Site-Selectivity in Ruthenium-Catalyzed C–H and C–C Activations

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Korkit Korvorapun

Contents

List of Abbreviations

A	ampere
Å	angstrom (Ångström)
Ac	acetyl
Ad	adamantane
Alk	alkyl
AMLA	ambiphilic metal ligand activation
aq.	aqueous
Ar	aryl
ATR	attenuated total reflection
BHT	3,5-di-*tert*-butyl-4-hydroxytoluene
BIES	base-assisted internal electrophilic substitution
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Bn	benzyl
BNDHP	1,1'binaphthyl-2,2'-diyl hydrogenphosphate
Boc	*tert*-butyloxycarbonyl
bpy	2,2'-bipyridine
Bu	butyl
Bz	benzoyl
cat.	catalytic
CMD	concerted metalation-deprotonation
CV	cyclic voltammetry
Cy	cyclohexyl
d	doublet
1,2-DCE	1,2-dichloroethane
D-CSA	*D*-camphorsulfonic acid
Dec	decyl
DFT	density-functional theory
DG	directing group
DIPEA	*N*,*N*-di-*iso*-propylethylamine
DMA	*N*,*N*-dimethylacetamide
DMEDA	*N*,*N*'-dimethylethylenediamine, Hünig's base
DMPO	5,5-dimethyl-1-pyrroline *N*-oxide
DMSO	dimethyl sulfoxide

DPEPhos	bis[(2-diphenylphosphino)phenyl] ether
dr	diastereomeric ratio
DTBP	di-*tert*-butyl peroxide
$E_{1/2}$	half-wave potential
ee	enantimeric excess
EI	electron ionization
EPR	electron paramagnetic resonance
equiv	equivalent
ESI	electrospray ionization
Et	ethyl
FTICR	fourier transform ion cyclotron resonance
g	gram
GC	gas chromatography
GPC	gel permeation chromatography
GVL	*γ*-valerolactone
h	hour
HATU	hexafluorophosphate azabenzotriazole tetramethyl uronium
hept	heptet
Het	heterocycle
Hex	hexyl
HFIP	1,1,1,3,3,3-hexafluoro-2-propanol
HMBC	heteronuclear multiple bond correlation
HOMO	highest occupied molecular orbital
HPLC	high-performance-liquid-chromatography
HR-MS	high resolution mass spectrometry
Hz	hertz
i	*iso*
IES	internal electrophilic substitution
Ile	isoleucine
IPr	1,3-bis(2,6-di-*iso*-propylphenyl)-1*H*-imidazole
IR	infrared
ISC	intersystem crossing
ISET	inner-sphere electron transfer
J	coupling constant

k	rate constant
L	ligand or liter
LED	light-emitting diode
LIFDI	liquid injection field desorption/ionization
LMCT	ligand-to-metal charge-transfer
LUMO	lowest unoccupied molecular orbital
m	multiplet
m	*meta*
M	molar
M	mega
µ	micro
m-CPBA	*m*-chloroperoxybenzoic acid
Me	methyl
Mes	mesitylene
MLCT	metal-to-ligand charge-transfer
m.p.	melting point
MPAA	monoprotected amino acid
MS	mass spectrometry
m/z	mass-to-charge ratio
n	*normal*
N	normality
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
NIS	*N*-iodosuccinimide
NMP	*N*-methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
NOESY	nuclear overhauser effect spectroscopy
o	*ortho*
Oct	octyl
OSET	outer-sphere electron transfer
p	pentet
p	*para*
Ph	phenyl
Phe	phenylalanine

Piv	pivaloyl
PMP	4-methoxyphenyl
Pr	propyl
PTS	polyoxyethanyl-*α*-tocopheryl sebacate
2-py	2-pyridyl
2-pym	2-pyrimidyl
pyr	pyrazole
q	quartet
rac	racemic or racemate
rt	room temperature
s	singlet or second
sat.	saturated
SDS	sodium dodecyl sulfate
SET	single-electron transfer
TBA	tetrabutylammonium
TBME	*tert*-butylmetylether
TBS	*tert*-butyldimethylsilyl
TEMPO	2,2,6,6-tetramethylpiperidin-1-oxyl
t	triplet
tert, *t*	*tertiary*
TD-DFT	time-dependent density-functional theory
Tf	trifluoromethanesulfonyl
TFA	Trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TM	transition metal
TMP	3,4,5-trimethoxyphenyl
TOF	time-of-flight
UV	ultraviolet
V	volt
Val	valine
Vis	visible

1 Introduction

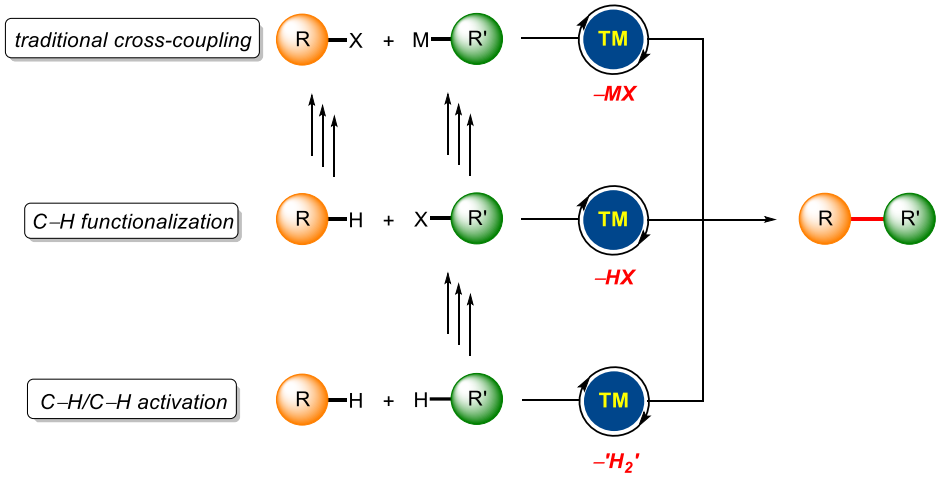
Regarding global warming issue, the scientific revolution has nowadays tended to reduce the use of non-renewable resources and to avoid the productions of chemical wastes and pollutants, which represent major environmental issues. Therefore, the development of sustainable chemistry has become a major goal for chemists. In 1998, Anastas and Warner published the *12 Principles of Green Chemistry* to diminish the impact of chemical processes on the environment and health, and to guide the development of green chemistry technologies.[1] Catalysis emerges as one of these principles in order to prevent stoichiometric transformations and reduce the amount of chemical waste. Thus, catalysis plays an important role in organic synthesis, with broad applications to academia as well as industries.[2]

1.1 Transition Metal-Catalyzed C–H Functionalization

A major breakthrough in modern organic synthesis over five decades has been represented by transition metal-catalyzed C–C and C–Het bond formations, allowing for the preparation and the synthetic modification of natural products and biological active compounds, among others.[3] Well-known transition metal catalyses, such as the Kumada-Corriu,[4] Mizoroki-Heck,[5] Sonogashira-Hagihara,[6] Negishi,[7] Stille,[8] Suzuki-Miyaura,[9] and Hiyama[10] cross-couplings afford new C–C bond formation for arylations, alkylations, alkenylations, and alkynylations. Due to these reactions emerging as a powerful toolbox for molecular synthesis with broad applications in crop protection, material sciences, and drug discovery,[11] these innovative transformations were recognized with the Nobel Prize in Chemistry in 2010 to R. F. Heck, E.-i. Negishi, and A. Suzuki.[12]

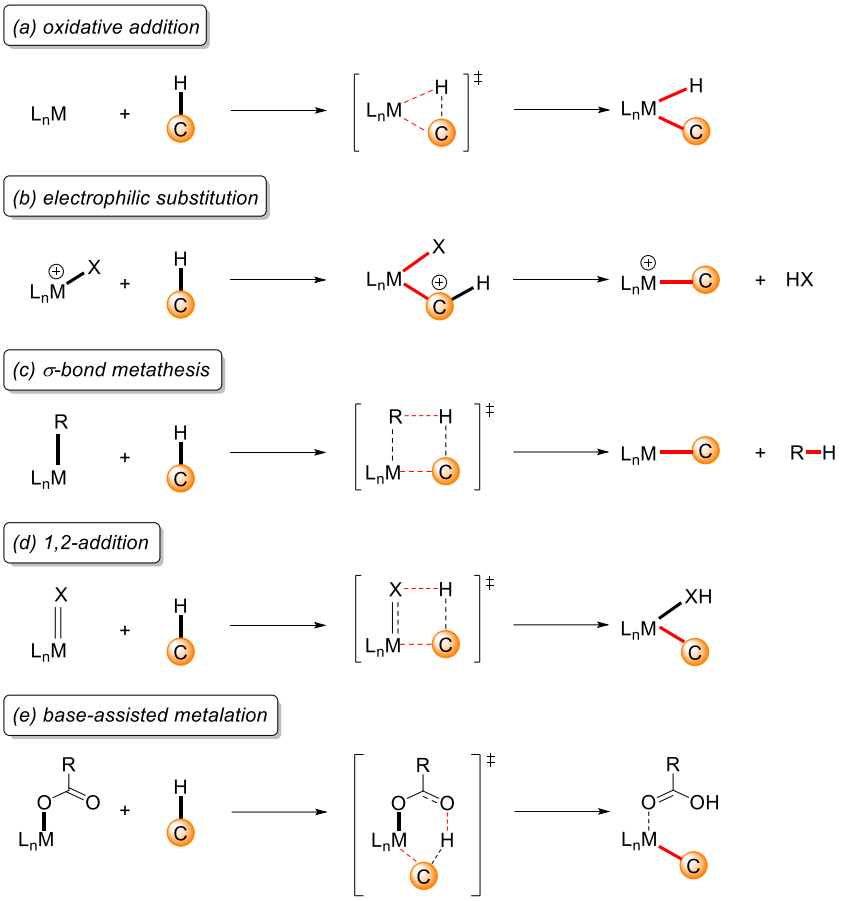
Despite this revolution in synthesis, cross-coupling reactions still display a number of drawbacks. First, a pre-functionalization of both substrates is obligatory, not only for organic (pseudo-)halides, but also for the employed organometallic reagents, which usually require multistep syntheses. Moreover, some of the nucleophiles are highly reactive and difficult to handle organometallic compounds, e.g. organomagnesium (RMgX) or organozinc (R_2Zn), and toxic organotin reagents ($RSnR'_3$) (Scheme 1). In addition to these operational issues, a generation of environmentally problematic metal-waste constitutes a disadvantage of traditional cross-coupling reactions. To avoid the use of these organometallic reagents, transition metal-catalyzed selective C–H functionalization has evolved as a powerful and sustainable method over the last decades

(Scheme 1).[13] Since the pre-functionlization for organometallic coupling partners is not necessary, the catalytic C–H activation strategy proves to be a more atom- and step-economical process. Furthermore, ideal oxidative C–H/C–H activations allow for the formation of new C–C bonds (Scheme 1).[13h, 14] Although the dehydrogenative transformation formally generates an equivalent of H_2 as the sole by-product, the oxidative process of the twofold C–H activations typically requires stoichiometric amounts of an oxidant, often silver(I) salts.



Scheme 1: General methods for the formation of C–C and C–Het bonds.

Since the C–H activation strategy has become more attractive, the nature of C–H bond cleavage has been extensively examined. Excluding radical-type outer-sphere mechanisms,[15] several modes of C–H bond activation have been categorized in five different pathways, depending on the electronic properties and the coordination environment of the metal center (Scheme 2).[16] The oxidative addition of a C–H bond is a typical reaction mechanism for electron-rich late transition metals in low oxidation states, such as ruthenium(0), rhodium(I), and palladium(0) (Scheme 2a). In contrast, most late transition metals in higher oxidation states act preferentially through an electrophilic substitution (Scheme 2b). The concerted pathway proceeding through four-centered transition state in which two σ-bond cleavage and two new σ-bond formation without any overall change in the oxidation state of the metal center is called σ-bond metathesis. This pathway is observed for early transition metals as well as lanthanides and actinides (Scheme 2c).[17] The 1,2-addition usually takes place for early transition metals with an unsaturated M=X bond, mostly metal imido complexes (Scheme 2d).[18] Moreover, the base-assisted C–H metalation occurs with metal-carboxylate or -carbonate complexes, leading to the formation of a new M–R bond (Scheme 2e).[16a, 19]



Scheme 2: Mechanistic pathways for C–H activations.

The base-assisted mechanism was further investigated and different transition states were identified (Figure 1). The concerted metalation-deprotonation (CMD)[20] and the ambiphilic metal ligand activation (AMLA),[21] which propose through a six-membered transition state, preferentially take place for electron-deficient substrates. A more strained four-membered transition state has been coined the internal electrophilic substitution (IES), which is mostly observed in C–H activations enabled by metal-alkoxy complexes.[22] Recently, the base-assisted internal electrophilic substitution (BIES) has been frequently observed through an electrophilic substitution-type pathway for electron-rich substrates.[23]

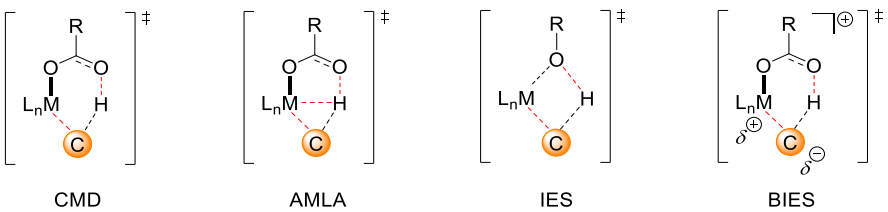


Figure 1: Proposed transition states for base-assisted C–H metalation.

Since C–H bonds are omnipresent in organic compounds with similar bond dissociations energies, site-selective functionalization has become a key challenge wthin the C–H activations concept. To conquer the regioselectivity issues, three different methods have been established (Figure 2).[24] The difference in reactivity among C–H bonds in heterocyclic compounds is highly related to their kinetic acidity, which leads to selective C–H transformations (Figure 2a).[25] The use of sterically hindered substituents in the substrate prevents the C–H activation process in the neighboring position, resulting in the selective functionalization of the less hindered C–H bond (Figure 2b).[26] However, the electronic or steric biased methods require specific substrates, which are considered as one of their drawbacks. The basic concept of proximity-induced C–H activation is representative of a general strategy for selective C–H transformations by using a Lewis-basic group (Figure 2c).[27] The chelation-assistance through directing groups (DG) brings the metal complex into close proximity to the desired C–H bond, typically at the *ortho* position. Over the years, a variety of N-heterocyclic compounds and Lewis basic functional groups have been identified as the directing groups in *ortho*-selective C–H activations (Figure 3).

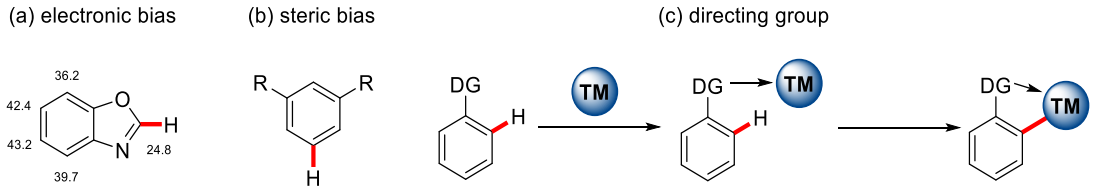


Figure 2: Site-selectivity control in C–H bond activation. pK_a values of C–H bonds of benzoxazole are given.

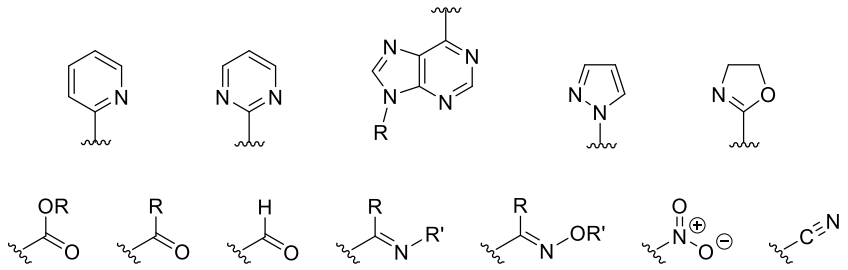


Figure 3: Selected examples of directing groups in C–H activation catalysis.

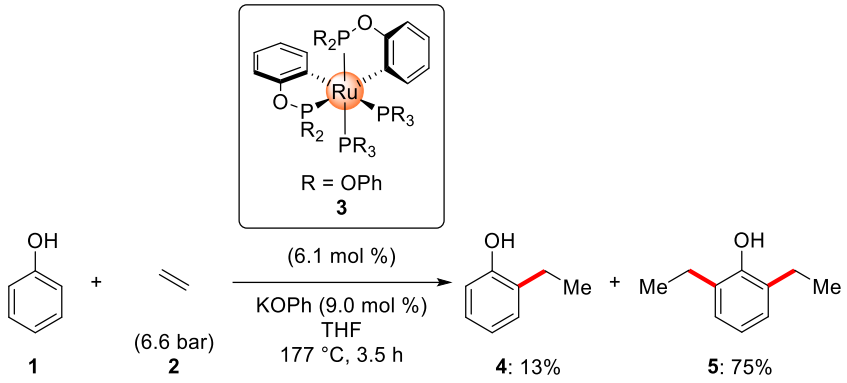
1.2 Ruthenium-Catalyzed Direct *ortho*-C–H Functionalizations

Over the last decade, transition metal-catalyzed C–H functionalization has gained significant momentum with notable achievements by means of 4d and 5d metal catalysis.[28] In addition to precious transition metals, ruthenium catalysis has emerged as an effective and inexpensive

alternative for several transformations.[19b, 29] In particular, site-selective C–H functionalizations on arenes have become more attractive.

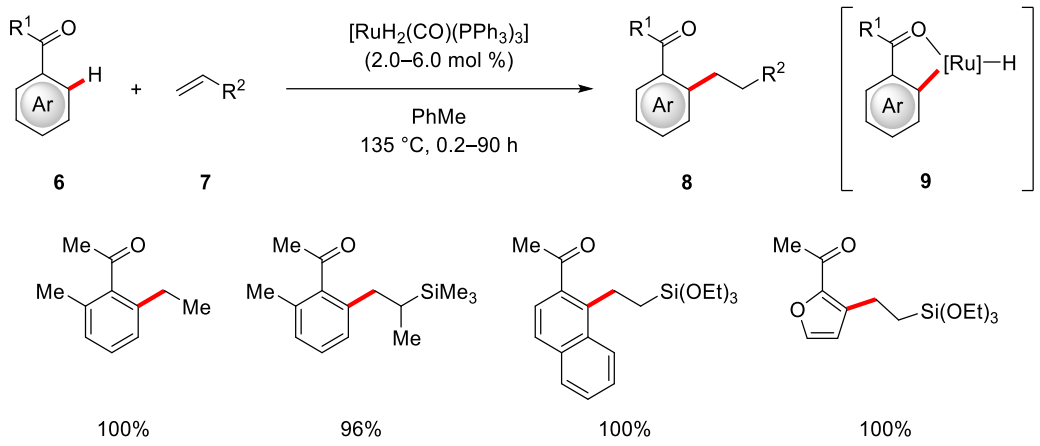
1.2.1 ortho-C–H Alkylations

In 1986, the first ruthenium-catalyzed C–H alkylation of phenol (**1**) was reported by Lewis and Smith (Scheme 3).[30] A triphenylphosphite was proven to be a transient directing group in the catalytic alkylation of phenol (**1**) with ethylene (**2**), affording the mono- and diethylated products **4** and **5** at the *ortho* position. The reaction was performed under high pressure and temperature of 6.6 bar and 177 °C, respectively.



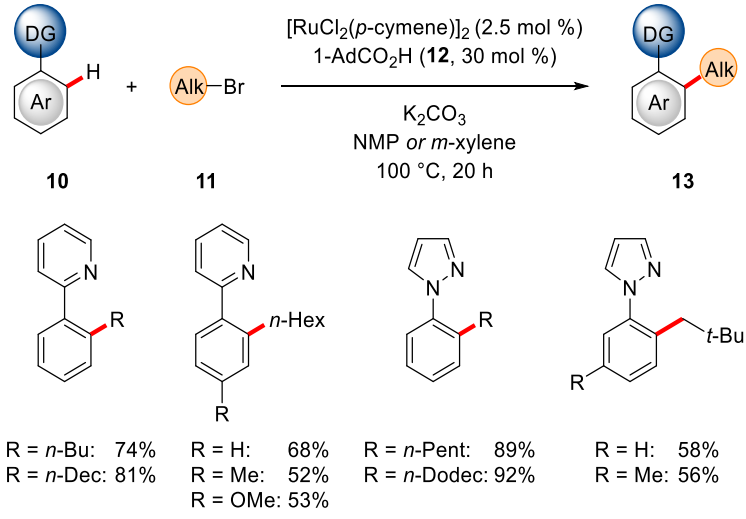
Scheme 3: Direct C–H alkylation of phenol (**1**) with ethylene (**2**).

Afterwards, the group of Murai successfully developed a general method for the *ortho*-C–H alkylations using $[RuH_2(CO)(PPh_3)_3]$ as the catalyst precursor (Scheme 4).[31] This effective protocol was applicable to a variety of aromatic ketones **6** and alkenes **7**, affording the desired alkylated ketones **8** with excellent levels of regioselectivity. In spite of no mechanistic studies, the *in situ* formed five-membered cyclometalated ruthenium complex **9** was proposed as an intermediate in the catalytic transformation, which undergoes olefin insertion followed by reductive elimination to deliver the *ortho*-alkylated products **8**.



Scheme 4: Ruthenium-catalyzed hydroarylations of ketones **6**.

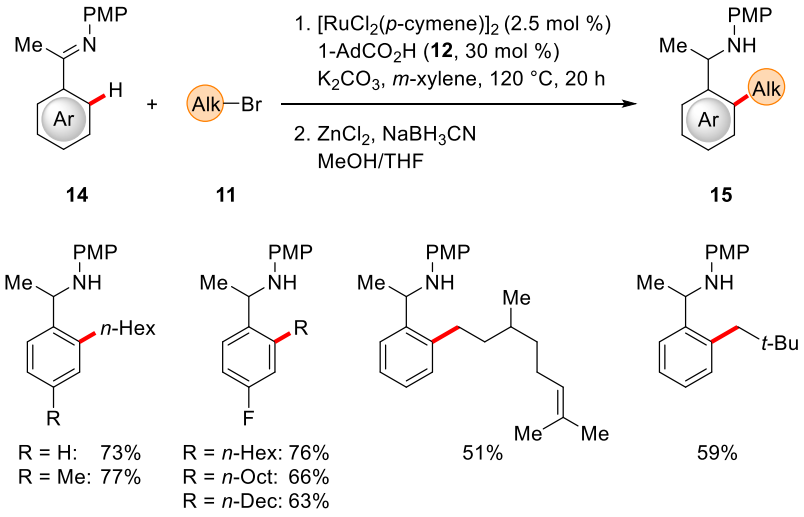
In contrast to hydroarylations *via* sensitive ruthenium hydrides,[32] the method for carboxylate-assisted direct alkylation of alkyl halides **11** was first reported by the group of Ackermann in 2009 (Scheme 5).[33] The catalytic alkylations were proven to be applicable to arylpyridines, arylpyrazoles, and arylimines. Moreover, the well-defined $[Ru(O_2CAd)_2(p\text{-cymene})]$ provided a catalytic efficacy comparable to the standard reaction conditions.



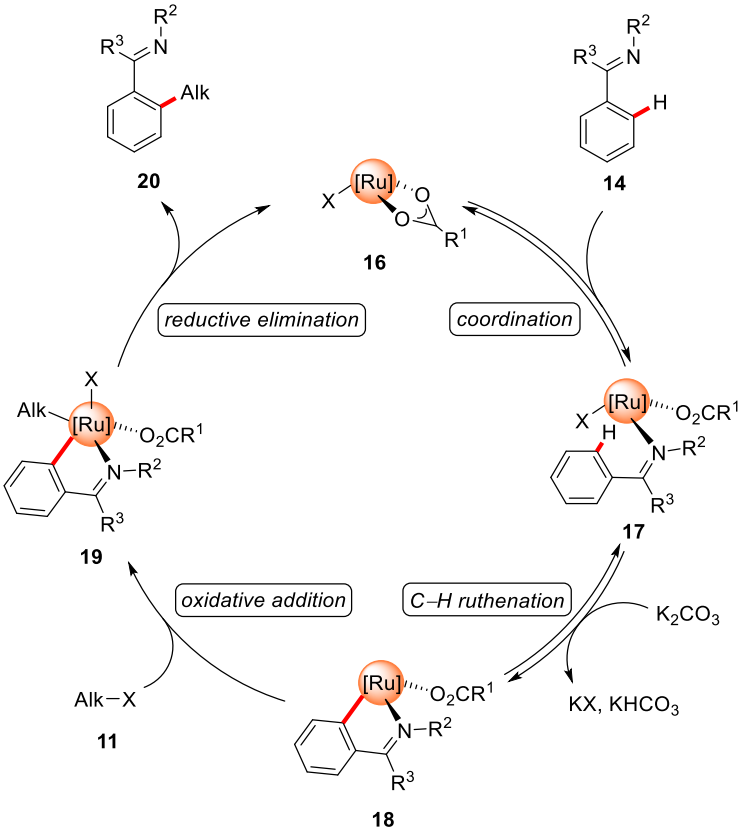
Scheme 5: Ruthenium-catalyzed direct C–H alkylations with primary alkyl bromides **11**.

Later, the versatility of carboxylate-assisted ruthenium-catalyzed *ortho*-C–H functionalization was mirrored by the direct alkylation of ketimines **14**, followed by reduction in one-pot fashion, affording the *ortho*-alkylated benzylamines **15** (Scheme 6).[34] Experiments with isotopically labeled substrates were indicative of a reversible carboxylate-assisted C–H bond cleavage to form ruthenacycle **18** (Scheme 7). Oxidative addition with alkyl halide **11** followed by reductive

elimination delivers the corresponding alkylated product **20** and regenerates the active ruthenium catalyst **16**.



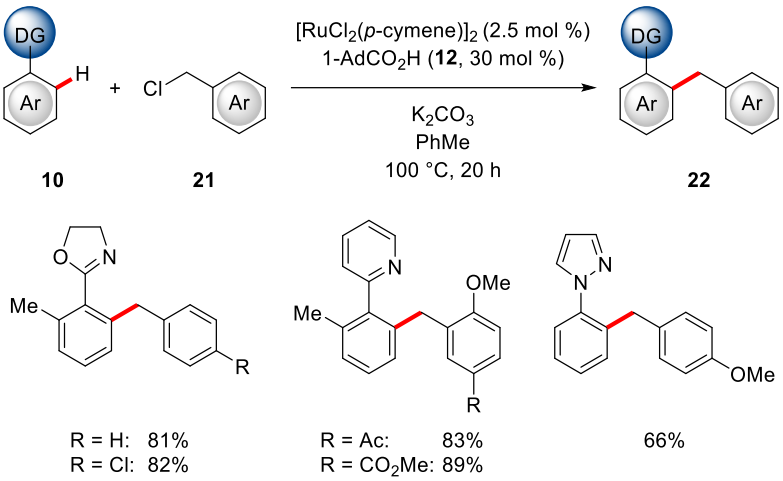
Scheme 6: Sequential direct C–H alkylations of ketimines **14** followed by reduction.



Scheme 7: Proposed catalytic cycle for direct alkylations.

1.2.2 ortho-C–H Benzylations

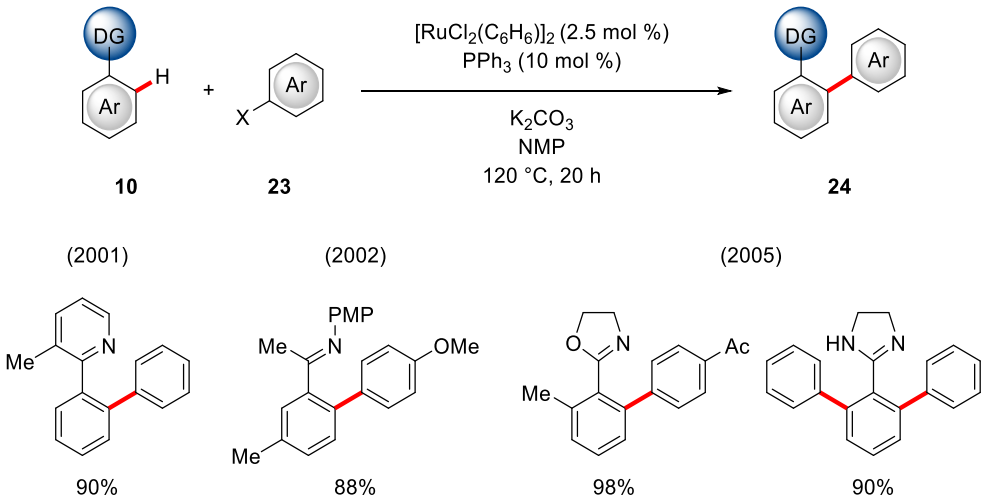
In continuation of the previous study, the group of Ackermann further demonstrated the power of carboxylate-assisted ruthenium catalysis, enabling *ortho*-selective C–H benzylations (Scheme 8).[35] In addition to pyridines and pyrazoles, transformative oxazolines were employed as the directing group in these direct C–H benzylations.



Scheme 8: Ruthenium(II)-catalyzed direct benzylations.

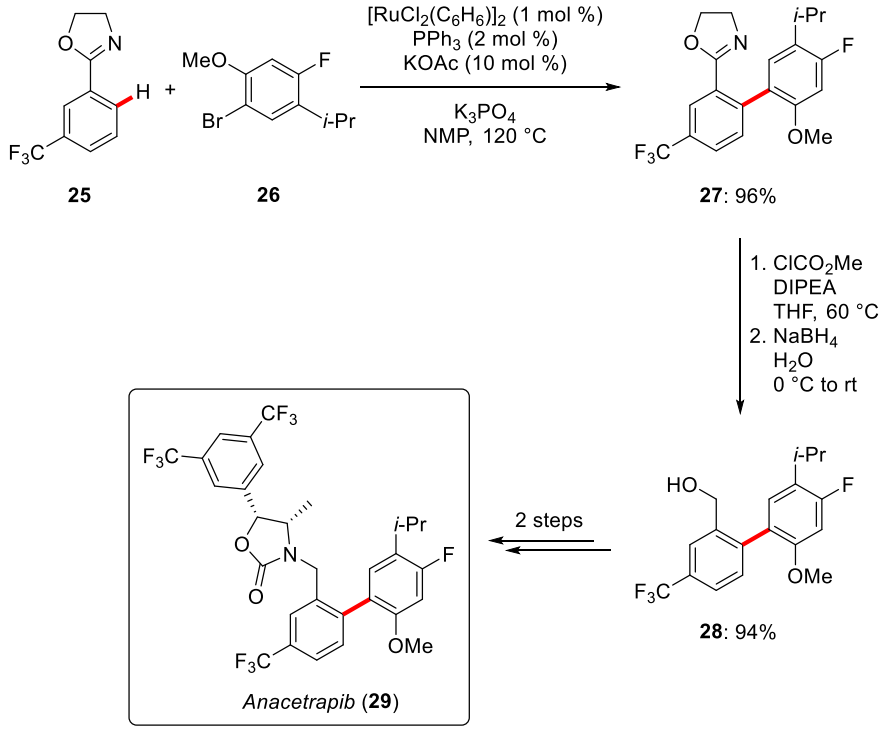
1.2.3 ortho-C–H Arylations

The group of Oi/Inoue developed ruthenium-phosphine catalysis for the first direct arylations of phenylpyridines in 2001 (Scheme 9).[36] Afterwards, the ruthenium catalysis under the same reaction condition allowed for *ortho*-selective arylation of synthetically useful ketimines,[37] oxazolines, and imidazolines.[38] The catalytic arylations selectively occurred at the less sterically-hindered *ortho* position when *meta*-substituted arenes were employed. It is noteworthy that impurities in NMP solvent exerted a major influence on the catalytic efficacy of ruthenium catalysis, leading to a lack of reproducibility.[39]



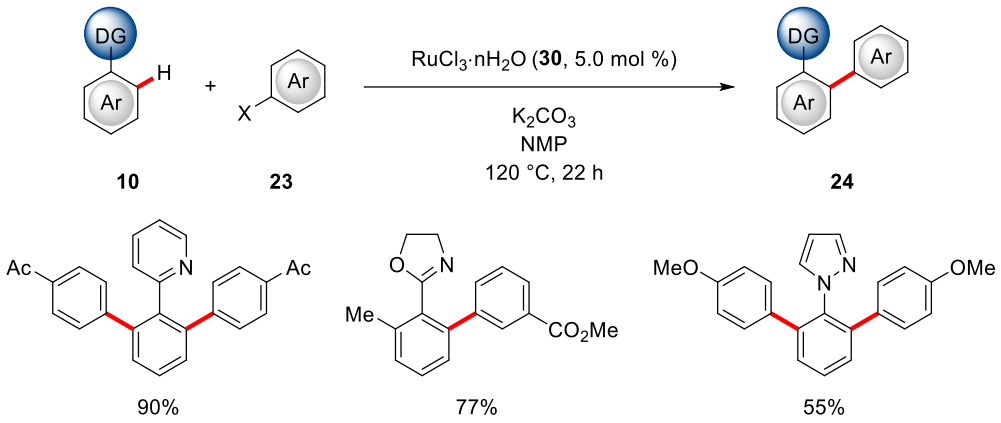
Scheme 9: Ruthenium-catalyzed direct C–H arylations.

In 2011, the modified direct arylation protocol with KOAc as the key additive enabled the formation of biaryl **27** on a multikilogram scale, as was demonstrated by the group of Ouellet (Scheme 10).[39] Oxazoline **27** was smoothly converted to benzyl alcohol **28**, which is an intermediate in the synthesis of *Anacetrapib* (**29**), a CETP inhibitor.



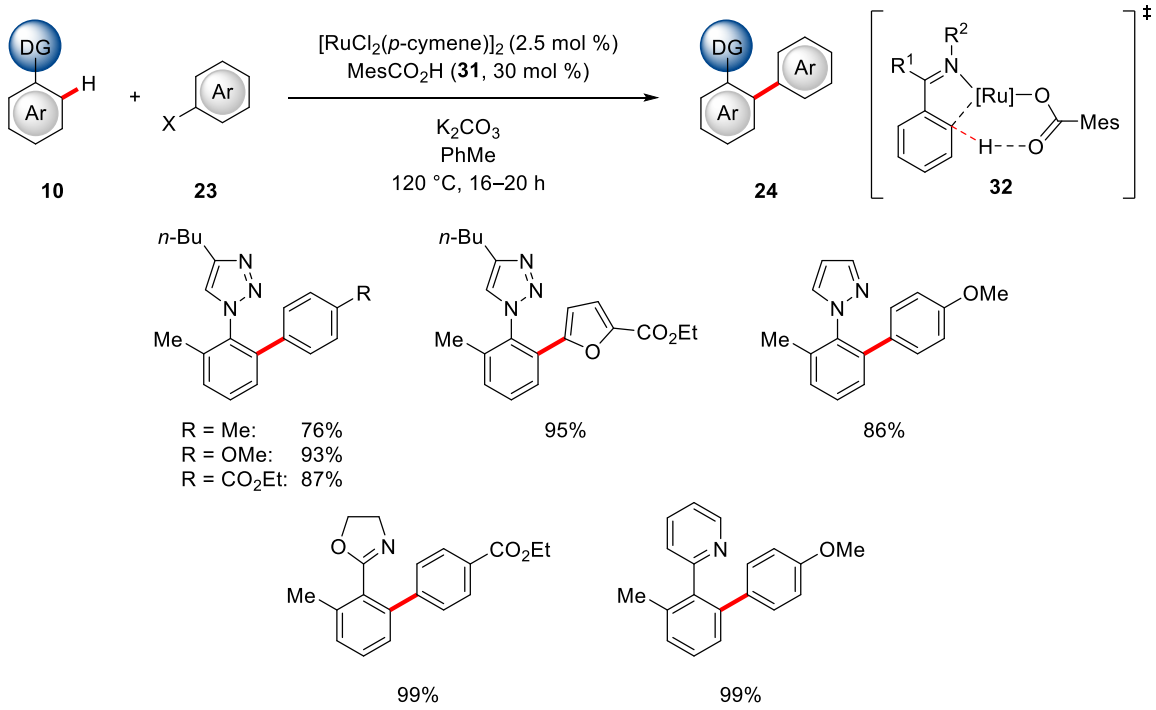
Scheme 10: Synthesis of the biaryl core of Anacetrapib (**29**).

In addition to ruthenium-phosphine catalysis, a simple $RuCl_3 \cdot nH_2O$ (**30**) catalyst allowed for *ortho*-selective C–H arylations under phosphine-free conditions, as was reported by the group of Ackermann in 2007 (Scheme 11).[40] The uncommon ruthenium(III)-catalyzed C–H activations were applicable to 2-alkenyl or 2-arylpyridines, 2-aryloxazoline, and arylpyrazoles.



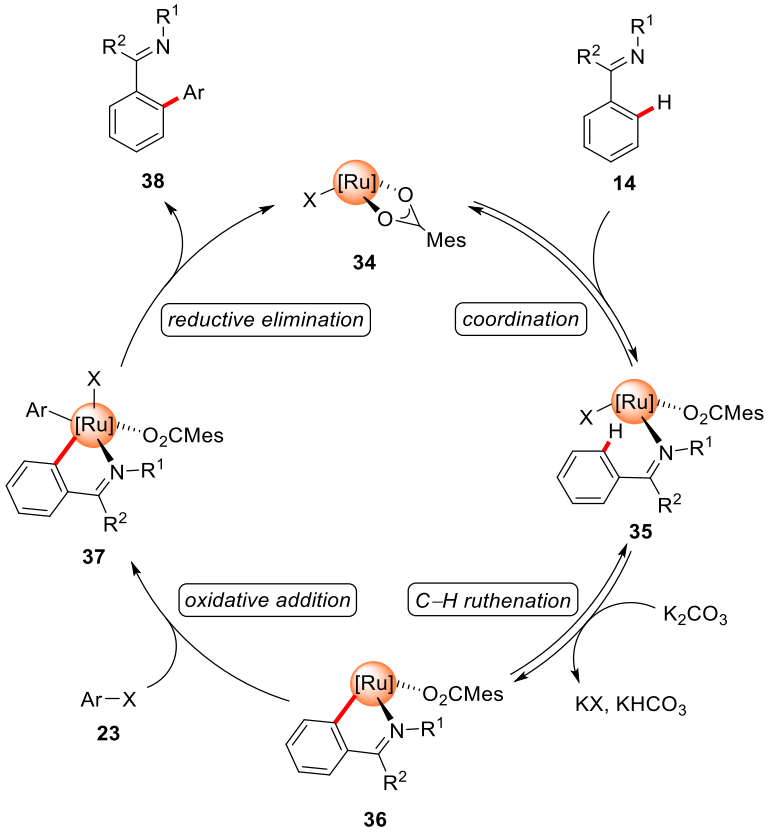
Scheme 11: Direct arylations by $RuCl_3 \cdot nH_2O$ (**30**) as a catalyst.

In 2008, the group of Ackermann disclosed the first general and robust method for ruthenium(II)-catalyzed direct C–H arylations using carboxylic acids as additives (Scheme 12).[41] Sterically hindered $MesCO_2H$ (**31**) proved to be an efficient additive in nonpolar solvent, PhMe, whereas phosphines and NHC ligands provided low catalytic efficacy. The ruthenium-carboxylate catalysis verified to be applicable to various aromatic substrates **10**. In particular, 1,2,3-triazoles, which are found in broad applications in drug discovery, crop protection, and material sciences, were simply converted to the *ortho*-arylated products **24**.[42] Furthermore, the C–H bond cleavage process was proposed to occur through a base-assisted metalation, involving a six-membered cyclic transition state **32**.



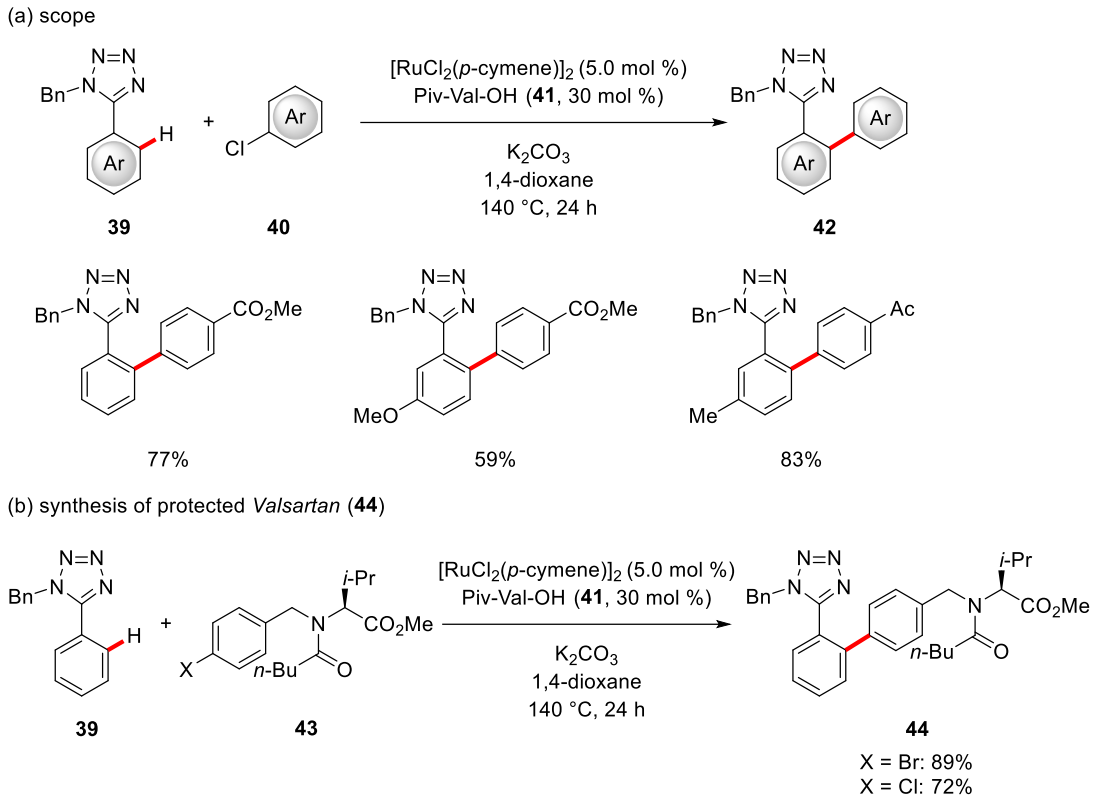
Scheme 12: Ruthenium-carboxylate catalysis for direct arylations through transition state **32**.

Afterwards, mechanistic insights of ruthenium-catalyzed *ortho*-arylations were studied.[43] Stoichiometric experiments of $[RuCl_2(p\text{-cymene})]_2$ and $MesCO_2H$ (**31**) led to the formation of the well-defined $[Ru(O_2CMes)_2(p\text{-cymene})]$ (**33**), which was highly effective for the catalytic arylations. Although ruthenium biscarboxylate complex **33** exhibited no reaction with aryl chloride, the reaction of complex **33** with 2-(4-methoxyphenyl)pyridine afforded the corresponding cyclometalated complex, which showed high catalytic efficacy in the arylation reactions. Furthermore, an observed H/D scrambling was indicative of a reversible, carboxylate-assisted C–H ruthenation, as shown in Scheme 13. Ruthenacycle **36** reacts with aryl halide **23** to form putative ruthenium(IV) intermediate **37**, which finally undergoes reductive elimination to give the *ortho*-arylated product **38** and regenerate the active catalyst **34**.



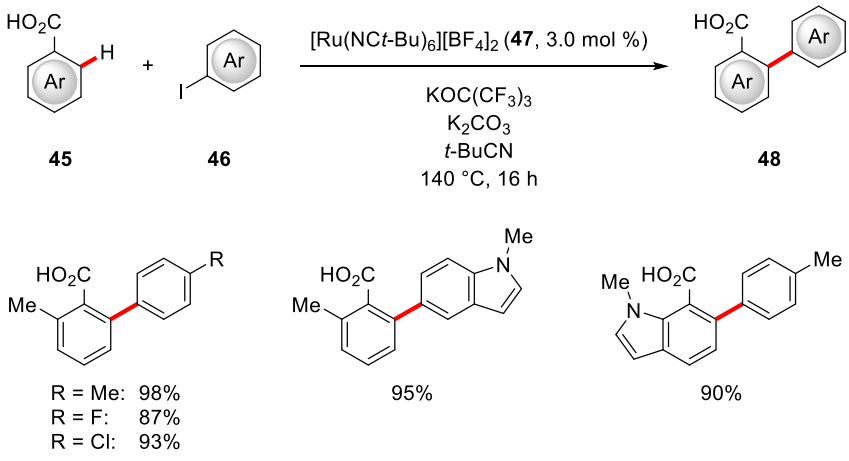
Scheme 13: Proposed catalytic cycle for direct arylations.

Thereafter, the group of Ackermann reported on a modified ruthenium-carboxylate catalysis, which allowed for the direct arylations of aryltetrazoles **39** (Scheme 14a).[44] In addition to the commercially available carboxylic acids,[44b] the use of monoprotected amino acid (MPAA) Piv-Val-OH (**41**) in ruthenium catalysis smoothly afforded the corresponding biaryl tetrazoles **42**,[44a] which are core structures of angiotensin II receptor blockers (ARBs). In particular, the powerful C–H arylations enabled the concise synthesis of antihypertensive *Valsartan* (**44**), as illustrated in Scheme 14b.



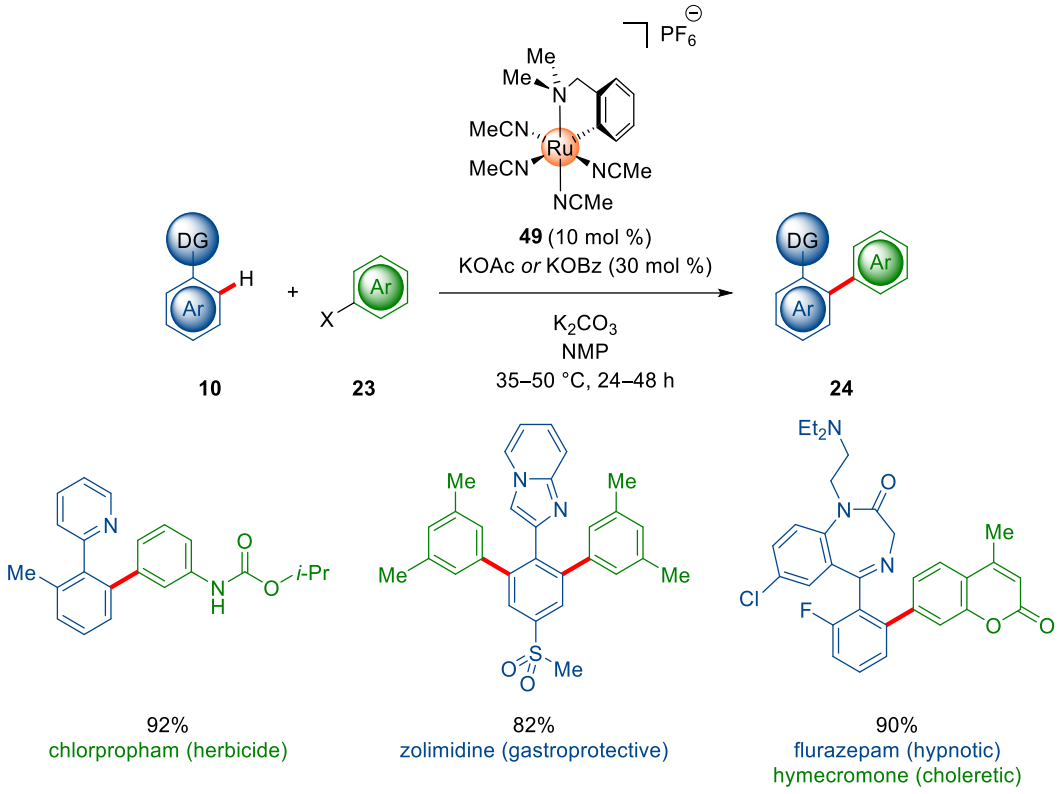
Scheme 14: Direct arylations of protected tetrazoles **39** using Piv-Val-OH (**41**) as a ligand and their application for synthesis of *Valsartan* (**44**).

In 2017, the group of Larrosa reported on direct C–H arylations of benzoic acids **45** and aryl iodides **46** using a cationic ruthenium(II) complex **47** (Scheme 15).[45] It is noteworthy that the addition of potassium perfluoro-*tert*-butoxide enhanced the catalytic efficacy.



Scheme 15: *ortho*-C–H Arylations of benzoic acids **45** by cationic ruthenium complex **47**.

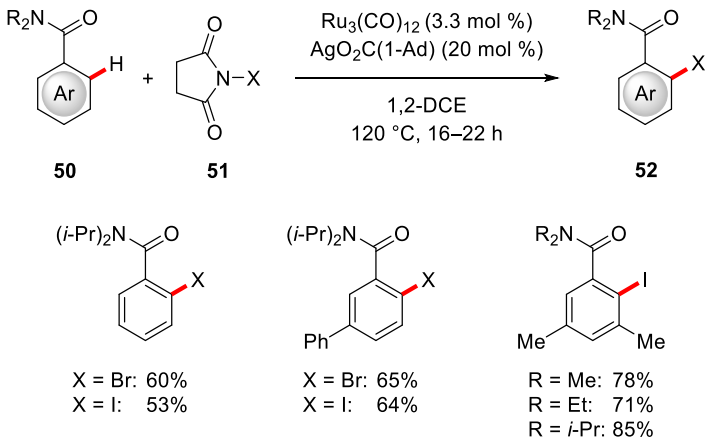
Subsequently, the cyclometalated ruthenium complex **49** allowed for the catalytic arylations at mild reaction temperature of 35–50 °C (Scheme 16).[46] In the presence of carboxylate salts, the power of the ruthenium catalysis was reflected by late-stage C–H arylations of relevant pharmaceuticals and natural products.



Scheme 16: Late-stage direct arylations of pharmaceuticals and natural products.

1.2.4 ortho-C–H Halogenations

In addition to the new C–C bond formations, the protocol for ruthenium-catalyzed direct brominations and iodinations of tertiary amides **50** was illustrated by the group of Ackermann in 2014 (Scheme 17).[47] Both experiments with 2,6-di-*tert*-butylpyridine and TEMPO were suggestive of a single-electron transfer mechanism for the catalytic C–H halogenations.



Scheme 17: *ortho*-Selective C–H halogenations of amides **50**.

1.3 Ruthenium-Catalyzed Remote *meta*-C–H Functionalizations

In contrast to a plethora of reports on *ortho*-C–H transformations, methods for the site-selective C–H bond activations at the *meta* position continue to be in high demand. Among those reports on *meta*-selective C–H functionalizations, they were classified into five categories (Figure 4).[48] First, the use of bulky substituents on the aromatic substrates can block the activation of C–H bonds in the adjacent positions,[49] leading to the C–H transformation at a less sterically-hindered *meta* position (Figure 4a).[50] However, this method is restricted to few transformations, mainly borylation or silylation. On the basis of chelation-assistance, the installation of a template on the arenes assists the coordination of the catalyst to come into close proximity to the targeted C–H bond at the *meta* or *para* position (Figure 4b).[51] Although the template assistance[52] is one of the favorite methods for remote functionalizations, the template design, installation, and subsequent removal require the number additional synthetic steps, which is addressed as the drawback of this strategy. The third method developed by Kuninobu/Kanai is a reversible hydrogen bonding linker, enabling C–H borylations at the *meta* position (Figure 4c).[53] However, the limitation to iridium catalysis and specific transformations is a weakness of this method. Inspired by the Catellani reaction,[54] norbornene and derivatives are employed as effective transient mediators to promote palladium-catalyzed *meta*-selective C–H transformations (Figure 4d).[55] Finally, the *in situ* formed cyclometalated ruthenium complexes by proximity-induced *ortho*-C–H metalation allow for the remote C–H functionalizations at the *para* position with respect to ruthenium (Figure 4e).[56] This phenomena is explained by the electronic bias of the ruthenacycles, identifying the Ru–C bond as an *ortho*/*para*-directing entity.

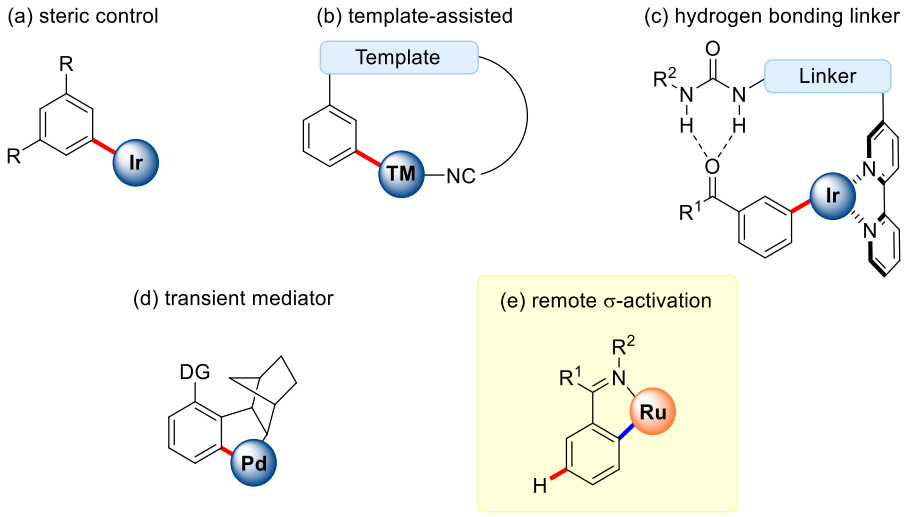
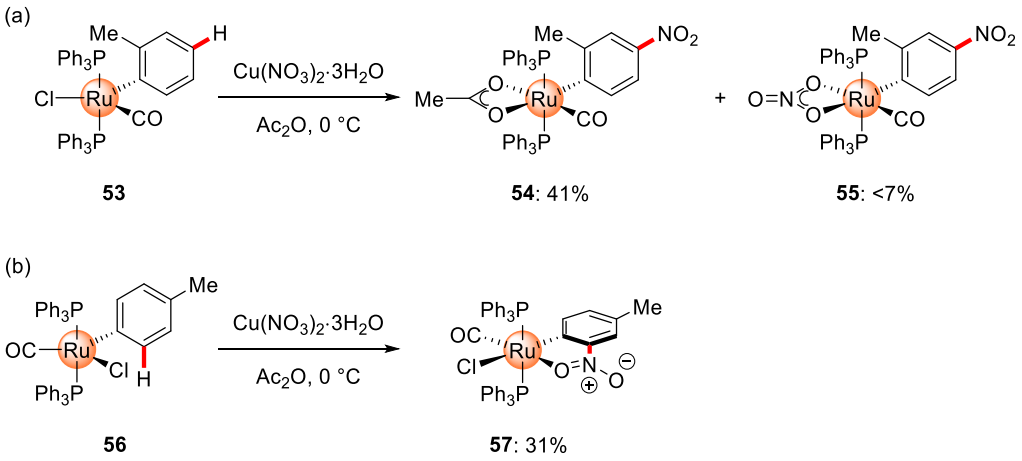


Figure 4: Methodologies for remote *meta*-C–H activations.

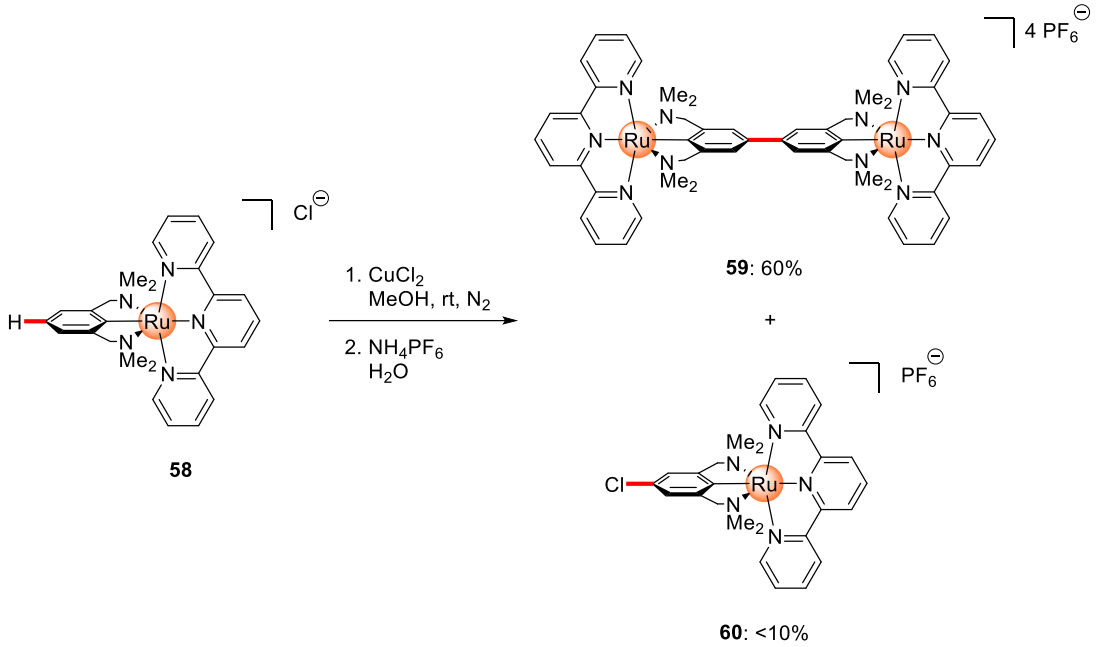
The inspiration for the ruthenium-catalyzed remote C–H functionalizations results from the reports on stoichiometric nitration of ruthenium aryl complexes by Roper/Wright in 1994 (Scheme 18).[57] The C–H nitrations of *o*-tolyl ruthenium complex **53** selectively occurred at the position *para* to the ruthenium metal center (Scheme 18a). In contrast, the reaction of *p*-tolyl ruthenium complex **56** led to the formation of very stable five-membered ruthenacycle **57** (Scheme 18b). The results were presumably clarified by *ortho*/*para*-directing effect of the metal center.



Scheme 18: Stoichiometric C–H nitrations.

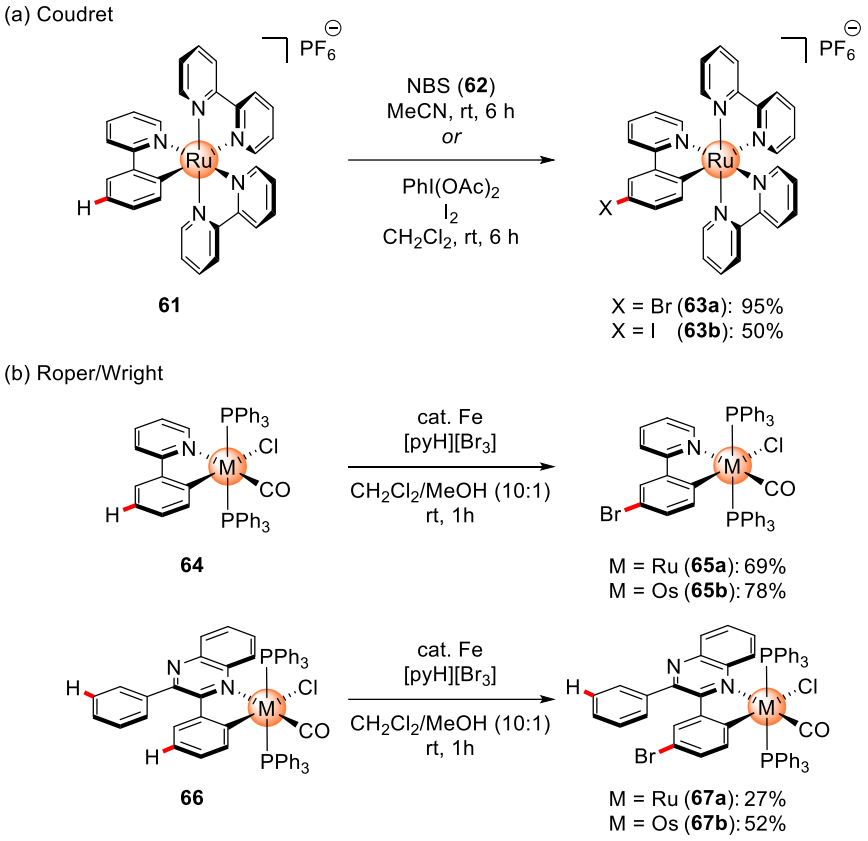
Later, the first chelation-assisted oxidative remote C–H/C–H functionalization was illustrated by the group of van Koten (Scheme 19).[58] The treatment of the cationic ruthenium complex **58** with $CuCl_2$ furnished the formation of a binuclear complex **59** and small amounts of chlorinated

ruthenium complex **60**. It is noteworthy that the reduced form of **59** strongly displayed electron resonance between the two metal centers through an ideally planar 4,4'-biphenyldiyl bridge.



Scheme 19: Oxidative homocoupling of ruthenium complex **58**.

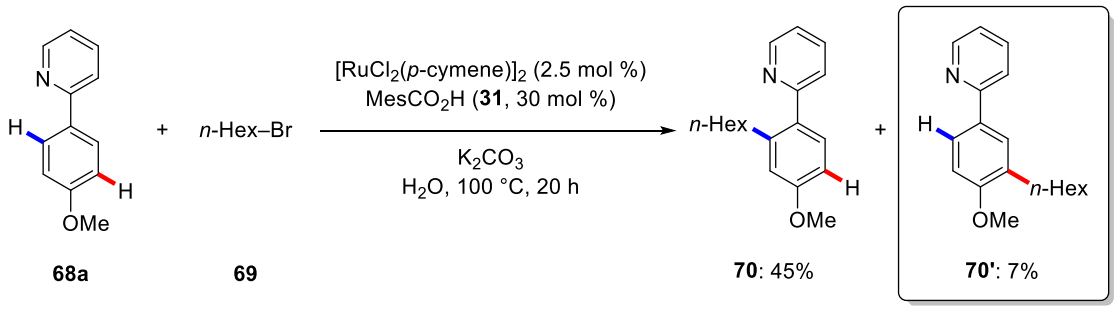
In addition, the group of Coudret reported on site-selective electrophilic C–H halogenations of cyclometalated ruthenium complex **61** at room temperature (Scheme 20a).[59] *N*-Bromosuccinimide (NBS, **62**) proved to be an efficient brominating agent, whereas *N*-iodosuccinimide (NIS) led to complex degradation. The treatment of complex **61** with the combination of molecular iodine and $PhI(OAc)_2$ smoothly delivered the desired iodinated ruthenacycle **63b**. Afterwards, Roper and Wright disclosed highly selective C–H brominations of arenes on the ruthenium and osmium complexes **64** (Scheme 20b).[60] The electrophilic substitutions using operational-simple pyridinium perbromide and a catalytic amount of iron powder occurred at the *para* position with respect to metal centers. Furthermore, the same regioselectivity was observed in brominations of metallacycles **66**, while no substitution occurred on the non-activated arene.[60a] This observation was suggestive of electronic directing effect of the metal centers, controlling positional selectivity of electrophilic functionalizations.



Scheme 20: Electrophilic C–H halogenations of cyclometalated complexes.

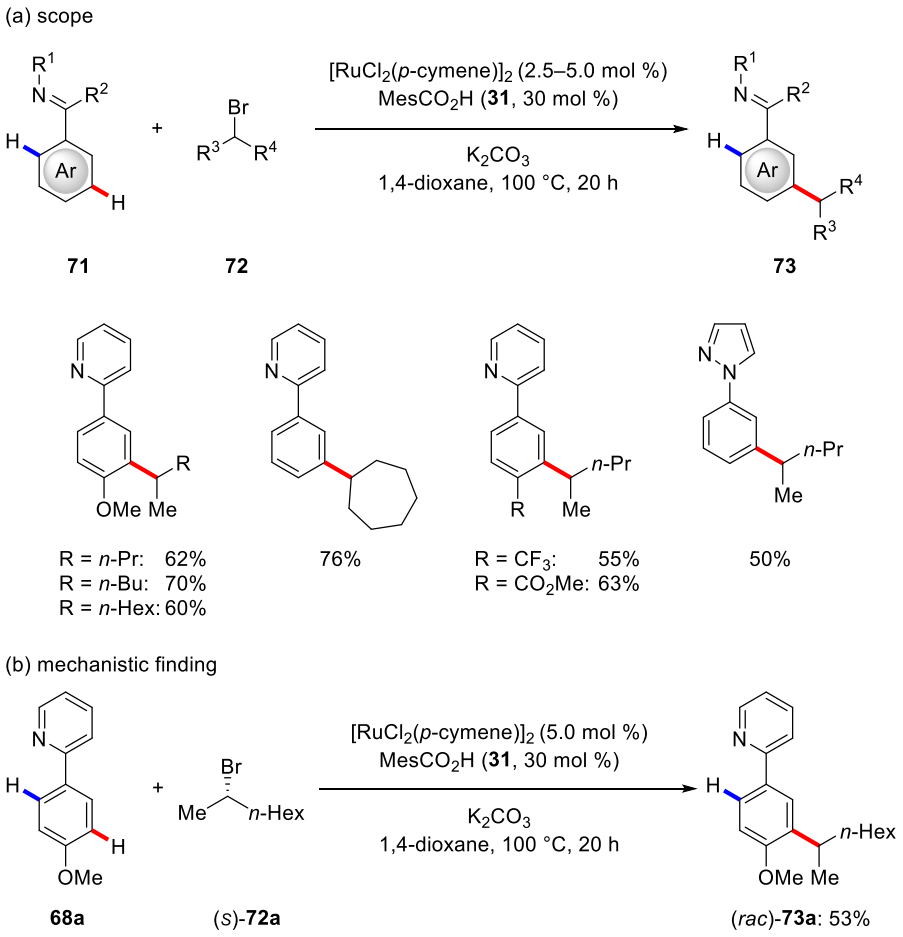
1.3.1 meta-C–H Alkylations

The first observation for catalytic remote C–H functionalization was reported by the group of Ackermann in 2011 (Scheme 21).[34] Chelation-assisted C–H alkylations with primary alkyl bromides typically furnished the *ortho*-alkylated products. However, the catalytic transformation of phenylpyridine **68a** with 1-bromohexane (**69**) delivered the *ortho*-alkylated product **70** along with the unprecendented *meta*-decorated arene **70'**, albeit in rather low yield.



Scheme 21: Ruthenium-catalyzed C–H alkylation with *n*-hexyl bromide (**69**).

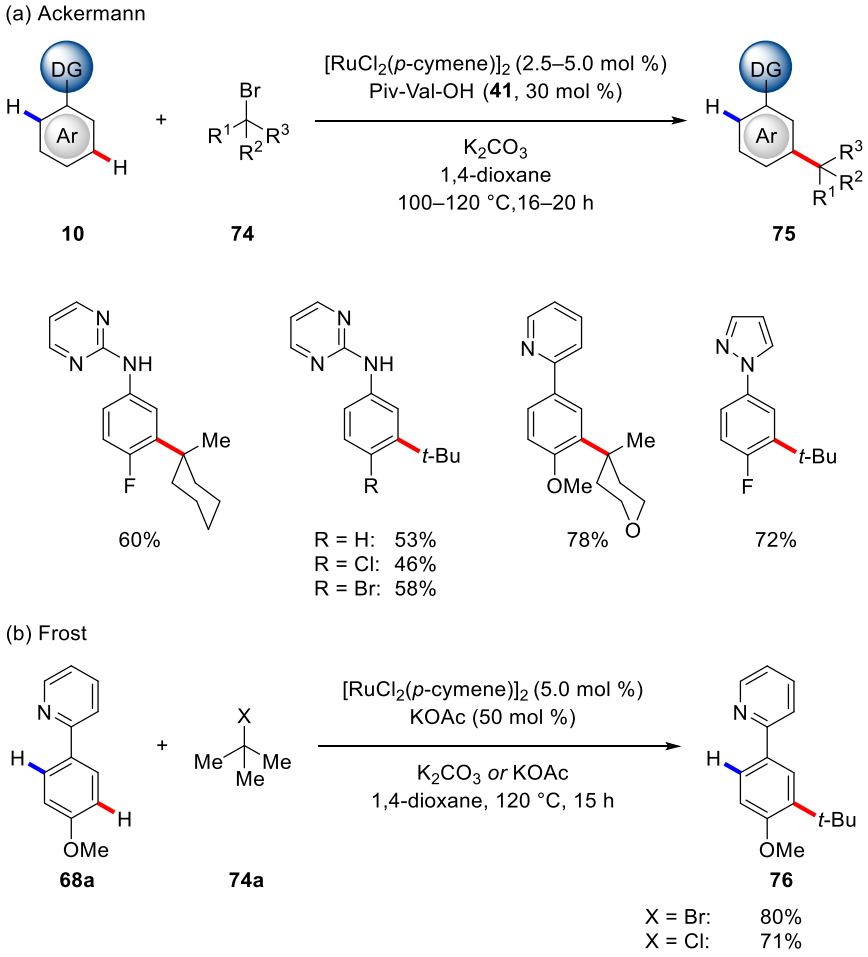
Inspired by the first observation, the group of Ackermann thereafter disclosed the methods for remote *meta*-C–H alkylations using secondary alkyl bromides **72** through an *ortho*-ruthenation strategy (Scheme 22).[61] The catalytic remote alkylations were applicable to pyridines, pyrimidines, and azoles as directing groups, leading to the formation of *meta*-alkylated arenes **73** with excellent levels of position-selectivity (Scheme 22a). Detailed mechanistic studies of this remote functionalization were supportive of a reversible C–H ruthenation and a subsequent site-selective alkylation, which was rationalized by the strong electronic effect of the Ru–C(sp^2) σ-bond. It is noteworthy that the enantiomerically-enriched alkyl bromide (*s*)-**72a** was converted to the racemic product **73a** (Scheme 22b).



Scheme 22: Remote *meta*-C–H alkylations with secondary alkyl bromides **72**.

In 2015, carboxylate-assisted ruthenium catalysis enabled tertiary *meta*-C–H alkylations was concurrently investigated by the group of Ackermann[62] and Frost[63] (Scheme 23). The highlight of Ackermann's protocol was the use of monoprotected amino acids **41** (MPAA) as the carboxylate ligand for the first time in ruthenium-catalyzed C–H activation (Scheme 23a). Furthermore, the

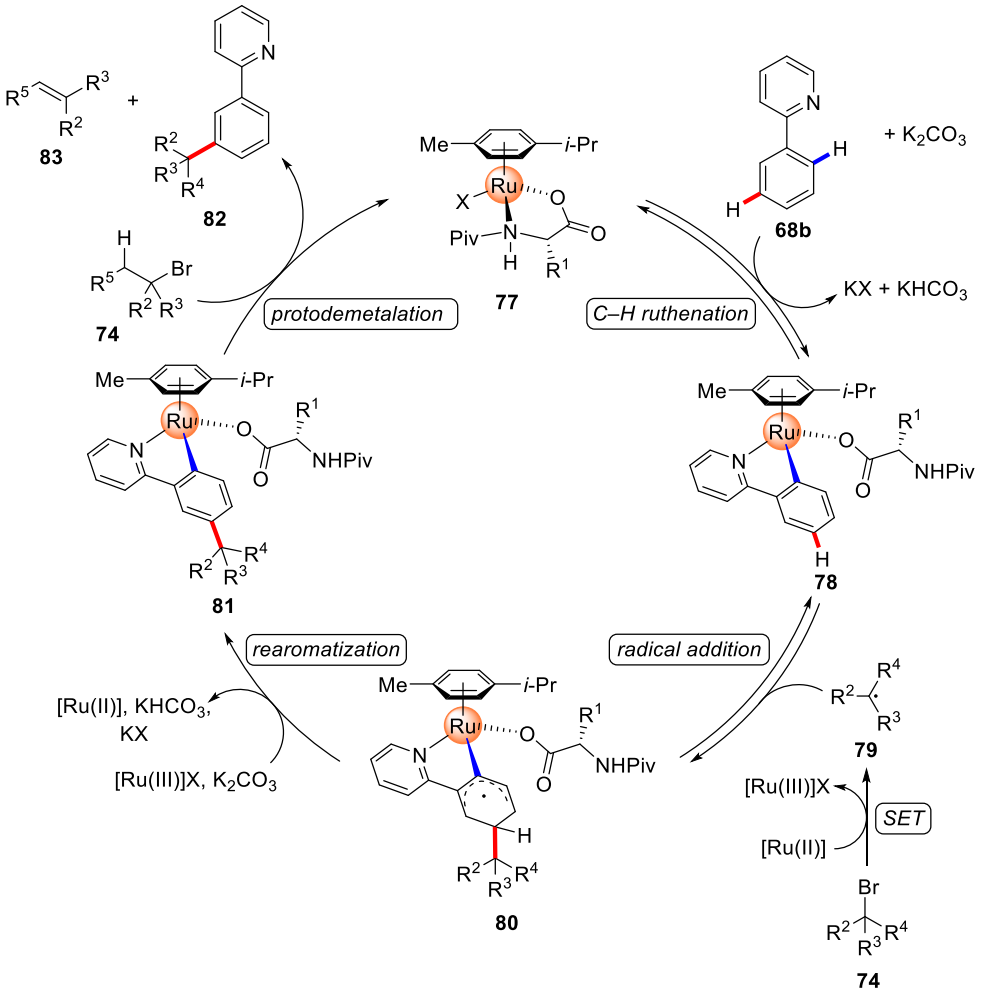
power of the effective transformations was reflected by broadly applicable directing groups. Particularly, removable *N*-pyrimidyl anilines were efficiently converted to the corresponding products **75**. Notably, the catalytic reactions with commercially available and less reactive tertiary alkyl chlorides **74a** under Frost's conditions provided the desired product **76** with high catalytic efficacy (Scheme 23b).



Scheme 23: Remote C–H transformations with tertiary alkyl halides **74**.

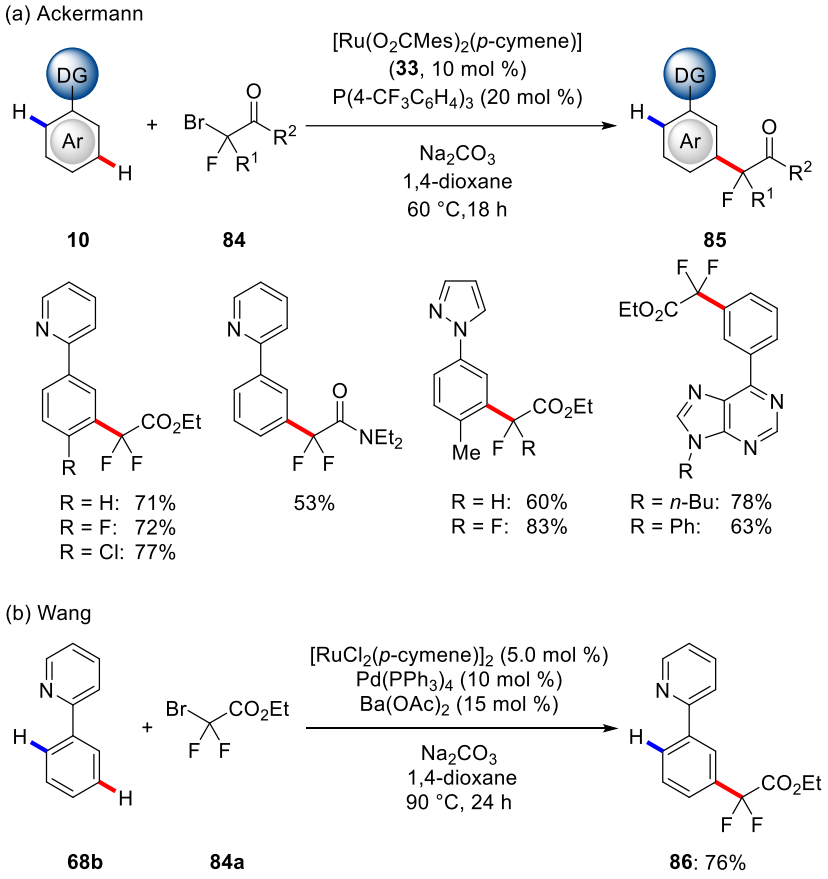
Mechanistic experiments by Ackermann, such as reactions with radical scavengers, reactions with diastereomerically pure alkyl bromides, and radical clock experiments, were supportive of a radical mechanism.[62] Based on such findings, the following catalytic cycle was proposed by Ackermann (Scheme 24). The *in situ* generated ruthenium complex **77** initially undergoes a reversible C–H ruthenation to form cyclometalated ruthenium intermediate **78**. Single-electron transfer from ruthenium(II) to alkyl halide **74** provides the corresponding radical **79**, which attacks on the arene at the *para* position with respect to the Ru–C bond to form radical intermediate **80**.

Then, rearomatization and hydrogen-atom abstraction afford the ruthenacycle intermediate **81**. Finally, complex **81** undergoes protodemetalation, delivering the *meta*-alkylated product **82** and regenerating the catalytically active complex **77**.



Scheme 24: Proposed catalytic cycle for remote C–H alkylations *via ortho*-ruthenation.

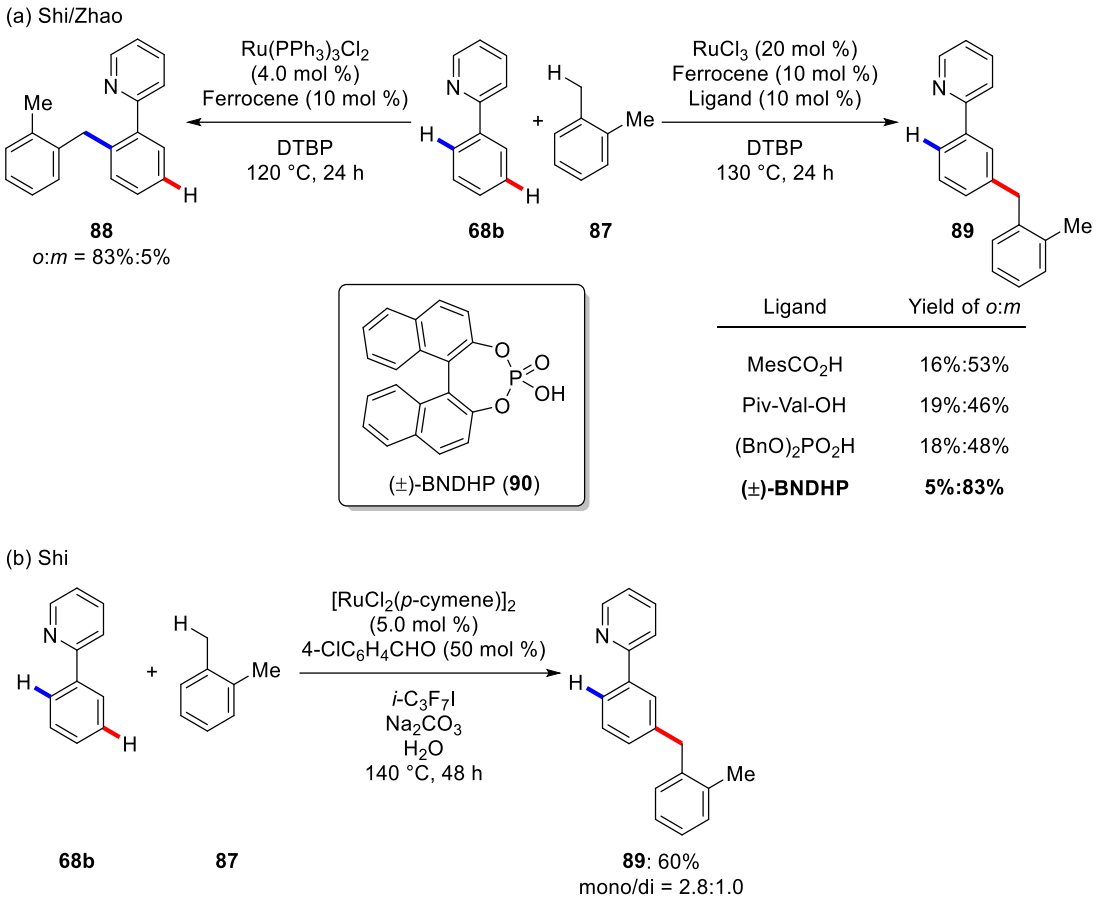
Since organofluorine compounds display an important role in agrochemicals, pharmaceuticals, and material sciences,[64] the installation of fluorine-containing groups has been of interest during the past decade.[65] In 2017, the group of Ackermann reported on the first remote *meta*-C–H mono- and difluoromethylations by the cooperative action of phosphine and carboxylate ligands in ruthenium(II) catalysis (Scheme 25a).[66] Later, the group of Wang disclosed a dual ruthenium and palladium catalysis, allowing for remote mono- and difluoromethylations (Scheme 25b).[67]



Scheme 25: Ruthenium catalysis for remote mono- and difluoromethylations.

1.3.2 meta-C–H Benzylations

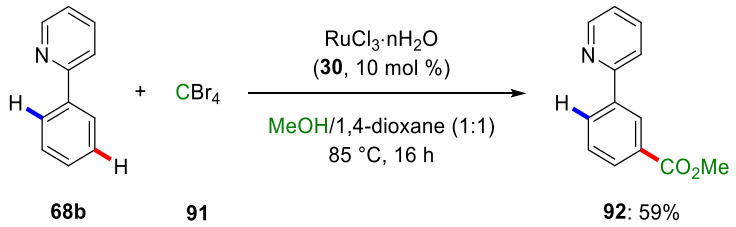
Although the benzyl radical is more stable than the alkyl radicals, the ruthenium catalysis of primary benzyl chlorides enabled direct *ortho*-C–H benzylations.[35] Taking into account atom- and step economical C–H/C–H activations[14] for the formation of new C–C bonds, oxidative ruthenium-catalyzed remote C–H benzylations of toluene derivatives **87** using di-*tert*-butylperoxide (DTBP) as a radical initiator were illustrated by the group of Shi/Zhao (Scheme 26a).[68] Even though the pre-functionalized substrates are not obligatory for the C–H/C–H activations, an excess of toluene derivative **87** is mandatory in the catalytic benzylations. $Ru(PPh_3)_3Cl_2$ catalyst provided the direct benzylated products **88** without additional ligands. Among the additive ligands, the combination between $RuCl_3$ and (±)-BNDHP was the most effective catalytic system, switching the site-selectivity of the oxidative C–H/C–H benzylations from *ortho* (**88**) to *meta* (**89**). Simultaneously, the group of Shi also reported on oxidative benzylations using perfluoroisopropyl iodide as a radical generator (Scheme 26b).[69]



Scheme 26: Oxidative ruthenium-catalyzed C–H/C–H benzylations with toluene derivatives **87**.

1.3.3 meta-C–H Carboxylations

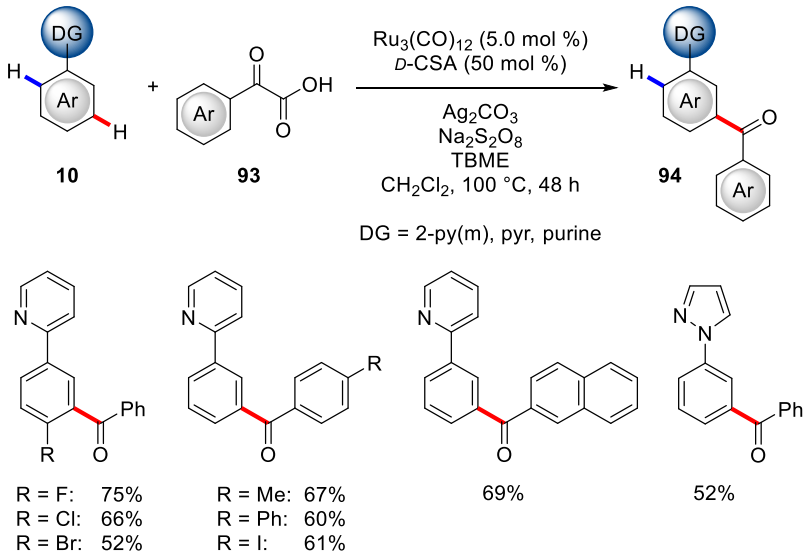
Carboxylation reactions are powerful methods for introducing a C-1 moiety into target molecules.[70] In 2017, the group of Greaney disclosed *meta*-selective carboxylation through a single-electron transfer process (Scheme 27).[71] Ruthenium-catalyzed *meta*-C–C bond formation followed by methanolysis was applicable to various arylheteroarenes, such as 2-arylpyridines (**68b**), 2-arylpyrimidines, and 6-arylpurines, thus affording *meta*-decorated arenes **92**.



Scheme 27: Ruthenium-catalyzed remote C–H carboxylation with CBr_4.

1.3.4 *meta*-C–H Acylation

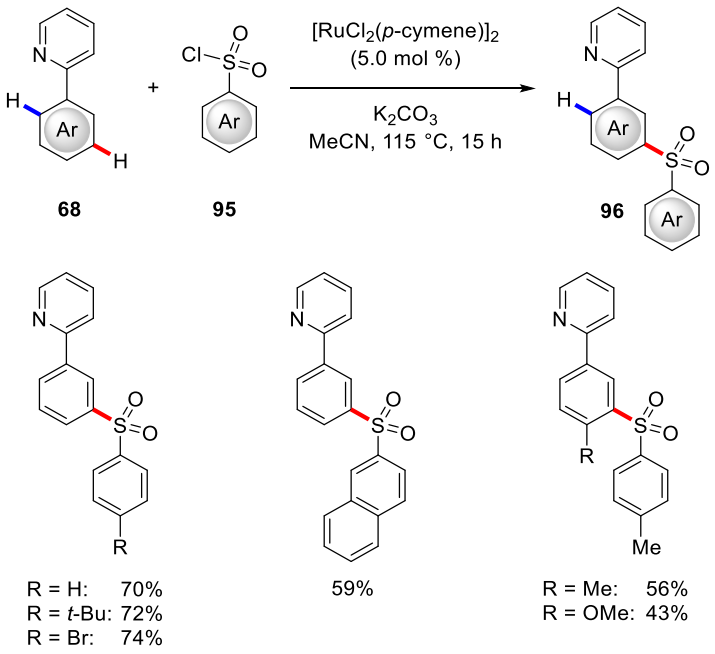
Recently, the group of Wang demonstrated a protocol for oxidative *meta*-C–H acylations, as shown in Scheme 28.[72] In the presence of a silver salt and a persulfate oxidant, the ketoacids **93** underwent oxidative decarboxylation to furnish an acyl radical, which is the key intermediate in the remote transformations. Radical intermediate selectively attacked on the arene of the *in situ* formed cyclometalated ruthenium complexes, leading to the formation of new *meta*-C–C bonds.



Scheme 28: Remote C–H acylations *via* oxidative decarboxylation.

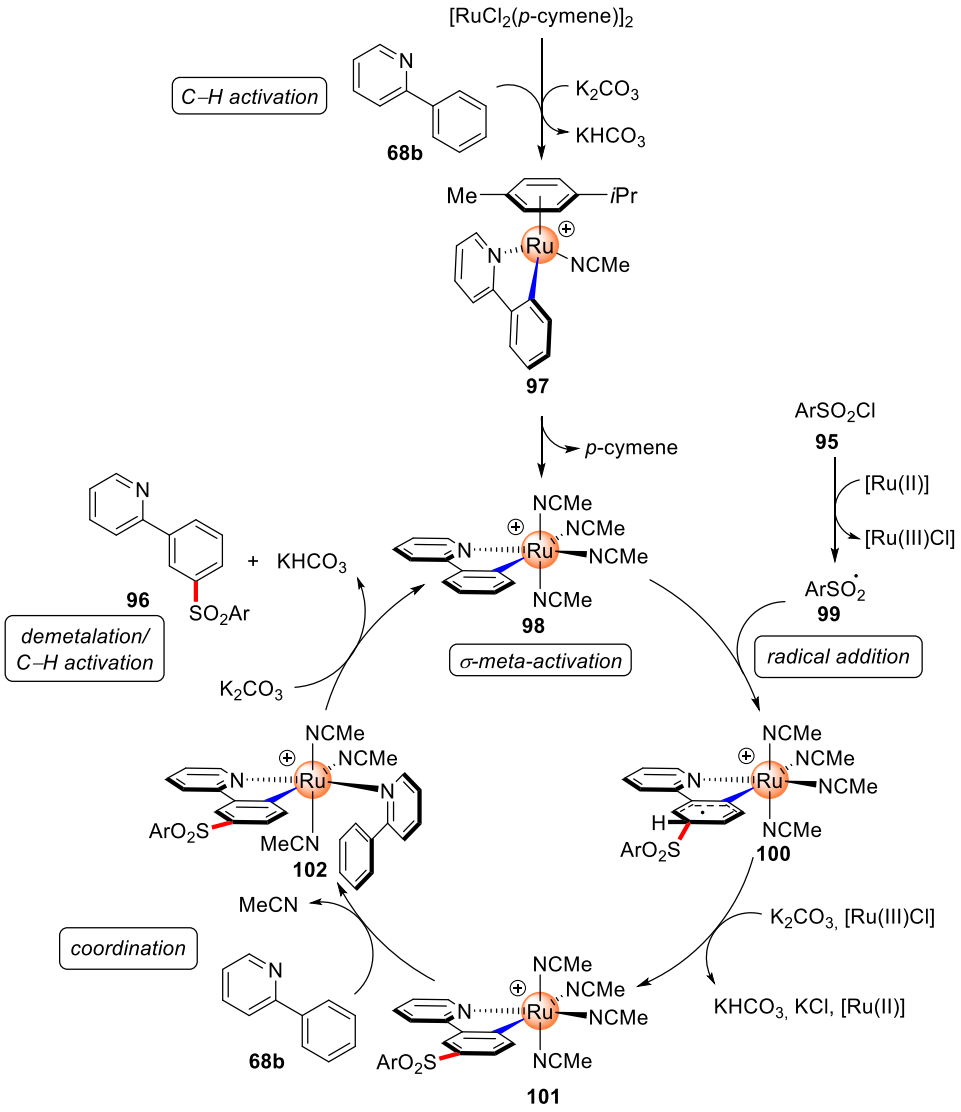
1.3.5 *meta*-C–H Sulfonylation

In addition to C–C bond, site-selective C–Het bond formation reactions have gained considerable attention over the last decade.[73] On the basis of remote functionalizations of ruthenacycles, the group of Frost first reported on a *meta*-selective C–H sulfonylation of 2-arylpyridines **68** and arylsulfonyl chlorides **95** in 2011 (Scheme 29).[74] Chelation-assisted C–H ruthenation led to the formation of a Ru–C bond, which exerts a strong *para*-directing effect for the subsequent proposed electrophilic sulfonylation.



Scheme 29: *meta*-C–H Sulfonylations of phenylpyridines **68** with sulfonyl chlorides **95.**

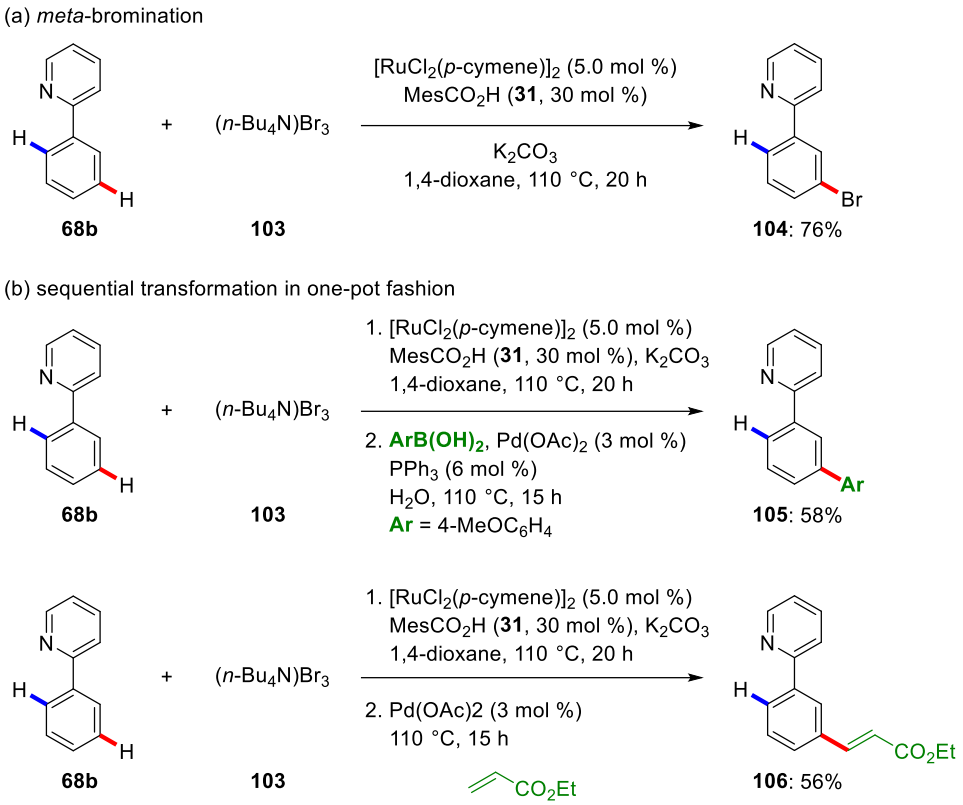
Afterwards, mechanistic experiments of *meta*-C–H sulfonylations were studied in more detail to unravel the catalyst working mode of such remote transformations.[75] It is noteworthy that the yields for the *meta*-sulfonylation of 2-phenylpyridine (**68b**) with *p*-tosyl chloride (**95a**) in the latter report[75] remarkably dropped from 80% to 50%, compared to the identical reaction conditions published earlier.[74] Among a series of well-defined cyclometalated ruthenium complexes in the catalytic sulfonylations, *p*-cymene-free ruthenacycle **98** provided a similar catalytic efficacy.[75] Moreover, dissociation of the *p*-cymene was observed during the course of the reaction by ^{1}H-NMR spectroscopy, which suggested cyclometalated complex **98** to be an active catalyst for this reaction. Reactions with various sulfonating agents and an experiment with radical scavenger TEMPO revealed that the catalytic sulfonylations likely proceeded *via* a radical mechanism, whereas a previously proposed electrophilic pathway could be ruled out. This is in good agreement with single-electron transfer (SET) mechanism for ruthenium-catalyzed *meta*-alkylation, which was earlier reported by the group of Ackermann.[62] On the basis of their findings, the catalytic cycle for remote sulfonylations was proposed,[75] which commences by C–H ruthenation followed by decoordination of *p*-cymene to form cationic cyclometalated complex **98** (Scheme 30). Sulfonyl radical **99**, which is generated from SET process from ruthenium(II), attacks at the position *para* to the Ru–C bond to form intermediate **100**. Rearomatization followed by ligand replacement furnish cationic ruthenium **102**, which undergoes demetalation and C–H ruthenation to deliver the desired product **96** and the active ruthenium intermediate **98**.



Scheme 30: Proposed catalytic cycle for *meta*-sulfonylation.

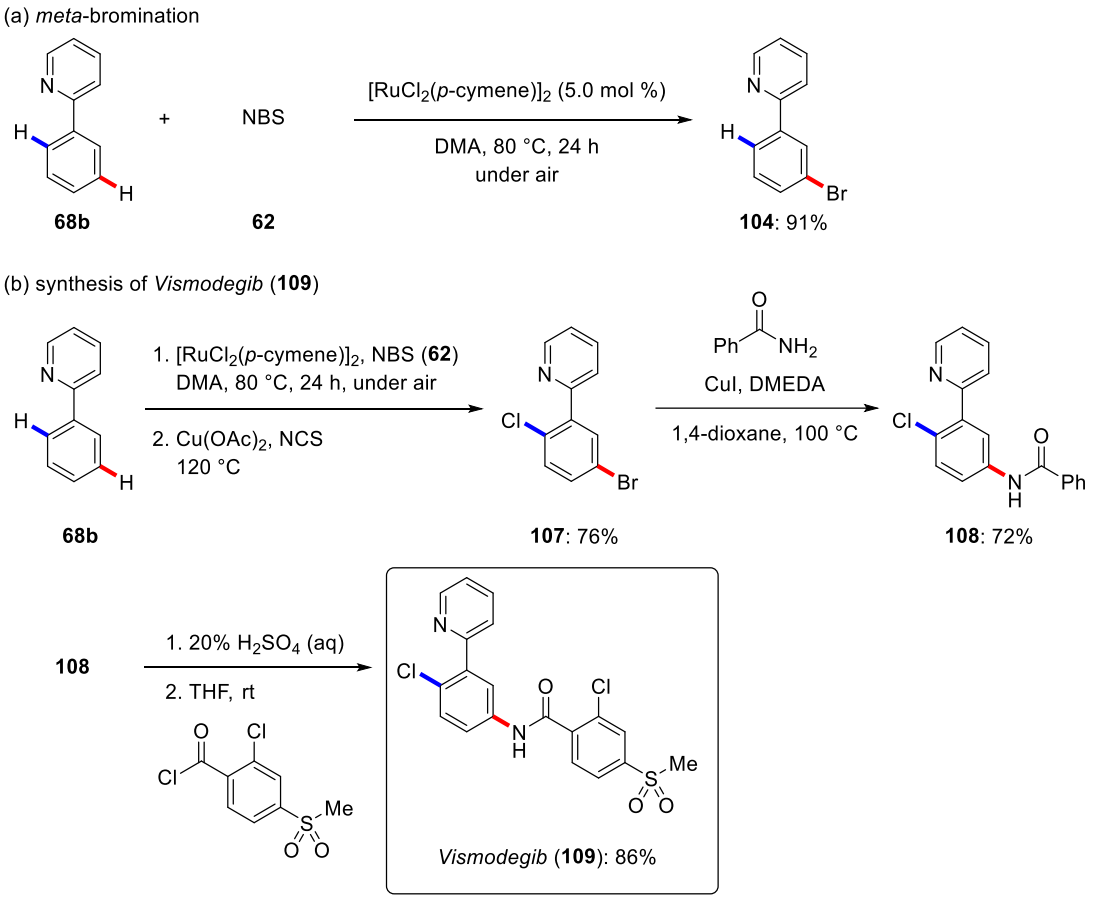
1.3.6 meta-C–H Brominations

Since aryl halides are typically used as starting materials for arylation reactions, a number of methods for direct C–H halogenation have been reported.[76] However, general methods for *meta*-selective halogenations continue to be scarce. In 2015, the group of Greaney disclosed ruthenium-catalyzed *meta*-C–H brominations of 2-phenylpyridine (**68b**) (Scheme 31a).[77] Tetrabutylammonium tribromide (**103**) was proven to be the most effective for remote brominations in Greaney's protocol. The synthetic utility of *meta*-brominations was reflected by late-stage transformations of the obtained adducts by Suzuki-Miyaura and Heck reactions in one-pot fashion, furnishing the *meta*-arylated product **105** or *meta*-alkenylated product **106**, respectively (Scheme 31b).



Scheme 31: Remote C–H brominations and sequential transformations.

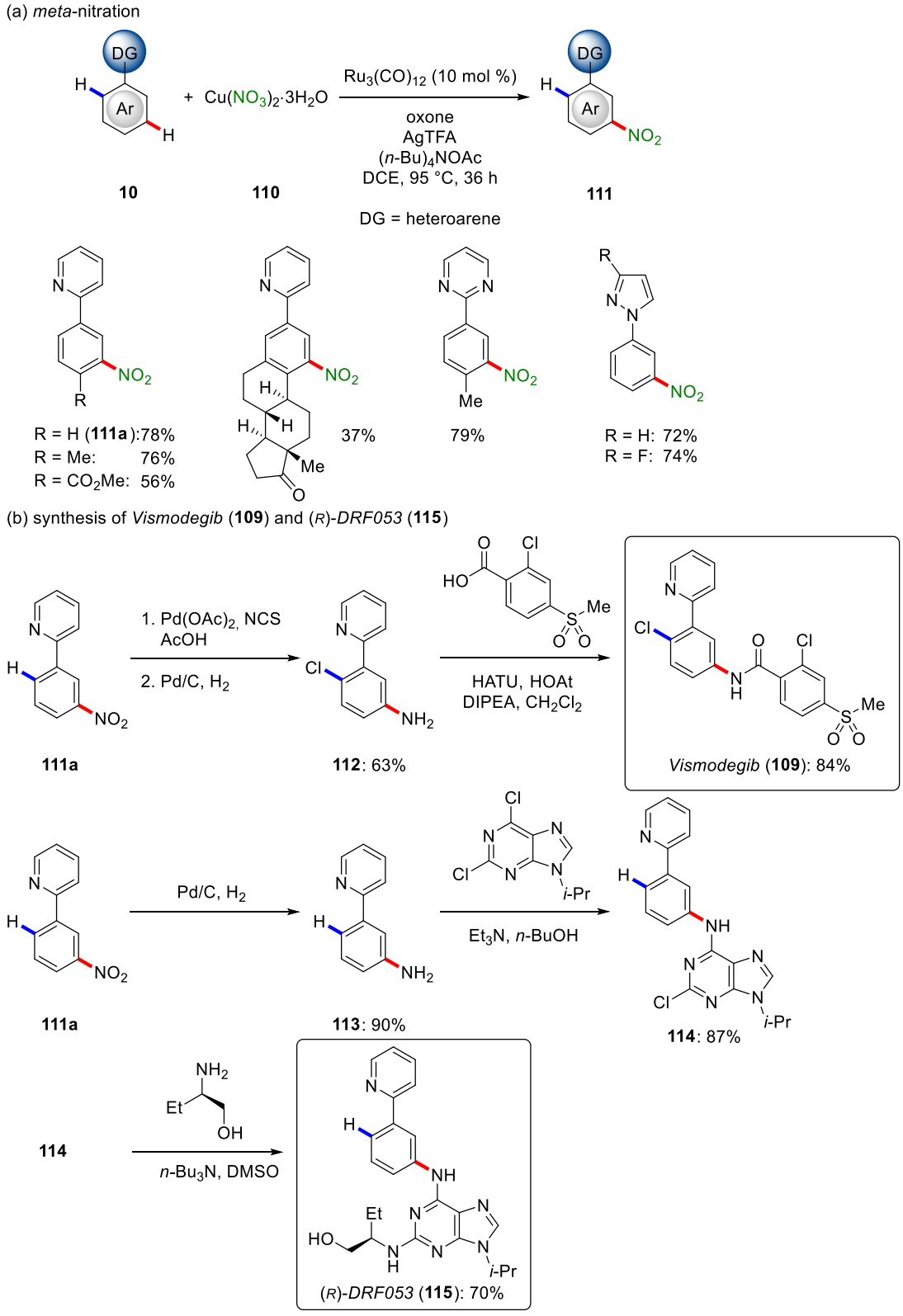
Concurrently, the group of Huang also reported on remote C–H brominations using *N*-bromosuccinimide (NBS, **62**) as a bromine source (Scheme 32a).[78] In addition to palladium-catalyzed coupling reactions, the power of *meta*-brominations was highlighted by the concise synthesis of anti-cancer drug *Vismodegib* (**109**), as shown in Scheme 32b. The sequential *meta*-bromination followed by *ortho*-chlorination in one-pot fashion delivered the desired intermediate **107**, which underwent copper-catalyzed amidation and substituent replacement to furnish the target molecule *Vismodegib* (**109**). Moreover, the cross-over H/D scrambling experiment suggested biscyclometalated complex as the key intermediate in the catalytic brominations. Remote *meta*-bromination was fully inhibited by the addition of radical scavenger BHT, which was indicative of a radical mechanism.



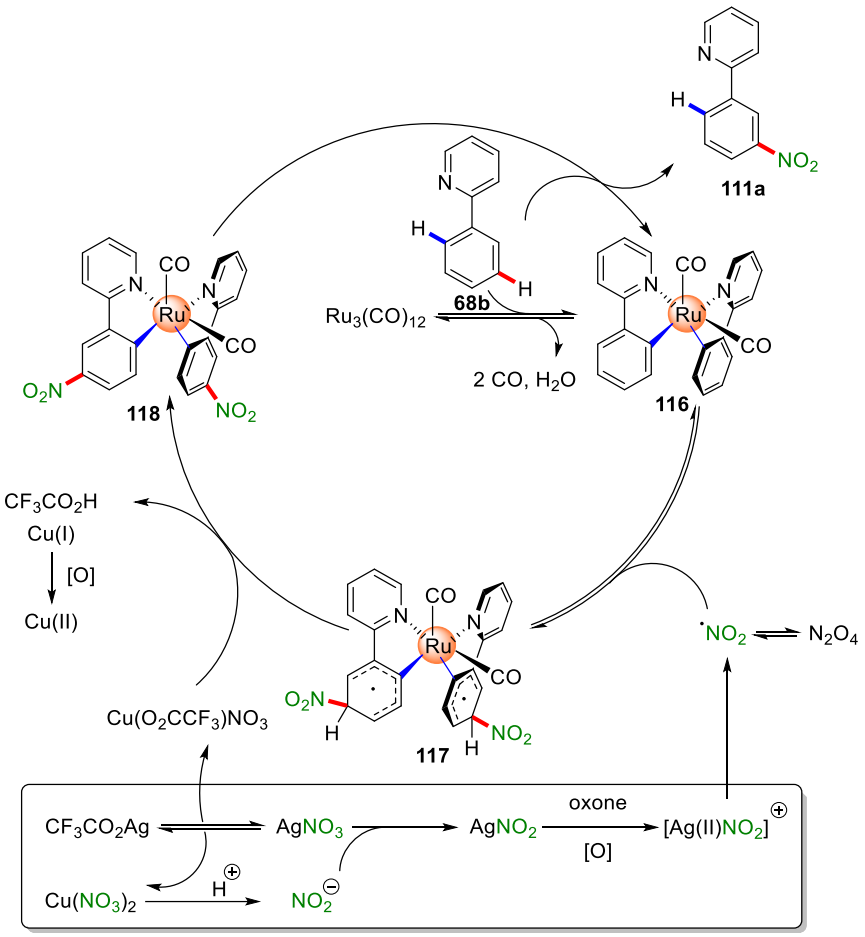
Scheme 32: Ruthenium-catalyzed *meta*-brominations and synthesis of *Vismodegib* (**109**).

1.3.7 meta-C–H Nitrations

The nitro group is a strongly electron-withdrawing group, which is frequently found in drug and material sciences.[79] Therefore, site-selective nitrations are in high demand.[80] The group of Zhang reported for the first time on a ruthenium-catalyzed *meta*-C–H nitration using $Cu(NO_3)_2{\cdot}3H_2O$ (**110**) (Scheme 33a).[81] The protocol for *meta*-nitrations was applicable to various directing group, such as pyridines, pyrimidines, pyrazoles, and ketoximes. Transformations of the obtained product **111a** led to the concise synthetic pathway of a marketed drug, *Vismodegib* (**109**), and a CDK/CK1 dual inhibitor (*R*)-*DRF053* (**115**) (Scheme 33b). On the basis of their mechanistic findings, a plausible mechanism commences by the formation of biscyclometalated ruthenium complex **116** (Scheme 34). Nitrogen dioxide radical, which is generated from anion exchange and a silver-mediated radical process, attacks on the arene at *para* to Ru–C bond, providing ruthenium intermediate **117**. Afterwards, oxidative rearomatization and ligand exchange afford the desired product **111a** and regenerate the active catalyst **116**.

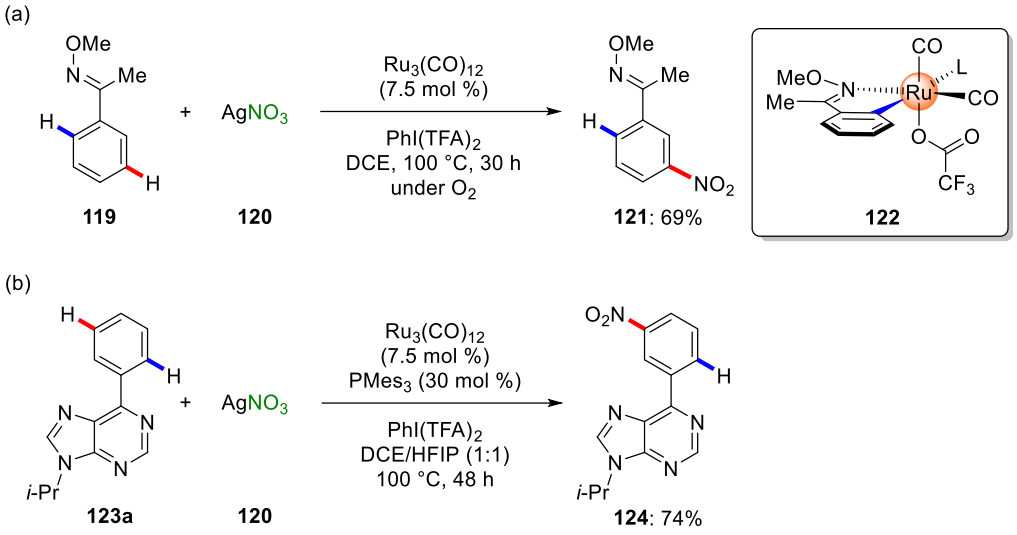


Scheme 33: Ruthenium-catalyzed *meta*-nitrations and their synthetic applications.



Scheme 34: Proposed catalytic cycle for ruthenium-catalyzed *meta*-nitrations.

Later, the group of Zhang improved the remote nitration protocol for transformable ketoximes **119** by using $PhI(TFA)_2$ as oxidant under an oxygen atmosphere (Scheme 35a).[82] Under the standard conditions, a monomeric octahedral ruthenium(II) complex **122** was isolated and confirmed by X-ray crystallography. Catalytic and stoichiometric reactions as well as DFT calculations prove ruthenacycle **122** to be an active intermediate in the catalytic nitration. Thereafter, a modified method using sterically hindered trimesitylphosphine was shown to be effective for the *meta*-nitration of 6-arylpurines **123a** and nucleosides (Scheme 35b).[83]



Scheme 35: Ruthenium-catalyzed remote C–H nitrations of ketoximes **119** and purines **123a**.

1.4 Ruthenium-Catalyzed Remote *para*-C–H Functionalizations

In contrast to the significant progress in *meta*-selective C–H transformations, challenging *para*-C–H functionalizations remain scarce. According to transition metal catalysis for *para*-selectivity, it can be achieved by three possible methodologies (Figure 5).[48b, 48c] The use of bulky ligand coordinated with iridium catalyst allowed for *para*-C–H borylations (Figure 5a).[84] It is noteworthy that the site-selectivity at the *para* position increased when sterically hindered substituents on the arene were employed. Moreover, cation/anion pairing can prevent *meta*-C–H activation, leading to C–H bond cleavage at the *para* position.[85] Nevertheless, this strategy is limited to iridium-catalyzed borylations. On the basis of proximity-induced C–H activation, the designed templates were installed to the target molecules, guiding the metal catalyst to be close to the desired C–H bond (Figure 5b).[51a, 86] The positional selectivity is directly controlled by the shape of the design template, enabling remote *meta*- or *para*-functionalizations. In addition, the electronic bias at the arene ring of cyclometalated ruthenium complexes leads to remote C–H transformations, furnishing the *para*-substituted products (Figure 5c).

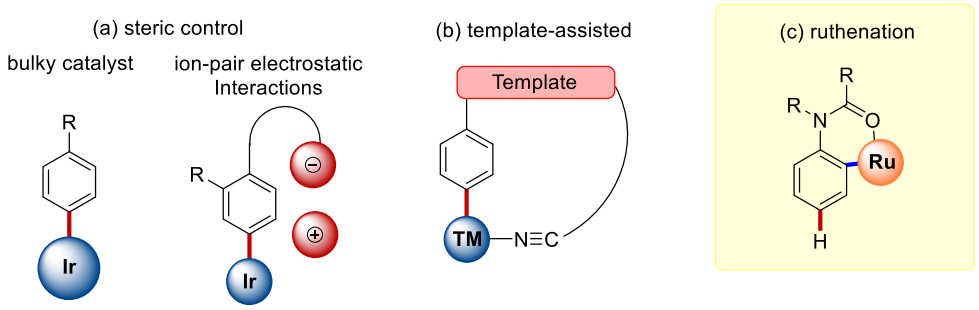
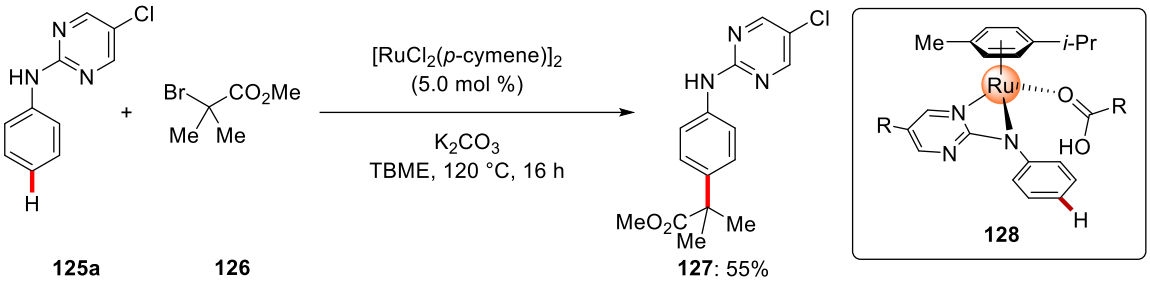


Figure 5: Methodologies for remote *para*-C–H activations.

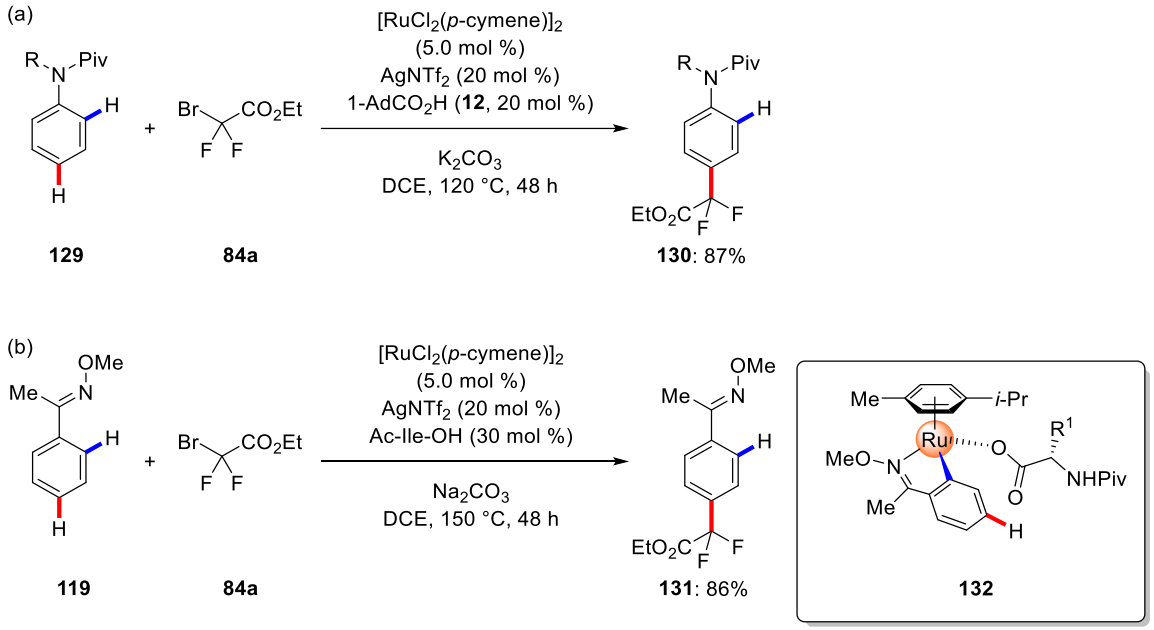
In 2017, the groups of Frost disclosed a ruthenium-catalyzed *para*-C–H functionalizations, leading to remote alkylations of *α*-bromo esters **126** (Scheme 36).[87] To avoid the second remote alkylation on the pyrimidine ring, chloro-substituent pyrimidine **125a** was employed in the remote transformations, smoothly delivering the corresponding *para*-alkylated adduct **127**. Mechanistic insights by experiments and DFT calculations were suggestive of a four-membered ruthenacycle **128** as the key intermediate.



Scheme 36: Ruthenium-catalyzed *para*-C–H alkylations with *α*-bromo esters **126**.

Thereafter, ruthenium-catalyzed *para*-C–H fluoroalkylations of anilides **129** with *α*-bromo esters **84a** were demonstrated by Zhao/Lan (Scheme 37a).[88] The combination between $AgNTf_2$ and carboxylic acid additive **12** under harsh reaction conditions of 120 °C selectively afforded the desired products **130**. Under the standard reaction conditions, 2-phenylpyridine (**68b**) was converted to the *meta*-difluoromethylated product, whereas the site-selectivity of phenylpyrazoles was controlled by the electron density of pyrazole rings. These findings were indicative of the electronic influence of the cyclometallic C–N bond on the *para* position. Moreover, the same group later employed similar reaction conditions for remote transformations of ketoximes **119** (Scheme 37b).[89] It is noteworthy that the well-defined monocylometalated

ruthenium complex **132** was proven to be the active intermediate by catalytic and stoichiometric experiments as well as DFT calculations.

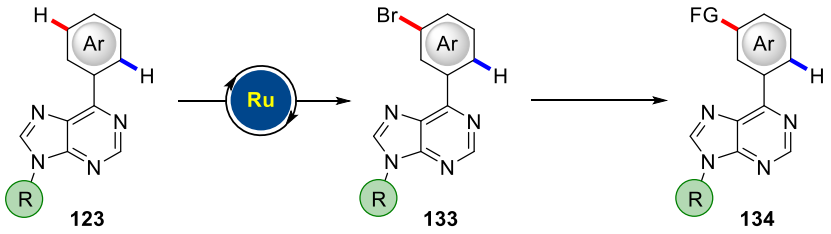


Scheme 37: Ruthenium-catalyzed *para*-C–H difluoroalkylations.

2 Objectives

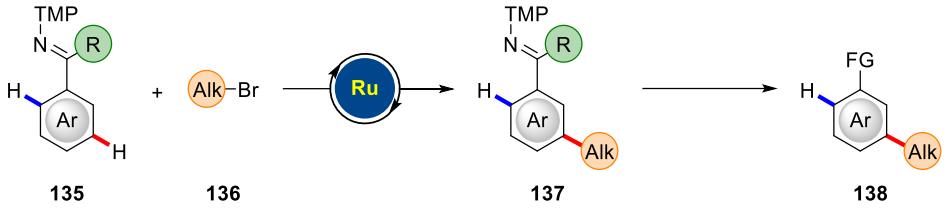
On the basis of sustainable chemistry, transition metal-catalyzed C–H activation has been recognized as a powerful platform in organic synthesis, accessing the selective formations of C–C and C–Het bonds.[13, 90] Control of site-selectivity is one of the key challenges for synthetically useful C–H transformations.[24a] Thus, the concept of chelation-assistance unravels the positional selectivity, enabling the functionalization of arenes at the *ortho* position.[27a, 27b]

Beside precious transition metals, ruthenium offers a highly reactive and cost-effective catalyst, with broadly transformative applications. Due to the distinctive character of the cyclometalated complexes, ruthenium catalysis accomplished the selective C–H transformations of arenes at the *ortho*,[29e] *meta*,[56b] or *para* positions.[87-89] However, the reports on ruthenium-catalyzed remote *meta*-C–H activations are limited to alkylations, sulfonylation, and nitrations. Since aryl halides are typically employed as starting materials in several catalytic transformations, a protocol for a *meta*-selective C–H bromination should be investigated (Scheme 38).



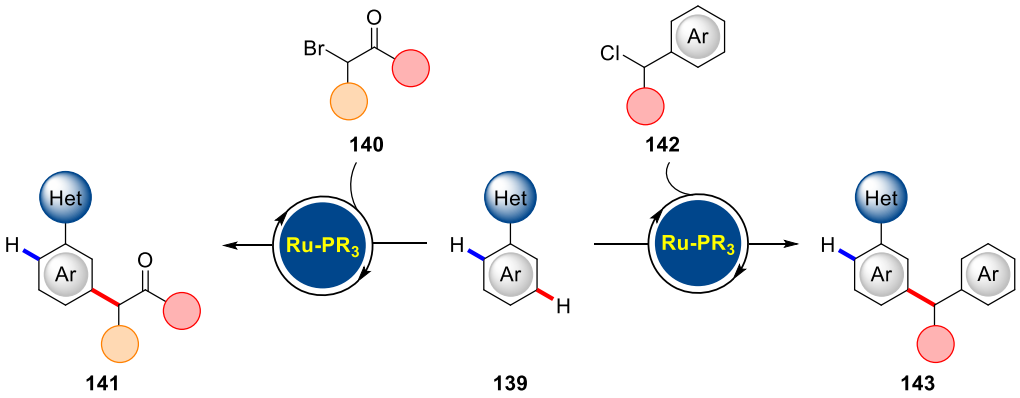
Scheme 38: Ruthenium-catalyzed romote *meta*-C–H brominations of purines **123**.

In addition, efficient protocols for ruthenium-catalyzed remote alkylations are generally restricted to strongly-coordinating directing groups, such as pyridines, pyrimidines, and pyrazoles.[61, 63] Inspired by the report from the group of Ackermann on remote alkylations of removable *N*-pyrimidyl anilines,[62] transformable ketimines **135** should be studied in remote *meta*-C–H functionalization (Scheme 39). Additionally, further modifications of the obtained products **137** should be investigated.



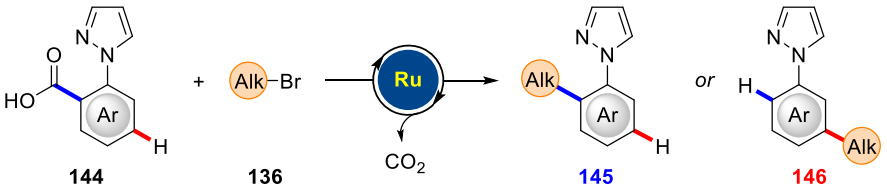
Scheme 39: Remote C–H alkylations of ketimines **135** and further transformations.

Typically, methods for remote C–H transformations require high reaction temperature of 100–120 °C.[56b] The synergistic ruthenium catalysis with phosphine ligands furnishing remote *meta*-C–H mono- or difluoromethylations at lower temperature of 60 °C, was demonstrated by the group of Ackermann.[66] Thus, the power of carboxylate-phosphine ruthenium catalysis should be further explored with *α*-bromo carbonyl compounds **140** and benzyl chlorides **142** (Scheme 40). Furthermore, detailed mechanistic insights should be investigated to rationalize the site-selectivity of C–C bond formations and to better understand the reaction mechanism.



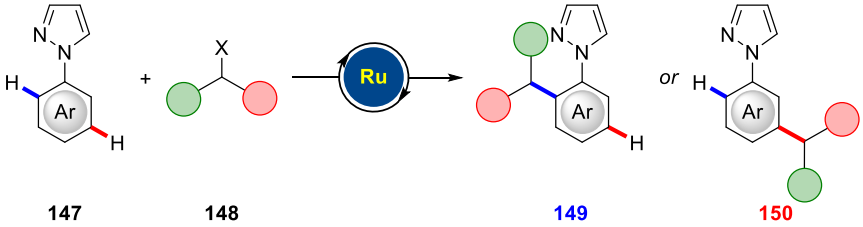
Scheme 40: Carboxylate-phosphine ruthenium catalysis for remote alkylation and benzylation.

Besides numerous reports on C–H functionalizations, a ruthenium-catalyzed decarbamoylative arylation of aromatic amides was illustrated by the group of Ackermann.[91] Therefore, a concept of ruthenium-catalyzed C–C activation should be applied for site-selective alkylations of primary, secondary, and tertiary alkyl halides **136** (Scheme 41).



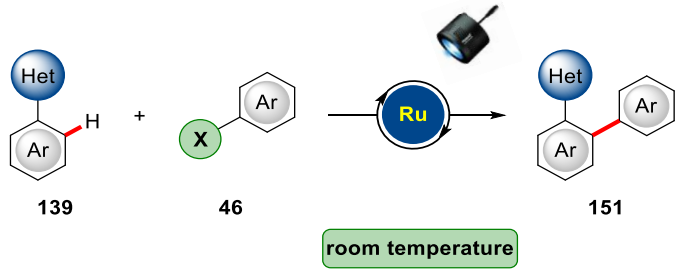
Scheme 41: Ruthenium catalysis for decarboxylative alkylations.

Since unprecedented *ortho*-alkylations of bromocyclohexane and bromonorbornane were observed in decarboxylative reactions, ruthenium-catalyzed C–H transformations of pyrazole derivatives **147** with a variety of secondary alkyl bromides **148** should be explored (Scheme 42). Moreover, mechanistic experiments should be conducted to elucidate the mechanistic pathway for *ortho*-selective alkylations.



Scheme 42: Site-selective C–H alkylation of secondary alkyl bromides.

Inspired by reports on photo-induced ruthenium-catalyzed remote C–H alkylations at room temperature,[92] the photoredox concept should be applied to direct C–H arylations to avoid the requirement of high reaction temperature of 100–140 °C (Scheme 43). In addition, mechanistic insights by experiments should be investigated to reveal the working mode of photoredox ruthenium catalysis.



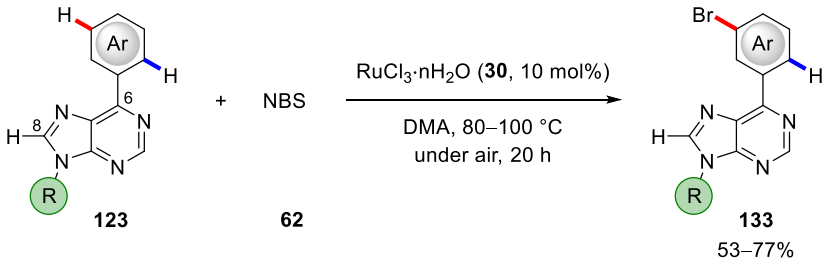
Scheme 43: Direct C–H arylations under photoredox ruthenium catalysis.

3 Results and Discussion

3.1 Ruthenium-Catalyzed *meta*-Selective Bromination

Aryl halides have played an important role in several organic transformations, especially in coupling reactions.[93] The electrophilic halogenation on arenes is a powerful transformation among direct C–H activations. However, the drawbacks of this method were reflected by multiple halogenated products. Moreover, halogenations at the benzylic position tend to be more efficient than at aromatic C–H bonds in the presence of light. Consequently, site-selective halogenation has been highly demanded in the synthetic methodology. Chelation-assistance has not allowed only for *ortho*-C–H halogenations,[47, 76] but also more challenging *meta*-C–H halogenations. However, the protocols were limited to pyridines, pyrimidines, and pyrazoles as directing groups.[77-78]

Due to a number of biologically active unnatural nucleosides,[94] late-stage transformations of nucleosides became more attractive in molecular syntheses. Although the most acidic C–H bond on purine ring is at the C8 position, a *meta*-selective C–H bromination on arene **123** using purine as the directing group was achieved by Dr. D. J. Burns in the Ackermann group (Scheme 44).[95]



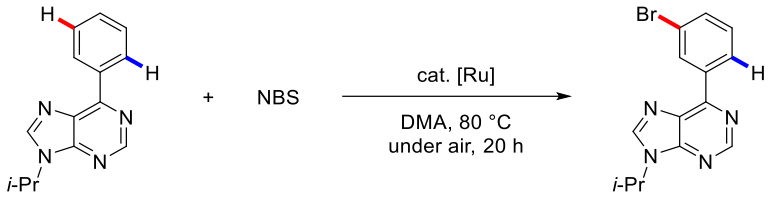
Scheme 44: Remote C–H bromination in the homogeneous system.

3.1.1 Optimization Studies

Having identified DMA as a good choice for the solvent (Table 1, entries 1–2),[95] some investigations concerning the nature of the catalyst and its loading were performed. A reduced catalytic loading significantly decreased the obtained yields of the *meta*-brominated product **133a** (entries 3–4). To reduce the metal waste, heterogeneous remote C–H bromination using ruthenium-sol-gel catalysts **152** was accomplished by Dr. S. Warratz (entry 5). In contrast to the homogeneous catalyst, a slight decrease of the product yields was observed in the reaction with lower catalytic loading (entries 6–7). Moreover, it was highlighted that the catalyst **152** could be

recovered and reused for 4–5 times without loss of catalytic efficacy.[95] In terms of sustainability, the heterogeneous catalyst **152** was therefore chosen to explore the scope of the *meta*-bromination.

Table 1: Ruthenium-catalyzed *meta*-bromination of purine **123a** with various catalytic loading.[a]



123a **62** **133a**

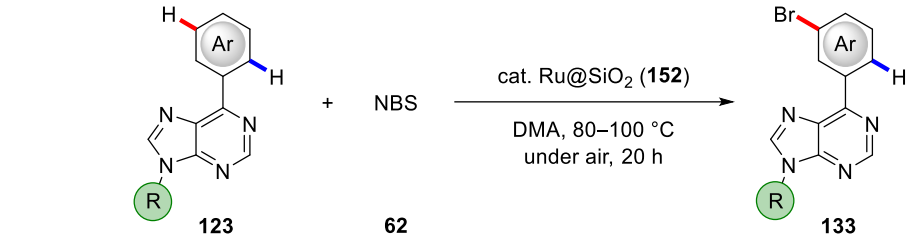
Entry	cat. [Ru]	133a (%)
1	$RuCl_3 \cdot nH_2O$ (**30**, 10 mol %)	77[b]
2	**30** (10 mol %)	---[c]
3	**30** (5 mol %)	25
4	**30** (2.5 mol %)	6
5	$Ru@SiO_2$ (**152**, 10 mol %)	63 (70)[d]
6	**152** (5 mol %)	68
7	**152** (2.5 mol %)	50

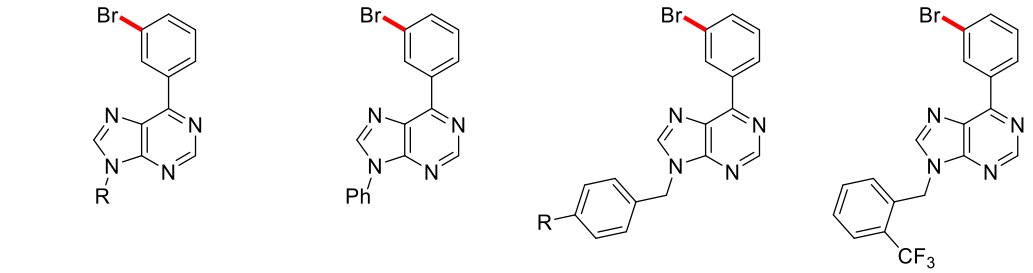
[a] Reaction conditions: **123a** (0.25 mmol), NBS (**62**, 0.50 mmol), [Ru] (x mol %), DMA (0.5 mL), 40 °C, 20 h, under N_2; yield of isolated products. [b] Reaction was performed by Dr. D. J. Burns. [c] DMA:H_2O (1:1). [d] Reaction was performed by Dr. S. Warratz.

3.1.2 Scope of the meta-Selective C–H Bromination

With the optimized catalytic system in hand, the versatility of heterogeneous remote C–H bromination was explored with various *N*-substituents of purine **123** (Scheme 45). Even though the *meta*-brominated adducts **133** were observed in excellent level of site-selectivity, the scope of purines in the heterogeneous ruthenium catalysis was limited to substituents on the aromatic motif.

The heterogeneous *meta*-bromination was not restricted to the assistance of purines **123**, but pyridines[95] and pyrimidines **139** were also efficiently converted to the desired products **153** (Scheme 46). The reaction of 2-(*o*-tolyl)pyrimidine (**139d**) delivered the monobrominated product **153c** as the major product in 62% yield and the dibrominated arene **153c'** as a side product in 13%. Moreover, the bromination of bromo-substituted pyrazole **147b** gave 23% of the corresponding adduct **153d**.





R = *i*-Pr (**133a**):63%, 70%[b]
R = *n*-Bu(**133b**):68%

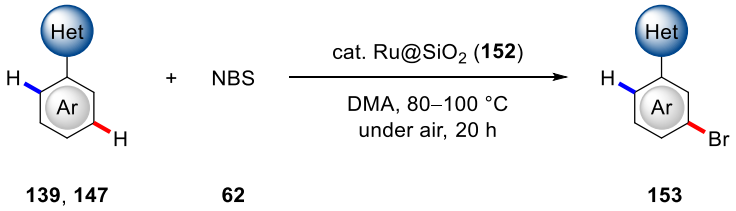
133c: 50%[c]

R = H (**133d**): 57%[b]
R = F (**133e**): 64%
R = Cl (**133f**): 64%

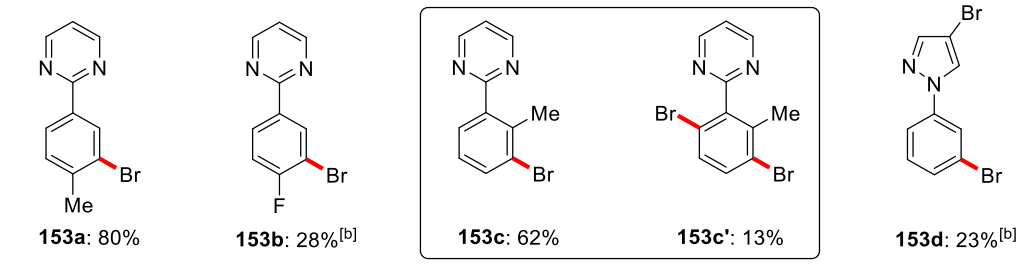
133g: 66%

[a] Reaction conditions: **123** (0.25 mmol), NBS (**62**, 0.50 mmol), **152** (10 mol %), DMA (0.50 mL), 80 °C, 20 h, under air; yield of isolated products. [b] Reactions were performed by Dr. S. Warratz. [c] 100 °C.

Scheme 45: Scope of *meta*-bromination in heterogeneous system.



139, **147** **62** **153**



153a: 80%

153b: 28%[b]

153c: 62%

153c': 13%

153d: 23%[b]

[a] Reaction conditions: **139**, or **147** (0.25 mmol), NBS (**62**, 0.50 mmol), **152** (10 mol %), DMA (0.50 mL), 80 °C, 20 h, under air; yield of isolated products. [b] 100 °C.

Scheme 46: *meta*-Bromination of different heteroarenes.

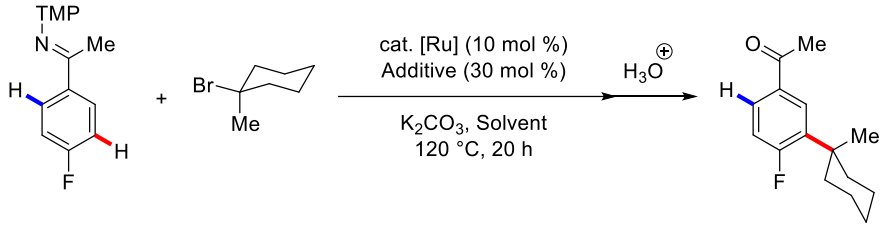
3.2 Ruthenium(II)-Catalyzed Remote *meta*-C–H Alkylation of Ketimines

During the past decade, full control of positional selectivity in C–H functionalization reactions has been identified as a major challenge.[24a] To achieve the selectivity, chelation-assistance has thus proven to be valuable for proximity-induced C–H functionalization.[27b] Unlike other *ortho*-metalations, *ortho*-C–H ruthenation process allowed not only for *ortho*-C–H transformations,[29e] but also more challenging *meta*-C–H functionalizations.[56b] In the early progress from the groups of Ackermann[61] and Frost,[63] pyridines and azoles were employed as the directing groups in the *meta*-C–H alkylations. The utility of these directing groups was limited, as they are difficult to modify or remove. The first report on the remote *meta*-alkylation of removable *N*-pyrimidylanilines was achieved by the group of Ackermann.[62]

3.2.1 Optimization Studies

To expand the versatility of ruthenium catalysis, Dr. J. Li in the Ackermann group developed a remote *meta*-C–H alkylation of ketimine **135** using $[RuCl_2(p\text{-cymene})]_2$ catalyst, 1-adamantanecarboxylic acid (1-AdCO_2H, **12**) as an additive in toluene as the solvent (Table 2, entry 1).[96] Then acid additives as the ligand of the ruthenium catalyst were tested. While pivalic acid showed similar efficacy to acid **12** (entry 2), MPAAs gave lower conversions (entries 3–4). However, the drawback of toluene is the radical-sensitive benzylic proton, resulting in the formation of *ortho*-benzylated adducts as a side product. To prevent the side reaction, Dr. S. De Sarkar found *tert*-butylbenzene (PhCMe_3) could be employed as the solvent instead of toluene and the twofold catalytic efficacy was observed (entry 5). After probing the additives and solvents (entries 6–10), the optimized reaction condition was to use a catalytic amount of acid **12** in PhCMe_3 (entry 7). In addition, it was found that carboxylic acid additive was essential in the ruthenium-catalyzed C–H activation (entry 11). Moreover, arenes on ruthenium complexes did not exert influence on the catalytic efficacy (entries 12–17). $RuCl_3$ catalysts failed to give any conversion (entries 18–19). Due to a reduced electronic density of imine, the reaction of *N*-(4-methoxyphenyl)imine provided the corresponding ketone **154aa** in moderate yield (entry 20).

Table 2: Optimization studies for the ruthenium(II)-catalyzed *meta*-alkylation of ketimine **135a**.[a]



135a **136a** **154aa**

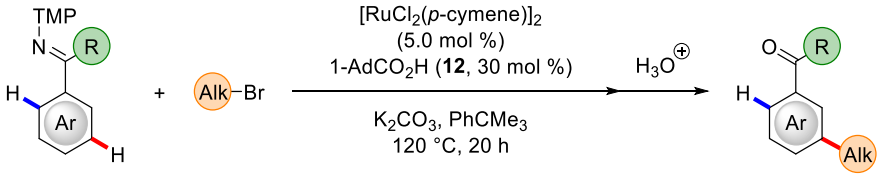
Entry	cat. [Ru]	Additive	Solvent	154aa (%)
1	$[RuCl_2(p\text{-cymene})]_2$	1-$AdCO_2H$ (**12**)	PhMe	58[b]
2	$[RuCl_2(p\text{-cymene})]_2$	PivOH	PhMe	62
3	$[RuCl_2(p\text{-cymene})]_2$	Piv-Val-OH (**41**)	PhMe	17
4	$[RuCl_2(p\text{-cymene})]_2$	Piv-Ile-OH (**155**)	PhMe	33[c]
5	$[RuCl_2(p\text{-cymene})]_2$	**155**	$PhCMe_3$	64[c]
6	$[RuCl_2(p\text{-cymene})]_2$	AcOH	$PhCMe_3$	14
7	**$[RuCl_2(p\text{-cymene})]_2$**	**12**	**$PhCMe_3$**	**73**
8	$[RuCl_2(p\text{-cymene})]_2$	**12**	PhH	54
9	$[RuCl_2(p\text{-cymene})]_2$	**12**	PhF	42
10	$[RuCl_2(p\text{-cymene})]_2$	**12**	$PhCF_3$	52
11	$[RuCl_2(p\text{-cymene})]_2$	---	$PhCMe_3$	---
12	$[RuCl_2(C_6H_6)]_2$	**12**	$PhCMe_3$	73
13	$[RuCl_2(PhCMe_3)]_2$	**12**	$PhCMe_3$	67
14	$[RuCl_2(C_6H_6)]_2$	**12**	1,4-dioxane	51
15	$[RuCl_2(p\text{-cymene})]_2$	**12**	1,4-dioxane	52[b]
16	$[RuCl_2(p\text{-cymene})]_2$	$MesCO_2H$ (**31**)	1,4-dioxane	30
17	$[RuCl_2(PhCMe_3)]_2$	**12**	1,4-dioxane	48
18	$RuCl_3$	**155**	$PhCMe_3$	---
19	$RuCl_3 \cdot nH_2O$ (**30**)	**155**	$PhCMe_3$	---
20	$[RuCl_2(p\text{-cymene})]_2$	**155**	$PhCMe_3$	44[d]

[a] Reaction conditions: **135a** (0.50 mmol), **136a** (1.50 mmol), [Ru] (10 mol %), additive (30 mol %), K_2CO_3 (1.00 mmol), solvent (2.0 mL), 120 °C, 20 h, under N_2, then hydrolysis by 2 N HCl, 3 h; yield of isolated products. [b] Reactions were performed by Dr. J. Li. [c] Reactions were performed by Dr. S. De Sarkar. [d] 4-Methoxyphenyl (PMP) instead of TMP. TMP = 3,4,5-trimethoxyphenyl.

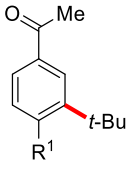
3.2.2 Scope of the meta-Selective C–H Alkylation of Ketimines

Having identified the optimal catalytic system, the versatility of ruthenium(II)-catalyzed remote *meta*-alkylation of ketimines **135** and tertiary alkyl bromides **136** was investigated (Scheme 47). In all cases, the ruthenium(II) biscarboxylate catalyst proved to be more effective than the ruthenium catalyst derived from Piv-Ile-OH (**155**). Acyclic and cyclic tertiary alkyl bromides **136** were smoothly reacted under the remote alkylation conditions. It is noteworthy that the less reactive alkyl chloride also furnished the desired *meta*-decorated arene **154ab** with similar catalytic efficacy, in contrast to *tert*-butyl iodide.[96] Moreover, the reaction of tertiary alkyl bromide **136f** containing a reactive primary alkyl chloride motif delivered the *meta*-alkylated ketone **154af** with excellent levels of chemo- and site-selectivity. Additionally, 3,4,5-trimethoxyphenylamine (TMP-NH_2) was recovered in a sustainable fashion in high yield after acidic hydrolysis, which could possibly be reused in further transformations.[96] However, strong electron-withdrawing substituents on the arenes **135k**–**135m** gave unsatisfactory results (**154kb**–**154mb**) under the optimized reaction conditions. Furthermore, ketimines **135n** and **135o** decorated with cyclic amine, methylenedioxy (**135p**), naphthalene (**135q**), and thiophene (**135r**) poorly reacted with *tert*-butyl bromide (**136b**). Steric hinderance of ketimines **135s** and **135t** changed the equilibrium to the inactive *Z*-isomer, resulting in inefficiency in the ruthenium catalysis.

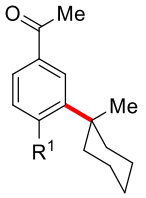
In addition to tertiary alkyl bromides **136a**–**136g**, the applicability of the remote C–H functionalization procedure was reflected by efficient *meta*-alkylation with various secondary alkyl bromides **136h**–**136q** (Scheme 48). A range of electronically different ketimines **135** performed efficiently with cyclic alkyl bromides **136h**–**136k**. The highly effective remote alkylation proved to be broadly applicable, tolerating a wealth of functional groups, including chlorides (**154ch**), esters (**154kh**), nitriles (**154lh**), and amines.[96] Unlike tertiary alkyl bromides, ketimines derived from amino-subtituted acetophenones (**135n** and **135o**) and 2-acetylnaphthalene (**135q**) were effortlessly reacted with both cyclic and acyclic secondary alkyl bromides. While the reaction of 4-bromopiperidine (**136p**) and 4-bromotetrahydropyran (**136q**) delivered the corresponding ketones **154qp**, **154ap**, and **154aq** in moderate yields, 3-bromotetrahydrofuran (**136r**) gave low yield of the corresponding product **154ar**. Moreover, the reaction of nitro-substituted ketimine **135m** failed to provide any conversion.



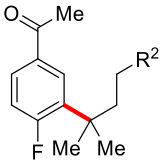
135 **136** **154**



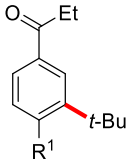
R^1 = H (**154bb**): 71%, 54%[b]
R^1 = F (**154ab**): 74%
R^1 = Cl (**154cb**): 62%, 65%[b]
R^1 = OMe (**154db**): 81%, 66%[b]
R^1 = Me (**154eb**): 46%, 40%[b]
R^1 = OBz (**154fb**): 61%, 44%[b]



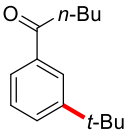
R^1 = H (**154ba**): 60%
R^1 = F (**154aa**): 73%



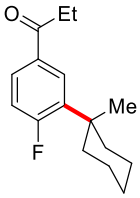
R^2 = H (**154ac**): 76%
R^2 = Me (**154ad**): 48%, 55%[c]
R^2 = Ph (**154ae**): 59%
R^2 = CH_2Cl (**154af**): 55%, 22%[b]



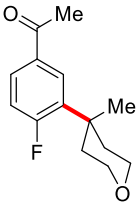
R^1 = H (**154gb**): 80%, 59%[b]
R^1 = F (**154hb**): 83%



154ib: 74%

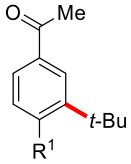


154ha: 70%

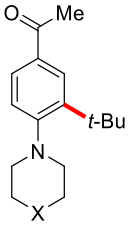


154ag: 57%

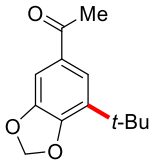
less successful examples



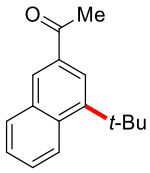
R^1 = Ph (**154jb**): 27%, 38%[b]
R^1 = CO_2Me (**154kb**): 13%, 28%[b]
R^1 = CN (**154lb**): 20%, 27%[b]
R^1 = NO_2 (**154mb**): ---, ---[b]



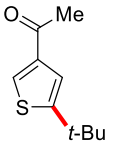
X = CH_2 (**154nb**): 14%
X = O (**154ob**): ---



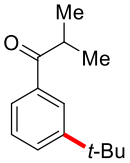
154pb: 35%



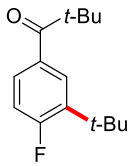
154qb: 38%, 19%[b]



154rb: 14%



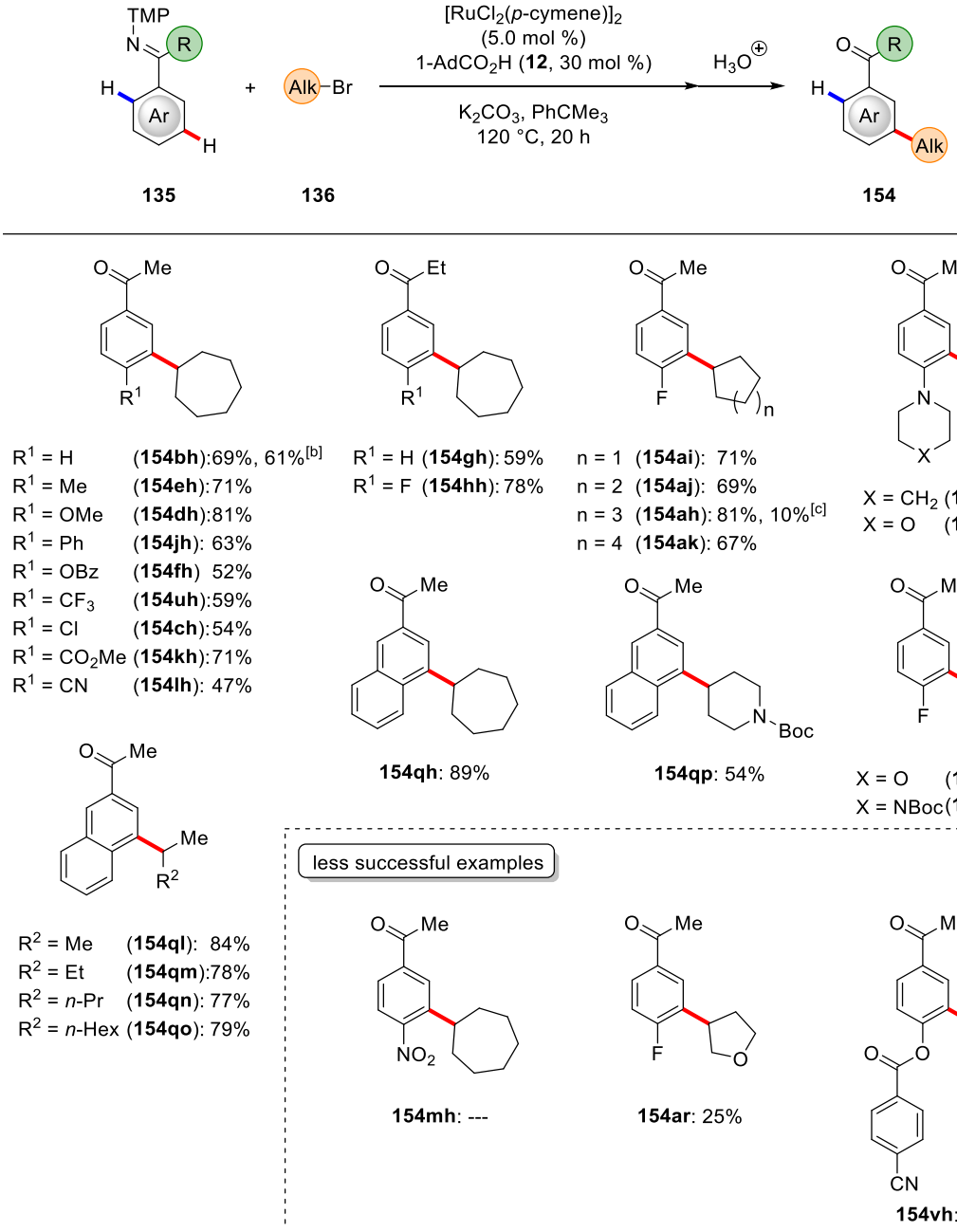
154sb: 13%[d], 30%[b]



154tb: ---, ---[b]

[a] Reaction conditions: **135** (0.50 mmol), **136** (1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), 1-$AdCO_2H$ (**12**, 30 mol %), K_2CO_3 (2.0 equiv), $PhCMe_3$ (2.0 mL), 120 °C, 20 h, under N_2, then hydrolysis by 2 N HCl, 3 h; yield of isolated products. [b] With Piv-Ile-OH (**155**) as the ligand. [c] $[RuCl_2(C_6H_6)]_2$. [d] PhMe.

Scheme 47: Remote *meta*-C–H alkylation with tertiary alkyl bromides.



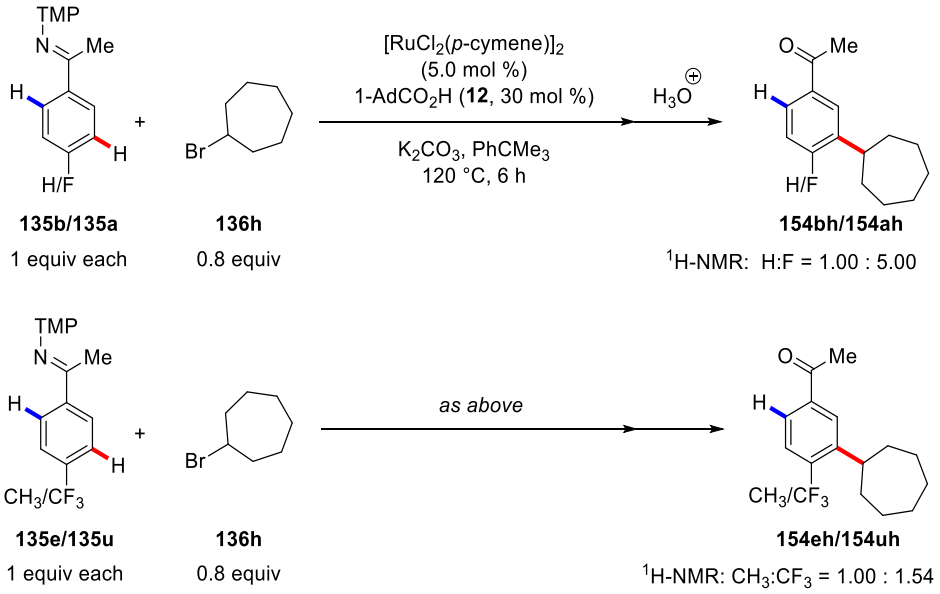
[a] Reaction conditions: **135** (0.50 mmol), **136** (1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), 1-$AdCO_2H$ (**12**, 30 mol %), K_2CO_3 (2.0 equiv), $PhCMe_3$ (2.0 mL), 120 °C, 20 h, under N_2, then hydrolysis by 2 N HCl, 3 h; yield of isolated products. [b] Alk–Br (0.75 mmol). [c] With Piv-Ile-OH (**155**) as the ligand.

Scheme 48: Remote *meta*-C–H alkylation with secondary alkyl bromides.

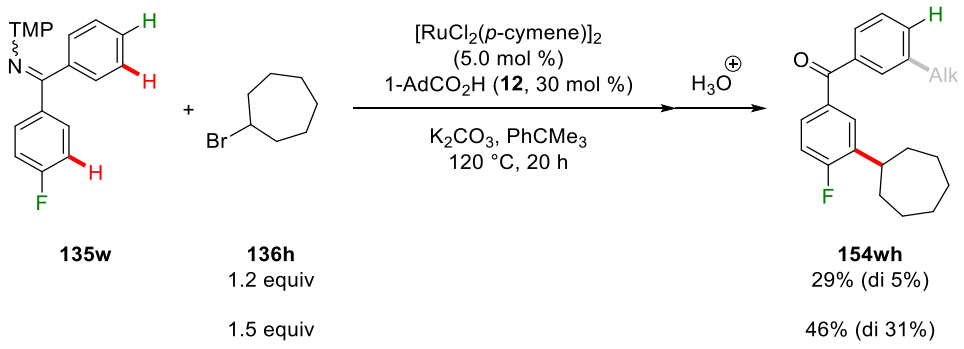
3.2.3 Mechanistic Studies

In order to delineate the working mode of the ruthenium(II)-catalyzed remote C–H activation, experimental mechanistic studies were conducted. To this end, intermolecular competition experiments highlighted electron-deficient arene to be conducted more preferentially (Scheme

49). Similarly, the *meta*-C–H alkylation of ketimine **135w** favorably occurred on the arene with fluorine substituent, delivering the monoalkylated product **154wh** as well as the dialkylated product (Scheme 50). It is noteworthy that the monoalkylated product on unsubstituted arene moiety was not observed even though the *E*/*Z* isomeric mixture of **135w** was employed. To rationalize this phenomenon, NOESY experiment was performed. According to the 2D-spectrum, the interconversion between *E*- and *Z*-isomer was observed even at ambient temperature with kinetic conversion rate $k_{BA}>k_{AB}$ (Figure 6).



Scheme 49: Intermolecular competition experiments for remote C–H alkylation. The conversion was determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard.



Scheme 50: Intramolecular competition experiments for remote C–H alkylation.

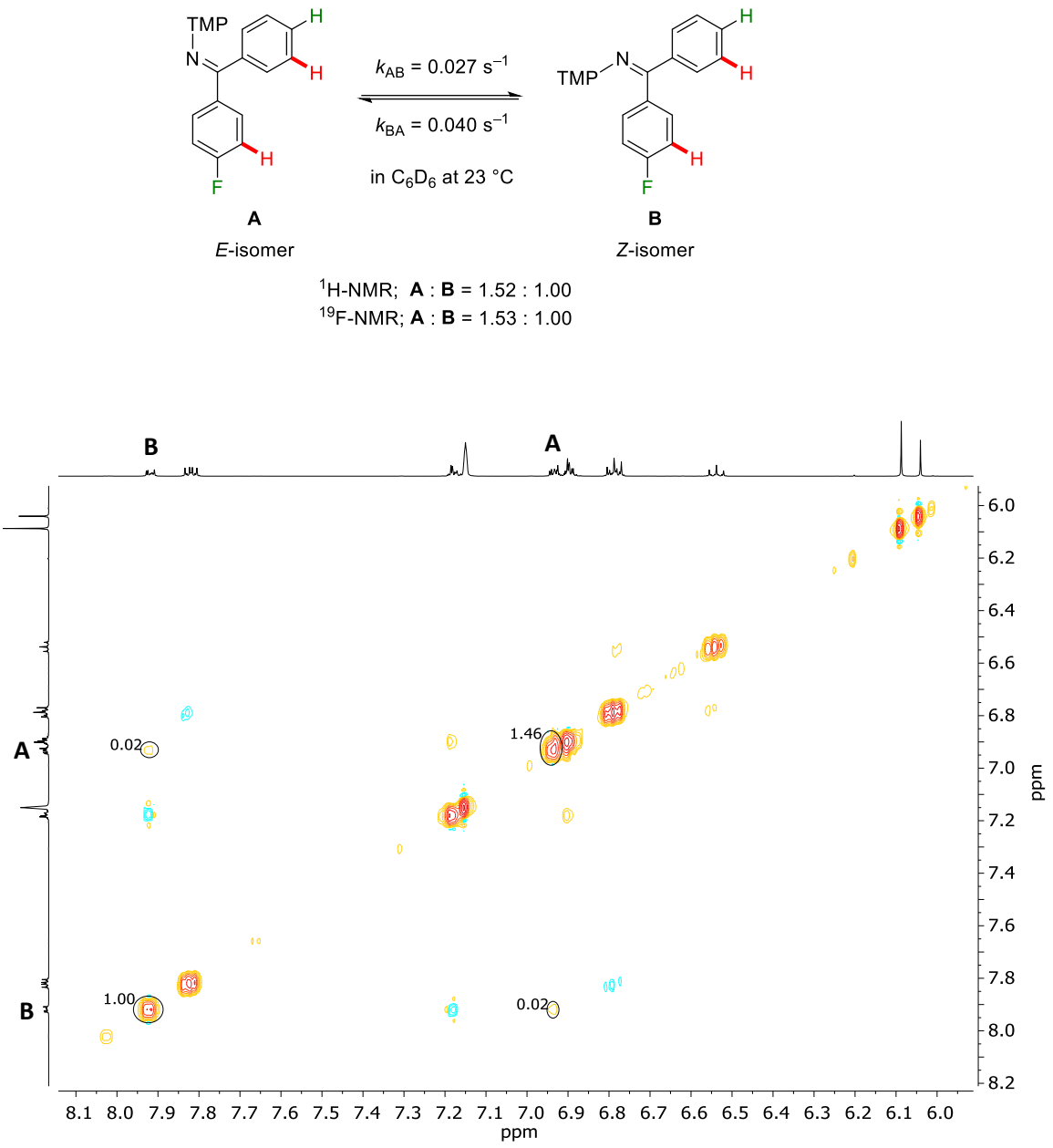
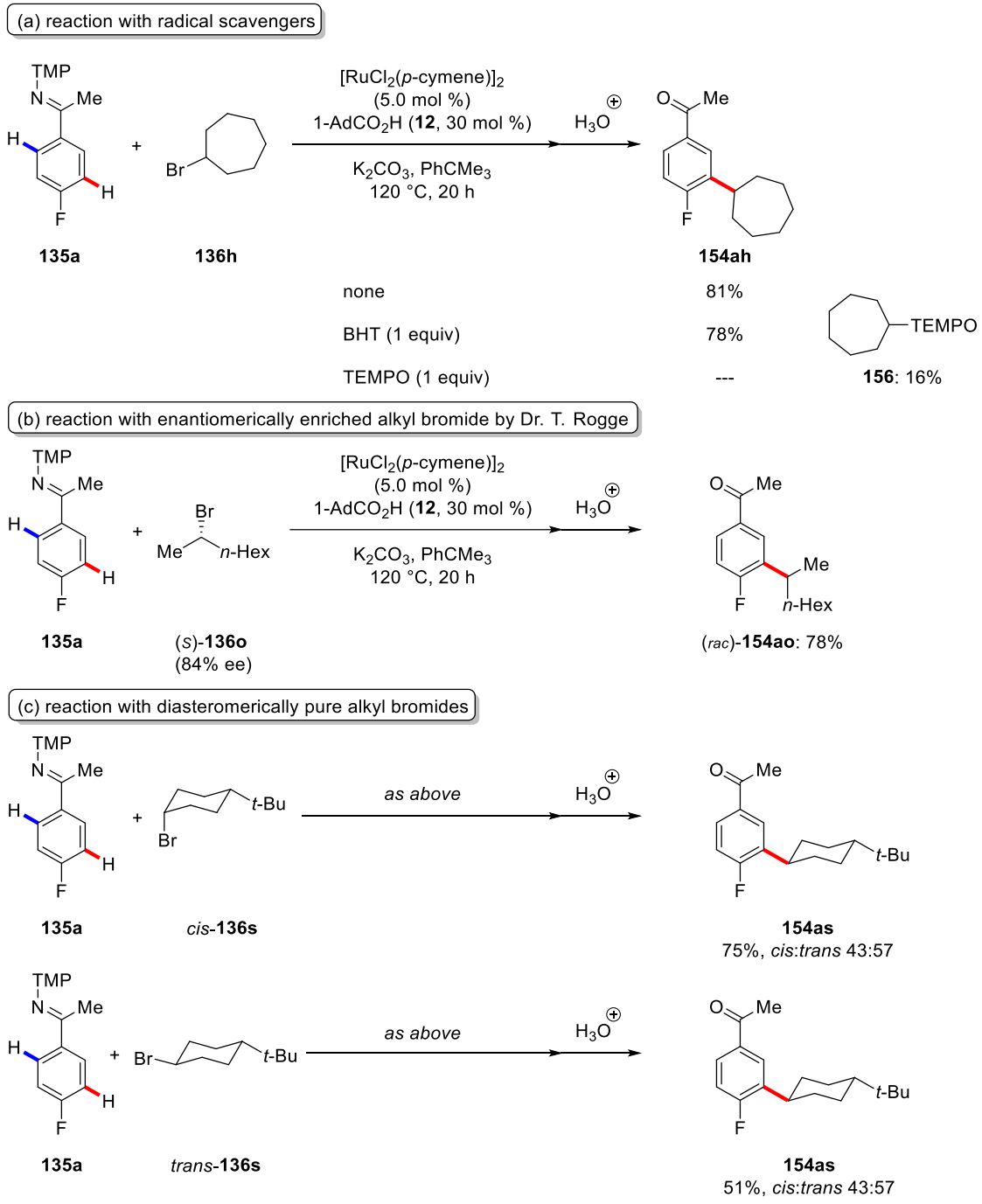


Figure 6: NOESY 2D-spectrum for isomeric mixture of ketimine **135w**.

To understand the nature of the C–X bond cleavage, the reaction was performed in the presence of radical scavengers (Scheme 51a). While BHT did not exert influence on the catatytic potency, the addition of the typically used radical trap TEMPO completely inhibited the catalytic C–H transformation. The TEMPO adduct **156** was isolated, which supported a homolytic C–X bond cleavage. Moreover, the reactions with enantiomerically enriched substrate (*s*)-**136o** and diasteromerically pure alkyl bromides **136s** delivered the isomeric mixtures **154ao** and **154as**, respectively, which are suggestive of a radical-type mechanism (Scheme 51b and c).

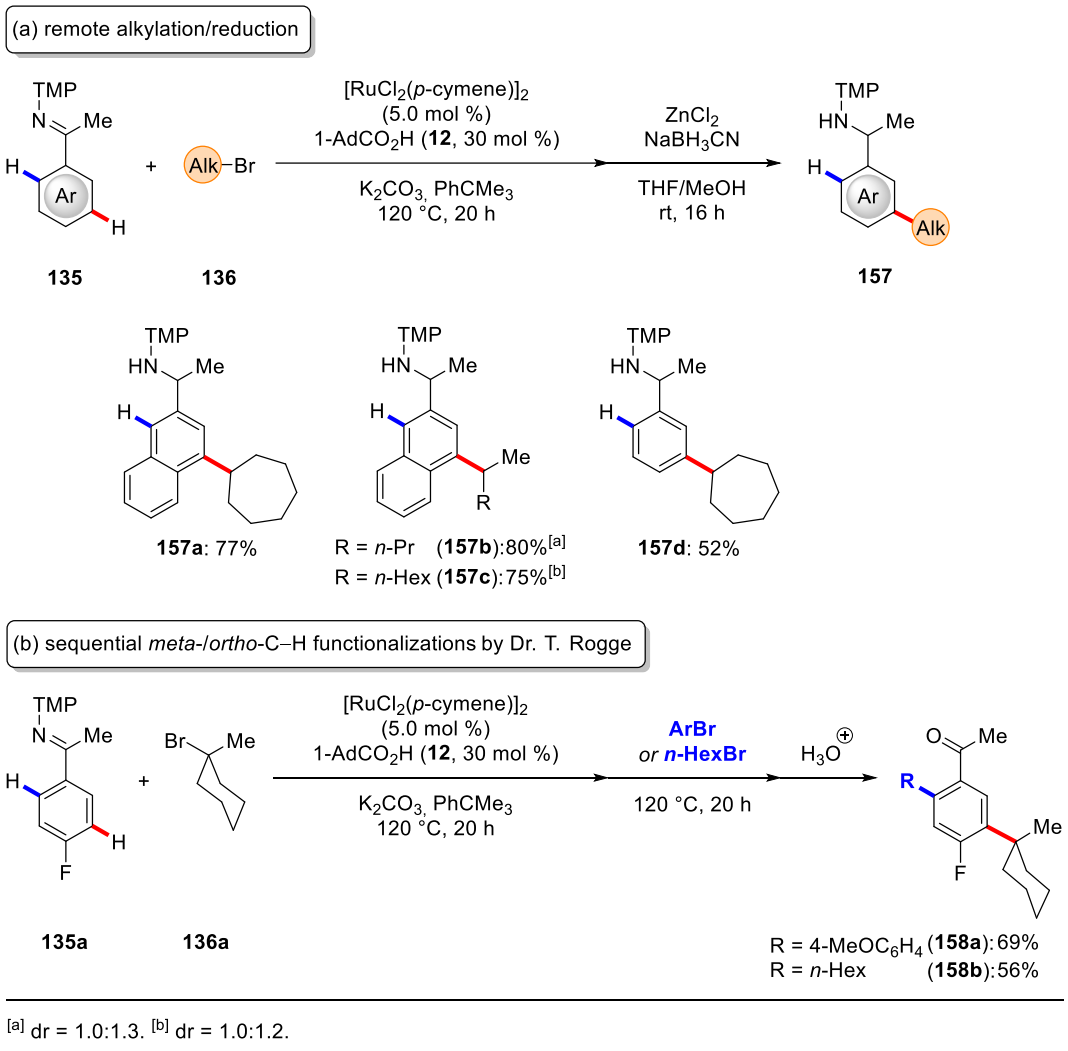


Scheme 51: Support for a radical-type mechanism of *meta*-C–H alkylation.

3.2.4 Late-Stage Diversification

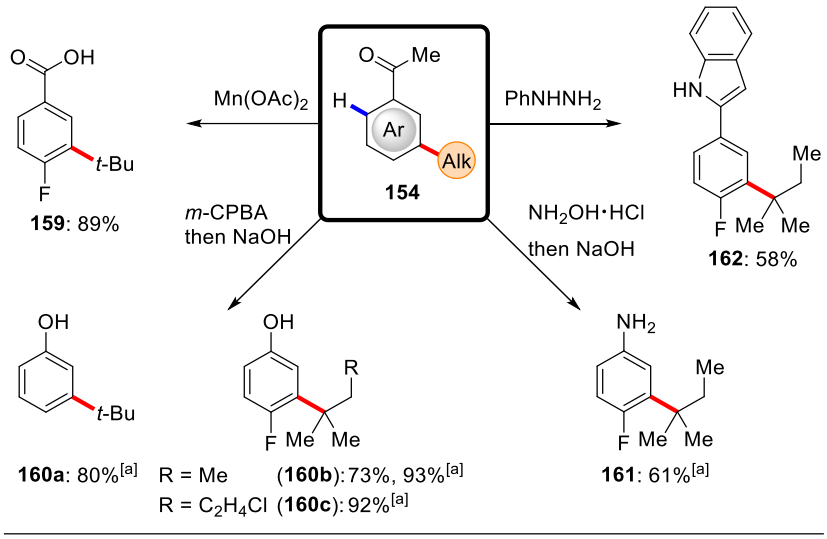
Finally, the power of efficient remote *meta*-C–H alkylation was illustrated by late-stage diversification of the thus obtained *meta*-alkylated arenes as depicted in Scheme 52. First, facile reduction of the obtained *meta*-alkylated ketimines in a one-pot fashion furnished benzylamine derivatives **157**. Second, the sequential twofold *meta*-/*ortho*-C–H functionalizations, performed

by Dr. T. Rogge, provided the approach for densely-tetrasubstituted arenes **158a** and **158b** without any additional catalysts. Moreover, the synthetic utilization of the *meta*-decorated arenes **154** was mirrored by transformative oxidation[97] to form valuable carboxylic acid **159** and Fischer indole synthesis (**162**) (Scheme 53). Since phenols and anilines are strong *ortho*-/*para*-directors in the electrophilic aromatic substitutions, the classical Friedel-Crafts reaction fails to provide *meta*-C–H transformations. Notably, classically transformative Baeyer-Villiger oxidation and Beckmann rearrangement[98] of ketones **154** impressively accessed to *meta*-alkylated phenols **160** and anilines **161**, respectively.



[a] dr = 1.0:1.3. [b] dr = 1.0:1.2.

Scheme 52: Sequential transformations in a one-pot fashion.



[a] Reactions were performed by Dr. D. J. Burns.

Scheme 53: Late-stage diversifications of the *meta*-alkylated arenes.

3.3 Sequential *meta*-/*ortho*-C–H Functionalizations by One-Pot Ruthenium(II/III) Catalysis

Since the earlier protocols for ruthenium(II)-catalyzed remote C–H secondary and tertiary alkylations,[61-63] sulfonylations,[74] brominations,[77-78] and nitrations[81] were performed at high reaction temperatures, the development of milder remote C–H transformations have been highly demanded in order to access to biorthogonal late-stage diversifications of biorelevant molecules and expand the range of tolerated functional groups. Further development in remote alkylations was achieved by Dr. Z. Ruan in the Ackermann group using a ruthenium(II) biscarboxylate complex cooperated with phosphine ligands.[66] The synergistic ruthenium catalysis was first accomplished *meta*-C–H mono- and difluoromethylation under milder conditions.

Acetic acid and propionic acid are important structural moieties of biologically and pharmaceutically active compounds, namely nonsteroidal anti-inflammatory drugs (NSAIDs), as depicted in Figure 7.[99] Among them, Ketoprofen, Flurbiprofen, and Fenoprofen contain *meta*-substituted pattern of arenes. Therefore, the remote *meta*-alkylations of *α*-halocarbonyl compounds have been of interest. In 2017, the group of Frost demonstrated protocols for the remote alkylation of *α*-halo esters and ketones. However, the reactions were still conducted at high reaction temperature of 120 °C.[100]

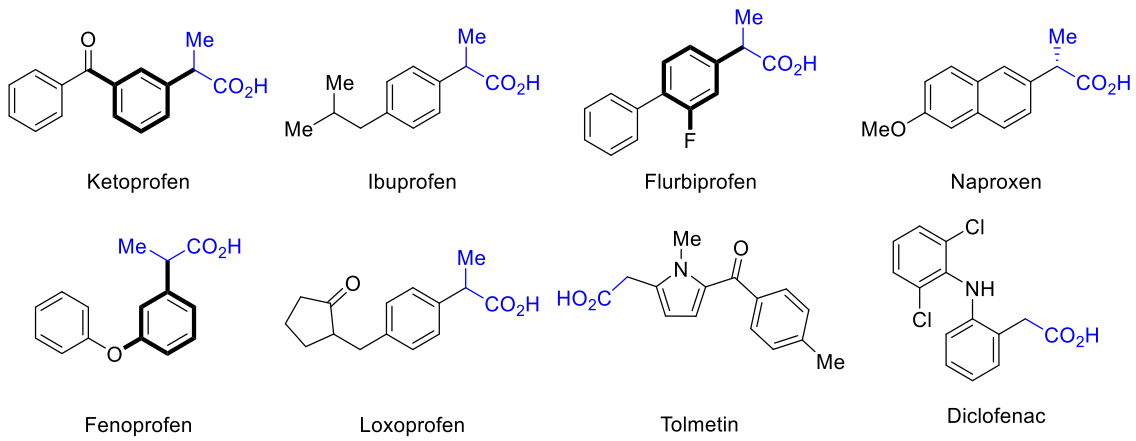
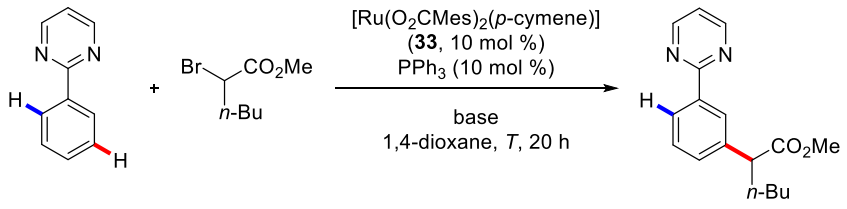


Figure 7: Selected nonsteroidal anti-inflammatory drugs (NSAIDs).

3.3.1 Optimization Studies

Initially, the remote alkylations were optimized by probing various reaction conditions for the transformation of 2-phenylpyrimidine (**139a**) with alkyl bromide **140a** (Table 3). It was found that a PPh_3 had a great influence on the formation of *meta*-alkylated product **141a** (entries 1–2). Moreover, the lower reaction temperatures significantly increased the catalytic efficacy (entries 2–6). Among the inorganic bases, K_2CO_3 proved to be most effective (entries 5–11).

Table 3: Bases and reaction temperatures for the remote *meta*-C–H alkylation.[a]



139a **140a** **141a**

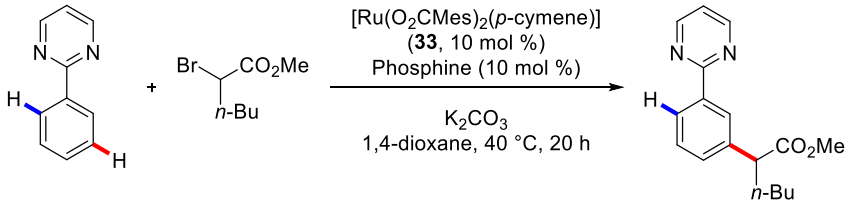
Entry	Base	*T* (°C)	141a (%)
1	K_2CO_3	120	30[b]
2	K_2CO_3	120	54
3	K_2CO_3	80	71
4	K_2CO_3	60	77
5	**K_2CO_3**	**40**	**82**
6	K_2CO_3	23	78
7	KOAc	40	70

Entry	Base	*T* (°C)	141a (%)
8	K_3PO_4	40	69
9	Li_2CO_3	40	(9)
10	Na_2CO_3	40	72
11	Cs_2CO_3	40	(3)

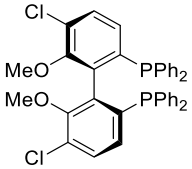
[a] Reaction conditions: **139a** (0.5 mmol), **140a** (1.5 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (**33**, 10 mol %), PPh_3 (10 mol %), base (1.0 mmol), 1,4-dioxane (2.0 mL), 20 h, under N_2; yield of isolated products. The yield in parentheses was determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [b] Without PPh_3.

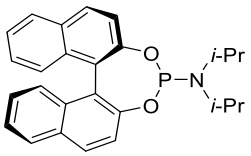
Among a variety of substituents on triarylphosphines, the cost-effective and commercially available PPh_3 was found as the optimal ligand for the remote *meta*-alkylations (Table 4, entry 3). Sterically-hindered triarylphosphines (entries 7–10), trialkylphosphines (entries 11–13) and phosphine oxides (entries 14–15) gave less satisfactory results. In addition, bidentate phosphine ligands failed to give any formation of **141a** (entries 16–17). It is noteworthy that chiral phosphoramidite ligand was also effective in the catalytic remote *meta*-alkylation. However, a racemic mixture of **141a** was observed by analytical HPLC (entry 18).

Table 4: Screening of different phosphine ligands for the remote *meta*-C–H alkylation.[a]



139a **140a** **141a**

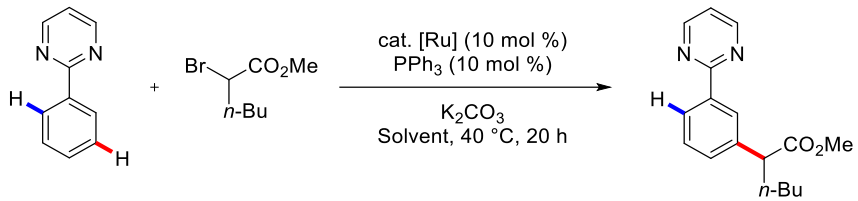
Entry	Phosphine	141a (%)	Entry	Phosphine	141a (%)
1	P(4-MeOC$_6$H$_4$)$_3$	67	13	P(*n*-Bu)$_3$	(4)
2	P(4-MeC$_6$H$_4$)$_3$	79	14	O=PPh$_3$	---
3	**PPh$_3$**	**82**	15	HPOPh$_2$	(4)
4	P(4-FC$_6$H$_4$)$_3$	76	16	*rac*-BINAP	---
5	P(4-CF$_3$C$_6$H$_4$)$_3$	71	17	(–)-Cl-MeO-BIPHEP 	---
6	P(2-furyl)$_3$	73			
7	P(2-MeC$_6$H$_4$)$_3$	---			
8	P(2,4,6-(MeO)$_3$C$_6$H$_2$)$_3$	---			
9	P(2,4,6-Me$_3$C$_6$H$_2$)$_3$	---			

Entry	Phosphine	141a (%)	Entry	Phosphine	141a (%)
10	$P(C_6F_5)_3$	---	18		76% (0% ee)[b]
11	$P(1\text{-Ad})_2n\text{-Bu}$	---			
12	PCy_3	(6)			

[a] Reaction conditions: **139a** (0.5 mmol), **140a** (1.5 mmol), $[Ru(O_2CMes)_2(p\text{-cymene})]$ (**33**, 10 mol %), phosphine (10 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), 40 °C, 20 h, under N_2; yield of isolated products. The yield in parentheses was determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [b] Enantiomerical excess (ee) was determined by chiral HPLC with *n*-hexane:*i*-PrOH (90:10).

Then carboxylate assistance was found to be of key importance to enable the remote *meta*-C–H alkylations, with the best results using $[Ru(O_2CAd)_2(p\text{-cymene})]$ (**163**) as the catalyst (Table 5, entry 3), while N. Kaplaneris found $[Ru(O_2CMes)_2(p\text{-cymene})]$ (**33**) performed more effectively in the remote transformations of imidates.[101] Other ruthenium sources fell short of the formation of *meta*-decorated arene **141a** (entries 7–9). Moreover, among other solvents, 1,4-dioxane proved to be the most efficient in the catalytic transformations (entries 10–13).

Table 5: Probing of ruthenium catalysts and solvents for the remote *meta*-C–H alkylation.[a]



139a **140a** **141a**

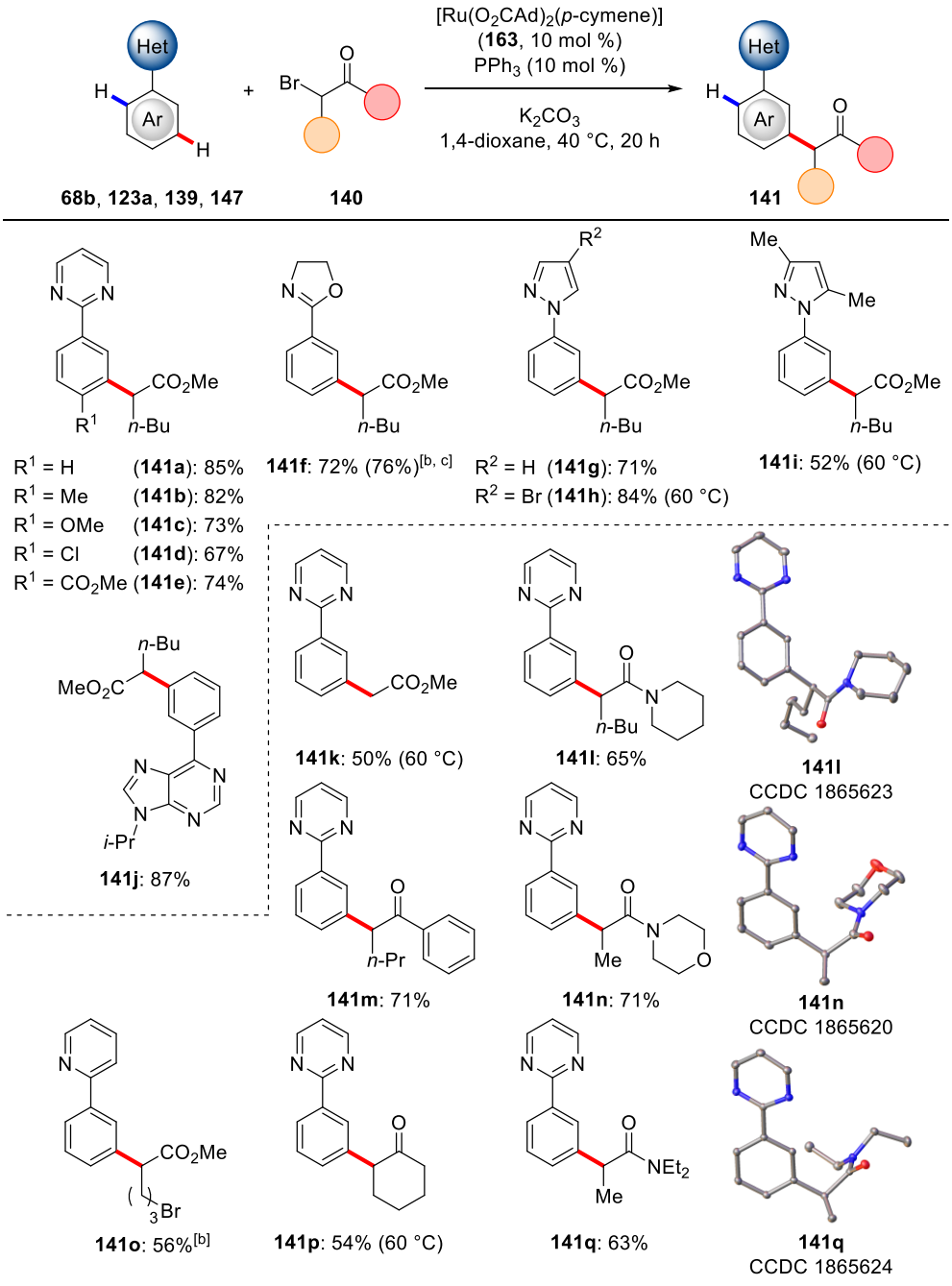
Entry	cat. [Ru]	Solvent	141a (%)
1	$[Ru(OAc)_2(p\text{-cymene})]$	1,4-dioxane	76
2	$[Ru(O_2CMes)_2(p\text{-cymene})]$ (**33**)	1,4-dioxane	82
3	**$[Ru(O_2CAd)_2(p\text{-cymene})]$ (163)**	**1,4-dioxane**	**85**
4	$[RuCl_2(p\text{-cymene})]_2$	1,4-dioxane	---[b]
5	$[RuCl_2(p\text{-cymene})]_2$	1,4-dioxane	(3)[b, c]
6	$[RuCl_2(p\text{-cymene})]_2$	1,4-dioxane	(1)[b, d]
7	$RuCl_3{\cdot}nH_2O$ (**30**)	1,4-dioxane	---[e]
8	$[Ru(t\text{-BuCN})_6][BF_4]_2$	1,4-dioxane	---[e]
9	$RuCl_2(PPh_3)_3$	1,4-dioxane	(2)[e, f]
10	**163**	2-MeTHF	77
11	**163**	cyclopentyl methyl ether	69

Entry	cat. [Ru]	Solvent	141a (%)
12	**163**	PhMe	71
13	**163**	1,2-DCE	72

[a] Reaction conditions: **139a** (0.5 mmol), **140a** (1.5 mmol), [Ru] (10 mol %), PPh_3 (10 mol %), K_2CO_3 (1.0 mmol), solvent (2.0 mL), 40 °C, 20 h, under N_2; yield of isolated products. The yield in parentheses was determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [b] 5.0 mol %. [c] Piv-Ile-OH (**155**, 30 mol %). [d] Piv-Phe-OH (30 mol %). [e] $MesCO_2H$ (**31**, 30 mol %). [f] Without PPh_3.

3.3.2 Scope of the meta-Selective C–H Alkylation with α-bromo carbonyl compounds

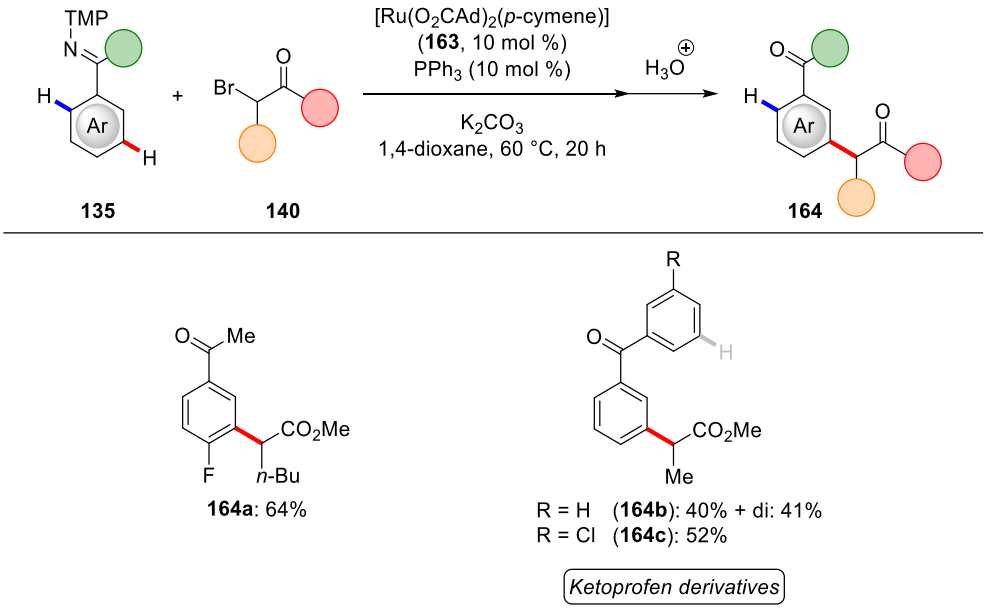
With the optimized ruthenium(II) biscarboxylate catalyst in hand, the robustness in the remote *meta*-alkylation of *α*-bromo carbonyl compounds **140** was explored (Scheme 54). Notably, the potent remote alkylation proved to be generally applicable, tolerating a wealth of functional groups, including halides, esters, ketones, and amides. In addition to 2-arylpyrimidines, the developed procedure was appropriate to transformable imidates (**141f**), removable pyrazoles (**141g**–**141i**), and purines (**141j**). It was highlighted that *α*-bromo-substituted esters, ketones, and amides were efficiently converted into the *meta*-alkylated arenes **141** with excellent levels of positional selectivity. Moreover, the reaction of methyl 2-bromoacetate (**140b**) afforded the desired *meta*-alkylated product **141k**, which is unlike ruthenium-catalyzed *ortho*-C–H alkylations with primary alkyl bromides.[33]



[a] Reaction conditions: **68b**, **123a**, **139**, or **147** (0.5 mmol), **140** (1.5 mmol), [Ru(O_2CAd)$_2$(*p*-cymene)] (**163**, 10 mol %), PPh_3 (10 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), 40 °C, 20 h, under N_2; yield of isolated products. [b] Reactions were performed by N. Kaplaneris. [c] [Ru(O_2CMes)$_2$(*p*-cymene)] (**33**) was used at 60 °C.

Scheme 54: Remote *meta*-alkylation under the synergistic ruthenium catalysis**.**

The synergistic ruthenium-catalyzed *meta*-C–H alkylation was also effective with arylketimines **135**, providing the *meta*-alkylated ketone **164** after acid hydrolysis (Scheme 55). Therefore, this protocol was applied for a step-economical synthesis of *Ketoprofen* derivatives **164b** and **164c**.



[a] Reaction conditions: **135** (0.5 mmol), **140** (1.5 mmol), [Ru(O_2CAd)$_2$(*p*-cymene)] (**163**, 10 mol %), PPh_3 (10 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), 60 °C, 20 h, under N_2, then hydrolysis by 2 N HCl, 3 h; yield of isolated products.

Scheme 55: Remote alkylation of ketimines **135** followed by acid hydrolysis.

In spite of the efficacy, robustness, and versatility of the ruthenium catalysis, *N*-pyrimidyl anilines, triazoles, tetrazoles, and acyclic imidates failed to give any conversion under the optimized ruthenium catalysis (Figure 8). Moreover, ineffective alkyl bromides are listed in Figure 8.

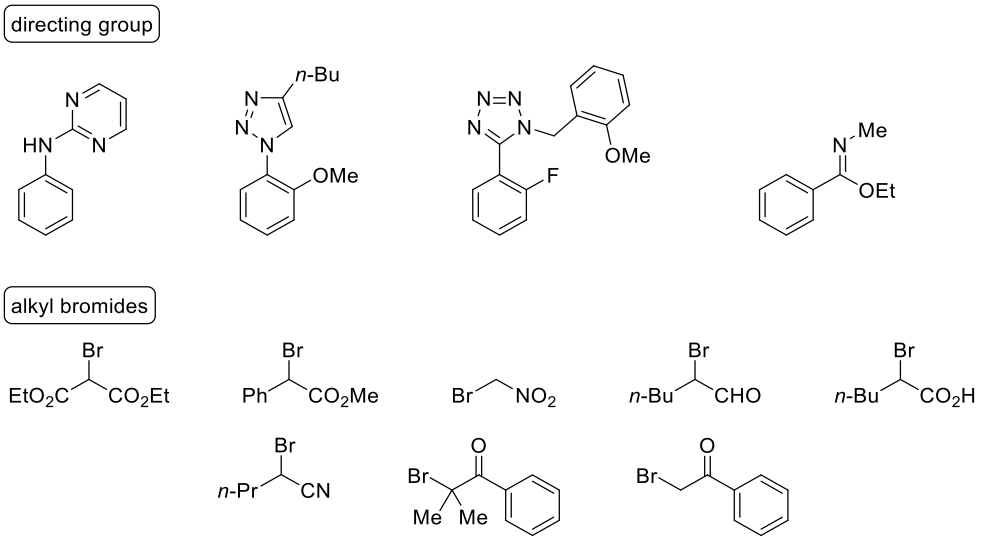
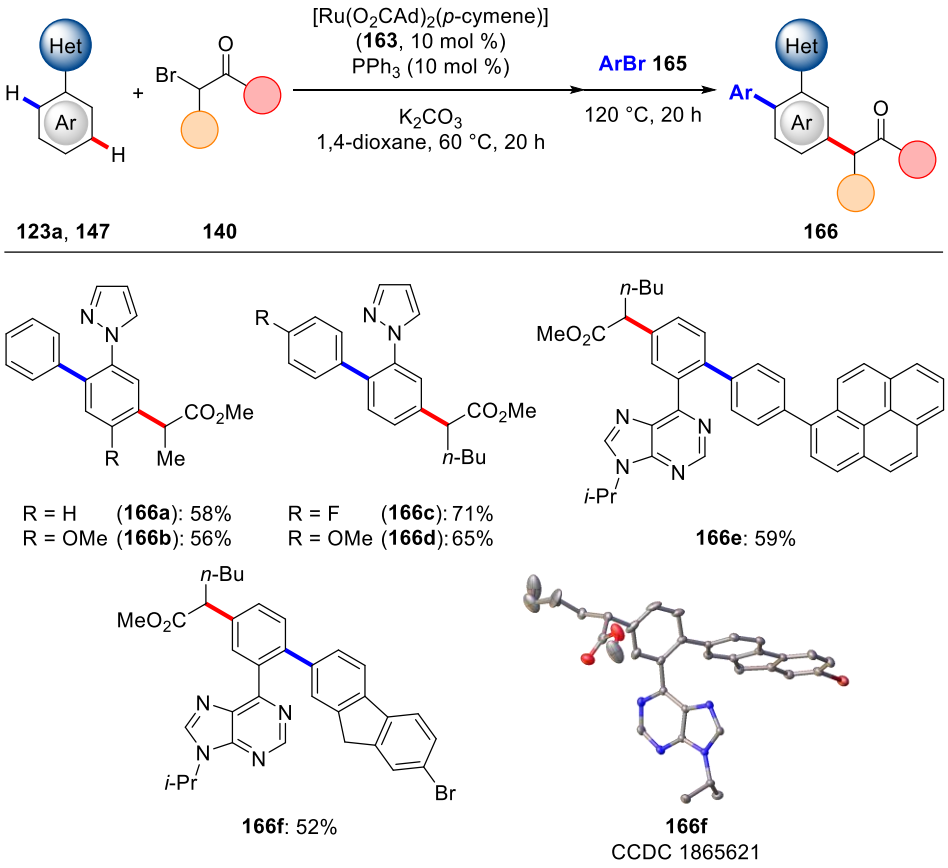


Figure 8: Inefficient directing groups and alkyl bromides in the synergistic ruthenium catalysis.

3.3.3 Scope of the Sequential meta-C–H Alkylation/ortho-C–H Arylation in One-Pot

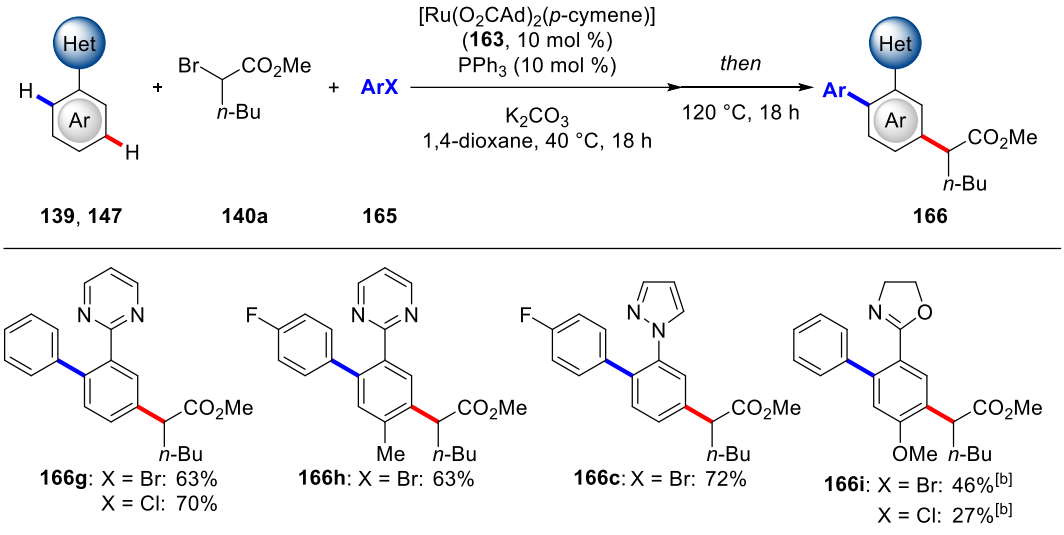
The potential of the synergistic ruthenium catalysis was explored through sequential *meta*-C–H alkylations followed by *ortho*-C–H arylations in a one-pot fashion. The operationally simple addition of the electrophilic aryl bromides **165** after completion of the *meta*-C–H functionalizations allowed for the twofold one-pot C–H transformations (Scheme 56). The sequential *meta*-C–H/*ortho*-C–H functionalizations under the synergistic ruthenium catalysis were applicable for removable pyrazoles (**166a**–**166d**) in excellent levels of positional selectivity. In particular, late-stage fluorescence labeling on purine bases (**166e**–**166f**) was achieved under the catalytic system.



[a] Reaction conditions: **123a** or **147** (0.5 mmol), **140** (1.5 mmol), [Ru(O$_2$CAd)$_2$(*p*-cymene)] (**163**, 10 mol %), PPh$_3$ (10 mol %), K$_2$CO$_3$ (2.0 mmol), 1,4-dioxane (2.0 mL), 60 °C, 20 h, under N$_2$, then ArBr **165** (1.0–1.5 mmol), 120 °C, 20 h; yield of isolated products.

Scheme 56: Sequential one-pot *meta*-alkylation followed by *ortho*-arylation under the carboxylate-phosphine ruthenium catalysis.

Due to the different reactivities of alkyl bromides **140** and aryl bromides **165**, a temperature-controlled sequential *meta*-C–H/*ortho*-C–H functionalization in a one-pot reaction of alkyl bromide **140a** and aryl halides **165** led to the formation of the corresponding products **166** with excellent levels of chemo- and positional selectivities (Scheme 57). This protocol was efficiently applicable to pyrimidines (**166g**–**166h**), removable pyrazoles (**166c**), and transformable oxazolines (**166i**).



[a] Reaction conditions: **139** or **147** (0.5 mmol), **140a** (1.5 mmol), **165** (1.5 mmol), [Ru(O$_2$CAd)$_2$(*p*-cymene)] (**163**, 10 mol %), PPh_3 (10 mol %), K_2CO_3 (2.0 mmol), 1,4-dioxane (2.0 mL), 40 °C, 18 h, under N_2, then 120 °C, 18 h; yield of isolated products. [b] [Ru(O$_2$CMes)$_2$(*p*-cymene)] (**33**) was used at 60 °C.

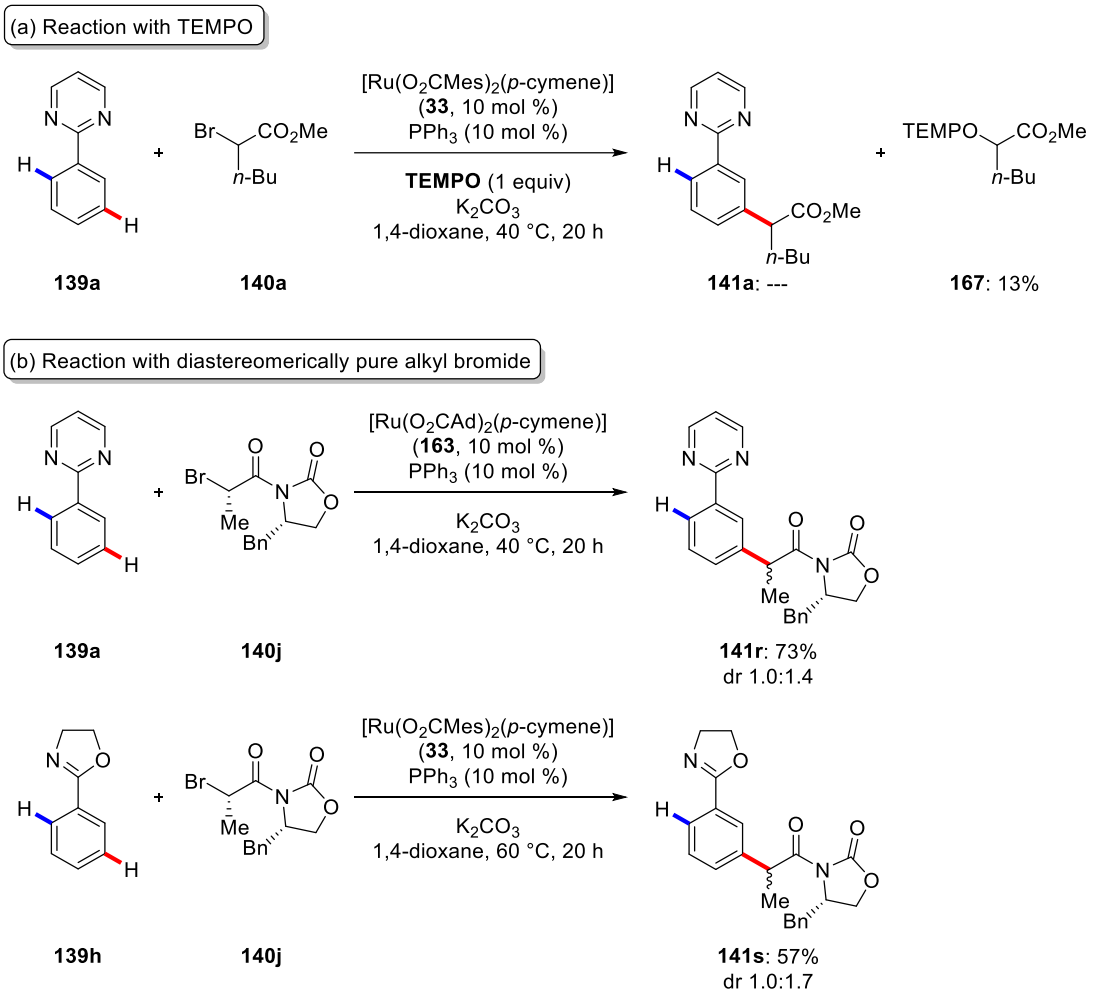
Scheme 57: Temperature controlled chemo-selective twofold C–H functionalizations.

3.3.4 Mechanistic Studies

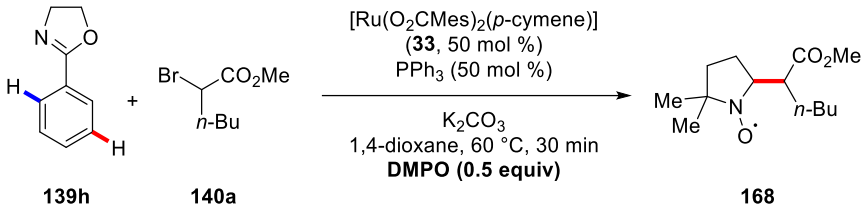
To understand its mode of action, the H/D exchange and KIE experiments were conducted by N. Kaplaneris.[101] The obtained results indicated that the C–H bond cleavage is a reversible process.

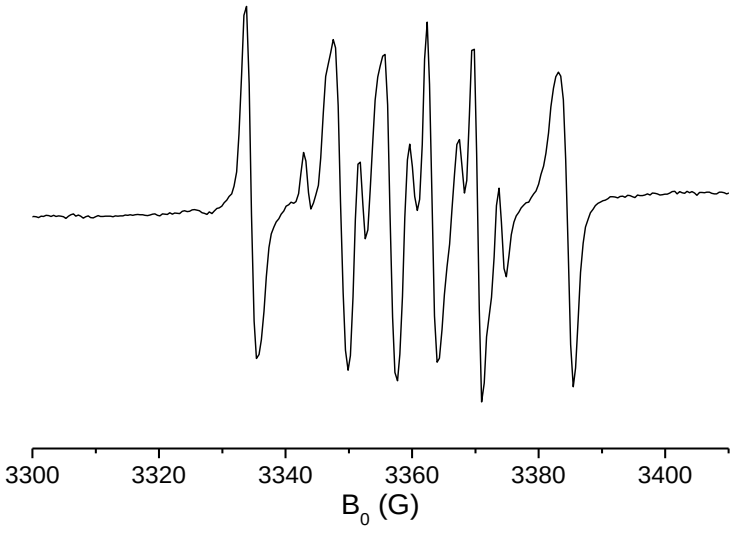
To delineate C–X bond cleavage event of the *meta*-C–H transformations, experiments with radical scavengers were conducted. The catalytic C–H activation was completely inhibited by the addition of TEMPO (Scheme 58a). The isolated TEMPO adduct **167** was supportive of the homolytic C–X bond cleavage. In addition, the stereochemically well-defined substrate **140j** was converted under the catalytic transformation to the diastereomeric mixtures **141r** and **141s**, which is again in good agreement with a single-electron transfer promoted C–X bond cleavage (Scheme 58b). Further strong support for a radical mechanism was obtained by EPR spectroscopic studies, in

collaboration with Dr. A. C. Stückl. Hence, 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO) was employed as a spin-trap label to indicate the *in situ* generation of an alkyl radical (Scheme 59).



Scheme 58: Experimental support for radical-type mechanism.

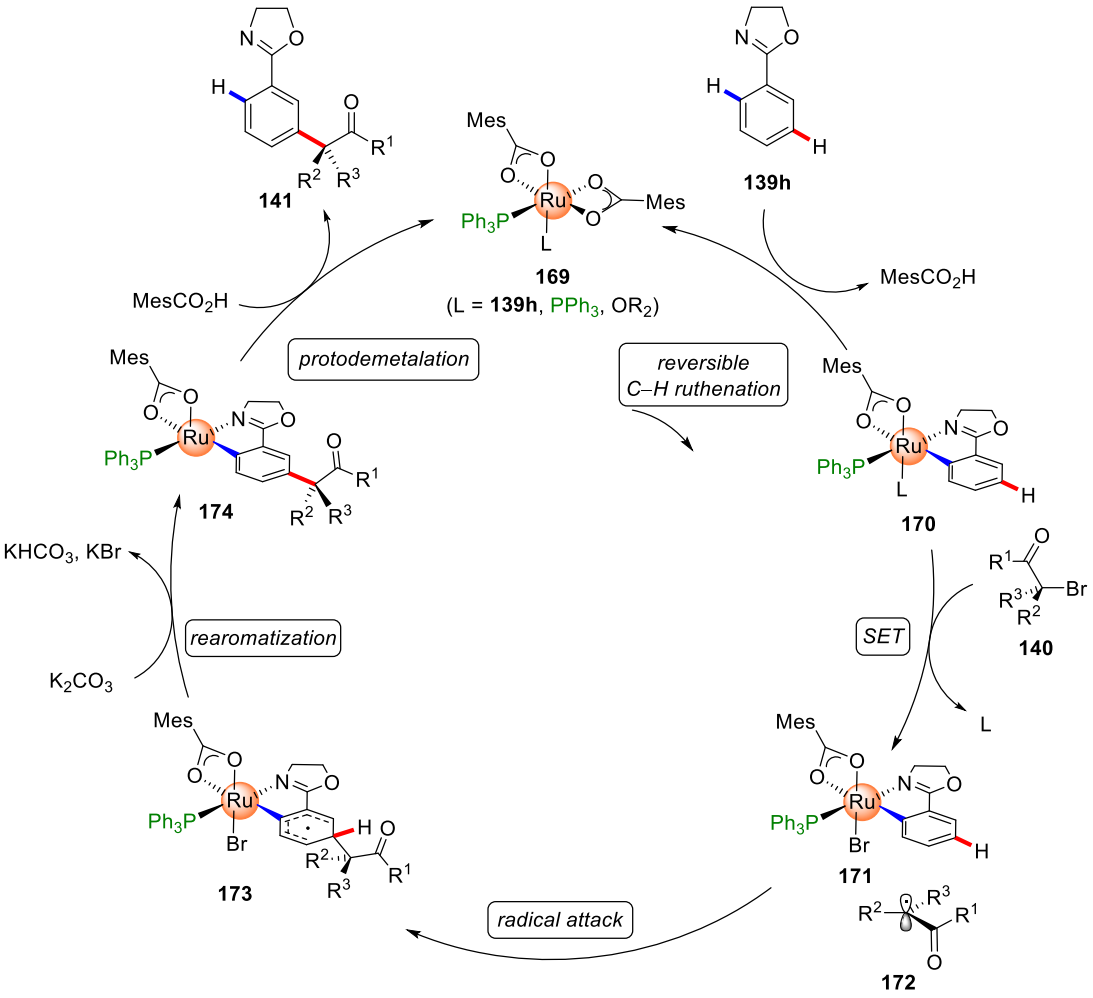




Scheme 59: EPR spectroscopic evidence for the *in situ* generation of an alkyl radical in ruthenium-catalyzed *meta*-alkylations.

3.3.5 Proposed Catalytic Cycle

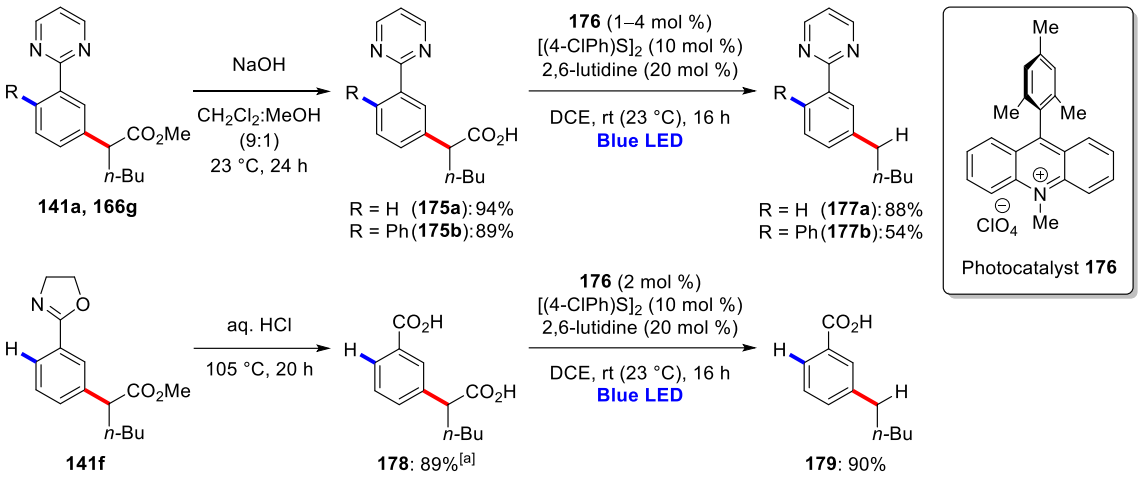
On the basis of the experimental and computational studies,[101] a plausible catalytic cycle commences with a reversible, carboxylate-assisted C–H ruthenation of arene **139h** (Scheme 60). Subsequently, single-electron transfer occurs from ruthenacycle **170** to alkyl halides **140**, forming the ruthenium(III) intermediate **171** and the alkyl radical **172**. Radical attack on the aromatic moiety at the position *para* to ruthenium generates ruthenacycle intermediate **173**. Rearomatization followed by protodemetalation delivers the desired *meta*-substituted product **141** and regenerates the catalytically active ruthenium(II) complex **169**.



Scheme 60: Proposed catalytic cycle for the remote *meta*-alkylation.

3.3.6 Late-Stage Diversification

Finally, the potential of the sequential *meta*-C–H/*ortho*-C–H functionalization strategy was reflected by the facile late-stage modification of the thus obtained arenes **141a** and **166g** (Scheme 61). The saponification of the ester group afforded the corresponding carboxylic acids **175** in high yields. Then, decarboxylative reduction under photoredox catalysis at room temperature[102] efficiently provided the *meta*-alkylated products **177**. Notably, carboxylic acid derivative **178**, which was modified by hydrolysis of adduct **141f**, underwent through a visible-light photoredox catalysis reduction manifold, leading to the chemo-selective decarboxylation of the aliphatic carboxylic acids.



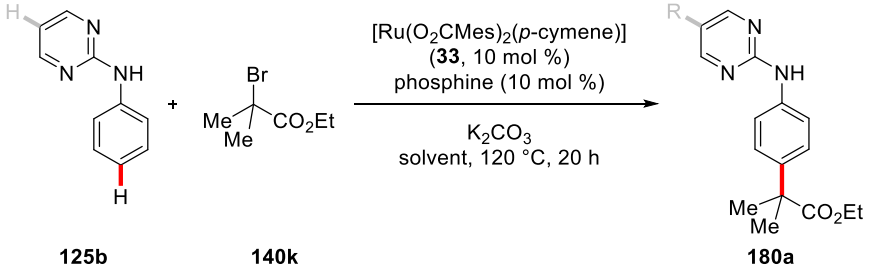
[a] Reaction was performed by N. Kaplaneris.

Scheme 61: Late-stage modification of the obtained *meta*-alkylated products.

3.3.7 Preliminary Studies on para-Selective C–H Alkylation

With respect to Frost's report on ruthenium-catalyzed *para*-C–H alkylation,[87] the synergistic ruthenium catalyst was examined on *para*-C–H functionalization (Table 6). The reaction between *N*-pyrimidyl aniline (**125b**) and alkyl bromide **140k** provided promising results in *m*-xylene as solvent (entries 1–3). Moreover, different electronic influence on phosphine ligand gave the similar results (entries 4–6). In addition to the corresponding product **180a**, the twofold alkylation of aniline **125b** was observed at the position *para* to NH group on both the phenyl and pyrimidine rings.

Table 6: Screening of phosphine ligands and solvents for the remote *para*-alkylation of **125b**.[a]



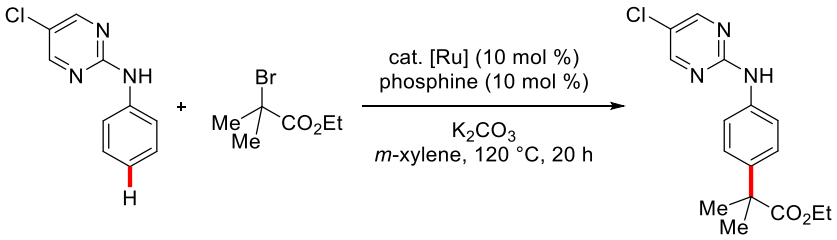
Entry	Phosphine	Solvent	180a (%)
1	PPh_3	1,4-dioxane	trace[b, c]
2	PPh_3	1,4-dioxane	12 (di 15)[b]
3	PPh_3	*m*-xylene	33[b]

Entry	Phosphine	Solvent	180a (%)
4	PPh_3	$PhCMe_3$	26 (di 23)
5	$P(4\text{-}FC_6H_4)_3$	*m*-xylene	28 (di 23)
6	$P(4\text{-}MeC_6H_4)_3$	*m*-xylene	26 (di 19)

[a] Reaction conditions: **125b** (0.25 mmol), **140k** (0.75 mmol), $[Ru(O_2CMes)_2(p\text{-cymene})]$ (**33**, 10 mol %), phosphine (10 mol %), K_2CO_3 (0.50 mmol), solvent (1.0 mL), 120 °C, 20 h, under N_2; yield of isolated products. [b] Reactions were performed by N. Kaplaneris. [c] 60 °C.

To avoid the formation of the dialkylated product, 4-chloropyrimidine **125a** was employed in the *para*-C–H alkylation (Table 7). The synergistic ruthenium catalysis with a phosphine ligand proved to be more powerful than the reaction without phosphine (entries 1–3). Different carboxylates on ruthenium precatalysts slightly dropped the yield of the corresponding product **180b** (entries 4–5), while the reaction of $[RuCl_2(p\text{-cymene})]_2$ without additional acids also delivered the *para*-alkylated product **180b** with similar catalytic efficacy (entry 6).

Table 7: Screening of ruthenium complexes and phosphine ligands for the remote *para*-alkylation of **125a**.[a]



125a **140k** **180b**

Entry	cat. [Ru]	Phosphine	180b (%)
1	$[Ru(O_2CMes)_2(p\text{-cymene})]$ (**33**)	-	37[b]
2	**33**	PPh_3	56[b]
3	**33**	$P(4\text{-}FC_6H_4)_3$	57[b]
4	$[Ru(OPiv)_2(p\text{-cymene})]$	PPh_3	49%
5	$[Ru(O_2CAd)_2(p\text{-cymene})]$ (**163**)	PPh_3	49%
6	$[RuCl_2(p\text{-cymene})]_2$	PPh_3	56%

[a] Reaction conditions: **125a** (0.25 mmol), **140k** (0.75 mmol), [Ru] (10 mol %), phosphine (10 mol %), K_2CO_3 (0.50 mmol), *m*-xylene (1.0 mL), 120 °C, 20 h, under N_2; yield of isolated products. [b] Reactions were performed by N. Kaplaneris.

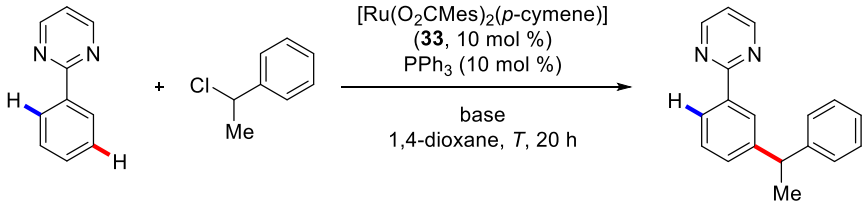
3.4 Late-Stage Diversification by Selectivity Switch in *meta*-C–H Activation

In 2009, Ackermann first reported on ruthenium-catalyzed direct C–H benzylations using primary benzyl chlorides.[35] On the principle of the atom- and step-economical C–H/C–H activation[14] for the construction of new C–C bonds, the groups of Shi/Zhao[68] and Shi[69] later reported on oxidative ruthenium-catalyzed remote C–H benzylations of toluene derivatives using di-*tert*-butylperoxide (DTBP) and heptafluoroisopropyl iodide (*i*-C_3F_7I) as the radical initiators, respectively. Even though the prefunctionalized substrates are not required for the C–H/C–H activation, an excess of toluene derivative is mandatory in these catalytic transformations.

3.4.1 Optimization Studies

The synergistic ruthenium catalysis with phosphine ligands was further examined for a remote *meta*-C–H benzylations of arene **139a** and secondary benzyl chloride **142a** (Table 8). First, the addition of triphenylphosphine significantly enhanced the catalytic efficacy (entries 1–2). Second, the reaction at lower reaction temperature of 40 °C dramatically increased the yield of the *meta*-benzylated product **143a** (entry 3), while the reaction at an ambient temperature of 23 °C furnished 47% of the corresponding product **143a** (entry 4). Third, among inorganic bases, K_2CO_3 and K_3PO_4 were found to be optimal bases in the catalytic transformation (entries 5–10).

Table 8: Bases and reaction temperatures for the remote *meta*-C–H benzylation.[a]



139a **142a** **143a**

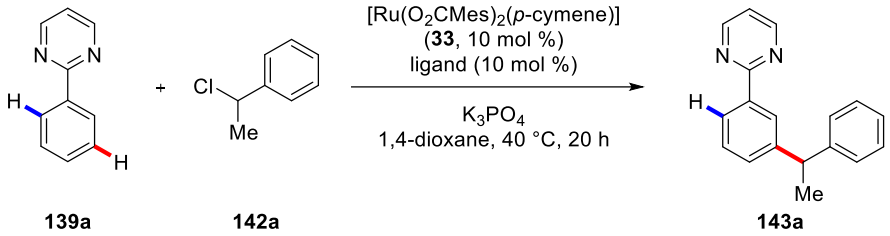
Entry	Base	*T* (°C)	143a (%)
1	K_2CO_3	120	16[b]
2	K_2CO_3	120	39
3	**K_2CO_3**	**40**	**62 (73)**
4	K_2CO_3	23	47 (52)
5	KOAc	23	41 (46)
6	K_3PO_4	23	51 (58)
7	**K_3PO_4**	**40**	**64 (76)**

Entry	Base	*T* (°C)	143a (%)
8	K_3PO_4	60	(64)
9	Li_3PO_4	40	(5)
10	Na_3PO_4	40	59 (73)

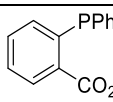
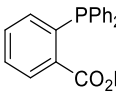
[a] Reaction conditions: **139a** (0.50 mmol), **142a** (1.50 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (**33**, 10 mol %), PPh_3 (10 mol %), base (1.00 mmol), 1,4-dioxane (2.0 mL), *T*, 20 h, under N_2; yield of isolated products. The yield in parentheses was determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [b] Without PPh_3.

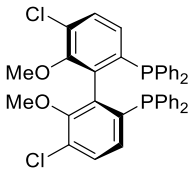
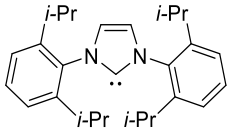
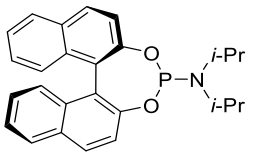
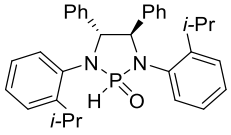
Among a variety triarylphosphines, PPh_3, tris(4-fluorophenyl)phosphine, and tris(4-trifluoromethylphenyl)phosphine provided similar results (Table 9, entries 1–10). Due to the reasonable price and commercial availability, PPh_3 was selected as the optimal ligand for the remote *meta*-C–H benzylation. While trialkylphosphines and phosphine oxides failed to give any conversion (entries 11–15), triphenyl or triethyl phosphites provided the low formation of the corresponding product **143a** (entries 16–17). Moreover, 2-(diphenylphosphino)benzoic acid gave unsatisfactory results with two different ruthenium sources (entries 18–19). In addition, no conversion was observed when bidentate phosphine ligands were employed (entries 20–21). Although *N*-Heterocyclic carbene (NHC) (entry 22) and chiral phosphine oxide (entry 24) were absolutely ineffective in the catalytic transformation, the chiral phosphoramidite ligand delivered 30% of the desired product **143a** (entry 23).

Table 9: Screening of phosphine ligands for the remote *meta*-C–H benzylation.[a]



139a **142a** **143a**

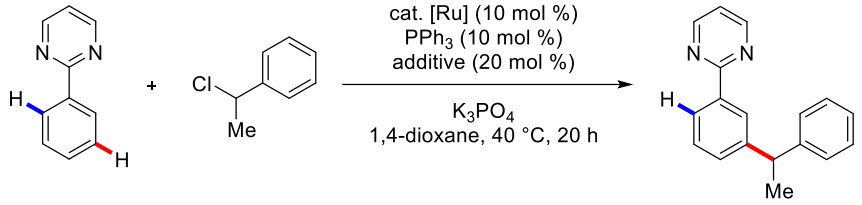
Entry	Ligand	143a (%)	Entry	Ligand	143a (%)
1	**PPh_3**	**64 (76)**	18		(8)[b]
2	**P(4-FC_6H_4)$_3$**	**65 (75)**			
3	**P(4-$CF_3C_6H_4$)$_3$**	**65 (74)**	19		---[c]
4	P(4-$MeOC_6H_4$)$_3$	(69)			
5	P(4-MeC_6H_4)$_3$	(46)	20	*rac*-BINAP	---[b]

Entry	Ligand	143a (%)	Entry	Ligand	143a (%)
6	$P(2\text{-}MeC_6H_4)_3$	---		(–)-Cl-MeO-BIPHEP	
7	$P(2,4,6\text{-}Me_3C_6H_2)_3$	---	21		---[b]
8	$P(2,4,6\text{-}(MeO)_3C_6H_2)_3$	---			
9	$P(C_6F_5)_3$	---			
10	$P(2\text{-furyl})_3$	(64)			
11	$P(1\text{-Ad})_2n\text{-Bu}$	(2)		IPr (NHC)	
12	$P(n\text{-Bu})_3$	(2)	22		(3)[b]
13	$O{=}PPh_3$	---			
14	$HPOPh_2$	---	23		(30)[b]
15	$n\text{-}Bu_2P(O)H$	---[b]			
16	$P(OPh)_3$	(21)[b]	24		---[b]
17	$P(OEt)_3$	(15)[b]			

[a] Reaction conditions: **139a** (0.50 mmol), **142a** (1.50 mmol), $[Ru(O_2CMes)_2(p\text{-cymene})]$ (**33**, 10 mol %), phosphine (10 mol %), K_3PO_4 (1.00 mmol), 1,4-dioxane (2.0 mL), 40 °C, 20 h, under N_2; yield of isolated products. The yield in parentheses was determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [b] $[Ru(OAc)_2(p\text{-cymene})]$ (**181**, 10 mol %). [c] $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %).

Afterwards, various ruthenium source and additives were tested in the remote benzylation (Table 10). No conversion was observed when the reaction was performed without a ruthenium catalyst (entry 1). Several ruthenium sources, such as $RuCl_3{\cdot}nH_2O$ (entries 2–3), $RuCl_2(PPh_3)_3$ (entry 4), $Ru(OAc)_2(PPh_3)_2$ (entries 5–7), $Ru(OAc)_2(PPh_3)_3$ (entry 8), and $[Ru(NCMe)_6]X_2$ (entries 9–10) provided unsatisfactory results. However, $Ru(OAc)_2(PPh_3)_2$[103] was highly catalytically effective when the reaction was performed at high reaction temperature of 100 °C (entry 6). Notably, carboxylate was found to be essential in this C–H functionalization (entries 11–16). Moreover, a variety of ruthenium(II) biscarboxylate precatalysts comparably provided the high catalytic efficacy. The 1:1 ratio of ruthenium catalysts to phosphine ligands furnished the best results for the *meta*-C–H benzylation (entries 17–21). In addition, the addition of phosphine ligand was required in the ruthenium-catalyzed remote C–H benzylations (entry 22).

Table 10: Ruthenium sources and additives for the remote *meta*-C–H benzylation.[a]



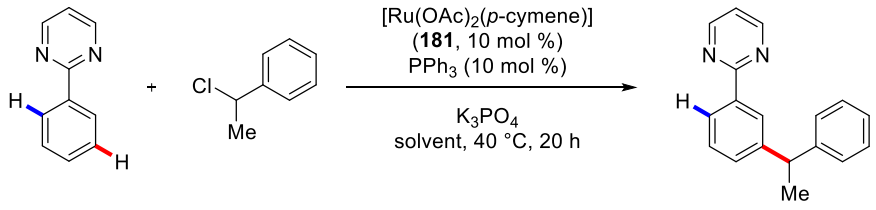
139a **142a** **143a**

Entry	cat. [Ru]	Additive	143a (%)
1	---	---	---
2	$RuCl_3 \cdot nH_2O$ (**30**)	$MesCO_2H$ (**31**)	---
3	**30**	KOAc	(6)[b, c, d]
4	$RuCl_2(PPh_3)_3$	**31**	---[e]
5	$Ru(OAc)_2(PPh_3)_2$	---	---
6	$Ru(OAc)_2(PPh_3)_2$	---	---[e], (3)[c, d, e], (68)[c, e, j]
7	$Ru(OAc)_2(PPh_3)_2$	---	(3)[c, d]
8	$Ru(OAc)_2(PPh_3)_3$	---	---[e]
9	$[Ru(NCMe)_6][BF_4]_2$	KOAc	---[c, d]
10	$[Ru(NCMe)_6][SbF_6]_2$	KOAc	---[c, d]
11	$[RuCl_2(p\text{-cymene})]_2$	---	---[f]
12	$[Ru(O_2CMes)_2(p\text{-cymene})]$ (**33**)	---	64 (76)
13	$[Ru(OAc)_2(p\text{-cymene})]$ (**181**)	---	69 (76)
14	$[Ru(O_2CAd)_2(p\text{-cymene})]$ (**163**)	---	68 (76)
15	$[Ru(OPiv)_2(p\text{-cymene})]$	---	68 (75)
16	**181**	---	68 (75)[c]
17	**181**	---	(5)[g]
18	**181**	---	(42)[h]
19	**181**	---	(3)[i]
20	**181**	---	(56)[g, h]
21	**181**	---	68 (76)[c, d]
22	**181**	---	(1)[c, d, e]

[a] Reaction conditions: **139a** (0.50 mmol), **142a** (1.50 mmol), [Ru] (10 mol %), PPh_3 (10 mol %), K_3PO_4 (1.00 mmol), 1,4-dioxane (2.0 mL), 40 °C, 20 h, under N_2; yield of isolated products. The yield in parentheses was determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [b] NMP (1.0 mL). [c] K_2CO_3. [d] 60 °C. [e] Without PPh_3. [f] $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %). [g] [Ru] (5.0 mol %). [h] PPh_3 (5.0 mol %). [i] PPh_3 (20 mol %). [j] 100 °C.

The synergistic ruthenium-catalyzed C–H transformations similarly showed high efficiency in various organic solvents (Table 11, entries 1–4), while the catalytic reaction failed to give any conversion in MeCN (entry 5).

Table 11: Screening of solvents for the remote *meta*-C–H benzylation.[a]



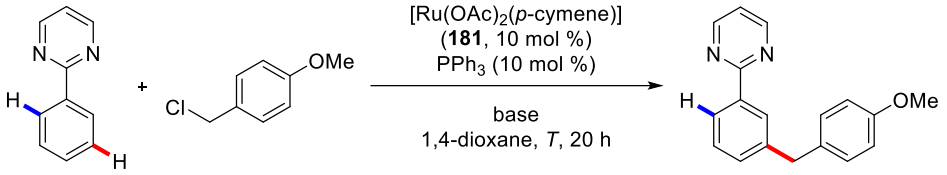
139a **142a** **143a**

Entry	Solvent	143a (%)
1	1,4-dioxane	69 (76)
2	2-MeTHF	65 (71)
3	PhMe	67 (76)
4	1,2-DCE	64 (70)
5	MeCN	---

[a] Reaction conditions: **139a** (0.50 mmol), **142a** (1.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 10 mol %), PPh_3 (10 mol %), K_3PO_4 (1.0 mmol), solvent (2.0 mL), 40 °C, 20 h, under N_2; yield of isolated products. The yield in parentheses was determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard.

In contrast to the report on a ruthenium-catalyzed direct C–H benzylation with primary benzyl chloride in 2009,[35] the reaction of pyrimidine **139a** and 4-methoxybenzyl chloride (**142b**) under the synergistic ruthenium catalysis conditions selectively afforded the *meta*-benzylated product **143b** (Table 12, entries 1–2), with the best results being accomplished using K_2CO_3 as base. In addition, no conversion was observed in the absence of phosphine ligands (entry 3). Although the remote C–H benzylations under photoredox catalysis furnished the corresponding product **143b** (entries 4–5), visible light was verified to be inessential in the remote C–H transformations by the control experiment under dark condition (entry 6).

Table 12: Reaction studies for remote *meta*-benzylation of primary benzyl chloride **142b**.[a]

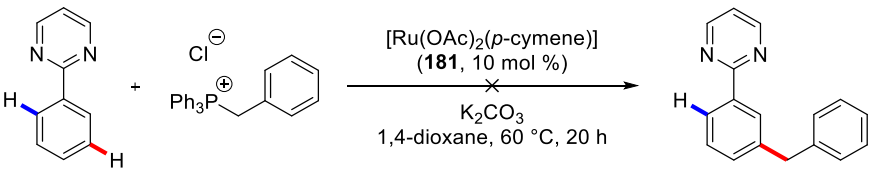


139a **142b** **143b**

Entry	Base	*T* (°C)	143b (%)
1	K_3PO_4	60	(37), [7]
2	K_2CO_3	60	59 (64), [5]
3	K_2CO_3	60	(3)[b]
4	K_2CO_3	30	67[c]
5	K_2CO_3	30	(36)[c, d], [3]
6	K_2CO_3	30	(52), [2]

[a] Reaction conditions: **139a** (0.50 mmol), **142b** (1.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 10 mol %), PPh_3 (10 mol %), base (1.00 mmol), 1,4-dioxane (2.0 mL), *T*, 20 h, under N_2; yield of isolated products. The yield in parentheses was determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. The yield of the *ortho*-benzylated products is given in square brackets. [b] Without PPh_3. [c] Under Blue LED (5 W). [d] 2 MeTHF.

Notably, the reaction of benzylphosphonium salt **182** under ruthenium catalyst did not deliver any formation of the corresponding product **143c** (Scheme 62). This finding was supportive of the benzylphosphonium not being an intermediate in the catalytic transformation.

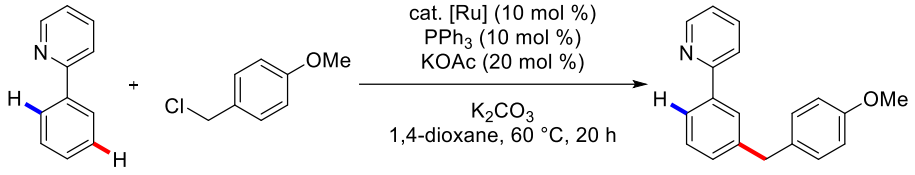


139a **182** **143c**

Scheme 62: Ruthenium-catalyzed benzylation of benzylphosphonium salt **182**.

In the remote C–H functionalization with primary benzyl chloride **142b**, cationic ruthenium(II) complexes and [Ru(OAc)$_2$(PPh$_3$)$_2$] were not effective (Table 13, entries 1–3), even though the reaction was conducted at high reaction temperature at 100 °C (entry 4).

Table 13: Various ruthenium sources for remote *meta*-benzylation of primary benzyl chloride **142b**.[a]



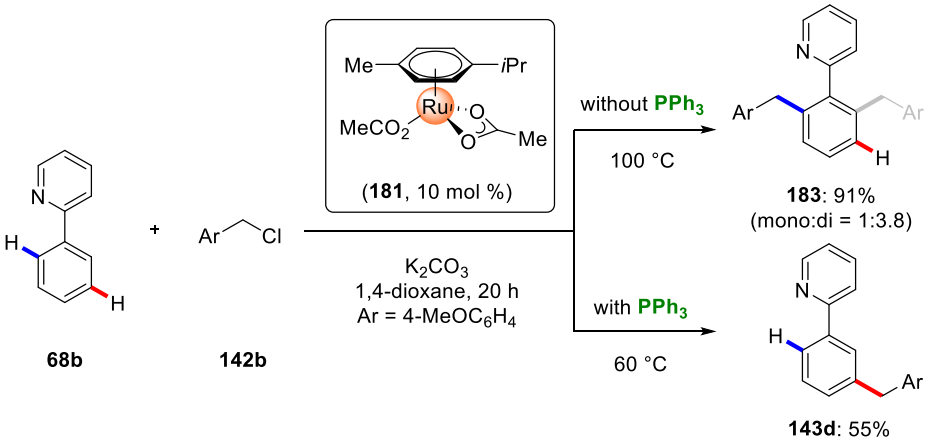
68b **142b** **143d**

Entry	cat. [Ru]	143d (%)	68b (%)
1	$[Ru(NCMe)_6][BF_4]_2$	---	96
2	$[Ru(NCMe)_6][SbF_4]_2$	---	88
3[b]	$[Ru(OAc)_2(PPh_3)_2]$	13	71
4[b, c]	$[Ru(OAc)_2(PPh_3)_2]$	32	---

[a] Reaction conditions: **68b** (0.50 mmol), **142b** (1.50 mmol), [Ru] (10 mol %), PPh_3 (10 mol %), KOAc (20 mol %), K_2CO_3 (1.00 mmol), 1,4-dioxane (2.0 mL), 60 °C, 20 h, under N_2. Yields were determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard [b] Without PPh_3 and KOAc. [c] 100 °C.

3.4.2 Effect of Phosphine Ligand to Site-Selectivity

The site-selectivity of the ruthenium-catalyzed C–H benzylation was controlled by the addition of a phosphine ligand, as shown in Scheme 63. The reaction without phosphine ligand afforded the *ortho*-benzylated products **183** with excellent levels of positional selectivity. It was found that the site-selectivity switched from *ortho* to *meta* position in the presence of phosphine ligands.

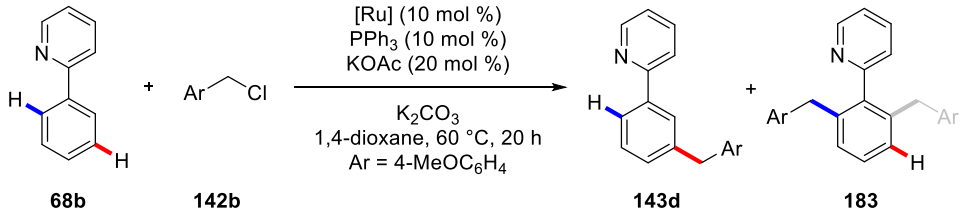


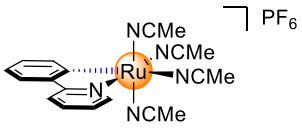
68b **142b**

Scheme 63: Influence of phosphine ligands to site-selectivity of ruthenium-catalyzed benzylation.

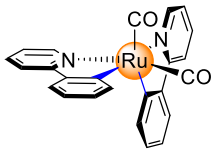
To elucidate the role of the carboxylate and phosphine ligands, the reactions were performed using the catalytic amount of monocyclometalated (**98**) or biscyclometalated (**184**) ruthenium complexes in the absence and presence of ligands (Table 14). It was verified in the reaction of ruthenacycle **98** that carboxylate ligand was essential in the C–H bond cleavage, while the addition of phosphine ligand controlled the site-selectivity of the C–H benzylations. On the other hand, biscyclometalated ruthenium complexes **184** was ineffective in any reaction conditions.

Table 14: Roles of carboxylate and phosphine ligands in ruthenium-catalyzed benzylation.[a]





98



184

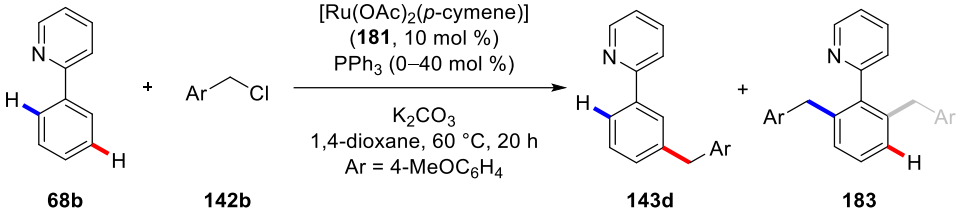
Entry	KOAc	PPh_3	[Ru]	143d (%)	183 (%)	68b (%)
1	✗	✗	**98**	9	14[b]	62
2			**184**	---	---	85
3	✗	✓	**98**	5	2[b]	83
4			**184**	---	---	90
5	✓	✗	**98**	---	76 (1.0:7.4) 66[c] (1.0:7.3)	---
6			**184**	---	---	87
7	✓	✓	**98**	80, 72[c]	15 (1.0:2.8)	---
8			**184**	---	---	90

[a] Reaction conditions: **68b** (0.50 mmol), **142b** (1.50 mmol), [Ru] (10 mol %), PPh_3 (10 mol %), KOAc (20 mol %), K_2CO_3 (1.00 mmol), 1,4-dioxane (2.0 mL), 60 °C, 20 h, under N_2. Yields were determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard and ratios of mono- to dibenzylated products were given in the parentheses. [b] Only monobenzylated product was observed. [c] Isolated yields.

Afterwards, the stoichiometry of ruthenium to phosphine was studied (Table 15 and Figure 9). Increasing amounts of PPh_3 up to 20 mol % had an impact on acceleration and inhibition of the

formation of **143d** and **183**, respectively. Higher loadings of PPh_3 poisoned the active catalyst and led to inhibition of any C–H benzylation.

Table 15: Stoichiometry of ruthenium to phosphine in the benzylation reaction.[a]



Entry	PPh_3 (x mol %)	143d (%)	183 (%)[b]
1	0	22	18 (1.0:2.6)
2	5	30	56 (1.0:1.3)
3	10	52	25 (1.0:7.3)
4	15	76	6 (1.0:1.0)
5	20	65	---
6	25	27	---
7	30	27	---
8	35	16	---
9	40	15	---

[a] Reaction conditions: **68b** (0.50 mmol), **142b** (1.50 mmol), [$Ru(OAc)_2$(*p*-cymene)] (**181**, 10 mol %), PPh_3 (x mol %), K_2CO_3 (1.00 mmol), 1,4-dioxane (2.0 mL), 60 °C, 20 h, under N_2. Yields were determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [b] Combined yield of mono- and dibenzylated products was given and the ratio of mono- to dibenzylated products was shown in the parentheses.

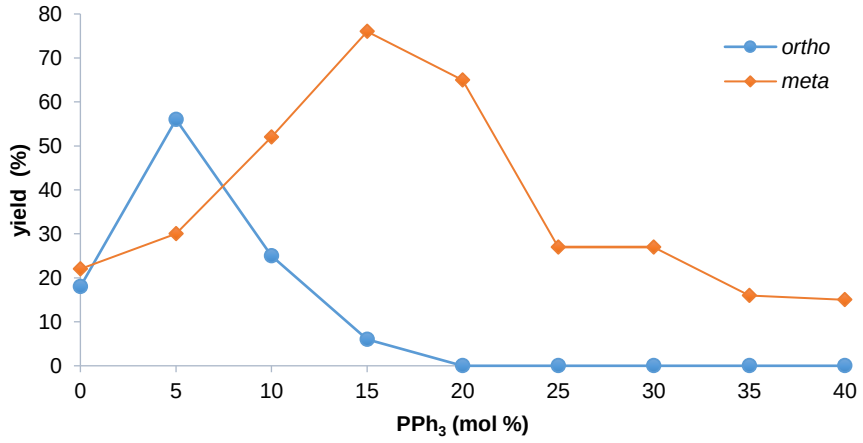
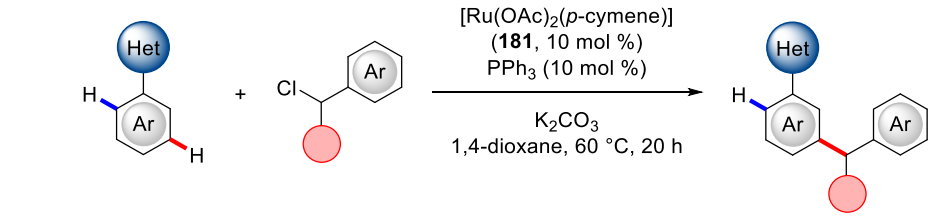


Figure 9: Site-selectivity of ruthenium-catalyzed benzylation with different amount of phosphine ligand at 60 °C.

3.4.3 Scope of the meta-Selective C–H Benzylation

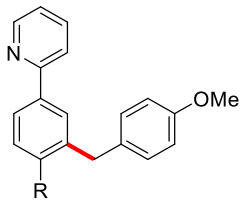
With the optimized conditions for the ruthenium-catalyzed *meta*-C–H benzylation in hand, the versatility of this remote C–H functionalization was explored with different heteroarenes **68**, **139** and benzyl chlorides **142** (Scheme 64). The protocol was highly effective for primary and secondary benzylation. Furthermore, the synergistic ruthenium catalysis was applicable to pyrimidines, pyridines, and synthetically transformative oxazolines. It was found that sterically hindered 1-chloro-2-(1-chloroethyl)benzene (**142e**) smoothly delivered the desired *meta*-benzylated products **143l**. The connectivity of *meta*-benzylated products **143** was established by two-dimensional nuclear magnetic resonance (2D-NMR) and X-ray crystal structure analyses.

The potential of the synergistic ruthenium-catalyzed *meta*-C–H transformation was also reflected by late-stage transformations of biorelevant purines **123** (Scheme 65). Notably, the robustness of ruthenium(II) catalysis proved to tolerate a wide range of functional groups, including ester (**185ah**), halides (**185ai**–**185ak**), ketone (**185hb**), and amide (**185kb**). Likewise, the twofold C–H functionalizations with dichloro-*p*-xylene (**142n**) effortlessly delivered bis-purine xylene **185an**. The positional selectivity of *meta*-benzylated products **185** was confirmed by 2D-NMR and X-ray crystal structure analysis.

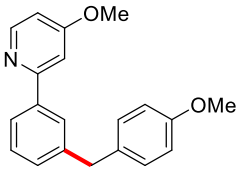


68, **139** **142** **143**

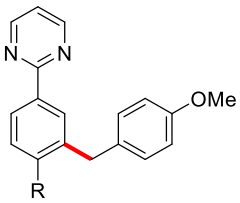
primary benzylation



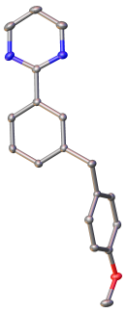
R = H (**143d**): 55%, (15)[b]
R = OMe (**143e**): 62%



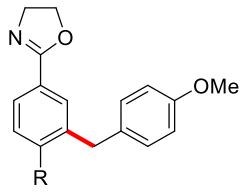
143f: 65%



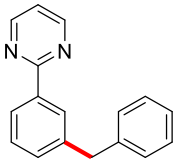
R = H (**143b**): 59%
R = F (**143g**): 51%, 46%[c]



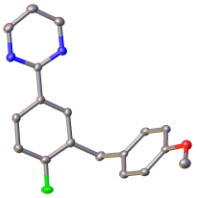
143b
CCDC 1915683



R = H (**143h**): 60%
R = Br (**143i**): 50%

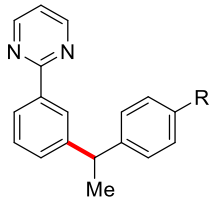


143c: 52%, 52%[d]

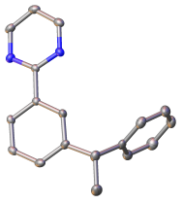


143g
CCDC 1915686

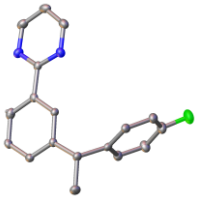
secondary benzylation



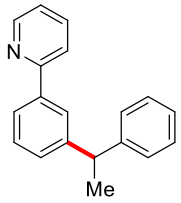
R = H (**143a**): 68%, (1%)[b]
R = F (**143j**): 81%



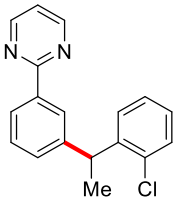
143a
CCDC 1915687



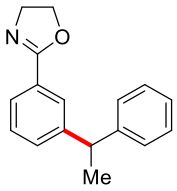
143j
CCDC 1915684



143k: 74%, 67%[d, e]



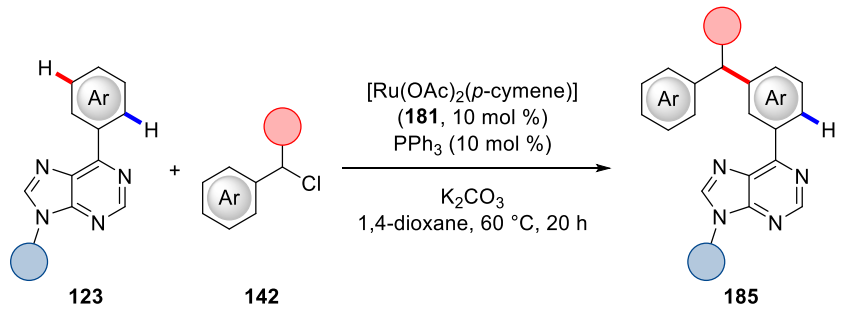
143l: 52%[f]



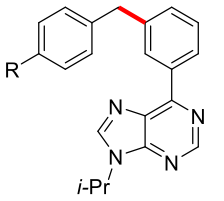
143m: 52%

[a] Reaction conditions: **68** or **139** (0.50 mmol), **142** (1.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 10 mol %), PPh_3 (10 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), 60 °C, 20 h, under N_2; yield of isolated products. [b] Without PPh_3 determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as internal standard. [c] 2-MeTHF. [d] K_3PO_4. [e] 40 °C. [f] 80 °C.

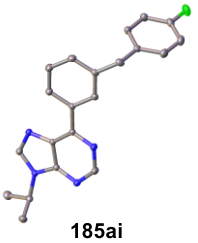
Scheme 64: Remote *meta*-C–H benzylation under ruthenium catalysis.



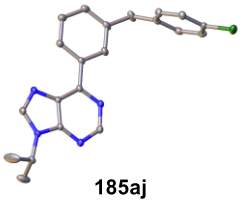
123 **142** **185**



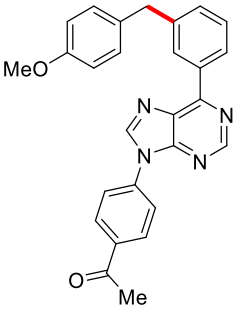
R = H (**185ac**):71%
R = OMe (**185ab**):74%
R = Me (**185af**): 62%
R = CF_3 (**185ag**):73%
R = CO_2Et (**185ah**):72%
R = F (**185ai**): 71%
R = Cl (**185aj**): 73%
R = Br (**185ak**):70%



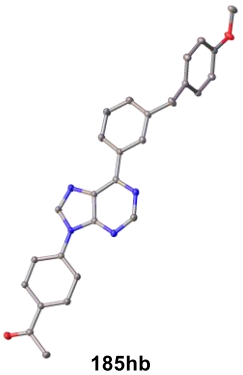
185ai
CCDC 1915675



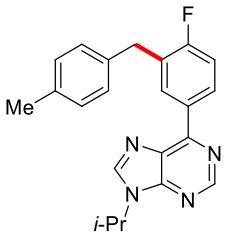
185aj
CCDC 1915610



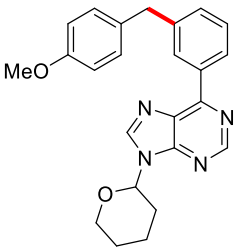
185hb: 68%



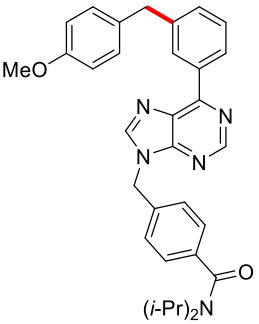
185hb
CCDC 1915681



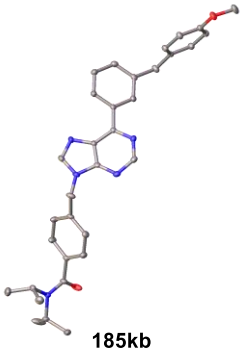
185if: 50%



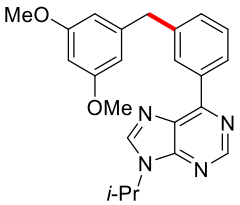
185jb: 75%



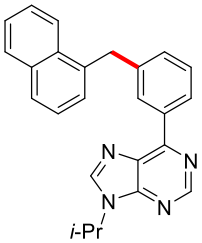
185kb: 63%



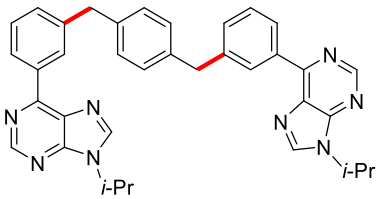
185kb
CCDC 1915682



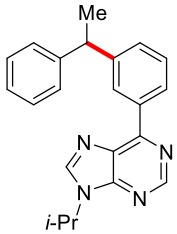
185al: 67%



185am: 67%[b]



185an: 48%[c]



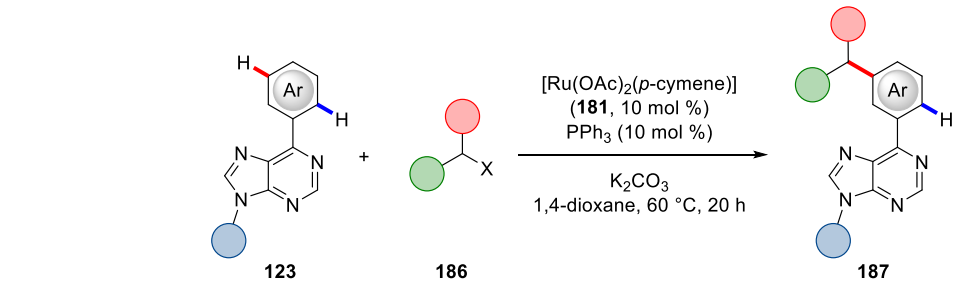
185aa: 87%, 82%[d]

[a] Reaction conditions: **123** (0.50 mmol), **142** (1.50 mmol), [$Ru(OAc)_2$(*p*-cymene)] (**181**, 10 mol %), PPh_3 (10 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), 60 °C, 20 h, under N_2; yield of isolated products. [b] 80 °C. [c] **123a** (1.25 mmol), **142n** (0.50 mmol). [d] K_3PO_4 at 40 °C.

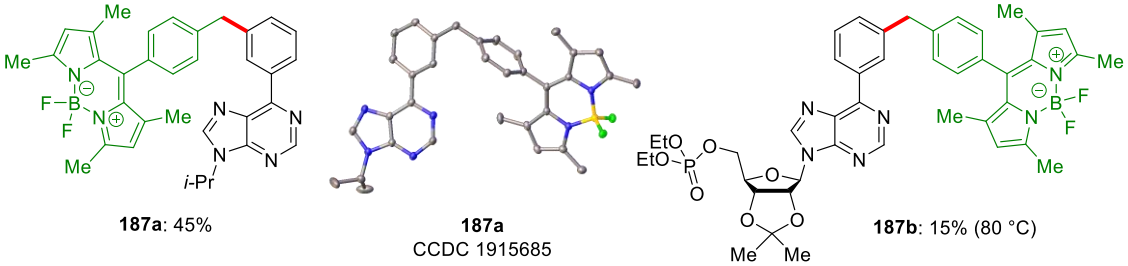
Scheme 65: Ruthenium-catalyzed *meta*-C–H benzylation of purines **123**.

3.4.4 Scope for Late-Stage Diversification through the remote meta-C–H Activation

In addition to simple and commercially available benzyl chlorides, the synergistic protocol for the remote C–H functionalizations was applicable to structurally complex electrophiles (Scheme 66). Late-stage diversification of purine bases with BODIPY fluorescence labels was accomplished by carboxylate-phosphine ruthenium catalysis (**187a** and **187b**). Notably, electrophiles bearing amino acids were smoothly transformed to the corresponding products **187c**–**187i** with high levels of chemo-selectivity without any evidence for racemization. It was highlighted that reactive unprotected hydroxyl groups in serine (**187f**) and tyrosine (**187i**) as well as free *NH*-indole in tryptophan (**187h**) were fully tolerated. In addition, more structurally complex peptides underwent the desired chemical ligation to form products **187j** and **187k**, featuring among others sensitive methionine. The synergistic ruthenium(II) catalyst verified also fully compatible with triglycerides derived from saturated and unsaturated fatty acids (**187l**–**187o**) and vitamin *D*-*α*-tocopherol (**187p**). Particularly, the chemo-selectivity of the *meta*-C–H transformation in the presence of unsaturated fatty acids (**187n** and **187o**) is noteworthy, since they are simply disposed to olefinic and allylic functionalizations. Remarkably, the late-stage modification of marketed drugs was accomplished, including transformations of neuroprotective agent gastrodin (**187q**–**187s**) and anti-inflammatory salicin (**187t**). The ruthenium catalysis was not restricted to benzylic electrophiles, but also synthetically useful monosaccharide bromoesters afforded the desired *meta*-alkylated products **187u**–**187w** with high catalytic efficacy. It is noteworthy that fully unprotected *OH*-free monosaccharides (**187t**) proved to be compatible for the first time in ruthenium catalysis. Notably, purine-uridine hybrids **187x** and **187y** were obtained by the synergistic catalysis *via* catalytic nucleoside ligation.



BODIPY Labeling

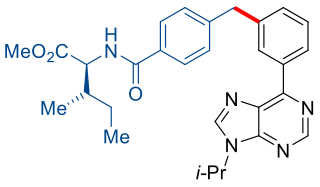


187a: 45%

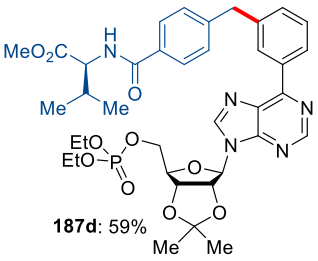
187a
CCDC 1915685

187b: 15% (80 °C)

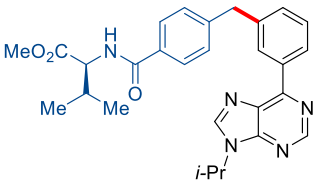
Amino Acids



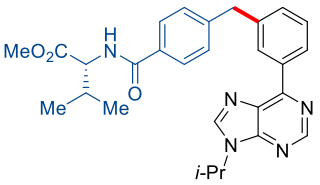
187c: 74%



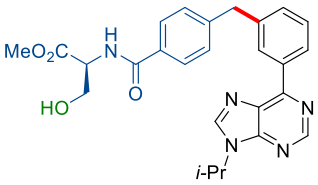
187d: 59%



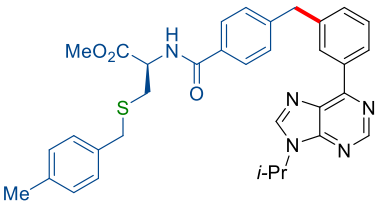
S-**187e**: 70% (>99% ee)
R-Cl (>99% ee)



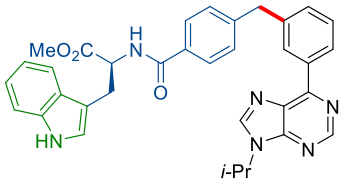
R-**187e**: 77% (>99% ee)
R-Cl (>99% ee)



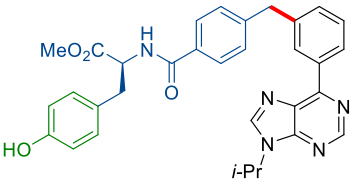
S-**187f**: 50% (98% ee, from R-Cl >99% ee)
rac-**187f**: 55% (0% ee, from R-Cl 0% ee)



187g: 79%



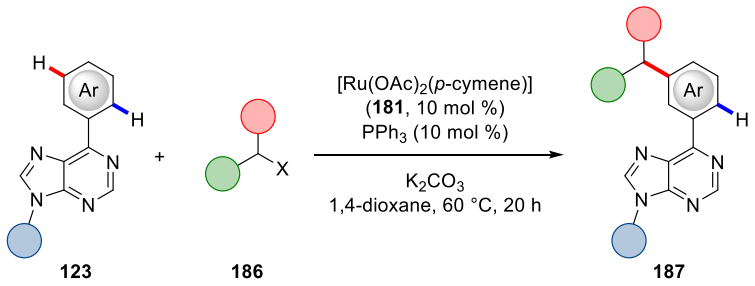
187h: 67%



187i: 53%

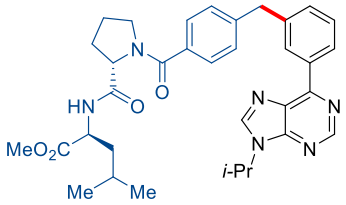
[a] Reaction conditions: **123** (0.50 mmol), **186** (1.00 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 10 mol %), PPh_3 (10 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), 60 °C, 20 h, under N_2; yield of isolated products.

Scheme 66: Late-stage diversification of structurally complex drugs and natural product molecules by remote *meta*-C–H functionalization.

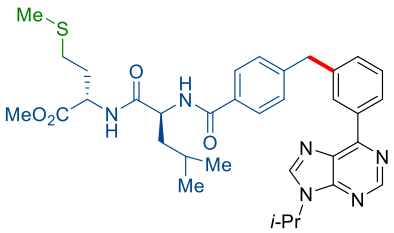


123 **186** **187**

Dipeptides

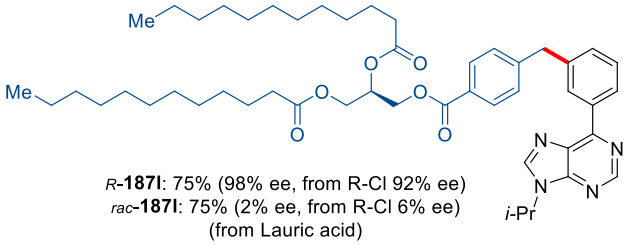


187j: 72%

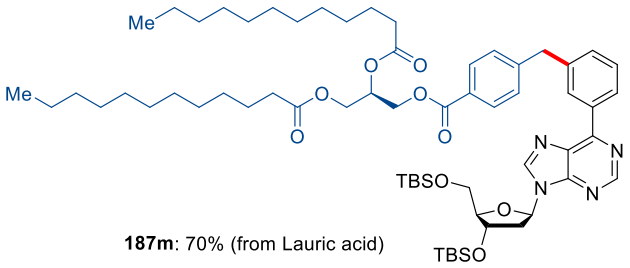


187k: 74%

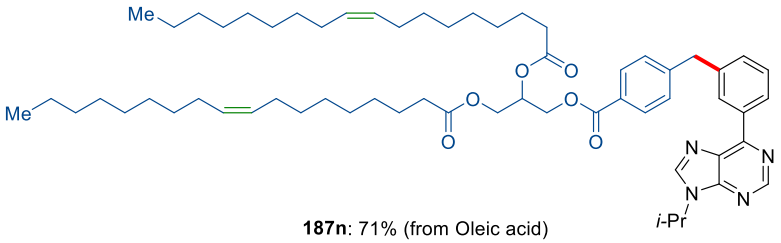
Triglycerides



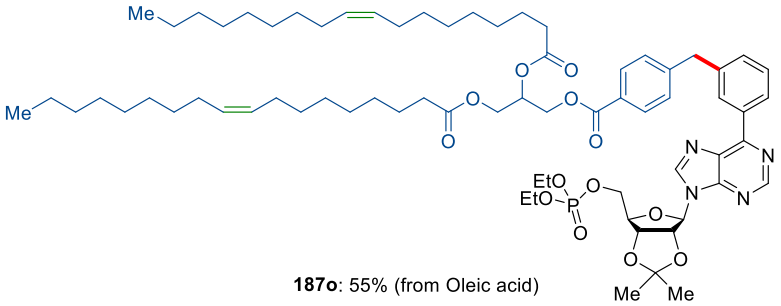
R-**187l**: 75% (98% ee, from R-Cl 92% ee)
rac-**187l**: 75% (2% ee, from R-Cl 6% ee)
(from Lauric acid)



187m: 70% (from Lauric acid)



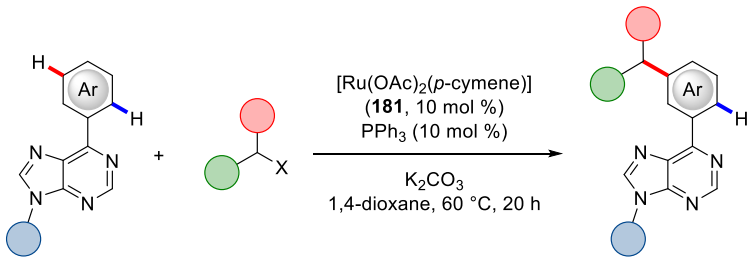
187n: 71% (from Oleic acid)



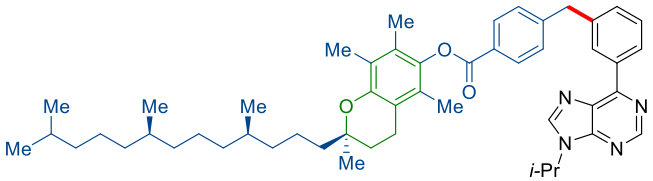
187o: 55% (from Oleic acid)

[a] Reaction conditions: **123** (0.50 mmol), **186** (1.00 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 10 mol %), PPh_3 (10 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), 60 °C, 20 h, under N_2; yield of isolated products.

Scheme 66 (cont.): Late-stage diversification of structurally complex drugs and natural product molecules by remote *meta*-C–H functionalization.

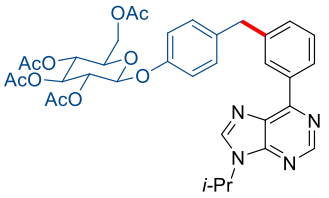


123 **186** **187**

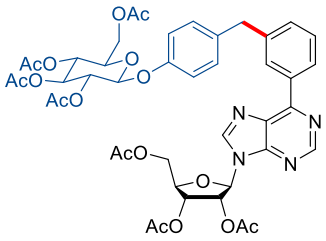


187p: 65% (from Vitamin E or *D*-Tocopherol)

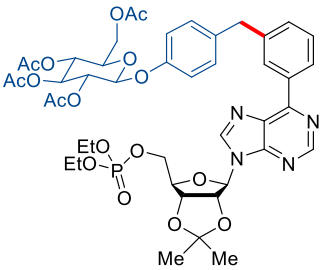
Monosaccharides



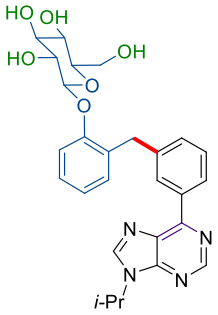
187q: 71% (from Gastrodin)



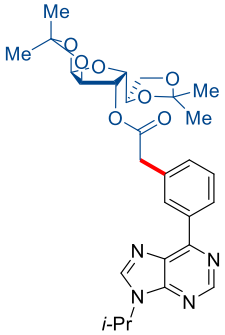
187r: 67% (from Gastrodin)



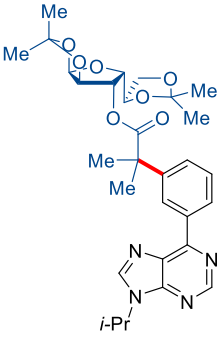
187s: 69% (from Gastrodin)



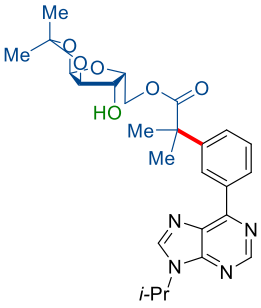
187t: 55% (from Salicin, 80 °C)



187u: 54%

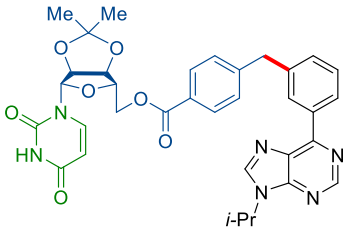


187v: 76%

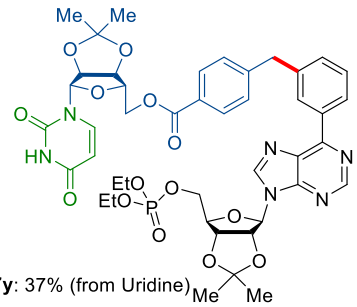


187w: 68%

Nucleoside Ligation



187x: 55% (from Uridine)

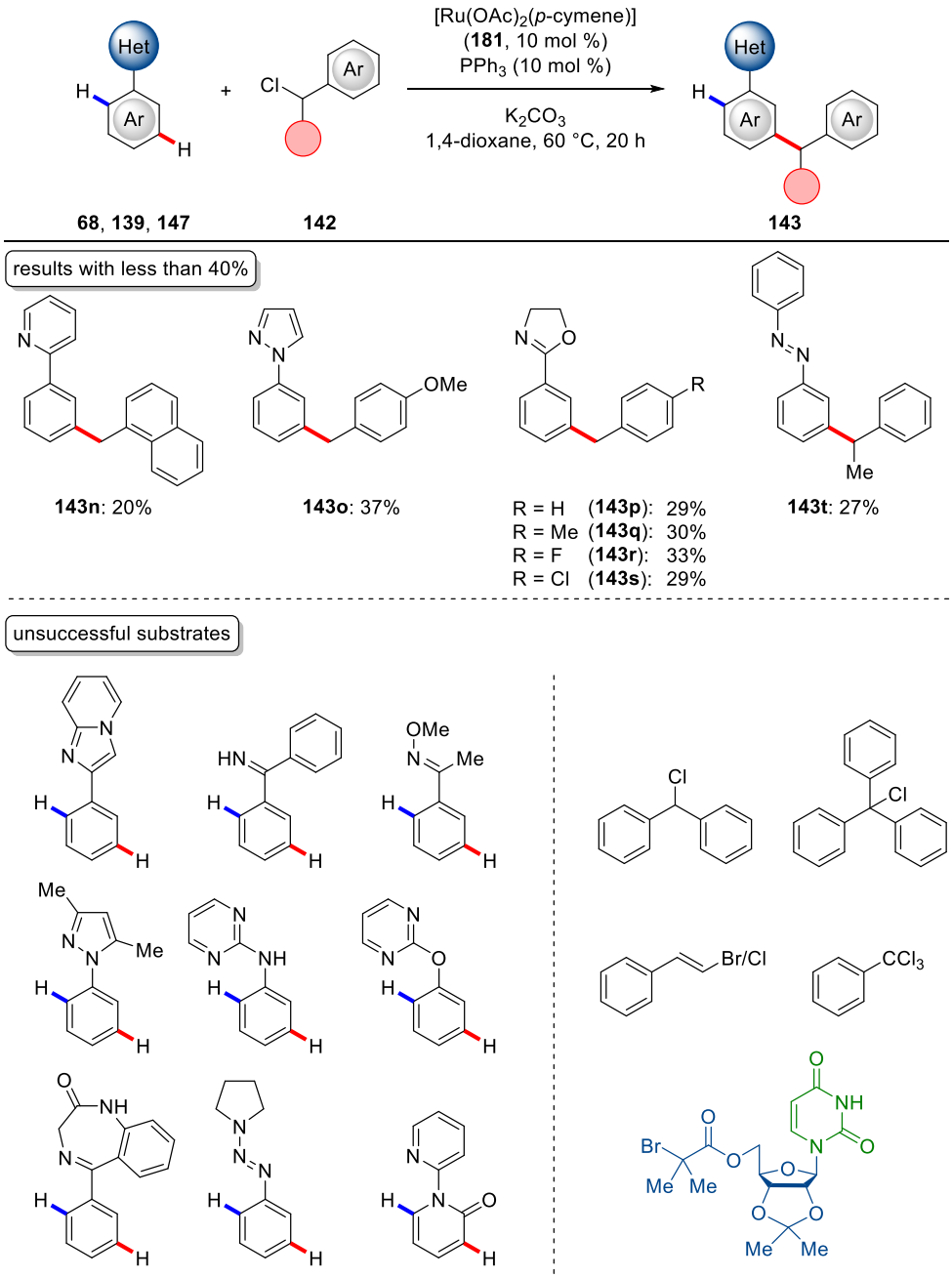


187y: 37% (from Uridine)

[a] Reaction conditions: **123** (0.50 mmol), **186** (1.00 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 10 mol %), PPh_3 (10 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), 60 °C, 20 h, under N_2; yield of isolated products.

Scheme 66 (cont.): Late-stage diversification of structurally complex drugs and natural product molecules by remote *meta*-C–H functionalization.

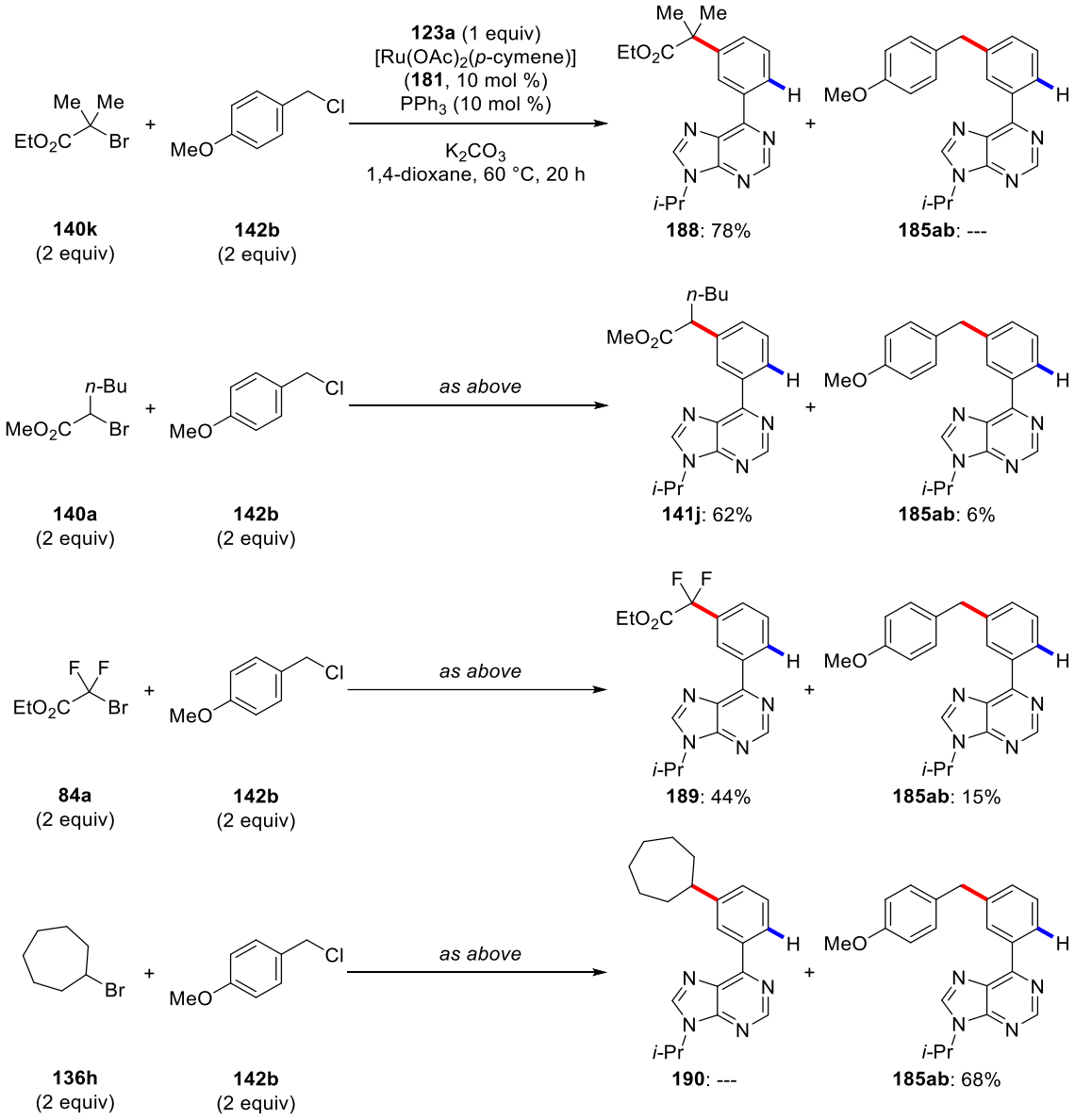
Although the synergistic ruthenium catalysis proved to be robust and versatile, low conversion of pyrazoles (**143o**) and azobenzenes (**143t**) was noted (Scheme 67). The reactions of oxazolinylbenzenes with different primary benzyl chlorides delivered the corresponding product **143p**–**143s** in low yields. Moreover, fully unreactive arenes, such as *O*-methyloximes, dimethylpyrazoles, *N*-pyrimidylanilines, benzodiazepines, 2-pyridylpyridone, and others, as well as ineffective alkyl chlorides or bromides are listed in Scheme 67.



Scheme 67: Unsuccessful results and ineffective substrates in the synergistic ruthenium-phosphine catalysis.

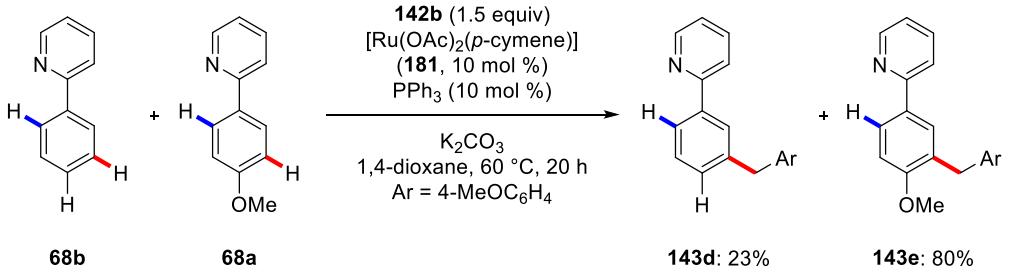
3.4.5 Mechanistic Studies

Since the carboxylate-phosphine ruthenium catalysis effectively transformed several electrophiles, competition experiments were conducted to examine their reactivities (Scheme 68). The results showed that primary benzyl chloride **142b** is less active than bromoesters **84a**, **140a**, and **140k**, whereas no reactivity was observed in case of bromocycloheptane (**136h**).



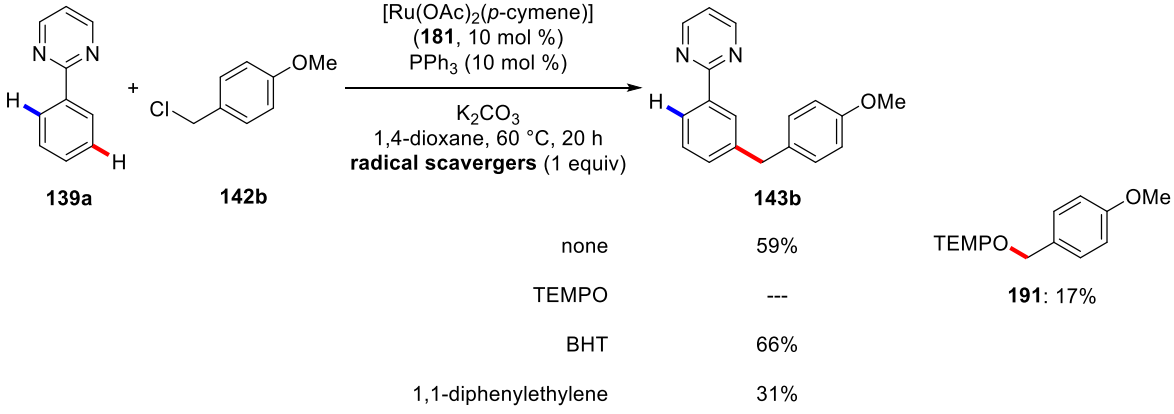
Scheme 68: Intermolecular competition experiments of electrophiles under the carboxylate-phosphine ruthenium catalysis.

Moreover, an intermolecular competition experiment of arenes **68a** and **68b** highlighted electron-rich arenes to be more efficiently converted (Scheme 69)



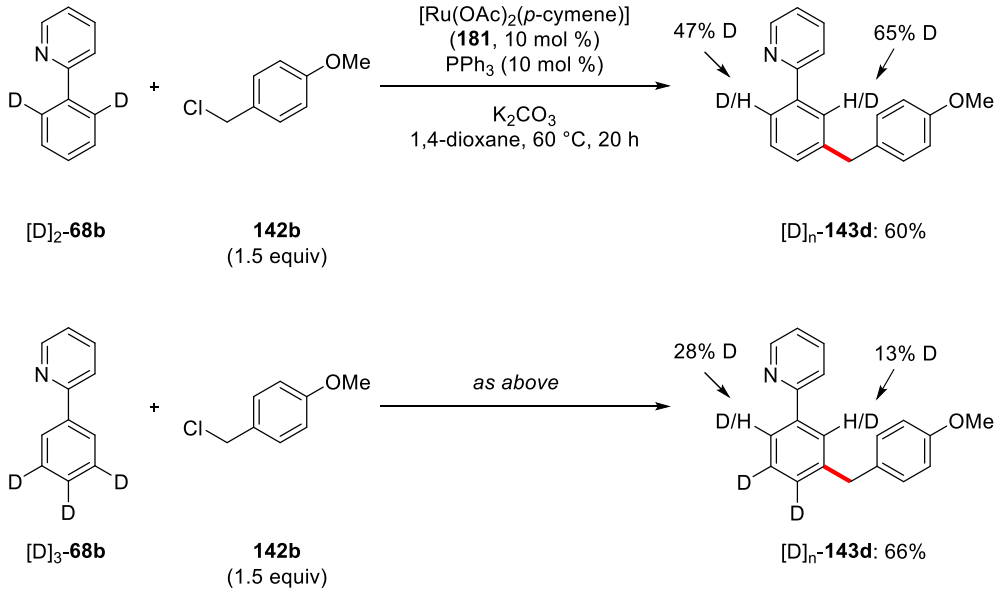
Scheme 69: Intermolecular competition experiment of pyridines **68a** and **68b**.

To understand the cleavage of C–X bond, experiments with radical scavengers were investigated (Scheme 70). The typically used radical scavenger TEMPO fully inhibited the synergistic C–H transformations. The isolated TEMPO adduct **191** strongly indicated the homolytic C–X bond cleavage. While the addition of BHT did not have any influence on the catatytic potential, the reaction with 1,1-diphenylethylene significantly reduced the formation of the *meta*-benzylated product **143b**. Moreover, the adduct derived from 1,1-diphenylethylene and benzyl chloride was detected by GC-MS spectrometry. These findings suggested a radical mechanism through homolytic C–X bond cleavage.



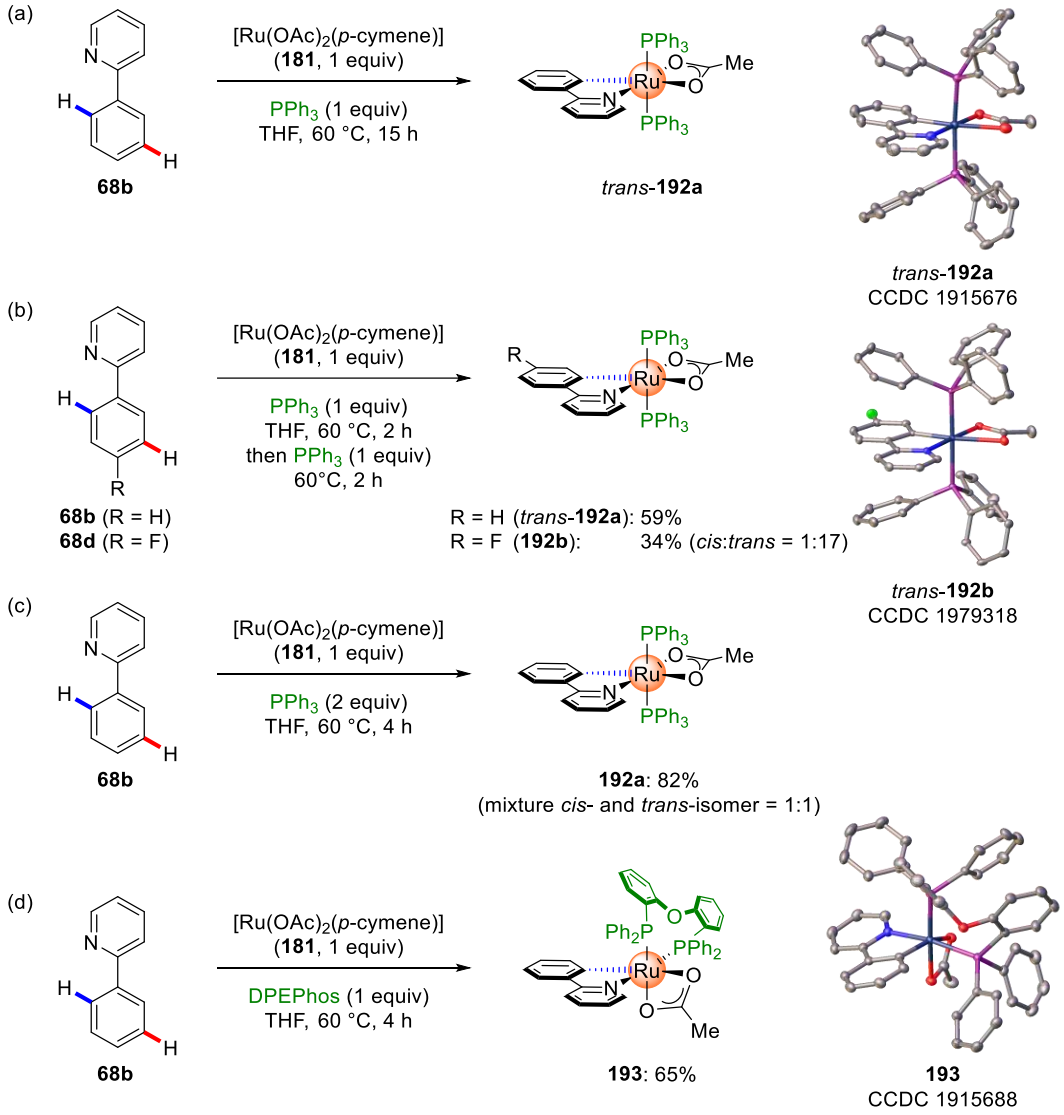
Scheme 70: *meta*-Benzylation in the presence of radical scavengers.

Afterwards, isotopically labelled substrates $[D]_2$-**68b** and $[D]_3$-**68b** were employed in the synergistic catalysis (Scheme 71). The substrates were efficiently converted into the corresponding product $[D]_n$-**143d**. The deuteration degree of product $[D]_n$-**143d** was measured by ^{1}H-NMR spectroscopy, where H/D scrambling at *ortho* position was observed. Owing to a trace amount of H_2O from K_2CO_3, it could not indicate proton source in protodemetalation process. However, it was suggestive of a reversible C–H metalation process.



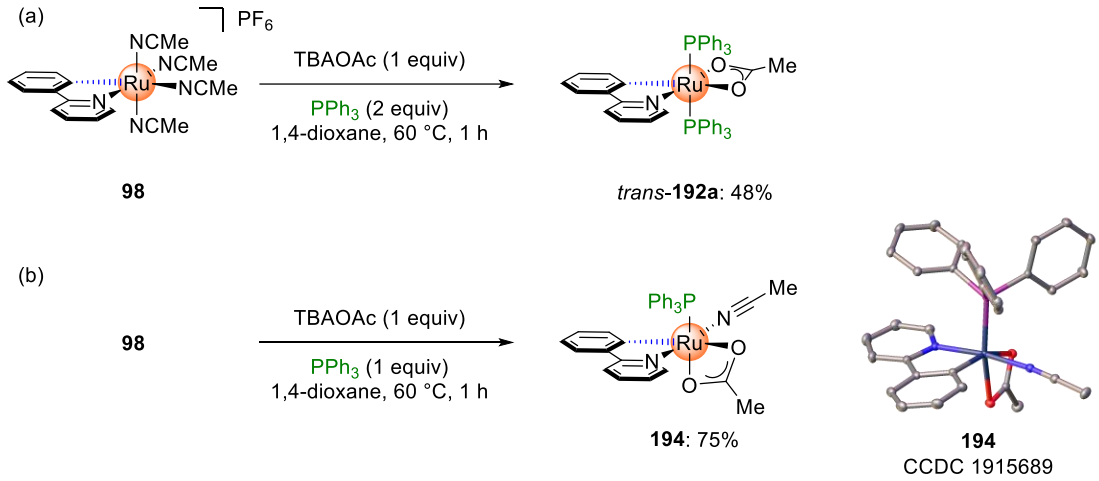
Scheme 71: Ruthenium-catalyzed *meta*-benzylation of isotopically labeled substrates $[D]_2$- and $[D]_3$-**68b**.

To delineate the mechanism of the synergistic C–H functionalization, the series of well-defined ruthenium intermediates were prepared (Scheme 72). First, ^{1}H-NMR spectroscopic studies revealed the *p*-cymene dissociation from the ruthenium precatalyst, which suggested *p*-cymene-coordinated ruthenacycle was not involved in the catalytic cycle. Second, the obtained single crystals from mixture of pyridine **68b**, $[Ru(OAc)_2(p\text{-cymene})]$ (**181**), and PPh_3 were analyzed by X-ray crystallography, providing the structure of ruthenacycle *trans*-**192a** with two phosphines (Scheme 72a). Due to two phosphine equivalents on complex *trans*-**192a**, an additional equivalent of phosphine was added into the complex mixture, affording 59% of complex *trans*-**192a** (Scheme 72b). Moreover, pyridine **68d** gave under the same conditions a 1:17 mixture of *cis*- and *trans*-ruthenacycle **192b**. The alternative protocol with two equivalents of phosphine ligands delivered a 1:1 mixture of *cis*- and *trans*-ruthenacycle **192a** (Scheme 72c). In the case of the bidentate phosphine ligand DPEPhos, monocyclometalated complex **193** was obtained and confirmed by X-ray crystal structure analysis (Scheme 72d).



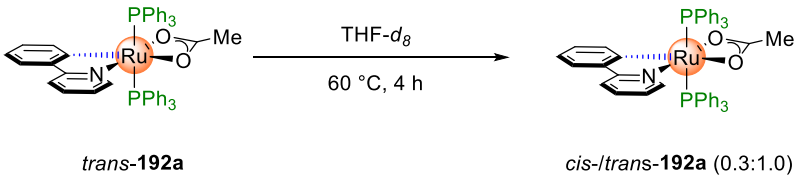
Scheme 72: Preparation of well-defined ruthenacycles **192** and **193**.

In addition, the carboxylate-phosphine ruthenium complex *trans*-**192a** could be derived from cationic monocyclometalated complex **98** with two equivalents of phosphine (Scheme 73a). In contrast, the reaction with one equivalent of phosphine smoothly delivered ruthenacycle **194** (Scheme 73b). The structure of complex **194** was established by X-ray crystallography.



Scheme 73: Ligand modification of cyclometalated ruthenium complex **98**.

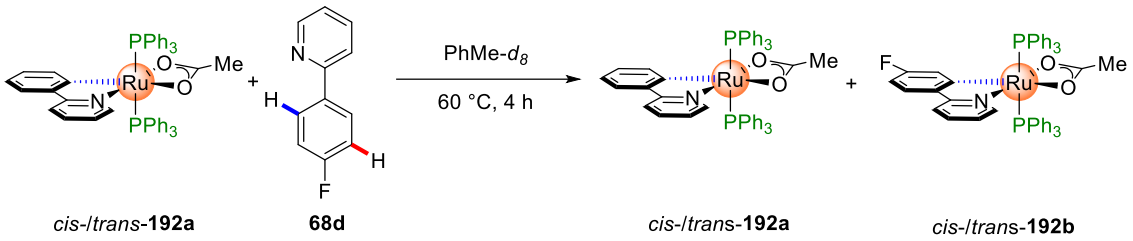
Having a series of well-defined ruthenacycles in hand, the isomerization of complex **192a** was examined by $^{31}P\{^{1}H\}$-NMR spectroscopy (Scheme 74). The solution of complex *trans*-**192a** in THF-d_8 was heated at 60 °C, affording a 0.3:1.0 mixture of *cis*- and *trans*-**192a**. This finding indicated that one of the phosphine ligands is simply labile in the ruthenium complex. These results are in good agreement with the Ru–P bond lengths of well-defined ruthenium complexes. According to X-ray crystallographic data, ruthenacycle *trans*-**192a** has Ru–P bond lengths of 2.3421 and 2.3355 Å, which are longer than complex **194** with a bond length of 2.2451 Å. In addition, bidentate phosphine ruthenium complex **193** has an axial Ru–P bond length of 2.2377 Å and an equatorial Ru–P bond length of 2.3263 Å. These data supported the weak coordination of phosphine ligand on ruthenium complex *trans*-**192a**.



Scheme 74: Isomerization of *trans*-**192a** by temperature.

Afterwards, the second C–H metalation of monocyclometalated complex *cis*-/*trans*-**192a** and pyridine **68d** was investigated (Table 16). $^{31}P\{^{1}H\}$-NMR spectroscopic studies did not detect any construction of the biscyclometalated ruthenium complex. However, ligand exchange of ruthenacycles *cis*-/*trans*-**192** with pyridine **68d** was observed in the presence and absence of K_2CO_3, leading to the formation of ruthenium complexes *cis*-/*trans*-**192b**.

Table 16: Studies on ligand exchange of ruthenacycle *cis*-/*trans*-**192a** and pyridine **68d**.



cis-/*trans*-**192a** **68d** *cis*-/*trans*-**192a** *cis*-/*trans*-**192b**

	cis-**192a**	*trans*-**192a**	*cis*-**192b**	*trans*-**192b**
without K_2CO_3	19%	6%	16%	59%
with K_2CO_3	33%	3%	13%	51%

In addition, redox properties of the novel ruthenacycles **192–194** were studied by cyclic voltammetry (Figure 10). The results of ruthenacycle **98** and **192–194** showed reversible one-electron redox processes at $E_{1/2}$ = 0.75 V (**98**), $E_{1/2}$ = 0.32 V (*trans*-**192a**), $E_{1/2}$ = 0.44 V (**193**), and $E_{1/2}$ = 0.47 V (**194**) versus Ag/AgCl. The change of the half wave potential ($E_{1/2}$) suggested that phosphine ligands significantly reduced oxidation potential of ruthenium(II/III) complexes. In contrast, the *p*-cymene-coordinated ruthenium complex **195** exhibited an irreversible oxidation event at E = 0.81 V.

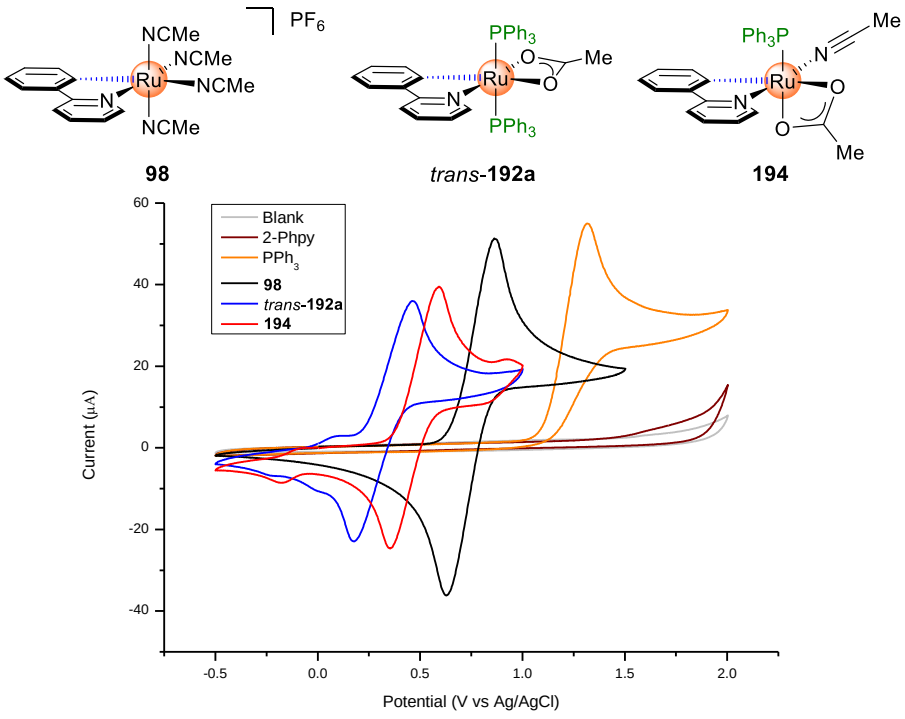


Figure 10: Cyclic voltammetry studies in 1,2-DCE containing 0.1 mol·L^{-1} *n*-Bu_4NPF_6, scan rate 100 mV·s^{-1}.

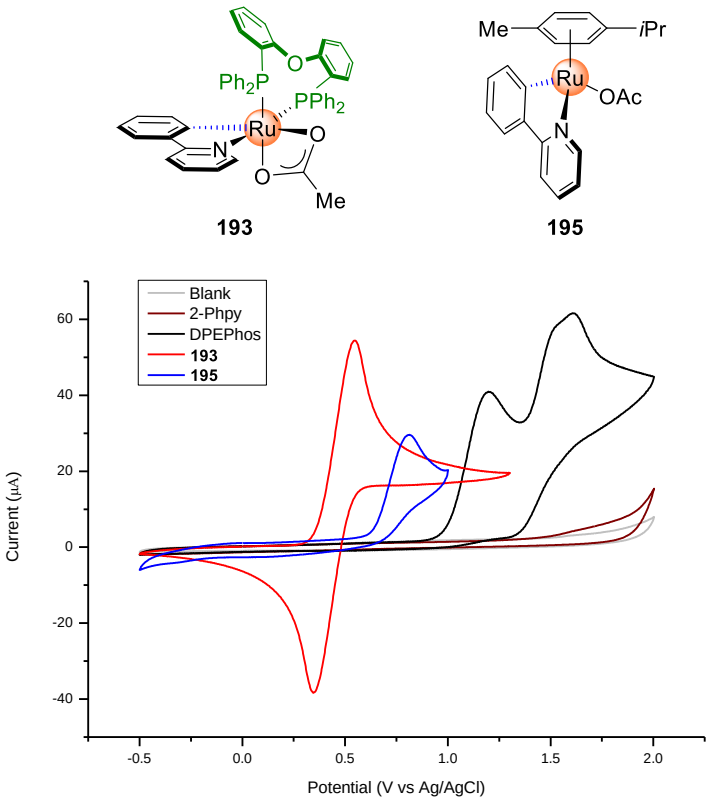
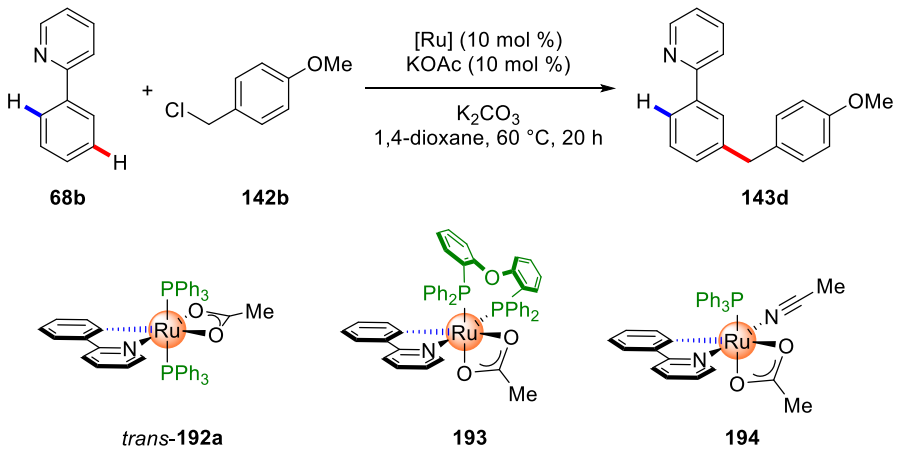


Figure 10 (cont.): Cyclic voltammetry studies in 1,2-DCE containing 0.1 mol·L^{-1} *n*-Bu_4NPF_6, scan rate 100 mV·s^{-1}.

Then, the catalytic efficacy of well-defined ruthenacycle **192a**–**194** was evaluated in the remote *meta*-C–H benzylations (Table 17). Complex *trans*-**192a** and **194** efficiently delivered the desired product **143d**, while bidentate phosphine ruthenium complex **193** failed to give any conversion of substrate **68b**.

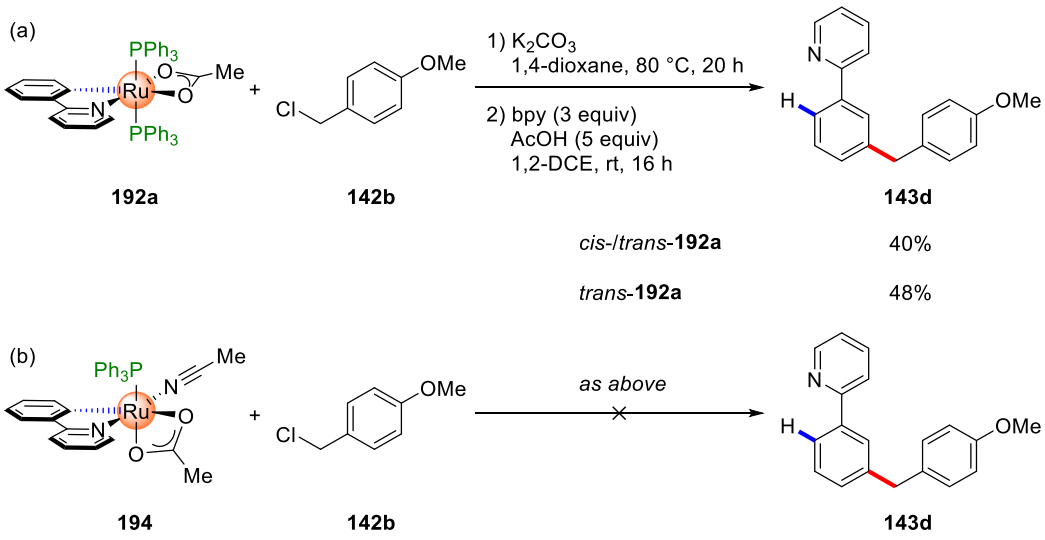
Table 17: Remote *meta*-C–H benzylation catalyzed by cyclometalated ruthenium complexes.[a]



Entry	[Ru]	143d (%)
1	*trans*-**192a**	54 (39)
2	**193**	--- (---)
3	**194**	59 (50)

[a] Reaction conditions: **68b** (0.50 mmol), **142b** (1.50 mmol), [Ru] (10 mol %), KOAc (10 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), 60 °C, 20 h, under N_2; yield of isolated products. The yield in parentheses was obtained in the absence of KOAc.

Furthermore, the stoichiometric experiments of ruthenacycle **192a** with benzyl chloride **142b** selectively afforded the corresponding product **143d** (Scheme 75a). It is noteworthy that demetalation by the addition of 2,2'-bipyridine and acetic acid was obligatory after the transformation. On the other hand, carboxylate-phosphine ruthenium complex **194** failed to provide the desired product **143d** (Scheme 75b).

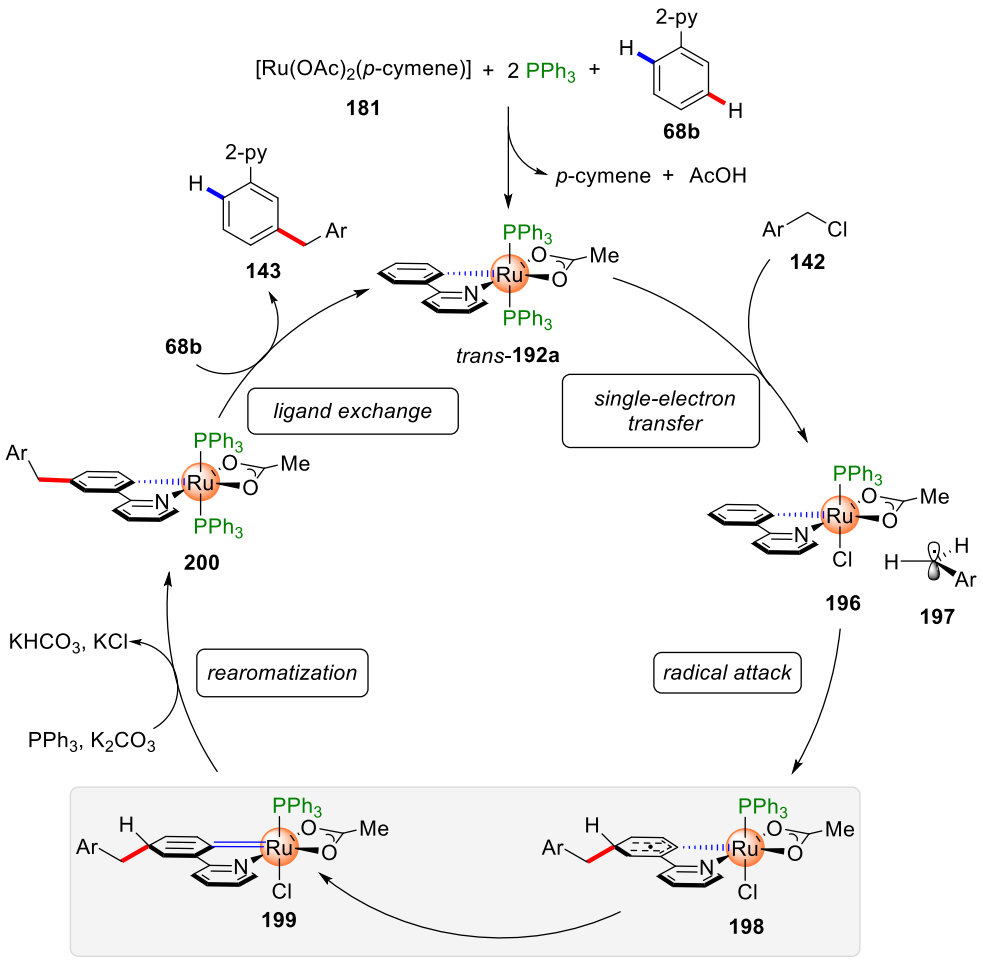


Scheme 75: Stoichiometric benzylation of ruthenacycle **192a** and **194**.

3.4.6 Proposed Catalytic Cycle

On the basis of experimental and computational findings,[104] a plausible catalytic cycle commences by carboxylate-assisted *ortho*-C–H ruthenation to generate complex *trans*-**192a** (Scheme 76). Then, single-electron transfer (SET) from the ruthenium(II) complex *trans*-**192a** to the benzyl halide **142**, generates the ruthenium-(III) intermediate **196**. The benzyl radical **197** attacks on the arene moiety at the position *para* to ruthenium, providing triplet species **198**. Next, ligand-to-metal charge-transfer leads to the significantly stabilized singlet ruthenacycle **199**.

Finally, rearomatization and ligand exchange delivers the desired *meta*-benzylated product **143** and regenerates ruthenium(II) complex *trans*-**192a**.



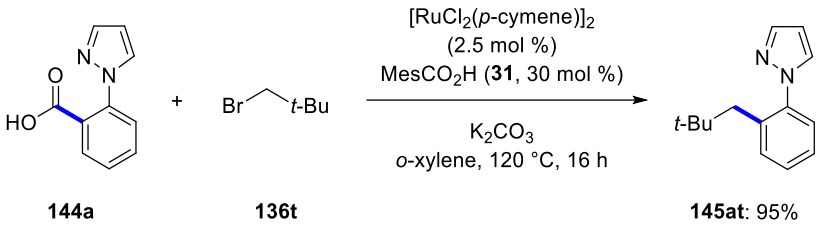
Scheme 76: Proposed catalytic cycle for ruthenium-catalyzed remote C–H benzylation.

3.5 Ruthenium(II)-Catalyzed Decarboxylative Alkylation

During the last decades, methods of site-selective C–H functionalizations have gained enormous attention.[13, 90] In particular, ruthenium catalysis allowed for *ortho*-,[33-34] *meta*-,[61-62, 96, 101] and *para*-selective[87-89] C–H alkylations. In contrast, ruthenium-catalyzed C–C bond activations remain seldom.[105]

Recently, the group of Ackermann reported the first ruthenium(II)-catalyzed decarbamoylative and decarboxylative C–C arylation of aromatic amides and acids.[91] Due to the versatility and robustness of the ruthenium catalyst, Dr. M. Moselage in the Ackermann group further developed the method for decarboxylative alkylations of acid **144a**, as shown in Scheme 77.[106] The C–C

alkylation with primary alkyl bromide **136t** efficiently delivered the *ortho*-alkylated product **145at** with excellent levels of positional selectivity.



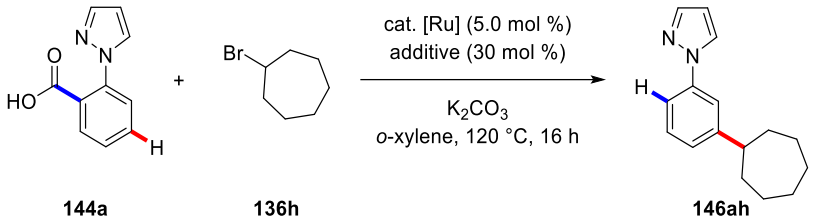
144a **136t** **145at**: 95%

Scheme 77: Ruthenium-catalyzed decarboxylative alkylation of primary alkyl bromide **136t**.

3.5.1 Optimization Studies for Decarboxylative meta-C–H Alkylation

In addition, the ruthenium catalysis enabled decarboxylative *meta*-C–H alkylations of secondary alkyl bromide **136h** (Table 18, entry 1). Different carboxylic acid additives were tested, however, $MesCO_2H$ (**31**) provided the best result (entries 1–3). The reaction without the addition of any acid additives still enabled product formation (entry 4), presumably because the acid starting material **144a** can act itself as carboxylate ligand. Moreover, the cationic ruthenium complexes were effective in the decarboxylative alkylations (entries 5–6). This indicated that a *p*-cymene cyclometalated ruthenium complex was likely not involved in the catalytic alkylation. Other ruthenium sources, such as $RuCl_3 \cdot nH_2O$ (**30**) or $Ru_3(CO)_{12}$, failed to provide the formation of the corresponding product **146ah** (entries 7–8). Furthermore, no conversion was observed when the reaction was performed without the catalyst (entry 9). It is noteworthy that the reaction in γ-valerolactone, a polar green solvent, did not allow any formation of product **146ah**, while the formation of ester *via* nucleophilic substitution of acid **144a** with alkyl bromide **136h** was observed (entry 10).

Table 18: Optimization studies for ruthenium-catalyzed decarboxylative *meta*-C–H alkylation.[a]

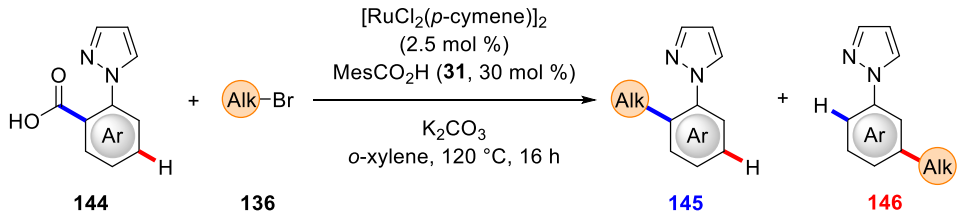


Entry	cat. [Ru]	Additive	146ah (%)
1	**$[RuCl_2(p\text{-cymene})]_2$**	**$MesCO_2H$ (31)**	**73[b]**
2	$[RuCl_2(p\text{-cymene})]_2$	1-$AdCO_2H$ (**12**)	49[b]
3	$[RuCl_2(p\text{-cymene})]_2$	PivOH	56
4	$[RuCl_2(p\text{-cymene})]_2$	---	39[b]
5	$[Ru(NCt\text{-Bu})_6][BF_4]_2$	**31**	60
6	$[Ru(NCt\text{-Bu})_6][SbF_6]_2$	**31**	49
7	$RuCl_3 \cdot nH_2O$ (**30**)	**31**	---
8	$Ru_3(CO)_{12}$	**31**	---
9	---	**31**	---
10	$[RuCl_2(p\text{-cymene})]_2$	**31**	trace[c]

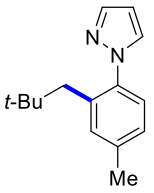
[a] Reaction conditions: **144a** (0.50 mmol), **136h** (1.50 mmol), [Ru] (5.0 mol %), additive (30 mol %), K_2CO_3 (1.0 mmol), *o*-xylene (1.0 mL), 120 °C, 16 h, under N_2; yield of isolated products. [b] Reactions were performed by Dr. M. Moselage. [c] γ-Valerolactone (GVL).

3.5.2 Scope of the Ruthenium-Catalyzed Decarboxylative Alkylation

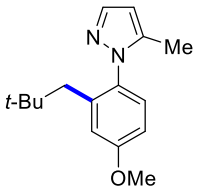
With the optimized conditions for the ruthenium-catalyzed decarboxylative alkylation in hand, the versatility of this remote transformation was explored with different acids **144** and alkyl bromides **136** (Scheme 78). Primary alkyl bromide **136t** was efficiently converted to the *ortho*-alkylated product **145et**. The decarboxylative alkylation of acid **144f** and alkyl bromide **136t** afforded the corresponding product **145ft** as well as *ortho*-benzylated adduct **201** as a side-product, which resulted from benzylic hydrogen abstraction of *o*-xylene solvent. Unprecedentedly, secondary alkyl bromides, such as bromocyclohexane (**136j**) and *exo*-2-bromonorbornane (**136u**), were mainly converted into the *ortho*-alkylated products **145aj**, **145fj**, and **145fu**. In contrast, cycloheptyl and cyclooctyl bromides **136h** and **136k**, respectively, were generally transformed into the *meta*-alkylated products **146**. Moreover, the catalytic functionalizations of tertiary alkyl bromides **136b** and **136v** furnished the corresponding *meta*-alkylated products **146eb**–**146gb** and **146av** with excellent levels of site-selectivity. The connectivity of the thus-obtained products **146eh** and **201** was unambiguously confirmed by X-ray crystal structure analyses.



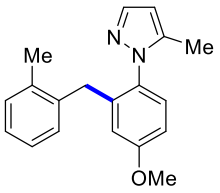
primary alkyl bromides - *ortho*



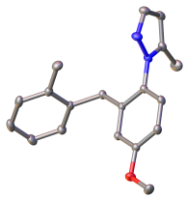
145et: 50%



145ft: 40%

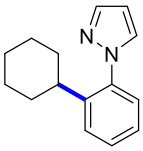


201: 37%

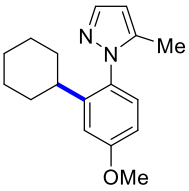


201
CCDC 1979319

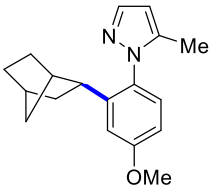
secondary alkyl bromides - *ortho*



145aj: 40%

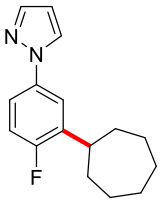


145fj: 33% (*o*/*m* = 10:1)

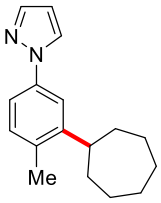


145fu: 54%

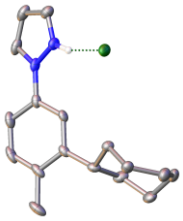
secondary alkyl bromides - *meta*



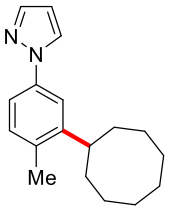
146gh: 64%



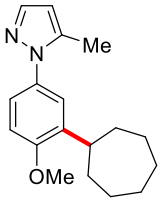
146eh: 59%



146eh[b]
CCDC 1979310

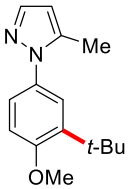


146ek: 35%

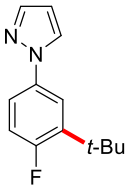


146fh: 28%

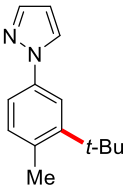
tertiary alkyl bromides - *meta*



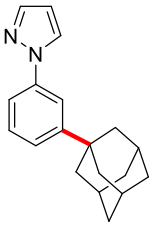
146fb: 54%



146gb: 54%



146eb: 28%

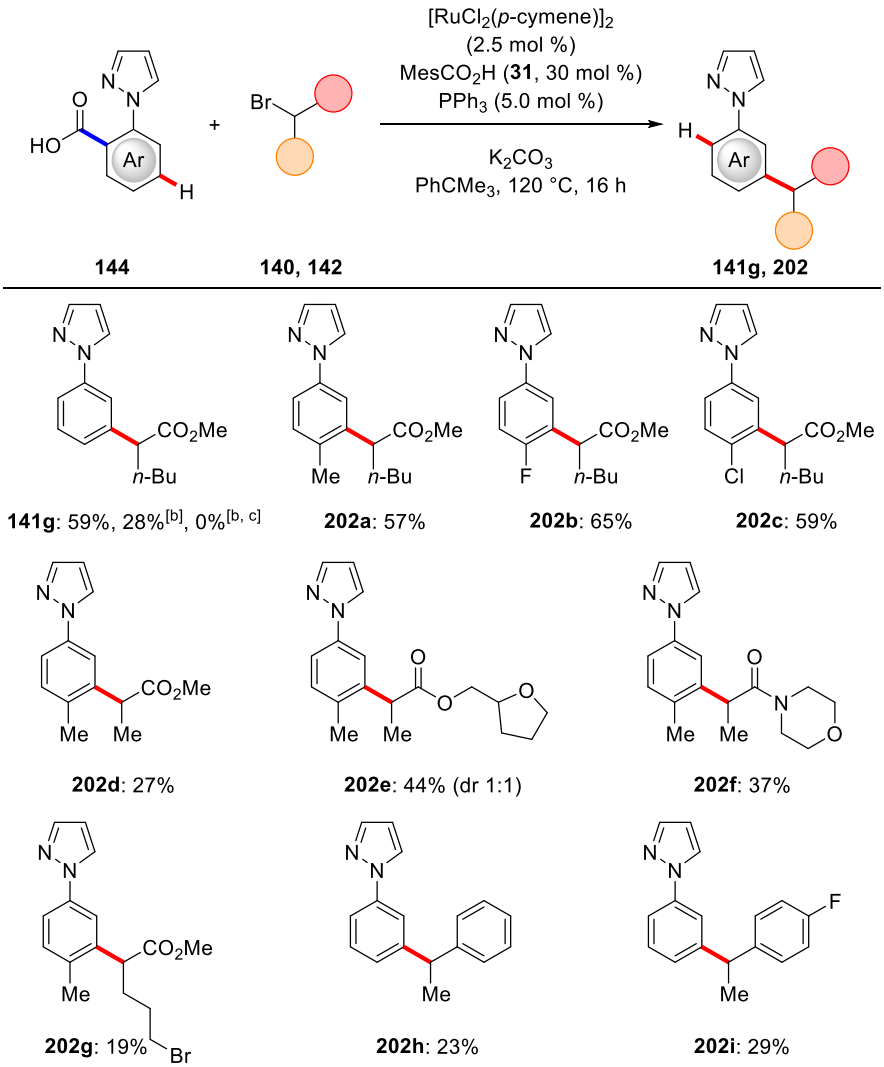


146av: 31%

[a] Reaction conditions: **144** (0.50 mmol), **136** (1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.5 mol %), $MesCO_2H$ (**31**, 30 mol %), K_2CO_3 (1.0 mmol), *o*-xylene (1.0 mL), 120 °C, 16 h, under N_2; yield of isolated products. [b] HCl adduct.

Scheme 78: Decarboxylative alkylations of acids **144** with primary, secondary, tertiary alkyl bromides **136**.

In addition, the catalyst was modified by the addition of a phosphine ligand and the replacement of $PhCMe_3$ as solvent, enabling decarboxylative alkylation with *α*-bromoesters and amides **140** (Scheme 79). Reactions of methyl 2-bromohexanoate (**140a**) provided the *meta*-alkylated product **141g** and **202a**–**202c** with good catalytic efficacy. High chemo- and positional-selectivities were observed in these decarboxylative transformations, although the corresponding products **202d**–**202g** were obtained in lower yields. Likewise, secondary benzyl chlorides **142** were converted to the desired products **202h**–**202i**, albeit in lower yields.



[a] Reaction conditions: **144** (0.50 mmol), **140** or **142** (1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.5 mol %), $MesCO_2H$ (**31**, 30 mol %), PPh_3 (5.0 mol %), K_2CO_3 (1.0 mmol), $PhCMe_3$ (1.0 mL), 120 °C, 16 h, under N_2; yield of isolated products. [b] *o*-Xylene. [c] Without PPh_3.

Scheme 79: Site-selective *meta*-C–H alkylation through decarboxylation.

Under the developed decarboxylative alkylation conditions, some pyrazole acids and some alkyl bromides gave rather unsatisfactory results, which are listed in Figure 11. It is noteworthy that nucleophilic substitutions of acids and alkyl bromides were mostly observed as a side reaction.

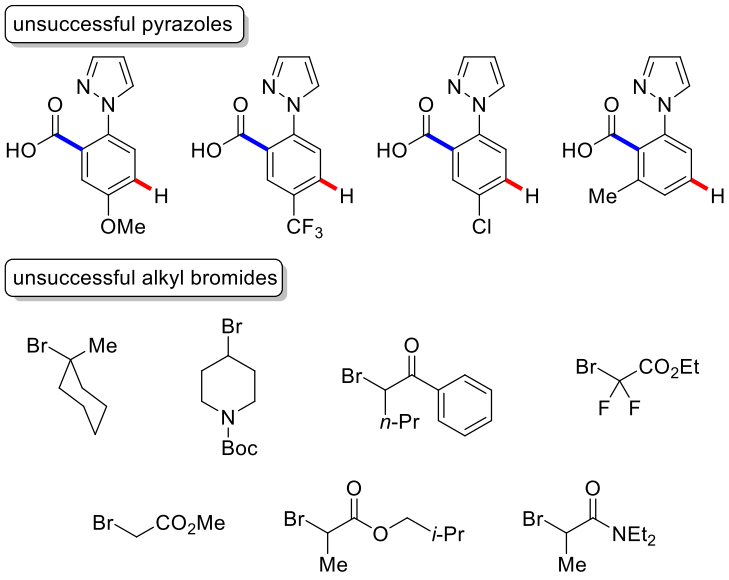
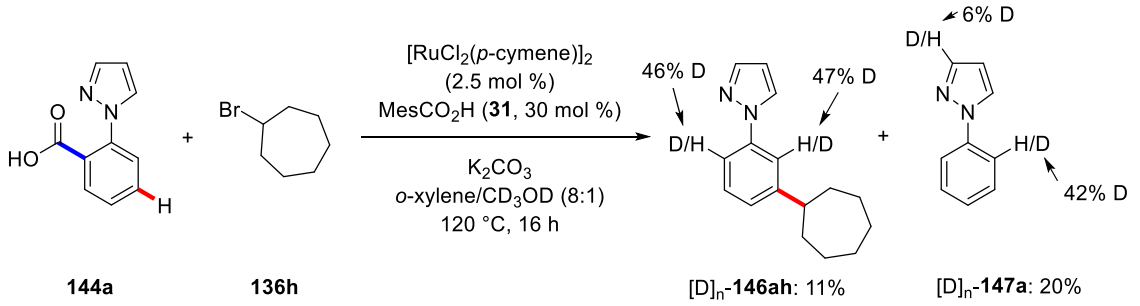


Figure 11: Inefficient acid arenes and alkyl bromides in decarboxylative alkylation.

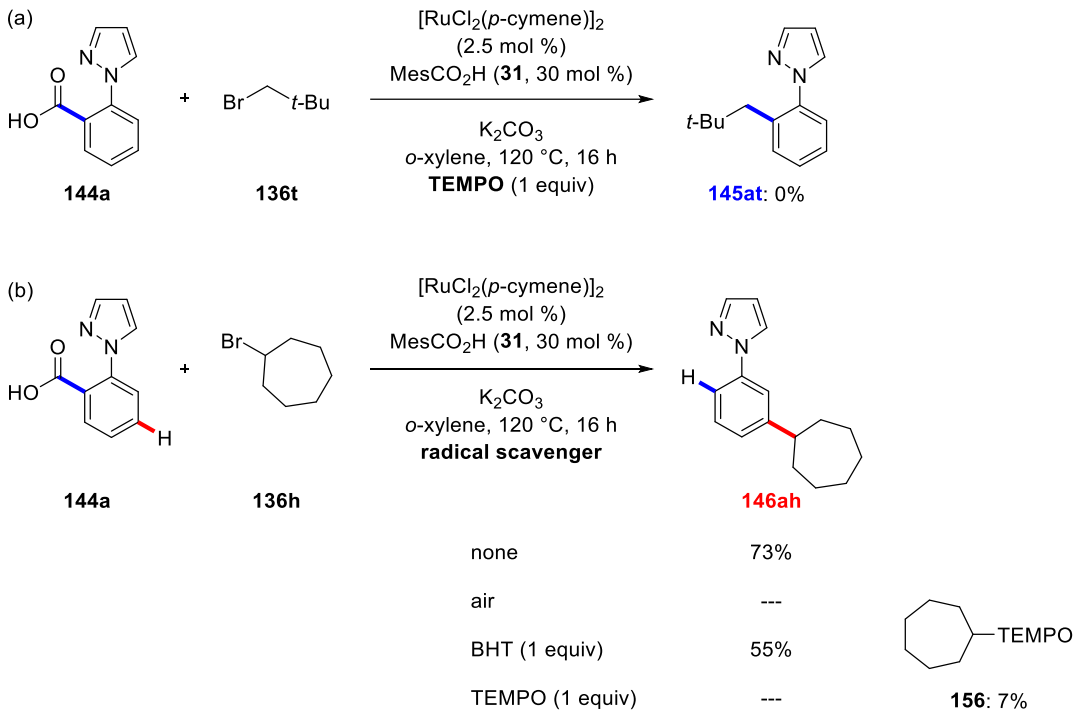
3.5.3 Mechanistic Studies

To unravel the working mode of this ruthenium-catalyzed decarboxylative alkylation, a reaction was conducted in the presence of deuterated co-solvent (Scheme 80). In the presence of alkyl bromide **136h**, the alkylated product [D]$_n$-**146ah** showed deuterium incorporation of 46% and 47% at the *ortho* positions. Moreover, the proto-decarboxylative compound [D]$_n$-**147a** was obtained with deuterium incorporation of 42% at the *ortho* position.



Scheme 80: Experiment with isotopically labeled co-solvent CD_3OD.

Then, reactions with radical scavengers were performed to explain the C–X bond cleavage process (Scheme 81). In the reaction of primary alkyl bromide **136t**, the addition of the radical trap TEMPO led to complete inhibition of the transformation (Scheme 81a). Unfortunately, the alkyl-TEMPO product could not be detected. The decarboxylative alkylation of acid **144a** with secondary alkyl bromide **136h** gave no formation of the corresponding product **146ah** when the reaction was conducted under air atmosphere (Scheme 81b). Moreover, the addition of radical scavenger BHT reduced the catalytic efficacy. Likewise, primary alkyl bromides, the reaction with bromocycloheptane (**136h**) was fully inhibited by the addition of TEMPO and the isolated alkyl-TEMPO adduct **156** can be explained by the homolytic C–X bond cleavage.



Scheme 81: Decarboxylative alkylation with radical scavengers.

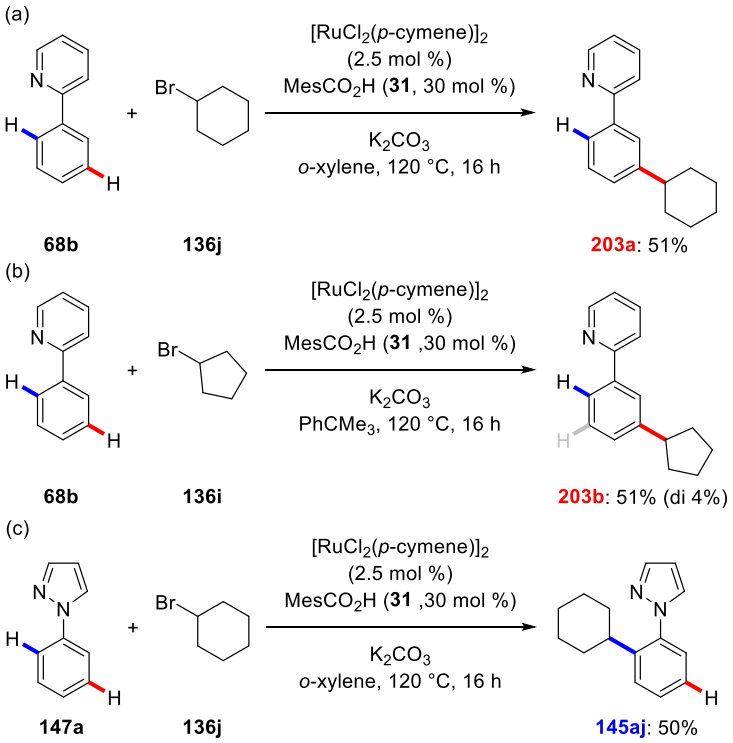
Furthermore, a substantial amount of free *p*-cymene was detected in the first period of the decarboxylative alkylation, which was conducted by J. Struwe.[106] It again suggested that *p*-cymene-coordinated ruthenacycle was not involved as an intermediate in the catalysis.

3.6 Ruthenium-Catalyzed C–H Alkylation of Pyrazoles: *ortho* versus *meta*

Over the last decades, ruthenium-catalyzed site-selective alkylations on the arene moiety have gained significant momentum.[29e, 56b] These studies showed that secondary and tertiary alkyl

bromides were selectively converted to the corresponding *meta*-[61-62, 96] or *para*-alkylated products under ruthenium catalysis,[87-89] whereas the reactions of primary alkyl bromides afforded the *ortho*-alkylated products.[33-34] As shown in Scheme 78 in section 3.5, ruthenium-catalyzed decarboxylative alkylation of bromocyclohexane (**136j**) and *exo*-2-bromonorbornane (**136u**) extraordinarily delivered the *ortho*-alkylated products. After these findings, it became of interest to investigate the mechanism for ruthenium-catalyzed *ortho*-alkylations.

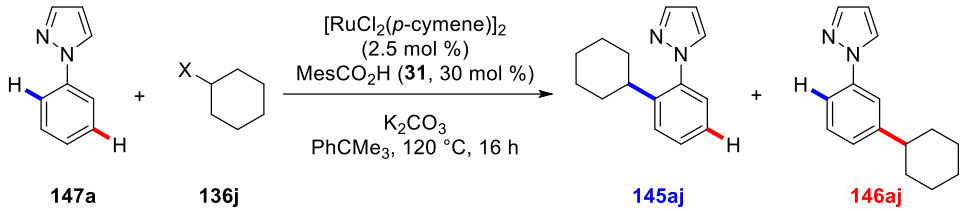
The site-selectivity of alkylation reactions was first examined through a ruthenium-catalyzed C–H functionalization of pyridine **68b** and pyrazole **147a** (Scheme 82). The catalytic transformation of pyridine **68b** with bromocyclohexane (**136j**) or bromocyclopentane (**136i**) afforded the corresponding *meta*-alkylated arenes **203a** and **203b**, respectively, with excellent levels of positional selectivity (Scheme 82a and b). Conversely, the C–H alkylation of pyrazole **147a** occurred at the *ortho* position (Scheme 82c). Moreover, trace amounts of benzylated adducts were observed by GC-MS spectrometry, when *o*-xylene was used as the solvent.



Scheme 82: Ruthenium-catalyzed C–H alkylation of pyridine **68b** and pyrazole **147a** with bromocyclohexane (**136j**) and bromocyclopentane (**136i**).

To prevent the side reaction, $PhCMe_3$ was employed as the solvent in the catalytic transformation (Scheme 83). The alkylation reaction of bromide **136j** gave a 5:1 mixture of the corresponding

ortho- and *meta*-alkylated products **145aj** and **146aj**, respectively. Likewise, cyclohexyl chloride and iodide were transformed into the *ortho*-alkylated product **145aj** as a major product.



147a **136j** **145aj** **146aj**

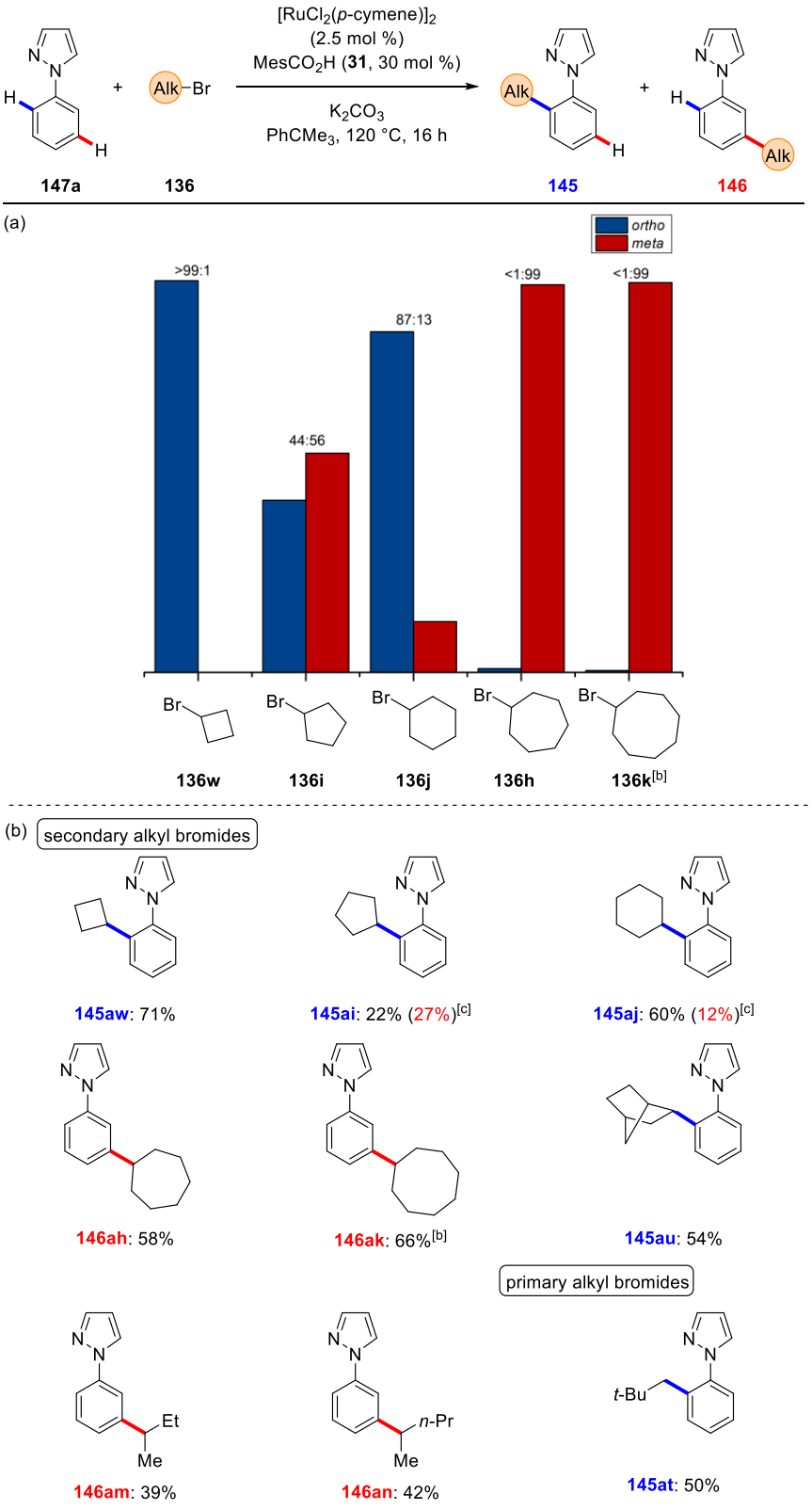
X = Cl	38%	5%
X = Br	60%	12%
X = I	53%	7%

Scheme 83: C–H Alkylation of pyrazole **147a** with cyclohexyl halides **136j**.

3.6.1 Site-Selectivity in Ruthenium-Catalyzed C–H Alkylation of Pyrazoles

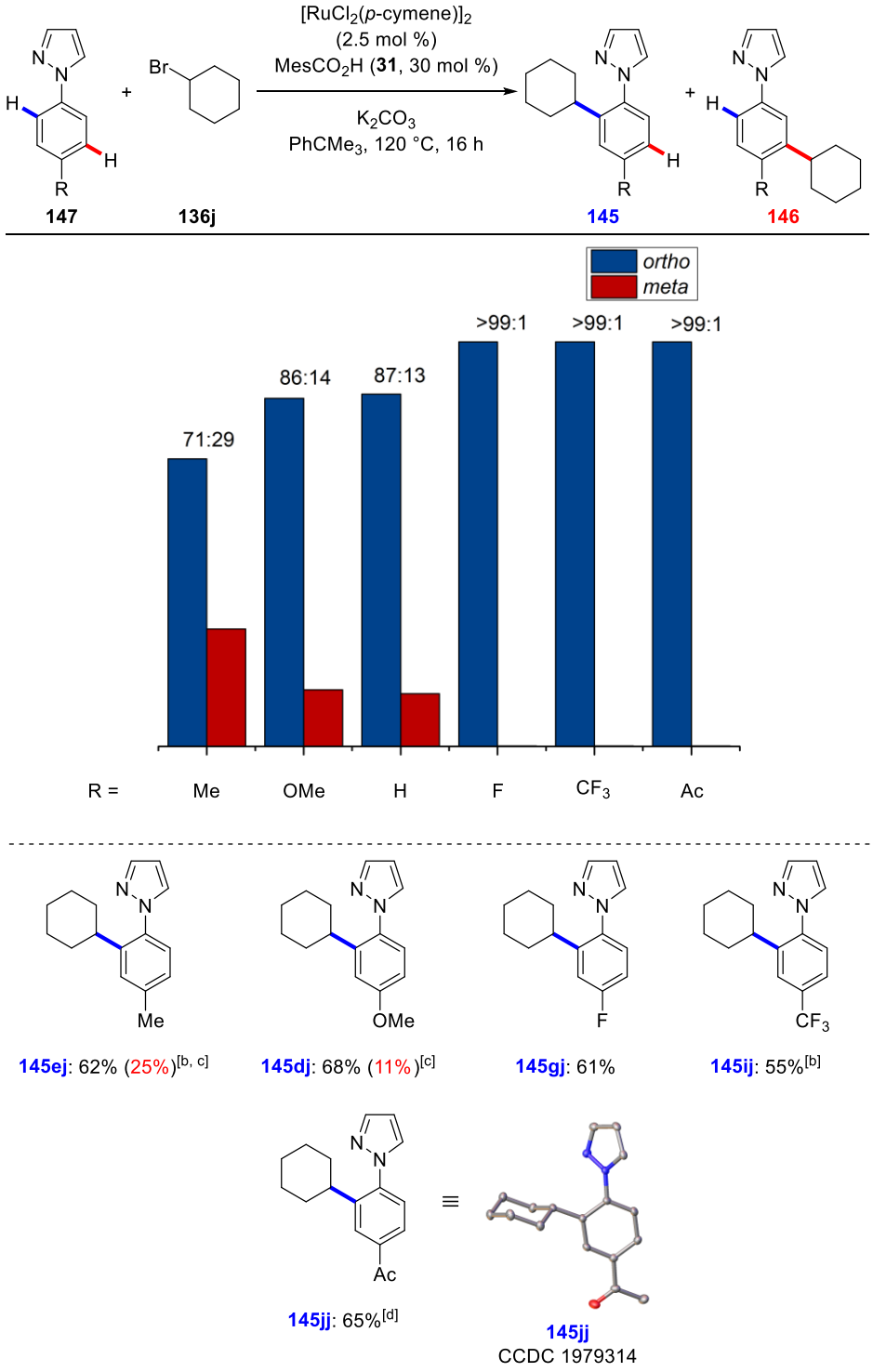
Then, the effect of the ring size of the bromocycloalkanes **136** on the positional selectivity was investigated (Scheme 84a). The catalytic alkylations of unsubstituted phenylpyrazole **147a** with bromocyclobutane (**136w**) and bromocyclohexane (**136j**) favorably gave the *ortho*-alkylated products **145aw** and **145aj**, respectively, while bromocycloheptane (**136h**) and bromocyclooctane (**136k**) preferentially delivered the *meta*-alkylated products **146ah** and **146ak**. Low site-selectivity was observed in the reaction of bromocyclopentane (**136i**). In addition, no formation of products was observed in the reactions of pyrazole **147a** with bromocyclopropane. Then, the scope of primary alkyl bromide as well as secondary alkyl bromides **136** was explored in the C–H alkylations (Scheme 84b). The reactions with neopentyl bromide (**136t**) or *exo*-2-bromonorbornane (**136u**) provided the *ortho*-alkylated products **145at** and **145au**, respectively. Acyclic secondary alkyl bromides **136m** and **136n** were efficiently converted into the *meta*-alkylated products **146am** and **146an**, respectively, with excellent levels of site-selectivity.

Afterwards, the electronic influence on the site-selectivity was probed by the reactions of the differently substituted pyrazolylarenes **147** with bromocyclohexane (**136j**) (Scheme 85). Electron-donating groups at the *para* position afforded a mixture of *ortho*- and *meta*-alkylated products **145** and **146**, while electron-withdrawing groups exclusively furnished the *ortho*-alkylated products **145gj**–**145jj**. The molecular structure of **145jj** was established by X-ray crystal structure analysis.



[a] Reaction conditions: **147a** (0.50 mmol), **136** (1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.5 mol %), $MesCO_2H$ (**31**, 30 mol %), K_2CO_3 (1.0 mmol), $PhCMe_3$ (1.0 mL), 120 °C, 16 h, under N_2; yield of isolated products. [b] The reactions were performed by J. Struwe. [c] The yield of *meta*-alkylated products **146** was given in the parentheses.

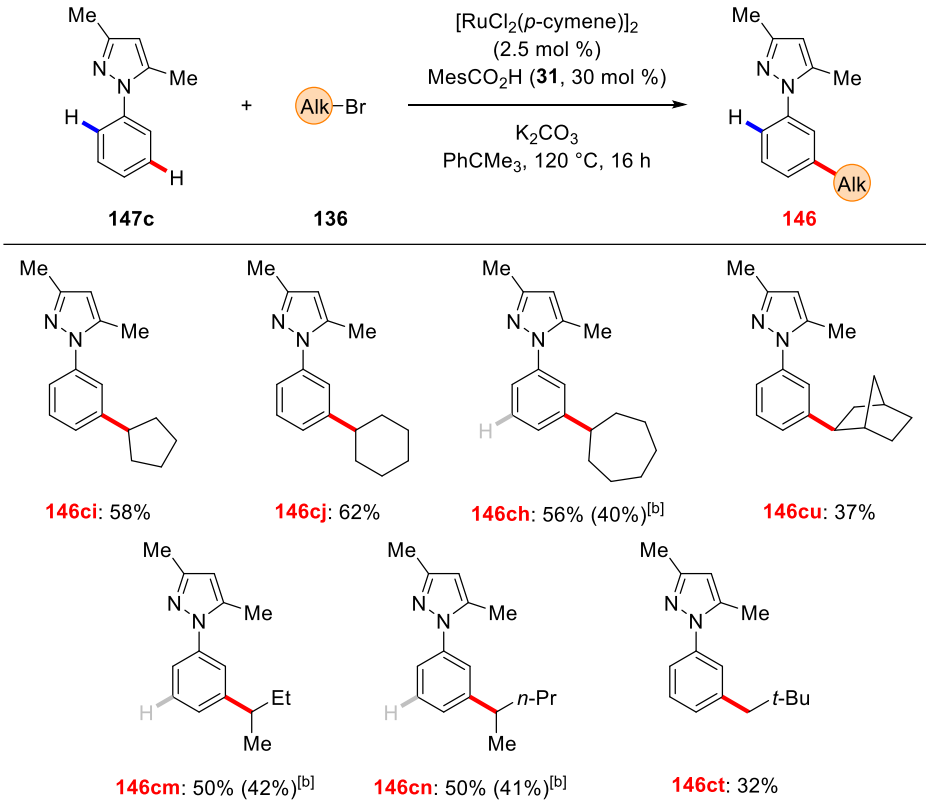
Scheme 84: (a) Positional selectivity of ruthenium-catalyzed C–H alkylation of pyrazole **147a** with various bromocycloalkanes **136** and (b) scope of C–H alkylations of phenylpyrazole **147a**.



[a] Reaction conditions: **147** (0.50 mmol), **136j** (1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.5 mol %), $MesCO_2H$ (**31**, 30 mol %), K_2CO_3 (1.0 mmol), $PhCMe_3$ (1.0 mL), 120 °C, 16 h, under N_2; yield of isolated products. [b] The reactions were performed by J. Struwe. [c] The yield of *meta*-alkylated products **146** was given in the parentheses. [d] Dialkylated products were obtained in 29% yield.

Scheme 85: Electronic effect on the site-selectivity of ruthenium-catalyzed C–H alkylation of pyrazoles **147** with bromocyclohexane **136j**.

In contrast to arylpyrazoles **147a** and **147d–147j**, the alkylation reactions of 3,5-dimethyl-1-phenyl-1*H*-pyrazole (**147c**) with cyclic or acyclic secondary alkyl bromides **136** solely furnished the *meta*-alkylated products **146** (Scheme 86). Moreover, the reaction of neopentyl bromide (**136t**) selectively provided the *meta*-alkylated arene **146ct**, albeit in lower yield.



[a] Reaction conditions: **147c** (0.50 mmol), **136** (0.75 mmol), $[RuCl_2(p\text{-cymene})]_2$ (2.5 mol %), $MesCO_2H$ (**31**, 30 mol %), K_2CO_3 (1.0 mmol), $PhCMe_3$ (1.0 mL), 120 °C, 16 h, under N_2; yield of isolated products. [b] The yield of di-*meta*-alkylated product is given in the parentheses.

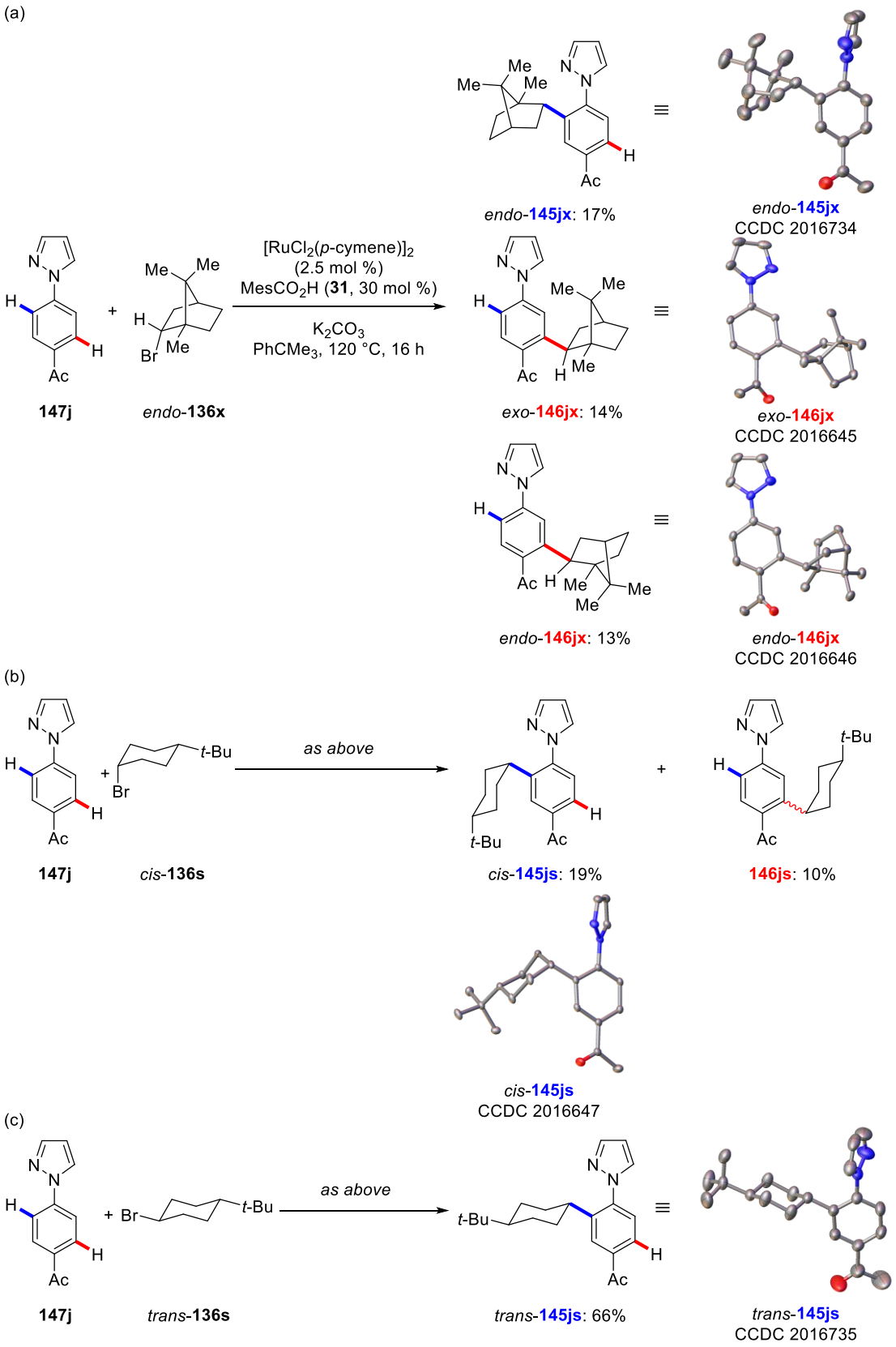
Scheme 86: *meta*-C–H Alkylations of pyrazole **147c** with alkyl bromides **136**.

3.6.2 Mechanistic Studies

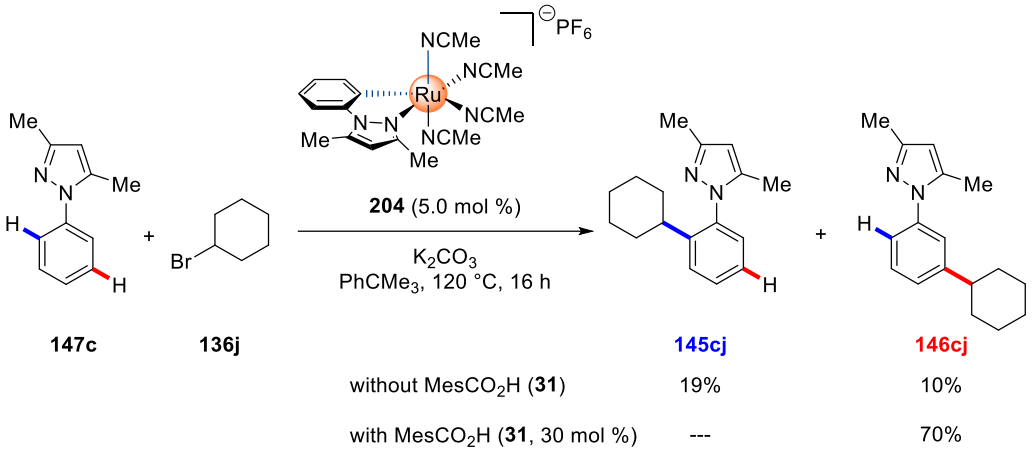
To delineate C–X bond cleavage event of the ruthenium-catalyzed C–H alkylations, the reactions of 1-phenylpyrazole (**147a**) with 2-bromocyclohexane (**136j**) in the presence of radical scarvengers were conducted by J. Struwe.[106] The catalytic alkylations were fully inhibited by the addition of TEMPO. Moreover, the lower catalytic efficacy was observed in the reactions with 1,1-diphenylethylene and the isolation of 2-cyclohexyl-1,1-diphenylethylene can be explained by homolytic C–X bond cleavage. The reaction mechanism was further studied by the alkylation reactions with diastereomerically pure electrophilles **136s** and **136x** (Scheme 87). The reaction

with *endo*-2-bromobornane (*endo*-**136x**) gave the *ortho*-alkylated product *endo*-**145jx** as well as a diastereomeric mixture of the *meta*-alkylated products **146jx** (Scheme 87a). Likewise, the stereochemistry of *tert*-butylcyclohexyl bromide *cis*-**136s** and *trans*-**136s** translated directly into the corresponding *ortho*-alkylated product *cis*-**145js** and *trans*-**145js**, respectively (Scheme 87b and c). Therefore, these results are strongly supportive of a concerted oxidative addition/reductive elimination mechanism to be operative for the *ortho*-alkylation. In contrast, the *meta*-functionlized product **146js** was obtained as *cis*- and *trans*-isomers from the alkylation reaction with the single diastereomer *cis*-**136s**, which is indicative of the formation of an alkyl radical *via* a single-electron transfer (SET) process. The site-selectivity and stereochemistry of the obtained products **145** and **146** were confirmed by 2D-NMR and X-ray analysis.

To elucidate the working mode of the ruthenium catalysis, the well-defined cationic cyclometalated ruthenium complex **204** was employed as the catalyst in the alkylation reaction (Scheme 88). In the presence of $MesCO_2H$ (**31**), the reaction afforded the *meta*-alkylated product **146cj** with excellent level of positional selectivity. While, the reaction in the absence of acid **31** resulted in a mixture of *ortho*- and *meta*-functionalized products **145cj** and **146cj**, which is in contrast to the standard reaction condition. Moreover, 62% of free *p*-cymene was observed in the first period of the catalytic alkylations by gas chromatography analysis, which was conducted by J. Struwe.[106]



Scheme 87: C–H Alkylation of pyrazole **147j** with diastereomerically pure alkyl bromides **136x** and **136s**.

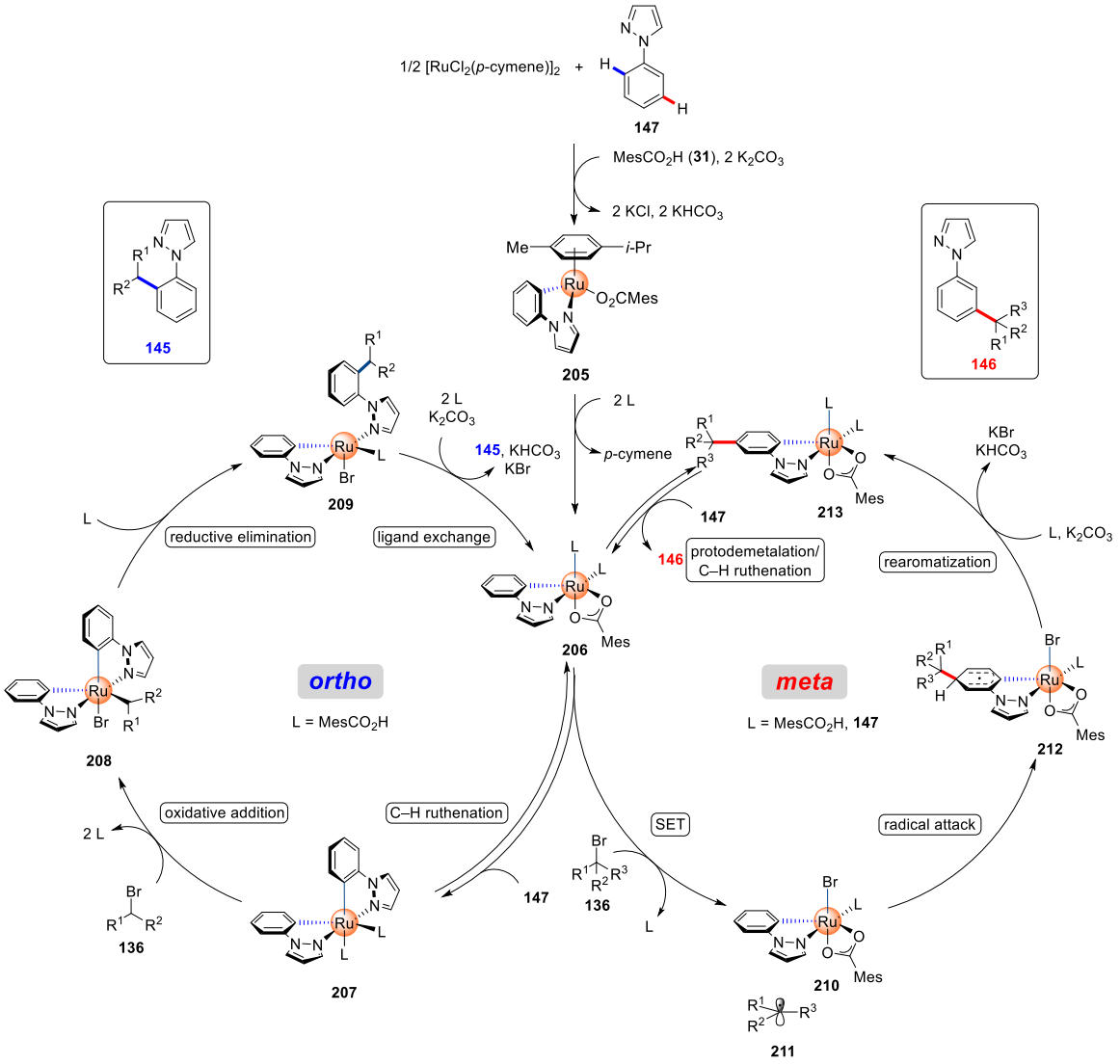


147c	136j		145cj	146cj
		without $MesCO_2H$ (**31**)	19%	10%
		with $MesCO_2H$ (**31**, 30 mol %)	---	70%

Scheme 88: C–H Alkylation catalyzed by the cationic cyclometalated ruthenium complex **204**.

3.6.3 Proposed Catalytic Cycle

On the basis of these findings in experiments and computations,[106] a plausible catalytic cycle for the *ortho*-C–H alkylation commences by a carboxylate-assisted C–H ruthenation and dissociation of *p*-cymene, therefore leading to the cyclometalated ruthenium complex **206** (Scheme 89, left). A second molecule of phenylpyrazole **147** coordinates to ruthenacycle **206** and undergoes C–H activation to form biscyclometalated complex **207**. The oxidative addition of alkyl bromide **136** to complex **207** generates the stable ruthenium(IV) intermediate **208**. Finally, reductive elimination followed by ligand exchange delivers the *ortho*-alkylated product **145** and ruthenacycle **206**. In contrast, *meta*-C–H alkylation occurs through a single-electron transfer (SET) process from ruthenium(II) complex **206** to alkyl bromides **136**, generating the ruthenacycle(III) intermediate **210** and a stabilized alkyl radical **211** (Scheme 89, right). Subsequently, the radical **211** preferentially attacks on the arene moiety at the position *para* to ruthenium, leading to triplet ruthenium intermediate **212**. Ligand-to-metal electron transfer and rearomatization furnish ruthenacycle **213**, which undergoes protodemetalation and C–H activation to afford the *meta*-alkylated product **146** and regenerate the active ruthenium species **206**.



Scheme 89: Proposed catalytic cycle for *ortho*- and *meta*-C–H alkylation.

3.7 Photo-Induced Ruthenium-Catalyzed C–H Arylations at Room Temperature

In addition to C–H alkylations, ruthenium-catalyzed direct arylations have become an important role in crop protection, material sciences, and drug discovery.[29b] The synthesis of biological active compounds, such as Anacetrapib, Valsartan, and Candesartan, through direct C–H arylations was contributed by Ouellet at Merck,[39] Ackermann,[44] and Seki,[107] respectively (Figure 12). In addition, the versatility of ruthenium-catalyzed C–H arylations was reflected by late-stage peptide[108] and nucleoside[109] transformations. In spite of major advances, those reports generally require high reaction temperatures of 100–140 °C.

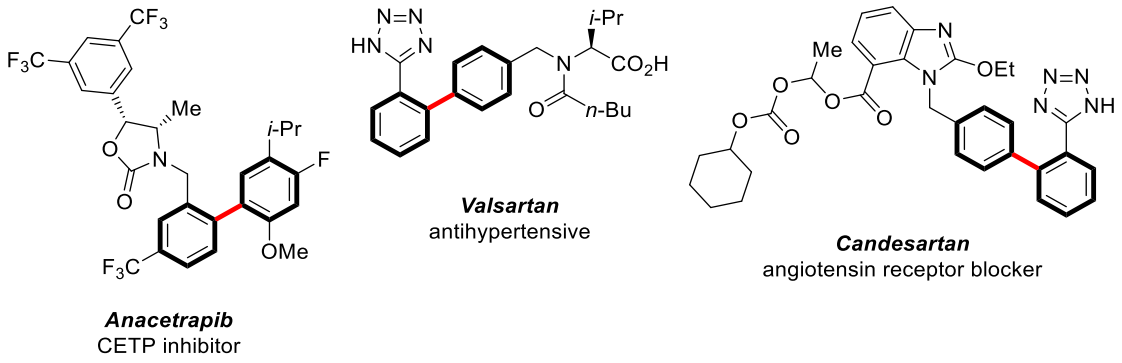
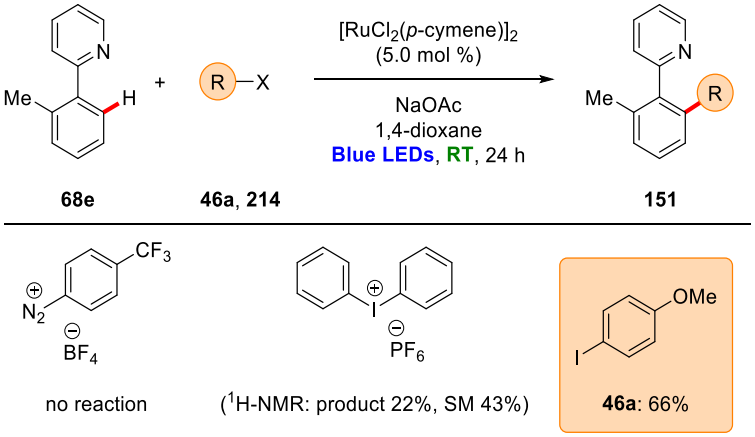


Figure 12: Selected examples of biologically active biaryl compounds.

Photoredox catalysis[110] allows for direct C–H functionalizations at room temperature, nonetheless, additional iridium[111] or ruthenium[112] photocatalysts are typically required in these catalytic transformations. To avoid this issue, the group of Ackermann[92] and then Greaney[113] disclosed visible-light-induced ruthenium-catalyzed remote C–H alkylations. According to those protocols, an *in situ* generated cyclometalated ruthenium complex performed as a catalyst for photocatalysis and cross couplings. The versatility of photo-induced ruthenium-catalyzed C–H transformations was further examined for direct arylations (Scheme 90). Among different arylating agents, 4-iodoanisole (**46a**) provided the best results for the photoredox arylations.



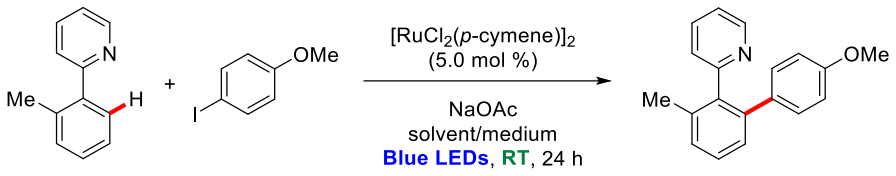
Scheme 90: Ruthenium-catalyzed direct C–H arylation under photoredox condition.

3.7.1 Optimization Studies

The reaction conditions for room temperature direct arylations were probed by using various organic solvents and micellar media (Table 19). DMA solvent provided the best catalytic efficacy for direct arylations (entries 1–9). Although the reaction in 1,4-dioxane gave slightly lower

efficiency, 1,4-dioxane was also chosen as the optimal solvents since it is easy to operate. It is noteworthy that the reaction in the dark furnished only a trace amount of product **151a**, which proved blue light to be essential in the catalytic transformations (entry 3). Moreover, environmentally benign water and micellar medium afforded the low to moderate yields of the corresponding product **151a** (entries 10–18).

Table 19: Reaction media for photo-induced direct arylation.[a]



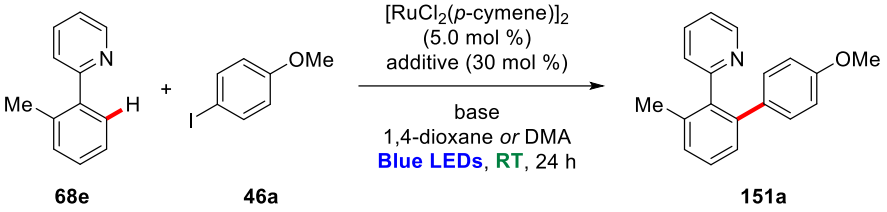
68e (1 equiv) **46a** (x equiv) **151a**

Entry	x equiv	Solvent/Medium	151a (%)
1	**1.5**	**1,4-dioxane**	**66 (68)**
2	2.0	1,4-dioxane	70 (72)
3	2.0	1,4-dioxane	(3)[b]
4	2.0	1,2-DCE	(22)[c]
5	2.0	PhMe	(12)
6	1.5	2-MeTHF	(17)
7	1.5	MeCN	(3)[c]
8	**1.5**	**DMA**	**84 (86)**[c]
9	1.5	NMP	(49)[c]
10	1.5	TPGS-750-M/H_2O (2 wt%)	(16)
11	1.5	SPGS-550-M/H_2O (2 wt%)	(38)
12	1.5	PTS/H_2O (5 wt%)	(30)
13	1.5	Triton X-100/H_2O (10 wt%)	(54)
14	1.5	Tween 20/H_2O (10 wt%)	(51)
15	1.5	Brij 93/H_2O (10 wt%)	(15)
16	1.5	Brij 35/H_2O (10 wt%)	(26)
17	1.5	SDS/H_2O (10 wt%)	(47)
18	1.5	H_2O	(19)

[a] Reaction conditions: **68e** (0.5 mmol), **46a** (x equiv), [$RuCl_2$(*p*-cymene)]$_2$ (5.0 mol %), NaOAc (1.0 mmol), solvent (2.0 mL), 30–35 °C, 24 h, under N_2, irradiate **Blue LEDs**; yield of isolated products. The conversion in the parentheses were determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [b] without light at 30–35 °C. [c] Reactions were performed by M. Waeterschoot.

Among acetate bases, KOAc in 1,4-dioxane or DMA similarly provided the high catalytic efficacy (Table 20, entries 1–5). While phosphate base failed to give any conversion (entry 6), the combination of carboxylic acid additives and K_2CO_3 smoothly delivered the corresponding product **151a** (entries 7–10).

Table 20: Screening of bases for photo-induced direct arylation.[a]



68e **46a** **151a**

Entry	Additive	Base	Solvent	151a (%)
1	---	LiOAc	1,4-dioxane	(9)[b]
2	---	NaOAc	1,4-dioxane	66 (68)
3	---	KOAc	1,4-dioxane	90 (92)[b]
4	---	CsOAc	1,4-dioxane	(27)[b]
5	---	KOAc	DMA	87 (88)
6	$MesCO_2H$ (**31**)	K_3PO_4	1,4-dioxane	---
7	**31**	K_2CO_3	1,4-dioxane	91 (93)
8	**31**	K_2CO_3	DMA	89 (88)
9	1-$AdCO_2H$ (**12**)	K_2CO_3	1,4-dioxane	86 (86)
10	PivOH	K_2CO_3	1,4-dioxane	93 (93)

[a] Reaction conditions: **68e** (0.50 mmol), **46a** (0.75 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), additive (30 mol %), base (1.0 mmol), solvent (2.0 mL), 30–35 °C, 24 h, under N_2, irradiate **Blue LEDs**; yield of isolated products. The conversion in the parentheses were determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [b] Reactions were performed by M. Waeterschoot.

Afterwards, various ruthenium sources were examined (Table 21). Well-defined carboxylate-coordinated ruthenium complexes were highly effective under photoredox conditions (entries 1–2). Due to their low solubility in 1,4-dioxane, cationic ruthenium complexes provided the unsatisfactory results (entries 3–4), while the reaction in DMA efficiently delivered the desired product **151a** in moderate yield (entry 5). Other ruthenium sources, such as $Ru_3(CO)_{12}$ and $RuCl_3{\cdot}nH_2O$ (**30**), failed to furnish product **151a** (entries 6–8).

Table 21: Ruthenium sources for photo-induced direct arylation.[a]

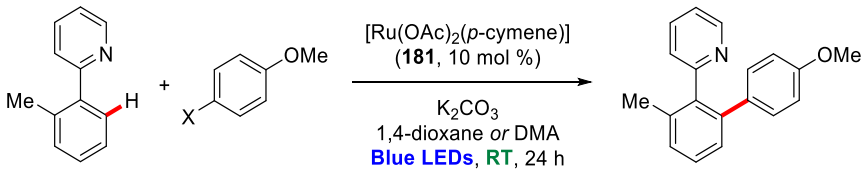
68e **46a** **151a**

Entry	cat. [Ru]	151a (%)
1	**[Ru(OAc)$_2$(*p*-cymene)] (181)**	**94 (95)[b]**
2	[Ru(O$_2$CMes)$_2$(*p*-cymene)] (**33**)	88 (91)[b]
3	[Ru(NC*t*-Bu)$_6$][BF$_4$]$_2$	(6)
4	[Ru(NC*t*-Bu)$_6$][PF$_6$]$_2$	(4)
5	[Ru(NC*t*-Bu)$_6$][PF$_6$]$_2$	(52)[c]
6	Ru$_3$(CO)$_{12}$	---[d]
7	RuCl$_3$·nH$_2$O (**30**)	---[d]
8	**30**	---[d, e]

[a] Reaction conditions: **68e** (0.50 mmol), **46a** (0.75 mmol), [Ru] (10 mol %), MesCO$_2$H (30 mol %), K$_2$CO$_3$ (1.0 mmol), 1,4-dioxane (2.0 mL), 30–35 °C, 24 h, under N$_2$, irradiate Blue LEDs; yield of isolated products. The conversion in the parentheses were determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [b] Without MesCO$_2$H. [c] DMA (2.0 mL). [d] Reactions were performed by M. Waeterschoot. [e] NMP (2.0 mL).

Notably, aryl iodide proved to be the most effective substrate in the photo-induced arylations (Table 22). The reactions of aryl bromide also furnished the desired arylated product **151a** with high catalytic efficacy (entries 2–3), while chloride and triflate delivered the moderate yields of the product **151a** (entries 4–6). In addition, control experiments verified the essential role of the ruthenium catalyst, carboxylate, base, and blue light, as conducted by M. Waeterschoot.[114]

Table 22: Screening of aryl (pseudo)halides for photo-induced direct arylation.[a]



68e **46a** **151a**

Entry	X	Solvent	151a (%)
1	I	1,4-dioxane	94 (95)
2	Br	1,4-dioxane	68 (69)
3	Br	DMA	75 (75)

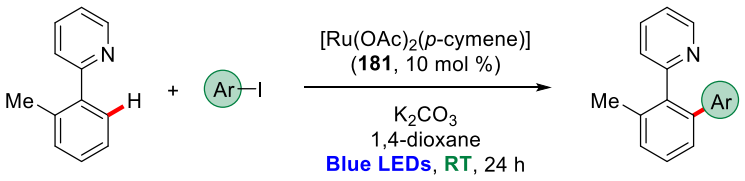
Entry	X	Solvent	151a (%)
4	Cl	1,4-dioxane	(43)
5	Cl	DMA	(6)
6	OTf	1,4-dioxane	39[b]

[a] Reaction conditions: **68e** (0.50 mmol), ArX **46a** (0.75 mmol), [$Ru(OAc)_2$(*p*-cymene)] (10 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane or DMA (2.0 mL), 30–35 °C, 24 h, under N_2, irradiate **Blue LEDs**; yield of isolated products. The conversion in the parentheses were determined by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [b] Reactions were performed by A. Casnati.

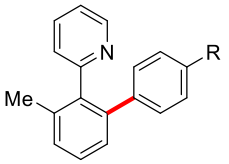
3.7.2 Scope of Photo-Induced Ruthenium-Catalyzed Direct C–H Arylation

Having the optimized reaction conditions in hand, the robustness of photo-induced ruthenium-catalyzed direct C–H arylation was explored by a variety of aryl iodides **46** (Scheme 91). Electron-donating and electron-withdrawing groups of *para*- and *meta*-substituted aryl halides **46** were well tolerated, providing the corresponding arylated products **151** with moderate to high efficacy. It is noteworthy that the ruthenium-catalyzed C–H arylation proved broadly applicable, tolerating sensitive functional groups, including halides (**151c**–**151e**, **151i**), ketone (**151k**), ester (**151f** and **151s**) and nitrile (**151l**). Sterically hindered 2-iodoanisole (**46m**) was also converted to the desired product **151m**. Furthermore, the ruthenium(II) catalysis was effective for (*NH*)-free indole (**151o**) and carbazole (**151t**). The connectivity of the thus-obtained products **151o** and **151t** was unambiguously confirmed by X-ray crystal structure analyses.

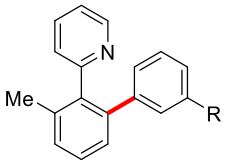
Besides monohaloarenes, the versatility of the room temperature ruthenium catalysis was mirrored by twofold (**216a** and **216b**) and threefold C–H functionalization (**216c**) (Scheme 92). The molecular structure of product **216b** was established by X-ray crystal structure analysis.



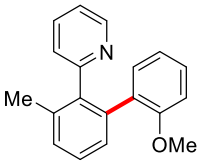
68e **46** **151**



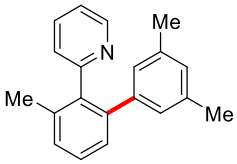
R = H (**151b**): 71%[b]
R = OMe (**151a**): 94%
R = F (**151c**): 67%[c]
3%[c, d]
R = Cl (**151d**): 68%[b]
0%[b, d]
R = Br (**151e**): 67%[c]
R = CO_2Me (**151f**): 72%[c, e]



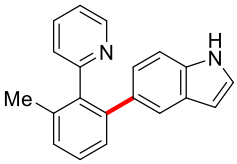
R = Me (**151g**): 88%
0%[b, d]
R = OMe (**151h**): 82%
R = F (**151i**): 56%
R = CF_3 (**151j**): 51%
0%[b, d]
R = Ac (**151k**): 69%
R = CN (**151l**): 50%[f]



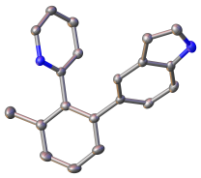
151m: 44%



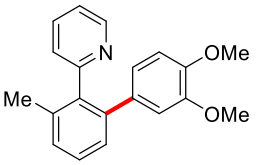
151n: 92%



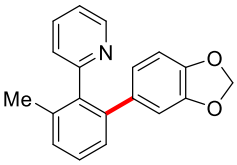
151o: 90%



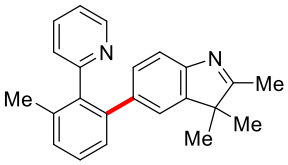
151o
CCDC 1968604



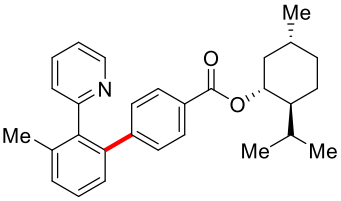
151p: 77%



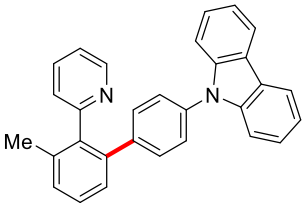
151q: 70%



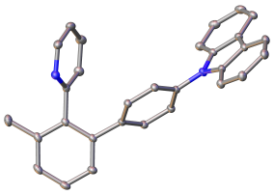
151r: 51%



151s: 44%



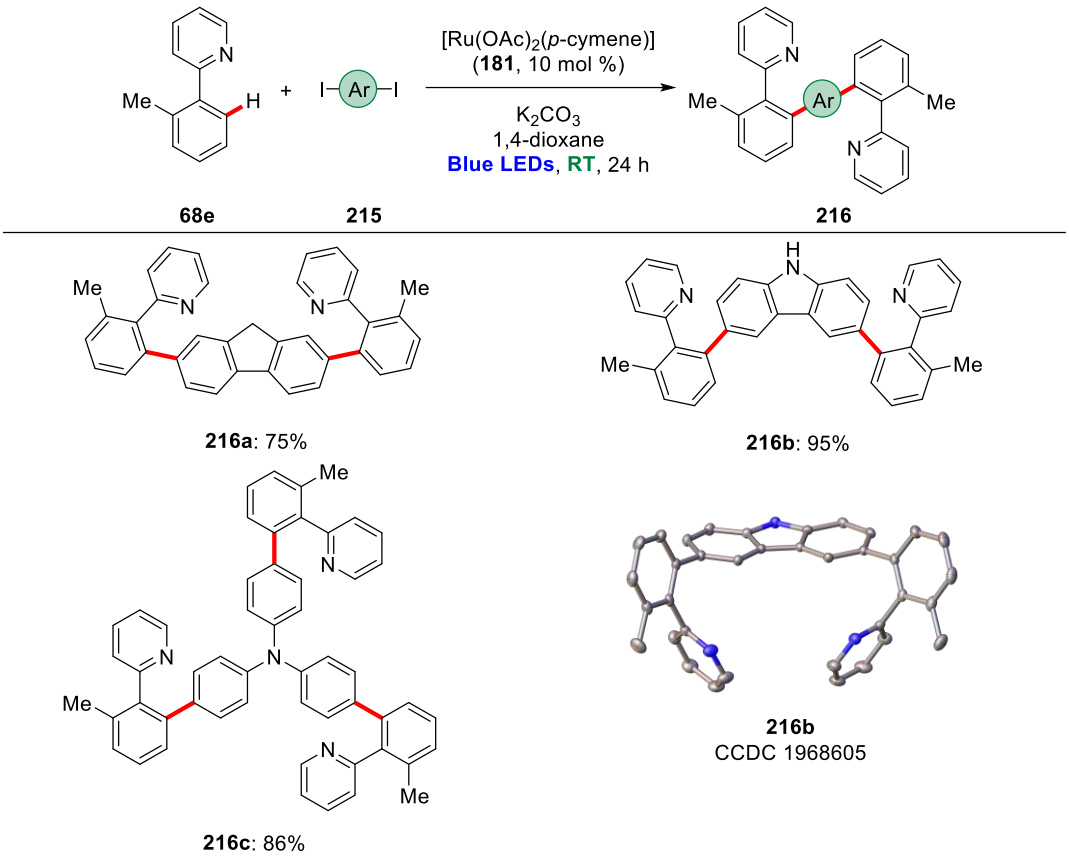
151t: 88%



151t
CCDC 1968602

[a] Reaction conditions: **68e** (0.50 mmol), **46** (0.75 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 10 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), 30–35 °C, 24 h, under N_2, **Blue LEDs**; yield of isolated products. [b] Reactions were performed by A. Casnati. [c] Reactions were performed by J. Struwe. [d] Without light at 30–35 °C. [e] 48 h. [f] DMA.

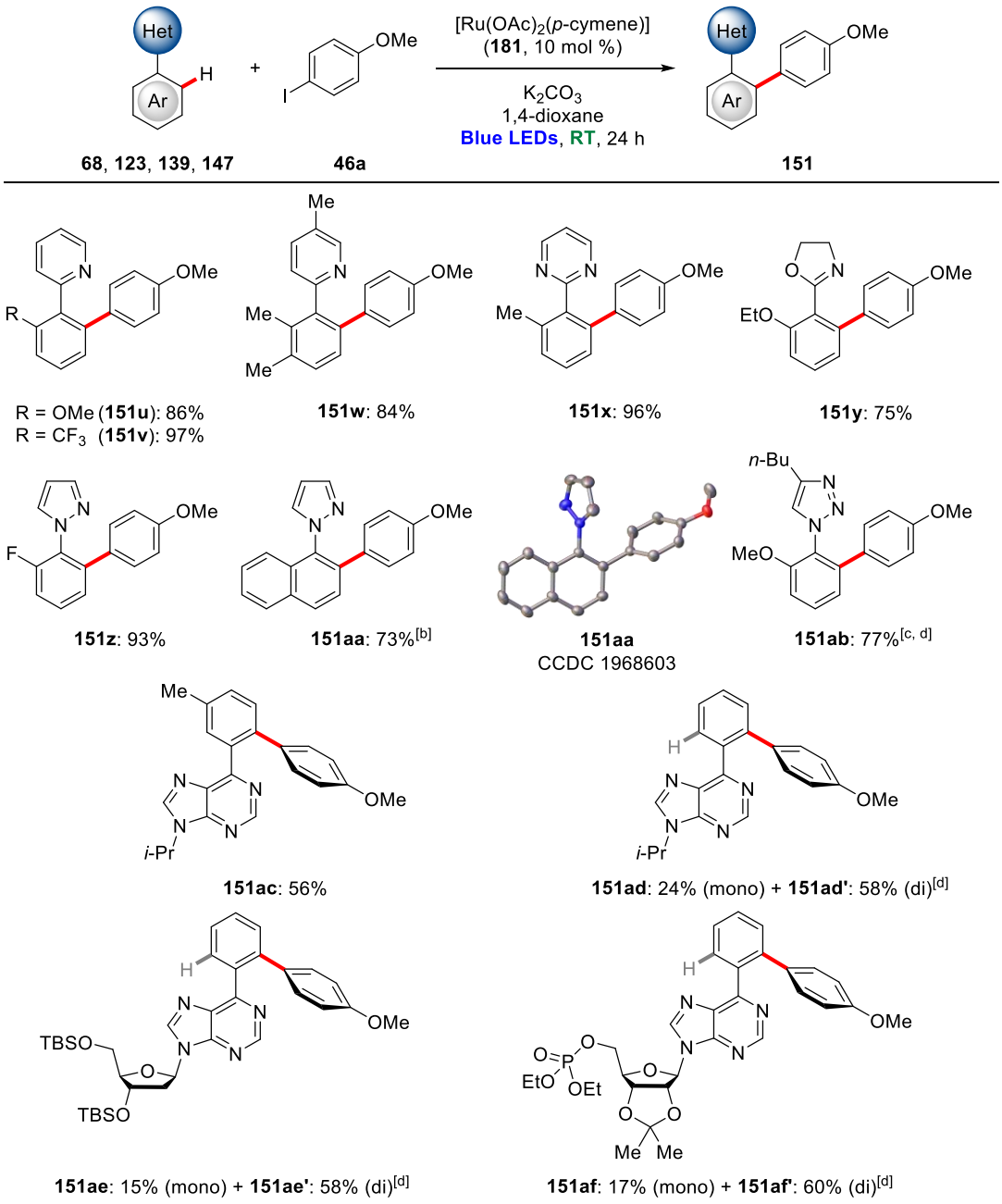
Scheme 91: Visible-light-induced ruthenium-catalyzed direct arylation of pyridine **68e**.



[a] Reaction conditions: **68e** (1.10–1.65 mmol), **215** (0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 10 mol %), K_2CO_3 (2.0–3.0 mmol), 1,4-dioxane (2.0 mL), 30–35 °C, 24 h, under N_2, **Blue LEDs**; yield of isolated products.

Scheme 92: Twofold and threefold C–H arylations of pyridine **68e**.

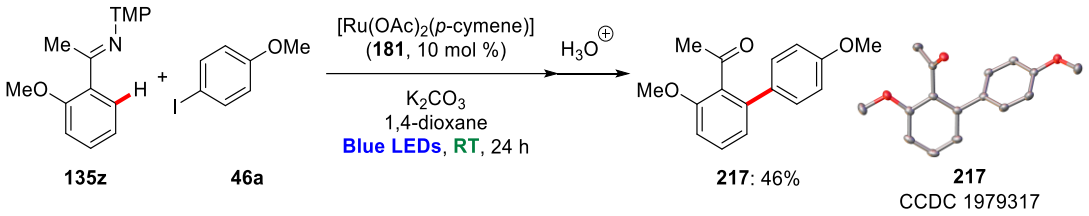
The photo-induced direct arylation was not limited to the assistance of pyridines. Indeed, arenes bearing pyrimidines (**151x**), transformable imidates (**151y**), removable pyrazoles (**151z** and **151aa**), and substituted click-triazoles (**151ab**) were effective in the photoredox direct arylations (Scheme 93). The potential of the visible-light-induced ruthenium-catalyzed direct arylation was highlighted by the late-stage diversification of biorelevant purines **151ac**–**151ad**, sensitive nucleoside **151ae**, and nucleotide **151af**.



[a] Reaction conditions: **68**, **123**, **139**, or **147** (0.50 mmol), **46a** (0.75 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 10 mol %), K_2CO_3 (1.0 mmol), 1,4-dioxane (2.0 mL), 30–35 °C, 24 h, under N_2, **Blue LEDs**; yield of isolated products. [b] Reactions were performed by M. Waeterschoot. [c] **46a** (1.50 mmol) and **181** (20 mol %). [d] DMA.

Scheme 93: Light-induced direct arylation of various heterorenes.

In addition, ketimine **135z** underwent the direct arylation followed by acidic hydrolysis to deliver the *ortho*-arylated acetophenone **217**, which was unambiguously confirmed by X-ray crystal structure analysis (Scheme 94).



Scheme 94: Photoredox arylation of ketimine **135z** at room temperature.

Despite of broad applicability of the reaction procedure, some unsuccessful starting materials, such as 2-pyridylindole, 1-naphthol, and 2-pyridylpyrrole, among others, as well as some ineffective aryl halides are listed in Figure 13.

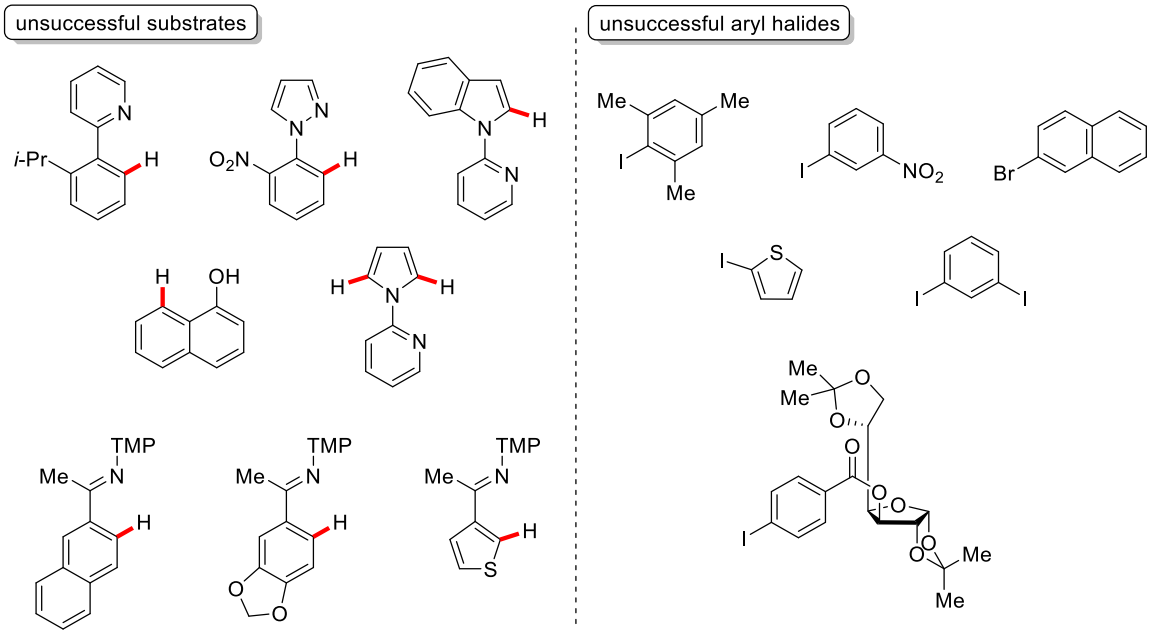
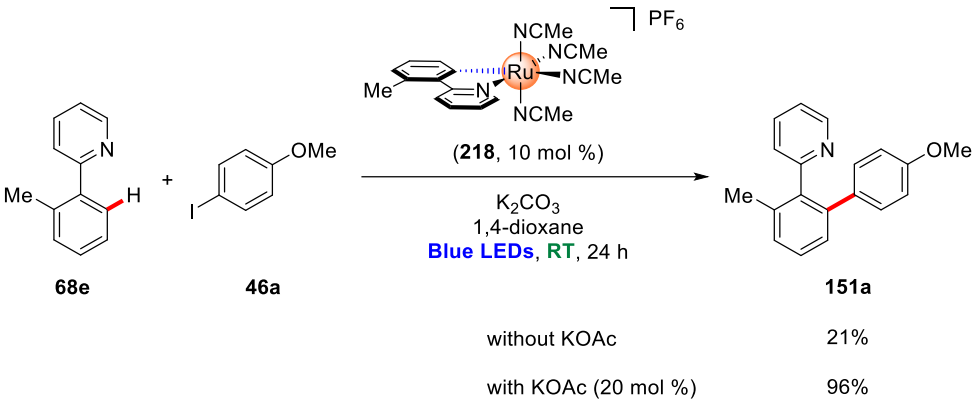


Figure 13: Unsuccessful substrates and aryl halides in the direct arylation.

3.7.3 Mechanistic Studies

Given the versatility of the room temperature photo-indued direct C–H arylations, mechanistic experiments were conducted to explain its working mode. A cationic monocyclometalated complex **218** proved to be highly effective in the presence of KOAc (Scheme 95). Moreover, the significant amount of free *p*-cymene was detected in the first period of the photo-induced transformation, which was found by J. Struwe.[114] These findings are suggestive of a *p*-cymene-free carboxylate-modified ruthenacycle as a catalytically active intermediate in the photoredox catalysis. Under the visible-light-driven direct arylations conditions, the quantum

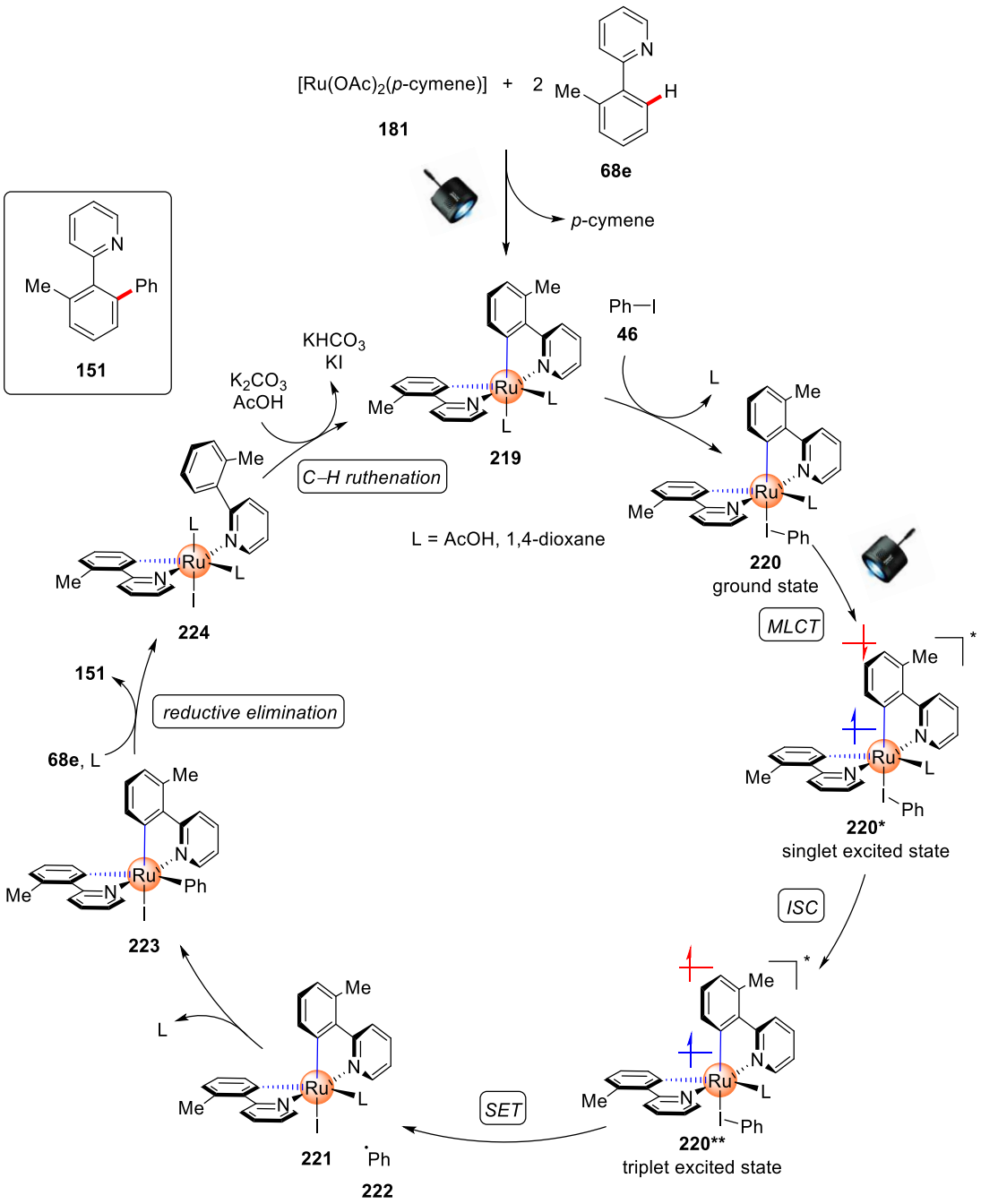
yield of Φ = 0.087 was observed.[114] Furthermore, an on/off light experiment performed by J. Struwe was indicative of the photoredox arylation not involving a radical chain process.[114]



Scheme 95: Light-driven direct arylation catalyzed by cyclometalated ruthenium **218**.

3.7.4 Plausible Catalytic Cycle

On the basis of the mechanistic findings in experiments and computations,[114] a plausible catalytic cycle was proposed, which commences by twofold carboxylate-assisted C–H ruthenation and dissociation of *p*-cymene, affording the corresponding biscyclometalated complex **219** (Scheme 96). The coordination of iodoarene to complex **219** leads to ruthenacycle **220**, which is excited by blue-light-absorption to form singlet excited species **220***. Relaxation through intersystem crossing (ISC) furnishes a long-lived triplet ruthenacycle **220****. Afterwards, an inner-sphere electron transfer (ISET) to iodoarene generates ruthenium(III) intermediate **221** and a phenyl radical (**222**), which readily recombine to form stable ruthenium(IV) intermediate **223**. Reductive elimination and ligand exchange deliver the arylated product **151** and ruthenium(II) complex **224**, which finally undergoes C–H bond activation to regenerate the photocatalytically active ruthenium(II) complex **219**.

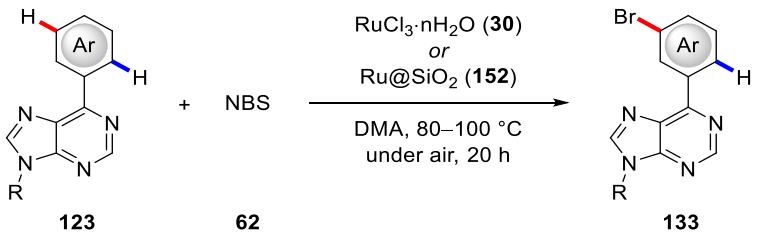


Scheme 96: Plausible catalytic cycle for visible-light-induced ruthenium-catalyzed direct arylation.

4 Summary and Outlook

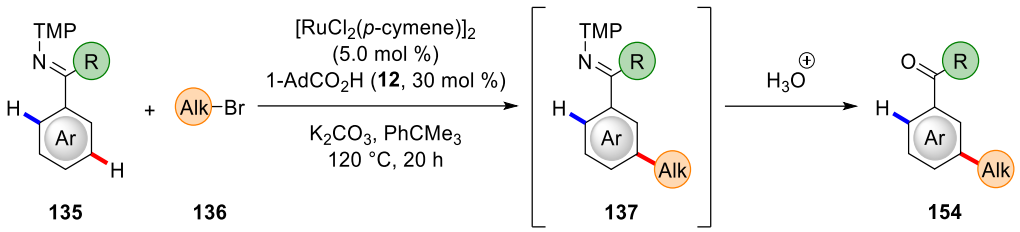
C–H and C–C activations have proven to bear great potential for the construction of C–C and C–Het bonds, with widespread applications to pharmaceutical, agrochemical chemistry, and material sciences. Ruthenium catalysis offers a powerful tool for site-selective C–H functionalizations. To further promote the catalytic C–H and C–C activation, a mechanistic understanding of the transformations is essential. Within this thesis, several new synthetic strategies were investigated for ruthenium-catalyzed site-selective C–H and C–C functionalization.

First, methods for remote *meta*-C–H bromination were developed (Scheme 97).[95] Both of homogeneous $RuCl_3 \cdot nH_2O$ (**30**) and heterogeneous ruthenium catalyst **152** showed comparable catalytic efficacy, furnishing the *meta*-brominated products **133** with excellent levels of positional selectivity. In addition to pyridine and pyrimidine, biorelevant purines **123** was for the first time employed as a directing group in remote C–H functionalization.



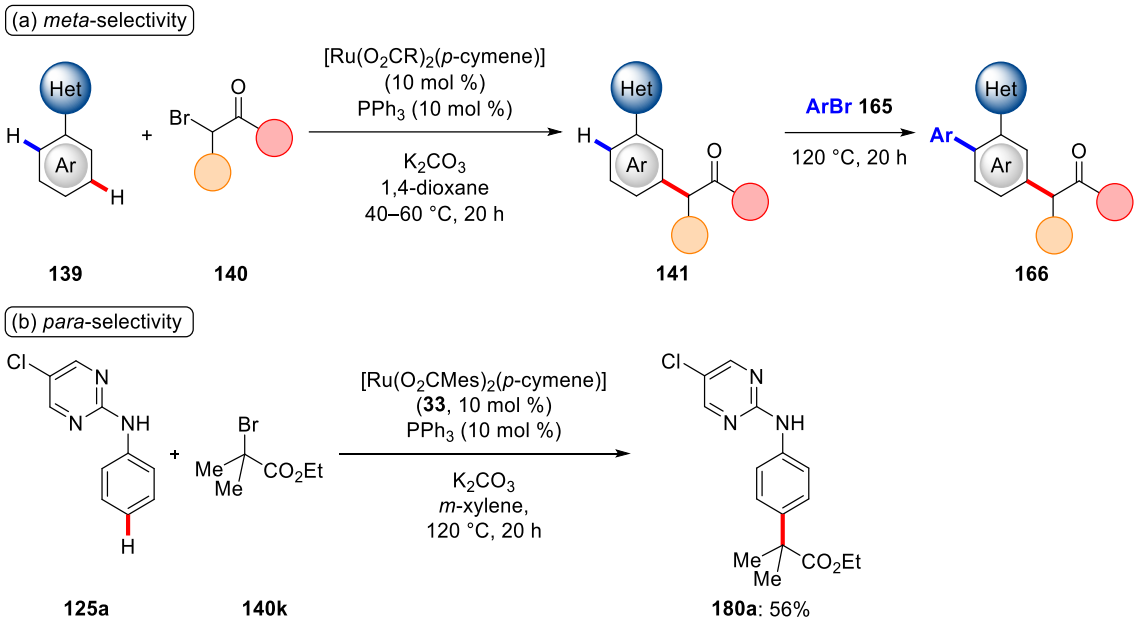
Scheme 97: Remote *meta*-C–H bromination of purine **123** by homogeneous or heterogenous ruthenium catalyst.

The second project focused on remote *meta*-C–H alkylations of arenes bearing with removable and transformable ketimines **135** (Scheme 98).[96] The alkylation reaction required $PhCMe_3$ as the solvent to prevent a side reaction at the benzylic position. Sequential one-pot remote alkylation followed by acid hydrolysis highlighted a broad substrate scope of different arylketimines **135** and a variety of secondary and tertiary alkyl bromides **136**. Moreover, the method was tolerant of various functional groups, valuable heterocycles, and structurally complex cholesterol. TMP-NH_2 could be recovered by an acid-base extraction. Mechanistic experiments gave strong support for a radical-type mechanism of *meta*-C–H alkylations. The power of this remote transformation set the stage for operationally simple one-pot protocols for the synthesis of *meta*-alkylated benzyl amines and the sequential twofold *meta*-/*ortho*-C–H activation. Furthermore, the transformation of the obtained alkylated phenones **154** provided a general platform to synthetically useful *meta*-substituted arenes, including anilines, phenols, acids, and indoles.



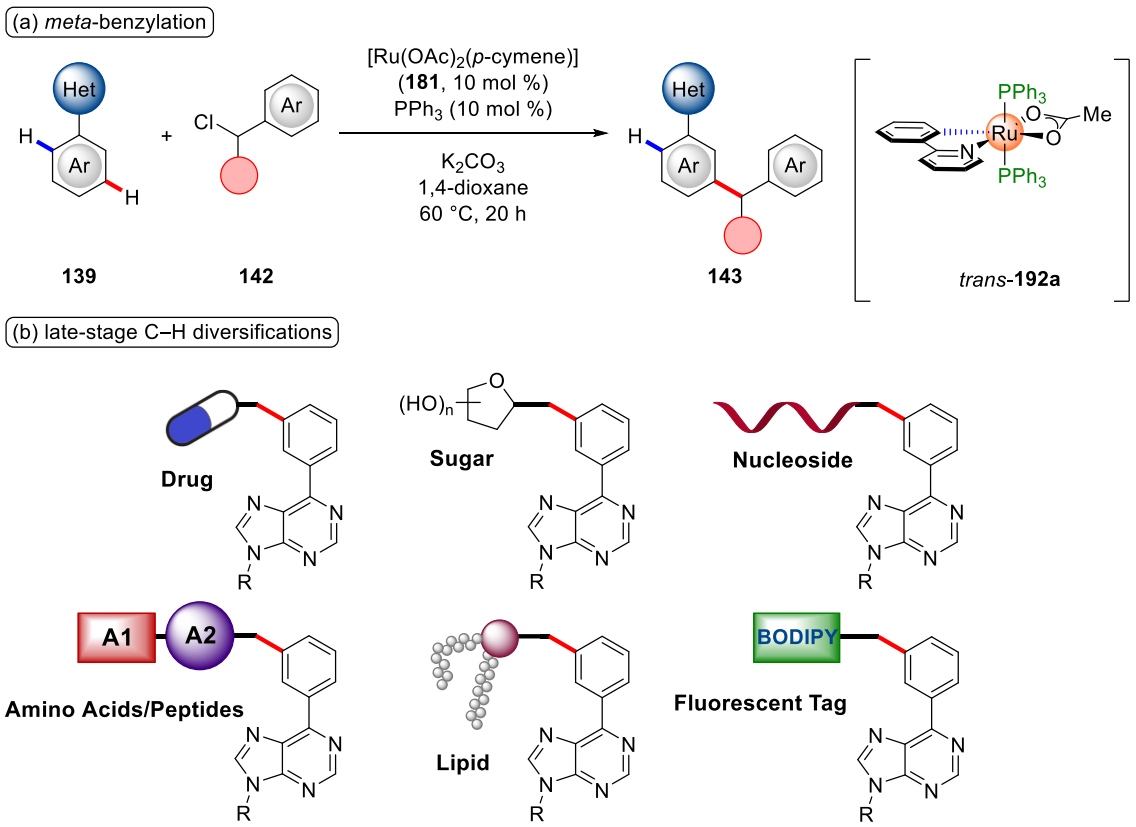
Scheme 98: Sequential one-pot ruthenium-catalyzed remote *meta*-alkylation.

In continuation of ruthenium-catalyzed remote transformations, the cooperation of carboxylate and phosphine ligands in ruthenium catalysis offered a general method for highly selective *meta*-C–H alkylations of *α*-bromo carbonyl compounds **140**, such as ketones, esters, and amides (Scheme 99a).[101] In contrast to the previous projects, the synergistic ruthenium catalysis was performed at lower reaction temperature. Moreover, the remote protocol was applicable to broad heterocyclic directing groups, such as pyridines, pyrimidines, removable pyrazoles, transformable oxazolines, and biologically relevant purines. In particular, remote alkylation of ketimine led to concise synthesis of an anti-inflammatory drug, *Ketoprofen* derivatives. Furthermore, the synergistic transformation was highlighted by sequential *meta*-alkylation/*ortho*-arylation in a user-friendly one-pot fashion, allowing for late-stage fluorescence labelling on purine bases. In addition to site-selectivity, the excellent chemo-selectivity of ruthenium-catalyzed twofold C–H activations was obtained by controlling reaction temperature. Detailed experimental mechanistic studies, including unprecedented EPR studies, were strongly supportive of a reversible C–H ruthenation and a single-electron transfer process, suggesting the formation of an arene-ligand-free cyclometalated ruthenium(III) complex. In contrast, the catalytic alkylation of *N*-pyrimidyl aniline **125a** took place on the arene at the position *para* to directing group, delivering the *para*-alkylated product **180a** (Scheme 99b). Detailed mechanistic investigations for *para*-selective transformation should be provided in the future.



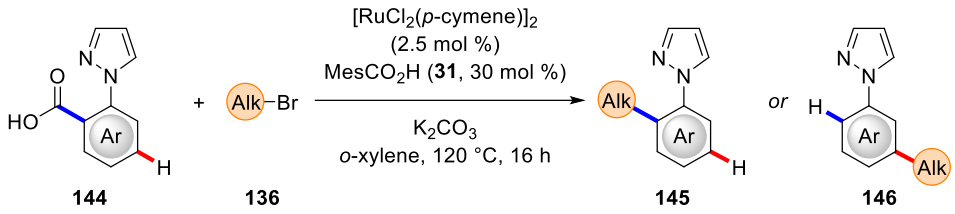
Scheme 99: Carboxylate-phosphine ruthenium catalysis for remote *meta*- or *para*-C–H alkylation.

In addition to *meta*-alkylation, the synergistic ruthenium catalysis proved to be a general tool for remote *meta*-benzylation (Scheme 100a).[104] The addition of phosphine ligand exerted an influence on positional selectivity of a ruthenium-catalyzed C–H benzylation. In addition to a broad substrate scope, the cooperative ruthenium catalysis set a stage for broadly effective late-stage C–H diversification of biologically relevant molecules and structurally complex drugs, including monosaccharides, nucleotides, triglycerides, amino acids, and peptides, as well as fluorescence label BODIPY (Scheme 100b). Particularly, fully unprotected *OH*-free monosaccharides proved to be tolerant. Mechanistic insights were suggestive of a reversible, carboxylate-assisted C–H ruthenation and a radical-involving mechanism. Moreover, the well-defined ruthenacycle *trans*-**192a** showed a reversible redox event and proved to be a key intermediate of the remote functionalization.



Scheme 100: Remote *meta*-benzylation and late-stage diversification.

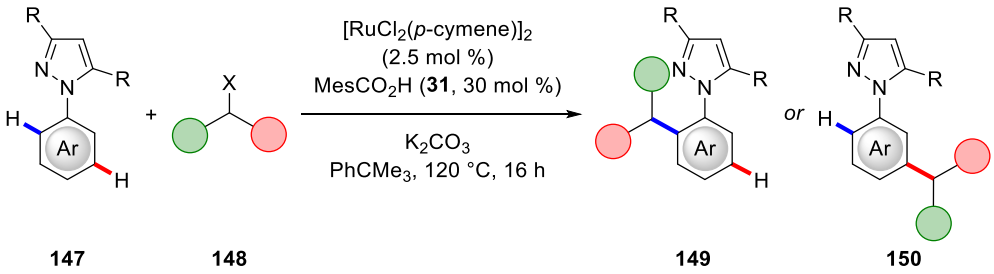
The next project focused on a ruthenium-catalyzed decarboxylative C–C activation enabled site-selective new C–C bond formation (Scheme 101).[106] Catalytic reaction of primary alkyl bromides provided the *ortho*-alkylated products **145**, whereas secondary and tertiary alkyl bromides mostly led to *meta*-selective alkylation. Surprisingly, the decarboxylative transformations of bromocyclohexane (**136j**) and *exo*-2-bromonorbornane (**136u**) afforded the alkylation at the *ortho* position, which were unusual for secondary alkyl halides. In case of *α*-bromo carbonyl compounds and secondary benzyl chlorides, the addition of phosphine ligand was essential for the decarboxylative alkylation. Mechanistic insights including experiments with radical scavengers and the observed benzylation as a side-reaction were supportive of the homolytic C–X bond cleavage of alkyl halide. Additionally, *p*-cymene-free cyclometalated ruthenium complex was proposed as a catalytically active species. To understand the working mode of C–C activation, more detailed mechanistic insights by experiment and computation should be investigated in the future.



Scheme 101: Ruthenium-catalyzed decarboxylative alkylation of acid **144**.

In spite of major breakthrough in C–C activation chemistry, the nucleophilic substitution of carboxylate to alkyl halide forming alkyl ester became the limitation of the decarboxylative transformation.

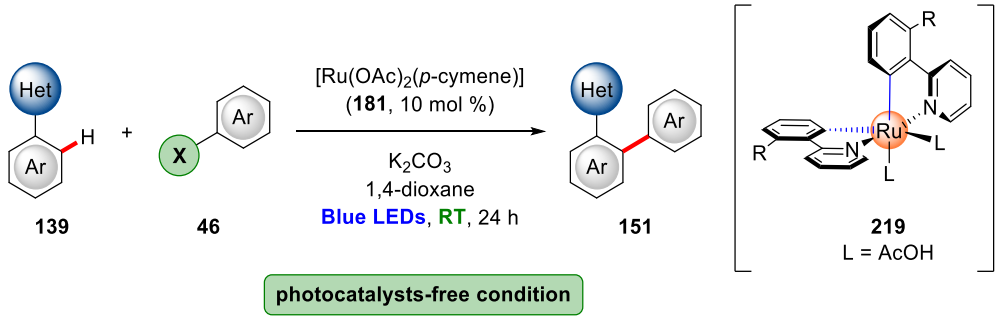
Owing to decarboxylative *ortho*-selective alkylation of bromocyclohexane and *exo*-2-bromonorbornane, positional selectivity in ruthenium-catalyzed C–H alkylation of pyrazoles was examined (Scheme 102).[106] Steric hindrance of alkyl halides and directing group of arenes had significant impacts on positional selectivity of the catalytic alkylation. Detailed mechanistic experiments were suggestive of two distinct mechanisms, a concerted oxidative addition/reductive elimination event for the *ortho*-C–H alkylation, while a SET pathway is proposed for the *meta*-functionalization. In addition, an arene-ligand-free ruthenacycle was identified as the catalytically active species in the catalysis.



Scheme 102: Site-selective *ortho*- or *meta*-alkylation of pyrazoles **147** under ruthenium catalysis.

The last project focused on integrating the chemistry of C–H activation and photoredox for direct arylation under exceedingly mild conditions (Scheme 103). Visible-light-induced ruthenium-catalyzed direct C–H arylation at room temperature was evolved without exogenous photocatalysts.[114] The catalytic method was tolerant of various functional groups and valuable heteroaromatic compounds, especially *NH*-free indole. In addition, twofold and threefold C–H activations of di- and triiodoarenes were highly effective. Notably, the power of this photoredox transformation set a stage for late-stage C–H arylation of sensitive nucleosides and nucleotides.

Detailed mechanistic investigations by experiments and computations were indicative of the *in situ* generated cyclometalated ruthenium complex **219** being a photocatalytically active species, which underwent light-induced metal-to-ligand charge-transfer and intersystem crossing to form long-lived triplet species. In addition, calculations were suggestive of an inner-sphere electron transfer process to be a preferable pathway.



Scheme 103: Visible-light-induced ruthenium-catalyzed direct arylation at room temperature.

5 Experimental Part

5.1 General Remarks

All reactions involving moisture- or air-sensitive reagents or products were performed under an atmosphere of nitrogen using pre-dried glassware and standard Schlenk techniques. If not otherwise mentioned yields refer to isolated compounds, estimated to be >95% pure as determined by ^{1}H-NMR.

Chromatography

Analytical thin layer chromatography (TLC) was performed on Merck, silica gel 60 F_{254} aluminum sheets. Detection was performed under UV light at 254 or 365 nm or developed by treatment with a potassium permanganate solution followed by careful warming or iodine spray technique. Chromatographic purification of products was accomplished by flash column chromatography on Merck Geduran® silica gel, grade 60 (0.040–0.063 mm, 230–400 mesh ASTM).

High-performance Liquid Chromatography

Analytical high-performance liquid chromatography (HPLC) for determination of the enantiomeric excess was performed on an Agilent *1260/1290 Infinity* equipped with Daicel *CHIRALPAK IA-3* or *IC-3* (4.6 mm × 250 mm, 3 µm particle size, 1 mL/min flow rate). Preparative HPLC from Agilent *1260 Infinity* equipped with VP 250/16 Nucleodur 100-10 C18 ec column.

Recycling Preparative HPLC

Recycling preparative HPLC or gel permeation chromatography (GPC) was performed on a Japan Analytical Industries (JAI) *LC-92XX II NEXT* system equipped with a JAIGEL 2.5HR or JAIGEL 2HH column. Chloroform was used as the solvent.

Cyclic Voltammetry

Cyclic Voltammetry (CV) spectra were measured using a Metrohm Autolab *PGSTAT204* workstation using a glassy-carbon disc electrode (3.0 mm diameter, CH Instruments) as a working electrode, a platinum wire (1.0 mm diameter, 99.99%, chempur) as a counter electrode and a

Ag/AgCl electrode as a reference electrode. The CV spectra were measured with *n*-Bu_4NPF_6 (0.1 M in 1,2-DCE, Sigma-Aldrich) as electrolyte and a sample concentration of 4 mM, at a 100 $mV \cdot s^{-1}$ scanning rate. The data were analysed with NOVA 2.1.3 software (Metrohm)

Electron Paramagnetic Resonance

Continuous-wave (CW) electron paramagnetic resonance (EPR) spectra were recorded at X-band microwave frequencies (9 GHz) using a Bruker *ElexSys E500* spectrometer with a Bruker *SuperX* CW bridge. The spectrometer was equipped with the Bruker *SHQ* rectangular microwave cavity (Bruker *4122SHQ*) and a helium flow cryostat (Oxford Instruments) for low temperature experiments.

Fluorescence Spectroscopy

Fluorescence excitation and emission data in solution were recorded on a Jasco® *FP-8500* spectrofluorometer. The scan speed was adjusted to 500 or 1000 nm/min. All compounds were measured at a concentration of 1 $mg \cdot L^{-1}$ in $CHCl_3$.

UV-VIS Spectroscopy

UV-Visible Spectroscopy was performed on a Jasco® *V-770* spectrophotometer. A baseline in the appropriate solvent was obtained prior to recording spectra.

Gas Chromatography

Gas chromatographic analysis (GC) was performed on an Agilent *7890A* GC system or Agilent *7890B* GC System equipped with an Agilent *HP-5* column (30 m, 0.320 mm diameter, 0.25 µm film thickness) and a flame-ionization detector (FID) using hydrogen as the carrier gas. Gas chromatography coupled with mass spectrometry (GC-MS) was performed on the same instrument equipped with an Agilent *HP-5MS* column (30 m, 0.250 mm diameter, 0.25 µm film thickness) and an Agilent *5875C* Triple-Axis-Detector or an Agilent *5977B* MSD. Mass spectra were obtained with electron-ionization (EI) at 70 eV in positive ion mode.

Infrared Spectroscopy

Infrared (IR) spectra were recorded on a Bruker *Alpha-P FT-IR* spectrometer with a diamond ATR probe in the range of 4000–400 cm^{-1}. Liquid samples were measured as film and solid samples neat. Analysis of the spectral data was carried out using *Opus 6* software. Absorption is given in wavenumbers (cm^{-1}).

Mass Spectrometry

Electron-ionization (EI) and EI high resolution mass spectra (HR-MS) were recorded on a Jeol *AccuTOF* instrument at 70 eV. Electrospray-ionization (ESI) mass spectra were obtained on Bruker micrOTOF and maXis instruments. All systems are equipped with *time-of-flight* (TOF) analyzers. Liquid injection field desorption/ionization (LIFDI) mass spectra were measured on a Jeol *AccuTOF* instrument with a Linden CMS. The ratios of mass to charge (*m*/*z*) are indicated and the intensity relative to the base peak (*I* = 100) is given in parenthesis.

Melting Points

Melting points (m.p.) were measured on a Stuart® Melting Point Apparatus SMP3 from Barloworld Scientific. All values are uncorrected.

Nuclear Magnetic Resonance Spectroscopy

Nuclear magnetic resonance (NMR) spectra were recorded on Varian *Mercury Plus 300*, *Inova 500*, *Inova 600* or Bruker *Avance III 300*, *Avance III HD 300*, *Avance III 400*, *Avance III HD 400*, *Avance Neo 400*, *Avance III HD 500* spectrometer. All measurements were performed at 298 K. Chemical shifts (δ) are reported in ppm. ^{1}H- and ^{13}C-NMR spectra were calibrated using the residual proton peak or carbon peak of the deuterated solvent, respectively (see table). For ^{19}F- and ^{31}P-NMR spectra were referenced using $CFCl_3$ and 85% phosphoric acid as external standard, respectively.

Solvent	^{1}H-NMR	^{13}C-NMR
$CDCl_3$	7.26 ppm	77.16 ppm
CD_2Cl_2	5.32 ppm	53.84 ppm
DMSO-d_6	2.50 ppm	39.52 ppm
Acetone-d_6	2.05 ppm	29.84, 206.26 ppm

Solvent	^{1}H-NMR	^{13}C-NMR
PhMe-d_8	2.08, 6.97, 7.01, 7.09 ppm	20.43, 125.13, 127.96, 128.87, 137.48 ppm
THF-d_8	1.72, 3.58 ppm	25.31, 67.21 ppm
MeCN-d_3	1.94 ppm	1.32, 118.26 ppm

The observed multiplicities are reported as follows: s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), hept (heptet), m (multiplet) or combinations thereof. The coupling constants *J* are given in Hertz (Hz). All spectra were analyzed using Mestrelab Research MestReNova v. 10.0.2 software.

Crystal Structure Analysis

X-ray structures were measured on a Bruker *D8* Venture four-circle-diffractometer from Bruker AXS GmbH equipped with a Photon II detector purchased from Bruker AXS GmbH and using microfocus IμS Cu/Mo radiation from Incoatec GmbH with HELIOS mirror optics and single-hole collimator from Bruker AXS GmbH.

Vacuum

A pressure of approx. $4 \cdot 10^{-1}$ mbar was measured on the employed rotary vane pump RZ6 from Vacuubrand®.

Solvents

All solvents used for work-up and purification were distilled prior to use. Solvents used in reactions involving air- or moisture-sensitive compounds were dried, distilled, and stored under an inert atmosphere of nitrogen or argon according to the following standard procedures.

Solvents purified by solvent purification system (*SPS-800*) from M. Braun: Dichloromethane, diethyl ether, *N*,*N*-dimethylformamide, tetrahydrofuran, toluene.

Solvents dried and distilled over Na using benzophenone as indicator: 1,4-Dioxane, *n*-hexane, toluene, *o*-xylene.

Solvents dried and distilled over CaH_2: 1,2-Dichloroethane, *N*,*N*-dimethylacetamide, *N*,*N*-dimethylformamide, dimethylsulfoxide, *N*-methyl-2-pyrrolidone, pyridine, triethylamine.

Solvents dried over molecular sieve and degassed by freeze-pump-thaw cycles: Acetonitrile (3 Å), acetonitrile-d_3 (3 Å), *tert*-butylbenzene (4 Å), chloroform-*d* (4 Å), dichloromethane-d_2 (4 Å), 2-methyltetrahydrofuran (4 Å), tetrahydrofuran-d_8 (4 Å), toluene-d_8 (4 Å).

Methanol was dried and distilled over $Mg(OMe)_2$.

Water was degassed before its use by repeated freeze-pump-thaw cycles.

Reagents

Chemicals obtained from commercial sources were used without further purification unless stated otherwise. K_2CO_3 was dried at 140 °C and $4 \cdot 10^{-1}$ mbar for 16 h and stored under an atmosphere of N_2.

The following compounds were synthesized according to previously described literature protocols:

2-Arylpyridines **68a**, **68d**, **68e**, **68h**,[115] ruthenacycle **98**, **218**,[46] purines **123a**, **123d**,[116] **123l**–**123n**,[117] ketimines **135**,[118] 1-bromo-1-methylcyclohexane (**136a**),[119] 2-arylpyrimidines **139a**–**139c**, **139e**–**139g**,[120] 2-(*o*-tolyl)pyrimidine (**139d**),[121] 4-butyl-1-(2-methoxyphenyl)-1*H*-1,2,3-triazole (**139m**),[41] arylpyrazoles **147a**, **147d**–**147j**,[122] 4-bromo-1-phenyl-1*H*-pyrazole (**147b**),[123] 3,5-dimethyl-1-phenyl-1*H*-pyrazole (**147c**),[124] $[Ru(O_2CAd)_2(p\text{-cymene})]$ (**163**),[33] $[Ru(OPiv)_2(p\text{-cymene})]$,[33] benzyl chlorides **142d**–**142e**, **186n**,[125] BODIPY **186a**,[126] 2,7-diiodo-9*H*-fluorene (**215a**),[127] 3,6-diiodo-9*H*-carbazole (**215b**),[128] and tris(4-iodophenyl)amine (**215c**).[129]

The following chemicals were kindly provided by the persons named below:

Karsten Rauch: $[RuCl_2(p\text{-cymene})]_2$, $[Ru(O_2CMes)_2(p\text{-cymene})]$ (**33**), $[Ru(OAc)_2(p\text{-cymene})]$ (**181**).

Dr. David J. Burns: purines **123e**–**123g**.

Dr. Svenja Warratz: $Ru@SiO_2$ (**152**), $[RuCl_2(PhCMe_3)]_2$, $Ru(OAc)_2(PPh_3)_2$, $Ru(OAc)_2(PPh_3)_3$.

Prof. Dr. Hongjun Ren: 1-(4-bromophenyl)pyrene (**165d**).

Nikolaos Kaplaneris: 5-chloro-*N*-phenylpyrimidin-2-amine (**125a**), 2-(4-methoxyphenyl)-4,5-dihydrooxazole (**139i**), 2-(4-bromophenyl)-4,5-dihydrooxazole (**139j**), 2-(2-ethoxyphenyl)-4,5-

dihydrooxazole (**139k**), 2-bromo-1-morpholinopropan-1-one (**140e**), methyl 2,5-dibromopentanoate (**140f**), 2-bromo-*N*,*N*-diethylpropanamide (**140h**), (tetrahydrofuran-2-yl)methyl 2-bromopropanoate (**140l**), benzoic acid **178**.

Dr. Torben Rogge: 2-(2-methoxyphenyl)pyridine (**68f**), 2-[2-(trifluoromethyl)phenyl]pyridine (**68g**).

Dr. Joachim Loup: chiral phosphoramidite ligands.

5.2 General Procedures

5.2.1 General Procedure A: Ruthenium-Catalyzed meta-Selective Bromination

A microwave vial was charged with purine **123** or heteroarene **68**, **139**, **147** (0.30 mmol), NBS (**62**, 107 mg, 0.60 mmol) and **152** (0.14 mmol[Ru]/g, 214 mg, 10 mol %) in DMA (0.6 mL) and the mixture was stirred open to air at 80–100 °C. After 20 h, the resulting mixture was filtered and washed with CH_2Cl_2 (20 mL). The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc) yielded *meta*-brominated products **133** or **153**.

5.2.2 General Procedure B: Ruthenium(II)-Catalyzed Remote meta-C–H Alkylations of Ketimines using 1-AdCO₂H as the Ligand

Ketimine **135** (0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 25.0 µmol, 5.0 mol %), 1-AdCO_2H (**12**, 27.3 mg, 0.15 mmol, 30 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL pressure tube. The tube was evacuated and purged with N_2 for three times. Alkyl bromide **136** (1.50 mmol) and $PhCMe_3$ (2.0 mL) were then added and the mixture was stirred at 120 °C for 20 h. At ambient temperature, HCl (2 N, 3.0 mL) was added, and the resulting mixture was stirred for an additional 3 h, and then extracted with EtOAc or Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc or *n*-pentane/Et_2O) yielded phenone **154**.

5.2.3 General Procedure C: Ruthenium(II)-Catalyzed Remote meta-C–H Alkylations of Ketimines using Piv-Ile-OH as the Ligand

Ketimine **135** (0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 25.0 µmol, 5.0 mol %), Piv-Ile-OH (**155**, 32.3 mg, 0.15 mmol, 30 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL pressure tube. The tube was evacuated and purged with N_2 for three times. Alkyl bromide **136** (1.50 mmol) and $PhCMe_3$ (2.0 mL) were then added and the mixture was stirred at 120 °C for 20 h. At ambient temperature, HCl (2 N, 3.0 mL) was added, and the resulting mixture was stirred for an additional 3 h, and then extracted with EtOAc or Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc or *n*-pentane/Et_2O) yielded phenone **154**.

5.2.4 General Procedure D: Ruthenium(II)-Catalyzed Remote meta-C–H Alkylations of Ketimines Followed by Reduction in One-Pot Fashion

Ketimine **135** (0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 25.0 µmol, 5.0 mol %), 1-$AdCO_2H$ (**12**, 27.3 mg, 0.15 mmol, 30 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL pressure tube. The tube was evacuated and purged with N_2 for three times. Alkyl bromide **136** (1.50 mmol) and $PhCMe_3$ (2.0 mL) were then added and the mixture was stirred at 120 °C for 20 h. Then, a solution of $ZnCl_2$ in THF (1.0 M, 0.50 mmol), $NaBH_3CN$ (63.5 mg, 2.00 mmol) and MeOH (1.5 mL) were successively added to the reaction mixture at ambient temperature. The reaction mixture was stirred at ambient temperature for 16 h and then distributed between Et_2O (8 mL) and sat. aq. K_2CO_3 (8 mL). The aqueous phase was extracted with Et_2O (2 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (SiO_2, *n*-hexane/EtOAc) yielded **157**.

5.2.5 General Procedure E: Ruthenium(II)-Catalyzed Remote meta-C–H Alkylations using PPh_3 as the Ligand

Heteroarene **68b**, **123a**, **139**, or **147** (0.50 mmol), $[Ru(O_2CAd)_2(p\text{-cymene})]$ (**163**, 29.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 for three times. Alkyl bromide **140** (1.50 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 40 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and

washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc) yielded *meta*-alkylated product **141**.

5.2.6 General Procedure F: Ruthenium(II)-Catalyzed Sequential meta-Alkylation/ortho-Arylation

Heteroarene **123a** or **147** (0.50 mmol), [Ru(O_2CAd)$_2$(*p*-cymene)] (**163**, 29.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (276 mg, 2.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 for three times. Alkyl bromide **140** (1.50 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, bromoarene **165** (1.00 or 1.50 mmol) was added to the reaction mixture at ambient temperature and the mixture was stirred at 120 °C for an additional 20 h. The resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc) yielded product **166**.

5.2.7 General Procedure G: Ruthenium(II)-Catalyzed Sequential meta-Alkylation/ortho-Arylation in One-Pot Fashion by Temperature Control

Heteroarene **139** or **147** (0.50 mmol), [Ru(O_2CAd)$_2$(*p*-cymene)] (**163**, 29.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (276 mg, 2.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 for three times. Alkyl bromide **140a** (1.50 mmol), bromoarene **165** (1.50 mmol), and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 40 °C. After 18 h, the reaction mixture was stirred at 120 °C for an additional 18 h. Afterwards, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc) yielded product **166**.

5.2.8 General Procedure H: Photocatalytic Decarboxylation

Carboxylic acid **175** or **178** (0.20 mmol), bis(4-chlorophenyl)disulfide (5.8 mg, 20.0 µmol, 10 mol %), and photocatalyst [Mes-Acr-Me][ClO_4] (**176**, 1.0–4.8 mol %) were placed in 10 mL vial. The vial was evacuated and purged with N_2 for three times. To the reaction mixture was added 2,6-lutidine (5 µL, 40.0 µmol, 20 mol %) and 1,2-DCE (8.0 mL). The mixture was degassed for

5 min. The reaction mixture was stirred under blue LED irradiation (8 W). After 16 h, the solvent was removed *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc or CH_2Cl_2/HOAc) yielded product **177** or **179**.

5.2.9 General Procedure I: Ruthenium(II)-Catalyzed meta-C–H Benzylation of Heteroarenes

Heteroarene **68**, **139** or purine **123** (0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 17.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Benzyl chloride **142** (1.50 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc) yielded *meta*-benzylated product **143** or **185**.

5.2.10 General Procedure J: Late-Satge Diversification through Ruthenium(II)-Catalyzed meta-C–H Activation

Purine **123** (0.25 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 8.9 mg, 25.0 µmol, 10 mol %), PPh_3 (6.6 mg, 25.0 µmol, 10 mol %) and K_2CO_3 (69 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Alkyl halide **186** (0.50 mmol) and 1,4-dioxane (1.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc) yielded *meta*-alkylated product **187**.

5.2.11 General Procedure K: Ruthenium(II)-Catalyzed C–C Alkylation of Acids 144

Carboxylic acid **144** (0.50 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (7.7 mg, 12.5 µmol, 2.5 mol %), $MesCO_2H$ (**31**, 24.6 mg, 0.15 mmol, 30 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Alkyl bromide **136** (1.50 mmol) and *o*-xylene (1.0 mL) were then added. The Schlenk tube was degassed and filled with N_2 three times and the mixture was stirred at 120 °C. After 16 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*.

Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc) yielded alkylated product **145** or **146**.

5.2.12 General Procedure L: Ruthenium(II)-Catalyzed C–C Alkylation of Acids 144 using PPh_3 as the Ligand

Carboxylic acid **144** (0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 12.5 µmol, 2.5 mol %), $MesCO_2H$ (**31**, 24.6 mg, 0.15 mmol, 30 mol %), PPh_3 (6.6 mg, 25.0 µmol, 5 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Alkyl bromide **140** or benzyl chloride **142** (1.50 mmol) and $PhCMe_3$ (1.0 mL) were then added. The Schlenk tube was degassed and filled with N_2 three times and the mixture was stirred at 120 °C. After 16 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc) yielded *meta*-alkylated product **141g** or **202**.

5.2.13 General Procedure M: Ruthenium-Catalyzed C–H Alkylations of Pyrazoles

Pyrazole **147** (0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 12.5 µmol, 2.5 mol %), $MesCO_2H$ (**31**, 24.6 mg, 0.15 mmol, 30 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Alkyl bromide **136** (0.75–1.50 mmol) and $PhCMe_3$ (1.0 mL) were then added and the mixture was stirred at 120 °C. After 16 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc) yielded alkylated product **145** or **146**.

5.2.14 General Procedure N: Photo-Induced Ruthenium-Catalyzed C–H Arylations at Room Temperature

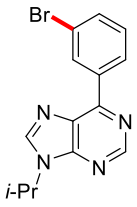
Heteroarene **68**, **123**, **139**, or **147** (0.50 mmol), $[Ru(OAc)_2(p\text{-cymene})]$ (**181**, 17.7 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a 10 mL vial. The vial was capped with a septum and wrapped with parafilm. The vial was evacuated and purged with N_2 three times. Aryl iodide **46** (0.75 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred under visible light irradiation (2 × Kessil A360N, temperature was maintained between 30 °C and 35 °C). After 24 h, the resulting mixture was filtered through a pad of silica gel and washed with

EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc) yielded *ortho*-arylated product **151**.

5.3 Experimental Procedures and Analytical Data

5.3.1 Ruthenium-Catalyzed meta-Selective Bromination

6-(3-Bromophenyl)-9-*iso*-propyl-9*H*-purine (133a)



The general procedure **A** was followed using purine **123a** (59.6 mg, 0.25 mmol) at 80 °C. After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **133a** (49.6 mg, 63%) as a white soild.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.99 (s, 1H), 8.94 (ddd, *J* = 2.1, 1.6, 0.4 Hz, 1H), 8.78 (ddd, *J* = 7.9, 1.6, 1.1 Hz, 1H), 8.18 (s, 1H), 7.62 (ddd, *J* = 7.9, 2.1, 1.1 Hz, 1H), 7.41 (ddd, *J* = 7.9, 7.9, 0.4 Hz, 1H), 4.97 (hept, *J* = 6.8 Hz, 1H), 1.66 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 152.8 (C_q), 152.2 (C_q), 151.9 (CH), 142.3 (CH), 137.7 (C_q), 133.7 (CH), 132.3 (CH), 131.5 (C_q), 130.1 (CH), 128.4 (CH), 122.8 (C_q), 47.3 (CH), 22.5 (CH_3).

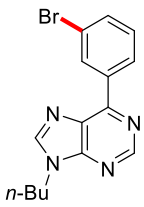
IR (ATR): $\tilde{\nu}$ = 2977, 1576, 1553, 1447, 1324, 1217, 786, 736, 698, 646 cm^{-1}.

m.p.: 120–121 °C.

MS (EI) *m*/*z* (relative intensity): 318 (68) [M(^{81}Br)]$^+$, 316 (69) [M(^{79}Br)]$^+$, 276 (92) [M(^{81}Br)–*i*-Pr]$^+$, 274 (94) [M(^{79}Br)–*i*-Pr]$^+$, 195 (100) [M–*i*-Pr–Br]$^+$, 141 (27), 44 (48).

HR-MS (ESI): *m*/*z* calcd for $C_{14}H_{14}{}^{79}BrN_4^+$ [M+H]$^+$ 317.0396, found 317.0399.

6-(3-Bromophenyl)-9-*n*-butyl-9*H*-purine (133b)



The general procedure **A** was followed using purine **123b** (75.7 mg, 0.30 mmol) at 80 °C. After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **133b** (67.7 mg, 68%) as a white soild.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.02 (s, 1H), 8.97 (dd, *J* = 2.0, 1.6 Hz, 1H), 8.80 (ddd, *J* = 7.9, 1.6, 1.3 Hz, 1H), 8.13 (s, 1H), 7.65 (ddd, *J* = 8.0, 2.0, 1.3 Hz, 1H), 7.43 (dd, *J* = 8.0, 7.9 Hz, 1H), 4.32 (t, *J* = 7.3 Hz, 2H), 2.00–1.87 (m, 2H), 1.47–1.33 (m, 2H), 0.98 (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 152.9 (C_q), 152.7 (C_q), 152.2 (CH), 144.6 (CH), 137.7 (C_q), 133.8 (CH), 132.4 (CH), 131.1 (C_q), 130.1 (CH), 128.5 (CH), 122.9 (C_q), 43.8 (CH_2), 31.9 (CH_2), 19.9 (CH_2), 13.5 (CH_3).

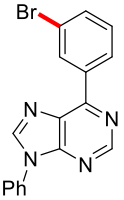
IR (ATR): $\tilde{\nu}$ = 2957, 1579, 1450, 1216, 869, 580, 693, 580, 498, 420 cm^{-1}.

m.p.: 70–71 °C.

MS (EI) *m*/*z* (relative intensity): 332 (13) [M(^{81}Br)]$^+$, 330 (75) [M(^{79}Br)]$^+$, 289 (100), 274 (42), 208 (26), 195 (77), 168 (28), 141 (33).

HR-MS (EI): *m*/*z* calcd for $C_{15}H_{15}{}^{79}BrN_4{}^+$ [M]$^+$ 330.0475, found 330.0476.

6-(3-Bromophenyl)-9-phenyl-9*H*-purine (133c)



The general procedure **A** was followed using purine **123c** (81.7 mg, 0.30 mmol) at 100 °C. After 20 h, purification by column chromatography (*n*-hexane/EtOAc 4:1) yielded **133c** (52.4 mg, 50%) as a white soild.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.08 (s, 1H), 9.01 (ddd, *J* = 2.1, 1.6, 0.4 Hz, 1H), 8.84 (ddd, *J* = 7.9, 1.6, 1.1 Hz, 1H), 8.41 (s, 1H), 7.77–7.73 (m, 2H), 7.67 (ddd, *J* = 8.0, 2.1, 1.1 Hz, 1H), 7.65–7.59 (m, 2H), 7.53–7.48 (m, 1H), 7.46 (ddd, *J* = 8.0, 7.9, 0.4 Hz, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 153.6 (C_q), 153.0 (CH), 152.4 (C_q), 143.6 (CH), 137.5 (C_q), 134.3 (C_q), 134.0 (CH), 132.5 (CH), 131.5 (C_q), 130.2 (CH), 130.0 (CH), 128.6 (CH), 128.5 (CH), 123.7 (CH), 122.9 (C_q).

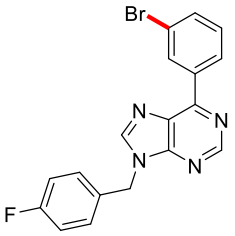
IR (ATR): $\tilde{\nu}$ = 3050, 1571, 1507, 1328, 1225, 1192, 928, 755, 686, 645 cm^{-1}.

m.p.: 180–181 °C.

MS (EI) *m*/*z* (relative intensity): 352 (97) [M(^{81}Br)]$^+$, 350 (100) [M(^{79}Br)]$^+$, 323 (17), 271 (42) [M–Br]$^+$, 244 (16), 141 (19), 77 (59), 51 (28).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{11}{}^{79}BrN_4{}^+$ [M]$^+$ 350.0162, found 350.0161.

6-(3-Bromophenyl)-9-(4-fluorobenzyl)-9*H*-purine (133e)



The general procedure **A** was followed using purine **123e** (91.3 mg, 0.30 mmol) at 80 °C. After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **133e** (74.1 mg, 64%) as a white soild.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.03 (s, 1H), 8.96 (dd, *J* = 1.9, 1.7 Hz, 1H), 8.79 (ddd, *J* = 7.9, 1.7, 1.1 Hz, 1H), 8.09 (s, 1H), 7.63 (ddd, *J* = 8.0, 1.9, 1.1 Hz, 1H), 7.41 (dd, *J* = 8.0, 7.9 Hz, 1H), 7.32 (dd, *J* = 8.8, 5.2 Hz, 2H), 7.04 (dd, *J* = 8.8, 8.9 Hz, 2H), 5.43 (s, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 162.7 (d, $^{1}J_{C-F}$ = 248 Hz, C_q), 153.0 (C_q), 152.5 (C_q), 152.5 (CH), 144.2 (CH), 137.5 (C_q), 133.8 (CH), 132.4 (CH), 130.9 (C_q), 130.9 (C_q), 130.1 (CH), 129.7 (d, $^{3}J_{C-F}$ = 8 Hz, CH), 128.4 (CH), 122.8 (C_q), 116.1 (d, $^{2}J_{C-F}$ = 22 Hz, CH), 46.6 (CH_2).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = −112.8 (tt, *J* = 8.9, 5.2 Hz).

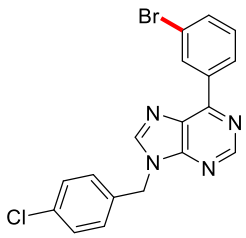
IR (ATR): $\tilde{\nu}$ = 3064, 1577, 1552, 1506, 1224, 1202, 765, 733, 697, 641 cm^{-1}.

m.p.: 155−156 °C.

MS (EI) *m*/*z* (relative intensity): 384 (36) [M(^{81}Br)]$^+$, 383 (38) [M(^{81}Br)−H]$^+$, 382 (36) [M(^{79}Br)]$^+$, 381 (32) [M(^{79}Br)−H]$^+$, 207 (91), 109 (100), 44 (59).

HR-MS (ESI): *m*/*z* calcd for $C_{18}H_{13}{}^{79}BrFN_4^+$ [M+H]$^+$ 383.0302, found 383.0300.

6-(3-Bromophenyl)-9-(4-chlorobenzyl)-9*H*-purine (133f)



The general procedure **A** was followed using purine **123f** (96.3 mg, 0.30 mmol) at 80 °C. After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **133f** (76.2 mg, 64%) as a white soild.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.03 (s, 1H), 8.96 (dd, *J* = 1.9, 1.7 Hz, 1H), 8.79 (ddd, *J* = 7.9, 1.7, 1.1 Hz, 1H), 8.10 (s, 1H), 7.64 (ddd, *J* = 8.0, 1.9, 1.1 Hz, 1H), 7.42 (dd, *J* = 8.0, 7.9 Hz, 1H), 7.33 (d_{AB}, *J* = 8.8 Hz, 2H), 7.26 (d_{AB}, *J* = 8.8 Hz, 2H), 5.43 (s, 2H).

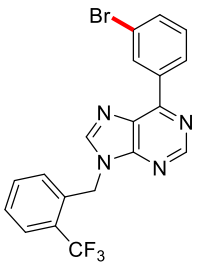
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 153.1 (C_q), 152.5 (C_q), 152.5 (CH), 144.2 (CH), 137.5 (C_q), 134.6 (C_q), 133.9 (CH), 133.5 (C_q), 132.4 (CH), 130.9 (C_q), 130.1 (CH), 129.3 (CH), 129.1 (CH), 128.4 (CH), 122.8 (C_q), 46.6 (CH_2).

IR (ATR): $\tilde{\nu}$ = 3058, 2926, 1578, 1495, 1324, 1213, 1091, 764, 695, 638 cm^{-1}.

m.p.: 166−167 °C.

HR-MS (ESI): *m*/*z* calcd for $C_{18}H_{13}{}^{79}Br^{35}ClN_4^+$ $[M+H]^+$ 399.0007, found 398.9993.

6-(3-Bromophenyl)-9-[2-(trifluoromethyl)benzyl]-9*H*-purine (133g)



The general procedure **A** was followed using purine **123g** (106 mg, 0.30 mmol) at 80 °C. After 20 h, purification by column chromatography (*n*-hexane/EtOAc 4:1) yielded **133g** (86.4 mg, 66%) as a white soild.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.05 (s, 1H), 8.98 (dd, *J* = 1.9, 1.8 Hz, 1H), 8.80 (ddd, *J* = 7.9, 1.8, 1.1 Hz, 1H), 8.09 (s, 1H), 7.75 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.64 (ddd, *J* = 8.0, 1.9, 1.1 Hz, 1H), 7.50−7.43 (m, 2H), 7.42 (dd, *J* = 8.0, 7.9 Hz, 1H), 7.22 (dd, *J* = 7.5, 1.6 Hz, 1H), 5.70 (s, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 153.3 (C_q), 152.9 (C_q), 152.7 (CH), 144.5 (CH), 137.5 (C_q), 133.9 (CH), 133.5 (q, $^3J_{C-F}$ = 2 Hz, C_q), 132.7 (q, $^4J_{C-F}$ = 1 Hz, CH), 132.5 (CH), 130.8 (C_q), 130.1 (CH), 129.7 (CH), 128.7 (CH), 128.5 (CH), 128.1 (q, $^2J_{C-F}$ = 31 Hz, C_q), 126.5 (q, $^3J_{C-F}$ = 6 Hz, CH), 124.2 (q, $^1J_{C-F}$ = 274 Hz, C_q), 122.9 (C_q), 43.5 (q, $^4J_{C-F}$ = 3 Hz, CH_2).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = −59.2 (s).

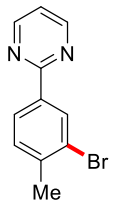
IR (ATR): $\tilde{\nu}$ = 3086, 1578, 1555, 1309, 1164, 1100, 1033, 774, 730, 633 cm^{-1}.

m.p.: 145−146 °C.

MS (EI) *m*/*z* (relative intensity): 434 (17) $[M(^{81}Br)]^+$, 433 (15) $[M(^{81}Br)-H]^+$, 432 (18) $[M(^{79}Br)]^+$, 431 (13) $[M(^{79}Br)-H]^+$, 365 (57) $[M(^{81}Br)-CF_3]^+$, 363 (51) $[M(^{79}Br)-CF_3]^+$, 207 (100), 159 (31), 44 (63).

HR-MS (ESI): *m*/*z* calcd for $C_{19}H_{13}{}^{79}BrF_3N_4$ $[M+H]^+$ 433.0270, found 433.0266.

2-(3-Bromo-4-methylphenyl)pyrimidine (153a)



The general procedure **A** was followed using 2-(*p*-tolyl)pyrimidine (**139b**, 51.1 mg, 0.30 mmol) at 80 °C. After 20 h, purification by column chromatography (*n*-hexane/CH_2Cl_2 1:1) yielded **153a** (60.1 mg, 80%) as a white soild.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.78 (d, *J* = 4.8 Hz, 2H), 8.63 (d, *J* = 1.8 Hz, 1H), 8.27 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.34 (d, *J* = 7.9 Hz, 1H), 7.17 (t, *J* = 4.8 Hz, 1H), 2.46 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 163.3 (C_q), 157.1 (CH), 140.5 (C_q), 136.9 (C_q), 131.9 (CH), 130.8 (CH), 126.8 (CH), 125.2 (C_q), 119.2 (CH), 23.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3069, 2971, 1566, 1541, 1409, 1374, 1032, 795, 676 cm^{-1}.

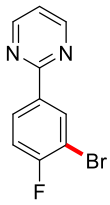
m.p.: 69−70 °C.

MS (ESI) *m/z* (relative intensity): 251 (98) $[M(^{81}Br)+H]^+$, 249 (100) $[M(^{79}Br)+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{11}H_{10}{}^{79}BrN_2{}^+$ $[M+H]^+$ 249.0022, found 249.0025.

The spectral data are in accordance with those reported in the literature.[78]

2-(3-Bromo-4-fluorophenyl)pyrimidine (153b)



The general procedure **A** was followed using 2-(4-fluorophenyl)pyrimidine (**139c**, 52.3 mg, 0.30 mmol) at 100 °C. After 20 h, purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc 7:2:1) yielded **153b** (21.3 mg, 28%) as a white soild.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.79 (d, *J* = 4.9 Hz, 2H), 8.70 (dd, *J* = 6.9, 2.2 Hz, 1H), 8.39 (ddd, *J* = 8.7, 4.9, 2.2 Hz, 1H), 7.22 (dd, *J* = 8.7, 8.3 Hz, 1H), 7.21 (t, *J* = 4.9 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 162.5 (d, $^5J_{C-F}$ = 1 Hz, C_q), 160.7 (d, $^1J_{C-F}$ = 251 Hz, C_q), 157.2 (CH), 135.0 (d, $^4J_{C-F}$ = 4 Hz, C_q), 133.5 (CH), 128.9 (d, $^3J_{C-F}$ = 8 Hz, CH), 119.3 (CH), 116.4 (d, $^2J_{C-F}$ = 23 Hz, CH), 109.4 (d, $^2J_{C-F}$ = 21 Hz, C_q).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = −104.7 (ddd, *J* = 8.3, 6.9, 4.9 Hz).

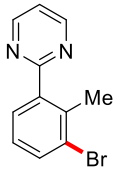
IR (ATR): $\tilde{\nu}$ = 2927, 1557, 1489, 1408, 1315, 1242, 810, 796, 675, 601 cm^{-1}.

m.p.: 112−114 °C.

MS (EI) *m/z* (relative intensity): 255 (9) $[M(^{81}Br)+H]^+$, 254 (96) $[M(^{81}Br)]^+$, 253 (16) $[M(^{79}Br)+H]^+$, 252 (100) $[M(^{79}Br)]^+$, 201 (56), 199 (57), 173 (47) $[M-Br]^+$, 120 (40), 100 (22), 91 (13), 69 (11).

HR-MS (EI): *m/z* calcd for $C_{10}H_6{}^{79}BrFN_2{}^+$ $[M]^+$ 251.9693, found 251.9693.

2-(3-Bromo-2-methylphenyl)pyrimidine (153c)



The general procedure **A** was followed using 2-(*o*-tolyl)pyrimidine (**139d**, 51.1 mg, 0.30 mmol) at 80 °C. After 20 h, purification by column chromatography (*n*-hexane/CH_2Cl_2/EtOAc 7:2:1) yielded **153c** (46.4 mg, 62%) as a colorless oil and dibrominated product **153c'** (12.9 mg, 13%) as a white soild.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.85 (d, *J* = 4.9 Hz, 2H), 7.65 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.60 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.25 (t, *J* = 4.9 Hz, 1H), 7.15 (dd, *J* = 7.9, 7.8 Hz, 1H), 2.51 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 167.4 (C_q), 157.0 (CH), 140.5 (C_q), 136.5 (C_q), 133.5 (CH), 129.5 (CH), 126.9 (CH), 126.8 (C_q), 118.9 (CH), 20.6 (CH_3).

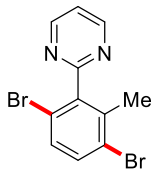
IR (ATR): $\tilde{\nu}$ = 3038, 1567, 1551, 1408, 1001, 777, 672 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 250 (71) $[M(^{81}Br)]^+$, 249 (100) $[M(^{81}Br)-H]^+$, 248 (74) $[M(^{79}Br)]^+$, 247 (95) $[M(^{79}Br)-H]^+$, 168 (93) $[M-HBr]^+$, 141 (10), 115 (26), 89 (30), 63 (17).

HR-MS (ESI): *m*/*z* calcd for $C_{11}H_{10}{}^{79}BrN_2^+$ $[M+H]^+$ 249.0022, found 249.0026.

The spectral data are in accordance with those reported in the literature.[78]

2-(3,6-Dibromo-2-methylphenyl)pyrimidine (153c')



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.91 (d, *J* = 5.0 Hz, 2H), 7.49 (d, *J* = 8.5 Hz, 1H), 7.37 (dq, *J* = 8.5, 0.6 Hz, 1H), 7.35 (t, *J* = 5.0 Hz, 1H), 2.15 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 166.9 (C_q), 157.4 (CH), 141.3 (C_q), 137.7 (C_q), 133.6 (CH), 131.1 (CH), 124.6 (C_q), 120.9 (C_q), 119.7 (CH), 21.1 (CH_3).

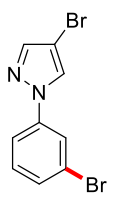
IR (ATR): $\tilde{\nu}$ = 2924, 1559, 1423, 1386, 1005, 813, 579 cm^{-1}.

m.p.: 71–72 °C.

MS (ESI) *m*/*z* (relative intensity): 331 (48) $[M(^{81}Br^{81}Br)+H]^+$, 329 (100) $[M(^{81}Br^{79}Br)+H]^+$, 327 (49) $[M(^{79}Br^{79}Br)+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{11}H_9{}^{79}Br^{81}BrN_2^+$ $[M+H]^+$ 328.9107, found 328.9111.

4-Bromo-1-(3-bromophenyl)-1*H*-pyrazole (153d)



The general procedure **A** was followed using 4-bromo-1-phenyl-1*H*-pyrazole (**147b**, 67.0 mg, 0.30 mmol) at 100 °C. After 20 h, purification by column chromatography (*n*-hexane/CH_2Cl_2 1:1) yielded **153d** (21.1 mg, 23%) as a white soild.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 0.7 Hz, 1H), 7.86 (dd, *J* = 2.1, 2.0 Hz, 1H), 7.67 (d, *J* = 0.7 Hz, 1H), 7.57 (ddd, *J* = 8.2, 2.1, 1.0 Hz, 1H), 7.44 (ddd, *J* = 8.1, 2.0, 1.0 Hz, 1H), 7.32 (dd, *J* = 8.2, 8.1 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 141.9 (CH), 140.5 (C_q), 130.7 (CH), 129.9 (CH), 126.9 (CH), 123.2 (C_q), 122.1 (CH), 117.2 (CH), 96.2 (C_q).

IR (ATR): $\tilde{\nu}$ = 3122, 1579, 1484, 1430, 1378, 1034, 954, 841, 774, 671 cm^{-1}.

m.p.: 63−64 °C.

MS (EI) *m/z* (relative intensity): 305 (5), 304 (50) [M(^{81}Br^{81}Br)]$^+$, 303 (10), 302 (100) [M(^{81}Br^{79}Br)]$^+$, 301 (5), 300 (51) [M(^{79}Br^{79}Br)]$^+$, 223 (7) [M(^{81}Br)−Br]$^+$, 221 (8) [M(^{79}Br)−Br]$^+$, 196 (16), 194 (14), 157 (18), 155 (18), 142 (45) [M−Br−Br]$^+$, 115 (17), 75 (20), 63 (12).

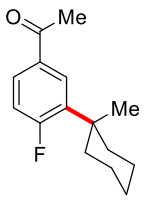
HR-MS (EI): *m/z* calcd for $C_9H_6{}^{79}Br_2N_2^+$ [M]$^+$ 299.8892, found 299.8897.

The spectral data are in accordance with those reported in the literature.[78]

5.3.2 Ruthenium(II)-Catalyzed Remote meta-C–H Alkylation of Ketimines

5.3.2.1 Characterization Data for 154

1-[4-Fluoro-3-(1-methylcyclohexyl)phenyl]ethan-1-one (154aa)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and 1-bromo-1-methylcyclohexane (**136a**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154aa** (85.1 mg, 73%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.99 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.78 (ddd, *J* = 8.4, 4.5, 2.3 Hz, 1H), 7.04 (dd, *J* = 12.4, 8.4 Hz, 1H), 2.57 (s, 3H), 2.13–2.01 (m, 2H), 1.73–1.53 (m, 4H), 1.53–1.33 (m, 4H), 1.29 (d, *J* = 1.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 196.9 (C_q), 165.2 (d, $^1J_{C-F}$ = 257 Hz, C_q), 136.8 (d, $^2J_{C-F}$ = 12 Hz, C_q), 133.2 (d, $^4J_{C-F}$ = 3 Hz, C_q), 129.1 (d, $^3J_{C-F}$ = 8 Hz, CH), 128.3 (d, $^3J_{C-F}$ = 11 Hz, CH), 116.7 (d, $^2J_{C-F}$ = 26 Hz, CH), 37.9 (d, $^3J_{C-F}$ = 4 Hz, C_q), 37.0 (d, $^4J_{C-F}$ = 4 Hz, CH_2), 26.5 (CH_3), 26.4 (CH_3), 26.2 (CH_2), 22.5 (CH_2).

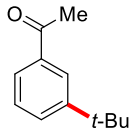
^{19}F-NMR (376 MHz, $CDCl_3$): δ = –101.0 (ddd, *J* = 12.7, 7.9, 4.6 Hz).

IR (ATR): $\tilde{\nu}$ = 2953, 2870, 1687, 1590, 1340, 1280, 1067, 830 cm^{-1}.

MS (EI) *m/z* (relative intensity): 234 (24) [M]$^+$, 219 (60) [M–Me]$^+$, 178 (35), 163 (62).

HR-MS (EI): *m/z* calcd for $C_{15}H_{19}FO^+$ [M]$^+$ 234.1414, found 234.1420.

1-[3-(*tert*-Butyl)phenyl]ethan-1-one (154bb)



The general procedure **B** was followed using ketimine **135b** (143 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154bb** (62.6 mg, 71%) as a colorless oil.

The general procedure **C** was followed using ketimine **135b** (143 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154bb** (48.0 mg, 54%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.01 (ddd, J = 2.1, 1.8, 0.5 Hz, 1H), 7.76 (ddd, J = 7.8, 1.8, 1.1 Hz, 1H), 7.61 (ddd, J = 7.8, 2.1, 1.1 Hz, 1H), 7.40 (ddd, J = 7.8, 7.8, 0.5 Hz, 1H), 2.61 (s, 3H), 1.36 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.3 (C_q), 151.6 (C_q), 136.9 (C_q), 130.2 (CH), 128.2 (CH), 125.7 (CH), 124.8 (CH), 34.9 (C_q), 31.3 (CH_3), 26.8 (CH_3).

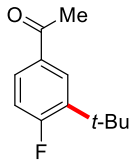
IR (ATR): $\tilde{\nu}$ = 2962, 2869, 1682, 1581, 1460, 1353, 1283, 967, 795 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 176 (21) $[M]^+$, 161 (100) $[M–Me]^+$, 133 (23) $[M–Ac]^+$, 115 (8).

HR-MS (EI): *m*/*z* calcd for $C_{12}H_{16}O^+$ $[M]^+$ 176.1196, found 176.1203.

The spectral data are in accordance with those reported in the literature.[130]

1-[3-(*tert*-Butyl)-4-fluorophenyl]ethan-1-one (154ab)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154ab** (72.0 mg, 74%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.97 (dd, J = 8.1, 2.3 Hz, 1H), 7.80 (ddd, J = 8.4, 4.5, 2.3 Hz, 1H), 7.06 (dd, J = 12.0, 8.4 Hz, 1H), 2.59 (s, 3H), 1.41 (d, J = 1.1 Hz, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.8 (C_q), 165.0 (d, $^1J_{C–F}$ = 257 Hz, C_q), 137.5 (d, $^2J_{C–F}$ = 12 Hz, C_q), 133.1 (d, $^4J_{C–F}$ = 3 Hz, C_q), 128.5 (d, $^3J_{C–F}$ = 10 Hz, CH), 127.9 (d, $^3J_{C–F}$ = 8 Hz, CH), 116.4 (d, $^2J_{C–F}$ = 25 Hz, CH), 34.5 (d, $^3J_{C–F}$ = 3 Hz, C_q), 29.8 (d, $^4J_{C–F}$ = 3 Hz, CH_3), 26.6 (CH_3).

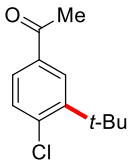
^{19}F-NMR (376 MHz, $CDCl_3$): δ = (–101.5)–(–101.8) (m).

IR (ATR): $\tilde{\nu}$ = 2961, 2873, 1683, 1606, 1490, 1355, 1235, 1094, 817 cm^{-1}.

MS (EI) *m/z* (relative intensity): 194 (18) $[M]^+$, 179 (100) $[M–Me]^+$, 151 (58) $[M–Ac]^+$, 136 (10).

HR-MS (EI): *m/z* calcd for $C_{12}H_{15}FO^+$ $[M]^+$ 194.1101, found 194.1106.

1-[3-(*tert*-Butyl)-4-chlorophenyl]ethan-1-one (154cb)



The general procedure **B** was followed using ketimine **135c** (160 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154cb** (64.8 mg, 62%) as a colorless oil.

The general procedure **C** was followed using ketimine **135c** (160 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154cb** (68.9 mg, 65%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 2.2 Hz, 1H), 7.69 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 2.59 (s, 3H), 1.51 (s, 9H).

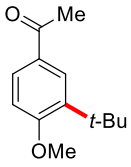
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 197.2 (C_q), 146.9 (C_q), 139.0 (C_q), 135.3 (C_q), 132.1 (CH), 127.6 (CH), 127.0 (CH), 36.3 (C_q), 29.5 (CH_3), 26.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2964, 1684, 1588, 1353, 1233, 1038, 818, 529 cm^{-1}.

MS (EI) *m/z* (relative intensity): 212 (9) $[M(^{37}Cl)]^+$, 210 (25) $[M(^{35}Cl)]^+$, 197 (28) $[M(^{37}Cl)–Me]^+$, 195 (82) $[M(^{35}Cl)–Me]^+$, 169 (34) $[M(^{37}Cl)–Ac]^+$, 167 (100) $[M(^{35}Cl)–Ac]^+$, 115 (26), 91 (13), 75 (9), 57 (10), 43 (81).

HR-MS (ESI): *m/z* calcd for $C_{12}H_{16}ClO^+$ $[M+H]^+$ 211.0884, found 211.0885.

1-[3-(*tert*-Butyl)-4-methoxyphenyl]ethan-1-one (154db)



The general procedure **B** was followed using ketimine **135d** (158 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 10:1) yielded **154db** (83.8 mg, 81%) as a colorless oil.

The general procedure **C** was followed using ketimine **135d** (158 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 10:1) yielded **154db** (67.6 mg, 66%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.94 (d, J = 2.3 Hz, 1H), 7.83 (dd, J = 8.5, 2.3 Hz, 1H), 6.89 (d, J = 8.5 Hz, 1H), 3.91 (s, 3H), 2.56 (s, 3H), 1.39 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 197.1 (C_q), 162.4 (C_q), 138.2 (C_q), 129.7 (C_q), 128.5 (CH), 127.0 (CH), 110.6 (CH), 55.2 (CH_3), 35.0 (C_q), 29.6 (CH_3), 26.4 (CH_3).

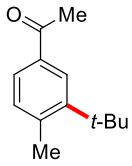
IR (ATR): $\tilde{\nu}$ = 2958, 1674, 1595, 1495, 1457, 1357, 1237, 1182, 1026, 970 cm^{-1}.

MS (EI) m/z (relative intensity): 206 (36) $[M]^+$, 191 (100) $[M–Me]^+$, 163 (42) $[M–Ac]^+$, 133 (18).

HR-MS (EI): m/z calcd for $C_{13}H_{18}O_2^+$ $[M]^+$ 206.1301, found 206.1297.

The spectral data are in accordance with those reported in the literature.[131]

1-(3-(*tert*-Butyl)-4-methylphenyl)ethan-1-one (154eb)



The general procedure **B** was followed using ketimine **135e** (150 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 70:1) yielded **154eb** (43.6 mg, 46%) as a colorless oil.

The general procedure **C** was followed using ketimine **135e** (150 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 70:1) yielded **154eb** (38.1 mg, 40%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, J = 1.9 Hz, 1H), 7.67 (ddd, J = 7.9, 1.9 Hz, 1H), 7.20 (d, J = 7.9 Hz, 1H), 2.60 (s, 3H), 2.58 (s, 3H), 1.44 (s, 9H).

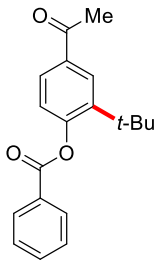
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 198.2 (C_q), 148.4 (C_q), 142.4 (C_q), 134.9 (C_q), 132.9 (CH), 126.0 (CH), 125.9 (CH), 35.9 (C_q), 30.7 (CH_3), 26.5 (CH_3), 23.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2963, 1681, 1601, 1355, 1267, 1237, 815 cm^{-1}.

MS (ESI) m/z (relative intensity): 213 (100) $[M+Na]^+$, 191 (20) $[M+H]^+$.

HR-MS (ESI): m/z calcd for $C_{13}H_{18}ONa^+$ $[M+Na]^+$ 213.1250, found 213.1253.

4-Acetyl-2-(*tert*-butyl)phenyl benzoate (154fb)



The general procedure **B** was followed using ketimine **135f** (203 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 9:1) yielded **154fb** (89.7 mg, 61%) as a viscous colorless oil.

The general procedure **C** was followed using ketimine **135f** (203 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 9:1) yielded **154fb** (65.1 mg, 44%) as a viscous colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.27–8.21 (m, 2H), 8.11 (d, J = 2.2 Hz, 1H), 7.87 (dd, J = 8.4, 2.2 Hz, 1H), 7.68 (tt, J = 6.7, 1.3 Hz, 1H), 7.59–7.52 (m, 2H), 7.20 (d, J = 8.4 Hz, 1H), 2.62 (s, 3H), 1.42 (s, 9H).

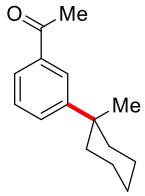
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 197.1 (C_q), 164.8 (C_q), 153.2 (C_q), 141.9 (C_q), 134.5 (C_q), 133.8 (CH), 130.2 (CH), 129.3 (C_q), 128.7 (CH), 127.6 (CH), 127.4 (CH), 124.4 (CH), 34.9 (C_q), 30.2 (CH_3), 26.7 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2964, 1736, 1682, 1599, 1356, 1237, 1190, 1083, 1053, 703 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 615 (11) $[2M+Na]^+$, 319 (100) $[M+Na]^+$, 297 (11) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{19}H_{20}O_3Na^+$ $[M+Na]^+$ 319.1305, found 319.1306.

1-[3-(1-Methylcyclohexyl)phenyl]ethan-1-one (154ba)



The general procedure **B** was followed using ketimine **135b** (143 mg, 0.50 mmol) and 1-bromo-1-methylcyclohexane (**136a**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154ba** (64.8 mg, 60%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.00 (dd, J = 1.9, 1.9 Hz, 1H), 7.76 (ddd, J = 7.7, 1.7, 1.1 Hz, 1H), 7.59 (ddd, J = 7.7, 2.1, 1.1 Hz, 1H), 7.40 (ddd, J = 7.7, 7.7, 0.5 Hz, 1H), 2.60 (s, 3H), 2.08–1.96 (m, 2H), 1.68–1.51 (m, 4H), 1.51–1.34 (m, 4H), 1.20 (s, 3H).

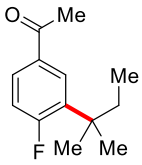
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 198.5 (C_q), 150.6 (C_q), 137.1 (C_q), 130.9 (CH), 128.4 (CH), 125.6 (CH), 125.6 (CH), 38.1 (C_q), 37.8 (CH_2), 30.3 (CH_3), 26.7 (CH_3), 26.2 (CH_2), 22.5 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2925, 2856, 1682, 1597, 1425, 1356, 1256, 1196, 1080, 965 cm^{-1}.

MS (EI) *m/z* (relative intensity): 216 (40) $[M]^+$, 201 (75) $[M–Me]^+$, 173 (26) $[M–Ac]^+$, 160 (32), 145 (48).

HR-MS (EI): *m/z* calcd for $C_{15}H_{20}O^+$ $[M]^+$ 216.1509, found 216.1512.

1-[4-Fluoro-3-(*tert*-pentyl)phenyl]ethan-1-one (154ac)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and 2-bromo-2-methylbutane (**136c**, 227 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154ac** (78.7 mg, 76%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.91 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.79 (ddd, *J* = 8.4, 4.5, 2.3 Hz, 1H), 7.03 (dd, *J* = 12.1, 8.4 Hz, 1H), 2.57 (s, 3H), 1.78 (qd, *J* = 7.5, 1.6 Hz, 2H), 1.36 (d, *J* = 1.2 Hz, 6H), 0.66 (td, *J* = 7.5, 0.6 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 196.9 (C_q), 164.9 (d, $^1J_{C–F}$ = 257 Hz, C_q), 136.0 (d, $^2J_{C–F}$ = 12 Hz, C_q), 133.1 (d, $^4J_{C–F}$ = 3 Hz, C_q), 129.1 (d, $^3J_{C–F}$ = 8 Hz, CH), 128.6 (d, $^3J_{C–F}$ = 10 Hz, CH), 116.3 (d, $^2J_{C–F}$ = 26 Hz, CH), 38.1 (d, $^3J_{C–F}$ = 3 Hz, C_q), 34.0 (d, $^4J_{C–F}$ = 4 Hz, CH_2), 27.6 (d, $^4J_{C–F}$ = 3 Hz, CH_3), 26.5 (CH_3), 9.3 (CH_3).

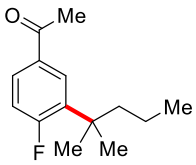
^{19}F-NMR (376 MHz, $CDCl_3$): δ = (–101.5)–(–101.7) (m).

IR (ATR): $\tilde{\nu}$ = 2965, 2877, 1683, 1604, 1491, 1355, 1252, 1094, 822 cm^{-1}.

MS (EI) *m/z* (relative intensity): 208 (7) $[M]^+$, 179 (100) $[M–Et]^+$, 151 (65), 136 (10).

HR-MS (EI): *m/z* calcd for $C_{13}H_{17}FO^+$ $[M]^+$ 208.1258, found 208.1266.

1-[4-Fluoro-3-(2-methylpentan-2-yl)phenyl]ethan-1-one (154ad)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and 2-bromo-2-methylpentane (**136d**, 249 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154ad** (53.3 mg, 48%) as a colorless oil.

The general procedure **C** was followed using ketimine **135a** (152 mg, 0.50 mmol), 2-bromo-2-methylpentane (**136d**, 249 mg, 1.50 mmol), and $[RuCl_2(C_6H_6)]_2$ (12.6 mg, 5 mol %). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154ad** (61.4 mg, 55%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.90 (dd, J = 8.0, 2.3 Hz, 1H), 7.79 (ddd, J = 8.4, 4.5, 2.3 Hz, 1H), 7.04 (dd, J = 12.1, 8.4 Hz, 1H), 2.57 (s, 3H), 1.74–1.68 (m, 2H), 1.37 (d, J = 1.1 Hz, 6H), 1.09–0.97 (m, 2H), 0.83 (t, J = 7.3 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 196.9 (C_q), 164.9 (d, $^1J_{C–F}$ = 257 Hz, C_q), 136.3 (d, $^2J_{C–F}$ = 12 Hz, C_q), 133.1 (d, $^4J_{C–F}$ = 3 Hz, C_q), 129.0 (d, $^3J_{C–F}$ = 8 Hz, CH), 128.5 (d, $^3J_{C–F}$ = 10 Hz, CH), 116.4 (d, $^2J_{C–F}$ = 26 Hz, CH), 44.0 (d, $^4J_{C–F}$ = 4 Hz, CH_2), 37.9 (d, $^3J_{C–F}$ = 3 Hz, C_q), 28.1 (d, $^4J_{C–F}$ = 3 Hz, CH_3), 26.5 (CH_3), 18.3 (CH_2), 14.6 (CH_3).

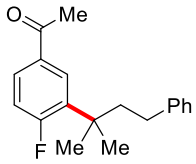
^{19}F-NMR (376 MHz, $CDCl_3$): δ = (–101.4)–(–101.7) (m).

IR (ATR): $\tilde{\nu}$ = 2958, 2931, 1683, 1583, 1490, 1355, 1247, 1097, 958 cm^{-1}.

MS (EI) *m/z* (relative intensity): 222 (5) $[M]^+$, 179 (100) $[M–Pr]^+$, 151 (56), 115 (6).

HR-MS (ESI): *m/z* calcd for $C_{14}H_{20}FO^+$ $[M+H]^+$ 223.1493, found 223.1493.

1-[3-(2-Methyl-4-phenylbutan-2-yl)phenyl]ethan-1-one (154ae)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and (3-bromo-3-methylbutyl)benzene (**136e**, 341 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154ae** (84.1 mg, 59%) as a colorless oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.98 (dd, J = 8.0, 2.3 Hz, 1H), 7.83 (ddd, J = 8.4, 4.5, 2.3 Hz, 1H), 7.26–7.21 (m, 2H), 7.17–7.12 (m, 1H), 7.12–7.06 (m, 3H), 2.60 (s, 3H), 2.36–2.30 (m, 2H), 2.12–2.06 (m, 2H), 1.47 (d, J = 1.0 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 197.0 (C_q), 164.9 (d, $^1J_{C–F}$ = 257 Hz, C_q), 142.5 (C_q), 135.7 (d, $^2J_{C–F}$ = 12 Hz, C_q), 133.2 (d, $^4J_{C–F}$ = 3 Hz, C_q), 129.0 (d, $^3J_{C–F}$ = 8 Hz, CH), 128.9 (d, $^3J_{C–F}$ = 10 Hz, CH), 128.3 (CH), 128.2 (CH), 125.6 (CH), 116.5 (d, $^2J_{C–F}$ = 26 Hz, CH), 43.6 (d, $^4J_{C–F}$ = 5 Hz, CH_2), 38.0 (d, $^3J_{C–F}$ = 3 Hz, C_q), 31.7 (CH_2), 28.2 (d, $^4J_{C–F}$ = 3 Hz, CH_3), 26.6 (CH_3).

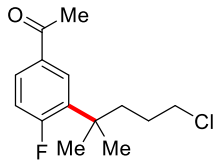
^{19}F-NMR (470 MHz, $CDCl_3$): δ = (–101.5)–(–101.7) (m).

IR (ATR): $\tilde{\nu}$ = 3026, 2965, 1683, 1491, 1355, 1257, 1220, 823, 698 cm^{-1}.

MS (EI) *m/z* (relative intensity): 284 (14) $[M]^+$, 179 (100), 151 (53), 105 (36), 91 (43), 77 (9), 65 (11), 43 (42).

HR-MS (EI): *m/z* calcd for $C_{19}H_{21}FO^+$ $[M]^+$ 284.1571, found 284.1577.

1-[3-(5-Chloro-2-methylpentan-2-yl)-4-fluorophenyl]ethan-1-one (154af)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and 4-bromo-1-chloro-4-methylpentane (**136f**, 299 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154af** (70.6 mg, 55%) as a colorless oil.

The general procedure **C** was followed using ketimine **135a** (152 mg, 0.50 mmol) and 4-bromo-1-chloro-4-methylpentane (**136f**, 299 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154af** (28.0 mg, 22%) as a colorless oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.91 (dd, *J* = 8.0, 2.3 Hz, 1H), 7.81 (ddd, *J* = 8.4, 4.5, 2.3 Hz, 1H), 7.07 (dd, *J* = 12.1, 8.4 Hz, 1H), 3.44 (t, *J* = 6.7 Hz, 2H), 2.58 (s, 3H), 1.92–1.86 (m, 2H), 1.54–1.46 (m, 2H), 1.41 (d, *J* = 1.0 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.9 (C_q), 164.8 (d, $^1J_{C-F}$ = 257 Hz, C_q), 135.4 (d, $^2J_{C-F}$ = 12 Hz, C_q), 133.2 (d, $^4J_{C-F}$ = 3 Hz, C_q), 128.9 (d, $^3J_{C-F}$ = 10 Hz, CH), 128.8 (d, $^3J_{C-F}$ = 8 Hz, CH), 116.5 (d, $^2J_{C-F}$ = 26 Hz, CH), 45.4 (CH_2), 38.8 (d, $^4J_{C-F}$ = 4 Hz, CH_2), 37.5 (d, $^3J_{C-F}$ = 3 Hz, C_q), 28.6 (CH_2), 28.1 (d, $^4J_{C-F}$ = 3 Hz, CH_3), 26.5 (CH_3).

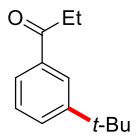
^{19}F-NMR (470 MHz, $CDCl_3$): δ = (–101.6)–(–101.7) (m).

IR (ATR): $\tilde{\nu}$ = 2961, 2874, 1682, 1581, 1477, 1258, 1090, 822 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 258 (1) $[M(^{37}Cl)]^+$, 256 (3) $[M(^{35}Cl)]^+$, 179 (100), 151 (48), 115 (5).

HR-MS (ESI): *m*/*z* calcd for $C_{14}H_{19}F^{35}ClO^+$ $[M+H]^+$ 257.1103, found 257.1103.

1-[3-(*tert*-Butyl)phenyl]propan-1-one (154gb)



The general procedure **B** was followed using ketimine **135g** (150 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 80:1) yielded **154gb** (76.2 mg, 80%) as a colorless oil.

The general procedure **C** was followed using ketimine **135g** (150 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 80:1) yielded **154gb** (55.8 mg, 59%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.02 (ddd, *J* = 2.0, 1.9, 0.5 Hz, 1H), 7.77 (ddd, *J* = 7.8, 1.9, 1.1 Hz, 1H), 7.59 (ddd, *J* = 7.8, 2.0, 1.1 Hz, 1H), 7.39 (ddd, *J* = 7.8, 7.8, 0.5 Hz, 1H), 3.01 (q, *J* = 7.3 Hz, 2H), 1.35 (s, 9H), 1.23 (t, *J* = 7.3 Hz, 3H).

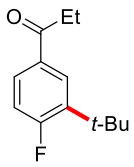
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 201.2 (C_q), 151.6 (C_q), 136.8 (C_q), 130.0 (CH), 128.2 (CH), 125.3 (CH), 124.7 (CH), 34.8 (C_q), 31.9 (CH_2), 31.2 (CH_3), 8.3 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2963, 2872, 1685, 1581, 1459, 1364, 1209, 850 cm^{-1}.

MS (EI) *m/z* (relative intensity): 190 (6) $[M]^+$, 161 (100) $[M–Et]^+$, 133 (13), 115 (10).

HR-MS (ESI): *m/z* calcd for $C_{13}H_{19}O^+$ $[M+H]^+$ 191.1430, found 191.1436.

1-[3-(*tert*-Butyl)-4-fluorophenyl]propan-1-one (154hb)



The general procedure **B** was followed using ketimine **135h** (159 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 80:1) yielded **154hb** (85.5 mg, 83%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.98 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.80 (ddd, *J* = 8.5, 4.5, 2.3 Hz, 1H), 7.05 (dd, *J* = 12.0, 8.5 Hz, 1H), 2.97 (q, *J* = 7.3 Hz, 2H), 1.40 (d, *J* = 1.2 Hz, 9H), 1.22 (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 199.7 (C_q), 164.9 (d, $^1J_{C–F}$ = 257 Hz, C_q), 137.5 (d, $^2J_{C–F}$ = 12 Hz, C_q), 132.9 (d, $^4J_{C–F}$ = 3 Hz, C_q), 128.1 (d, $^3J_{C–F}$ = 10 Hz, CH), 127.7 (d, $^3J_{C–F}$ = 7 Hz, CH), 116.4 (d, $^2J_{C–F}$ = 25 Hz, CH), 34.4 (d, $^3J_{C–F}$ = 3 Hz, C_q), 31.7 (CH_2), 29.7 (d, $^4J_{C–F}$ = 4 Hz, CH_3), 8.3 (CH_3).

^{19}F-NMR (470 MHz, $CDCl_3$) δ = (–102.0)–(–102.1) (m).

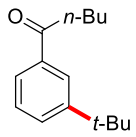
IR (ATR): $\tilde{\nu}$ = 2945, 2022, 1686, 1605, 1458, 1366, 1210, 1089, 800 cm^{-1}.

m.p.: 44–45 °C.

MS (EI) *m/z* (relative intensity): 208 (7) $[M]^+$, 193 (14) $[M–Me]^+$, 179 (100) $[M–Et]^+$, 165 (22).

HR-MS (EI): *m/z* calcd for $C_{13}H_{17}FO^+$ $[M]^+$ 208.1258, found 208.1263.

1-[3-(*tert*-Butyl)phenyl]pentan-1-one (154ib)



The general procedure **B** was followed using ketimine **135i** (164 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 100:1) yielded **154ib** (81.0 mg, 74%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.02–7.99 (m, 1H), 7.76 (ddd, *J* = 7.8, 1.7, 1.1 Hz, 1H), 7.59 (ddd, *J* = 7.8, 2.1, 1.1 Hz, 1H), 7.39 (ddd, *J* = 7.8, 7.8, 0.5 Hz, 1H), 2.97 (dd, *J* = 7.7, 7.1 Hz, 2H), 1.77–1.68 (m, 2H), 1.47–1.37 (m, 2H), 1.35 (s, 9H), 0.96 (t, *J* = 7.3 Hz, 3H).

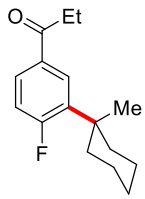
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 200.9 (C_q), 151.6 (C_q), 136.9 (C_q), 130.0 (CH), 128.2 (CH), 125.4 (CH), 124.7 (CH), 38.4 (CH_2), 34.8 (C_q), 31.3 (CH_3), 26.6 (CH_2), 22.5 (CH_2), 13.9 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2959, 2871, 1684, 1598, 1462, 1365, 1285, 1243, 1020, 793 cm^{-1}.

MS (EI) *m/z* (relative intensity): 218 (5) $[M]^+$, 203 (8) $[M–Me]^+$, 176 (32) $[M–Pr]^+$, 161 (100) $[M–Bu]^+$.

HR-MS (EI): *m/z* calcd for $C_{15}H_{22}O^+$ $[M]^+$ 218.1665, found 218.1682.

1-[4-Fluoro-3-(1-methylcyclohexyl)phenyl]propan-1-one (154ha)



The general procedure **B** was followed using ketimine **135h** (159 mg, 0.50 mmol) and 1-bromo-1-methylcyclohexane (**136a**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 70:1) yielded **154ha** (87.3 mg, 70%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.00 (dd, *J* = 8.1, 2.3 Hz, 1H), 7.80 (ddd, *J* = 8.4, 4.5, 2.3 Hz, 1H), 7.04 (dd, *J* = 12.4, 8.4 Hz, 1H), 2.98 (q, *J* = 7.2 Hz, 2H), 2.16–2.01 (m, 2H), 1.75–1.53 (m, 4H), 1.53–1.34 (m, 4H), 1.30 (d, *J* = 1.0 Hz, 3H), 1.22 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 199.5 (C_q), 165.0 (d, $^1J_{C–F}$ = 256 Hz, C_q), 136.7 (d, $^2J_{C–F}$ = 11 Hz, C_q), 132.8 (d, $^4J_{C–F}$ = 3 Hz, C_q), 128.8 (d, $^3J_{C–F}$ = 8 Hz, CH), 127.7 (d, $^3J_{C–F}$ = 10 Hz, CH), 116.7 (d, $^2J_{C–F}$ = 26 Hz, CH), 38.0 (d, $^3J_{C–F}$ = 4 Hz, C_q), 37.1 (d, $^4J_{C–F}$ = 4 Hz, CH_2), 31.7 (CH_2), 26.6 (CH_3), 26.4 (CH_2), 22.7 (CH_2), 8.4 (CH_3).

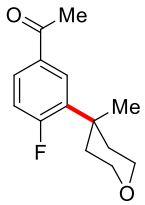
^{19}F-NMR (282 MHz, $CDCl_3$): δ = –101.4 (ddd, *J* = 12.7, 8.2, 4.8 Hz).

IR (ATR): $\tilde{\nu}$ = 2927, 2858, 1685, 1581, 1488, 1451, 1228, 1182, 799 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 248 (8) $[M]^+$, 219 (100) $[M–Et]^+$, 163 (22), 133 (12).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{21}FO^+$ $[M]^+$ 248.1571, found 248.1579.

1-[4-Fluoro-3-(4-methyltetrahydro-2*H*-pyran-4-yl)phenyl]ethan-1-one (154ag)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and 4-bromo-4-methyltetrahydro-2*H*-pyran (**136g**, 269 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 3:1) yielded **154ag** (66.9 mg, 57%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.93 (dd, *J* = 7.9, 2.3 Hz, 1H), 7.82 (ddd, *J* = 8.4, 4.6, 2.3 Hz, 1H), 7.09 (dd, *J* = 12.4, 8.4 Hz, 1H), 3.80 (d_{AB}dd, *J* = 11.0, 9.1, 3.1 Hz, 2H), 3.70 (d_{AB}dd, *J* = 11.0, 6.2, 3.8 Hz, 2H), 2.58 (s, 3H), 2.20 (ddd, *J* = 12.7, 9.1, 3.8 Hz, 2H), 1.91–1.82 (m, 2H), 1.40 (d, *J* = 1.0 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 196.7 (C_q), 165.0 (d, $^1J_{C–F}$ = 257 Hz, C_q), 135.9 (d, $^2J_{C–F}$ = 11 Hz, C_q), 133.3 (d, $^4J_{C–F}$ = 3 Hz, C_q), 128.8 (d, $^3J_{C–F}$ = 11 Hz, CH), 128.2 (d, $^3J_{C–F}$ = 8 Hz, CH), 116.9 (d, $^2J_{C–F}$ = 26 Hz, CH), 64.2 (CH_2), 36.7 (d, $^4J_{C–F}$ = 4 Hz, CH_2), 35.5 (d, $^3J_{C–F}$ = 3 Hz, C_q), 26.5 (CH_3), 25.3 (d, $^4J_{C–F}$ = 3 Hz, CH_3).

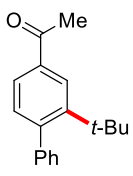
^{19}F-NMR (376 MHz, $CDCl_3$): δ = –101.8 (ddd, *J* = 12.4, 7.9, 4.6 Hz).

IR (ATR): $\tilde{\nu}$ = 2932, 2853, 1683, 1605, 1490, 1356, 1244, 1106, 826 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 236 (10) $[M]^+$, 221 (14) $[M–Me]^+$, 192 (53), 177 (65), 163 (90), 149 (49), 133 (20), 83 (22), 49 (22), 43 (100).

HR-MS (EI): *m*/*z* calcd for $C_{14}H_{17}FO_2^+$ $[M]^+$ 236.1207, found 236.1226.

1-[2-(*tert*-Butyl)-[1,1'-biphenyl]-4-yl]ethan-1-one (154jb)



The general procedure **B** was followed using ketimine **135j** (181 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154jb** (34.1 mg, 27%) as a colorless oil.

The general procedure **C** was followed using ketimine **135j** (181 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154jb** (48.0 mg, 38%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.18 (dd, *J* = 1.9, 0.4 Hz, 1H), 7.74 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.39–7.34 (m, 3H), 7.27–7.23 (m, 2H), 7.12 (dd, *J* = 7.9, 0.4 Hz, 1H), 2.64 (s, 3H), 1.22 (s, 9H).

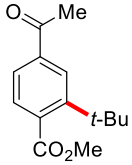
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 198.2 (C_q), 148.3 (C_q), 147.1 (C_q), 144.2 (C_q), 135.9 (C_q), 132.9 (CH), 129.5 (CH), 127.3 (CH), 127.0 (CH), 126.7 (CH), 124.9 (CH), 36.7 (C_q), 32.5 (CH_3), 26.7 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2964, 1686, 1596, 1398, 1354, 1236, 770, 707 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 527 (74) $[2M+Na]^+$, 275 (100) $[M+Na]^+$, 253 (13) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{18}H_{20}ONa^+$ $[M+Na]^+$ 275.1406, found 275.1407.

Methyl 4-acetyl-2-(*tert*-butyl)benzoate (154kb)



The general procedure **B** was followed using ketimine **135k** (172 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 10:1) yielded **154kb** (15.6 mg, 13%) as a colorless oil.

The general procedure **C** was followed using ketimine **135k** (172 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 10:1) yielded **154kb** (32.3 mg, 28%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.10 (dd, *J* = 1.7, 0.5 Hz, 1H), 7.77 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.36 (dd, *J* = 7.9, 0.5 Hz, 1H), 3.92 (s, 3H), 2.61 (s, 3H), 1.42 (s, 9H).

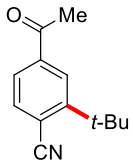
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 197.5 (C_q), 171.5 (C_q), 148.1 (C_q), 137.7 (C_q), 136.9 (C_q), 128.8 (CH), 126.8 (CH), 125.4 (CH), 52.6 (CH_3), 36.1 (C_q), 31.3 (CH_3), 26.8 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2954, 1729, 1687, 1434, 1291, 1255, 1121, 1069 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 234 (2) $[M]^+$, 219 (43) $[M–Me]^+$, 203 (58) $[M–OMe]^+$, 187 (100), 177 (23) $[M–t\text{-}Bu]^+$, 115 (29), 91 (17), 43 (79).

HR-MS (EI): *m*/*z* calcd for $C_{14}H_{18}O_3^+$ $[M]^+$ 234.1250, found 234.1261.

4-Acetyl-2-(*tert*-butyl)benzonitrile (154lb)



The general procedure **B** was followed using ketimine **135l** (155 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 10:1) yielded **154lb** (19.8 mg, 20%) as a colorless oil.

The general procedure **C** was followed using ketimine **135l** (155 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 10:1) yielded **154lb** (26.7 mg, 27%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.06 (dd, J = 1.6, 0.6 Hz, 1H), 7.82 (d_{AB}d, J = 7.9, 1.6 Hz, 1H), 7.78 (d_{AB}d, J = 7.9, 0.6 Hz, 1H), 2.63 (s, 3H), 1.55 (s, 9H).

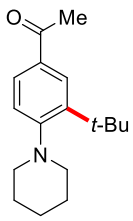
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.9 (C_q), 154.3 (C_q), 139.6 (C_q), 135.8 (CH), 125.7 (CH), 125.7 (CH), 119.3 (C_q), 114.7 (C_q), 35.9 (C_q), 30.1 (CH_3), 26.9 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2967, 2223, 1692, 1483, 1404, 1288, 1237, 835 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 201 (10) $[M]^+$, 186 (100) $[M–Me]^+$, 158 (31) $[M–Ac]^+$, 143 (14) $[M–t\text{-Bu}]^+$, 115 (14), 43 (29).

HR-MS (EI): *m*/*z* calcd for $C_{13}H_{15}NO^+$ $[M]^+$ 201.1148, found 201.1150.

1-[3-(*tert*-Butyl)-4-(piperidin-1-yl)phenyl]ethan-1-one (154nb)



The general procedure **B** was followed using ketimine **135n** (184 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, to the reaction mixture was added HCl (2 N, 3.0 mL) and the resulting mixture was stirred for additional 3 h, and then neutralized with sat. aq. $NaHCO_3$ solution until pH 8. The reaction mixture was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (*n*-hexane/EtOAc 19:1 to 9:1) yielded **154nb** (18.7 mg, 14%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.01 (d, J = 2.2 Hz, 1H), 7.80 (dd, J = 8.2, 2.2 Hz, 1H), 7.39 (d, J = 8.2 Hz, 1H), 2.90–2.63 (m, 4H), 2.58 (s, 3H), 1.89–1.65 (m, 4H), 1.46 (s, 9H), 1.45–1.23 (m, 2H).

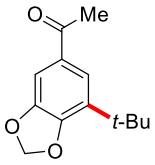
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 197.8 (C_q), 159.7 (C_q), 147.7 (C_q), 134.3 (C_q), 127.1 (CH), 127.1 (CH), 125.7 (CH), 55.3 (CH_2), 35.8 (C_q), 30.7 (CH_3), 26.6 (CH_3), 26.2 (CH_2), 24.3 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2932, 1682, 1594, 1352, 1237, 1216, 918, 833 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 259 (65) $[M]^+$, 258 (38) $[M–H]^+$, 244 (100) $[M–Me]^+$, 230 (8), 216 (64), 202 (17), 188 (14), 43 (44).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{25}NO^+$ $[M]^+$ 259.1931, found 259.1934.

1-[7-(*tert*-Butyl)benzo[*d*][1,3]dioxol-5-yl]ethan-1-one (154pb)



The general procedure **B** was followed using ketimine **135p** (165 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 10:1) yielded **154pb** (38.8 mg, 35%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.52 (d, *J* = 1.7 Hz, 1H), 7.31 (d, *J* = 1.7 Hz, 1H), 6.04 (s, 2H), 2.54 (s, 3H), 1.38 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.4 (C_q), 149.2 (C_q), 147.9 (C_q), 132.3 (C_q), 131.4 (C_q), 121.6 (CH), 106.3 (CH), 101.1 (CH_2), 34.1 (C_q), 29.3 (CH_3), 26.6 (CH_3).

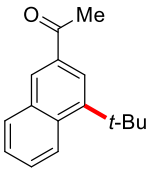
IR (ATR): $\tilde{\nu}$ = 2961, 2908, 1669, 1588, 1419, 1290, 1252, 1044, 966, 867 cm^{-1}.

m.p.: 114–115 °C.

MS (ESI) *m*/*z* (relative intensity): 463 (67) $[2M+Na]^+$, 243 (100) $[M+Na]^+$, 221 (94) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{13}H_{16}O_3Na^+$ $[M+Na]^+$ 243.0992, found 243.0988.

1-[4-(*tert*-Butyl)naphthalen-2-yl]ethan-1-one (154qb)



The general procedure **B** was followed using ketimine **135q** (168 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154qb** (42.9 mg, 38%) as a white solid.

The general procedure **C** was followed using ketimine **135q** (168 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154qb** (21.0 mg, 19%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.49 (dddd, *J* = 8.8, 1.1, 0.9, 0.8 Hz, 1H), 8.32 (ddd *J* = 1.7, 0.9, 0.7 Hz, 1H), 8.10 (d, *J* = 1.7 Hz, 1H), 7.99 (dddd, *J* = 8.0, 1.7, 0.8, 0.7 Hz, 1H), 7.61 (ddd, *J* = 8.8, 6.9, 1.7 Hz, 1H), 7.52 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 2.73 (s, 3H), 1.66 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.2 (C_q), 146.8 (C_q), 134.2 (C_q), 133.9 (C_q), 133.5 (C_q), 131.2 (CH), 129.8 (CH), 127.1 (CH), 126.9 (CH), 125.4 (CH), 120.9 (CH), 36.3 (C_q), 31.8 (CH_3), 26.6 (CH_3).

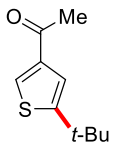
IR (ATR): $\tilde{\nu}$ = 2965, 1679, 1388, 1288, 1240, 1213, 894, 791, 758 cm^{-1}.

m.p.: 71–72 °C.

MS (EI) *m*/*z* (relative intensity): 226 (46) $[M]^+$, 211 (100) $[M–Me]^+$, 165 (14), 152 (19), 141 (10), 43 (92).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{18}O^+$ $[M]^+$ 226.1352, found 226.1361.

1-[5-(*tert*-Butyl)thiophen-3-yl]ethan-1-one (154rb)



The general procedure **B** was followed using ketimine **135r** (146 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154rb** (25.4 mg, 14%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 1.4 Hz, 1H), 7.26 (d, *J* = 1.4 Hz, 1H), 2.49 (s, 3H), 1.38 (s, 9H).

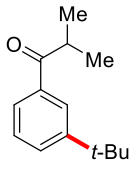
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 192.7 (C_q), 158.7 (C_q), 142.1 (C_q), 130.2 (CH), 120.7 (CH), 34.6 (C_q), 32.3 (CH_3), 27.1 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3098, 2963, 1668, 1395, 1232, 853, 792, 647, 598 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 205 (100) $[M+Na]^+$, 183 (48) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{10}H_{14}OSNa^+$ $[M+Na]^+$ 205.0658, found 205.0660.

1-[3-(*tert*-Butyl)phenyl]-2-methylpropan-1-one (154sb)



The general procedure **B** was followed using ketimine **135s** (157 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol) in PhMe (2.0 mL). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154sb** (13.6 mg, 13%) as a colorless oil.

The general procedure **C** was followed using ketimine **135s** (157 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154sb** (30.6 mg, 30%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.01 (ddd, *J* = 2.0, 1.7, 0.5 Hz, 1H), 7.76 (ddd, *J* = 7.7, 1.7, 1.1 Hz, 1H), 7.59 (ddd, *J* = 7.8, 2.0, 1.1 Hz, 1H), 7.39 (ddd, *J* = 7.8, 7.7, 0.5 Hz, 1H), 3.57 (hept, *J* = 6.8 Hz, 1H), 1.36 (s, 9H), 1.23 (d, *J* = 6.8 Hz, 6H).

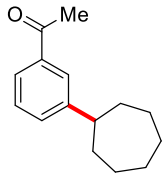
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 204.6 (C_q), 151.6 (C_q), 136.0 (C_q), 129.8 (CH), 128.2 (CH), 125.5 (CH), 125.1 (CH), 35.5 (CH), 34.9 (C_q), 31.3 (CH_3), 19.3 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2965, 1682, 1467, 1365, 1213, 1162, 991, 743, 696 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 204 (4) $[M]^+$, 189 (4) $[M–Me]^+$, 161 (100) $[M–i\text{-}Pr]^+$, 133 (16) $[M–C(O)i\text{-}Pr]^+$, 105 (19), 91 (16), 77 (9), 43 (19).

HR-MS (EI): *m*/*z* calcd for $C_{14}H_{20}O^+$ $[M]^+$ 204.1509, found 204.1519.

1-(3-Cycloheptylphenyl)ethan-1-one (154bh)



The general procedure **B** was followed using ketimine **135b** (143 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154bh** (74.6 mg, 69%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.81–7.77 (m, 1H), 7.74 (ddd, *J* = 7.0, 1.8, 1.8 Hz, 1H), 7.42–7.32 (m, 2H), 2.79–2.67 (m, 1H), 2.59 (s, 3H), 1.97–1.47 (m, 12H).

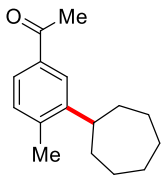
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.2 (C_q), 150.3 (C_q), 137.1 (C_q), 131.5 (CH), 128.4 (CH), 126.3 (CH), 125.7 (CH), 47.0 (CH), 36.7 (CH_2), 27.9 (CH_2), 27.2 (CH_2), 26.7 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3352, 2921, 2853, 1681, 1582, 1434, 1356, 1270, 793 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 216 (60) $[M]^+$, 201 (100) $[M–Me]^+$, 146 (36), 131 (64).

HR-MS (EI): *m*/*z* calcd for $C_{15}H_{20}O^+$ $[M]^+$ 216.1509, found 216.1510.

1-(3-Cycloheptyl-4-methylphenyl)ethan-1-one (154eh)



The general procedure **B** was followed using ketimine **135e** (150 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154eh** (82.3 mg, 71%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, J = 1.8 Hz, 1H), 7.65 (dd, J = 7.9, 1.8 Hz, 1H), 7.20 (d, J = 7.9 Hz, 1H), 2.95–2.83 (m, 1H), 2.57 (s, 3H), 2.38 (s, 3H), 1.90–1.78 (m, 4H), 1.78–1.46 (m, 8H).

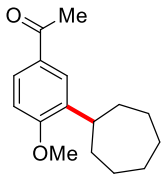
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 198.1 (C_q), 148.4 (C_q), 140.4 (C_q), 135.4 (C_q), 130.2 (CH), 125.5 (CH), 125.4 (CH), 41.8 (CH), 35.9 (CH_2), 27.6 (CH_2), 27.5 (CH_2), 26.5 (CH_3), 19.7 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2920, 2853, 1678, 1602, 1444, 1353, 1242, 813 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 230 (42) $[M]^+$, 215 (100) $[M–Me]^+$, 145 (40), 115 (18).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{22}O^+$ $[M]^+$ 230.1665, found 230.1673.

1-(3-Cycloheptyl-4-methoxyphenyl)ethan-1-one (154dh)



The general procedure **B** was followed using ketimine **135d** (158 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 10:1) yielded **154dh** (99.7 mg, 81%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, J = 2.3 Hz, 1H), 7.78 (dd, J = 8.5, 2.3 Hz, 1H), 6.84 (d, J = 8.5 Hz, 1H), 3.88 (s, 3H), 3.17–3.02 (m, 1H), 2.54 (s, 3H), 1.93–1.45 (m, 12H).

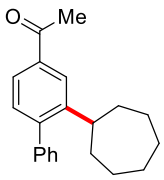
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 197.1 (C_q), 160.2 (C_q), 138.2 (C_q), 130.0 (C_q), 127.9 (CH), 127.1 (CH), 109.5 (CH), 55.5 (CH_3), 38.9 (CH), 35.2 (CH_2), 27.8 (CH_2), 27.4 (CH_2), 26.3 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2919, 2852, 1672, 1596, 1495, 1354, 1241, 1025, 810 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 246 (95) $[M]^+$, 231 (100) $[M–Me]^+$, 161 (57), 147 (26).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{22}O_2^+$ $[M]^+$ 246.1614, found 246.1630.

1-(2-Cycloheptyl-[1,1'-biphenyl]-4-yl)ethan-1-one (154jh)



The general procedure **B** was followed using ketimine **135j** (181 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154jh** (92.4 mg, 63%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 1.8 Hz, 1H), 7.75 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.46–7.32 (m, 3H), 7.28–7.22 (m, 3H), 2.89–2.77 (m, 1H), 2.62 (s, 3H), 1.85–1.61 (m, 6H), 1.57–1.46 (m, 4H), 1.39–1.23 (m, 2H).

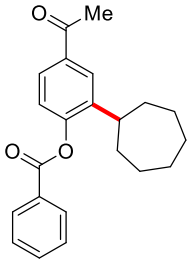
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 197.9 (C_q), 147.9 (C_q), 145.2 (C_q), 140.9 (C_q), 136.4 (C_q), 130.0 (CH), 128.8 (CH), 128.0 (CH), 127.1 (CH), 126.3 (CH), 125.1 (CH), 41.6 (CH), 36.8 (CH_2), 27.7 (CH_2), 27.3 (CH_2), 26.7 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2919, 2852, 1681, 1597, 1458, 1353, 1277, 1008, 827 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 292 (85) $[M]^+$, 221 (46), 165 (41), 115 (6).

HR-MS (ESI): *m*/*z* calcd for $C_{21}H_{25}O^+$ $[M+H]^+$ 293.1900, found 293.1905.

4-Acetyl-2-cycloheptylphenyl benzoate (154fh)



The general procedure **B** was followed using ketimine **135f** (203 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 95:5) yielded **154fh** (88.1 mg, 52%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.25–8.20 (m, 2H), 7.98 (d, *J* = 2.2 Hz, 1H), 7.83 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.71–7.65 (m, 1H), 7.58–7.52 (m, 2H), 7.23 (d, *J* = 8.4 Hz, 1H), 2.92 (tt, *J* = 10.5, 3.4 Hz, 1H), 2.62 (s, 3H), 1.95–1.87 (m, 2H), 1.83–1.39 (m, 10H).

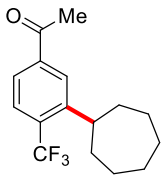
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 197.3 (C_q), 164.8 (C_q), 151.7 (C_q), 141.9 (C_q), 135.2 (C_q), 133.9 (CH), 130.2 (CH), 129.1 (C_q), 128.7 (CH), 127.9 (CH), 127.0 (CH), 122.7 (CH), 40.2 (CH), 35.4 (CH_2), 27.6 (CH_2), 27.4 (CH_2), 26.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2922, 1737, 1683, 1600, 1451, 1238, 1081, 1056, 1023, 707 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 336 (2) $[M]^+$, 231 (10) $[M–Bz]^+$, 135 (15), 105 (100), 77 (35), 51 (5), 43 (13).

HR-MS (ESI): *m/z* calcd for $C_{22}H_{24}O_3Na^+$ $[M+Na]^+$ 359.1618, found 359.1622.

1-[3-Cycloheptyl-4-(trifluoromethyl)phenyl]ethan-1-one (154uh)



The general procedure **B** was followed using ketimine **135u** (177 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154uh** (84.0 mg, 59%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.99 (s, 1H), 7.78 (dq, *J* = 8.2, 0.8 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 1H), 3.15–3.06 (m, 1H), 2.63 (s, 3H), 1.91–1.78 (m, 4H), 1.78–1.51 (m, 8H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 197.4 (C_q), 149.9 (q, $^3J_{C-F}$ = 2 Hz, C_q), 139.8 (C_q), 130.7 (q, $^2J_{C-F}$ = 30 Hz, C_q), 127.8 (CH), 125.9 (q, $^3J_{C-F}$ = 6 Hz, CH), 125.2 (CH), 124.1 (q, $^1J_{C-F}$ = 273 Hz, C_q), 41.6 (q, $^4J_{C-F}$ = 2 Hz, CH), 36.9 (CH_2), 27.5 (CH_2), 27.4 (CH_2), 26.8 (CH_3).

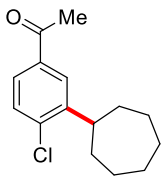
^{19}F-NMR (376 MHz, $CDCl_3$): δ = –59.5 (s).

IR (ATR): $\tilde{\nu}$ = 2925, 2856, 1692, 1574, 1415, 1310, 1238, 1154, 1035, 829 cm^{-1}.

MS (EI) *m/z* (relative intensity): 284 (35) $[M]^+$, 214 (55), 199 (100), 151 (23).

HR-MS (ESI): *m/z* calcd for $C_{16}H_{19}F_3NaO^+$ $[M+Na]^+$ 307.1280, found 307.1286.

1-(4-Chloro-3-cycloheptylphenyl)ethan-1-one (154ch)



The general procedure **B** was followed using ketimine **135c** (160 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154ch** (68.1 mg, 54%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 2.2, 0.4 Hz, 1H), 7.66 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.41 (dd, *J* = 8.3, 0.4 Hz, 1H), 3.27–3.14 (m, 1H), 2.58 (s, 3H), 1.98–1.52 (m, 12H).

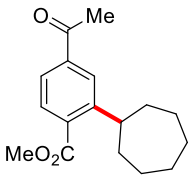
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 197.1 (C_q), 147.2 (C_q), 138.2 (C_q), 135.8 (C_q), 129.5 (CH), 127.2 (CH), 126.5 (CH), 42.3 (CH), 35.4 (CH_2), 27.8 (CH_2), 27.4 (CH_2), 26.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2922, 2854, 1684, 1591, 1406, 1355, 1235, 1038, 815, 523 cm^{-1}.

MS (EI) *m/z* (relative intensity): 252 (17) $[M(^{37}Cl)]^+$, 250 (48) $[M(^{35}Cl)]^+$, 237 (27) $[M(^{37}Cl)–Me]^+$, 235 (81) $[M(^{35}Cl)–Me]^+$, 215 (44) $[M–Cl]^+$, 180 (41), 165 (73), 115 (27), 55 (23), 43 (100).

HR-MS (EI): *m/z* calcd for $C_{15}H_{19}ClO^+$ $[M]^+$ 250.1119, found 250.1118.

Methyl 4-acetyl-2-cycloheptylbenzoate (154kh)



The general procedure **B** was followed using ketimine **135k** (172 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 10:1) yielded **154kh** (97.9 mg, 71%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.94 (dd, *J* = 1.2, 1.2 Hz, 1H), 7.76–7.72 (m, 2H), 3.93 (s, 3H), 3.40 (tt, *J* = 10.3, 3.2 Hz, 1H), 2.62 (s, 3H), 1.99–1.49 (m, 12H).

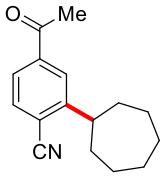
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 197.6 (C_q), 168.1 (C_q), 150.8 (C_q), 139.1 (C_q), 133.4 (C_q), 129.6 (CH), 126.8 (CH), 125.0 (CH), 52.3 (CH_3), 42.1 (CH), 36.8 (CH_2), 27.8 (CH_2), 27.6 (CH_2), 26.9 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2921, 2854, 1723, 1686, 1433, 1270, 1233, 1096, 1065, 785 cm^{-1}.

MS (EI) *m/z* (relative intensity): 274 (28) $[M]^+$, 259 (17) $[M–Me]^+$, 243 (73), 199 (34), 181 (28), 115 (23), 59 (18), 43 (100).

HR-MS (ESI): *m/z* calcd for $C_{17}H_{23}O_3^+$ $[M+H]^+$ 275.1642, found 275.1646.

4-Acetyl-2-cycloheptylbenzonitrile (154lh)



The general procedure **B** was followed using ketimine **135l** (155 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 10:1) yielded **154lh** (56.3 mg, 47%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.92 (dd, *J* = 1.7, 0.5 Hz, 1H), 7.79 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.68 (dd, *J* = 8.1, 0.5 Hz, 1H), 3.17 (tt, *J* = 10.3, 3.4 Hz, 1H), 2.62 (s, 3H), 2.00–1.55 (m, 12H).

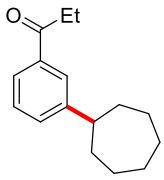
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.8 (C_q), 153.9 (C_q), 140.1 (C_q), 133.0 (CH), 126.1 (CH), 125.6 (CH), 117.4 (C_q), 115.3 (C_q), 44.9 (CH), 36.0 (CH_2), 27.7 (CH_2), 27.4 (CH_2), 26.9 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2923, 2855, 2224, 1688, 1410, 1357, 1241, 831, 541 cm^{-1}.

MS (EI) *m/z* (relative intensity): 241 (25) $[M]^+$, 240 (12) $[M–H]^+$, 226 (79) $[M–Me]^+$, 212 (27), 198 (34) $[M–Ac]^+$, 186 (24), 172 (29), 156 (100), 128 (20), 115 (19), 55 (32), 43 (76).

HR-MS (ESI): *m/z* calcd for $C_{16}H_{19}NONa^+$ $[M+Na]^+$ 264.1359, found 264.1364.

1-(3-Cycloheptylphenyl)propan-1-one (154gh)



The general procedure **B** was followed using ketimine **135g** (150 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 80:1) yielded **154gh** (67.7 mg, 59%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.81–7.77 (m, 1H), 7.77–7.72 (m, 1H), 7.41–7.30 (m, 2H), 2.99 (q, *J* = 7.3 Hz, 2H), 2.78–2.66 (m, 1H), 1.97–1.45 (m, 12H), 1.22 (t, *J* = 7.3 Hz, 3H).

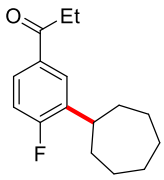
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 201.0 (C_q), 150.3 (C_q), 137.0 (C_q), 131.3 (CH), 128.4 (CH), 126.1 (CH), 125.3 (CH), 47.0 (CH), 36.7 (CH_2), 31.9 (CH_2), 27.9 (CH_2), 27.2 (CH_2), 8.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3391, 2921, 2853, 1683, 1582, 1482, 1348, 1233, 1161, 781 cm^{-1}.

MS (EI) *m/z* (relative intensity): 230 (5) $[M]^+$, 201 (100) $[M–Et]^+$, 179 (13), 131 (8).

HR-MS (ESI): *m/z* calcd for $C_{16}H_{23}O^+$ $[M+H]^+$ 231.1743, found 231.1749.

1-(3-Cycloheptyl-4-fluorophenyl)propan-1-one (154hh)



The general procedure **B** was followed using ketimine **135h** (159 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 80:1) yielded **154hh** (96.9 mg, 78%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 7.3, 2.3 Hz, 1H), 7.76 (ddd, *J* = 8.5, 4.9, 2.3 Hz, 1H), 7.03 (dd, *J* = 9.9, 8.5 Hz, 1H), 3.07–2.91 (m, 3H), 1.94–1.47 (m, 12H), 1.21 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 199.4 (C_q), 162.8 (d, $^1J_{C–F}$ = 252 Hz, C_q), 136.6 (d, $^2J_{C–F}$ = 16 Hz, C_q), 133.2 (d, $^4J_{C–F}$ = 3 Hz, C_q), 128.3 (d, $^3J_{C–F}$ = 7 Hz, CH), 127.3 (d, $^3J_{C–F}$ = 10 Hz, CH), 115.3 (d, $^2J_{C–F}$ = 24 Hz, CH), 39.6 (CH), 35.3 (CH_2), 31.7 (CH_2), 27.8 (CH_2), 27.3 (CH_2), 8.4 (CH_3).

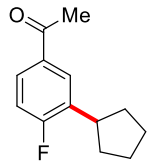
^{19}F-NMR (282 MHz, $CDCl_3$): δ = (–111.4)–(–111.6) (m).

IR (ATR): $\tilde{\nu}$ = 2923, 2855, 1685, 1586, 1492, 1350, 1237, 1150, 797 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 248 (6) $[M]^+$, 219 (100) $[M–Et]^+$, 149 (10), 109 (13).

HR-MS (ESI): *m*/*z* calcd for $C_{16}H_{22}FO^+$ $[M+H]^+$ 249.1649, found 249.1654.

1-(3-Cyclopentyl-4-fluorophenyl)ethan-1-one (154ai)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and bromocyclopentane (**136i**, 224 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154ai** (73.0 mg, 71%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 7.3, 2.3 Hz, 1H), 7.76 (ddd, *J* = 8.5, 4.9, 2.3 Hz, 1H), 7.04 (dd, *J* = 9.9, 8.5 Hz, 1H), 3.32–3.16 (m, 1H), 2.57 (d, *J* = 0.5 Hz, 3H), 2.14–1.97 (m, 2H), 1.91–1.52 (m, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.6 (C_q), 164.0 (d, $^1J_{C–F}$ = 253 Hz, C_q), 133.4 (d, $^2J_{C–F}$ = 16 Hz, C_q), 133.3 (d, $^4J_{C–F}$ = 3 Hz, C_q), 128.5 (d, $^3J_{C–F}$ = 7 Hz, CH), 128.0 (d, $^3J_{C–F}$ = 10 Hz, CH), 115.3 (d, $^2J_{C–F}$ = 24 Hz, CH), 38.8 (d, $^3J_{C–F}$ = 1 Hz, CH), 33.1 (d, $^4J_{C–F}$ = 1 Hz, CH_2), 26.5 (CH_3), 25.4 (CH_2).

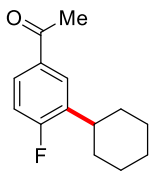
^{19}F-NMR (282 MHz, $CDCl_3$): δ = –109.7 (ddd, *J* = 9.9, 7.3, 5.0 Hz).

IR (ATR): $\tilde{\nu}$ = 3348, 2954, 2871, 1682, 1585, 1492, 1356, 1250, 1112, 822 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 206 (23) $[M]^+$, 191 (100) $[M–Me]^+$, 163 (16), 149 (20).

HR-MS (EI): *m*/*z* calcd for $C_{13}H_{15}FO^+$ $[M]^+$ 206.1101, found 206.1112.

1-(3-Cyclohexyl-4-fluorophenyl)ethan-1-one (154aj)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and bromocyclohexane (**136j**, 245 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154aj** (76.3 mg, 69%) as a colorless oil

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 7.2, 2.3 Hz, 1H), 7.77 (ddd, *J* = 8.5, 4.9, 2.3 Hz, 1H), 7.05 (dd, *J* = 9.9, 8.5 Hz, 1H), 2.94–2.81 (m, 1H), 2.57 (s, 3H), 1.90–1.71 (m, 5H), 1.57–1.18 (m, 5H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.7 (C_q), 163.5 (d, $^1J_{C-F}$ = 253 Hz, C_q), 134.9 (d, $^2J_{C-F}$ = 16 Hz, C_q), 133.4 (d, $^4J_{C-F}$ = 3 Hz, C_q), 128.3 (d, $^3J_{C-F}$ = 7 Hz, CH), 128.0 (d, $^3J_{C-F}$ = 10 Hz, CH), 115.3 (d, $^2J_{C-F}$ = 24 Hz, CH), 37.2 (d, $^3J_{C-F}$ = 2 Hz, CH), 32.9 (CH_2), 26.8 (CH_2), 26.6 (CH_3), 26.1 (CH_2).

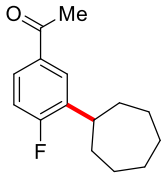
^{19}F-NMR (282 MHz, $CDCl_3$): δ = –111.6 (ddd, J = 9.9, 7.2, 4.9 Hz).

IR (ATR): $\tilde{\nu}$ = 2926, 2852, 1682, 1586, 1492, 1355, 1254, 1107, 820 cm^{-1}.

MS (EI) m/z (relative intensity): 220 (23) $[M]^+$, 205 (100) $[M–Me]^+$, 149 (23), 109 (12).

HR-MS (EI): m/z calcd for $C_{14}H_{17}FO^+$ $[M]^+$ 220.1258, found 220.1262.

1-(3-Cycloheptyl-4-fluorophenyl)ethan-1-one (154ah)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154ah** (94.7 mg, 81%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.88 (dd, J = 7.3, 2.3 Hz, 1H), 7.75 (ddd, J = 8.5, 4.9, 2.3 Hz, 1H), 7.04 (dd, J = 9.8, 8.5 Hz, 1H), 3.08–2.94 (m, 1H), 2.55 (s, 3H), 1.95–1.46 (m, 12H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 196.9 (C_q), 163.1 (d, $^1J_{C-F}$ = 253 Hz, C_q), 136.8 (d, $^2J_{C-F}$ = 16 Hz, C_q), 133.5 (d, $^4J_{C-F}$ = 3 Hz, C_q), 128.6 (d, $^3J_{C-F}$ = 7 Hz, CH), 127.9 (d, $^3J_{C-F}$ = 10 Hz, CH), 115.4 (d, $^2J_{C-F}$ = 24 Hz, CH), 39.5 (d, $^3J_{C-F}$ = 1 Hz, CH), 35.2 (d, $^4J_{C-F}$ = 1 Hz, CH_2), 27.7 (CH_2), 27.2 (CH_2), 26.5 (CH_3).

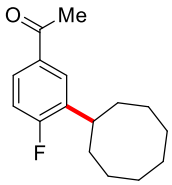
^{19}F-NMR (282 MHz, $CDCl_3$): δ = (–111.0)–(–111.1) (m).

IR (ATR): $\tilde{\nu}$ = 2921, 1682, 1585, 1492, 1416, 1355, 1243, 1170, 1104, 819 cm^{-1}.

MS (EI) m/z (relative intensity): 234 (41) $[M]^+$, 219 (100) $[M–Me]^+$, 164 (40), 149 (70).

HR-MS (EI): m/z calcd for $C_{15}H_{19}FO^+$ $[M]^+$ 234.1414, found 234.1416.

1-(3-Cyclooctyl-4-fluorophenyl)ethan-1-one (154ak)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and bromocyclooctane (**136k**, 287 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154ak** (82.7 mg, 67%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.87 (dd, J = 7.3, 2.3 Hz, 1H), 7.75 (ddd, J = 8.5, 4.9, 2.3 Hz, 1H), 7.04 (dd, J = 9.9, 8.5 Hz, 1H), 3.20–3.05 (m, 1H), 2.57 (s, 3H), 1.90–1.73 (m, 6H), 1.73–1.50 (m, 8H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.7 (C_q), 163.1 (d, $^{1}J_{C-F}$ = 253 Hz, C_q), 137.2 (d, $^{2}J_{C-F}$ = 16 Hz, C_q), 133.4 (d, $^{4}J_{C-F}$ = 3 Hz, C_q), 128.8 (d, $^{3}J_{C-F}$ = 7 Hz, CH), 127.8 (d, $^{3}J_{C-F}$ = 10 Hz, CH), 115.4 (d, $^{2}J_{C-F}$ = 24 Hz, CH), 37.3 (CH), 33.4 (CH_2), 26.7 (CH_2), 26.6 (CH_3), 26.4 (CH_2), 26.0 (CH_2).

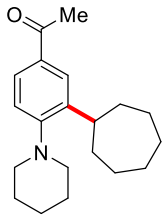
^{19}F-NMR (282 MHz, $CDCl_3$): δ = (–110.5)–(–110.7) (m).

IR (ATR): $\tilde{\nu}$ = 2919, 2852, 1682, 1585, 1492, 1355, 1283, 1108, 822 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 248 (47) $[M]^+$, 233 (38) $[M–Me]^+$, 164 (69), 149 (100).

HR-MS (ESI): *m*/*z* calcd for $C_{16}H_{22}FO^+$ $[M+H]^+$ 249.1649, found 249.1654.

1-[3-Cycloheptyl-4-(piperidin-1-yl)phenyl]ethan-1-one (154nh)



The general procedure **B** was followed using ketimine **135n** (184 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, to the reaction mixture was added HCl (2 N, 3.0 mL) and the resulting mixture was stirred for additional 3 h, and then neutralized with sat. aq. $NaHCO_3$ solution until pH 8. The reaction mixture was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 95:5) yielded **154nh** (105 mg, 70%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, J = 2.2 Hz, 1H), 7.70 (dd, J = 8.3, 2.2 Hz, 1H), 7.01 (d, J = 8.3 Hz, 1H), 3.15 (tt, J = 10.1, 3.2 Hz, 1H), 2.86 (dd, J = 5.3, 5.1 Hz, 4H), 2.55 (s, 3H), 1.89–1.45 (m, 18H).

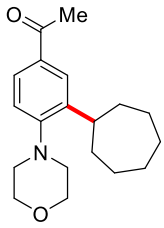
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 197.6 (C_q), 156.0 (C_q), 145.1 (C_q), 132.2 (C_q), 127.4 (CH), 126.9 (CH), 119.0 (CH), 54.2 (CH_2), 38.9 (CH), 36.8 (CH_2), 28.0 (CH_2), 27.7 (CH_2), 26.5 (CH_2), 26.4 (CH_3), 24.3 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2917, 2852, 1676, 1595, 1354, 1266, 920, 827, 599 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 299 (100) $[M]^+$, 284 (19) $[M–Me]^+$, 242 (30), 228 (35), 217 (35), 200 (19), 186 (38), 172 (27), 144 (14), 130 (14), 43 (42).

HR-MS (EI): *m*/*z* calcd for $C_{20}H_{29}NO^+$ $[M]^+$ 299.2244, found 299.2260.

1-(3-Cycloheptyl-4-morpholinophenyl)ethan-1-one (154oh)



The general procedure **B** was followed using ketimine **135o** (186 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, to the reaction mixture was added HCl (2 N, 3.0 mL) and the resulting mixture was stirred for additional 3 h, and then neutralized with sat. aq. $NaHCO_3$ solution until pH 8. The reaction mixture was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 4:1) yielded **154oh** (88.0 mg, 58%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 2.2 Hz, 1H), 7.73 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.06 (d, *J* = 8.3 Hz, 1H), 3.93–3.83 (m, 4H), 3.18 (tt, *J* = 9.9, 3.6 Hz, 1H), 2.98–2.88 (m, 4H), 2.56 (s, 3H), 1.90–1.43 (m, 12H).

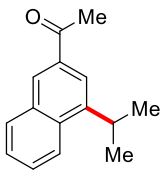
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 197.3 (C_q), 154.0 (C_q), 145.1 (C_q), 133.0 (C_q), 127.6 (CH), 126.9 (CH), 119.2 (CH), 67.3 (CH_2), 53.2 (CH_2), 39.1 (CH), 36.8 (CH_2), 28.0 (CH_2), 27.7 (CH_2), 26.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2915, 2850, 1677, 1595, 1450, 1355, 1235, 1114, 919, 828 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 301 (100) $[M]^+$, 286 (11) $[M–Me]^+$, 244 (18), 228 (29), 219 (28), 200 (24), 186 (25), 172 (40), 144 (16), 130 (15), 43 (37).

HR-MS (EI): *m*/*z* calcd for $C_{19}H_{27}NO_2^+$ $[M]^+$ 301.2036, found 301.2047.

1-(4-*iso*-Propylnaphthalen-2-yl)ethan-1-one (154ql)



The general procedure **B** was followed using ketimine **135q** (168 mg, 0.50 mmol) and 2-bromopropane (**136l**, 185 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154ql** (89.3 mg, 84%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.32 (br s, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 1.7 Hz, 1H), 7.99 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.64 (ddd, *J* = 8.5, 6.8, 1.2 Hz, 1H), 7.54 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 3.75 (hept, *J* = 6.9 Hz, 1H), 2.73 (s, 3H), 1.44 (d, *J* = 6.9 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.2 (C_q), 145.3 (C_q), 134.0 (C_q), 133.6 (C_q), 133.0 (C_q), 130.4 (CH), 128.7 (CH), 128.2 (CH), 126.0 (CH), 123.3 (CH), 119.4 (CH), 28.8 (CH), 26.6 (CH_3), 23.4 (CH_3).

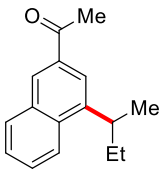
IR (ATR): $\tilde{\nu}$ = 3063, 2960, 1671, 1397, 1271, 1229, 1194, 1142, 882 cm^{-1}.

m.p.: 60–62 °C.

MS (EI) *m*/*z* (relative intensity): 212 (58) $[M]^+$, 197 (100) $[M–Me]^+$, 152 (25), 115 (8).

HR-MS (EI): *m*/*z* calcd for $C_{15}H_{16}O^+$ $[M]^+$ 212.1196, found 212.1209.

1-[4-(*sec*-Butyl)naphthalen-2-yl]ethan-1-one (154qm)



The general procedure **B** was followed using ketimine **135q** (168 mg, 0.50 mmol) and 2-bromobutane (**136m**, 206 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154qm** (87.7 mg, 78%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 1.5 Hz, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 8.01–7.94 (m, 2H), 7.63 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1H), 7.54 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 3.52 (dt, *J* = 6.9, 6.9 Hz, 1H), 2.73 (s, 3H), 1.98–1.83 (m, 1H), 1.83–1.67 (m, 1H), 1.41 (d, *J* = 6.9 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 3H).

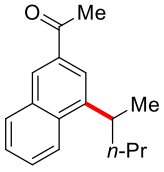
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.2 (C_q), 144.5 (C_q), 134.1 (C_q), 134.0 (C_q), 133.0 (C_q), 130.4 (CH), 128.6 (CH), 128.1 (CH), 126.0 (CH), 123.3 (CH), 120.1 (CH), 35.5 (CH), 30.5 (CH_2), 26.6 (CH_3), 21.1 (CH_3), 12.3 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3056, 2961, 1674, 1622, 1425, 1396, 1278, 1174, 885 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 226 (52) $[M]^+$, 197 (100) $[M–Et]^+$, 153 (25), 127 (10).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{18}O^+$ $[M]^+$ 226.1352, found 226.1365.

1-[4-(Pentan-2-yl)naphthalen-2-yl]ethan-1-one (154qn)



The general procedure **B** was followed using ketimine **135q** (168 mg, 0.50 mmol) and 2-bromopentane (**136n**, 227 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154qn** (91.8 mg, 77%) as a light yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 1.5 Hz, 1H), 8.16 (d, *J* = 8.6 Hz, 1H), 8.00–7.95 (m, 2H), 7.63 (ddd, *J* = 8.6, 6.8, 1.5 Hz, 1H), 7.55 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 3.61 (dt, *J* = 6.9, 6.9 Hz, 1H), 2.74 (s, 3H), 1.91–1.61 (m, 2H), 1.48–1.25 (m, 5H), 0.92 (t, *J* = 7.3 Hz, 3H).

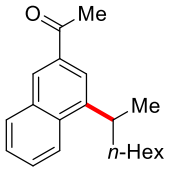
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.2 (C_q), 144.8 (C_q), 134.0 (C_q), 134.0 (C_q), 133.0 (C_q), 130.5 (CH), 128.6 (CH), 128.1 (CH), 126.0 (CH), 123.2 (CH), 120.2 (CH), 40.0 (CH_2), 33.6 (CH), 26.6 (CH_3), 21.6 (CH_3), 20.9 (CH_2), 14.3 (CH_3). j

IR (ATR): $\tilde{\nu}$ = 2957, 2928, 1675, 1623, 1453, 1375, 1277, 1194, 885 cm^{-1}.

MS (EI) *m/z* (relative intensity): 240 (53) $[M]^+$, 197 (100) $[M–Pr]^+$, 153 (26), 127 (11).

HR-MS (EI): *m/z* calcd for $C_{17}H_{20}O^+$ $[M]^+$ 240.1509, found 240.1523.

1-[4-(Octan-2-yl)naphthalen-2-yl]ethan-1-one (154qo)



The general procedure **B** was followed using ketimine **135q** (168 mg, 0.50 mmol) and 2-bromooctane (**136o**, 290 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154qo** (111.9 mg, 79%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.32 (s, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 8.01–7.94 (m, 2H), 7.63 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1H), 7.54 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 3.59 (dt, *J* = 6.9, 6.9 Hz, 1H), 2.74 (s, 3H), 1.93–1.79 (m, 1H), 1.79–1.64 (m, 1H), 1.41 (d, *J* = 6.9 Hz, 3H), 1.37–1.16 (m, 8H), 0.92–0.75 (m, 3H).

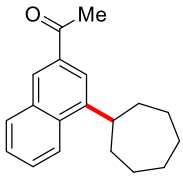
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.2 (C_q), 144.8 (C_q), 134.0 (C_q), 134.0 (C_q), 133.0 (C_q), 130.5 (CH), 128.6 (CH), 128.1 (CH), 126.0 (CH), 123.2 (CH), 120.1 (CH), 37.8 (CH_2), 33.9 (CH), 31.8 (CH_2), 29.5 (CH_2), 27.8 (CH_2), 26.6 (CH_3), 22.7 (CH_2), 21.6 (CH_3), 14.1 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2956, 2954, 1677, 1454, 1352, 1276, 1195, 885 cm^{-1}.

MS (EI) *m/z* (relative intensity): 282 (50) $[M]^+$, 191 (100), 153 (22), 127 (5).

HR-MS (EI): *m/z* calcd for $C_{20}H_{26}O^+$ $[M]^+$ 282.1978, found 282.1994.

1-(4-Cycloheptylnaphthalen-2-yl)ethan-1-one (154qh)



The general procedure **B** was followed using ketimine **135q** (168 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154qh** (117.9 mg, 89%) as a light yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.29 (br s, 1H), 8.13 (d, J = 8.5 Hz, 1H), 7.99–7.93 (m, 2H), 7.67–7.59 (m, 1H), 7.57–7.49 (m, 1H), 3.55–3.41 (m, 1H), 2.72 (d, J = 1.5 Hz, 3H), 2.14–1.99 (m, 2H), 1.99–1.56 (m, 10H).

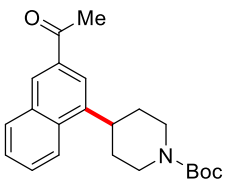
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.2 (C_q), 146.5 (C_q), 134.0 (C_q), 133.4 (C_q), 133.0 (C_q), 130.5 (CH), 128.5 (CH), 128.2 (CH), 126.0 (CH), 123.4 (CH), 120.3 (CH), 41.2 (CH), 36.3 (CH_2), 27.9 (CH_2), 27.7 (CH_2), 26.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2919, 2852, 1674, 1457, 1397, 1260, 1194, 885 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 266 (100) $[M]^+$, 209 (16), 183 (28), 153 (40).

HR-MS (EI): *m*/*z* calcd for $C_{19}H_{22}O^+$ $[M]^+$ 266.1665, found 266.1661.

tert-Butyl 4-(3-acetylnaphthalen-1-yl)piperidine-1-carboxylate (154qp)



The general procedure **B** was followed using ketimine **135q** (168 mg, 0.50 mmol) and *tert*-butyl 4-bromopiperidine-1-carboxylate (**136p**, 396 mg, 1.50 mmol) was added by syringe pump over 5.5 h at 140 °C. After 20 h, to the reaction mixture was added HCl (2 N, 3.0 mL) and the resulting mixture was stirred for additional 3 h, and then neutralized with sat. aq. $NaHCO_3$ solution until pH 8. The reaction mixture was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-pentane/Et_2O 3:1) yielded **154qp** (96.3 mg, 54%) as a white solid

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.32 (d, J = 1.6 Hz, 1H), 8.11 (d, J = 8.4 Hz, 1H), 8.01–7.96 (m, 1H), 7.93 (d, J = 1.6 Hz, 1H), 7.64 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H), 7.55 (ddd, J = 8.0, 6.9, 1.2 Hz, 1H), 4.34 (br d, J = 13.1 Hz, 2H), 3.46 (tt, J = 11.8, 3.3 Hz, 1H), 2.96 (t, J = 12.8 Hz, 2H), 2.71 (s, 3H), 2.03–1.92 (m, 2H), 1.92–1.72 (m, 2H), 1.50 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 197.9 (C_q), 154.6 (C_q), 142.2 (C_q), 134.0 (C_q), 133.4 (C_q), 133.1 (C_q), 130.6 (CH), 129.2 (CH), 128.4 (CH), 126.2 (CH), 122.8 (CH), 120.2 (CH), 79.5 (C_q), 44.6 (CH_2), 37.8 (CH), 32.8 (CH_2), 28.5 (CH_3), 26.5 (CH_3).

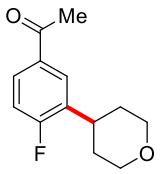
IR (ATR): $\tilde{\nu}$ = 2973, 2855, 1673, 1426, 1363, 1228, 1163, 1122, 891, 753 cm^{-1}.

m.p.: 139–140 °C.

MS (EI) *m*/*z* (relative intensity): 353 (10) $[M]^+$, 280 (10) $[M–Ot\text{-}Bu]^+$, 253 (46) $[M–Boc]^+$, 198 (21), 165 (9), 152 (14), 83 (17), 69 (9), 57 (100), 43 (61).

HR-MS (EI): *m/z* calcd for $C_{22}H_{27}NO_3^+$ $[M]^+$ 353.1985, found 353.1980.

1-[4-Fluoro-3-(tetrahydro-2*H*-pyran-4-yl)phenyl]ethan-1-one (154aq)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and 4-bromotetrahydro-2*H*-pyran (**136q**, 248 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 10:1 to 3:1) yielded **154aq** (46.7 mg, 42%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 7.3, 2.4 Hz, 1H), 7.81 (ddd, *J* = 8.5, 5.1, 2.4 Hz, 1H), 7.08 (dd, *J* = 9.9, 8.5 Hz, 1H), 4.08 (ddt, *J* = 11.7, 4.3, 1.1 Hz, 2H), 3.55 (ddd, *J* = 11.8, 11.7, 2.1 Hz, 2H), 3.13 (ddt, *J* = 12.1, 7.6, 3.8 Hz, 1H), 2.57 (s, 3H), 1.94–1.82 (m, 2H), 1.78–1.71 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 196.6 (C_q), 163.7 (d, $^1J_{C-F}$ = 254 Hz, C_q), 133.7 (d, $^4J_{C-F}$ = 3 Hz, C_q), 132.9 (d, $^2J_{C-F}$ = 15 Hz, C_q), 128.6 (d, $^3J_{C-F}$ = 10 Hz, CH), 128.3 (d, $^3J_{C-F}$ = 7 Hz, CH), 115.6 (d, $^2J_{C-F}$ = 24 Hz, CH), 68.2 (CH_2), 34.6 (d, $^3J_{C-F}$ = 2 Hz, CH), 32.3 (d, $^4J_{C-F}$ = 1 Hz, CH_2), 26.5 (CH_3).

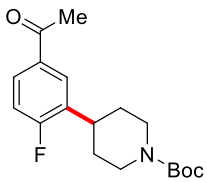
^{19}F-NMR (376 MHz, $CDCl_3$): δ = –111.5 (ddd, *J* = 9.9, 7.3, 5.1 Hz).

IR (ATR): $\tilde{\nu}$ = 2952, 2843, 1682, 1586, 1494, 1356, 1234, 1087, 821 cm^{-1}.

MS (EI) *m/z* (relative intensity): 222 (44) $[M]^+$, 207 (33) $[M–Me]^+$, 178 (31), 163 (71), 149 (60), 133 (14), 101 (19), 58 (17), 43 (100).

HR-MS (EI): *m/z* calcd for $C_{13}H_{15}FO_2^+$ $[M]^+$ 222.1051, found 222.1050.

tert-Butyl 4-(5-acetyl-2-fluorophenyl)piperidine-1-carboxylate (154ap)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and *tert*-butyl 4-bromopiperidine-1-carboxylate (**136p**, 396 mg, 1.50 mmol) was added in 3 portions after 3 h and 6 h at 140 °C. After 20 h, to the reaction mixture was added HCl (2 N, 3.0 mL) and the resulting mixture was stirred for additional 3 h, and then neutralized with sat. aq. $NaHCO_3$ solution until pH 8. The reaction mixture was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-pentane/Et_2O 3:1) yielded **154ap** (83.1 mg, 52%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.86 (dd, J = 7.2, 2.3 Hz, 1H), 7.81 (ddd, J = 8.5, 5.0, 2.3 Hz, 1H), 7.09 (dd, J = 9.9, 8.5 Hz, 1H), 4.27 (d, J = 13.0 Hz, 2H), 3.03 (tt, J = 12.3, 3.7 Hz, 1H), 2.83 (dd, J = 13.0, 12.6 Hz, 2H), 2.58 (s, 3H), 1.81 (d_{AB}, J = 12.6 Hz, 2H), 1.69 (d_{AB}ddd, J = 12.6, 12.6, 12.3, 4.1 Hz, 2H), 1.49 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.4 (C_q), 163.5 (d, $^{1}J_{C–F}$ = 253 Hz, C_q), 154.6 (C_q), 133.7 (d, $^{4}J_{C–F}$ = 3 Hz, C_q), 132.8 (d, $^{2}J_{C–F}$ = 15 Hz, C_q), 128.6 (d, $^{3}J_{C–F}$ = 10 Hz, CH), 128.2 (d, $^{3}J_{C–F}$ = 7 Hz, CH), 115.6 (d, $^{2}J_{C–F}$ = 24 Hz, CH), 79.6 (C_q), 44.3 (CH_2), 35.7 (d, $^{3}J_{C–F}$ = 2 Hz, CH), 31.7 (CH_2), 28.6 (CH_3), 26.6 (CH_3).

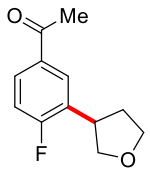
^{19}F-NMR (282 MHz, $CDCl_3$): δ = –111.5 (ddd, J = 9.9, 7.2, 5.0 Hz).

IR (ATR): $\tilde{\nu}$ = 2975, 2930, 1685, 1587, 1420, 1365, 1233, 1166, 1021, 819 cm^{-1}.

MS (EI) m/z (relative intensity): 321 (2) $[M]^+$, 266 (7) $[M–t\text{-Bu}]^+$, 248 (21) $[M–t\text{-Bu–Me}]^+$, 221 (51), 83 (9), 57 (100), 43 (40).

HR-MS (EI): m/z calcd for $C_{18}H_{24}FNO_3^+$ $[M]^+$ 321.1735, found 321.1742.

1-[4-Fluoro-3-(tetrahydrofuran-3-yl)phenyl]ethan-1-one (154ar)



The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and 3-bromotetrahydrofuran (**136r**, 226 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 10:1 to 4:1) yielded **154ar** (26.1 mg, 25%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.93 (dd, J = 7.3, 2.3 Hz, 1H), 7.83 (ddd, J = 8.5, 5.0, 2.3 Hz, 1H), 7.10 (dd, J = 9.7, 8.5 Hz, 1H), 4.19–4.12 (m, 1H), 4.08 (ddd, J = 8.3, 8.1, 5.0 Hz, 1H), 3.94 (ddd, J = 8.3, 7.4, 7.4 Hz, 1H), 3.81–3.74 (m, 1H), 3.69 (p, J = 7.4 Hz, 1H), 2.58 (s, 3H), 2.45–2.32 (m, 1H), 2.13–2.01 (m, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.4 (C_q), 163.7 (d, $^{1}J_{C–F}$ = 254 Hz, C_q), 133.7 (d, $^{4}J_{C–F}$ = 3 Hz, C_q), 130.0 (d, $^{2}J_{C–F}$ = 15 Hz, C_q), 128.8 (d, $^{3}J_{C–F}$ = 10 Hz, CH), 128.7 (d, $^{3}J_{C–F}$ = 6 Hz, CH), 115.6 (d, $^{2}J_{C–F}$ = 24 Hz, CH), 73.0 (d, $^{4}J_{C–F}$ = 2.0 Hz, CH_2), 68.2 (CH_2), 37.9 (d, $^{3}J_{C–F}$ = 1.6 Hz, CH), 33.0 (CH_2), 26.6 (CH_3).

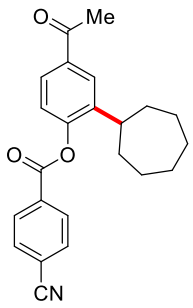
^{19}F-NMR (282 MHz, $CDCl_3$): δ = –109.6 (ddd, J = 9.7, 7.3, 5.0 Hz).

IR (ATR): $\tilde{\nu}$ = 2876, 1684, 1588, 1496, 1359, 1254, 1063, 830, 572 cm^{-1}.

MS (ESI) m/z (relative intensity): 231 (100) $[M+Na]^+$, 209 (41) $[M+H]^+$.

HR-MS (ESI): m/z calcd for $C_{12}H_{13}FO_2Na^+$ $[M+Na]^+$ 231.0792, found 231.0794.

4-Acetyl-2-cycloheptylphenyl 4-cyanobenzoate (154vh)



The general procedure **B** was followed using ketimine **135v** (108 mg, 0.25 mmol) and bromocycloheptane (**136h**, 133 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 9:1) yielded **154vh** (10.2 mg, 11%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 8.7 Hz, 2H), 7.98 (d, *J* = 2.2 Hz, 1H), 7.87 (d, *J* = 8.7 Hz, 2H), 7.84 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 1H), 2.85 (tt, *J* = 10.4, 3.3 Hz, 1H), 2.62 (s, 3H), 1.95–1.37 (m, 12H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 197.0 (C_q), 163.1 (C_q), 151.0 (C_q), 141.6 (C_q), 135.5 (C_q), 132.8 (C_q), 132.5 (CH), 130.5 (CH), 128.0 (CH), 127.1 (CH), 122.4 (CH), 117.6 (C_q), 117.3 (C_q), 40.4 (CH), 35.5 (CH_2), 27.7 (CH_2), 27.5 (CH_2), 26.7 (CH_3).

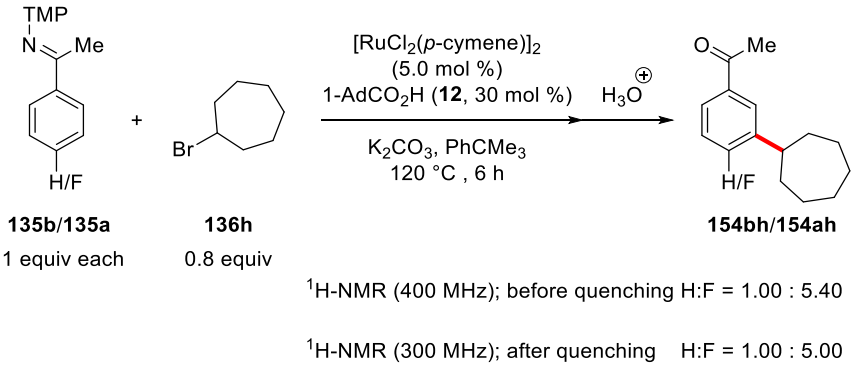
IR (ATR): $\tilde{\nu}$ = 2924, 2856, 2232, 1743, 1684, 1239, 1081, 1018, 761 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 384 (100) $[M+Na]^+$, 362 (47) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{23}H_{23}NO_3Na^+$ $[M+Na]^+$ 384.1570, found 384.1575.

5.3.2.2 Mechanistic Studies

5.3.2.2.1 Intermolecular Competition Experiments



Ketimine **135b** (143 mg, 0.50 mmol), **135a** (152 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 25.0 µmol, 5.0 mol %), 1-$AdCO_2H$ (**12**, 27.3 mg, 0.15 mmol, 30 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL pressure tube. The tube was evacuated and purged with N_2 for three times. Bromocycloheptane (**136h**, 70.8 mg, 0.40 mmol) and $PhCMe_3$ (2.0 mL) were then added and the mixture was stirred at 120 °C for 6 h. At ambient temperature, the

resulting mixture was filtered and washed with EtOAc. The filtrate was concentrated *in vacuo*. The crude mixture was analyzed by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene (84.1 mg, 0.50 mmol) as the internal standard (Figure 14). The mixture was dissolved with Et_2O (10 mL) and then treated with HCl (2 N, 3.0 mL). The resulting mixture was stirred at ambient temperature for 3 h, and then extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The crude mixture was again analyzed by ^{1}H-NMR spectroscopy (Figure 15).

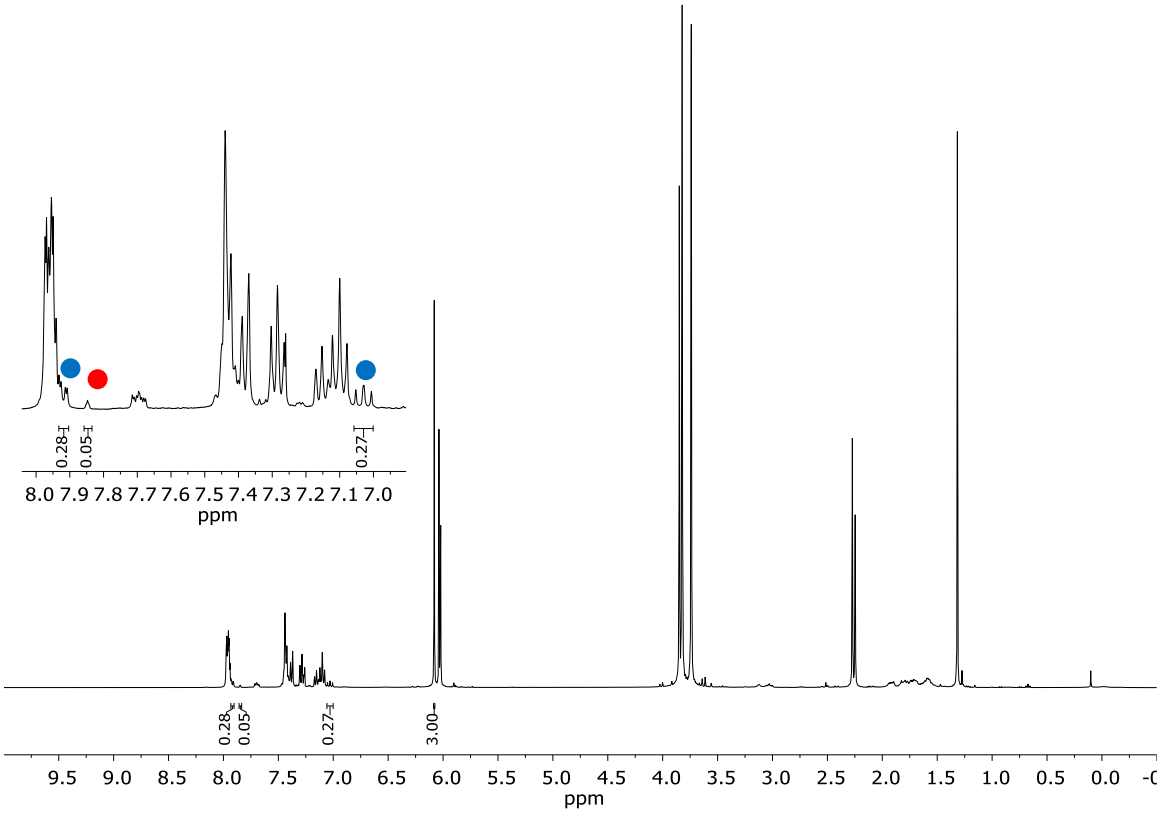


Figure 14: ^{1}H-NMR spectrum for a crude mixture before hydrolysis (H = ●, F = ●).

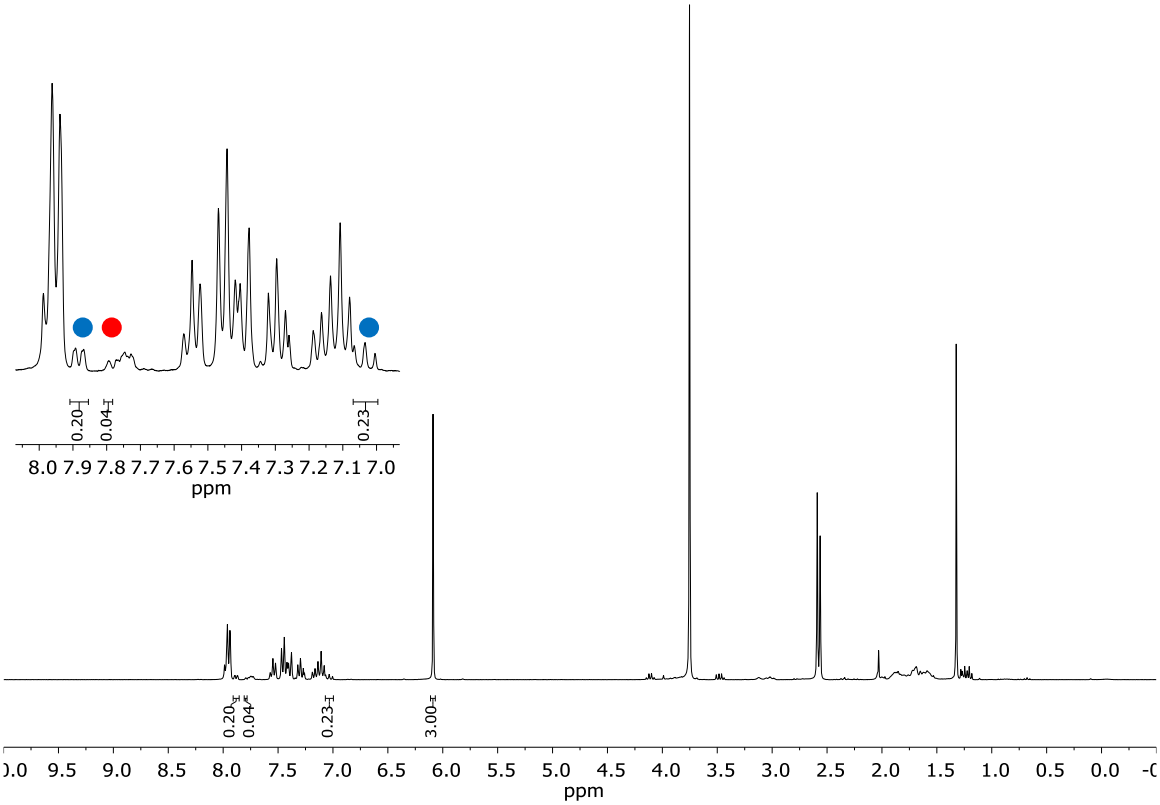
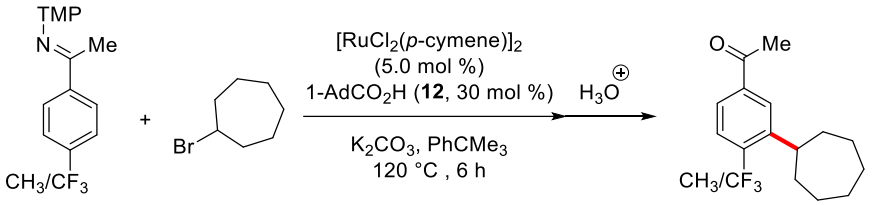


Figure 15: ^{1}H-NMR spectrum for a crude mixture after hydrolysis (**154bh** (H)=●, **154ah** (F)=●).



135e/135u 1 equiv each

136h 0.8 equiv

154eh/154uh

^{1}H-NMR (400 MHz); before quenching CH_3:CF_3 = 1.00 : 1.48

^{1}H-NMR (300 MHz); after quenching CH_3:CF_3 = 1.00 : 1.57

Ketimine **135e** (150 mg, 0.50 mmol), **135u** (177 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 25.0 µmol, 5.0 mol %), 1-$AdCO_2H$ (**12**, 27.3 mg, 0.15 mmol, 30 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL pressure tube. The tube was evacuated and purged with N_2 for three times. Bromocycloheptane (**136h**, 70.8 mg, 0.40 mmol) and $PhCMe_3$ (2.0 mL) were then added and the mixture was stirred at 120 °C for 6 h. At ambient temperature, the resulting mixture was filtered and washed with EtOAc. The filtrate was concentrated *in vacuo*. The crude mixture was analyzed by ^{1}H-NMR spectroscopy using 1,3,5-trimethoxybenzene (84.1 mg, 0.50 mmol) as the internal standard (Figure 16). The mixture was dissolved with Et_2O (10 mL) and then treated with HCl (2 N, 3.0 mL). The resulting mixture was stirred at ambient temperature for

3 h, and then extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The crude mixture was again analyzed by ^{1}H-NMR spectroscopy (Figure 17).

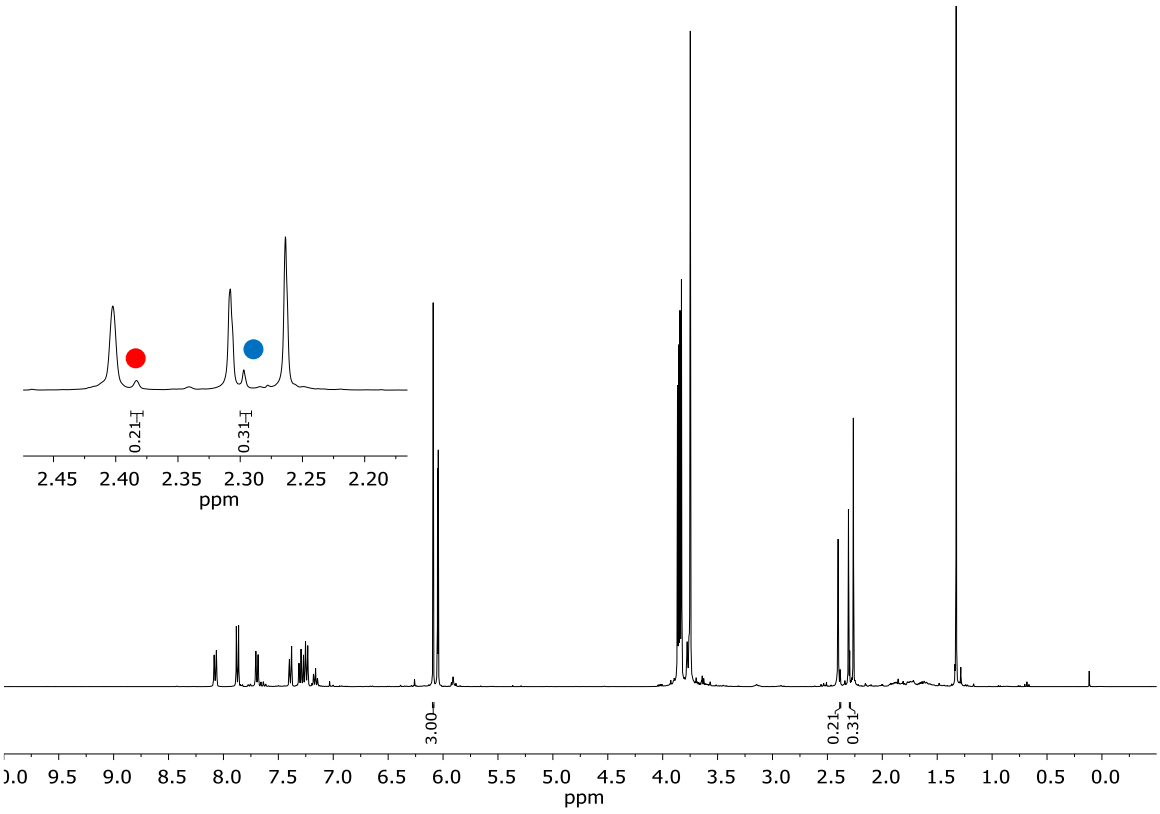


Figure 16: ^{1}H-NMR spectrum for a crude mixture before hydrolysis (CH_3 = ●, CF_3 = ●).

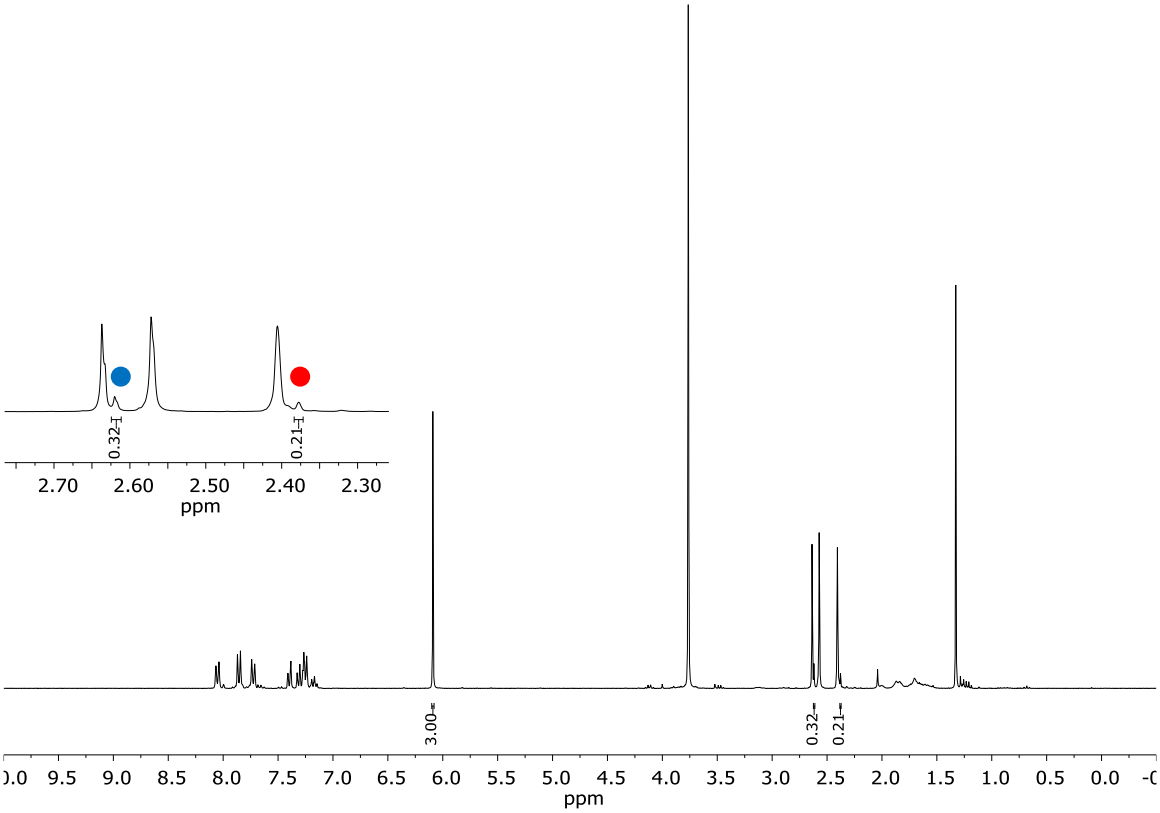
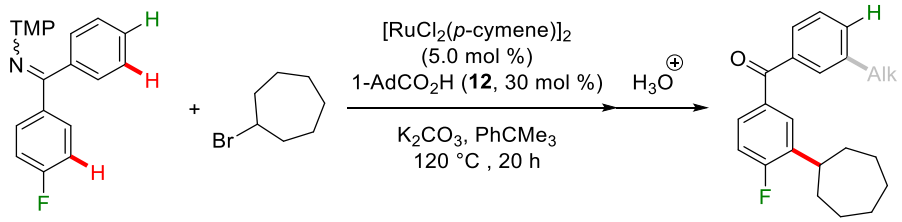


Figure 17: ^{1}H-NMR spectrum for a crude mixture after hydrolysis (**154eh** (CH_3)=●, **154uh** (CF_3)=●).

5.3.2.2.2 Intramolecular Competition Experiment



135w | **136h** 1.2 equiv | 1.5 equiv | **154wh** 29% (di 5%) | 46% (di 31%)

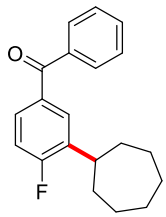
Alkyl bromide 136h (1.2 equiv)

The general procedure **B** was followed using ketimine **135w** (183 mg, 0.50 mmol) and bromocycloheptane (**136h**, 107 mg, 0.60 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 100:1) followed by recycling preparative HPLC yielded monoalkylated **154wh** (43.0 mg, 29%) as a colorless oil as well as dialkylated **154wh'** (9.1 mg, 5%) as a colorless oil and recovered unreacted ketone (43.2 mg, 43%) as a colorless oil.

Alkyl bromide 136h (1.5 equiv)

The general procedure **B** was followed using ketimine **135w** (183 mg, 0.50 mmol) and bromocycloheptane (**136h**, 133 mg, 0.75 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 100:1) followed by recycling preparative HPLC yielded monoalkylated **154wh** (68.1 mg, 46%) as a colorless oil as well as dialkylated **154wh'** (62.2 mg, 31%) as a colorless oil and recovered unreacted ketone (8.1 mg, 8%) as a colorless oil.

(3-Cycloheptyl-4-fluorophenyl)(phenyl)methanone (154wh)



^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.78–7.75 (m, 3H), 7.61–7.57 (m, 2H), 7.51–7.47 (m, 2H), 7.07 (dd, *J* = 9.9, 8.4 Hz, 1H), 3.05 (tt, *J* = 10.7, 3.5 Hz, 1H), 1.94–1.88 (m, 2H), 1.84–1.77 (m, 2H), 1.75–1.65 (m, 4H), 1.63–1.53 (m, 4H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 195.7 (C_q), 162.8 (d, $^{1}J_{C-F}$ = 253 Hz, C_q), 137.7 (C_q), 136.7 (d, $^{2}J_{C-F}$ = 16 Hz, C_q), 133.6 (d, $^{4}J_{C-F}$ = 3 Hz, C_q), 132.3 (CH), 130.5 (d, $^{3}J_{C-F}$ = 7 Hz, CH), 129.9 (CH), 129.7 (d, $^{3}J_{C-F}$ = 10 Hz, CH), 128.3 (CH), 115.2 (d, $^{2}J_{C-F}$ = 24 Hz, CH), 39.5 (CH), 35.2 (CH_2), 27.7 (CH_2), 27.3 (CH_2).

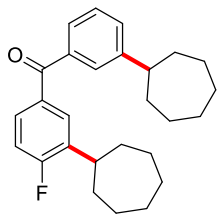
^{19}F-NMR (470 MHz, $CDCl_3$): δ = (–111.7)–(–111.8) (m).

IR (ATR): $\tilde{\nu}$ = 2924, 2855, 1657, 1599, 1490, 1446, 1281, 1092, 713 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 296 (92) $[M]^+$, 226 (68), 149 (53), 105 (100).

HR-MS (ESI): *m*/*z* calcd for $C_{20}H_{22}FO^+$ $[M+H]^+$ 297.1649, found 297.1654.

(3-Cycloheptyl-4-fluorophenyl)(3-cycloheptylphenyl)methanone (154wh')



^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.74 (dd, *J* = 7.3, 2.3 Hz, 1H), 7.62 (ddd, *J* = 8.5, 5.0, 2.3 Hz, 1H), 7.60–7.59 (m, 1H), 7.56 (ddd, *J* = 7.4, 1.6, 1.6 Hz, 1H), 7.42 (ddd, *J* = 7.6, 1.6, 1.6 Hz, 1H), 7.38 (dd, *J* = 7.6, 7.4 Hz, 1H), 7.08 (dd, *J* = 9.9, 8.5 Hz, 1H), 3.06 (tt, *J* = 10.7, 3.5 Hz, 1H), 2.74 (tt, *J* = 10.7, 3.6 Hz, 1H), 1.97–1.89 (m, 4H), 1.85–1.77 (m, 4H), 1.74–1.65 (m, 8H), 1.63–1.51 (m, 8H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 195.9 (C_q), 162.7 (d, $^{1}J_{C-F}$ = 252 Hz, C_q), 150.1 (C_q), 137.7 (C_q), 136.5 (d, $^{2}J_{C-F}$ = 16 Hz, C_q), 133.8 (d, $^{4}J_{C-F}$ = 3 Hz, C_q), 130.9 (CH), 130.6 (d, $^{3}J_{C-F}$ = 7 Hz, CH), 129.6 (d, $^{3}J_{C-F}$ = 10 Hz, CH), 128.3 (CH), 128.2 (CH), 127.3 (CH), 115.2 (d, $^{2}J_{C-F}$ = 24 Hz, CH), 46.9 (CH), 39.3 (CH), 36.8 (CH_2), 35.3 (CH_2), 27.8 (CH_2), 27.8 (CH_2), 27.3 (CH_2), 27.2 (CH_2).

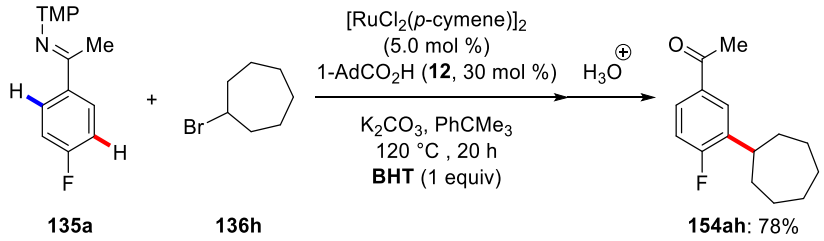
^{19}F-NMR (282 MHz, $CDCl_3$): δ = (–112.1)–(–112.2) (m).

IR (ATR): $\tilde{\nu}$ = 2919, 1657, 1583, 1284, 1246, 1170, 1091, 833, 806, 755 cm^{-1}.

MS (EI) *m/z* (relative intensity): 392 (100) $[M]^+$, 310 (22), 219 (57), 201 (22), 149 (24), 55 (19).

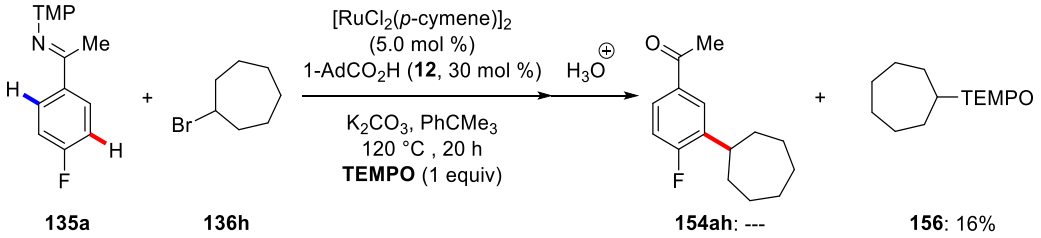
HR-MS (EI): *m/z* calcd for $C_{27}H_{33}FO^+$ $[M]^+$ 392.2510, found 392.2523.

5.3.2.2.3 Reactions with Radical Scavengers



135a **136h** **154ah**: 78%

Ketimine **135a** (152 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 25.0 µmol, 5.0 mol %), 1-$AdCO_2H$ (**12**, 27.3 mg, 0.15 mmol, 30 mol %), K_2CO_3 (138 mg, 1.00 mmol) and BHT (110 mg, 0.50 mmol) were placed in a pre-dried 25 mL pressure tube. The tube was evacuated and purged with N_2 for three times. Bromocycloheptane (**136h**, 266 mg, 1.50 mmol) and $PhCMe_3$ (2.0 mL) were then added and the mixture was stirred at 120 °C for 20 h. At ambient temperature, HCl (2 N, 3.0 mL) was added, and the resulting mixture was stirred for additional 3 h, and then extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-pentane/Et_2O 50:1) yielded product **154ah** (91.0 mg, 78%) as a colorless oil.

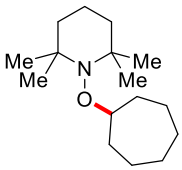


135a **136h** **154ah**: --- **156**: 16%

Ketimine **135a** (152 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 25.0 µmol, 5.0 mol %), 1-$AdCO_2H$ (**12**, 27.3 mg, 0.15 mmol, 30 mol %), K_2CO_3 (138 mg, 1.00 mmol) and TEMPO (78.5 mg, 0.50 mmol) were placed in a pre-dried 25 mL pressure tube. The tube was evacuated and purged with N_2 for three times. Bromocycloheptane (**136h**, 266 mg, 1.50 mmol) and $PhCMe_3$ (2.0 mL) were then added and the mixture was stirred at 120 °C for 20 h. At ambient temperature, HCl (2 N,

3.0 mL) was added, and the resulting mixture was stirred for additional 3 h, and then extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-pentane/Et_2O 50:1) yielded TEMPO-adduct **156** (20.0 mg, 16%) as a colorless oil.

1-(Cycloheptyloxy)-2,2,6,6-tetramethylpiperidine (156)



^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.82 (tt, J = 8.5, 4.4 Hz, 1H), 2.07–1.95 (m, 2H), 1.71–1.41 (m, 13H), 1.40–1.22 (m, 3H), 1.11 (s, 12H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 83.8 (CH), 59.7 (C_q), 40.3 (CH_2), 34.4 (CH_3), 33.5 (CH_2), 28.6 (CH_2), 23.4 (CH_2), 20.4 (CH_3), 17.3 (CH_2).

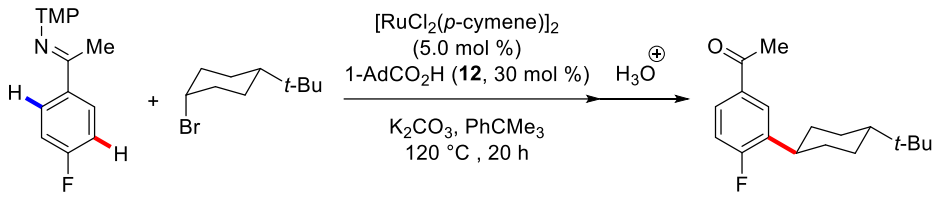
IR (ATR): $\tilde{\nu}$ = 2924, 2856, 1458, 1359, 1132, 1006, 973 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 254 (100) $[M+H]^+$, 126 (33).

HR-MS (ESI): *m*/*z* calcd for $C_{16}H_{32}NO^+$ $[M+H]^+$ 254.2478, found 254.2479.

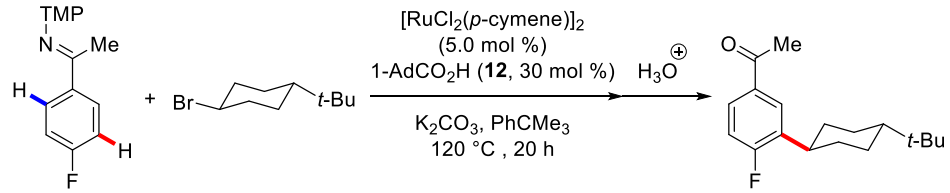
The spectral data are in accordance with those reported in the literature.[132]

*5.3.2.2.4 Reactions with Diastereomerically Pure Alkyl Bromide **136s***



135a *cis*-**136s** **154as** 75%, *cis*:*trans* 43:57

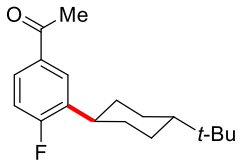
The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and *cis*-1-bromo-4-(*tert*-butyl)cyclohexane (*cis*-**136s**, 329 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154as** as a mixture of *cis*- and *trans*-isomers (*cis*-**154as**/*trans*-**154as** 43:57, 104 mg, 75%).



135a *trans*-**136s** **154as**
51%, *cis*:*trans* 43:57

The general procedure **B** was followed using ketimine **135a** (152 mg, 0.50 mmol) and *trans*-1-bromo-4-(*tert*-butyl)cyclohexane (*trans*-**136s**, 329 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-pentane/Et_2O 50:1) yielded **154as** as a mixture of *cis*- and *trans*-isomers (*cis*-**154as**/*trans*-**154as** 43:57, 71.2 mg, 51%).

1-{3-[*trans*-4-(*tert*-Butyl)cyclohexyl]-4-fluorophenyl}ethan-1-one (*trans*-154as)



White solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.88 (dd, J = 7.1, 2.3 Hz, 1H), 7.77 (ddd, J = 8.5, 4.9, 2.3 Hz, 1H), 7.05 (dd, J = 9.9, 8.5 Hz, 1H), 2.83 (tt, J = 12.2, 3.4 Hz, 1H), 2.58 (s, 3H), 2.00–1.86 (m, 4H), 1.60–1.42 (m, 2H), 1.28–1.05 (m, 3H), 0.89 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.7 (C_q), 163.7 (d, $^1J_{C-F}$ = 253 Hz, C_q), 134.7 (d, $^2J_{C-F}$ = 16 Hz, C_q), 133.5 (d, $^4J_{C-F}$ = 3 Hz, C_q), 128.3 (d, $^3J_{C-F}$ = 7 Hz, CH), 128.0 (d, $^3J_{C-F}$ = 10 Hz, CH), 115.4 (d, $^2J_{C-F}$ = 24 Hz, CH), 47.7 (CH), 37.2 (d, $^3J_{C-F}$ = 2 Hz, CH), 33.3 (CH_2), 32.5 (C_q), 27.6 (CH_3), 27.6 (CH_2), 26.6 (CH_3).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = –111.5 (ddd, J = 9.9, 7.1, 4.9 Hz).

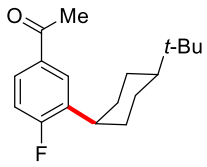
IR (ATR): $\tilde{\nu}$ = 2940, 2859, 1681, 1606, 1491, 1354, 1281, 1116, 825, 570 cm^{-1}.

m.p.: 54–55 °C.

MS (EI) *m*/*z* (relative intensity): 276 (32) $[M]^+$, 261 (11) $[M–Me]^+$, 220 (71) $[M–Bu]^+$, 205 (100), 177 (25), 151 (34), 57 (94), 43 (96).

HR-MS (EI): *m*/*z* calcd for $C_{18}H_{25}FO^+$ $[M]^+$ 276.1884, found 276.1896.

1-{3-[*cis*-4-(*tert*-Butyl)cyclohexyl]-4-fluorophenyl}ethan-1-one (*cis*-154as)



Colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.11 (ddd, J = 7.6, 2.3, 0.8 Hz, 1H), 7.79 (dddd, J = 8.5, 4.8, 2.3, 0.5 Hz, 1H), 7.05 (dd, J = 11.0, 8.5 Hz, 1H), 3.35–3.26 (m, 1H), 2.59 (s, 3H), 2.17–2.07 (m, 2H), 1.88–1.73 (m, 2H), 1.72–1.60 (m, 2H), 1.26 (qd, J = 12.1, 3.5 Hz, 2H), 1.14 (tt, J = 11.2, 3.0 Hz, 1H), 0.85 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.7 (C_q), 164.2 (d, $^{1}J_{C-F}$ = 254 Hz, C_q), 133.8 (d, $^{2}J_{C-F}$ = 14 Hz, C_q), 132.9 (d, $^{4}J_{C-F}$ = 3 Hz, C_q), 129.7 (d, $^{3}J_{C-F}$ = 6 Hz, CH), 128.0 (d, $^{3}J_{C-F}$ = 10 Hz, CH), 115.4 (d, $^{2}J_{C-F}$ = 24 Hz, CH), 47.4 (CH), 32.7 (C_q), 31.1 (CH), 29.9 (CH_2), 29.9 (CH_2), 27.6 (CH_3), 26.6 (CH_3), 23.3 (CH_2).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = –107.9 (ddd, J = 11.0, 7.6, 4.8 Hz).

IR (ATR): $\tilde{\nu}$ = 2941, 2866, 1687, 1584, 1491, 1357, 1254, 1112, 828, 575 cm^{-1}.

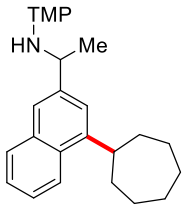
MS (EI) *m*/*z* (relative intensity): 276 (2) $[M]^+$, 261 (3) $[M–Me]^+$, 220 (29) $[M–Bu]^+$, 205 (23), 177 (14), 149 (10), 57 (26), 43 (100).

HR-MS (EI): *m*/*z* calcd for $C_{18}H_{25}FO^+$ $[M]^+$ 276.1884, found 276.1884.

5.3.2.3 Late-Stage Diversifications

Remote meta-C–H Alkylations Followed by Reduction in One-Pot Fashion

***N*-[1-(4-Cycloheptylnaphthalen-2-yl)ethyl]-3,4,5-trimethoxyaniline (157a)**



The general procedure **D** was followed using ketimine **135q** (168 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **157a** (167 mg, 77%) as a white solid as well as alkylated phenone **154qh** (4.1 mg, 3%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.10 (d, J = 7.9 Hz, 1H), 7.84–7.80 (m, 1H), 7.69 (br s, 1H), 7.52–7.40 (m, 3H), 5.85 (s, 2H), 4.59 (q, J = 6.7 Hz, 1H), 4.07 (br s, 1H), 3.74 (s, 3H), 3.70 (s, 6H), 3.56–3.47 (m, 1H), 2.14–2.03 (m, 2H), 1.96–1.75 (m, 6H), 1.75–1.63 (m, 4H), 1.61 (d, J = 6.7 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 153.6 (C_q), 146.4 (C_q), 144.2 (C_q), 142.3 (C_q), 134.1 (C_q), 130.3 (C_q), 129.8 (C_q), 128.8 (CH), 125.4 (CH), 125.2 (CH), 123.1 (CH), 122.1 (CH), 121.3 (CH), 91.1 (CH), 60.9

(CH_3), 55.7 (CH_3), 54.5 (CH), 40.9 (CH), 36.5 (CH_2), 36.2 (CH_2), 27.8 (CH_2), 27.8 (CH_2), 27.6 (CH_2), 27.6 (CH_2), 24.6 (CH_3).

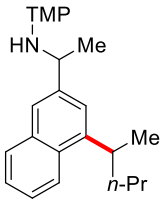
IR (ATR): $\tilde{\nu}$ = 3362, 2919, 1604, 1507, 1446, 1235, 1123, 1009, 810, 749 cm^{-1}.

m.p.: 158–159 °C.

MS (EI) *m/z* (relative intensity): 433 (80) $[M]^+$, 418 (18) $[M–Me]^+$, 251 (100), 183 (24), 168 (35), 155 (16), 55 (24).

HR-MS (EI): *m/z* calcd for $C_{28}H_{35}NO_3^+$ $[M]^+$ 433.2611, found 433.2628.

3,4,5-Trimethoxy-*N*-{1-[4-(pentan-2-yl)naphthalen-2-yl]ethyl}aniline (157b)



The general procedure **D** was followed using ketimine **135q** (168 mg, 0.50 mmol) and 2-bromopentane (**136n**, 227 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1 to 4:1) yielded **157b** (164 mg, 80%, dr 1.0:1.3) as a viscous yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$, determined as a diastereomeric mixture (1.0:1.3)): δ = 8.12–8.06 (m, 2H), 7.84–7.78 (m, 2H), 7.69–7.66 (m, 2H), 7.50–7.40 (m, 4H), 7.38 (d, *J* = 1.7 Hz, 2H), 5.81 (s, 2H), 5.80 (s, 2H), 4.58 (qd, *J* = 6.7, 3.4 Hz, 2H), 4.03 (br s, 2H), 3.71 (s, 3H), 3.70 (s, 3H), 3.67 (s, 6H), 3.67 (s, 6H), 3.65–3.55 (m, 2H), 1.86–1.62 (m, 4H), 1.59 (d, *J* = 6.7 Hz, 3H), 1.59 (d, *J* = 6.7 Hz, 3H), 1.36 (d, *J* = 6.9 Hz, 6H), 1.40–1.20 (m, 4H), 0.90 (t, *J* = 7.1 Hz, 3H), 0.85 (t, *J* = 7.2 Hz, 3H).

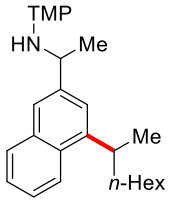
^{13}C-NMR (75 MHz, $CDCl_3$, determined as a diastereomeric mixture (1.0:1.3)): δ = 153.7 (4 × C_q), 144.7 (C_q), 144.6 (C_q), 144.2 (C_q), 144.2 (C_q), 142.3 (C_q), 142.3 (C_q), 134.2 (2 × C_q), 131.0 (2 × C_q), 129.9 (2 × C_q), 128.9 (CH), 128.8 (CH), 125.4 (2 × CH), 125.3 (2 × CH), 123.1 (2 × CH), 122.4 (CH), 122.3 (CH), 121.3 (CH), 121.2 (CH), 91.2 (2 × CH), 91.1 (2 × CH), 61.0 (2 × CH_3), 55.7 (2 × CH_3), 55.7 (2 × CH_3), 54.6 (CH), 54.5 (CH), 40.3 (CH_2), 40.0 (CH_2), 33.5 (CH), 33.4 (CH), 24.8 (2 × CH_3), 22.0 (CH_3), 21.7 (CH_3), 20.9 (CH_2), 20.8 (CH_2), 14.2 (CH_3), 14.2 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3390, 2958, 1610, 1509, 1452, 1234, 1128, 1012, 784, 748 cm^{-1}.

MS (EI) *m/z* (relative intensity): 407 (49) $[M]^+$, 392 (15) $[M–Me]^+$, 295 (14), 225 (100) $[M–NHTMP]^+$, 183 (30) $[NH_2TMP]^+$, 168 (42) $[TMP]^+$, 155 (35), 91 (11), 43 (23).

HR-MS (EI): *m/z* calcd for $C_{26}H_{33}NO_3^+$ $[M]^+$ 407.2455, found 407.2446.

3,4,5-Trimethoxy-*N*-{1-[4-(octan-2-yl)naphthalen-2-yl]ethyl}aniline (157c)



The general procedure **D** was followed using ketimine **135q** (168 mg, 0.50 mmol) and 2-bromooctane (**136o**, 290 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1 to 4:1) yielded **157c** (169 mg, 75%, dr 1.0:1.2) as a viscous yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$, determined as a diastereomeric mixture (1.0:1.2)): δ = 8.11–8.06 (m, 2H), 7.83–7.78 (m, 2H), 7.68 (br s, 2H), 7.49–7.41 (m, 4H), 7.40–7.36 (m, 2H), 5.82 (s, 2H), 5.81 (s, 2H), 4.58 (q, *J* = 6.7 Hz, 2H), 4.02 (br s, 2H), 3.71 (s, 3H), 3.70 (s, 3H), 3.68 (s, 6H), 3.67 (s, 6H), 3.62–3.52 (m, 2H), 1.89–1.73 (m, 2H), 1.73–1.63 (m, 2H), 1.59 (d, *J* = 6.7 Hz, 3H), 1.58 (d, *J* = 6.7 Hz, 3H), 1.36 (d, *J* = 6.9 Hz, 3H), 1.35 (d, *J* = 6.9 Hz, 3H), 1.33–1.17 (m, 16H), 0.91–0.80 (m, 6H).

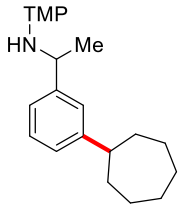
^{13}C-NMR (75 MHz, $CDCl_3$, determined as a diastereomeric mixture (1.0:1.2)): δ = 153.7 (4 × C_q), 144.8 (C_q), 144.7 (C_q), 144.2 (C_q), 144.2 (C_q), 142.3 (C_q), 142.3 (C_q), 134.2 (C_q), 134.2 (C_q), 131.0 (C_q), 131.0 (C_q), 129.9 (2 × C_q), 128.8 (CH), 128.8 (CH), 125.4 (2 × CH), 125.3 (2 × CH), 123.1 (2 × CH), 122.3 (CH), 122.3 (CH), 121.2 (2 × CH), 91.1 (4 × CH), 61.0 (CH_3), 61.0 (CH_3), 55.7 (4 × CH_3), 54.5 (2 × CH), 38.1 (CH_2), 37.7 (CH_2), 33.8 (CH), 33.7 (CH), 31.8 (CH_2), 31.7 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 27.8 (CH_2), 27.7 (CH_2), 24.8 (2 × CH_3), 22.7 (CH_2), 22.6 (CH_2), 22.0 (CH_3), 21.7 (CH_3), 14.1 (CH_3), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3383, 2926, 1608, 1507, 1451, 1232, 1125, 1011, 782, 746 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 449 (65) $[M]^+$, 434 (19) $[M–Me]^+$, 267 (100), 183 (35), 168 (39), 155 (16), 43 (13).

HR-MS (EI): *m*/*z* calcd for $C_{29}H_{39}NO_3^+$ $[M]^+$ 449.2924, found 449.2921.

***N*-[1-(3-Cycloheptylphenyl)ethyl]-3,4,5-trimethoxyaniline (157d)**



The general procedure **D** was followed using ketimine **135b** (285 mg, 1.00 mmol) and bromocycloheptane (**136h**, 531 mg, 3.0 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **157d** (200 mg, 52%) as a light yellow oil as well as alkylated phenone **154bh** (51.3 mg, 24%) as a colorless oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.23 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.19–7.15 (m, 2H), 7.08–7.04 (m, 1H), 5.76 (s, 2H), 4.39 (q, *J* = 6.7 Hz, 1H), 3.92 (br s, 1H), 3.72 (s, 3H), 3.69 (s, 6H), 2.65 (tt, *J* = 10.6, 3.6 Hz, 1H), 1.92–1.84 (m, 2H), 1.82–1.74 (m, 2H), 1.74–1.53 (m, 8H), 1.51 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 153.6 (C_q), 150.4 (C_q), 145.3 (C_q), 144.2 (C_q), 129.7 (C_q), 128.6 (CH), 125.2 (CH), 124.4 (CH), 122.8 (CH), 90.9 (CH), 61.0 (CH_3), 55.7 (CH_3), 54.4 (CH), 47.0 (CH), 37.0 (CH_2), 36.7 (CH_2), 27.9 (CH_2), 27.9 (CH_2), 27.2 (CH_2), 27.2 (CH_2), 24.8 (CH_3).

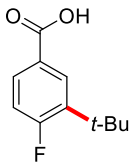
IR (ATR): $\tilde{\nu}$ = 3356, 2996, 2850, 1599, 1507, 1447, 1205, 1126, 1008, 812 cm^{-1}.

MS (EI) *m/z* (relative intensity): 383 (92) $[M]^+$, 201 (100), 168 (78), 119 (15).

HR-MS (EI): *m/z* calcd for $C_{24}H_{33}NO_3^+$ $[M]^+$ 383.2455, found 383.2469.

Oxidation of Phenone

3-(*tert*-Butyl)-4-fluorobenzoic acid (159)



A mixture of phenone **154ab** (97.5 mg, 0.50 mmol) and anhydrous $Mn(OAc)_2$ (1.0 mg, 5.8 µmol) in acetic acid (1.0 mL) was stirred at 100 °C under an oxygen atmosphere for 15 h.[97] The reaction mixture was concentrated *in vacuo* to give a crude mixture. The crude mixture was dissolved with EtOAc and washed with HCl (1 N, 10 mL). The organic phase was dried over anhydrous Na_2SO_4. Filtration followed by evaporation gave a crude product. Purification of the residue by column chromatography (*n*-hexane/EtOAc 9:1 to 1:1) yielded the corresponding product **159** (87.4 mg, 89%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.11 (dd, *J* = 8.0, 2.2 Hz, 1H), 7.98 (ddd, *J* = 8.5, 4.6, 2.2 Hz, 1H), 7.08 (dd, *J* = 12.0, 8.5 Hz, 1H), 1.42 (d, *J* = 1.0 Hz, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 171.4 (C_q), 165.6 (d, $^1J_{C-F}$ = 258 Hz, C_q), 137.6 (d, $^2J_{C-F}$ = 13 Hz, C_q), 130.4 (d, $^3J_{C-F}$ = 11 Hz, CH), 130.1 (d, $^3J_{C-F}$ = 8 Hz, CH), 124.9 (d, $^4J_{C-F}$ = 3 Hz, C_q), 116.7 (d, $^2J_{C-F}$ = 26 Hz, CH), 34.4 (d, $^3J_{C-F}$ = 3 Hz, C_q), 29.7 (d, $^4J_{C-F}$ = 3 Hz, CH_3).

^{19}F-NMR (470 MHz, $CDCl_3$): δ = (–100.4)–(–100.5) (m).

mp.: 154–155 °C.

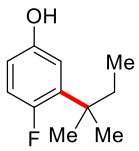
IR (ATR): $\tilde{\nu}$ = 2964, 1683, 1428, 1294, 1258, 1217, 1089, 839, 772 cm^{-1}.

MS (EI) *m/z* (relative intensity): 196 (14) $[M]^+$, 181 (100) $[M–Me]^+$, 153 (79), 109 (15).

HR-MS (EI): *m/z* calcd for $C_{11}H_{13}FO_2^+$ $[M]^+$ 196.0894, found 196.0902.

Baeyer-Villiger Oxidation of Phenone

4-Fluoro-3-(*tert*-pentyl)phenol (160b)



Phenone **154ac** (83.5 mg, 0.40 mmol) and *m*-CPBA (207 mg, 1.20 mmol) were placed in a pre-dried 10 mL pressure tube and CH_2Cl_2 (3.0 mL) was added. The mixture was stirred at 60 °C. After 6 h, the mixture was concentrated *in vacuo*. The residue was dissolved in EtOH (1.5 mL) and aq. NaOH solution (50%, 1.5 mL) and stirred at ambient temperature for 16 h. Then, the resulting mixture was neutralized with HCl (1 N) until pH 7 and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-pentane/Et_2O 10:1 to 1:1) yielded phenol **160b** (53.5 mg, 73%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 6.84 (dd, *J* = 12.0, 8.6 Hz, 1H), 6.73 (dd, *J* = 6.6, 3.2 Hz, 1H), 6.62 (ddd, *J* = 8.6, 3.3, 3.2 Hz, 1H), 1.75 (qd, *J* = 7.5, 1.4 Hz, 2H), 1.30 (d, *J* = 1.0 Hz, 6H), 0.69 (td, *J* = 7.5, 0.6 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 156.2 (d, $^1J_{C–F}$ = 240 Hz, C_q), 150.8 (d, $^4J_{C–F}$ = 2 Hz, C_q), 136.7 (d, $^2J_{C–F}$ = 13 Hz, C_q), 116.6 (d, $^2J_{C–F}$ = 27 Hz, CH), 115.3 (d, $^3J_{C–F}$ = 6 Hz, CH), 113.3 (d, $^3J_{C–F}$ = 9 Hz, CH), 38.0 (d, $^3J_{C–F}$ = 3 Hz, C_q), 34.1 (d, $^4J_{C–F}$ = 4 Hz, CH_2), 27.6 (d, $^4J_{C–F}$ = 3 Hz, CH_3), 9.4 (CH_3).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = (–120.2)–(–120.4) (m).

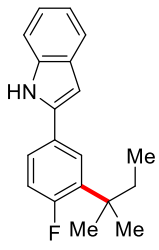
IR (ATR): $\tilde{\nu}$ = 3315, 2965, 1482, 1440, 1194, 811, 761, 738 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 182 (36) $[M]^+$, 153 (100) $[M–Et]^+$, 125 (81).

HR-MS (EI): *m*/*z* calcd for $C_{11}H_{15}FO^+$ $[M]^+$ 182.1101, found 182.1103.

Fischer Indole Synthesis

2-[4-Fluoro-3-(*tert*-pentyl)phenyl]-1*H*-indole (162)



The indole was prepared by a modified literature procedure.[133] Phenone **154ac** (104 mg, 0.50 mmol), phenylhydrazine hydrochloride salt (145 mg, 1.00 mmol), and polyphosphoric acid (0.5 mL) in a microwave tube were stirred at 120 °C under microwave irradiation for 1 h. Then, sat. aq. $NaHCO_3$ solution (20 mL) and EtOAc (20 mL) were added. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and

concentrated *in vacuo*. Purification by column chromatography (*n*-hexane/EtOAc 20:1 and Et_3N 1%) yielded indole **162** (81.2 mg, 58%) as a pale yellow solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.27 (br s, 1H), 7.63 (d, J = 7.9 Hz, 1H), 7.54 (dd, J = 7.7, 2.4 Hz, 1H), 7.46 (ddd, J = 8.3, 4.4, 2.4 Hz, 1H), 7.41 (dd, J = 8.1, 1.1 Hz, 1H), 7.20 (ddd, J = 8.1, 7.1, 1.2 Hz, 1H), 7.13 (ddd, J = 7.9, 7.1, 1.1 Hz, 1H), 7.07 (dd, J = 12.3, 8.3 Hz, 1H), 6.76 (dd, J = 2.2, 0.9 Hz, 1H), 1.84 (qd, J = 7.5, 1.5 Hz, 2H), 1.42 (d, J = 1.1 Hz, 6H), 0.74 (t, J = 7.5 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 161.6 (d, $^1J_{C–F}$ = 250 Hz, C_q), 137.7 (C_q), 136.7 (C_q), 136.2 (d, $^2J_{C–F}$ = 12 Hz, C_q), 129.3 (C_q), 128.2 (d, $^4J_{C–F}$ = 3 Hz, C_q), 125.6 (d, $^3J_{C–F}$ = 6 Hz, CH), 124.4 (d, $^3J_{C–F}$ = 9 Hz, CH), 122.2 (CH), 120.5 (CH), 120.3 (CH), 116.9 (d, $^2J_{C–F}$ = 26 Hz, CH), 110.8 (CH), 99.7 (d, $^6J_{C–F}$ = 1 Hz, CH), 38.1 (d, $^3J_{C–F}$ = 3 Hz, C_q), 34.1 (d, $^4J_{C–F}$ = 4 Hz, CH_2), 27.7 (d, $^4J_{C–F}$ = 3 Hz, CH_3), 9.5 (CH_3).

^{19}F-NMR (470 MHz, $CDCl_3$): δ = (–109.9)–(–110.1) (m).

IR (ATR): $\tilde{\nu}$ = 3423, 2967, 1480, 1454, 1230, 797, 747 cm^{-1}.

m.p.: 142–144 °C.

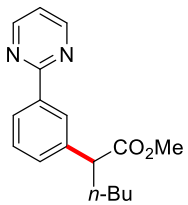
MS (ESI) *m*/*z* (relative intensity): 561 (25), 490 (45), 381 (77), 312 (41), 282 (74) $[M+H]^+$, 118 (100).

HR-MS (ESI): *m*/*z* calcd for $C_{19}H_{21}FN^+$ $[M+H]^+$ 282.1653, found 282.1642.

5.3.3 Sequential meta-/ortho-C–H Functionalizations by One-Pot Ruthenium(II/III) Catalysis

5.3.3.1 Characterization Data for 141

Methyl 2-[3-(pyrimidin-2-yl)phenyl]hexanoate (141a)



The general procedure **E** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **141a** (121 mg, 85%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.81 (d, J = 4.8 Hz, 2H), 8.40–8.37 (m, 1H), 8.37–8.30 (m, 1H), 7.49–7.42 (m, 2H), 7.19 (t, J = 4.8 Hz, 1H), 3.70–3.63 (m, 4H), 2.15 (dddd, J = 13.4, 9.4, 8.0, 5.7 Hz, 1H), 1.85 (dddd, J = 13.4, 9.4, 7.4, 5.7 Hz, 1H), 1.41–1.17 (m, 4H), 0.87 (t, J = 7.0 Hz, 3H).

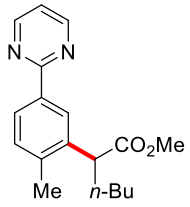
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.4 (C_q), 164.5 (C_q), 157.1 (CH), 139.7 (C_q), 137.8 (C_q), 130.0 (CH), 128.8 (CH), 127.9 (CH), 127.0 (CH), 119.0 (CH), 52.0 (CH_3), 51.7 (CH), 33.4 (CH_2), 29.9 (CH_2), 22.5 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2953, 2860, 1732, 1567, 1555, 1409, 1158, 775, 697 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 284 (24) $[M]^+$, 228 (59) $[M–Bu]^+$, 225 (83) $[M–CO_2Me]^+$, 183 (14), 169 (100) $[M–Bu–CO_2Me]^+$.

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{20}N_2O_2^+$ $[M]^+$ 284.1519, found 284.1524.

Methyl 2-[2-methyl-5-(pyrimidin-2-yl)phenyl]hexanoate (141b)



The general procedure **E** was followed using 2-(*p*-tolyl)pyrimidine (**139b**, 85.3 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 9:1) yielded **141b** (123 mg, 82%) as a white soild.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.78 (d, *J* = 4.8 Hz, 2H), 8.43 (d, *J* = 1.8 Hz, 1H), 8.21 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.14 (t, *J* = 4.8 Hz, 1H), 3.88 (dd, *J* = 8.1, 7.0 Hz, 1H), 3.65 (s, 3H), 2.44 (s, 3H), 2.31–2.17 (m, 1H), 1.91–1.77 (m, 1H), 1.41–1.22 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.4 (C_q), 164.5 (C_q), 157.0 (CH), 139.1 (C_q), 138.2 (C_q), 135.8 (C_q), 130.7 (CH), 126.8 (CH), 126.5 (CH), 118.7 (CH), 51.9 (CH_3), 47.2 (CH), 32.8 (CH_2), 30.0 (CH_2), 22.7 (CH_2), 20.0 (CH_3), 14.0 (CH_3).

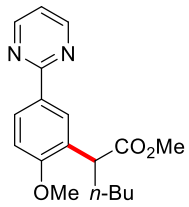
IR (ATR): $\tilde{\nu}$ = 2953, 2859, 1726, 1549, 1417, 1158, 796, 782 cm^{-1}.

m.p.: 58–59 °C.

MS (EI) *m*/*z* (relative intensity): 298 (34) $[M]^+$, 283 (13) $[M–Me]^+$, 255 (18) $[M–Pr]^+$, 239 (49) $[M–CO_2Me]^+$, 183 (100), 168 (22).

HR-MS (EI): *m*/*z* calcd for $C_{18}H_{22}N_2O_2^+$ $[M]^+$ 298.1676, found 298.1675.

Methyl 2-[2-methoxy-5-(pyrimidin-2-yl)phenyl]hexanoate (141c)



The general procedure **E** was followed using 2-(4-methoxyphenyl)pyrimidine (**139e**, 93.3 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **141c** (115 mg, 73%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.75 (d, *J* = 4.8 Hz, 2H), 8.38 (d, *J* = 2.2 Hz, 1H), 8.34 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.10 (t, *J* = 4.8 Hz, 1H), 6.97 (d, *J* = 8.6 Hz, 1H), 4.02 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.89 (s, 3H), 3.66 (s, 3H), 2.15 (dddd, *J* = 13.0, 9.7, 7.6, 5.6 Hz, 1H), 1.83 (dddd, *J* = 13.3, 9.7, 7.6, 5.4 Hz, 1H), 1.39–1.20 (m, 4H), 0.87 (t, *J* = 7.0 Hz, 3H).

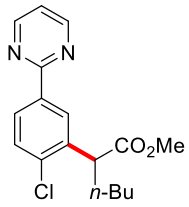
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.6 (C_q), 164.3 (C_q), 159.1 (C_q), 157.0 (CH), 130.1 (C_q), 128.7 (CH), 128.3 (CH), 128.3 (C_q), 118.2 (CH), 110.5 (CH), 55.8 (CH_3), 51.8 (CH_3), 44.5 (CH), 32.0 (CH_2), 29.9 (CH_2), 22.6 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2953, 2859, 1732, 1567, 1402, 1246, 1026, 798 cm^{-1}.

MS (EI) *m/z* (relative intensity): 314 (41) $[M]^+$, 255 (47) $[M–CO_2Me]^+$, 199 (100), 169 (27).

HR-MS (EI): *m/z* calcd for $C_{18}H_{22}N_2O_3^+$ $[M]^+$ 314.1625, found 314.1629.

Methyl 2-[2-chloro-5-(pyrimidin-2-yl)phenyl]hexanoate (141d)



The general procedure **E** was followed using 2-(4-chlorophenyl)pyrimidine (**139f**, 95.5 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 9:1) yielded **141d** (107 mg, 67%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 4.8 Hz, 2H), 8.51 (d, *J* = 2.1 Hz, 1H), 8.28 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.19 (t, *J* = 4.8 Hz, 1H), 4.20 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.69 (s, 3H), 2.19 (dddd, *J* = 13.5, 9.9, 7.6, 4.9 Hz, 1H), 1.88 (dddd, *J* = 16.0, 9.9, 7.6, 5.2 Hz, 1H), 1.40–1.31 (m, 3H), 1.30–1.23 (m, 1H), 0.88 (t, *J* = 7.2 Hz, 3H).

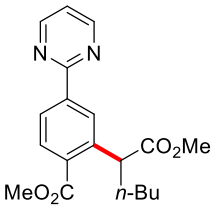
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 173.7 (C_q), 163.5 (C_q), 157.1 (CH), 137.4 (C_q), 136.7 (C_q), 136.6 (C_q), 129.8 (CH), 128.6 (CH), 127.8 (CH), 119.2 (CH), 52.1 (CH_3), 47.5 (CH), 32.6 (CH_2), 29.7 (CH_2), 22.6 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2955, 2861, 1733, 1568, 1551, 1416, 1165, 1036, 797 cm^{-1}.

MS (EI) *m/z* (relative intensity): 320 (3) [M(^{37}Cl)]$^+$, 318 (9) [M(^{35}Cl)]$^+$, 283 (100) [M–Cl]$^+$, 264 (8) [M(^{37}Cl)–Bu]$^+$, 262 (26) [M(^{35}Cl)–Bu]$^+$, 261 (12) [M(^{35}Cl)–CO_2Me]$^+$, 259 (35) [M(^{35}Cl)–CO_2Me]$^+$, 203 (65), 168 (19).

HR-MS (EI): *m/z* calcd for $C_{17}H_{19}{}^{35}ClN_2O_2^+$ [M]$^+$ 318.1130, found 318.1136.

Methyl 2-(1-methoxy-1-oxohexan-2-yl)-4-(pyrimidin-2-yl)benzoate (141e)



The general procedure **E** was followed using methyl 4-(pyrimidin-2-yl)benzoate (**139g**, 107 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **141e** (126 mg, 74%) as a white solid.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.83 (d, *J* = 4.8 Hz, 2H), 8.56 (d, *J* = 1.7 Hz, 1H), 8.38 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.22 (t, *J* = 4.8 Hz, 1H), 4.64 (dd, *J* = 7.4, 7.4 Hz, 1H), 3.93 (s, 3H), 3.65 (s, 3H), 2.26–2.20 (m, 1H), 1.91–1.83 (m, 1H), 1.39–1.29 (m, 3H), 1.29–1.20 (m, 1H), 0.86 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.3 (C_q), 167.7 (C_q), 163.5 (C_q), 157.2 (CH), 140.9 (C_q), 140.7 (C_q), 131.5 (C_q), 130.8 (CH), 128.6 (CH), 126.3 (CH), 119.5 (CH), 52.2 (CH_3), 52.0 (CH_3), 47.3 (CH), 33.2 (CH_2), 30.0 (CH_2), 22.6 (CH_2), 14.0 (CH_3).

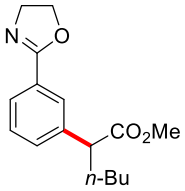
IR (ATR): $\tilde{\nu}$ = 2953, 2859, 1726, 1549, 1417, 1158, 796, 782 cm^{-1}.

m.p.: 77–78 °C.

MS (EI) *m/z* (relative intensity): 342 (7) [M]$^+$, 310 (74) [M–Et]$^+$, 282 (100) [M–CO_2Me]$^+$, 267 (97) [M–Me–CO_2Me]$^+$, 239 (74) [M–Pr–CO_2Me]$^+$, 211 (28), 169 (19), 59 (12).

HR-MS (EI): *m/z* calcd for $C_{19}H_{22}N_2O_4^+$ [M]$^+$ 342.1574, found 342.1582.

Methyl 2-[3-(4,5-dihydrooxazol-2-yl)phenyl]hexanoate (141f)



The general procedure **E** was followed using 2-phenyl-4,5-dihydrooxazole (**139h**, 73.6 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 4:1) yielded **141f** (99.2 mg, 72%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.83 (ddd, *J* = 7.6, 1.7, 1.6 Hz, 1H), 7.43 (ddd, *J* = 7.7, 1.7, 1.6 Hz, 1H), 7.36 (ddd, *J* = 7.7, 7.6, 0.6 Hz, 1H), 4.43 (td, *J* = 9.6, 0.8 Hz, 2H), 4.05 (td, *J* = 9.6, 0.8 Hz, 2H), 3.64 (s, 3H), 3.57 (dd, *J* = 7.8, 7.7 Hz, 1H), 2.09 (dddd, *J* = 13.3, 9.4, 7.8, 5.6 Hz, 1H), 1.78 (dddd, *J* = 13.5, 9.4, 7.7, 5.9 Hz, 1H), 1.39–1.11 (m, 4H), 0.86 (t, *J* = 7.1 Hz, 3H).

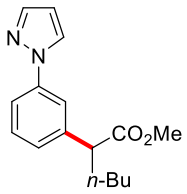
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.1 (C_q), 164.4 (C_q), 139.5 (C_q), 130.6 (CH), 128.5 (CH), 128.0 (C_q), 127.8 (CH), 126.9 (CH), 67.6 (CH_2), 55.0 (CH_2), 52.0 (CH_3), 51.5 (CH), 33.2 (CH_2), 29.8 (CH_2), 22.5 (CH_2), 13.9 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2952, 2872, 1733, 1649, 1357, 1160, 950, 709 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 298 (14) $[M+Na]^+$, 276 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{16}H_{22}NO_3^+$ $[M+H]^+$ 276.1594, found 276.1597.

Methyl 2-[3-(1*H*-pyrazol-1-yl)phenyl]hexanoate (141g)



The general procedure **E** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **141g** (97.0 mg, 71%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.93 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.72 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.67 (dd, *J* = 2.3, 1.7 Hz, 1H), 7.58 (ddd, *J* = 8.0, 2.3, 1.1 Hz, 1H), 7.40 (dd, *J* = 8.0, 7.8 Hz, 1H), 7.24 (ddd, *J* = 7.8, 1.7, 1.1 Hz, 1H), 6.46 (dd, *J* = 2.5, 1.8 Hz, 1H), 3.67 (s, 3H), 3.61 (dd, *J* = 7.9, 7.6 Hz, 1H), 2.11 (dddd, *J* = 13.5, 9.3, 7.9, 5.8 Hz, 1H), 1.82 (dddd, *J* = 13.5, 9.3, 7.6, 6.0 Hz, 1H), 1.41–1.16 (m, 4H), 0.87 (t, *J* = 7.0 Hz, 3H).

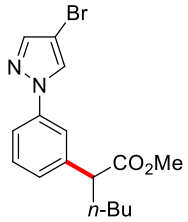
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.1 (C_q), 141.0 (CH), 140.8 (C_q), 140.3 (C_q), 129.5 (CH), 126.7 (CH), 125.9 (CH), 118.9 (CH), 117.9 (CH), 107.5 (CH), 52.0 (CH_3), 51.6 (CH), 33.3 (CH_2), 29.8 (CH_2), 22.5 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2953, 2860, 1732, 1593, 1520, 1392, 1160, 1044, 747, 695 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 272 (79) $[M]^+$, 216 (67) $[M–Bu]^+$, 213 (72) $[M–CO_2Me]^+$, 185 (47) $[M–Et–CO_2Me]^+$, 171 (37) $[M–Pr–CO_2Me]^+$, 157 (100) $[M–Bu–CO_2Me]^+$, 130 (19), 115 (18), 77 (16).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{20}N_2O_2^+$ $[M]^+$ 272.1519, found 272.1526.

Methyl 2-[3-(4-bromo-1*H*-pyrazol-1-yl)phenyl]hexanoate (141h)



The general procedure **E** was followed using 4-bromo-1-phenyl-1*H*-pyrazole (**147b**, 112 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol) at 60 °C. After 20 h, purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **141h** (147 mg, 84%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 0.7 Hz, 1H), 7.67 (d, *J* = 0.7 Hz, 1H), 7.61 (dd, *J* = 2.2, 2.0 Hz, 1H), 7.53 (ddd, *J* = 8.0, 2.2, 1.1 Hz, 1H), 7.40 (dd, *J* = 8.0, 7.9 Hz, 1H), 7.29–7.24 (m, 1H), 3.67 (s, 3H), 3.60 (dd, *J* = 7.9, 7.6 Hz, 1H), 2.11 (dddd, *J* = 13.6, 9.5, 7.9, 5.8 Hz, 1H), 1.80 (dddd, *J* = 13.5, 9.5, 7.6, 6.0 Hz, 1H), 1.38–1.17 (m, 4H), 0.87 (t, *J* = 7.1 Hz, 3H).

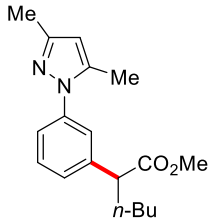
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 173.9 (C_q), 141.4 (CH), 141.0 (C_q), 139.8 (C_q), 129.6 (CH), 127.0 (CH), 126.5 (CH), 118.6 (CH), 117.8 (CH), 95.6 (C_q), 52.1 (CH_3), 51.6 (CH), 33.4 (CH_2), 29.8 (CH_2), 22.5 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2953, 2860, 1731, 1593, 1336, 1160, 953, 791, 694 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 352 (86) $[M(^{81}Br)]^+$, 350 (88) $[M(^{79}Br)]^+$, 296 (88) $[M(^{81}Br)–Bu]^+$, 294 (100) $[M(^{79}Br)–Bu]^+$, 293 (63) $[M(^{81}Br)–CO_2Me]^+$, 291 (63) $[M(^{79}Br)–CO_2Me]^+$, 264 (54) $[M(^{81}Br)–Et–CO_2Me]^+$, 262 (39) $[M(^{79}Br)–Et–CO_2Me]^+$, 251 (45) $[M(^{81}Br)–Pr–CO_2Me]^+$, 249 (41) $[M(^{79}Br)–Pr–CO_2Me]^+$, 237 (94) $[M(^{81}Br)–Bu–CO_2Me]^+$, 235 (94) $[M(^{79}Br)–Bu–CO_2Me]^+$, 212 (24) $[M–Br–Bu]^+$, 183 (31), 155 (31), 115 (41), 91 (61), 77 (36).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{19}{}^{79}BrN_2O_2^+$ $[M]^+$ 350.0624, found 350.0630.

Methyl 2-[3-(3,5-dimethyl-1*H*-pyrazol-1-yl)phenyl]hexanoate (141i)



The general procedure **E** was followed using 3,5-dimethyl-1-phenyl-1*H*-pyrazole (**147c**, 86.2 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol) at 60 °C. After 20 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **141i** (78.3 mg, 52%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.42–7.36 (m, 2H), 7.35–7.26 (m, 2H), 6.00–5.98 (m, 1H), 3.66 (s, 3H), 3.58 (dd, *J* = 7.9, 7.5 Hz, 1H), 2.30 (s, 3H), 2.29 (s, 3H), 2.08 (dddd, *J* = 13.5, 9.2, 7.9, 5.9 Hz, 1H), 1.79 (dddd, *J* = 13.5, 9.2, 7.5, 6.0 Hz, 1H), 1.38–1.15 (m, 4H), 0.87 (t, *J* = 7.1 Hz, 3H).

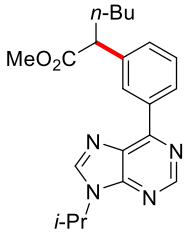
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.1 (C_q), 148.9 (C_q), 140.2 (C_q), 140.0 (C_q), 139.3 (C_q), 129.1 (CH), 126.7 (CH), 124.3 (CH), 123.4 (CH), 106.9 (CH), 52.0 (CH_3), 51.5 (CH), 33.4 (CH_2), 29.8 (CH_2), 22.5 (CH_2), 14.0 (CH_3), 13.6 (CH_3), 12.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2953, 2860, 1734, 1607, 1591, 1494, 1160, 779, 700 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 300 (100) $[M]^+$, 257 (51) $[M–Pr]^+$, 244 (38) $[M–Bu]^+$, 241 (59) $[M–CO_2Me]^+$, 213 (44) $[M–Et–CO_2Me]^+$, 199 (44) $[M–Pr–CO_2Me]^+$, 186 (82) $[M–Bu–CO_2Me]^+$, 144 (12), 115 (13), 77 (10).

HR-MS (EI): *m*/*z* calcd for $C_{18}H_{24}N_2O_2^+$ $[M]^+$ 300.1832, found 300.1837.

Methyl 2-[3-(9-*iso*-propyl-9*H*-purin-6-yl)phenyl]hexanoate (141j)



The general procedure **E** was followed using purine **123a** (119 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **141j** (159 mg, 87%) as a light yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.74 (ddd, *J* = 6.6, 2.5, 1.7 Hz, 1H), 8.69–8.66 (m, 1H), 8.19 (s, 1H), 7.55–7.47 (m, 2H), 4.99 (hept, *J* = 6.8 Hz, 1H), 3.71 (t, *J* = 7.7 Hz, 1H), 3.67 (s, 3H), 2.23–2.09 (m, 1H), 1.95–1.80 (m, 1H), 1.67 (d, *J* = 6.8 Hz, 6H), 1.41–1.19 (m, 4H), 0.87 (t, *J* = 7.0 Hz, 3H).

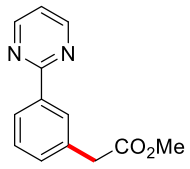
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.4 (C_q), 154.4 (C_q), 152.0 (C_q), 151.9 (CH), 141.9 (CH), 139.7 (C_q), 136.0 (C_q), 131.5 (C_q), 130.1 (CH), 129.3 (CH), 128.9 (CH), 128.8 (CH), 52.0 (CH_3), 51.8 (CH), 47.3 (CH), 33.4 (CH_2), 29.9 (CH_2), 22.7 (CH_3), 22.5 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2953, 2872, 1732, 1568, 1324, 1218, 1160, 799, 702, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 366 (63) $[M]^+$, 323 (30) $[M–Pr]^+$, 310 (100) $[M–Bu]^+$, 307 (49) $[M–CO_2Me]^+$, 278 (58) $[M–Et–CO_2Me]^+$, 265 (95) $[M–Pr–CO_2Me]^+$, 251 (49) $[M–Bu–CO_2Me]^+$, 236 (25), 209 (41), 59 (12).

HR-MS (EI): *m*/*z* calcd for $C_{21}H_{26}N_4O_2^+$ $[M]^+$ 366.2050, found 366.2055.

Methyl 2-[3-(pyrimidin-2-yl)phenyl]acetate (141k)



The general procedure **E** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol) and methyl 2-bromoacetate (**140b**, 230 mg, 1.50 mmol) at 60 °C. After 20 h, purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **141k** (57.0 mg, 50%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.78 (d, *J* = 4.8 Hz, 2H), 8.36 (d, *J* = 1.7 Hz, 1H), 8.34 (ddd, *J* = 6.7, 1.8, 1.7 Hz, 1H), 7.52–7.36 (m, 2H), 7.16 (t, *J* = 4.8 Hz, 1H), 3.73 (s, 2H), 3.69 (s, 3H).

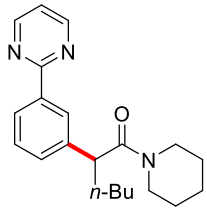
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 171.6 (C_q), 164.3 (C_q), 157.0 (CH), 137.8 (C_q), 134.3 (C_q), 131.5 (CH), 129.0 (CH), 128.7 (CH), 126.8 (CH), 119.0 (CH), 52.0 (CH_3), 41.1 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2952, 1735, 1568, 1556, 1411, 1159, 1013, 789, 769 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 228 (35) $[M]^+$, 213 (34) $[M–Me]^+$, 185 (15), 169 (100) $[M–CO_2Me]^+$, 116 (11), 89 (13).

HR-MS (EI): *m*/*z* calcd for $C_{13}H_{12}N_2O_2^+$ $[M]^+$ 228.0893, found 228.0898.

1-(Piperidin-1-yl)-2-[3-(pyrimidin-2-yl)phenyl]hexan-1-one (141l)



The general procedure **E** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol) and 2-bromo-1-(piperidin-1-yl)hexan-1-one (**140c**, 394 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 4:1) yielded **141l** (110 mg, 65%) as a white soild.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 4.8 Hz, 2H), 8.33–8.28 (m, 2H), 7.47–7.39 (m, 2H), 7.18 (t, *J* = 4.8 Hz, 1H), 3.83 (dd, *J* = 7.6, 6.8 Hz, 1H), 3.71–3.61 (m, 1H), 3.53–3.35 (m, 3H), 2.16 (dddd, *J* = 13.4, 10.1, 7.6, 4.6 Hz, 1H), 1.75 (dddd, *J* = 13.2, 10.1, 6.8, 5.0 Hz, 1H), 1.57–1.24 (m, 8H), 1.24–0.99 (m, 2H), 0.86 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 171.0 (C_q), 164.5 (C_q), 157.1 (CH), 141.4 (C_q), 137.7 (C_q), 129.8 (CH), 129.0 (CH), 127.8 (CH), 126.4 (CH), 119.0 (CH), 48.8 (CH), 46.7 (CH_2), 43.2 (CH_2), 34.9 (CH_2), 30.2 (CH_2), 26.2 (CH_2), 25.7 (CH_2), 24.6 (CH_2), 22.8 (CH_2), 14.1 (CH_3).

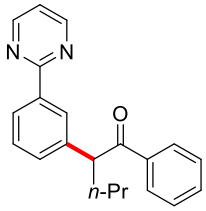
IR (ATR): $\tilde{\nu}$ = 2932, 2855, 1633, 1567, 1554, 1408, 1249, 1011, 776, 701 cm^{-1}.

m.p.: 72–73 °C.

MS (EI) *m/z* (relative intensity): 337 (21) $[M]^+$, 281 (35) $[M–Bu]^+$, 238 (14), 225 (17), 169 (34), 112 (100), 84 (13), 69 (42), 41 (15).

HR-MS (EI): *m/z* calcd for $C_{21}H_{27}N_3O^+$ $[M]^+$ 337.2149, found 337.2145.

1-Phenyl-2-[3-(pyrimidin-2-yl)phenyl]pentan-1-one (141m)



The general procedure **E** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol) and 2-bromo-1-phenylpentan-1-one (**140d**, 362 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 4:1) yielded **141m** (113 mg, 71%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 4.9 Hz, 2H), 8.43 (dd, *J* = 1.8, 1.8 Hz, 1H), 8.30 (ddd, *J* = 7.0, 1.9, 1.8 Hz, 1H), 8.03–7.98 (m, 2H), 7.49–7.35 (m, 5H), 7.17 (t, *J* = 4.9 Hz, 1H), 4.70 (dd, *J* = 7.3, 7.3 Hz, 1H), 2.23 (dddd, *J* = 13.6, 10.0, 7.3, 5.7 Hz, 1H), 1.88 (dddd, *J* = 13.6, 10.0, 7.3, 5.6 Hz, 1H), 1.45–1.22 (m, 2H), 0.93 (t, *J* = 7.4 Hz, 3H).

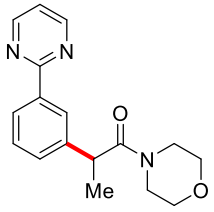
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 199.8 (C_q), 164.3 (C_q), 157.1 (CH), 140.2 (C_q), 138.0 (C_q), 136.9 (C_q), 132.7 (CH), 130.3 (CH), 129.1 (CH), 128.6 (CH), 128.4 (CH), 128.2 (CH), 126.8 (CH), 119.1 (CH), 53.5 (CH), 36.4 (CH_2), 21.0 (CH_2), 14.2 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2957, 1679, 1567, 1554, 1409, 1204, 783, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity): 316 (11) $[M]^+$, 274 (6) $[M–Pr]^+$, 211 (31) $[M–Bz]^+$, 169 (60) $[M–Pr–Bz]^+$, 105 (100) $[Bz]^+$, 77 (13).

HR-MS (EI): *m/z* calcd for $C_{21}H_{20}N_2O^+$ $[M]^+$ 316.1570, found 316.1584.

1-Morpholino-2-[3-(pyrimidin-2-yl)phenyl]propan-1-one (141n)



The general procedure **E** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol) and 2-bromo-1-morpholinopropan-1-one (**140e**, 334 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 2:3) yielded **141n** (105 mg, 71%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.81 (d, *J* = 4.8 Hz, 2H), 8.38–8.28 (m, 2H), 7.47 (dd, *J* = 7.9, 7.8 Hz, 1H), 7.38 (ddd, *J* = 7.8, 1.5, 1.5 Hz, 1H), 7.20 (t, *J* = 4.8 Hz, 1H), 3.97 (q, *J* = 6.8 Hz, 1H), 3.88–3.76 (m, 1H), 3.75–3.61 (m, 1H), 3.60–3.29 (m, 5H), 3.21–3.10 (m, 1H), 1.52 (d, *J* = 6.8 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 171.9 (C_q), 164.2 (C_q), 157.1 (CH), 142.2 (C_q), 138.1 (C_q), 129.3 (CH), 129.2 (CH), 127.2 (CH), 126.7 (CH), 119.2 (CH), 66.8 (CH_2), 66.3 (CH_2), 46.1 (CH_2), 43.4 (CH), 42.5 (CH_2), 20.7 (CH_3).

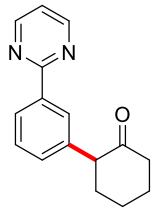
IR (ATR): $\tilde{\nu}$ = 2971, 2855, 1641, 1558, 1415, 1232, 1121, 834, 789, 699 cm^{-1}.

m.p.: 123–125 °C.

MS (EI) *m*/*z* (relative intensity): 297 (8) $[M]^+$, 267 (42), 210 (31), 183 (98), 168 (54), 114 (100), 70 (58).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{19}N_3O_2^+$ $[M]^+$ 297.1472, found 297.1479.

2-[3-(Pyrimidin-2-yl)phenyl]cyclohexan-1-one (141p)



The general procedure **E** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol) and 2-bromocyclohexan-1-one (**140g**, 266 mg, 1.50 mmol) at 60 °C. After 20 h, purification by column chromatography (*n*-hexane/EtOAc 4:1) yielded **141p** (68.7 mg, 54%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.79 (d, *J* = 4.8 Hz, 2H), 8.35 (ddd, *J* = 7.8, 1.7, 1.2 Hz, 1H), 8.24 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.47 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.29 (ddd, *J* = 7.7, 1.7, 1.2 Hz, 1H), 7.17 (t, *J* = 4.8 Hz, 1H), 3.74 (dd, *J* = 12.4, 5.4 Hz, 1H), 2.60–2.53 (m, 1H), 2.53–2.43 (m, 1H), 2.39–2.30 (m, 1H), 2.23–2.07 (m, 2H), 2.07–1.98 (m, 1H), 1.92–1.80 (m, 2H).

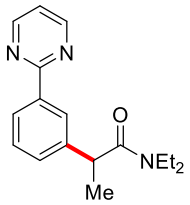
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 209.7 (C_q), 164.6 (C_q), 157.0 (CH), 139.1 (C_q), 137.5 (C_q), 131.1 (CH), 128.5 (CH), 128.3 (CH), 126.7 (CH), 119.0 (CH), 57.5 (CH), 42.3 (CH_2), 35.3 (CH_2), 27.9 (CH_2), 25.5 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2935, 2862, 1706, 1567, 1554, 1408, 1125, 784, 699 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 252 (67) $[M]^+$, 224 (73), 209 (47), 207 (53), 195 (100), 183 (64), 168 (35), 156 (20), 129 (29), 115 (26), 103 (15).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{16}N_2O^+$ $[M]^+$ 252.1257, found 252.1259.

_N_,_N_-Diethyl-2-[3-(pyrimidin-2-yl)phenyl]propanamide (141q)



The general procedure **E** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol) and 2-bromo-*N*,*N*-diethylpropanamide (**140h**, 313 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:2) yielded **141q** (89.0 mg, 63%) as a white soild.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.81 (d, *J* = 4.9 Hz, 2H), 8.35 (br s, 1H), 8.31 (ddd, *J* = 5.1, 3.7, 1.7 Hz, 1H), 7.47–7.41 (m, 2H), 7.19 (t, *J* = 4.9 Hz, 1H), 3.96 (q, *J* = 6.9 Hz, 1H), 3.53 (dq, *J* = 14.1, 7.1 Hz, 1H), 3.37 (dq, *J* = 14.5, 7.1 Hz, 1H), 3.24 (dq, *J* = 14.1, 7.1 Hz, 1H), 3.11 (dq, *J* = 14.5, 7.1 Hz, 1H), 1.50 (d, *J* = 6.9 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.01 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 172.5 (C_q), 164.5 (C_q), 157.1 (CH), 142.8 (C_q), 137.9 (C_q), 129.3 (CH), 129.1 (CH), 127.3 (CH), 126.5 (CH), 119.0 (CH), 43.2 (CH), 41.7 (CH_2), 40.3 (CH_2), 21.1 (CH_3), 14.4 (CH_3), 12.9 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2973, 1623, 1551, 1411, 1269, 1082, 789, 700, 636 cm^{-1}.

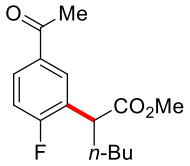
m.p.: 133–134 °C.

MS (EI) *m*/*z* (relative intensity): 283 (19) $[M]^+$, 226 (4) $[M–2Et]^+$, 210 (4) $[M–NEt_2]^+$, 183 (17) $[M–C(O)NEt_2]^+$, 168 (19) $[M–Me–C(O)NEt_2]^+$, 100 (100) $[C(O)NEt_2]^+$, 72 (44).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{21}N_3O^+$ $[M]^+$ 283.1679, found 283.1672.

5.3.3.2 Characterization Data for 164

Methyl 2-(5-acetyl-2-fluorophenyl)hexanoate (164a)



The general procedure **E** was followed using ketimine **135a** (152 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 20 h, HCl (2 N, 3.0 mL) was added at ambient temperature, and the resulting mixture was stirred for an additional 3 h, extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-pentane/Et_2O 20:1) yielded phenone **164a** (85.1 mg, 64%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.99 (dd, *J* = 7.1, 2.3 Hz, 1H), 7.87 (ddd, *J* = 8.6, 5.0, 2.3 Hz, 1H), 7.12 (dd, *J* = 9.5, 8.6 Hz, 1H), 3.93 (dd, *J* = 7.7, 7.5 Hz, 1H), 3.68 (s, 3H), 2.59 (s, 3H), 2.13 (dddd, *J* = 12.8, 9.8, 7.5, 5.5 Hz, 1H), 1.88–1.73 (m, 1H), 1.42–1.15 (m, 4H), 0.87 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.3 (C_q), 173.3 (C_q), 163.4 (d, $^1J_{C–F}$ = 254 Hz, C_q), 133.7 (d, $^4J_{C–F}$ = 3 Hz, C_q), 129.9 (d, $^3J_{C–F}$ = 6 Hz, CH), 129.3 (d, $^3J_{C–F}$ = 10 Hz, CH), 126.9 (d, $^2J_{C–F}$ = 16 Hz, C_q), 115.7 (d, $^2J_{C–F}$ = 24 Hz, CH), 52.2 (CH_3), 43.7 (d, $^3J_{C–F}$ = 2 Hz, CH), 32.2 (CH_2), 29.6 (CH_2), 26.6 (CH_3), 22.4 (CH_2), 13.9 (CH_3).

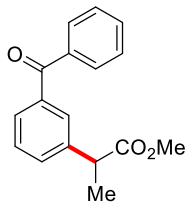
^{19}F-NMR (282 MHz, $CDCl_3$): δ = –110.4 (ddd, *J* = 9.5, 7.1, 5.0 Hz).

IR (ATR): $\tilde{\nu}$ = 2956, 1736, 1686, 1590, 1358, 1253, 1171, 827, 567 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 266 (2) $[M]^+$, 251 (58) $[M–Me]^+$, 223 (5) $[M–Ac]^+$, 210 (100) $[M–Bu]^+$, 178 (27) $[M–Bu–OMe]^+$, 163 (15), 151 (68) $[M–Bu–CO_2Me]^+$, 136 (12).

HR-MS (EI): *m*/*z* calcd for $C_{15}H_{19}FO_3^+$ $[M]^+$ 266.1313, found 266.1318.

Methyl 2-(3-benzoylphenyl)propanoate (164b)



The general procedure **E** was followed using ketimine **135x** (174 mg, 0.50 mmol) and methyl 2-bromopropanoate (**140i**, 251 mg, 1.50 mmol). After 20 h, HCl (2 N, 3.0 mL) was added at ambient temperature, and the resulting mixture was stirred for an additional 3 h, extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 10:1 to 4:1) yielded phenone **164b** (53.3 mg, 40%) as a colorless oil and **164b'** (72.3 mg, 41%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.83–7.78 (m, 2H), 7.75 (dd, *J* = 1.8, 1.8 Hz, 1H), 7.68 (ddd, *J* = 7.6, 1.8, 1.3 Hz, 1H), 7.63–7.56 (m, 1H), 7.54 (dddd, *J* = 7.7, 1.8, 1.3, 0.5 Hz, 1H), 7.52–7.40 (m, 3H), 3.81 (q, *J* = 7.2 Hz, 1H), 3.68 (s, 3H), 1.54 (d, *J* = 7.2 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.3 (C_q), 174.4 (C_q), 140.7 (C_q), 137.8 (C_q), 137.4 (C_q), 132.4 (CH), 131.4 (CH), 130.0 (CH), 129.1 (CH), 128.9 (CH), 128.5 (CH), 128.2 (CH), 52.2 (CH_3), 45.3 (CH), 18.6 (CH_3).

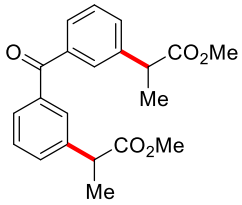
IR (ATR): $\tilde{\nu}$ = 2981, 2951, 1733, 1657, 1447, 1281, 1206, 1164, 703, 642 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 268 (31) $[M]^+$, 209 (100) $[M–CO_2Me]^+$, 191 (24), 105 (71) $[Bz]^+$, 77 (51).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{16}O_3^+$ $[M]^+$ 268.1094, found 268.1097.

The spectral data are in accordance with those reported in the literature.[134]

Dimethyl 2,2'-[carbonylbis(3,1-phenylene)]dipropionate (164b')



^{1}H-NMR (600 MHz, $CDCl_3$, 2 diastereomers): δ = 7.75–7.74 (m, 4H), 7.67 (ddd, *J* = 7.7, 1.6, 1.6 Hz, 2H), 7.67 (ddd, *J* = 7.7, 1.6, 1.6 Hz, 2H), 7.56–7.53 (m, 4H), 7.44 (dd, *J* = 7.7, 7.7 Hz, 4H), 3.80 (q, *J* = 7.2 Hz, 4H), 3.68 (s, 6H), 3.68 (s, 6H), 1.54 (d, *J* = 7.2 Hz, 6H), 1.54 (d, *J* = 7.2 Hz, 6H).

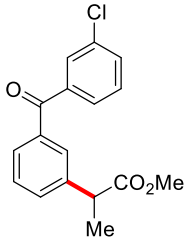
^{13}C-NMR (125 MHz, $CDCl_3$, 2 diastereomers): δ = 196.0 (C_q), 174.3 (C_q), 140.8 (C_q), 140.7 (C_q), 137.7 (C_q), 137.7 (C_q), 131.5 (CH), 131.5 (CH), 129.2 (CH), 129.1 (CH), 128.9 (CH), 128.5 (CH), 128.5 (CH), 52.2 (CH_3), 45.3 (CH), 18.6 (CH_3), 18.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2981, 2952, 1731, 1659, 1434, 1287, 1162, 1067, 742, 696 cm^{-1}.

MS (EI) *m/z* (relative intensity): 354 (4) $[M]^+$, 322 (60) $[M–OMe]^+$, 295 (54) $[M–CO_2Me]^+$, 235 (100) $[M–2CO_2Me]^+$, 191 (59), 131 (56), 103 (53), 77 (19), 59 (12), 43 (17).

HR-MS (EI): *m/z* calcd for $C_{21}H_{22}O_5^+$ $[M]^+$ 354.1462, found 354.1458.

Methyl 2-[3-(3-chlorobenzoyl)phenyl]propanoate (164c)



The general procedure **E** was followed using ketimine **135y** (191 mg, 0.50 mmol) and methyl 2-bromopropanoate (**140i**, 251 mg, 1.50 mmol). After 20 h, HCl (2 N, 3.0 mL) was added at ambient temperature, and the resulting mixture was stirred for an additional 3 h, extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 10:1) yielded phenone **164c** (78.6 mg, 52%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.77 (ddd, *J* = 2.1, 1.6, 0.5 Hz, 1H), 7.74 (td, *J* = 1.8, 0.9 Hz, 1H), 7.69–7.63 (m, 2H), 7.59–7.53 (m, 2H), 7.49–7.40 (m, 2H), 3.81 (q, *J* = 7.2 Hz, 1H), 3.69 (s, 3H), 1.54 (d, *J* = 7.2 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 194.7 (C_q), 174.2 (C_q), 140.9 (C_q), 139.1 (C_q), 137.2 (C_q), 134.5 (C_q), 132.3 (CH), 131.8 (CH), 129.9 (CH), 129.6 (CH), 129.1 (CH), 128.8 (CH), 128.6 (CH), 128.0 (CH), 52.2 (CH_3), 45.3 (CH), 18.6 (CH_3).

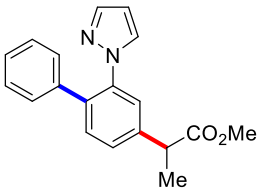
IR (ATR): $\tilde{\nu}$ = 2981, 2952, 1733, 1661, 1434, 1281, 1203, 1163, 737, 679 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 304 (10) [M(^{37}Cl)]$^+$, 302 (32) [M(^{35}Cl)]$^+$, 245 (34) [M(^{37}Cl)–CO_2Me]$^+$, 243 (100) [M(^{35}Cl)–CO_2Me]$^+$, 191 (24), 141 (19), 139 (57), 113 (10), 111 (30), 103 (19), 77 (12), 43 (24).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{15}{}^{35}ClO_3^+$ [M]$^+$ 302.0704, found 302.0712.

5.3.3.3 Characterization Data for 166

Methyl 2-[2-(1*H*-pyrazol-1-yl)-[1,1'-biphenyl]-4-yl]propanoate (166a)



The general procedure **F** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol), methyl 2-bromopropanoate (**140i**, 251 mg, 1.50 mmol), and bromobenzene (**165a**, 236 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **166a** (88.3 mg, 58%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.63 (dd, *J* = 1.9, 0.6 Hz, 1H), 7.57–7.55 (m, 1H), 7.43 (d_{AB}d, *J* = 8.1, 0.8 Hz, 1H), 7.41 (d_{AB}d, *J* = 8.1, 1.7 Hz, 1H), 7.30–7.24 (m, 3H), 7.11–7.06 (m, 2H), 7.05 (dd, *J* = 2.4, 0.6 Hz, 1H), 6.18 (dd, *J* = 2.4, 1.9 Hz, 1H), 3.83 (q, *J* = 7.2 Hz, 1H), 3.70 (s, 3H), 1.58 (d, *J* = 7.2 Hz, 3H).

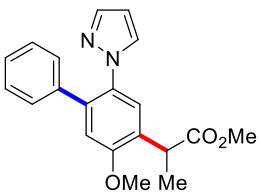
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.3 (C_q), 140.8 (C_q), 140.2 (CH), 138.5 (C_q), 138.1 (C_q), 135.3 (C_q), 131.3 (CH), 131.2 (CH), 128.4 (CH), 128.3 (CH), 127.3 (CH), 127.2 (CH), 125.7 (CH), 106.3 (CH), 52.2 (CH_3), 45.0 (CH), 18.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2980, 2950, 1732, 1519, 1442, 1200, 1164, 1042, 739, 699 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 306 (38) [M]$^+$, 305 (100) [M–H]$^+$, 247 (23) [M–CO_2Me]$^+$, 245 (29).

HR-MS (ESI): *m*/*z* calcd for $C_{19}H_{19}N_2O_2^+$ [M+H]$^+$ 307.1441, found 307.1443.

Methyl 2-[5-methoxy-2-(1*H*-pyrazol-1-yl)-[1,1'-biphenyl]-4-yl]propanoate (166b)



The general procedure **F** was followed using 1-(4-methoxyphenyl)-1*H*-pyrazole (**147d**, 87.1 mg, 0.50 mmol), methyl 2-bromopropanoate (**140i**, 251 mg, 1.50 mmol), and bromobenzene (**165a**, 236 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc 7:1) yielded **166b** (94.5 mg, 56%) as a viscous colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.59 (dd, J = 2.0, 0.6 Hz, 1H), 7.44 (s, 1H), 7.28–7.24 (m, 3H), 7.12–7.09 (m, 2H), 7.04 (dd, J = 2.3, 0.6 Hz, 1H), 6.91 (s, 1H), 6.15 (dd, J = 2.3, 2.0 Hz, 1H), 4.07 (q, J = 7.2 Hz, 1H), 3.88 (s, 3H), 3.68 (s, 3H), 1.52 (d, J = 7.2 Hz, 3H).

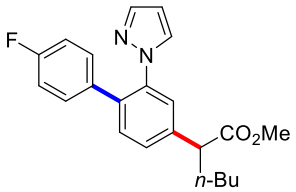
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.7 (C_q), 156.2 (C_q), 139.8 (CH), 138.3 (C_q), 136.7 (C_q), 131.7 (C_q), 131.3 (CH), 129.4 (C_q), 128.3 (CH), 128.2 (CH), 127.4 (CH), 126.6 (CH), 112.4 (CH), 106.0 (CH), 55.9 (CH_3), 52.0 (CH_3), 39.2 (CH), 17.1 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2981, 2947, 1733, 1518, 1488, 1222, 1036, 750, 700 cm^{-1}.

MS (EI) m/z (relative intensity): 336 (96) $[M]^+$, 335 (100) $[M–H]^+$, 277 (81) $[M–CO_2Me]^+$, 261 (29), 165 (11), 59 (13).

HR-MS (ESI): m/z calcd for $C_{20}H_{21}N_2O_3^+$ $[M+H]^+$ 337.1547, found 337.1547.

Methyl 2-[4'-fluoro-2-(1*H*-pyrazol-1-yl)-[1,1'-biphenyl]-4-yl]hexanoate (166c)



The general procedure **F** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol), methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol), and 1-bromo-4-fluorobenzene (**165b**, 263 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **166c** (130 mg, 71%) as a viscous light yellow oil.

The general procedure **G** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol), methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol), and 1-bromo-4-fluorobenzene (**165b**, 263 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc 15:1) yielded **166c** (133 mg, 72%) as a viscous light yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.63 (dd, J = 1.9, 0.6 Hz, 1H), 7.53 (d, J = 1.9 Hz, 1H), 7.42 (d_{AB}d, J = 8.1, 1.9 Hz, 1H), 7.39 (d_{AB}d, J = 8.1, 0.5 Hz, 1H), 7.09 (dd, J = 2.4, 0.6 Hz, 1H), 7.04 (dd, J = 8.9, 5.4 Hz, 2H), 6.96 (dd, J = 8.9, 8.6 Hz, 2H), 6.21 (dd, J = 2.4, 1.9 Hz, 1H), 3.69 (s, 3H), 3.63 (dd, J = 7.7, 7.7 Hz, 1H), 2.19–2.07 (m, 1H), 1.89–1.78 (m, 1H), 1.41–1.23 (m, 4H), 0.89 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 174.1 (C_q), 162.2 (d, $^1J_{C–F}$ = 247 Hz, C_q), 140.4 (CH), 140.0 (C_q), 138.6 (C_q), 134.6 (C_q), 134.2 (d, $^4J_{C–F}$ = 3 Hz, C_q), 131.2 (CH), 131.1 (CH), 130.1 (d, $^3J_{C–F}$ = 8 Hz, CH), 127.8 (CH), 126.4 (CH), 115.4 (d, $^2J_{C–F}$ = 21 Hz, CH), 106.5 (CH), 52.1 (CH_3), 51.2 (CH), 33.3 (CH_2), 29.8 (CH_2), 22.4 (CH_2), 13.9 (CH_3).

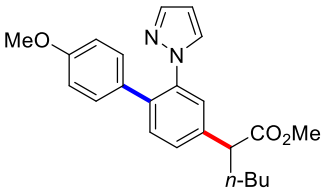
^{19}F-NMR (376 MHz, $CDCl_3$): δ = –114.7 (tt, J = 8.6, 5.4 Hz).

IR (ATR): $\tilde{\nu}$ = 2954, 2860, 1733, 1489, 1222, 1158, 1040, 828, 749 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 366 (52) $[M]^+$, 365 (100) $[M–H]^+$, 307 (15) $[M–CO_2Me]^+$, 263 (10), 251 (24).

HR-MS (ESI): *m*/*z* calcd for $C_{22}H_{23}FN_2O_2Na^+$ $[M+Na]^+$ 389.1636, found 389.1627.

Methyl 2-[4'-methoxy-2-(1*H*-pyrazol-1-yl)-[1,1'-biphenyl]-4-yl]hexanoate (166d)



The general procedure **F** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol), methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol), and 1-bromo-4-methoxybenzene (**165c**, 281 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **166d** (122 mg, 65%) as a viscous light yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.64 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.52 (dd, *J* = 1.2, 1.2 Hz, 1H), 7.41–7.38 (m, 2H), 7.09 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.00 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.20 (dd, *J* = 2.4, 1.8 Hz, 1H), 3.79 (s, 3H), 3.68 (s, 3H), 3.62 (dd, *J* = 8.2, 7.3 Hz, 1H), 2.22–2.04 (m, 1H), 1.91–1.76 (m, 1H), 1.43–1.21 (m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H).

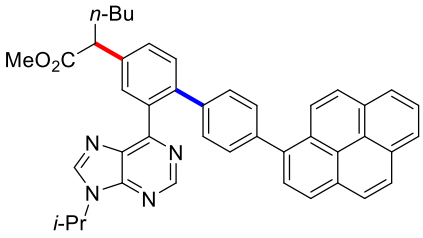
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.0 (C_q), 158.9 (C_q), 140.1 (CH), 139.2 (C_q), 138.4 (C_q), 135.1 (C_q), 131.3 (CH), 131.0 (CH), 130.4 (C_q), 129.5 (CH), 127.5 (CH), 126.2 (CH), 113.9 (CH), 106.3 (CH), 55.2 (CH_3), 52.1 (CH_3), 51.2 (CH), 33.3 (CH_2), 29.9 (CH_2), 22.5 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2954, 1733, 1609, 1489, 1245, 1161, 1039, 826, 750 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 378 (62) $[M]^+$, 377 (100) $[M–H]^+$, 319 (10) $[M–CO_2Me]^+$, 263 (19), 261 (15).

HR-MS (ESI): *m*/*z* calcd for $C_{23}H_{26}N_2O_3Na^+$ $[M+Na]^+$ 401.1836, found 401.1825.

Methyl 2-[2-(9-*iso*-propyl-9*H*-purin-6-yl)-4'-(pyren-1-yl)-[1,1'-biphenyl]-4-yl]hexanoate (166e)



The general procedure **F** was followed using purine **123a** (119 mg, 0.50 mmol), methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol), and 1-(4-bromophenyl)pyrene (**165d**, 357 mg, 1.00 mmol). Purification by column

chromatography (*n*-hexane/EtOAc 3:1) yielded **166e** (190 mg, 59%) as a light yellow solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.98 (s, 1H), 8.20–8.13 (m, 3H), 8.07 (s, 2H), 8.04 (d, *J* = 7.6 Hz, 1H), 8.02 (s, 1H), 8.01–7.95 (m, 2H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.80 (d, *J* = 1.9 Hz, 1H), 7.67 (d_{AB}, *J* = 8.0 Hz, 1H), 7.61 (d_{AB}d, *J* = 8.0, 1.9 Hz, 1H), 7.39 (d_{AB}, *J* = 8.5 Hz, 2H), 7.34 (d_{AB}, *J* = 8.5 Hz, 2H), 4.94 (hept, *J* = 6.8 Hz, 1H), 3.77–3.67 (m, 4H), 2.29–2.11 (m, 1H), 1.99–1.83 (m, 1H), 1.64 (d, *J* = 6.8 Hz, 6H), 1.48–1.26 (m, 4H), 0.92 (t, *J* = 6.9 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.3 (C_q), 158.7 (C_q), 151.9 (CH), 151.1 (C_q), 141.8 (CH), 140.5 (C_q), 139.9 (C_q), 139.1 (C_q), 138.5 (C_q), 137.3 (C_q), 134.8 (C_q), 132.6 (C_q), 131.4 (C_q), 130.8 (C_q), 130.8 (CH), 130.4 (C_q), 129.9 (CH), 129.2 (CH), 129.1 (CH), 128.3 (C_q), 127.4 (CH), 127.3 (CH), 127.3 (CH), 127.2 (CH), 125.9 (CH), 125.0 (CH), 125.0 (CH), 124.9 (C_q), 124.8 (C_q), 124.7 (CH), 124.5 (CH), 52.0 (CH_3), 51.4 (CH), 47.3 (CH), 33.5 (CH_2), 30.0 (CH_2), 22.6 (CH_3), 22.6 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3038, 2951, 1732, 1580, 1328, 1214, 1162, 846, 722, 647 cm^{-1}.

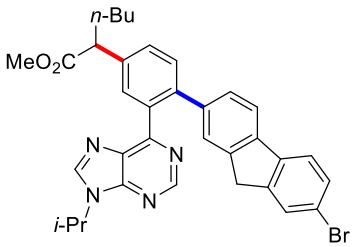
m.p.: 109–110 °C.

MS (EI) *m*/*z* (relative intensity): 642 (100) $[M]^+$, 641 (76) $[M–H]^+$, 599 (17) $[M–Pr]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{43}H_{38}N_4O_2Na^+$ $[M+Na]^+$ 665.2887, found 665.2887.

Em: **λmax** (1.0 mg/L in $CHCl_3$, Ex 280 nm) = 434 nm.

Methyl 2-[4-(7-bromo-9*H*-fluoren-2-yl)-3-(9-*iso*-propyl-9*H*-purin-6-yl)phenyl]hexanoate (166f)



The general procedure **F** was followed using purine **123a** (119 mg, 0.50 mmol), methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol), and 2,7-dibromofluorene (**165e**, 486 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **166f** (158 mg, 52%) as a light yellow solid.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.86 (s, 1H), 7.91 (s, 1H), 7.71 (d, *J* = 1.8 Hz, 1H), 7.61 (d, *J* = 1.6 Hz, 1H), 7.55 (d_{AB}, *J* = 8.0 Hz, 1H), 7.54 (d_{AB}d, *J* = 8.0, 1.7 Hz, 1H), 7.52 (d, *J* = 8.1 Hz, 1H), 7.46–7.43 (m, 2H), 7.42–7.41 (m, 1H), 7.08 (dd, *J* = 7.9, 1.6 Hz, 1H), 4.86 (hept, *J* = 6.8 Hz, 1H), 3.74 (br s, 2H), 3.69–3.65 (m, 4H), 2.19–2.11 (m, 1H), 1.90–1.82 (m, 1H), 1.58 (d, *J* = 6.8 Hz, 6H), 1.38–1.27 (m, 4H), 0.89 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.3 (C_q), 158.7 (C_q), 151.8 (CH), 151.1 (C_q), 145.3 (C_q), 142.5 (C_q), 141.9 (CH), 140.7 (C_q), 140.4 (C_q), 140.1 (C_q), 138.9 (C_q), 138.3 (C_q), 134.7 (C_q), 132.6 (C_q), 130.9 (CH), 130.8 (CH), 129.8 (CH), 129.1 (CH), 128.3 (CH), 128.1 (CH), 125.7 (CH), 120.9 (CH), 120.2 (C_q), 119.1 (CH), 52.0 (CH_3), 51.4 (CH), 47.3 (CH), 36.7 (CH_2), 33.5 (CH_2), 30.0 (CH_2), 22.6 (CH_2), 22.5 (CH_3), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2952, 2870, 1732, 1577, 1455, 1327, 1214, 1162, 812, 647 cm^{-1}.

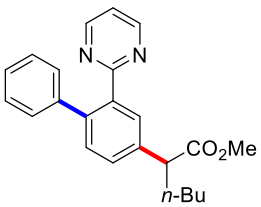
m.p.: 92–94 °C.

MS (EI) *m*/*z* (relative intensity): 610 (71) $[M(^{81}Br)]^+$, 609 (100) $[M(^{81}Br)–H]^+$, 608 (69) $[M(^{79}Br)]^+$, 607 (81) $[M(^{79}Br)–H]^+$, 43 (17).

HR-MS (ESI): *m*/*z* calcd for $C_{34}H_{34}{}^{79}BrN_4O_2^+$ $[M+H]^+$ 609.1860, found 609.1857.

Em: **λmax** (1.0 mg/L in $CHCl_3$, Ex 280 nm) = 441 nm.

Methyl 2-[2-(pyrimidin-2-yl)-[1,1'-biphenyl]-4-yl]hexanoate (166g)



The general procedure **G** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol), methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol), and bromobenzene (**165a**, 236 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc 7:1) yielded **166g** (113 mg, 63%) as a light yellow oil.

In case of using chlorobenzene (**165a'**) (169 mg, 1.50 mmol), the reaction provided product **166g** (126 mg, 70%).

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.63 (d, *J* = 4.9 Hz, 2H), 7.72 (d, *J* = 1.9 Hz, 1H), 7.48 (d_{AB}d, *J* = 7.9, 1.9 Hz, 1H), 7.43 (d_{AB}, *J* = 7.9 Hz, 1H), 7.24–7.18 (m, 3H), 7.13–7.11 (m, 2H), 7.09 (t, *J* = 4.9 Hz, 1H), 3.67 (s, 3H), 3.65 (dd, *J* = 8.0, 7.4 Hz, 1H), 2.15 (dddd, *J* = 13.3, 9.6, 8.0, 5.3 Hz, 1H), 1.85 (dddd, *J* = 13.3, 9.3, 7.4, 5.8 Hz, 1H), 1.39–1.23 (m, 4H), 0.88 (t, *J* = 7.1 Hz, 3H).

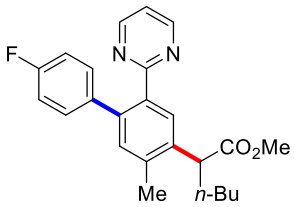
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.3 (C_q), 167.8 (C_q), 156.6 (CH), 141.2 (C_q), 140.3 (C_q), 138.4 (C_q), 138.3 (C_q), 130.9 (CH), 130.2 (CH), 129.0 (CH), 128.7 (CH), 127.9 (CH), 126.4 (CH), 118.4 (CH), 52.0 (CH_3), 51.4 (CH), 33.4 (CH_2), 29.9 (CH_2), 22.6 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2953, 1732, 1566, 1553, 1437, 1400, 1161, 818, 747, 700 cm^{-1}.

MS (EI) *m/z* (relative intensity): 360 (39) $[M]^+$, 359 (100) $[M–H]^+$, 301 (6) $[M–CO_2Me]^+$, 257 (13) $[M–CO_2Me–Pr]^+$, 245 (20) $[M–CO_2Me–Bu]^+$.

HR-MS (ESI): *m/z* calcd for $C_{23}H_{24}N_2O_2Na^+$ $[M+Na]^+$ 383.1730, found 383.1730.

Methyl 2-[4'-fluoro-5-methyl-2-(pyrimidin-2-yl)-[1,1'-biphenyl]-4-yl]hexanoate (166h)



The general procedure **G** was followed using 2-(*p*-tolyl)pyrimidine (**139b**, 85.3 mg, 0.50 mmol), methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol), and 1-bromo-4-fluorobenzene (**165b**, 263 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc 7:1) yielded **166h** (124 mg, 63%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.61 (d, *J* = 4.8 Hz, 2H), 7.76 (s, 1H), 7.22 (s, 1H), 7.11–7.03 (m, 3H), 6.90 (dd, *J* = 8.8, 8.8 Hz, 2H), 3.88 (dd, *J* = 8.4, 6.7 Hz, 1H), 3.65 (s, 3H), 2.46 (s, 3H), 2.27–2.13 (m, 1H), 1.88–1.73 (m, 1H), 1.42–1.22 (m, 4H), 0.89 (t, *J* = 6.8 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.3 (C_q), 167.5 (C_q), 161.6 (d, $^1J_{C–F}$ = 245 Hz, C_q), 156.5 (CH), 138.7 (C_q), 137.4 (C_q), 137.3 (d, $^4J_{C–F}$ = 3 Hz, C_q), 137.2 (C_q), 136.2 (C_q), 132.6 (CH), 130.4 (d, $^3J_{C–F}$ = 8 Hz, CH), 129.3 (CH), 118.2 (CH), 114.7 (d, $^2J_{C–F}$ = 21 Hz, CH), 51.9 (CH_3), 46.8 (CH), 32.9 (CH_2), 30.0 (CH_2), 22.6 (CH_2), 19.8 (CH_3), 14.0 (CH_3).

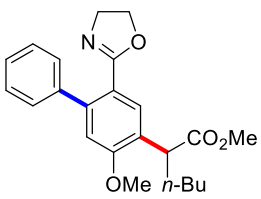
^{19}F-NMR (282 MHz, $CDCl_3$): δ = –116.6 (tt, *J* = 8.8, 5.4 Hz).

IR (ATR): $\tilde{\nu}$ = 2954, 1733, 1565, 1495, 1421, 1219, 1160, 837, 812 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 807 (18) $[2M+Na]^+$, 415 (48) $[M+Na]^+$, 393 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{24}H_{26}FN_2O_2^+$ $[M+H]^+$ 393.1973, found 393.1973.

Methyl 2-[2-(4,5-dihydrooxazol-2-yl)-5-methoxy-[1,1'-biphenyl]-4-yl]hexanoate (166i)



The general procedure **G** was followed using 2-(4-methoxyphenyl)-4,5-dihydrooxazole (**139i**, 88.6 mg, 0.50 mmol), methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol), and bromobenzene (**165a**, 236 mg, 1.50 mmol). Purification by column chromatography (*n*-hexane/EtOAc 3:2) yielded **166i** (87.2 mg, 46%) as a colorless oil.

In case of using chlorobenzene (**165a'**) (169 mg, 1.50 mmol), the reaction provided product **166i** (52.2 mg, 27%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.71 (s, 1H), 7.41–7.31 (m, 5H), 6.82 (s, 1H), 4.14–4.03 (m, 2H), 4.00 (dd, *J* = 7.7, 7.6 Hz, 1H), 3.88 (dd, *J* = 10.0, 8.9 Hz, 2H), 3.86 (s, 3H), 3.67 (s, 3H), 2.10 (dddd, *J* = 13.1, 9.6, 7.7, 5.5 Hz, 1H), 1.78 (dddd, *J* = 13.4, 9.6, 7.6, 5.7 Hz, 1H), 1.40–1.20 (m, 4H), 0.88 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 174.5 (C_q), 165.7 (C_q), 158.2 (C_q), 142.3 (C_q), 141.5 (C_q), 130.6 (CH), 128.3 (CH), 127.9 (CH), 127.2 (CH), 127.1 (C_q), 119.8 (C_q), 112.6 (CH), 67.5 (CH_2), 55.8 (CH_3), 55.0 (CH_2), 51.9 (CH_3), 43.8 (CH), 32.0 (CH_2), 29.8 (CH_2), 22.5 (CH_2), 13.9 (CH_3).

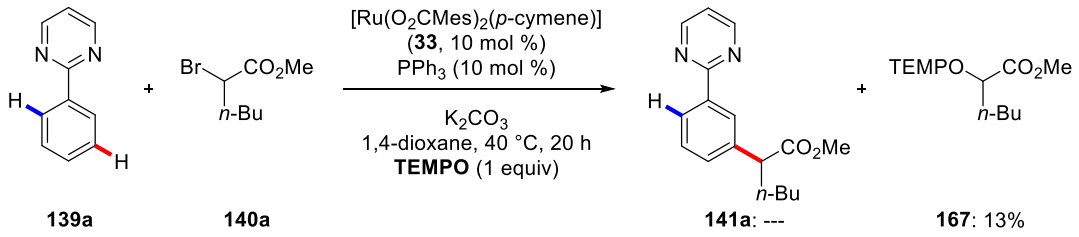
IR (ATR): $\tilde{\nu}$ = 2953, 1733, 1647, 1609, 1487, 1346, 1224, 1166, 752, 700 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 785 (80) $[2M+Na]^+$, 763 (37) $[2M+H]^+$, 404 (27) $[M+Na]^+$, 382 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{23}H_{28}NO_4^+$ $[M+H]^+$ 382.2013, found 382.2011.

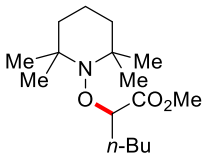
5.3.3.4 Mechanistic Studies

5.3.3.4.1 Reaction with TEMPO



2-Phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol), $[Ru(O_2CMes)_2(p\text{-cymene})]$ (**33**, 28.1 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %), K_2CO_3 (138 mg, 1.00 mmol), and TEMPO (78.2 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 for three times. Methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 40 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 30:1) followed by recycling preparative HPLC yielded TEMPO-adduct **167** (18.1 mg, 13%) as a colorless oil.

Methyl 2-[(2,2,6,6-tetramethylpiperidin-1-yl)oxy]hexanoate (167)



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 4.25–4.20 (m, 1H), 3.70 (s, 3H), 1.88–1.74 (m, 2H), 1.50–1.14 (m, 13H), 1.12 (s, 3H), 1.10 (s, 3H), 1.01 (s, 3H), 0.89 (t, *J* = 7.2 Hz, 3H).

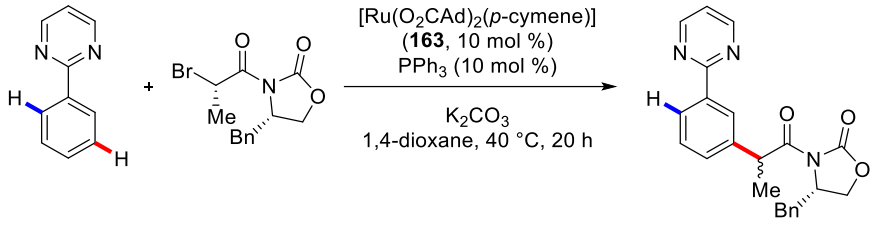
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 174.1 (C_q), 85.7 (CH), 60.3 (C_q), 59.4 (C_q), 51.3 (CH_3), 40.3 (CH_2), 40.2 (CH_2), 33.5 (CH_3), 32.9 (CH_3), 31.8 (CH_2), 26.8 (CH_2), 22.6 (CH_2), 20.2 (CH_3), 20.1 (CH_3), 17.1 (CH_2), 13.9 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2931, 2872, 1742, 1458, 1375, 1261, 1170, 1132, 1034, 791 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 285 (1) $[M]^+$, 270 (4) $[M–Me]^+$, 156 (100) $[TEMPO]^+$, 123 (29), 83 (15), 69 (22), 55 (26), 41 (18).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{31}NO_3^+$ $[M]^+$ 285.2298, found 285.2309.

5.3.3.4.2 Reactions with Diastereomerically Pure Alkyl Bromide

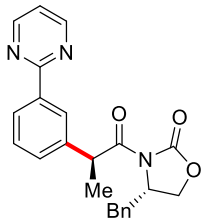


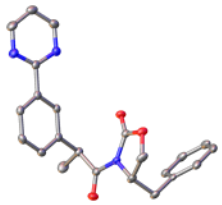
139a **140j** **141r**: 73%
dr 1.0:1.4

The general procedure **E** was followed using 2-phenylpyrimidine (**139a**, 102 mg, 0.65 mmol) and (*s*)-4-benzyl-3-((*s*)-2-bromopropanoyl)oxazolidin-2-one (**140j**, 156 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **141r** (141 mg, 73%, dr 1.0:1.4). Two diastereomers was separated by recycling preparative HPLC to provide isomer **A** (57.3 mg, 30%) as a white solid and isomer **B** (41.8 mg, 36%) as a colorless oil.

(*s*)-4-Benzyl-3-{(*s*)-2-[3-(pyrimidin-2-yl)phenyl]propanoyl}oxazolidin-2-one (141rA)

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 4.8 Hz, 2H), 8.46 (dd, *J* = 1.8, 1.7 Hz, 1H), 8.33 (ddd, *J* = 7.7, 1.8, 1.4 Hz, 1H), 7.52 (ddd, *J* = 7.7, 1.7, 1.4 Hz, 1H), 7.45 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.36–7.31 (m, 2H), 7.30–7.27 (m, 1H), 7.24–7.21 (m, 2H), 7.18 (t, *J* = 4.8 Hz, 1H), 5.23 (q, *J* = 7.0 Hz, 1H), 4.62





141rA
CCDC 1865622

(dddd, *J* = 9.8, 7.6, 3.3, 2.4 Hz, 1H), 4.11 (d_{AB}d, *J* = 9.1, 2.4 Hz, 1H), 4.07 (d_{AB}dd, *J* = 9.1, 7.6, 0.6 Hz, 1H), 3.37 (dd, *J* = 13.3, 3.3 Hz, 1H), 2.81 (dd, *J* = 13.3, 9.8 Hz, 1H), 1.63 (d, *J* = 7.0 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.4 (C_q), 164.5 (C_q), 157.1 (CH), 152.8 (C_q), 140.6 (C_q), 137.9 (C_q), 135.3 (C_q), 130.6 (CH), 129.4 (CH), 128.9 (CH), 128.8 (CH), 127.9 (CH), 127.3 (CH), 127.1 (CH), 119.0 (CH), 65.9 (CH_2), 55.8 (CH), 43.4 (CH), 38.0 (CH_2), 19.5 (CH_3).

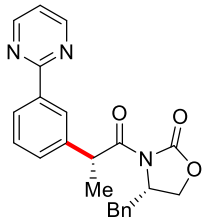
IR (ATR): $\tilde{\nu}$ = 2977, 1771, 1694, 1554, 1410, 1357, 1209, 760, 745, 699 cm^{-1}.

m.p.: 140–141 °C.

MS (EI) *m*/*z* (relative intensity): 387 (33) $[M]^+$, 210 (100), 183 (51), 168 (34), 91 (14) [Bn].

HR-MS (EI): *m*/*z* calcd for $C_{23}H_{21}N_3O_3^+$ $[M]^+$ 387.1577, found 387.1583.

(*s*)-4-Benzyl-3-{(*R*)-2-[3-(pyrimidin-2-yl)phenyl]propanoyl}oxazolidin-2-one (141rB)



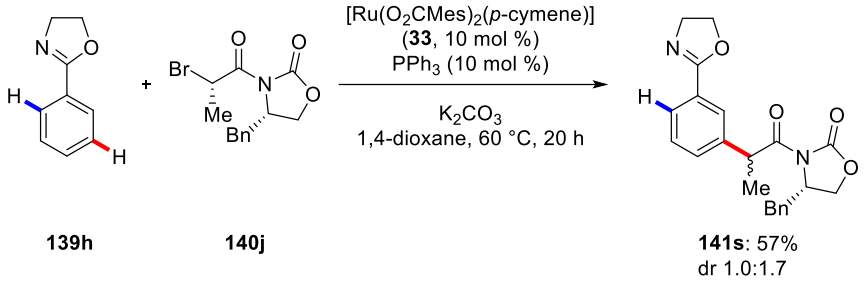
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 4.8 Hz, 1H), 8.53 (dd, *J* = 1.8, 1.7 Hz, 1H), 8.37 (ddd, *J* = 7.8, 1.8, 1.4 Hz, 1H), 7.56 (ddd, *J* = 7.7, 1.7, 1.4 Hz, 1H), 7.49 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.20–7.18 (m, 3H), 7.17 (t, *J* = 4.8 Hz, 1H), 7.03–6.99 (m, 2H), 5.22 (q, *J* = 7.1 Hz, 1H), 4.76 (dddd, *J* = 9.2, 8.1, 3.4, 3.3 Hz, 1H), 4.19 (dd, *J* = 9.0, 8.1 Hz, 1H), 4.08 (dd, *J* = 9.0, 3.3 Hz, 1H), 3.17 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.60 (dd, *J* = 13.5, 9.2 Hz, 1H), 1.60 (d, *J* = 7.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.3 (C_q), 164.4 (C_q), 157.1 (CH), 152.8 (C_q), 140.6 (C_q), 138.0 (C_q), 135.0 (C_q), 130.6 (CH), 129.3 (CH), 128.9 (CH), 128.7 (CH), 128.1 (CH), 127.1 (CH), 127.0 (CH), 119.0 (CH), 65.9 (CH_2), 55.1 (CH), 43.5 (CH), 37.5 (CH_2), 19.3 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2977, 1772, 1693, 1555, 1410, 1356, 1210, 734, 699 cm^{-1}.

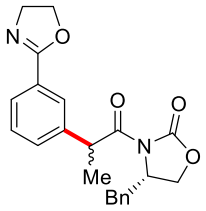
MS (EI) *m*/*z* (relative intensity): 387 (29) $[M]^+$, 210 (100), 183 (47), 168 (34), 91 (18) [Bn].

HR-MS (EI): *m*/*z* calcd for $C_{23}H_{21}N_3O_3^+$ $[M]^+$ 387.1577, found 387.1586.



The general procedure **E** was followed using [Ru(O_2CMes)$_2$(*p*-cymene)] (**33**, 28.1 mg, 50.0 µmol, 10 mol %), 2-phenyl-4,5-dihydrooxazole (**139h**, 57.6 mg, 0.39 mmol) and (*s*)-4-benzyl-3-((*s*)-2-bromopropanoyl)oxazolidin-2-one (**140j**, 93.8 mg, 0.30 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:2) yielded **141s** (65.1 mg, 57%, dr 1.0:1.7). Two diastereomers was separated by recycling preparative HPLC to provide isomer **A** (23.8 mg, 21%) as a colorless oil and isomer **B** (41.2 mg, 36%) as a colorless oil.

(4*s*)-4-Benzyl-3-{2-[3-(4,5-dihydrooxazol-2-yl)phenyl]propanoyl}oxazolidin-2-one (141s)



Diastereomer **A**:

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.00 (dd, *J* = 1.7, 1.6 Hz, 1H), 7.88 (ddd, *J* = 7.8, 1.6, 1.5 Hz, 1H), 7.54 (ddd, *J* = 7.7, 1.7, 1.5 Hz, 1H), 7.40 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.23–7.19 (m, 3H), 7.02–6.98 (m, 2H), 5.14 (q, *J* = 7.0 Hz, 1H), 4.74 (dddd, *J* = 9.2, 8.2, 3.4, 3.3 Hz, 1H), 4.42 (t, *J* = 9.6 Hz, 2H), 4.19 (dd, *J* = 9.0, 8.2 Hz, 1H), 4.09 (dd, *J* = 9.0, 3.3 Hz, 1H), 4.05 (t, *J* = 9.6 Hz, 2H), 3.13 (dd, *J* = 13.5, 3.4 Hz, 1H), 2.59 (dd, *J* = 13.5, 9.2 Hz, 1H), 1.54 (d, *J* = 7.0 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.0 (C_q), 164.3 (C_q), 152.8 (C_q), 140.4 (C_q), 134.9 (C_q), 131.2 (CH), 129.3 (CH), 128.8 (CH), 128.6 (CH), 128.2 (C_q), 127.9 (CH), 127.1 (CH), 127.1 (CH), 67.6 (CH_2), 65.9 (CH_2), 55.0 (CH), 55.0 (CH_2), 43.2 (CH), 37.5 (CH_2), 19.2 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2978, 2933, 1779, 1697, 1650, 1360, 1214, 1068, 948, 706 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 378 (100) $[M]^+$, 201 (96), 174 (76), 143 (29), 131 (42), 103 (35), 91 (20) [Bn], 77 (13).

HR-MS (EI): *m*/*z* calcd for $C_{22}H_{22}N_2O_4^+$ $[M]^+$ 378.1574, found 378.1590.

Diastereomer **B**:

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.94 (dd, *J* = 1.7, 1.6 Hz, 1H), 7.84 (ddd, *J* = 7.7, 1.6, 1.5 Hz, 1H), 7.49 (ddd, *J* = 7.8, 1.7, 1.5 Hz, 1H), 7.39–7.31 (m, 3H), 7.30–7.24 (m, 1H), 7.24–7.18 (m, 2H), 5.15 (q, *J* = 7.0 Hz, 1H), 4.61 (dddd, *J* = 9.8, 7.4, 3.3, 2.6 Hz, 1H), 4.42 (t, *J* = 9.5 Hz, 2H), 4.12 (dd, *J* = 9.1, 2.6 Hz, 1H), 4.10–4.02 (m, 3H), 3.35 (dd, *J* = 13.3, 3.3 Hz, 1H), 2.80 (dd, *J* = 13.3, 9.8 Hz, 1H), 1.57 (d, *J* = 7.0 Hz, 3H).

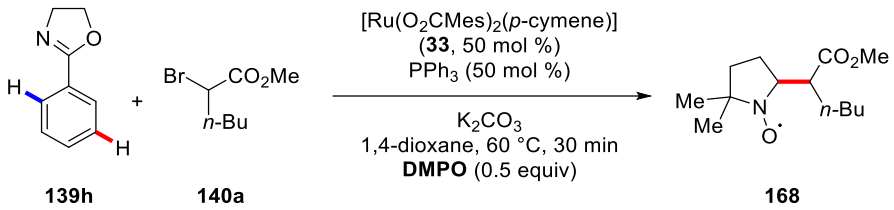
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 174.2 (C_q), 164.4 (C_q), 152.8 (C_q), 140.5 (C_q), 135.3 (C_q), 131.3 (CH), 129.4 (CH), 128.9 (CH), 128.6 (CH), 128.1 (C_q), 127.8 (CH), 127.3 (CH), 127.1 (CH), 67.6 (CH_2), 65.9 (CH_2), 55.7 (CH), 54.9 (CH_2), 43.1 (CH), 37.9 (CH_2), 19.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2976, 2932, 1777, 1696, 1650, 1359, 1212, 1069, 948, 706 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 378 (87) $[M]^+$, 201 (100), 174 (83), 143 (40), 131 (47), 115 (15), 103 (42), 91 (58) [Bn], 77 (18), 65 (13).

HR-MS (EI): *m*/*z* calcd for $C_{22}H_{22}N_2O_4^+$ $[M]^+$ 378.1574, found 378.1583.

5.3.3.4.3 Spin Trapping with DMPO



139h **140a** **168**

A mixture of 2-phenyl-4,5-dihydrooxazole (**139h**, 17.7 mg, 0.12 mmol), methyl 2-bromohexanoate (**140a**, 75.3 mg, 0.36 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (**33**, 33.7 mg, 60 µmol), PPh_3 (15.7 mg, 60 µmol), K_2CO_3 (33.2 mg, 0.24 mmol) and DMPO (6.8 mg, 60 µmol) in 1,4-dioxane (3.0 mL) was heated to 60 °C for 30 min in a glovebox with N_2-atmosphere. A filtered sample was transferred to an EPR-tube and measured directly (Figure 18).

DMPO itself gave small background signals which are different to the strong ones observed after the reaction. The observed spectrum is in accordance to reported DMPO-adducts with alkyl radicals.[135]

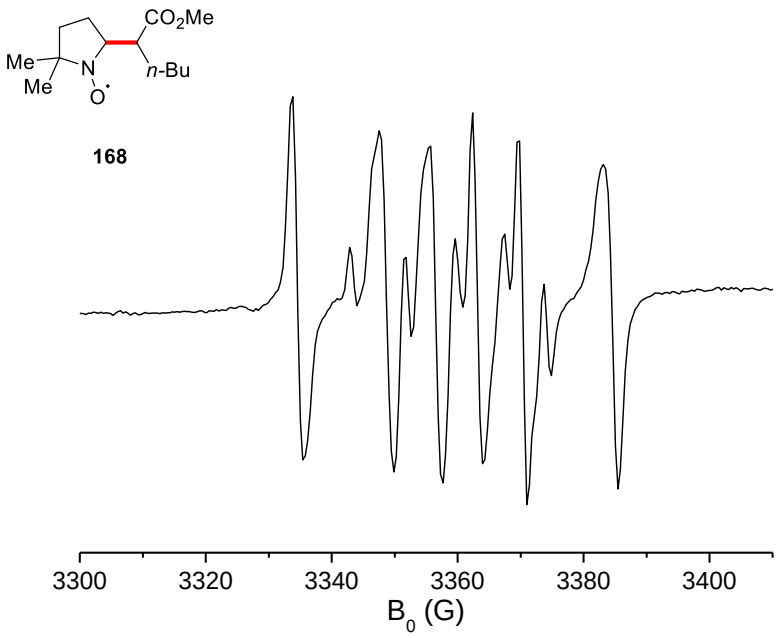
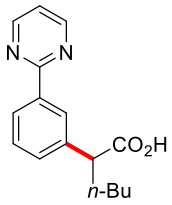


Figure 18: EPR spectroscopic studies for the synergistic ruthenium catalytic system.

5.3.3.5 Late-Stage Diversifications

Saponification of Esters

2-[3-(Pyrimidin-2-yl)phenyl]hexanoic acid (175a)



To a solution of **141a** (569 mg, 2.00 mmol) in CH_2Cl_2/MeOH (9:1, 20 mL) was added NaOH in MeOH (2 M, 2.0 mL). The reaction mixture was stirred at ambient temperature. After 24 h, the reaction mixture was concentrated *in vacuo* and acidified with 2 N HCl until pH 1–2. The resulting mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (CH_2Cl_2/MeOH 50:1) yielded product **175a** (508 mg, 94%) as a viscous colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 10.54 (br s, 1H), 8.85 (d, *J* = 4.9 Hz, 2H), 8.38 (dd, *J* = 1.8, 1.7 Hz, 1H), 8.30 (ddd, *J* = 7.3, 1.7, 1.7 Hz, 1H), 7.51 (ddd, *J* = 7.7, 1.8, 1.7 Hz, 1H), 7.44 (dd, *J* = 7.7, 7.3 Hz, 1H), 7.19 (t, *J* = 4.9 Hz, 1H), 3.69 (dd, *J* = 7.8, 7.7 Hz, 1H), 2.19 (dddd, *J* = 13.2, 9.5, 7.8, 5.6 Hz, 1H), 1.89 (dddd, *J* = 13.2, 9.5, 7.7, 5.3 Hz, 1H), 1.43–1.19 (m, 4H), 0.87 (t, *J* = 6.9 Hz, 3H).

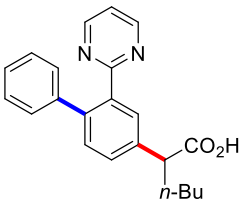
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 178.5 (C_q), 164.3 (C_q), 157.1 (CH), 139.4 (C_q), 137.4 (C_q), 130.4 (CH), 128.8 (CH), 128.0 (CH), 127.3 (CH), 119.1 (CH), 51.8 (CH), 32.8 (CH_2), 29.8 (CH_2), 22.5 (CH_2), 13.9 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2956, 2930, 1704, 1556, 1411, 1168, 907, 727, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 270 (28) $[M]^+$, 225 (50) $[M–CO_2H]^+$, 214 (51) $[M–Bu]^+$, 196 (23) $[M–CO_2H–Et]^+$, 183 (27) $[M–CO_2H–Pr]^+$, 169 (79) $[M–CO_2H–Bu]^+$, 84 (10), 58 (41) [Bu], 43 (100) [Pr].

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{18}N_2O_2^+$ $[M]^+$ 270.1363, found 270.1377.

2-[2-(Pyrimidin-2-yl)-[1,1'-biphenyl]-4-yl]hexanoic acid (175b)



To a solution of **166g** (113 mg, 0.31 mmol) in CH_2Cl_2/MeOH (9:1, 3.0 mL) was added NaOH in MeOH (2 M, 0.3 mL). The reaction mixture was stirred at ambient temperature. After 24 h, the reaction mixture was concentrated *in vacuo* and acidified with 2 N HCl until pH 1–2. The resulting mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (CH_2Cl_2/MeOH 50:1) yielded product **175b** (96.4 mg, 89%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.72 (d, *J* = 5.0 Hz, 2H), 7.68 (d, *J* = 1.8 Hz, 1H), 7.50 (d_{AB}d, *J* = 8.0, 1.8 Hz, 1H), 7.43 (d_{AB}, *J* = 8.0 Hz, 1H), 7.23–7.17 (m, 3H), 7.15 (t, *J* = 5.0 Hz, 1H), 7.12–7.06 (m, 2H), 3.64 (dd, *J* = 7.7, 7.7 Hz, 1H), 2.23–2.08 (m, 1H), 1.86 (dddd, *J* = 13.4, 9.4, 7.7, 5.5 Hz, 1H), 1.41–1.21 (m, 4H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 177.3 (C_q), 167.5 (C_q), 156.6 (CH), 140.9 (C_q), 140.4 (C_q), 138.5 (C_q), 137.4 (C_q), 130.9 (CH), 130.5 (CH), 129.1 (CH), 128.9 (CH), 127.9 (CH), 126.5 (CH), 118.6 (CH), 51.3 (CH), 32.7 (CH_2), 29.8 (CH_2), 22.6 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2955, 2929, 1710, 1567, 1439, 1401, 1176, 910, 732, 701 cm^{-1}.

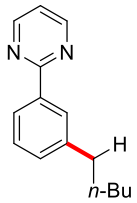
m.p.: 79–80 °C.

MS (EI) *m*/*z* (relative intensity): 346 (40) $[M]^+$, 345 (100) $[M–H]^+$, 288 (6) $[M–Bu]^+$, 271 (8) $[M–CO_2H–Et]^+$, 257 (12) $[M–CO_2H–Pr]^+$, 244 (12) $[M–CO_2H–Bu]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{22}H_{22}N_2O_2Na^+$ $[M+Na]^+$ 369.1573, found 369.1569.

Photocatalytic Decarboxylations

2-(3-Pentylphenyl)pyrimidine (177a)



The general procedure **H** was followed using substrate **175a** (54.1 mg, 0.20 mmol) and photocatalyst [Mes-Acr-Me][ClO_4] (**176**, 1.0 mg, 2.4 µmol, 1.2 mol %). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **177a** (39.9 mg, 88%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.81 (d, *J* = 4.8 Hz, 2H), 8.27–8.23 (m, 2H), 7.41 (dd, *J* = 8.3, 7.6 Hz, 1H), 7.31 (ddd, *J* = 7.6, 1.9, 1.3 Hz, 1H), 7.18 (t, *J* = 4.8 Hz, 1H), 2.71 (dd, *J* = 8.0, 7.6 Hz, 2H), 1.76–1.59 (m, 2H), 1.41–1.30 (m, 4H), 0.93–0.86 (m, 3H).

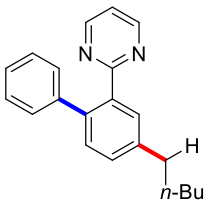
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.9 (C_q), 157.1 (CH), 143.3 (C_q), 137.4 (C_q), 130.9 (CH), 128.4 (CH), 128.0 (CH), 125.5 (CH), 118.9 (CH), 36.1 (CH_2), 31.7 (CH_2), 31.3 (CH_2), 22.6 (CH_2), 14.1 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2927, 2856, 1568, 1553, 1423, 1408, 782, 697, 636 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 226 (47) $[M]^+$, 197 (7) $[M–Et]^+$, 183 (45) $[M–Pr]^+$, 170 (93), 169 (100) $[M–Bu]^+$, 116 (8), 89 (7).

HR-MS (ESI): *m*/*z* calcd for $C_{15}H_{19}N_2^+$ $[M+H]^+$ 227.1543, found 227.1538.

2-(4-Pentyl-[1,1'-biphenyl]-2-yl)pyrimidine (177b)



The general procedure **H** was followed using substrate **175b** (34.7 mg, 0.10 mmol) and photocatalyst [Mes-Acr-Me][ClO_4] (**176**, 2.0 mg, 4.8 µmol, 4.8 mol %). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **177b** (16.3 mg, 54%) as a light yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.63 (d, *J* = 4.9 Hz, 2H), 7.61 (dd, *J* = 1.9, 0.6 Hz, 1H), 7.39 (d_{AB}d, *J* = 7.8, 0.6 Hz, 1H), 7.34 (d_{AB}d, *J* = 7.8, 1.9 Hz, 1H), 7.25–7.18 (m, 3H), 7.15–7.10 (m, 2H), 7.08 (t, *J* = 4.9 Hz, 1H), 2.71 (dd, *J* = 7.9, 7.7 Hz, 2H), 1.76–1.65 (m, 2H), 1.41–1.31 (m, 4H), 0.94–0.87 (m, 3H).

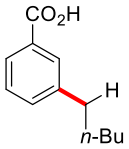
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 168.3 (C_q), 156.7 (CH), 142.2 (C_q), 141.6 (C_q), 138.8 (C_q), 138.0 (C_q), 130.6 (CH), 130.4 (CH), 129.5 (CH), 129.1 (CH), 127.9 (CH), 126.2 (CH), 118.3 (CH), 35.5 (CH_2), 31.6 (CH_2), 31.1 (CH_2), 22.5 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2927, 2856, 1566, 1552, 1423, 1397, 817, 770, 699 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 302 (37) $[M]^+$, 301 (100) $[M–H]^+$, 244 (27) $[M–Bu]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{21}H_{23}N_2^+$ $[M+H]^+$ 303.1856, found 303.1860.

3-Pentylbenzoic acid (179)



The general procedure **H** was followed using substrate **178** (47.3 mg, 0.20 mmol) and photocatalyst [Mes-Acr-Me][ClO_4] (**176**, 2.0 mg, 4.8 µmol, 2.4 mol %). After 16 h, purification by column chromatography (CH_2Cl_2/HOAc 100:1) yielded **179** (34.5 mg, 90%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 11.48 (br s, 1H), 7.98–7.91 (m, 2H), 7.43 (ddd, *J* = 7.7, 1.6, 1.6 Hz, 1H), 7.38 (dd, *J* = 7.8, 7.7 Hz, 1H), 2.67 (dd, *J* = 7.9, 7.6 Hz, 2H), 1.73–1.58 (m, 2H), 1.44–1.25 (m, 4H), 0.91 (t, *J* = 6.8 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 172.6 (C_q), 143.3 (C_q), 133.9 (CH), 130.1 (CH), 129.5 (C_q), 128.4 (CH), 127.6 (CH), 35.7 (CH_2), 31.4 (CH_2), 31.0 (CH_2), 22.5 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2925, 2854, 1678, 1451, 1275, 946, 739, 666 cm^{-1}.

m.p.: 58–59 °C.

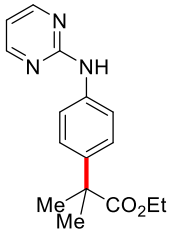
MS (EI) *m*/*z* (relative intensity): 192 (41) $[M]^+$, 149 (10) $[M–Pr]^+$, 136 (100) $[M–Bu]^+$, 135 (85), 105 (10), 92 (37), 91 (47), 77 (19), 58 (22) [Bu], 43 (66) [Pr].

HR-MS (EI): *m*/*z* calcd for $C_{12}H_{16}O_2^+$ $[M]^+$ 192.1145, found 192.1149.

The spectral data are in accordance with those reported in the literature.[136]

5.3.3.6 Characterization Data for 180

Ethyl 2-methyl-2-[4-(pyrimidin-2-ylamino)phenyl]propanoate (180a)



Pyrimidyl aniline **125b** (42.8 mg, 0.25 mmol), [Ru(O_2CMes)$_2$(*p*-cymene)] (**33**, 14.1 mg, 25.0 µmol, 10 mol %), PPh_3 (6.6 mg, 25.0 µmol, 10 mol %) and K_2CO_3 (69.1 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 for three times. Ethyl 2-bromo-2-methylpropanoate (**140k**, 146 mg, 0.75 mmol) and $PhCMe_3$ (1.0 mL) were then added and the mixture was stirred at 120 °C. After 20 h, the resulting mixture was filtered through a pad of siliga gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of

the residue by column chromatography (*n*-hexane/EtOAc 6:1) yielded monoalkylated product **180a** (18.9 mg, 26%) as a colorless oil and dialkylated product **180a'** (22.8 mg, 23%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.42 (d, J = 4.8 Hz, 2H), 7.56 (d, J = 8.7 Hz, 2H), 7.35 (br s, 1H), 7.32 (d, J = 8.7 Hz, 2H), 6.71 (t, J = 4.8 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 1.57 (s, 6H), 1.19 (t, J = 7.1 Hz, 3H).

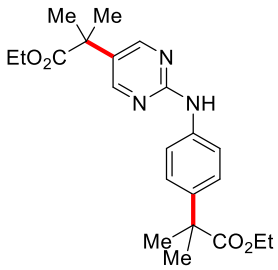
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 176.8 (C_q), 160.2 (C_q), 158.1 (CH), 139.1 (C_q), 137.8 (C_q), 126.3 (CH), 119.4 (CH), 112.6 (CH), 60.8 (CH_2), 45.9 (C_q), 26.5 (CH_3), 14.1 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2975, 1720, 1579, 1522, 1446, 1415, 1243, 1143, 796 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 308 (22) $[M+Na]^+$, 286 (100) $[M+H]^+$, 212 (9).

HR-MS (ESI): *m/z* calcd for $C_{16}H_{20}N_3O_2^+$ $[M+H]^+$ 286.1550, found 286.1556.

Ethyl 2-{2-{[4-(1-ethoxy-2-methyl-1-oxopropan-2-yl)phenyl]amino}pyrimidin-5-yl}-2-methyl propanoate (180a')



^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.44 (s, 2H), 7.55 (d, J = 8.9 Hz, 2H), 7.44 (br s, 1H), 7.31 (d, J = 8.9 Hz, 2H), 4.13 (q, J = 7.1 Hz, 2H), 4.11 (q, J = 7.1 Hz, 2H), 1.59 (s, 6H), 1.56 (s, 6H), 1.21 (t, J = 7.1 Hz, 3H), 1.18 (t, J = 7.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 176.6 (C_q), 175.4 (C_q), 158.8 (C_q), 155.8 (CH), 138.9 (C_q), 137.8 (C_q), 128.2 (C_q), 126.2 (CH), 119.2 (CH), 61.3 (CH_2), 60.7 (CH_2), 46.0 (C_q), 43.1 (C_q), 26.6 (CH_3), 26.0 (CH_3), 14.1 (CH_3).

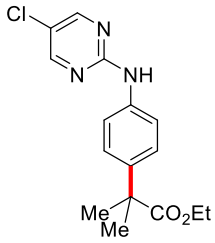
IR (ATR): $\tilde{\nu}$ = 3390, 2978, 1709, 1595, 1519, 1436, 1249, 1144, 800 cm^{-1}.

m.p.: 105–106 °C.

MS (EI) *m/z* (relative intensity): 399 (15) $[M]^+$, 326 (100) $[M–CO_2Et]^+$, 298 (14), 252 (14).

HR-MS (EI): *m/z* calcd for $C_{22}H_{29}N_3O_4^+$ $[M]^+$ 399.2153, found 399.2168.

Ethyl 2-{4-[(5-chloropyrimidin-2-yl)amino]phenyl}-2-methylpropanoate (180b)



Pyrimidyl aniline **125a** (51.5 mg, 0.25 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 12.5 µmol, 5.0 mol %), PPh_3 (6.6 mg, 25.0 µmol, 10 mol %) and K_2CO_3 (69.1 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 for three times. Ethyl 2-bromo-2-methylpropanoate (**140k**, 146 mg, 0.75 mmol) and *m*-xylene (1.0 mL) were then added and the mixture was stirred at 120 °C. After 20 h, the resulting mixture was filtered through a pad of siliga gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 10:1) yielded **180b** (44.4 mg, 56%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.34 (s, 2H), 7.52 (d, *J* = 8.8 Hz, 2H), 7.40–7.29 (m, 3H), 4.12 (q, *J* = 7.1 Hz, 2H), 1.57 (s, 6H), 1.19 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 176.7 (C_q), 158.2 (C_q), 156.2 (CH), 139.5 (C_q), 137.3 (C_q), 126.3 (CH), 120.8 (C_q), 119.3 (CH), 60.8 (CH_2), 45.9 (C_q), 26.5 (CH_3), 14.1 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2981, 1718, 1612, 1522, 1429, 1241, 1149, 1026, 839, 779 cm^{-1}.

m.p.: 92–94 °C.

MS (ESI) *m*/*z* (relative intensity): 344 (13) $[M(^{37}Cl)+Na]^+$, 342 (40) $[M(^{35}Cl)+Na]^+$, 322 (33) $[M(^{37}Cl)+H]^+$, 320 (100) $[M(^{35}Cl)+H]^+$, 246 (9).

HR-MS (ESI): *m*/*z* calcd for $C_{16}H_{19}{}^{35}ClN_3O_2^+$ $[M+H]^+$ 320.1160, found 320.1164.

The spectral data are in accordance with those reported in the literature.[87]

5.3.3.7 Fluorescence Spectra

Concentration of sample: 1 mg/L in $CHCl_3$

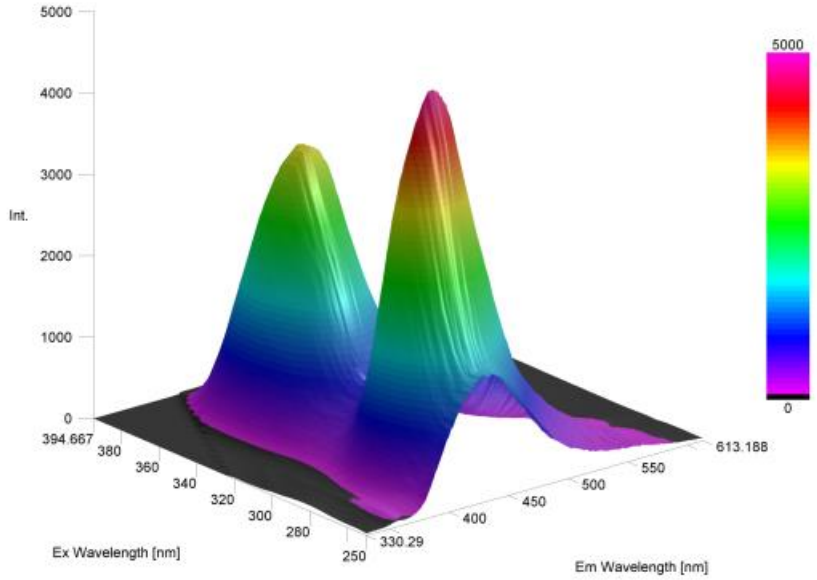


Figure 19: Excitation/emission fluorescence spectrum of **166e**.

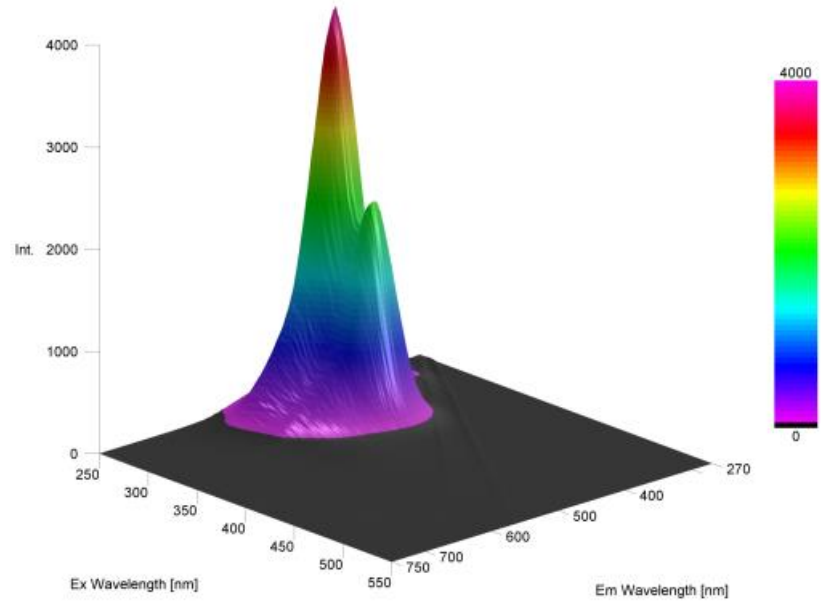


Figure 20: Excitation/emission fluorescence spectrum of **166f**.

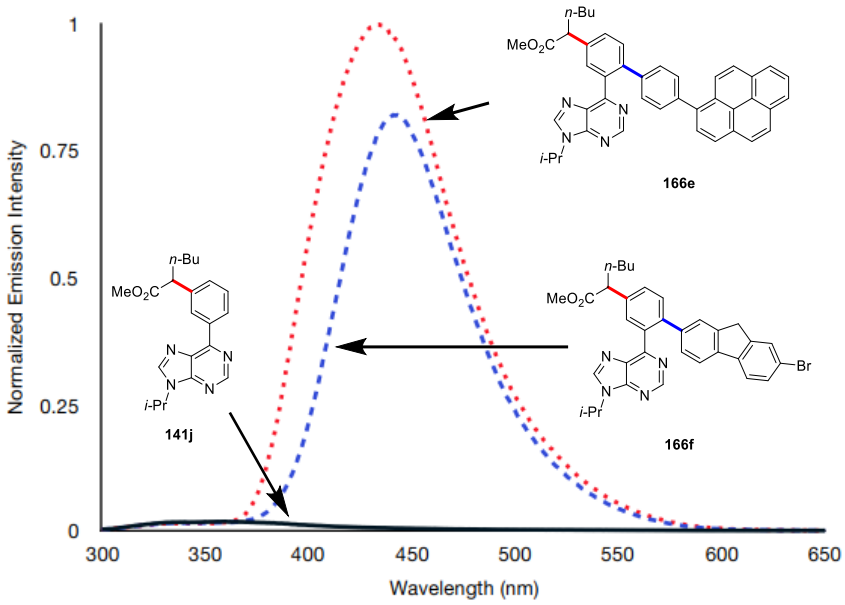


Figure 21: Emission fluorescence spectra of **141j**, **166e**, and **166f** (excitation at 280 nm)**.**

5.3.3.8 X-Ray Crystallographic Analysis

A suitable crystal was selected and the crystal was mounted on a MITIGEN holder in NVH oil on a Bruker D8 Venture diffractometer. The crystal was kept at 100 K during data collection. Using Olex2,[137] the structure was solved with the XT[138] structure solution program using Intrinsic Phasing and refined with the XL[139] refinement package using Least Squares minimisation.

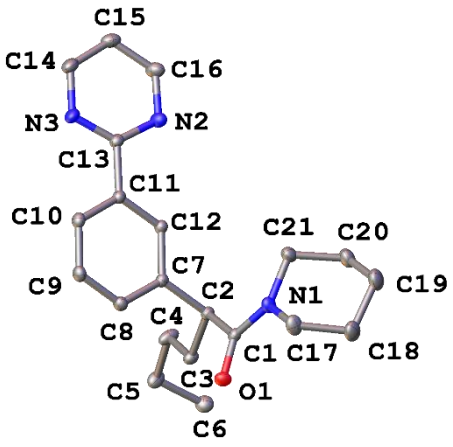


Figure 22: Molecular structure of **141l** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{21}H_{27}N_3O$ (*M* = 337.45 g/mol): triclinic, space group P-1 (no. 2), *a* = 10.1934(6) Å, *b* = 10.7135(6) Å, *c* = 17.2661(11) Å, *α* = 89.316(2)°, *β* = 85.141(2)°, *γ* = 82.592(2)°, *V* = 1863.12(19) Å^3, *Z* = 4, *T* = 99.99 K, μ(MoKα) = 0.075 mm^{-1}, *Dcalc* = 1.203 g/cm^3, 105267 reflections measured (4.504° ≤ 2Θ ≤ 63.066°), 12396 unique (R_{int} = 0.0272, R_{sigma} = 0.0158) which were used in all calculations. The final R_1 was 0.0394 (I > 2σ(I)) and wR_2 was 0.1119 (all data).

Table 23: Crystal data and structure refinement for **141l**.

Compound	**141l**
CCDC	1865623
Identification code	mo_0069_CG_0m
Empirical formula	$C_{21}H_{27}N_3O$
Formula weight	337.45
Temperature/K	99.99
Crystal system	triclinic
Space group	P-1
a/Å	10.1934(6)
b/Å	10.7135(6)
c/Å	17.2661(11)
α/°	89.316(2)
β/°	85.141(2)
γ/°	82.592(2)
Volume/Å^3	1863.12(19)
Z	4
ρ_{calc}g/cm^3	1.203
μ/mm^{-1}	0.075
F(000)	728.0
Crystal size/mm^3	0.417 × 0.182 × 0.144
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.504 to 63.066
Index ranges	-14 ≤ h ≤ 14, -15 ≤ k ≤ 15, -25 ≤ l ≤ 25
Reflections collected	105267

Independent reflections	12396 [R_{int} = 0.0272, R_{sigma} = 0.0158]
Data/restraints/parameters	12396/0/453
Goodness-of-fit on F^2	1.043
Final R indexes [I>=2σ (I)]	R_1 = 0.0394, wR_2 = 0.1086
Final R indexes [all data]	R_1 = 0.0432, wR_2 = 0.1119
Largest diff. peak/hole / e $Å^{-3}$	0.46/-0.19

Table 24: Selected bond lengths [Å] for **141l**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C1	1.2355(9)	C7	C8	1.3975(10)
N1	C1	1.3513(10)	C7	C12	1.3944(10)
N1	C17	1.4651(10)	C8	C9	1.3913(11)
N1	C21	1.4627(10)	C9	C10	1.3896(11)
N2	C13	1.3399(10)	C10	C11	1.3963(10)
N2	C16	1.3364(11)	C11	C12	1.3993(10)
N3	C13	1.3420(10)	C11	C13	1.4850(10)
N3	C14	1.3402(11)	C14	C15	1.3800(13)
C1	C2	1.5304(10)	C15	C16	1.3876(12)
C2	C3	1.5348(10)	C17	C18	1.5238(13)
C2	C7	1.5221(10)	C18	C19	1.5261(14)
C3	C4	1.5233(11)	C19	C20	1.5285(14)
C4	C5	1.5284(11)	C20	C21	1.5262(12)
C5	C6	1.5198(12)			

Table 25: Selected bond angles [°] for **141l**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C1	N1	C17	119.50(7)	C10	C9	C8	120.53(7)
C1	N1	C21	126.89(7)	C9	C10	C11	119.87(7)
C21	N1	C17	113.30(7)	C10	C11	C12	119.40(7)
C16	N2	C13	116.50(7)	C10	C11	C13	120.52(6)
C14	N3	C13	116.07(7)	C12	C11	C13	120.00(6)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
O1	C1	N1	121.74(7)	C7	C12	C11	120.87(7)
O1	C1	C2	119.41(7)	N2	C13	N3	125.84(7)
N1	C1	C2	118.77(6)	N2	C13	C11	117.18(6)
C1	C2	C3	110.00(6)	N3	C13	C11	116.95(7)
C7	C2	C1	107.55(6)	N3	C14	C15	122.84(8)
C7	C2	C3	112.95(6)	C14	C15	C16	116.30(8)
C4	C3	C2	111.68(6)	N2	C16	C15	122.44(8)
C3	C4	C5	113.94(7)	N1	C17	C18	110.21(7)
C6	C5	C4	112.75(7)	C17	C18	C19	110.35(8)
C8	C7	C2	120.00(6)	C18	C19	C20	110.57(8)
C12	C7	C2	120.91(6)	C21	C20	C19	111.20(8)
C12	C7	C8	119.08(7)	N1	C21	C20	110.04(7)
C9	C8	C7	120.22(7)				

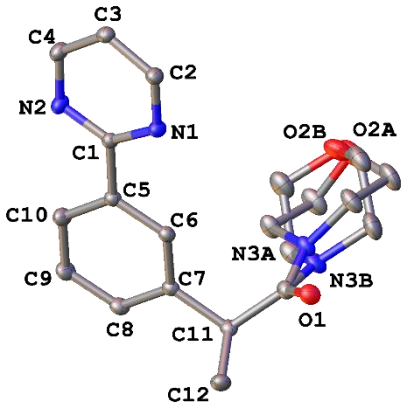


Figure 23: Molecular structure of **141n** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{17}H_{19}N_3O_2$ (*M* = 297.35 g/mol): monoclinic, space group $P2_1/n$ (no. 14), *a* = 10.0431(10) Å, *b* = 9.7828(11) Å, *c* = 15.4733(11) Å, *β* = 99.887(4)°, *V* = 1497.7(2) Å^3, *Z* = 4, *T* = 100.01 K, μ(MoKα) = 0.088 mm^{-1}, *Dcalc* = 1.319 g/cm^3, 20654 reflections measured (4.506° ≤ 2Θ ≤ 65.196°), 5448 unique (R_{int} = 0.0229, R_{sigma} = 0.0212) which were used in all calculations. The final R_1 was 0.0406 (I > 2σ(I)) and wR_2 was 0.1176 (all data).

Table 26: Crystal data and structure refinement for **141n**.

Compound	**141n**
CCDC	1865620
Identification code	mo_0090_CG_0m
Empirical formula	$C_{17}H_{19}N_3O_2$
Formula weight	297.35
Temperature/K	100.01
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	10.0431(10)
b/Å	9.7828(11)
c/Å	15.4733(11)
α/°	90
β/°	99.887(4)
γ/°	90
Volume/Å^3	1497.7(2)
Z	4
ρ_{calc}g/cm^3	1.319
μ/mm^{-1}	0.088
F(000)	632.0
Crystal size/mm^3	0.283 × 0.2 × 0.138
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.506 to 65.196
Index ranges	-15 ≤ h ≤ 15, -14 ≤ k ≤ 14, -23 ≤ l ≤ 23
Reflections collected	20654
Independent reflections	5448 [R_{int} = 0.0229, R_{sigma} = 0.0212]
Data/restraints/parameters	5448/0/255
Goodness-of-fit on F^2	1.038
Final R indexes [I>=2σ (I)]	R_1 = 0.0406, wR_2 = 0.1135
Final R indexes [all data]	R_1 = 0.0452, wR_2 = 0.1176
Largest diff. peak/hole / e Å^{-3}	0.46/-0.22

Table 27: Bond lengths [Å] for **141n**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C13	1.2275(10)	C2	C3	1.3850(10)
O2A	C15A	1.416(5)	C3	C4	1.3853(11)
O2A	C16A	1.423(5)	C5	C6	1.3979(10)
O2B	C15B	1.445(12)	C5	C10	1.3956(10)
O2B	C16B	1.416(14)	C6	C7	1.3931(10)
N1	C1	1.3396(9)	C7	C8	1.3968(10)
N1	C2	1.3404(9)	C7	C11	1.5198(10)
N2	C1	1.3408(9)	C8	C9	1.3907(11)
N2	C4	1.3355(10)	C9	C10	1.3914(11)
N3A	C13	1.375(2)	C11	C12	1.5282(11)
N3A	C14A	1.469(2)	C11	C13	1.5296(10)
N3A	C17A	1.463(2)	C14A	C15A	1.5151(17)
N3B	C13	1.348(7)	C14B	C15B	1.502(6)
N3B	C14B	1.465(7)	C16A	C17A	1.5144(18)
N3B	C17B	1.477(7)	C16B	C17B	1.504(6)
C1	C5	1.4831(10)			

Table 28: Bond angles [°] for **141n**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C15A	O2A	C16A	109.0(3)	C6	C7	C11	121.72(6)
C16B	O2B	C15B	109.9(6)	C8	C7	C11	119.39(6)
C1	N1	C2	116.51(6)	C9	C8	C7	120.35(7)
C4	N2	C1	116.43(7)	C8	C9	C10	120.49(7)
C13	N3A	C14A	124.20(17)	C9	C10	C5	119.79(7)
C13	N3A	C17A	117.43(16)	C7	C11	C12	110.30(6)
C17A	N3A	C14A	114.48(15)	C7	C11	C13	110.77(6)
C13	N3B	C14B	127.1(5)	C12	C11	C13	110.99(6)
C13	N3B	C17B	120.7(5)	O1	C13	N3A	121.07(11)
C14B	N3B	C17B	110.7(5)	O1	C13	N3B	121.3(3)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N1	C1	N2	125.59(7)	O1	C13	C11	120.96(7)
N1	C1	C5	117.24(6)	N3A	C13	C11	117.73(11)
N2	C1	C5	117.17(6)	N3B	C13	C11	115.9(3)
N1	C2	C3	122.54(7)	N3A	C14A	C15A	109.85(13)
C2	C3	C4	116.08(7)	N3B	C14B	C15B	110.2(3)
N2	C4	C3	122.82(7)	O2A	C15A	C14A	111.18(16)
C6	C5	C1	120.28(6)	O2B	C15B	C14B	111.1(6)
C10	C5	C1	120.35(7)	O2A	C16A	C17A	111.01(15)
C10	C5	C6	119.36(7)	O2B	C16B	C17B	111.8(6)
C7	C6	C5	121.13(6)	N3A	C17A	C16A	110.80(13)
C6	C7	C8	118.87(7)	N3B	C17B	C16B	109.6(4)

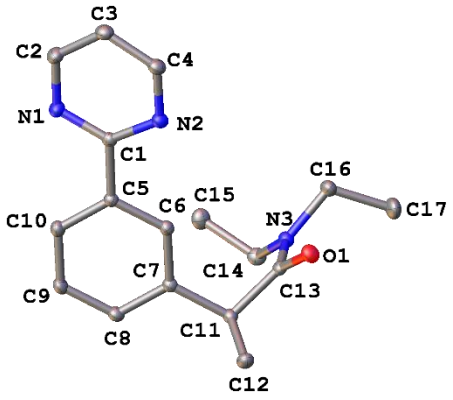


Figure 24: Molecular structure of **141q** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{17}H_{21}N_3O$ (M = 283.37 g/mol): monoclinic, space group $P2_1/n$ (no. 14), a = 10.0808(7) Å, b = 9.7488(6) Å, c = 15.9224(12) Å, β = 108.079(3)°, V = 1487.53(18) Å^3, Z = 4, T = 100.01 K, μ(MoKα) = 0.081 mm^{-1}, *Dcalc* = 1.265 g/cm^3, 18332 reflections measured (4.97° ≤ 2Θ ≤ 61.044°), 4530 unique (R_{int} = 0.0270, R_{sigma} = 0.0240) which were used in all calculations. The final R_1 was 0.0395 (I > 2σ(I)) and wR_2 was 0.1064 (all data).

Table 29: Crystal data and structure refinement for **141q**.

Compound	**141q**
CCDC	1865624
Identification code	mo_0087_CG_0m
Empirical formula	$C_{17}H_{21}N_3O$
Formula weight	283.37
Temperature/K	100.01
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	10.0808(7)
b/Å	9.7488(6)
c/Å	15.9224(12)
α/°	90
β/°	108.079(3)
γ/°	90
Volume/Å^3	1487.53(18)
Z	4
ρ_{calc}g/cm^3	1.265
μ/mm^{-1}	0.081
F(000)	608.0
Crystal size/mm^3	0.54 × 0.516 × 0.182
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.97 to 61.044
Index ranges	-14 ≤ h ≤ 12, -13 ≤ k ≤ 13, -22 ≤ l ≤ 22
Reflections collected	18332
Independent reflections	4530 [R_{int} = 0.0270, R_{sigma} = 0.0240]
Data/restraints/parameters	4530/0/193
Goodness-of-fit on F^2	1.053
Final R indexes [I>=2σ (I)]	R_1 = 0.0395, wR_2 = 0.1026
Final R indexes [all data]	R_1 = 0.0432, wR_2 = 0.1064
Largest diff. peak/hole / e Å^{-3}	0.44/-0.29

Table 30: Bond lengths [Å] for **141q**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C13	1.2356(10)	C5	C6	1.3983(11)
N1	C1	1.3419(10)	C5	C10	1.3982(11)
N1	C2	1.3397(11)	C6	C7	1.3955(11)
N2	C1	1.3431(10)	C7	C8	1.3948(11)
N2	C4	1.3389(11)	C7	C11	1.5238(11)
N3	C13	1.3527(11)	C8	C9	1.3923(11)
N3	C14	1.4674(11)	C9	C10	1.3901(12)
N3	C16	1.4708(11)	C11	C12	1.5323(12)
C1	C5	1.4836(11)	C11	C13	1.5302(11)
C2	C3	1.3851(12)	C14	C15	1.5207(12)
C3	C4	1.3869(12)	C16	C17	1.5198(13)

Table 31: Bond angles [°] for **141q**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C2	N1	C1	116.25(7)	C6	C7	C11	121.59(7)
C4	N2	C1	116.39(7)	C8	C7	C6	118.79(7)
C13	N3	C14	125.90(7)	C8	C7	C11	119.62(7)
C13	N3	C16	118.00(7)	C9	C8	C7	120.46(7)
C14	N3	C16	116.03(7)	C10	C9	C8	120.60(7)
N1	C1	N2	125.83(7)	C9	C10	C5	119.56(7)
N1	C1	C5	116.91(7)	C7	C11	C12	110.89(7)
N2	C1	C5	117.26(7)	C7	C11	C13	109.21(6)
N1	C2	C3	122.64(8)	C13	C11	C12	111.01(7)
C2	C3	C4	116.37(8)	O1	C13	N3	121.27(8)
N2	C4	C3	122.47(8)	O1	C13	C11	119.69(7)
C6	C5	C1	119.88(7)	N3	C13	C11	118.87(7)
C10	C5	C1	120.60(7)	N3	C14	C15	113.59(7)
C10	C5	C6	119.52(7)	N3	C16	C17	112.62(7)
C7	C6	C5	121.05(7)				

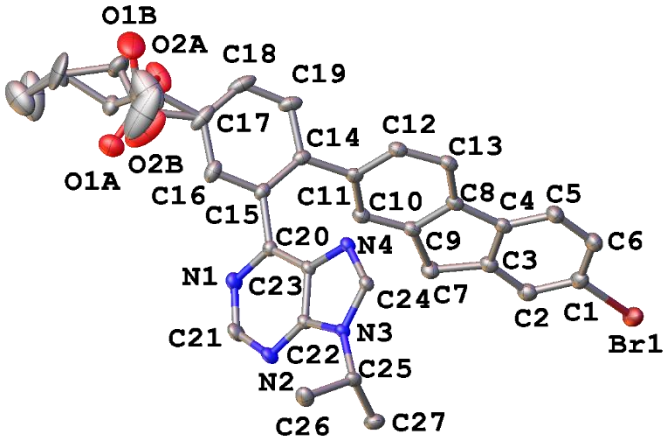


Figure 25: Molecular structure of **166f** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{34}H_{33}BrN_4O_2$ (*M* = 609.55 g/mol): triclinic, space group P-1 (no. 2), *a* = 8.4938(10) Å, *b* = 10.8107(10) Å, *c* = 16.6719(19) Å, *α* = 104.927(3)°, *β* = 95.326(4)°, *γ* = 99.344(4)°, *V* = 1445.0(3) Å^3, *Z* = 2, *T* = 99.98 K, μ(MoKα) = 1.461 mm^{-1}, *Dcalc* = 1.401 g/cm^3, 47834 reflections measured (4.91° ≤ 2Θ ≤ 61.12°), 8840 unique (R_{int} = 0.0269, R_{sigma} = 0.0227) which were used in all calculations. The final R_1 was 0.0380 (I > 2σ(I)) and wR_2 was 0.0989 (all data).

Table 32: Crystal data and structure refinement for **166f**.

Compound	**166f**
CCDC	1865621
Identification code	mo_0133_CG_0m
Empirical formula	$C_{34}H_{33}BrN_4O_2$
Formula weight	609.55
Temperature/K	99.98
Crystal system	triclinic
Space group	P-1
a/Å	8.4938(10)
b/Å	10.8107(10)
c/Å	16.6719(19)
α/°	104.927(3)

β/°	95.326(4)
γ/°	99.344(4)
Volume/Å^3	1445.0(3)
Z	2
ρ_{calc}g/cm^3	1.401
μ/mm^{-1}	1.461
F(000)	632.0
Crystal size/mm^3	0.518 × 0.179 × 0.08
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.91 to 61.12
Index ranges	-12 ≤ h ≤ 12, -15 ≤ k ≤ 15, -23 ≤ l ≤ 23
Reflections collected	47834
Independent reflections	8840 [R_{int} = 0.0269, R_{sigma} = 0.0227]
Data/restraints/parameters	8840/12/439
Goodness-of-fit on F^2	1.028
Final R indexes [I>=2σ (I)]	R_1 = 0.0380, wR_2 = 0.0968
Final R indexes [all data]	R_1 = 0.0417, wR_2 = 0.0989
Largest diff. peak/hole / e Å^{-3}	1.48/-0.69

Table 33: Bond lengths [Å] for **166f**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Br1	C1	1.8987(17)	C9	C10	1.389(2)
O1A	C29A	1.205(5)	C10	C11	1.399(2)
O1B	C29B	1.158(10)	C11	C12	1.406(2)
O2A	C29A	1.323(5)	C11	C14	1.481(2)
O2A	C30A	1.430(9)	C12	C13	1.386(2)
O2B	C29B	1.340(12)	C14	C15	1.402(2)
O2B	C30B	1.482(16)	C14	C19	1.404(2)
N1	C20	1.3455(18)	C15	C16	1.398(2)
N1	C21	1.345(2)	C15	C20	1.486(2)
N2	C21	1.336(2)	C16	C17	1.399(3)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N2	C22	1.3367(17)	C17	C18	1.381(3)
N3	C22	1.3702(17)	C17	C28A	1.484(3)
N3	C24	1.3710(17)	C17	C28B	1.672(5)
N3	C25	1.4744(18)	C18	C19	1.383(3)
N4	C23	1.3870(17)	C20	C23	1.3936(19)
N4	C24	1.3135(18)	C22	C23	1.4075(19)
C1	C2	1.390(2)	C25	C26	1.519(2)
C1	C6	1.393(3)	C25	C27	1.519(2)
C2	C3	1.393(2)	C28A	C29A	1.511(6)
C3	C4	1.403(2)	C28A	C31A	1.518(4)
C3	C7	1.508(2)	C28B	C29B	1.562(12)
C4	C5	1.389(2)	C28B	C31B	1.541(7)
C4	C8	1.470(2)	C31A	C32A	1.608(9)
C5	C6	1.389(2)	C31B	C32B	1.471(12)
C7	C9	1.513(2)	C32A	C33	1.455(10)
C8	C9	1.404(2)	C32B	C33	1.503(8)
C8	C13	1.388(2)	C33	C34	1.519(4)

Table 34: Bond angles [°] for **166f**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C29A	O2A	C30A	116.2(4)	C16	C17	C28A	127.1(2)
C29B	O2B	C30B	111.8(10)	C16	C17	C28B	106.4(3)
C21	N1	C20	118.61(13)	C18	C17	C16	118.68(16)
C21	N2	C22	111.67(13)	C18	C17	C28A	114.3(2)
C22	N3	C24	105.33(11)	C18	C17	C28B	134.6(3)
C22	N3	C25	128.54(11)	C17	C18	C19	120.60(16)
C24	N3	C25	125.95(12)	C18	C19	C14	121.59(17)
C24	N4	C23	103.60(11)	N1	C20	C15	117.32(13)
C2	C1	Br1	119.06(13)	N1	C20	C23	118.64(13)
C2	C1	C6	122.32(16)	C23	C20	C15	123.59(12)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C6	C1	Br1	118.62(13)	N2	C21	N1	128.40(14)
C1	C2	C3	117.71(15)	N2	C22	N3	127.91(13)
C2	C3	C4	120.18(15)	N2	C22	C23	125.94(13)
C2	C3	C7	129.15(14)	N3	C22	C23	106.08(11)
C4	C3	C7	110.67(14)	N4	C23	C20	132.92(13)
C3	C4	C8	108.08(13)	N4	C23	C22	110.08(12)
C5	C4	C3	121.42(15)	C20	C23	C22	116.64(12)
C5	C4	C8	130.49(15)	N4	C24	N3	114.91(12)
C4	C5	C6	118.55(16)	N3	C25	C26	110.44(12)
C5	C6	C1	119.82(16)	N3	C25	C27	111.12(12)
C3	C7	C9	102.45(13)	C26	C25	C27	112.39(13)
C9	C8	C4	108.69(13)	C17	C28A	C29A	107.6(3)
C13	C8	C4	129.92(14)	C17	C28A	C31A	110.0(2)
C13	C8	C9	121.39(14)	C29A	C28A	C31A	111.4(3)
C8	C9	C7	110.09(14)	C29B	C28B	C17	105.5(5)
C10	C9	C7	129.85(14)	C31B	C28B	C17	106.7(4)
C10	C9	C8	120.05(14)	C31B	C28B	C29B	105.6(6)
C9	C10	C11	119.26(14)	O1A	C29A	O2A	123.0(4)
C10	C11	C12	119.62(14)	O1A	C29A	C28A	125.3(4)
C10	C11	C14	122.39(14)	O2A	C29A	C28A	111.6(4)
C12	C11	C14	117.96(13)	O1B	C29B	O2B	124.3(10)
C13	C12	C11	121.52(14)	O1B	C29B	C28B	129.0(10)
C12	C13	C8	118.14(14)	O2B	C29B	C28B	106.7(7)
C15	C14	C11	123.91(13)	C28A	C31A	C32A	113.2(4)
C15	C14	C19	118.03(15)	C32B	C31B	C28B	102.1(6)
C19	C14	C11	118.06(14)	C33	C32A	C31A	104.5(6)
C14	C15	C20	124.28(13)	C31B	C32B	C33	136.5(8)
C16	C15	C14	119.77(14)	C32A	C33	C34	113.8(5)
C16	C15	C20	115.83(14)	C32B	C33	C34	114.2(5)
C15	C16	C17	121.27(17)				

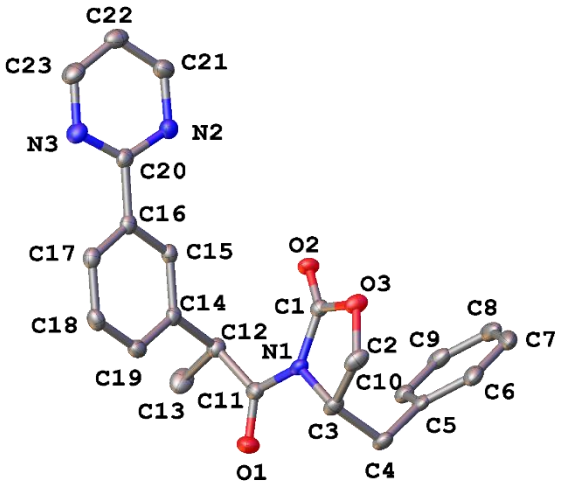


Figure 26: Molecular structure of **141rA** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{23}H_{21}N_3O_3$ (*M* = 387.43 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 6.2748(5) Å, *b* = 13.1370(11) Å, *c* = 24.081(2) Å, *V* = 1985.1(3) Å^3, *Z* = 4, *T* = 101.23 K, μ(CuKα) = 0.708 mm^{-1}, *Dcalc* = 1.296 g/cm^3, 16924 reflections measured (7.342° ≤ 2Θ ≤ 149.108°), 4024 unique (R_{int} = 0.0197, R_{sigma} = 0.0181) which were used in all calculations. The final R_1 was 0.0259 (I > 2σ(I)) and wR_2 was 0.0659 (all data).

Table 35: Crystal data and structure refinement for **141rA**.

Compound	**141rA**
CCDC	1865622
Identification code	cu_0123_CG_0m
Empirical formula	$C_{23}H_{21}N_3O_3$
Formula weight	387.43
Temperature/K	101.23
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	6.2748(5)
b/Å	13.1370(11)
c/Å	24.081(2)
α/°	90

β/°	90
γ/°	90
Volume/Å^3	1985.1(3)
Z	4
ρ_{calc}g/cm^3	1.296
μ/mm^{-1}	0.708
F(000)	816.0
Crystal size/mm^3	0.49 × 0.21 × 0.092
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	7.342 to 149.108
Index ranges	-7 ≤ h ≤ 7, -13 ≤ k ≤ 16, -30 ≤ l ≤ 29
Reflections collected	16924
Independent reflections	4024 [R_{int} = 0.0197, R_{sigma} = 0.0181]
Data/restraints/parameters	4024/0/263
Goodness-of-fit on F^2	1.077
Final R indexes [I>=2σ (I)]	R_1 = 0.0259, wR_2 = 0.0658
Final R indexes [all data]	R_1 = 0.0260, wR_2 = 0.0659
Largest diff. peak/hole / e Å^{-3}	0.14/-0.18
Flack parameter	0.03(3)

Table 36: Bond lengths [Å] for **141rA**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C11	1.2140(18)	C6	C7	1.389(2)
O2	C1	1.1994(17)	C7	C8	1.385(3)
O3	C1	1.3474(16)	C8	C9	1.387(2)
O3	C2	1.4597(18)	C9	C10	1.394(2)
N1	C1	1.3927(17)	C11	C12	1.516(2)
N1	C3	1.4654(18)	C12	C13	1.530(2)
N1	C11	1.3999(18)	C12	C14	1.5263(18)
N2	C20	1.3424(19)	C14	C15	1.390(2)
N2	C21	1.339(2)	C14	C19	1.393(2)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N3	C20	1.3420(18)	C15	C16	1.3984(19)
N3	C23	1.335(2)	C16	C17	1.397(2)
C2	C3	1.517(2)	C16	C20	1.484(2)
C3	C4	1.5420(18)	C17	C18	1.388(2)
C4	C5	1.509(2)	C18	C19	1.390(2)
C5	C6	1.397(2)	C21	C22	1.381(2)
C5	C10	1.398(2)	C22	C23	1.384(2)

Table 37: Bond angles [°] for **141rA**.

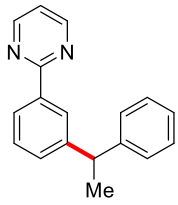
Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C1	O3	C2	109.68(11)	O1	C11	N1	118.31(13)
C1	N1	C3	110.80(11)	O1	C11	C12	123.74(13)
C1	N1	C11	128.92(12)	N1	C11	C12	117.87(12)
C11	N1	C3	120.23(11)	C11	C12	C13	110.38(12)
C21	N2	C20	116.29(13)	C11	C12	C14	109.18(11)
C23	N3	C20	116.49(13)	C14	C12	C13	111.37(11)
O2	C1	O3	122.29(13)	C15	C14	C12	120.41(12)
O2	C1	N1	129.25(13)	C15	C14	C19	119.20(12)
O3	C1	N1	108.45(11)	C19	C14	C12	120.34(13)
O3	C2	C3	104.65(11)	C14	C15	C16	120.93(13)
N1	C3	C2	99.96(11)	C15	C16	C20	119.57(13)
N1	C3	C4	112.47(11)	C17	C16	C15	119.20(13)
C2	C3	C4	114.86(12)	C17	C16	C20	121.23(13)
C5	C4	C3	114.11(11)	C18	C17	C16	120.01(13)
C6	C5	C4	121.66(14)	C17	C18	C19	120.30(13)
C6	C5	C10	117.99(14)	C18	C19	C14	120.36(13)
C10	C5	C4	120.35(13)	N2	C20	C16	117.40(12)
C7	C6	C5	120.85(15)	N3	C20	N2	125.43(13)
C8	C7	C6	120.45(14)	N3	C20	C16	117.16(13)
C7	C8	C9	119.67(15)	N2	C21	C22	122.92(15)

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C8	C9	C10	119.81(16)	C21	C22	C23	115.97(15)
C9	C10	C5	121.22(14)	N3	C23	C22	122.89(14)

5.3.4 Late-Stage Diversification by Selectivity Switch in meta-C–H Activation

5.3.4.1 Characterization Data for 143 and 183

2-[3-(1-Phenylethyl)phenyl]pyrimidine (143a)



The general procedure **I** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol) and (1-chloroethyl)benzene (**142a**, 211 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) followed by recycling preparative HPLC yielded **143a** (88.6 mg, 68%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.76 (d, *J* = 4.9 Hz, 2H), 8.38 (dd, *J* = 1.8, 1.8 Hz, 1H), 8.28 (ddd, *J* = 7.6, 1.8, 1.3 Hz, 1H), 7.40 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.33–7.29 (m, 1H), 7.29–7.24 (m, 4H), 7.20–7.14 (m, 1H), 7.11 (t, *J* = 4.9 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 1H), 1.71 (d, *J* = 7.2 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.7 (C_q), 157.0 (CH), 146.6 (C_q), 146.1 (C_q), 137.5 (C_q), 130.1 (CH), 128.6 (CH), 128.3 (CH), 127.5 (CH), 127.3 (CH), 126.0 (CH), 125.9 (CH), 118.9 (CH), 44.9 (CH), 21.9 (CH_3).

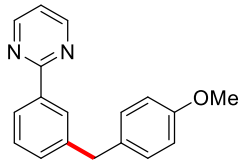
IR (ATR): $\tilde{\nu}$ = 3027, 2966, 1567, 1553, 1422, 1407, 794, 765, 698 cm^{-1}.

m.p.: 78–79 °C.

MS (EI) *m/z* (relative intensity): 260 (42) $[M]^+$, 259 (14) $[M–H]^+$, 245 (100) $[M–Me]^+$, 190 (6), 165 (18), 122 (7).

HR-MS (EI): *m/z* calcd for $C_{18}H_{16}N_2^+$ $[M]^+$ 260.1308, found 260.1321.

2-[3-(4-Methoxybenzyl)phenyl]pyrimidine (143b)



The general procedure **I** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **143b** (82.2 mg, 59%) as a white soild.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.79 (d, J = 4.8 Hz, 2H), 8.32 (ddd, J = 1.8, 1.7, 0.6 Hz, 1H), 8.28 (ddd, J = 7.7, 1.7, 1.5 Hz, 1H), 7.41 (dd, J = 7.7, 7.6 Hz, 1H), 7.31–7.28 (m, 1H), 7.17 (t, J = 4.8 Hz, 1H), 7.16 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 4.03 (s, 2H), 3.78 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.7 (C_q), 157.9 (C_q), 157.0 (CH), 141.9 (C_q), 137.6 (C_q), 133.1 (C_q), 131.3 (CH), 129.8 (CH), 128.7 (CH), 128.5 (CH), 125.9 (CH), 118.9 (CH), 113.9 (CH), 55.3 (CH_3), 41.1 (CH_2).

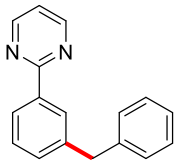
IR (ATR): $\tilde{\nu}$ = 3033, 2908, 1567, 1555, 1509, 1407, 1242, 1033, 786, 696 cm^{-1}.

m.p.: 90–92 °C.

MS (EI) m/z (relative intensity): 276 (100) $[M]^+$, 275 (53) $[M–H]^+$, 261 (39) $[M–Me]^+$, 245 (12) $[M–OMe]^+$, 231 (8), 121 (12).

HR-MS (EI): m/z calcd for $C_{18}H_{16}N_2O^+$ $[M]^+$ 276.1257, found 276.1264.

2-(3-Benzylphenyl)pyrimidine (143c)



The general procedure **I** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol) and benzyl chloride (**142c**, 190 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **143c** (63.7 mg, 52%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.79 (d, J = 4.9 Hz, 2H), 8.36–8.34 (m, 1H), 8.31 (ddd, J = 7.8, 1.8, 1.3 Hz, 1H), 7.43 (ddd, J = 7.8, 7.7, 0.6 Hz, 1H), 7.34–7.20 (m, 6H), 7.16 (t, J = 4.9 Hz, 1H), 4.10 (s, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.6 (C_q), 157.0 (CH), 141.4 (C_q), 140.9 (C_q), 137.7 (C_q), 131.4 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.4 (CH), 126.0 (CH), 118.9 (CH), 42.0 (CH_2).

IR (ATR): $\tilde{\nu}$ = 3024, 2918, 1566, 1553, 1425, 1408, 778, 759, 701, 635 cm^{-1}.

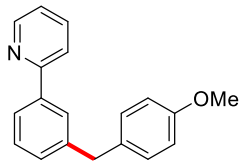
m.p.: 76–78 °C.

MS (EI) m/z (relative intensity): 246 (98) $[M]^+$, 245 (100) $[M–H]^+$, 190 (8), 165 (24), 152 (5), 122 (7), 91 (8) $[Bn]^+$, 43 (19).

HR-MS (EI): m/z calcd for $C_{17}H_{14}N_2^+$ $[M]^+$ 246.1151, found 246.1149.

The spectral data are in accordance with those reported in the literature.[69]

2-[3-(4-Methoxybenzyl)phenyl]pyridine (143d)



The general procedure **I** was followed using 2-phenylpyridine (**68b**, 77.6 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **143d** (75.4 mg, 55%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.69 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H), 7.86 (ddd, *J* = 1.7, 1.5, 0.6 Hz, 1H), 7.81 (ddd, *J* = 7.8, 1.7, 1.2 Hz, 1H), 7.76–7.67 (m, 2H), 7.39 (ddd, *J* = 7.8, 7.7, 0.6 Hz, 1H), 7.25–7.19 (m, 2H), 7.15 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.03 (s, 2H), 3.78 (s, 3H).

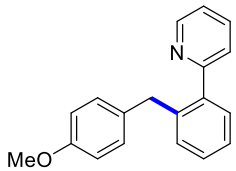
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 157.9 (C_q), 157.4 (C_q), 149.5 (CH), 142.0 (C_q), 139.5 (C_q), 136.5 (CH), 133.0 (C_q), 129.8 (CH), 129.4 (CH), 128.8 (CH), 127.4 (CH), 124.6 (CH), 121.9 (CH), 120.6 (CH), 113.8 (CH), 55.3 (CH_3), 41.1 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2906, 2834, 1583, 1509, 1461, 1242, 1033, 811, 774, 696 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 275 (100) $[M]^+$, 274 (94) $[M–H]^+$, 260 (45) $[M–Me]^+$, 230 (12), 121 (12), 78 (11), 51 (6).

HR-MS (EI): *m*/*z* calcd for $C_{19}H_{17}NO^+$ $[M]^+$ 275.1305, found 275.1312.

2-[2-(4-Methoxybenzyl)phenyl]pyridine (183)



2-Phenylpyridine (**68b**, 233 mg, 1.50 mmol), $[Ru(OAc)_2(p\text{-cymene})]$ (**181**, 17.7 mg, 50.0 µmol, 10.0 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. 4-Methoxybenzyl chloride (**142b**, 78.3 mg, 0.50 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 100 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 8:1) yielded monobenzylated product **183** (26.4 mg, 19%) as a colorless oil and dibenzylated product **183'** (71.2 mg, 72%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.67 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.64 (ddd, *J* = 7.5, 1.8 Hz, 1H), 7.39–7.18 (m, 6H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.71 (d, *J* = 8.8 Hz, 2H), 4.05 (s, 2H), 3.73 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 159.8 (C_q), 157.5 (C_q), 149.0 (CH), 140.5 (C_q), 139.1 (C_q), 136.0 (CH), 133.3 (C_q), 130.4 (CH), 129.7 (CH), 129.7 (CH), 128.3 (CH), 126.1 (CH), 124.1 (CH), 121.6 (CH), 113.5 (CH), 55.2 (CH_3), 37.9 (CH_2).

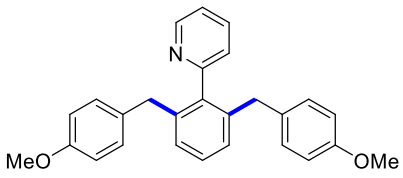
IR (ATR): $\tilde{\nu}$ = 3003, 2907, 2834, 1585, 1510, 1468, 1245, 1176, 1036, 753 cm^{-1}.

MS (EI) *m/z* (relative intensity): 275 (75) $[M]^+$, 274 (100) $[M–H]^+$, 260 (30) $[M–Me]^+$, 230 (18), 167 (45).

HR-MS (ESI): *m/z* calcd for $C_{19}H_{18}NO^+$ $[M+H]^+$ 276.1383, found 276.1384.

The spectral data are in accordance with those reported in the literature.[35]

2-[2,6-Bis(4-methoxybenzyl)phenyl]pyridine (183')



^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.69 (ddd, *J* = 4.9, 1.8, 1.1 Hz, 1H), 7.54 (ddd, *J* = 7.8, 7.7, 1.8 Hz, 1H), 7.25 (t, *J* = 7.7 Hz, 1H), 7.20 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 7.09 (d, *J* = 7.7 Hz, 2H), 6.92 (ddd, *J* = 7.8, 1.2, 1.1 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 4H), 6.73 (d, *J* = 8.7 Hz, 4H), 3.75 (s, 6H), 3.72 (d_{AB}, *J* = 15.6 Hz, 2H), 3.65 (d_{AB}, *J* = 15.6 Hz, 2H).

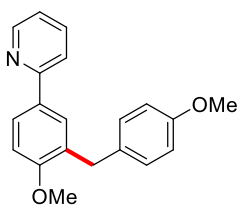
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.8 (C_q), 157.5 (C_q), 149.2 (CH), 140.2 (C_q), 139.4 (C_q), 135.5 (CH), 132.9 (C_q), 129.6 (CH), 128.0 (CH), 127.8 (CH), 125.2 (CH), 121.6 (CH), 113.4 (CH), 55.2 (CH_3), 38.5 (CH_2).

IR (ATR): $\tilde{\nu}$ = 3002, 2906, 2834, 1610, 1508, 1241, 1175, 1033, 789, 750 cm^{-1}.

MS (EI) *m/z* (relative intensity): 395 (94) $[M]^+$, 394 (100) $[M–H]^+$, 380 (12) $[M–Me]^+$, 286 (29), 272 (25), 242 (9), 121 (9).

HR-MS (ESI): *m/z* calcd for $C_{27}H_{26}NO_2^+$ $[M+H]^+$ 396.1958, found 396.1962.

2-[4-Methoxy-3-(4-methoxybenzyl)phenyl]pyridine (143e)



The general procedure **I** was followed using 2-(4-methoxyphenyl)pyridine (**68a**, 92.6 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 6:1) yielded **143e** (94.9 mg, 62%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.64 (ddd, *J* = 4.9, 1.9, 1.1 Hz, 1H), 7.86 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.78 (d, *J* = 2.3 Hz, 1H), 7.67 (ddd, *J* = 8.0, 7.3, 1.9 Hz, 1H), 7.61 (ddd, *J* = 8.0, 1.2, 1.1 Hz, 1H), 7.18 (d, *J* = 8.5 Hz, 2H), 7.14 (ddd, *J* = 7.3, 4.9, 1.2 Hz, 1H), 6.96 (d, *J* = 8.6 Hz, 1H), 6.82 (d, *J* = 8.5 Hz, 2H), 4.00 (s, 2H), 3.87 (s, 3H), 3.77 (s, 3H).

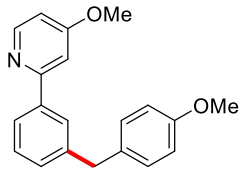
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 158.3 (C_q), 157.7 (C_q), 157.3 (C_q), 149.5 (CH), 136.5 (CH), 133.0 (C_q), 131.7 (C_q), 130.3 (C_q), 129.7 (CH), 128.9 (CH), 126.1 (CH), 121.3 (CH), 119.8 (CH), 113.6 (CH), 110.6 (CH), 55.5 (CH_3), 55.2 (CH_3), 35.2 (CH_2).

IR (ATR): $\tilde{\nu}$ = 3003, 2931, 2834, 1607, 1584, 1507, 1463, 1240, 1026, 779 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 306 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{20}H_{20}NO_2^+$ $[M+H]^+$ 306.1489, found 306.1494.

4-Methoxy-2-[3-(4-methoxybenzyl)phenyl]pyridine (143f)



The general procedure **I** was followed using 4-methoxy-2-phenylpyridine (**68c**, 92.6 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 7:3) yielded **143f** (99.5 mg, 65%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.51 (dd, *J* = 5.8, 0.5 Hz, 1H), 7.84–7.82 (m, 1H), 7.77 (ddt, *J* = 7.8, 1.8, 0.9 Hz, 1H), 7.38 (ddd, *J* = 7.8, 7.7, 0.6 Hz, 1H), 7.23–7.19 (m, 1H), 7.20 (dd, *J* = 2.5, 0.5 Hz, 1H), 7.14 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.77 (dd, *J* = 5.8, 2.5 Hz, 1H), 4.01 (s, 2H), 3.90 (s, 3H), 3.78 (s, 3H).

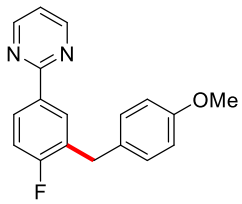
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 166.3 (C_q), 159.1 (C_q), 157.9 (C_q), 150.7 (CH), 141.9 (C_q), 139.4 (C_q), 133.0 (C_q), 129.8 (CH), 129.5 (CH), 128.7 (CH), 127.5 (CH), 124.6 (CH), 113.8 (CH), 108.0 (CH), 107.0 (CH), 55.3 (CH_3), 55.2 (CH_3), 41.1 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2936, 2835, 1590, 1563, 1509, 1243, 1175, 1032, 794, 699 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 305 (64) $[M]^+$, 304 (100) $[M–H]^+$, 290 (25) $[M–Me]^+$, 260 (6) $[M–Me–OMe]^+$, 121 (8), 43 (9).

HR-MS (EI): *m*/*z* calcd for $C_{20}H_{19}NO_2^+$ $[M]^+$ 305.1410, found 305.1408.

2-[4-Fluoro-3-(4-methoxybenzyl)phenyl]pyrimidine (143g)



The general procedure **I** was followed using 2-(4-fluorophenyl)pyrimidine (**139c**, 87.1 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 6:1) yielded **143g** (74.6 mg, 51%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.75 (d, J = 4.8 Hz, 2H), 8.36–8.27 (m, 2H), 7.20 (d, J = 8.7 Hz, 2H), 7.14 (dd, J = 9.6, 8.5 Hz, 1H), 7.14 (t, J = 4.8 Hz, 1H), 6.83 (d, J = 8.7 Hz, 2H), 4.03 (s, 2H), 3.77 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 163.8 (C_q), 162.8 (d, $^{1}J_{C–F}$ = 248 Hz, C_q), 157.9 (C_q), 157.0 (CH), 133.6 (d, $^{4}J_{C–F}$ = 3 Hz, C_q), 131.8 (C_q), 131.1 (d, $^{3}J_{C–F}$ = 6 Hz, CH), 129.5 (CH), 128.6 (d, $^{2}J_{C–F}$ = 16 Hz, C_q), 128.1 (d, $^{3}J_{C–F}$ = 9 Hz, CH), 118.8 (CH), 115.6 (d, $^{2}J_{C–F}$ = 23 Hz, CH), 113.9 (CH), 55.2 (CH_3), 34.3 (d, $^{3}J_{C–F}$ = 3 Hz, CH_2).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = (–114.8)–(–115.0) (m).

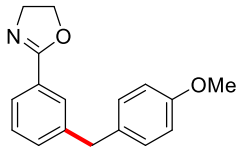
IR (ATR): $\tilde{\nu}$ = 3010, 2936, 1556, 1514, 1494, 1415, 1240, 1028, 796, 568 cm^{-1}.

m.p.: 89–90 °C.

MS (EI) *m*/*z* (relative intensity): 294 (100) $[M]^+$, 293 (55) $[M–H]^+$, 279 (24) $[M–Me]^+$, 263 (11) $[M–OMe]^+$, 121 (13), 91 (4) $[Bn]^+$, 77 (4), 43 (6).

HR-MS (EI): *m*/*z* calcd for $C_{18}H_{15}FN_2O^+$ $[M]^+$ 294.1163, found 294.1167.

2-[3-(4-Methoxybenzyl)phenyl]-4,5-dihydrooxazole (143h)



The general procedure **I** was followed using 2-phenyl-4,5-dihydrooxazole (**139h**, 73.6 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 7:3) yielded **143h** (80.7 mg, 60%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.83–7.80 (m, 1H), 7.77 (ddd, J = 7.2, 1.7, 1.7 Hz, 1H), 7.35–7.27 (m, 2H), 7.10 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 4.41 (td, J = 9.4, 0.8 Hz, 2H), 4.04 (td, J = 9.4, 0.8 Hz, 2H), 3.94 (s, 2H), 3.77 (s, 3H).

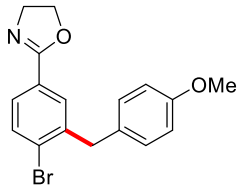
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.6 (C_q), 157.9 (C_q), 141.7 (C_q), 132.7 (C_q), 131.7 (CH), 129.7 (CH), 128.5 (CH), 128.4 (CH), 127.8 (C_q), 125.8 (CH), 113.9 (CH), 67.5 (CH_2), 55.3 (CH_3), 54.9 (CH_2), 40.9 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2904, 2835, 1647, 1509, 1242, 1176, 1033, 952, 801, 707 cm^{-1}.

MS (EI) *m/z* (relative intensity): 267 (100) $[M]^+$, 266 (34) $[M–H]^+$, 252 (16) $[M–Me]^+$, 236 (16) $[M–OMe]^+$, 223 (10), 208 (10), 165 (15), 152 (14), 121 (25), 105 (17), 89 (6), 77 (7).

HR-MS (EI): *m/z* calcd for $C_{17}H_{17}NO_2^+$ $[M]^+$ 267.1254, found 267.1262.

2-[4-Bromo-3-(4-methoxybenzyl)phenyl]-4,5-dihydrooxazole (143i)



The general procedure **I** was followed using 2-(4-bromophenyl)-4,5-dihydrooxazole (**139j**, 113 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 7:3) yielded **143i** (87.2 mg, 50%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.78 (dd, *J* = 2.0, 0.5 Hz, 1H), 7.64 ($d_{AB}d$, *J* = 8.3, 2.0 Hz, 1H), 7.60 ($d_{AB}d$, *J* = 8.3, 0.5 Hz, 1H), 7.12 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 4.40 (td, *J* = 9.5, 0.8 Hz, 2H), 4.08 (s, 2H), 4.02 (td, *J* = 9.5, 0.8 Hz, 2H), 3.78 (s, 3H).

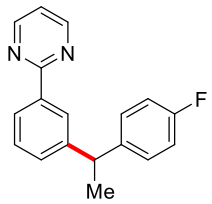
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 163.8 (C_q), 158.0 (C_q), 140.9 (C_q), 132.9 (CH), 131.0 (C_q), 130.5 (CH), 129.7 (CH), 128.1 (C_q), 127.3 (CH), 127.1 (C_q), 113.9 (CH), 67.7 (CH_2), 55.2 (CH_3), 55.0 (CH_2), 40.9 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2903, 1648, 1509, 1243, 1176, 1074, 1023, 811, 722 cm^{-1}.

MS (EI) *m/z* (relative intensity): 347 (98) $[M(^{81}Br)]^+$, 345 (100) $[M(^{79}Br)]^+$, 316 (16), 266 (40) $[M–Br]^+$, 223 (22), 195 (18), 152 (26), 121 (39).

HR-MS (EI): *m/z* calcd for $C_{17}H_{16}{}^{79}BrNO_2^+$ $[M]^+$ 345.0359, found 345.0354.

2-{3-[1-(4-Fluorophenyl)ethyl]phenyl}pyrimidine (143j)



The general procedure **I** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol) and 1-(1-chloroethyl)-4-fluorobenzene (**142d**, 238 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **143j** (113 mg, 81%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 4.9 Hz, 2H), 8.34 (ddt, *J* = 1.9, 1.5, 0.6 Hz, 1H), 8.28 (dddd, *J* = 7.7, 1.5, 1.2, 0.3 Hz, 1H), 7.42 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.30 (dddd, *J* = 7.7, 1.9, 1.2, 0.6 Hz, 1H), 7.25–7.20 (m, 2H), 7.18 (t, *J* = 4.9 Hz, 1H), 6.97 (dd, *J* = 8.7, 8.7 Hz, 2H), 4.26 (q, *J* = 7.3 Hz, 1H), 1.70 (d, *J* = 7.3 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.7 (C_q), 161.2 (d, $^1J_{C-F}$ = 244 Hz, C_q), 157.1 (CH), 146.5 (C_q), 141.8 (d, $^4J_{C-F}$ = 3 Hz, C_q), 137.7 (C_q), 130.0 (CH), 128.9 (d, $^3J_{C-F}$ = 8 Hz, CH), 128.7 (CH), 127.2 (CH), 126.1 (CH), 119.0 (CH), 115.0 (d, $^2J_{C-F}$ = 21 Hz, CH), 44.2 (CH), 22.1 (CH_3).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = –117.5 (tt, *J* = 8.7, 5.4 Hz).

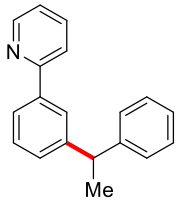
IR (ATR): $\tilde{\nu}$ = 2961, 1567, 1554, 1505, 1406, 1219, 1158, 835, 782, 690 cm^{-1}.

m.p.: 88–90 °C.

MS (EI) *m/z* (relative intensity): 278 (38) $[M]^+$, 263 (100) $[M–Me]^+$, 243 (11), 208 (7), 183 (17).

HR-MS (EI): *m/z* calcd for $C_{18}H_{15}FN_2^+$ $[M]^+$ 278.1214, found 278.1211.

2-[3-(1-Phenylethyl)phenyl]pyridine (143k)



The general procedure **I** was followed using 2-phenylpyridine (**68b**, 77.6 mg, 0.50 mmol) and (1-chloroethyl)benzene (**142a**, 211 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) followed by recycling preparative HPLC yielded **143k** (96.2 mg, 74%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.67 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H), 7.89 (dd, *J* = 1.9, 1.9 Hz, 1H), 7.78 (ddd, *J* = 7.7, 1.9, 1.2 Hz, 1H), 7.75–7.65 (m, 2H), 7.38 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.32–7.13 (m, 7H), 4.25 (q, *J* = 7.2 Hz, 1H), 1.70 (d, *J* = 7.2 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 157.5 (C_q), 149.5 (CH), 146.8 (C_q), 146.1 (C_q), 139.4 (C_q), 136.5 (CH), 128.7 (CH), 128.3 (CH), 128.2 (CH), 127.6 (CH), 126.3 (CH), 126.0 (CH), 124.7 (CH), 121.9 (CH), 120.6 (CH), 44.9 (CH), 22.0 (CH_3).

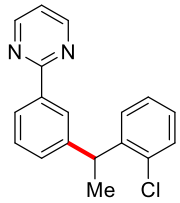
IR (ATR): $\tilde{\nu}$ = 2966, 1583, 1565, 1433, 1414, 761, 696, 614 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 259 (63) $[M]^+$, 258 (100) $[M–H]^+$, 244 (90) $[M–Me]^+$, 165 (20), 78 (12), 51 (9).

HR-MS (ESI): *m*/*z* calcd for $C_{19}H_{18}N^+$ $[M+H]^+$ 260.1434, found 260.1435.

The spectral data are in accordance with those reported in the literature.[68-69]

2-{3-[1-(2-Chlorophenyl)ethyl]phenyl}pyrimidine (143l)



The general procedure **I** was followed using 2-phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol) and 1-chloro-2-(1-chloroethyl)benzene (**142e**, 263 mg, 1.50 mmol) at 80 °C. After 20 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **143l** (76.3 mg, 52%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 4.8 Hz, 2H), 8.39 (ddd, *J* = 1.9, 1.7, 0.8 Hz, 1H), 8.30 (ddd, *J* = 7.7, 1.7, 1.4 Hz, 1H), 7.42 (ddd, *J* = 7.7, 7.7, 0.8 Hz, 1H), 7.36 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.33 (dddd, *J* = 7.7, 1.9, 1.4, 0.6 Hz, 1H), 7.27 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.21 (ddd, *J* = 7.6, 7.5, 1.5 Hz, 1H), 7.17 (t, *J* = 4.8 Hz, 1H), 7.13 (ddd, *J* = 7.6, 7.5, 2.0 Hz, 1H), 4.77 (q, *J* = 7.2 Hz, 1H), 1.70 (d, *J* = 7.2 Hz, 3H).

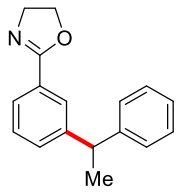
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.7 (C_q), 157.1 (CH), 145.2 (C_q), 143.5 (C_q), 137.6 (C_q), 133.8 (C_q), 130.3 (CH), 129.5 (CH), 128.6 (CH), 128.6 (CH), 127.4 (CH), 127.3 (CH), 126.9 (CH), 126.1 (CH), 118.9 (CH), 41.2 (CH), 21.2 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2968, 1567, 1553, 1422, 1407, 1034, 793, 757, 699, 635 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 296 (31) $[M(^{37}Cl)]^+$, 294 (89) $[M(^{35}Cl)]^+$, 281 (35) $[M(^{37}Cl)–Me]^+$, 279 (100) $[M(^{35}Cl)–Me]^+$, 259 (24) $[M–Cl]^+$, 243 (60) $[M–Me–Cl]^+$, 190 (26), 165 (12), 129 (10), 122 (10), 103 (14), 77 (13).

HR-MS (ESI): *m*/*z* calcd for $C_{18}H_{16}{}^{35}ClN_2^+$ $[M+H]^+$ 295.0997, found 295.0999.

2-[3-(1-Phenylethyl)phenyl]-4,5-dihydrooxazole (143m)



The general procedure **I** was followed using 2-phenyl-4,5-dihydrooxazole (**139h**, 73.6 mg, 0.50 mmol) and (1-chloroethyl)benzene (**142a**, 211 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1)

followed by recycling preparative HPLC yielded **143m** (65.6 mg, 52%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.89–7.87 (m, 1H), 7.79–7.74 (m, 1H), 7.35–7.26 (m, 4H), 7.24–7.15 (m, 3H), 4.42 (td, *J* = 9.5, 0.6 Hz, 2H), 4.19 (q, *J* = 7.3 Hz, 1H), 4.05 (t, *J* = 9.5 Hz, 2H), 1.66 (d, *J* = 7.3 Hz, 3H).

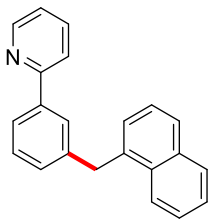
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 164.8 (C_q), 146.6 (C_q), 145.9 (C_q), 130.7 (CH), 128.4 (CH), 127.8 (C_q), 127.6 (CH), 127.2 (CH), 126.1 (CH), 126.0 (CH), 67.5 (CH_2), 54.9 (CH_2), 44.7 (CH), 21.7 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2967, 2875, 1647, 1450, 1356, 1264, 1178, 1066, 947, 700 cm^{-1}.

MS (EI) *m/z* (relative intensity): 251 (69) $[M]^+$, 236 (100) $[M–Me]^+$, 221 (12), 193 (40), 192 (40), 178 (15), 165 (68), 103 (19), 89 (9), 77 (16).

HR-MS (EI): *m/z* calcd for $C_{17}H_{17}NO^+$ $[M]^+$ 251.1305, found 251.1316.

2-[3-(Naphthalen-1-ylmethyl)phenyl]pyridine (143n)



The general procedure **I** was followed using 2-phenylpyridine (**68b**, 77.6 mg, 0.50 mmol) and 1-(chloromethyl)naphthalene (**142m**, 265 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded **143n** (28.8 mg, 20%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.70 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H), 8.09–8.02 (m, 1H), 7.96 (dddd, *J* = 1.8, 1.2, 0.6, 0.6 Hz, 1H), 7.91–7.85 (m, 1H), 7.82 (dddd, *J* = 7.7, 1.2, 1.2, 0.6 Hz, 1H), 7.79 (dtt, *J* = 8.1, 0.9, 0.5 Hz, 1H), 7.71 (d_{AB}dd, *J* = 8.0, 7.0, 1.8 Hz, 1H), 7.67 (d_{AB}dd, *J* = 8.0, 1.6, 1.0 Hz, 1H), 7.50–7.41 (m, 3H), 7.37 (ddd, *J* = 7.7, 7.7, 0.6 Hz, 1H), 7.37–7.33 (m, 1H), 7.24–7.18 (m, 2H), 4.56 (s, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 157.4 (C_q), 149.5 (CH), 141.1 (C_q), 139.5 (C_q), 136.5 (CH), 136.4 (C_q), 133.8 (C_q), 132.0 (C_q), 129.3 (CH), 128.8 (CH), 128.6 (CH), 127.3 (CH), 127.1 (CH), 125.9 (CH), 125.5 (CH), 124.7 (CH), 124.2 (CH), 121.9 (CH), 120.6 (CH), 39.2 (CH_2).

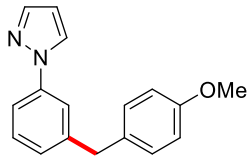
IR (ATR): $\tilde{\nu}$ = 3045, 1584, 1565, 1461, 1435, 769, 744 cm^{-1}.

MS (EI) *m/z* (relative intensity): 295 (75) $[M]^+$, 294 (100) $[M–H]^+$, 215 (27), 147 (14), 115 (7), 43 (10).

HR-MS (EI): *m/z* calcd for $C_{22}H_{17}N^+$ $[M]^+$ 295.1356, found 295.1350.

The spectral data are in accordance with those reported in the literature.[68]

1-[3-(4-Methoxybenzyl)phenyl]-1*H*-pyrazole (143o)



The general procedure **I** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded **143o** (48.9 mg, 37%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.71 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.57–7.55 (m, 1H), 7.52–7.48 (m, 1H), 7.36 (ddd, *J* = 7.8, 7.7, 0.5 Hz, 1H), 7.13 (d, *J* = 8.8 Hz, 2H), 7.10 (dddd, *J* = 7.7, 2.2, 0.9, 0.5 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.44 (dd, *J* = 2.5, 1.8 Hz, 1H), 3.99 (s, 2H), 3.78 (s, 3H).

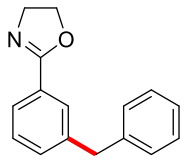
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 158.1 (C_q), 143.3 (C_q), 141.0 (CH), 140.3 (C_q), 132.6 (C_q), 129.9 (CH), 129.4 (CH), 126.9 (CH), 126.8 (CH), 119.8 (CH), 116.9 (CH), 114.0 (CH), 107.4 (CH), 55.2 (CH_3), 41.0 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2835, 1608, 1592, 1509, 1391, 1242, 1176, 1033, 786, 747 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 264 (100) $[M]^+$, 249 (22) $[M–Me]^+$, 152 (13), 121 (21), 77 (9).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{16}N_2O^+$ $[M]^+$ 264.1257, found 264.1270.

2-(3-Benzylphenyl)-4,5-dihydrooxazole (143p)



The general procedure **I** was followed using 2-phenyl-4,5-dihydrooxazole (**139h**, 73.6 mg, 0.50 mmol) and benzyl chloride (**142c**, 190 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 7:3) followed by recycling preparative HPLC yielded **143p** (33.9 mg, 29%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.84 (s, 1H), 7.79 (d, *J* = 7.4 Hz, 1H), 7.37–7.16 (m, 7H), 4.42 (t, *J* = 9.8 Hz, 2H), 4.05 (t, *J* = 9.8 Hz, 2H), 4.02 (s, 2H).

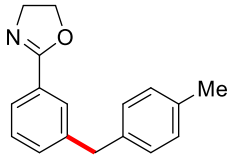
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.5 (C_q), 141.3 (C_q), 140.5 (C_q), 131.8 (CH), 128.8 (CH), 128.6 (CH), 128.4 (CH), 127.8 (C_q), 126.1 (CH), 125.9 (CH), 67.6 (CH_2), 54.9 (CH_2), 41.8 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2903, 1647, 1600, 1493, 1357, 1263, 1179, 1065, 952, 700 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 237 (100) $[M]^+$, 236 (34) $[M–H]^+$, 207 (84), 193 (13), 165 (55), 152 (15), 91 (31) $[Bn]^+$, 65 (9).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{15}NO^+$ $[M]^+$ 237.1148, found 237.1149.

2-[3-(4-Methylbenzyl)phenyl]-4,5-dihydrooxazole (143q)



The general procedure **I** was followed using 2-phenyl-4,5-dihydrooxazole (**139h**, 73.6 mg, 0.50 mmol) and 4-methylbenzyl chloride (**142f**, 211 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 7:3) followed by recycling preparative HPLC yielded **143q** (37.4 mg, 30%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.83 (ddd, *J* = 1.7, 1.7, 0.7 Hz, 1H), 7.77 (ddd, *J* = 7.4, 1.7, 1.7 Hz, 1H), 7.32 (ddd, *J* = 7.6, 7.4, 0.7 Hz, 1H), 7.28 (ddd, *J* = 7.6, 1.7, 1.7 Hz, 1H), 7.11–7.06 (m, 4H), 4.41 (t, *J* = 9.5 Hz, 2H), 4.05 (t, *J* = 9.5 Hz, 2H), 3.97 (s, 2H), 2.31 (s, 3H).

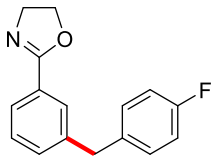
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 164.7 (C_q), 141.7 (C_q), 137.6 (C_q), 135.7 (C_q), 131.8 (CH), 129.2 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 127.8 (C_q), 125.9 (CH), 67.5 (CH_2), 54.9 (CH_2), 41.4 (CH_2), 21.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2903, 1648, 1513, 1356, 1262, 1180, 1064, 951, 797, 707 cm^{-1}.

MS (EI) *m/z* (relative intensity): 251 (100) $[M]^+$, 236 (5) $[M–Me]^+$, 221 (16), 206 (14), 193 (10), 179 (12), 165 (24), 105 (15) $[MeBn]^+$.

HR-MS (EI): *m/z* calcd for $C_{17}H_{17}NO^+$ $[M]^+$ 251.1305, found 251.1308.

2-[3-(4-Fluorobenzyl)phenyl]-4,5-dihydrooxazole (143r)



The general procedure **I** was followed using 2-phenyl-4,5-dihydrooxazole (**139h**, 73.6 mg, 0.50 mmol) and 4-fluorobenzyl chloride (**142i**, 217 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 7:3) followed by recycling preparative HPLC yielded **143r** (42.7 mg, 33%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.84–7.74 (m, 2H), 7.34 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.30–7.24 (m, 1H), 7.13 (dd, *J* = 8.8, 5.4 Hz, 2H), 6.96 (dd, *J* = 8.8, 8.7 Hz, 2H), 4.42 (t, *J* = 9.5 Hz, 2H), 4.05 (t, *J* = 9.5 Hz, 2H), 3.97 (s, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.5 (C_q), 161.3 (d, $^{1}J_{C–F}$ = 244 Hz, C_q), 141.1 (C_q), 136.2 (d, $^{4}J_{C–F}$ = 3 Hz, C_q), 131.7 (CH), 130.2 (d, $^{3}J_{C–F}$ = 8 Hz, CH), 128.5 (CH), 127.9 (C_q), 126.0 (CH), 115.2 (d, $^{2}J_{C–F}$ = 21 Hz, CH), 67.6 (CH_2), 54.9 (CH_2), 41.0 (CH_2).

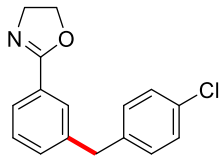
^{19}F-NMR (282 MHz, $CDCl_3$): δ = (–117.1)–(–117.3) (m).

IR (ATR): $\tilde{\nu}$ = 2877, 1648, 1602, 1507, 1357, 1219, 1157, 1065, 952, 707 cm^{-1}.

MS (EI) *m/z* (relative intensity): 255 (100) $[M]^+$, 254 (32) $[M–H]^+$, 225 (88), 211 (13), 183 (38), 165 (16), 109 (34) $[FBn]^+$, 89 (9), 43 (22).

HR-MS (EI): *m/z* calcd for $C_{16}H_{14}FNO^+$ $[M]^+$ 255.1054, found 255.1063.

2-[3-(4-Chlorobenzyl)phenyl]-4,5-dihydrooxazole (143s)



The general procedure **I** was followed using 2-phenyl-4,5-dihydrooxazole (**139h**, 73.6 mg, 0.50 mmol) and 4-chlorobenzyl chloride (**142j**, 242 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 7:3) followed by recycling preparative HPLC yielded **143s** (39.0 mg, 29%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.90–7.70 (m, 2H), 7.33 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.10 (d, *J* = 8.3 Hz, 2H), 4.42 (t, *J* = 9.4 Hz, 2H), 4.05 (br s, 2H), 3.97 (s, 2H).

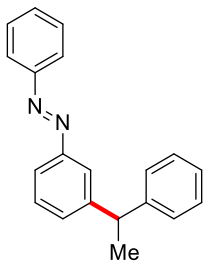
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 164.4 (C_q), 140.7 (C_q), 139.0 (C_q), 131.9 (C_q), 131.7 (CH), 130.1 (CH), 128.5 (CH), 128.0 (C_q), 126.2 (CH), 67.6 (CH_2), 54.9 (CH_2), 41.1 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2903, 1649, 1490, 1357, 1264, 1181, 1084, 980, 791, 709 cm^{-1}.

MS (EI) *m/z* (relative intensity): 273 (34) $[M(^{37}Cl)]^+$, 272 (29) $[M(^{37}Cl)–H]^+$, 271 (100) $[M(^{35}Cl)]^+$, 270 (37) $[M(^{35}Cl)–H]^+$, 243 (30), 241 (89), 193 (14), 178 (11), 165 (56), 127 (9) $[^{37}ClBn]^+$, 125 (23) $[^{35}ClBn]^+$, 103 (17), 89 (17).

HR-MS (EI): *m/z* calcd for $C_{16}H_{14}{}^{35}ClNO^+$ $[M]^+$ 271.0758, found 271.0758.

(*E*)-1-Phenyl-2-[3-(1-phenylethyl)phenyl]diazene (143t)



The general procedure **I** was followed using azobenzene (**139l**, 91.2 mg, 0.50 mmol) and (1-chloroethyl)benzene (**142a**, 211 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane to *n*-hexane/EtOAc 100:1) followed by recycling preparative HPLC yielded **143t** (39.1 mg, 27%) as an orange oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.96–7.91 (m, 2H), 7.88 (dd, *J* = 1.9, 1.8 Hz, 1H), 7.77 (ddd, *J* = 7.8, 1.9, 1.3 Hz, 1H), 7.57–7.48 (m, 3H), 7.45 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.38–7.27 (m, 5H), 7.27–7.19 (m, 1H), 4.30 (q, *J* = 7.2 Hz, 1H), 1.75 (d, *J* = 7.2 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 152.7 (C_q), 152.6 (C_q), 147.4 (C_q), 145.8 (C_q), 130.8 (CH), 130.4 (CH), 129.0 (CH), 128.4 (CH), 127.6 (CH), 126.1 (CH), 122.7 (CH), 122.5 (CH), 120.1 (CH), 44.8 (CH), 21.9 (CH_3).

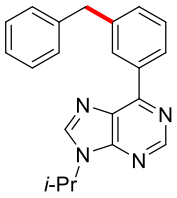
IR (ATR): $\tilde{\nu}$ = 2967, 1598, 1492, 1449, 1150, 1027, 763, 690, 529 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 286 (68) $[M]^+$, 209 (9) $[M–Ph]^+$, 181 (88) $[M–Ph–N_2]^+$, 166 (60), 165 (68), 105 (48) $[EtPh]^+$, 77 (100) $[Ph]^+$.

HR-MS (EI): *m*/*z* calcd for $C_{20}H_{18}N_2^+$ $[M]^+$ 286.1465, found 286.1461.

5.3.4.2 Characterization Data for 185

6-(3-Benzylphenyl)-9-*iso*-propyl-9*H*-purine (185ac)



The general procedure **I** was followed using purine **123a** (119 mg, 0.50 mmol) and benzyl chloride (**142c**, 190 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **185ac** (116 mg, 71%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.68 (ddd, *J* = 7.7, 1.8, 1.3 Hz, 1H), 8.62 (ddd, *J* = 1.8, 1.3, 0.6 Hz, 1H), 8.18 (s, 1H), 7.48 (ddd, *J* = 7.7, 7.7, 0.6 Hz, 1H), 7.32 (dddd, *J* = 7.7, 1.3, 1.3, 0.6 Hz, 1H), 7.30–7.15 (m, 5H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.14 (s, 2H), 1.67 (d, *J* = 6.8 Hz, 6H).

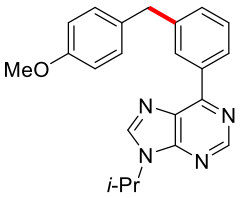
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 154.7 (C_q), 152.0 (C_q), 151.9 (CH), 141.8 (CH), 141.4 (C_q), 140.9 (C_q), 135.9 (C_q), 131.5 (C_q and CH), 129.9 (CH), 128.9 (CH), 128.7 (CH), 128.4 (CH), 127.9 (CH), 126.0 (CH), 47.3 (CH), 42.1 (CH_2), 22.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2977, 1567, 1494, 1324, 1217, 783, 700, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 328 (42) $[M]^+$, 327 (41) $[M–H]^+$, 285 (100) $[M–i\text{-}Pr]^+$, 165 (8), 91 (6).

HR-MS (EI): *m*/*z* calcd for $C_{21}H_{20}N_4^+$ $[M]^+$ 328.1682, found 328.1685.

9-*iso*-Propyl-6-[3-(4-methoxybenzyl)phenyl]-9*H*-purine (185ab)



The general procedure **I** was followed using purine **123a** (119 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **185ab** (133 mg, 74%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.66 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 8.59 (ddd, *J* = 1.8, 1.5, 0.6 Hz, 1H), 8.18 (s, 1H), 7.47 (ddd, *J* = 7.8, 7.7, 0.6 Hz, 1H), 7.30 (dddd, *J* = 7.7, 1.5, 1.2, 0.6 Hz, 1H), 7.16 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.07 (s, 2H), 3.77 (s, 3H), 1.67 (d, *J* = 6.8 Hz, 6H).

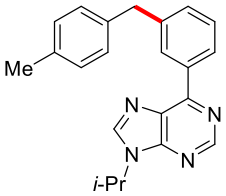
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 157.9 (C_q), 154.8 (C_q), 152.0 (C_q), 151.9 (CH), 141.9 (C_q), 141.8 (CH), 135.8 (C_q), 133.1 (C_q), 131.5 (C_q), 131.4 (CH), 129.8 (CH), 129.8 (CH), 128.7 (CH), 127.8 (CH), 113.8 (CH), 55.3 (CH_3), 47.3 (CH), 41.2 (CH_2), 22.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2977, 1567, 1509, 1324, 1243, 1217, 1033, 791, 703, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 358 (84) $[M]^+$, 357 (30) $[M–H]^+$, 343 (14) $[M–Me]^+$, 315 (100) [M–*i*-Pr]$^+$, 301 (43), 121 (13), 43 (8).

HR-MS (EI): *m*/*z* calcd for $C_{22}H_{22}N_4O^+$ $[M]^+$ 358.1788, found 358.1796.

9-*iso*-Propyl-6-[3-(4-methylbenzyl)phenyl]-9*H*-purine (185af)



The general procedure **I** was followed using purine **123a** (119 mg, 0.50 mmol) and 4-methylbenzyl chloride (**142f**, 211 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **185af** (106 mg, 62%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.67 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 8.61 (ddd, *J* = 1.8, 1.2, 0.6 Hz, 1H), 8.18 (s, 1H), 7.47 (ddd, *J* = 7.8, 7.7, 0.6 Hz, 1H), 7.31 (dddd, *J* = 7.7, 1.2, 1.2, 0.6 Hz, 1H), 7.14 (d_{AB}, *J* = 8.0 Hz, 2H), 7.09 (d_{AB}, *J* = 8.0 Hz, 2H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.09 (s, 2H), 2.30 (s, 3H), 1.67 (d, *J* = 6.8 Hz, 6H).

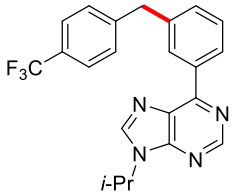
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 154.9 (C_q), 152.1 (C_q), 152.0 (CH), 141.9 (CH), 141.8 (C_q), 138.0 (C_q), 135.9 (C_q), 135.5 (C_q), 131.5 (C_q), 131.5 (CH), 129.9 (CH), 129.1 (CH), 128.8 (CH), 128.8 (CH), 127.9 (CH), 47.2 (CH), 41.6 (CH_2), 22.6 (CH_3), 21.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2977, 2919, 1567, 1495, 1445, 1324, 1217, 790, 702, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 342 (75) $[M]^+$, 341 (27) $[M–H]^+$, 327 (2) $[M–Me]^+$, 299 (100) [M–*i*-Pr]$^+$, 285 (11), 165 (6), 142 (7).

HR-MS (EI): *m*/*z* calcd for $C_{22}H_{22}N_4^+$ $[M]^+$ 342.1839, found 342.1845.

9-*iso*-Propyl-6-{3-[4-(trifluoromethyl)benzyl]phenyl}-9*H*-purine (185ag)



The general procedure **I** was followed using purine **123a** (119 mg, 0.50 mmol) and 4-(trifluoromethyl)benzyl chloride (**142g**, 292 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **185ag** (146 mg, 73%) as a colorless oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.70 (ddd, *J* = 7.8, 1.5, 1.3 Hz, 1H), 8.61 (dd, *J* = 1.7, 1.5 Hz, 1H), 8.18 (s, 1H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.50 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.31 (ddd, *J* = 7.7, 1.7, 1.3 Hz, 1H), 4.99 (hept, *J* = 6.9 Hz, 1H), 4.18 (s, 2H), 1.68 (d, *J* = 6.9 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 154.6 (C_q), 152.1 (C_q), 152.0 (CH), 145.1 (C_q), 142.0 (CH), 140.4 (C_q), 136.2 (C_q), 131.5 (C_q), 131.5 (CH), 130.0 (CH), 129.2 (CH), 129.0 (CH), 128.4 (q, $^2J_{C–F}$ = 32 Hz, C_q), 128.3 (CH), 125.4 (q, $^3J_{C–F}$ = 4 Hz, CH), 124.3 (q, $^1J_{C–F}$ = 270 Hz, C_q), 47.3 (CH), 41.8 (CH_2), 22.6 (CH_3).

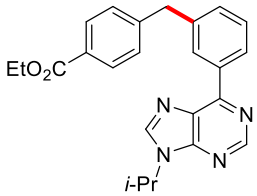
^{19}F-NMR (470 MHz, $CDCl_3$): δ = –62.3 (s).

IR (ATR): $\tilde{\nu}$ = 2980, 1568, 1321, 1219, 1107, 1065, 1018, 788, 703, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 396 (46) $[M]^+$, 395 (58) $[M–H]^+$, 353 (100) [M–*i*-Pr]$^+$, 333 (17).

HR-MS (EI): *m*/*z* calcd for $C_{22}H_{19}F_3N_4^+$ $[M]^+$ 396.1556, found 396.1557.

Ethyl 4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoate (185ah)



The general procedure **I** was followed using purine **123a** (119 mg, 0.50 mmol) and ethyl 4-(chloromethyl)benzoate (**142h**, 298 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **185ah** (144 mg, 72%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.00 (s, 1H), 8.69 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 8.60 (ddd, *J* = 1.8, 1.8, 0.6 Hz, 1H), 8.18 (s, 1H), 7.96 (d, *J* = 8.6 Hz, 2H), 7.49 (ddd, *J* = 7.8, 7.7, 0.6 Hz, 1H), 7.34–7.27

(m, 3H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 4.18 (s, 2H), 1.67 (d, *J* = 6.8 Hz, 6H), 1.37 (t, *J* = 7.1 Hz, 3H).

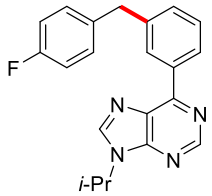
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 166.4 (C_q), 154.5 (C_q), 152.0 (C_q), 151.9 (CH), 146.2 (C_q), 141.9 (CH), 140.5 (C_q), 136.0 (C_q), 131.5 (C_q), 131.4 (CH), 130.0 (CH), 129.7 (CH), 128.9 (CH), 128.8 (CH), 128.4 (C_q), 128.1 (CH), 60.8 (CH_2), 47.3 (CH), 42.0 (CH_2), 22.6 (CH_3), 14.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2978, 1711, 1567, 1325, 1272, 1219, 1101, 1021, 703, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 400 (60) $[M]^+$, 399 (100) $[M–H]^+$, 371 (10) $[M–Et]^+$, 357 (47) $[M–i\text{-}Pr]^+$, 329 (21) $[M–i\text{-}Pr–Et]^+$, 311 (48), 285 (19), 283 (26) $[M–i\text{-}Pr–CO_2Et]^+$, 165 (9), 156 (11), 142 (9).

HR-MS (EI): *m*/*z* calcd for $C_{24}H_{24}N_4O_2^+$ $[M]^+$ 400.1894, found 400.1883.

6-[3-(4-Fluorobenzyl)phenyl]-9-*iso*-propyl-9*H*-purine (185ai)



The general procedure **I** was followed using purine **123a** (119 mg, 0.50 mmol) and 4-fluorobenzyl chloride (**142i**, 217 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **185ai** (123 mg, 71%) as a white solid.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.68 (ddd, *J* = 7.8, 1.8, 1.3 Hz, 1H), 8.59 (dd, *J* = 2.0, 1.8 Hz, 1H), 8.18 (s, 1H), 7.48 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.29 (ddd, *J* = 7.7, 2.0, 1.3 Hz, 1H), 7.19 (dd, *J* = 8.8, 5.4 Hz, 2H), 6.96 (dd, *J* = 8.8, 8.7 Hz, 2H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.09 (s, 2H), 1.67 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 161.3 (d, $^{1}J_{C–F}$ = 244 Hz, C_q), 154.6 (C_q), 152.0 (C_q), 151.9 (CH), 141.8 (CH), 141.2 (C_q), 136.6 (d, $^{4}J_{C–F}$ = 3 Hz, C_q), 136.0 (C_q), 131.5 (C_q), 131.3 (CH), 130.2 (d, $^{3}J_{C–F}$ = 8 Hz, CH), 129.8 (CH), 128.8 (CH), 128.0 (CH), 115.1 (d, $^{2}J_{C–F}$ = 21 Hz, CH), 47.3 (CH), 41.2 (CH_2), 22.6 (CH_3).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = –117.4 (tt, *J* = 8.7, 5.4 Hz).

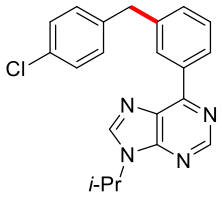
IR (ATR): $\tilde{\nu}$ = 2980, 1567, 1506, 1444, 1326, 1221, 834, 794, 704, 651 cm^{-1}.

m.p.: 95–96 °C.

MS (EI) *m*/*z* (relative intensity): 346 (41) $[M]^+$, 345 (38) $[M–H]^+$, 303 (100) $[M–i\text{-}Pr]^+$, 183 (5), 109 (9), 43 (6).

HR-MS (EI): *m/z* calcd for $C_{21}H_{19}FN_4^+$ $[M]^+$ 346.1588, found 346.1591.

6-[3-(4-Chlorobenzyl)phenyl]-9-*iso*-propyl-9*H*-purine (185aj)



The general procedure **I** was followed using purine **123a** (119 mg, 0.50 mmol) and 4-chlorobenzyl chloride (**142j**, 242 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **185aj** (132 mg, 73%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.68 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 8.58 (ddd, *J* = 1.8, 1.2, 0.6 Hz, 1H), 8.18 (s, 1H), 7.48 (ddd, *J* = 7.8, 7.7, 0.6 Hz, 1H), 7.29 (dddd, *J* = 7.7, 1.2, 1.2, 0.6 Hz, 1H), 7.25 (d, *J* = 8.9 Hz, 2H), 7.17 (d, *J* = 8.9 Hz, 2H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.09 (s, 2H), 1.67 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 154.6 (C_q), 152.0 (C_q), 151.9 (CH), 141.8 (CH), 140.8 (C_q), 139.4 (C_q), 136.0 (C_q), 131.8 (C_q), 131.5 (C_q), 131.3 (CH), 130.2 (CH), 129.9 (CH), 128.8 (CH), 128.5 (CH), 128.1 (CH), 47.3 (CH), 41.4 (CH_2), 22.6 (CH_3).

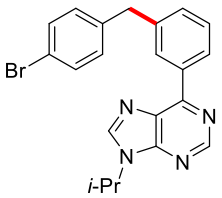
IR (ATR): $\tilde{\nu}$ = 2977, 1567, 1490, 1448, 1324, 1217, 1089, 781, 700, 647 cm^{-1}.

m.p.: 104–105 °C.

MS (EI) *m/z* (relative intensity): 364 (16) $[M(^{37}Cl)]^+$, 363 (25) $[M(^{37}Cl)–H]^+$, 362 (46) $[M(^{35}Cl)]^+$, 361 (51) $[M(^{35}Cl)–H]^+$, 321 (35) $[M(^{37}Cl)–i\text{-Pr}]^+$, 319 (100) $[M(^{35}Cl)–i\text{-Pr}]^+$, 283 (16) $[M–i\text{-Pr}–Cl]^+$, 165 (7), 142 (10), 125 (9), 43 (7).

HR-MS (EI): *m/z* calcd for $C_{21}H_{19}{}^{35}ClN_4^+$ $[M]^+$ 362.1293, found 362.1287.

6-[3-(4-Bromobenzyl)phenyl]-9-*iso*-propyl-9*H*-purine (185ak)



The general procedure **I** was followed using purine **123a** (119 mg, 0.50 mmol) and 4-bromobenzyl chloride (**142k**, 308 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **185ak** (142 mg, 70%) as a pale yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.00 (s, 1H), 8.68 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 8.59 (ddd, *J* = 1.8, 1.2, 0.6 Hz, 1H), 8.16 (s, 1H), 7.47 (ddd, *J* = 7.8, 7.7, 0.6 Hz, 1H), 7.38 (d, *J* = 8.6 Hz, 2H), 7.28 (dddd,

J = 7.7, 1.2, 1.2, 0.6 Hz, 1H), 7.10 (d, *J* = 8.6 Hz, 2H), 4.96 (hept, *J* = 6.8 Hz, 1H), 4.06 (s, 2H), 1.65 (d, *J* = 6.8 Hz, 6H).

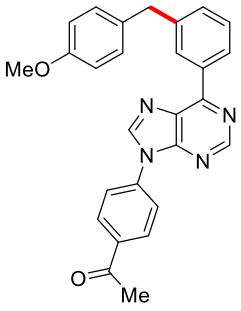
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 154.5 (C_q), 152.0 (C_q), 151.8 (CH), 141.8 (CH), 140.7 (C_q), 139.9 (C_q), 136.0 (C_q), 131.4 (C_q), 131.4 (CH), 131.3 (CH), 130.6 (CH), 129.8 (CH), 128.8 (CH), 128.1 (CH), 119.8 (C_q), 47.2 (CH), 41.4 (CH_2), 22.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2977, 1567, 1486, 1325, 1218, 1070, 1011, 781, 703, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 408 (48) $[M(^{81}Br)]^+$, 407 (64) $[M(^{81}Br)–H]^+$, 406 (48) $[M(^{79}Br)]^+$, 405 (55) $[M(^{79}Br)–H]^+$, 365 (100) $[M(^{81}Br)–i\text{-Pr}]^+$, 363 (100) $[M(^{79}Br)–i\text{-Pr}]^+$, 283 (39) $[M–i\text{-Pr}–Br]^+$, 165 (14), 142 (11).

HR-MS (EI): *m*/*z* calcd for $C_{21}H_{19}{}^{79}BrN_4^+$ $[M]^+$ 406.0788, found 406.0778.

1-{4-{6-[3-(4-Methoxybenzyl)phenyl]-9*H*-purin-9-yl}phenyl}ethan-1-one (185hb)



The general procedure **I** was followed using purine **123h** (157 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 7:3) yielded **185hb** (147 mg, 68%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.09 (s, 1H), 8.70 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 8.64 (ddd, *J* = 1.9, 1.8, 0.9 Hz, 1H), 8.46 (s, 1H), 8.21 (d, *J* = 8.9 Hz, 2H), 7.97 (d, *J* = 8.9 Hz, 2H), 7.50 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.35 (ddd, *J* = 7.7, 1.9, 1.2 Hz, 1H), 7.18 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.09 (s, 2H), 3.78 (s, 3H), 2.69 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 196.4 (C_q), 157.9 (C_q), 155.8 (C_q), 153.1 (CH), 152.0 (C_q), 142.3 (CH), 142.1 (C_q), 138.2 (C_q), 136.4 (C_q), 135.4 (C_q), 133.0 (C_q), 131.8 (CH), 131.6 (C_q), 130.1 (CH), 129.9 (CH), 129.8 (CH), 128.8 (CH), 128.0 (CH), 122.9 (CH), 113.9 (CH), 55.3 (CH_3), 41.2 (CH_2), 26.8 (CH_3).

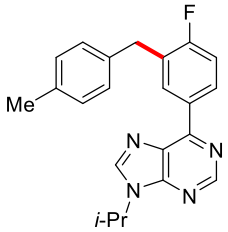
IR (ATR): $\tilde{\nu}$ = 3112, 1679, 1557, 1509, 1233, 1173, 1026, 928, 835, 786 cm^{-1}.

m.p.: 159–160 °C.

MS (EI) *m*/*z* (relative intensity): 434 (100) $[M]^+$, 433 (63) $[M–H]^+$, 419 (53) $[M–Me]^+$, 210 (9), 121 (9), 43 (16).

HR-MS (EI): *m*/*z* calcd for $C_{27}H_{22}N_4O_2^+$ $[M]^+$ 434.1737, found 434.1743.

6-[4-Fluoro-3-(4-methylbenzyl)phenyl]-9-*iso*-propyl-9*H*-purine (185if)



The general procedure **I** was followed using purine **123i** (128 mg, 0.50 mmol) and 4-methylbenzyl chloride (**142f**, 211 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) followed by recycling preparative HPLC yielded **185if** (90.5 mg, 50%) as a white soild.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.98 (s, 1H), 8.76 (ddd, *J* = 8.6, 5.2, 2.3 Hz, 1H), 8.71 (dd, *J* = 7.5, 2.3 Hz, 1H), 8.16 (s, 1H), 7.21 (dd, *J* = 9.5, 8.6 Hz, 1H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.08 (d, *J* = 7.9 Hz, 2H), 4.96 (hept, *J* = 6.8 Hz, 1H), 4.10 (s, 2H), 2.29 (s, 3H), 1.66 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 162.7 (d, $^{1}J_{C-F}$ = 251 Hz, C_q), 153.6 (C_q), 151.9 (C_q), 151.8 (CH), 141.7 (CH), 136.7 (C_q), 135.5 (C_q), 132.6 (d, $^{3}J_{C-F}$ = 6 Hz, CH), 131.9 (d, $^{4}J_{C-F}$ = 3 Hz, C_q), 131.1 (C_q), 130.2 (d, $^{3}J_{C-F}$ = 9 Hz, CH), 129.0 (CH), 128.6 (d, $^{2}J_{C-F}$ = 16 Hz, C_q), 128.4 (CH), 115.6 (d, $^{2}J_{C-F}$ = 23 Hz, CH), 47.3 (CH), 34.9 (d, $^{3}J_{C-F}$ = 3 Hz, CH_2), 22.6 (CH_3), 21.0 (CH_3).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = (–113.6)–(–113.8) (m).

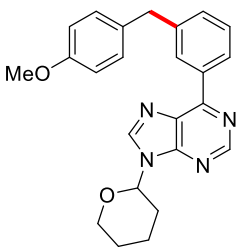
IR (ATR): $\tilde{\nu}$ = 2978, 1574, 1502, 1446, 1326, 1219, 834, 806, 646 cm^{-1}.

m.p.: 72–74 °C.

MS (EI) *m*/*z* (relative intensity): 360 (90) $[M]^+$, 359 (26) $[M–H]^+$, 345 (2) $[M–Me]^+$, 317 (100) [M–*i*-Pr]$^+$, 303 (9).

HR-MS (EI): *m*/*z* calcd for $C_{22}H_{21}FN_4^+$ $[M]^+$ 360.1745, found 360.1748.

6-[3-(4-Methoxybenzyl)phenyl]-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (185jb)



The general procedure **I** was followed using purine **123j** (140 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **185jb** (150 mg, 75%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.68 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 8.61 (ddd, *J* = 1.8, 1.8, 0.6 Hz, 1H), 8.32 (s, 1H), 7.46 (ddd, *J* = 7.8, 7.7, 0.6 Hz, 1H), 7.30 (ddd, *J* = 7.7, 1.8, 1.2 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 5.82 (dd, *J* = 9.9, 3.0 Hz, 1H), 4.20–4.13 (m, 1H), 4.06 (s, 2H), 3.82–3.73 (m, 1H), 3.74 (s, 3H), 2.19–1.98 (m, 3H), 1.86–1.58 (m, 3H).

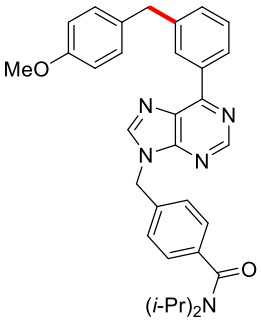
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 157.8 (C_q), 154.8 (C_q), 152.1 (CH), 151.5 (C_q), 141.8 (C_q and CH), 135.6 (C_q), 132.9 (C_q), 131.4 (CH), 131.0 (C_q), 129.7 (CH), 128.6 (CH), 127.8 (CH), 113.7 (CH), 81.9 (CH), 68.7 (CH_2), 55.1 (CH_3), 41.1 (CH_2), 31.7 (CH_2), 24.8 (CH_2), 22.8 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2946, 1567, 1509, 1323, 1243, 1083, 1042, 734, 701, 643 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 400 (41) $[M]^+$, 372 (11) $[M–Et]^+$, 316 (100) $[M–THP]^+$, 315 (76), 301 (52), 121 (22), 85 (33), 67 (11), 41 (12).

HR-MS (EI): *m*/*z* calcd for $C_{24}H_{24}N_4O_2^+$ $[M]^+$ 400.1894, found 400.1903.

N,*N*-Di-*iso*-propyl-4-{{6-[3-(4-methoxybenzyl)phenyl]-9*H*-purin-9-yl}methyl}benzamide (185kb)



The general procedure **I** was followed using purine **123k** (207 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 2:3) yielded **185kb** (167 mg, 63%) as a white soild.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.04 (s, 1H), 8.68 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 8.62 (ddd, *J* = 1.8, 1.8, 0.6 Hz, 1H), 8.10 (s, 1H), 7.47 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.33–7.28 (m, 5H), 7.15 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 5.47 (s, 2H), 4.06 (s, 2H), 3.75 (s, 3H), 3.87–3.39 (br, 2H), 1.78–0.88 (br, 12H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 170.1 (C_q), 157.9 (C_q), 155.0 (C_q), 152.6 (CH), 152.4 (C_q), 144.0 (CH), 142.0 (C_q), 139.2 (C_q), 135.7 (C_q), 133.1 (C_q), 131.6 (CH), 130.9 (C_q), 129.9 (CH), 129.8 (CH), 128.8 (CH), 127.9 (CH), 127.8 (CH), 126.4 (CH), 113.8 (CH), 55.2 (CH_3), 51.6–50.0 (br, CH), 46.8 (CH_2), 46.6–45.2 (br, CH), 41.1 (CH_2), 20.6 (CH_3).

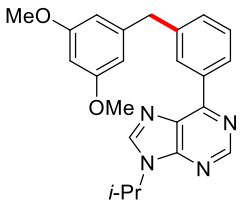
IR (ATR): $\tilde{\nu}$ = 2967, 1623, 1568, 1509, 1439, 1323, 1244, 1035, 794, 703 cm^{-1}.

m.p.: 68–70 °C.

MS (EI) *m*/*z* (relative intensity): 533 (56) $[M]^+$, 532 (10) $[M–H]^+$, 518 (5) $[M–Me]^+$, 490 (21) $[M–i\text{-}Pr]^+$, 433 (100) $[M–N(i\text{-}Pr)_2]^+$, 405 (18) $[M–C(O)N(i\text{-}Pr)_2]^+$, 315 (25), 217 (14), 118 (19), 91 (23) $[Bn]^+$, 58 (14), 43 (52).

HR-MS (EI): *m*/*z* calcd for $C_{33}H_{35}N_5O_2^+$ $[M]^+$ 533.2785, found 533.2807.

6-[3-(3,5-Dimethoxybenzyl)phenyl]-9-*iso*-propyl-9*H*-purine (185al)



The general procedure **I** was followed using purine **123a** (119 mg, 0.50 mmol) and 3,5-dimethoxybenzyl chloride (**142l**, 280 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **185al** (130 mg, 67%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.99 (s, 1H), 8.67 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 8.62 (ddd, *J* = 1.8, 1.5, 0.6 Hz, 1H), 8.14 (s, 1H), 7.46 (ddd, *J* = 7.8, 7.7, 0.6 Hz, 1H), 7.32 (dddd, *J* = 7.7, 1.5, 1.2, 0.6 Hz, 1H), 6.40 (d, *J* = 2.3 Hz, 2H), 6.29 (t, *J* = 2.3 Hz, 1H), 4.94 (hept, *J* = 6.8 Hz, 1H), 4.05 (s, 2H), 3.72 (s, 6H), 1.63 (d, *J* = 6.8 Hz, 6H).

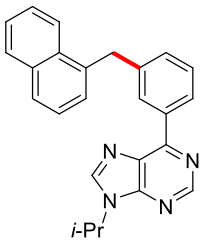
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 160.6 (C_q), 154.5 (C_q), 151.9 (C_q), 151.8 (CH), 143.1 (C_q), 141.7 (CH), 140.9 (C_q), 135.8 (C_q), 131.3 (C_q), 131.3 (CH), 129.8 (CH), 128.6 (CH), 127.9 (CH), 107.0 (CH), 98.0 (CH), 55.1 (CH_3), 47.2 (CH), 42.2 (CH_2), 22.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2936, 1567, 1457, 1324, 1204, 1145, 1063, 791, 703, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 388 (97) $[M]^+$, 387 (58) $[M–H]^+$, 373 (4) $[M–Me]^+$, 345 (100) [M–*i*-Pr]$^+$, 331 (10) [M–*i*-Pr–Me]$^+$, 313 (20), 299 (8), 173 (8), 151 (6), 43 (14).

HR-MS (EI): *m*/*z* calcd for $C_{23}H_{24}N_4O_2^+$ $[M]^+$ 388.1894, found 388.1894.

9-*iso*-Propyl-6-[3-(naphthalen-1-ylmethyl)phenyl]-9*H*-purine (185am)



The general procedure **I** was followed using purine **123a** (119 mg, 0.50 mmol) and 1-(chloromethyl)naphthalene (**142m**, 265 mg, 1.50 mmol) at 80 °C. After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **185am** (127 mg, 67%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.02 (s, 1H), 8.73 (ddd, *J* = 1.8, 1.5, 0.6 Hz, 1H), 8.67 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 8.17 (s, 1H), 8.09–8.03 (m, 1H), 7.89–7.83 (m, 1H), 7.76 (br d, *J* = 8.1 Hz, 1H), 7.48–7.40 (m, 4H), 7.35 (ddt, *J* = 7.0, 1.4, 0.8 Hz, 1H), 7.26 (dddd, *J* = 7.6, 1.5, 1.2, 0.6 Hz, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.61 (s, 2H), 1.67 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 154.8 (C_q), 152.0 (C_q), 151.9 (CH), 141.8 (CH), 141.0 (C_q), 136.5 (C_q), 135.9 (C_q), 133.8 (C_q), 132.0 (C_q), 131.5 (C_q), 131.2 (CH), 129.9 (CH), 128.7 (CH), 128.5 (CH), 127.9 (CH), 127.3 (CH), 127.1 (CH), 125.9 (CH), 125.5 (CH), 125.4 (CH), 124.2 (CH), 47.3 (CH), 39.2 (CH_2), 22.6 (CH_3).

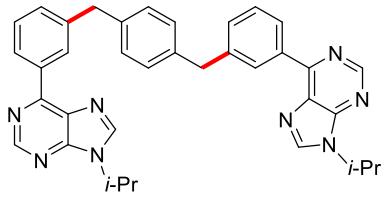
IR (ATR): $\tilde{\nu}$ = 2978, 1569, 1444, 1324, 1225, 791, 705, 647, 571 cm^{-1}.

m.p.: 114–116 °C.

MS (ESI) *m*/*z* (relative intensity): 757 (6) $[2M+H]^+$, 401 (2) $[M+Na]^+$, 379 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{25}H_{23}N_4^+$ $[M+H]^+$ 379.1917, found 379.1920.

1,4-Bis[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzene (185an)



Purine **123a** (297 mg, 1.25 mmol), *α*,*α*'-dichloro-*p*-xylene (**142n**, 87.6 mg, 0.50 mmol), $[Ru(OAc)_2(p\text{-cymene})]$ (**181**, 17.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (276 mg, 2.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. 1,4-Dioxane (2.0 mL) was then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 1:2) yielded **185an** (139 mg, 48%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.99 (s, 2H), 8.65 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 2H), 8.61 (ddd, *J* = 1.8, 1.8, 0.6 Hz, 2H), 8.15 (s, 2H), 7.45 (ddd, *J* = 7.8, 7.7, 0.6 Hz, 2H), 7.30 (ddd, *J* = 7.7, 1.8, 1.2 Hz, 2H), 7.16 (s, 4H), 4.96 (hept, *J* = 6.8 Hz, 2H), 4.08 (s, 4H), 1.65 (d, *J* = 6.8 Hz, 12H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 154.7 (C_q), 151.9 (C_q), 151.8 (CH), 141.7 (CH), 141.5 (C_q), 138.6 (C_q), 135.8 (C_q), 131.4 (C_q and CH), 129.9 (CH), 128.9 (CH), 128.6 (CH), 127.8 (CH), 47.2 (CH), 41.6 (CH_2), 22.6 (CH_3).

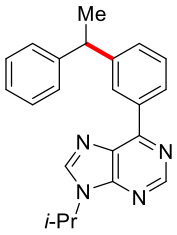
IR (ATR): $\tilde{\nu}$ = 2975, 1570, 1441, 1326, 1218, 790, 699, 646, 582 cm^{-1}.

m.p.: 156–158 °C.

MS (EI) *m*/*z* (relative intensity): 578 (100) $[M]^+$, 536 (17) $[M–i\text{-Pr}]^+$, 493 (12) $[M–i\text{-Pr}–i\text{-Pr}]^+$, 285 (21), 246 (12), 209 (17), 43 (6).

HR-MS (EI): *m*/*z* calcd for $C_{36}H_{34}N_8^+$ $[M]^+$ 578.2901, found 578.2900.

9-*iso*-Propyl-6-[3-(1-phenylethyl)phenyl]-9*H*-purine (185aa)



The general procedure **I** was followed using purine **123a** (119 mg, 0.50 mmol) and (1-chloroethyl)benzene (**142a**, 211 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **185aa** (149 mg, 87%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.68 (dd, *J* = 1.8, 1.6 Hz, 1H), 8.66 (ddd, *J* = 7.7, 1.6, 1.4 Hz, 1H), 8.18 (s, 1H), 7.47 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.35–7.33 (m, 1H), 7.31–7.27 (m, 4H), 7.19–7.16 (m, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.32 (q, *J* = 7.2 Hz, 1H), 1.74 (d, *J* = 7.2 Hz, 3H), 1.67 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 154.9 (C_q), 152.0 (C_q), 151.9 (CH), 146.7 (C_q), 146.1 (C_q), 141.8 (CH), 135.8 (C_q), 131.5 (C_q), 130.2 (CH), 128.6 (CH), 128.6 (CH), 128.3 (CH), 127.9 (CH), 127.6 (CH), 125.9 (CH), 47.3 (CH), 45.0 (CH), 22.7 (CH_3), 22.0 (CH_3).

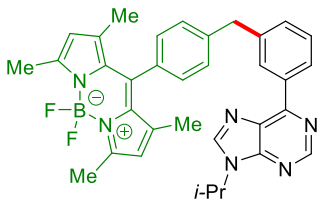
IR (ATR): $\tilde{\nu}$ = 2973, 1566, 1494, 1446, 1324, 1218, 799, 700, 646, 573 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 342 (81) $[M]^+$, 341 (63) $[M–H]^+$, 327 (34) $[M–Me]^+$, 299 (95) [M–*i*-Pr]$^+$, 285 (100) [M–*i*-Pr–Me]$^+$, 165 (14), 142 (8).

HR-MS (EI): *m*/*z* calcd for $C_{22}H_{22}N_4^+$ $[M]^+$ 342.1839, found 342.1832.

5.3.4.3 Characterization Data for 187

5,5-Difluoro-10-{4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]phenyl}-1,3,7,9-tetramethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinine (187a)



The general procedure **J** was followed using purine **123a** (23.9 mg, 0.10 mmol) and benzyl chloride **186a** (75 mg, 0.20 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 7:3) yielded **187a** (26.1 mg, 45%) as an orange solid.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.00 (s, 1H), 8.71 (ddd, *J* = 7.8, 1.7, 1.3 Hz, 1H), 8.57 (dd, *J* = 2.0, 1.7 Hz, 1H), 8.18 (s, 1H), 7.50 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 2H), 7.31 (ddd, *J* = 7.7, 2.0, 1.3 Hz, 1H), 7.20 (d, *J* = 8.1 Hz, 2H), 5.96 (s, 2H), 4.99 (hept, *J* = 6.8 Hz, 1H), 4.22 (s, 2H), 2.54 (s, 6H), 1.68 (d, *J* = 6.8 Hz, 6H), 1.39 (s, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 155.1 (C_q), 154.6 (C_q), 152.0 (C_q), 151.9 (CH), 143.1 (C_q), 141.8 (C_q and CH), 141.8 (C_q), 141.0 (C_q), 136.0 (C_q), 132.7 (C_q), 131.4 (C_q), 131.2 (CH), 129.8 (CH), 129.7 (CH), 128.8 (CH), 128.1 (CH), 128.0 (CH), 121.0 (CH), 47.3 (CH), 41.7 (CH_2), 22.7 (CH_3), 14.6 (CH_3), 14.5 (CH_3).

^{11}B-NMR (128 MHz, $CDCl_3$): δ = 0.8 (t, $^1J_{B-F}$ = 33.1 Hz).

^{19}F-NMR (376 MHz, $CDCl_3$): δ = –146.3 (q, $^1J_{F-B}$ = 33.1 Hz).

IR (ATR): $\tilde{\nu}$ = 2925, 1542, 1508, 1306, 1191, 1155, 976, 731, 703, 647 cm^{-1}.

m.p.: 170–172 °C (decomp.).

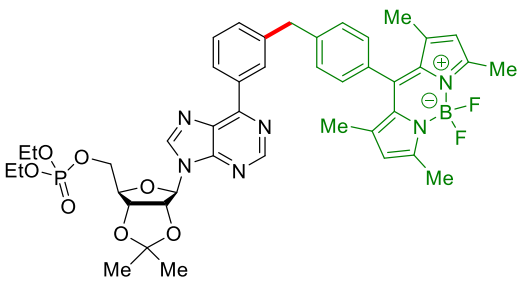
MS (ESI) *m/z* (relative intensity): 1150 (5) $[2M+H]^+$, 597 (4) $[M+Na]^+$, 575 (100) $[M+H]^+$, 177 (6), 117 (19).

HR-MS (ESI): *m/z* calcd for $C_{34}H_{34}BF_2N_6^+$ $[M+H]^+$ 575.2906, found 575.2903.

UV-Vis: λ_{max} (1.0 mg/L in $CHCl_3$) = 502 nm.

E_m: λ_{max} (1.0 mg/L in $CHCl_3$) = 514 nm.

{(3a*R*,4*R*,6*R*,6a*R*)-6-{6-{3-[4-(5,5-Difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinin-10-yl)benzyl]phenyl}-9*H*-purin-9-yl}-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}methyl diethyl phosphate (187b)



The general procedure **J** was followed using purine **123l** (50.5 mg, 0.10 mmol) and benzyl chloride **186a** (75 mg, 0.20 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:7) yielded **187b** (12.9 mg, 15%) as an orange solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.71 (d, *J* = 7.8 Hz, 1H), 8.57 (s, 1H), 8.29 (s, 1H), 7.50 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.27 (d, *J* = 2.6 Hz, 1H), 5.97 (s, 2H), 5.45 (dd, *J* = 6.3, 2.6 Hz, 1H), 5.13 (dd, *J* = 6.3, 3.0 Hz, 1H), 4.58–4.51 (m, 1H), 4.30 (ddd, *J* = 10.8, 6.3, 4.4 Hz, 1H), 4.26–4.17 (m, 1H), 4.22 (s, 2H), 4.13–3.98 (m, 4H), 2.54 (s, 6H), 1.66 (s, 3H), 1.42 (s, 3H), 1.40 (s, 6H), 1.31–1.22 (m, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 155.3 (C_q), 155.1 (C_q), 152.5 (CH), 151.7 (C_q), 143.2 (CH), 143.1 (C_q), 141.8 (C_q), 141.8 (C_q), 141.2 (C_q), 135.7 (C_q), 132.8 (C_q), 131.7 (C_q), 131.6 (CH), 131.5 (C_q), 129.9

(CH), 129.8 (CH), 128.9 (CH), 128.3 (CH), 128.1 (CH), 121.1 (CH), 114.8 (C_q), 91.1 (CH), 85.2 (d, $^3J_{C–P}$ = 8 Hz, CH), 84.2 (CH), 81.3 (CH), 66.6 (d, $^2J_{C–P}$ = 6 Hz, CH_2), 64.1 (d, $^2J_{C–P}$ = 6 Hz, CH_2), 64.1 (d, $^2J_{C–P}$ = 6 Hz, CH_2), 41.6 (CH_2), 27.2 (CH_3), 25.3 (CH_3), 16.1 (d, $^3J_{C–P}$ = 7 Hz, CH_3), 16.1 (d, $^3J_{C–P}$ = 7 Hz, CH_3), 14.6 (t, $^4J_{C–F}$ = 2 Hz, CH_3), 14.4 (CH_3).

^{11}B-NMR (128 MHz, $CDCl_3$): δ = 0.8 (t, $^1J_{B–F}$ = 33.0 Hz).

^{19}F-NMR (376 MHz, $CDCl_3$): δ = –146.3 (q, $^1J_{F–B}$ = 33.0 Hz).

^{31}P-NMR (162 MHz, $CDCl_3$): δ = (–0.8)–(–1.2) (m).

IR (ATR): $\tilde{\nu}$ = 2927, 1543, 1509, 1306, 1192, 1155, 1020, 972, 752, 643 cm^{-1}.

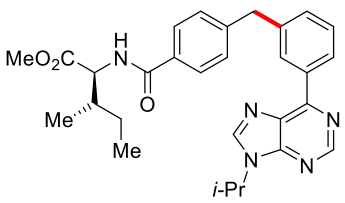
MS (ESI) *m*/*z* (relative intensity): 863 (100) $[M+Na]^+$, 841 (13) $[M+H]^+$, 821 (16) $[M–F]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{43}H_{48}BF_2N_6O_7PNa^+$ $[M+Na]^+$ 863.3283, found 863.3273.

UV-Vis: λ_{max} (1.0 mg/L in $CHCl_3$) = 502 nm.

E_m: λ_{max} (1.0 mg/L in $CHCl_3$) = 514 nm.

Methyl {4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoyl}-*L*-isoleucinate (187c)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride **186b** (149 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **187c** (92.4 mg, 74%) as a viscous colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.00 (s, 1H), 8.68 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 8.60 (dd, *J* = 1.8, 1.6 Hz, 1H), 8.18 (s, 1H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.48 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.31–7.27 (m, 1H), 6.61 (d, *J* = 8.5 Hz, 1H), 4.97 (hept, *J* = 6.8 Hz, 1H), 4.79 (dd, *J* = 8.5, 4.9 Hz, 1H), 4.16 (s, 2H), 3.74 (s, 3H), 2.06–1.85 (m, 1H), 1.66 (d, *J* = 6.8 Hz, 6H), 1.58–1.42 (m, 1H), 1.31–1.13 (m, 1H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H).

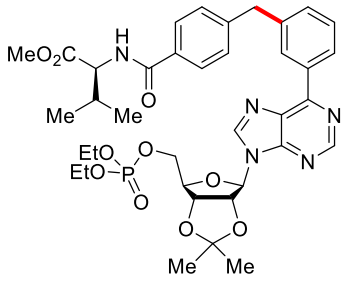
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 172.4 (C_q), 166.8 (C_q), 154.5 (C_q), 152.0 (C_q), 151.9 (CH), 145.0 (C_q), 141.9 (CH), 140.5 (C_q), 136.0 (C_q), 131.9 (C_q), 131.4 (C_q), 131.4 (CH), 129.9 (CH), 129.1 (CH), 128.8 (CH), 128.1 (CH), 127.2 (CH), 56.7 (CH), 52.1 (CH_3), 47.3 (CH), 41.9 (CH_2), 38.3 (CH), 25.4 (CH_2), 22.6 (CH_3), 15.5 (CH_3), 11.7 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3311, 2966, 1737, 1646, 1569, 1496, 1326, 1218, 733, 647 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 499 (9) $[M]^+$, 440 (53) $[M–CO_2Me]^+$, 355 (100) $[M–(H\text{-}Leu\text{-}OMe)]^+$, 328 (19), 285 (32), 156 (12).

HR-MS (EI): *m*/*z* calcd for $C_{29}H_{33}N_5O_3^+$ $[M]^+$ 499.2578, found 499.2586.

Methyl {4-{3-{9-{(3a*R*,4*R*,6*R*,6a*R*)-6-{[(diethoxyphosphoryl)oxy]methyl}-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}-9*H*-purin-6-yl}benzyl}benzoyl}-*L*-valinate (187d)



The general procedure **J** was followed using purine **123l** (126 mg, 0.25 mmol) and benzyl chloride *S*-**186c** (142 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:3) yielded **187d** (110 mg, 59%) as a viscous colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.02 (s, 1H), 8.68 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 8.60 (dd, *J* = 1.8, 1.6 Hz, 1H), 8.29 (s, 1H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.49 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.33 (d, *J* = 8.3 Hz, 2H), 7.31 (ddd, *J* = 7.7, 1.8, 1.4 Hz, 1H), 6.58 (d, *J* = 8.7 Hz, 1H), 6.26 (d, *J* = 2.5 Hz, 1H), 5.45 (dd, *J* = 6.3, 2.5 Hz, 1H), 5.13 (dd, *J* = 6.3, 3.1 Hz, 1H), 4.76 (dd, *J* = 8.7, 4.9 Hz, 1H), 4.53 (dddd, *J* = 4.9, 4.5, 3.1, 1.2 Hz, 1H), 4.29 (ddd, *J* = 11.0, 6.2, 4.5 Hz, 1H), 4.21 (ddd, *J* = 11.0, 6.9, 4.9 Hz, 1H), 4.17 (s, 2H), 4.10–4.00 (m, 4H), 3.76 (s, 3H), 2.25 (pd, *J* = 6.9, 4.9 Hz, 1H), 1.65 (s, 3H), 1.41 (s, 3H), 1.27 (td, *J* = 7.1, 1.0 Hz, 3H), 1.24 (td, *J* = 7.1, 1.0 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 172.5 (C_q), 166.9 (C_q), 155.0 (C_q), 152.4 (CH), 151.6 (C_q), 144.9 (C_q), 143.1 (CH), 140.7 (C_q), 135.7 (C_q), 132.0 (C_q), 131.6 (C_q and CH), 130.0 (CH), 129.1 (CH), 128.9 (CH), 128.2 (CH), 127.3 (CH), 114.7 (C_q), 91.1 (CH), 85.3 (d, $^3J_{C–P}$ = 8 Hz, CH), 84.2 (CH), 81.4 (CH), 66.6 (d, $^2J_{C–P}$ = 6 Hz, CH_2), 64.0 (d, $^2J_{C–P}$ = 6 Hz, CH_2), 63.9 (d, $^2J_{C–P}$ = 6 Hz, CH_2), 57.4 (CH), 52.2 (CH_3), 41.9 (CH_2), 31.7 (CH), 27.3 (CH_3), 25.4 (CH_3), 19.1 (CH_3), 18.0 (CH_3), 16.1 (d, $^3J_{C–P}$ = 7 Hz, CH_3).

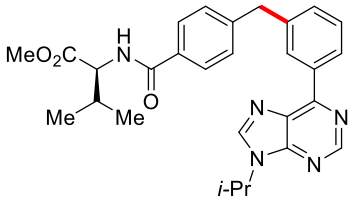
^{31}P{^{1}H }-NMR (121 MHz, $CDCl_3$): δ = –1.1 (s).

IR (ATR): $\tilde{\nu}$ = 3327, 2981, 1739, 1648, 1569, 1498, 1260, 1209, 1020, 733 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 774 (33) $[M+Na]^+$, 752 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{37}H_{47}N_5O_{10}P^+$ $[M+H]^+$ 752.3055, found 752.3055.

Methyl {4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoyl}-*L*-valinate (*S*-187e)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride *S*-**186c** (142 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded *S*-**187e** (85.3 mg, 70%) as a white solid.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.00 (s, 1H), 8.68 (ddd, *J* = 7.8, 1.6, 1.2 Hz, 1H), 8.60 (dd, *J* = 1.8, 1.6 Hz, 1H), 8.18 (s, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.49 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.30 (ddd, *J* = 7.7, 1.8, 1.2 Hz, 1H), 6.57 (d, *J* = 8.7 Hz, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.76 (dd, *J* = 8.7, 4.9 Hz, 1H), 4.17 (s, 2H), 3.75 (s, 3H), 2.25 (heptd, *J* = 6.9, 4.9 Hz, 1H), 1.67 (d, *J* = 6.8 Hz, 6H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 172.5 (C_q), 167.0 (C_q), 154.5 (C_q), 152.0 (C_q), 151.9 (CH), 145.0 (C_q), 141.9 (CH), 140.6 (C_q), 136.1 (C_q), 132.0 (C_q), 131.4 (C_q), 131.4 (CH), 129.9 (CH), 129.1 (CH), 128.9 (CH), 128.1 (CH), 127.2 (CH), 57.4 (CH), 52.2 (CH_3), 47.3 (CH), 41.9 (CH_2), 31.7 (CH), 22.6 (CH_3), 19.1 (CH_3), 18.0 (CH_3).

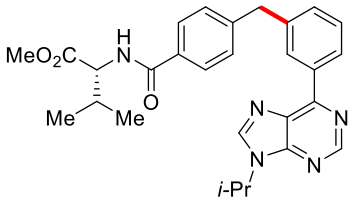
IR (ATR): $\tilde{\nu}$ = 3321, 2965, 1737, 1644, 1568, 1495, 1325, 1214, 783, 646 cm^{-1}.

m.p.: 62–64 °C.

MS (EI) *m*/*z* (relative intensity): 485 (14) $[M]^+$, 453 (8) $[M–OMe]^+$, 426 (49) $[M–CO_2Me]^+$, 355 (100) $[M–(H\text{-}Val\text{-}OMe)]^+$, 328 (23), 285 (34), 165 (7), 156 (13), 142 (8), 43 (16).

HR-MS (EI): *m*/*z* calcd for $C_{28}H_{31}N_5O_3^+$ $[M]^+$ 485.2421, found 485.2409.

Methyl {4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoyl}-*D*-valinate (*R*-187e)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride *R*-**186c** (142 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded *R*-**187e** (92.9 mg, 77%) as a viscous colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.68 (ddd, *J* = 7.8, 1.5, 1.3 Hz, 1H), 8.61 (dd, *J* = 1.7, 1.5 Hz, 1H), 8.18 (s, 1H), 7.73 (d, *J* = 8.5 Hz, 2H), 7.49 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.33 (d, *J* = 8.5 Hz, 2H), 7.30 (ddd, *J* = 7.7, 1.7, 1.3 Hz, 1H), 6.57 (d, *J* = 8.7 Hz, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.76 (dd,

J = 8.7, 4.9 Hz, 1H), 4.18 (s, 2H), 3.76 (s, 3H), 2.25 (pd, *J* = 6.9, 4.9 Hz, 1H), 1.67 (d, *J* = 6.8 Hz, 6H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H).

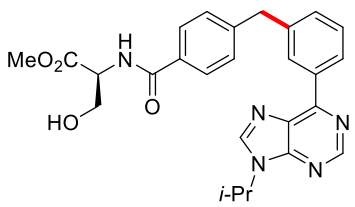
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 172.5 (C_q), 167.0 (C_q), 154.5 (C_q), 152.0 (C_q), 151.9 (CH), 145.0 (C_q), 141.9 (CH), 140.6 (C_q), 136.1 (C_q), 132.0 (C_q), 131.5 (C_q), 131.4 (CH), 129.9 (CH), 129.2 (CH), 128.9 (CH), 128.1 (CH), 127.2 (CH), 57.4 (CH), 52.2 (CH_3), 47.3 (CH), 41.9 (CH_2), 31.7 (CH), 22.7 (CH_3), 19.1 (CH_3), 18.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3319, 2966, 1736, 1644, 1568, 1495, 1325, 1213, 703, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 485 (10) $[M]^+$, 426 (46) $[M–CO_2Me]^+$, 355 (100) $[M–(H\text{-}Val\text{-}OMe)]^+$, 328 (15), 285 (31), 156 (14).

HR-MS (ESI): *m*/*z* calcd for $C_{28}H_{32}N_5O_3^+$ $[M+H]^+$ 486.2500, found 486.2497.

Methyl {4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoyl}-*L*-serinate (*S*-187f)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride *S*-**186d** (136 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:9) yielded *S*-**187f** (59.1 mg, 50%) as a colorless oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.99 (s, 1H), 8.64 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 8.55 (dd, *J* = 1.7, 1.6 Hz, 1H), 8.19 (s, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.48 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.30–7.26 (m, 1H), 7.28 (d, *J* = 8.3 Hz, 2H), 7.12 (d, *J* = 7.3 Hz, 1H), 4.97 (hept, *J* = 6.8 Hz, 1H), 4.81 (ddd, *J* = 7.3, 3.7, 3.5 Hz, 1H), 4.14 (s, 2H), 4.02 (dd, *J* = 11.2, 3.7 Hz, 1H), 3.97 (dd, *J* = 11.2, 3.5 Hz, 1H), 3.77 (s, 3H), 3.18 (br s, 1H), 1.66 (d, *J* = 6.8 Hz, 6H).

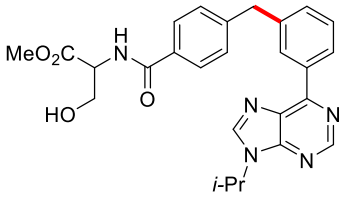
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 171.0 (C_q), 167.5 (C_q), 154.6 (C_q), 152.1 (C_q), 152.0 (CH), 145.3 (C_q), 142.1 (CH), 140.6 (C_q), 136.0 (C_q), 131.5 (CH), 131.4 (C_q), 131.3 (C_q), 130.0 (CH), 129.2 (CH), 129.0 (CH), 128.2 (CH), 127.4 (CH), 63.4 (CH_2), 55.1 (CH), 52.8 (CH_3), 47.3 (CH), 41.8 (CH_2), 22.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3355, 2980, 1741, 1644, 1569, 1497, 1326, 1219, 703, 647 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 473 (7) $[M]^+$, 472 (5) $[M–H]^+$, 455 (5) $[M–H_2O]^+$, 443 (32) $[M–CHOH]^+$, 414 (8) $[M–CO_2Me]^+$, 400 (13), 372 (12), 355 (100) $[M–(H\text{-}Ser\text{-}OMe)]^+$, 328 (23), 285 (41), 165 (10), 156 (20), 142 (13).

HR-MS (EI): *m*/*z* calcd for $C_{26}H_{27}N_5O_4^+$ $[M]^+$ 473.2058, found 473.2079.

Methyl {4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoyl}-*D*/*L*-serinate (*rac*-187f)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride *rac*-**186d** (136 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:9) yielded *rac*-**187f** (65.5 mg, 55%) as a white solid.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.99 (s, 1H), 8.65 (ddd, *J* = 7.8, 1.6, 1.5 Hz, 1H), 8.57 (dd, *J* = 1.6, 1.6 Hz, 1H), 8.18 (s, 1H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.48 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.31–7.28 (m, 1H), 7.29 (d, *J* = 8.3 Hz, 2H), 7.09 (d, *J* = 7.2 Hz, 1H), 4.97 (hept, *J* = 6.8 Hz, 1H), 4.83 (ddd, *J* = 7.2, 3.7, 3.5 Hz, 1H), 4.15 (s, 2H), 4.03 (dd, *J* = 11.3, 3.7 Hz, 1H), 3.99 (dd, *J* = 11.3, 3.5 Hz, 1H), 3.78 (s, 3H), 3.01 (br s, 1H), 1.66 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.9 (C_q), 167.3 (C_q), 154.5 (C_q), 152.0 (C_q), 151.9 (CH), 145.3 (C_q), 142.0 (CH), 140.5 (C_q), 136.0 (C_q), 131.4 (C_q and CH), 131.3 (C_q), 129.9 (CH), 129.1 (CH), 128.9 (CH), 128.1 (CH), 127.3 (CH), 63.5 (CH_2), 55.2 (CH), 52.8 (CH_3), 47.3 (CH), 41.9 (CH_2), 22.6 (CH_3).

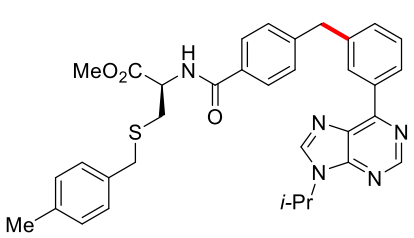
IR (ATR): $\tilde{\nu}$ = 3333, 2976, 1739, 1643, 1569, 1496, 1326, 1218, 703, 646 cm^{-1}.

m.p.: 73–75 °C.

MS (EI) *m*/*z* (relative intensity): 473 (4) $[M]^+$, 472 (3) $[M–H]^+$, 455 (11) $[M–H_2O]^+$, 443 (29) $[M–CHOH]^+$, 414 (5) $[M–CO_2Me]^+$, 400 (9), 372 (7), 355 (100) $[M–(H\text{-}Ser\text{-}OMe)]^+$, 328 (16), 311 (14), 285 (38), 165 (9), 156 (20), 142 (13).

HR-MS (EI): *m*/*z* calcd for $C_{26}H_{27}N_5O_4^+$ $[M]^+$ 473.2058, found 473.2055.

Methyl *N*-{4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoyl}-*S*-(4-methylbenzyl)-*L*-cysteinate (187g)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride **186e** (196 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **187g** (117 mg, 79%) as a viscous colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.69 (ddd, *J* = 7.8, 1.6, 1.3 Hz, 1H), 8.62 (dd, *J* = 1.9, 1.6 Hz, 1H), 8.18 (s, 1H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.49 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.33 (d, *J* = 8.3 Hz,

2H), 7.30 (ddd, *J* = 7.7, 1.9, 1.3 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 2H), 7.06 (d, *J* = 7.8 Hz, 2H), 6.86 (d, *J* = 7.5 Hz, 1H), 4.98 (hept, *J* = 6.9 Hz, 1H), 4.98 (ddd, *J* = 7.5, 5.3, 5.1 Hz, 1H), 4.17 (s, 2H), 3.76 (s, 3H), 3.67 (d_{AB}, *J* = 13.5 Hz, 1H), 3.66 (d_{AB}, *J* = 13.5 Hz, 1H), 3.01 (d_{AB}d, *J* = 13.9, 5.1 Hz, 1H), 2.96 (d_{AB}d, *J* = 13.9, 5.3 Hz, 1H), 2.27 (s, 3H), 1.67 (d, *J* = 6.9 Hz, 6H).

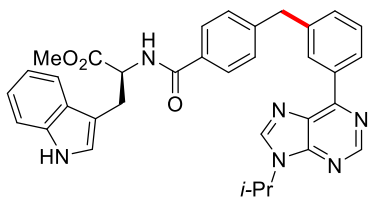
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 171.2 (C_q), 166.7 (C_q), 154.5 (C_q), 152.0 (C_q), 151.9 (CH), 145.2 (C_q), 141.9 (CH), 140.5 (C_q), 136.8 (C_q), 136.1 (C_q), 134.4 (C_q), 131.4 (C_q), 131.4 (CH), 129.9 (CH), 129.2 (CH), 129.1 (CH), 128.8 (CH), 128.6 (CH), 128.1 (CH), 127.3 (CH), 52.7 (CH_3), 52.0 (CH), 47.3 (CH), 41.9 (CH_2), 36.5 (CH_2), 33.5 (CH_2), 22.6 (CH_3), 21.1 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3329, 2979, 1741, 1650, 1569, 1494, 1325, 1216, 731, 647 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 1209 (16) $[2M+Na]^+$, 1187 (9) $[2M+H]^+$, 616 (100) $[M+Na]^+$, 594 (47) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{34}H_{35}N_5O_3SNa^+$ $[M+Na]^+$ 616.2353, found 616.2372.

Methyl {4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoyl}-*L*-tryptophanate (187h)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride **186f** (186 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:2) yielded **187h** (96.5 mg, 67%) as a viscous colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.67 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 8.58 (dd, *J* = 1.8, 1.6 Hz, 1H), 8.23 (br s, 1H), 8.18 (s, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.53 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.48 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.32 (d, *J* = 8.2, 1.0 Hz, 1H), 7.30–7.26 (m, 1H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.16 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 7.06 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 6.97 (d, *J* = 2.4 Hz, 1H), 6.63 (d, *J* = 7.7 Hz, 1H), 5.12 (dt, *J* = 7.7, 5.3 Hz, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.13 (s, 2H), 3.69 (s, 3H), 3.42 (d, *J* = 5.3 Hz, 2H), 1.67 (d, *J* = 6.8 Hz, 6H).

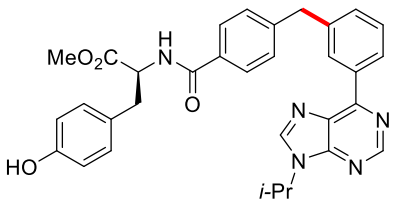
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 172.2 (C_q), 166.6 (C_q), 154.5 (C_q), 152.0 (C_q), 151.8 (CH), 144.9 (C_q), 142.0 (CH), 140.6 (C_q), 136.0 (C_q), 135.9 (C_q), 131.7 (C_q), 131.4 (CH), 131.4 (C_q), 129.9 (CH), 129.1 (CH), 128.9 (CH), 128.1 (CH), 127.5 (C_q), 127.2 (CH), 122.7 (CH), 122.2 (CH), 119.6 (CH), 118.6 (CH), 111.2 (CH), 110.0 (C_q), 53.4 (CH), 52.4 (CH_3), 47.3 (CH), 41.8 (CH_2), 27.7 (CH_2), 22.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3300, 2980, 1737, 1644, 1570, 1495, 1327, 1218, 736, 647 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 1168 (5) $[2M+Na]^+$, 1145 (19) $[2M+H]^+$, 595 (10) $[M+Na]^+$, 573 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{34}H_{33}N_6O_3^+$ $[M+H]^+$ 573.2609, found 573.2608.

Methyl {4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoyl}-*L*-tyrosinate (187i)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride **186g** (174 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:2) yielded **187i** (72.2 mg, 53%) as a viscous colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.62 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 8.53 (dd, *J* = 1.8, 1.6 Hz, 1H), 8.20 (s, 1H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.45 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.28–7.25 (m, 1H), 7.23 (d, *J* = 8.3 Hz, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 6.86 (br s, 1H), 6.69 (d, *J* = 8.5 Hz, 2H), 6.59 (d, *J* = 7.7 Hz, 1H), 5.00 (dt, *J* = 7.7, 5.6 Hz, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.10 (s, 2H), 3.72 (s, 3H), 3.16 (dd, *J* = 14.0, 5.6 Hz, 1H), 3.09 (dd, *J* = 14.0, 5.6 Hz, 1H), 1.66 (d, *J* = 6.8 Hz, 6H).

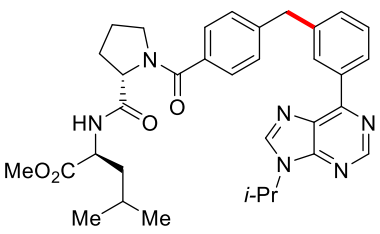
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 172.0 (C_q), 166.8 (C_q), 155.3 (C_q), 154.7 (C_q), 152.0 (C_q), 151.9 (CH), 145.1 (C_q), 142.1 (CH), 140.6 (C_q), 135.8 (C_q), 131.6 (C_q), 131.5 (CH), 131.3 (C_q), 130.3 (CH), 130.0 (CH), 129.1 (CH), 128.9 (CH), 128.1 (CH), 127.2 (CH), 127.1 (C_q), 115.6 (CH), 53.7 (CH), 52.4 (CH_3), 47.4 (CH), 41.8 (CH_2), 37.1 (CH_2), 22.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3269, 2978, 1736, 1639, 1569, 1326, 1217, 784, 703, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 549 (3) $[M]^+$, 490 (5) $[M–CO_2Me]^+$, 443 (100) [M–(4-OHBn)]$^+$, 400 (40) [M–(4-OHBn)–*i*Pr]$^+$, 372 (24), 355 (58) [M–(H-Tyr-OMe)]$^+$, 328 (37), 313 (18), 285 (45), 178 (8), 147 (7), 107 (19), 43 (8).

HR-MS (EI): *m*/*z* calcd for $C_{32}H_{31}N_5O_4^+$ $[M]^+$ 549.2371, found 549.2387.

Methyl {4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoyl}-*L*-prolyl-*L*-leucinate (187j)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride **186h** (198 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:4) yielded **187j** (107 mg, 72%) as a viscous colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.99 (s, 1H), 8.68 (d, *J* = 7.8 Hz, 1H), 8.58 (s, 1H), 8.18 (s, 1H), 7.48 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.78 (dd, *J* = 7.9, 4.7 Hz, 1H), 4.54 (ddd, *J* = 8.0, 7.8, 4.5 Hz, 1H), 4.14 (s, 2H), 3.71 (s, 3H), 3.54–3.48 (m, 1H), 3.48–3.42 (m, 1H), 2.48–2.38 (m, 1H), 2.06–1.97 (m, 2H), 1.83–1.75 (m, 1H), 1.66 (d, *J* = 6.8 Hz, 6H), 1.67–1.53 (m, 3H), 0.88 (d, *J* = 6.1 Hz, 3H), 0.87 (d, *J* = 6.4 Hz, 3H).

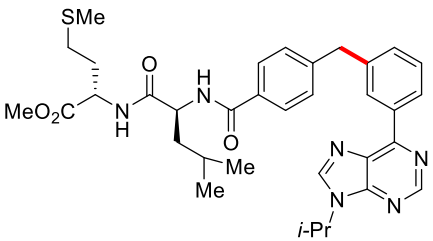
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 173.0 (C_q), 170.9 (C_q), 170.7 (C_q), 154.5 (C_q), 152.0 (C_q), 151.9 (CH), 143.4 (C_q), 141.9 (CH), 140.6 (C_q), 136.0 (C_q), 133.9 (C_q), 131.4 (C_q and CH), 129.9 (CH), 128.8 (CH), 128.8 (CH), 128.1 (CH), 127.2 (CH), 59.6 (CH), 52.2 (CH_3), 51.1 (CH), 50.4 (CH_2), 47.3 (CH), 41.9 (CH_2), 41.2 (CH_2), 27.0 (CH_2), 25.5 (CH_2), 25.0 (CH), 22.8 (CH_3), 22.6 (CH_3), 21.9 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3282, 2957, 1743, 1681, 1614, 1570, 1428, 1327, 1221, 648 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 596 (5) $[M]^+$, 424 (30) [M–(C(O)-Leu-OMe)]$^+$, 355 (100) [M–(H-Pro-Leu-OMe)]$^+$, 328 (11), 285 (18), 156 (9), 43 (6).

HR-MS (EI): *m*/*z* calcd for $C_{34}H_{40}N_6O_4^+$ $[M]^+$ 596.3106, found 596.3124.

Methyl {4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoyl}-*L*-leucyl-*L*-methioninate (187k)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride **186i** (215 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:2) yielded **187k** (117 mg, 74%) as a viscous colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.00 (s, 1H), 8.68 (ddd, *J* = 7.8, 1.6, 1.3 Hz, 1H), 8.59 (dd, *J* = 1.9, 1.6 Hz, 1H), 8.19 (s, 1H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.48 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.30 (d, *J* = 8.3 Hz, 2H), 7.28 (ddd, *J* = 7.7, 1.9, 1.3 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.61 (d, *J* = 8.2 Hz, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.72–4.66 (m, 2H), 4.15 (s, 2H), 3.74 (s, 3H), 2.45 (t, *J* = 7.4 Hz, 2H), 2.17–2.09 (m,

1H), 2.02–1.93 (m, 1H), 1.99 (s, 3H), 1.79–1.61 (m, 3H), 1.67 (d, *J* = 6.8 Hz, 6H), 0.95 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.3 Hz, 3H).

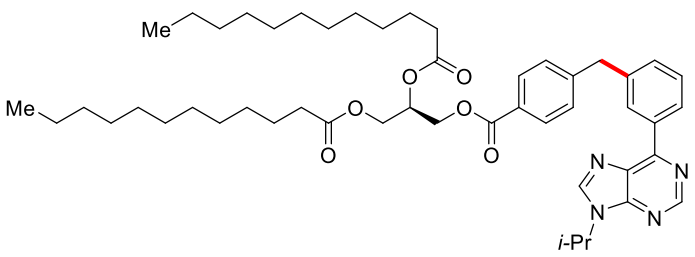
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 171.9 (C_q), 171.7 (C_q), 167.1 (C_q), 154.4 (C_q), 152.0 (C_q), 151.8 (CH), 145.2 (C_q), 142.0 (CH), 140.5 (C_q), 135.9 (C_q), 131.5 (C_q), 131.4 (C_q and CH), 129.9 (CH), 129.2 (CH), 128.9 (CH), 128.1 (CH), 127.2 (CH), 52.5 (CH_3), 52.0 (CH), 51.6 (CH), 47.3 (CH), 41.9 (CH_2), 41.1 (CH_2), 31.5 (CH_2), 30.0 (CH_2), 24.9 (CH), 22.9 (CH_3), 22.6 (CH_3), 22.3 (CH_3), 15.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3272, 2954, 1742, 1632, 1568, 1325, 1218, 784, 703, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 630 (1) $[M]^+$, 615 (1) $[M–Me]^+$, 569 (6) $[M–SMe_2]^+$, 556 (33) $[M–EtSMe]^+$, 500 (32) $[M–EtSMe–Bu]^+$, 468 (11) $[M–EtSMe–Bu–OMe]^+$, 440 (20) $[M–EtSMe–Bu–CO_2Me]^+$, 355 (100) $[M–(H\text{-}Leu\text{-}Met\text{-}OMe)]^+$, 328 (17), 313 (7), 285 (30), 156 (10), 43 (8).

HR-MS (EI): *m*/*z* calcd for $C_{34}H_{42}N_6O_4S^+$ $[M]^+$ 630.2983, found 630.2984.

(*R*)-3-{{4-[3-(9-*iso*-Propyl-9*H*-purin-6-yl)benzyl]benzoyl}oxy}propane-1,2-diyl didodecanoate (*R*-187l)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride *R*-**186j** (305 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 4:1) yielded *R*-**187l** (153 mg, 75%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.70 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 8.62 (dd, *J* = 1.8, 1.6 Hz, 1H), 8.18 (s, 1H), 7.93 (d, *J* = 8.3 Hz, 2H), 7.49 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.31–7.27 (m, 1H), 5.40 (dddd, *J* = 6.0, 5.9, 4.4, 4.3 Hz, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.49 (d_{AB}d, *J* = 11.9, 4.3 Hz, 1H), 4.39 (d_{AB}d, *J* = 11.9, 6.0 Hz, 1H), 4.37 (dd, *J* = 11.9, 4.4 Hz, 1H), 4.22 (dd, *J* = 11.9, 5.9 Hz, 1H), 4.18 (s, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.31 (t, *J* = 7.6 Hz, 2H), 1.68 (d, *J* = 6.8 Hz, 6H), 1.64–1.55 (m, 4H), 1.33–1.17 (m, 32H), 0.87 (t, *J* = 7.0 Hz, 3H), 0.87 (t, *J* = 7.1 Hz, 3H).

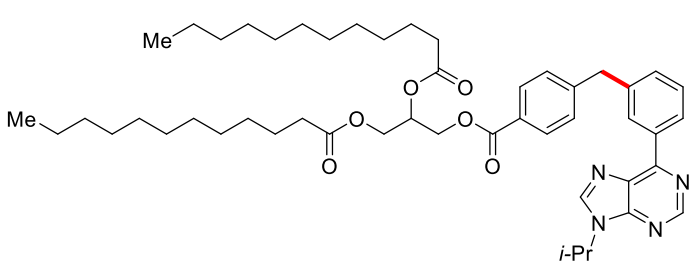
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 173.3 (C_q), 172.9 (C_q), 165.9 (C_q), 154.6 (C_q), 152.1 (C_q), 152.0 (CH), 146.9 (C_q), 142.0 (CH), 140.4 (C_q), 136.2 (C_q), 131.5 (C_q), 131.5 (CH), 130.0 (CH), 130.0 (CH), 129.1 (CH), 129.0 (CH), 128.3 (CH), 127.5 (C_q), 68.9 (CH), 62.7 (CH_2), 62.2 (CH_2), 47.2 (CH), 42.0 (CH_2), 34.2 (CH_2), 34.0 (CH_2), 31.9 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 24.9 (CH_2), 24.8 (CH_2), 22.7 (CH_2), 22.6 (CH_3), 14.1 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2923, 2853, 1726, 1569, 1326, 1269, 1102, 783, 703, 647 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 1622 (33) $[2M+H]^+$, 834 (32) $[M+Na]^+$, 812 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{49}H_{71}N_4O_6^+$ $[M+H]^+$ 811.5368, found 811.5372.

3-{{4-[3-(9-*iso*-Propyl-9*H*-purin-6-yl)benzyl]benzoyl}oxy}propane-1,2-diyl didodecanoate (*rac*-187l)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride *rac*-**186j** (305 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 4:1) yielded *rac*-**187l** (153 mg, 75%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.00 (s, 1H), 8.70 (ddd, *J* = 7.8, 1.7, 1.5 Hz, 1H), 8.62 (dd, *J* = 1.8, 1.7 Hz, 1H), 8.18 (s, 1H), 7.93 (d, *J* = 8.3 Hz, 2H), 7.49 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.31–7.27 (m, 1H), 5.40 (dddd, *J* = 5.9, 5.8, 4.3, 4.2 Hz, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.48 (d_{AB}d, *J* = 11.9, 4.3 Hz, 1H), 4.39 (d_{AB}d, *J* = 11.9, 5.8 Hz, 1H), 4.37 (dd, *J* = 11.9, 4.2 Hz, 1H), 4.22 (dd, *J* = 11.9, 5.9 Hz, 1H), 4.17 (s, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.67 (d, *J* = 6.8 Hz, 6H), 1.65–1.53 (m, 4H), 1.34–1.15 (m, 32H), 0.86 (t, *J* = 6.6 Hz, 3H), 0.86 (t, *J* = 6.6 Hz, 3H).

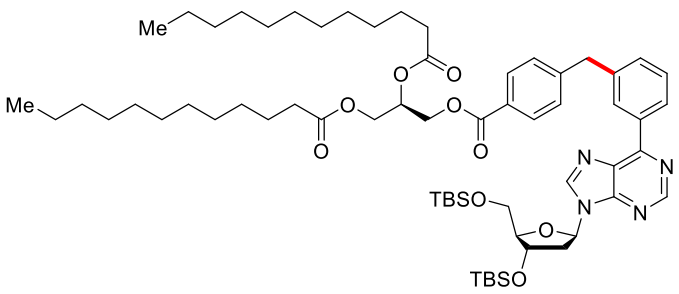
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 173.1 (C_q), 172.7 (C_q), 165.8 (C_q), 154.4 (C_q), 152.0 (C_q), 151.9 (CH), 146.7 (C_q), 141.9 (CH), 140.3 (C_q), 136.1 (C_q), 131.4 (C_q), 131.3 (CH), 129.9 (CH), 129.9 (CH), 129.0 (CH), 128.9 (CH), 128.2 (CH), 127.4 (C_q), 68.9 (CH), 62.7 (CH_2), 62.2 (CH_2), 47.3 (CH), 42.0 (CH_2), 34.3 (CH_2), 34.1 (CH_2), 31.9 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 29.1 (CH_2), 25.0 (CH_2), 24.9 (CH_2), 22.7 (CH_2), 22.6 (CH_3), 14.2 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2922, 2853, 1725, 1569, 1326, 1269, 1102, 783, 704, 647 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 834 (1) $[M+Na]^+$, 812 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{49}H_{71}N_4O_6^+$ $[M+H]^+$ 811.5368, found 811.5352.

(*R*)-3-{{4-{3-{9-{(2*R*,4*R*,5*R*)-4-[(*tert*-Butyldimethylsilyl)oxy]-5-{[(*tert*-butyldimethylsilyl)oxy]methyl}tetrahydrofuran-2-yl}-9*H*-purin-6-yl}benzyl}benzoyl}oxy}propane-1,2-diyl didodecanoate (187m)



The general procedure **J** was followed using purine **123m** (135 mg, 0.25 mmol) and benzyl chloride *R*-**186j** (305 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 6:1) yielded **187m** (195 mg, 70%) as a yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.99 (s, 1H), 8.70 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 8.61 (dd, *J* = 1.8, 1.6 Hz, 1H), 8.42 (s, 1H), 7.93 (d, *J* = 8.3 Hz, 2H), 7.49 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.31–7.27 (m, 1H), 6.57 (dd, *J* = 6.7, 6.3 Hz, 1H), 5.40 (dddd, *J* = 6.0, 5.9, 4.4, 4.3 Hz, 1H), 4.65 (ddd, *J* = 5.9, 3.6, 3.3 Hz, 1H), 4.49 (d_{AB}d, *J* = 11.9, 4.3 Hz, 1H), 4.40 (d_{AB}d, *J* = 11.9, 6.0 Hz, 1H), 4.37 (dd, *J* = 11.9, 4.4 Hz, 1H), 4.22 (dd, *J* = 11.9, 5.9 Hz, 1H), 4.17 (s, 2H), 4.06 (ddd, *J* = 4.3, 3.3, 3.3 Hz, 1H), 3.88 (d_{AB}d, *J* = 11.2, 4.3 Hz, 1H), 3.80 (d_{AB}d, *J* = 11.2, 3.3 Hz, 1H), 2.71 (ddd, *J* = 13.0, 6.7, 5.9 Hz, 1H), 2.49 (ddd, *J* = 13.0, 6.3, 3.6 Hz, 1H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.31 (t, *J* = 7.6 Hz, 2H), 1.67–1.54 (m, 4H), 1.33–1.17 (m, 32H), 0.93 (s, 9H), 0.91 (s, 9H), 0.87 (t, *J* = 6.9 Hz, 3H), 0.87 (t, *J* = 6.9 Hz, 3H), 0.12 (s, 6H), 0.09 (s, 3H), 0.09 (s, 3H).

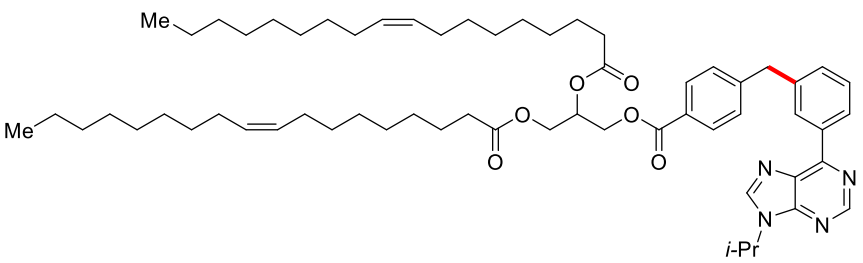
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 173.3 (C_q), 172.9 (C_q), 165.9 (C_q), 154.7 (C_q), 152.2 (CH), 152.0 (C_q), 146.9 (C_q), 142.8 (CH), 140.4 (C_q), 136.0 (C_q), 131.7 (C_q), 131.5 (CH), 130.0 (CH), 129.1 (CH), 129.0 (CH), 128.4 (CH), 127.5 (C_q), 88.0 (CH), 84.5 (CH), 72.0 (CH), 68.9 (CH), 62.8 (CH_2), 62.7 (CH_2), 62.2 (CH_2), 42.0 (CH_2), 41.1 (CH_2), 34.2 (CH_2), 34.0 (CH_2), 31.9 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 25.9 (CH_3), 25.8 (CH_3), 24.9 (CH_2), 24.8 (CH_2), 22.7 (CH_2), 18.4 (C_q), 18.0 (C_q), 14.1 (CH_3), –4.7 (CH_3), –4.8 (CH_3), –5.4 (CH_3), –5.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2925, 2854, 1727, 1570, 1256, 1107, 835, 778, 703, 646 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 2227 (38) $[2M+H]^+$, 1136 (39) $[M+Na]^+$, 1114 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{63}H_{101}N_4O_9Si_2^+$ $[M+H]^+$ 1113.7102, found 1113.7102.

3-{{4-[3-(9-*iso*-Propyl-9*H*-purin-6-yl)benzyl]benzoyl}oxy}propane-1,2-diyl dioleate (187n)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride **186k** (387 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 4:1) yielded **187n** (174 mg, 71%) as a pale yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.00 (s, 1H), 8.70 (ddd, *J* = 7.8, 1.7, 1.5 Hz, 1H), 8.62 (dd, *J* = 1.8, 1.7 Hz, 1H), 8.18 (s, 1H), 7.93 (d, *J* = 8.3 Hz, 2H), 7.49 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.31–7.27 (m, 1H), 5.44–5.25 (m, 5H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.48 (d_{AB}d, *J* = 11.9, 4.3 Hz, 1H), 4.39 (d_{AB}d, *J* = 11.9, 5.6 Hz, 1H), 4.37 (dd, *J* = 11.9, 4.1 Hz, 1H), 4.22 (dd, *J* = 11.9, 5.9 Hz, 1H), 4.18 (s, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 2.08–1.91 (m, 8H), 1.67 (d, *J* = 6.8 Hz, 6H), 1.64–1.52 (m, 4H), 1.37–1.18 (m, 40H), 0.87 (t, *J* = 6.6 Hz, 3H), 0.87 (t, *J* = 6.6 Hz, 3H).

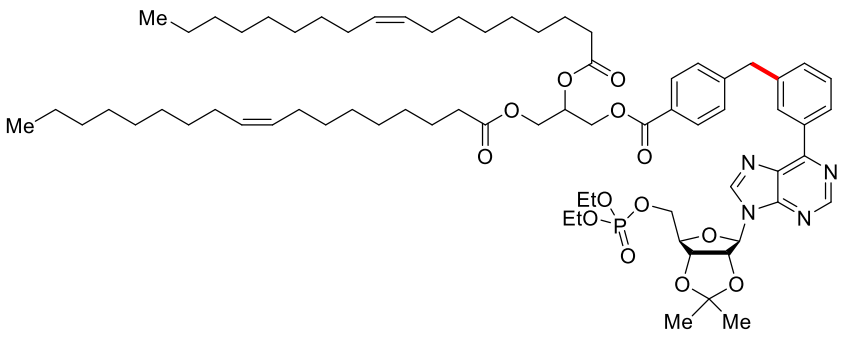
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 173.1 (C_q), 172.7 (C_q), 165.8 (C_q), 154.4 (C_q), 152.0 (C_q), 151.9 (CH), 146.7 (C_q), 141.8 (CH), 140.3 (C_q), 136.1 (C_q), 131.4 (C_q), 131.3 (CH), 129.9 (CH), 129.9 (CH), 129.6 (CH), 129.6 (CH), 129.0 (CH), 128.8 (CH), 128.2 (CH), 127.4 (C_q), 68.9 (CH), 62.7 (CH_2), 62.2 (CH_2), 47.3 (CH), 42.0 (CH_2), 34.2 (CH_2), 34.1 (CH_2), 31.9 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.1 (CH_2), 29.1 (CH_2), 27.3 (CH_2), 27.2 (CH_2), 24.9 (CH_2), 24.9 (CH_2), 22.7 (CH_2), 22.6 (CH_3), 14.2 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2923, 2853, 1726, 1570, 1458, 1269, 1175, 1096, 703, 647 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 1951 (14) $[2M+H]^+$, 976 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{61}H_{91}N_4O_6^+$ $[M+H]^+$ 975.6933, found 975.6929.

3-{{4-{3-{9-{(3a*R*,4*R*,6*R*,6a*R*)-6-{[(Diethoxyphosphoryl)oxy]methyl}-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}-9*H*-purin-6-yl}benzyl}benzoyl}oxy}propane-1,2-diyl dioleate (187o)



The general procedure **J** was followed using purine **123l** (126 mg, 0.25 mmol) and benzyl chloride **186k** (387 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:2) yielded **187o** (172 mg, 55%) as a greenish yellow oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.69 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 8.61 (dd, *J* = 1.9, 1.6 Hz, 1H), 8.28 (s, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.48 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.31–7.28 (m, 1H), 6.26 (d, *J* = 2.6 Hz, 1H), 5.45 (dd, *J* = 6.3, 2.6 Hz, 1H), 5.39 (dddd, *J* = 6.0, 5.9, 4.3, 4.3 Hz, 1H), 5.36–5.27 (m, 4H), 5.13 (dd, *J* = 6.3, 3.1 Hz, 1H), 4.53 (dddd, *J* = 4.5, 4.5, 3.1, 1.1 Hz, 1H), 4.48 (d_{AB}d, *J* = 11.9, 4.3 Hz, 1H), 4.38 (d_{AB}d, *J* = 11.9, 6.0 Hz, 1H), 4.36 (dd, *J* = 11.9, 4.3 Hz, 1H), 4.29 (ddd, *J* = 10.9, 6.3, 4.5 Hz, 1H), 4.21 (dd, *J* = 11.9, 5.9 Hz, 1H), 4.20 (ddd, *J* = 10.9, 6.8, 4.5 Hz, 1H), 4.17 (s, 2H), 4.09–4.00 (m, 4H), 2.30 (t, *J* = 7.5 Hz, 2H), 2.30 (t, *J* = 7.6 Hz, 2H), 2.06–1.95 (m, 8H), 1.64 (s, 3H), 1.63–1.55 (m, 4H), 1.41 (s, 3H), 1.36–1.19 (m, 46H), 0.86 (t, *J* = 7.2 Hz, 3H), 0.86 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 173.1 (C_q), 172.7 (C_q), 165.7 (C_q), 154.9 (C_q), 152.3 (CH), 151.6 (C_q), 146.6 (C_q), 143.1 (CH), 140.4 (C_q), 135.7 (C_q), 131.6 (C_q and CH), 129.9 (CH), 129.9 (CH), 129.8 (CH), 129.6 (CH), 129.6 (CH), 129.0 (CH), 128.9 (CH), 128.3 (CH), 127.4 (C_q), 114.6 (C_q), 91.0 (CH), 85.3 (d, $^{3}J_{C-P}$ = 8 Hz, CH), 84.2 (CH), 81.3 (CH), 68.9 (CH), 66.6 (d, $^{2}J_{C-P}$ = 6 Hz, CH_2), 64.1 (d, $^{2}J_{C-P}$ = 5 Hz, CH_2), 64.1 (d, $^{2}J_{C-P}$ = 5 Hz, CH_2), 62.7 (CH_2), 62.2 (CH_2), 42.0 (CH_2), 34.2 (CH_2), 34.1 (CH_2), 31.9 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 27.3 (CH_2), 27.2 (CH_3), 27.2 (CH_2), 25.4 (CH_3), 24.9 (CH_2), 24.9 (CH_2), 22.7 (CH_2), 16.11 (d, $^{3}J_{C-P}$ = 7 Hz, CH_3), 14.2 (CH_3).

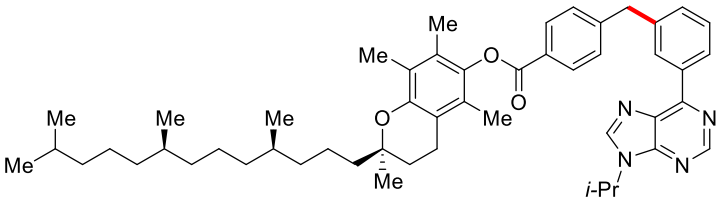
^{31}P-NMR (162 MHz, $CDCl_3$): δ = (–0.8)–(–1.2) (m).

IR (ATR): $\tilde{\nu}$ = 2923, 2853, 1741, 1569, 1268, 1097, 1021, 703, 645 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 2484 (15) $[2M+H]^+$, 1264 (32) $[M+Na]^+$, 1242 (100) $[M+H]^+$, 632 (4) $[M+H+Na]^{2+}$.

HR-MS (ESI): *m*/*z* calcd for $C_{70}H_{106}N_4O_{13}P^+$ $[M+H]^+$ 1241.7489, found 1241.7480.

(*R*)-2,5,7,8-Tetramethyl-2-[(4*R*,8*R*)-4,8,12-trimethyltridecyl]chroman-6-yl 4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoate (187p)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride **186l** (292 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **187p** (127 mg, 65%) as a viscous pale yellow oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.03 (s, 1H), 8.73 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 8.68 (dd, *J* = 1.7, 1.6 Hz, 1H), 8.19 (s, 1H), 8.18 (d, *J* = 8.3 Hz, 2H), 7.52 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.36 (ddd, *J* = 7.7, 1.7, 1.4 Hz, 1H), 4.99 (hept, *J* = 6.8 Hz, 1H), 4.23 (s, 2H), 2.61 (dd, *J* = 7.0, 6.8 Hz, 2H), 2.12 (s, 3H), 2.05 (s, 3H), 2.01 (s, 3H), 1.83 (dt, *J* = 13.9, 7.0 Hz, 1H), 1.80–1.73 (m, 1H), 1.68 (d, *J* = 6.8 Hz, 6H), 1.62–1.02 (m, 24H), 0.90–0.83 (m, 12H).

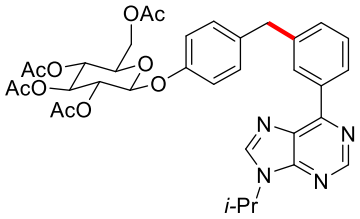
^{13}C-NMR (125 MHz, $CDCl_3$, 1:1 Conformer A and B): δ = 164.9 (C_q), 154.4 (C_q), 152.0 (C_q), 151.9 (CH), 149.3 (C_q), 146.9 (C_q), 141.9 (CH), 140.5 (C_q), 140.3 (C_q), 136.1 (C_q), 131.5 (C_q), 131.4 (CH), 130.3 (CH), 130.0 (CH), 129.0 (CH), 128.9 (CH), 128.2 (CH), 127.5 (C_q), 126.8 (C_q), 125.0 (C_q), 122.9 (C_q), 117.3 (C_q), 75.0 (C_q), 47.3 (CH), 42.1 (CH_2), 40.4 and 39.7 (CH_2), 39.4 (CH_2), 37.5 (CH_2), 37.5 (CH_2), 37.3 (CH_2), 32.8 (CH), 32.8 and 32.7 (CH), 31.3 and 31.1 (CH_2), 28.0 (CH), 24.8 (CH_2), 24.5 (CH_2), 24.2 and 23.8 (CH_3), 22.8 (CH_3), 22.7 (CH_3), 22.6 (CH_3), 21.1 (CH_2), 20.7 (CH_2), 19.8 (CH_3), 19.7 (CH_3), 13.1 (CH_3), 12.3 (CH_3), 11.9 (CH_3). Conformer A and B originate from the hindered rotation around the C–C bond to the ester group.

IR (ATR): $\tilde{\nu}$ = 2925, 1732, 1571, 1459, 1327, 1273, 1237, 1092, 704, 648 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 808 (14) $[M+Na]^+$, 786 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{51}H_{69}N_4O_3^+$ $[M+H]^+$ 785.5364, found 785.5349.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(Acetoxymethyl)-6-{4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]phenoxy} tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (187q)



The general procedure **J** was followed using purine **123a** (119 mg, 0.50 mmol) and benzyl chloride **186m** (473 mg, 1.00 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **187q** (240 mg, 71%) as a white solid.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 9.00 (s, 1H), 8.67 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 8.58 (ddd, *J* = 1.8, 1.8, 0.6 Hz, 1H), 8.18 (s, 1H), 7.47 (ddd, *J* = 7.8, 7.7, 0.5 Hz, 1H), 7.29 (ddd, *J* = 7.7, 1.8, 1.2 Hz, 1H), 7.16 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 5.29–5.22 (m, 2H), 5.14 (dd, *J* = 9.9, 9.7 Hz, 1H), 5.03 (d, *J* = 7.8 Hz, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.27 (dd, *J* = 12.3, 5.3 Hz, 1H), 4.14 (dd, *J* = 12.3, 2.5 Hz, 1H), 4.08 (s, 2H), 3.82 (ddd, *J* = 9.9, 5.3, 2.5 Hz, 1H), 2.04 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 1.68 (d, *J* = 6.8 Hz, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.4 (C_q), 170.0 (C_q), 169.2 (C_q), 169.1 (C_q), 155.2 (C_q), 154.6 (C_q), 152.0 (C_q), 151.9 (CH), 141.8 (CH), 141.4 (C_q), 136.1 (C_q), 135.9 (C_q), 131.5 (C_q), 131.3 (CH), 129.9 (CH), 129.8 (CH), 128.7 (CH), 128.0 (CH), 117.1 (CH), 99.3 (CH), 72.8 (CH), 72.0 (CH), 71.2 (CH), 68.4 (CH), 62.0 (CH_2), 47.3 (CH), 41.6 (CH_2), 22.6 (CH_3), 20.7 (CH_3), 20.7 (CH_3), 20.7 (CH_3), 20.6 (CH_3).

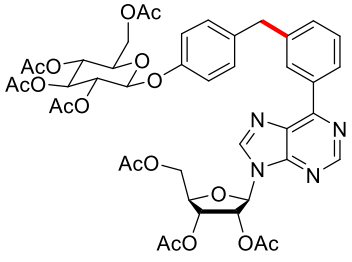
IR (ATR): $\tilde{\nu}$ = 2977, 1746, 1570, 1508, 1367, 1213, 1035, 704, 647, 598 cm^{-1}.

m.p.: 182–184 °C.

MS (ESI) *m*/*z* (relative intensity): 697 (8) $[M+Na]^+$, 675 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{35}H_{39}N_4O_{10}^+$ $[M+H]^+$ 675.2661, found 675.2656.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(Acetoxymethyl)-6-{4-{3-{9-[(2*R*,3*R*,4*R*,5*R*)-3,4-diacetoxy-5-(acetoxymethyl) tetrahydrofuran-2-yl]-9*H*-purin-6-yl}benzyl}phenoxy}tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (187r)



The general procedure **J** was followed using purine **123n** (182 mg, 0.40 mmol) and benzyl chloride **186m** (379 mg, 0.80 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 2:3) yielded **187r** (231 mg, 67%) as a viscous pale yellow oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.64 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 8.56 (dd, *J* = 1.8, 1.7 Hz, 1H), 8.27 (s, 1H), 7.47 (dd, *J* = 7.8, 7.6 Hz, 1H), 7.30 (ddd, *J* =

7.6, 1.7, 1.2 Hz, 1H), 7.16 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.29 (d, *J* = 5.4 Hz, 1H), 6.00 (dd, *J* = 5.5, 5.4 Hz, 1H), 5.70 (dd, *J* = 5.5, 4.5 Hz, 1H), 5.28–5.22 (m, 2H), 5.14 (dd, *J* = 10.0, 9.1 Hz, 1H), 5.02 (d, *J* = 7.6 Hz, 1H), 4.49–4.45 (m, 2H), 4.42–4.37 (m, 1H), 4.27 (dd, *J* = 12.3, 5.3 Hz, 1H), 4.13 (dd, *J* = 12.3, 2.4 Hz, 1H), 4.07 (s, 2H), 3.82 (ddd, *J* = 10.1, 5.3, 2.4 Hz, 1H), 2.16 (s, 3H), 2.13 (s, 3H), 2.08 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H).

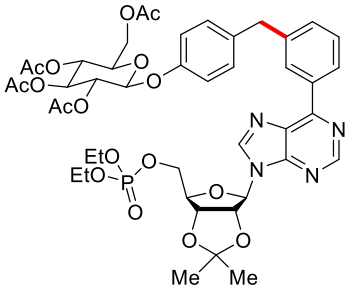
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.4 (C_q), 170.1 (C_q), 170.0 (C_q), 169.4 (C_q), 169.2 (C_q), 169.1 (C_q), 155.3 (C_q), 155.2 (C_q), 152.5 (CH), 151.9 (C_q), 142.4 (CH), 141.5 (C_q), 135.9 (C_q), 135.5 (C_q), 131.6 (CH), 131.6 (C_q), 129.9 (CH), 129.8 (CH), 128.8 (CH), 128.0 (CH), 117.1 (CH), 99.3 (CH), 86.4 (CH), 80.4 (CH), 73.1 (CH), 72.8 (CH), 72.0 (CH), 71.2 (CH), 70.7 (CH), 68.3 (CH), 63.1 (CH_2), 62.0 (CH_2), 41.2 (CH_2), 20.8 (CH_3), 20.7 (CH_3), 20.7 (CH_3), 20.6 (CH_3), 20.6 (CH_3), 20.6 (CH_3), 20.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 1745, 1569, 1508, 1368, 1216, 1038, 907, 703, 642, 600 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 913 (37) $[M+Na]^+$, 891 (100) $[M+H]^+$, 465 (38).

HR-MS (ESI): *m*/*z* calcd for $C_{43}H_{47}N_4O_{17}^+$ $[M+H]^+$ 891.2931, found 891.2923.

(2*R*,3*R*,4*S*,5*R*,6*S*)-2-(Acetoxymethyl)-6-{4-{3-{9-{(3a*R*,4*R*,6*R*,6a*R*)-6-{[(diethoxyphosphoryl)oxy]methyl}-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}-9*H*-purin-6-yl}benzyl}phenoxy}tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (187s)



The general procedure **J** was followed using purine **123l** (99.0 mg, 0.20 mmol) and benzyl chloride **186m** (189 mg, 0.40 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:4) yielded **187s** (130 mg, 69%) as a viscous pale yellow oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.99 (s, 1H), 8.64 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 8.55 (dd, *J* = 1.6, 1.6 Hz, 1H), 8.26 (s, 1H), 7.45 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.28 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 7.14 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 6.24 (d, *J* = 2.5 Hz, 1H), 5.43 (dd, *J* = 6.3, 2.5 Hz, 1H), 5.27–5.20 (m, 2H), 5.12 (dd, *J* = 10.1, 9.1 Hz, 1H), 5.10 (dd, *J* = 6.3, 3.0 Hz, 1H), 5.01 (d, *J* = 7.7 Hz, 1H), 4.51 (dddd, *J* = 5.1, 4.5, 3.0, 1.2 Hz, 1H), 4.27 (ddd, *J* = 11.0, 6.4, 4.5 Hz, 1H), 4.25 (dd, *J* = 12.2, 5.3 Hz, 1H), 4.19 (ddd, *J* = 11.0, 6.9, 5.1 Hz, 1H), 4.11 (dd, *J* = 12.2, 2.4 Hz, 1H), 4.07–3.99 (m, 6H), 3.80 (ddd, *J* = 10.1, 5.3, 2.4 Hz, 1H), 2.02 (s, 3H), 2.01 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.62 (s, 3H), 1.39 (s, 3H), 1.25 (td, *J* = 7.2, 1.1 Hz, 3H), 1.22 (td, *J* = 7.1, 1.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 170.4 (C_q), 170.0 (C_q), 169.2 (C_q), 169.1 (C_q), 155.2 (C_q), 155.1 (C_q), 152.4 (CH), 151.6 (C_q), 143.1 (CH), 141.5 (C_q), 135.9 (C_q), 135.6 (C_q), 131.6 (C_q), 131.6 (CH), 129.9 (CH), 129.8 (CH), 128.8 (CH), 128.1 (CH), 117.1 (CH), 114.7 (C_q), 99.3 (CH), 91.0 (CH), 85.3 (d, $^3J_{C-P}$ = 8 Hz, CH), 84.2 (CH), 81.4 (CH), 72.8 (CH), 72.0 (CH), 71.2 (CH), 68.3 (CH), 66.6 (d, $^2J_{C-P}$ = 5 Hz, CH_2), 64.1 (d, $^2J_{C-P}$ = 6 Hz, CH_2), 64.1 (d, $^2J_{C-P}$ = 6 Hz, CH_2), 62.0 (CH_2), 41.2 (CH_2), 27.2 (CH_3), 25.4 (CH_3), 20.7 (CH_3), 20.7 (CH_3), 20.7 (CH_3), 20.6 (CH_3), 16.1 (d, $^3J_{C-P}$ = 7 Hz, CH_3).

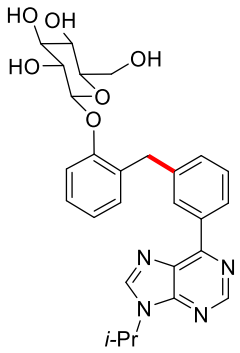
^{31}P{^{1}H}-NMR (121 MHz, $CDCl_3$): δ = –1.1 (s).

IR (ATR): $\tilde{\nu}$ = 2985, 1754, 1569, 1508, 1373, 1213, 1029, 733, 702, 645 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 1904 (8) $[2M+Na]^+$, 1882 (13) $[2M+H]^+$, 963 (66) $[M+Na]^+$, 941 (100) $[M+H]^+$, 655 (3), 482 (12).

HR-MS (ESI): *m*/*z* calcd for $C_{44}H_{54}N_4O_{17}P^+$ $[M+H]^+$ 941.3216, found 941.3219.

(2*R*,3*S*,4*S*,5*R*,6*S*)-2-(Hydroxymethyl)-6-{2-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]phenoxy} tetrahydro-2*H*-pyran-3,4,5-triol (187t)



The general procedure **J** was followed using purine **123a** (119 mg, 0.50 mmol) and benzyl chloride **186n** (305 mg, 1.00 mmol) at 80 °C. After 20 h, purification by column chromatography (CH_2Cl_2/acetone 1:1) followed by reverse phase HPLC (H_2O/MeCN 60:40) yielded **187t** (139 mg, 55%) as a viscous colorless oil.

^{1}H-NMR (600 MHz, acetone-d_6): δ = 8.96 (s, 1H), 8.90 (dd, *J* = 1.7, 1.7 Hz, 1H), 8.70 (ddd, *J* = 7.6, 1.7, 1.6 Hz, 1H), 8.63 (s, 1H), 7.49 (ddd, *J* = 7.6, 1.7, 1.6 Hz, 1H), 7.46 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.31 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.19 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.16 (ddd, *J* = 8.3, 7.2, 1.7 Hz, 1H), 6.97 (ddd, *J* = 7.4, 7.2, 1.5 Hz, 1H), 5.26 (br s, 1H), 5.02 (hept, *J* = 6.8 Hz, 1H), 5.02 (d, *J* = 7.6 Hz, 1H), 4.48 (br s, 1H), 4.30 (br s, 1H), 4.19 (d_{AB}, *J* = 14.2 Hz, 1H), 4.13 (d_{AB}, *J* = 14.2 Hz, 1H), 3.90–3.84 (m, 1H), 3.75–3.66 (m, 3H), 3.55 (t, *J* = 8.9 Hz, 1H), 3.53–3.49 (m, 1H), 3.46 (t, *J* = 9.2 Hz, 1H), 1.69 (d, *J* = 6.8 Hz, 6H).

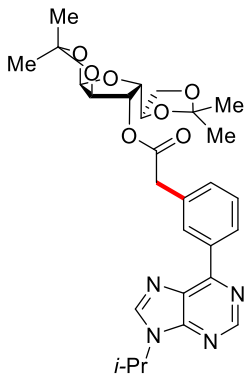
^{13}C-NMR (125 MHz, acetone-d_6): δ = 156.4 (C_q), 154.4 (C_q), 153.1 (C_q), 152.4 (CH), 144.6 (CH), 142.3 (C_q), 136.5 (C_q), 132.2 (CH), 131.9 (C_q), 131.6 (CH), 131.4 (C_q), 131.0 (CH), 129.0 (CH), 128.3 (CH), 128.1 (CH), 122.7 (CH), 116.1 (CH), 102.1 (CH), 78.2 (CH), 77.7 (CH), 74.5 (CH), 71.3 (CH), 62.7 (CH_2), 48.4 (CH), 37.2 (CH_2), 22.4 (CH_3), 22.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3340, 2919, 1572, 1491, 1454, 1328, 1223, 1072, 1043, 648 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 529 (42) $[M+Na]^+$, 507 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{27}H_{31}N_4O_6^+$ $[M+H]^+$ 507.2238, found 507.2249.

(3a*R*,5*R*,6*S*,6a*R*)-5-[(*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3] dioxol-6-yl 2-[3-(9-*iso*-propyl-9*H*-purin-6-yl)phenyl]acetate (187u)



The general procedure **J** was followed using purine **123a** (119 mg, 0.50 mmol) and alkyl bromide **186o** (381 mg, 1.00 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 3:2) yielded **187u** (145 mg, 54%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.00 (s, 1H), 8.76 (ddd, *J* = 7.8, 1.7, 1.5 Hz, 1H), 8.68 (dd, *J* = 1.7, 1.6 Hz, 1H), 8.18 (s, 1H), 7.52 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.45 (ddd, *J* = 7.7, 1.6, 1.5 Hz, 1H), 5.85 (d, *J* = 3.6 Hz, 1H), 5.30 (d, *J* = 2.9 Hz, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.47 (d, *J* = 3.6 Hz, 1H), 4.18 (d_{AB}d, *J* = 8.0, 2.9 Hz, 1H), 4.16 (d_{AB}dd, *J* = 8.0, 5.7, 4.8 Hz, 1H), 3.98 (d_{AB}d, *J* = 8.6, 5.7 Hz, 1H), 3.96 (d_{AB}d, *J* = 8.6, 4.8 Hz, 1H), 3.82 (d_{AB}, *J* = 15.3 Hz, 1H), 3.80 (d_{AB}, *J* = 15.3 Hz, 1H), 1.67 (d, *J* = 6.8 Hz, 6H), 1.49 (s, 3H), 1.36 (s, 3H), 1.26 (s, 3H), 1.20 (s, 3H).

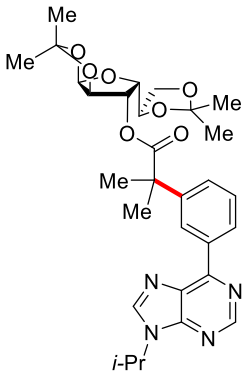
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 169.8 (C_q), 154.0 (C_q), 152.1 (C_q), 151.9 (CH), 141.9 (CH), 136.1 (C_q), 133.7 (C_q), 131.6 (CH), 131.4 (C_q), 130.2 (CH), 128.9 (CH), 128.8 (CH), 112.2 (C_q), 109.2 (C_q), 105.0 (CH), 83.2 (CH), 79.9 (CH), 76.4 (CH), 72.3 (CH), 67.2 (CH_2), 47.3 (CH), 41.4 (CH_2), 26.9 (CH_3), 26.8 (CH_3), 26.3 (CH_3), 25.1 (CH_3), 22.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2984, 1742, 1570, 1372, 1215, 1072, 1018, 843, 703, 647 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 1100 (12) $[2M+Na]^+$, 561 (43) $[M+Na]^+$, 539 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{28}H_{35}N_4O_7^+$ $[M+H]^+$ 539.2500, found 539.2490.

(3a*R*,5*R*,6*S*,6a*R*)-5-[(*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl 2-[3-(9-*iso*-propyl-9*H*-purin-6-yl)phenyl]-2-methylpropanoate (187v)



The general procedure **J** was followed using purine **123a** (119 mg, 0.50 mmol) and alkyl bromide **186p** (409 mg, 1.00 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **187v** (241 mg, 76%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.00 (s, 1H), 8.79 (dd, *J* = 1.8, 1.7 Hz, 1H), 8.74 (ddd, *J* = 7.5, 1.7, 1.7 Hz, 1H), 8.18 (s, 1H), 7.52 (dd, *J* = 7.7, 7.5 Hz, 1H), 7.49 (ddd, *J* = 7.7, 1.8, 1.7 Hz, 1H), 5.66 (d, *J* = 3.6 Hz, 1H), 5.31 (d, *J* = 3.1 Hz, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.48 (d, *J* = 3.6 Hz, 1H), 4.16 (dd, *J* = 8.0, 3.1 Hz, 1H), 4.01 (ddd, *J* = 8.0, 6.1, 5.3 Hz, 1H), 3.88 (d_{AB}d, *J* = 8.6, 6.1 Hz, 1H), 3.85 (d_{AB}d, *J* = 8.6, 5.3 Hz, 1H), 1.71 (s, 3H), 1.68–1.66 (m, 9H), 1.48 (s, 3H), 1.36 (s, 3H), 1.23 (s, 3H), 1.19 (s, 3H).

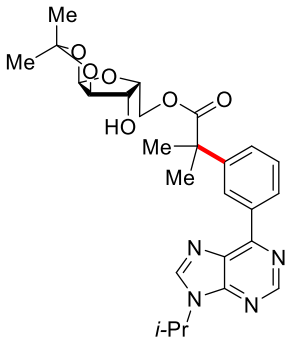
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 175.1 (C_q), 154.3 (C_q), 152.0 (C_q), 151.9 (CH), 144.5 (C_q), 141.9 (CH), 135.9 (C_q), 131.4 (C_q), 128.6 (CH), 128.5 (CH), 128.0 (CH), 126.9 (CH), 112.1 (C_q), 109.1 (C_q), 105.1 (CH), 83.0 (CH), 80.2 (CH), 76.3 (CH), 72.3 (CH), 67.3 (CH_2), 47.3 (CH), 47.1 (C_q), 26.9 (CH_3), 26.8 (CH_3), 26.8 (CH_3), 26.3 (CH_3), 26.1 (CH_3), 25.1 (CH_3), 22.7 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2983, 1737, 1569, 1372, 1217, 1140, 1073, 1020, 845, 647 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 1156 (6) $[2M+Na]^+$, 589 (14) $[M+Na]^+$, 567 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{30}H_{39}N_4O_7^+$ $[M+H]^+$ 567.2813, found 567.2812.

[(3a*R*,5*R*,6*S*,6a*R*)-6-Hydroxy-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl]methyl 2-[3-(9-*iso*-propyl-9*H*-purin-6-yl)phenyl]-2-methylpropanoate (187w)



The general procedure **J** was followed using purine **123a** (119 mg, 0.50 mmol) and alkyl bromide **186q** (339 mg, 1.00 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:1) followed by recycling preparative HPLC yielded **187w** (169 mg, 68%) as a viscous colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.97 (s, 1H), 8.58 (ddd, *J* = 6.7, 2.3, 2.1 Hz, 1H), 8.28 (dd, *J* = 2.3, 1.4 Hz, 1H), 8.22 (s, 1H), 7.58–7.53 (m, 2H), 5.92 (d, *J* = 3.5 Hz, 1H), 5.78 (d, *J* = 4.5 Hz, 1H), 4.99 (hept, *J* = 6.8 Hz, 1H), 4.74 (dd, *J* = 10.3, 10.3 Hz, 1H), 4.40 (d, *J* = 3.5 Hz, 1H), 4.28 (ddd, *J* = 10.3, 4.6, 3.2 Hz, 1H), 4.13 (dd, *J* = 10.3, 4.6 Hz, 1H), 3.85

(dd, *J* = 4.5, 3.2 Hz, 1H), 1.70 (s, 3H), 1.68 (d, *J* = 6.8 Hz, 3H), 1.68 (d, *J* = 6.8 Hz, 3H), 1.57 (s, 3H), 1.40 (s, 3H), 1.24 (s, 3H).

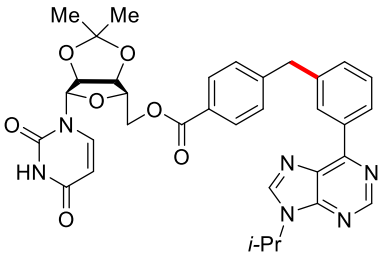
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 176.1 (C_q), 155.0 (C_q), 152.1 (C_q), 151.7 (CH), 145.4 (C_q), 142.6 (CH), 135.1 (C_q), 131.4 (C_q), 128.9 (CH), 128.8 (CH), 127.2 (CH), 111.6 (C_q), 105.0 (CH), 85.6 (CH), 77.6 (CH), 72.7 (CH), 60.7 (CH_2), 47.6 (CH), 47.1 (C_q), 28.0 (CH_3), 26.9 (CH_3), 26.2 (CH_3), 25.8 (CH_3), 22.7 (CH_3), 22.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2978, 1729, 1569, 1326, 1217, 1147, 1070, 1012, 702, 647 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 1016 (65) $[2M+Na]^+$, 994 (6) $[2M+H]^+$, 519 (66) $[M+Na]^+$, 497 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{26}H_{33}N_4O_6^+$ $[M+H]^+$ 497.2395, found 497.2384.

{(3a*R*,4*R*,6*R*,6a*R*)-6-[2,4-Dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}methyl 4-[3-(9-*iso*-propyl-9*H*-purin-6-yl)benzyl]benzoate (187x)



The general procedure **J** was followed using purine **123a** (59.6 mg, 0.25 mmol) and benzyl chloride **186r** (219 mg, 0.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:3) yielded **187x** (87.3 mg, 55%) as a white solid.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.62 (d, *J* = 2.1 Hz, 1H), 8.99 (s, 1H), 8.66 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 8.54 (dd, *J* = 1.8, 1.6 Hz, 1H), 8.20 (s, 1H), 7.88 (d, *J* = 8.3 Hz, 2H), 7.50 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.33–7.30 (m, 1H), 7.30 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 1H), 5.64 (d, *J* = 2.1 Hz, 1H), 5.52 (dd, *J* = 8.1, 2.1 Hz, 1H), 5.03 (dd, *J* = 6.3, 2.1 Hz, 1H), 4.97 (hept, *J* = 6.8 Hz, 1H), 4.90 (dd, *J* = 6.3, 3.4 Hz, 1H), 4.61 (dd, *J* = 12.1, 3.4 Hz, 1H), 4.55 (ddd, *J* = 4.9, 3.4, 3.4 Hz, 1H), 4.44 (dd, *J* = 12.1, 4.9 Hz, 1H), 4.17 (d_{AB}, *J* = 15.5 Hz, 1H), 4.15 (d_{AB}, *J* = 15.5 Hz, 1H), 1.66 (d, *J* = 6.8 Hz, 6H), 1.56 (s, 3H), 1.35 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 165.8 (C_q), 162.8 (C_q), 154.6 (C_q), 152.0 (C_q), 151.9 (CH), 149.9 (C_q), 147.1 (C_q), 142.1 (CH), 140.8 (CH), 140.1 (C_q), 136.1 (C_q), 131.5 (CH), 131.3 (C_q), 130.0 (CH), 129.6 (CH), 129.0 (CH), 128.9 (CH), 128.3 (CH), 127.3 (C_q), 114.3 (C_q), 102.3 (CH), 95.0 (CH), 85.4 (CH), 85.1 (CH), 81.2 (CH), 64.4 (CH_2), 47.3 (CH), 42.0 (CH_2), 27.2 (CH_3), 25.3 (CH_3), 22.6 (CH_3).

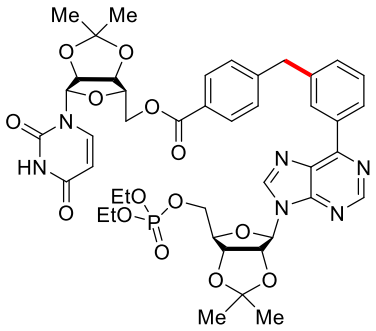
IR (ATR): $\tilde{\nu}$ = 2983, 1688, 1570, 1456, 1378, 1270, 1216, 1087, 750, 647 cm^{-1}.

m.p.: 87–90 °C.

MS (ESI) *m/z* (relative intensity): 661 (3) $[M+Na]^+$, 639 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{34}H_{35}N_6O_7^+$ $[M+H]^+$ 639.2562, found 639.2562.

{(3a*R*,4*R*,6*R*,6a*R*)-6-[2,4-Dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}methyl 4-{3-{9-{(3a*R*,4*R*,6*R*,6a*R*)-6-{[(diethoxyphosphoryl)oxy]methyl}-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}-9*H*-purin-6-yl}benzyl}benzoate (187y)



The general procedure **J** was followed using purine **123l** (126 mg, 0.25 mmol) and benzyl chloride **186r** (219 mg, 0.50 mmol). After 20 h, purification by column chromatography (CH_2Cl_2/acetone 3:1) yielded **187y** (83.5 mg, 37%) as a viscous colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.24 (d, *J* = 2.2 Hz, 1H), 9.01 (s, 1H), 8.66 (ddd, *J* = 7.8, 1.6, 1.4 Hz, 1H), 8.55 (dd, *J* = 1.6, 1.6 Hz, 1H), 8.31 (s, 1H), 7.88 (d, *J* = 8.3 Hz, 2H), 7.50 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.34 (ddd, *J* = 7.7, 1.6, 1.4 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 1H), 6.26 (d, *J* = 2.5 Hz, 1H), 5.66 (d, *J* = 2.1 Hz, 1H), 5.51 (dd, *J* = 8.1, 2.2 Hz, 1H), 5.45 (dd, *J* = 6.3, 2.5 Hz, 1H), 5.13 (dd, *J* = 6.3, 3.1 Hz, 1H), 5.02 (dd, *J* = 6.3, 2.1 Hz, 1H), 4.90 (dd, *J* = 6.3, 3.3 Hz, 1H), 4.62 (dd, *J* = 12.1, 3.3 Hz, 1H), 4.56–4.51 (m, 2H), 4.45 (dd, *J* = 12.1, 4.8 Hz, 1H), 4.29 (ddd, *J* = 11.1, 6.3, 4.6 Hz, 1H), 4.20 (ddd, *J* = 11.1, 6.9, 5.3 Hz, 1H), 4.18 (d_{AB}, *J* = 15.5 Hz, 1H), 4.15 (d_{AB}, *J* = 15.5 Hz, 1H), 4.11–4.01 (m, 4H), 1.64 (s, 3H), 1.57 (s, 3H), 1.41 (s, 3H), 1.35 (s, 3H), 1.27 (td, *J* = 7.1, 0.9 Hz, 3H), 1.24 (td, *J* = 7.1, 1.0 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 165.8 (C_q), 162.5 (C_q), 155.0 (C_q), 152.3 (CH), 151.6 (C_q), 149.9 (C_q), 147.0 (C_q), 143.4 (CH), 140.7 (CH), 140.3 (C_q), 135.7 (C_q), 131.8 (CH), 131.6 (C_q), 130.0 (CH), 129.6 (CH), 129.1 (CH), 129.0 (CH), 128.4 (CH), 127.4 (C_q), 114.7 (C_q), 114.3 (C_q), 102.4 (CH), 94.9 (CH), 91.0 (CH), 85.4 (CH), 85.3 (d, $^3J_{C-P}$ = 8 Hz, CH), 85.1 (CH), 84.2 (CH), 81.4 (CH), 81.2 (CH), 66.6 (d, $^2J_{C-P}$ = 5 Hz, CH_2), 64.4 (CH_2), 64.1 (d, $^2J_{C-P}$ = 5 Hz, CH_2), 64.1 (d, $^2J_{C-P}$ = 6 Hz, CH_2), 42.0 (CH_2), 27.2 (CH_3), 27.2 (CH_3), 25.4 (CH_3), 25.3 (CH_3), 16.1 (d, $^3J_{C-P}$ = 7 Hz, CH_3).

^{31}P{^{1}H }-NMR (121 MHz, $CDCl_3$): δ = –1.1 (s).

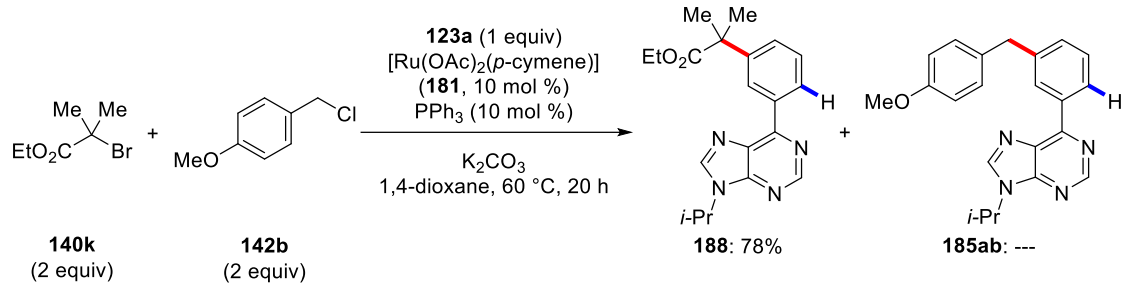
IR (ATR): $\tilde{\nu}$ = 3493, 2988, 1694, 1571, 1382, 1270, 1213, 1088, 1029, 866 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 1832 (2) $[2M+Na]^+$, 1811 (4) $[2M+H]^+$, 928 (12) $[M+Na]^+$, 906 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{43}H_{50}N_6O_{14}P^+$ $[M+H]^+$ 905.3117, found 905.3120.

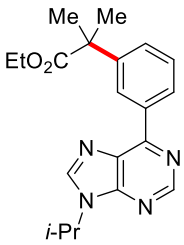
5.3.4.4 Mechanistic Studies

5.3.4.4.1 Competition Experiments of Alkyl Halides



Purine **123a** (119 mg, 0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 17.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Ethyl 2-bromo-2-methylpropanoate (**140k**, 195 mg, 1.00 mmol), 4-methoxybenzyl chloride (**142b**, 157 mg, 1.00 mmol), and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 3:1) yielded **188** (137 mg, 78%) as a colorless oil.

Ethyl 2-[3-(9-*iso*-propyl-9*H*-purin-6-yl)phenyl]-2-methylpropanoate (188)



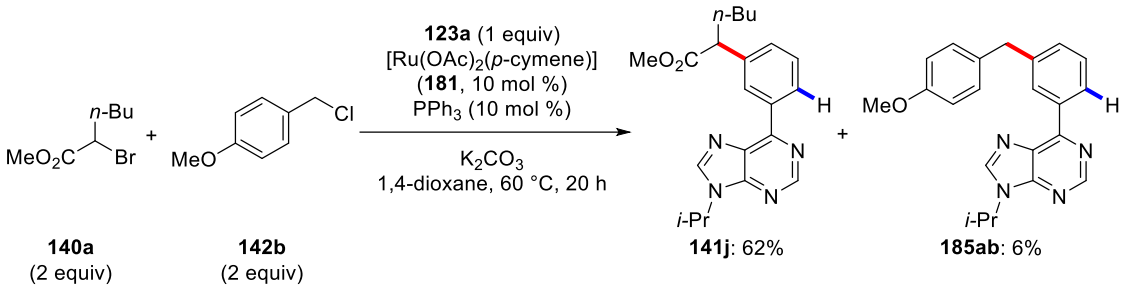
^{1}H-NMR (600 MHz, $CDCl_3$): δ = 9.01 (s, 1H), 8.81 (dd, *J* = 1.8, 1.7 Hz, 1H), 8.71 (ddd, *J* = 7.5, 1.7, 1.6 Hz, 1H), 8.18 (s, 1H), 7.51 (dd, *J* = 7.8, 7.5 Hz, 1H), 7.48 (ddd, *J* = 7.8, 1.8, 1.6 Hz, 1H), 4.98 (hept, *J* = 6.8 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.68 (s, 6H), 1.67 (d, *J* = 6.8 Hz, 6H), 1.18 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 176.5 (C_q), 154.6 (C_q), 152.0 (C_q), 151.9 (CH), 145.2 (C_q), 141.8 (CH), 135.8 (C_q), 131.5 (C_q), 128.4 (CH), 128.4 (CH), 128.3 (CH), 126.8 (CH), 60.8 (CH_2), 47.2 (CH), 46.8 (C_q), 26.7 (CH_3), 22.7 (CH_3), 14.1 (CH_3).

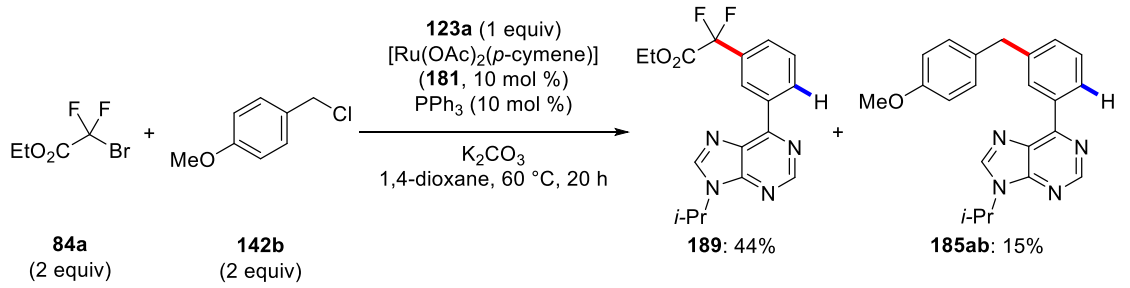
IR (ATR): $\tilde{\nu}$ = 2977, 1722, 1567, 1324, 1218, 1142, 1025, 798, 702, 646 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 352 (18) $[M]^+$, 323 (4) $[M–Et]^+$, 279 (89) $[M–CO_2Et]^+$, 237 (100) $[M–C(Me)_2CO_2Et]^+$, 221 (12).

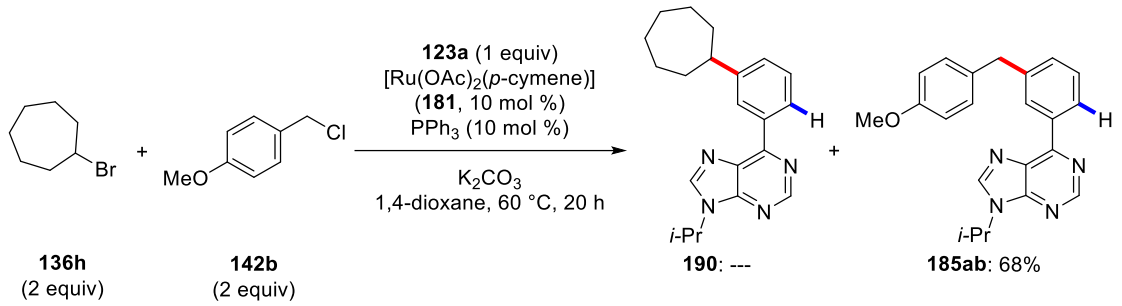
HR-MS (EI): *m*/*z* calcd for $C_{20}H_{24}N_4O_2^+$ $[M]^+$ 352.1894, found 352.1897.



Purine **123a** (119 mg, 0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 17.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Methyl 2-bromohexanoate (**140a**, 209 mg, 1.00 mmol), 4-methoxybenzyl chloride (**142b**, 157 mg, 1.00 mmol), and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 3:1) yielded **141j**[101] (114 mg, 62%) as a colorless oil and **185ab** (11.3 mg, 6%) as a colorless oil.

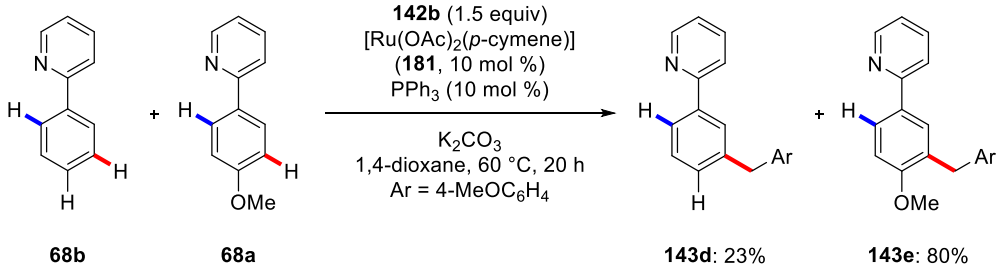


Purine **123a** (119 mg, 0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 17.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Ethyl 2-bromo-2,2-difluoroacetate (**84a**, 203 mg, 1.00 mmol), 4-methoxybenzyl chloride (**142b**, 157 mg, 1.00 mmol), and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 3:1) yielded **189**[103] (79.3 mg, 44%) as a colorless oil and **185ab** (27.7 mg, 15%) as a colorless oil.



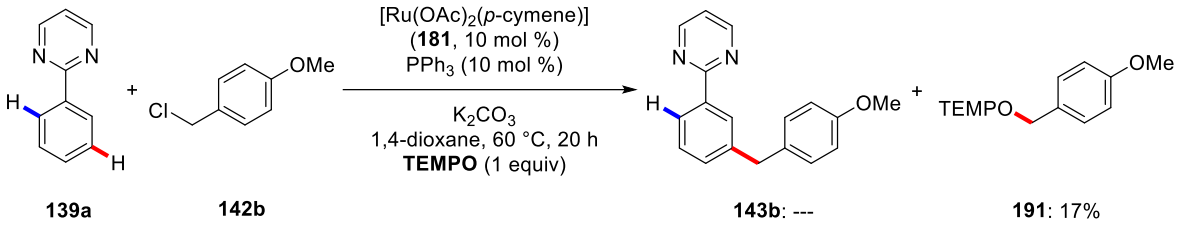
Purine **123a** (119 mg, 0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 17.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Bromocycloheptane (**136h**, 177 mg, 1.00 mmol), 4-Methoxybenzyl chloride (**142b**, 157 mg, 1.00 mmol), and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 3:1) yielded **185ab** (122 mg, 68%) as a colorless oil.

5.3.4.4.2 Intermolecular Competition Experiment



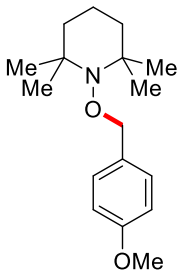
2-Phenylpyridine (**68b**, 77.6 mg, 0.50 mmol), 2-(4-methoxyphenyl)pyridine (**68a**, 92.6 mg, 0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 17.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. 4-Methoxybenzyl chloride (**142b**, 117 mg, 0.75 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 6:1) yielded **143d** (32.1 mg, 23%) as a colorless oil, **143e** (122 mg, 80%) as a colorless oil, and recovered **68b** (43.1 mg, 56%) as a colorless oil.

5.3.4.4.3 Reactions with Radical Scavengers



2-Phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 17.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %), K_2CO_3 (138 mg, 1.00 mmol) and TEMPO (78.2 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. 4-Methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 20:1) followed by recycling preparative HPLC yielded TEMPO-adduct **191** (23.0 mg, 17%) as a colorless oil and recovered **139a** (61.0 mg, 78%) as a colorless oil.

1-[(4-Methoxybenzyl)oxy]-2,2,6,6-tetramethylpiperidine (191)



^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.74 (s, 2H), 3.81 (s, 3H), 1.62–1.31 (m, 6H), 1.26 (s, 6H), 1.13 (s, 6H).

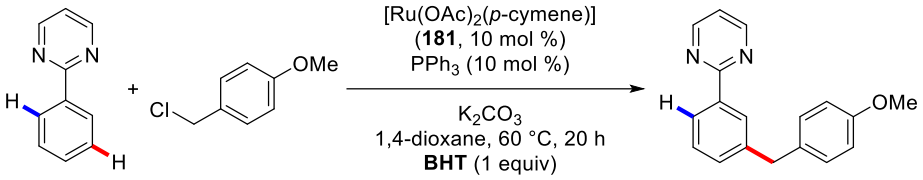
^{13}C-NMR (75 MHz, $CDCl_3$): δ = 159.0 (C_q), 130.4 (C_q), 129.2 (CH), 113.6 (CH), 78.4 (CH_2), 60.0 (C_q), 55.3 (CH_3), 39.7 (CH_2), 33.2 (CH_3), 20.3 (CH_3), 17.1 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2930, 1613, 1513, 1359, 1247, 1173, 1036, 821, 695, 603 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 278 (100) $[M+H]^+$, 243 (3), 137 (16).

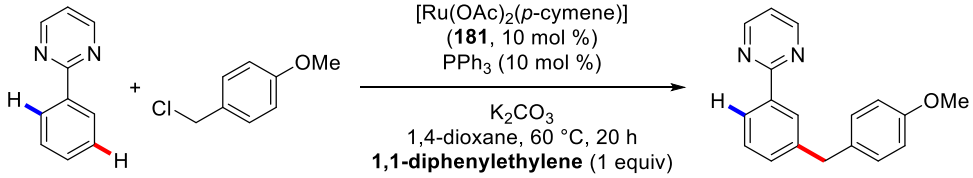
HR-MS (ESI): *m/z* calcd for $C_{17}H_{28}NO_2^+$ $[M+H]^+$ 278.2115, found 278.2120.

The spectral data are in accordance with those reported in the literature.[140]



139a **142b** **143b**: 66%

2-Phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 17.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %), K_2CO_3 (138 mg, 1.00 mmol) and BHT (110 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. 4-Methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 10:1) yielded **143b** (91.4 mg, 66%) as a colorless oil.

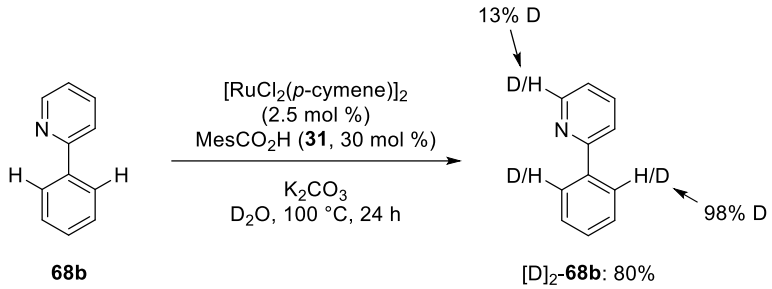


139a **142b** **143b**: 31%

2-Phenylpyrimidine (**139a**, 78.1 mg, 0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 17.7 mg, 50.0 µmol, 10 mol %), PPh_3 (13.1 mg, 50.0 µmol, 10 mol %), K_2CO_3 (138 mg, 1.00 mmol) and 1,1-diphenylethylene (90.1 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. 4-Methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered throough a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 10:1) yielded **143b** (42.3 mg, 31%) as a colorless oil and recovered **139a** (39.2 mg, 50%) as a colorless oil.

5.3.4.4.4 Isotopic Studies

*Preparation of [D]$_2$-**68b***



2-Phenylpyridine (**68b**, 776 mg, 5.00 mmol), [RuCl$_2$(*p*-cymene)]$_2$ (76.5 mg, 0.13 mmol, 2.5 mol %), MesCO$_2$H (**31**, 246 mg, 1.50 mmol, 30 mol %) and K_2CO_3 (1.38 g, 10.0 mmol) were placed in a pre-dried 50 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. D_2O (17 mL) was then added and the mixture was stirred at 100 °C. After 24 h, the resulting mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 10:1) yielded [D]$_2$-**68b** (630 mg, 80%) as a colorless oil. The degree of deuteration was determined by ^{1}H-NMR spectroscopy (Figure 27).

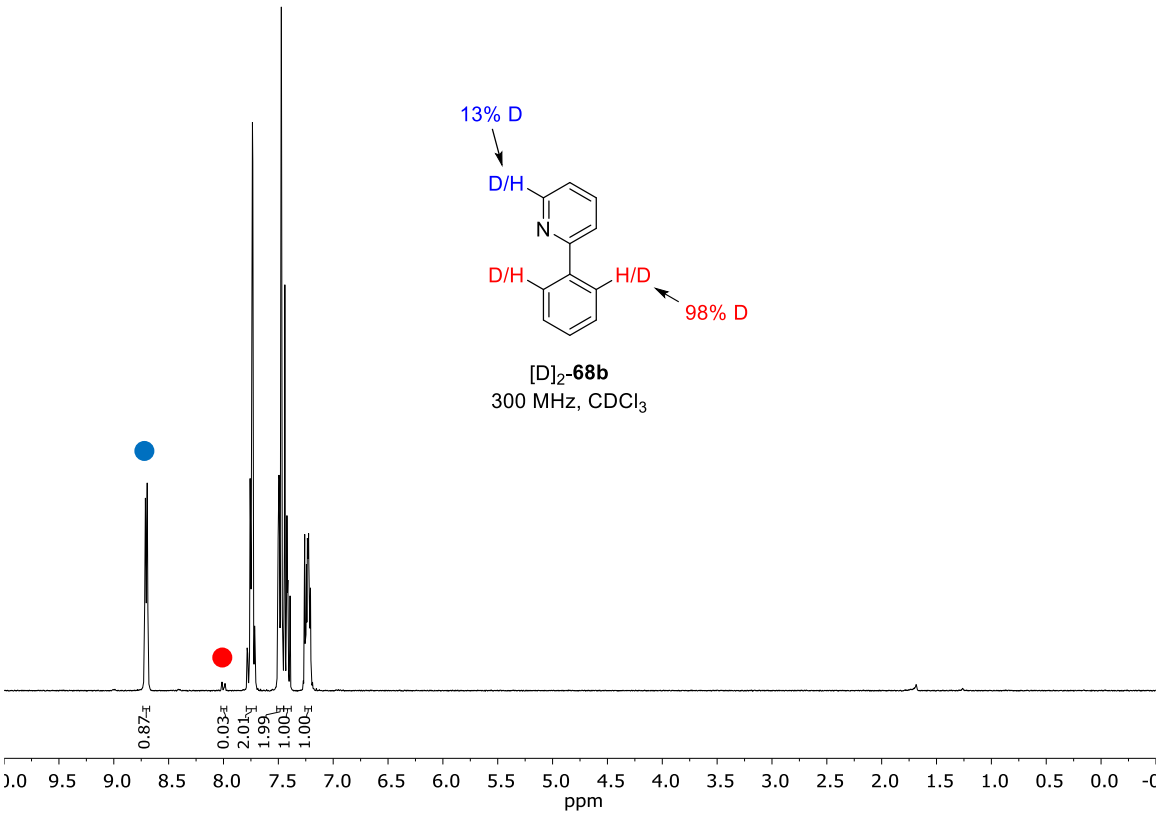
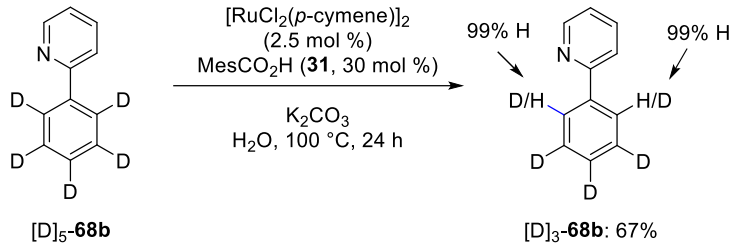


Figure 27: ^{1}H-NMR spectrum of [D]$_2$-**68b**.

*Preparation of [D]$_3$-**68b***



[D]$_5$-2-Phenylpyridine ([D]$_5$-**68b**, 481 mg, 3.00 mmol), [RuCl$_2$(*p*-cymene)]$_2$ (45.9 mg, 75.0 µmol, 2.5 mol %), MesCO$_2$H (**31**, 148 mg, 0.90 mmol, 30 mol %) and K$_2$CO$_3$ (829 mg, 6.00 mmol) were placed in a pre-dried 50 mL Schlenk tube. The tube was evacuated and purged with N$_2$ three times. H$_2$O (10 mL) was then added and the mixture was stirred at 100 °C. After 24 h, the resulting mixture was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried over Na$_2$SO$_4$ and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 10:1) yielded [D]$_3$-**68b** (317 mg, 67%) as a colorless oil. The degree of deuteration was determined by ^{1}H-NMR spectroscopy (Figure 28).

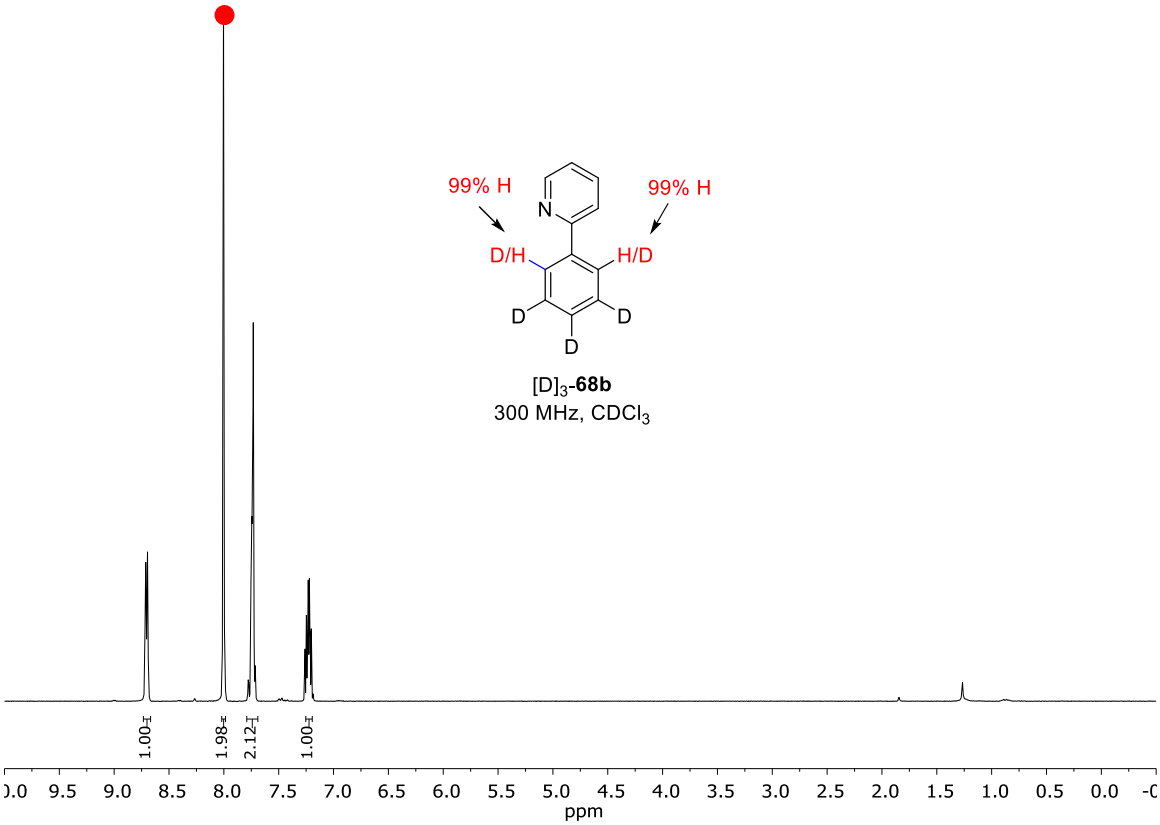
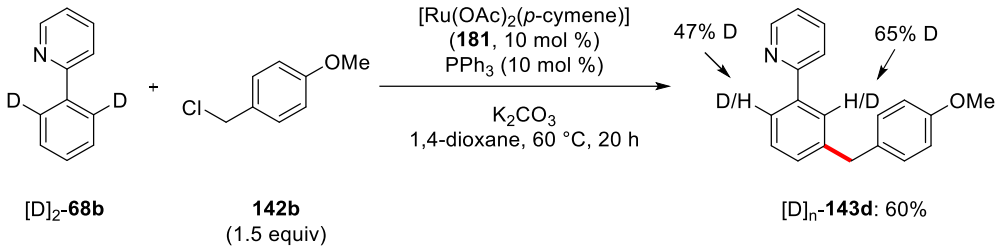


Figure 28: ^{1}H-NMR spectrum of [D]$_3$-**68b**.

*Ruthenium-Catalyzed meta-Benzylation of [D]$_2$-**68b***



The general procedure **I** was followed using [D]$_2$-**68b** (78.6 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded [D]$_n$-**143d** (83.6 mg, 60%) as a colorless oil. The degree of deuteration was determined by ^{1}H-NMR spectroscopy (Figure 29).

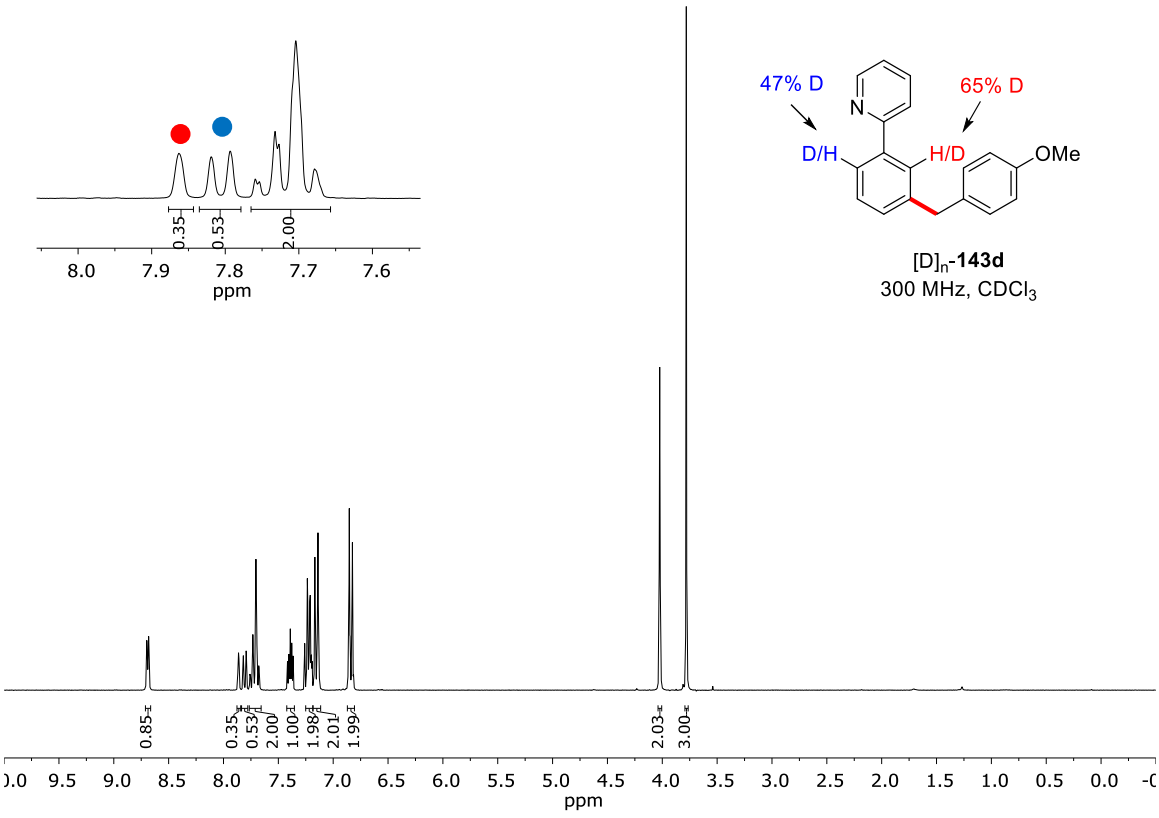
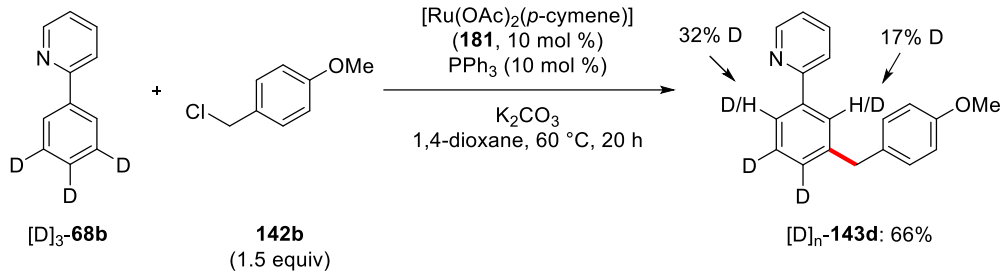


Figure 29: ^{1}H-NMR spectrum of [D]$_n$-**143d**.

*Ruthenium-Catalyzed meta-Benzylation of [D]$_3$-**68b***



The general procedure **I** was followed using [D]$_3$-**68b** (79.1 mg, 0.50 mmol) and 4-methoxybenzyl chloride (**142b**, 235 mg, 1.50 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded [D]$_n$-**143d** (92.4 mg, 66%) as a colorless oil. The degree of deuteration was determined by ^{1}H-NMR spectroscopy (Figure 30).

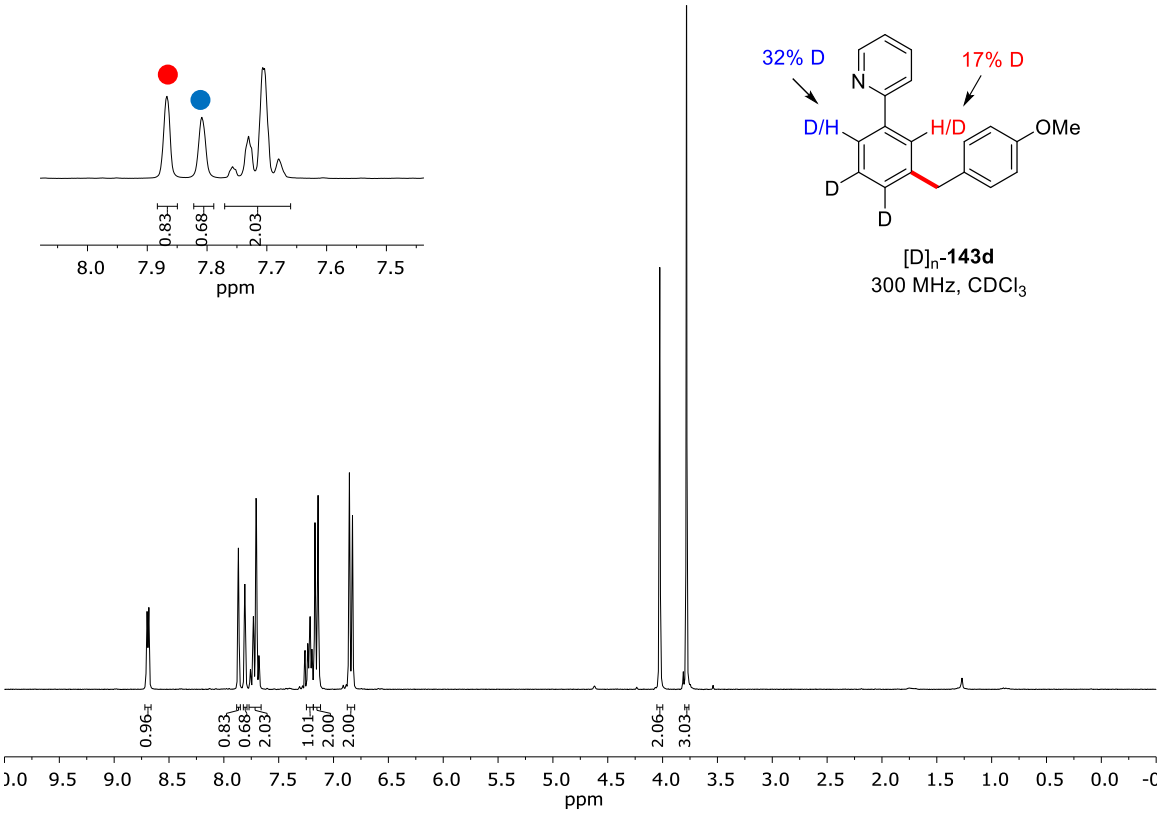
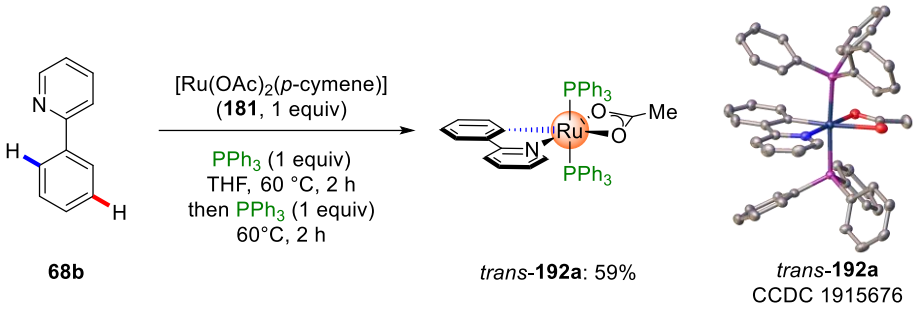


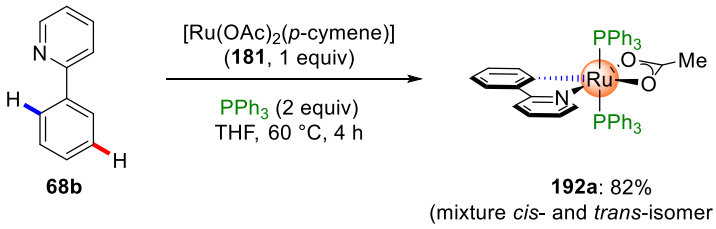
Figure 30: ^{1}H-NMR spectrum of [D]$_n$-**143d**.

5.3.4.4.5 Cyclometallic Complex Studies

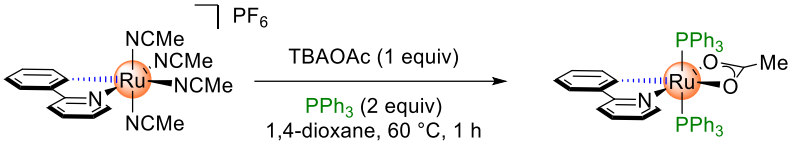
*Preparation of Ruthenacycle **192a***



2-Phenylpyridine (**68b**, 77.6 mg, 0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 177 mg, 0.50 mmol), and PPh_3 (131 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. THF (2.0 mL) was added and the mixture was stirred at 60 °C. After 2 h, an additional PPh_3 (131 mg, 0.50 mmol) was added into the reaction mixture at ambient temperature and the mixture was again stirred at 60 °C for an additional 2 h. An orange solid formed during this time and the reaction was cooled to ambient temperature. The orange solid was collected and washed with THF (5.0 mL) and dry *n*-hexane (2 × 10 mL). The orange solid was dried under vacuum, providing complex *trans*-**192a** (249 mg, 59%). Suitable crystals of *trans*-**192a** for X-ray crystallography were grown by slow crystallization from THF/*n*-hexane (*see X-Ray Crystallographic Analysis section*).



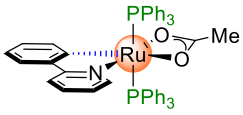
2-Phenylpyridine (**68b**, 155 mg, 1.00 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 353 mg, 1.00 mmol), and PPh_3 (525 mg, 2.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. THF (2.0 mL) was added and the mixture was stirred at 60 °C for 4 h. An orange solid formed during this time and the reaction was cooled to ambient temperature. The orange solid was collected and washed with THF (5.0 mL) and dry *n*-hexane (2 × 10 mL). The orange solid was dried under vacuum, providing complex **192a** (690 mg, 82%).



98 *trans*-**192a**: 48%

Ruthenacycle **98** (282 mg, 0.50 mmol), TBAOAc (151 mg, 0.50 mmol), and PPh_3 (262 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. 1,4-Dioxane (1.6 mL) was added and the mixture was stirred at 60 °C for 1 h. Then, the reaction was cooled to ambient temperature. The orange solid was collected and washed with THF (5.0 mL) and dry *n*-hexane (2 × 10 mL). The orange solid was dried under vacuum, providing complex *trans*-**192a** (203 mg, 48%).

Characteristic Data for *trans*-**192a**



^{1}H-NMR (300 MHz, CD_2Cl_2): δ = 8.79 (d, J = 5.7 Hz, 1H), 7.90 (d, J = 7.4 Hz, 1H), 7.30–7.06 (m, 30H), 6.93–6.84 (m, 1H), 6.74 (dd, J = 7.4, 1.7 Hz, 1H), 6.64 (d, J = 8.2 Hz, 1H), 6.53 (ddd, J = 7.4, 7.1, 1.7 Hz, 1H), 6.46 (dd, J = 7.4, 7.1 Hz, 1H), 6.34 (ddd, J = 7.2, 5.7, 1.5 Hz, 1H), 0.77 (s, 3H).

^{13}C-NMR (75 MHz, CD_2Cl_2): δ = 184.5 (dd, J = 23, 11 Hz, C_q), 180.9 (C_q), 169.8 (C_q), 153.2 (CH), 148.8 (C_q), 140.7 (CH), 134.7 (t, $^2J_{C–P} + {}^4J_{C–P}$ = 11 Hz, CH), 133.0 (t, $^1J_{C–P} + {}^3J_{C–P}$ = 35 Hz, C_q), 131.9 (CH), 129.1 (CH), 127.7 (t, $^3J_{C–P} + {}^5J_{C–P}$ = 9 Hz, CH), 125.3 (CH), 123.5 (CH), 118.8 (CH), 118.0 (CH), 117.9 (CH), 22.8 (CH_3).

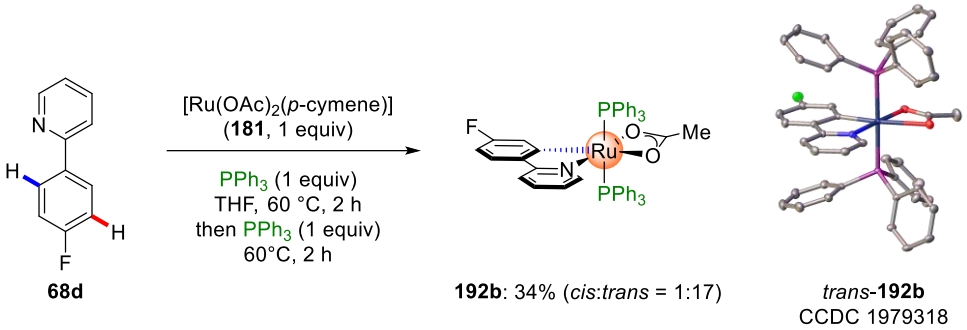
^{31}P{^{1}H}-NMR (121 MHz, CD_2Cl_2): δ = 41.2 (s).

IR (ATR): $\tilde{\nu}$ = 3047, 1536, 1431, 1090, 1067, 745, 693, 672, 510, 493 cm^{-1}.

m.p.: 100–103 °C (decomp.).

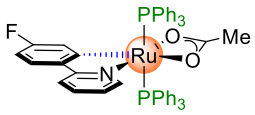
MS (LIFDI) *m*/*z* (relative intensity): 839.2 (100) $[M]^+$.

*Preparation of Ruthenacycle **192b***



2-(4-Fluorophenyl)pyridine (**68d**, 86.6 mg, 0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 177 mg, 0.50 mmol), and PPh_3 (131 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. THF (2.0 mL) was added and the mixture was stirred at 60 °C. After 2 h, an additional PPh_3 (131 mg, 0.50 mmol) was added into the reaction mixture at ambient temperature and the mixture was again stirred at 60 °C for an additional 2 h. An orange solid formed during this time and the reaction was cooled to ambient temperature. The orange solid was collected and washed with THF (5.0 mL) and dry *n*-hexane (2 × 10 mL). The orange solid was dried under vacuum, providing complex **192b** (145 mg, 34%, *cis*:*trans* = 1:17). Suitable crystals of *trans*-**192b** for X-ray crystallography were grown by slow crystallization from CH_2Cl_2/*n*-hexane (*see X-Ray Crystallographic Analysis section*).

Characteristic Data for **192b**



^{1}H-NMR (300 MHz, CD_2Cl_2, determined as a mixture of *cis*- and *trans*-isomer 1:16): δ = 8.78 (d, *J* = 5.7 Hz, 1H, *trans*-isomer), 8.22 (d, *J* = 5.7 Hz, 1H, *cis*-isomer), 7.54 (dd, *J* = 10.7, 2.6 Hz, 1H, *trans*-isomer), 7.33–7.06 (m, 30H, *trans*-isomer), 6.91 (ddd, *J* = 7.9, 7.5, 1.5 Hz, 1H, *trans*-isomer), 6.69 (dd, *J* = 8.7, 5.9 Hz, 1H, *trans*-isomer), 6.60 (d, *J* = 7.9 Hz, 1H, *trans*-isomer), 6.51 (ddd, *J* = 8.5, 8.5, 2.5 Hz, 1H, *cis*-isomer), 6.35 (ddd, *J* = 7.5, 5.7, 1.4 Hz, 1H, *trans*-isomer), 6.14 (ddd, *J* = 8.9, 8.7, 2.6 Hz, 1H, *trans*-isomer), 1.07 (s, 3H, *cis*-isomer), 0.77 (s, 3H, *trans*-isomer). Due to overlapping, some proton peaks of *cis*-**192b** could determined by ^{1}H-NMR.

^{19}F{^{1}H}-NMR (282 MHz, CD_2Cl_2, determined as a mixture of *cis*- and *trans*-isomer 1:16): δ = –116.7 (s, *cis*-isomer), –116.9 (s, *trans*-isomer).

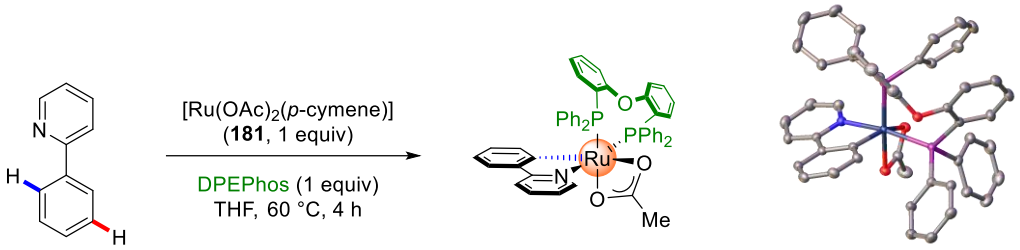
^{31}P{^{1}H}-NMR (121 MHz, CD_2Cl_2, determined as a mixture of *cis*- and *trans*-isomer 1:16): δ = 56.5 (d, *J* = 31.8 Hz, 1P, *cis*-isomer), 51.7 (d, *J* = 31.8 Hz, 1P, *cis*-isomer), 41.1 (s, *trans*-isomer).

IR (ATR): $\tilde{\nu}$ = 3053, 1585, 1541, 1430, 1090, 855, 740, 693, 510, 405 cm^{-1}.

m.p.: 130–133 °C (decomp.).

MS (LIFDI) *m*/*z* (relative intensity): 857.2 (100) $[M]^+$.

*Preparation of Ruthenacycle **193***



68b **193**: 65% **193** CCDC 1915688

2-Phenylpyridine (**68b**, 77.6 mg, 0.50 mmol), $[Ru(OAc)_2(p\text{-cymene})]$ (**181**, 177 mg, 0.50 mmol), and bis[2-(diphenylphosphino)phenyl]ether (DPEPhos, 269 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. THF (2.0 mL) was added and the mixture was stirred at 60 °C for 4 h. A yellow solid formed during this time and the reaction was cooled to ambient temperature. The yellow solid was collected and washed with dry *n*-hexane (2 × 10 mL). The yellow solid was dried under vacuum, providing complex **193** (276 mg, 65%). Suitable crystals of **193** for X-ray crystallography were grown by slow crystallization from THF/*n*-hexane (*see X-Ray Crystallographic Analysis section*).

^{1}H-NMR (400 MHz, CD_2Cl_2): δ = 7.94–7.89 (m, 1H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.54–7.06 (m, 20H), 6.91 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.87–6.79 (m, 2H), 6.74–6.62 (m, 5H), 6.57 (dd, *J* = 8.3, 8.3 Hz, 1H), 6.43 (dd, *J* = 6.5, 6.5 Hz, 1H), 6.23 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.08 (dd, *J* = 8.7, 8.7 Hz, 2H), 0.87 (d, *J* = 1.7 Hz, 3H).

^{13}C-NMR (100 MHz, CD_2Cl_2): δ = 184.5 (d, $^3J_{C-P}$ = 2 Hz, C_q), 182.0 (dd, $^3J_{C-P}$ = 17, 8 Hz, C_q), 164.5 (C_q), 160.7 (d, $^2J_{C-P}$ = 8 Hz, C_q), 158.9 (d, $^2J_{C-P}$ = 8 Hz, C_q), 151.1 (CH), 146.6 (d, $^2J_{C-P}$ = 1 Hz, C_q), 145.3 (d, $^4J_{C-P}$ = 4 Hz, CH), 136.8 (d, $^1J_{C-P}$ = 42 Hz, C_q), 136.3 (d, $^1J_{C-P}$ = 43 Hz, C_q), 136.1–135.5 (m, CH), 135.4 (CH), 135.2 (d, $^1J_{C-P}$ = 39 Hz, C_q), 135.2–134.6 (br, CH), 134.0 (d, $^1J_{C-P}$ = 37 Hz, C_q), 134.1–133.6 (m, CH), 131.6 (d, $^2J_{C-P}$ = 9 Hz, CH), 131.3 (CH), 131.1 (CH), 129.3 (CH), 128.6 (d, $^4J_{C-P}$ = 2 Hz, CH), 127.9 (d, $^4J_{C-P}$ = 2 Hz, CH), 127.8 (d, $^3J_{C-P}$ = 7 Hz, CH), 127.7 (d, $^3J_{C-P}$ = 7 Hz, CH), 127.4 (d, $^1J_{C-P}$ = 39 Hz, C_q), 127.2 (d, $^3J_{C-P}$ = 9 Hz, CH), 126.9 (d, $^3J_{C-P}$ = 8 Hz, CH), 125.7 (CH), 125.4 (d, $^1J_{C-P}$ = 38 Hz, C_q), 124.7

(d, $^{3}J_{C–P}$ = 6 Hz, CH), 124.4 (d, $^{3}J_{C–P}$ = 5 Hz, CH), 123.3 (d, $^{3}J_{C–P}$ = 6 Hz, CH), 122.9 (CH), 120.1 (d, $^{4}J_{C–P}$ = 3 Hz, CH), 119.7 (CH), 118.6 (br, CH), 117.6 (d, $^{4}J_{C–P}$ = 2 Hz, CH), 23.6 (d, $^{4}J_{C–P}$ = 2 Hz, CH_3).

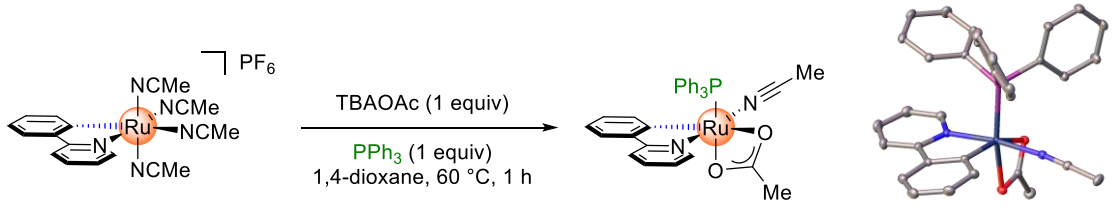
$^{31}P\{^{1}H\}$-NMR (162 MHz, CD_2Cl_2): δ = 59.5 (d, J = 37.7 Hz), 46.7 (d, J = 37.7 Hz).

IR (ATR): $\tilde{\nu}$ = 3050, 1578, 1454, 1433, 1232, 1091, 744, 695, 673, 518 cm^{-1}.

m.p.: 215–217 °C (decomp.).

MS (LIFDI) m/z (relative intensity): 853.1 (100) $[M]^+$.

*Preparation of Ruthenacycle **194***



98 **194**: 75% **194** CCDC 1915689

Ruthenacycle **98** (282 mg, 0.50 mmol), TBAOAc (151 mg, 0.50 mmol), and PPh_3 (131 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. 1,4-Dioxane (1.6 mL) was added and the mixture was stirred at 60 °C for 1 h. Then, the reaction was cooled to ambient temperature. The orange solid was collected and washed with THF (5.0 mL) and dry *n*-hexane (2 × 10 mL). The orange solid was dried under vacuum, providing complex **194** (234 mg, 75%). Suitable crystals of **194** for X-ray crystallography were grown by slow crystallization from CH_2Cl_2/*n*-hexane (*see X-Ray Crystallographic Analysis section*).

^{1}H-NMR (300 MHz, CD_2Cl_2): δ = 8.44 (d, J = 5.9 Hz, 1H), 7.61 (d, J = 7.6 Hz, 1H), 7.47–7.34 (m, 3H), 7.30–7.19 (m, 3H), 7.19–7.08 (m, 12H), 6.83 (ddd, J = 7.5, 7.3, 1.5 Hz, 1H), 6.78–6.67 (m, 2H), 2.12 (s, 3H), 1.89 (s, 3H).

^{13}C-NMR (100 MHz, CD_2Cl_2): δ = 187.3 (d, $^{2}J_{C–P}$ = 16 Hz, C_q), 185.3 (C_q), 167.4 (C_q), 151.8 (CH), 146.6 (C_q), 140.0 (CH), 135.7 (d, $^{1}J_{C–P}$ = 43 Hz, C_q), 134.7 (CH), 133.6 (d, $^{2}J_{C–P}$ = 10 Hz, CH), 129.1 (d, $^{4}J_{C–P}$ = 2 Hz, CH), 127.9 (d, $^{3}J_{C–P}$ = 9 Hz, CH), 126.8 (CH), 123.9 (CH), 122.1 (C_q), 120.6 (CH), 119.1 (CH), 118.0 (CH), 24.7 (CH_3), 4.9 (CH_3).

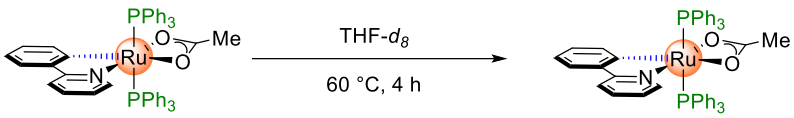
$^{31}P\{^{1}H\}$-NMR (162 MHz, CD_2Cl_2): δ = 65.7 (s).

IR (ATR): $\tilde{\nu}$ = 3052, 2241, 1538, 1474, 1434, 1092, 751, 696, 664, 518 cm^{-1}.

m.p.: 147–149 °C (decomp.).

MS (LIFDI) *m/z* (relative intensity): 618.2 (100) $[M]^+$.

*Isomerization of Ruthenacycle trans-**192a***



trans-**192a** *cis*-/*trans*-**192a** (0.3:1.0)

The NMR tube equipped with J. Young valve was charged with the solution of *trans*-**192a** (42.0 mg, 50 µmol) in THF-d_8 (0.5 mL). Then, the tube was heated at 60 °C. After 4 h, the tube was cooled to ambient temperature and measured $^{31}P\{^1H\}$-NMR spectroscopy (Figure 31).

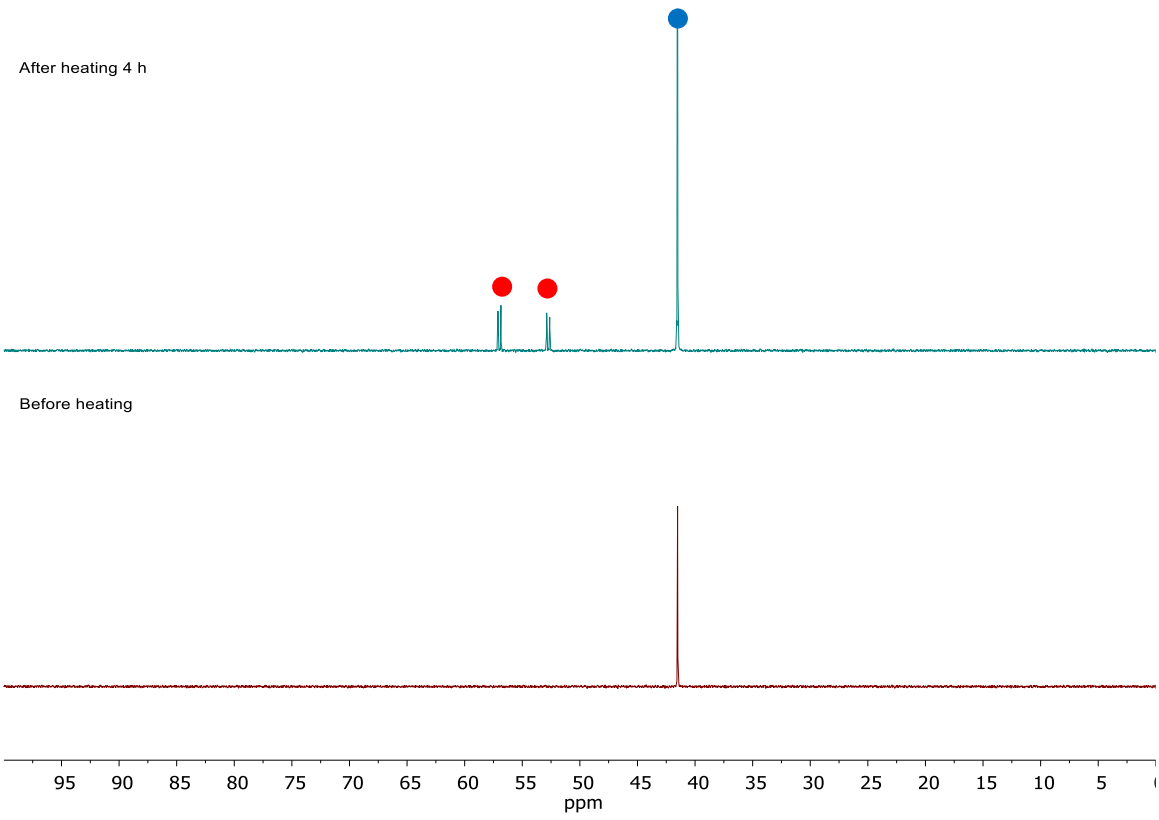
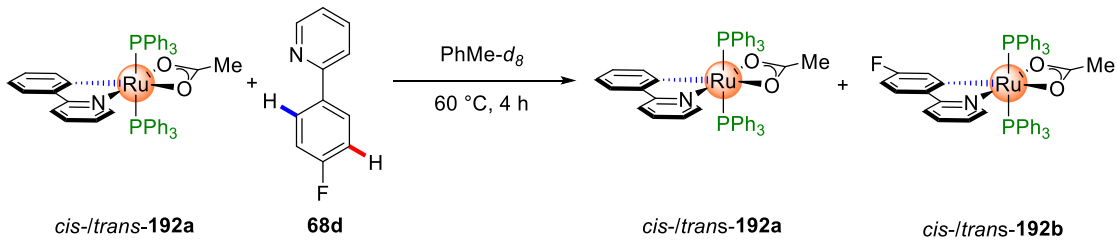


Figure 31: Isomerization of ruthenacycle *trans*-**192a** determined by $^{31}P\{^1H\}$-NMR spectroscopy (*cis*-isomer = ●, *trans*-isomer = ●).

*Ligand Exchange of Ruthenacycle cis-/trans-**192a** with pyridine **68d***



cis-/trans-**192a** **68d** *cis-/trans*-**192a** *cis-/trans*-**192b**

The NMR tube equipped with J. Young valve was charged with the solution of *cis-/trans*-**192a** (42.0 mg, 50 µmol, *cis*:*trans* = 1:10) and pyridine **68d** (8.7 mg, 50 µmol) in PhMe-d_8 (0.5 mL). K_2CO_3 (7.0 mg, 50 µmol) was then added and the tube was heated at 60 °C. After 4 h, the tube was cooled to ambient temperature and measured $^{31}P\{^1H\}$-NMR spectroscopy.

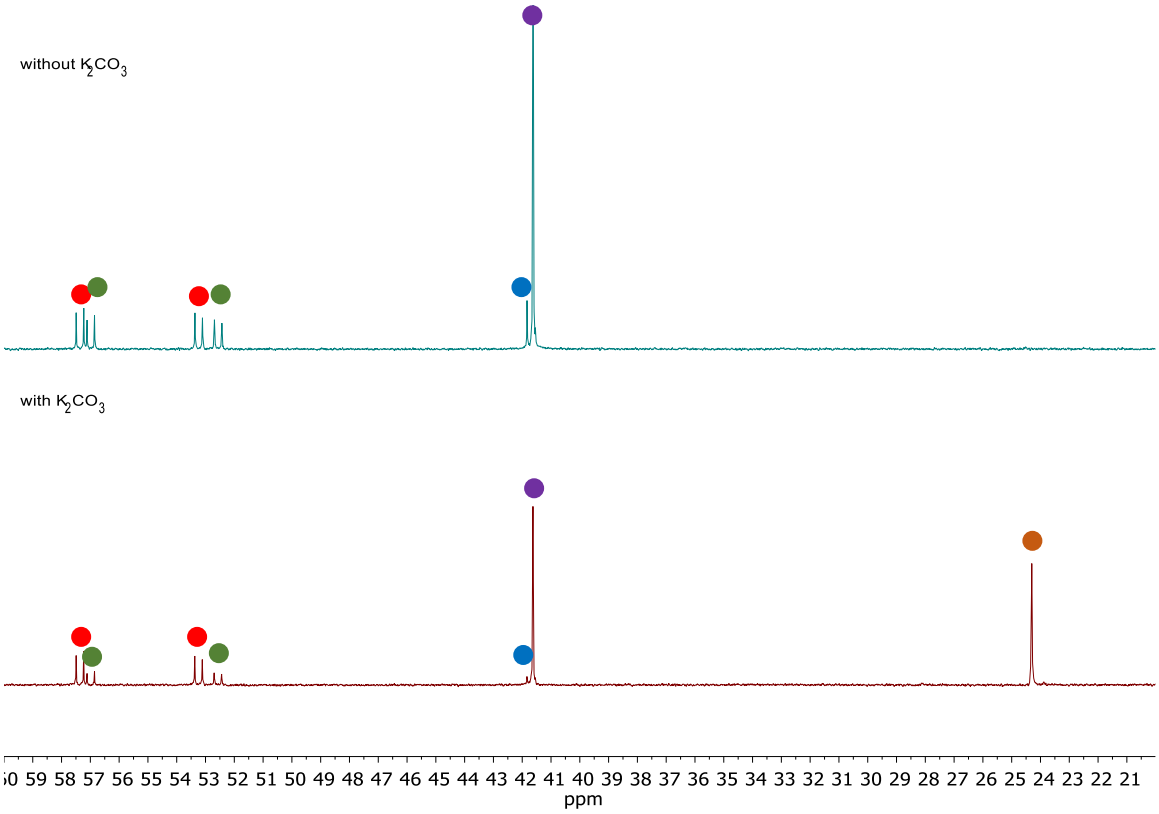
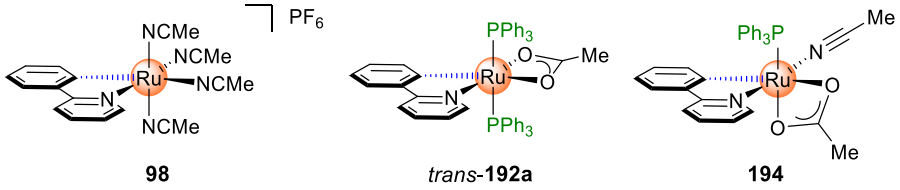


Figure 32: Ligand exchange of ruthenacycle **192a** with **68d** determined by $^{31}P\{^1H\}$-NMR spectroscopy (*cis*-**192a** = ●, *trans*-**192a** = ●, *cis*-**192b** = ●, *trans*-**192b** = ●, O=PPh_3 = ●).

Cyclic Voltammetry

Cyclic voltammetric analysis was carried out with a Metrohm Autolab PGSTAT204 workstation and analysis was performed with Nova 2.1.4 software. A glassy-carbon electrode (3 mm-diameter, disc-electrode) was used as the working electrode, a Pt wire was used as the auxiliary electrode and a Ag/AgCl electrode was used as the reference. 1,2-DCE with 0.1 mol·L^{-1} n-Bu_4NPF_6 as conducting salt served as electrolytes for the measurements. 1,2-DCE was dried and degassed prior to its use. Measurements were carried out at a scan rate of 100 mV·s^{-1}.



98 *trans*-**192a** **194**

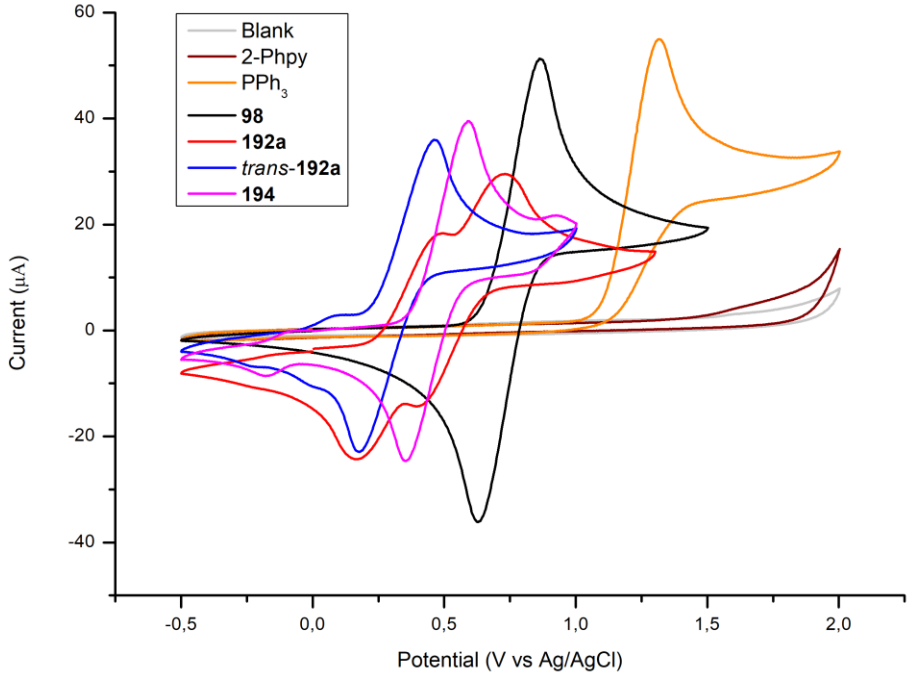
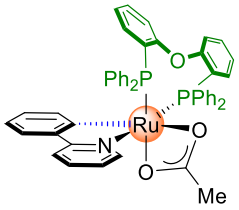
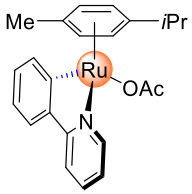


Figure 33: Cyclic voltammogram at 100 mV·s^{-1} in 1,2-DCE. *n*-Bu_4NPF_6 (0.1 M in 1,2-DCE), concentration of substrates 4 mM. $E_{1/2}$ of **98** = 0.75 V, $E_{1/2}$ of *cis*-/*trans*-**192a** = 0.33 and 0.56 V, $E_{1/2}$ of *trans*-**192a** = 0.32 V, $E_{1/2}$ of **194** = 0.47 V.



193



195

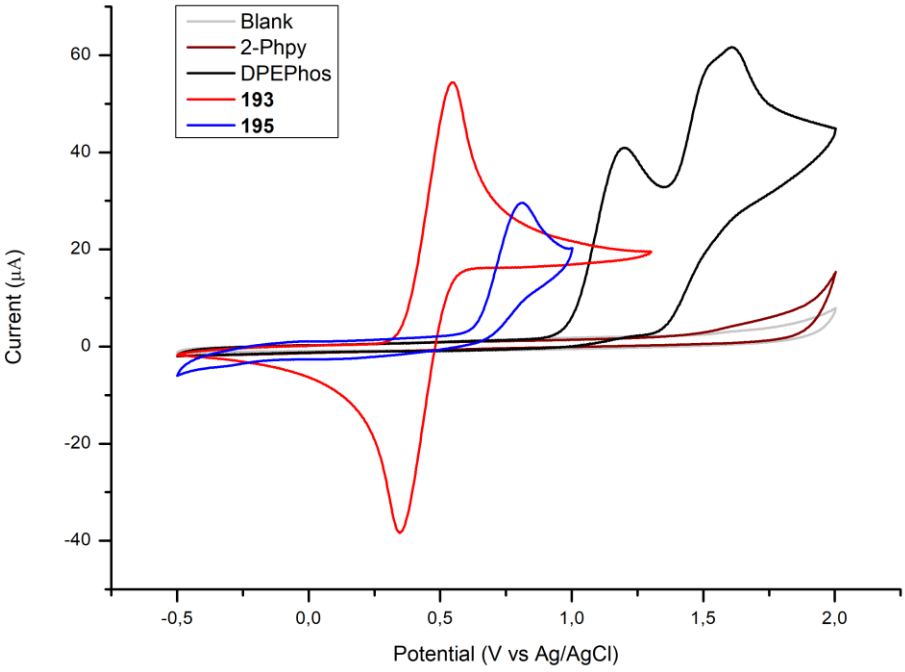
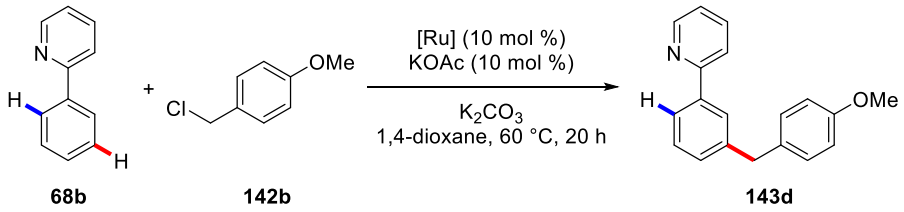
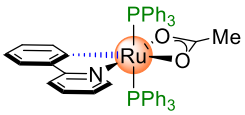


Figure 34: Cyclic voltammogram at 100 mV·s^{-1} in 1,2-DCE. *n*-Bu_4NPF_6 (0.1 M in 1,2-DCE), concentration of substrates 4 mM. $E_{1/2}$ of **193** = 0.44 V, E_{ox} of **195** = 0.81 V.

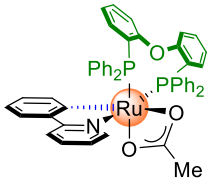
*Catalytic Reactions with Ruthenacycle trans-**192a**, **193**, and **194***



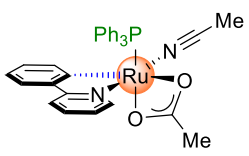
68b **142b** **143d**



trans-**192a**



193



194

Reactions with Ruthenacycle *trans*-**192a**

2-Phenylpyridine (**68b**, 38.8 mg, 0.25 mmol), *trans*-**192a** (21.0 mg, 25.0 µmol, 10 mol %), KOAc (2.5 mg, 25.0 µmol, 10 mol %) and K_2CO_3 (69 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. 4-Methoxybenzyl chloride (**142b**, 118 mg, 0.75 mmol) and 1,4-dioxane (1.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 10:1) yielded *meta*-benzylated product **143d** (37.2 mg, 54%). In case of the condition without KOAc, the reaction gave the product **143d** (26.8 mg, 39%).

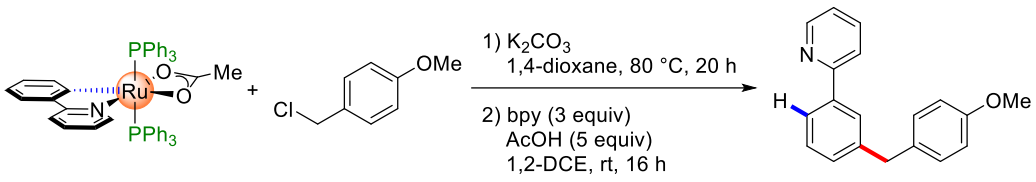
Reactions with Ruthenacycle **193**

2-Phenylpyridine (**68b**, 38.8 mg, 0.25 mmol), **193** (21.3 mg, 25.0 µmol, 10 mol %), KOAc (2.5 mg, 25.0 µmol, 10 mol %) and K_2CO_3 (69 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. 4-Methoxybenzyl chloride (**142b**, 118 mg, 0.75 mmol) and 1,4-dioxane (1.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was determined by gas chromatography. Both reactions with and without KOAc did not afford any conversion of the product **143d**.

Reactions with Ruthenacycle **194**

2-Phenylpyridine (**68b**, 77.6 mg, 0.5 mmol), **194** (30.9 mg, 50.0 µmol, 10 mol %), KOAc (5.0 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (139 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. 4-Methoxybenzyl chloride (**142b**, 235 mg, 1.5 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred at 60 °C. After 20 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 10:1) yielded *meta*-benzylated product **194** (81.0 mg, 59%). In case of the condition without KOAc, the reaction gave the product **194** (68.7 mg, 50%).

*Stoichiometric Reactions of Ruthenacycle **192a***



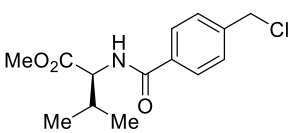
192a **142b** **143d**

cis-/*trans*-**192a**	40%
trans-**192a**	48%

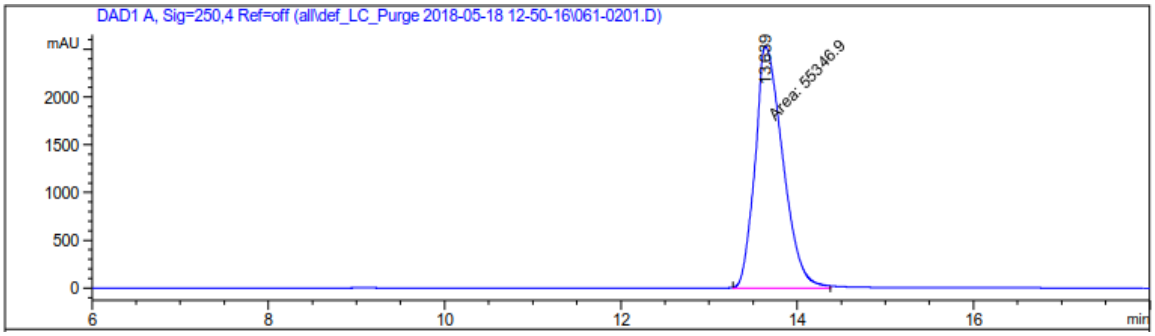
Ruthenacycle **192a** (84.0 mg, 0.10 mmol) and K_2CO_3 (28.0 mg, 0.20 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. 4-Methoxybenzyl chloride (**142b**, 23.5 mg, 0.15 mmol) and 1,4-dioxane (1.0 mL) were then added and the mixture was stirred at 80 °C for 20 h. At ambient temperature, 2,2'-bipyridine (46.9 mg, 0.30 mmol), AcOH (30.0 mg, 0.50 mmol) and 1,2-DCE (1.0 mL) were added, and the resulting mixture was stirred at ambient temperature for 16 h. Then, the reaction mixture was quenched with sat. aq. $NaHCO_3$ solution (10 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (*n*-hexane/EtOAc 10:1) yielded *meta*-benzylated product **143d** (in case of *cis*-/*trans*-**192a**: 11.0 mg, 40%, in case of *trans*-**192a**: 13.2 mg, 48%) as a colorless oil.

5.3.4.5 Racemization Examination

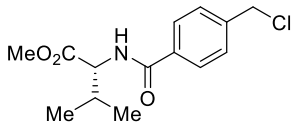
Benzyl chlorides *S*-**186c** and *R*-**186c** were examined by HPLC with a Daicel *CHIRALPAK IA-3* (4.6 mm x 250 mm, 3 µm particle size) *n*-hexane/*i*-PrOH 80:20, 1 mL/min flow rate, detection at 250 nm. *S*-**186c**: t_r = 13.6 min. *R*-**186c**: t_r = 9.9 min.



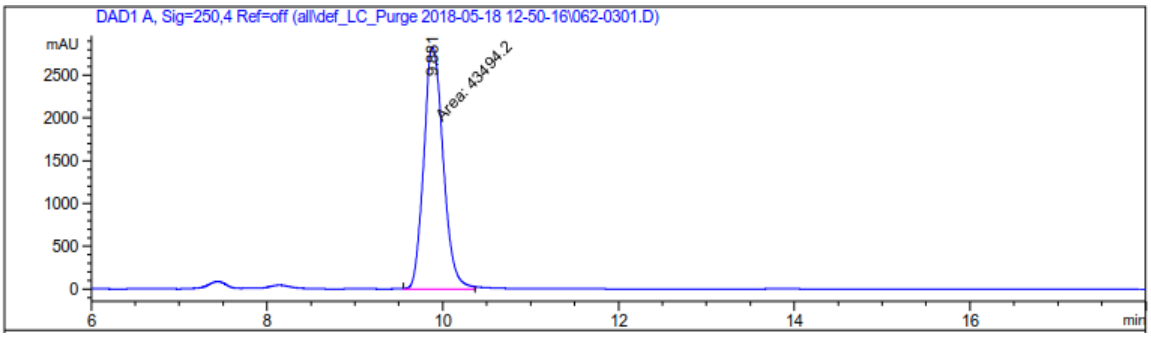
S-**186c**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.639	MF	0.3646	5.53469e4	2529.80151	100.0000

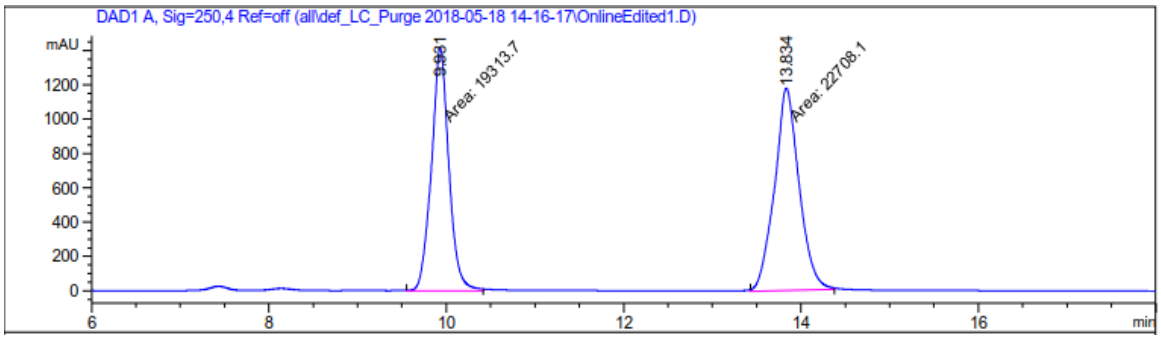


R-**186c**



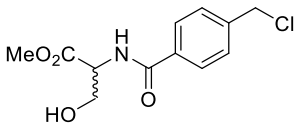
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.881	FM	0.2566	4.34942e4	2824.75732	100.0000

Mixture of *S*-**186c** and *R*-**186c**

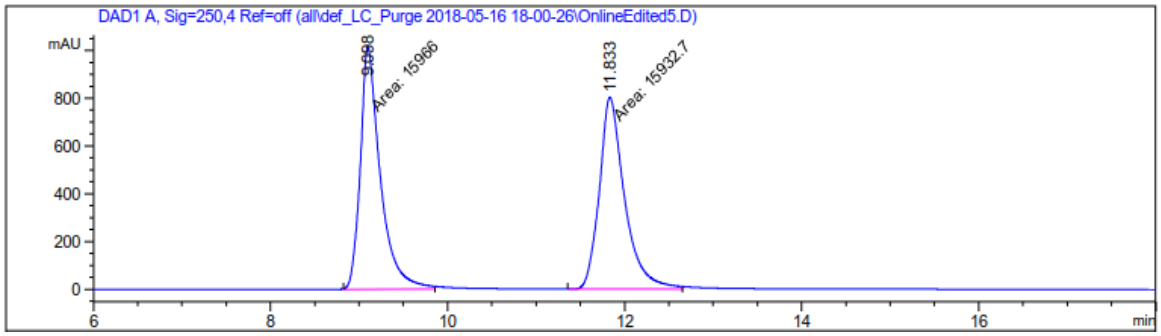


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.931	MF	0.2272	1.93137e4	1416.54846	45.9611
2	13.834	MM	0.3209	2.27081e4	1179.35181	54.0389

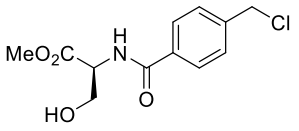
Benzyl chlorides *rac*-**186d** and *S*-**186d** were examined by HPLC with a Daicel *CHIRALPAK IA-3* (4.6 mm x 250 mm, 3 µm particle size) *n*-hexane/*i*-PrOH 70:30, 1 mL/min flow rate, detection at 250 nm. *S*-**186d**: t_r = 11.8 min. *R*-**186d**: t_r = 9.1 min.



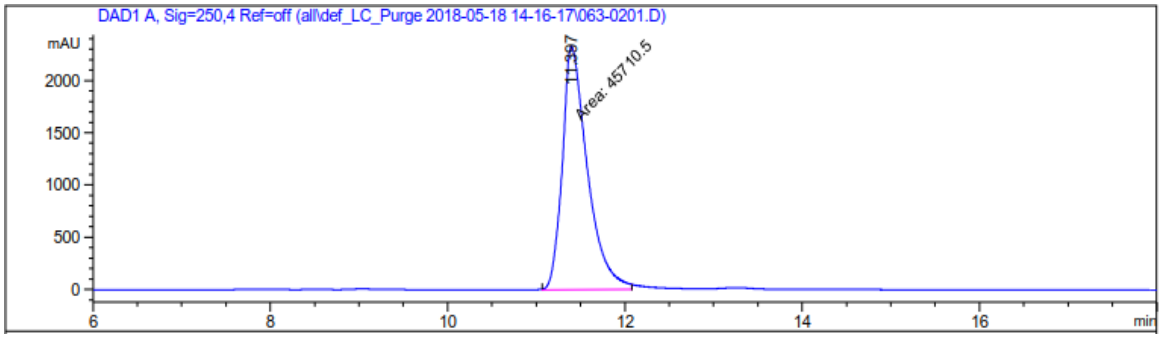
rac-**186d**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.098	FM	0.2622	1.59660e4	1014.76837	50.0523
2	11.833	MF	0.3308	1.59327e4	802.82697	49.9477

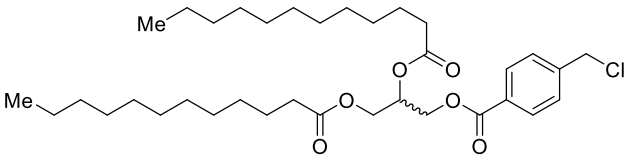


S-**186d**

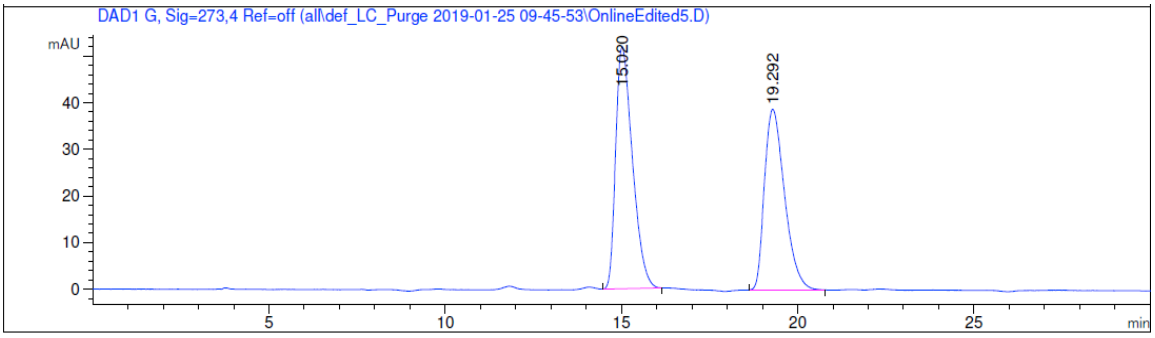


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.397	FM	0.3281	4.57105e4	2322.30566	100.0000

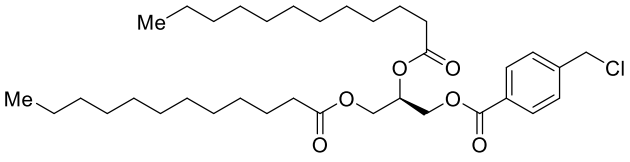
Benzyl chlorides *rac*-**186j** and *R*-**186j** were examined by HPLC with a Daicel *CHIRALPAK IC-3* (4.6 mm x 250 mm, 3 µm particle size) *n*-hexane/EtOAc 95:5, 1 mL/min flow rate, detection at 273 nm. *R*-**186j**: t_r = 15.0 min. *S*-**186j**: t_r = 19.3 min.



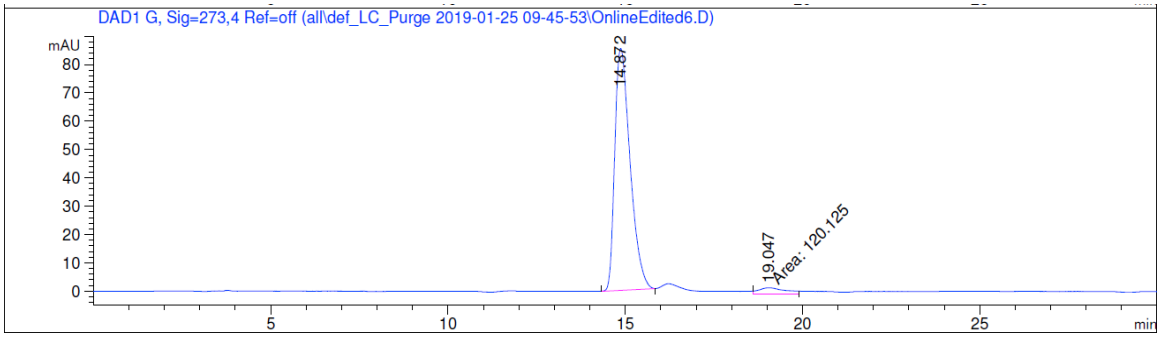
rac-**186j**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.020	BB	0.4839	1714.88147	51.84497	52.7173
2	19.292	BB	0.5489	1538.09607	38.76307	47.2827

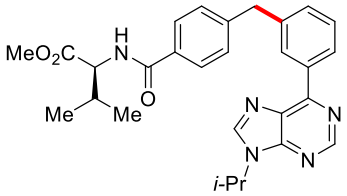


R-**186j**

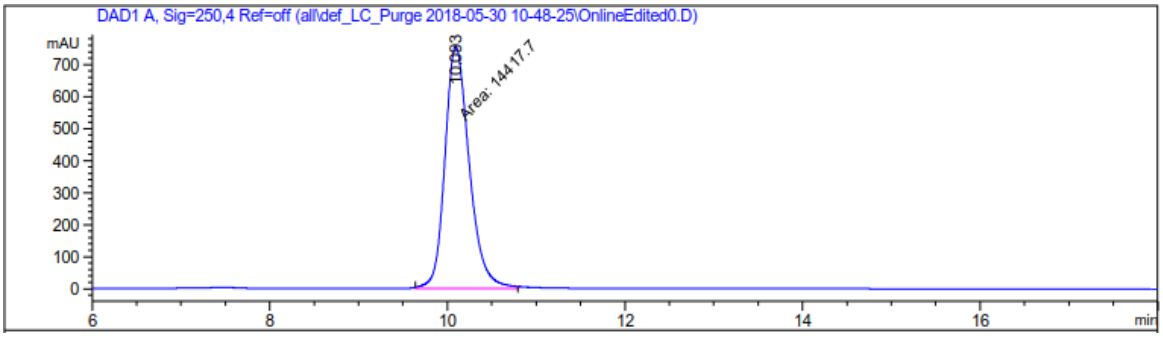


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.872	BB	0.4534	2565.91406	85.42355	95.5278
2	19.047	MM	0.8916	120.12537	2.24563	4.4722

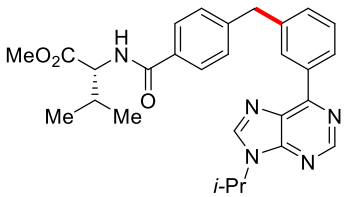
Compound *S*-**187e** and *R*-**187e** were examined by HPLC with a Daicel *CHIRALPAK IA-3* (4.6 mm x 250 mm, 3 µm particle size) *n*-hexane/*i*-PrOH 50:50, 1 mL/min flow rate, detection at 250 nm. *S*-**187e**: t_r = 10.1 min. *R*-**187e**: t_r = 7.8 min.



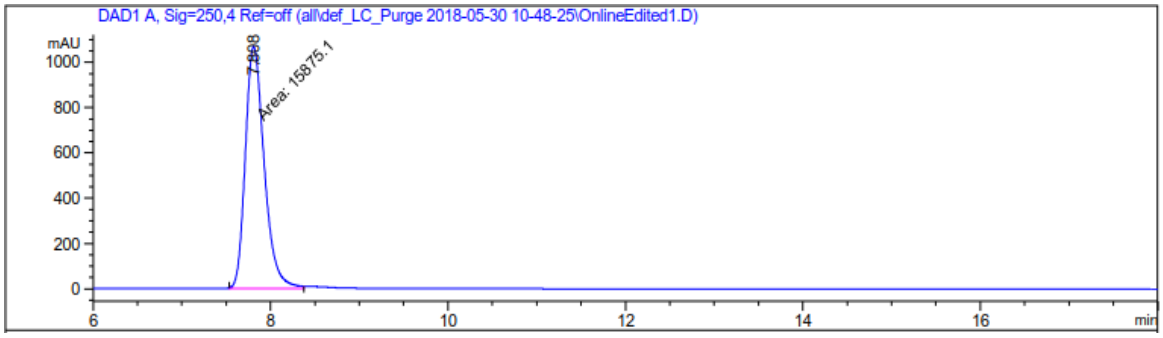
S-**187e**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.093	MF	0.3179	1.44177e4	755.91595	100.0000

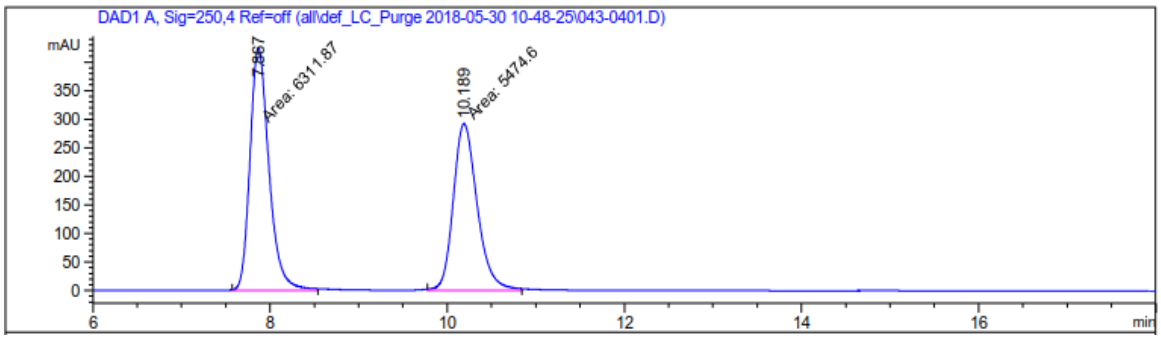


R-**187e**



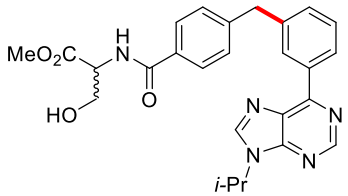
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.808	FM	0.2474	1.58751e4	1069.53699	100.0000

Mixture of *S*-**187e** and *R*-**187e**

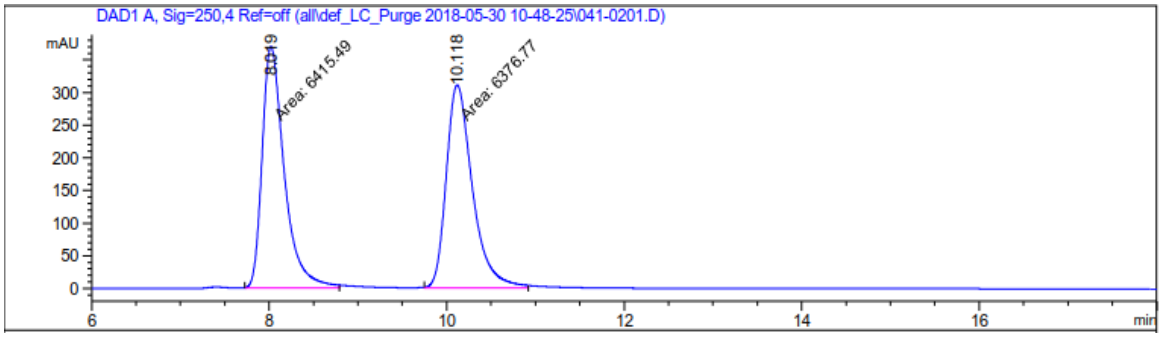


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.867	MF	0.2481	6311.86572	423.93903	53.5518
2	10.189	FM	0.3124	5474.60303	292.04456	46.4482

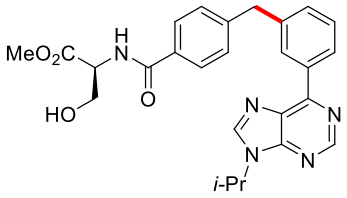
Compound *rac*-**187f** and *S*-**187f** were examined by HPLC with a Daicel *CHIRALPAK IA-3* (4.6 mm x 250 mm, 3 µm particle size) *n*-hexane/*i*-PrOH 50:50, 1 mL/min flow rate, detection at 250 nm. *S*-**187f**: t_r = 10.1 min. *R*-**187f**: t_r = 8.0 min.



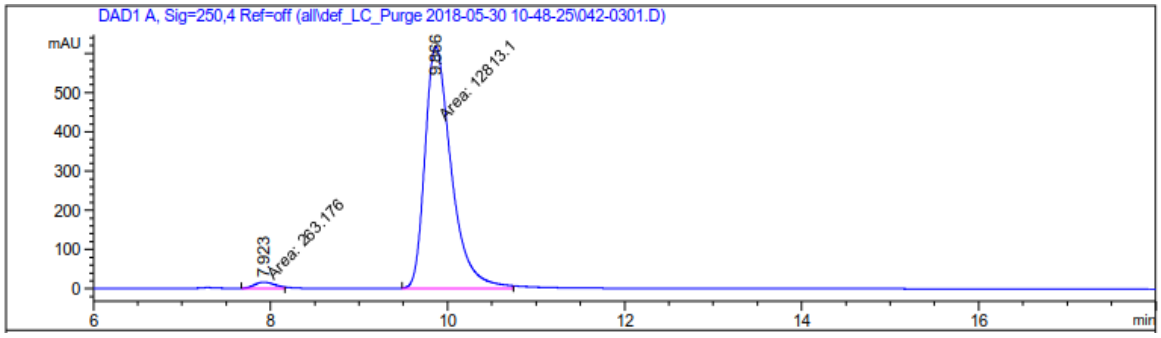
rac-**187f**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.019	FM	0.2891	6415.49023	369.85632	50.1513
2	10.118	MF	0.3419	6376.77344	310.82327	49.8487

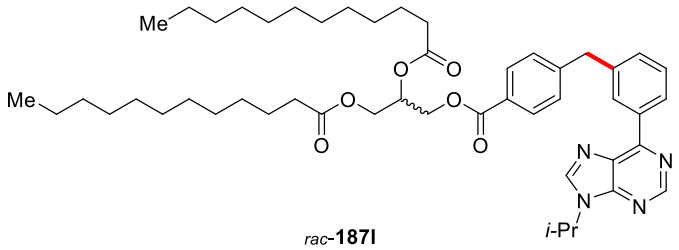


S-**187f**

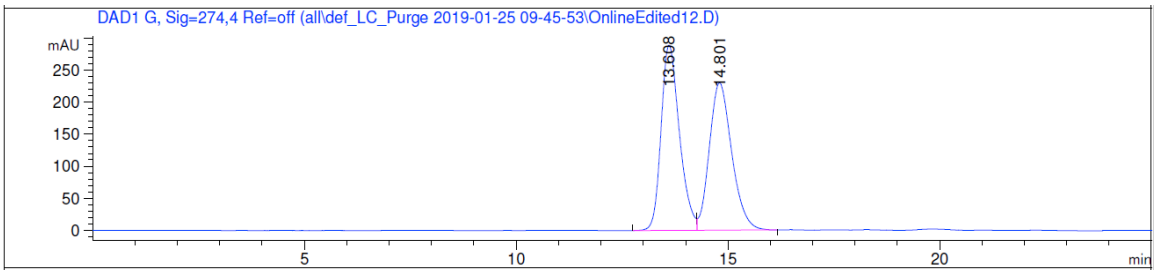


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.923	MF	0.2709	263.17639	16.19169	2.0126
2	9.866	MF	0.3459	1.28131e4	617.32446	97.9874

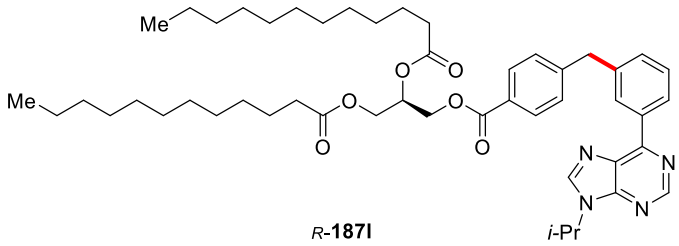
Compound *rac*-**187l** and *R*-**187l** were examined by HPLC with a Daicel *CHIRALPAK IC-3* (4.6 mm x 250 mm, 3 µm particle size) *n*-hexane/EtOAc 85:15, 1 mL/min flow rate, detection at 274 nm. *R*-**187l**: t_r = 13.6 min. *S*-**187l**: t_r = 14.8 min.



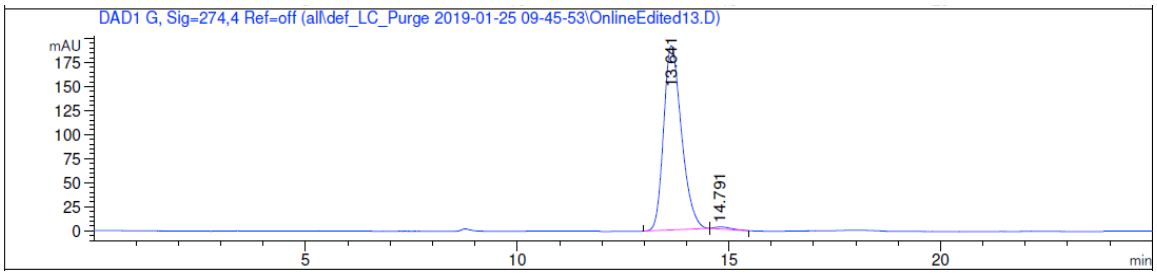
rac-**187l**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.608	BV	0.4571	8689.30371	288.75269	50.7088
2	14.801	VB	0.5668	8446.39355	229.82544	49.2912



R-**187l**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.641	BB	0.4463	5623.72949	191.69371	99.0091
2	14.791	BB	0.3248	56.28119	2.05320	0.9909

5.3.4.6 Fluorescence Spectra

Concentration of sample: 1 mg/L in $CHCl_3$

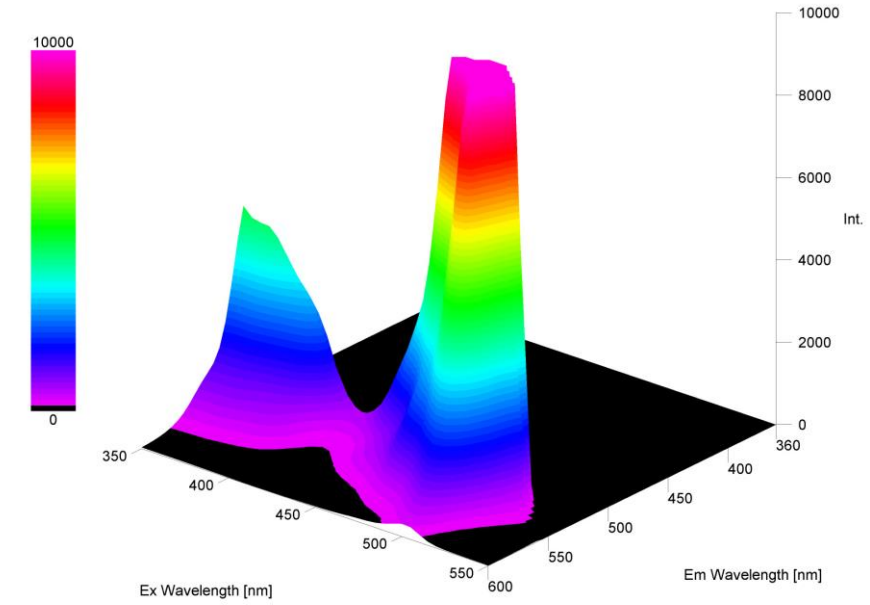


Figure 35: Excitation/emission fluorescence spectrum of **187a**.

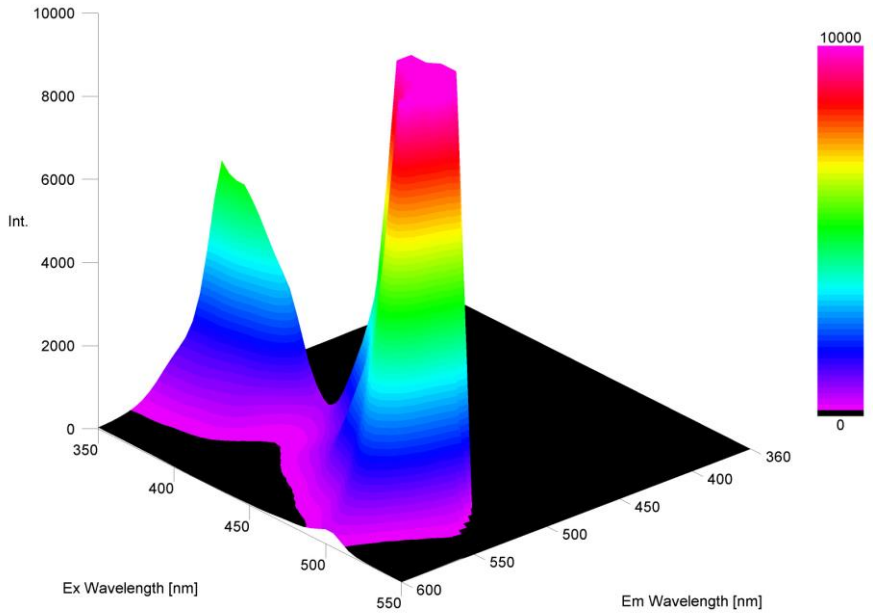


Figure 36: Excitation/emission fluorescence spectrum of **187b**.

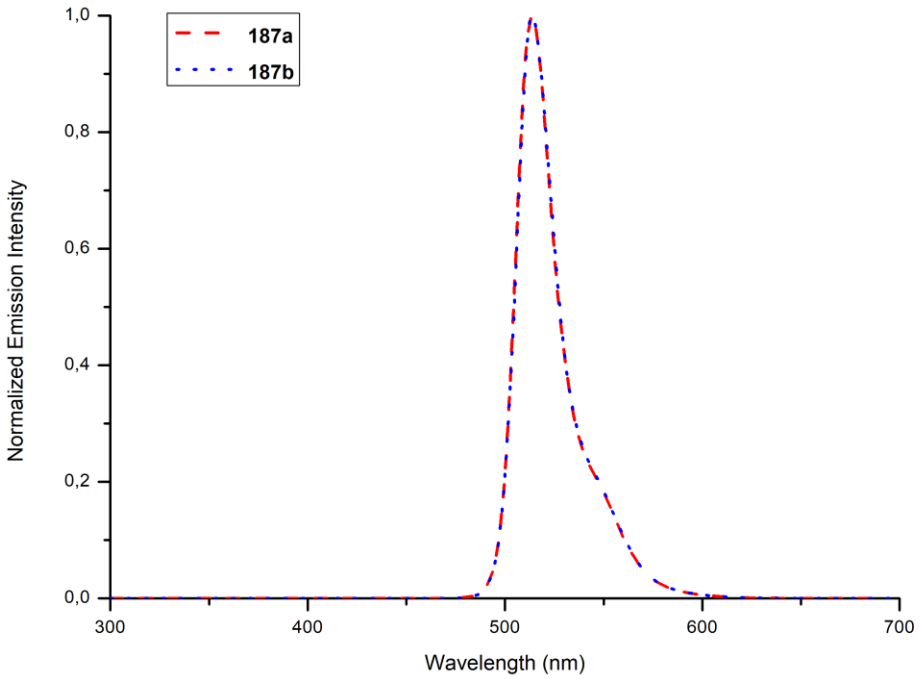


Figure 37: Emission fluorescence spectra of **187a** and **187b** (excitation at 502 nm).

5.3.4.7 X-Ray Crystallographic Analysis

A suitable crystal was selected and the crystal was mounted on a MITIGEN holder in NVH oil on a Bruker D8 Venture diffractometer. The crystal was kept at 100 or 150 K during data collection. Using Olex2,[137] the structure was solved with the XT[138] structure solution program using Intrinsic Phasing and refined with the XL[139] refinement package using Least Squares minimisation.

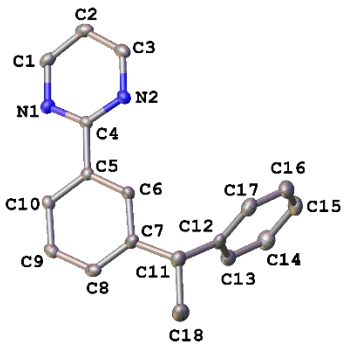


Figure 38: Molecular structure of **143a** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{18}H_{16}N_2$ (*M* = 260.33 g/mol): orthorhombic, space group $Pca2_1$ (no. 29), *a* = 12.2928(3) Å, *b* = 6.01020(10) Å, *c* = 36.9034(9) Å, *V* = 2726.50(10) Å^3, *Z* = 8, *T* = 99.97 K, μ(MoKα) = 0.075 mm^{-1}, *Dcalc* = 1.268 g/cm^3, 28332 reflections measured (6.624° ≤ 2Θ ≤ 59.142°), 7604 unique (R_{int} = 0.0264, R_{sigma} = 0.0245) which were used in all calculations. The final R_1 was 0.0431 (I > 2σ(I)) and wR_2 was 0.1162 (all data).

Table 38: Crystal data and structure refinement for **143a**.

Compound	**143a**
CCDC number	1915687
Identification code	Pca21
Empirical formula	$C_{18}H_{16}N_2$
Formula weight	260.33
Temperature/K	99.97
Crystal system	orthorhombic
Space group	$Pca2_1$
a/Å	12.2928(3)
b/Å	6.01020(10)
c/Å	36.9034(9)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2726.50(10)
Z	8
ρ_{calc}g/cm^3	1.268
μ/mm^{-1}	0.075
F(000)	1104.0
Crystal size/mm^3	0.309 × 0.268 × 0.244
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.624 to 59.142
Index ranges	-17 ≤ h ≤ 17, -8 ≤ k ≤ 8, -51 ≤ l ≤ 51
Reflections collected	28332

Independent reflections	7604 [R_{int} = 0.0264, R_{sigma} = 0.0245]
Data/restraints/parameters	7604/151/452
Goodness-of-fit on F^2	1.050
Final R indexes [I>=2σ (I)]	R_1 = 0.0431, wR_2 = 0.1153
Final R indexes [all data]	R_1 = 0.0443, wR_2 = 0.1162
Largest diff. peak/hole / e $Å^{-3}$	0.52/-0.25
Flack parameter	-0.2(5)

Table 39: Bond lengths [Å] for **143a**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N1	C1	1.342(3)	C7	C11	1.541(3)
N1	C4	1.337(2)	C8	C9	1.403(3)
N2	C3	1.334(3)	C9	C10	1.388(3)
N2	C4	1.342(3)	C11	C12	1.524(3)
C1	C2	1.378(3)	C11	C18	1.522(3)
C2	C3	1.391(3)	C12	C13	1.393(3)
C4	C5	1.486(3)	C12	C17	1.384(4)
C5	C6	1.394(3)	C13	C14	1.397(3)
C5	C10	1.396(3)	C14	C15	1.388(4)
C6	C7	1.399(3)	C15	C16	1.379(4)
C7	C8	1.391(3)	C16	C17	1.385(4)

Table 40: Bond angles [°] for **143a**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C4	N1	C1	116.03(18)	C7	C8	C9	120.75(19)
C3	N2	C4	116.4(2)	C10	C9	C8	120.37(19)
N1	C1	C2	122.9(2)	C9	C10	C5	119.62(19)
C1	C2	C3	116.23(19)	C12	C11	C7	109.22(17)
N2	C3	C2	122.4(2)	C18	C11	C7	113.9(2)
N1	C4	N2	126.02(18)	C18	C11	C12	111.3(2)
N1	C4	C5	117.10(17)	C13	C12	C11	122.1(2)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N2	C4	C5	116.87(17)	C17	C12	C11	119.1(2)
C6	C5	C4	119.36(17)	C17	C12	C13	118.8(2)
C6	C5	C10	119.46(18)	C12	C13	C14	120.3(2)
C10	C5	C4	121.18(17)	C15	C14	C13	119.8(2)
C5	C6	C7	121.70(19)	C16	C15	C14	119.9(2)
C6	C7	C11	117.46(19)	C15	C16	C17	120.1(2)
C8	C7	C6	118.1(2)	C12	C17	C16	121.1(2)
C8	C7	C11	124.44(19)				

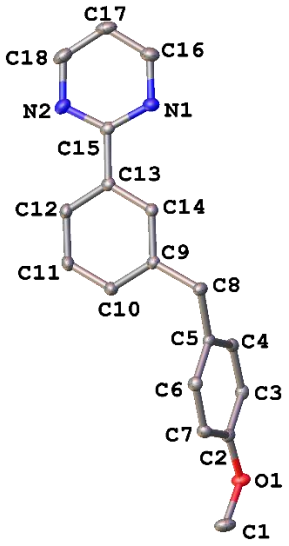


Figure 39: Molecular structure of **143b** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{18}H_{16}N_2O$ (*M* = 276.33 g/mol): orthorhombic, space group Pbca (no. 61), *a* = 18.7085(6) Å, *b* = 6.2302(2) Å, *c* = 24.4878(10) Å, *V* = 2854.24(17) Å^3, *Z* = 8, *T* = 100.0 K, μ(MoKα) = 0.081 mm^{-1}, *Dcalc* = 1.286 g/cm^3, 37416 reflections measured (4.354° ≤ 2Θ ≤ 59.152°), 3996 unique (R_{int} = 0.0318, R_{sigma} = 0.0169) which were used in all calculations. The final R_1 was 0.0436 (I > 2σ(I)) and wR_2 was 0.1102 (all data).

Table 41: Crystal data and structure refinement for **143b**.

Compound	**143b**
CCDC number	1915683

Identification code	Pbca
Empirical formula	$C_{18}H_{16}N_2O$
Formula weight	276.33
Temperature/K	100.0
Crystal system	orthorhombic
Space group	Pbca
a/Å	18.7085(6)
b/Å	6.2302(2)
c/Å	24.4878(10)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2854.24(17)
Z	8
ρ_{calc}g/cm^3	1.286
μ/mm^{-1}	0.081
F(000)	1168.0
Crystal size/mm^3	0.251 × 0.204 × 0.076
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.354 to 59.152
Index ranges	-21 ≤ h ≤ 25, -8 ≤ k ≤ 8, -33 ≤ l ≤ 33
Reflections collected	37416
Independent reflections	3996 [R_{int} = 0.0318, R_{sigma} = 0.0169]
Data/restraints/parameters	3996/0/191
Goodness-of-fit on F^2	1.068
Final R indexes [I>=2σ (I)]	R_1 = 0.0436, wR_2 = 0.1080
Final R indexes [all data]	R_1 = 0.0469, wR_2 = 0.1102
Largest diff. peak/hole / e Å^{-3}	0.37/-0.23

Table 42: Bond lengths [Å] for **143b**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C1	1.4292(13)	C6	C7	1.3970(14)
O1	C2	1.3748(12)	C8	C9	1.5199(13)
N1	C15	1.3420(13)	C9	C10	1.3965(14)
N1	C16	1.3384(14)	C9	C14	1.3961(13)
N2	C15	1.3436(13)	C10	C11	1.3915(14)
N2	C18	1.3394(15)	C11	C12	1.3880(14)
C2	C3	1.3954(13)	C12	C13	1.3999(14)
C2	C7	1.3883(14)	C13	C14	1.3976(13)
C3	C4	1.3854(14)	C13	C15	1.4850(14)
C4	C5	1.4001(13)	C16	C17	1.3807(17)
C5	C6	1.3907(13)	C17	C18	1.3810(18)
C5	C8	1.5123(13)			

Table 43: Bond angles [°] for **143b**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C2	O1	C1	117.38(8)	C14	C9	C8	119.58(9)
C16	N1	C15	116.26(10)	C14	C9	C10	118.70(9)
C18	N2	C15	116.37(10)	C11	C10	C9	120.51(9)
O1	C2	C3	115.48(9)	C12	C11	C10	120.57(9)
O1	C2	C7	124.56(9)	C11	C12	C13	119.69(9)
C7	C2	C3	119.95(9)	C12	C13	C15	119.76(9)
C4	C3	C2	119.97(9)	C14	C13	C12	119.40(9)
C3	C4	C5	121.13(9)	C14	C13	C15	120.79(9)
C4	C5	C8	120.37(9)	C9	C14	C13	121.12(9)
C6	C5	C4	117.99(9)	N1	C15	N2	125.58(10)
C6	C5	C8	121.62(9)	N1	C15	C13	117.25(9)
C5	C6	C7	121.62(9)	N2	C15	C13	117.17(9)
C2	C7	C6	119.33(9)	N1	C16	C17	122.81(11)
C5	C8	C9	115.13(8)	C16	C17	C18	116.37(10)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C10	C9	C8	121.71(9)	N2	C18	C17	122.60(11)

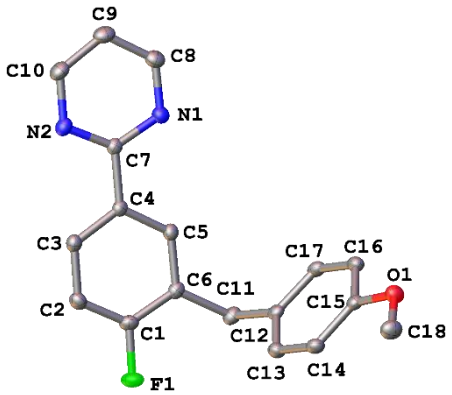


Figure 40: Molecular structure of **143g** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{18}H_{15}FN_2O$ (*M* = 294.32 g/mol): monoclinic, space group $P2_1/c$ (no. 14), *a* = 8.1191(4) Å, *b* = 5.6386(3) Å, *c* = 31.0628(17) Å, *β* = 93.276(2)°, *V* = 1419.74(13) Å^3, *Z* = 4, *T* = 99.98 K, μ(MoKα) = 0.096 mm^{-1}, *Dcalc* = 1.377 g/cm^3, 20105 reflections measured (5.026° ≤ 2Θ ≤ 59.122°), 3964 unique (R_{int} = 0.0168, R_{sigma} = 0.0125) which were used in all calculations. The final R_1 was 0.0370 (I > 2σ(I)) and wR_2 was 0.1001 (all data).

Table 44: Crystal data and structure refinement for **143g**.

Compound	**143g**
CCDC number	1915686
Identification code	mo_0182_CG_0m
Empirical formula	$C_{18}H_{15}FN_2O$
Formula weight	294.32
Temperature/K	99.98
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	8.1191(4)
b/Å	5.6386(3)

c/Å	31.0628(17)
α/°	90
β/°	93.276(2)
γ/°	90
Volume/Å^3	1419.74(13)
Z	4
ρ_{calc}g/cm^3	1.377
μ/mm^{-1}	0.096
F(000)	616.0
Crystal size/mm^3	0.426 × 0.412 × 0.326
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.026 to 59.122
Index ranges	-11 ≤ h ≤ 11, -7 ≤ k ≤ 7, -43 ≤ l ≤ 39
Reflections collected	20105
Independent reflections	3964 [R_{int} = 0.0168, R_{sigma} = 0.0125]
Data/restraints/parameters	3964/0/200
Goodness-of-fit on F^2	1.039
Final R indexes [I>=2σ (I)]	R_1 = 0.0370, wR_2 = 0.0984
Final R indexes [all data]	R_1 = 0.0389, wR_2 = 0.1001
Largest diff. peak/hole / e Å^{-3}	0.43/-0.19

Table 45: Bond lengths [Å] for **143g**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
F1	C1	1.3658(10)	C4	C7	1.4836(12)
O1	C15	1.3692(11)	C5	C6	1.3964(12)
O1	C18	1.4255(12)	C6	C11	1.5157(12)
N1	C7	1.3444(12)	C8	C9	1.3867(14)
N1	C8	1.3381(12)	C9	C10	1.3840(15)
N2	C7	1.3431(11)	C11	C12	1.5145(12)
N2	C10	1.3342(12)	C12	C13	1.3920(12)
C1	C2	1.3830(13)	C12	C17	1.3964(13)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C1	C6	1.3860(13)	C13	C14	1.3952(13)
C2	C3	1.3880(12)	C14	C15	1.3929(12)
C3	C4	1.3963(12)	C15	C16	1.3945(13)
C4	C5	1.3949(12)	C16	C17	1.3873(13)

Table 46: Bond angles [°] for **143g**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C15	O1	C18	116.57(8)	N2	C7	N1	125.87(8)
C8	N1	C7	116.46(8)	N2	C7	C4	116.77(8)
C10	N2	C7	116.10(8)	N1	C8	C9	122.20(9)
F1	C1	C2	117.78(8)	C10	C9	C8	116.53(9)
F1	C1	C6	118.51(8)	N2	C10	C9	122.85(9)
C2	C1	C6	123.71(8)	C12	C11	C6	111.51(7)
C1	C2	C3	118.22(8)	C13	C12	C11	120.96(8)
C2	C3	C4	120.48(8)	C13	C12	C17	117.98(8)
C3	C4	C7	119.94(8)	C17	C12	C11	121.03(8)
C5	C4	C3	119.27(8)	C12	C13	C14	121.67(8)
C5	C4	C7	120.79(8)	C15	C14	C13	119.26(8)
C4	C5	C6	121.60(8)	O1	C15	C14	124.28(8)
C1	C6	C5	116.69(8)	O1	C15	C16	115.79(8)
C1	C6	C11	122.40(8)	C14	C15	C16	119.92(8)
C5	C6	C11	120.90(8)	C17	C16	C15	119.86(8)
N1	C7	C4	117.36(8)	C16	C17	C12	121.29(8)

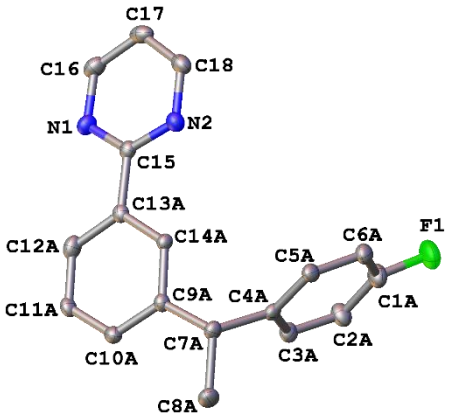


Figure 41: Molecular structure of **143j** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{18}H_{15}FN_2$ (*M* = 278.32 g/mol): monoclinic, space group $P2_1/c$ (no. 14), *a* = 19.3115(8) Å, *b* = 5.8472(3) Å, *c* = 12.7090(5) Å, *β* = 106.294(2)°, *V* = 1377.44(11) Å^3, *Z* = 4, *T* = 100.01 K, μ(MoKα) = 0.089 mm^{-1}, *Dcalc* = 1.342 g/cm^3, 39008 reflections measured (4.394° ≤ 2Θ ≤ 59.996°), 4019 unique (R_{int} = 0.0356, R_{sigma} = 0.0218) which were used in all calculations. The final R_1 was 0.0533 (I > 2σ(I)) and wR_2 was 0.1230 (all data).

Table 47: Crystal data and structure refinement for **143j**.

Compound	**143j**
CCDC number	1915684
Identification code	mo_0065_CG_0m
Empirical formula	$C_{18}H_{15}FN_2$
Formula weight	278.32
Temperature/K	100.01
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	19.3115(8)
b/Å	5.8472(3)
c/Å	12.7090(5)
α/°	90
β/°	106.294(2)

γ/°	90
Volume/Å^3	1377.44(11)
Z	4
ρ_{calc}g/cm^3	1.342
μ/mm^{-1}	0.089
F(000)	584.0
Crystal size/mm^3	0.29 × 0.17 × 0.065
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.394 to 59.996
Index ranges	-26 ≤ h ≤ 27, -8 ≤ k ≤ 8, -17 ≤ l ≤ 17
Reflections collected	39008
Independent reflections	4019 [R_{int} = 0.0356, R_{sigma} = 0.0218]
Data/restraints/parameters	4019/36/295
Goodness-of-fit on F^2	1.183
Final R indexes [I>=2σ (I)]	R_1 = 0.0533, wR_2 = 0.1197
Final R indexes [all data]	R_1 = 0.0588, wR_2 = 0.1230
Largest diff. peak/hole / e Å^{-3}	0.40/-0.33

Table 48: Selected bond lengths [Å] for **143j**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
F1	C1A	1.374(3)	C7A	C8A	1.528(3)
N1	C15	1.3446(17)	C7A	C9A	1.528(3)
N1	C16	1.3374(19)	C9A	C10A	1.391(3)
N2	C15	1.3429(17)	C9A	C14A	1.395(3)
N2	C18	1.3355(18)	C10A	C11A	1.388(4)
C1A	C2A	1.373(4)	C11A	C12A	1.375(4)
C1A	C6A	1.382(4)	C12A	C13A	1.399(4)
C2A	C3A	1.382(4)	C13A	C14A	1.395(3)
C3A	C4A	1.396(3)	C13A	C15	1.478(3)
C4A	C5A	1.392(3)	C16	C17	1.379(2)
C4A	C7A	1.526(3)	C17	C18	1.380(2)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C5A	C6A	1.395(4)			

Table 49: Selected bond angles [°] for **143j**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C16	N1	C15	116.14(12)	C10A	C9A	C14A	117.9(2)
C18	N2	C15	116.38(12)	C14A	C9A	C7A	118.4(2)
F1	C1A	C6A	114.0(4)	C11A	C10A	C9A	120.9(2)
C2A	C1A	F1	122.3(4)	C12A	C11A	C10A	120.2(3)
C2A	C1A	C6A	123.7(3)	C11A	C12A	C13A	120.8(3)
C1A	C2A	C3A	117.9(3)	C12A	C13A	C15	122.2(3)
C2A	C3A	C4A	121.3(2)	C14A	C13A	C12A	118.0(2)
C3A	C4A	C7A	120.0(2)	C14A	C13A	C15	119.7(3)
C5A	C4A	C3A	118.6(2)	C13A	C14A	C9A	122.2(2)
C5A	C4A	C7A	121.4(3)	N1	C15	C13A	118.11(19)
C4A	C5A	C6A	121.4(2)	N2	C15	N1	125.54(13)
C1A	C6A	C5A	117.1(3)	N2	C15	C13A	116.36(19)
C4A	C7A	C8A	111.63(18)	N1	C16	C17	122.83(13)
C4A	C7A	C9A	109.42(19)	C16	C17	C18	116.39(13)
C8A	C7A	C9A	114.46(18)	N2	C18	C17	122.71(14)
C10A	C9A	C7A	123.7(2)				

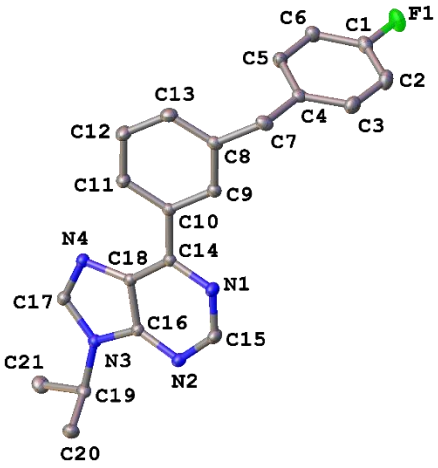


Figure 42: Molecular structure of **185ai** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{21}H_{19}FN_4$ (*M* = 346.40 g/mol): monoclinic, space group $P2_1/c$ (no. 14), *a* = 11.2425(7) Å, *b* = 9.3295(6) Å, *c* = 16.3348(11) Å, *β* = 94.764(2)°, *V* = 1707.39(19) Å^3, *Z* = 4, *T* = 99.98 K, μ(MoKα) = 0.090 mm^{-1}, *Dcalc* = 1.348 g/cm^3, 5632 reflections measured (5.004° ≤ 2Θ ≤ 63.084°), 5632 unique (R_{int} = 0.0, R_{sigma} = 0.0206) which were used in all calculations. The final R_1 was 0.0392 (I > 2σ(I)) and wR_2 was 0.1096 (all data).

Table 50: Crystal data and structure refinement for **185ai**.

Compound	**185ai**
CCDC number	1915675
Identification code	mo_0272_CG_0m_4
Empirical formula	$C_{21}H_{19}FN_4$
Formula weight	346.40
Temperature/K	99.98
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	11.2425(7)
b/Å	9.3295(6)
c/Å	16.3348(11)
α/°	90

β/°	94.764(2)
γ/°	90
Volume/Å^3	1707.39(19)
Z	4
ρ_{calc}g/cm^3	1.348
μ/mm^{-1}	0.090
F(000)	728.0
Crystal size/mm^3	0.424 × 0.247 × 0.21
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.004 to 63.084
Index ranges	-16 ≤ h ≤ 16, 13 ≤ k ≤ 0, 24 ≤ l ≤ 0
Reflections collected	5632
Independent reflections	5632 [R_{int} = 0.0, R_{sigma} = 0.0206]
Data/restraints/parameters	5632/0/237
Goodness-of-fit on F^2	1.041
Final R indexes [I>=2σ (I)]	R_1 = 0.0392, wR_2 = 0.1076
Final R indexes [all data]	R_1 = 0.0428, wR_2 = 0.1096
Largest diff. peak/hole / e Å^{-3}	0.44/-0.27

Table 51: Bond lengths [Å] for **185ai**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
F1	C1	1.3554(11)	C4	C7	1.5150(12)
N1	C14	1.3502(10)	C5	C6	1.3911(13)
N1	C15	1.3397(11)	C7	C8	1.5132(12)
N2	C15	1.3367(11)	C8	C9	1.3925(11)
N2	C16	1.3337(10)	C8	C13	1.3960(12)
N3	C16	1.3730(10)	C9	C10	1.4001(11)
N3	C17	1.3691(10)	C10	C11	1.4004(11)
N3	C19	1.4762(10)	C10	C14	1.4770(11)
N4	C17	1.3179(11)	C11	C12	1.3882(12)
N4	C18	1.3913(10)	C12	C13	1.3908(12)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C1	C2	1.3774(13)	C14	C18	1.4032(11)
C1	C6	1.3841(12)	C16	C18	1.4076(11)
C2	C3	1.3891(14)	C19	C20	1.5227(13)
C3	C4	1.3948(12)	C19	C21	1.5200(12)
C4	C5	1.3969(11)			

Table 52: Bond angles [°] for **185ai**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C15	N1	C14	119.49(7)	C9	C10	C11	119.40(7)
C16	N2	C15	111.22(7)	C9	C10	C14	119.41(7)
C16	N3	C19	125.59(7)	C11	C10	C14	121.19(7)
C17	N3	C16	105.56(7)	C12	C11	C10	119.80(8)
C17	N3	C19	128.70(7)	C11	C12	C13	120.20(8)
C17	N4	C18	104.01(7)	C12	C13	C8	120.91(8)
F1	C1	C2	118.70(8)	N1	C14	C10	117.00(7)
F1	C1	C6	118.57(8)	N1	C14	C18	117.75(7)
C2	C1	C6	122.73(9)	C18	C14	C10	125.25(7)
C1	C2	C3	117.97(8)	N2	C15	N1	128.32(8)
C2	C3	C4	121.76(8)	N2	C16	N3	126.86(7)
C3	C4	C5	118.12(8)	N2	C16	C18	126.84(7)
C3	C4	C7	120.23(8)	N3	C16	C18	106.29(7)
C5	C4	C7	121.63(8)	N4	C17	N3	114.51(7)
C6	C5	C4	121.33(8)	N4	C18	C14	134.05(7)
C1	C6	C5	118.10(8)	N4	C18	C16	109.63(7)
C8	C7	C4	114.04(7)	C14	C18	C16	116.32(7)
C9	C8	C7	120.19(8)	N3	C19	C20	109.47(7)
C9	C8	C13	118.62(8)	N3	C19	C21	110.16(7)
C13	C8	C7	121.19(8)	C21	C19	C20	112.01(7)
C8	C9	C10	121.07(7)				

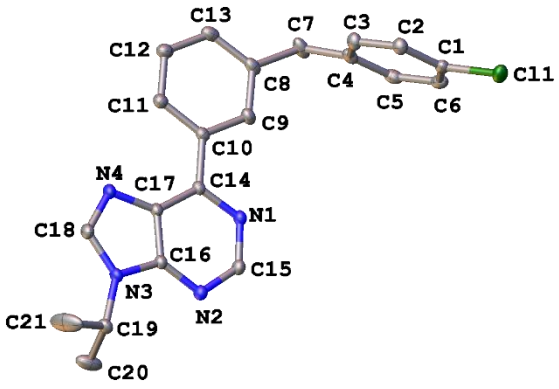


Figure 43: Molecular structure of **185aj** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{21}H_{19}ClN_4$ (*M* = 362.85 g/mol): triclinic, space group P-1 (no. 2), *a* = 8.9649(8) Å, *b* = 9.9520(7) Å, *c* = 11.7814(11) Å, *α* = 100.554(3)°, *β* = 105.986(3)°, *γ* = 111.878(2)°, *V* = 888.28(13) Å^3, *Z* = 2, *T* = 100.0 K, μ(MoKα) = 0.227 mm^{-1}, *Dcalc* = 1.357 g/cm^3, 12425 reflections measured (4.656° ≤ 2Θ ≤ 63.036°), 5883 unique (R_{int} = 0.0176, R_{sigma} = 0.0255) which were used in all calculations. The final R_1 was 0.0376 (I > 2σ(I)) and wR_2 was 0.1059 (all data).

Table 53: Crystal data and structure refinement for **185aj**.

Compound	**185aj**
CCDC number	1915610
Identification code	mo_0273_CG_0m
Empirical formula	$C_{21}H_{19}ClN_4$
Formula weight	362.85
Temperature/K	100.0
Crystal system	triclinic
Space group	P-1
a/Å	8.9649(8)
b/Å	9.9520(7)
c/Å	11.7814(11)
α/°	100.554(3)
β/°	105.986(3)
γ/°	111.878(2)

Volume/Å^3	888.28(13)
Z	2
ρ_{calc}g/cm^3	1.357
μ/mm^{-1}	0.227
F(000)	380.0
Crystal size/mm^3	0.287 × 0.198 × 0.162
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.656 to 63.036
Index ranges	-13 ≤ h ≤ 9, -14 ≤ k ≤ 14, -17 ≤ l ≤ 17
Reflections collected	12425
Independent reflections	5883 [R_{int} = 0.0176, R_{sigma} = 0.0255]
Data/restraints/parameters	5883/0/237
Goodness-of-fit on F^2	1.078
Final R indexes [I>=2σ (I)]	R_1 = 0.0376, wR_2 = 0.1031
Final R indexes [all data]	R_1 = 0.0407, wR_2 = 0.1059
Largest diff. peak/hole / e Å^{-3}	0.49/-0.52

Table 54: Bond lengths [Å] for **185aj**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Cl1	C1	1.7425(10)	C4	C7	1.5099(15)
N1	C14	1.3485(12)	C5	C6	1.3913(15)
N1	C15	1.3365(12)	C7	C8	1.5123(14)
N2	C15	1.3376(12)	C8	C9	1.3949(13)
N2	C16	1.3310(12)	C8	C13	1.3933(15)
N3	C16	1.3715(11)	C9	C10	1.4013(13)
N3	C18	1.3729(12)	C10	C11	1.3992(13)
N3	C19	1.4755(12)	C10	C14	1.4782(13)
N4	C17	1.3905(12)	C11	C12	1.3905(13)
N4	C18	1.3172(12)	C12	C13	1.3885(15)
C1	C2	1.3885(13)	C14	C17	1.4048(12)
C1	C6	1.3821(14)	C16	C17	1.4063(12)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C2	C3	1.3915(14)	C19	C20	1.5140(16)
C3	C4	1.3956(14)	C19	C21	1.5035(16)
C4	C5	1.3920(15)			

Table 55: Bond angles [°] for **185aj**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C15	N1	C14	119.56(8)	C9	C10	C14	119.50(8)
C16	N2	C15	111.07(8)	C11	C10	C9	119.16(9)
C16	N3	C18	105.30(8)	C11	C10	C14	121.32(8)
C16	N3	C19	124.64(8)	C12	C11	C10	119.88(9)
C18	N3	C19	130.03(8)	C13	C12	C11	120.36(10)
C18	N4	C17	104.07(8)	C12	C13	C8	120.72(9)
C2	C1	Cl1	119.39(8)	N1	C14	C10	117.03(8)
C6	C1	Cl1	118.85(8)	N1	C14	C17	117.62(8)
C6	C1	C2	121.76(9)	C17	C14	C10	125.36(8)
C1	C2	C3	118.39(9)	N1	C15	N2	128.45(9)
C2	C3	C4	121.37(9)	N2	C16	N3	126.45(8)
C3	C4	C7	121.12(9)	N2	C16	C17	126.96(8)
C5	C4	C3	118.47(9)	N3	C16	C17	106.58(8)
C5	C4	C7	120.31(9)	N4	C17	C14	134.12(8)
C6	C5	C4	121.19(9)	N4	C17	C16	109.54(8)
C1	C6	C5	118.82(9)	C14	C17	C16	116.33(8)
C4	C7	C8	115.92(8)	N4	C18	N3	114.51(8)
C9	C8	C7	120.82(10)	N3	C19	C20	110.46(8)
C13	C8	C7	120.33(9)	N3	C19	C21	110.84(9)
C13	C8	C9	118.79(9)	C21	C19	C20	112.70(12)
C8	C9	C10	121.08(9)				

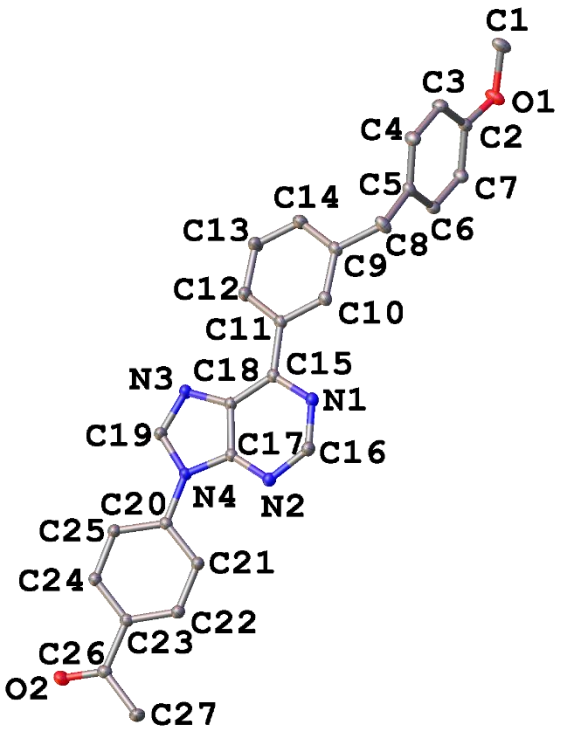


Figure 44: Molecular structure of **185hb** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{27}H_{22}N_4O_2$ (*M* = 434.48 g/mol): triclinic, space group P-1 (no. 2), *a* = 6.3344(7) Å, *b* = 12.4251(18) Å, *c* = 13.9524(19) Å, *α* = 106.848(5)°, *β* = 91.291(5)°, *γ* = 93.640(5)°, *V* = 1047.9(2) Å^3, *Z* = 2, *T* = 100.01 K, μ(MoKα) = 0.089 mm^{-1}, *Dcalc* = 1.377 g/cm^3, 38890 reflections measured (5.22° ≤ 2Θ ≤ 63.094°), 7003 unique (R_{int} = 0.0243, R_{sigma} = 0.0175) which were used in all calculations. The final R_1 was 0.0393 (I > 2σ(I)) and wR_2 was 0.1124 (all data).

Table 56: Crystal data and structure refinement for **185hb**.

Compound	**185hb**
CCDC number	1915681
Identification code	mo_0250_CG_0m
Empirical formula	$C_{27}H_{22}N_4O_2$
Formula weight	434.48
Temperature/K	100.01
Crystal system	triclinic
Space group	P-1

a/Å	6.3344(7)
b/Å	12.4251(18)
c/Å	13.9524(19)
α/°	106.848(5)
β/°	91.291(5)
γ/°	93.640(5)
Volume/Å^3	1047.9(2)
Z	2
ρ_{calc}g/cm^3	1.377
μ/mm^{-1}	0.089
F(000)	456.0
Crystal size/mm^3	0.567 × 0.17 × 0.062
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.22 to 63.094
Index ranges	-9 ≤ h ≤ 9, -18 ≤ k ≤ 18, -20 ≤ l ≤ 20
Reflections collected	38890
Independent reflections	7003 [R_{int} = 0.0243, R_{sigma} = 0.0175]
Data/restraints/parameters	7003/0/300
Goodness-of-fit on F^2	1.045
Final R indexes [I>=2σ (I)]	R_1 = 0.0393, wR_2 = 0.1089
Final R indexes [all data]	R_1 = 0.0433, wR_2 = 0.1124
Largest diff. peak/hole / e Å^{-3}	0.47/-0.23

Table 57: Bond lengths [Å] for **185hb**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C1	1.4302(11)	C8	C9	1.5137(12)
O1	C2	1.3665(10)	C9	C10	1.3900(12)
O2	C26	1.2206(11)	C9	C14	1.3993(13)
N1	C15	1.3497(11)	C10	C11	1.4028(11)
N1	C16	1.3356(11)	C11	C12	1.4009(12)
N2	C16	1.3425(11)	C11	C15	1.4799(12)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N2	C17	1.3333(10)	C12	C13	1.3930(13)
N3	C18	1.3907(11)	C13	C14	1.3911(13)
N3	C19	1.3055(11)	C15	C18	1.4012(11)
N4	C17	1.3881(10)	C17	C18	1.4052(11)
N4	C19	1.3875(11)	C20	C21	1.3907(12)
N4	C20	1.4193(11)	C20	C25	1.3985(11)
C2	C3	1.3901(12)	C21	C22	1.3892(12)
C2	C7	1.3984(12)	C22	C23	1.3957(12)
C3	C4	1.3973(12)	C23	C24	1.3966(12)
C4	C5	1.3902(12)	C23	C26	1.4906(12)
C5	C6	1.3994(12)	C24	C25	1.3853(12)
C5	C8	1.5085(12)	C26	C27	1.5076(13)
C6	C7	1.3844(12)			

Table 58: Bond angles [°] for **185hb**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C2	O1	C1	116.58(7)	C14	C13	C12	120.74(9)
C16	N1	C15	119.31(7)	C13	C14	C9	120.36(8)
C17	N2	C16	111.49(7)	N1	C15	C11	116.88(7)
C19	N3	C18	104.44(7)	N1	C15	C18	117.56(8)
C17	N4	C20	129.35(7)	C18	C15	C11	125.50(8)
C19	N4	C17	105.13(7)	N1	C16	N2	128.45(8)
C19	N4	C20	125.52(7)	N2	C17	N4	128.29(8)
O1	C2	C3	124.61(8)	N2	C17	C18	125.97(8)
O1	C2	C7	115.72(8)	N4	C17	C18	105.73(7)
C3	C2	C7	119.66(8)	N3	C18	C15	132.49(8)
C2	C3	C4	119.19(8)	N3	C18	C17	110.28(7)
C5	C4	C3	121.92(8)	C15	C18	C17	117.21(7)
C4	C5	C6	117.86(8)	N3	C19	N4	114.39(7)
C4	C5	C8	121.14(8)	C21	C20	N4	120.61(7)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C6	C5	C8	120.92(8)	C21	C20	C25	120.25(8)
C7	C6	C5	121.06(8)	C25	C20	N4	119.14(7)
C6	C7	C2	120.24(8)	C22	C21	C20	119.57(8)
C5	C8	C9	116.24(7)	C21	C22	C23	120.87(8)
C10	C9	C8	119.52(8)	C22	C23	C24	118.79(8)
C10	C9	C14	118.68(8)	C22	C23	C26	122.55(8)
C14	C9	C8	121.75(8)	C24	C23	C26	118.65(7)
C9	C10	C11	121.58(8)	C25	C24	C23	120.92(8)
C10	C11	C15	118.78(7)	C24	C25	C20	119.50(8)
C12	C11	C10	119.01(8)	O2	C26	C23	120.55(8)
C12	C11	C15	122.14(8)	O2	C26	C27	121.26(8)
C13	C12	C11	119.62(8)	C23	C26	C27	118.16(7)

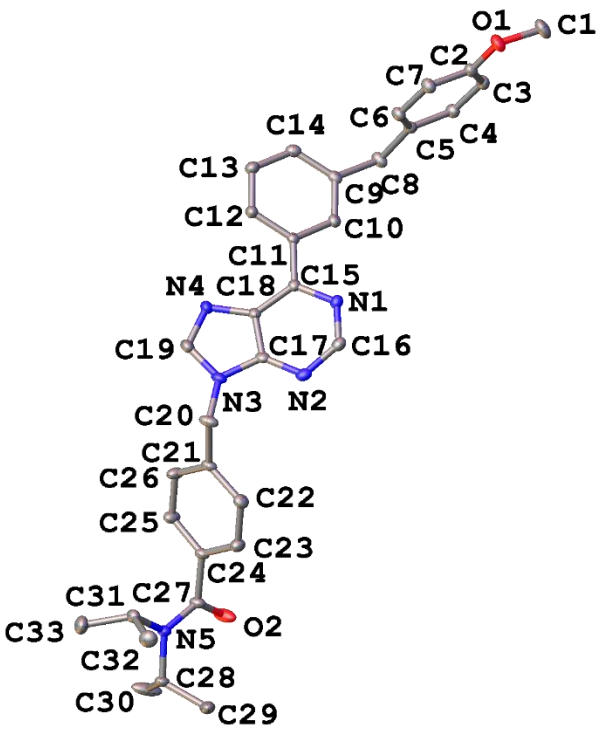


Figure 45: Molecular structure of **185kb** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{33}H_{35}N_5O_2$ (*M* = 533.66 g/mol): monoclinic, space group $P2_1/n$ (no. 14), *a* = 10.1416(6) Å, *b* = 27.4937(13) Å, *c* = 10.2461(6) Å, *β* = 101.977(2)°, *V* = 2794.7(3) Å^3, *Z* = 4, *T* = 100.0 K, μ(MoKα) = 0.081 mm^{-1}, *Dcalc* = 1.268 g/cm^3, 44140 reflections measured (5.03° ≤ 2Θ ≤ 62.986°), 9275 unique (R_{int} = 0.0219, R_{sigma} = 0.0176) which were used in all calculations. The final R_1 was 0.0409 (I > 2σ(I)) and wR_2 was 0.1117 (all data).

Table 59: Crystal data and structure refinement for **185kb.**

Compound	**185kb**
CCDC number	1915682
Identification code	mo_0241_CG_0m
Empirical formula	$C_{33}H_{35}N_5O_2$
Formula weight	533.66
Temperature/K	100.0
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	10.1416(6)
b/Å	27.4937(13)
c/Å	10.2461(6)
α/°	90
β/°	101.977(2)
γ/°	90
Volume/Å^3	2794.7(3)
Z	4
ρ_{calc}g/cm^3	1.268
μ/mm^{-1}	0.081
F(000)	1136.0
Crystal size/mm^3	0.438 × 0.434 × 0.37
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.03 to 62.986
Index ranges	-14 ≤ h ≤ 14, -40 ≤ k ≤ 40, -15 ≤ l ≤ 14
Reflections collected	44140

Independent reflections	9275 [R_{int} = 0.0219, R_{sigma} = 0.0176]
Data/restraints/parameters	9275/0/366
Goodness-of-fit on F^2	1.039
Final R indexes [I>=2σ (I)]	R_1 = 0.0409, wR_2 = 0.1081
Final R indexes [all data]	R_1 = 0.0455, wR_2 = 0.1117
Largest diff. peak/hole / e $Å^{-3}$	0.46/-0.24

Table 60: Bond lengths [Å] for **185kb**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C1	1.4265(12)	C8	C9	1.5110(12)
O1	C2	1.3681(10)	C9	C10	1.3938(12)
O2	C27	1.2366(11)	C9	C14	1.3978(12)
N1	C15	1.3529(10)	C10	C11	1.3999(11)
N1	C16	1.3418(11)	C11	C12	1.4006(11)
N2	C16	1.3392(12)	C11	C15	1.4787(11)
N2	C17	1.3324(11)	C12	C13	1.3941(12)
N3	C17	1.3718(11)	C13	C14	1.3936(12)
N3	C19	1.3727(12)	C15	C18	1.3996(11)
N3	C20	1.4611(11)	C17	C18	1.4062(11)
N4	C18	1.3921(10)	C20	C21	1.5135(12)
N4	C19	1.3156(11)	C21	C22	1.3898(12)
N5	C27	1.3496(11)	C21	C26	1.3963(12)
N5	C28	1.4869(10)	C22	C23	1.3948(12)
N5	C31	1.4843(11)	C23	C24	1.3904(12)
C2	C3	1.3954(12)	C24	C25	1.3940(12)
C2	C7	1.3937(12)	C24	C27	1.5105(11)
C3	C4	1.3942(12)	C25	C26	1.3939(12)
C4	C5	1.3964(11)	C28	C29	1.5193(13)
C5	C6	1.3940(11)	C28	C30	1.5176(14)
C5	C8	1.5155(12)	C31	C32	1.5266(14)
C6	C7	1.3892(12)	C31	C33	1.5277(13)

Table 61: Bond angles [°] for **185kb**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C2	O1	C1	116.90(7)	N1	C15	C11	117.52(7)
C16	N1	C15	119.01(7)	N1	C15	C18	118.02(7)
C17	N2	C16	111.16(7)	C18	C15	C11	124.46(7)
C17	N3	C19	106.04(7)	N2	C16	N1	128.49(8)
C17	N3	C20	125.94(8)	N2	C17	N3	127.32(8)
C19	N3	C20	127.37(8)	N2	C17	C18	126.84(8)
C19	N4	C18	104.00(7)	N3	C17	C18	105.80(7)
C27	N5	C28	120.29(7)	N4	C18	C15	133.51(7)
C27	N5	C31	122.97(7)	N4	C18	C17	110.02(7)
C31	N5	C28	116.05(7)	C15	C18	C17	116.45(7)
O1	C2	C3	124.48(8)	N4	C19	N3	114.12(8)
O1	C2	C7	115.57(8)	N3	C20	C21	115.36(7)
C7	C2	C3	119.95(8)	C22	C21	C20	119.83(8)
C4	C3	C2	119.17(8)	C22	C21	C26	118.82(8)
C3	C4	C5	121.69(8)	C26	C21	C20	121.09(8)
C4	C5	C8	119.26(7)	C21	C22	C23	120.83(8)
C6	C5	C4	117.99(8)	C24	C23	C22	120.03(8)
C6	C5	C8	122.74(7)	C23	C24	C25	119.44(7)
C7	C6	C5	121.27(8)	C23	C24	C27	118.20(8)
C6	C7	C2	119.92(8)	C25	C24	C27	122.36(8)
C9	C8	C5	115.97(7)	C26	C25	C24	120.14(8)
C10	C9	C8	120.18(8)	C25	C26	C21	120.51(8)
C10	C9	C14	118.59(8)	O2	C27	N5	123.26(8)
C14	C9	C8	121.21(8)	O2	C27	C24	119.35(8)
C9	C10	C11	121.30(7)	N5	C27	C24	117.35(7)
C10	C11	C12	119.37(7)	N5	C28	C29	112.50(7)
C10	C11	C15	119.10(7)	N5	C28	C30	112.69(7)
C12	C11	C15	121.53(7)	C30	C28	C29	112.42(9)
C13	C12	C11	119.70(8)	N5	C31	C32	111.04(7)
C14	C13	C12	120.27(8)	N5	C31	C33	111.36(8)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C13	C14	C9	120.76(8)	C32	C31	C33	112.64(8)

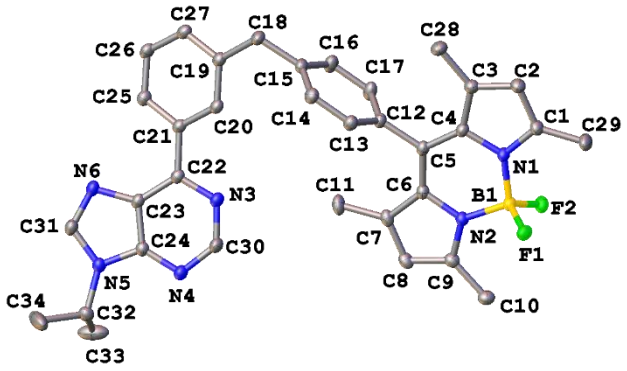


Figure 46: Molecular structure of **187a** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{34}H_{33}BF_2N_6$ (*M* = 574.47 g/mol): triclinic, space group P-1 (no. 2), *a* = 10.4593(10) Å, *b* = 16.8136(17) Å, *c* = 16.9094(11) Å, *α* = 94.418(2)°, *β* = 94.020(3)°, *γ* = 90.953(3)°, *V* = 2956.8(5) Å^3, *Z* = 4, *T* = 100.0 K, μ(MoKα) = 0.086 mm^{-1}, *Dcalc* = 1.290 g/cm^3, 108206 reflections measured (4.646° ≤ 2Θ ≤ 61.34°), 18151 unique (R_{int} = 0.0389, R_{sigma} = 0.0271) which were used in all calculations. The final R_1 was 0.0464 (I > 2σ(I)) and wR_2 was 0.1302 (all data).

Table 62: Crystal data and structure refinement for **187a**.

Compound	**187a**
CCDC number	1915685
Identification code	0408_CG_0m
Empirical formula	$C_{34}H_{33}BF_2N_6$
Formula weight	574.47
Temperature/K	100.0
Crystal system	triclinic
Space group	P-1
a/Å	10.4593(10)
b/Å	16.8136(17)
c/Å	16.9094(11)

α/°	94.418(2)
β/°	94.020(3)
γ/°	90.953(3)
Volume/Å^3	2956.8(5)
Z	4
ρ_{calc}g/cm^3	1.290
μ/mm^{-1}	0.086
F(000)	1208.0
Crystal size/mm^3	0.607 × 0.465 × 0.242
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.646 to 61.34
Index ranges	-14 ≤ h ≤ 15, -24 ≤ k ≤ 24, -24 ≤ l ≤ 24
Reflections collected	108206
Independent reflections	18151 [R_{int} = 0.0389, R_{sigma} = 0.0271]
Data/restraints/parameters	18151/0/787
Goodness-of-fit on F^2	1.031
Final R indexes [I>=2σ (I)]	R_1 = 0.0464, wR_2 = 0.1217
Final R indexes [all data]	R_1 = 0.0569, wR_2 = 0.1302
Largest diff. peak/hole / e Å^{-3}	0.41/-0.39

Table 63: Selected bond lengths [Å] for **187a**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
F1	B1	1.3996(14)	C6	C7	1.4289(15)
F2	B1	1.3927(14)	C7	C8	1.3877(17)
N1	C1	1.3475(14)	C7	C11	1.4966(16)
N1	C4	1.4020(14)	C8	C9	1.4069(16)
N1	B1	1.5470(15)	C9	C10	1.4859(16)
N2	C6	1.4010(14)	C12	C13	1.3906(16)
N2	C9	1.3491(14)	C12	C17	1.3926(16)
N2	B1	1.5453(15)	C13	C14	1.3928(16)
N3	C22	1.3502(14)	C14	C15	1.3921(17)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N3	C30	1.3373(15)	C15	C16	1.3950(17)
N4	C24	1.3329(14)	C15	C18	1.5119(16)
N4	C30	1.3398(15)	C16	C17	1.3896(16)
N5	C24	1.3710(14)	C18	C19	1.5179(16)
N5	C31	1.3715(15)	C19	C20	1.3929(16)
N5	C32	1.4766(15)	C19	C27	1.3986(15)
N6	C23	1.3863(14)	C20	C21	1.3993(16)
N6	C31	1.3127(16)	C21	C22	1.4786(15)
C1	C2	1.4041(16)	C21	C25	1.4015(15)
C1	C29	1.4879(16)	C22	C23	1.3978(16)
C2	C3	1.3863(16)	C23	C24	1.4073(16)
C3	C4	1.4261(16)	C25	C26	1.3905(16)
C3	C28	1.4987(16)	C26	C27	1.3877(17)
C4	C5	1.3954(15)	C32	C33	1.500(2)
C5	C6	1.3939(16)	C32	C34	1.5037(19)
C5	C12	1.4910(15)			

Table 64: Selected bond angles [°] for **187a**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C1	N1	C4	108.40(9)	C12	C13	C14	120.02(11)
C1	N1	B1	125.97(9)	C15	C14	C13	121.08(11)
C4	N1	B1	125.63(9)	C14	C15	C16	118.40(10)
C6	N2	B1	125.75(9)	C14	C15	C18	121.26(11)
C9	N2	C6	108.57(9)	C16	C15	C18	120.29(11)
C9	N2	B1	125.66(9)	C17	C16	C15	120.88(11)
C30	N3	C22	118.63(10)	C16	C17	C12	120.25(11)
C24	N4	C30	111.08(10)	C15	C18	C19	113.56(10)
C24	N5	C31	105.50(10)	C20	C19	C18	121.67(10)
C24	N5	C32	125.65(10)	C20	C19	C27	118.66(11)
C31	N5	C32	128.73(10)	C27	C19	C18	119.64(10)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C31	N6	C23	103.92(10)	C19	C20	C21	121.09(10)
N1	C1	C2	109.01(10)	C20	C21	C22	119.32(10)
N1	C1	C29	123.13(11)	C20	C21	C25	119.37(10)
C2	C1	C29	127.85(11)	C25	C21	C22	121.30(10)
C3	C2	C1	108.62(10)	N3	C22	C21	117.52(10)
C2	C3	C4	106.09(10)	N3	C22	C23	118.04(10)
C2	C3	C28	124.72(11)	C23	C22	C21	124.44(10)
C4	C3	C28	129.18(11)	N6	C23	C22	133.07(11)
N1	C4	C3	107.86(9)	N6	C23	C24	109.96(10)
C5	C4	N1	120.38(10)	C22	C23	C24	116.93(10)
C5	C4	C3	131.61(10)	N4	C24	N5	127.74(11)
C4	C5	C12	118.72(10)	N4	C24	C23	126.21(10)
C6	C5	C4	121.09(10)	N5	C24	C23	106.02(10)
C6	C5	C12	120.19(10)	C26	C25	C21	119.71(11)
N2	C6	C7	107.79(10)	C27	C26	C25	120.35(10)
C5	C6	N2	120.33(10)	C26	C27	C19	120.78(11)
C5	C6	C7	131.71(10)	N3	C30	N4	129.10(11)
C6	C7	C11	128.87(11)	N6	C31	N5	114.60(10)
C8	C7	C6	106.15(10)	N5	C32	C33	111.27(10)
C8	C7	C11	124.97(11)	N5	C32	C34	110.42(11)
C7	C8	C9	108.55(10)	C33	C32	C34	113.29(14)
N2	C9	C8	108.93(10)	F1	B1	N1	110.21(9)
N2	C9	C10	122.61(10)	F1	B1	N2	110.45(9)
C8	C9	C10	128.47(11)	F2	B1	F1	108.57(9)
C13	C12	C5	120.36(10)	F2	B1	N1	110.56(9)
C13	C12	C17	119.37(10)	F2	B1	N2	110.59(9)
C17	C12	C5	120.24(10)	N2	B1	N1	106.46(9)

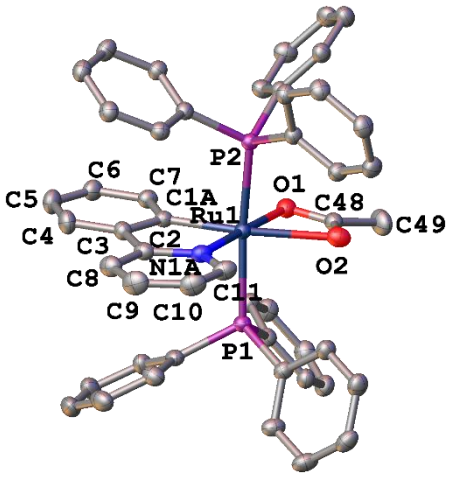


Figure 47: Molecular structure of *trans*-**192a** with thermal ellipoids at 50% probability level. The hydrogen atoms and THF are omitted for clarity.

Crystal Data for $C_{55}H_{53}NO_{3.5}P_2Ru$ (M = 946.99 g/mol): monoclinic, space group $P2_1/n$ (no. 14), a = 11.9019(7) Å, b = 15.2039(9) Å, c = 24.7562(15) Å, β = 93.907(3)°, V = 4469.4(5) Å^3, Z = 4, T = 99.99 K, μ(MoKα) = 0.471 mm^{-1}, *Dcalc* = 1.407 g/cm^3, 13699 reflections measured (4.57° ≤ 2Θ ≤ 61.146°), 13699 unique (R_{int} = 0, R_{sigma} = 0.0303) which were used in all calculations. The final R_1 was 0.0435 (I > 2σ(I)) and wR_2 was 0.1183 (all data).

Table 65: Crystal data and structure refinement for *trans*-**192a**.

Compound	*trans*-**192a**
CCDC number	1915676
Identification code	0473_CG_0m_4
Empirical formula	$C_{55}H_{53}NO_{3.5}P_2Ru$
Formula weight	946.99
Temperature/K	99.99
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	11.9019(7)
b/Å	15.2039(9)
c/Å	24.7562(15)
α/°	90

β/°	93.907(3)
γ/°	90
Volume/Å^3	4469.4(5)
Z	4
ρ_{calc}g/cm^3	1.407
μ/mm^{-1}	0.471
F(000)	1968.0
Crystal size/mm^3	0.317 × 0.086 × 0.063
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.57 to 61.146
Index ranges	-16 ≤ h ≤ 16, 0 ≤ k ≤ 21, 0 ≤ l ≤ 35
Reflections collected	13699
Independent reflections	13699 [R_{int} = 0, R_{sigma} = 0.0303]
Data/restraints/parameters	13699/30/587
Goodness-of-fit on F^2	1.048
Final R indexes [I>=2σ (I)]	R_1 = 0.0435, wR_2 = 0.1132
Final R indexes [all data]	R_1 = 0.0516, wR_2 = 0.1183
Largest diff. peak/hole / e Å^{-3}	1.34/-0.94

Table 66: Selected bond lengths [Å] for *trans*-**192a**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Ru1	P1	2.3421(5)	C16	C17	1.392(3)
Ru1	P2	2.3355(5)	C18	C19	1.395(3)
Ru1	O1	2.1592(16)	C18	C23	1.395(3)
Ru1	O2	2.3317(17)	C19	C20	1.387(3)
Ru1	N1	2.0554(18)	C20	C21	1.380(4)
Ru1	C1	2.0031(17)	C21	C22	1.380(4)
P1	C12	1.8378(19)	C22	C23	1.386(3)
P1	C18	1.828(2)	C24	C25	1.397(3)
P1	C24	1.8314(19)	C24	C29	1.392(3)
P2	C30	1.832(2)	C25	C26	1.389(3)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
P2	C36	1.8312(19)	C26	C27	1.392(3)
P2	C42	1.837(2)	C27	C28	1.383(3)
O1	C48	1.264(2)	C28	C29	1.393(3)
O2	C48	1.261(2)	C30	C31	1.390(3)
N1	C2	1.387(3)	C30	C35	1.398(3)
N1	C11	1.379(3)	C31	C32	1.398(3)
C1	C3	1.382(3)	C32	C33	1.382(3)
C1	C7	1.386(2)	C33	C34	1.390(3)
C2	C3	1.451(3)	C34	C35	1.386(3)
C2	C8	1.397(3)	C36	C37	1.393(3)
C3	C4	1.397(3)	C36	C41	1.398(3)
C4	C5	1.385(3)	C37	C38	1.392(3)
C5	C6	1.387(3)	C38	C39	1.384(3)
C6	C7	1.383(3)	C39	C40	1.381(3)
C8	C9	1.381(3)	C40	C41	1.386(3)
C9	C10	1.390(4)	C42	C43	1.392(3)
C10	C11	1.385(3)	C42	C47	1.397(3)
C12	C13	1.394(3)	C43	C44	1.386(3)
C12	C17	1.388(3)	C44	C45	1.387(3)
C13	C14	1.394(3)	C45	C46	1.384(3)
C14	C15	1.383(3)	C46	C47	1.395(3)
C15	C16	1.386(3)	C48	C49	1.489(3)

Table 67: Selected bond angles [°] for *trans*-**192a**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
P2	Ru1	P1	172.681(17)	C17	C12	P1	119.96(15)
O1	Ru1	P1	91.03(4)	C17	C12	C13	118.84(18)
O1	Ru1	P2	92.19(4)	C14	C13	C12	120.6(2)
O1	Ru1	O2	57.94(6)	C15	C14	C13	120.0(2)
O2	Ru1	P1	85.36(4)	C14	C15	C16	119.67(19)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
O2	Ru1	P2	90.78(4)	C15	C16	C17	120.4(2)
N1	Ru1	P1	88.04(5)	C12	C17	C16	120.5(2)
N1	Ru1	P2	88.70(5)	C19	C18	P1	122.35(16)
N1	Ru1	O1	179.02(6)	C19	C18	C23	118.57(19)
N1	Ru1	O2	121.66(6)	C23	C18	P1	119.01(16)
C1	Ru1	P1	93.47(5)	C20	C19	C18	120.7(2)
C1	Ru1	P2	92.29(5)	C21	C20	C19	119.8(2)
C1	Ru1	O1	101.95(6)	C22	C21	C20	120.3(2)
C1	Ru1	O2	159.78(6)	C21	C22	C23	120.1(2)
C1	Ru1	N1	78.41(7)	C22	C23	C18	120.5(2)
C12	P1	Ru1	115.92(7)	C25	C24	P1	117.64(15)
C18	P1	Ru1	115.73(6)	C29	C24	P1	123.60(15)
C18	P1	C12	101.27(9)	C29	C24	C25	118.73(18)
C18	P1	C24	103.56(9)	C26	C25	C24	120.78(19)
C24	P1	Ru1	115.02(6)	C25	C26	C27	119.8(2)
C24	P1	C12	103.44(9)	C28	C27	C26	119.8(2)
C30	P2	Ru1	115.18(6)	C27	C28	C29	120.3(2)
C30	P2	C42	104.39(9)	C24	C29	C28	120.51(19)
C36	P2	Ru1	115.02(6)	C31	C30	P2	122.18(15)
C36	P2	C30	102.04(9)	C31	C30	C35	118.87(18)
C36	P2	C42	102.48(9)	C35	C30	P2	118.83(15)
C42	P2	Ru1	115.91(6)	C30	C31	C32	120.29(19)
C48	O1	Ru1	95.11(13)	C33	C32	C31	120.39(19)
C48	O2	Ru1	87.27(13)	C32	C33	C34	119.54(19)
C2	N1	Ru1	115.92(13)	C35	C34	C33	120.31(19)
C11	N1	Ru1	126.77(16)	C34	C35	C30	120.59(18)
C11	N1	C2	117.31(18)	C37	C36	P2	122.21(14)
C3	C1	Ru1	118.20(13)	C37	C36	C41	118.53(17)
C3	C1	C7	118.03(17)	C41	C36	P2	119.20(15)
C7	C1	Ru1	123.77(14)	C38	C37	C36	120.64(19)
N1	C2	C3	113.97(17)	C39	C38	C37	120.21(19)

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
N1	C2	C8	121.79(19)	C40	C39	C38	119.51(18)
C8	C2	C3	124.23(19)	C39	C40	C41	120.67(19)
C1	C3	C2	113.47(17)	C40	C41	C36	120.42(19)
C1	C3	C4	120.81(18)	C43	C42	P2	118.07(15)
C4	C3	C2	125.70(19)	C43	C42	C47	118.63(18)
C5	C4	C3	120.1(2)	C47	C42	P2	123.20(15)
C4	C5	C6	119.6(2)	C44	C43	C42	120.85(19)
C7	C6	C5	119.4(2)	C43	C44	C45	120.17(19)
C6	C7	C1	122.04(19)	C46	C45	C44	119.8(2)
C9	C8	C2	119.7(2)	C45	C46	C47	120.1(2)
C8	C9	C10	119.2(2)	C46	C47	C42	120.46(18)
C11	C10	C9	120.0(2)	O1	C48	C49	119.0(2)
N1	C11	C10	122.0(2)	O2	C48	O1	119.45(19)
C13	C12	P1	121.20(15)	O2	C48	C49	121.5(2)

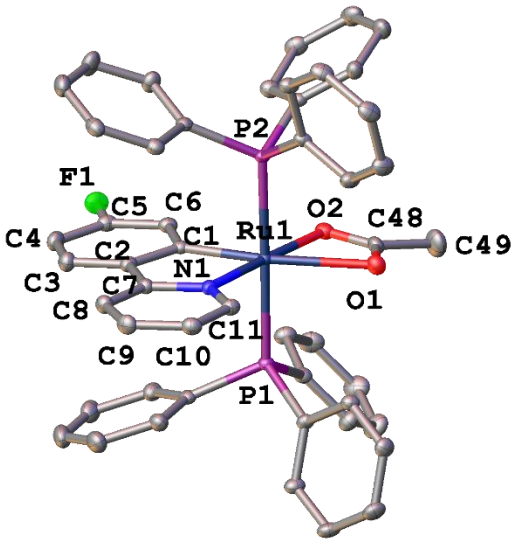


Figure 48: Molecular structure of *trans*-**192b** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{50}H_{42}Cl_2FNO_2P_2Ru$ (M = 941.75 g/mol): monoclinic, space group Pc (no. 7), a = 12.5538(4) Å, b = 20.7915(6) Å, c = 17.2221(5) Å, β = 109.9250(10)°, V = 4226.1(2) Å^3, Z = 4, T = 100.0 K, μ(MoKα) = 0.620 mm^{-1}, *Dcalc* = 1.480 g/cm^3, 196620 reflections measured (4.656° ≤ 2Θ ≤

63.094°), 28065 unique (R_{int} = 0.0236, R_{sigma} = 0.0164) which were used in all calculations. The final R_1 was 0.0240 (I > 2σ(I)) and wR_2 was 0.0645 (all data).

Table 68: Crystal data and structure refinement for *trans*-**192b**.

Compound	*trans*-**192b**
CCDC number	1979318
Identification code	0497_CG_0m
Empirical formula	$C_{50}H_{42}Cl_2FNO_2P_2Ru$
Formula weight	941.75
Temperature/K	100.0
Crystal system	monoclinic
Space group	Pc
a/Å	12.5538(4)
b/Å	20.7915(6)
c/Å	17.2221(5)
α/°	90
β/°	109.9250(10)
γ/°	90
Volume/Å^3	4226.1(2)
Z	4
ρ_{calc}g/cm^3	1.480
μ/mm^{-1}	0.620
F(000)	1928.0
Crystal size/mm^3	0.344 × 0.309 × 0.17
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.656 to 63.094
Index ranges	-18 ≤ h ≤ 18, -30 ≤ k ≤ 30, -25 ≤ l ≤ 25
Reflections collected	196620
Independent reflections	28065 [R_{int} = 0.0236, R_{sigma} = 0.0164]
Data/restraints/parameters	28065/2/1085
Goodness-of-fit on F^2	1.069

Final R indexes [I>=2σ (I)]	R_1 = 0.0240, wR_2 = 0.0639
Final R indexes [all data]	R_1 = 0.0250, wR_2 = 0.0645
Largest diff. peak/hole / e Å^{-3}	0.62/-0.98
Flack parameter	-0.004(4)

Table 69: Selected bond angles [°] for *trans*-**192b**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Ru1	P1	2.3514(9)	C15	C16	1.385(4)
Ru1	P2	2.3266(10)	C16	C17	1.393(3)
Ru1	O1	2.3822(19)	C18	C19	1.399(3)
Ru1	O2	2.1251(19)	C18	C23	1.397(3)
Ru1	N1	2.056(2)	C19	C20	1.397(4)
Ru1	C1	1.981(2)	C20	C21	1.382(4)
Ru1	C48	2.598(2)	C21	C22	1.384(4)
P1	C12	1.830(2)	C22	C23	1.402(4)
P1	C18	1.833(3)	C24	C25	1.399(3)
P1	C24	1.821(2)	C24	C29	1.399(4)
P2	C30	1.840(2)	C25	C26	1.394(3)
P2	C36	1.836(3)	C26	C27	1.393(4)
P2	C42	1.826(2)	C27	C28	1.388(4)
F1	C5	1.366(3)	C28	C29	1.382(4)
O1	C48	1.267(3)	C30	C31	1.401(3)
O2	C48	1.260(3)	C30	C35	1.396(3)
N1	C7	1.369(3)	C31	C32	1.385(3)
N1	C11	1.354(3)	C32	C33	1.394(4)
C1	C2	1.410(3)	C33	C34	1.382(4)
C1	C6	1.404(3)	C34	C35	1.393(4)
C2	C3	1.399(3)	C36	C37	1.395(3)
C2	C7	1.460(4)	C36	C41	1.402(3)
C3	C4	1.399(4)	C37	C38	1.395(3)
C4	C5	1.383(3)	C38	C39	1.389(4)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C5	C6	1.375(3)	C39	C40	1.386(4)
C7	C8	1.396(3)	C40	C41	1.389(3)
C8	C9	1.376(4)	C42	C43	1.396(3)
C9	C10	1.397(3)	C42	C47	1.408(3)
C10	C11	1.385(3)	C43	C44	1.396(4)
C12	C13	1.397(3)	C44	C45	1.385(4)
C12	C17	1.396(3)	C45	C46	1.385(4)
C13	C14	1.386(3)	C46	C47	1.385(3)
C14	C15	1.392(4)	C48	C49	1.516(4)

Table 70: Selected bond angles [°] for *trans*-**192b**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
P1	Ru1	O1	87.75(5)	N1	C11	C10	123.1(2)
P1	Ru1	C48	88.14(6)	C13	C12	P1	119.17(19)
P2	Ru1	P1	178.80(3)	C17	C12	P1	121.85(18)
P2	Ru1	O1	92.96(5)	C17	C12	C13	118.5(2)
P2	Ru1	C48	92.95(6)	C14	C13	C12	120.9(3)
O1	Ru1	C48	29.06(7)	C13	C14	C15	120.0(3)
O2	Ru1	P1	90.88(6)	C16	C15	C14	119.8(2)
O2	Ru1	P2	90.31(6)	C15	C16	C17	120.1(3)
O2	Ru1	O1	57.81(7)	C16	C17	C12	120.7(2)
O2	Ru1	C48	28.79(8)	C19	C18	P1	117.76(18)
N1	Ru1	P1	88.41(6)	C23	C18	P1	123.57(19)
N1	Ru1	P2	90.40(6)	C23	C18	C19	118.6(2)
N1	Ru1	O1	120.61(7)	C20	C19	C18	120.8(2)
N1	Ru1	O2	178.31(8)	C21	C20	C19	120.1(3)
N1	Ru1	C48	149.61(8)	C20	C21	C22	119.8(2)
C1	Ru1	P1	90.08(7)	C21	C22	C23	120.6(3)
C1	Ru1	P2	89.58(7)	C18	C23	C22	120.1(3)
C1	Ru1	O1	160.14(9)	C25	C24	P1	119.70(17)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C1	Ru1	O2	102.52(9)	C25	C24	C29	119.0(2)
C1	Ru1	N1	79.02(9)	C29	C24	P1	121.23(19)
C1	Ru1	C48	131.16(10)	C26	C25	C24	120.0(2)
C12	P1	Ru1	112.99(8)	C27	C26	C25	120.4(2)
C12	P1	C18	105.23(12)	C28	C27	C26	119.5(2)
C18	P1	Ru1	115.22(8)	C29	C28	C27	120.3(2)
C24	P1	Ru1	118.05(9)	C28	C29	C24	120.7(3)
C24	P1	C12	101.52(11)	C31	C30	P2	117.07(17)
C24	P1	C18	102.05(11)	C35	C30	P2	125.08(19)
C30	P2	Ru1	116.23(8)	C35	C30	C31	117.8(2)
C36	P2	Ru1	117.38(8)	C32	C31	C30	121.3(2)
C36	P2	C30	99.83(12)	C31	C32	C33	120.3(2)
C42	P2	Ru1	113.34(9)	C34	C33	C32	119.0(2)
C42	P2	C30	105.57(11)	C33	C34	C35	120.9(3)
C42	P2	C36	102.59(11)	C34	C35	C30	120.7(3)
C48	O1	Ru1	84.96(15)	C37	C36	P2	119.89(18)
C48	O2	Ru1	96.92(16)	C37	C36	C41	119.4(2)
C7	N1	Ru1	116.60(16)	C41	C36	P2	120.64(17)
C11	N1	Ru1	124.81(15)	C36	C37	C38	119.9(2)
C11	N1	C7	118.6(2)	C39	C38	C37	120.3(2)
C2	C1	Ru1	117.31(18)	C40	C39	C38	119.9(2)
C6	C1	Ru1	125.20(17)	C39	C40	C41	120.3(2)
C6	C1	C2	117.5(2)	C40	C41	C36	120.1(2)
C1	C2	C7	113.7(2)	C43	C42	P2	121.87(19)
C3	C2	C1	122.2(2)	C43	C42	C47	118.5(2)
C3	C2	C7	124.1(2)	C47	C42	P2	119.48(17)
C2	C3	C4	119.4(2)	C44	C43	C42	120.4(2)
C5	C4	C3	117.6(2)	C45	C44	C43	120.4(2)
F1	C5	C4	118.0(2)	C44	C45	C46	119.7(2)
F1	C5	C6	117.9(2)	C45	C46	C47	120.5(2)
C6	C5	C4	124.0(2)	C46	C47	C42	120.4(2)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C5	C6	C1	119.3(2)	O1	C48	Ru1	65.98(13)
N1	C7	C2	113.4(2)	O1	C48	C49	120.2(2)
N1	C7	C8	120.4(2)	O2	C48	Ru1	54.29(12)
C8	C7	C2	126.2(2)	O2	C48	O1	120.2(2)
C9	C8	C7	120.4(2)	O2	C48	C49	119.5(3)
C8	C9	C10	119.3(2)	C49	C48	Ru1	170.5(2)
C11	C10	C9	118.2(2)				

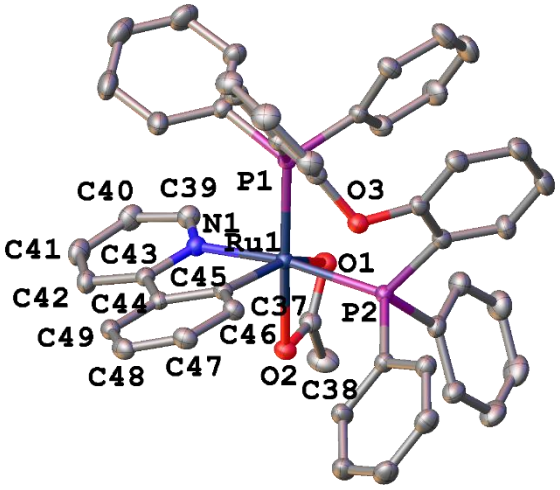


Figure 49: Molecular structure of **193** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{49}H_{39}NO_3P_2Ru$ (*M* = 852.82 g/mol): monoclinic, space group C2/c (no. 15), *a* = 19.1587(12) Å, *b* = 20.6734(11) Å, *c* = 20.6880(9) Å, *β* = 107.466(2)°, *V* = 7816.2(7) Å^3, *Z* = 8, *T* = 149.96 K, μ(MoKα) = 0.529 mm^{-1}, *Dcalc* = 1.449 g/cm^3, 182744 reflections measured (5.086° ≤ 2Θ ≤ 63.122°), 13014 unique (R_{int} = 0.0258, R_{sigma} = 0.0112) which were used in all calculations. The final R_1 was 0.0217 (I > 2σ(I)) and wR_2 was 0.0600 (all data).

Table 71: Crystal data and structure refinement for **193**.

Compound	**193**
CCDC number	1915688
Identification code	0527_CG_0m

Empirical formula	$C_{49}H_{39}NO_3P_2Ru$
Formula weight	852.82
Temperature/K	149.96
Crystal system	monoclinic
Space group	C2/c
a/Å	19.1587(12)
b/Å	20.6734(11)
c/Å	20.6880(9)
α/°	90
β/°	107.466(2)
γ/°	90
Volume/Å^3	7816.2(7)
Z	8
ρ_{calc}g/cm^3	1.449
μ/mm^{-1}	0.529
F(000)	3504.0
Crystal size/mm^3	0.529 × 0.31 × 0.154
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.086 to 63.122
Index ranges	-28 ≤ h ≤ 28, -29 ≤ k ≤ 29, -28 ≤ l ≤ 30
Reflections collected	182744
Independent reflections	13014 [R_{int} = 0.0258, R_{sigma} = 0.0112]
Data/restraints/parameters	13014/0/506
Goodness-of-fit on F^2	1.052
Final R indexes [I>=2σ (I)]	R_1 = 0.0217, wR_2 = 0.0583
Final R indexes [all data]	R_1 = 0.0240, wR_2 = 0.0600
Largest diff. peak/hole / e Å^{-3}	0.44/-0.54

Table 72: Selected bond lengths [Å] for **193**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Ru1	P1	2.2377(3)	C15	C16	1.3885(17)
Ru1	P2	2.3263(3)	C16	C17	1.3830(18)
Ru1	O1	2.2928(8)	C17	C18	1.3903(16)
Ru1	O2	2.1987(8)	C19	C20	1.3870(14)
Ru1	N1	2.0836(9)	C19	C24	1.3922(15)
Ru1	C37	2.5928(11)	C20	C21	1.3865(17)
Ru1	C45	2.0302(10)	C21	C22	1.3808(19)
P1	C1	1.8379(11)	C22	C23	1.3910(16)
P1	C7	1.8263(10)	C23	C24	1.3990(15)
P1	C13	1.8506(10)	C25	C26	1.3963(15)
P2	C24	1.8388(10)	C25	C30	1.3989(16)
P2	C25	1.8503(11)	C26	C27	1.3934(17)
P2	C31	1.8325(11)	C27	C28	1.381(2)
O1	C37	1.2627(13)	C28	C29	1.389(2)
O2	C37	1.2700(13)	C29	C30	1.3893(17)
O3	C14	1.3899(13)	C31	C32	1.3923(15)
O3	C19	1.3839(13)	C31	C36	1.3966(15)
N1	C39	1.3452(14)	C32	C33	1.3908(15)
N1	C43	1.3561(13)	C33	C34	1.3822(18)
C1	C2	1.3936(15)	C34	C35	1.3881(17)
C1	C6	1.3966(15)	C35	C36	1.3897(16)
C2	C3	1.3926(16)	C37	C38	1.5027(16)
C3	C4	1.377(2)	C39	C40	1.3827(16)
C4	C5	1.380(2)	C40	C41	1.3874(18)
C5	C6	1.3904(18)	C41	C42	1.3819(16)
C7	C8	1.3952(15)	C42	C43	1.3977(14)
C7	C12	1.3906(14)	C43	C44	1.4616(14)
C8	C9	1.3844(16)	C44	C45	1.4264(14)
C9	C10	1.385(2)	C44	C49	1.4016(14)
C10	C11	1.379(2)	C45	C46	1.4080(14)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C11	C12	1.3948(16)	C46	C47	1.3919(15)
C13	C14	1.3961(15)	C47	C48	1.3908(16)
C13	C18	1.4026(15)	C48	C49	1.3826(16)
C14	C15	1.3863(15)			

Table 73: Selected bond angles [°] for **193**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
P1	Ru1	P2	96.827(9)	C18	C13	P1	122.74(8)
P1	Ru1	O1	111.67(2)	O3	C14	C13	119.50(9)
P1	Ru1	C37	140.68(3)	C15	C14	O3	117.78(10)
P2	Ru1	C37	88.90(3)	C15	C14	C13	122.62(10)
O1	Ru1	P2	90.52(2)	C14	C15	C16	119.60(11)
O1	Ru1	C37	29.14(3)	C17	C16	C15	119.49(11)
O2	Ru1	P1	169.67(2)	C16	C17	C18	120.21(11)
O2	Ru1	P2	86.58(2)	C17	C18	C13	121.78(11)
O2	Ru1	O1	58.41(3)	O3	C19	C20	122.38(10)
O2	Ru1	C37	29.29(3)	O3	C19	C24	115.08(9)
N1	Ru1	P1	93.69(3)	C20	C19	C24	122.43(10)
N1	Ru1	P2	169.30(3)	C21	C20	C19	118.66(11)
N1	Ru1	O1	83.73(3)	C22	C21	C20	120.59(11)
N1	Ru1	O2	82.72(3)	C21	C22	C23	119.98(11)
N1	Ru1	C37	81.68(3)	C22	C23	C24	120.86(11)
C45	Ru1	P1	91.38(3)	C19	C24	P2	116.57(8)
C45	Ru1	P2	101.60(3)	C19	C24	C23	117.42(10)
C45	Ru1	O1	152.61(3)	C23	C24	P2	126.01(9)
C45	Ru1	O2	97.50(3)	C26	C25	P2	123.27(9)
C45	Ru1	N1	80.07(4)	C26	C25	C30	118.14(10)
C45	Ru1	C37	125.59(4)	C30	C25	P2	118.58(8)
C1	P1	Ru1	112.82(3)	C27	C26	C25	120.49(12)
C1	P1	C13	99.47(5)	C28	C27	C26	120.65(12)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C7	P1	Ru1	113.34(3)	C27	C28	C29	119.63(12)
C7	P1	C1	100.59(5)	C28	C29	C30	119.83(13)
C7	P1	C13	102.72(5)	C29	C30	C25	121.24(12)
C13	P1	Ru1	124.57(3)	C32	C31	P2	122.92(8)
C24	P2	Ru1	123.17(3)	C32	C31	C36	118.78(10)
C24	P2	C25	99.76(5)	C36	C31	P2	118.23(8)
C25	P2	Ru1	111.22(3)	C33	C32	C31	120.69(10)
C31	P2	Ru1	117.34(3)	C34	C33	C32	120.16(11)
C31	P2	C24	101.20(5)	C33	C34	C35	119.70(11)
C31	P2	C25	100.65(5)	C34	C35	C36	120.33(11)
C37	O1	Ru1	88.72(6)	C35	C36	C31	120.32(11)
C37	O2	Ru1	92.83(6)	O1	C37	Ru1	62.14(5)
C19	O3	C14	118.07(8)	O1	C37	O2	119.99(10)
C39	N1	Ru1	125.21(7)	O1	C37	C38	120.32(10)
C39	N1	C43	119.79(9)	O2	C37	Ru1	57.88(5)
C43	N1	Ru1	114.43(7)	O2	C37	C38	119.68(10)
C2	C1	P1	122.72(8)	C38	C37	Ru1	177.39(9)
C2	C1	C6	118.59(10)	N1	C39	C40	122.52(11)
C6	C1	P1	118.67(8)	C39	C40	C41	118.15(11)
C3	C2	C1	120.69(12)	C42	C41	C40	119.64(10)
C4	C3	C2	120.18(13)	C41	C42	C43	119.79(10)
C3	C4	C5	119.69(12)	N1	C43	C42	119.94(10)
C4	C5	C6	120.74(12)	N1	C43	C44	113.83(9)
C5	C6	C1	120.10(12)	C42	C43	C44	126.20(9)
C8	C7	P1	115.36(8)	C45	C44	C43	116.48(9)
C12	C7	P1	125.30(8)	C49	C44	C43	121.34(9)
C12	C7	C8	119.31(10)	C49	C44	C45	122.16(9)
C9	C8	C7	120.16(11)	C44	C45	Ru1	112.30(7)
C10	C9	C8	120.18(12)	C46	C45	Ru1	132.00(8)
C11	C10	C9	120.14(11)	C46	C45	C44	115.37(9)
C10	C11	C12	120.01(12)	C47	C46	C45	122.18(10)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C7	C12	C11	120.09(11)	C48	C47	C46	120.97(10)
C14	C13	P1	120.96(8)	C49	C48	C47	119.01(10)
C14	C13	C18	116.28(9)	C48	C49	C44	120.24(10)

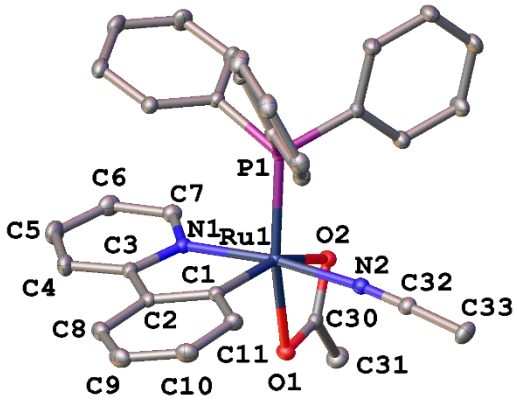


Figure 50: Molecular structure of **194** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{33}H_{29}N_2O_2PRu$ (*M* = 617.62 g/mol): orthorhombic, space group $Pna2_1$ (no. 33), *a* = 16.2264(8) Å, *b* = 9.3716(4) Å, *c* = 17.7053(10) Å, *V* = 2692.4(2) Å^3, *Z* = 4, *T* = 100.1 K, μ(MoKα) = 0.676 mm^{-1}, *Dcalc* = 1.524 g/cm^3, 57514 reflections measured (4.602° ≤ 2Θ ≤ 63.044°), 8977 unique (R_{int} = 0.0242, R_{sigma} = 0.0160) which were used in all calculations. The final R_1 was 0.0155 (I > 2σ(I)) and wR_2 was 0.0412 (all data).

Table 74: Crystal data and structure refinement for **194**.

Compound	**194**
CCDC number	1915689
Identification code	Pna21
Empirical formula	$C_{33}H_{29}N_2O_2PRu$
Formula weight	617.62
Temperature/K	100.1
Crystal system	orthorhombic
Space group	$Pna2_1$
a/Å	16.2264(8)

b/Å	9.3716(4)
c/Å	17.7053(10)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2692.4(2)
Z	4
ρ_{calc}g/cm^3	1.524
μ/mm^{-1}	0.676
F(000)	1264.0
Crystal size/mm^3	0.305 × 0.139 × 0.09
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.602 to 63.044
Index ranges	-23 ≤ h ≤ 23, -13 ≤ k ≤ 13, -26 ≤ l ≤ 26
Reflections collected	57514
Independent reflections	8977 [R_{int} = 0.0242, R_{sigma} = 0.0160]
Data/restraints/parameters	8977/1/354
Goodness-of-fit on F^2	1.034
Final R indexes [I>=2σ (I)]	R_1 = 0.0155, wR_2 = 0.0408
Final R indexes [all data]	R_1 = 0.0160, wR_2 = 0.0412
Largest diff. peak/hole / e Å^{-3}	0.37/-0.43
Flack parameter	-0.032(5)

Table 75: Bond lengths [Å] for **194**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Ru1	P1	2.2451(5)	C9	C10	1.393(3)
Ru1	O1	2.2216(12)	C10	C11	1.389(2)
Ru1	O2	2.2956(11)	C12	C13	1.397(2)
Ru1	N1	2.0531(13)	C12	C17	1.394(2)
Ru1	N2	2.0148(14)	C13	C14	1.395(2)
Ru1	C1	2.0085(15)	C14	C15	1.394(3)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
P1	C12	1.8372(16)	C15	C16	1.388(3)
P1	C18	1.8283(16)	C16	C17	1.391(2)
P1	C24	1.8394(16)	C18	C19	1.396(2)
O1	C30	1.267(2)	C18	C23	1.400(2)
O2	C30	1.2635(19)	C19	C20	1.395(2)
N1	C3	1.3643(19)	C20	C21	1.381(2)
N1	C7	1.345(2)	C21	C22	1.393(3)
N2	C32	1.147(2)	C22	C23	1.390(2)
C1	C2	1.424(2)	C24	C25	1.396(2)
C1	C11	1.412(2)	C24	C29	1.398(2)
C2	C3	1.456(2)	C25	C26	1.395(2)
C2	C8	1.403(2)	C26	C27	1.383(3)
C3	C4	1.396(2)	C27	C28	1.390(3)
C4	C5	1.380(3)	C28	C29	1.390(2)
C5	C6	1.394(3)	C30	C31	1.507(2)
C6	C7	1.383(2)	C32	C33	1.460(2)
C8	C9	1.382(3)			

Table 76: Bond angles [°] for **194**.

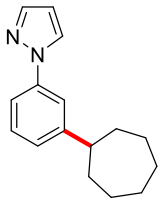
Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
P1	Ru1	O2	105.56(3)	C5	C4	C3	120.03(16)
O1	Ru1	P1	163.66(3)	C4	C5	C6	118.98(16)
O1	Ru1	O2	58.10(4)	C7	C6	C5	118.58(16)
N1	Ru1	P1	92.21(4)	N1	C7	C6	122.93(16)
N1	Ru1	O1	88.19(5)	C9	C8	C2	120.10(15)
N1	Ru1	O2	91.65(5)	C8	C9	C10	119.48(16)
N2	Ru1	P1	93.88(4)	C11	C10	C9	120.47(16)
N2	Ru1	O1	87.33(5)	C10	C11	C1	122.38(16)
N2	Ru1	O2	91.42(5)	C13	C12	P1	123.40(12)
N2	Ru1	N1	172.18(6)	C17	C12	P1	118.07(12)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C1	Ru1	P1	95.99(4)	C17	C12	C13	118.48(14)
C1	Ru1	O1	100.17(5)	C14	C13	C12	120.72(16)
C1	Ru1	O2	157.26(5)	C15	C14	C13	119.83(16)
C1	Ru1	N1	80.16(6)	C16	C15	C14	119.97(16)
C1	Ru1	N2	94.33(6)	C15	C16	C17	119.78(16)
C12	P1	Ru1	121.81(5)	C16	C17	C12	121.19(15)
C12	P1	C24	101.16(7)	C19	C18	P1	121.80(12)
C18	P1	Ru1	113.59(5)	C19	C18	C23	118.57(14)
C18	P1	C12	102.78(7)	C23	C18	P1	119.34(12)
C18	P1	C24	101.24(7)	C20	C19	C18	120.50(15)
C24	P1	Ru1	113.57(5)	C21	C20	C19	120.46(16)
C30	O1	Ru1	92.44(9)	C20	C21	C22	119.60(18)
C30	O2	Ru1	89.14(10)	C23	C22	C21	120.18(17)
C3	N1	Ru1	115.95(10)	C22	C23	C18	120.66(15)
C7	N1	Ru1	125.24(11)	C25	C24	P1	119.44(12)
C7	N1	C3	118.82(13)	C25	C24	C29	119.11(14)
C32	N2	Ru1	174.61(14)	C29	C24	P1	121.43(12)
C2	C1	Ru1	113.99(11)	C26	C25	C24	120.21(15)
C11	C1	Ru1	129.80(12)	C27	C26	C25	120.23(16)
C11	C1	C2	115.52(14)	C26	C27	C28	119.99(16)
C1	C2	C3	115.34(13)	C27	C28	C29	120.04(16)
C8	C2	C1	122.04(14)	C28	C29	C24	120.42(15)
C8	C2	C3	122.62(15)	O1	C30	C31	120.13(15)
N1	C3	C2	113.71(13)	O2	C30	O1	120.31(15)
N1	C3	C4	120.63(15)	O2	C30	C31	119.57(15)
C4	C3	C2	125.62(15)	N2	C32	C33	177.99(19)

5.3.5 Ruthenium(II)-Catalyzed Decarboxylative Alkylation

5.3.5.1 Characterization Data for 145, 146, and 201

1-(3-Cycloheptylphenyl)-1*H*-pyrazole (146ah)



The general procedure **K** was followed using 2-(1*H*-pyrazol-1-yl)benzoic acid (**144a**, 94.1 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol) and $[Ru(NC\textit{t}\text{-}Bu)_6][BF_4]_2$ (19.3 mg, 25.0 µmol, 5.0 mol %). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *meta*-alkylated product **146ah** (71.8 mg, 60%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.92 (dd, *J* = 2.5, 0.7 Hz, 1H), 7.72 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.57 (dd, *J* = 2.2, 1.8 Hz, 1H), 7.43 (ddd, *J* = 7.9, 2.2, 1.3 Hz, 1H), 7.34 (dd, *J* = 7.9, 7.7 Hz, 1H), 7.12 (ddd, *J* = 7.7, 1.8, 1.3 Hz, 1H), 6.45 (dd, *J* = 2.5, 1.8 Hz, 1H), 2.74 (tt, *J* = 10.6, 3.6 Hz, 1H), 1.99–1.91 (m, 2H), 1.85–1.77 (m, 2H), 1.76–1.50 (m, 8H).

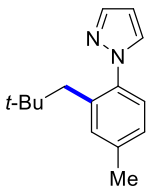
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 151.7 (C_q), 140.8 (CH), 140.2 (C_q), 129.2 (CH), 126.8 (CH), 124.9 (CH), 117.9 (CH), 116.3 (CH), 107.3 (CH), 47.1 (CH), 36.7 (CH_2), 27.8 (CH_2), 27.2 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2919, 2852, 1607, 1590, 1518, 1392, 1043, 784, 744, 697 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 240 (100) $[M]^+$, 239 (36) $[M–H]^+$, 225 (10), 211 (17), 197 (26), 183 (29), 171 (53), 158 (61), 144 (14), 130 (15), 115 (23), 77 (12).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{20}N_2^+$ $[M]^+$ 240.1621, found 240.1633.

1-(4-Methyl-2-neopentylphenyl)-1*H*-pyrazole (145et)



The general procedure **K** was followed using 5-methyl-2-(1*H*-pyrazol-1-yl)benzoic acid (**144e**, 101 mg, 0.50 mmol) and neopentyl bromide (**136t**, 227 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded *ortho*-alkylated product **145et** (57.0 mg, 50%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.68 (dd, *J* = 2.0, 0.7 Hz, 1H), 7.54 (dd, *J* = 2.1, 0.7 Hz, 1H), 7.15 (d, *J* = 8.5 Hz, 1H), 7.11–7.06 (m, 2H), 6.39 (dd, *J* = 2.1, 2.0 Hz, 1H), 2.69 (s, 2H), 2.39 (s, 3H), 0.68 (s, 9H).

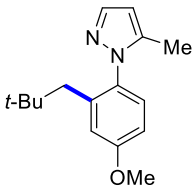
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 139.7 (CH), 138.0 (C_q), 137.2 (C_q), 135.1 (C_q), 133.5 (CH), 130.9 (CH), 127.4 (CH), 126.4 (CH), 105.9 (CH), 44.0 (CH_2), 32.1 (C_q), 29.4 (CH_3), 21.2 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2950, 2865, 1518, 1476, 1395, 1234, 1044, 818, 746 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 228 (29) $[M]^+$, 213 (30) $[M–Me]^+$, 172 (100) $[M–t\text{-}Bu]^+$, 171 (67), 144 (52), 130 (9), 115 (9), 57 (13), 43 (14).

HR-MS (EI): *m*/*z* calcd for $C_{15}H_{20}N_2^+$ $[M]^+$ 228.1621, found 228.1632.

1-(4-Methoxy-2-neopentylphenyl)-5-methyl-1*H*-pyrazole (145ft)



The general procedure **K** was followed using 5-methoxy-2-(5-methyl-1*H*-pyrazol-1-yl)benzoic acid (**144f**, 116 mg, 0.50 mmol) and neopentyl bromide (**136t**, 227 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *ortho*-alkylated product **145ft** (51.2 mg, 40%) as a colorless oil and *ortho*-benzylated product **201** (54.3 mg, 37%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 1.8 Hz, 1H), 7.10 (d, *J* = 8.6 Hz, 1H), 6.84 (d, *J* = 2.9 Hz, 1H), 6.81 (dd, *J* = 8.6, 2.9 Hz, 1H), 6.13 (dq, *J* = 1.8, 0.8 Hz, 1H), 3.84 (s, 3H), 2.47 (br s, 2H), 2.13 (d, *J* = 0.8 Hz, 3H), 0.75 (s, 9H).

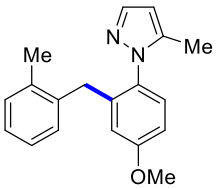
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.7 (C_q), 139.5 (C_q), 138.9 (CH), 138.8 (C_q), 132.2 (C_q), 128.8 (CH), 117.7 (CH), 111.6 (CH), 105.2 (CH), 55.4 (CH_3), 44.1 (CH_2), 32.2 (C_q), 29.7 (CH_3), 11.8 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2952, 1608, 1505, 1464, 1279, 1238, 1052, 922, 813, 770 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 258 (42) $[M]^+$, 243 (100) $[M–Me]^+$, 202 (65) $[M–t\text{-}Bu]^+$, 187 (74) $[M–CH_2t\text{-}Bu]^+$, 174 (18), 160 (13), 57 (12), 41 (13).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{22}N_2O^+$ $[M]^+$ 258.1727, found 258.1738.

1-[4-Methoxy-2-(2-methylbenzyl)phenyl]-5-methyl-1*H*-pyrazole (201)



^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 1.8 Hz, 1H), 7.16 (d, *J* = 8.6 Hz, 1H), 7.12–7.05 (m, 3H), 6.94 (dd, *J* = 7.0, 1.2 Hz, 1H), 6.81 (dd, *J* = 8.6, 2.9 Hz, 1H), 6.56 (d, *J* = 2.9 Hz, 1H), 6.11 (dd, *J* = 1.8, 0.8 Hz, 1H), 3.75 (s, 3H), 3.66 (s, 2H), 2.09 (s, 3H), 1.98 (d, *J* = 0.8 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 159.9 (C_q), 140.4 (C_q), 139.9 (C_q), 139.5 (CH), 137.3 (C_q), 136.6 (C_q), 131.6 (C_q), 130.2 (CH), 130.0 (CH), 129.0 (CH), 126.5 (CH), 125.9 (CH), 115.8 (CH), 111.2 (CH), 105.1 (CH), 55.4 (CH_3), 34.5 (CH_2), 19.6 (CH_3), 11.2 (CH_3).

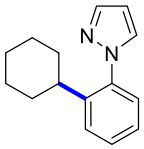
IR (ATR): $\tilde{\nu}$ = 2961, 1610, 1499, 1438, 1280, 1217, 1110, 1045, 799, 742 cm^{-1}.

m.p.: 65–66 °C

MS (EI) *m*/*z* (relative intensity): 292 (100) $[M]^+$, 291 (22) $[M–H]^+$, 277 (38) $[M–Me]^+$, 264 (35), 250 (9), 210 (16), 179 (12), 174 (17), 165 (15), 152 (12), 43 (13).

HR-MS (EI): *m*/*z* calcd for $C_{19}H_{20}N_2O^+$ $[M]^+$ 292.1570, found 292.1571.

1-(2-Cyclohexylphenyl)-1*H*-pyrazole (145aj)



The general procedure **K** was followed using 2-(1*H*-pyrazol-1-yl)benzoic acid (**144a**, 94.1 mg, 0.50 mmol) and bromocyclohexane (**136j**, 245 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 20:1) followed by recycling preparative HPLC yielded *ortho*-alkylated product **145aj** (45.4 mg, 40%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.55 (dd, *J* = 2.3, 0.7 Hz, 1H), 7.42–7.38 (m, 2H), 7.29–7.24 (m, 2H), 6.44 (dd, *J* = 2.3, 1.9 Hz, 1H), 2.44 (tt, *J* = 12.0, 3.1 Hz, 1H), 1.82–1.66 (m, 5H), 1.48–1.33 (m, 2H), 1.30–1.16 (m, 3H).

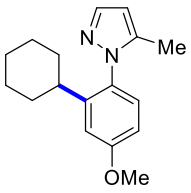
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 144.0 (C_q), 140.0 (CH), 138.9 (C_q), 130.9 (CH), 128.8 (CH), 127.1 (CH), 126.9 (CH), 126.0 (CH), 105.9 (CH), 38.3 (CH), 34.3 (CH_2), 26.8 (CH_2), 26.1 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2924, 2851, 1515, 1448, 1394, 1043, 938, 745, 620 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 226 (74) $[M]^+$, 225 (100) $[M–H]^+$, 208 (14), 197 (21), 183 (39), 169 (46), 157 (17), 143 (13), 130 (25), 115 (17).

HR-MS (ESI): *m*/*z* calcd for $C_{15}H_{19}N_2^+$ $[M+H]^+$ 227.1543, found 227.1552.

1-(2-Cyclohexyl-4-methoxyphenyl)-5-methyl-1*H*-pyrazole (145fj)



The general procedure **K** was followed using 5-methoxy-2-(5-methyl-1*H*-pyrazol-1-yl)benzoic acid (**144f**, 116 mg, 0.50 mmol) and bromocyclohexane (**136j**, 245 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *ortho*-alkylated product **145fj** (44.3 mg, 33%, as a 10:1 mixture of *ortho* and *meta* product) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$, determined as a 10:1 mixture of *ortho*- and *meta*-isomer): δ = 7.54 (d, *J* = 1.7 Hz, 1H), 7.24 (d, *J* = 2.6 Hz, 1H, *meta*-isomer), 7.18 (dd, *J* = 8.6, 2.6 Hz, 1H, *meta*-isomer), 7.10

(d, *J* = 8.6 Hz, 1H), 6.90 (d, *J* = 2.9 Hz, 1H), 6.77 (dd, *J* = 8.6, 2.9 Hz, 1H), 6.16–6.13 (m, 1H), 3.86 (s, 3H, *meta*-isomer), 3.85 (s, 3H), 2.98 (tt, *J* = 11.7, 3.2 Hz, 1H, *meta*-isomer), 2.29 (s, 3H, *meta*-isomer), 2.07 (s, 3H), 2.03 (tt, *J* = 11.9, 3.2 Hz, 1H), 1.88–1.60 (m, 5H), 1.45–1.04 (m, 5H). Some proton peaks of *meta* isomer could observed by ^{1}H-NMR spectroscopy.

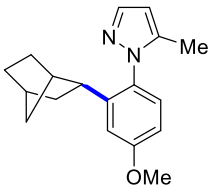
^{13}C-NMR (125 MHz, $CDCl_3$, determined as a 10:1 mixture of *ortho* and *meta* isomer): δ = 160.0 (C_q), 147.4 (C_q), 139.8 (C_q), 139.2 (CH, *meta*-isomer), 139.0 (CH), 136.9 (C_q, *meta*-isomer), 132.8 (C_q, *meta*-isomer), 130.6 (C_q), 128.9 (CH), 123.8 (CH, *meta*-isomer), 123.0 (CH, *meta*-isomer), 112.8 (CH), 110.8 (CH), 110.2 (CH, *meta*-isomer), 106.1 (CH, *meta*-isomer), 104.7 (CH), 55.7 (CH_3, *meta*-isomer), 55.4 (CH_3), 38.7 (CH), 36.9 (CH, *meta*-isomer), 33.1 (CH_2, *meta*-isomer), 27.1 (CH_2, *meta*-isomer), 26.8 (CH_2), 26.4 (CH_2, *meta*-isomer), 26.1 (CH_2), 12.3 (CH_3, *meta*-isomer), 11.6 (CH_3). Due to overlapping, some carbon peaks of *meta*-isomer could not be detected by ^{13}C-NMR spectroscopy.

IR (ATR): $\tilde{\nu}$ = 2924, 2850, 1608, 1506, 1445, 1294, 1242, 1051, 922, 770 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 270 (38) $[M]^+$, 269 (12) $[M–H]^+$, 255 (100) $[M–Me]^+$, 241 (6), 227 (17), 213 (12), 187 (10).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{22}N_2O^+$ $[M]^+$ 270.1727, found 270.1727.

1-[*exo*-2-(Bicyclo[2.2.1]heptan-2-yl)-4-methoxyphenyl]-5-methyl-1*H*-pyrazole (145fu)



The general procedure **K** was followed using 5-methoxy-2-(5-methyl-1*H*-pyrazol-1-yl)benzoic acid (**144f**, 116 mg, 0.50 mmol) and *exo*-2-bromonorbornane (**136u**, 263 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *ortho*-alkylated product **145fu** (76.5 mg, 54%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 1.9 Hz, 1H), 7.10 (d, *J* = 8.5 Hz, 1H), 6.94 (d, *J* = 2.8 Hz, 1H), 6.75 (dd, *J* = 8.5, 2.8 Hz, 1H), 6.14 (dq, *J* = 1.9, 0.8 Hz, 1H), 3.85 (s, 3H), 2.50–2.17 (m, 3H), 2.08 (s, 3H), 1.56 (dt, *J* = 9.8, 2.0 Hz, 1H), 1.52–1.24 (m, 4H), 1.19 (ddt, *J* = 9.7, 2.2, 1.4 Hz, 1H), 1.13–0.96 (m, 2H).

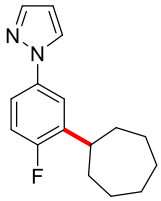
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 159.8 (C_q), 147.0 (C_q), 139.6 (C_q), 139.1 (CH), 131.3 (C_q), 129.0 (CH), 112.9 (CH), 109.9 (CH), 104.7 (CH), 55.4 (CH_3), 42.2 (CH), 41.5 (CH), 39.4 (CH_2), 36.7 (CH), 36.5 (CH_2), 30.7 (CH_2), 28.4 (CH_2), 11.7 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2950, 2869, 1607, 1503, 1299, 1225, 1111, 1041, 922, 769 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 282 (88) $[M]^+$, 267 (68) $[M–Me]^+$, 253 (100), 241 (26), 226 (50), 200 (16), 115 (12), 77 (11), 67 (14), 43 (24).

HR-MS (EI): *m*/*z* calcd for $C_{18}H_{22}N_2O^+$ $[M]^+$ 282.1727, found 282.1736.

1-(3-Cycloheptyl-4-fluorophenyl)-1*H*-pyrazole (146gh)



The general procedure **K** was followed using 5-fluoro-2-(1*H*-pyrazol-1-yl)benzoic acid (**144g**, 103 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 15:1) yielded *meta*-alkylated product **146gh** (82.6 mg, 64%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.71 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.58 (dd, *J* = 6.4, 2.8 Hz, 1H), 7.38 (ddd, *J* = 8.8, 4.3, 2.8 Hz, 1H), 7.06 (dd, *J* = 9.9, 8.8 Hz, 1H), 6.45 (dd, *J* = 2.5, 1.8 Hz, 1H), 3.04 (tt, *J* = 10.4, 3.5 Hz, 1H), 2.01–1.49 (m, 12H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 158.3 (d, $^1J_{C–F}$ = 244 Hz, C_q), 140.8 (CH), 137.5 (d, $^2J_{C–F}$ = 17 Hz, C_q), 136.4 (d, $^4J_{C–F}$ = 3 Hz, C_q), 126.8 (CH), 119.4 (d, $^3J_{C–F}$ = 6 Hz, CH), 117.7 (d, $^3J_{C–F}$ = 9 Hz, CH), 115.9 (d, $^2J_{C–F}$ = 25 Hz, CH), 107.4 (CH), 39.8 (CH), 35.3 (CH_2), 27.8 (CH_2), 27.4 (CH_2).

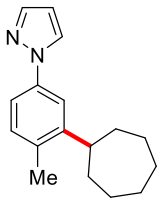
^{19}F-NMR (282 MHz, $CDCl_3$): δ = –121.6 (ddd, *J* = 9.9, 6.4, 4.3 Hz).

IR (ATR): $\tilde{\nu}$ = 2922, 2855, 1519, 1494, 1393, 1220, 1039, 811, 744, 635 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 258 (100) $[M]^+$, 229 (9), 215 (9), 201 (17), 188 (43), 176 (35), 133 (16), 41 (12).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{19}FN_2^+$ $[M]^+$ 258.1527, found 258.1531.

1-(3-Cycloheptyl-4-methylphenyl)-1*H*-pyrazole (146eh)



The general procedure **K** was followed using 5-methyl-2-(1*H*-pyrazol-1-yl)benzoic acid (**144e**, 101 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *meta*-alkylated product **146eh** (74.5 mg, 59%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 2.5, 0.7 Hz, 1H), 7.71 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.56 (d, *J* = 2.4 Hz, 1H), 7.32 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.17 (d, *J* = 8.2 Hz, 1H), 6.44 (dd, *J* = 2.5, 1.8 Hz, 1H), 2.91 (tt, *J* = 10.4, 3.1 Hz, 1H), 2.35 (s, 3H), 1.96–1.49 (m, 12H).

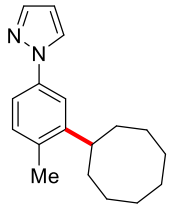
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 149.3 (C_q), 140.5 (CH), 138.6 (C_q), 132.8 (C_q), 130.7 (CH), 126.6 (CH), 117.0 (CH), 116.0 (CH), 107.0 (CH), 42.2 (CH), 36.0 (CH_2), 27.8 (CH_2), 27.7 (CH_2), 19.1 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2920, 2853, 1611, 1518, 1391, 1334, 1043, 808, 743 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 254 (100) $[M]^+$, 239 (11) $[M–Me]^+$, 225 (9), 211 (19), 197 (24), 185 (35), 172 (38), 128 (16), 115 (21), 41 (14).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{22}N_2^+$ $[M]^+$ 254.1778, found 254.1783.

1-(3-Cyclooctyl-4-methylphenyl)-1*H*-pyrazole (146ek)



The general procedure **K** was followed using 5-methyl-2-(1*H*-pyrazol-1-yl)benzoic acid (**144e**, 101 mg, 0.50 mmol) and bromocyclooctane (**136k**, 287 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *meta*-alkylated product **146ek** (46.4 mg, 35%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.71 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.54 (d, *J* = 2.4 Hz, 1H), 7.32 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.18 (d, *J* = 8.2 Hz, 1H), 6.44 (dd, *J* = 2.4, 1.8 Hz, 1H), 3.08–2.99 (m, 1H), 2.36 (s, 3H), 1.88–1.54 (m, 14H).

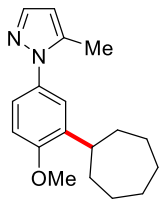
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 150.2 (C_q), 140.6 (CH), 138.6 (C_q), 132.8 (C_q), 130.8 (CH), 126.7 (CH), 117.5 (CH), 116.0 (CH), 107.1 (CH), 39.6 (CH), 34.3 (CH_2), 26.7 (CH_2), 26.4 (CH_2), 19.2 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2917, 2850, 1611, 1585, 1518, 1392, 1334, 1043, 809, 743 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 268 (100) $[M]^+$, 253 (8) $[M–Me]^+$, 225 (11), 211 (17), 197 (24), 185 (46), 172 (41), 128 (14), 115 (19), 41 (21).

HR-MS (EI): *m*/*z* calcd for $C_{18}H_{24}N_2^+$ $[M]^+$ 268.1934, found 268.1941.

1-(3-Cycloheptyl-4-methoxyphenyl)-5-methyl-1*H*-pyrazole (146fh)



The general procedure **K** was followed using 5-methoxy-2-(5-methyl-1*H*-pyrazol-1-yl)benzoic acid (**144f**, 116 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *meta*-alkylated product **146fh** (39.3 mg, 28%) as a colorless oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.54 (d, J = 1.8 Hz, 1H), 7.23 (d, J = 2.7 Hz, 1H), 7.16 (dd, J = 8.6, 2.7 Hz, 1H), 6.88 (d, J = 8.6 Hz, 1H), 6.16 (dq, J = 1.8, 0.9 Hz, 1H), 3.87 (s, 3H), 3.13 (tt, J = 10.2, 3.3 Hz, 1H), 2.29 (s, 3H), 1.92–1.84 (m, 2H), 1.82–1.74 (m, 2H), 1.73–1.65 (m, 2H), 1.64–1.50 (m, 6H).

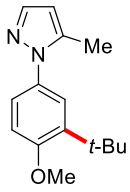
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 155.6 (C_q), 139.3 (CH), 138.9 (C_q), 138.6 (C_q), 132.8 (C_q), 124.1 (CH), 122.9 (CH), 110.3 (CH), 106.1 (CH), 55.7 (CH_3), 38.8 (CH), 35.4 (CH_2), 27.9 (CH_2), 27.4 (CH_2), 12.3 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2920, 2852, 1499, 1442, 1238, 1102, 1028, 921, 811, 771 cm^{-1}.

MS (EI) m/z (relative intensity): 284 (100) $[M]^+$, 269 (5) $[M–Me]^+$, 255 (8), 241 (9), 227 (20), 215 (15), 201 (14), 171 (11), 55 (9), 41 (13).

HR-MS (EI): m/z calcd for $C_{18}H_{24}N_2O^+$ $[M]^+$ 284.1883, found 284.1891.

1-[3-(*tert*-Butyl)-4-methoxyphenyl]-5-methyl-1*H*-pyrazole (146fb)



The general procedure **K** was followed using 5-methoxy-2-(5-methyl-1*H*-pyrazol-1-yl)benzoic acid (**144f**, 116 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *meta*-alkylated product **146fb** (65.9 mg, 54%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.54 (dq, J = 1.8, 0.5 Hz, 1H), 7.32 (d, J = 2.7 Hz, 1H), 7.21 (dd, J = 8.6, 2.7 Hz, 1H), 6.92 (d, J = 8.6 Hz, 1H), 6.17 (dq, J = 1.8, 0.8 Hz, 1H), 3.88 (s, 3H), 2.30 (dd, J = 0.8, 0.5 Hz, 3H), 1.39 (s, 9H).

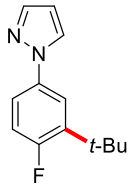
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 157.8 (C_q), 139.2 (CH), 139.0 (C_q), 138.5 (C_q), 132.5 (C_q), 124.1 (CH), 123.5 (CH), 111.4 (CH), 106.1 (CH), 55.3 (CH_3), 35.1 (C_q), 29.6 (CH_3), 12.3 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2955, 1497, 1454, 1234, 1091, 1027, 922, 814, 772 cm^{-1}.

MS (EI) m/z (relative intensity): 244 (76) $[M]^+$, 229 (100) $[M–Me]^+$, 214 (23) $[M–2Me]^+$, 201 (25), 171 (9), 77 (8), 43 (9).

HR-MS (EI): m/z calcd for $C_{15}H_{20}N_2O^+$ $[M]^+$ 244.1570, found 244.1577.

1-[3-(*tert*-Butyl)-4-fluorophenyl]-1*H*-pyrazole (146gb)



The general procedure **K** was followed using 5-fluoro-2-(1*H*-pyrazol-1-yl)benzoic acid (**144g**, 103 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 25:1) yielded *meta*-alkylated product **146gb** (59.1 mg, 54%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.71 (dd, *J* = 1.9, 0.6 Hz, 1H), 7.65 (dd, *J* = 7.1, 2.8 Hz, 1H), 7.42 (ddd, *J* = 8.7, 3.9, 2.8 Hz, 1H), 7.07 (dd, *J* = 11.8, 8.7 Hz, 1H), 6.45 (dd, *J* = 2.5, 1.9 Hz, 1H), 1.43 (d, *J* = 1.1 Hz, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 160.2 (d, $^{1}J_{C-F}$ = 248 Hz, C_q), 140.8 (CH), 138.4 (d, $^{2}J_{C-F}$ = 13 Hz, C_q), 136.1 (d, $^{4}J_{C-F}$ = 3 Hz, C_q), 126.9 (CH), 119.1 (d, $^{3}J_{C-F}$ = 6 Hz, CH), 118.4 (d, $^{3}J_{C-F}$ = 9 Hz, CH), 116.9 (d, $^{2}J_{C-F}$ = 26 Hz, CH), 107.4 (CH), 34.6 (d, $^{3}J_{C-F}$ = 3 Hz, C_q), 29.8 (d, $^{4}J_{C-F}$ = 4 Hz, CH_3).

^{19}F-NMR (282 MHz, $CDCl_3$): δ = (–112.1)–(–112.2) (m).

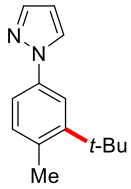
IR (ATR): $\tilde{\nu}$ = 2961, 1518, 1491, 1395, 1211, 1044, 949, 812, 744, 640 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 218 (67) $[M]^+$, 203 (100) $[M–Me]^+$, 175 (74).

HR-MS (EI): *m*/*z* calcd for $C_{13}H_{15}FN_2^+$ $[M]^+$ 218.1214, found 218.1221.

The analytical data correspond with those reported in the literature.[62]

1-[3-(*tert*-Butyl)-4-methylphenyl]-1*H*-pyrazole (146eb)



The general procedure **K** was followed using 5-methyl-2-(1*H*-pyrazol-1-yl)benzoic acid (**144e**, 101 mg, 0.50 mmol) and *tert*-butyl bromide (**136b**, 206 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 25:1) yielded *meta*-alkylated product **146eb** (30.4 mg, 28%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.73 (d, *J* = 2.4 Hz, 1H), 7.71 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.35 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.18 (d, *J* = 8.2 Hz, 1H), 6.44 (dd, *J* = 2.4, 1.8 Hz, 1H), 2.57 (s, 3H), 1.46 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 149.3 (C_q), 140.6 (CH), 138.1 (C_q), 134.6 (C_q), 133.4 (CH), 126.7 (CH), 117.7 (CH), 116.6 (CH), 107.1 (CH), 36.1 (C_q), 30.7 (CH_3), 22.9 (CH_3).

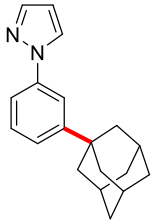
IR (ATR): $\tilde{\nu}$ = 2959, 1610, 1517, 1492, 1395, 1045, 949, 811, 745 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 214 (52) $[M]^+$, 199 (100) $[M–Me]^+$, 184 (9) $[M–2Me]^+$, 171 (18), 115 (10), 91 (9), 77 (6), 41 (7).

HR-MS (EI): *m*/*z* calcd for $C_{14}H_{18}N_2^+$ $[M]^+$ 214.1465, found 214.1475.

The spectral data are in accordance with those reported in the literature.[103]

1-[3-(Adamantan-1-yl)phenyl]-1*H*-pyrazole (146av)



The general procedure **K** was followed using 2-(1*H*-pyrazol-1-yl)benzoic acid (**144a**, 94.1 mg, 0.50 mmol) and 1-bromoadamantane (**136v**, 324 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *meta*-alkylated product **146av** (42.7 mg, 31%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.93 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.74 (d, *J* = 2.0 Hz, 1H), 7.73 (d, *J* = 1.7 Hz, 1H), 7.45 (ddd, *J* = 7.8, 2.0, 1.6 Hz, 1H), 7.39 (dd, *J* = 7.8, 7.6 Hz, 1H), 7.30 (dt, *J* = 7.6, 1.6 Hz, 1H), 6.46 (dd, *J* = 2.5, 1.7 Hz, 1H), 2.16–2.08 (m, 3H), 2.00–1.93 (m, 6H), 1.85–1.72 (m, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 153.0 (C_q), 140.8 (CH), 140.1 (C_q), 128.9 (CH), 126.8 (CH), 123.1 (CH), 116.5 (CH), 116.4 (CH), 107.3 (CH), 43.2 (CH_2), 36.8 (CH_2), 36.5 (C_q), 29.0 (CH).

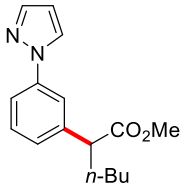
IR (ATR): $\tilde{\nu}$ = 2899, 2846, 1606, 1518, 1391, 1032, 945, 781, 743, 696 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 278 (100) $[M]^+$, 235 (8), 221 (65), 184 (9).

HR-MS (EI): *m*/*z* calcd for $C_{19}H_{22}N_2^+$ $[M]^+$ 278.1778, found 278.1784.

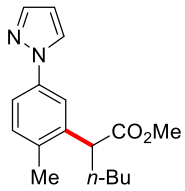
5.3.5.2 Characterization Data for 141g and 202

Methyl 2-[3-(1*H*-pyrazol-1-yl)phenyl]hexanoate (141g)



The general procedure **L** was followed using 2-(1*H*-pyrazol-1-yl)benzoic acid (**144a**, 94.1 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *meta*-alkylated product **141g** (80.1 mg, 59%) as a colorless oil. The analytical data of **141g** are in section 5.3.3.1.

Methyl 2-[2-methyl-5-(1*H*-pyrazol-1-yl)phenyl]hexanoate (202a)



The general procedure **L** was followed using 5-methyl-2-(1*H*-pyrazol-1-yl)benzoic acid (**144e**, 101 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 15:1) yielded *meta*-alkylated product **202a** (82.1 mg, 57%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.89 (dd, *J* = 2.5, 0.7 Hz, 1H), 7.70 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.63 (d, *J* = 2.4 Hz, 1H), 7.49 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 1H), 6.44 (dd, *J* = 2.5, 1.8 Hz, 1H), 3.85 (dd, *J* = 8.1, 7.0 Hz, 1H), 3.66 (s, 3H), 2.39 (s, 3H), 2.15 (dddd, *J* = 13.2, 10.0, 8.1, 5.0 Hz, 1H), 1.78 (dddd, *J* = 13.7, 10.0, 7.0, 5.5 Hz, 1H), 1.37–1.19 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H).

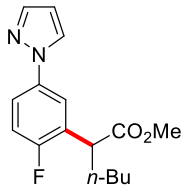
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.2 (C_q), 140.7 (CH), 139.0 (C_q), 138.7 (C_q), 134.3 (C_q), 131.2 (CH), 126.7 (CH), 117.8 (CH), 117.7 (CH), 107.3 (CH), 52.0 (CH_3), 47.1 (CH), 33.0 (CH_2), 29.9 (CH_2), 22.6 (CH_2), 19.5 (CH_3), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2954, 1732, 1613, 1520, 1392, 1161, 1043, 956, 815, 747 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 286 (62) $[M]^+$, 271 (4) $[M–Me]^+$, 257 (9) $[M–Et]^+$, 243 (39) $[M–Pr]^+$, 230 (60) $[M–Bu]^+$, 227 (83) $[M–CO_2Me]^+$, 213 (23) $[M–CO_2Me–Me]^+$, 199 (18) $[M–CO_2Me–Et]^+$, 185 (31) $[M–CO_2Me–Pr]^+$, 171 (100) $[M–CO_2Me–Bu]^+$, 157 (17), 128 (14), 115 (24), 41 (18).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{22}N_2O_2^+$ $[M]^+$ 286.1676, found 286.1681.

Methyl 2-[2-fluoro-5-(1*H*-pyrazol-1-yl)phenyl]hexanoate (202b)



The general procedure **L** was followed using 5-fluoro-2-(1*H*-pyrazol-1-yl)benzoic acid (**144g**, 103 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *meta*-alkylated product **202b** (93.9 mg, 65%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.71 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.68 (dd, *J* = 6.2, 2.8 Hz, 1H), 7.56 (ddd, *J* = 8.9, 4.4, 2.8 Hz, 1H), 7.13 (dd, *J* = 9.5, 8.9 Hz, 1H), 6.46 (dd, *J* = 2.5, 1.8 Hz, 1H), 3.96 (t, *J* = 7.7 Hz, 1H), 3.69 (s, 3H), 2.20–2.05 (m, 1H), 1.89–1.74 (m, 1H), 1.45–1.13 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 173.3 (C_q), 158.7 (d, $^1J_{C–F}$ = 245 Hz, C_q), 141.0 (CH), 136.6 (d, $^4J_{C–F}$ = 3 Hz, C_q), 127.5 (d, $^2J_{C–F}$ = 17 Hz, C_q), 126.9 (CH), 120.0 (d, $^3J_{C–F}$ = 4 Hz, CH), 119.6 (d, $^3J_{C–F}$ = 9 Hz, CH), 116.2 (d, $^2J_{C–F}$ = 25 Hz, CH), 107.6 (CH), 52.2 (CH_3), 43.7 (d, $^3J_{C–F}$ = 2 Hz, CH), 32.4 (CH_2), 29.7 (CH_2), 22.4 (CH_2), 13.9 (CH_3).

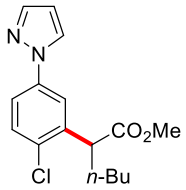
^{19}F-NMR (282 MHz, $CDCl_3$): δ = –120.9 (ddd, *J* = 9.5, 6.2, 4.4 Hz).

IR (ATR): $\tilde{\nu}$ = 2955, 2861, 1734, 1520, 1500, 1394, 1224, 1039, 819, 747 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 290 (77) $[M]^+$, 247 (9) $[M–Pr]^+$, 234 (60) $[M–Bu]^+$, 231 (70) $[M–CO_2Me]^+$, 203 (14) $[M–CO_2Me–Et]^+$, 189 (24) $[M–CO_2Me–Pr]^+$, 175 (100) $[M–CO_2Me–Bu]^+$, 148 (13), 133 (10).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{19}FN_2O_2^+$ $[M]^+$ 290.1425, found 290.1434.

Methyl 2-[2-chloro-5-(1*H*-pyrazol-1-yl)phenyl]hexanoate (202c)



The general procedure **L** was followed using 5-chloro-2-(1*H*-pyrazol-1-yl)benzoic acid (**144h**, 111 mg, 0.50 mmol) and methyl 2-bromohexanoate (**140a**, 314 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *meta*-alkylated product **202c** (91.2 mg, 59%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.73 (d, *J* = 2.6 Hz, 1H), 7.72 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.56 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 1H), 6.47 (dd, *J* = 2.5, 1.8 Hz, 1H), 4.18 (dd, *J* = 7.7, 7.6 Hz, 1H), 3.69 (s, 3H), 2.13 (dddd, *J* = 13.1, 9.7, 7.7, 5.5 Hz, 1H), 1.82 (dddd, *J* = 13.4, 9.7, 7.6, 5.5 Hz, 1H), 1.41–1.18 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H).

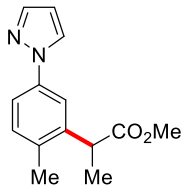
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 173.5 (C_q), 141.3 (CH), 139.1 (C_q), 138.3 (C_q), 131.5 (C_q), 130.4 (CH), 126.7 (CH), 119.2 (CH), 118.9 (CH), 107.9 (CH), 52.2 (CH_3), 47.4 (CH), 32.9 (CH_2), 29.6 (CH_2), 22.5 (CH_2), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2954, 2860, 1733, 1519, 1481, 1392, 1166, 1032, 818, 746 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 308 (17) $[M(^{37}Cl)]^+$, 306 (47) $[M(^{35}Cl)]^+$, 271 (100) $[M–Cl]^+$, 252 (8) $[M(^{37}Cl)–Bu]^+$, 250 (24) $[M(^{35}Cl)–Bu]^+$, 249 (12) $[M(^{37}Cl)–CO_2Me]^+$, 247 (35) $[M(^{35}Cl)–CO_2Me]^+$, 193 (23) $[M(^{37}Cl)–CO_2Me–Bu]^+$, 191 (58) $[M(^{35}Cl)–CO_2Me–Bu]^+$, 155 (12), 115 (13), 59 (13), 43 (35).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{19}{}^{35}ClN_2O_2^+$ $[M]^+$ 306.1130, found 306.1136.

Methyl 2-[2-methyl-5-(1*H*-pyrazol-1-yl)phenyl]propanoate (202d)



The general procedure **L** was followed using 5-methyl-2-(1*H*-pyrazol-1-yl)benzoic acid (**144e**, 101 mg, 0.50 mmol) and methyl 2-bromopropanoate (**140i**, 251 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *meta*-alkylated product **202d** (33.3 mg, 27%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.88 (dd, *J* = 2.5, 0.7 Hz, 1H), 7.70 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.59 (d, *J* = 2.4 Hz, 1H), 7.47 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 1H), 6.44 (dd, *J* = 2.5, 1.8 Hz, 1H), 3.99 (q, *J* = 7.2 Hz, 1H), 3.67 (s, 3H), 2.38 (s, 3H), 1.54 (d, *J* = 7.2 Hz, 3H).

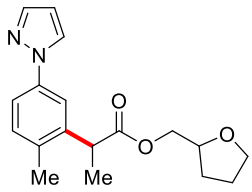
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 174.6 (C_q), 140.7 (CH), 140.2 (C_q), 138.7 (C_q), 134.0 (C_q), 131.3 (CH), 126.7 (CH), 117.8 (CH), 117.7 (CH), 107.3 (CH), 52.1 (CH_3), 41.5 (CH), 19.2 (CH_3), 17.9 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2951, 1731, 1613, 1520, 1393, 1335, 1199, 1045, 946, 750 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 244 (59) $[M]^+$, 212 (8) $[M–OMe]^+$, 185 (100) $[M–CO_2Me]^+$, 170 (13) $[M–CO_2Me–Me]^+$, 157 (12), 143 (11), 115 (17), 91 (12), 77 (7), 59 (9), 43 (10).

HR-MS (EI): *m*/*z* calcd for $C_{14}H_{16}N_2O_2^+$ $[M]^+$ 244.1206, found 244.1210.

(Tetrahydrofuran-2-yl)methyl 2-[2-methyl-5-(1*H*-pyrazol-1-yl)phenyl]propanoate (202e)



The general procedure **L** was followed using 5-methyl-2-(1*H*-pyrazol-1-yl)benzoic acid (**144e**, 101 mg, 0.50 mmol) and (tetrahydrofuran-2-yl)methyl 2-bromopropanoate (**140l**, 356 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 7:1) yielded *meta*-alkylated product **202e** (68.6 mg, 44%, as a diastereomeric mixture (1:1)) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$, determined as a diastereomeric mixture (1:1)): δ = 7.91 (dd, *J* = 2.5, 0.7 Hz, 1H), 7.91 (dd, *J* = 2.5, 0.7 Hz, 1H), 7.69 (dd, *J* = 1.8, 0.7 Hz, 2H), 7.61 (d, *J* = 2.4 Hz, 1H), 7.60 (d, *J* = 2.4 Hz, 1H), 7.49 (dd, *J* = 8.2, 2.4 Hz, 2H), 7.23 (d, *J* = 8.2 Hz, 2H), 6.43 (dd, *J* = 2.5, 1.8 Hz, 2H), 4.22–3.98 (m, 8H), 3.82–3.67 (m, 4H), 2.39 (s, 6H), 1.97–1.71 (m, 6H), 1.54 (d, *J* = 7.1 Hz, 3H), 1.54 (d, *J* = 7.1 Hz, 3H), 1.54–1.43 (m, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$, determined as a diastereomeric mixture (1:1)): δ = 174.1 (C_q), 174.0 (C_q), 140.7 (2 × CH), 140.1 (C_q), 140.1 (C_q), 138.7 (2 × C_q), 134.0 (2 × C_q), 131.2 (2 × CH), 126.7 (2 × CH), 117.8 (CH), 117.8 (CH), 117.6 (CH), 117.6 (CH), 107.2 (2 × CH), 76.4 (CH), 76.3 (CH), 68.4 (CH_2),

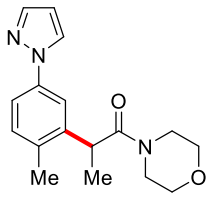
68.3 (CH_2), 66.8 (CH_2), 66.6 (CH_2), 41.6 (CH), 41.6 (CH), 28.0 (CH_2), 27.8 (CH_2), 25.7 (CH_2), 25.7 (CH_2), 19.2 (2 × CH_3), 17.9 (CH_3), 17.9 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2975, 2873, 1730, 1613, 1520, 1393, 1187, 1044, 947, 749 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 314 (42) $[M]^+$, 271 (13), 244 (9) $[M–THF]^+$, 230 (21) $[M–CH_2THF]^+$, 212 (31) $[M–OCH_2THF]^+$, 186 (98), 185 (100) $[M–CO_2CH_2THF]^+$, 171 (37) $[M–CO_2CH_2THF–Me]^+$, 143 (14), 115 (24), 91 (15), 71 (71), 43 (61), 41 (26).

HR-MS (EI): *m*/*z* calcd for $C_{18}H_{22}N_2O_3^+$ $[M]^+$ 314.1625, found 314.1637.

2-[2-Methyl-5-(1*H*-pyrazol-1-yl)phenyl]-1-morpholinopropan-1-one (202f)



The general procedure **L** was followed using 5-methyl-2-(1*H*-pyrazol-1-yl)benzoic acid (**144e**, 101 mg, 0.50 mmol) and 2-bromo-1-morpholinopropan-1-one (**140e**, 333 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded *meta*-alkylated product **202f** (54.8 mg, 37%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.68 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.54 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.44 (d, *J* = 2.4 Hz, 1H), 7.25 (d, *J* = 8.2 Hz, 1H), 6.43 (dd, *J* = 2.5, 1.8 Hz, 1H), 3.95 (q, *J* = 6.8 Hz, 1H), 3.88–3.77 (m, 1H), 3.73–3.61 (m, 1H), 3.60–3.41 (m, 3H), 3.34–3.22 (m, 1H), 3.18–3.04 (m, 2H), 2.37 (s, 3H), 1.44 (d, *J* = 6.8 Hz, 3H).

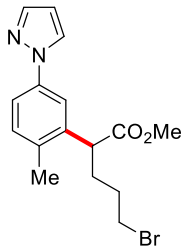
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 172.1 (C_q), 141.2 (C_q), 140.8 (CH), 139.1 (C_q), 132.2 (C_q), 131.7 (CH), 126.6 (CH), 117.9 (CH), 117.0 (CH), 107.4 (CH), 66.8 (CH_2), 66.2 (CH_2), 45.7 (CH_2), 42.5 (CH_2), 40.0 (CH), 18.9 (CH_3), 18.7 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2969, 2856, 1643, 1519, 1429, 1394, 1228, 1114, 1029, 753 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 299 (20) $[M]^+$, 269 (34), 212 (29), 185 (100), 170 (14), 158 (9), 143 (12), 114 (99), 91 (14), 70 (68), 43 (24).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{21}N_3O_2^+$ $[M]^+$ 299.1628, found 299.1629.

Methyl 5-bromo-2-[2-methyl-5-(1*H*-pyrazol-1-yl)phenyl]pentanoate (202g)



The general procedure **L** was followed using 5-methyl-2-(1*H*-pyrazol-1-yl)benzoic acid (**144e**, 101 mg, 0.50 mmol) and methyl 2,5-dibromopentanoate (**140f**, 411 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *meta*-alkylated product **202g** (33.5 mg, 19%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.89 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.71 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.61 (d, *J* = 2.4 Hz, 1H), 7.49 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 6.45 (dd, *J* = 2.5, 1.8 Hz, 1H), 3.88 (dd, *J* = 8.1, 6.7 Hz, 1H), 3.67 (s, 3H), 3.43–3.37(m, 2H), 2.40 (s, 3H), 2.33–2.22 (m, 1H), 2.07–1.73 (m, 3H).

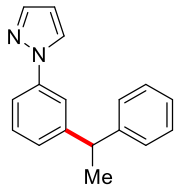
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 173.6 (C_q), 140.8 (CH), 138.8 (C_q), 138.2 (C_q), 134.3 (C_q), 131.5 (CH), 126.7 (CH), 118.1 (CH), 117.7 (CH), 107.4 (CH), 52.2 (CH_3), 46.3 (CH), 33.0 (CH_2), 31.5 (CH_2), 30.7 (CH_2), 19.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2951, 1730, 1613, 1520, 1434, 1393, 1198, 1162, 1043, 748 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 352 (22) [M(^{81}Br)]$^+$, 350 (22) [M(^{79}Br)]$^+$, 293 (28) [M(^{81}Br)–CO_2Me]$^+$, 291 (28) [M(^{79}Br)–CO_2Me]$^+$, 271 (100) [M–Br]$^+$, 243 (47) [M–Br–Et]$^+$, 211 (70) [M–Br–CO_2Me]$^+$, 185 (23), 183 (28), 171 (64), 157 (15), 143 (10), 128 (14), 115 (20), 91 (9).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{19}{}^{79}BrN_2O_2^+$ [M]$^+$ 350.0624, found 350.0643.

1-[3-(1-Phenylethyl)phenyl]-1*H*-pyrazole (202h)



The general procedure **L** was followed using 2-(1*H*-pyrazol-1-yl)benzoic acid (**144a**, 94.1 mg, 0.50 mmol) and (1-chloroethyl)benzene (**142a**, 211 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) followed by recycling preparative HPLC yielded *meta*-benzylated product **202h** (28.8 mg, 23%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.89 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.72 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.63 (dddd, *J* = 2.0, 1.8, 0.5, 0.5 Hz, 1H), 7.49 (ddd, *J* = 7.8, 2.0, 1.1 Hz, 1H), 7.36 (dd, *J* = 7.8, 7.7 Hz, 1H), 7.33–7.18 (m, 5H), 7.15 (dddd, *J* = 7.7, 1.8, 1.1, 0.6 Hz, 1H), 6.45 (dd, *J* = 2.5, 1.8 Hz, 1H), 4.23 (q, *J* = 7.2 Hz, 1H), 1.70 (d, *J* = 7.2 Hz, 3H).

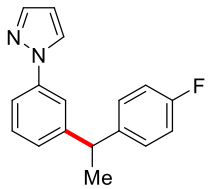
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 148.0 (C_q), 145.6 (C_q), 140.8 (CH), 140.2 (C_q), 129.3 (CH), 128.4 (CH), 127.5 (CH), 126.7 (CH), 126.1 (CH), 125.7 (CH), 118.7 (CH), 116.9 (CH), 107.4 (CH), 44.8 (CH), 21.8 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2969, 1592, 1519, 1493, 1393, 1044, 945, 750, 702 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 248 (83) $[M]^+$, 233 (100) $[M–Me]^+$, 206 (17), 179 (12), 165 (30), 115 (8), 77 (13).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{16}N_2^+$ $[M]^+$ 248.1308, found 248.1314.

1-{3-[1-(4-Fluorophenyl)ethyl]phenyl}-1*H*-pyrazole (202i)



The general procedure **L** was followed using 2-(1*H*-pyrazol-1-yl)benzoic acid (**144a**, 94.1 mg, 0.50 mmol) and 1-(1-chloroethyl)-4-fluorobenzene (**142d**, 238 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *meta*-benzylated product **202i** (38.4 mg, 29%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.89 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.72 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.61 (dd, *J* = 2.2, 2.0 Hz, 1H), 7.48 (ddd, *J* = 7.9, 2.2, 1.0 Hz, 1H), 7.36 (dd, *J* = 7.9, 7.8 Hz, 1H), 7.20 (ddd, *J* = 8.9, 5.4, 0.6 Hz, 2H), 7.13–7.11 (m, 1H), 6.98 (dd, *J* = 8.9, 8.7 Hz, 2H), 6.45 (dd, *J* = 2.5, 1.8 Hz, 1H), 4.21 (q, *J* = 7.3 Hz, 1H), 1.67 (d, *J* = 7.3 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 161.2 (d, $^{1}J_{C–F}$ = 244 Hz, C_q), 147.8 (C_q), 141.3 (d, $^{4}J_{C–F}$ = 3 Hz, C_q), 140.9 (CH), 140.2 (C_q), 129.3 (CH), 128.9 (d, $^{3}J_{C–F}$ = 8 Hz, CH), 126.7 (CH), 125.6 (CH), 118.6 (CH), 116.9 (CH), 115.1 (d, $^{2}J_{C–F}$ = 21 Hz, CH), 107.5 (CH), 44.1 (CH), 22.0 (CH_3).

^{19}F-NMR (376 MHz, $CDCl_3$): δ = –117.1 (tt, *J* = 8.7, 5.4 Hz)

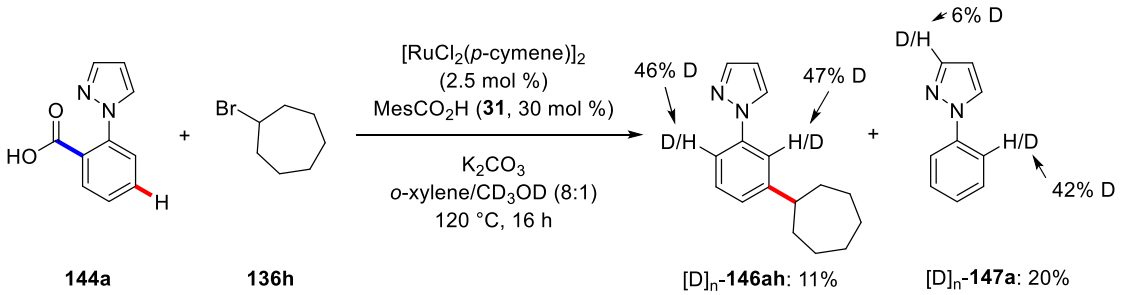
IR (ATR): $\tilde{\nu}$ = 2968, 1607, 1592, 1508, 1393, 1222, 1040, 945, 837, 749 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 266 (77) $[M]^+$, 251 (100) $[M–Me]^+$, 231 (8) $[M–Me–F]^+$, 224 (14), 183 (25).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{15}FN_2^+$ $[M]^+$ 266.1214, found 266.1216.

5.3.5.3 Mechanistic Studies

5.3.5.3.1 Isotopic Studies



2-(1*H*-Pyrazol-1-yl)benzoic acid (**144a**, 94.1 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 13 µmol, 2.5 mol %), $MesCO_2H$ (**31**, 24.6 mg, 150 µmol, 30 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Bromocycloheptane (**136h**, 266 mg, 1.50 mmol), *o*-xylene (0.8 mL) and D_3COD (0.1 mL) were then added. The Schlenk tube was degassed and filled with N_2 three times and the mixture was stirred at 120 °C. After 16 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc 25:1) yielded $[D]_n$-**146ah** (13.4 mg, 11%) and $[D]_n$-**147a** (14.6 mg, 20%). The degree of deuteration was determined by ^{1}H-NMR spectroscopy (Figure 51 and Figure 52).

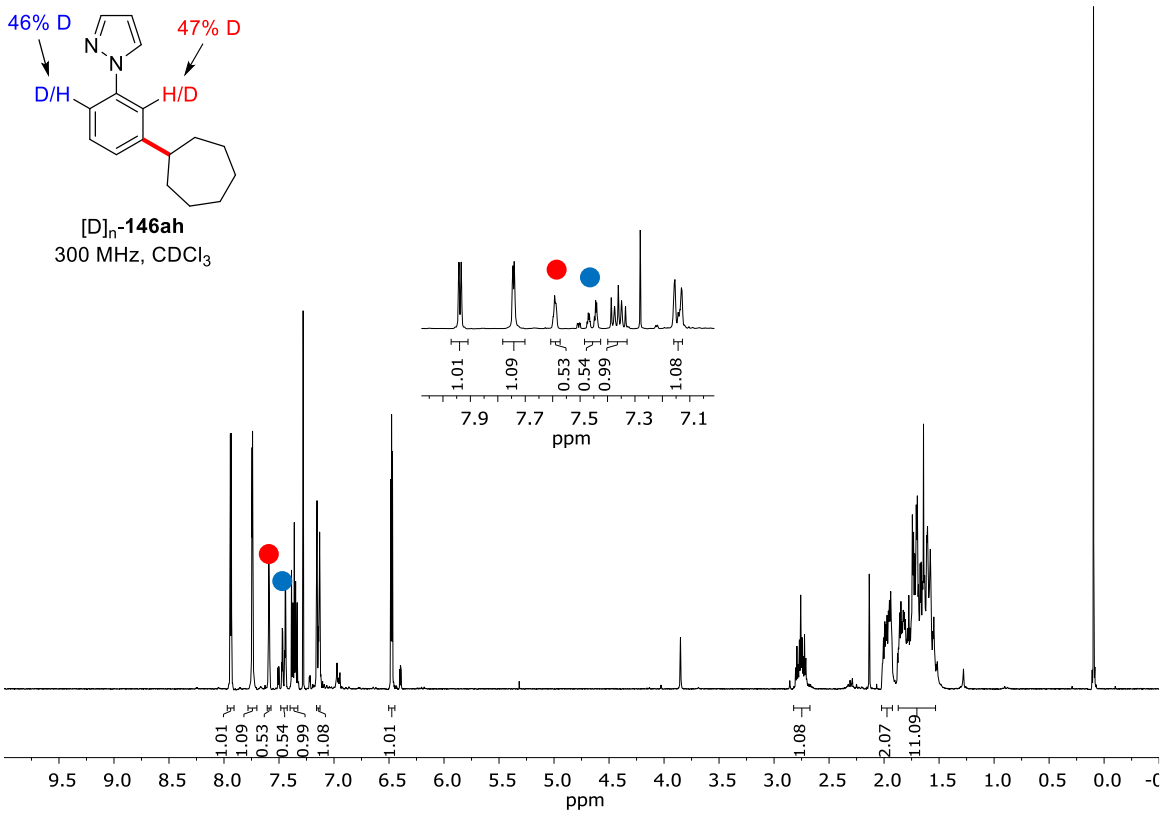


Figure 51: ^{1}H-NMR spectrum of $[D]_n$-**146ah**.

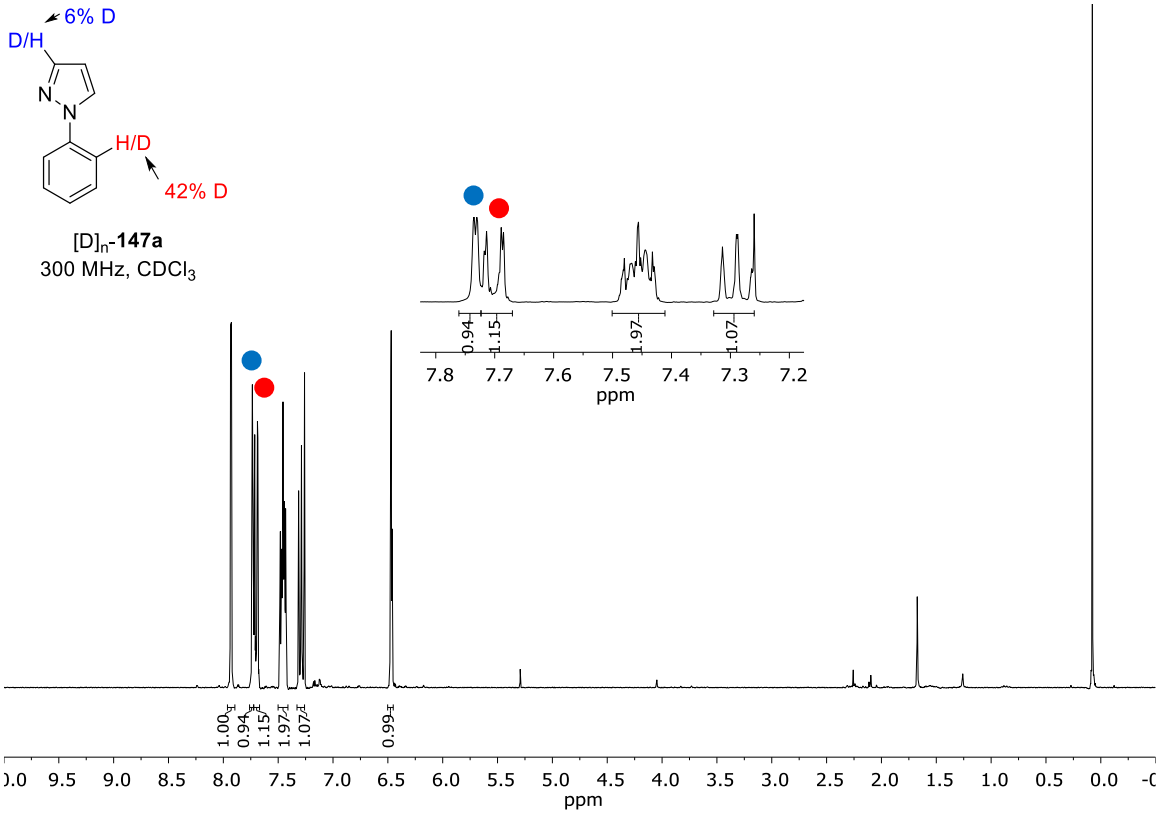
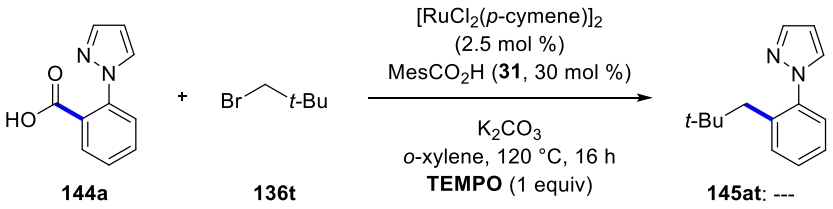


Figure 52: ^{1}H-NMR spectrum of $[D]_n$-**147a**.

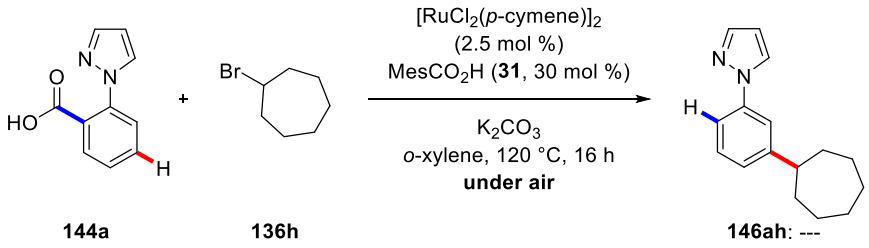
5.3.5.3.2 Reactions with Radical Scavengers

Primary Alkylations

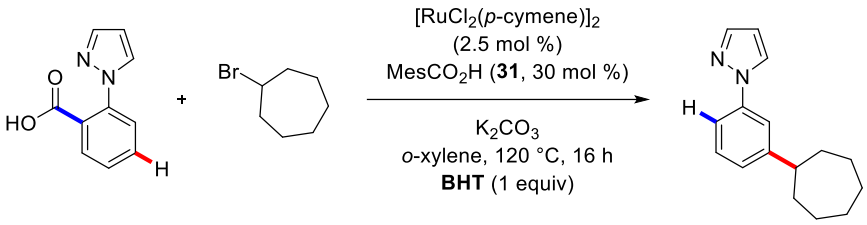


2-(1*H*-Pyrazol-1-yl)benzoic acid (**144a**, 94.1 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 13 µmol, 2.5 mol %), $MesCO_2H$ (**31**, 24.6 mg, 150 µmol, 30 mol %), K_2CO_3 (138 mg, 1.00 mmol) and TEMPO (78.2 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Neopentyl bromide (**136t**, 227 mg, 1.50 mmol) and *o*-xylene (1.0 mL) were then added. The Schlenk tube was degassed and filled with N_2 three times and the mixture was stirred at 120 °C. After 16 h, the resulting mixture was determined by GC-MS spectrometry. The reaction did not provide any formation of product **145at**.

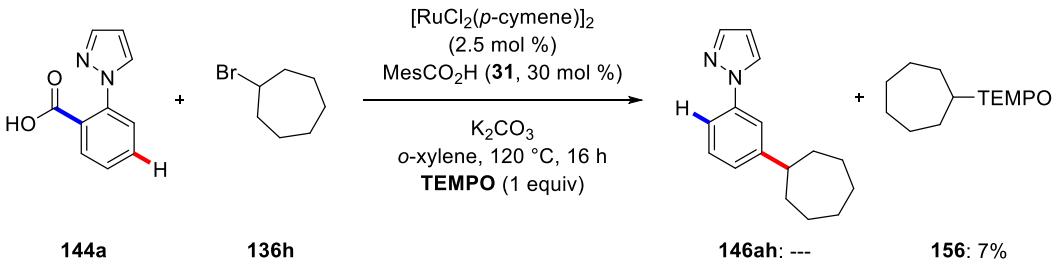
Secondary Alkylation



To a pre-dried 25 mL Schlenk tube charged with 2-(1*H*-pyrazol-1-yl)benzoic acid (**144a**, 94.1 mg, 0.50 mmol), bromocycloheptane (**136h**, 266 mg, 1.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 13 µmol, 2.5 mol %), $MesCO_2H$ (**31**, 24.6 mg, 150 µmol, 30 mol %) and K_2CO_3 (138 mg, 1.00 mmol) was added *o*-xylene (1.0 mL) under air atmosphere. The mixture was then stirred at 120 °C. After 16 h, the resulting mixture was determined by GC-MS spectrometry. The reaction did not provide any formation of product **146ah**.



2-(1*H*-Pyrazol-1-yl)benzoic acid (**144a**, 94.1 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 13 µmol, 2.5 mol %), $MesCO_2H$ (**31**, 24.6 mg, 150 µmol, 30 mol %), K_2CO_3 (138 mg, 1.00 mmol) and BHT (110 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Bromocycloheptane (**136h**, 266 mg, 1.50 mmol) and *o*-xylene (1.0 mL) were then added. The Schlenk tube was degassed and filled with N_2 three times and the mixture was stirred at 120 °C. After 16 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc 25:1) yielded **146ah** (66.0 mg, 55%) as a colorless oil.



2-(1*H*-Pyrazol-1-yl)benzoic acid (**144a**, 94.1 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 13 µmol, 2.5 mol %), $MesCO_2H$ (**31**, 24.6 mg, 150 µmol, 30 mol %), K_2CO_3 (138 mg, 1.00 mmol) and TEMPO (78.2 mg, 0.50 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Bromocycloheptane (**136h**, 266 mg, 1.50 mmol) and *o*-xylene (1.0 mL) were then added. The Schlenk tube was degassed and filled with N_2 three times and the mixture was stirred at 120 °C. After 16 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-pentane/Et_2O 50:1) yielded TEMPO-adduct **156** (9.2 mg, 7%) as a colorless oil. The analytical data of **156** are in section 5.3.2.2.3.

5.3.5.4 X-Ray Crystallographic Analysis

A suitable crystal was selected and the crystal was mounted on a MITIGEN holder in NVH oil on a Bruker D8 Venture diffractometer. The crystal was kept at 100 K during data collection. Using Olex2,[137] the structure was solved with the XT[138] structure solution program using Intrinsic Phasing and refined with the XL[139] refinement package using Least Squares minimisation.

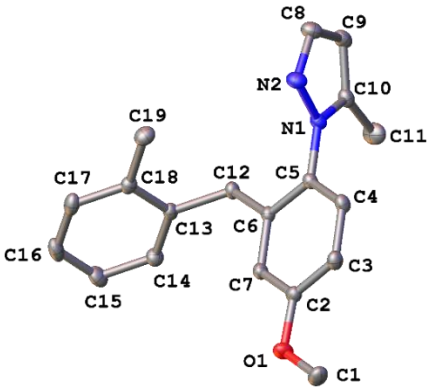


Figure 53: Molecular structure of **201** with thermal ellipsoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{19}H_{20}N_2O$ (*M* = 292.37 g/mol): triclinic, space group P-1 (no. 2), *a* = 8.7004(7) Å, *b* = 9.8431(8) Å, *c* = 10.0077(7) Å, *α* = 86.914(3)°, *β* = 82.448(3)°, *γ* = 66.641(2)°, *V* = 779.98(11) Å^3, *Z* = 2, *T* = 100.0 K, μ(MoKα) = 0.078 mm^{-1}, *Dcalc* = 1.245 g/cm^3, 26231 reflections measured (4.508° ≤ 2Θ ≤ 61.054°), 4757 unique (R_{int} = 0.0192, R_{sigma} = 0.0154) which were used in all calculations. The final R_1 was 0.0417 (I > 2σ(I)) and wR_2 was 0.1196 (all data).

Table 77: Crystal data and structure refinement for **201**.

Compound	**201**
CCDC number	1979319
Identification code	mo_0190_CG_0m
Empirical formula	$C_{19}H_{20}N_2O$
Formula weight	292.37
Temperature/K	100.0
Crystal system	triclinic
Space group	P-1

a/Å	8.7004(7)
b/Å	9.8431(8)
c/Å	10.0077(7)
α/°	86.914(3)
β/°	82.448(3)
γ/°	66.641(2)
Volume/Å^3	779.98(11)
Z	2
ρ_{calc}g/cm^3	1.245
μ/mm^{-1}	0.078
F(000)	312.0
Crystal size/mm^3	0.464 × 0.395 × 0.391
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.508 to 61.054
Index ranges	-12 ≤ h ≤ 12, -14 ≤ k ≤ 14, -14 ≤ l ≤ 14
Reflections collected	26231
Independent reflections	4757 [R_{int} = 0.0192, R_{sigma} = 0.0154]
Data/restraints/parameters	4757/0/202
Goodness-of-fit on F^2	1.042
Final R indexes [I>=2σ (I)]	R_1 = 0.0417, wR_2 = 0.1185
Final R indexes [all data]	R_1 = 0.0429, wR_2 = 0.1196
Largest diff. peak/hole / e Å^{-3}	0.42/-0.32

Table 78: Bond lengths [Å] for **201**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C1	1.4290(11)	C6	C12	1.5167(11)
O1	C2	1.3627(10)	C8	C9	1.4025(13)
N1	N2	1.3649(10)	C9	C10	1.3788(12)
N1	C5	1.4298(10)	C10	C11	1.4905(13)
N1	C10	1.3624(11)	C12	C13	1.5089(11)
N2	C8	1.3313(12)	C13	C14	1.3948(11)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C2	C3	1.3924(12)	C13	C18	1.4043(11)
C2	C7	1.3958(11)	C14	C15	1.3922(12)
C3	C4	1.3892(12)	C15	C16	1.3870(15)
C4	C5	1.3883(11)	C16	C17	1.3886(14)
C5	C6	1.4002(11)	C17	C18	1.3954(12)
C6	C7	1.3923(11)	C18	C19	1.5046(12)

Table 79: Bond angles [°] for **201**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C2	O1	C1	116.64(7)	N2	C8	C9	111.89(8)
N2	N1	C5	118.22(7)	C10	C9	C8	105.48(8)
C10	N1	N2	112.59(7)	N1	C10	C9	105.90(8)
C10	N1	C5	129.18(7)	N1	C10	C11	123.30(8)
C8	N2	N1	104.14(7)	C9	C10	C11	130.80(8)
O1	C2	C3	124.21(8)	C13	C12	C6	113.98(7)
O1	C2	C7	115.63(7)	C14	C13	C12	119.86(7)
C3	C2	C7	120.16(8)	C14	C13	C18	119.50(8)
C4	C3	C2	118.64(8)	C18	C13	C12	120.63(7)
C5	C4	C3	121.15(8)	C15	C14	C13	121.17(8)
C4	C5	N1	118.36(7)	C16	C15	C14	119.35(9)
C4	C5	C6	120.72(8)	C15	C16	C17	119.86(8)
C6	C5	N1	120.79(7)	C16	C17	C18	121.44(8)
C5	C6	C12	121.52(7)	C13	C18	C19	120.86(8)
C7	C6	C5	117.83(7)	C17	C18	C13	118.66(8)
C7	C6	C12	120.65(7)	C17	C18	C19	120.47(8)
C6	C7	C2	121.47(7)				

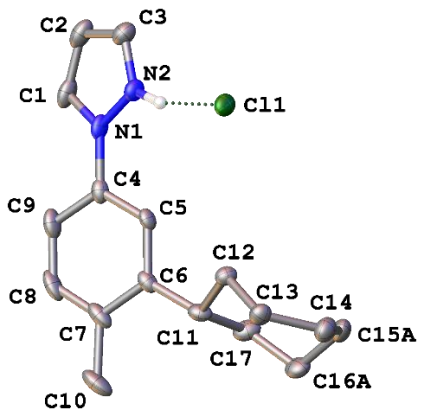


Figure 54: Molecular structure of **146eh** with thermal ellipsoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{34}H_{51}Cl_3N_4O_2$ (*M* = 654.13 g/mol): orthorhombic, space group Pbcn (no. 60), *a* = 5.2607(4) Å, *b* = 16.9010(10) Å, *c* = 39.466(3) Å, *V* = 3509.0(4) Å^3, *Z* = 4, *T* = 99.99 K, μ(MoKα) = 0.296 mm^{-1}, *Dcalc* = 1.238 g/cm^3, 29694 reflections measured (4.128° ≤ 2Θ ≤ 59.152°), 4931 unique (R_{int} = 0.0287, R_{sigma} = 0.0209) which were used in all calculations. The final R_1 was 0.0503 (I > 2σ(I)) and wR_2 was 0.1112 (all data).

Table 80: Crystal data and structure refinement for **146eh**.

Compound	**146eh**
CCDC number	1979310
Identification code	mo_0079_CG_0m
Empirical formula	$C_{34}H_{51}Cl_3N_4O_2$
Formula weight	654.13
Temperature/K	99.99
Crystal system	orthorhombic
Space group	Pbcn
a/Å	5.2607(4)
b/Å	16.9010(10)
c/Å	39.466(3)
α/°	90
β/°	90

γ/°	90
Volume/Å^3	3509.0(4)
Z	4
ρ_{calc}g/cm^3	1.238
μ/mm^{-1}	0.296
F(000)	1400.0
Crystal size/mm^3	0.406 × 0.197 × 0.167
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.128 to 59.152
Index ranges	-7 ≤ h ≤ 7, -23 ≤ k ≤ 22, -54 ≤ l ≤ 54
Reflections collected	29694
Independent reflections	4931 [R_{int} = 0.0287, R_{sigma} = 0.0209]
Data/restraints/parameters	4931/4/229
Goodness-of-fit on F^2	1.217
Final R indexes [I>=2σ (I)]	R_1 = 0.0503, wR_2 = 0.1090
Final R indexes [all data]	R_1 = 0.0554, wR_2 = 0.1112
Largest diff. peak/hole / e Å^{-3}	0.30/-0.34

Table 81: Bond lengths [Å] for **146eh**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N1	N2	1.3510(19)	C7	C10	1.508(3)
N1	C1	1.349(2)	C8	C9	1.375(3)
N1	C4	1.430(2)	C11	C12	1.536(2)
N2	C3	1.333(2)	C11	C17	1.540(2)
C1	C2	1.372(3)	C12	C13	1.533(2)
C2	C3	1.385(3)	C13	C14	1.527(2)
C4	C5	1.385(2)	C14	C15B	1.533(7)
C4	C9	1.388(2)	C14	C15A	1.565(3)
C5	C6	1.398(2)	C15B	C16B	1.512(11)
C6	C7	1.411(2)	C16B	C17	1.696(7)
C6	C11	1.514(2)	C17	C16A	1.499(3)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C7	C8	1.390(3)	C15A	C16A	1.532(4)

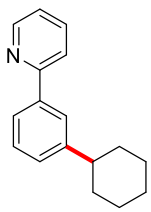
Table 82: Bond angles [°] for **146eh**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N2	N1	C4	122.97(13)	C8	C7	C10	119.42(16)
C1	N1	N2	108.07(15)	C9	C8	C7	122.69(16)
C1	N1	C4	128.96(15)	C8	C9	C4	118.25(17)
C3	N2	N1	108.80(14)	C6	C11	C12	113.02(13)
N1	C1	C2	108.71(16)	C6	C11	C17	108.88(14)
C1	C2	C3	105.80(17)	C12	C11	C17	114.08(14)
N2	C3	C2	108.61(17)	C13	C12	C11	113.08(13)
C5	C4	N1	120.33(14)	C14	C13	C12	116.43(15)
C5	C4	C9	121.04(17)	C13	C14	C15B	109.6(3)
C9	C4	N1	118.63(15)	C13	C14	C15A	116.02(16)
C4	C5	C6	120.40(14)	C16B	C15B	C14	107.8(5)
C5	C6	C7	119.05(16)	C15B	C16B	C17	112.1(6)
C5	C6	C11	120.19(14)	C11	C17	C16B	119.5(3)
C7	C6	C11	120.71(16)	C16A	C17	C11	114.48(18)
C6	C7	C10	122.02(18)	C16A	C15A	C14	114.1(2)
C8	C7	C6	118.55(17)	C17	C16A	C15A	111.8(2)

5.3.6 Ruthenium-Catalyzed C–H Alkylation of Pyrazoles: ortho versus meta

5.3.6.1 Characterization Data for 145, 146, and 203

2-(3-Cyclohexylphenyl)pyridine (203a)



2-Phenylpyridine (**68b**, 77.6 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 13 µmol, 2.5 mol %), $MesCO_2H$ (**31**, 24.6 mg, 150 µmol, 30 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Bromocyclohexane (**136j**, 245 mg, 1.50 mmol) and *o*-xylene (1.0 mL) were then added and the mixture was stirred at 120 °C. After 16 h, the resulting

mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc 10:1) yielded *meta*-alkylated product **203a** (60.5 mg, 51%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.70 (ddd, *J* = 4.8, 1.5, 1.5 Hz, 1H), 7.87 (dddd, *J* = 1.9, 1.8, 0.6, 0.6 Hz, 1H), 7.77 (ddd, *J* = 7.8, 1.9, 1.3 Hz, 1H), 7.75–7.70 (m, 2H), 7.40 (ddd, *J* = 7.8, 7.7, 0.6 Hz, 1H), 7.27 (dddd, *J* = 7.7, 1.8, 1.3, 0.6 Hz, 1H), 7.22 (ddd, *J* = 5.4, 4.8, 3.1 Hz, 1H), 2.61 (tt, *J* = 11.6, 3.4 Hz, 1H), 1.99–1.81 (m, 4H), 1.77 (dtt, *J* = 10.5, 3.1, 1.5 Hz, 1H), 1.59–1.37 (m, 4H), 1.37–1.19 (m, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 157.7 (C_q), 149.5 (CH), 148.5 (C_q), 139.3 (C_q), 136.5 (CH), 128.6 (CH), 127.4 (CH), 125.5 (CH), 124.3 (CH), 121.8 (CH), 120.6 (CH), 44.8 (CH), 34.5 (CH_2), 27.0 (CH_2), 26.2 (CH_2).

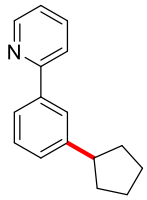
IR (ATR): $\tilde{\nu}$ = 2921, 2849, 1583, 1564, 1461, 1434, 1152, 768, 741, 698 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 237 (91) $[M]^+$, 236 (100) $[M–H]^+$, 222 (9), 208 (45), 194 (51), 182 (97), 180 (32), 169 (49), 167 (44), 155 (29) $[M–Cy]^+$, 115 (9), 78 (13), 43 (24), 41 (19).

HR-MS (ESI): *m*/*z* calcd for $C_{17}H_{20}N^+$ $[M+H]^+$ 238.1590, found 238.1598.

The spectral data are in accordance with those reported in the literature.[61, 113]

2-(3-Cyclopentylphenyl)pyridine (203b)



2-Phenylpyridine (**68b**, 77.6 mg, 0.50 mmol), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 13 µmol, 2.5 mol %), $MesCO_2H$ (**31**, 24.6 mg, 150 µmol, 30 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Bromocyclopentane (**136i**, 224 mg, 1.50 mmol) and $PhCMe_3$ (1.0 mL) were then added and the mixture was stirred at 120 °C. After 16 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc 10:1) yielded *meta*-alkylated product **203b** (56.9 mg, 51%) as a colorless oil and di-*meta*-alkylated product **203b'** (5.2 mg, 4%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.70 (ddd, *J* = 4.8, 1.7, 1.1 Hz, 1H), 7.90 (dd, *J* = 1.9, 1.7 Hz, 1H), 7.77 (ddd, *J* = 7.7, 1.9, 1.4 Hz, 1H), 7.75–7.70 (m, 2H), 7.40 (dd, *J* = 7.7, 7.6 Hz, 1H), 7.31 (ddd, *J* = 7.6, 1.7, 1.4 Hz, 1H), 7.22 (ddd, *J* = 6.0, 4.8, 2.6 Hz, 1H), 3.09 (tt, *J* = 9.0, 7.2 Hz, 1H), 2.19–2.07 (m, 2H), 1.91–1.62 (m, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 157.8 (C_q), 149.6 (CH), 147.1 (C_q), 139.3 (C_q), 136.6 (CH), 128.6 (CH), 127.7 (CH), 125.8 (CH), 124.3 (CH), 121.9 (CH), 120.7 (CH), 46.1 (CH), 34.7 (CH_2), 25.6 (CH_2).

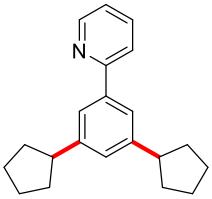
IR (ATR): $\tilde{\nu}$ = 2949, 2866, 1584, 1564, 1461, 1434, 1151, 769, 742, 698 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 246 (24) $[M+Na]^+$, 224 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{16}H_{18}N^+$ $[M+H]^+$ 224.1434, found 224.1436.

The spectral data are in accordance with those reported in the literature.[113]

2-(3,5-Dicyclopentylphenyl)pyridine (203b')



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.71–8.66 (m, 1H), 7.76–7.69 (m, 2H), 7.67 (s, 2H), 7.23–7.19 (m, 1H), 7.18 (s, 1H), 3.06 (tt, *J* = 8.4, 7.9 Hz, 2H), 2.18–2.04 (m, 4H), 1.90–1.77 (m, 4H), 1.77–1.60 (m, 8H).

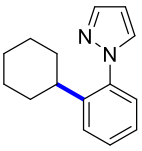
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 158.2 (C_q), 149.6 (CH), 146.9 (C_q), 139.3 (C_q), 136.5 (CH), 126.8 (CH), 123.3 (CH), 121.8 (CH), 120.8 (CH), 46.2 (CH), 34.7 (CH_2), 25.6 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2949, 2866, 1585, 1566, 1474, 1441, 991, 874, 783, 743 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 291 (35) $[M]^+$, 290 (19) $[M-H]^+$, 263 (30), 250 (100), 222 (17), 220 (9), 194 (20), 182 (13), 167 (10), 43 (10), 41 (10).

HR-MS (EI): *m*/*z* calcd for $C_{21}H_{25}N^+$ $[M]^+$ 291.1982, found 291.1982.

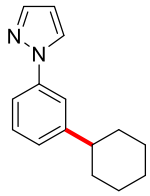
1-(2-Cyclohexylphenyl)-1*H*-pyrazole (145aj)



The general procedure **M** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol) and bromocyclohexane (**136j**, 245 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *ortho*-alkylated product **145aj** (68.0 mg, 60%) as a colorless oil and *meta*-alkylated product **146aj** (13.1 mg, 12%) as a colorless oil.

In case of using *o*-xylene (1.0 mL) as a solvent, the reaction provided the product **145aj** (57.1 mg, 50%). The analytical data of **145aj** are in section 5.3.5.1.

1-(3-Cyclohexylphenyl)-1*H*-pyrazole (146aj)



^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 2.3 Hz, 1H), 7.72 (d, *J* = 1.9 Hz, 1H), 7.59 (dd, *J* = 2.1, 1.7 Hz, 1H), 7.46 (ddd, *J* = 7.9, 2.1, 1.2 Hz, 1H), 7.36 (dd, *J* = 7.9, 7.8 Hz, 1H), 7.14 (ddd, *J* = 7.8, 1.7, 1.2 Hz, 1H), 6.46 (dd, *J* = 2.3, 1.9 Hz, 1H), 2.58 (tt, *J* = 12.2, 3.7 Hz, 1H), 1.92 (ddd, *J* = 12.5, 3.7, 2.4 Hz, 2H), 1.86 (ddd, *J* = 13.0, 3.5, 3.1 Hz, 2H), 1.76 (dtt, *J* = 12.8, 3.0, 1.5 Hz, 1H), 1.48 (dddd, *J* = 12.6, 12.5, 12.2, 3.1 Hz, 2H), 1.40 (ddddd, *J* = 13.0, 12.8, 12.6, 3.0, 2.4 Hz, 2H), 1.27 (dtt, *J* = 12.8, 12.8, 3.5 Hz, 1H).

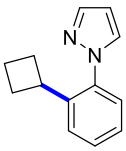
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 149.7 (C_q), 140.8 (CH), 140.1 (C_q), 129.1 (CH), 126.7 (CH), 125.0 (CH), 118.0 (CH), 116.6 (CH), 107.3 (CH), 44.7 (CH), 34.4 (CH_2), 26.9 (CH_2), 26.2 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2924, 2851, 1608, 1591, 1519, 1448, 1393, 1044, 950, 748 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 226 (100) $[M]^+$, 225 (29) $[M–H]^+$, 211 (14), 197 (18), 183 (20), 171 (40), 170 (29), 158 (24), 144 (10) $[M–Cy]^+$, 115 (14), 77 (9).

HR-MS (EI): *m*/*z* calcd for $C_{15}H_{18}N_2^+$ $[M]^+$ 226.1465, found 226.1471.

1-(2-Cyclobutylphenyl)-1*H*-pyrazole (145aw)



The general procedure **M** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol) and bromocyclobutane (**136w**, 203 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *ortho*-alkylated product **145aw** (70.5 mg, 71%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.71 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.53 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.46–7.36 (m, 2H), 7.30–7.24 (m, 2H), 6.42 (dd, *J* = 2.4, 1.9 Hz, 1H), 3.70–3.56 (m, 1H), 2.10– 1.82 (m, 5H), 1.80–1.68 (m, 1H).

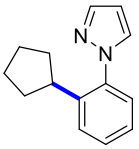
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 141.5 (C_q), 140.1 (CH), 138.8 (C_q), 130.5 (CH), 128.5 (CH), 127.2 (CH), 126.3 (CH), 126.3 (CH), 106.0 (CH), 36.4 (CH), 29.3 (CH_2), 18.4 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2972, 2865, 1516, 1498, 1394, 1044, 938, 750, 622 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 198 (17) $[M]^+$, 197 (7) $[M–H]^+$, 169 (100), 142 (9), 130 (6), 115 (12), 77 (7).

HR-MS (EI): *m*/*z* calcd for $C_{13}H_{14}N_2^+$ $[M]^+$ 198.1151, found 198.1152.

1-(2-Cyclopentylphenyl)-1*H*-pyrazole (145ai)



The general procedure **M** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol) and bromocyclopentane (**136i**, 224 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) followed by recycling preparative HPLC yielded *ortho*-alkylated product **145ai** (23.2 mg, 22%) as a colorless oil and *meta*-alkylated product **146ai** (28.9 mg, 27%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.57 (dd, *J* = 2.3, 0.7 Hz, 1H), 7.46–7.36 (m, 2H), 7.29–7.22 (m, 2H), 6.43 (dd, *J* = 2.3, 1.9 Hz, 1H), 2.92 (ddt, *J* = 10.0, 8.6, 7.5 Hz, 1H), 1.97–1.68 (m, 4H), 1.66–1.47 (m, 4H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 142.9 (C_q), 140.0 (CH), 139.6 (C_q), 130.9 (CH), 128.9 (CH), 127.0 (CH), 126.7 (CH), 126.0 (CH), 105.9 (CH), 39.7 (CH), 34.8 (CH_2), 25.8 (CH_2).

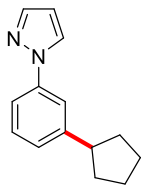
IR (ATR): $\tilde{\nu}$ = 2951, 2867, 1516, 1453, 1394, 1043, 938, 744, 621 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 212 (73) $[M]^+$, 211 (51) $[M–H]^+$, 194 (11), 183 (34), 169 (100), 156 (18), 143 (12), 130 (19), 128 (14), 115 (24), 91 (15), 77 (14), 58 (23), 43 (70).

HR-MS (EI): *m*/*z* calcd for $C_{14}H_{16}N_2^+$ $[M]^+$ 212.1308, found 212.1315.

The spectral data are in accordance with those reported in the literature.[141]

1-(3-Cyclopentylphenyl)-1*H*-pyrazole (146ai)



^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.92 (dd, *J* = 2.5, 0.7 Hz, 1H), 7.72 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.61 (ddd, *J* = 2.3, 1.6, 0.6 Hz, 1H), 7.45 (ddd, *J* = 7.9, 2.3, 1.2 Hz, 1H), 7.35 (dd, *J* = 7.9, 7.7 Hz, 1H), 7.18 (dddd, *J* = 7.7, 1.6, 1.2, 0.6 Hz, 1H), 6.46 (dd, *J* = 2.5, 1.8 Hz, 1H), 3.07 (tt, *J* = 9.1, 7.2 Hz, 1H), 2.19–2.04 (m, 2H), 1.91–1.56 (m, 6H).

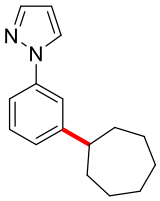
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 148.2 (C_q), 140.8 (CH), 140.1 (C_q), 129.1 (CH), 126.7 (CH), 125.2 (CH), 118.2 (CH), 116.5 (CH), 107.3 (CH), 46.0 (CH), 34.6 (CH_2), 25.6 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2950, 2867, 1608, 1589, 1518, 1392, 1043, 785, 746, 698 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 212 (100) $[M]^+$, 211 (36) $[M–H]^+$, 197 (8), 184 (42), 183 (35), 171 (59), 158 (12), 144 (14), 129 (10), 115 (27), 77 (14).

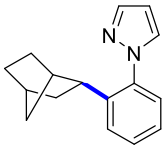
HR-MS (EI): *m*/*z* calcd for $C_{14}H_{16}N_2^+$ $[M]^+$ 212.1308, found 212.1316.

1-(3-Cycloheptylphenyl)-1*H*-pyrazole (146ah)



The general procedure **M** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol) and bromocycloheptane (**136h**, 266 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *meta*-alkylated product **146ah** (69.9 mg, 58%) as a colorless oil. The analytical data of **146ah** are in section 5.3.5.1.

1-[*exo*-2-(Bicyclo[2.2.1]heptan-2-yl)phenyl]-1*H*-pyrazole (145au)



The general procedure **M** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol) and *exo*-2-bromonorbornane (**136u**, 263 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *ortho*-alkylated product **145au** (64.4 mg, 54%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.55 (dd, *J* = 2.3, 0.7 Hz, 1H), 7.43 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.38 (ddd, *J* = 8.0, 6.6, 2.2 Hz, 1H), 7.26 (d_{AB}d, *J* = 7.8, 2.2 Hz, 1H), 7.25 (d_{AB}dd, *J* = 7.8, 6.6, 1.5 Hz, 1H), 6.43 (dd, *J* = 2.3, 1.9 Hz, 1H), 2.69 (dd, *J* = 9.0, 5.8 Hz, 1H), 2.32 (ddd, *J* = 2.7, 1.7, 1.4 Hz, 1H), 2.27 (ddd, *J* = 3.9, 2.5, 2.2 Hz, 1H), 1.58 (ddd, *J* = 9.8, 2.2, 1.7 Hz, 1H), 1.52–1.45 (m, 3H), 1.38 (ddd, *J* = 12.2, 9.0, 2.4 Hz, 1H), 1.20 (ddd, *J* = 9.8, 2.5, 1.4 Hz, 1H), 1.16–1.09 (m, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 143.7 (C_q), 140.0 (CH), 139.7 (C_q), 131.0 (CH), 128.7 (CH), 127.1 (CH), 126.4 (CH), 125.9 (CH), 105.9 (CH), 42.6 (CH), 41.7 (CH), 39.5 (CH_2), 36.9 (CH), 36.5 (CH_2), 30.5 (CH_2), 28.6 (CH_2).

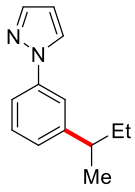
IR (ATR): $\tilde{\nu}$ = 2949, 2869, 1515, 1454, 1394, 1043, 938, 747, 624 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 238 (100) $[M]^+$, 237 (50) $[M–H]^+$, 223 (10), 209 (80), 197 (45), 182 (83), 169 (99), 156 (27), 142 (13), 130 (22), 128 (18), 115 (27), 77 (19), 41 (13).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{18}N_2^+$ $[M]^+$ 238.1465, found 238.1467.

The spectral data are in accordance with those reported in the literature.[141-142]

1-[3-(*sec*-Butyl)phenyl]-1*H*-pyrazole (146am)



The general procedure **M** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol) and 2-bromobutane (**136m**, 206 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *meta*-alkylated product **146am** (39.3 mg, 39%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.92 (dd, *J* = 2.5, 0.7 Hz, 1H), 7.73 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.56 (dd, *J* = 2.2, 1.6 Hz, 1H), 7.46 (ddd, *J* = 7.9, 2.2, 1.2 Hz, 1H), 7.36 (dd, *J* = 7.9, 7.7 Hz, 1H), 7.12 (dddd, *J* = 7.7, 1.6, 1.2, 0.3 Hz, 1H), 6.46 (dd, *J* = 2.5, 1.8 Hz, 1H), 2.68 (h, *J* = 7.0 Hz, 1H), 1.71–1.58 (m, 2H), 1.28 (d, *J* = 7.0 Hz, 3H), 0.85 (t, *J* = 7.4 Hz, 3H).

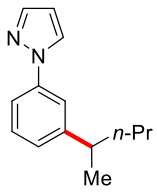
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.4 (C_q), 140.9 (CH), 140.2 (C_q), 129.2 (CH), 126.8 (CH), 125.3 (CH), 118.2 (CH), 116.6 (CH), 107.4 (CH), 41.8 (CH), 31.1 (CH_2), 21.8 (CH_3), 12.2 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2960, 1609, 1591, 1519, 1392, 1042, 945, 787, 745, 698 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 200 (47) $[M]^+$, 185 (7) $[M–Me]^+$, 171 (100) $[M–Et]^+$, 156 (9) $[M–Me–Et]^+$, 144 (11) [M–*sec*-Bu]$^+$, 130 (8), 117 (7), 103 (8), 77 (9).

HR-MS (EI): *m*/*z* calcd for $C_{13}H_{16}N_2^+$ $[M]^+$ 200.1308, found 200.1311.

1-[3-(Pentan-2-yl)phenyl]-1*H*-pyrazole (146an)



The general procedure **M** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol) and 2-bromopentane (**136n**, 227 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *meta*-alkylated product **146an** (45.0 mg, 42%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.92 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.73 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.56 (dd, *J* = 2.1, 1.7 Hz, 1H), 7.46 (ddd, *J* = 7.9, 2.1, 1.3 Hz, 1H), 7.36 (dd, *J* = 7.9, 7.7 Hz, 1H), 7.12 (ddd, *J* = 7.7, 1.7, 1.3 Hz, 1H), 6.46 (dd, *J* = 2.5, 1.8 Hz, 1H), 2.78 (h, *J* = 7.0 Hz, 1H), 1.67–1.51 (m, 2H), 1.36–1.15 (m, 2H), 1.28 (d, *J* = 7.0 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.7 (C_q), 140.9 (CH), 140.2 (C_q), 129.2 (CH), 126.8 (CH), 125.2 (CH), 118.1 (CH), 116.6 (CH), 107.4 (CH), 40.5 (CH_2), 39.8 (CH), 22.2 (CH_3), 20.8 (CH_2), 14.1 (CH_3).

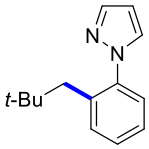
IR (ATR): $\tilde{\nu}$ = 2957, 1609, 1591, 1519, 1392, 1042, 948, 787, 743, 698 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 214 (45) $[M]^+$, 199 (3) $[M–Me]^+$, 185 (7) $[M–Et]^+$, 171 (100) $[M–n\text{-}Pr]^+$, 157 (13) $[M–n\text{-}Pr–Me]^+$, 144 (13), 130 (9), 103 (9), 77 (11), 58 (26), 43 (78).

HR-MS (EI): *m*/*z* calcd for $C_{14}H_{18}N_2^+$ $[M]^+$ 214.1465, found 214.1466.

The spectral data are in accordance with those reported in the literature.[61]

1-(2-Neopentylphenyl)-1*H*-pyrazole (145at)



The general procedure **M** was followed using 1-phenyl-1*H*-pyrazole (**147a**, 72.1 mg, 0.50 mmol) and neopentyl bromide (**136t**, 227 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *ortho*-alkylated product **145at** (53.2 mg, 50%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.70 (dd, *J* = 2.0, 0.7 Hz, 1H), 7.58 (dd, *J* = 2.2, 0.7 Hz, 1H), 7.34–7.26 (m, 4H), 6.41 (dd, *J* = 2.2, 2.0 Hz, 1H), 2.75 (s, 2H), 0.68 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 140.4 (C_q), 140.0 (CH), 135.5 (C_q), 133.0 (CH), 130.9 (CH), 127.6 (CH), 126.8 (CH), 126.7 (CH), 106.1 (CH), 43.9 (CH_2), 32.1 (C_q), 29.3 (CH_3).

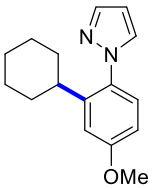
IR (ATR): $\tilde{\nu}$ = 2950, 1517, 1476, 1394, 1364, 1044, 939, 748, 718 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 214 (23) $[M]^+$, 199 (28) $[M–Me]^+$, 158 (100) $[M–t\text{-}Bu]^+$, 157 (74), 130 (55), 103 (9), 77 (11), 57 (15), 41 (13).

HR-MS (EI): *m*/*z* calcd for $C_{14}H_{18}N_2^+$ $[M]^+$ 214.1465, found 214.1470.

The spectral data are in accordance with those reported in the literature.[33]

1-(2-Cyclohexyl-4-methoxyphenyl)-1*H*-pyrazole (145dj)



The general procedure **M** was followed using 1-(4-methoxyphenyl)-1*H*-pyrazole (**147d**, 87.1 mg, 0.50 mmol) and bromocyclohexane (**136j**, 245 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *ortho*-alkylated product **145dj** (86.6 mg, 68%) as a colorless oil and *meta*-alkylated product **146dj** (14.7 mg, 11%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.69 (dd, *J* = 2.0, 0.7 Hz, 1H), 7.49 (dd, *J* = 2.2, 0.7 Hz, 1H), 7.20 (d, *J* = 8.6 Hz, 1H), 6.90 (d, *J* = 2.9 Hz, 1H), 6.76 (dd, *J* = 8.6, 2.9 Hz, 1H), 6.40 (dd, *J* = 2.2, 2.0 Hz, 1H), 3.85 (s, 3H), 2.32 (tt, *J* = 12.0, 3.1 Hz, 1H), 1.80–1.62 (m, 5H), 1.43–1.30 (m, 2H), 1.27–1.11 (m, 3H).

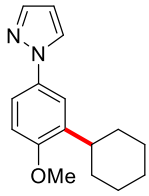
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.9 (C_q), 145.9 (C_q), 139.9 (CH), 132.4 (C_q), 131.3 (CH), 128.1 (CH), 112.7 (CH), 110.7 (CH), 105.8 (CH), 55.4 (CH_3), 38.5 (CH), 34.2 (CH_2), 26.7 (CH_2), 26.0 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2924, 2850, 1607, 1517, 1288, 1241, 1041, 944, 810, 747 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 256 (100) $[M]^+$, 255 (90) $[M–H]^+$, 239 (14), 227 (17), 213 (31), 199 (28), 184 (10), 160 (13), 115 (9), 77 (8), 41 (9).

HR-MS (ESI): *m*/*z* calcd for $C_{16}H_{20}N_2ONa^+$ $[M+Na]^+$ 279.1468, found 279.1470.

1-(3-Cyclohexyl-4-methoxyphenyl)-1*H*-pyrazole (146dj)



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.83 (dd, *J* = 2.3, 0.8 Hz, 1H), 7.70 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.52 (d, *J* = 2.7 Hz, 1H), 7.40 (dd, *J* = 8.7, 2.7 Hz, 1H), 6.89 (d, *J* = 8.7 Hz, 1H), 6.43 (dd, *J* = 2.3, 1.8 Hz, 1H), 3.86 (s, 3H), 3.00 (tt, *J* = 11.5, 3.1 Hz, 1H), 1.91–1.80 (m, 4H), 1.80–1.72 (m, 1H), 1.51–1.36 (m, 4H), 1.35–1.18 (m, 1H).

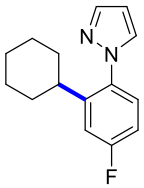
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 155.5 (C_q), 140.4 (CH), 137.5 (C_q), 134.0 (C_q), 126.9 (CH), 118.7 (CH), 117.6 (CH), 110.7 (CH), 106.9 (CH), 55.7 (CH_3), 36.9 (CH), 33.1 (CH_2), 27.0 (CH_2), 26.3 (CH_2).

IR (ATR): $\tilde{\nu}$ = 2925, 2850, 1517, 1499, 1238, 1047, 955, 809, 747, 638 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 256 (100) $[M]^+$, 255 (9) $[M–H]^+$, 213 (21), 200 (10), 187 (13), 185 (9), 157 (12), 145 (10), 130 (10), 115 (8), 77 (6), 41 (9).

HR-MS (ESI): *m*/*z* calcd for $C_{16}H_{20}N_2ONa^+$ $[M+Na]^+$ 279.1468, found 279.1472.

1-(2-Cyclohexyl-4-fluorophenyl)-1*H*-pyrazole (145gj)



The general procedure **M** was followed using 1-(4-fluorophenyl)-1*H*-pyrazole (**147g**, 81.1 mg, 0.50 mmol) and bromocyclohexane (**136j**, 245 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *ortho*-alkylated product **145gj** (74.2 mg, 61%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 2.0 Hz, 1H), 7.51 (d, *J* = 2.2 Hz, 1H), 7.25 (dd, *J* = 8.5, 5.5 Hz, 1H), 7.08 (dd, *J* = 10.1, 2.9 Hz, 1H), 6.93 (ddd, *J* = 8.5, 8.2, 2.9 Hz, 1H), 6.43 (dd, *J* = 2.2, 2.0 Hz, 1H), 2.37 (tt, *J* = 12.1, 2.6 Hz, 1H), 1.81–1.63 (m, 5H), 1.42–1.12 (m, 5H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 163.0 (d, $^1J_{C–F}$ = 248 Hz, C_q), 147.2 (d, $^3J_{C–F}$ = 7 Hz, C_q), 140.4 (CH), 135.3 (d, $^4J_{C–F}$ = 3 Hz, C_q), 131.3 (CH), 128.9 (d, $^3J_{C–F}$ = 9 Hz, CH), 114.1 (d, $^2J_{C–F}$ = 23 Hz, CH), 113.1 (d, $^2J_{C–F}$ = 23 Hz, CH), 106.3 (CH), 38.6 (d, $^4J_{C–F}$ = 1 Hz, CH), 34.2 (CH_2), 26.7 (CH_2), 26.1 (CH_2).

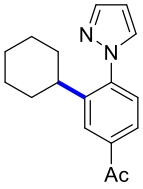
^{19}F-NMR (376 MHz, $CDCl_3$): δ = (–112.1)–(–112.3) (m).

IR (ATR): $\tilde{\nu}$ = 2926, 2852, 1517, 1498, 1395, 1238, 953, 866, 817, 747 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 245 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{15}H_{18}N_2F^+$ $[M+H]^+$ 245.1449, found 245.1450.

1-[3-Cyclohexyl-4-(1*H*-pyrazol-1-yl)phenyl]ethan-1-one (145jj)



The general procedure **M** was followed using 1-[4-(1*H*-pyrazol-1-yl)phenyl]ethan-1-one (**147j**, 93.1 mg, 0.50 mmol) and bromocyclohexane (**136j**, 245 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *ortho*-alkylated product **145jj** (86.6 mg, 65%) as a white solid, di-*ortho*-alkylated product **145jj'** (36.8 mg, 21%) as a white solid and dialkylated product **145jj''** (14.4 mg, 8%) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 2.0 Hz, 1H), 7.83 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.75 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.59 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 6.48 (dd, *J* = 2.4, 1.9 Hz, 1H), 2.64 (s, 3H), 2.62 (tt, *J* = 12.0, 3.1 Hz, 1H), 1.82–1.73 (m, 4H), 1.73–1.67 (m, 1H), 1.54–1.40 (m, 2H), 1.32–1.16 (m, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 197.4 (C_q), 144.0 (C_q), 142.7 (C_q), 140.8 (CH), 137.0 (C_q), 130.9 (CH), 127.6 (CH), 126.9 (CH), 126.4 (CH), 106.7 (CH), 38.3 (CH), 34.1 (CH_2), 26.8 (CH_3), 26.6 (CH_2), 25.9 (CH_2).

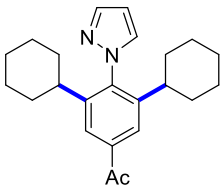
IR (ATR): $\tilde{\nu}$ = 2920, 2850, 1679, 1602, 1519, 1396, 1264, 939, 834, 752 cm^{-1}.

m.p.: 75–77 °C.

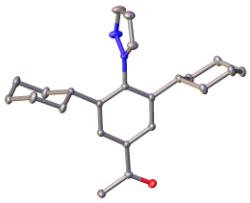
MS (EI) *m*/*z* (relative intensity): 268 (96) $[M]^+$, 267 (100) $[M–H]^+$, 251 (10), 239 (16), 225 (41) $[M–Ac]^+$, 211 (29), 199 (11), 185 (10), 168 (13), 157 (11), 115 (11), 58 (27), 43 (98).

HR-MS (ESI): *m*/*z* calcd for $C_{17}H_{20}N_2ONa^+$ $[M+Na]^+$ 291.1468, found 291.1471.

1-[3,5-Dicyclohexyl-4-(1*H*-pyrazol-1-yl)phenyl]ethan-1-one (145jj')



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.78 (s, 2H), 7.74 (dd, *J* = 2.0, 0.6 Hz, 1H), 7.41 (dd, *J* = 2.2, 0.6 Hz, 1H), 6.47 (dd, *J* = 2.2, 2.0 Hz, 1H), 2.64 (s, 3H), 1.90 (tt, *J* = 11.9, 3.3 Hz, 2H), 1.85–1.77 (m, 2H), 1.77–1.58 (m, 8H), 1.48–1.33 (m, 4H), 1.27–1.04 (m, 6H).



145jj'
CCDC 1979313

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 197.9 (C_q), 146.6 (C_q), 141.1 (C_q), 140.1 (CH), 137.8 (C_q), 131.6 (CH), 124.2 (CH), 106.0 (CH), 39.0 (CH), 34.7 (CH_2), 34.1 (CH_2), 26.8 (CH_3), 26.7 (CH_2), 26.6 (CH_2), 25.9 (CH_2).

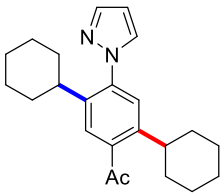
IR (ATR): $\tilde{\nu}$ = 2922, 2850, 1692, 1444, 1393, 1271, 1193, 939, 875, 766 cm^{-1}.

m.p.: 138–140 °C.

MS (EI) *m/z* (relative intensity): 350 (100) $[M]^+$, 349 (77) $[M–H]^+$, 321 (12), 307 (25) $[M–Ac]^+$, 295 (25), 267 (23) $[M–Cy]^+$, 252 (32), 184 (11) $[M–Cy–Cy]^+$, 115 (8), 55 (13), 43 (62), 41 (18).

HR-MS (ESI): *m/z* calcd for $C_{23}H_{30}N_2ONa^+$ $[M+Na]^+$ 373.2250, found 373.2251.

1-[2,5-Dicyclohexyl-4-(1*H*-pyrazol-1-yl)phenyl]ethan-1-one (145jj'')



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.74 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.56 (dd, *J* = 2.3, 0.7 Hz, 1H), 7.45 (s, 1H), 7.26 (s, 1H), 6.46 (dd, *J* = 2.3, 1.9 Hz, 1H), 3.00 (tt, *J* = 11.6, 3.3 Hz, 1H), 2.60 (s, 3H), 2.51 (tt, *J* = 12.0, 3.0 Hz, 1H), 1.88–1.66 (m, 10H), 1.45–1.31 (m, 6H), 1.29–1.14 (m, 4H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 203.4 (C_q), 144.8 (C_q), 140.8 (C_q), 140.7 (C_q), 140.5 (CH), 139.6 (C_q), 130.9 (CH), 126.5 (CH), 125.5 (CH), 106.4 (CH), 39.7 (CH), 37.9 (CH), 34.5 (CH_2), 34.2 (CH_2), 30.9 (CH_3), 26.8 (CH_2), 26.7 (CH_2), 26.1 (CH_2), 26.0 (CH_2).

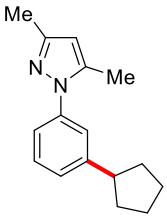
IR (ATR): $\tilde{\nu}$ = 2922, 2852, 1691, 1517, 1449, 1402, 1218, 953, 883, 760 cm^{-1}.

m.p.: 165–167 °C.

MS (EI) *m/z* (relative intensity): 350 (100) $[M]^+$, 349 (85) $[M–H]^+$, 335 (13) $[M–Me]^+$, 318 (12), 307 (21) $[M–Ac]^+$, 293 (18), 267 (11) $[M–Cy]^+$, 58 (24), 43 (73).

HR-MS (ESI): *m/z* calcd for $C_{23}H_{31}N_2O^+$ $[M+H]^+$ 351.2431, found 351.2437.

1-(3-Cyclopentylphenyl)-3,5-dimethyl-1*H*-pyrazole (146ci)



The general procedure **M** was followed using 3,5-dimethyl-1-phenyl-1*H*-pyrazole (**147c**, 86.2 mg, 0.50 mmol) and bromocyclopentane (**136i**, 112 mg, 0.75 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *meta*-alkylated product **146ci** (69.3 mg, 58%) as a colorless oil.

^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.34 (dd, J = 7.8, 7.8 Hz, 1H), 7.30 (dd, J = 2.1, 2.0 Hz, 1H), 7.22 (ddd, J = 7.8, 2.0, 1.0 Hz, 1H), 7.20 (ddd, J = 7.8, 2.1, 1.0 Hz, 1H), 5.98 (s, 1H), 3.04 (tt, J = 9.6, 7.5 Hz, 1H), 2.30 (s, 3H), 2.29 (d, J = 0.7 Hz, 3H), 2.12–2.06 (m, 2H), 1.84–1.77 (m, 2H), 1.73–1.65 (m, 2H), 1.65–1.57 (m, 2H).

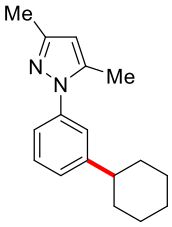
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 148.6 (C_q), 147.7 (C_q), 139.7 (C_q), 139.2 (C_q), 128.6 (CH), 126.0 (CH), 123.7 (CH), 122.0 (CH), 106.6 (CH), 45.8 (CH), 34.6 (CH_2), 25.6 (CH_2), 13.6 (CH_3), 12.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2951, 2867, 1606, 1589, 1557, 1492, 1380, 792, 702 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 240 (100) $[M]^+$, 239 (33) $[M–H]^+$, 212 (32), 211 (27), 199 (96), 169 (10), 130 (9), 115 (18), 91 (16), 77 (10), 43 (27), 41 (15).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{20}N_2^+$ $[M]^+$ 240.1621, found 240.1623.

1-(3-Cyclohexylphenyl)-3,5-dimethyl-1*H*-pyrazole (146cj)



The general procedure **M** was followed using 3,5-dimethyl-1-phenyl-1*H*-pyrazole (**147c**, 86.2 mg, 0.50 mmol) and bromocyclohexane (**136j**, 122 mg, 0.75 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *meta*-alkylated product **146cj** (79.3 mg, 62%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.34 (dd, J = 7.9, 7.7 Hz, 1H), 7.27 (ddd, J = 2.3, 1.6, 0.6 Hz, 1H), 7.21 (ddd, J = 7.9, 2.3, 1.2 Hz, 1H), 7.19 (dddd, J = 7.7, 1.6, 1.2, 0.6 Hz, 1H), 6.00–5.97 (m, 1H), 2.55 (tt, J = 11.6, 3.3 Hz, 1H), 2.30 (d, J = 0.4 Hz, 3H), 2.29 (d, J = 0.7 Hz, 3H), 1.96–1.71 (m, 5H), 1.52–1.18 (m, 5H).

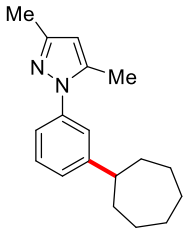
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 149.1 (C_q), 148.6 (C_q), 139.8 (C_q), 139.2 (C_q), 128.6 (CH), 125.7 (CH), 123.4 (CH), 122.1 (CH), 106.6 (CH), 44.5 (CH), 34.4 (CH_2), 26.9 (CH_2), 26.2 (CH_2), 13.6 (CH_3), 12.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2922, 2850, 1605, 1590, 1492, 1446, 1380, 792, 701 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 254 (100) $[M]^+$, 253 (34) $[M–H]^+$, 239 (8) $[M–Me]^+$, 225 (26), 213 (12), 211 (11), 199 (74), 186 (15), 115 (11), 91 (9), 77 (8), 41 (10).

HR-MS (EI): *m*/*z* calcd for $C_{17}H_{22}N_2^+$ $[M]^+$ 254.1778, found 254.1773.

1-(3-Cycloheptylphenyl)-3,5-dimethyl-1*H*-pyrazole (146ch)



The general procedure **M** was followed using 3,5-dimethyl-1-phenyl-1*H*-pyrazole (**147c**, 86.2 mg, 0.50 mmol) and bromocycloheptane (**136h**, 133 mg, 0.75 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded *meta*-alkylated product **146ch** (75.5 mg, 56%) as a colorless oil and di-*meta*-alkylated product **146ch'** (72.8 mg, 40%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.32 (dd, *J* = 7.9, 7.8 Hz, 1H), 7.25 (dd, *J* = 2.1, 2.0 Hz, 1H), 7.19 (ddd, *J* = 7.9, 2.1, 1.1 Hz, 1H), 7.18–7.15 (m, 1H), 5.98 (s, 1H), 2.71 (tt, *J* = 10.5, 3.5 Hz, 1H), 2.30 (s, 3H), 2.29 (d, *J* = 0.8 Hz, 3H), 1.98–1.90 (m, 2H), 1.79 (dtd, *J* = 13.2, 6.6, 3.5 Hz, 2H), 1.74–1.47 (m, 8H).

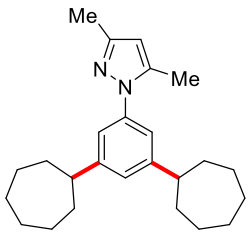
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 151.1 (C_q), 148.7 (C_q), 139.8 (C_q), 139.3 (C_q), 128.7 (CH), 125.6 (CH), 123.3 (CH), 121.9 (CH), 106.6 (CH), 46.9 (CH), 36.7 (CH_2), 27.9 (CH_2), 27.2 (CH_2), 13.5 (CH_3), 12.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2919, 2853, 1605, 1589, 1492, 1444, 1380, 975, 789, 702 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 268 (100) $[M]^+$, 267 (23) $[M–H]^+$, 253 (8) $[M–Me]^+$, 239 (21), 225 (35), 211 (20), 199 (69), 186 (64), 115 (15), 77 (10).

HR-MS (EI): *m*/*z* calcd for $C_{18}H_{24}N_2^+$ $[M]^+$ 268.1934, found 268.1944.

1-(3,5-Dicycloheptylphenyl)-3,5-dimethyl-1*H*-pyrazole (146ch')



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.01 (d, *J* = 1.7 Hz, 2H), 6.98 (t, *J* = 1.7 Hz, 1H), 5.96 (q, *J* = 0.7 Hz, 1H), 2.67 (tt, *J* = 10.6, 3.6 Hz, 2H), 2.30 (s, 3H), 2.27 (d, *J* = 0.7 Hz, 3H), 1.93 (dddd, *J* = 13.5, 6.6, 3.5, 1.6 Hz, 4H), 1.78 (dtt, *J* = 13.1, 6.6, 3.1 Hz, 4H), 1.74–1.47 (m, 16H).

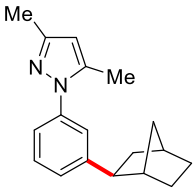
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 150.8 (C_q), 148.5 (C_q), 139.6 (C_q), 139.3 (C_q), 124.3 (CH), 120.5 (CH), 106.4 (CH), 47.0 (CH), 36.8 (CH_2), 27.9 (CH_2), 27.2 (CH_2), 13.6 (CH_3), 12.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2917, 2852, 1597, 1557, 1455, 1383, 975, 776, 709 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 364 (100) $[M]^+$, 363 (23) $[M–H]^+$, 349 (8) $[M–Me]^+$, 335 (13), 321 (26), 309 (12), 295 (68), 282 (63), 267 (13), 225 (12), 199 (10), 55 (19), 44 (38).

HR-MS (EI): *m*/*z* calcd for $C_{25}H_{36}N_2^+$ $[M]^+$ 364.2873, found 364.2869.

1-[*exo*-3-(Bicyclo[2.2.1]heptan-2-yl)phenyl]-3,5-dimethyl-1*H*-pyrazole (146cu)



The general procedure **M** was followed using 3,5-dimethyl-1-phenyl-1*H*-pyrazole (**147c**, 86.2 mg, 0.50 mmol) and *exo*-2-bromonorbornane (**136u**, 131 mg, 0.75 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 30:1) yielded *meta*-alkylated product **146cu** (49.6 mg, 37%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.33 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.28–7.25 (m, 1H), 7.22–7.16 (m, 2H), 6.00–5.97 (m, 1H), 2.78 (dd, *J* = 8.9, 5.8 Hz, 1H), 2.43–2.38 (m, 1H), 2.38–2.33 (m, 1H), 2.30 (d, *J* = 0.4 Hz, 3H), 2.29 (d, *J* = 0.8 Hz, 3H), 1.80 (dddd, *J* = 12.2, 8.9, 2.3, 0.8 Hz, 1H), 1.72–1.63 (m, 1H), 1.63–1.50 (m, 3H), 1.40–1.23 (m, 2H), 1.23–1.16 (m, 1H).

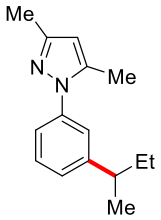
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 148.7 (C_q), 148.6 (C_q), 139.7 (C_q), 139.2 (C_q), 128.6 (CH), 125.9 (CH), 123.6 (CH), 121.8 (CH), 106.6 (CH), 47.2 (CH), 42.9 (CH), 39.3 (CH_2), 36.9 (CH), 36.2 (CH_2), 30.6 (CH_2), 28.9 (CH_2), 13.6 (CH_3), 12.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2949, 2868, 1605, 1588, 1556, 1493, 1380, 789, 701 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 266 (100) $[M]^+$, 265 (19) $[M–H]^+$, 251 (5) $[M–Me]^+$, 237 (12), 199 (68), 186 (41), 128 (9), 115 (14), 84 (14), 77 (10), 67 (12), 49 (19).

HR-MS (EI): *m*/*z* calcd for $C_{18}H_{22}N_2^+$ $[M]^+$ 266.1778, found 266.1792.

1-[3-(*sec*-Butyl)phenyl]-3,5-dimethyl-1*H*-pyrazole (146cm)



The general procedure **M** was followed using 3,5-dimethyl-1-phenyl-1*H*-pyrazole (**147c**, 86.1 mg, 0.50 mmol) and 2-bromobutane (**136m**, 103 mg, 0.75 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded *meta*-alkylated product **146cm** (57.5 mg, 50%) as a colorless oil and di-*meta*-alkylated product **146cm'** (60.2 mg, 42%, as a diastereomeric mixture (1:1)) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.35 (ddd, J = 7.6, 7.5, 0.9 Hz, 1H), 7.24–7.22 (m, 1H), 7.22 (ddd, J = 7.5, 2.2, 1.2 Hz, 1H), 7.17 (dddd, J = 7.6, 1.7, 1.2, 0.5 Hz, 1H), 5.99–5.97 (m, 1H), 2.65 (h, J = 7.0 Hz, 1H), 2.30 (s, 3H), 2.28 (d, J = 0.7 Hz, 3H), 1.67–1.56 (m, 2H), 1.26 (d, J = 7.0 Hz, 3H), 0.83 (t, J = 7.4 Hz, 3H).

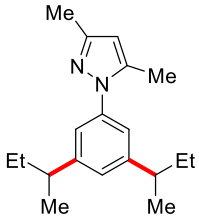
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.8 (C_q), 148.7 (C_q), 139.8 (C_q), 139.3 (C_q), 128.7 (CH), 126.0 (CH), 123.6 (CH), 122.3 (CH), 106.7 (CH), 41.6 (CH), 31.1 (CH_2), 21.7 (CH_3), 13.5 (CH_3), 12.4 (CH_3), 12.2 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2960, 1607, 1590, 1557, 1492, 1379, 974, 791, 702 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 228 (53) $[M]^+$, 213 (18) $[M–Me]^+$, 199 (100) $[M–Et]^+$, 184 (7) $[M–Me–Et]^+$, 143 (10), 115 (7), 77 (7).

HR-MS (EI): *m*/*z* calcd for $C_{15}H_{20}N_2^+$ $[M]^+$ 228.1621, found 228.1627.

1-(3,5-Di-*sec*-butylphenyl)-3,5-dimethyl-1*H*-pyrazole (146cm')



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.03 (d, J = 1.6 Hz, 2H), 6.96 (t, J = 1.6 Hz, 1H), 5.98 (s, 1H), 2.62 (h, J = 7.0 Hz, 2H), 2.30 (s, 3H), 2.26 (d, J = 0.8 Hz, 3H), 1.66–1.53 (m, 4H), 1.25 (d, J = 7.0 Hz, 6H), 0.83 (t, J = 7.4 Hz, 6H). Proton signals of two diastereomers are identical.

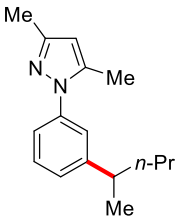
^{13}C-NMR (100 MHz, $CDCl_3$, determined as a diastereomeric mixture (1:1)): δ = 148.5 (2 × C_q), 148.4 (4 × C_q), 139.7 (2 × C_q), 139.3 (2 × C_q), 125.2 (CH), 125.2 (CH), 121.1 (2 × CH), 121.1 (2 × CH), 106.4 (2 × CH), 41.6 (4 × CH), 31.2 (2 × CH_2), 31.1 (2 × CH_2), 21.7 (4 × CH_3), 13.6 (2 × CH_3), 12.3 (2 × CH_3), 12.2 (2 × CH_3), 12.2 (2 × CH_3).

IR (ATR): $\tilde{\nu}$ = 2959, 2925, 1598, 1557, 1460, 1381, 875, 778, 710 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 284 (51) $[M]^+$, 269 (20) $[M–Me]^+$, 255 (100) $[M–Et]^+$, 225 (15), 199 (14), 115 (7).

HR-MS (EI): *m*/*z* calcd for $C_{19}H_{28}N_2^+$ $[M]^+$ 284.2247, found 284.2246.

3,5-Dimethyl-1-[3-(pentan-2-yl)phenyl]-1*H*-pyrazole (146cn)



The general procedure **M** was followed using 3,5-dimethyl-1-phenyl-1*H*-pyrazole (**147c**, 86.1 mg, 0.50 mmol) and 2-bromopentane (**136n**, 113 mg, 0.75 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded *meta*-alkylated product **146cn** (61.0 mg, 50%) as a colorless oil and di-*meta*-alkylated product **146cn'** (64.1 mg, 41%, as a diastereomeric mixture (1:1)) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.34 (ddd, *J* = 7.7, 7.5, 0.7 Hz, 1H), 7.24–7.23 (m, 1H), 7.22 (ddd, *J* = 7.7, 2.2, 1.3 Hz, 1H), 7.16 (dddd, *J* = 7.5, 1.4, 1.3, 0.5 Hz, 1H), 5.99 (q, *J* = 0.8 Hz, 1H), 2.75 (h, *J* = 7.0 Hz, 1H), 2.30 (s, 3H), 2.28 (d, *J* = 0.8 Hz, 3H), 1.65–1.48 (m, 2H), 1.34–1.14 (m, 2H), 1.25 (d, *J* = 7.0 Hz, 3H), 0.87 (t, *J* = 7.3 Hz, 3H).

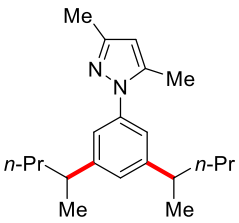
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 149.1 (C_q), 148.7 (C_q), 139.8 (C_q), 139.3 (C_q), 128.7 (CH), 126.0 (CH), 123.6 (CH), 122.3 (CH), 106.7 (CH), 40.5 (CH_2), 39.6 (CH), 22.1 (CH_3), 20.8 (CH_2), 14.1 (CH_3), 13.5 (CH_3), 12.3 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2956, 1607, 1557, 1492, 1380, 974, 890, 792, 702 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 242 (50) $[M]^+$, 227 (5) $[M–Me]^+$, 213 (13) $[M–Et]^+$, 199 (100) $[M–n\text{-}Pr]^+$, 143 (9), 115 (7), 77 (7), 58 (8), 43 (30).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{22}N_2^+$ $[M]^+$ 242.1778, found 242.1778.

1-[3,5-Di(pentan-2-yl)phenyl]-3,5-dimethyl-1*H*-pyrazole (146cn')



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.02 (d, *J* = 1.6 Hz, 2H), 6.96 (t, *J* = 1.6 Hz, 1H), 5.98 (s, 1H), 2.71 (h, *J* = 7.0 Hz, 2H), 2.31 (s, 3H), 2.26 (d, *J* = 0.7 Hz, 3H), 1.63–1.46 (m, 4H), 1.34–1.14 (m, 4H), 1.24 (d, *J* = 7.0 Hz, 6H), 0.86 (t, *J* = 7.3 Hz, 6H). Proton signals of two diastereomers are identical.

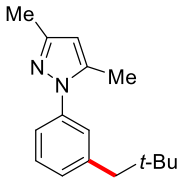
^{13}C-NMR (100 MHz, $CDCl_3$, determined as a diastereomeric mixture (1:1)): δ = 148.8 (4 × C_q), 148.5 (2 × C_q), 139.7 (2 × C_q), 139.3 (2 × C_q), 125.1 (CH), 125.1 (CH), 121.0 (4 × CH), 106.5 (2 × CH), 40.6 (2 × CH_2), 40.6 (2 × CH_2), 39.6 (4 × CH), 22.1 (4 × CH_3), 20.8 (4 × CH_2), 14.1 (4 × CH_3), 13.6 (2 × CH_3), 12.3 (2 × CH_3).

IR (ATR): $\tilde{\nu}$ = 2956, 2926, 1599, 1557, 1459, 1383, 876, 777, 710 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 312 (66) $[M]^+$, 297 (4) $[M–Me]^+$, 283 (14) $[M–Et]^+$, 270 (100) [M–*n*-Pr]$^+$, 269 (85) $[M–Et–Me]^+$, 227 (13) [M–*n*-Pr–*n*-Pr]$^+$, 225 (17), 199 (14), 115 (6), 43 (19), 41 (11).

HR-MS (EI): *m*/*z* calcd for $C_{21}H_{32}N_2^+$ $[M]^+$ 312.2560, found 312.2568.

3,5-Dimethyl-1-(3-neopentylphenyl)-1*H*-pyrazole (146ct)



The general procedure **M** was followed using 3,5-dimethyl-1-phenyl-1*H*-pyrazole (**147c**, 86.1 mg, 0.50 mmol) and neopentyl bromide (**136t**, 113 mg, 0.75 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 20:1) yielded *meta*-alkylated product **146ct** (39.2 mg, 32%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.33 (ddd, *J* = 8.0, 7.5, 0.6 Hz, 1H), 7.27 (ddd, *J* = 8.0, 2.2, 1.3 Hz, 1H), 7.16 (ddd, *J* = 2.2, 1.7, 0.6 Hz, 1H), 7.11 (ddd, *J* = 7.5, 1.7, 1.3 Hz, 1H), 5.99–5.97 (m, 1H), 2.54 (s, 2H), 2.30 (d, *J* = 0.4 Hz, 3H), 2.29 (d, *J* = 0.8 Hz, 3H), 0.93 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.7 (C_q), 140.7 (C_q), 139.4 (C_q), 139.3 (C_q), 129.4 (CH), 128.2 (CH), 126.7 (CH), 122.5 (CH), 106.6 (CH), 50.0 (CH_2), 31.8 (C_q), 29.4 (CH_3), 13.5 (CH_3), 12.4 (CH_3).

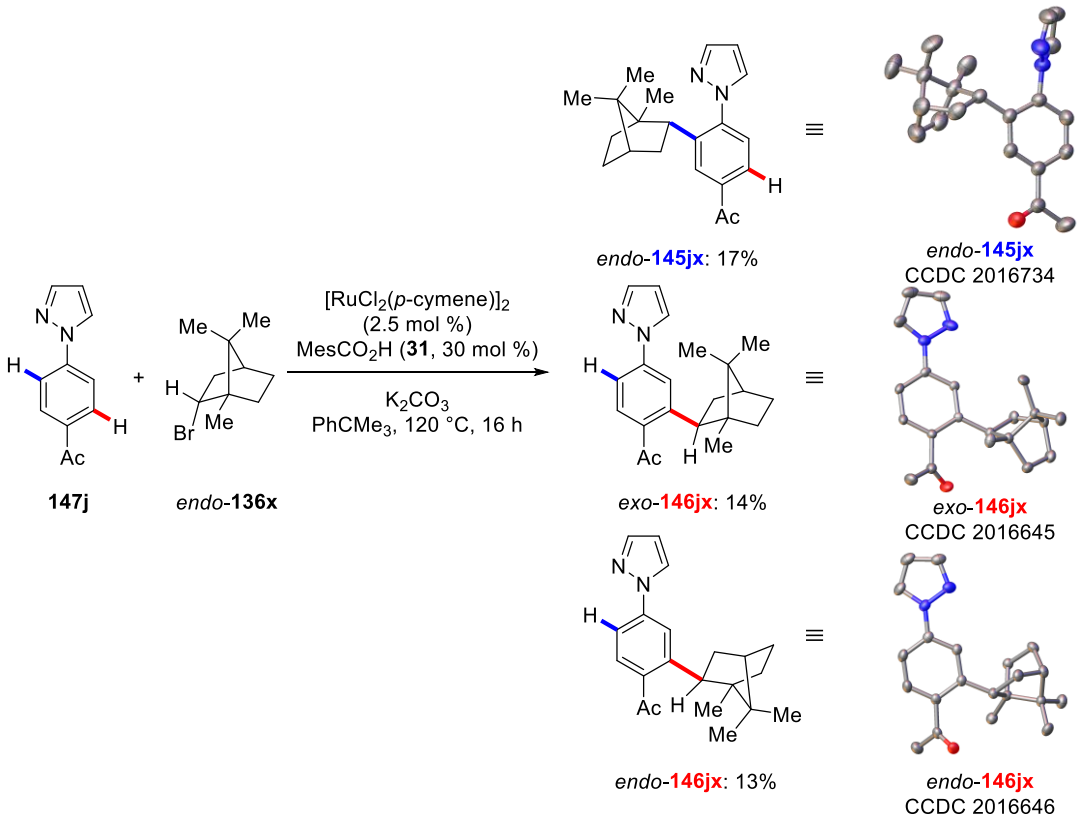
IR (ATR): $\tilde{\nu}$ = 2951, 1607, 1557, 1494, 1380, 1363, 975, 797, 742, 702 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 242 (27) $[M]^+$, 227 (13) $[M–Me]^+$, 186 (100) [M–*t*-Bu]$^+$, 171 (6) [M–CH_2*t*-Bu]$^+$, 144 (10), 130 (6), 115 (5), 57 (15), 41 (10).

HR-MS (EI): *m*/*z* calcd for $C_{16}H_{22}N_2^+$ $[M]^+$ 242.1778, found 242.1782.

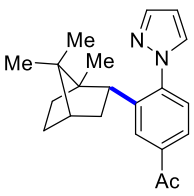
5.3.6.2 Mechanistic Studies

5.3.6.2.1 Reactions with Diastereomerically Pure Alkyl Bromides



The general procedure **M** was followed using 1-[4-(1*H*-pyrazol-1-yl)phenyl]ethan-1-one (**147j**, 93.1 mg, 0.50 mmol) and *endo*-2-bromobornane (*endo*-**136x**, 327 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *ortho*-alkylated product *endo*-**145jx** (27.4 mg, 17%) as a white solid, *meta*-alkylated product *exo*-**146jx** (22.0 mg, 14%) as a white solid and *meta*-alkylated product *endo*-**146jx** (21.0 mg, 13%) as a white solid.

1-[4-(1*H*-Pyrazol-1-yl)-3-(*endo*-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)phenyl]ethan-1-one (*endo*-145jx)



^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 2.0 Hz, 1H), 7.86 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.72 (d, *J* = 2.0 Hz, 1H), 7.57 (d, *J* = 2.3 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 6.44 (dd, *J* = 2.3, 2.0 Hz, 1H), 3.86 (ddd, *J* = 11.7, 5.7, 2.3 Hz, 1H), 2.67 (s, 3H), 2.34–2.18 (m, 1H), 1.93–1.80 (m, 1H), 1.77 (dd, *J* = 4.4, 4.4 Hz, 1H), 1.53–1.33 (m, 3H), 1.22–1.10 (m, 1H), 0.84 (s, 6H), 0.20 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 197.6 (C_q), 144.8 (C_q), 140.7 (CH), 139.6 (C_q), 136.3 (C_q), 131.4 (CH), 130.5 (CH), 127.2 (CH), 126.6 (CH), 106.8 (CH), 50.5 (C_q), 50.5 (C_q), 45.6 (CH), 42.1 (CH), 35.4 (CH_2), 28.8 (CH_2), 28.6 (CH_2), 26.9 (CH_3), 19.8 (CH_3), 18.5 (CH_3), 14.3 (CH_3).

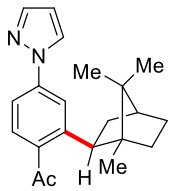
IR (ATR): $\tilde{\nu}$ = 2951, 1684, 1602, 1518, 1395, 1239, 937, 909, 827, 728 cm^{-1}.

m.p.: 97–98 °C.

MS (ESI) *m/z* (relative intensity): 667 (12) $[2M+Na]^+$, 645 (3) $[2M+H]^+$, 345 (35) $[M+Na]^+$, 323 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{21}H_{27}N_2O^+$ $[M+H]^+$ 323.2118, found 323.2119.

1-[4-(1*H*-Pyrazol-1-yl)-2-(*exo*-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)phenyl]ethan-1-one (*exo*-146jx)



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.97–7.92 (m, 2H), 7.75 (d, *J* = 1.7 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.55 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.49 (dd, *J* = 2.5, 1.7 Hz, 1H), 4.03 (dd, *J* = 9.1, 8.7 Hz, 1H), 2.63 (s, 3H), 2.26 (ddt, *J* = 12.2, 8.7, 3.4 Hz, 1H), 1.89–1.77 (m, 2H), 1.73 (dd, *J* = 12.2, 9.1 Hz, 1H), 1.61–1.54 (m, 2H), 1.43–1.32 (m, 1H), 0.93 (s, 3H), 0.86 (s, 3H), 0.68 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 202.6 (C_q), 145.8 (C_q), 141.8 (CH), 141.6 (C_q), 138.4 (C_q), 130.5 (CH), 126.8 (CH), 119.3 (CH), 115.3 (CH), 108.3 (CH), 50.7 (C_q), 48.6 (C_q), 46.5 (CH), 45.8 (CH), 39.7 (CH_2), 35.4 (CH_2), 31.0 (CH_3), 27.4 (CH_2), 21.8 (CH_3), 21.1 (CH_3), 13.6 (CH_3).

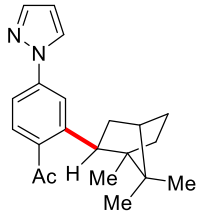
IR (ATR): $\tilde{\nu}$ = 2952, 2878, 1682, 1605, 1577, 1390, 1247, 1043, 948, 749 cm^{-1}.

m.p.: 129–131 °C.

MS (ESI) *m/z* (relative intensity): 667 (6) $[2M+Na]^+$, 645 (2) $[2M+H]^+$, 345 (37) $[M+Na]^+$, 323 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{21}H_{27}N_2O^+$ $[M+H]^+$ 323.2118, found 323.2118.

1-[4-(1*H*-Pyrazol-1-yl)-2-(*endo*-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)phenyl]ethan-1-one (*endo*-146jx)



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.97 (dd, J = 2.5, 0.7 Hz, 1H), 7.84 (d, J = 1.9 Hz, 1H), 7.77 (d, J = 1.7 Hz, 1H), 7.61–7.56 (m, 2H), 6.51 (dd, J = 2.5, 1.7 Hz, 1H), 4.25 (ddd, J = 11.6, 5.6, 2.3 Hz, 1H), 2.58 (s, 3H), 2.34–2.23 (m, 1H), 1.93–1.84 (m, 1H), 1.81 (dd, J = 4.4, 4.4 Hz, 1H), 1.52 (dd, J = 13.3, 5.6 Hz, 1H), 1.47–1.39 (m, 2H), 1.21–1.14 (m, 1H), 1.04 (s, 3H), 0.93 (s, 3H), 0.61 (s, 3H).

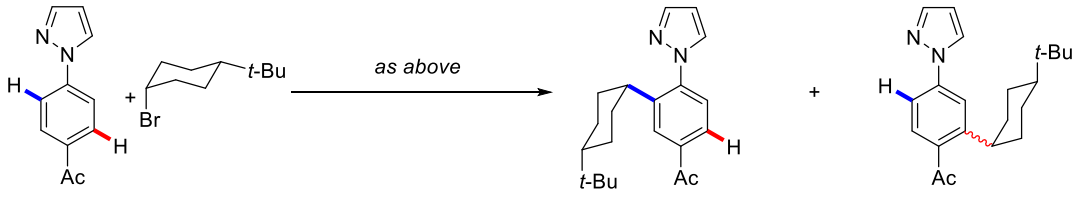
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 203.3 (C_q), 144.0 (C_q), 141.8 (CH), 141.1 (C_q), 139.7 (C_q), 129.4 (CH), 126.9 (CH), 120.3 (CH), 115.8 (CH), 108.3 (CH), 51.4 (C_q), 50.6 (C_q), 45.6 (CH), 42.7 (CH), 35.4 (CH_2), 31.0 (CH_3), 28.9 (CH_2), 28.7 (CH_2), 20.0 (CH_3), 18.8 (CH_3), 14.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2938, 2882, 1683, 1603, 1389, 1247, 1038, 909, 828, 762 cm^{-1}.

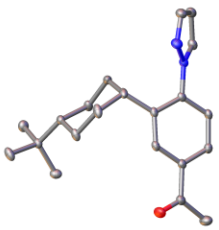
m.p.: 118–120 °C.

MS (EI) *m*/*z* (relative intensity): 322 (1) $[M]^+$, 308 (7), 304 (10), 289 (8), 279 (14) $[M–Ac]^+$, 213 (94), 211 (100), 196 (42), 169 (16), 95 (10).

HR-MS (EI): *m*/*z* calcd for $C_{21}H_{26}N_2O^+$ $[M]^+$ 322.2040, found 322.2037.



147j *cis*-**136s** *cis*-**145js**: 19% **146js**: 10%

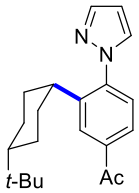


cis-**145js**
CCDC 2016647

The general procedure **M** was followed using 1-[4-(1*H*-pyrazol-1-yl)phenyl]ethan-1-one (**147j**, 93.1 mg, 0.50 mmol) and *cis*-1-bromo-4-(*tert*-butyl)cyclohexane (*cis*-**136s**, 312 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1 to 4:1) yielded *ortho*-alkylated product *cis*-**145js** (31.2 mg, 19%) as a white solid, *meta*-alkylated product **146js**

(16.5 mg, 10%) as a 1:1.3 mixture of *cis*- and *trans*-isomer as a colorless oil, and starting material **147j** (35.2 mg, 38%) as a white solid.

1-{3-[*cis*-4-(*tert*-Butyl)cyclohexyl]-4-(1*H*-pyrazol-1-yl)phenyl}ethan-1-one (*cis*-145js)



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 2.0 Hz, 1H), 7.85 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.74 (d, *J* = 2.0 Hz, 1H), 7.60 (d, *J* = 2.2 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 6.46 (dd, *J* = 2.2, 2.0 Hz, 1H), 3.39–3.32 (m, 1H), 2.64 (s, 3H), 1.79–1.70 (m, 2H), 1.67–1.52 (m, 4H), 1.38–1.24 (m, 2H), 1.08 (tt, *J* = 11.1, 3.8 Hz, 1H), 0.84 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 197.5 (C_q), 143.4 (C_q), 143.0 (C_q), 140.9 (CH), 136.6 (C_q), 130.8 (CH), 129.2 (CH), 127.5 (CH), 126.5 (CH), 106.9 (CH), 46.6 (CH), 32.9 (C_q), 32.2 (CH), 29.9 (CH_2), 27.7 (CH_3), 26.9 (CH_3), 23.1 (CH_2).

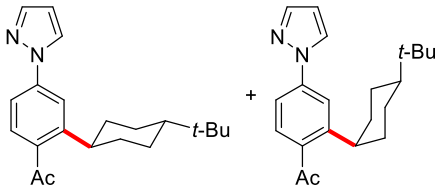
IR (ATR): $\tilde{\nu}$ = 2934, 1678, 1596, 1420, 1393, 1359, 1260, 939, 826, 771 cm^{-1}.

m.p.: 98–99 °C.

MS (EI) *m*/*z* (relative intensity): 324 (31) $[M]^+$, 323 (100) $[M–H]^+$, 309 (18) $[M–Me]^+$, 267 (47) [M–*t*-Bu]$^+$, 250 (14), 225 (24) [M–*t*-Bu–Ac]$^+$, 211 (21), 199 (11), 183 (6), 169 (10), 157 (5), 115 (4).

HR-MS (EI): *m*/*z* calcd for $C_{21}H_{28}N_2O^+$ $[M]^+$ 324.2196, found 324.2173.

Mixture of 1-{2-[*trans*-4-(*tert*-Butyl)cyclohexyl]-4-(1*H*-pyrazol-1-yl)phenyl}ethan-1-one (*trans*-146js) and 1-{2-[*cis*-4-(*tert*-Butyl)cyclohexyl]-4-(1*H*-pyrazol-1-yl)phenyl}ethan-1-one (*cis*-146js)



trans-**146js** *cis*-**146js**

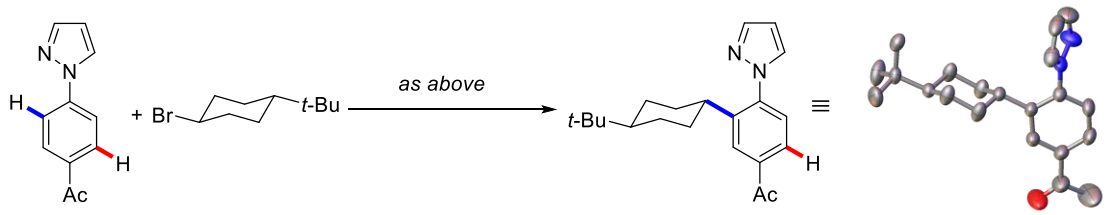
^{1}H-NMR (400 MHz, $CDCl_3$, determined as 1:1.3 mixture of *cis*-**146js** and *trans*-**146js**): δ = 7.97 (d, *J* = 2.5 Hz, 1H, *cis*-isomer), 7.96 (d, *J* = 2.7 Hz, 1H, *trans*-isomer), 7.90 (d, *J* = 2.3 Hz, 1H, *cis*-isomer), 7.77 (d, *J* = 2.3 Hz, 1H, *trans*-isomer), 7.76–7.73 (m, 2H), 7.64 (d, *J* = 8.4 Hz, 1H, *cis*-isomer), 7.63 (d, *J* = 8.5 Hz, 1H, *trans*-isomer), 7.56 (dd, *J* = 8.4, 2.3 Hz, 1H, *cis*-isomer), 7.53 (dd, *J* = 8.5, 2.3 Hz, 1H, *trans*-isomer), 6.51–6.47 (m, 2H), 3.78–3.69 (m, 1H, *cis*-isomer), 3.17 (tt, *J* = 12.2, 3.4 Hz, 1H, *trans*-isomer), 2.60 (s, 6H), 2.00–1.78 (m, 8H), 1.69–1.59 (m, 2H, *cis*-isomer), 1.57–1.45 (m, 2H, *trans*-isomer), 1.40–1.28 (m, 2H, *cis*-isomer), 1.25–1.05 (m, 4H), 0.88 (s, 9H, *cis*-isomer), 0.86 (s, 9H, *trans*-isomer). Some proton peaks could not be identified due to overlapping.

^{13}C-NMR (100 MHz, $CDCl_3$, determined as 1:1.3 mixture of *cis*-**146js** and *trans*-**146js**): δ = 202.6 (C_q of *cis*-isomer), 202.2 (C_q of *trans*-isomer), 149.6 (C_q of *trans*-isomer), 149.1 (C_q of *cis*-isomer), 142.0 (C_q of *trans*-isomer), 141.8 (CH of *cis*-isomer), 141.8 (CH of *trans*-isomer), 141.5 (C_q of *cis*-isomer), 137.0 (C_q of *cis*-isomer), 136.6 (C_q of *trans*-isomer), 130.2 (CH of *cis*-isomer), 130.0 (CH of *trans*-isomer), 126.9 (CH of *trans*-isomer), 126.8 (CH of *cis*-isomer), 118.9 (CH of *cis*-isomer), 117.7 (CH of *trans*-isomer), 115.6 (CH of *trans*-isomer), 115.4 (CH of *cis*-isomer), 108.3 (CH of *cis*-isomer), 108.3 (CH of *trans*-isomer), 48.0 (CH of *trans*-isomer), 46.1 (CH of *cis*-isomer), 40.1 (CH of *trans*-isomer), 34.9 (CH_2 of *trans*-isomer), 33.3 (CH of *cis*-isomer), 32.9 (C_q of *cis*-isomer), 32.6 (C_q of *trans*-isomer), 31.1 (CH_2 of *cis*-isomer), 30.7 (CH_3 of *trans*-isomer), 30.6 (CH_3 of *cis*-isomer), 27.8 (CH_2 of *trans*-isomer), 27.8 (CH_3 of *cis*- and *trans*-isomer), 23.4 (CH_2 of *cis*-isomer).

IR (ATR): $\tilde{\nu}$ = 2936, 2857, 1682, 1605, 1576, 1391, 1246, 1043, 945, 747 cm^{-1}.

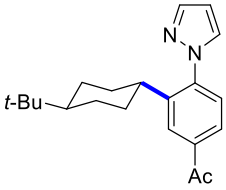
MS (EI) *m*/*z* (relative intensity): 324 (5) $[M]^+$, 309 (100) $[M–Me]^+$, 306 (19), 291 (11), 267 (8) [M–*t*-Bu]$^+$, 249 (24), 235 (23), 222 (38), 209 (18), 195 (12), 183 (8), 157 (6), 115 (8).

HR-MS (EI): *m*/*z* calcd for $C_{21}H_{28}N_2O^+$ $[M]^+$ 324.2196, found 324.2195.



The general procedure **M** was followed using 1-[4-(1*H*-pyrazol-1-yl)phenyl]ethan-1-one (**147j**, 93.1 mg, 0.50 mmol) and *trans*-1-bromo-4-(*tert*-butyl)cyclohexane (*trans*-**136s**, 312 mg, 1.50 mmol). After 16 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded *ortho*-alkylated product *trans*-**145js** (107 mg, 66%) as a white solid.

1-{3-[*trans*-4-(*tert*-Butyl)cyclohexyl]-4-(1*H*-pyrazol-1-yl)phenyl}ethan-1-one (*trans*-145js)



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 2.0 Hz, 1H), 7.83 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.76 (d, *J* = 1.9 Hz, 1H), 7.59 (d, *J* = 2.2 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 6.48 (dd, *J* = 2.2, 1.9 Hz, 1H), 2.64 (s, 3H), 2.58 (tt, *J* = 12.2, 3.2 Hz, 1H), 1.88–1.79 (m, 4H), 1.56–1.43 (m, 2H), 1.14–0.92 (m, 3H), 0.84 (s, 9H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 197.5 (C_q), 143.9 (C_q), 143.0 (C_q), 141.0 (CH), 137.2 (C_q), 131.0 (CH), 127.7 (CH), 127.1 (CH), 126.6 (CH), 106.9 (CH), 47.8 (CH), 38.4 (CH), 34.6 (CH_2), 32.6 (C_q), 27.7 (CH_3), 27.7 (CH_2), 26.9 (CH_3).

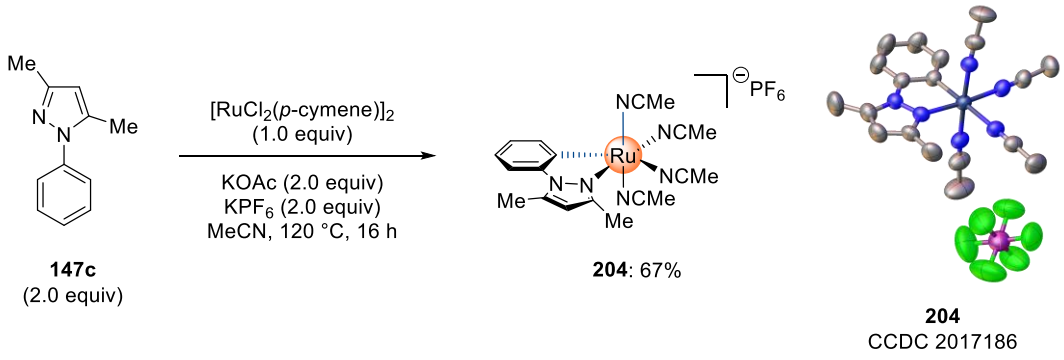
IR (ATR): $\tilde{\nu}$ = 2920, 2854, 1690, 1601, 1390, 1224, 935, 824, 770, 624 cm^{-1}.

m.p.: 109–110 °C.

MS (EI) *m/z* (relative intensity): 324 (34) $[M]^+$, 323 (100) $[M–H]^+$, 309 (19) $[M–Me]^+$, 267 (46) [M–*t*-Bu]$^+$, 250 (14), 225 (25) [M–*t*-Bu–Ac]$^+$, 211 (22), 199 (12), 169 (12).

HR-MS (EI): *m/z* calcd for $C_{21}H_{28}N_2O^+$ $[M]^+$ 324.2196, found 324.2175.

*5.3.6.2.2 Synthesis of Cyclometalated Ruthenium Complex **204***



An oven-dried pressure tube was charged with 3,5-dimethyl-1-phenyl-1*H*-pyrazole (**147c**, 172 mg, 1.00 mmol), $[RuCl_2(p\text{-cymene})]_2$ (306 mg, 0.50 mmol), KOAc (196 mg, 2.00 mmol), and KPF_6 (368 mg, 2.00 mmol). After evacuation and refilling with N_2 for three times, MeCN (6.5 mL) was added and the tube was sealed. The reaction mixture was stirred at 120 °C. After 16 h, the reaction was cooled down to the ambient temperature. The crude mixture was loaded on an aluminium oxide (Al_2O_3, neutral, conditioned with CH_2Cl_2) column and eluted with MeCN/CH_2Cl_2 (1:1) using N_2 instead of air. The pale green band was collected and the solvent was removed under reduced pressure. The complex was dissolved in MeCN (10 mL) and precipitated with Et_2O, affording the desired complex **204** (391 mg, 67%) as a green solid. The complex **204** was transferred to the glovebox subsequently. Suitable crystals of **204** for X-ray crystallography were grown by slow crystallization from MeCN/Et_2O (*see X-Ray Crystallographic Analysis section*).

^{1}H-NMR (300 MHz, MeCN-d_3): δ = 7.95–7.90 (m, 1H), 7.45–7.40 (m, 1H), 7.00–6.89 (m, 2H), 6.08 (s, 1H), 2.70 (s, 3H), 2.51 (s, 6H), 2.05 (s, 6H), 1.96 (s, 3H).

^{13}C-NMR (100 MHz, MeCN-d_3): δ = 166.3 (C_q), 152.9 (C_q), 148.7 (C_q), 141.1 (C_q), 139.9 (CH), 124.2 (CH), 123.3 (C_q), 122.4 (C_q), 121.9 (CH), 112.6 (CH), 110.1 (CH), 15.1 (CH_3), 14.7 (CH_3), 4.36 (CH_3), 3.8 (CH_3).

^{19}F-NMR (376 MHz, MeCN-d_3): δ = (–71.8)–(–74.0) (m).

^{31}P-NMR (162 MHz, MeCN-d_3): δ = –144.6 (hept, J = 708 Hz).

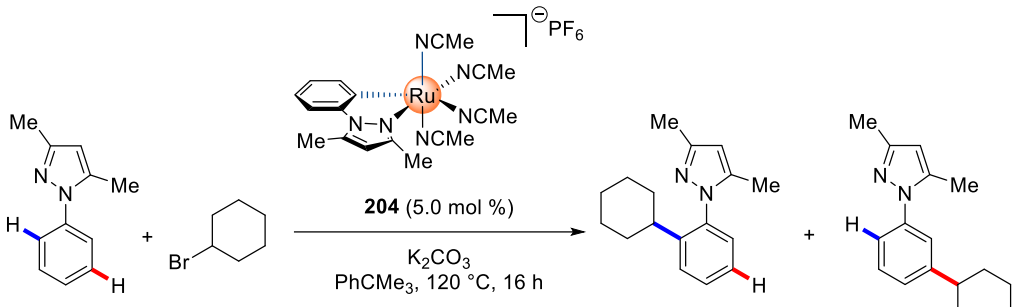
IR (ATR): $\tilde{\nu}$ = 2274, 1546, 1460, 1436, 1419, 1032, 832, 737, 719, 556 cm^{-1}.

m.p.: >170 °C (decomp.)

MS (ESI) *m*/*z* (relative intensity): 396 (100) $[M–MeCN–PF_6]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{17}H_{20}N_5Ru^+$ $[M–MeCN–PF_6]^+$ 396.0761, found 396.0759.

*5.3.6.2.3 Catalytic C–H Alkylation with Cyclometalated Complex **204***

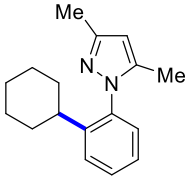


	145cj	146cj
without $MesCO_2H$ (**31**)	19%	10%
with $MesCO_2H$ (**31**, 30 mol %)	---	70%

3,5-Dimethyl-1-phenyl-1*H*-pyrazole (**147c**, 86.2 mg, 0.50 mmol), complex **204** (14.5 mg, 25 µmol, 5.0 mol %), $MesCO_2H$ (**31**, 24.6 mg, 150 µmol, 30 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a pre-dried 25 mL Schlenk tube. The tube was evacuated and purged with N_2 three times. Bromocyclohexane (**136j**, 123 mg, 0.75 mmol) and $PhCMe_3$ (1.0 mL) were then added and the mixture was stirred at 120 °C. After 16 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc 30:1) yielded *meta*-alkylated product **146cj** (89.5 mg, 70%) as a colorless oil.

In case of the reaction without $MesCO_2H$ (**31**), the reaction provided *ortho*-alkylated product **145cj** (24.4 mg, 19%) as a colorless oil, *meta*-alkylated product **146cj** (13.1 mg, 10%) as a colorless oil, and starting material **147c** (34.4 mg, 38%) as a colorless oil.

1-(2-Cyclohexylphenyl)-3,5-dimethyl-1*H*-pyrazole (145cj)



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.40–7.36 (m, 2H), 7.26–7.21 (m, 1H), 7.18–7.14 (m, 1H), 5.95 (s, 1H), 2.29 (d, *J* = 1.1 Hz, 3H), 2.16 (tt, *J* = 12.0, 2.8 Hz, 1H), 2.04 (d, *J* = 0.9 Hz, 3H), 1.82–1.61 (m, 5H), 1.44–1.29 (m, 2H), 1.24–1.14 (m, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.3 (C_q), 146.2 (C_q), 140.5 (C_q), 137.8 (C_q), 129.3 (CH), 128.3 (CH), 127.3 (CH), 126.2 (CH), 104.9 (CH), 38.5 (CH), 34.1 (CH_2), 26.9 (CH_2), 26.2 (CH_2), 13.8 (CH_3), 11.6 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2924, 2851, 1555, 1498, 1448, 1028, 774, 754, 530 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 277 (2) $[M+Na]^+$, 255 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{17}H_{23}N_2^+$ $[M+H]^+$ 255.1856, found 255.1859.

5.3.6.3 X-Ray Crystallographic Analysis

A suitable crystal was selected and the crystal was mounted on a MITIGEN holder in NVH oil on a Bruker D8 Venture diffractometer. The crystal was kept at 100 or 300 K during data collection. Using Olex2,[137] the structure was solved with the XT[138] structure solution program using Intrinsic Phasing and refined with the XL[139] refinement package using Least Squares minimisation.

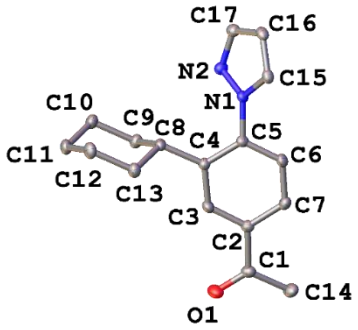


Figure 55: Molecular structure of **145jj** with thermal ellipsoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{17}H_{20}N_2O$ (*M* = 268.35 g/mol): monoclinic, space group P2/c (no. 13), *a* = 20.7094(15) Å, *b* = 5.3605(4) Å, *c* = 27.2622(18) Å, *β* = 106.154(2)°, *V* = 2907.0(4) Å^3, *Z* = 8, *T* = 100.0 K, μ(MoKα) = 0.077 mm^{-1}, *Dcalc* = 1.226 g/cm^3, 56579 reflections measured (4.4° ≤ 2Θ ≤ 57.528°), 7532 unique (R_{int} = 0.0559, R_{sigma} = 0.0337) which were used in all calculations. The final R_1 was 0.0648 (I > 2σ(I)) and wR_2 was 0.1690 (all data).

Table 83: Crystal data and structure refinement for **145jj**.

Compound	**145jj**
CCDC number	1979314
Identification code	0700_CG_0m
Empirical formula	$C_{17}H_{20}N_2O$
Formula weight	268.35
Temperature/K	100.0
Crystal system	monoclinic
Space group	P2/c
a/Å	20.7094(15)
b/Å	5.3605(4)
c/Å	27.2622(18)
α/°	90
β/°	106.154(2)
γ/°	90
Volume/Å^3	2907.0(4)
Z	8
ρ_{calc}g/cm^3	1.226
μ/mm^{-1}	0.077
F(000)	1152.0
Crystal size/mm^3	0.405 × 0.162 × 0.145
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.4 to 57.528
Index ranges	-28 ≤ h ≤ 27, -7 ≤ k ≤ 7, -36 ≤ l ≤ 36
Reflections collected	56579

Independent reflections	7532 [R_{int} = 0.0559, R_{sigma} = 0.0337]
Data/restraints/parameters	7532/0/363
Goodness-of-fit on F^2	1.122
Final R indexes [I>=2σ (I)]	R_1 = 0.0648, wR_2 = 0.1655
Final R indexes [all data]	R_1 = 0.0709, wR_2 = 0.1690
Largest diff. peak/hole / e $Å^{-3}$	0.45/-0.29

Table 84: Selected bond lengths [Å] for **145jj**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C1	1.214(2)	C4	C8	1.515(2)
N1	N2	1.363(2)	C5	C6	1.390(2)
N1	C5	1.427(2)	C6	C7	1.387(3)
N1	C15	1.361(2)	C8	C9	1.536(3)
N2	C17	1.331(2)	C8	C13	1.539(3)
C1	C2	1.503(2)	C9	C10	1.527(2)
C1	C14	1.503(3)	C10	C11	1.527(3)
C2	C3	1.393(2)	C11	C12	1.529(3)
C2	C7	1.395(3)	C12	C13	1.530(3)
C3	C4	1.399(2)	C15	C16	1.367(3)
C4	C5	1.402(2)	C16	C17	1.402(3)

Table 85: Selected bond angles [°] for **145jj**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N2	N1	C5	120.98(15)	C6	C5	N1	116.44(16)
C15	N1	N2	111.92(15)	C6	C5	C4	122.00(16)
C15	N1	C5	126.38(15)	C7	C6	C5	120.32(17)
C17	N2	N1	103.99(15)	C6	C7	C2	119.21(16)
O1	C1	C2	120.17(17)	C4	C8	C9	111.09(15)
O1	C1	C14	121.75(17)	C4	C8	C13	111.69(15)
C2	C1	C14	118.07(16)	C9	C8	C13	110.35(15)
C3	C2	C1	118.47(16)	C10	C9	C8	111.31(15)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C3	C2	C7	119.51(16)	C11	C10	C9	111.27(15)
C7	C2	C1	121.99(16)	C10	C11	C12	110.86(16)
C2	C3	C4	122.55(17)	C11	C12	C13	111.47(16)
C3	C4	C5	116.26(16)	C12	C13	C8	110.97(15)
C3	C4	C8	119.85(16)	N1	C15	C16	106.98(16)
C5	C4	C8	123.89(16)	C15	C16	C17	104.77(16)
C4	C5	N1	121.56(16)	N2	C17	C16	112.33(16)

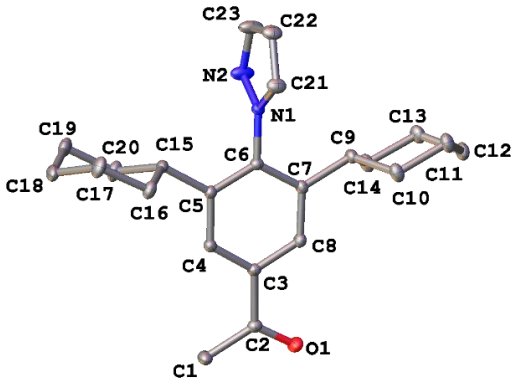


Figure 56: Molecular structure of **145jj'** with thermal ellipsoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{23}H_{30}N_2O$ (*M* = 350.49 g/mol): triclinic, space group P-1 (no. 2), *a* = 5.8157(4) Å, *b* = 10.5817(8) Å, *c* = 16.4884(12) Å, *α* = 79.072(3)°, *β* = 84.757(2)°, *γ* = 81.344(3)°, *V* = 982.88(12) Å^3, *Z* = 2, *T* = 100.01 K, μ(MoKα) = 0.072 mm^{-1}, *Dcalc* = 1.184 g/cm^3, 36020 reflections measured (5.042° ≤ 2Θ ≤ 57.588°), 5088 unique (R_{int} = 0.0191, R_{sigma} = 0.0142) which were used in all calculations. The final R_1 was 0.0395 (I > 2σ(I)) and wR_2 was 0.1053 (all data).

Table 86: Crystal data and structure refinement for **145jj'**.

Compound	**145jj'**
CCDC number	1979313
Identification code	0687_CG_0m
Empirical formula	$C_{23}H_{30}N_2O$
Formula weight	350.49

Temperature/K	100.01
Crystal system	triclinic
Space group	P-1
a/Å	5.8157(4)
b/Å	10.5817(8)
c/Å	16.4884(12)
α/°	79.072(3)
β/°	84.757(2)
γ/°	81.344(3)
Volume/Å^3	982.88(12)
Z	2
ρ_{calc}g/cm^3	1.184
μ/mm^{-1}	0.072
F(000)	380.0
Crystal size/mm^3	0.817 × 0.269 × 0.16
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.042 to 57.588
Index ranges	-7 ≤ h ≤ 7, -14 ≤ k ≤ 14, -22 ≤ l ≤ 22
Reflections collected	36020
Independent reflections	5088 [R_{int} = 0.0191, R_{sigma} = 0.0142]
Data/restraints/parameters	5088/0/236
Goodness-of-fit on F^2	1.059
Final R indexes [I>=2σ (I)]	R_1 = 0.0395, wR_2 = 0.1044
Final R indexes [all data]	R_1 = 0.0407, wR_2 = 0.1053
Largest diff. peak/hole / e Å^{-3}	0.40/-0.25

Table 87: Bond lengths [Å] for **145jj'**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C2	1.2196(11)	C9	C10	1.5348(13)
N1	N2	1.3537(11)	C9	C14	1.5352(12)
N1	C6	1.4326(11)	C10	C11	1.5313(13)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N1	C21	1.3516(11)	C11	C12	1.5273(14)
N2	C23	1.3333(13)	C12	C13	1.5263(14)
C1	C2	1.5020(12)	C13	C14	1.5282(12)
C2	C3	1.5045(12)	C15	C16	1.5364(13)
C3	C4	1.3963(12)	C15	C20	1.5359(13)
C3	C8	1.3934(12)	C16	C17	1.5339(13)
C4	C5	1.4015(12)	C17	C18	1.5254(14)
C5	C6	1.4026(12)	C18	C19	1.5208(15)
C5	C15	1.5196(11)	C19	C20	1.5319(13)
C6	C7	1.4054(12)	C21	C22	1.3716(13)
C7	C8	1.3911(12)	C22	C23	1.3967(14)
C7	C9	1.5153(12)			

Table 88: Bond angles [°] for **145jj'**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N2	N1	C6	120.46(7)	C7	C8	C3	121.68(8)
C21	N1	N2	112.15(8)	C7	C9	C10	111.30(7)
C21	N1	C6	127.32(8)	C7	C9	C14	110.43(7)
C23	N2	N1	103.86(8)	C10	C9	C14	110.53(7)
O1	C2	C1	121.09(8)	C11	C10	C9	111.04(8)
O1	C2	C3	119.40(8)	C12	C11	C10	111.30(8)
C1	C2	C3	119.49(8)	C13	C12	C11	110.34(8)
C4	C3	C2	123.33(8)	C12	C13	C14	111.18(8)
C8	C3	C2	117.19(8)	C13	C14	C9	112.24(8)
C8	C3	C4	119.42(8)	C5	C15	C16	110.95(7)
C3	C4	C5	121.15(8)	C5	C15	C20	111.40(7)
C4	C5	C6	117.53(8)	C20	C15	C16	110.98(7)
C4	C5	C15	120.29(7)	C17	C16	C15	112.20(8)
C6	C5	C15	122.17(8)	C18	C17	C16	111.59(8)
C5	C6	N1	119.12(7)	C19	C18	C17	110.59(8)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C5	C6	C7	122.69(8)	C18	C19	C20	110.94(8)
C7	C6	N1	118.19(7)	C19	C20	C15	111.72(8)
C6	C7	C9	122.69(8)	N1	C21	C22	107.31(8)
C8	C7	C6	117.50(8)	C21	C22	C23	104.11(9)
C8	C7	C9	119.79(8)	N2	C23	C22	112.56(9)

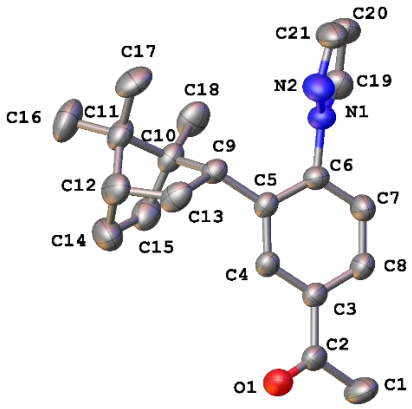


Figure 57: Molecular structure of *endo*-**145jx** with thermal ellipsoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{21}H_{26}N_2O$ (*M* = 322.44 g/mol): monoclinic, space group Cc (no. 9), *a* = 10.588(6) Å, *b* = 19.131(10) Å, *c* = 10.302(6) Å, *β* = 118.335(11)°, *V* = 1836.9(17) Å^3, *Z* = 4, *T* = 300 K, μ(MoKα) = 0.072 mm^{-1}, *Dcalc* = 1.166 g/cm^3, 35887 reflections measured (4.862° ≤ 2Θ ≤ 55.924°), 4332 unique (R_{int} = 0.0350, R_{sigma} = 0.0234) which were used in all calculations. The final R_1 was 0.0420 (I > 2σ(I)) and wR_2 was 0.1202 (all data).

Table 89: Crystal data and structure refinement for *endo*-**145jx**.

Compound	*endo*-**145jx**
CCDC number	2016734
Identification code	mo_1053_CG_0m
Empirical formula	$C_{21}H_{26}N_2O$
Formula weight	322.44
Temperature/K	300

Crystal system	monoclinic
Space group	Cc
a/Å	10.588(6)
b/Å	19.131(10)
c/Å	10.302(6)
α/°	90
β/°	118.335(11)
γ/°	90
Volume/Å^3	1836.9(17)
Z	4
ρ_{calc}g/cm^3	1.166
μ/mm^{-1}	0.072
F(000)	696.0
Crystal size/mm^3	0.386 × 0.191 × 0.052
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.862 to 55.924
Index ranges	-13 ≤ h ≤ 13, -24 ≤ k ≤ 25, -13 ≤ l ≤ 13
Reflections collected	35887
Independent reflections	4332 [R_{int} = 0.0350, R_{sigma} = 0.0234]
Data/restraints/parameters	4332/2/221
Goodness-of-fit on F^2	1.075
Final R indexes [I>=2σ (I)]	R_1 = 0.0420, wR_2 = 0.1132
Final R indexes [all data]	R_1 = 0.0489, wR_2 = 0.1202
Largest diff. peak/hole / e Å^{-3}	0.21/-0.18
Flack parameter	0.1(4)

Table 90: Bond lengths [Å] for *endo*-**145jx**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C2	1.215(3)	C9	C10	1.559(3)
N1	N2	1.353(3)	C9	C13	1.559(3)
N1	C6	1.432(3)	C10	C11	1.567(3)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N1	C19	1.340(4)	C10	C15	1.534(4)
N2	C21	1.318(4)	C10	C18	1.506(4)
C1	C2	1.502(4)	C11	C12	1.534(4)
C2	C3	1.489(3)	C11	C16	1.530(4)
C3	C4	1.395(3)	C11	C17	1.528(4)
C3	C8	1.385(3)	C12	C13	1.539(4)
C4	C5	1.394(3)	C12	C14	1.518(5)
C5	C6	1.410(3)	C14	C15	1.542(5)
C5	C9	1.513(3)	C19	C20	1.364(5)
C6	C7	1.382(3)	C20	C21	1.385(6)
C7	C8	1.371(4)			

Table 91: Bond angles [°] for *endo*-**145jx**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N2	N1	C6	120.5(2)	C9	C10	C11	100.54(18)
C19	N1	N2	112.1(2)	C15	C10	C9	108.8(2)
C19	N1	C6	126.9(2)	C15	C10	C11	101.5(2)
C21	N2	N1	104.4(3)	C18	C10	C9	114.0(2)
O1	C2	C1	120.7(2)	C18	C10	C11	116.5(2)
O1	C2	C3	121.1(2)	C18	C10	C15	114.0(2)
C3	C2	C1	118.3(2)	C12	C11	C10	93.0(2)
C4	C3	C2	119.4(2)	C16	C11	C10	113.3(3)
C8	C3	C2	121.2(2)	C16	C11	C12	114.8(3)
C8	C3	C4	119.3(2)	C17	C11	C10	115.0(2)
C5	C4	C3	122.8(2)	C17	C11	C12	113.7(3)
C4	C5	C6	115.57(19)	C17	C11	C16	107.0(3)
C4	C5	C9	123.3(2)	C11	C12	C13	103.3(2)
C6	C5	C9	121.14(19)	C14	C12	C11	102.7(3)
C5	C6	N1	122.2(2)	C14	C12	C13	106.8(2)
C7	C6	N1	115.9(2)	C12	C13	C9	103.6(2)
C7	C6	C5	121.9(2)	C12	C14	C15	102.9(3)

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C8	C7	C6	120.7(2)	C10	C15	C14	104.0(2)
C7	C8	C3	119.6(2)	N1	C19	C20	106.6(3)
C5	C9	C10	116.03(17)	C19	C20	C21	105.2(3)
C5	C9	C13	117.54(19)	N2	C21	C20	111.8(3)
C13	C9	C10	101.97(19)				

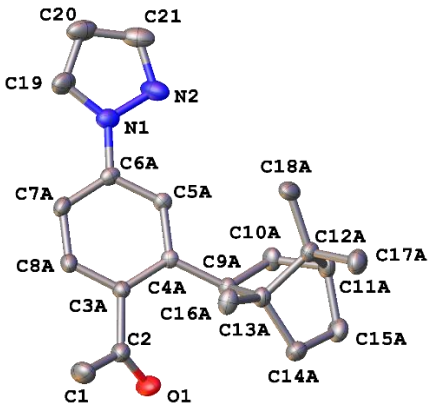


Figure 58: Molecular structure of *exo*-**146jx** with thermal ellipsoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{21}H_{26}N_2O$ (*M* = 322.44 g/mol): orthorhombic, space group Pbca (no. 61), *a* = 18.2576(9) Å, *b* = 9.0892(4) Å, *c* = 21.3228(9) Å, *V* = 3538.5(3) Å^3, *Z* = 8, *T* = 100.0 K, μ(MoKα) = 0.074 mm^{-1}, *Dcalc* = 1.211 g/cm^3, 108209 reflections measured (3.82° ≤ 2Θ ≤ 59.25°), 4981 unique (R_{int} = 0.0595, R_{sigma} = 0.0246) which were used in all calculations. The final R_1 was 0.0759 (I > 2σ(I)) and wR_2 was 0.1690 (all data).

Table 92: Crystal data and structure refinement for *exo*-**146jx**.

Compound	*exo*-**146jx**
CCDC number	2016645
Identification code	mo_1036_CG_0m
Empirical formula	$C_{21}H_{26}N_2O$
Formula weight	322.44

Temperature/K	100.0
Crystal system	orthorhombic
Space group	Pbca
a/Å	18.2576(9)
b/Å	9.0892(4)
c/Å	21.3228(9)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	3538.5(3)
Z	8
ρ_{calc}g/cm^3	1.211
μ/mm^{-1}	0.074
F(000)	1392.0
Crystal size/mm^3	0.409 × 0.367 × 0.307
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.82 to 59.25
Index ranges	-24 ≤ h ≤ 25, -12 ≤ k ≤ 12, -29 ≤ l ≤ 29
Reflections collected	108209
Independent reflections	4981 [R_{int} = 0.0595, R_{sigma} = 0.0246]
Data/restraints/parameters	4981/252/354
Goodness-of-fit on F^2	1.203
Final R indexes [I>=2σ (I)]	R_1 = 0.0759, wR_2 = 0.1676
Final R indexes [all data]	R_1 = 0.0789, wR_2 = 0.1690
Largest diff. peak/hole / e Å^{-3}	0.44/-0.26

Table 93: Selected bond lengths [Å] for *exo*-**146jx**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C2	1.217(2)	C9A	C10A	1.558(4)
N1	N2	1.368(3)	C9A	C13A	1.587(3)
N1	C6A	1.396(3)	C10A	C11A	1.525(4)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N1	C19	1.354(3)	C11A	C12A	1.541(5)
N2	C21	1.328(3)	C11A	C15A	1.544(4)
C1	C2	1.511(3)	C12A	C13A	1.569(5)
C2	C3A	1.529(3)	C12A	C17A	1.530(5)
C3A	C4A	1.415(3)	C12A	C18A	1.544(4)
C3A	C8A	1.398(3)	C13A	C14A	1.560(3)
C4A	C5A	1.396(3)	C13A	C16A	1.516(3)
C4A	C9A	1.521(3)	C14A	C15A	1.552(4)
C5A	C6A	1.394(3)	C19	C20	1.369(3)
C6A	C7A	1.386(3)	C20	C21	1.393(4)
C7A	C8A	1.386(3)			

Table 94: Selected bond angles [°] for *exo*-**146jx**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N2	N1	C6A	120.4(2)	C11A	C10A	C9A	103.5(2)
C19	N1	N2	111.42(18)	C10A	C11A	C12A	103.2(2)
C19	N1	C6A	128.1(2)	C10A	C11A	C15A	106.6(2)
C21	N2	N1	104.2(2)	C12A	C11A	C15A	102.6(2)
O1	C2	C1	120.21(19)	C11A	C12A	C13A	93.6(3)
O1	C2	C3A	121.8(2)	C11A	C12A	C18A	114.4(3)
C1	C2	C3A	118.0(2)	C17A	C12A	C11A	112.8(3)
C4A	C3A	C2	124.5(3)	C17A	C12A	C13A	114.6(2)
C8A	C3A	C2	115.6(3)	C17A	C12A	C18A	106.8(3)
C8A	C3A	C4A	119.9(2)	C18A	C12A	C13A	114.5(3)
C3A	C4A	C9A	121.3(2)	C12A	C13A	C9A	104.4(2)
C5A	C4A	C3A	116.99(19)	C14A	C13A	C9A	102.92(18)
C5A	C4A	C9A	121.7(2)	C14A	C13A	C12A	100.0(2)
C6A	C5A	C4A	122.1(2)	C16A	C13A	C9A	116.66(19)
C5A	C6A	N1	117.5(3)	C16A	C13A	C12A	117.2(2)
C7A	C6A	N1	121.7(3)	C16A	C13A	C14A	113.4(2)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C7A	C6A	C5A	120.8(2)	C15A	C14A	C13A	102.73(19)
C6A	C7A	C8A	117.7(2)	C11A	C15A	C14A	103.7(2)
C7A	C8A	C3A	122.4(2)	N1	C19	C20	107.2(2)
C4A	C9A	C10A	117.1(2)	C19	C20	C21	104.8(2)
C4A	C9A	C13A	119.31(18)	N2	C21	C20	112.3(2)
C10A	C9A	C13A	102.3(2)				

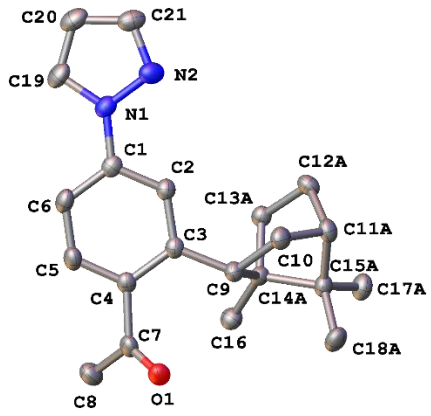


Figure 59: Molecular structure of *endo*-**146jx** with thermal ellipsoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{21}H_{26}N_2O$ (*M* = 322.44 g/mol): orthorhombic, space group Pbca (no. 61), *a* = 18.2383(3) Å, *b* = 9.1329(2) Å, *c* = 21.4131(4) Å, *V* = 3566.75(12) Å^3, *Z* = 8, *T* = 100.0 K, μ(CuKα) = 0.573 mm^{-1}, *Dcalc* = 1.201 g/cm^3, 136327 reflections measured (8.258° ≤ 2Θ ≤ 159.994°), 3880 unique (R_{int} = 0.0354, R_{sigma} = 0.0087) which were used in all calculations. The final R_1 was 0.0524 (I > 2σ(I)) and wR_2 was 0.1295 (all data).

Table 95: Crystal data and structure refinement for *endo*-**146jx**.

Compound	*endo*-**146jx**
CCDC number	2016646
Identification code	1041_Pbca
Empirical formula	$C_{21}H_{26}N_2O$
Formula weight	322.44
Temperature/K	100.0

Crystal system	orthorhombic
Space group	Pbca
a/Å	18.2383(3)
b/Å	9.1329(2)
c/Å	21.4131(4)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	3566.75(12)
Z	8
ρ_{calc}g/cm^3	1.201
μ/mm^{-1}	0.573
F(000)	1392.0
Crystal size/mm^3	0.26 × 0.247 × 0.197
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	8.258 to 159.994
Index ranges	-23 ≤ h ≤ 23, -11 ≤ k ≤ 11, -27 ≤ l ≤ 27
Reflections collected	136327
Independent reflections	3880 [R_{int} = 0.0354, R_{sigma} = 0.0087]
Data/restraints/parameters	3880/60/287
Goodness-of-fit on F^2	1.138
Final R indexes [I>=2σ (I)]	R_1 = 0.0524, wR_2 = 0.1291
Final R indexes [all data]	R_1 = 0.0531, wR_2 = 0.1295
Largest diff. peak/hole / e Å^{-3}	0.31/-0.24

Table 96: Selected bond lengths [Å] for *endo*-**146jx**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C7	1.2166(19)	C9	C10	1.568(2)
N1	N2	1.365(2)	C9	C14A	1.588(2)
N1	C1	1.419(2)	C10	C11A	1.562(3)
N1	C19	1.363(2)	C11A	C12A	1.538(3)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N2	C21	1.332(2)	C11A	C15A	1.556(3)
C1	C2	1.391(2)	C12A	C13A	1.557(3)
C1	C6	1.385(2)	C13A	C14A	1.543(3)
C2	C3	1.397(2)	C14A	C15A	1.571(3)
C3	C4	1.412(2)	C14A	C16	1.490(2)
C3	C9	1.514(2)	C15A	C17A	1.531(3)
C4	C5	1.396(2)	C15A	C18A	1.526(3)
C4	C7	1.505(2)	C19	C20	1.363(3)
C5	C6	1.383(2)	C20	C21	1.397(3)
C7	C8	1.509(2)			

Table 97: Selected bond angles [°] for *endo*-**146jx**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N2	N1	C1	120.35(13)	C11A	C10	C9	102.96(13)
C19	N1	N2	111.27(14)	C12A	C11A	C10	108.17(17)
C19	N1	C1	128.28(14)	C12A	C11A	C15A	102.42(18)
C21	N2	N1	104.44(14)	C15A	C11A	C10	102.76(15)
C2	C1	N1	119.06(14)	C11A	C12A	C13A	102.78(16)
C6	C1	N1	120.49(14)	C14A	C13A	C12A	104.05(15)
C6	C1	C2	120.44(14)	C13A	C14A	C9	109.29(15)
C1	C2	C3	121.79(14)	C13A	C14A	C15A	101.35(15)
C2	C3	C4	117.61(13)	C15A	C14A	C9	100.24(15)
C2	C3	C9	120.51(13)	C16	C14A	C9	114.26(15)
C4	C3	C9	121.84(13)	C16	C14A	C13A	113.31(17)
C3	C4	C7	123.97(13)	C16	C14A	C15A	116.93(16)
C5	C4	C3	119.47(14)	C11A	C15A	C14A	93.20(14)
C5	C4	C7	116.52(13)	C17A	C15A	C11A	113.62(17)
C6	C5	C4	122.23(15)	C17A	C15A	C14A	113.88(18)
C5	C6	C1	118.33(14)	C18A	C15A	C11A	113.71(18)
O1	C7	C4	121.79(15)	C18A	C15A	C14A	115.15(18)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
O1	C7	C8	120.83(15)	C18A	C15A	C17A	107.10(18)
C4	C7	C8	117.36(14)	N1	C19	C20	107.22(16)
C3	C9	C10	117.07(13)	C19	C20	C21	105.15(15)
C3	C9	C14A	113.48(14)	N2	C21	C20	111.92(17)
C10	C9	C14A	102.80(13)				

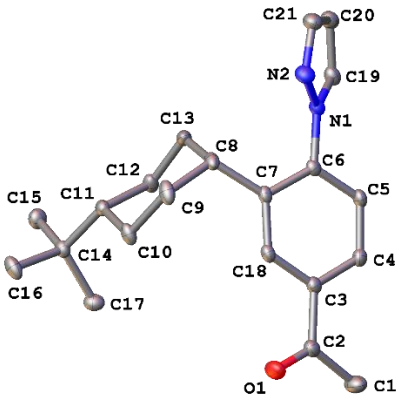


Figure 60: Molecular structure of *cis*-**145js** with thermal ellipsoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{21}H_{28}N_2O$ (*M* =324.45 g/mol): orthorhombic, space group $Pna2_1$ (no. 33), *a* = 16.476(3) Å, *b* = 18.989(4) Å, *c* = 5.7847(9) Å, *V* = 1809.9(6) Å^3, *Z* = 4, *T* = 100.0 K, μ(MoKα) = 0.073 mm^{-1}, *Dcalc* = 1.191 g/cm^3, 130203 reflections measured (4.29° ≤ 2Θ ≤ 57.42°), 4675 unique (R_{int} = 0.0354, R_{sigma} = 0.0114) which were used in all calculations. The final R_1 was 0.0296 (I > 2σ(I)) and wR_2 was 0.0774 (all data).

Table 98: Crystal data and structure refinement for *cis*-**145js**.

Compound	*cis*-**145js**
CCDC number	2016647
Identification code	1048_Pna21
Empirical formula	$C_{21}H_{28}N_2O$
Formula weight	324.45
Temperature/K	100.0
Crystal system	orthorhombic

Space group	$Pna2_1$
a/Å	16.476(3)
b/Å	18.989(4)
c/Å	5.7847(9)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1809.9(6)
Z	4
ρ_{calc}g/cm^3	1.191
μ/mm^{-1}	0.073
F(000)	704.0
Crystal size/mm^3	0.384 × 0.19 × 0.038
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.29 to 57.42
Index ranges	-22 ≤ h ≤ 22, -25 ≤ k ≤ 25, -7 ≤ l ≤ 7
Reflections collected	130203
Independent reflections	4675 [R_{int} = 0.0354, R_{sigma} = 0.0114]
Data/restraints/parameters	4675/1/221
Goodness-of-fit on F^2	1.040
Final R indexes [I>=2σ (I)]	R_1 = 0.0296, wR_2 = 0.0761
Final R indexes [all data]	R_1 = 0.0308, wR_2 = 0.0774
Largest diff. peak/hole / e Å^{-3}	0.22/-0.15
Flack parameter	-0.08(19)

Table 99: Bond lengths [Å] for *cis*-**145js**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C2	1.2190(18)	C7	C18	1.3894(18)
N1	N2	1.3637(16)	C8	C9	1.533(2)
N1	C6	1.4277(16)	C8	C13	1.546(2)
N1	C19	1.3601(17)	C9	C10	1.5394(18)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N2	C21	1.3305(18)	C10	C11	1.5307(18)
C1	C2	1.501(2)	C11	C12	1.5341(18)
C2	C3	1.4988(18)	C11	C14	1.5557(17)
C3	C4	1.3937(18)	C12	C13	1.528(2)
C3	C18	1.4004(18)	C14	C15	1.5342(18)
C4	C5	1.3911(18)	C14	C16	1.5357(19)
C5	C6	1.3915(18)	C14	C17	1.5319(19)
C6	C7	1.4135(17)	C19	C20	1.373(2)
C7	C8	1.5241(18)	C20	C21	1.407(2)

Table 100: Bond angles [°] for *cis*-**145js**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N2	N1	C6	120.79(11)	C7	C8	C13	110.17(12)
C19	N1	N2	112.21(11)	C9	C8	C13	109.05(11)
C19	N1	C6	126.99(12)	C8	C9	C10	116.27(12)
C21	N2	N1	103.96(12)	C11	C10	C9	112.75(11)
O1	C2	C1	120.92(13)	C10	C11	C12	107.91(10)
O1	C2	C3	120.01(13)	C10	C11	C14	113.33(10)
C3	C2	C1	119.07(12)	C12	C11	C14	113.90(11)
C4	C3	C2	122.61(12)	C13	C12	C11	111.60(12)
C4	C3	C18	119.37(12)	C12	C13	C8	112.68(11)
C18	C3	C2	118.01(12)	C15	C14	C11	109.82(11)
C5	C4	C3	119.40(12)	C15	C14	C16	107.92(11)
C4	C5	C6	120.13(12)	C16	C14	C11	110.02(11)
C5	C6	N1	117.22(11)	C17	C14	C11	112.27(10)
C5	C6	C7	121.87(11)	C17	C14	C15	108.55(11)
C7	C6	N1	120.91(11)	C17	C14	C16	108.15(11)
C6	C7	C8	121.26(11)	C7	C18	C3	122.76(12)
C18	C7	C6	116.18(12)	N1	C19	C20	106.89(13)
C18	C7	C8	122.48(11)	C19	C20	C21	104.55(13)
C7	C8	C9	116.23(12)	N2	C21	C20	112.37(13)

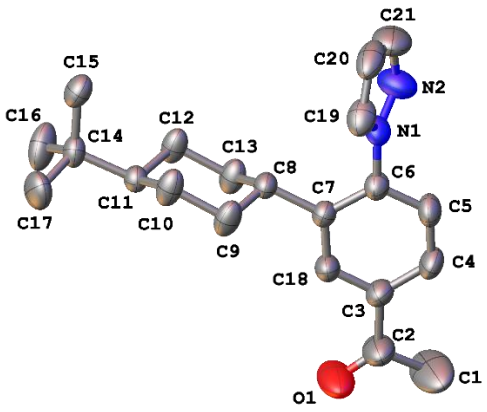


Figure 61: Molecular structure of *trans*-**145js** with thermal ellipsoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{21}H_{28}N_2O$ (*M* = 324.45 g/mol): triclinic, space group P-1 (no. 2), *a* = 5.9333(2) Å, *b* = 10.3005(3) Å, *c* = 16.2603(5) Å, *α* = 98.9640(10)°, *β* = 99.7430(10)°, *γ* = 91.3860(10)°, *V* = 966.16(5) Å^3, *Z* = 2, *T* = 300.0 K, μ(MoKα) = 0.068 mm^{-1}, *Dcalc* = 1.115 g/cm^3, 7889 reflections measured (5.104° ≤ 2Θ ≤ 55.832°), 7889 unique (R_{int} = ?, R_{sigma} = 0.0275) which were used in all calculations. The final R_1 was 0.0670 (I > 2σ(I)) and wR_2 was 0.1864 (all data).

Table 101: Crystal data and structure refinement for *trans*-**145js**.

Compound	*trans*-**145js**
CCDC number	2016735
Identification code	mo_1054_CG_0m_4
Empirical formula	$C_{21}H_{28}N_2O$
Formula weight	324.45
Temperature/K	300.0
Crystal system	triclinic
Space group	P-1
a/Å	5.9333(2)
b/Å	10.3005(3)
c/Å	16.2603(5)
α/°	98.9640(10)
β/°	99.7430(10)
γ/°	91.3860(10)

Volume/Å^3	966.16(5)
Z	2
ρ_{calc}g/cm^3	1.115
μ/mm^{-1}	0.068
F(000)	352.0
Crystal size/mm^3	0.376 × 0.302 × 0.084
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.104 to 55.832
Index ranges	-7 ≤ h ≤ 7, -13 ≤ k ≤ 13, -21 ≤ l ≤ 21
Reflections collected	7889
Independent reflections	7889 [R_{int} = ?, R_{sigma} = 0.0275]
Data/restraints/parameters	7889/0/222
Goodness-of-fit on F^2	1.074
Final R indexes [I>=2σ (I)]	R_1 = 0.0670, wR_2 = 0.1752
Final R indexes [all data]	R_1 = 0.0850, wR_2 = 0.1864
Largest diff. peak/hole / e Å^{-3}	0.27/-0.17

Table 102: Bond lengths [Å] for *trans*-**145js**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C2	1.189(4)	C7	C18	1.384(3)
N1	N2	1.343(3)	C8	C9	1.514(3)
N1	C6	1.427(3)	C8	C13	1.517(3)
N1	C19	1.351(3)	C9	C10	1.527(3)
N2	C21	1.333(4)	C10	C11	1.528(3)
C1	C2	1.484(4)	C11	C12	1.519(3)
C2	C3	1.490(3)	C11	C14	1.560(2)
C3	C4	1.390(3)	C12	C13	1.527(3)
C3	C18	1.385(3)	C14	C15	1.531(3)
C4	C5	1.371(3)	C14	C16	1.521(3)
C5	C6	1.387(3)	C14	C17	1.536(3)
C6	C7	1.396(3)	C19	C20	1.353(4)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C7	C8	1.518(2)	C20	C21	1.368(5)

Table 103: Bond angles [°] for *trans*-**145js**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N2	N1	C6	120.08(18)	C9	C8	C13	109.65(16)
N2	N1	C19	112.0(2)	C13	C8	C7	110.92(16)
C19	N1	C6	127.9(2)	C8	C9	C10	111.17(18)
C21	N2	N1	103.2(3)	C9	C10	C11	112.48(18)
O1	C2	C1	119.8(3)	C10	C11	C14	114.00(16)
O1	C2	C3	120.8(3)	C12	C11	C10	107.91(16)
C1	C2	C3	119.4(3)	C12	C11	C14	114.16(16)
C4	C3	C2	122.1(2)	C11	C12	C13	112.26(18)
C18	C3	C2	118.7(2)	C8	C13	C12	111.61(17)
C18	C3	C4	119.1(2)	C15	C14	C11	111.49(17)
C5	C4	C3	119.49(19)	C15	C14	C17	108.29(19)
C4	C5	C6	120.5(2)	C16	C14	C11	110.63(17)
C5	C6	N1	118.02(18)	C16	C14	C15	108.7(2)
C5	C6	C7	121.44(19)	C16	C14	C17	108.3(2)
C7	C6	N1	120.52(17)	C17	C14	C11	109.31(18)
C6	C7	C8	122.51(17)	C7	C18	C3	122.8(2)
C18	C7	C6	116.55(17)	N1	C19	C20	107.0(3)
C18	C7	C8	120.80(17)	C19	C20	C21	104.8(2)
C9	C8	C7	113.61(17)	N2	C21	C20	112.9(3)

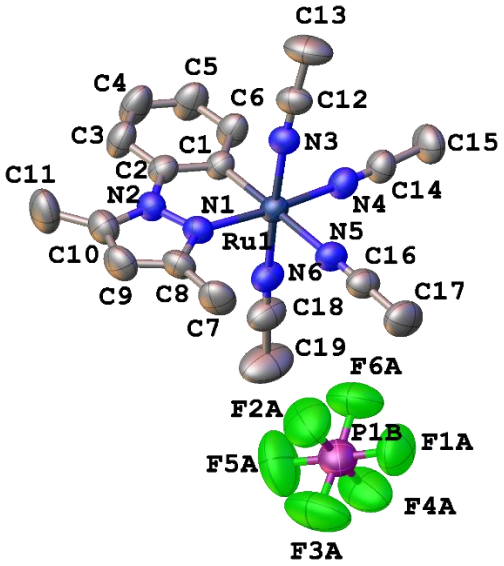


Figure 62: Molecular structure of **204** with thermal ellipsoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{19}H_{23}F_6N_6PRu$ (*M* = 581.47 g/mol): monoclinic, space group $P2_1/n$ (no. 14), *a* = 12.6946(6) Å, *b* = 12.8467(6) Å, *c* = 15.4440(9) Å, *β* = 96.350(2)°, *V* = 2503.2(2) Å^3, *Z* = 4, *T* = 300 K, μ(MoKα) = 0.753 mm^{-1}, *Dcalc* = 1.543 g/cm^3, 54797 reflections measured (3.946° ≤ 2Θ ≤ 55.846°), 5985 unique (R_{int} = 0.0233, R_{sigma} = 0.0138) which were used in all calculations. The final R_1 was 0.0299 (I > 2σ(I)) and wR_2 was 0.0764 (all data).

Table 104: Crystal data and structure refinement for **204**.

Compound	**204**
CCDC number	2017186
Identification code	mo_1055_CG_0m
Empirical formula	$C_{19}H_{23}F_6N_6PRu$
Formula weight	581.47
Temperature/K	300
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	12.6946(6)
b/Å	12.8467(6)
c/Å	15.4440(9)

α/°	90
β/°	96.350(2)
γ/°	90
Volume/Å^3	2503.2(2)
Z	4
ρ_{calc}g/cm^3	1.543
μ/mm^{-1}	0.753
F(000)	1168.0
Crystal size/mm^3	0.369 × 0.338 × 0.128
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.946 to 55.846
Index ranges	-16 ≤ h ≤ 16, -16 ≤ k ≤ 16, -20 ≤ l ≤ 20
Reflections collected	54797
Independent reflections	5985 [R_{int} = 0.0233, R_{sigma} = 0.0138]
Data/restraints/parameters	5985/6/359
Goodness-of-fit on F^2	1.187
Final R indexes [I>=2σ (I)]	R_1 = 0.0299, wR_2 = 0.0756
Final R indexes [all data]	R_1 = 0.0314, wR_2 = 0.0764
Largest diff. peak/hole / e Å^{-3}	0.37/-0.37

Table 105: Selected bond lengths [Å] for **204**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Ru1	N1	2.0616(18)	C3	C4	1.383(4)
Ru1	N3	2.0128(19)	C4	C5	1.363(4)
Ru1	N4	2.020(2)	C5	C6	1.380(3)
Ru1	N5	2.156(2)	C7	C8	1.491(4)
Ru1	N6	2.010(2)	C8	C9	1.386(4)
Ru1	C1	2.020(2)	C9	C10	1.359(4)
N1	N2	1.382(3)	C10	C11	1.501(4)
N1	C8	1.333(3)	C12	C13	1.458(4)
N2	C2	1.428(3)	C14	C15	1.449(3)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N2	C10	1.359(3)	C16	C17	1.449(4)
N3	C12	1.127(3)	C18	C19	1.463(4)
N4	C14	1.133(3)	P1B	F1A	1.539(4)
N5	C16	1.129(3)	P1B	F2A	1.571(4)
N6	C18	1.123(3)	P1B	F3A	1.513(7)
C1	C2	1.397(3)	P1B	F4A	1.542(4)
C1	C6	1.400(3)	P1B	F5A	1.584(5)
C2	C3	1.381(3)	P1B	F6A	1.557(6)

Table 106: Selected bond angles [°] for **204**.

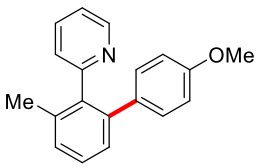
Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N1	Ru1	N5	100.39(7)	C10	C9	C8	108.1(2)
N3	Ru1	N1	93.27(7)	N2	C10	C11	124.8(3)
N3	Ru1	N4	86.93(8)	C9	C10	N2	106.5(2)
N3	Ru1	N5	91.04(7)	C9	C10	C11	128.7(3)
N3	Ru1	C1	89.56(8)	N3	C12	C13	178.7(3)
N4	Ru1	N1	173.12(7)	N4	C14	C15	178.6(3)
N4	Ru1	N5	86.49(7)	N5	C16	C17	179.3(3)
N6	Ru1	N1	89.52(8)	N6	C18	C19	178.9(4)
N6	Ru1	N3	177.21(8)	C2	C3	C4	118.8(2)
N6	Ru1	N4	90.29(8)	C5	C4	C3	120.3(2)
N6	Ru1	N5	88.48(8)	C4	C5	C6	120.2(2)
N6	Ru1	C1	90.94(8)	C5	C6	C1	122.1(2)
C1	Ru1	N1	79.15(8)	N1	C8	C7	122.5(2)
C1	Ru1	N4	93.97(8)	N1	C8	C9	109.1(2)
C1	Ru1	N5	179.26(9)	C9	C8	C7	128.5(2)
N2	N1	Ru1	114.91(12)	F1A	P1B	F2A	92.8(3)
C8	N1	Ru1	138.28(17)	F1A	P1B	F4A	90.4(4)
C8	N1	N2	106.50(18)	F1A	P1B	F5A	176.7(4)
N1	N2	C2	115.17(17)	F1A	P1B	F6A	80.3(4)
C10	N2	N1	109.84(19)	F2A	P1B	F5A	88.4(4)

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C10	N2	C2	134.9(2)	F3A	P1B	F1A	101.3(6)
C12	N3	Ru1	173.41(19)	F3A	P1B	F2A	89.9(5)
C14	N4	Ru1	177.2(2)	F3A	P1B	F4A	93.1(4)
C16	N5	Ru1	173.7(2)	F3A	P1B	F5A	81.7(5)
C18	N6	Ru1	176.8(2)	F3A	P1B	F6A	176.2(5)
C2	C1	Ru1	116.00(15)	F4A	P1B	F2A	175.1(5)
C2	C1	C6	115.5(2)	F4A	P1B	F5A	88.3(4)
C6	C1	Ru1	128.49(17)	F4A	P1B	F6A	90.4(4)
C1	C2	N2	114.66(19)	F6A	P1B	F2A	86.5(4)
C3	C2	N2	122.3(2)	F6A	P1B	F5A	96.7(5)
C3	C2	C1	123.0(2)				

5.3.7 Photo-Induced Ruthenium-Catalyzed C–H Arylations at Room Temperature

5.3.7.1 Characterization Data for 151 and 214

2-(4'-Methoxy-3-methyl-[1,1'-biphenyl]-2-yl)pyridine (151a)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 1-iodo-4-methoxybenzene (**46a**, 176 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 7:1) yielded **151a** (129 mg, 94%) as a viscous colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.64 (ddd, *J* = 4.9, 1.9, 1.1 Hz, 1H), 7.46 (ddd, *J* = 7.8, 7.7, 1.9 Hz, 1H), 7.34 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.28–7.23 (m, 2H), 7.09 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 6.88 (ddd, *J* = 7.8, 1.2, 1.1 Hz, 1H), 6.68 (d, *J* = 8.8 Hz, 2H), 3.73 (s, 3H), 2.17 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.8 (C_q), 158.0 (C_q), 148.9 (CH), 140.8 (C_q), 139.3 (C_q), 136.7 (C_q), 135.7 (CH), 134.1 (C_q), 130.7 (CH), 129.0 (CH), 128.0 (CH), 127.6 (CH), 125.6 (CH), 121.2 (CH), 113.1 (CH), 55.1 (CH_3), 20.5 (CH_3).

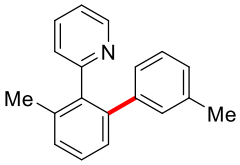
IR (ATR): $\tilde{\nu}$ = 2954, 2835, 1609, 1585, 1511, 1458, 1244, 1178, 1029, 748 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 275 (48) $[M]^+$, 274 (100) $[M–H]^+$, 260 (24) $[M–Me]^+$, 231 (20).

HR-MS (ESI): *m*/*z* calcd for $C_{19}H_{18}NO^+$ $[M+H]^+$ 276.1383, found 276.1381.

The spectral data are in accordance with those reported in the literature.[41]

2-(3,3'-Dimethyl-[1,1'-biphenyl]-2-yl)pyridine (151g)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 1-iodo-3-methylbenzene (**46g**, 164 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 15:1) yielded **151g** (114 mg, 88%) as a viscous colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.63 (ddd, *J* = 4.9, 1.9, 1.1 Hz, 1H), 7.45 (ddd, *J* = 7.8, 7.7, 1.9 Hz, 1H), 7.35 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.30–7.25 (m, 2H), 7.09 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 7.03–6.98 (m, 1H), 6.94–6.91 (m, 2H), 6.89 (ddd, *J* = 7.8, 1.2, 1.1 Hz, 1H), 6.87–6.83 (m, 1H), 2.20 (s, 3H), 2.19 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.7 (C_q), 148.7 (CH), 141.5 (C_q), 141.3 (C_q), 139.3 (C_q), 137.1 (C_q), 136.6 (C_q), 135.6 (CH), 130.5 (CH), 129.3 (CH), 128.0 (CH), 127.5 (CH), 127.4 (CH), 126.9 (CH), 126.7 (CH), 125.6 (CH), 121.2 (CH), 21.2 (CH_3), 20.5 (CH_3).

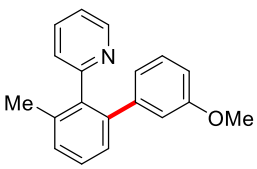
IR (ATR): $\tilde{\nu}$ = 3058, 2920, 1584, 1562, 1459, 1423, 1024, 776, 746, 705 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 282 (52) $[M+Na]^+$, 260 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{19}H_{18}N^+$ $[M+H]^+$ 260.1434, found 260.1428.

The spectral data are in accordance with those reported in the literature.[143]

2-(3'-Methoxy-3-methyl-[1,1'-biphenyl]-2-yl)pyridine (151h)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 1-iodo-3-methoxybenzene (**46h**, 176 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 7:1) yielded **151h** (114 mg, 82%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.64 (ddd, *J* = 4.9, 1.9, 1.1 Hz, 1H), 7.46 (ddd, *J* = 7.7, 7.6, 1.9 Hz, 1H), 7.36 (dd, *J* = 7.9, 7.1 Hz, 1H), 7.31–7.27 (m, 2H), 7.10 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 7.07 (dd, *J*

= 8.2, 7.6 Hz, 1H), 6.90 (ddd, *J* = 7.7, 1.2, 1.1 Hz, 1H), 6.72 (ddd, *J* = 7.6, 1.6, 1.0 Hz, 1H), 6.67 (ddd, *J* = 8.2, 2.6, 1.0 Hz, 1H), 6.59 (dd, *J* = 2.6, 1.6 Hz, 1H), 3.59 (s, 3H), 2.19 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.7 (C_q), 158.7 (C_q), 148.7 (CH), 143.0 (C_q), 141.0 (C_q), 139.2 (C_q), 136.7 (C_q), 135.8 (CH), 129.5 (CH), 128.6 (CH), 128.0 (CH), 127.4 (CH), 125.6 (CH), 122.0 (CH), 121.3 (CH), 114.6 (CH), 112.8 (CH), 55.0 (CH_3), 20.4 (CH_3).

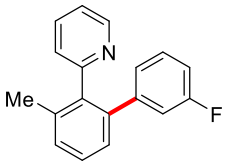
IR (ATR): $\tilde{\nu}$ = 2955, 1576, 1463, 1413, 1226, 1039, 778, 747, 702 cm^{-1}.

MS (EI) *m/z* (relative intensity): 275 (41) $[M]^+$, 274 (100) $[M–H]^+$, 258 (20), 231 (15).

HR-MS (ESI): *m/z* calcd for $C_{19}H_{17}NONa^+$ $[M+Na]^+$ 298.1202, found 298.1207.

The spectral data are in accordance with those reported in the literature.[143]

2-(3'-Fluoro-3-methyl-[1,1'-biphenyl]-2-yl)pyridine (151i)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 1-fluoro-3-iodobenzene (**46i**, 167 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 15:1) yielded **151i** (73.3 mg, 56%) as a viscous colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.63 (ddd, *J* = 4.9, 1.8, 1.1 Hz, 1H), 7.48 (ddd, *J* = 7.8, 7.7, 1.8 Hz, 1H), 7.37 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.31 (ddd, *J* = 7.6, 1.6, 0.8 Hz, 1H), 7.27–7.23 (m, 1H), 7.12 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 7.11–7.04 (m, 1H), 6.91 (ddd, *J* = 7.8, 1.2, 1.1 Hz, 1H), 6.85–6.78 (m, 3H), 2.18 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 162.2 (d, $^{1}J_{C–F}$ = 245 Hz, C_q), 159.2 (C_q), 149.0 (CH), 143.9 (d, $^{3}J_{C–F}$ = 8 Hz, C_q), 140.0 (d, $^{4}J_{C–F}$ = 2 Hz, C_q), 139.3 (C_q), 136.8 (C_q), 135.8 (CH), 129.8 (CH), 128.9 (d, $^{3}J_{C–F}$ = 8 Hz, CH), 128.1 (CH), 127.4 (CH), 125.5 (CH), 125.4 (d, $^{4}J_{C–F}$ = 3 Hz, CH), 121.5 (CH), 116.5 (d, $^{2}J_{C–F}$ = 22 Hz, CH), 113.1 (d, $^{2}J_{C–F}$ = 21 Hz, CH), 20.4 (CH_3).

^{19}F-NMR (376 MHz, $CDCl_3$): δ = (–114.1)–(–114.2) (m).

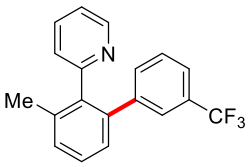
IR (ATR): $\tilde{\nu}$ = 3061, 1611, 1577, 1461, 1416, 1194, 1156, 874, 779, 699 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 286 (67) $[M+Na]^+$, 264 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{18}H_{15}FN^+$ $[M+H]^+$ 264.1183, found 264.1184.

The spectral data are in accordance with those reported in the literature.[143]

2-[3-Methyl-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl]pyridine (151j)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 1-iodo-3-(trifluoromethyl)benzene (**46j**, 204 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 15:1) yielded **151j** (80.2 mg, 51%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.62 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.48 (ddd, *J* = 7.8, 7.7, 1.8 Hz, 1H), 7.41–7.31 (m, 4H), 7.30–7.22 (m, 3H), 7.11 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 6.89 (ddd, *J* = 7.8, 1.2, 1.0 Hz, 1H), 2.20 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.0 (C_q), 149.1 (CH), 142.3 (C_q), 139.7 (C_q), 139.4 (C_q), 136.9 (C_q), 135.9 (CH), 132.8 (CH), 130.0 (CH), 129.9 (q, $^{2}J_{C–F}$ = 32 Hz, C_q), 128.2 (CH), 128.0 (CH), 127.3 (CH), 126.5 (q, $^{3}J_{C–F}$ = 4 Hz, CH), 125.5 (CH), 124.0 (q, $^{1}J_{C–F}$ = 272 Hz, C_q), 122.9 (q, $^{3}J_{C–F}$ = 4 Hz, CH), 121.5 (CH), 20.4 (CH_3).

^{19}F-NMR (376 MHz, $CDCl_3$): δ = –62.8 (s).

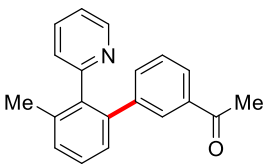
IR (ATR): $\tilde{\nu}$ = 3063, 1585, 1430, 1333, 1271, 1162, 1119, 1070, 783, 748 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 336 (100) $[M+Na]^+$, 314 (98) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{19}H_{14}F_3NNa^+$ $[M+Na]^+$ 336.0971, found 336.0976.

The spectral data are in accordance with those reported in the literature.[144]

1-[3'-Methyl-2'-(pyridin-2-yl)-[1,1'-biphenyl]-3-yl]ethan-1-one (151k)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 1-(3-iodophenyl)ethan-1-one (**46k**, 185 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **151k** (99.0 mg, 69%) as a yellow oil.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.64 (ddd, *J* = 4.9, 1.9, 1.1 Hz, 1H), 7.73 (ddd, *J* = 7.7, 1.6, 1.5 Hz, 1H), 7.64 (dd, *J* = 1.6, 1.6 Hz, 1H), 7.46 (ddd, *J* = 7.8, 7.7, 1.9 Hz, 1H), 7.39 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.35–7.31 (m, 2H), 7.29 (ddd, *J* = 7.6, 1.5, 0.7 Hz, 1H), 7.25 (ddd, *J* = 7.7, 7.7, 0.5 Hz, 1H), 7.11 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 6.90 (ddd, *J* = 7.8, 1.2, 1.1 Hz, 1H), 2.41 (s, 3H), 2.19 (s, 3H).

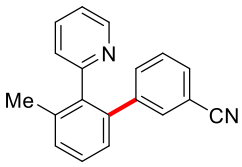
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.0 (C_q), 159.3 (C_q), 149.0 (CH), 141.9 (C_q), 140.1 (C_q), 139.3 (C_q), 136.9 (C_q), 136.4 (C_q), 136.0 (CH), 134.1 (CH), 130.2 (CH), 129.9 (CH), 128.3 (CH), 128.0 (CH), 127.4 (CH), 125.9 (CH), 125.6 (CH), 121.5 (CH), 26.6 (CH_3), 20.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 3060, 1681, 1584, 1562, 1425, 1357, 1242, 782, 749, 698 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 287 (39) $[M]^+$, 286 (100) $[M–H]^+$, 244 (30) $[M–Ac]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{20}H_{18}NO^+$ $[M+H]^+$ 288.1383, found 288.1385.

3'-Methyl-2'-(pyridin-2-yl)-[1,1'-biphenyl]-3-carbonitrile (151l)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 3-iodobenzonitrile (**46l**, 172 mg, 0.75 mmol) in DMA (2.0 mL). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 4:1) yielded **151l** (68.0 mg, 50%) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.62 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.51 (ddd, *J* = 7.8, 7.7, 1.8 Hz, 1H), 7.42–7.36 (m, 3H), 7.34 (ddd, *J* = 7.7, 1.6, 0.8 Hz, 1H), 7.29 (ddd, *J* = 7.9, 1.5, 1.5 Hz, 1H), 7.24–7.19 (m, 2H), 7.13 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 6.91 (ddd, *J* = 7.8, 1.2, 1.0 Hz, 1H), 2.18 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 158.7 (C_q), 149.2 (CH), 142.9 (C_q), 139.3 (C_q), 138.9 (C_q), 137.0 (C_q), 135.9 (CH), 134.0 (CH), 132.9 (CH), 130.3 (CH), 129.9 (CH), 128.4 (CH), 128.3 (CH), 127.2 (CH), 125.5 (CH), 121.7 (CH), 118.7 (C_q), 111.8 (C_q), 20.4 (CH_3).

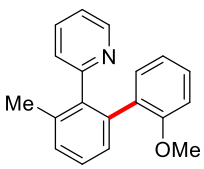
IR (ATR): $\tilde{\nu}$ = 2924, 2225, 1585, 1456, 1422, 1149, 1025, 785, 754, 699 cm^{-1}.

m.p.: 97–99 °C.

MS (ESI) *m*/*z* (relative intensity): 563 (5) $[2M+Na]^+$, 293 (100) $[M+Na]^+$, 271 (74) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{19}H_{14}N_2Na^+$ $[M+Na]^+$ 293.1049, found 293.1051.

2-(2'-Methoxy-3-methyl-[1,1'-biphenyl]-2-yl)pyridine (151m)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 1-iodo-2-methoxybenzene (**46m**, 176 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 6:1) yielded **151m** (60.5 mg, 44%) as a light yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.55 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.40 (ddd, *J* = 7.8, 7.7, 1.9 Hz, 1H), 7.34 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.29 (ddd, *J* = 7.6, 1.7, 0.7 Hz, 1H), 7.21 (ddd, *J* = 7.5, 1.7, 0.7 Hz, 1H), 7.13 (ddd, *J* = 8.2, 7.4, 1.8 Hz, 1H), 7.05–7.01 (m, 1H), 7.01 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 6.78 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.67 (d, *J* = 8.2 Hz, 1H), 3.54 (s, 3H), 2.22 (s, 3H).

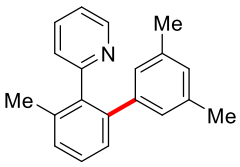
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.5 (C_q), 156.2 (C_q), 148.4 (CH), 140.1 (C_q), 137.9 (C_q), 136.2 (C_q), 135.0 (CH), 131.8 (CH), 130.5 (C_q), 129.5 (CH), 128.2 (CH), 128.1 (CH), 127.6 (CH), 124.8 (CH), 121.0 (CH), 119.9 (CH), 110.1 (CH), 55.1 (CH_3), 20.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2930, 1583, 1496, 1462, 1419, 1238, 1126, 1024, 787, 745 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 573 (27) $[2M+Na]^+$, 298 (100) $[M+Na]^+$, 276 (96) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{19}H_{17}NONa^+$ $[M+Na]^+$ 298.1202, found 298.1204.

2-(3,3',5'-Trimethyl-[1,1'-biphenyl]-2-yl)pyridine (151n)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 1-iodo-3,5-dimethylbenzene (**46n**, 174 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 15:1) yielded **151n** (126 mg, 92%) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.63 (ddd, *J* = 4.9, 1.8, 1.1 Hz, 1H), 7.46 (ddd, *J* = 7.8, 7.6, 1.8 Hz, 1H), 7.34 (dd, *J* = 8.3, 6.7 Hz, 1H), 7.29–7.24 (m, 2H), 7.09 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 6.90 (ddd, *J* = 7.8, 1.2, 1.1 Hz, 1H), 6.76–6.74 (m, 1H), 6.70–6.68 (m, 2H), 2.18 (s, 3H), 2.15–2.14 (m, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.8 (C_q), 148.6 (CH), 141.4 (C_q), 141.4 (C_q), 139.3 (C_q), 136.9 (C_q), 136.6 (C_q), 135.6 (CH), 129.2 (CH), 127.9 (CH), 127.8 (CH), 127.6 (CH), 127.5 (CH), 125.6 (CH), 121.1 (CH), 21.1 (CH_3), 20.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2917, 1583, 1562, 1460, 1426, 1025, 851, 784, 748, 704 cm^{-1}.

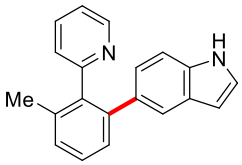
m.p.: 55–57 °C.

MS (ESI) *m*/*z* (relative intensity): 569 (20) $[2M+Na]^+$, 296 (100) $[M+Na]^+$, 274 (90) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{20}H_{19}NNa^+$ $[M+Na]^+$ 296.1410, found 296.1412.

The spectral data are in accordance with those reported in the literature.[46]

5-[3-Methyl-2-(pyridin-2-yl)phenyl]-1*H*-indole (151o)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 5-iodo-1*H*-indole (**46o**, 182 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **151o** (128 mg, 90%) as a white solid.

^{1}H-NMR (400 MHz, DMSO-d_6): δ = 10.96 (s, 1H), 8.58 (ddd, J = 4.9, 1.9, 1.1 Hz, 1H), 7.50 (ddd, J = 7.8, 7.7, 1.9 Hz, 1H), 7.36 (dd, J = 8.3, 6.8 Hz, 1H), 7.29–7.24 (m, 4H), 7.15 (ddd, J = 7.7, 4.9, 1.2 Hz, 1H), 7.11 (ddd, J = 8.4, 0.9, 0.9 Hz, 1H), 6.89 (ddd, J = 7.8, 1.2, 1.1 Hz, 1H), 6.69 (dd, J = 8.4, 1.7 Hz, 1H), 6.28 (ddd, J = 3.0, 1.9, 0.9 Hz, 1H), 2.06 (s, 3H).

^{13}C-NMR (100 MHz, DMSO-d_6): δ = 159.5 (C_q), 148.6 (CH), 142.0 (C_q), 139.5 (C_q), 135.9 (C_q), 135.8 (CH), 134.4 (C_q), 132.0 (C_q), 128.2 (CH), 127.9 (CH), 127.7 (CH), 127.3 (C_q), 125.5 (CH), 125.3 (CH), 122.9 (CH), 121.4 (CH), 120.7 (CH), 110.4 (CH), 101.2 (CH), 20.3 (CH_3).

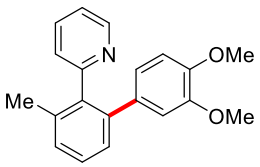
IR (ATR): $\tilde{\nu}$ = 3137, 1592, 1454, 1420, 1316, 888, 766, 730 cm^{-1}.

m.p.: 189–191 °C.

MS (ESI) *m*/*z* (relative intensity): 307 (15) $[M+Na]^+$, 285 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{20}H_{17}N_2^+$ $[M+H]^+$ 285.1386, found 285.1388.

2-(3',4'-Dimethoxy-3-methyl-[1,1'-biphenyl]-2-yl)pyridine (151p)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 4-iodo-1,2-dimethoxybenzene (**46p**, 198 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **151p** (118 mg, 77%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.65 (ddd, J = 4.9, 1.8, 1.1 Hz, 1H), 7.47 (ddd, J = 7.8, 7.7, 1.8 Hz, 1H), 7.35 (dd, J = 7.6, 7.5 Hz, 1H), 7.30–7.26 (m, 2H), 7.11 (ddd, J = 7.7, 4.9, 1.2 Hz, 1H), 6.88 (ddd, J = 7.8, 1.2, 1.1 Hz, 1H), 6.77 (d_{AB}d, J = 8.2, 2.0 Hz, 1H), 6.72 (d_{AB}, J = 8.2 Hz, 1H), 6.48 (d, J = 2.0 Hz, 1H), 3.82 (s, 3H), 3.56 (s, 3H), 2.17 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 160.0 (C_q), 148.7 (CH), 147.7 (C_q), 147.4 (C_q), 140.8 (C_q), 139.2 (C_q), 136.7 (C_q), 136.0 (CH), 134.3 (C_q), 129.2 (CH), 128.1 (CH), 127.4 (CH), 125.6 (CH), 121.5 (CH), 121.3 (CH), 113.3 (CH), 110.4 (CH), 55.7 (CH_3), 55.5 (CH_3), 20.4 (CH_3).

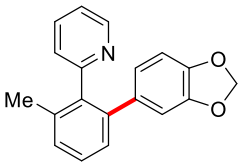
IR (ATR): $\tilde{\nu}$ = 2933, 1584, 1512, 1462, 1247, 1138, 1024, 788, 748 cm^{-1}.

m.p.: 90–92 °C.

MS (ESI) *m*/*z* (relative intensity): 633 (17) $[2M+Na]^+$, 328 (100) $[M+Na]^+$, 306 (79) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{20}H_{19}NO_2Na^+$ $[M+Na]^+$ 328.1308, found 328.1308.

2-[2-(Benzo[*d*][1,3]dioxol-5-yl)-6-methylphenyl]pyridine (151q)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 5-iodobenzo[*d*][1,3]dioxole (**46q**, 186 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 7:1) yielded **151q** (102 mg, 70%) as a viscous colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.64 (ddd, *J* = 4.9, 1.9, 1.1 Hz, 1H), 7.50 (ddd, *J* = 7.8, 7.7, 1.9 Hz, 1H), 7.33 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.27 (ddd, *J* = 7.6, 1.5, 0.7 Hz, 1H), 7.23 (ddd, *J* = 7.5, 1.5, 0.7 Hz, 1H), 7.11 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 6.92 (ddd, *J* = 7.8, 1.2, 1.1 Hz, 1H), 6.59 (dd, *J* = 6.3, 0.5 Hz, 1H), 6.58 (s, 1H), 6.54–6.51 (m, 1H), 5.86 (s, 2H), 2.16 (s, 3H).

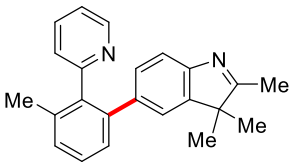
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.6 (C_q), 148.9 (CH), 146.9 (C_q), 146.0 (C_q), 140.8 (C_q), 139.3 (C_q), 136.7 (C_q), 135.8 (CH), 135.7 (C_q), 129.2 (CH), 128.0 (CH), 127.5 (CH), 125.5 (CH), 123.2 (CH), 121.3 (CH), 110.1 (CH), 107.6 (CH), 100.7 (CH_2), 20.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2892, 1584, 1459, 1337, 1223, 1036, 936, 784, 748, 638 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 601 (5) $[2M+Na]^+$, 312 (100) $[M+Na]^+$, 290 (98) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{19}H_{15}NO_2Na^+$ $[M+Na]^+$ 312.0995, found 312.0999.

2,3,3-Trimethyl-5-[3-methyl-2-(pyridin-2-yl)phenyl]-3*H*-indole (151r)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 5-iodo-2,3,3-trimethyl-3*H*-indole (**46r**, 214 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **151r** (83.7 mg, 51%) as a viscous dark yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.63 (ddd, *J* = 4.9, 1.9, 1.1 Hz, 1H), 7.38–7.33 (m, 2H), 7.37 (ddd, *J* = 7.8, 7.7, 1.9 Hz, 1H), 7.33–7.30 (m, 1H), 7.29 (ddd, *J* = 7.1, 1.7, 0.7 Hz, 1H), 7.17 (dd, *J* = 7.9, 1.8 Hz,

1H), 7.04 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 6.82 (ddd, *J* = 7.8, 1.2, 1.1 Hz, 1H), 6.77 (dd, *J* = 1.8, 0.6 Hz, 1H), 2.20 (s, 6H), 1.03 (s, 6H).

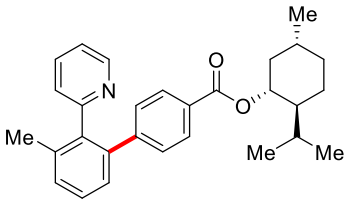
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 187.9 (C_q), 159.9 (C_q), 151.9 (C_q), 148.6 (CH), 144.8 (C_q), 141.3 (C_q), 139.4 (C_q), 138.6 (C_q), 136.7 (C_q), 135.7 (CH), 129.3 (CH), 128.6 (CH), 128.0 (CH), 127.4 (CH), 125.7 (CH), 123.3 (CH), 121.1 (CH), 119.0 (CH), 53.2 (C_q), 22.9 (CH_3), 20.4 (CH_3), 15.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2961, 1577, 1456, 1426, 1204, 1025, 834, 791, 749, 733 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 675 (49) $[2M+Na]^+$, 653 (17) $[2M+H]^+$, 349 (47) $[M+Na]^+$, 327 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{23}H_{23}N_2^+$ $[M+H]^+$ 327.1856, found 327.1851.

(1*R*,2*S*,5*R*)-2-*iso*-Propyl-5-methylcyclohexyl 3'-methyl-2'-(pyridin-2-yl)-[1,1'-biphenyl]-4-carboxylate (151s)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and (1*R*,2*S*,5*R*)-2-*iso*-propyl-5-methylcyclohexyl 4-iodobenzoate (**46s**, 290 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **151s** (94.6 mg, 44%) as a viscous colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.63 (ddd, *J* = 4.9, 1.8, 1.1 Hz, 1H), 7.81 (d, *J* = 8.6 Hz, 2H), 7.47 (ddd, *J* = 7.8, 7.7, 1.8 Hz, 1H), 7.37 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.32 (ddd, *J* = 7.6, 1.6, 0.8 Hz, 1H), 7.26 (ddd, *J* = 7.5, 1.6, 0.8 Hz, 1H), 7.15 (d, *J* = 8.6 Hz, 2H), 7.12 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 6.90 (ddd, *J* = 7.8, 1.2, 1.1 Hz, 1H), 4.89 (ddd, *J* = 10.9, 10.9, 4.2 Hz, 1H), 2.19 (s, 3H), 2.09 (dddd, *J* = 12.1, 4.2, 3.9, 1.6 Hz, 1H), 1.93 (heptd, *J* = 7.0, 2.7 Hz, 1H), 1.75–1.67 (m, 2H), 1.60–1.46 (m, 2H), 1.17–1.00 (m, 2H), 0.97–0.84 (m, 1H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.90 (d, *J* = 7.0 Hz, 3H), 0.77 (d, *J* = 7.0 Hz, 3H).

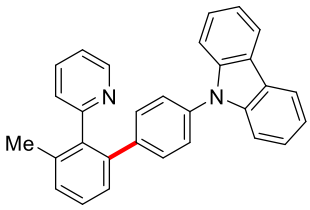
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 166.0 (C_q), 159.1 (C_q), 149.0 (CH), 146.3 (C_q), 140.2 (C_q), 139.2 (C_q), 136.9 (C_q), 135.9 (CH), 130.0 (CH), 129.5 (CH), 128.9 (CH), 128.6 (C_q), 128.1 (CH), 127.4 (CH), 125.5 (CH), 121.5 (CH), 74.7 (CH), 47.2 (CH), 40.9 (CH_2), 34.3 (CH_2), 31.4 (CH), 26.4 (CH), 23.5 (CH_2), 22.0 (CH_3), 20.8 (CH_3), 20.4 (CH_3), 16.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2954, 2868, 1707, 1457, 1267, 1178, 1099, 767, 735, 702 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 878 (24) $[2M+Na]^+$, 856 (3) $[2M+H]^+$, 450 (100) $[M+Na]^+$, 428 (87) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{29}H_{33}NO_2Na^+$ $[M+Na]^+$ 450.2404, found 450.2407.

9-[3'-Methyl-2'-(pyridin-2-yl)-[1,1'-biphenyl]-4-yl]-9*H*-carbazole (151t)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol) and 9-(4-iodophenyl)-9*H*-carbazole (**46t**, 277 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 7:1) yielded **151t** (182 mg, 88%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.69 (ddd, *J* = 4.9, 1.8, 1.1 Hz, 1H), 8.13 (ddd, *J* = 7.8, 1.0, 1.0 Hz, 2H), 7.56 (ddd, *J* = 7.8, 7.7, 1.8 Hz, 1H), 7.44 (dd, *J* = 7.5, 7.4 Hz, 1H), 7.42–7.26 (m, 12H), 7.17 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 7.02 (ddd, *J* = 7.8, 1.2, 1.1 Hz, 1H), 2.26 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 159.4 (C_q), 149.0 (CH), 140.9 (C_q), 140.7 (C_q), 140.4 (C_q), 139.5 (C_q), 136.9 (C_q), 135.7 (CH), 135.7 (C_q), 131.0 (CH), 129.8 (CH), 128.2 (CH), 127.4 (CH), 126.1 (CH), 125.8 (CH), 125.7 (CH), 123.3 (C_q), 121.5 (CH), 120.2 (CH), 119.8 (CH), 109.7 (CH), 20.5 (CH_3).

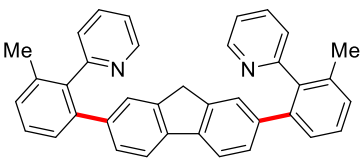
IR (ATR): $\tilde{\nu}$ = 3023, 1582, 1515, 1451, 1316, 1229, 841, 742, 719 cm^{-1}.

m.p.: 178–180 °C.

MS (ESI) *m*/*z* (relative intensity): 843 (38) $[2M+Na]^+$, 821 (4) $[2M+H]^+$, 433 (57) $[M+Na]^+$, 411 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{30}H_{23}N_2^+$ $[M+H]^+$ 411.1856, found 411.1858.

2,7-Bis[3-methyl-2-(pyridin-2-yl)phenyl]-9*H*-fluorene (216a)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 186 mg, 1.10 mmol), 2,7-diiodo-9*H*-fluorene (**215a**, 209 mg, 0.50 mmol) and K_2CO_3 (276 mg, 2.00 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **216a** (189 mg, 75%) as a pale yellow solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.63 (ddd, *J* = 5.0, 1.9, 1.0 Hz, 2H), 7.44 (dd, *J* = 8.0, 0.8 Hz, 2H), 7.41 (ddd, *J* = 7.8, 7.7, 1.9 Hz, 2H), 7.37 (dd, *J* = 7.8, 7.2 Hz, 2H), 7.33–7.28 (m, 4H), 7.22 (dd, *J* = 1.7,

0.8 Hz, 2H), 7.06 (ddd, *J* = 7.7, 5.0, 1.2 Hz, 2H), 7.03 (dd, *J* = 8.0, 1.7 Hz, 2H), 6.90 (ddd, *J* = 7.8, 1.2, 1.0 Hz, 2H), 3.60 (s, 2H), 2.19 (s, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.7 (C_q), 148.8 (CH), 142.9 (C_q), 141.4 (C_q), 140.2 (C_q), 139.5 (C_q), 139.4 (C_q), 136.7 (C_q), 135.7 (CH), 129.3 (CH), 128.4 (CH), 128.0 (CH), 127.6 (CH), 126.2 (CH), 125.6 (CH), 121.2 (CH), 118.9 (CH), 36.7 (CH_2), 20.5 (CH_3).

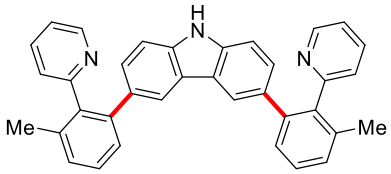
IR (ATR): $\tilde{\nu}$ = 2920, 1584, 1562, 1455, 1411, 1275, 1024, 826, 785, 746 cm^{-1}.

m.p.: 175–177 °C.

MS (ESI) *m*/*z* (relative intensity): 1024 (30) $[2M+Na]^+$, 1002 (48) $[2M+H]^+$, 523 (29) $[M+Na]^+$, 501 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{37}H_{29}N_2^+$ $[M+H]^+$ 501.2325, found 501.2328.

3,6-Bis[3-methyl-2-(pyridin-2-yl)phenyl]-9*H*-carbazole (216b)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 186 mg, 1.10 mmol), 3,6-diiodo-9*H*-carbazole (**215b**, 210 mg, 0.50 mmol) and K_2CO_3 (276 mg, 2.00 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **216b** (238 mg, 95%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.63 (ddd, *J* = 5.0, 1.9, 1.1 Hz, 2H), 8.39 (s, 1H), 7.73–7.71 (m, 2H), 7.38 (dd, *J* = 7.5, 7.3 Hz, 2H), 7.37–7.34 (m, 2H), 7.35 (ddd, *J* = 7.7, 7.6, 1.9 Hz, 2H), 7.30 (ddd, *J* = 7.3, 1.8, 0.8 Hz, 2H), 7.01 (ddd, *J* = 7.6, 5.0, 1.2 Hz, 2H), 6.98 (d_{AB}d, *J* = 8.4, 1.6 Hz, 2H), 6.96 (d_{AB}d, *J* = 8.4, 0.8 Hz, 2H), 6.89 (ddd, *J* = 7.7, 1.2, 1.1 Hz, 2H), 2.20 (s, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 159.9 (C_q), 148.7 (CH), 141.9 (C_q), 139.5 (C_q), 138.4 (C_q), 136.6 (C_q), 135.7 (CH), 132.9 (C_q), 128.9 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 125.7 (CH), 122.9 (C_q), 121.1 (CH), 121.0 (CH), 109.6 (CH), 20.6 (CH_3).

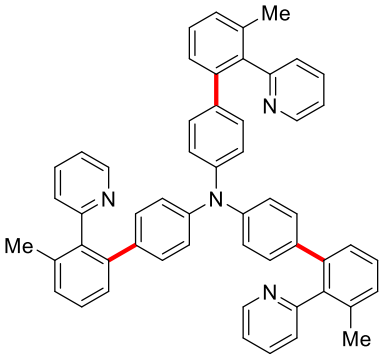
IR (ATR): $\tilde{\nu}$ = 3411, 3023, 1585, 1455, 1287, 1235, 1025, 784, 746, 618 cm^{-1}.

m.p.: 256–257 °C.

MS (ESI) *m*/*z* (relative intensity): 1003 (17) $[2M+H]^+$, 524 (37) $[M+Na]^+$, 502 (100) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{36}H_{28}N_3^+$ $[M+H]^+$ 502.2278, found 502.2279.

Tris[3'-methyl-2'-(pyridin-2-yl)-[1,1'-biphenyl]-4-yl]amine (216c)



The general procedure **N** was followed using 2-(*o*-tolyl)pyridine (**68e**, 279 mg, 1.65 mmol), tris(4-iodophenyl)amine (**215c**, 312 mg, 0.50 mmol) and K_2CO_3 (415 mg, 3.00 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **216c** (323 mg, 86%) as a off-white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.62 (ddd, *J* = 4.9, 1.9, 1.1 Hz, 3H), 7.47 (ddd, *J* = 7.8, 7.7, 1.9 Hz, 3H), 7.35 (dd, *J* = 8.4, 6.7 Hz, 3H), 7.29–7.26 (m, 6H), 7.11 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 3H), 6.89 (ddd, *J* = 7.8, 1.2, 1.1 Hz, 3H), 6.86 (d, *J* = 8.6 Hz, 6H), 6.67 (d, *J* = 8.6 Hz, 6H), 2.19 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 159.7 (C_q), 148.7 (CH), 145.5 (C_q), 140.9 (C_q), 139.3 (C_q), 136.6 (C_q), 135.9 (C_q), 135.5 (CH), 130.3 (CH), 129.2 (CH), 128.0 (CH), 127.2 (CH), 125.7 (CH), 122.9 (CH), 121.2 (CH), 20.5 (CH_3).

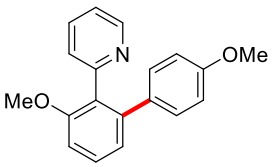
IR (ATR): $\tilde{\nu}$ = 3028, 1584, 1506, 1458, 1318, 1269, 834, 785, 746, 580 cm^{-1}.

m.p.: >190 °C (decomp.).

MS (ESI) *m*/*z* (relative intensity): 747 (80) $[M+H]^+$, 374 (100) $[M+2H]^{2+}$.

HR-MS (ESI): *m*/*z* calcd for $C_{54}H_{43}N_4^+$ $[M+H]^+$ 747.3482, found 747.3486.

2-(3,4'-Dimethoxy-[1,1'-biphenyl]-2-yl)pyridine (151u)



The general procedure **N** was followed using 2-(2-methoxyphenyl)pyridine (**68f**, 92.7 mg, 0.50 mmol) and 1-iodo-4-methoxybenzene (**46a**, 176 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **151u** (125 mg, 86%) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.60 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.49 (ddd, *J* = 7.8, 7.7, 1.9 Hz, 1H), 7.40 (dd, *J* = 8.3, 7.8 Hz, 1H), 7.08 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 7.04 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.02 (ddd, *J* = 7.8, 1.2, 1.0 Hz, 1H), 7.01 (d, *J* = 8.9 Hz, 2H), 6.98 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.68 (d, *J* = 8.9 Hz, 2H), 3.77 (s, 3H), 3.72 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 158.1 (C_q), 157.2 (C_q), 157.0 (C_q), 148.8 (CH), 142.3 (C_q), 135.4 (CH), 133.4 (C_q), 130.5 (CH), 129.0 (CH), 129.0 (C_q), 126.2 (CH), 122.4 (CH), 121.2 (CH), 113.0 (CH), 109.6 (CH), 55.9 (CH_3), 55.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2935, 2835, 1586, 1514, 1463, 1242, 1174, 1121, 1021, 733 cm^{-1}.

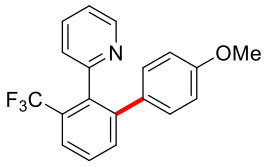
m.p.: 111–112 °C.

MS (ESI) *m/z* (relative intensity): 314 (16) $[M+Na]^+$, 292 (100) $[M+H]^+$, 236 (12).

HR-MS (ESI): *m/z* calcd for $C_{19}H_{18}NO_2^+$ $[M+H]^+$ 292.1332, found 292.1336.

The spectral data are in accordance with those reported in the literature.[43]

2-[4'-Methoxy-3-(trifluoromethyl)-[1,1'-biphenyl]-2-yl]pyridine (151v)



The general procedure **N** was followed using 2-[2-(trifluoromethyl)phenyl]pyridine (**68g**, 112 mg, 0.50 mmol) and 1-iodo-4-methoxybenzene (**46a**, 176 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **151v** (161 mg, 97%) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.57 (ddd, *J* = 4.9, 1.8, 1.1 Hz, 1H), 7.78–7.74 (m, 1H), 7.60–7.52 (m, 2H), 7.49 (ddd, *J* = 7.8, 7.7, 1.8 Hz, 1H), 7.12 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 7.02 (ddd, *J* = 7.8, 1.2, 1.1 Hz, 1H), 6.97 (d, *J* = 8.9 Hz, 2H), 6.68 (d, *J* = 8.9 Hz, 2H), 3.73 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 158.4 (C_q), 156.8 (C_q), 148.4 (CH), 142.9 (C_q), 138.3 (q, $^3J_{C-F}$ = 2 Hz, C_q), 135.3 (CH), 133.6 (CH), 132.4 (C_q), 130.7 (CH), 129.2 (q, $^2J_{C-F}$ = 30 Hz, C_q), 128.2 (CH), 125.6 (q, $^5J_{C-F}$ = 2 Hz, CH), 124.9 (q, $^3J_{C-F}$ = 5 Hz, CH), 124.0 (q, $^1J_{C-F}$ = 274 Hz, C_q), 122.0 (CH), 113.2 (CH), 55.1 (CH_3).

^{19}F-NMR (376 MHz, $CDCl_3$): δ = –57.1 (s).

IR (ATR): $\tilde{\nu}$ = 2934, 1609, 1517, 1445, 1323, 1247, 1166, 1119, 1025, 748 cm^{-1}.

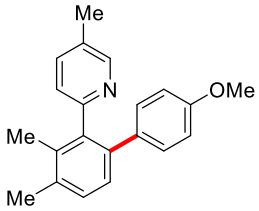
m.p.: 83–85 °C.

MS (ESI) *m/z* (relative intensity): 681 (3) $[2M+Na]^+$, 352 (22) $[M+Na]^+$, 330 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{19}H_{15}F_3NO^+$ $[M+H]^+$ 330.1100, found 330.1114.

The spectral data are in accordance with those reported in the literature.[43]

2-(4'-Methoxy-3,4-dimethyl-[1,1'-biphenyl]-2-yl)-5-methylpyridine (151w)



The general procedure **N** was followed using 2-(2,3-dimethylphenyl)-5-methylpyridine (**68h**, 98.7 mg, 0.50 mmol) and 1-iodo-4-methoxybenzene (**46a**, 176 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 7:1) yielded **151w** (127 mg, 84%) as a viscous colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.47 (ddd, *J* = 2.4, 0.8, 0.8 Hz, 1H), 7.26 (ddd, *J* = 8.0, 2.4, 0.8 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.77 (dd, *J* = 8.0, 0.8 Hz, 1H), 6.67 (d, *J* = 8.8 Hz, 2H), 3.73 (s, 3H), 2.35 (s, 3H), 2.30 (s, 3H), 2.03 (s, 3H).

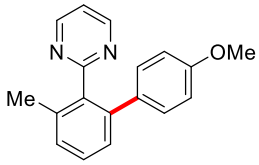
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 157.8 (C_q), 157.3 (C_q), 149.1 (CH), 139.4 (C_q), 138.7 (C_q), 136.3 (CH), 135.9 (C_q), 135.1 (C_q), 134.6 (C_q), 130.6 (CH), 130.3 (C_q), 129.4 (CH), 127.1 (CH), 125.1 (CH), 113.0 (CH), 55.1 (CH_3), 20.4 (CH_3), 18.2 (CH_3), 16.9 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2924, 1609, 1514, 1465, 1242, 1176, 1030, 816, 574 cm^{-1}.

MS (EI) *m*/*z* (relative intensity): 303 (63) $[M]^+$, 302 (100) $[M–H]^+$, 288 (26) $[M–Me]^+$, 258 (13), 244 (9).

HR-MS (ESI): *m*/*z* calcd for $C_{21}H_{22}NO^+$ $[M+H]^+$ 304.1696, found 304.1698.

2-(4'-Methoxy-3-methyl-[1,1'-biphenyl]-2-yl)pyrimidine (151x)



The general procedure **N** was followed using 2-(*o*-tolyl)pyrimidine (**139d**, 85.1 mg, 0.50 mmol) and 1-iodo-4-methoxybenzene (**46a**, 176 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **151x** (132 mg, 96%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.68 (d, *J* = 4.9 Hz, 2H), 7.36 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.28–7.24 (m, 2H), 7.09 (t, *J* = 4.9 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.69 (d, *J* = 8.7 Hz, 2H), 3.74 (s, 3H), 2.19 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 168.4 (C_q), 158.0 (C_q), 156.6 (CH), 140.5 (C_q), 138.2 (C_q), 135.9 (C_q), 134.0 (C_q), 130.1 (CH), 129.0 (CH), 128.5 (CH), 127.6 (CH), 118.4 (CH), 113.2 (CH), 55.1 (CH_3), 20.0 (CH_3).

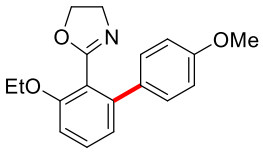
IR (ATR): $\tilde{\nu}$ = 2936, 1607, 1556, 1510, 1460, 1236, 1184, 1023, 848, 790 cm^{-1}.

m.p.: 109–110 °C.

MS (EI) *m/z* (relative intensity): 276 (100) $[M]^+$, 275 (80) $[M–H]^+$, 261 (41) $[M–Me]^+$, 232 (22), 168 (18).

HR-MS (ESI): *m/z* calcd for $C_{18}H_{17}N_2O^+$ $[M+H]^+$ 277.1335, found 277.1337.

2-(3-Ethoxy-4'-methoxy-[1,1'-biphenyl]-2-yl)-4,5-dihydrooxazole (151y)



The general procedure **N** was followed using 2-(2-ethoxyphenyl)-4,5-dihydrooxazole (**139k**, 95.7 mg, 0.50 mmol) and 1-iodo-4-methoxybenzene (**46a**, 176 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **151y** (112 mg, 75%) as a white solid.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 8.9 Hz, 2H), 7.37–7.34 (m, 1H), 6.96 (dd, *J* = 7.7, 0.9 Hz, 1H), 6.89–6.86 (m, 1H), 6.90 (d, *J* = 8.9 Hz, 2H), 4.22 (t, *J* = 9.4 Hz, 2H), 4.10 (q, *J* = 7.0 Hz, 2H), 3.85 (t, *J* = 9.4 Hz, 2H), 3.83 (s, 3H), 1.40 (t, *J* = 7.0 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 162.8 (C_q), 158.9 (C_q), 157.5 (C_q), 142.9 (C_q), 133.0 (C_q), 130.5 (CH), 129.5 (CH), 121.9 (CH), 118.2 (C_q), 113.5 (CH), 110.6 (CH), 67.2 (CH_2), 64.5 (CH_2), 55.2 (CH_3), 55.1 (CH_2), 14.7 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2979, 1667, 1568, 1516, 1460, 1240, 1121, 1033, 939, 792 cm^{-1}.

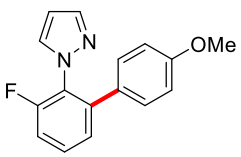
m.p.: 88–90 °C.

MS (ESI) *m/z* (relative intensity): 320 (35) $[M+Na]^+$, 298 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{18}H_{20}NO_3^+$ $[M+H]^+$ 298.1438, found 298.1441.

The spectral data are in accordance with those reported in the literature.[145]

1-(3-Fluoro-4'-methoxy-[1,1'-biphenyl]-2-yl)-1*H*-pyrazole (151z)



The general procedure **N** was followed using 1-(2-fluorophenyl)-1*H*-pyrazole (**147k**, 81.1 mg, 0.50 mmol) and 1-iodo-4-methoxybenzene (**46a**, 176 mg, 0.75 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 7:1) yielded **151z** (124 mg, 93%) as a colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.68 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.44 (ddd, *J* = 8.2, 8.0, 5.4 Hz, 1H), 7.27 (ddd, *J* = 8.0, 1.4, 1.3 Hz, 1H), 7.25 (ddd, *J* = 2.5, 0.7, 0.6 Hz, 1H), 7.20 (ddd, *J* = 9.5, 8.2, 1.4 Hz, 1H), 7.00 (d, *J* = 8.9 Hz, 2H), 6.78 (d, *J* = 8.9 Hz, 2H), 6.29 (dd, *J* = 2.5, 1.9 Hz, 1H), 3.78 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.3 (C_q), 158.2 (d, $^{1}J_{C–F}$ = 252.0 Hz, C_q), 141.1 (C_q), 140.6 (CH), 132.1 (CH), 129.9 (d, $^{3}J_{C–F}$ = 8.8 Hz, CH), 129.5 (d, $^{4}J_{C–F}$ = 2.5 Hz, C_q), 129.4 (CH), 126.8 (d, $^{2}J_{C–F}$ = 12.4 Hz, C_q), 125.8 (d, $^{4}J_{C–F}$ = 3.5 Hz, CH), 114.9 (d, $^{2}J_{C–F}$ = 20.4 Hz, CH), 113.8 (CH), 106.5 (CH), 55.2 (CH_3).

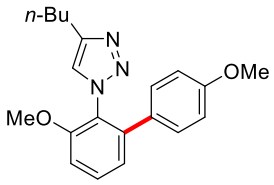
^{19}F-NMR (376 MHz, $CDCl_3$): δ = –122.3 (dd, *J* = 9.5, 5.4 Hz)

IR (ATR): $\tilde{\nu}$ = 2837, 1608, 1515, 1467, 1242, 1180, 1095, 1023, 938, 743 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 559 (5) $[2M+Na]^+$, 291 (100) $[M+Na]^+$, 269 (16) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{16}H_{13}FN_2ONa^+$ $[M+Na]^+$ 291.0904, found 291.0906.

4-Butyl-1-(3,4'-dimethoxy-[1,1'-biphenyl]-2-yl)-1*H*-1,2,3-triazole (151ab)



The general procedure **N** was followed using 4-butyl-1-(2-methoxyphenyl)-1*H*-1,2,3-triazole (**139m**, 116 mg, 0.50 mmol), 1-iodo-4-methoxybenzene (**46a**, 352 mg, 1.50 mmol) and $[Ru(OAc)_2(p\text{-cymene})]$ (**181**, 35.3 mg, 0.10 mmol, 20 mol %) in DMA (2.0 mL). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **151ab** (129 mg, 77%) as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.48 (dd, *J* = 8.3, 7.8 Hz, 1H), 7.07 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.03 (t, *J* = 0.7 Hz, 1H), 7.02 (dd, *J* = 8.3, 1.2 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 6.73 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H), 3.74 (s, 3H), 2.67 (t, *J* = 7.5 Hz, 2H), 1.60–1.51 (m, 2H), 1.28–1.17 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.1 (C_q), 155.2 (C_q), 147.4 (C_q), 140.7 (C_q), 130.7 (CH), 129.7 (C_q), 129.4 (CH), 124.5 (C_q), 123.7 (CH), 122.2 (CH), 113.6 (CH), 110.5 (CH), 56.2 (CH_3), 55.1 (CH_3), 31.4 (CH_2), 25.1 (CH_2), 21.9 (CH_2), 13.8 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2932, 1610, 1516, 1471, 1244, 1176, 1122, 1021, 833, 790 cm^{-1}.

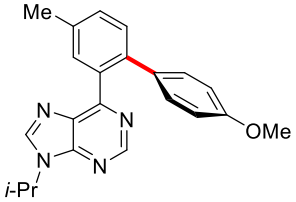
m.p.: 60–62 °C.

MS (EI) *m/z* (relative intensity): 337 (3) $[M]^+$, 308 (59) $[M–Et]^+$, 294 (40) $[M–Pr]^+$, 278 (13) $[M–Pr–Me]^+$, 266 (100) $[M–Bu–Me]^+$, 251 (61) $[M–Bu–OMe]^+$, 236 (36), 223 (25), 155 (10), 139 (12), 127 (12).

HR-MS (EI): *m/z* calcd for $C_{20}H_{23}N_3O_2^+$ $[M]^+$ 337.1785, found 337.1791.

The spectral data are in accordance with those reported in the literature.[145]

9-*iso*-Propyl-6-(4'-methoxy-4-methyl-[1,1'-biphenyl]-2-yl)-9*H*-purine (151ac)



The general procedure **N** was followed using purine **123o** (63.1 mg, 0.25 mmol) and 1-iodo-4-methoxybenzene (**46a**, 87.8 mg, 0.38 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 3:2 to 1:1) yielded **151ac** (50.1 mg, 56%) as a viscous light yellow oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.85 (s, 1H), 7.97 (s, 1H), 7.52 (ddd, *J* = 1.9, 0.7, 0.7 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.33 (ddd, *J* = 7.8, 1.9, 0.7 Hz, 1H), 7.05 (d, *J* = 8.8 Hz, 2H), 6.65 (d, *J* = 8.8 Hz, 2H), 4.89 (hept, *J* = 6.8 Hz, 1H), 3.71 (s, 3H), 2.44 (s, 3H), 1.62 (d, *J* = 6.8 Hz, 6H).

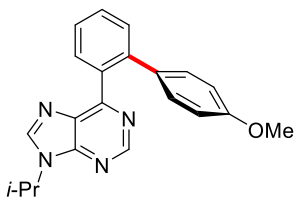
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.4 (C_q), 158.1 (C_q), 151.8 (CH), 151.1 (C_q), 141.9 (CH), 138.5 (C_q), 136.5 (C_q), 134.1 (C_q), 133.7 (C_q), 132.6 (C_q), 131.3 (CH), 130.5 (CH), 130.4 (CH), 130.2 (CH), 113.2 (CH), 55.1 (CH_3), 47.2 (CH), 22.4 (CH_3), 21.0 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2977, 1576, 1494, 1329, 1242, 1177, 1037, 820, 734, 648 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 739 (38) $[2M+Na]^+$, 717 (5) $[2M+H]^+$, 381 (24) $[M+Na]^+$, 359 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{22}H_{23}N_4O^+$ $[M+H]^+$ 359.1866, found 359.1868.

9-*iso*-Propyl-6-(4'-methoxy-[1,1'-biphenyl]-2-yl)-9*H*-purine (151ad)



The general procedure **N** was followed using purine **123a** (59.6 mg, 0.25 mmol) and 1-iodo-4-methoxybenzene (**46a**, 87.8 mg, 0.38 mmol) in DMA (1.0 mL). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 3:2) yielded monoarylated product **151ad** (20.5 mg, 24%) as a viscous yellow oil and diarylated product **151ad'** (65.0 mg, 58%) as a viscous colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.84 (s, 1H), 7.99 (s, 1H), 7.76–7.73 (m, 1H), 7.55–7.43 (m, 3H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.67 (d, *J* = 8.8 Hz, 2H), 4.90 (hept, *J* = 6.8 Hz, 1H), 3.72 (s, 3H), 1.63 (d, *J* = 6.8 Hz, 6H).

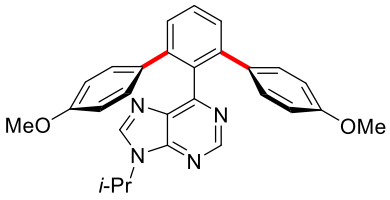
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.1 (C_q), 158.3 (C_q), 151.8 (CH), 151.2 (C_q), 142.0 (CH), 141.4 (C_q), 134.3 (C_q), 133.8 (C_q), 132.7 (C_q), 131.0 (CH), 130.6 (CH), 130.3 (CH), 129.7 (CH), 126.9 (CH), 113.3 (CH), 55.1 (CH_3), 47.2 (CH), 22.5 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2977, 1580, 1517, 1495, 1330, 1243, 1215, 1035, 833, 763 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 367 (28) $[M+Na]^+$, 345 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{21}H_{21}N_4O^+$ $[M+H]^+$ 345.1710, found 345.1713.

6-(4,4''-Dimethoxy-[1,1':3',1''-terphenyl]-2'-yl)-9-*iso*-propyl-9*H*-purine (151ad')



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.71 (s, 1H), 7.84 (s, 1H), 7.54 (dd, *J* = 8.3, 7.3 Hz, 1H), 7.42 (d, *J* = 7.3 Hz, 1H), 7.42 (d, *J* = 8.3 Hz, 1H), 7.03 (d, *J* = 8.8 Hz, 4H), 6.57 (d, *J* = 8.8 Hz, 4H), 4.78 (hept, *J* = 6.8 Hz, 1H), 3.67 (s, 6H), 1.53 (d, *J* = 6.8 Hz, 6H).

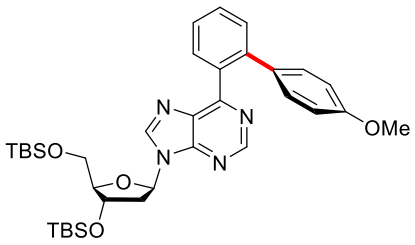
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.4 (C_q), 158.1 (C_q), 151.2 (CH), 150.4 (C_q), 141.7 (CH), 141.6 (C_q), 134.1 (C_q), 133.7 (C_q), 133.4 (C_q), 130.2 (CH), 129.0 (CH), 129.0 (CH), 112.9 (CH), 55.1 (CH_3), 47.0 (CH), 22.3 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2977, 1609, 1592, 1513, 1455, 1330, 1244, 1176, 1031, 803 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 923 (58) $[2M+Na]^+$, 901 (9) $[2M+H]^+$, 473 (60) $[M+Na]^+$, 451 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{28}H_{27}N_4O_2^+$ $[M+H]^+$ 451.2129, found 451.2130.

9-{(2*R*,4*R*,5*R*)-4-[(*tert*-Butyldimethylsilyl)oxy]-5-{[(*tert*-butyldimethylsilyl)oxy]methyl} tetrahydrofuran-2-yl}-6-(4'-methoxy-[1,1'-biphenyl]-2-yl)-9*H*-purine (151ae)



The general procedure **N** was followed using purine **123m** (135 mg, 0.25 mmol) and 1-iodo-4-methoxybenzene (**46a**, 87.8 mg, 0.38 mmol) in DMA (1.0 mL). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded monoarylated product **151ae** (24.4 mg, 15%) as a viscous colorless oil and diarylated product **151ae'** (109 mg, 58%) as a viscous colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.83 (s, 1H), 8.22 (s, 1H), 7.73 (ddd, *J* = 7.5, 1.1, 1.1 Hz, 1H), 7.55–7.49 (m, 2H), 7.46 (ddd, *J* = 7.5, 5.8, 2.9 Hz, 1H), 7.07 (d, *J* = 8.8 Hz, 2H), 6.68 (d, *J* = 8.8 Hz, 2H), 6.51 (dd, *J* = 7.2, 6.0 Hz, 1H), 4.63 (ddd, *J* = 5.9, 3.3, 3.2 Hz, 1H), 4.03 (ddd, *J* = 4.3, 3.3, 3.2 Hz, 1H), 3.85 (d_{AB}d, *J* = 11.2, 4.3 Hz, 1H), 3.77 (d_{AB}d, *J* = 11.2, 3.3 Hz, 1H), 3.73 (s, 3H), 2.68 (ddd, *J* = 13.1, 7.2, 5.9 Hz, 1H), 2.44 (ddd, *J* = 13.1, 6.0, 3.3 Hz, 1H), 0.92 (s, 9H), 0.89 (s, 9H), 0.11 (s, 6H), 0.06 (s, 3H), 0.05 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.3 (C_q), 158.3 (C_q), 152.1 (CH), 151.1 (C_q), 142.8 (CH), 141.4 (C_q), 134.2 (C_q), 133.7 (C_q), 132.8 (C_q), 131.0 (CH), 130.7 (CH), 130.3 (CH), 129.7 (CH), 126.9 (CH), 113.3 (CH), 88.0 (CH), 84.3 (CH), 72.1 (CH), 62.9 (CH_2), 55.1 (CH_3), 41.0 (CH_2), 25.9 (CH_3), 25.8 (CH_3), 18.4 (C_q), 18.0 (C_q), –4.7 (CH_3), –4.8 (CH_3), –5.4 (CH_3), –5.5 (CH_3).

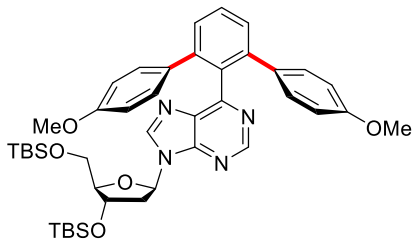
IR (ATR): $\tilde{\nu}$ = 2929, 2857, 1581, 1252, 1109, 1032, 834, 778 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 669 (84) $[M+Na]^+$, 647 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{35}H_{51}N_4O_4Si_2^+$ $[M+H]^+$ 647.3443, found 647.3447.

The spectral data are in accordance with those reported in the literature.[109]

9-{(2*R*,4*R*,5*R*)-4-[(*tert*-Butyldimethylsilyl)oxy]-5-{[(*tert*-butyldimethylsilyl)oxy]methyl} tetrahydrofuran-2-yl}-6-(4,4''-dimethoxy-[1,1':3',1''-terphenyl]-2'-yl)-9*H*-purine (151ae')



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.71 (s, 1H), 8.07 (s, 1H), 7.53 (dd, *J* = 7.8, 7.6 Hz, 1H), 7.42 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.40 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.04 (d, *J* = 8.8 Hz, 2H), 7.04 (d, *J* = 8.8 Hz, 2H), 6.59 (d, *J* = 8.8 Hz, 2H), 6.57 (d, *J* = 8.8 Hz, 2H), 6.40 (dd, *J* = 7.4, 6.0 Hz, 1H), 4.54 (ddd, *J* = 5.7, 3.1, 3.1 Hz, 1H), 4.00 (ddd, *J* = 4.1, 3.3, 3.1 Hz, 1H), 3.81 (d_{AB}d, *J* = 11.2, 4.1 Hz, 1H), 3.74 (d_{AB}d, *J* = 11.2, 3.3 Hz, 1H), 3.68

(s, 3H), 3.67 (s, 3H), 2.49 (ddd, *J* = 13.1, 7.4, 5.7 Hz, 1H), 2.37 (ddd, *J* = 13.1, 6.0, 3.1 Hz, 1H), 0.91 (s, 9H), 0.89 (s, 9H), 0.10 (s, 6H), 0.05 (s, 3H), 0.04 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.4 (C_q), 158.1 (C_q), 158.1 (C_q), 151.5 (CH), 150.3 (C_q), 142.4 (CH), 141.7 (C_q), 141.7 (C_q), 134.1 (C_q), 133.7 (C_q), 133.6 (C_q), 133.2 (C_q), 130.2 (CH), 130.1 (CH), 129.2 (CH), 129.1 (CH), 129.0 (CH), 113.0 (CH), 112.9 (CH), 88.0 (CH), 84.1 (CH), 72.2 (CH), 62.9 (CH_2), 55.0 (CH_3), 41.2 (CH_2), 25.9 (CH_3), 25.7 (CH_3), 18.4 (C_q), 18.0 (C_q), –4.7 (CH_3), –4.9 (CH_3), –5.4 (CH_3), –5.6 (CH_3).

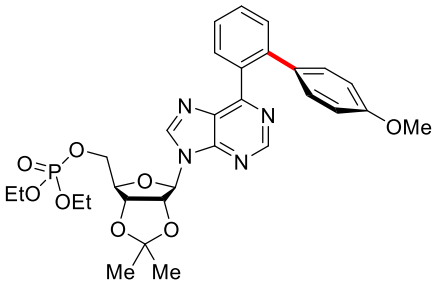
IR (ATR): $\tilde{\nu}$ = 2929, 2857, 1610, 1579, 1513, 1245, 1113, 1031, 830, 777 cm^{-1}.

MS (ESI) *m*/*z* (relative intensity): 775 (100) $[M+Na]^+$, 753 (49) $[M+H]^+$.

HR-MS (ESI): *m*/*z* calcd for $C_{42}H_{56}N_4O_5Si_2Na^+$ $[M+Na]^+$ 775.3681, found 775.3679.

The spectral data are in accordance with those reported in the literature.[109]

Diethyl {{(3a*R*,4*R*,6*R*,6a*R*)-6-[6-(4'-methoxy-[1,1'-biphenyl]-2-yl)-9*H*-purin-9-yl]-2,2-dimethyl tetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}methyl} phosphate (151af)



The general procedure **N** was followed using purine **123l** (126 mg, 0.25 mmol) and 1-iodo-4-methoxybenzene (**46a**, 87.8 mg, 0.38 mmol) in DMA (1.0 mL). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 3:7) yielded monoarylated product **151af** (26.7 mg, 17%) as a viscous light yellow oil and diarylated product **151af'** (107 mg, 60%) as a viscous colorless oil.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.86 (s, 1H), 8.09 (s, 1H), 7.72 (ddd, *J* = 7.5, 0.9, 0.9 Hz, 1H), 7.56–7.50 (m, 2H), 7.47 (ddd, *J* = 7.5, 6.3, 2.4 Hz, 1H), 7.07 (d, *J* = 8.8 Hz, 2H), 6.69 (d, *J* = 8.8 Hz, 2H), 6.18 (d, *J* = 2.7 Hz, 1H), 5.39 (dd, *J* = 6.3, 2.7 Hz, 1H), 5.09 (dd, *J* = 6.3, 3.2 Hz, 1H), 4.49 (dddd, *J* = 4.9, 4.6, 3.2, 1.1 Hz, 1H), 4.27 (ddd, *J* = 11.1, 6.4, 4.6 Hz, 1H), 4.20 (ddd, *J* = 11.1, 7.0, 4.9 Hz, 1H), 4.12–4.00 (m, 4H), 3.74 (s, 3H), 1.64 (s, 3H), 1.40 (s, 3H), 1.28 (td, *J* = 7.1, 1.0 Hz, 3H), 1.24 (td, *J* = 7.1, 1.0 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.7 (C_q), 158.4 (C_q), 152.4 (CH), 150.8 (C_q), 143.2 (CH), 141.5 (C_q), 133.9 (C_q), 133.6 (C_q), 132.8 (C_q), 131.0 (CH), 130.8 (CH), 130.2 (CH), 129.9 (CH), 126.9 (CH), 114.8 (C_q), 113.4 (CH), 90.7 (CH), 84.9 (d, $^{3}J_{C-P}$ = 8 Hz, CH), 84.0 (CH), 81.2 (CH), 66.5 (d, $^{2}J_{C-P}$ = 6 Hz, CH_2),

64.1 (d, $^{2}J_{C–P}$ = 6 Hz, CH_2), 64.1 (d, $^{2}J_{C–P}$ = 6 Hz, CH_2), 55.1 (CH_3), 27.2 (CH_3), 25.3 (CH_3), 16.1 (d, $^{3}J_{C–P}$ = 7 Hz, CH_3).

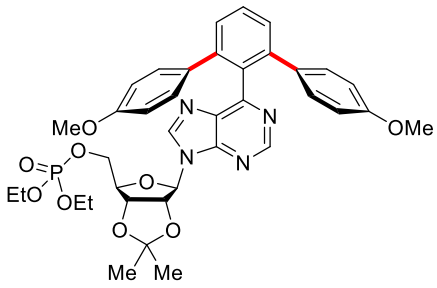
$^{31}P\{^{1}H\}$-NMR (162 MHz, $CDCl_3$): δ = –1.0 (s).

IR (ATR): $\tilde{\nu}$ = 2984, 1582, 1517, 1244, 1208, 1019, 834, 763, 728 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 1243 (11) $[2M+Na]^+$, 1221 (35) $[2M+H]^+$, 633 (25) $[M+Na]^+$, 611 (100) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{30}H_{36}N_4O_8P^+$ $[M+H]^+$ 611.2265, found 611.2266.

{(3a*R*,4*R*,6*R*,6a*R*)-6-[6-(4,4''-Dimethoxy-[1,1':3',1''-terphenyl]-2'-yl)-9*H*-purin-9-yl]-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}methyl diethyl phosphate (151af')



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.73 (s, 1H), 7.94 (s, 1H), 7.53 (dd, *J* = 7.9, 7.4 Hz, 1H), 7.42 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.41 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 2H), 7.01 (d, *J* = 8.8 Hz, 2H), 6.59 (d, *J* = 8.8 Hz, 2H), 6.58 (d, *J* = 8.8 Hz, 2H), 6.07 (d, *J* = 2.7 Hz, 1H), 5.22 (dd, *J* = 6.3, 2.7 Hz, 1H), 5.04 (dd, *J* = 6.3, 3.2 Hz, 1H), 4.43 (dddd, *J* = 4.9, 4.8, 3.2, 1.0 Hz, 1H), 4.19 (ddd, *J* = 11.4, 6.7, 4.9 Hz, 1H), 4.14–4.01 (m, 5H), 3.68 (s, 6H), 1.61 (s, 3H), 1.37 (s, 3H), 1.27 (td, *J* = 7.1, 1.0 Hz, 3H), 1.25 (td, *J* = 7.1, 1.0 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 159.9 (C_q), 158.2 (C_q), 158.1 (C_q), 151.7 (CH), 150.0 (C_q), 143.0 (CH), 141.7 (C_q), 141.6 (C_q), 134.1 (C_q), 133.5 (C_q), 133.4 (C_q), 132.9 (C_q), 130.1 (CH), 130.1 (CH), 129.1 (CH), 129.1 (CH), 114.7 (C_q), 113.0 (CH), 112.9 (CH), 90.5 (CH), 84.7 (d, $^{3}J_{C–P}$ = 8 Hz, CH), 83.9 (CH), 81.1 (CH), 66.3 (d, $^{2}J_{C–P}$ = 6 Hz, CH_2), 64.1 (d, $^{2}J_{C–P}$ = 6 Hz, CH_2), 55.0 (CH_3), 27.1 (CH_3), 25.3 (CH_3), 16.0 (d, $^{3}J_{C–P}$ = 6 Hz, CH_3).

$^{31}P\{^{1}H\}$-NMR (162 MHz, $CDCl_3$): δ = –1.0 (s).

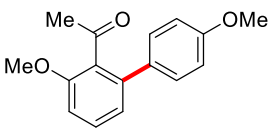
IR (ATR): $\tilde{\nu}$ = 2985, 1580, 1514, 1245, 1024, 835, 803, 732 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 739 (100) $[M+Na]^+$, 717 (19) $[M+H]^+$.

HR-MS (ESI): *m/z* calcd for $C_{37}H_{41}N_4O_9PNa^+$ $[M+Na]^+$ 739.2503, found 739.2501.

5.3.7.2 Photo-Induced Ruthenium-Catalyzed C–H Arylation of Ketimine 135z

1-(3,4'-Dimethoxy-[1,1'-biphenyl]-2-yl)ethan-1-one (217)



Ketimine **135z** (158 mg, 0.50 mmol), [Ru(OAc)$_2$(*p*-cymene)] (**181**, 17.7 mg, 50.0 µmol, 10 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a 10 mL vial. The vial was capped with a septum and wrapped with parafilm. The vial was evacuated and purged with N_2 three times. 1-Iodo-4-methoxybenzene (**46a**, 176 mg, 0.75 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred under visible light irradiation (2 × Kessil A360N, temperature was maintained between 30 °C and 35 °C) for 24 h. At ambient temperature, HCl (2 N, 3.0 mL) was added, and the resulting mixture was stirred for an additional 3 h, and then extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc 7:1) yielded *ortho*-arylated product **217** (58.4 mg, 46%) as a light yellow solid.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.36 (dd, *J* = 8.4, 7.7 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 2H), 6.95 (dd, *J* = 7.7, 0.9 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.91 (dd, *J* = 8.4, 0.9 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 2.14 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 205.2 (C_q), 159.2 (C_q), 155.5 (C_q), 139.6 (C_q), 132.0 (C_q), 131.1 (C_q), 130.0 (CH), 129.8 (CH), 122.2 (CH), 113.9 (CH), 109.5 (CH), 55.9 (CH_3), 55.2 (CH_3), 32.4 (CH_3).

IR (ATR): $\tilde{\nu}$ = 2938, 1687, 1566, 1514, 1462, 1247, 1176, 1020, 834, 795 cm^{-1}.

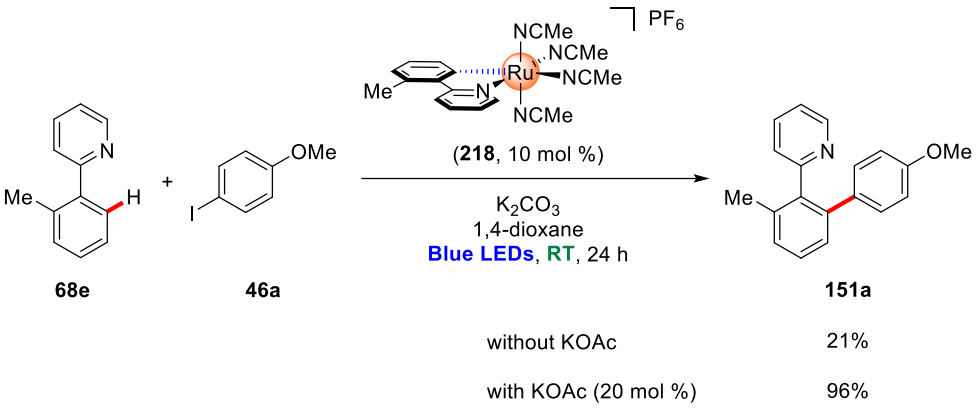
m.p.: 127–129 °C.

MS (ESI) *m*/*z* (relative intensity): 535 (13) $[2M+Na]^+$, 404 (27), 279 (100) $[M+Na]^+$, 257 (11) $[M+H]^+$, 148 (31).

HR-MS (ESI): *m*/*z* calcd for $C_{16}H_{16}O_3Na^+$ $[M+Na]^+$ 279.0992, found 279.0994.

The spectral data are in accordance with those reported in the literature.[146]

5.3.7.3 Photo-Induced C–H Arylation by Ruthenacycle 218



2-(*o*-Tolyl)pyridine (**68e**, 84.6 mg, 0.50 mmol), ruthenacycle **218** (28.9 mg, 50.0 µmol, 10 mol %), KOAc (9.8 mg, 0.10 mmol, 20 mol %) and K_2CO_3 (138 mg, 1.00 mmol) were placed in a 10 mL vial. The vial was capped with a septum and wrapped with parafilm. The vial was evacuated and purged with N_2 three times. 1-Iodo-4-methoxybenzene (**46a**, 176 mg, 0.75 mmol) and 1,4-dioxane (2.0 mL) were then added and the mixture was stirred under visible light irradiation (2 × Kessil A360N, temperature was maintained between 30 °C and 35 °C). After 24 h, the resulting mixture was filtered through a pad of silica gel and washed with EtOAc. The filtrate was concentrated *in vacuo*. Purification of the residue by column chromatography (SiO_2, *n*-hexane/EtOAc 7:1) yielded *ortho*-arylated product **151a** (145 mg, 96%) as a viscous colorless oil.

In case of the reaction without KOAc, the reaction provided the arylated product **151a** (32.3 mg, 21%) as a viscous colorless oil.

5.3.7.4 X-Ray Crystallographic Analysis

A suitable crystal was selected and the crystal was mounted on a MITIGEN holder in NVH oil on a Bruker D8 Venture diffractometer. The crystal was kept at 100 or 150 K during data collection. Using Olex2,[137] the structure was solved with the XT[138] structure solution program using Intrinsic Phasing and refined with the XL[139] refinement package using Least Squares minimisation.

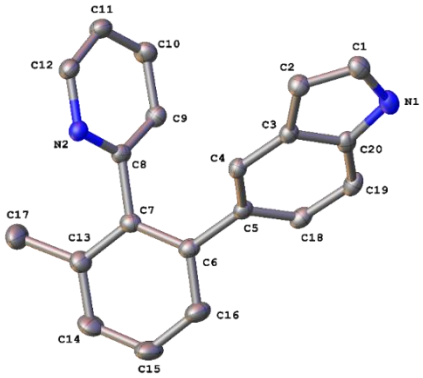


Figure 63: Molecular structure of **151o** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{20}H_{16}N_2$ (*M* = 284.35 g/mol): orthorhombic, space group $Pca2_1$ (no. 29), *a* = 15.2112(6) Å, *b* = 8.9415(4) Å, *c* = 22.0568(12) Å, *V* = 3000.0(2) Å^3, *Z* = 8, *T* = 150.04 K, μ(MoKα) = 0.074 mm^{-1}, *Dcalc* = 1.259 g/cm^3, 48106 reflections measured (4.556° ≤ 2Θ ≤ 57.456°), 7738 unique (R_{int} = 0.0299, R_{sigma} = 0.0205) which were used in all calculations. The final R_1 was 0.0434 (I > 2σ(I)) and wR_2 was 0.1161 (all data).

Table 107: Crystal data and structure refinement for **151o**.

Compound	**151o**
CCDC number	1968604
Identification code	0764_CG_Pca21
Empirical formula	$C_{20}H_{16}N_2$
Formula weight	284.35
Temperature/K	150.04
Crystal system	orthorhombic
Space group	$Pca2_1$
a/Å	15.2112(6)
b/Å	8.9415(4)
c/Å	22.0568(12)
α/°	90
β/°	90
γ/°	90

Volume/Å^3	3000.0(2)
Z	8
ρ_{calc}g/cm^3	1.259
μ/mm^{-1}	0.074
F(000)	1200.0
Crystal size/mm^3	0.418 × 0.311 × 0.126
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.556 to 57.456
Index ranges	-20 ≤ h ≤ 19, -12 ≤ k ≤ 12, -29 ≤ l ≤ 29
Reflections collected	48106
Independent reflections	7738 [R_{int} = 0.0299, R_{sigma} = 0.0205]
Data/restraints/parameters	7738/1/405
Goodness-of-fit on F^2	1.063
Final R indexes [I>=2σ (I)]	R_1 = 0.0434, wR_2 = 0.1138
Final R indexes [all data]	R_1 = 0.0460, wR_2 = 0.1161
Largest diff. peak/hole / e Å^{-3}	0.30/-0.27
Flack parameter	-0.1(6)

Table 108: Bond lengths [Å] for **151o**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N1	C1	1.375(3)	C7	C8	1.497(3)
N1	C20	1.378(3)	C7	C13	1.413(3)
N2	C8	1.346(3)	C8	C9	1.388(3)
N2	C12	1.345(3)	C9	C10	1.385(3)
C1	C2	1.360(3)	C10	C11	1.385(3)
C2	C3	1.437(3)	C11	C12	1.383(4)
C3	C4	1.401(3)	C13	C14	1.389(3)
C3	C20	1.418(3)	C13	C17	1.512(3)
C4	C5	1.391(3)	C14	C15	1.385(4)
C5	C6	1.490(3)	C15	C16	1.386(4)
C5	C18	1.415(3)	C18	C19	1.389(3)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C6	C7	1.408(3)	C19	C20	1.395(3)
C6	C16	1.393(3)			

Table 109: Bond angles [°] for **151o**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C1	N1	C20	108.50(19)	N2	C8	C9	122.3(2)
C12	N2	C8	117.4(2)	C9	C8	C7	119.9(2)
C2	C1	N1	110.4(2)	C10	C9	C8	119.4(2)
C1	C2	C3	106.9(2)	C11	C10	C9	118.7(2)
C4	C3	C2	134.3(2)	C12	C11	C10	118.4(2)
C4	C3	C20	119.2(2)	N2	C12	C11	123.7(2)
C20	C3	C2	106.47(19)	C7	C13	C17	122.4(2)
C5	C4	C3	119.8(2)	C14	C13	C7	118.8(2)
C4	C5	C6	120.93(19)	C14	C13	C17	118.8(2)
C4	C5	C18	119.6(2)	C15	C14	C13	121.2(2)
C18	C5	C6	119.4(2)	C14	C15	C16	119.9(2)
C7	C6	C5	122.82(19)	C15	C16	C6	120.8(2)
C16	C6	C5	118.1(2)	C19	C18	C5	121.8(2)
C16	C6	C7	119.0(2)	C18	C19	C20	117.8(2)
C6	C7	C8	120.4(2)	N1	C20	C3	107.7(2)
C6	C7	C13	120.2(2)	N1	C20	C19	130.6(2)
C13	C7	C8	119.3(2)	C19	C20	C3	121.6(2)
N2	C8	C7	117.79(19)				

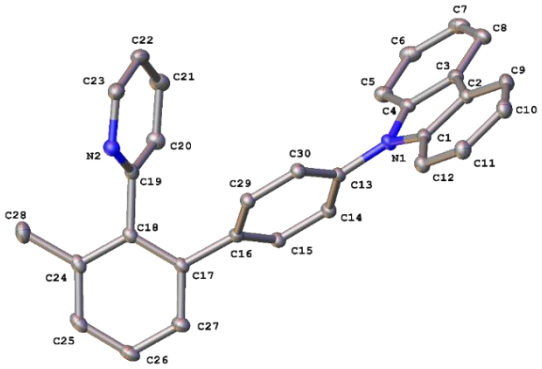


Figure 64: Molecular structure of **151t** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{30}H_{22}N_2$ (*M* = 410.49 g/mol): triclinic, space group P-1 (no. 2), *a* = 8.0802(7) Å, *b* = 9.6205(6) Å, *c* = 15.0324(11) Å, *α* = 105.143(4)°, *β* = 91.497(3)°, *γ* = 110.285(3)°, *V* = 1049.19(14) Å^3, *Z* = 2, *T* = 100.0 K, μ(MoKα) = 0.076 mm^{-1}, *Dcalc* = 1.299 g/cm^3, 54130 reflections measured (4.714° ≤ 2Θ ≤ 61.172°), 6426 unique (R_{int} = 0.0207, R_{sigma} = 0.0113) which were used in all calculations. The final R_1 was 0.0412 (I > 2σ(I)) and wR_2 was 0.1124 (all data).

Table 110: Crystal data and structure refinement for **151t**.

Compound	**151t**
CCDC number	1968602
Identification code	0773_CG_0m
Empirical formula	$C_{30}H_{22}N_2$
Formula weight	410.49
Temperature/K	100.0
Crystal system	triclinic
Space group	P-1
a/Å	8.0802(7)
b/Å	9.6205(6)
c/Å	15.0324(11)
α/°	105.143(4)
β/°	91.497(3)
γ/°	110.285(3)
Volume/Å^3	1049.19(14)

Z	2
ρ_{calc}g/cm^3	1.299
μ/mm^{-1}	0.076
F(000)	432.0
Crystal size/mm^3	0.497 × 0.38 × 0.311
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.714 to 61.172
Index ranges	-11 ≤ h ≤ 11, -11 ≤ k ≤ 13, -21 ≤ l ≤ 21
Reflections collected	54130
Independent reflections	6426 [R_{int} = 0.0207, R_{sigma} = 0.0113]
Data/restraints/parameters	6426/0/290
Goodness-of-fit on F^2	1.032
Final R indexes [I>=2σ (I)]	R_1 = 0.0412, wR_2 = 0.1107
Final R indexes [all data]	R_1 = 0.0430, wR_2 = 0.1124
Largest diff. peak/hole / e Å^{-3}	0.41/-0.24

Table 111: Bond lengths [Å] for **151t**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N1	C1	1.3952(11)	C13	C30	1.3980(11)
N1	C4	1.3969(11)	C14	C15	1.3918(11)
N1	C13	1.4143(10)	C15	C16	1.3968(12)
N2	C19	1.3440(11)	C16	C17	1.4865(11)
N2	C23	1.3421(12)	C16	C29	1.4001(11)
C1	C2	1.4092(11)	C17	C18	1.4072(12)
C1	C12	1.3929(12)	C17	C27	1.3976(12)
C2	C3	1.4433(12)	C18	C19	1.4947(12)
C2	C9	1.3959(12)	C18	C24	1.4059(11)
C3	C4	1.4105(12)	C19	C20	1.3966(12)
C3	C8	1.3980(12)	C20	C21	1.3872(13)
C4	C5	1.3935(12)	C21	C22	1.3873(14)
C5	C6	1.3889(12)	C22	C23	1.3854(13)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C6	C7	1.4010(14)	C24	C25	1.3961(13)
C7	C8	1.3858(14)	C24	C28	1.5068(13)
C9	C10	1.3871(13)	C25	C26	1.3888(14)
C10	C11	1.4043(13)	C26	C27	1.3890(12)
C11	C12	1.3905(12)	C29	C30	1.3890(11)
C13	C14	1.3941(11)			

Table 112: Bond angles [°] for **151t**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C1	N1	C4	108.37(7)	C15	C14	C13	119.96(8)
C1	N1	C13	126.14(7)	C14	C15	C16	120.94(8)
C4	N1	C13	125.09(7)	C15	C16	C17	120.58(7)
C23	N2	C19	117.42(8)	C15	C16	C29	118.55(8)
N1	C1	C2	108.97(7)	C29	C16	C17	120.87(7)
C12	C1	N1	129.22(8)	C18	C17	C16	120.52(7)
C12	C1	C2	121.80(8)	C27	C17	C16	119.72(8)
C1	C2	C3	106.89(7)	C27	C17	C18	119.75(8)
C9	C2	C1	119.55(8)	C17	C18	C19	119.00(7)
C9	C2	C3	133.55(8)	C24	C18	C17	120.19(8)
C4	C3	C2	106.96(7)	C24	C18	C19	120.80(8)
C8	C3	C2	133.46(8)	N2	C19	C18	117.08(7)
C8	C3	C4	119.55(8)	N2	C19	C20	122.34(8)
N1	C4	C3	108.81(7)	C20	C19	C18	120.53(8)
C5	C4	N1	129.16(8)	C21	C20	C19	119.21(8)
C5	C4	C3	121.96(8)	C20	C21	C22	118.80(9)
C6	C5	C4	117.38(9)	C23	C22	C21	118.15(8)
C5	C6	C7	121.36(9)	N2	C23	C22	124.05(9)
C8	C7	C6	121.02(8)	C18	C24	C28	121.08(8)
C7	C8	C3	118.70(9)	C25	C24	C18	118.70(8)
C10	C9	C2	119.16(8)	C25	C24	C28	120.23(8)

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C9	C10	C11	120.49(8)	C26	C25	C24	121.27(8)
C12	C11	C10	121.37(9)	C25	C26	C27	119.98(8)
C11	C12	C1	117.59(8)	C26	C27	C17	120.10(9)
C14	C13	N1	119.99(7)	C30	C29	C16	120.87(8)
C14	C13	C30	119.64(7)	C29	C30	C13	120.00(7)
C30	C13	N1	120.36(7)				

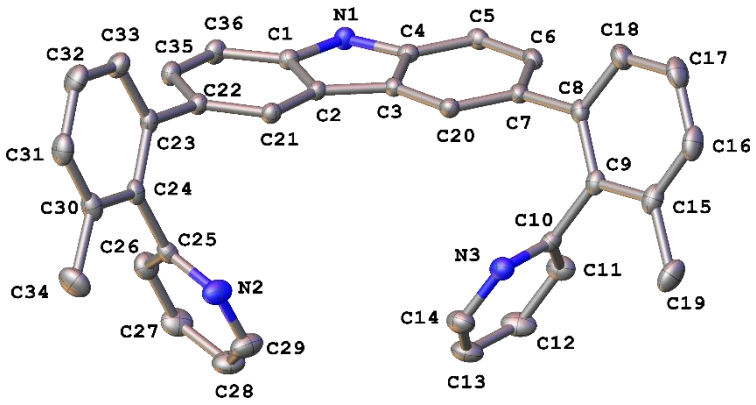


Figure 65: Molecular structure of **216b** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{37}Cl_2H_{29}N_3$ (*M* = 586.53 g/mol): monoclinic, space group $P2_1/n$ (no. 14), *a* = 8.3699(11) Å, *b* = 13.291(3) Å, *c* = 27.082(3) Å, *β* = 90.799(7)°, *V* = 3012.4(8) Å^3, *Z* = 4, *T* = 100.0 K, μ(MoKα) = 0.247 mm^{-1}, *Dcalc* = 1.293 g/cm^3, 99832 reflections measured (5.074° ≤ 2Θ ≤ 59.19°), 8420 unique (R_{int} = 0.0300, R_{sigma} = 0.0153) which were used in all calculations. The final R_1 was 0.0438 (I > 2σ(I)) and wR_2 was 0.1151 (all data).

Table 113: Crystal data and structure refinement for **216b**.

Compound	**216b**
CCDC number	1968605
Identification code	mo_0856_CG_0m
Empirical formula	$C_{37}Cl_2H_{29}N_3$
Formula weight	586.53
Temperature/K	100.0

Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	8.3699(11)
b/Å	13.291(3)
c/Å	27.082(3)
α/°	90
β/°	90.799(7)
γ/°	90
Volume/Å^3	3012.4(8)
Z	4
ρ_{calc}g/cm^3	1.293
μ/mm^{-1}	0.247
F(000)	1224.0
Crystal size/mm^3	0.401 × 0.105 × 0.068
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.074 to 59.19
Index ranges	-11 ≤ h ≤ 11, -18 ≤ k ≤ 18, -36 ≤ l ≤ 37
Reflections collected	99832
Independent reflections	8420 [R_{int} = 0.0300, R_{sigma} = 0.0153]
Data/restraints/parameters	8420/0/359
Goodness-of-fit on F^2	1.029
Final R indexes [I>=2σ (I)]	R_1 = 0.0438, wR_2 = 0.1092
Final R indexes [all data]	R_1 = 0.0518, wR_2 = 0.1151
Largest diff. peak/hole / e Å^{-3}	0.38/-0.25

Table 114: Bond lengths [Å] for **216b**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N1	C1	1.3865(13)	C12	C13	1.3809(19)
N1	C4	1.3839(13)	C13	C14	1.3822(18)
N2	C25	1.3426(14)	C15	C16	1.3906(18)
N2	C29	1.3387(16)	C15	C19	1.5081(18)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
N3	C10	1.3413(14)	C16	C17	1.384(2)
N3	C14	1.3428(15)	C17	C18	1.3877(17)
C1	C2	1.4178(14)	C21	C22	1.3926(14)
C1	C36	1.3938(14)	C22	C23	1.4926(14)
C2	C3	1.4449(14)	C22	C35	1.4057(15)
C2	C21	1.3957(14)	C23	C24	1.4034(15)
C3	C4	1.4143(14)	C23	C33	1.4011(15)
C3	C20	1.3951(14)	C24	C25	1.4917(15)
C4	C5	1.3957(14)	C24	C30	1.4077(15)
C5	C6	1.3846(15)	C25	C26	1.3925(15)
C6	C7	1.4097(15)	C26	C27	1.3807(18)
C7	C8	1.4920(14)	C27	C28	1.3798(19)
C7	C20	1.3905(14)	C28	C29	1.3806(18)
C8	C9	1.3988(15)	C30	C31	1.3941(17)
C8	C18	1.3991(15)	C30	C34	1.5071(17)
C9	C10	1.4915(15)	C31	C32	1.3862(18)
C9	C15	1.4054(15)	C32	C33	1.3891(16)
C10	C11	1.3911(15)	C35	C36	1.3869(15)
C11	C12	1.3866(17)			

Table 115: Bond angles [°] for **216b**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C4	N1	C1	108.68(9)	C9	C15	C19	120.39(11)
C29	N2	C25	117.28(10)	C16	C15	C9	118.64(11)
C10	N3	C14	117.44(10)	C16	C15	C19	120.96(11)
N1	C1	C2	108.94(9)	C17	C16	C15	121.01(11)
N1	C1	C36	130.21(10)	C16	C17	C18	120.15(11)
C36	C1	C2	120.81(9)	C17	C18	C8	120.33(11)
C1	C2	C3	106.60(9)	C7	C20	C3	119.18(9)
C21	C2	C1	120.12(9)	C22	C21	C2	119.33(9)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C21	C2	C3	133.17(9)	C21	C22	C23	119.78(9)
C4	C3	C2	106.47(9)	C21	C22	C35	119.56(9)
C20	C3	C2	133.42(9)	C35	C22	C23	120.52(9)
C20	C3	C4	120.10(9)	C24	C23	C22	121.73(9)
N1	C4	C3	109.26(9)	C33	C23	C22	118.57(10)
N1	C4	C5	129.60(10)	C33	C23	C24	119.63(10)
C5	C4	C3	121.13(9)	C23	C24	C25	119.84(9)
C6	C5	C4	117.72(9)	C23	C24	C30	120.11(10)
C5	C6	C7	122.07(9)	C30	C24	C25	120.05(10)
C6	C7	C8	119.67(9)	N2	C25	C24	116.84(9)
C20	C7	C6	119.78(9)	N2	C25	C26	122.47(10)
C20	C7	C8	120.51(9)	C26	C25	C24	120.69(10)
C9	C8	C7	121.29(9)	C27	C26	C25	119.06(11)
C9	C8	C18	118.98(10)	C28	C27	C26	118.89(11)
C18	C8	C7	119.72(10)	C27	C28	C29	118.40(12)
C8	C9	C10	120.19(9)	N2	C29	C28	123.87(12)
C8	C9	C15	120.85(10)	C24	C30	C34	121.00(11)
C15	C9	C10	118.97(10)	C31	C30	C24	118.94(11)
N3	C10	C9	115.86(9)	C31	C30	C34	120.05(11)
N3	C10	C11	122.62(10)	C32	C31	C30	121.13(11)
C11	C10	C9	121.50(10)	C31	C32	C33	120.04(11)
C12	C11	C10	118.82(11)	C32	C33	C23	120.13(11)
C13	C12	C11	119.07(11)	C36	C35	C22	122.20(10)
C12	C13	C14	118.31(11)	C35	C36	C1	117.93(9)
N3	C14	C13	123.70(11)				

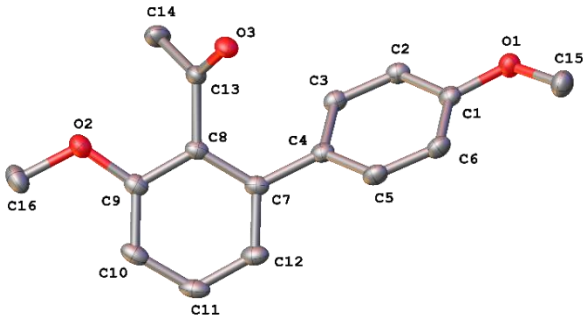


Figure 66: Molecular structure of **217** with thermal ellipoids at 50% probability level. The hydrogen atoms are omitted for clarity.

Crystal Data for $C_{16}H_{16}O_3$ (*M* = 256.29 g/mol): monoclinic, space group $P2_1/c$ (no. 14), *a* = 7.9023(5) Å, *b* = 17.4162(12) Å, *c* = 10.1964(7) Å, *β* = 110.822(2)°, *V* = 1311.66(15) Å^3, *Z* = 4, *T* = 100.0 K, μ(MoKα) = 0.089 mm^{-1}, *Dcalc* = 1.298 g/cm^3, 26466 reflections measured (4.678° ≤ 2Θ ≤ 57.442°), 3377 unique (R_{int} = 0.0225, R_{sigma} = 0.0127) which were used in all calculations. The final R_1 was 0.0418 (I > 2σ(I)) and wR_2 was 0.1093 (all data).

Table 116: Crystal data and structure refinement for **217**.

Compound	**217**
CCDC number	1979317
Identification code	mo_0859_CG_0m
Empirical formula	$C_{16}H_{16}O_3$
Formula weight	256.29
Temperature/K	100.0
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	7.9023(5)
b/Å	17.4162(12)
c/Å	10.1964(7)
α/°	90
β/°	110.822(2)
γ/°	90
Volume/Å^3	1311.66(15)

Z	4
ρ_{calc}g/cm^3	1.298
μ/mm^{-1}	0.089
F(000)	544.0
Crystal size/mm^3	0.337 × 0.214 × 0.153
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.678 to 57.442
Index ranges	-10 ≤ h ≤ 10, -23 ≤ k ≤ 23, -13 ≤ l ≤ 13
Reflections collected	26466
Independent reflections	3377 [R_{int} = 0.0225, R_{sigma} = 0.0127]
Data/restraints/parameters	3377/0/175
Goodness-of-fit on F^2	1.053
Final R indexes [I>=2σ (I)]	R_1 = 0.0418, wR_2 = 0.1058
Final R indexes [all data]	R_1 = 0.0461, wR_2 = 0.1093
Largest diff. peak/hole / e Å^{-3}	0.96/-0.20

Table 117: Bond lengths [Å] for **217**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C1	1.3673(13)	C4	C7	1.4862(15)
O1	C15	1.4269(14)	C5	C6	1.3906(16)
O2	C9	1.3657(14)	C7	C8	1.4033(15)
O2	C16	1.4313(13)	C7	C12	1.4032(15)
O3	C13	1.2140(13)	C8	C9	1.4053(14)
C1	C2	1.3973(15)	C8	C13	1.5093(14)
C1	C6	1.3900(15)	C9	C10	1.3945(15)
C2	C3	1.3841(15)	C10	C11	1.3865(18)
C3	C4	1.4034(14)	C11	C12	1.3837(17)
C4	C5	1.3947(15)	C13	C14	1.5069(15)

Table 118: Bond angles [°] for **217**.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C1	O1	C15	117.16(9)	C12	C7	C8	118.91(10)
C9	O2	C16	117.64(9)	C7	C8	C9	119.60(9)
O1	C1	C2	115.67(9)	C7	C8	C13	121.25(9)
O1	C1	C6	124.33(10)	C9	C8	C13	119.09(9)
C6	C1	C2	119.99(10)	O2	C9	C8	115.57(9)
C3	C2	C1	120.12(10)	O2	C9	C10	123.48(10)
C2	C3	C4	121.00(10)	C10	C9	C8	120.91(10)
C3	C4	C7	122.38(9)	C11	C10	C9	118.81(11)
C5	C4	C3	117.69(10)	C12	C11	C10	121.22(10)
C5	C4	C7	119.86(9)	C11	C12	C7	120.52(11)
C6	C5	C4	122.11(10)	O3	C13	C8	120.05(10)
C1	C6	C5	119.08(10)	O3	C13	C14	121.23(10)
C8	C7	C4	122.87(9)	C14	C13	C8	118.72(9)
C12	C7	C4	118.18(10)				

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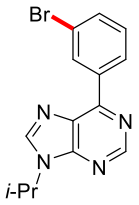
7 Appendix: NMR spectra



133a
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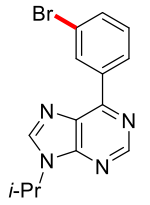

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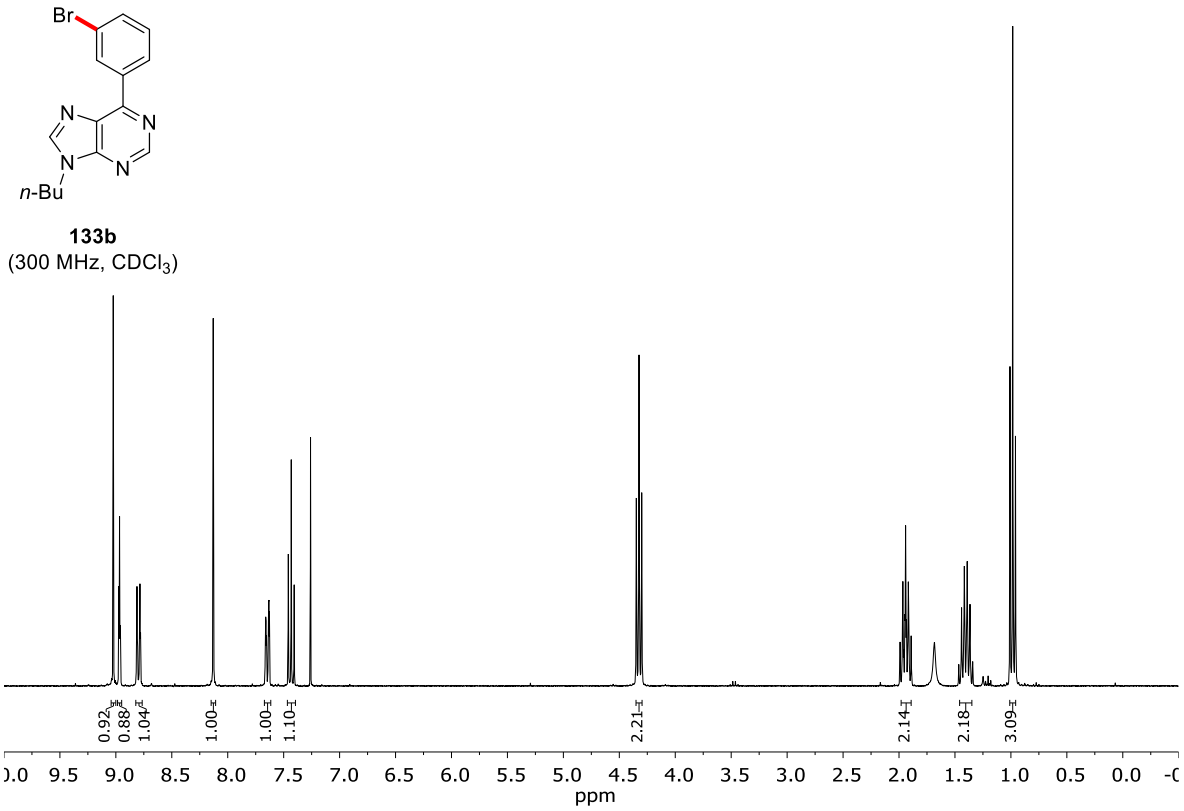

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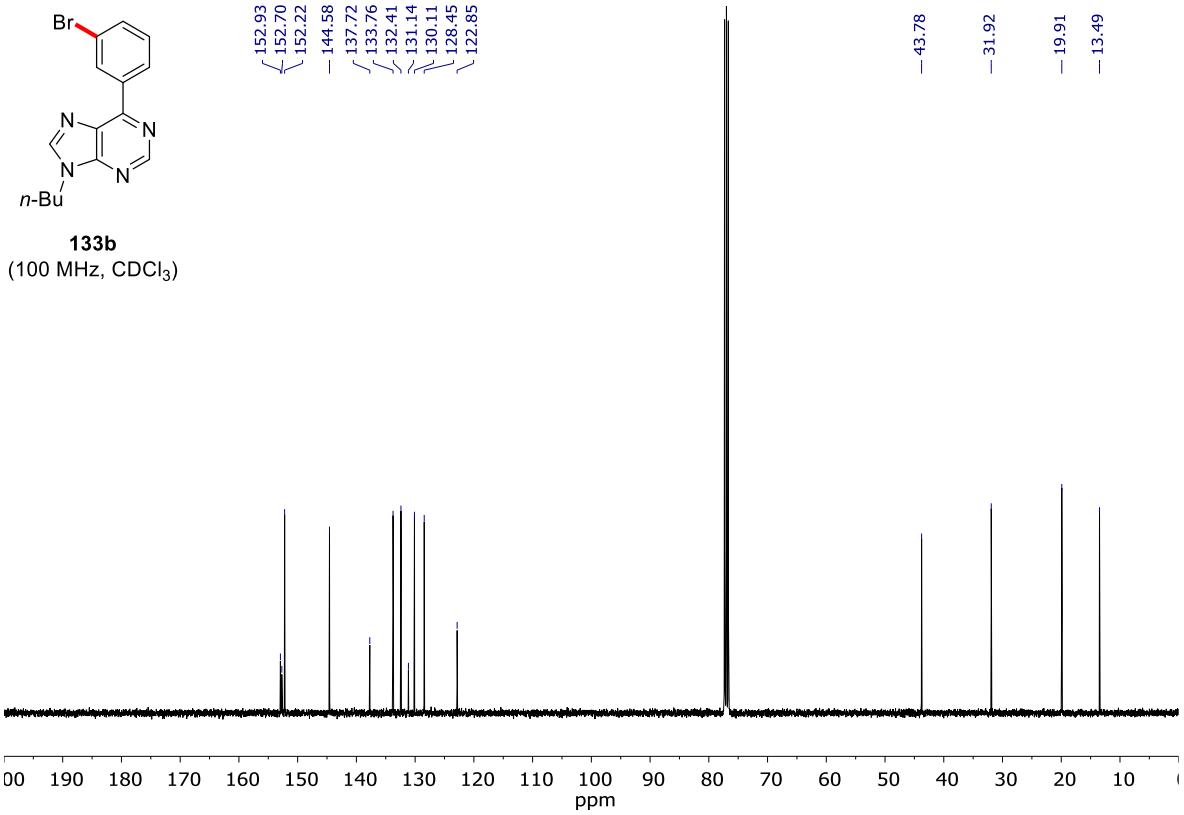
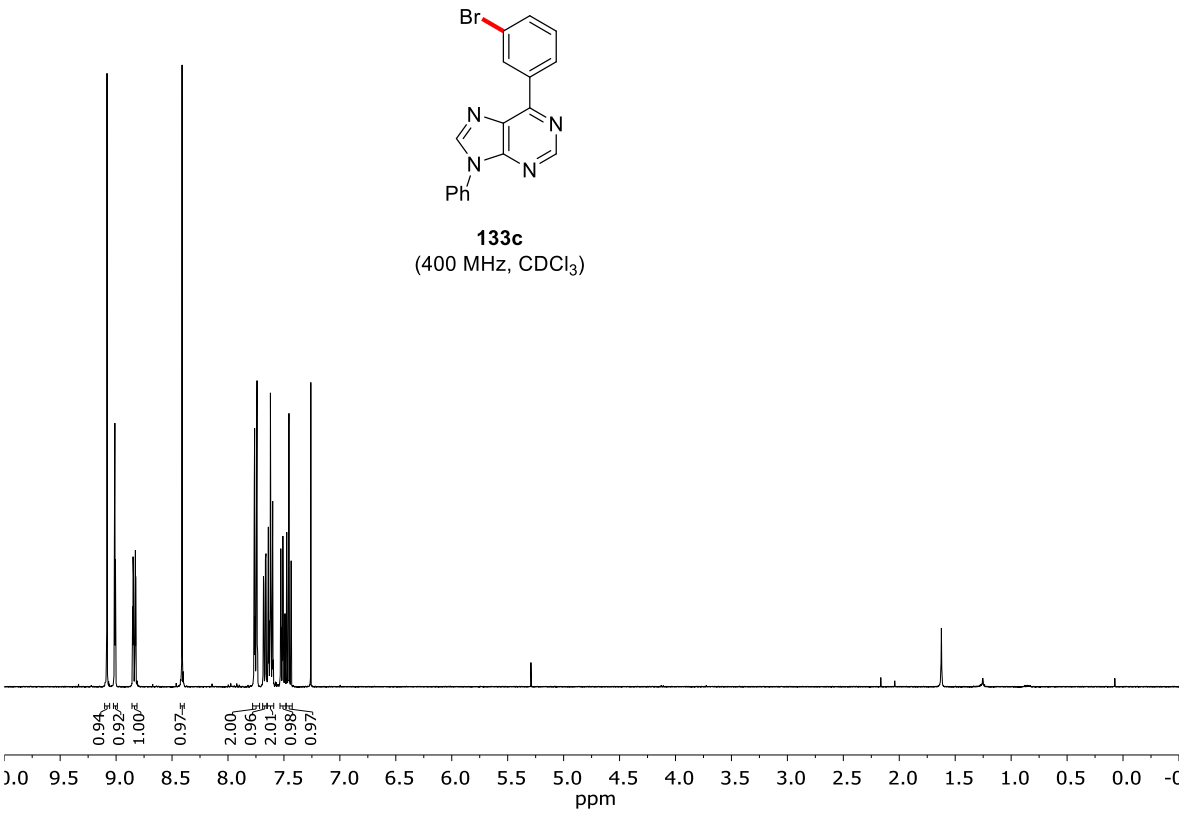
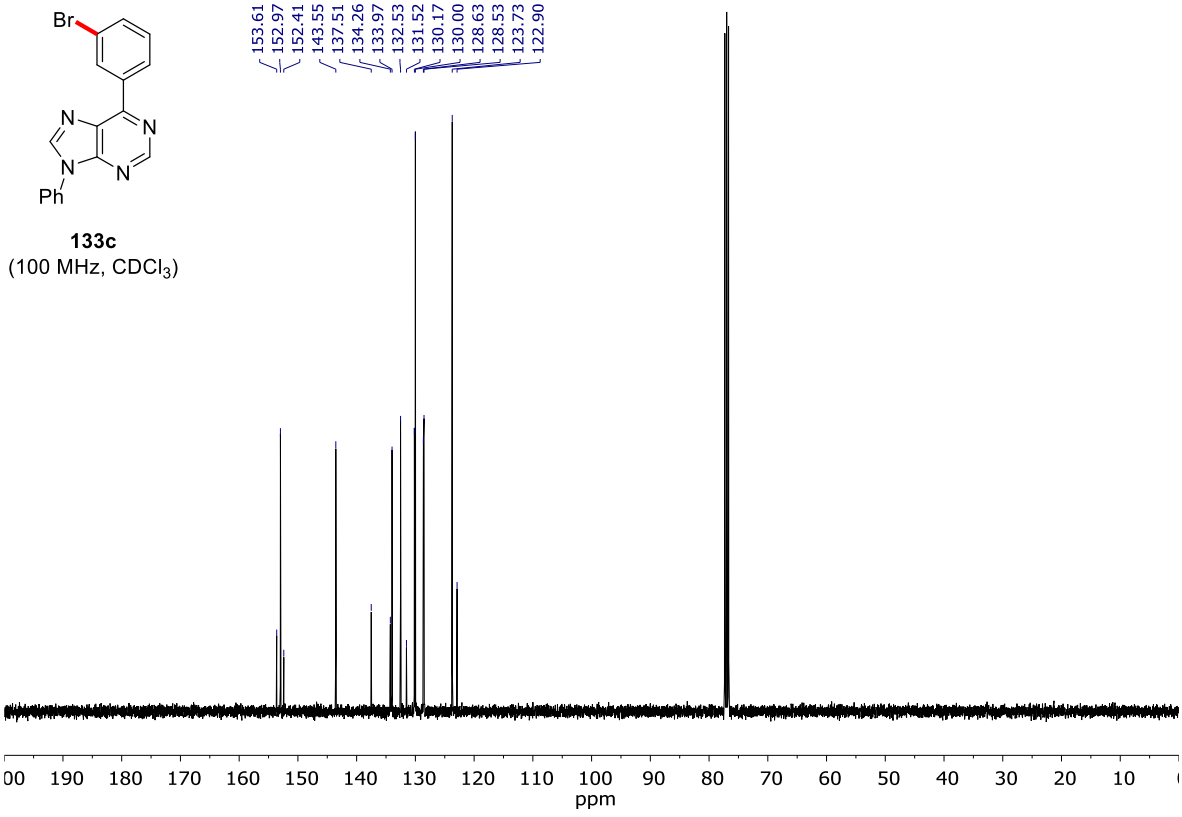


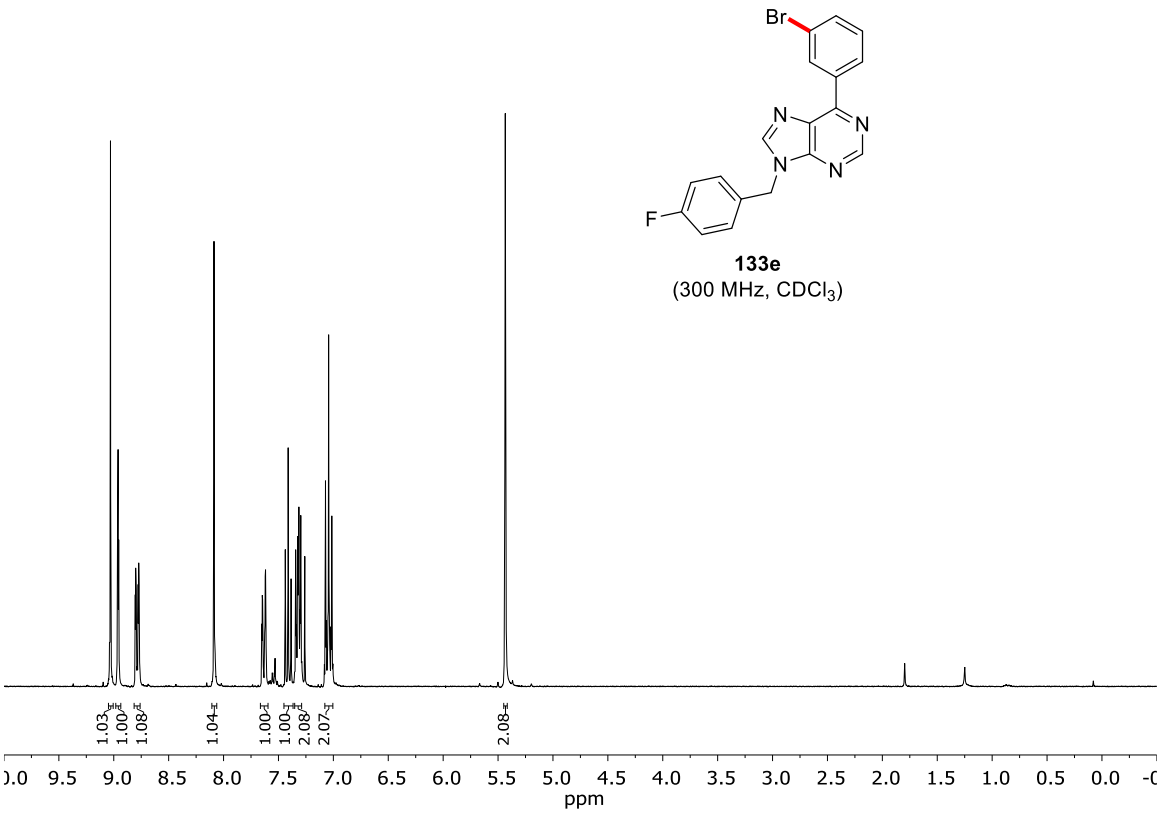
133b
(100 MHz, $CDCl_3$)



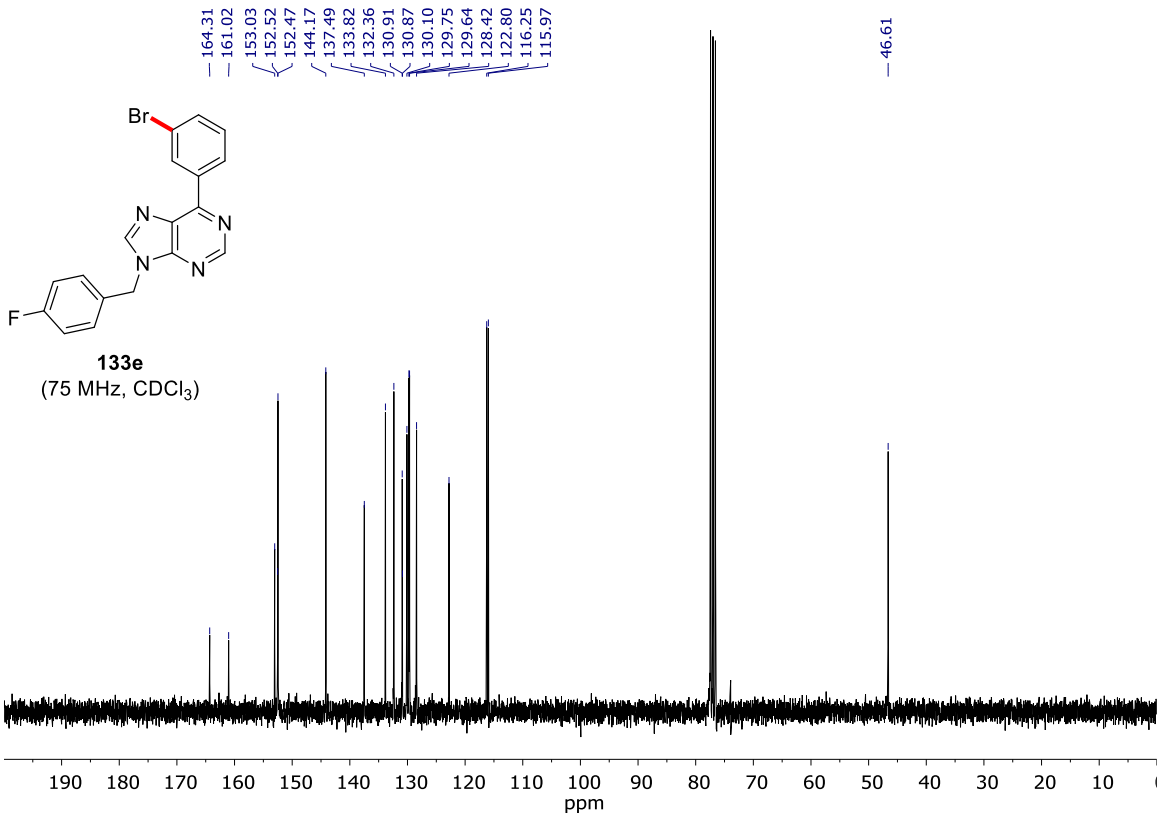
133c
(400 MHz, $CDCl_3$)



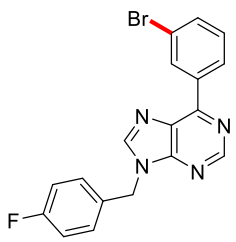
133c
(100 MHz, $CDCl_3$)



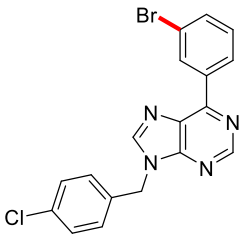
133e
(300 MHz, $CDCl_3$)



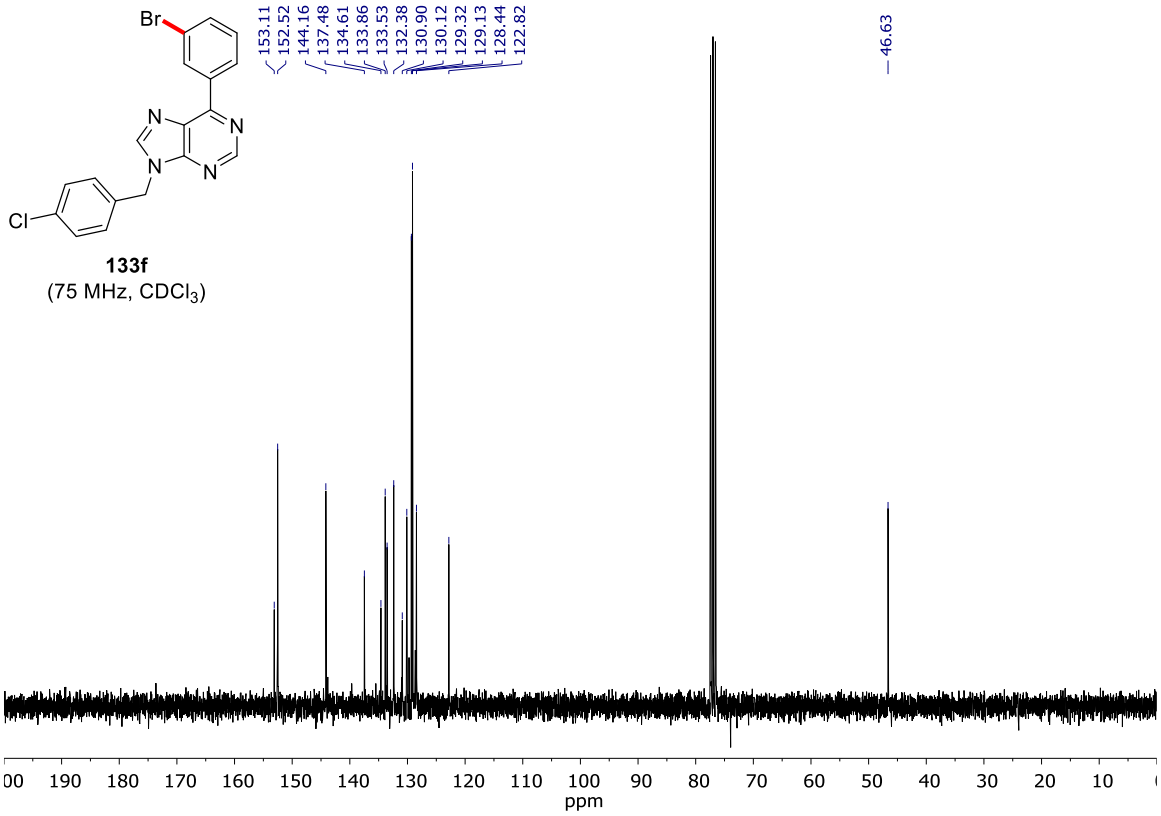
133e
(75 MHz, $CDCl_3$)



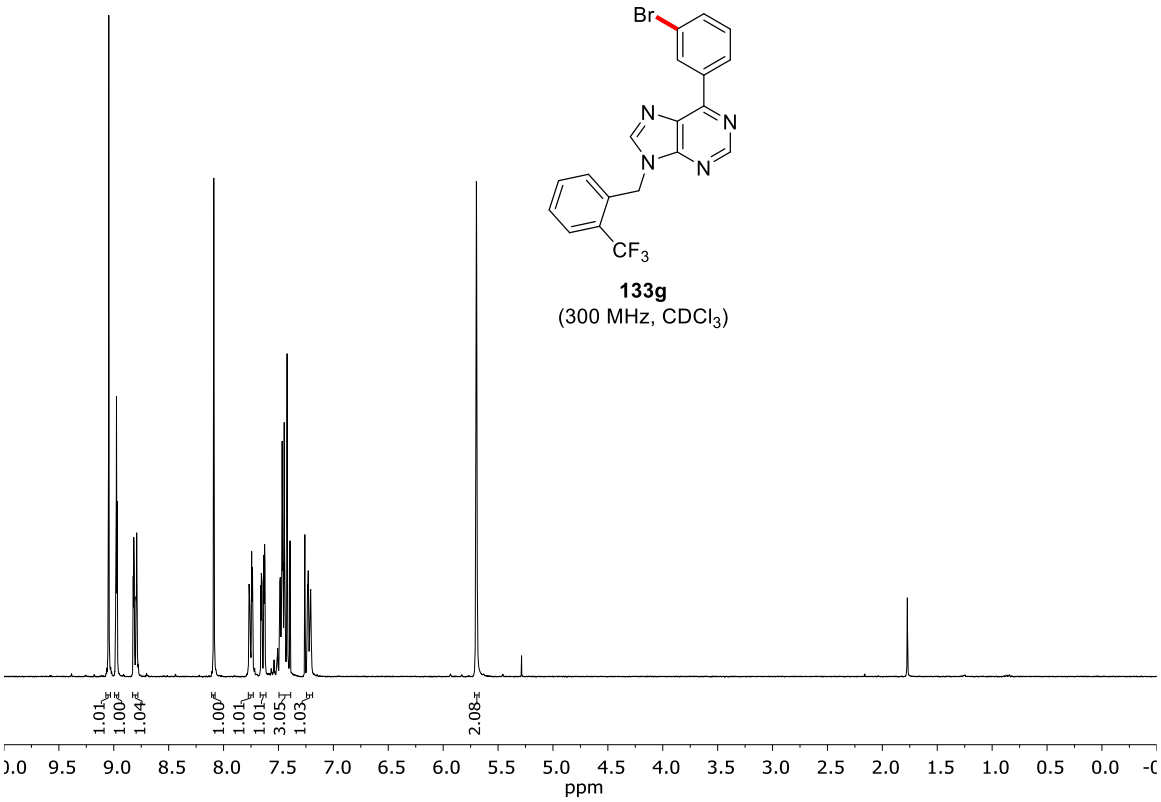
133e
^{19}F-NMR
(282 MHz, $CDCl_3$)



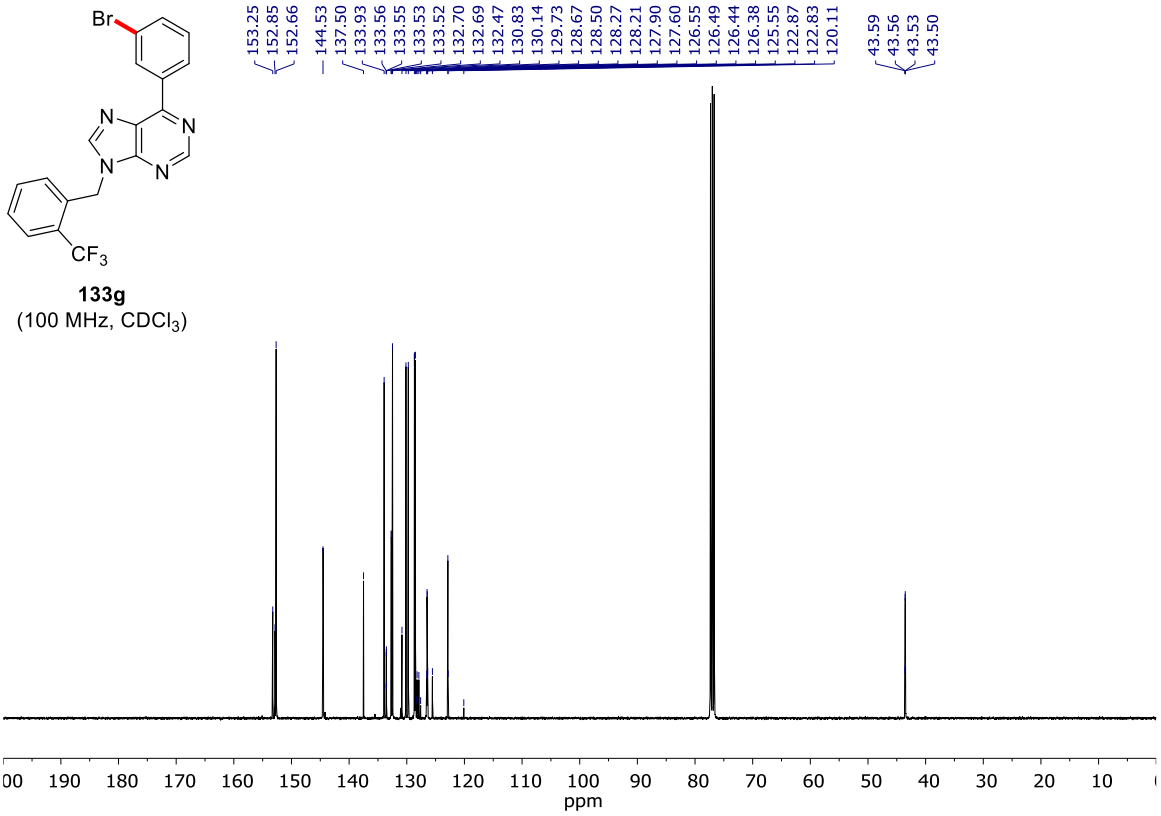
133f
(300 MHz, $CDCl_3$)



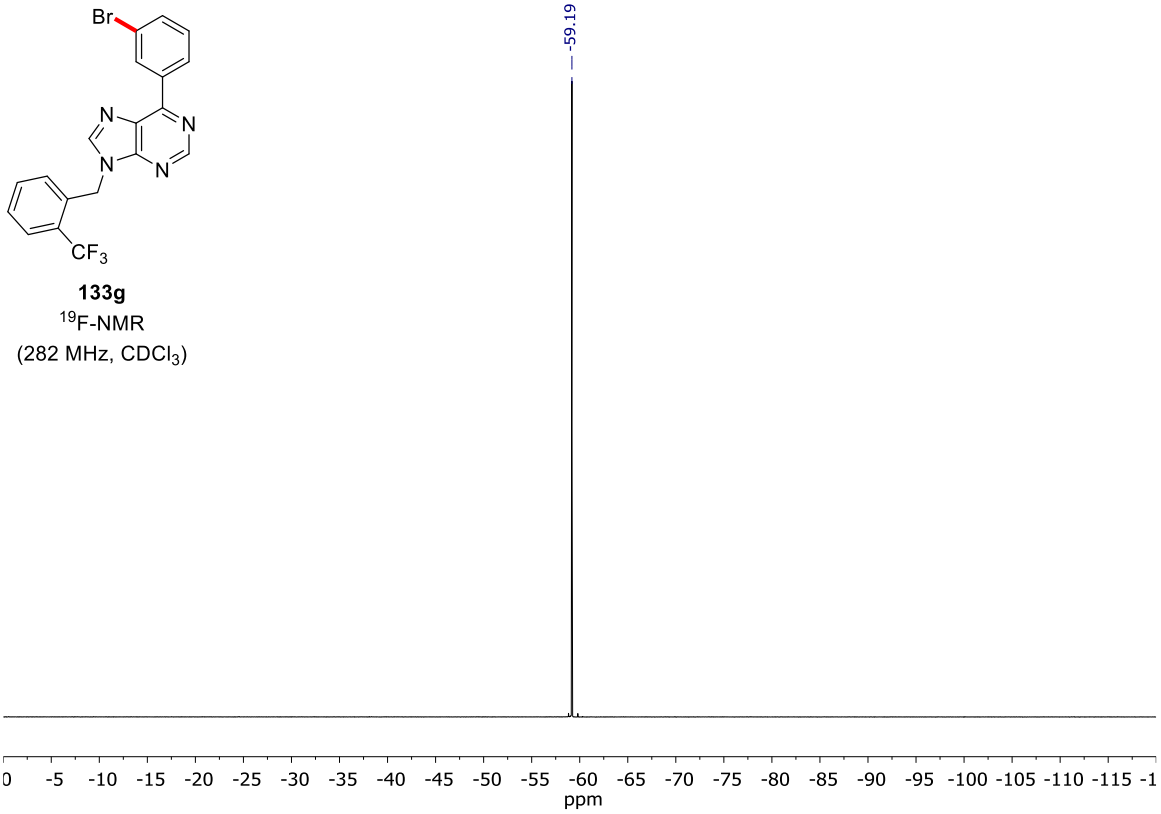
133f
(75 MHz, $CDCl_3$)



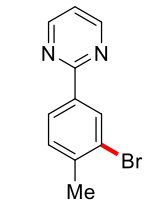
133g
(300 MHz, $CDCl_3$)



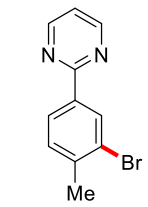
133g
(100 MHz, $CDCl_3$)



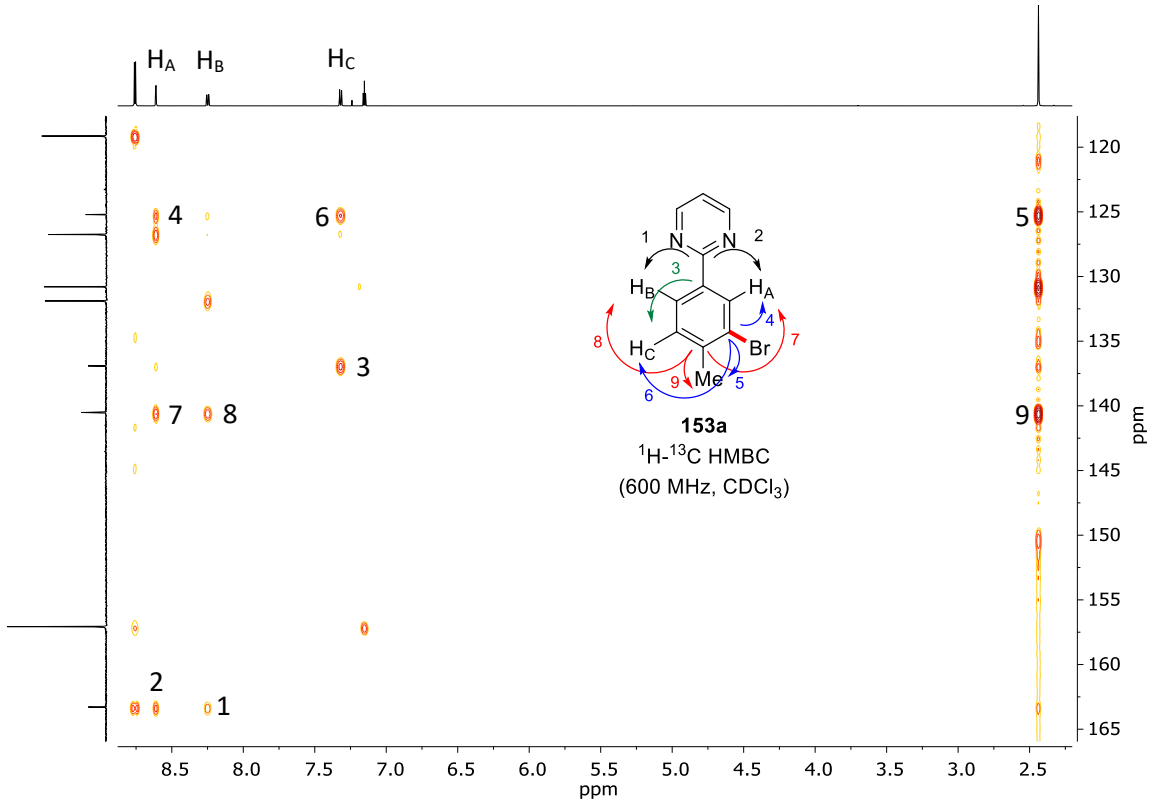
133g
^{19}F-NMR
(282 MHz, $CDCl_3$)

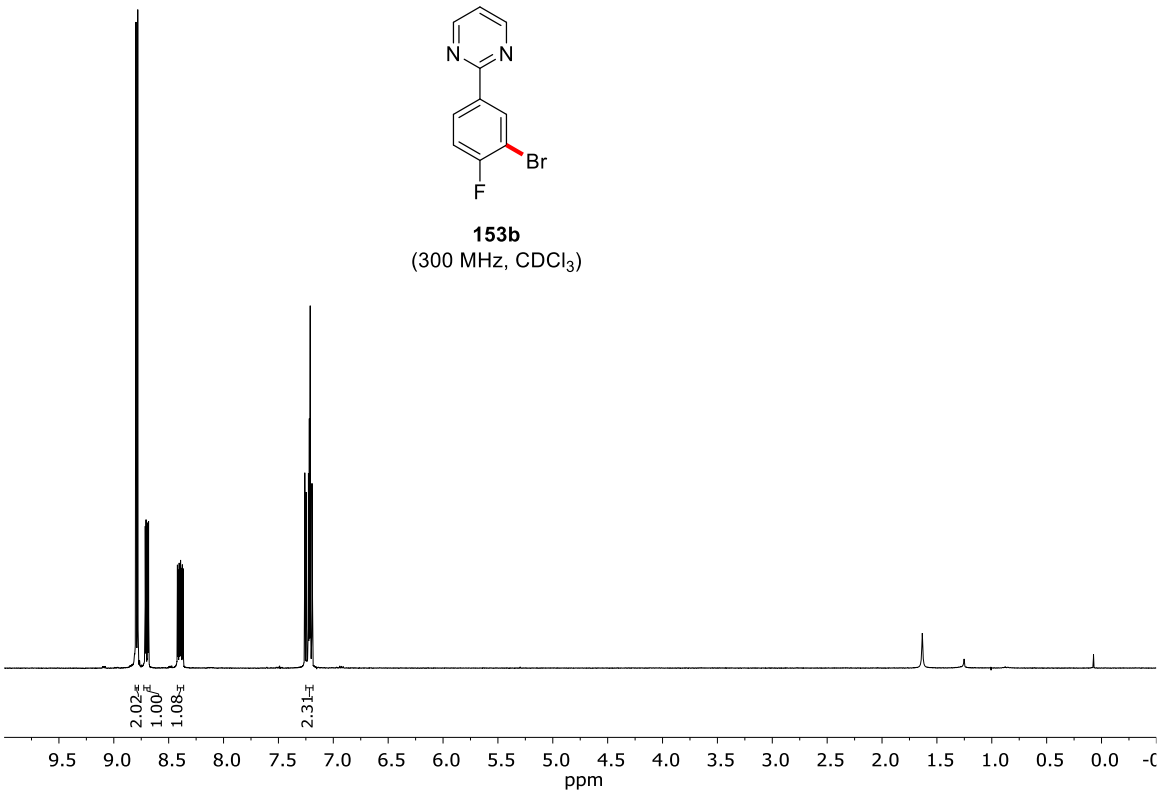


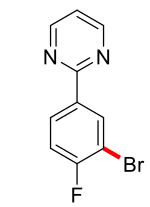
153a
(600 MHz, $CDCl_3$)



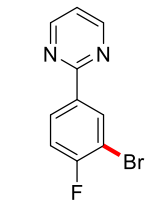
153a
(125 MHz, $CDCl_3$)


HA HB HC
4
6
3
7 8
2
1
5
9
1
2
3
HB
HA
4
HC
Br
7
8
9
Me
5
6
153a
1H-13C HMBC
(600 MHz, CDCl3)
ppm
ppm

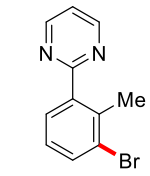

N
N
Br
F
153b
(300 MHz, CDCl3)
2.02
1.00
1.08
2.31
ppm



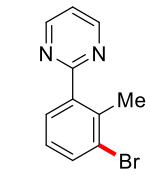
153b
(125 MHz, $CDCl_3$)



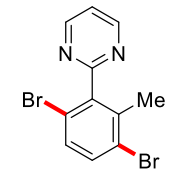
153b
^{19}F-NMR
(282 MHz, $CDCl_3$)



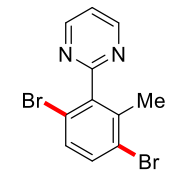
153c
(500 MHz, $CDCl_3$)



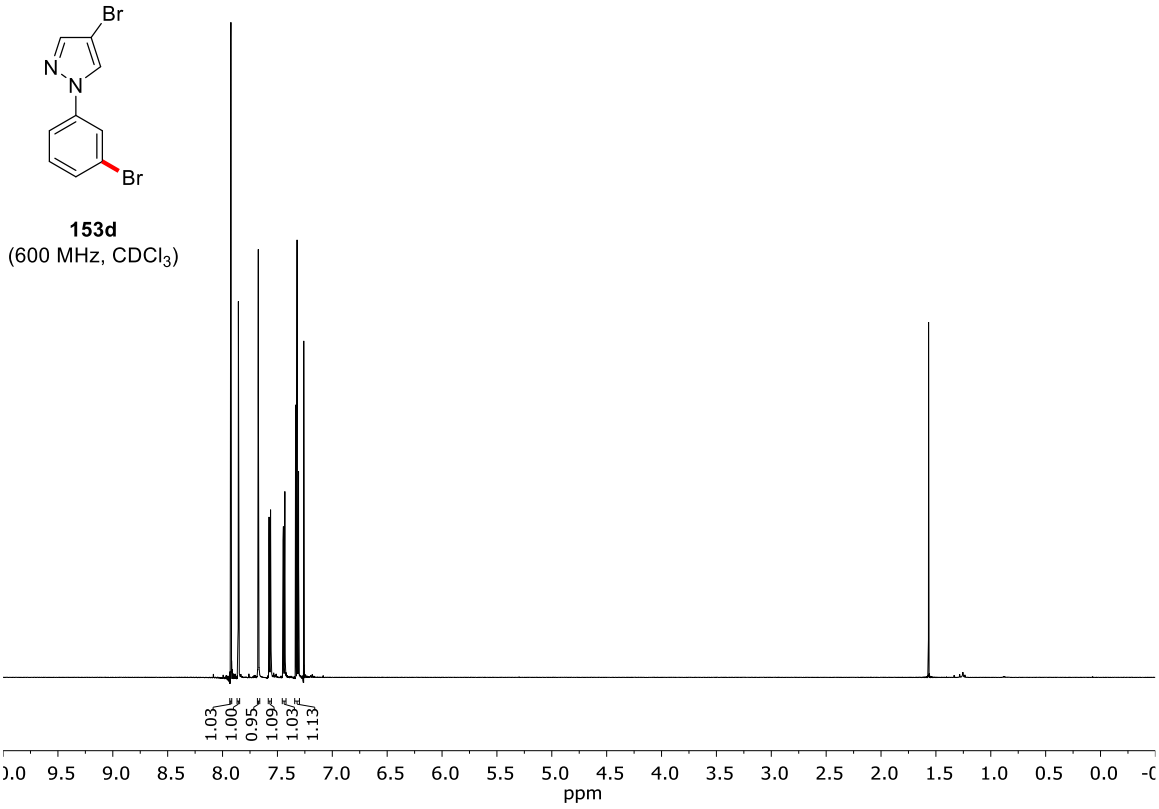
153c
(125 MHz, $CDCl_3$)

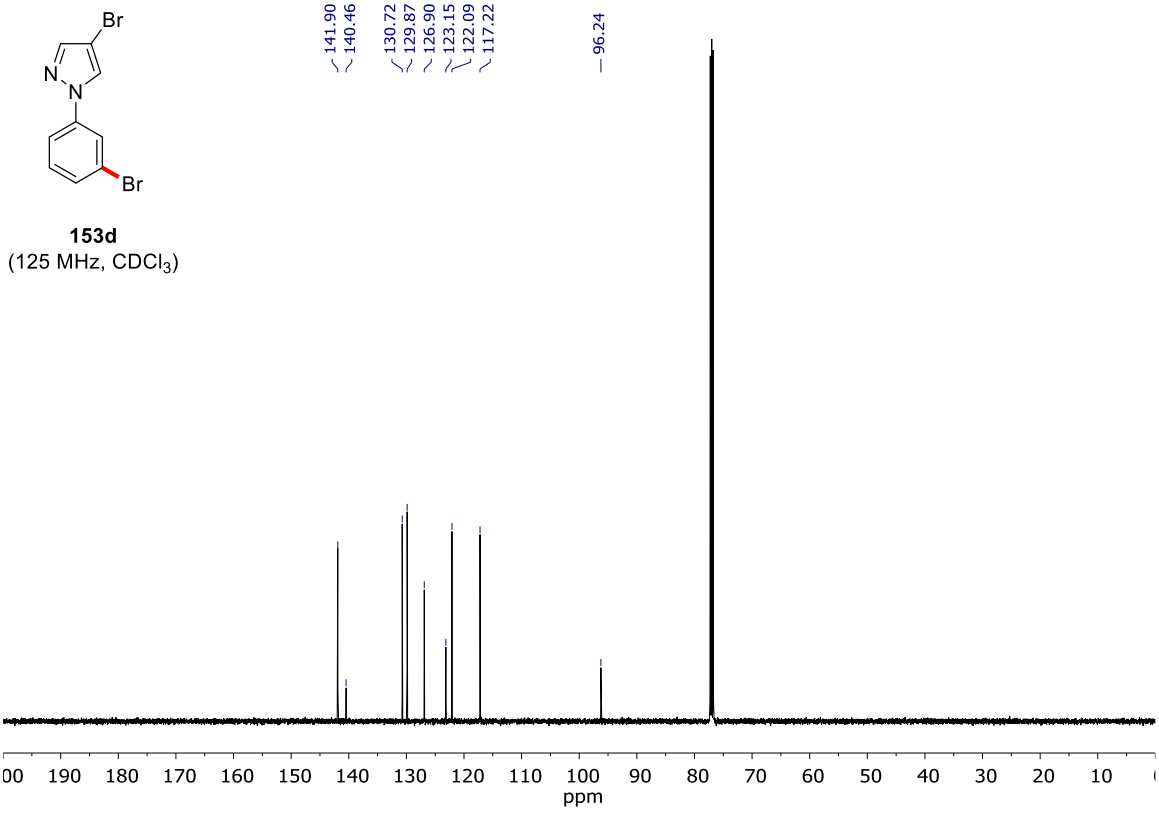


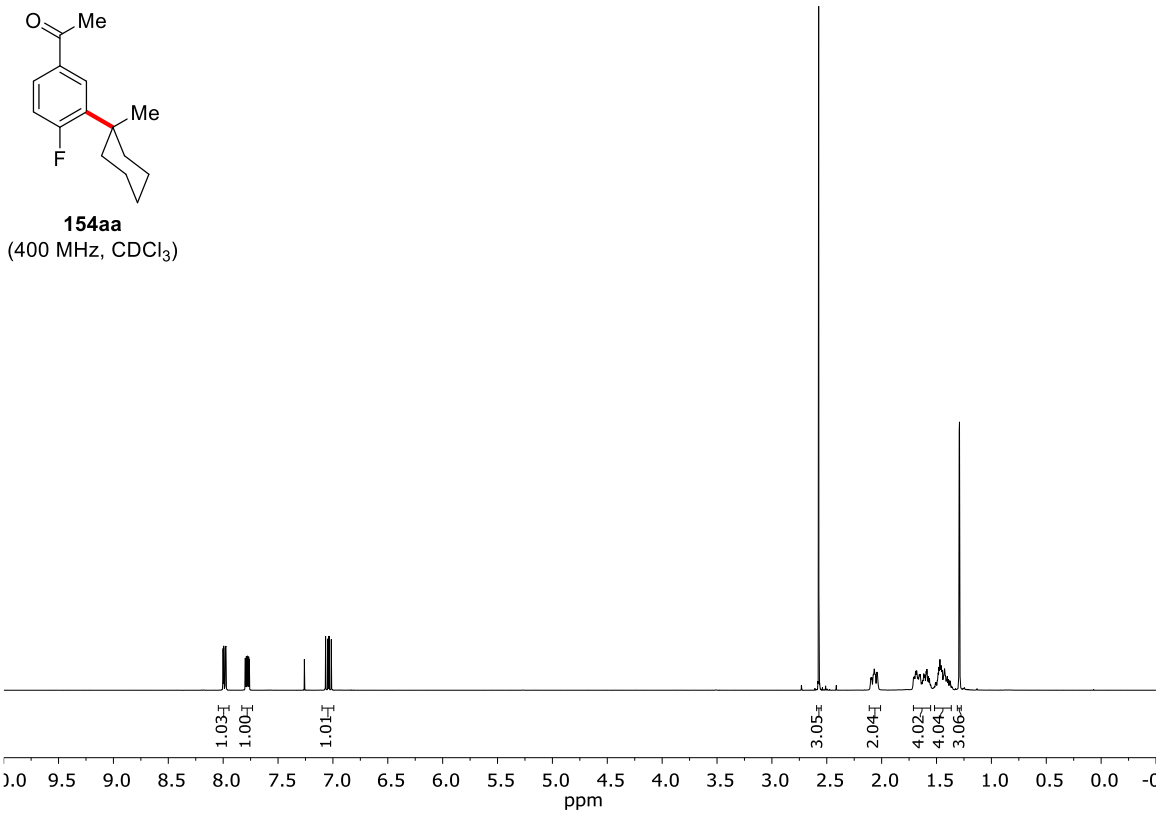
153c'
(400 MHz, $CDCl_3$)



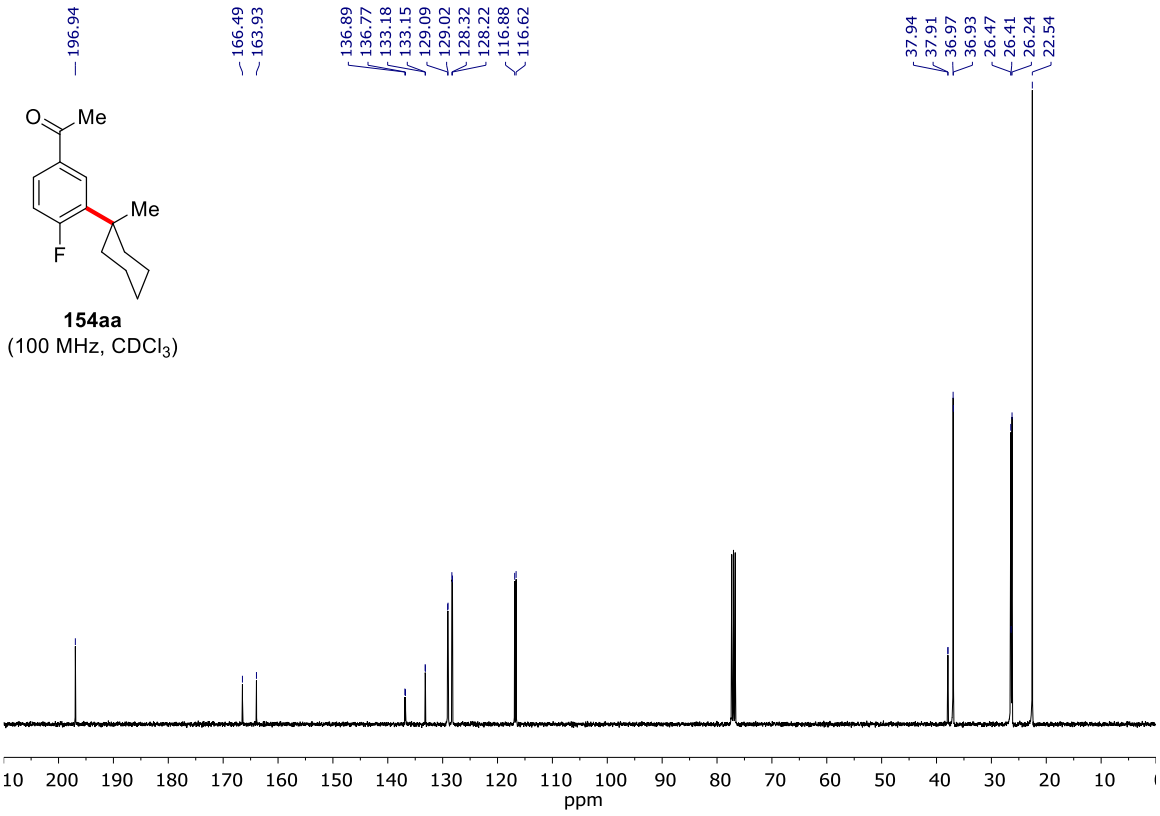
153c'
(125 MHz, $CDCl_3$)


Br
N
N
Br
153d
(600 MHz, CDCl3)
1.03
1.00
0.95
1.09
1.03
1.13
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

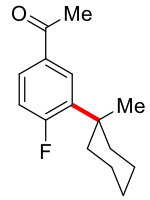

Br
N
N
Br
153d
(125 MHz, CDCl3)
141.90
140.46
130.72
129.87
126.90
123.15
122.09
117.22
96.24
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm



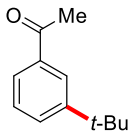
154aa
(400 MHz, $CDCl_3$)



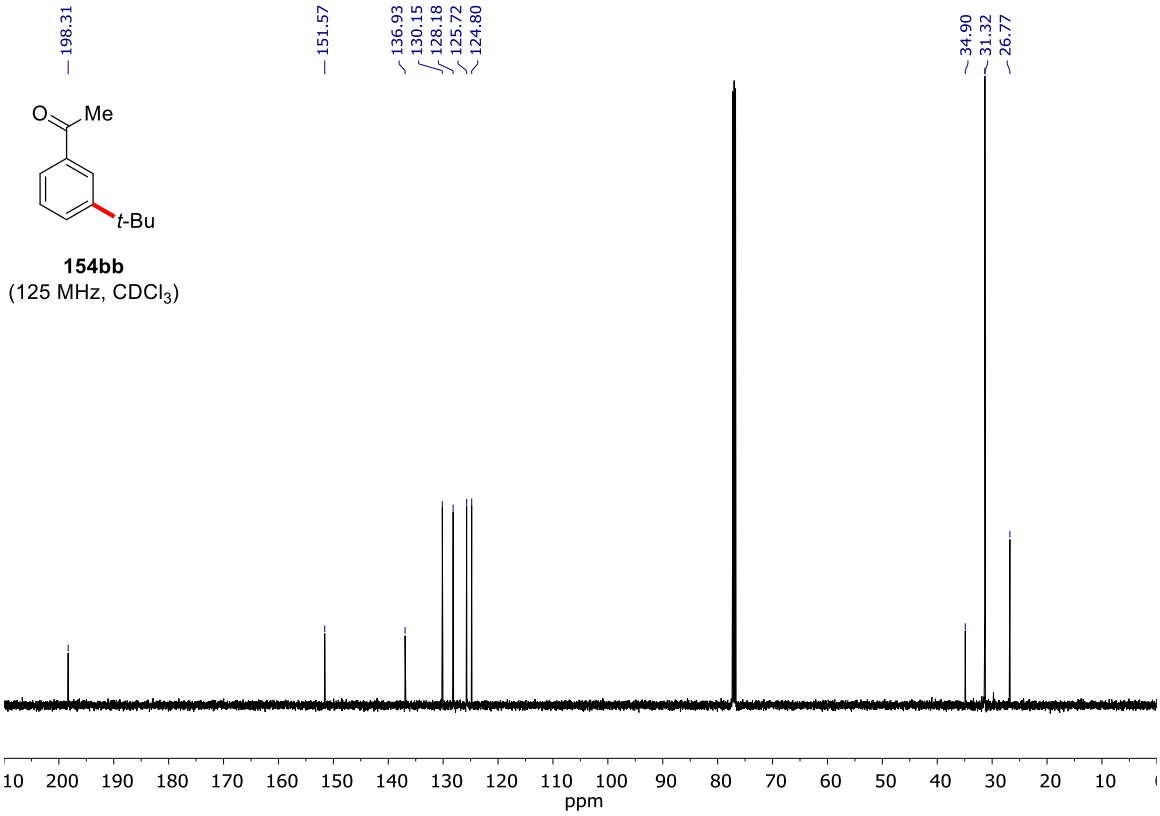
154aa
(100 MHz, $CDCl_3$)



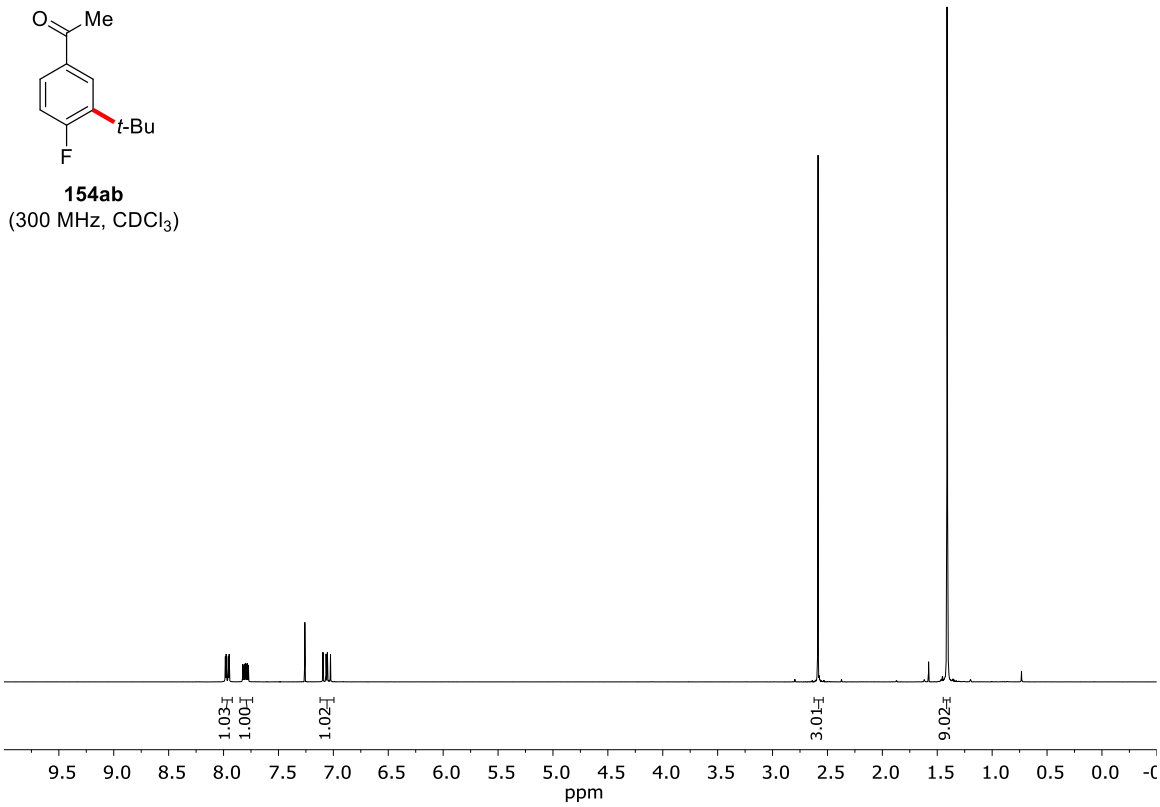
154aa
^{19}F-NMR
(376 MHz, $CDCl_3$)



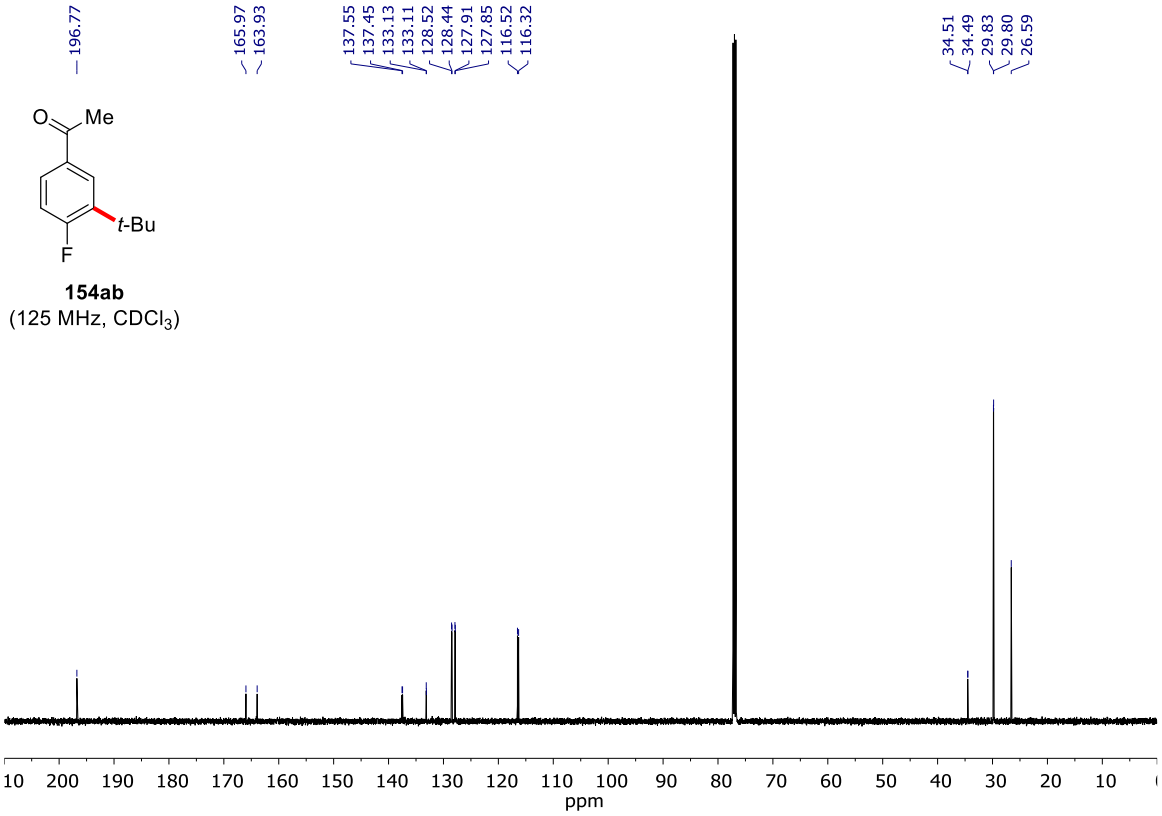
154bb
(300 MHz, $CDCl_3$)



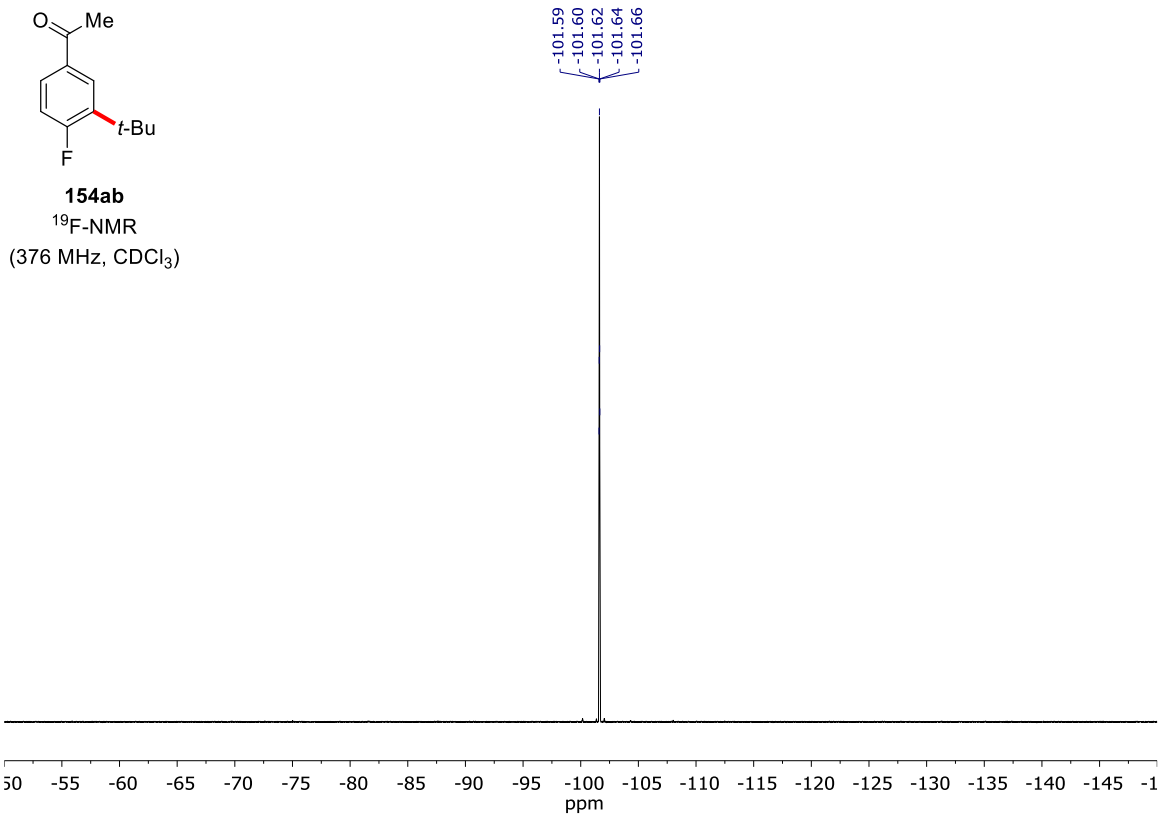
154bb
(125 MHz, $CDCl_3$)



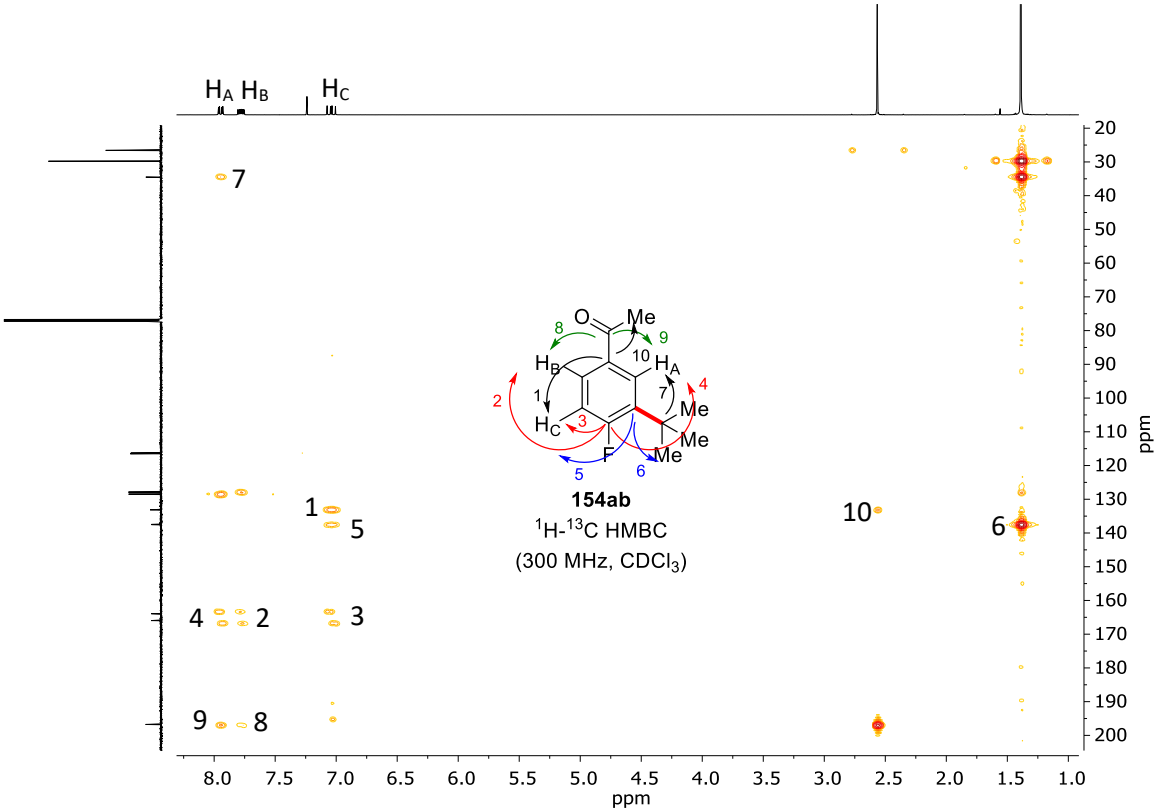
154ab
(300 MHz, $CDCl_3$)



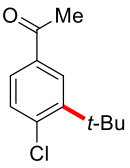
154ab
(125 MHz, $CDCl_3$)



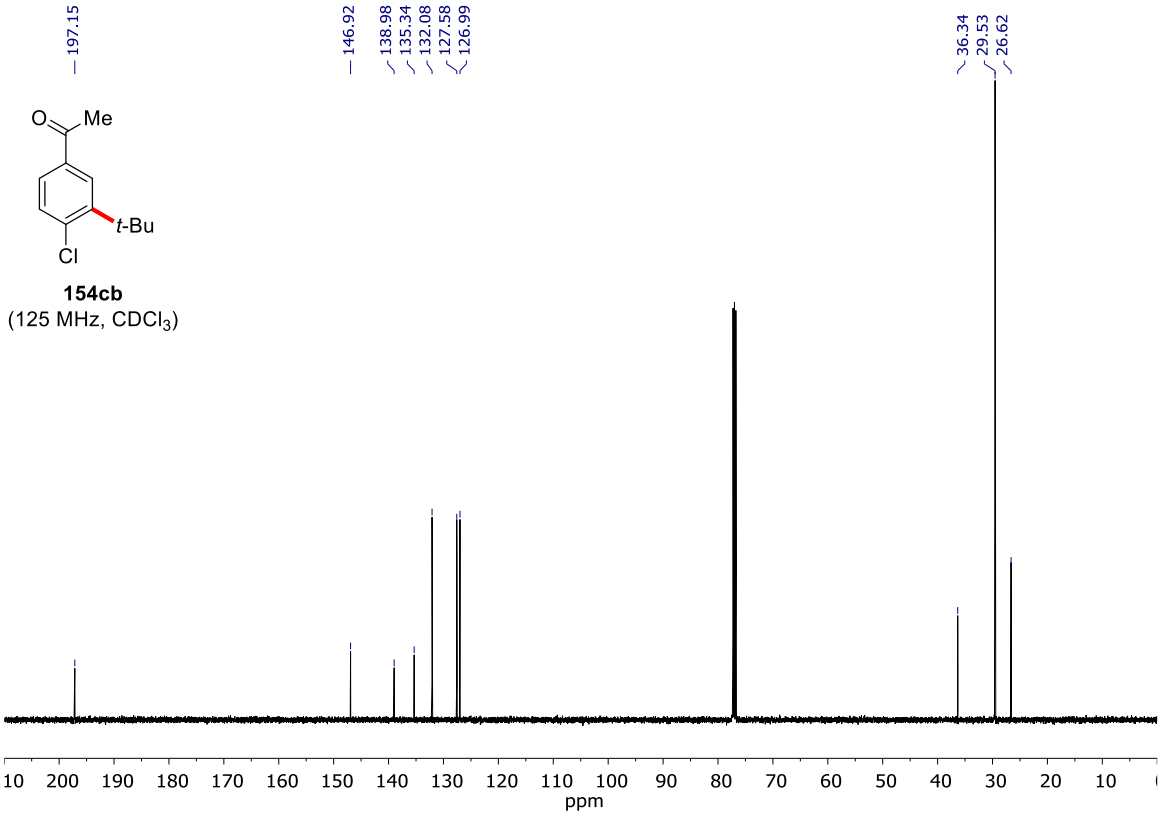
154ab
^{19}F-NMR
(376 MHz, $CDCl_3$)

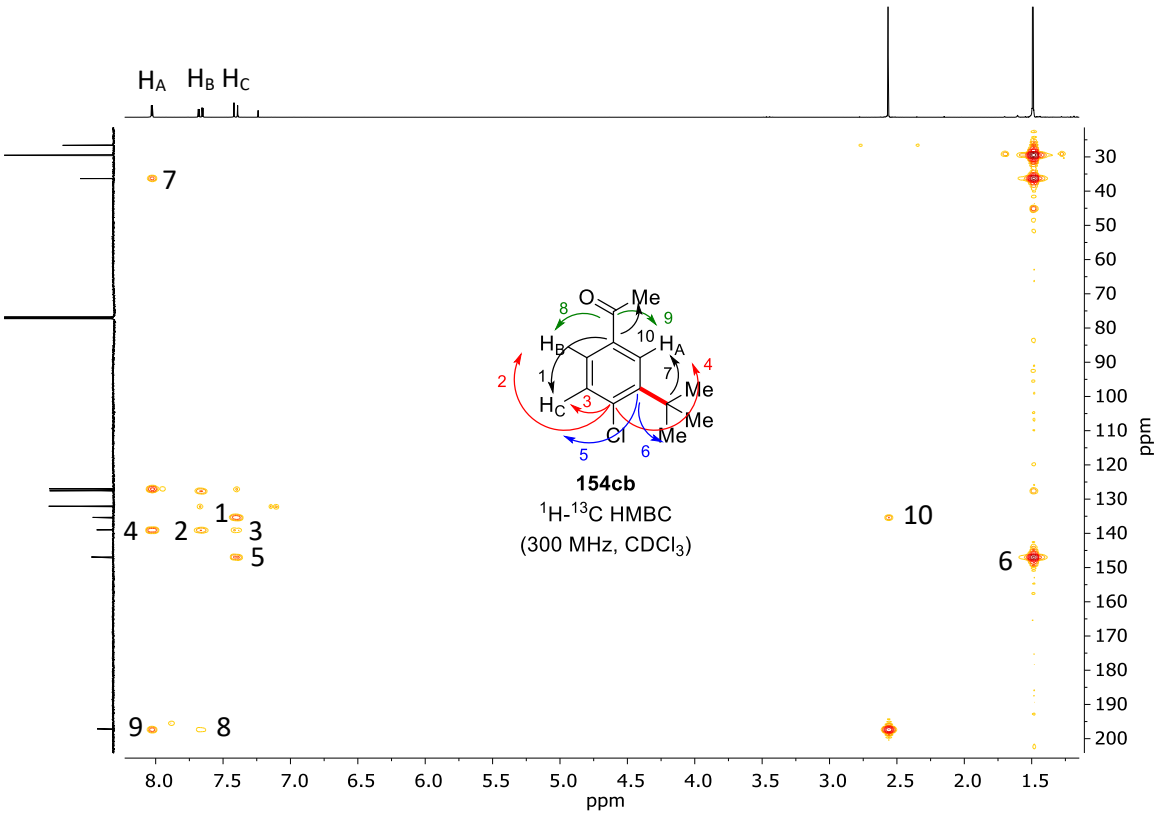


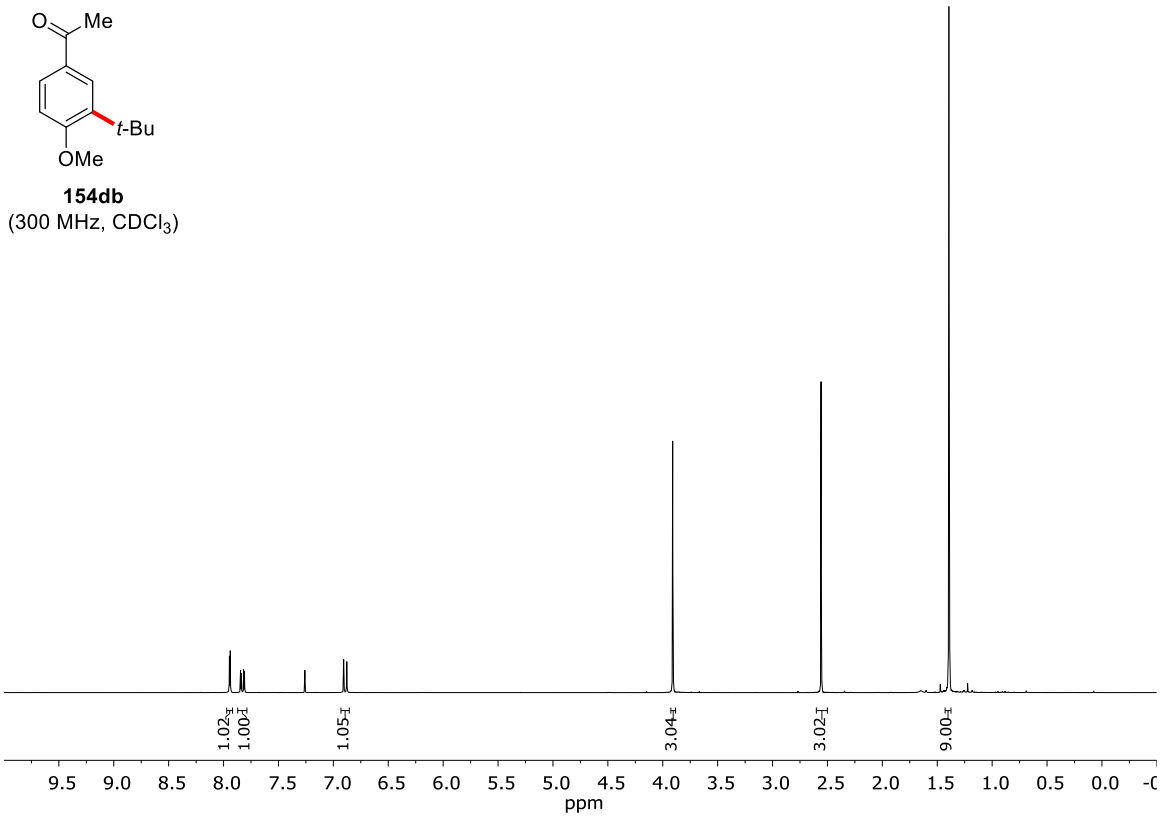
154ab
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



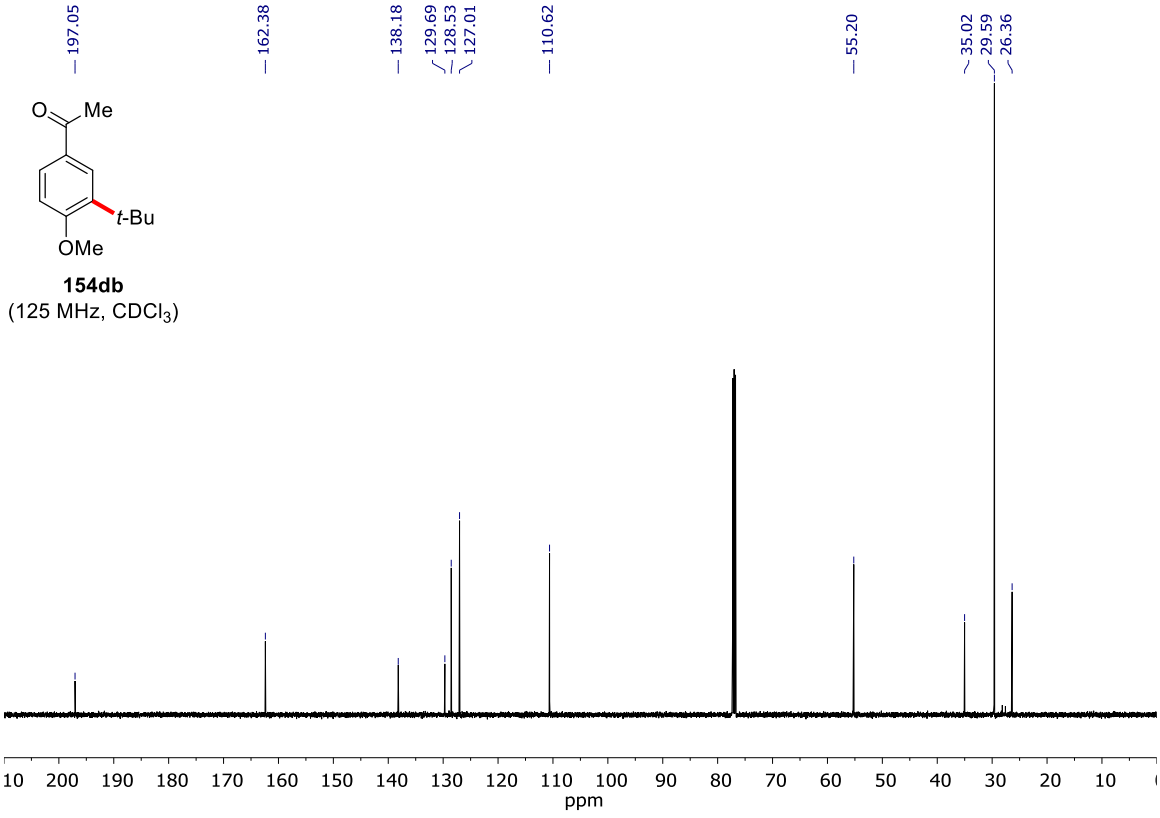
154cb
(300 MHz, $CDCl_3$)


197.15
146.92
138.98
135.34
132.08
127.58
126.99
36.34
29.53
26.62
O
Me
t-Bu
Cl
154cb
(125 MHz, CDCl3)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

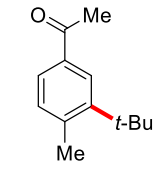

HA HB HC
7
4 2 1 3 5
9 8
10
6
O
Me
8
9
10
HB
HA
1
7
4
2
HC
3
Me
Me
Cl
Me
5
6
154cb
1H-13C HMBC
(300 MHz, CDCl3)
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
ppm
30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200
ppm



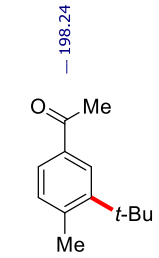
154db
(300 MHz, $CDCl_3$)



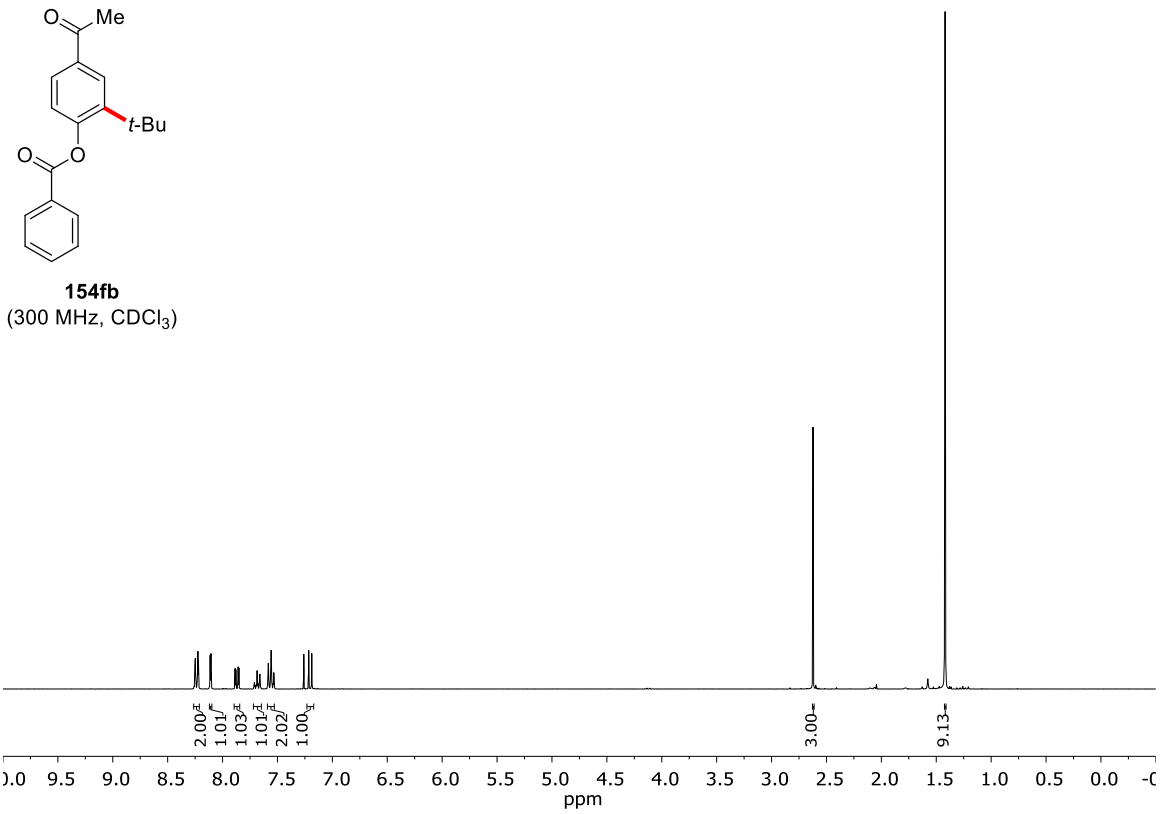
154db
(125 MHz, $CDCl_3$)



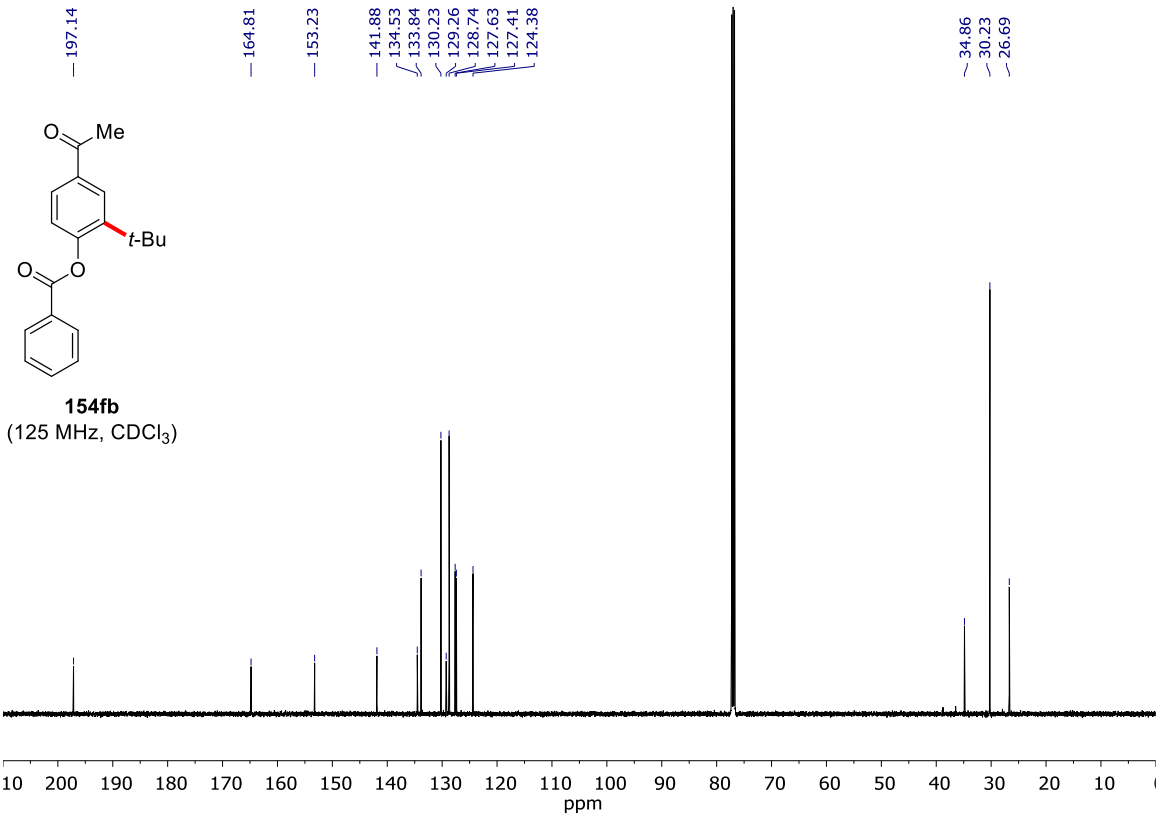
154eb
(400 MHz, $CDCl_3$)



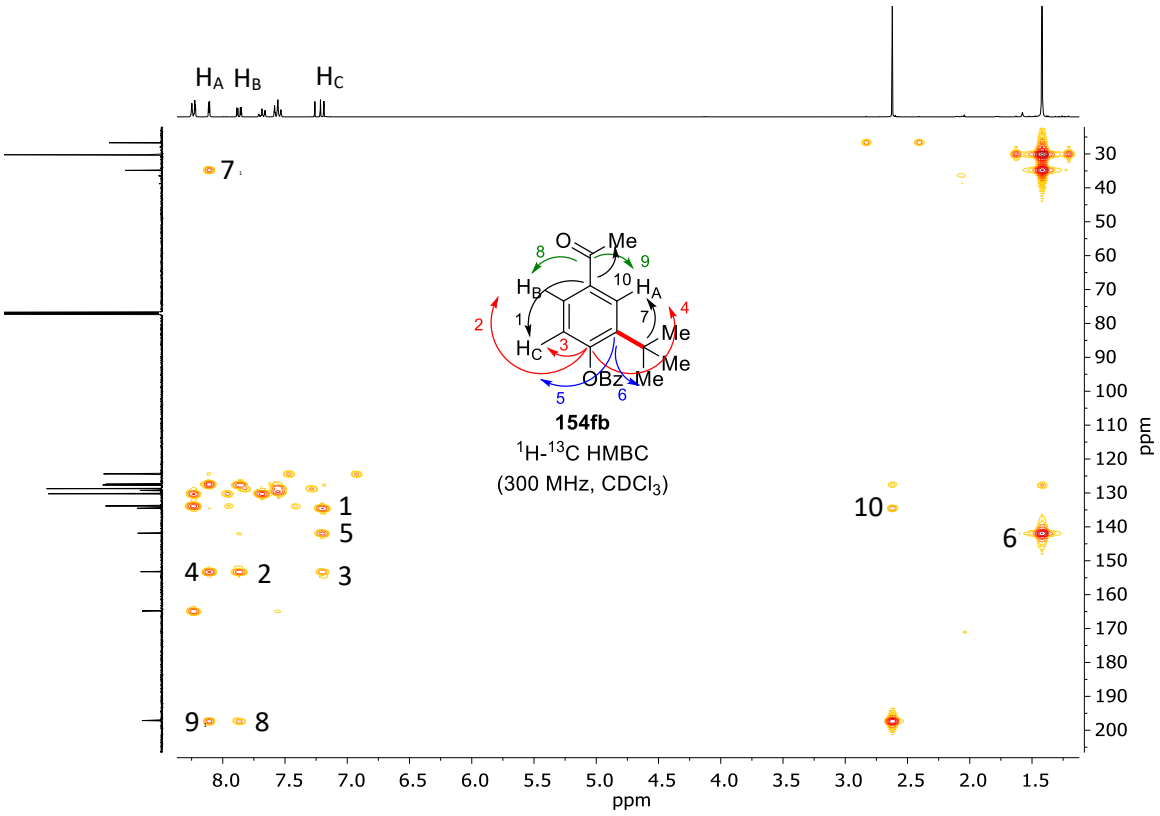
154eb
(100 MHz, $CDCl_3$)



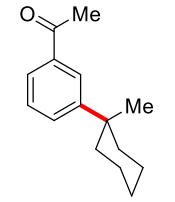
154fb
(300 MHz, $CDCl_3$)



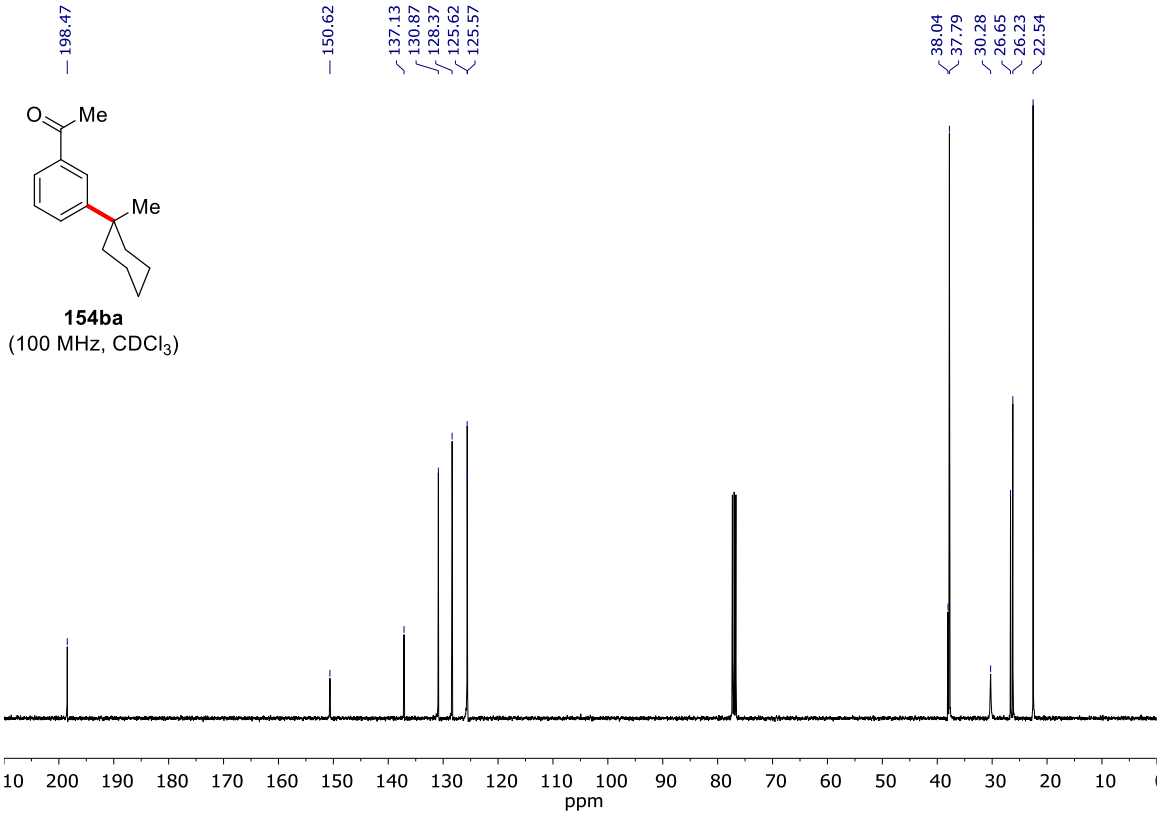
154fb
(125 MHz, $CDCl_3$)



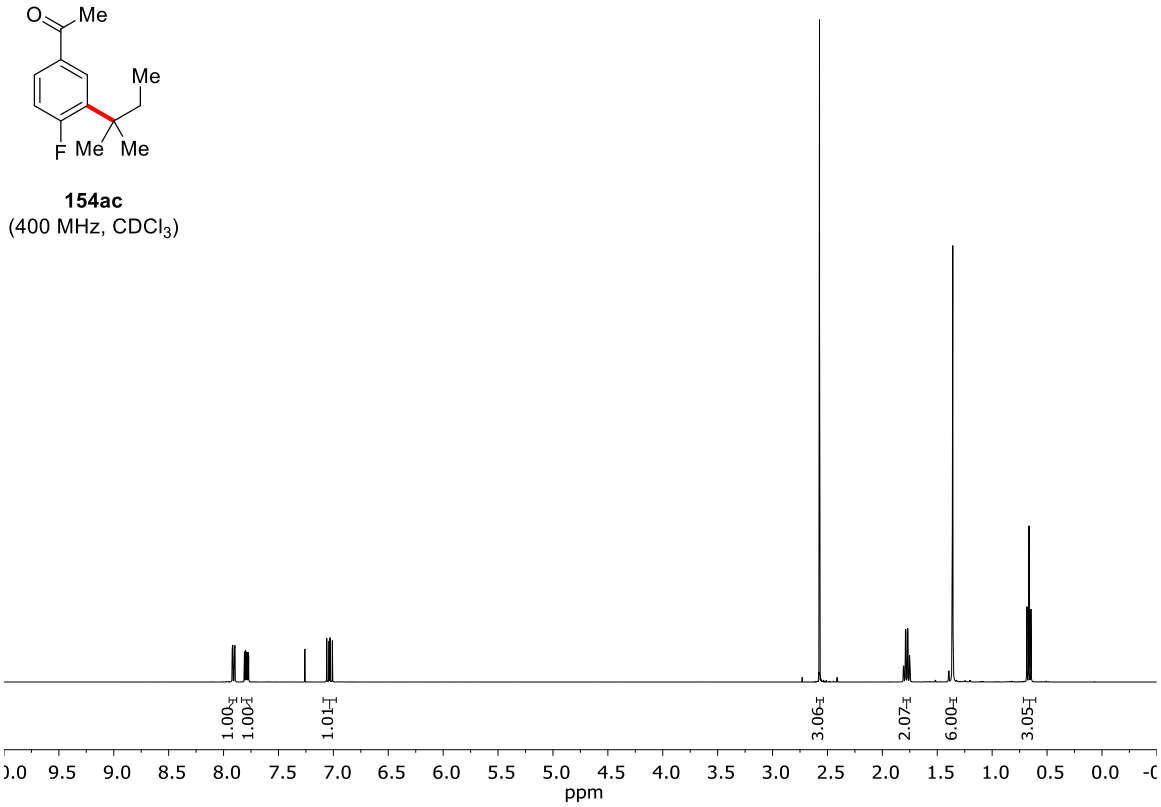
154fb
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



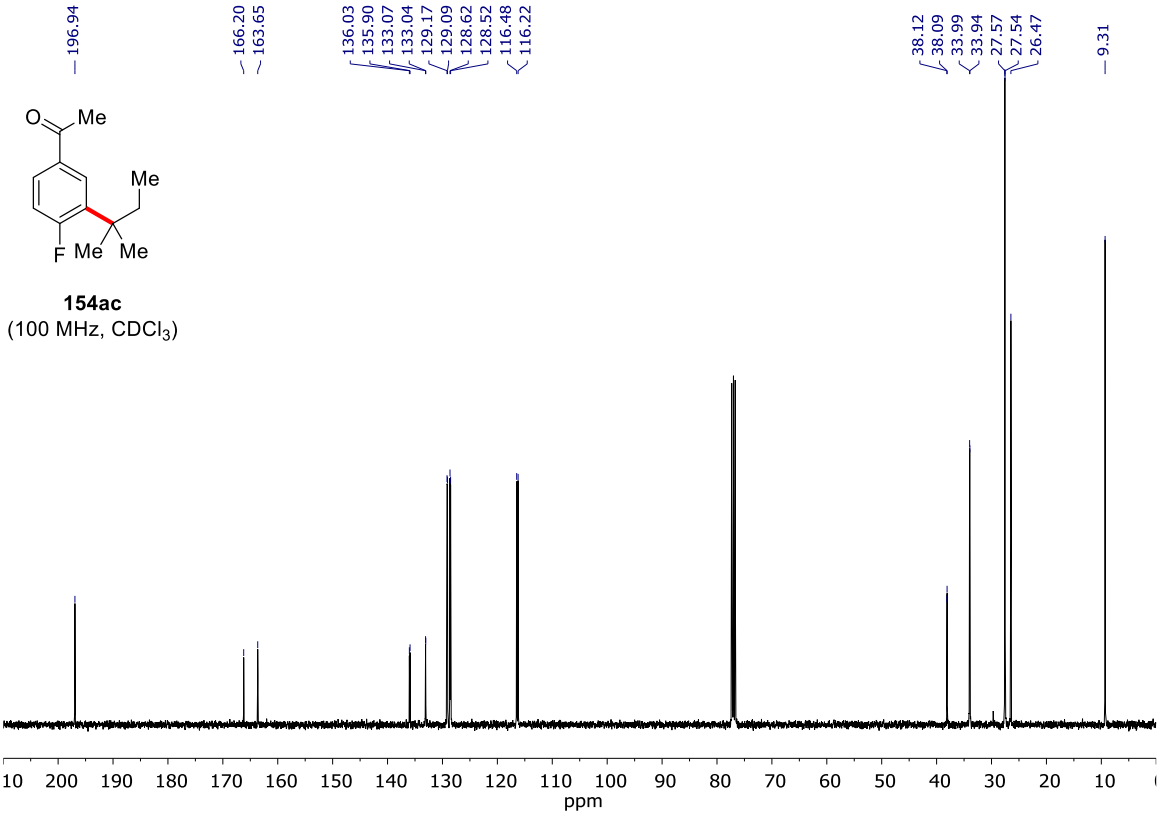
154ba
(400 MHz, $CDCl_3$)



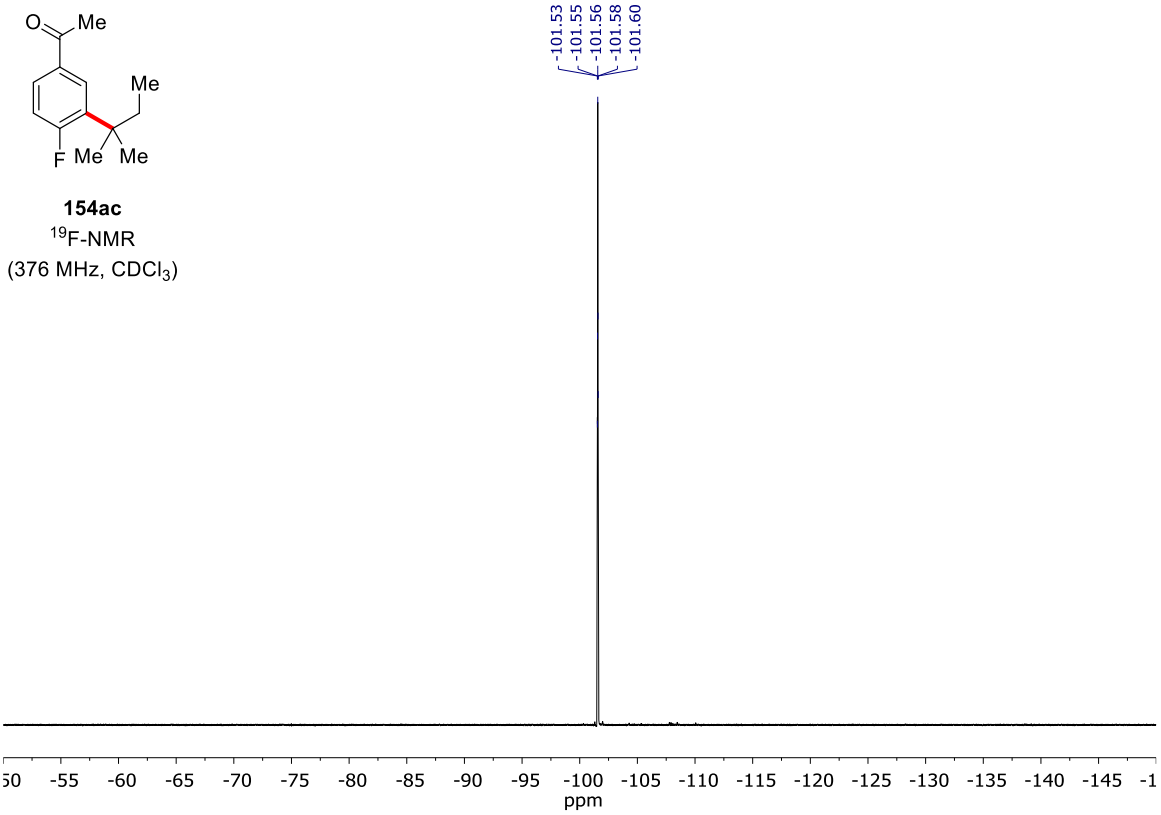
154ba
(100 MHz, $CDCl_3$)



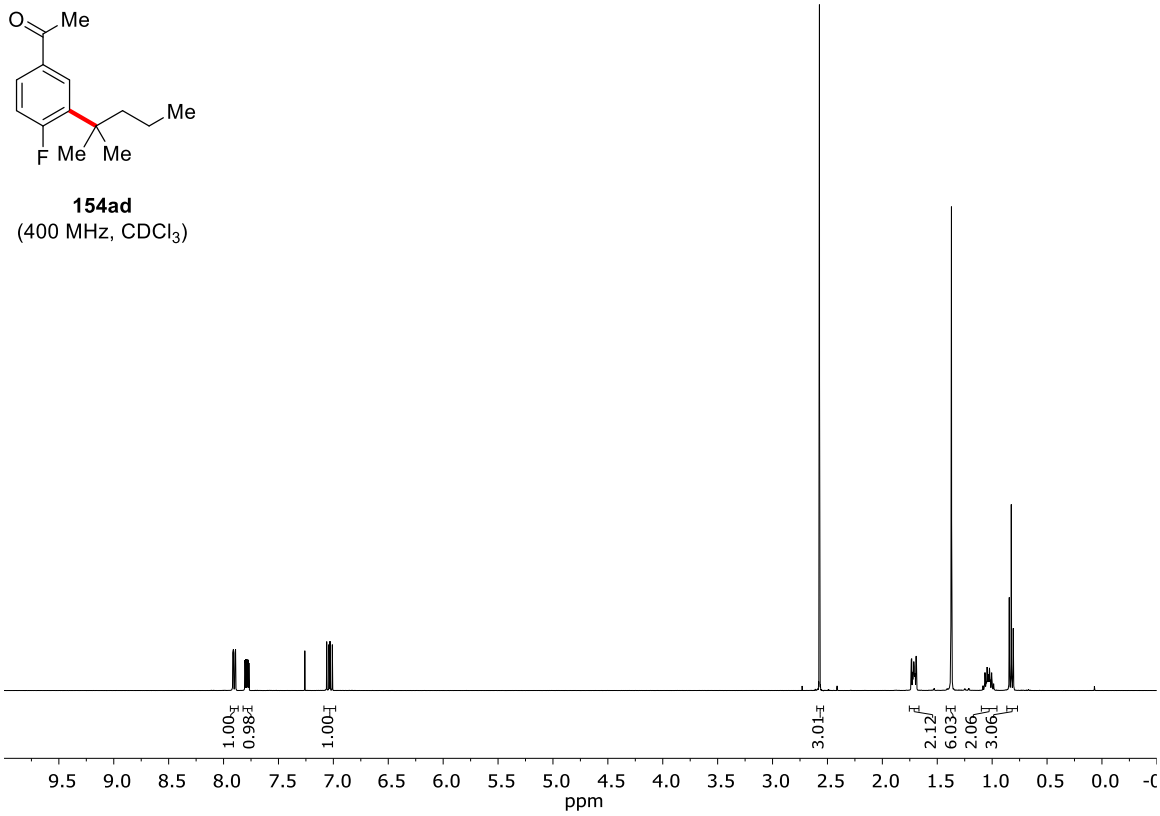
154ac
(400 MHz, $CDCl_3$)



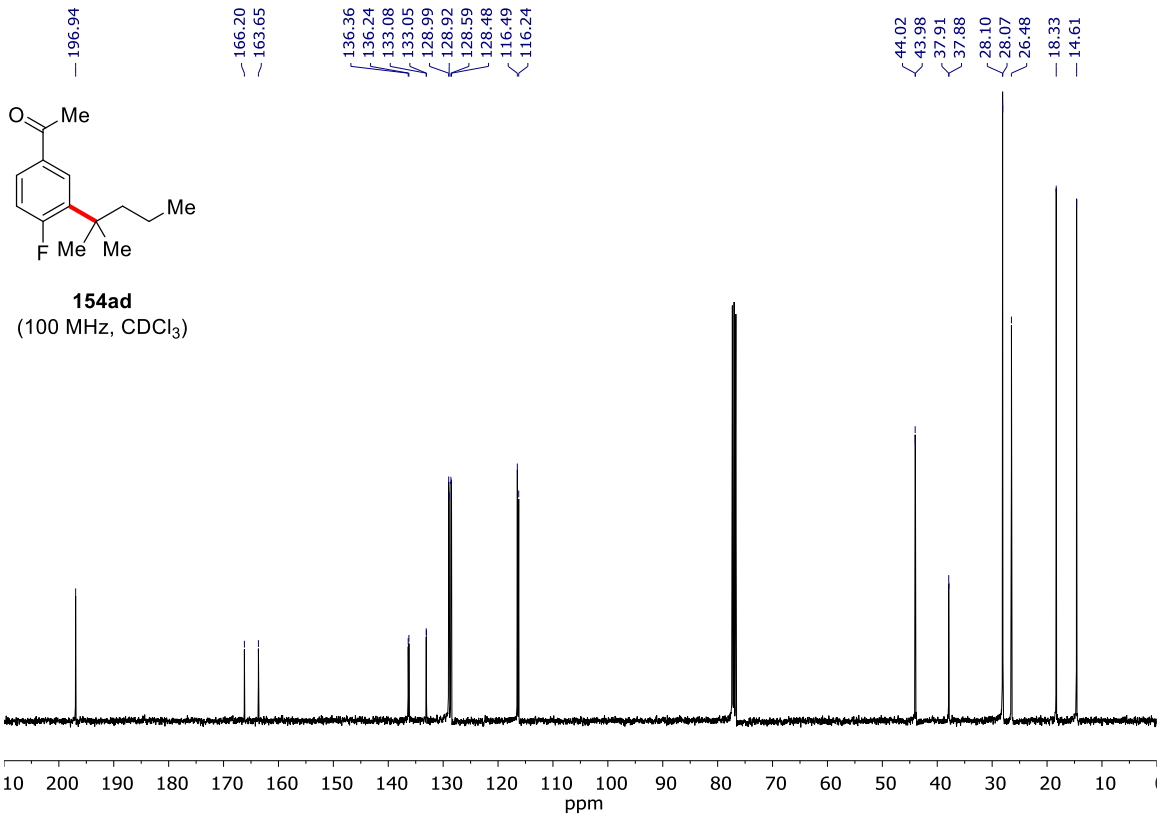
154ac
(100 MHz, $CDCl_3$)



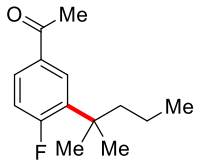
154ac
^{19}F-NMR
(376 MHz, $CDCl_3$)



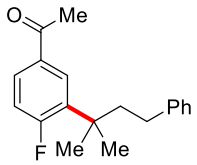
154ad
(400 MHz, $CDCl_3$)



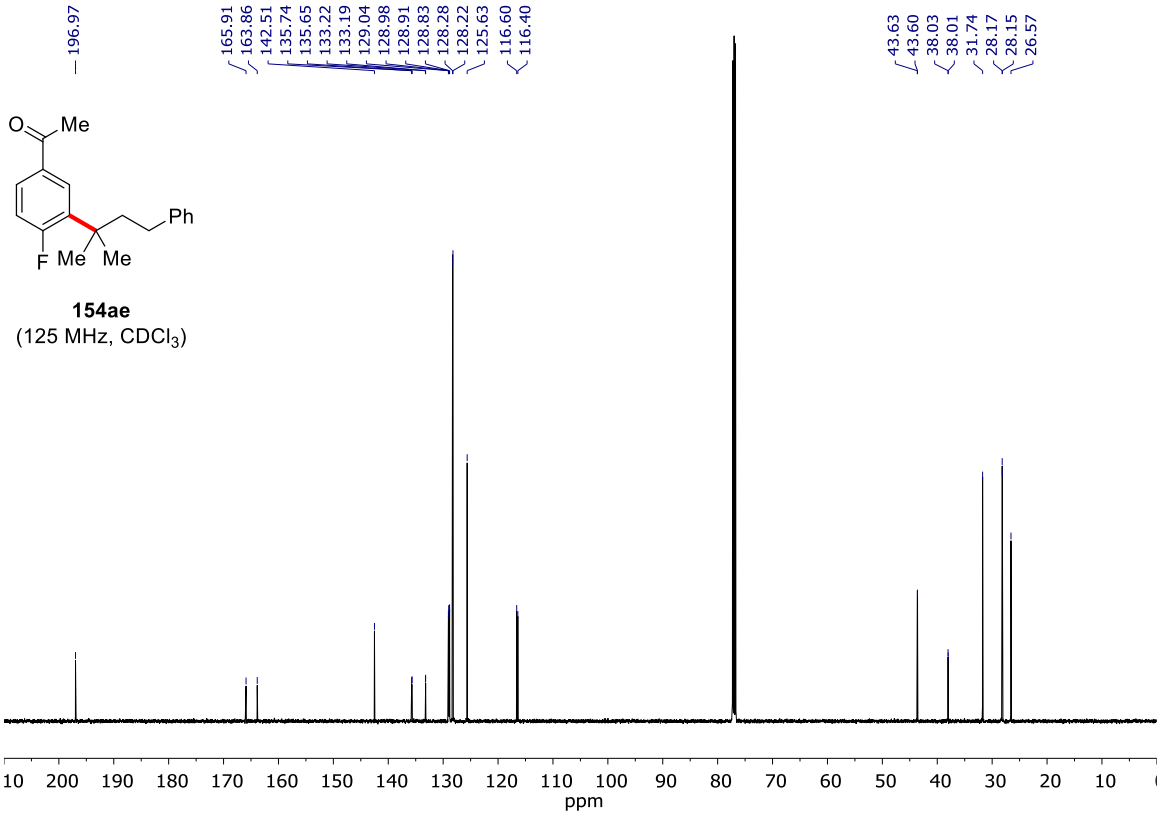
154ad
(100 MHz, $CDCl_3$)



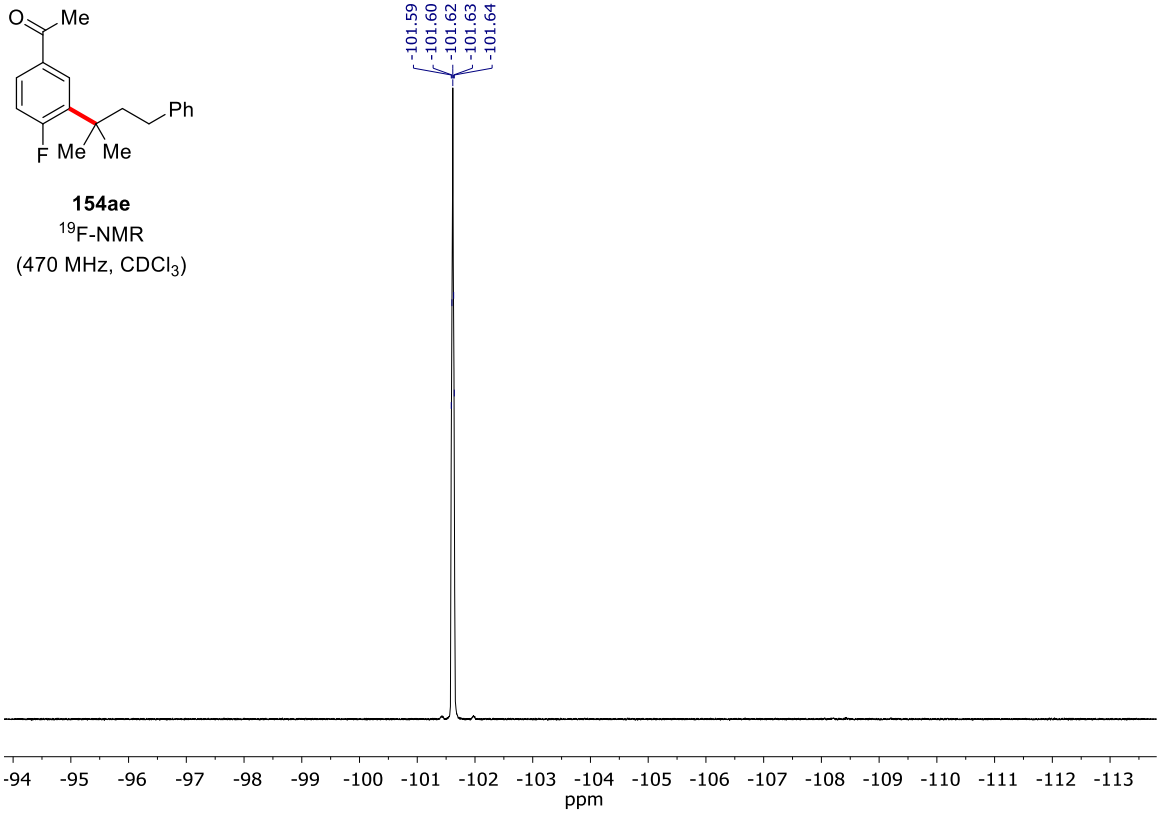
154ad
^{19}F-NMR
(376 MHz, $CDCl_3$)



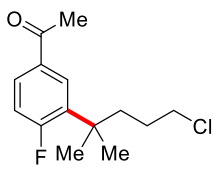
154ae
(500 MHz, $CDCl_3$)



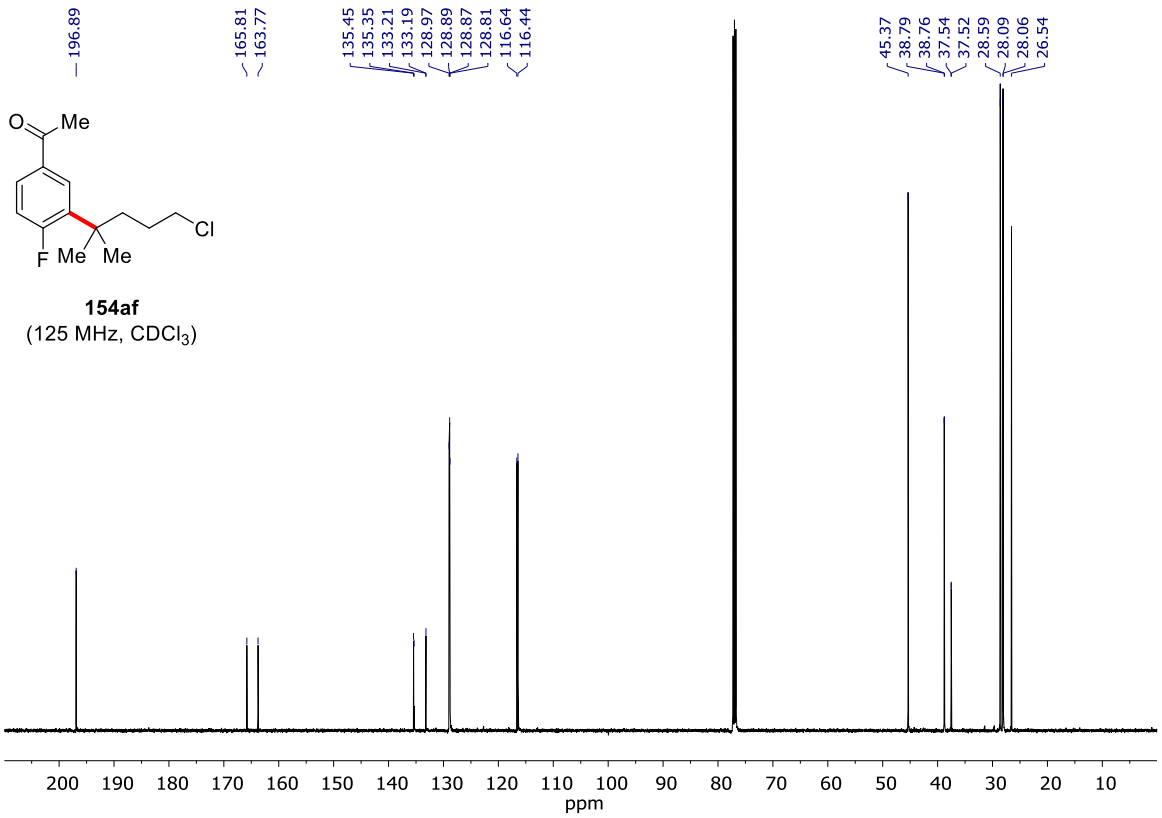
154ae
(125 MHz, $CDCl_3$)



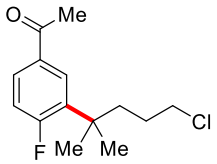
154ae
^{19}F-NMR
(470 MHz, $CDCl_3$)



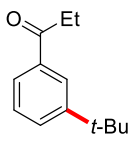
154af
(500 MHz, $CDCl_3$)



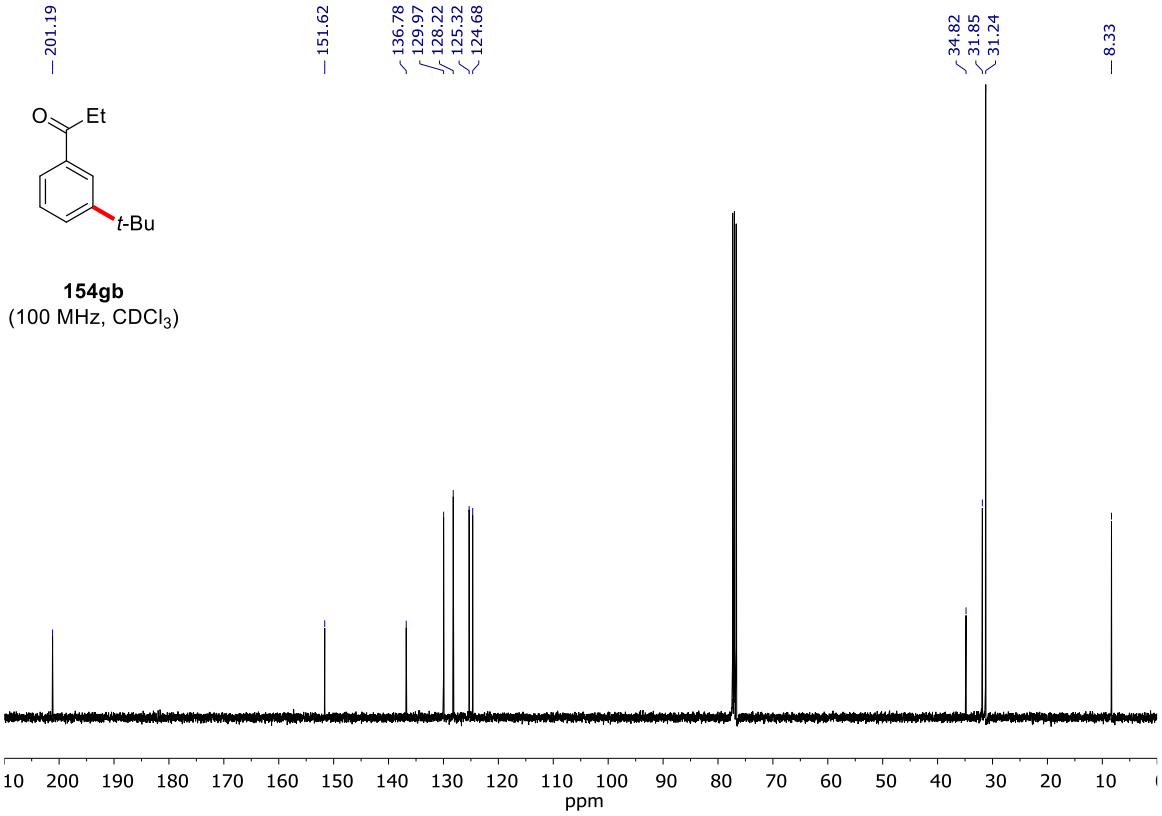
154af
(125 MHz, $CDCl_3$)



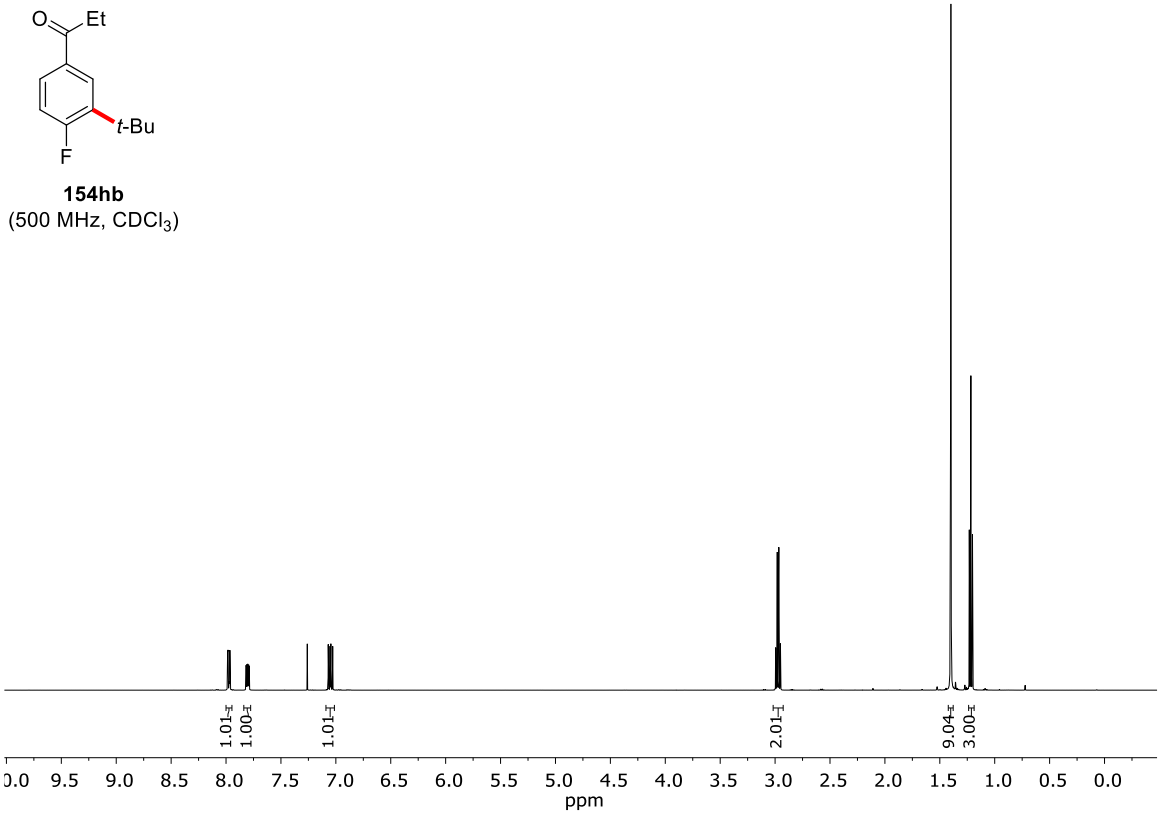
154af
^{19}F-NMR
(470 MHz, $CDCl_3$)



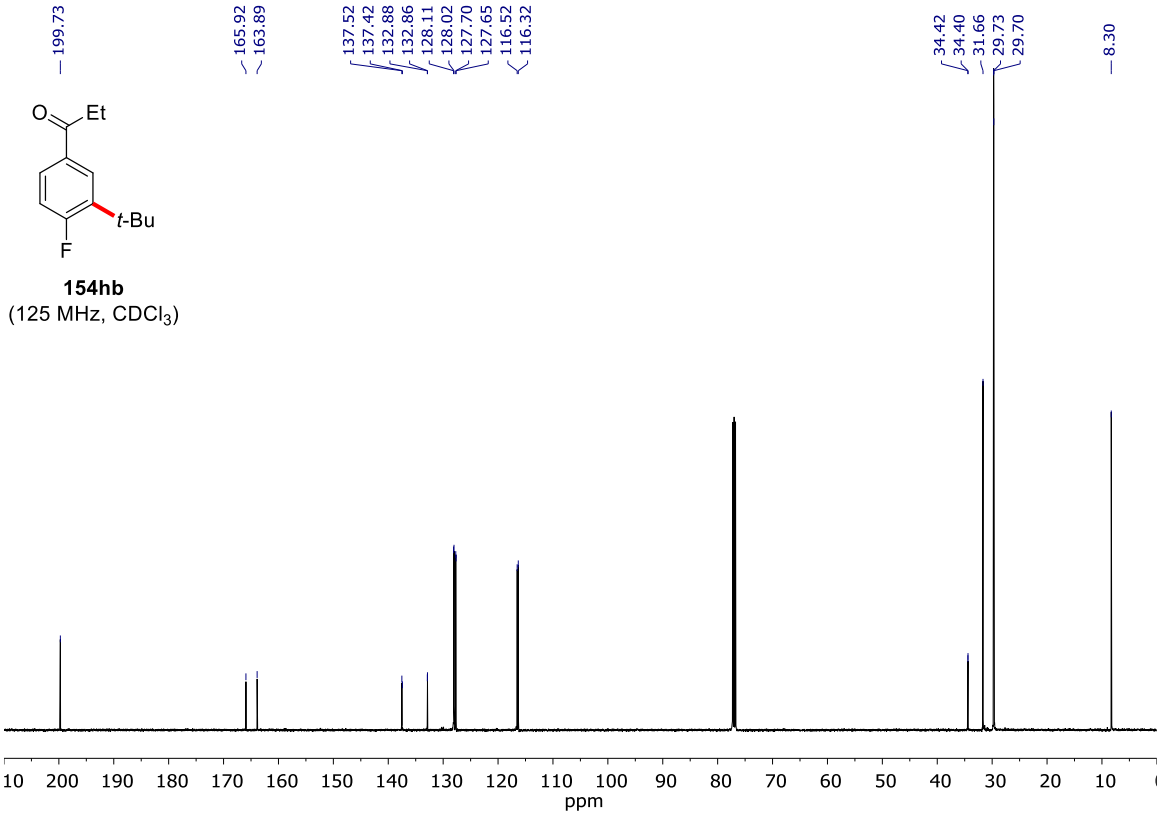
154gb
(400 MHz, $CDCl_3$)



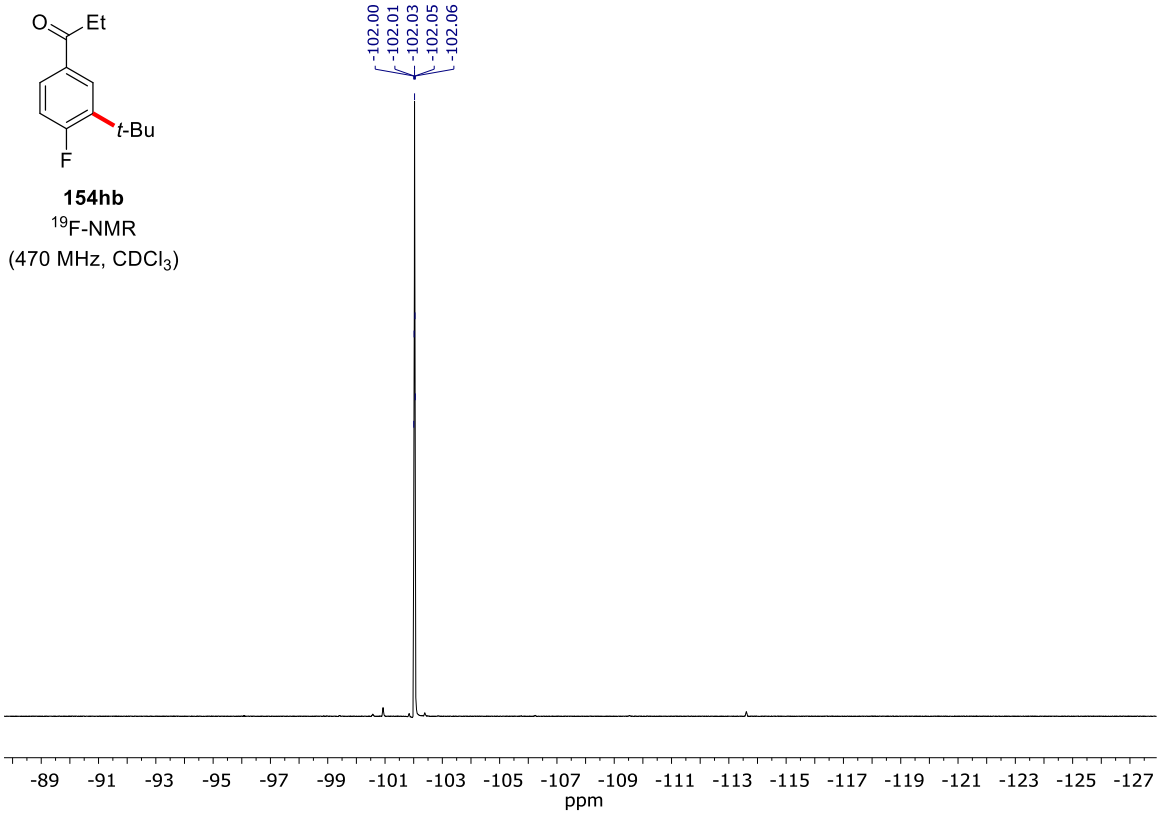
154gb
(100 MHz, $CDCl_3$)



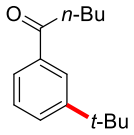
154hb
(500 MHz, $CDCl_3$)



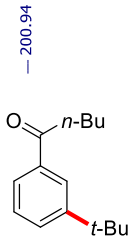
154hb
(125 MHz, $CDCl_3$)



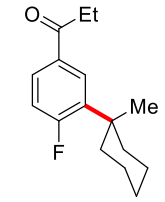
154hb
^{19}F-NMR
(470 MHz, $CDCl_3$)



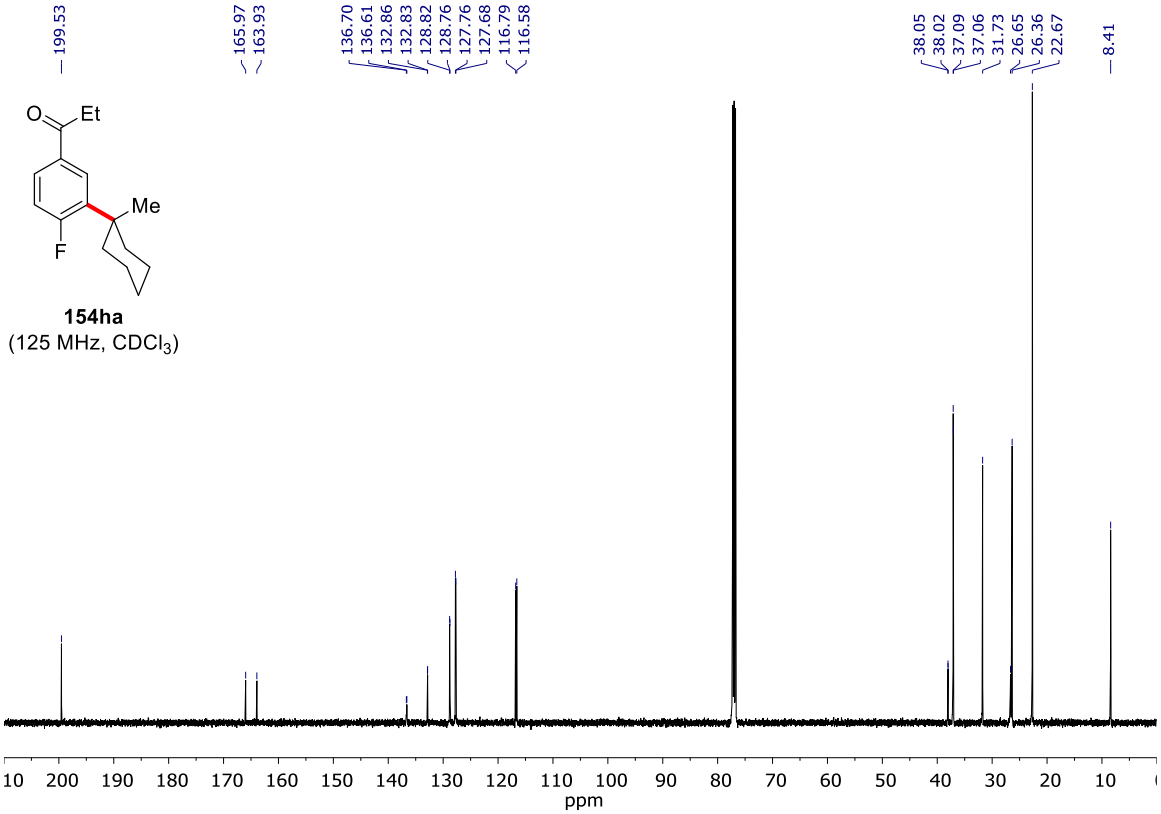
154ib
(400 MHz, $CDCl_3$)



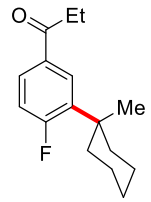
154ib
(100 MHz, $CDCl_3$)



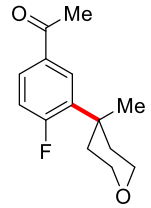
154ha
(300 MHz, $CDCl_3$)



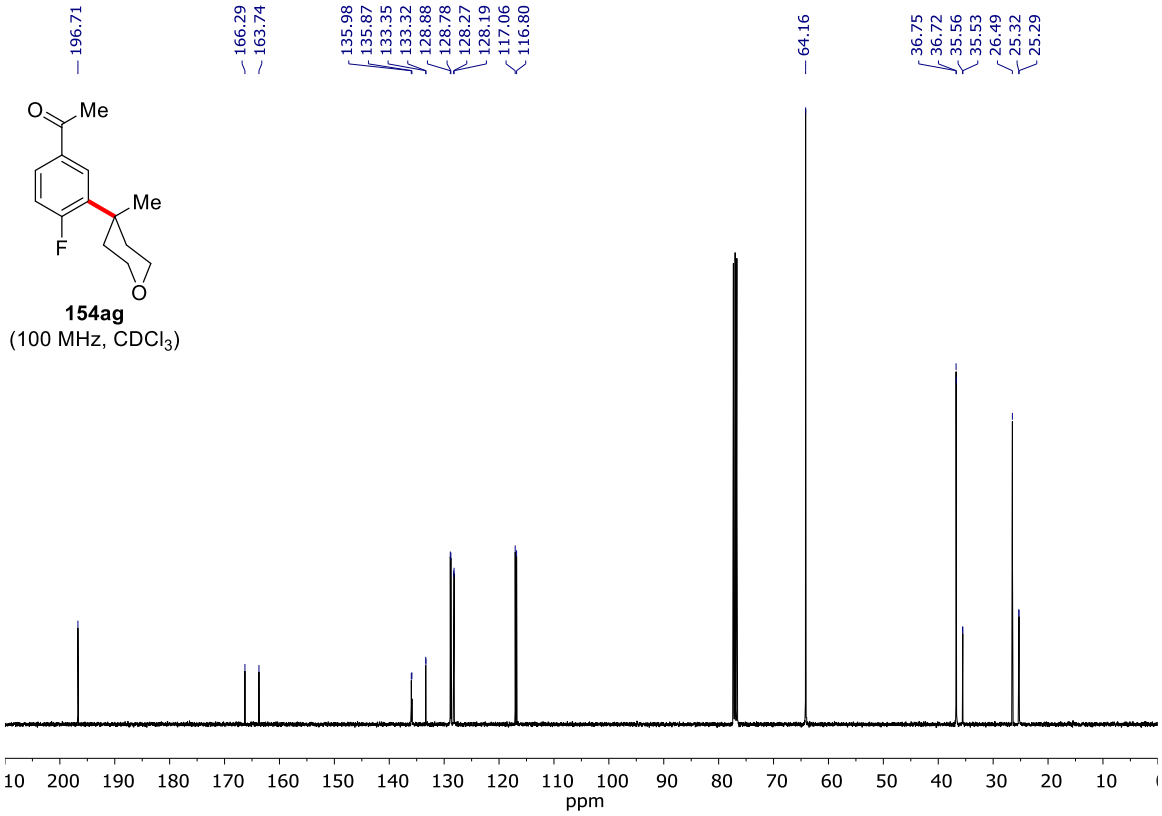
154ha
(125 MHz, $CDCl_3$)



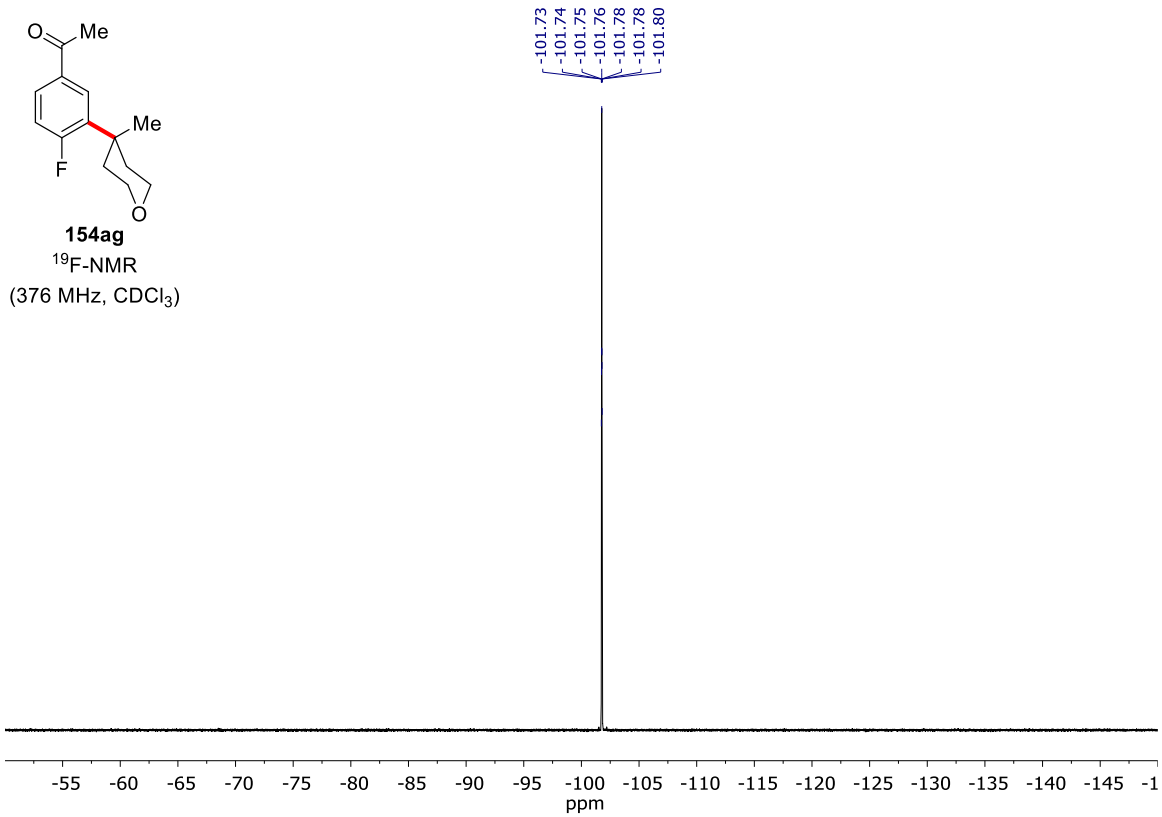
154ha
^{19}F-NMR
(282 MHz, $CDCl_3$)



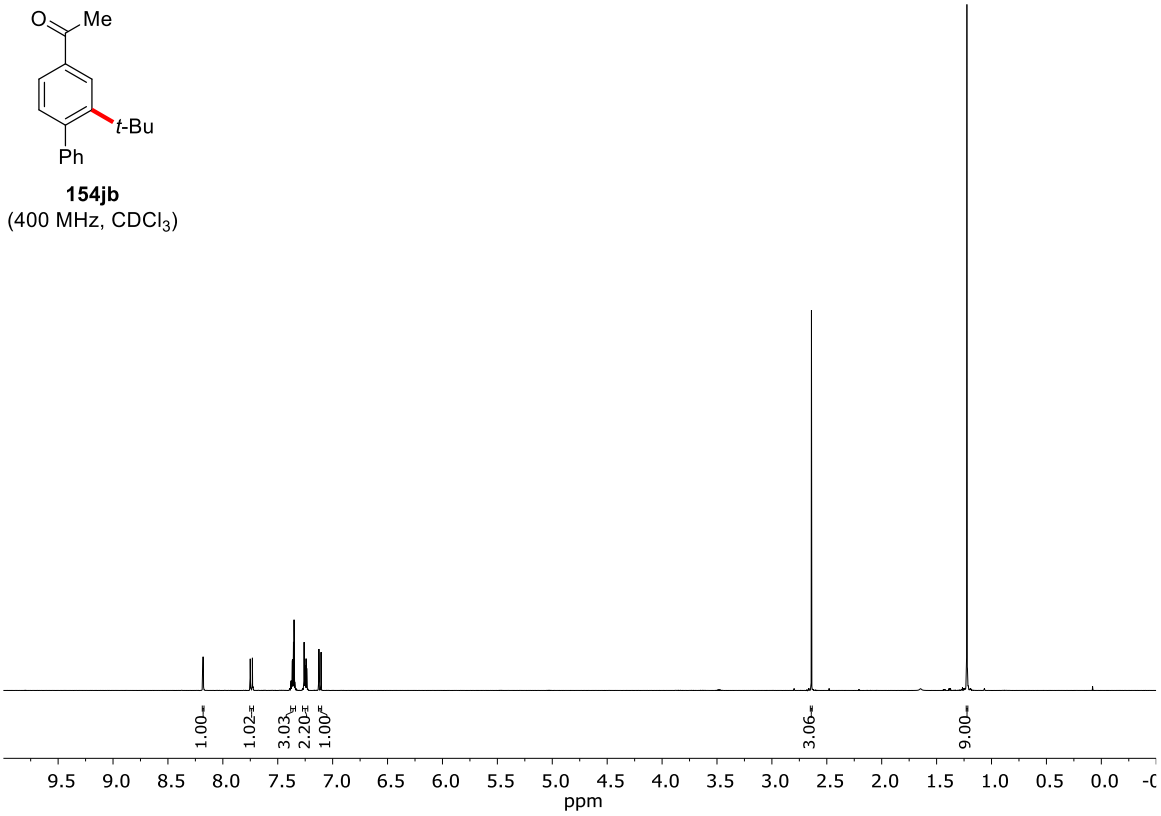
154ag
(400 MHz, $CDCl_3$)

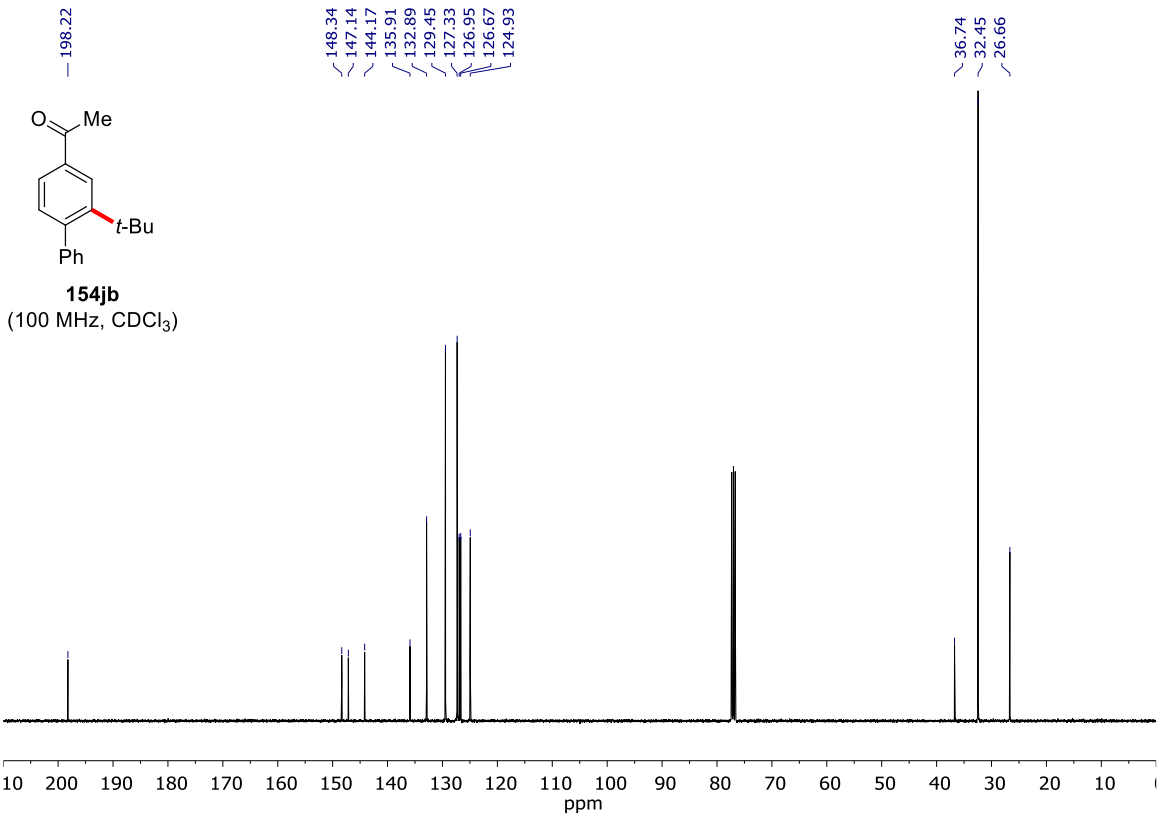


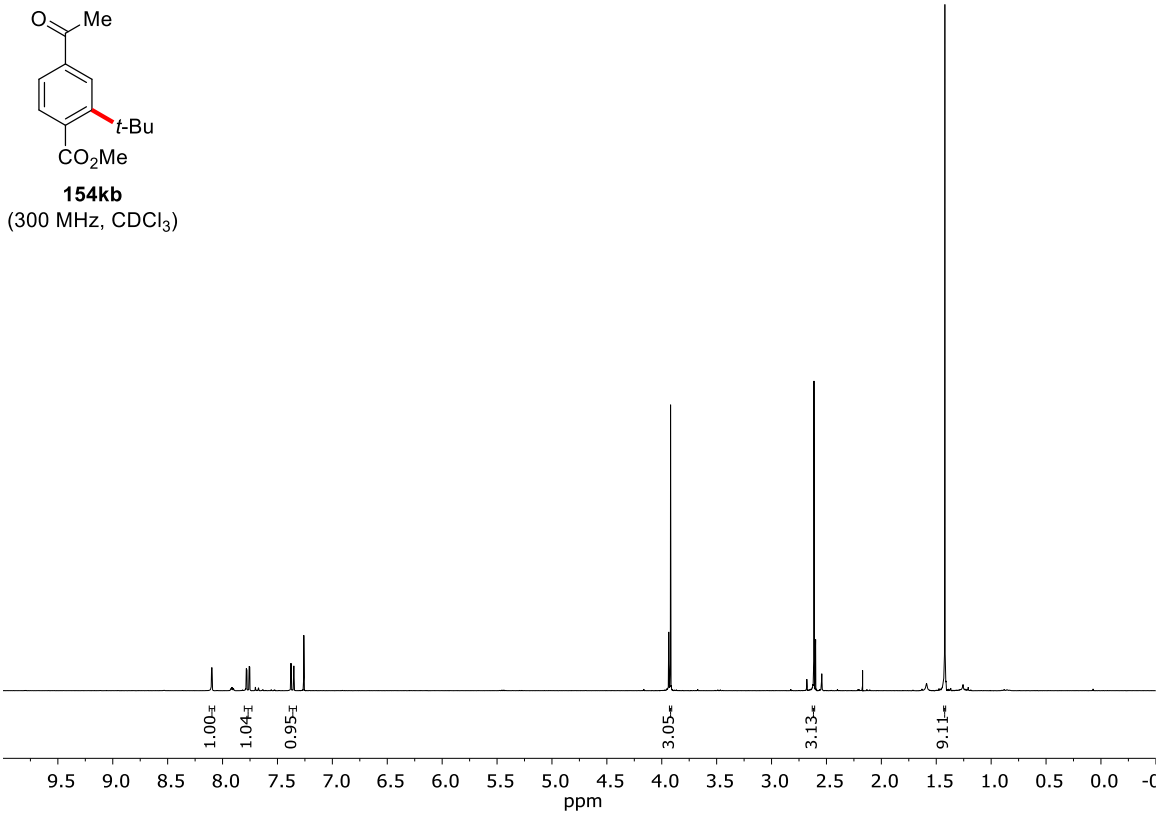
154ag
(100 MHz, $CDCl_3$)



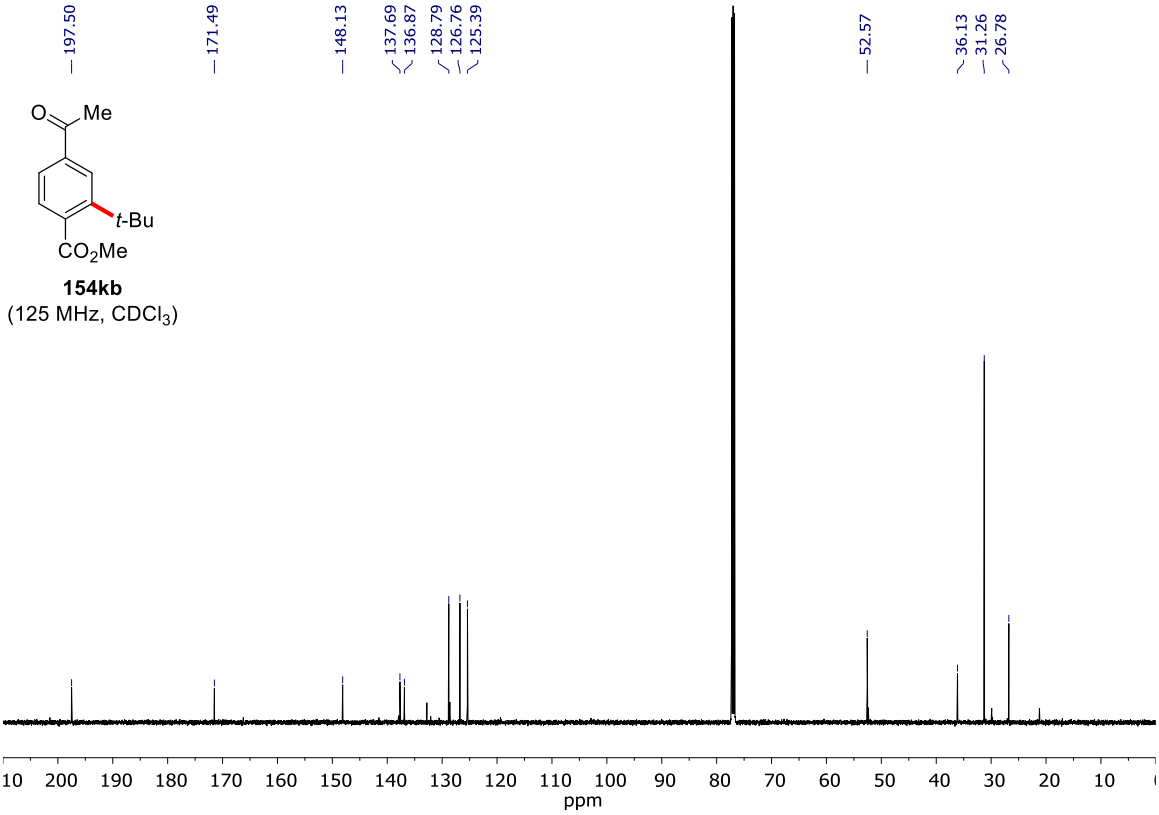
154ag
^{19}F-NMR
(376 MHz, $CDCl_3$)


O
Me
t-Bu
Ph
154jb
(400 MHz, CDCl3)
1.00
1.02
3.03
2.20
1.00
3.06
9.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

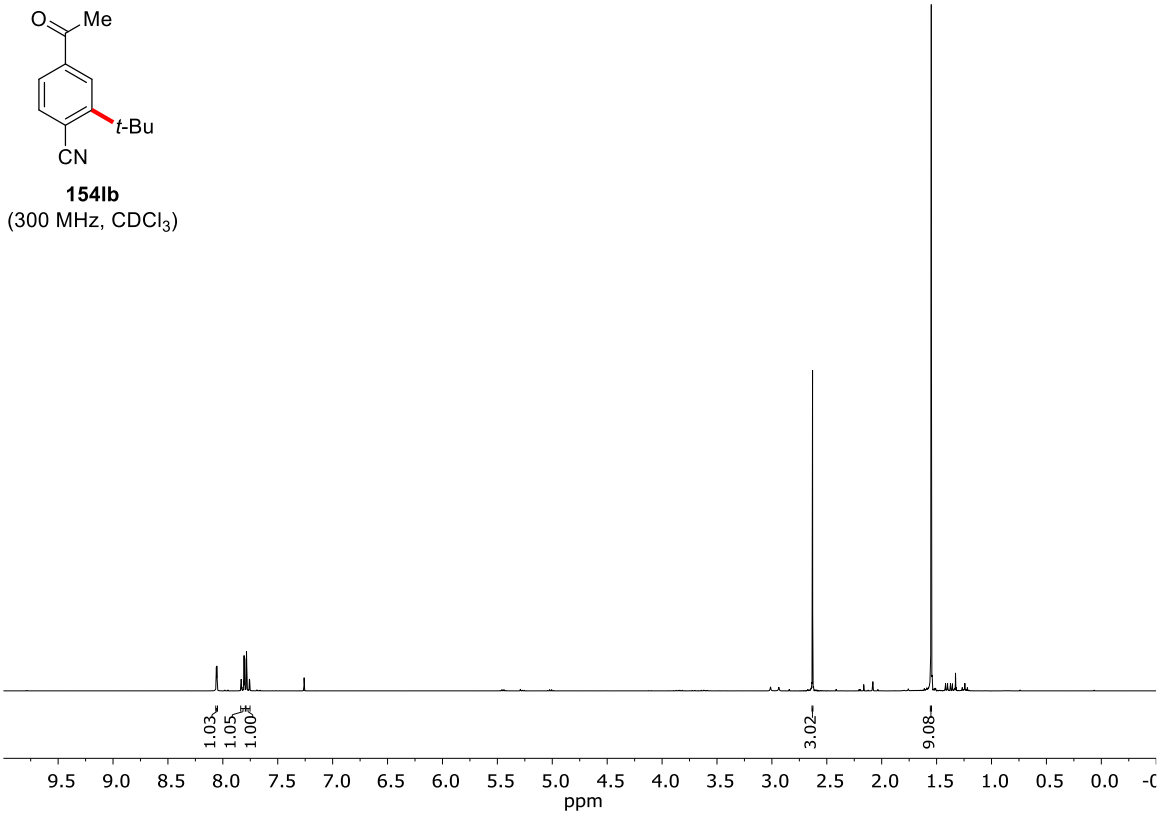

198.22
148.34
147.14
144.17
135.91
132.89
129.45
127.33
126.95
126.67
124.93
36.74
32.45
26.66
O
Me
t-Bu
Ph
154jb
(100 MHz, CDCl3)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm



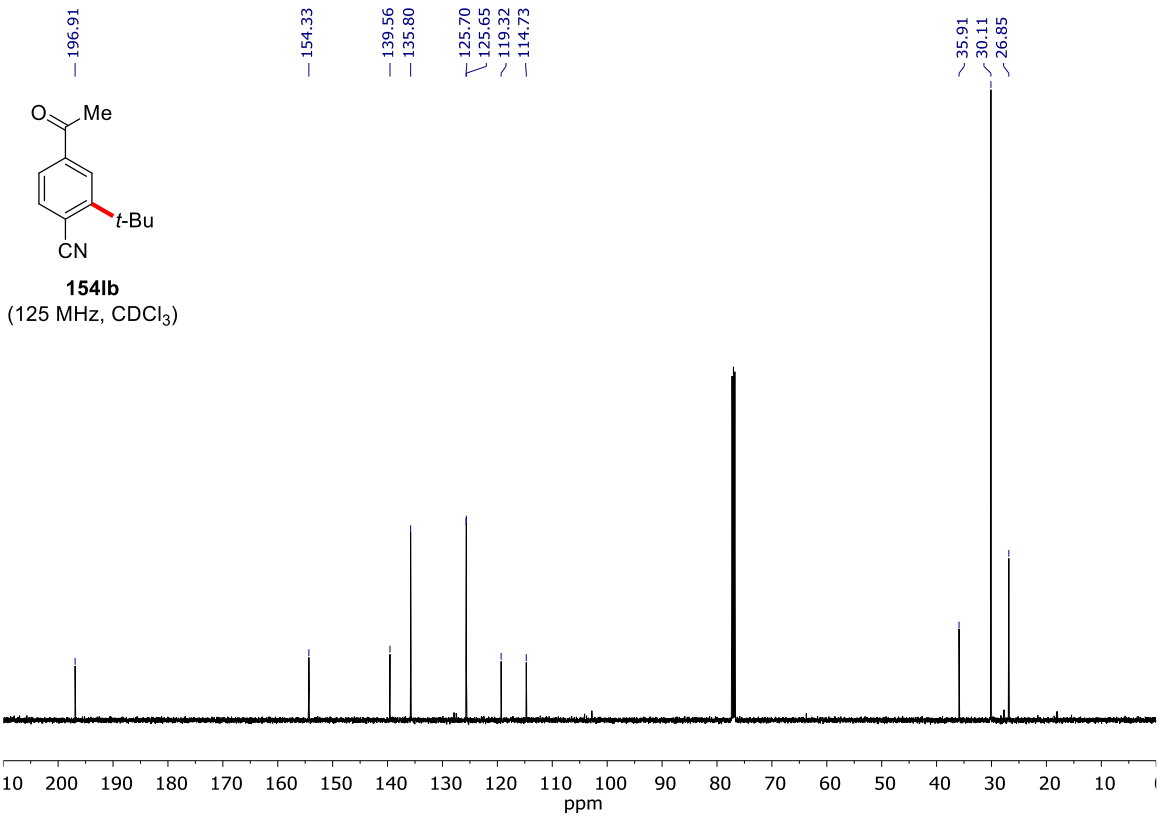
154kb
(300 MHz, $CDCl_3$)



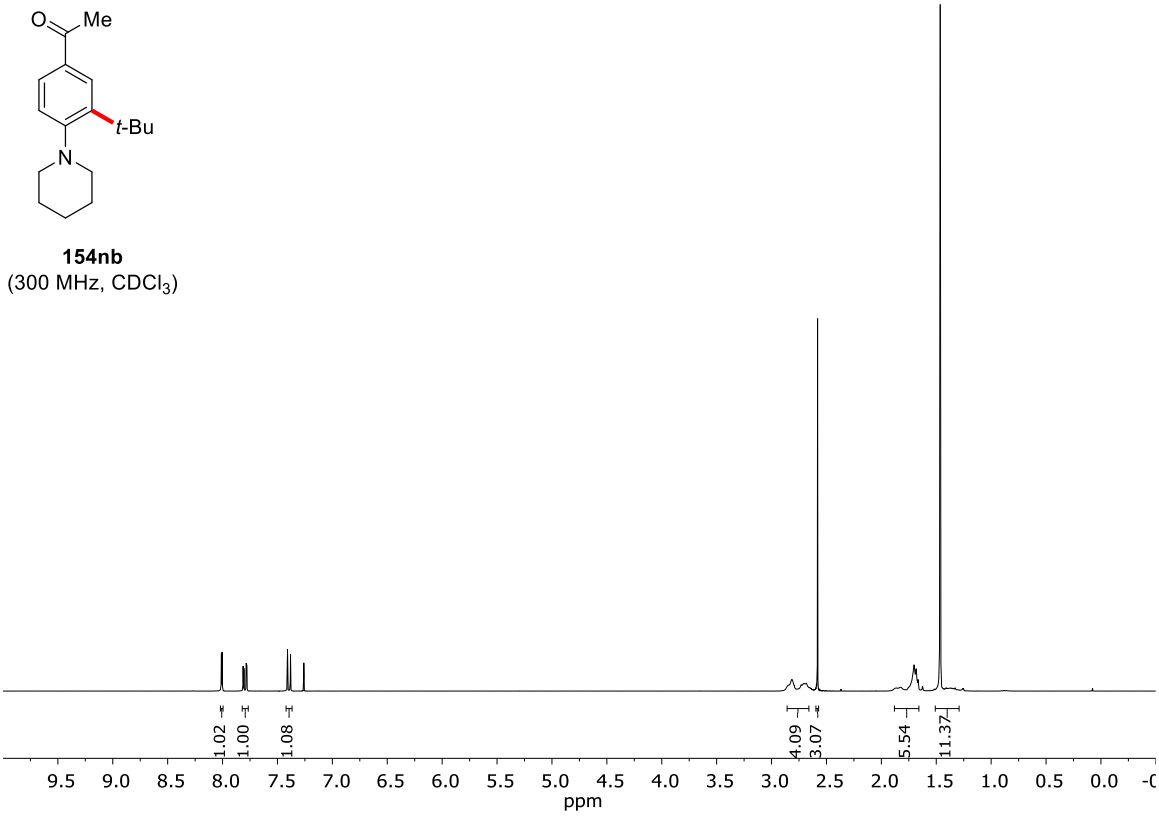
154kb
(125 MHz, $CDCl_3$)



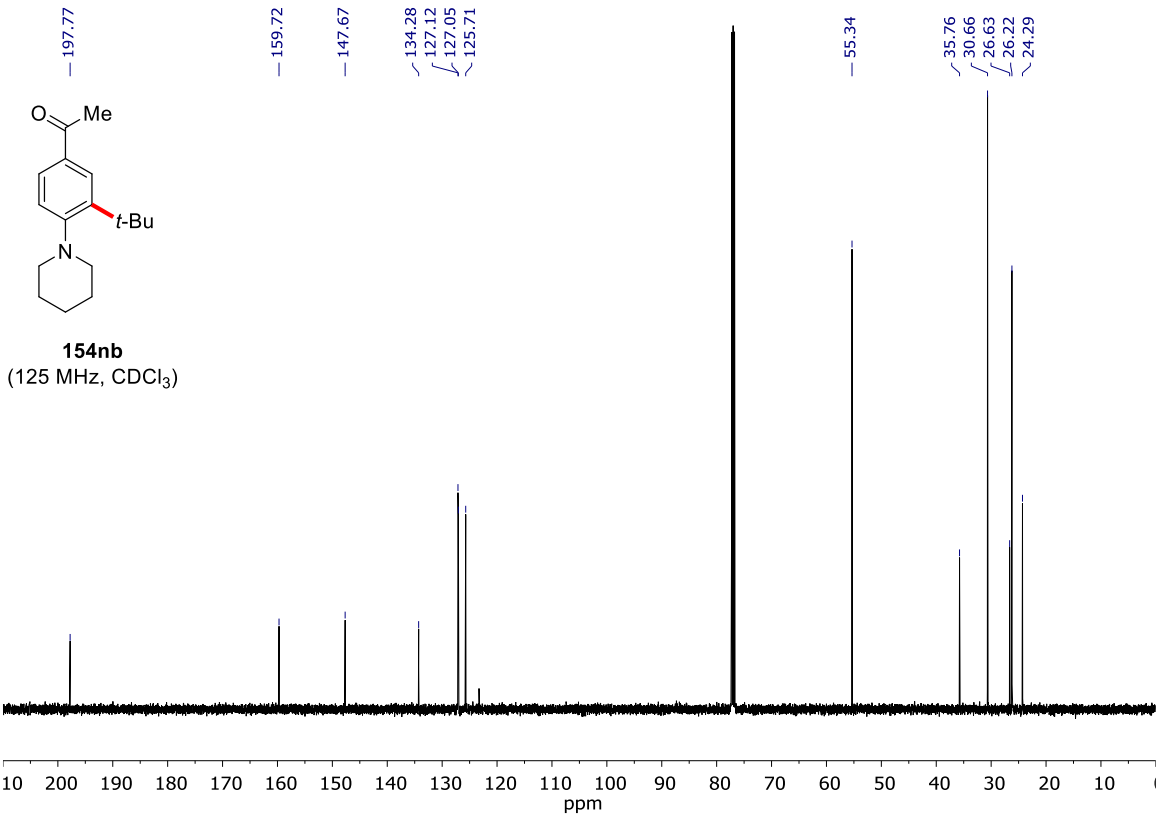
154lb
(300 MHz, $CDCl_3$)



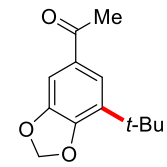
154lb
(125 MHz, $CDCl_3$)



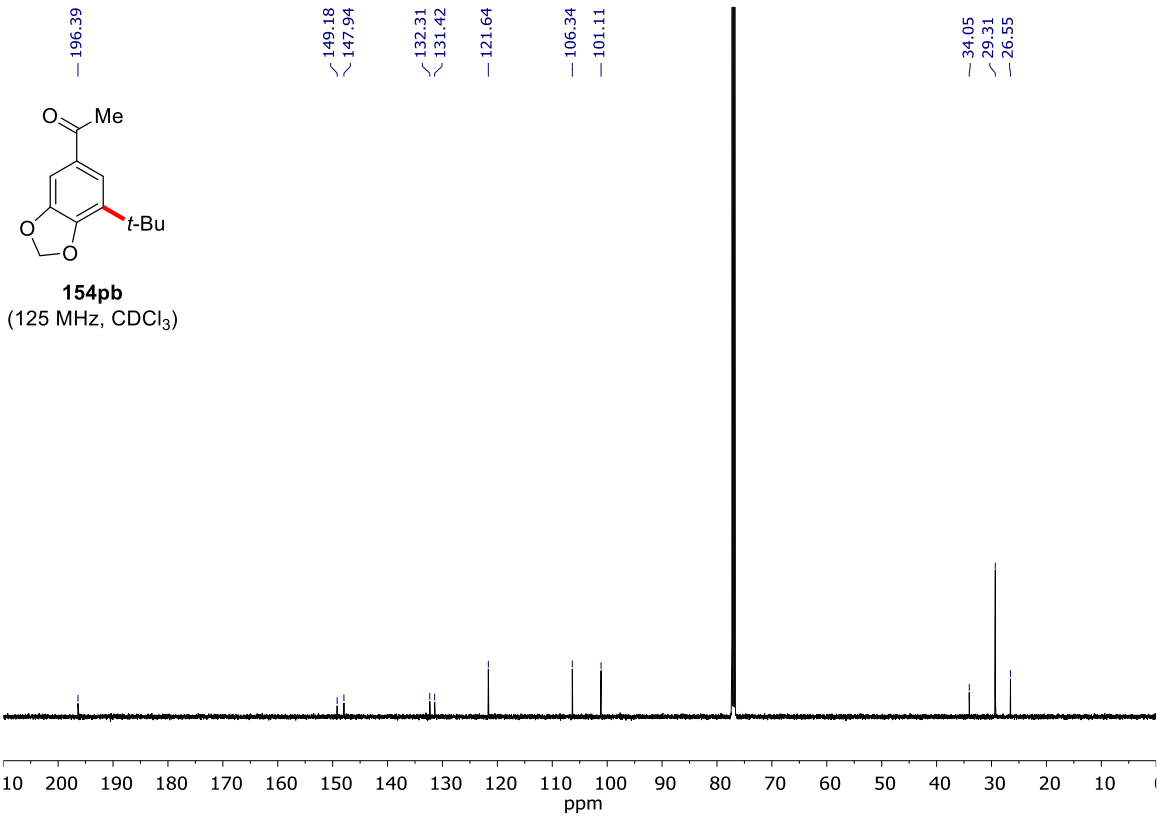
154nb
(300 MHz, $CDCl_3$)



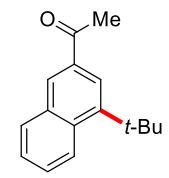
154nb
(125 MHz, $CDCl_3$)



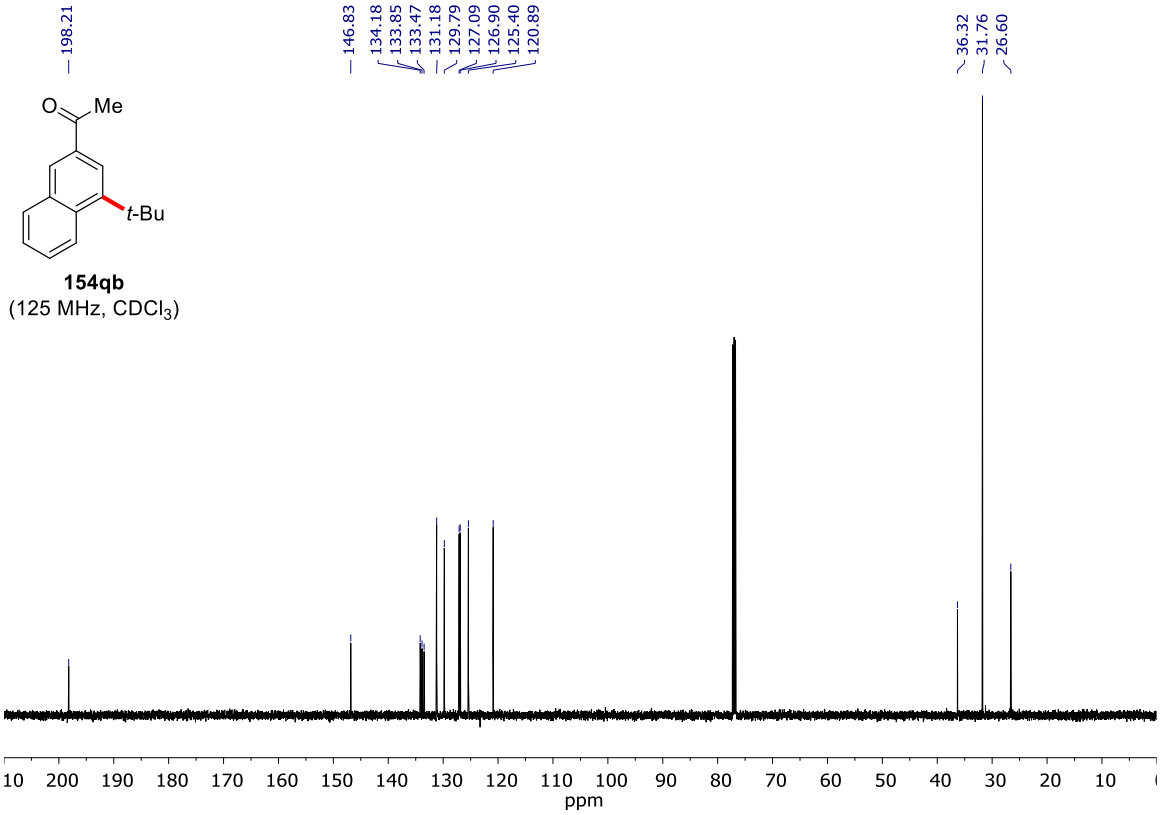
154pb
(300 MHz, $CDCl_3$)



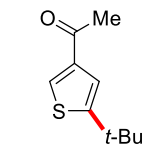
154pb
(125 MHz, $CDCl_3$)



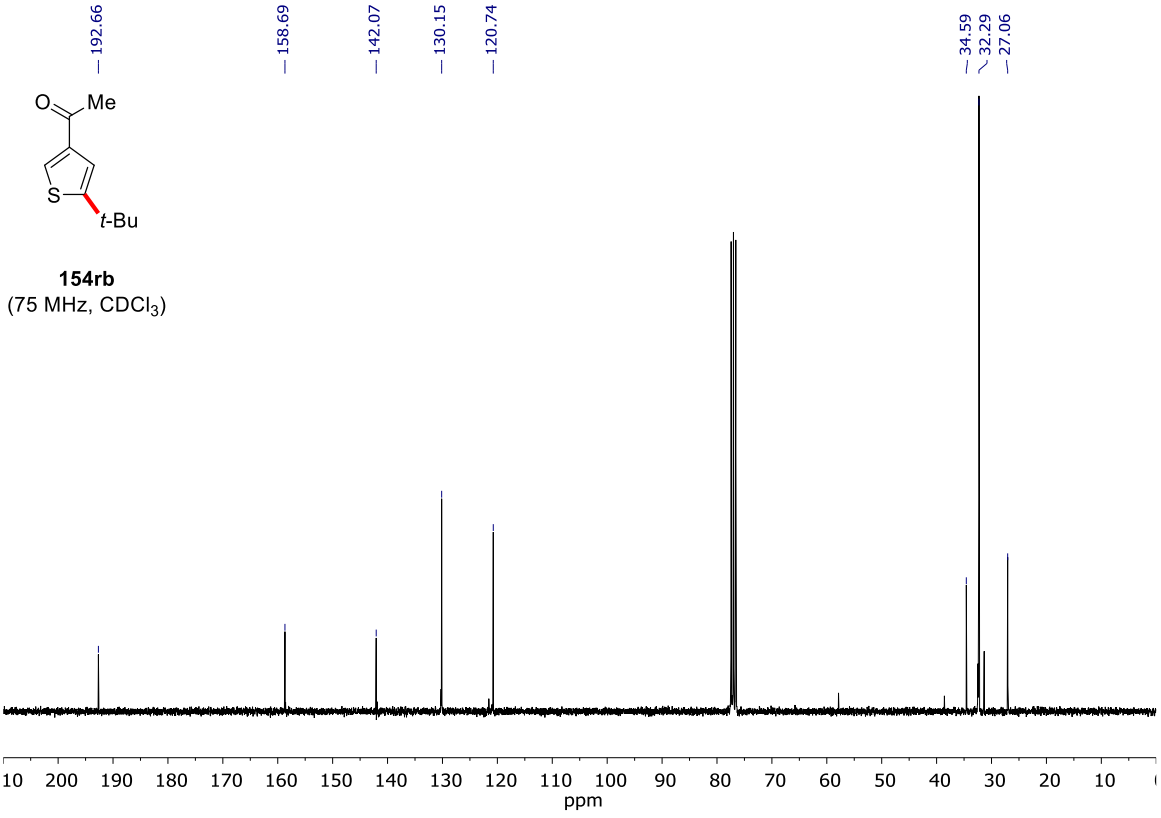
154qb
(300 MHz, $CDCl_3$)



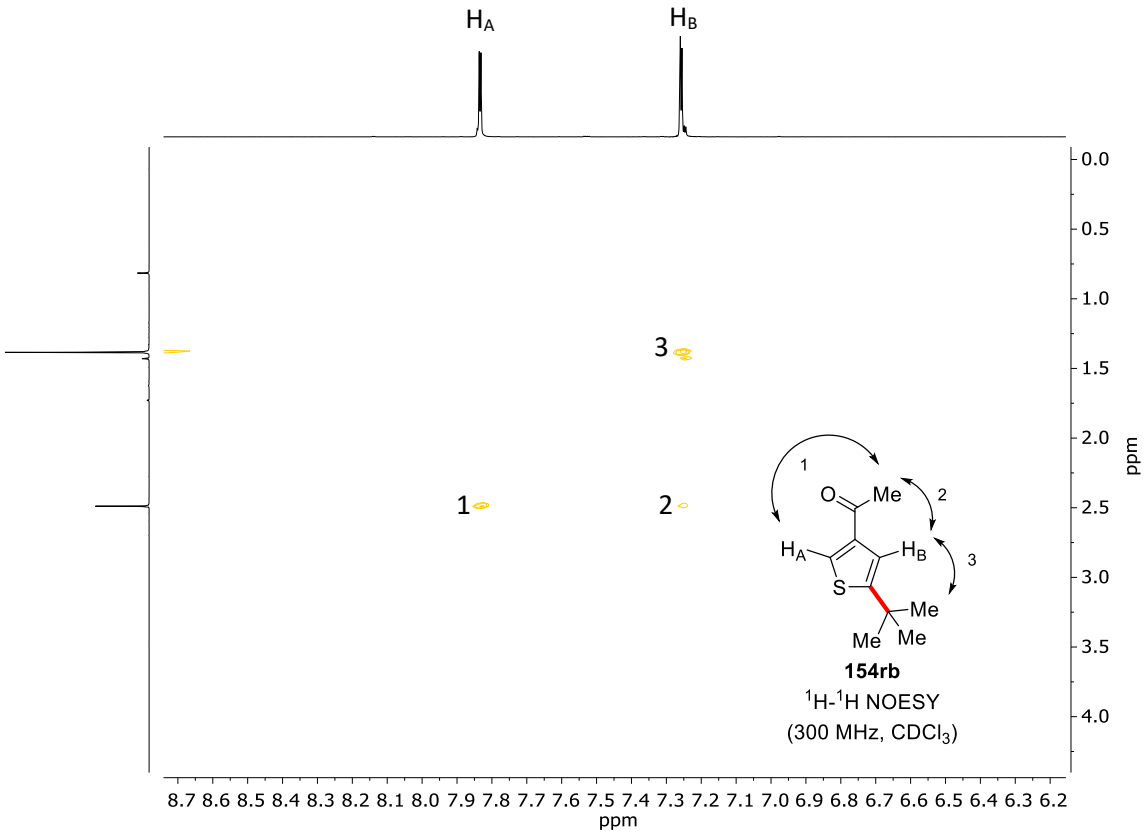
154qb
(125 MHz, $CDCl_3$)



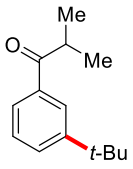
154rb
(300 MHz, $CDCl_3$)



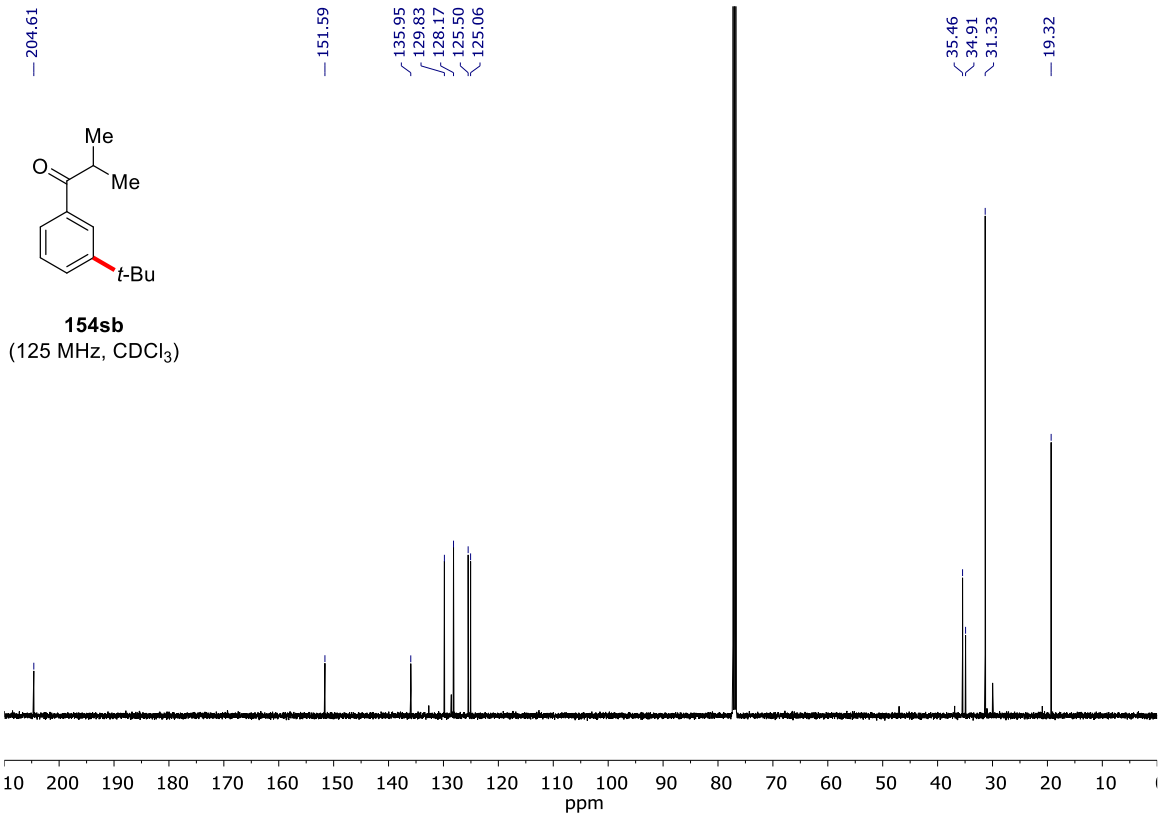
154rb
(75 MHz, $CDCl_3$)



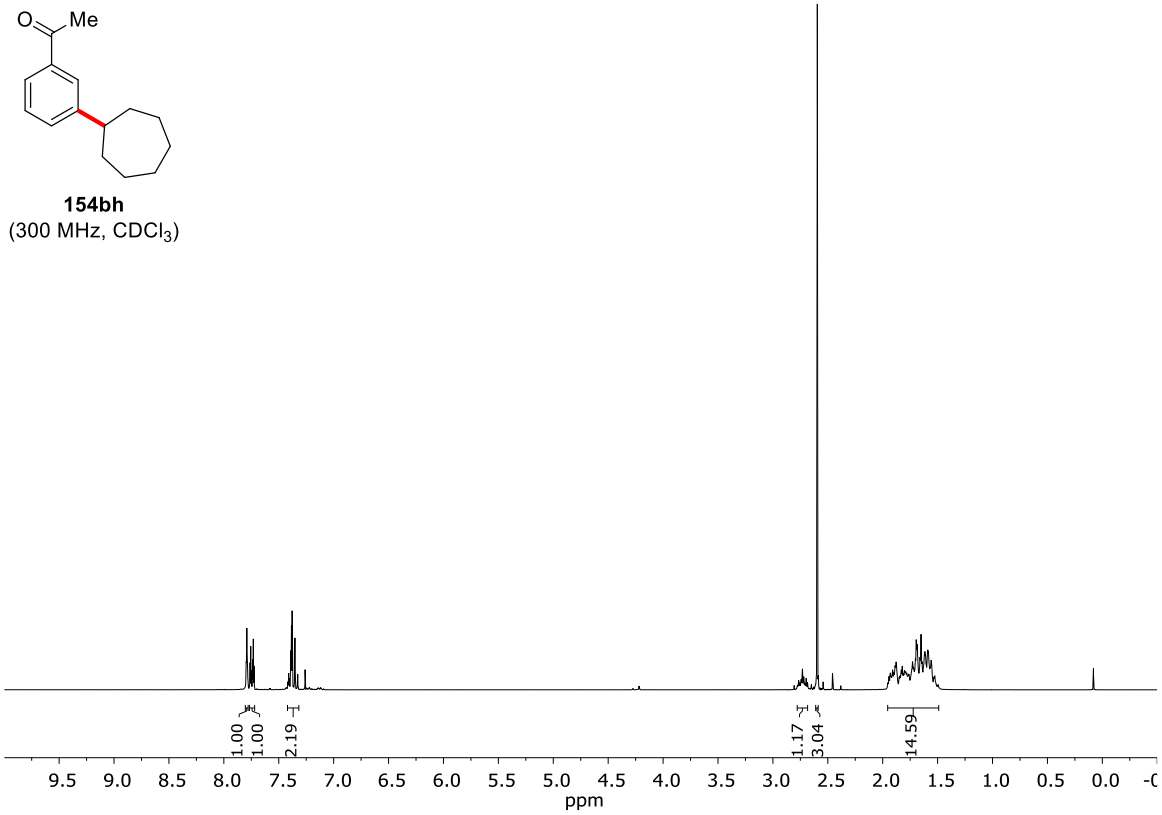
154rb
^{1}H-^{1}H NOESY
(300 MHz, $CDCl_3$)



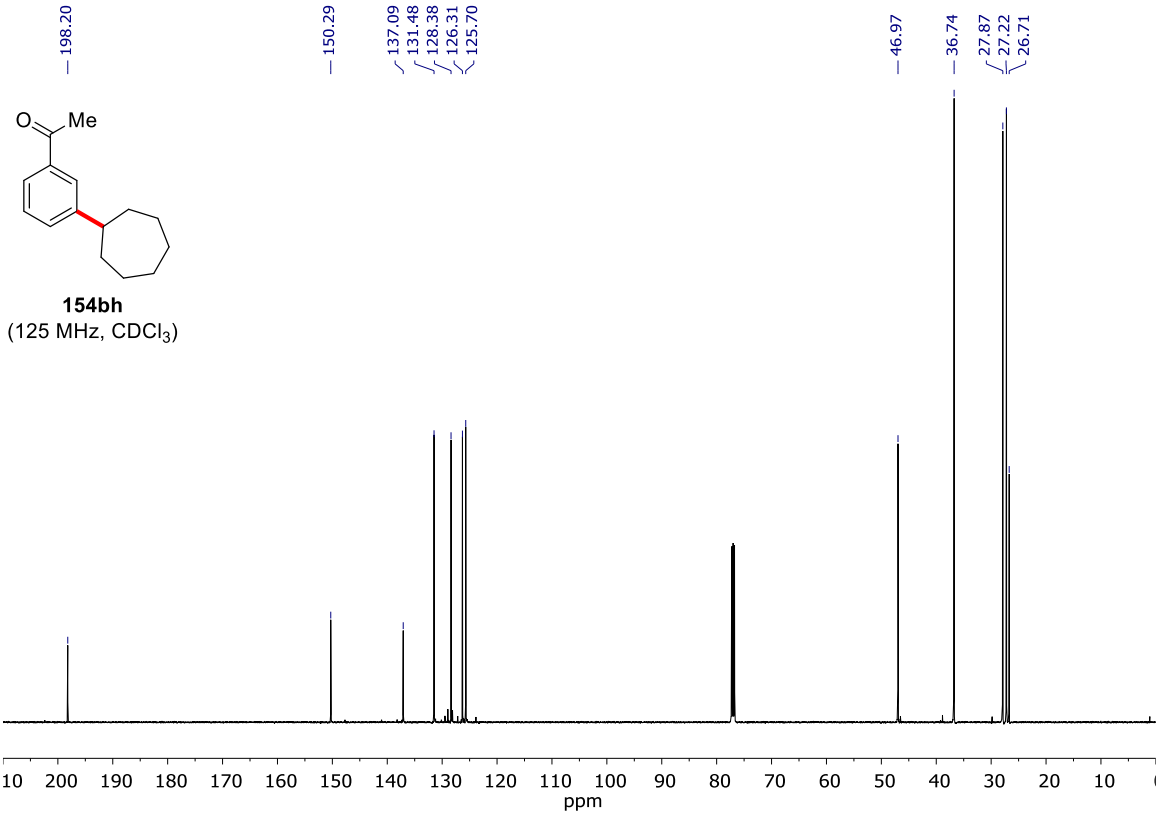
154sb
(300 MHz, $CDCl_3$)



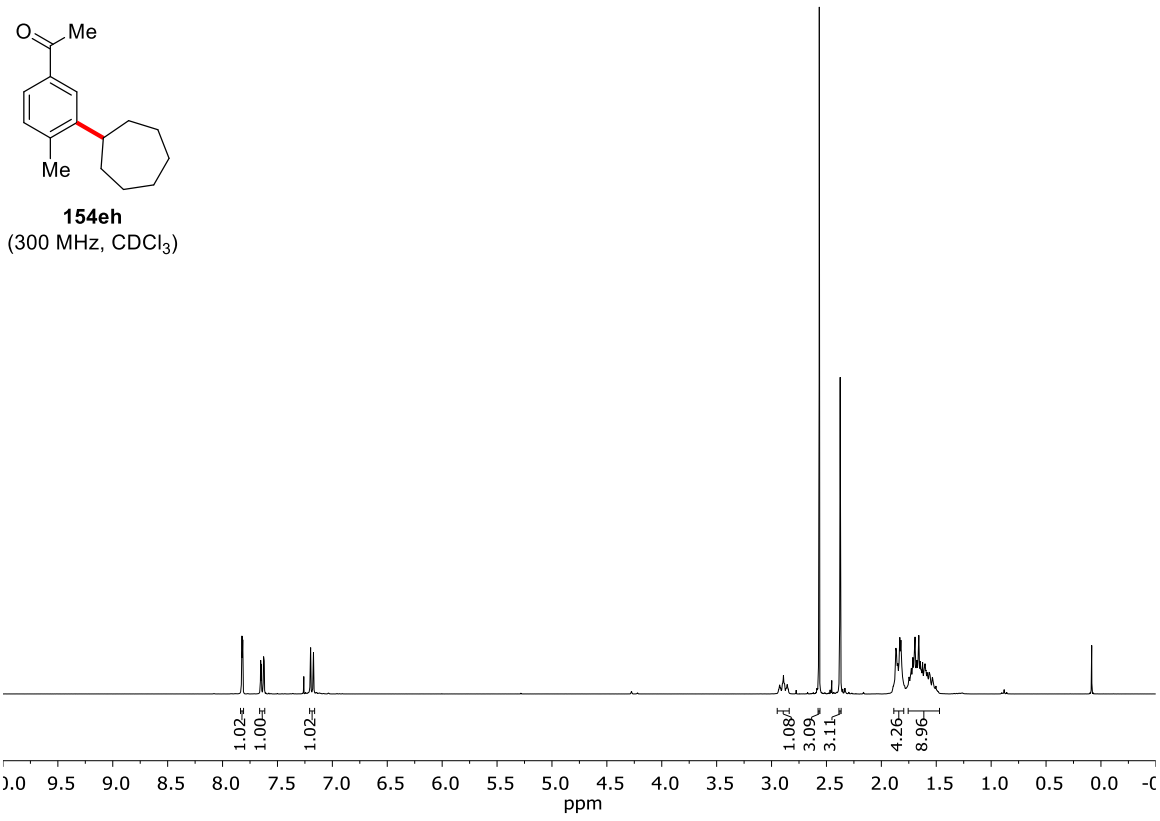
154sb
(125 MHz, $CDCl_3$)



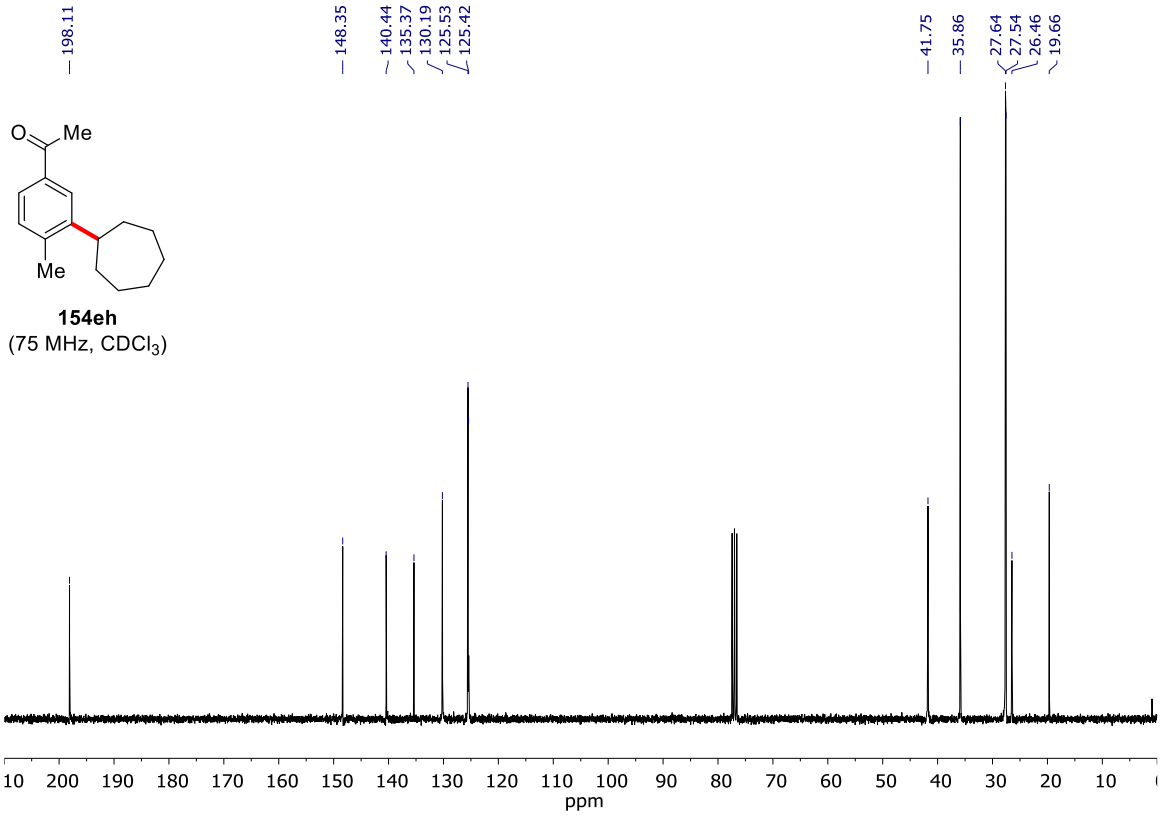
154bh
(300 MHz, $CDCl_3$)



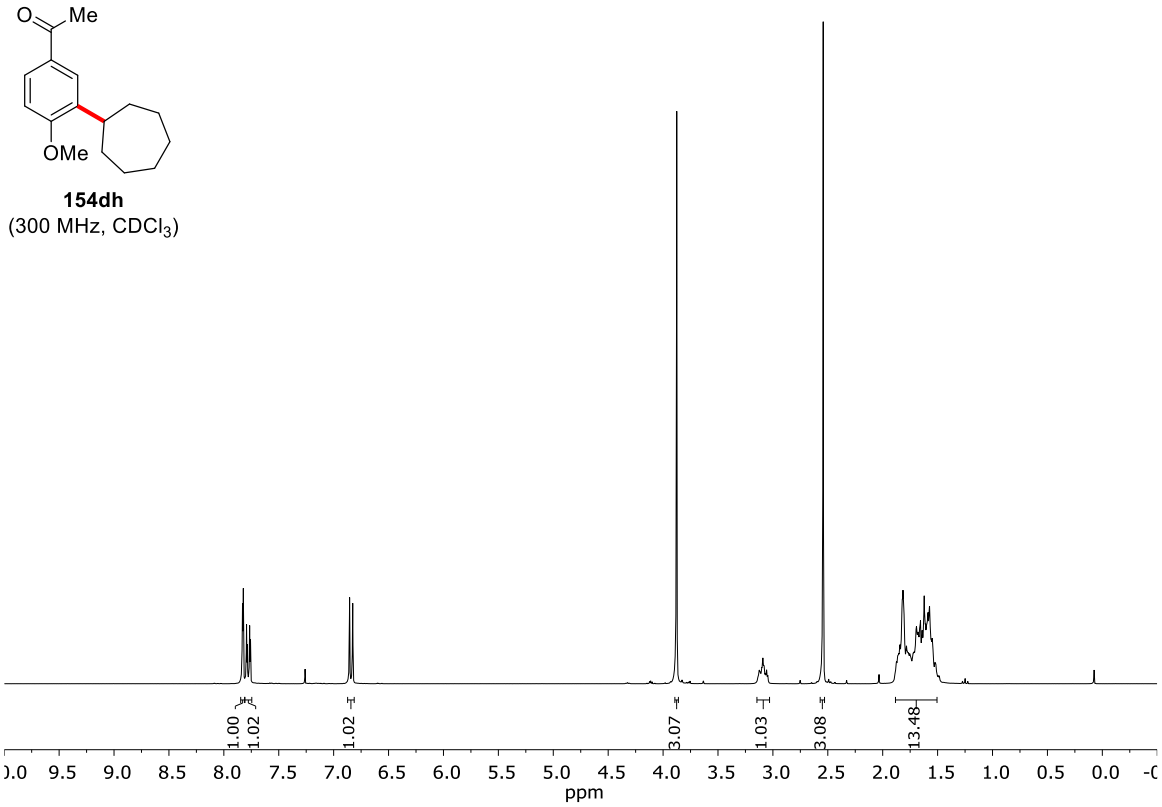
154bh
(125 MHz, $CDCl_3$)



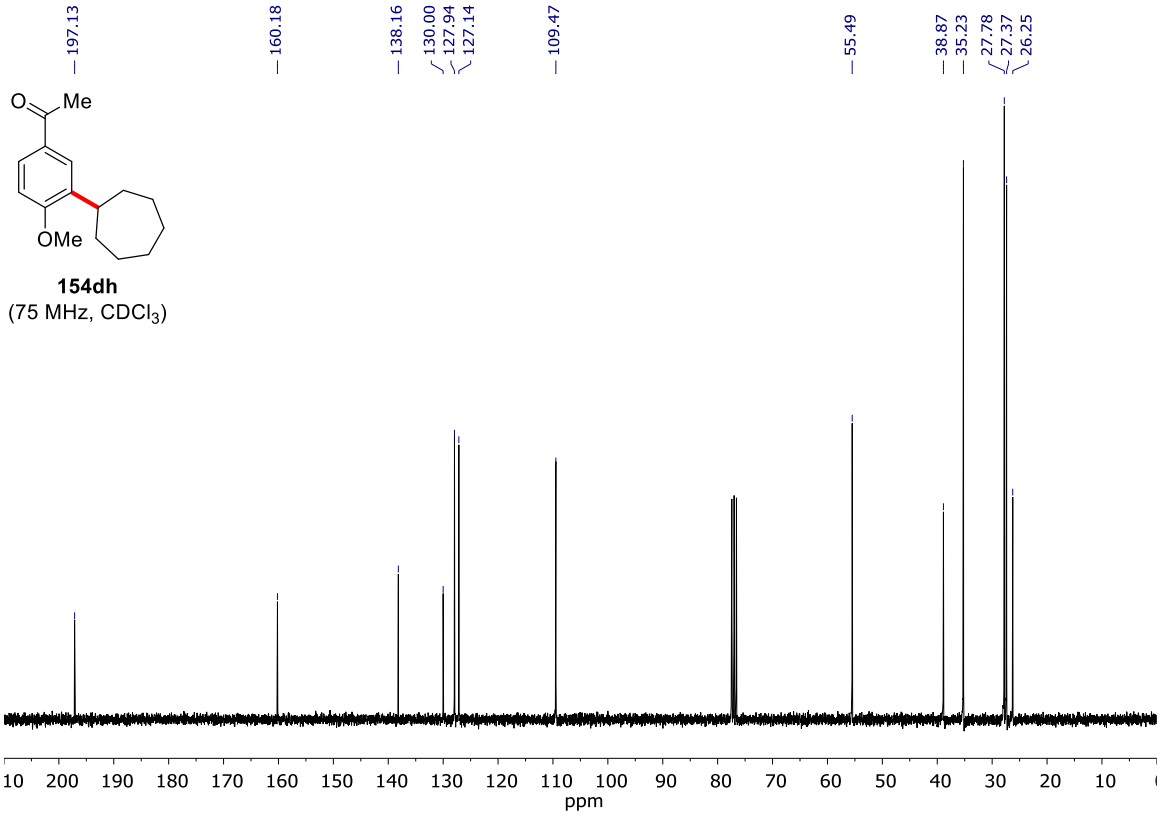
154eh
(300 MHz, $CDCl_3$)



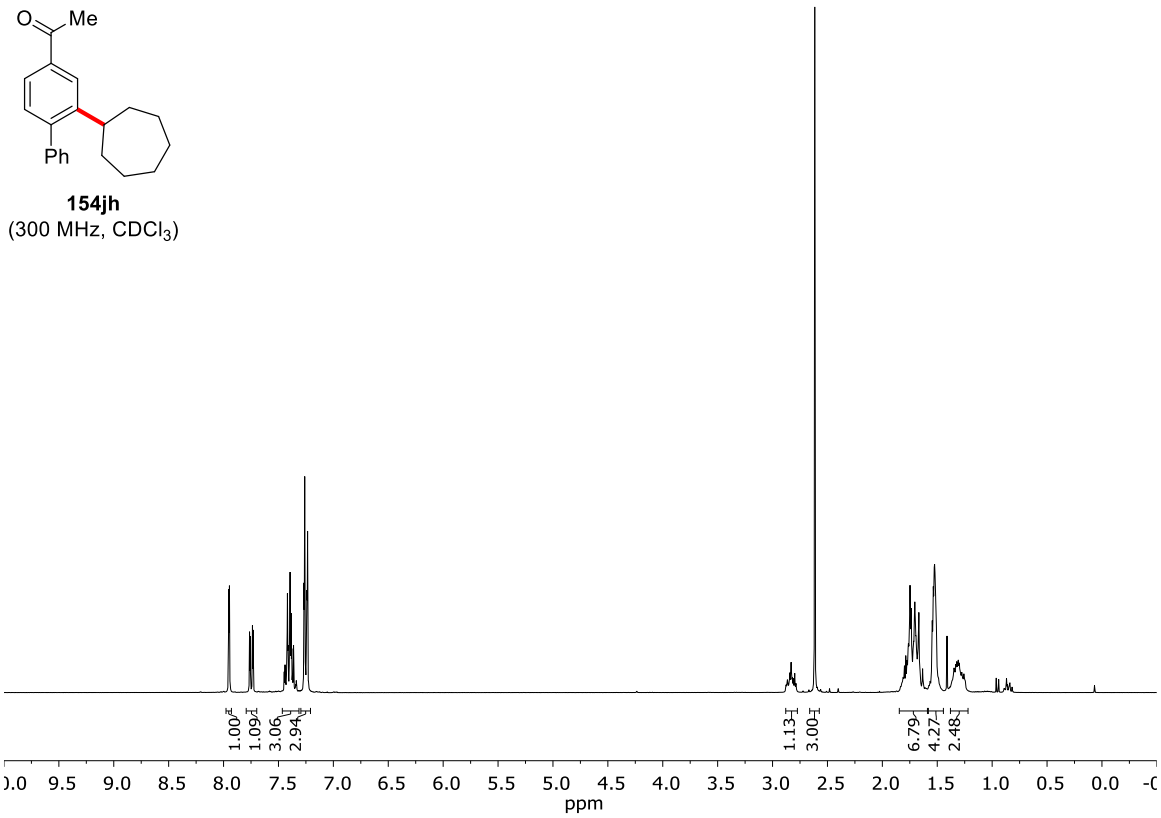
154eh
(75 MHz, $CDCl_3$)



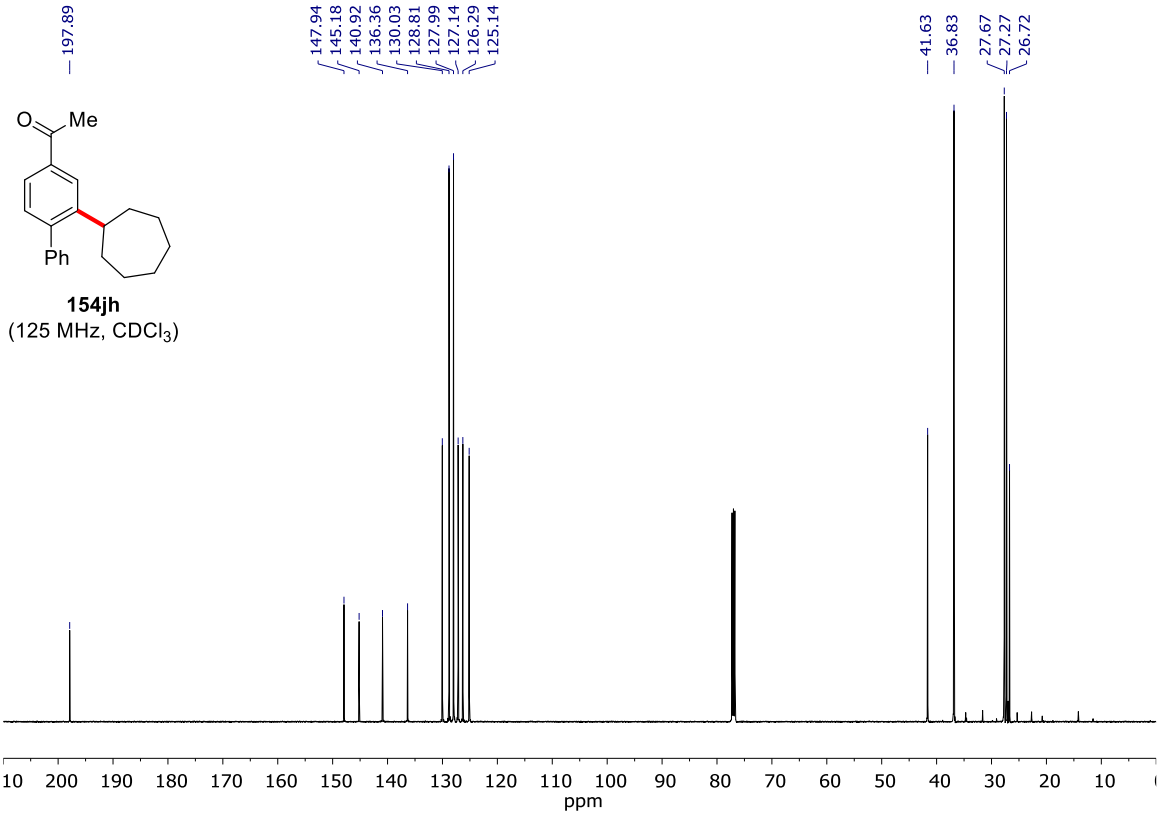
154dh
(300 MHz, $CDCl_3$)



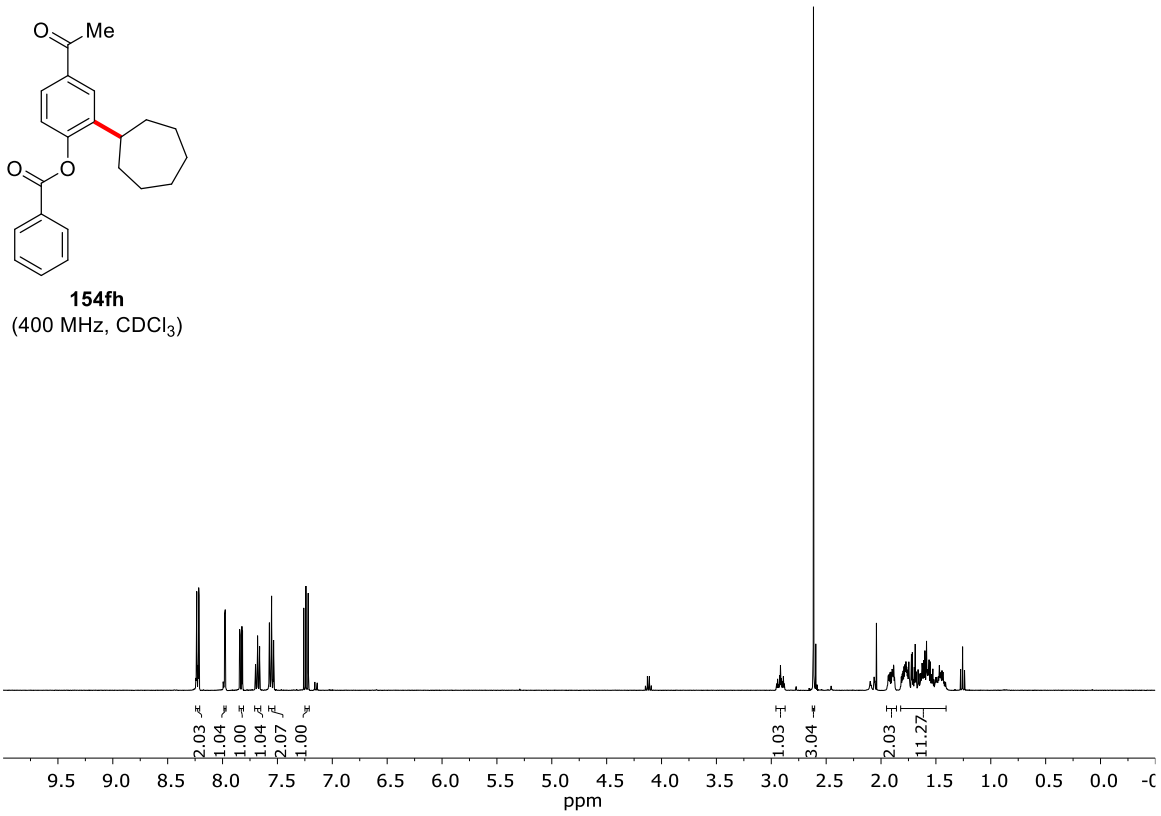
154dh
(75 MHz, $CDCl_3$)



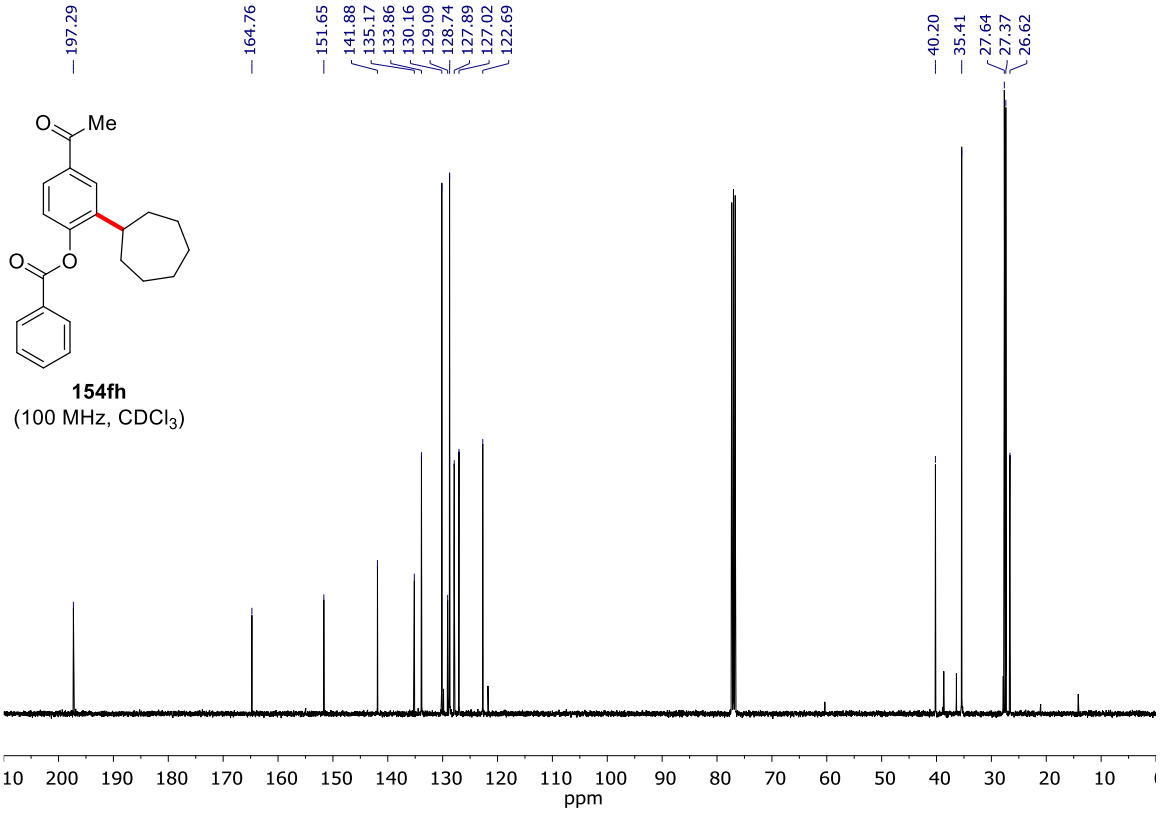
154jh
(300 MHz, $CDCl_3$)



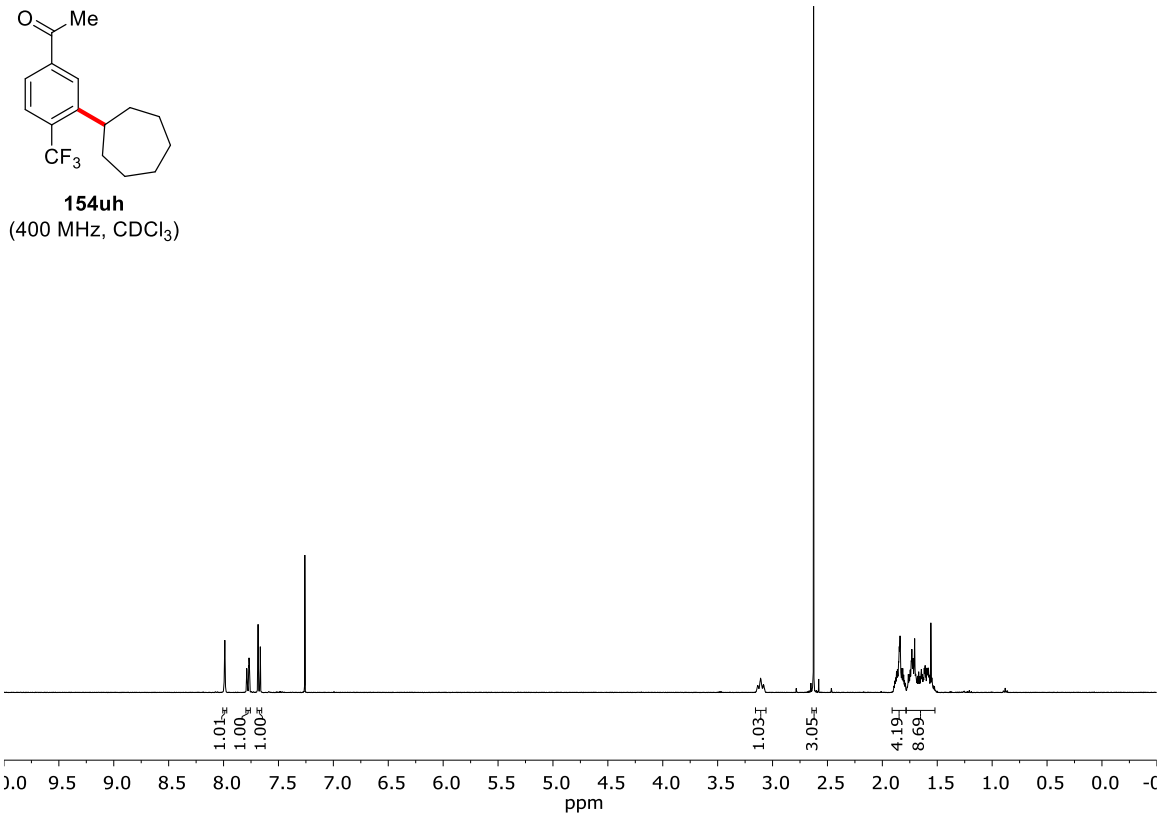
154jh
(125 MHz, $CDCl_3$)



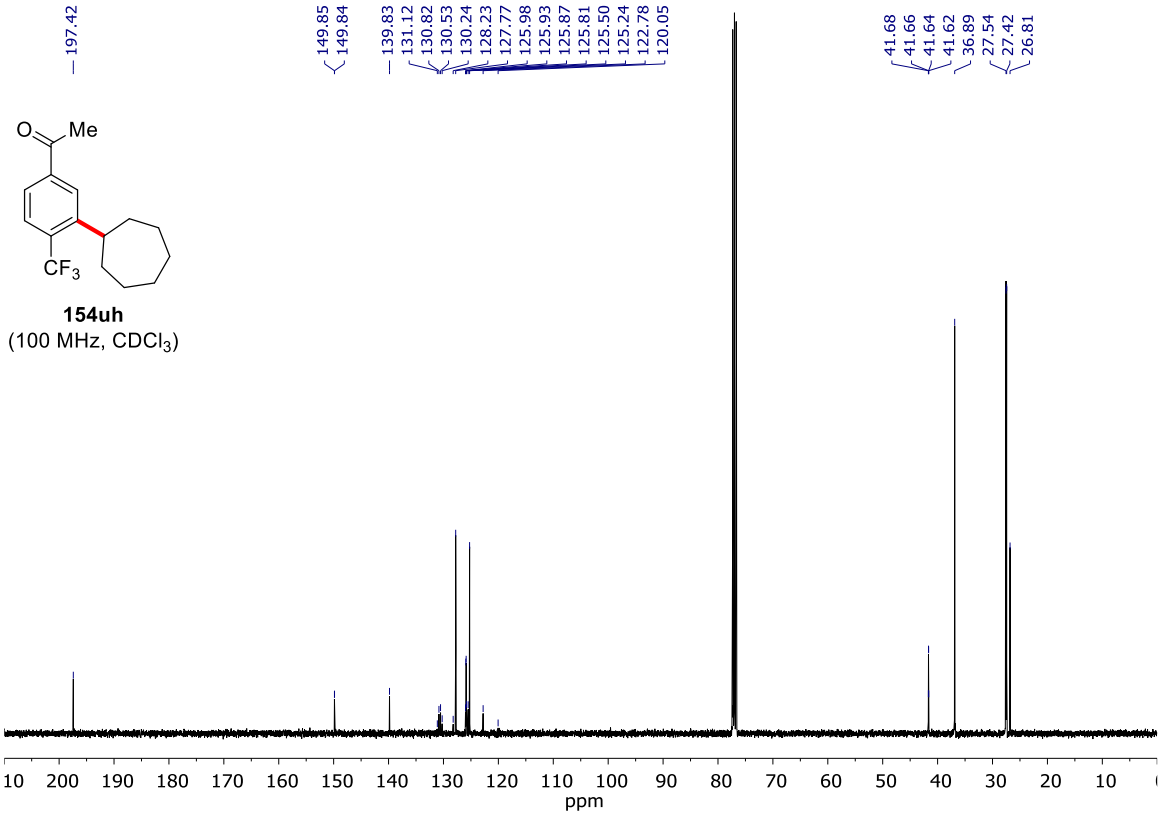
154fh
(400 MHz, $CDCl_3$)



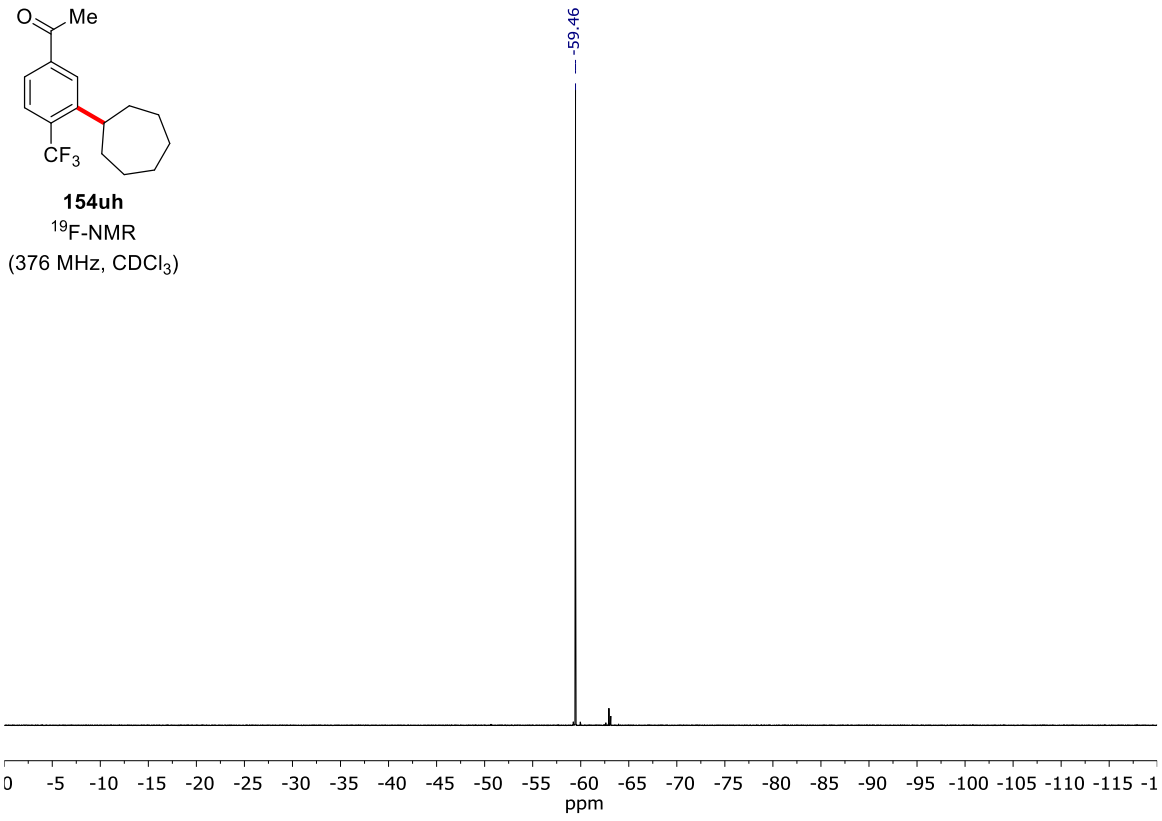
154fh
(100 MHz, $CDCl_3$)



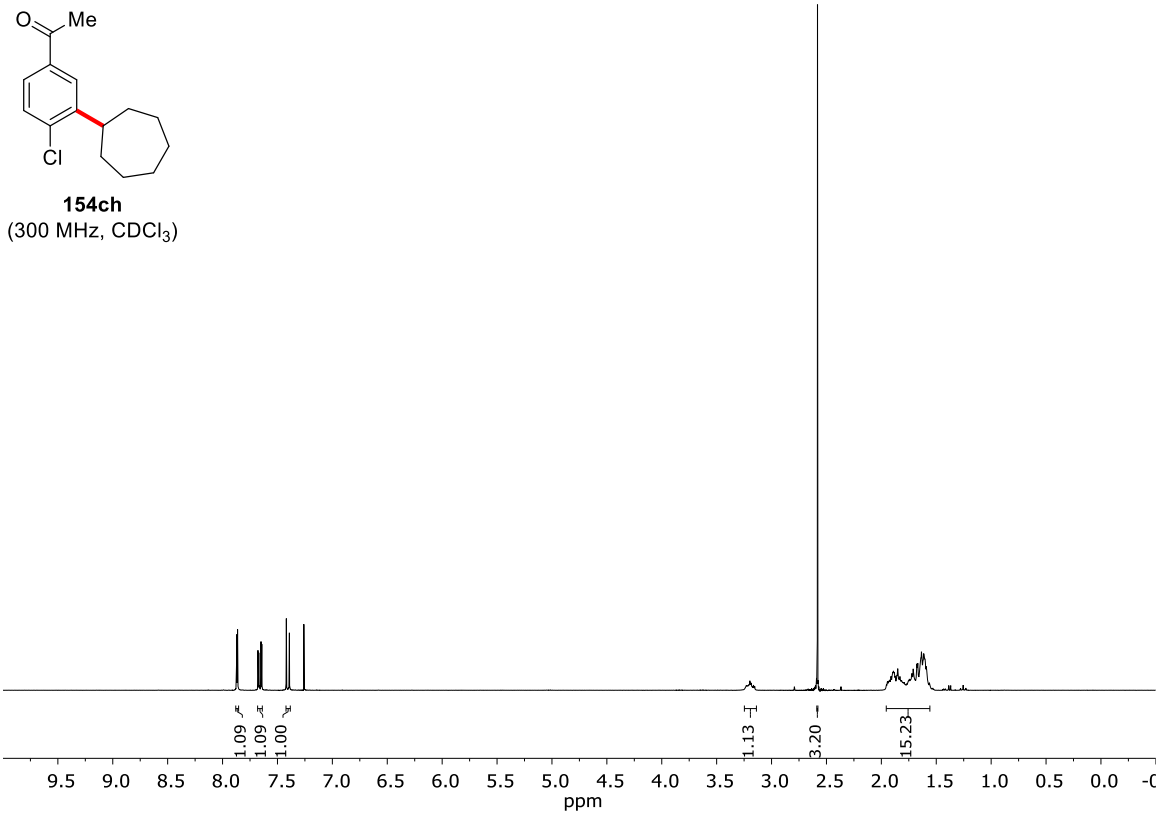
154uh
(400 MHz, $CDCl_3$)



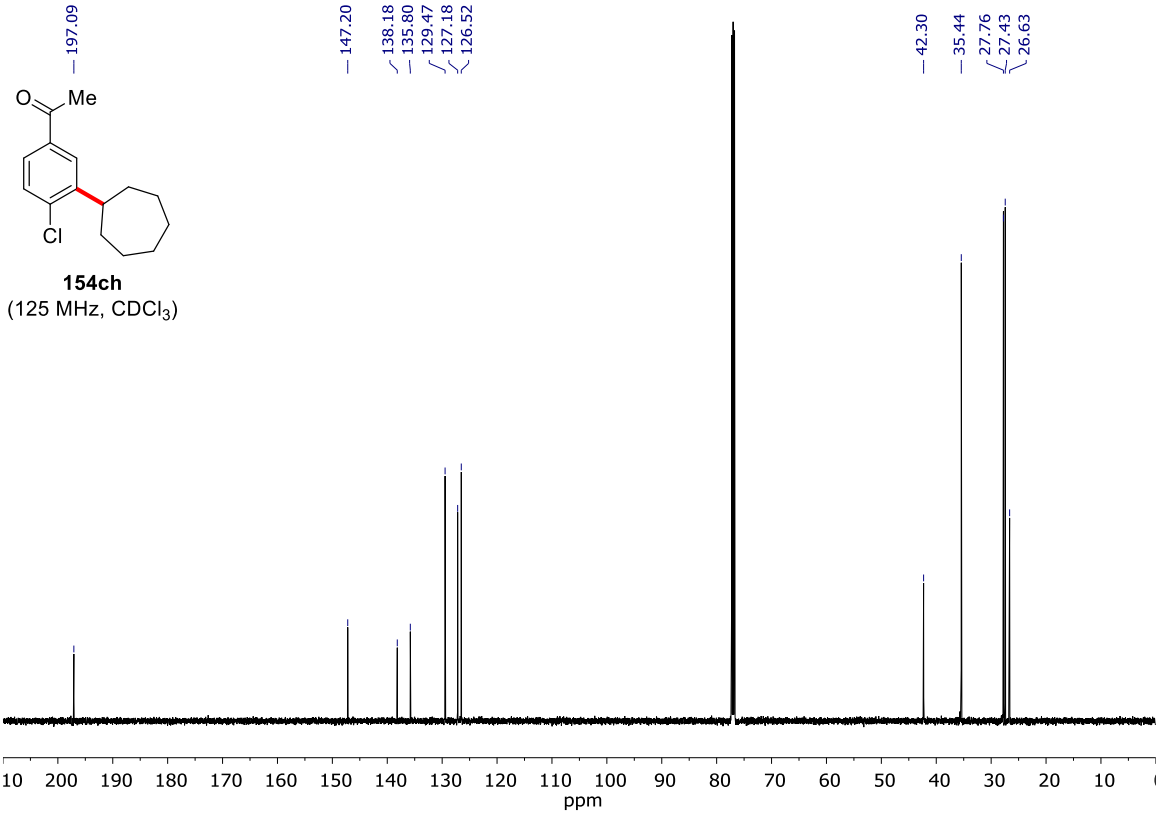
154uh
(100 MHz, $CDCl_3$)



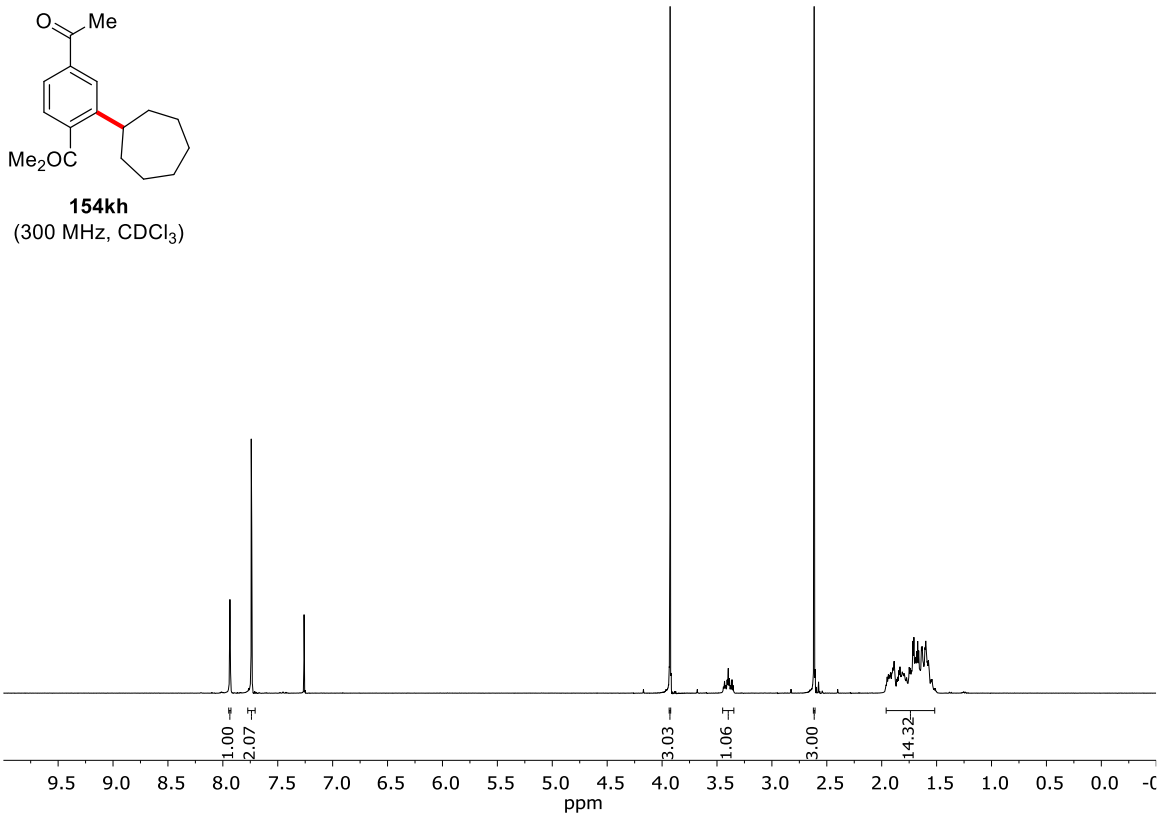
154uh
^{19}F-NMR
(376 MHz, $CDCl_3$)

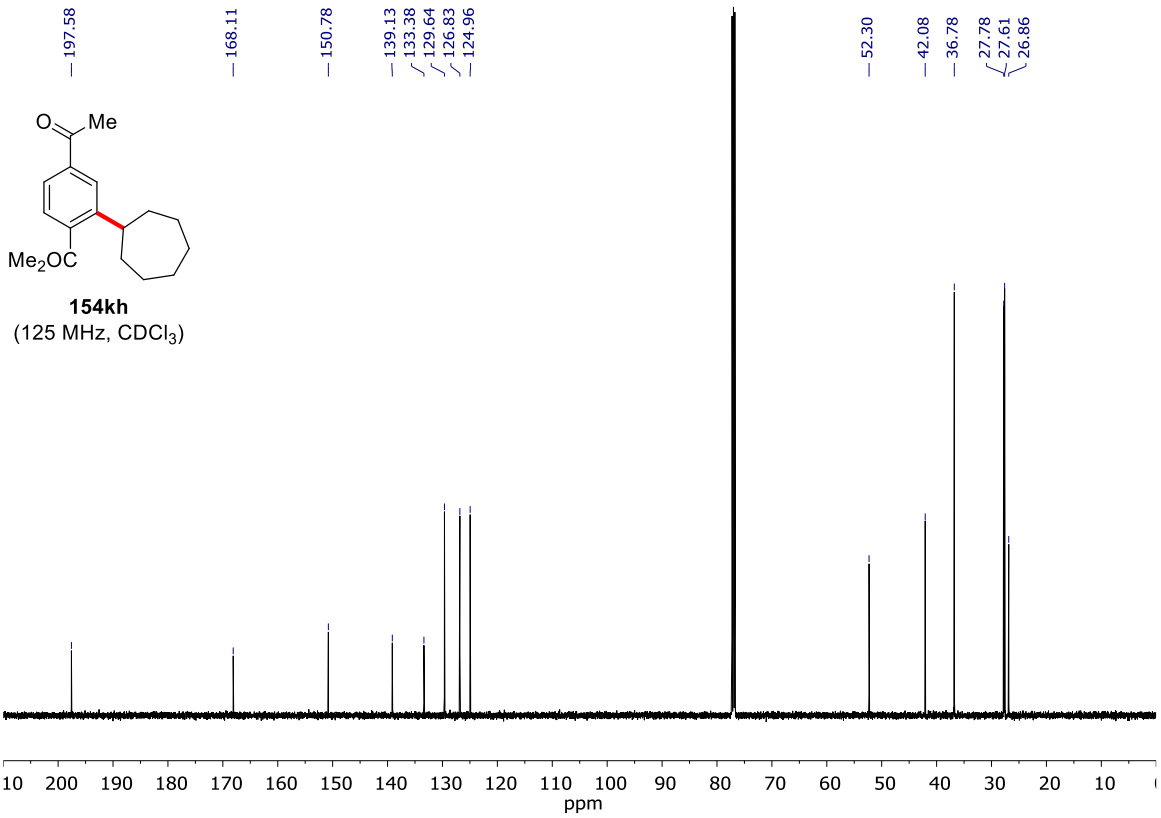


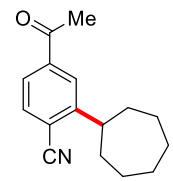
154ch
(300 MHz, $CDCl_3$)



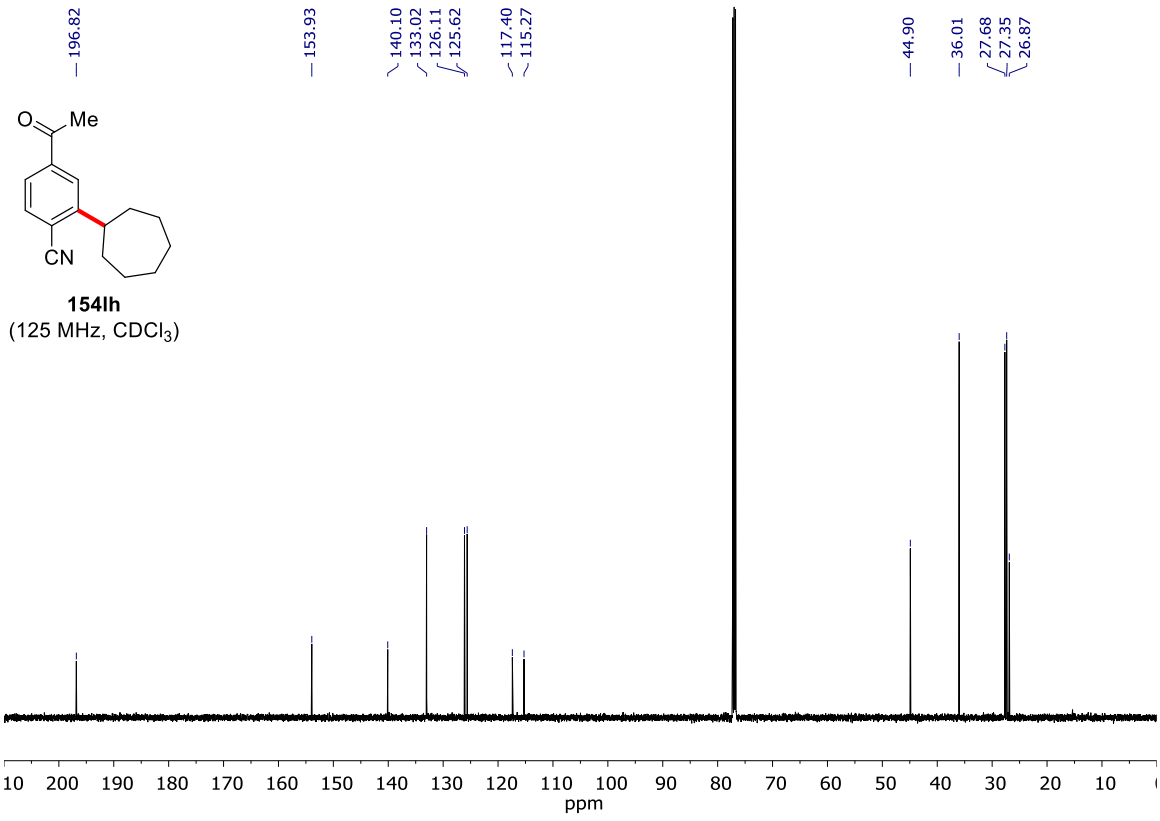
154ch
(125 MHz, $CDCl_3$)


O
Me
Me2OC
154kh
(300 MHz, CDCl3)
1.00
2.07
3.03
1.06
3.00
14.32
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

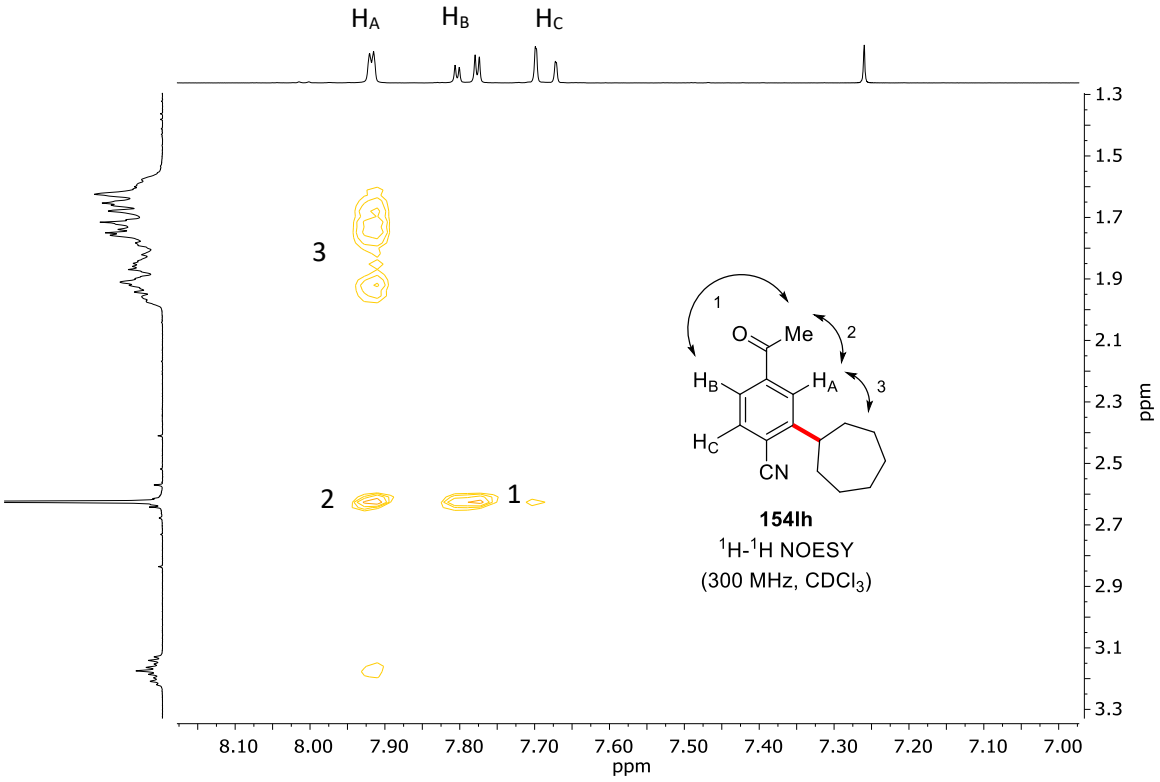

197.58
168.11
150.78
139.13
133.38
129.64
126.83
124.96
52.30
42.08
36.78
27.78
27.61
26.86
O
Me
Me2OC
154kh
(125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

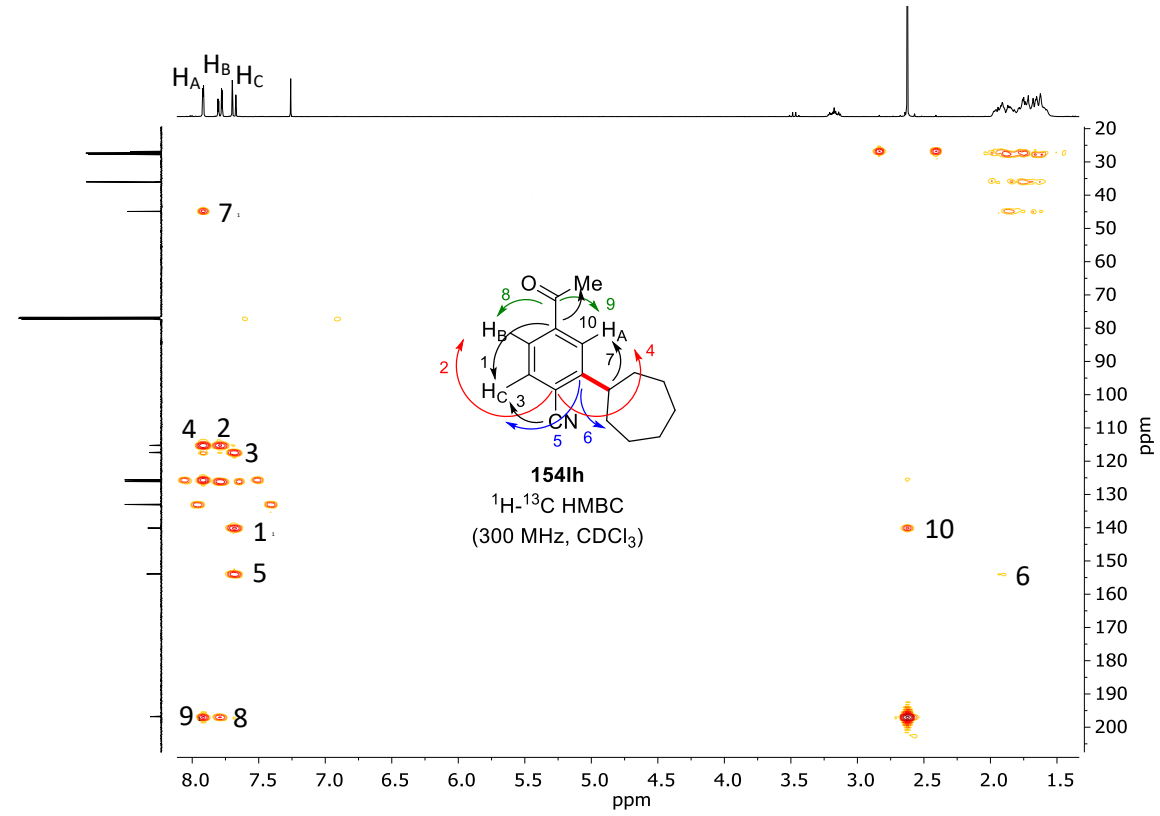


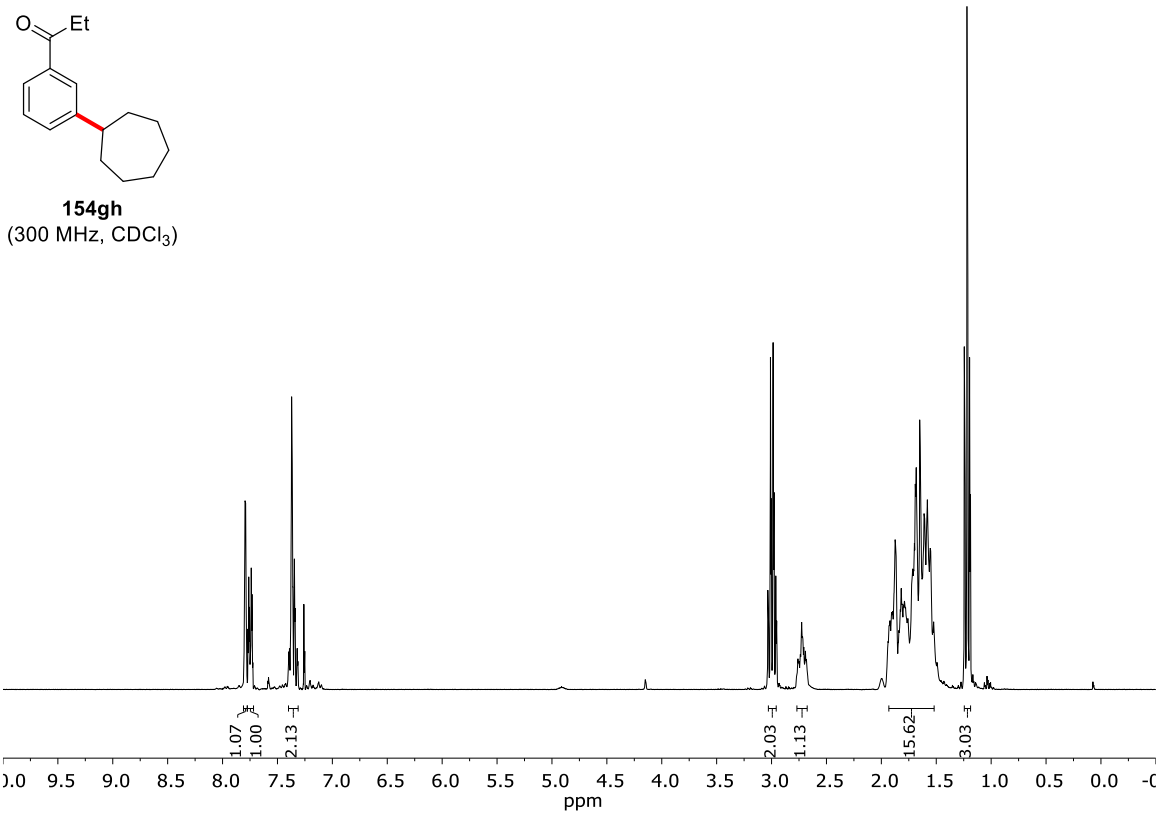
154lh
(300 MHz, $CDCl_3$)

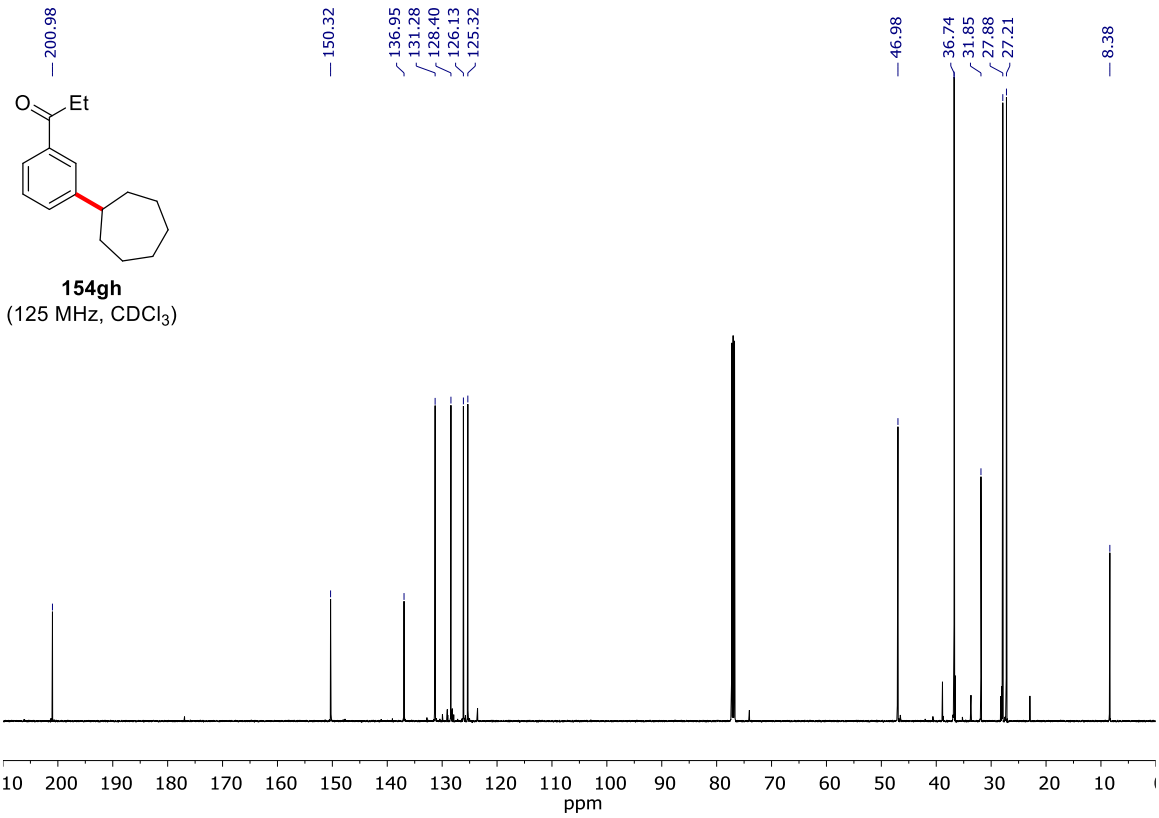


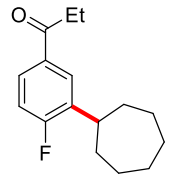
154lh
(125 MHz, $CDCl_3$)


HA
HB
HC
3
2
1
O
Me
HB
HA
HC
CN
1
2
3
154lh
1H-1H NOESY
(300 MHz, CDCl3)
ppm
8.10
8.00
7.90
7.80
7.70
7.60
7.50
7.40
7.30
7.20
7.10
7.00
1.3
1.5
1.7
1.9
2.1
2.3
2.5
2.7
2.9
3.1
3.3

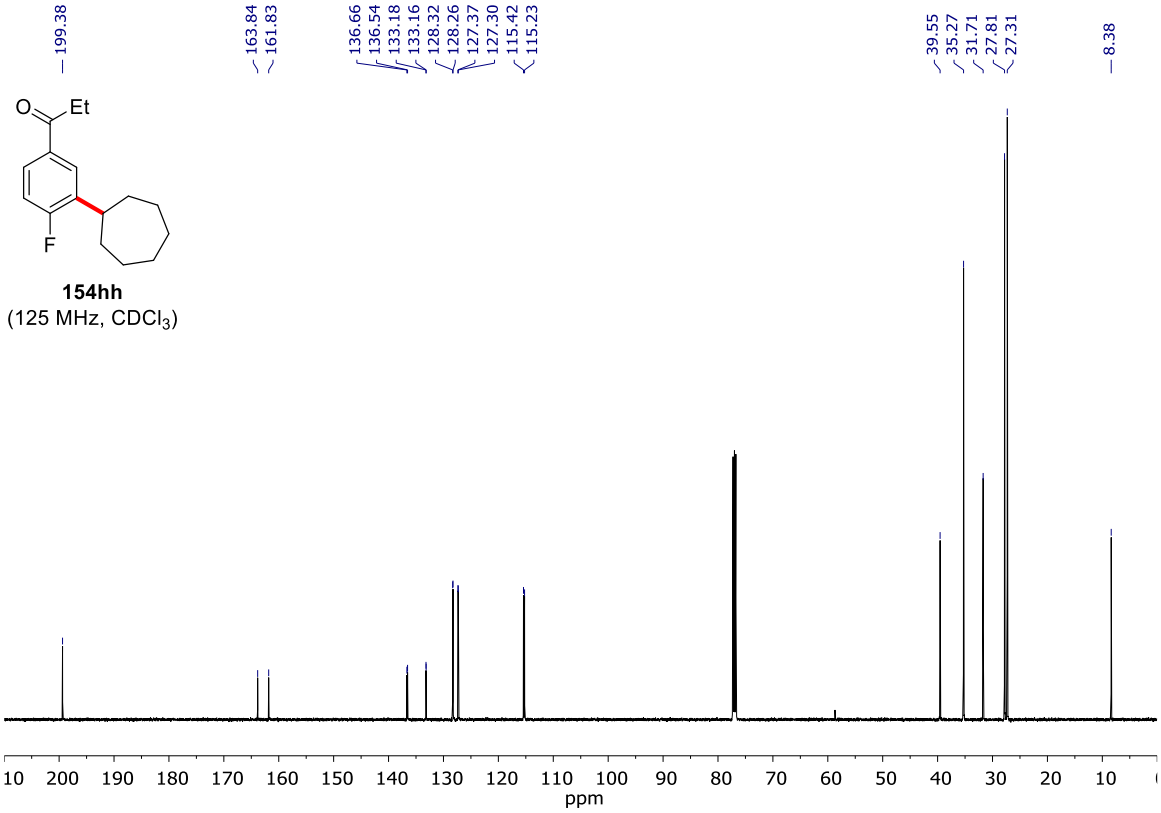

HA
HB
HC
7
4
2
3
1
5
9
8
10
6
O
Me
HB
HA
HC
CN
1
2
3
4
5
6
7
8
9
10
154lh
1H-13C HMBC
(300 MHz, CDCl3)
ppm
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200


O
Et
154gh
(300 MHz, CDCl3)
1.07
1.00
2.13
2.03
1.13
15.62
3.03
ppm

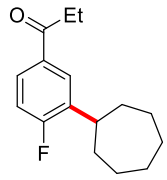

200.98
150.32
136.95
131.28
128.40
126.13
125.32
46.98
36.74
31.85
27.88
27.21
8.38
O
Et
154gh
(125 MHz, CDCl3)
ppm



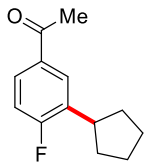
154hh
(300 MHz, $CDCl_3$)



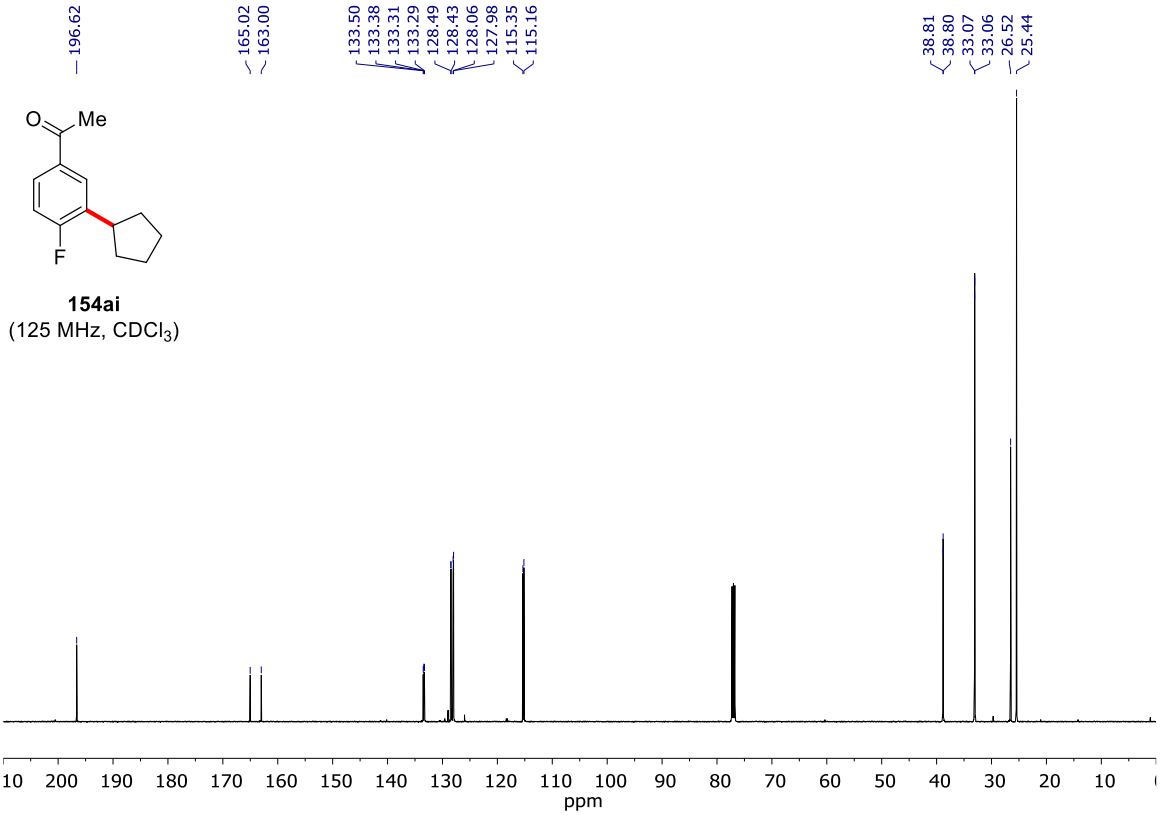
154hh
(125 MHz, $CDCl_3$)



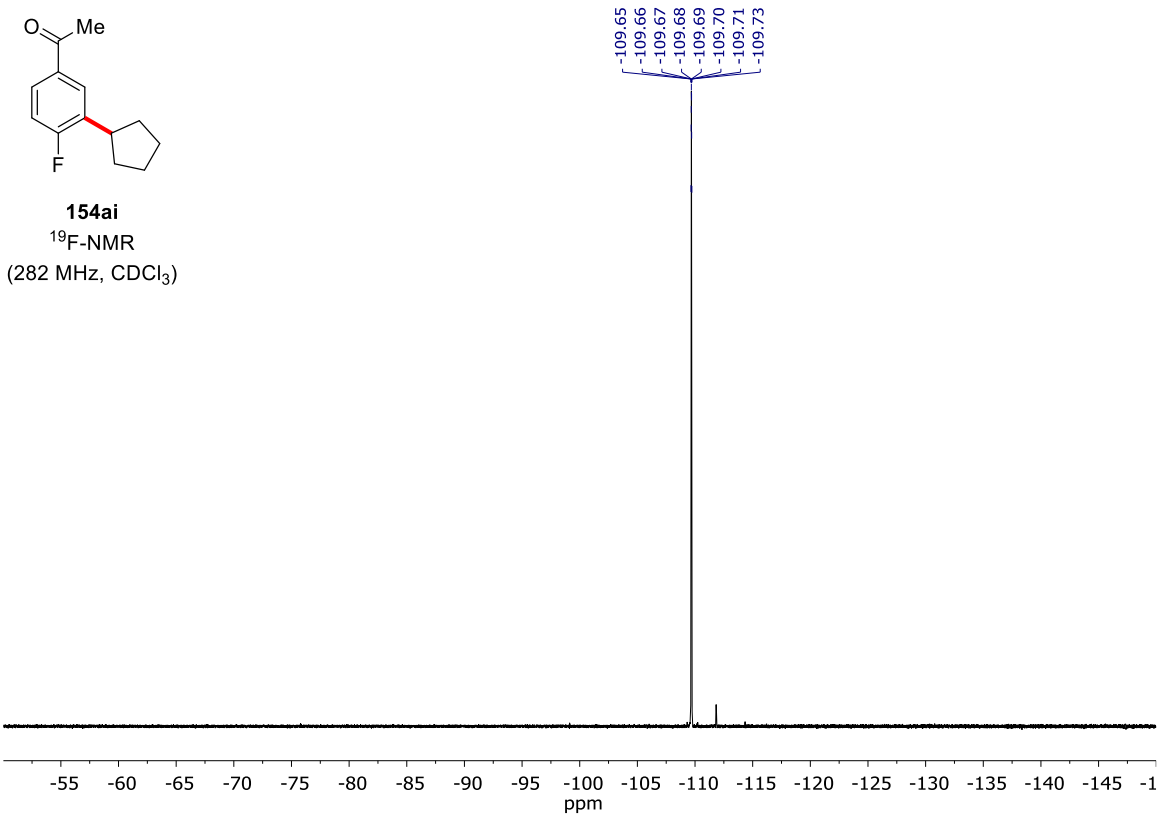
154hh
^{19}F-NMR
(282 MHz, $CDCl_3$)



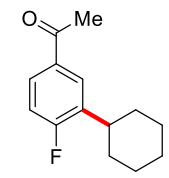
154ai
(300 MHz, $CDCl_3$)



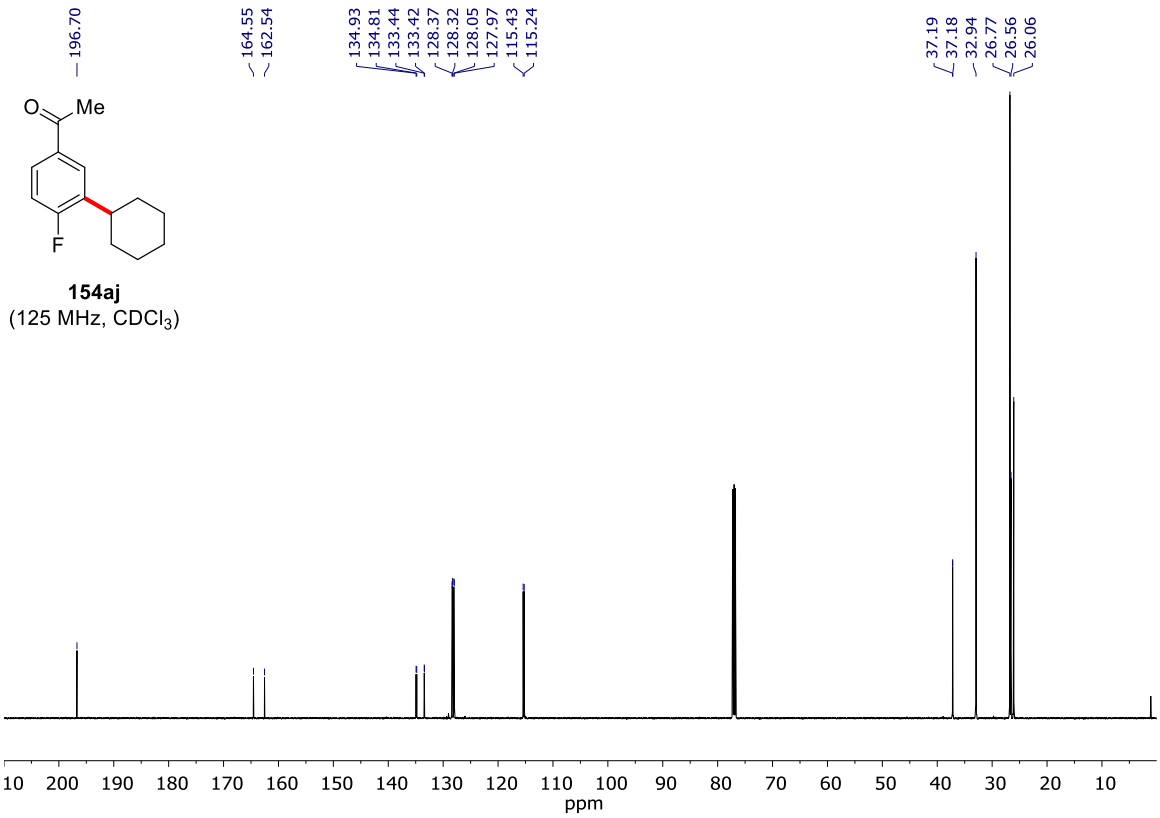
154ai
(125 MHz, $CDCl_3$)



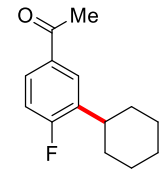
154ai
^{19}F-NMR
(282 MHz, $CDCl_3$)



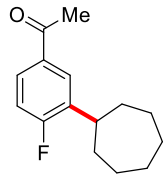
154aj
(300 MHz, $CDCl_3$)



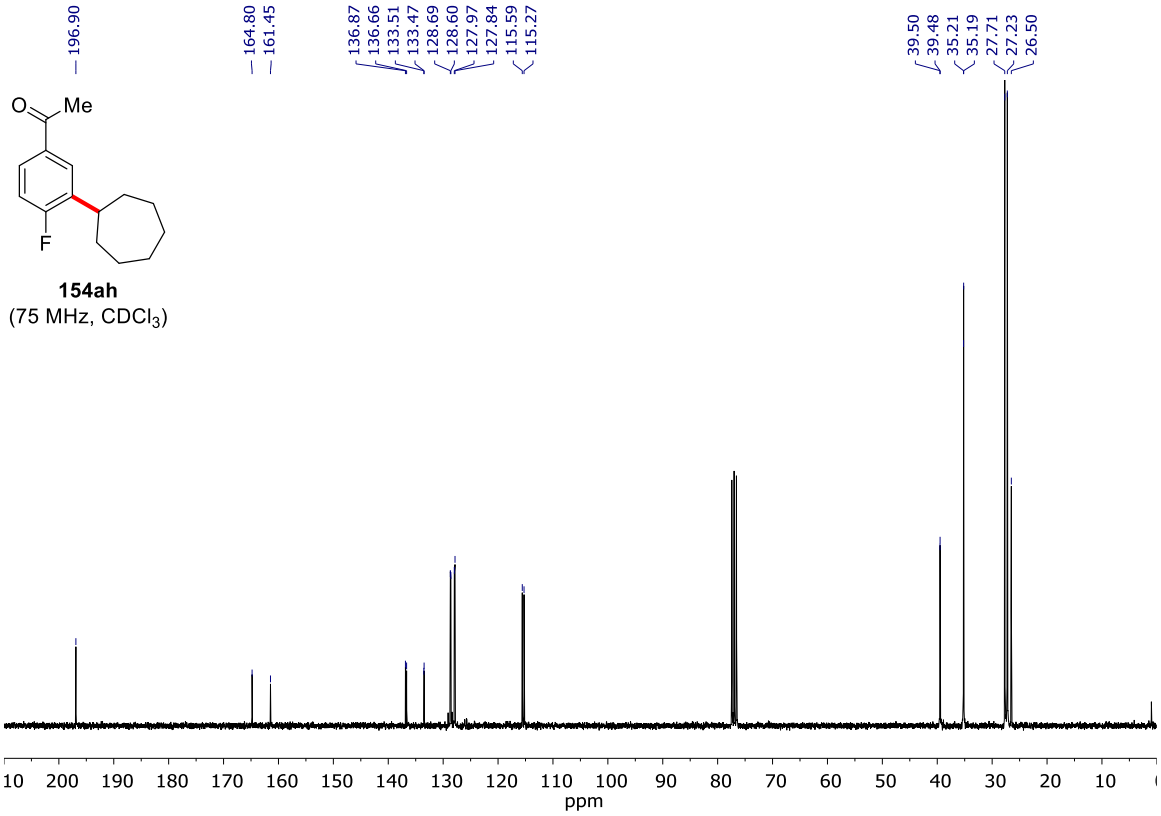
154aj
(125 MHz, $CDCl_3$)



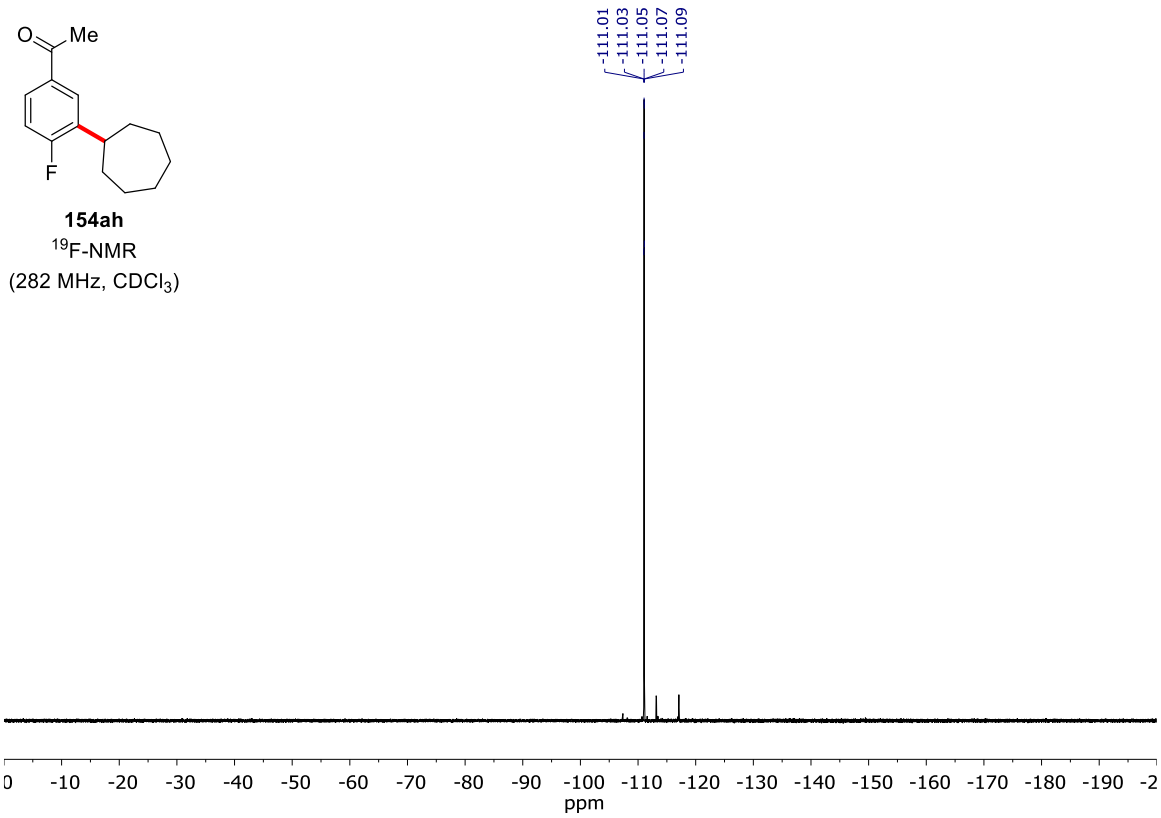
154aj
^{19}F-NMR
(282 MHz, $CDCl_3$)



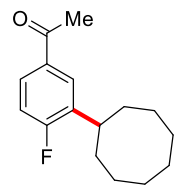
154ah
(300 MHz, $CDCl_3$)



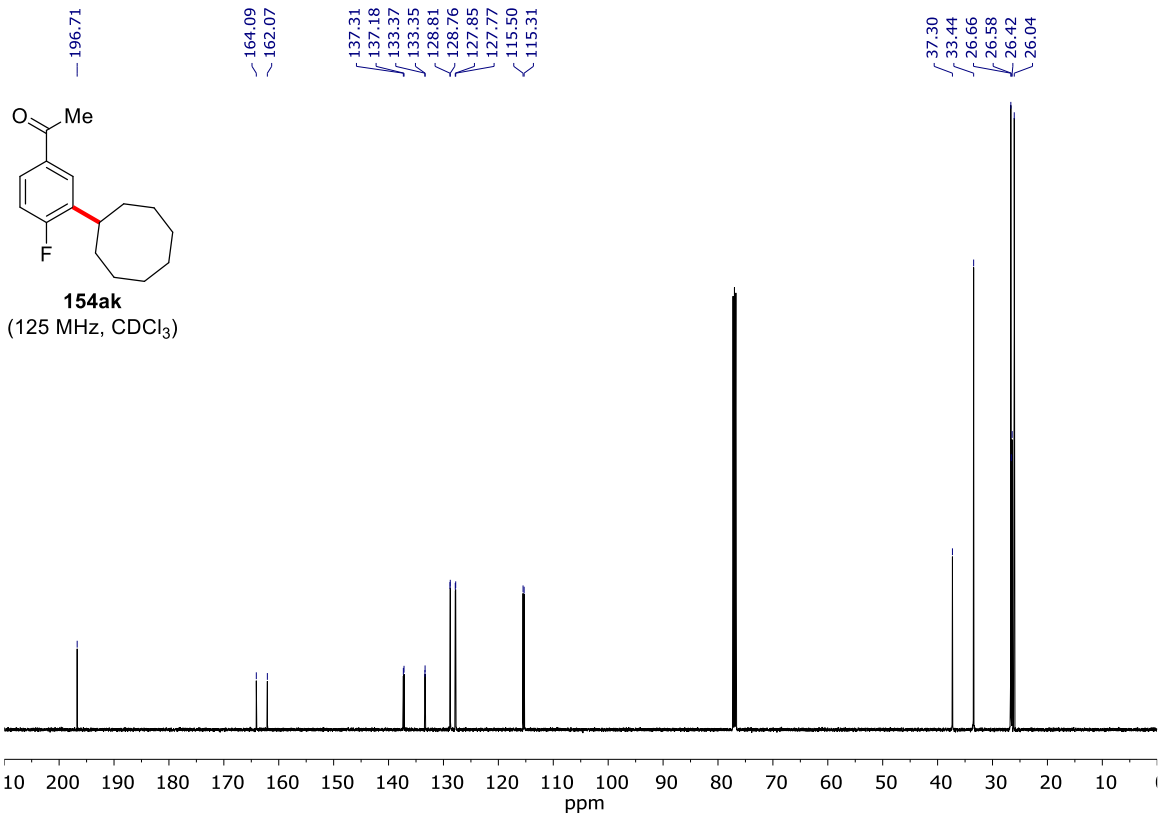
154ah
(75 MHz, $CDCl_3$)



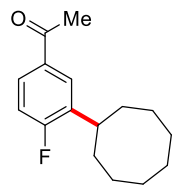
154ah
^{19}F-NMR
(282 MHz, $CDCl_3$)



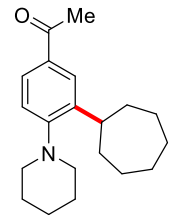
154ak
(300 MHz, $CDCl_3$)



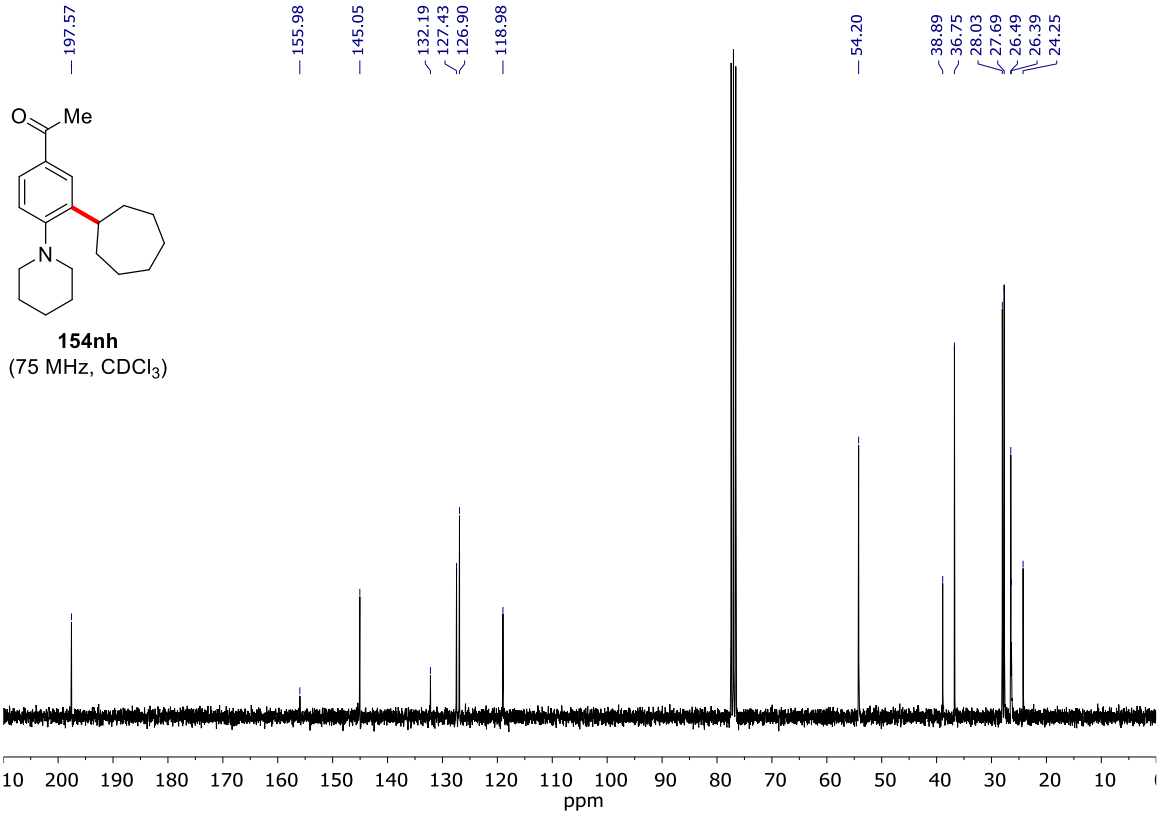
154ak
(125 MHz, $CDCl_3$)



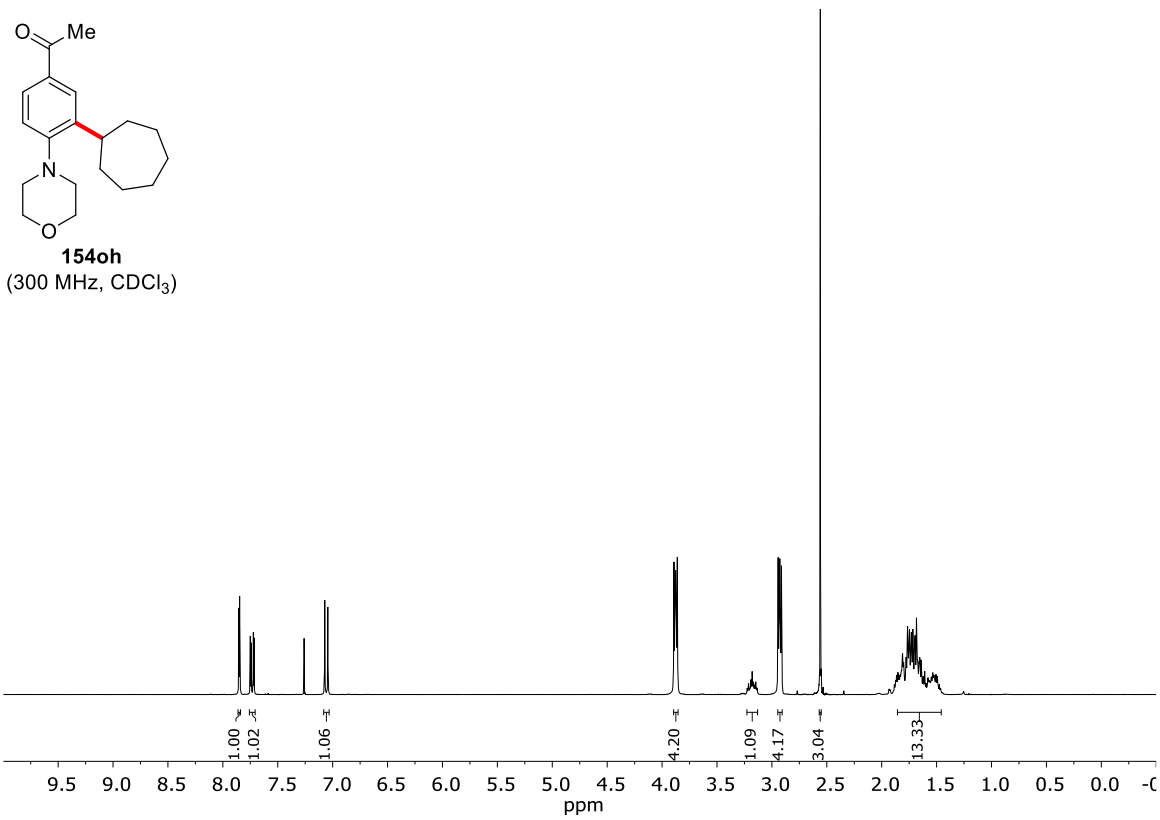
154ak
^{19}F-NMR
(282 MHz, $CDCl_3$)



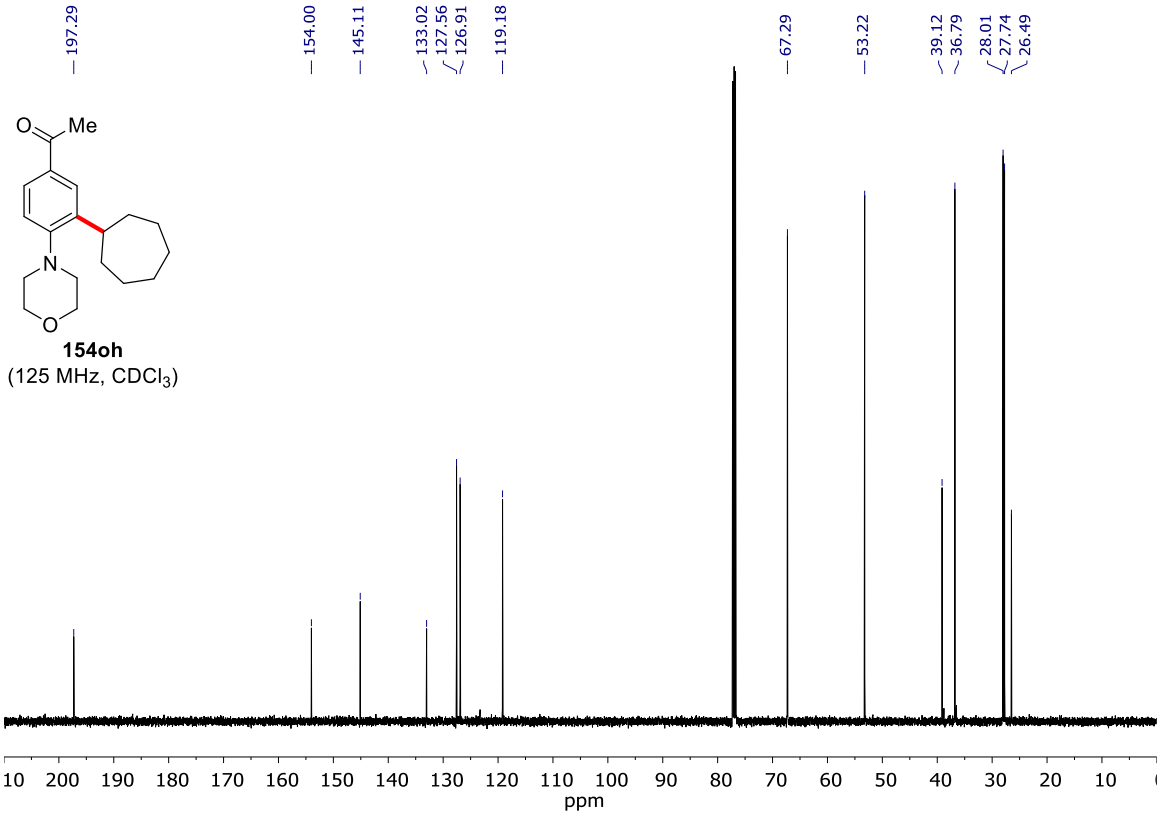
154nh
(300 MHz, $CDCl_3$)

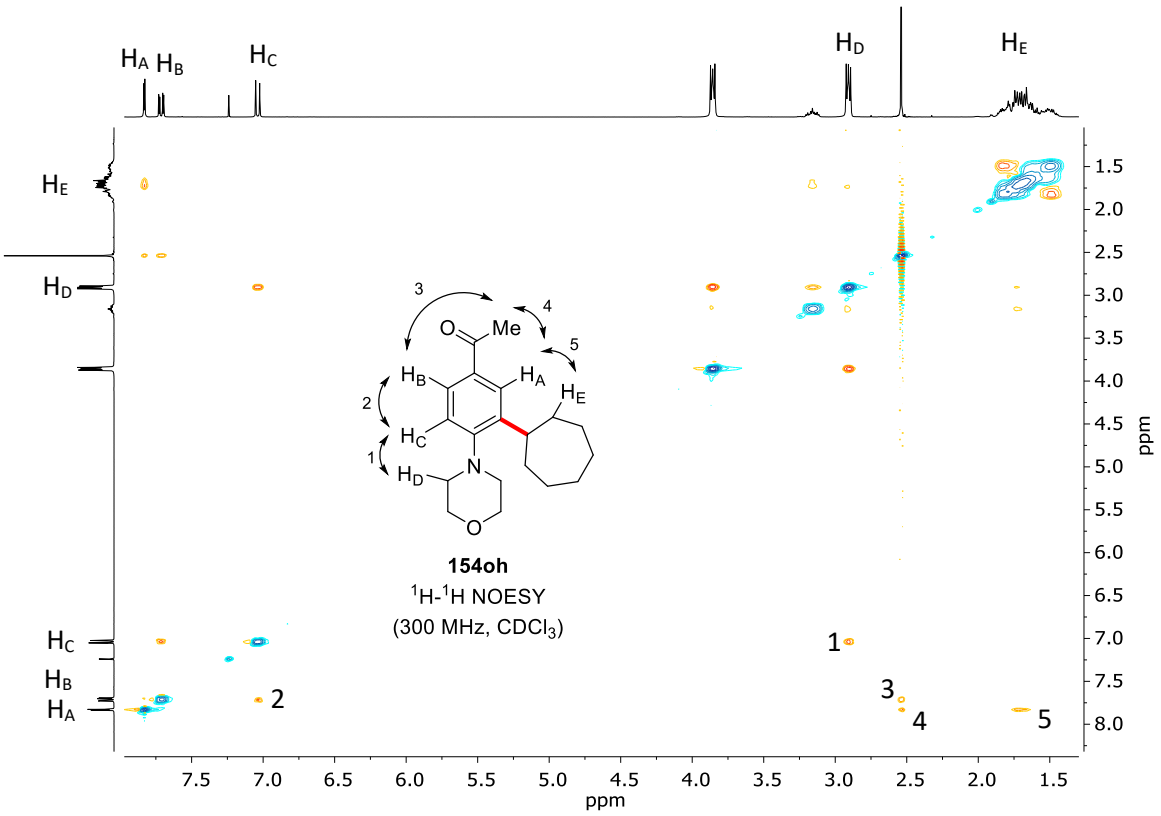


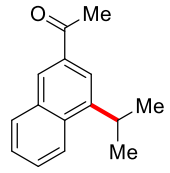
154nh
(75 MHz, $CDCl_3$)



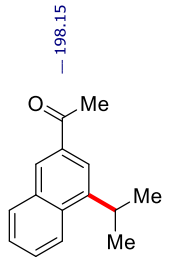
154oh
(300 MHz, $CDCl_3$)


197.29
154.00
145.11
133.02
127.56
126.91
119.18
67.29
53.22
39.12
36.79
28.01
27.74
26.49
O
Me
N
O
154oh
(125 MHz, CDCl3)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

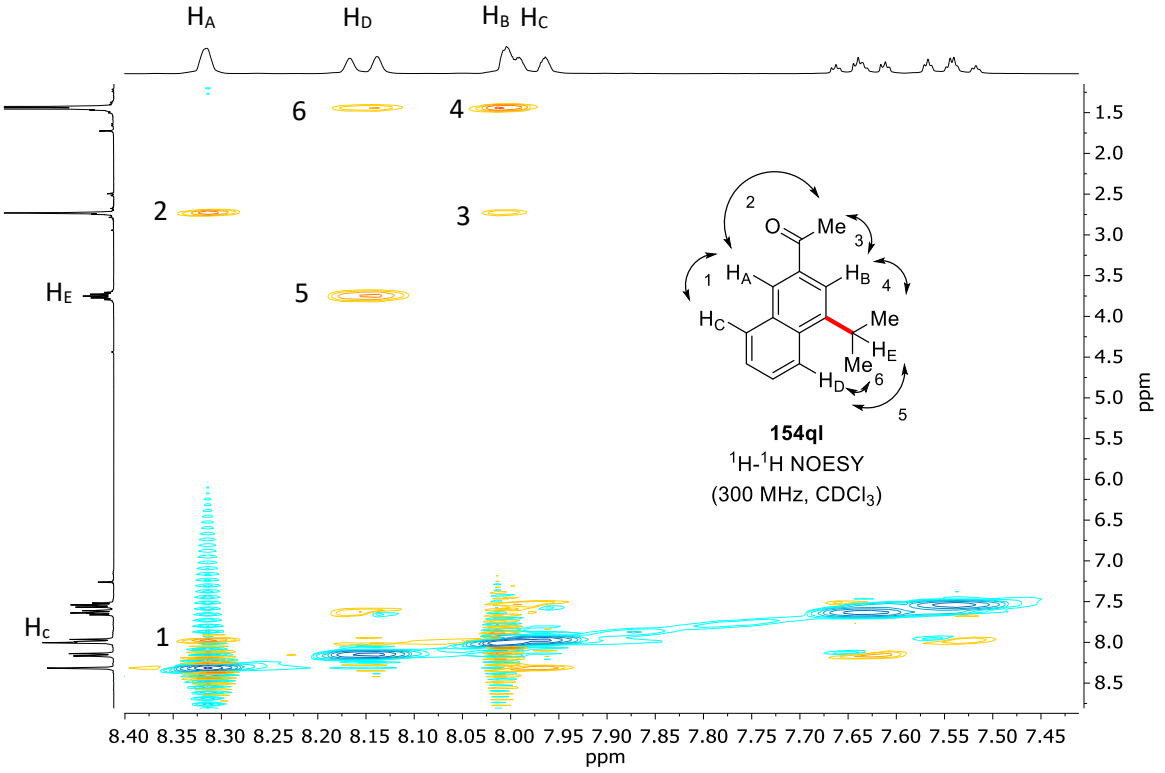

HA HB
HC
HD
HE
HE
HD
HC
HB
HA
2
1
3
4
5
O
Me
HB
HA
HE
HC
HD
N
O
154oh
1H-1H NOESY
(300 MHz, CDCl3)
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
ppm
1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0
ppm

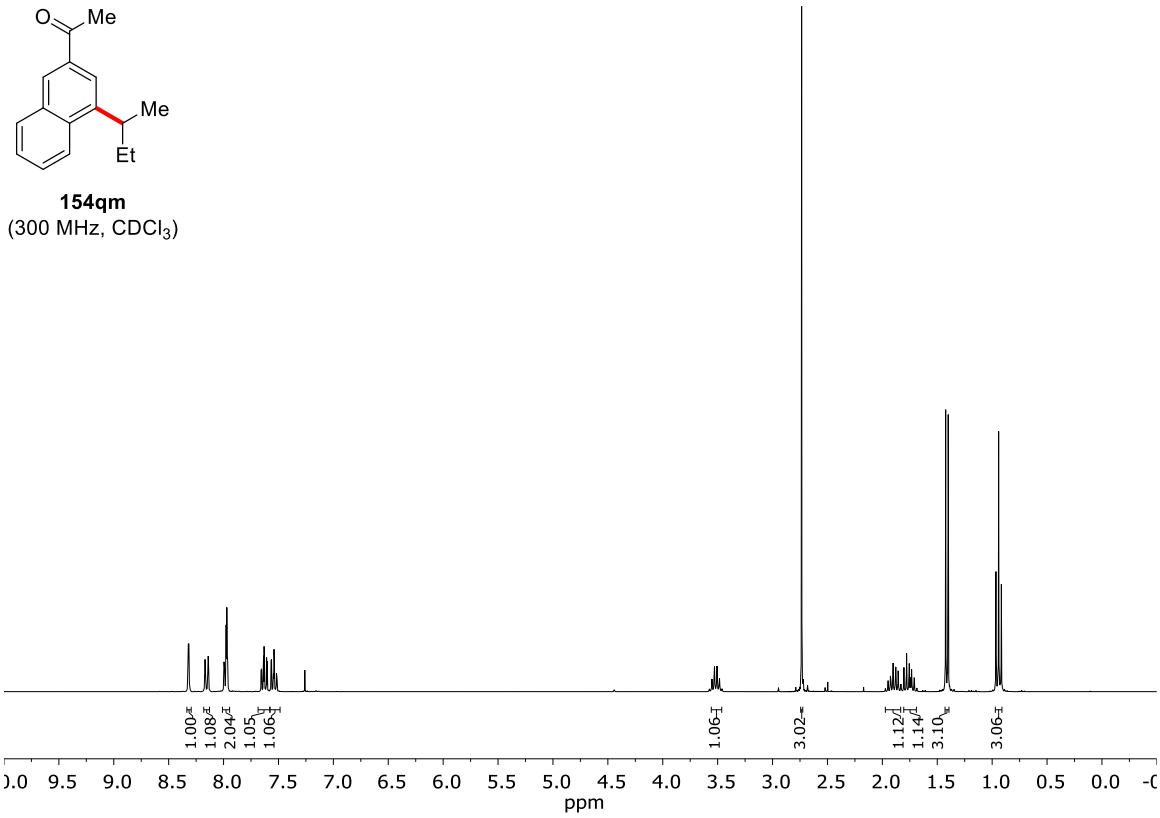


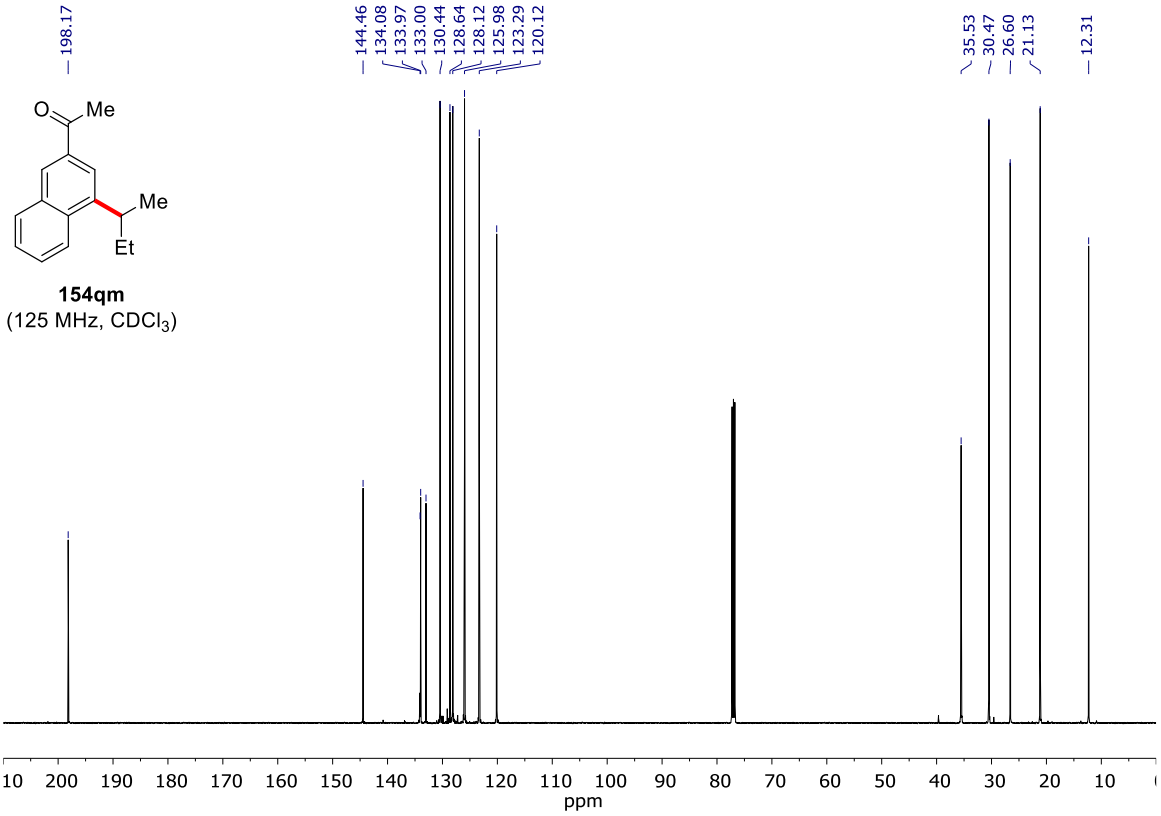
154ql
(300 MHz, $CDCl_3$)



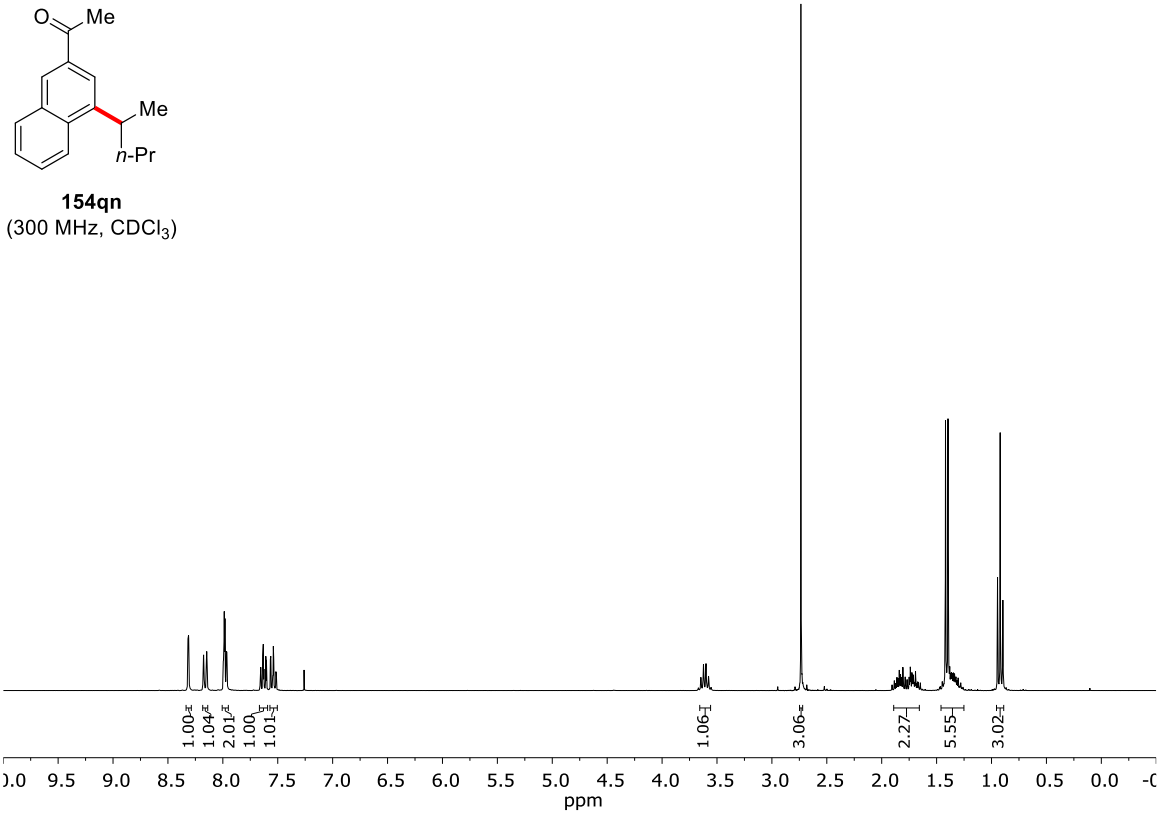
154ql
(125 MHz, $CDCl_3$)


HA
HD
HB HC
6
4
2
3
HE
5
Hc
1
O
Me
HA
HB
HC
Me
HE
Me
HD
154ql
1H-1H NOESY
(300 MHz, CDCl3)
8.40 8.35 8.30 8.25 8.20 8.15 8.10 8.05 8.00 7.95 7.90 7.85 7.80 7.75 7.70 7.65 7.60 7.55 7.50 7.45
ppm
ppm

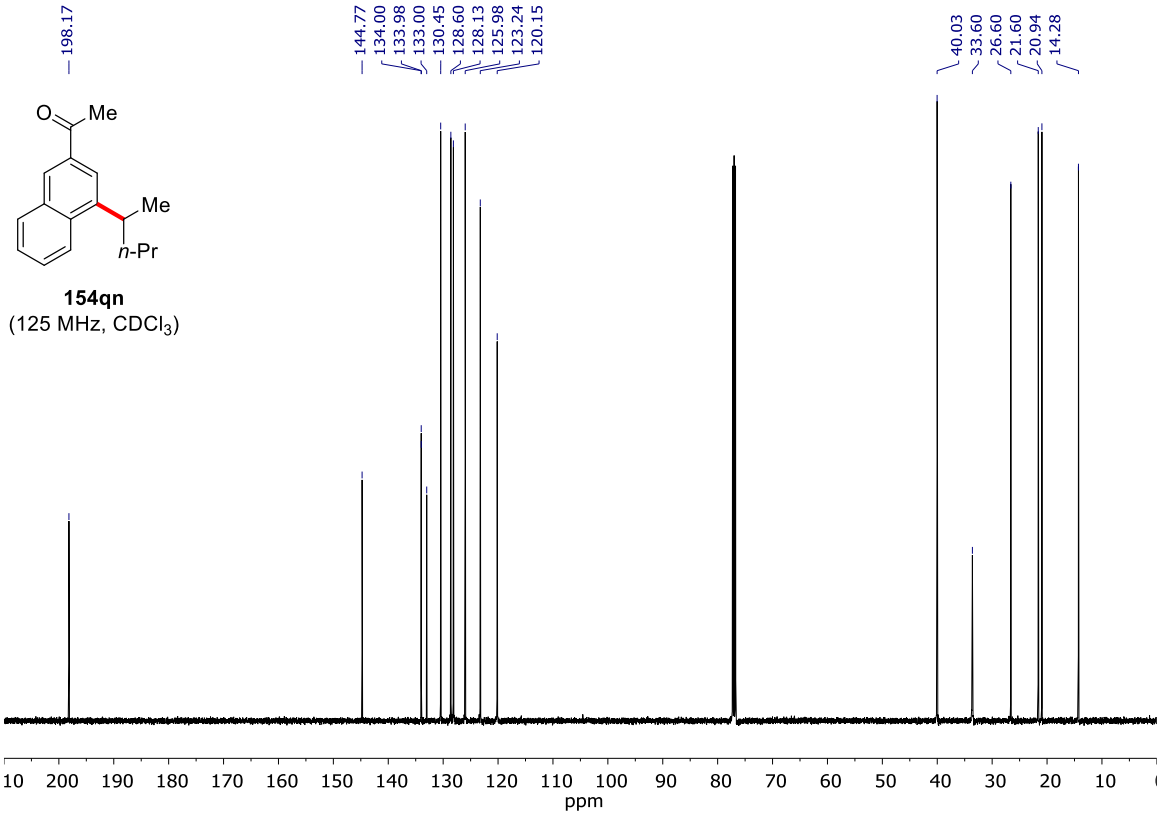

O
Me
Me
Et
154qm
(300 MHz, CDCl3)
1.00
1.08
2.04
1.05
1.06
1.06
3.02
1.12
1.14
3.10
3.06
ppm



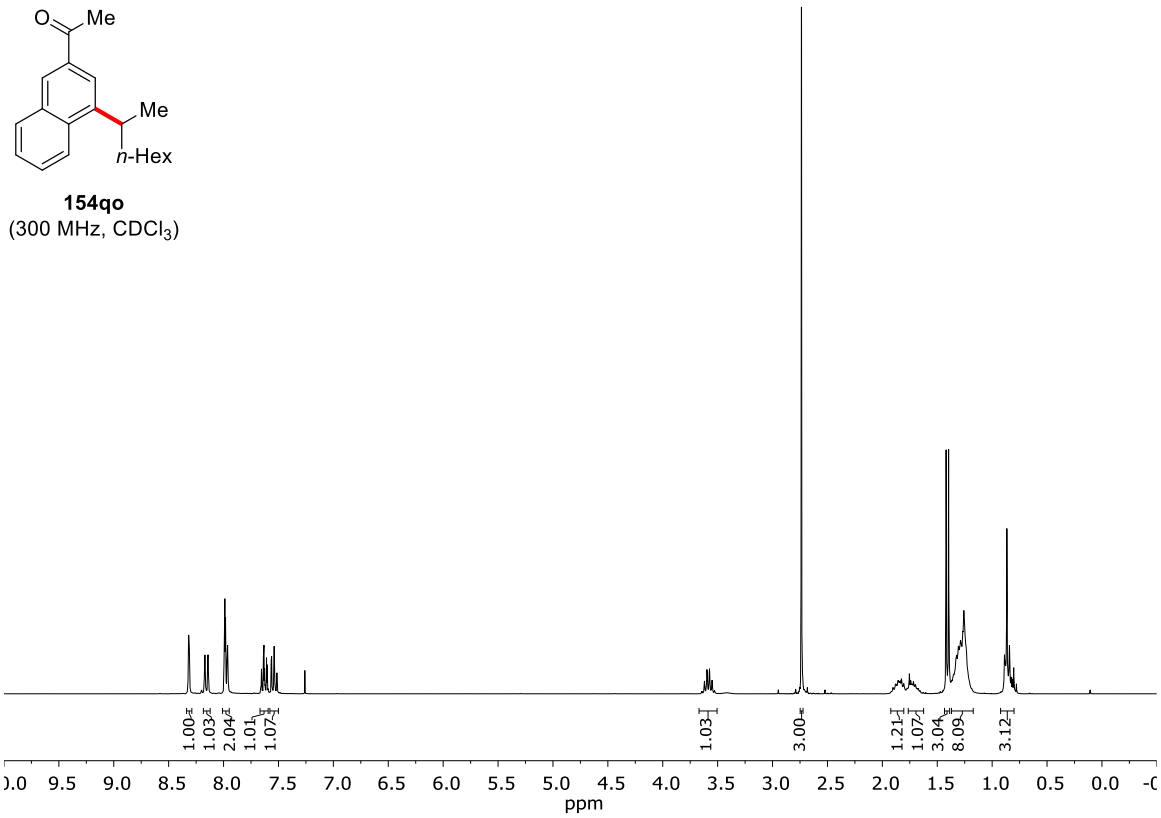
154qm
(125 MHz, $CDCl_3$)



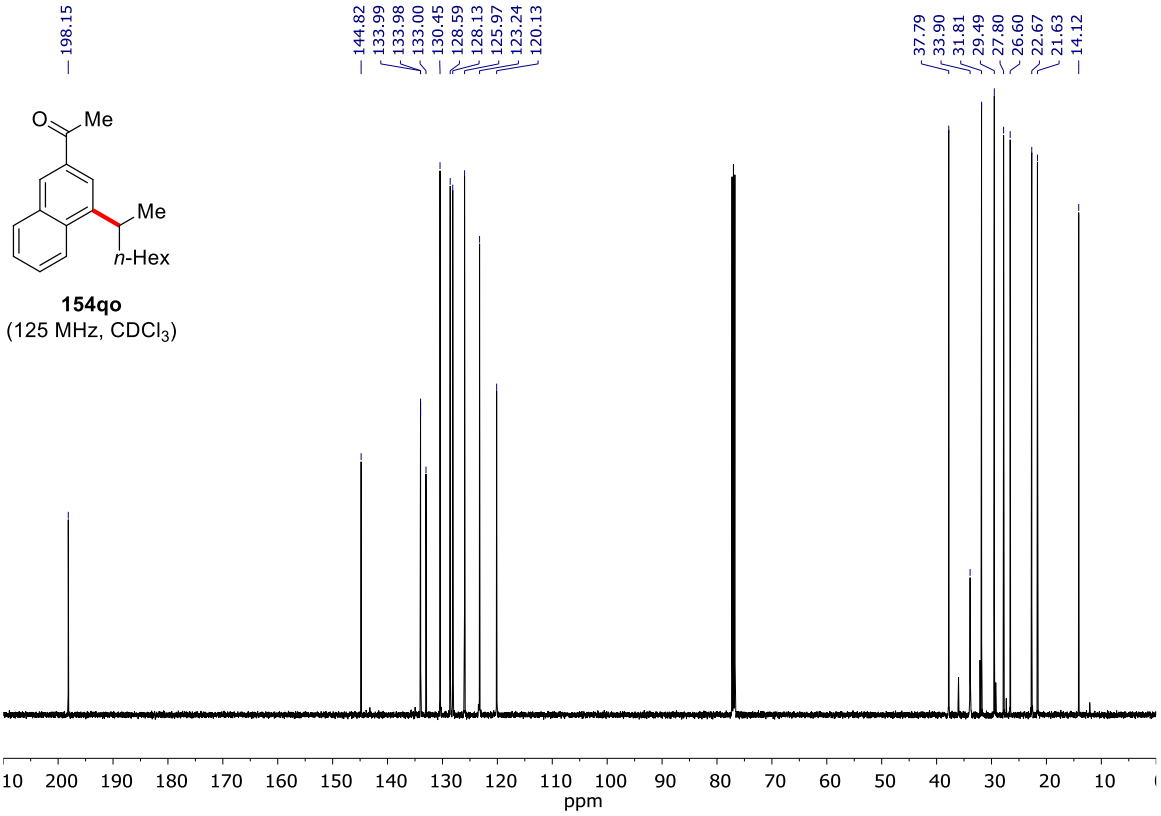
154qn
(300 MHz, $CDCl_3$)



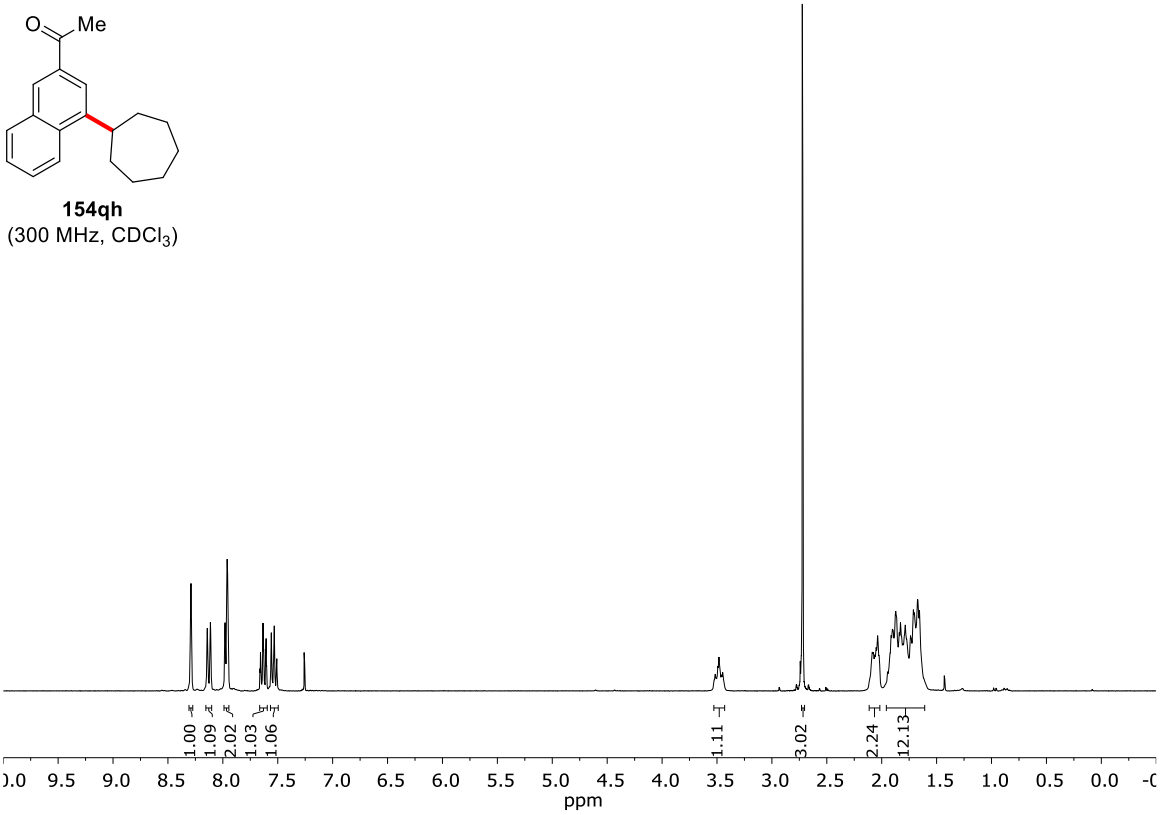
154qn
(125 MHz, $CDCl_3$)



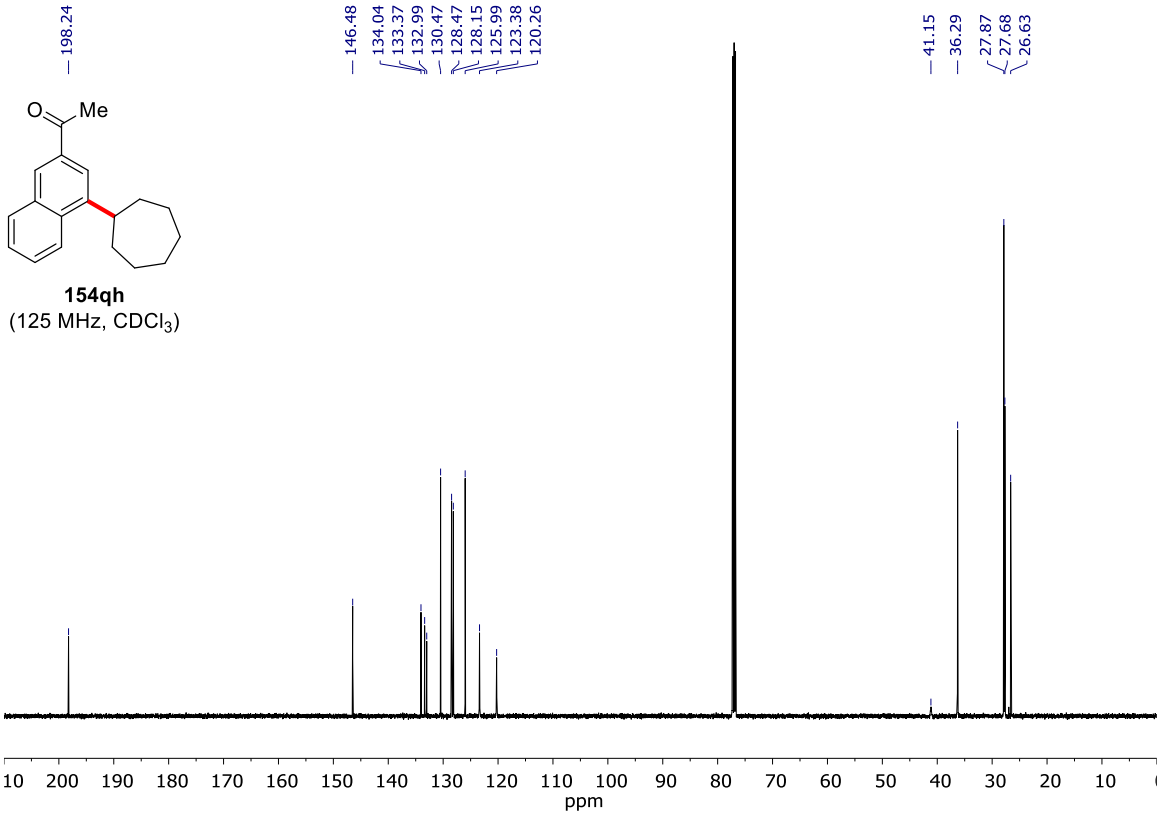
154qo
(300 MHz, $CDCl_3$)



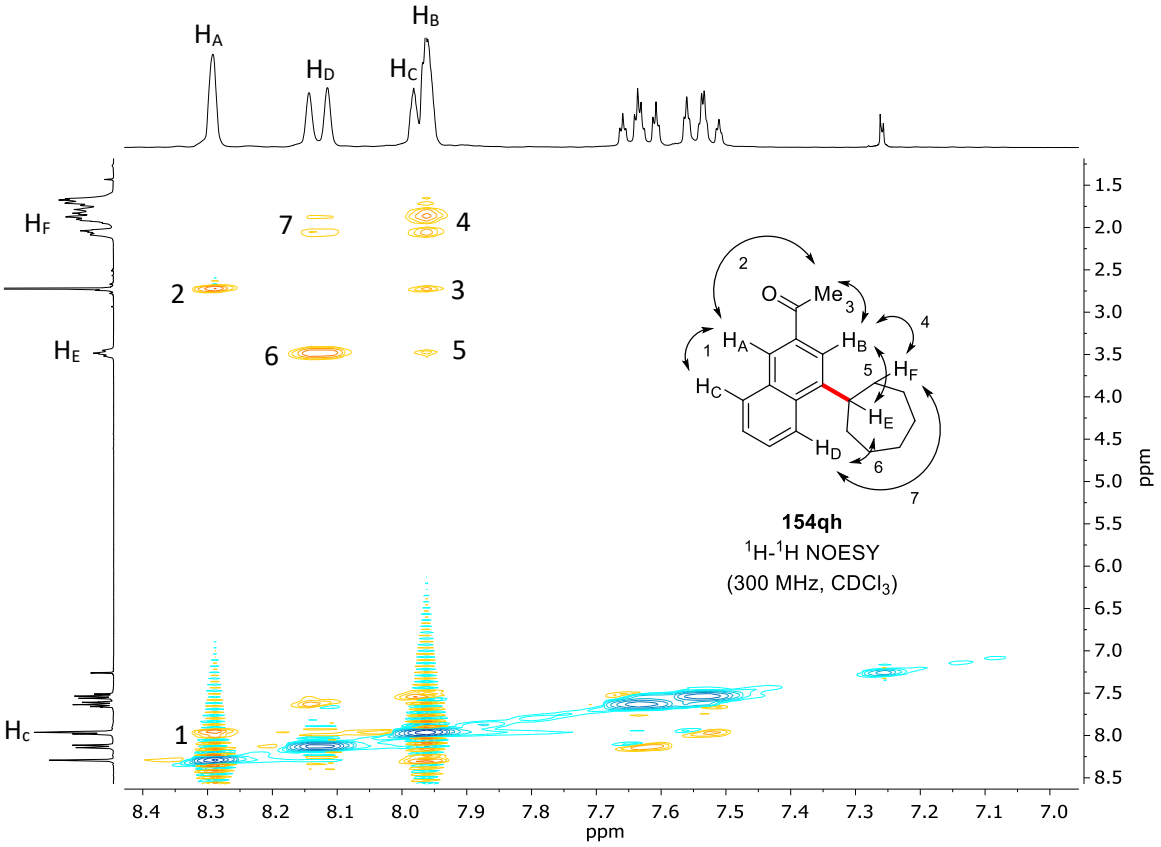
154qo
(125 MHz, $CDCl_3$)



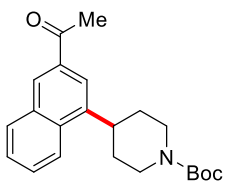
154qh
(300 MHz, $CDCl_3$)



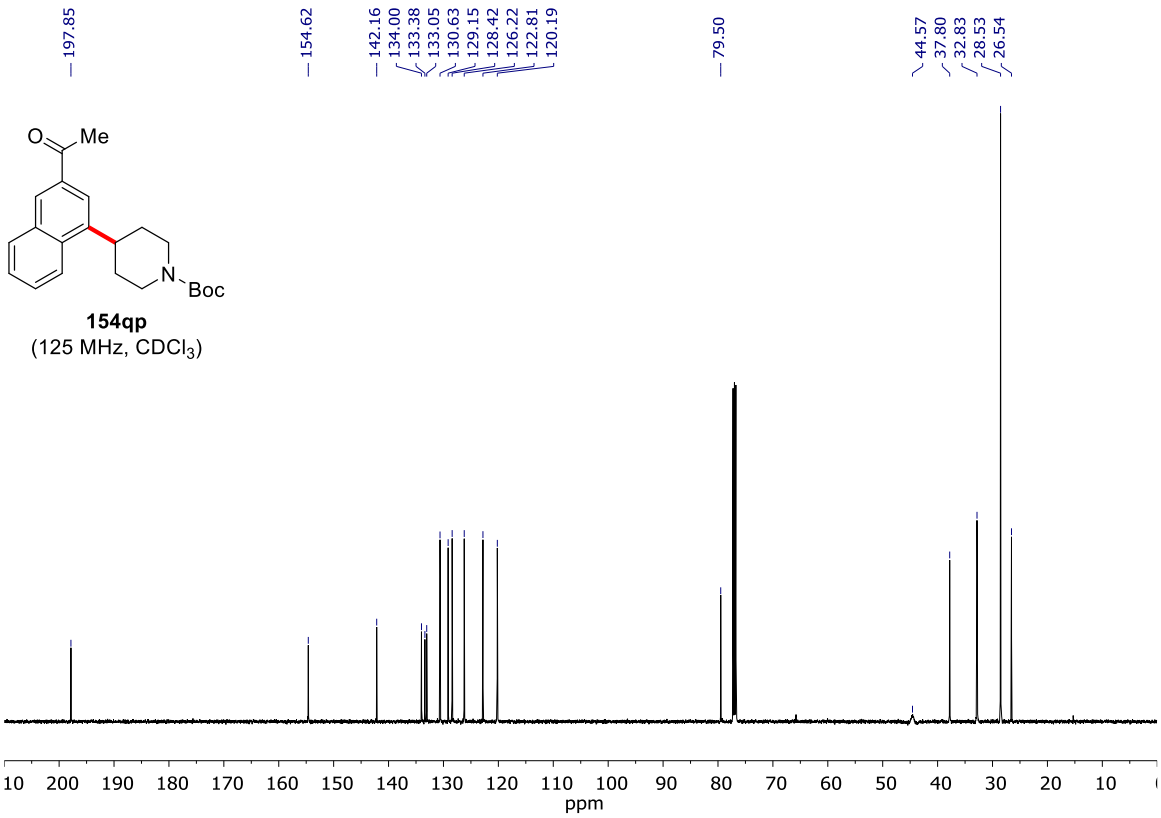
154qh
(125 MHz, $CDCl_3$)



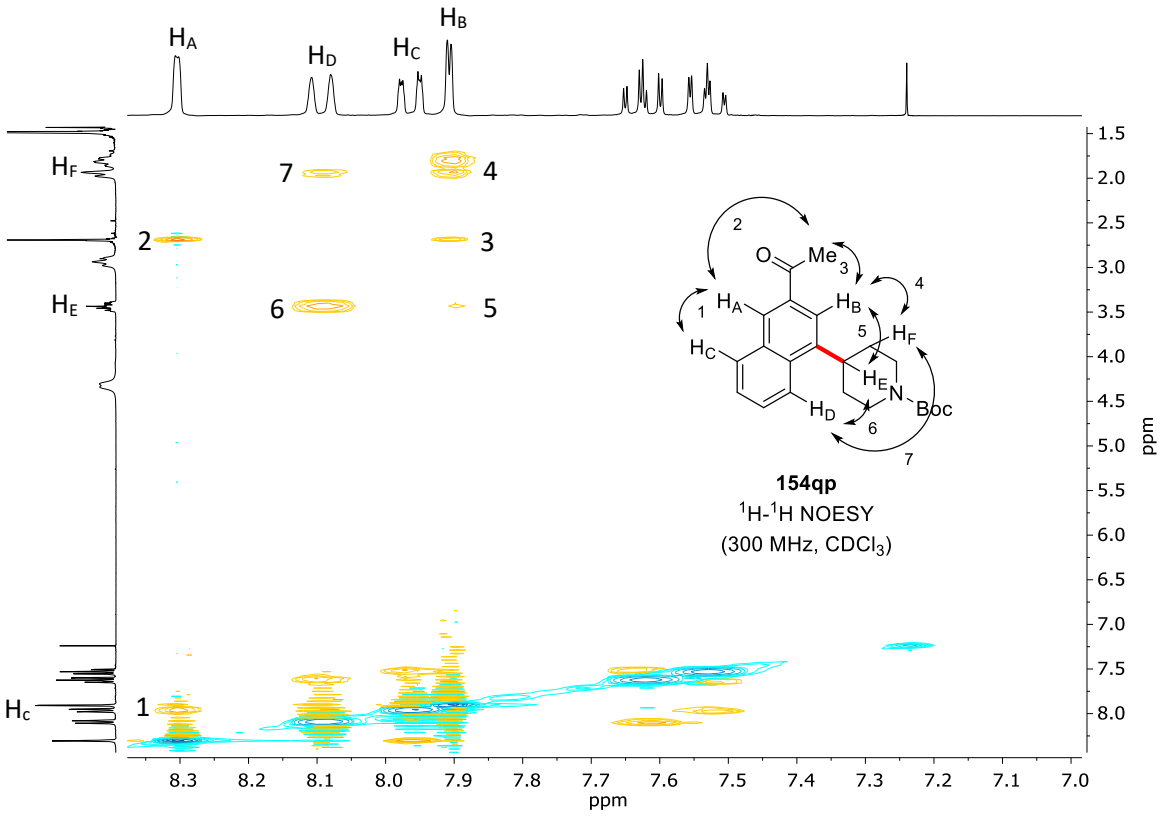
154qh
^{1}H-^{1}H NOESY
(300 MHz, $CDCl_3$)



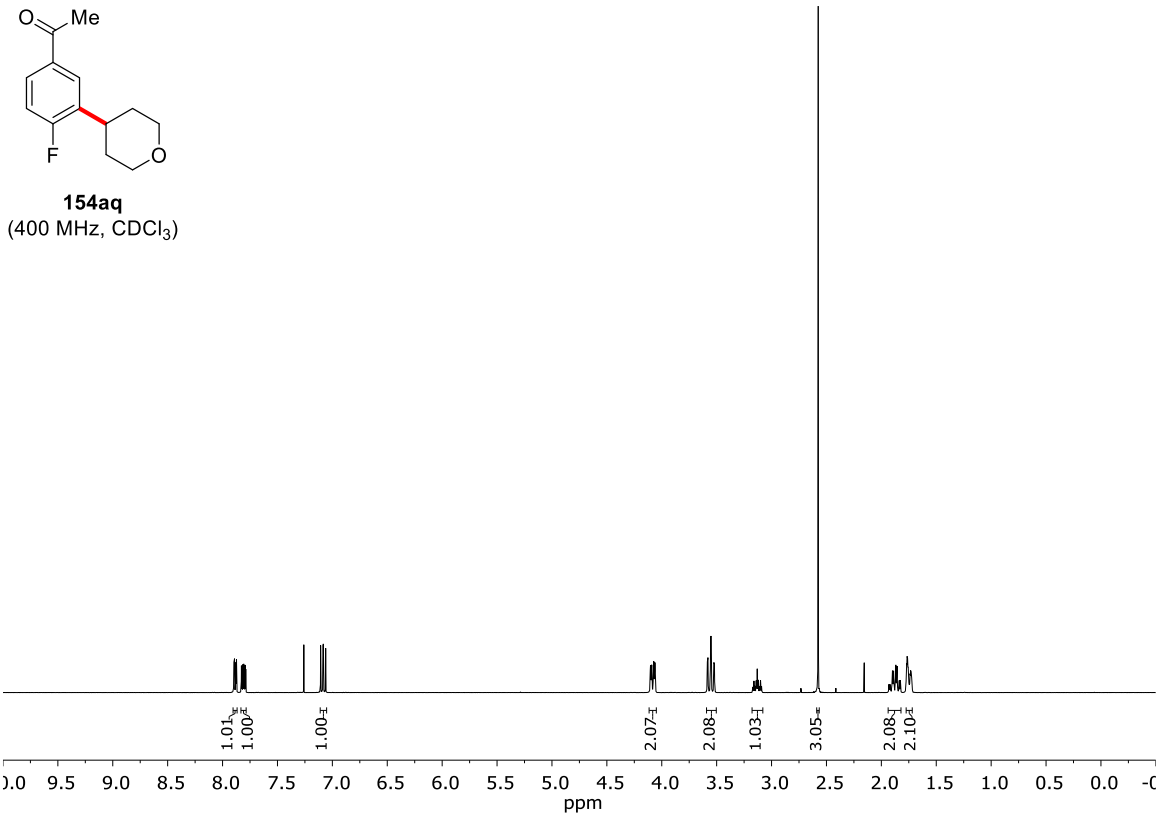
154qp
(300 MHz, $CDCl_3$)



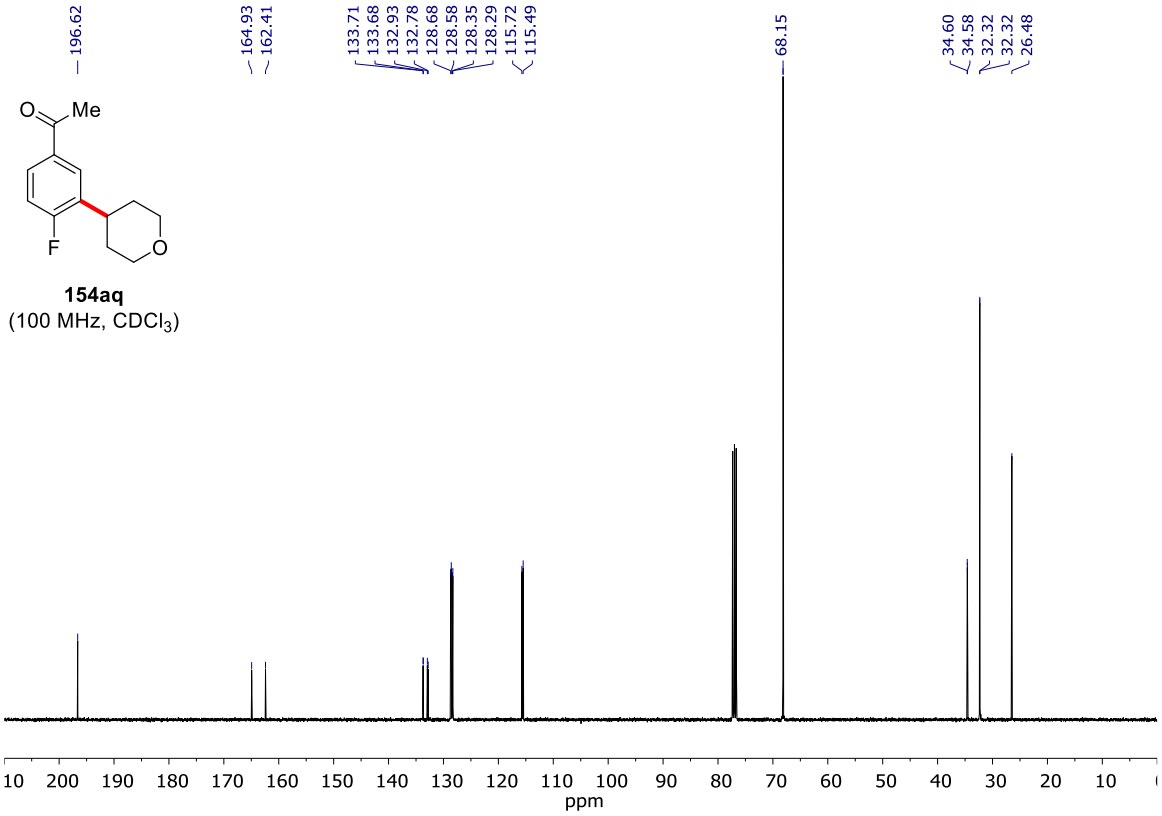
154qp
(125 MHz, $CDCl_3$)



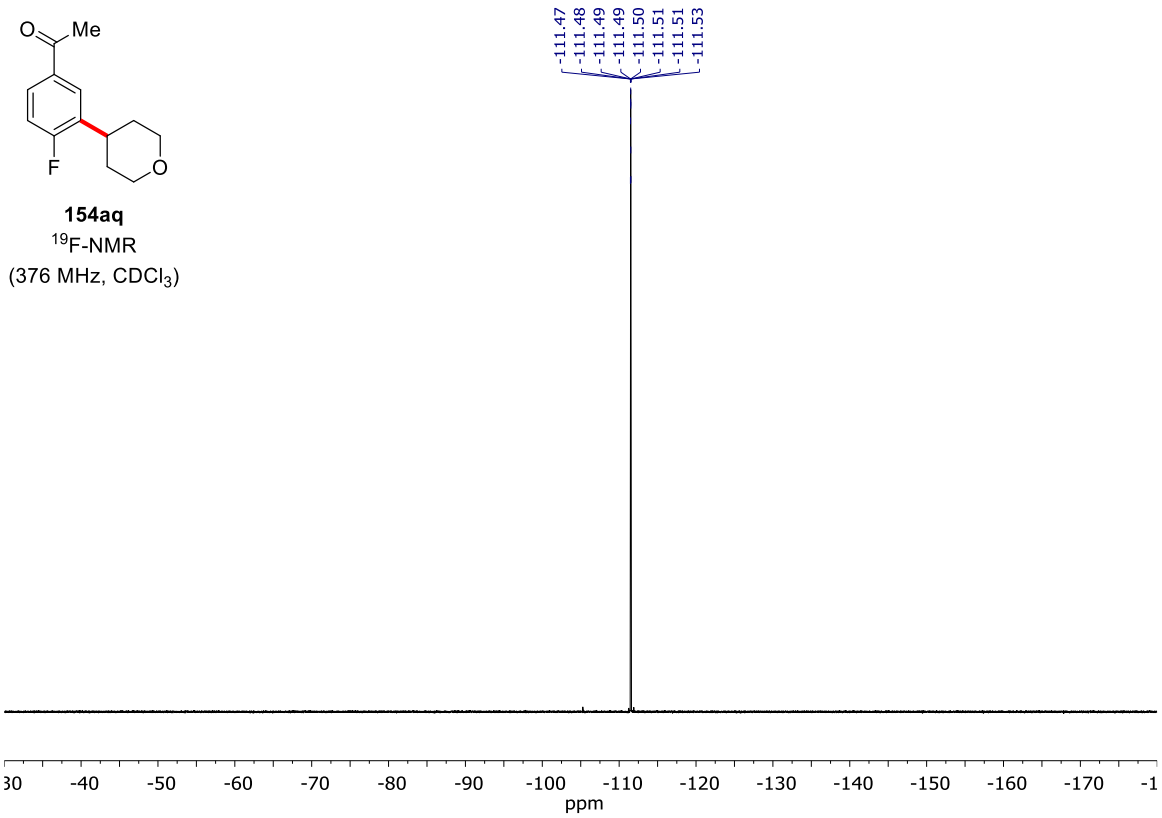
154qp
^{1}H-^{1}H NOESY
(300 MHz, $CDCl_3$)



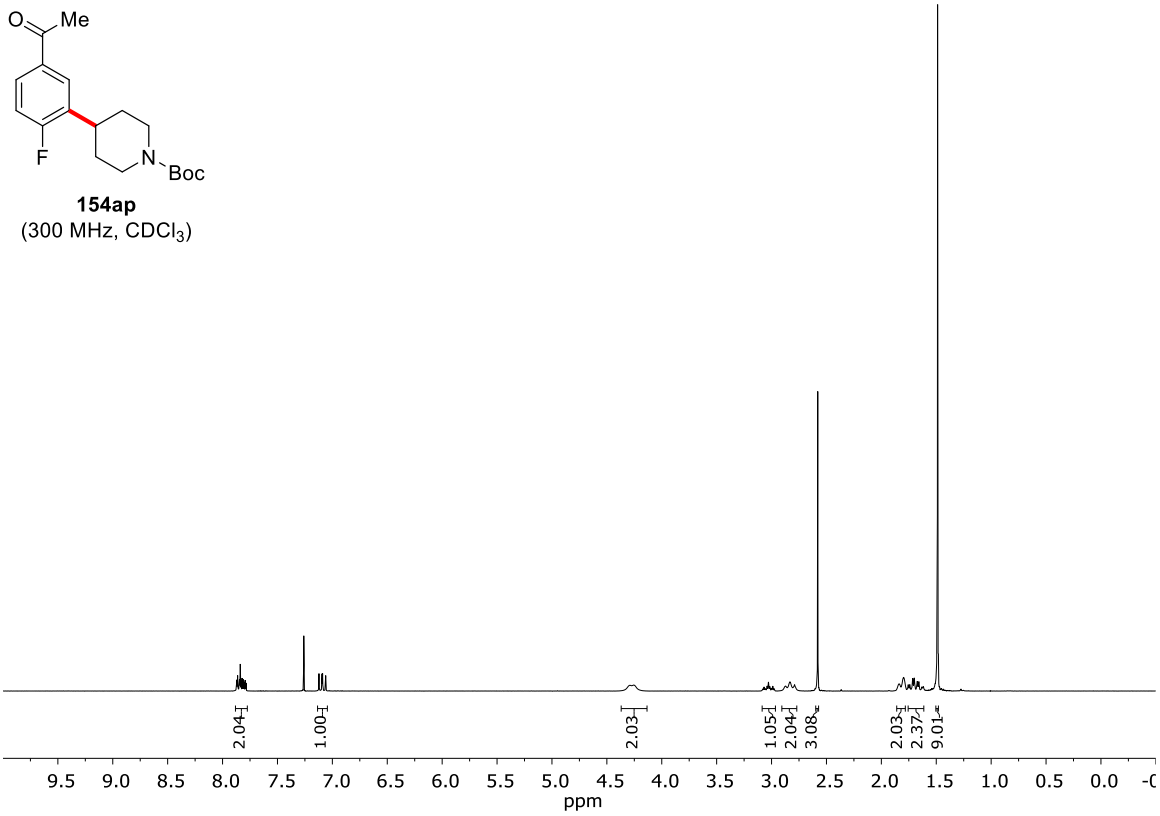
154aq
(400 MHz, $CDCl_3$)



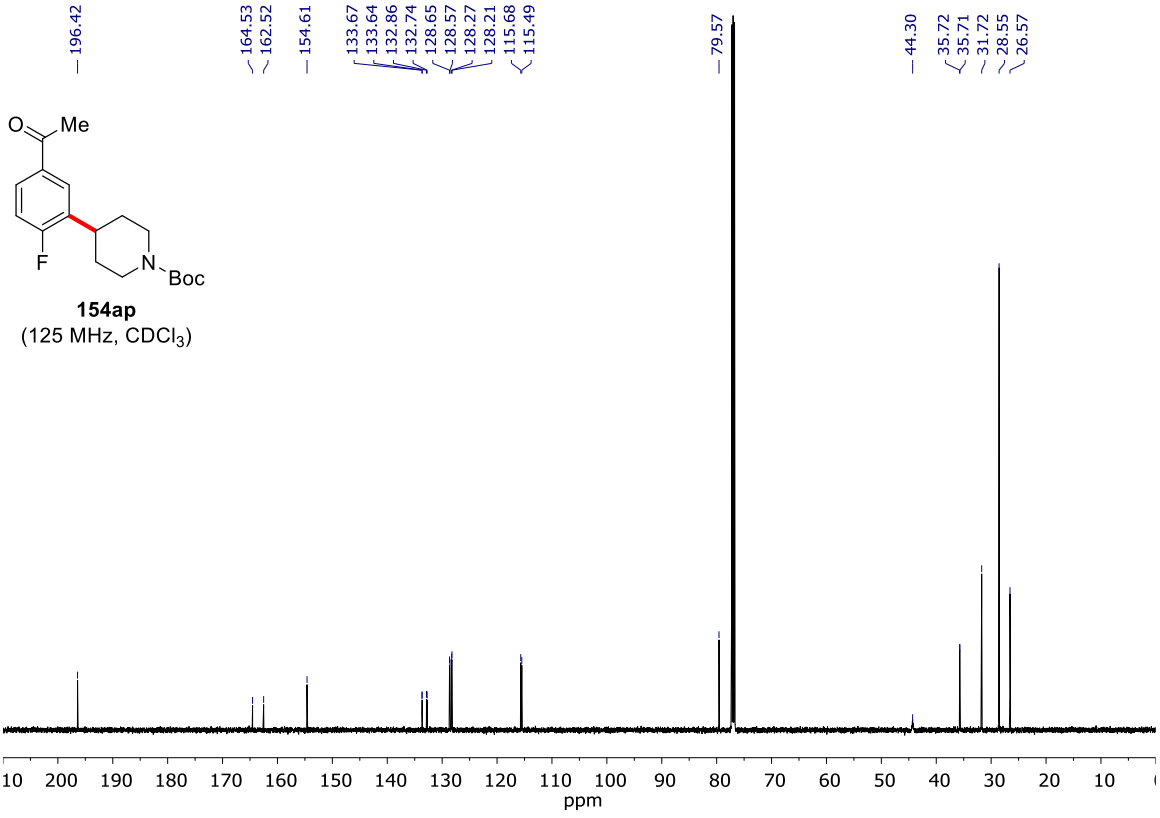
154aq
(100 MHz, $CDCl_3$)



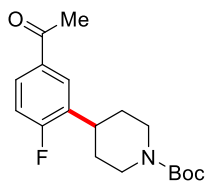
154aq
^{19}F-NMR
(376 MHz, $CDCl_3$)



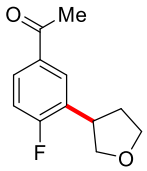
154ap
(300 MHz, $CDCl_3$)



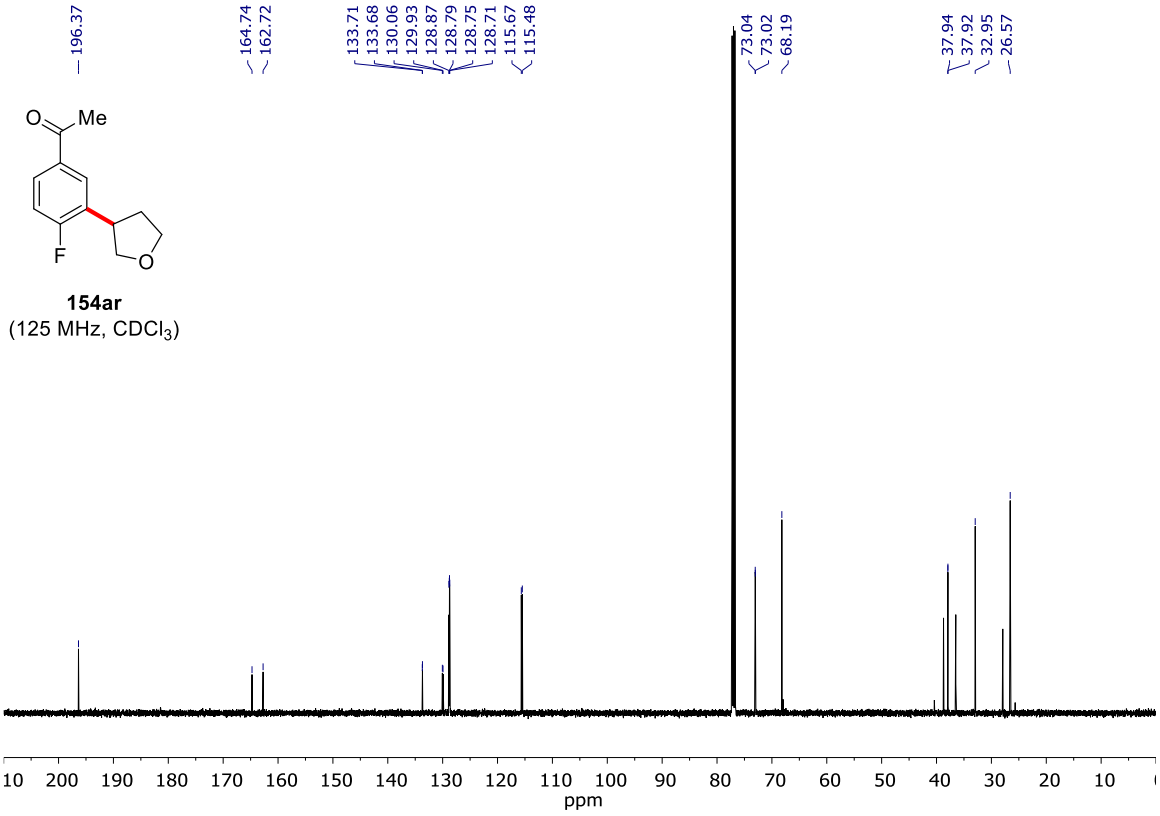
154ap
(125 MHz, $CDCl_3$)



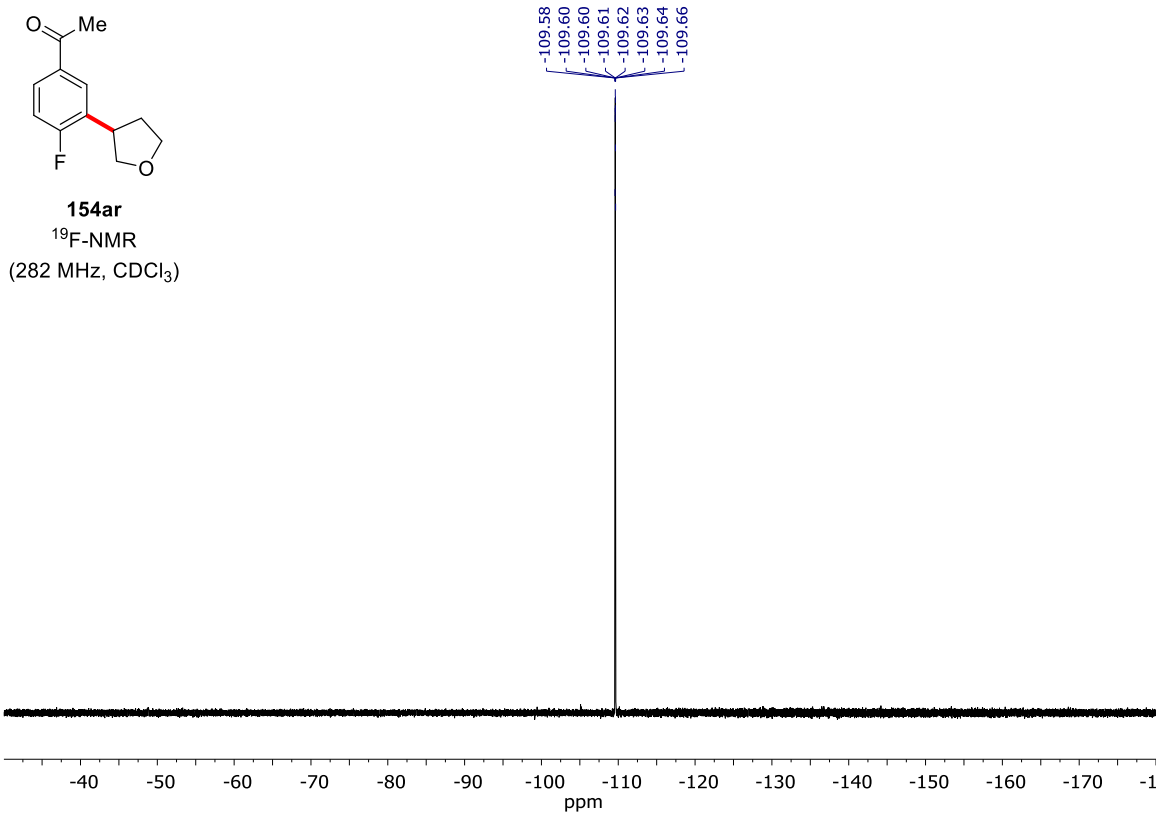
154ap
^{19}F-NMR
(282 MHz, $CDCl_3$)



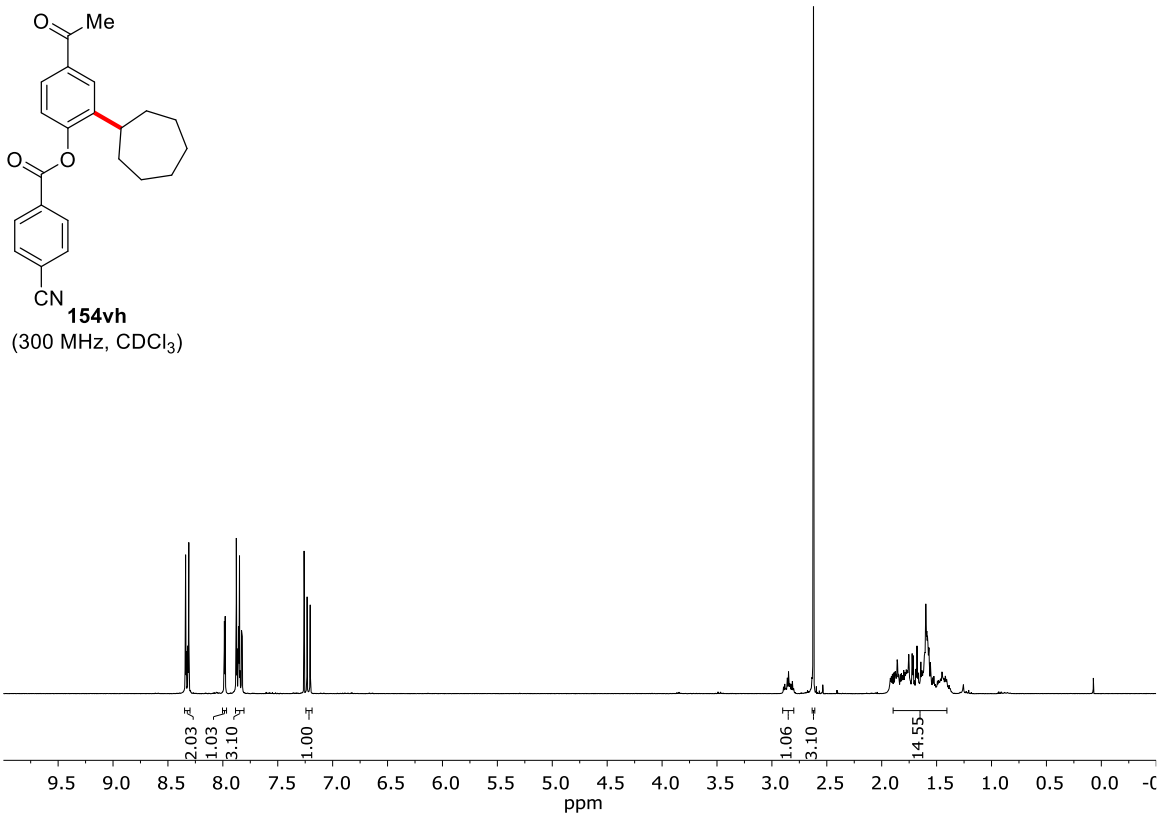
154ar
(300 MHz, $CDCl_3$)

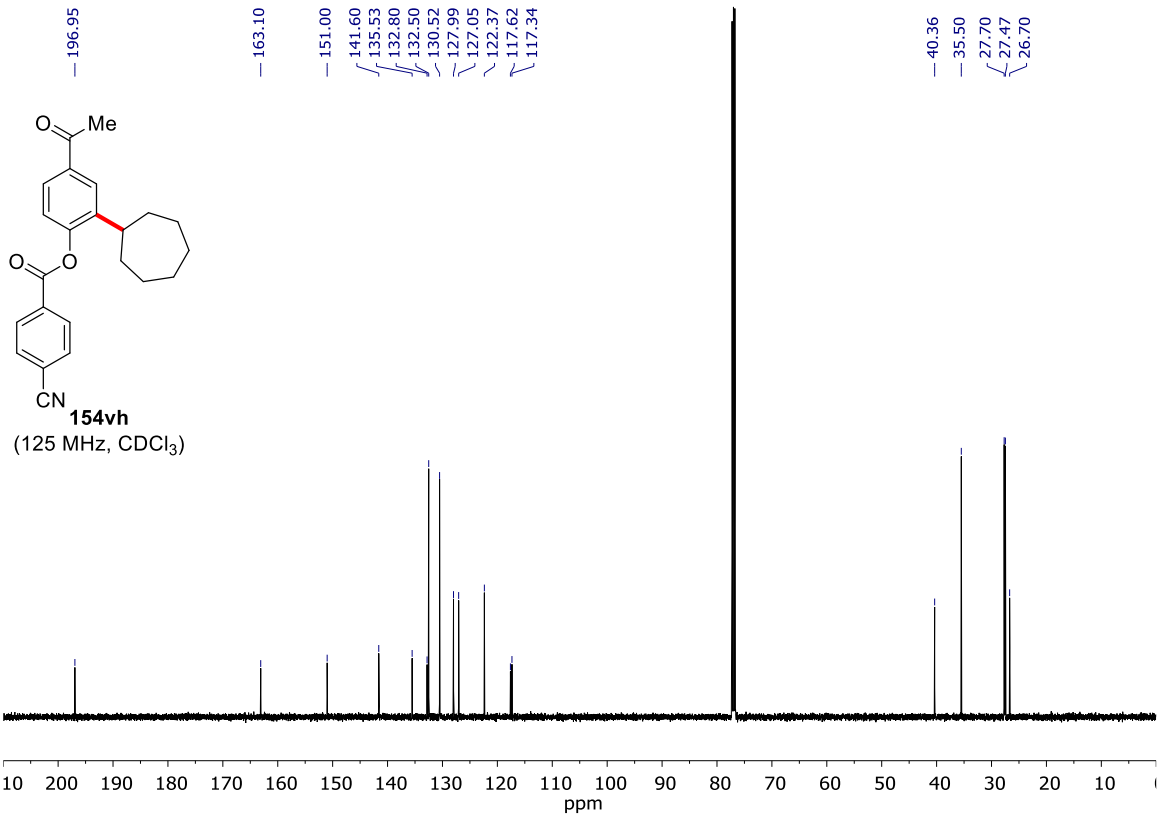


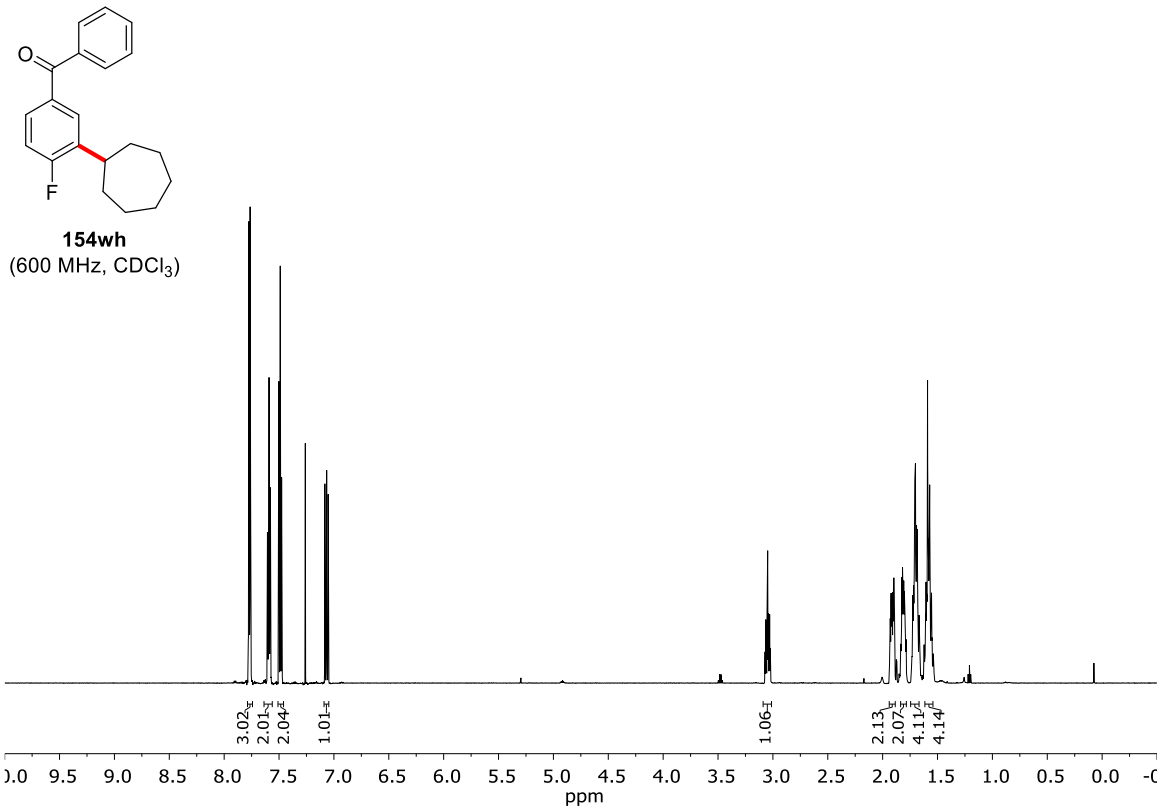
154ar
(125 MHz, $CDCl_3$)

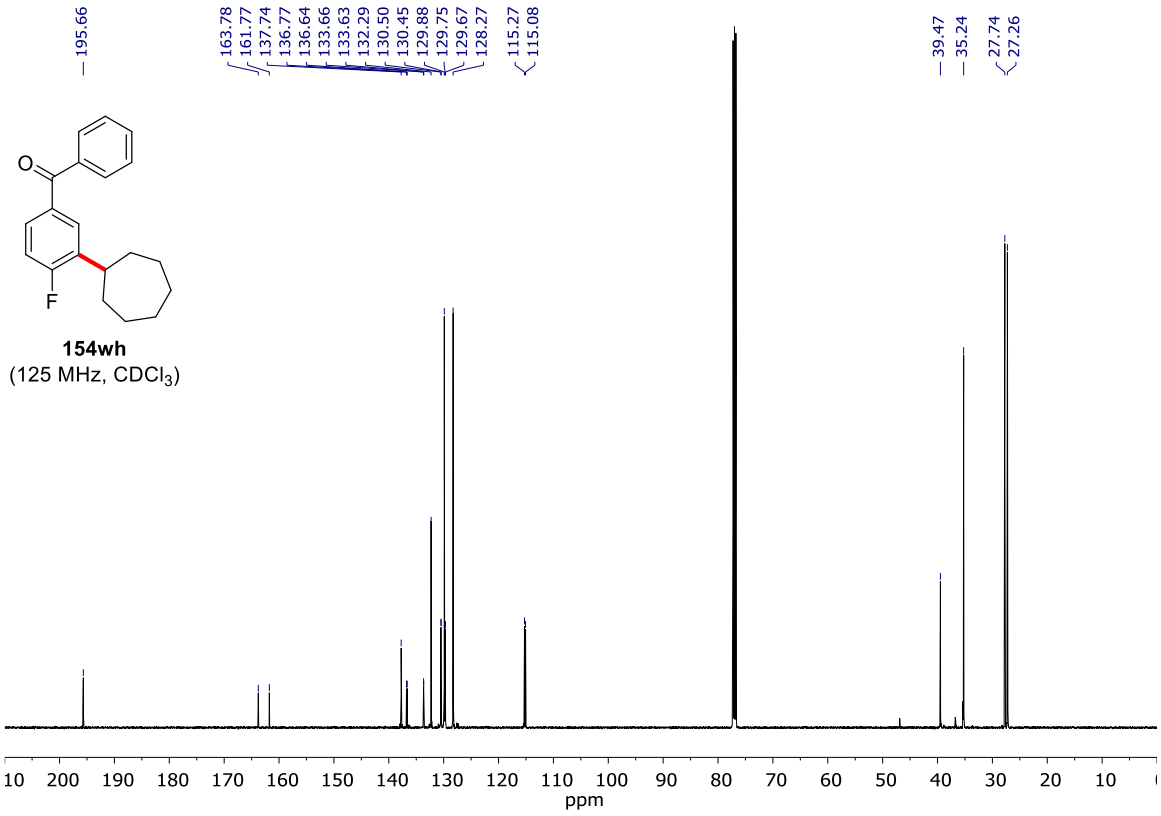


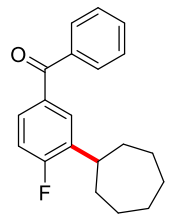
154ar
^{19}F-NMR
(282 MHz, $CDCl_3$)


Me
O
O
O
CN
154vh
(300 MHz, CDCl3)
2.03
1.03
3.10
1.00
1.06
3.10
14.55
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

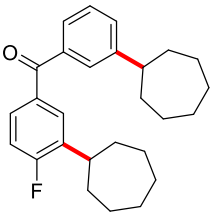

196.95
163.10
151.00
141.60
135.53
132.80
132.50
130.52
127.99
127.05
122.37
117.62
117.34
40.36
35.50
27.70
27.47
26.70
Me
O
O
O
CN
154vh
(125 MHz, CDCl3)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm


O
F
154wh
(600 MHz, CDCl3)
3.02
2.01
2.04
1.01
1.06
2.13
2.07
4.11
4.14
ppm

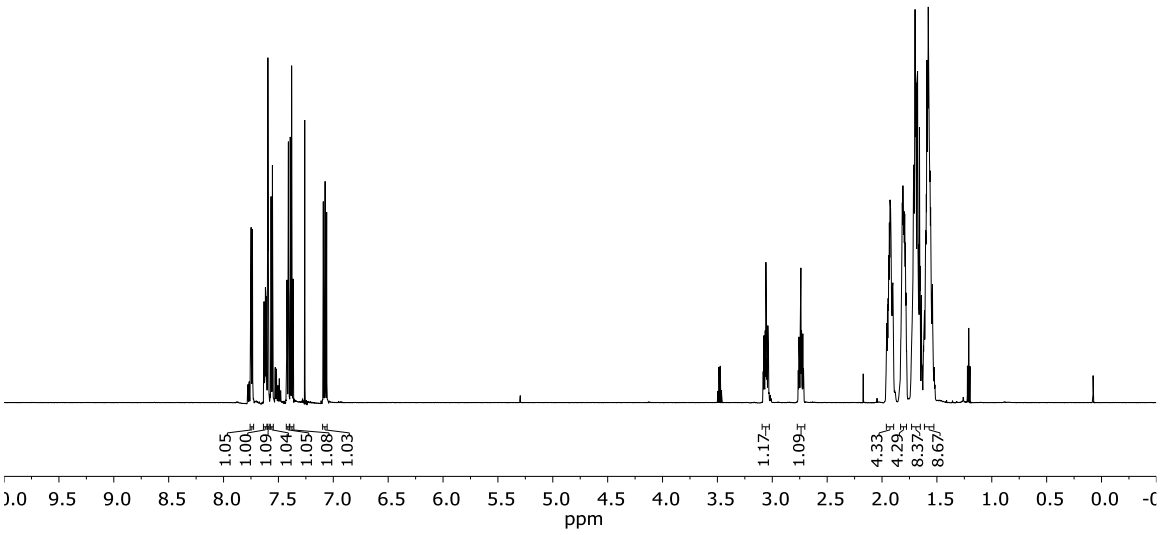

195.66
163.78
161.77
137.74
136.77
136.64
133.66
133.63
132.29
130.50
130.45
129.88
129.75
129.67
128.27
115.27
115.08
39.47
35.24
27.74
27.26
O
F
154wh
(125 MHz, CDCl3)
ppm

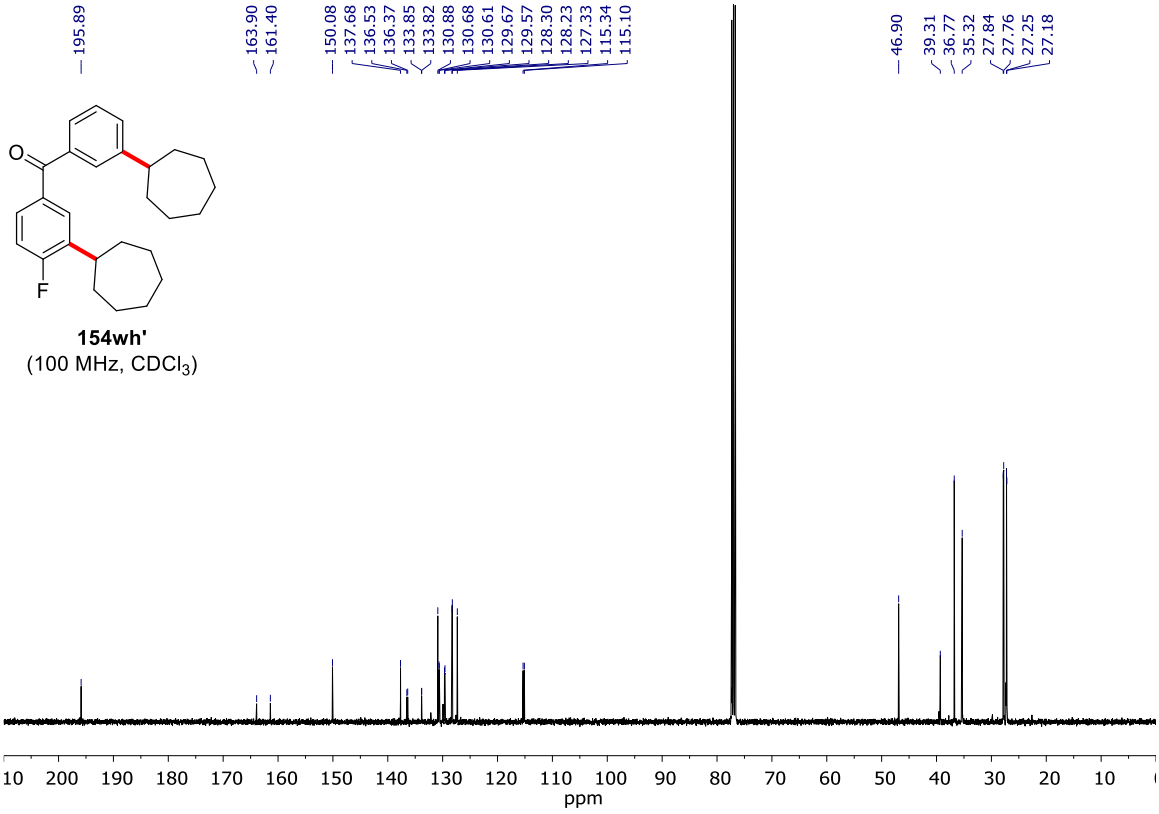


154wh
^{19}F-NMR
(470 MHz, $CDCl_3$)

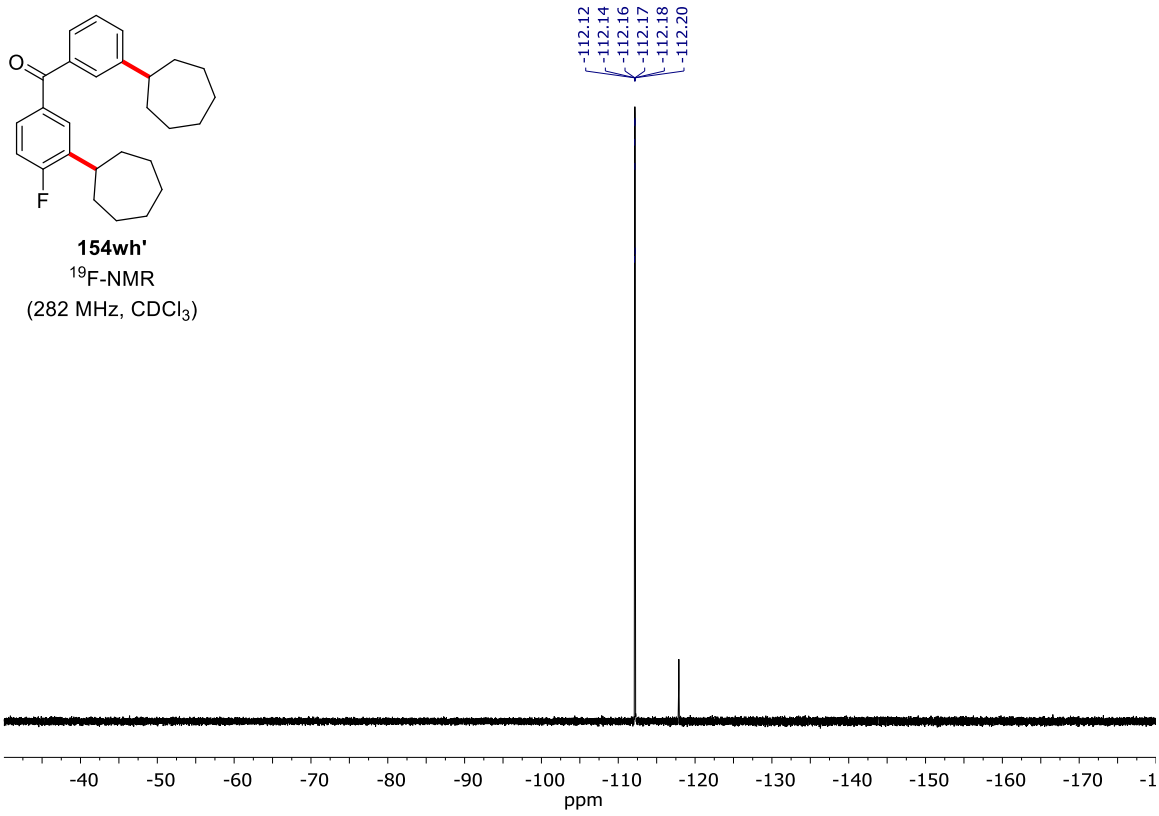


154wh'
(600 MHz, $CDCl_3$)

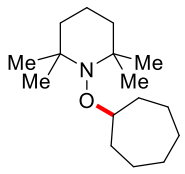




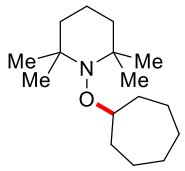
154wh'
(100 MHz, $CDCl_3$)



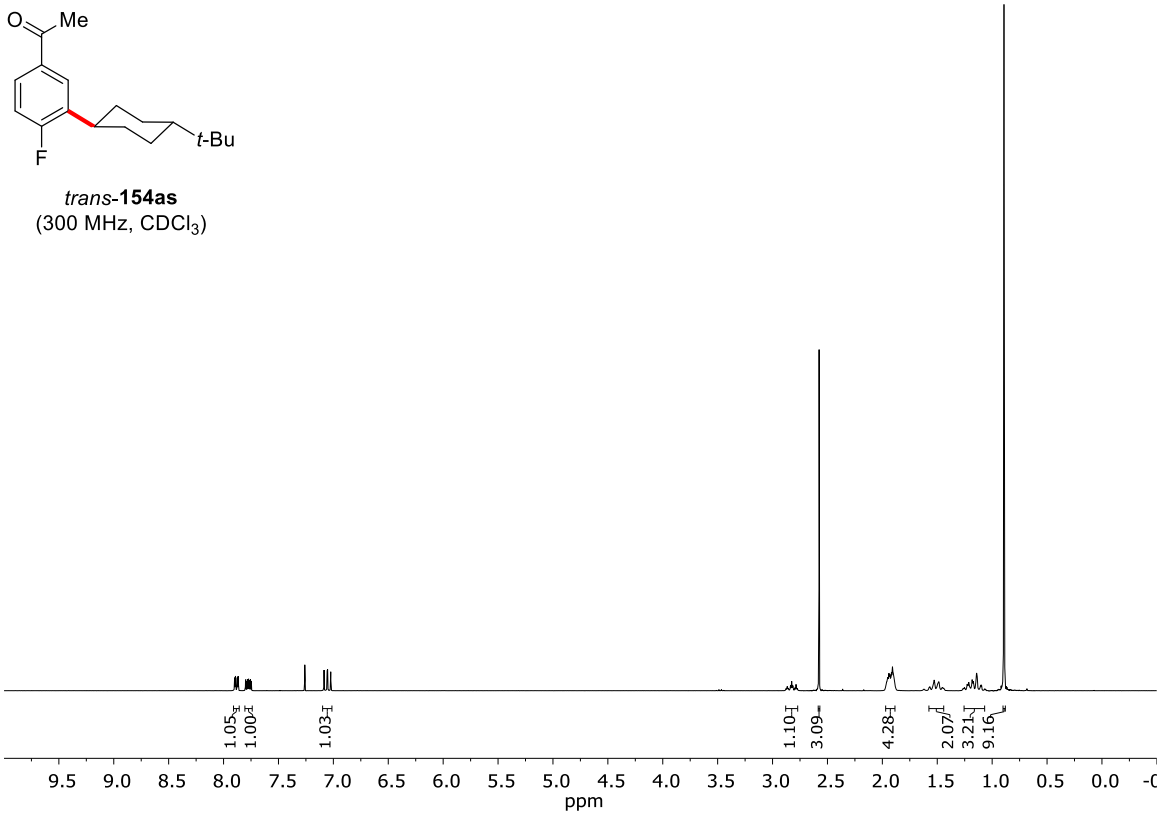
154wh'
^{19}F-NMR
(282 MHz, $CDCl_3$)



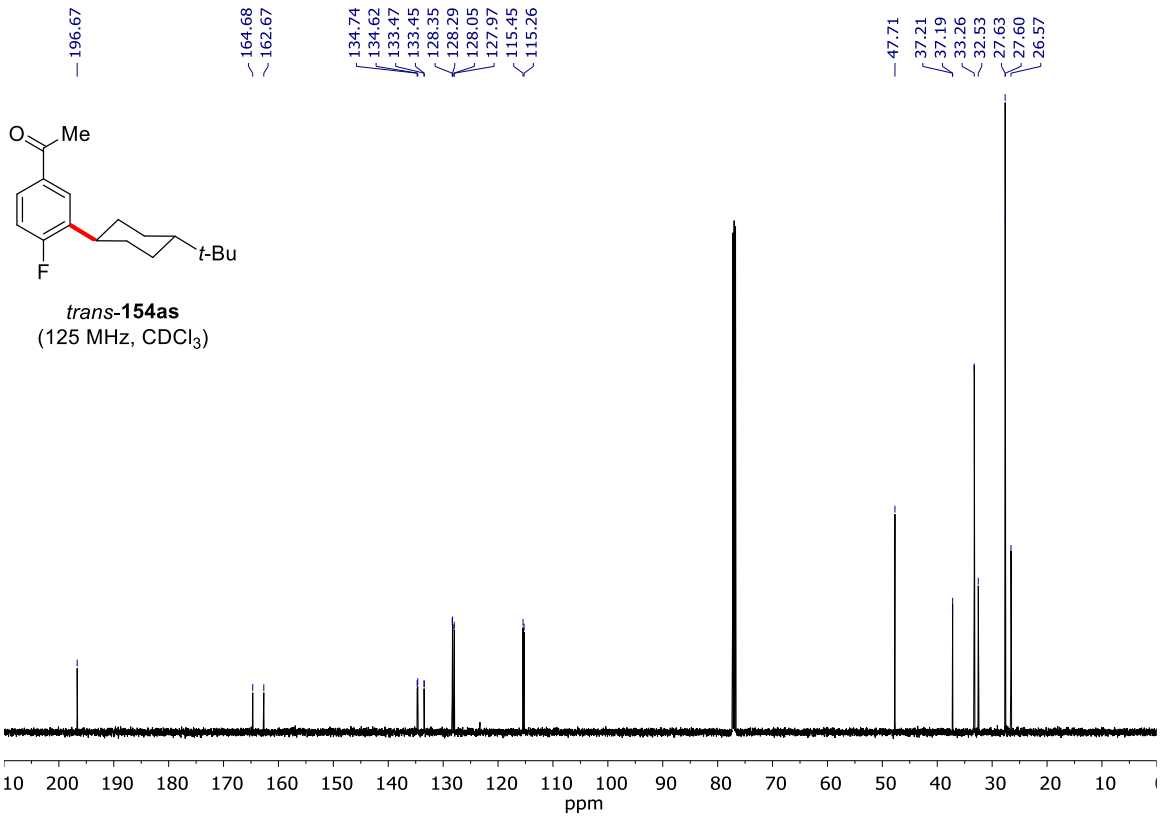
156
(300 MHz, $CDCl_3$)



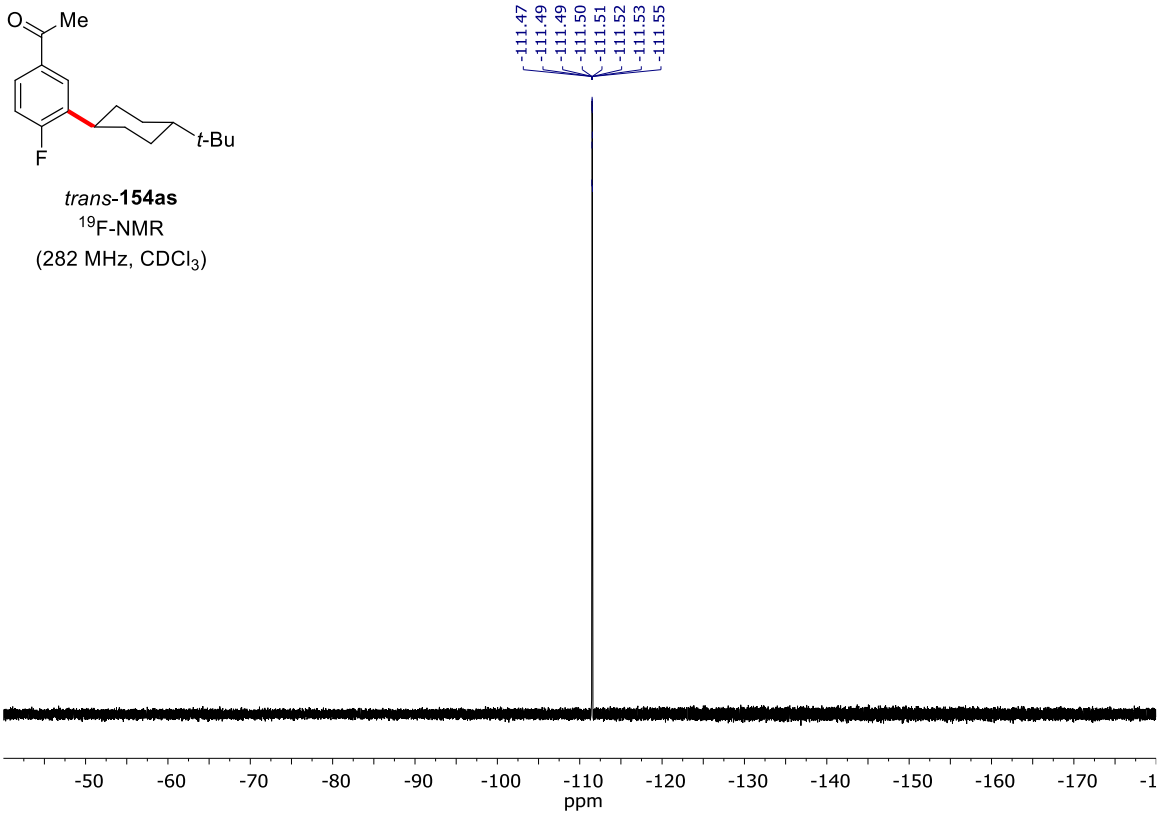
156
(75 MHz, $CDCl_3$)



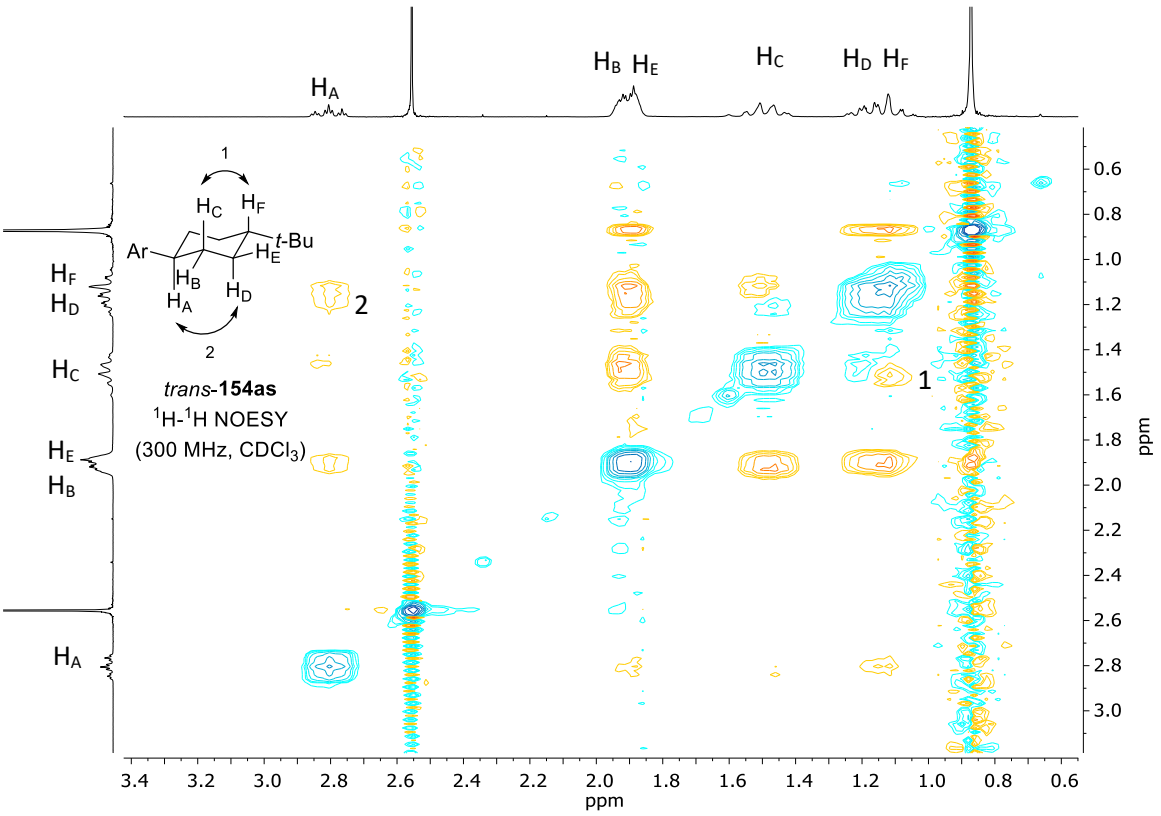
trans-**154as**
(300 MHz, $CDCl_3$)



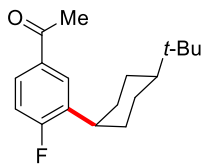
trans-**154as**
(125 MHz, $CDCl_3$)



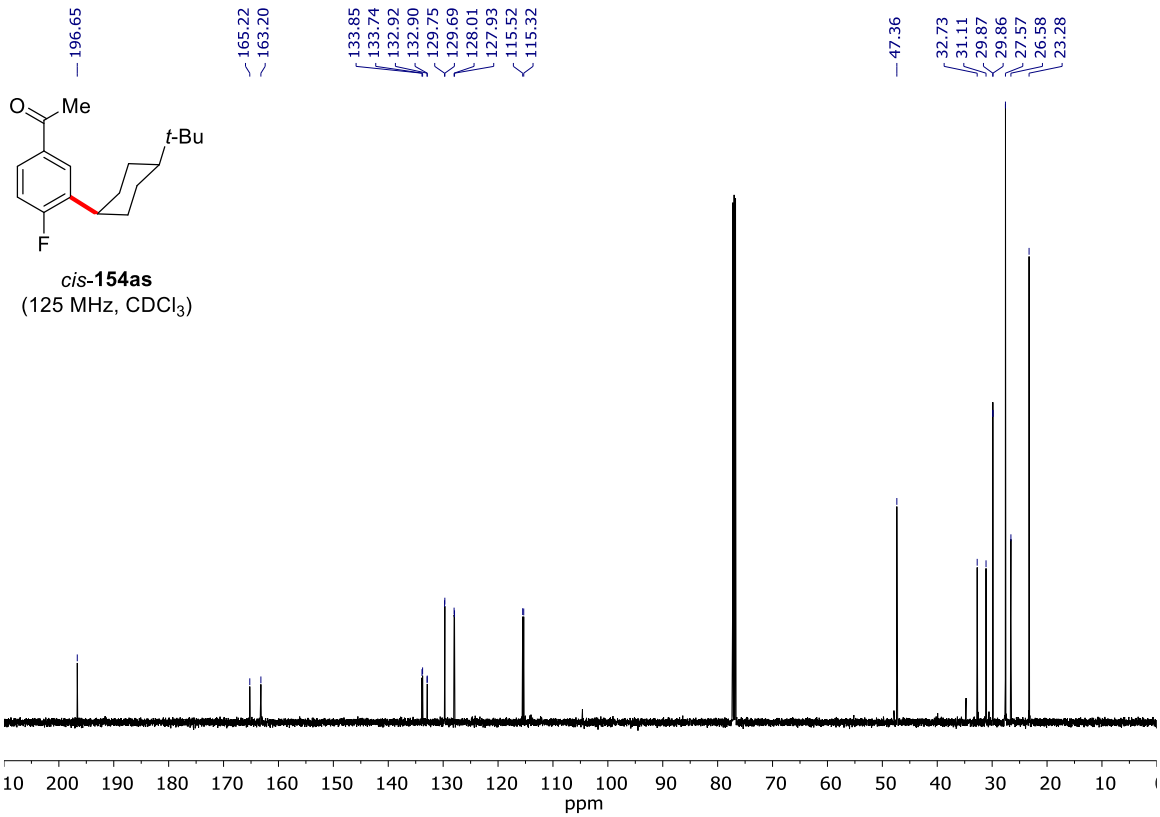
trans-**154as**
^{19}F-NMR
(282 MHz, $CDCl_3$)



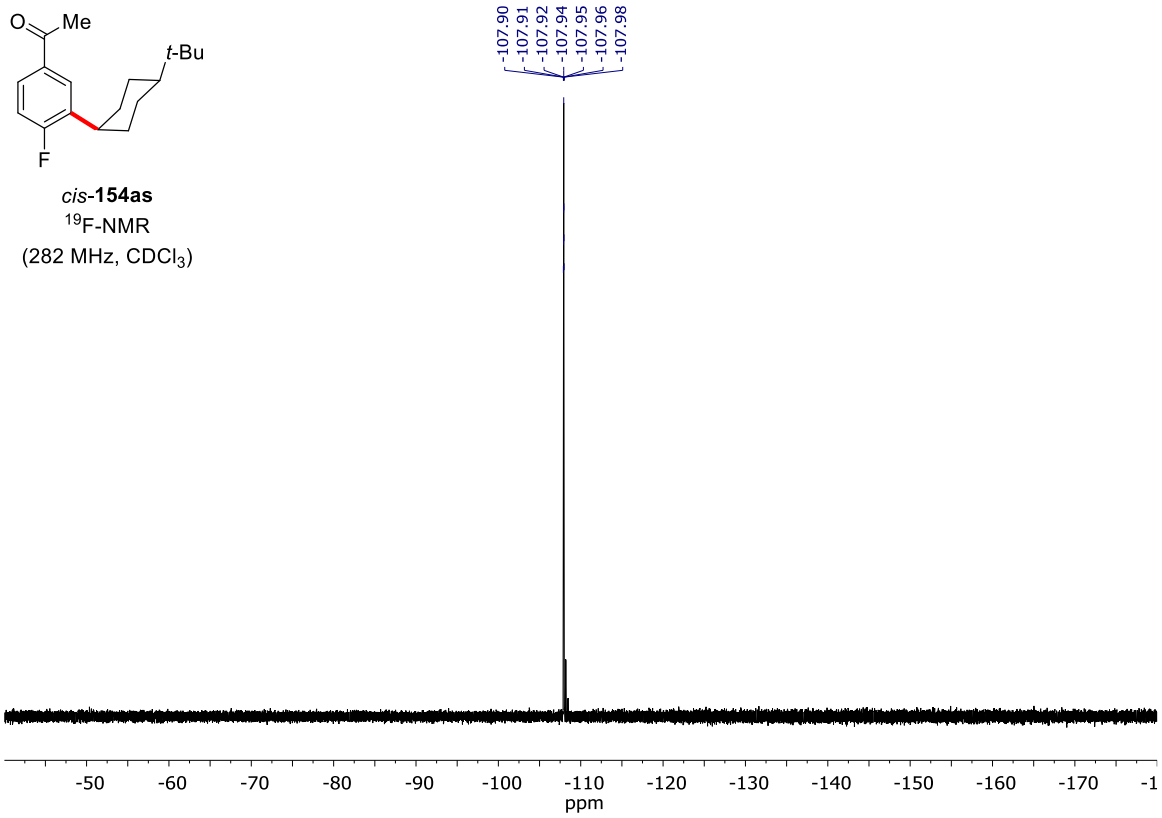
trans-**154as**
^{1}H-^{1}H NOESY
(300 MHz, $CDCl_3$)



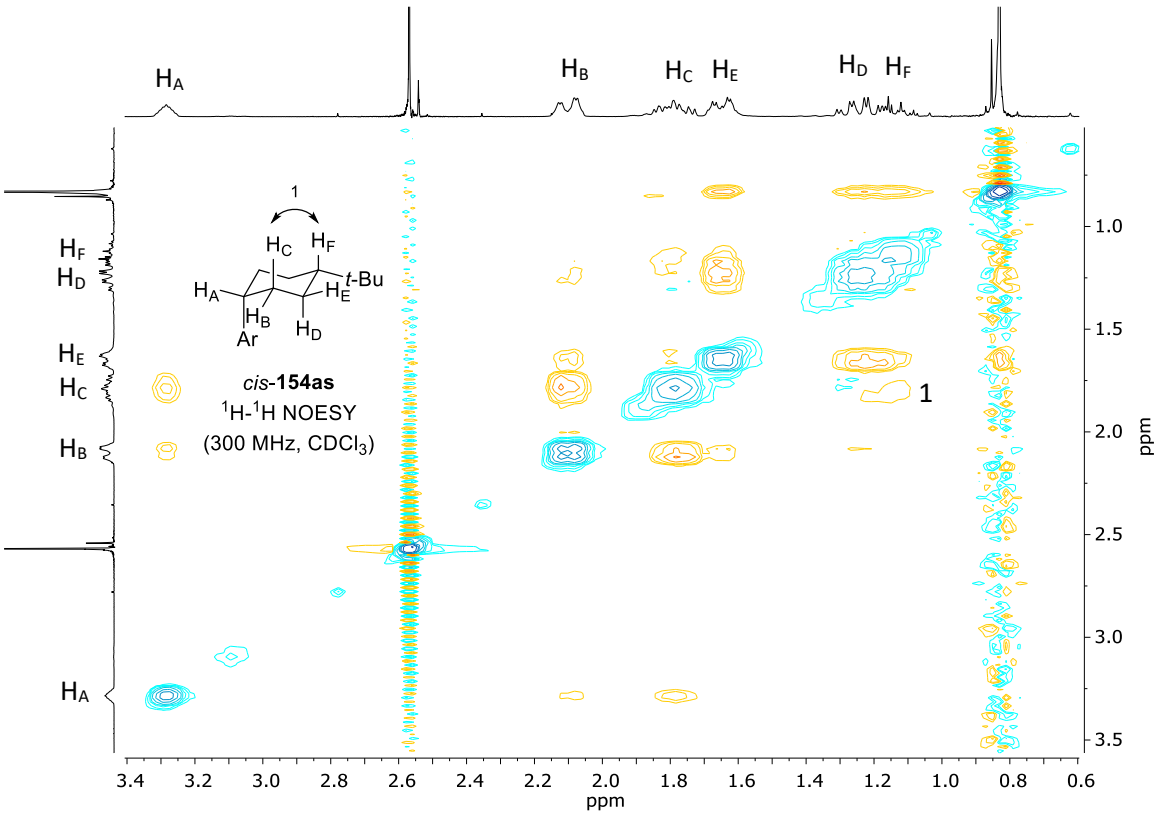
cis-**154as**
(300 MHz, $CDCl_3$)

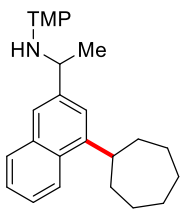


cis-**154as**
(125 MHz, $CDCl_3$)

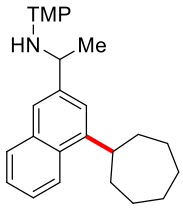


cis-**154as**
^{19}F-NMR
(282 MHz, $CDCl_3$)

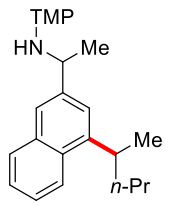




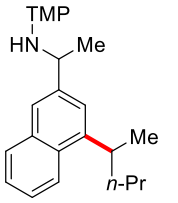
157a
(400 MHz, $CDCl_3$)



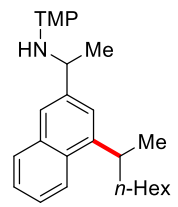
157a
(100 MHz, $CDCl_3$)



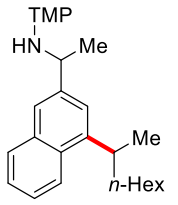
157b
(300 MHz, $CDCl_3$)



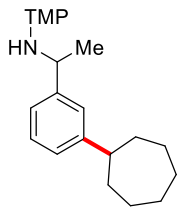
157b
(75 MHz, $CDCl_3$)



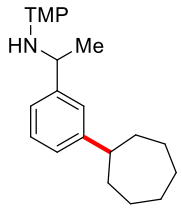
157c
(300 MHz, $CDCl_3$)



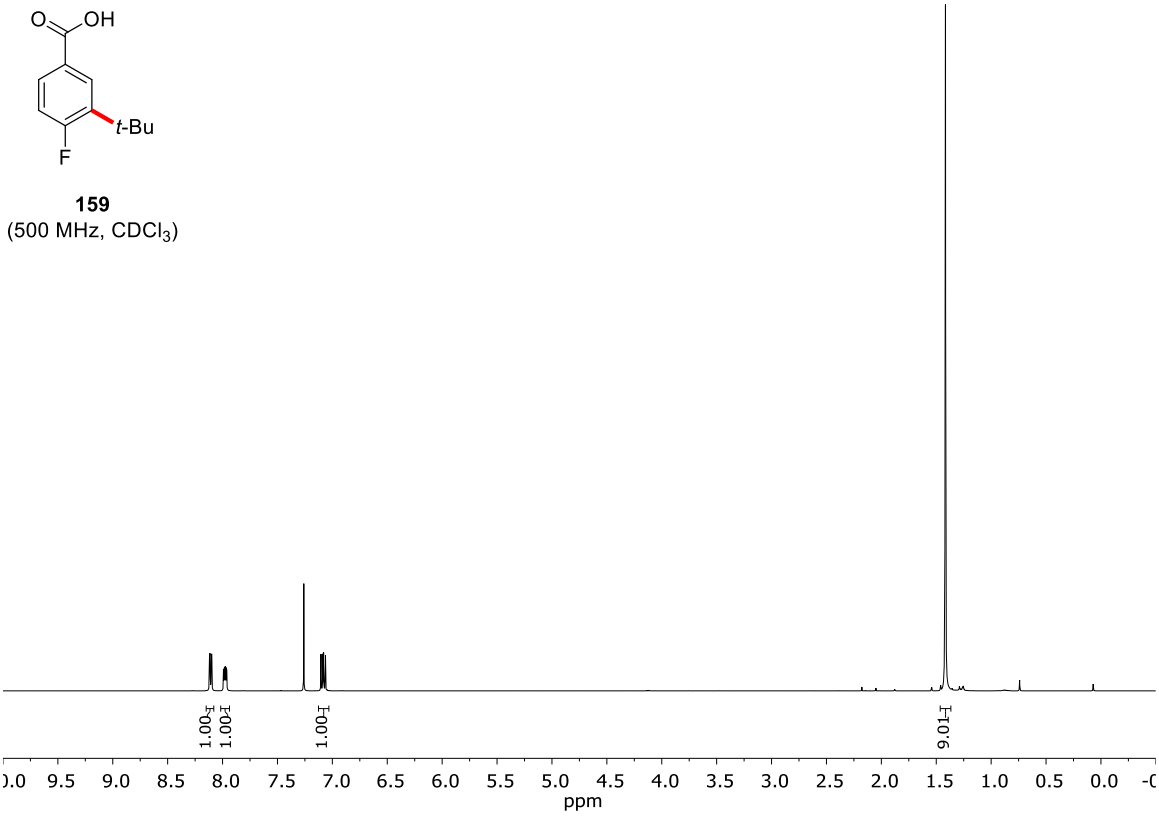
157c
(75 MHz, $CDCl_3$)



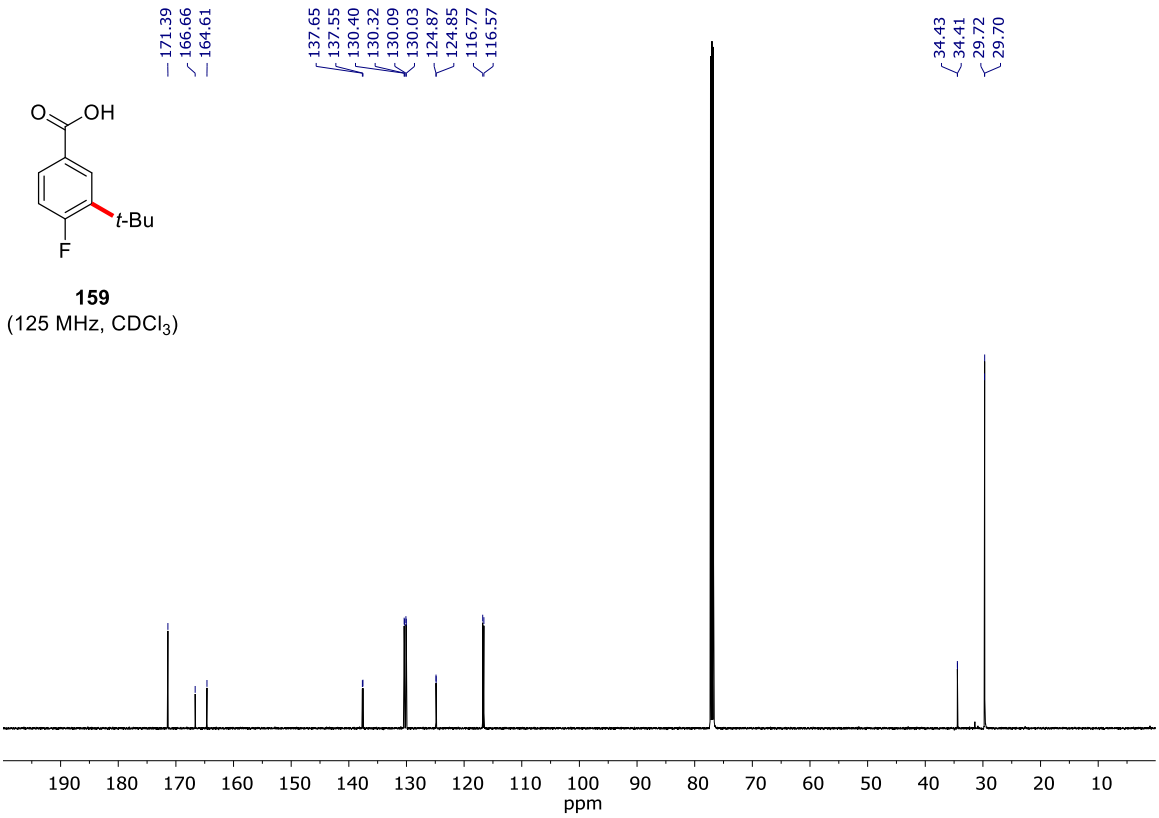
157d
(500 MHz, $CDCl_3$)



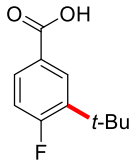
157d
(125 MHz, $CDCl_3$)



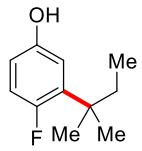
159
(500 MHz, $CDCl_3$)



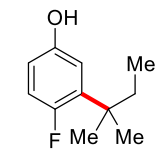
159
(125 MHz, $CDCl_3$)



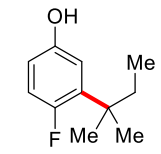
159
^{19}F-NMR
(470 MHz, $CDCl_3$)



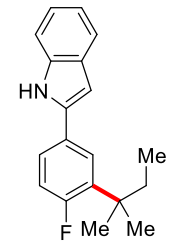
160b
(300 MHz, $CDCl_3$)



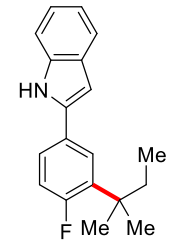
160b
(125 MHz, $CDCl_3$)



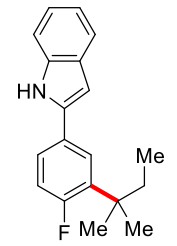
160b
^{19}F-NMR
(282 MHz, $CDCl_3$)



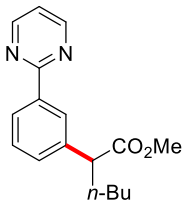
162
(500 MHz, $CDCl_3$)



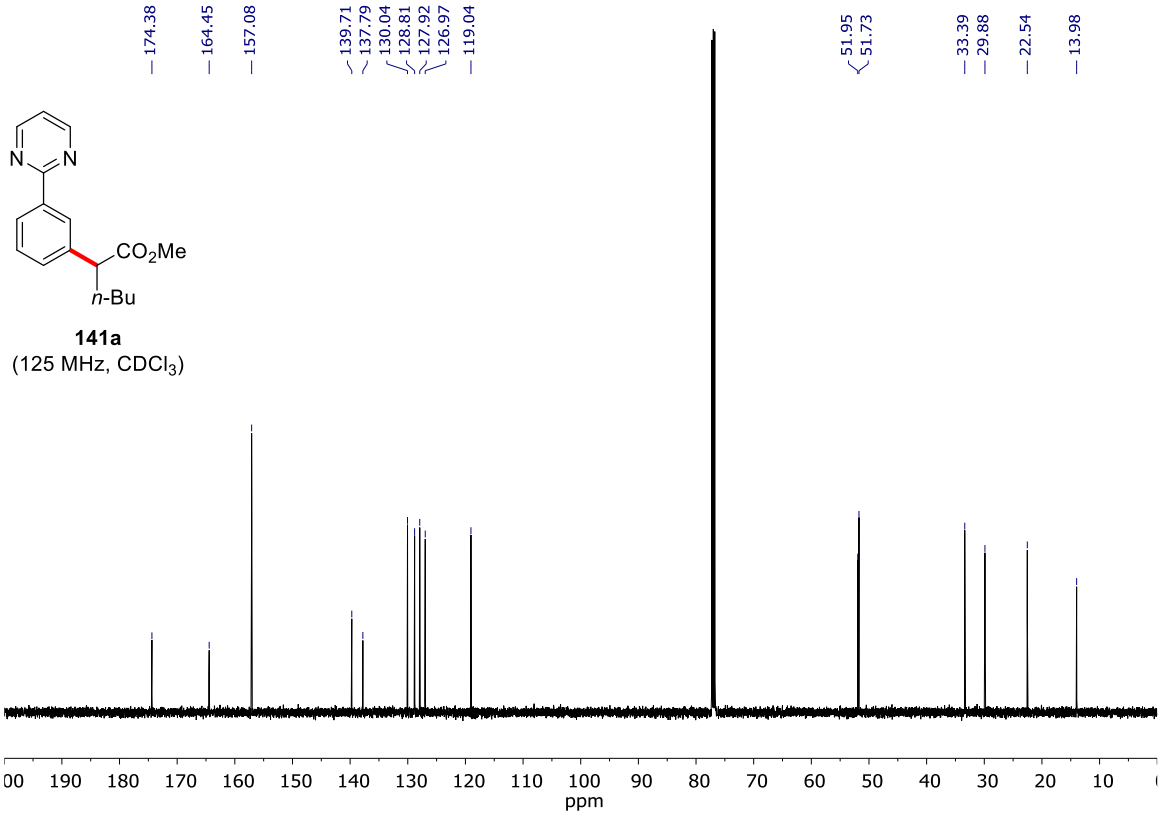
162
(125 MHz, $CDCl_3$)



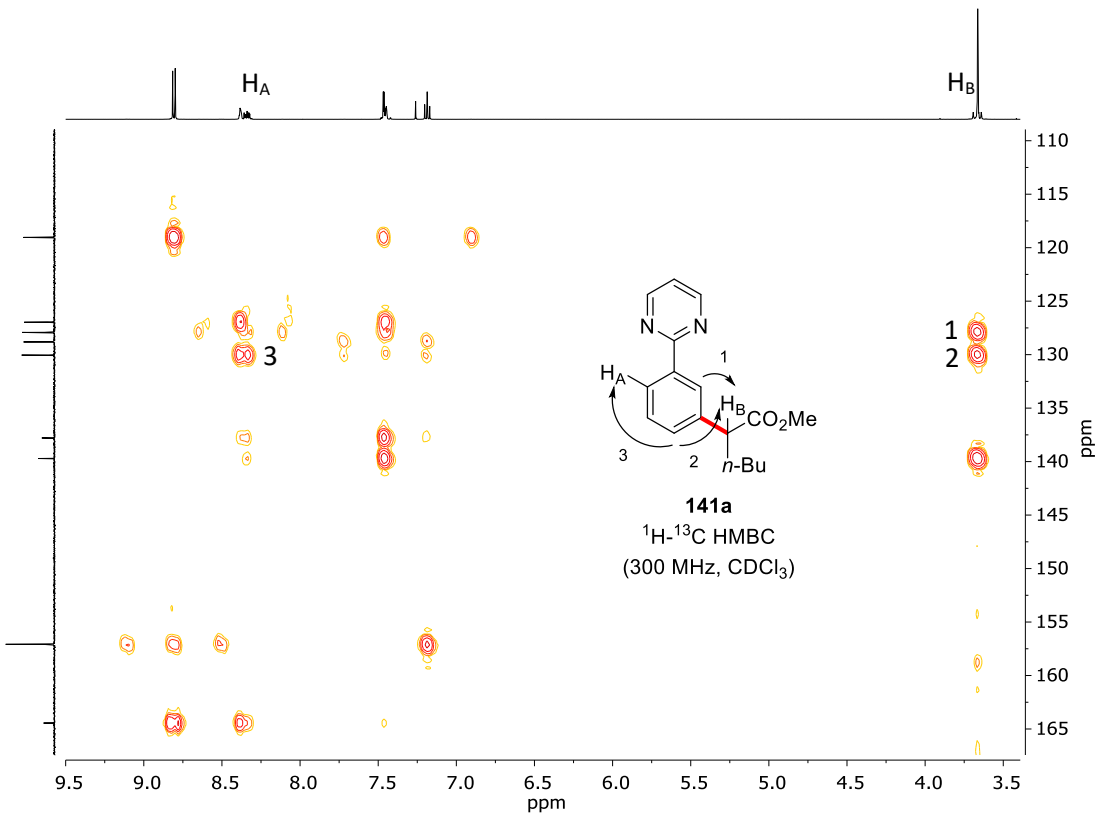
162
^{19}F-NMR
(470 MHz, $CDCl_3$)



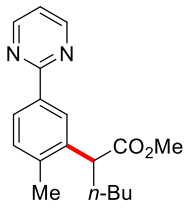
141a
(300 MHz, $CDCl_3$)



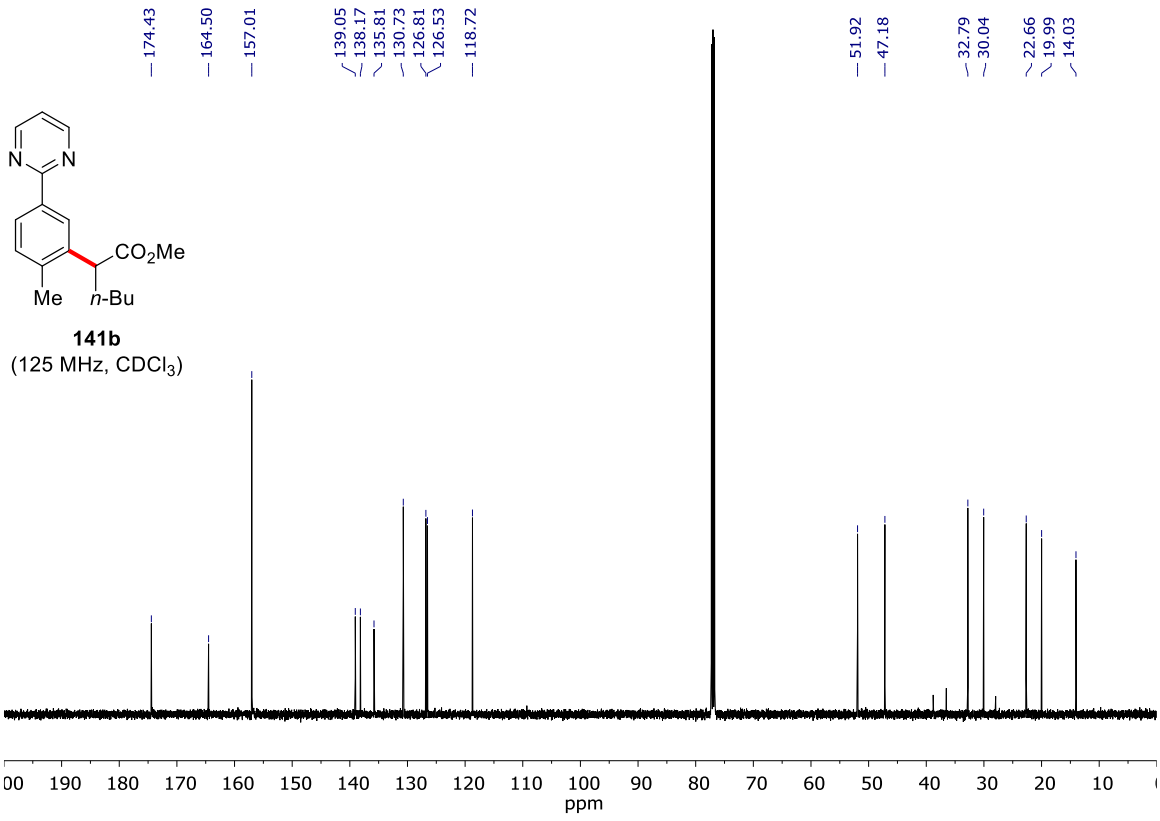
141a
(125 MHz, $CDCl_3$)



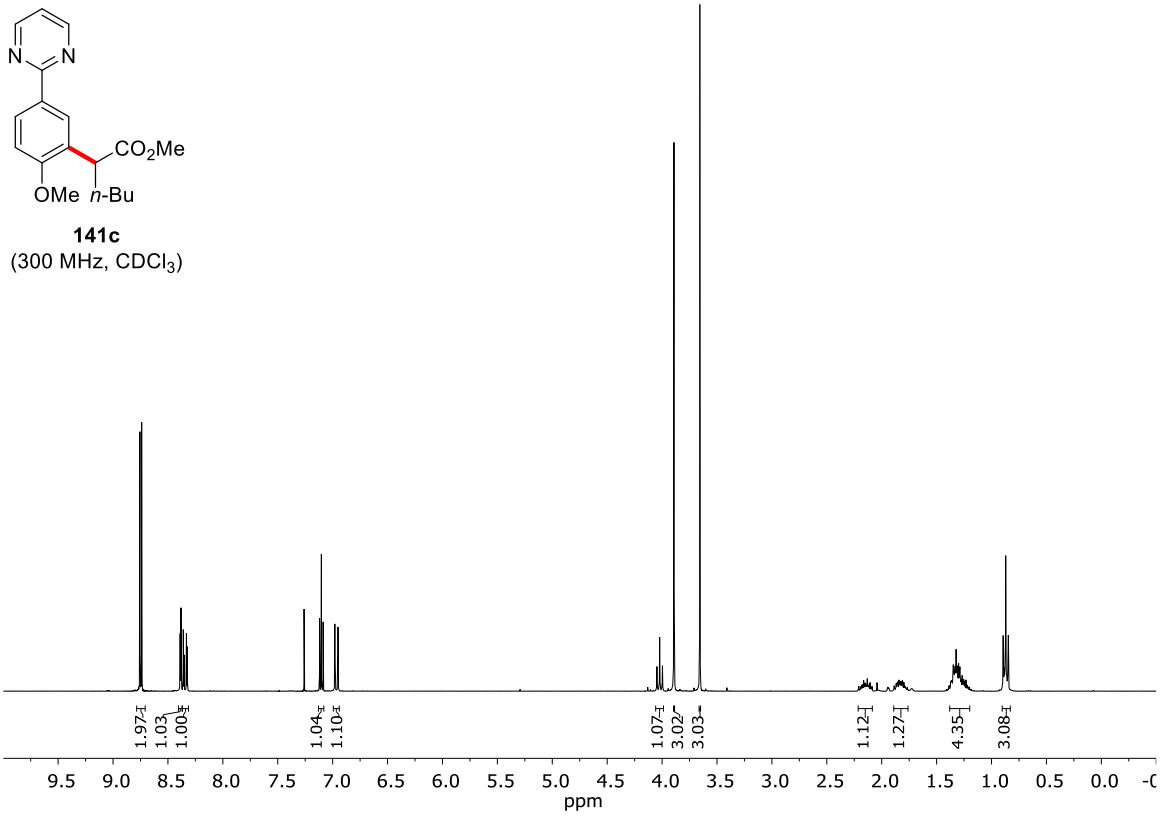
141a
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



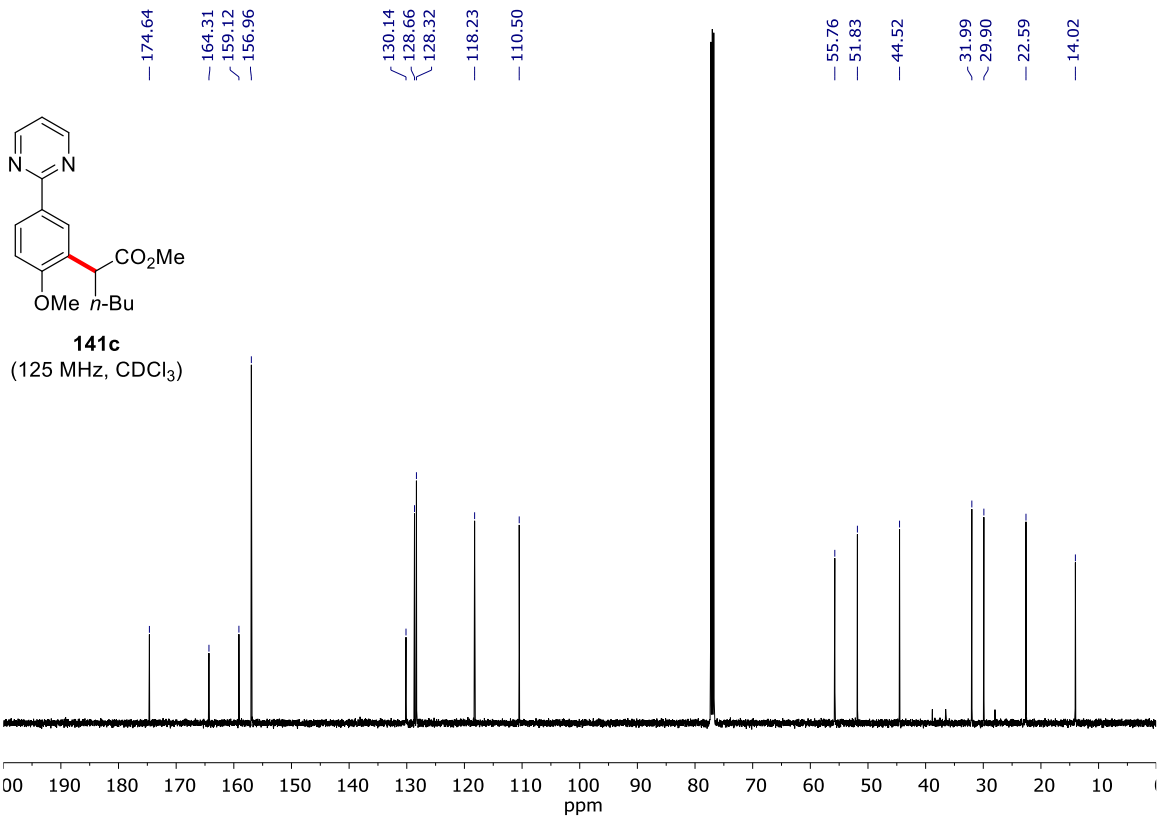
141b
(300 MHz, $CDCl_3$)



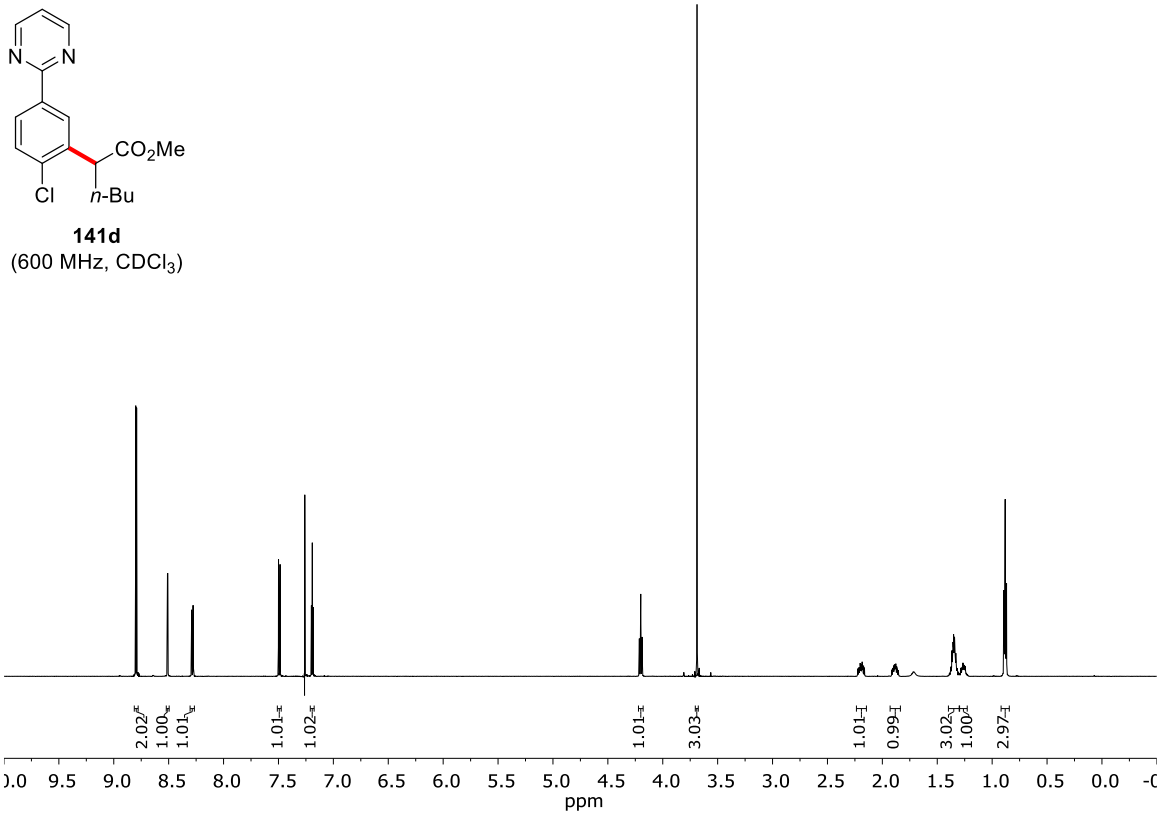
141b
(125 MHz, $CDCl_3$)



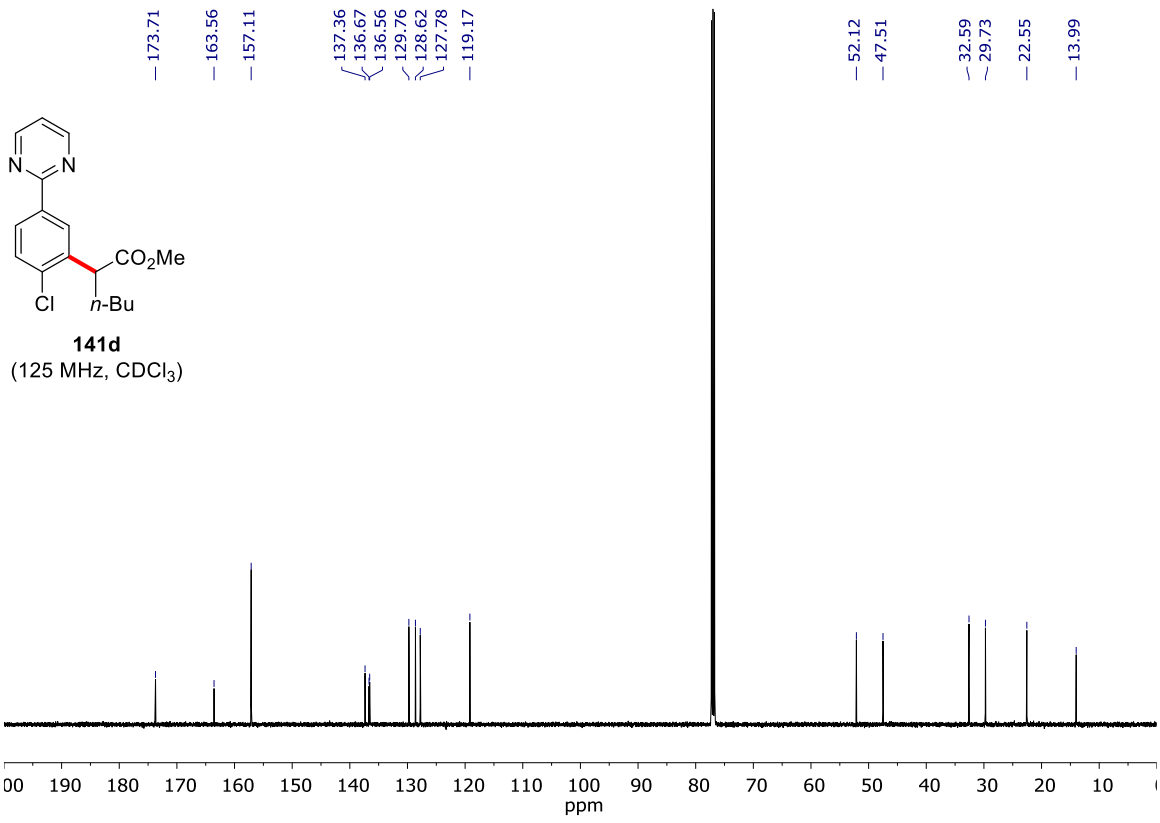
141c
(300 MHz, $CDCl_3$)



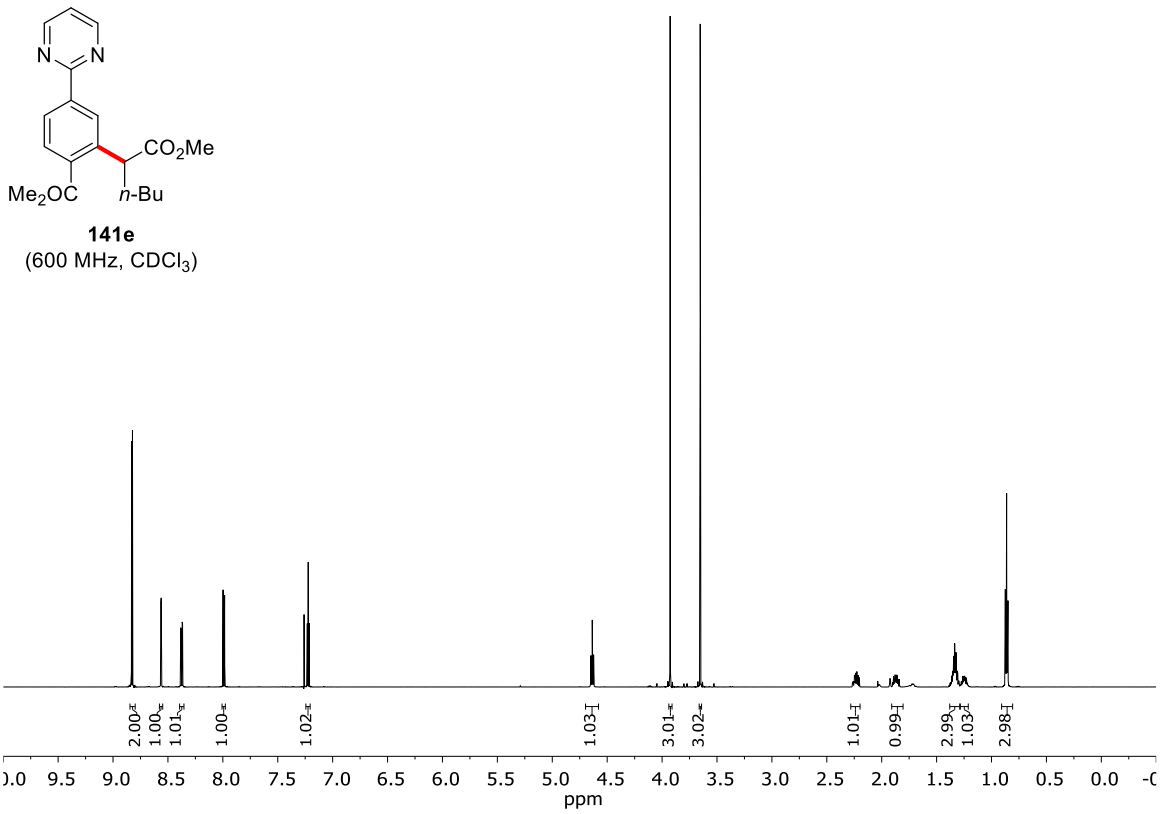
141c
(125 MHz, $CDCl_3$)

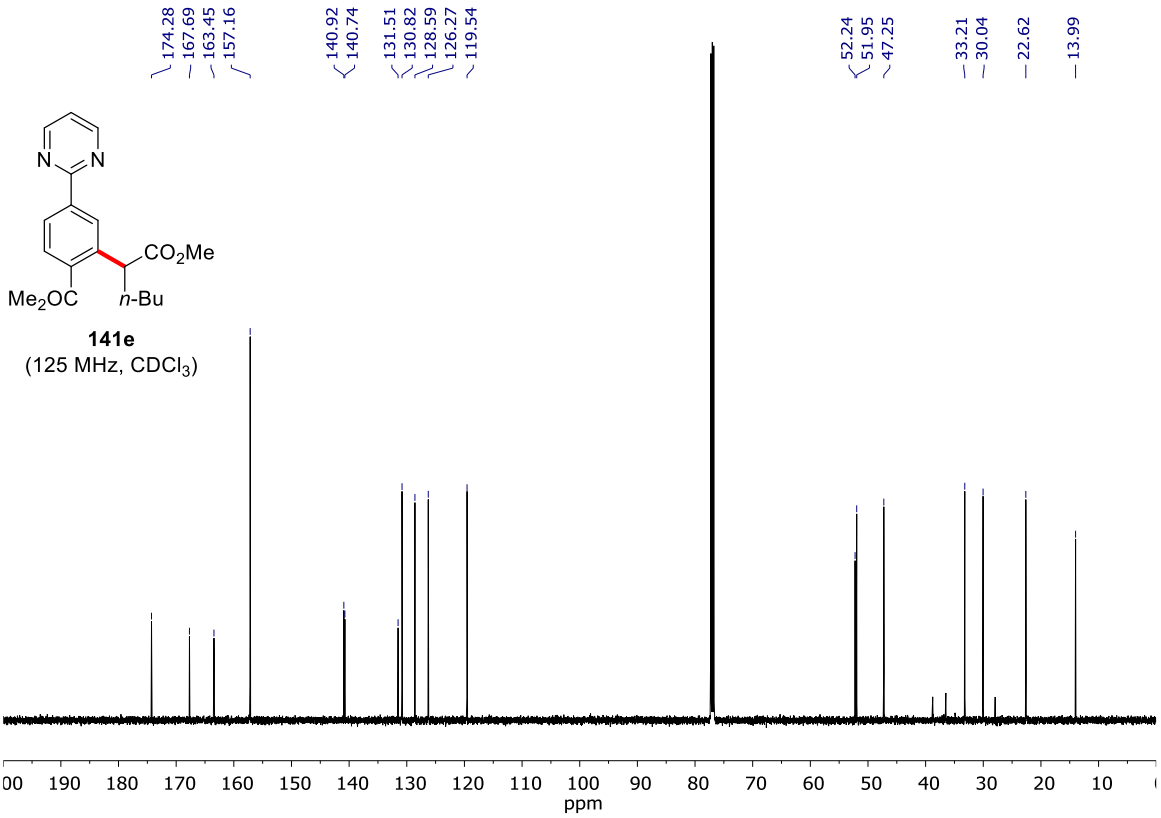


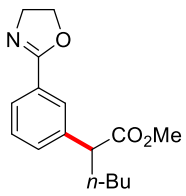
141d
(600 MHz, $CDCl_3$)



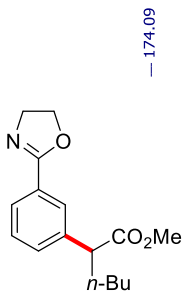
141d
(125 MHz, $CDCl_3$)


CO2Me
Me2OC
n-Bu
141e
(600 MHz, CDCl3)
2.00
1.00
1.01
1.00
1.02
1.03
3.01
3.02
1.01
0.99
2.99
1.03
2.98
ppm

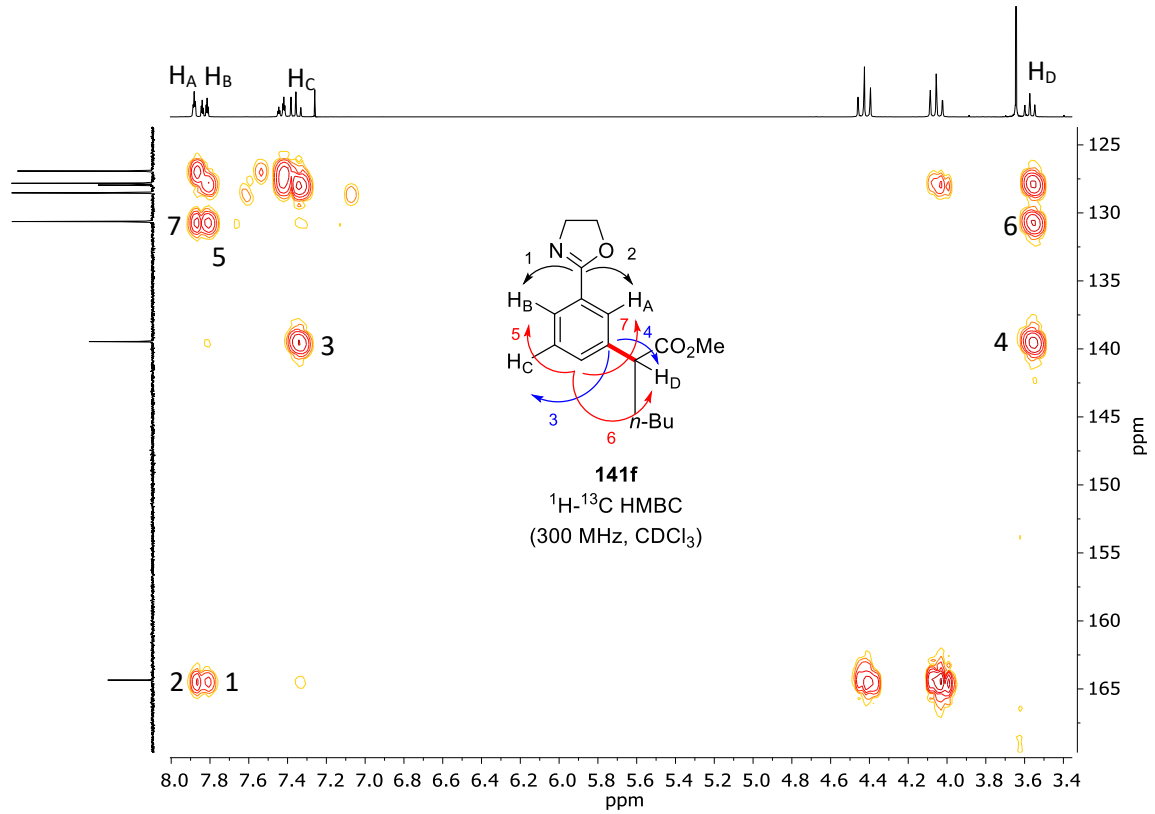

174.28
167.69
163.45
157.16
140.92
140.74
131.51
130.82
128.59
126.27
119.54
52.24
51.95
47.25
33.21
30.04
22.62
13.99
CO2Me
Me2OC
n-Bu
141e
(125 MHz, CDCl3)
ppm



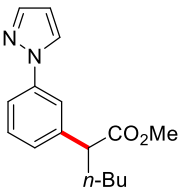
141f
(300 MHz, $CDCl_3$)



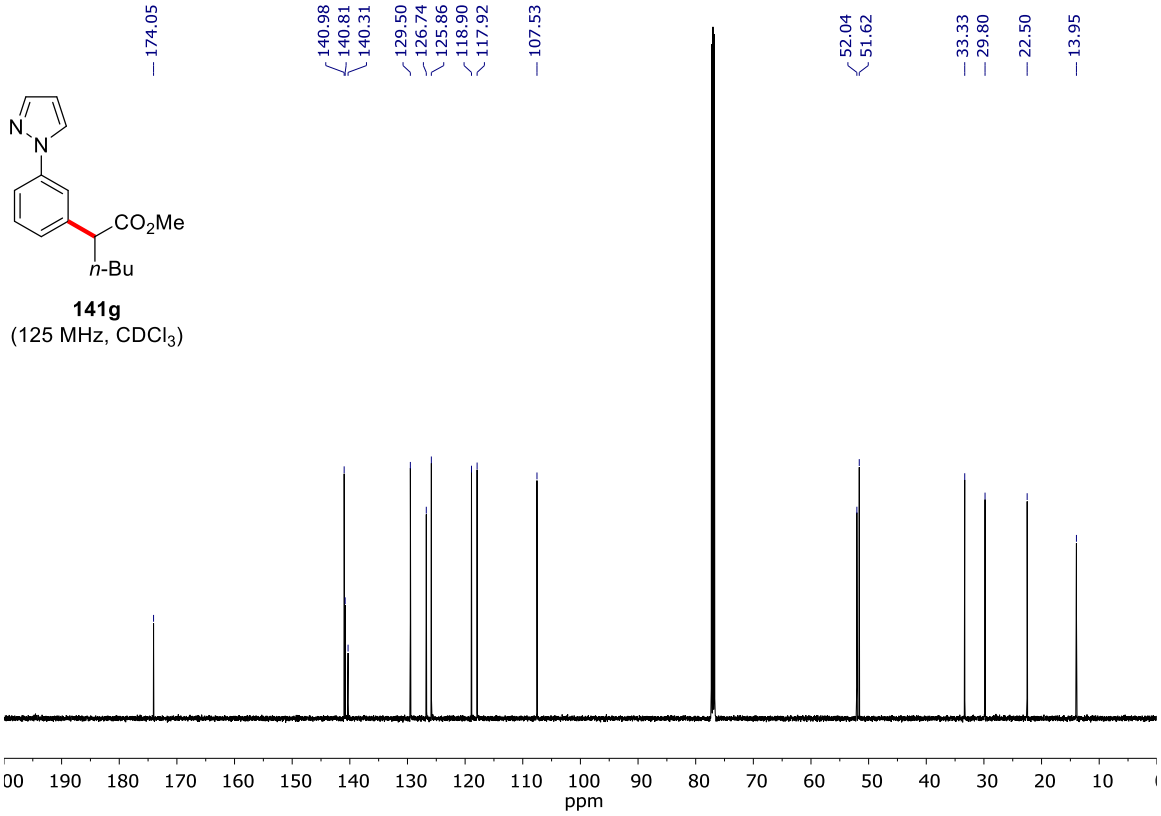
141f
(125 MHz, $CDCl_3$)



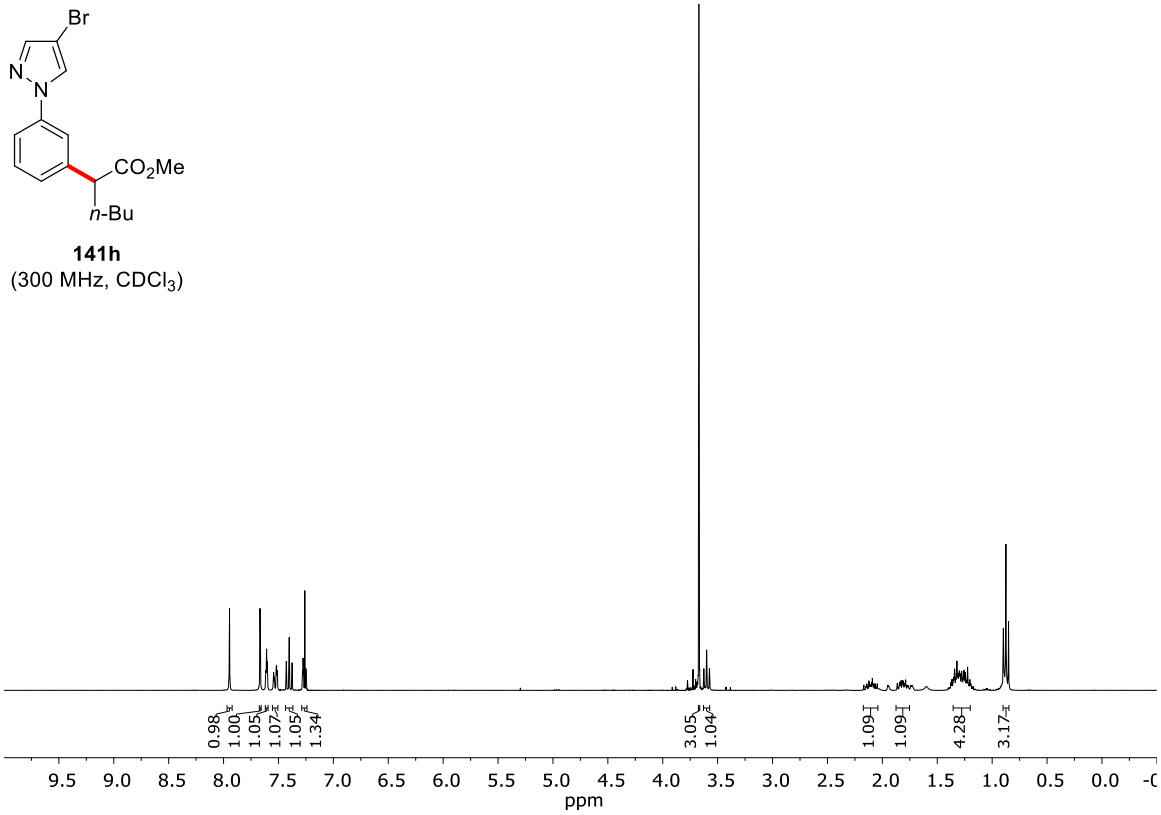
141f
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



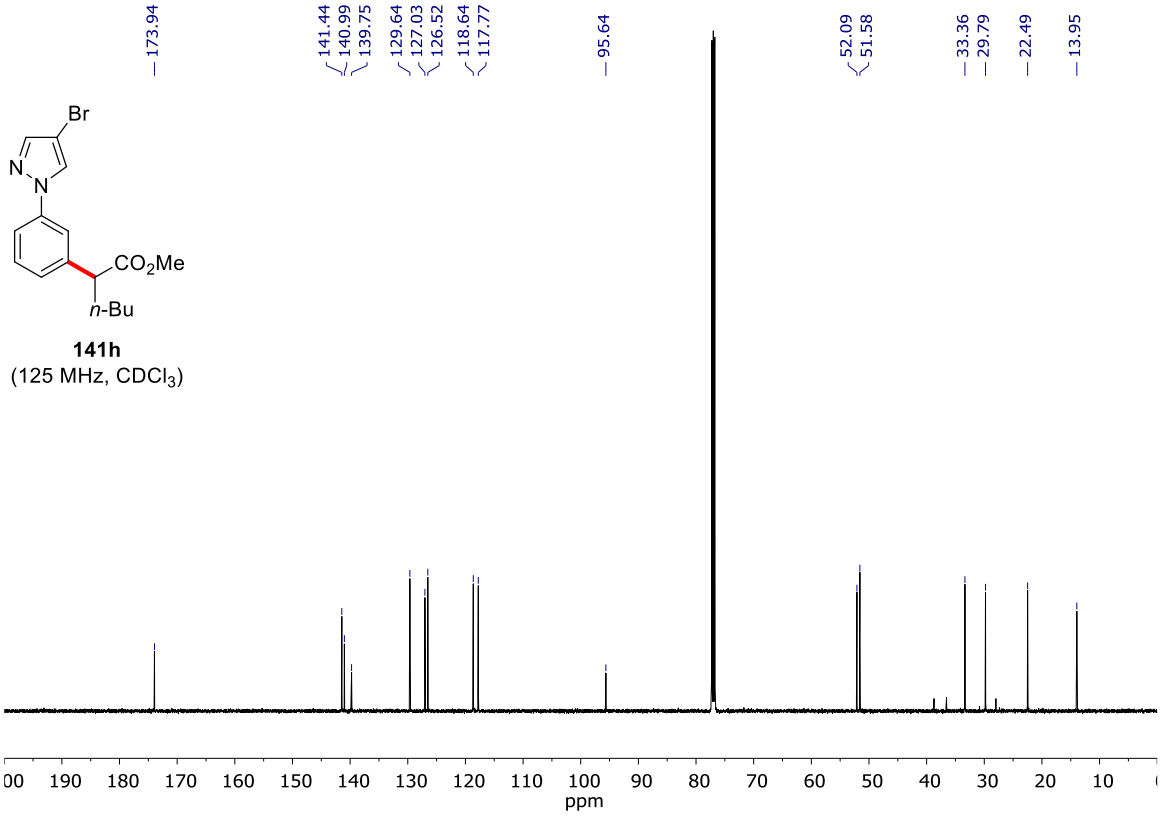
141g
(300 MHz, $CDCl_3$)



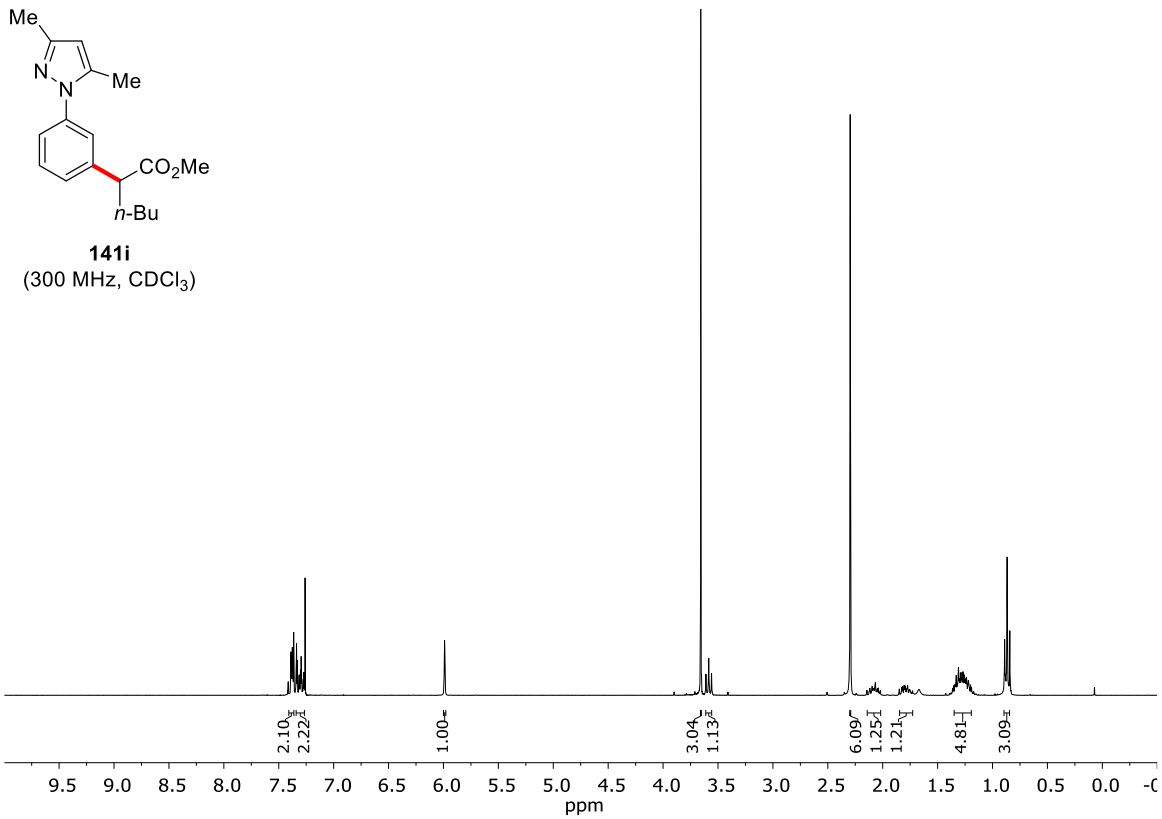
141g
(125 MHz, $CDCl_3$)



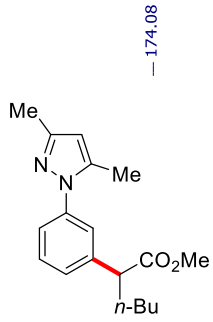
141h
(300 MHz, $CDCl_3$)



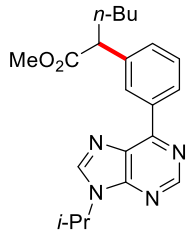
141h
(125 MHz, $CDCl_3$)



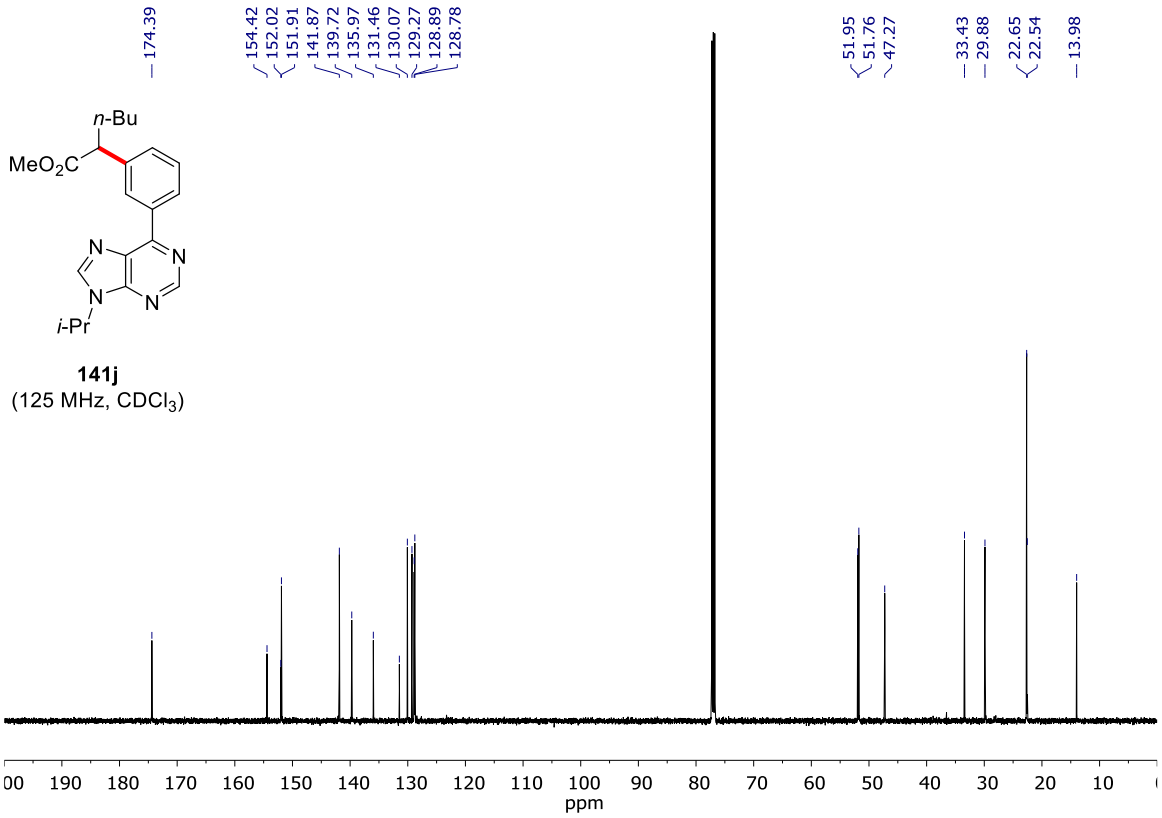
141i
(300 MHz, $CDCl_3$)



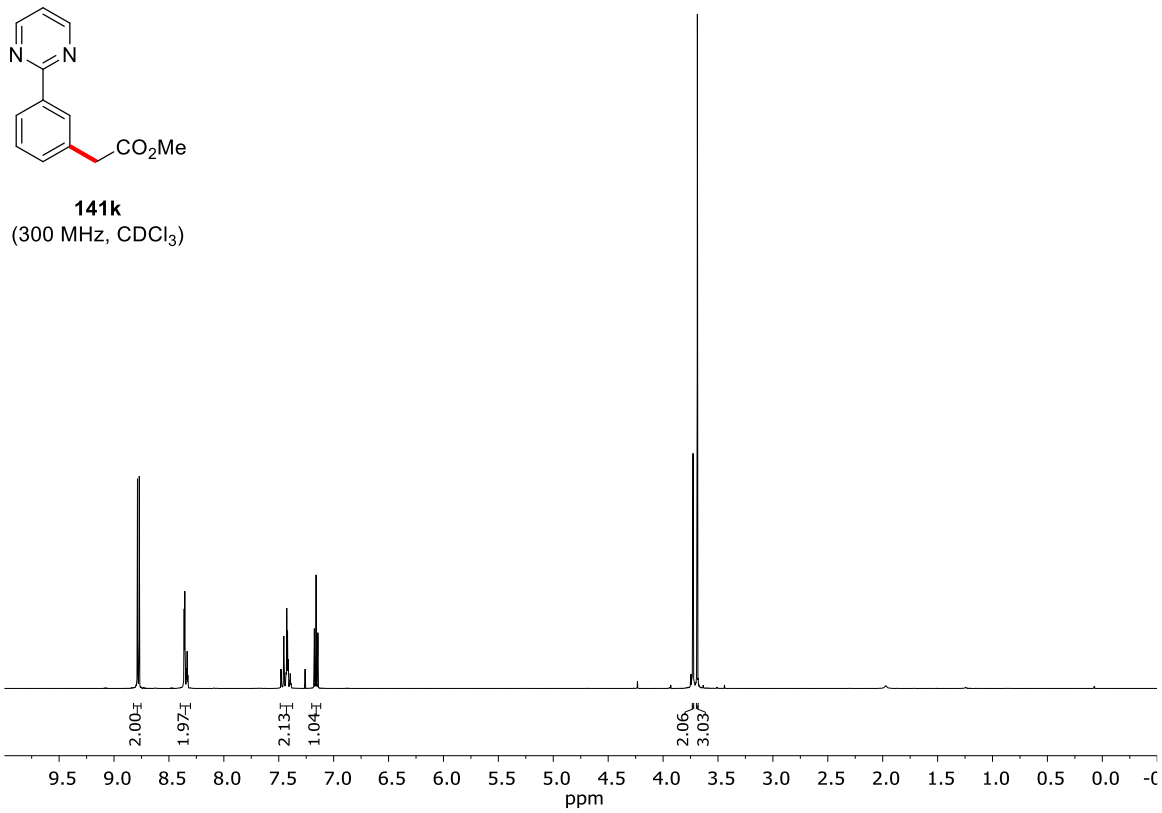
141i
(125 MHz, $CDCl_3$)



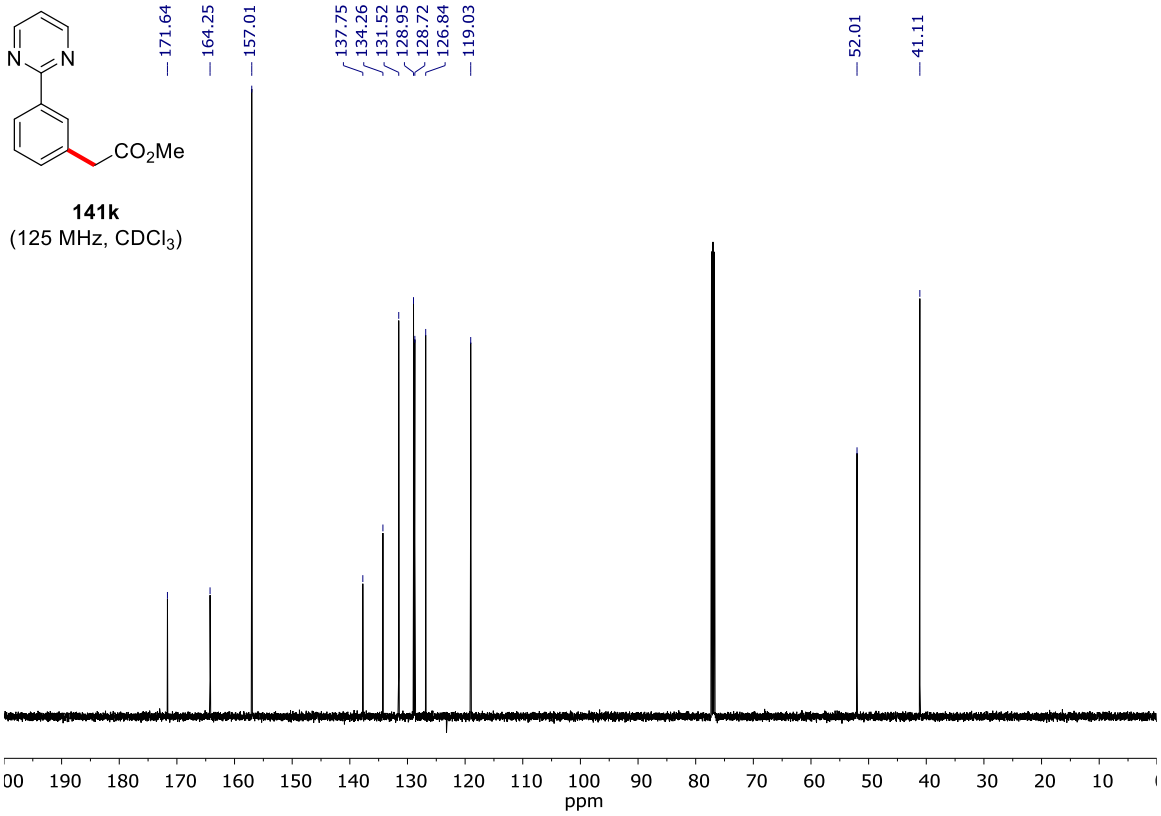
141j
(300 MHz, $CDCl_3$)



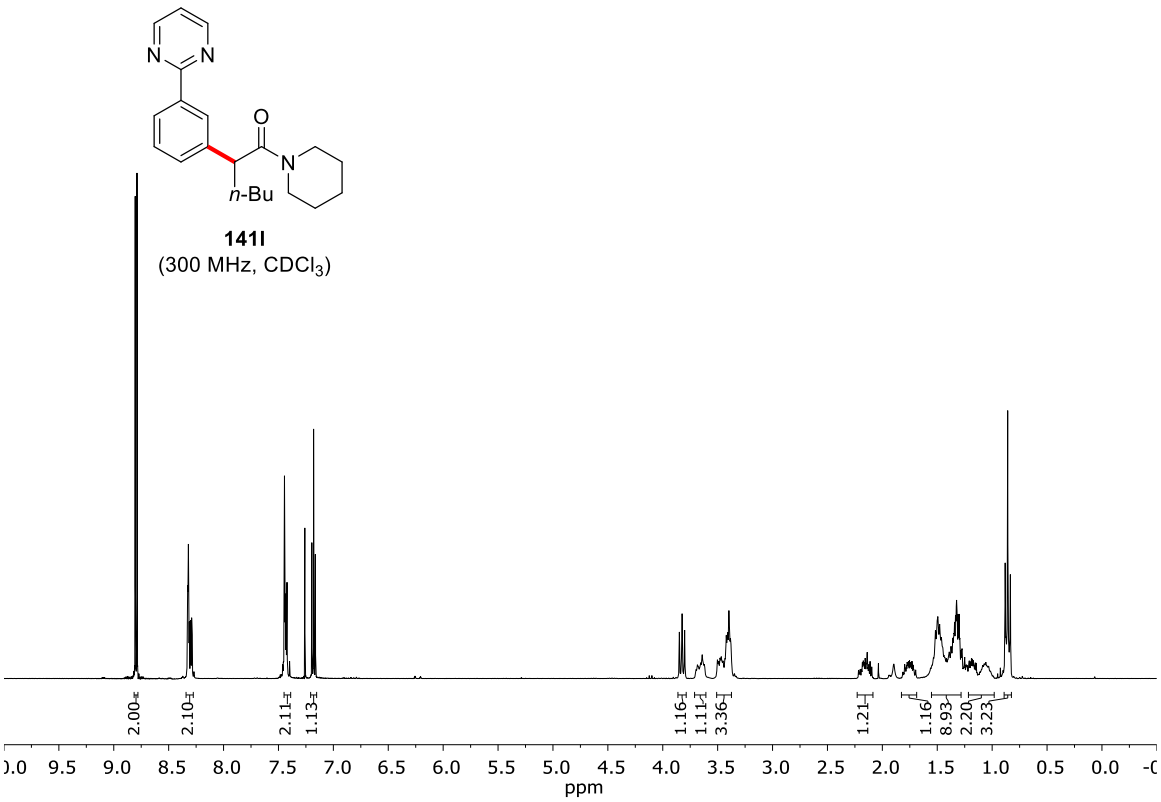
141j
(125 MHz, $CDCl_3$)



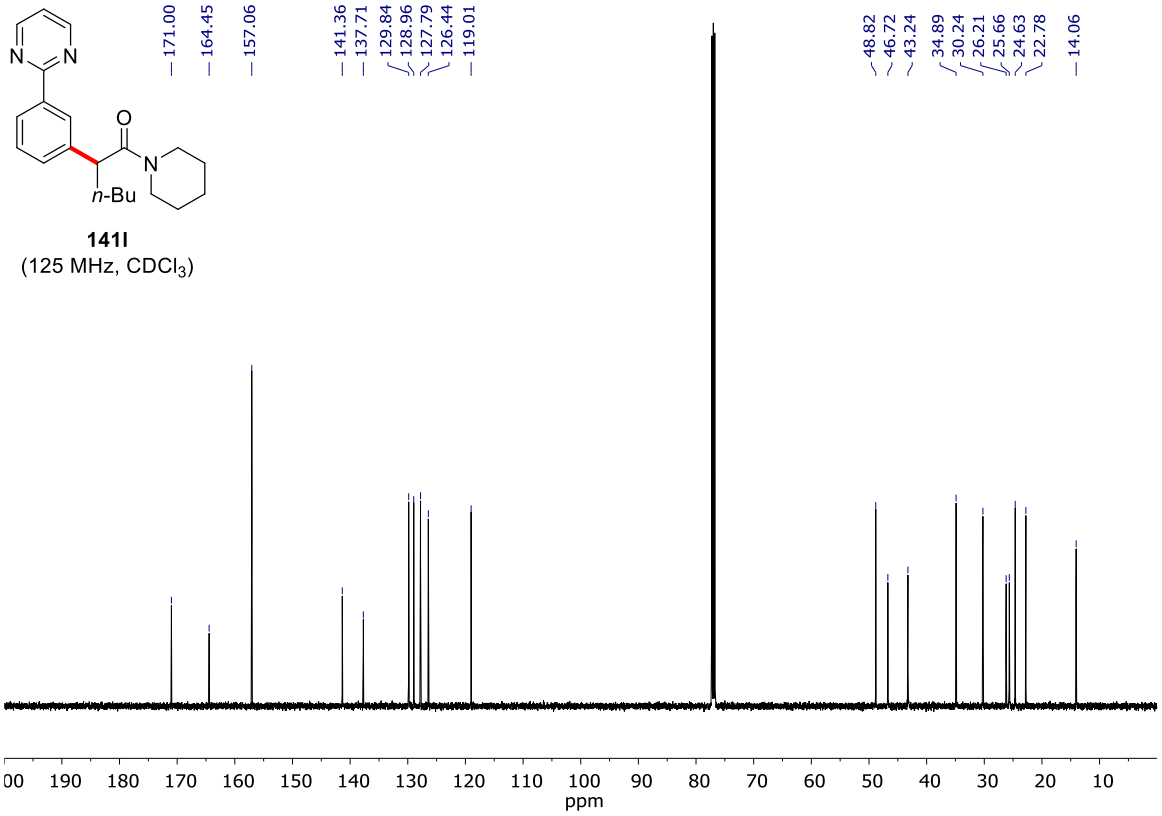
141k
(300 MHz, $CDCl_3$)



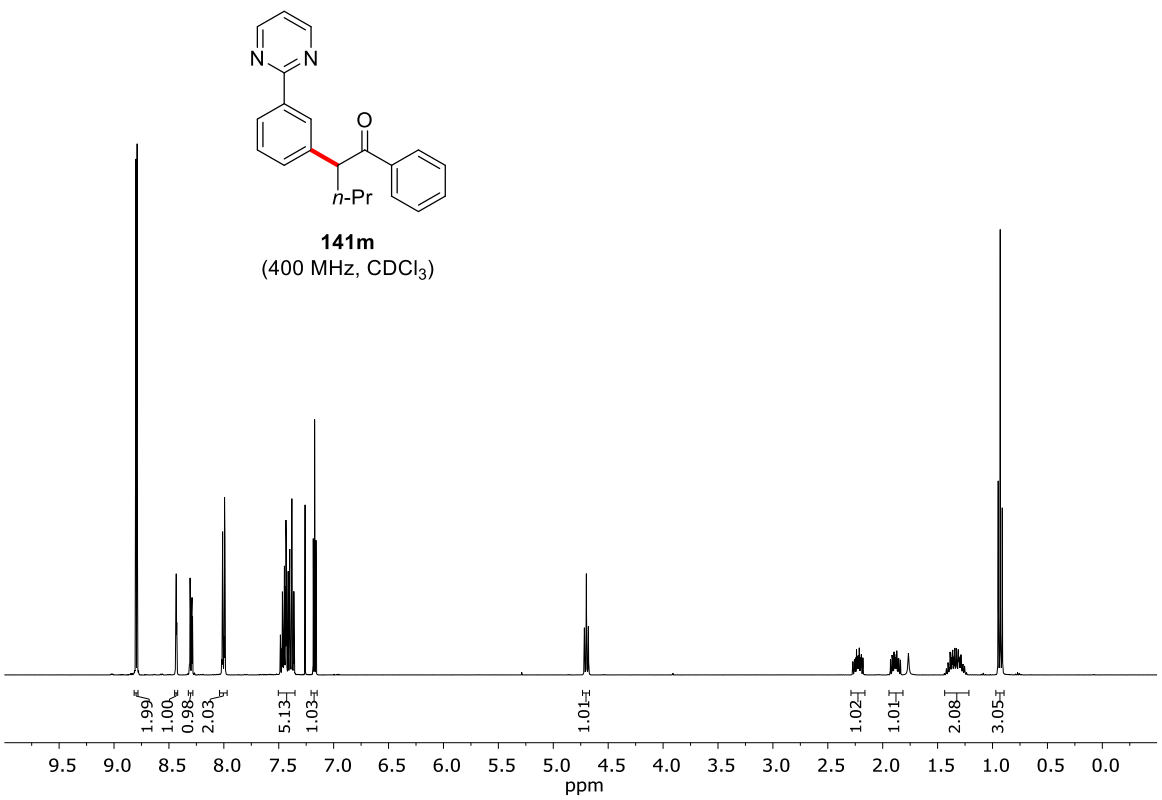
141k
(125 MHz, $CDCl_3$)



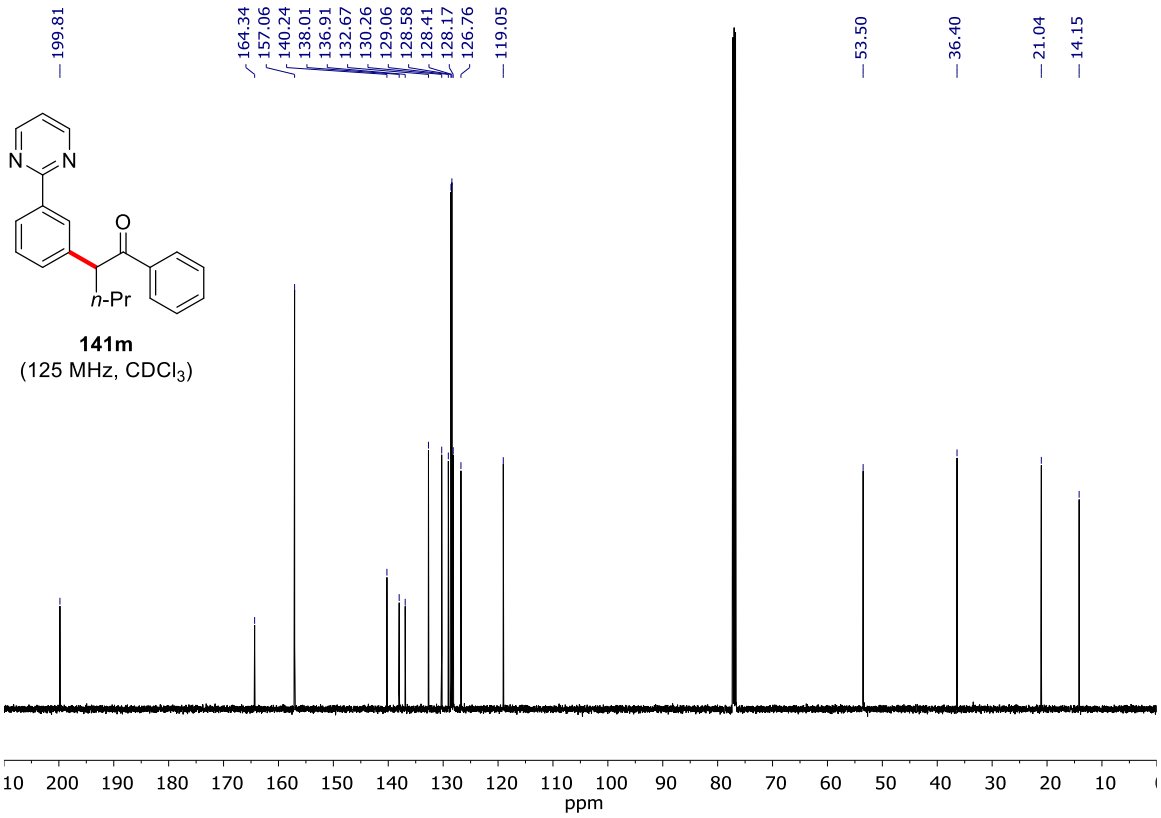
141l
(300 MHz, $CDCl_3$)



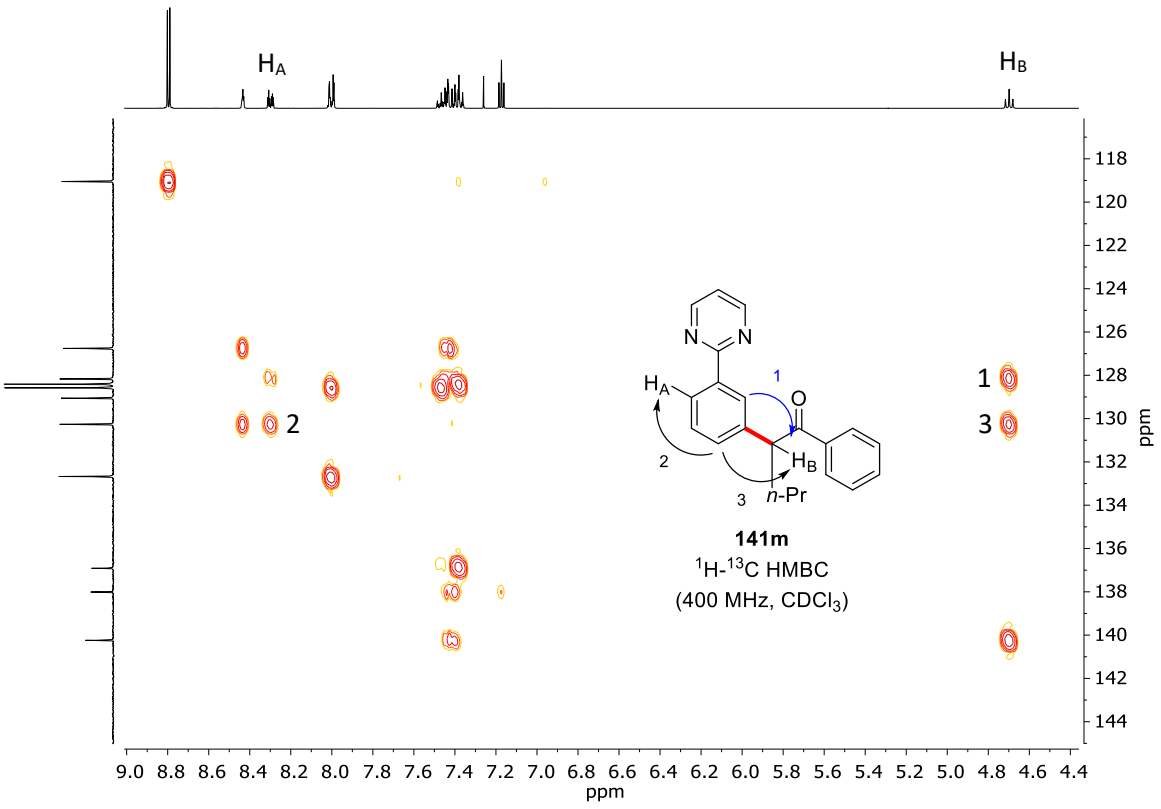
141l
(125 MHz, $CDCl_3$)



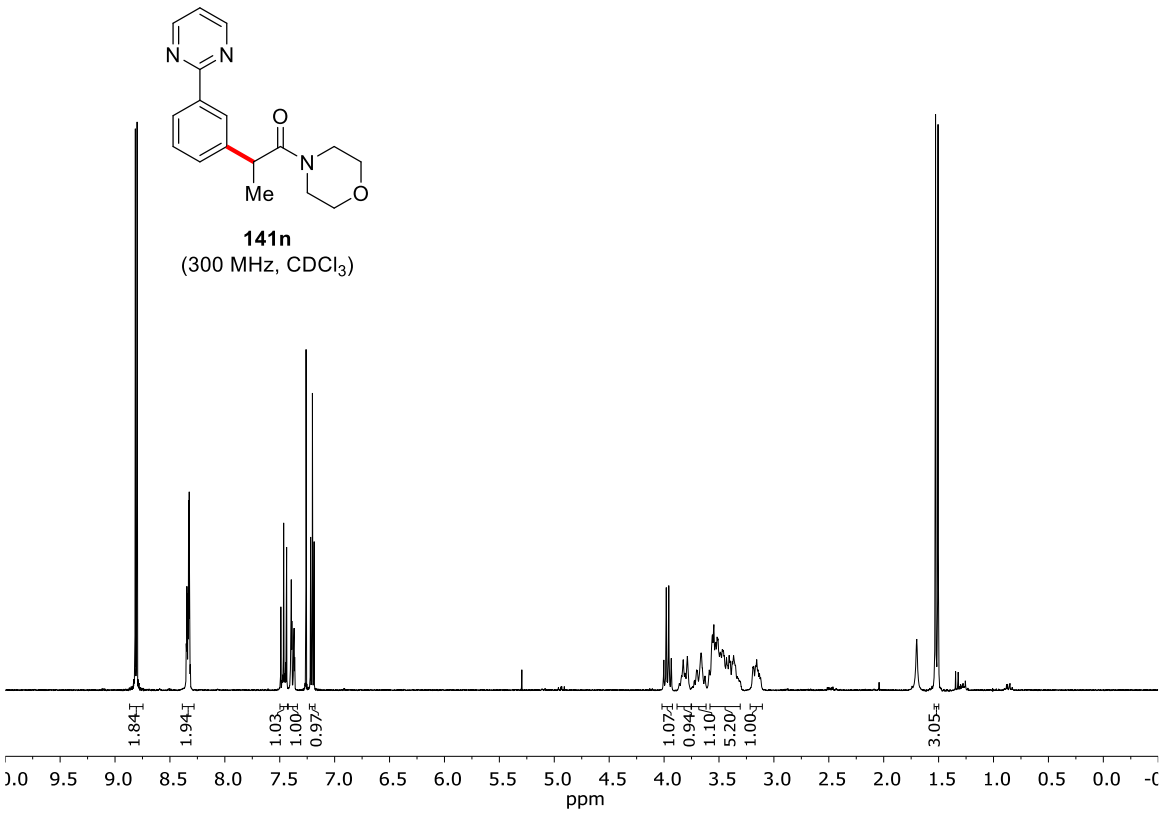
141m
(400 MHz, $CDCl_3$)



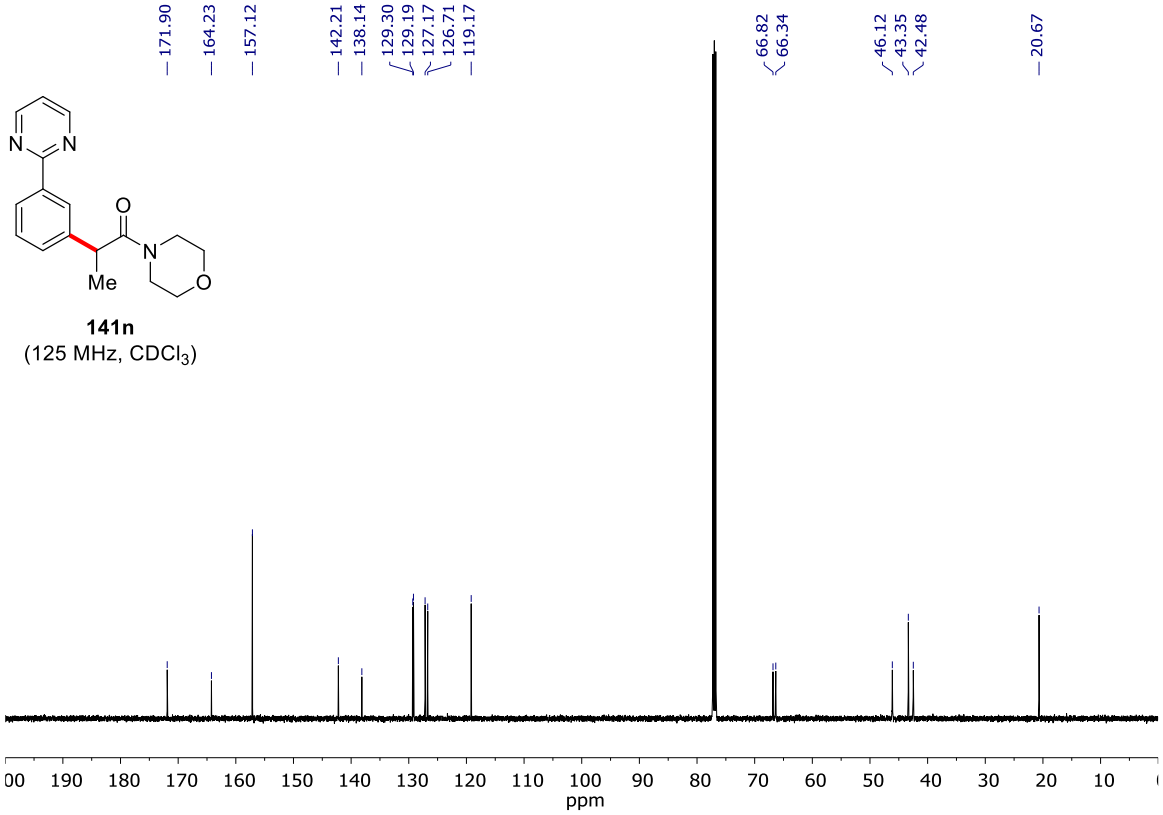
141m
(125 MHz, $CDCl_3$)



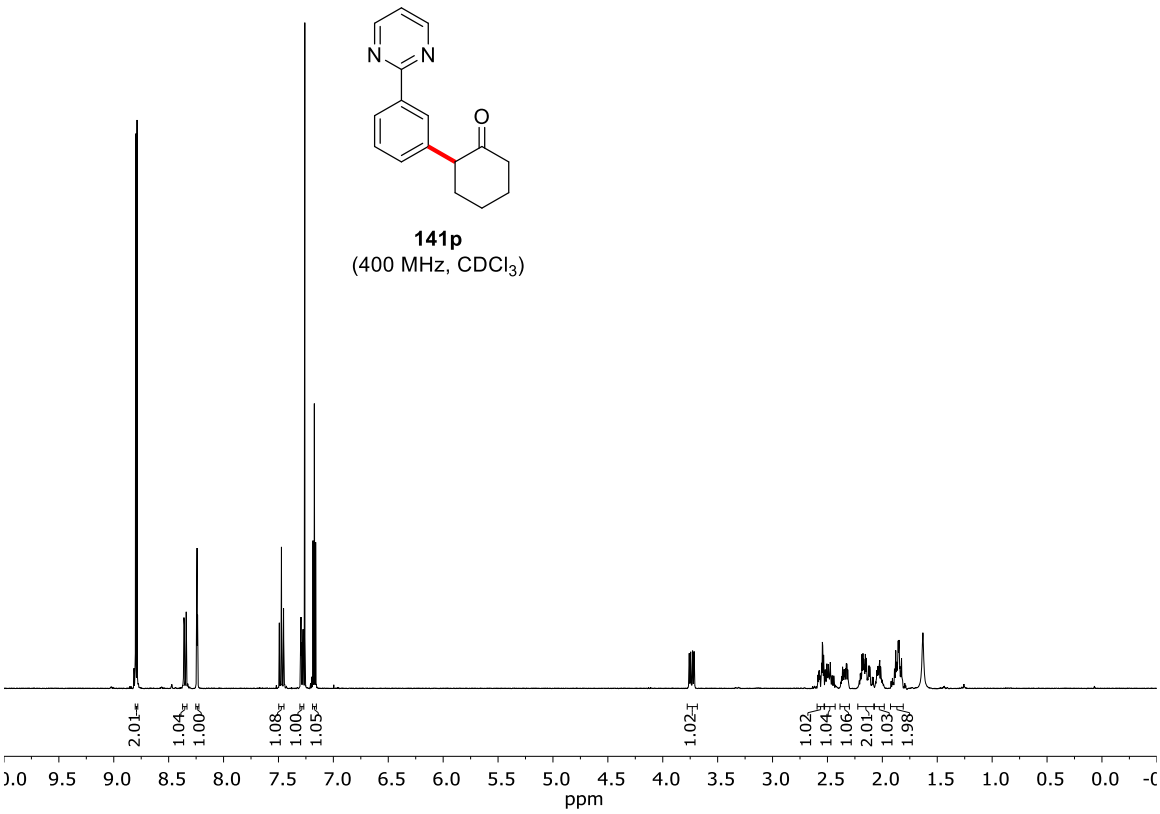
141m
^{1}H-^{13}C HMBC
(400 MHz, $CDCl_3$)

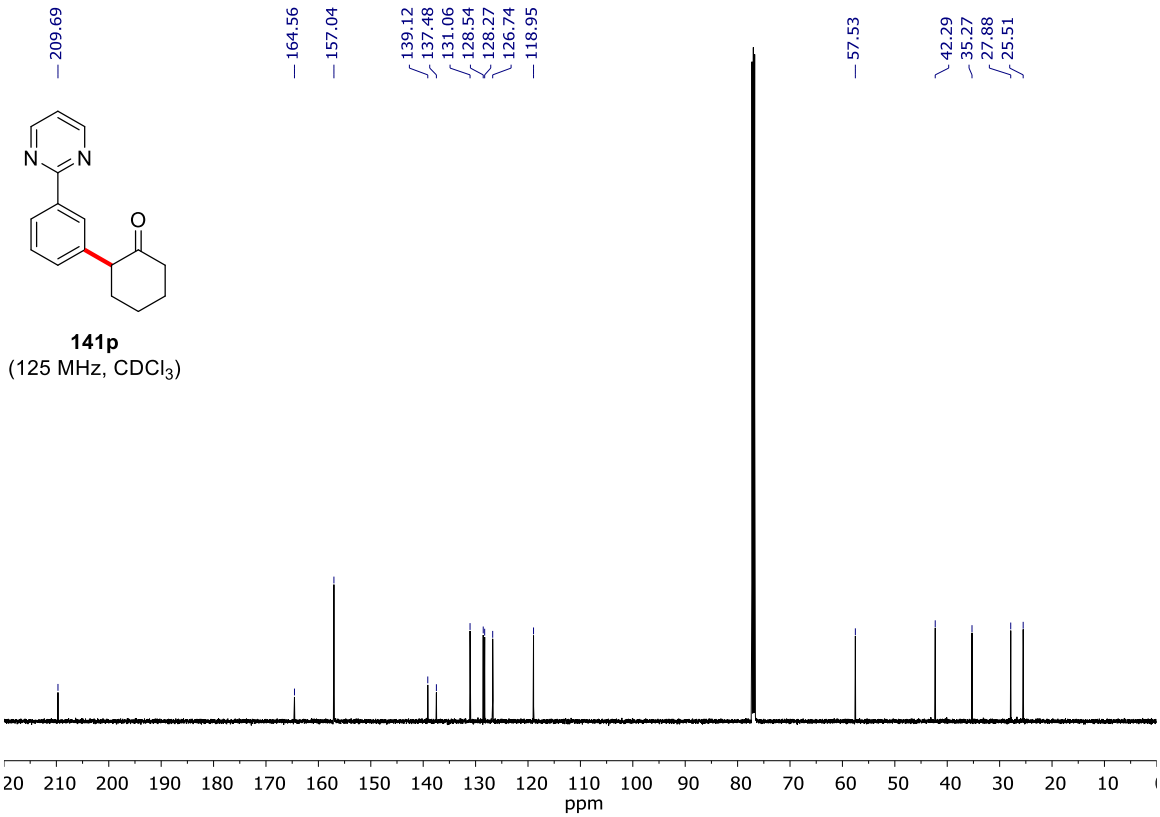


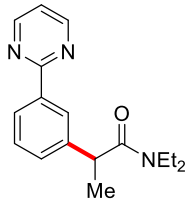
141n
(300 MHz, $CDCl_3$)



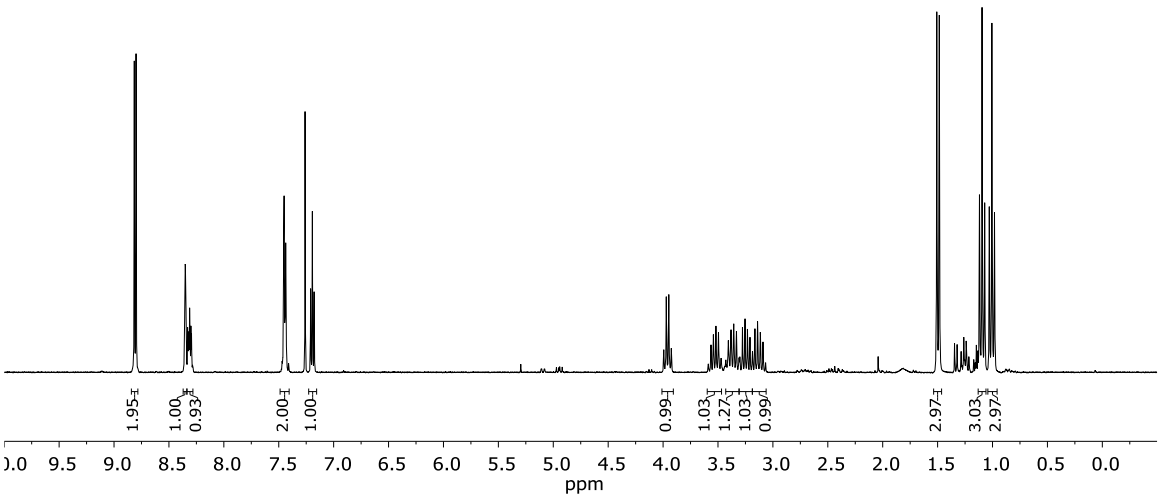
141n
(125 MHz, $CDCl_3$)

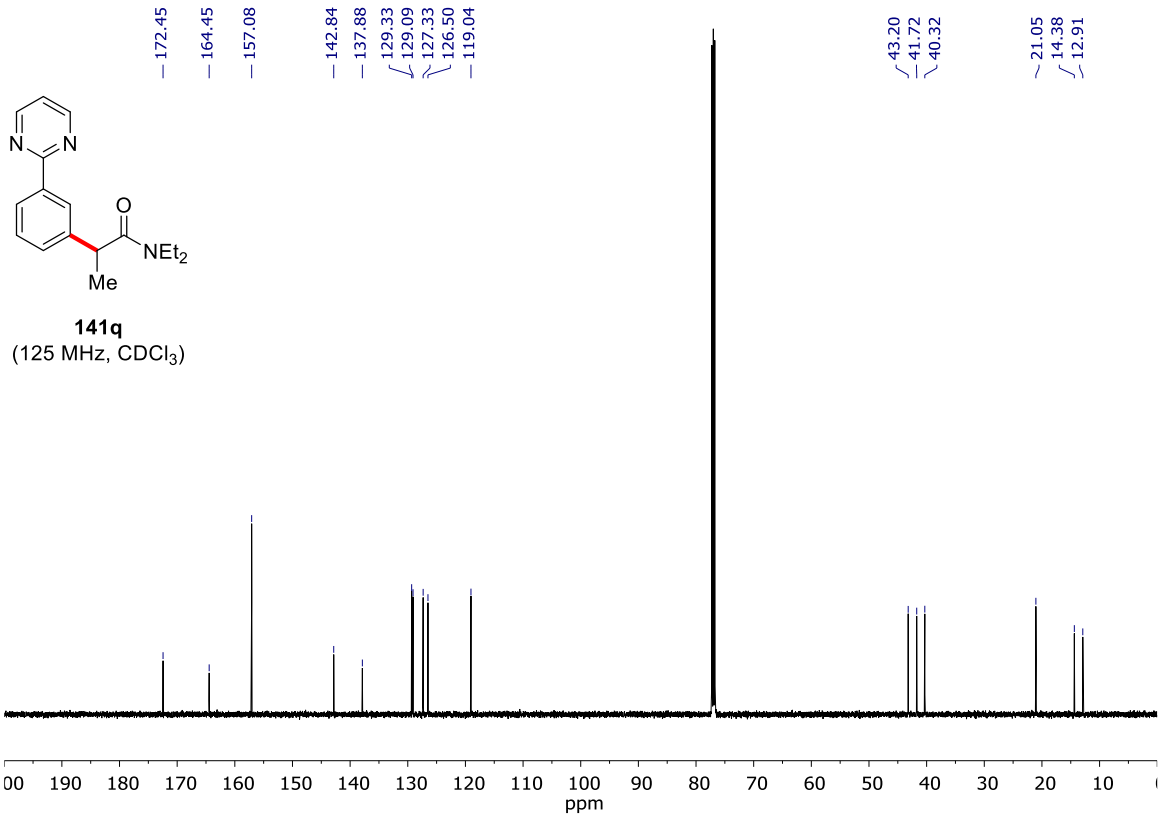

141p
(400 MHz, CDCl3)
2.01
1.04
1.00
1.08
1.00
1.05
1.02
1.02
1.04
1.06
2.01
1.03
1.98
ppm


209.69
164.56
157.04
139.12
137.48
131.06
128.54
128.27
126.74
118.95
57.53
42.29
35.27
27.88
25.51
141p
(125 MHz, CDCl3)
ppm

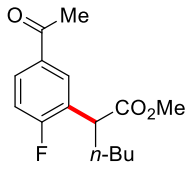


141q
(300 MHz, $CDCl_3$)

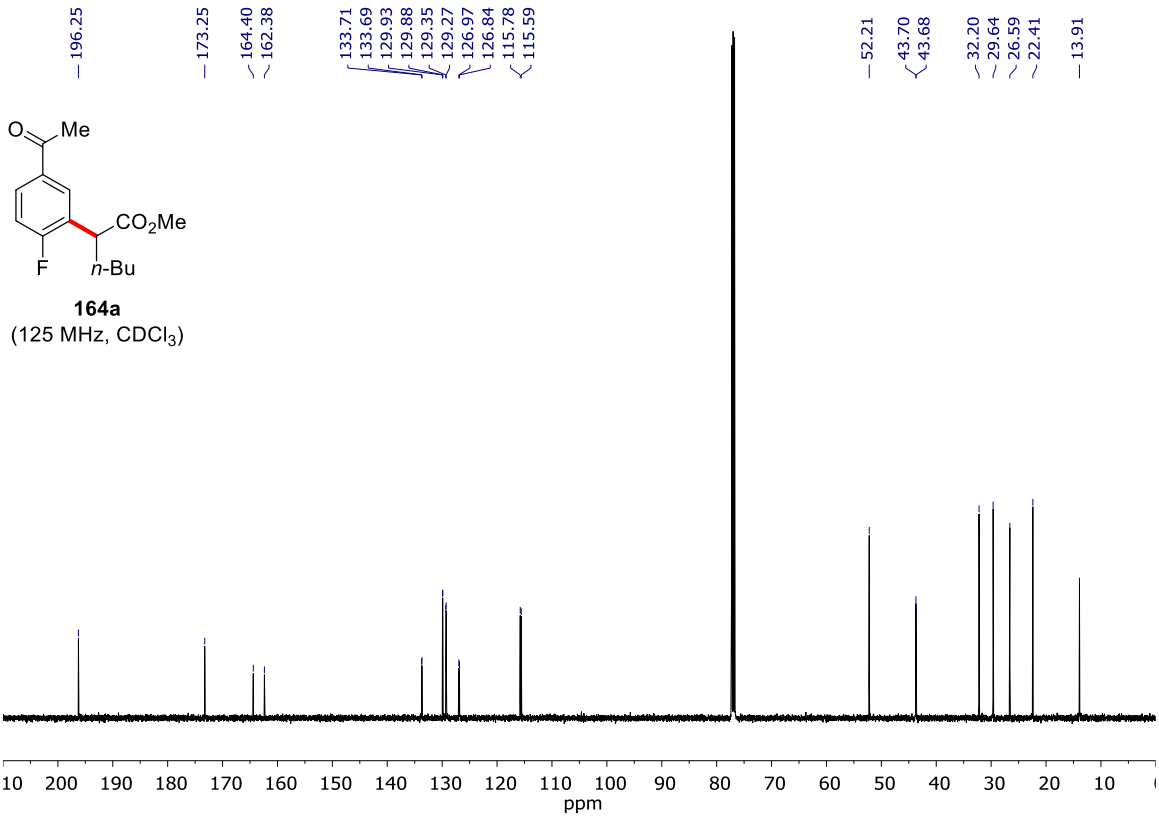




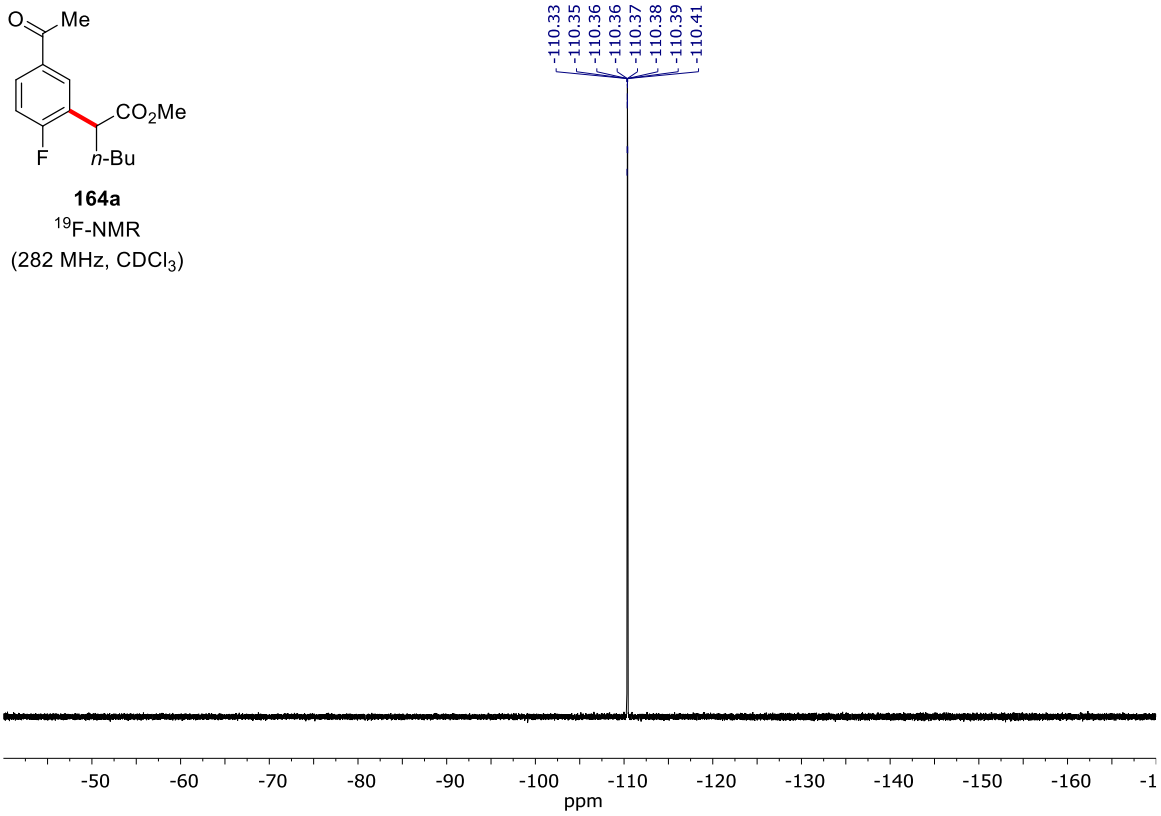
141q
(125 MHz, $CDCl_3$)



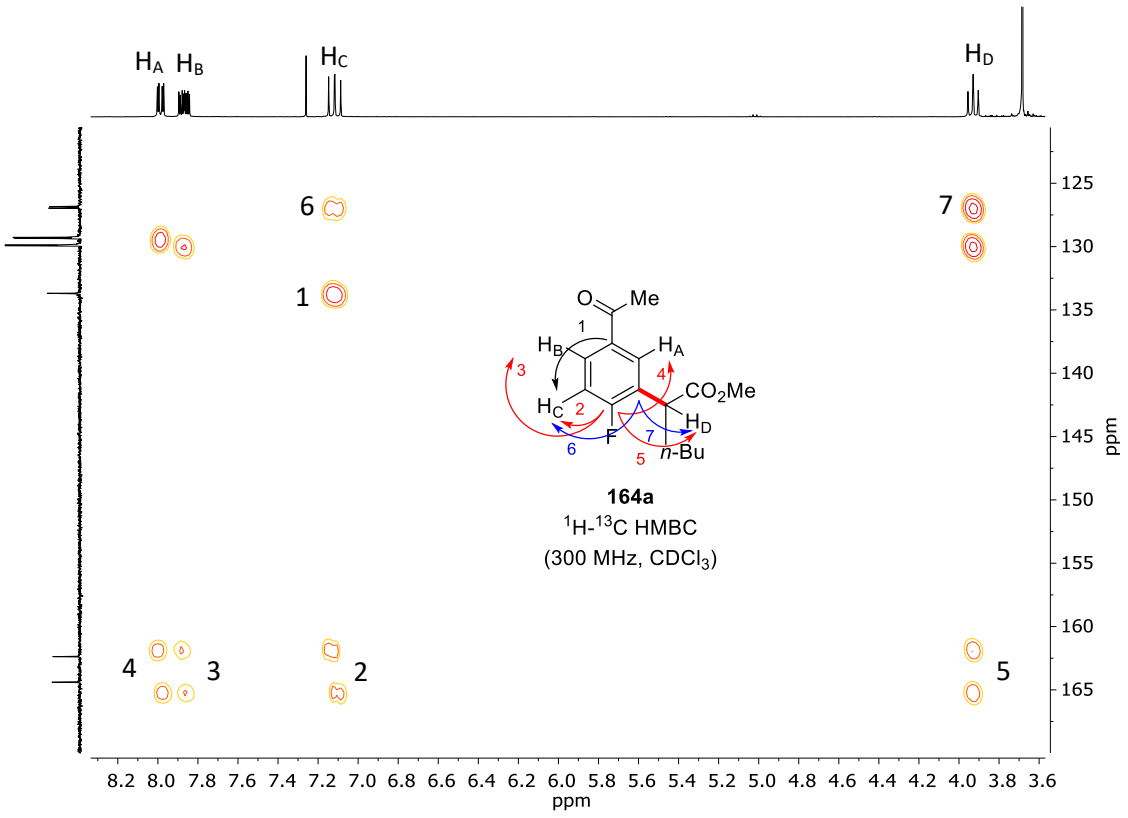
164a
(300 MHz, $CDCl_3$)



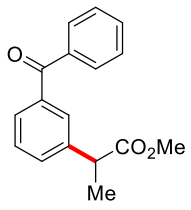
164a
(125 MHz, $CDCl_3$)



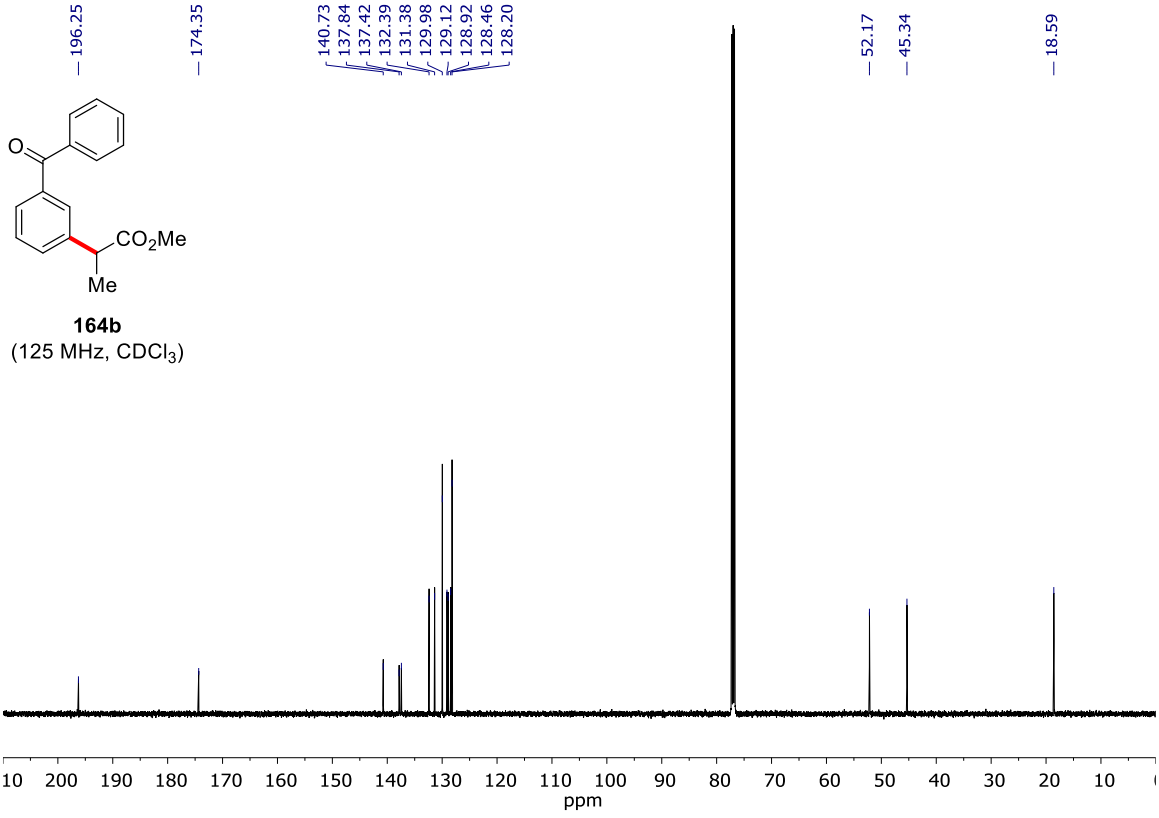
164a
^{19}F-NMR
(282 MHz, $CDCl_3$)



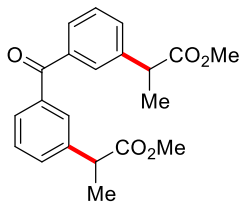
164a
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



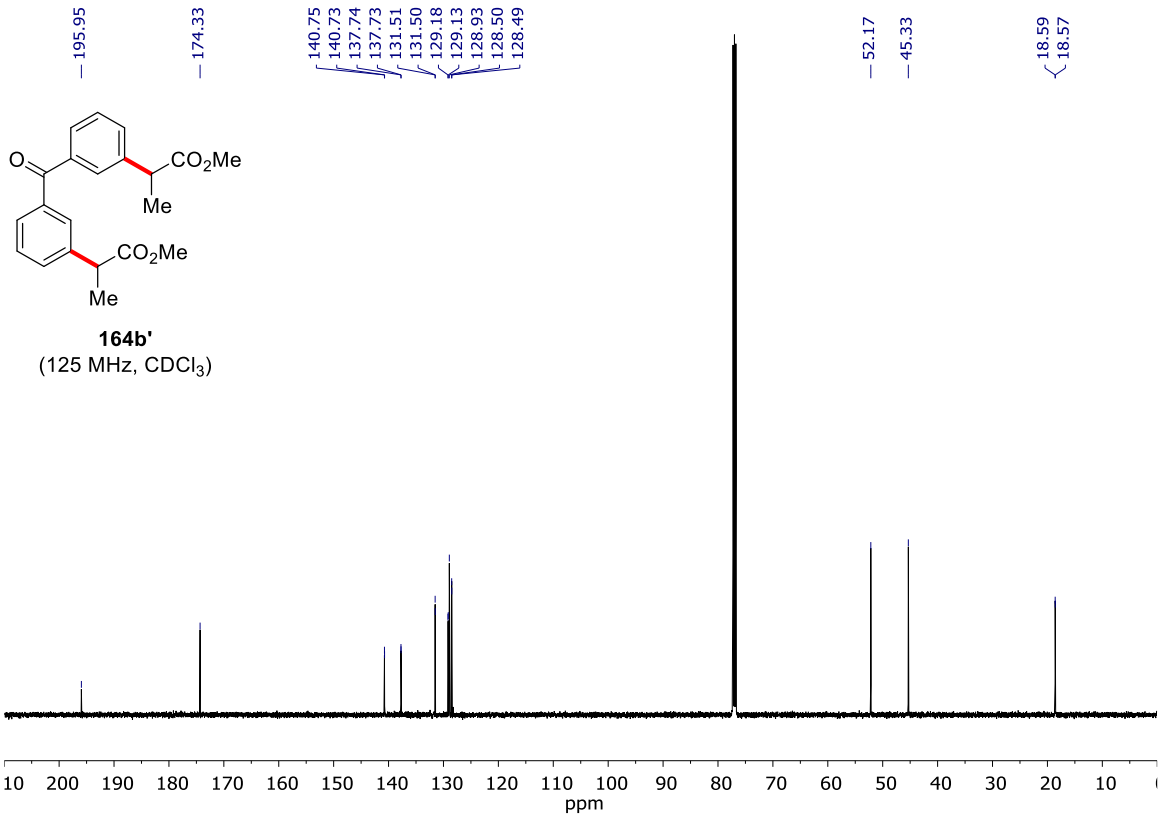
164b
(300 MHz, $CDCl_3$)



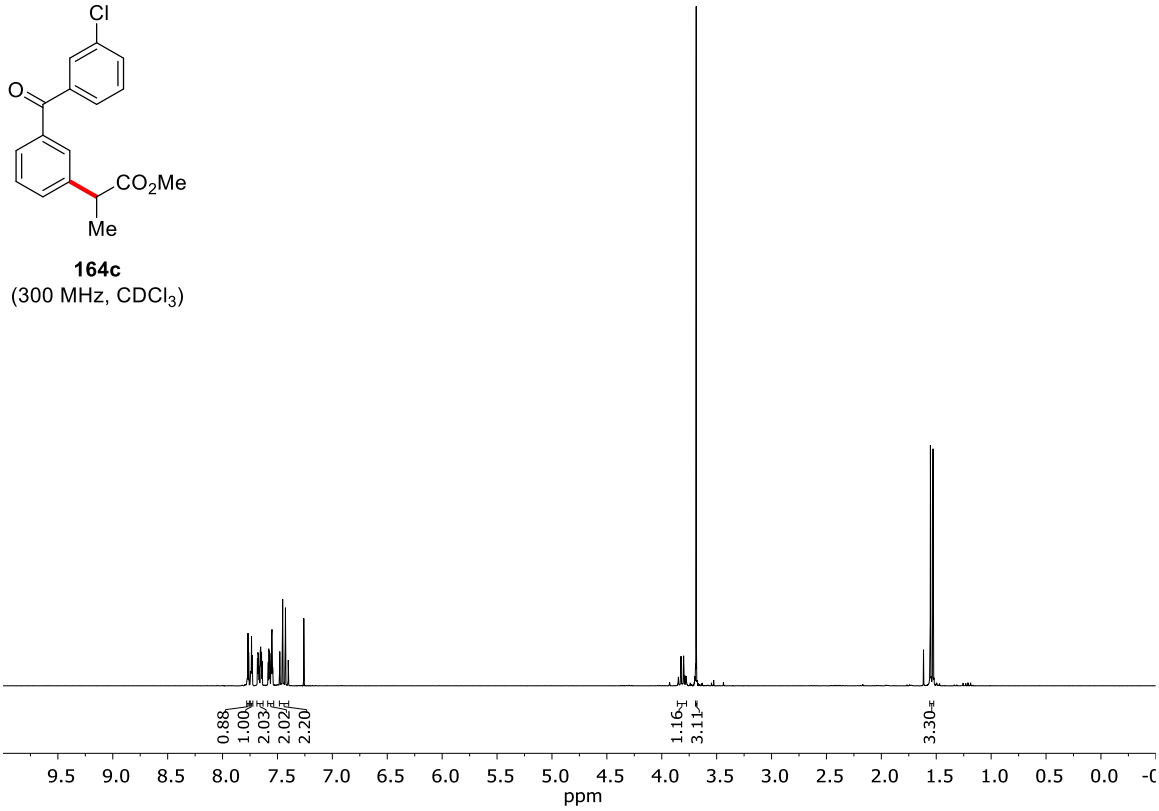
164b
(125 MHz, $CDCl_3$)



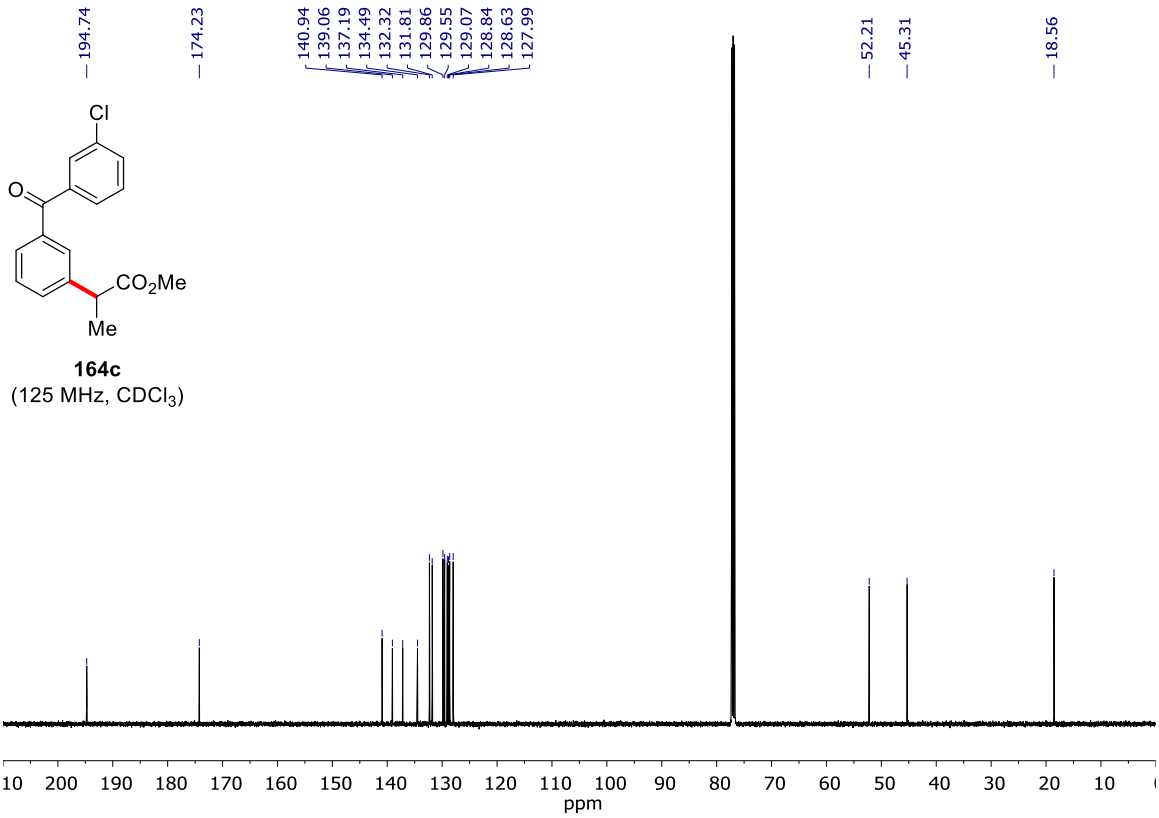
164b'
(600 MHz, $CDCl_3$)



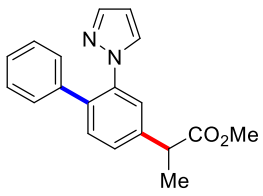
164b'
(125 MHz, $CDCl_3$)



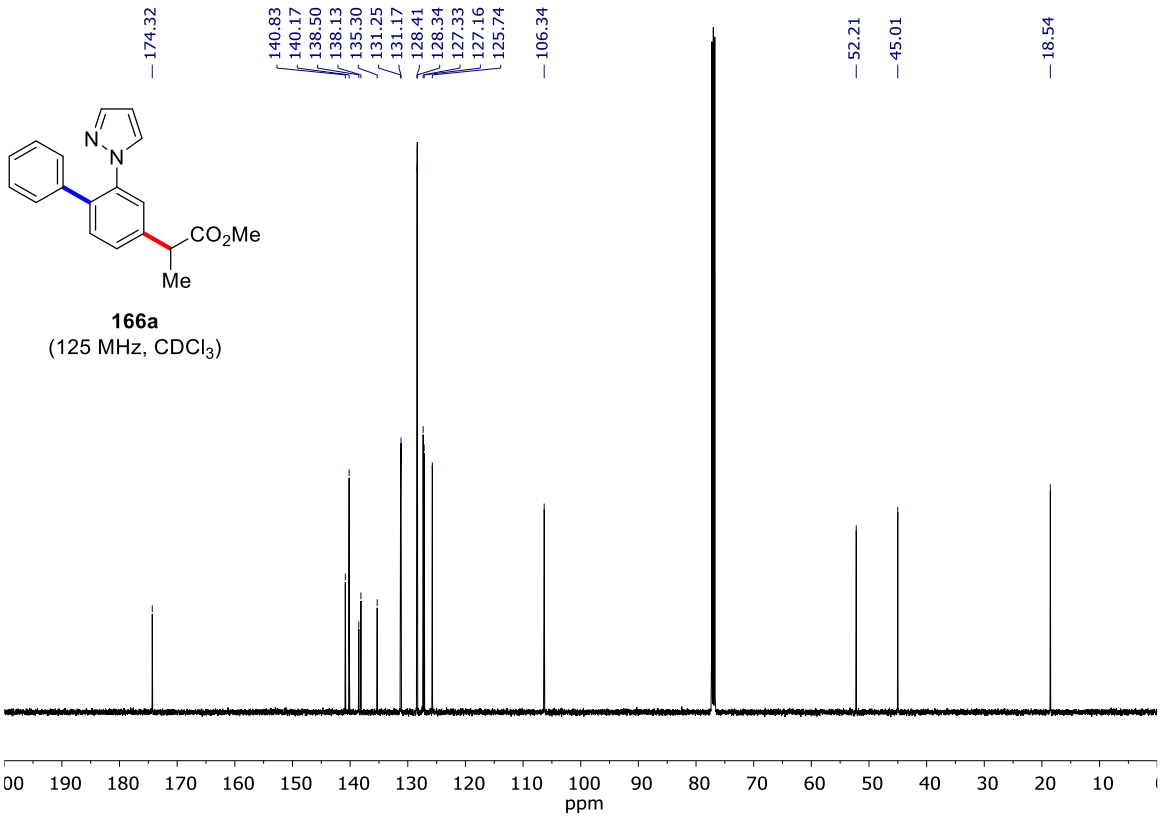
164c
(300 MHz, $CDCl_3$)



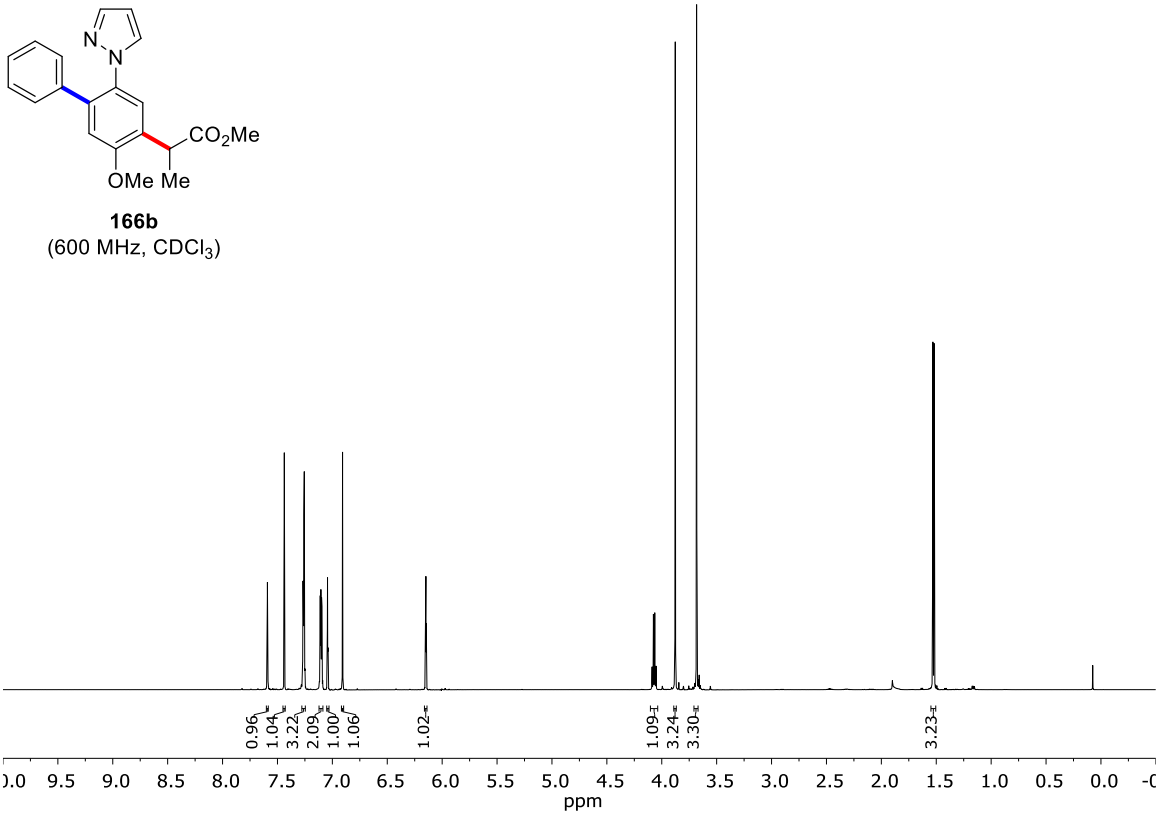
164c
(125 MHz, $CDCl_3$)



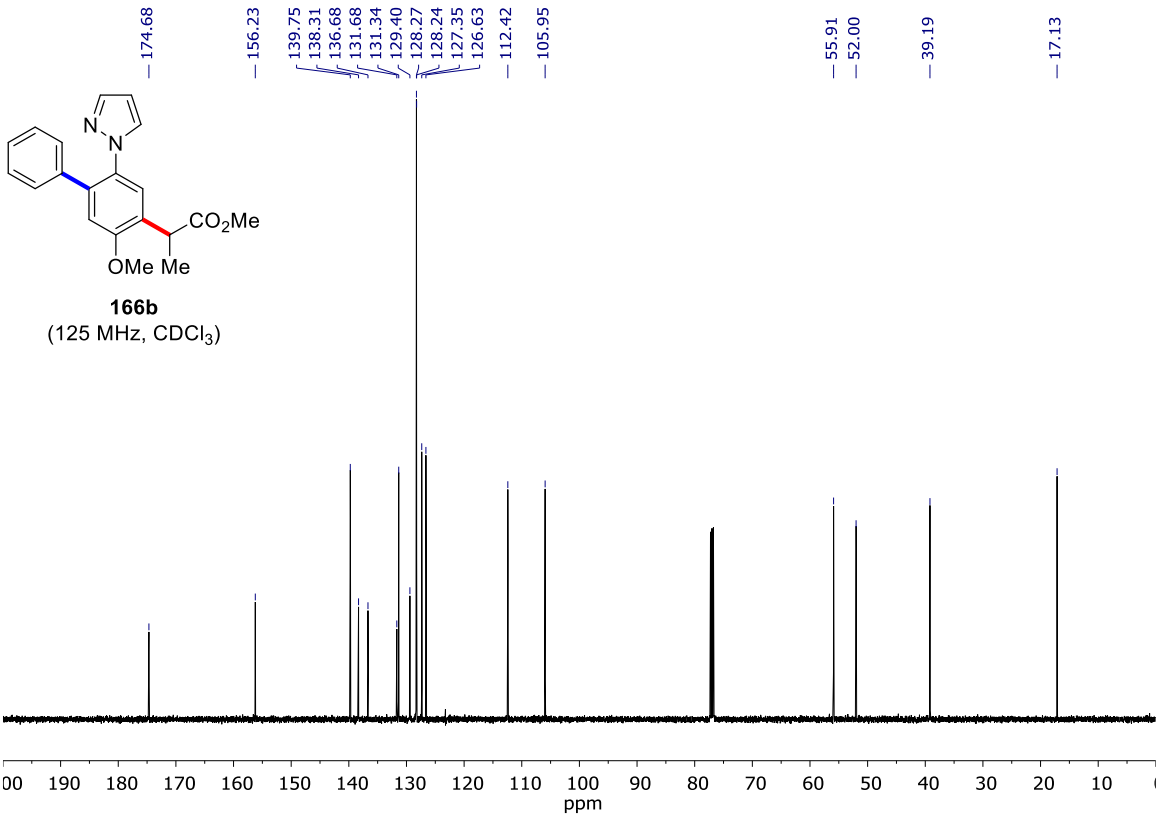
166a
(300 MHz, $CDCl_3$)



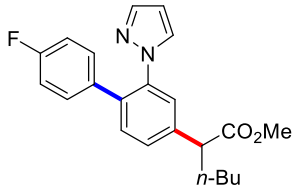
166a
(125 MHz, $CDCl_3$)



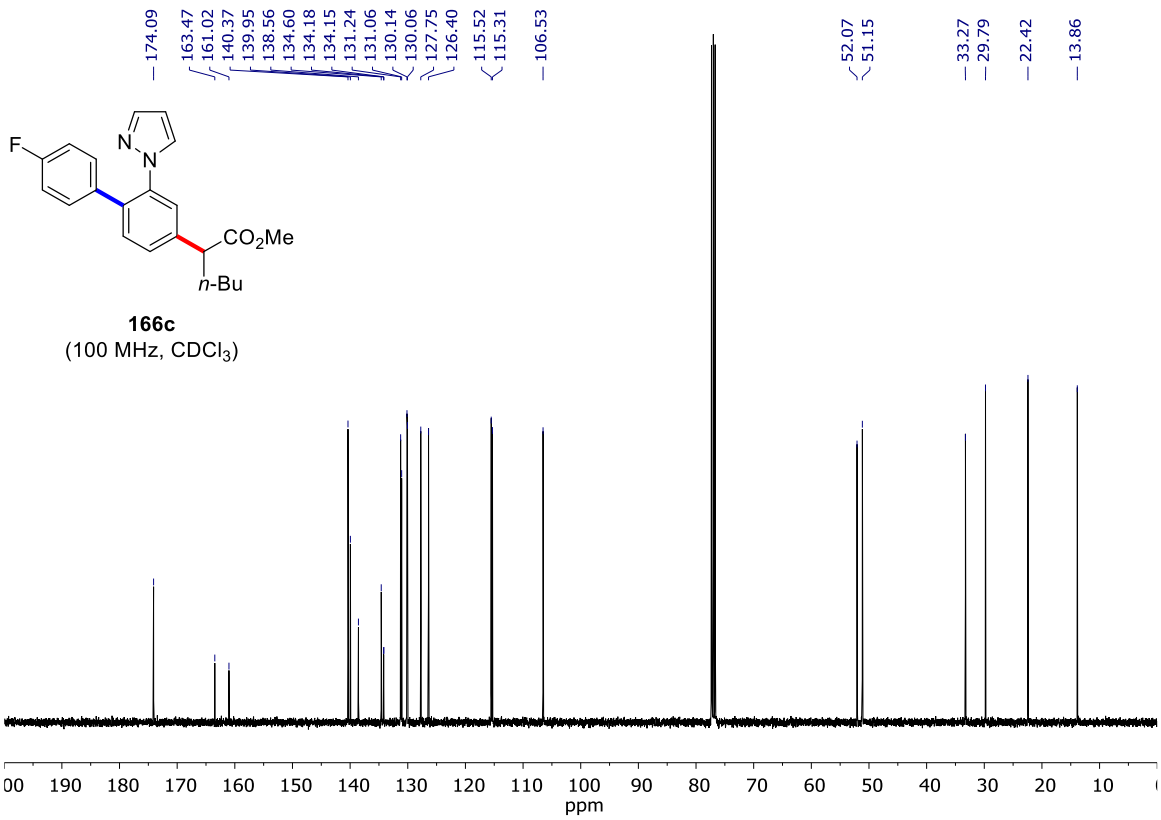
166b
(600 MHz, $CDCl_3$)



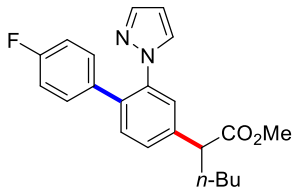
166b
(125 MHz, $CDCl_3$)



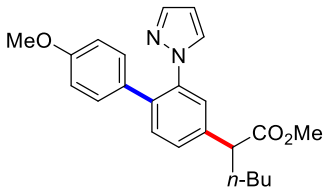
166c
(400 MHz, $CDCl_3$)



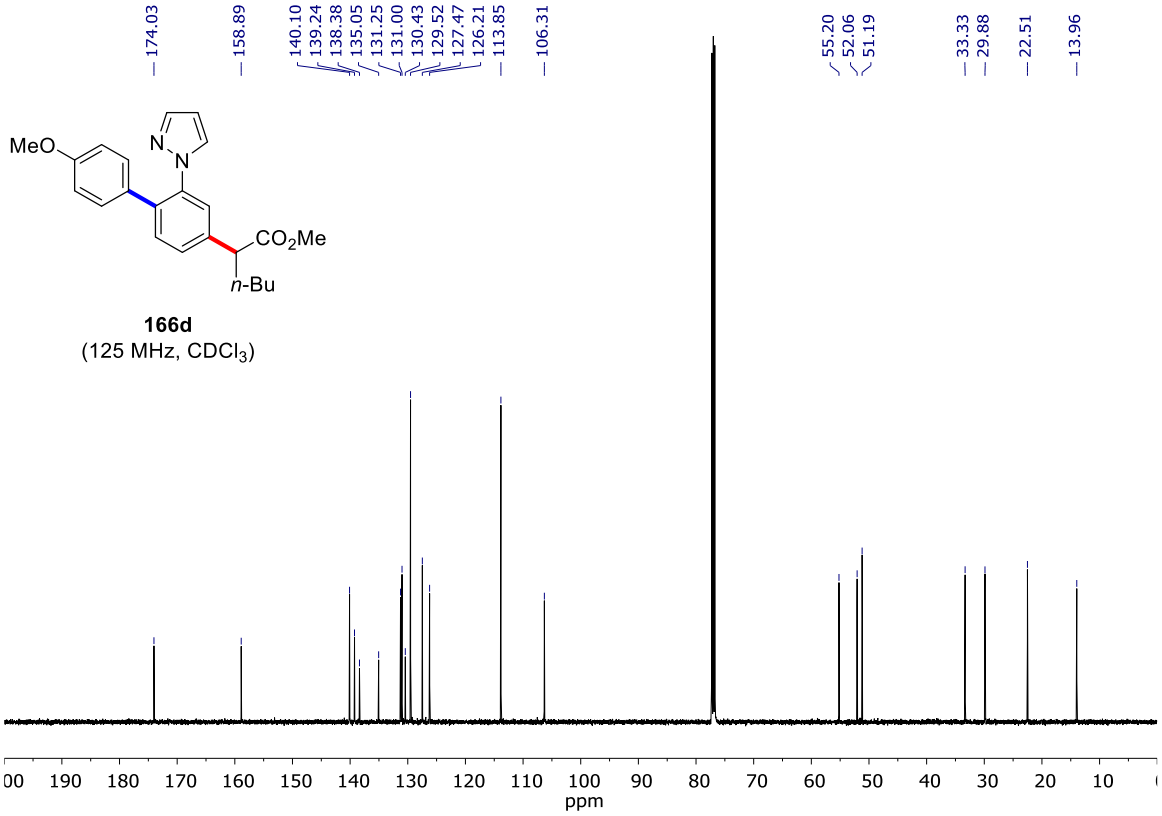
166c
(100 MHz, $CDCl_3$)



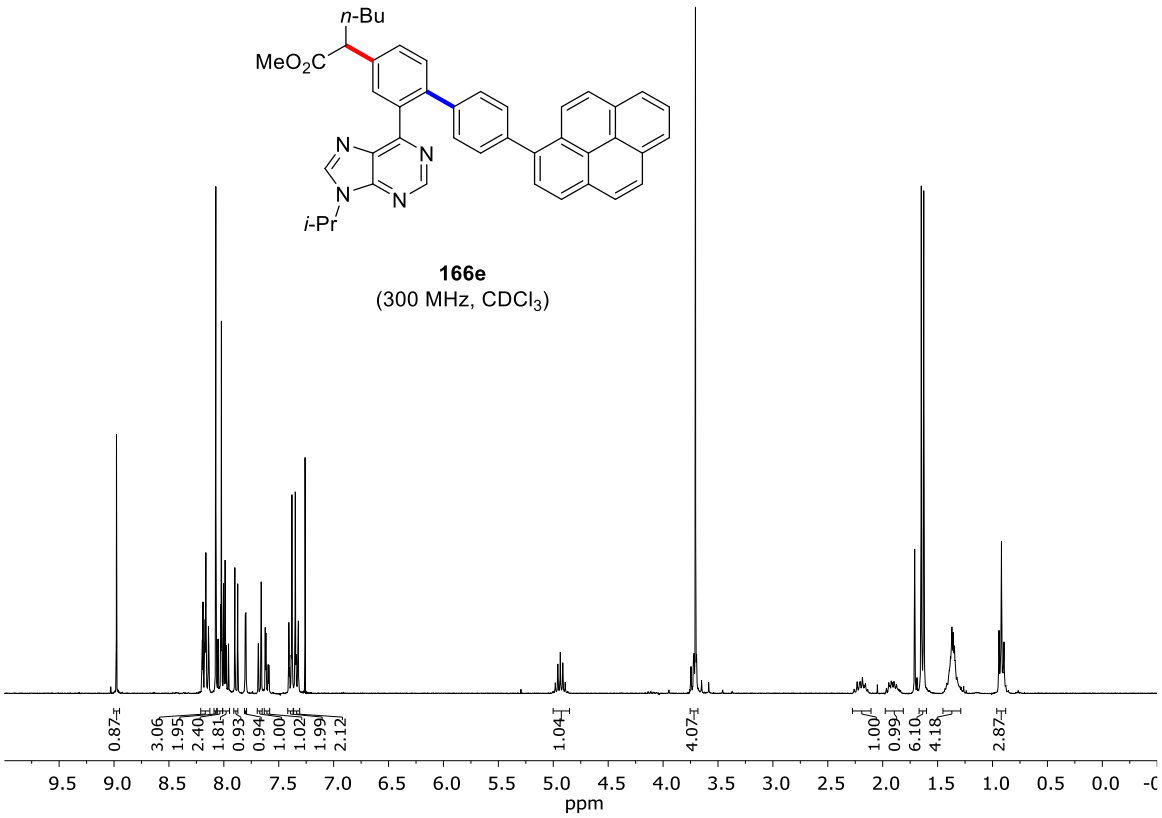
166c
^{19}F-NMR
(376 MHz, $CDCl_3$)



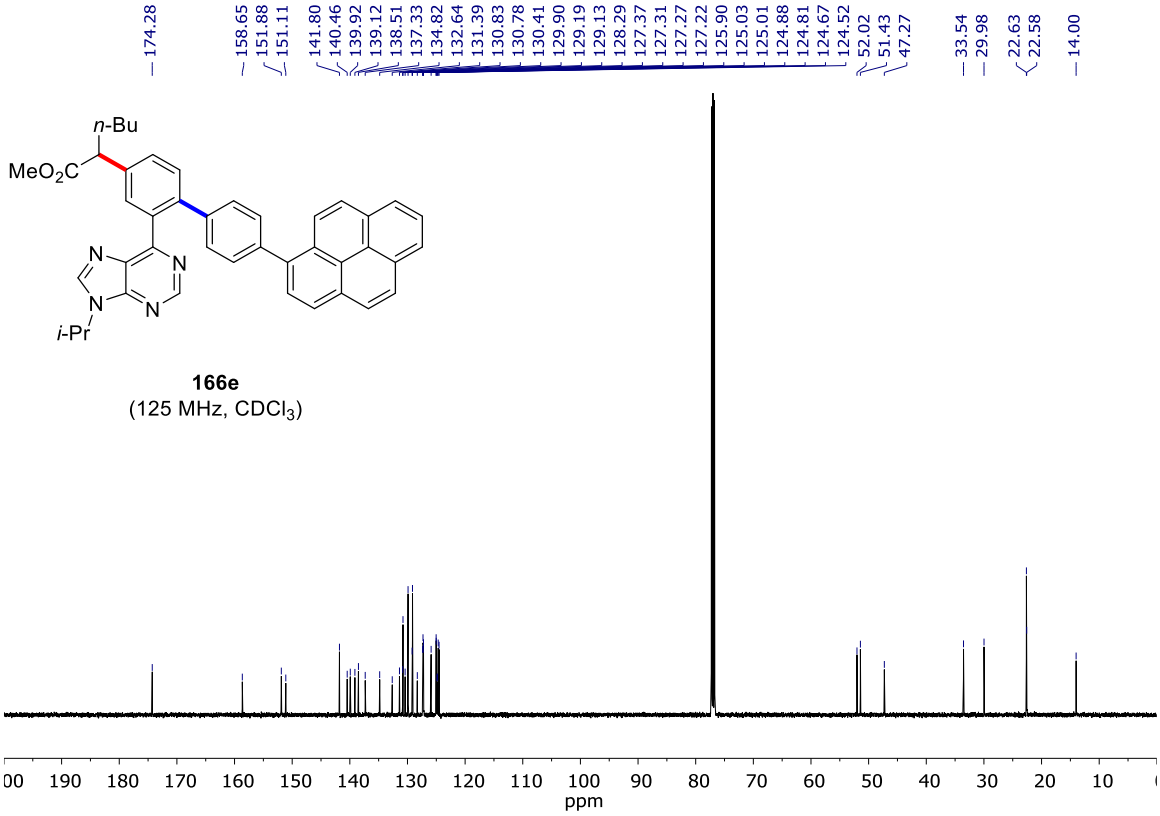
166d
(300 MHz, $CDCl_3$)

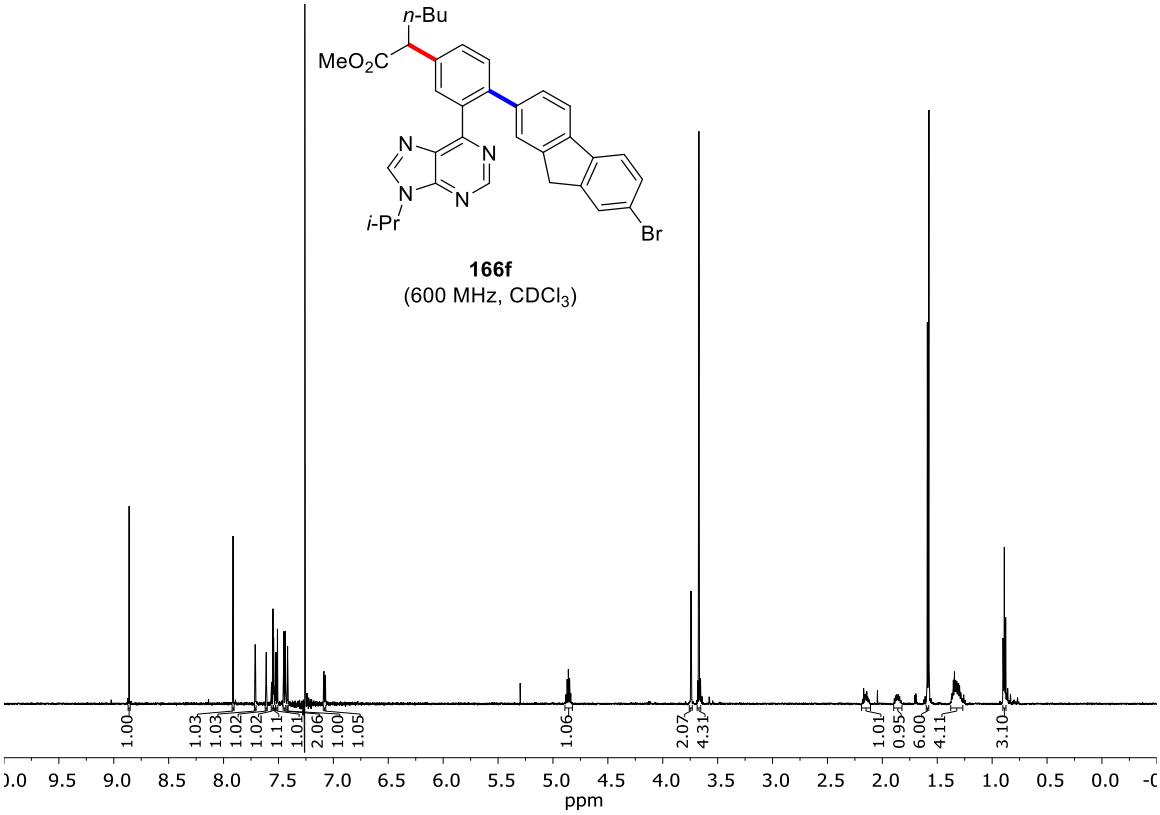


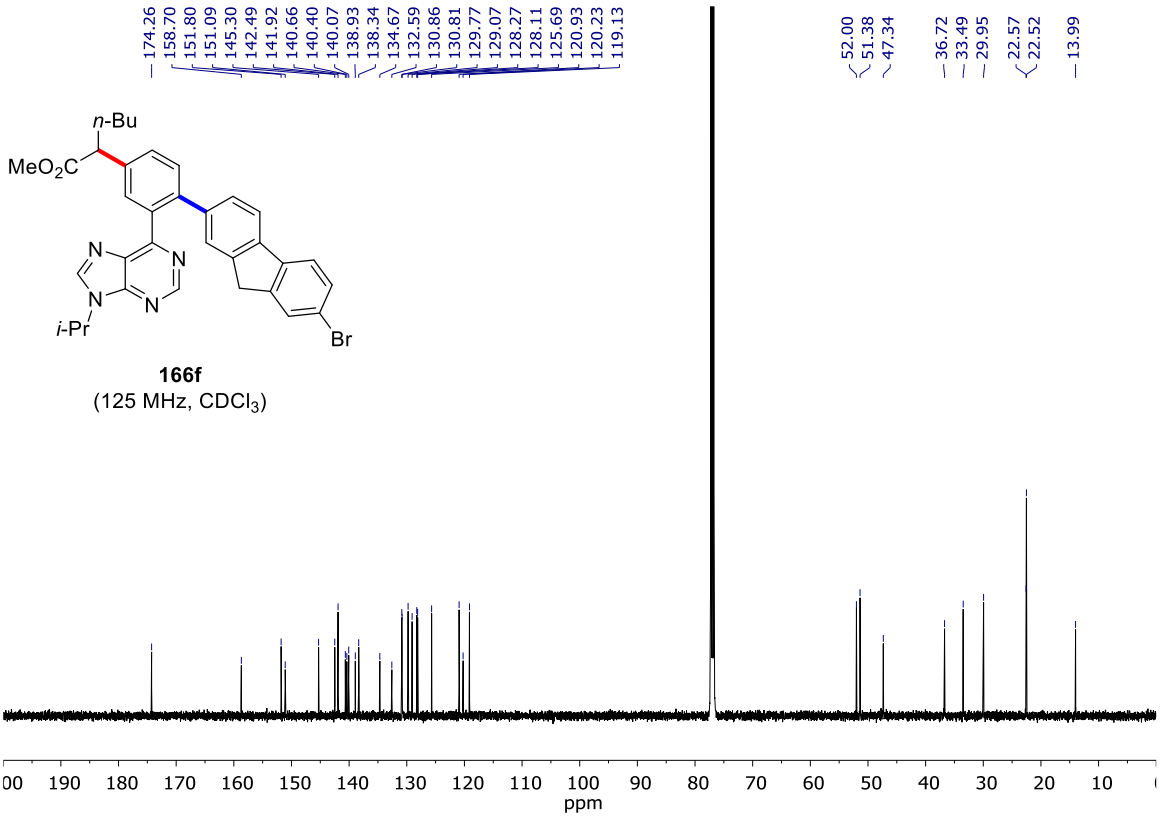
166d
(125 MHz, $CDCl_3$)



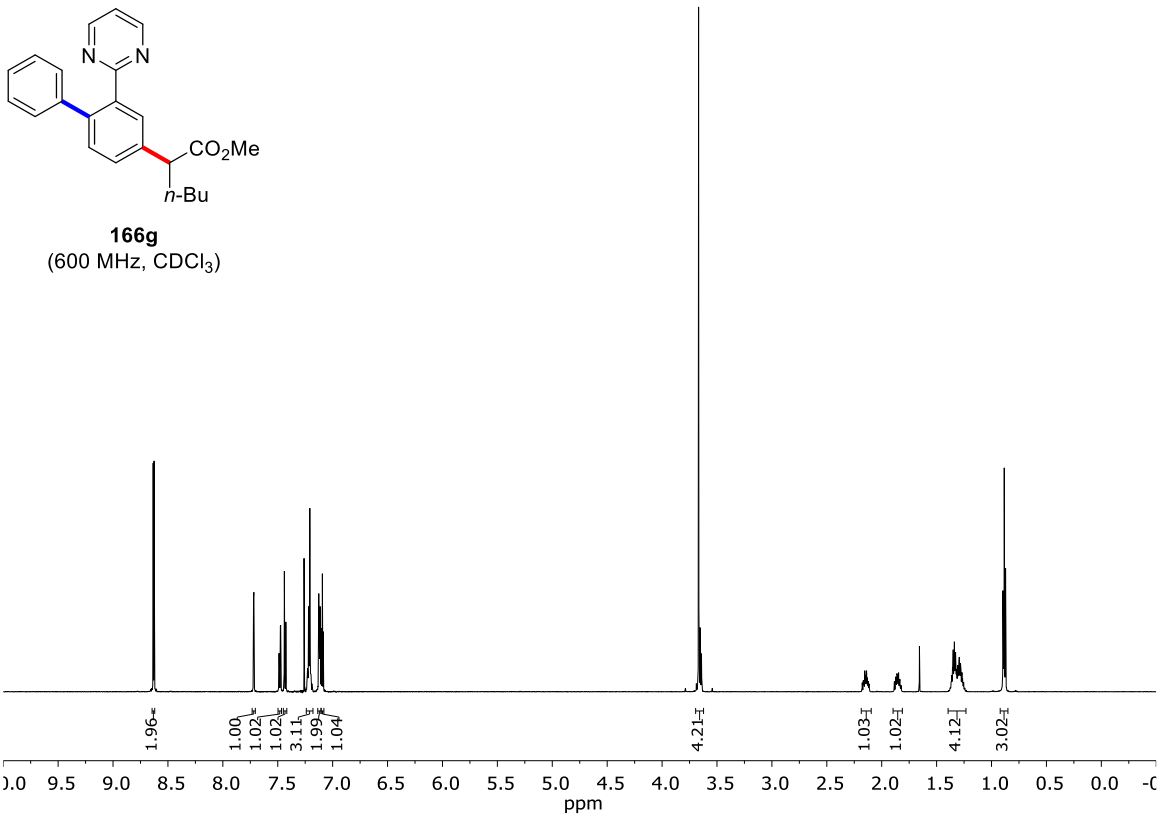
166e
(300 MHz, $CDCl_3$)


174.28
158.65
151.88
151.11
141.80
140.46
139.92
139.12
138.51
137.33
134.82
132.64
131.39
130.83
130.78
130.41
129.90
129.19
129.13
128.29
127.37
127.31
127.27
127.22
125.90
125.03
125.01
124.88
124.81
124.67
124.52
52.02
51.43
47.27
33.54
29.98
22.63
22.58
14.00
n-Bu
MeO2C
N
N
N
N
i-Pr
166e
(125 MHz, CDCl3)
ppm

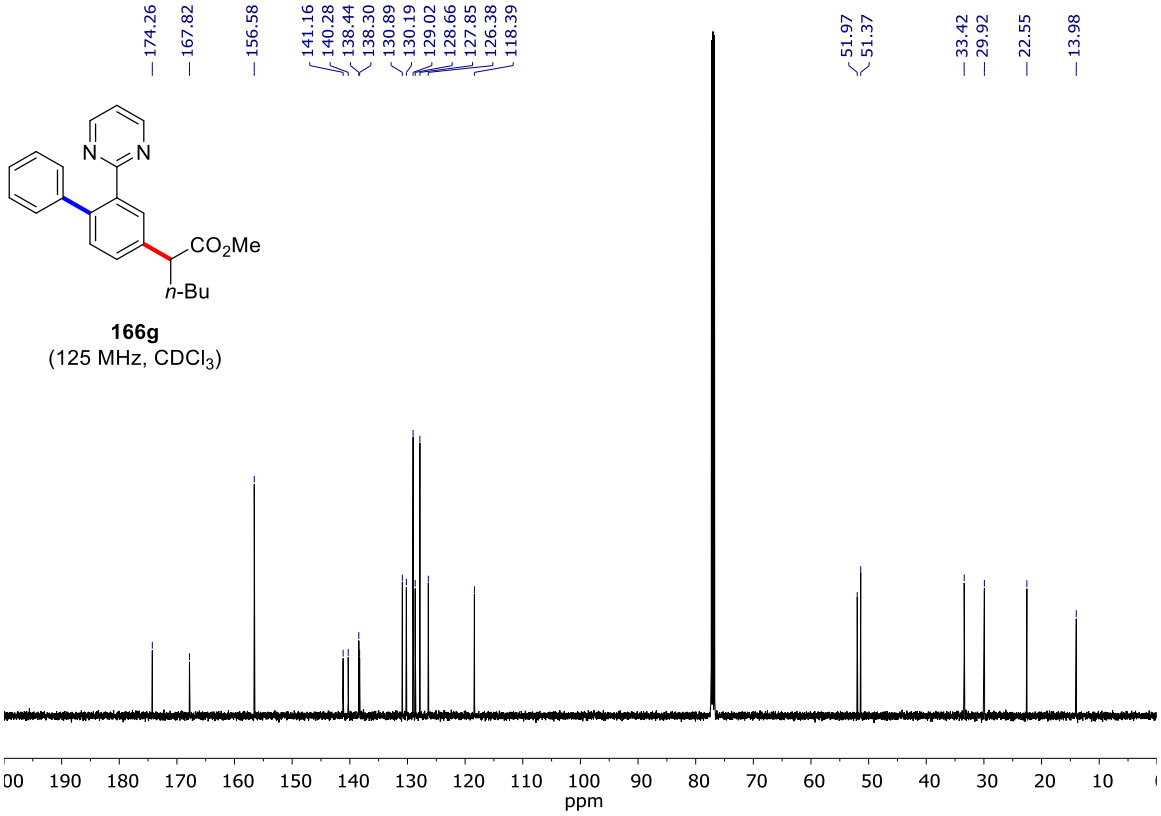

n-Bu
MeO2C
N
N
N
N
i-Pr
Br
166f
(600 MHz, CDCl3)
1.00
1.03
1.03
1.02
1.02
1.11
1.01
2.06
1.00
1.05
1.06
2.07
4.31
1.01
0.95
6.00
4.11
3.10
ppm



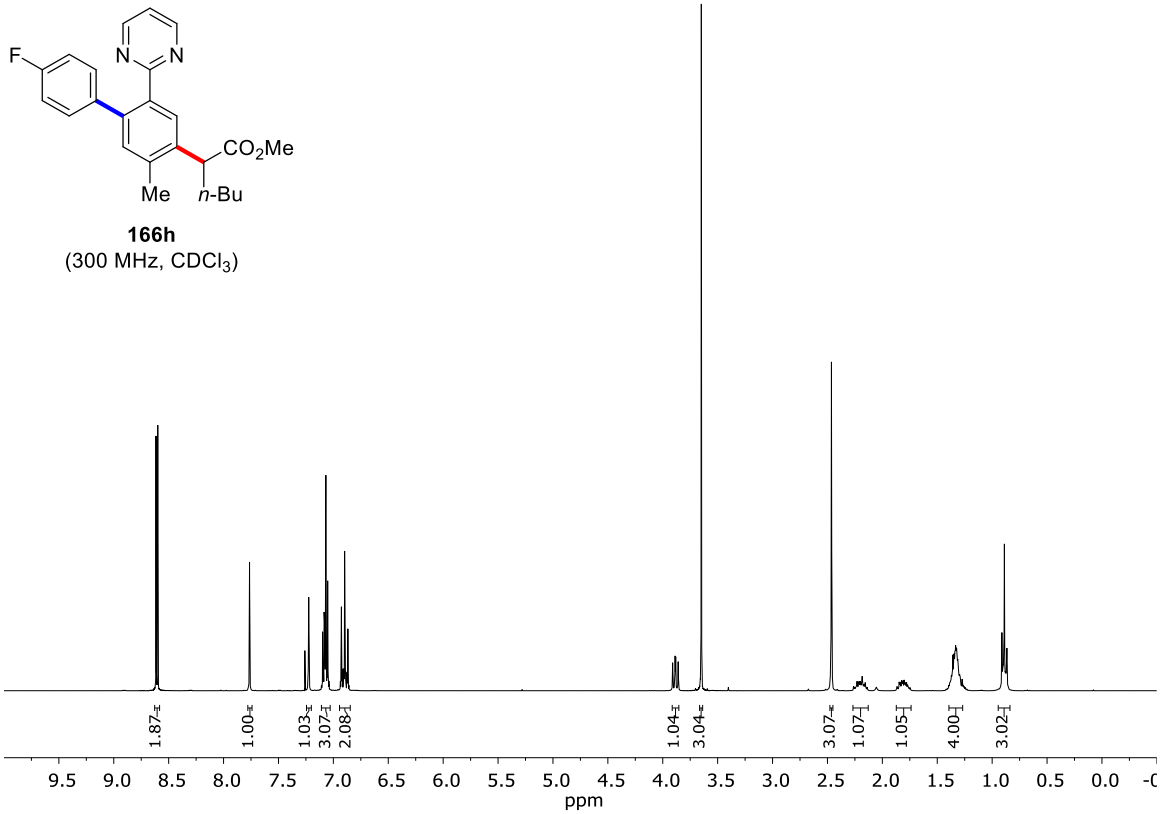
166f
(125 MHz, $CDCl_3$)



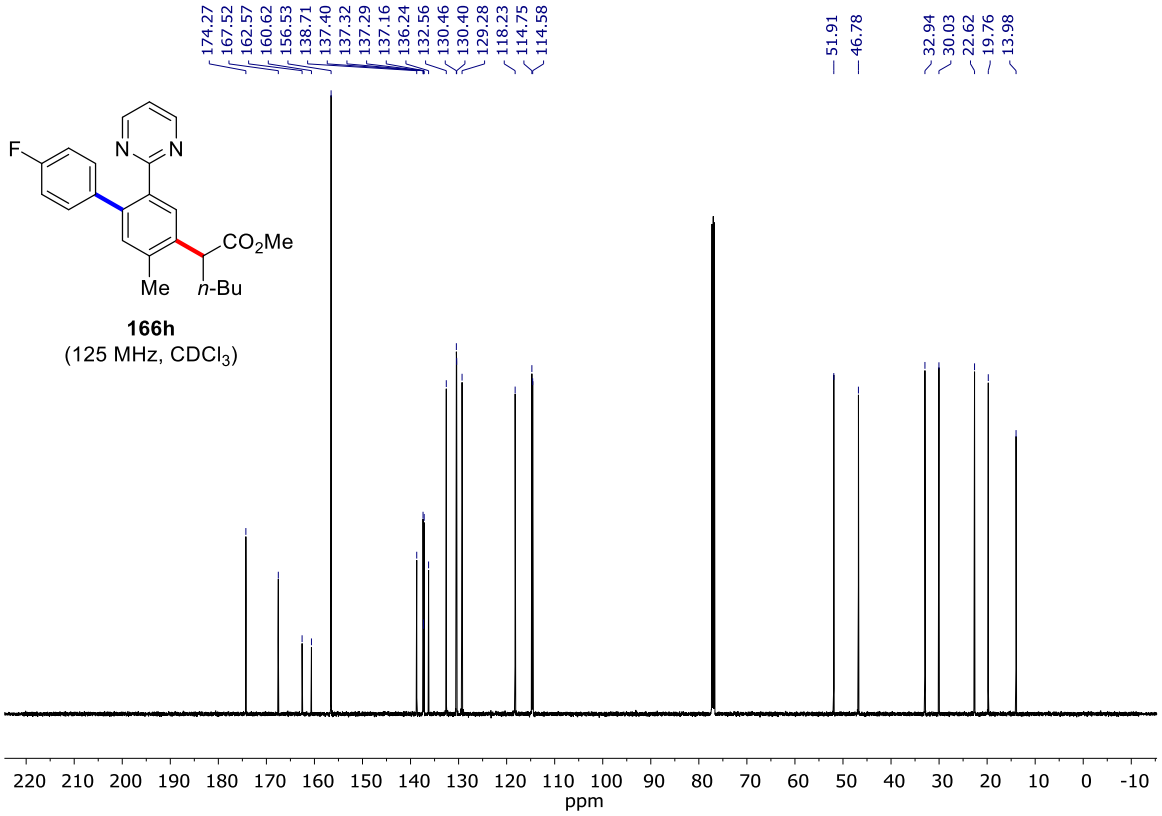
166g
(600 MHz, $CDCl_3$)



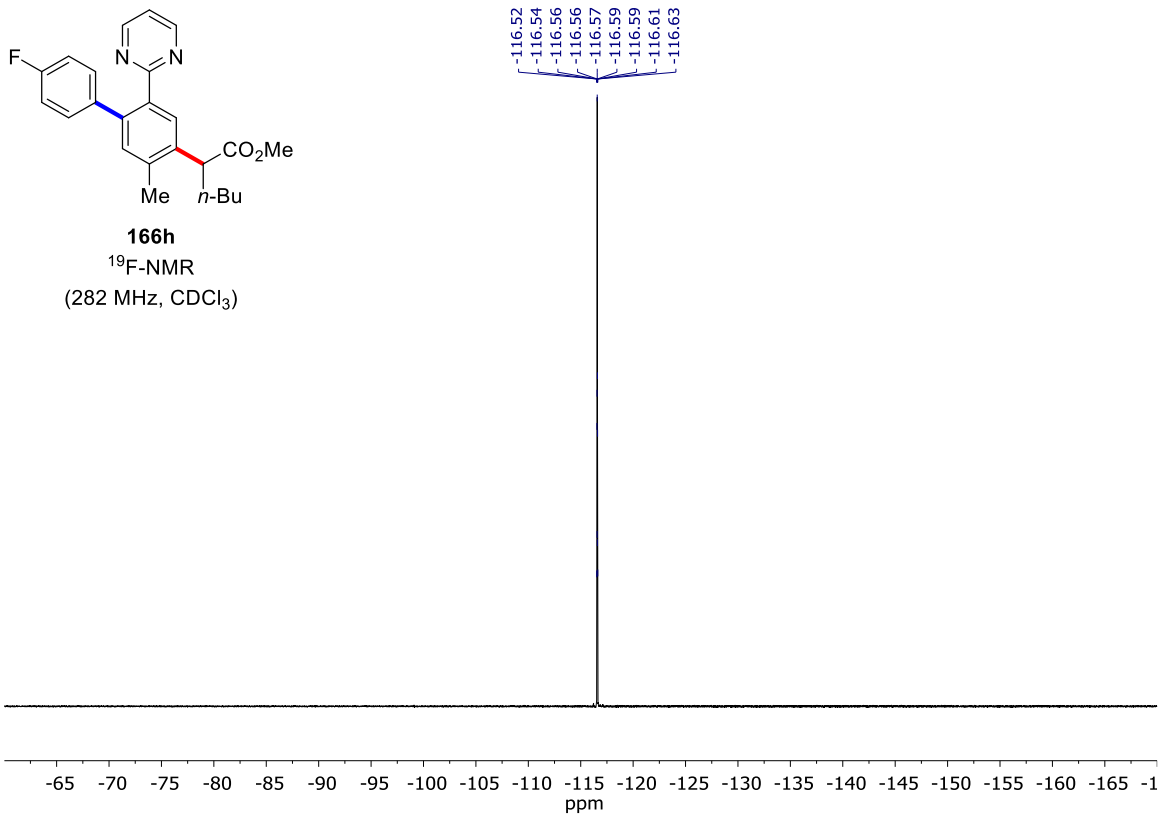
166g
(125 MHz, $CDCl_3$)



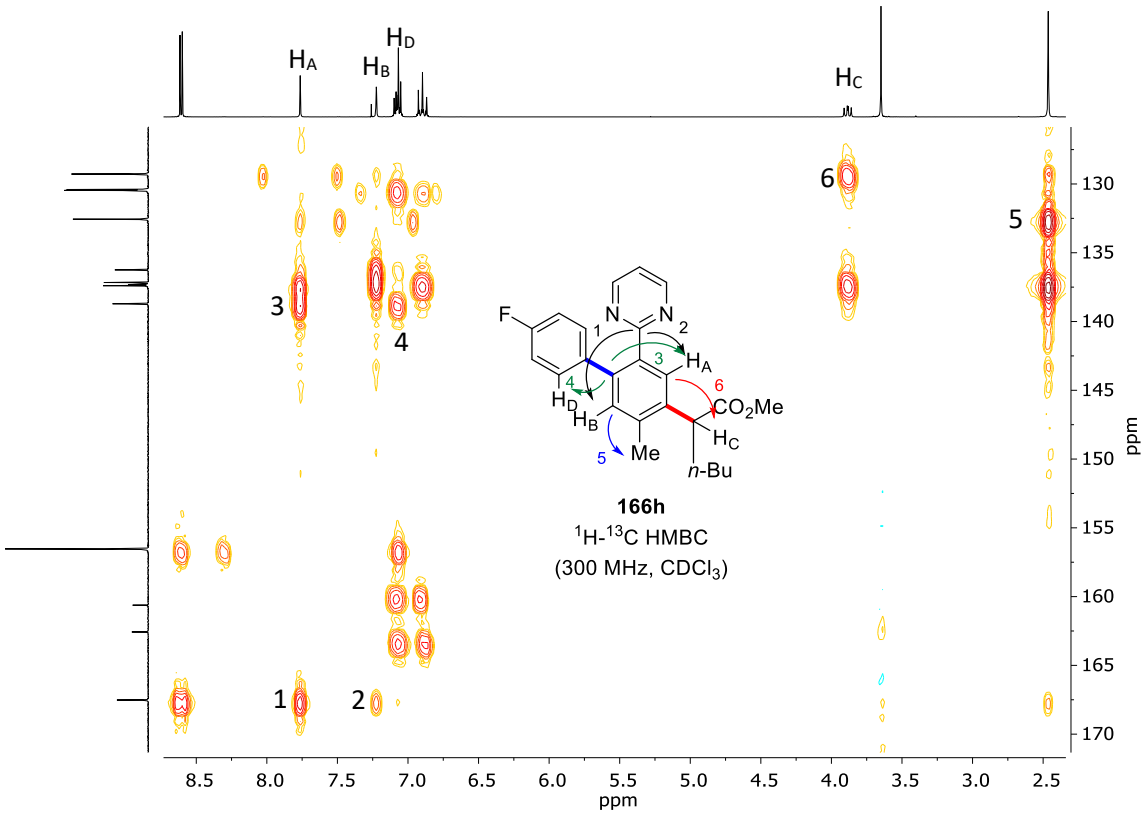
166h
(300 MHz, $CDCl_3$)



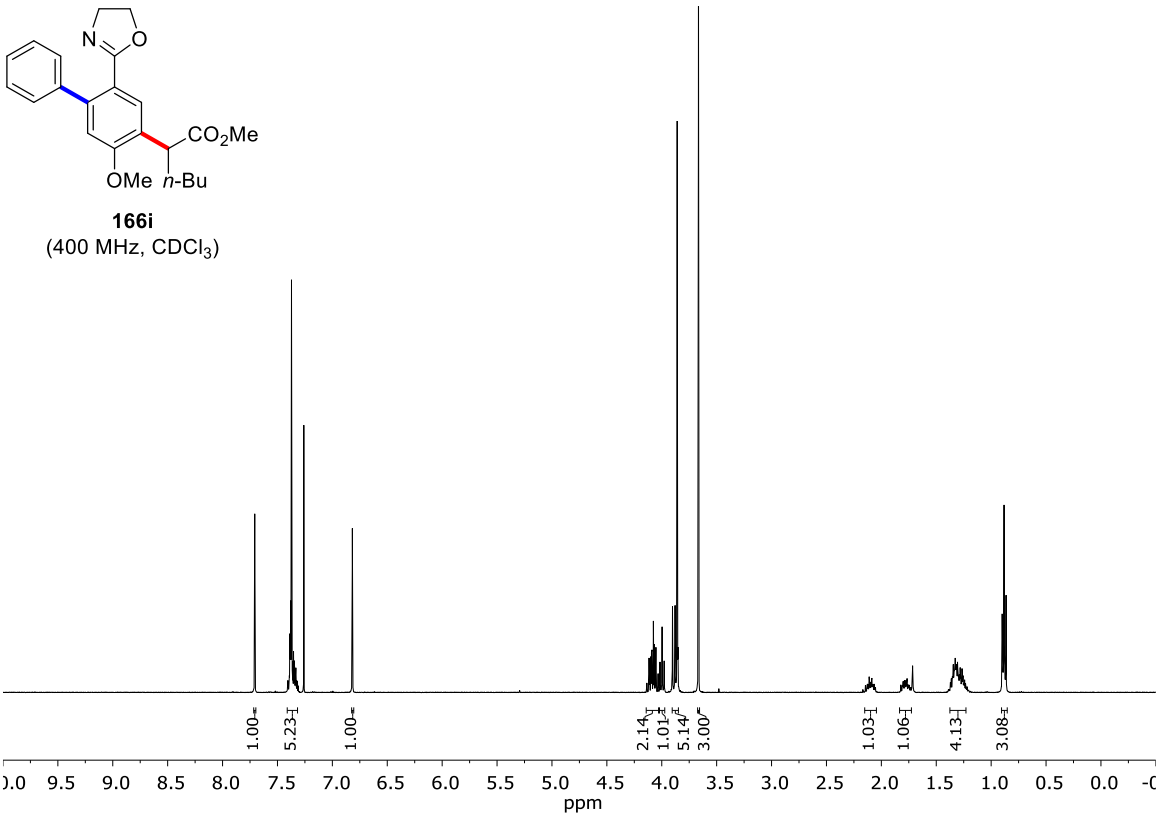
166h
(125 MHz, $CDCl_3$)



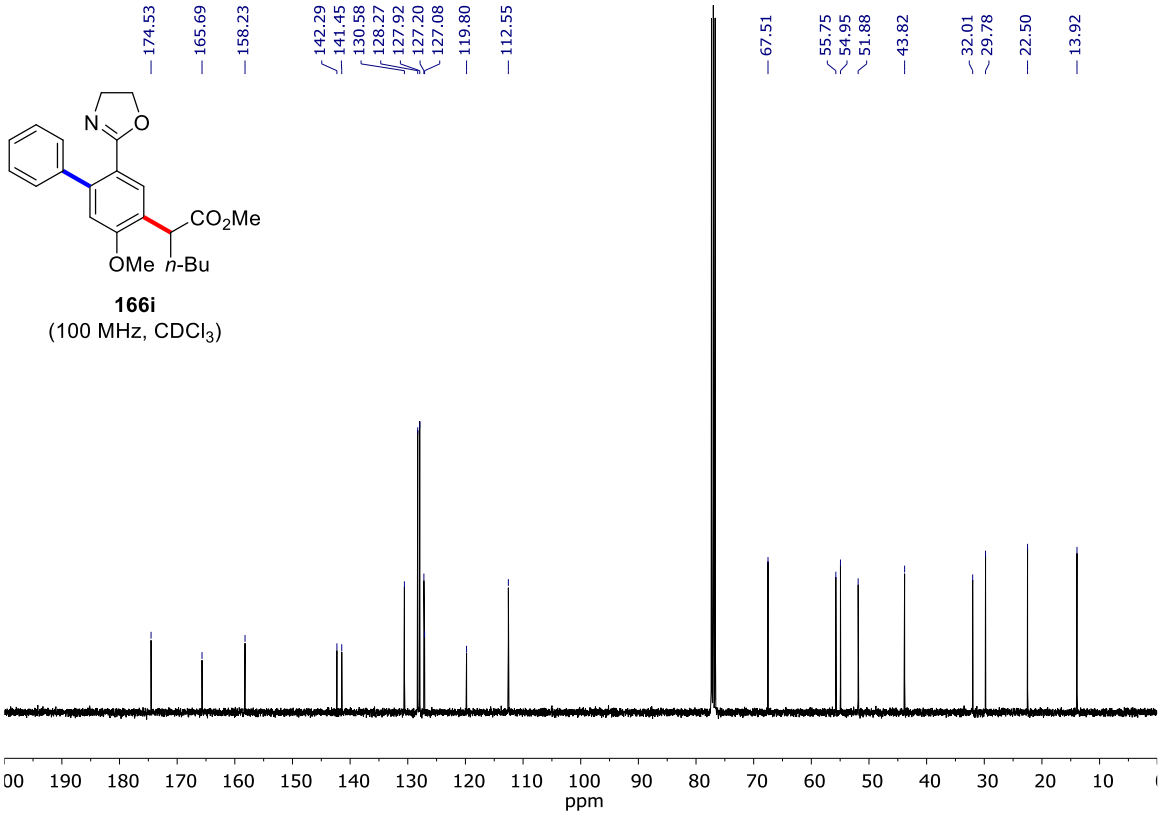
166h
^{19}F-NMR
(282 MHz, $CDCl_3$)



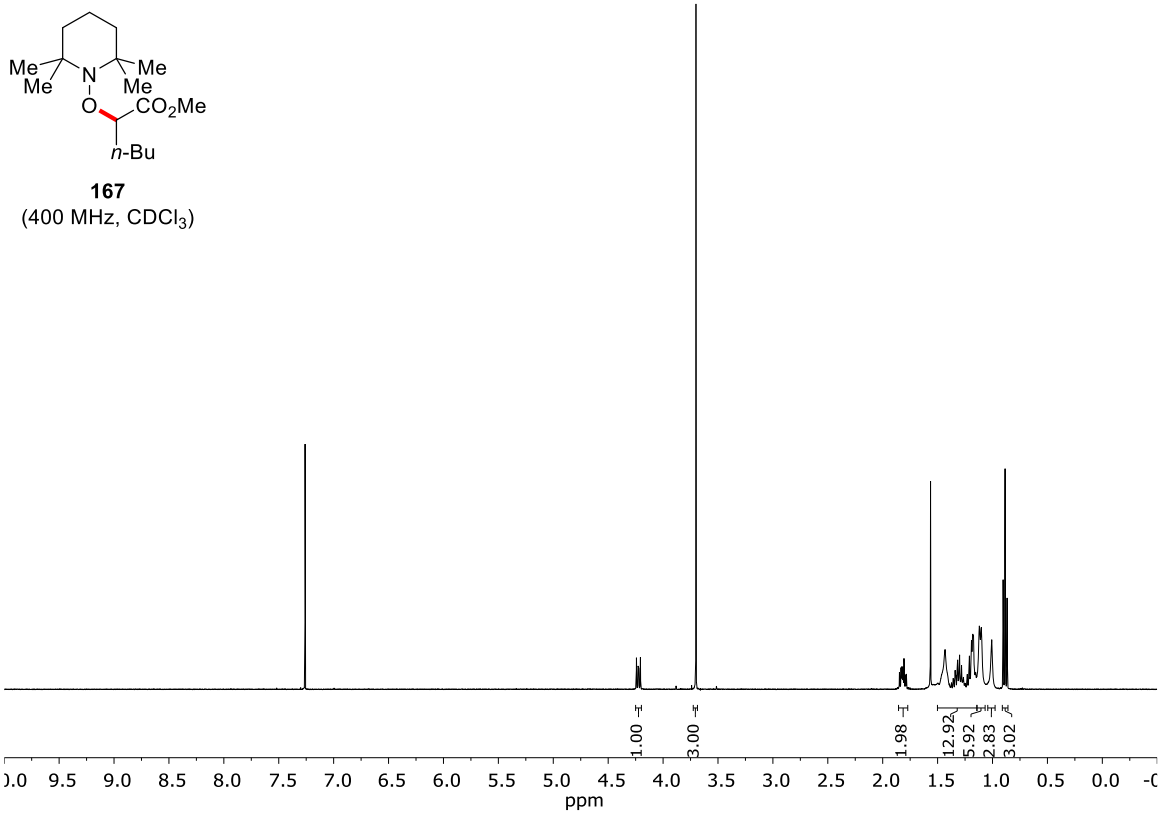
166h
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



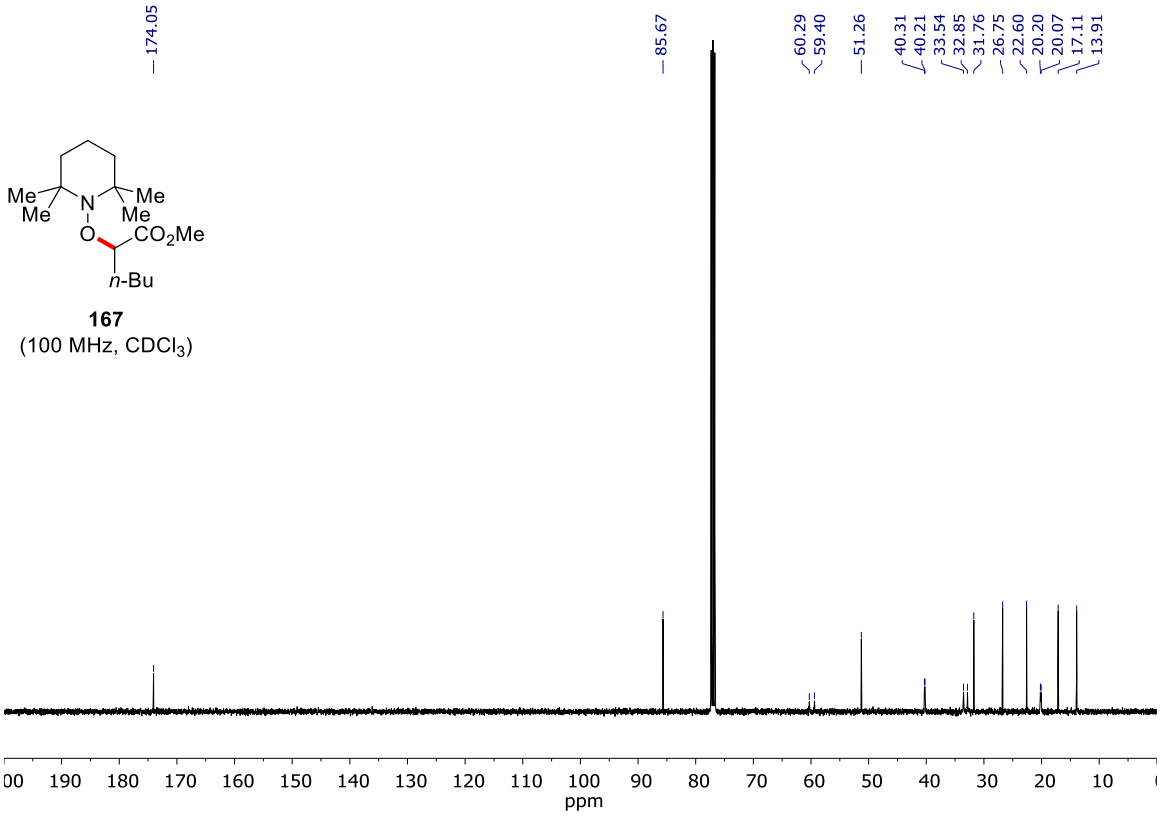
166i
(400 MHz, $CDCl_3$)



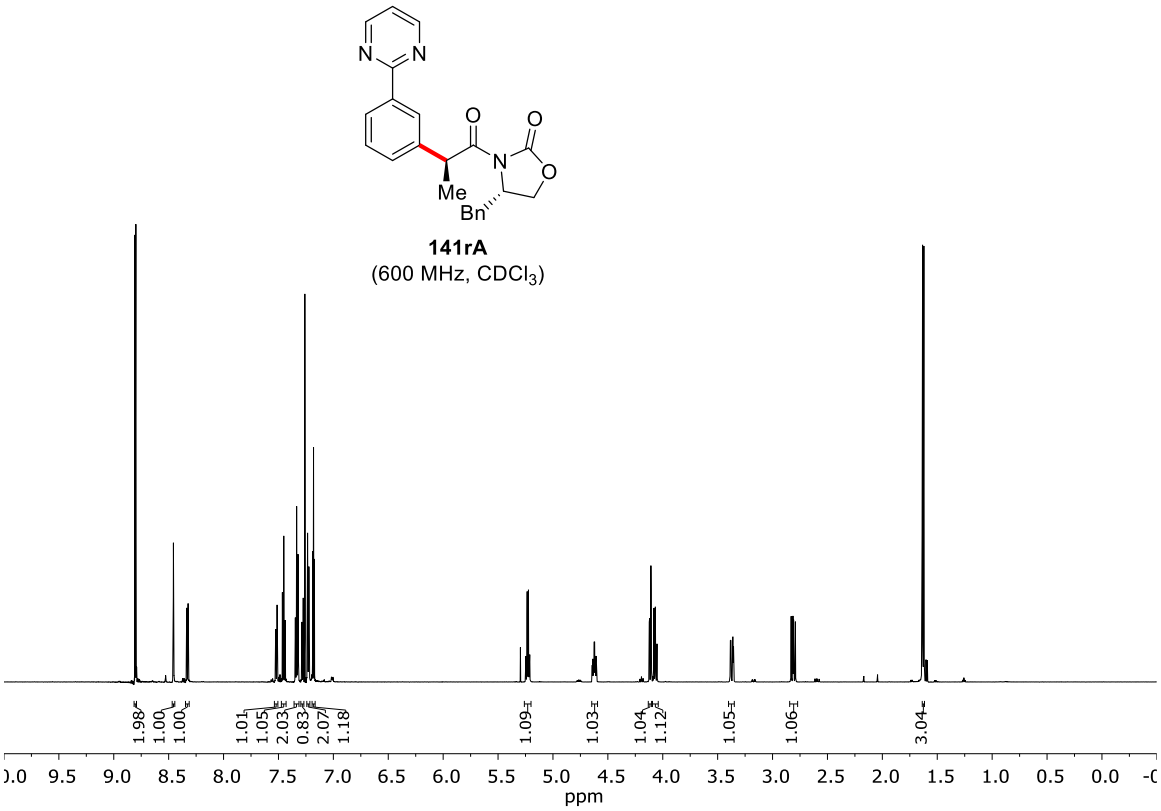
166i
(100 MHz, $CDCl_3$)



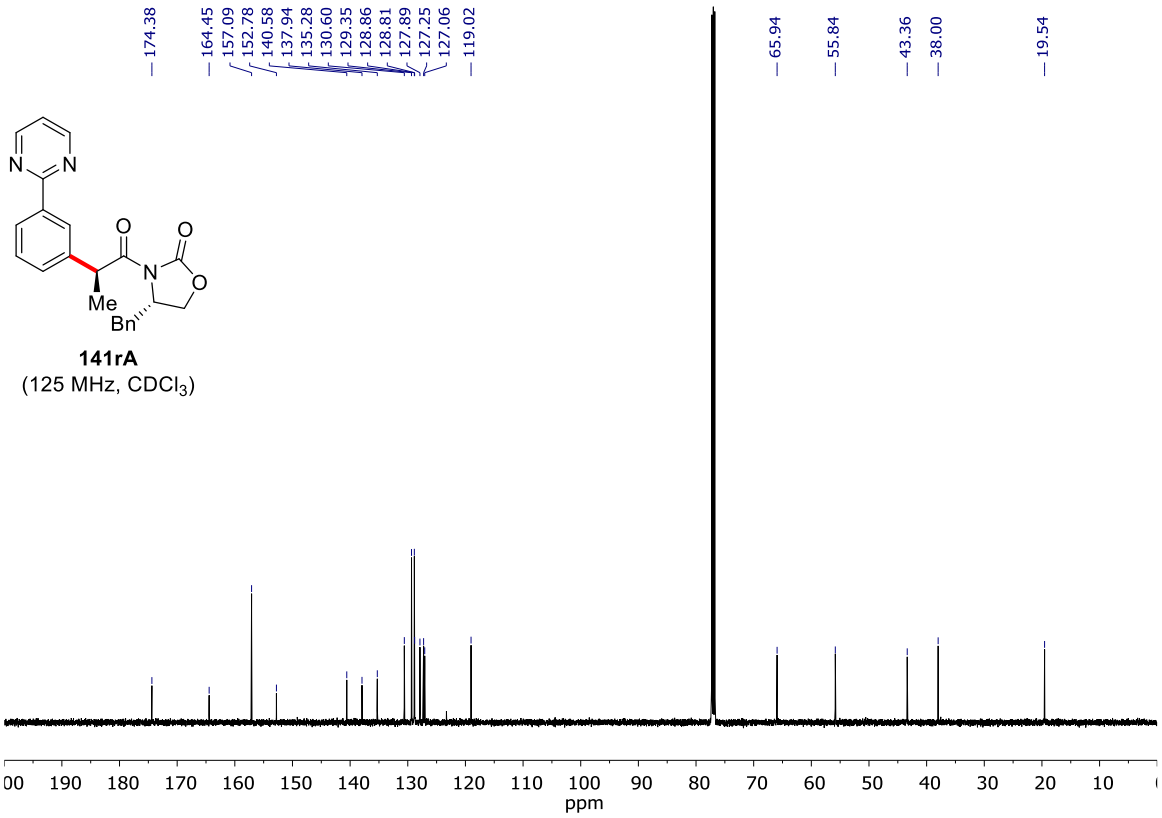
167
(400 MHz, $CDCl_3$)



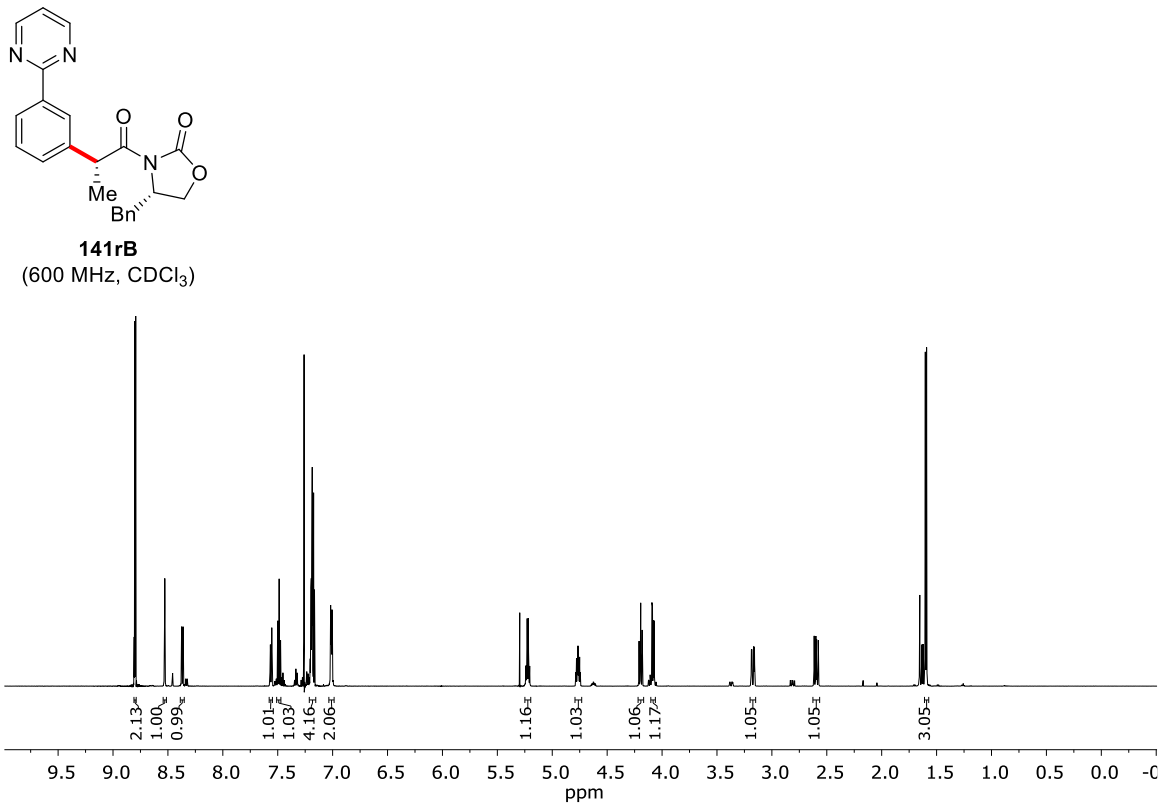
167
(100 MHz, $CDCl_3$)



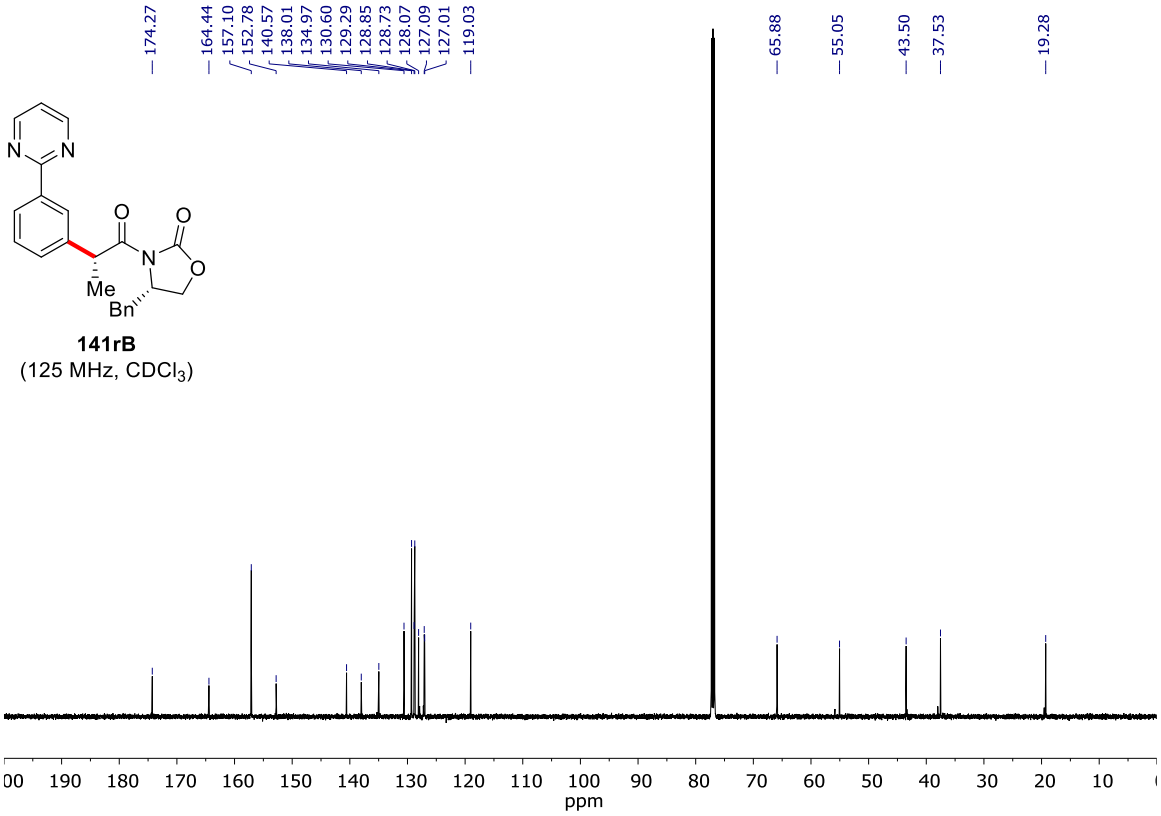
141rA
(600 MHz, $CDCl_3$)



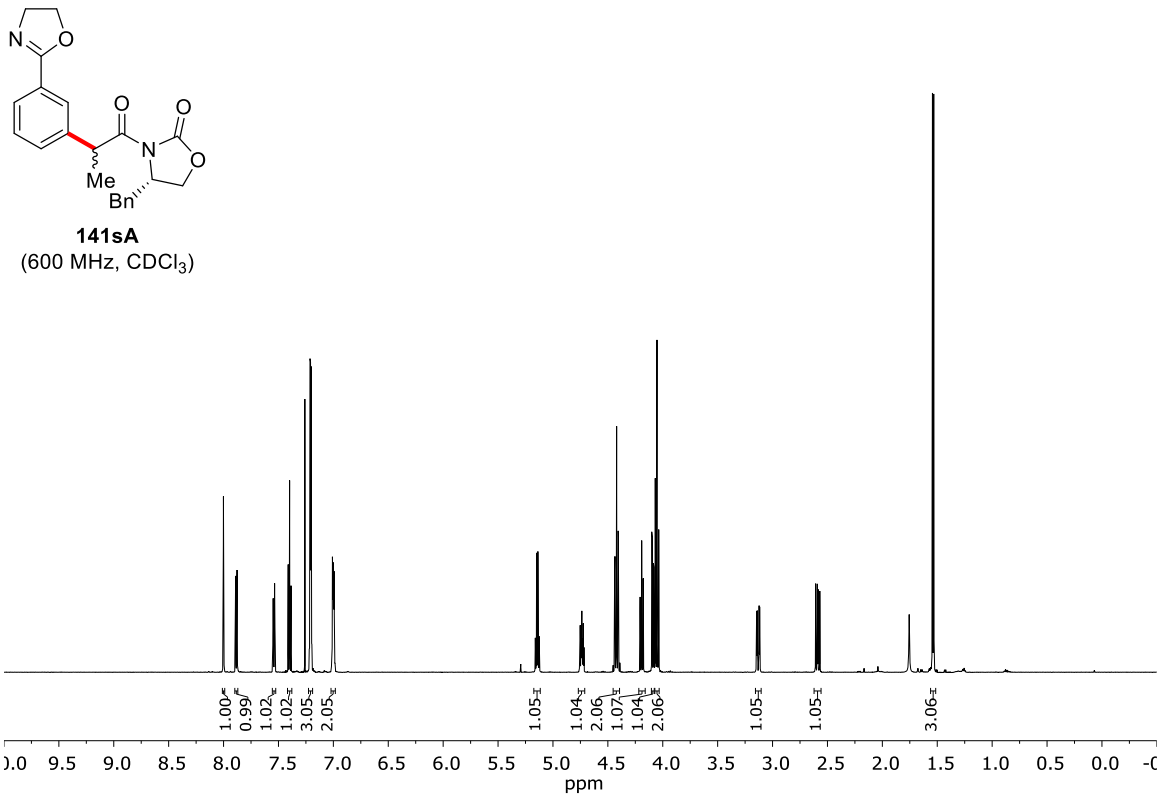
141rA
(125 MHz, $CDCl_3$)



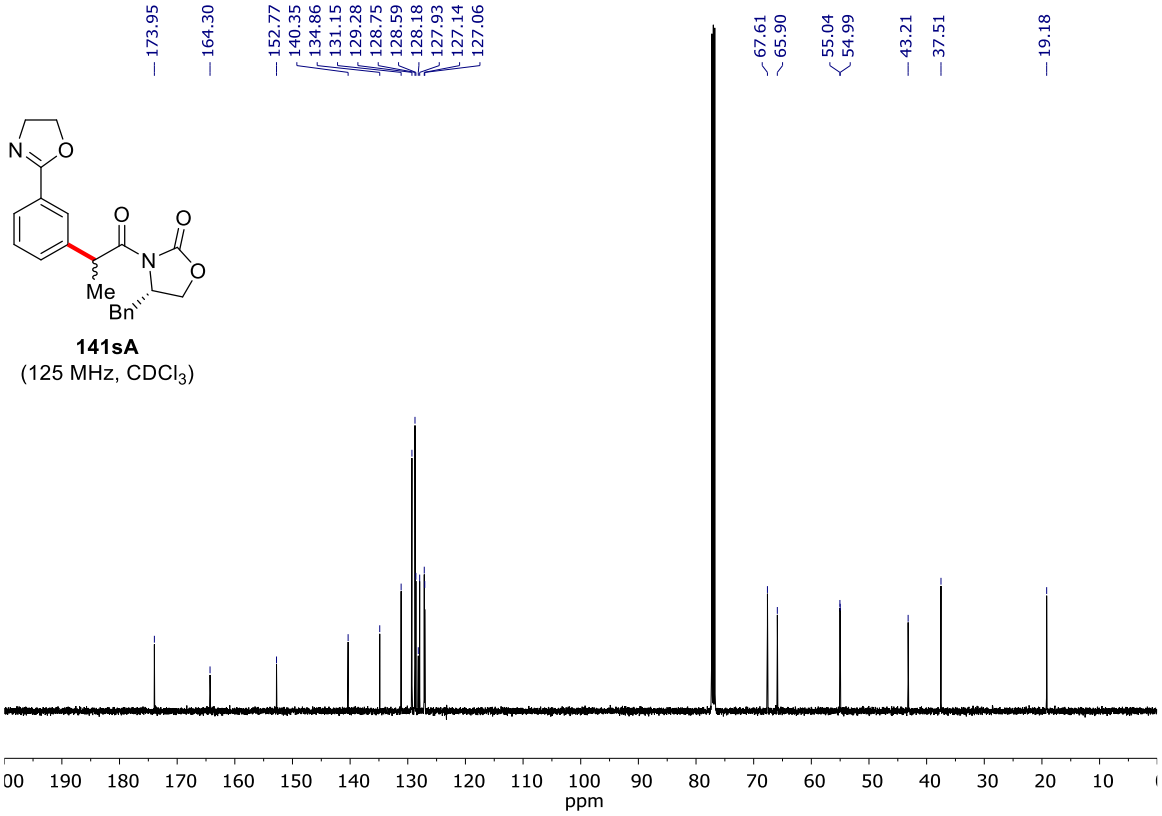
141rB
(600 MHz, $CDCl_3$)



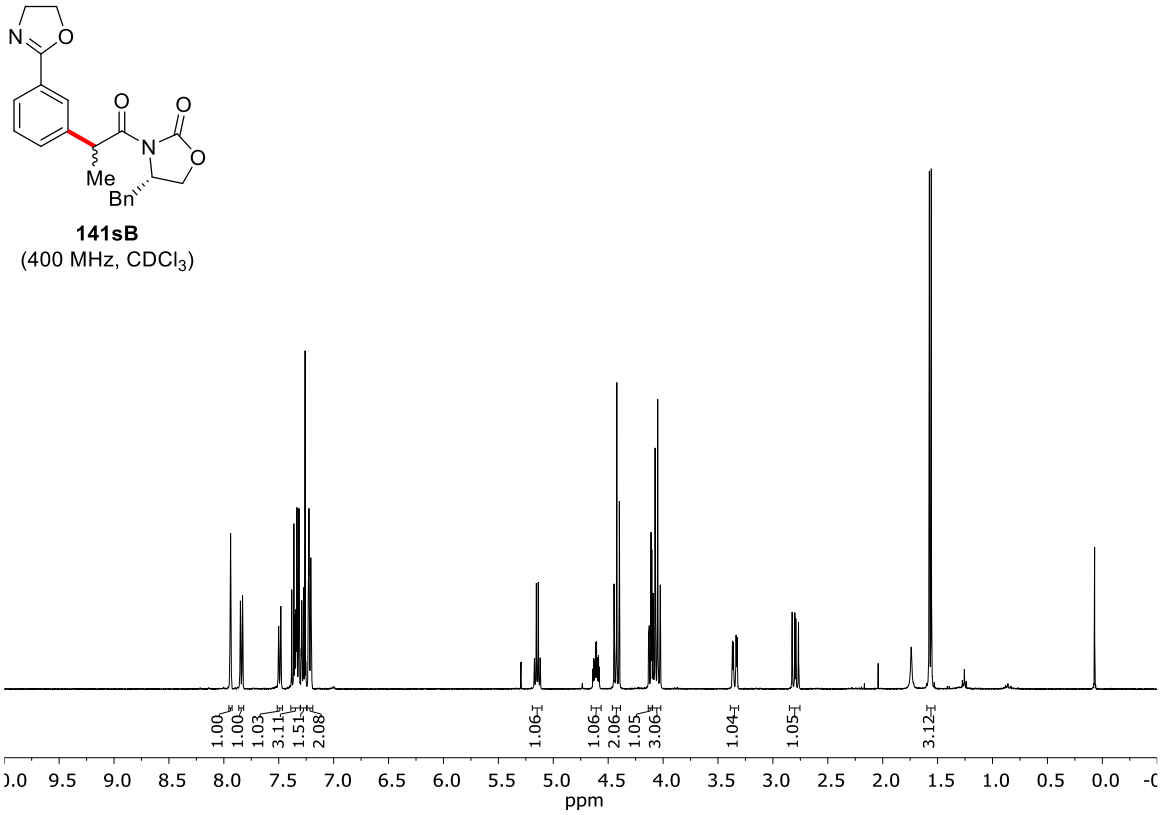
141rB
(125 MHz, $CDCl_3$)



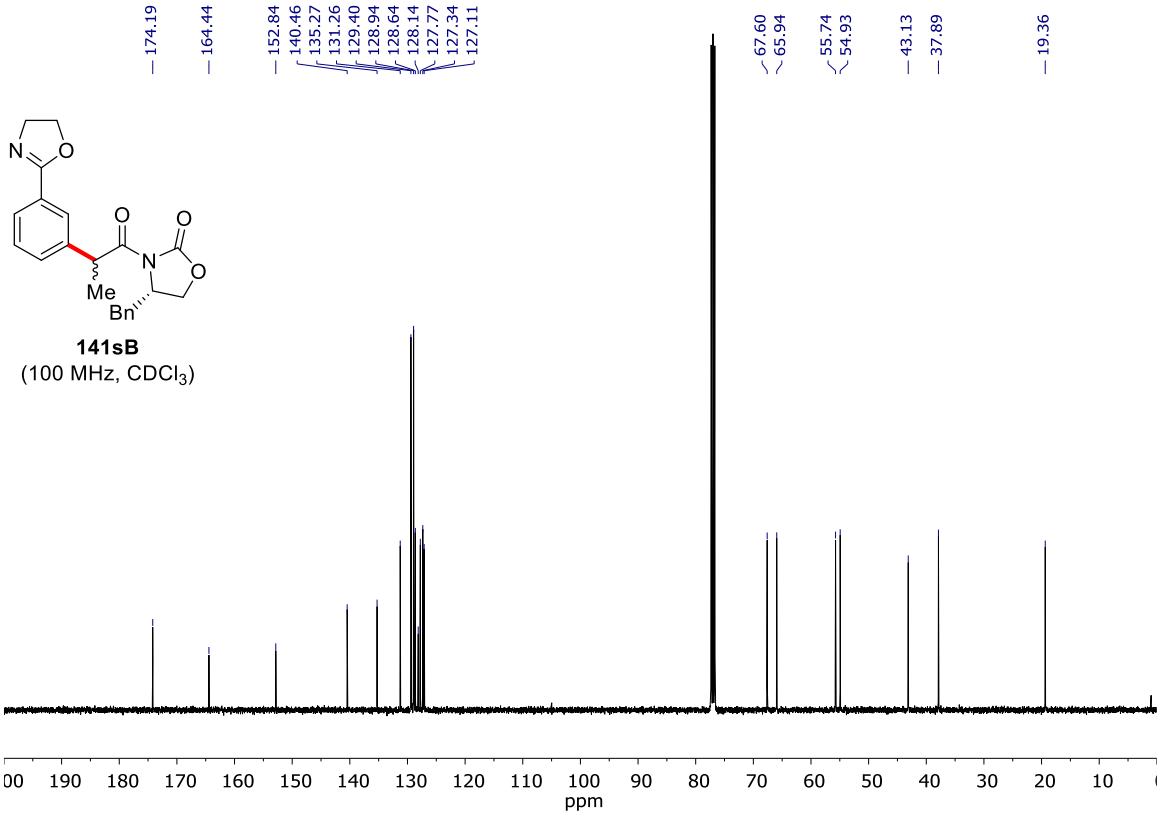
141sA
(600 MHz, $CDCl_3$)



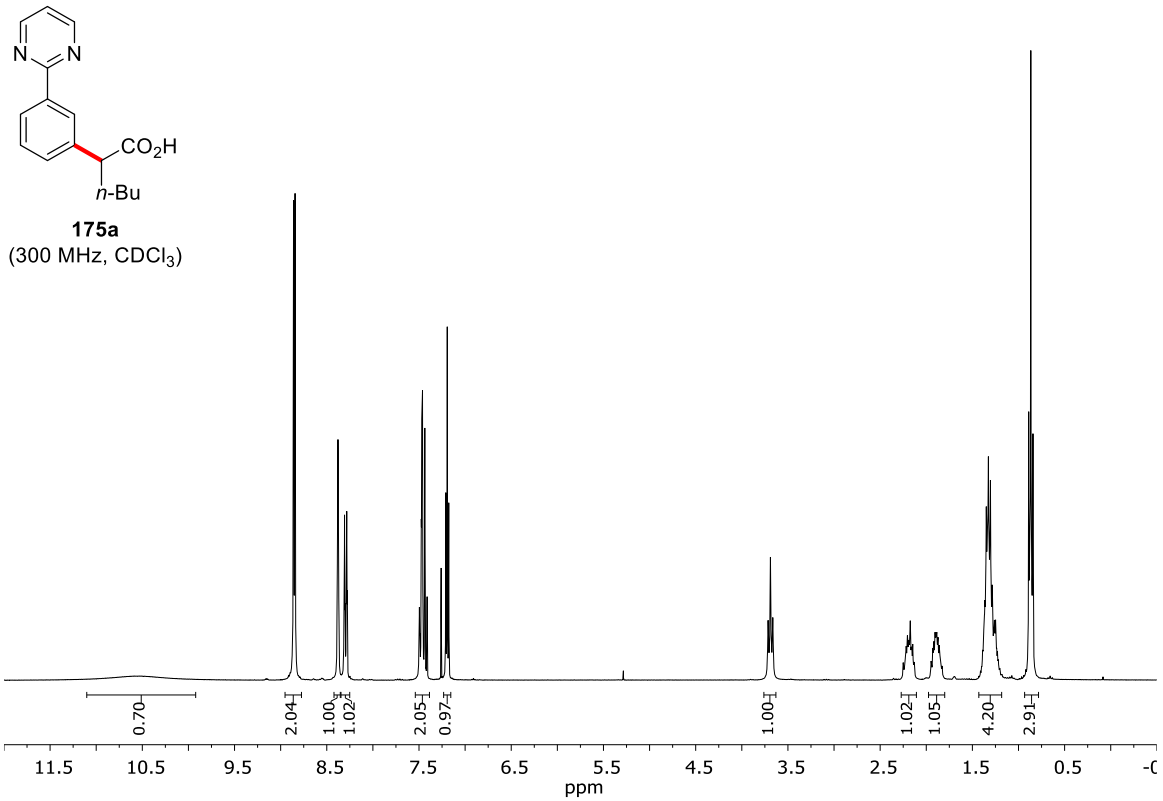
141sA
(125 MHz, $CDCl_3$)



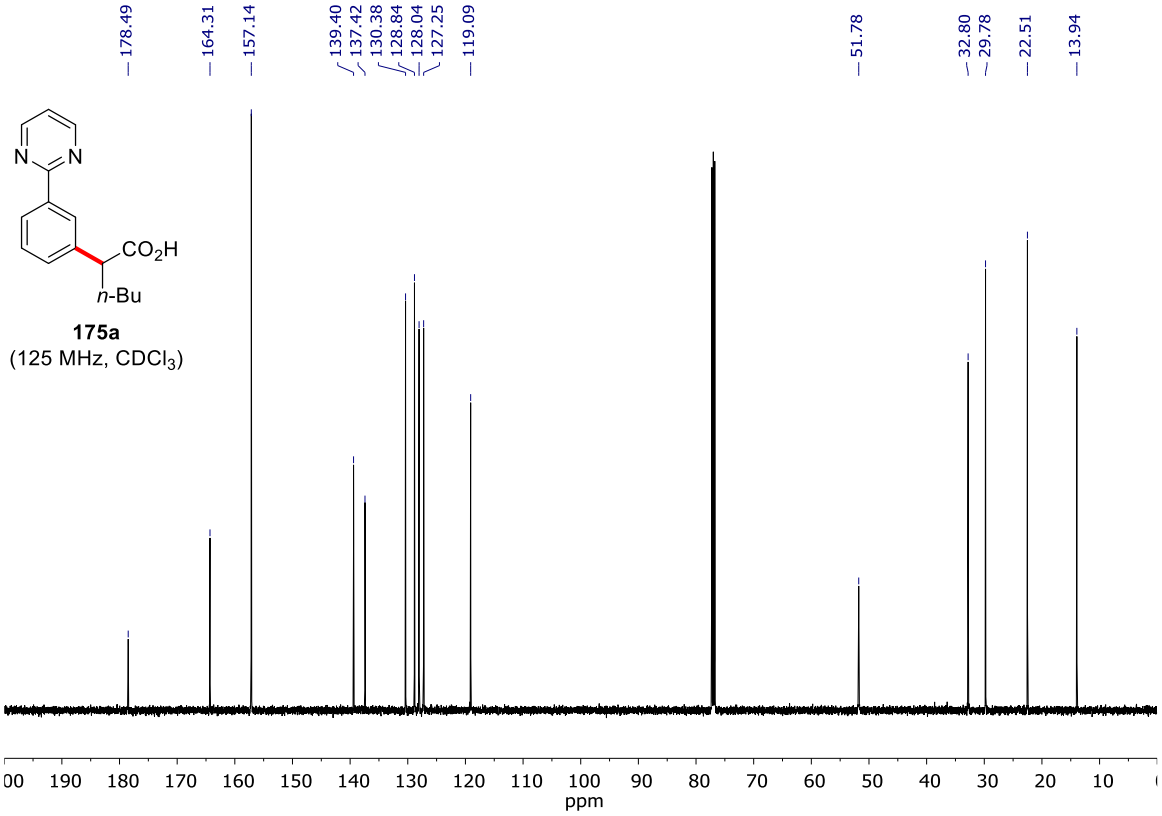
141sB
(400 MHz, $CDCl_3$)

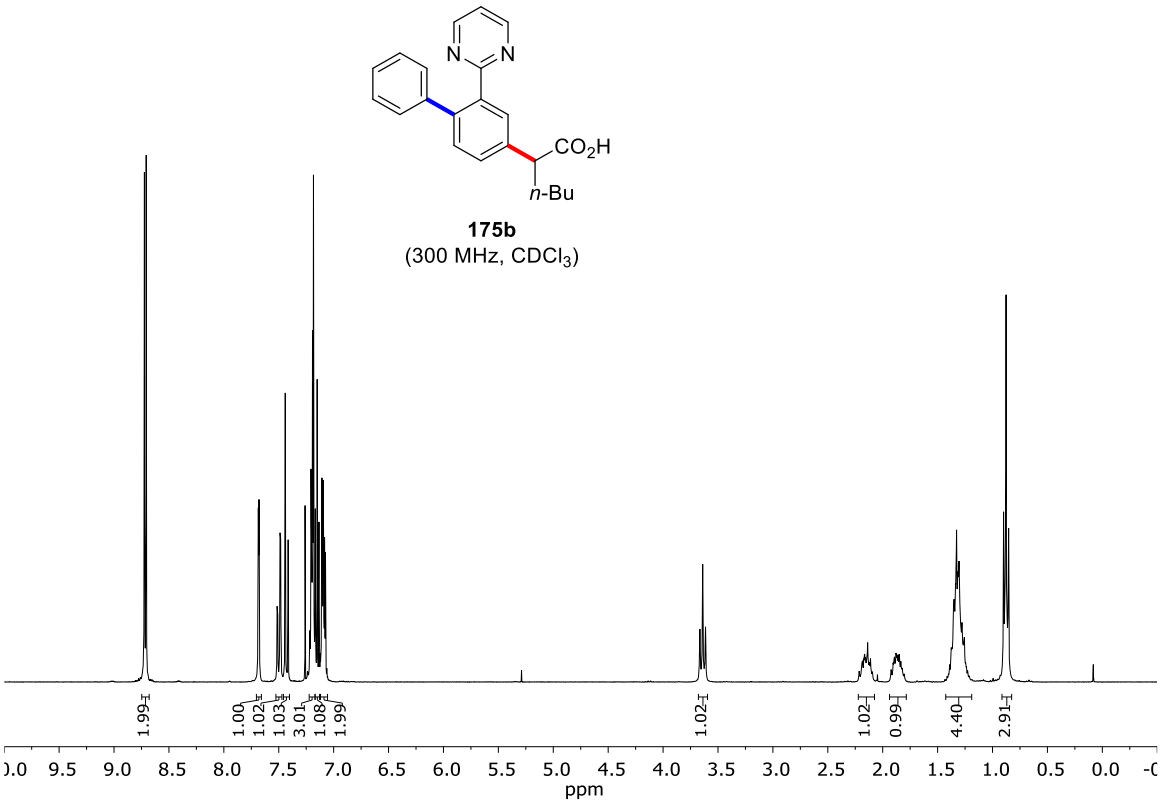


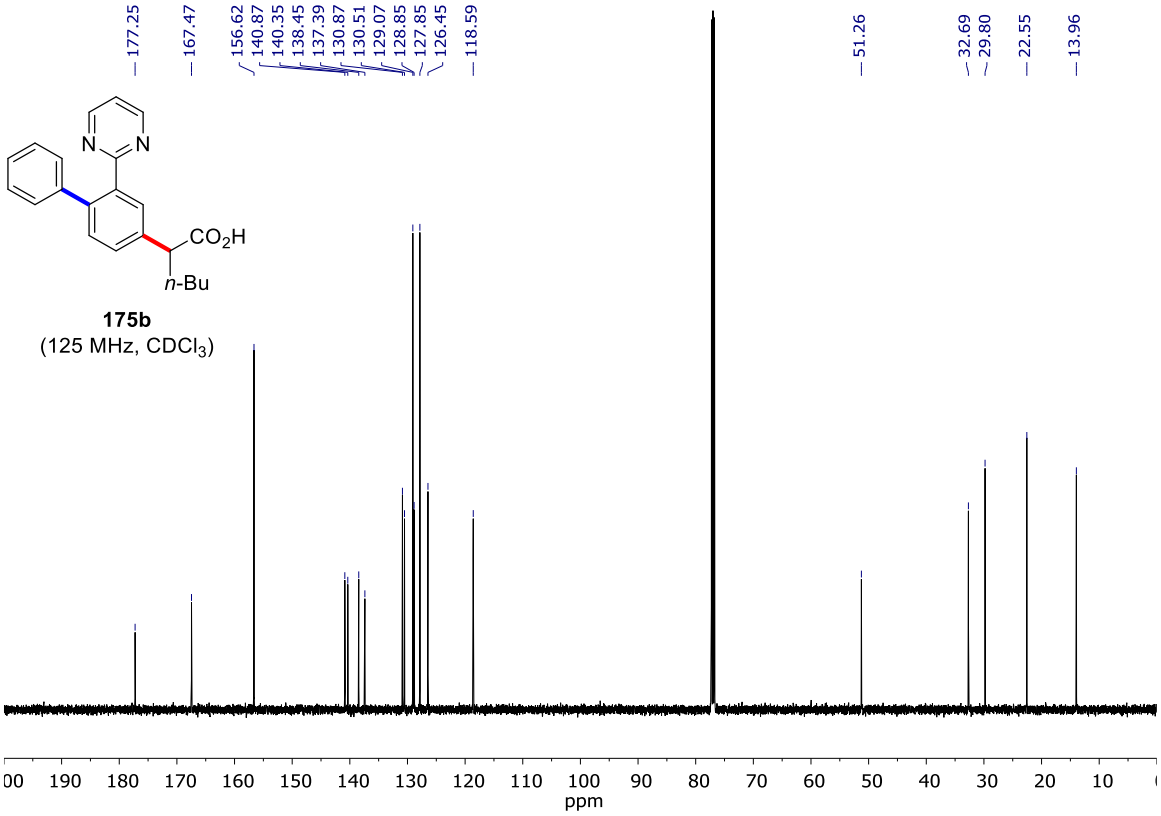
141sB
(100 MHz, $CDCl_3$)

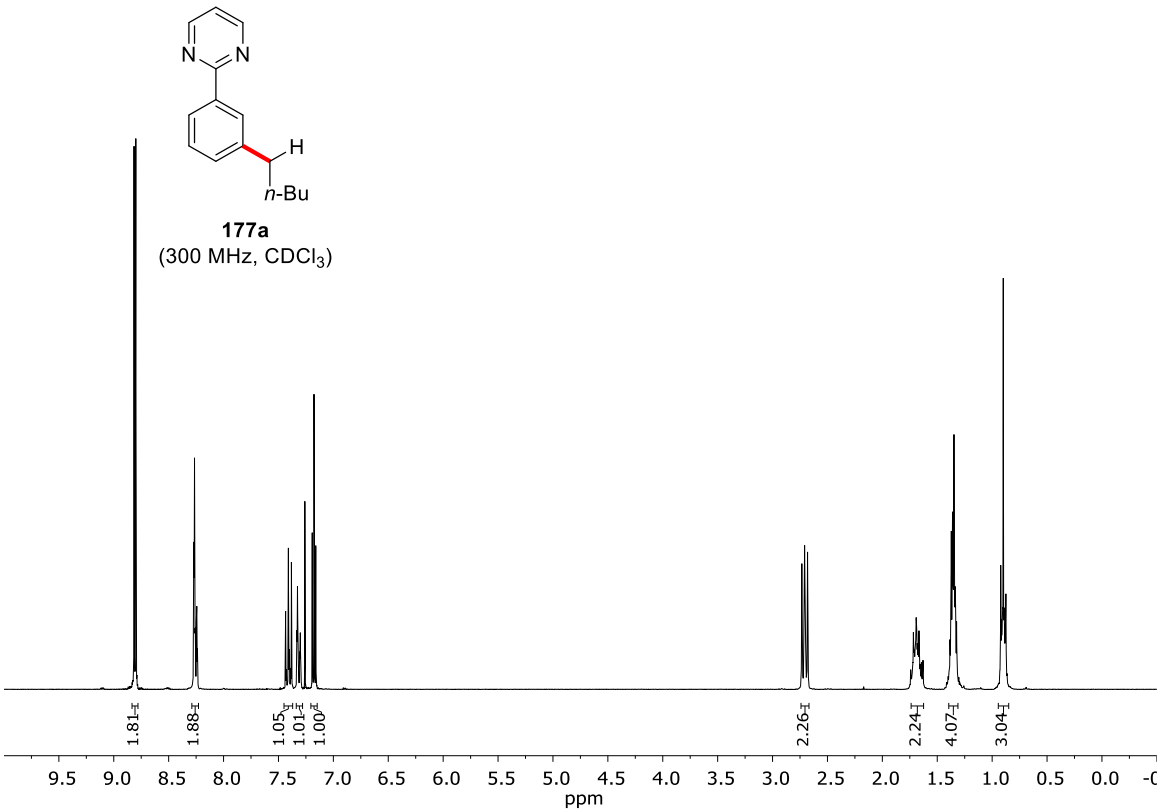


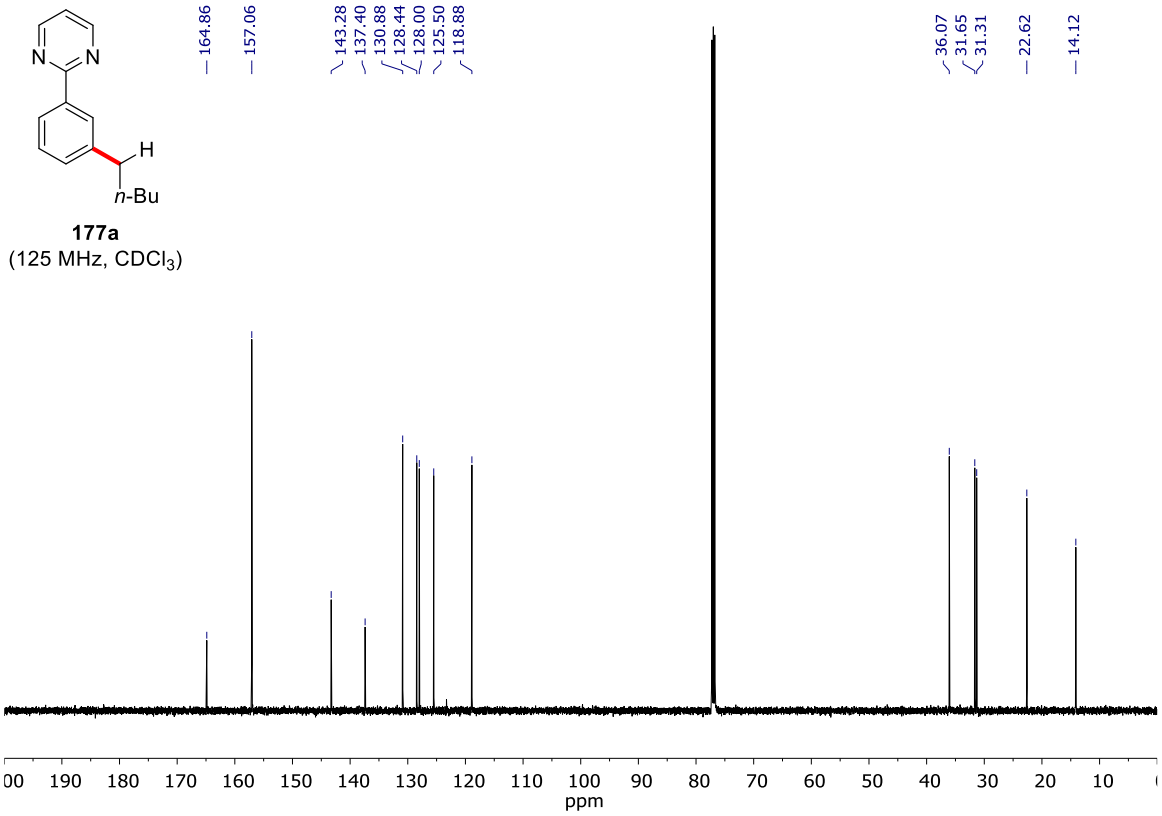
175a
(300 MHz, $CDCl_3$)


178.49
164.31
157.14
139.40
137.42
130.38
128.84
128.04
127.25
119.09
51.78
32.80
29.78
22.51
13.94
CO2H
n-Bu
175a
(125 MHz, CDCl3)
ppm

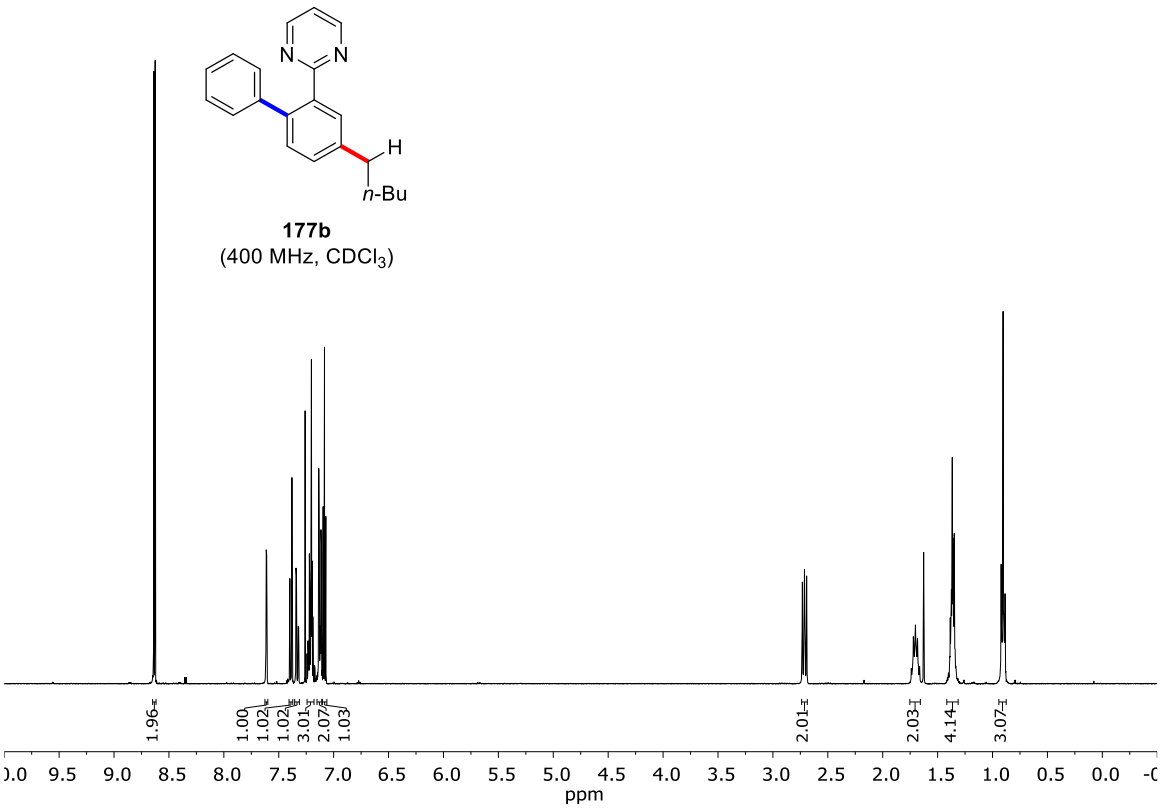

CO2H
n-Bu
175b
(300 MHz, CDCl3)
1.99
1.00
1.02
1.03
3.01
1.08
1.99
1.02
1.02
0.99
4.40
2.91
ppm


177.25
167.47
156.62
140.87
140.35
138.45
137.39
130.87
130.51
129.07
128.85
127.85
126.45
118.59
51.26
32.69
29.80
22.55
13.96
N
N
CO2H
n-Bu
175b
(125 MHz, CDCl3)
ppm

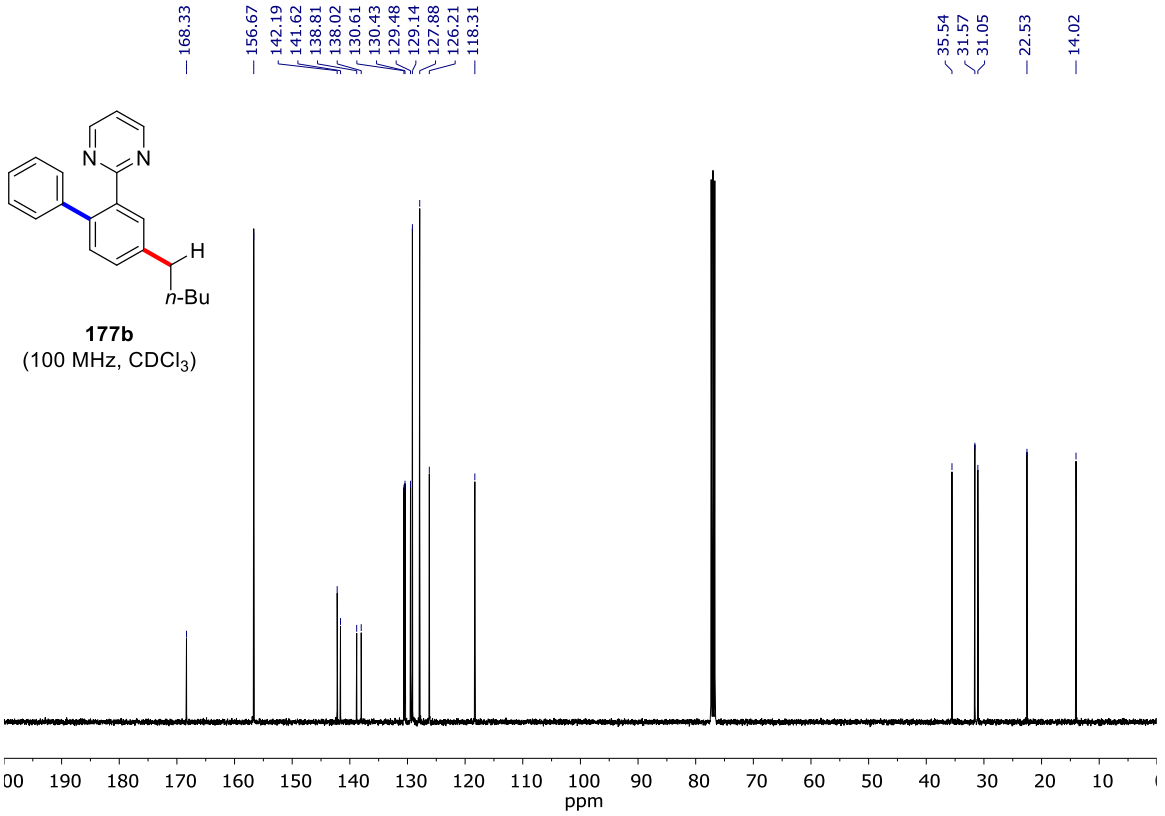

N
N
H
n-Bu
177a
(300 MHz, CDCl3)
1.81
1.88
1.05
1.01
1.00
2.26
2.24
4.07
3.04
ppm



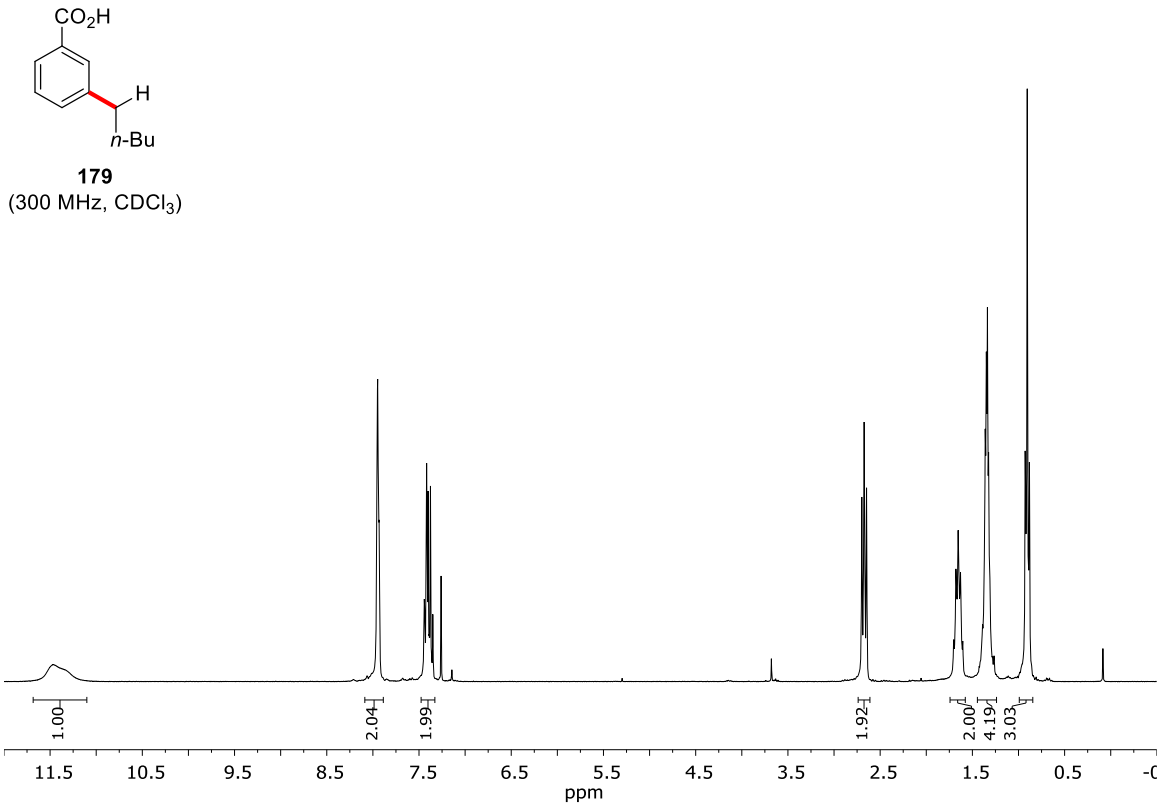
177a
(125 MHz, $CDCl_3$)



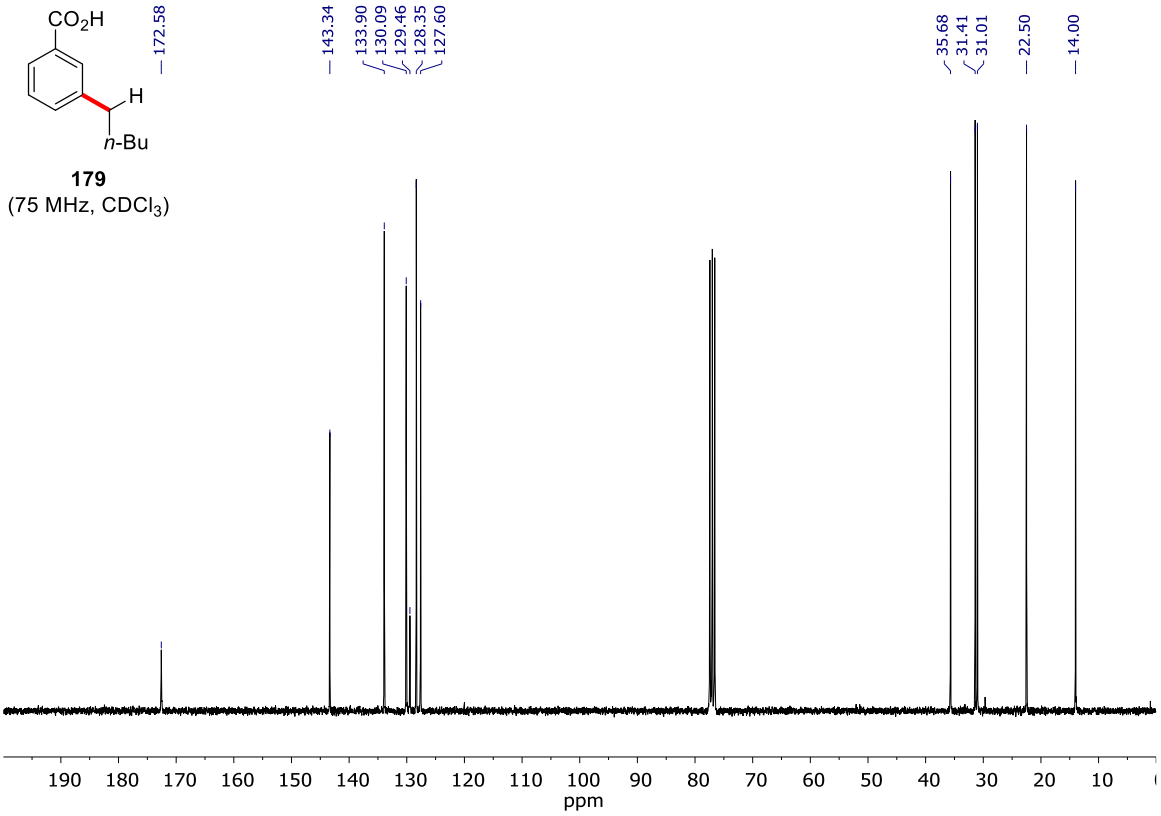
177b
(400 MHz, $CDCl_3$)



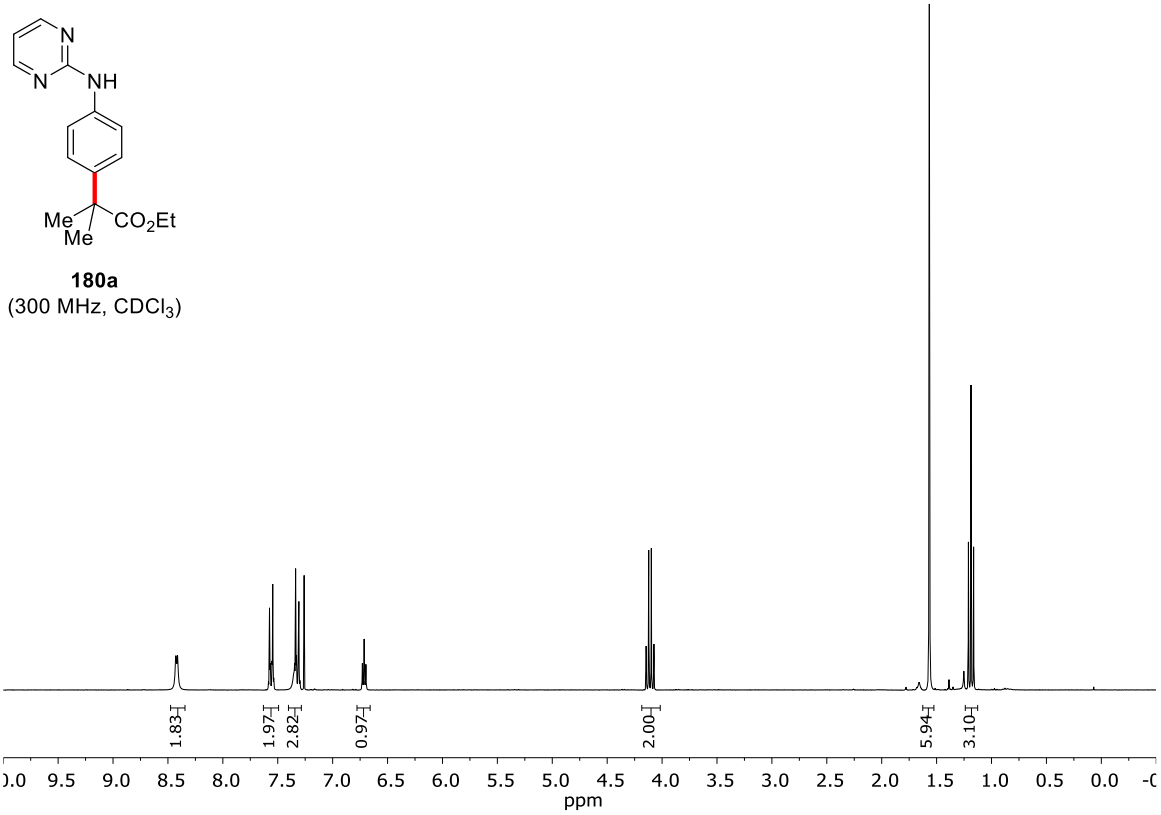
177b
(100 MHz, $CDCl_3$)



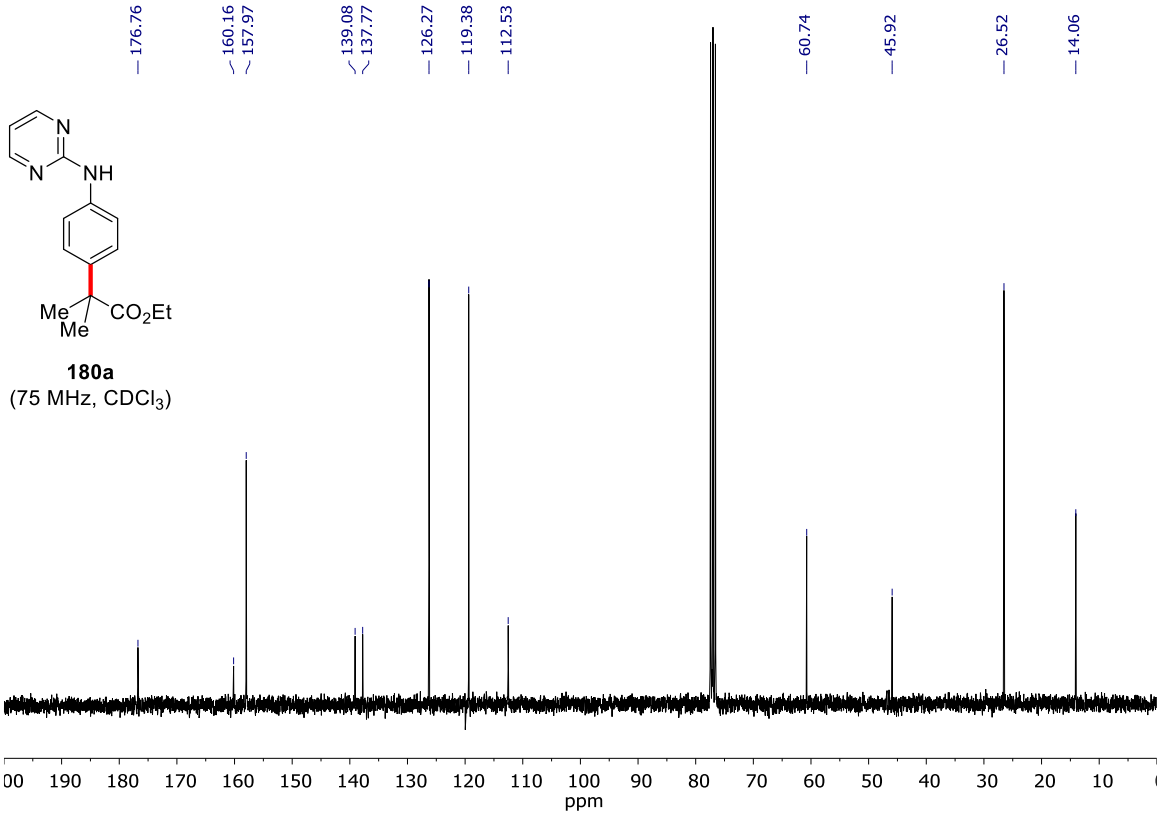
179
(300 MHz, $CDCl_3$)



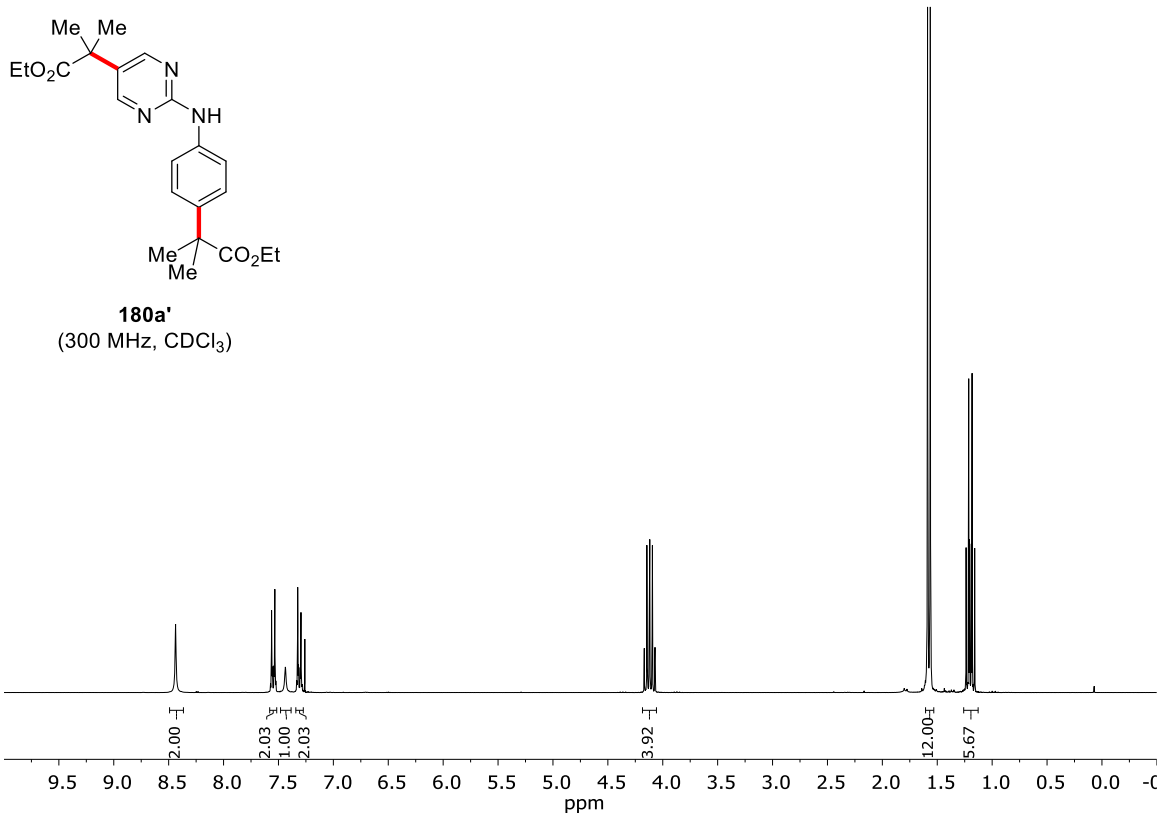
179
(75 MHz, $CDCl_3$)



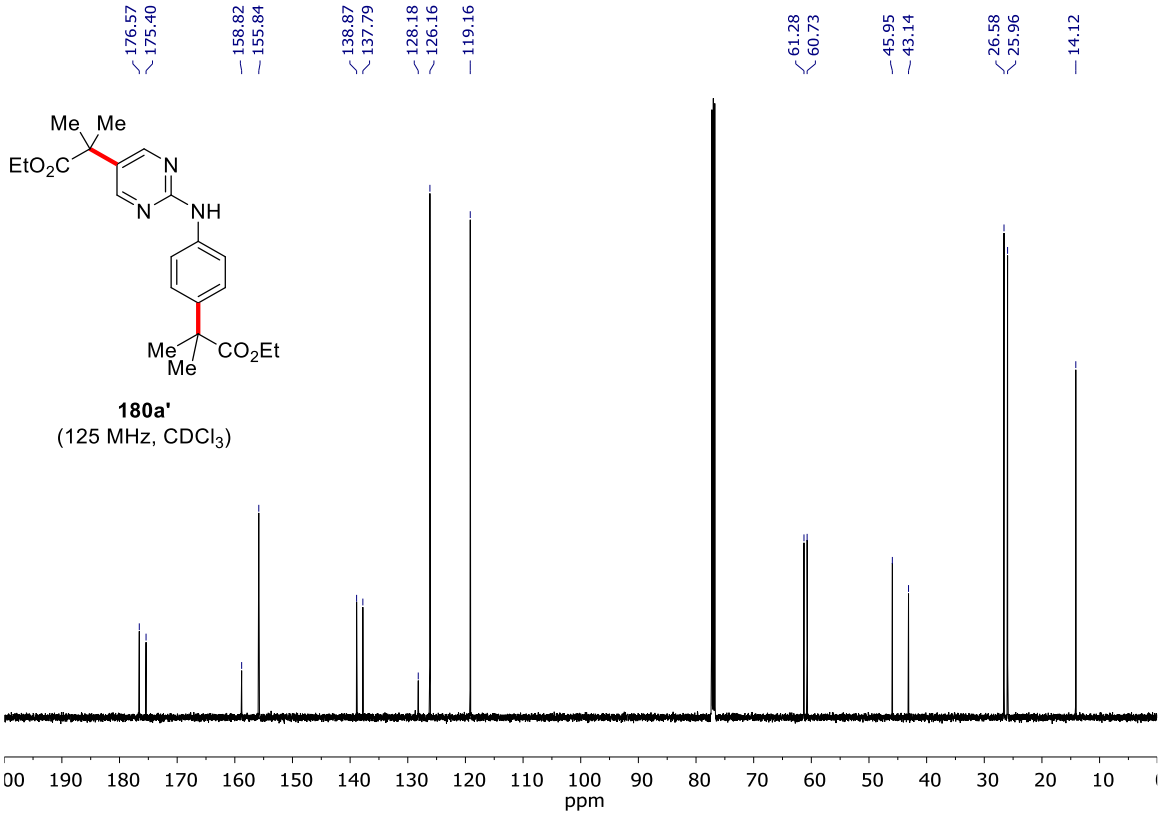
180a
(300 MHz, $CDCl_3$)



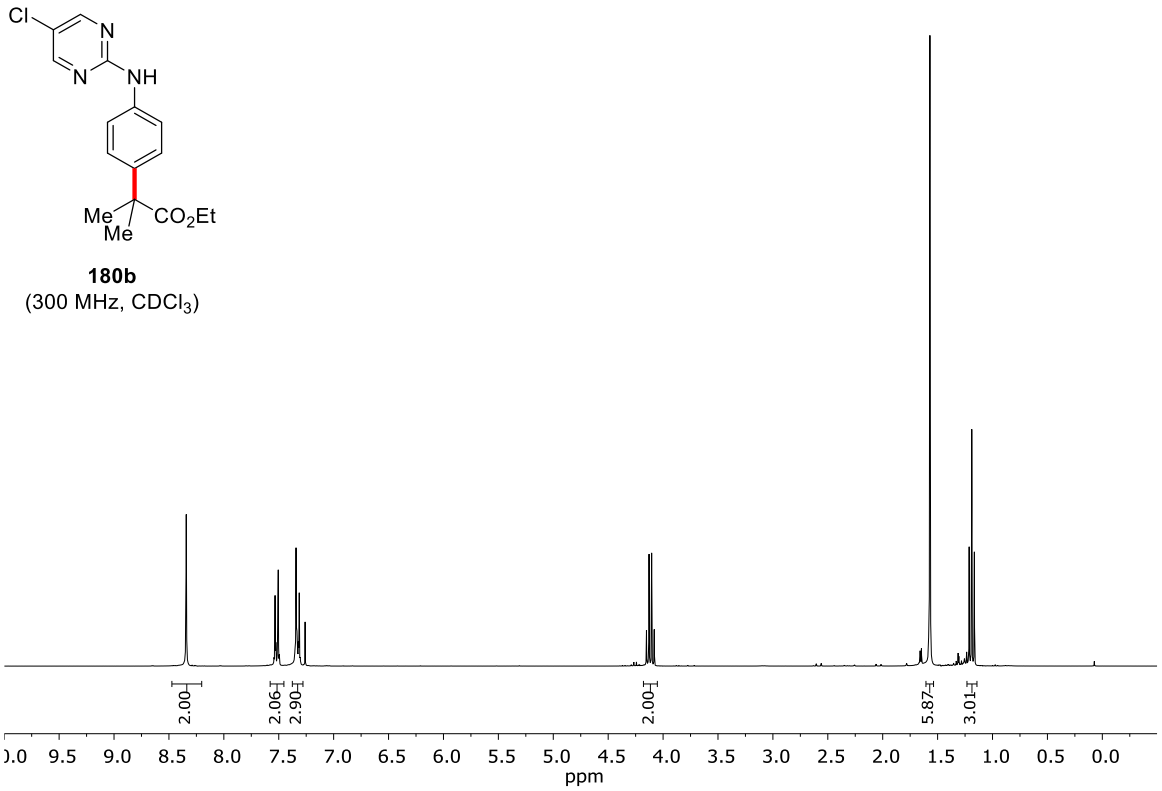
180a
(75 MHz, $CDCl_3$)



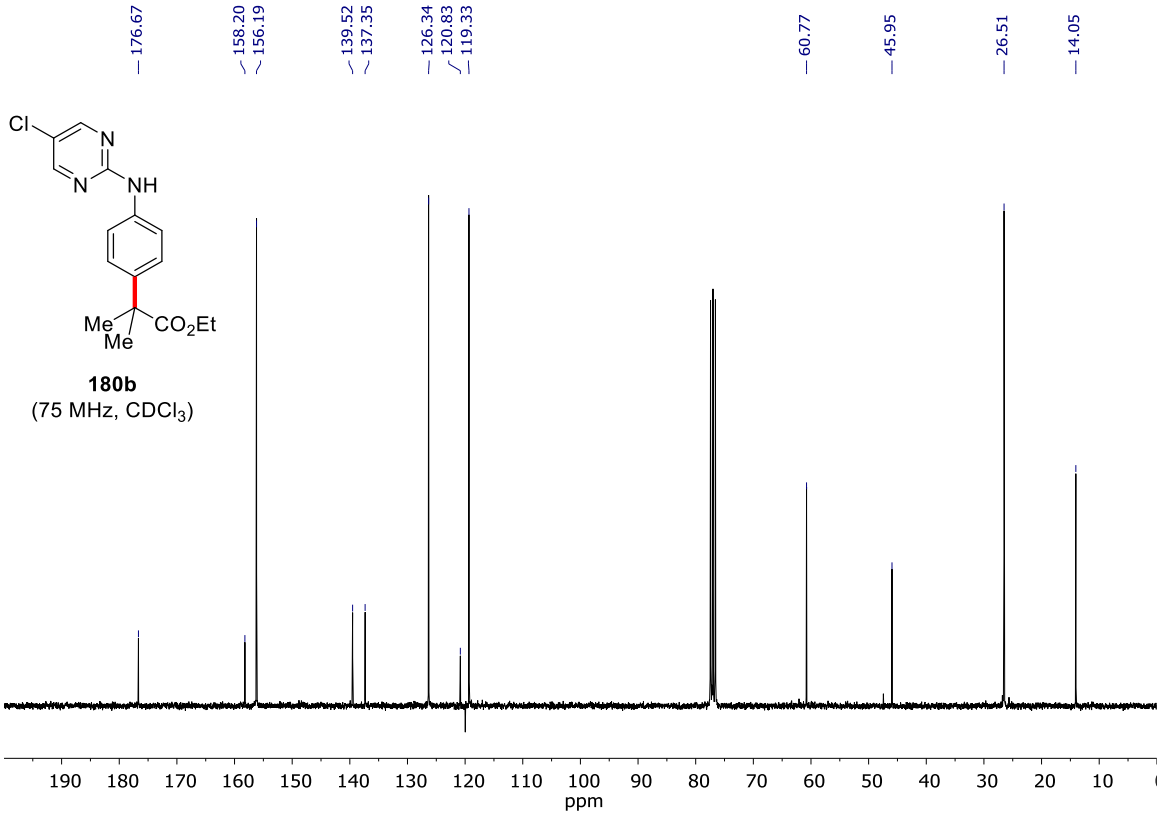
180a'
(300 MHz, $CDCl_3$)



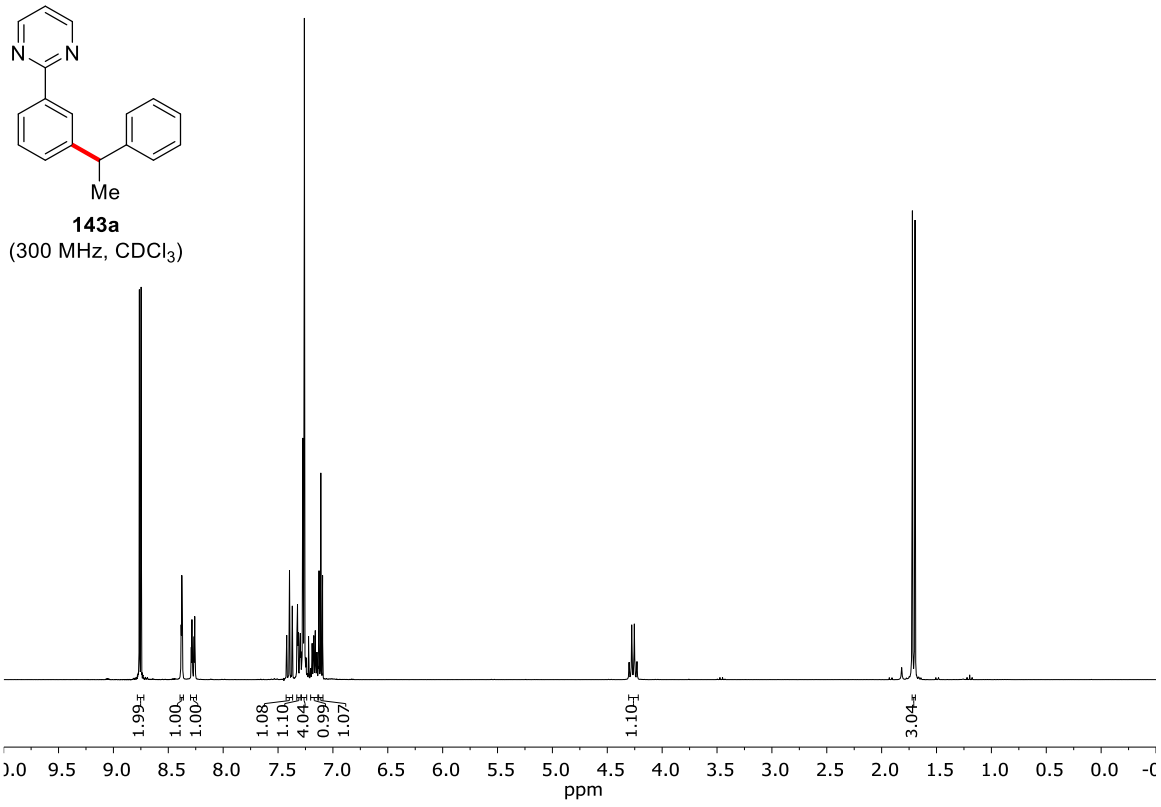
180a'
(125 MHz, $CDCl_3$)



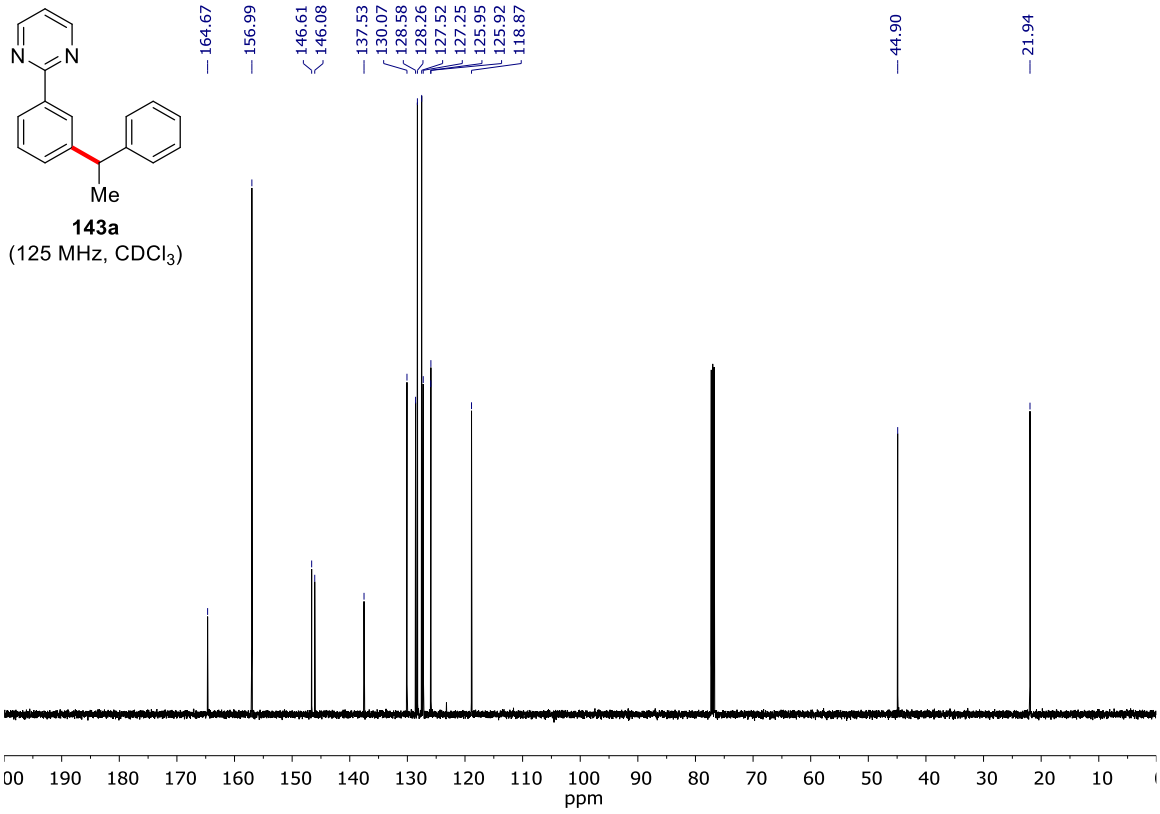
180b
(300 MHz, $CDCl_3$)

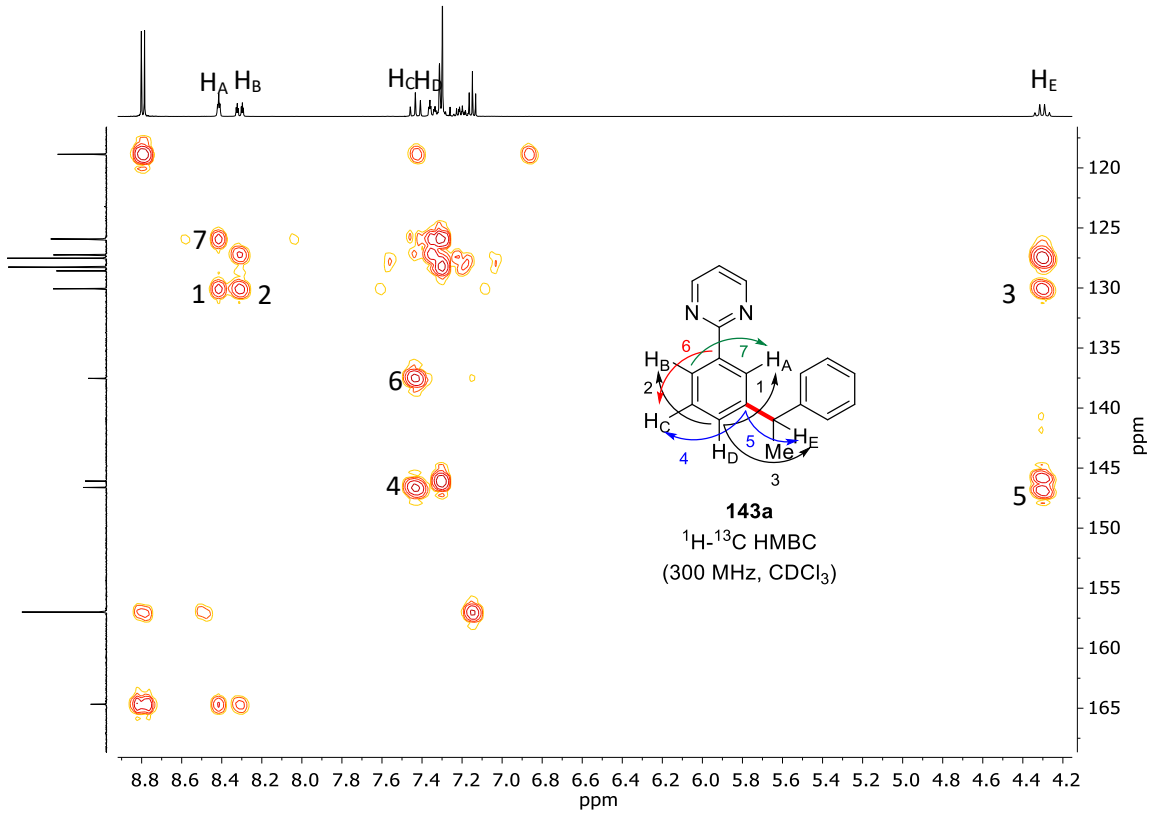


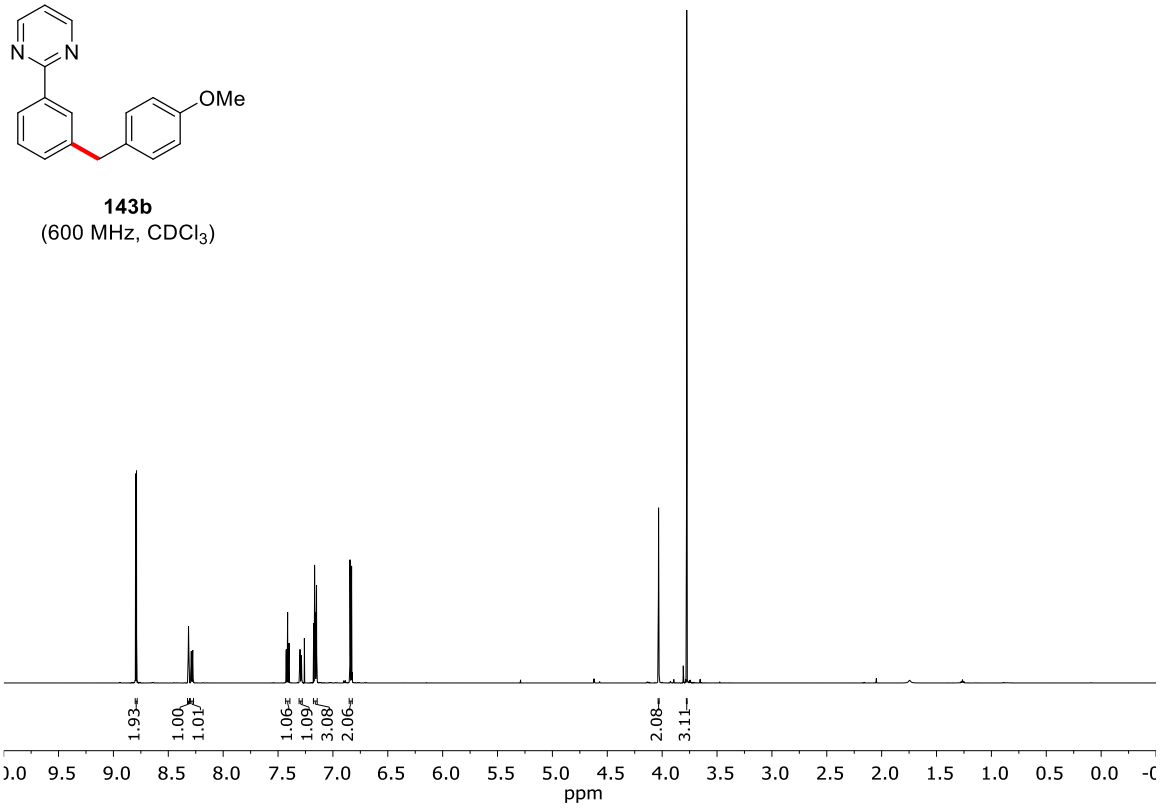
180b
(75 MHz, $CDCl_3$)

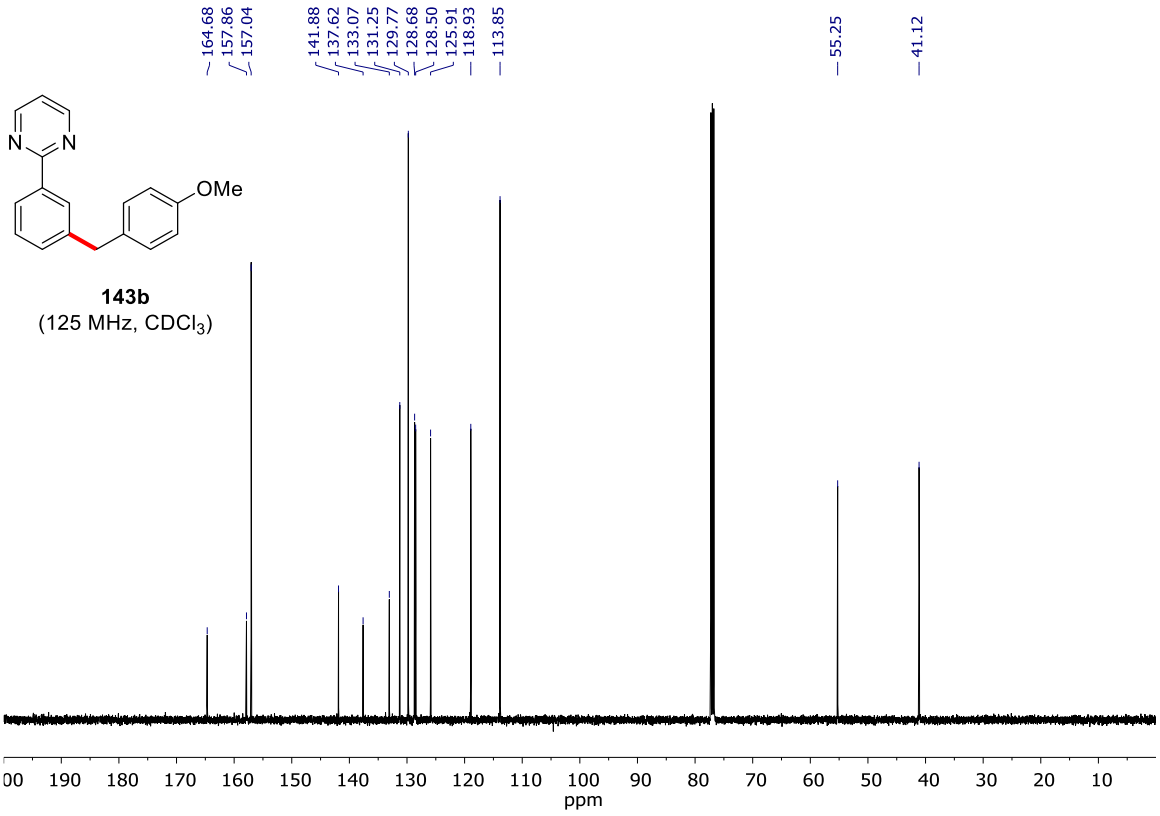


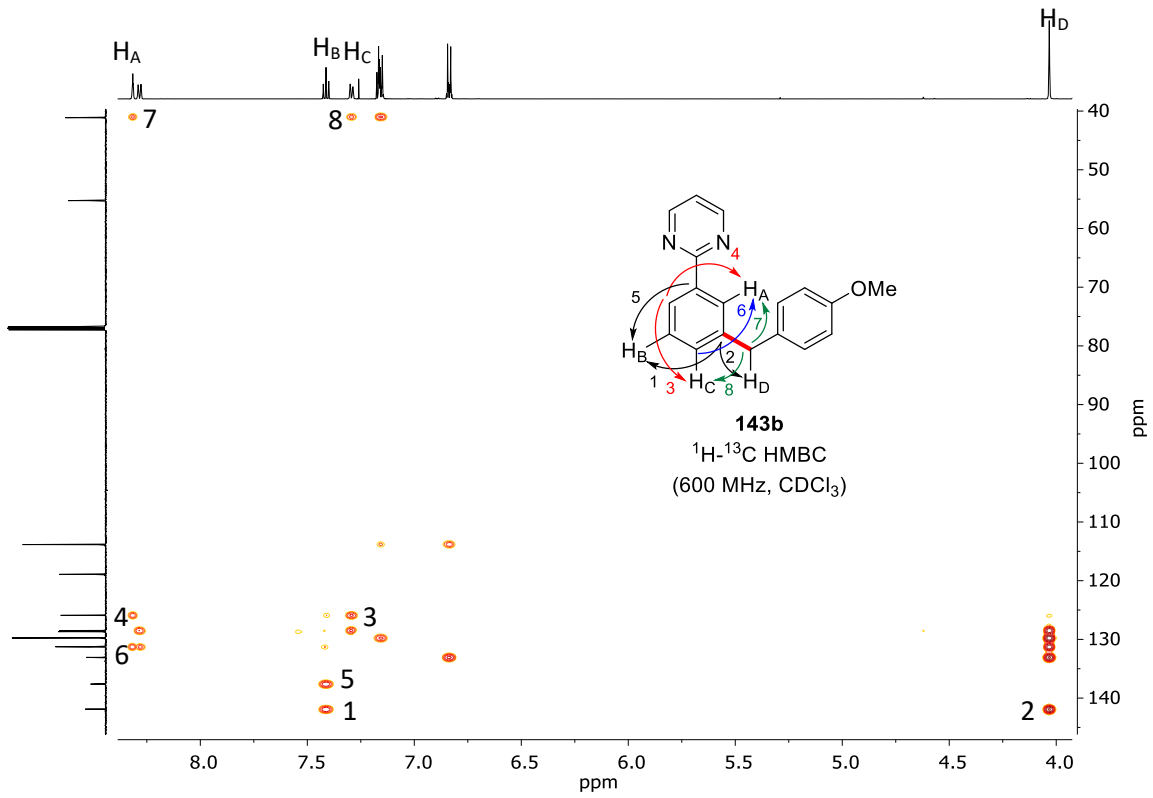
143a
(300 MHz, $CDCl_3$)

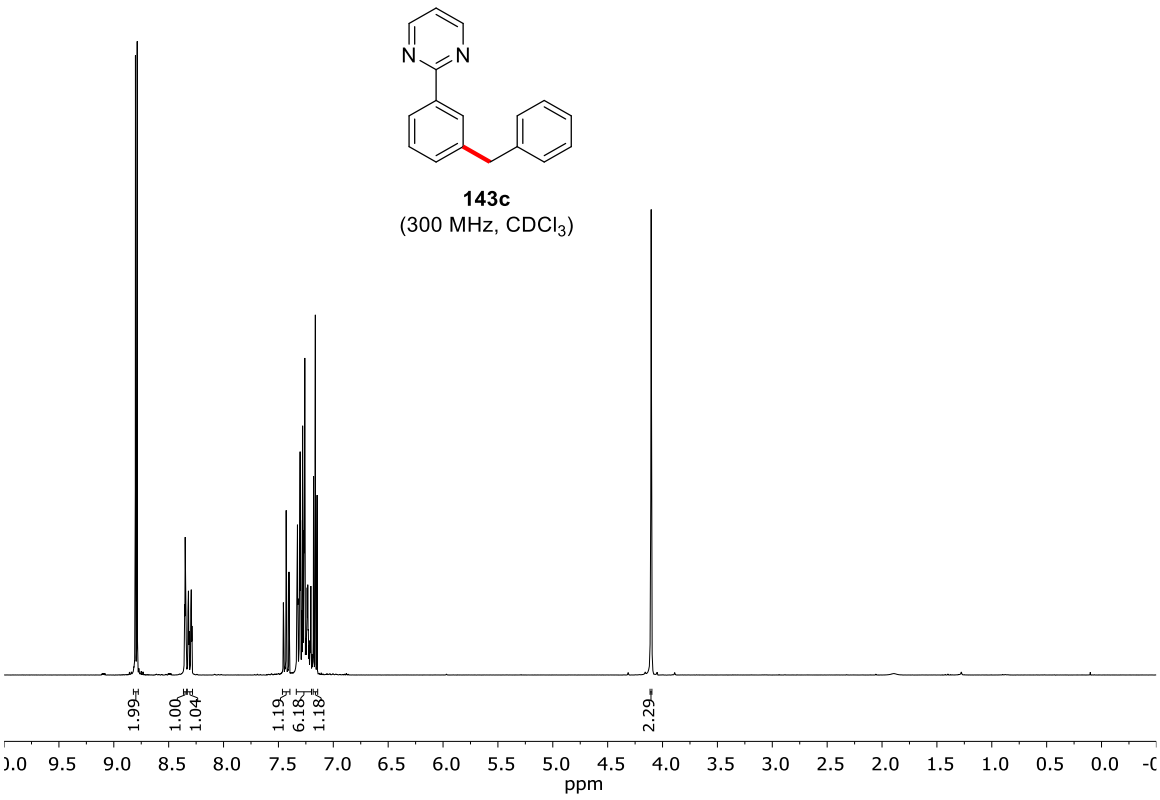

164.67
156.99
146.61
146.08
137.53
130.07
128.58
128.26
127.52
127.25
125.95
125.92
118.87
44.90
21.94
Me
143a
(125 MHz, CDCl3)
ppm

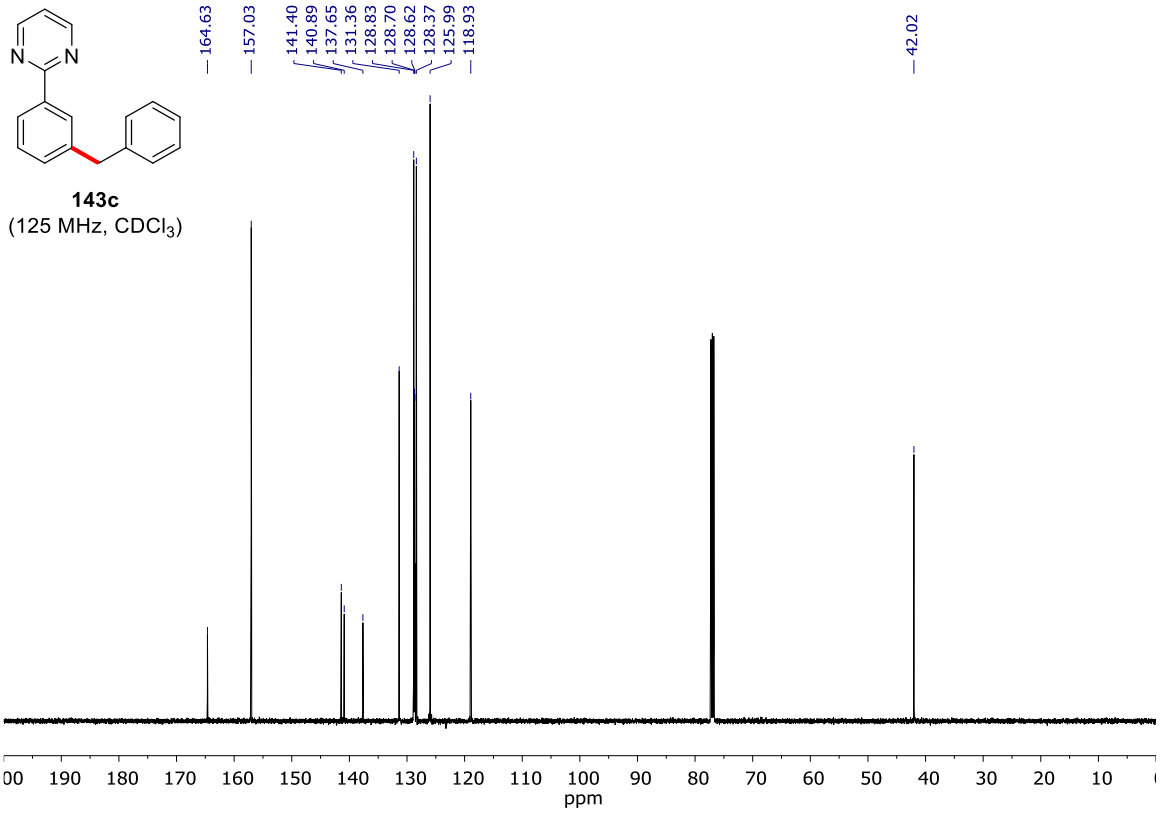

HA HB
HC HD
HE
7
1
2
6
4
3
5
143a
1H-13C HMBC
(300 MHz, CDCl3)
ppm


N
N
OMe
143b
(600 MHz, CDCl3)
1.93
1.00
1.01
1.06
1.09
3.08
2.06
2.08
3.11
ppm

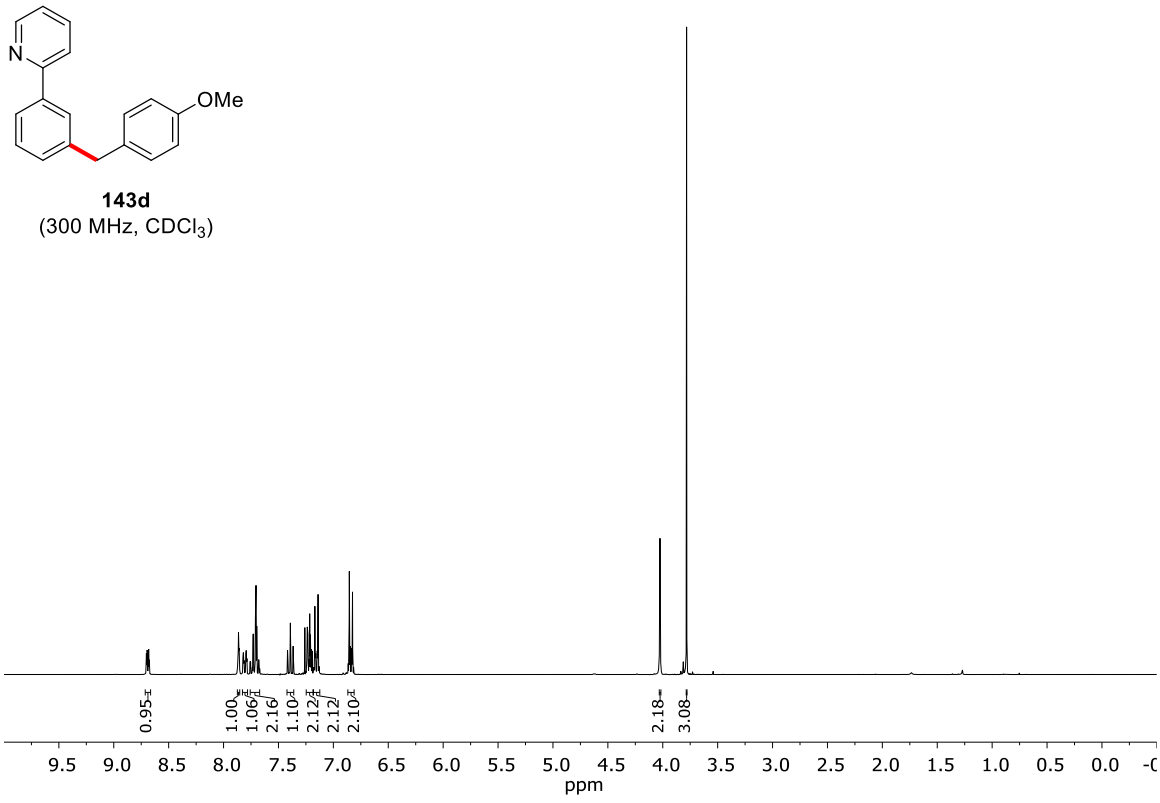

164.68
157.86
157.04
141.88
137.62
133.07
131.25
129.77
128.68
128.50
125.91
118.93
113.85
55.25
41.12
N
N
OMe
143b
(125 MHz, CDCl3)
ppm


H_A
H_B H_C
H_D
7
8
4
6
3
5
1
2
OMe
143b
^{1}H-^{13}C HMBC
(600 MHz, CDCl$_3$)
ppm
ppm

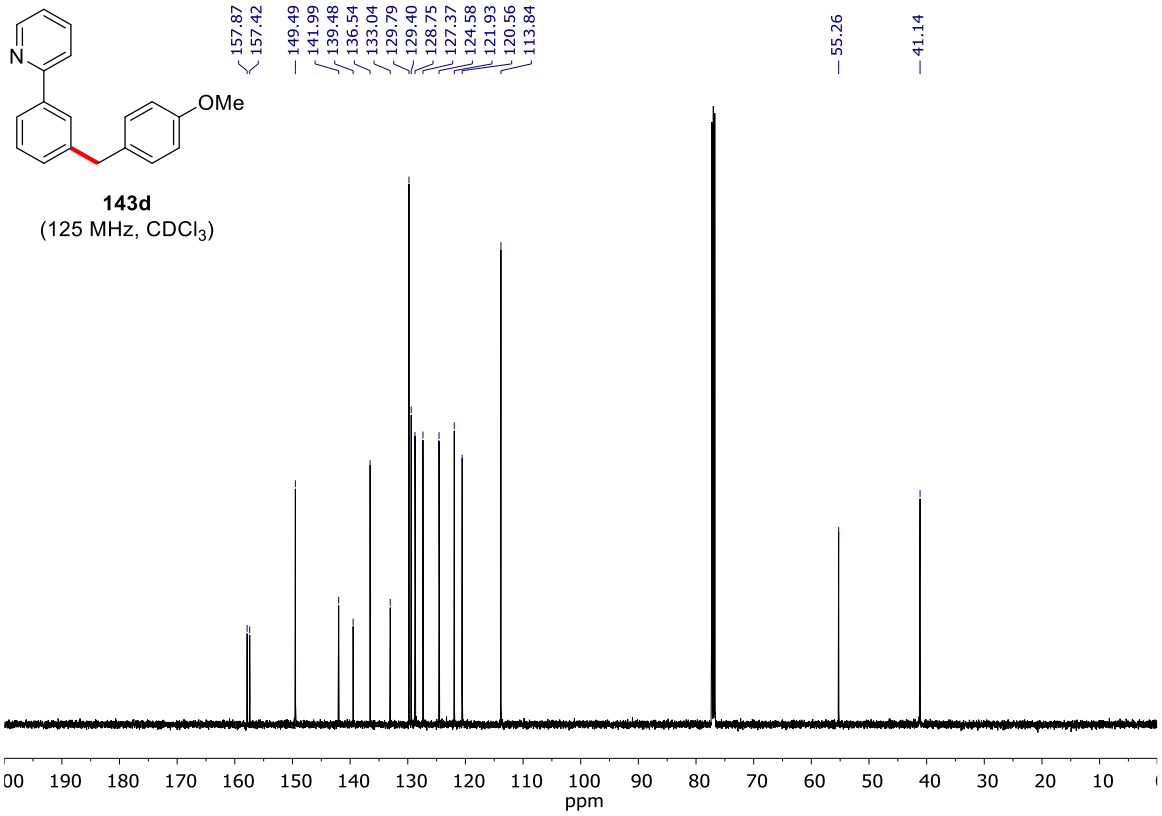

143c
(300 MHz, CDCl$_3$)
1.99
1.00
1.04
1.19
6.18
1.18
2.29
ppm



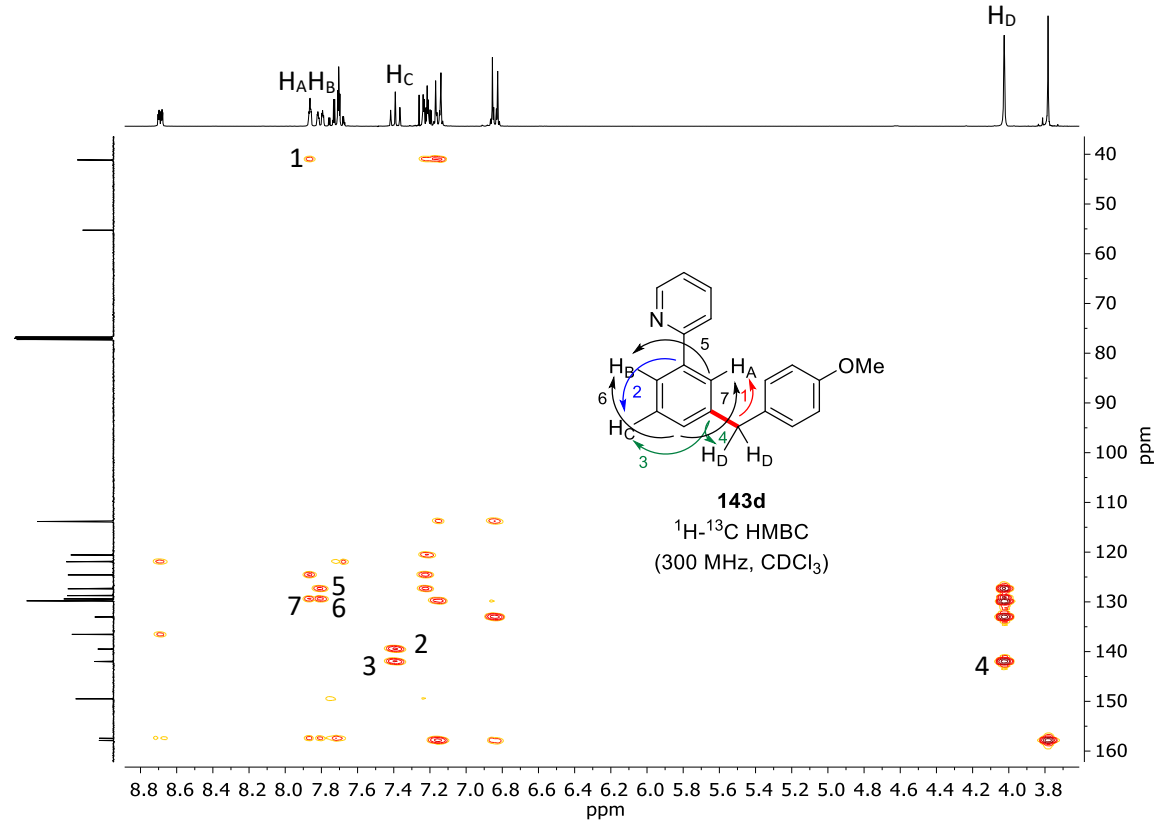
143c
(125 MHz, $CDCl_3$)



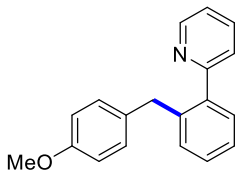
143d
(300 MHz, $CDCl_3$)



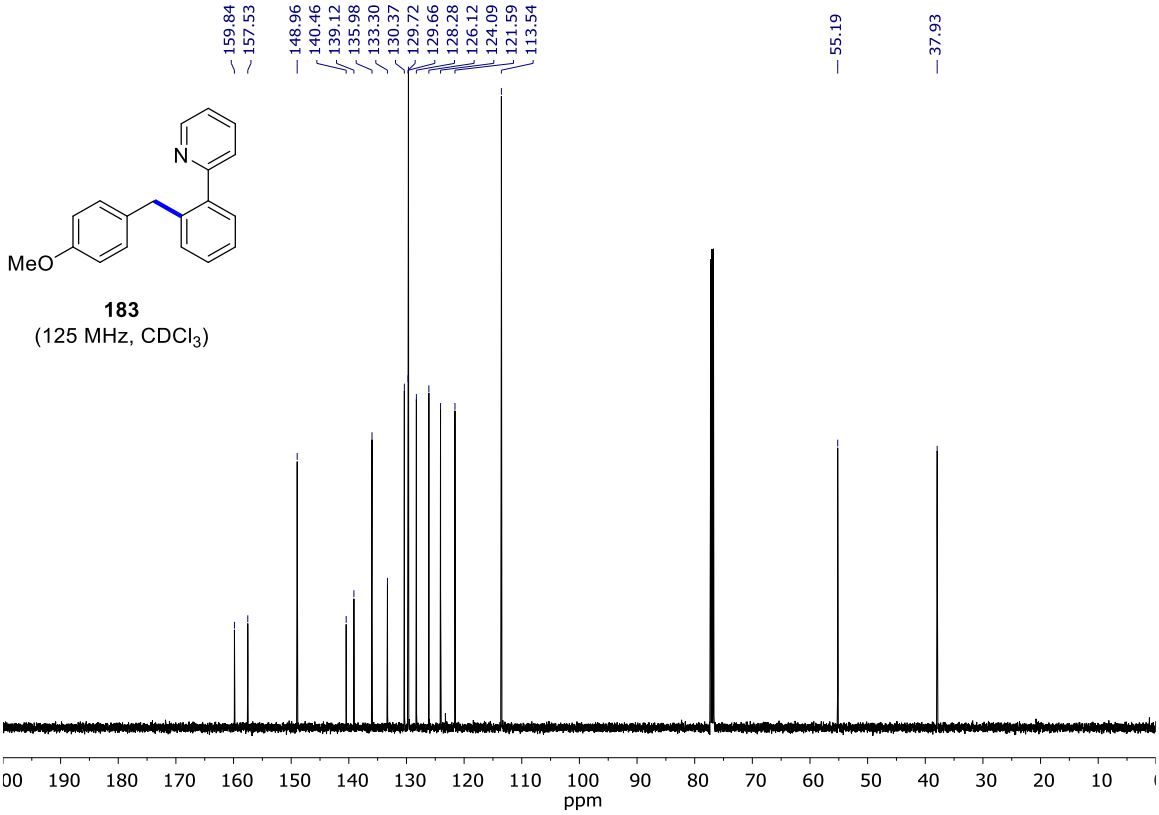
143d
(125 MHz, $CDCl_3$)



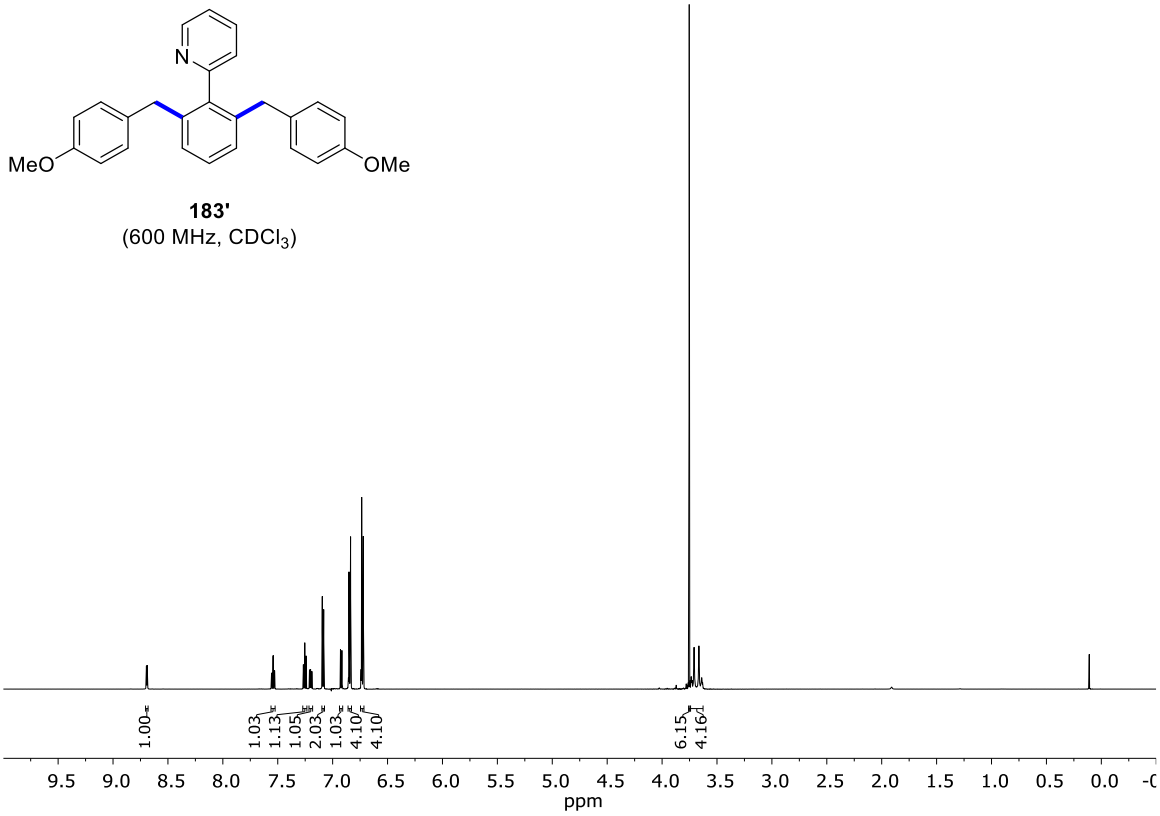
143d
^1H-^{13}C HMBC
(300 MHz, $CDCl_3$)

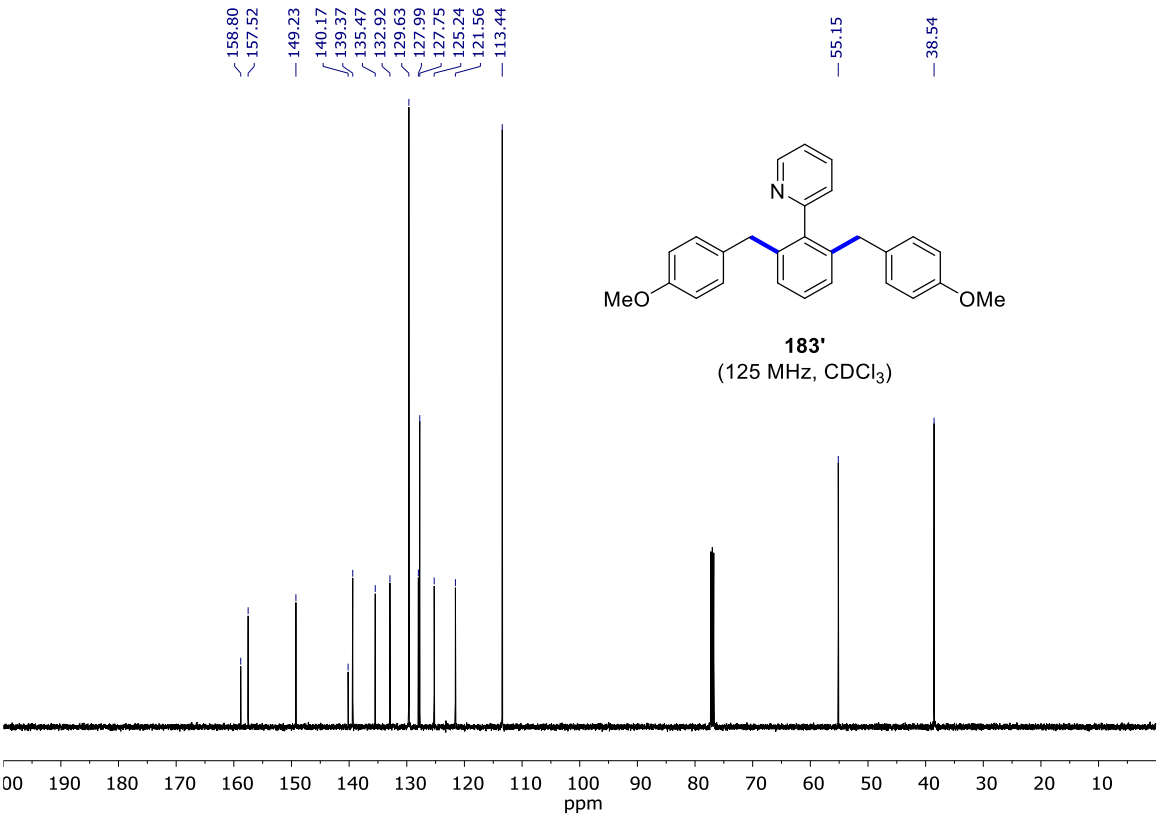


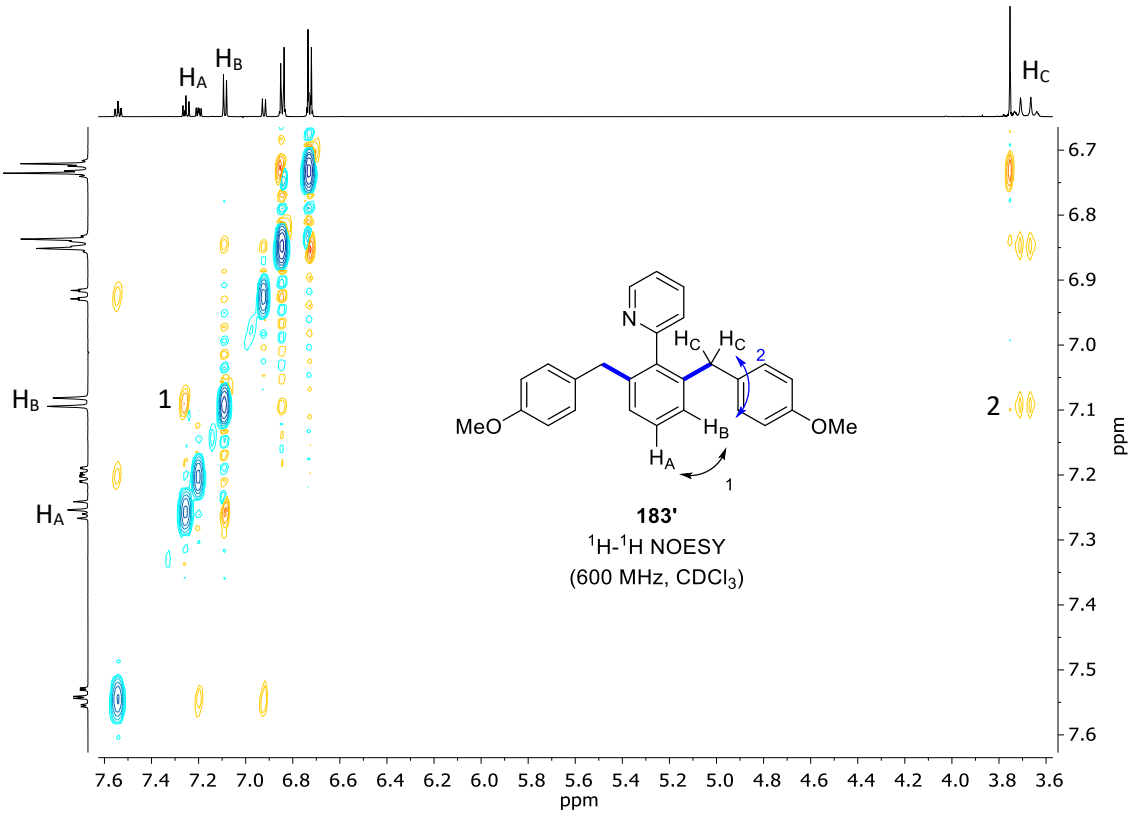
183
(300 MHz, $CDCl_3$)



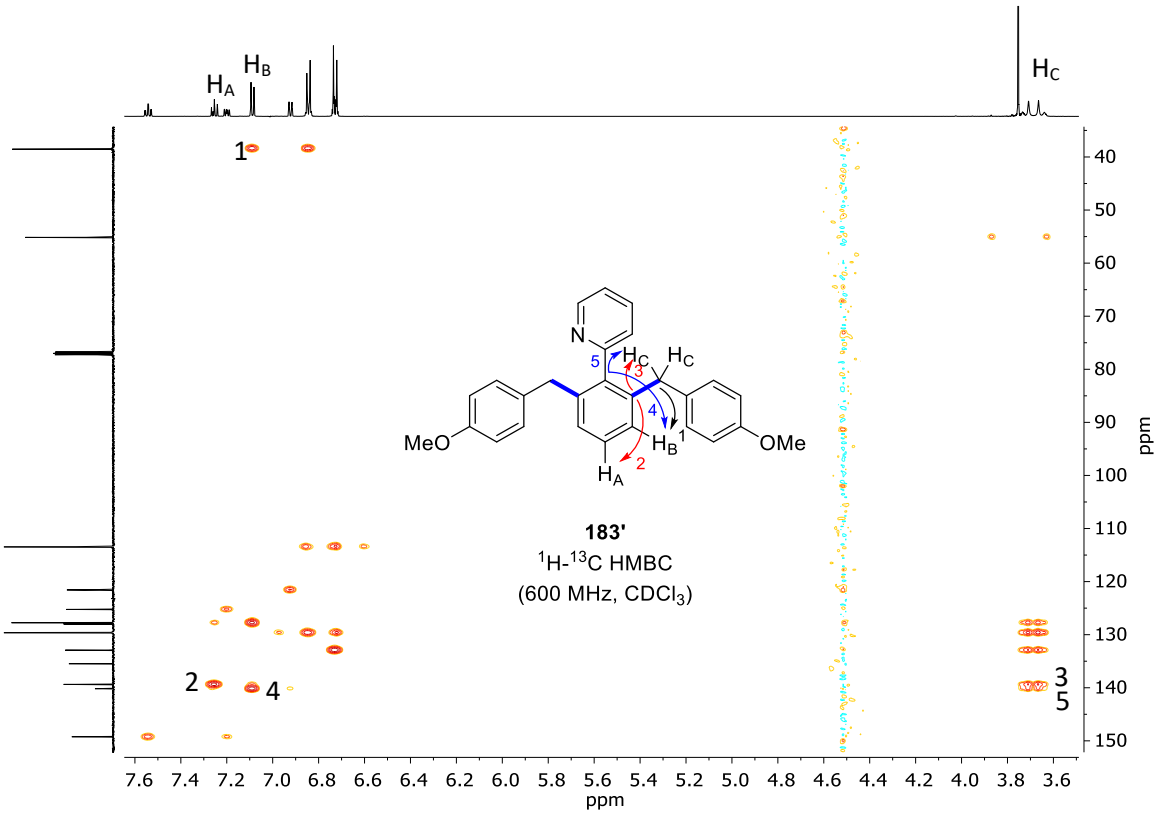
183
(125 MHz, $CDCl_3$)


N
MeO
OMe
183'
(600 MHz, CDCl3)
1.00
1.03
1.13
1.05
2.03
1.03
4.10
4.10
6.15
4.16
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

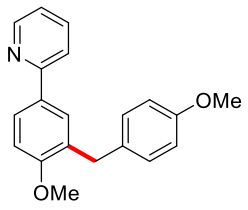

158.80
157.52
149.23
140.17
139.37
135.47
132.92
129.63
127.99
127.75
125.24
121.56
113.44
55.15
38.54
N
MeO
OMe
183'
(125 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm



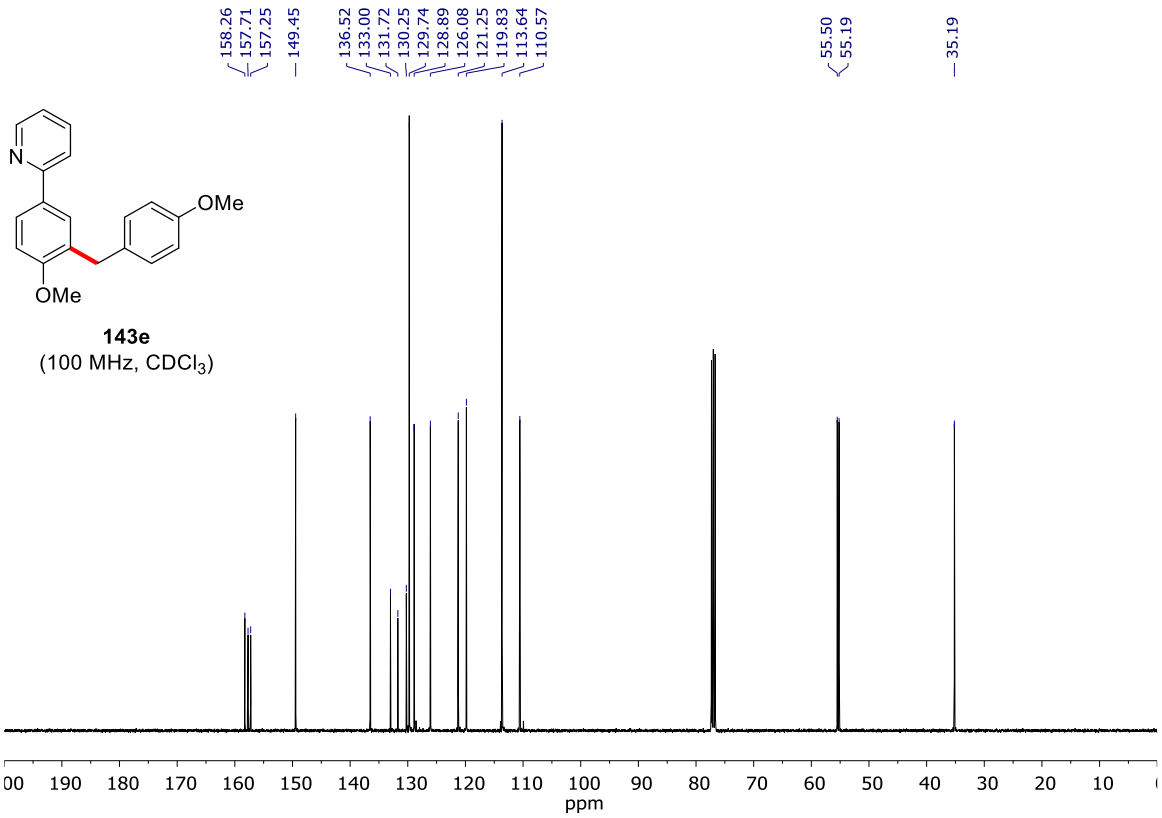
183'
^{1}H-^{1}H NOESY
(600 MHz, $CDCl_3$)



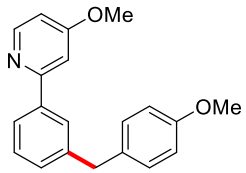
183'
^{1}H-^{13}C HMBC
(600 MHz, $CDCl_3$)



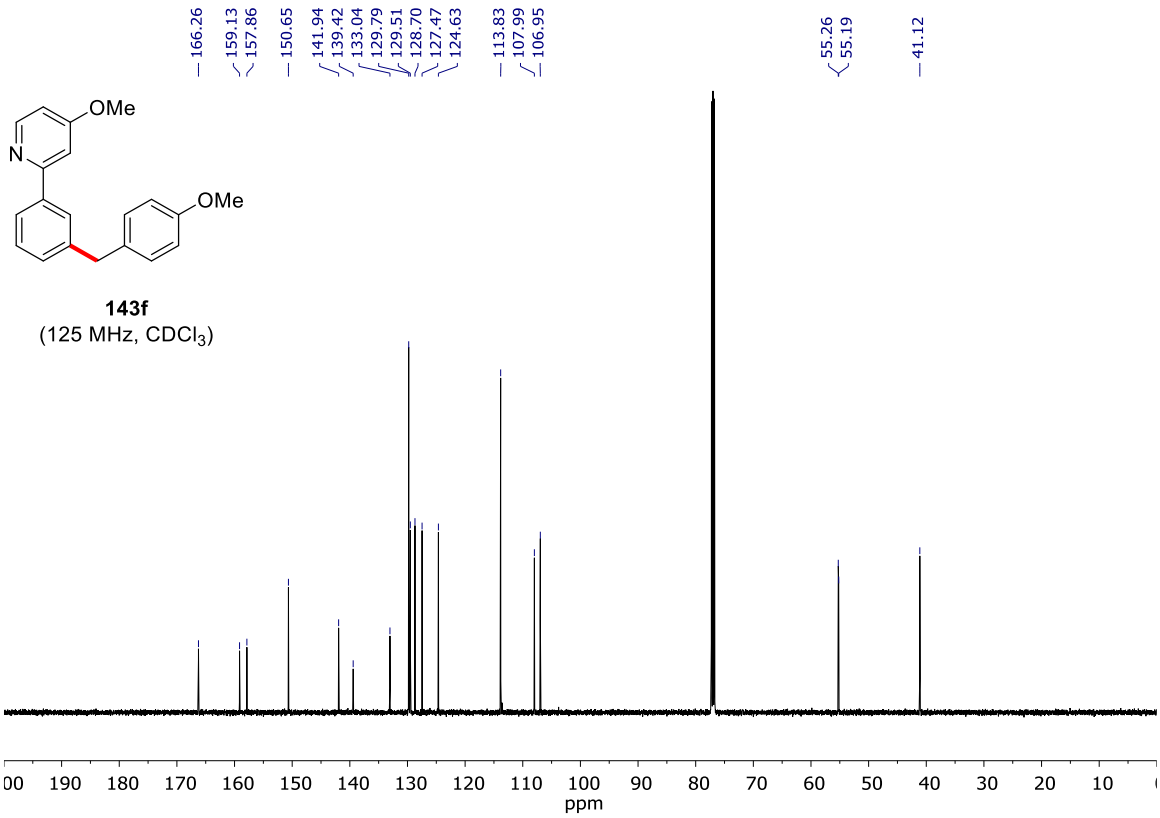
143e
(400 MHz, $CDCl_3$)



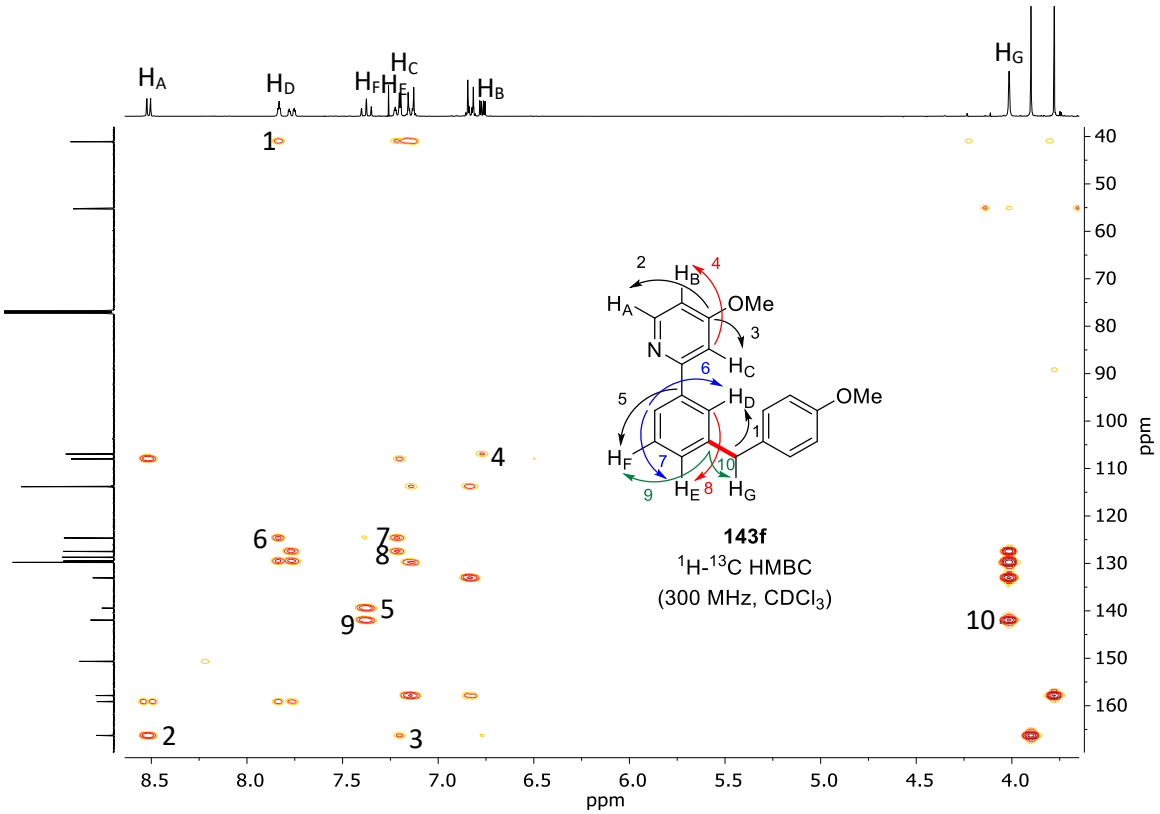
143e
(100 MHz, $CDCl_3$)



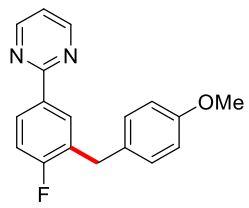
143f
(300 MHz, $CDCl_3$)



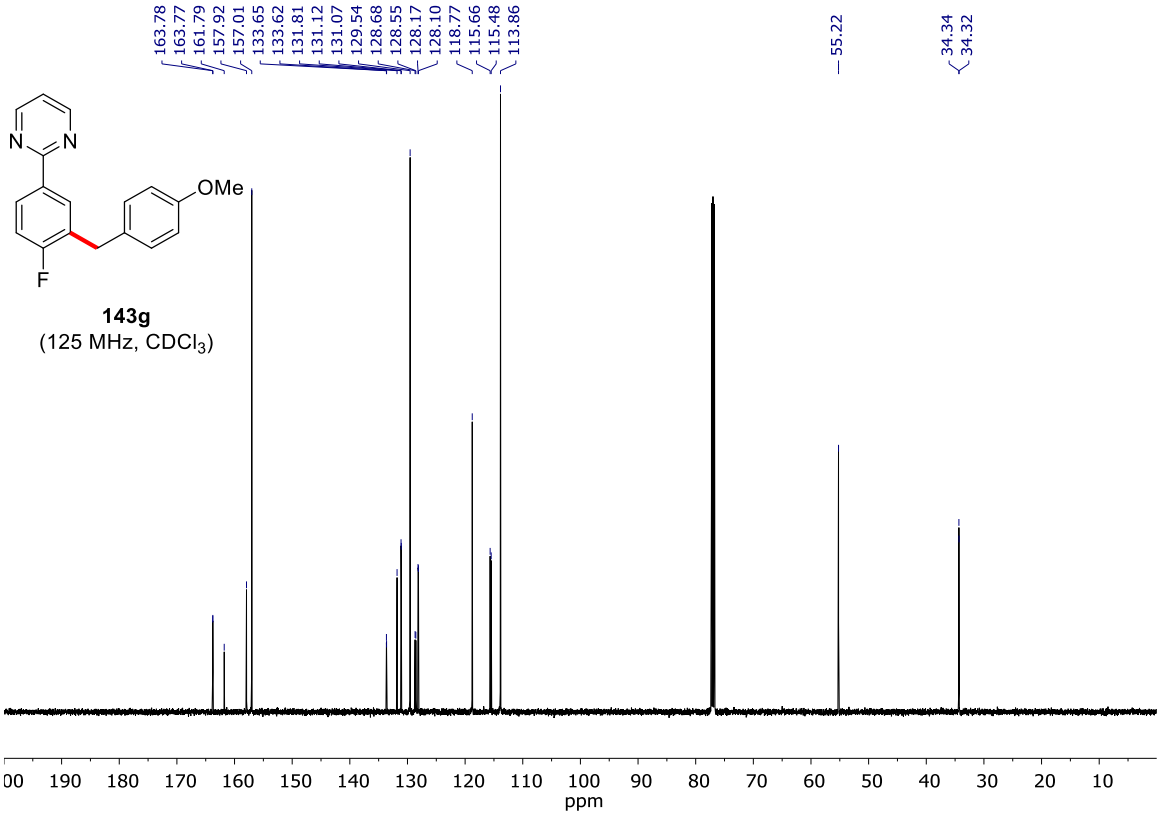
143f
(125 MHz, $CDCl_3$)



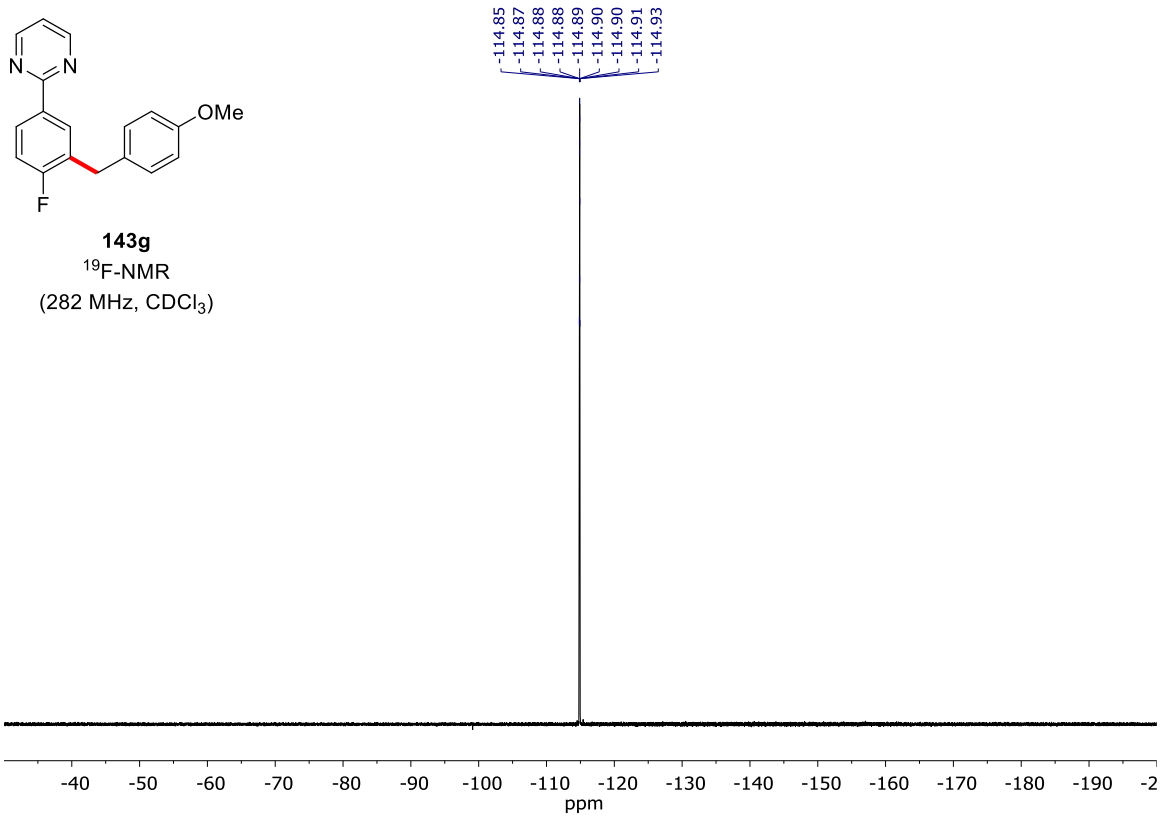
143f
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



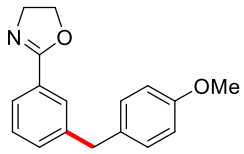
143g
(300 MHz, $CDCl_3$)



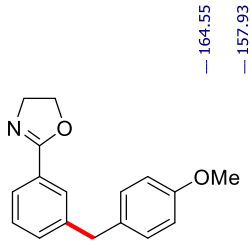
143g
(125 MHz, $CDCl_3$)



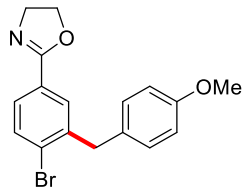
143g
^{19}F-NMR
(282 MHz, $CDCl_3$)



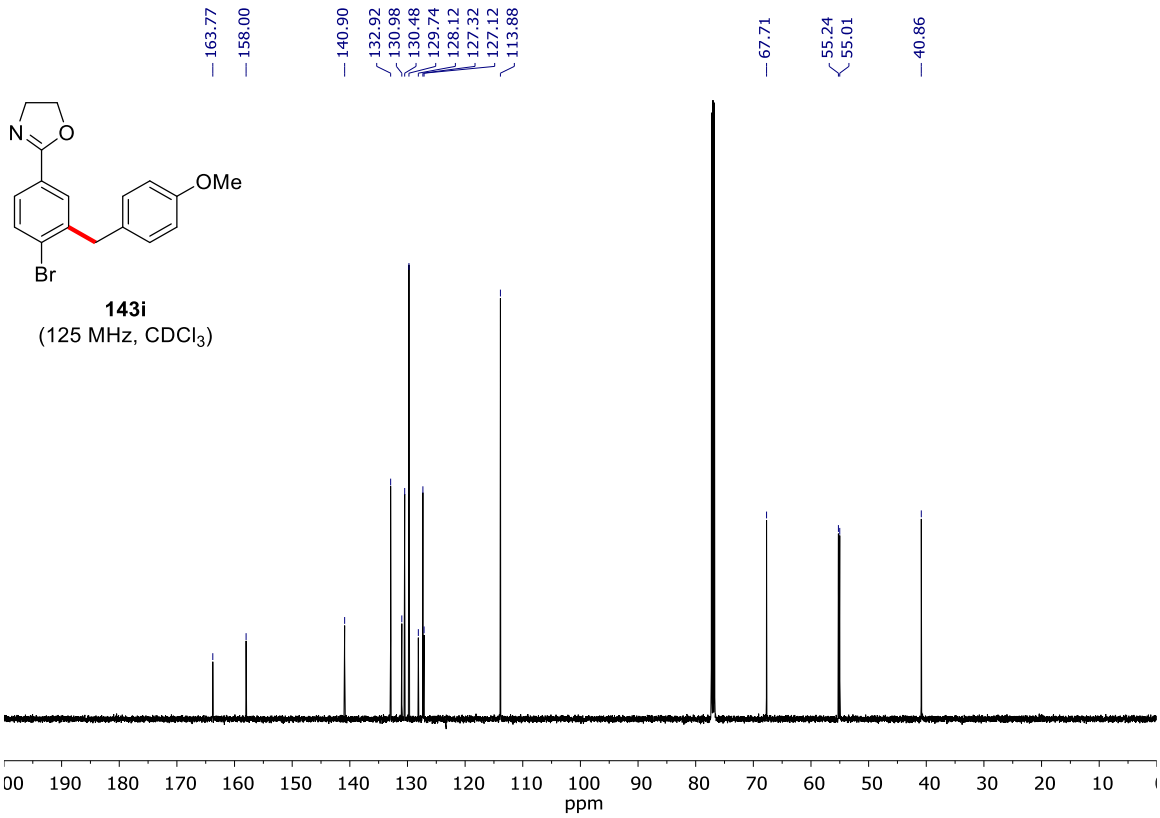
143h
(300 MHz, $CDCl_3$)



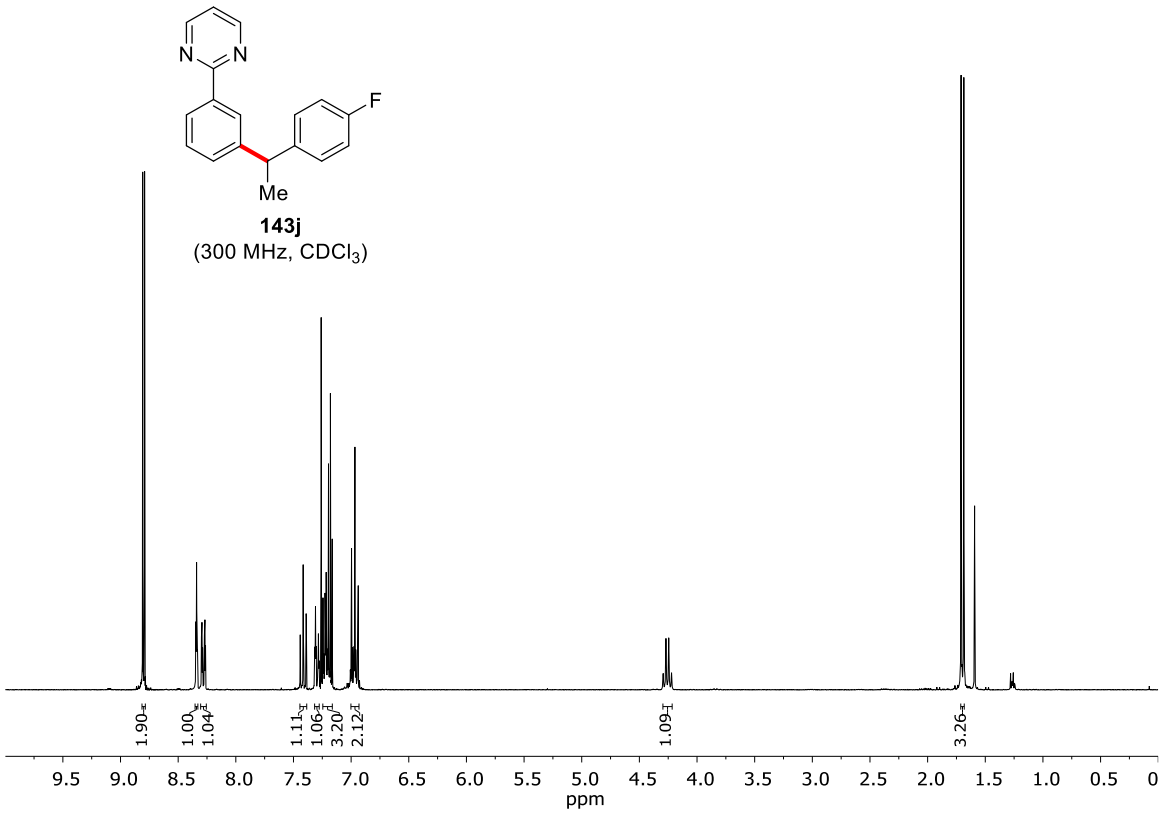
143h
(125 MHz, $CDCl_3$)

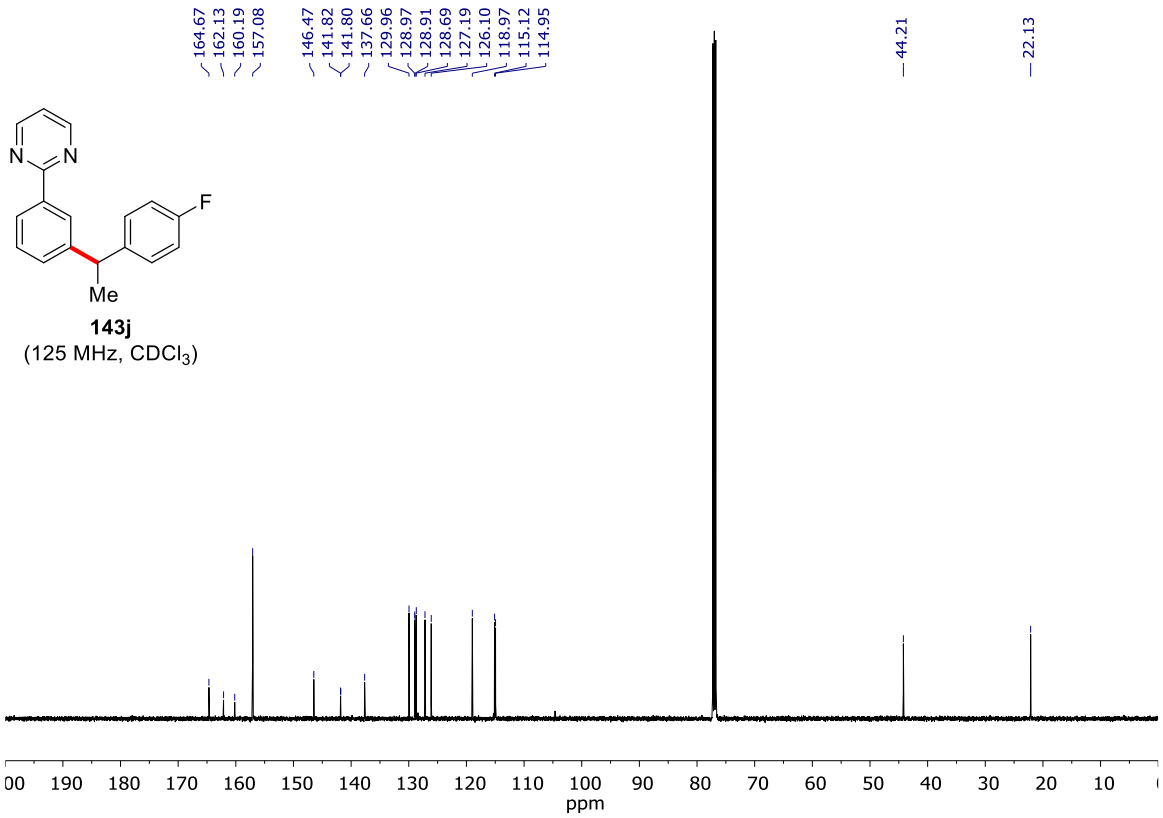


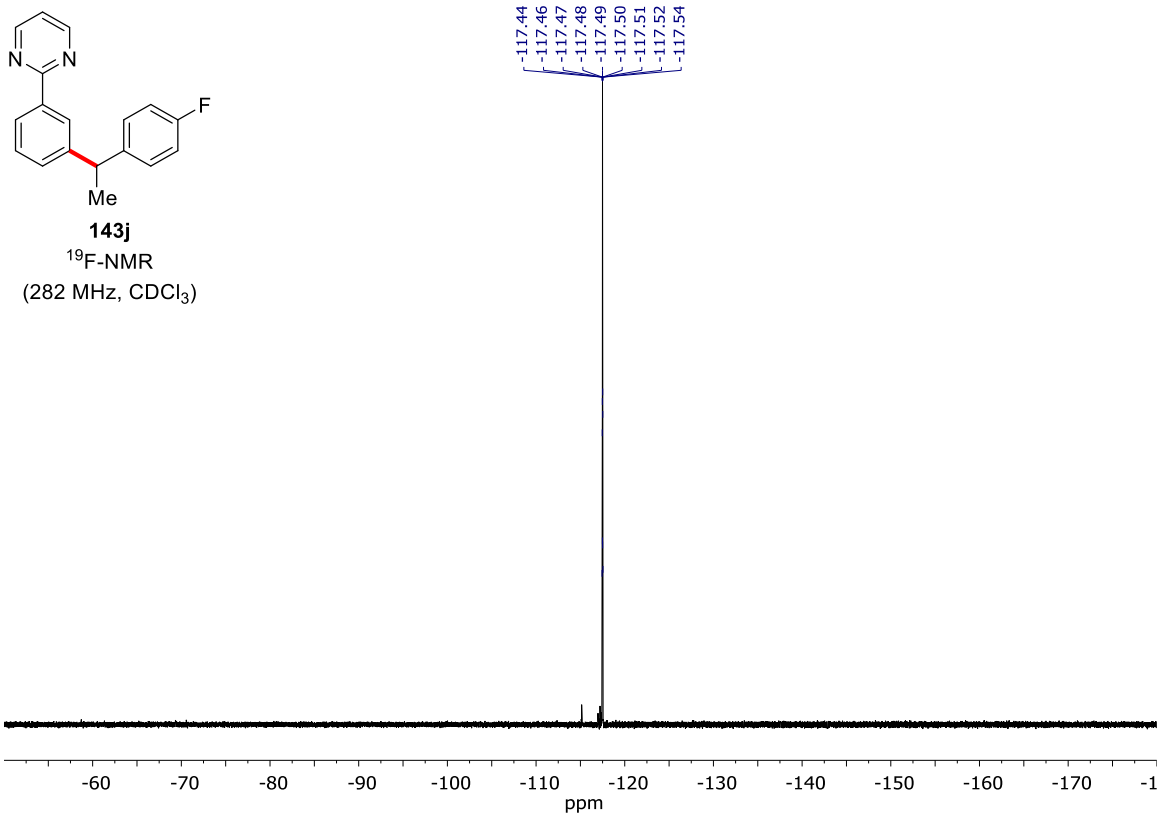
143i
(300 MHz, $CDCl_3$)



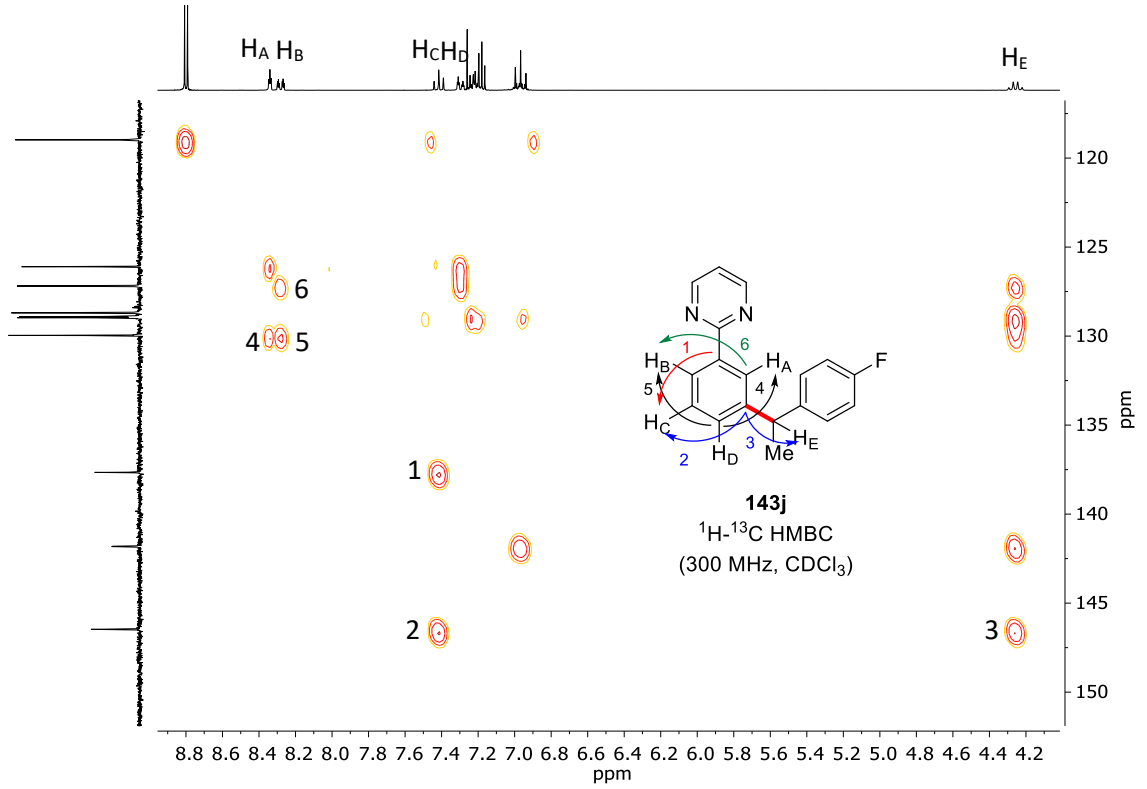
143i
(125 MHz, $CDCl_3$)


N
N
F
Me
143j
(300 MHz, CDCl3)
1.90
1.00
1.04
1.11
1.06
3.20
2.12
1.09
3.26
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
ppm

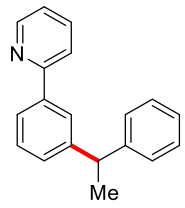

164.67
162.13
160.19
157.08
146.47
141.82
141.80
137.66
129.96
128.97
128.91
128.69
127.19
126.10
118.97
115.12
114.95
44.21
22.13
N
N
F
Me
143j
(125 MHz, CDCl3)
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm



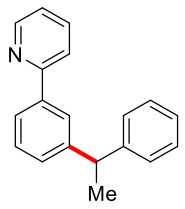
143j
^{19}F-NMR
(282 MHz, $CDCl_3$)



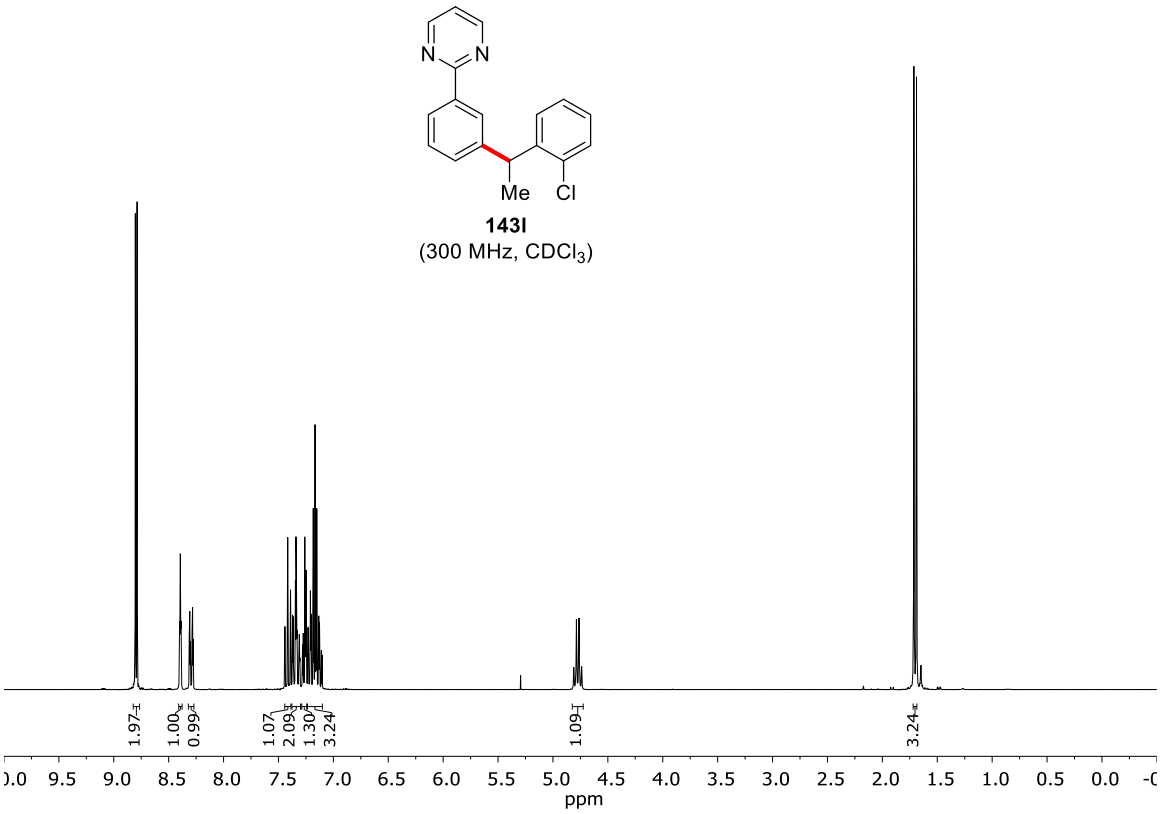
143j
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



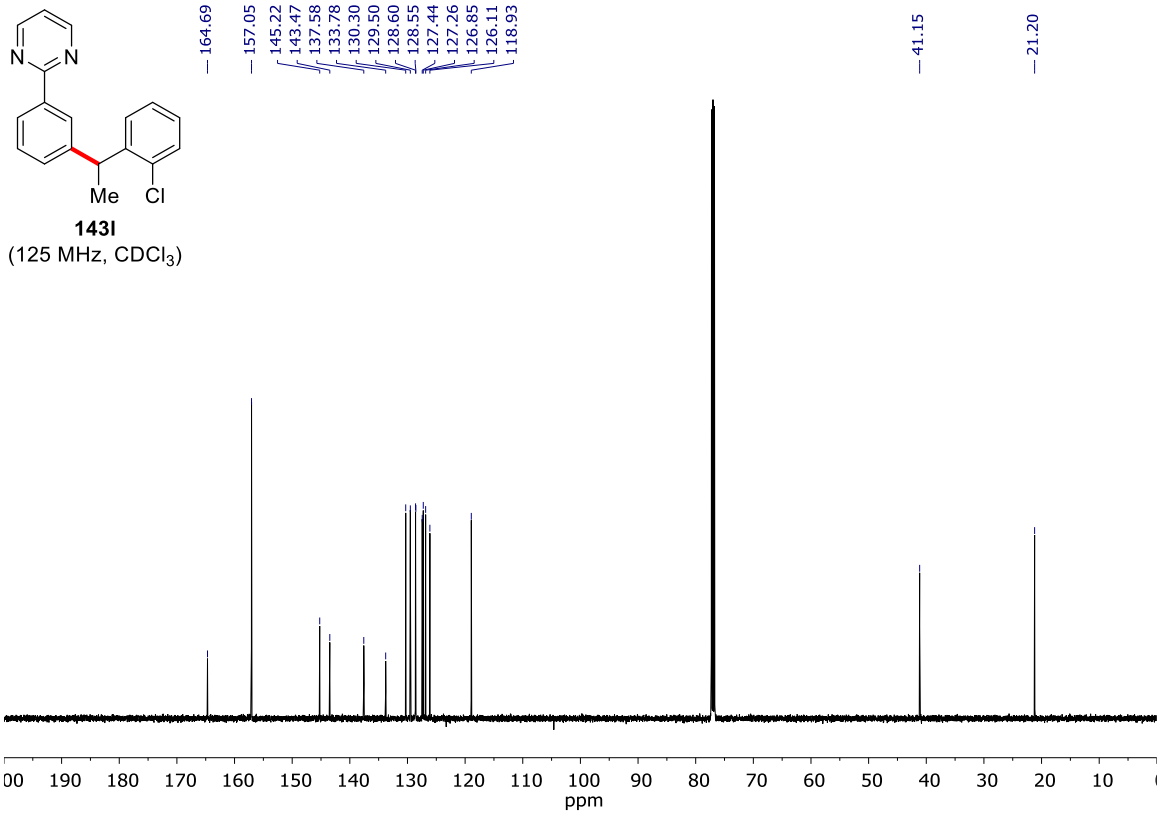
143k
(300 MHz, $CDCl_3$)



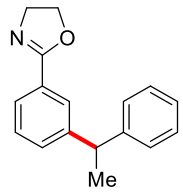
143k
(125 MHz, $CDCl_3$)



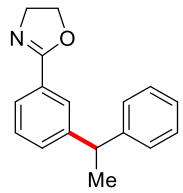
143l
(300 MHz, $CDCl_3$)



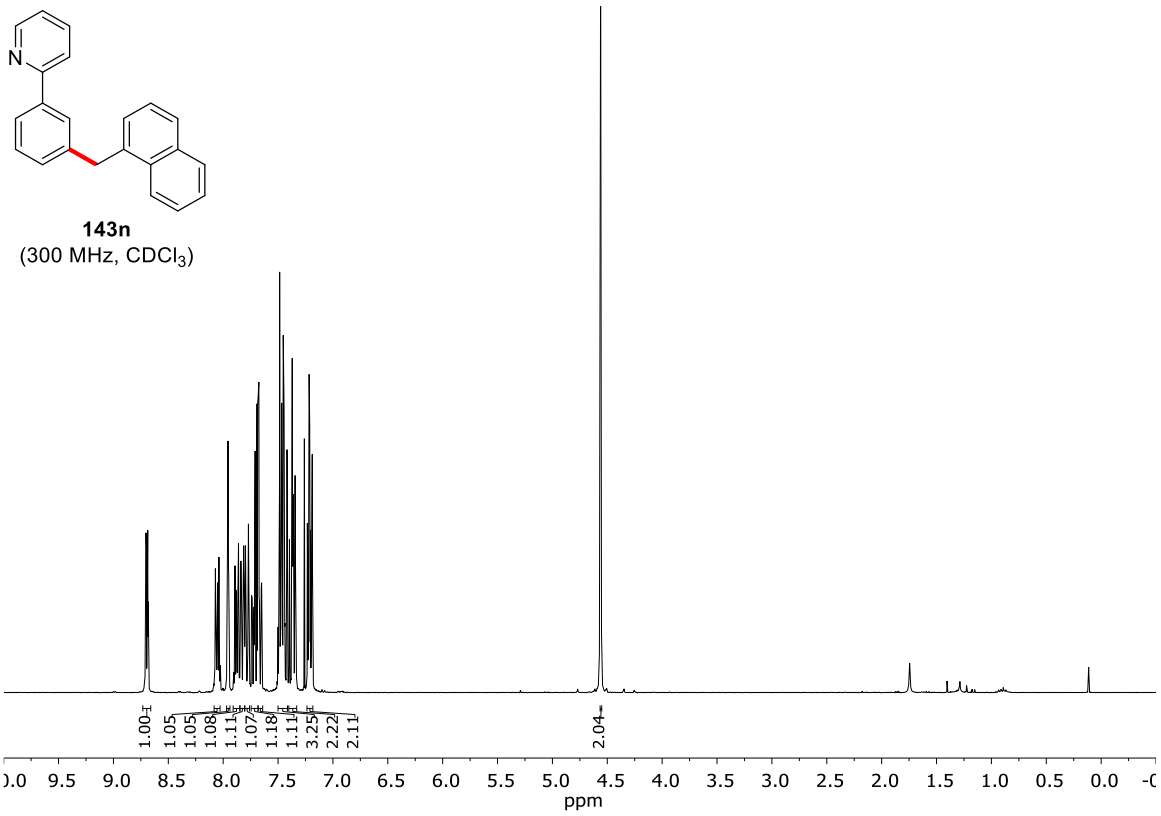
143l
(125 MHz, $CDCl_3$)

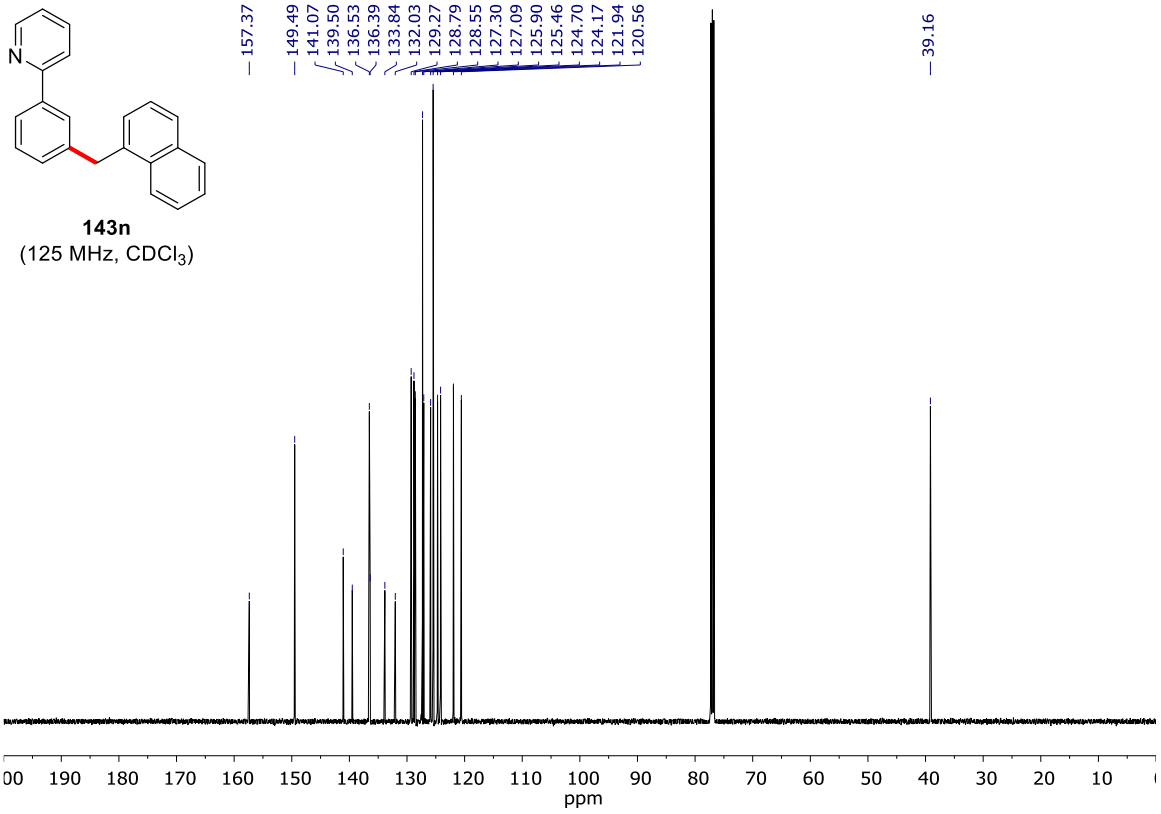


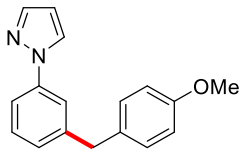
143m
(400 MHz, $CDCl_3$)



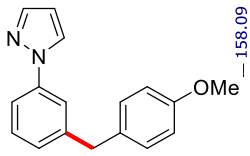
143m
(100 MHz, $CDCl_3$)


N
143n
(300 MHz, CDCl3)
1.00
1.05
1.05
1.08
1.11
1.07
1.18
1.11
3.25
2.22
2.11
2.04
ppm

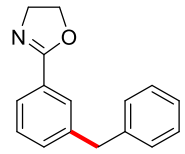

N
143n
(125 MHz, CDCl3)
157.37
149.49
141.07
139.50
136.53
136.39
133.84
132.03
129.27
128.79
128.55
127.30
127.09
125.90
125.46
124.70
124.17
121.94
120.56
39.16
ppm



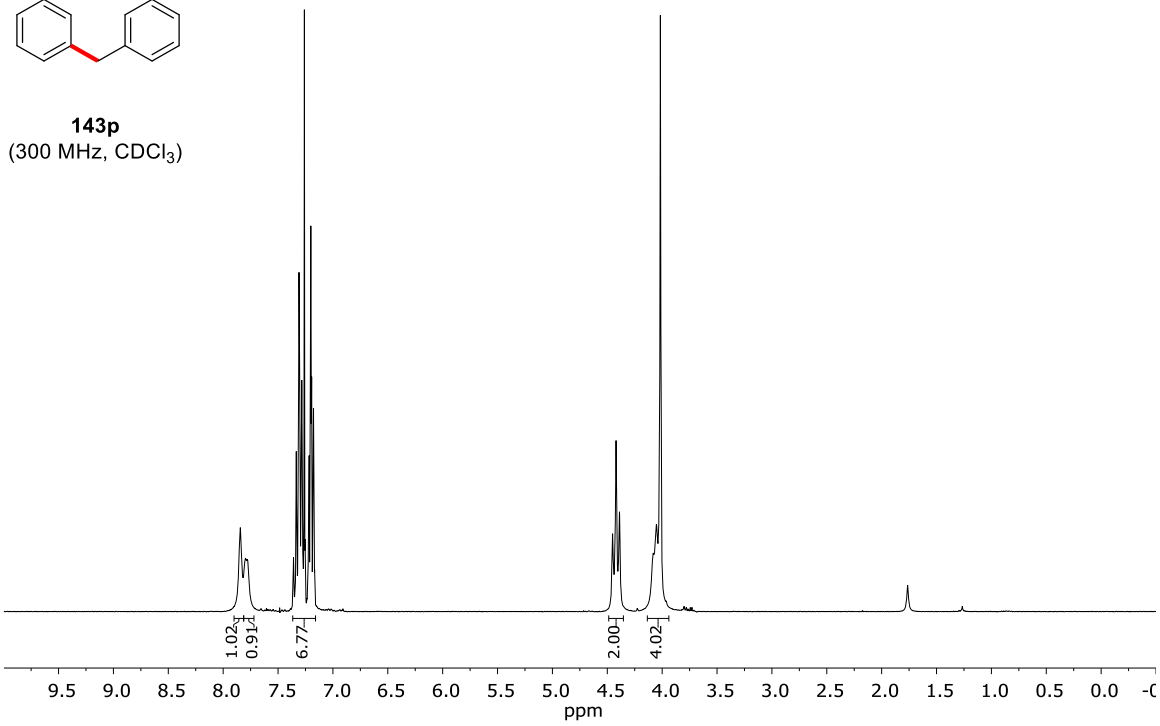
143o
(400 MHz, $CDCl_3$)

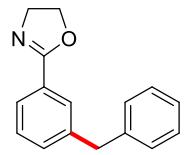


143o
(100 MHz, $CDCl_3$)

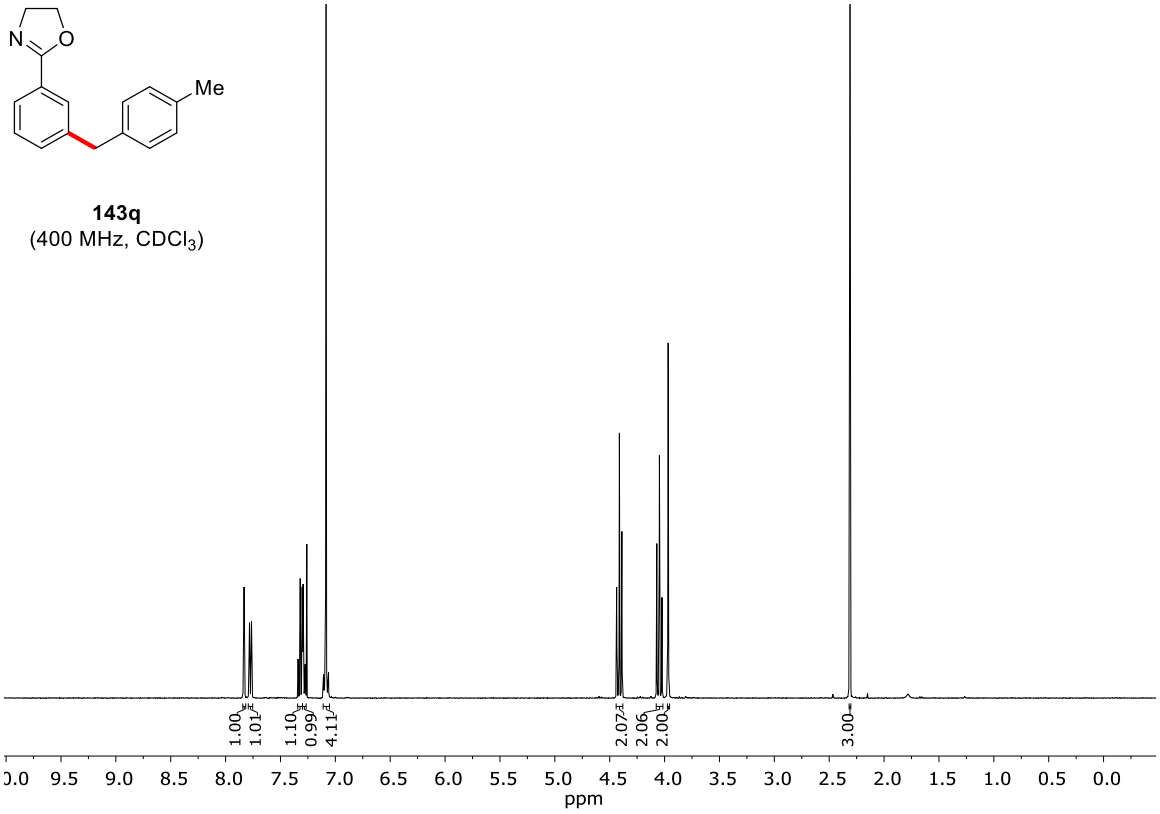


143p
(300 MHz, $CDCl_3$)

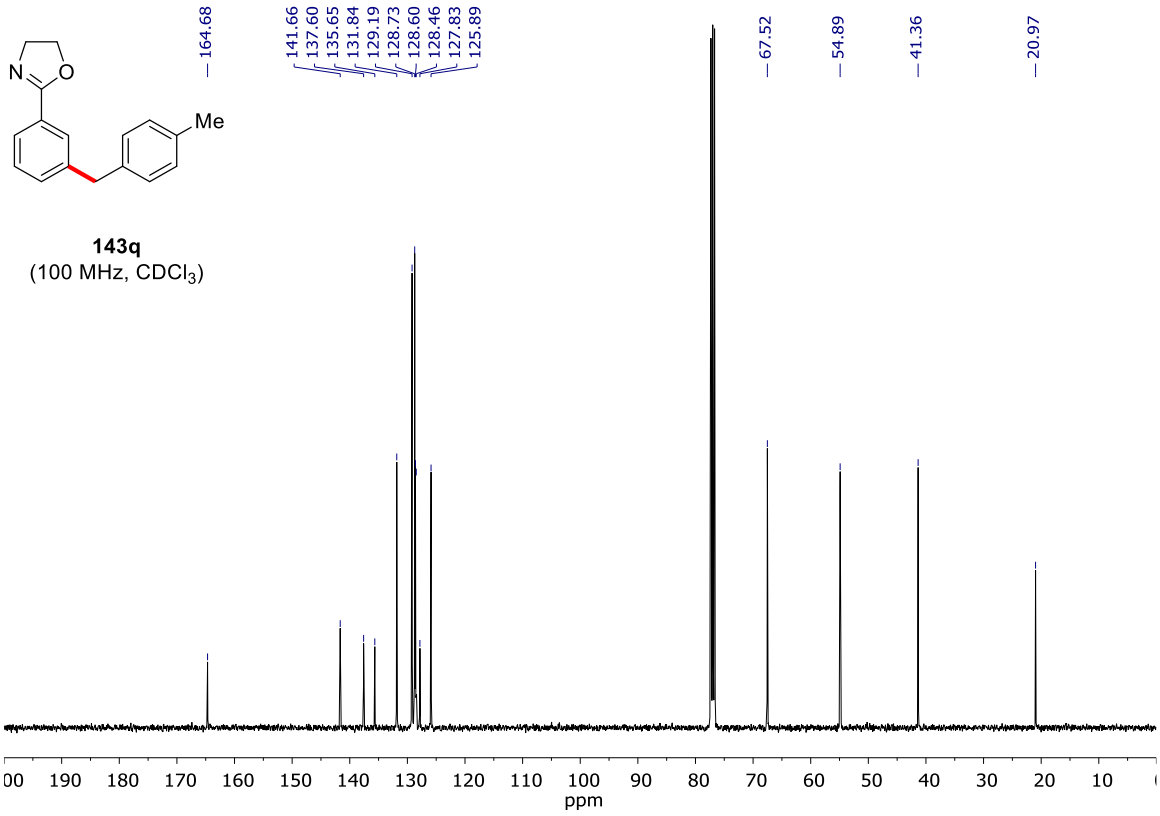




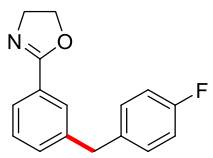
143p
(125 MHz, $CDCl_3$)



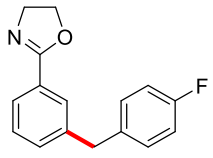
143q
(400 MHz, $CDCl_3$)



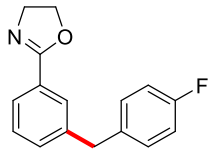
143q
(100 MHz, $CDCl_3$)



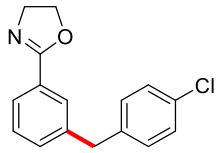
143r
(300 MHz, $CDCl_3$)



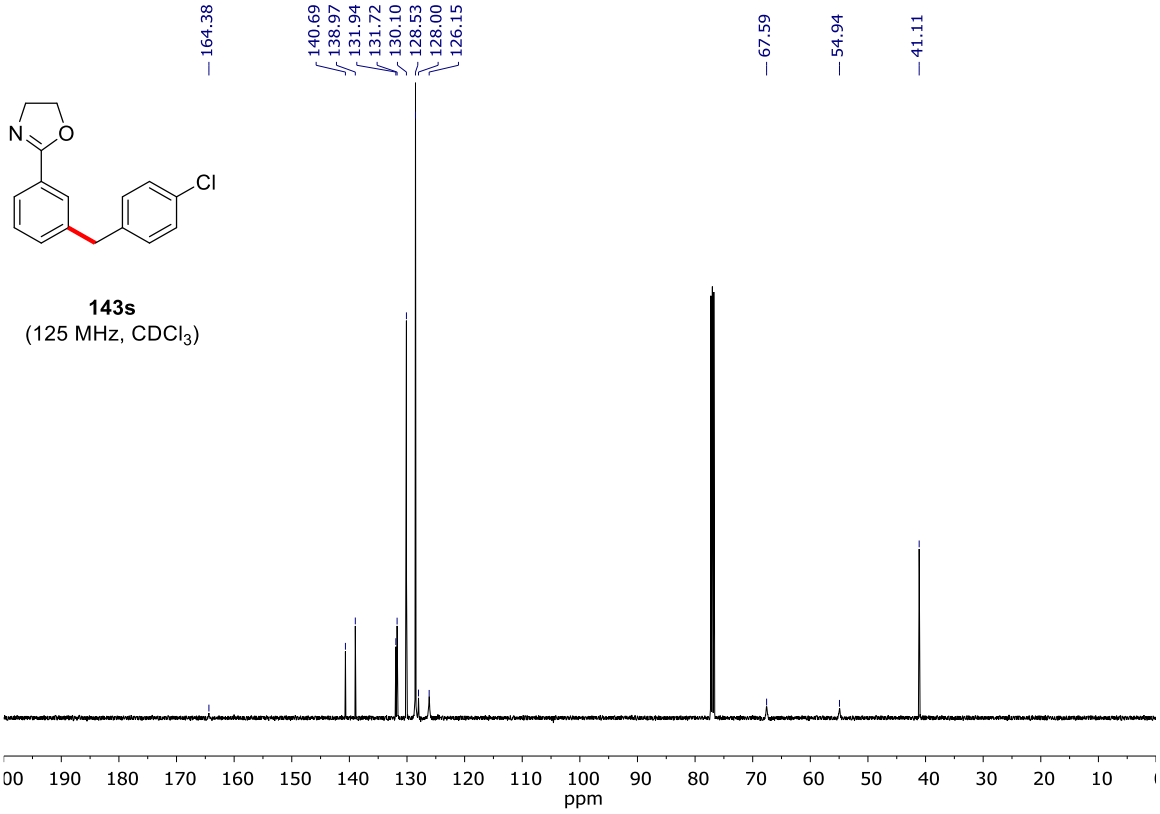
143r
(125 MHz, $CDCl_3$)



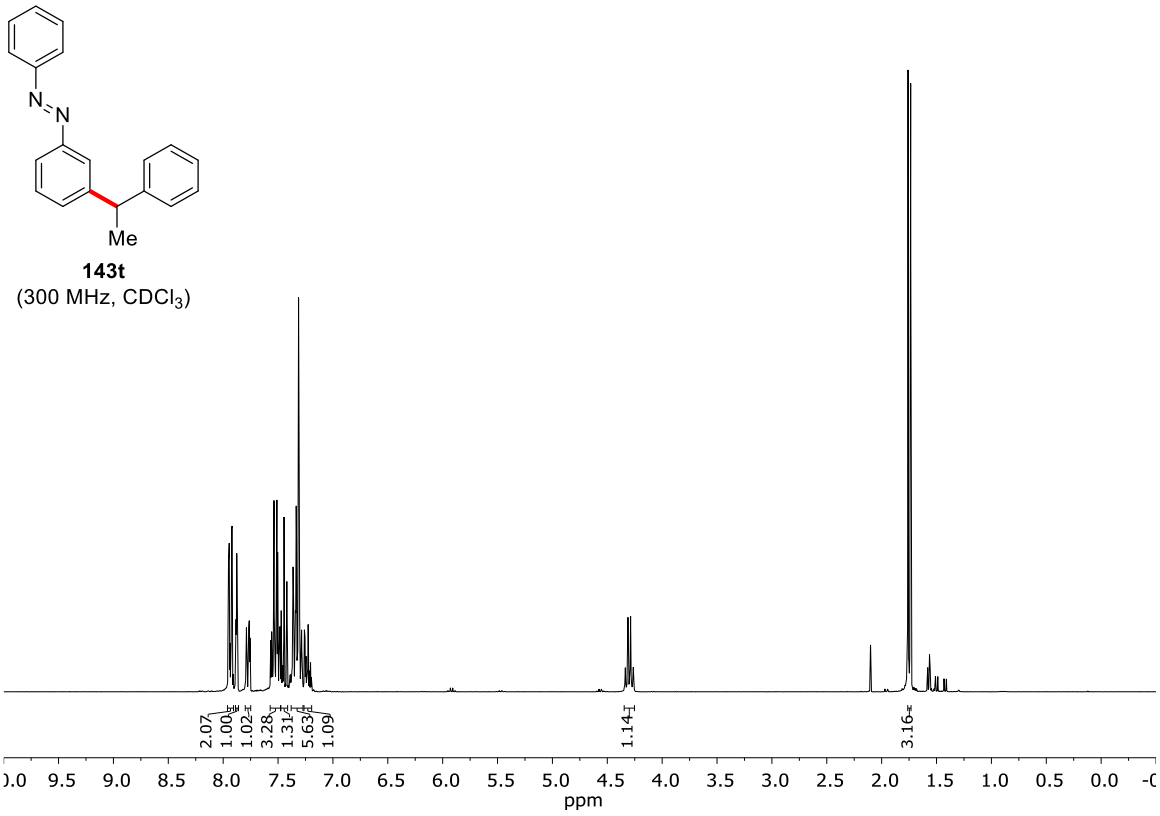
143r
^{19}F-NMR
(282 MHz, $CDCl_3$)



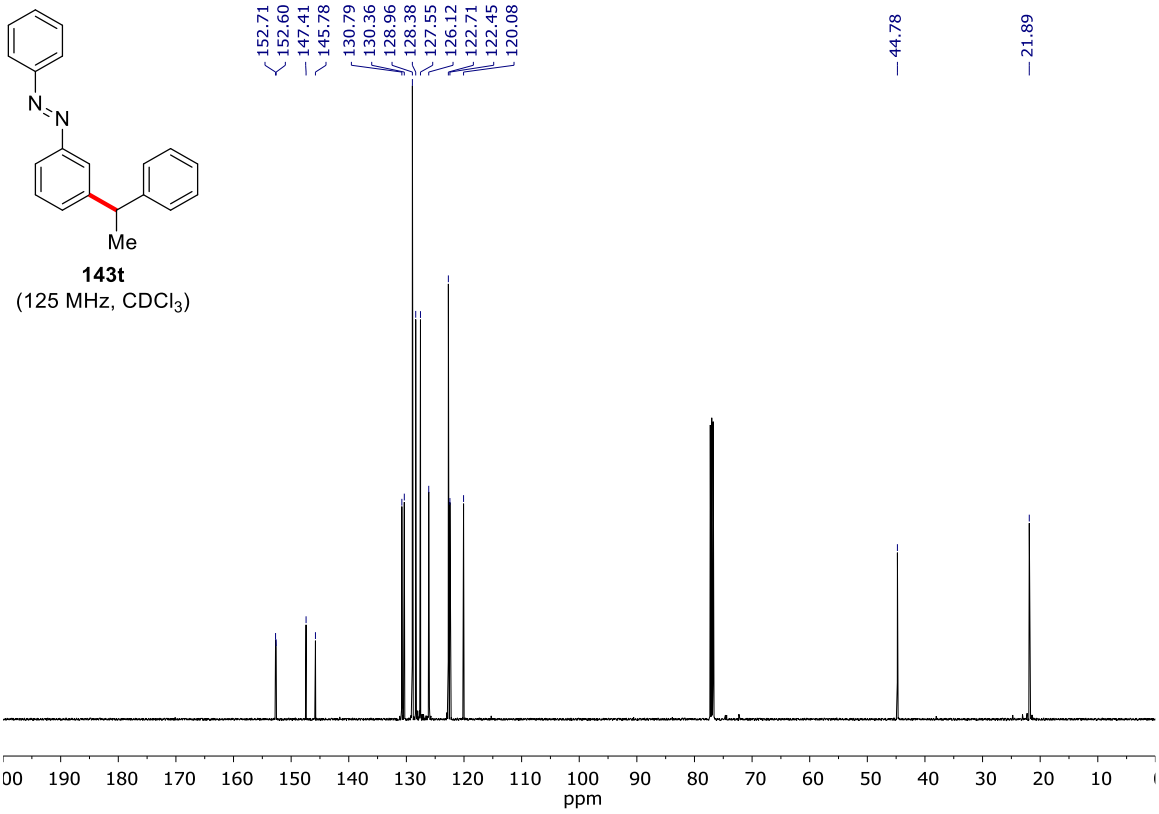
143s
(600 MHz, $CDCl_3$)



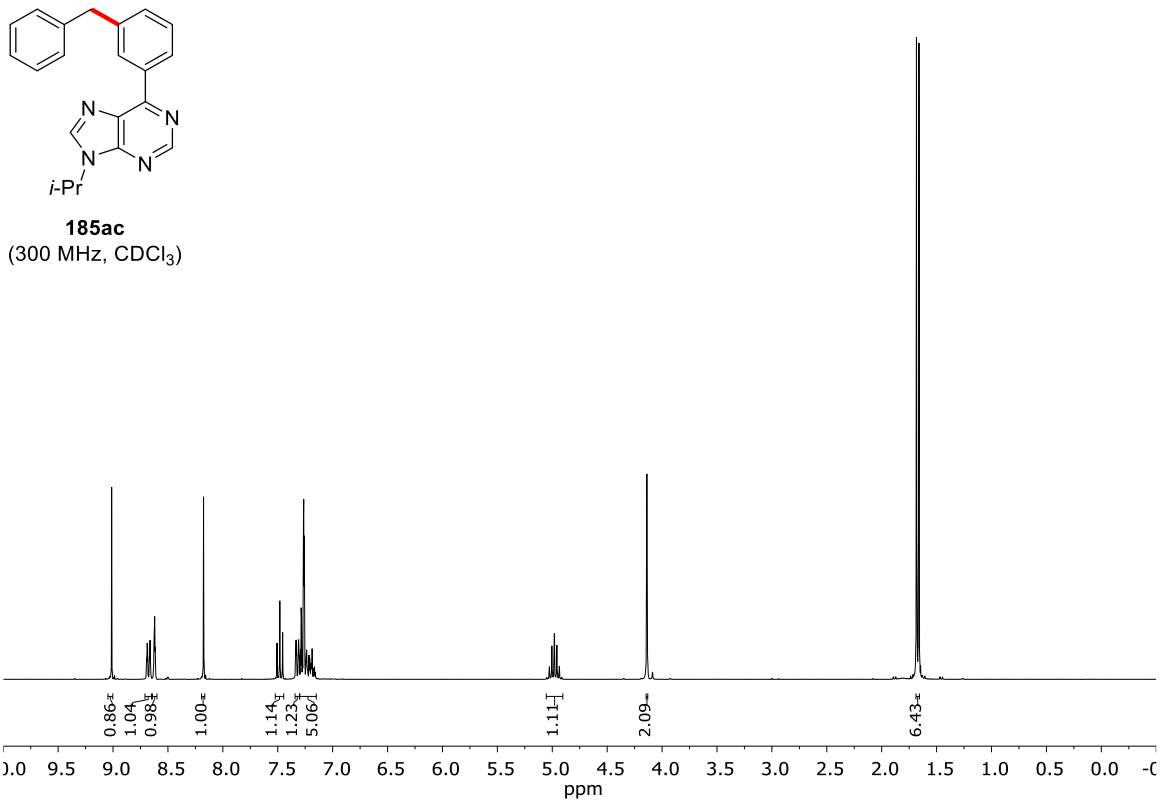
143s
(125 MHz, $CDCl_3$)



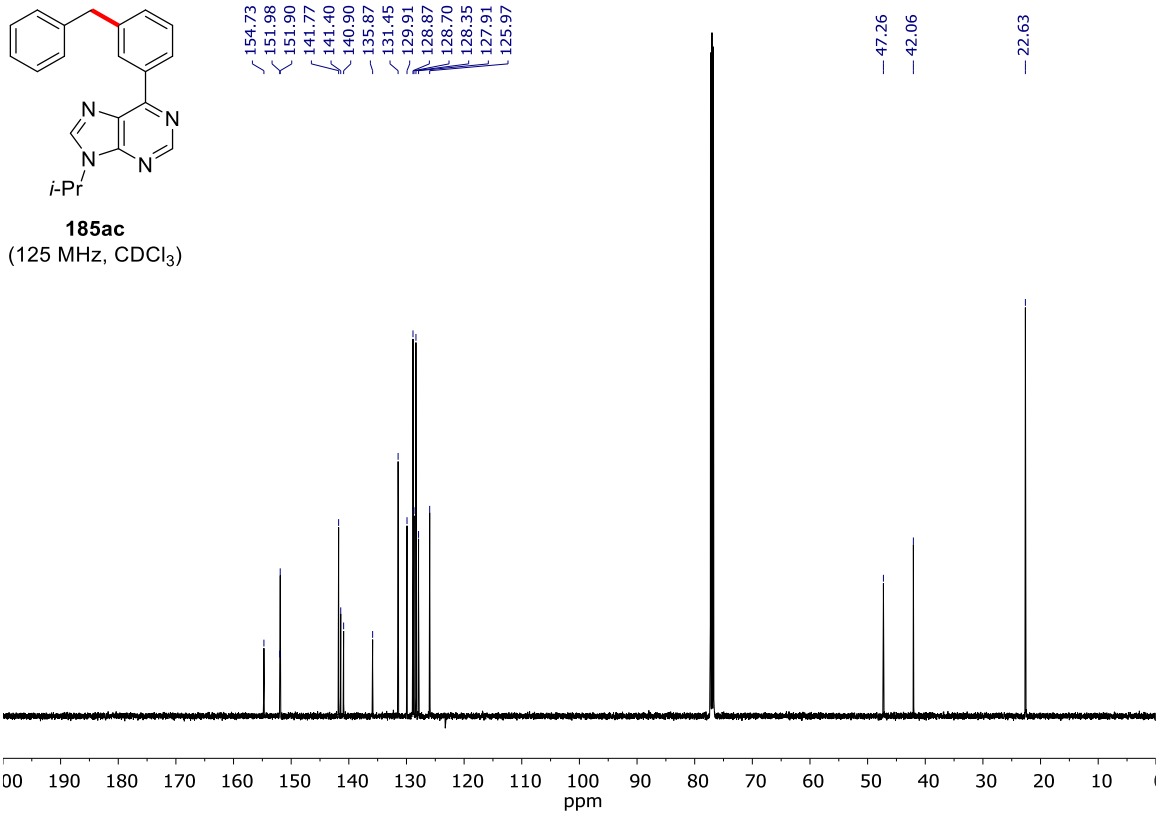
143t
(300 MHz, $CDCl_3$)



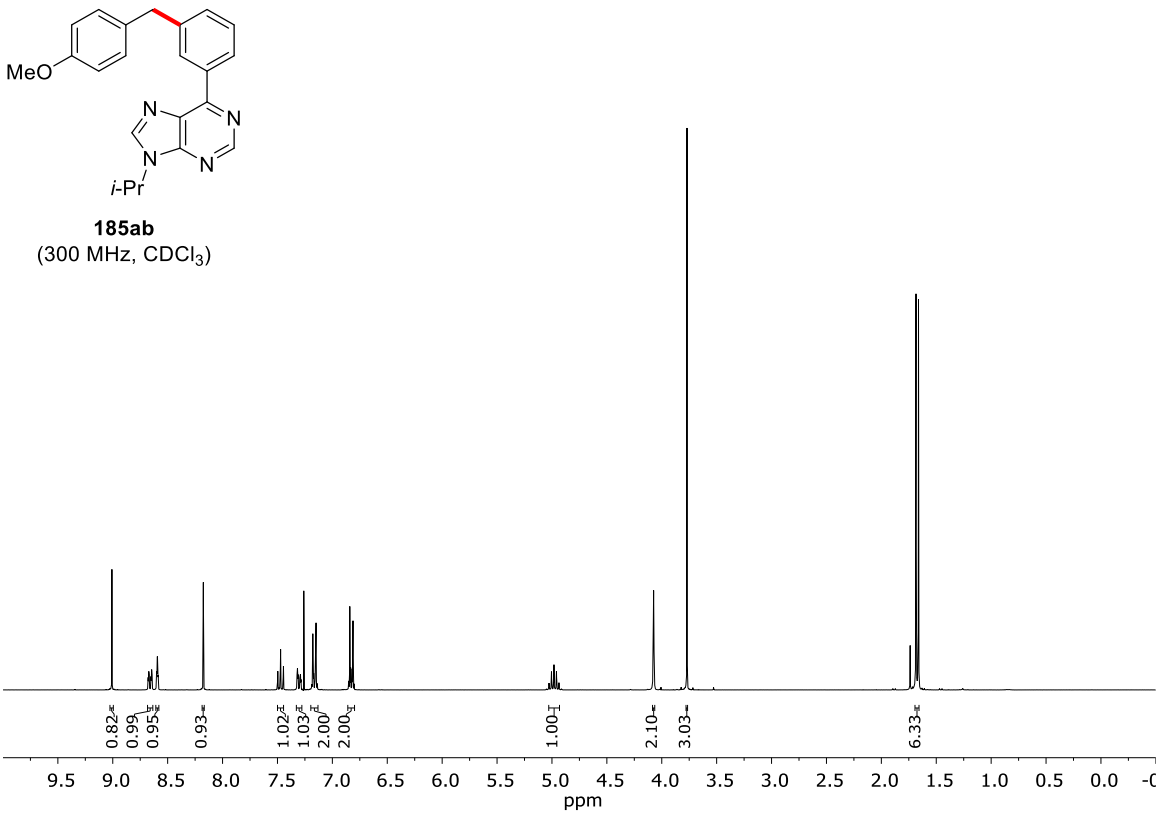
143t
(125 MHz, $CDCl_3$)



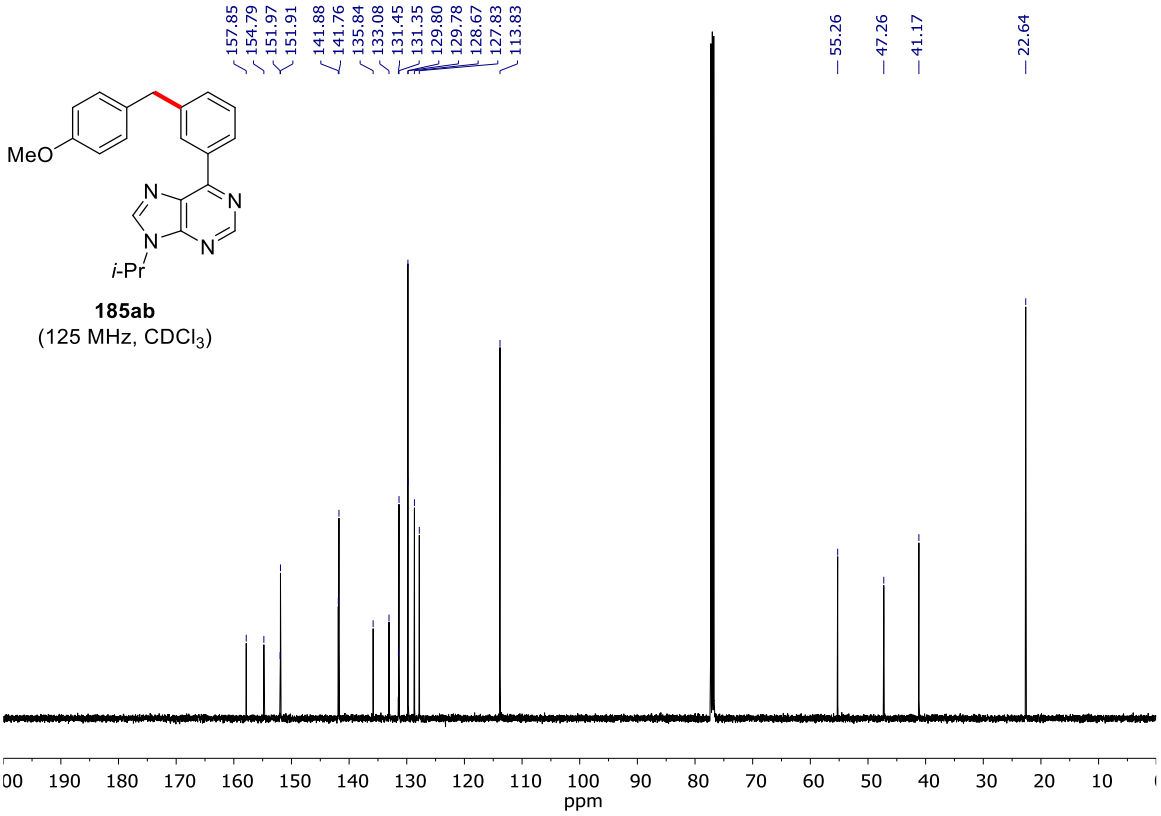
185ac
(300 MHz, $CDCl_3$)

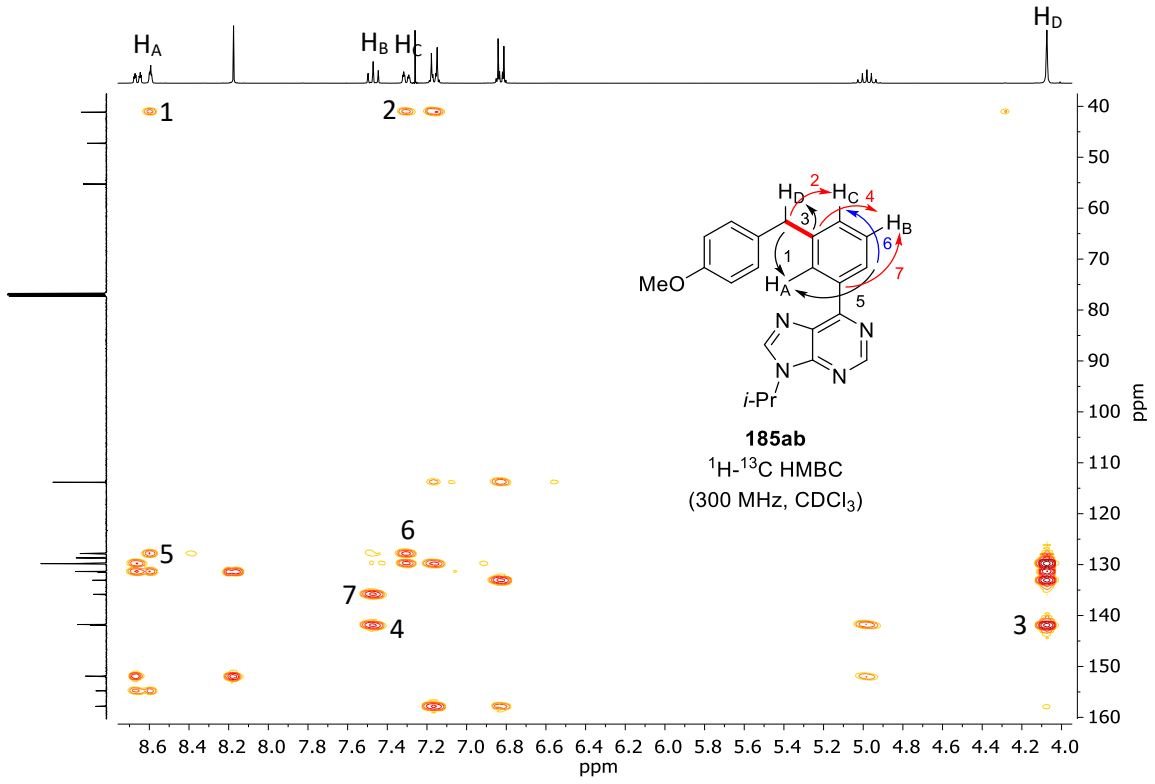


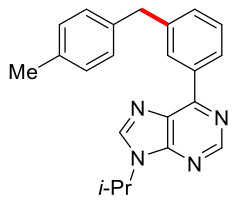
185ac
(125 MHz, $CDCl_3$)



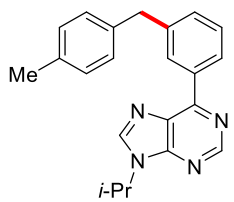
185ab
(300 MHz, $CDCl_3$)


157.85
154.79
151.97
151.91
141.88
141.76
135.84
133.08
131.45
131.35
129.80
129.78
128.67
127.83
113.83
55.26
47.26
41.17
22.64
MeO
N
N
N
N
i-Pr
185ab
(125 MHz, CDCl3)
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

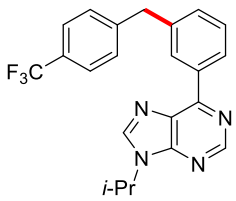

HA
HB HC
HD
1
2
5
6
7
4
3
HD 2 HC 4
3
HB
6
1
HA
7
5
MeO
N
N
N
N
i-Pr
185ab
1H-13C HMBC
(300 MHz, CDCl3)
40 50 60 70 80 90 100 110 120 130 140 150 160
ppm
8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0
ppm



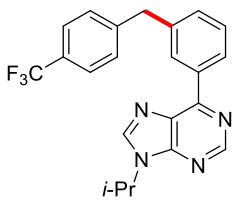
185af
(400 MHz, $CDCl_3$)



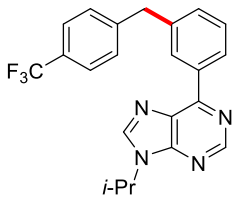
185af
(100 MHz, $CDCl_3$)



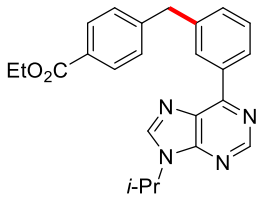
185ag
(500 MHz, $CDCl_3$)



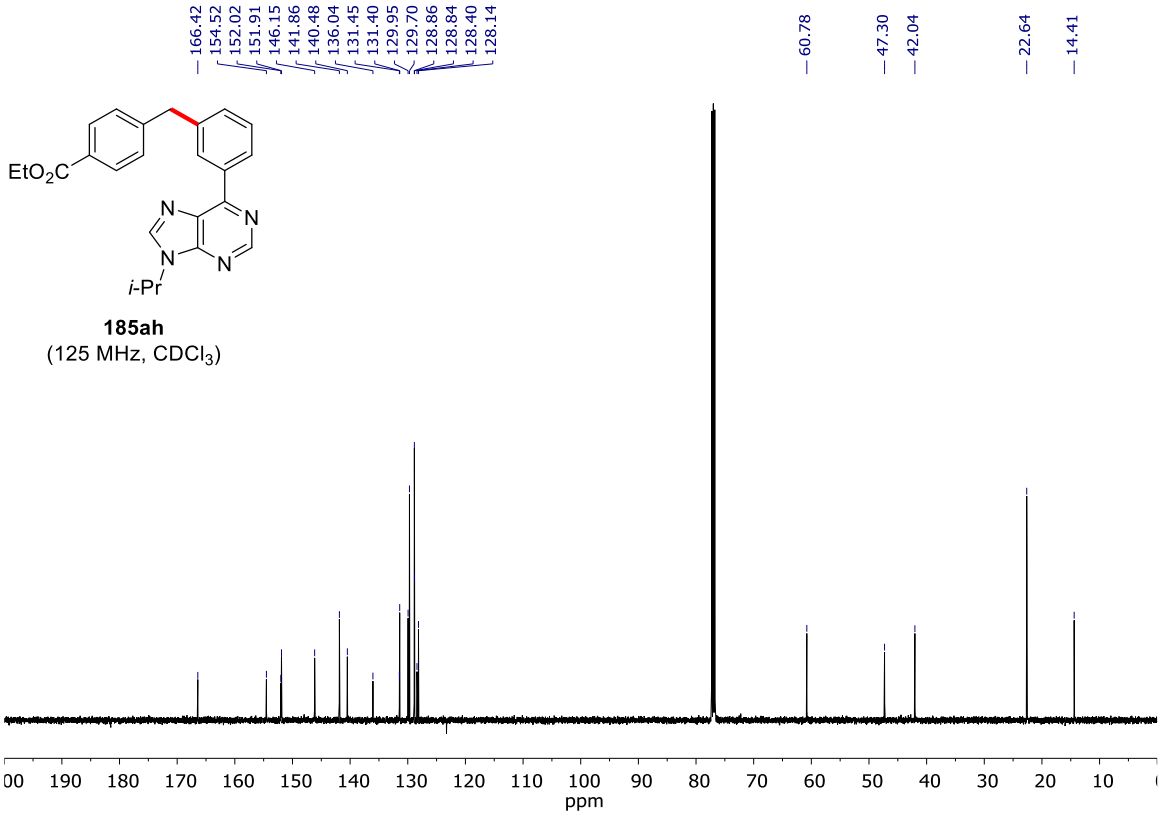
185ag
(125 MHz, $CDCl_3$)



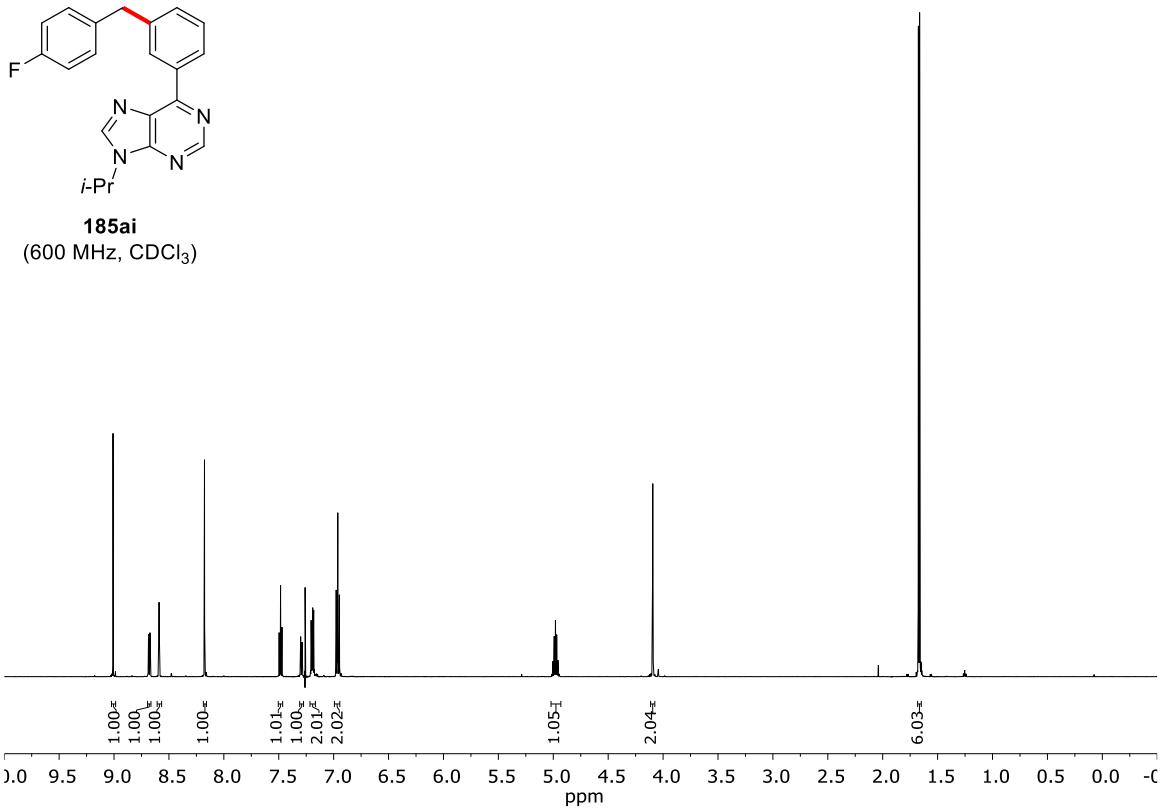
185ag
^{19}F-NMR
(470 MHz, $CDCl_3$)



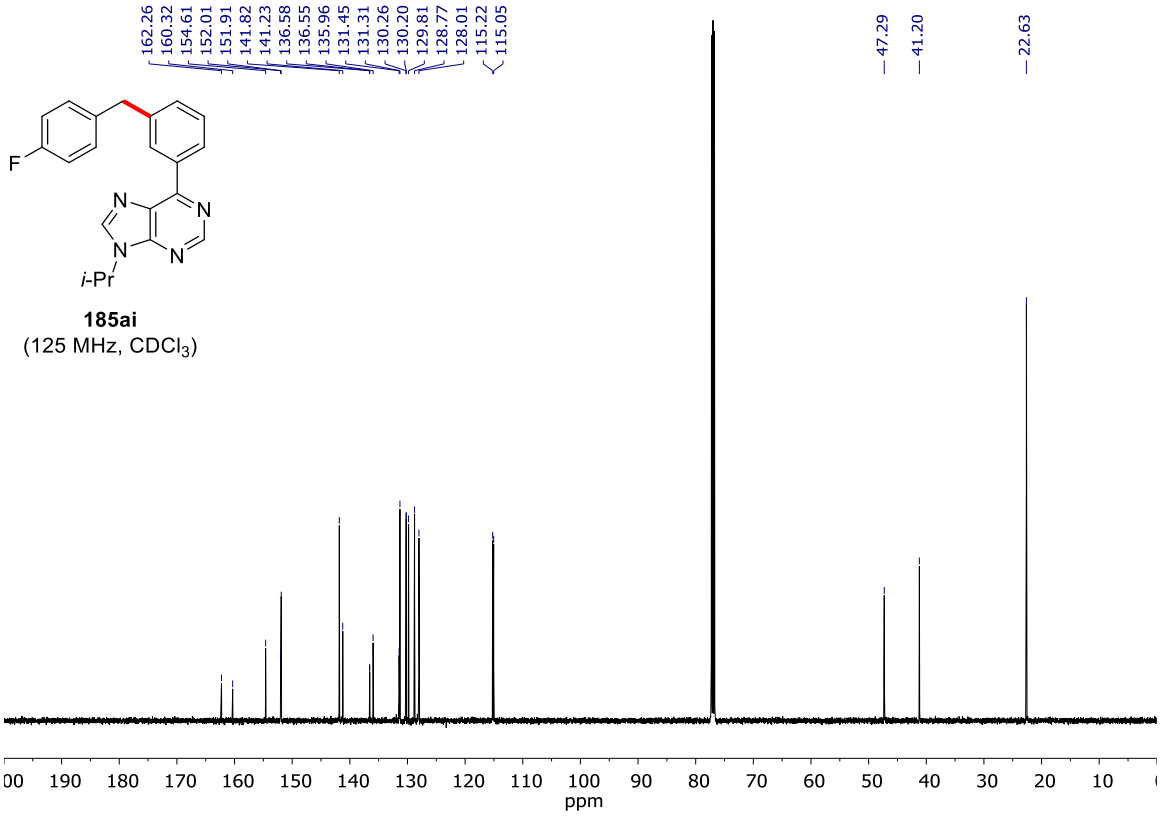
185ah
(300 MHz, $CDCl_3$)



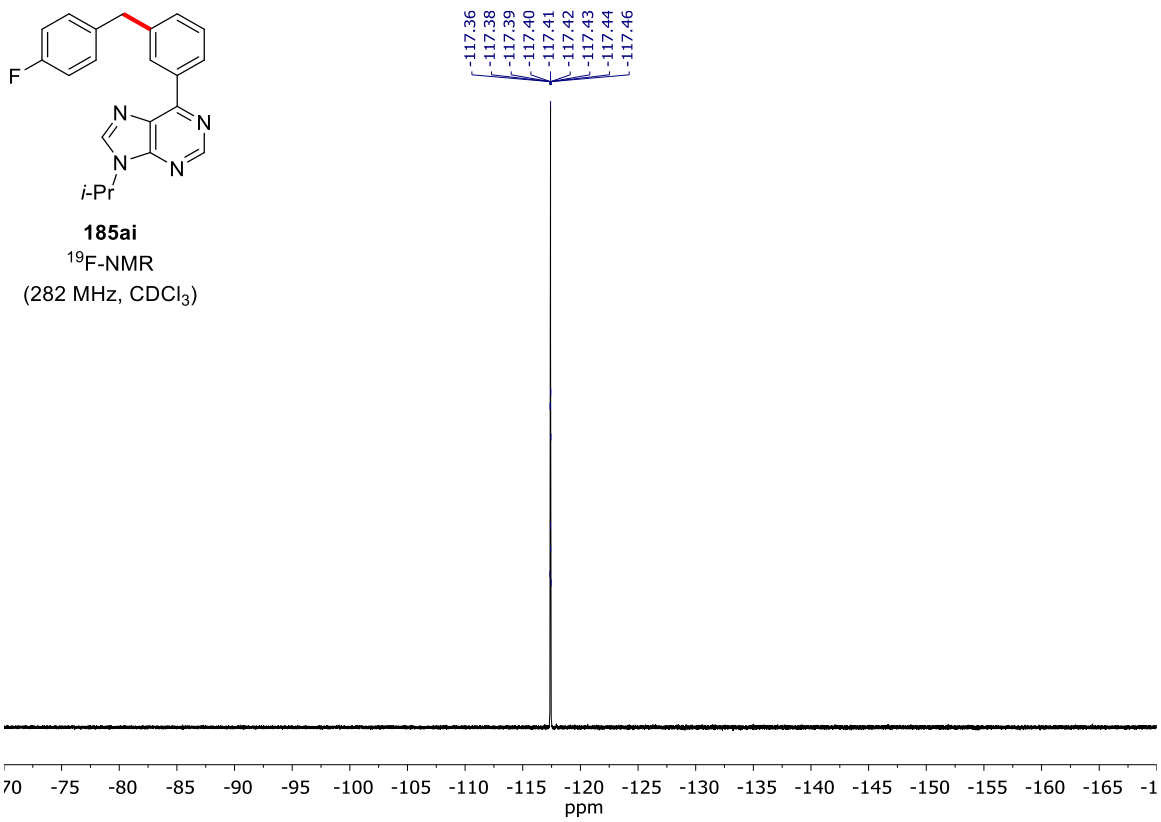
185ah
(125 MHz, $CDCl_3$)



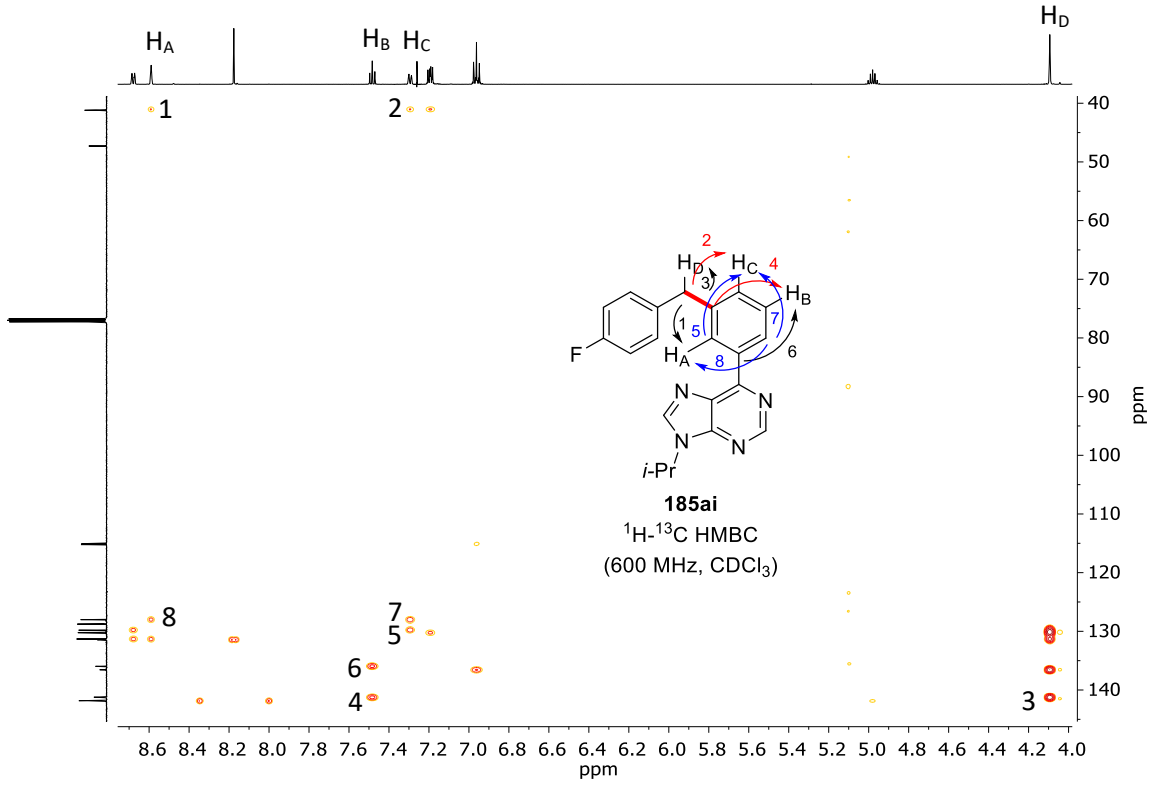
185ai
(600 MHz, $CDCl_3$)



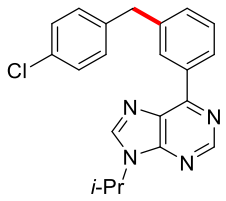
185ai
(125 MHz, $CDCl_3$)



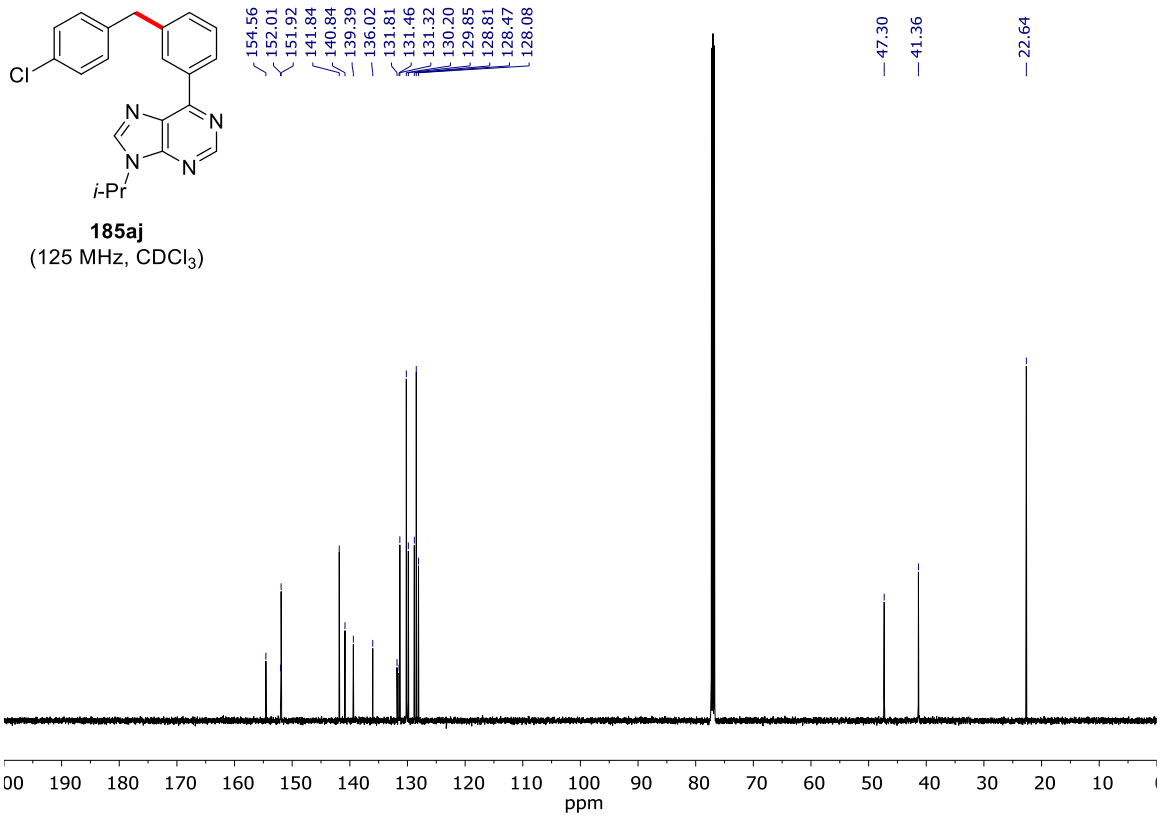
185ai
^{19}F-NMR
(282 MHz, $CDCl_3$)



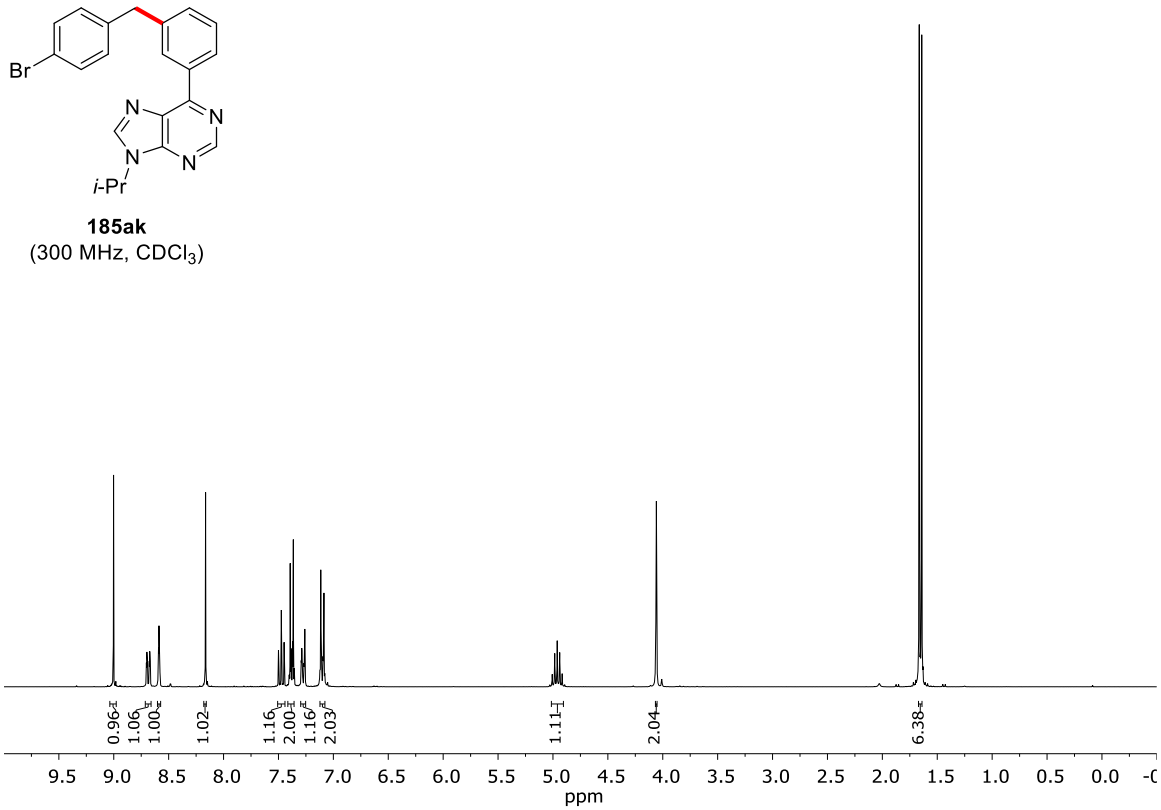
185ai
^{1}H-^{13}C HMBC
(600 MHz, $CDCl_3$)



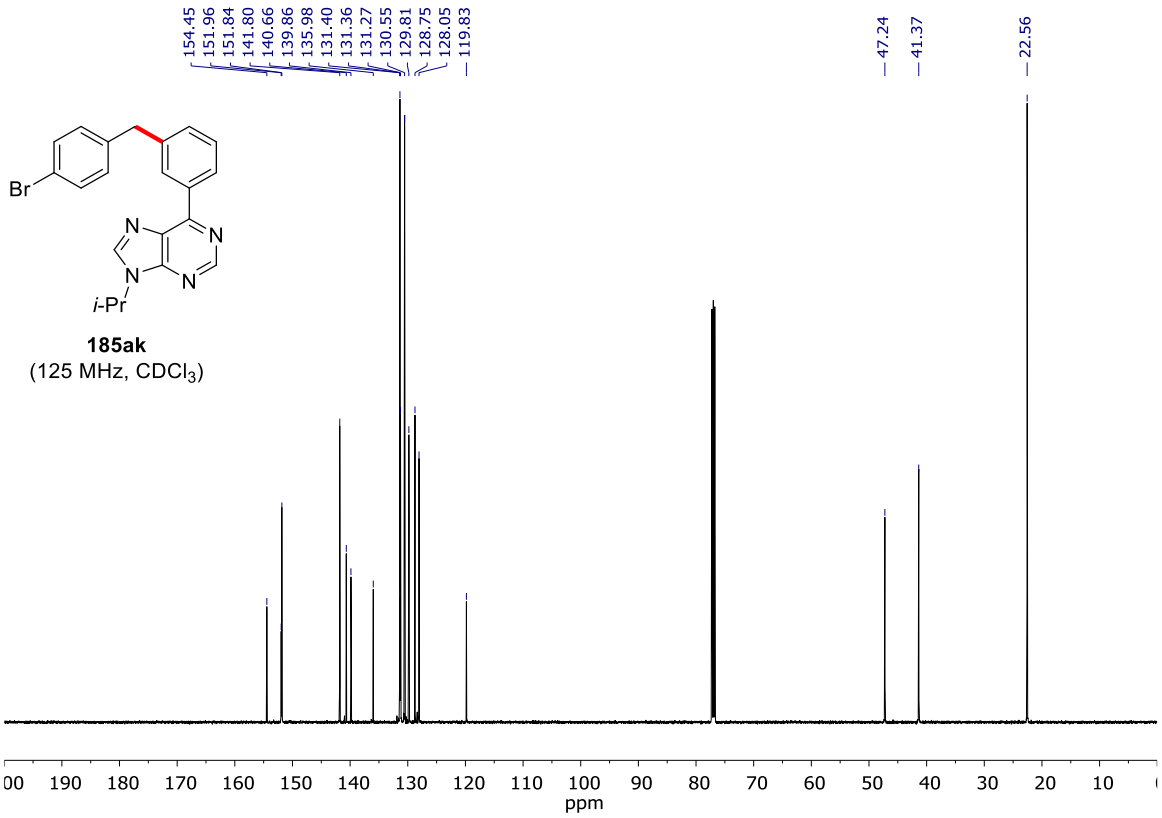
185aj
(300 MHz, $CDCl_3$)

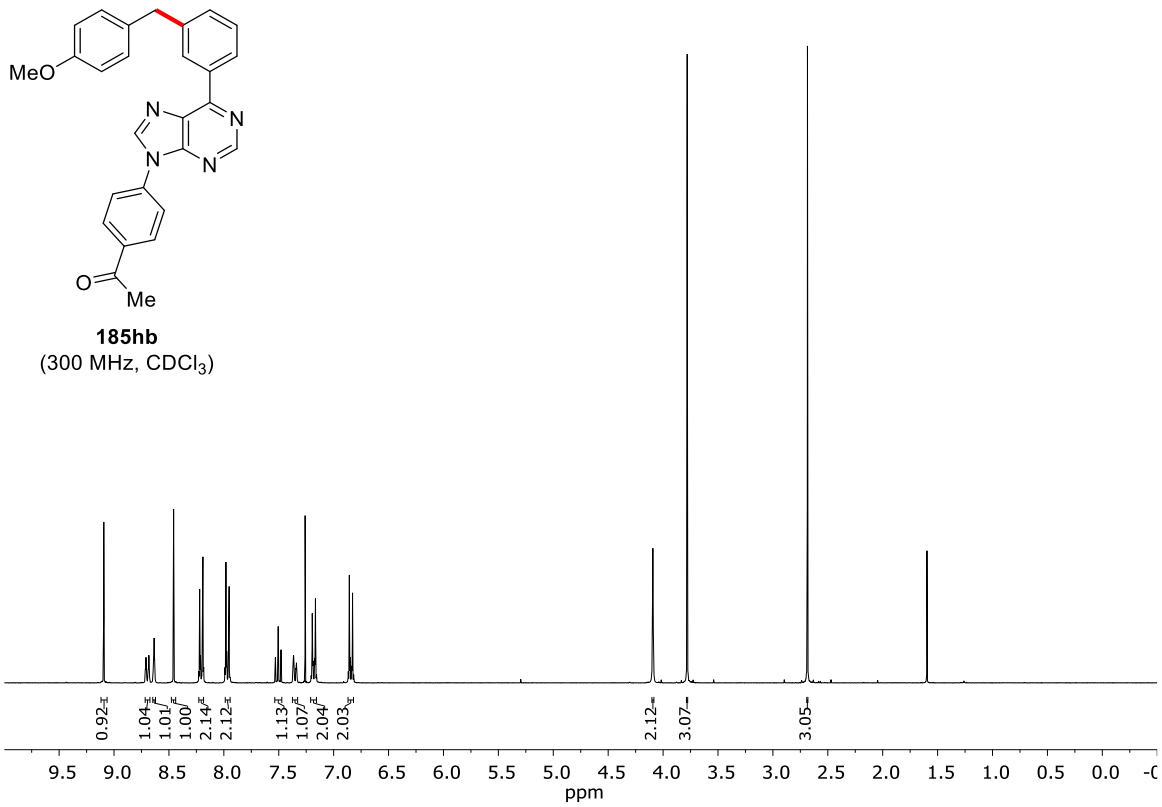


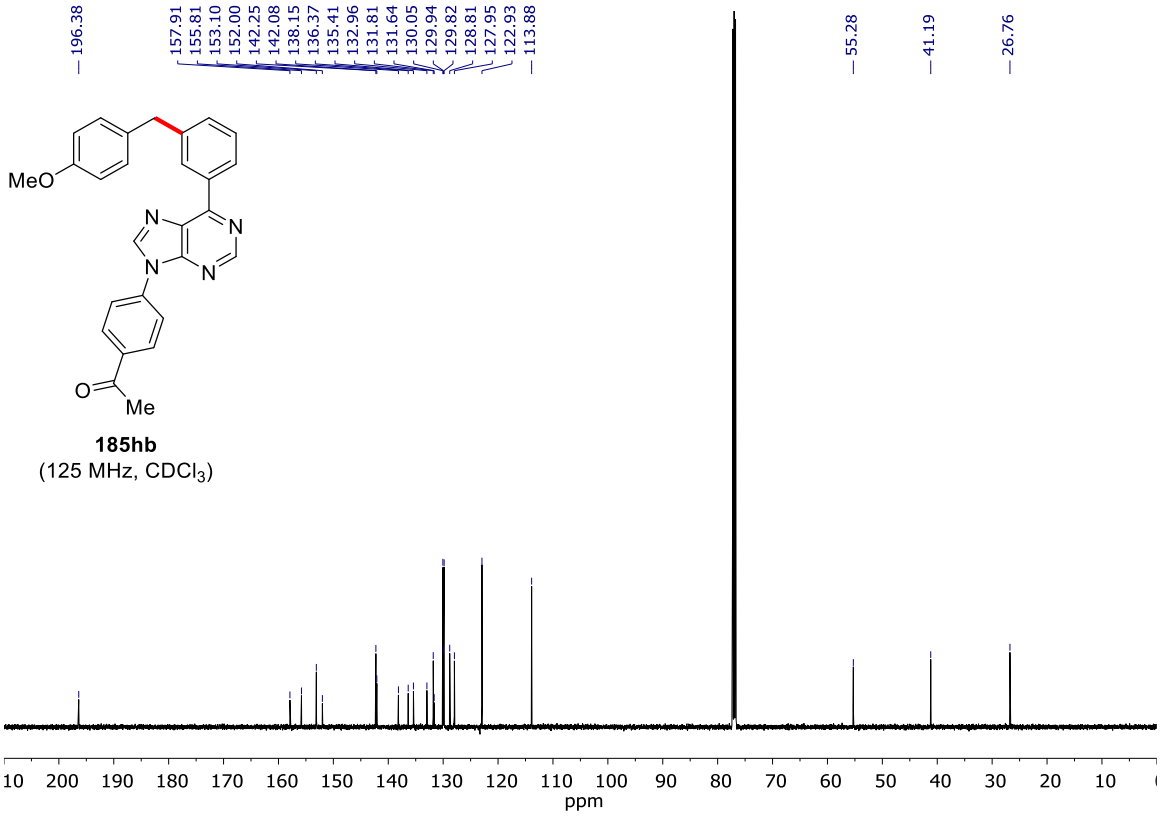
185aj
(125 MHz, $CDCl_3$)

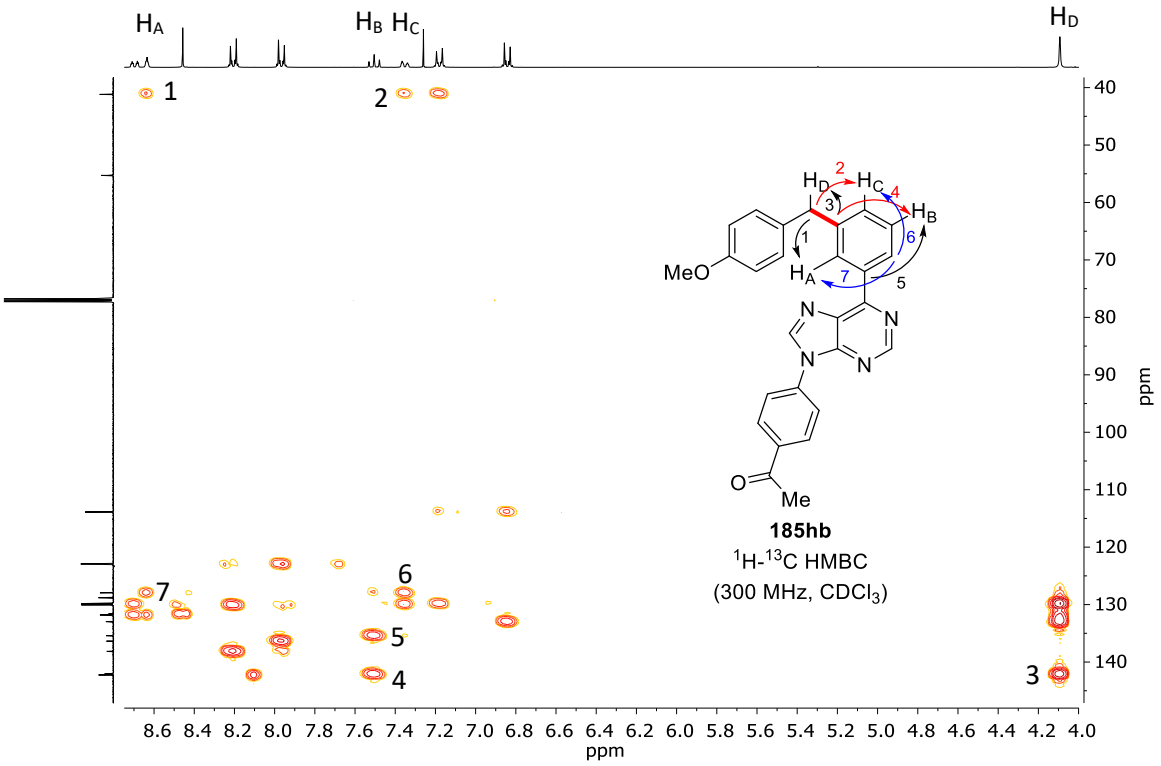


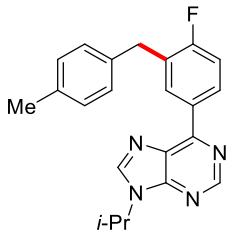
185ak
(300 MHz, $CDCl_3$)


154.45
151.96
151.84
141.80
140.66
139.86
135.98
131.40
131.36
131.27
130.55
129.81
128.75
128.05
119.83
47.24
41.37
22.56
Br
N
N
N
N
i-Pr
185ak
(125 MHz, CDCl3)
ppm

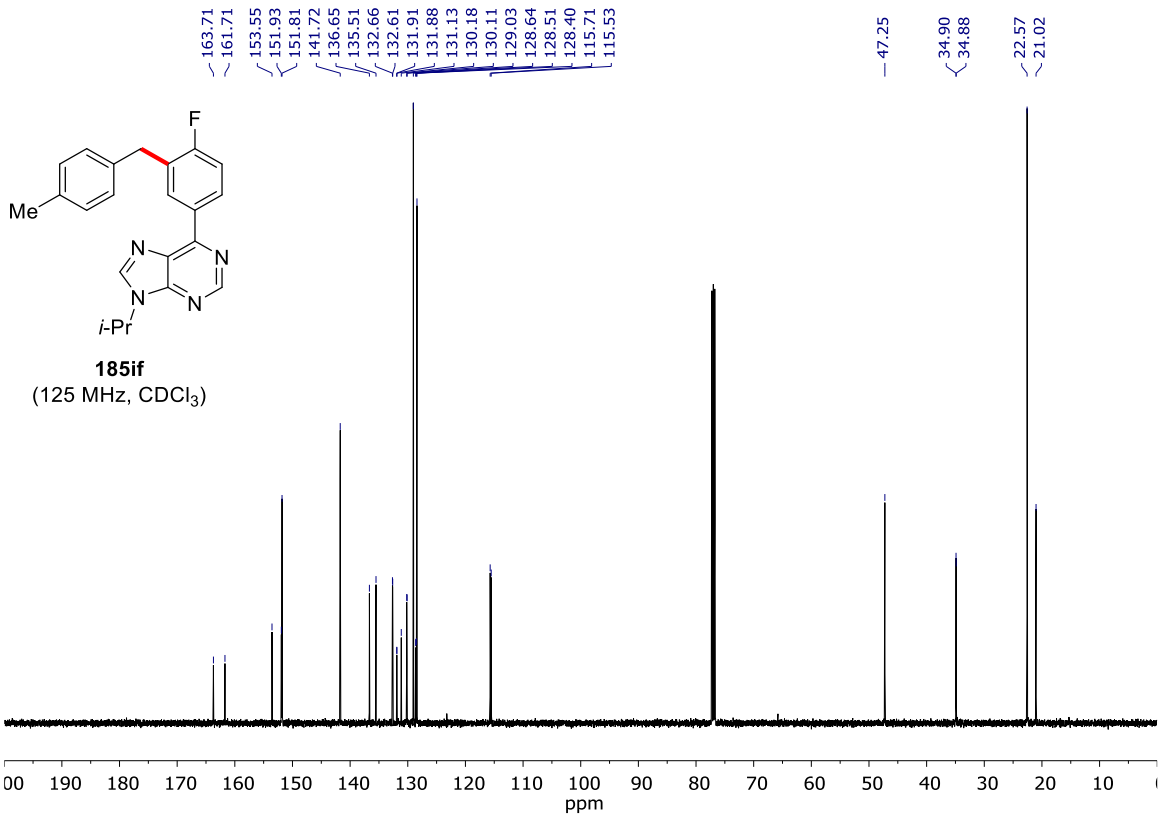

MeO
N
N
N
N
O
Me
185hb
(300 MHz, CDCl3)
0.92
1.04
1.01
1.00
2.14
2.12
1.13
1.07
2.04
2.03
2.12
3.07
3.05
ppm


196.38
157.91
155.81
153.10
152.00
142.25
142.08
138.15
136.37
135.41
132.96
131.81
131.64
130.05
129.94
129.82
128.81
127.95
122.93
113.88
55.28
41.19
26.76
MeO
N
N
N
N
O
Me
185hb
(125 MHz, CDCl3)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

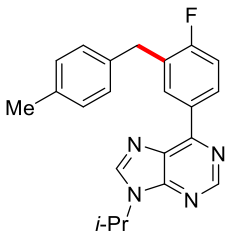

HA
HB HC
HD
1
2
6
7
5
4
3
HD
HC
HB
HA
MeO
N
N
N
N
O
Me
185hb
1H-13C HMBC
(300 MHz, CDCl3)
40 50 60 70 80 90 100 110 120 130 140
ppm
8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0
ppm



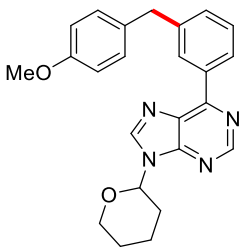
185if
(300 MHz, $CDCl_3$)



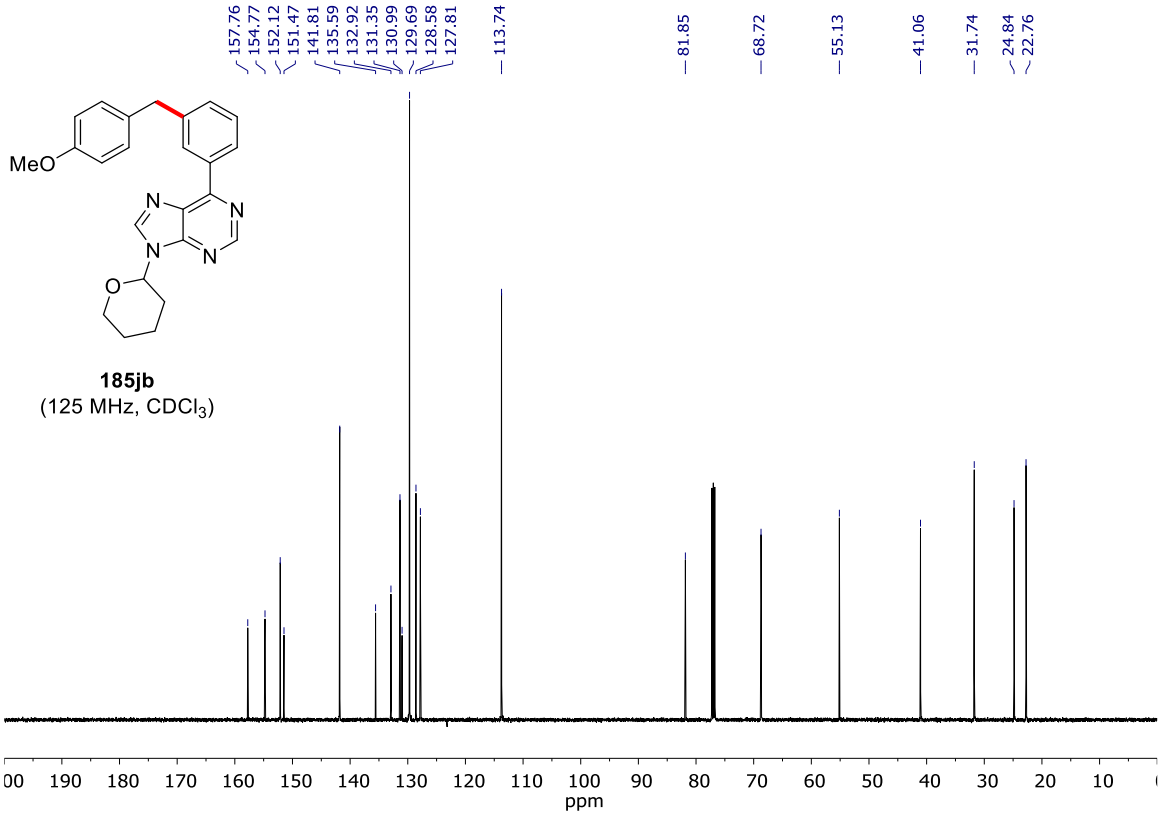
185if
(125 MHz, $CDCl_3$)

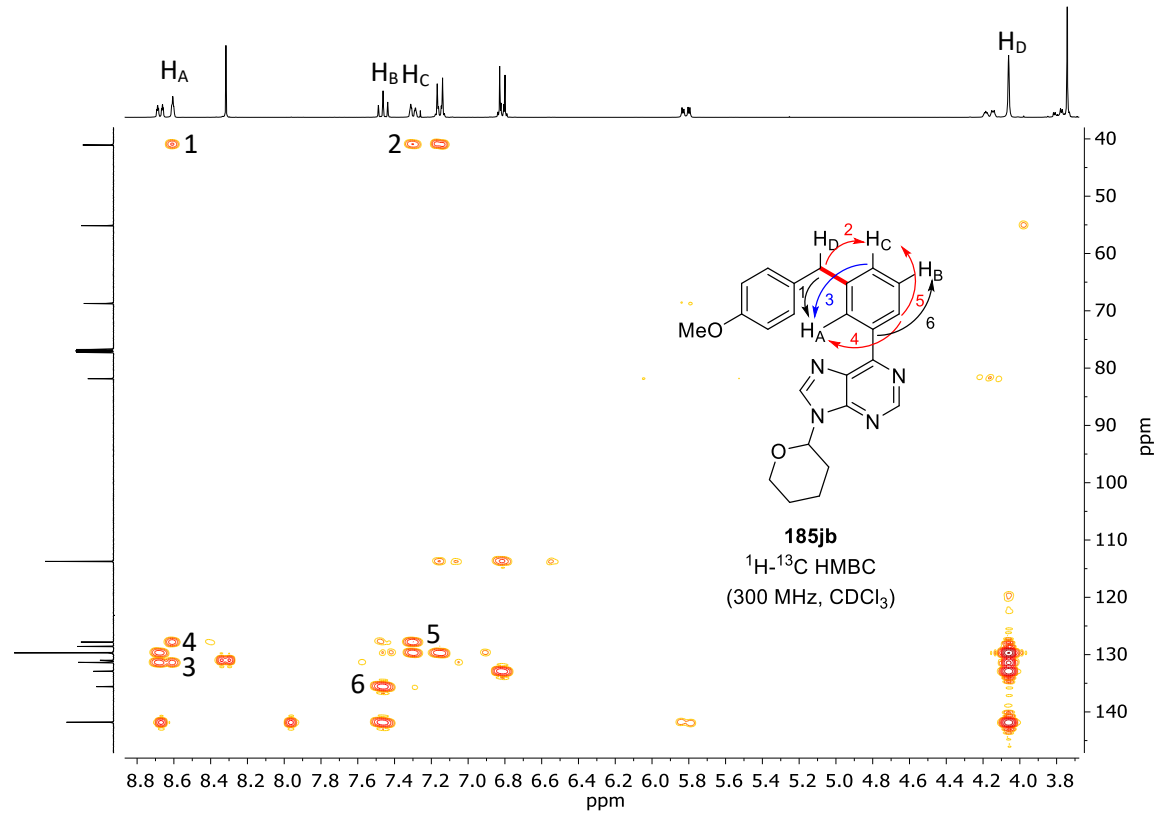


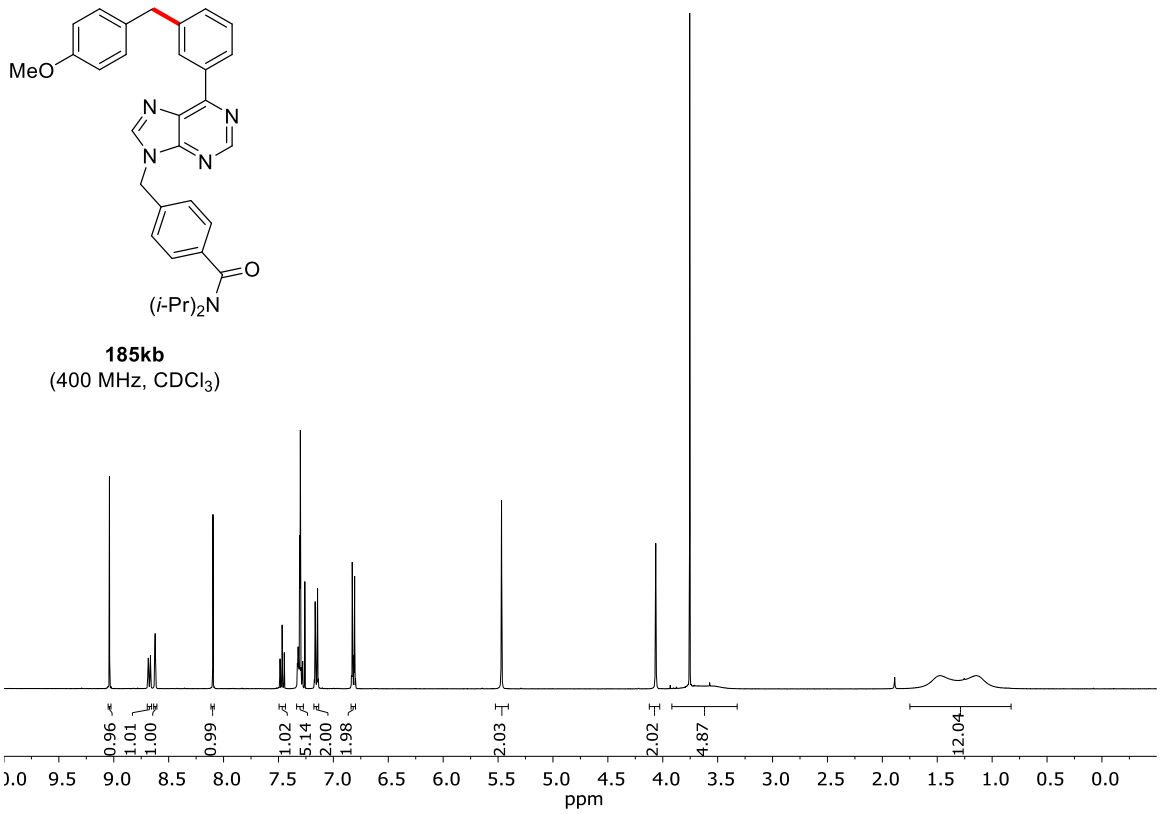
185if
^{19}F-NMR
(282 MHz, $CDCl_3$)



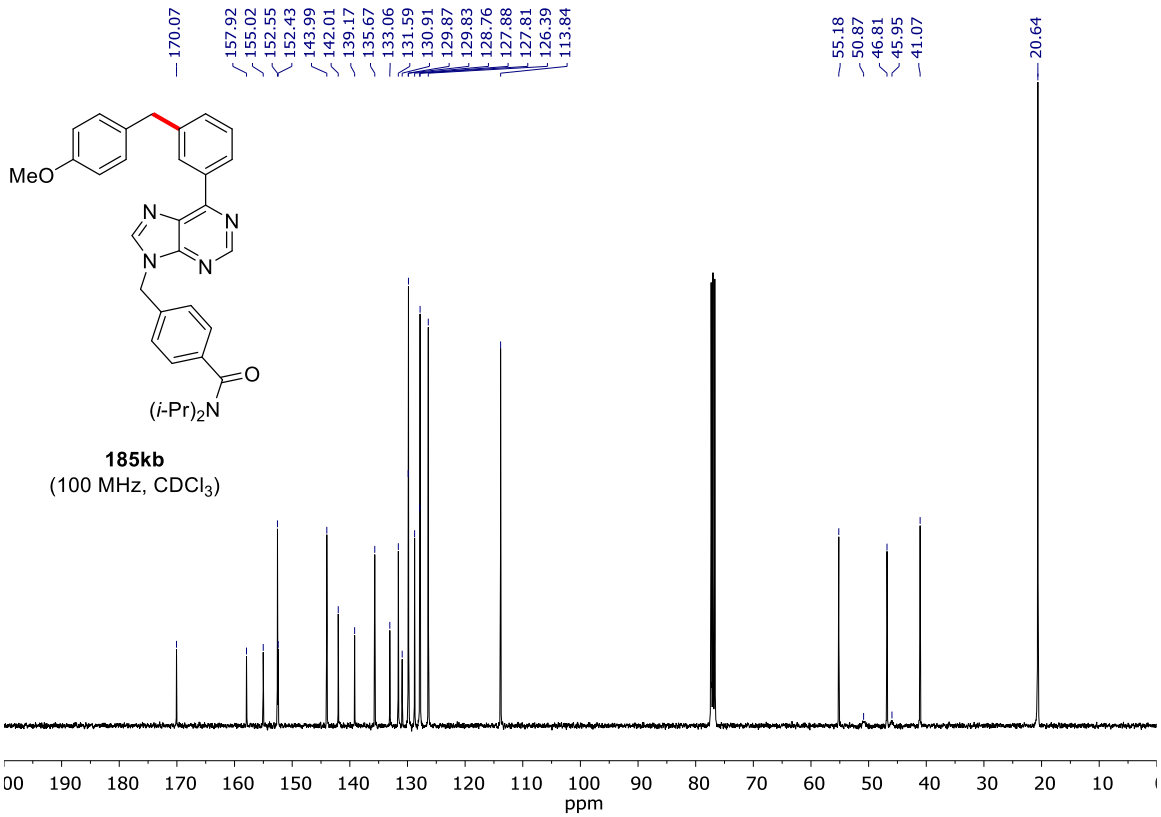
185jb
(300 MHz, $CDCl_3$)


157.76
154.77
152.12
151.47
141.81
135.59
132.92
131.35
130.99
129.69
128.58
127.81
113.74
81.85
68.72
55.13
41.06
31.74
24.84
22.76
MeO
N
N
N
N
O
185jb
(125 MHz, CDCl3)
ppm

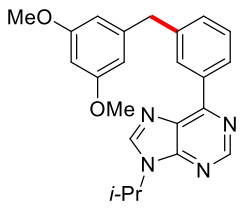

HA
HB HC
HD
1
2
4
3
5
6
HD
2
HC
HB
1
3
5
6
HA
4
MeO
N
N
N
N
O
185jb
1H-13C HMBC
(300 MHz, CDCl3)
ppm
ppm



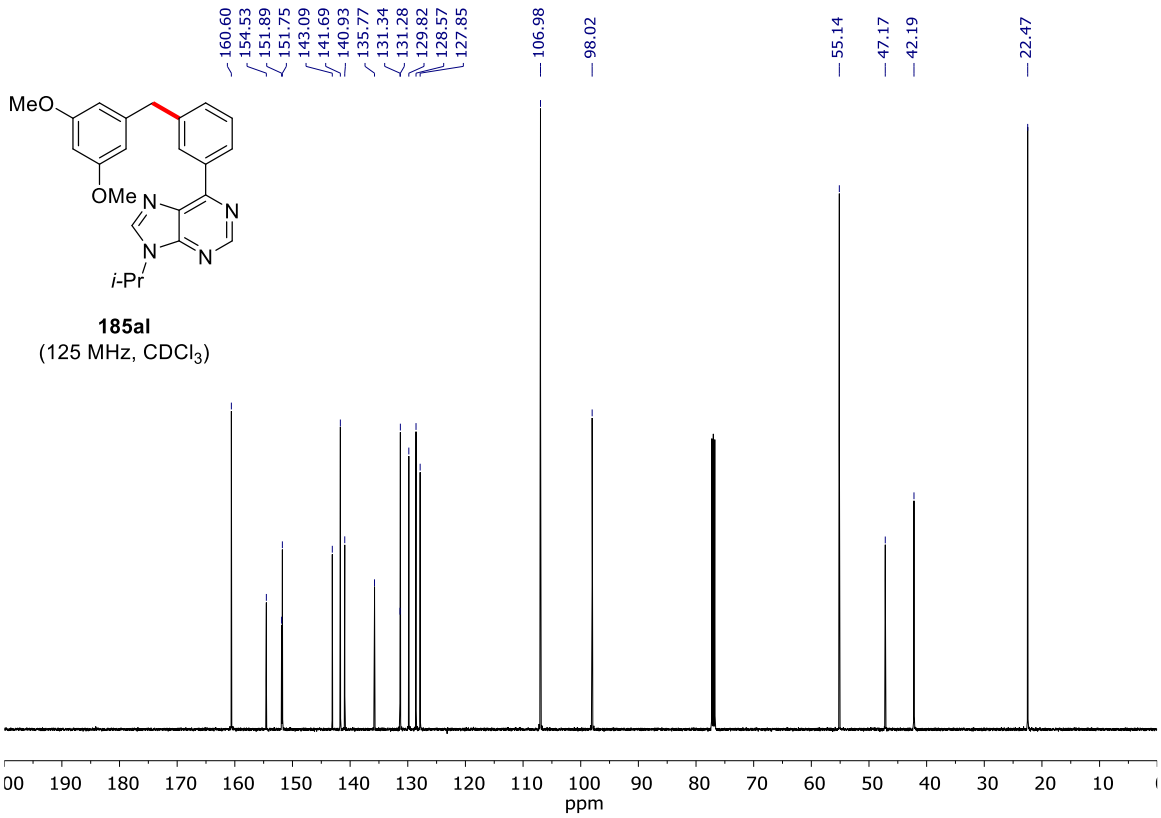
185kb
(400 MHz, $CDCl_3$)



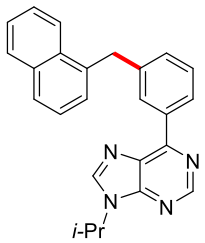
185kb
(100 MHz, $CDCl_3$)



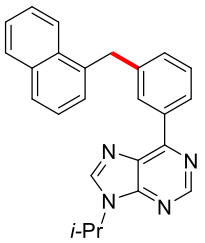
185al
(300 MHz, $CDCl_3$)



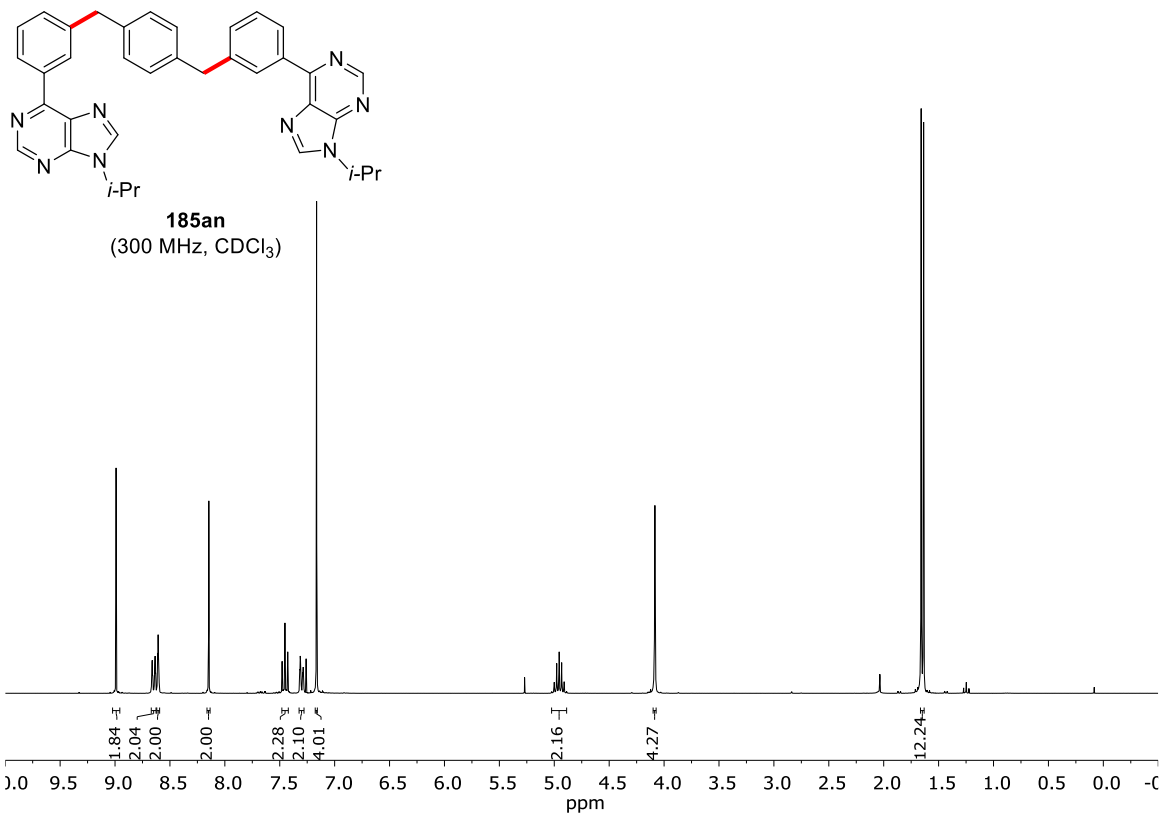
185al
(125 MHz, $CDCl_3$)

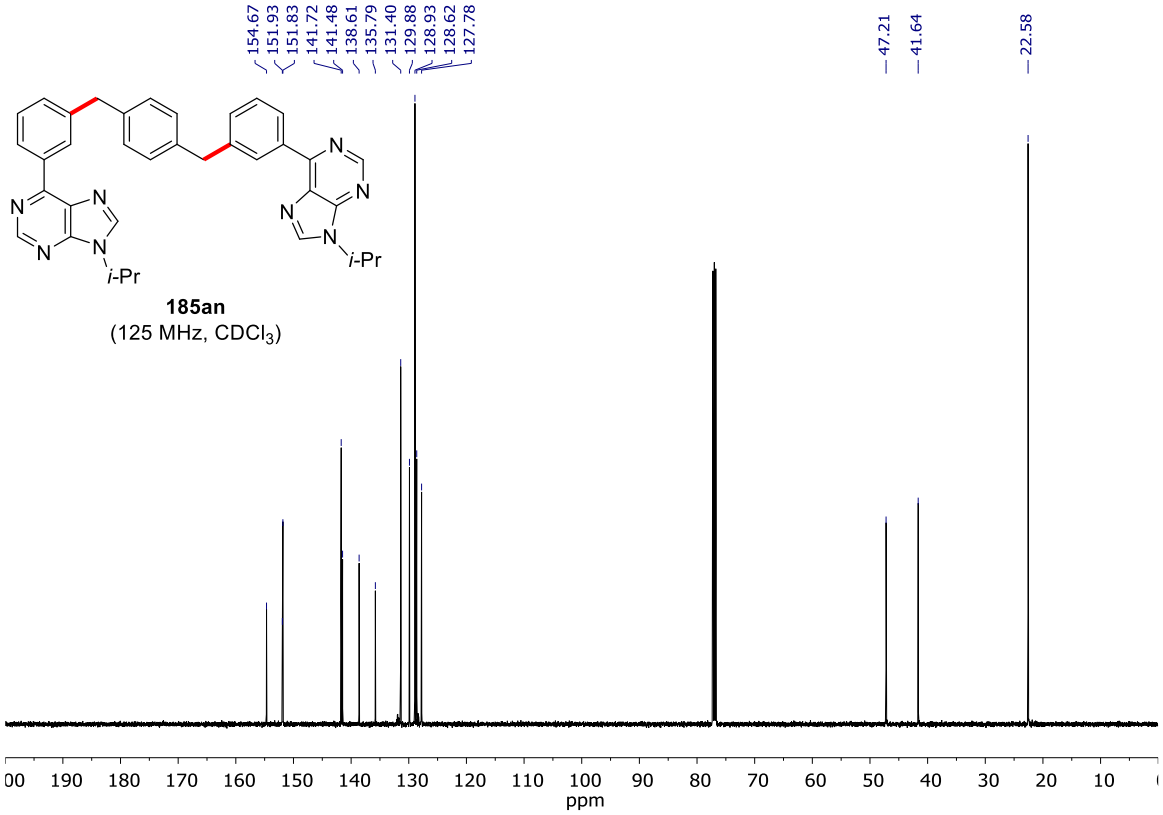


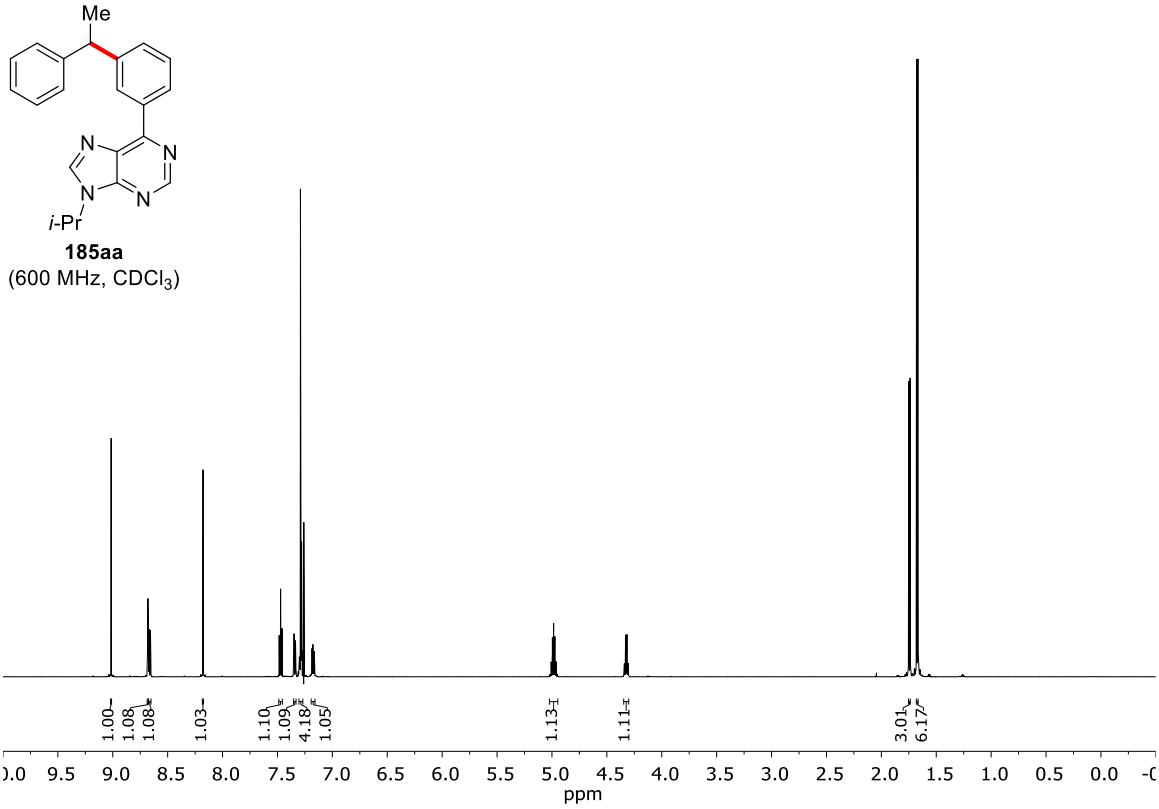
185am
(300 MHz, $CDCl_3$)



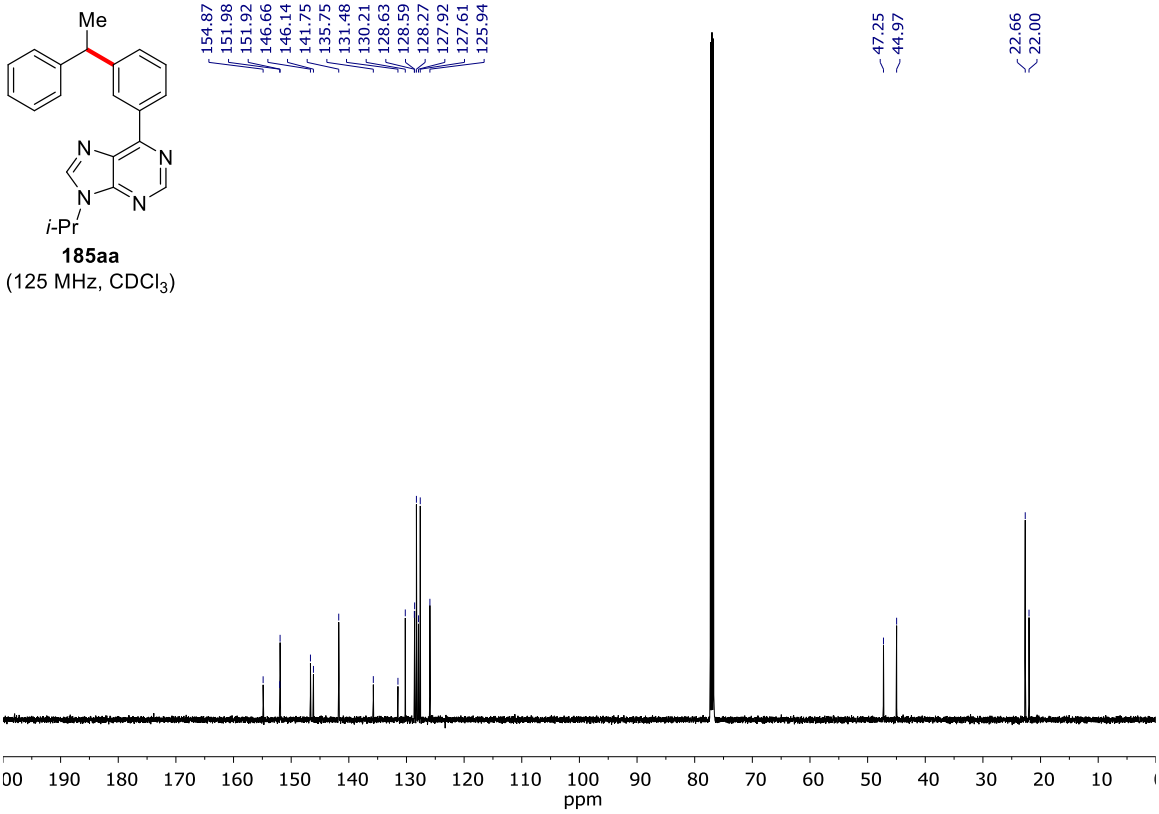
185am
(125 MHz, $CDCl_3$)


i-Pr
185an
(300 MHz, CDCl3)
1.84
2.04
2.00
2.00
2.28
2.10
4.01
2.16
4.27
12.24
ppm

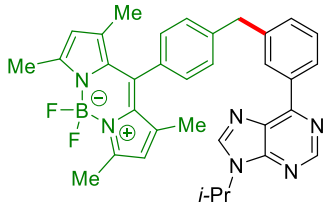

154.67
151.93
151.83
141.72
141.48
138.61
135.79
131.40
129.88
128.93
128.62
127.78
47.21
41.64
22.58
i-Pr
185an
(125 MHz, CDCl3)
ppm



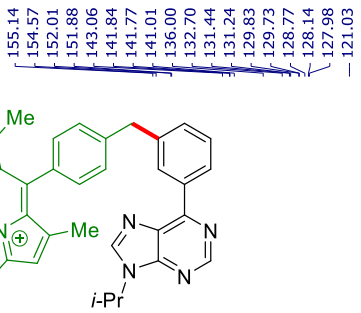
185aa
(600 MHz, $CDCl_3$)



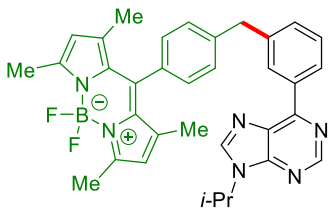
185aa
(125 MHz, $CDCl_3$)



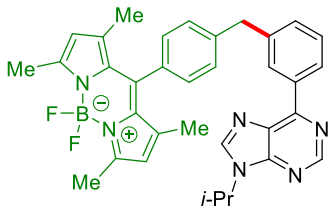
187a
(600 MHz, $CDCl_3$)



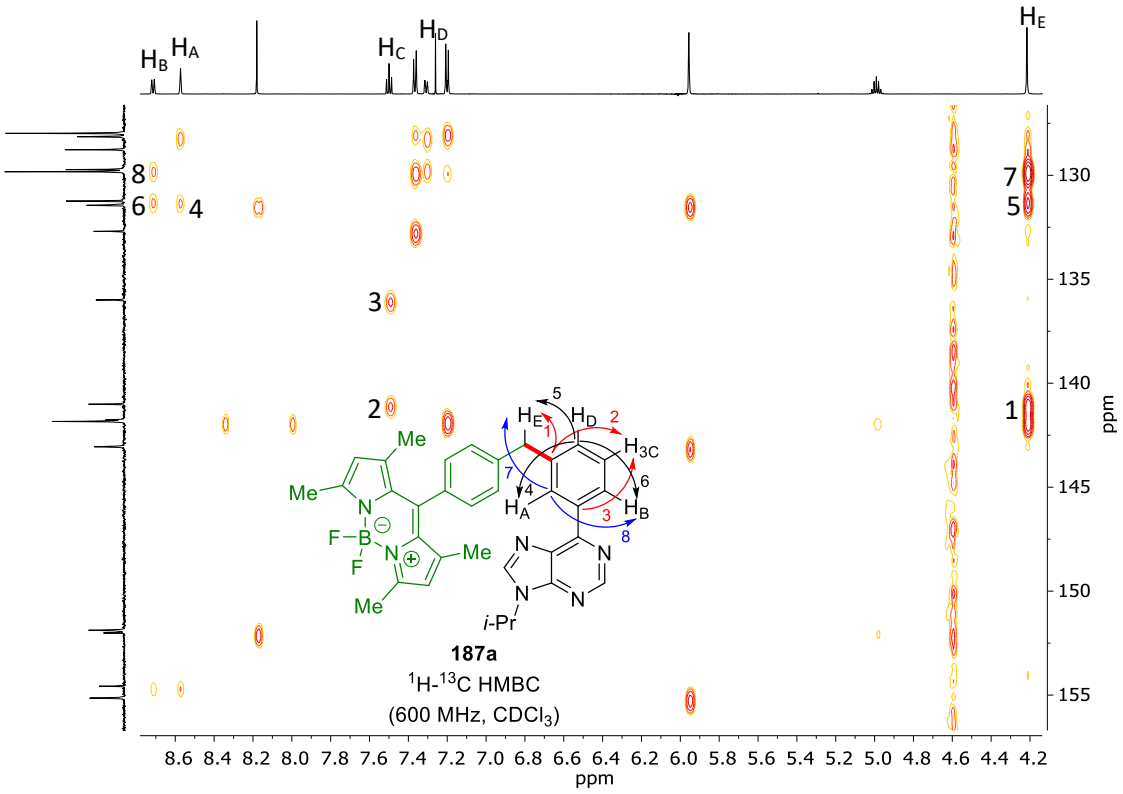
187a
(125 MHz, $CDCl_3$)



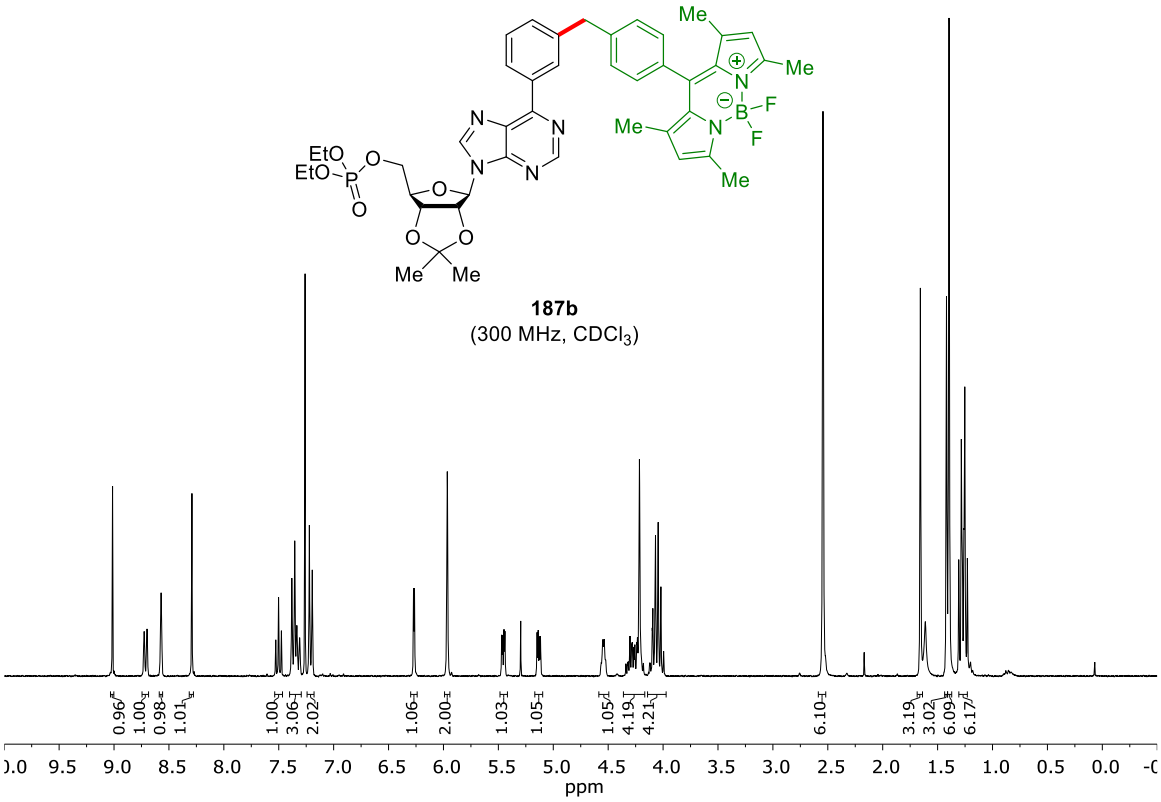
187a
^{11}B-NMR
(128 MHz, $CDCl_3$)



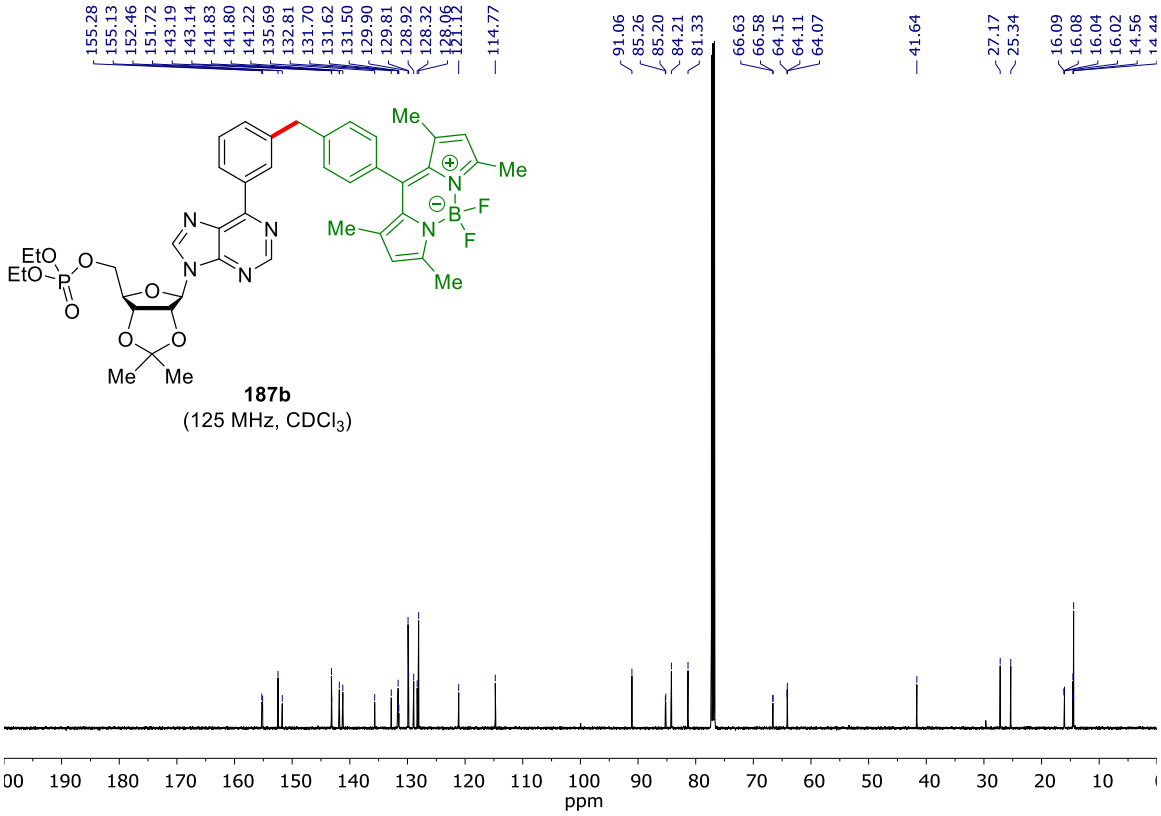
187a
^{19}F-NMR
(376 MHz, $CDCl_3$)



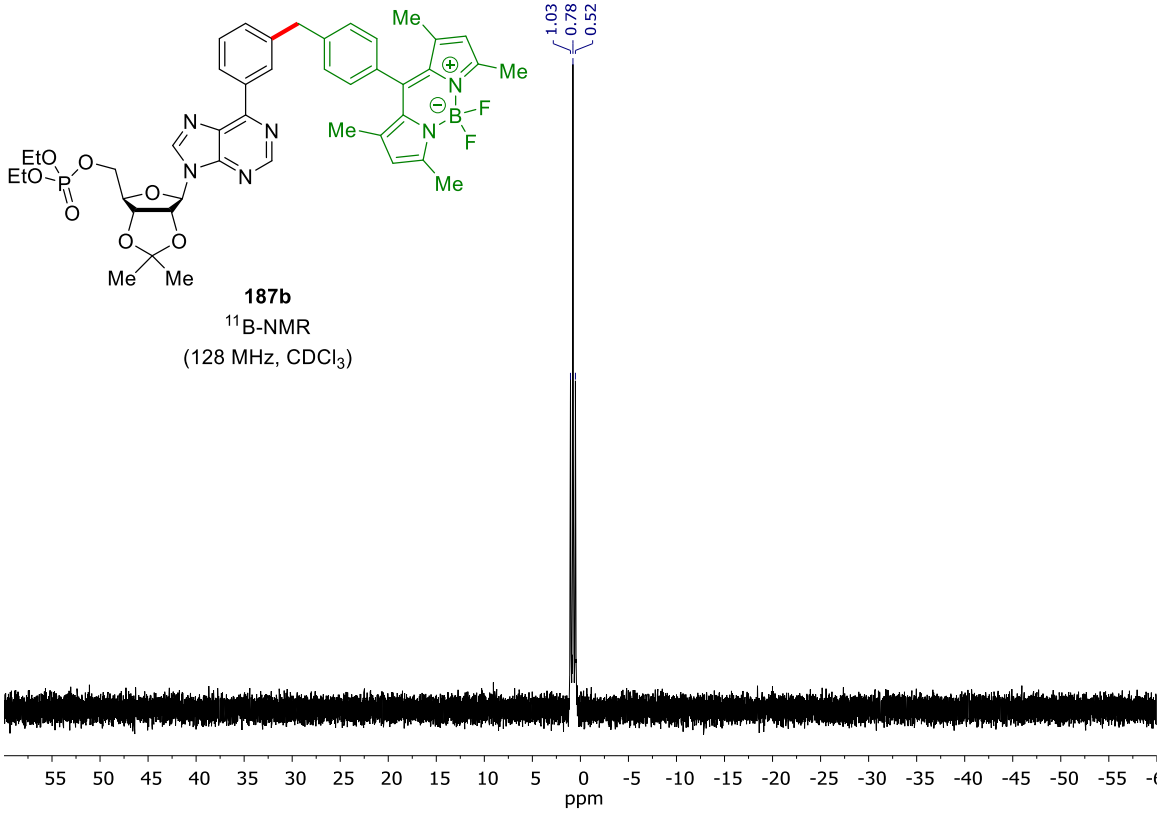
187a
^{1}H-^{13}C HMBC
(600 MHz, $CDCl_3$)



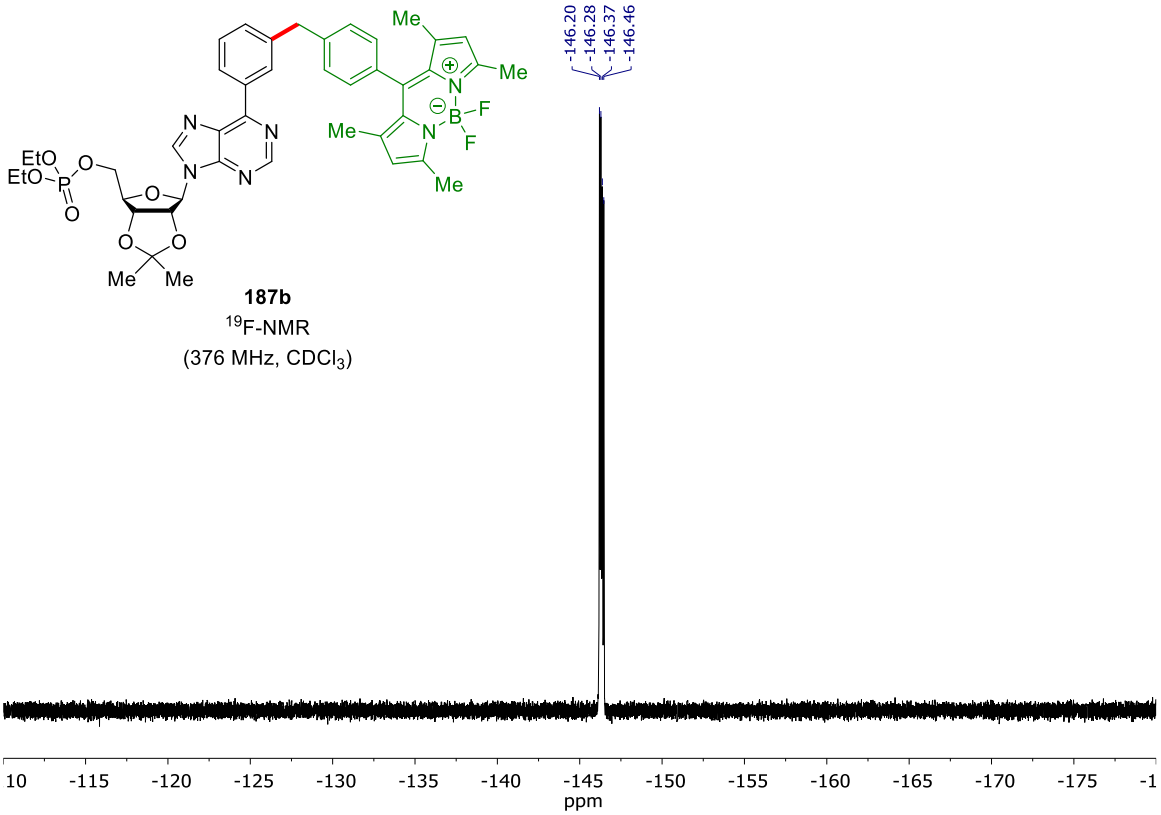
187b
(300 MHz, $CDCl_3$)



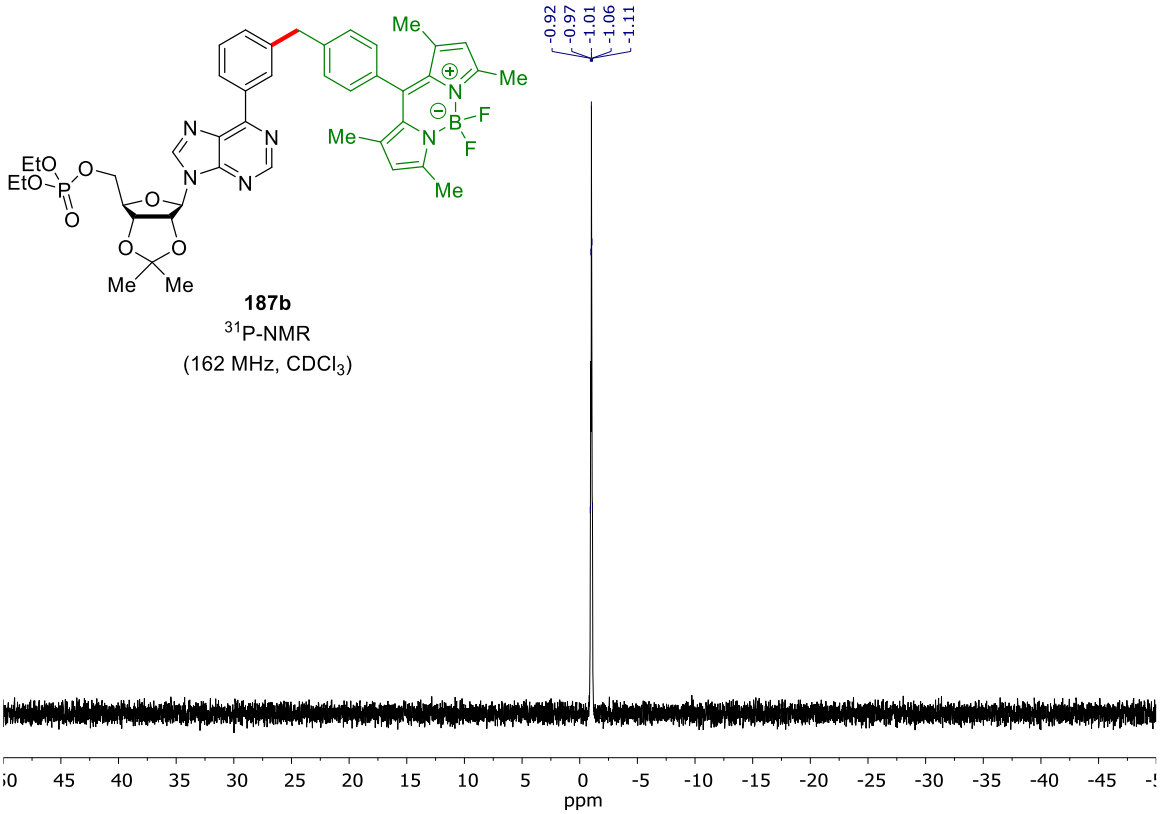
187b
(125 MHz, $CDCl_3$)



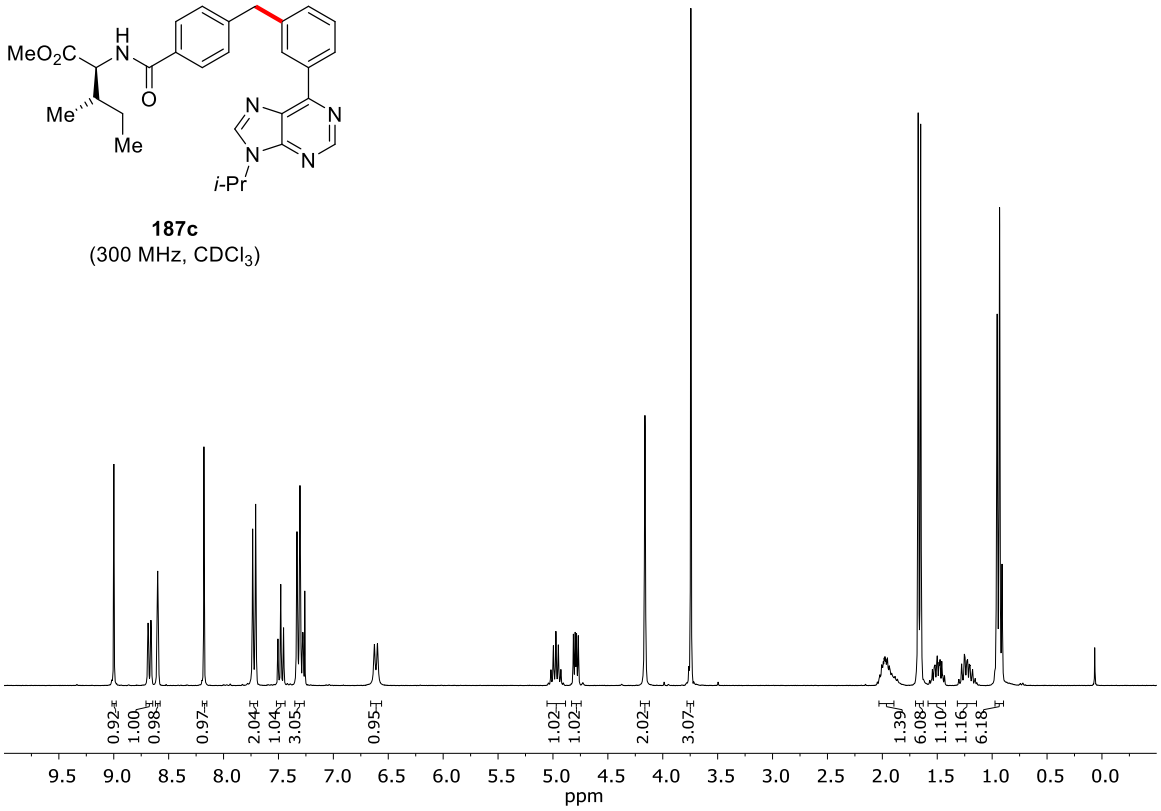
187b
^{11}B-NMR
(128 MHz, $CDCl_3$)



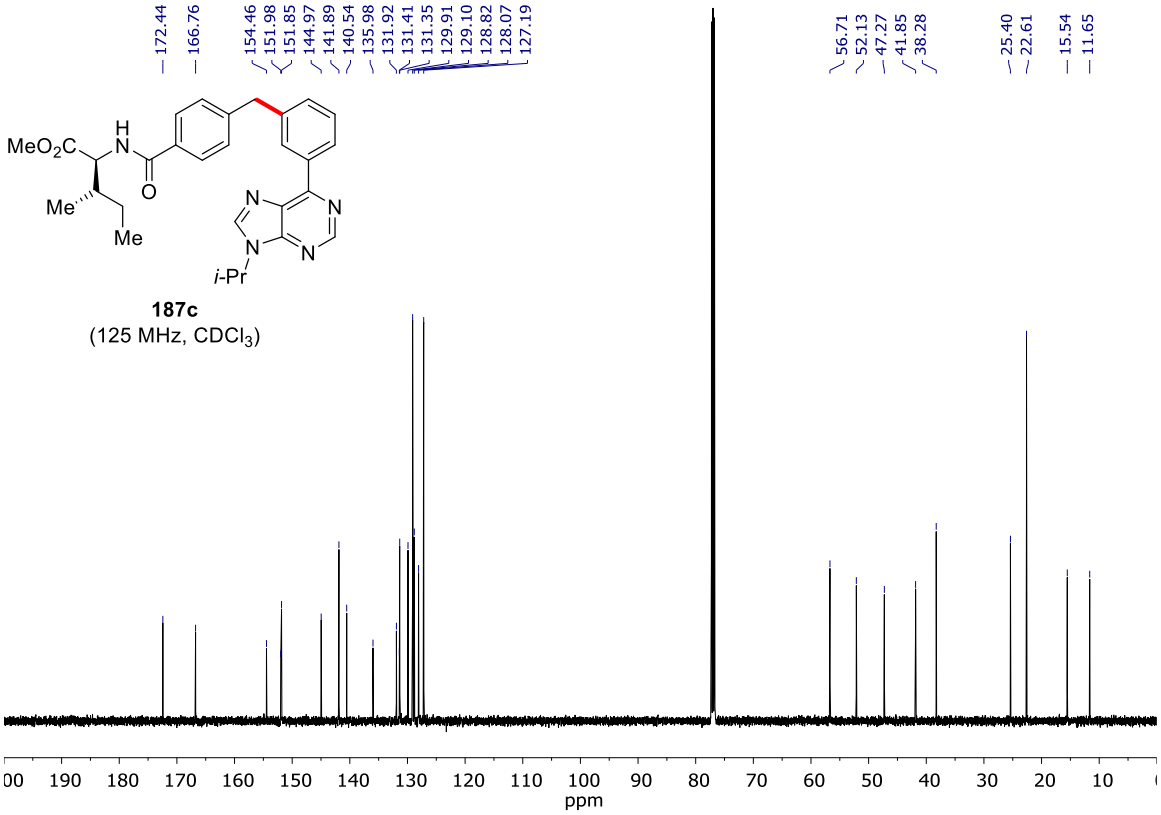
187b
^{19}F-NMR
(376 MHz, $CDCl_3$)



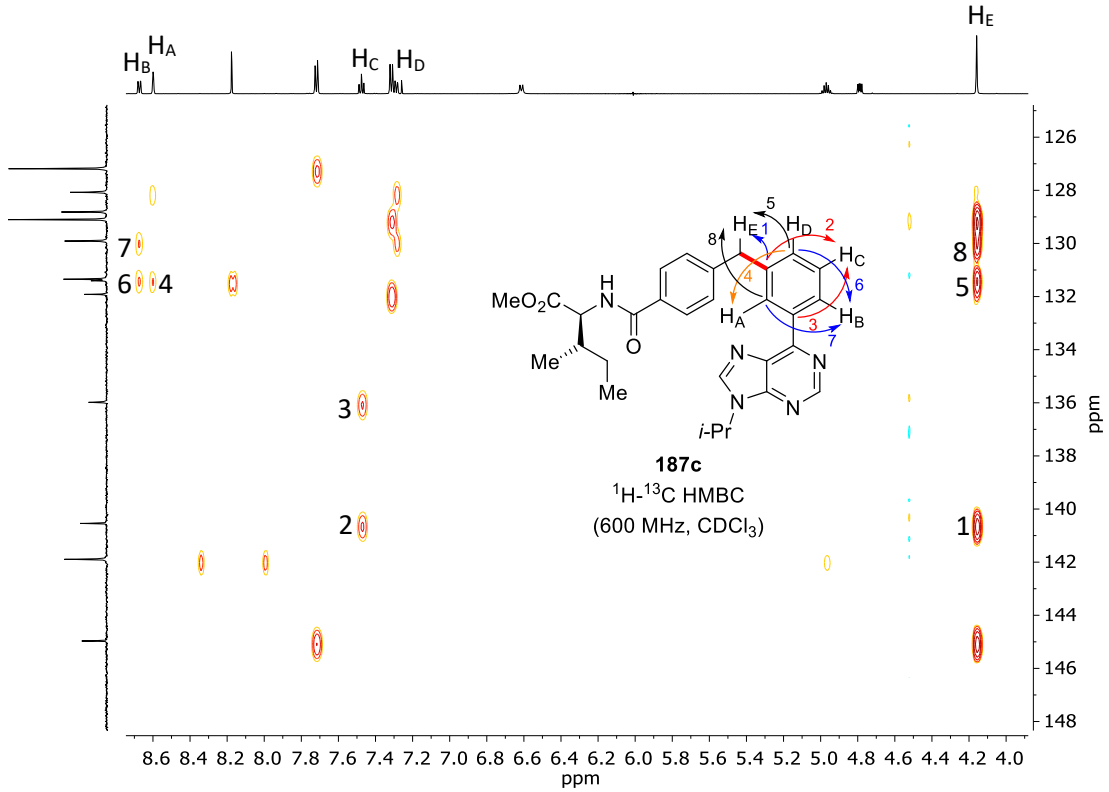
187b
^{31}P-NMR
(162 MHz, $CDCl_3$)



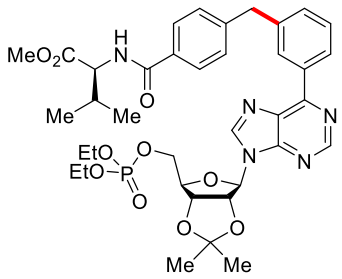
187c
(300 MHz, $CDCl_3$)



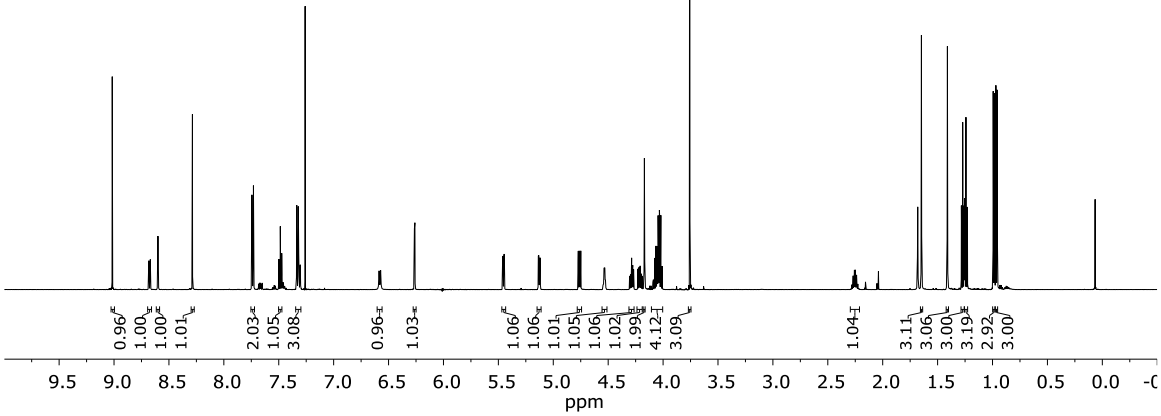
187c
(125 MHz, $CDCl_3$)

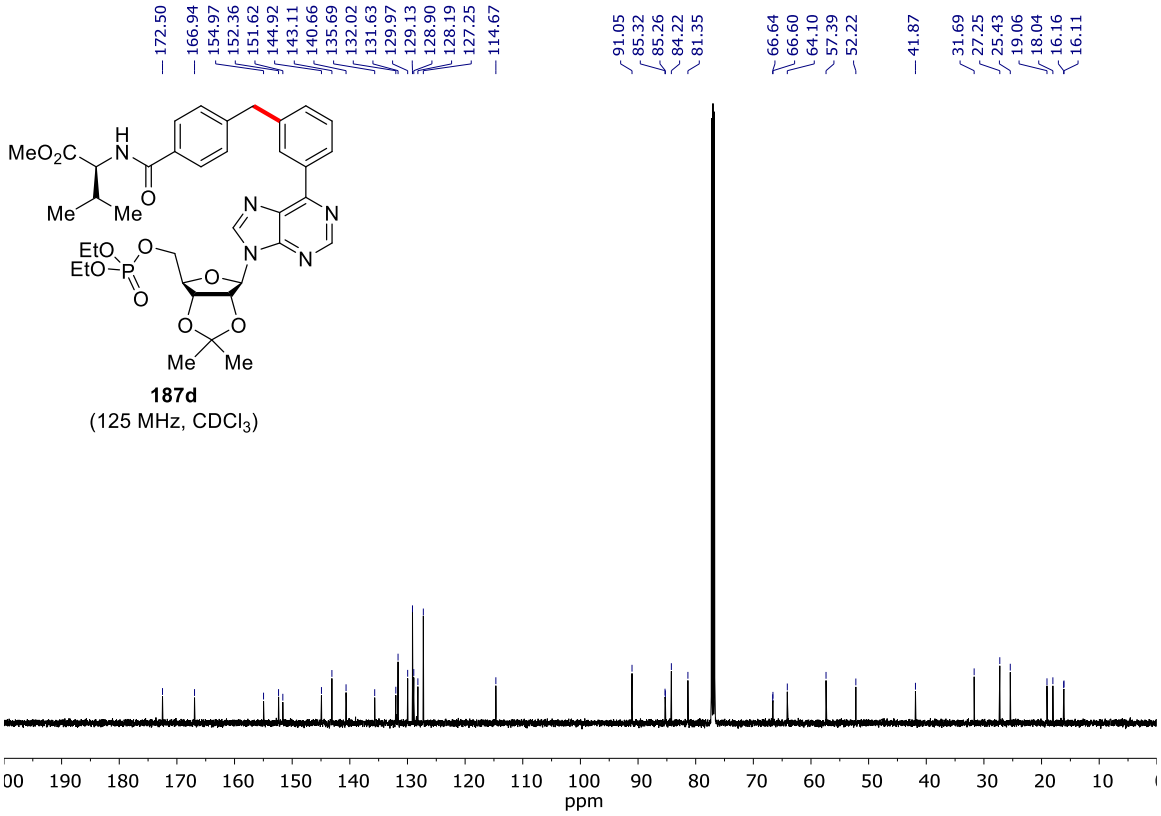


187c
^{1}H-^{13}C HMBC
(600 MHz, $CDCl_3$)

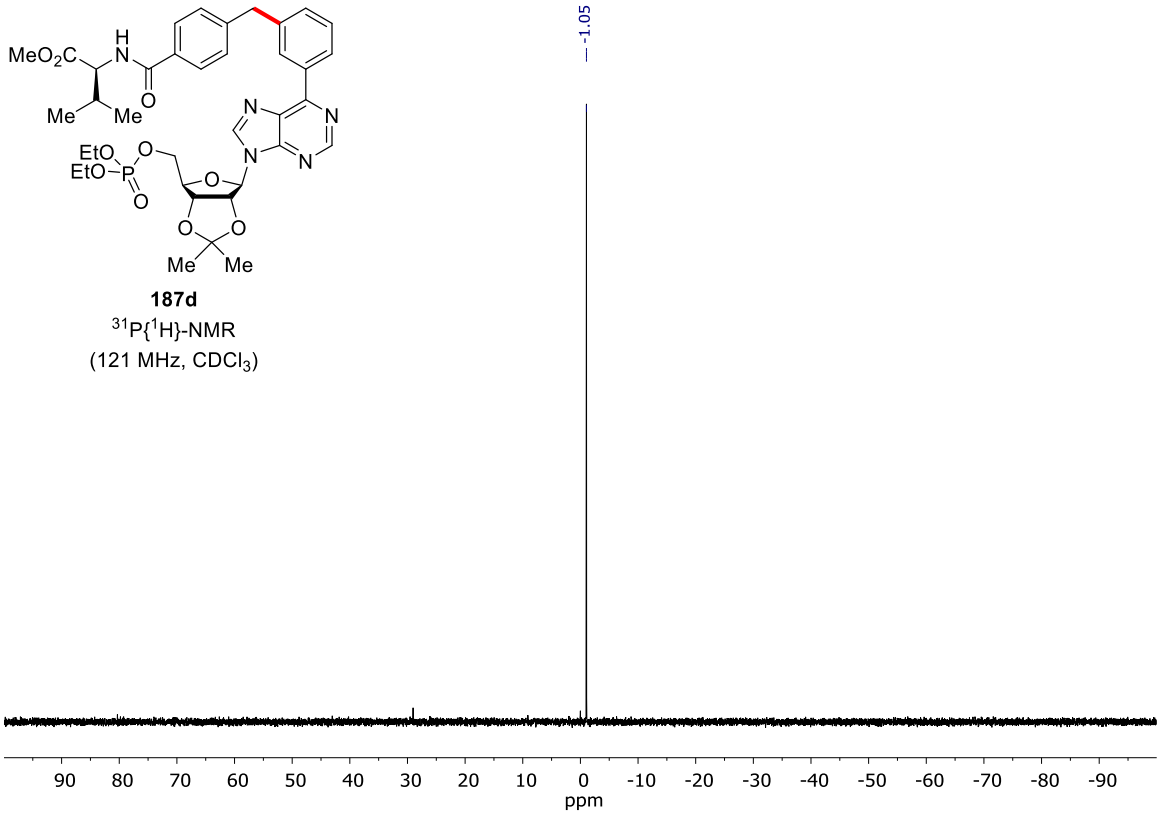


187d
(600 MHz, $CDCl_3$)

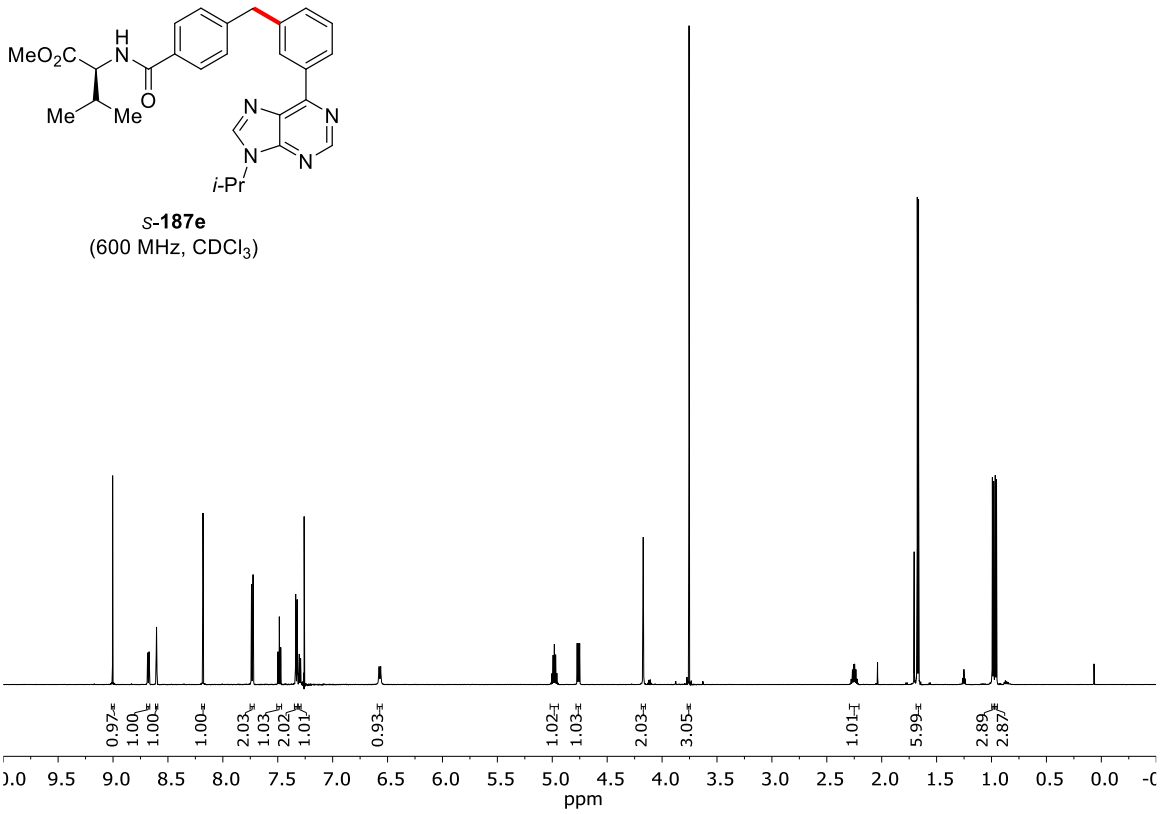




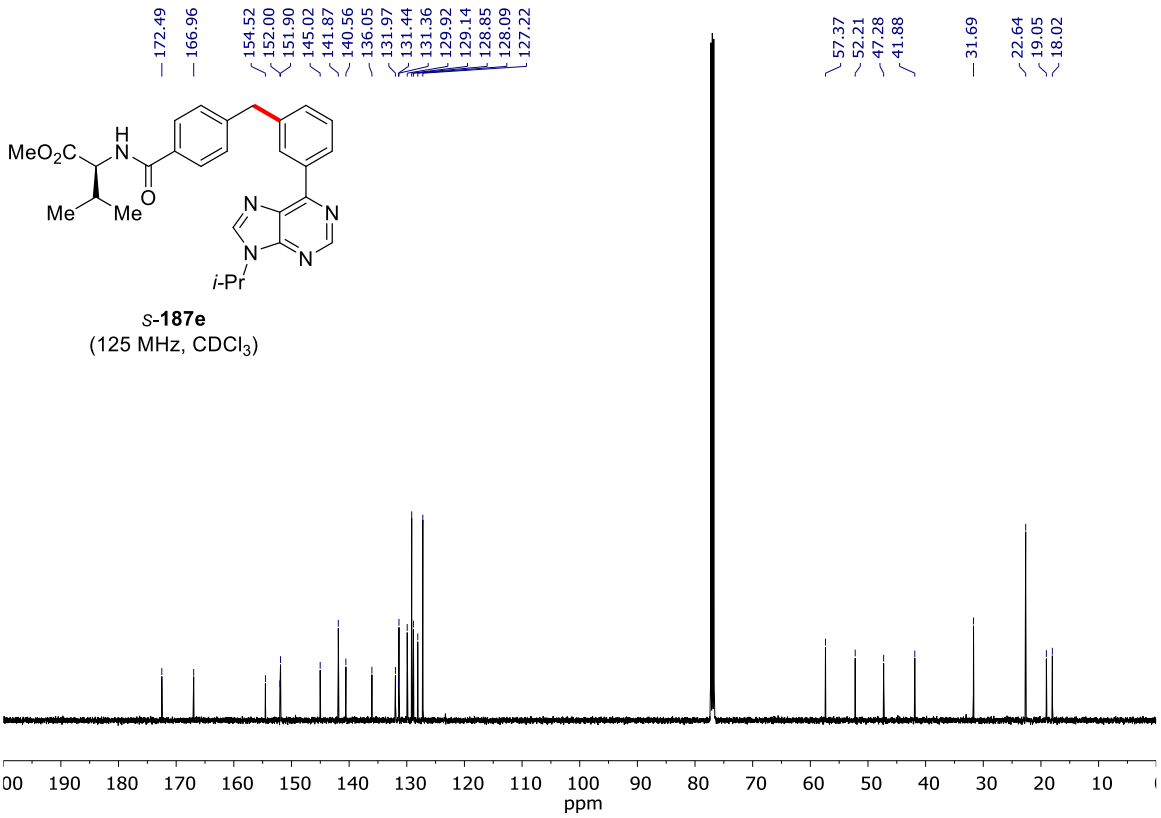
187d
(125 MHz, $CDCl_3$)



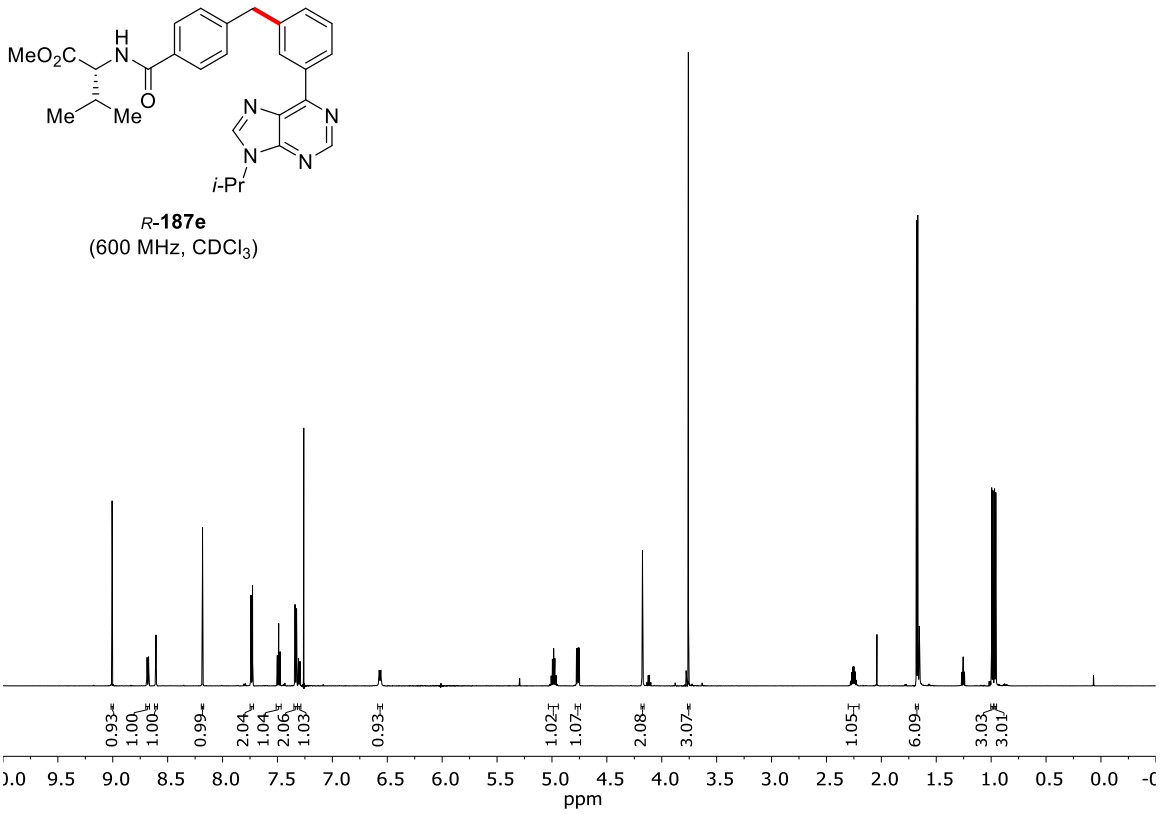
187d
$^{31}P\{^{1}H\}$-NMR
(121 MHz, $CDCl_3$)



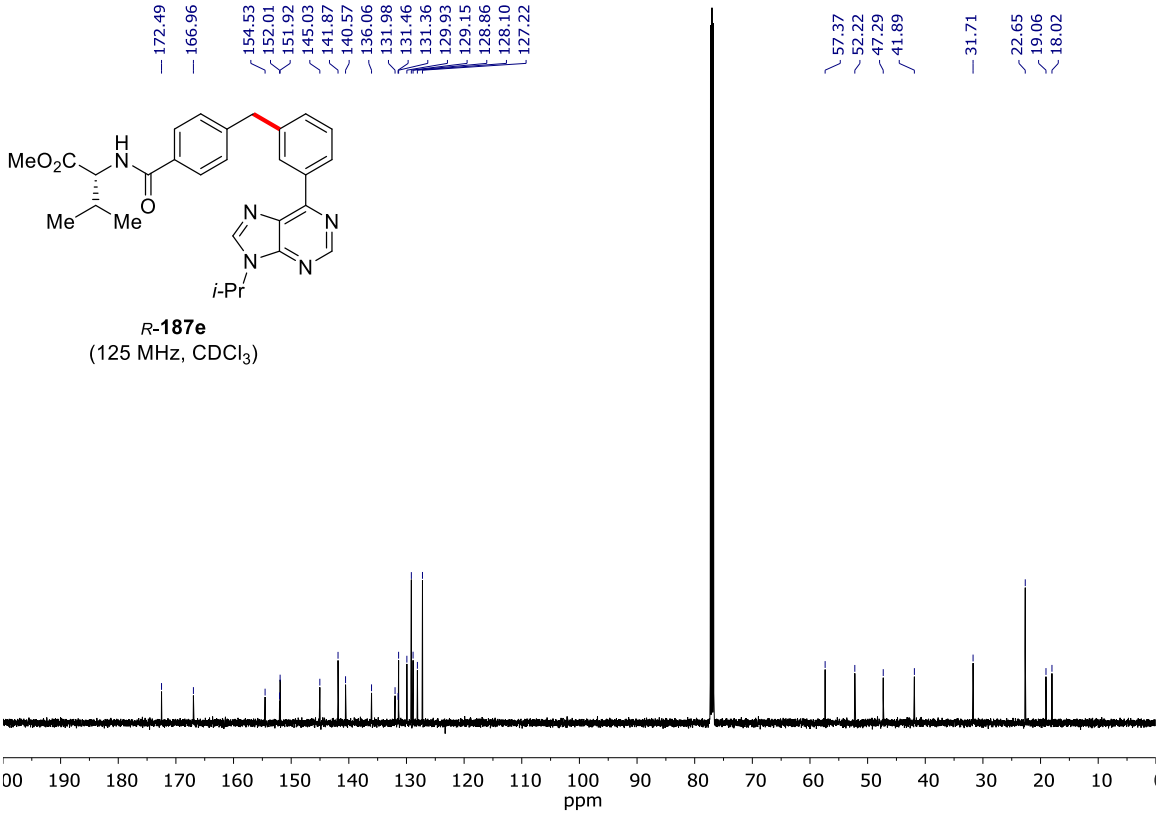
S-**187e**
(600 MHz, $CDCl_3$)



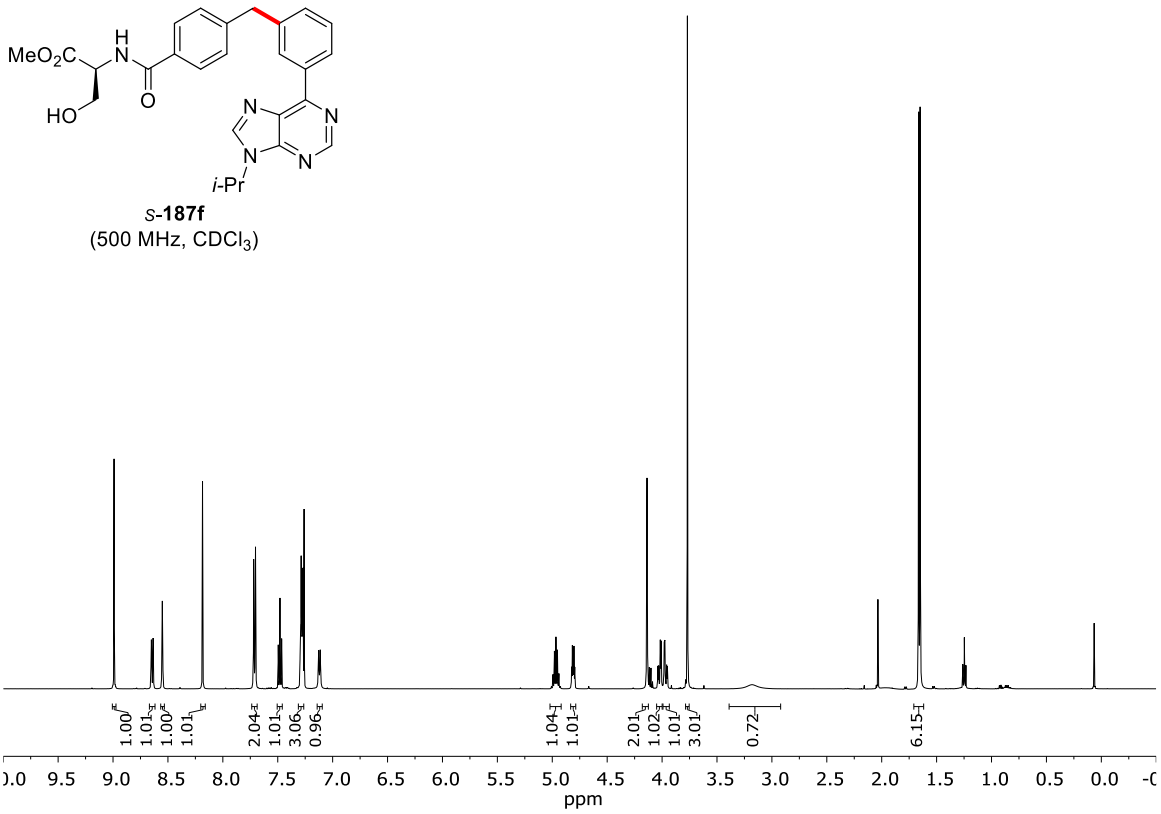
S-**187e**
(125 MHz, $CDCl_3$)



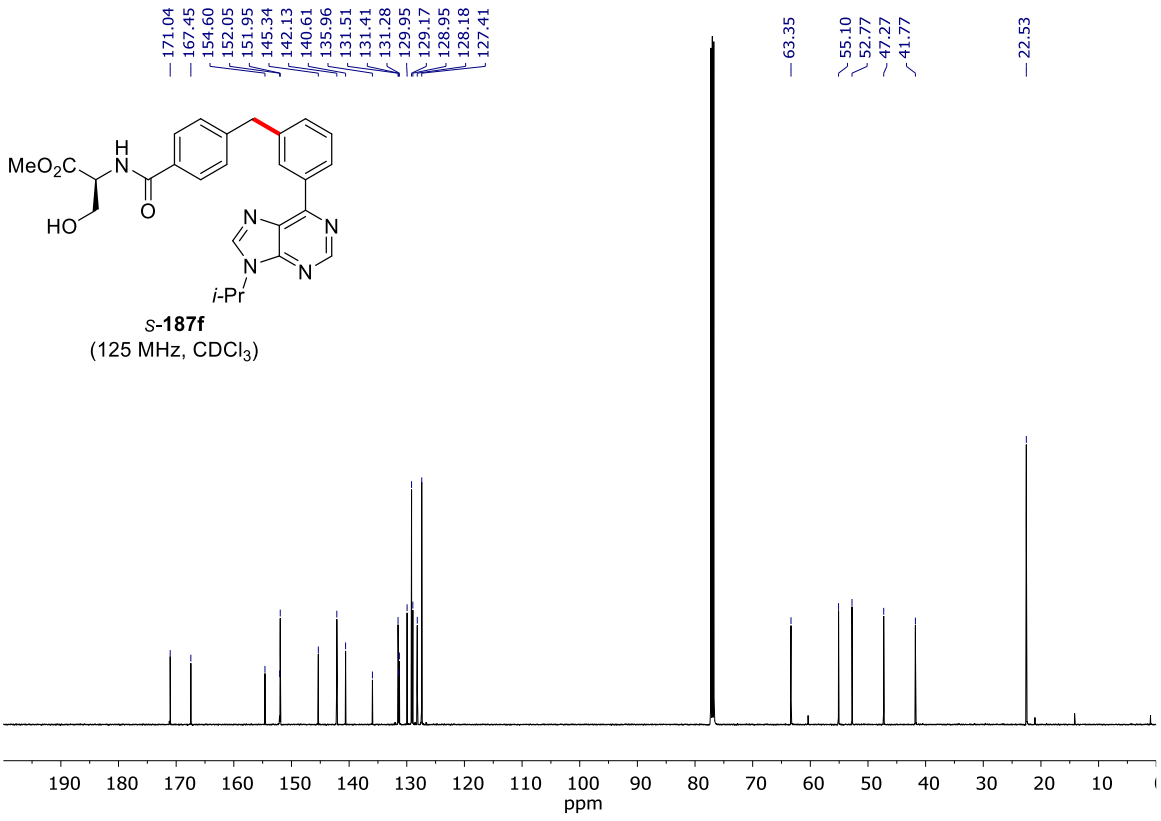
R-**187e**
(600 MHz, $CDCl_3$)



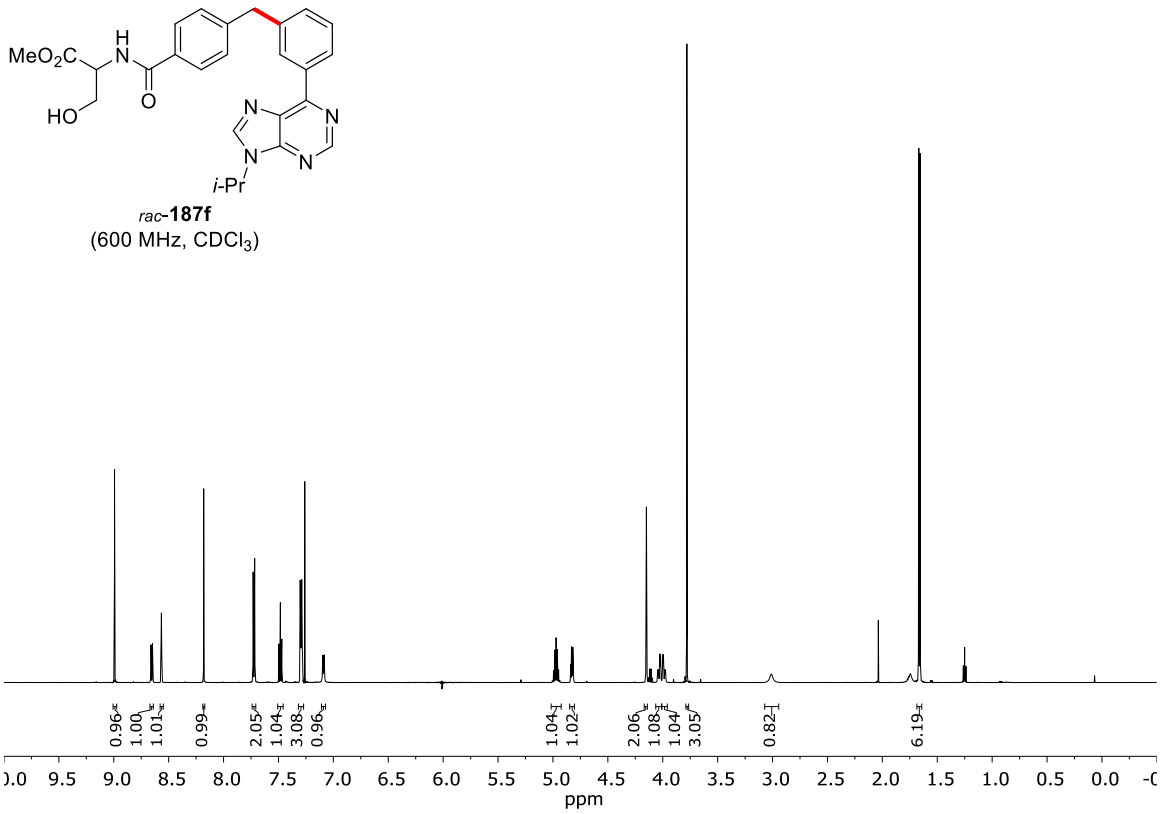
R-**187e**
(125 MHz, $CDCl_3$)



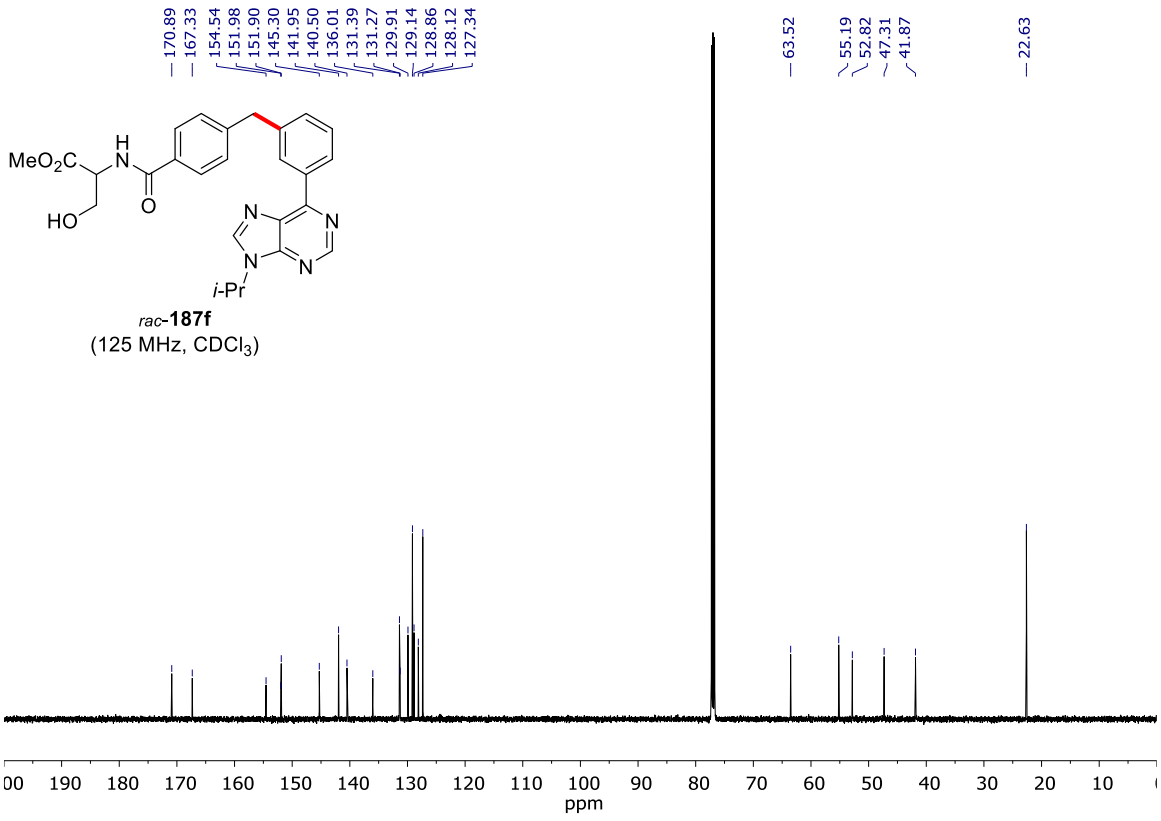
S-**187f**
(500 MHz, $CDCl_3$)



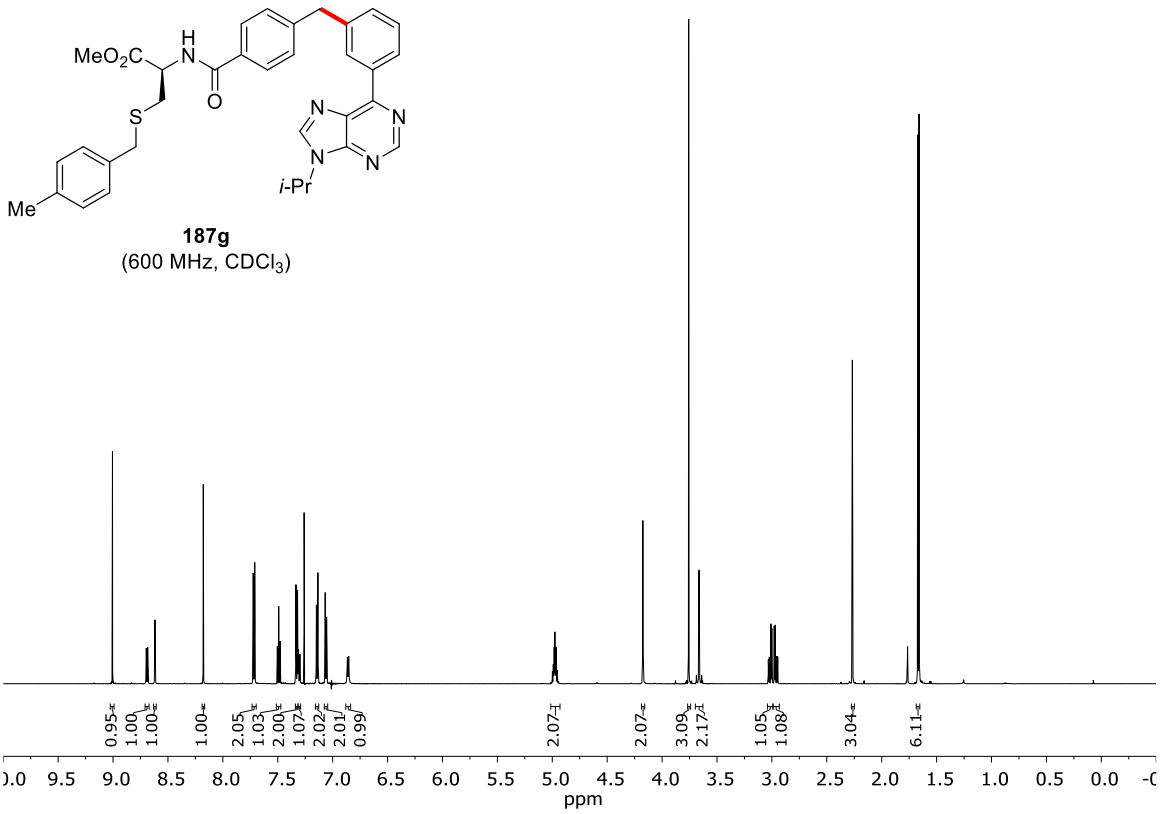
S-**187f**
(125 MHz, $CDCl_3$)



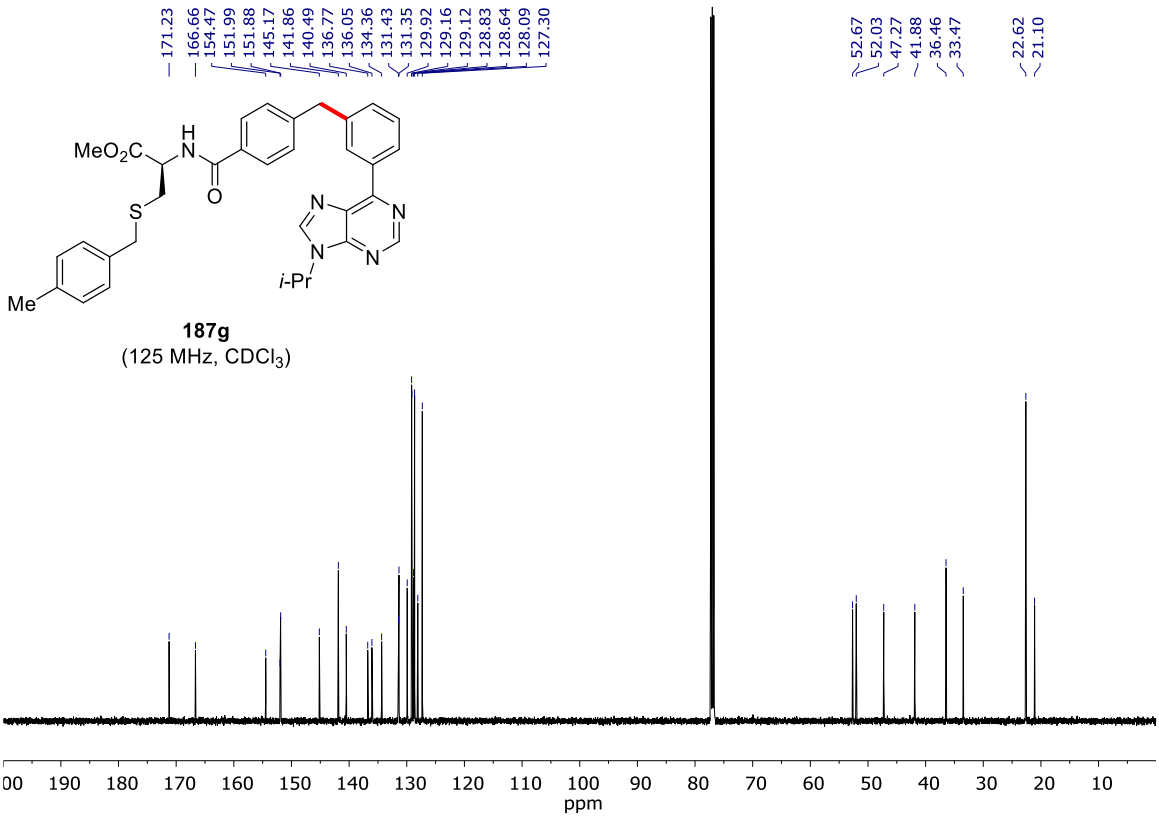
rac-**187f**
(600 MHz, $CDCl_3$)



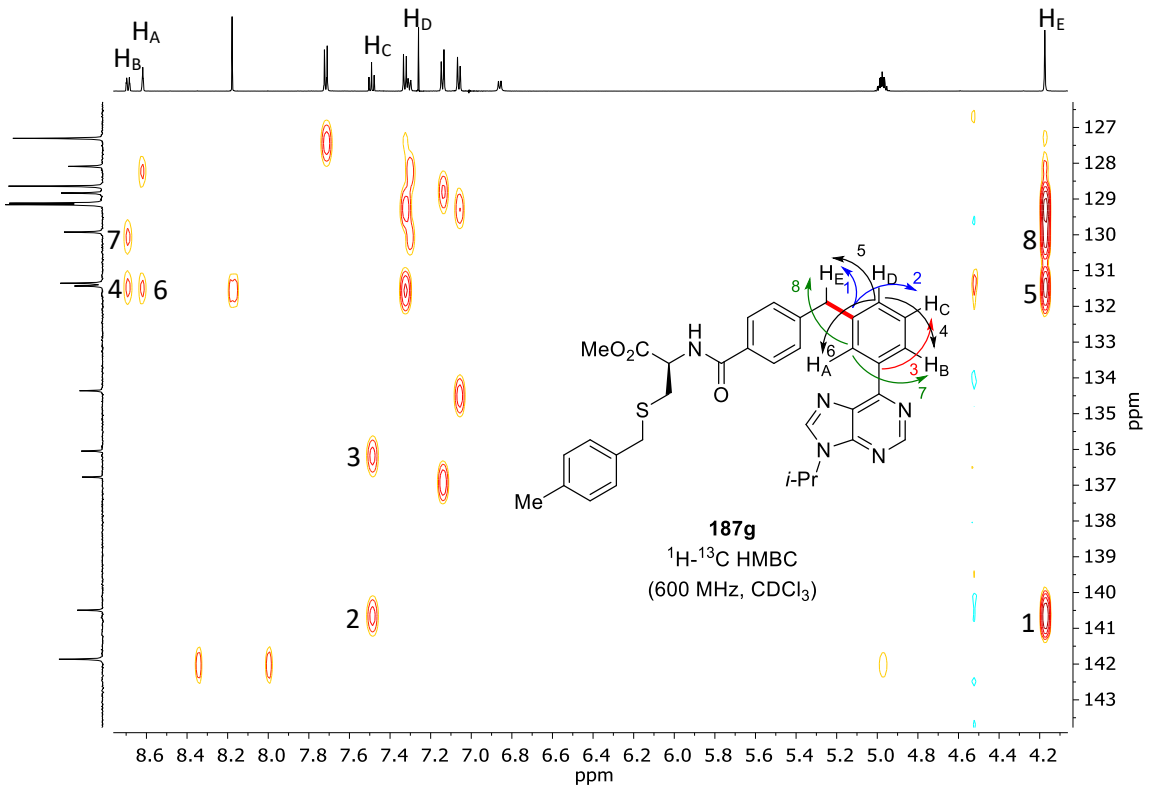
rac-**187f**
(125 MHz, $CDCl_3$)



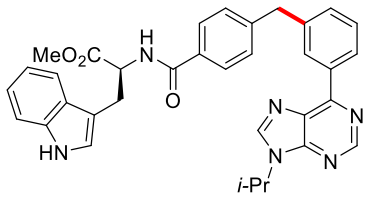
187g
(600 MHz, $CDCl_3$)



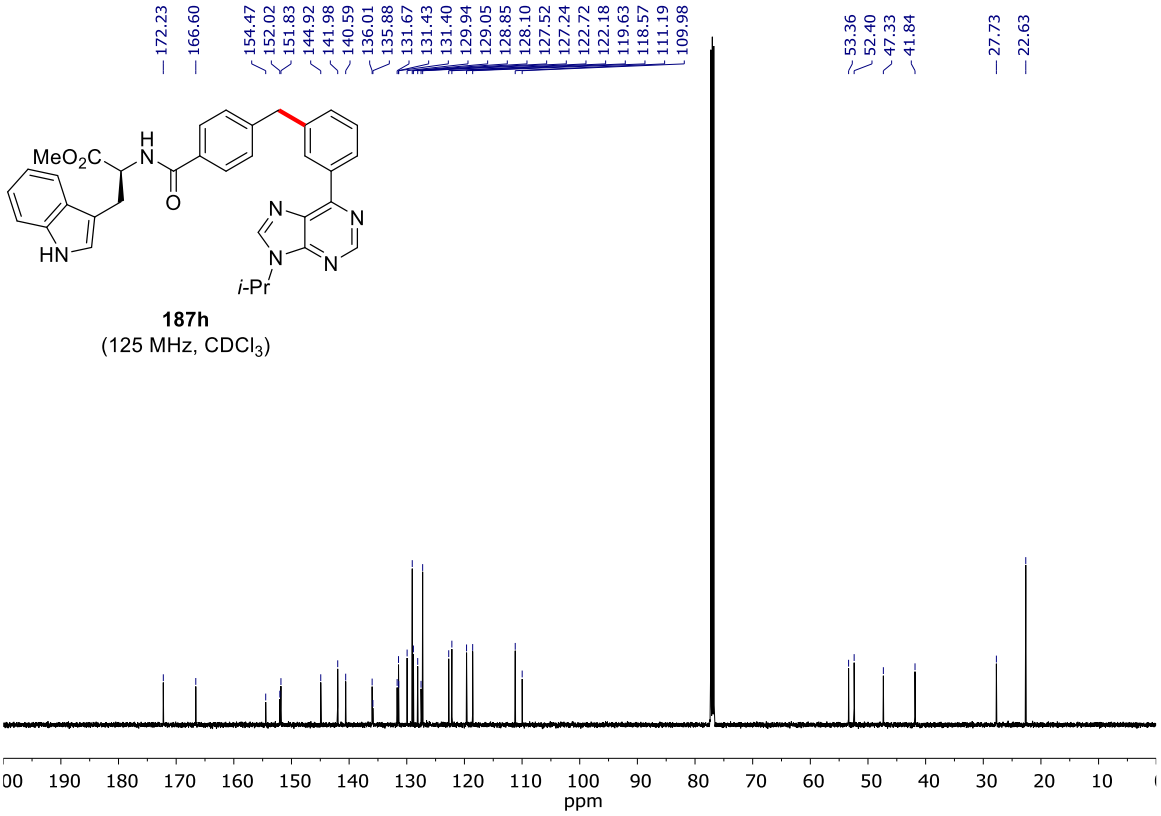
187g
(125 MHz, $CDCl_3$)



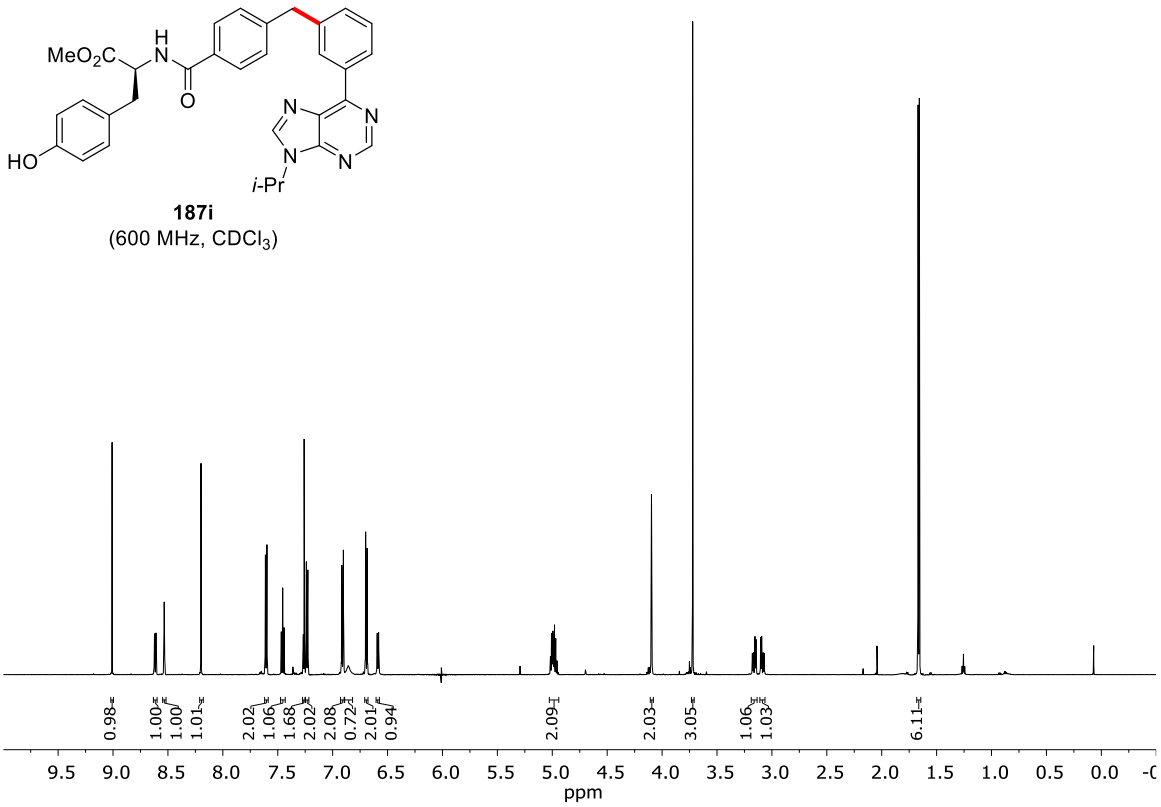
187g
^{1}H-^{13}C HMBC
(600 MHz, $CDCl_3$)



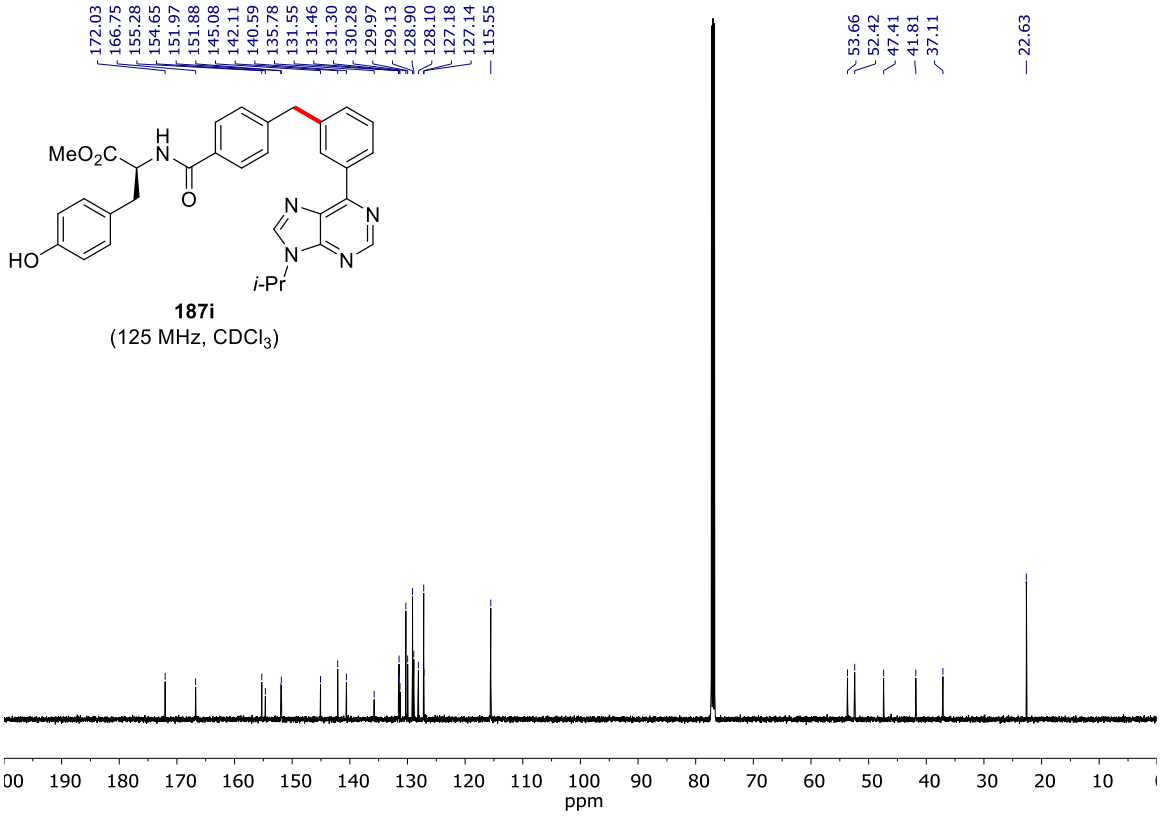
187h
(300 MHz, $CDCl_3$)



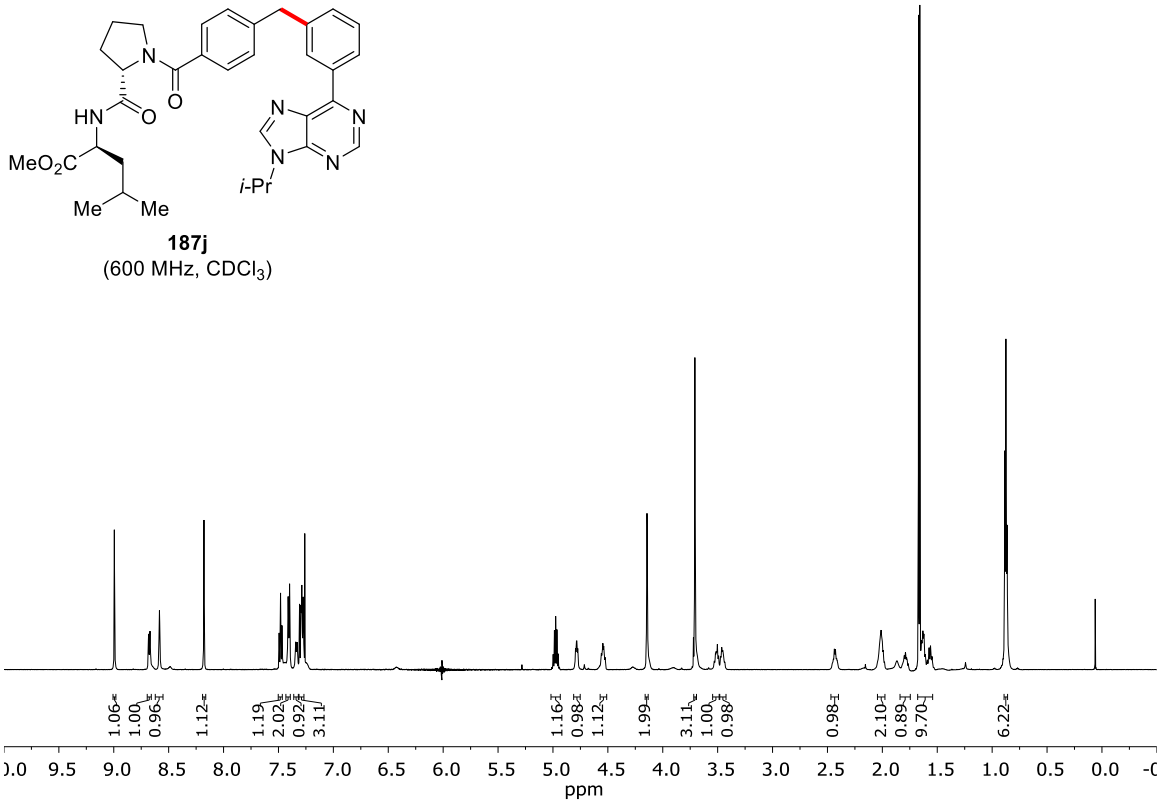
187h
(125 MHz, $CDCl_3$)



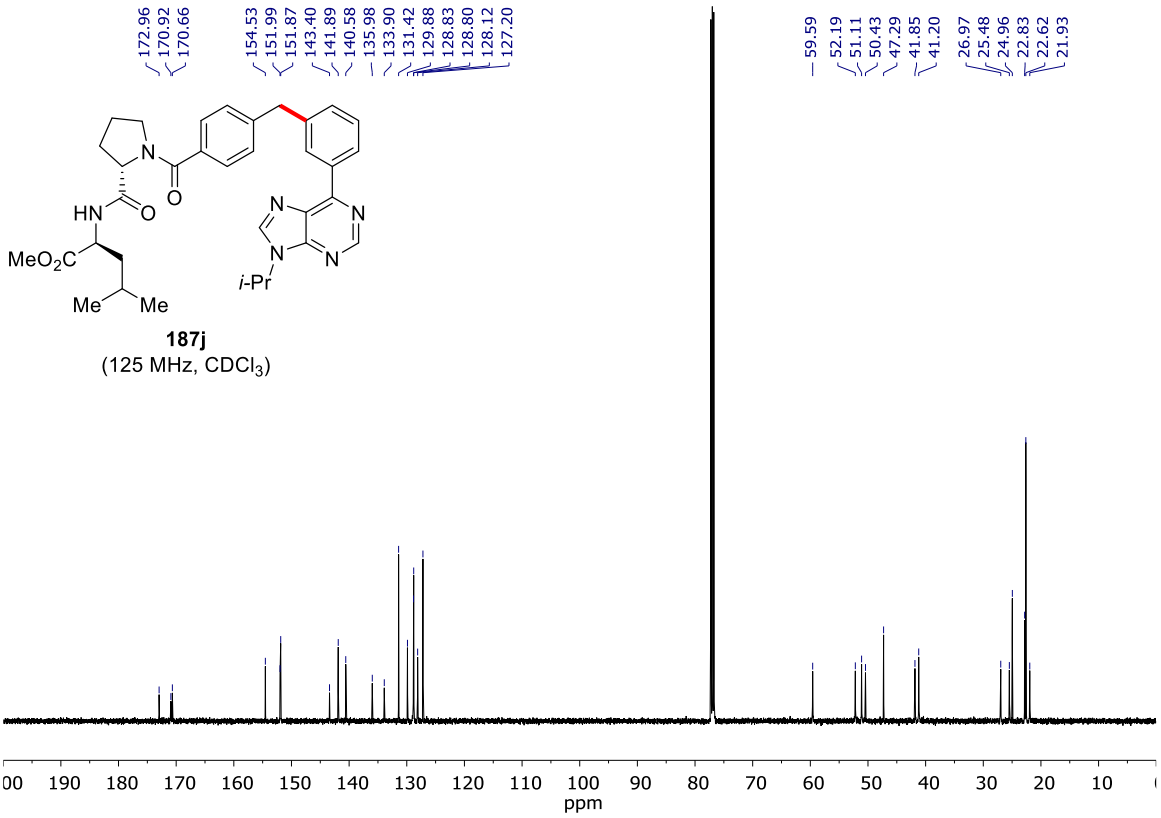
187i
(600 MHz, $CDCl_3$)



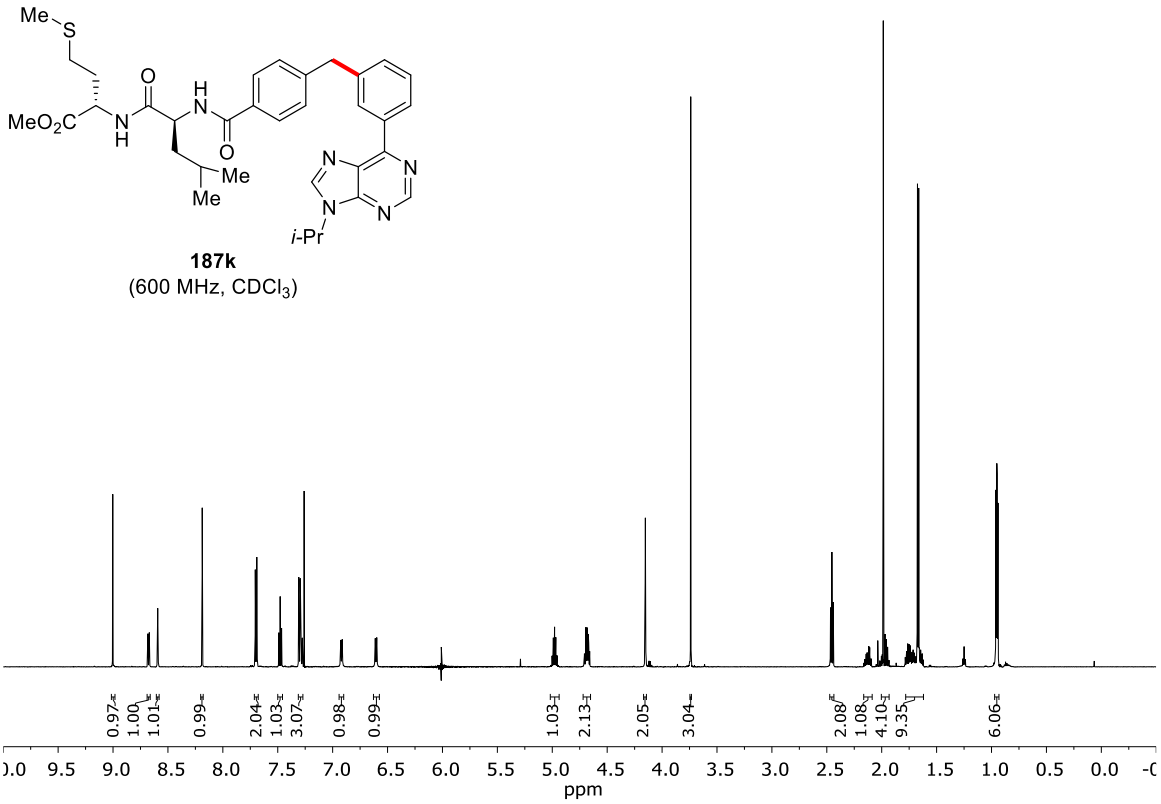
187i
(125 MHz, $CDCl_3$)



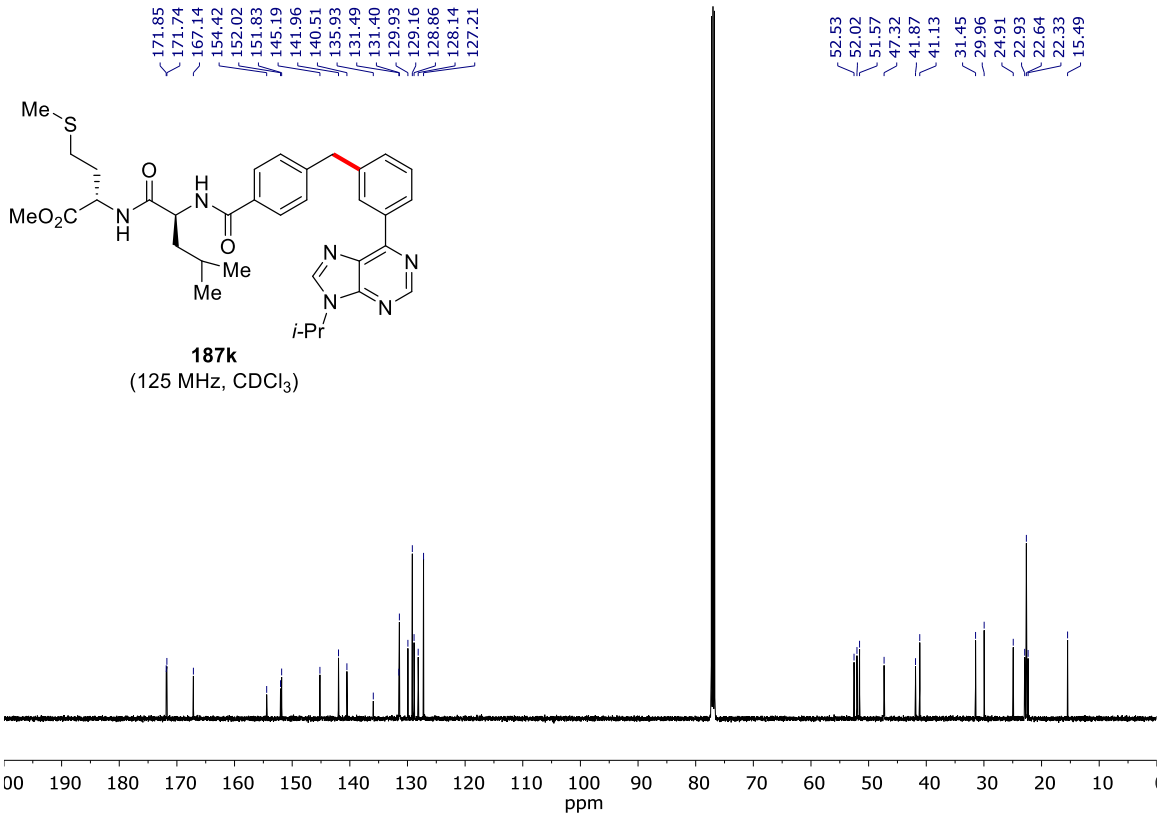
187j
(600 MHz, $CDCl_3$)

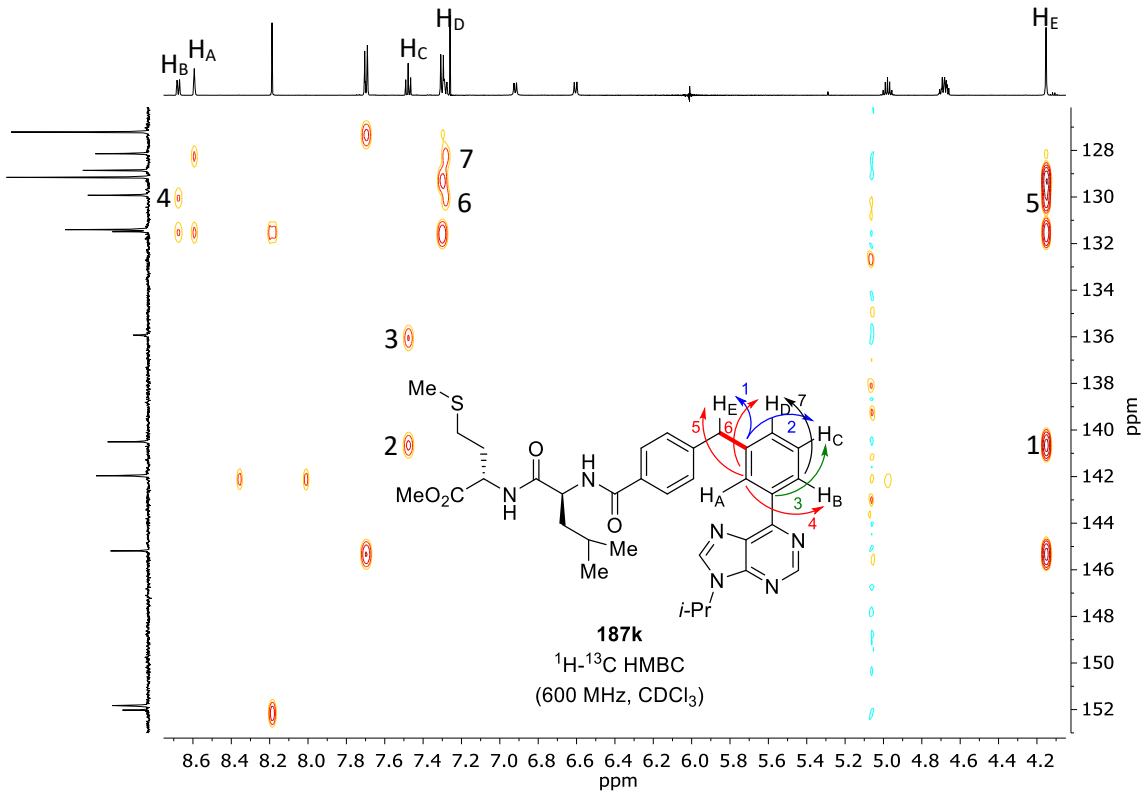


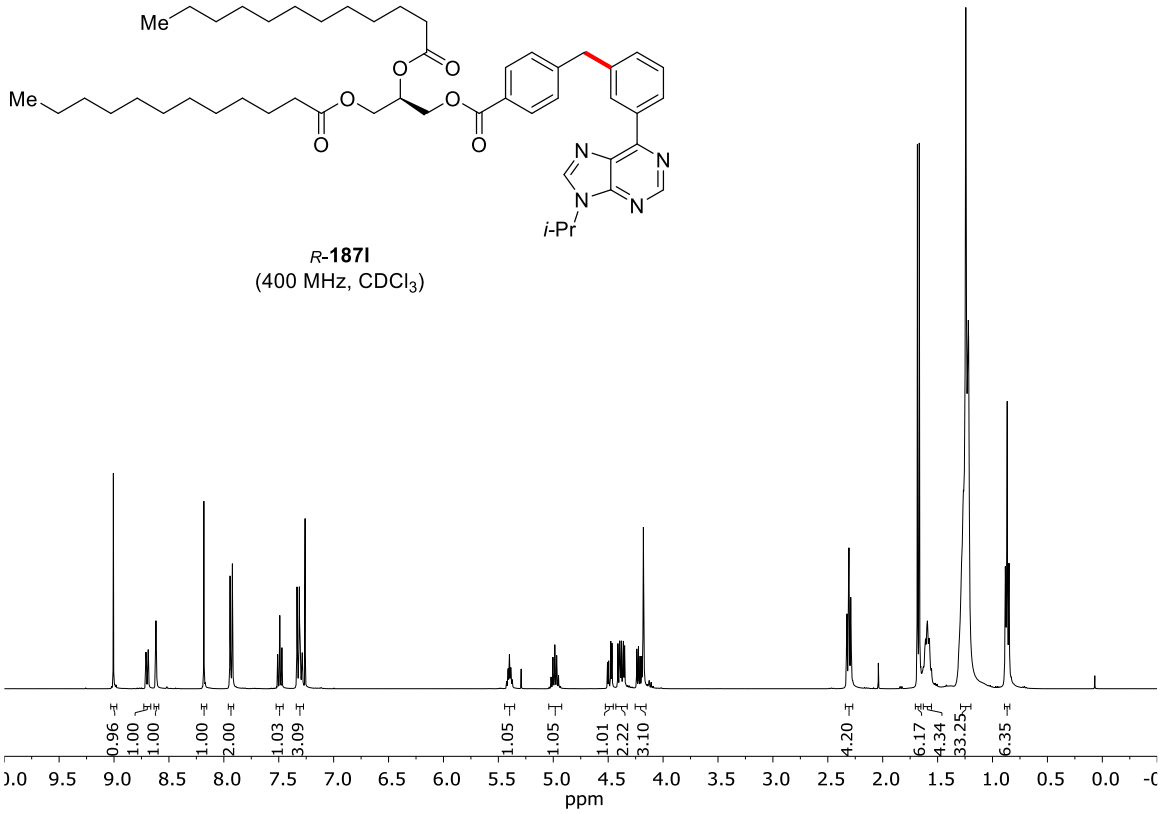
187j
(125 MHz, $CDCl_3$)



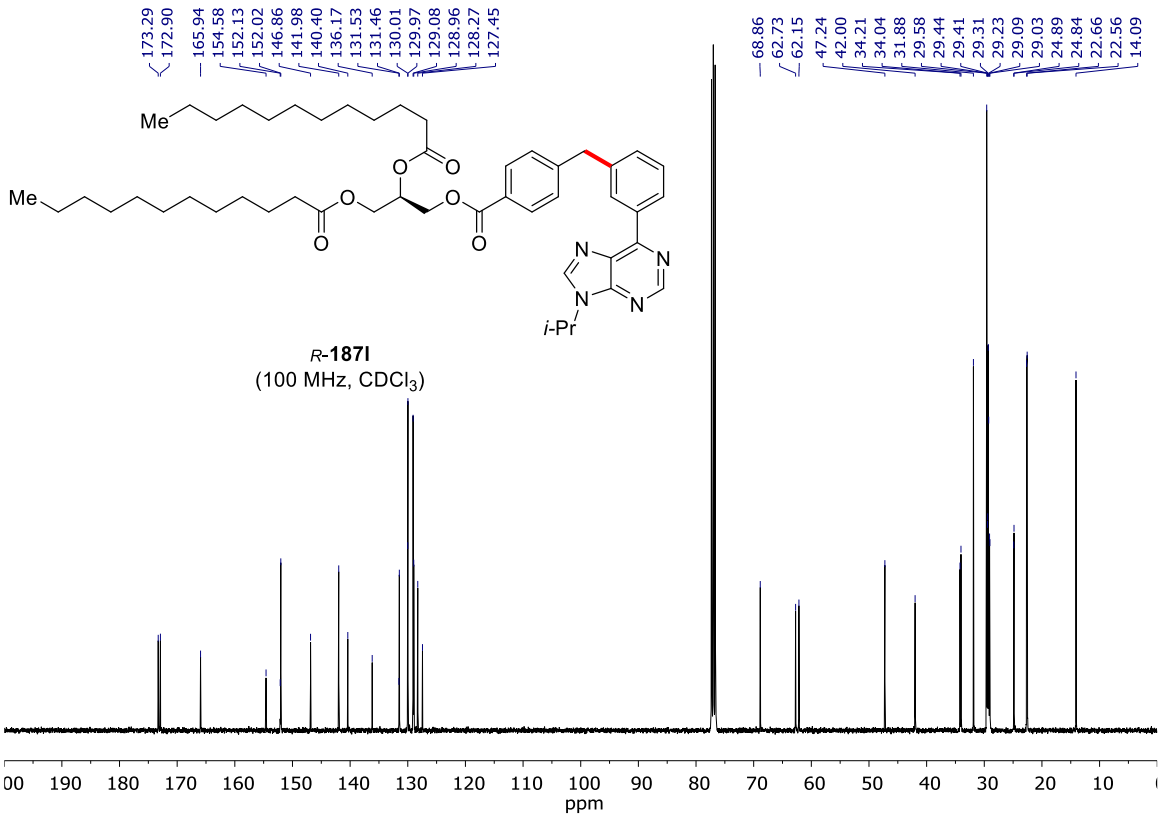
187k
(600 MHz, $CDCl_3$)


171.85
171.74
167.14
154.42
152.02
151.83
145.19
141.96
140.51
135.93
131.49
131.40
129.93
129.16
128.86
128.14
127.21
52.53
52.02
51.57
47.32
41.87
41.13
31.45
29.96
24.91
22.93
22.64
22.33
15.49
Me
S
MeO2C
N
H
O
H
N
O
Me
Me
N
N
N
N
i-Pr
187k
(125 MHz, CDCl3)
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

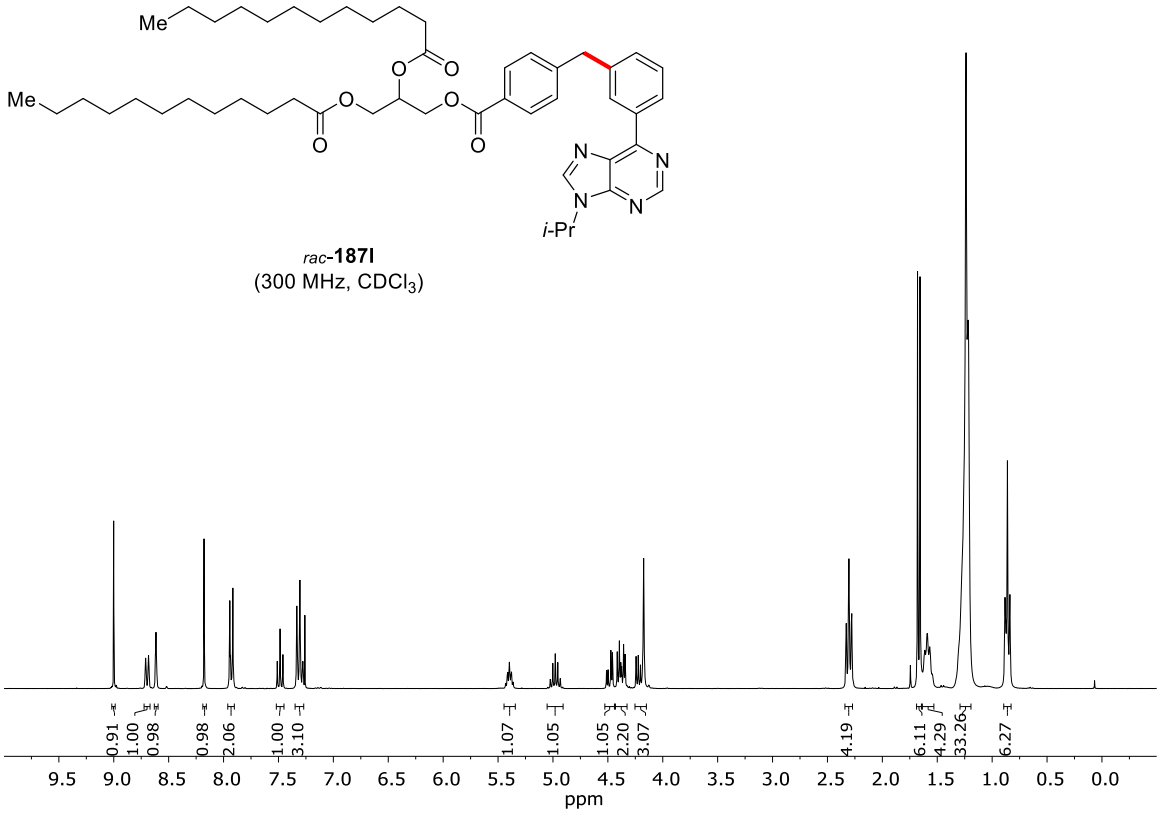

HB
HA
HC
HD
HE
4
7
6
3
2
5
1
Me
S
MeO2C
N
H
O
H
N
O
Me
Me
N
N
N
N
i-Pr
HE
HD
HC
HA
HB
1
2
3
4
5
6
7
187k
1H-13C HMBC
(600 MHz, CDCl3)
128
130
132
134
136
138
140
142
144
146
148
150
152
ppm
8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2
ppm



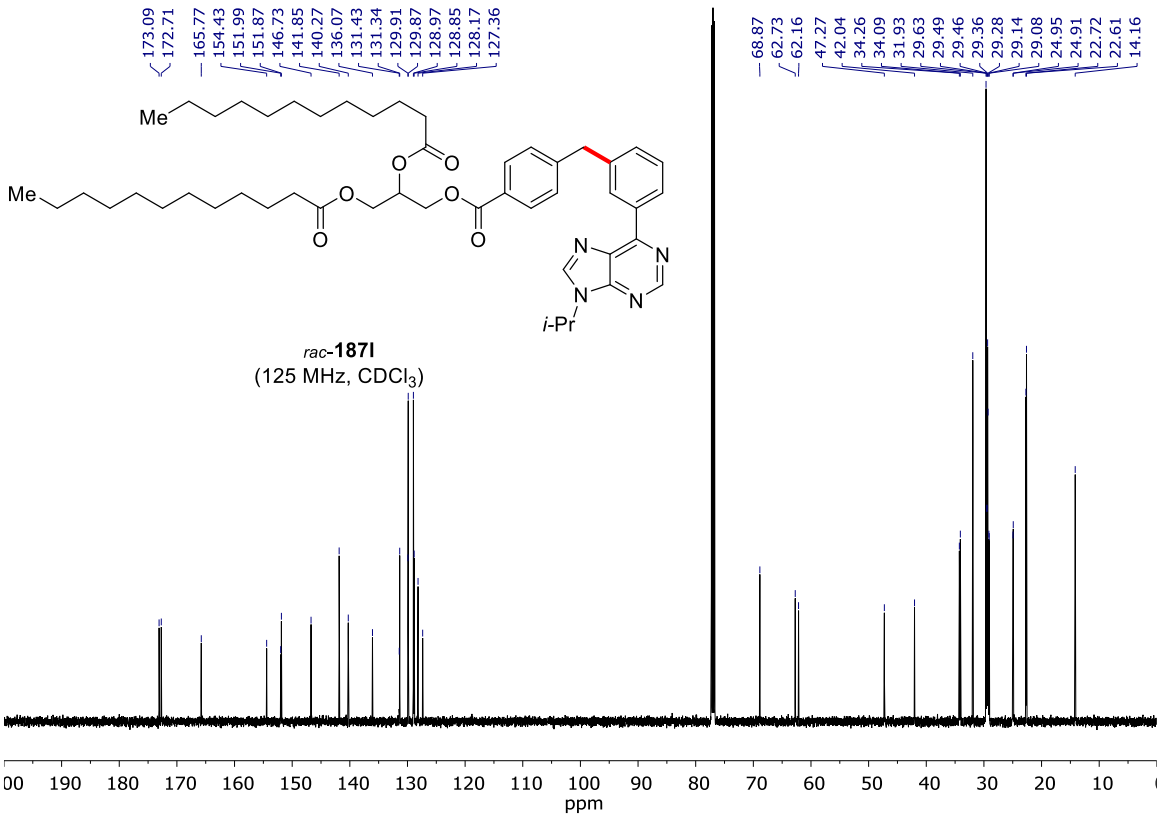
R-**187l**
(400 MHz, $CDCl_3$)



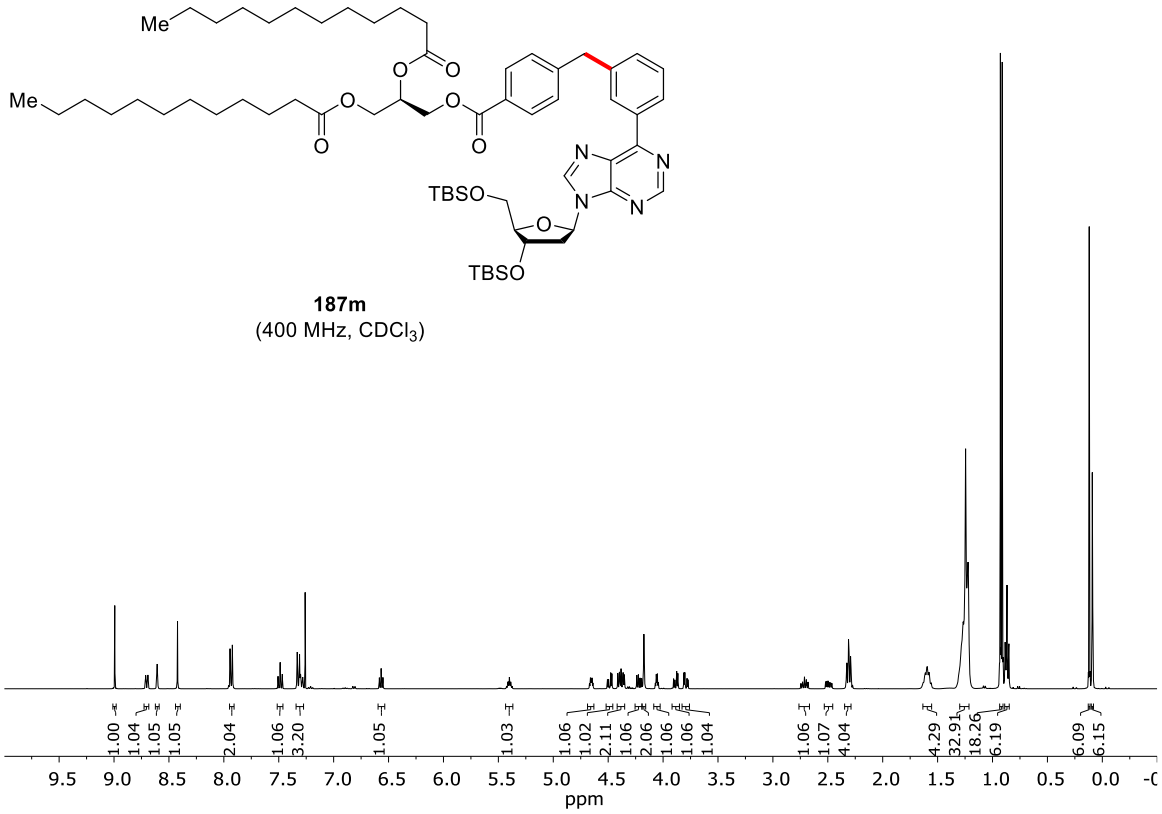
R-**187l**
(100 MHz, $CDCl_3$)



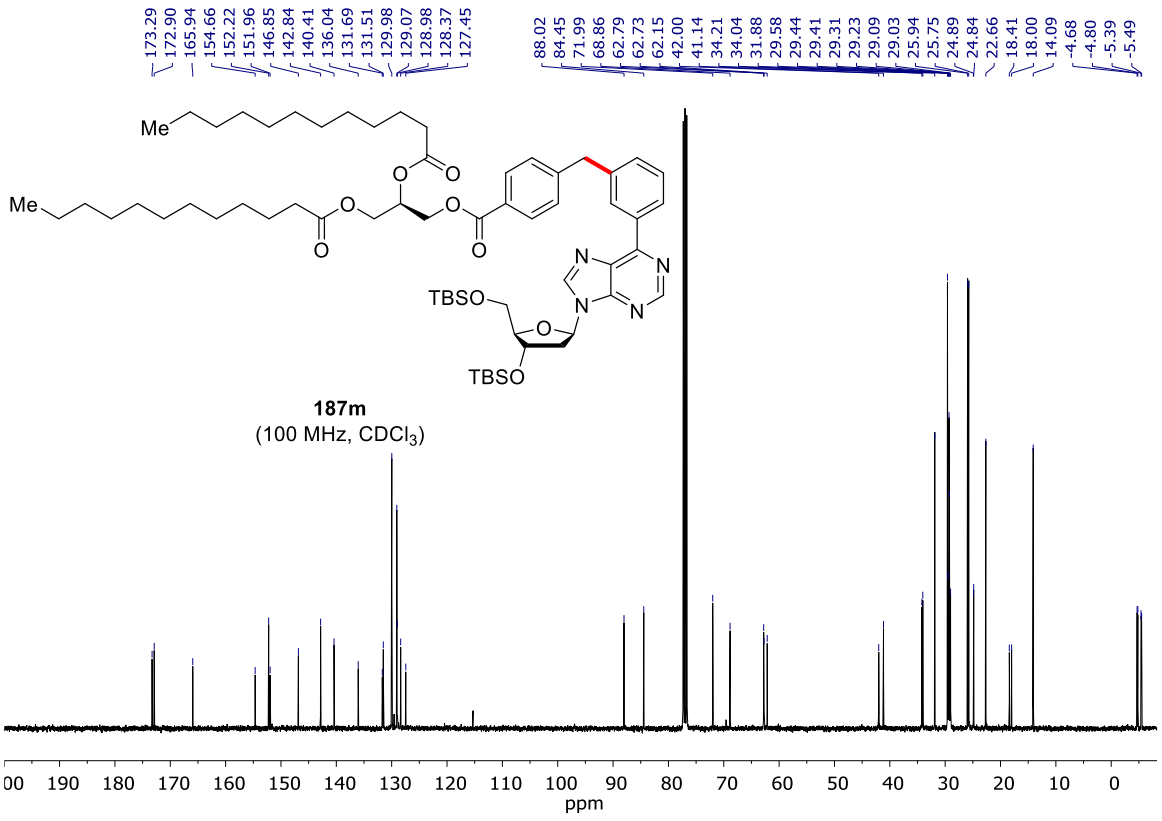
rac-**187l**
(300 MHz, $CDCl_3$)



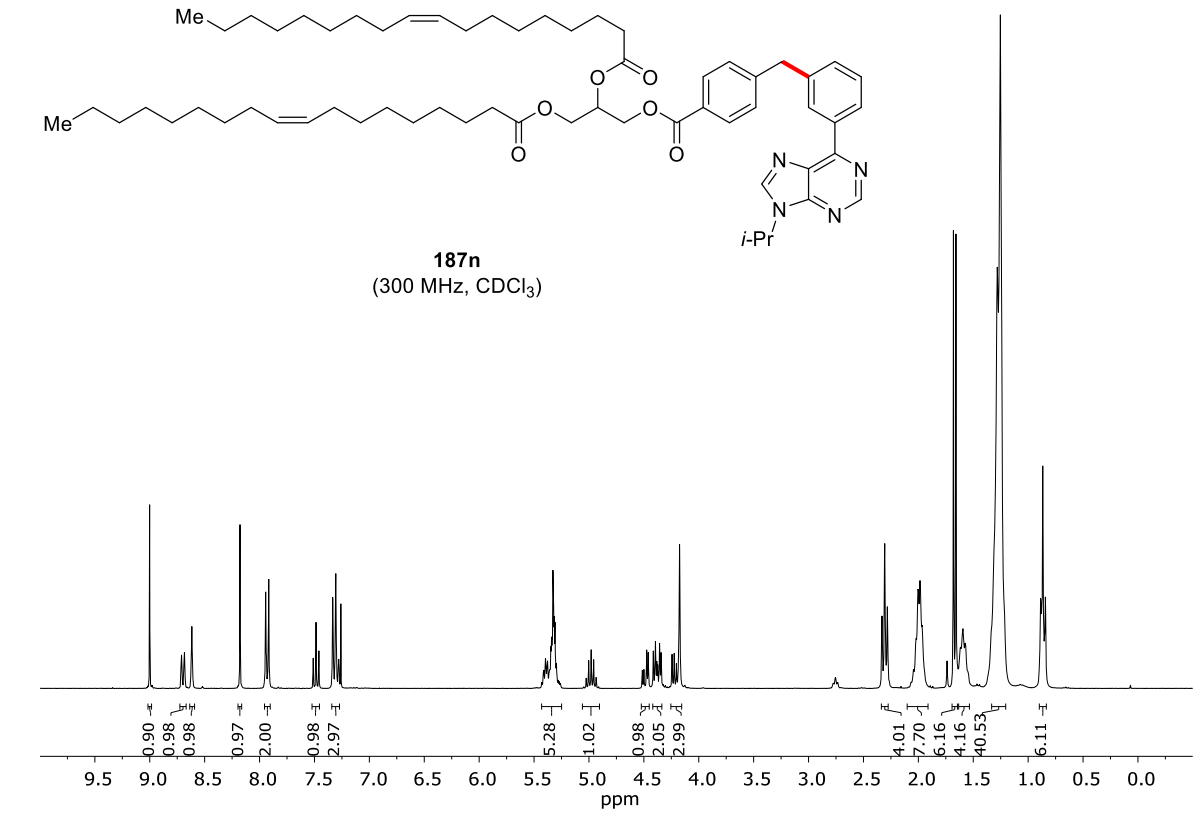
rac-**187l**
(125 MHz, $CDCl_3$)

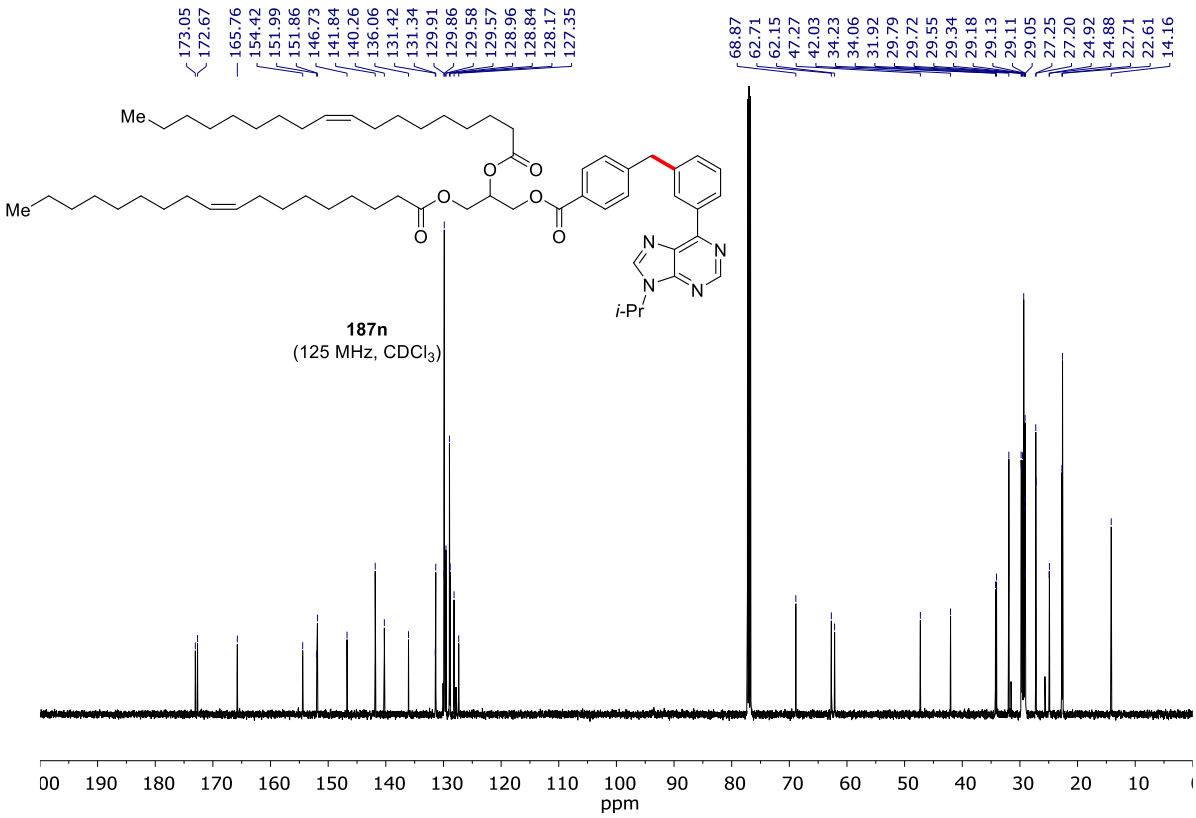


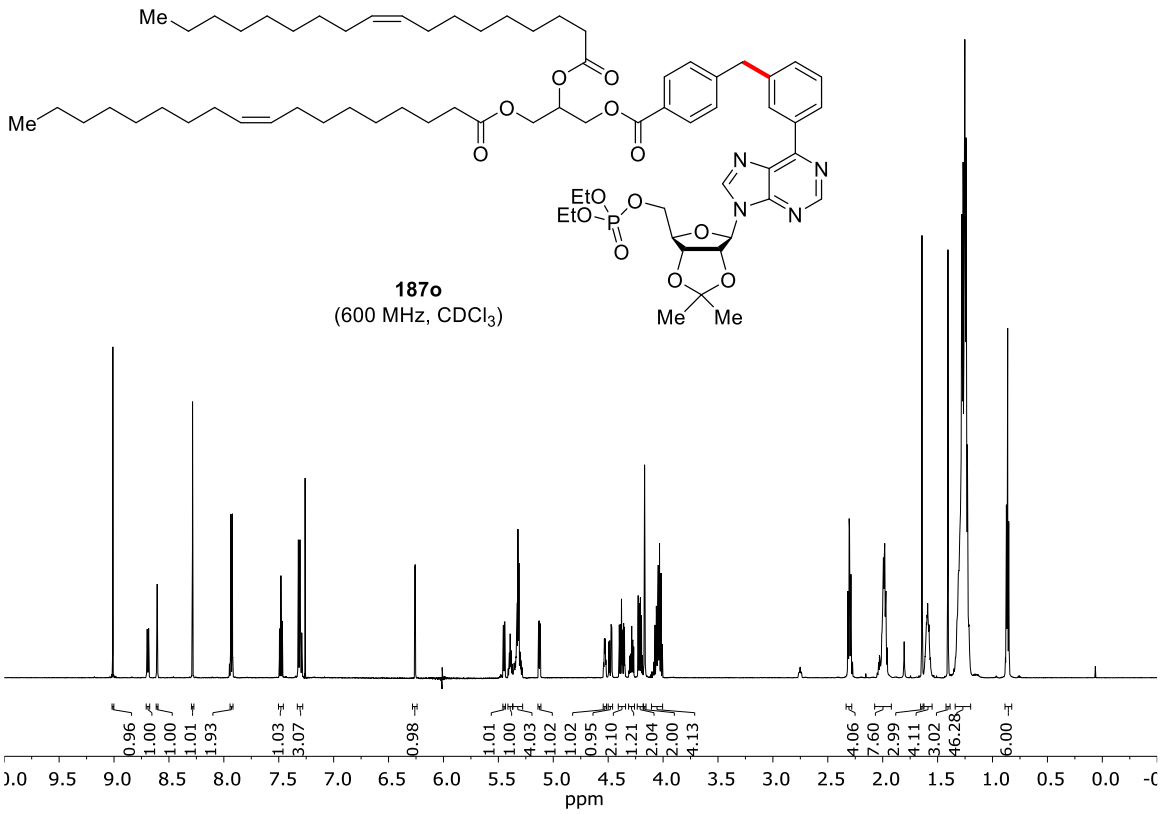
187m
(400 MHz, $CDCl_3$)

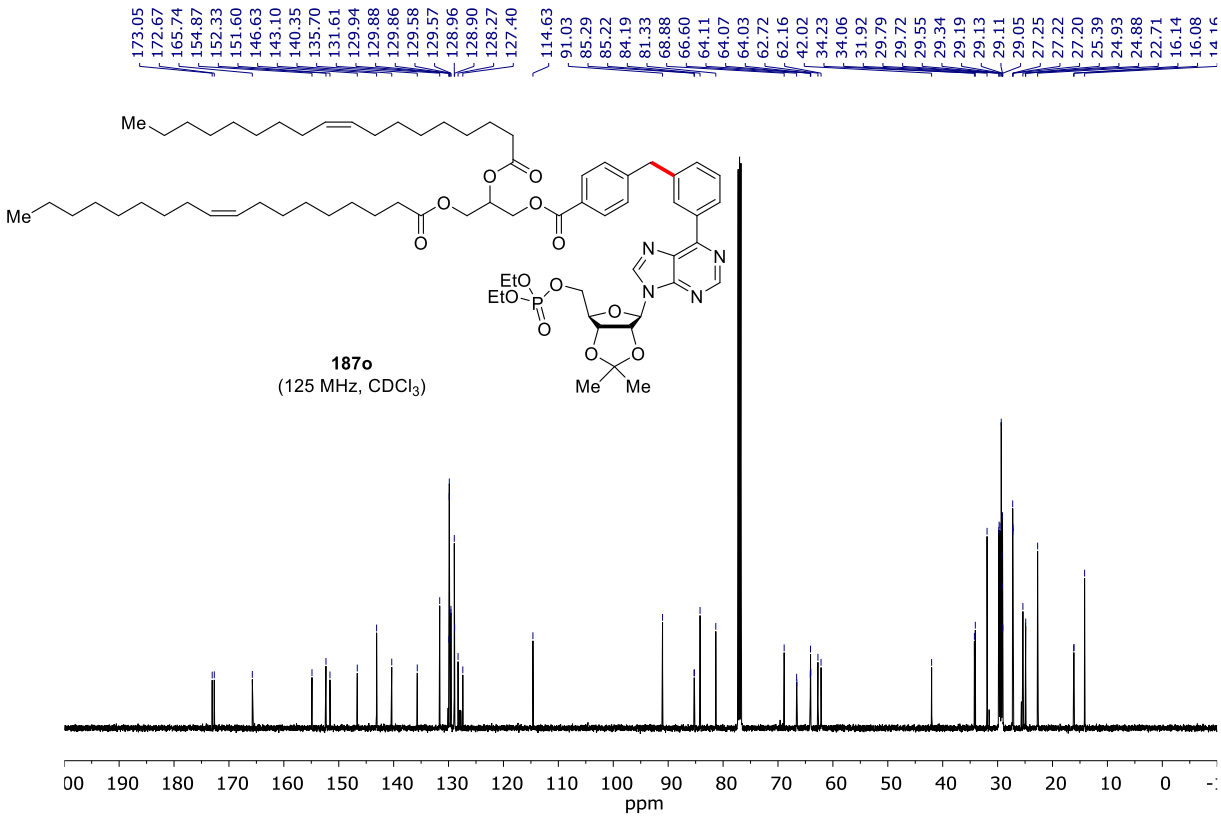


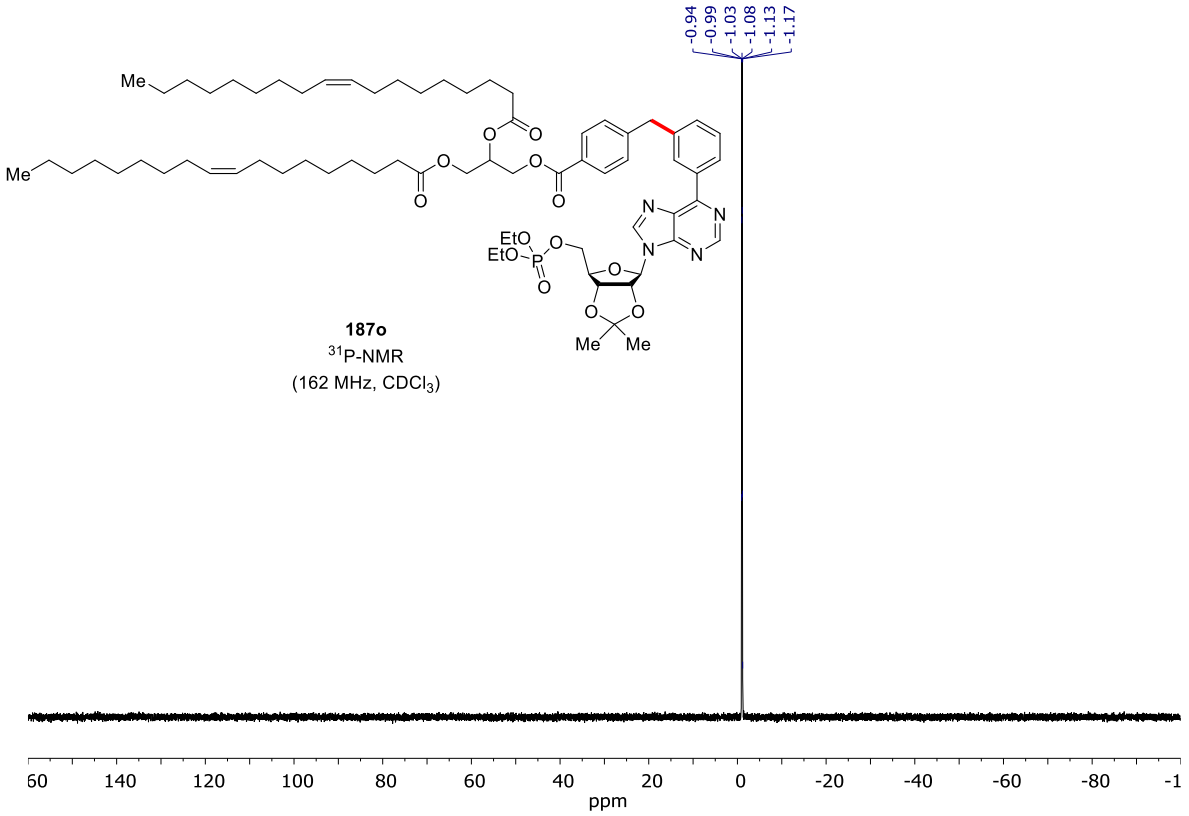
187m
(100 MHz, $CDCl_3$)


Me
Me
O
O
O
O
O
O
N
N
N
N
i-Pr
187n
(300 MHz, CDCl3)
0.90
0.98
0.98
0.97
2.00
0.98
2.97
5.28
1.02
0.98
2.05
2.99
4.01
7.70
6.16
4.16
40.53
6.11
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

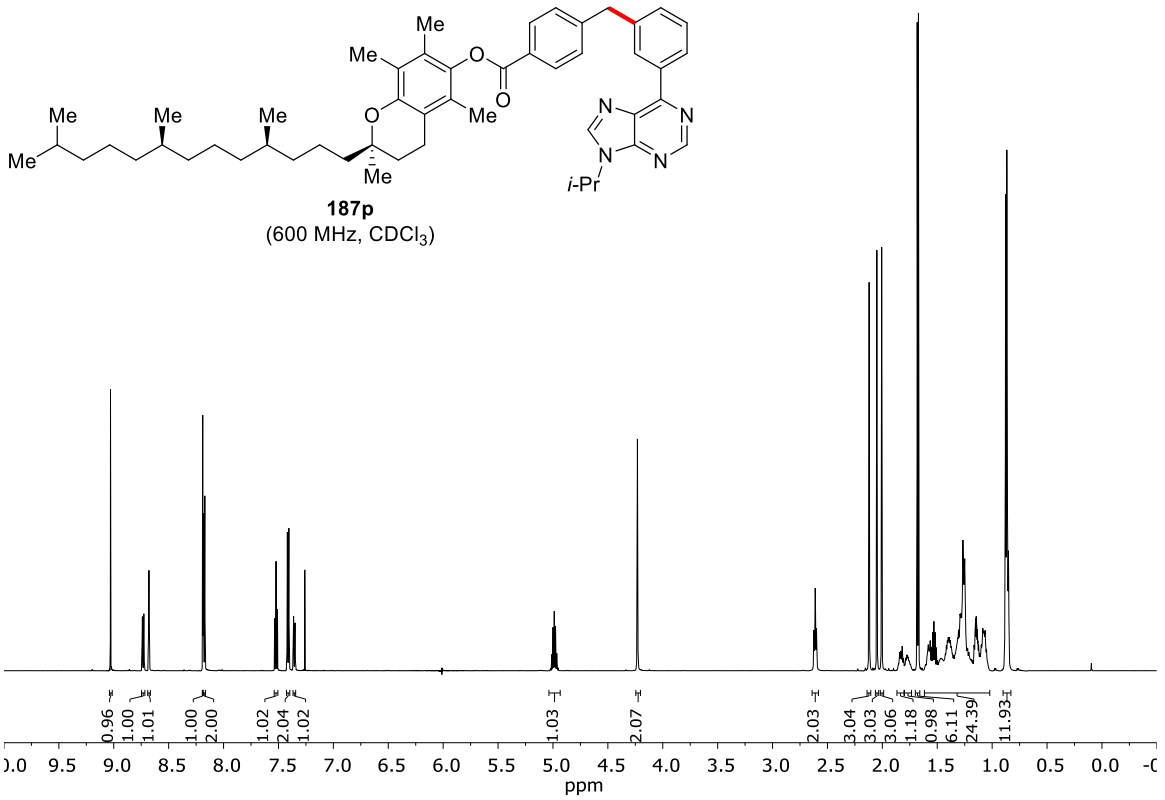

173.05
172.67
165.76
154.42
151.99
151.86
146.73
141.84
140.26
136.06
131.42
131.34
129.91
129.86
129.58
129.57
128.96
128.84
128.17
127.35
68.87
62.71
62.15
47.27
42.03
34.23
34.06
31.92
29.79
29.72
29.55
29.34
29.18
29.13
29.11
29.05
27.25
27.20
24.92
24.88
22.71
22.61
14.16
Me
Me
O
O
O
O
O
O
N
N
N
N
i-Pr
187n
(125 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm


Me
Me
EtO
EtO
Me
Me
187o
(600 MHz, CDCl3)
ppm

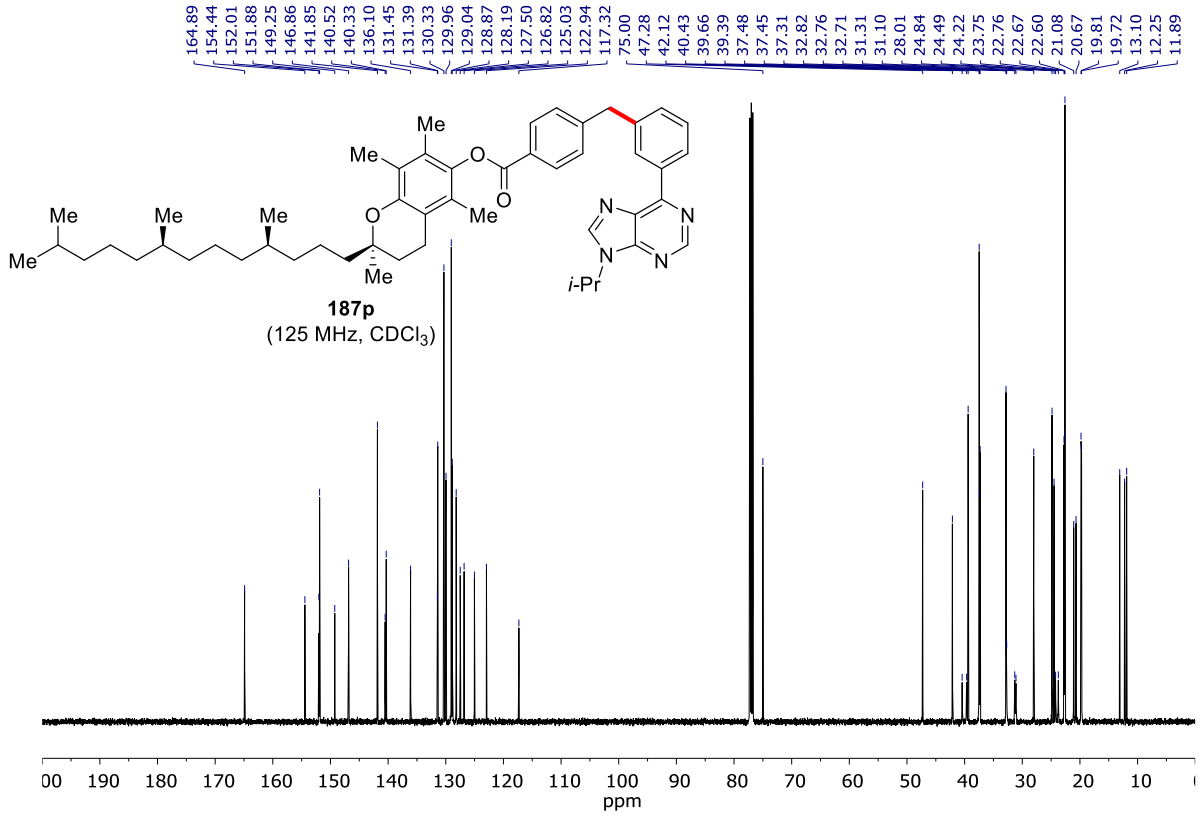

173.05
172.67
165.74
154.87
152.33
151.60
146.63
143.10
140.35
135.70
131.61
129.94
129.88
129.86
129.58
129.57
128.96
128.90
128.27
127.40
114.63
91.03
85.29
85.22
84.19
81.33
68.88
66.60
64.11
64.07
64.03
62.72
62.16
42.02
34.23
34.06
31.92
29.79
29.72
29.55
29.34
29.19
29.13
29.11
29.05
27.25
27.22
27.20
25.39
24.93
24.88
22.71
16.14
16.08
Me
Me
EtO
EtO
Me
Me
187o
(125 MHz, CDCl3)
ppm



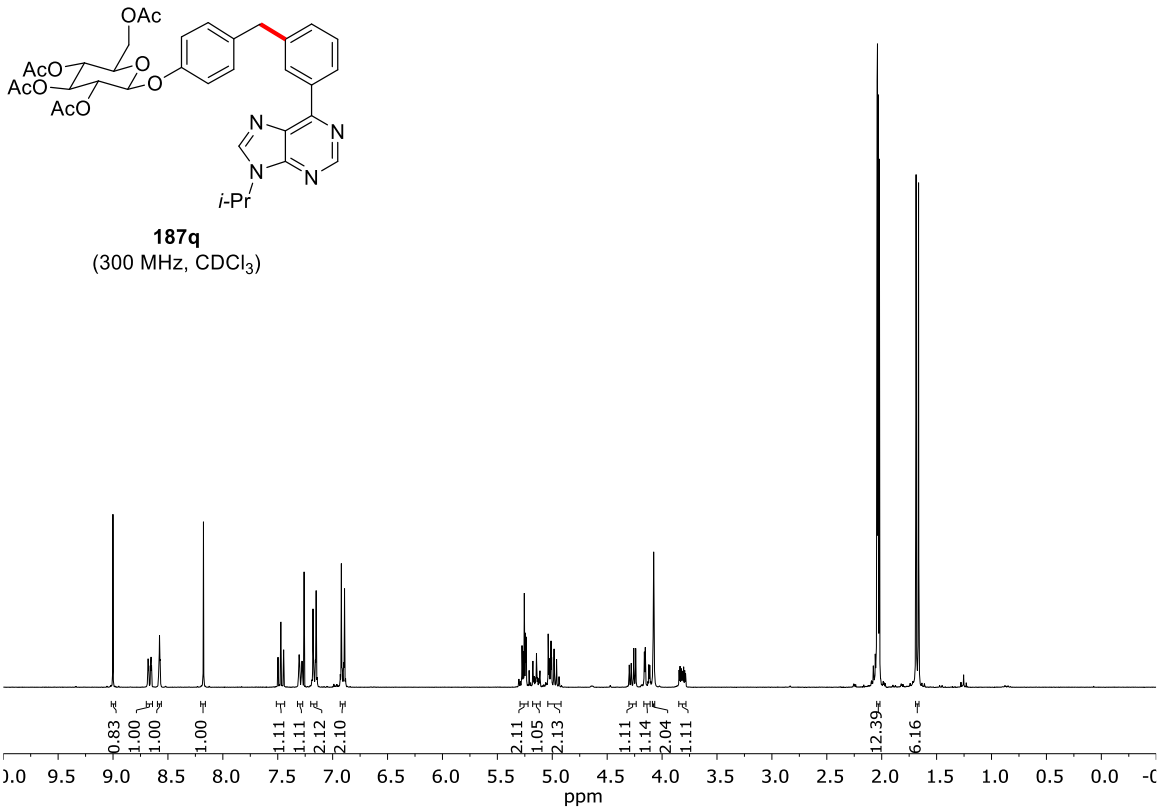
187o
^{31}P-NMR
(162 MHz, $CDCl_3$)



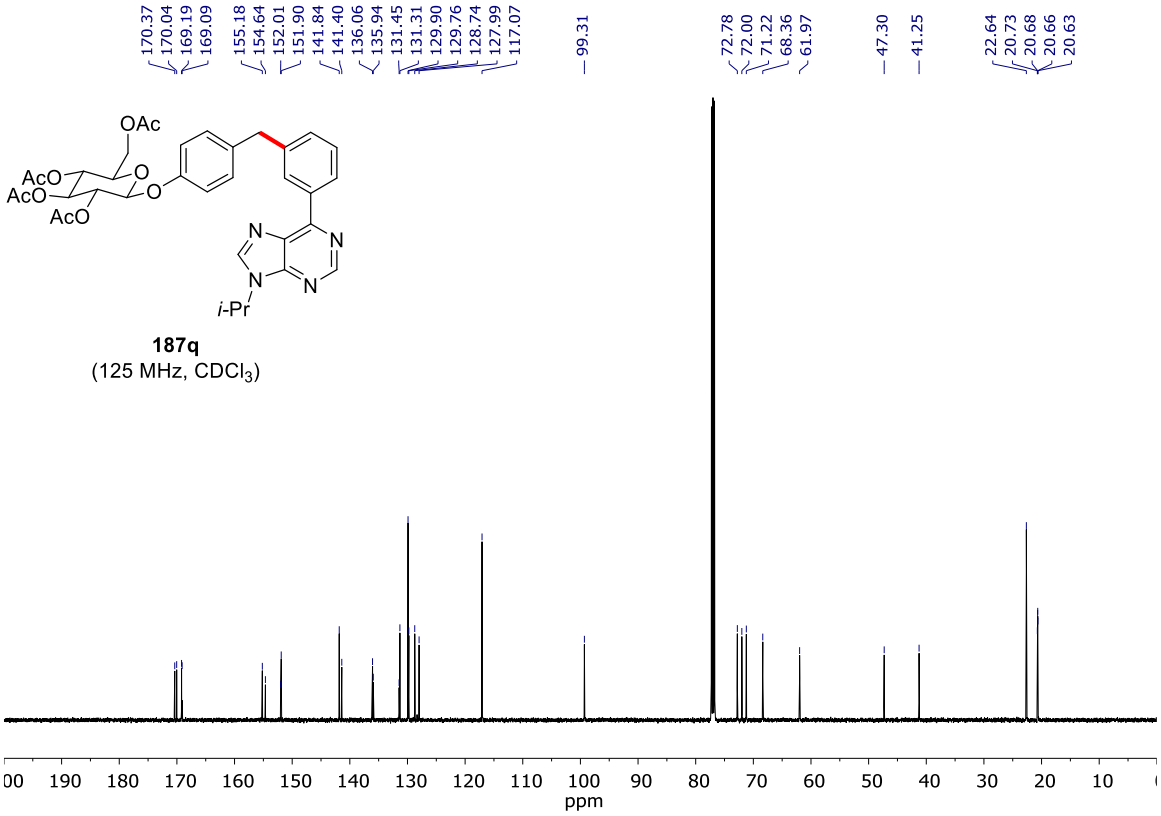
187p
(600 MHz, $CDCl_3$)

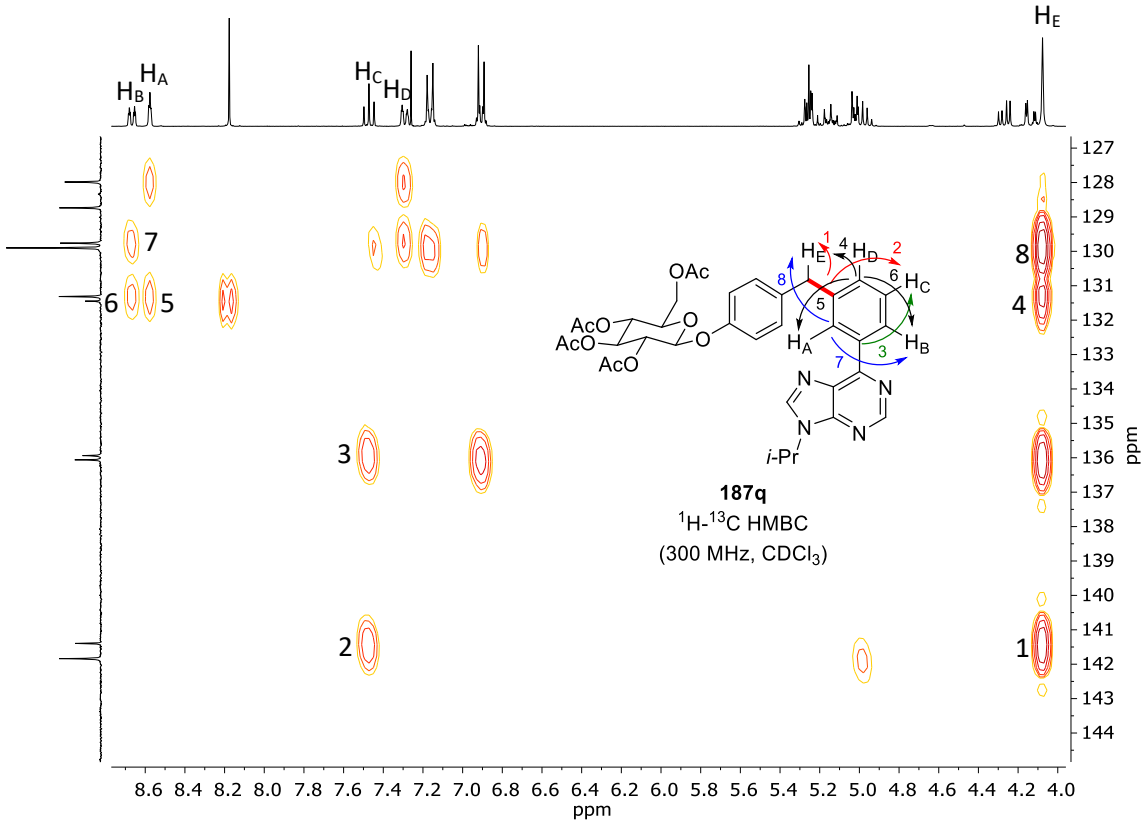


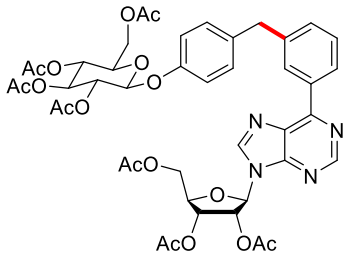
187p
(125 MHz, $CDCl_3$)



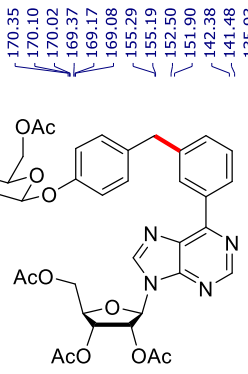
187q
(300 MHz, $CDCl_3$)


170.37
170.04
169.19
169.09
155.18
154.64
152.01
151.90
141.84
141.40
136.06
135.94
131.45
131.31
129.90
129.76
128.74
127.99
117.07
99.31
72.78
72.00
71.22
68.36
61.97
47.30
41.25
22.64
20.73
20.68
20.66
20.63
OAc
AcO
AcO
AcO
O
O
N
N
N
N
i-Pr
187q
(125 MHz, CDCl3)
ppm

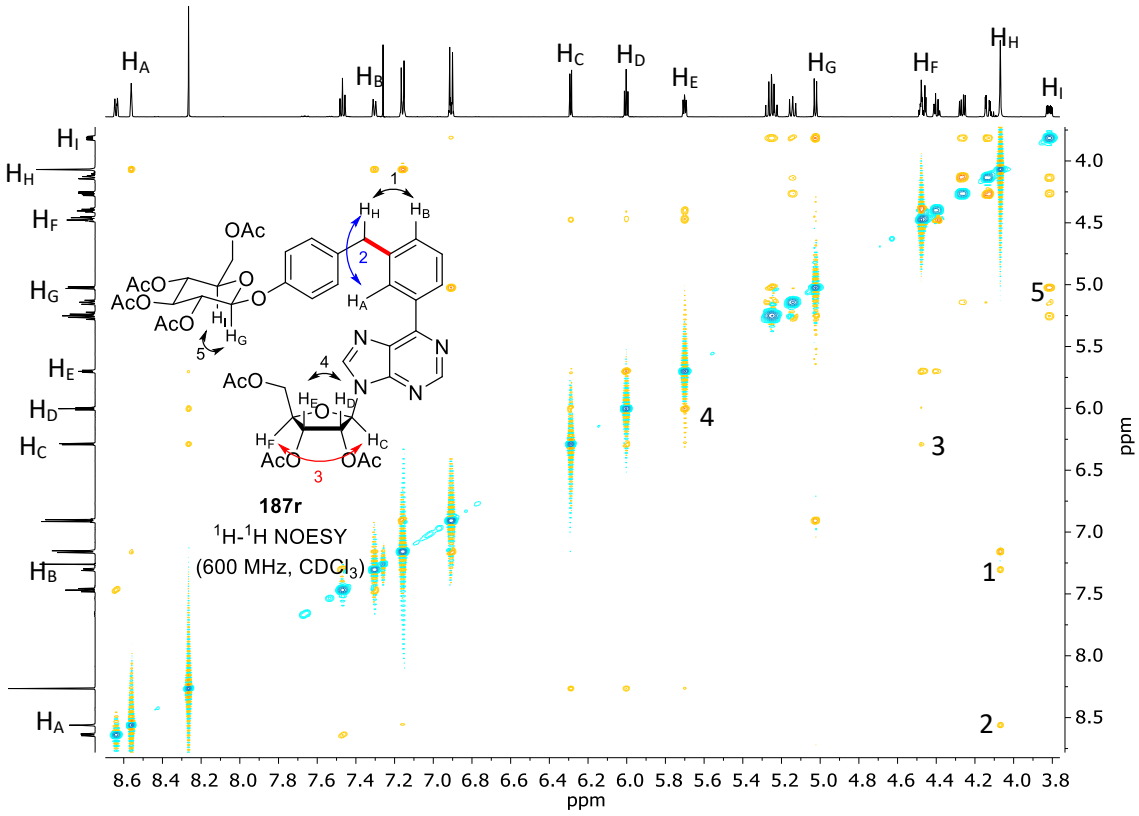

HE
HA
HB
HC
HD
7
6
5
3
2
8
4
1
OAc
AcO
AcO
AcO
O
O
N
N
N
N
i-Pr
187q
1H-13C HMBC
(300 MHz, CDCl3)
ppm
ppm

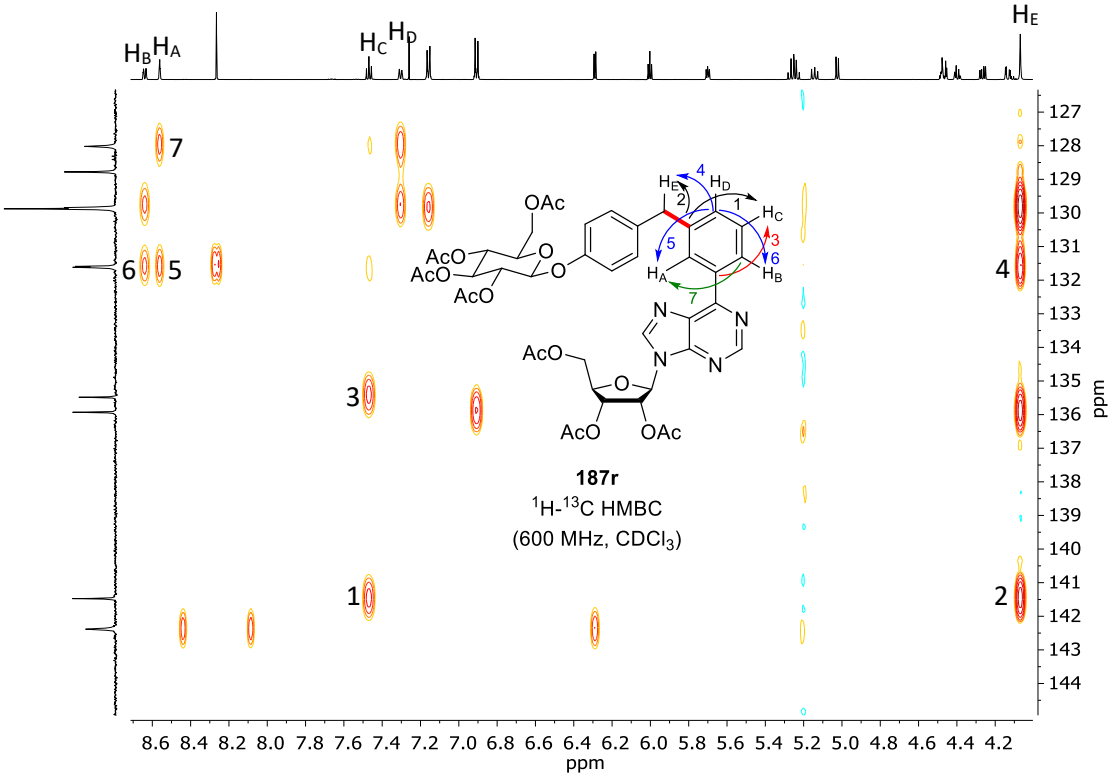


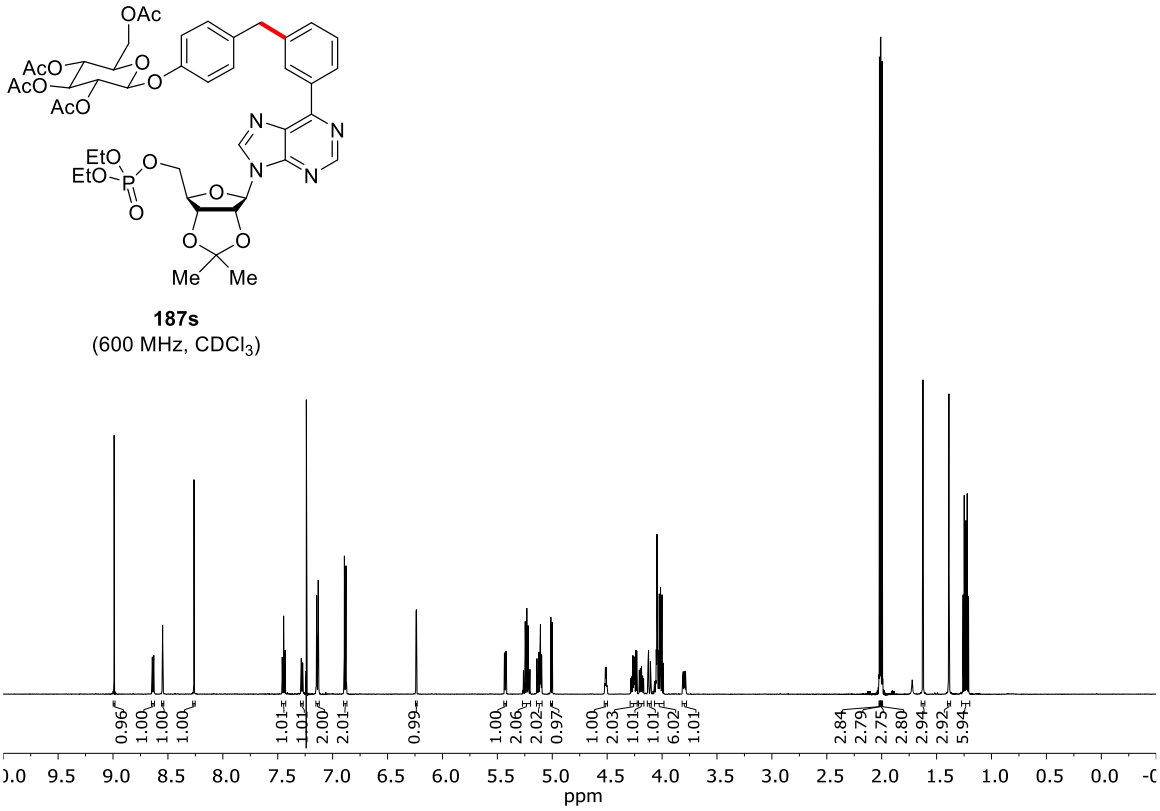
187r
(600 MHz, $CDCl_3$)



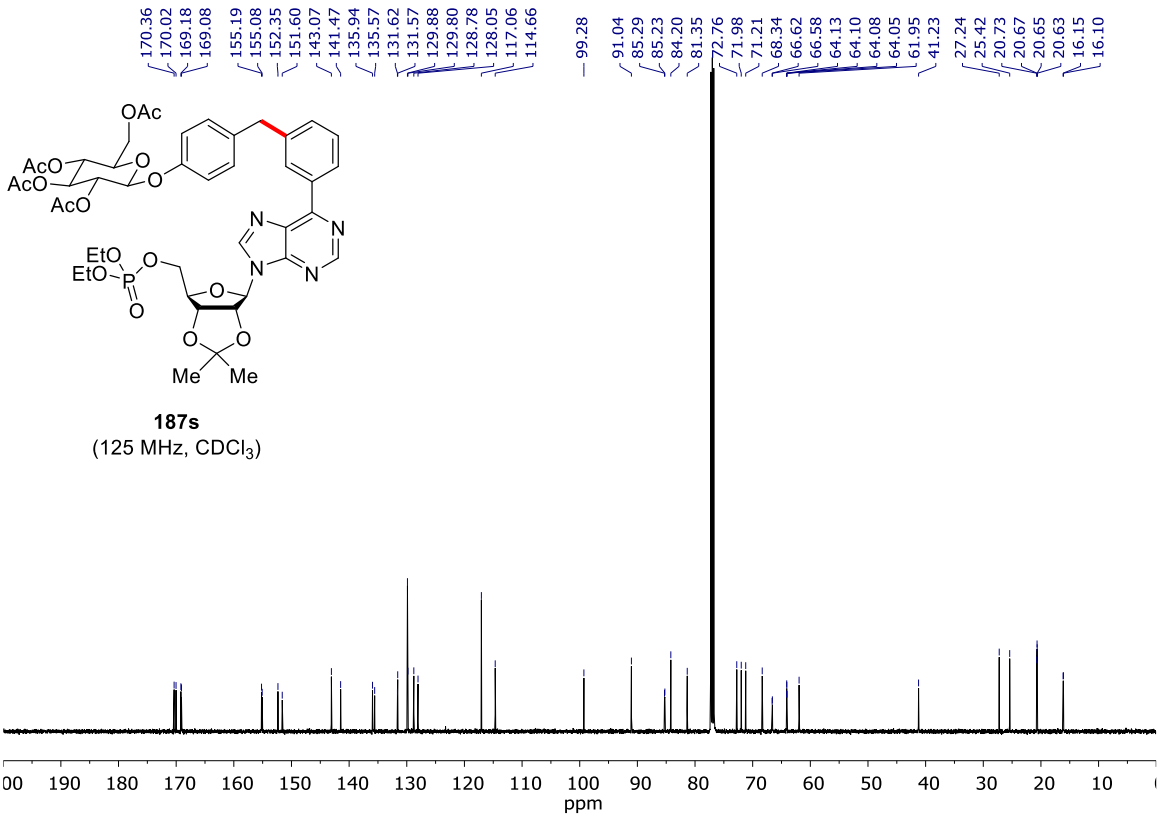
187r
(125 MHz, $CDCl_3$)


187r
^{1}H-^{1}H NOESY
(600 MHz, CDCl$_3$)
ppm

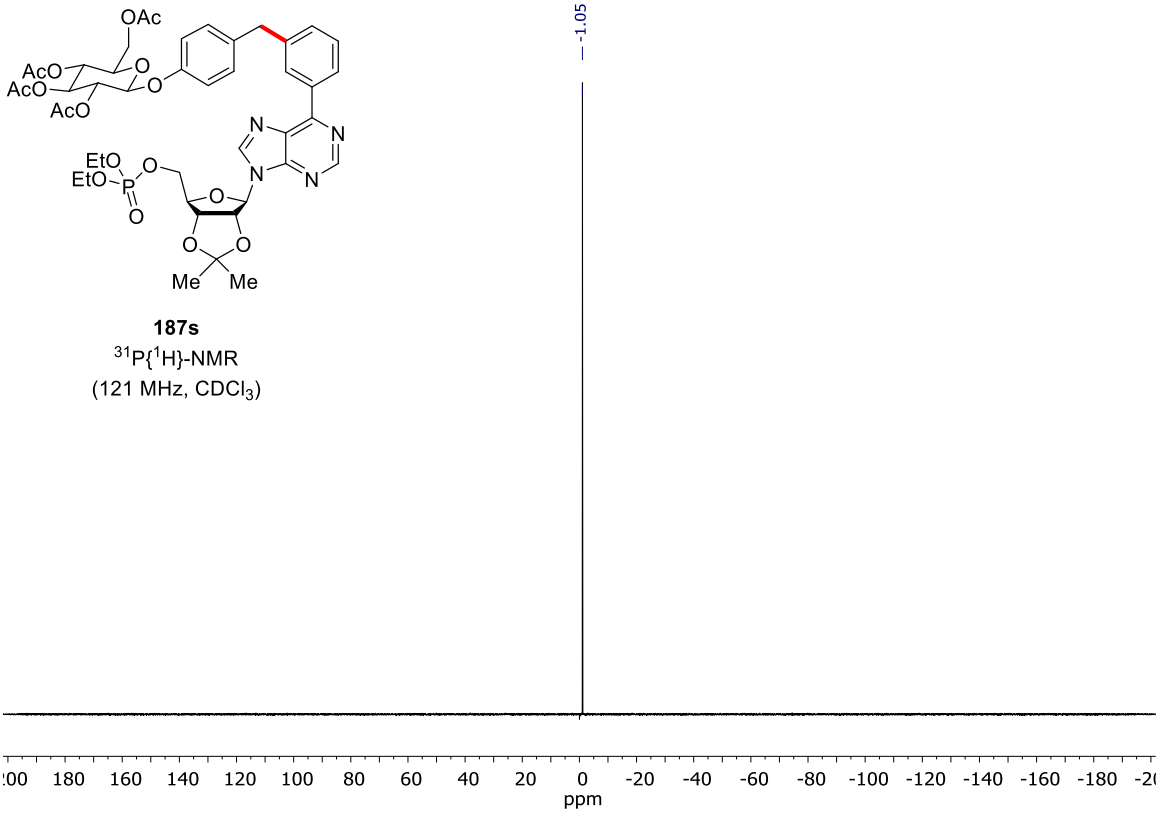

187r
^{1}H-^{13}C HMBC
(600 MHz, CDCl$_3$)
ppm



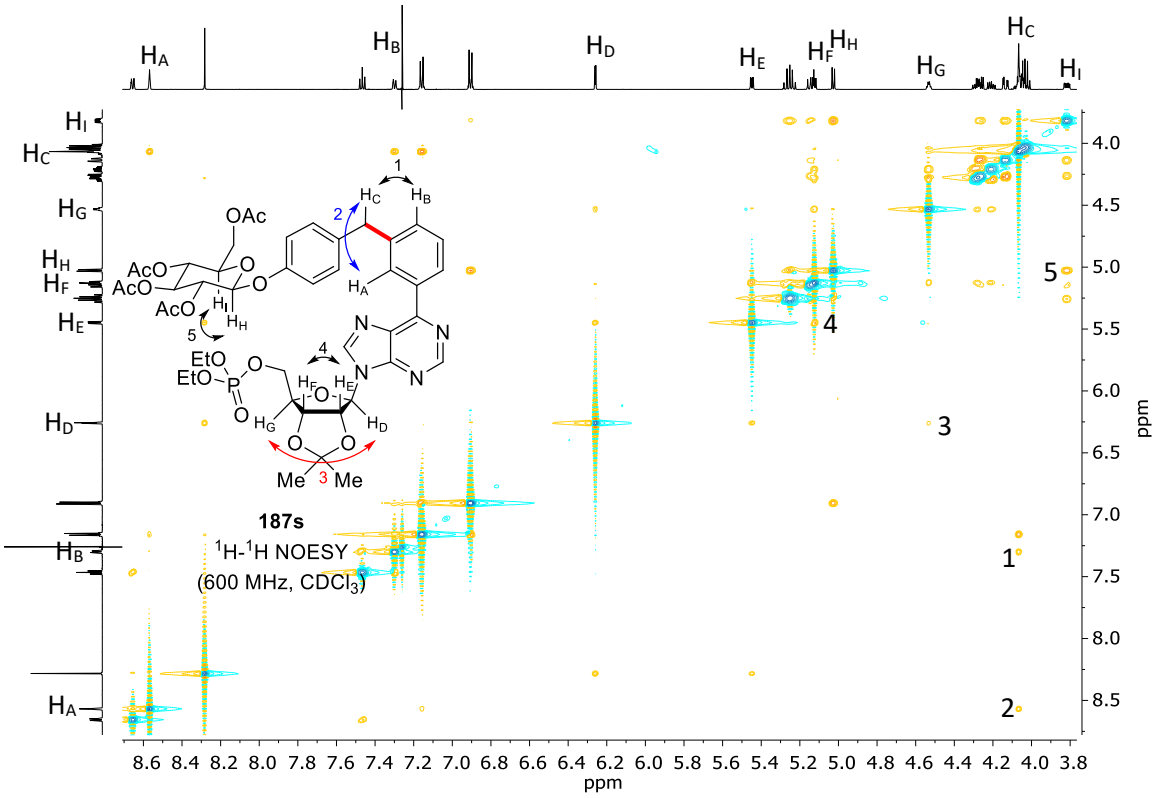
187s
(600 MHz, $CDCl_3$)



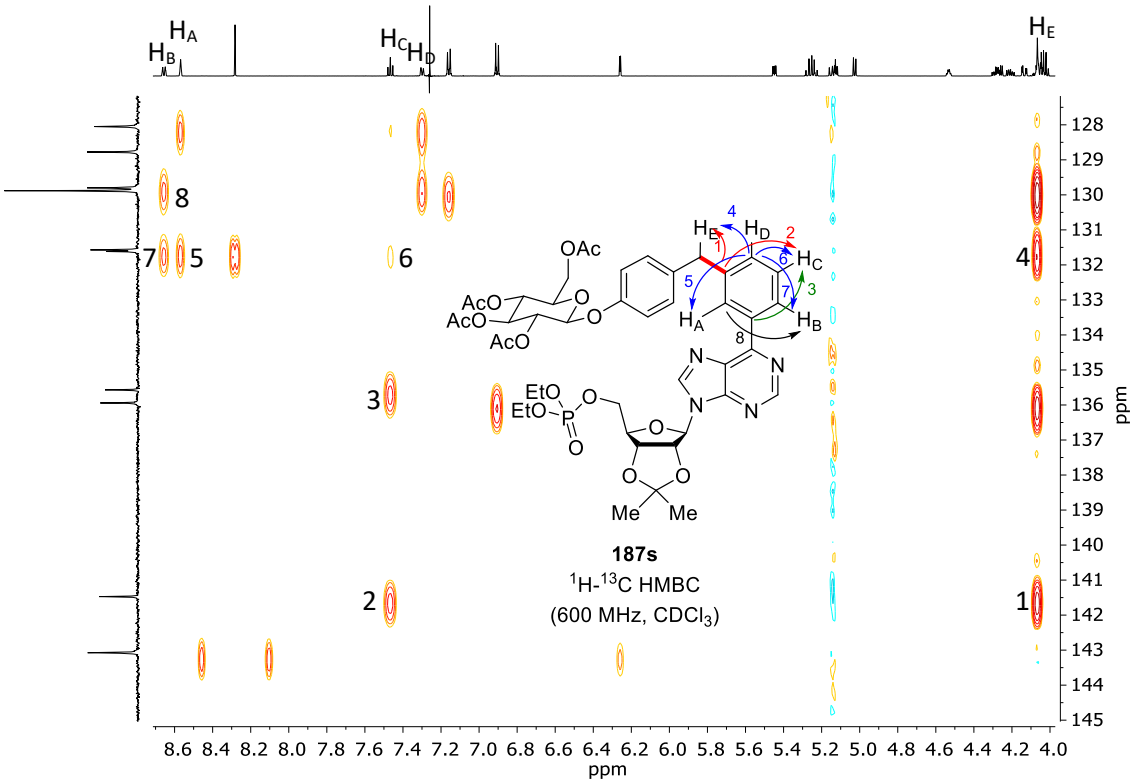
187s
(125 MHz, $CDCl_3$)

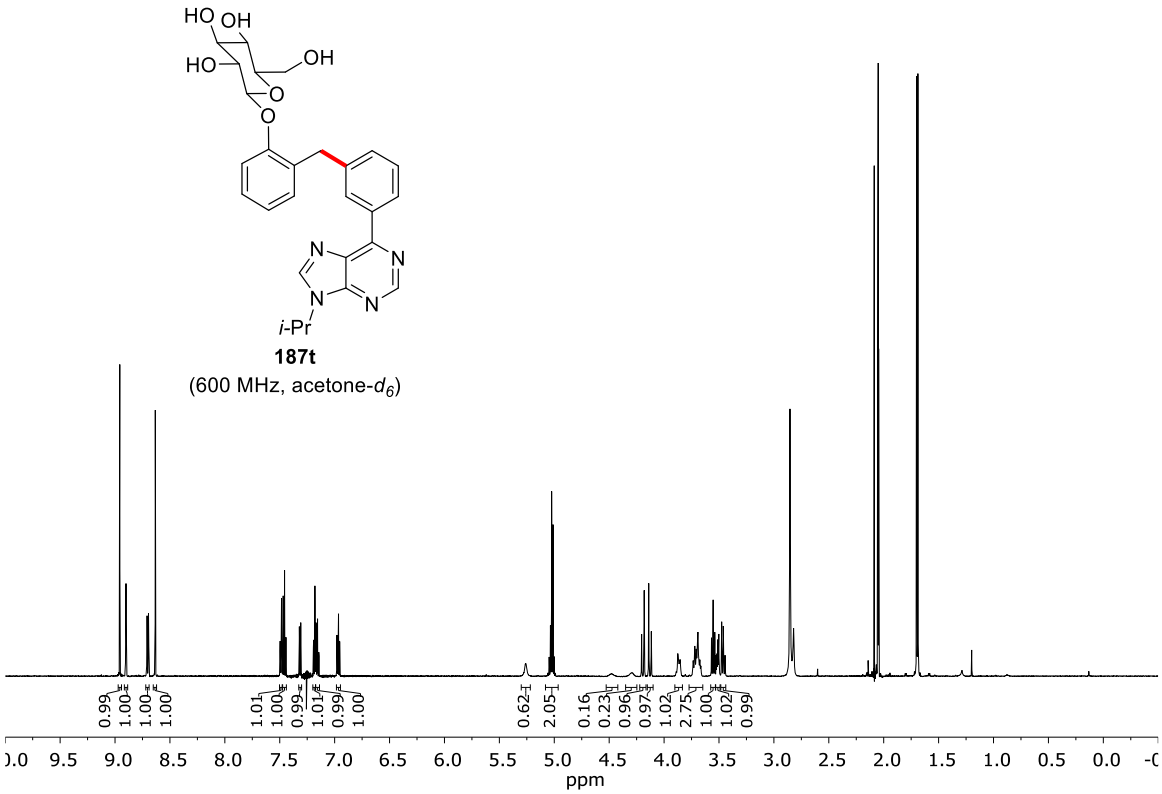


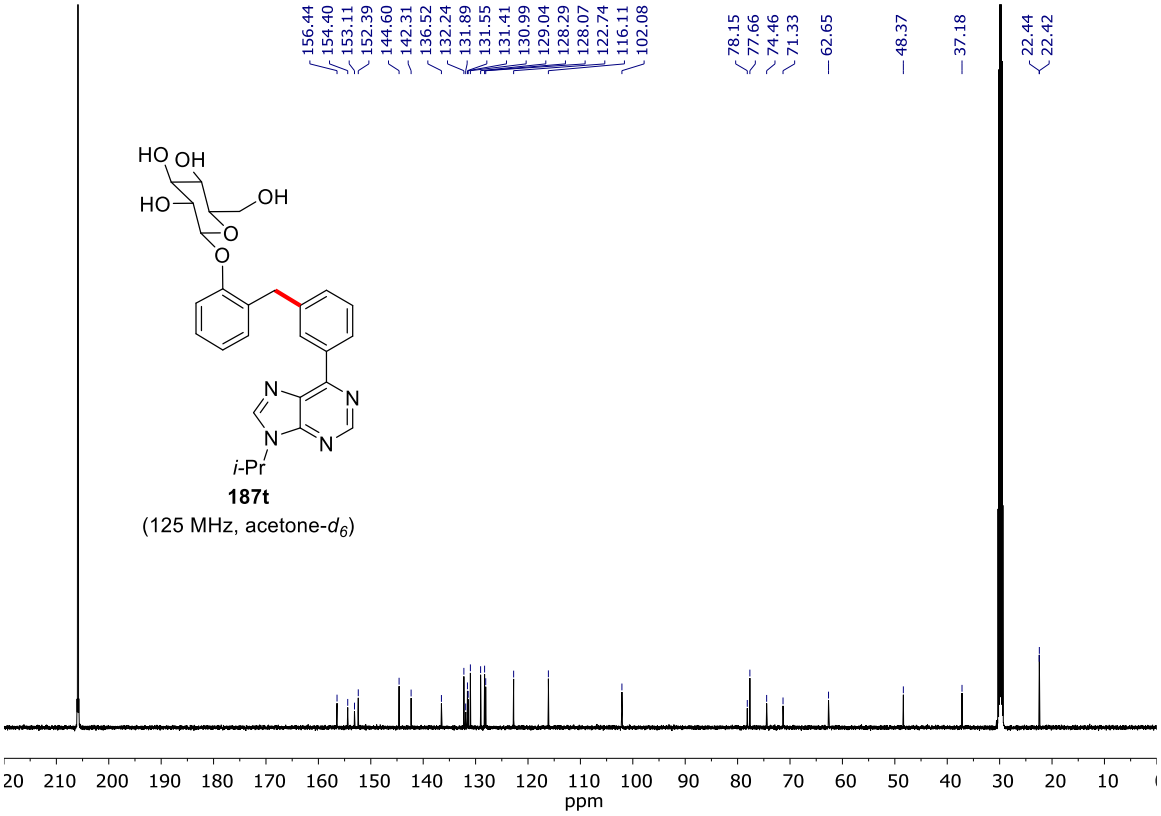
187s
$^{31}P\{^{1}H\}$-NMR
(121 MHz, $CDCl_3$)



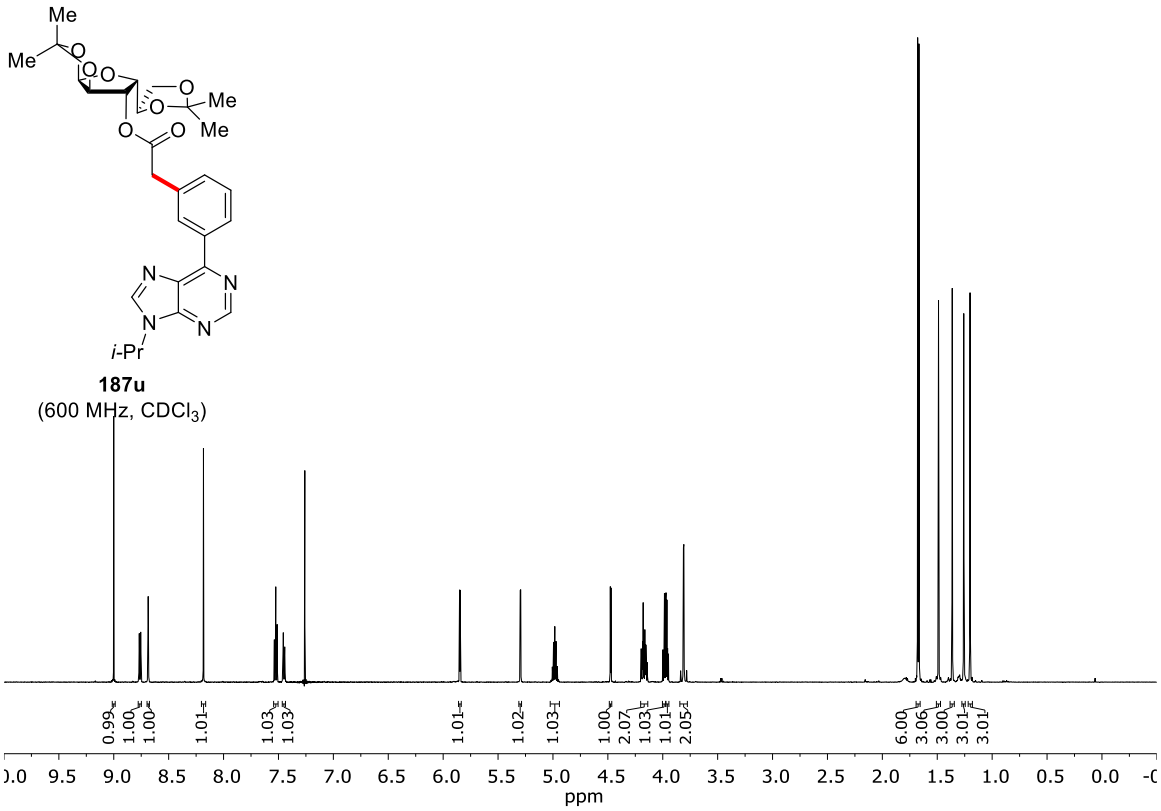
187s
^{1}H-^{1}H NOESY
(600 MHz, $CDCl_3$)


HA
HB
HC
HD
HE
8
7
5
6
4
3
2
1
OAc
AcO
AcO
AcO
EtO
EtO
Me
Me
ppm
187s
1H-13C HMBC
(600 MHz, CDCl3)

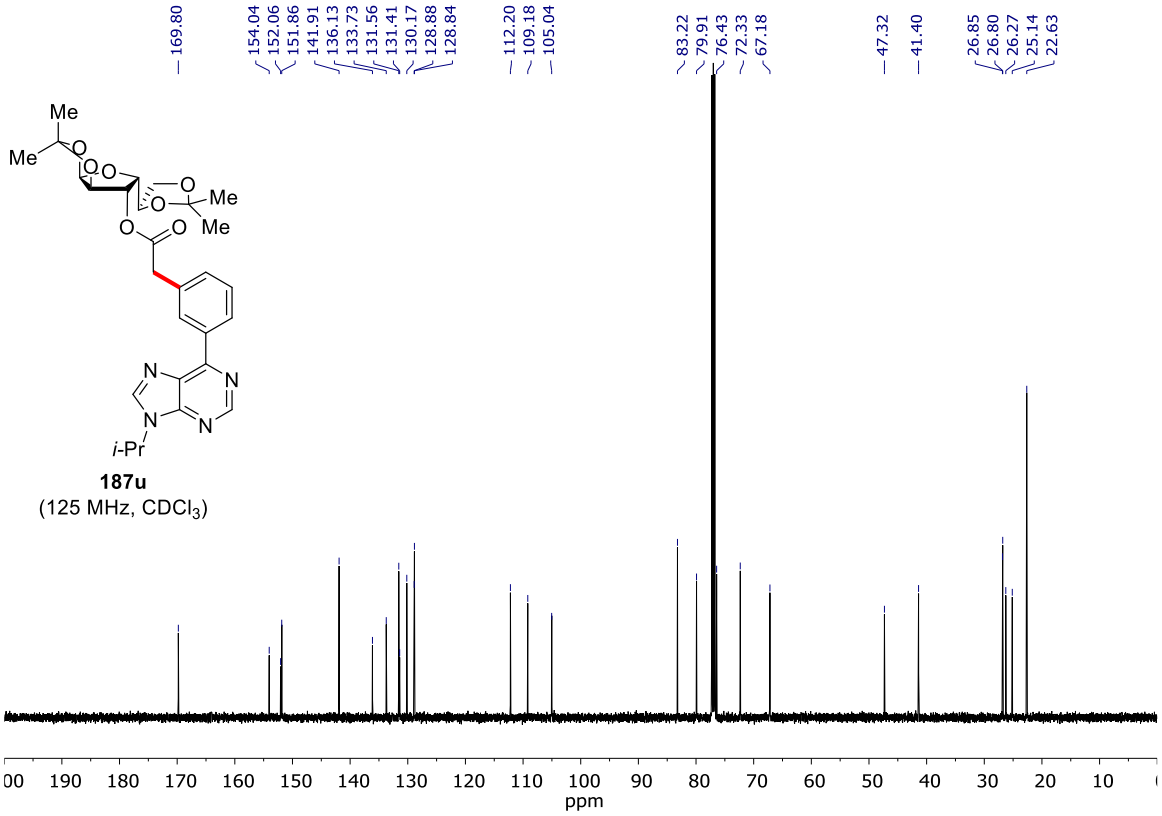

HO
OH
HO
OH
i-Pr
187t
(600 MHz, acetone-d6)
ppm

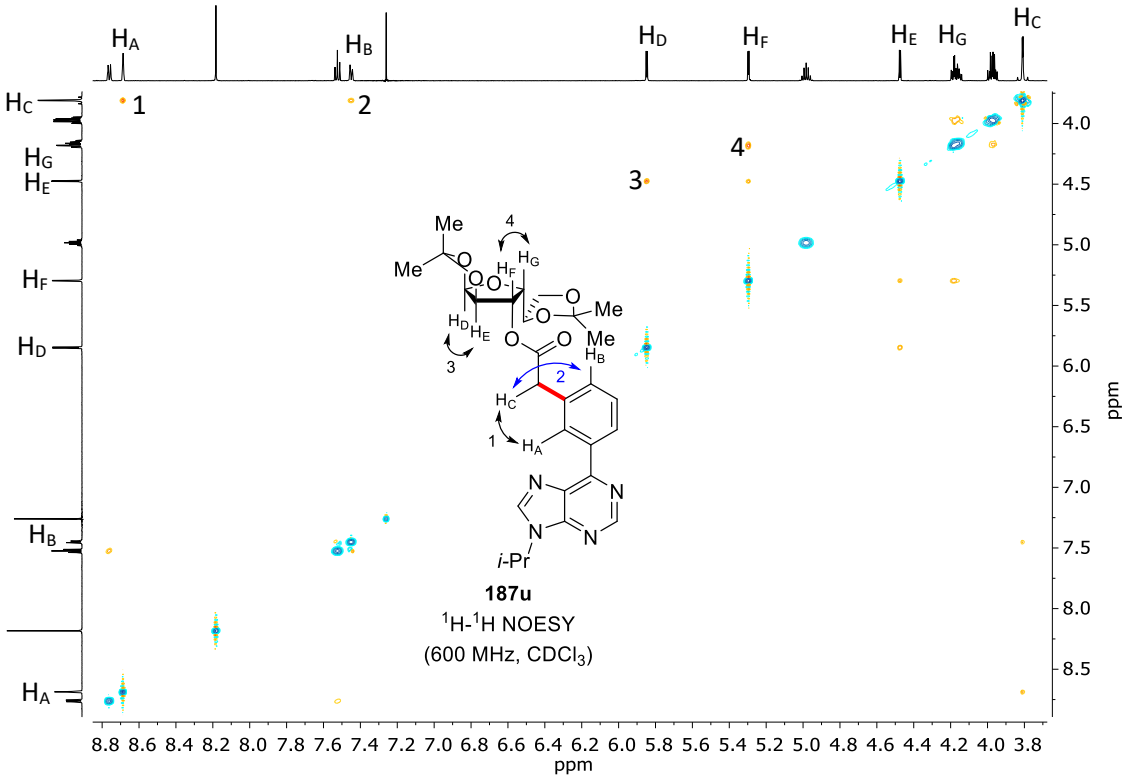


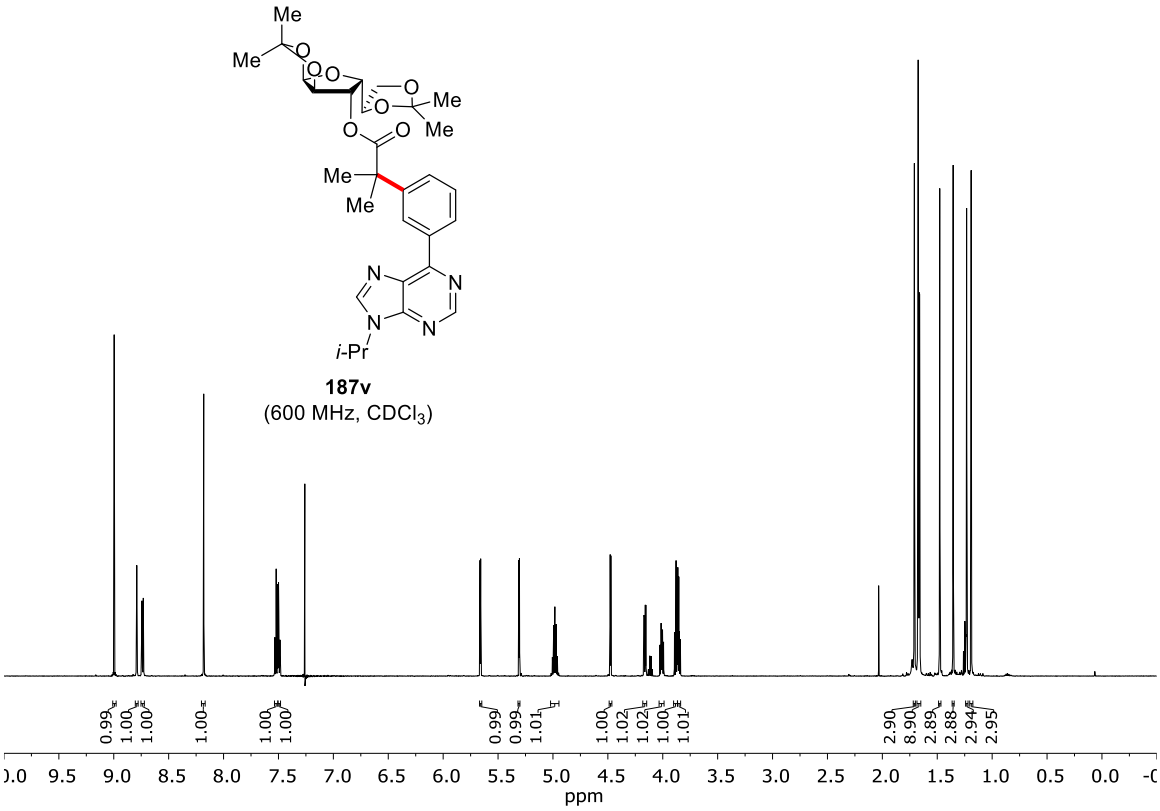
187t
(125 MHz, acetone-d_6)



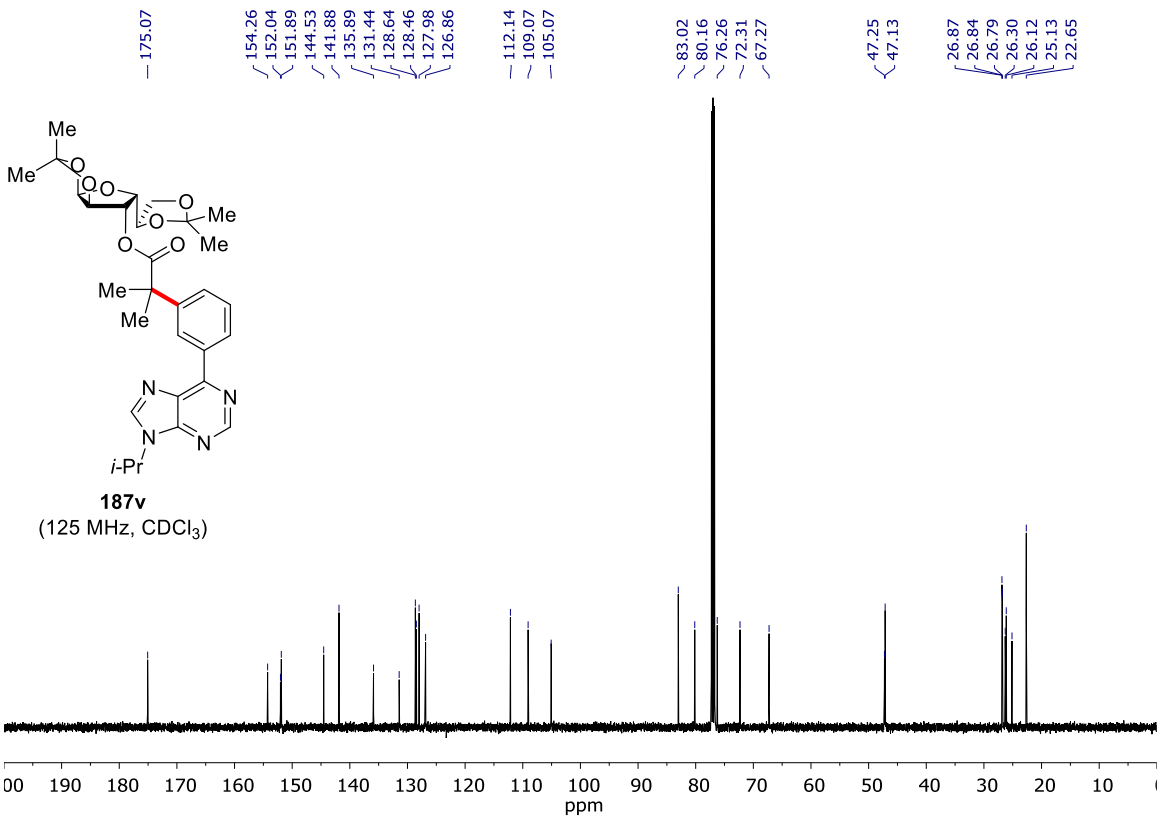
187u
(600 MHz, $CDCl_3$)


169.80
154.04
152.06
151.86
141.91
136.13
133.73
131.56
131.41
130.17
128.88
128.84
112.20
109.18
105.04
83.22
79.91
76.43
72.33
67.18
47.32
41.40
26.85
26.80
26.27
25.14
22.63
Me
Me
O
O
O
O
Me
O
Me
O
O
N
N
N
N
i-Pr
187u
(125 MHz, CDCl3)
ppm

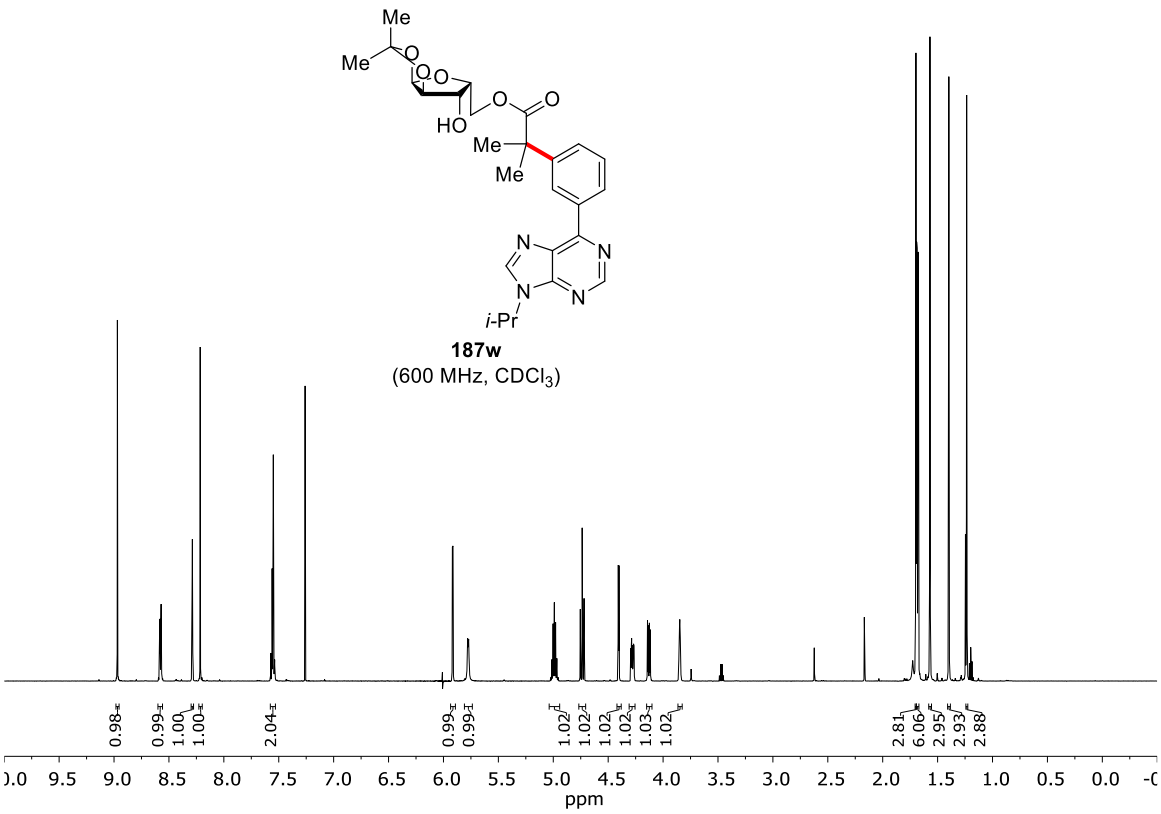

HA
HB
HD
HF
HE
HG
HC
1
2
3
4
HC
HG
HE
HF
HD
HB
HA
ppm
Me
Me
O
O
O
O
Me
O
Me
O
O
HF
HG
HD
HE
4
3
2
1
HC
HA
HB
N
N
N
N
i-Pr
187u
1H-1H NOESY
(600 MHz, CDCl3)
ppm



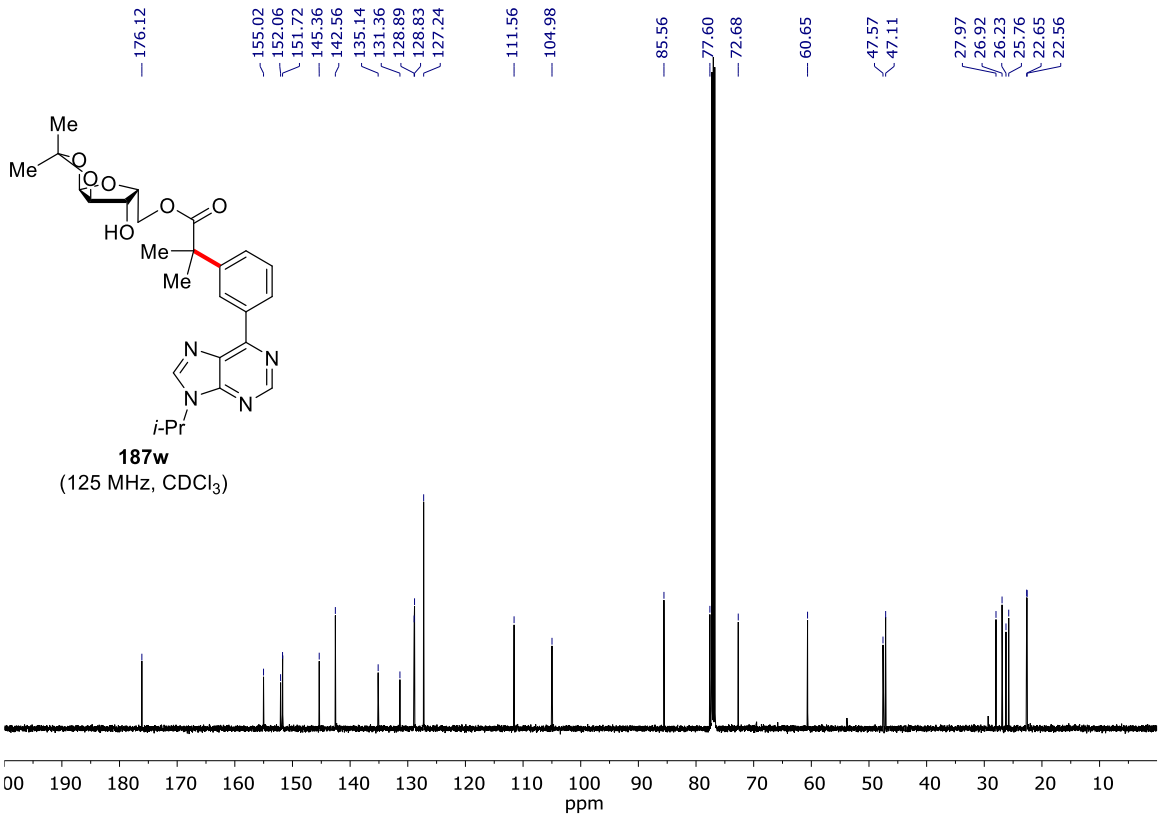
187v
(600 MHz, $CDCl_3$)



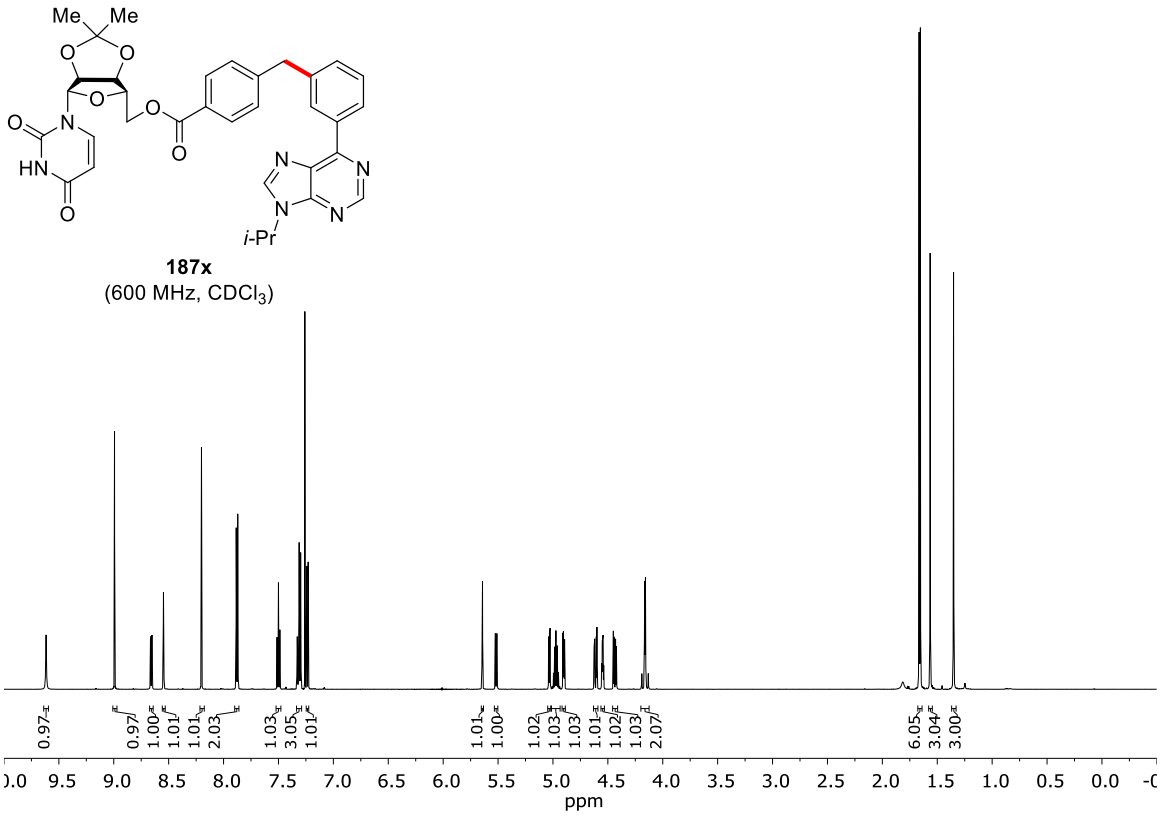
187v
(125 MHz, $CDCl_3$)



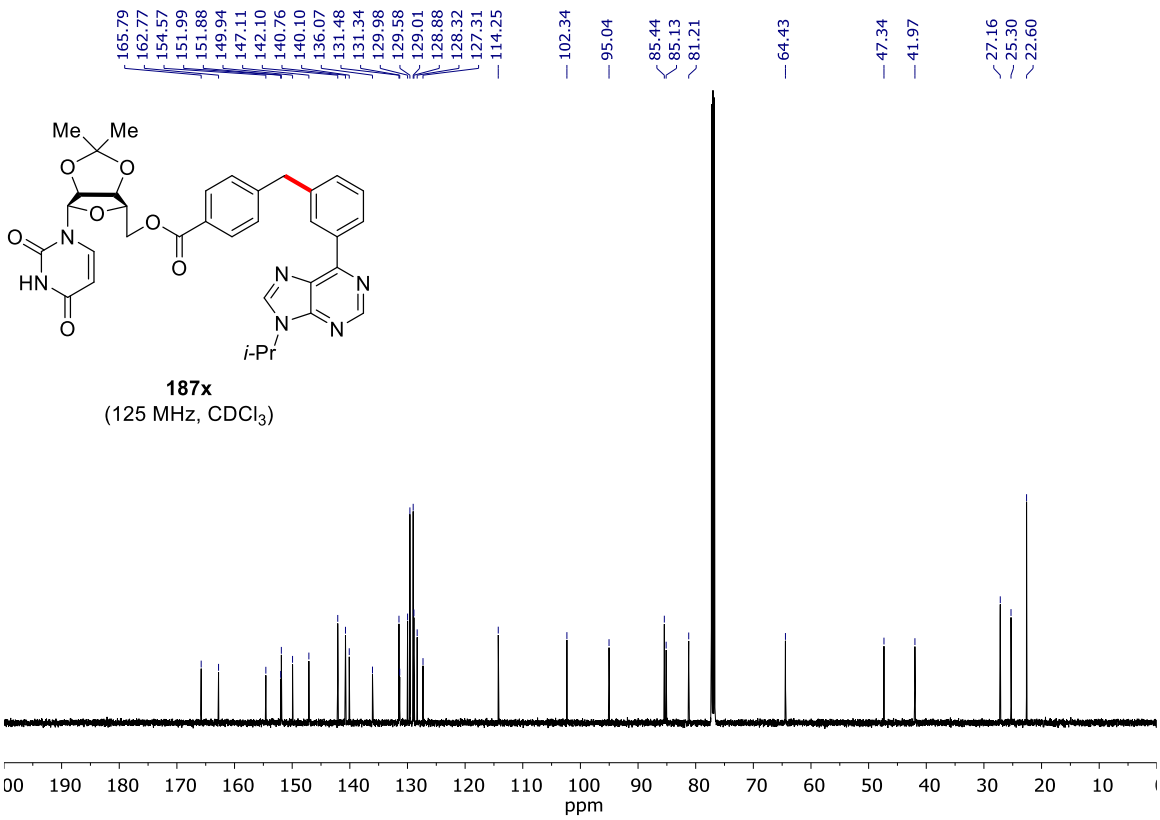
187w
(600 MHz, $CDCl_3$)



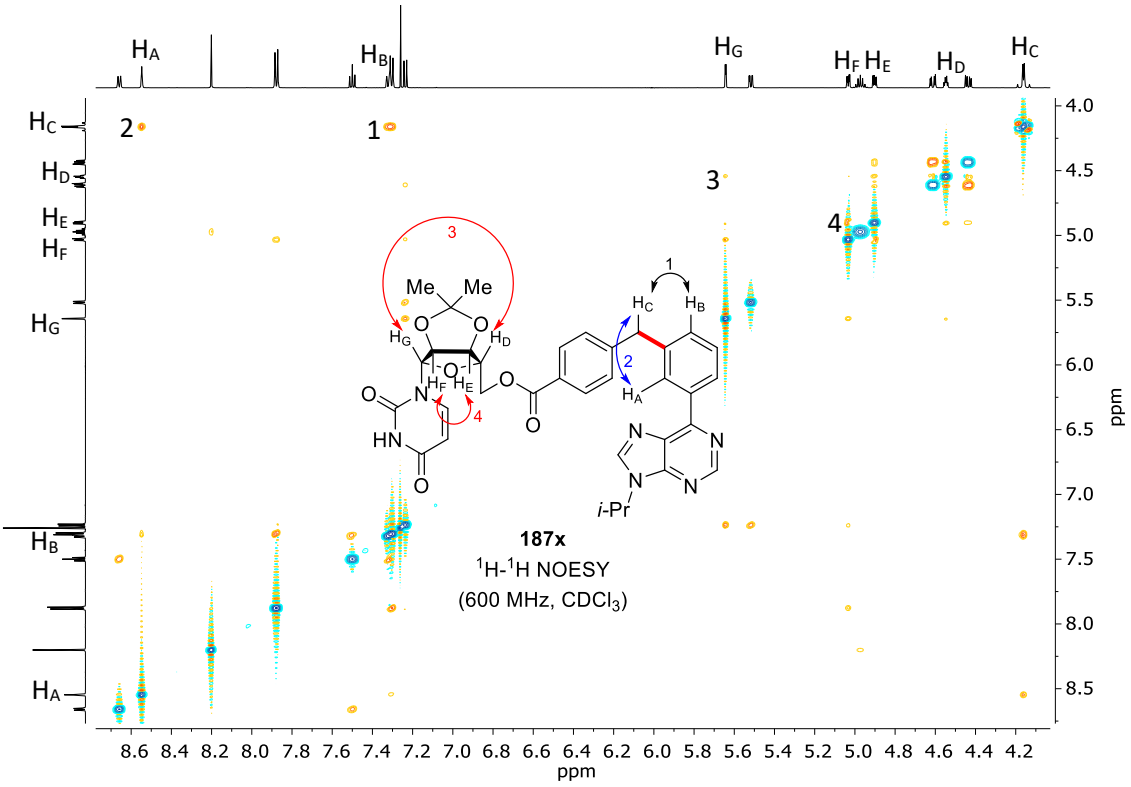
187w
(125 MHz, $CDCl_3$)

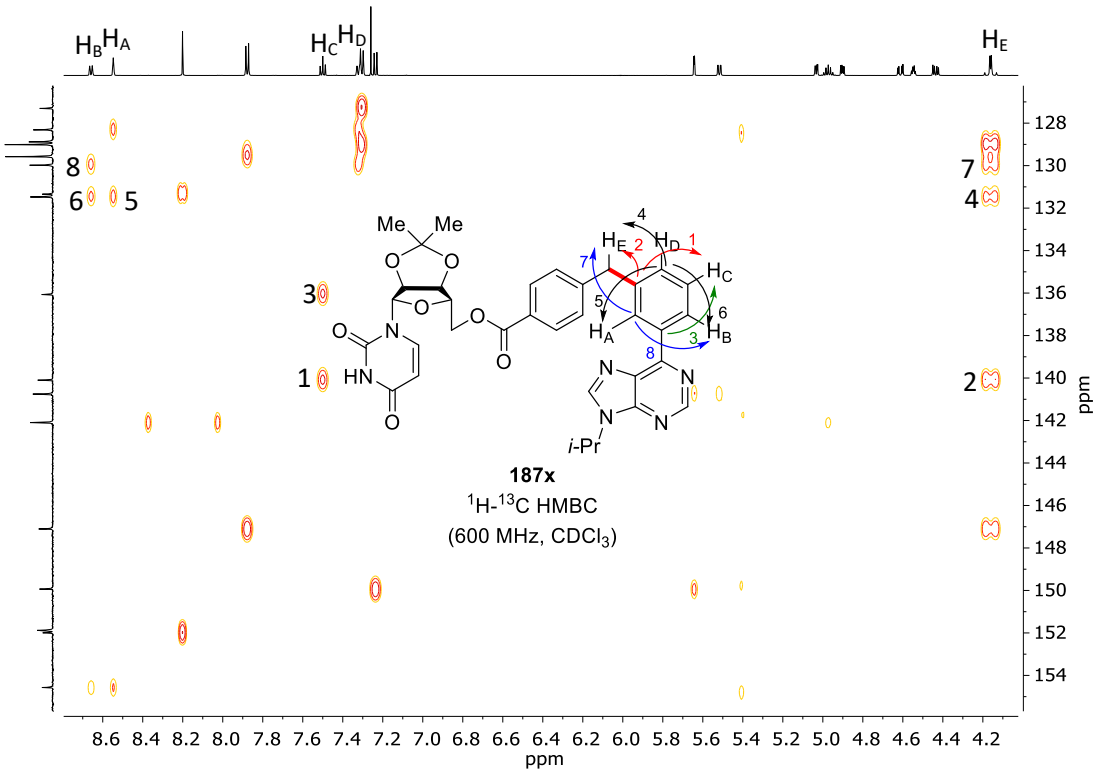


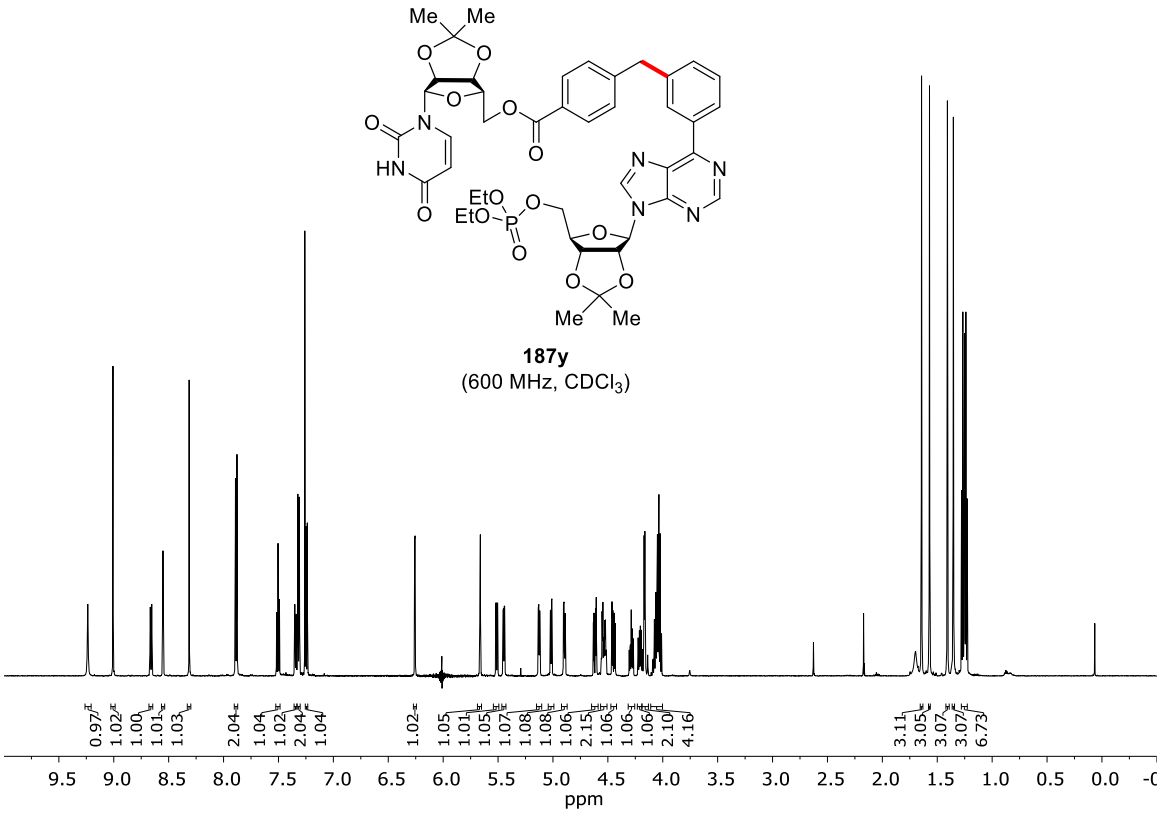
187x
(600 MHz, $CDCl_3$)



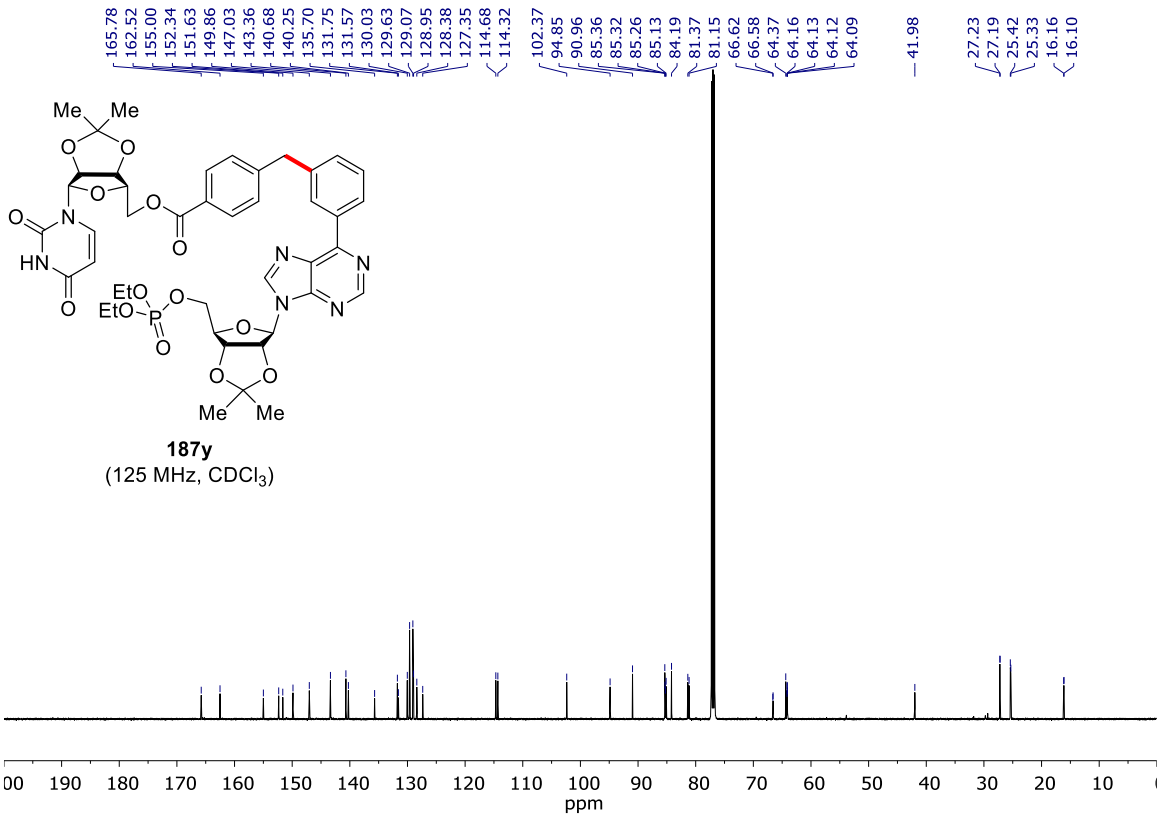
187x
(125 MHz, $CDCl_3$)


HA
HB
HG
HF HE
HD
HC
2
1
3
4
Me
Me
O
HN
N
i-Pr
187x
1H-1H NOESY
(600 MHz, CDCl3)
ppm

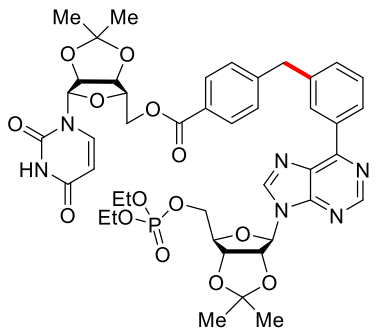

HB HA
HC HD
HE
8
6
5
7
4
3
1
2
Me
Me
O
HN
N
i-Pr
187x
1H-13C HMBC
(600 MHz, CDCl3)
ppm



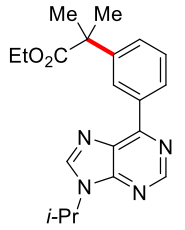
187y
(600 MHz, $CDCl_3$)



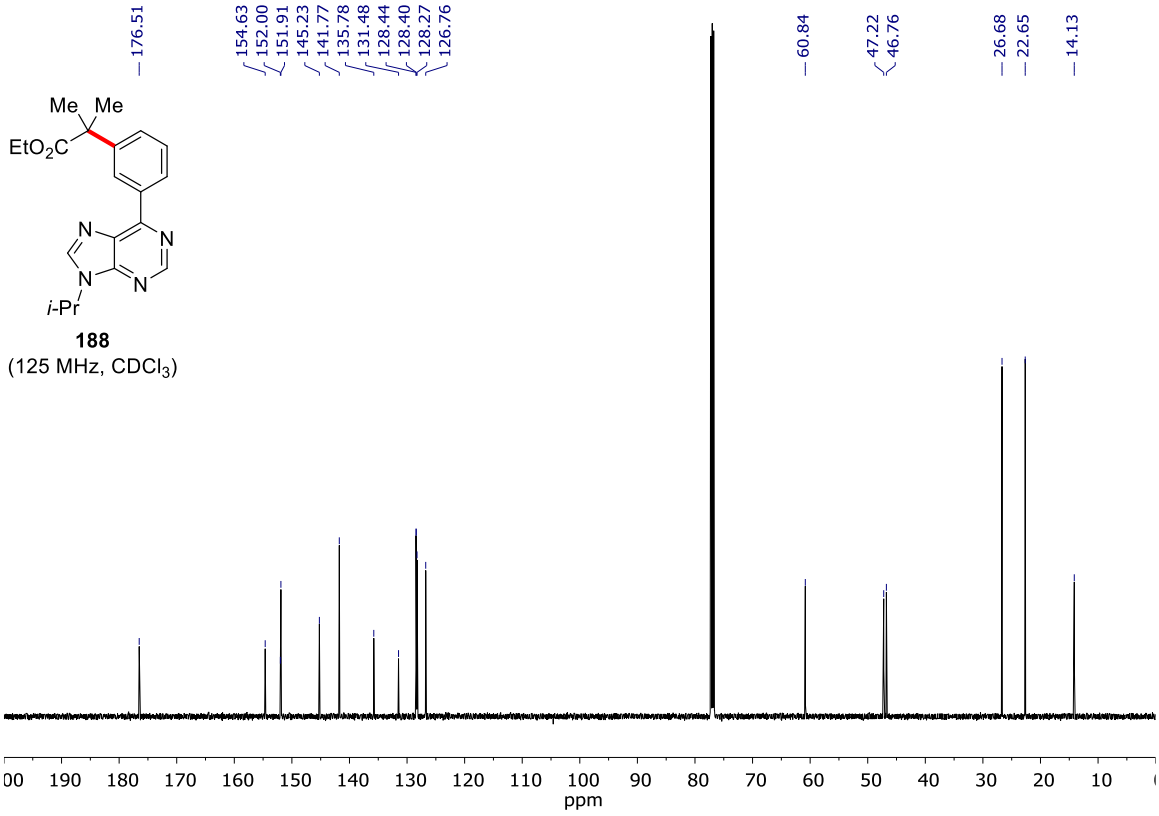
187y
(125 MHz, $CDCl_3$)



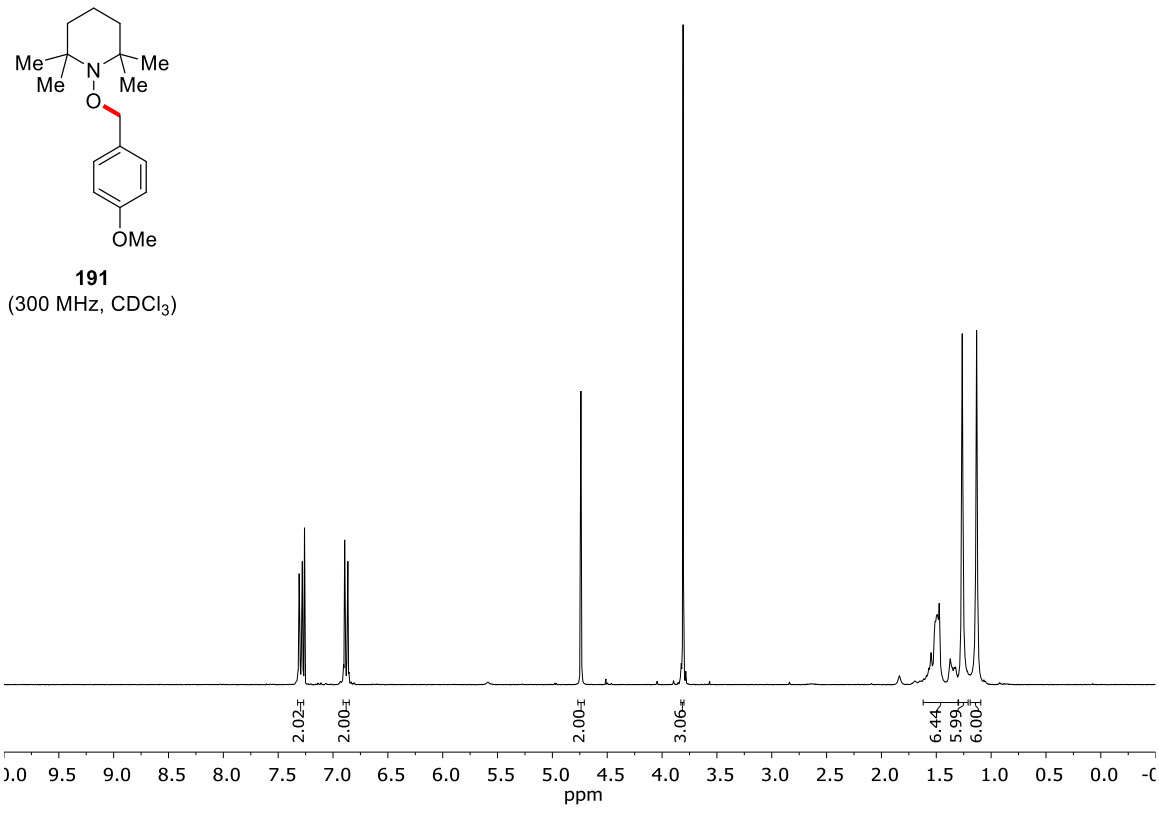
187y
$^{31}P\{^{1}H\}$-NMR
(121 MHz, $CDCl_3$)



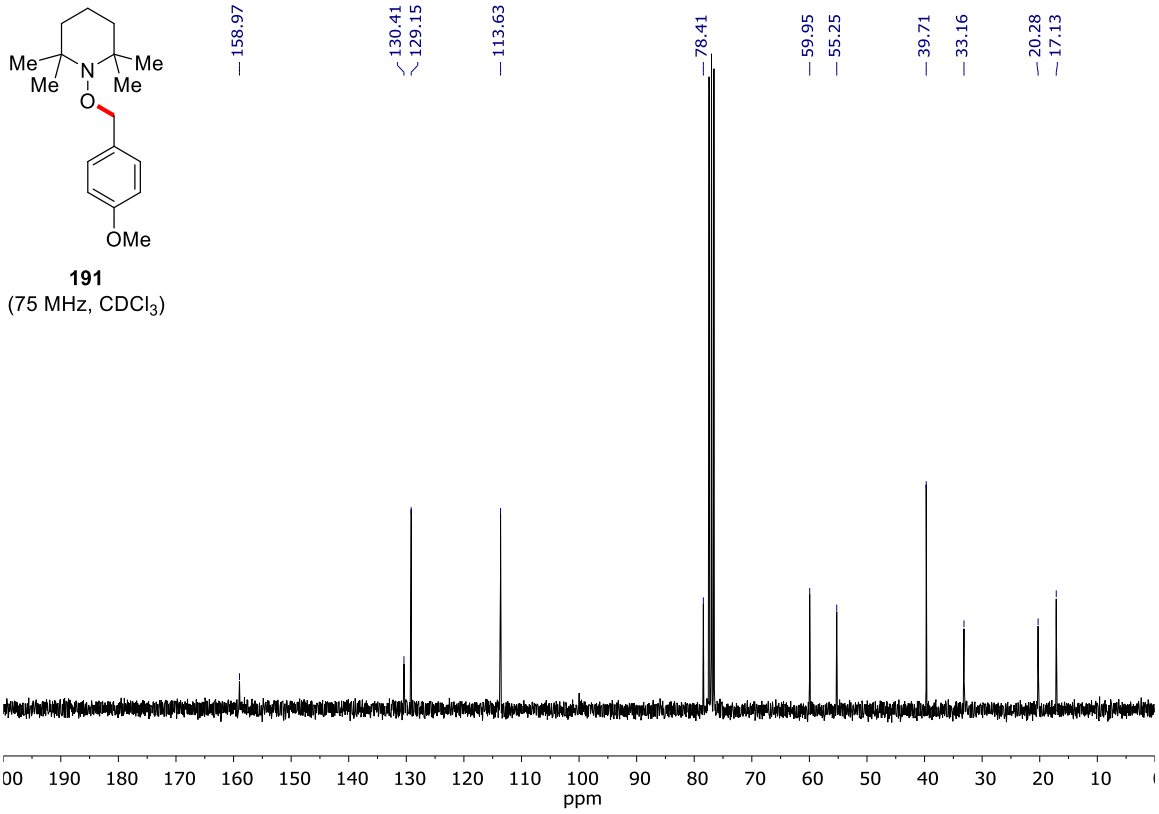
188
(600 MHz, $CDCl_3$)



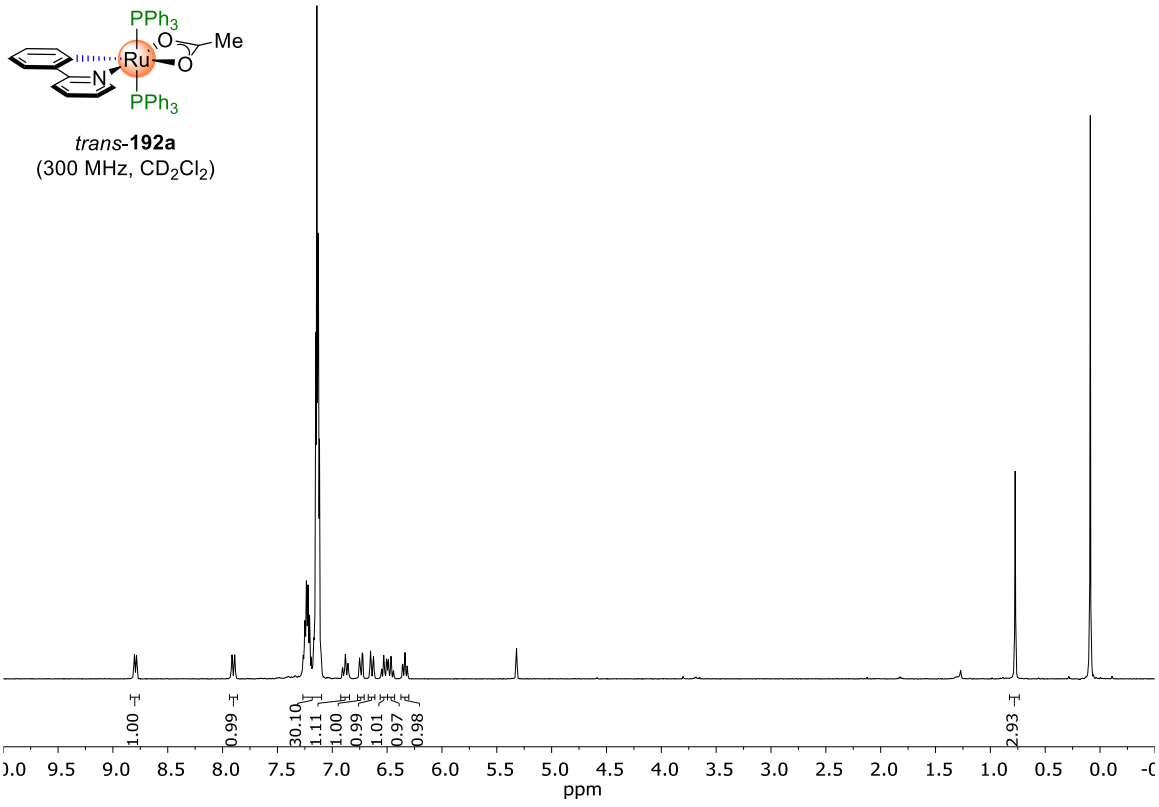
188
(125 MHz, $CDCl_3$)



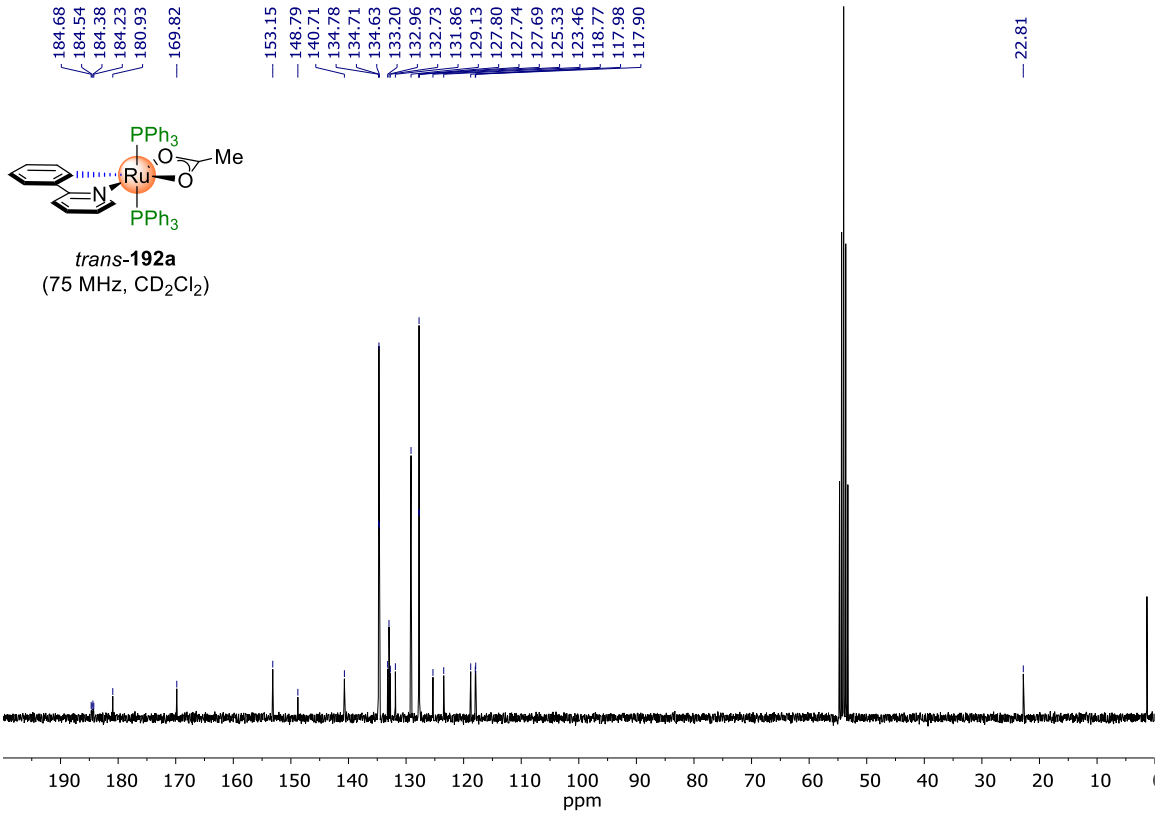
191
(300 MHz, $CDCl_3$)



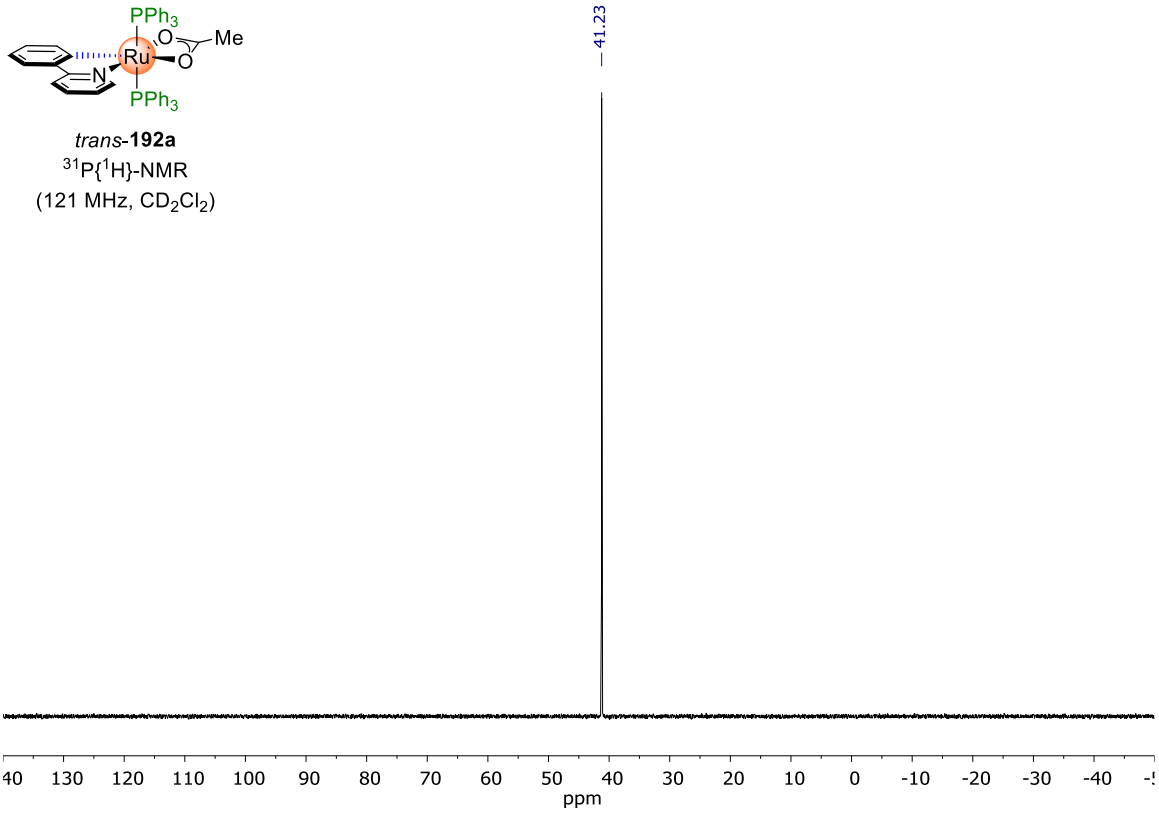
191
(75 MHz, $CDCl_3$)



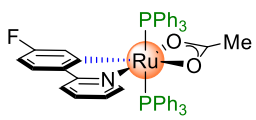
trans-**192a**
(300 MHz, CD_2Cl_2)



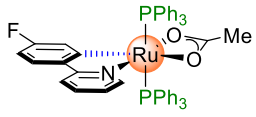
trans-**192a**
(75 MHz, CD_2Cl_2)



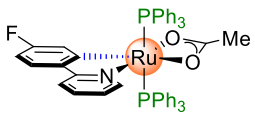
trans-**192a**
$^{31}P\{^1H\}$-NMR
(121 MHz, CD_2Cl_2)



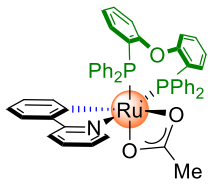
192b
(300 MHz, CD_2Cl_2)



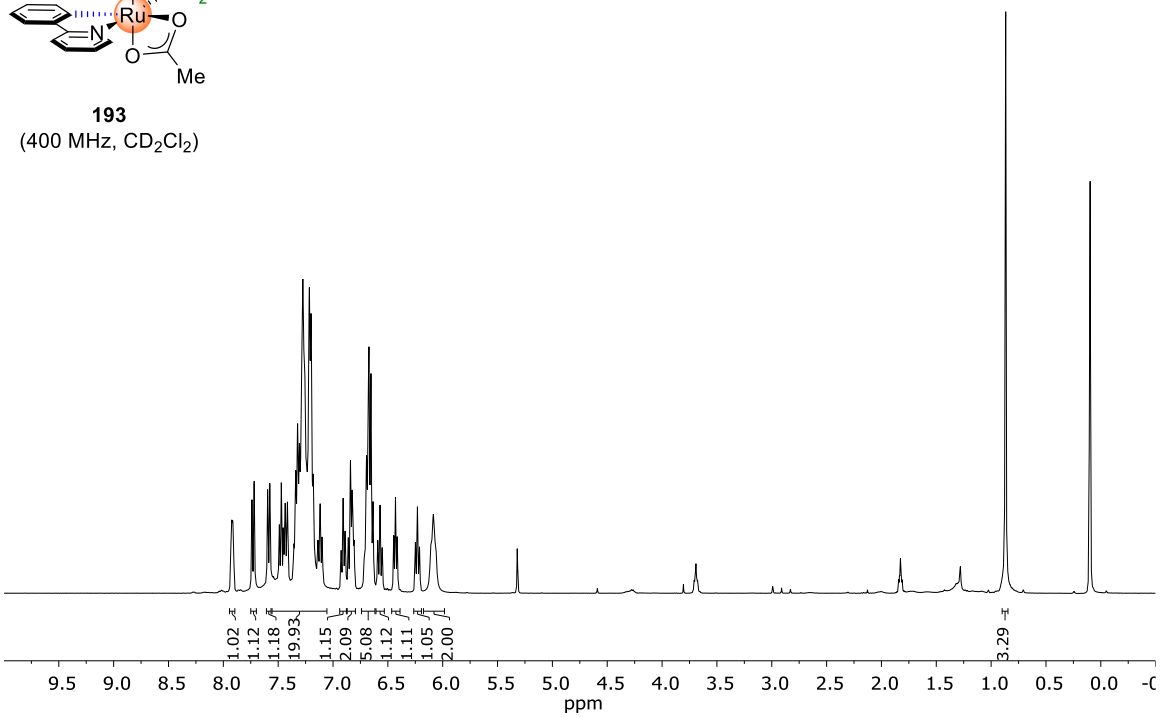
192b
$^{19}F\{^1H\}$-NMR
(282 MHz, CD_2Cl_2)

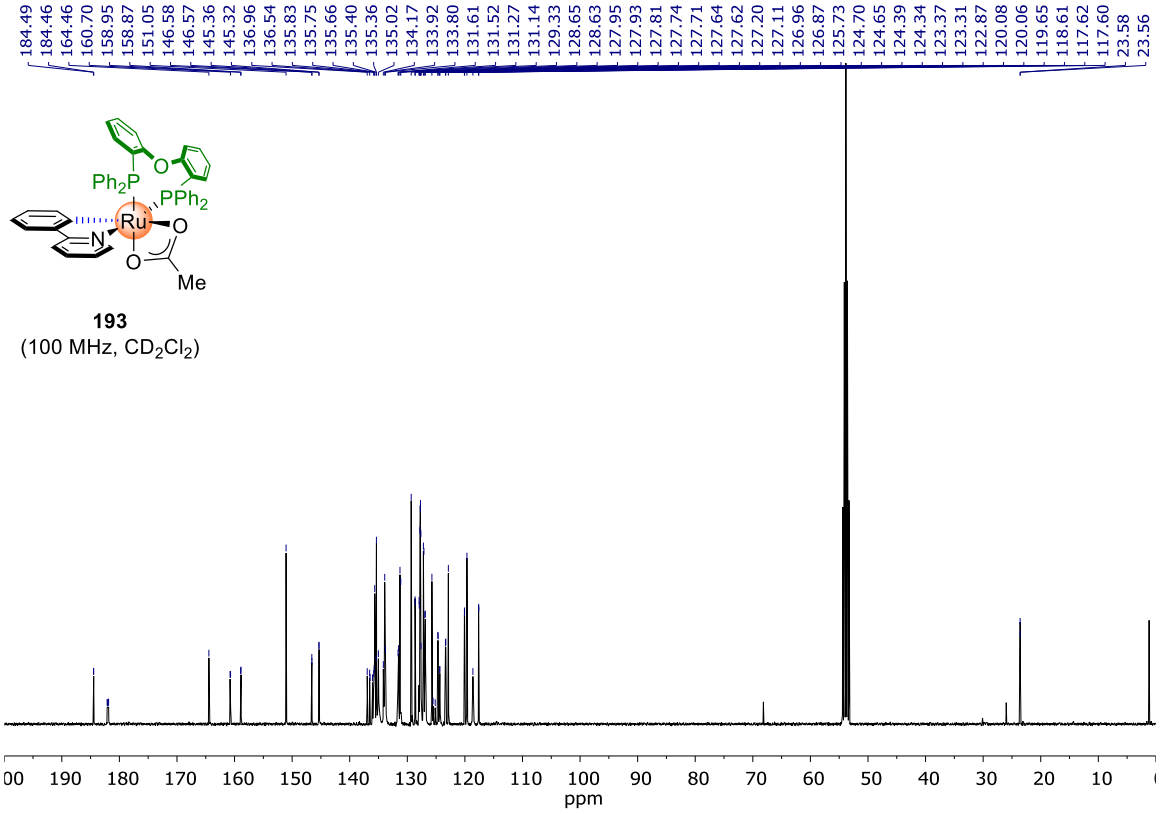


192b
$^{31}P\{^{1}H\}$-NMR
(121 MHz, CD_2Cl_2)

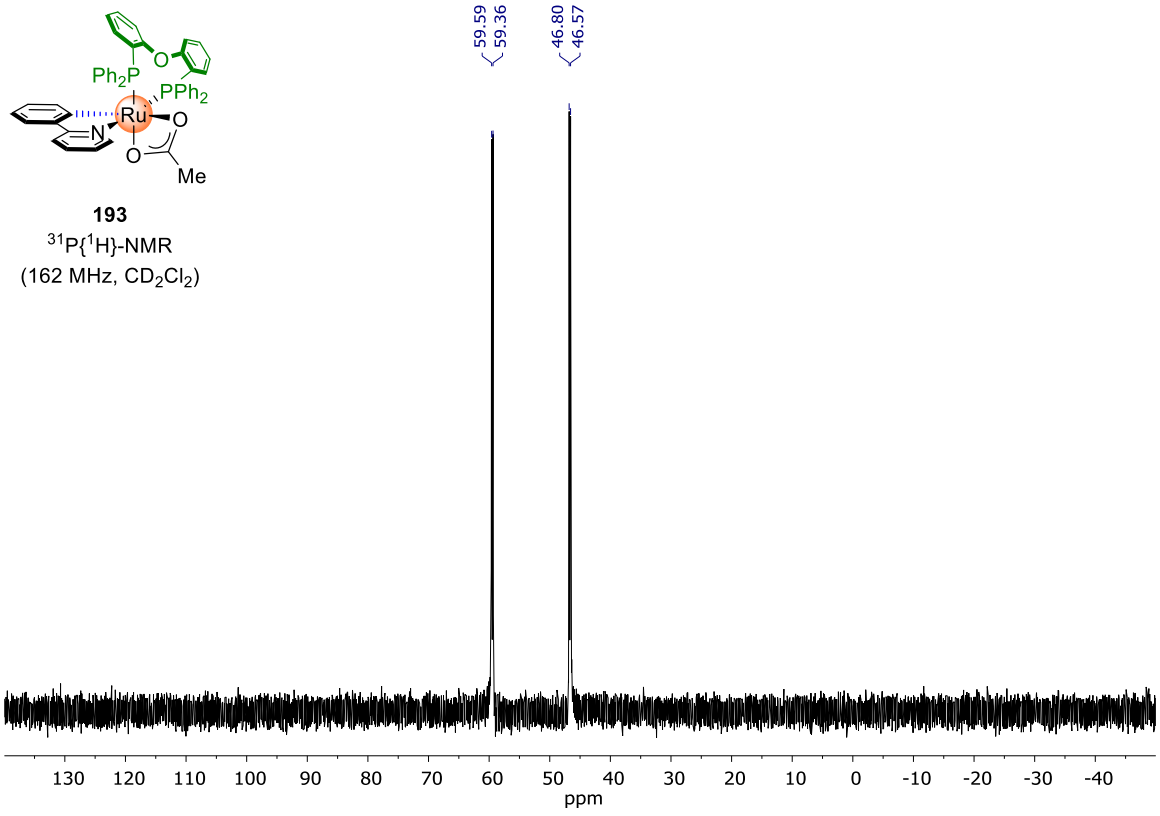


193
(400 MHz, CD_2Cl_2)

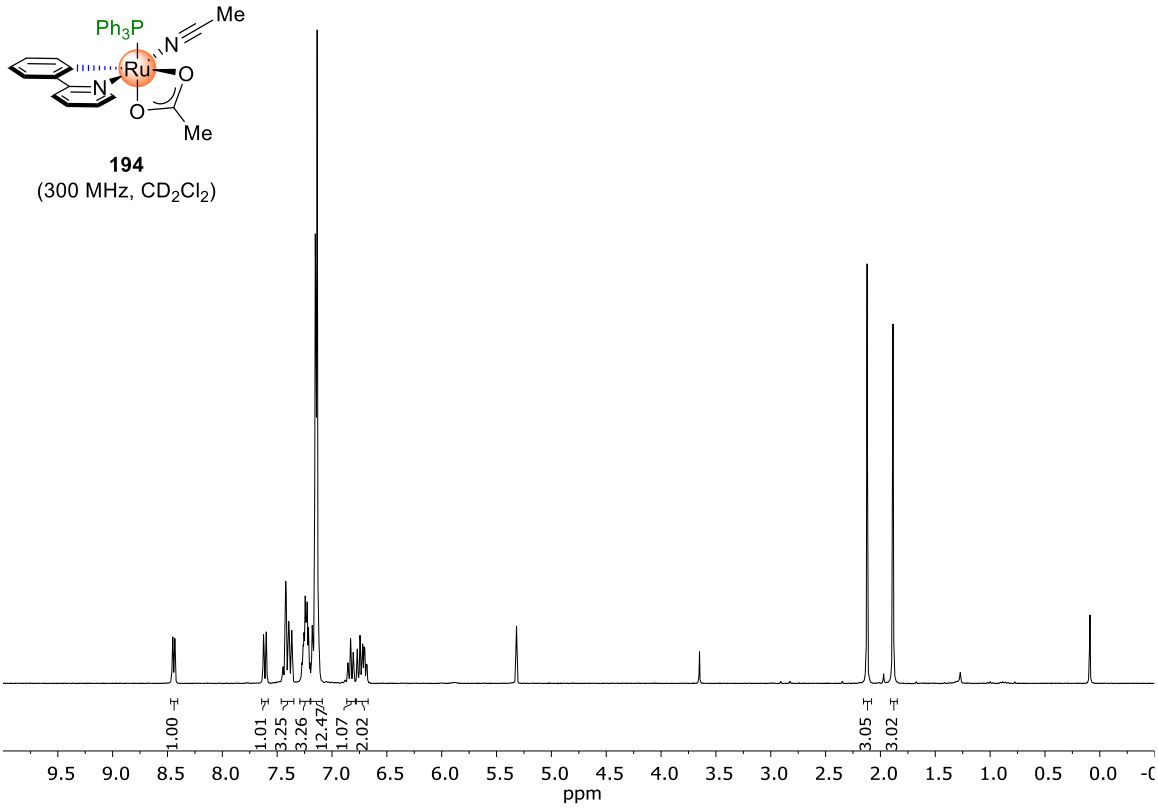


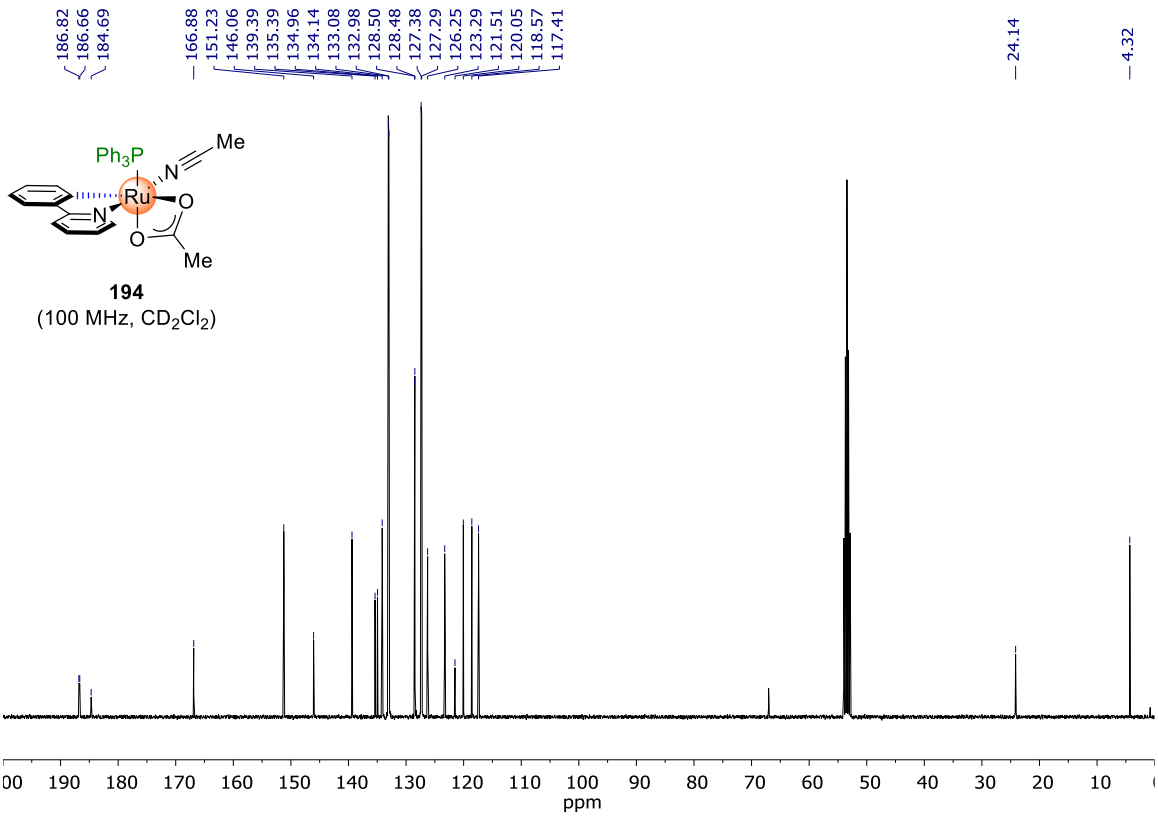


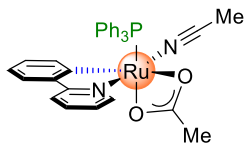
193
(100 MHz, CD_2Cl_2)



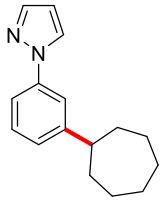
193
$^{31}P\{^1H\}$-NMR
(162 MHz, CD_2Cl_2)


Ph3P
Me
N
Ru
O
N
O
Me
194
(300 MHz, CD2Cl2)
1.00
1.01
3.25
3.26
12.47
1.07
2.02
3.05
3.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

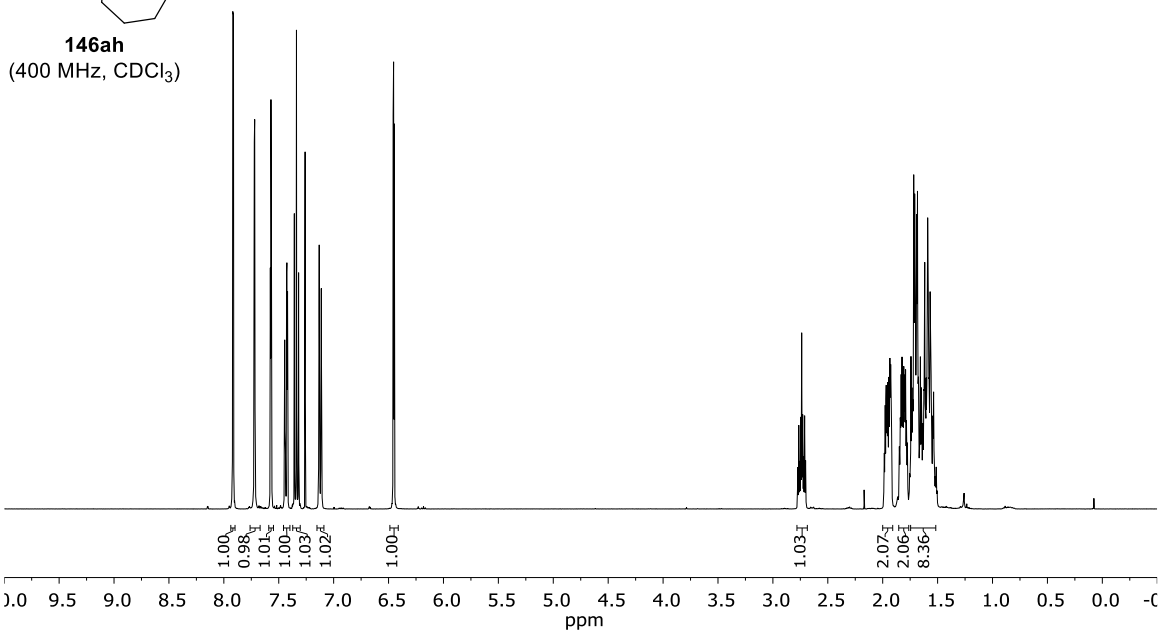

186.82
186.66
184.69
166.88
151.23
146.06
139.39
135.39
134.96
134.14
133.08
132.98
128.50
128.48
127.38
127.29
126.25
123.29
121.51
120.05
118.57
117.41
24.14
4.32
Ph3P
Me
N
Ru
O
N
O
Me
194
(100 MHz, CD2Cl2)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm

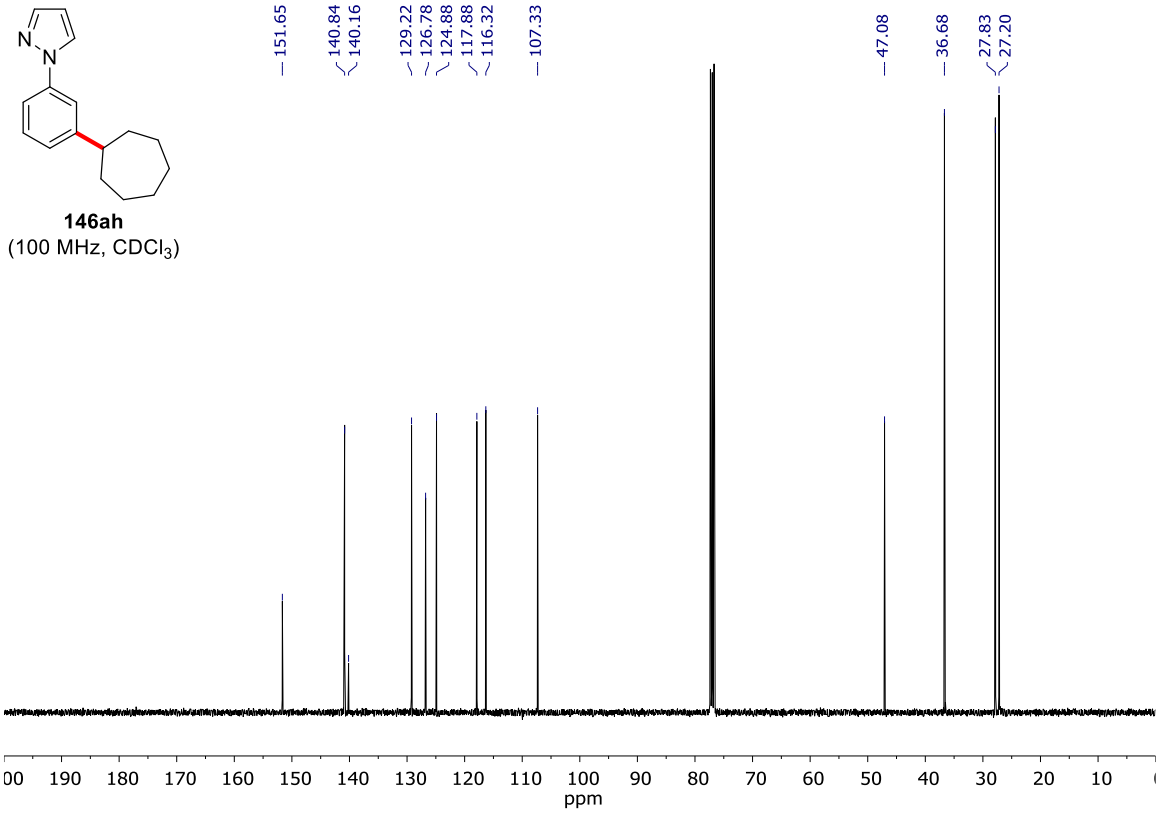


194
$^{31}P\{^{1}H\}$-NMR
(162 MHz, CD_2Cl_2)

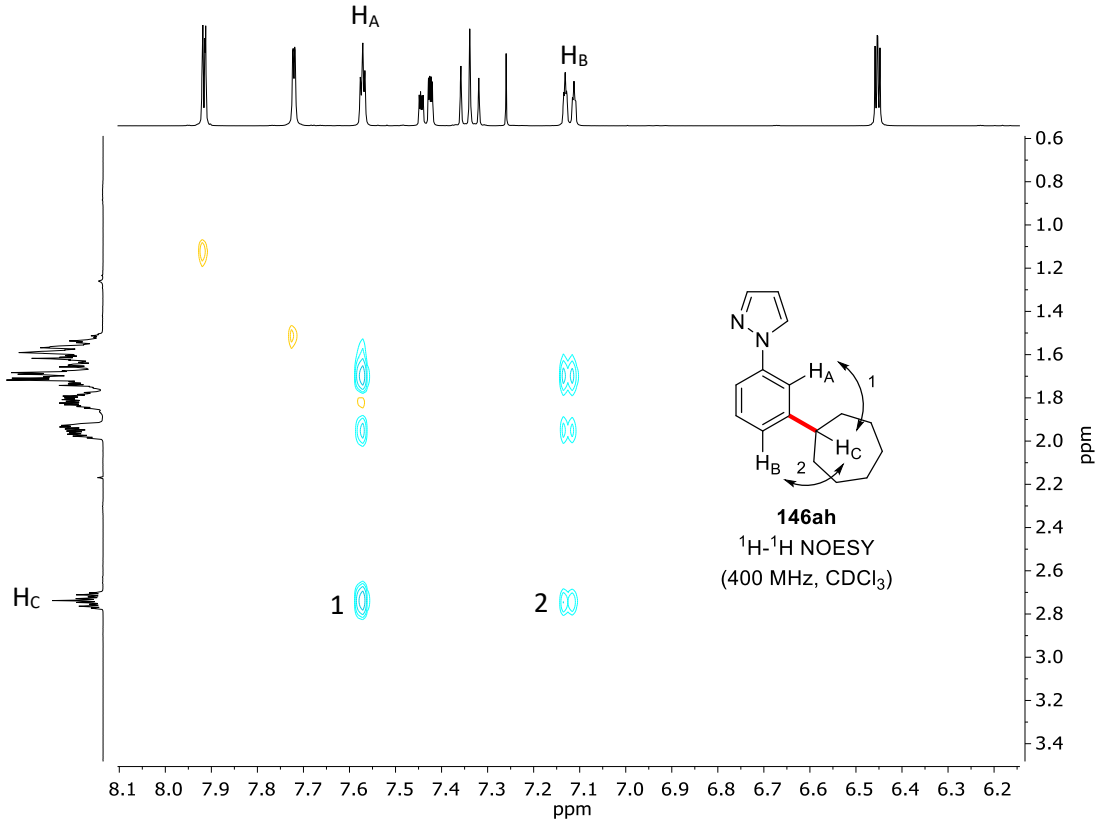


146ah
(400 MHz, $CDCl_3$)

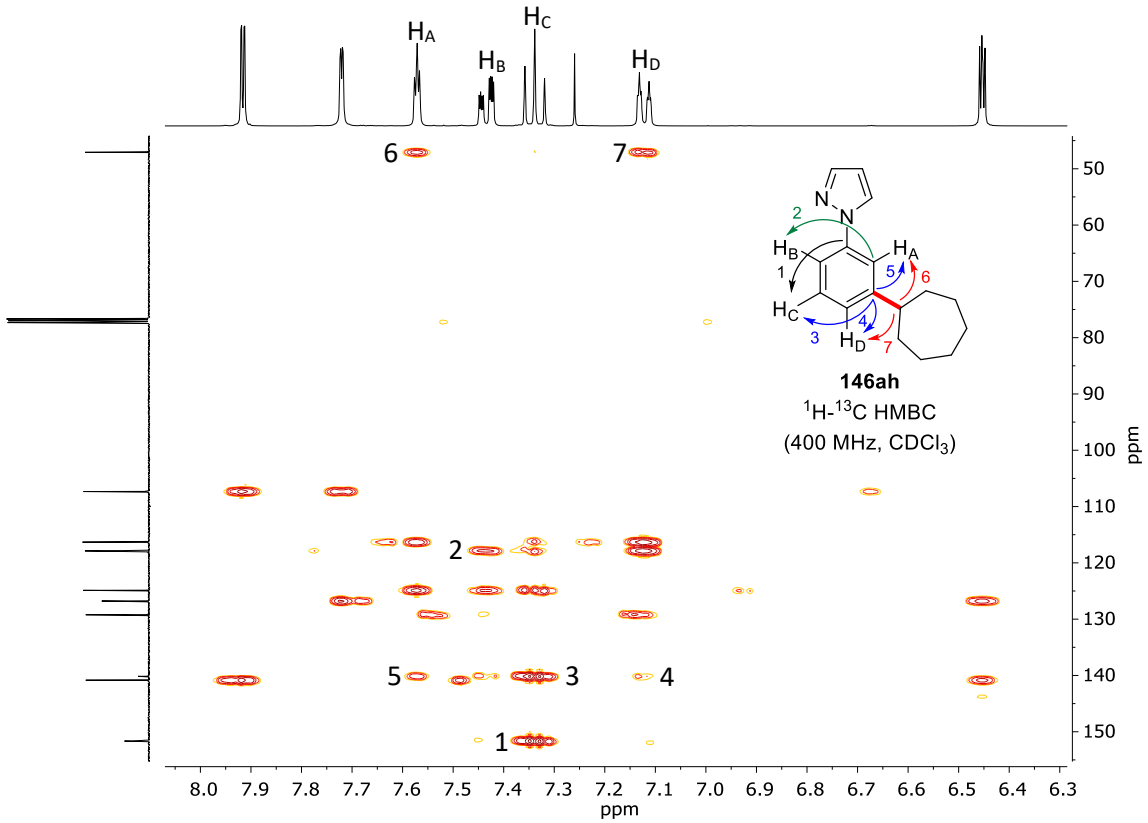


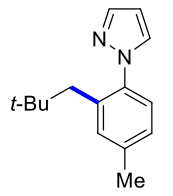


146ah
(100 MHz, $CDCl_3$)

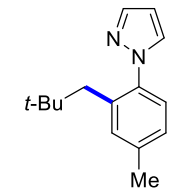


146ah
^1H-^1H NOESY
(400 MHz, $CDCl_3$)

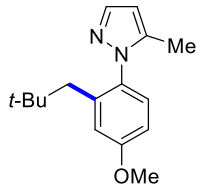




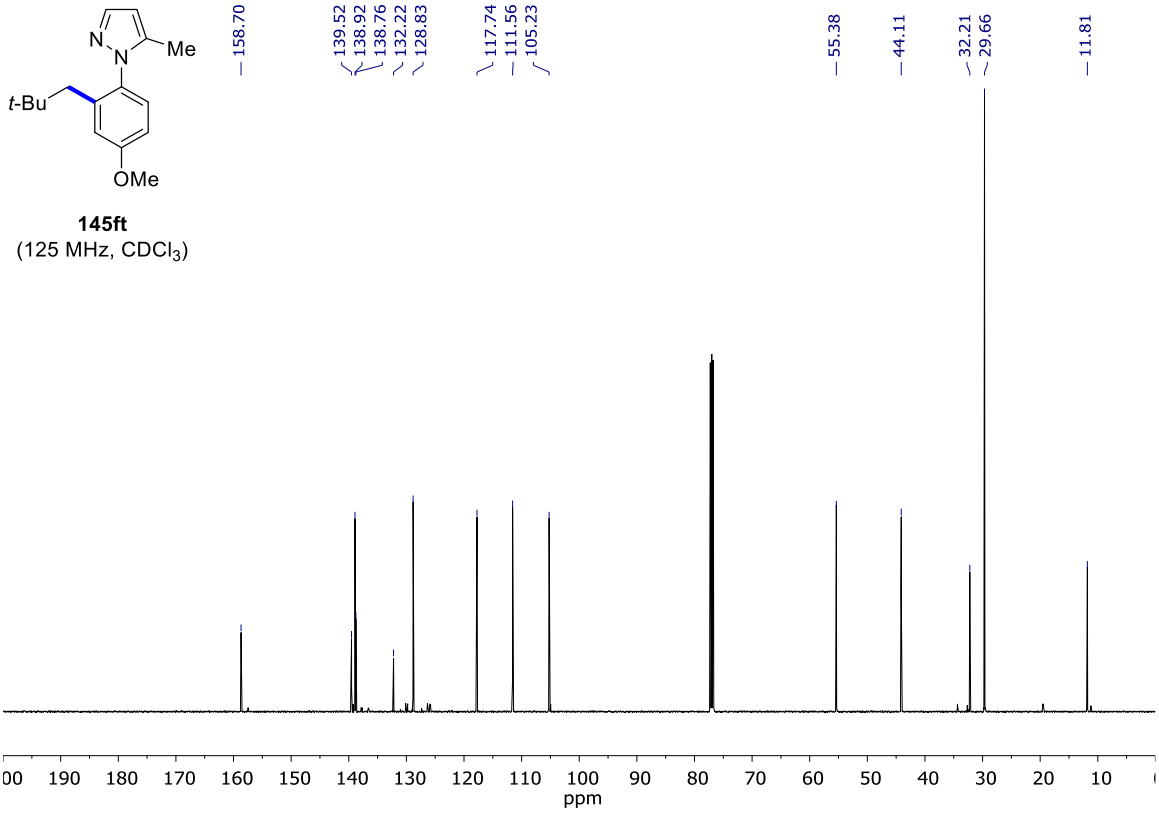
145et
(300 MHz, $CDCl_3$)



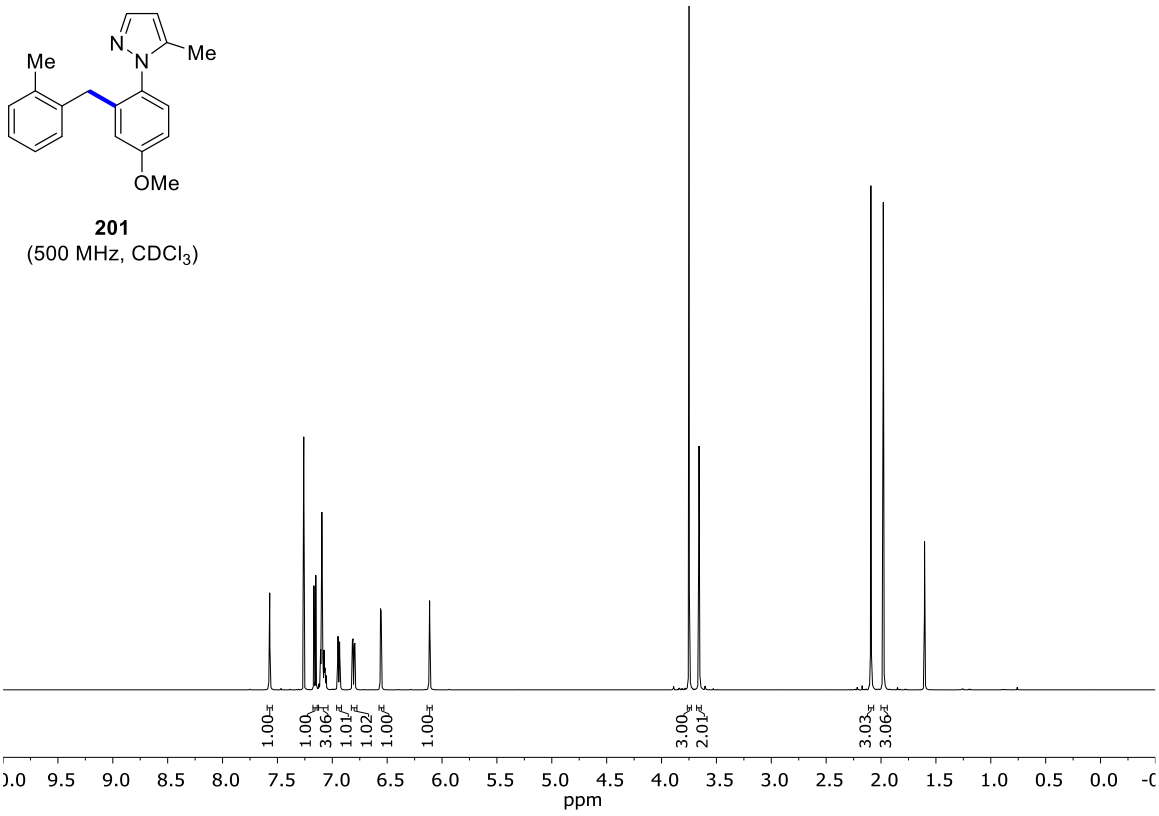
145et
(125 MHz, $CDCl_3$)



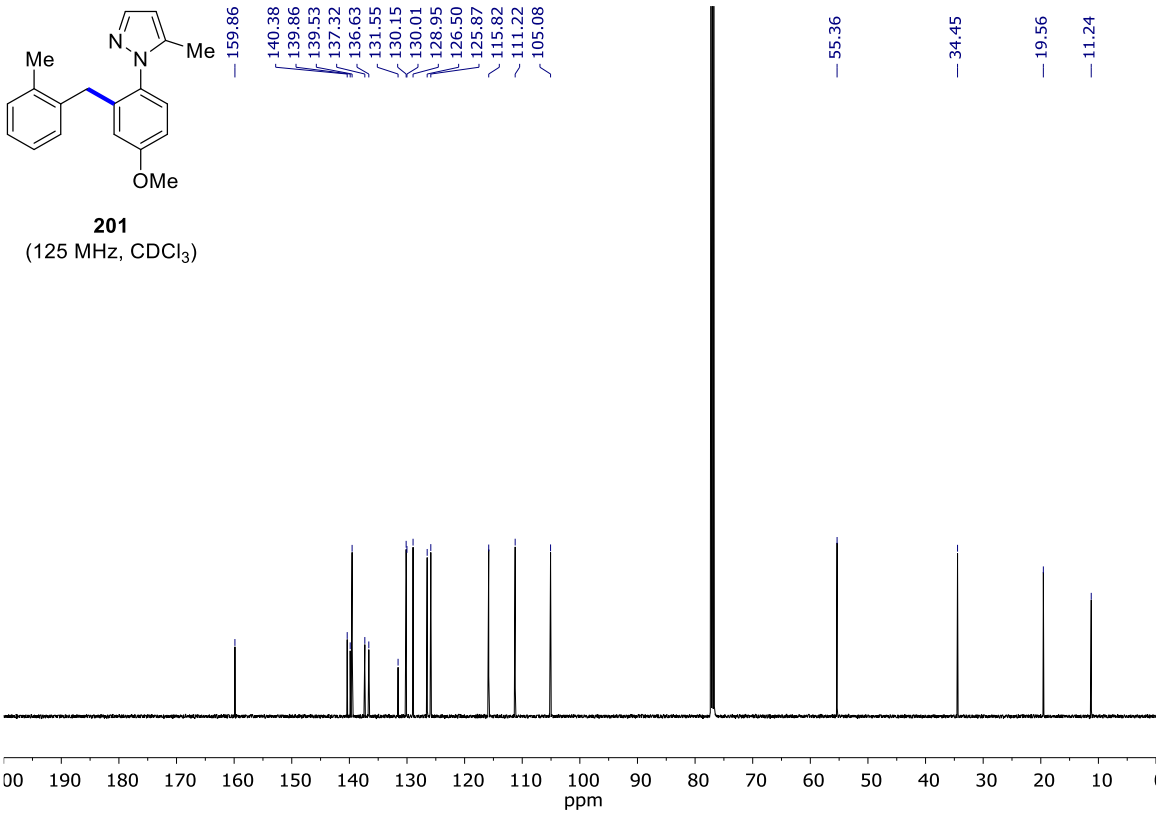
145ft
(500 MHz, $CDCl_3$)



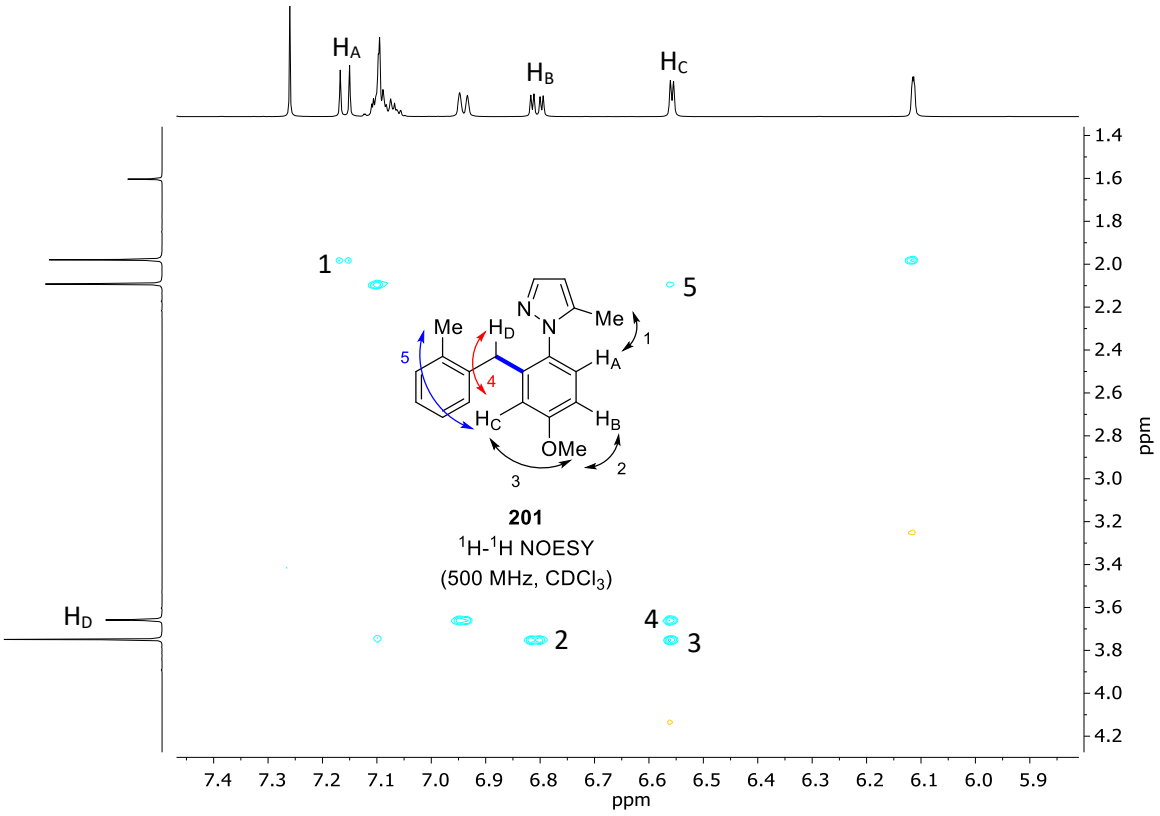
145ft
(125 MHz, $CDCl_3$)



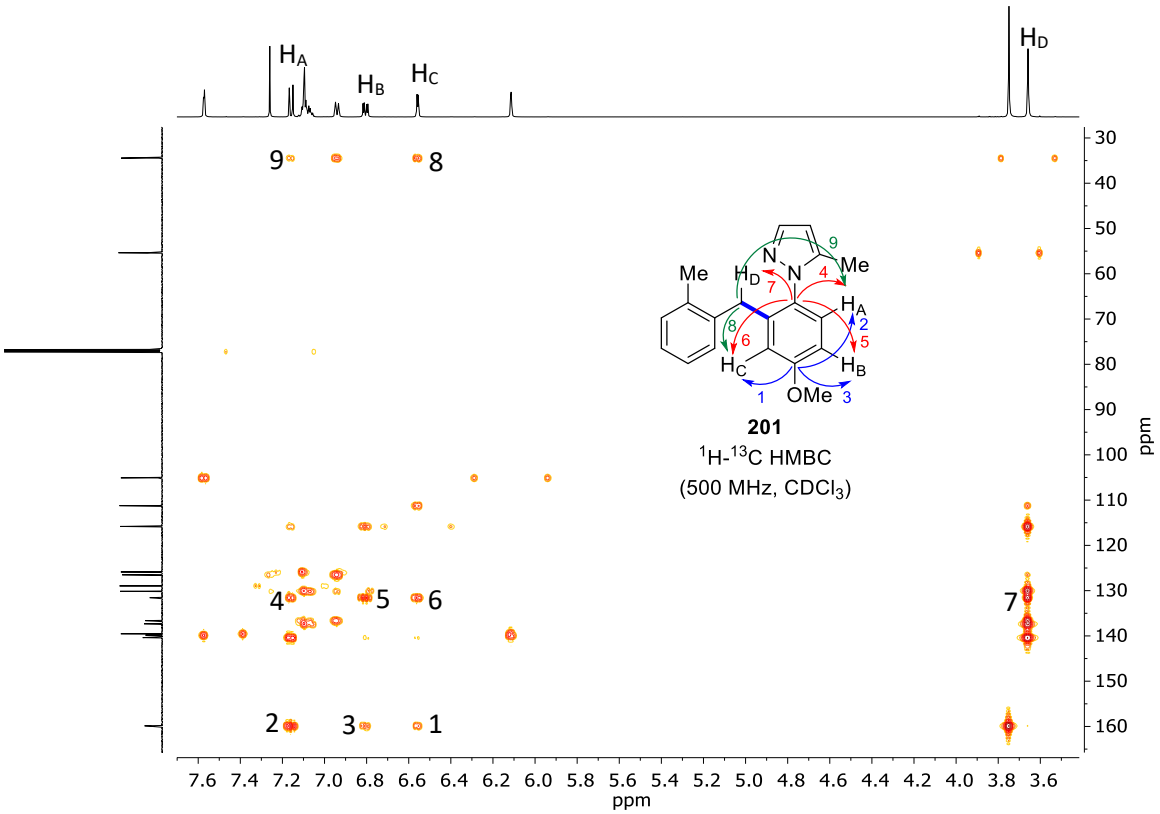
201
(500 MHz, $CDCl_3$)



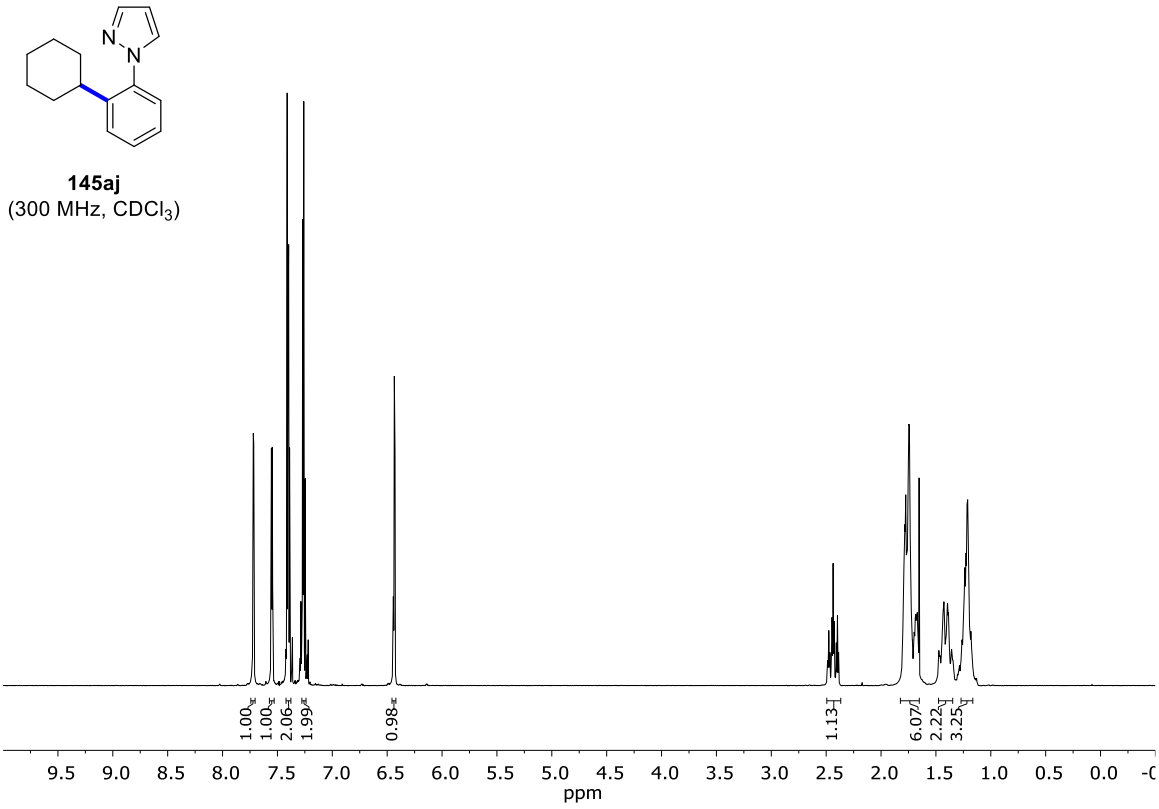
201
(125 MHz, $CDCl_3$)



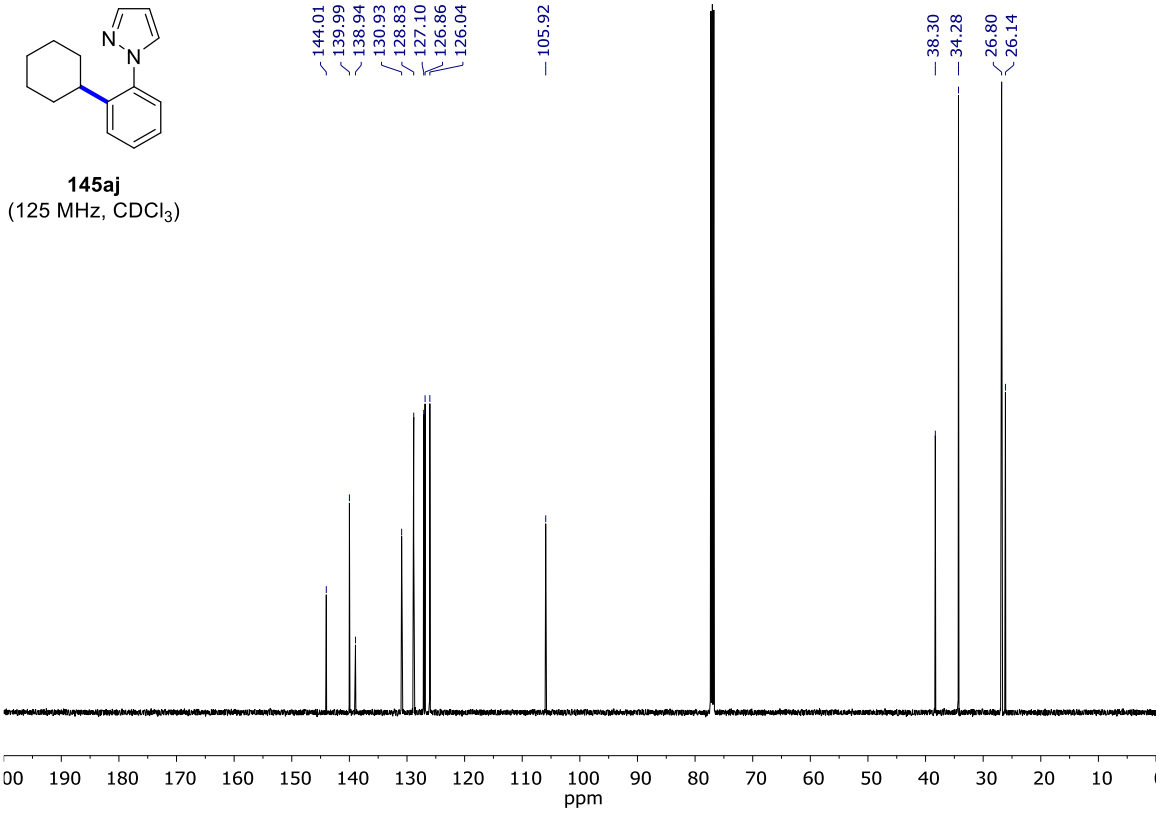
201
^1H-^1H NOESY
(500 MHz, $CDCl_3$)



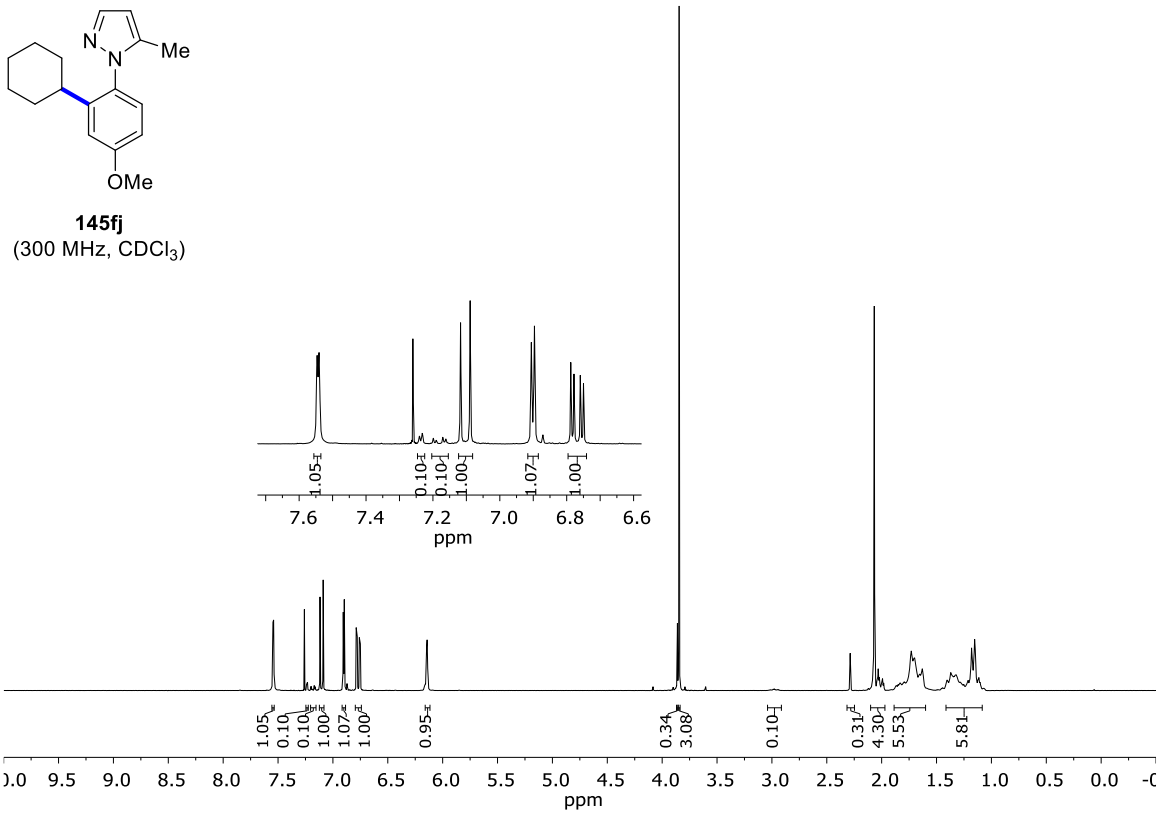
201
^{1}H-^{13}C HMBC
(500 MHz, $CDCl_3$)



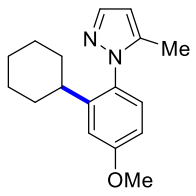
145aj
(300 MHz, $CDCl_3$)



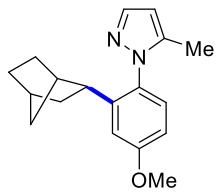
145aj
(125 MHz, $CDCl_3$)



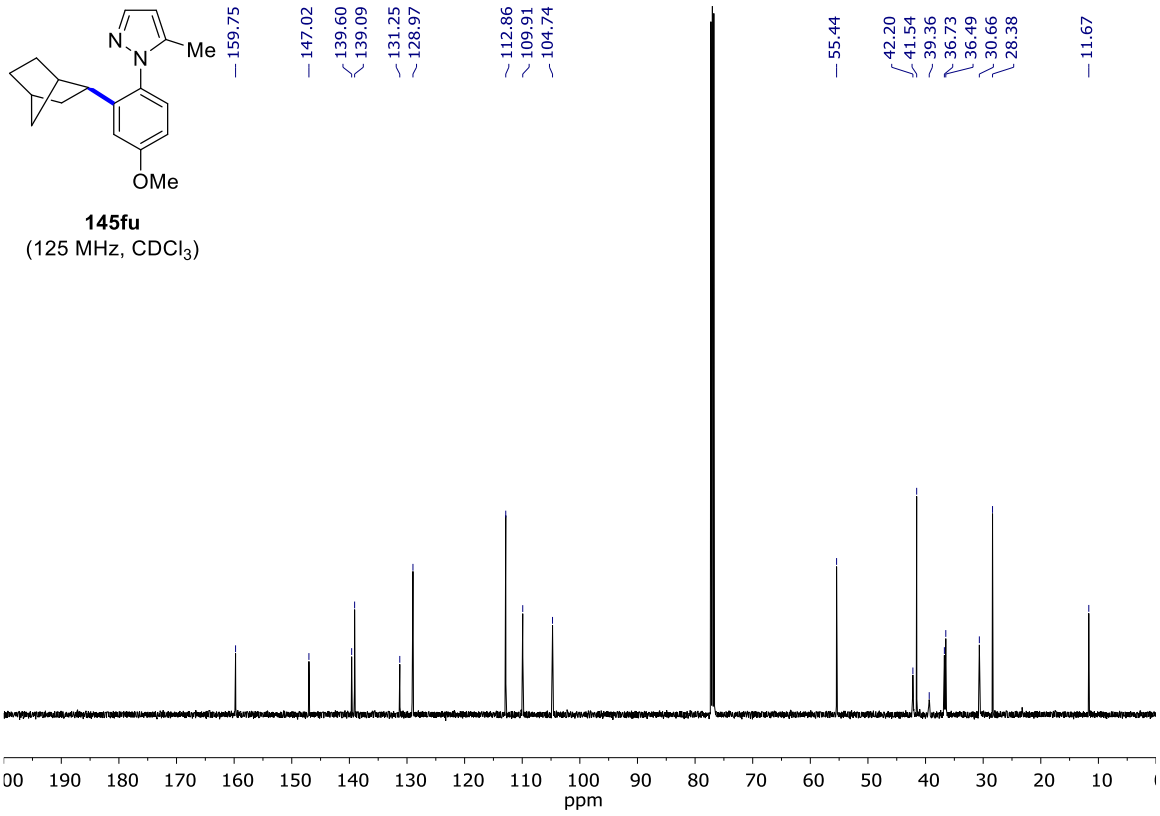
145fj
(300 MHz, $CDCl_3$)



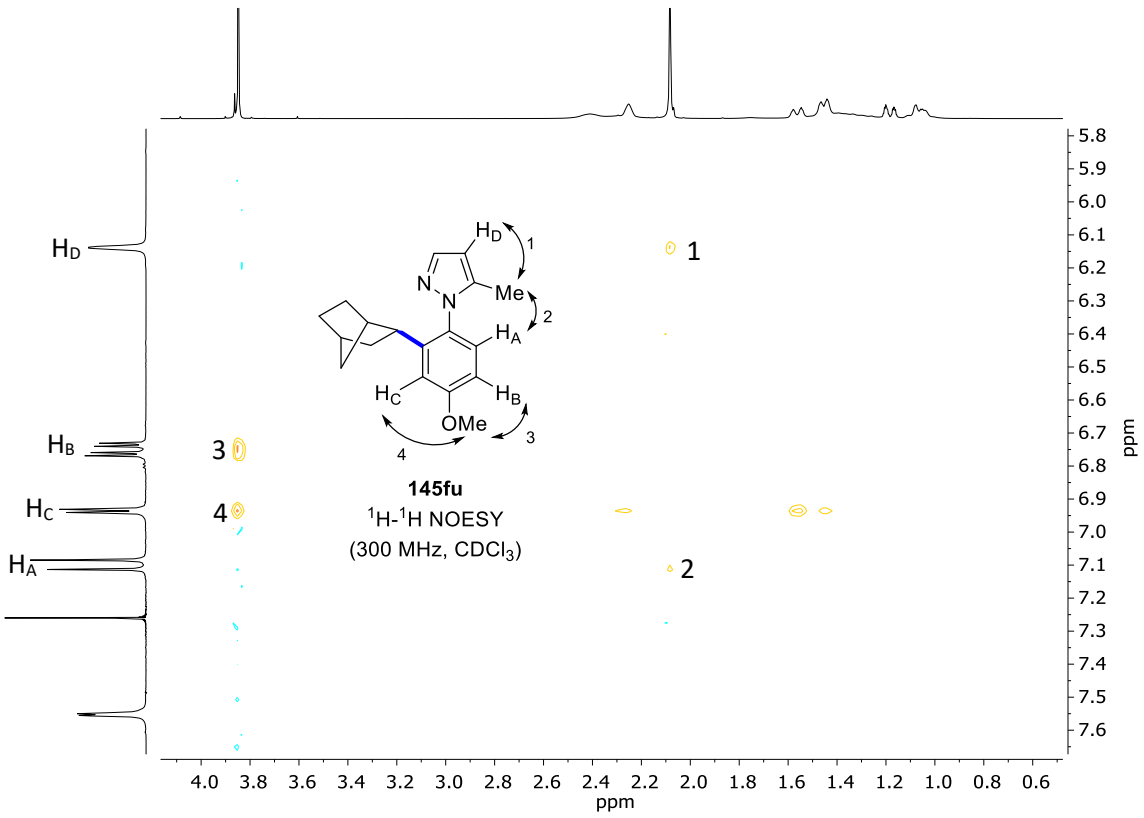
145fj
(125 MHz, $CDCl_3$)



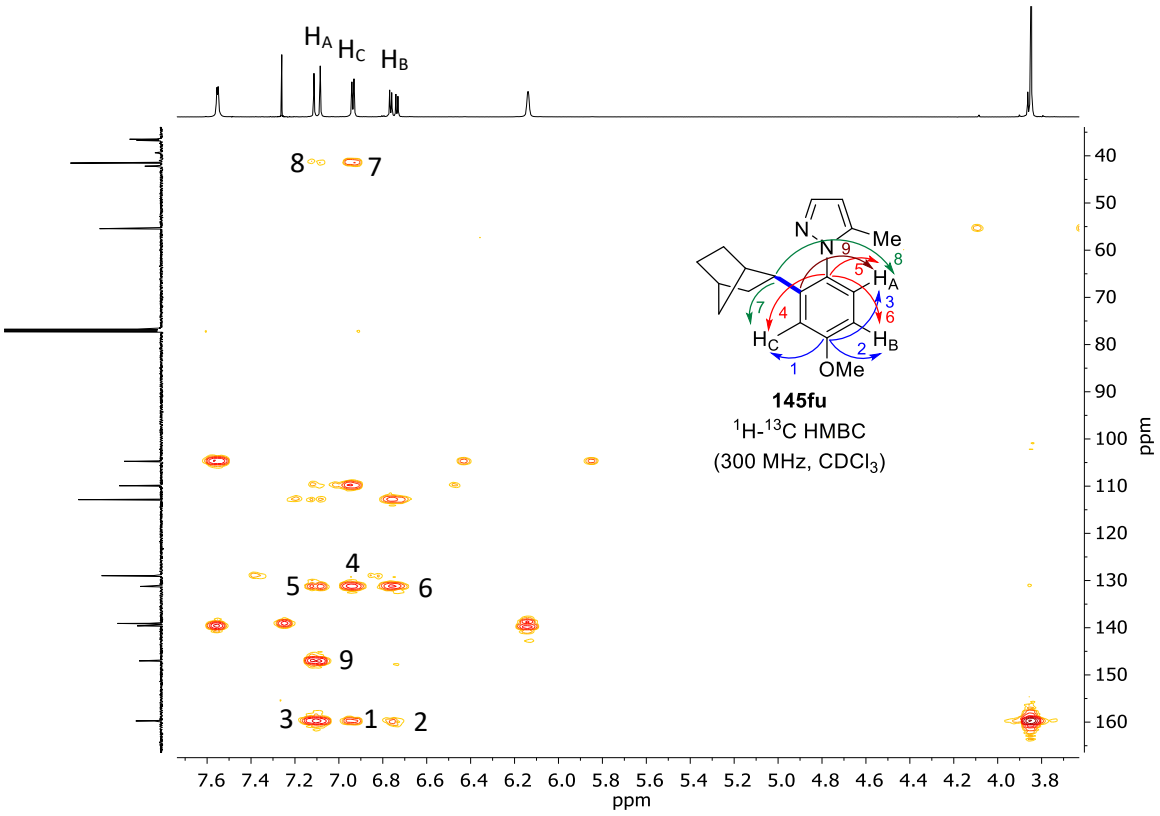
145fu
(300 MHz, $CDCl_3$)



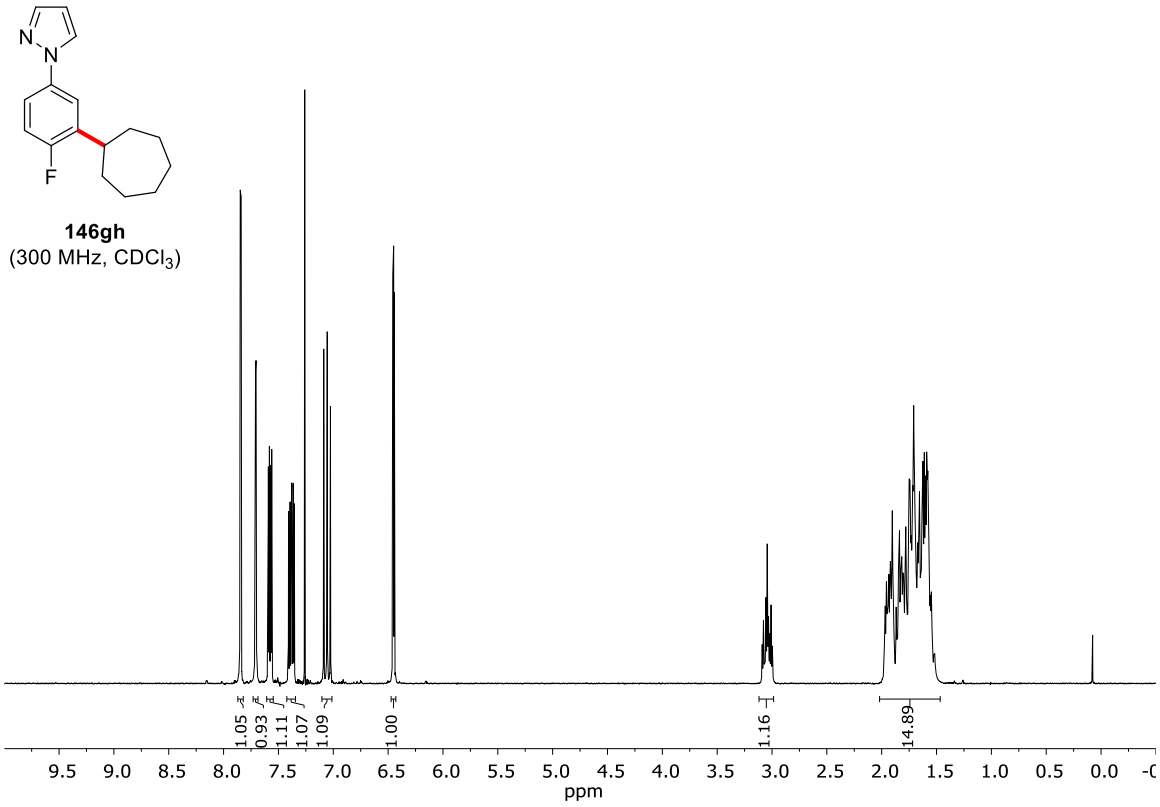
145fu
(125 MHz, $CDCl_3$)



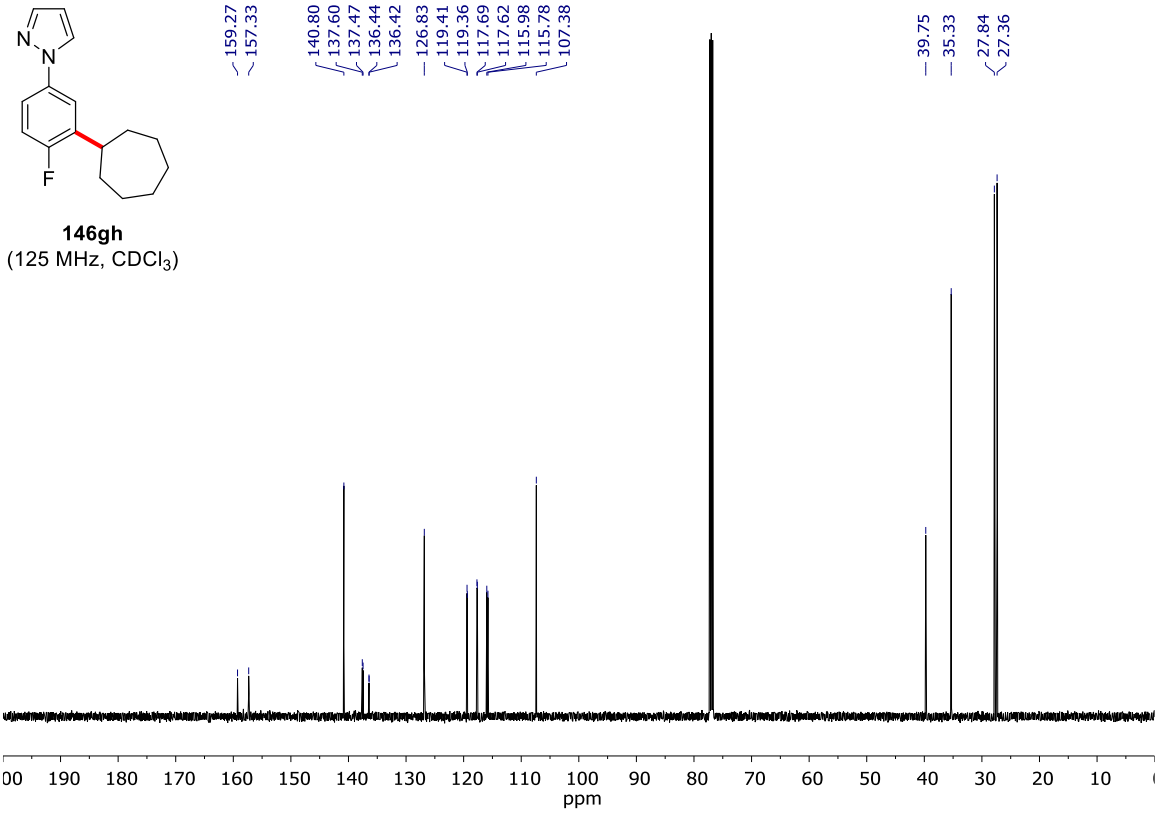
145fu
^1H-^1H NOESY
(300 MHz, $CDCl_3$)



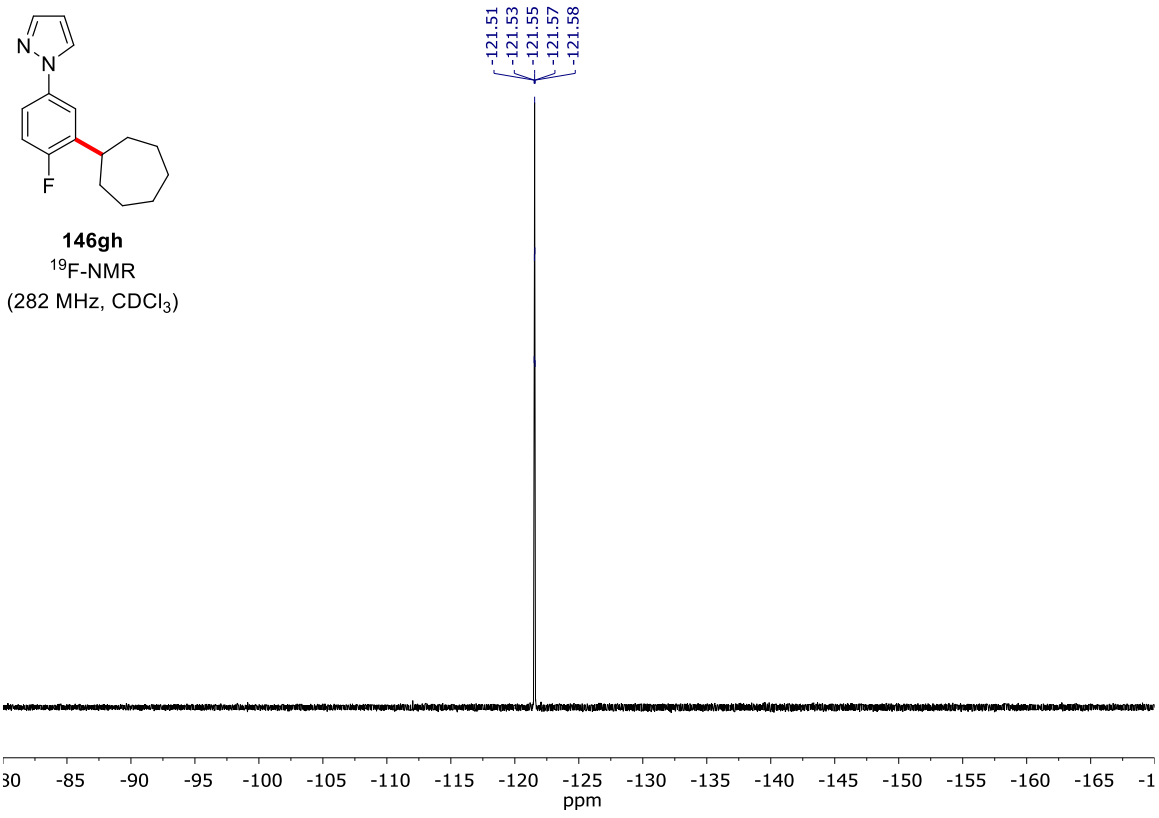
145fu
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



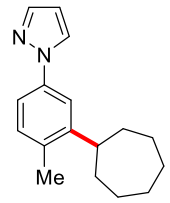
146gh
(300 MHz, $CDCl_3$)



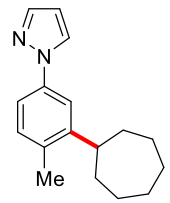
146gh
(125 MHz, $CDCl_3$)



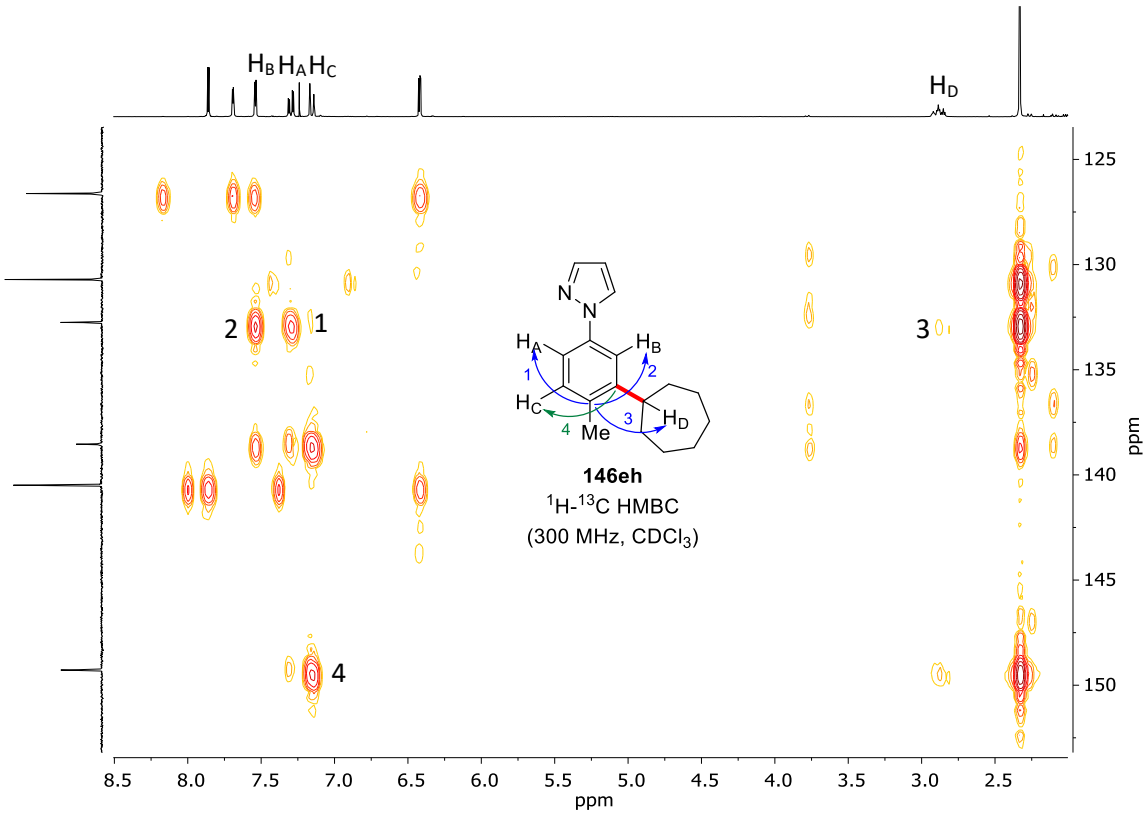
146gh
^{19}F-NMR
(282 MHz, $CDCl_3$)



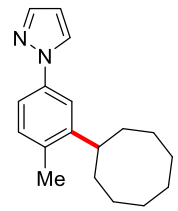
146eh
(300 MHz, $CDCl_3$)



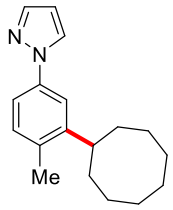
146eh
(125 MHz, $CDCl_3$)



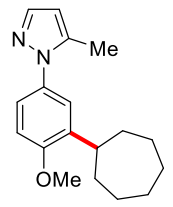
146eh
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



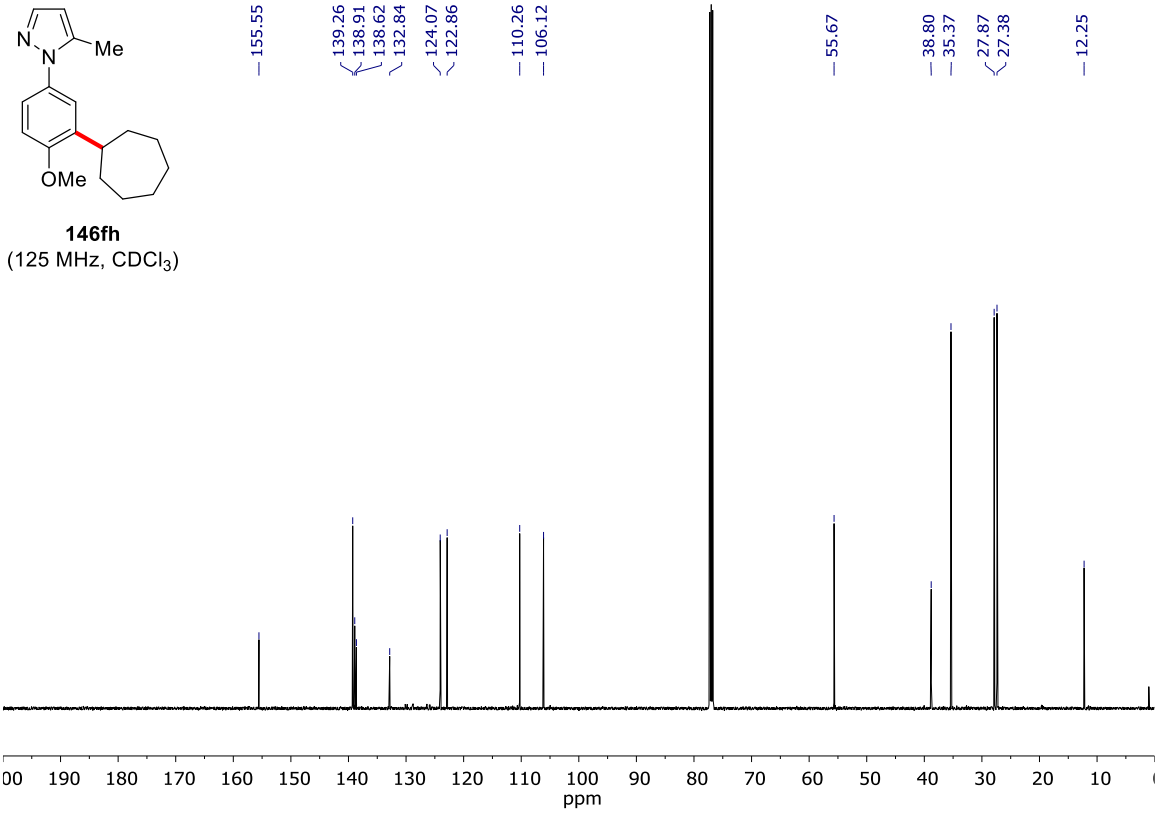
146ek
(400 MHz, $CDCl_3$)



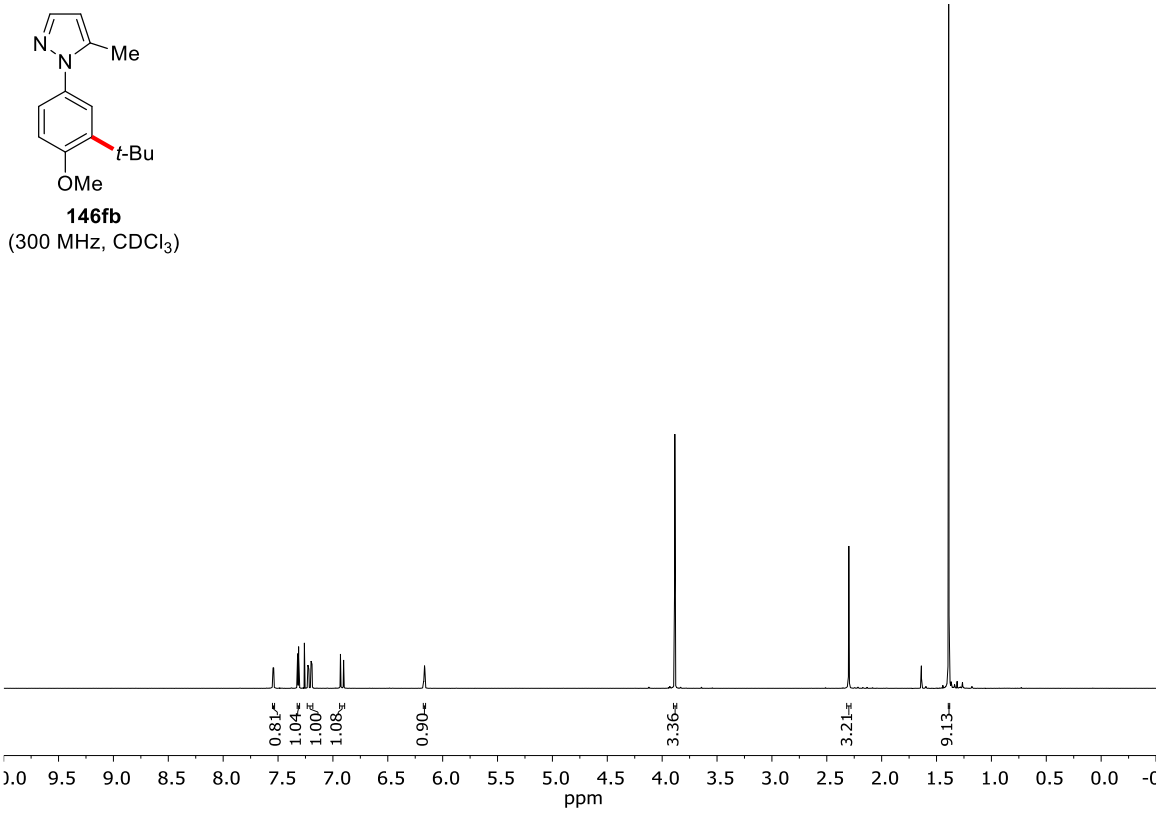
146ek
(100 MHz, $CDCl_3$)



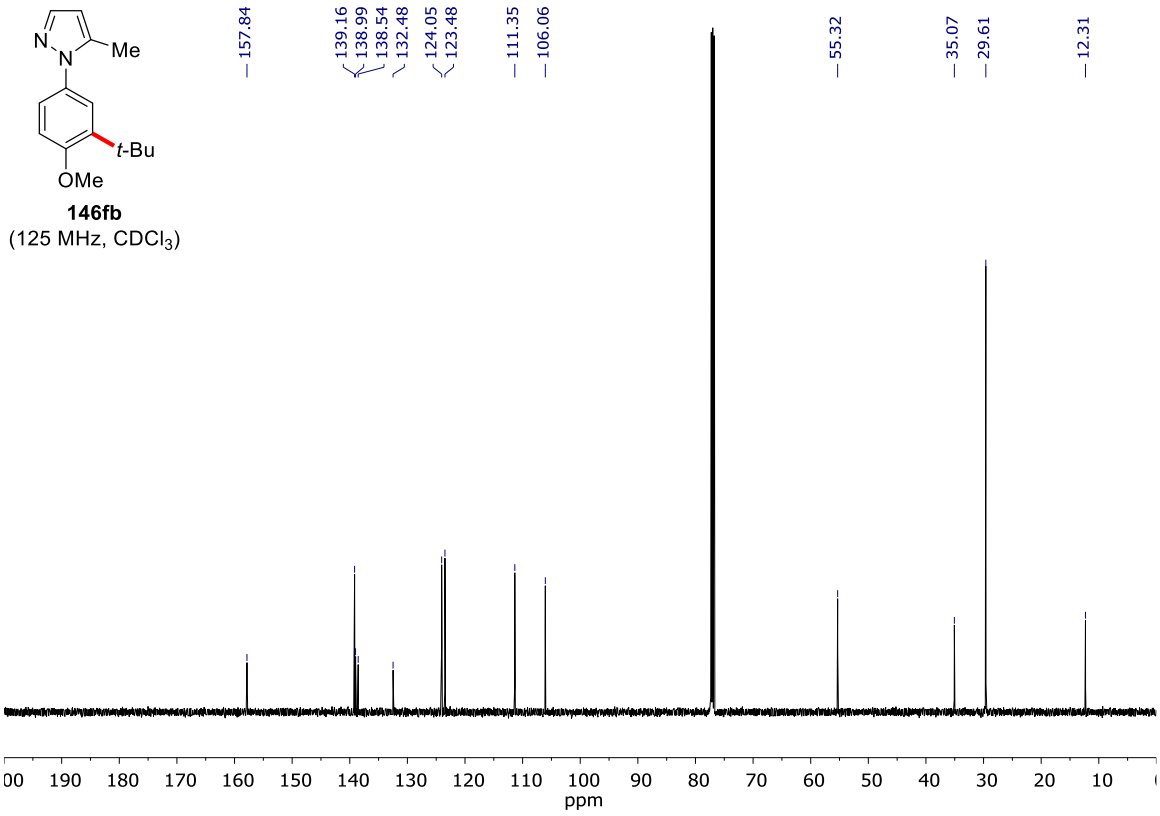
146fh
(500 MHz, $CDCl_3$)

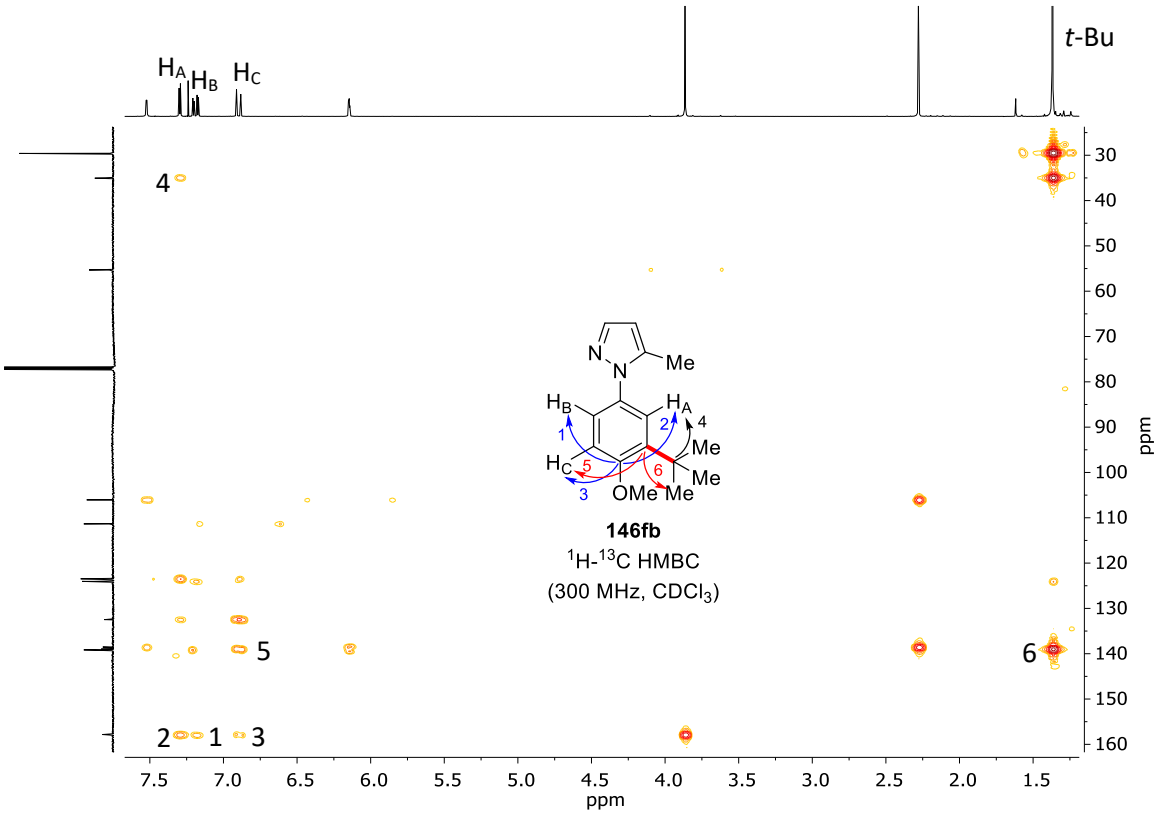


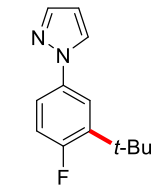
146fh
(125 MHz, $CDCl_3$)



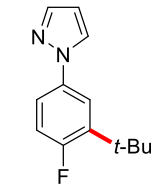
146fb
(300 MHz, $CDCl_3$)


157.84
139.16
138.99
138.54
132.48
124.05
123.48
111.35
106.06
55.32
35.07
29.61
12.31
Me
t-Bu
OMe
146fb
(125 MHz, CDCl3)
ppm

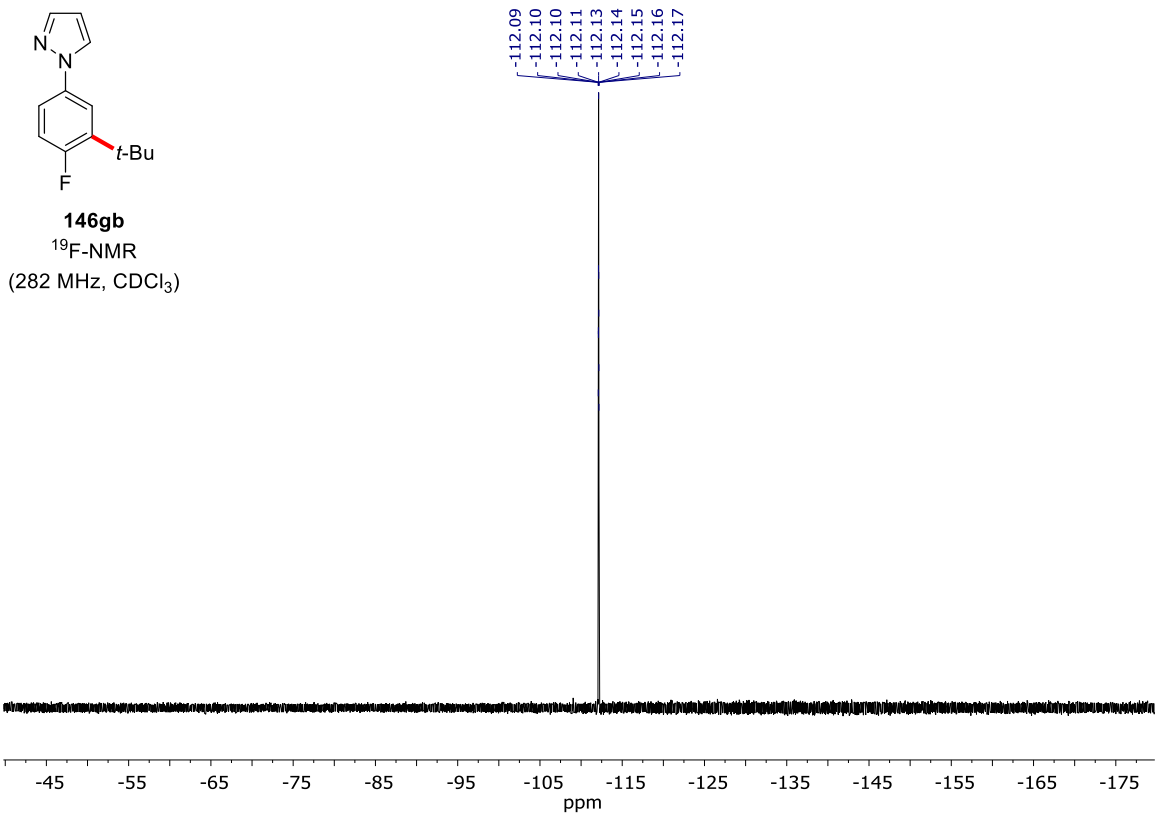

t-Bu
HA
HB
HC
4
5
6
2
1
3
Me
OMe
146fb
1H-13C HMBC
(300 MHz, CDCl3)
ppm



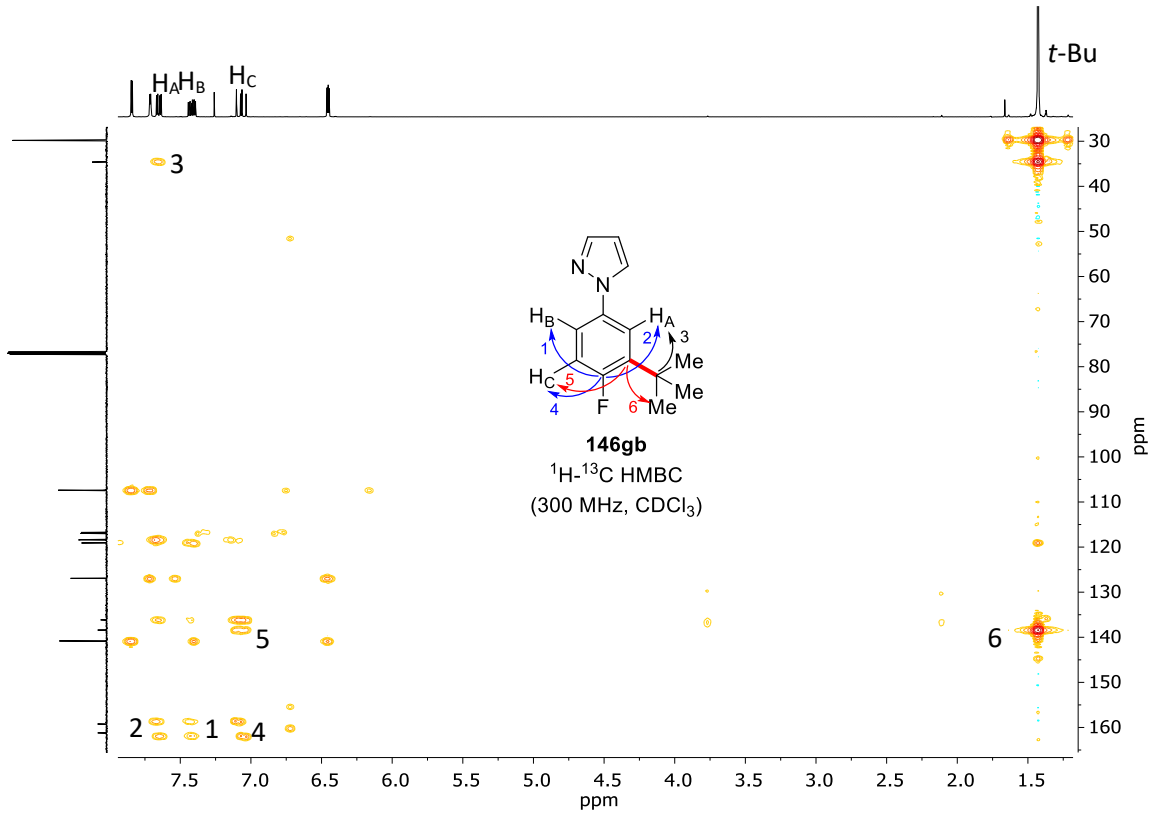
146gb
(300 MHz, $CDCl_3$)



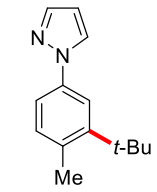
146gb
(125 MHz, $CDCl_3$)



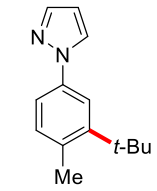
146gb
^{19}F-NMR
(282 MHz, $CDCl_3$)



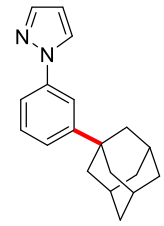
146gb
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



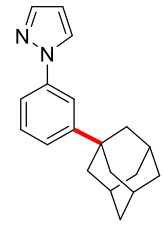
146eb
(300 MHz, $CDCl_3$)



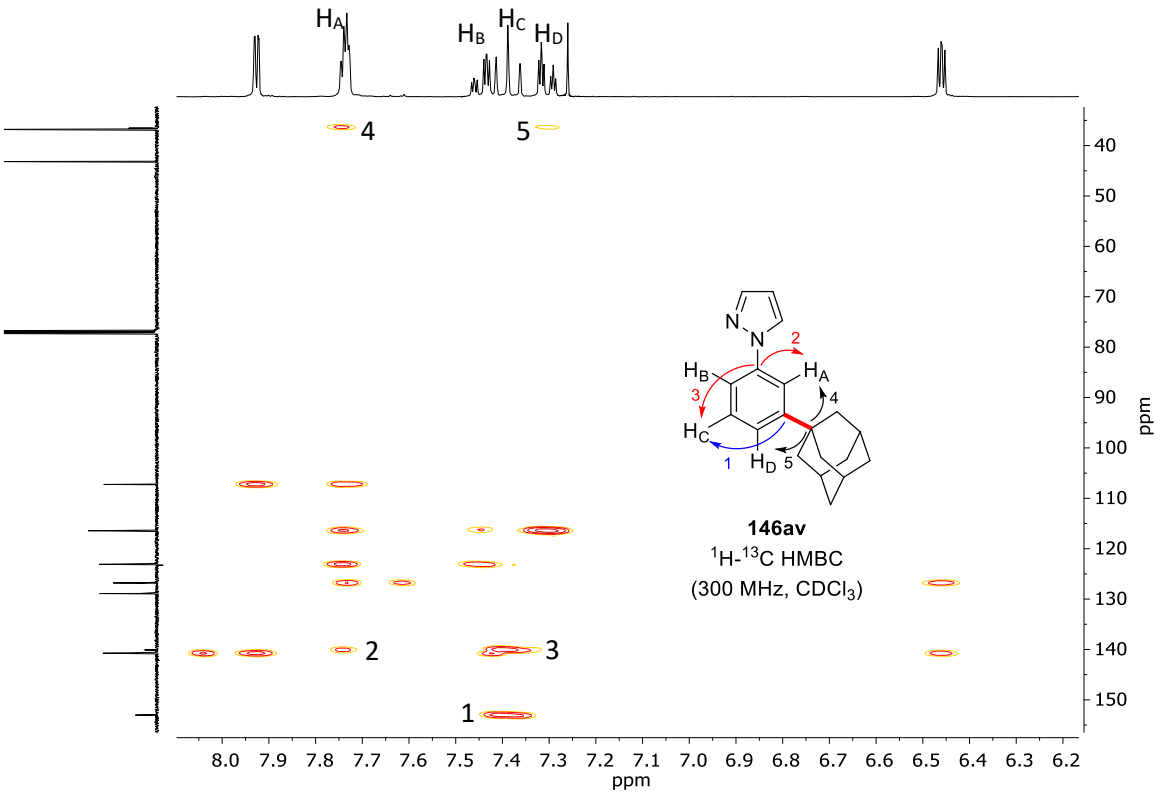
146eb
(125 MHz, $CDCl_3$)



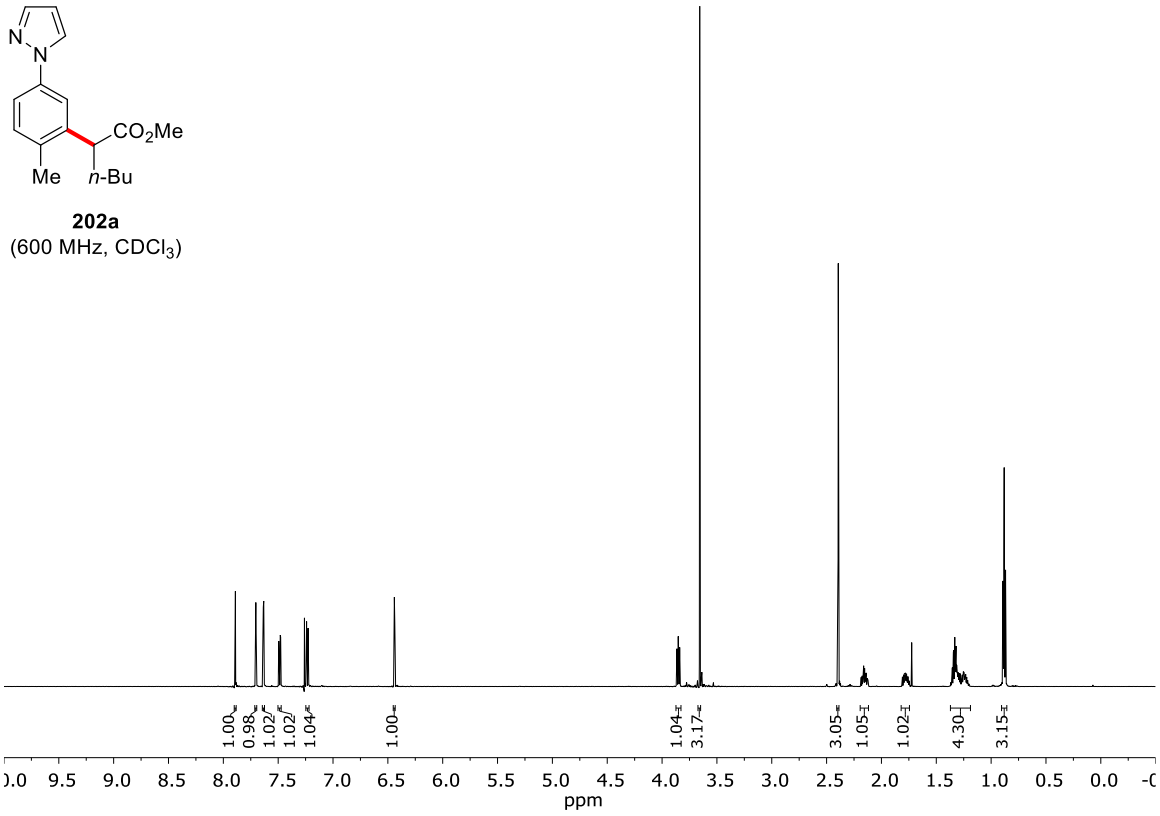
146av
(300 MHz, $CDCl_3$)



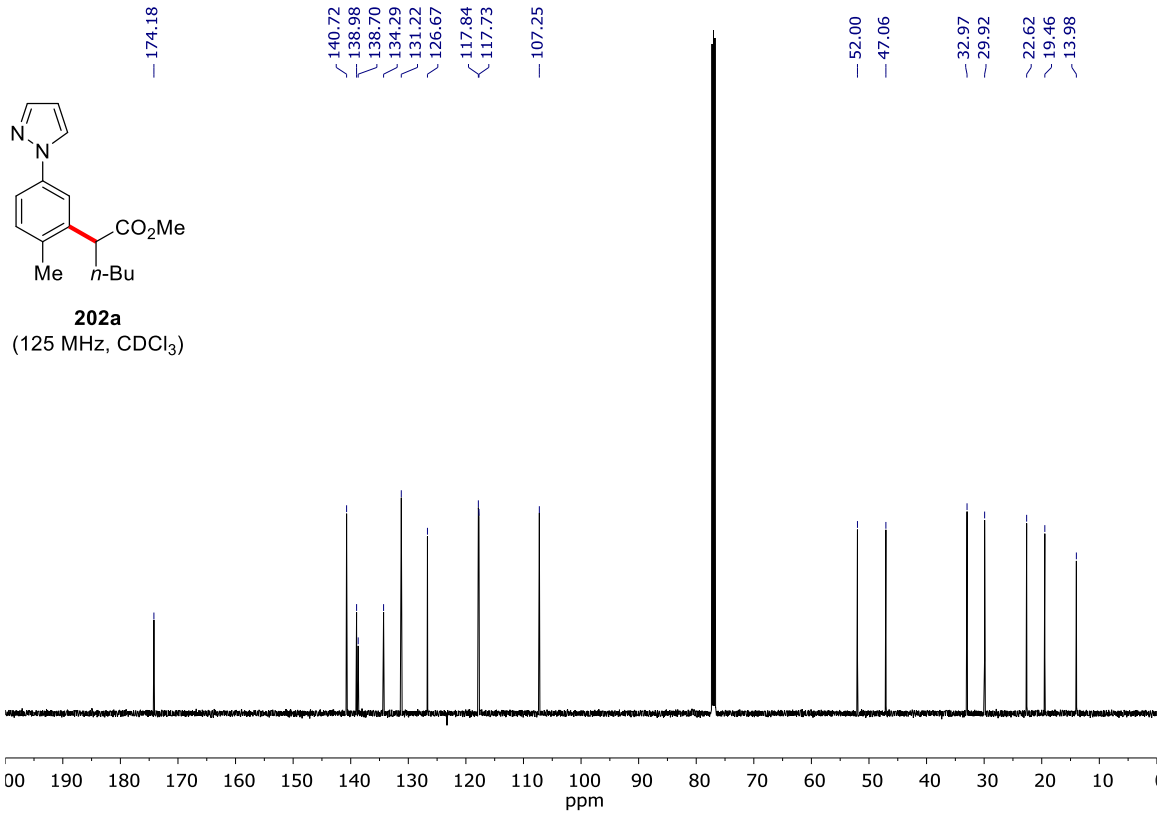
146av
(125 MHz, $CDCl_3$)

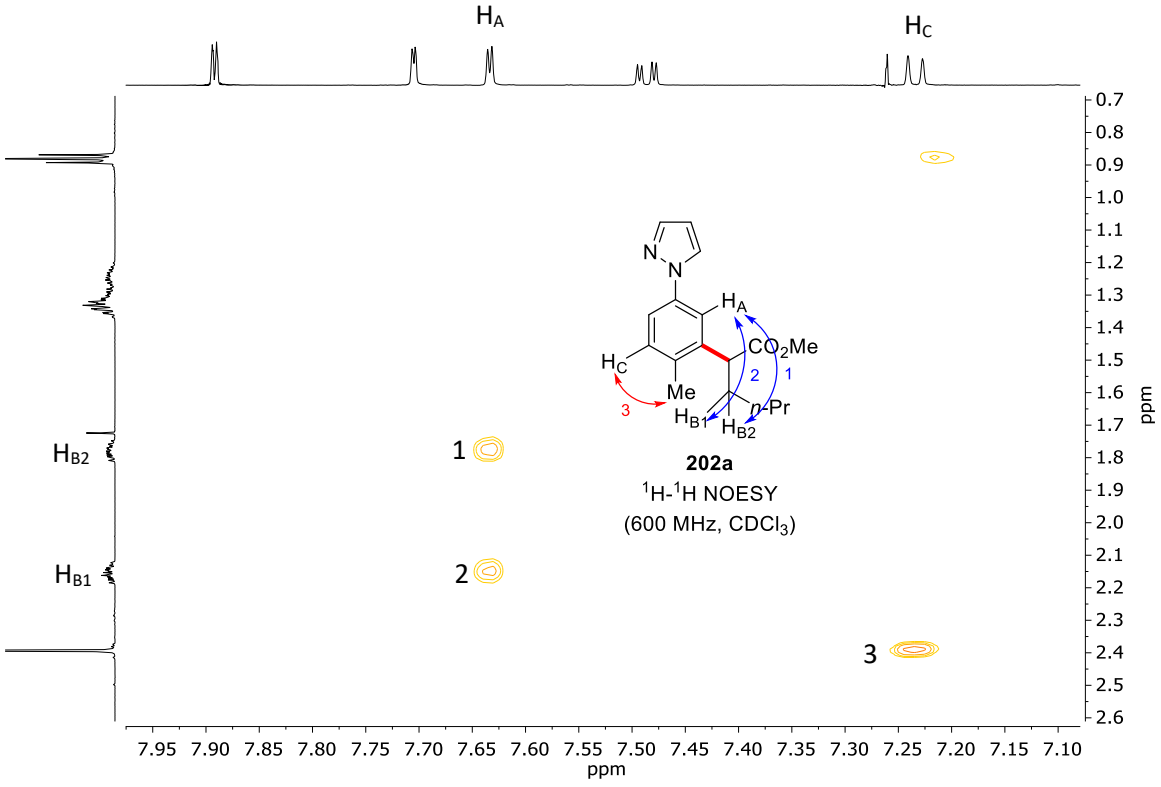


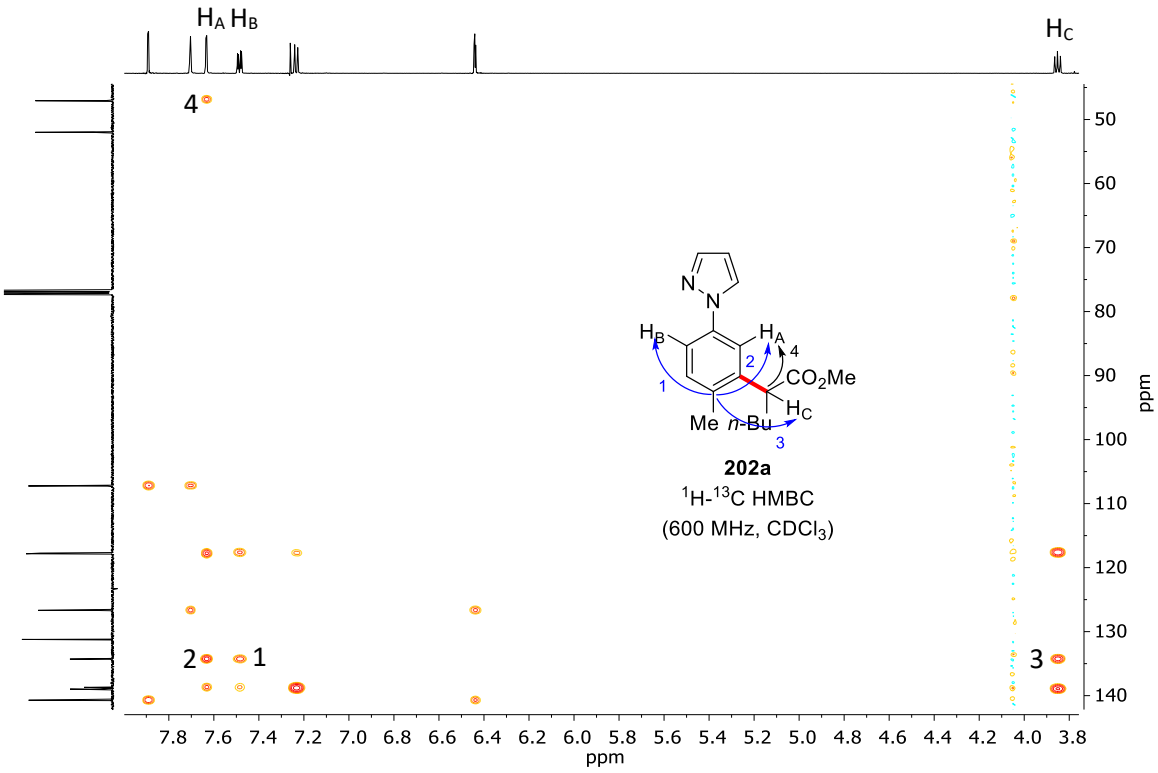
146av
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



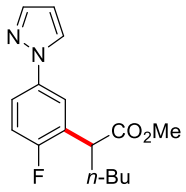
202a
(600 MHz, $CDCl_3$)


174.18
140.72
138.98
138.70
134.29
131.22
126.67
117.84
117.73
107.25
52.00
47.06
32.97
29.92
22.62
19.46
13.98
CO2Me
Me
n-Bu
202a
(125 MHz, CDCl3)
ppm

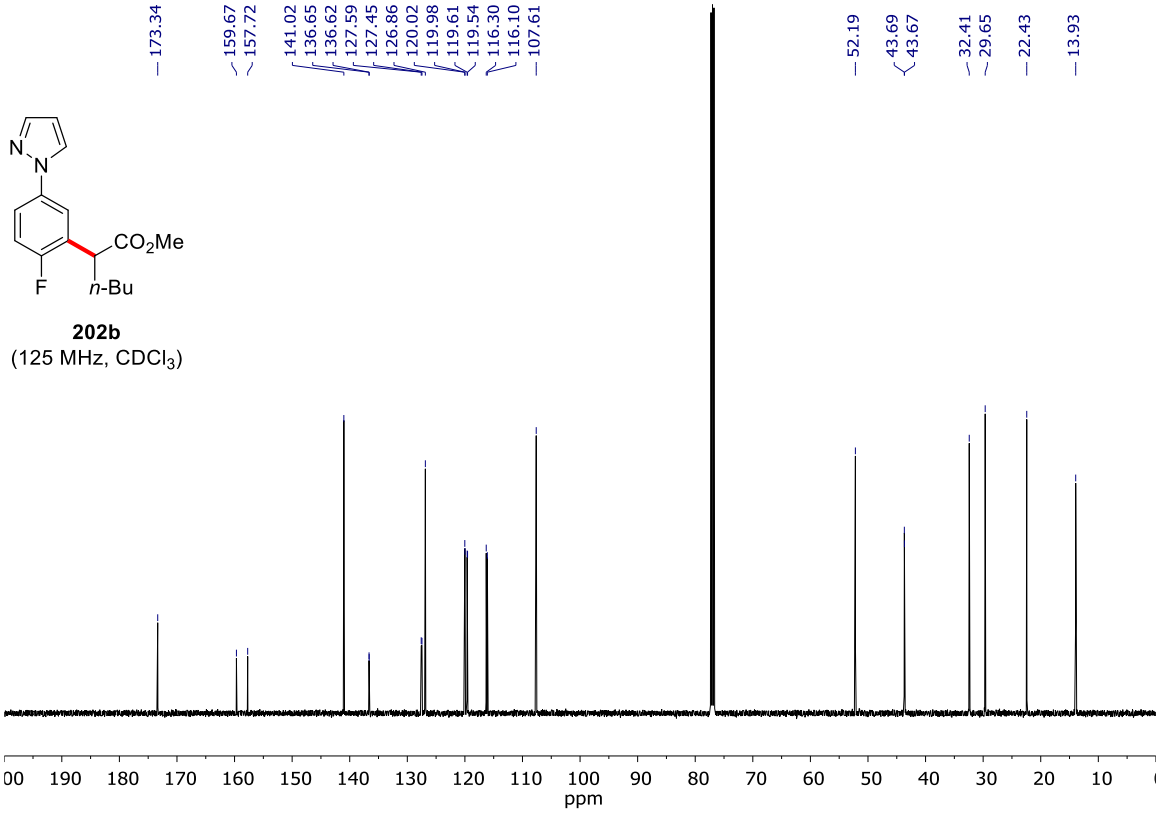

HA
HC
HB2
HB1
1
2
3
CO2Me
Me
n-Pr
202a
1H-1H NOESY
(600 MHz, CDCl3)
ppm



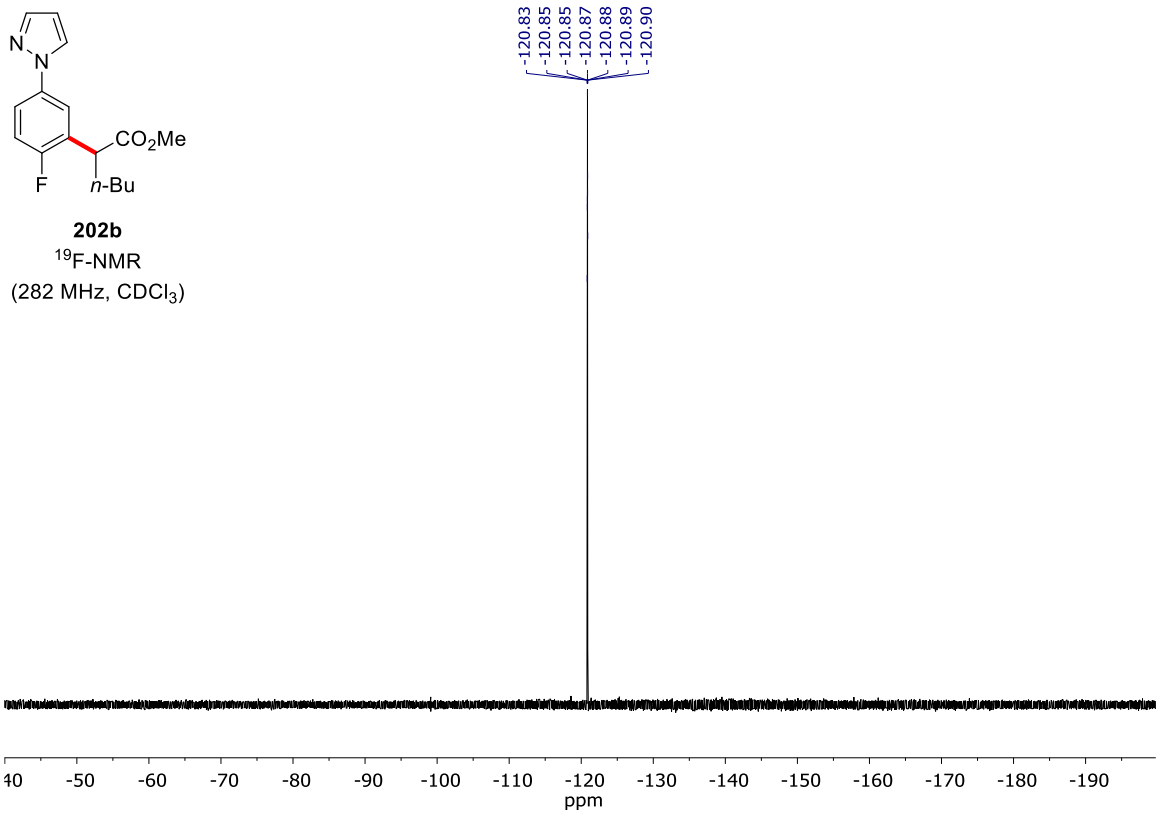
202a
^{1}H-^{13}C HMBC
(600 MHz, $CDCl_3$)



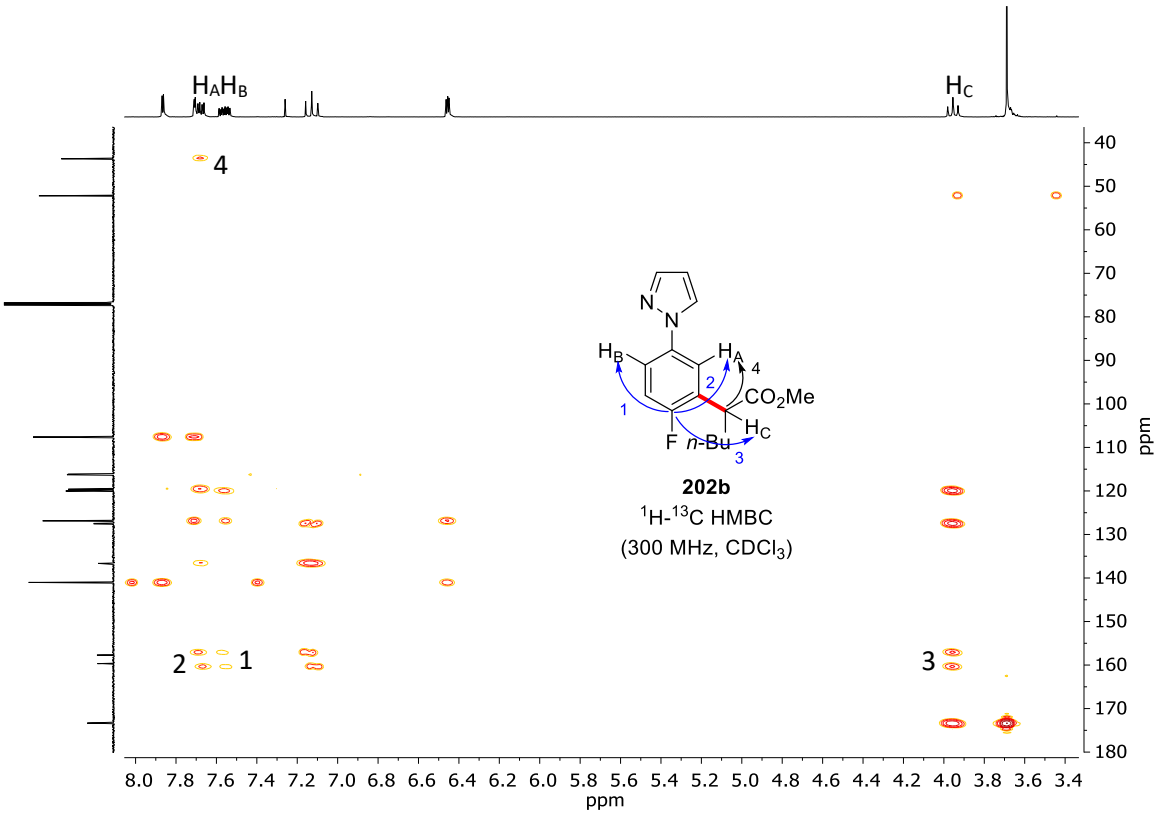
202b
(300 MHz, $CDCl_3$)



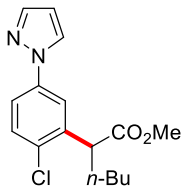
202b
(125 MHz, $CDCl_3$)



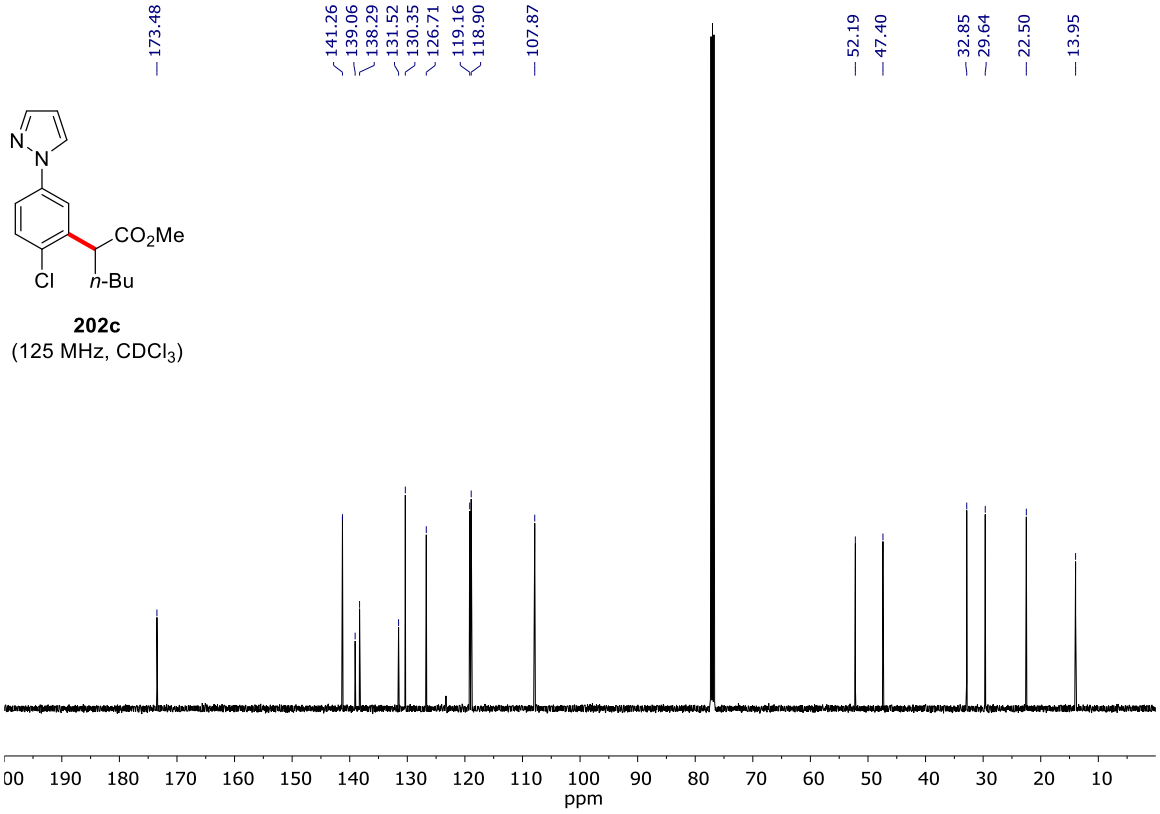
202b
^{19}F-NMR
(282 MHz, $CDCl_3$)



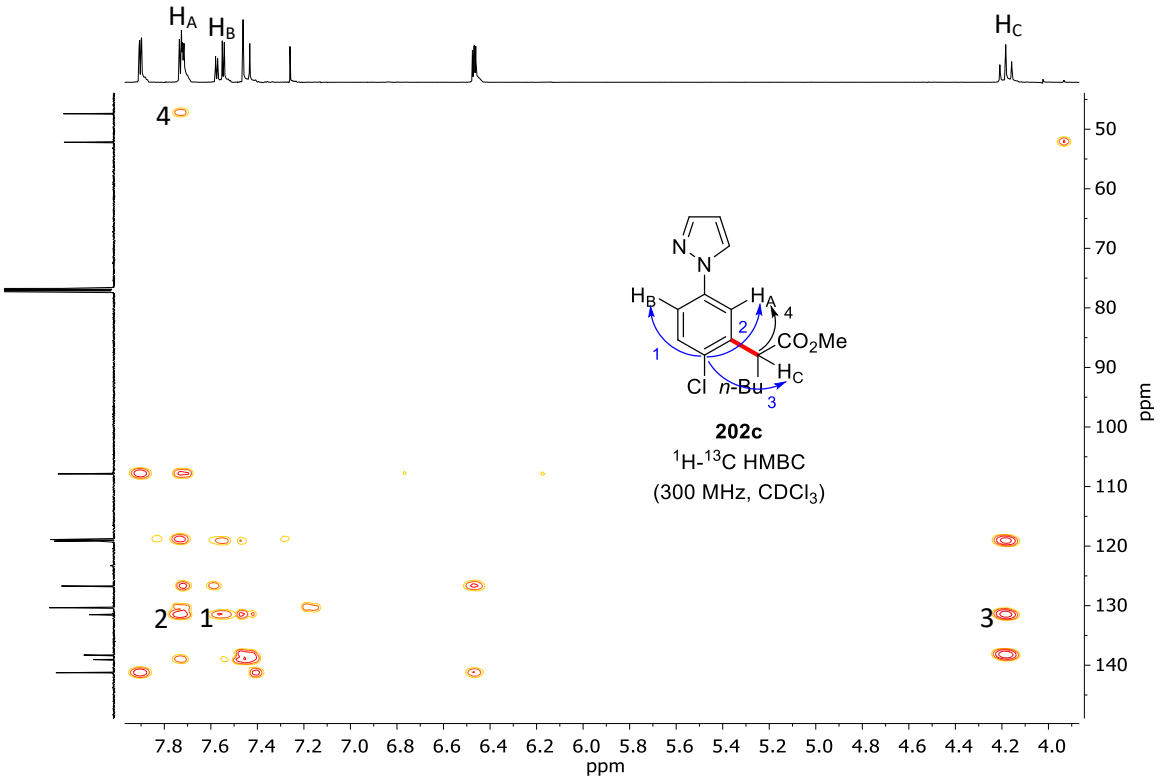
202b
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



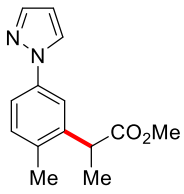
202c
(300 MHz, $CDCl_3$)



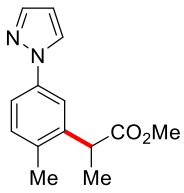
202c
(125 MHz, $CDCl_3$)



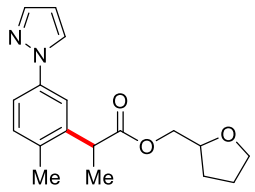
202c
^1H-^{13}C HMBC
(300 MHz, $CDCl_3$)



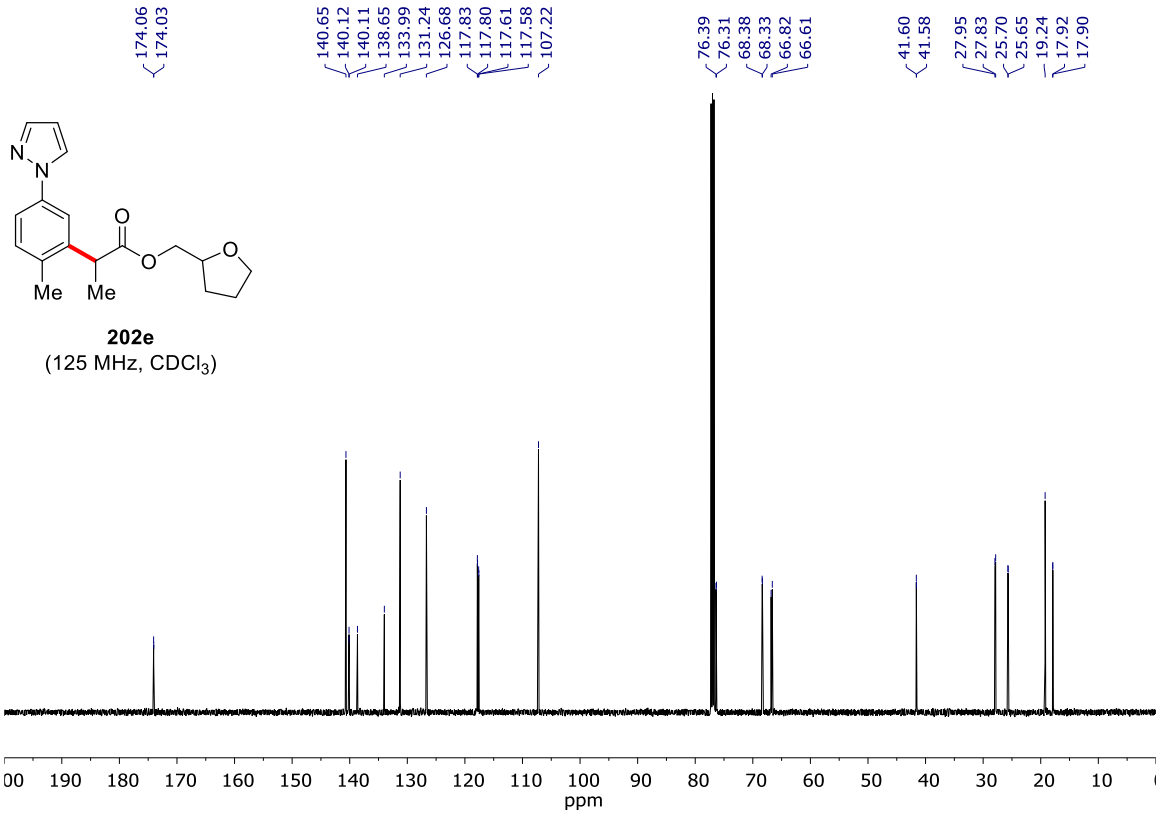
202d
(300 MHz, $CDCl_3$)



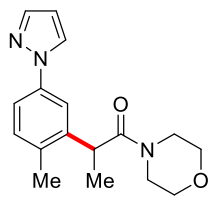
202d
(125 MHz, $CDCl_3$)



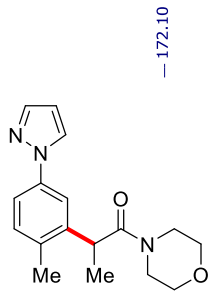
202e
(300 MHz, $CDCl_3$)



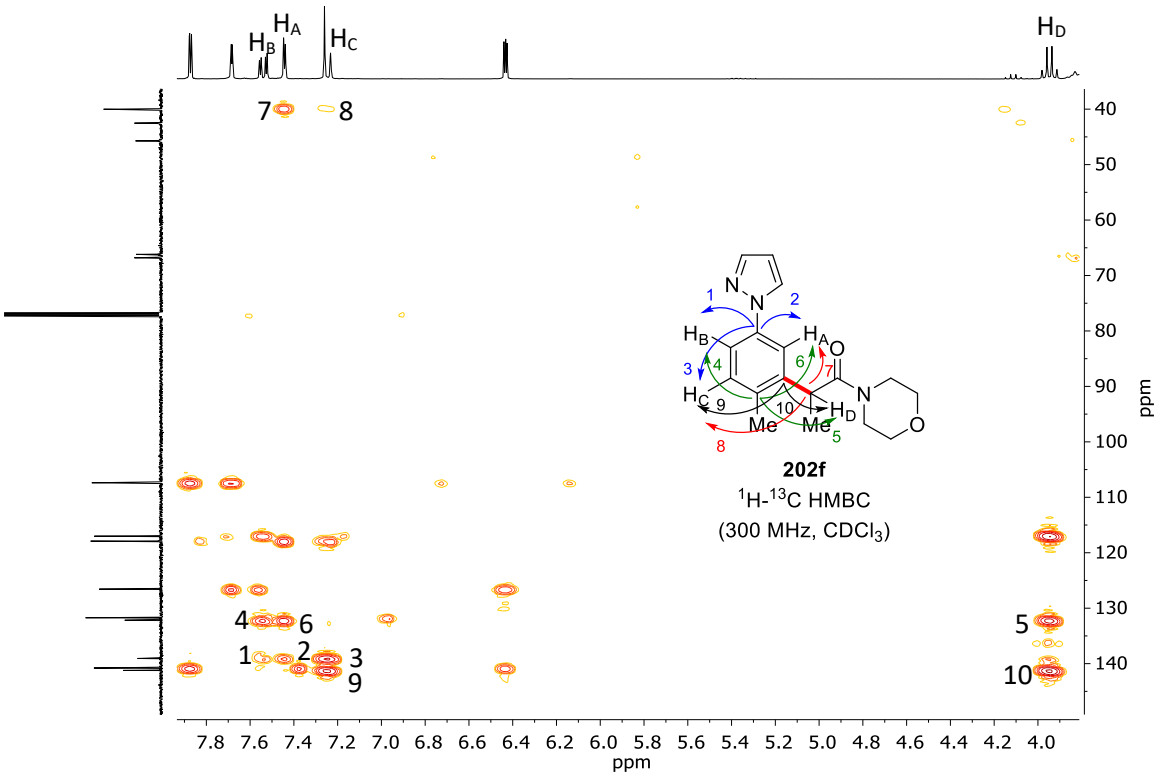
202e
(125 MHz, $CDCl_3$)



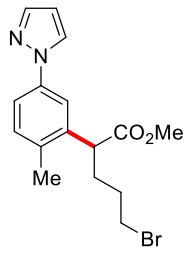
202f
(300 MHz, $CDCl_3$)



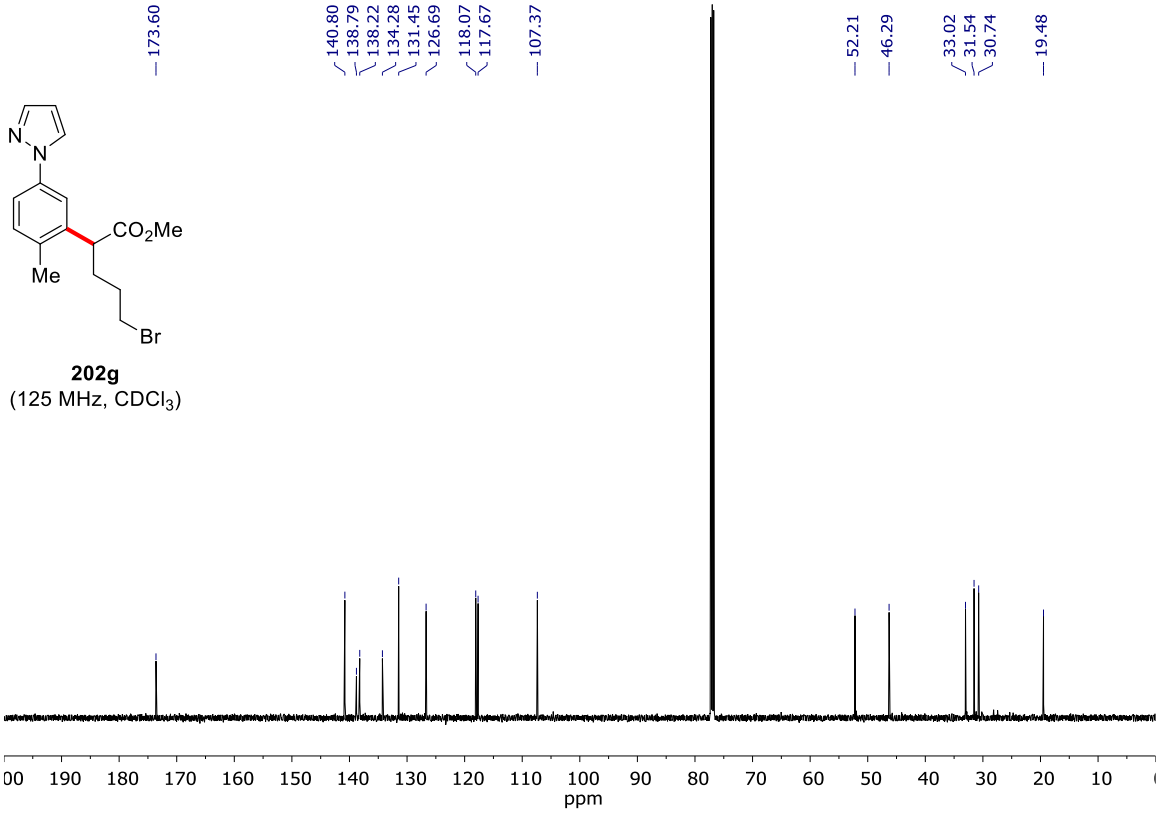
202f
(125 MHz, $CDCl_3$)



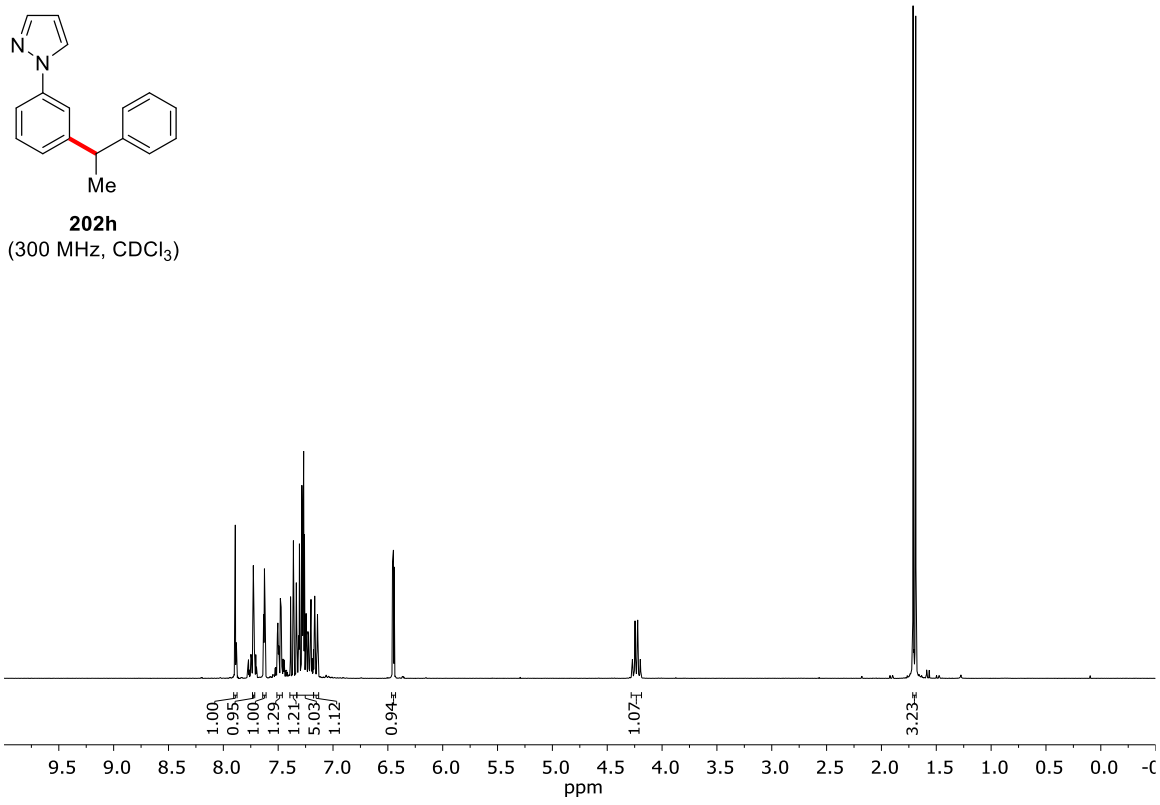
202f
^{1}H-^{13}C HMBC
(300 MHz, $CDCl_3$)



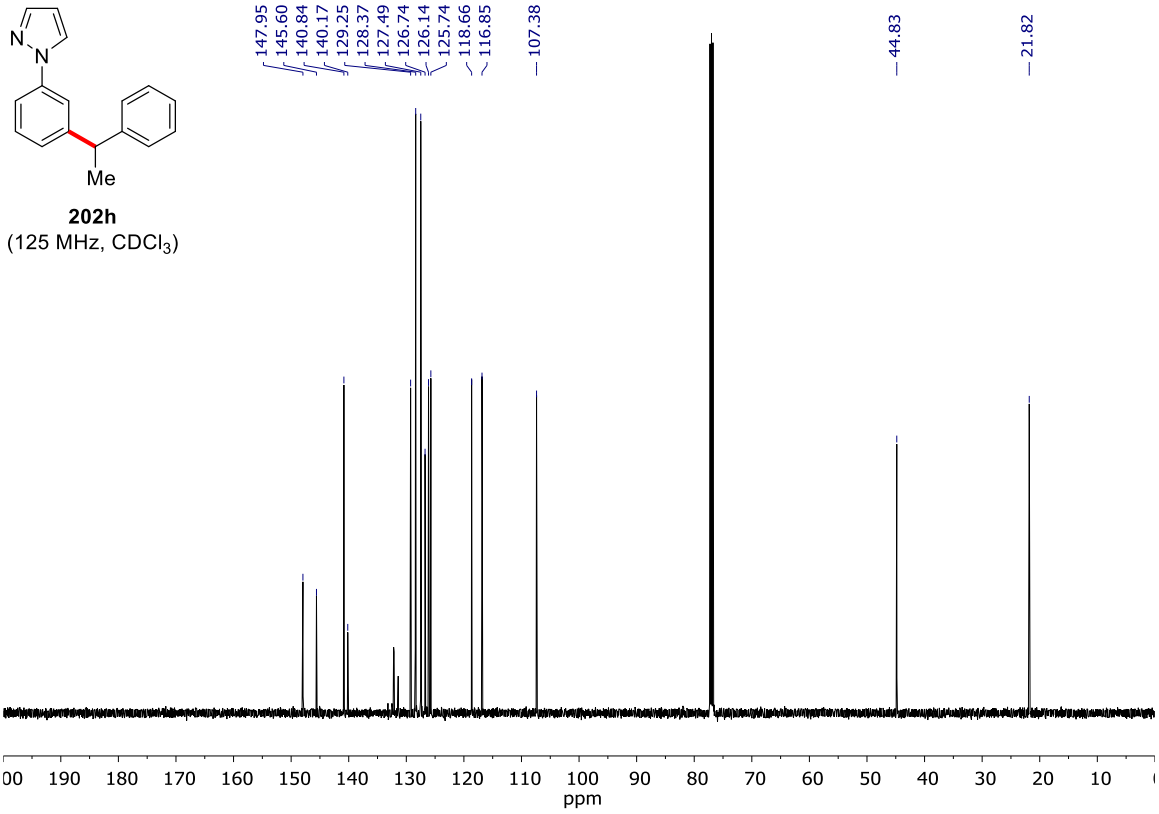
202g
(300 MHz, $CDCl_3$)



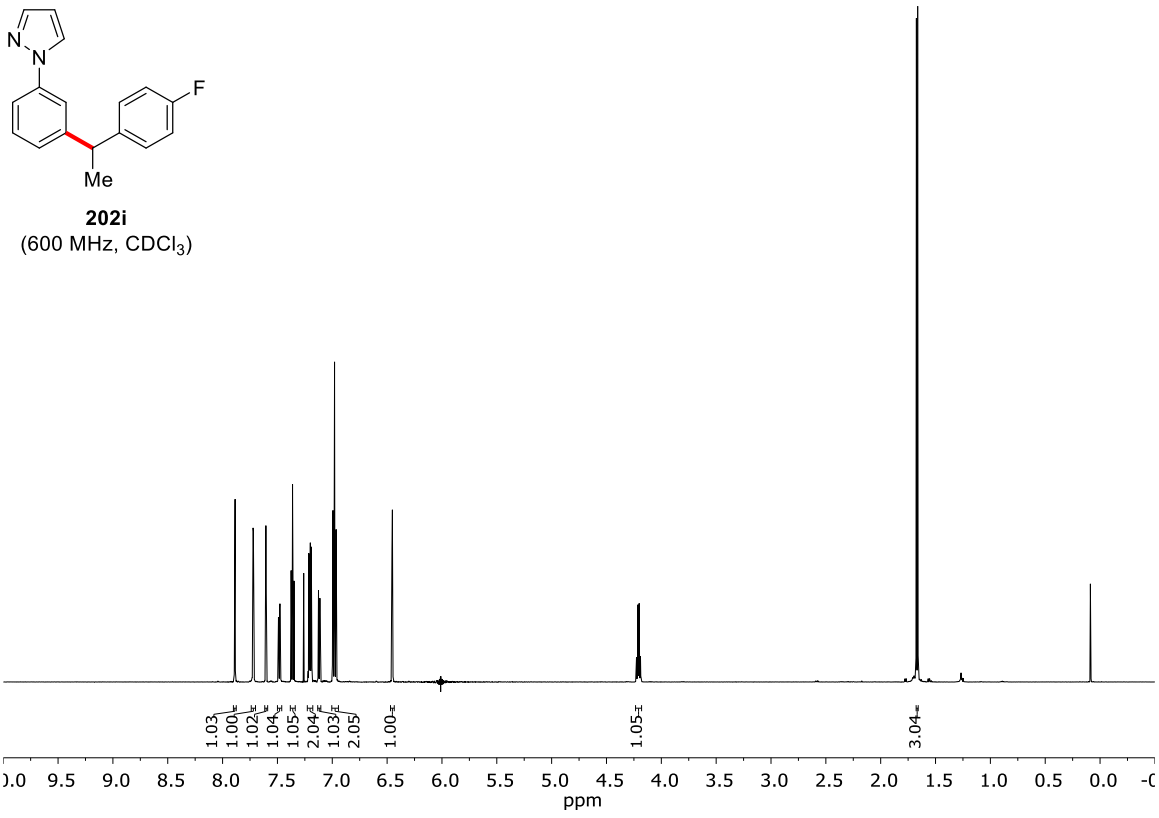
202g
(125 MHz, $CDCl_3$)



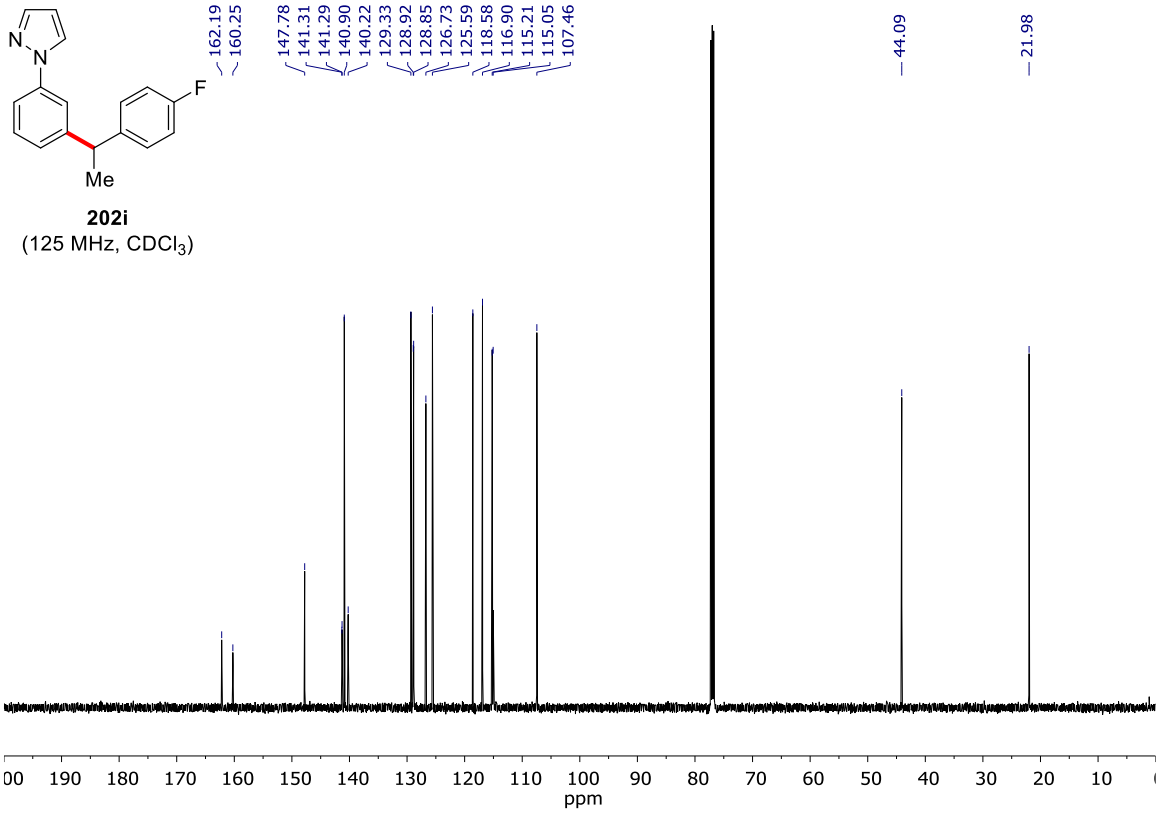
202h
(300 MHz, $CDCl_3$)



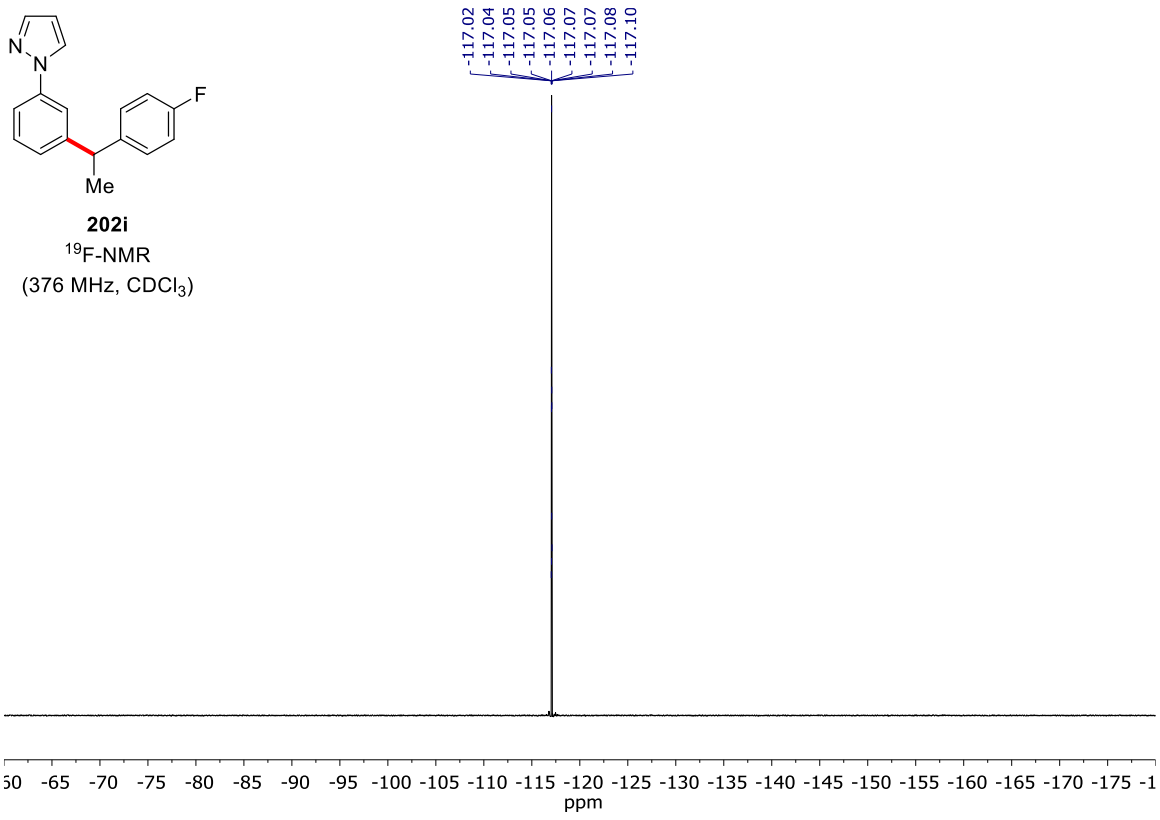
202h
(125 MHz, $CDCl_3$)



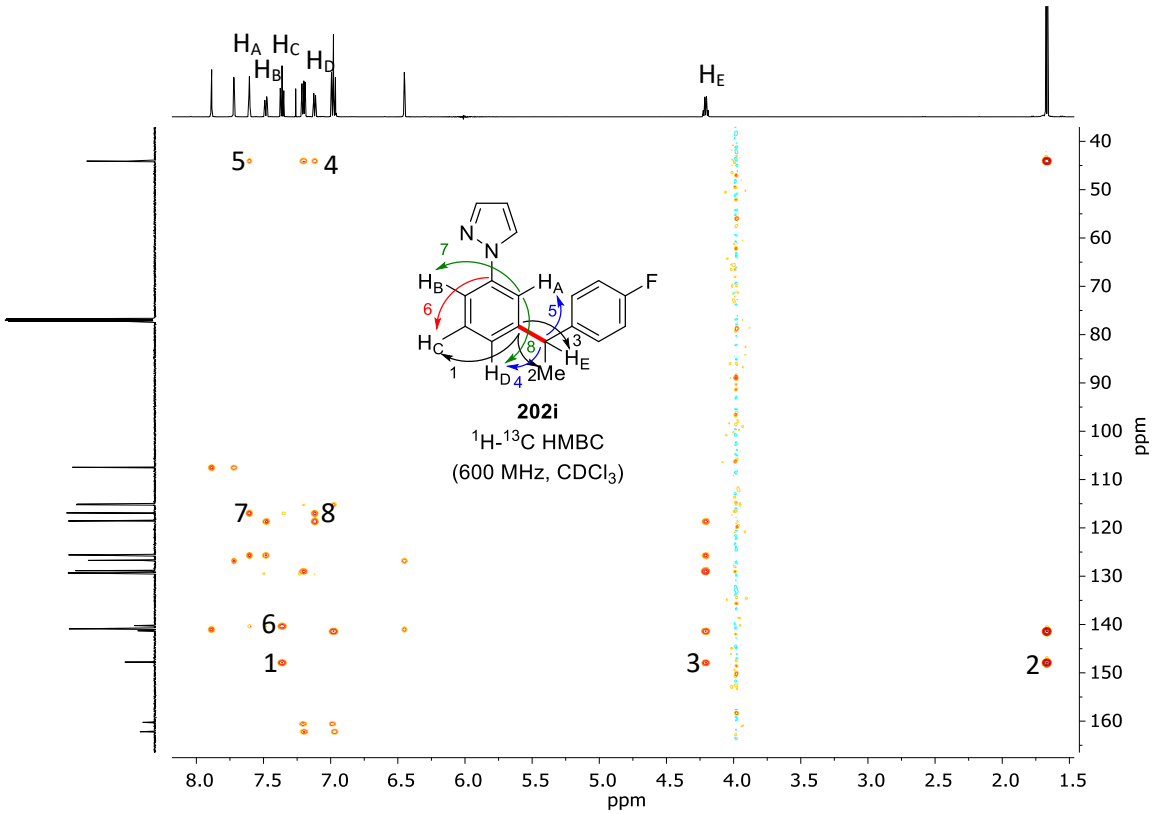
202i
(600 MHz, $CDCl_3$)



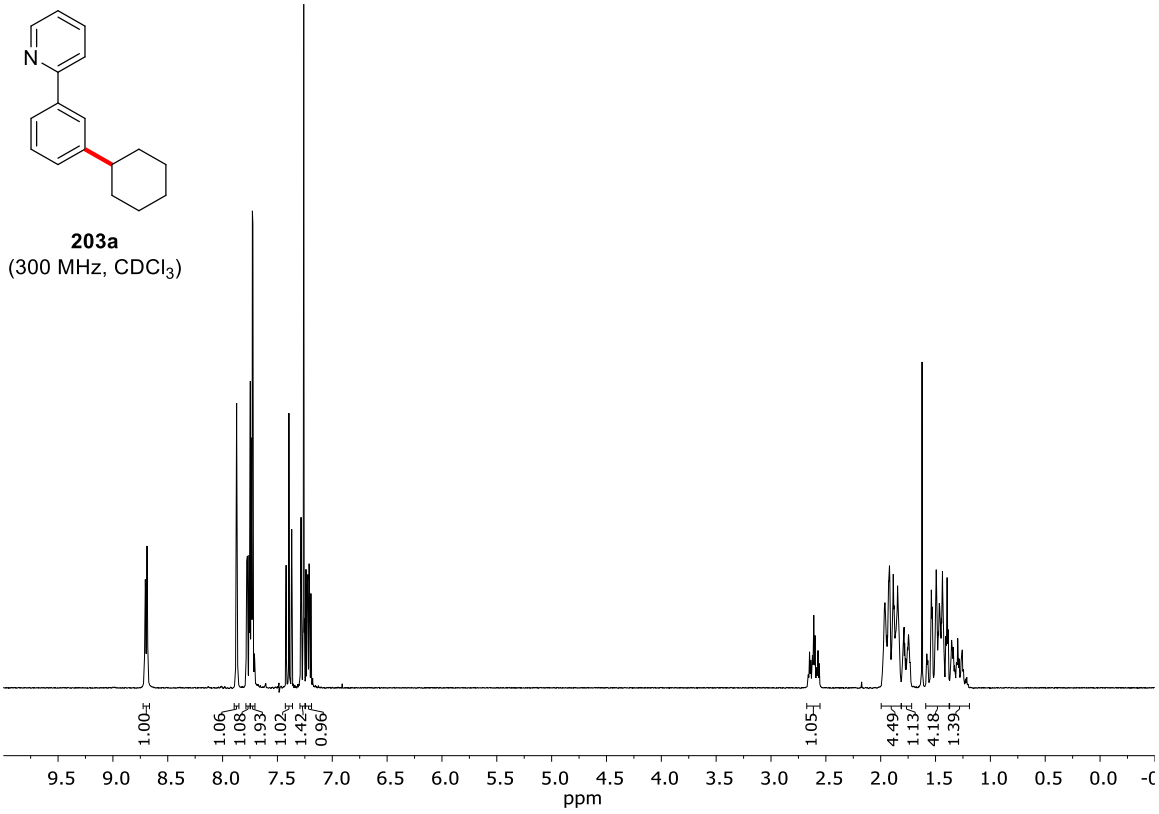
202i
(125 MHz, $CDCl_3$)



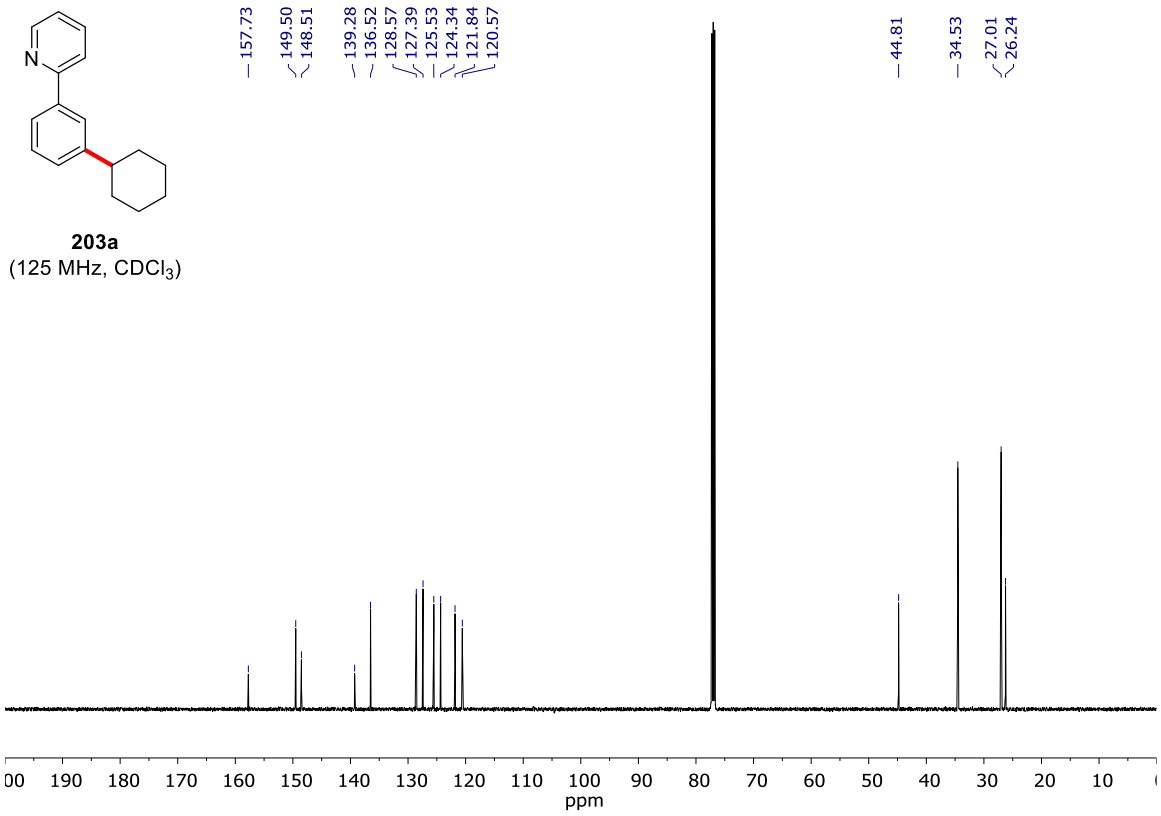
202i
^{19}F-NMR
(376 MHz, $CDCl_3$)



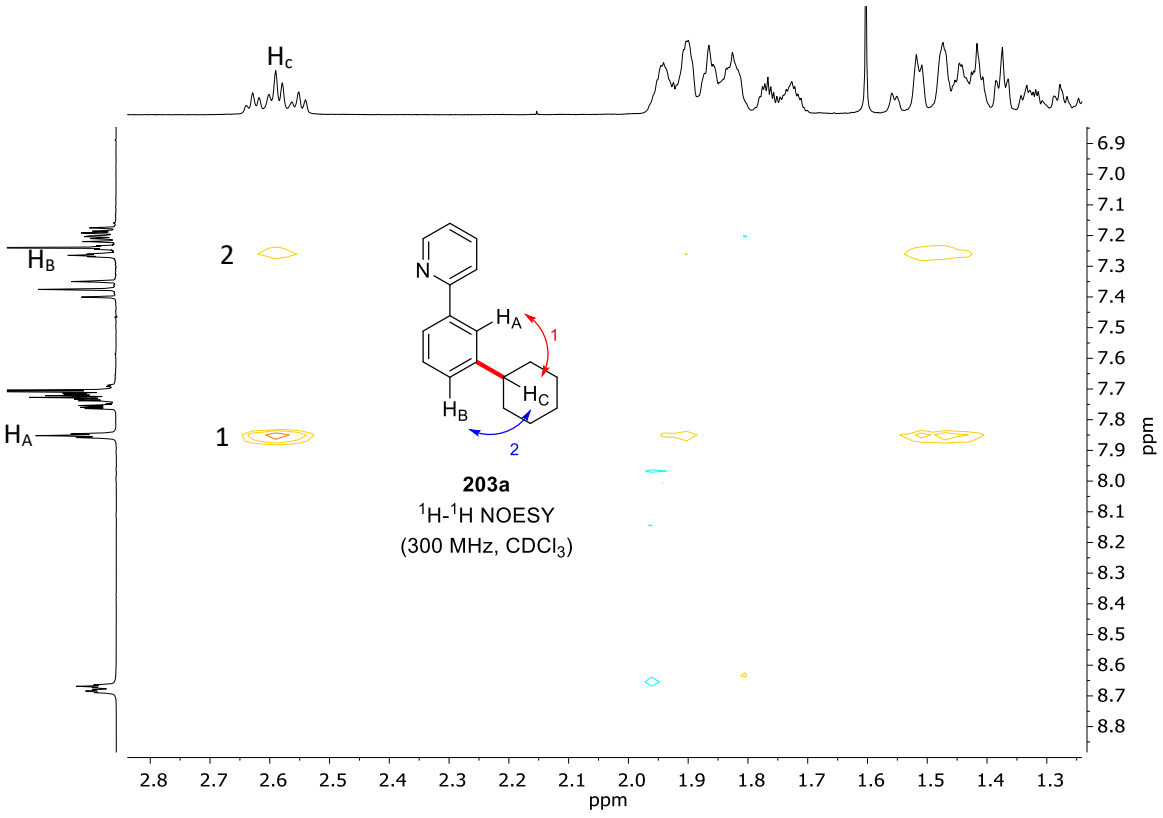
202i
^{1}H-^{13}C HMBC
(600 MHz, $CDCl_3$)



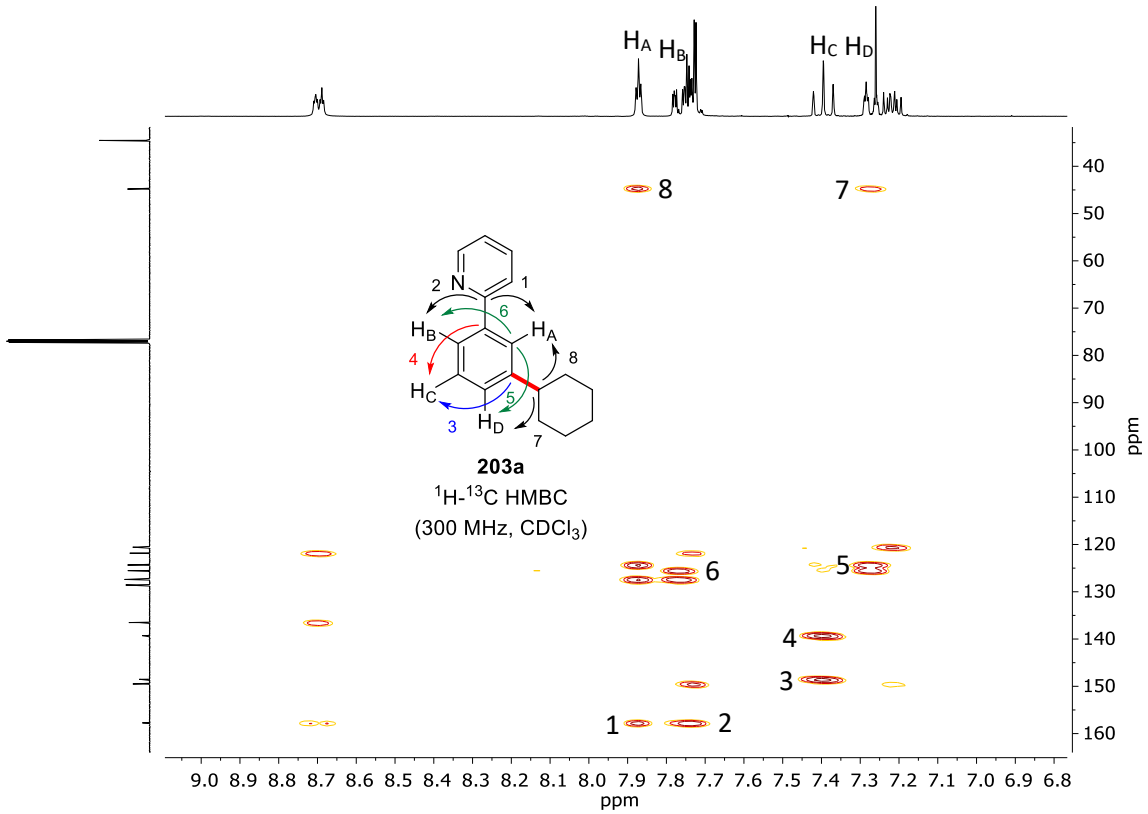
203a
(300 MHz, $CDCl_3$)

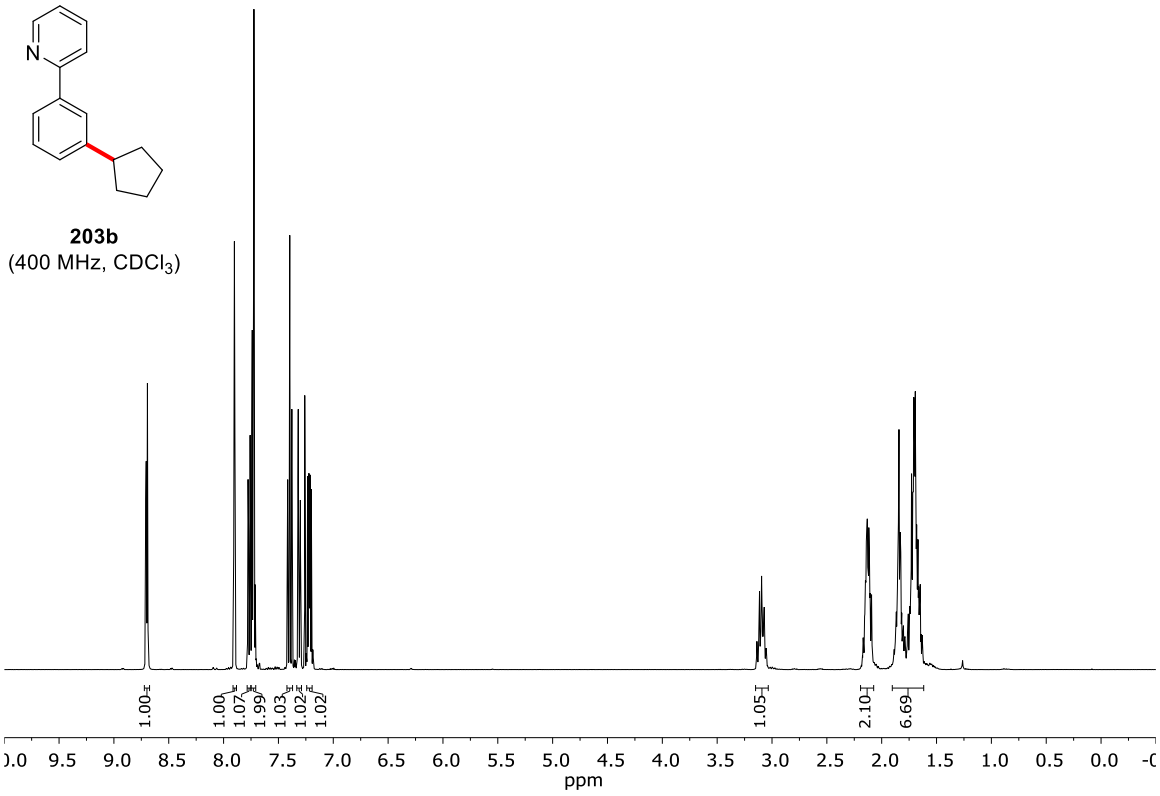


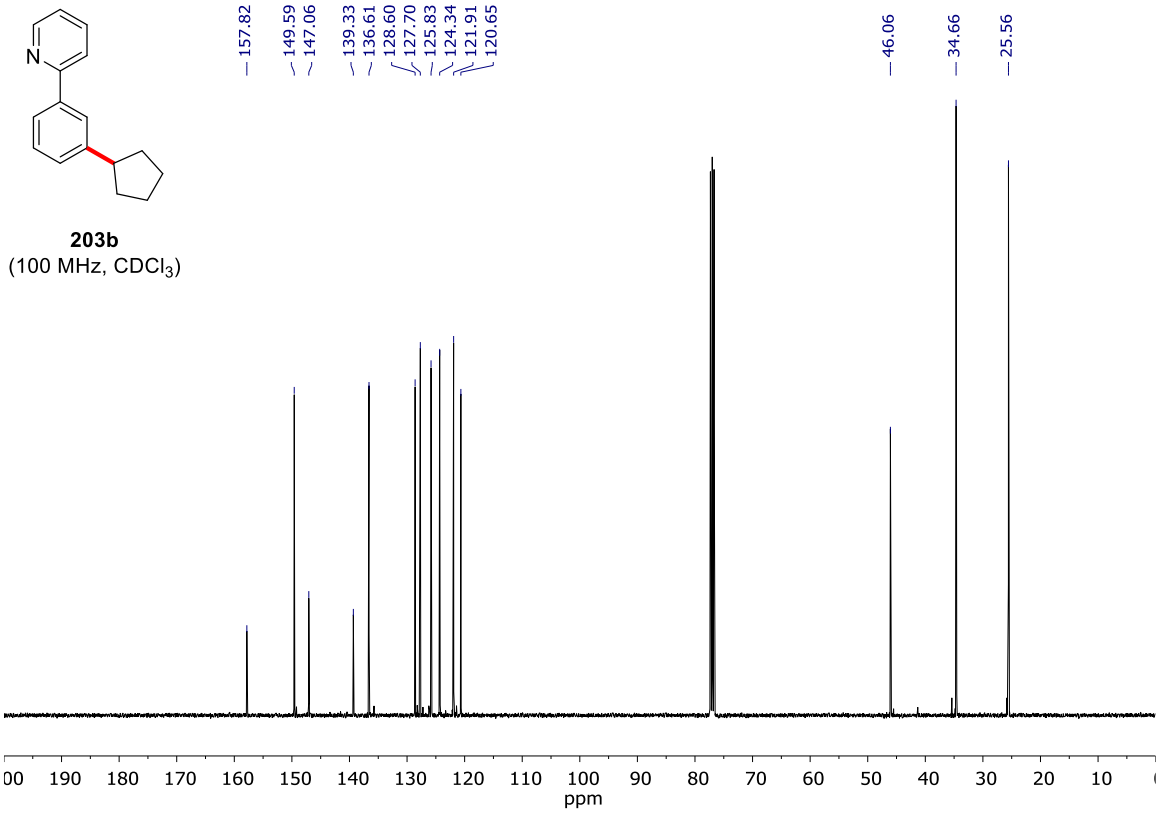
203a
(125 MHz, $CDCl_3$)



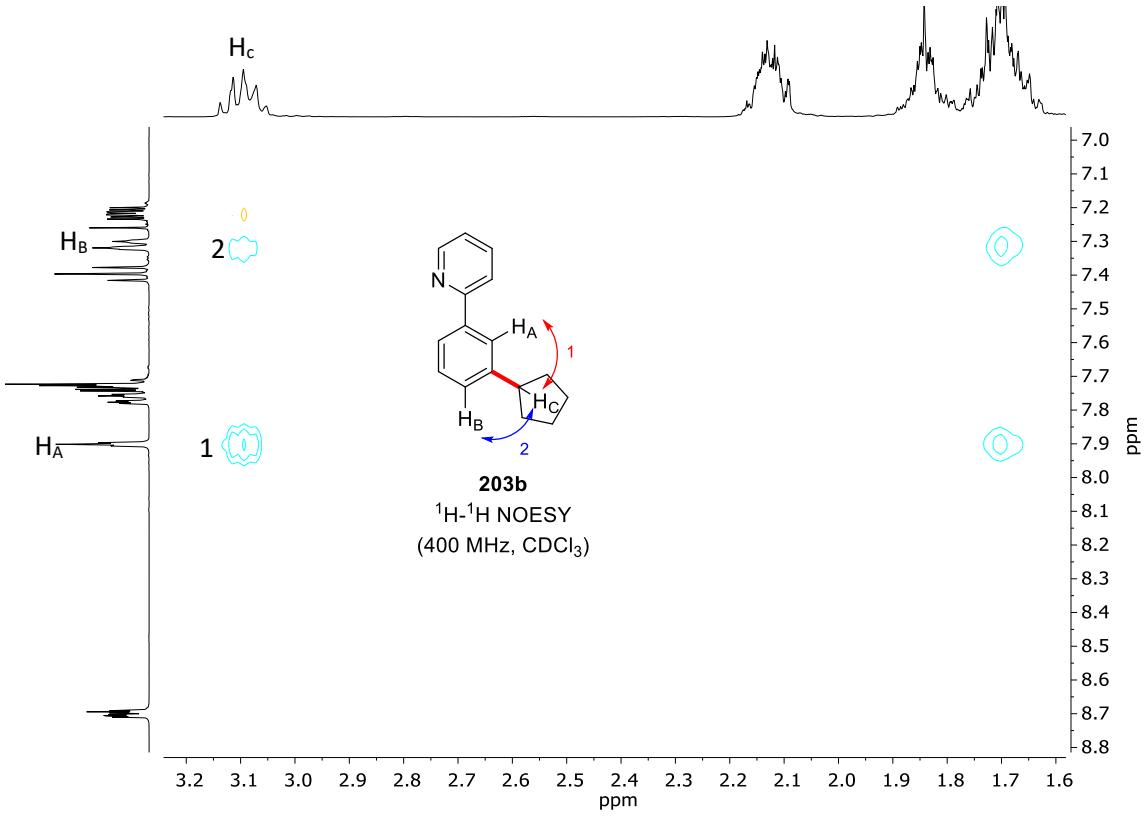
203a
^1H-^1H NOESY
(300 MHz, $CDCl_3$)


HA HB
HC HD
8
7
6
5
4
3
1
2
203a
1H-13C HMBC
(300 MHz, CDCl3)
ppm
ppm

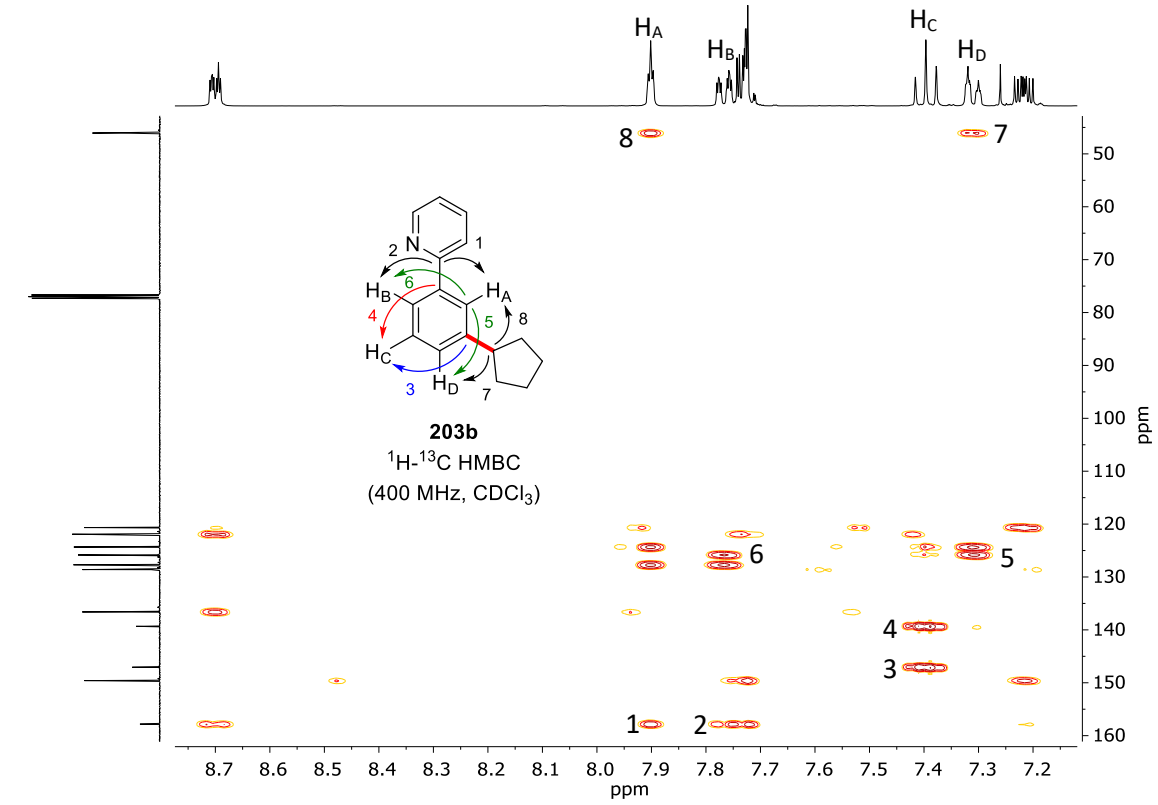

203b
(400 MHz, CDCl3)
1.00
1.00
1.07
1.99
1.03
1.02
1.02
1.05
2.10
6.69
ppm

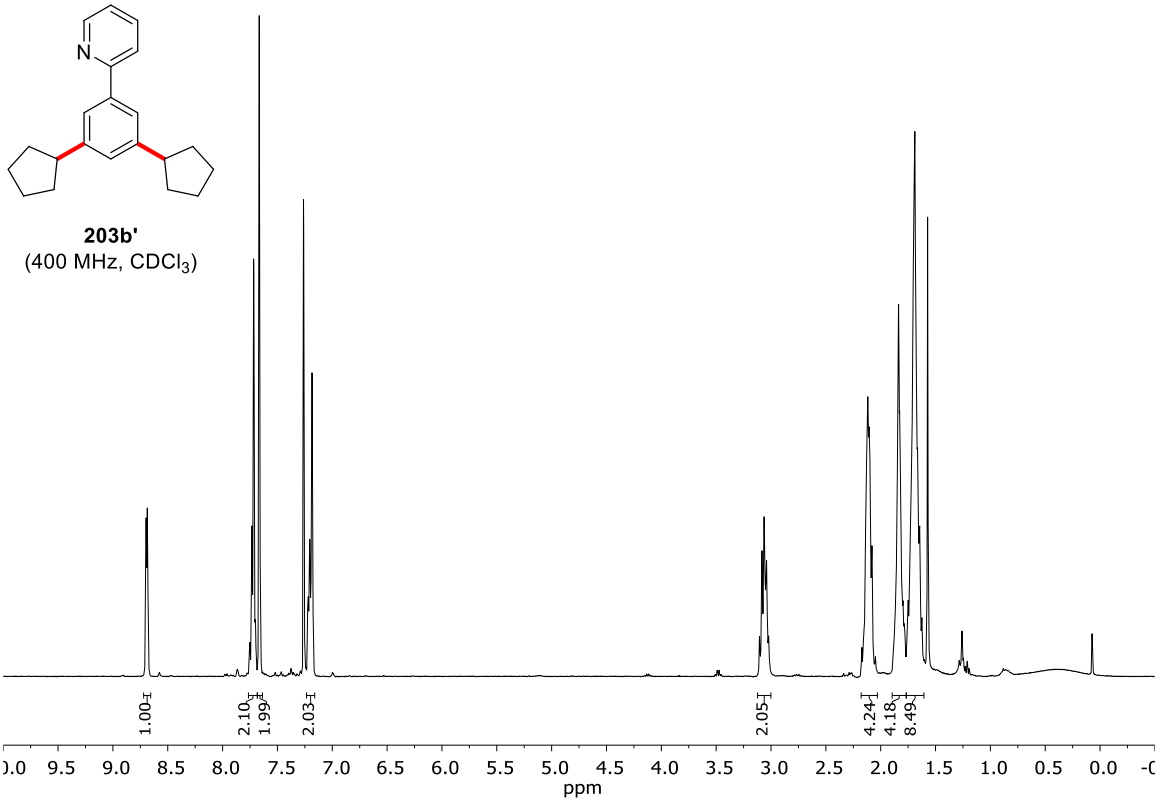


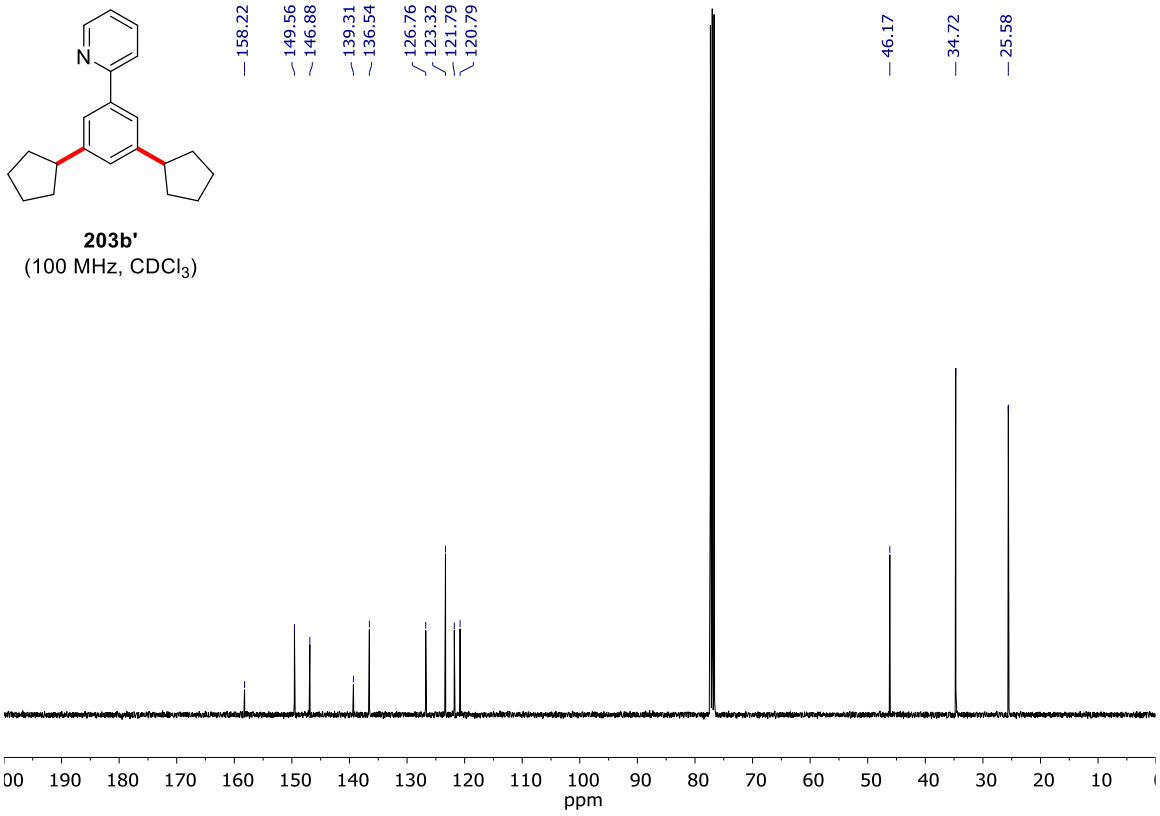
203b
(100 MHz, $CDCl_3$)



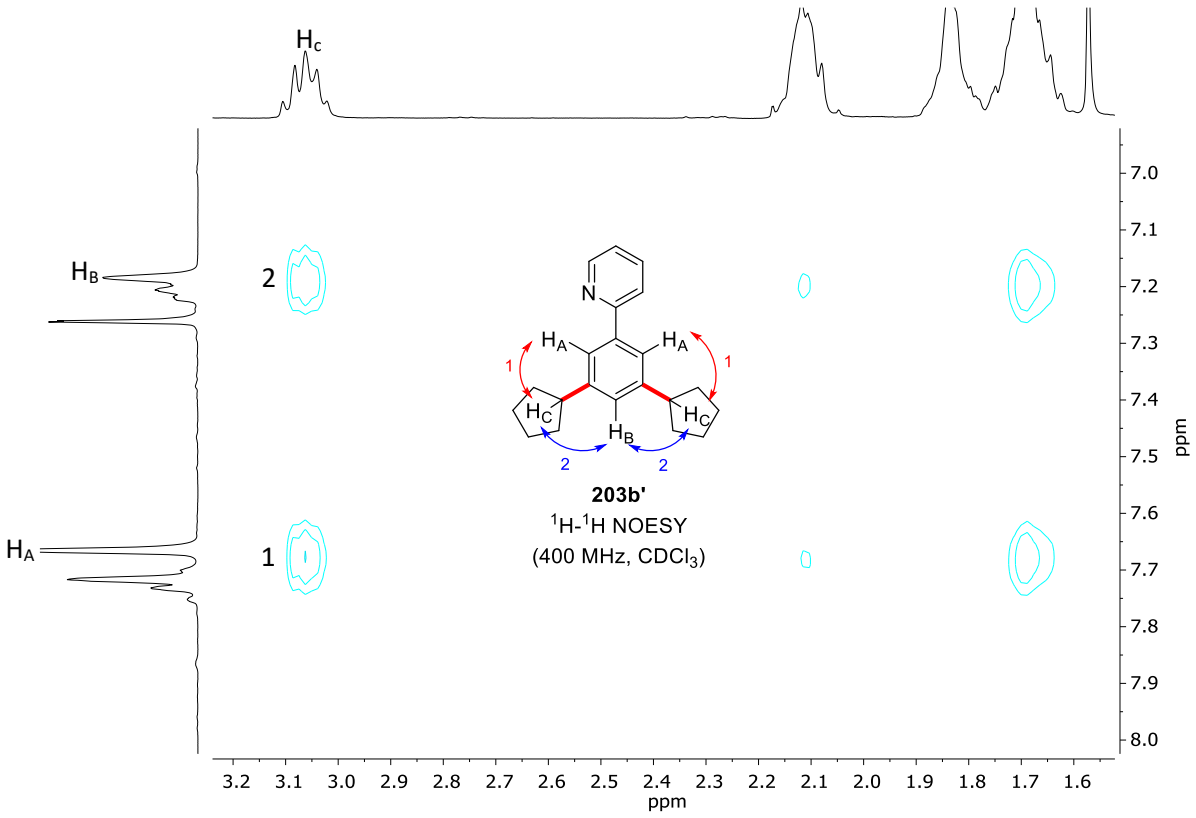
203b
^1H-^1H NOESY
(400 MHz, $CDCl_3$)


HA
HB
HC
HD
8
7
6
5
4
3
1
2
203b
1H-13C HMBC
(400 MHz, CDCl3)
ppm
ppm

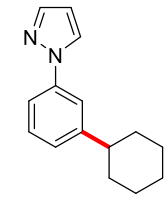

203b'
(400 MHz, CDCl3)
1.00
2.10
1.99
2.03
2.05
4.24
4.18
8.49
ppm



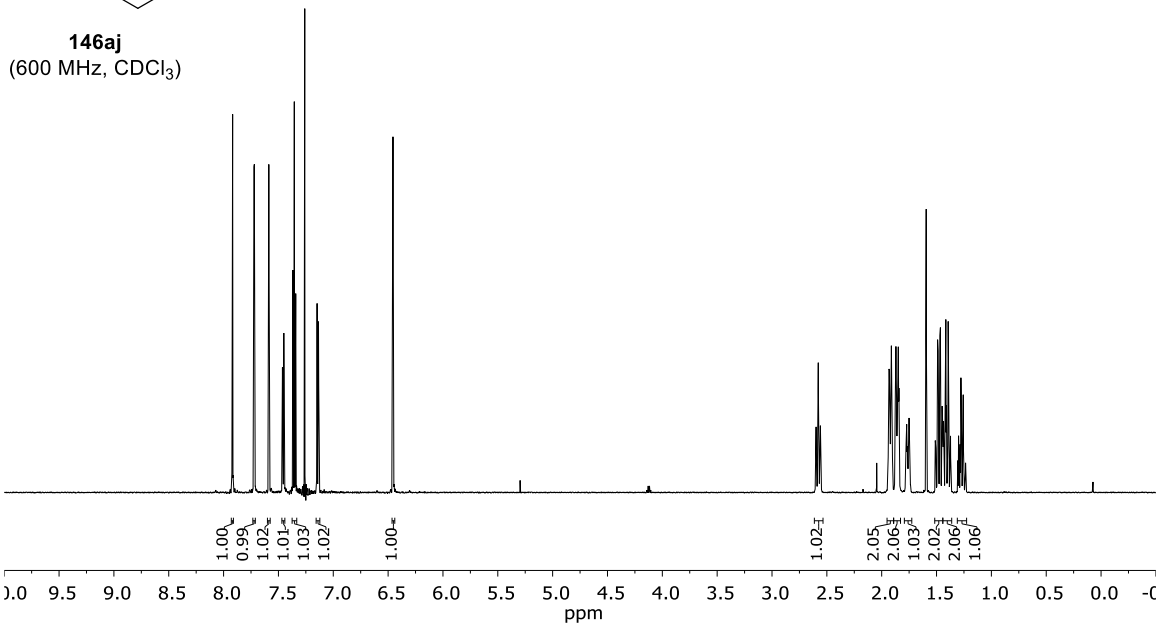
203b'
(100 MHz, $CDCl_3$)

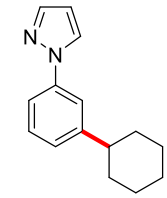


203b'
^1H-^1H NOESY
(400 MHz, $CDCl_3$)

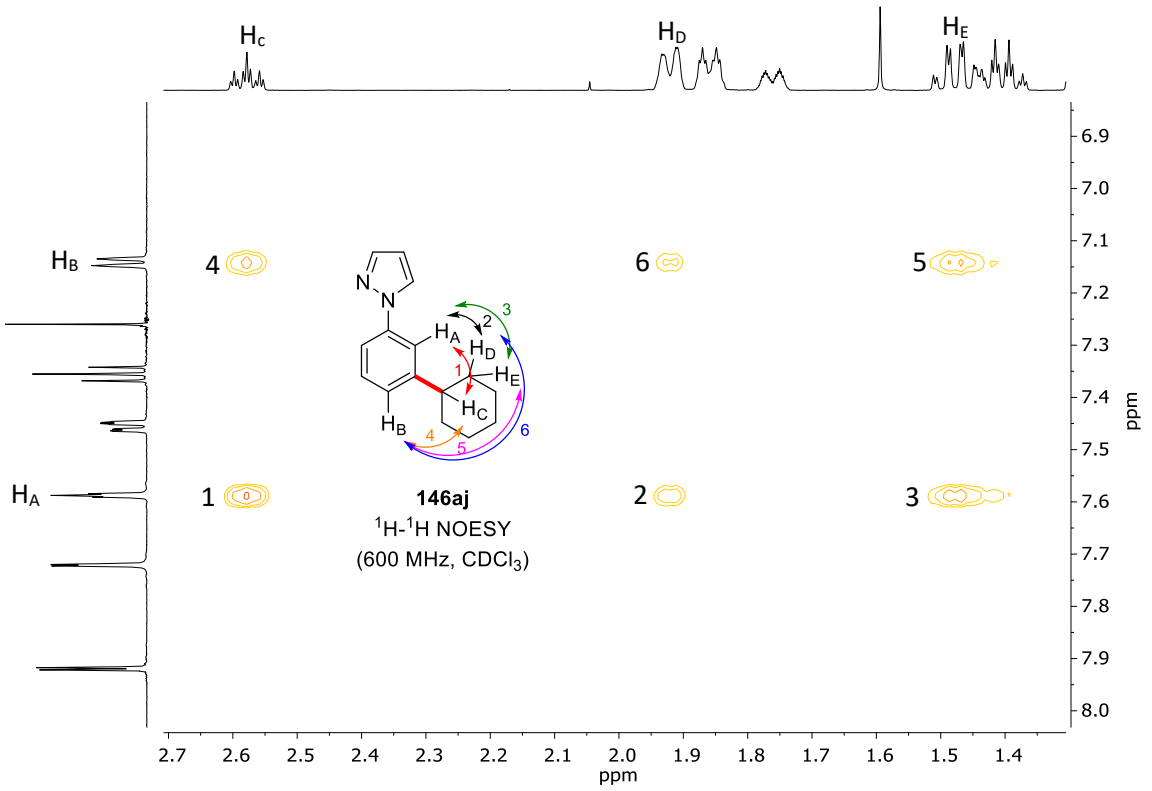


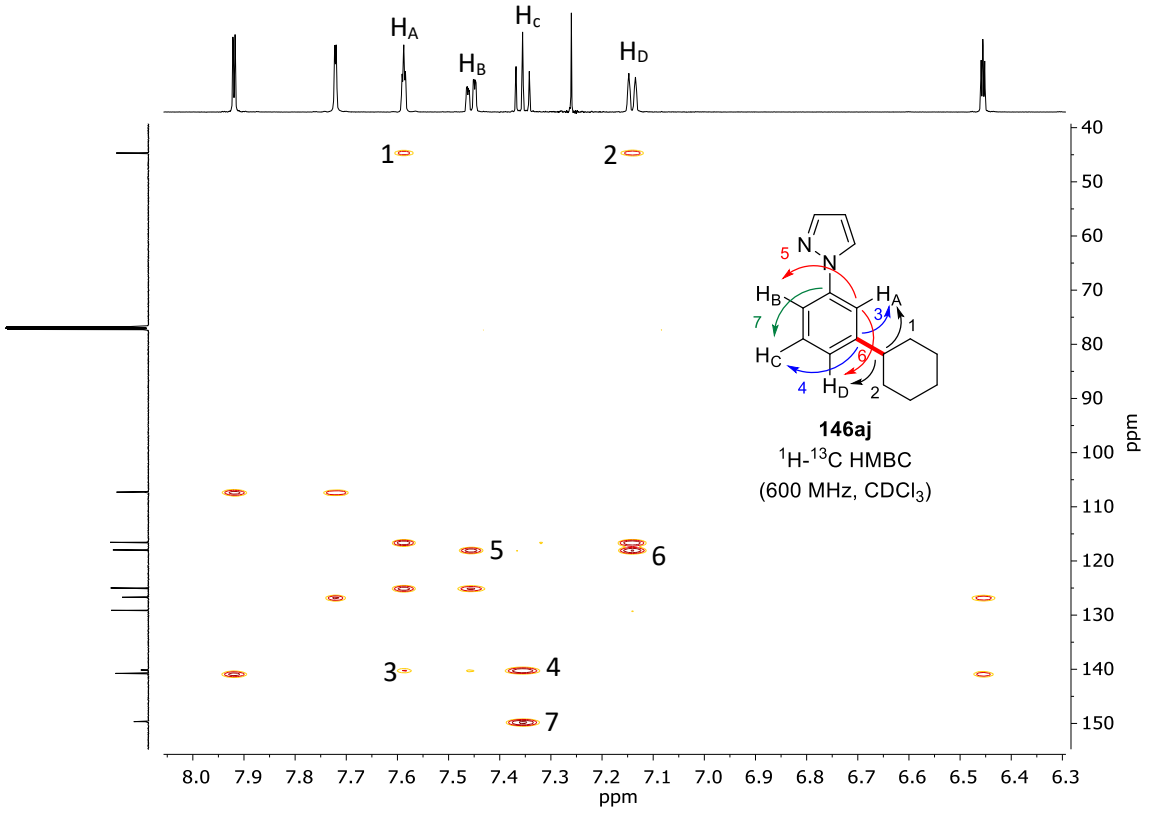
146aj
(600 MHz, $CDCl_3$)

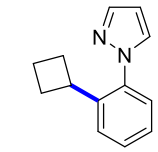




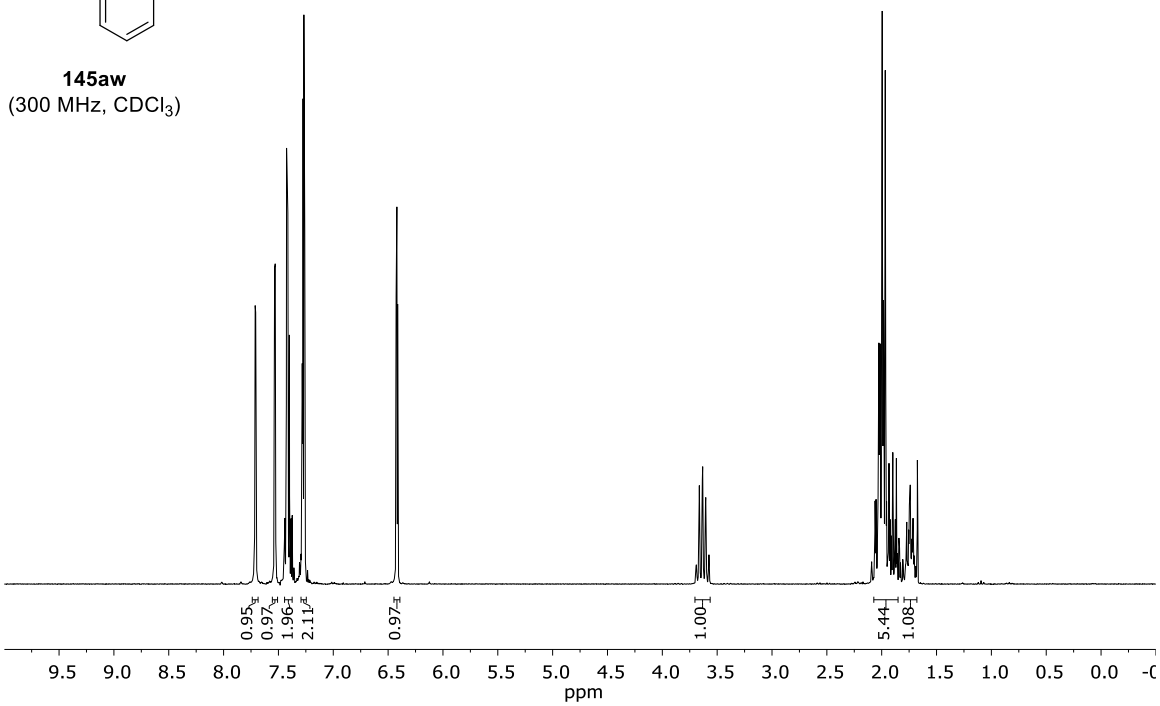
146aj
(125 MHz, $CDCl_3$)

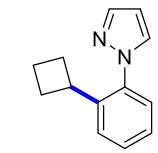

Hc
HD
HE
HB
HA
4
6
5
1
2
3
146aj
1H-1H NOESY
(600 MHz, CDCl3)
ppm
ppm


HA
HB
Hc
HD
1
2
5
6
3
4
7
146aj
1H-13C HMBC
(600 MHz, CDCl3)
ppm
ppm

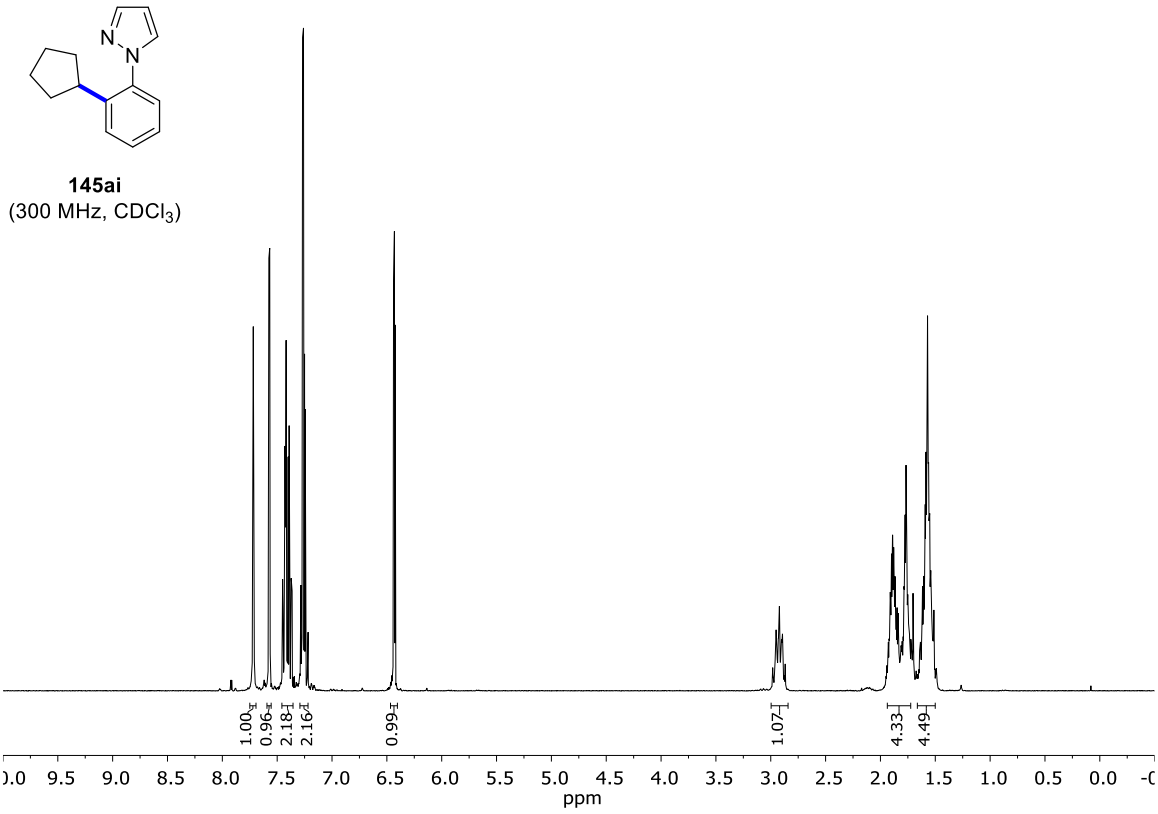


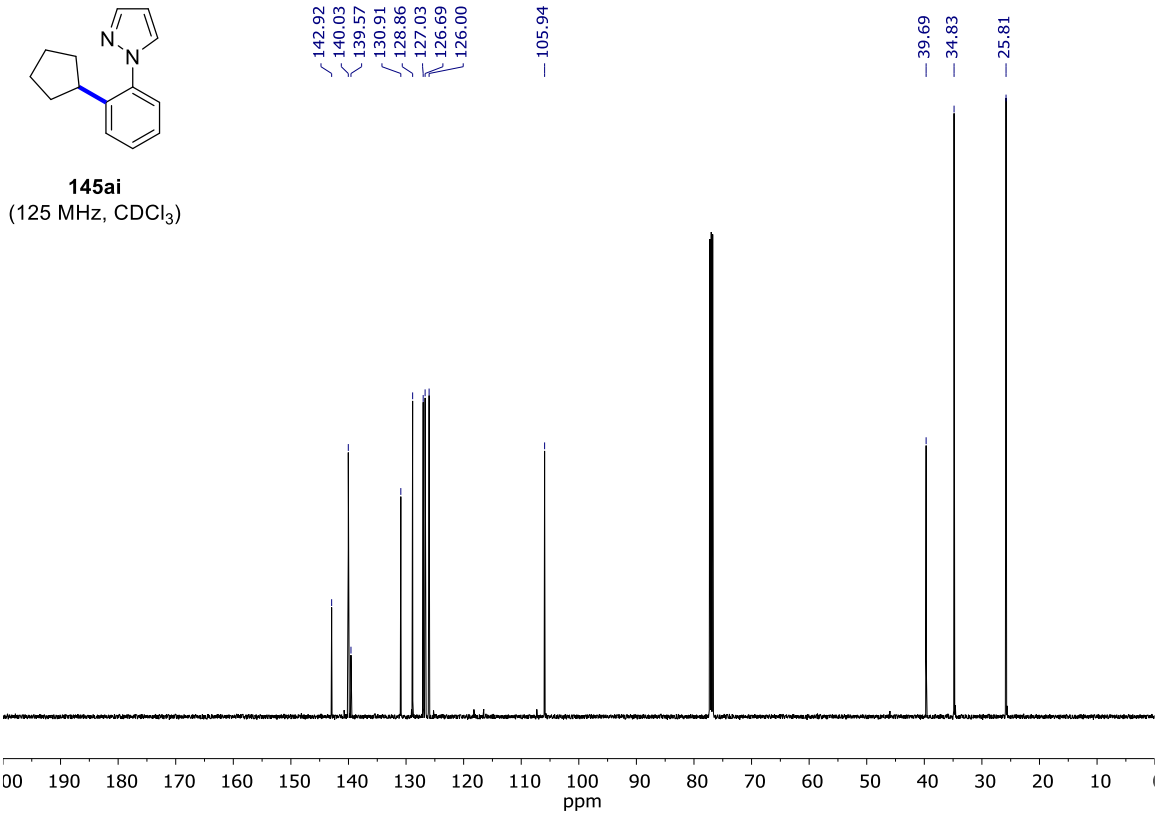
145aw
(300 MHz, $CDCl_3$)

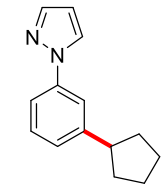




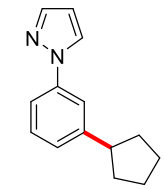
145aw
(125 MHz, $CDCl_3$)


145ai
(300 MHz, CDCl3)
1.00
0.96
2.18
2.16
0.99
1.07
4.33
4.49
ppm

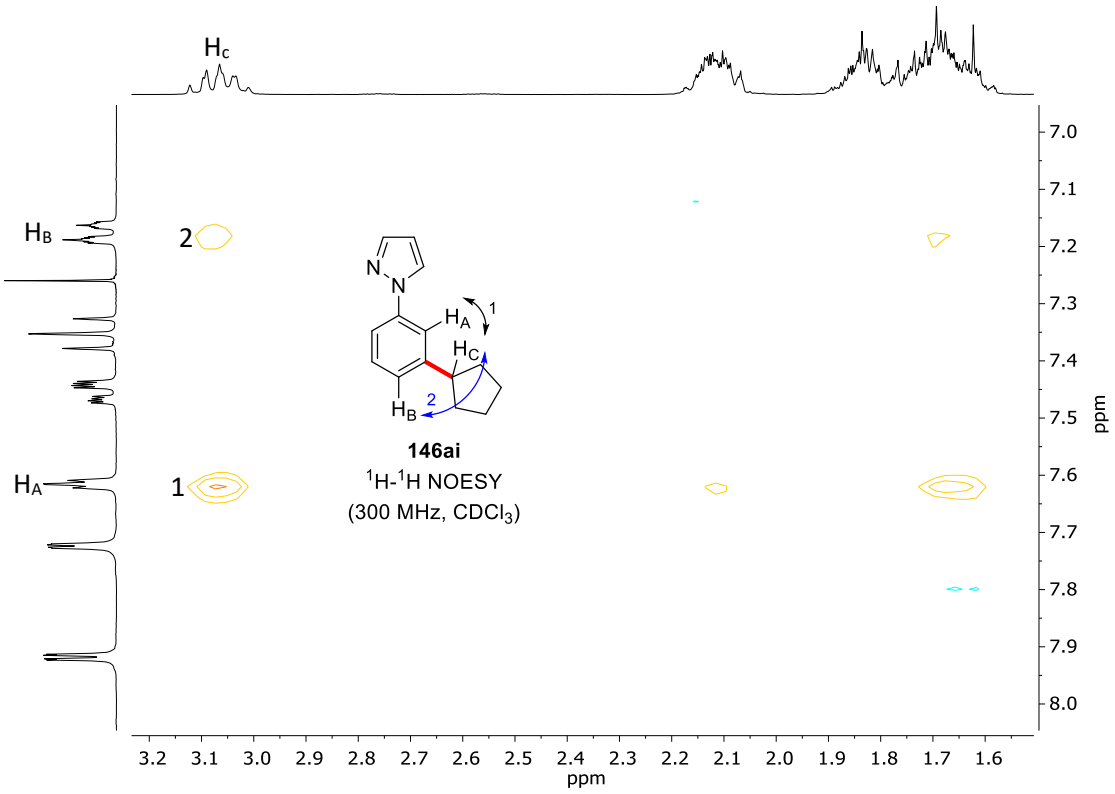

145ai
(125 MHz, CDCl3)
142.92
140.03
139.57
130.91
128.86
127.03
126.69
126.00
105.94
39.69
34.83
25.81
ppm

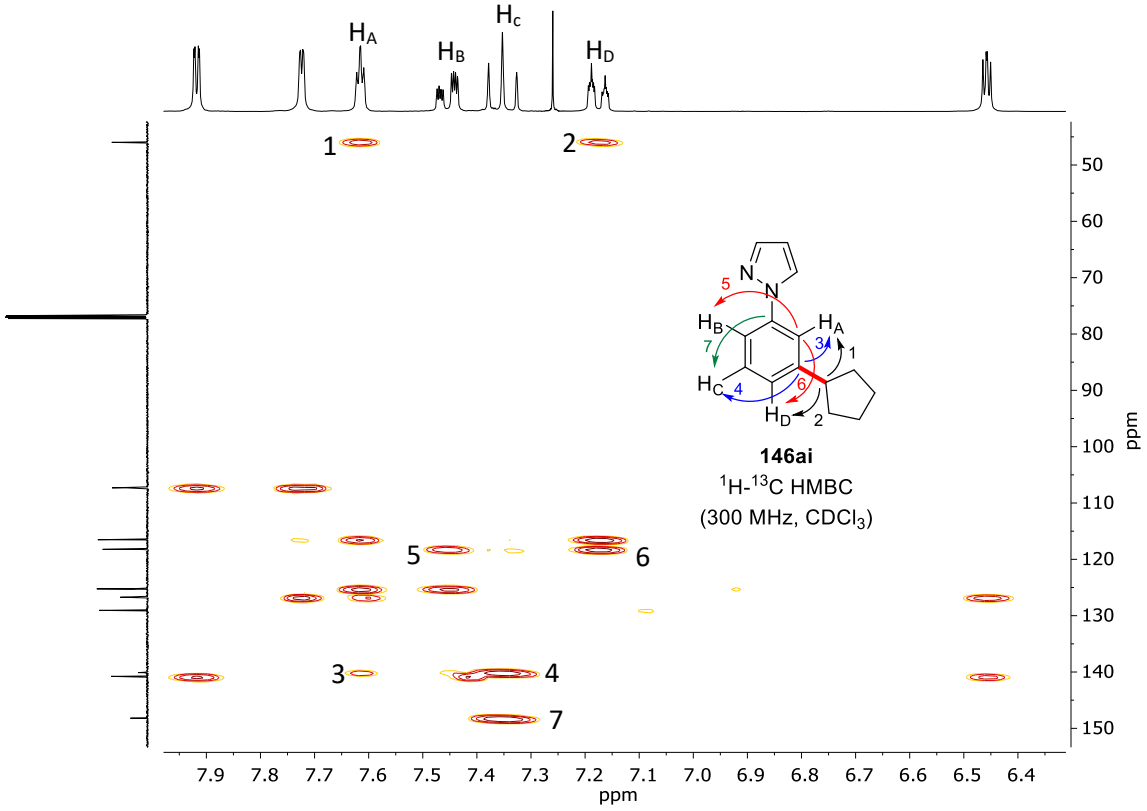


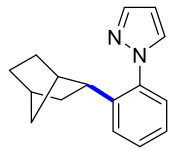
146ai
(300 MHz, $CDCl_3$)



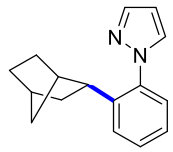
146ai
(125 MHz, $CDCl_3$)


Hc
HB
HA
2
1
N
N
HA
1
HC
HB
2
146ai
1H-1H NOESY
(300 MHz, CDCl3)
7.0
7.1
7.2
7.3
7.4
7.5
7.6
7.7
7.8
7.9
8.0
ppm
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
ppm

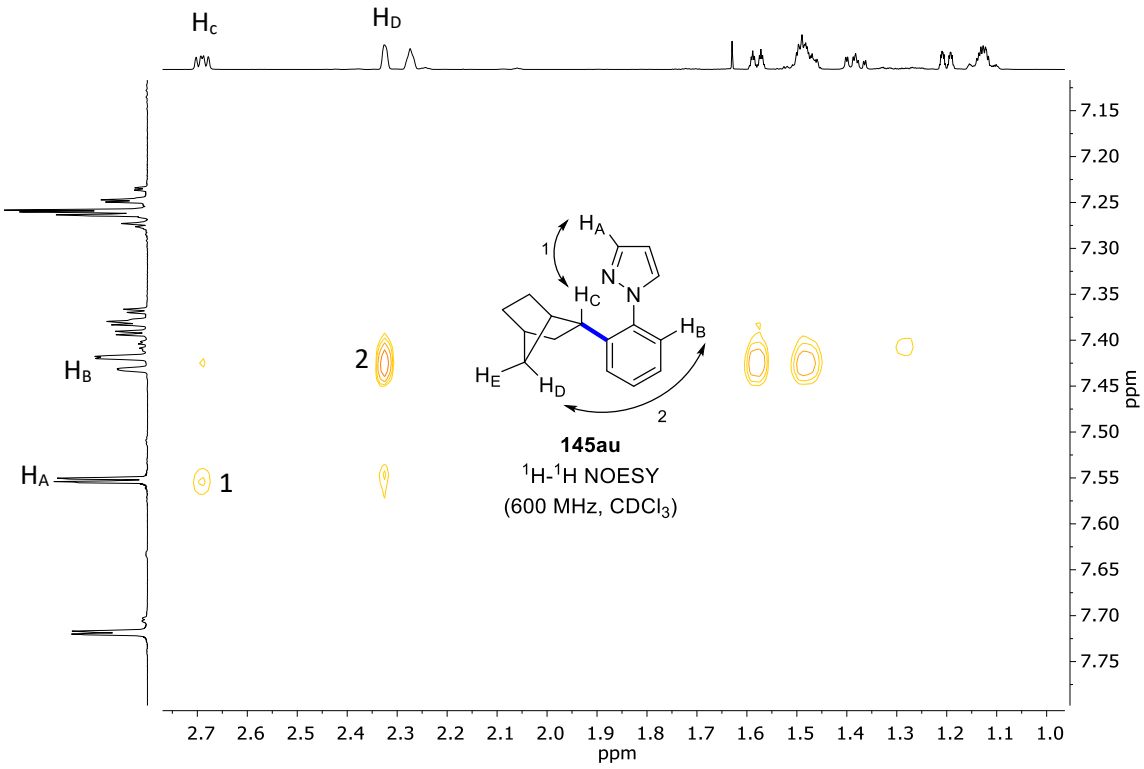

HA
HB
Hc
HD
1
2
5
6
3
4
7
N
N
5
HB
7
HA
3
4
1
HC
6
HD
2
146ai
1H-13C HMBC
(300 MHz, CDCl3)
50
60
70
80
90
100
110
120
130
140
150
ppm
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
6.5
6.4
ppm

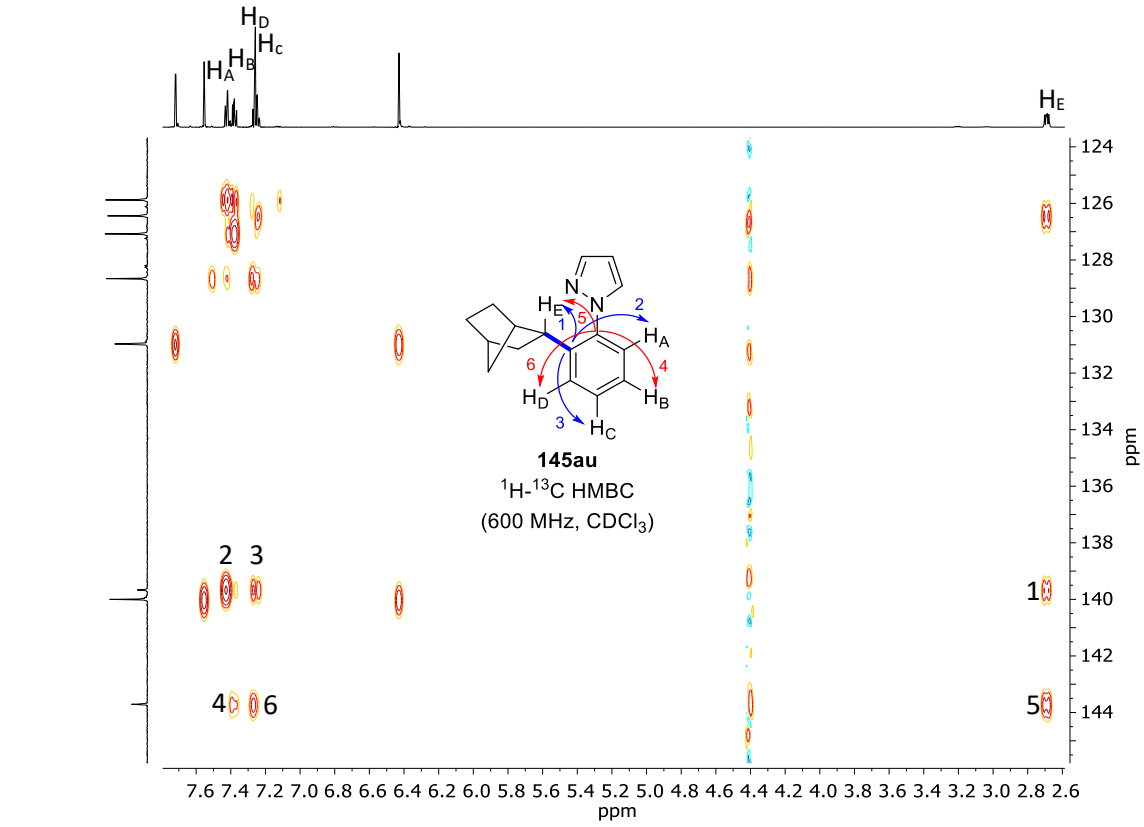


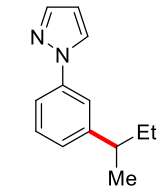
145au
(600 MHz, $CDCl_3$)



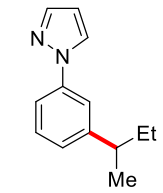
145au
(125 MHz, $CDCl_3$)


Hc
HD
HB
HA
1
2
HA
HC
HB
HE
HD
1
2
145au
1H-1H NOESY
(600 MHz, CDCl3)
7.15
7.20
7.25
7.30
7.35
7.40
7.45
7.50
7.55
7.60
7.65
7.70
7.75
ppm
2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0
ppm

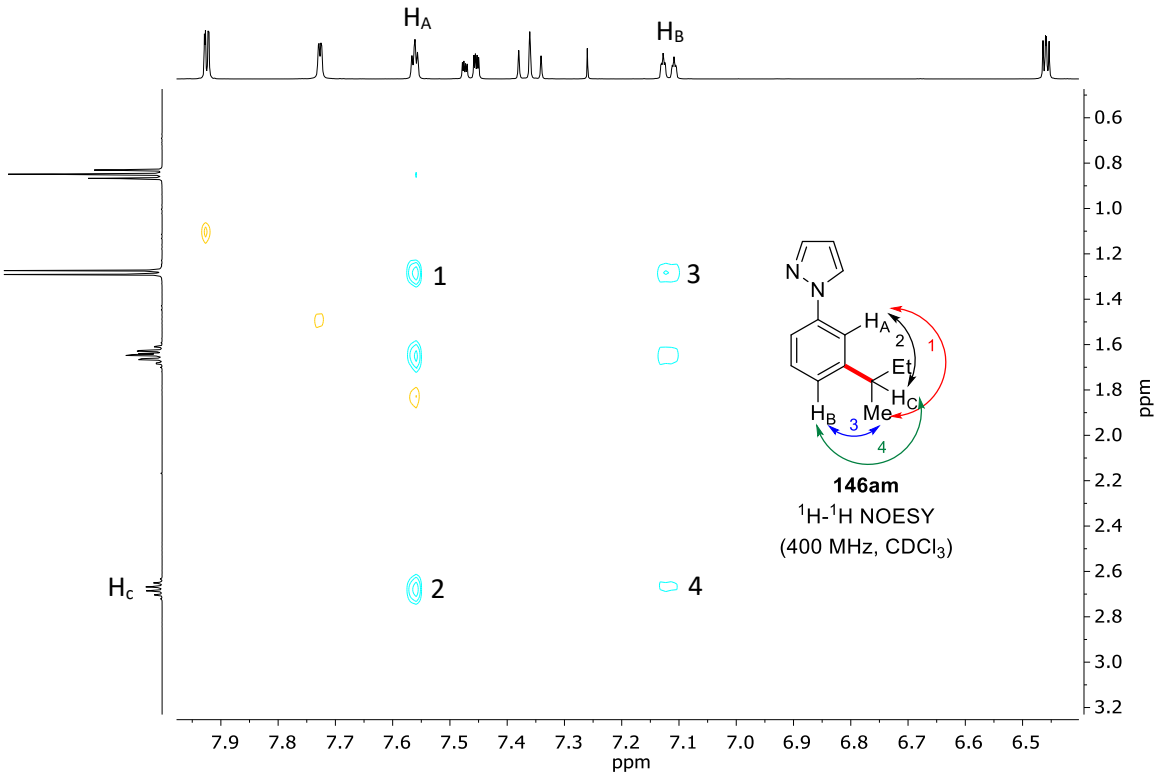

HD
HA
HB
Hc
HE
HE
1
5
2
HA
6
4
HD
HB
3
HC
145au
1H-13C HMBC
(600 MHz, CDCl3)
2 3
4 6
1
5
124
126
128
130
132
134
136
138
140
142
144
ppm
7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6
ppm

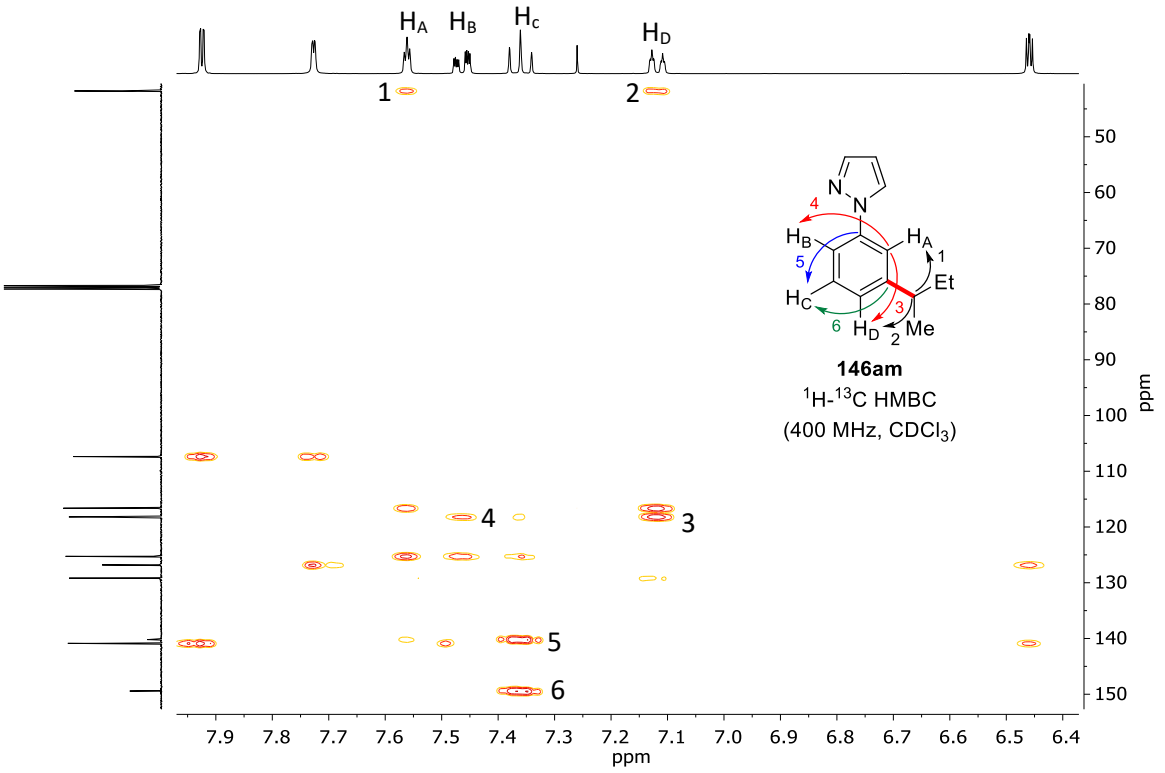


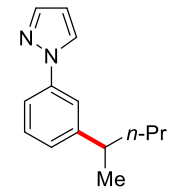
146am
(400 MHz, $CDCl_3$)



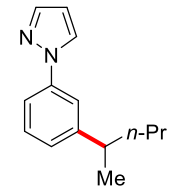
146am
(100 MHz, $CDCl_3$)


HA
HB
HC
1
2
3
4
146am
1H-1H NOESY
(400 MHz, CDCl3)
ppm

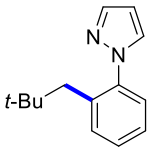

HA
HB
Hc
HD
1
2
3
4
5
6
146am
1H-13C HMBC
(400 MHz, CDCl3)
ppm



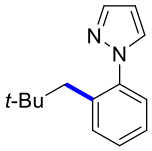
146an
(400 MHz, $CDCl_3$)



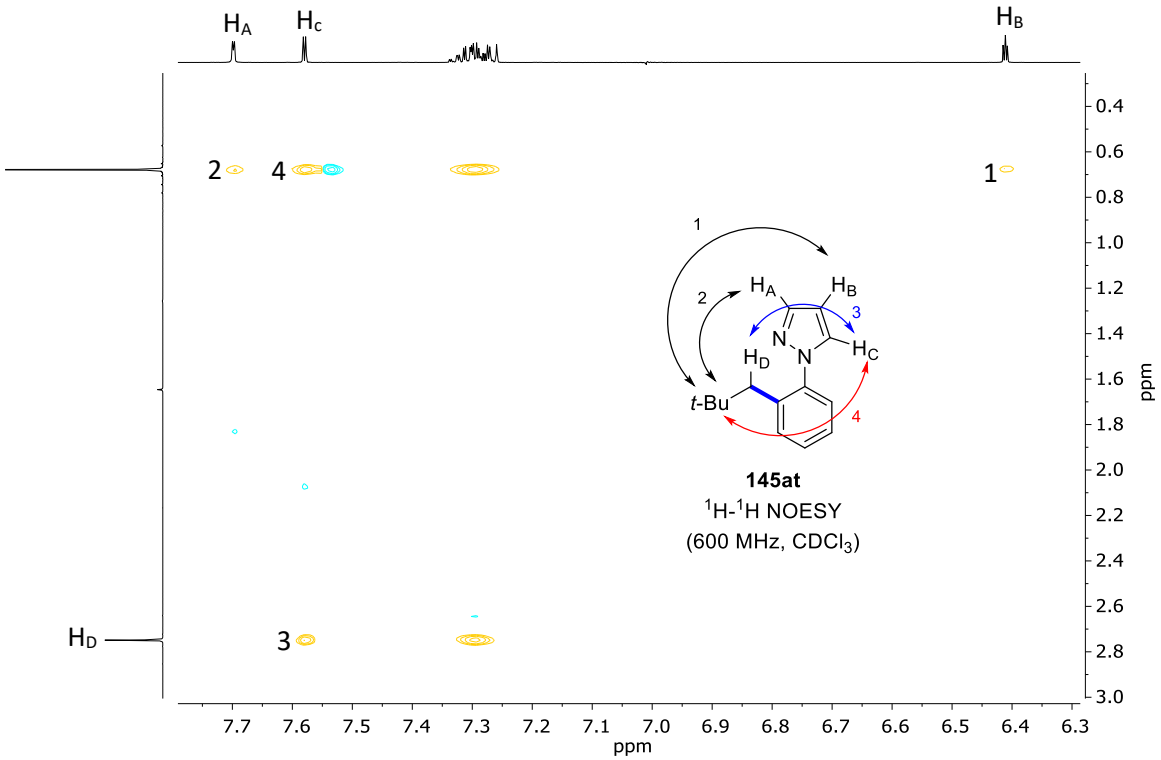
146an
(100 MHz, $CDCl_3$)



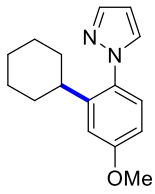
145at
(600 MHz, $CDCl_3$)



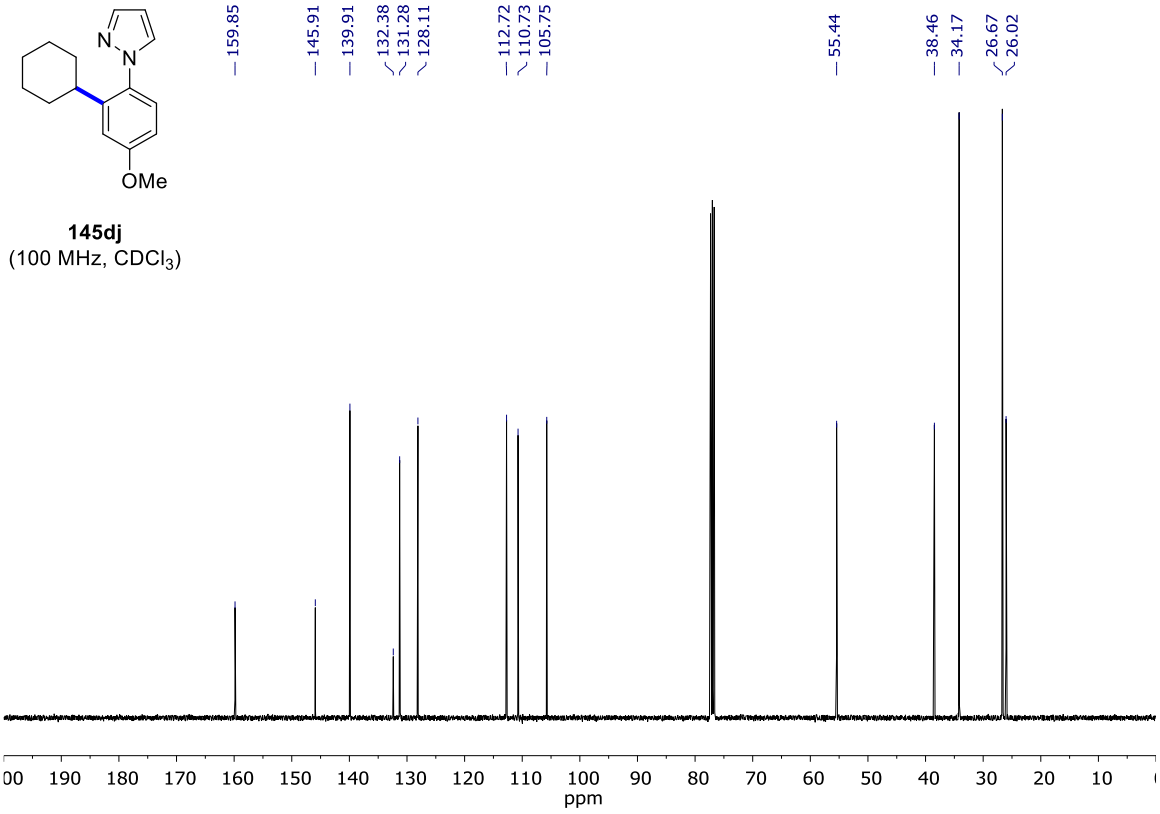
145at
(100 MHz, $CDCl_3$)



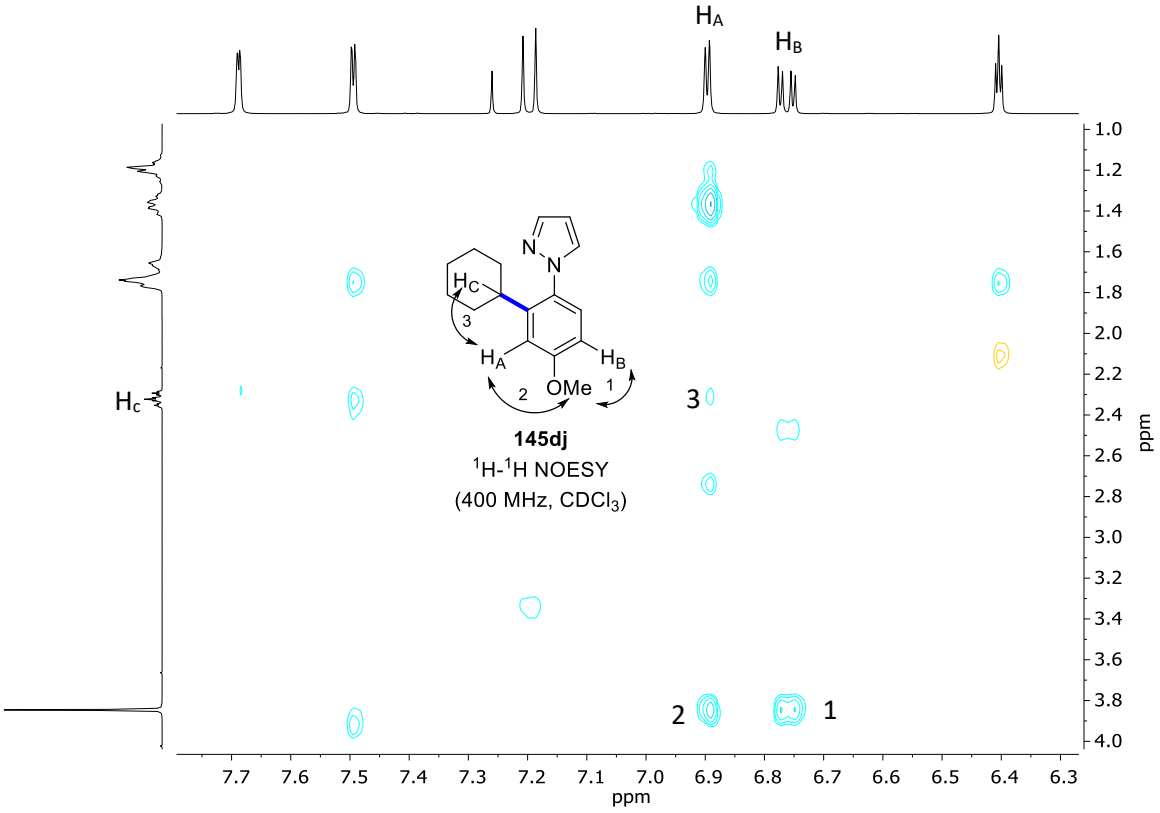
145at
^{1}H-^{1}H NOESY
(600 MHz, $CDCl_3$)



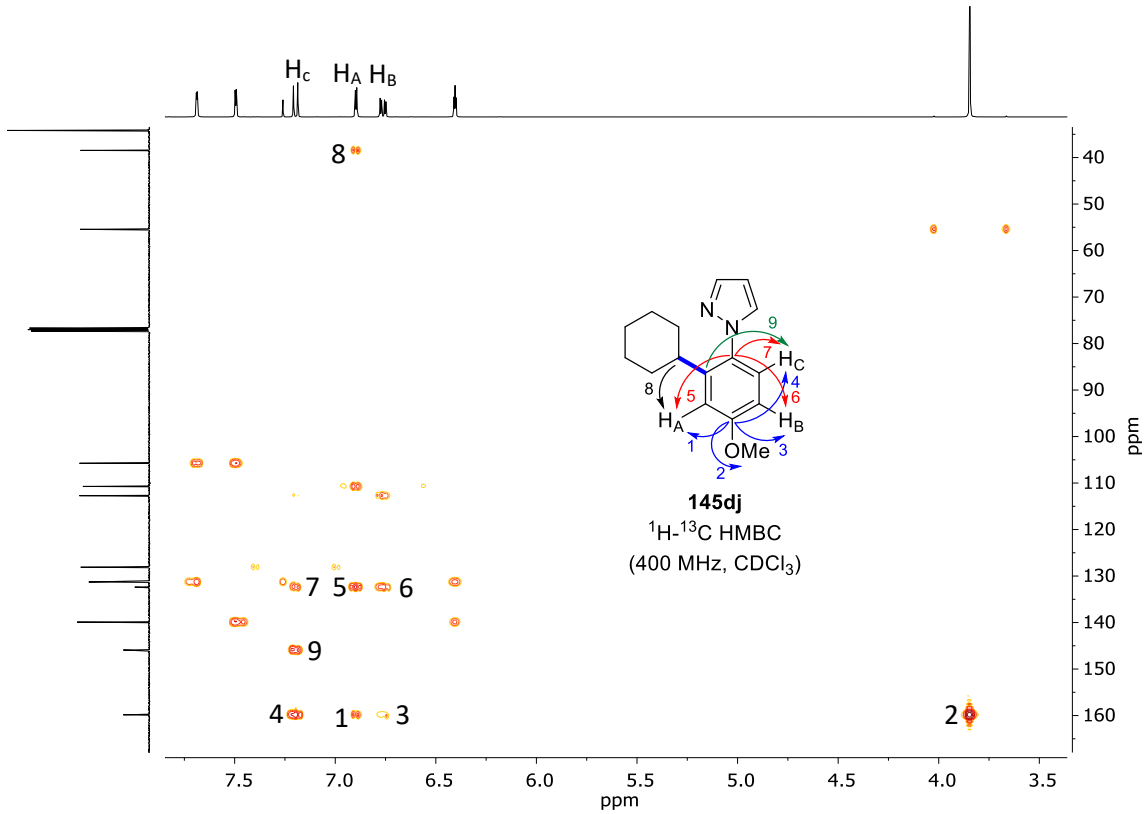
145dj
(400 MHz, $CDCl_3$)



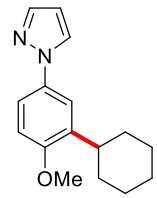
145dj
(100 MHz, $CDCl_3$)



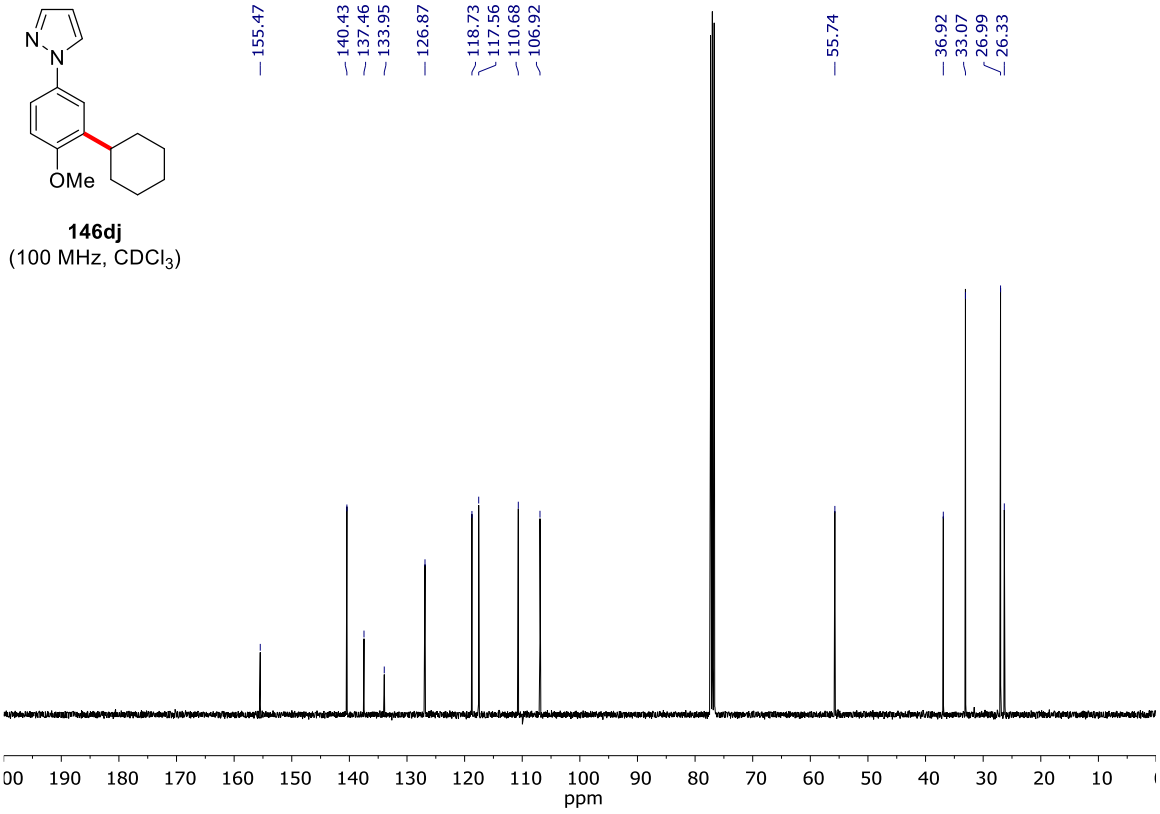
145dj
^1H-^1H NOESY
(400 MHz, $CDCl_3$)



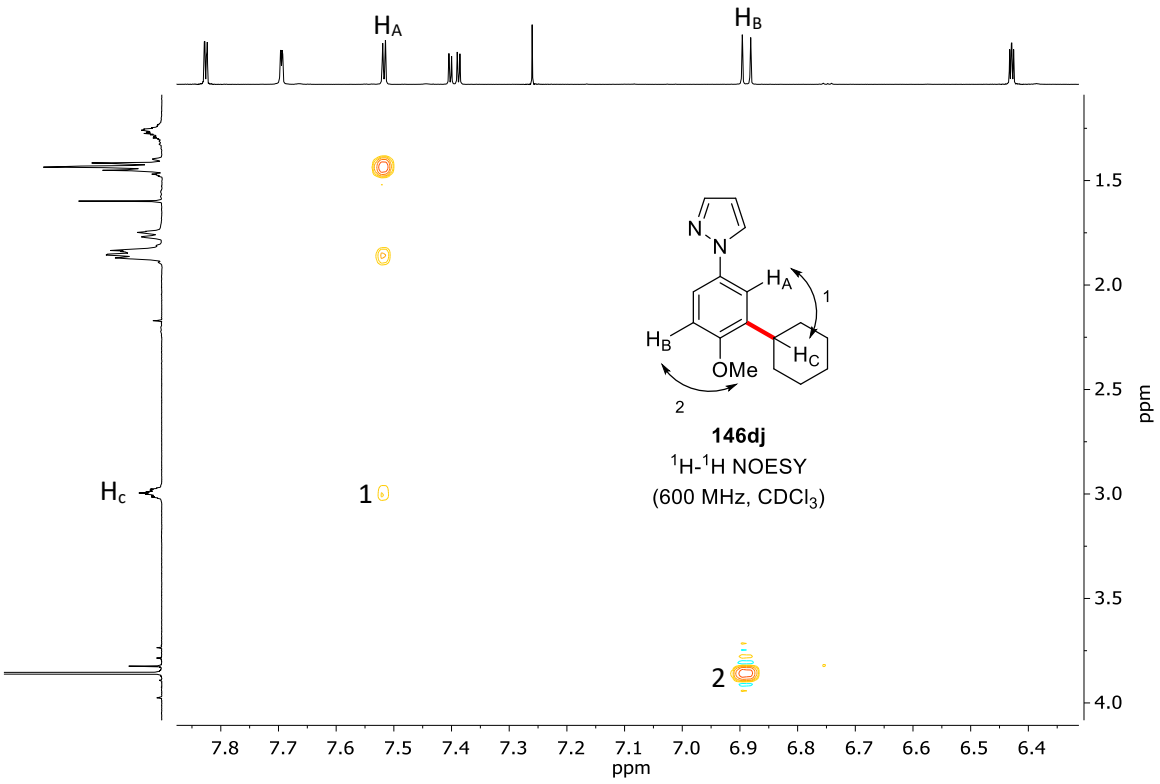
145dj
^{1}H-^{13}C HMBC
(400 MHz, $CDCl_3$)



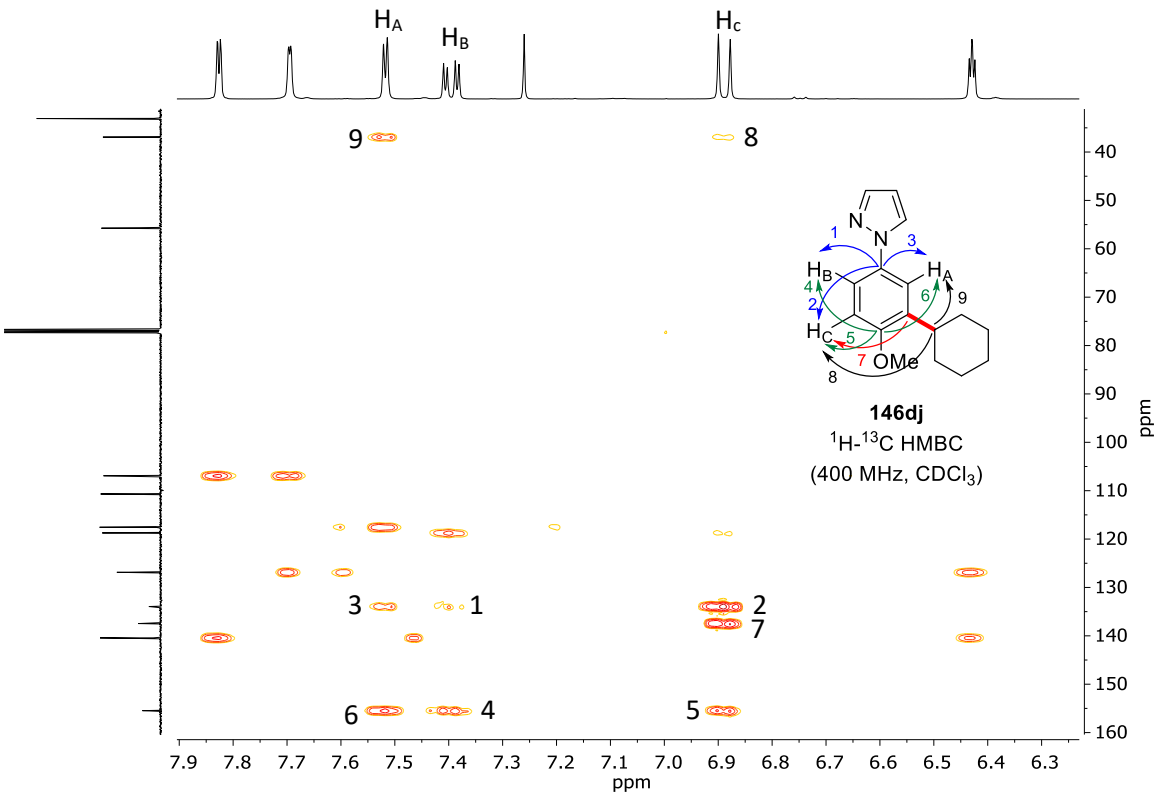
146dj
(400 MHz, $CDCl_3$)

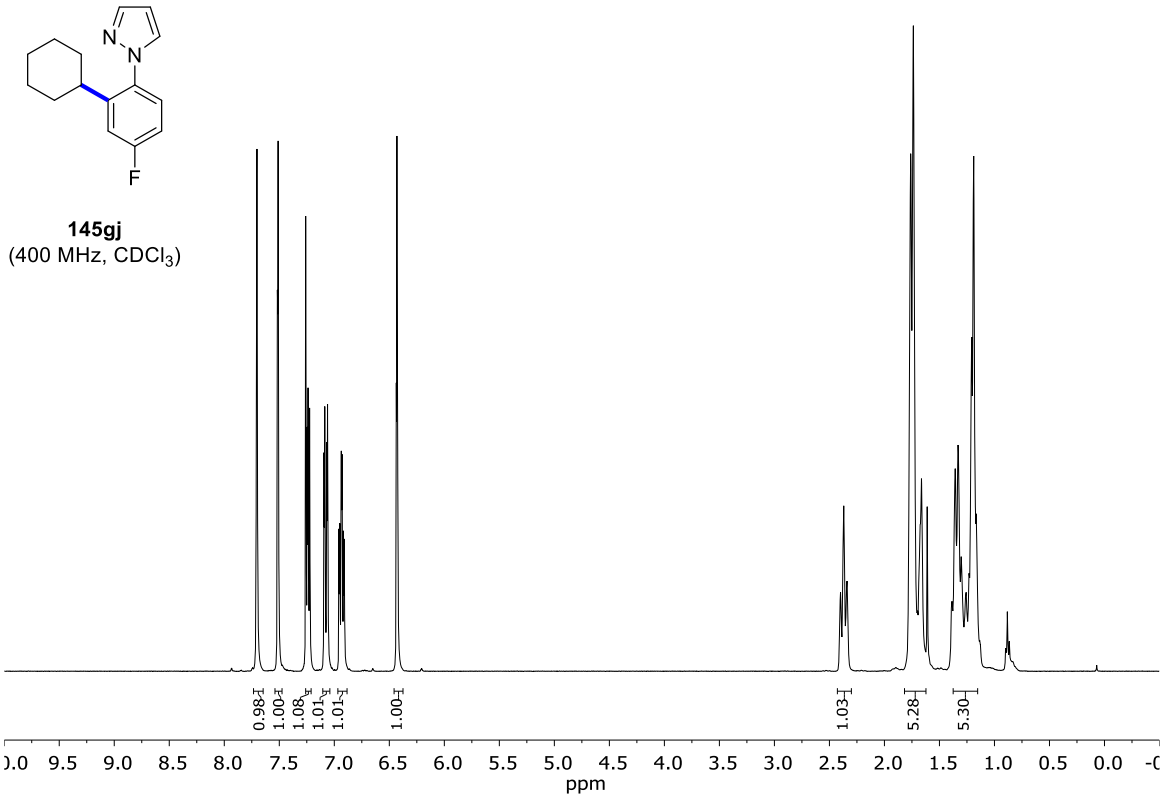


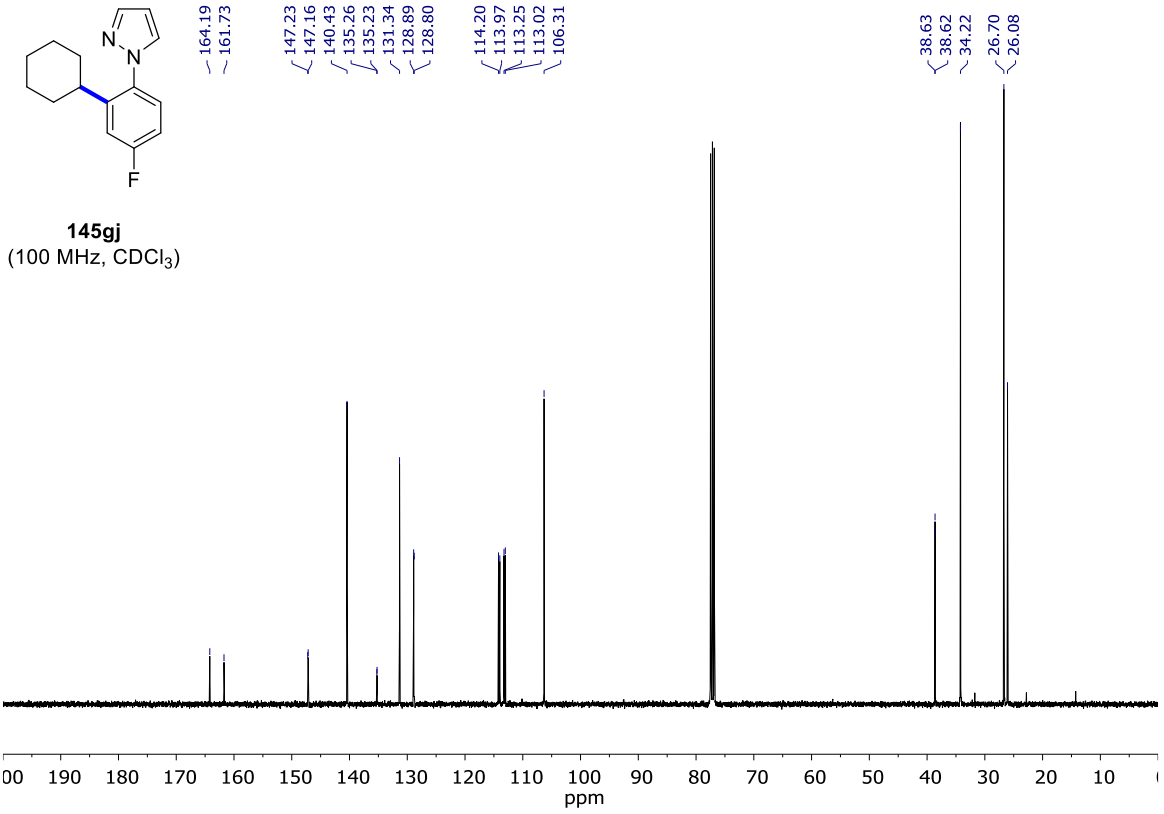
146dj
(100 MHz, $CDCl_3$)



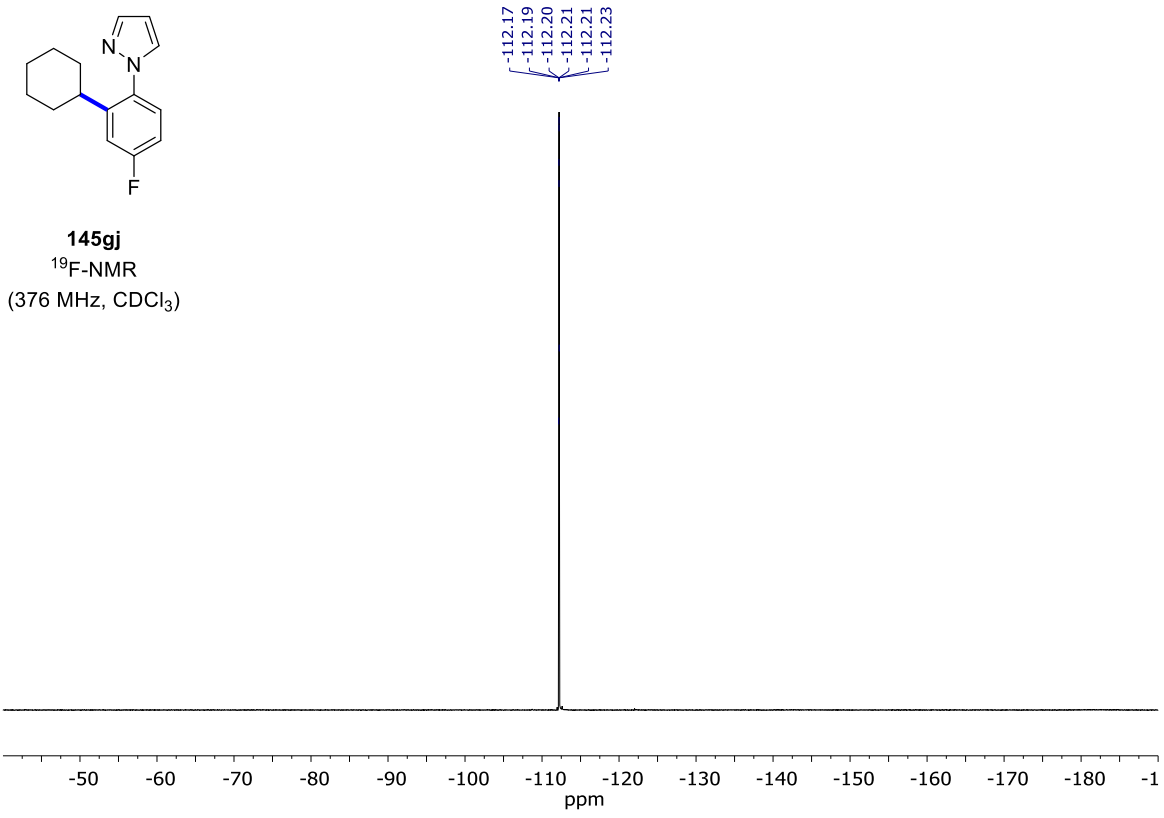
146dj
^1H-^1H NOESY
(600 MHz, $CDCl_3$)


HA
HB
HC
9
8
3
1
2
7
6
4
5
ppm
146dj
1H-13C HMBC
(400 MHz, CDCl3)

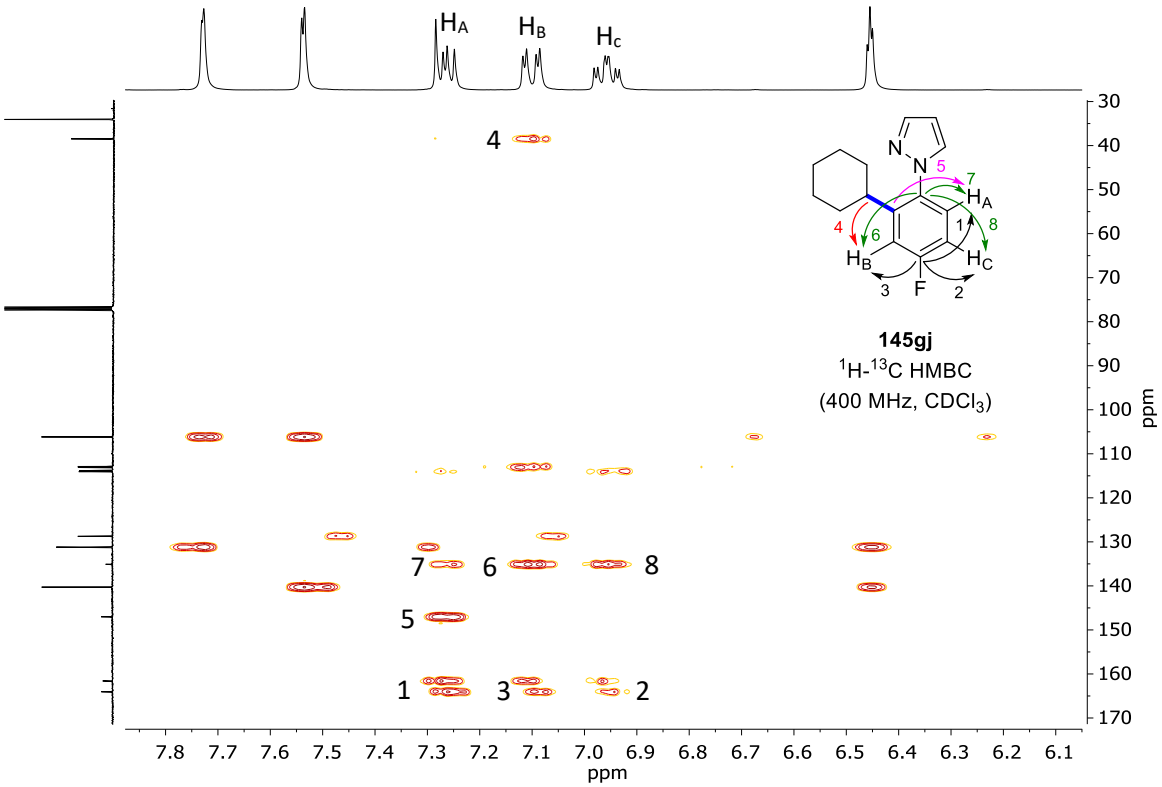

F
145gj
(400 MHz, CDCl3)
0.98
1.00
1.08
1.01
1.01
1.00
1.03
5.28
5.30
ppm



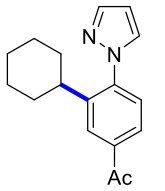
145gj
(100 MHz, $CDCl_3$)



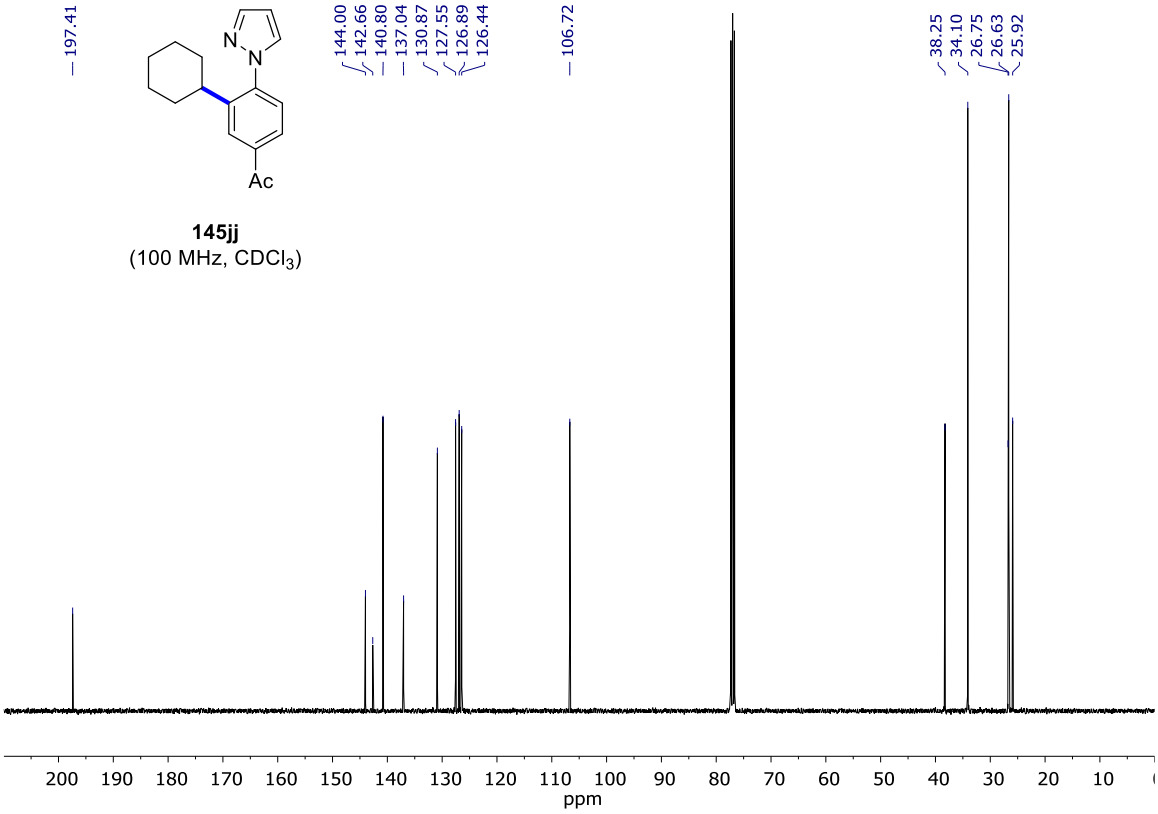
145gj
^{19}F-NMR
(376 MHz, $CDCl_3$)



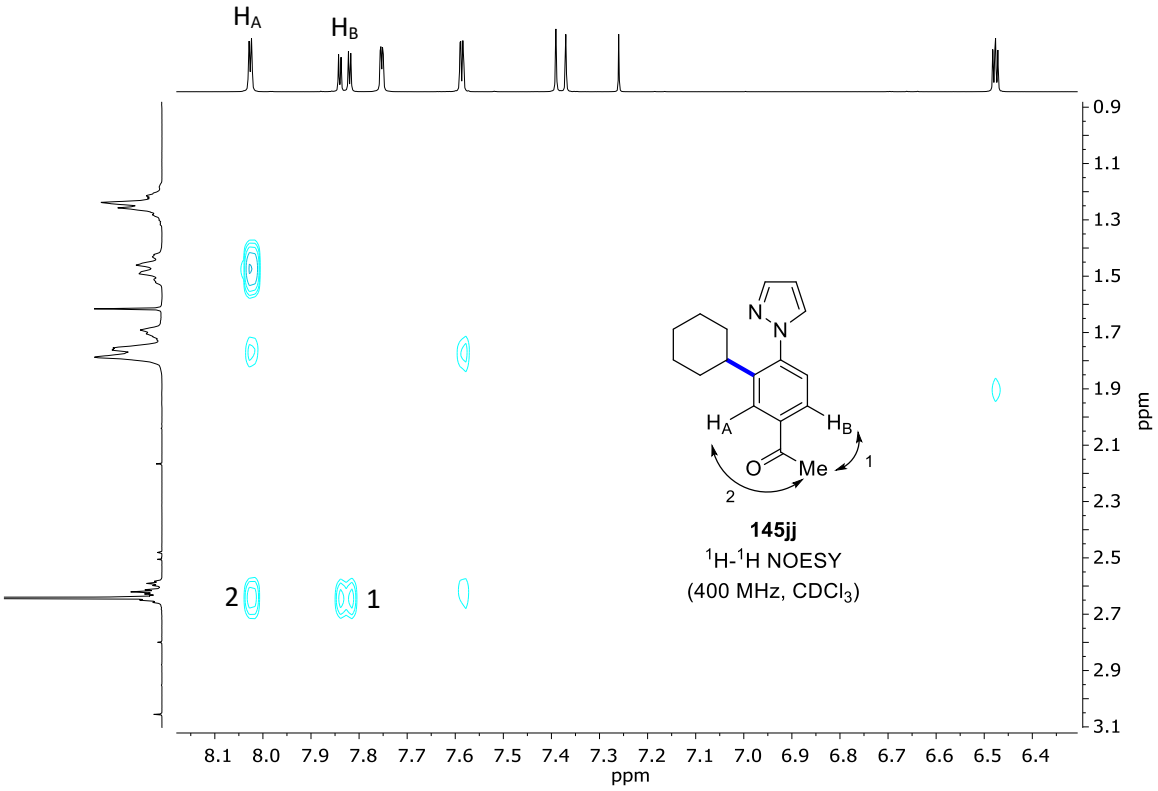
145gj
^{1}H-^{13}C HMBC
(400 MHz, $CDCl_3$)



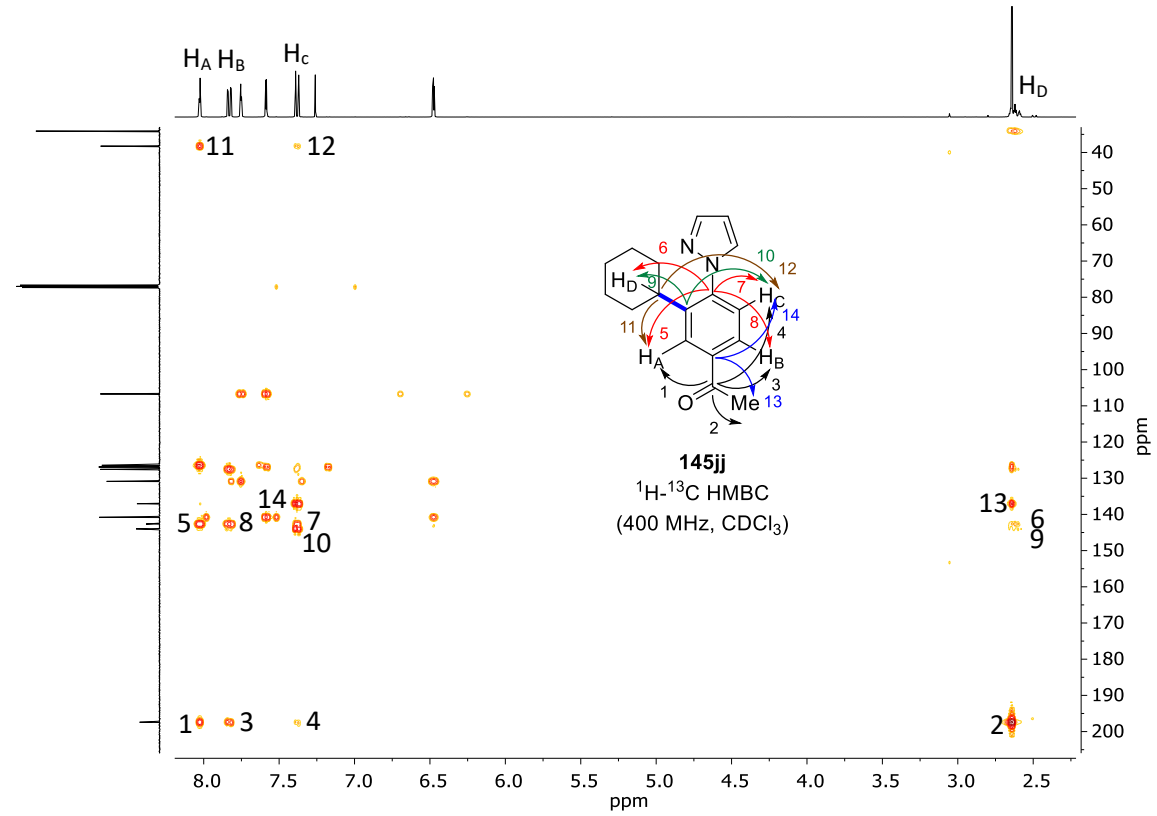
145jj
(400 MHz, $CDCl_3$)



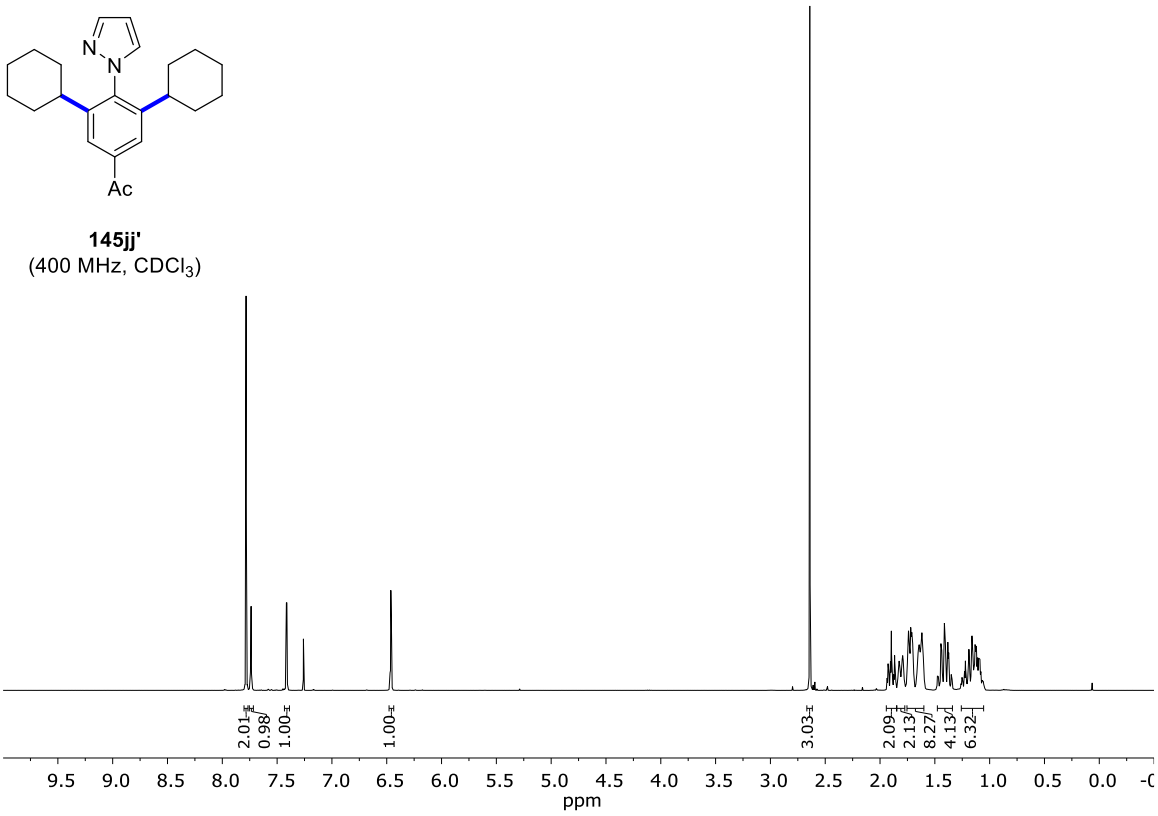
145jj
(100 MHz, $CDCl_3$)



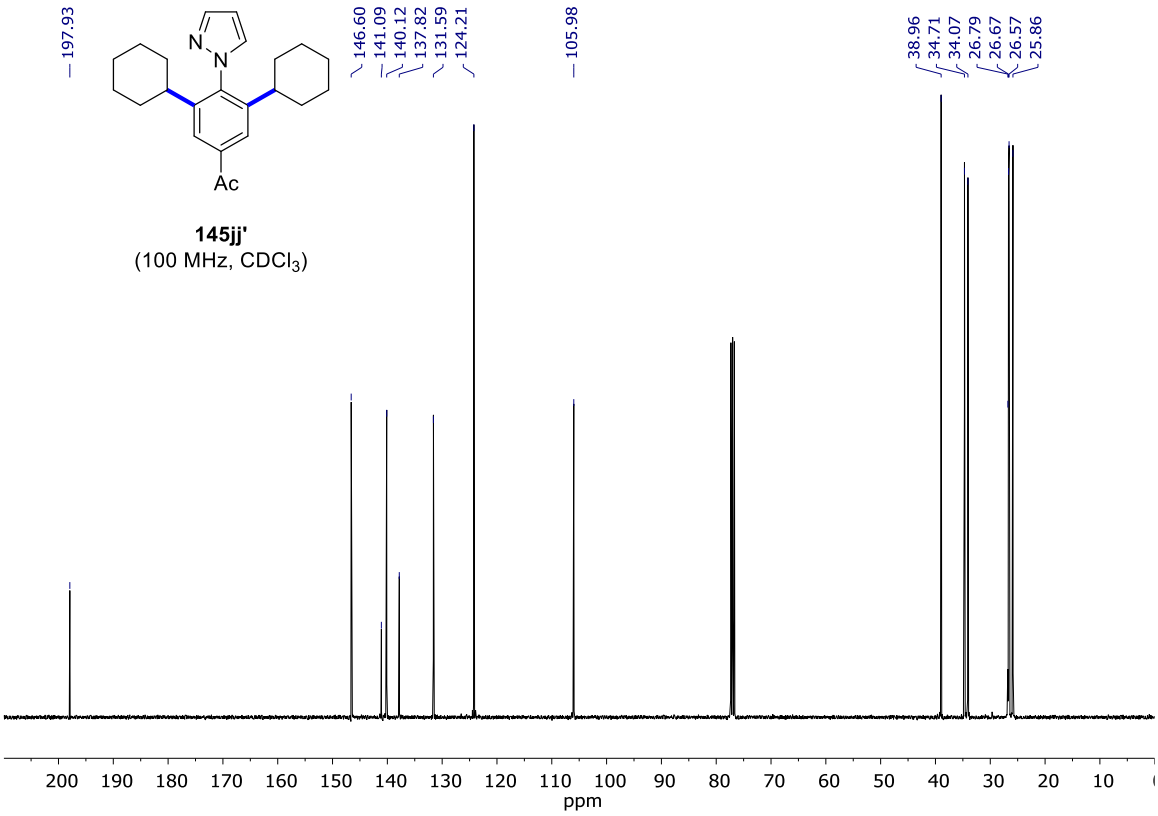
145jj
^1H-^1H NOESY
(400 MHz, $CDCl_3$)



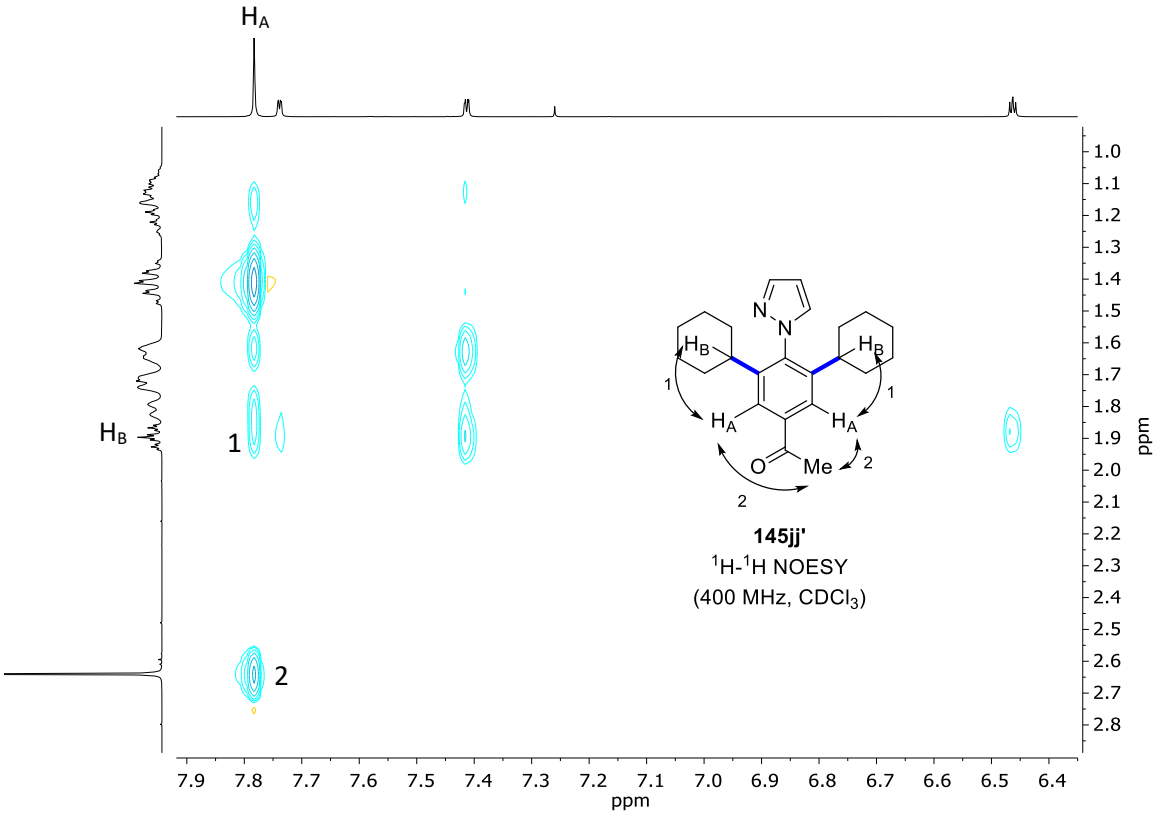
145jj
^{1}H-^{13}C HMBC
(400 MHz, $CDCl_3$)



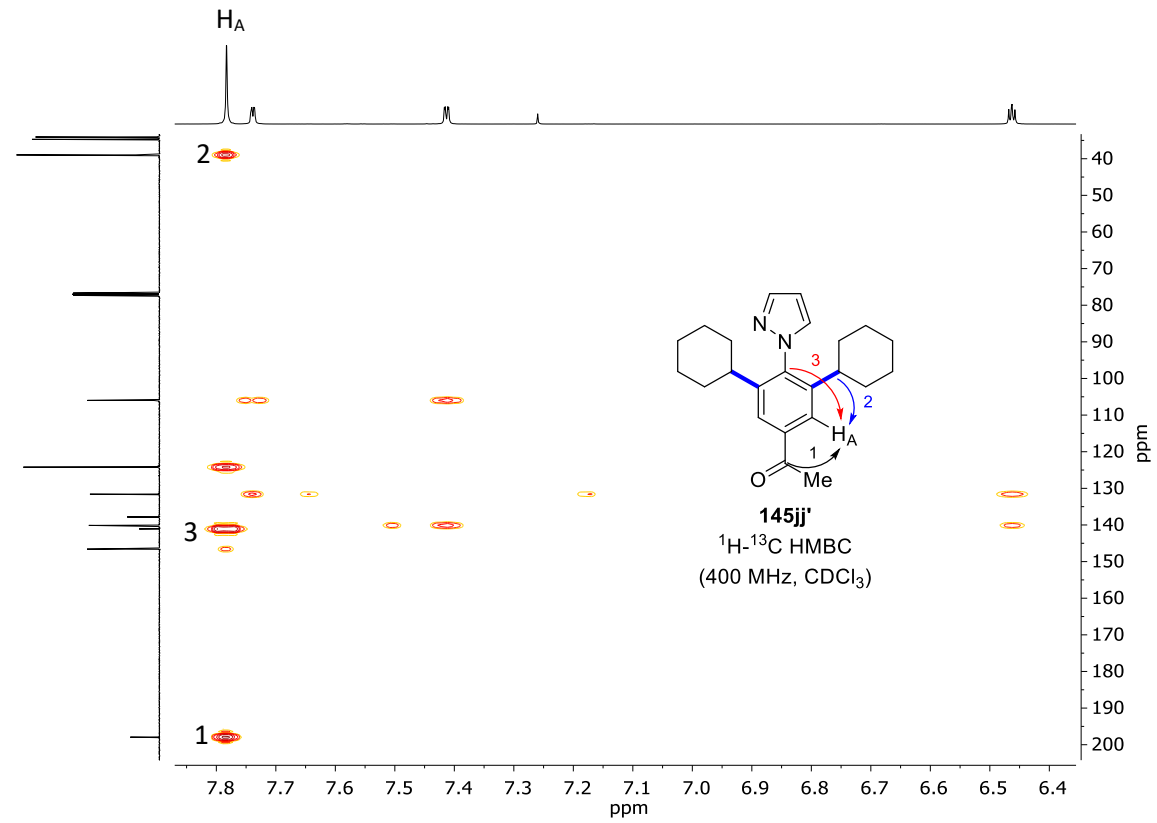
145jj'
(400 MHz, $CDCl_3$)



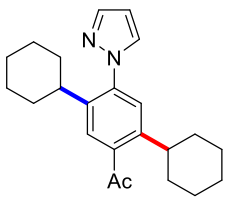
145jj'
(100 MHz, $CDCl_3$)



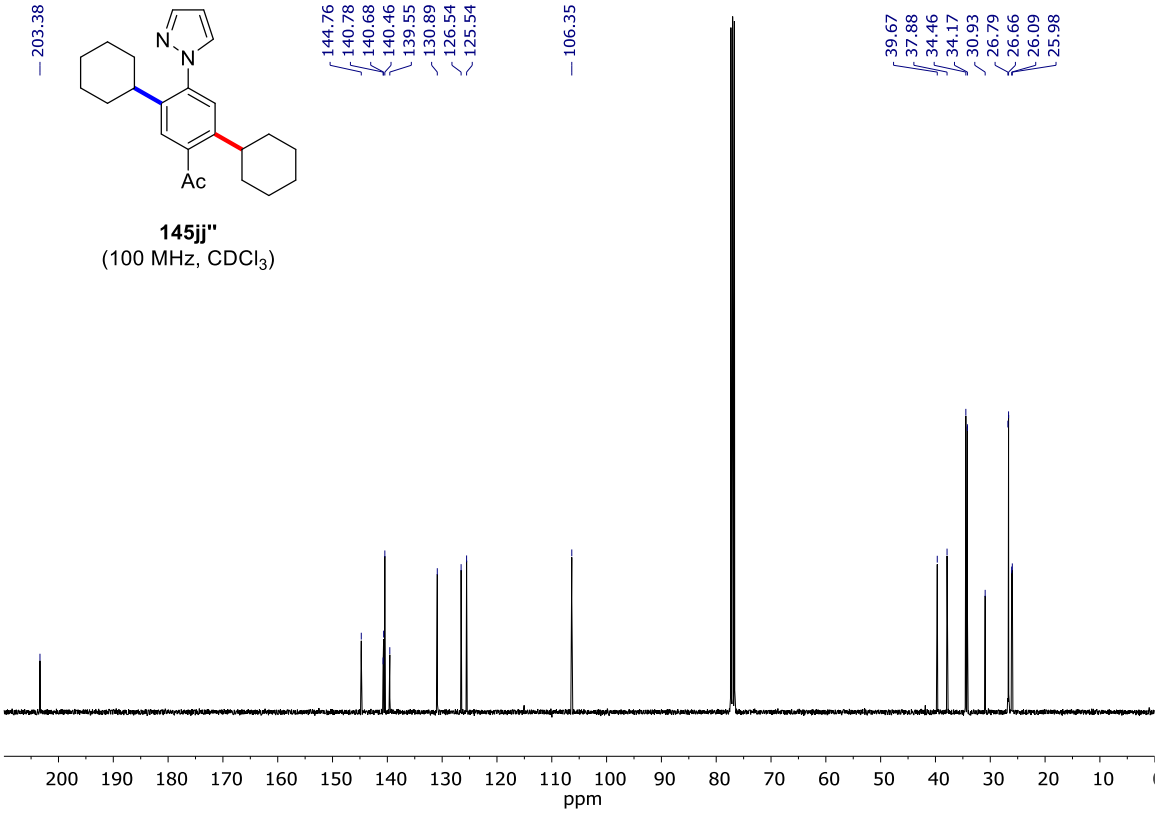
145jj'
^1H-^1H NOESY
(400 MHz, $CDCl_3$)



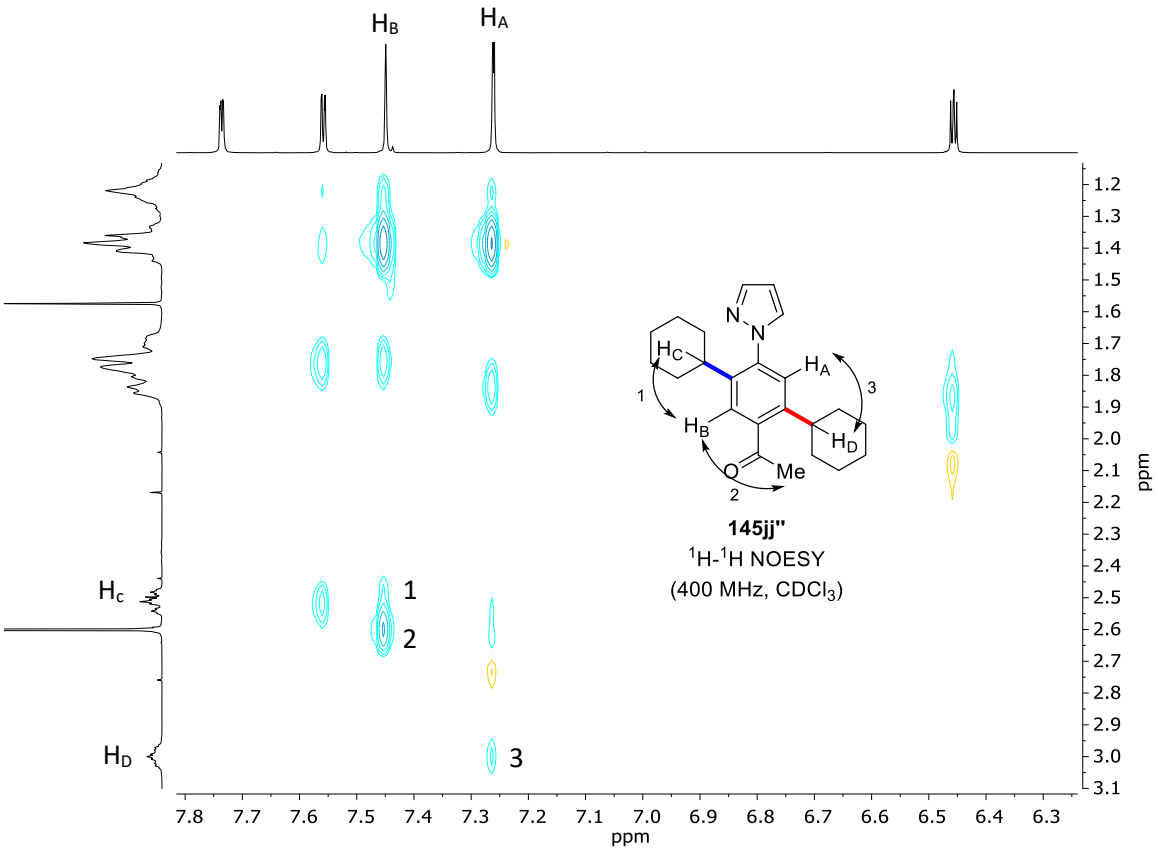
145jj'
^{1}H-^{13}C HMBC
(400 MHz, $CDCl_3$)



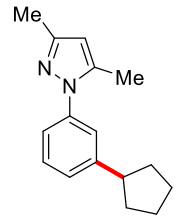
145jj''
(400 MHz, $CDCl_3$)



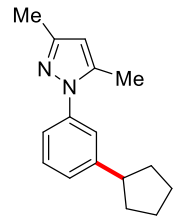
145jj''
(100 MHz, $CDCl_3$)



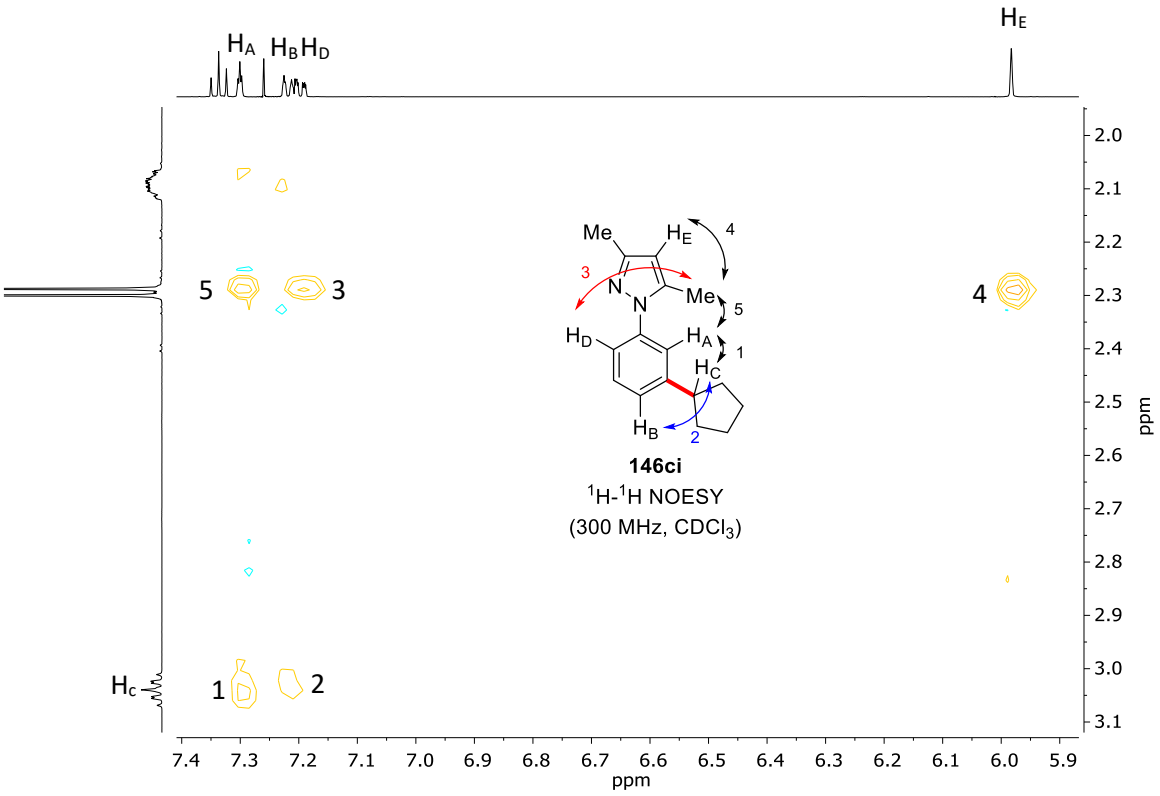
145jj''
^{1}H-^{1}H NOESY
(400 MHz, $CDCl_3$)

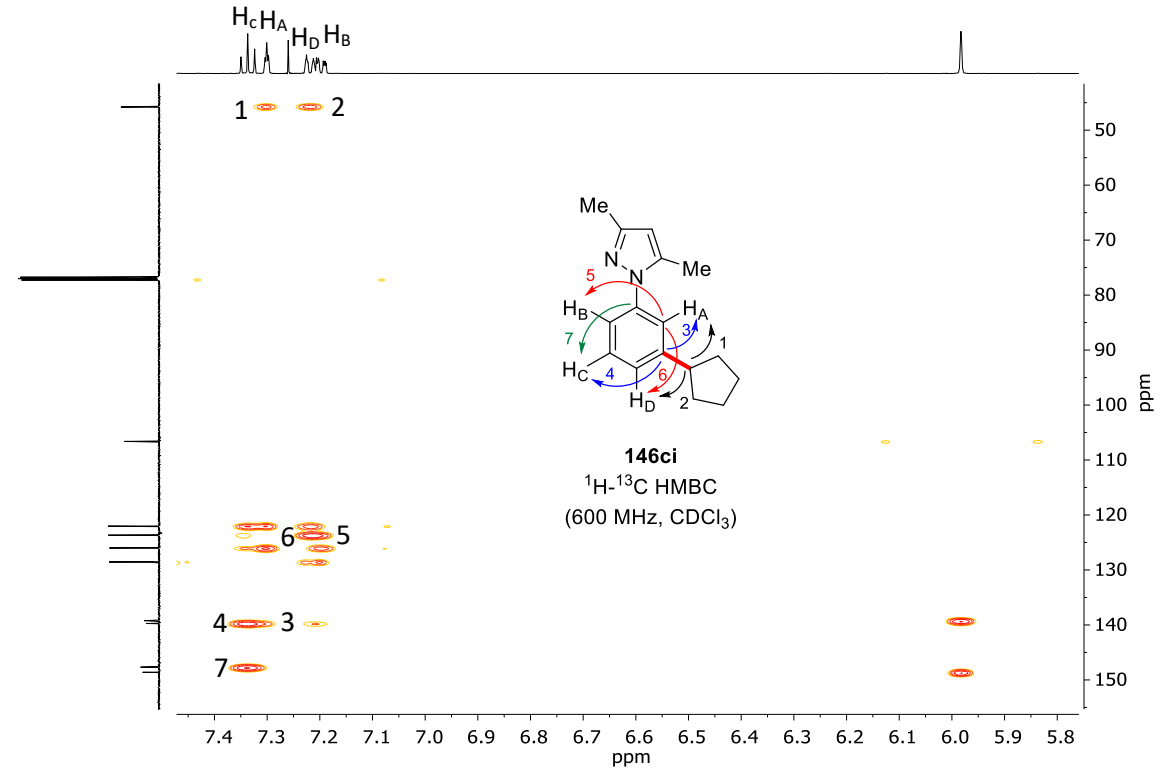


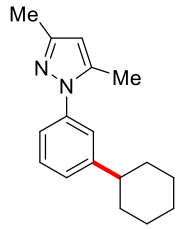
146ci
(600 MHz, $CDCl_3$)



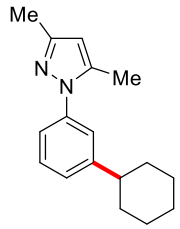
146ci
(125 MHz, $CDCl_3$)


HA HBHD
HE
Me
HE
4
3
N
N
Me
5
HD
HA
1
HC
HB
2
5
3
4
Hc
1
2
146ci
1H-1H NOESY
(300 MHz, CDCl3)
2.0
2.1
2.2
2.3
2.4
2.5
2.6
2.7
2.8
2.9
3.0
3.1
ppm
7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9
ppm

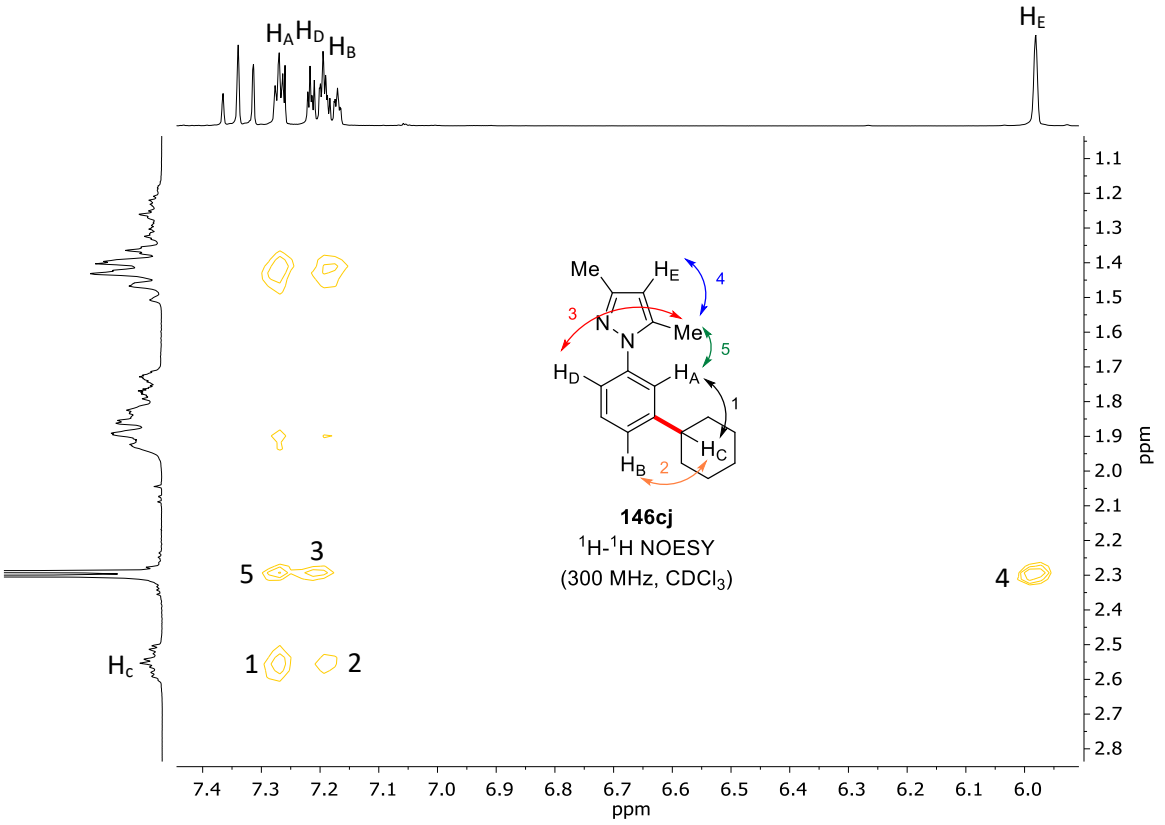

HcHA HD HB
1
2
Me
N
N
Me
5
HB
HA
7
3
1
HC
4
6
HD
2
6
5
4
3
7
146ci
1H-13C HMBC
(600 MHz, CDCl3)
50
60
70
80
90
100
110
120
130
140
150
ppm
7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8
ppm

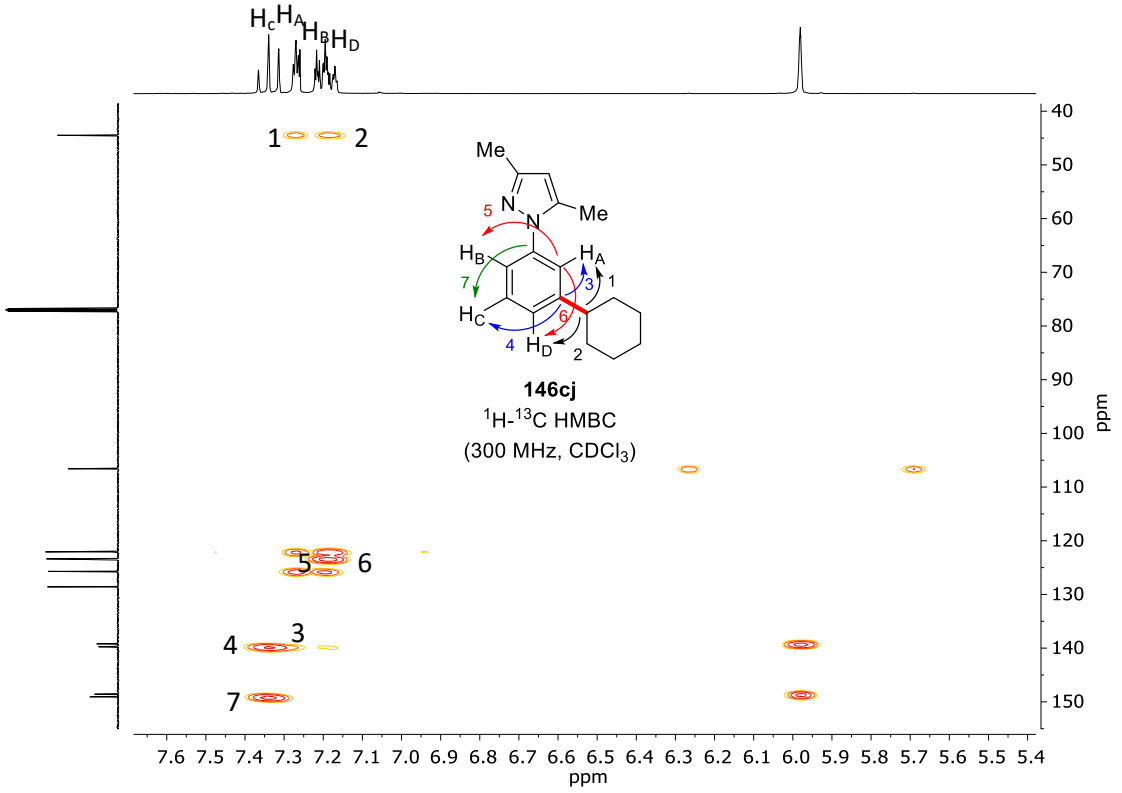


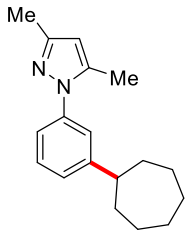
146cj
(300 MHz, $CDCl_3$)



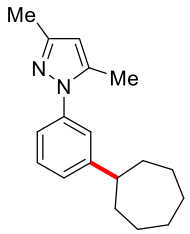
146cj
(125 MHz, $CDCl_3$)


HA HD HB
HE
Me
HE
4
3
N
N
Me
5
HD
HA
1
HC
HB
2
146cj
1H-1H NOESY
(300 MHz, CDCl3)
5
3
4
1
2
Hc
7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2 6.1 6.0
ppm
1.1 1.2 1.3 1.4 1.5 1.6 1.7 1.8 1.9 2.0 2.1 2.2 2.3 2.4 2.5 2.6 2.7 2.8
ppm

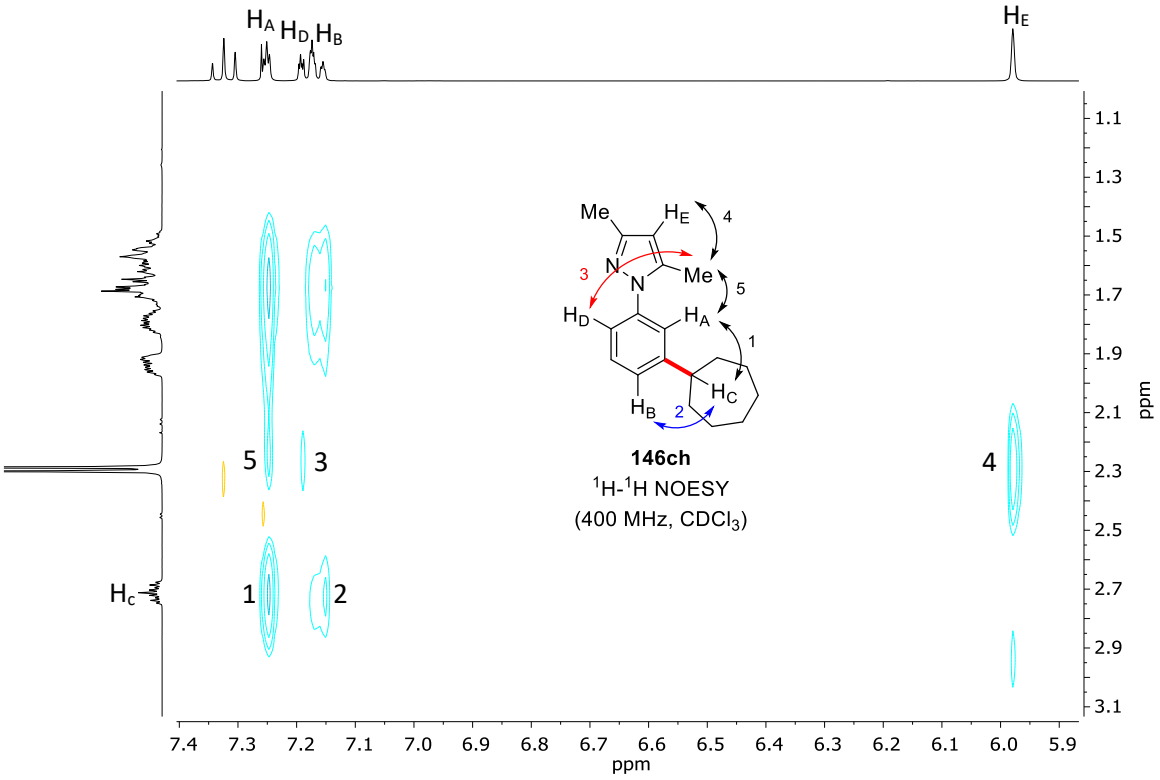

Hc HA HB HD
1
2
Me
N
N
Me
5
HB
HA
7
3
1
HC
6
4
HD
2
146cj
1H-13C HMBC
(300 MHz, CDCl3)
5
6
4
3
7
7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3 6.2 6.1 6.0 5.9 5.8 5.7 5.6 5.5 5.4
ppm
40 50 60 70 80 90 100 110 120 130 140 150
ppm



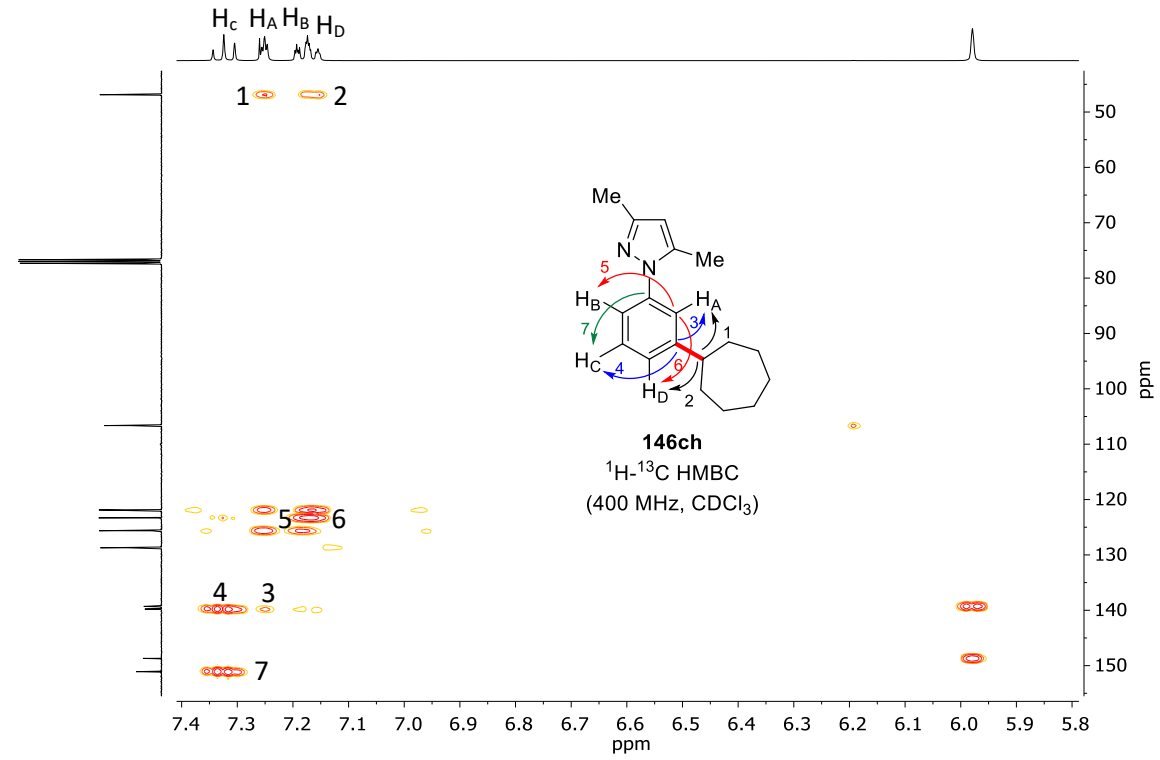
146ch
(400 MHz, $CDCl_3$)



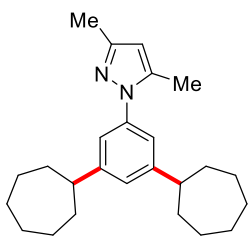
146ch
(100 MHz, $CDCl_3$)



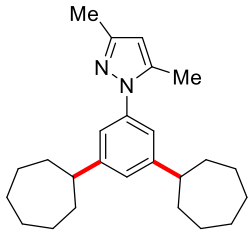
146ch
^{1}H-^{1}H NOESY
(400 MHz, $CDCl_3$)



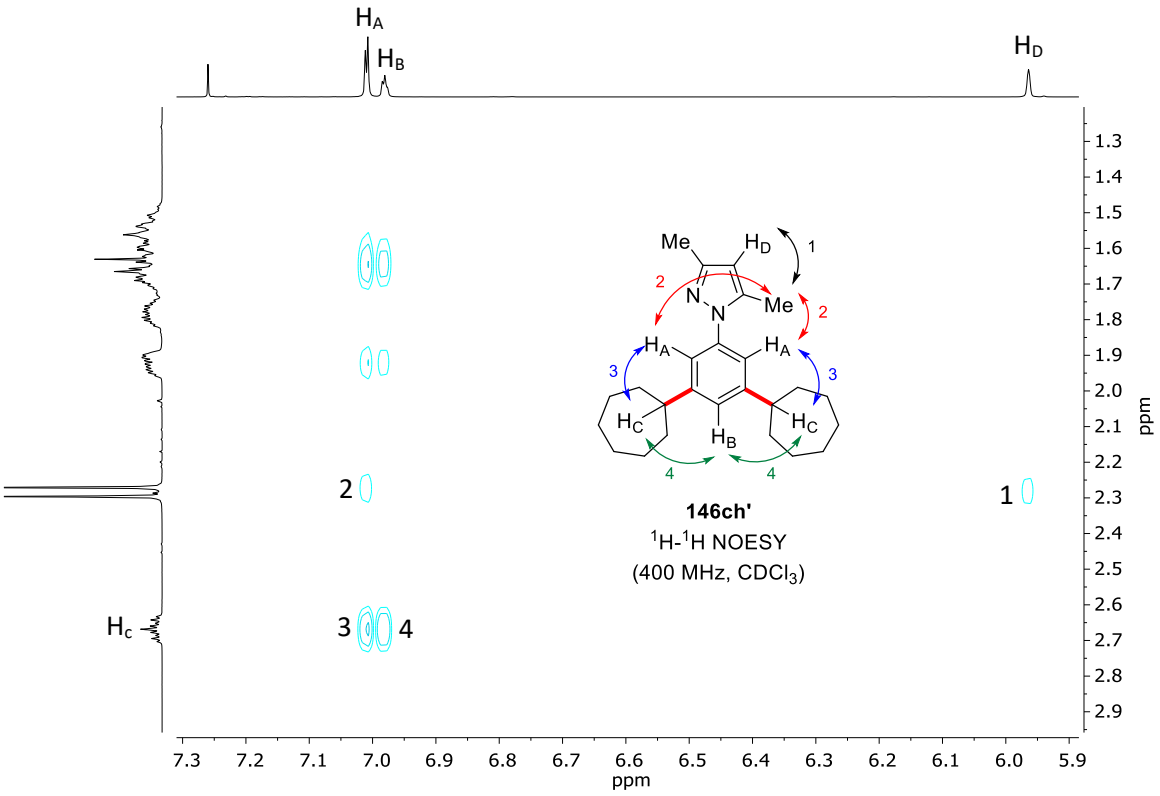
146ch
^{1}H-^{13}C HMBC
(400 MHz, $CDCl_3$)



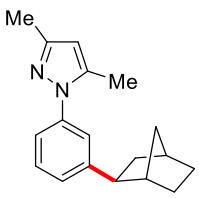
146ch'
(400 MHz, $CDCl_3$)



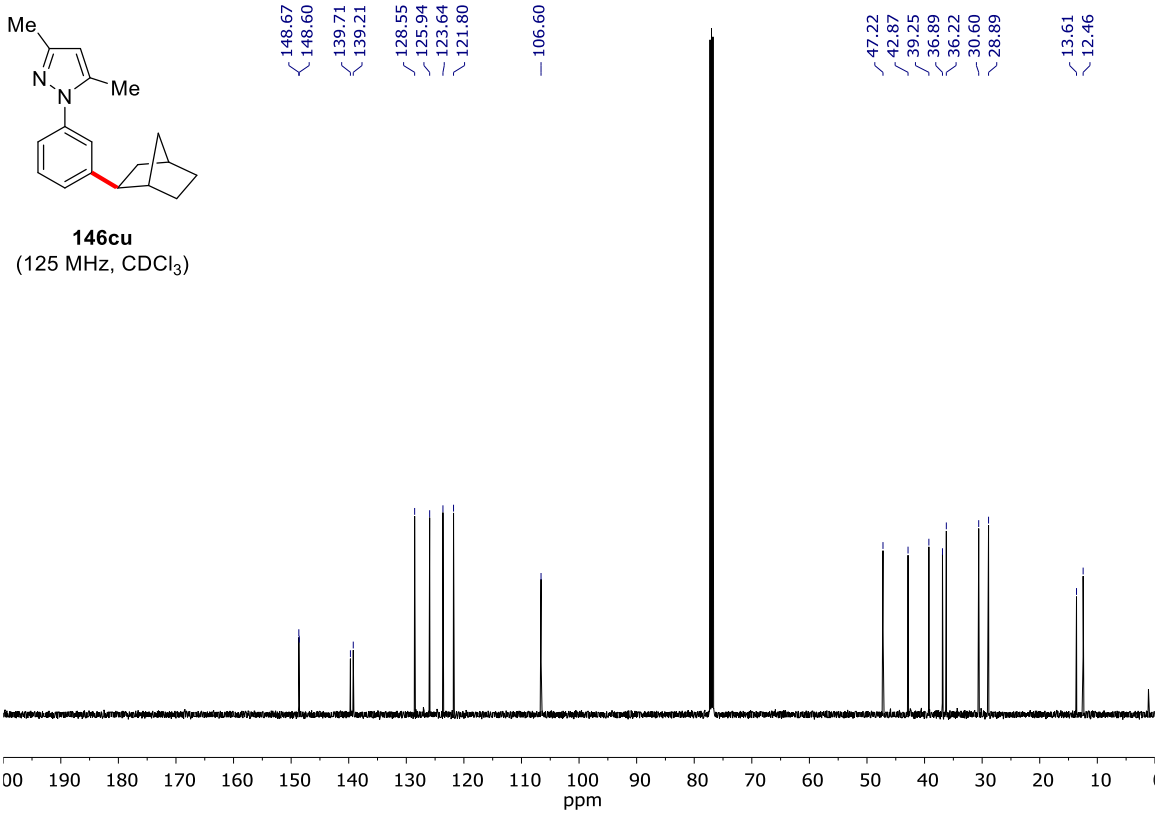
146ch'
(100 MHz, $CDCl_3$)



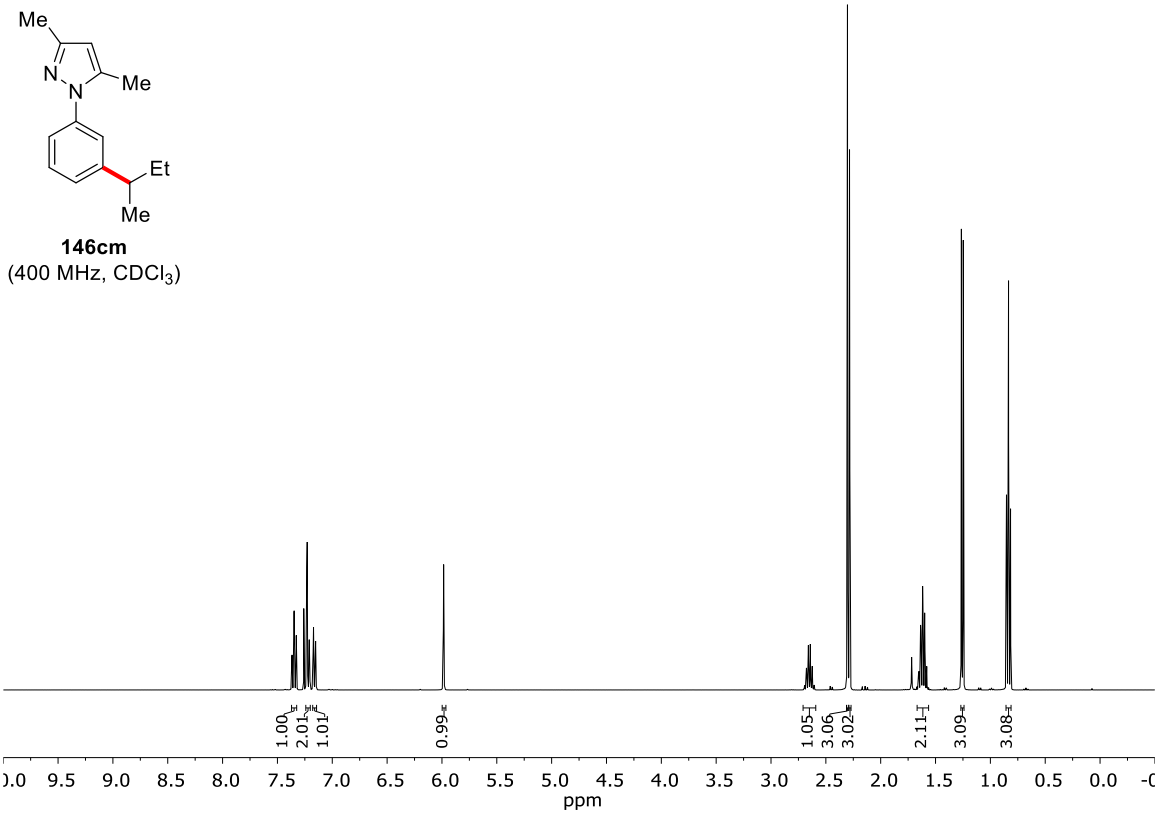
146ch'
^{1}H-^{1}H NOESY
(400 MHz, $CDCl_3$)



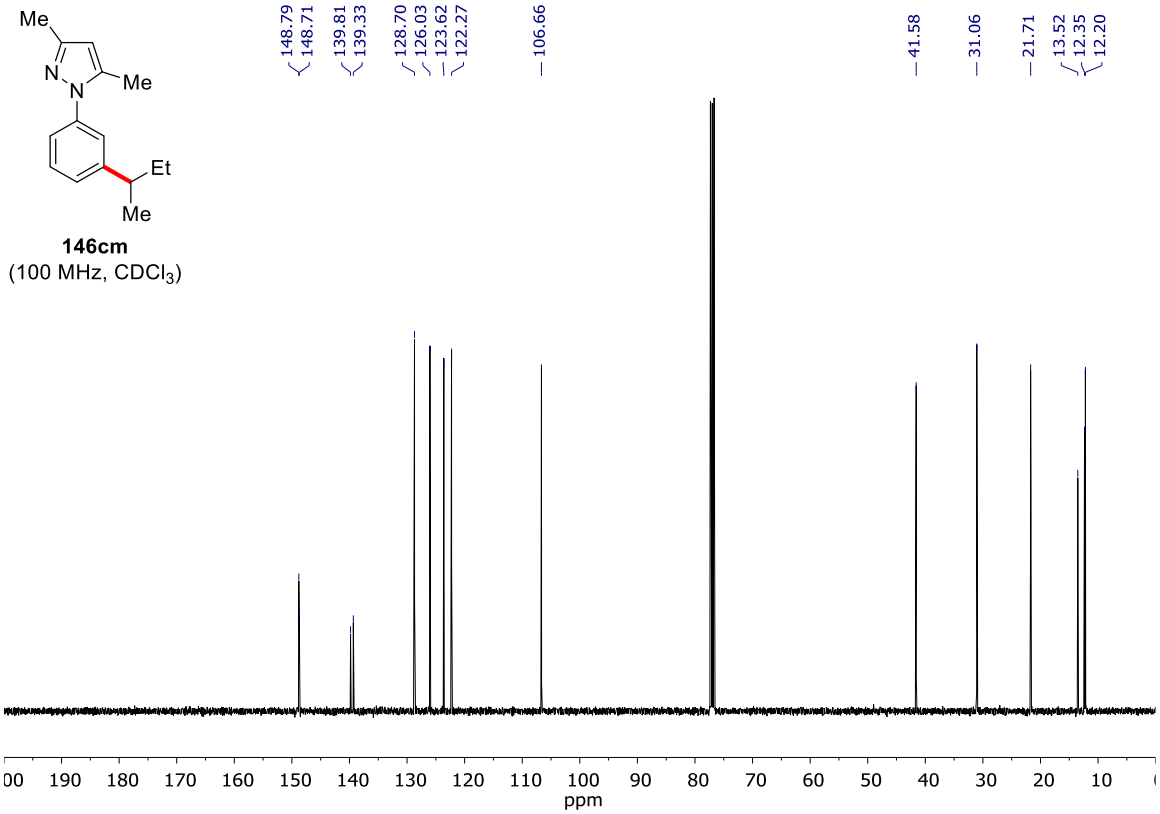
146cu
(300 MHz, $CDCl_3$)

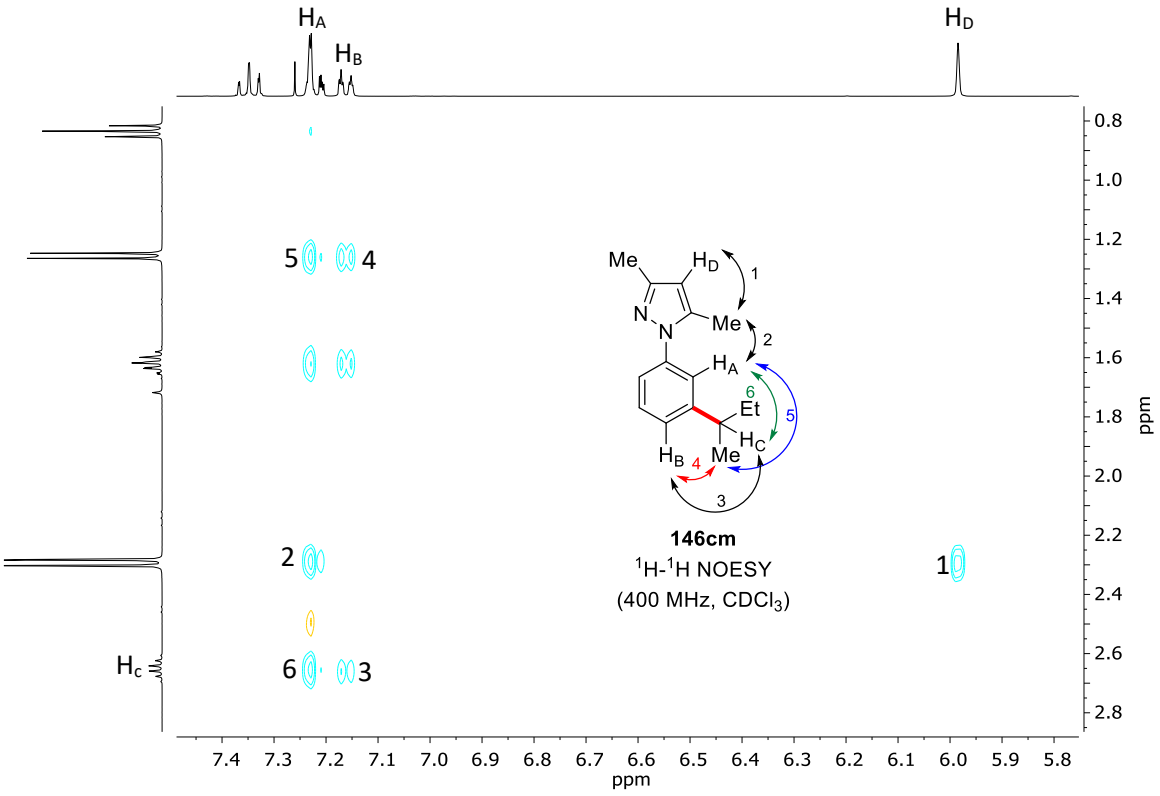


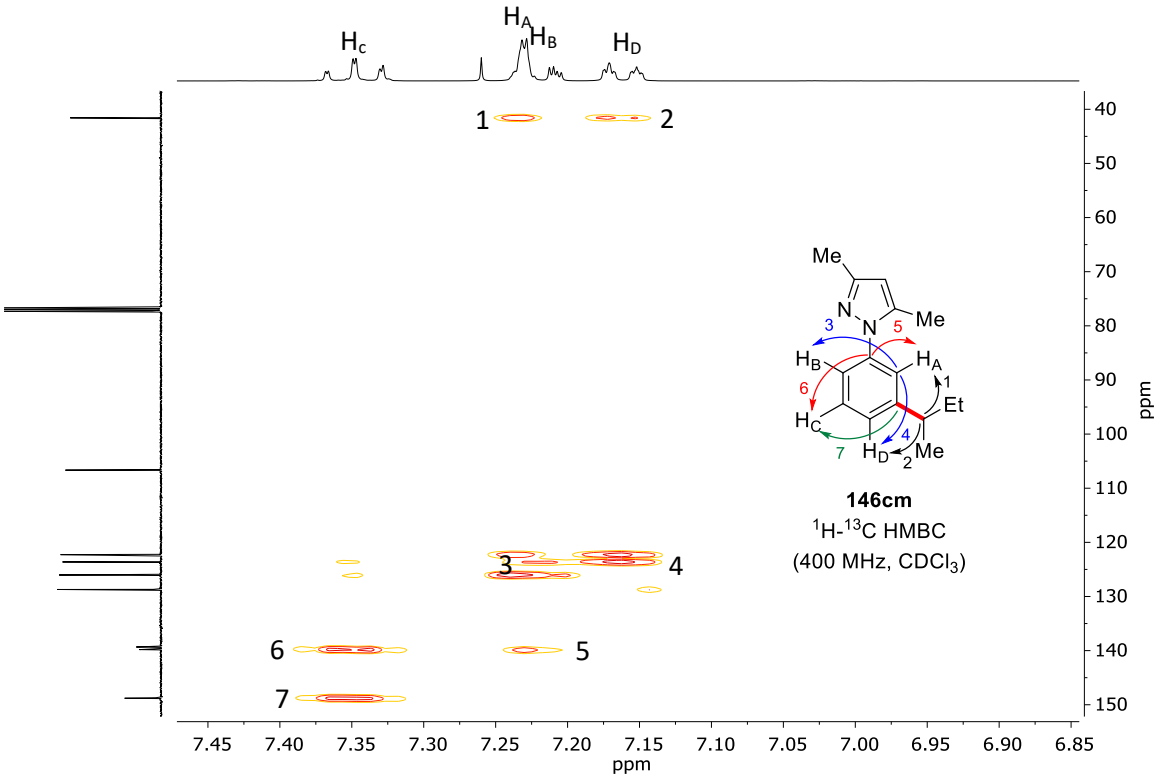
146cu
(125 MHz, $CDCl_3$)



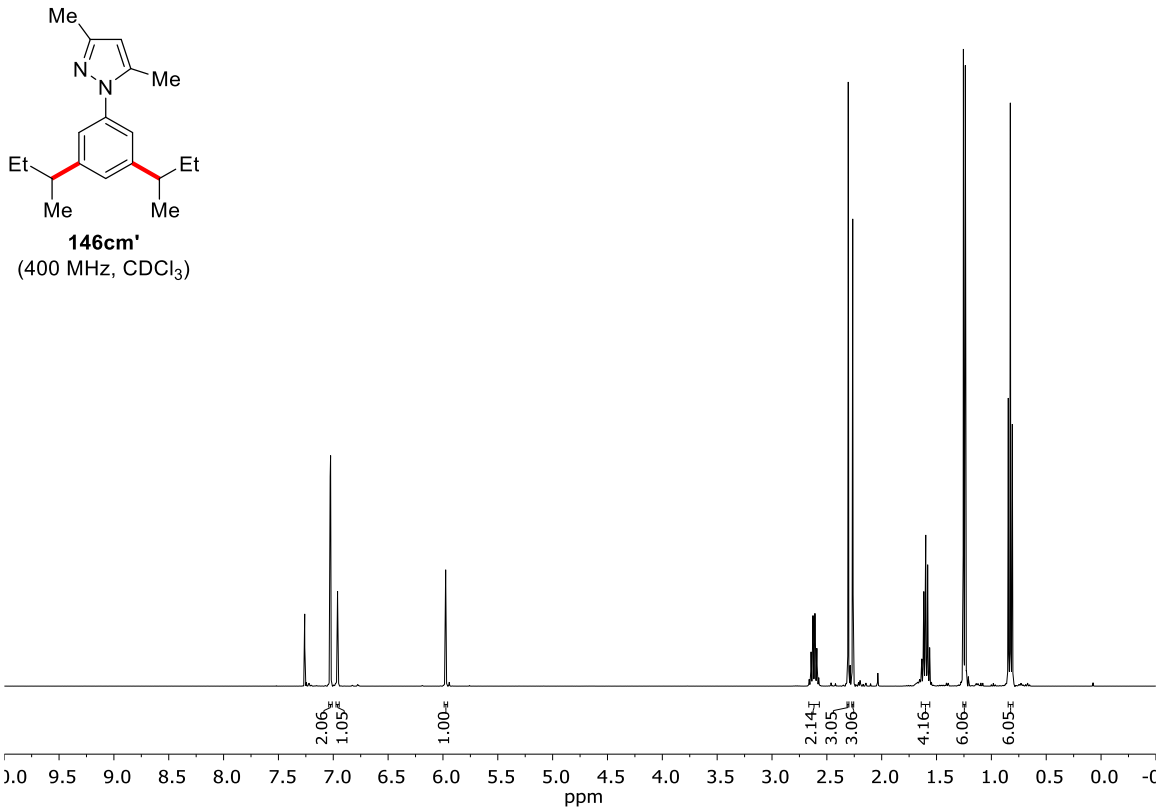
146cm
(400 MHz, $CDCl_3$)


Me
N
N
Me
Et
Me
146cm
(100 MHz, CDCl3)
148.79
148.71
139.81
139.33
128.70
126.03
123.62
122.27
106.66
41.58
31.06
21.71
13.52
12.35
12.20
ppm

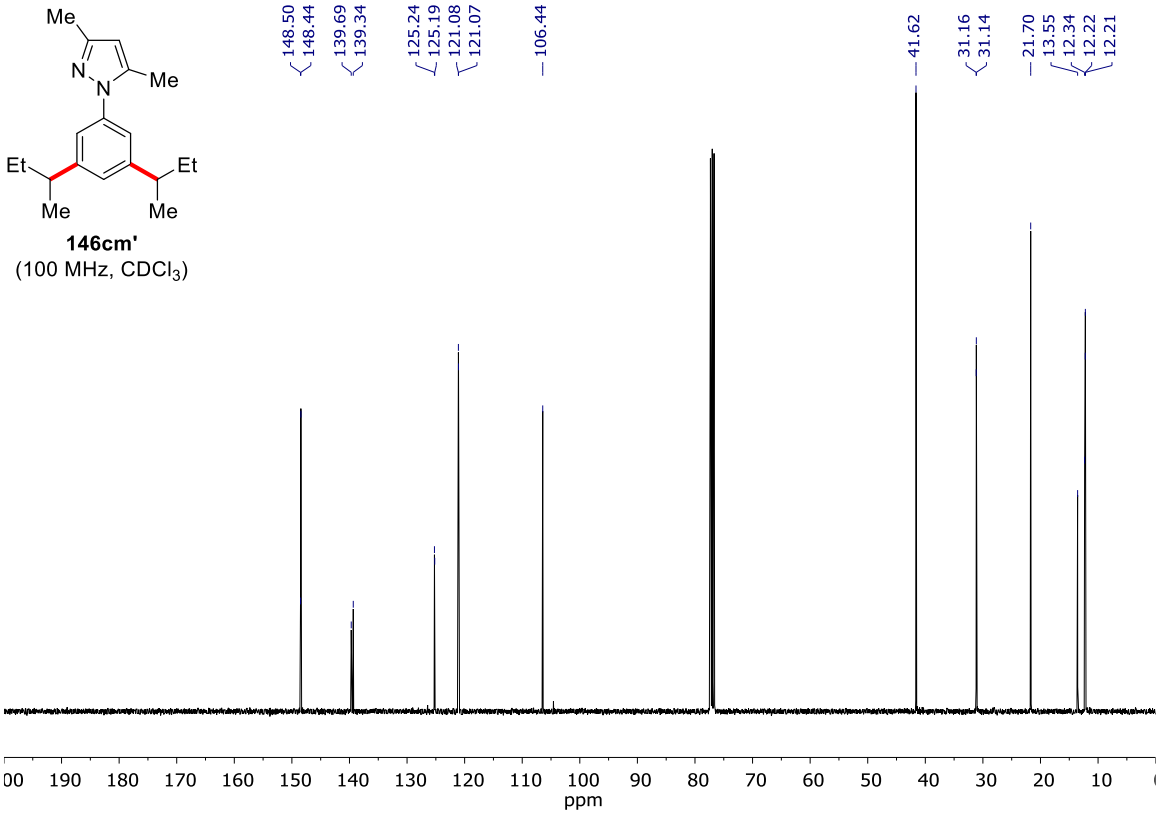

HA
HB
HD
5
4
2
6
3
1
HC
Me
HD
1
N
N
Me
2
HA
6
Et
5
HC
HB
4
Me
3
146cm
1H-1H NOESY
(400 MHz, CDCl3)
ppm

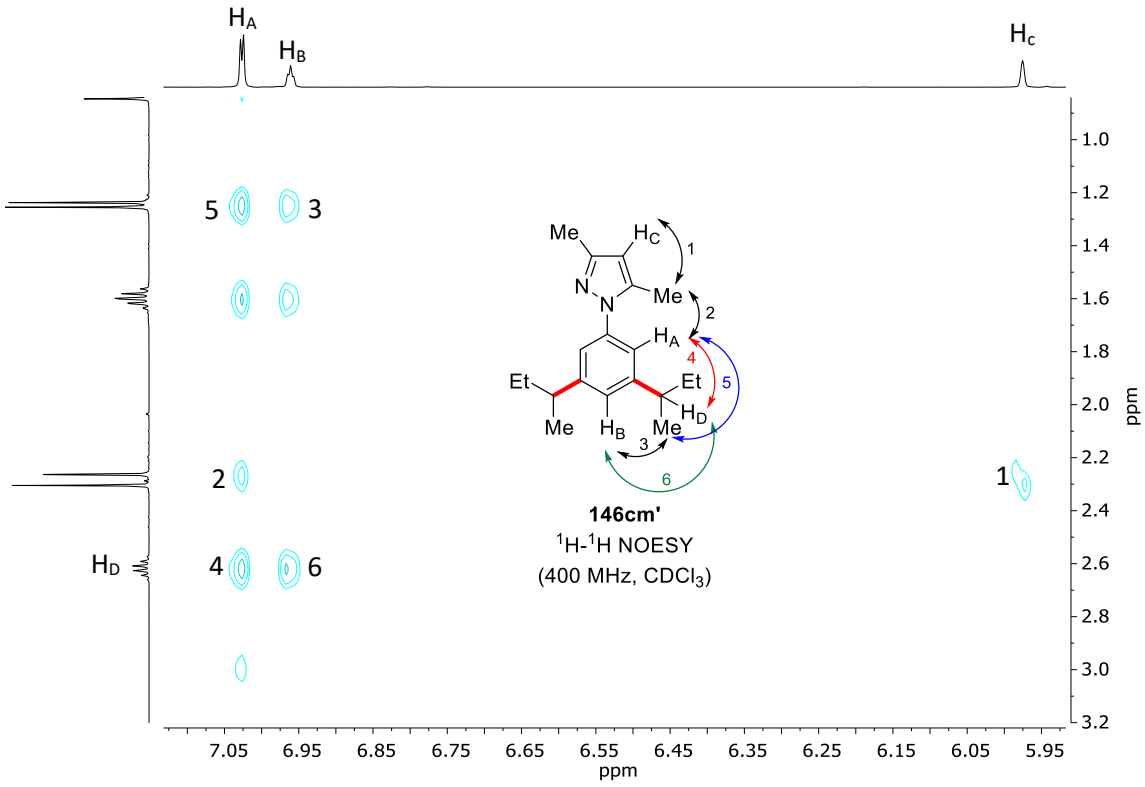


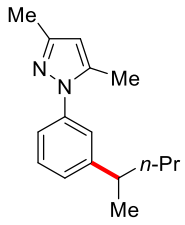
146cm
^{1}H-^{13}C HMBC
(400 MHz, $CDCl_3$)



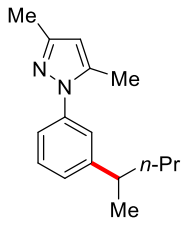
146cm'
(400 MHz, $CDCl_3$)


Me
N
N
Me
Et
Et
Me
Me
146cm'
(100 MHz, CDCl3)
148.50
148.44
139.69
139.34
125.24
125.19
121.08
121.07
106.44
41.62
31.16
31.14
21.70
13.55
12.34
12.22
12.21
ppm

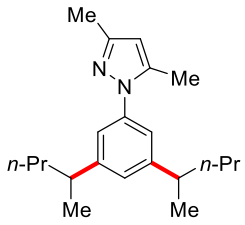

HA
HB
Hc
5
3
2
HD
4
6
1
Me
HC
N
N
Me
HA
Et
Et
HD
Me
HB
Me
146cm'
1H-1H NOESY
(400 MHz, CDCl3)
ppm
ppm



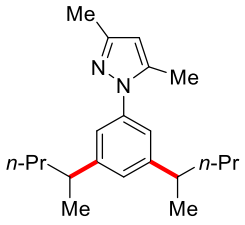
146cn
(400 MHz, $CDCl_3$)



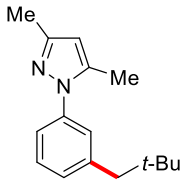
146cn
(100 MHz, $CDCl_3$)



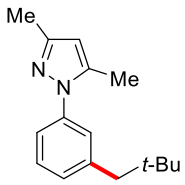
146cn'
(400 MHz, $CDCl_3$)



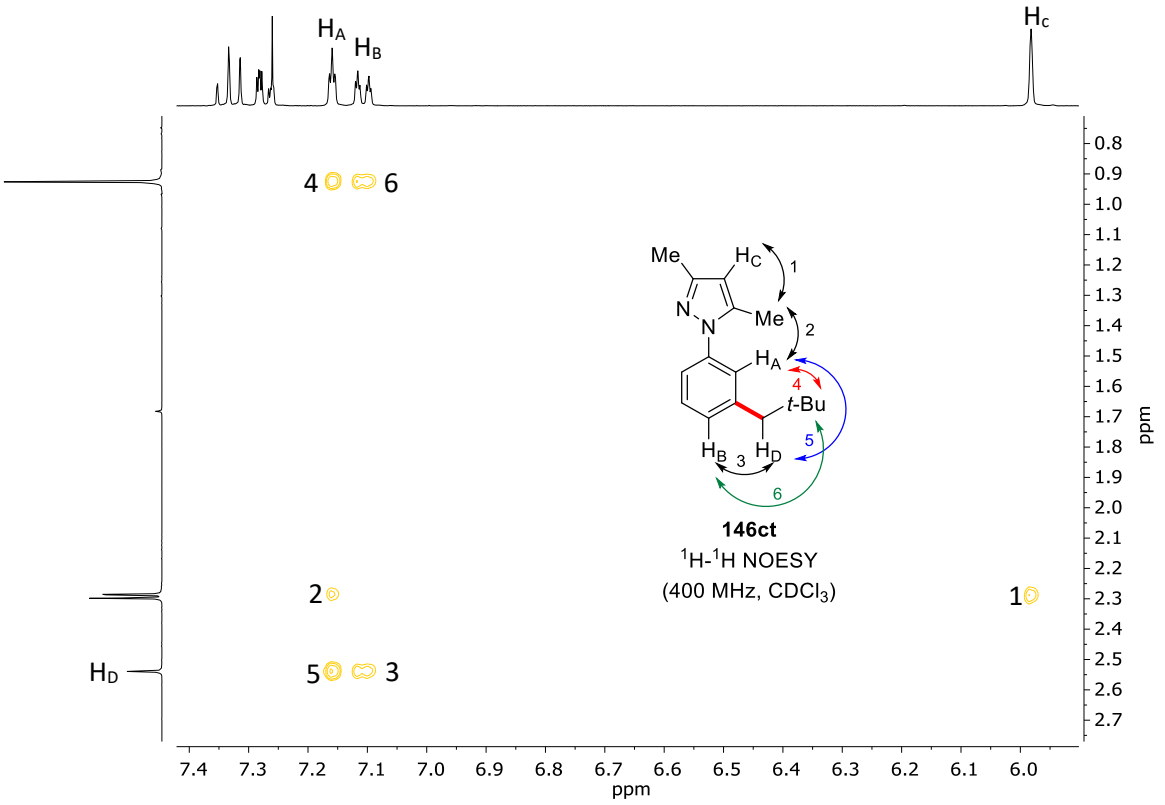
146cn'
(100 MHz, $CDCl_3$)

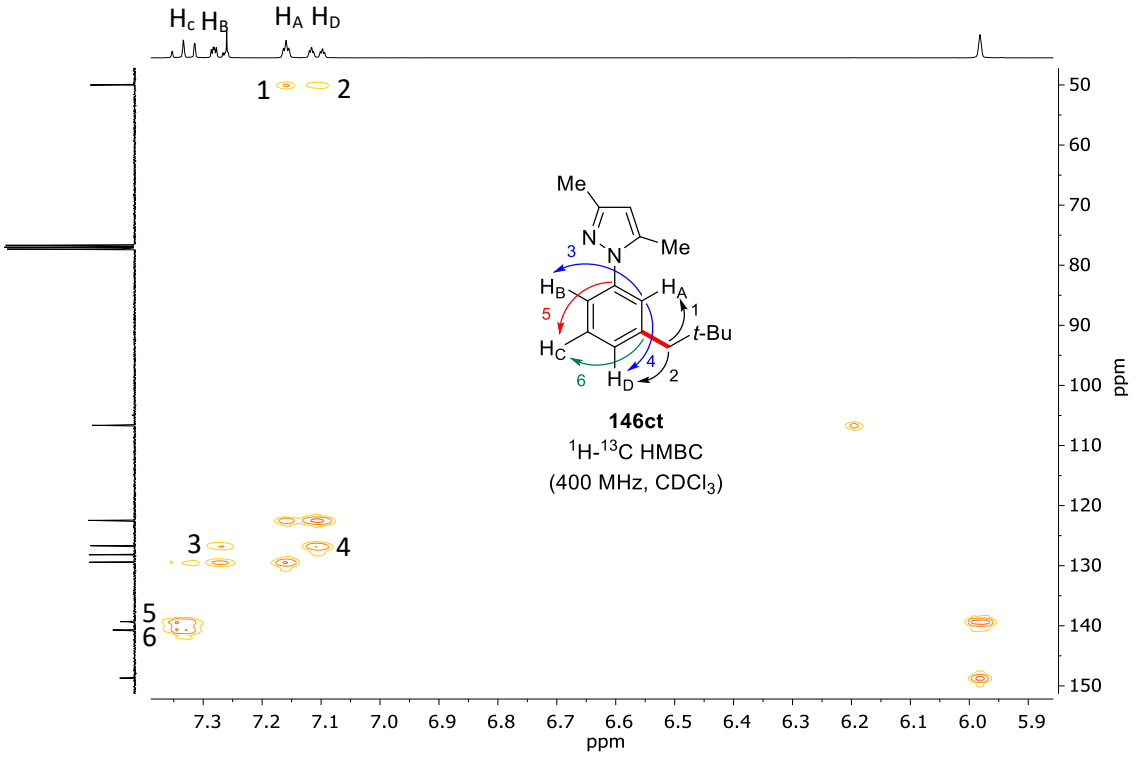


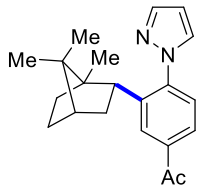
146ct
(400 MHz, $CDCl_3$)



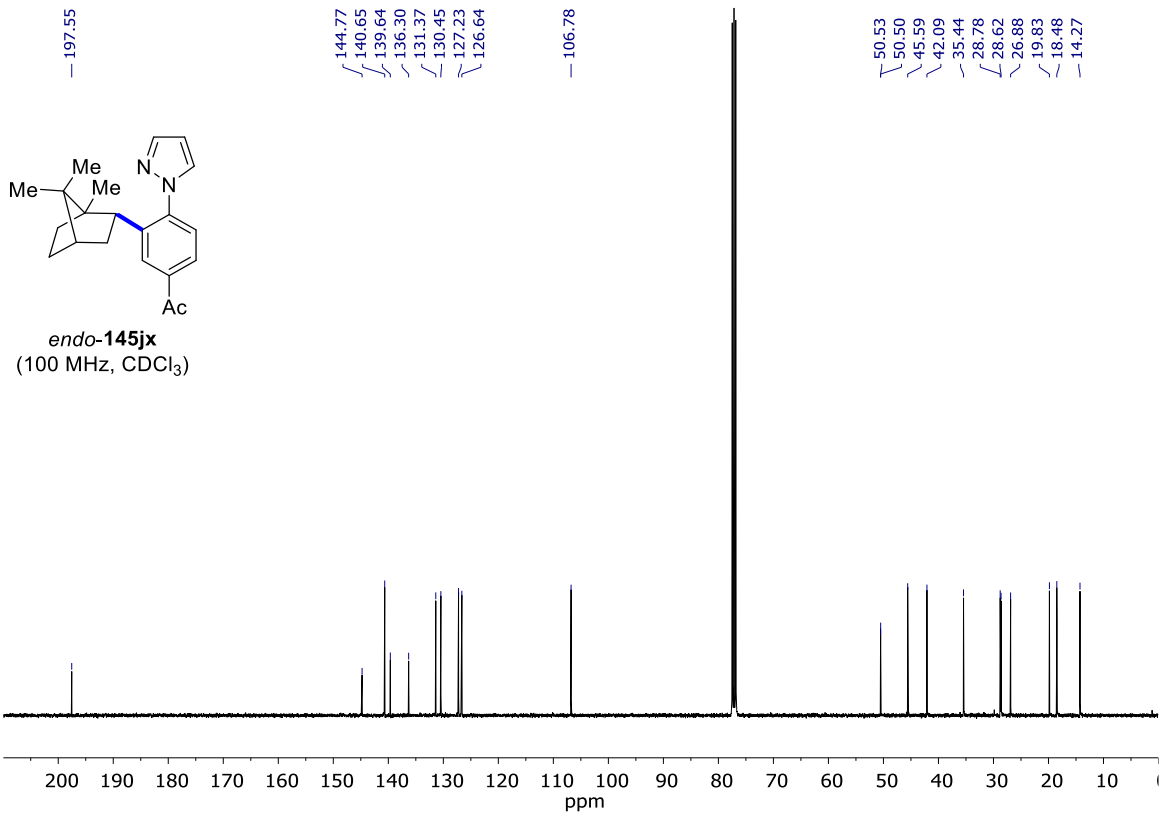
146ct
(100 MHz, $CDCl_3$)


HA HB
Hc
4 6
2
1
HD
5 3
Me
Hc
1
N
N
Me
2
HA
4
t-Bu
HB 3 HD
5
6
146ct
1H-1H NOESY
(400 MHz, CDCl3)
ppm
ppm

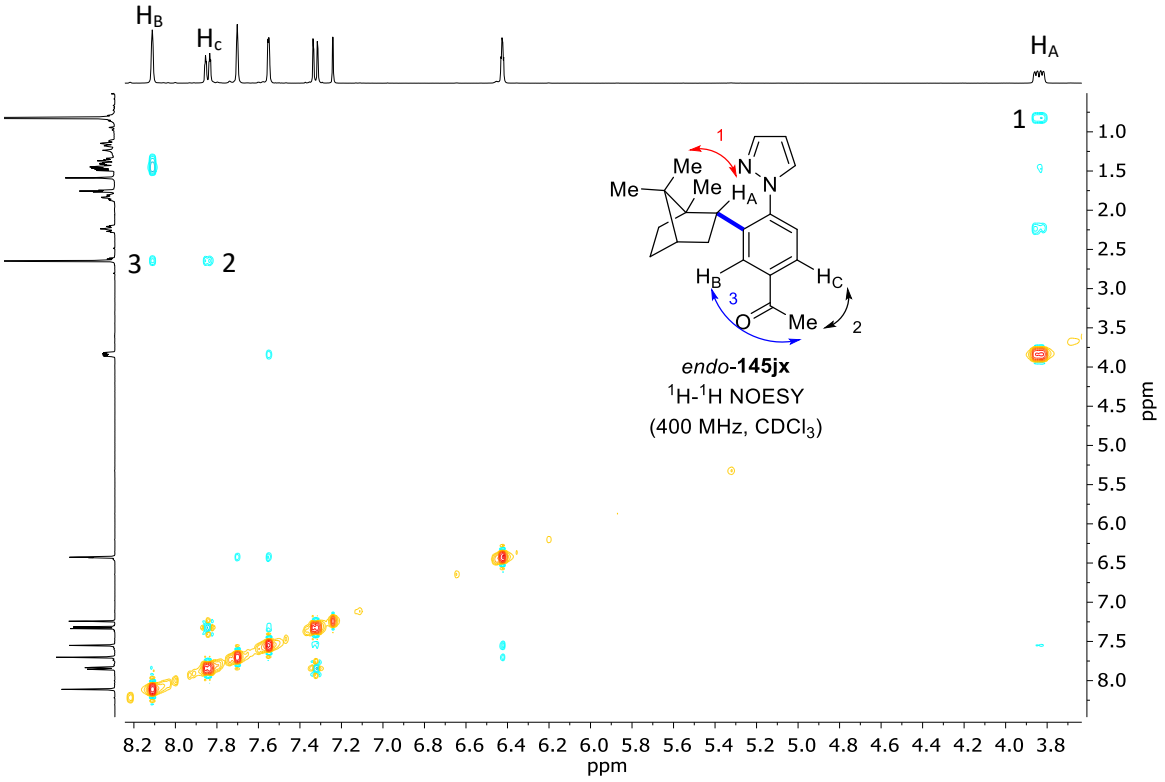

Hc HB
HA HD
1 2
3 4
5
6
Me
N
N
Me
3
HB
HA
5
1
t-Bu
Hc
6
HD
4
2
146ct
1H-13C HMBC
(400 MHz, CDCl3)
ppm
ppm



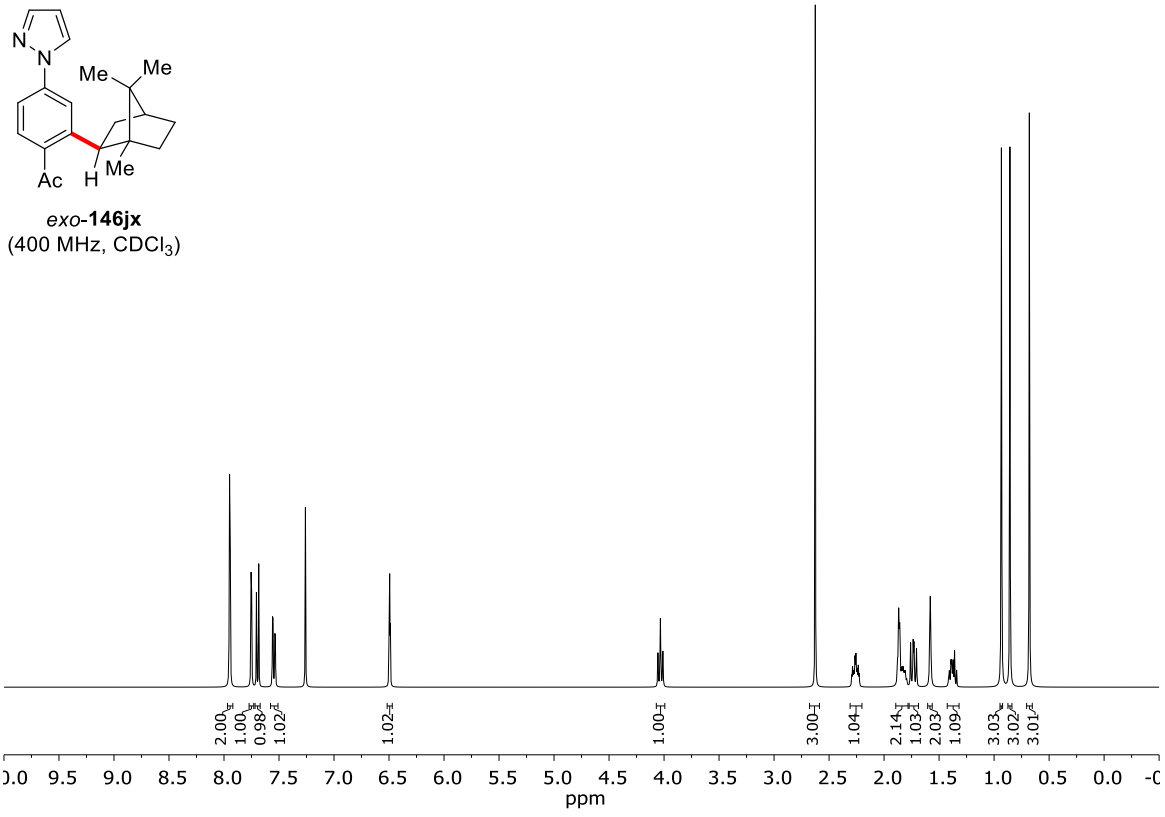
endo-**145jx**
(300 MHz, $CDCl_3$)



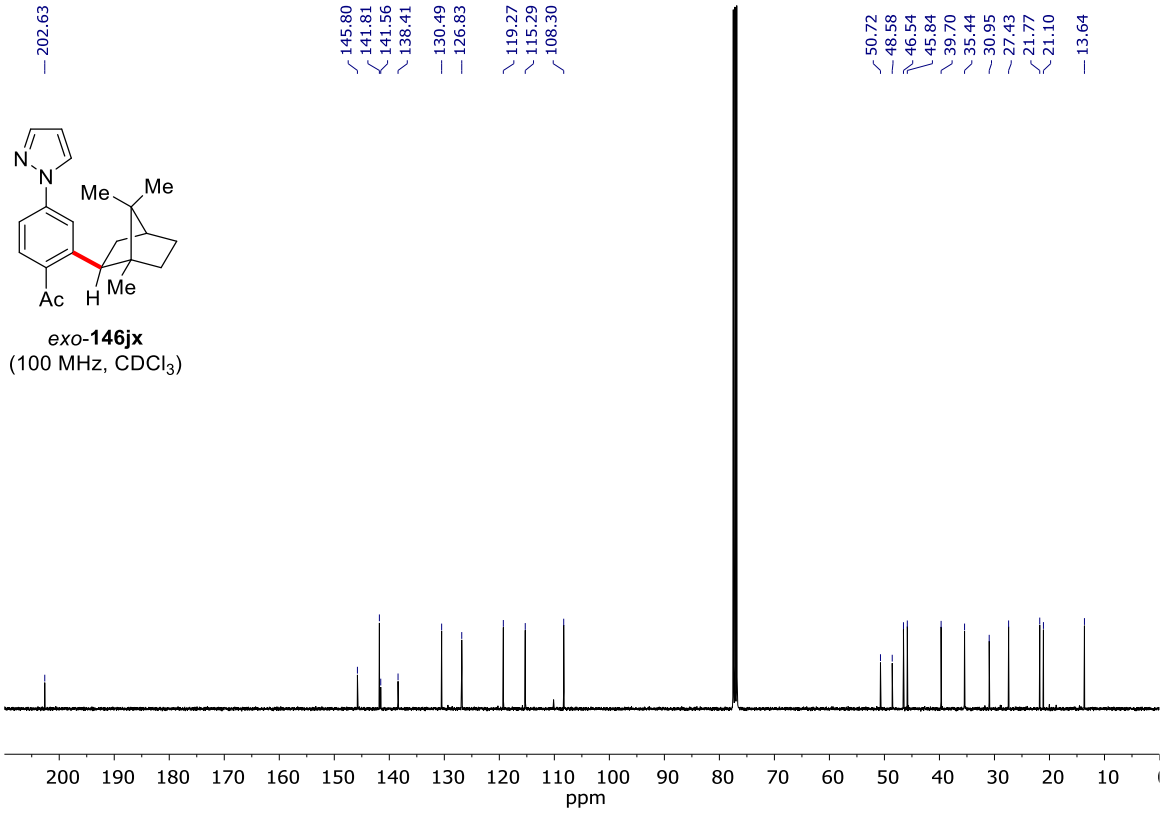
endo-**145jx**
(100 MHz, $CDCl_3$)



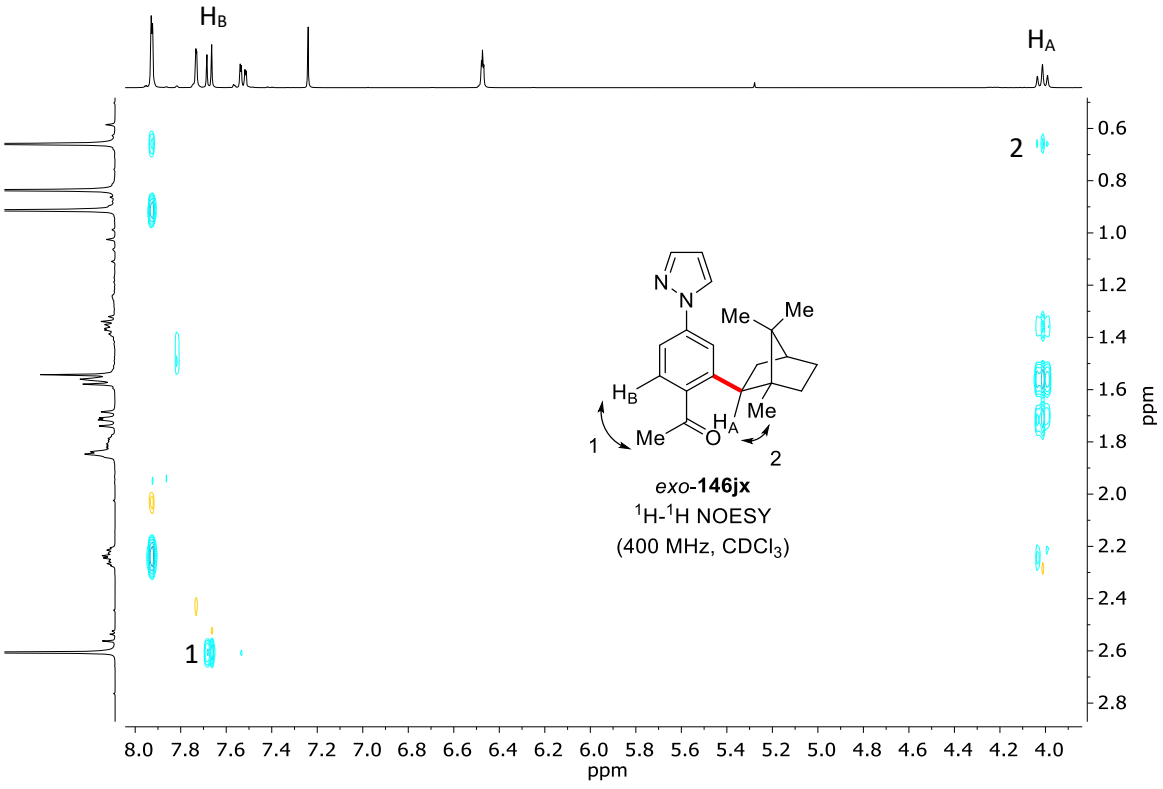
endo-**145jx**
^{1}H-^{1}H NOESY
(400 MHz, $CDCl_3$)



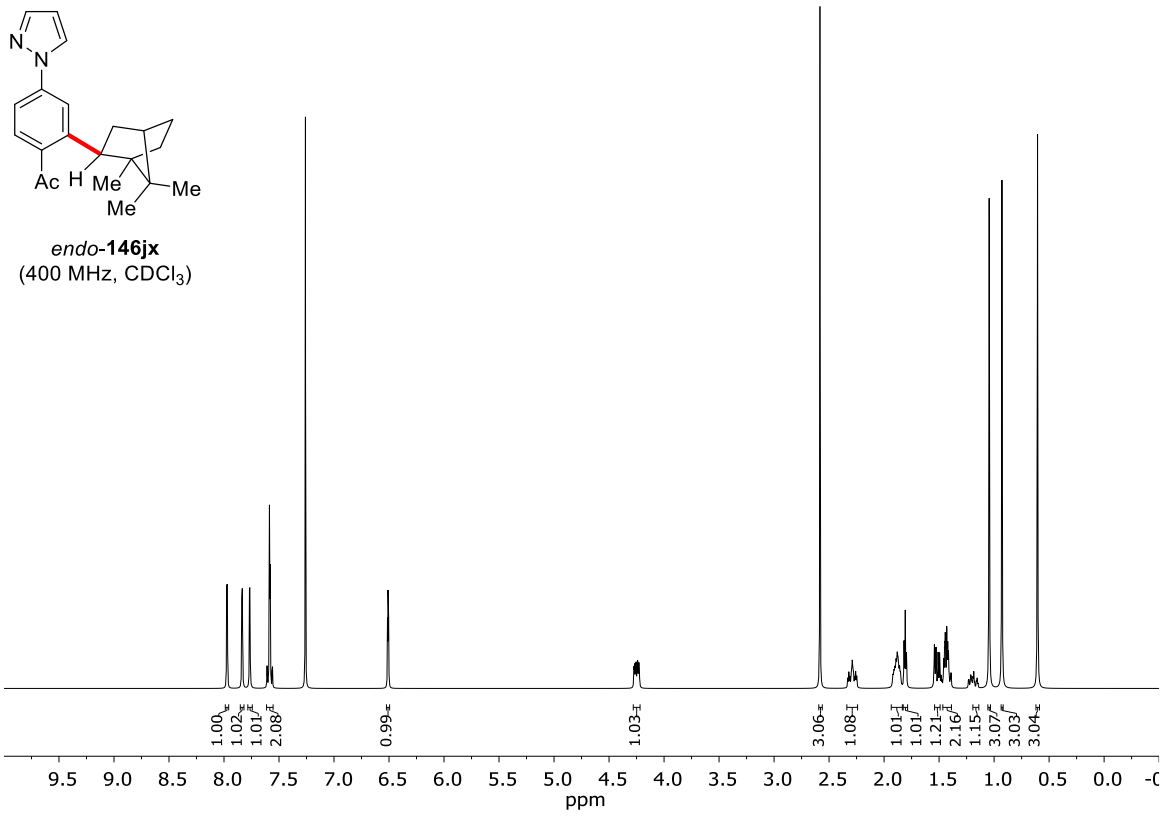
exo-**146jx**
(400 MHz, $CDCl_3$)



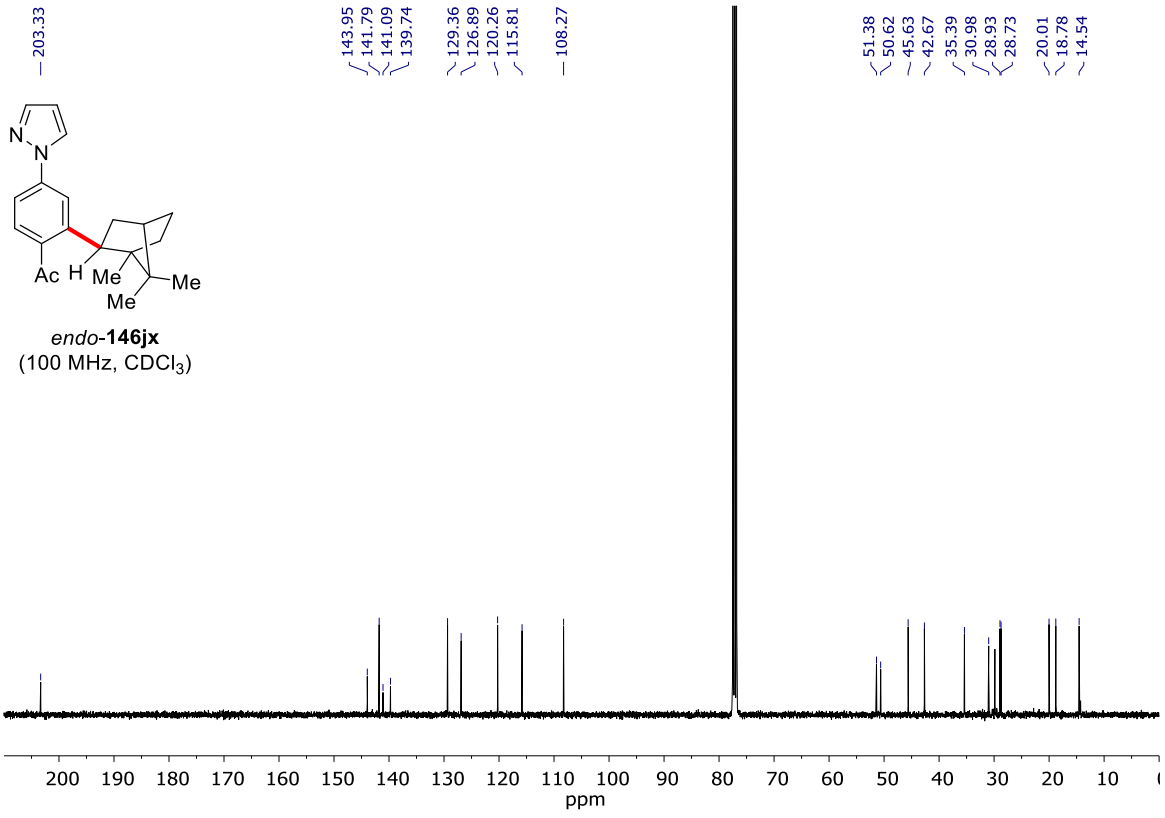
exo-**146jx**
(100 MHz, $CDCl_3$)



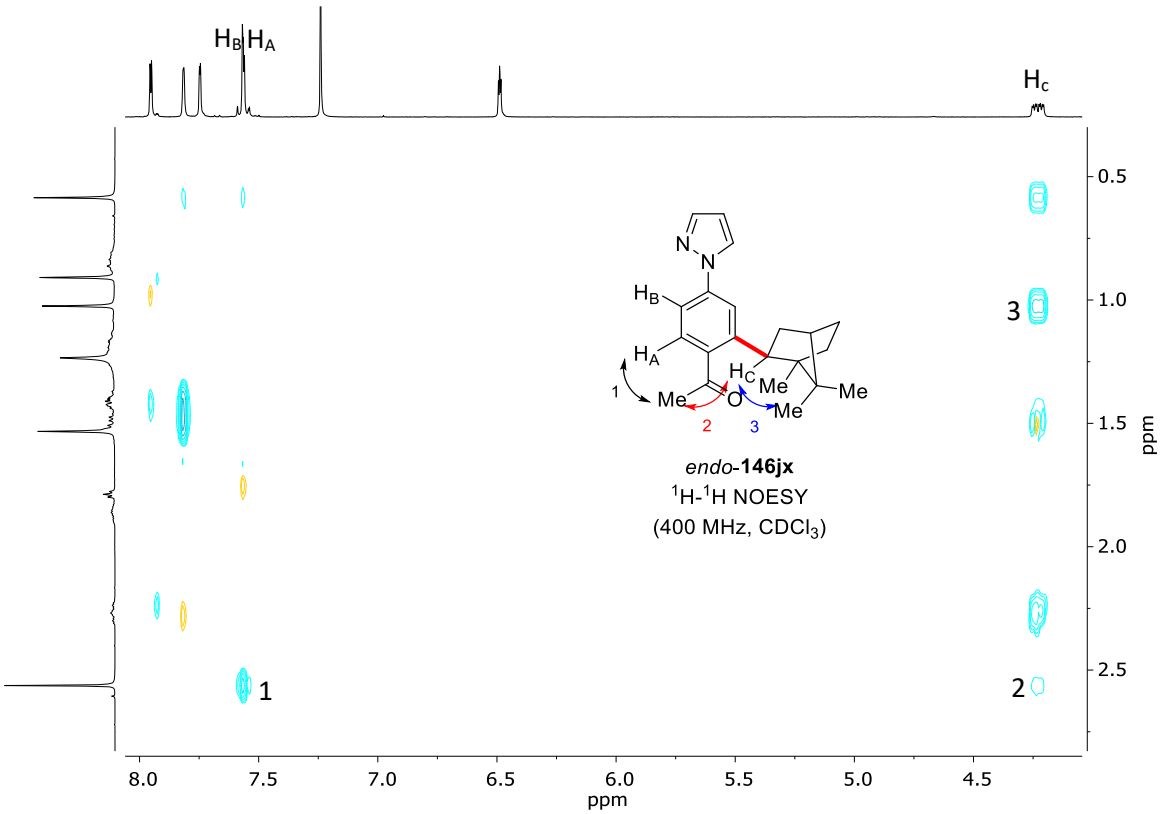
exo-**146jx**
^{1}H-^{1}H NOESY
(400 MHz, $CDCl_3$)



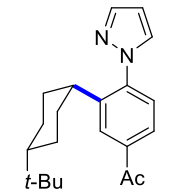
endo-**146jx**
(400 MHz, $CDCl_3$)



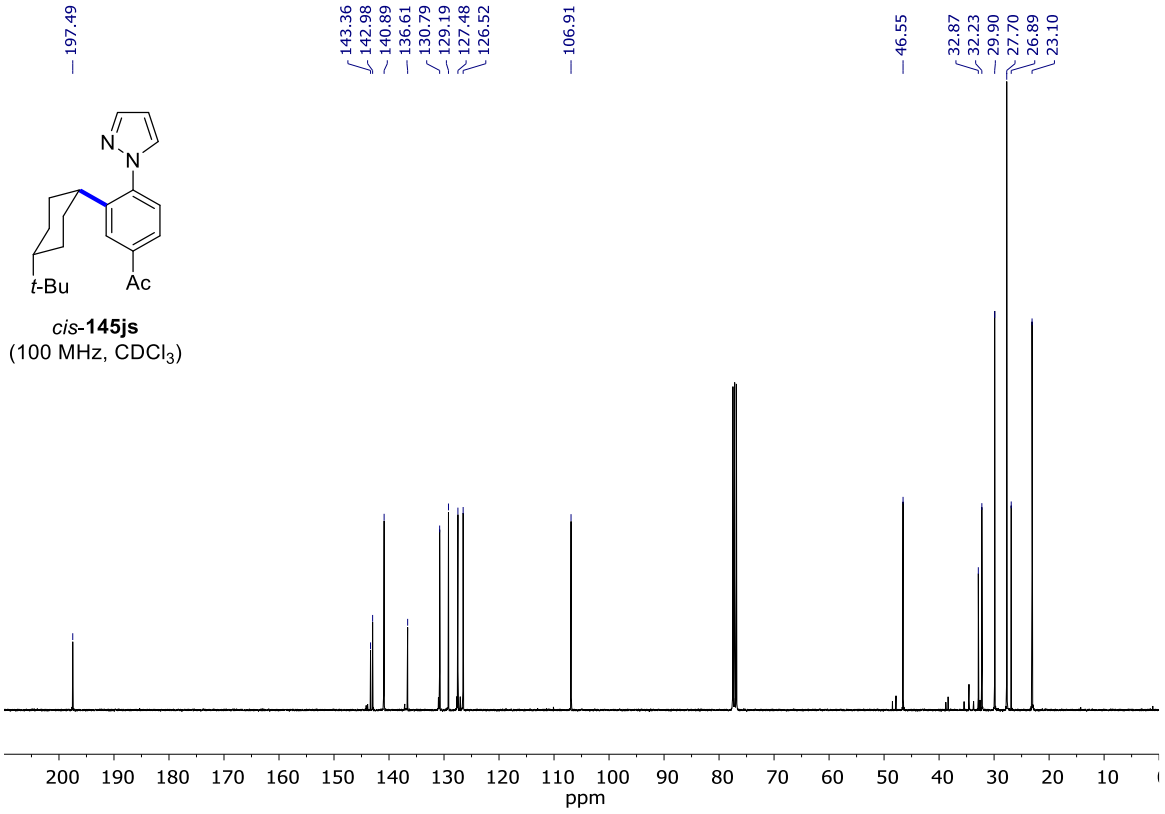
endo-**146jx**
(100 MHz, $CDCl_3$)

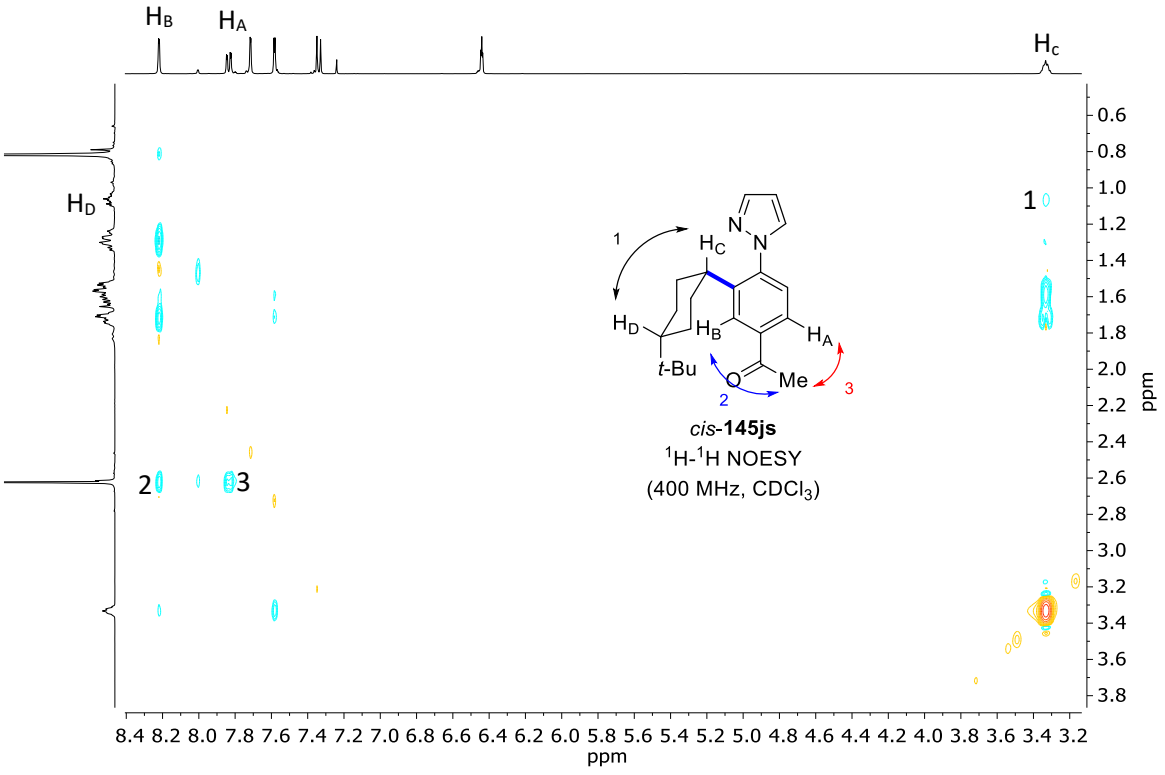


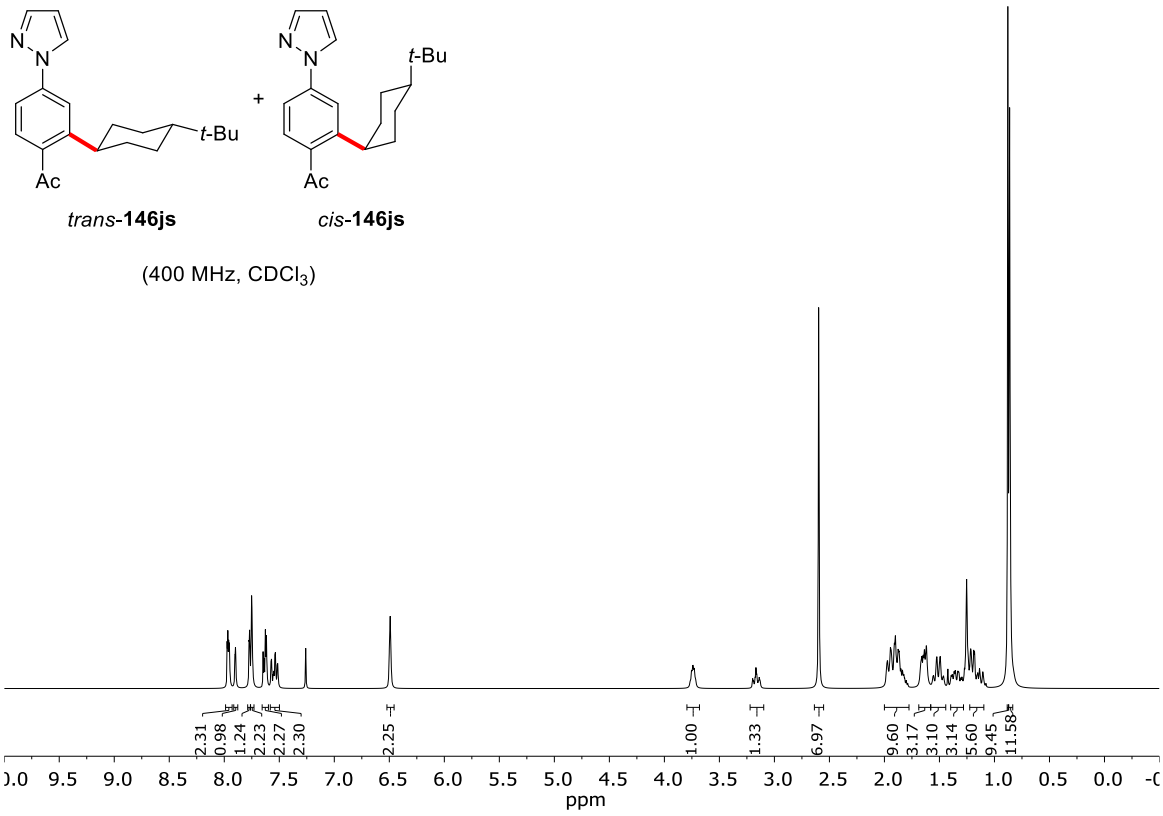
endo-**146jx**
^{1}H-^{1}H NOESY
(400 MHz, $CDCl_3$)



cis-**145js**
(400 MHz, $CDCl_3$)

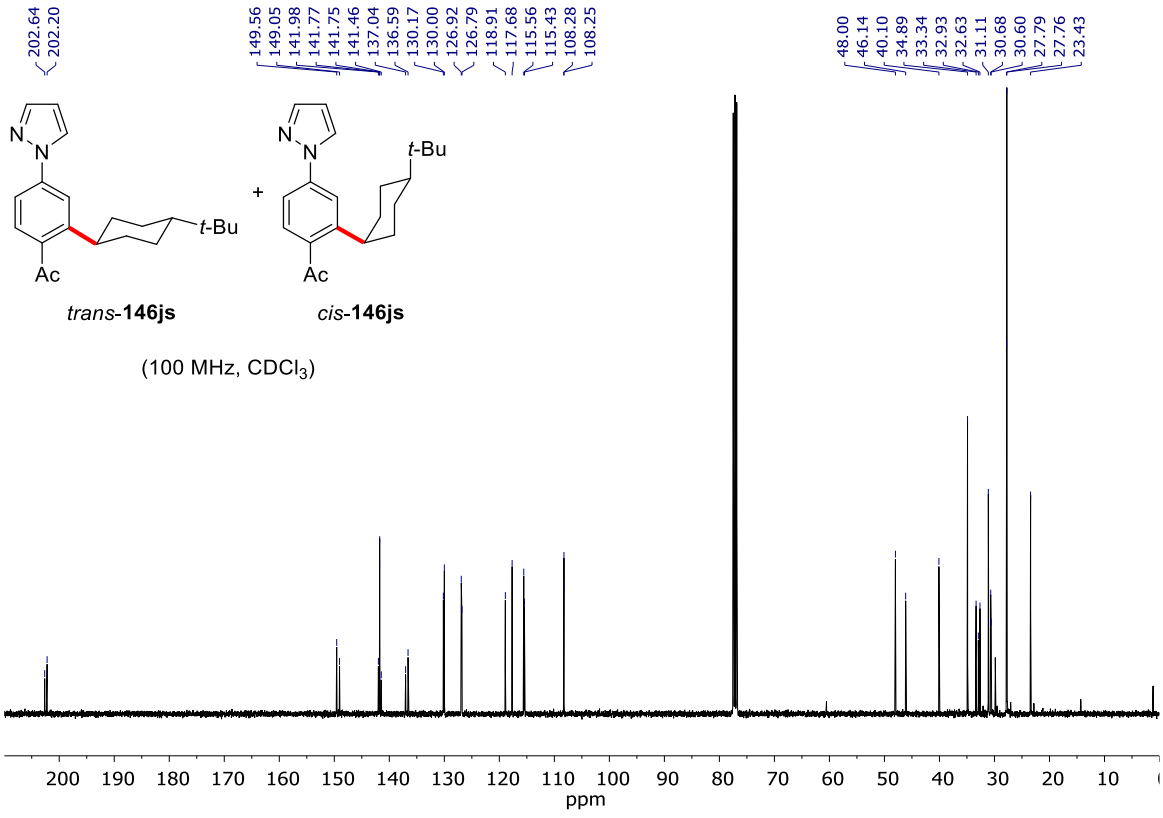

197.49
143.36
142.98
140.89
136.61
130.79
129.19
127.48
126.52
106.91
46.55
32.87
32.23
29.90
27.70
26.89
23.10
t-Bu
Ac
cis-145js
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm


HB
HA
HC
HD
1
2
3
t-Bu
Me
cis-145js
1H-1H NOESY
(400 MHz, CDCl3)
8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2
ppm
0.6 0.8 1.0 1.2 1.4 1.6 1.8 2.0 2.2 2.4 2.6 2.8 3.0 3.2 3.4 3.6 3.8
ppm



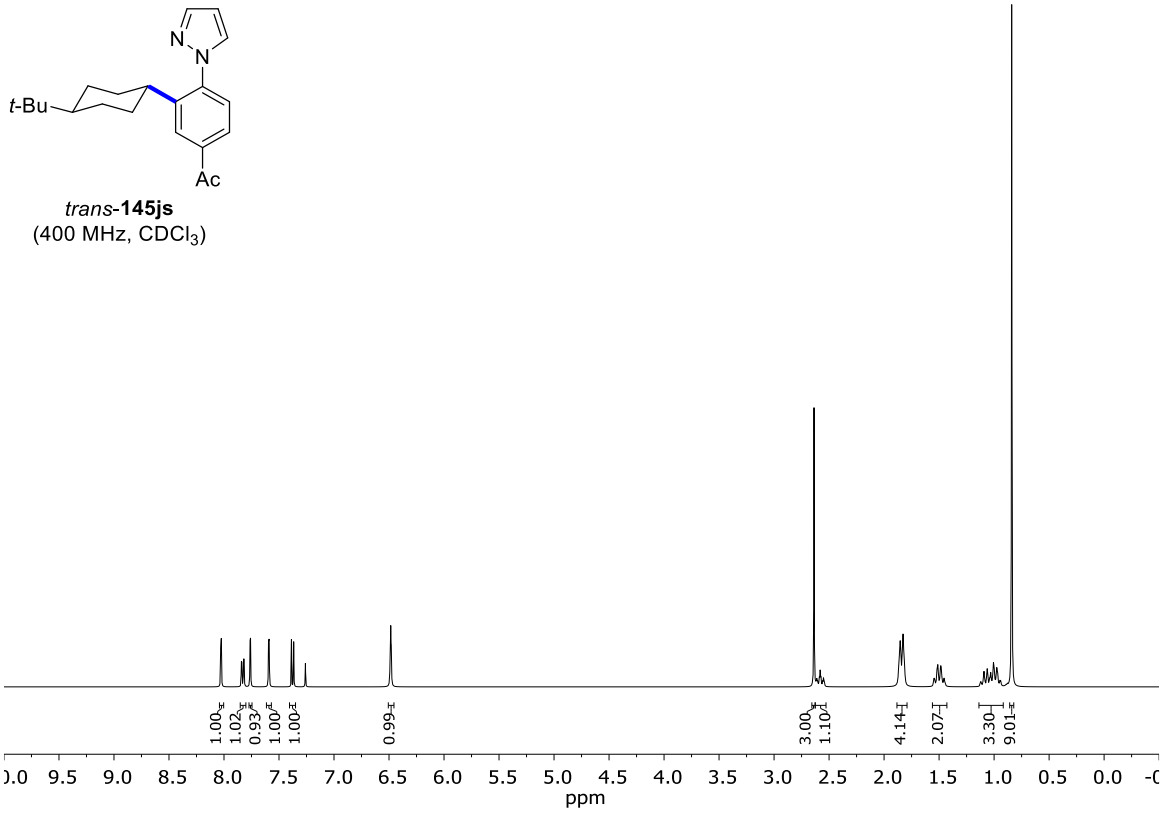
trans-**146js** *cis*-**146js**

(400 MHz, $CDCl_3$)

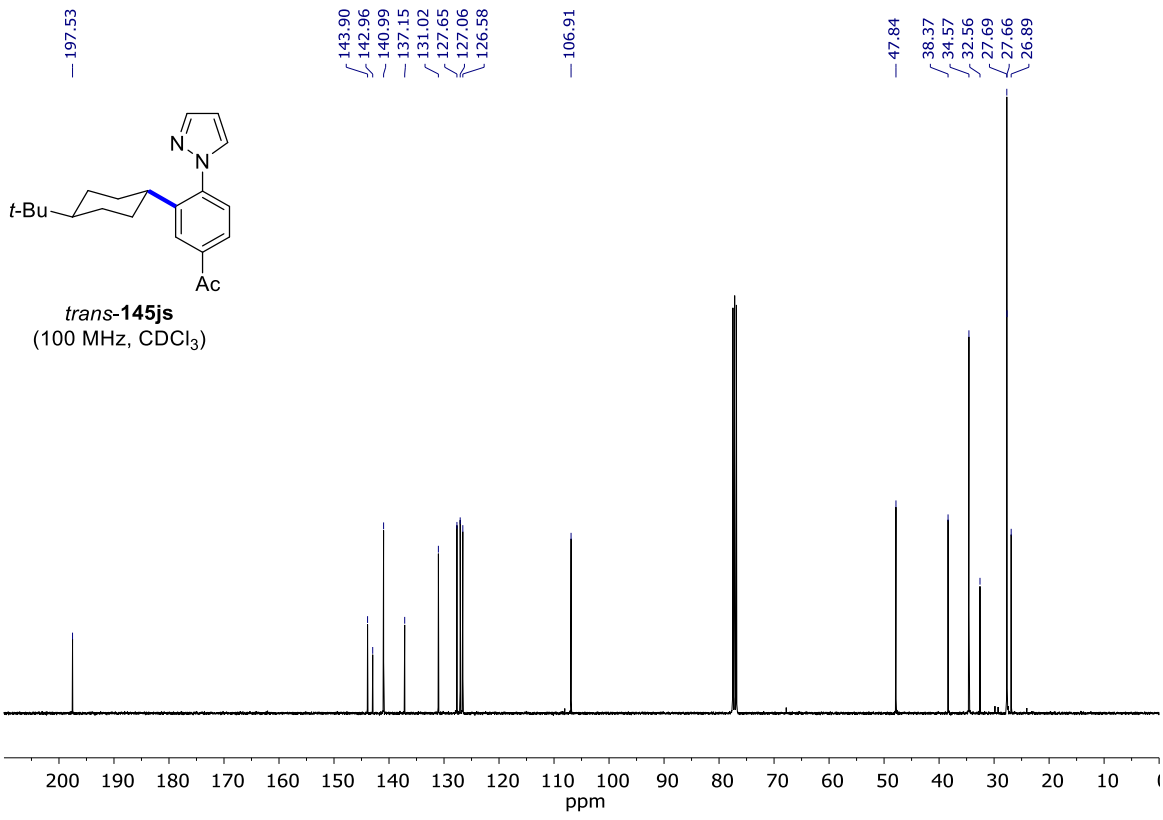


trans-**146js** *cis*-**146js**

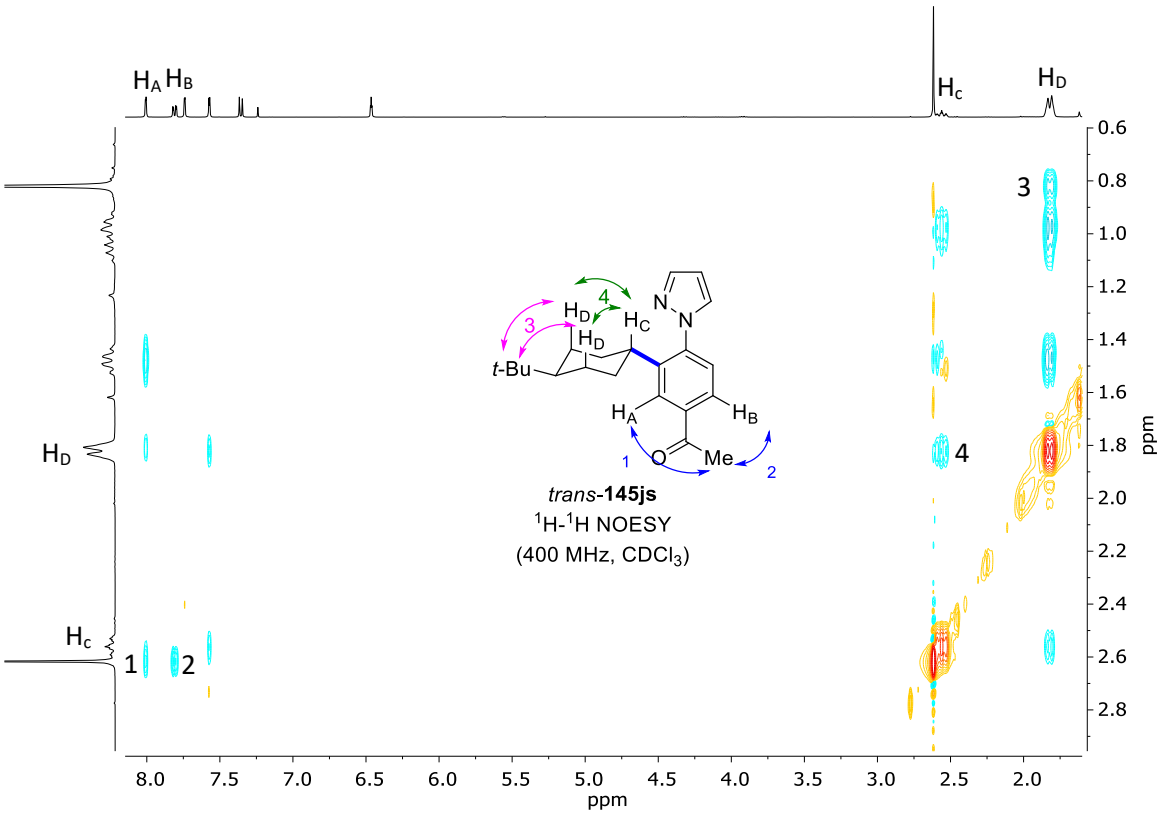
(100 MHz, $CDCl_3$)



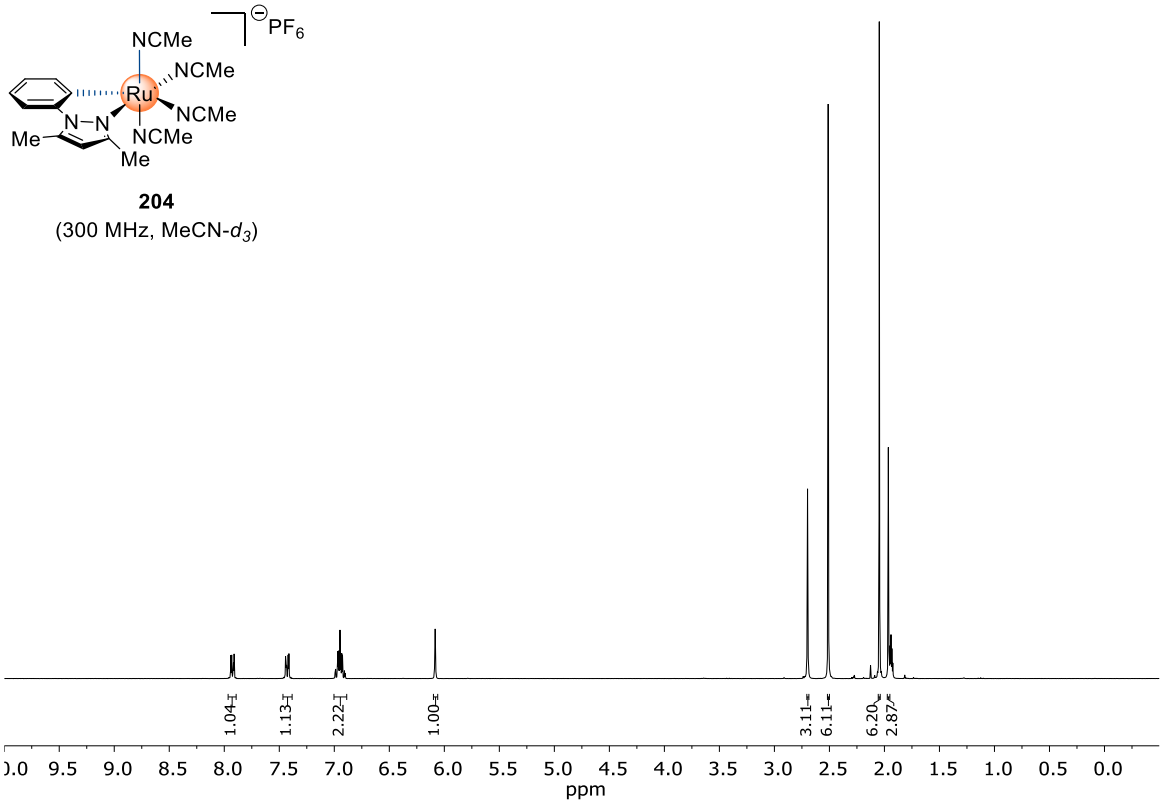
trans-**145js**
(400 MHz, $CDCl_3$)



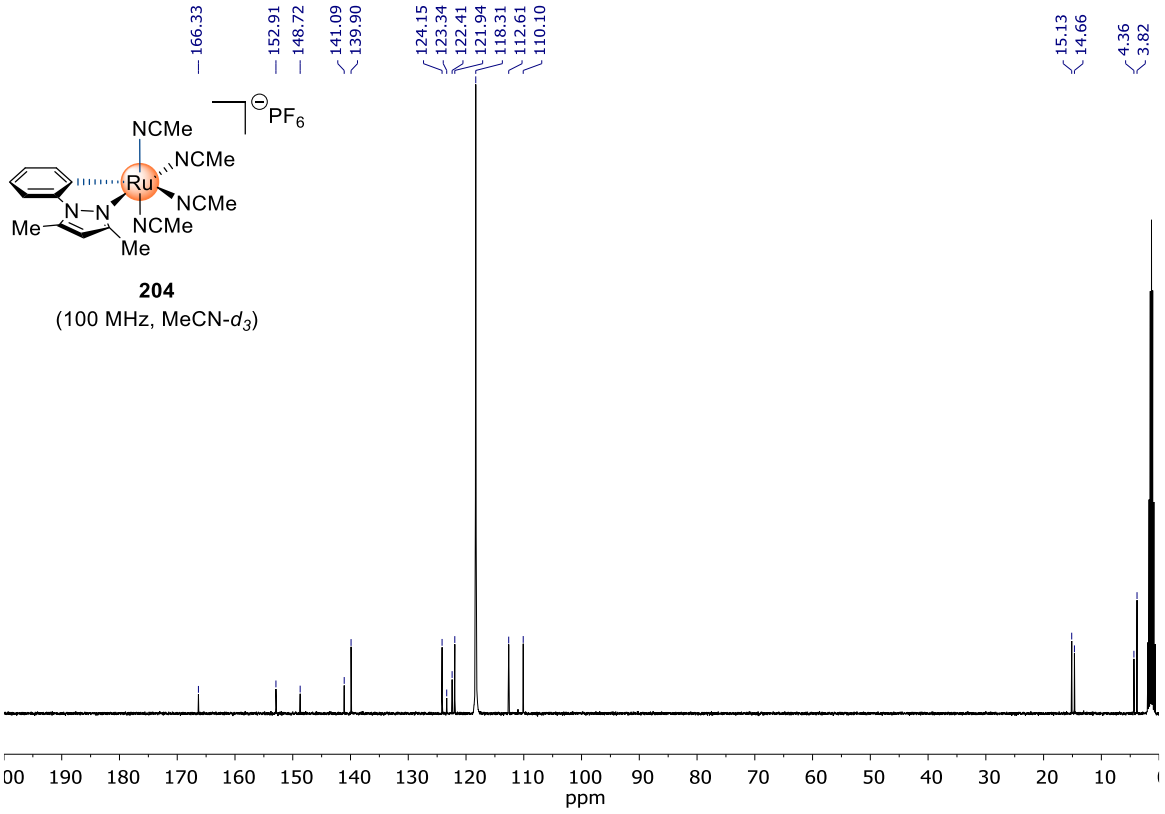
trans-**145js**
(100 MHz, $CDCl_3$)



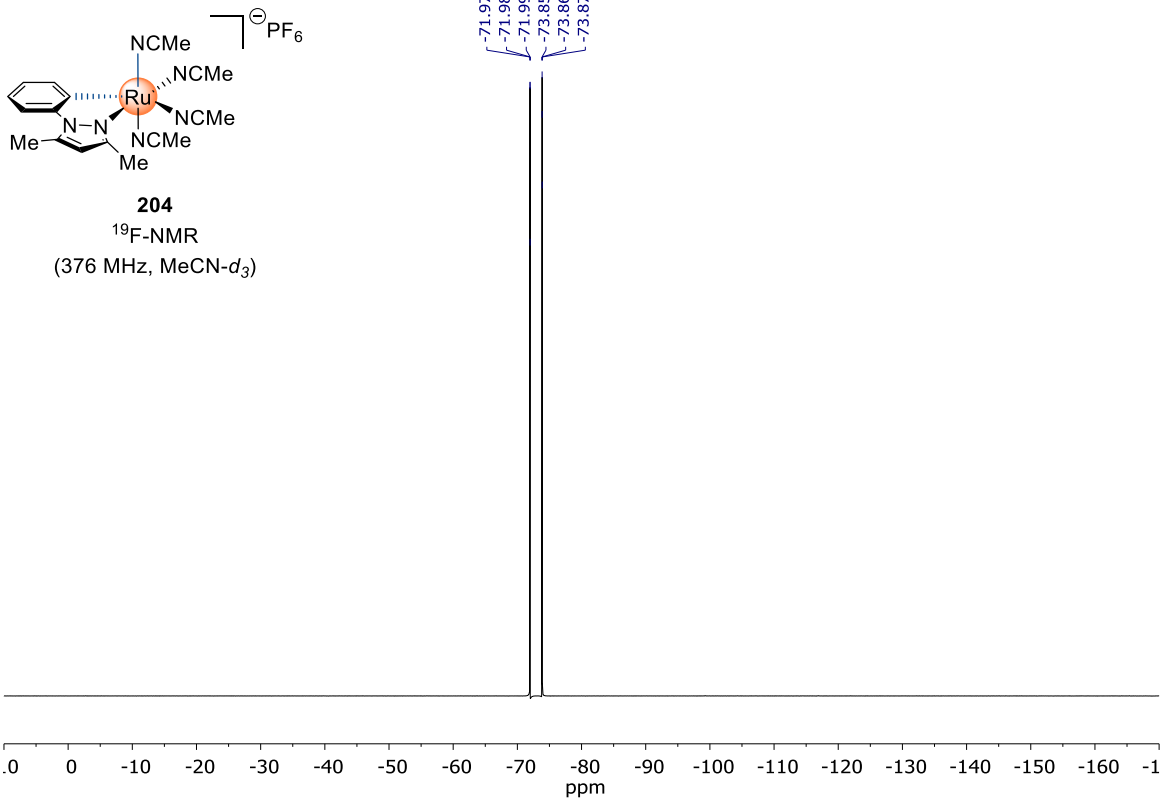
trans-**145js**
^{1}H-^{1}H NOESY
(400 MHz, $CDCl_3$)



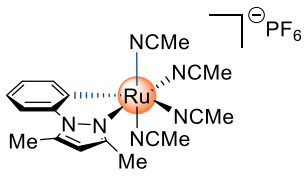
204
(300 MHz, MeCN-d_3)



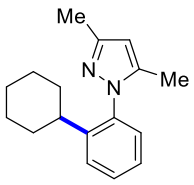
204
(100 MHz, MeCN-d_3)



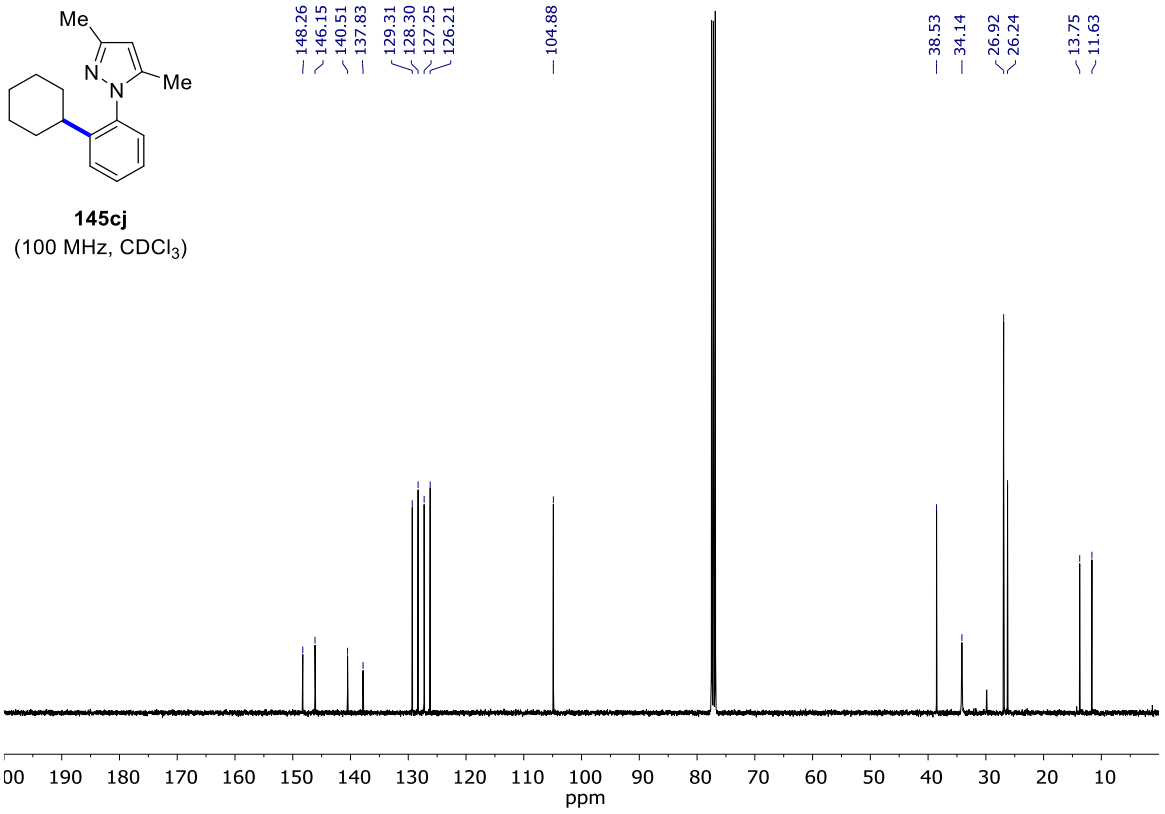
204
^{19}F-NMR
(376 MHz, MeCN-d_3)



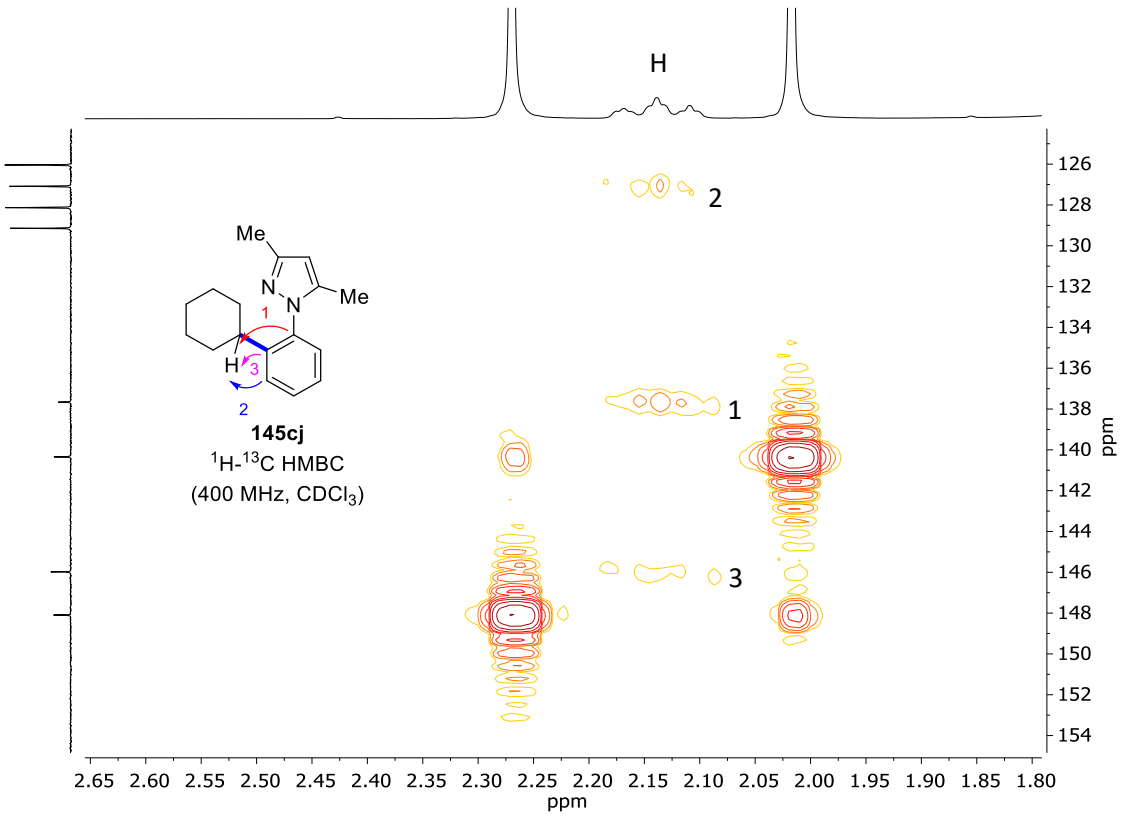
204
^{31}P-NMR
(162 MHz, MeCN-d_3)



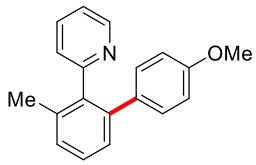
145cj
(400 MHz, $CDCl_3$)



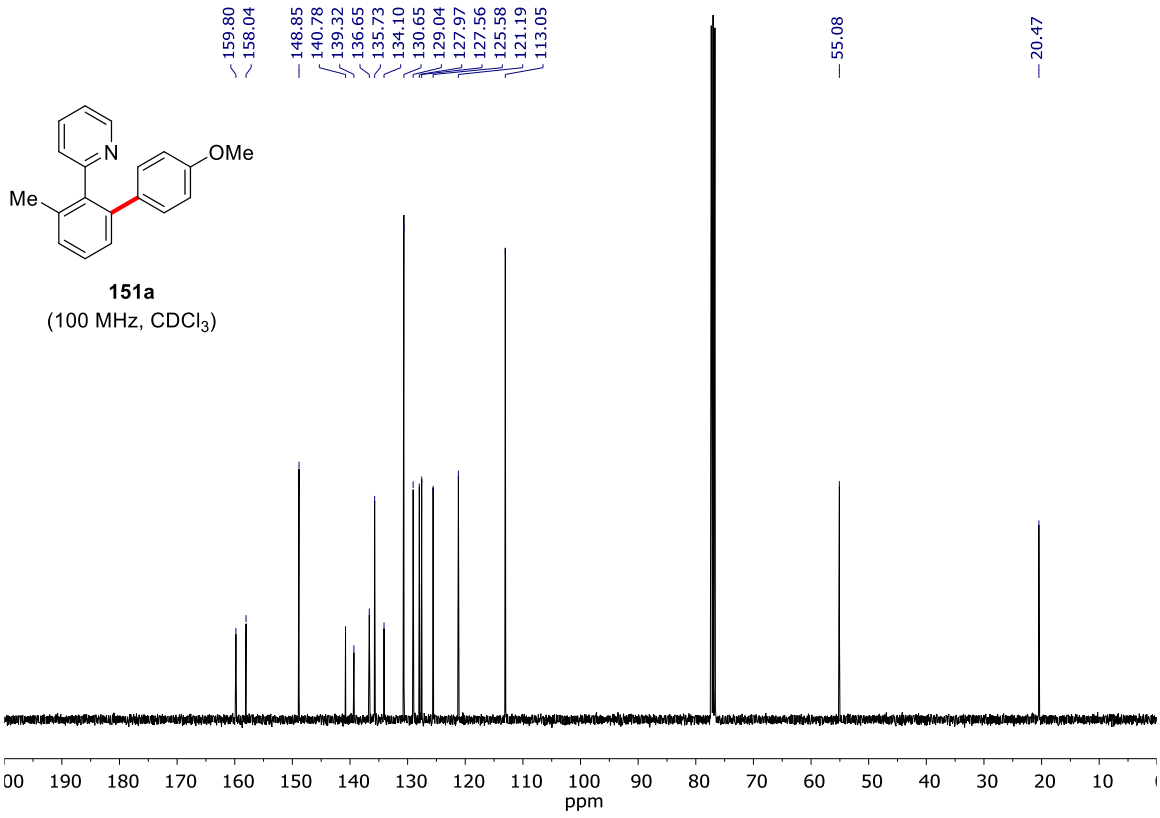
145cj
(100 MHz, $CDCl_3$)



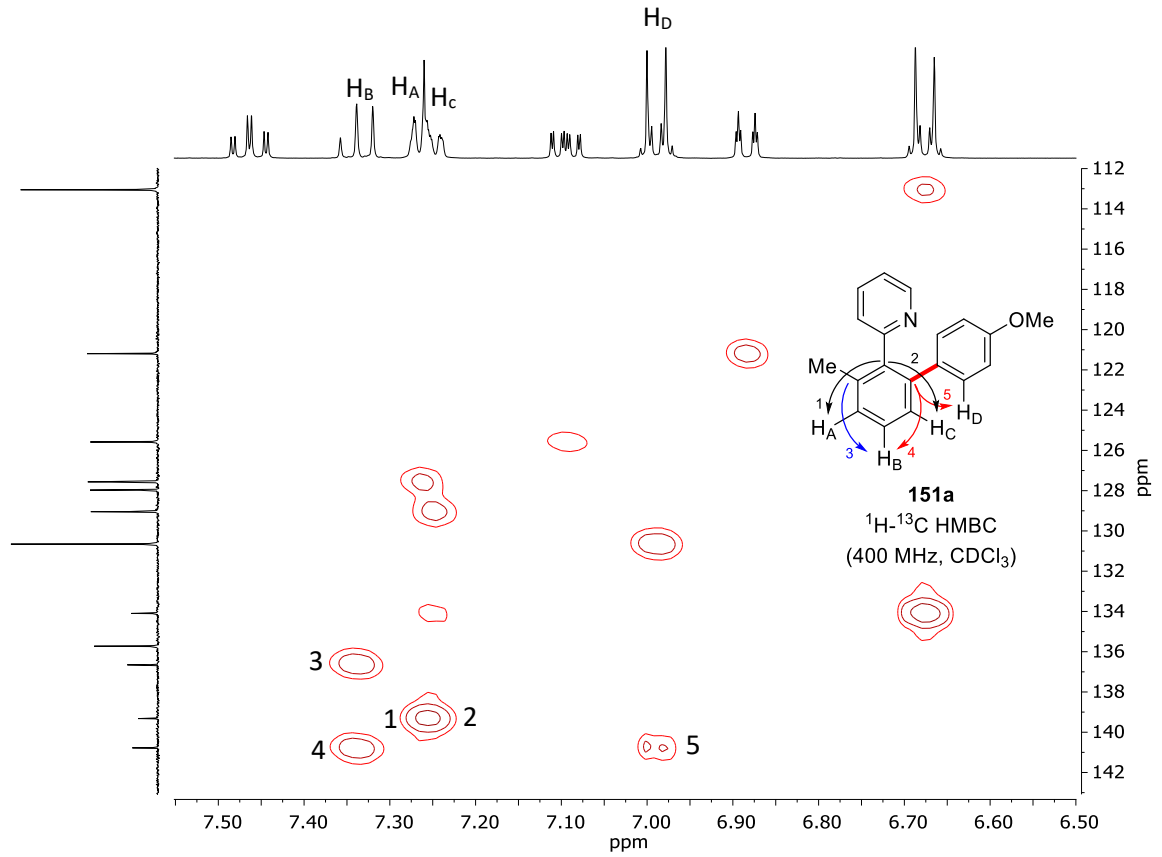
145cj
^{1}H-^{13}C HMBC
(400 MHz, $CDCl_3$)

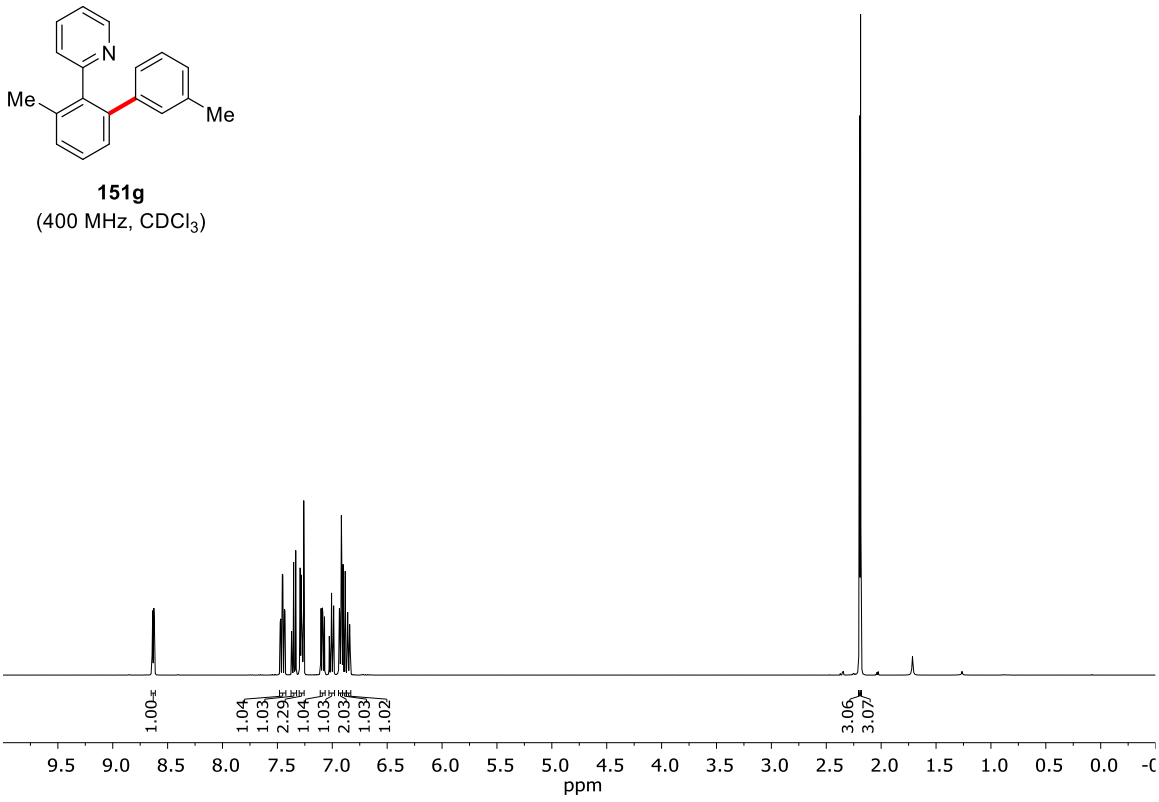


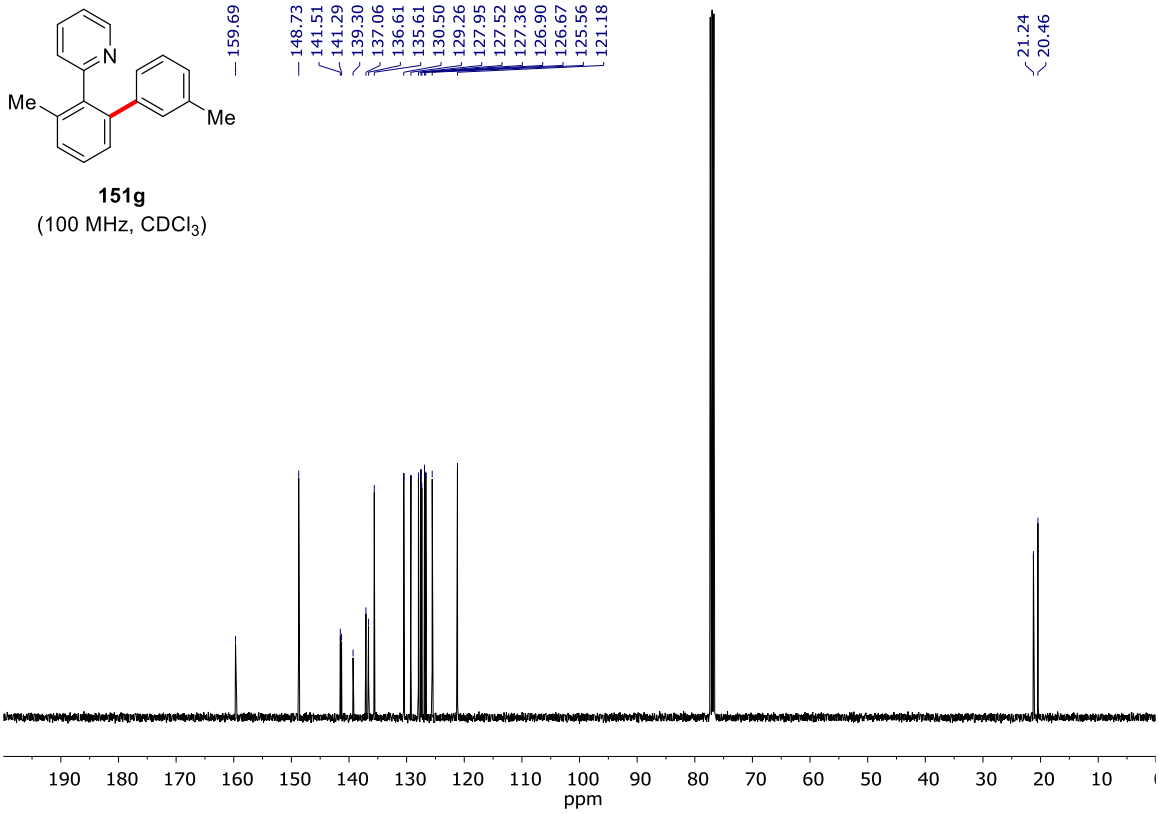
151a
(400 MHz, $CDCl_3$)



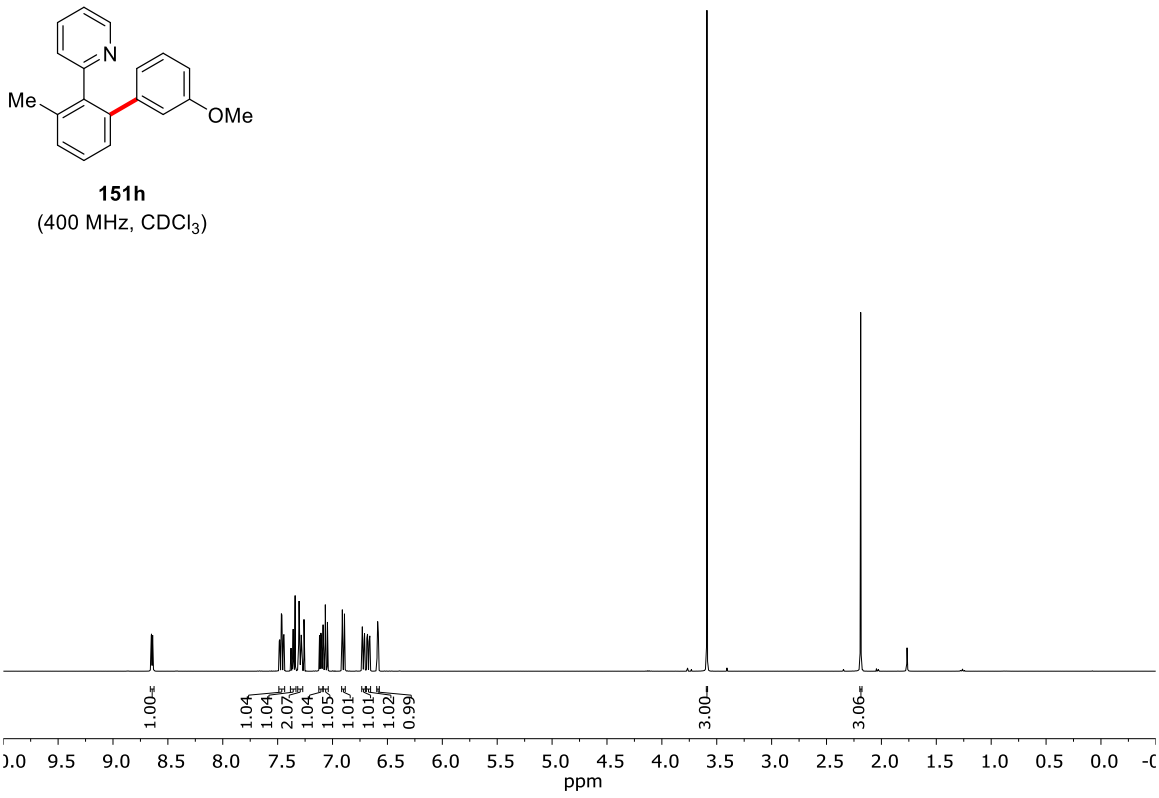
151a
(100 MHz, $CDCl_3$)


H_D
H_B H_A H_C
N
OMe
Me
1
2
3
4
5
H_A
H_B
H_C
H_D
151a
^{1}H-^{13}C HMBC
(400 MHz, CDCl$_3$)
ppm
ppm

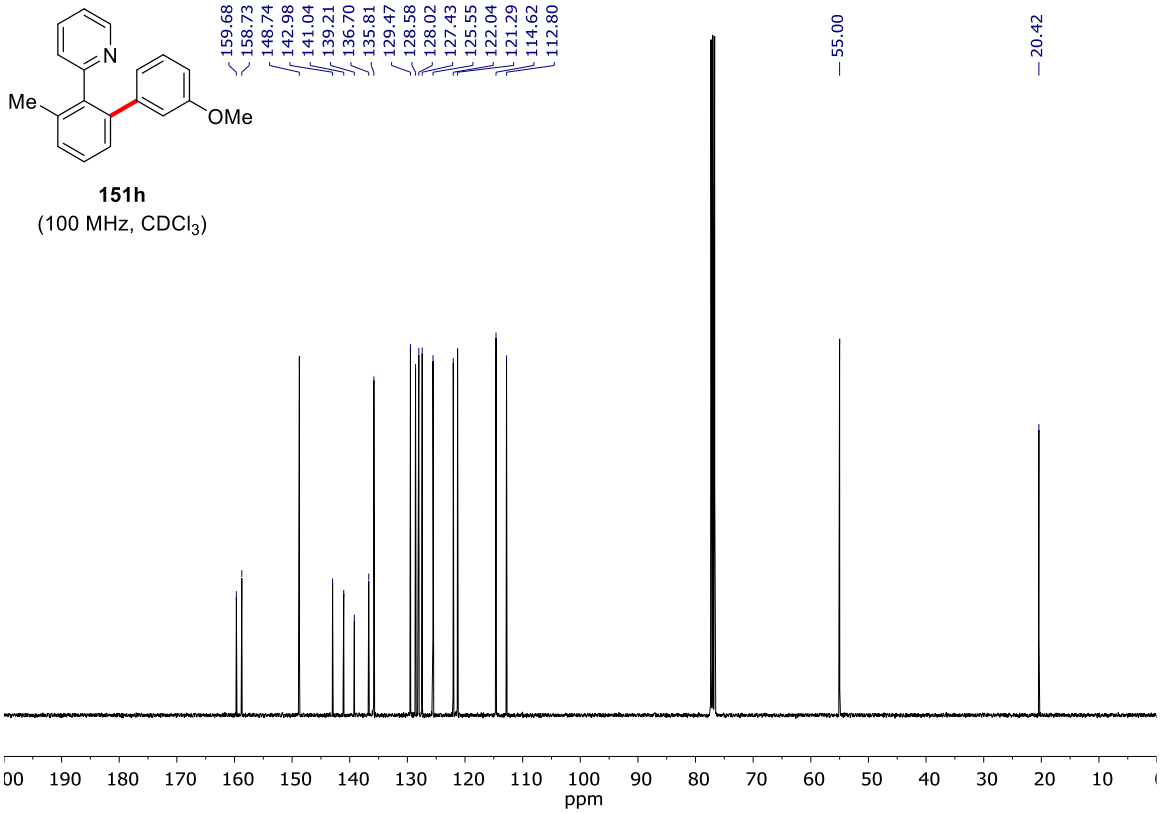

N
Me
Me
151g
(400 MHz, CDCl$_3$)
1.00
1.04
1.03
2.29
1.04
1.03
2.03
1.03
1.02
3.06
3.07
ppm



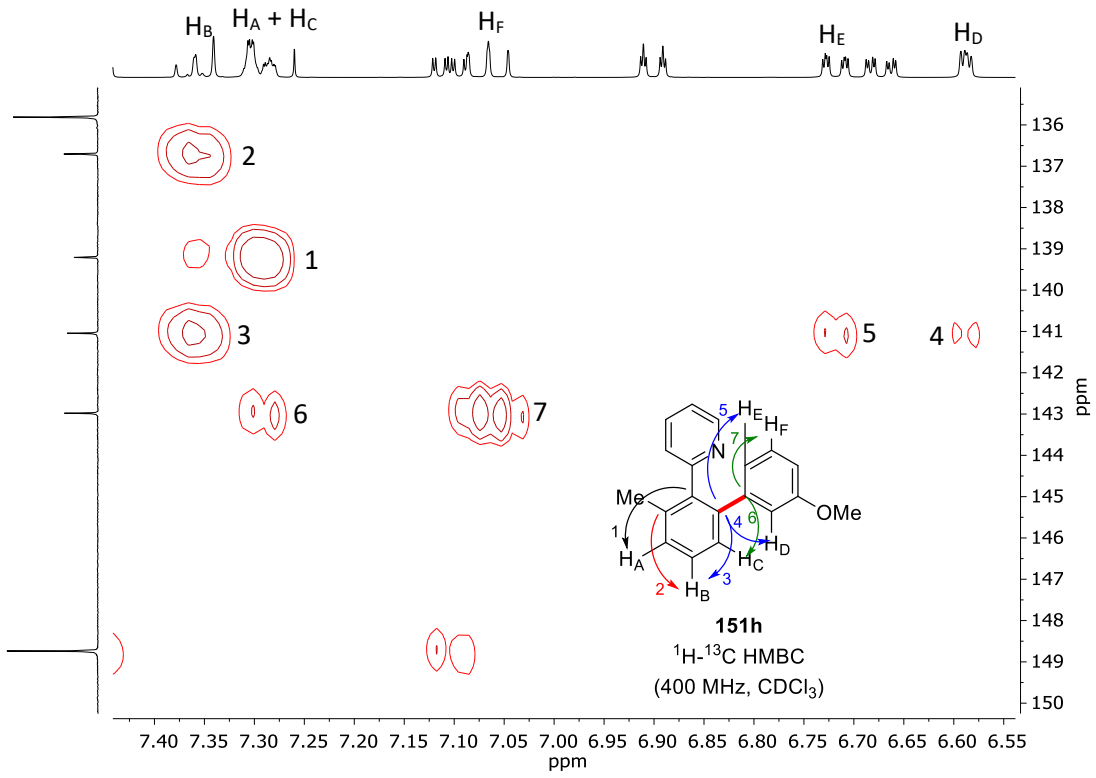
151g
(100 MHz, $CDCl_3$)



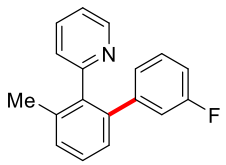
151h
(400 MHz, $CDCl_3$)



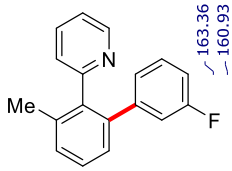
151h
(100 MHz, $CDCl_3$)



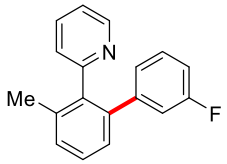
151h
^{1}H-^{13}C HMBC
(400 MHz, $CDCl_3$)



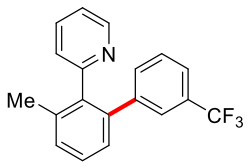
151i
(400 MHz, $CDCl_3$)



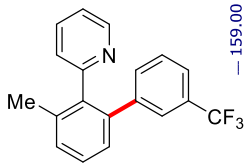
151i
(100 MHz, $CDCl_3$)



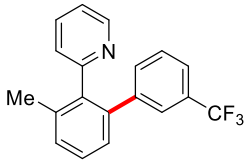
151i
^{19}F-NMR
(376 MHz, $CDCl_3$)



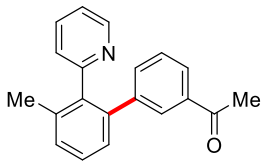
151j
(400 MHz, $CDCl_3$)



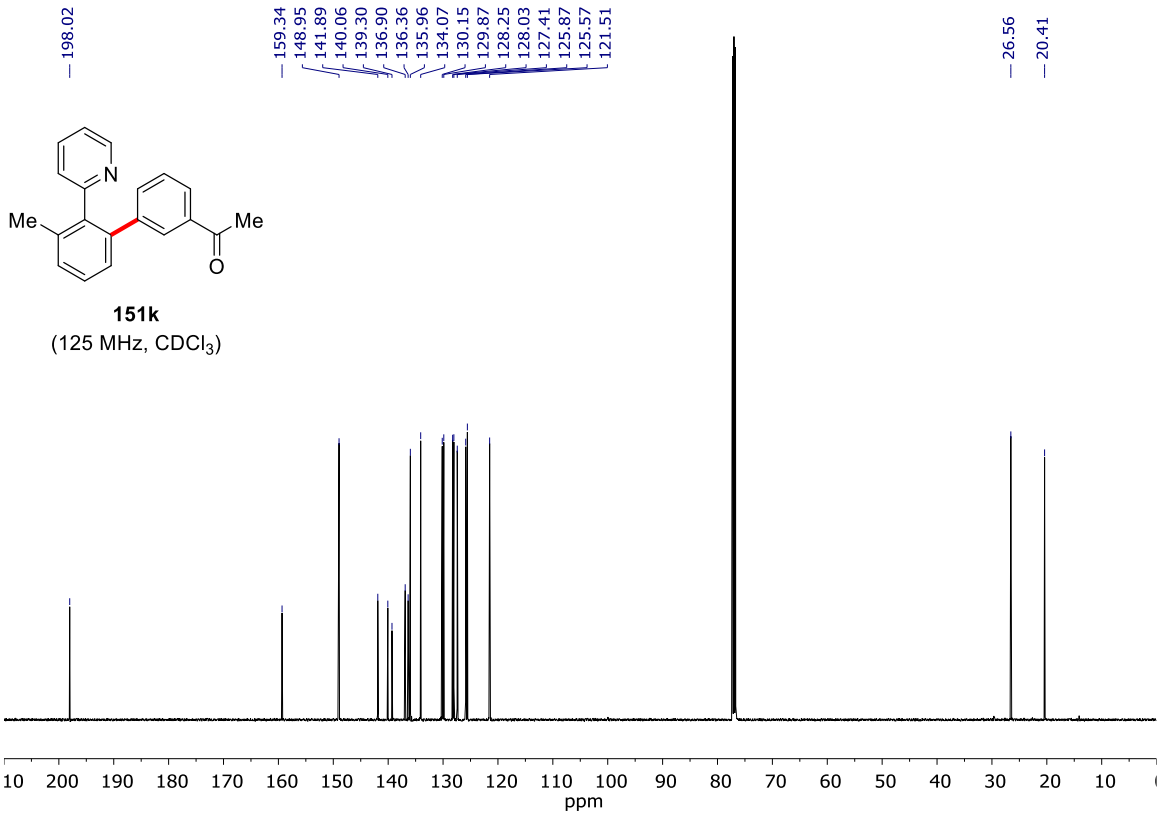
151j
(100 MHz, $CDCl_3$)



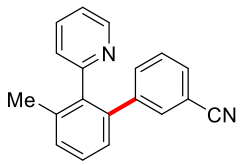
151j
^{19}F-NMR
(376 MHz, $CDCl_3$)



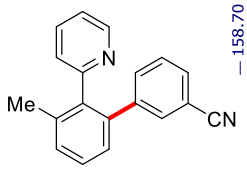
151k
(500 MHz, $CDCl_3$)



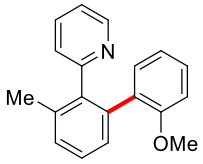
151k
(125 MHz, $CDCl_3$)



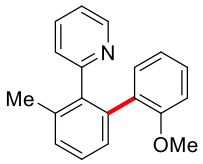
151l
(400 MHz, $CDCl_3$)



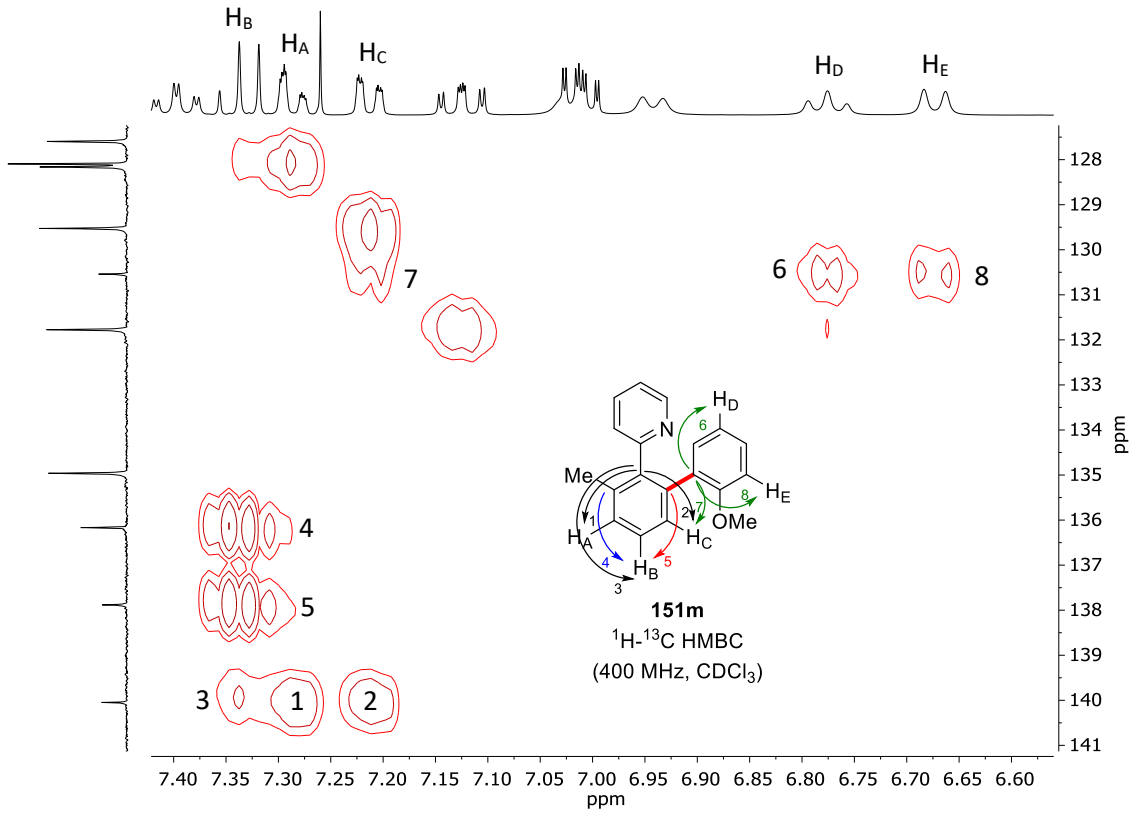
151l
(100 MHz, $CDCl_3$)



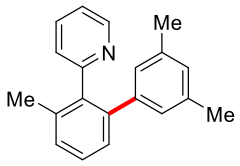
151m
(400 MHz, $CDCl_3$)



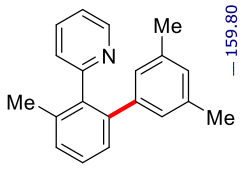
151m
(100 MHz, $CDCl_3$)



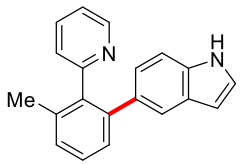
151m
^{1}H-^{13}C HMBC
(400 MHz, $CDCl_3$)



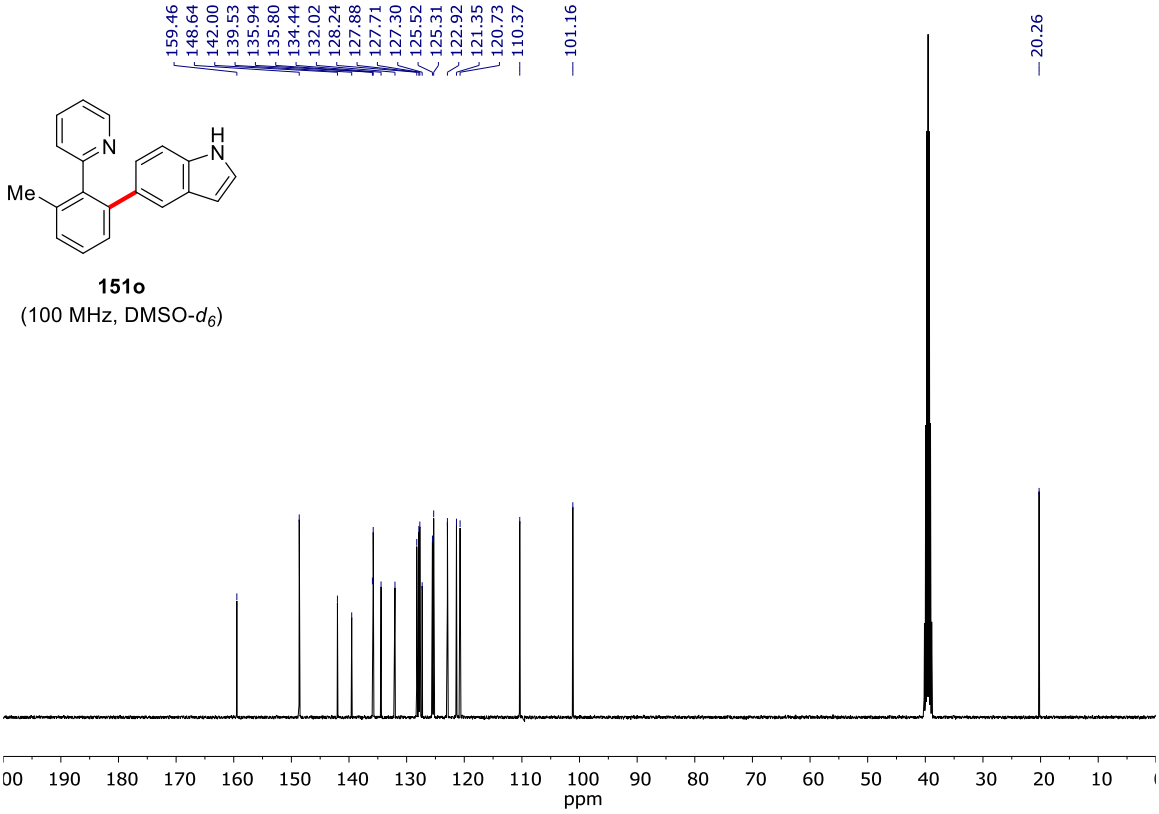
151n
(400 MHz, $CDCl_3$)



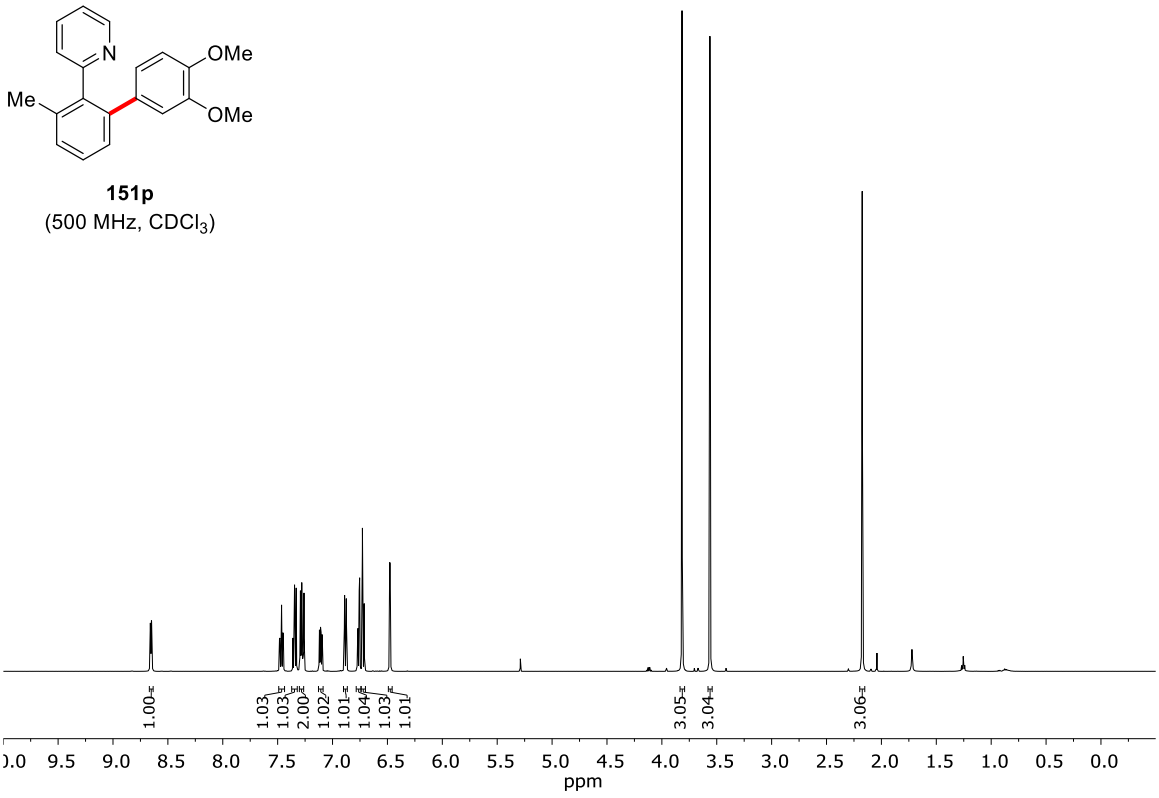
151n
(100 MHz, $CDCl_3$)



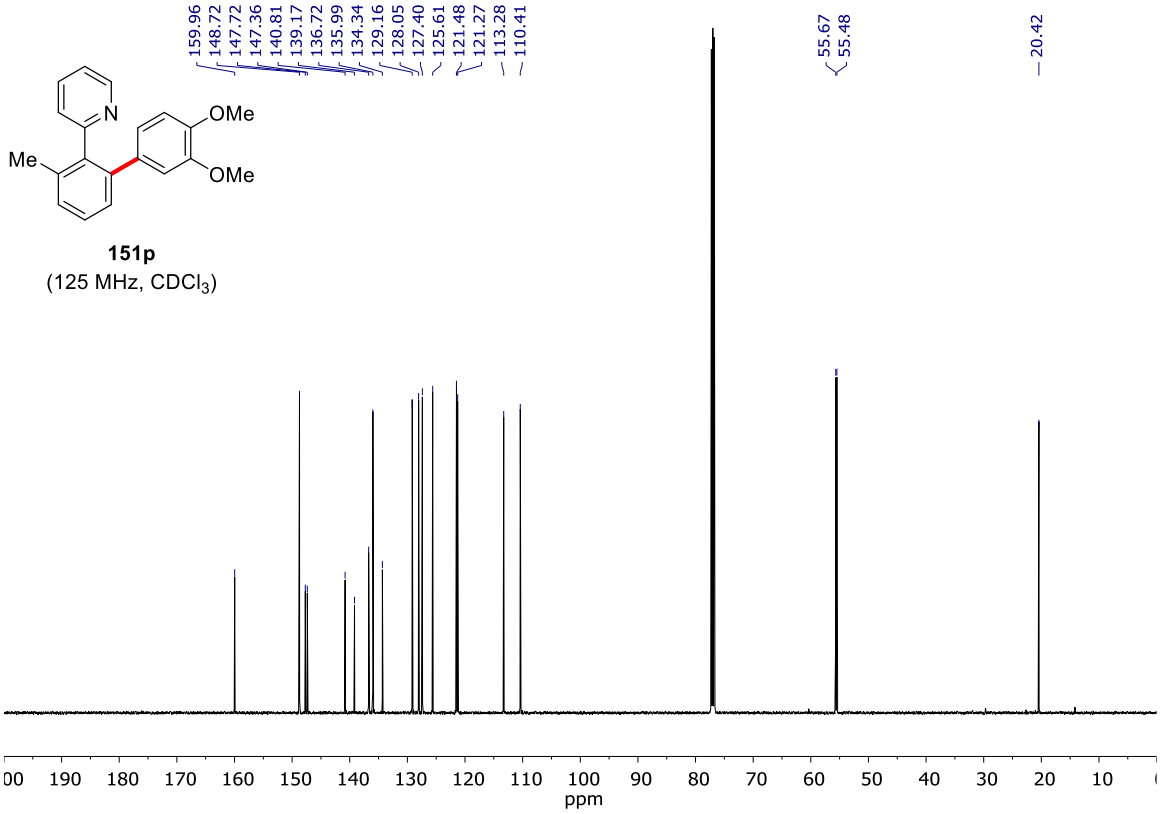
151o
(400 MHz, DMSO-d_6)



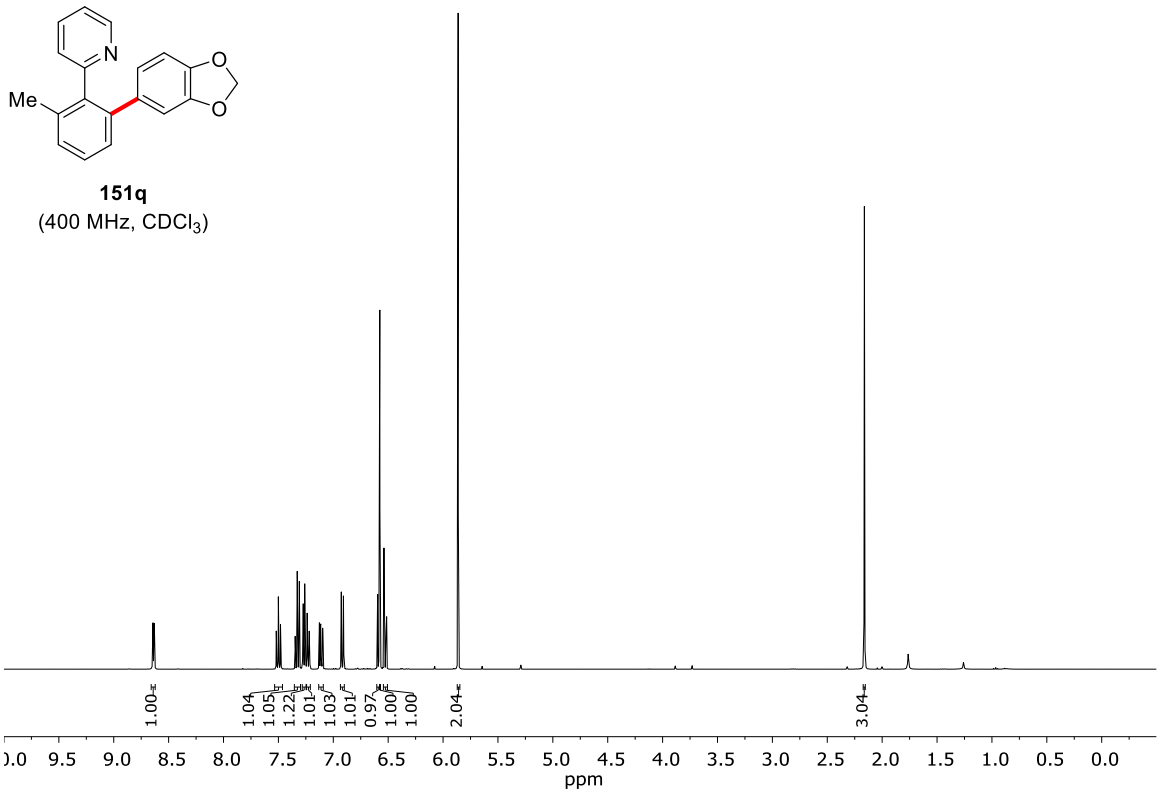
151o
(100 MHz, DMSO-d_6)



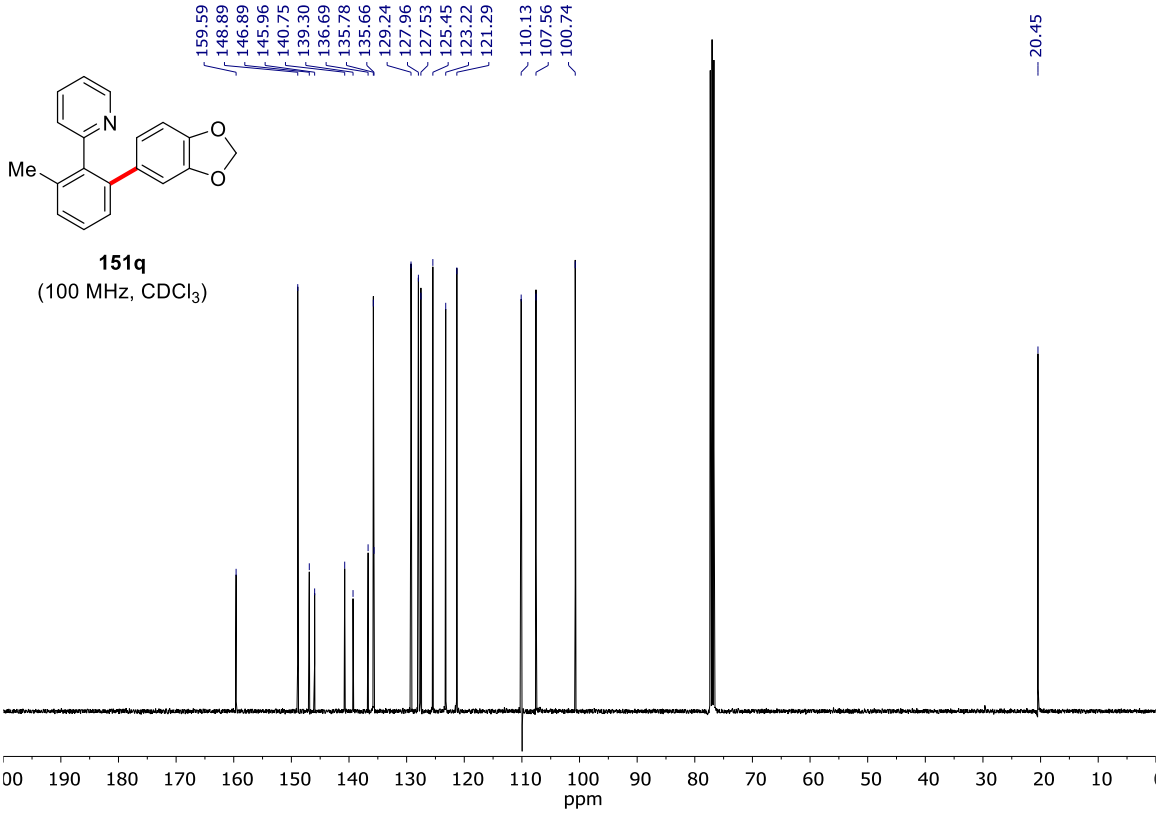
151p
(500 MHz, $CDCl_3$)



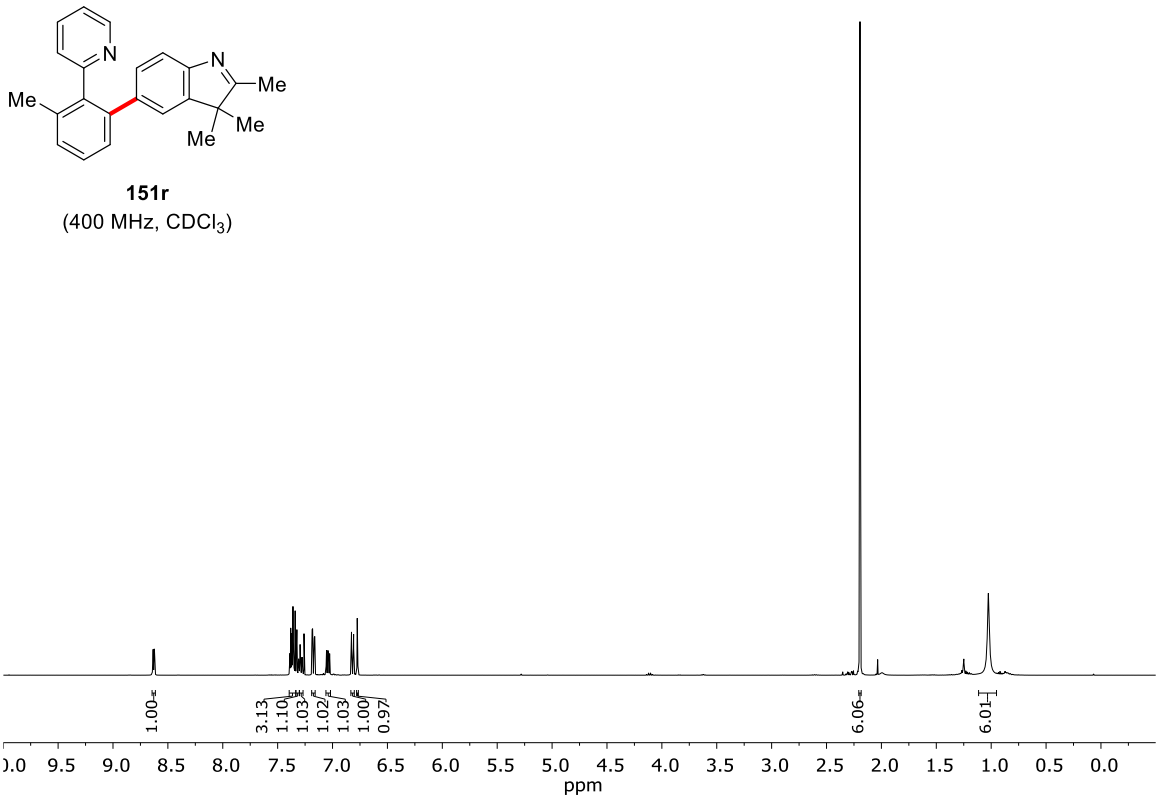
151p
(125 MHz, $CDCl_3$)



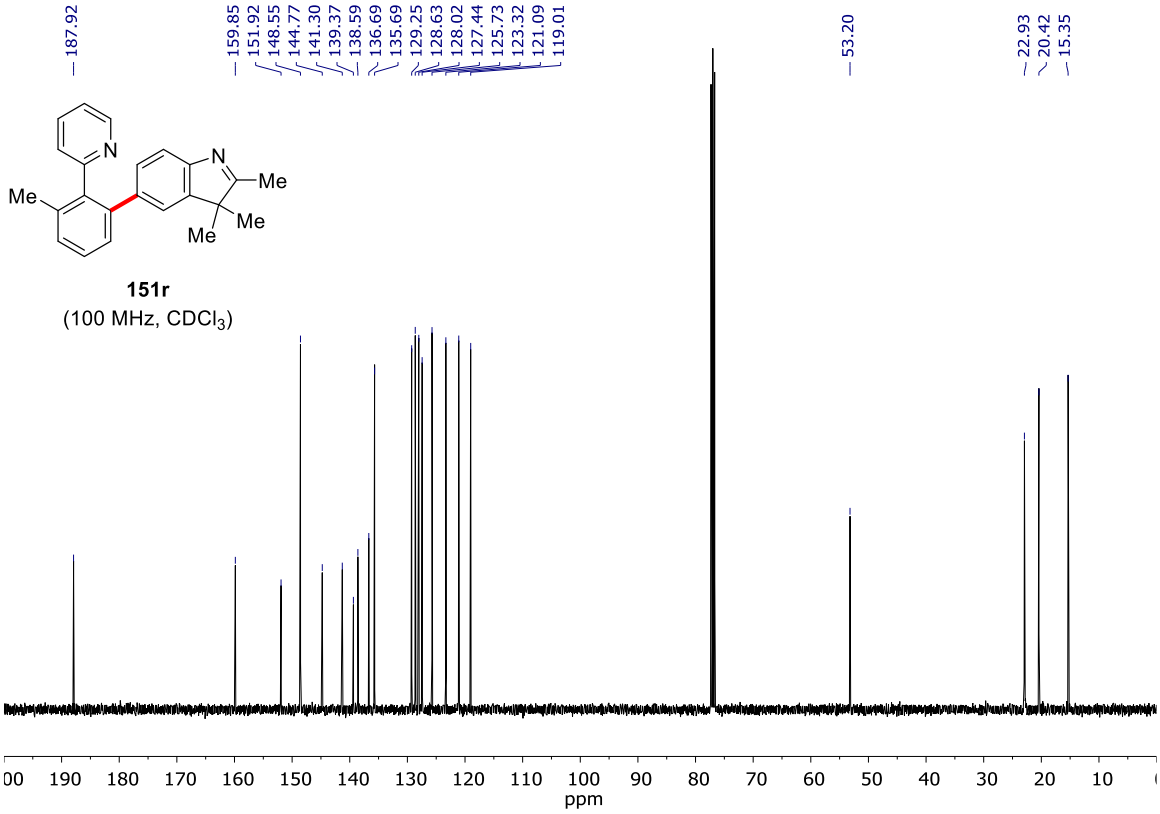
151q
(400 MHz, $CDCl_3$)



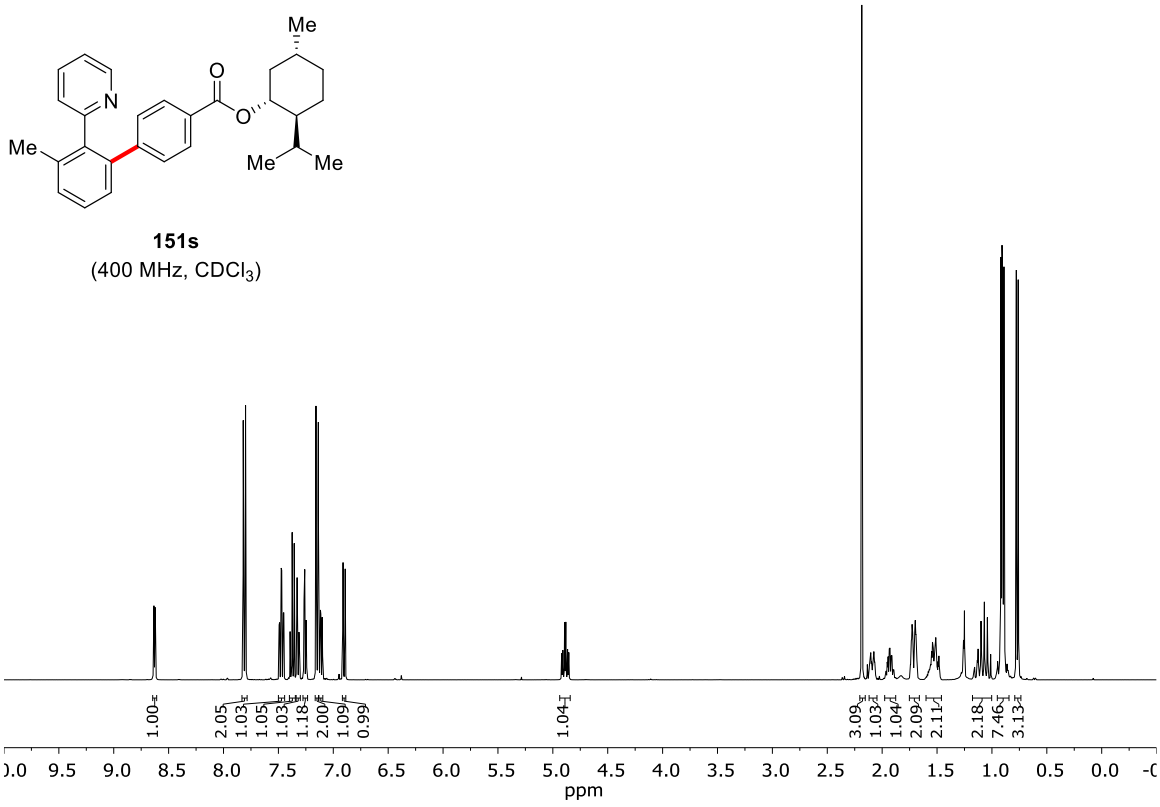
151q
(100 MHz, $CDCl_3$)



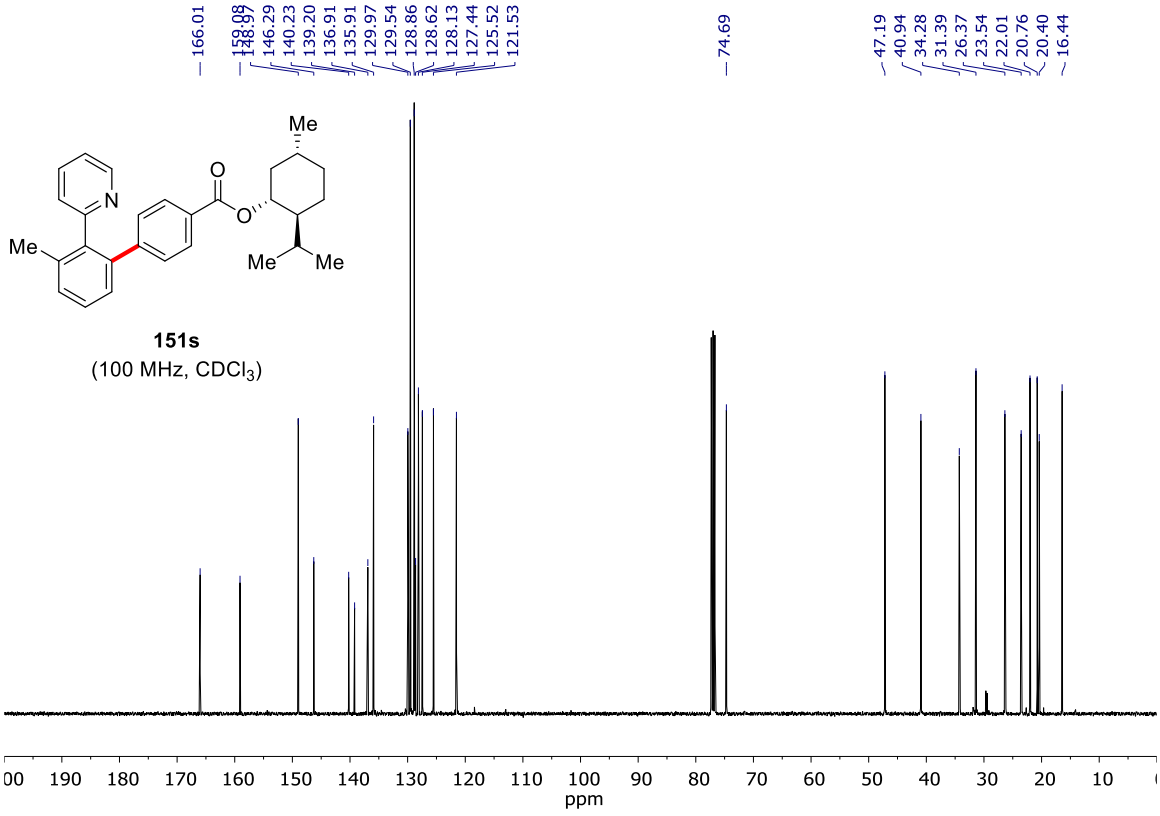
151r
(400 MHz, $CDCl_3$)



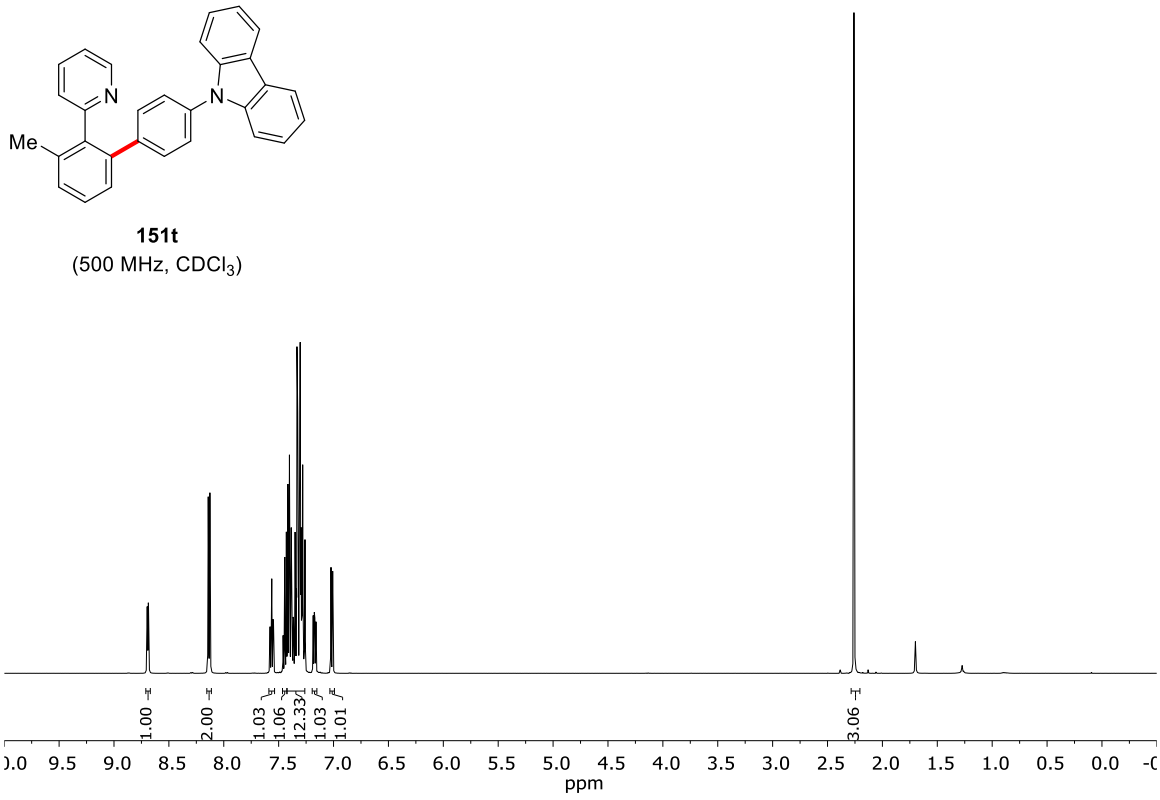
151r
(100 MHz, $CDCl_3$)



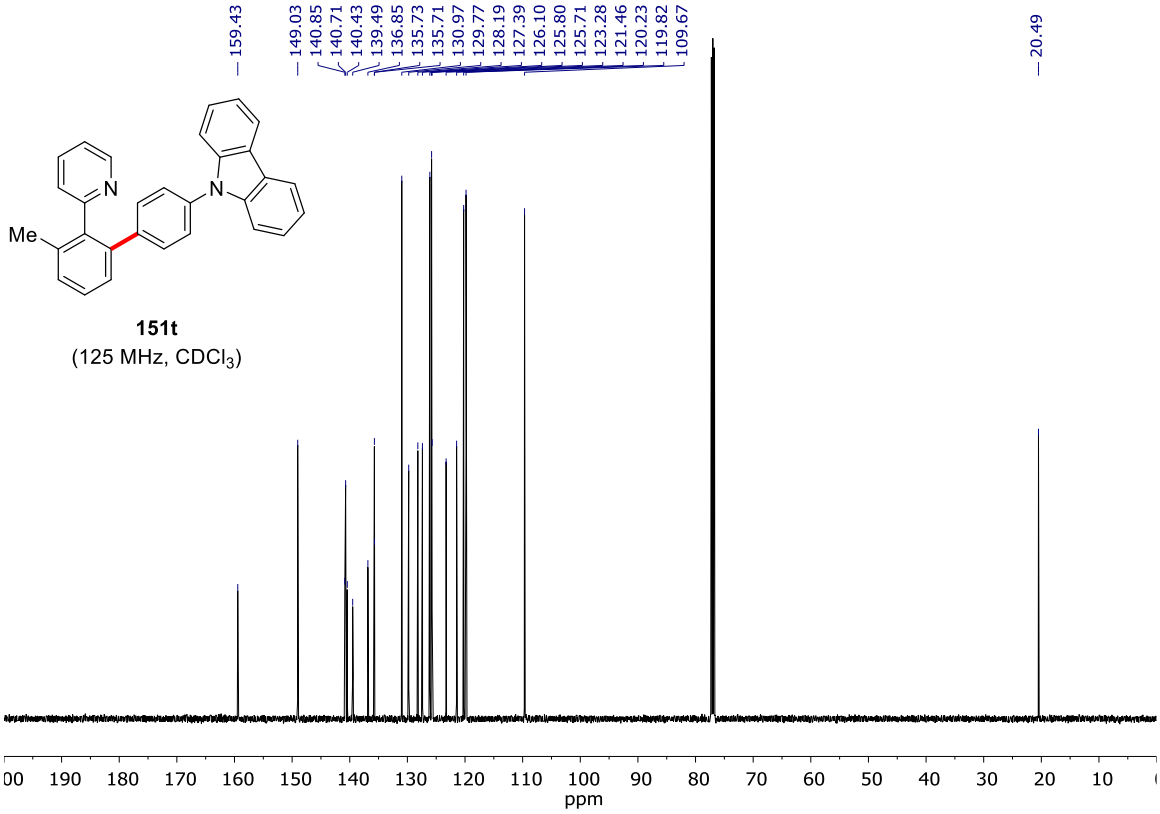
151s
(400 MHz, $CDCl_3$)



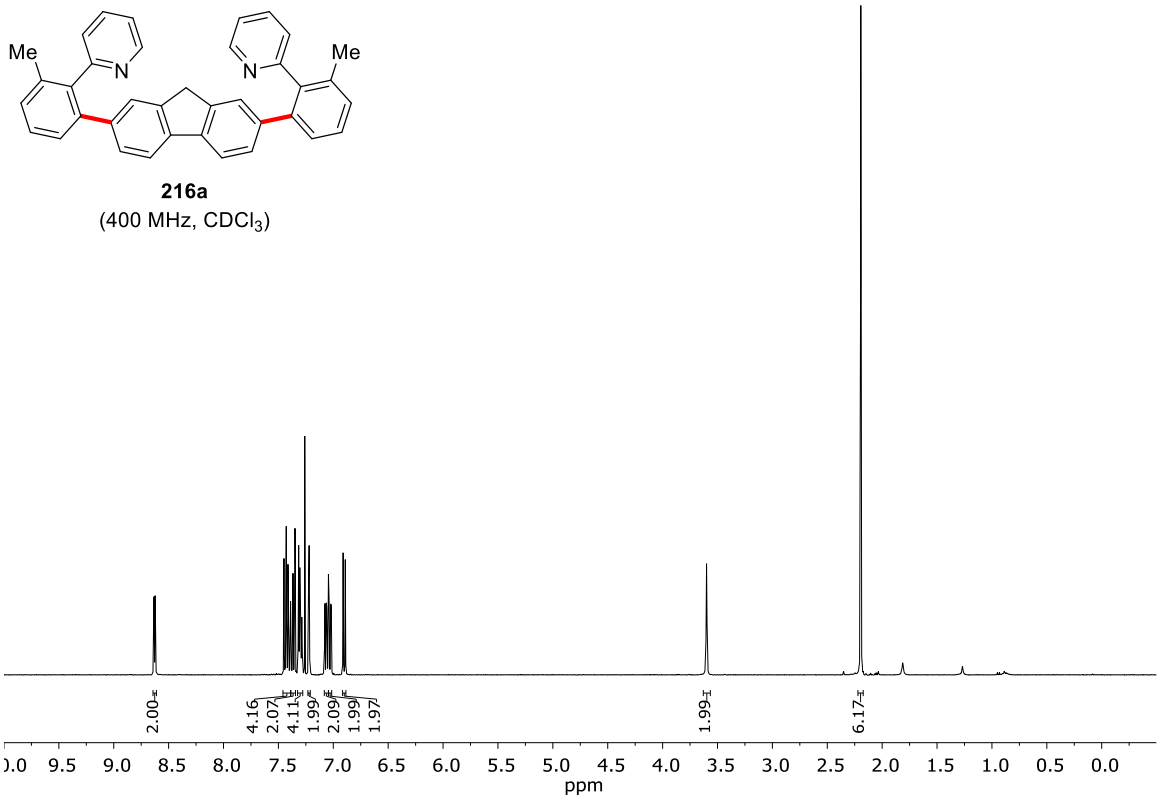
151s
(100 MHz, $CDCl_3$)



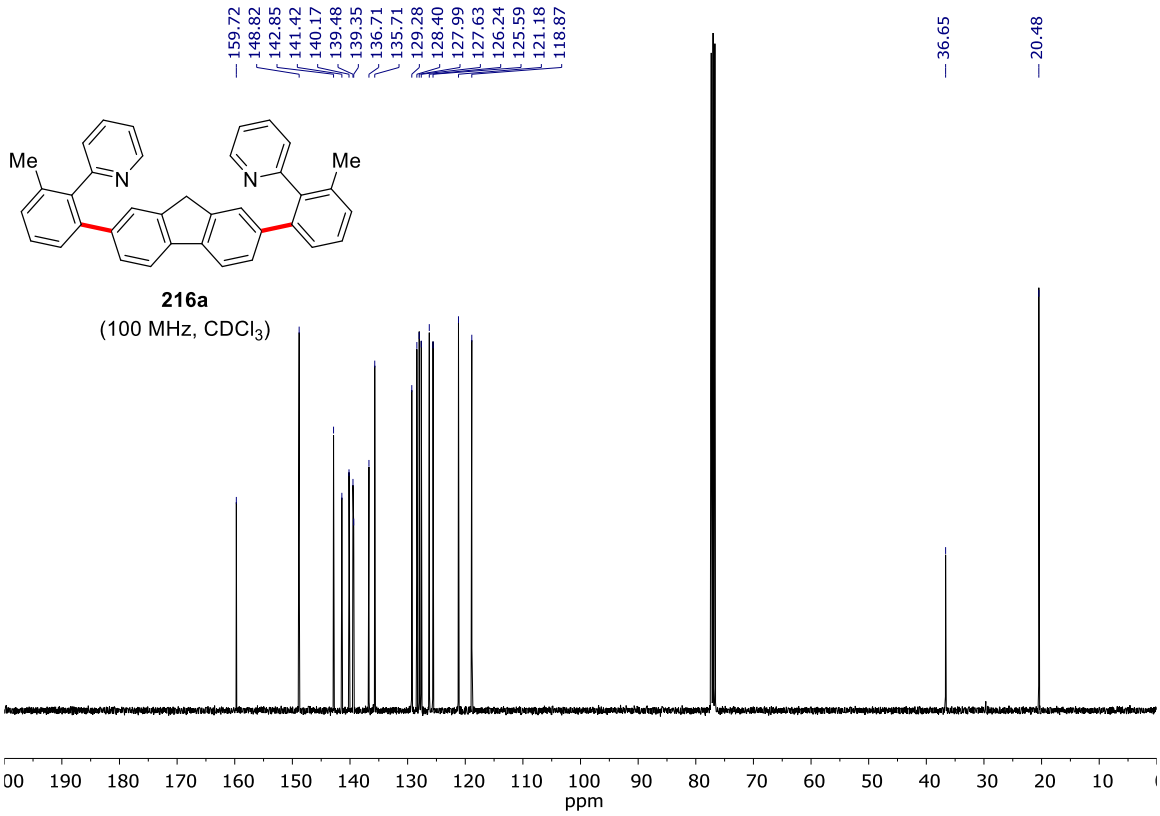
151t
(500 MHz, $CDCl_3$)



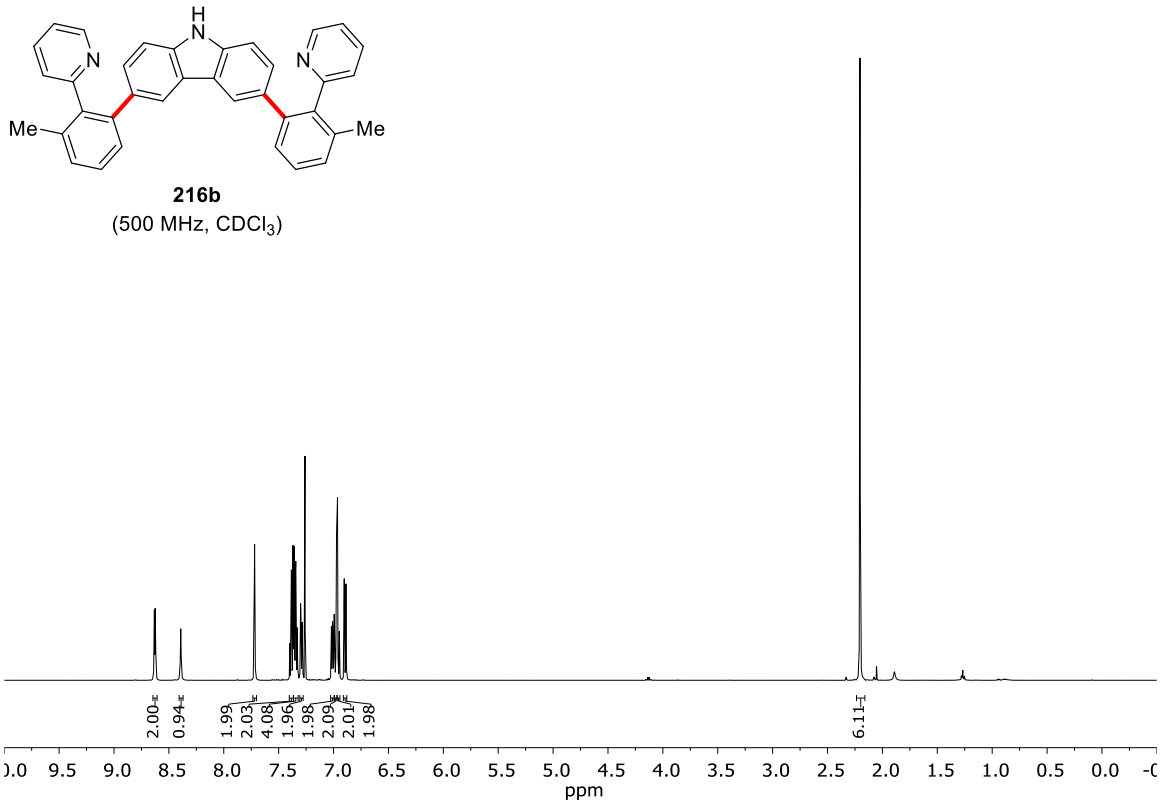
151t
(125 MHz, $CDCl_3$)



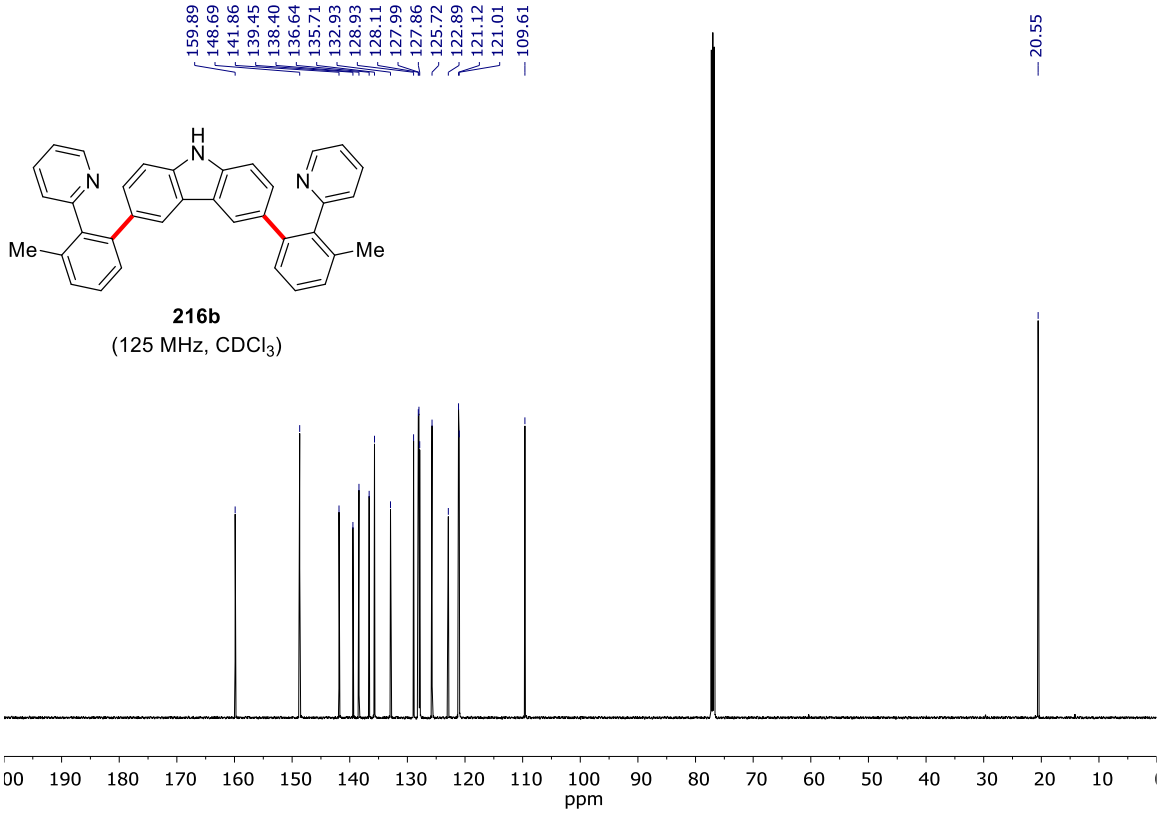
216a
(400 MHz, $CDCl_3$)



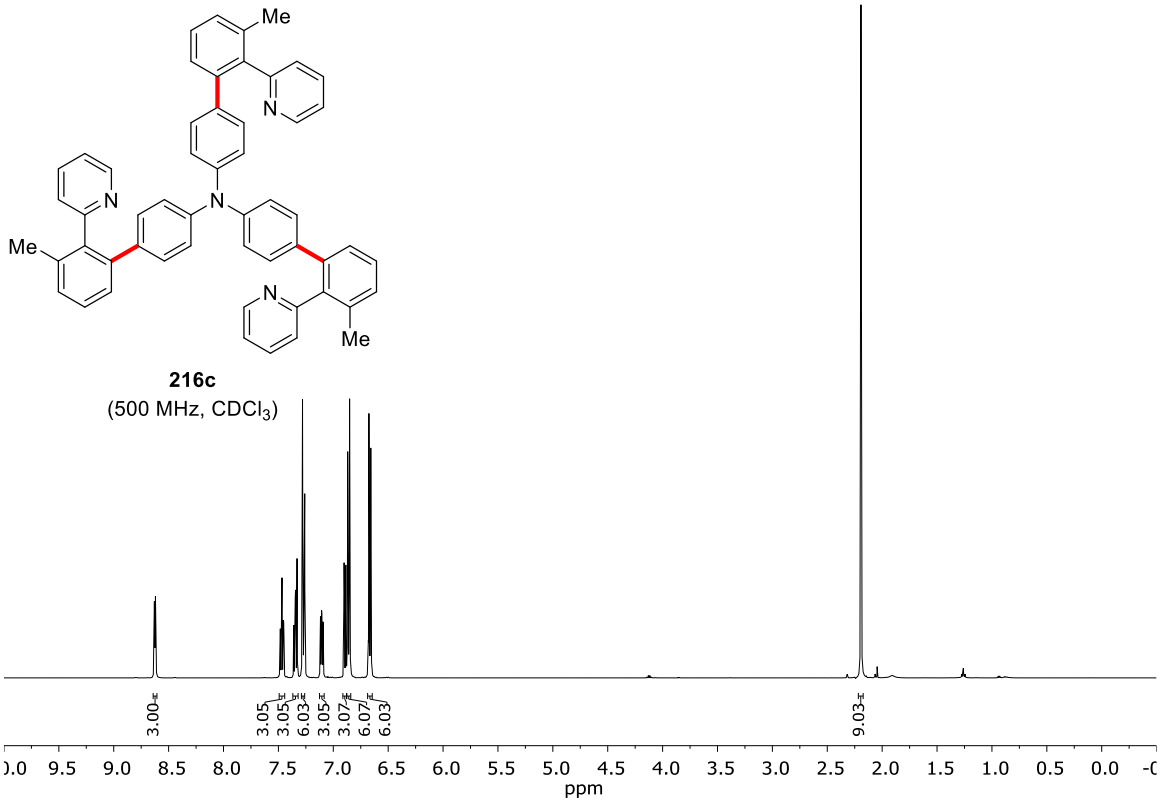
216a
(100 MHz, $CDCl_3$)



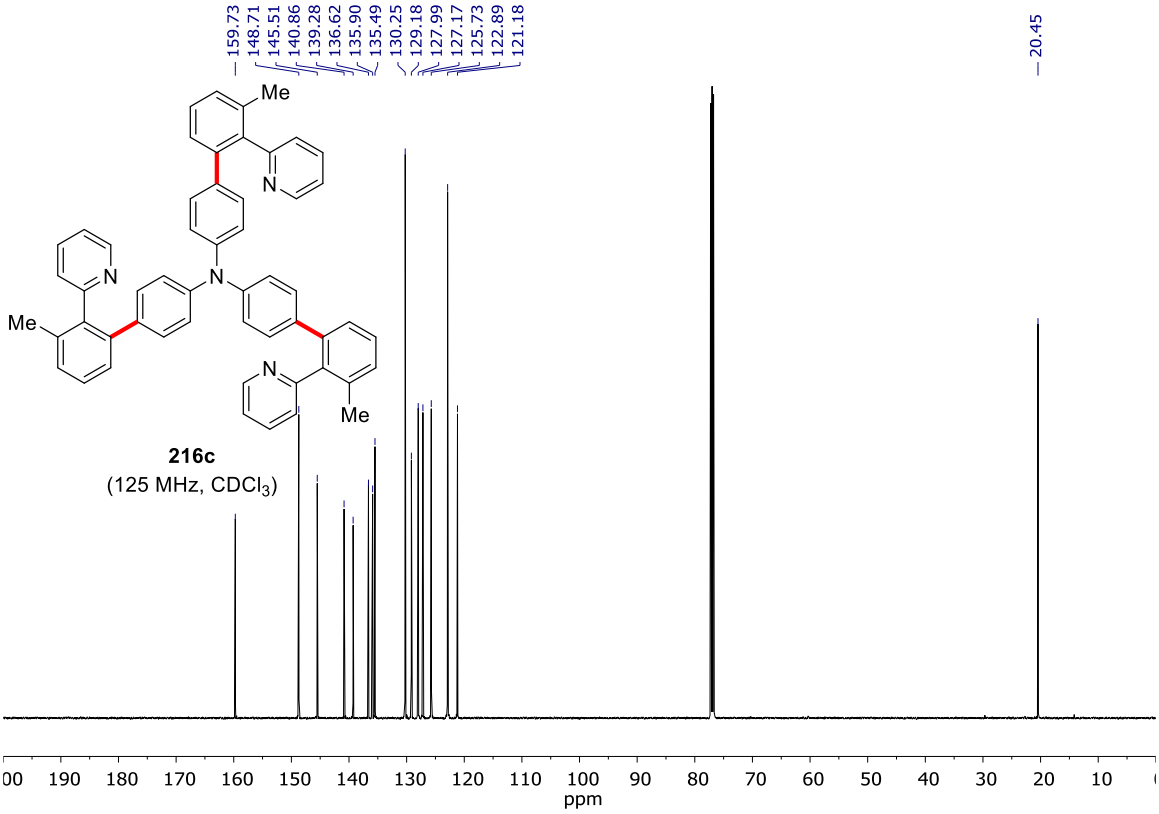
216b
(500 MHz, $CDCl_3$)

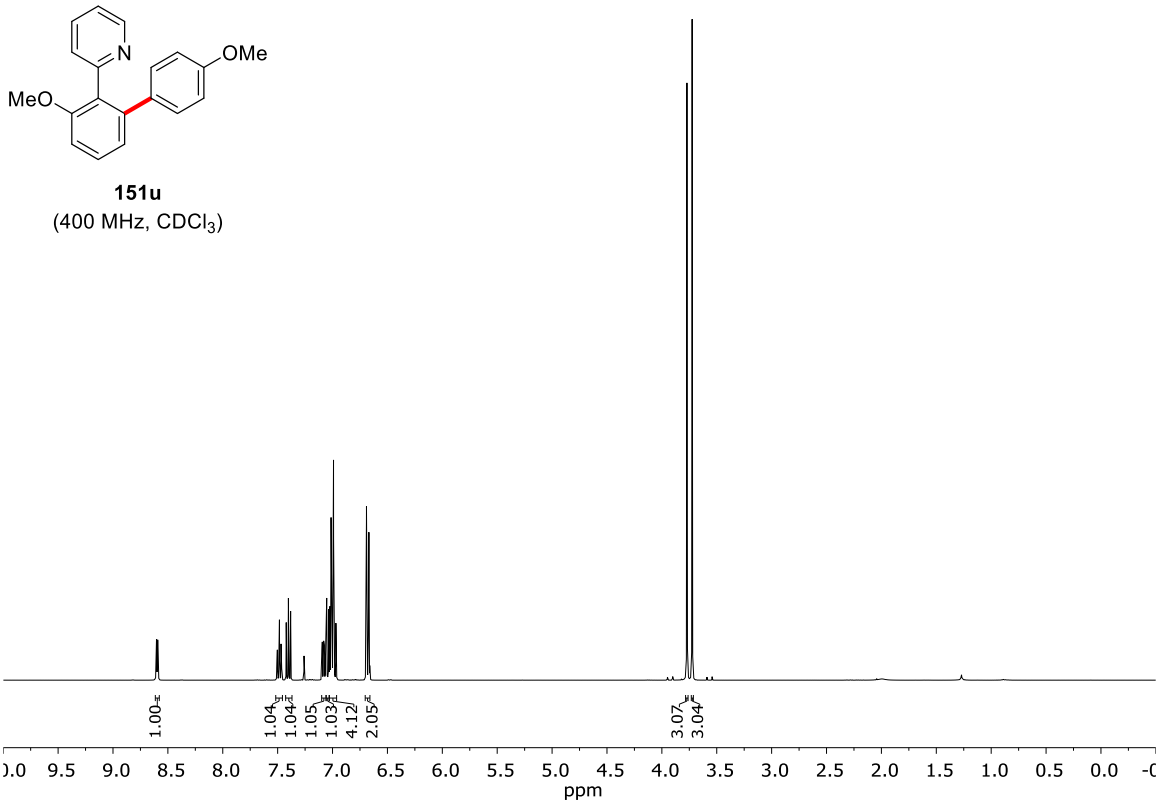


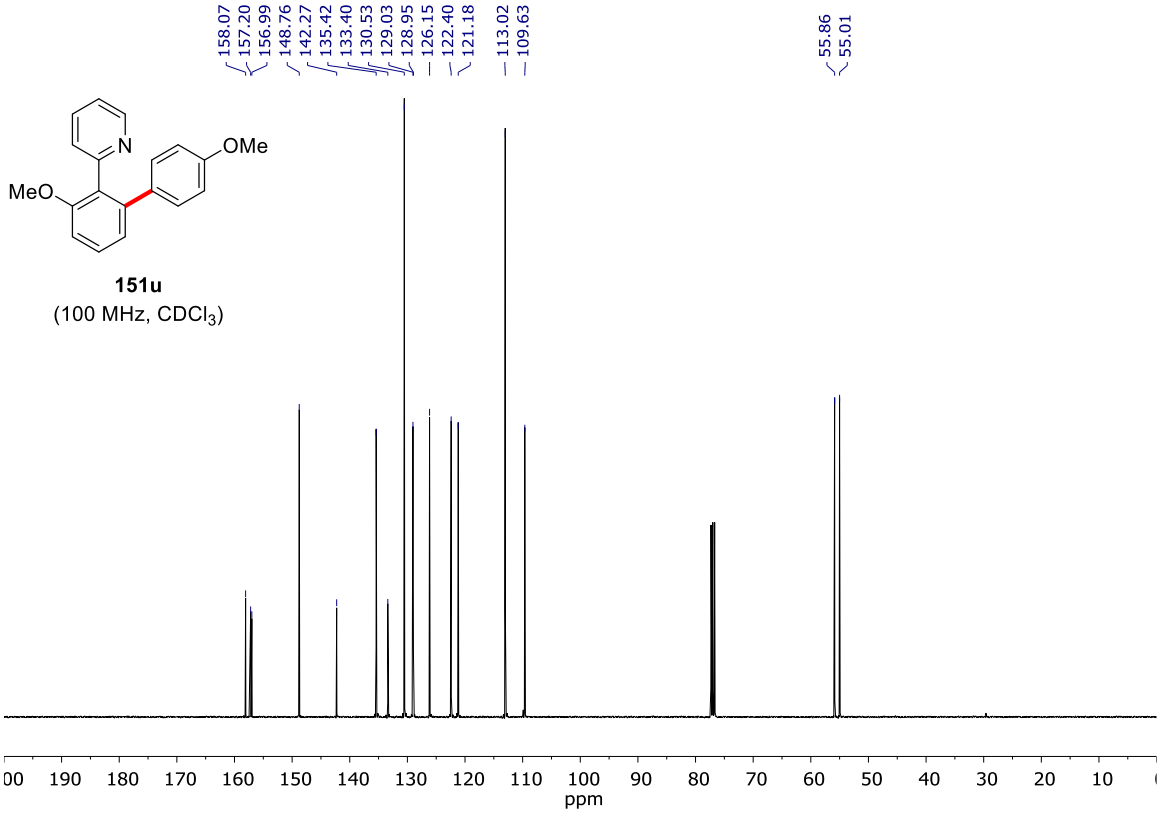
216b
(125 MHz, $CDCl_3$)



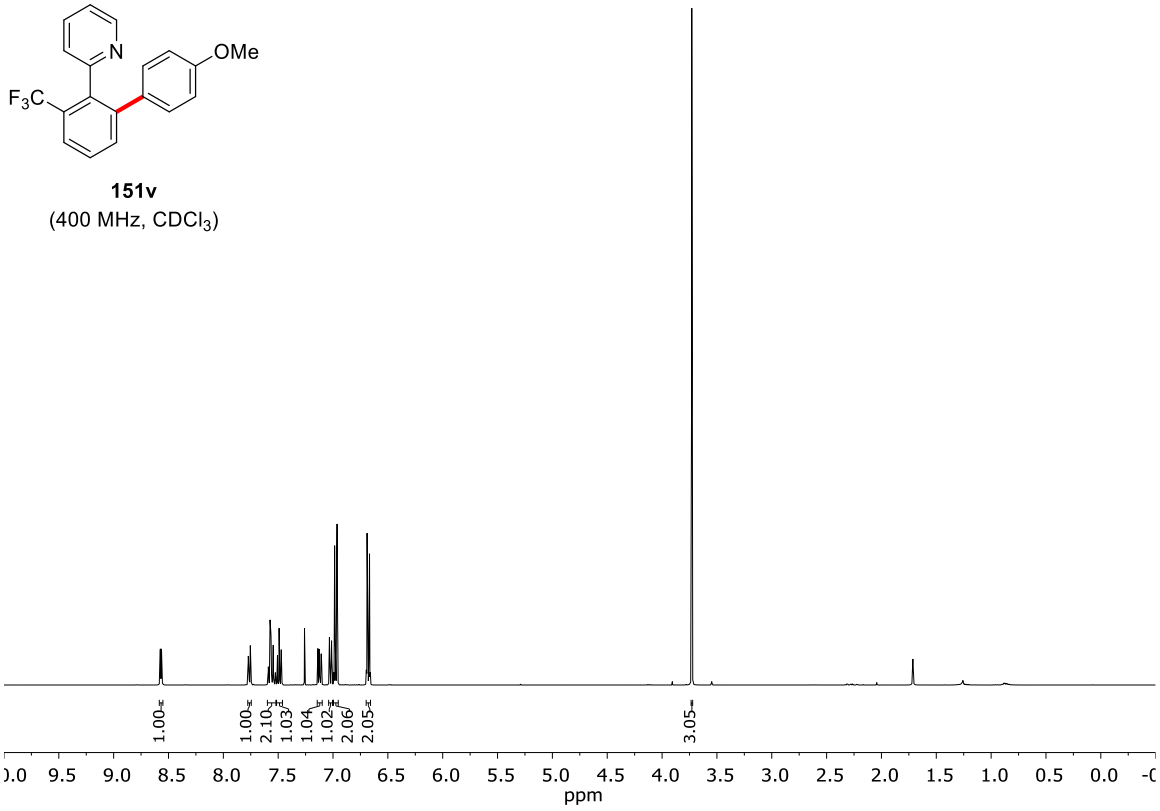
216c
(500 MHz, $CDCl_3$)


159.73
148.71
145.51
140.86
139.28
136.62
135.90
135.49
130.25
129.18
127.99
127.17
125.73
122.89
121.18
20.45
Me
N
N
Me
N
Me
216c
(125 MHz, CDCl3)
ppm

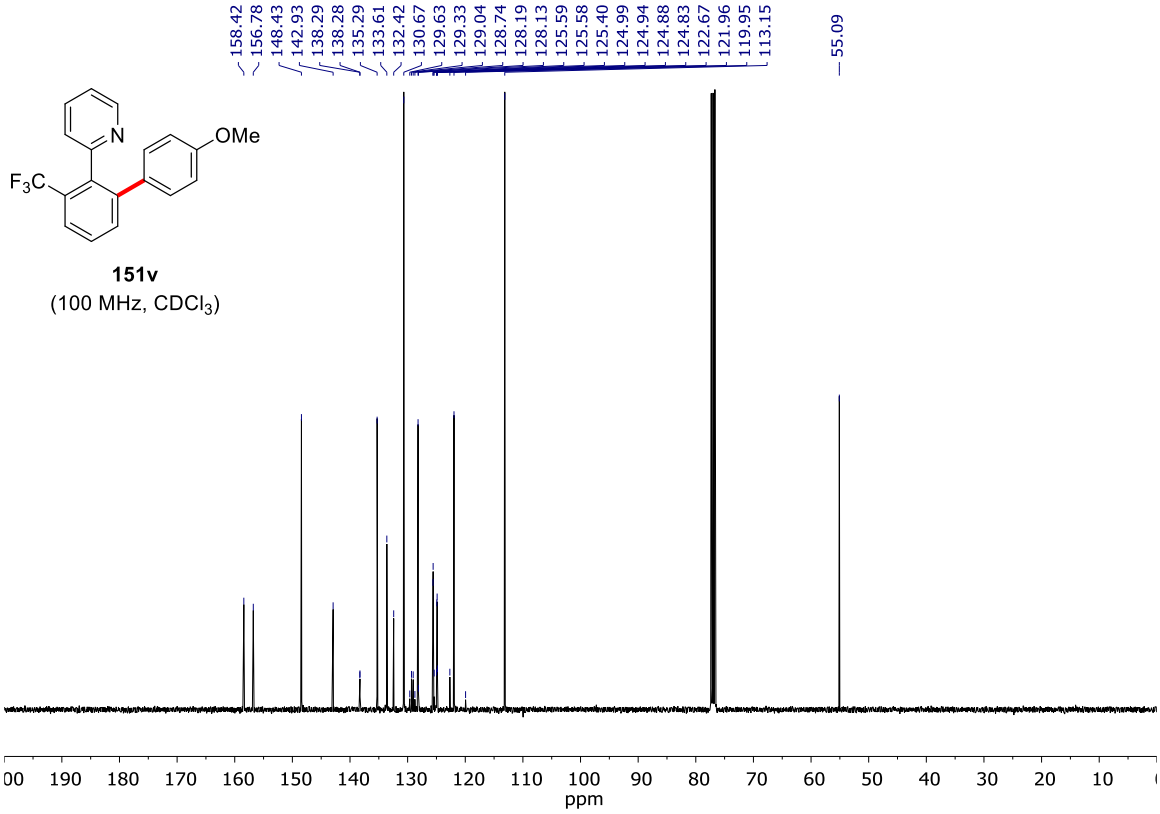

N
OMe
MeO
151u
(400 MHz, CDCl3)
1.00
1.04
1.04
1.05
1.03
4.12
2.05
3.07
3.04
ppm



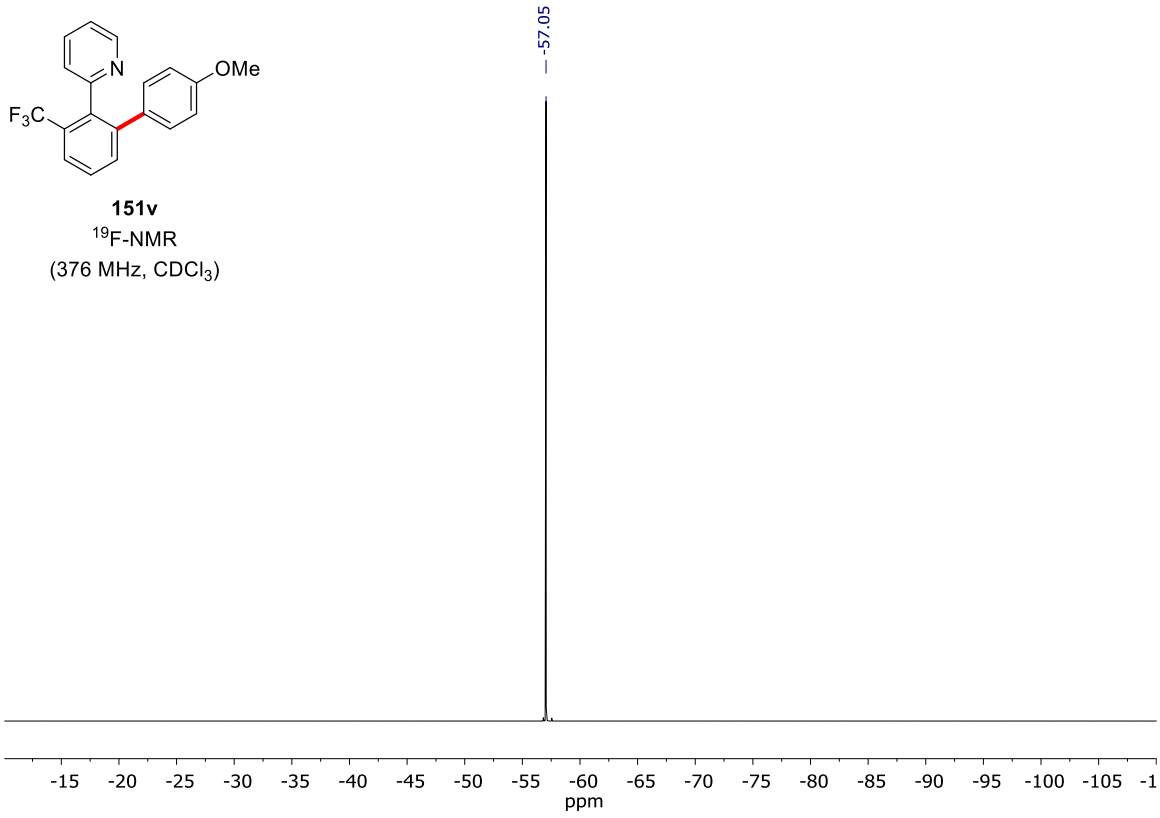
151u
(100 MHz, $CDCl_3$)



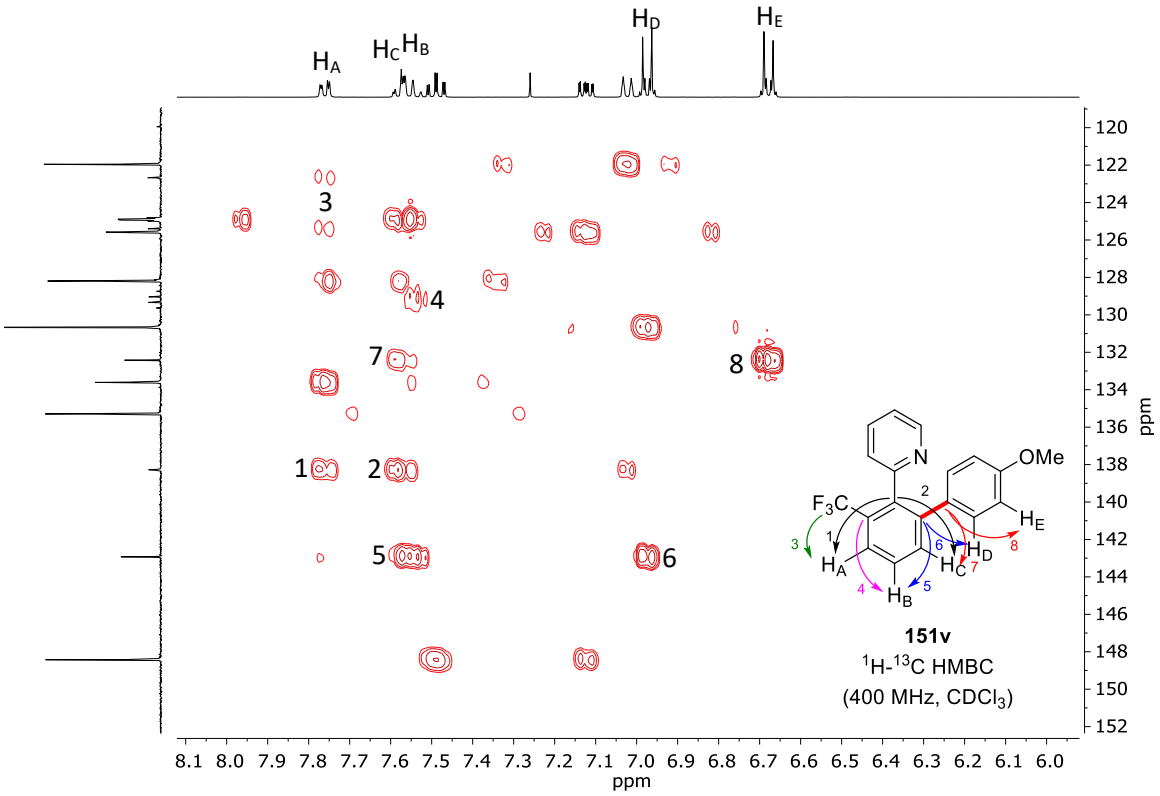
151v
(400 MHz, $CDCl_3$)



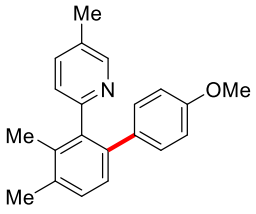
151v
(100 MHz, $CDCl_3$)



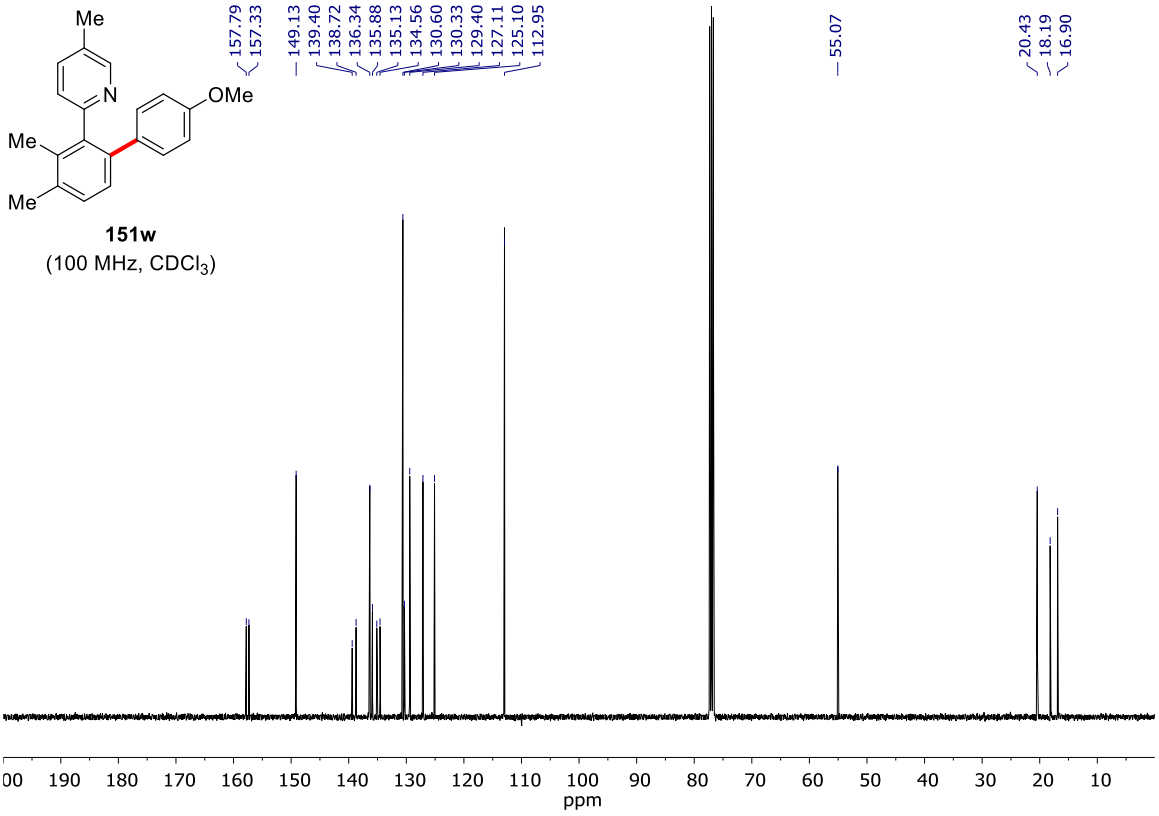
151v
^{19}F-NMR
(376 MHz, $CDCl_3$)



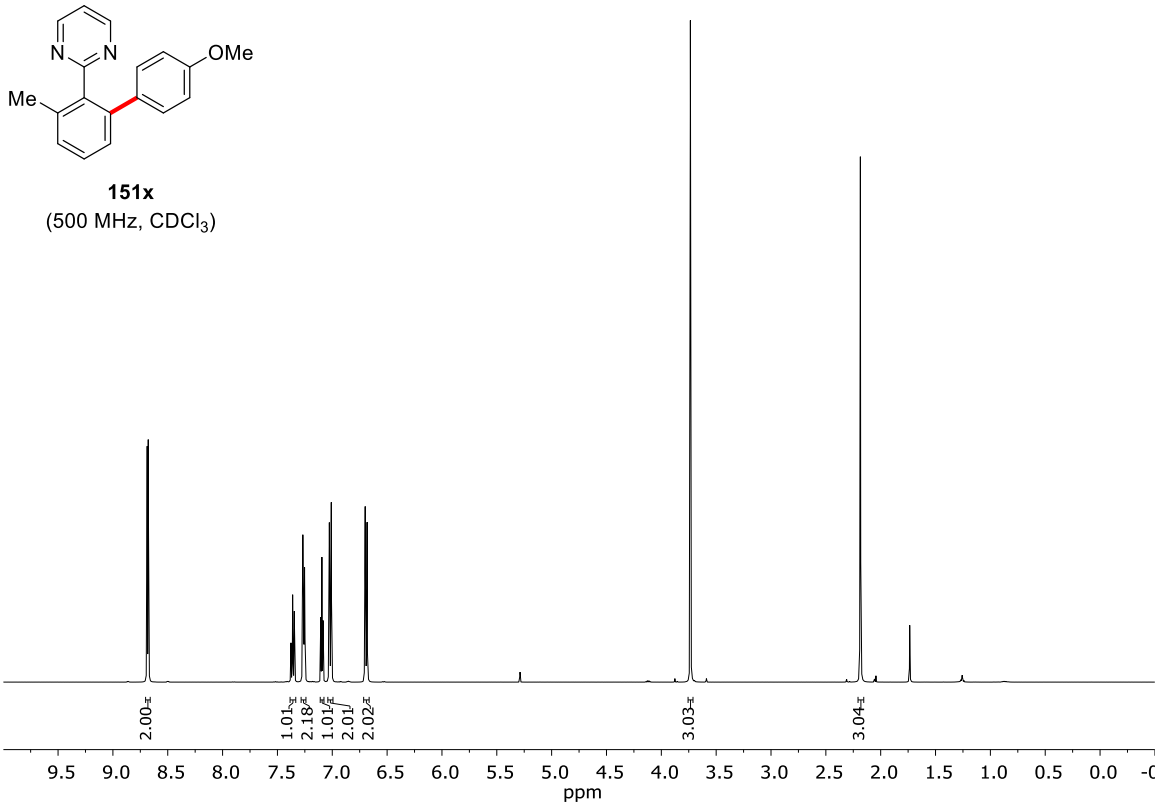
151v
^{1}H-^{13}C HMBC
(400 MHz, $CDCl_3$)



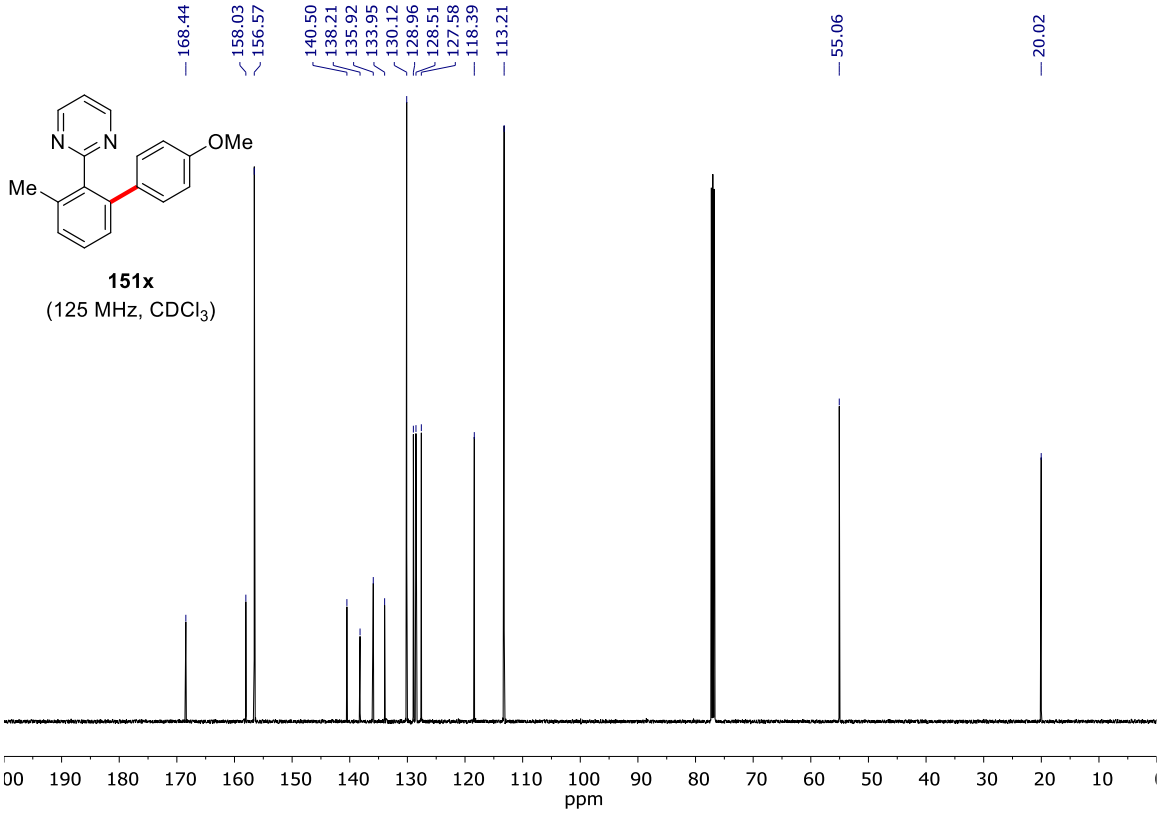
151w
(400 MHz, $CDCl_3$)



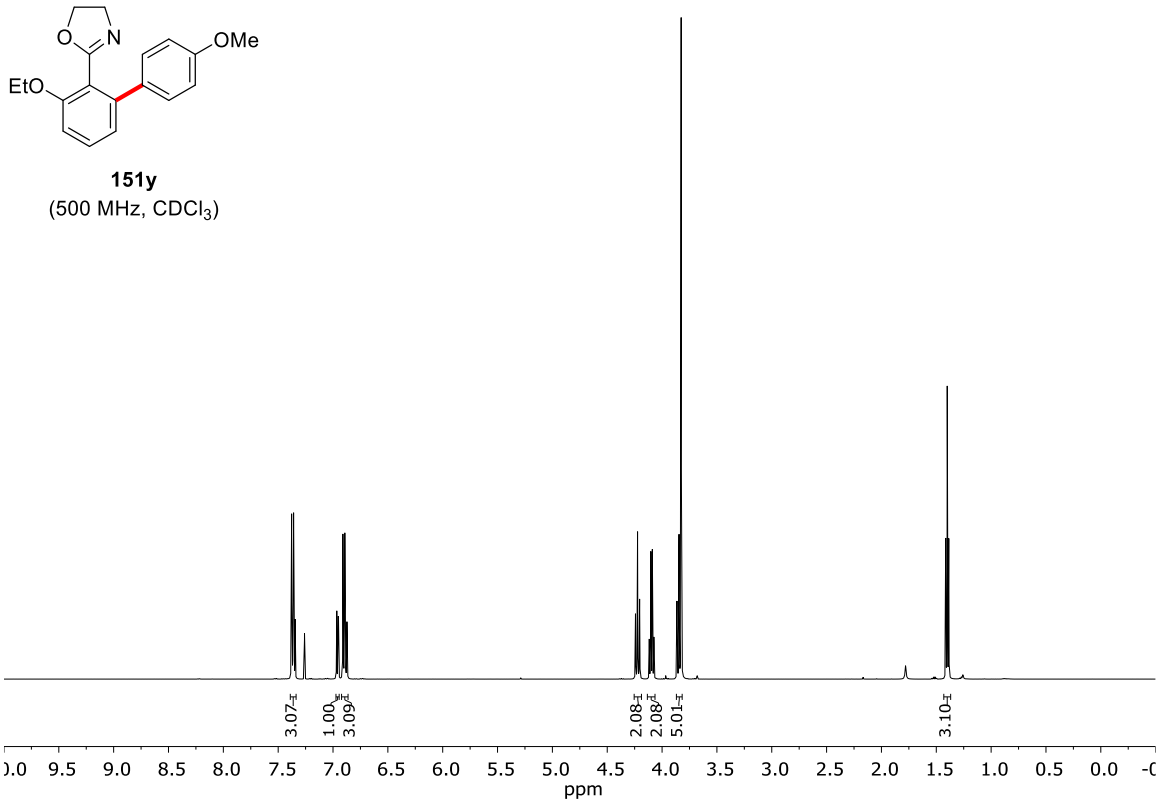
151w
(100 MHz, $CDCl_3$)



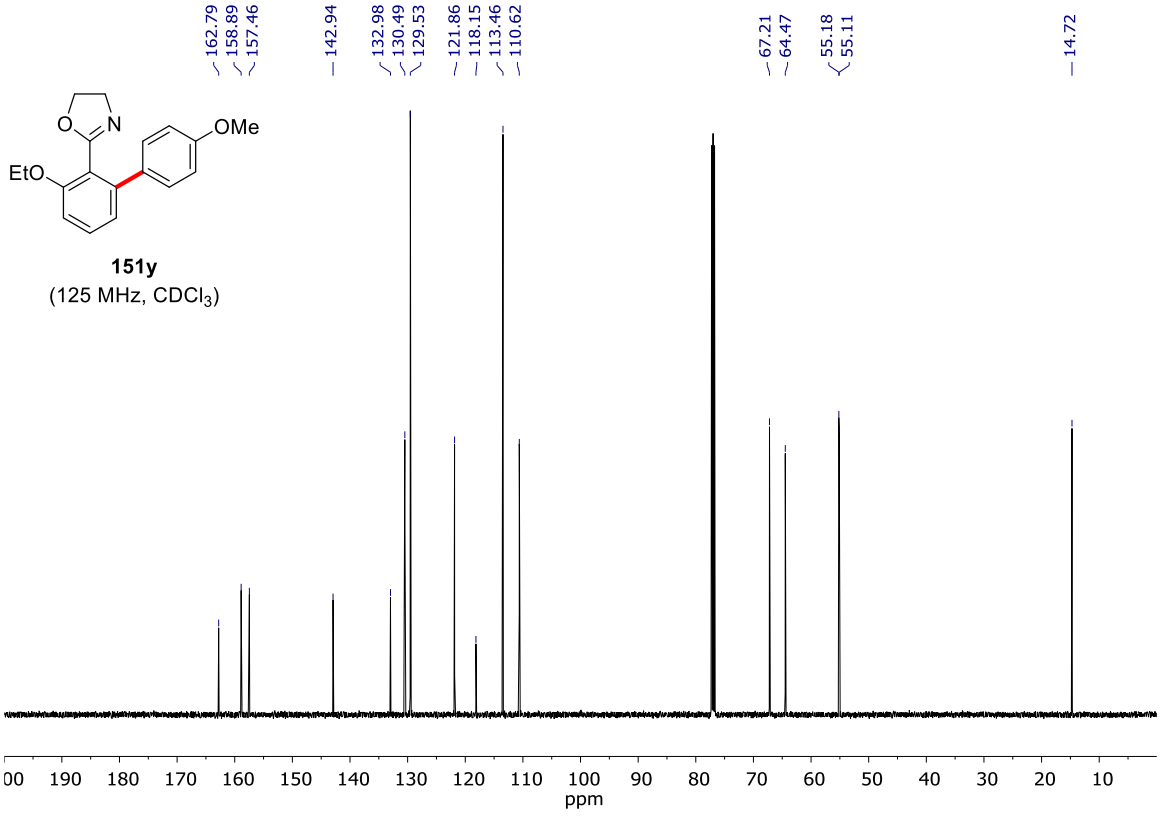
151x
(500 MHz, $CDCl_3$)



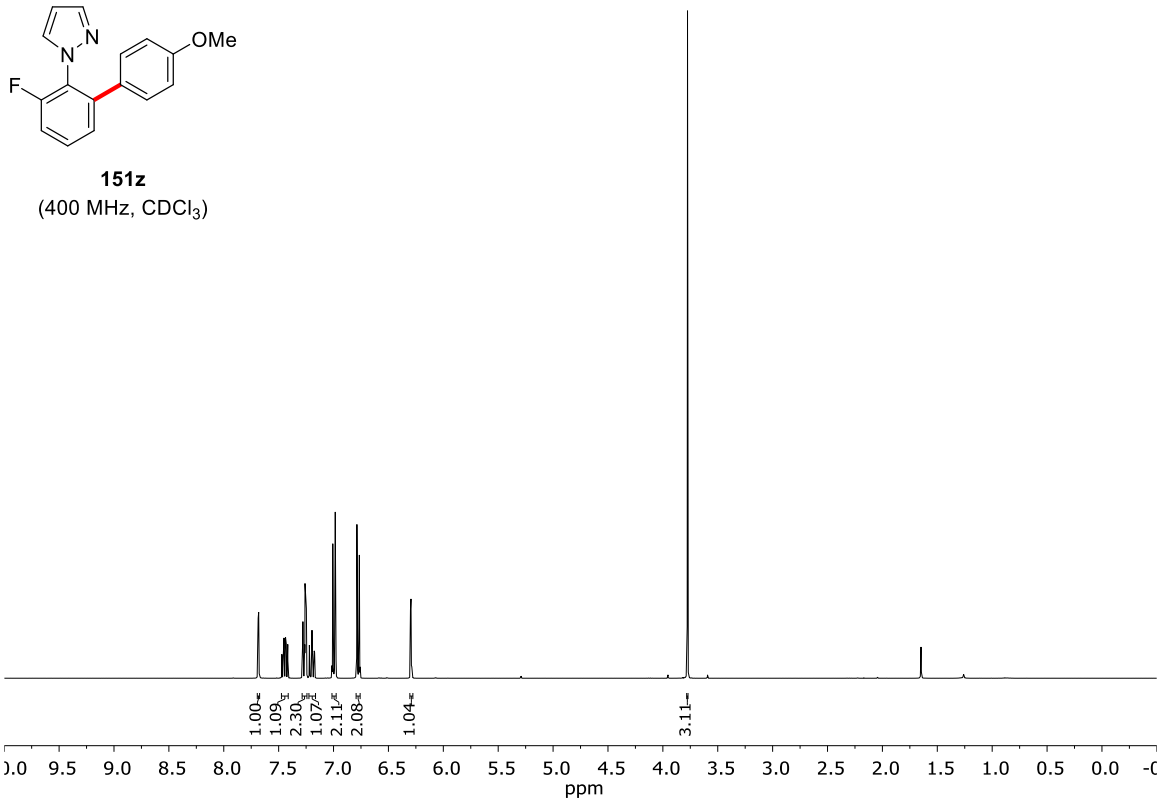
151x
(125 MHz, $CDCl_3$)



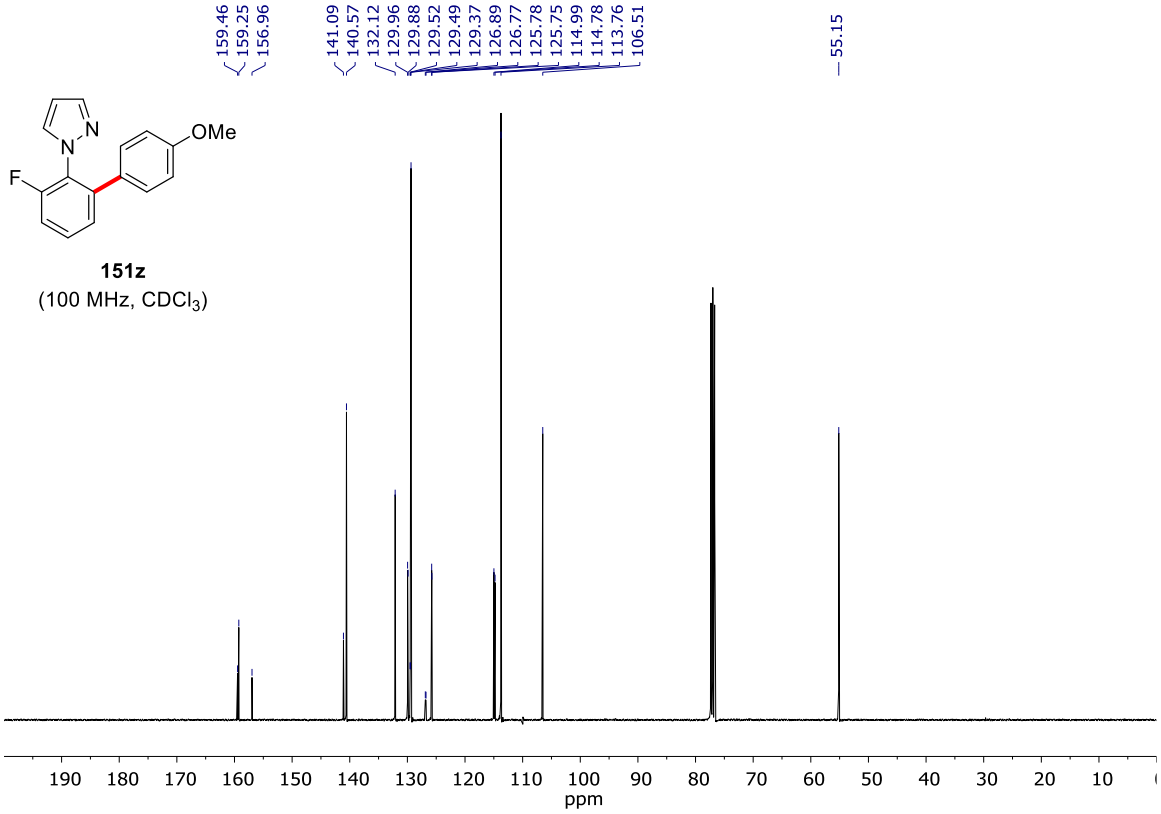
151y
(500 MHz, $CDCl_3$)



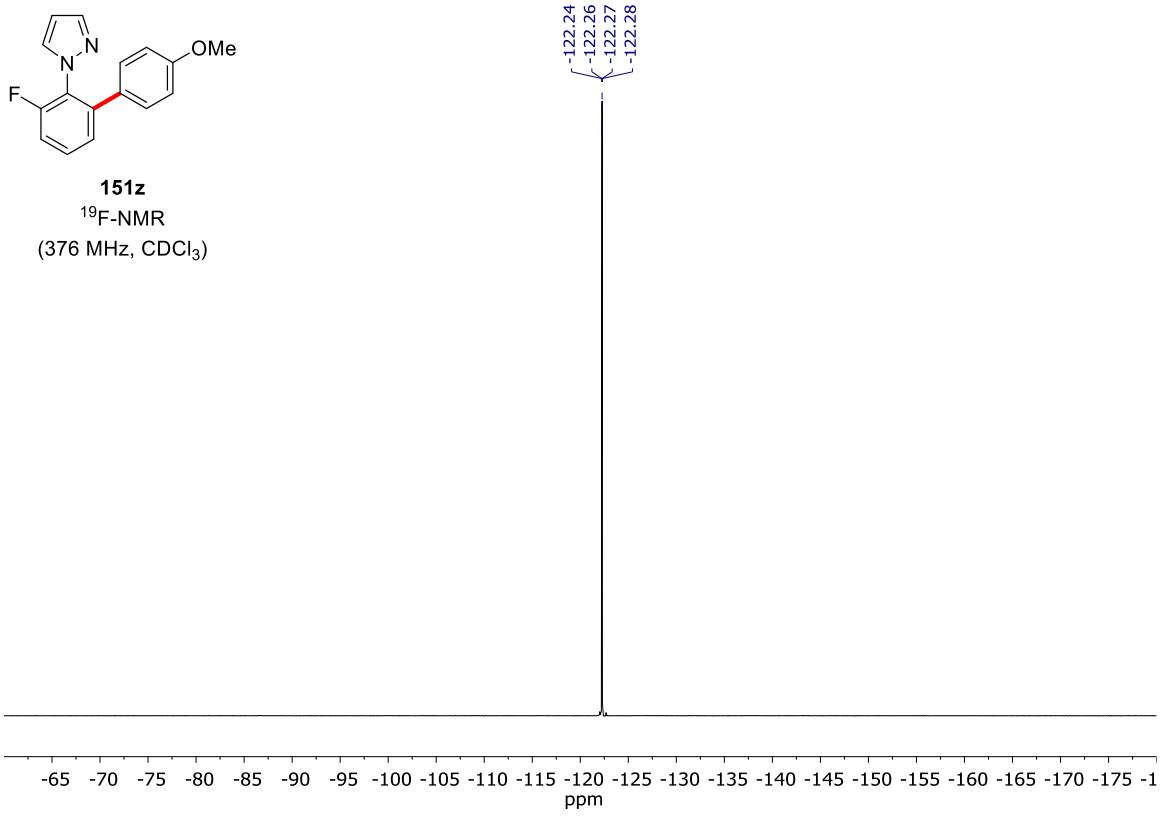
151y
(125 MHz, $CDCl_3$)



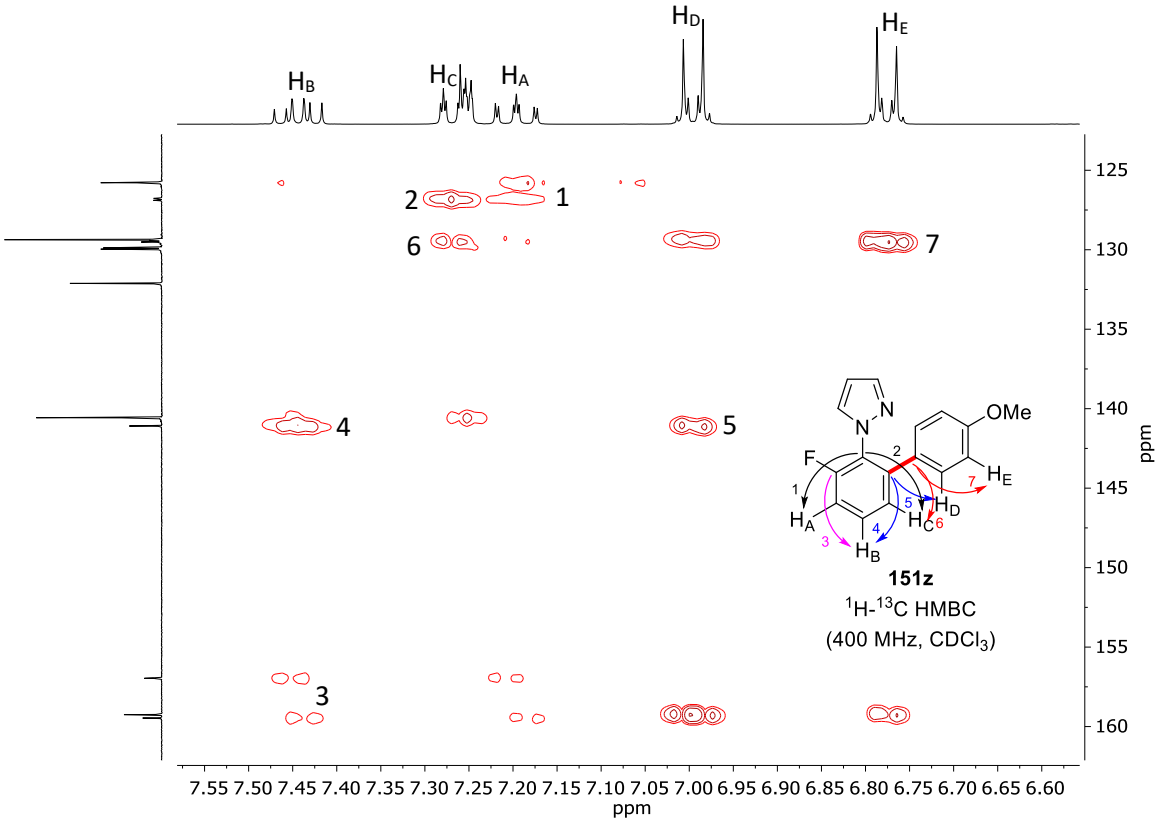
151z
(400 MHz, $CDCl_3$)



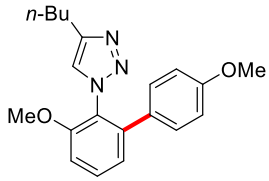
151z
(100 MHz, $CDCl_3$)



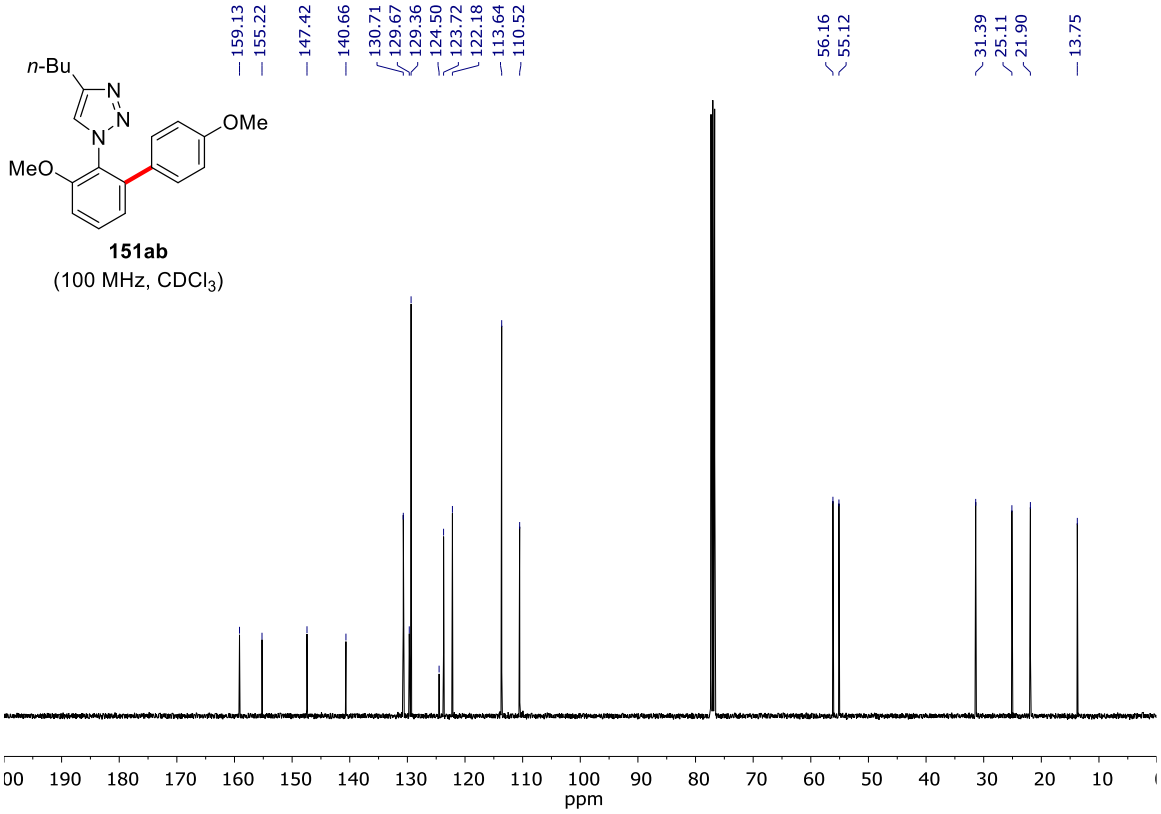
151z
^{19}F-NMR
(376 MHz, $CDCl_3$)



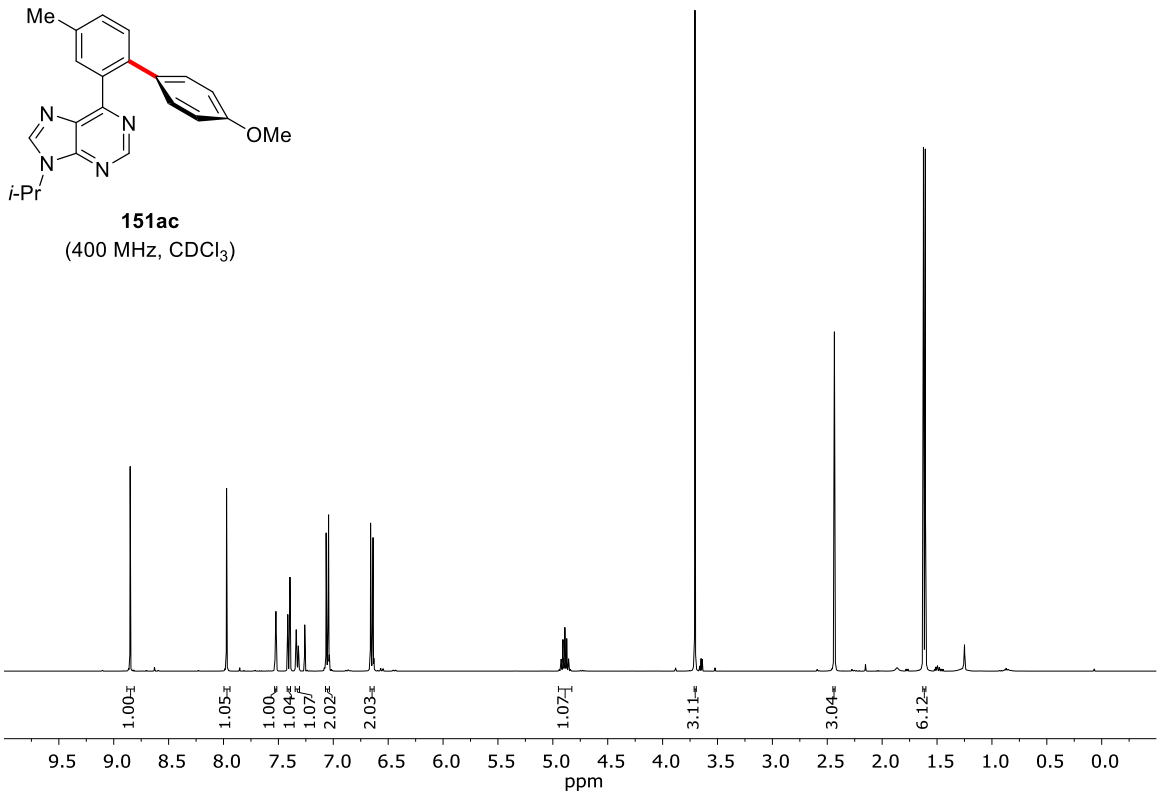
151z
^{1}H-^{13}C HMBC
(400 MHz, $CDCl_3$)



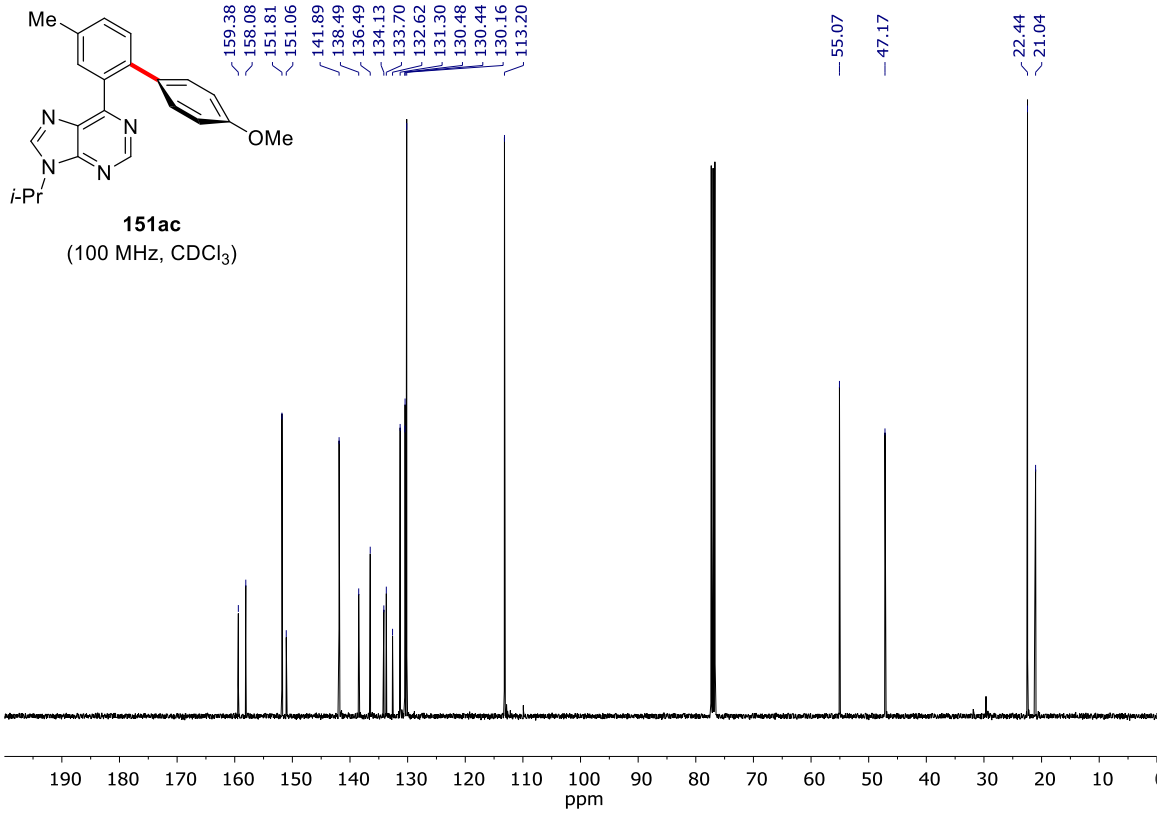
151ab
(400 MHz, $CDCl_3$)



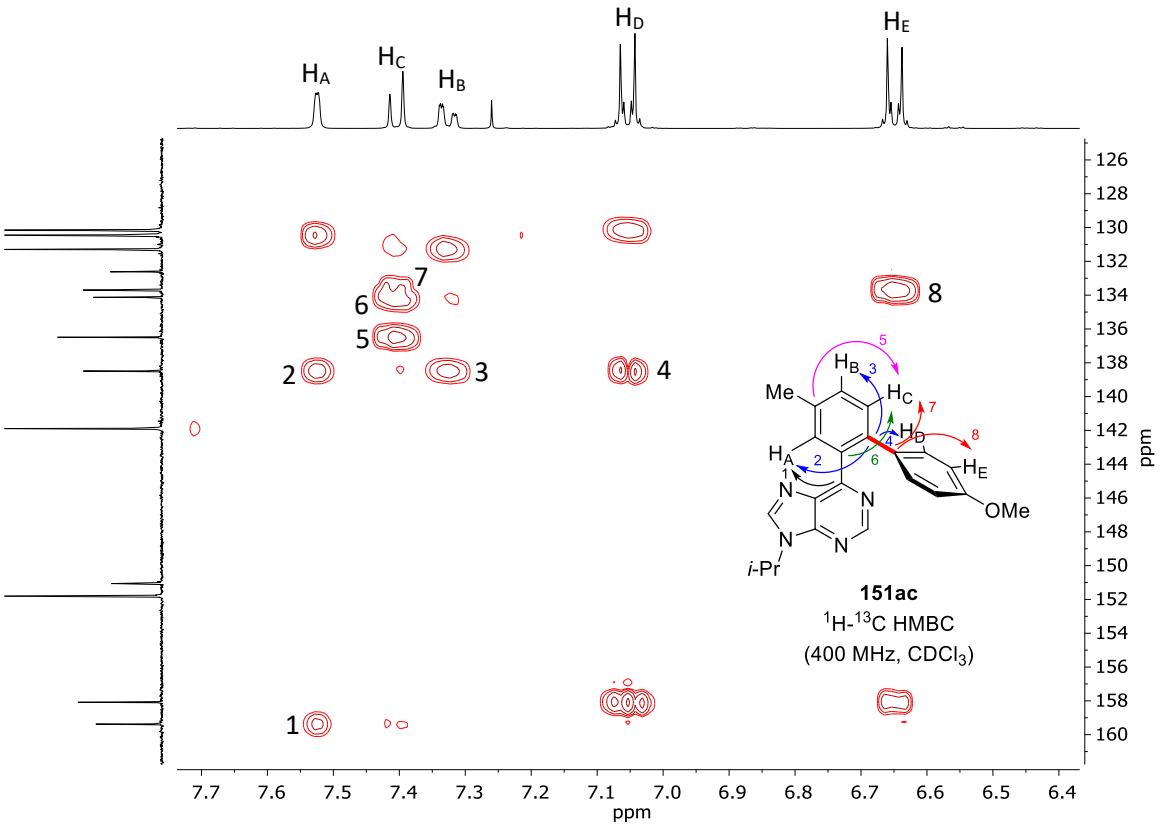
151ab
(100 MHz, $CDCl_3$)



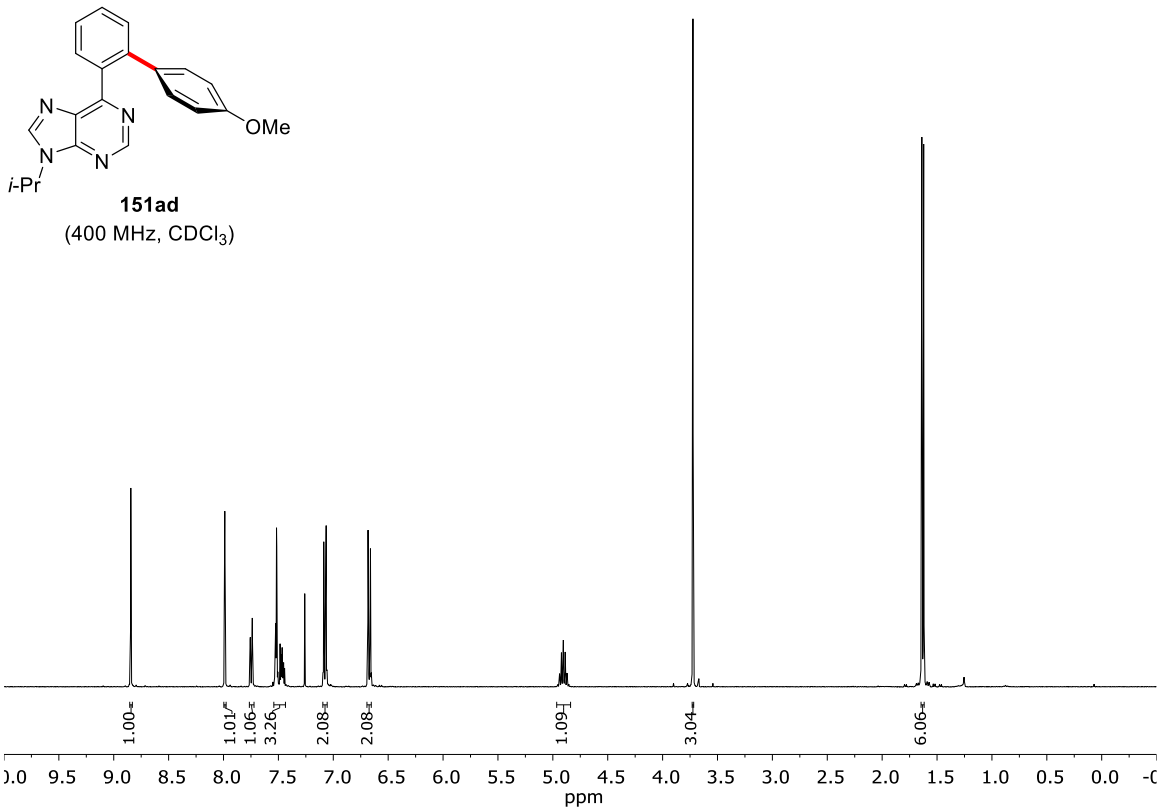
151ac
(400 MHz, $CDCl_3$)

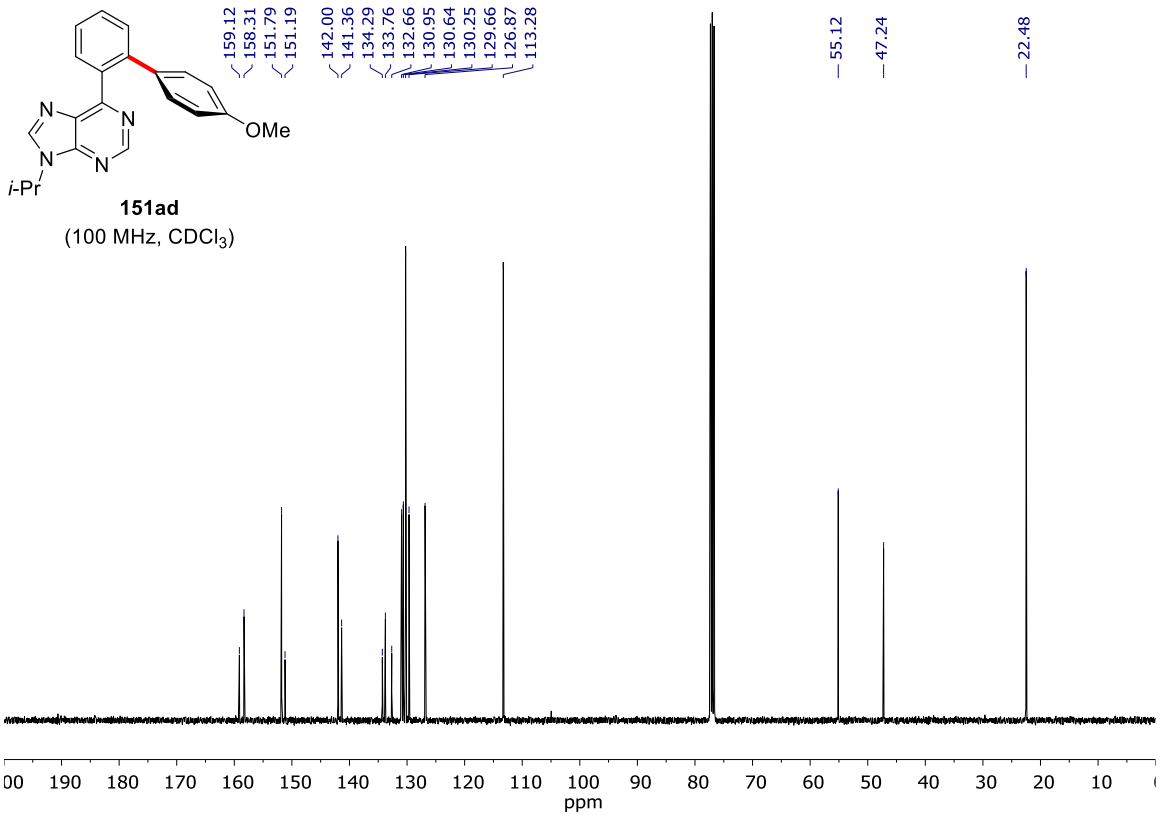


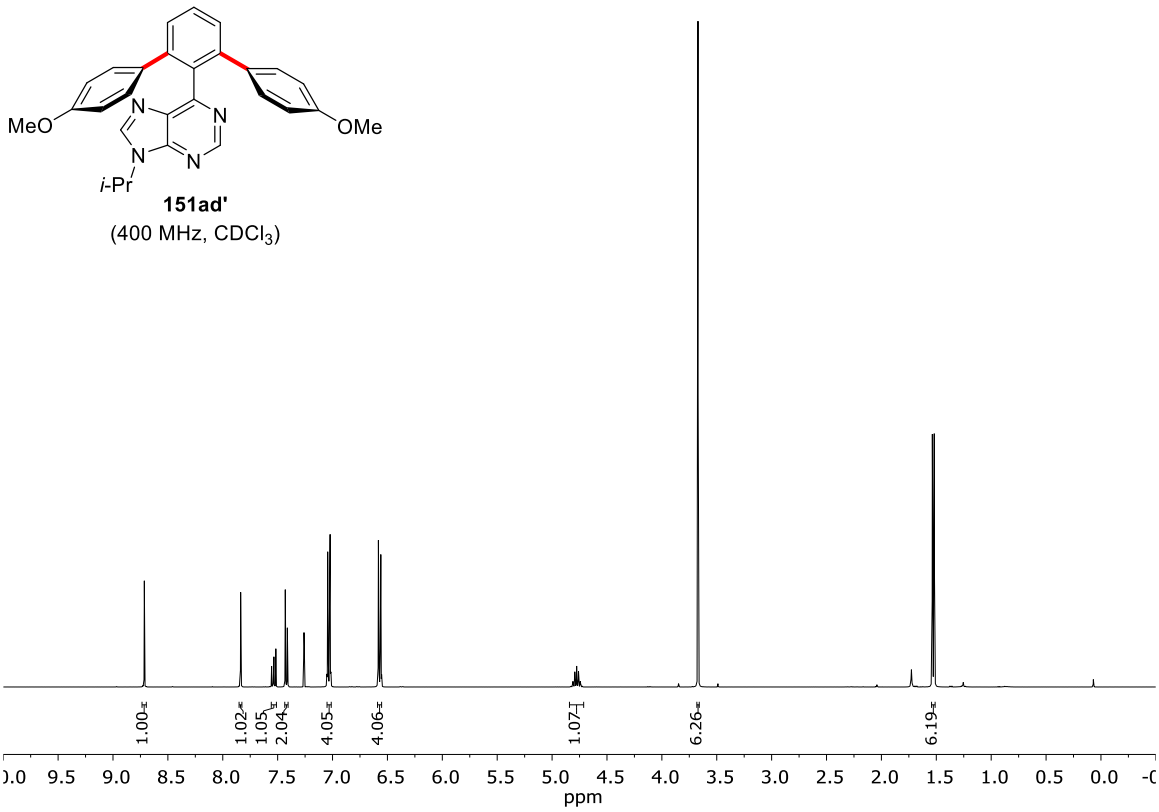
151ac
(100 MHz, $CDCl_3$)

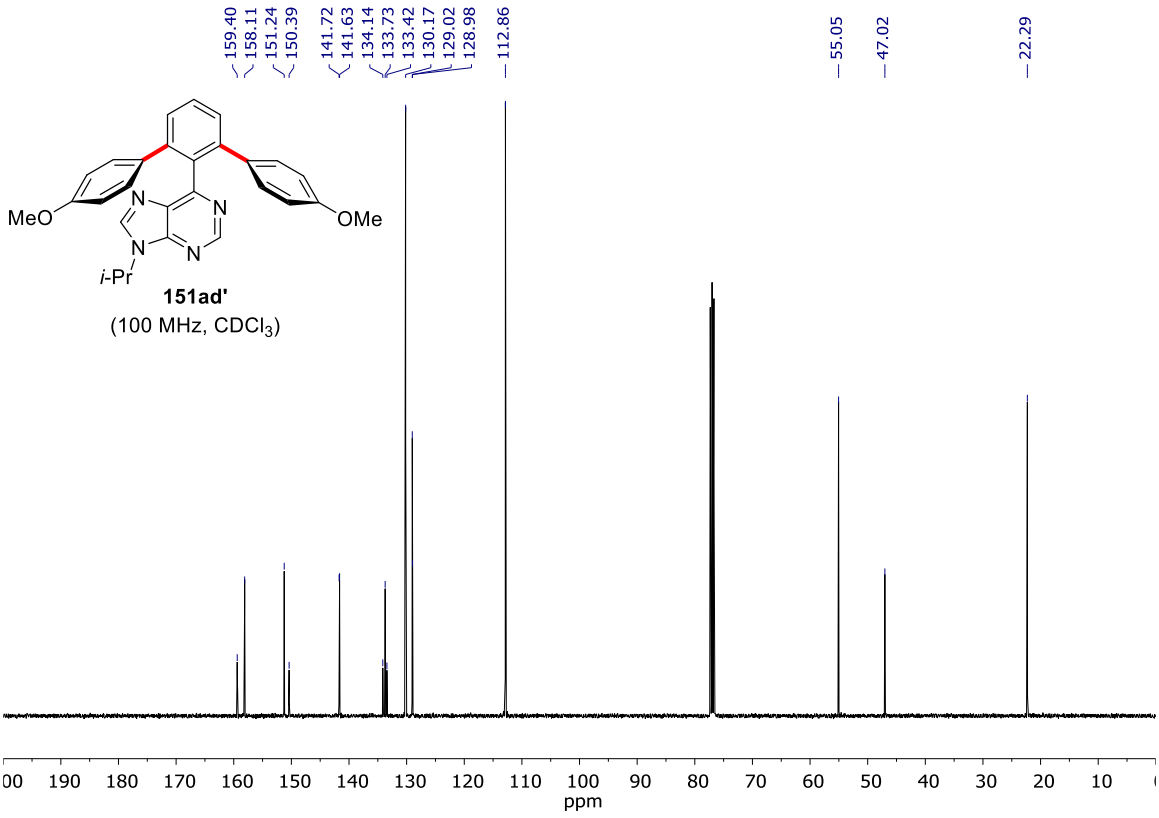


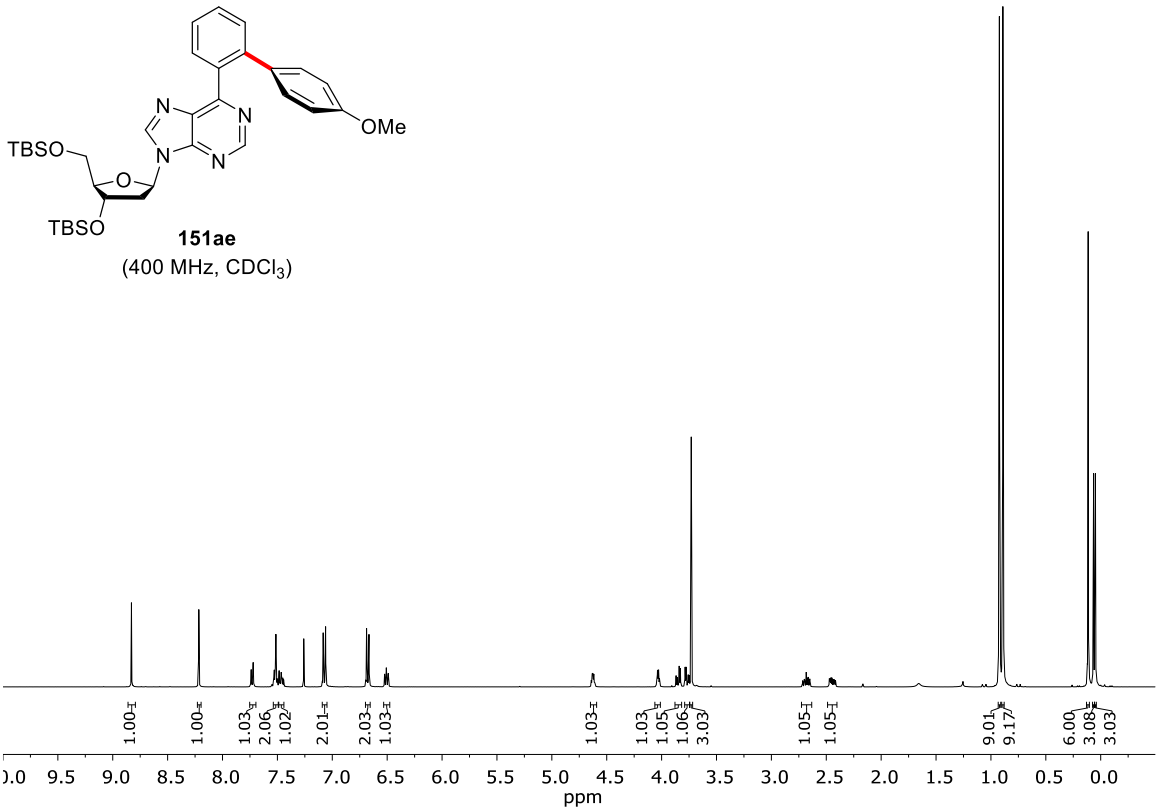
151ac
^1H-^{13}C HMBC
(400 MHz, $CDCl_3$)

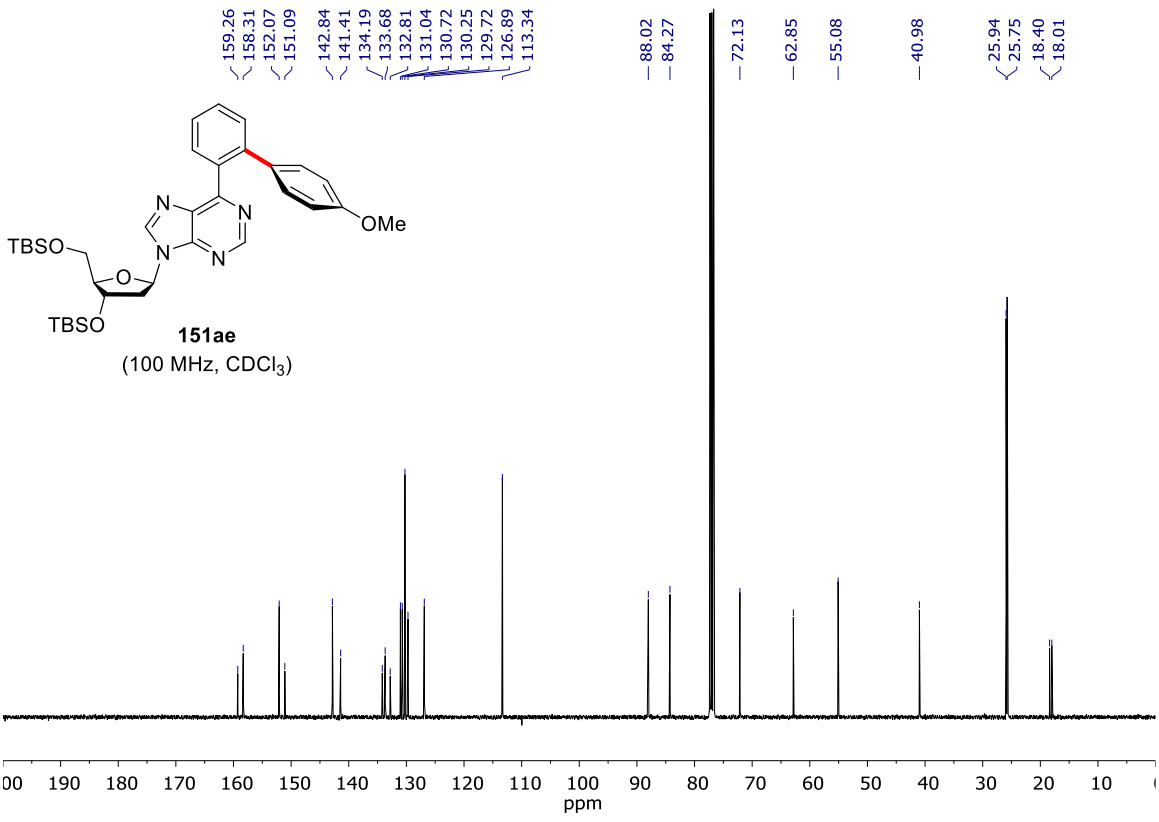

OMe
i-Pr
151ad
(400 MHz, CDCl3)
1.00
1.01
1.06
3.26
2.08
2.08
1.09
3.04
6.06
ppm

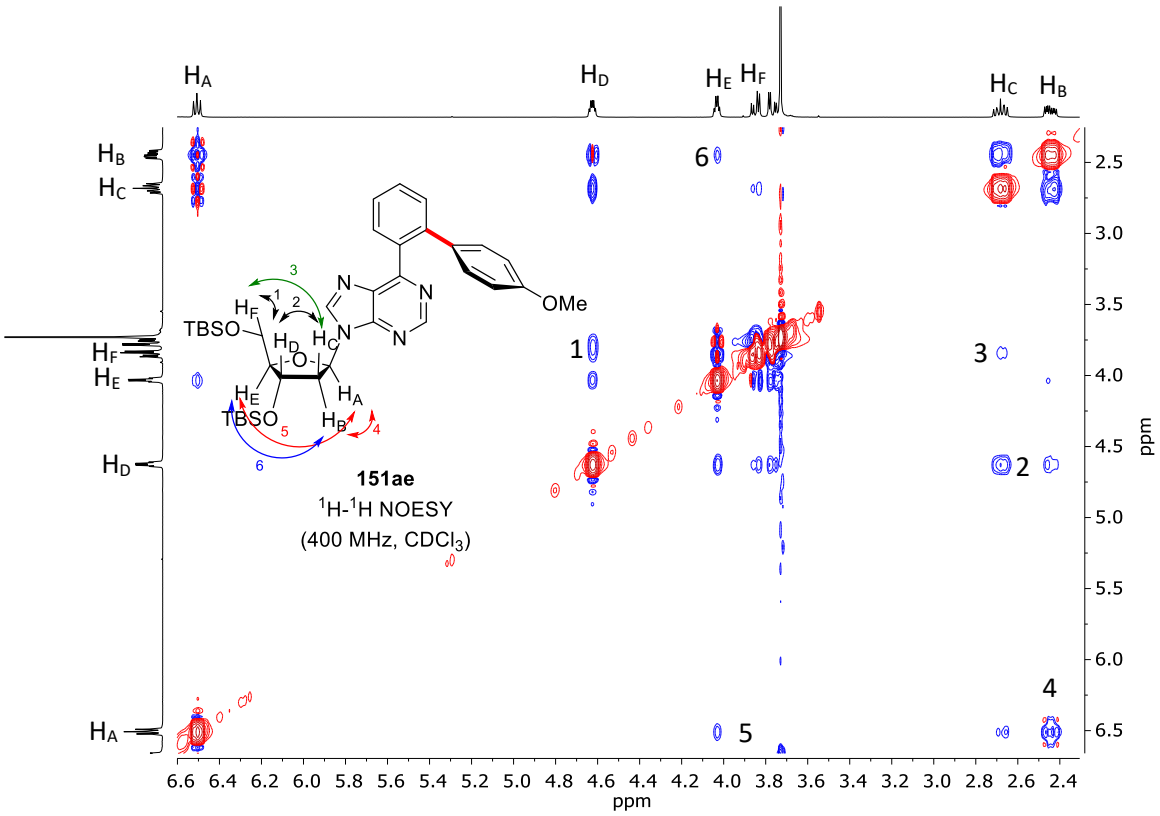

OMe
i-Pr
151ad
(100 MHz, CDCl3)
159.12
158.31
151.79
151.19
142.00
141.36
134.29
133.76
132.66
130.95
130.64
130.25
129.66
126.87
113.28
55.12
47.24
22.48
ppm

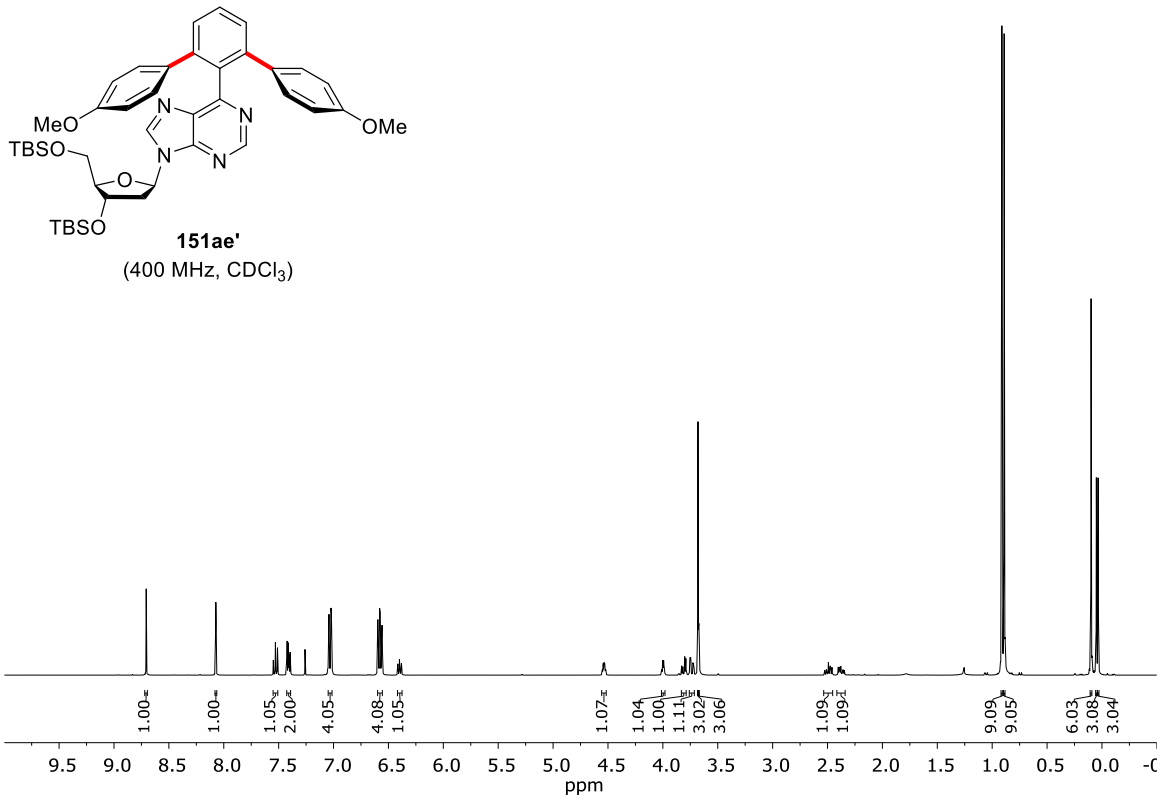

MeO
OMe
N
N
N
N
i-Pr
151ad'
(400 MHz, CDCl3)
1.00
1.02
1.05
2.04
4.05
4.06
1.07
6.26
6.19
ppm

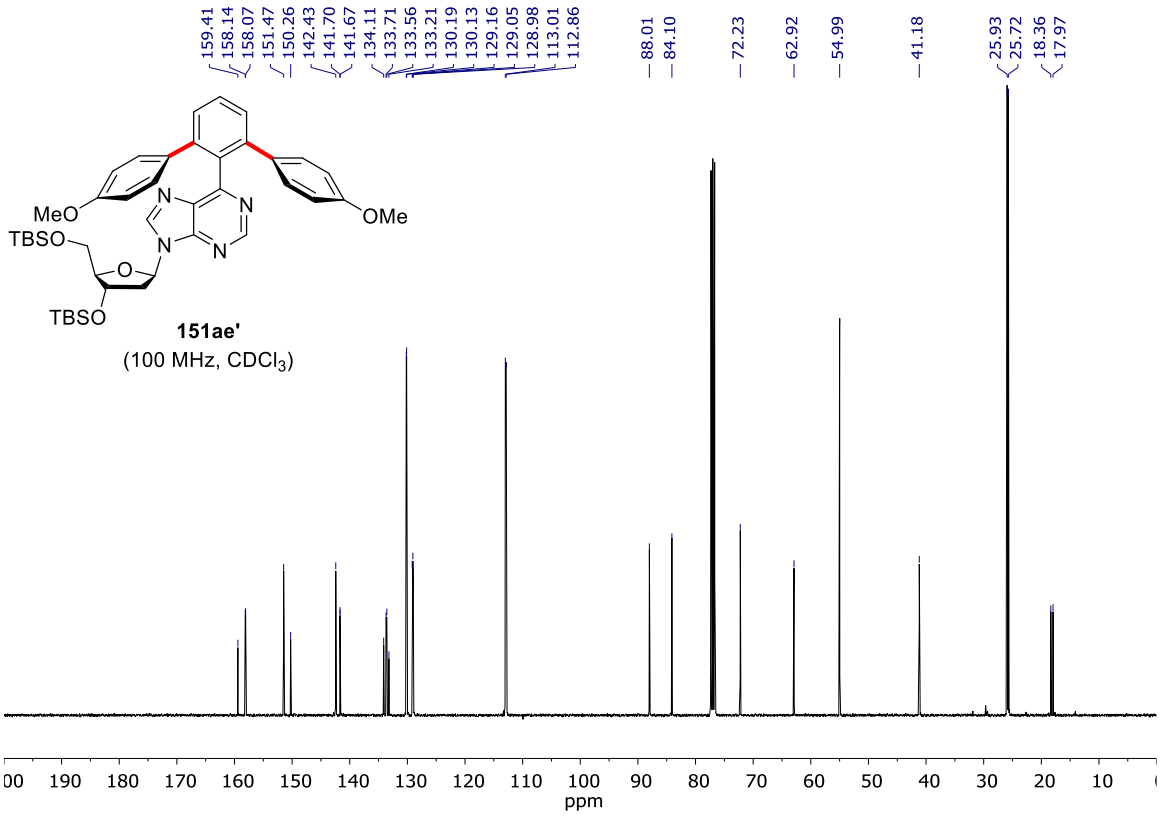

159.40
158.11
151.24
150.39
141.72
141.63
134.14
133.73
133.42
130.17
129.02
128.98
112.86
55.05
47.02
22.29
MeO
OMe
N
N
N
N
i-Pr
151ad'
(100 MHz, CDCl3)
ppm


TBSO
TBSO
OMe
N
N
N
N
O
151ae
(400 MHz, CDCl3)
1.00
1.00
1.03
2.06
1.02
2.01
2.03
1.03
1.03
1.03
1.05
1.06
3.03
1.05
1.05
9.01
9.17
6.00
3.08
3.03
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

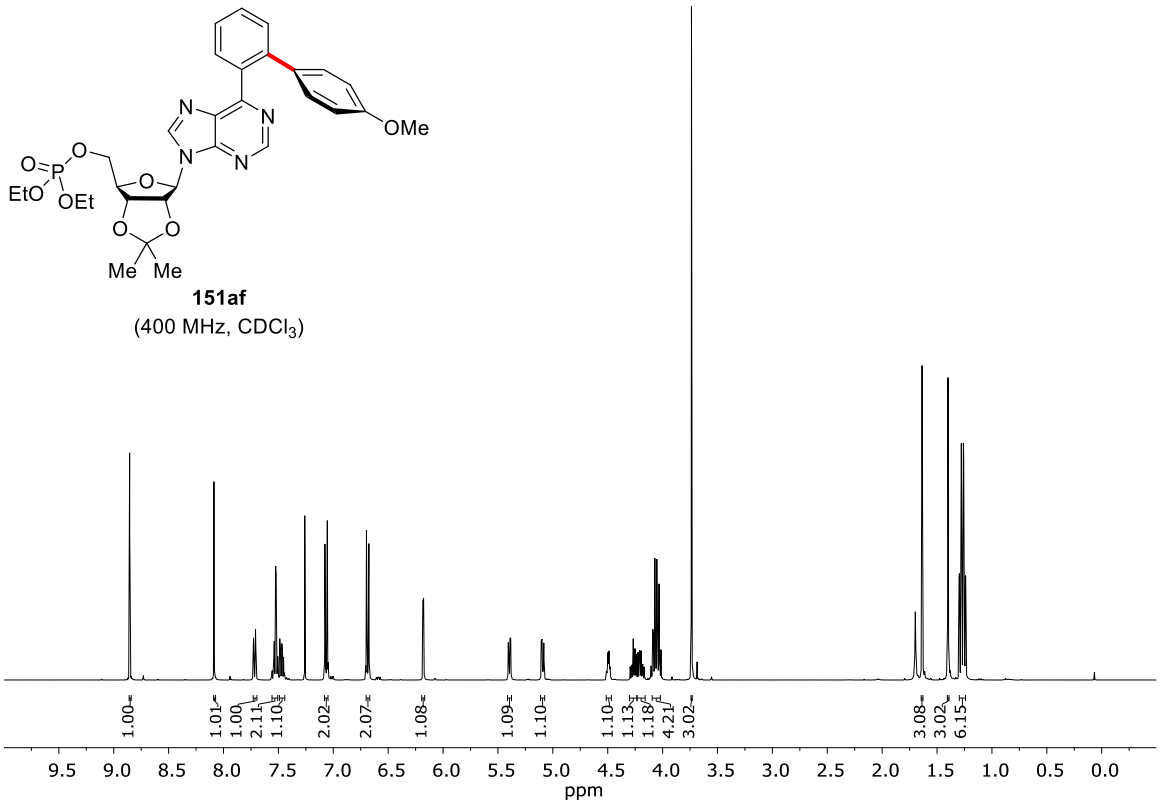

159.26
158.31
152.07
151.09
142.84
141.41
134.19
133.68
132.81
131.04
130.72
130.25
129.72
126.89
113.34
88.02
84.27
72.13
62.85
55.08
40.98
25.94
25.75
18.40
18.01
TBSO
TBSO
OMe
N
N
N
N
O
151ae
(100 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm


HA
HD
HE HF
HC HB
HB
HC
HF
HE
HD
HA
OMe
TBSO
TBSO
151ae
1H-1H NOESY
(400 MHz, CDCl3)
ppm
ppm

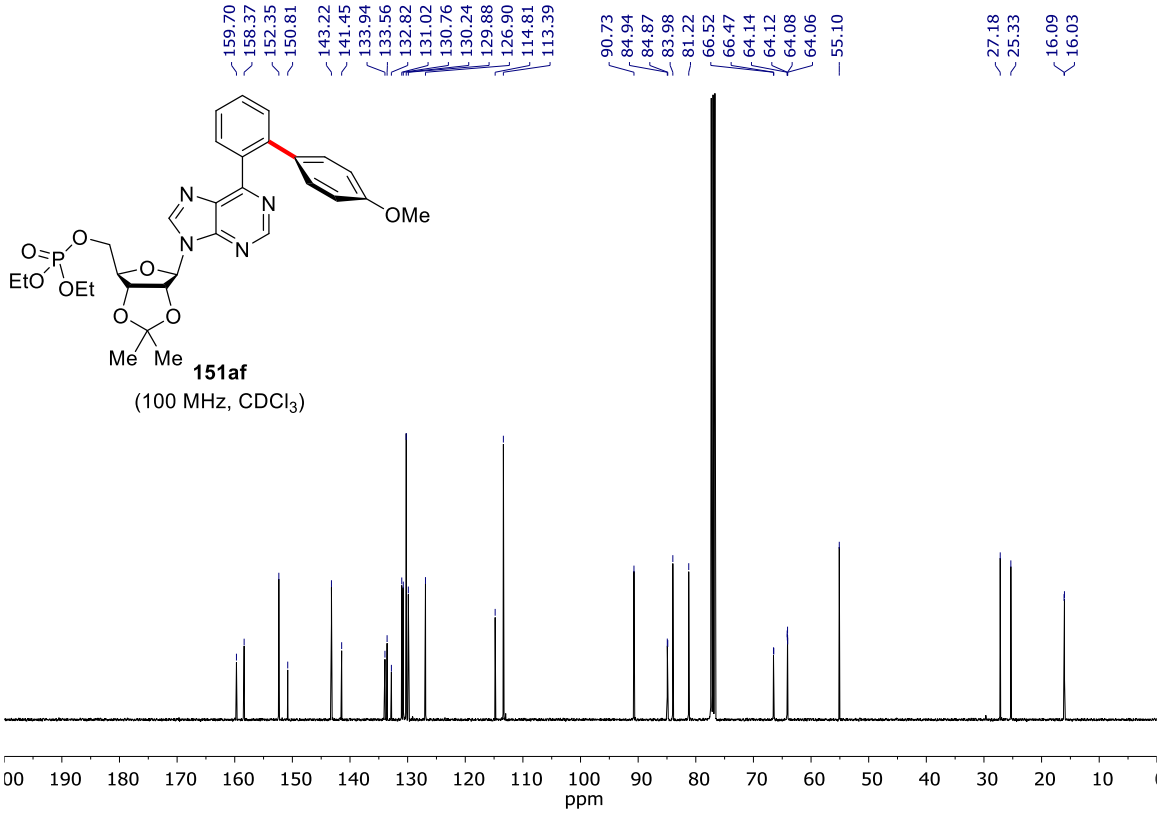

MeO
TBSO
TBSO
OMe
151ae'
(400 MHz, CDCl3)
ppm

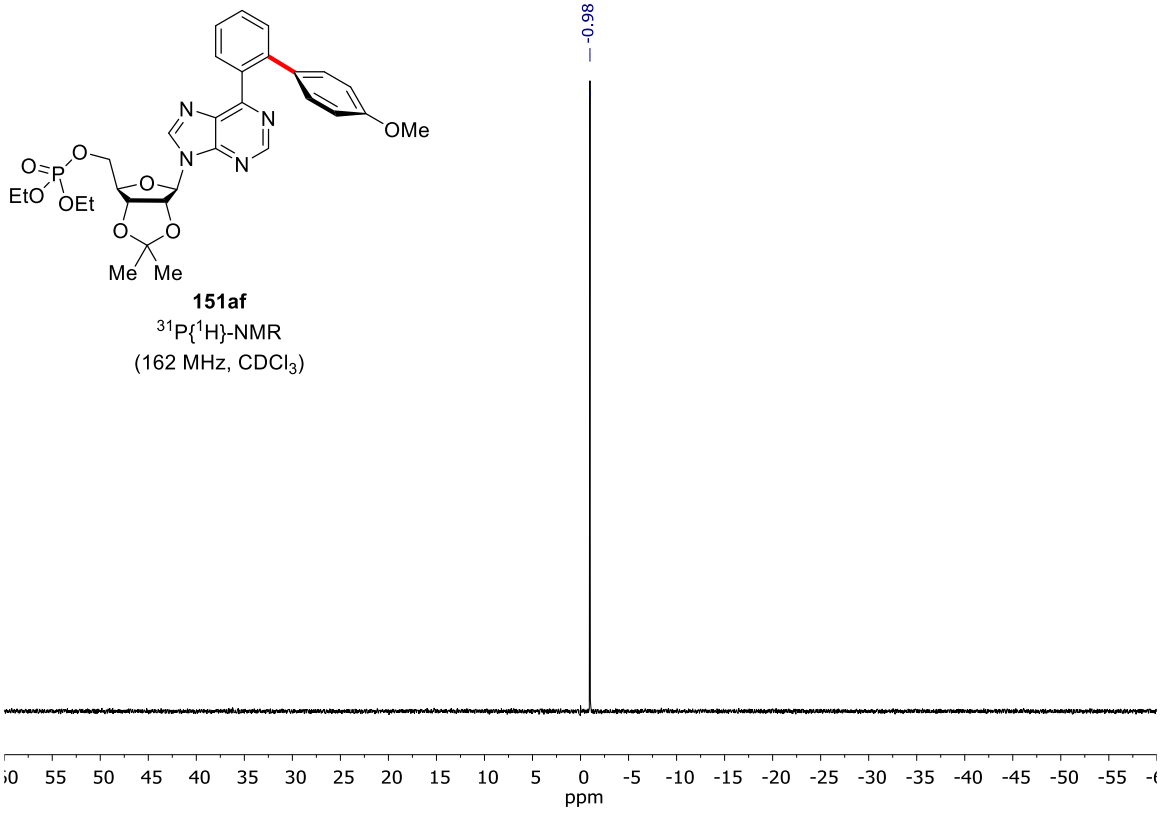


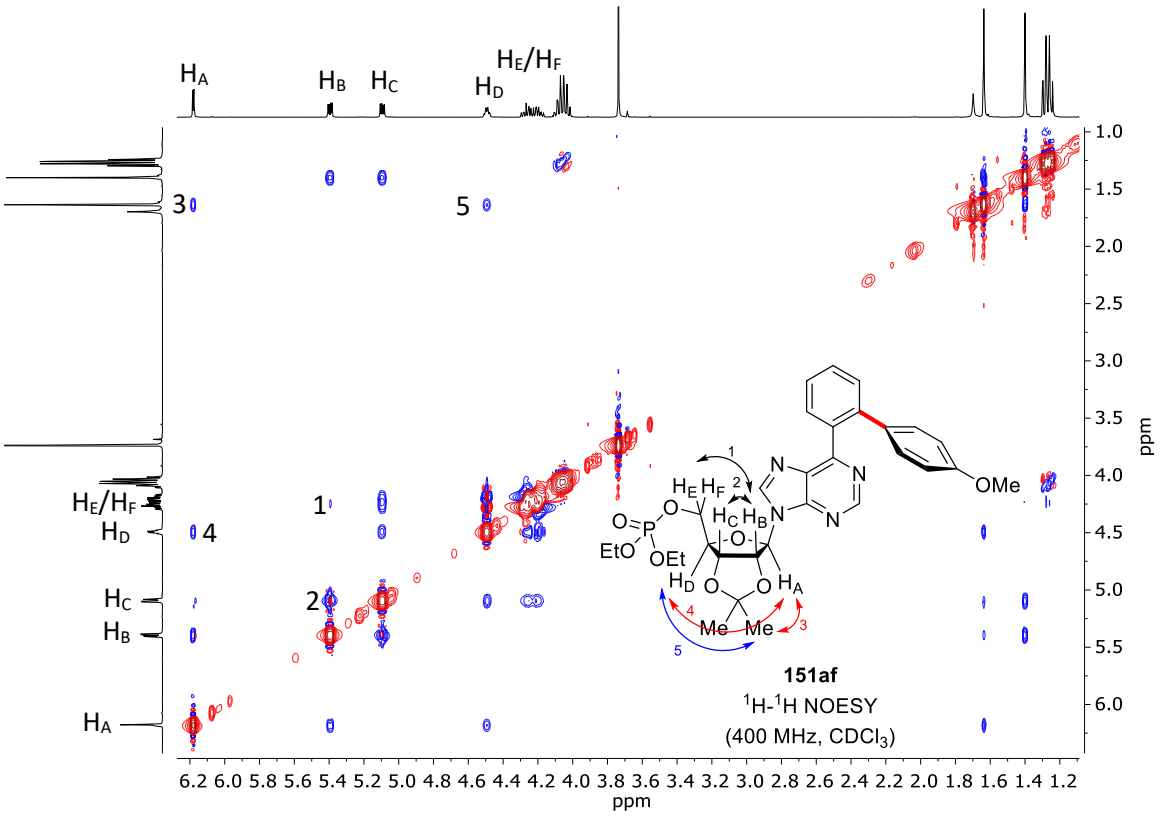
151ae'
(100 MHz, $CDCl_3$)

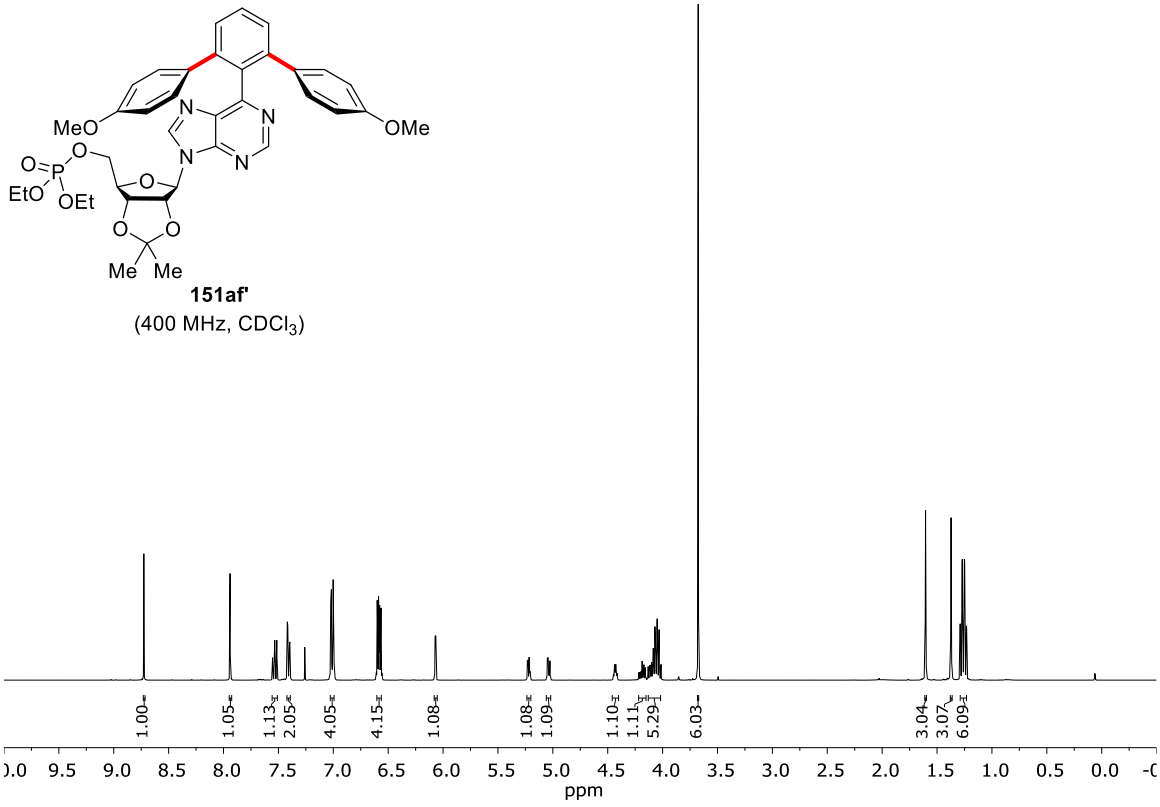


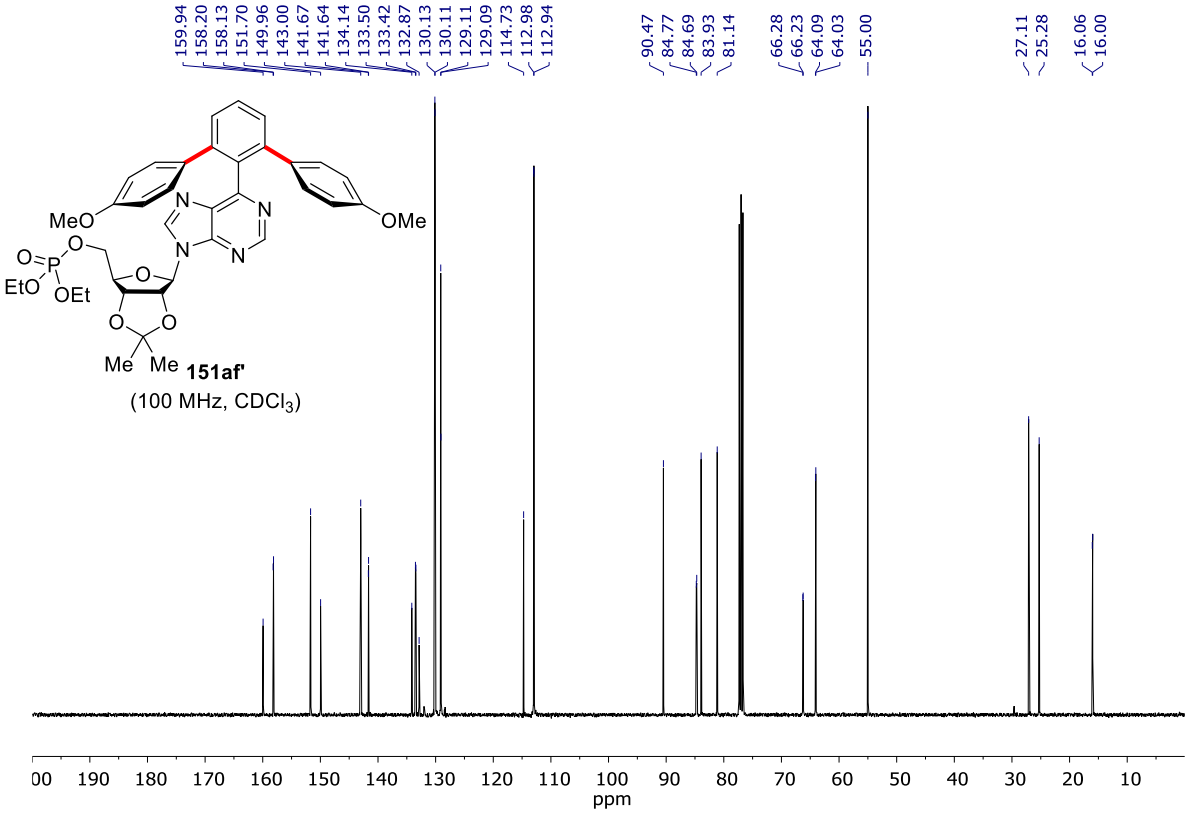
151af
(400 MHz, $CDCl_3$)


159.70
158.37
152.35
150.81
143.22
141.45
133.94
133.56
132.82
131.02
130.76
130.24
129.88
126.90
114.81
113.39
90.73
84.94
84.87
83.98
81.22
66.52
66.47
64.14
64.12
64.08
64.06
55.10
27.18
25.33
16.09
16.03
OMe
EtO
OEt
Me
Me
151af
(100 MHz, CDCl3)
ppm

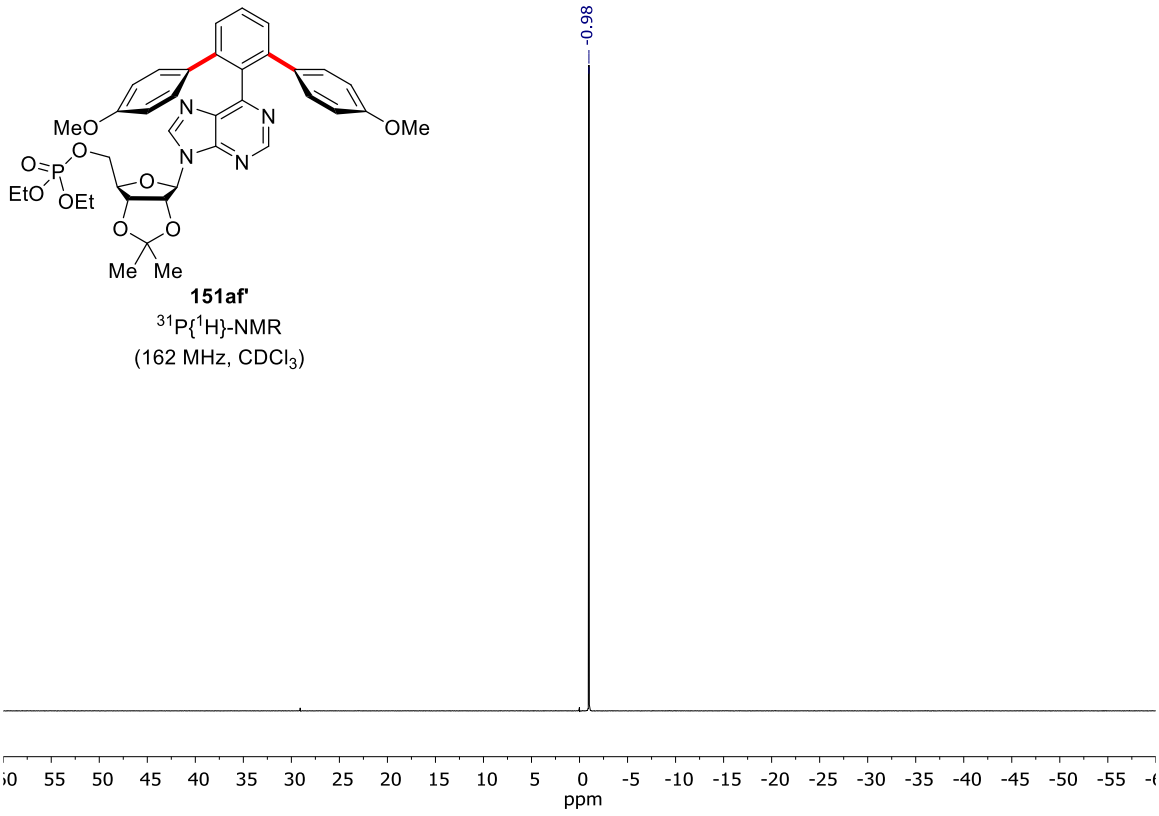

-0.98
OMe
EtO
OEt
Me
Me
151af
31P{1H}-NMR
(162 MHz, CDCl3)
ppm


HA
HB
HC
HD
HE/HF
3
5
1
4
2
OMe
151af
1H-1H NOESY
(400 MHz, CDCl3)
ppm

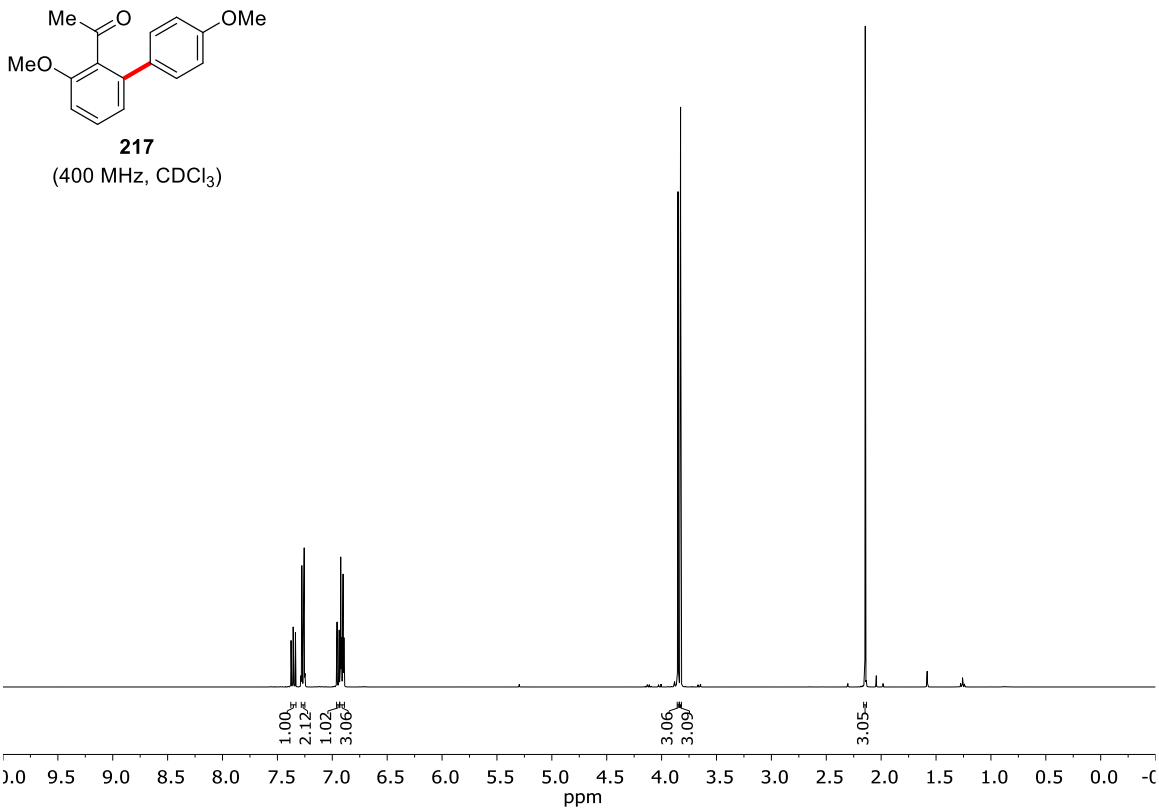

MeO
OMe
EtO
OEt
Me
Me
151af'
(400 MHz, CDCl3)
ppm



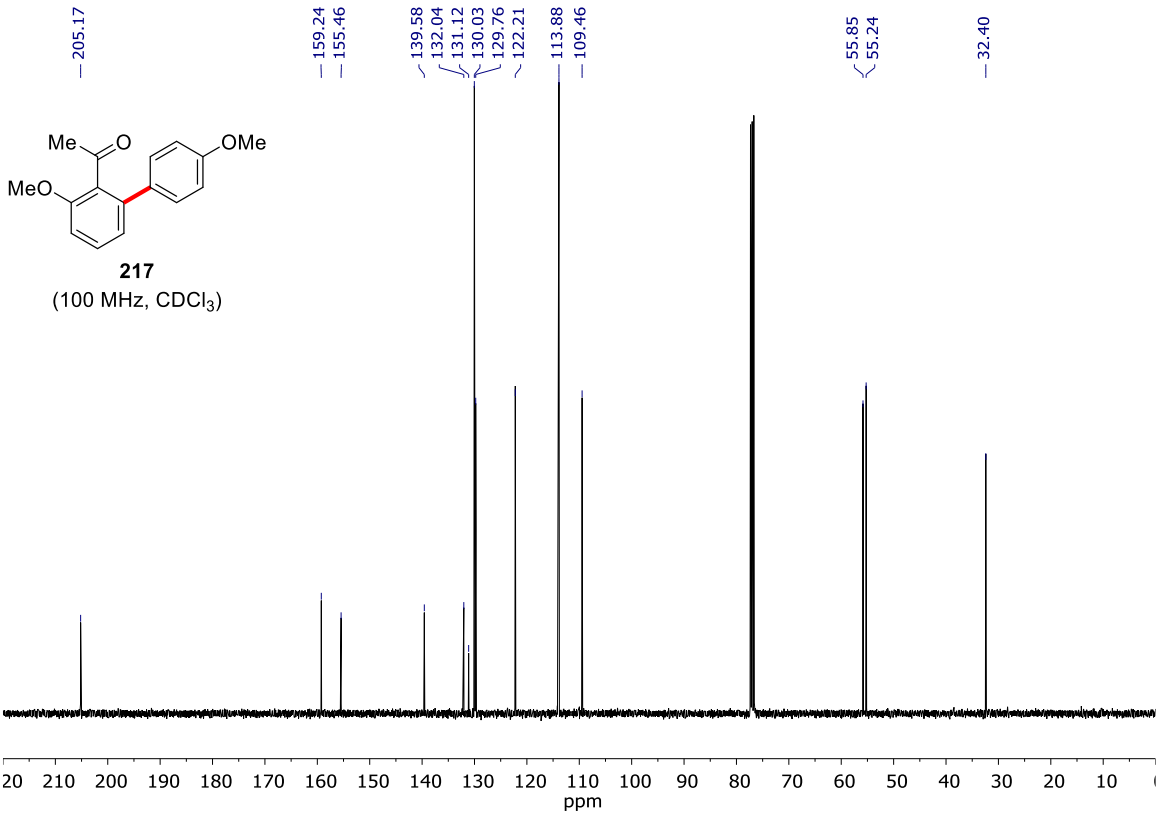
151af'
(100 MHz, $CDCl_3$)



151af'
$^{31}P\{^{1}H\}$-NMR
(162 MHz, $CDCl_3$)



217
(400 MHz, $CDCl_3$)



217
(100 MHz, $CDCl_3$)

Curriculum Vitae

PERSONAL INFORMATION

Name:	Korkit Korvorapun
Date of Birth:	16.12.1988
Place of Birth:	Bangkok, Thailand
Nationality:	Thai

ACADEMIC EDUCATION

05/2015–09/2020	**Ph.D. Thesis** under the supervision of Prof. Dr. Lutz Ackermann Georg-August-Universität Göttingen, Göttingen, Germany Title: *"Site-Selectivity in Ruthenium-Catalyzed C–H and C–C Activations"*
06/2011–09/2014	**Master of Science (M.Sc.)** in Organic Chemistry (GPA 4.00) **Master Thesis** under the supervision of Prof. Dr. Manat Pohmakotr (major advisor) and Assoc. Prof. Dr. Darunee Soorukram (co-advisor) Mahidol University, Bangkok, Thailand Title: *"Fluoride-Catalyzed Nucleophilic Addition of $PhSCF_2SiMe_3$ to Nitrones: Asymmetric Synthesis of Polyhydroxylated Pyrrolizidines and Indolizidines"*
05/2007–03/2011	**Bachelor of Science (B.Sc.)** in Chemistry (GPA 3.79 with the first class honors) **Bachelor Thesis** under the supervision of Prof. Dr. Manat Pohmakotr (major advisor) and Assoc. Prof. Dr. Darunee Soorukram (co-advisor) Mahidol University, Bangkok, Thailand Title: *"Preliminary Study of the Reaction of $PhSCF_2SiMe_3$ with Nitrile Oxides and Nitrones"*

SCHOOL EDUCATION

2001–2007 Suksanareewittaya School (Secondary School), Bangkok, Thailand

PUBLICATIONS

9) **K. Korvorapun**,' M. Moselage,' J. Struwe, T. Rogge, A. M. Messinis, L. Ackermann, "*Regiodivergent C–H and Decarboxylative Alkylation by Ruthenium Catalysis: ortho versus meta Position-Selectivity*" *Angew. Chem. Int. Ed.* **2020**, *59*, DOI: 10.1002/anie.202007144.

8) **K. Korvorapun**,' J. Struwe,' R. Kuniyil, A. Zangarelli, A. Casnati, M. Waeterschoot, L. Ackermann, *"Photo-Induced Ruthenium-Catalyzed C–H Arylations at Ambient Temperature" Angew. Chem. Int. Ed.* **2020**, *59*, DOI: 10.1002/anie.202003035.

7) **K. Korvorapun**, R. C. Samanta, T. Rogge, L. Ackermann, *"Ruthenium-Catalyzed Remote C–H Functionalizations",* in *Remote C-H Bond Functionalizations: Methods and Strategies in Organic Synthesis* (Eds.: D. Maiti, S. Guin), Wiley-VCH, Weinheim, **2020**.

6) **K. Korvorapun**, R. Kuniyil, L. Ackermann, "*Late-Stage Diversification by Selectivity Switch in meta-C–H Activation: Evidence for Singlet Stabilization*" *ACS Catal.* **2020**, *10*, 435–440.

5) P. Gandeepan, J. Koeller, **K. Korvorapun**, J. Mohr, L. Ackermann, "*Visible-Light-Enabled Ruthenium-Catalyzed meta-C–H Alkylation at Room Temperature*" *Angew. Chem. Int. Ed.* **2019**, *58*, 9820–9825.

4) **K. Korvorapun**,' N. Kaplaneris,' T. Rogge, S. Warratz, A. C. Stückl, L. Ackermann, *"Sequential meta-/ortho-C–H Functionalizations by One-Pot Ruthenium(II/III) Catalysis" ACS Catal.* **2018**, *8*, 886–892. 'equal contribution

3) J. Li,' **K. Korvorapun**,' S. De Sarkar,' T. Rogge, D. J. Burns, S. Warratz, L. Ackermann, *"Ruthenium(II)-catalysed remote C–H alkylations as a versatile platform to meta-decorated arenes" Nat. Commun.* **2017**, *8*, 15430. 'equal contribution

2) S. Warratz, D. J. Burns, C. Zhu, **K. Korvorapun**, T. Rogge, J. Scholz, C. Jooss, D. Gelman, L. Ackermann, *"meta-C–H Bromination on Purine Bases by Heterogeneous Ruthenium Catalysis" Angew. Chem. Int. Ed.* **2017**, *56*, 1557–1560.

1) **K. Korvorapun**, D. Soorukram, C. Kuhakarn, P. Tuchinda, V. Reutrakul, M. Pohmakotr, *"Stereoselective Nucleophilic Addition of $PhSCF_2SiMe_3$ to Chiral Cyclic Nitrones: Asymmetric Synthesis of gem-Difluoromethylenated Polyhydroxypyrrolizidines and -indolizidines" Chem. Asian J.* **2015**, *10*, 948–968.

CONFERENCES

05/2013	*The International Conference of the International Congress for Innovation in Chemistry* (PERCH-CIC Congress VIII), Pattaya, Thailand (Poster Presentation)
09/2017	*ICASEC Summer School on Organic Catalysis for Energy Conversion*, Göttingen, Germany (Poster Presentation)
05/2018	*Göttinger Chemie-Forum 2018*, Göttingen, Germany (Poster Presentation)
09/2018	*Jahrestagung der Fachgruppe Nachhaltige Chemie*, Aachen, Germany (Poster Presentation)

Erklärung

Hiermit versichere ich, dass ich die vorliegende Dissertation im Zeitraum von Mai 2015 bis September 2020 am Institut für Organische und Biomolekulare Chemie der Georg-August-Universität Göttingen auf Anregung und unter Anleitung von

Herrn Prof. Dr. Lutz Ackermann

selbstständig durchgeführt und keine anderen als die angegeben Hilfsmittel und Quellen verwendet habe.

Göttingen, den 16.09.2020

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