C–H Activation by Iron(III), Manganese(II) and Rhoda(III)electro Catalysis

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Zhigao Shen

from Hunan, China

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Thesis Committee

Prof. Dr. Lutz Ackermann, Institute of Organic and Biomolecular Chemistry

Prof. Dr. Konrad Koszinowski, Institute of Organic and Biomolecular Chemistry

Members of the Examination Board

Reviewer: Prof. Dr. Lutz Ackermann, Institute of Organic and Biomolecular Chemistry

Second Reviewer: Prof. Dr. Konrad Koszinowski, Institute of Organic and Biomolecular Chemistry

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Prof. Dr. Johannes C. L. Walker, Institute of Organic and Biomolecular Chemistry

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Contents

List of Abbreviations

Ac	acetyl
acac	acetylacetonate
Alk	alkyl
AMLA	ambiphillic metal-ligand activation
aq	aqueous
Ar	aryl
atm	atmospheric pressure
BIES	base-assisted internal electrophilic substitution
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
Bu	butyl
Calc.	calculated
cat.	catalytic
CCE	constant current electrolysis
CMD	concerted metalation deprotonation
Cp	cyclopentadienyl
Cp*	pentamethylcyclopentadienyl
$CypCO_2H$	cyclopentanecarboxylic acid
CV	cyclic voltammetry
Cy	cyclohexyl
δ	chemical shift
d	doublet
DCE	1,2-dichloroethane
dd	doublet of doublets
DG	directing group
DMF	*N,N*-dimethylformamide
DMSO	dimethylsulfoxide

dt	doublet of triplets
ee	enantiomeric excess
EI	electron ionization
equiv	equivalent
ESI	electrospray ionization
Et	ethyl
g	gram
GC	gas chromatography
GF	graphite felt
h	hour
HFIP	1,1,1,3,3,3-hexafluoro-2-propanol
HRMS	high resolution mass spectromethy
Hz	hertz
i	*iso*
IMes	1,3-bis(2,4,6-trimethylphenyl)imidazole-2-ylidene
IPr	1,3-bis(2,6-*iso*-propylphenyl)imidazole-2-ylidene
IR	infrared spectroscopy
J	coupling constant
KIE	kinetic isotope effect
L	ligand
m	meta
m	multiplet
M	molar
mol	mole
$[M]^+$	molecular ion peak
mA	Milliamper
Me	methyl
Mes	mesityl
mg	milligram

MHz	megahertz
min	minute
mL	milliliter
mmol	millimolar
M.p.	melting point
MS	mass spectromethy
m/z	mass to charge ratio
NMR	nuclear magnetic resonance
o	*ortho*
p	*para*
Ph	phenyl
PMP	*para*-methoxyphenyl
Piv	pivaloyl
ppm	parts per million
Pr	propyl
Py	pyridyl
pym	pyrimidyl
q	quartet
Q	8-aminoquinoline
rt.	room temperature
s	singlet
sat.	saturated
SET	single electron transfer
SPS	solvent purification system
t	*tert*
t	triplet
T	temperature
TFE	2,2,2-trifluoroethanol
THF	tetrahydrofuran

TLC	thin layer chromatography
TM	transition metal
TMS	trimethylsilyl
TS	transition state
V	Volt
X	(pseudo-)halide

1 Introduction

Urea was first isolated in urine in 1773.[1] And almost half a century later, the German scientist Friedrich Wöhler from Göttingen realized the synthesis of urea by heating an aqueous solution of ammonium cyanate which is regarded as the first organic compound obtained from inorganic mixtures.[2] Since then, organic chemistry has been viewed as an essential part of chemistry. Now, urea is widely used in agricultural industry improving the yields of crops, which helped to relieve the starvation all around the world significantly. Over the last century, different types of reactions have been developed. So, with all these chemical methods in hand, scientists synthesized different kinds of polymers, life-saving drugs, pesticides, dyes and finished the total synthesis of many natural compounds. Due to resource and energy consumption, waste generation, byproducts and the use of dangerous chemicals, chemistry continues to be regarded as one contributing factor to pollution. A new concept, sustainable development, was proposed by Brundtland that meets the present needs without compromising the ability of future generations to meet their own needs.[3] It's urgent to remove or at least to minimize the disadvantages.

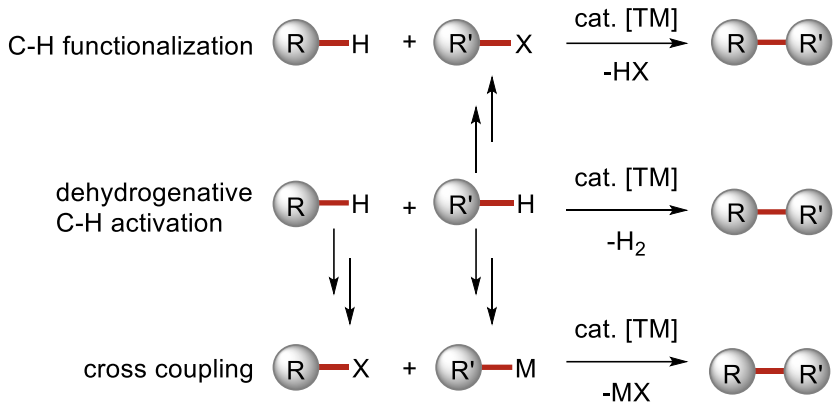
Thereafter, the development of more environment-friendly, resource-,[4] atom-[5] and step-economic[6] reactions are highly desirable. Many interests in chemical academia have been paid to Domino reactions[7] which can construct several C–C and C–Het bonds in a single step and some reactions also have been modified to work in green solvents, such as biomass-derived glycerol.[8] With the insightful understanding of chemical processes and the development of new ligands, stoichiometric reactions can work in catalytic version with high efficiency and the temperature of some reactions can be decreased dramatically. In addition, CO_2 can also be used to synthesize value-added products, polymers and widely used chemical materials.[9] Throughout the development of chemistry, chemists are guided by the principles 12 Principles of Green Chemistry proposed by Anastas and Warner.[10]

1.1 C–H Functionalization

Organic chemistry mainly studies the cleavage and formation of bonds in a practical and selective fashion, and the formation of carbon-carbon (C–C)[11] and C–Heteroatom (C–Het)[12] bonds is the most important part, since it can serve as a valuable tool for scientists to design and synthesize different kinds of functional materials and bioactive molecules. Original works in coupling reactions were realized by Glaser[13] in the late of 19th century and Ullmann[14] in the early of 20th century using stoichiometric or catalytic amounts of copper. Now highly efficient transition-metal catalyzed organic reactions have made a huge impact on organic transformations for C–C and C–Het bond formations. In the recent decades, significant progress have been further witnessed in this area by the invention of a variety of named cross-coupling reactions, such as the Kumada-Corriu-coupling,[15] Mizoroki-Heck-coupling,[16] Negishi-coupling,[17] Stille-coupling,[18] Hiyama-coupling,[19] Suzuki-Miyaura-coupling,[20] and Sonogashira-coupling[21] reactions. Thus, transition metal-catalyzed cross-coupling reactions performed as a powerful tool in organic synthesis, with applications ranging from the construction of natural product and useful materials to the modifications of biologically active chemicals,[11, 12] and their significance was further reflected by Heck, Negishi and Suzuki being collectively awarded with the Nobel Prize in chemistry in 2010.[23]

Based on transition-metal catalysis, this newly acquired ability to forge carbon–carbon bonds between or within functionalized and often sensitive substrates provided new opportunities, particularly in total synthesis but also in medicinal chemistry as well as in chemical biology and nanotechnology. Prominent among these processes are the palladium-catalyzed C–C bond-forming reactions. The historical, mechanistic, theoretical, and practical aspects of these processes have been amply discussed. Indeed, these protocols have revolutionized organic syntheses, albeit a few problems still exist. First, the use of pre-functionalized starting materials is needed, such as the organic (pseudo)halides. And even for the widely used organic nucleophiles, multiple synthetic steps, difficulty in storing and handling make them user unfriendly, e.g. RMgX, R_2Zn, and toxic R'_3RSn.

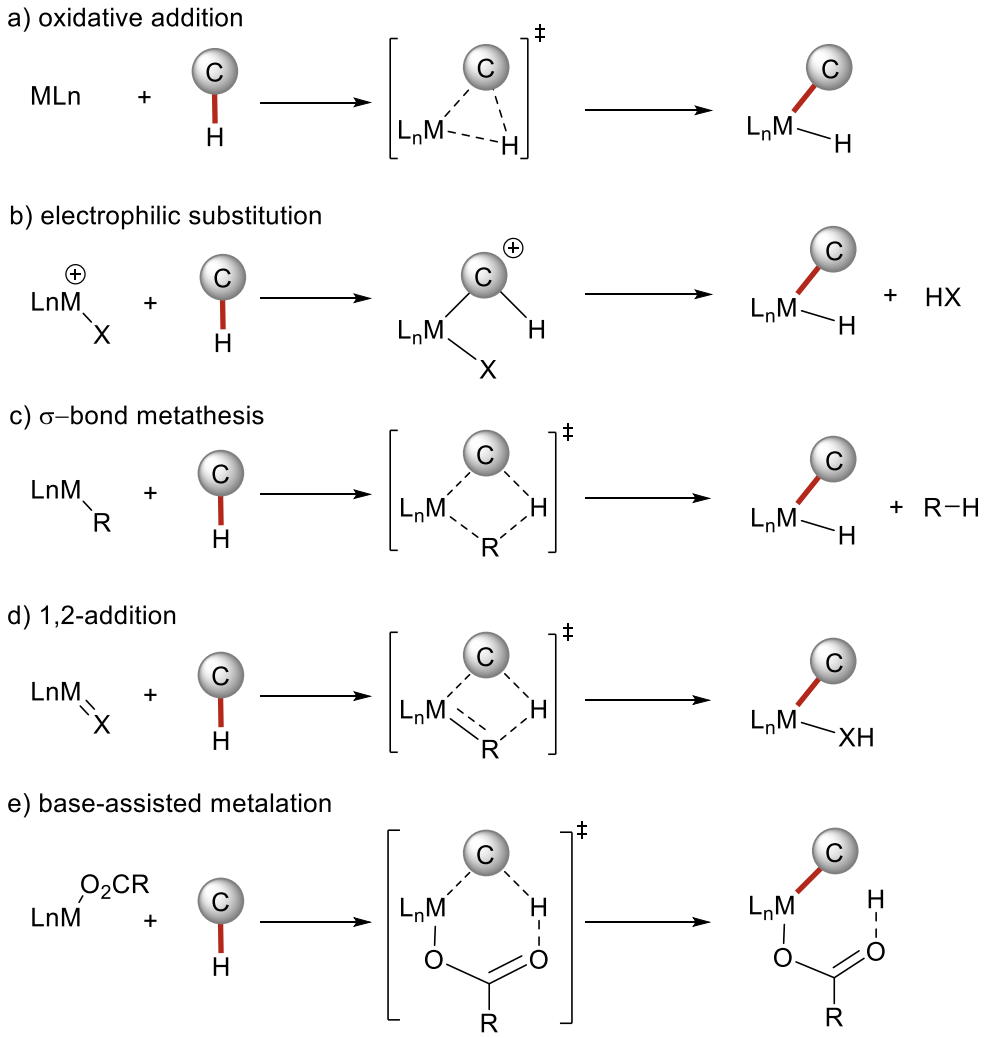
Therefore, the selective C–H functionalization can serve as an elegant tool to diminish these problems,[24] combining the broad practicability of cross-couplings with the nature of green chemistry—atom economy and environmentally friendly methods (Scheme 1.1). Moreover, two-fold C–H dehydrogenative activation also contribute to the formation of C–C bonds while external oxidants are required in the dehydrative step.[25]



Scheme 1.1. Comparison of traditional cross-coupling *vs.* C–H activation.

The last thirty years have seen many examples of C–H activation at different metal centers, usually with good regio- and chemoselectivity and under mild conditions. The selective transformation of ubiquitous but inert C–H bonds to other functional groups has far-reaching practical implications, ranging from more efficient strategies for fine chemical synthesis to the replacement of current petrochemical feedstocks by less expensive and more readily available alkanes.[26] All the potential practical applications have inspired chemists to study how these organometallic reactions occur, and what their inherent advantages and limitations for practical alkane conversion and late-stage functionalization are. As the transition metal-facilitated cleavage of the C–H bonds is the common key step in the above-mentioned C–H functionalization strategies, it has been heavily examined. Excluding outer-sphere mechanisms, such as carbene/nitrene insertions[27] or radical reactions[28], the bond dissociation proceeds generally *via* five different pathways, depending on the nature of the metal, the ligands and oxidation states.[29] These methods (Scheme 1.2) are oxidative addition, electrophilic substitution, σ-bond metathesis, 1,2-addition and base-assisted metalation. Electron-rich complexes of late transition metals

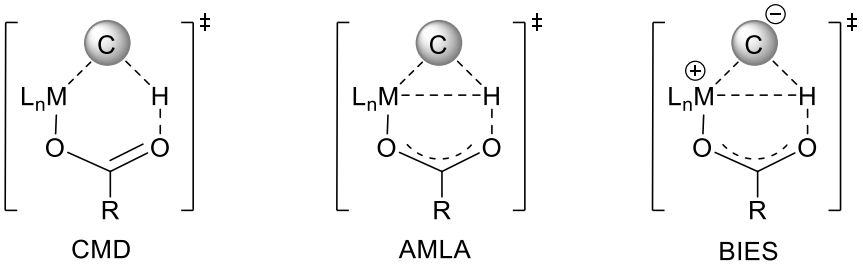
are prone to cleave the inert C–H bonds by oxidative addition, while this mode of action is unfavorable for early transition metals.[29b] Most late transition metals in higher oxidation states often act as a Lewis acid to cleave C–H bond by an electrophilic substitution mode. The σ-bond metathesis is observed for early transition metals which cannot undergo oxidative addition. Metals containing an unsaturated M=X bond tend to undergo C–H activation *via* 1,2-addition. This fashion can be found in early transition metals.



Scheme 1.2. Mechanistic pathways for the C–H activation.

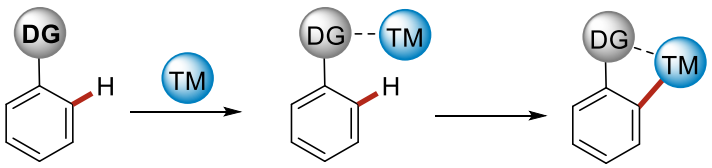
Besides the mechanistic scenarios, many examples proceed via the base-assisted C–H metalation events (Scheme 1.3). Further research on this base-assisted C–H activation led to the proposal of several transition states. The base-assisted deprotonation takes place *via* a six- or five-membered transition state respectively in the presence of

carboxylate or a secondary phosphine oxide.[29a, 30] This C–H cleavage mode was classified as Concerted Metalation-Deprotonation (CMD)[30b] and ambiphillic metal-ligand activation (AMLA).[31] An additional mechanism is the base assisted intramolecular electrophilic substitution (BIES), which is common for base assisted electrophilic transition metals.[32]

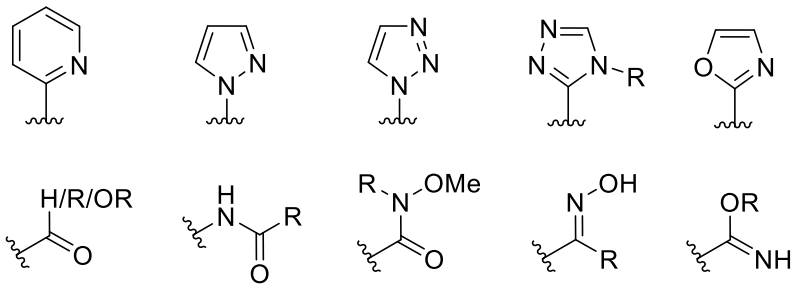


Scheme 1.3. Transition states for the C–H cleavage in base-assisted C–H metalation.

Although many modes have been proposed for the C–H cleavage, another big challenge about C–H activation is the regioselectivity due to the almost equal bond dissociation energies and acidities among several C–H bonds.[33] This issue can be tackled through steric hindrance, electronic bias, or the incorporation of directing groups.[34] The lone pair of the directing groups can coordinate to the transition metal, thus bringing the catalyst in close proximity to the desired C–H bond (Scheme 1.4).[35] Remarkably, different templates[36] and strategies[37] have been developed for the *para*- and *meta*- C–H activation. Even free amine and hydroxyl groups could be used as directing groups to control the selectivity.[38]



Scheme 1.4. Regioselective C–H activation using directing groups(DGs).



Scheme 1.5. Common directing groups for proximity induced C–H activation.

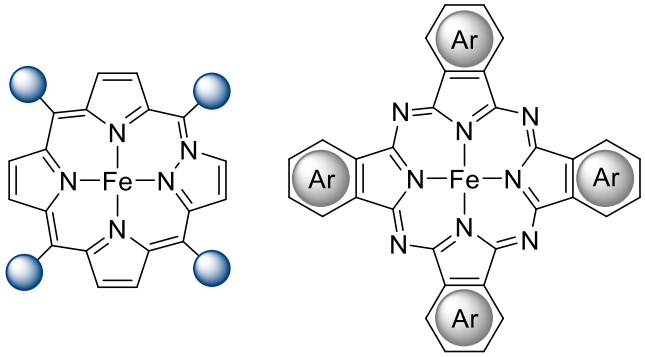
1.2 Iron-Catalyzed C–H Activation

Iron is the most abundant transition metal on the earth. The great abundance (6.3% abundance of iron in the Earth's crust) and widespread distribution allow for the low cost as well as low biological toxicity in sharp contrast to the majority of other precious metals (e.g., 0.00000007% abundance of rhodium in the Earth's crust).[39] So the use of iron as a substituent to precious metals is desirable in terms of both economy and sustainability.

Organoiron chemistry was arguably initiated by the synthesis of pentacarbonyliron in 1891, independently by Mond[40] and Berthelot.[41] Another important breakthrough of iron-chemistry was reported by the use of simple iron salt as precatalysts in reactions with Grignard reagent, including homocouplings, by Kharasch in 1941.[42] A subsequent milestone was the preparation of ferrocene accomplished by Pauson and Keary in 1951, which was formulated as dicyclopentadienyl iron.[43] Then a sandwich structure of ferrocene was proposed by Woodward and Wilkinson.[44] Transformative application of ferrocene made a great contribution to organic chemistry, especially for asymmetric synthesis.[45] A milestone in organoiron catalysis was the application of iron salts as catalysts in cross-couplings between Grignard reagents and vinyl bromides by *Kochi* in 1971,[46] which, remarkably, preceded before studies with palladium catalysts. Despite the loss of interest in iron-catalyzed cross-couplings due to the development of palladium catalysis, it has recently witnessed a renaissance. In fact, iron complexes are often too diverse in their reactivity compared with neighboring metals[47] and noble metals,[48] and

hence it is difficult to design catalytic cycles of significance. Thus, the design of appropriate ligands for iron chemistry is in high demand.

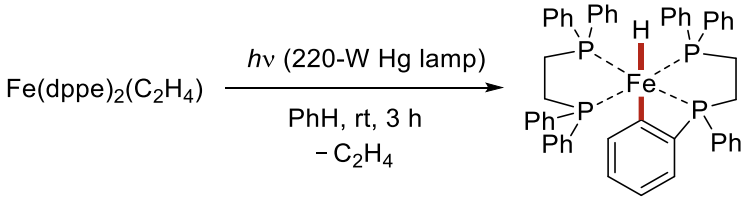
Chemists have received many inspirations from enzymes to accelerate the design and exploitation of ligands compatible with iron, including heme proteins.[49] In heme proteins, the iron is coordinated with four atoms that located in a macrocyclic porphyrin ring system. Thus, many types of porphyrins have been prepared to conduct different transformations catalyzed by iron (Scheme 1.6), which mostly limited to the carbene migration reactions and oxygenation reactions.[50] Thus ligands with new scaffold are in high need for efficient C–H activation.



1 **2**

Scheme 1.6. Common structure of Fe-porphrin.

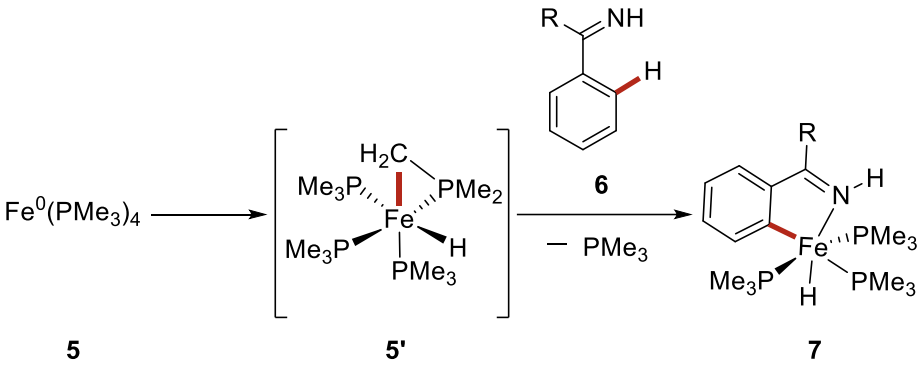
It should be highlighted that the first stoichiometric iron-mediated C–H activation was described as early as in 1968 by Hata.[51] Ultraviolet-light irradiation of $Fe(dppe)_2(C_2H_4)$ **3** resulted the loss of ethylene and shift of a hydrogen atom from a phenyl group of the ligand to the iron atom forming the new iron complex $HFe(C_6H_4PPhCH_2CH_2PPh_3)(dppe)$ **4** (Scheme 1.7).



3 **4**

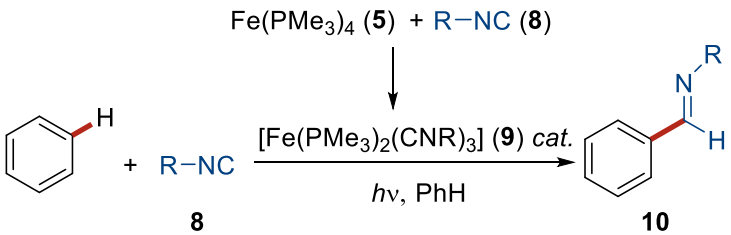
Scheme 1.7. Synthesis of cyclometalated complex **4**.

Among others, $Fe(PMe_3)_4$, first synthesized by Schmidabauer[52] in 1975, has shown significant efficiency in directing group-assisted C–H cleavage, which indicating the feasibility of stoichiometric C–H activation with low-valent iron complex (Scheme 1.8).[53] Importantly, $Fe(PMe_3)_4$ tended to exist as an iron(II) species due to C–H activation of the phosphine ligand.[54] $Fe(PMe_3)_4$ showed great potential for the application of catalytic C–H activations.



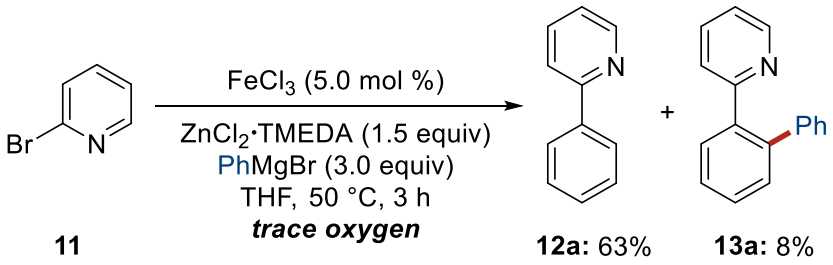
Scheme 1.8. Stoichiometric *ortho*-C–H metalation of imines with $Fe(PMe_3)_4$.

Indeed, the first contribution of a catalytic C–H activation using an iron complex was made by Jones in 1987.[55] Here, the combination between the catalyst derived from $Fe(PMe_3)_4$ and isocyanide ligands allowed for the formation of aldimines **10** from unactivated benzene under UV irradiation. Control experiment conducted in C_6D_6 proved that the solvent rather than the PMe_3 ligand was the source of the aldimine's hydrogen. The authors suggested that light was indispensable for the coordination of an isocyanide ligand to generate a reactive intermediate **9** capable to insert into an inert C–H bond (Scheme 1.9). Four decades after its original discovery, $Fe(PMe_3)_4$ was finally confirmed to be viable in iron-catalyzed C–H activation free of additional ligands, as elegantly described by Kakiuchi and Ackermann for the carbonyl-assisted hydroarylation of alkenes and allenes respectively.[56]



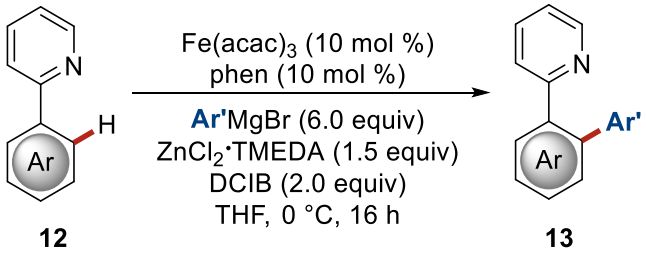
Scheme 1.9. Aldimine synthesis by iron-catalyzed C–H activation.

In 2008, in the area of iron-catalyzed C–H activation was disclosed by Nakamura and coworkers via an iron-catalyzed oxidative C–H activation was disclosed.[57] This discovery was originated from an intended iron-catalyzed cross-coupling reaction.[58] Besides the desired product **12a**, a small amount of the *ortho*-arylated phenylpyridine **13a** was formed. Later, oxygen and 2,2'-bipyridine were identified as being pivotal to the C–H arylation (Scheme 1.10).



Scheme 1.10. Iron-catalyzed C–H arylation as a byproduct of a cross-coupling reation.

Extensive optimization of this iron-catalyzed arylation proved that 1,2-dichloro-2-methylpropane (DCIB) was the very essential oxidant and phenanthroline served as the best ligand.[57] Surprisingly, the zinc salt was essential for the reaction also. It was postulated that the zinc additive was responsible for the *in situ* generation of arylzinc species, while Mg-free Ph_2Zn and PhZnBr were unable to deliver the product, with or without TMEDA (Scheme 1.11).

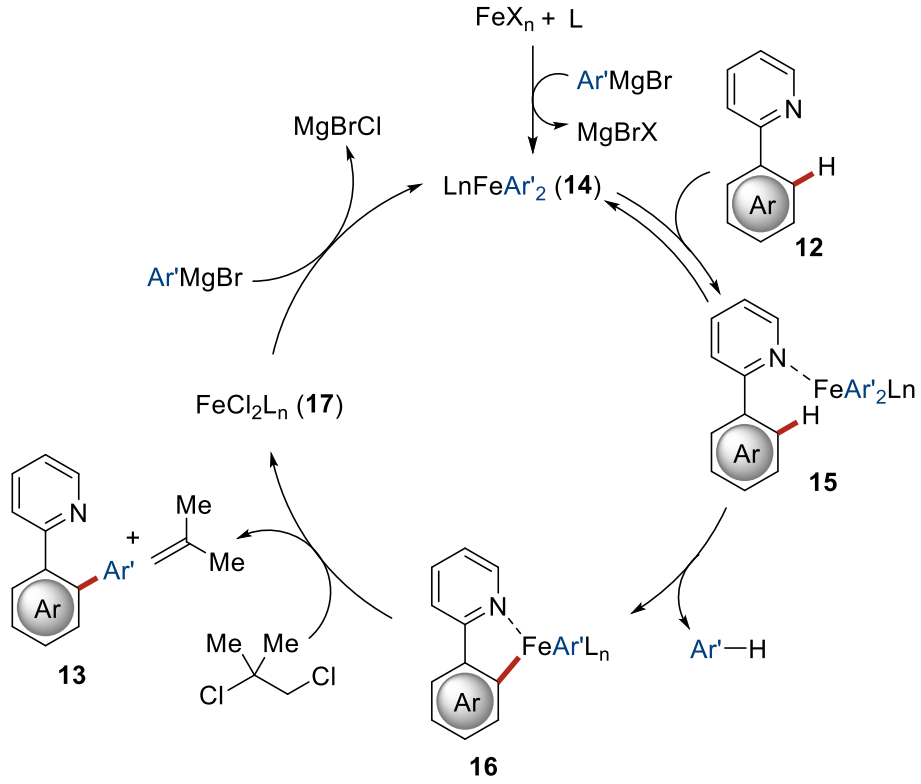


Scheme 1.11. First example of iron-catalyzed C–H arylation.

Enormous efforts have been made on iron-catalyzed C(sp^2)–H arylation, including the application of more synthetically useful amides[59] and imines[60] as the directing groups,

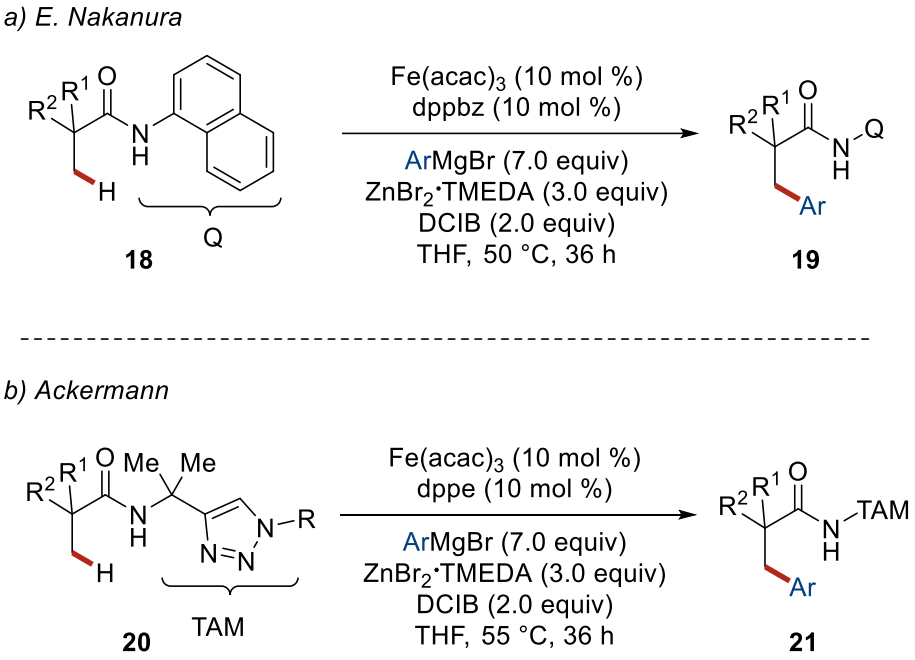
the use of environmentally benign oxygen as the oxidant,[61] the C(sp^2)–H arylation of alkenes,[62] the direct use of Grignard reagents without zinc additives,[63] and the exploitation of metallic magnesium avoiding the use of dangerous and sensitive organometallic reagents.[64]

Despite the significant contributions, a well-established mechanism was not shown in their original reports, then Nakamura and coworkers suggested a catalytic cycle on the basis of KIE studies and stoichiometric reactions (Scheme 1.12).[63] The catalytic cycle starts through the formation of an aryliron intermediate **14** by transmetalation from the aryl Grignard reagent to the iron center. Then, a reversible chelation of the iron center by the pyridine takes place followed by an irreversible C–H metalation with synergistic elimination of an arene *via* σ-bond metathesis. Next, the cyclometalated species **16** undergoes a reductive elimination with the assistance of DCIB to produce the desired arylated product **13**, isobutene and dichloroiron species. Finally, a transmetalation between dichloroiron species **17** and the Grignard reagent takes place to regenerate the active catalyst **14**.



Scheme 1.12. Catalytic cycle of the oxidative iron-catalyzed C–H arylation.

Later the introduction of bidentate directing groups allowed for the challenging iron-catalyzed C(sp^3) –H activation expanding the scope beyond oxidative arylations with organometallic reagents (Scheme 1.13a).[65] After optimization they discovered that 8-aminoquinoline directing group was optimal which was initially introduced by Daugulis for palladium-catalyzed C–H activations.[66] The KIE study and priority for terminal methyl group over internal methylene groups suggested an inner-sphere C–H activation process rather than a radical pathway. A biologically compatible triazole directing group was developed by Ackermann group which were effective for iron-catalyzed C(sp^3)–H and C(sp^2)–H arylations (Scheme 1.13b).[67]

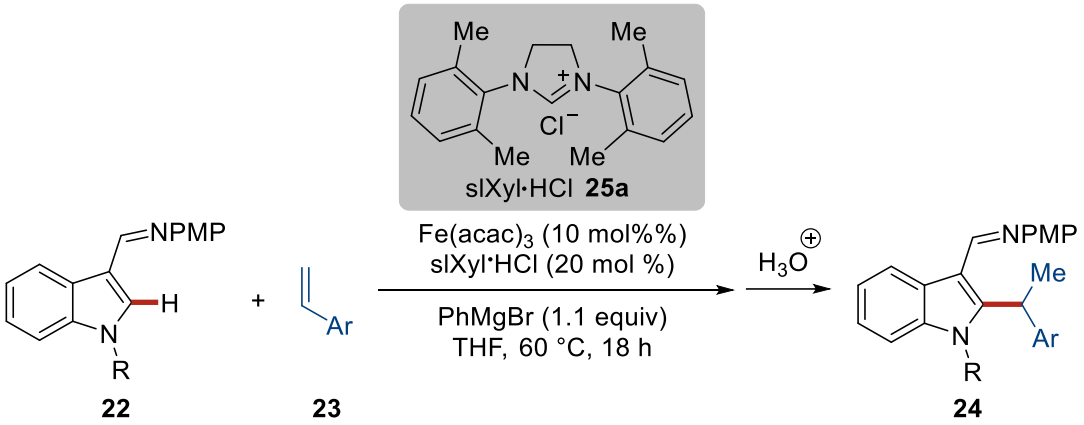


Scheme 1.13. Bidentate directing group enabled Iron-catalyzed C(sp^3)–H arylation.

After those pioneering studies, under the assistance of bidentate directing groups further important progress were realized by the research groups of Nakamura, Ackermann and Cook, among others. Thus, C–H alkylations with alkyl halides, alkenes, alkyl tosylates or Grignard reagents became available.[68] Alkynyl bromides were used for the preparation of the alkynylated product under iron-catalysis.[69] *N*-chloroamines proved to be a good aminating reagents.[70] Organoboron reagents proved viable for C–H alkenylations and arylations.[71] Various annulations with alkynes and allenes were reported to deliver

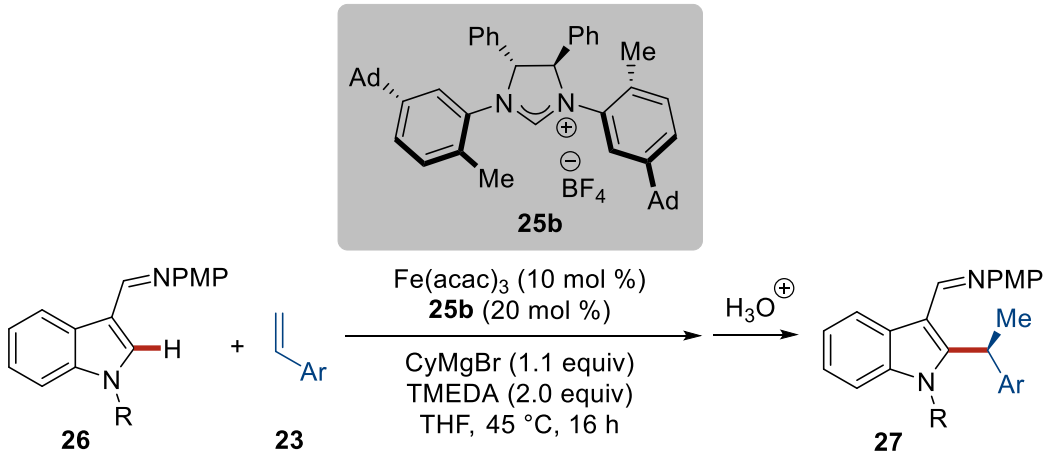
heteroarenes in the presence of iron catalyst.[72] C(sp^3)–H and C(sp^2)–H methylations were also achieved.[73]

Yoshikai reported an iron-catalyzed C–H activation in which a rare branched product **24** was formed enabled by a modification of the N-heterocyclic carbene scaffold **25** (Scheme 1.14). Alkynes were also suitable coupling partner after a slight modification of the reaction conditions.[74]



Scheme 1.14. Iron-catalyzed hydroarylation of styrenes.

The very first highly enantioselective iron-catalyzed C–H activation was realized by Ackermann and coworkers (Scheme 1.15a).[75] Shortly afterwards an asymmetric arylation of ferrocene was reported by Butenschoen,[76] giving the planar-chiral product in moderate enantiomeric excess (Scheme 1.15b).

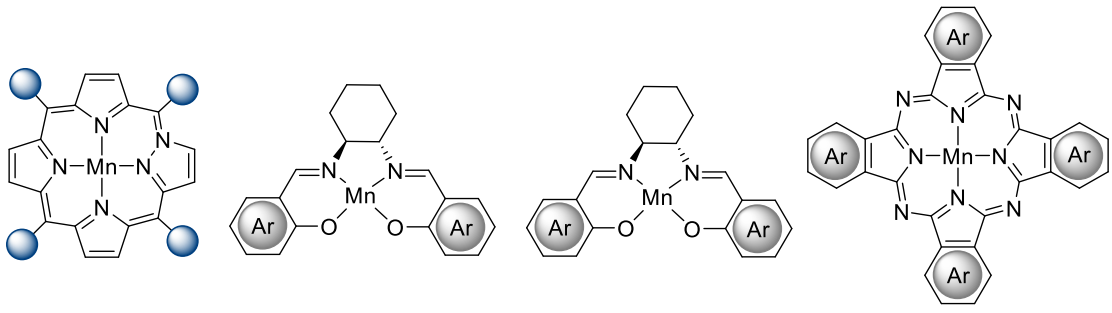


Scheme 1.15. Enantioselective iron-catalyzed C–H alkylation.

1.3 Manganese-catalyzed C–H Activations

In the last few decades, significant attention has been paid to the development of sustainable and economic strategies for molecular synthesis. Despite significant advances, expensive transition metals, are predominantly needed to gain high efficiency, such as palladium, rhodium, ruthenium, and iridium complexes.[24b, 24c, 24g] Recent progress in this fast developing arena suggested the use of earth-abundant 3d transition metal complexes as catalysts in C–H activation.[24a, 24d]

Manganese is the third most abundant transition metal just after iron, titanium and the twelfth most abundant element on earth.[39] In addition, it represents an essential trace element in the human body, with manganese cores served as an assistance factor.[77] Therefore, it is promising to utilize it as a catalyst due to its low price, availability and low toxicity.[78] The function of manganese in many enzymes inspired chemists to design ligands (Scheme 1.16), which can realize similar transformations accomplishing the C–H functionalization by outer–sphere mechanisms for a variety of transformations.[79]



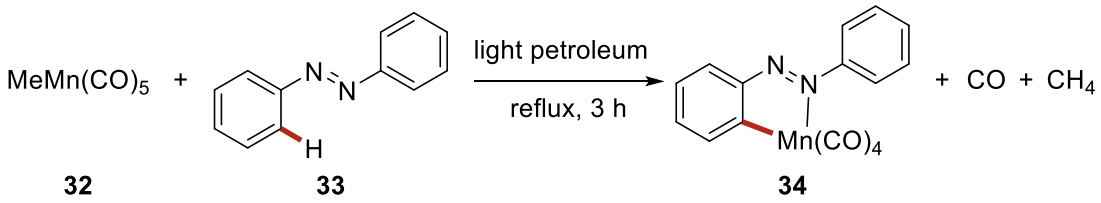
28 **29** **30** **31**

Scheme 1.16. Typical manganese complexes **28**-**31** for C–H functionalizations.

This chapter will focus on the manganese-catalyzed reactions under chelation assistance. There are two parts in this chapter: i) manganese(I)-catalyzed C–H functionalization, ii) low-valent manganese(II)-catalyzed C–H functionalizations.

1.3.1 Manganese(I)-catalyzed C–H Functionalization

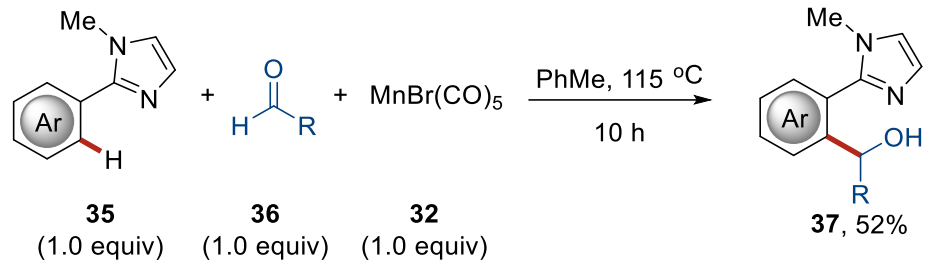
The discovery of metal catalyzed C–H bond cleavage is often inspired by the stoichiometric investigations with metal complexes. The first manganese-catalyzed C–H activation traces back to the synthesis of the manganese complex **34** from [$MnMe(CO)_5$] **32** through a C–H scission event, reported by Stone and Bruce in 1970 (Scheme 1.17).[80] The engagement of manganese(I) in the C–H activation was subsequently confirmed as various well-defined manganacycles were reported by different groups respectively, such as Woodgate[81] and Liebeskind[82] among others.



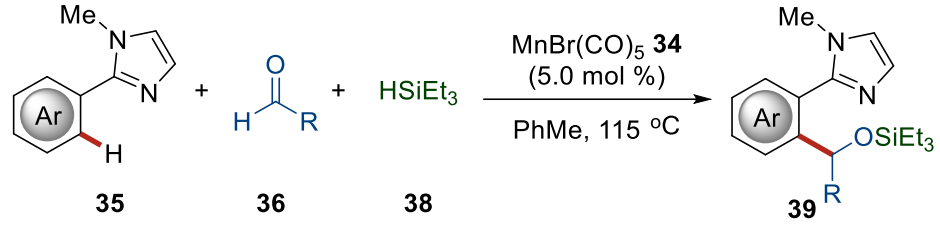
Scheme 1.17. Stoichiometric manganese-mediated C–H activation.

In 2007, the first catalytic manganese(I)-catalyzed C–H activation was achieved by Kuninobu and Takai.[83] They initiated the exploration by the stoichiometric C–H bond activation and insertion into aldehyde **36** with the manganese complex [$MnBr(CO)_5$]. After the reaction mixture was heated for 10 hours the desired alcohol **37** was obtained in 52% yield (Scheme 1.18a). Despite the fact that the stoichiometric C–H bond scission and insertion of aldehyde proceeded smoothly with [$MnBr(CO)_5$], only trace amount of alcohol **37** was produced with catalytic amounts of the manganese complex **32**. After optimization, triethylsilane **38** was found to be essential for regenerating the catalyst (Scheme 1.18b). A probable catalytic cycle was put forward based on mechanistic studies (Scheme 1.19). The catalytic cycle was initiated by the formation of a five-membered manganacycle **40** followed by the insertion into polar C=O bond to form the seven-membered manganese complex **41**. Finally, the silylethers **39** are formed *via* release of H_2 and regeneration of the manganese(I) catalyst by the action of Et_3SiH **38**.

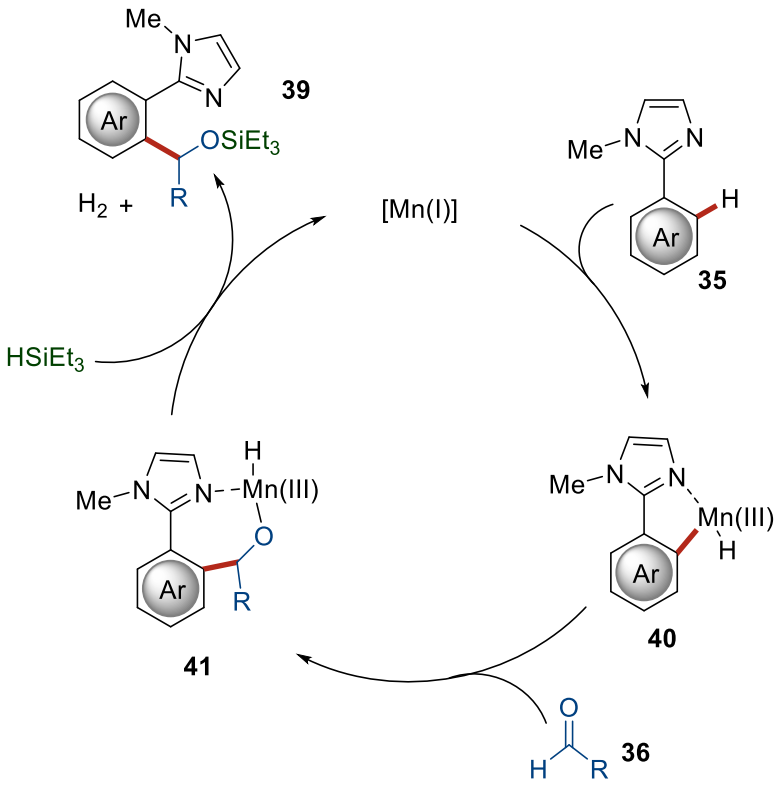
a) stoichiometric reaction



b) catalytic reaction

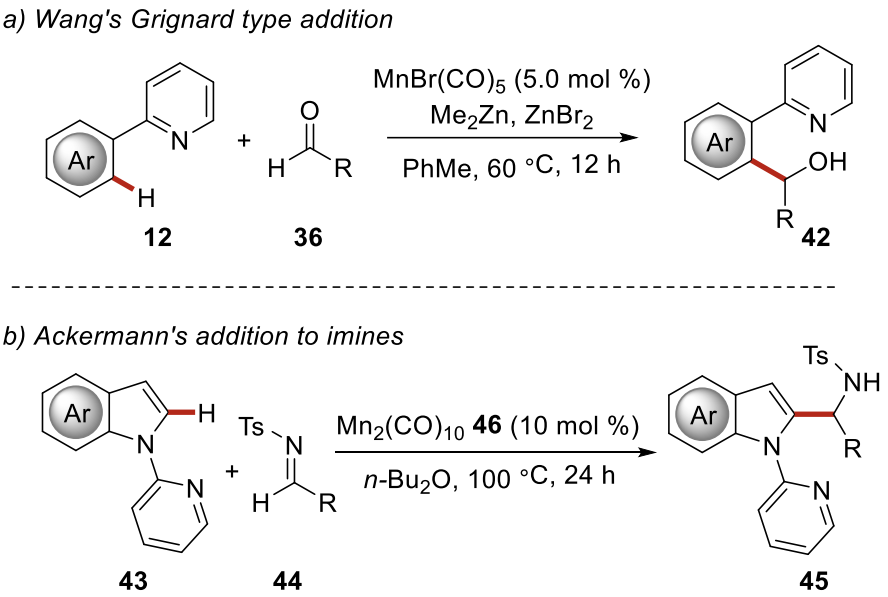


Scheme 1.18. Manganese(I)-catalyzed C–H addition to aldehydes **36**.



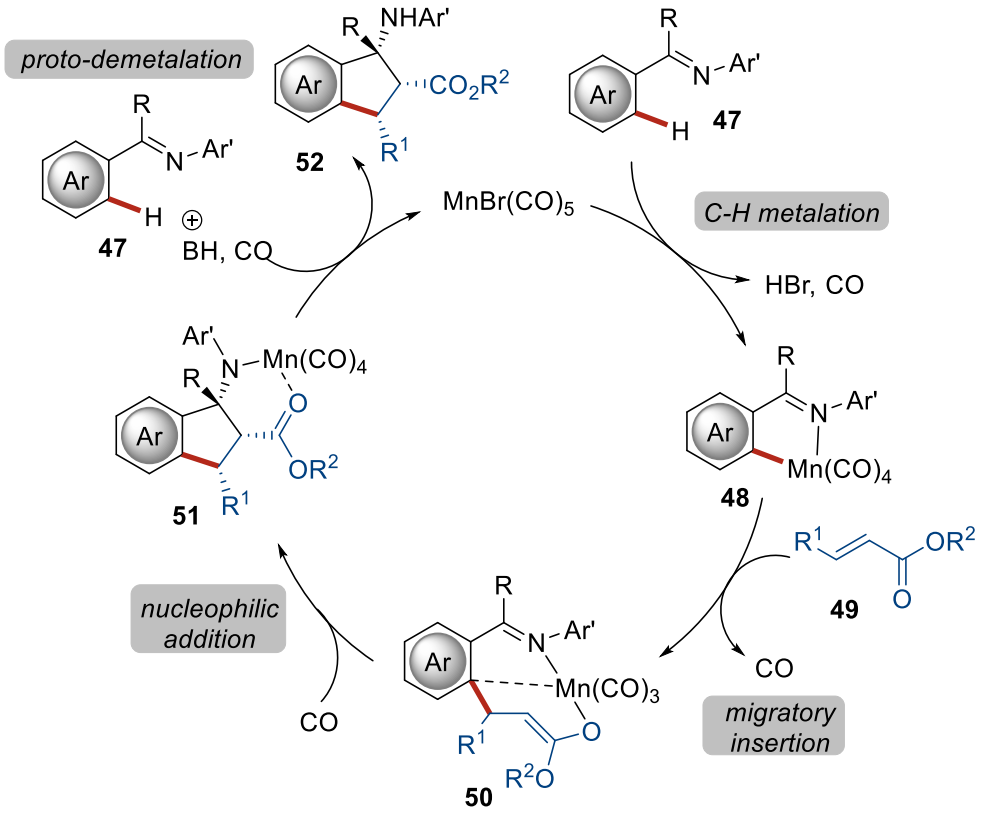
Scheme 1.19. Proposed catalytic cycle for manganese(I)-catalyzed C–H addition to aldehydes **36**.

In 2015, Wang developed a manganese-catalyzed Grignard-type nucleophilic addition of C(sp^2)–H bonds to aldehydes to access secondary alcohols (Scheme 1.20a),[84] which circumvents the limitation of previous rhodium and palladium catalytic systems. During the mechanistic studies, the authors found that [$MnMe(CO)_5$] was an effective catalyst. Nitriles were also viable coupling partners to give ketones under this reaction. Later, Ackermann and Wang extended this kind nucleophilic transformation, as attack to C=Het double bond led to functionalized amines (Scheme 1.20b).[85]

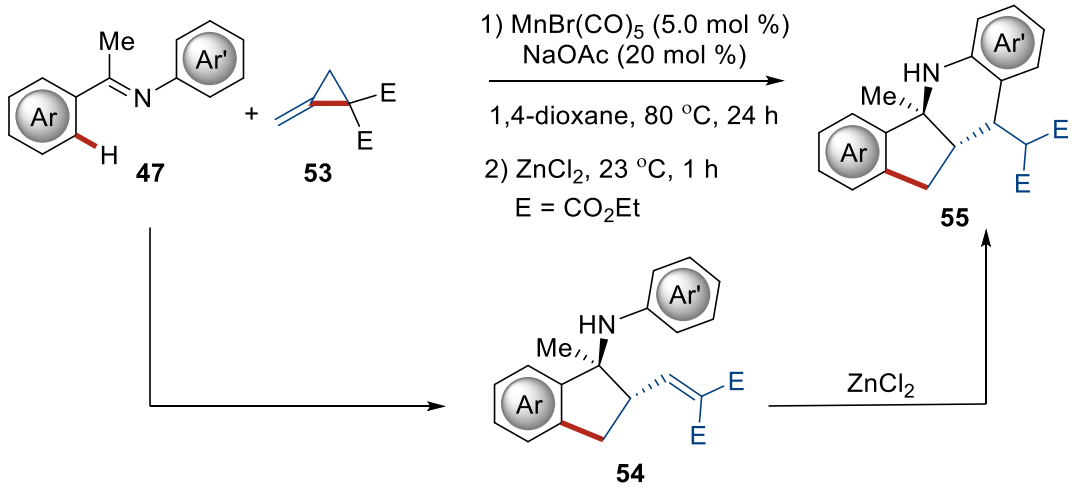


Scheme 1.20. Manganese-catalyzed nucleophilic addition.

The extension of these C–H addition strategies from polar C=Het multiple bonds to nonpolar C=C double bonds was accomplished by Wang and co-workers.[86] The addition reaction showed a broad substrate scope, good functional group tolerance, and complete mono-selectivity. Ketimines **47** are also good substrates to form five-membered manganacycle **48**. Ackermann's group found an intramolecular nucleophile attack can occur to furnish useful *β*-amino acids **52** after the insertion of acrylate **49** to the complex **48** (Scheme 1.21).[87] Using the same strategy, methylenecyclopropanes **53** (MCPs) containing electron-withdrawing groups were employed in the manganese-catalyzed C–H activation. The intramolecular nucleophile addition followed by zinc-mediated hydroarylation of the alkene **54** provided the desired product **55** (Scheme 1.22).[88]

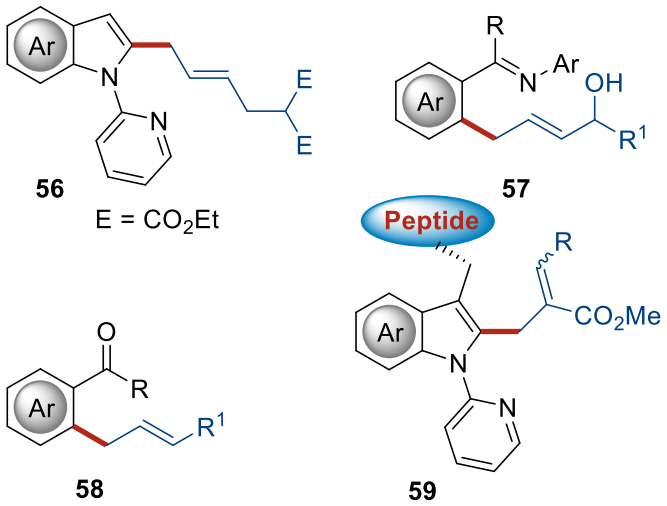


Scheme 1.21. Mechanism for the synthesis of *β*-amino acids.



Scheme 1.22. C–H/C–C activation with MCP catalyzed by Manganese(I).

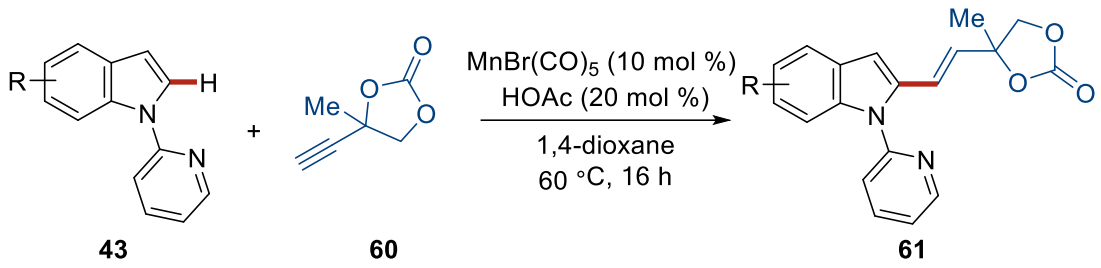
Alkenes with leaving groups are also good coupling partners in the manganese-catalyzed C–H activations. Thus, alkenes with different leaving groups were designed by Ackermann for the unprecedented allylations on different functional molecules,[89] remarkably this manifold was used for the diversification of peptides[90] (Scheme 1.23).



Scheme 1.23. Products derived by manganese(I)-catalyzed C–H allylation.

Alkynes are very important synthons widely used in the synthesis of high-value products, showed high reactivity towards manganese-catalyzed C–H activation. The first use of catalytic amounts of Brønsted acids in manganese-catalyzed C–H activation enabling chemoselective hydroarylations was achieved by Ackermann, which is fully tolerant of *β*-O leaving groups (Scheme 1.24).[91] At the same time, indoles were successfully allenated by alkynes bearing a leaving group in the presence of $[MnBr(CO)_5]$. Optically active multisubstituted allenes were prepared with high enantiomeric excess through a highly efficient chirality transfer.[92] A general and scalable strategy was developed to regioselectively synthesize *N*-heterocycles by using alkyne coupling partners with ketimine and a simple manganese-based catalyst. This procedure overcomes the previous limitations of C–H activation with unsymmetrical alkyne coupling partners and was also demonstrated to be effective with unpolarized aliphatic alkynes, with the desired products obtained with complete regioselectivity.[93] The manganese-catalyzed C–H alkenylation with terminal alkynes was realized by Wang, highlighting not only a practical catalytic system comprised of easily available $[MnBr(CO)_5]$ and Cy_2NH but also high levels control in regio-, chemo- and stereoselectivity.[94]

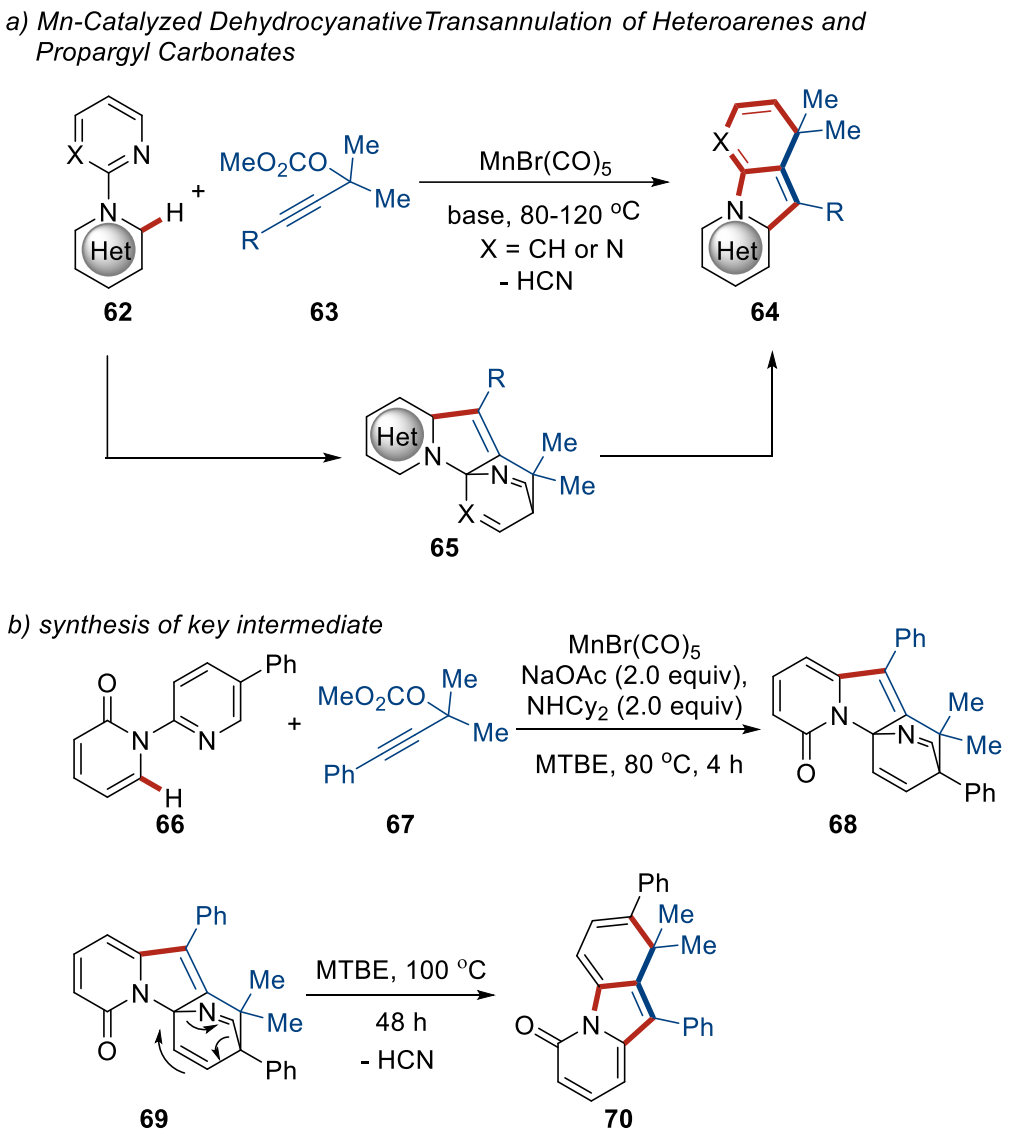
Ackermann's hydroarylation



43 **60** **61**

Scheme 1.24. Mn(I) catalyzed hydroarylation of alkynes.

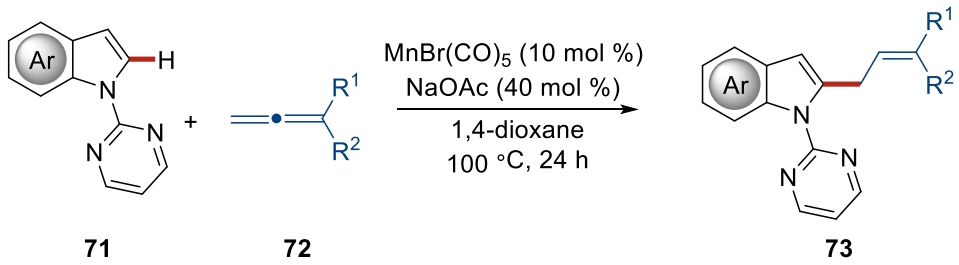
Domino reactions *via* C–H allenylation, Diels–Alder (DA) reaction, and retro Diels–Alder reaction pathway were realized by manganese catalysis in Ackermann and Li group respectively (Scheme 1.25).[95] To shed light into this cascade process, a stable DA adduct **68** was isolated after the coupling of substrates **66** and **67** at a lower temperature, which proved to be an intermediate en route to the final product **70** *via* a retro-Diels-Alder event with extrusion of HCN.



scheme 1.25. Manganese(I) catalyzed domino reactions.

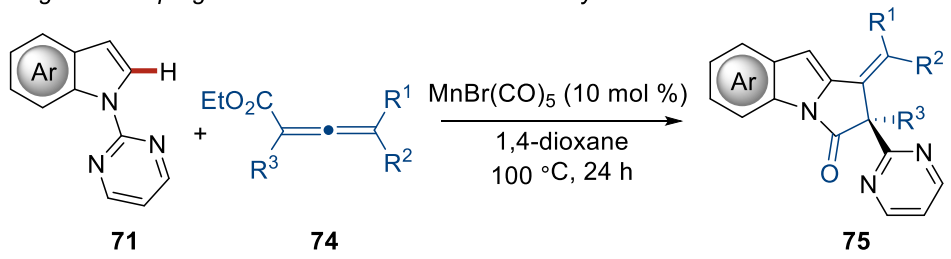
With the great success of allenes in the construction of complex compounds, it represents an appealing partner in manganese-catalyzed C–H functionalization. In 2017, allylation of indole was achieved by Wang's group using 1,1-dimethylallene (Scheme 1.26a).[96] A manganese(I)-catalyzed region- and stereoselective 1,2-diheteroarylation of allenes was discovered by Wang and Rueping respectively,[97] which features the combination of C–H hydroarylation along with a Smiles rearrangement (Scheme 1.26 b). In the same year, polycyclization enabled by manganese(I)/silver(I) relay catalysis through one-pot manganese-catalyzed C–H allylation and silver-catalyzed Pavarov reaction was established by Wang (Scheme 1.26c).[98]

a) Wang's allylation with allenes



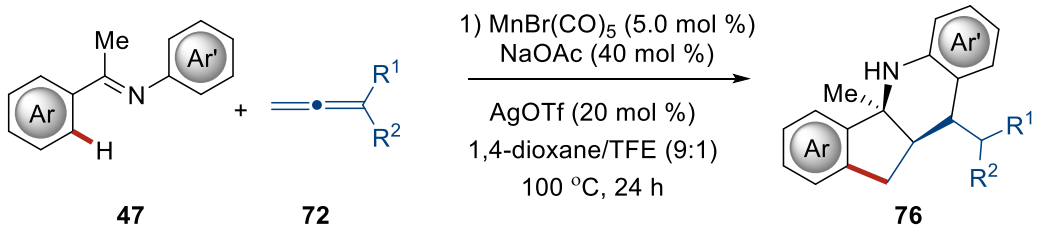
71 **72** **73**

b) Wang and Rueping's cascade C—H activation and cyclization



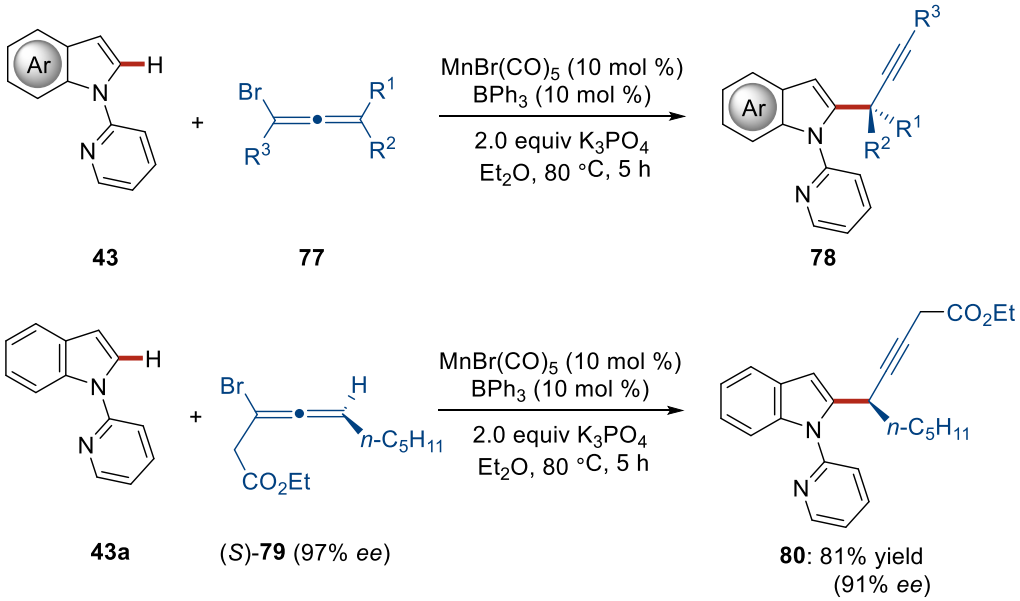
71 **74** **75**

c) Wang's cascade C—H activation and Povarov reaction



47 **72** **76**

Scheme 1.26. Manganese(I) catalyzed transformations with allenes **72** and **74**.



43 **77** **78**

43a (*S*)-**79** (97% *ee*) **80**: 81% yield (91% *ee*)

Scheme 1.27. Manganese(I) catalyzed C–H propargylation with bromoallenes **77** and (*S*)-**79**.

Bromoallenes were efficiently employed in direct C–H propargylations with high selectivity under the synergy of manganese(I) and a Lewis acid. The axial chirality in the bromoallene (*S*)-**79** could be successfully transferred to the central chirality at the propargylic position, a motif difficult to obtain by traditional methods (Scheme 1.27).[99] Manganese-catalyzed C–H annulation of ketimines **47** with allenes providing an approach to stereoselective synthesis of 1-aminoindanes **81** was also described.[100]

With the rapidly growing interest in the application of photochemistry in organic synthesis, a photoredox Minisci reaction with unactivated iodoalkanes catalyzed by $Mn_2(CO)_{10}$ was developed, which was successfully employed in the late-stage functionalization of complex drugs.[101] Manganese-mediated photochemical generation of aryl radicals was likewise exploited for the direct C–H arylations of (het)arenes (Scheme 1.28).[102]

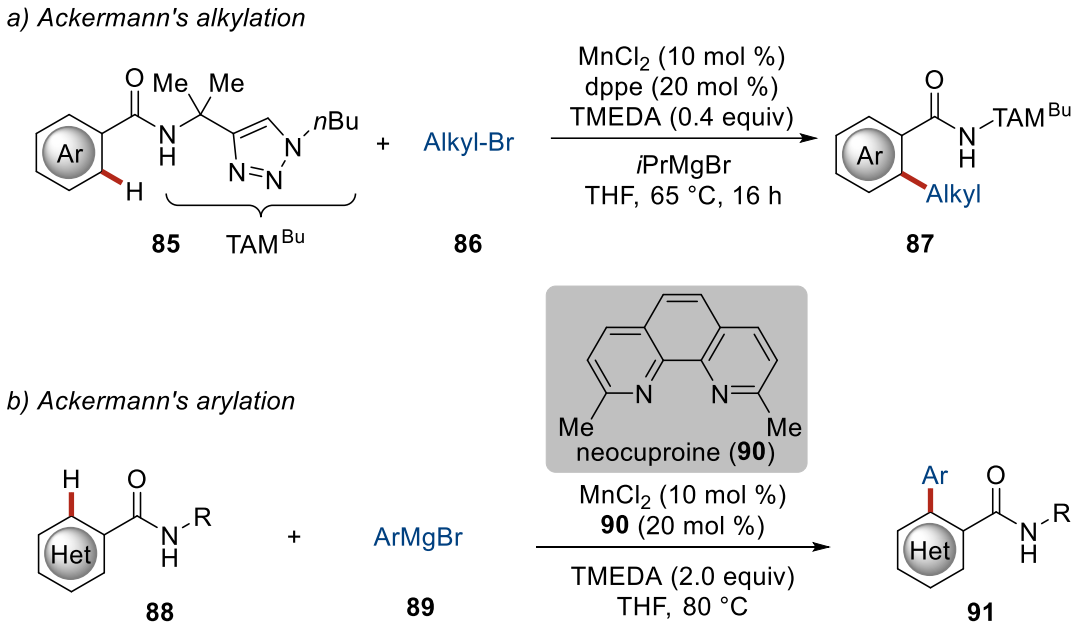
Scheme 1.28. Visible-light and manganese-catalyzed reactions.

Manganese(I) catalysis displayed great power in meaningful cyanation and aminocarboxylation.[103] Lastly, challenging C–H/C–F functionalization could be accomplished by manganese(I). It is noteworthy that C–F bonds are generally relatively inert due to the high bond energy and the reluctance of organofluorine compounds to coordinate to metal centers.[104] Despite these challenges, C–H/C–F activation has been successfully employed in the manganese-catalyzed perfluoroallylation and monofluoroalkenylation.[105]

1.3.2 Low-valent Manganese(II)-catalyzed C–H Functionalization

Despite a plethora of transformations enabled by manganese(I)-catalyzed C–H functionalization, these methods are restricted to the addition of double bonds. The Ackermann group reported the first low-valent $MnCl_2$-catalyzed C–H alkylation with alkyl

bromides **86** (Scheme 1.29a). The unprecedented manganese(II)-catalyzed C–H cleavage occurred without the use of expensive phosphine ligands in the absence of zinc, providing versatile access to alkylated benzamides through assistance of the removable TAM (triazolyl-methyl) group (Scheme 1.29a).[106] Versatile manganese-catalyzed C–H arylations on synthetically meaningful pyridines were accomplished with sustainable $MnCl_2$ as the catalyst as disclosed one year later.[107] The oxidative C–H functionalization proved viable with a user-friendly and safe continuous flow setup.



Scheme 1.29. Low-valent manganese(II)-catalyzed C–H functionalization.

Later, Nakamura reported a manganese-catalyzed C–H methylation, using MeMgBr, a catalytic amount of $MnCl_2 \cdot 2LiCl$, and an organic dihalide as the oxidant (Scheme 1.29b).[108]

1.4 Rhodium-catalyzed C–H Activation

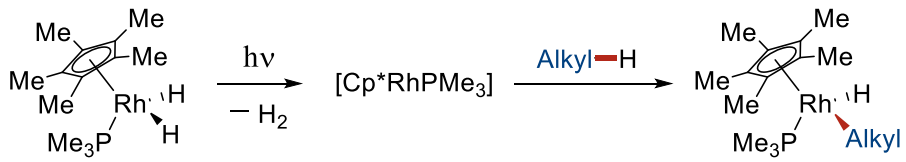
As the formation of C–C bond is the most important objective within synthetic chemistry, different types of coupling reactions have been developed to achieve the formation of C–C bonds. Most of these transformations proceed in the presence of palladium. Many new reactions catalyzed by rhodium complexes show great potential.[109] In addition, rhodium often shuttles between rhodium(I) and rhodium(III) oxidation states in the catalytic cycle

that does not require organometallic reagents. Cycloadditions, hydroacylation reactions, and allylic functionalization are representative examples for rhodium-catalyzed C–C bonds formations.[110] Rhodium-derived complexes also provide a powerful tool for the asymmetric hydrogenation of prochiral unsaturated compounds to give optically pure alcohols, amines and other hydrocarbons.[111]

The utility of C–H activation in lieu of substrate prefunctionalization has featured a tantalizing alternative to classical cross-coupling reactions but the challenges ahead are the selectivity and reactivity associated with otherwise inert C–H bonds. Literature reports on selectivity based on steric effects, acidity, and electronic and directing group effects are now numerous. The designs of directing groups and ligands allow the rhodium to conduct the cleavage of inert C–H bond efficiently with good selectivity. For this part, rhodium-catalyzed C–H activation will be divided into two parts: (i) rhodium-catalyzed inner-sphere C–H activation (ii) rhodaelectro-catalyzed C–H activation.

1.4.1 Rh-catalyzed Inner-sphere C–H Activation

Due to the difficulty to control the selectivity, simple benzene and linear hydrocarbons were ideal model substrates to explore the process of C–H cleavage in the early stages of C–H activation. In 1984, Bergman and Jones found that photolysis of Cp*Rh(PMe_3)H_2 **96** in a hydrocarbon solvent led to the loss of H_2 and the C–H activation of solvent.[112] Unfortunately, the 16-electron Cp*Rh(PMe_3) **97** viewed to be accountable for hydrocarbon oxidative addition was not detectable (Scheme 1.30).

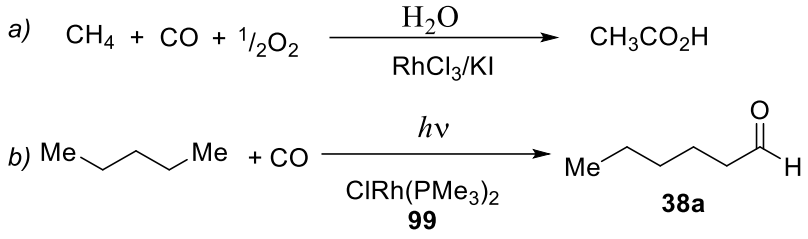


96 **97** **98**

Scheme 1.30. Early study of C–H activation by Bergman.

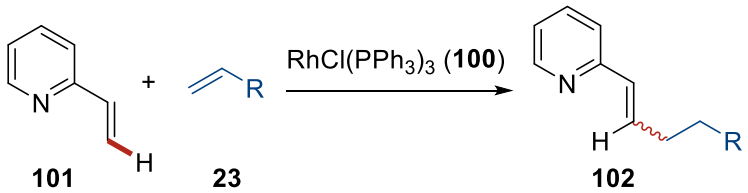
Inspired by the early rhodium-mediated C–H activation, the inert methane successfully underwent carboxylation to release acetic acid catalyzed by $RhCl_3$ under aqueous

conditions with the use of oxygen as the oxidant (Scheme 1.31a).[113] However, the yield of this process was not mentioned. Besides the alkane carboxylation, photochemical transformations of alkanes to aldehyde **38a** catalyzed by $RhCl(PMe_3)_3$ (**99**) have also been observed (Scheme 1.31b).[114] Mechanistic studies by Goldman provided evidence that the CO-dissociated species is not responsible for the C–H activation step. Goldman proposed that the principal photo-process in this reaction involves direct C–H oxidation addition to the four-coordinate rhodium(I) center to deliver a six-coordinate intermediate, which then undergoes CO insertion in the following step.[115]



Scheme 1.31. Rh(I) catalyzed transformations of hydrocarbons.

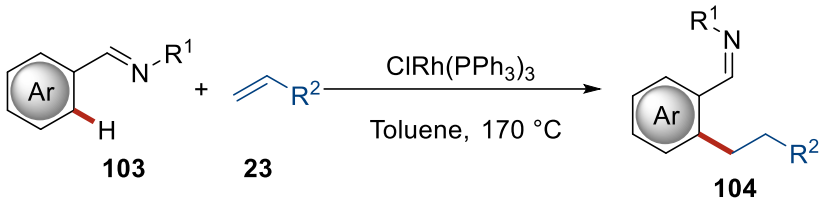
Alkynes tend to experience dimerization or polymerization in the presence rhodium complexes especially at high temperatures.[116] In the early stage of rhodium catalyzed $C(sp^2)$–H activation, alkenes are the ideal substrates for the position-selective C–H activation. In one of the earliest reports of rhodium-catalyzed C–C bond formation by C–H activation, Lim and Kang showed that pyridine functioned as a directing group to achieve C–H alkylation, albeit without tolerance of any other functional groups.[117]



Scheme 1.32. Rhodium-catalyzed C–H alkylation.

Subsequently, the imine functionality enjoyed widespread use and development in the realm of C–H bond functionalization by Rhodium (I). Specifically, $RhCl(PPh_3)_3$ (**100** Wilkinson's catalyst) was determined to be the optimal catalyst for this transformation.[118] Furthermore, the overalkylation that plagued aryl ketone alkylation could be avoided in this

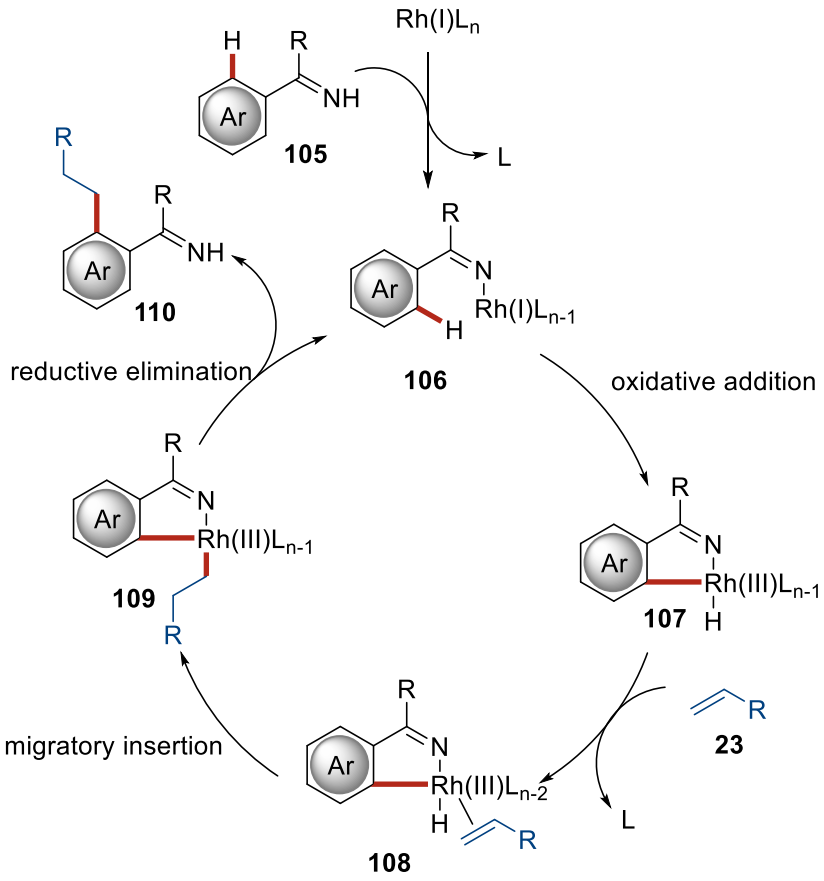
case. It was further discovered by Jun and co-workers that imines **103** were capable to undergo alkylation to generate the corresponding imines **104** (Scheme 1.33).[119]



103 **23** **104**

Scheme 1.33. Imine directed alkylation.

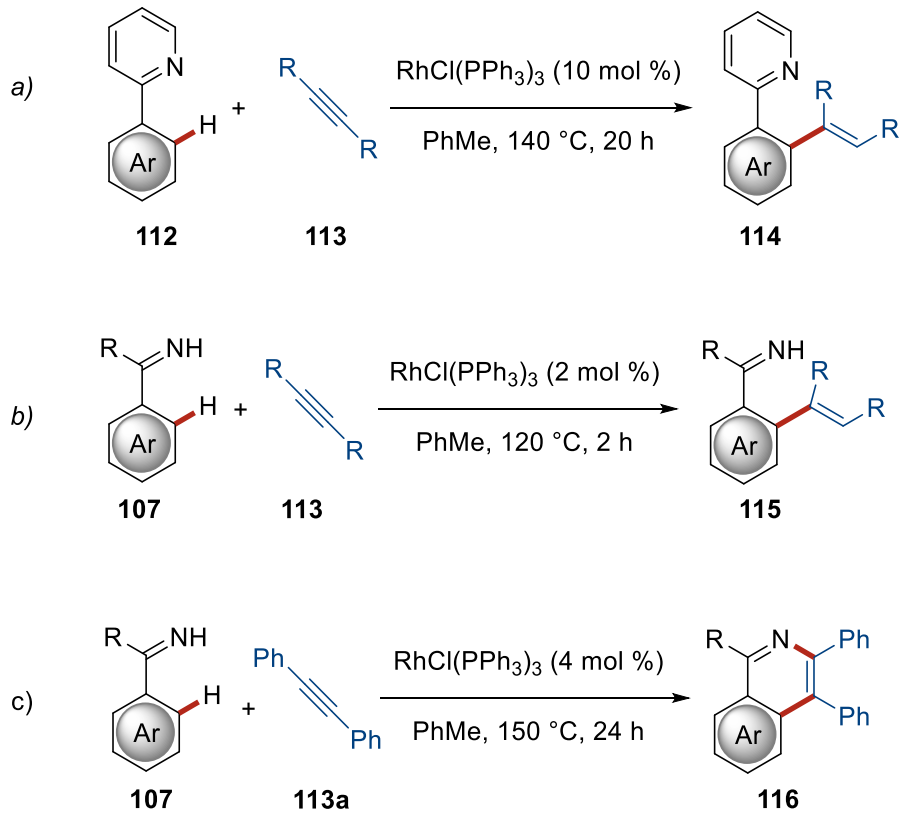
The widely accepted mechanism for chelation-assisted C–H bond alkylation catalyzed by rhodium(I) demonstrated in Scheme 1.34. Initial coordination of rhodium by the chelating heteroatom of imine **105** followed by facile C–H bond activation gives metallacyclic intermediate **107**. Dissociation of a phosphine ligand, followed by olefin binding and hydride insertion, gives **108**. Reductive elimination of **109** produces the product **110** and closes the catalytic cycle.[120] The reductive elimination step has been demonstrated to be rate limiting in C–H alkylation reactions.



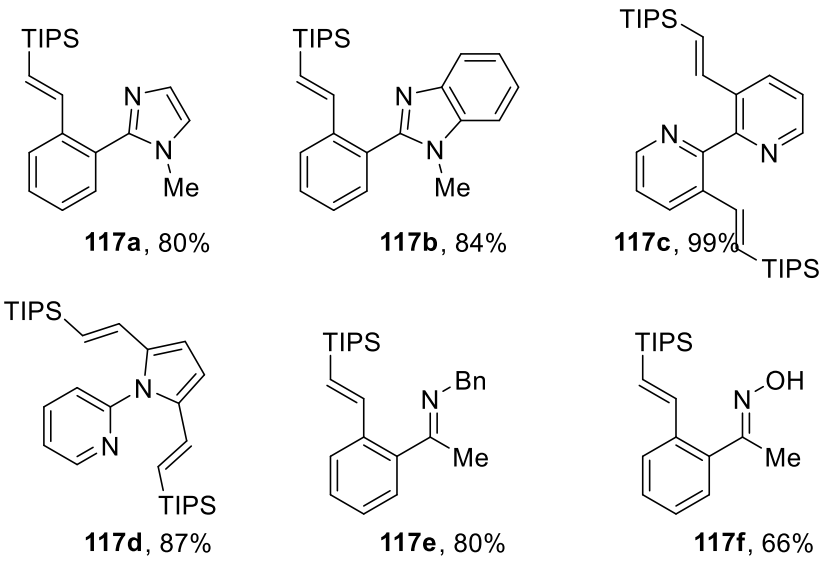
Scheme 1.34. Mechanism for rhodium(I) catalyzed alkylation.

While the hydroarylation of olefins has seen broad success using rhodium(I)-catalyzed chelation-assisted methods, the tendency of alkynes, in particular terminal alkynes, to undergo rhodium-catalyzed alkyne dimerization or trimerization has made their use problematic.[116] Internal alkynes, much like internal olefins, are often unreactive in C–H bond functionalization reactions. Under assistance of the reliable mechanism, several groups have successfully developed heteroatom-chelated vinylation methods. Lim and Kang reported the first example of chelation-assisted hydroarylation of an internal alkyne **113** realizing the *ortho*-alkenylation of 2-phenylpyridines by using Wilkinson's catalyst (Scheme 1.35a).[121] The scope of alkyne was limited primarily to internal and symmetrical alkynes. Terminal alkynes generated mainly polymeric materials,[116] and unsymmetrical alkynes, such as 2-hepyne, led to regioisomeric mixtures.[122] Internal alkynes were smoothly used for the alkenylation with the assistance of imine using $RhCl(PPh_3)_3$ as the catalyst (Scheme 1.35b). It was also discovered by Jun that increased temperatures and

prolonged reaction times ultimately produced isoquinoline products **116** in nearly quantitative amounts (Scheme 1.35c).[123] When triisopropylsilylacetylene is used as the coupling partner, the substrate scope of the alkenylation in the presence of a $RhCl(PPh_3)_3$ catalyst was expanded to imidazole and benzimidazole directing groups (Scheme 1.36).[122]

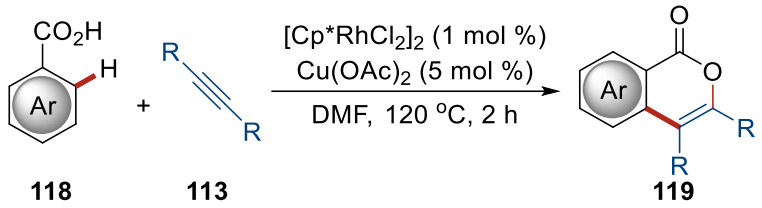


Scheme 1.35. Rh(I) catalyzed C–H alkenylation.



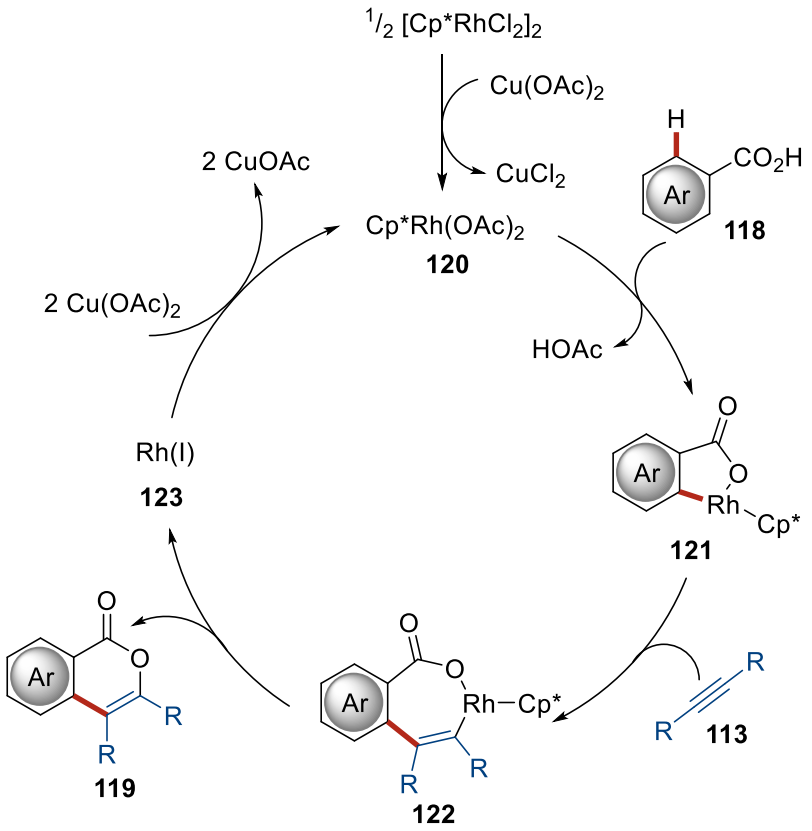
Scheme 1.36. Alkenylation by using triisopropylsilylacetylene.

Carboxylate groups can also function as effective directing groups in oxidative coupling of benzoic acids and alkynes using a rhodium(III)-copper(II) co-catalytic system, where the copper(II) serves to oxidize the rhodium catalyst in order to reinitiate the catalytic cycle (Scheme 1.37). A series of isocoumarin derivatives **119** was thereby synthesized from benzoic acids and internal alkynes using $[Cp^*RhCl_2]_2$ as the catalyst.[124] Both electron-deficient and electron-rich benzoic acids were suitable substrates, and alkyl or aryl substituted alkynes were used.



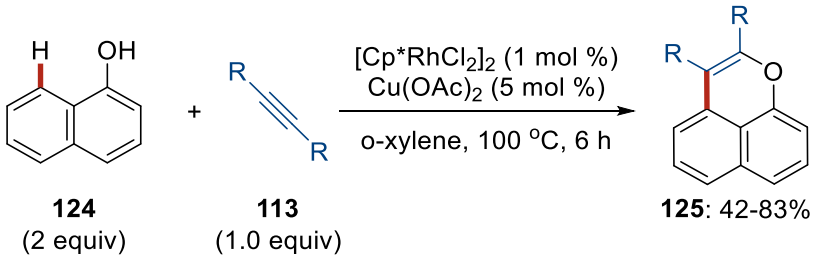
Scheme 1.37. Oxidative coupling of benzoic acids with alkynes.

A plausible mechanism for the reaction of benzoic acid **118** with alkyne **113** is shown in Scheme 1.38. Coordination of the carboxylate oxygen to Cp*Rh(III) $(OAc)_2$ **120** is followed by *ortho* rhodation to form a rhodacycle intermediate **121**. Afterwards alkyne insertion and reductive elimination occurs to produce isocoumarin **119**. The resulting rhodium(I) species **123** is oxidized in the presence of the copper cocatalyst to regenerate Rh(III)Cp*$(OAc)_2$.



Scheme 1.38. Plausible mechanism for rhodium-catalyzed isocoumarin synthesis.

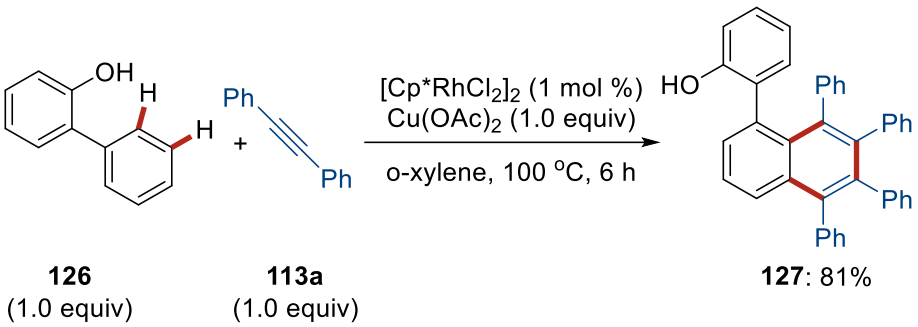
Encouraged by the significant breakthrough of the carboxylate-assisted C–H activation reported by Miura, the reactions of 1-naphthols (**124**) (Scheme 1.39) and analogues including 4-hydroxycoumarin, quinolinone and 9-phenylxanthen-9-ol were discovered to undergo peri C–H bond cleavage to produce fused pyran derivatives.[125]



Scheme 1.39. The coupling of 1-naphthols with alkynes.

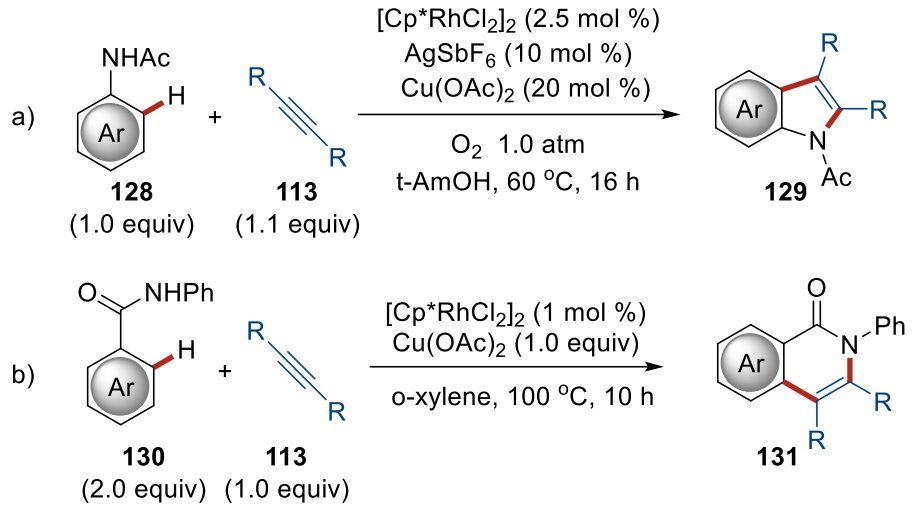
In contrast to the couplings described above (Scheme 1.39), treatment of equimolar amounts of 2-phenylphenol **126**, diphenylacetylene, $Cu(OAc)_2 \cdot H_2O$, and KI in the presence

of $[Cp^*RhCl_2]_2$ (1 mol%) selectively furnished 5-(2-hydroxyphenyl)-1,2,3,4-tetraphenyl-naphthalene **127** in 81% yield (Scheme 1.40).[125]



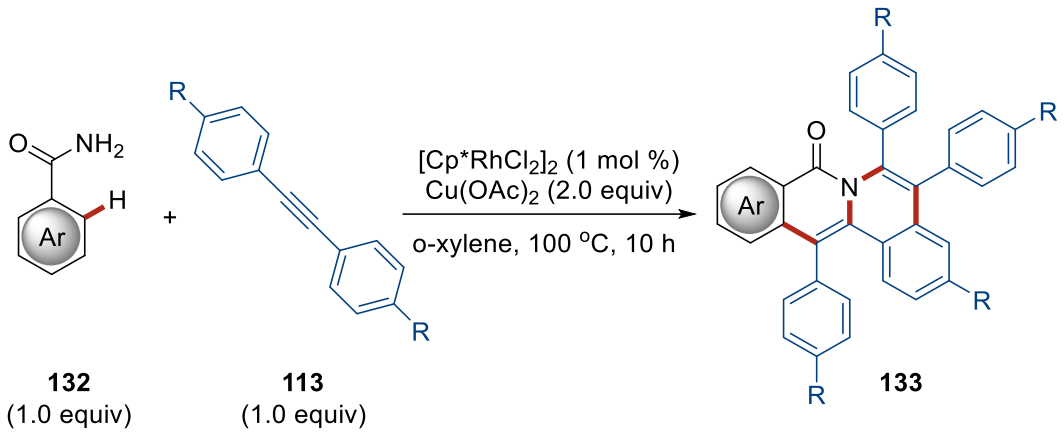
Scheme 1.40. The coupling of 2-phenylphenol with diphenylacetylene.

In 2008, Fagnou found that alkynes oxidatively coupled with acetanilides **128** by using rhodium(III) catalyst and $Cu(OAc)_2$ as the oxidant through *ortho* C–H bond cleavage to furnish *N*-acetylindoles **129** (Scheme 1.41a).[126] Meanwhile, Miura found that benzanilides **130**, which possess two types of cleavable *ortho* C–H bonds on aniline and benzoic acid moieties, undergo the oxidative coupling with alkynes involving the selective cleavage of the latter to produce isoquinolinone derivatives **131**.[127]



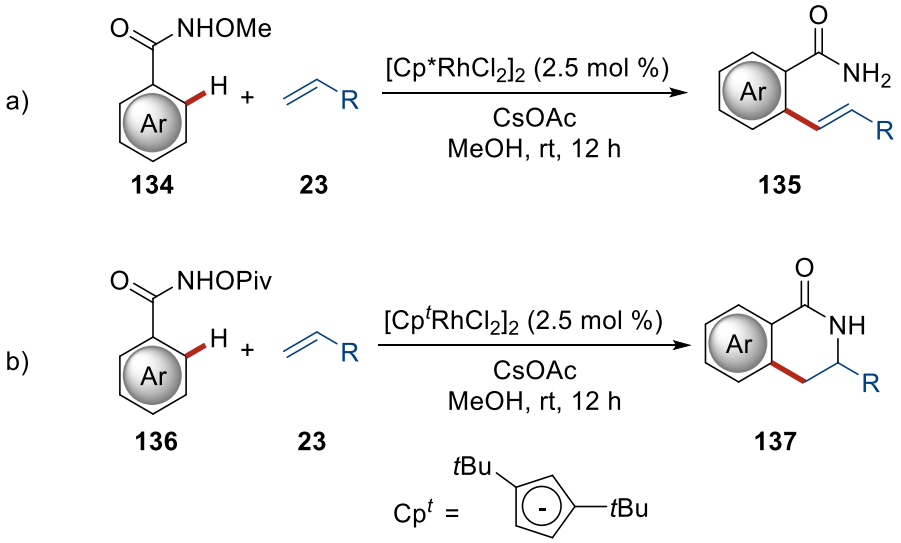
Scheme 1.41. The coupling of *N*-acylanilines with alkynes.

Under similar conditions, *N*-unsubstituted benzamides **132** undergo a cascade coupling accompanied by two C–H and two N–H bond cleavages to construct a tetracyclic dibenzoquinolizinone framework **133** (Scheme 1.42).



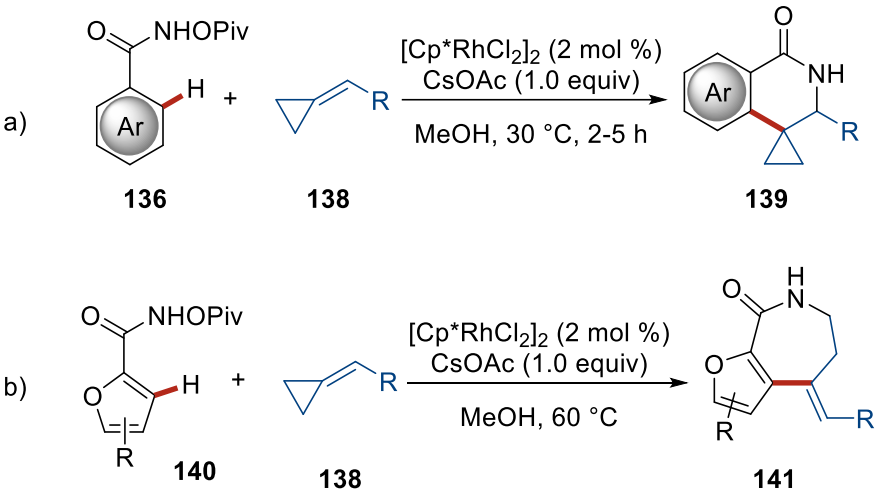
Scheme 1.42. The coupling of *N*-unsubstituted benzamides with diarylacetylenes.

In 2011, Glorius reported a rhodium-catalyzed oxidative olefination by chelation-assisted C–H activation of *N*-methoxy benzamides **134**. In this mild process, the N–O bond serves as an internal oxidant. In addition, a small modification of the substituent of the directing/oxidizing group results in the selective generation of valuable tetrahydroisoquinolinone products **135** (Scheme 1.43a).[128] After changing the Cp ligand from Cp* to much bulkier Cp^t, synthesis of dihydroisoquinolones **137** from aliphatic alkenes and *O*-pivaloyl benzhydroxamic acids **136** mediated by a rhodium precatalyst was achieved with excellent regioselectivity (Scheme 1.43b).[129]



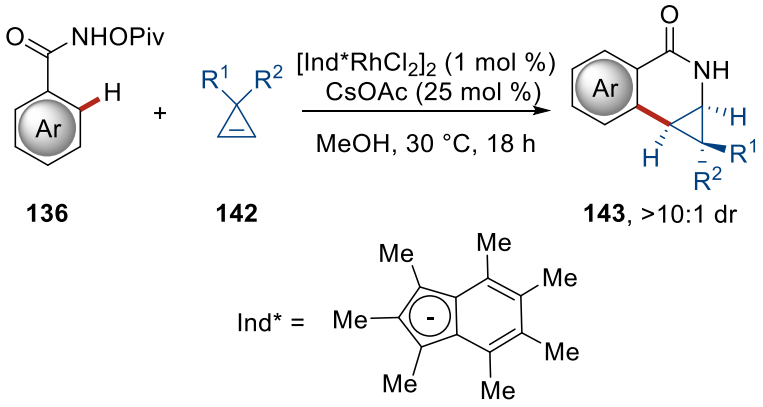
Scheme 1.43. Rhodium-catalyzed olefination and tetrahydroisoquinolinone synthesis.

Inspired by this oxidizing group, an unprecedented rhodium-catalyzed C–H activation of benzamides and methylenecyclopropanes **138** for the selective synthesis of spiro dihydroisoquinolinones **139** was reported by Cui (Scheme 1.44a).[130] Interestingly, when the furan-derived amide **140** coupled with methylenecyclopropanes under higher temperature, a furan-fused azepinone **141** was formed in high yield (Scheme 1.44b).



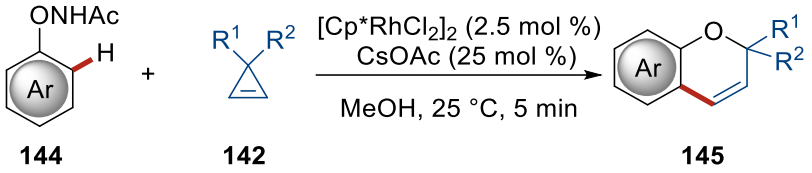
Scheme 1.44. Synthesis of spiro dihydroisoquinolinones **139** and furan-fused azepinone **141**.

Another diastereoselective coupling of arylhydroxamates **136** and cyclopropenes **142** was successfully developed by rhodium catalysis (Scheme 1.45). Through ligand development, the diastereoselectivity of this reaction was improved using a heptamethylindenyl (Ind*) ligand. In addition, the nature of the *O*-substituted ester of benzhydroxamic acid proved important for achieving high diastereoselectivity.[131]



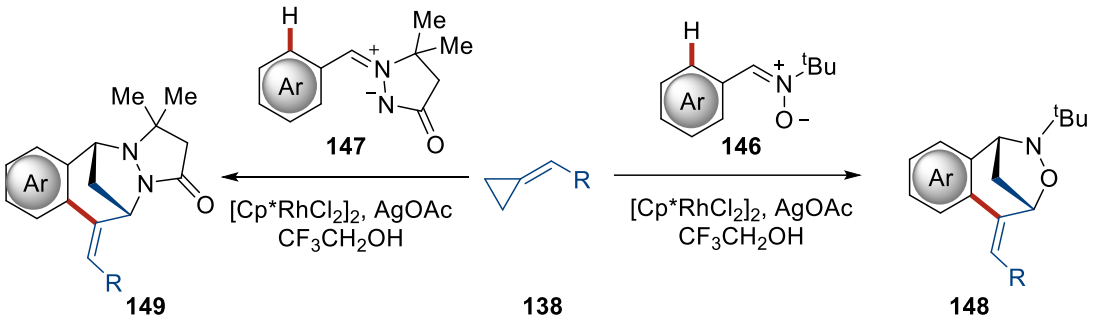
Scheme 1.45. Benzamidation of cyclopropenes *via* rhodium(III) catalyzed C–H activation.

In 2014, Wang group reported the use of cyclopropene as a three-carbon unit in rhodium(III)-catalyzed C–H bond activation.[132] An efficient rhodium(III)-catalyzed synthesis of 2*H*-chromene **145** from *N*-phenoxyacetamides **144** and cyclopropenes through C–H activation has been achieved (Scheme 1.46). The reaction proceeded at room temperature without using external oxidants.



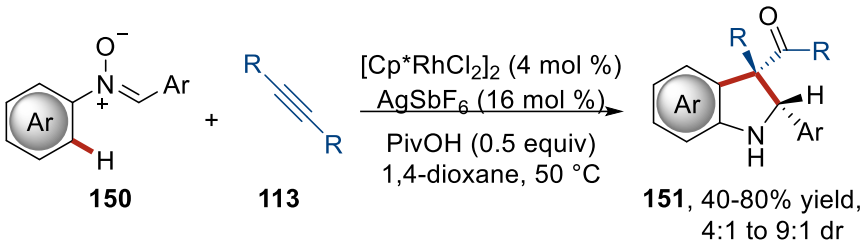
Scheme 1.46. Synthesis of 2*H*-chromene **145** from *N*-phenoxyacetamides **144** and cyclopropenes **142**.

A combination of C–H activation with ring opening of cyclopropanols by rhodium(III)-catalysis, offering an efficient route to access *β*-aryl ketones was reported by Li.[133] The reaction proceeded under mild conditions with ample scope, high regioselectivity, and excellent functional group tolerance. Both oxime ethers and *N*-pyrimidylindoles proved to be viable substrates. In 2018, Li reported rhodium(III)-catalyzed C–H activation of nitrones **146** and azomethine imines **147**, followed by a dipolar cycloaddition with alkylidenecyclopropanes **138** (ACPs) (Scheme 1.47). Taking advantage of the ring strain in ACPs, the reaction with aryl nitrones delivered bridged [3.2.1] bicyclic isoxazolidines **148**, and reaction with azomethine imines afforded bridged tricyclic pyrazolones **149** under the same conditions.[134]



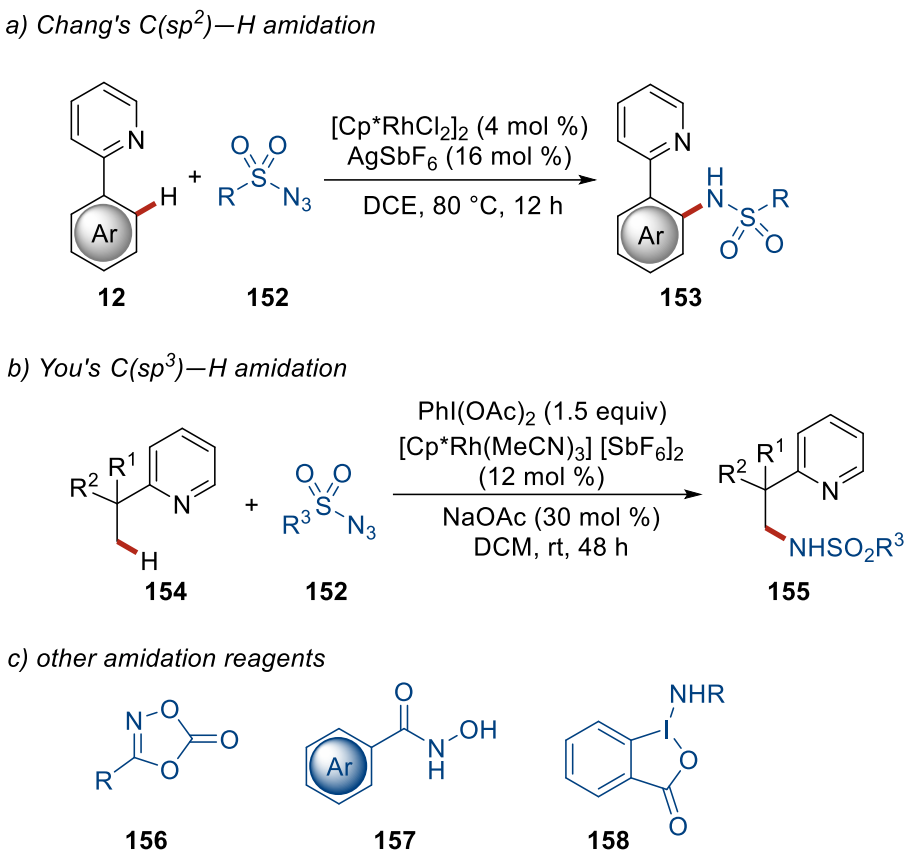
Scheme 1.47. Coupling of nitrones **146** and azomethine imines **147** with alkylidenecyclopropanes **138**.

The arylnitrones **150** were coupled with internal alkynes **113** to form indolines **151** in the presence of rhodium(III) catalyst free of external oxidants (Scheme 1.48). A dual role of the rhodium catalyst is proposed, initially enabling the C–H cleavage and *O*-atom transfer process. The cyclization worked well under mild conditions furnishing the desired products **151** with moderate to high diastereoselectivity.[135]



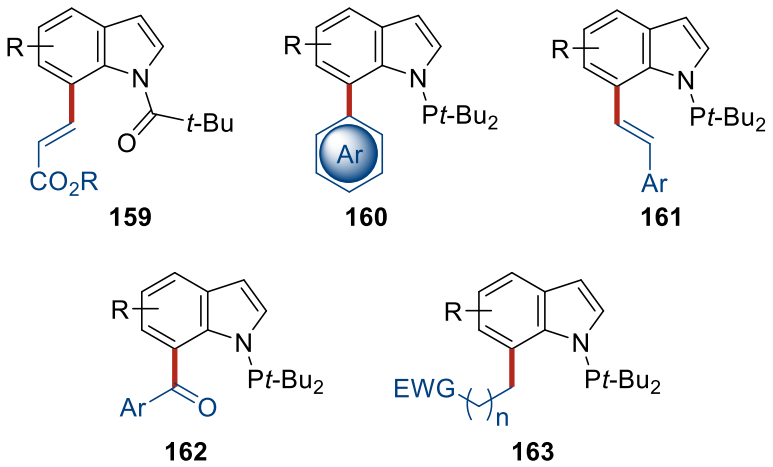
Scheme 1.48. Cyclization of arylnitrones to indolines.

In 2012, Chang and coworkers reported the first rhodium(III)-catalyzed C–H amidation reaction using sulfonyl azides as the amino source, releasing N_2 as the sole byproduct without the use of external oxidants (Scheme 1.49a).[136] A more challenging rhodium(III)-catalyzed chelation-assisted activation of unreactive C(sp^3)–H bonds has been disclosed in You's lab (Scheme 1.49b), thus providing a practical and step-economic route to 2-(pyridine-2-yl)ethanamine derivatives *via* an intermolecular amidation. In contrast to Chang's system, external oxidant $PhI(OAc)_2$ was responsible for the generation of nitrene, which undergoes subsequent migratory insertion.[137] Dioxazolone, *N*-methoxyamide and amidobenziodoxolones were also successfully developed as suitable nitrogenation sources to perform the rhodium(III)-catalyzed chelation-assisted C–H activation (Scheme 1.49c).[138]



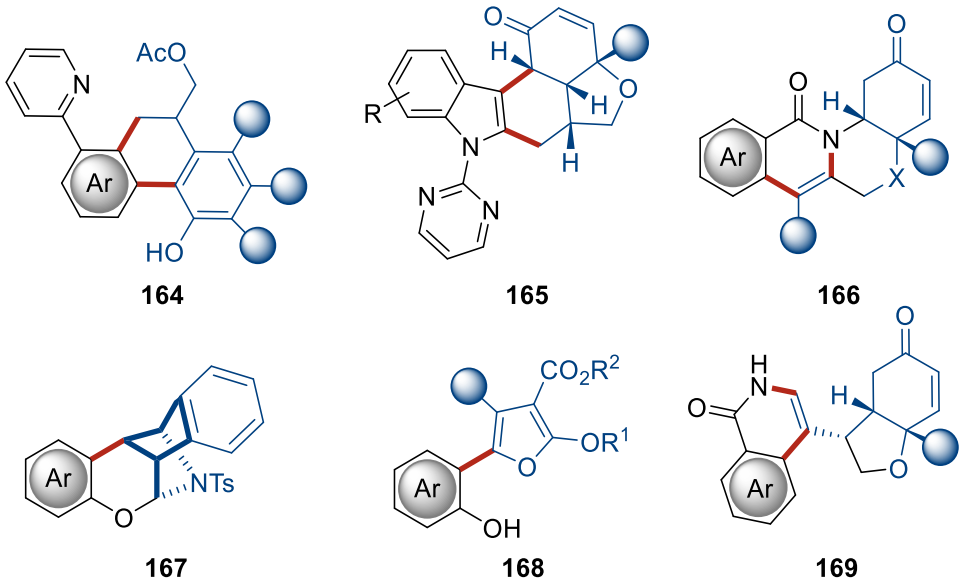
Scheme 1.49. Rhodium(III)-catalyzed C–H amidation.

Despite the plethora of C2 functionalization of indole, the selective C7 transformation of indole is scarce. Through elaborate modification of the directing groups, C7 olefination, arylation, methylation and alkylation were available in Shi's and Ma's lab (Scheme 1.50).[139]



Scheme 1.50. Products obtained *via* C7 functionalization of indole by rhodium(III).

Further important functional groups have been directly introduced to useful molecules under the assistance of rhodium catalyst, such as Br, I, CN and N_3.[140] Many structurally complex molecules become available *via* strategic chelation-assisted and rhodium-catalyzed C–H functionalizations (Scheme 1.51).[141]



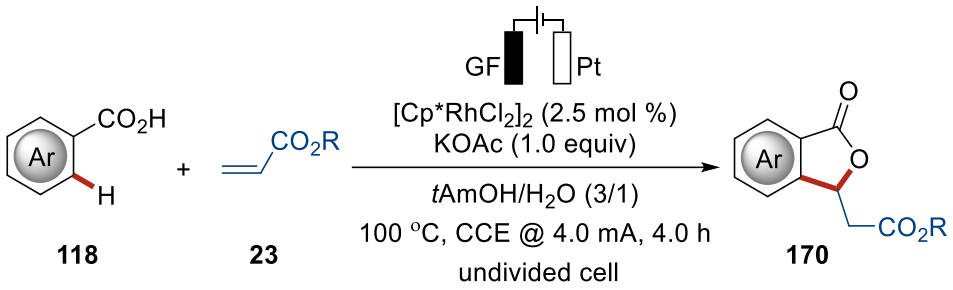
Scheme 1.51. Complex structures obtained by rhodium(III) catalyzed C–H activation.

1.4.2 Rhodaelectro-catalyzed C–H Activation

In the last a few years, the use of electricity as a redox reagent to drive chemical reactions has emerged as an increasingly-viable platform.[142] Significant achievements have been realized by the merger of metallaelectrocatalysis and C–H activation, thus eliminating the use of toxic and expensive oxidants.[143] The exploitation of efficient and more environmentally-friendly synthetic methods is still highly desirable. Many opportunities lie ahead to explore rhodaelectro-catalyzed C–H activation. Thus, when replacing the chemical oxidants with electricity, new reaction pathway and new reaction manifold will be found.

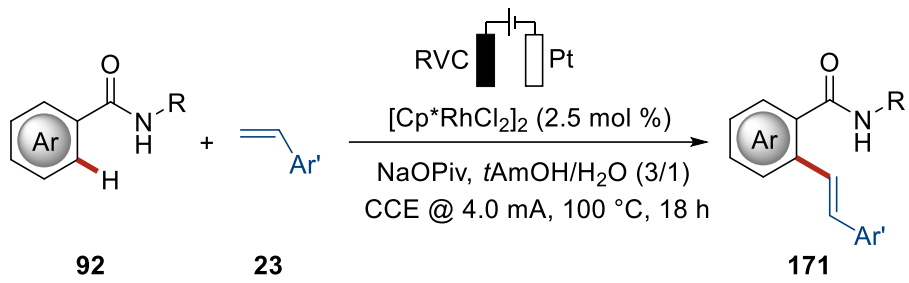
In 2018, Ackermann and coworkers reported the first rhodaelectro-catalyzed C–H activation (Scheme 1.52).[144] Hence, cross-dehydrogenative C–H/C–H alkenylations were realized *via* weakly-coordinating benzoic acids **118** and alkenes **23**. This report serves as

the proof of concept for the 4d-metal electrocatalyzed C–H activation. The optimal reaction conditions featured a user-friendly undivided cell setup, KOAc as the additive and full water tolerance.



Scheme 1.52. First rhodaelectro-catalyzed C–H activation.

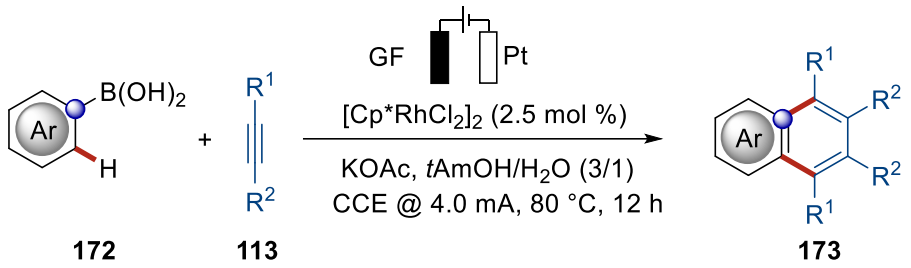
In contrast to the alkenylation with *α,β*-unsaturated carbonyl compounds under rhodaelectro-catalysis, Ackermann recently reported an intriguing alkenylation reaction using unactivated alkenes **23** with weakly coordinating benzamides **92** (Scheme 1.53).[145] The rhodaelectro-catalyzed C–H alkenylation was shown to proceed with ample substrate scope, including heterocycles and valuable electrophilic functional groups, such as chloride, bromo and nitrile. Likewise, a variety of alkenes proved to be amenable, especially oxidation-sensitive hydroxyl substituents. A gram-scale reaction without the decrease of yield highlighted the synthetic utility of the rhodaelectro-catalyzed C–H activation.



Scheme 1.53. Rhodaelectro-catalyzed C–H alkenylation.

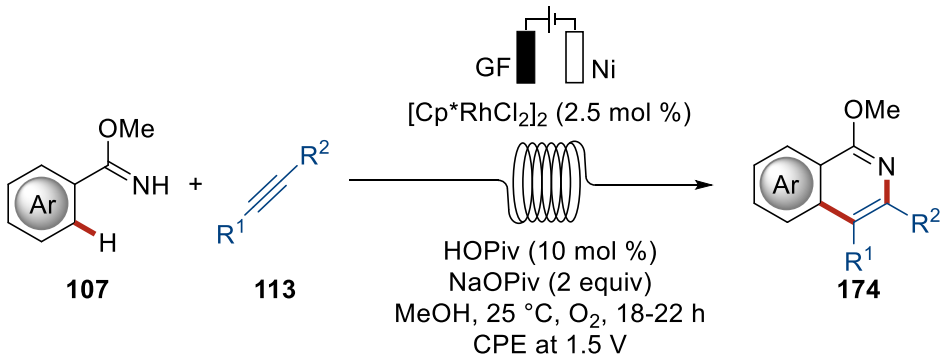
Electrooxidative C–B/C–H [2+2+2] cyclization was realized with a variety of boronic acids *via* versatile rhodium catalysis (Scheme 1.54).[146] The C–B/C–H annulation was efficiently established with ample scope and remarkable levels of functional group tolerance, such as chloro, ester and cyano substituents, in a user-friendly undivided cell setup. Notably, the

chemoselectivity of the conversion of sensitive iodo-substituted boronic acids could be significantly improved as compared to transformations with the typical chemical oxidants, such as AgOAc and $Cu(OAc)_2$.



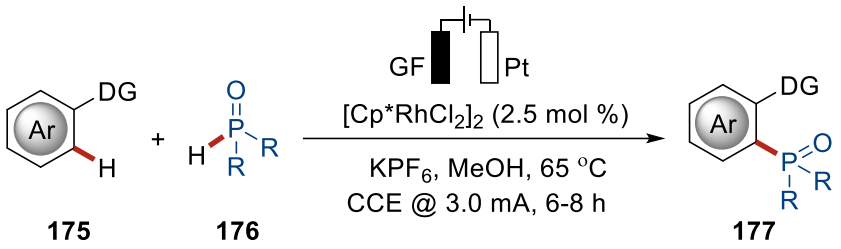
Scheme 1.54. Electrooxidative C–B/C–H [2+2+2] cyclization.

Ackermann also found a robust flow-rhodaelectro-catalyzed alkynes cyclization utilizing aryl imidates **107** as the substrates (Scheme 1.55).[147] It is worth noting that C–H/N–H alkyne annulations were amenable to an electroflow setup. This strategy represents a user-friendly tool for the efficient upscaling of a reaction with significantly improved control of heat and mass transfer. This challenging flow-rhodaelectro-catalyzed alkyne annulations gave access to isoquinolines **174** as well as azo-tetracycles by an intramolecular reaction.



Scheme 1.55. Flow-rhodaelectro-catalyzed alkyne cyclization.

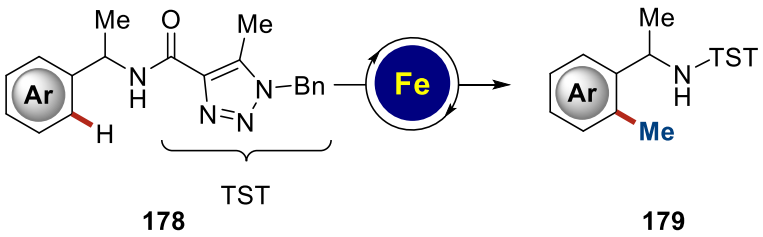
The Xu group then disclosed a phosphorylation using a *N*–coordinating directing groups (Scheme 1.56).[148] The broadly applicable concept of rhodaelectro-catalysis was further utilized for the effective C–H phosphorylation using diphenylphosphines **26**. To demonstrate the scalability, a decagram scale reaction was successfully performed, illustrating the potential for future industrial applications.



Scheme 1.56. Rhodaelectro-catalyzed C–H phosphorylation.

2 Objectives

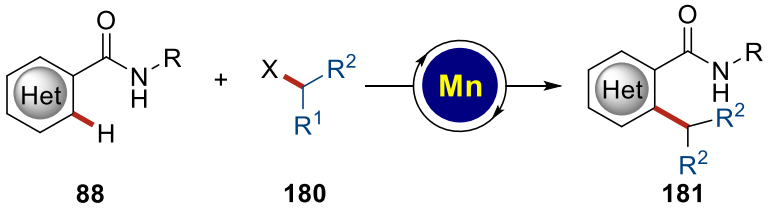
The methyl group is widely found among various bioactive compounds, and the introduction of a single methyl substituent can significantly impact the biological activities and physical properties of pharmacologically relevant drug molecules by favoring the bioactive conformation or changing drug metabolism and pharmacokinetic (DMPK) properties.[149] Ackermann[73b] and Nakamura[73a] introduced a widely applicable iron-catalyzed methylation protocol for C(sp^2)-H bonds. Benzylamines represent the key molecular motif of various natural products and bioactive molecules.[150] With our continued interests in iron chemistry, the development of methylation of benzylamines catalyzed by iron continues to be in high demand (Scheme 2.1).



178 179

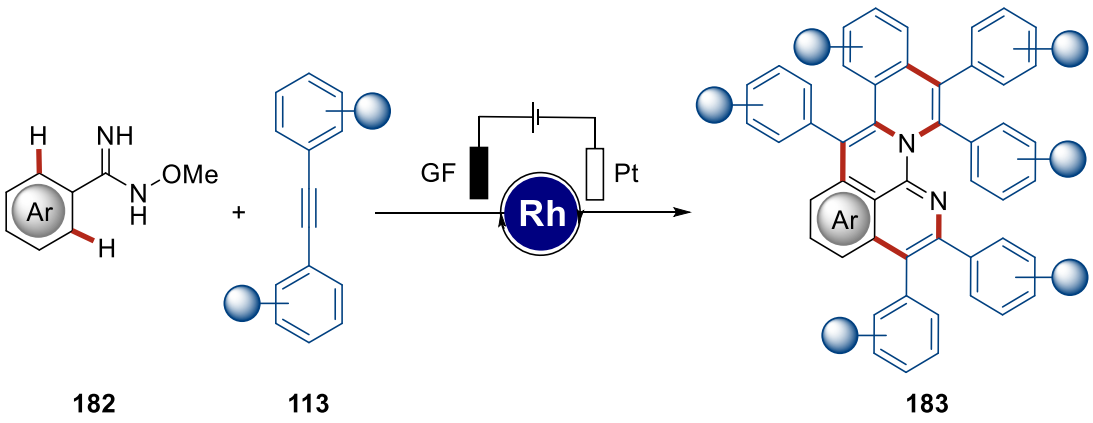
Scheme 2.1. Iron-catalyzed C–H methylation.

Alkylation is a very important strategy to form C(sp^3)–C(sp^3) and C(sp^2)–C(sp^3) bonds. Noble metals played an important role in the C–H alkyations.[151] Recently inexpensive 3d metal catalysts have gained considerable momentum for alkylations as a more environmentally-benign and economically-attractive alternative.[24a, 24d] under the assistance of triazole directing groups, the first example of manganese(II)-catalyzed alkylation was reported by Ackermann's group.[106] Pyridinylamides including picolinamide, nicotinamide, and isonicotinamide are key structural units of numerous biologically active molecules, with notable applications to the life science.[152]. Thus, it is of high importance to introduce alkyl groups into pyridinylamides in the presence of manganese(II) in order to achieve derivatization of pyridinylamides or gain mechanistic insight into manganese(II)-catalyzed C–H activation (Scheme 2.2).



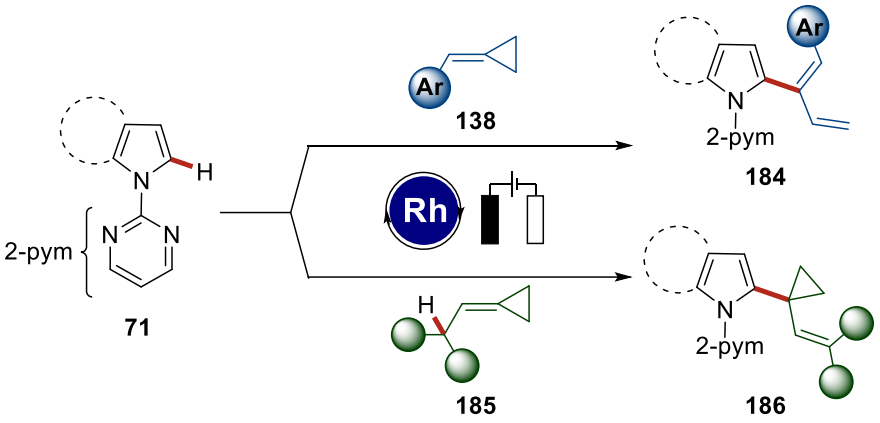
Scheme 2.2. Envisioned manganese(II)-catalyzed C–H alkylation.

Cross-dehydrogenative couplings present the most atom-economic transformation in C–H activation. However, to achieve these transformations sacrificial oxidants are needed, which greatly reduces the atom economy of C–H activation. Furthermore, most transformations rely on expensive silver salts as oxidants, which drive the cost of the overall reactions.[24, 25] The assembly of atomically precise aza-PAHs in an efficient and economic manner has received considerable attention. However, the synthesis of PAHs and aza-PAHs generally relies on stepwise elaborations, largely involving Diels–Alder cycloadditions, dehydrogenative cyclization, and transition-metal-catalyzed cross-couplings that require prefunctionalized substrates.[153] Transition-metal-catalyzed oxidative C–H activation/annulation has been proven to be a powerful tool for PAH syntheses.[154] The electrooxidative alkyne annulation was recently likewise merged with a multiple C–H domino strategy catalyzed by rhodium(III).[146] With our ongoing interest in material syntheses by metalla-electrocatalysis, it is promising to develop a one-step approach to the assembly of aza-PAHs *via* rhodaelectro-catalyzed cascade C–H annulations (Scheme 2.3).



Scheme 2.3. Synthesis of aza-nanographene *via* rhodaelectro-catalyzed Domino C−H annulations.

Among a variety of pharmaceuticals, biologically active molecules and natural products, 1,3-dienes[155] and cyclopropanes[156] represent a vital structure unit for their bioactivities. Ene-yne metathesis, Wittig-type olefinations, Mizoroki-Heck reactions and cross-coupling are among the traditional ways to synthesize 1,3-dienes,[157] while these procedures require the prefunctionalization of the substrates. Thus far, very few examples demonstrated the cyclopropylations by cleavage of C–H bonds[158] as cyclopropanes, the smallest rings, are prone to undergo ring-opening through metal-insertion or fragmentation.[159] The exploitation of efficient and more environmentally-friendly synthetic methods is still highly desirable. With our continued interest in rhodaelectro-catalyzed C–H activation,[144-147] we wondered whether the C–H dienylation and cyclopropylation could be realized through rhodaelectro-catalysis (Scheme 2.4).

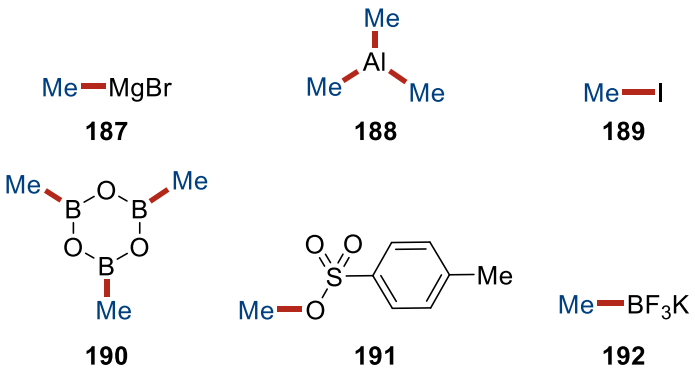


Scheme 2.4. Dienylation and cyclopropylation enabled by rhodaelectro-catalysis.

3 Results and Discussion

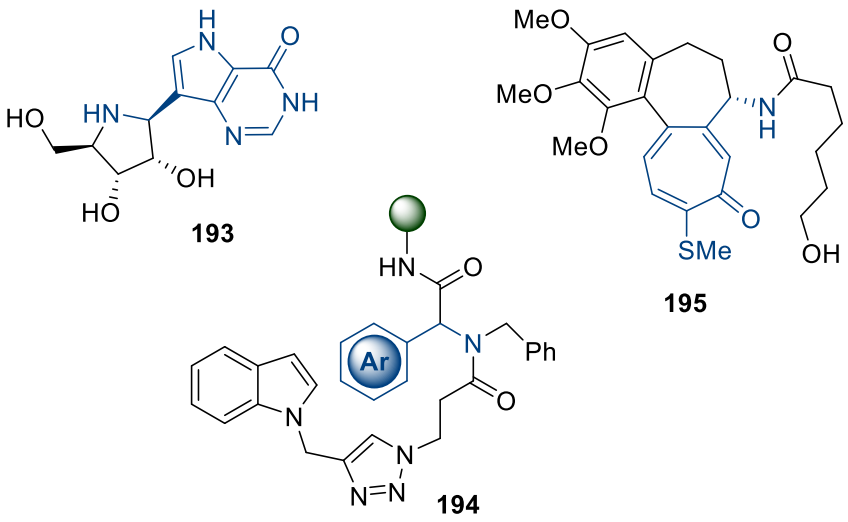
3.1 Triazole-Enabled C–H Activation of Benzylamines by Iron-Catalysis

Since the methyl group plays a very important role for the biological activities and physical properties of pharmacologically relevant drug molecules, many methylation reagents have been developed for direct C–H methylations, such as MeMgBr **187**, $AlMe_3$ **188**, MeI **189**, $Me_3B_3O_3$ **190**, MeOTs **191** and $MeBF_3K$ **192** (Scheme 3.1).[160] Bidentate directing groups were confirmed to be effective in iron-catalyzed C–H methylation.[73] In the previous reports, most of the methylation occurred on electron-deficient aromatic compounds.



Scheme 3.1. Common methylation reagents.

Benzylamines are widely distributed among bioactive molecules (Scheme 3.2).[150] In this context, we became interested in the development of an economical method for the methylation of electron-rich benzylamines. As shown in former studies, MeMgBr served as a suitable methylation reagent under the assistance of triazole directing group.[73b] We, hence, started to explore the feasibility of iron-mediated methylation of protected benzylamines **178a** using MeMgBr as user-friendly and safe methylation reagent.

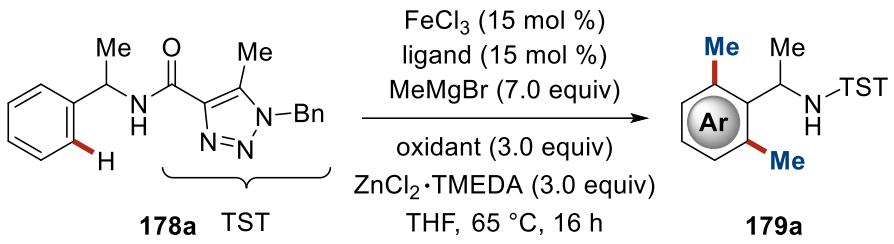


Scheme 3.2. Biological compounds **193-195** containing benzylamines.

3.1.1 Optimization Studies

At the outset of our studies, Dr. Cera designed the tri-substituted triazole TST, which enabled the envisioned iron-catalyzed C–H methylation of benzylamide **178a**. Dr. Cera conducted the following optimization (Table 3.1). Preliminary results revealed that nitrogen or NHC ligands fell short in enabling the desired C–H methylation (Table 3.1, Entries 1-3). The bidentate dppe ligand gave only unsatisfactory result (Entry 4), which could be rationalized with the need for a more rigid coordination environment at iron. In good agreement with this hypothesis, dppz and dppen led to the formation of the desired compound **179a** in synthetically useful yields (Entries 5 and 6), particularly, when using 2,3-dichlorobutane as the oxidizing agent.

Table 3.1. Optimization of iron-catalyzed C–H methylations of benzylamine **178a**.[a]



Entry	Ligand	Oxidant	Yield [%]
1	--	DCB	--
2	D*t*bpy	DCB	--
3	IPr·HCl	DCB	--
4	dppe	DCB	21
5	dppz	DCB	45
6	dppen	DCIB	53
7	dppen	DCB	86

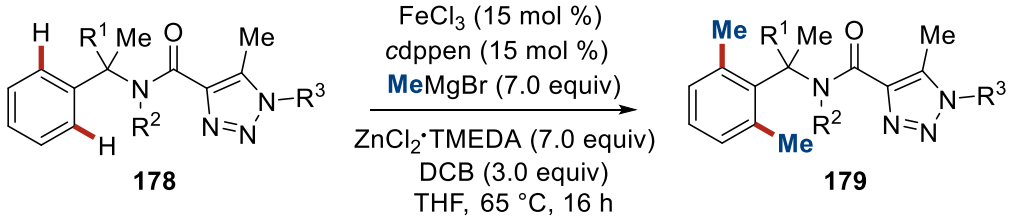
[a] Reaction conditions: **178a** (0.20 mmol), $FeCl_3$ (15 mol %), ligand (15 mol %), MeMgBr (1.40 mmol), $ZnCl_2$•TMEDA (0.60 mmol), oxidant (0.60 mmol), THF (0.5 M), 65 °C, 16 h, isolated yields. dppe = 1,2-bis(diphenylphosphino)ethane; dppbz = 1,2-bis(diphenylphosphino)benzene; dppen = 1,2-bis(diphenylphosphino)ethene. DCB = 2,3-dichlorobutane. DCIB = 1,2-dichloro-2-methylpropane.

3.1.2 Scope of Triazole-Assisted C–H Methylation

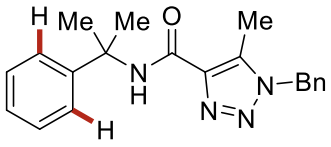
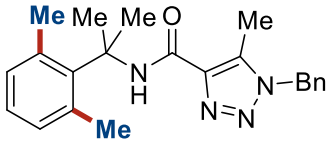
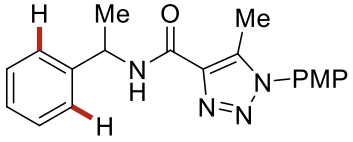
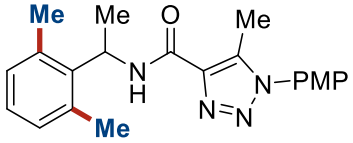
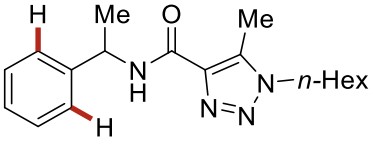
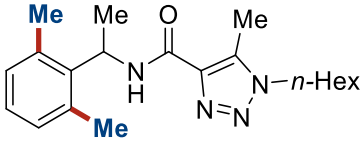
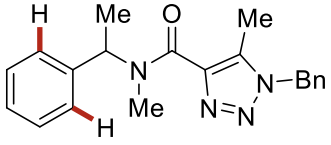
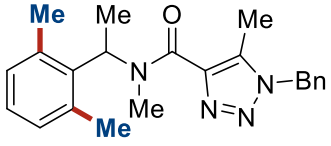
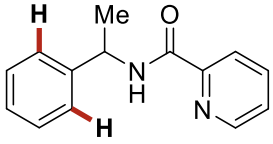
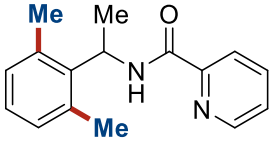
With the optimized reaction conditions in hand, we explored the influence exerted by the TST substitution pattern on the catalytic efficacy. Thus, various directing groups were tolerated in the C–H methylation **178** (Table 3.2), with the sterically congested *gem*-disubstituted benzylamine **178b** being efficiently converted. The iron-catalyzed C–H activation proved amenable to differently *N*-substituted triazoles, including alkyl- and aryl-decorated derivatives **178c** and **178d**. The amide **178e** without free NH-group failed to undergo C–H methylation, probably due to an anionic bidentate coordination mode at iron.

It is particularly noteworthy that the frequently used, picolinic acid-derived[161] benzylamine **178f** was less effective under otherwise identical reaction conditions.

Table 3.2. Influence of the TST substitution pattern.



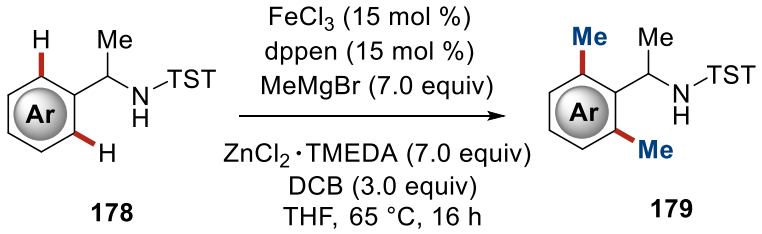
178 **179**

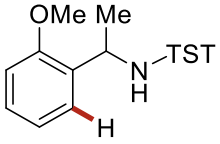
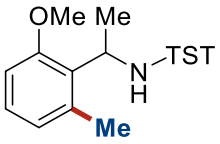
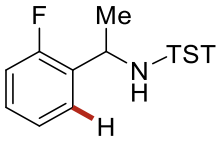
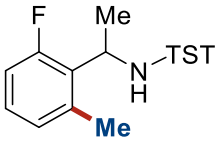
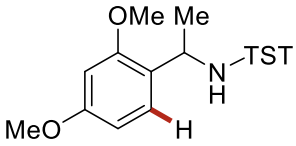
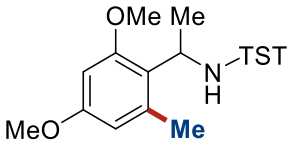
Entry	Substrate	Product	Yield [%]
1	 **178b**	 **179b**	83
2	 **178c**	 **179c**	89
3	 **178d**	 **179d**	70
4	 **178e**	 **179e**	--
5	 **178f**	 **179f**	51

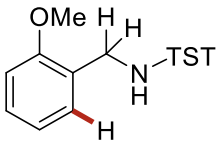
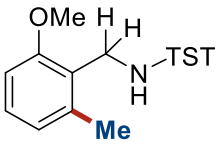
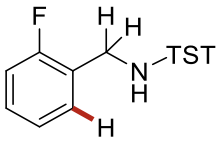
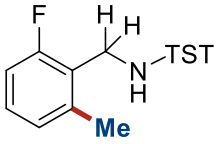
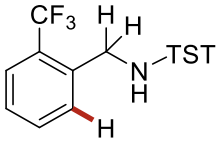
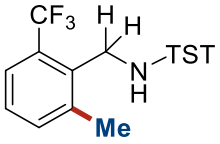
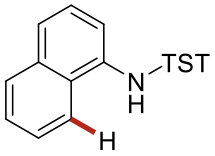
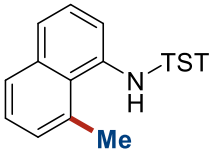
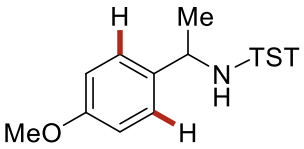
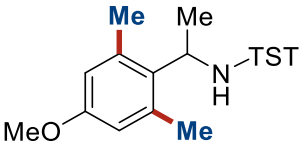
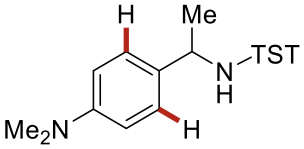
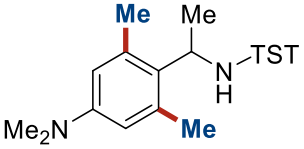
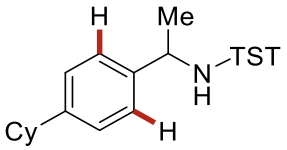
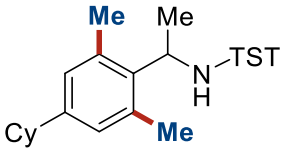
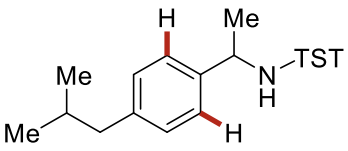
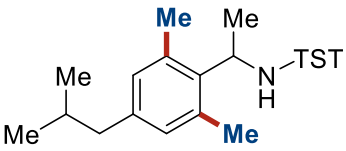
[a] Reaction conditions: **178** (0.20 mmol), $FeCl_3$ (15 mol %), dppen (15 mol %), MeMgBr (1.40 mmol), $ZnCl_2$•TMEDA (0.60 mmol), DCB (0.60 mmol), THF (0.5 M), 65 °C, 16 h, isolated yields.

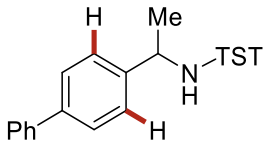
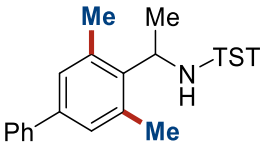
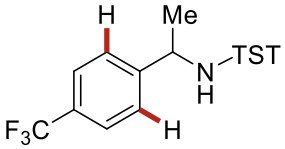
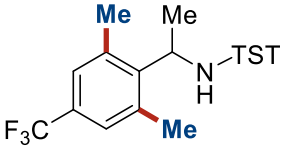
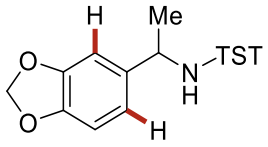
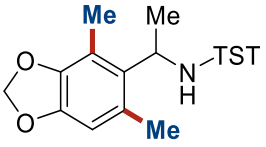
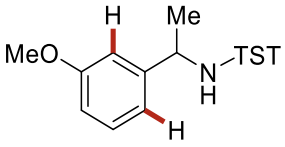
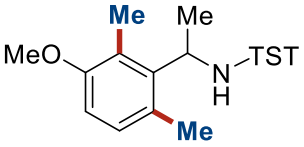
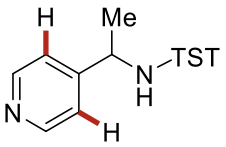
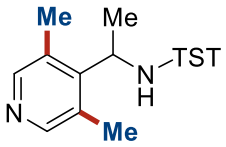
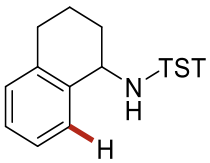
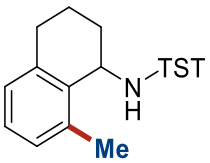
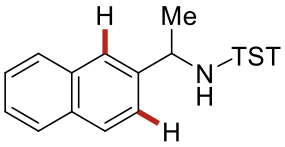
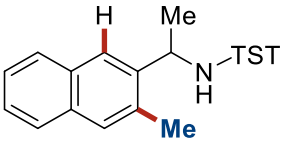
After the optimal TST group was confirmed, we probed the versatility of the iron-catalyzed C–H activation with differently substituted benzylamines **178** (Table 3.3). To our delight, *ortho*-functionalized substrates furnished the products **178g**-**178l** in good to excellent yields. The naphthalene derivative **178m** underwent an unusual *peri*-C–H methylation, thereby furnishing the product **179m** with excellent levels of positional selectivity. *Para*- and *meta*-substituted substrates were directly converted to the twofold methylated products **179n**-**179u**. Given the practical importance of nitrogen-containing heterocycles, it is noteworthy that pyridine **179v** could be obtained in synthetically useful yields as well. Likewise, bicyclic substrate delivered the desired product **179w** featuring the sertraline motif – an important pharmacophore in medicinal chemistry.[162]

Table 3.3. TST-assisted iron-catalyzed C–H methylation.



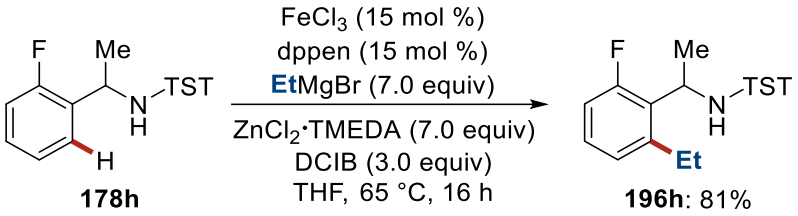
Entry	Substrate	Product	Yield [%]
1	 **178g**	 **179g**	88
2	 **178h**	 **179h**	86
3	 **178i**	 **179i**	80

4	 **178j**	 **179j**	90
5	 **178k**	 **179k**	92
6	 **178l**	 **179l**	80
7	 **178m**	 **179m**	66
8	 **178n**	 **179n**	75
9	 **178o**	 **179o**	62
10	 **178p**	 **179p**	80
11	 **178q**	 **179q**	77

12	 **178r**	 **179r**	84
13	 **178s**	 **179s**	84
14	 **178t**	 **179t**	90
15	 **178u**	 **179u**	89
16	 **178v**	 **179v**	52
17	 **178w**	 **179w**	83
18	 **178x**	 **179x**	91

[a] Reaction conditions: **178** (0.20 mmol), $FeCl_3$ (15 mol %), dppen (15 mol %), MeMgBr (1.4 mmol), $ZnCl_2$•TMEDA (0.60 mmol), DCB (0.60 mmol), THF (0.5 M), 65 °C, 16 h, isolated yields.

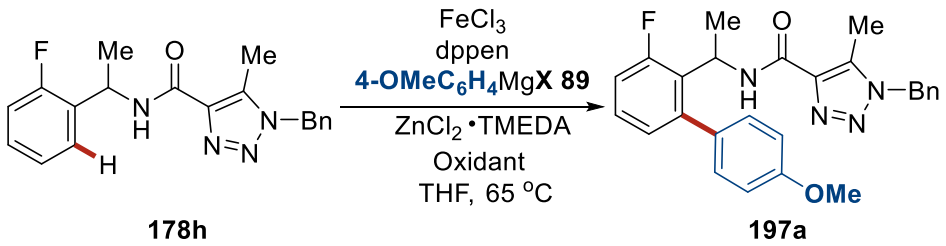
The iron-catalyzed C–H activation strategy was not limited to direct methylation reactions. Indeed, the versatility of our approach was reflected by a high-yielding C–H ethylation of benzylamine **178h**, with the best results being achieved by employing DCIB as the oxidant (Scheme 3.3).



Scheme 3.3. TST-assisted iron-catalyzed C–H ethylation.

Then we did some optimization for the iron-catalyzed C–H arylation (Table 3.4). We found that DCIB was more effective than 2,3-DCB giving the desired product **197a** in 87% yield (entry 3).

Table 3.4. Optimization of iron-catalyzed C–H arylation.[a]

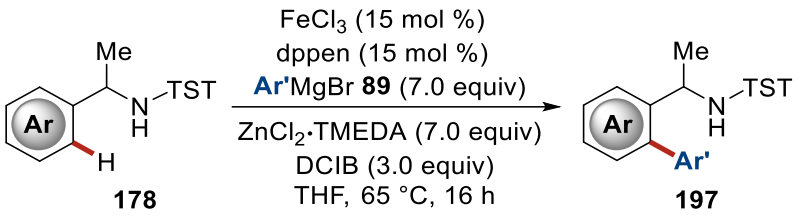


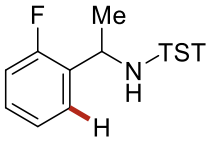
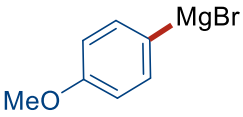
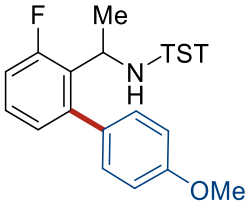
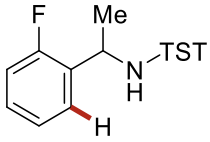
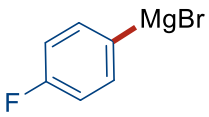
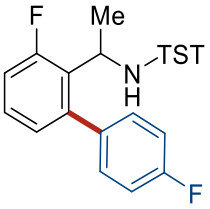
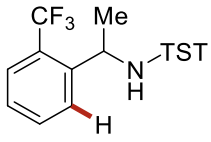
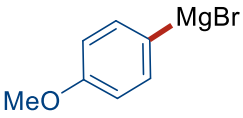
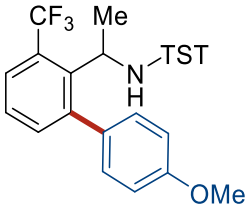
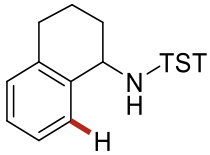
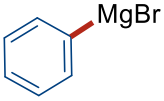
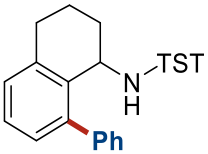
entry	Oxidant	X	Yield [%]
1	2,3-DCB	Br	17
2	2,3-DCB	Cl	--
3	DCIB	Br	87

[a] Reaction conditions: **178h** (0.20 mmol), $FeCl_3$ (15 mol %), $ZnCl_2$·TMEDA (0.6 mmol), ligand (15 mol %), PhMgX (1.4 mmol), Oxidant (0.6 mmol), isolated yield.

Next, we tested the versatility of the iron-catalyzed C–H arylation (Table 3.5). Both electron-deficient and electron-rich Grignard reagents furnished the products in excellent yields (**197a**-**197c**). Bicyclic amine **178w** was also a reactive substrate in the C–H arylation.

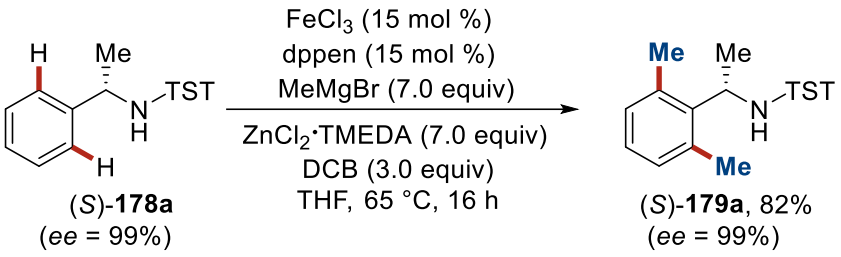
Table 3.5. TST-assisted iron-catalyzed C–H arylation.[a]



Entry	Substrate	Ar'MgBr	Product	Yield [%]
1	 178h	 89a	 197a	75
2	 178h	 89b	 197b	83
3	 178l	 89a	 197c	89
4	 178w	 89c	 197d	76

[a] Reaction conditions: 1a (0.20 mmol), $FeCl_3$ (15 mol %), $ZnCl_2$·TMEDA (0.60 mmol), dppen (15 mol %), Ar'MgBr (1.4 mmol), DCIB (0.6 mmol), isolated yield.

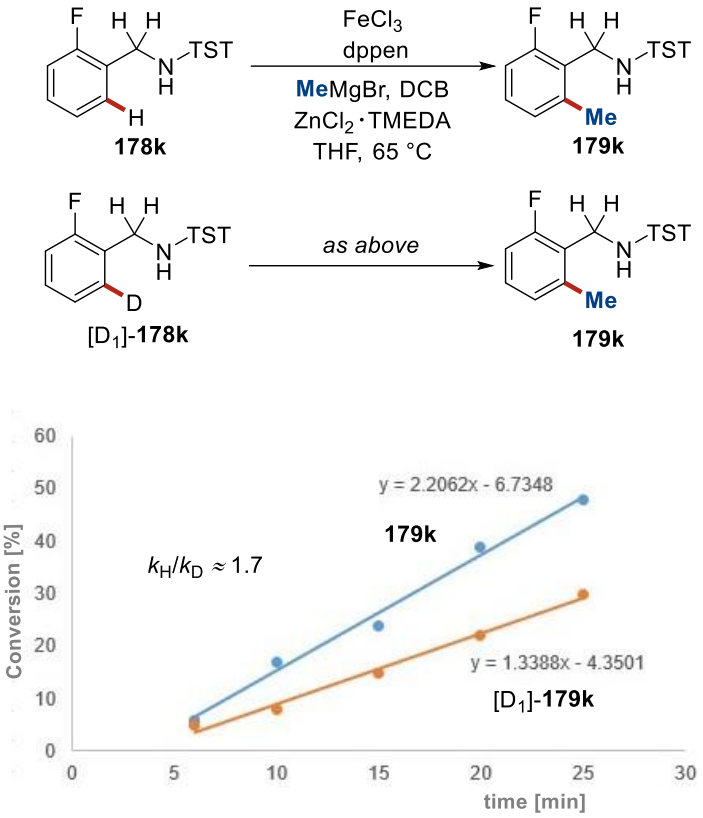
The synthetic utility of the iron-catalyzed C–H activation strategy was among others mirrored by the racemization-free modification of the enantiomerically-enriched benzylamine (*S*)-**178a** (Scheme 3.4).



Scheme 3.4. Racemization-free C–H methylation of benzylamine (*S*)-**178a**.

3.1.3 KIE studies of Iron-catalyzed Methylation

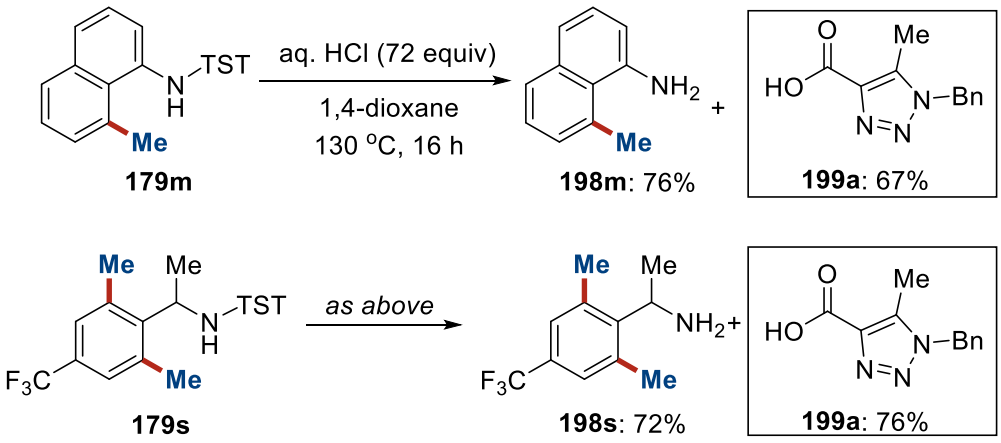
As to the catalyst mode of action, we conducted kinetic studies through independent experiments and the conversions were determined by ^{19}F NMR. To this end, we unraveled a kinetic isotope effect (KIE) of $k_H/k_D \approx 1.7$, being suggestive that the C–H cleavage is before or in the rate-determining step (Scheme 3.5). The outstanding efficacy of the iron-catalyzed C–H activation was further reflected by a 48% conversion of substrate **178k** within only 25 minutes.



Scheme 3.5. KIE studies by independent experiments.

3.1.4 Deprotection of 179

Finally, the TST group could be removed in a traceless fashion, furnishing the free primary benzylamines **198m** and **198s**, while the reusable TST acid **199a** was recovered in high yield (Scheme 3.6).[163]



Scheme 3.6. Removal of TST group in a traceless fashion.

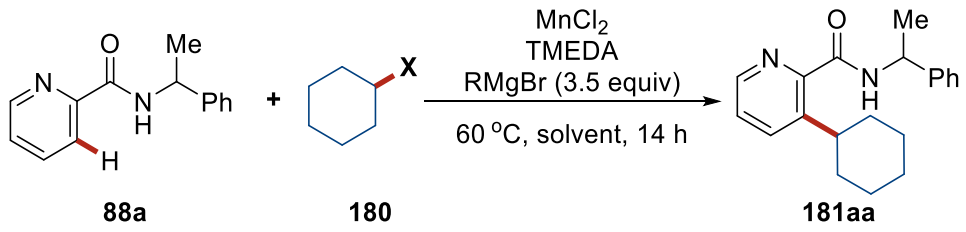
3.2 Manganese-catalyzed Pyridinyl C–H Alkylation

In the past few years, direct C–H alkylations of unreactive arenes with alkyl halides have been achieved in a site-selective manner by chelation assistance.[164] However, those works were mostly realized by expensive and toxic rare 4d and 5d transition metals.[151] Particularly, secondary C–H alkylations continue to be scarce, since in many cases *β*–H elimination is more favorable in presence of those metals. Recently much attention has shifted to less expensive earth-abundant 3d transition metals for C–H activations such as nickel,[165] iron[68, 73] and manganese.[106]

3.3.1 Optimization of Pyridinyl Alkylation

Pyridinylamides represent a key unit in a variety of bioactive molecules. Therefore, it is urgent to develop some efficient approaches to perform alkylation of pyridinylamide. We initiated the study of pyridinyl C–H alkylation by using cyclohexyl halide **180** as the alkylation reagents in the presence of $MnCl_2$ (Table 3.6). Various bases including alkyl and phenyl Grignard reagents were tested, which showed that ethylmagnesium bromide was superior to others (entries 1-4). The chlorocyclohexane even featured higher reactivity for this pyridinyl C–H alkylation reaction, while iodocyclohexane gave a modest yield (entries 5-6). It was found that no alkylated product was formed in the absence of the manganese catalyst or TMEDA additive (entries 7-8). Finally, the best result was obtained using 10 mol % of $MnCl_2$ combined with 1.0 equivalent of TMEDA (entries 9-12).

Table 3.6. Optimization of pyridinyl C–H alkylation with a secondary alkyl halide.[a]



88a **180** **181aa**

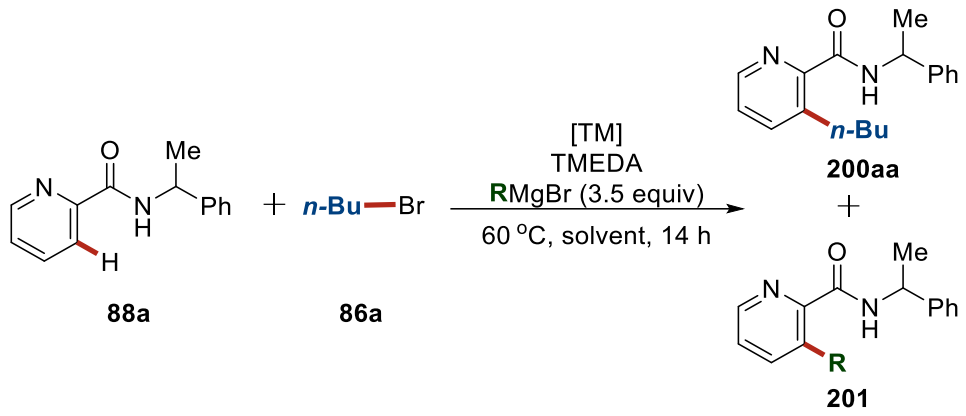
Entry	[Mn] [mol %]	TMEDA [equiv]	X	RMgBr	Yield [%]

1	$MnCl_2$ (20)	2.0	Br	*i*-PrMgBr (2.8 M in THF)	65
2	$MnCl_2$ (20)	2.0	Br	EtMgBr (2.8 M in THF)	69
3	$MnCl_2$ (20)	2.0	Br	*t*-BuCH_2MgBr (1.5 M in THF)	56
4	$MnCl_2$ (20)	2.0	Br	PhMgBr (2.3 M in THF)	45
5	$MnCl_2$ (20)	2.0	Cl	EtMgBr (2.8 M in THF)	78
6	$MnCl_2$ (20)	2.0	I	EtMgBr (2.8 M in THF)	48
7	--	2.0	Cl	EtMgBr (2.8 M in THF)	0
8	$MnCl_2$ (20)	--	Cl	EtMgBr (2.8 M in THF)	0
9	$MnCl_2$ (10)	2.0	Cl	EtMgBr (2.8 M in THF)	76
10	$MnCl_2$ (5)	2.0	Cl	EtMgBr (2.8 M in THF)	54
11	$MnCl_2$ (10)	1.0	Cl	EtMgBr (2.8 M in THF)	79
12	$MnCl_2$ (10)	0.5	Cl	EtMgBr (2.8 M in THF)	64

[a] Reaction conditions: **88a** (0.20 mmol), **180** (3.0 equiv), $MnCl_2$ catalyst, TMEDA, RMgBr (3.5 equiv), THF (0.6 mL) under N_2 at 60 °C for 14 h, isolated yield.

Dr. Huang finished the optimization of the primary alkylation by the reaction of *N*-(1-phenylethyl)picolinamide **88a** and *n*-butyl bromide **86a** catalyzed by cost-efficient $MnCl_2$ (Table 3.7). The assessment of different Grignard reagent showed that bulkier Grignard reagents are more efficient to form the butylated product. When *t*-BuCH_2MgBr was used, only butylation was observed without formation of any alkylated product generated by Grignard reagent (entries 1-7). Dr. Huang also studied other manganese catalysts, such as $Mn(OAc)_2$, $Mn_2(CO)_{10}$ and $MnBr(CO)_5$, without any alkylated product (entries 8-10). Control experiment without the manganese catalyst did not give the desired product, which confirmed that manganese is key for the catalytic reaction (entry 14). Decreased amounts of TMEDA gave less product as well (entry 15).

Table 3.7. Optimization of pyridinyl C–H primary alkylation.



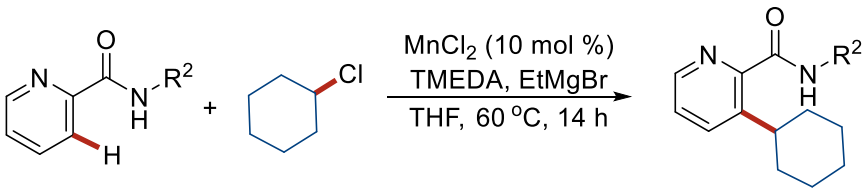
Entry	[TM] (mol %)	TMEDA [equiv]	RMgBr	Yield [%] 200aa/201
1	$MnCl_2$ (20)	2.0	PhMgBr (2.3 M in THF)	45/35
2	$MnCl_2$ (20)	2.0	MeMgBr (3.0 M in THF)	55/29
3	$MnCl_2$ (20)	2.0	EtMgBr (3.4 M in THF)	46/37
4	$MnCl_2$ (20)	2.0	*i*-PrMgBr (2.4 M in THF)	58/20
5	$MnCl_2$ (20)	2.0	*i*-PrMgBr (3.0 M in 2-MeTHF)	59/22
6	$MnCl_2$ (20)	2.0	*i*-PrMgCl (2.0 M in THF)	40/31
7	$MnCl_2$ (20)	2.0	*t*-BuCH_2MgBr (1.5 M in THF)	69/0
8	$Mn(OAc)_2$ (20)	2.0	*t*-BuCH_2MgBr (1.5 M in THF)	0/0
9	$Mn_2(CO)_{10}$ (10)	2.0	*t*-BuCH_2MgBr (1.5 M in THF)	0/0
10	$MnBr(CO)_5$ (20)	2.0	*t*-BuCH_2MgBr (1.5 M in THF)	0/0
11	$Fe(acac)_3$ (10)	2.0	*t*-BuCH_2MgBr (1.5 M in THF)	0/0
12	$FeCl_3$ (10)	2.0	*t*-BuCH_2MgBr (1.5 M in THF)	0/0
13	$MnCl_2$ (10)	2.0	*t*-BuCH_2MgBr (1.5 M in THF)	42/0
14	--	2.0	*t*-BuCH_2MgBr (1.5 M in THF)	0/0
15	$MnCl_2$ (20)	1.0	*t*-BuCH_2MgBr (1.5 M in THF)	50/0

[a] Reaction conditions: **88a** (0.20 mmol), *n*-BuBr (3.0 equiv), [Mn] catalyst, TMEDA, RMgBr (3.5 equiv), THF (0.2 mL) under N_2 at 60 °C for 14 h, isolated yield.

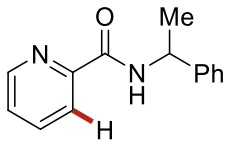
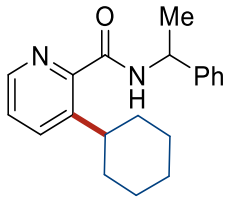
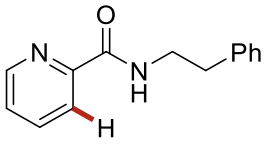
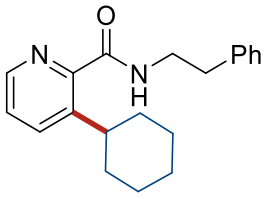
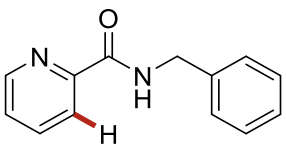
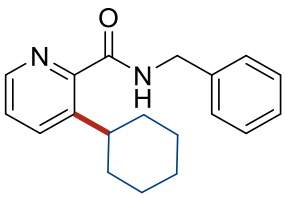
3.2.2 Scope of Manganese Catalyzed Alkylation

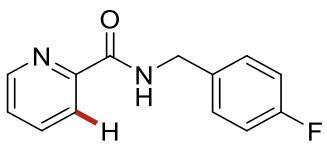
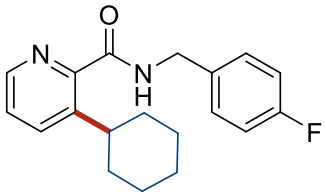
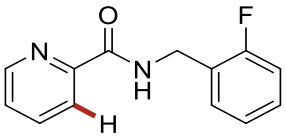
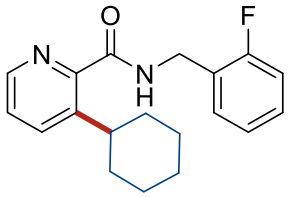
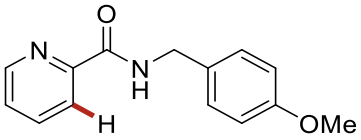
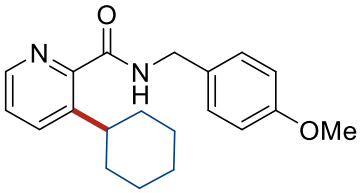
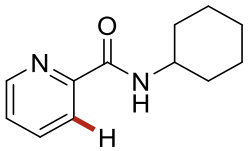
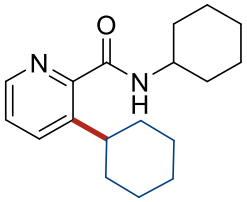
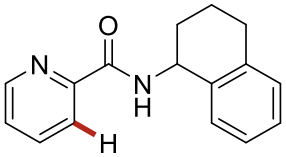
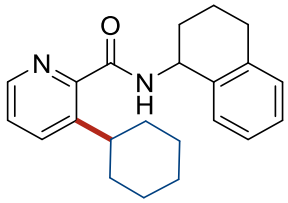
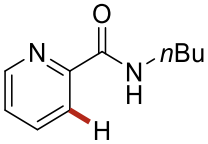
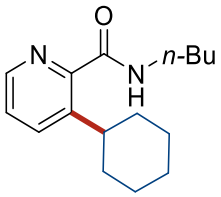
After the optimization of the pyridinyl C–H alkylation, the scope and limitation of the secondary alkylation was evaluated (Table 3.8). A variety of 3-cyclohexylated picolinamides **181aa-181ja** was synthesized with high catalytic efficiency. Quinoline was also viable to be cyclohexylated (**181ka**). Significantly, the importance of the reaction was underlined by furnishing the compound **181fa** on gram scale with a comparable catalytic efficiency.

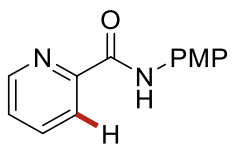
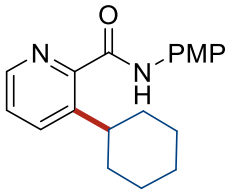
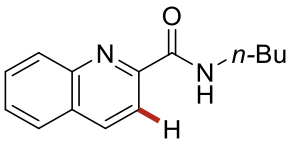
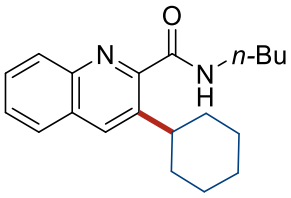
Table 3.8. Scope of manganese-catalyzed alkylation with chlorocyclohexane.



88 **180a** **181**

Entry	Substrate	Product	Yield [%]
1	 **88a**	 **181aa**	79
2	 **88b**	 **181ba**	94
3	 **88c**	 **181ca**	77

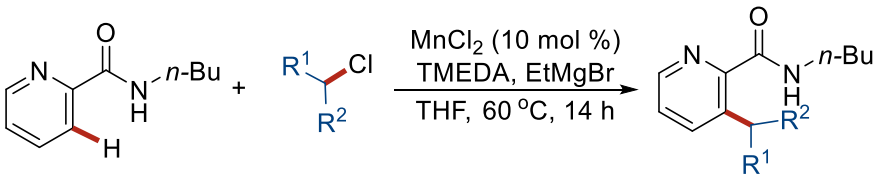
4	 **88d**	 **181da**	84
5	 **88e**	 **181ea**	83
6	 **88f**	 **181fa**	88 81 (1.3 g scale)
7	 **88g**	 **181ga**	80
8	 **88h**	 **181ha**	82
9	 **88i**	 **181ia**	92

10	 **88j**	 **181ja**	46
11	 **88k**	 **181ka**	26

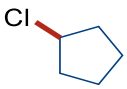
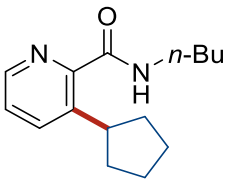
[a] Reaction conditions: **88** (0.20 mmol), **180a** (3.0 equiv), $MnCl_2$ catalyst, TMEDA, EtMgBr (3.5 equiv), THF (0.6 mL) under N_2 at 60 °C for 14 h, isolated yield.

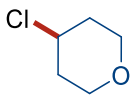
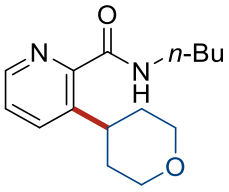
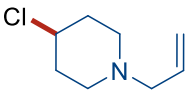
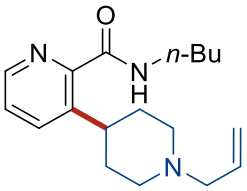
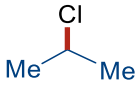
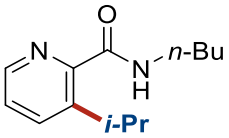
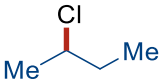
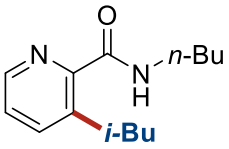
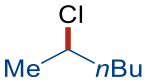
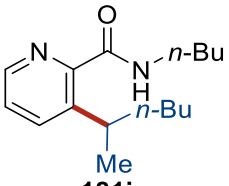
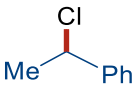
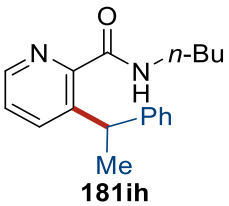
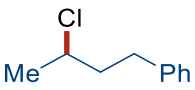
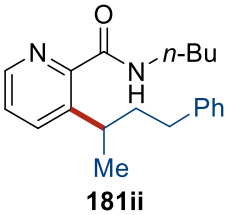
Then, various secondary alkyl chlorides were tested (Table 3.9). The versatility of the optimized methodology was further documented through the cyclopentylation and isopropylation of picolinamides (**181ib**, **181ie**). The cyclic secondary alkylchlorides with different ring size afforded the corresponding pyridinylamides **181if-181ik**.

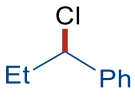
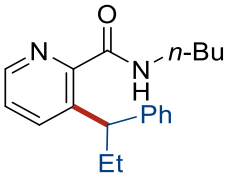
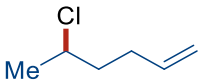
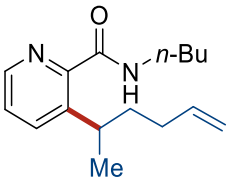
Table 3.9. Scope of manganese-catalyzed secondary alkylation with alkyl chlorides **180**.



88i **180** **181**

Entry	Substrate	Product	Yield (%)
1	 **180b**	 **181ib**	57

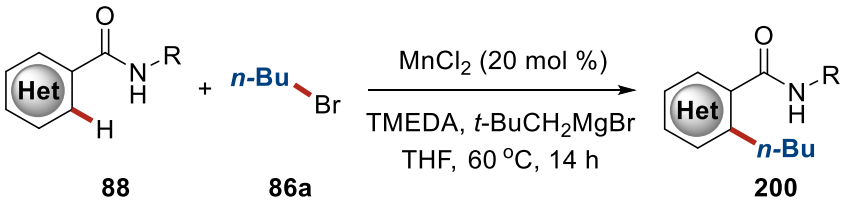
2	 **180c**	 **181ic**	60
3	 **180d**	 **181id**	77
4	 **180e**	 **181ie**	62
5	 **180f**	 **181if**	75
6	 **180g**	 **181ig**	82
7	 **180h**	 **181ih**	37
8	 **180i**	 **181ii**	52

9	 **180j**	 **181ij**	59
10	 **180k**	 **181ik**	59

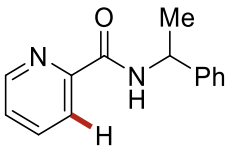
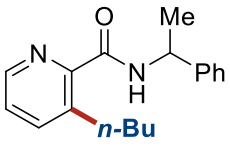
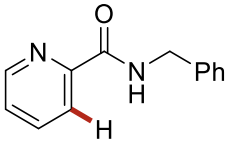
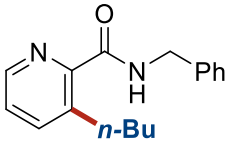
[a] Reaction conditions: **88i** (0.20 mmol), **180** (3.0 equiv), $MnCl_2$ (10 mol %), TMEDA, EtMgBr (3.5 equiv), THF (0.6 mL) under N_2 at 60 °C for 14 h, isolated yield.

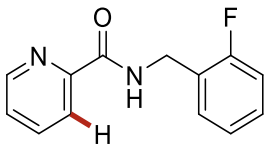
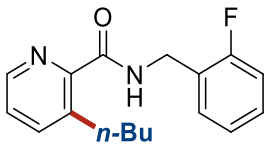
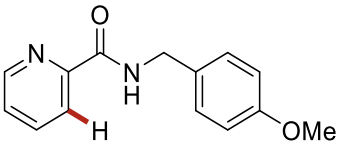
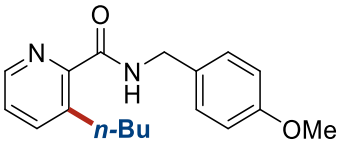
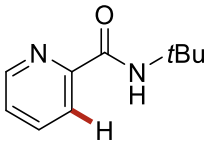
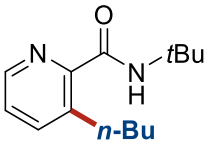
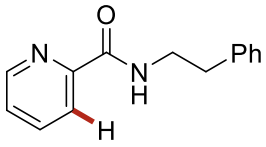
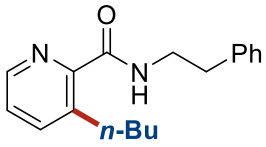
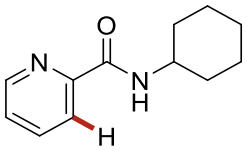
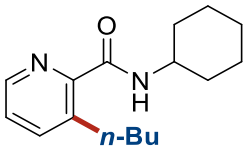
Next, we turned our attention to the manganese-catalyzed *n*-butylation with differently substituted picolinamides **88** (Table 3.10). Variation of substituents on the amides **88** were tolerated in this reaction to achieve products **200aa-200ga**.

Table 3.10. Scope of manganese catalyzed butylation.



88 **86a** **200**

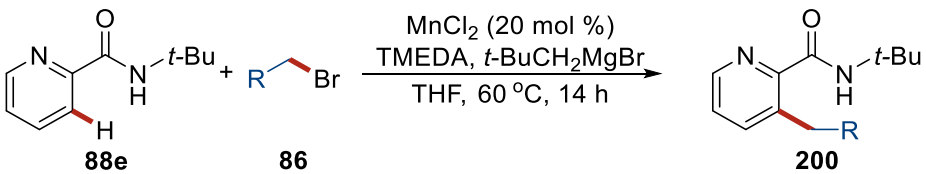
Entry	Substrate	Product	Yield [%]
1	 **88a**	 **200aa**	69
2	 **88b**	 **200ba**	65

3	 **88c**	 **200ca**	56
4	 **88d**	 **200da**	56
5	 **88e**	 **200ea**	75
6	 **88f**	 **200fa**	75
7	 **88g**	 **200ga**	77

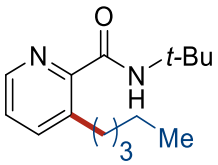
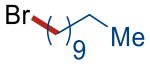
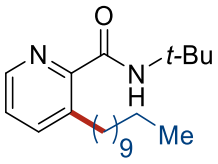
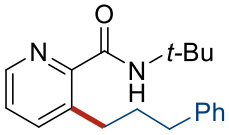
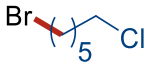
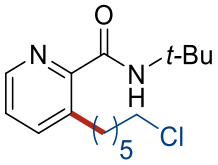
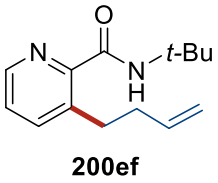
[a] Reaction conditions: **88** (0.20 mmol), *n*-BuBr (3.0 equiv), $MnCl_2$ (10 mol %), TMEDA (2.0 equiv), *t*-$BuCH_2MgBr$ (3.5 equiv), THF (0.2 mL) under N_2 at 60 °C for 14 h, isolated yield.

Different primary alkylbromides **86** were probed thereafter (Table 3.11). Interestingly, terminal alkene and alkyl chlorides were tolerated by this primary alkylation catalyst (**200ee** and **200ef**).

Table 3.11. Scope of manganese catalyzed primary alkylation of pyridine.

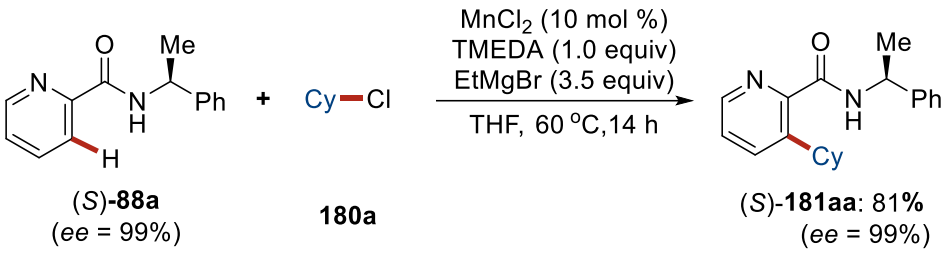


88e **86** **200**

Entry	Substrate	Product	Yield [%]
1	 **86b**	 **200eb**	71
2	 **86c**	 **200ec**	53
3	 **86d**	 **200ed**	74
4	 **86e**	 **200ee**	73
5	 **86f**	 **200ef**	52

[a] Reaction conditions: **88e** (0.20 mmol), **86** (3.0 equiv), $MnCl_2$ (10 mol %), TMEDA (2.0 equiv), *t*-$BuCH_2MgBr$ (3.5 equiv), THF (0.2 mL) under N_2 at 60 °C for 14 h, isolated yield.

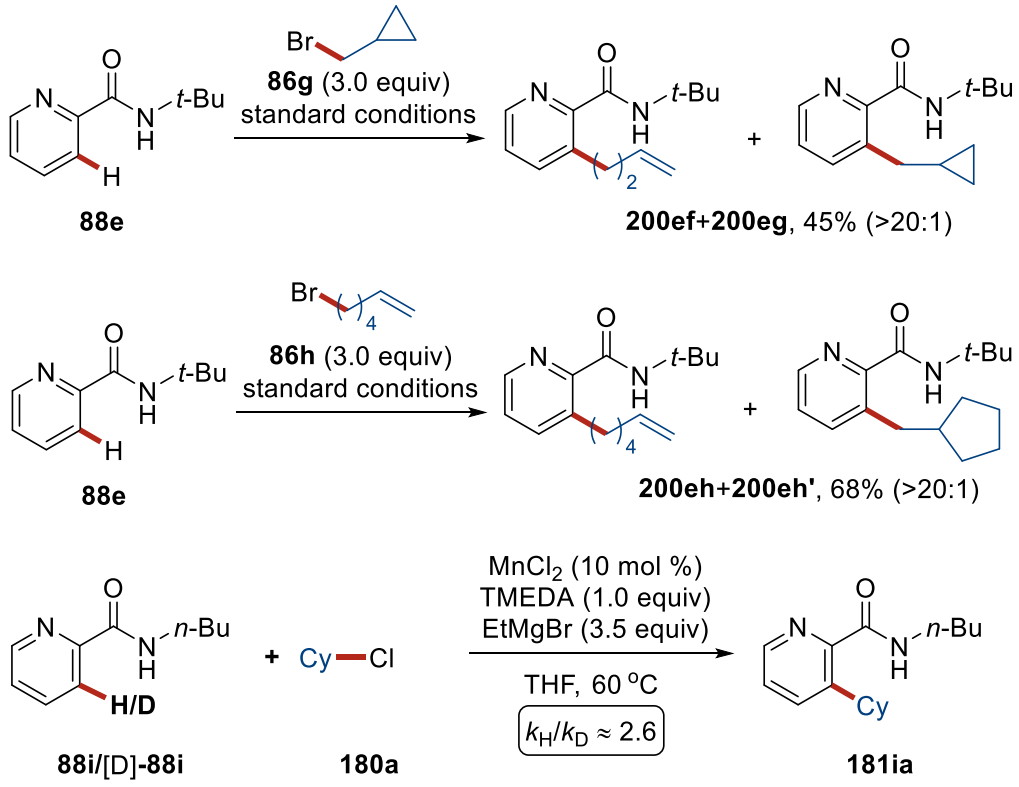
The synthetic utility of our manganese-catalyzed C–H alkylation strategy was reflected by the derivatization of the optically enriched *N*-(1-phenylethyl)picolinamide **88a** without racemization of the stereogenic center (Scheme 3.8).



Scheme 3.8. Racemization-free C–H cyclohexylation of pyridine (*S*)-**88a.**

3.2.3 Mechanistic Studies of Manganese Catalyzed Alkylation

As to the elucidation of the reaction mechanism (Scheme 3.9), we subjected bromomethylcyclopropane **86g** to the optimized conditions and obtained the ring-opening product **200ef**, which indicated a radical pathway in the activation of the C–Br bond. However, the application of 6-bromohex-1-ene **86h** only yielded the linear compound **200eh**. Then we performed independent reactions observing a kinetic isotopic effect (KIE) of $k_H/k_D \approx 2.6$, thus indicating the C–H cleavage as the rate-determining step.



Scheme 3.9. Mechanistic studies of manganese-catalyzed C–H alkylation.

3.3 Rhodaelectro-Catalyzed Domino Alkyne Annulations to access Aza-Polycyclic Aromatic Hydrocarbons

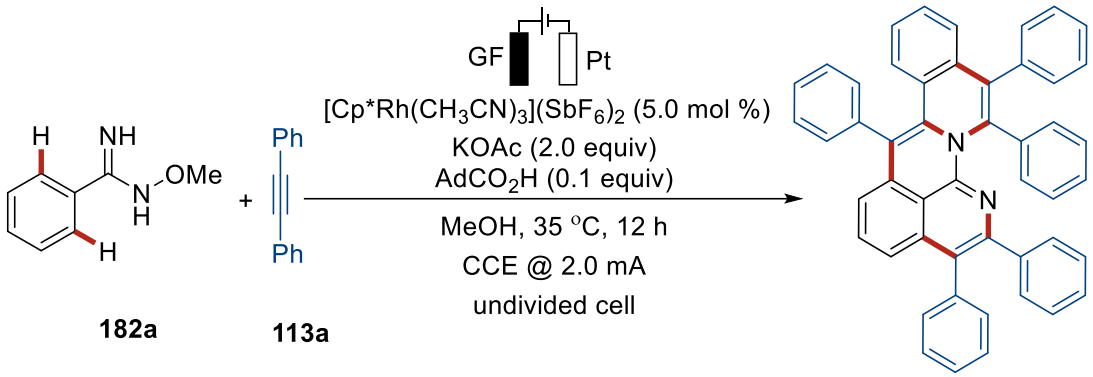
To meet the rising demand for the development of sustainable and green synthetic methodology, electrosynthesis has emerged as a powerful strategy in which stoichiometric amounts of oxidizing and reducing reagents as well as electron transfer events can be replaced by electric current. Therefore, the generation of waste can be diminished and broader functional groups tolerance can be accomplished. The first rhodaelecto-catalyzed annulation to form polycyclic aromatic hydrocarbons was reported by Ackermann.[146] Different transformations have been realized by rhodaelectro-catalysis, such as olefination,[145] alkylation[144] and annulation.[146, 147] Numerous examples of the formation of diverse heterocyclic compounds through the cleavage of C–H/N–H or C–H/O–H bonds followed by annulation reactions with alkynes catalyzed by Rhodium(III) have been reported.[127-134] Thus far, only a few examples achieved the double C–H activation and related C–C or C–X (X=N, O) bond formation.[127, 166] A multiple C–H activation and annulation strategy in the presence of rhodaelectro-catalysis to synthesize aza-polycyclic aromatic hydrocarbons is envisioned to be highly desirable.

3.3.1 Optimization of Rhodaelectro-Catalyzed Domino Annulations

On the basis of previous studies,[127, 146, 166] Dr. Kong from the Ackermann team designed a new directing group to investigate the C–H activation and alkyne annulation cascade *via* rhodaelectro-catalysis. The optimization was finished by Dr. Kong. Hence, I performed key control experiments. When cationic rhodium(III) catalyst $[Cp^*Rh(CH_3CN)_3](SbF_6)_2$ was employed as catalyst, the product was obtained in 90% yield (Table 3.12, entry 1). Higher loading of the catalyst did not show a decrease of the efficiency (entry 3). When the reaction was attempted without electricity, only trace amounts of the desired product **183aa** was formed (entry 4). No product was observed in the absence of the rhodium catalyst

(entry 5). A nitrogen atmosphere failed to improve the yield of this reaction (entry 6). The replacement of electricity by $Cu(OAc)_2$ furnished the product in much lower yield (entry 7). The use of other electrode materials led to a sharp decrease of the yield.

Table 3.12. Control experiments for the rhodaelectro-catalyzed cascade reactions.[a]



182a **113a** **183aa**

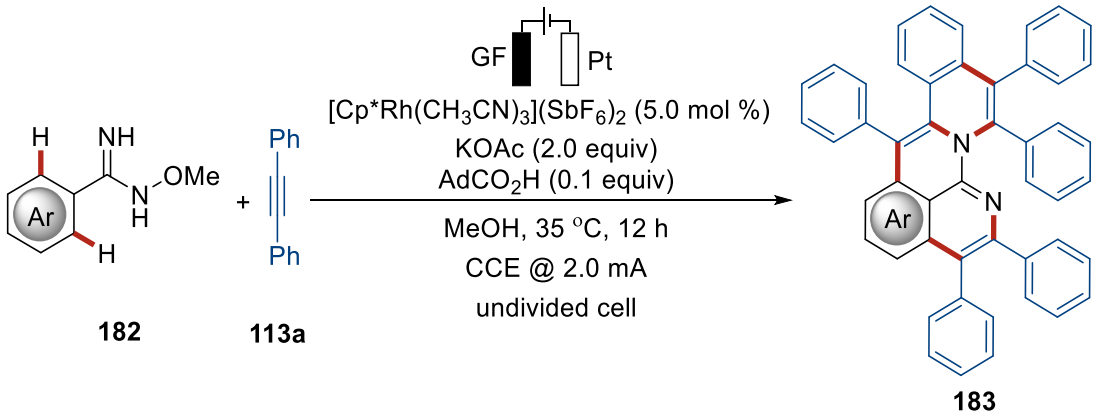
Entry	Variation of standard condotion	Yield [%]
1	no	90
2	$[Cp^*RhCl_2]_2$ (2.5 mol %)	75
3	$[Cp^*Rh(CH_3CN)_3](SbF_6)_2$ (2.5 mol %)	89
4	without electricity	trace
5	Without rhodium catalyst	0
6	under N_2	60
7	$Cu(OAc)_2$ (4 equiv) instead of electricity	25
8	platinum plate as anode electrode	67
9	nickel foam as cathode electrode	65

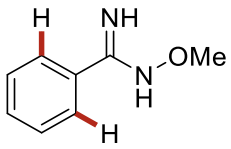
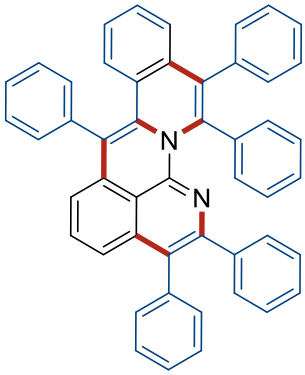
[a] Undivided cell, graphite felt anode (GF), platinum plate cathode (Pt), **182a** (0.20 mmol), **113a** (0.70 mmol), $[Cp^*Rh(CH_3CN)_3](SbF_6)_2$ (5.0 mol %), KOAc (2.0 equiv), $AdCO_2H$ (0.1 equiv), MeOH (4 mL), 35 °C under air, isolated yield.

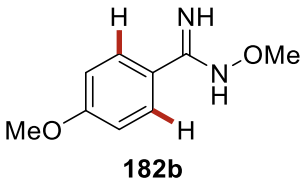
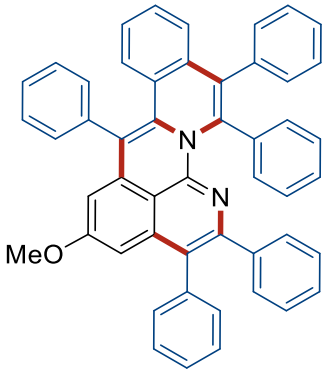
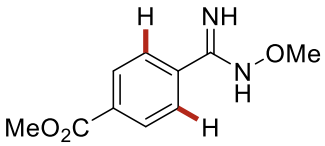
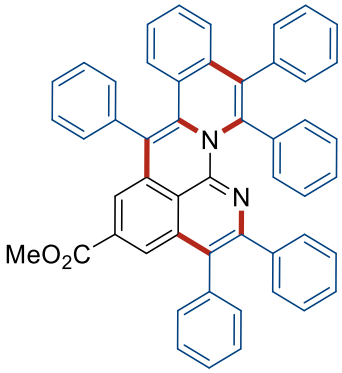
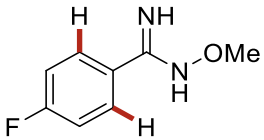
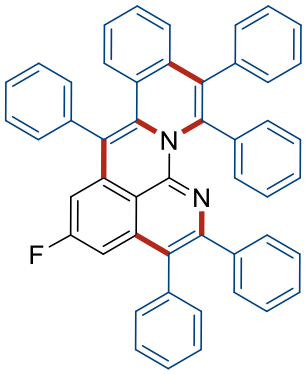
3.3.2 Scope of Rhodaelectro-catalyzed C–H Activation and Annulation Cascade

With the optimal reaction conditions in hand, the scope of the electrocatalysis was examined with different imidamides **182** (Table 3.13). A broad range of aryl imidamides **182** bearing electron-donating (**182b**) and electron-withdrawing groups (**182c**) proved applicable to the electrocatalysis.

Table 3.13. Rhodaelectro-catalyzed C–H activation with imidamide **182**.



Entry	Substrate	Product	Yield [%]
1	 **182a**	 **183aa**	90

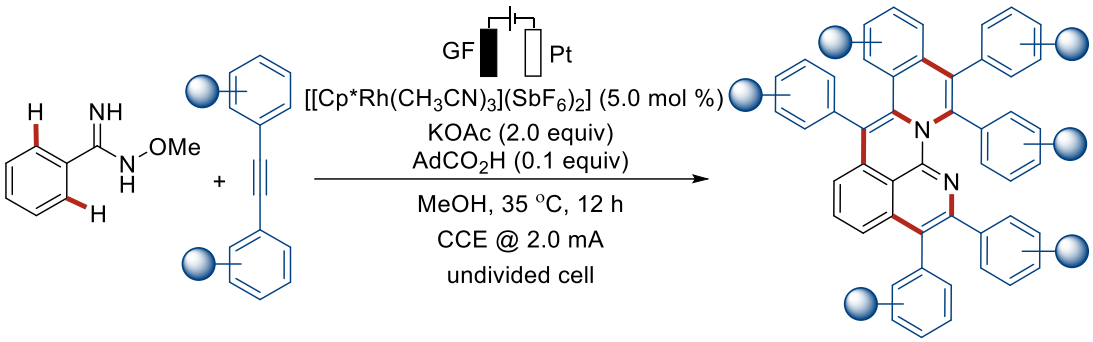
2	 **182b**	 **183ba**	76
3	 **182c**	 **183ca**	57
4	 **182d**	 **183da**	73

[a] Undivided cell, graphite felt anode (GF), platinum plate cathode (Pt), **182** (0.20 mmol), **113a** (0.70 mmol), $[Cp^*Rh(CH_3CN)_3](SbF_6)_2$ (5.0 mol %), KOAc (2.0 equiv), $AdCO_2H$ (0.1 equiv), MeOH (4.0 mL), 35 °C under air, isolated yield.

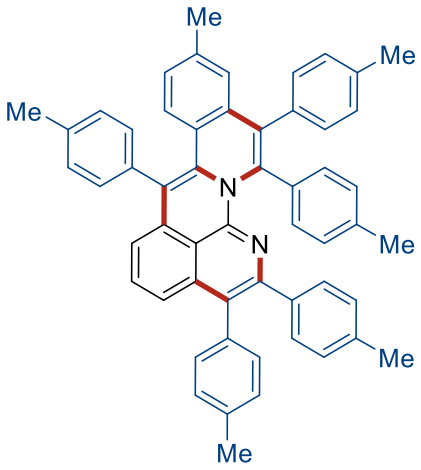
Subsequently, a variety of alkynes **113** was evaluated in the rhodaelectro-catalyzed cascade C–H activations (Table 3.14). Alkynes **113** with electron-donating substituents on the arene motif delivered the desired products **183ab**, **183ac**, and **183ad**. The trimethylsilyl

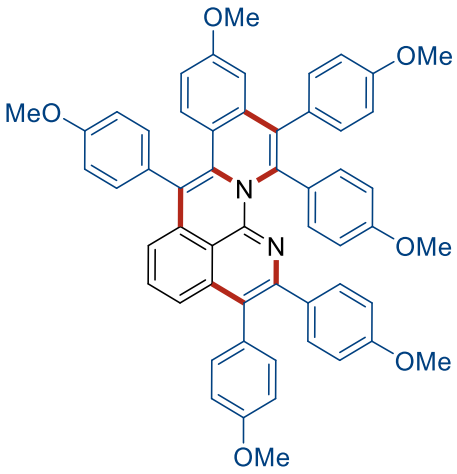
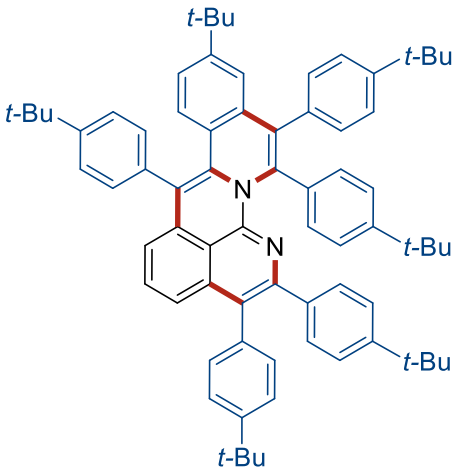
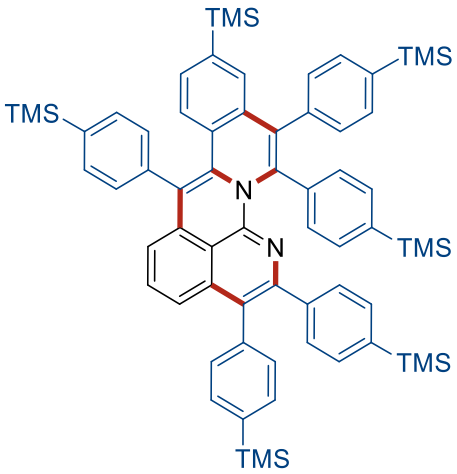
group was well tolerated under the electrolysis conditions, serving as a handle for further transformations, such as Hiyama cross-couplings.[167] The cascade annulative reaction proceeded equally well with *meta*-substituted alkyne **113f**, affording the desired product **183af** in high yield and selectivity. Remarkably, challenging unsymmetrical alkyne **113g** delivered the corresponding product with only two regioisomers and good selectivity.

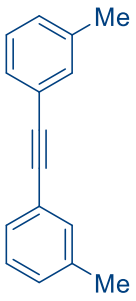
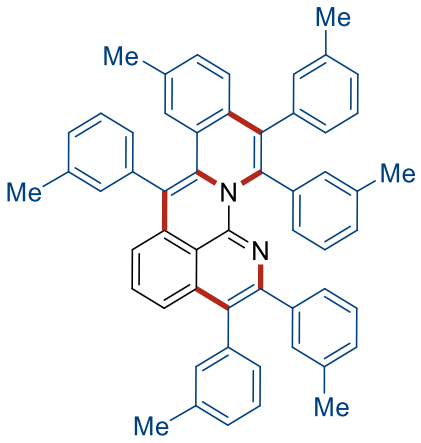
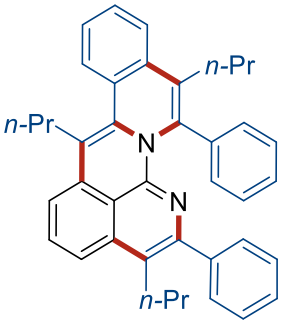
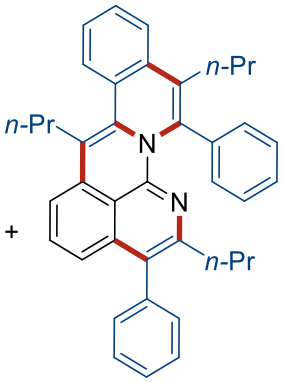
Table 3.14. Rhodaelectro-catalyzed C–H activation with alkyne **113**.



182a **113** **183**

Entry	Substrate	Product	Yield [%]
1	 **113b**	 **183ab**	81

2	 **113c**	 **183ac**	92
3	 **113d**	 **183ad**	45
4	 **113e**	 **183ae**	67

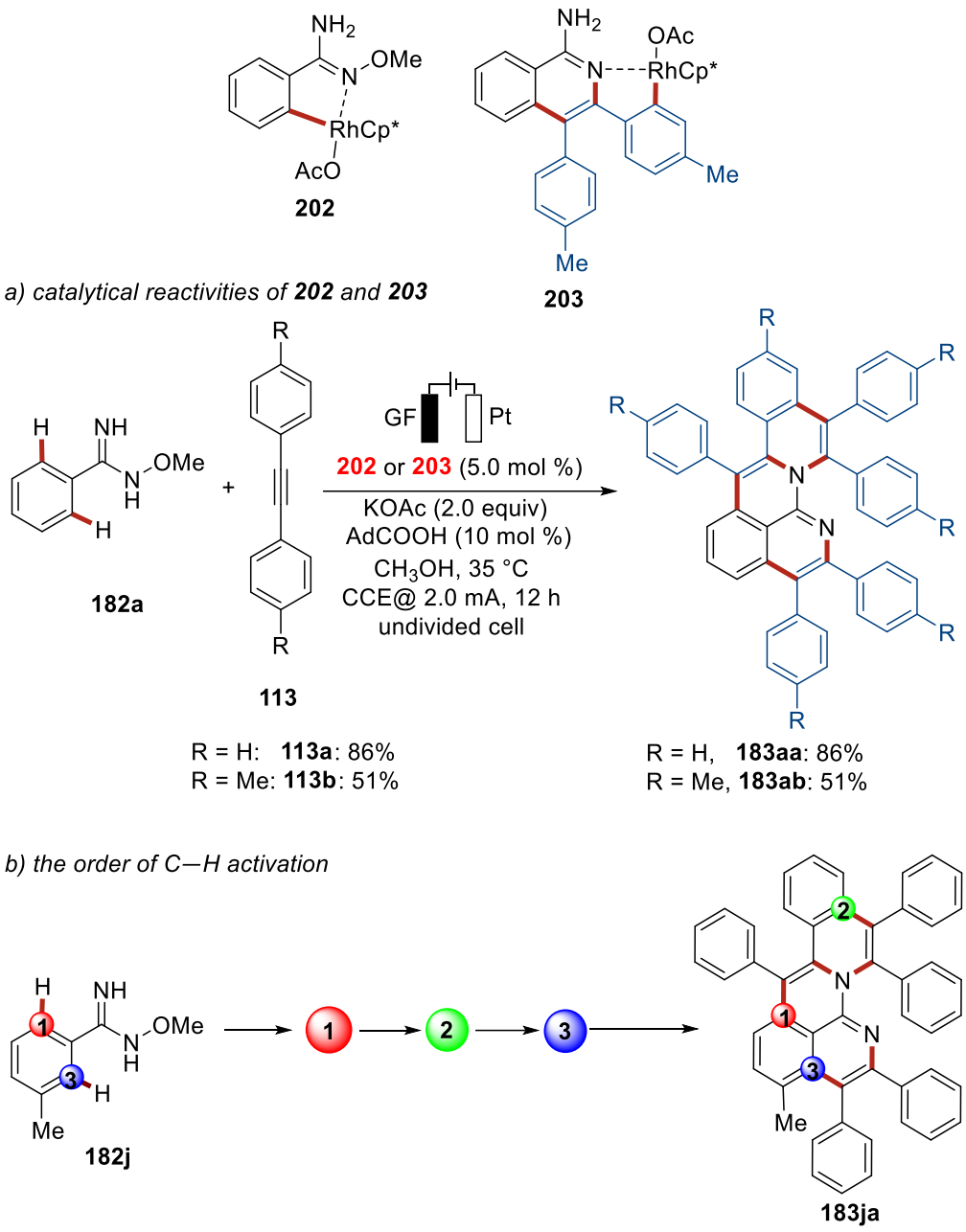
5	 **113f**	 **183af**	71
6	 **113g**	 **183ag** +  **183ag'**	51 (**183ga**) 19 (**183ga**)

[a] Undivided cell, graphite felt anode (GF), platinum plate cathode (Pt), **182a** (0.20 mmol), **113** (0.70 mmol), $[Cp^*Rh(CH_3CN)_3](SbF_6)_2$ (5.0 mol %), KOAc (0.40 mmol, 2.0 equiv), $AdCO_2H$ (0.1 equiv), solvent (4.0 mL), 35 °C under air, isolated yield.

3.3.3 Mechanistic Studies

The high efficacy of the rhodaelectro-catalyzed cascade C–H activation for aza-PAHs synthesis motivated us to delineate its mode of action (Scheme 3.10). Both rhodacycles **202** and **203** showed catalytic reactivity for the electrocatalysis (Scheme 3.10a). This suggested that the three C–H activation steps took place in an order of 1→2→3 (Scheme 3.10b), which was further substantiated by the structure of PAH **183ja** when unsymmetrical substrate **182j** was employed. As *N*-methoxylamide was widely used in rhodium- and ruthenium- catalyzed C–H annulation,[168] a similar pathway might proceed for our new *N*-

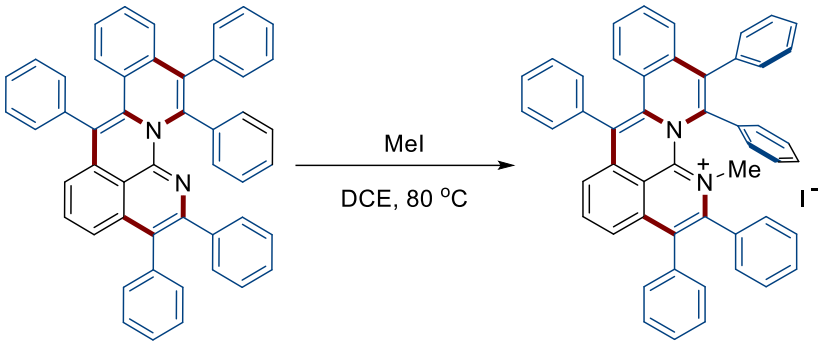
methoxylamide directing group, as N–O bond cleavage was observed on rhodacycle **203** and the products **183**.



Scheme 3.10. mechanistic studies of Rhodaelectro-catalyzed C–H activation with alkyne **113**.

3.3.4 Derivatization of Product 183aa

The obtained aza-PAHs **183** could be easily transformed to valuable functional molecular analogs. Treating aza-PAH **183aa** with iodomethane thus afforded a cationic nitrogen-doped nanographene **204** in 93 % yield (Scheme 3.11).



183aa **204**, 93%

Scheme 3.11. Methylation of **183aa**.

3.4 Rhodaelectro-Catalyzed Switchable Indole Dienylation/ Cyclopropylation

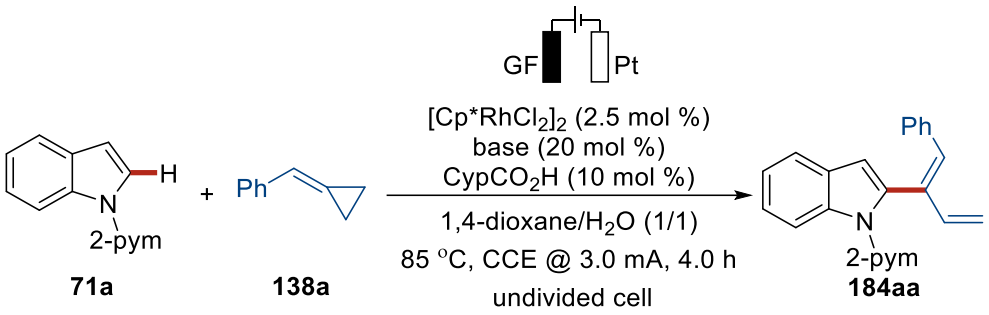
Conjugated dienes and cyclopropanes are key structural motifs in many natural products and drugs.[155, 156] These two structures can easily be transferred to other complex molecules. Rhodium(III) showed strong power in electricity-enabled C–H activations.

3.4.1 Optimization Studies for the Switchable Dienylation and Cyclopropylation

Numerous examples of C–H functionalization of indoles catalysed by rhodium(III) have been reported with the assistance of pyrimidine.[141d] Therefore, we chose 2-indolepyrimidine **71a** as the model substrate and a constant current of 3.0 mA was applied in an undivided cell setup. The optimization for the rhodaelectro-catalyzed dienylation was commenced by testing the effect of different carboxylate salts (Table 3.15). Initially, the commercially available NaOAc was used to give the dienylated product **184a** in good yield with good *Z/E* ratio. The sterically encumbered NaOPiv failed to improve the regioselectivity of this transformation. Aromatic carboxylate salts failed to increase the yield and selectivity of the reaction (entries 3-4). Fortunately, the desired product **184a** was

obtained in 85% yield and 4.5/1 *Z/E* ratio by NaO_2CAd (entry 5). Then, weaker bases were also tested but not give better results (entries 6-7).

Table 3.15. Screening of the bases.[a]



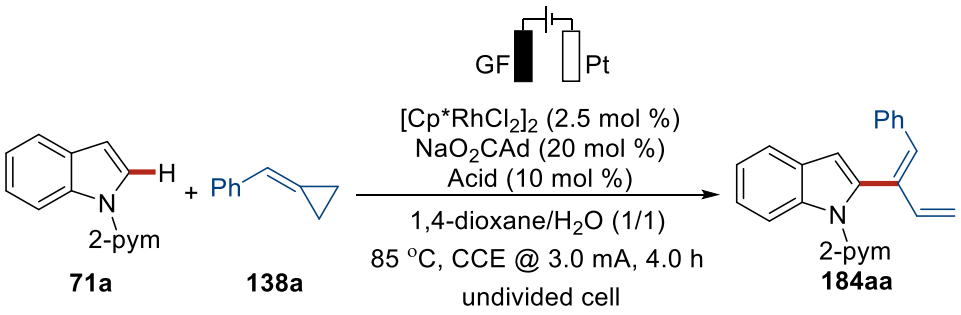
71a **138a** **184aa**

Entry	Base	Yield [%]	*Z/E*
1	NaOAc	72	3.9/1
2	NaOPiv	78	3.5/1
3	NaO_2CMes	60	4.0/1
4	NaO_2CPh	82	3.6/1
5	**NaO_2CAd**	**85**	**4.5/1**
6	NaO_2CCF_3	72	3.5/1
7	NaO_3SCF_3	trace	--

[a] Undivided cell, graphite felt anode (GF), platinum plate cathode, **71a** (0.10 mmol) **138a** (0.16 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), base (20 mol %), $CypCO_2H$ (10 mol %), solvent (4.0 mL), 85 °C, CCE @ 3.0 mA, under air, yield of isolated product, *Z/E* ratio determined by ^1H NMR, $CypCO_2H$ = cyclopentanecarboxylic acid.

Next, we turned to the evaluation of the effect exerted by the acids (Table 3.16). The use of acetic acid showed lower efficiency than $CypCO_2H$ (entries 1-2). Other carboxylic acids with bulkier group also gave similar efficiency (entries 3-4). We also tried stronger carboxylic acids, but reaction efficiency was not improved (entries 5-6).

Table 3.16. Screening of different acids.[a]

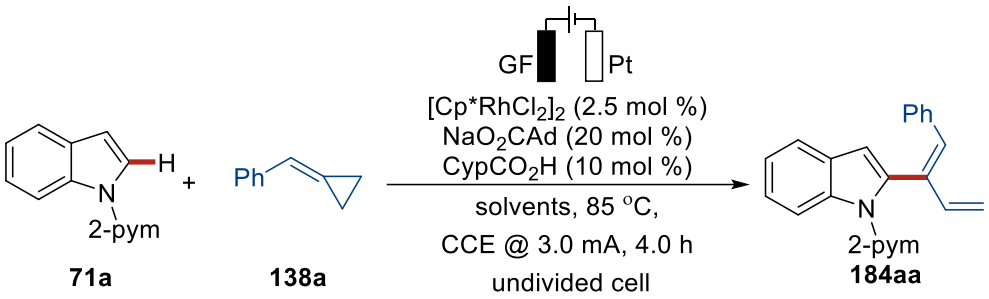


Entry	Acid	Yield [%]	*Z/E*
1	$CypCO_2H$	85	4.5/1
2	AcOH	76	3.6/1
3	PivOH	82	3.3/1
4	$AdCO_2H$	82	4.0/1
5	$PhCO_2H$	79	3.7/1
6	$MesCO_2H$	78	3.8/1

[a] Undivided cell, graphite felt anode (GF), platinum plate cathode (Pt), **71a** (0.10 mmol) **138a** (0.16 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), NaO_2CAd (20 mol %), acid (10 mol %), solvent (4.0 mL), 85 °C, CCE @ 3.0 mA, under air, 4.0 h, yield of isolated product, *Z/E* ratio determined by ^1H NMR.

Then, we resorted to the optimization of different solvents (Table 3.17). The variation of the ratio between 1,4-dioxane and water were conducted, yet not improve the efficiency of the reaction (entries 1-3). Another mixture of solvents *t*-AmOH/H_2O (3/1) (entry 4), often used for the electrochemistry,[144] furnished the dienylated product **184aa** in lower yield and *Z/E* ratio. The electrocatalysis was applicable to water-free system while with lower efficiency (entries 5-6).

Table 3.17. Optimization of solvents.



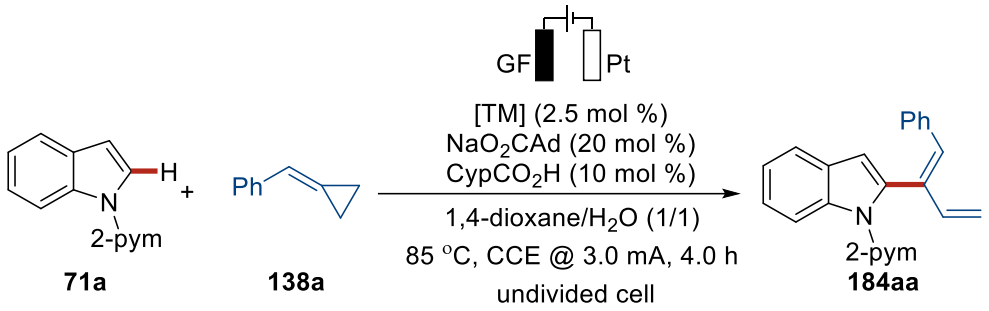
71a **138a** **184aa**

Entry	Solvent	Yield (%)	*Z/E*
1	1,4-dioxane/H_2O (1/1)	85	4.5/1
2	H_2O	trace	--
3	1,4-dioxane/H_2O (2/1)	72	3.4/1
4	*t*-AmOH/H_2O (3/1)	82	2.5/1
5	DMF	trace	--
6	EtOH	74	3.7/1

[a] Undivided cell, graphite felt anode (GF), platinum plate cathode (Pt), **71a** (0.10 mmol) **184a** (0.16 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), base (20 mol %), acid (10 mol %), solvent (4.0 mL), 85 °C, CCE @ 3.0 mA, under air, yield of isolated product, *Z/E* ratio determined by ^1H NMR.

Subsequently, control experiments were conducted (Table 3.18). The absence of the catalyst $[Cp^*RhCl_2]_2$ resulted in no conversion of the starting material (Table 3.20, entry 2). Reactions in the absence of NaO_2CAd or $CpCO_2H$ gave worse results. A low yield was obtained without electricity (entry 5). Other transition metal catalysts were tested, yet failed to assemble the desired product (entries 6-7).

Table 3.18. Control experiments.[a]



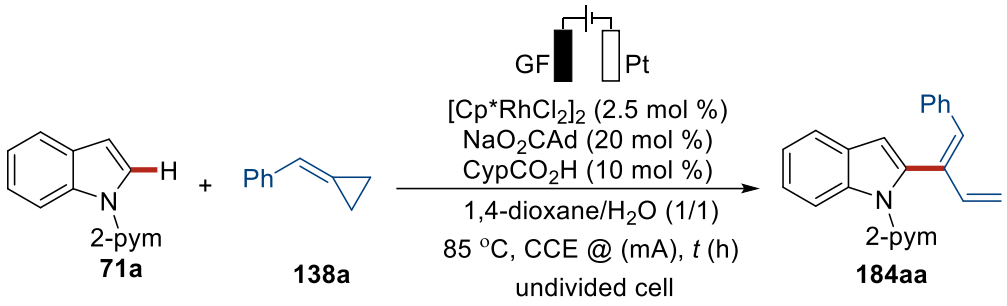
71a **138a** **184aa**

Entry	[TM]	Base	Acid	Yield [%]	*Z/E*
1	$[Cp^*RhCl_2]_2$	NaO_2CAd	$CypCO_2H$	85	4.5/1
2	--	NaO_2CAd	$CypCO_2H$	--	--
3	$[Cp^*RhCl_2]_2$	--	$CypCO_2H$	32	3.2/1
4	$[Cp^*RhCl_2]_2$	NaO_2CAd	--	72	3.6/1
5[b]	$[Cp^*RhCl_2]_2$	NaO_2CAd	$CypCO_2H$	24	2.4/1
6	$[RuCl_2(p\text{-cymene})]_2$	NaO_2CAd	$CypCO_2H$	--	--
7	$Pd(OAc)_2$	NaO_2CAd	$CypCO_2H$	--	--

[a] Undivided cell, graphite felt anode (GF), platinum plate cathode (Pt), **71a** (0.10 mmol) **138a** (0.16 mmol), [M] (2.5 mol %), NaO_2CAd (20 mol %), $CypCO_2H$ (10 mol %), 1,4-Dioxane/H_2O (1/1) (4.0 mL), 85 °C, CCE @ 3.0 mA, under air, yield of isolated product, *Z/E* ratio determined by ^1H NMR. [b] Without electricity, 12 h.

Small variation of the current did not give better results (Table 3.19, entries 2-3). An increased amount of NaO_2CAd displayed better selectivity (entry 4). The C–H dienylation proceeded well at larger scale and higher temperature with the desired product obtained in higher yield and selectivity.

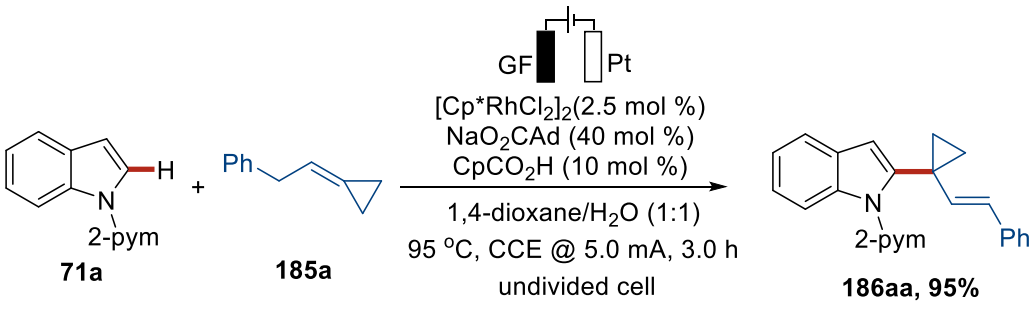
Table 3.19. Further optimization of rhodaelectro-C–H-dienylation.[a]



Entry	Current (mA)	*t* [H]	Yield [%]	*Z/E*
1	3.0	4.0	85	4.5/1
2	2.0	6.0	87	3.8/1
3	4.0	3.0	72	3.2/1
4[b]	3.0	4.0	82	6.0/1
5[b, c]	5.0	3.0	87	6.5/1
6[b, c, d]	5.0	3.0	89	7.0/1

[a] Undivided cell, graphite felt anode (GF), platinum plate cathode (Pt), **71a** (0.10 mmol) **138a** (0.16 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), NaO_2CAd (20 mol %), $CypCO_2H$ (10 mol %), 1,4-dioxane/H_2O (1/1) 4.0 mL, 85 °C, CCE @ 3.0 mA, under air, yield of isolated product, *Z/E* ratio determined by ^1H NMR. [b] NaO_2CAd (40 mol %). [c] reaction performed on 0.2 mmol scale. [d] at 95 °C.

With the optimized reaction conditions for the novel C–H dienylation reaction in hand, a benzyl substituted cyclopropane **185a** was employed (Scheme 3.12), in which a unique direct C–H cyclopropanylated indole **186aa** was formed in high yield without the detection of (*Z*)-conformation.

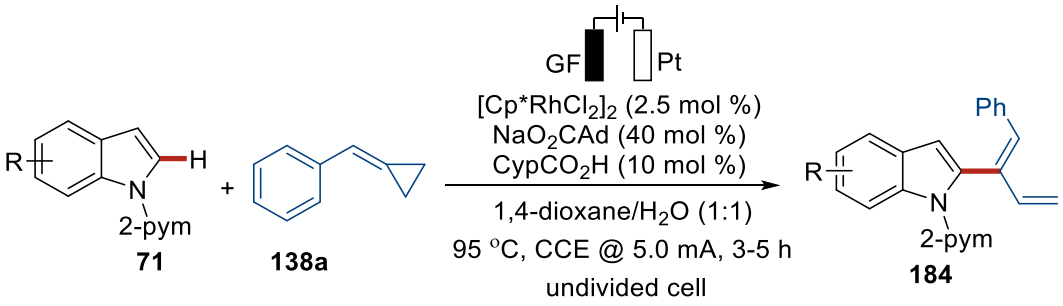


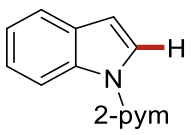
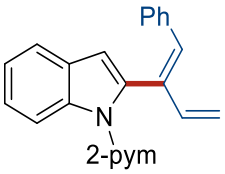
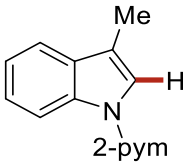
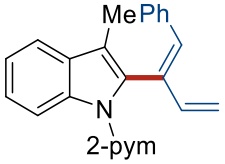
Scheme 3.12. Cyclopropanylation of indole.

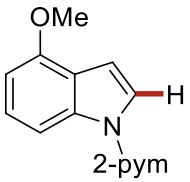
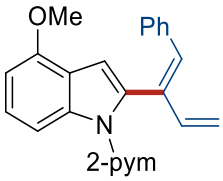
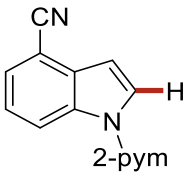
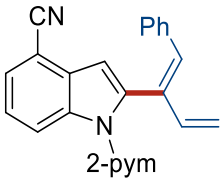
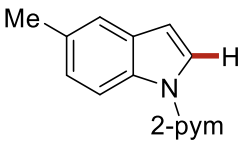
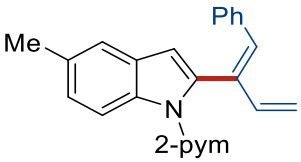
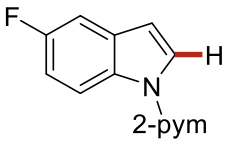
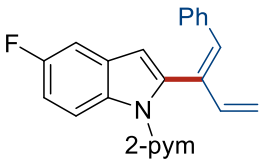
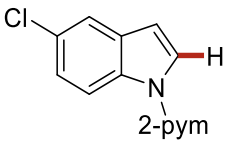
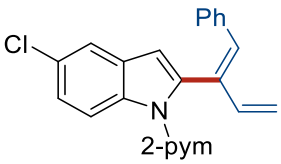
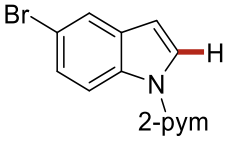
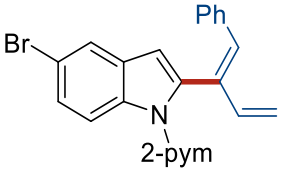
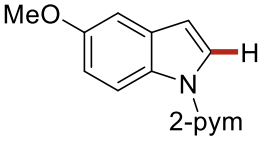
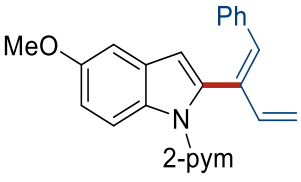
3.4.2 Scope of the Switchable Dienylation and Cyclopropanylation

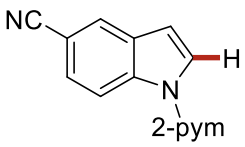
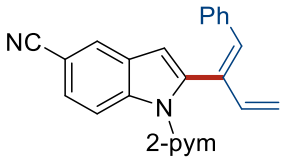
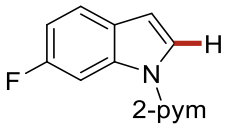
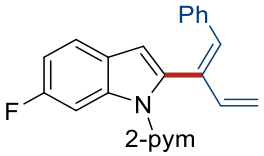
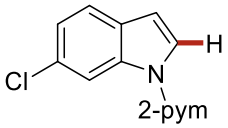
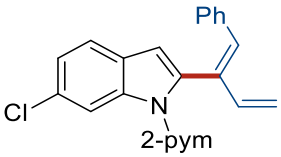
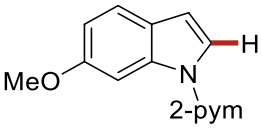
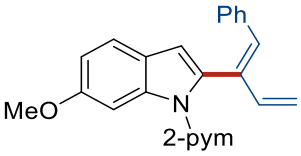
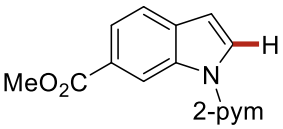
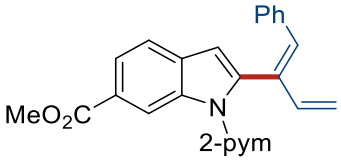
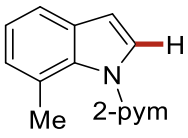
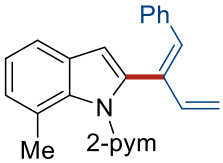
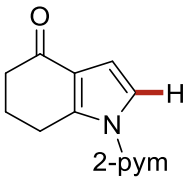
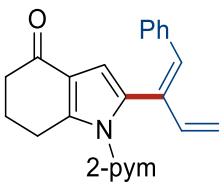
With the optimized reaction conditions for electrochemical C–H dienylations in hand, the versatility was explored with substituted indoles **71** (Table 3.20). Although 3- or 7-methyl indoles delivered the desired products in moderate yields, 3-methyl indole showed much a better selectivity (**184ba, 184oa**). Fluorine and methoxy-substituted indoles **71c** and **71f** were transformed efficiently, while 6-substituted indoles (**184ka**, **184ma**) was converted less efficiently. Various functional group was tolerated, such as chloride, bromide and cyan. Interestingly, indoles **71n** with ester functionality at the 6-position delivered **184na** in high yield and good selectivity. This dienylation protocol was applicable to pyrrole **71p**.

Table 3.20. Electrochemical C–H dienylation of different indoles **71** with **185a**.[a]



Entry	Substrate	Product	Yield [%]	*Z/E*
1	 **71a**	 **184aa**	89	7.0/1
2	 **71b**	 **184ba**	69	9.6/1

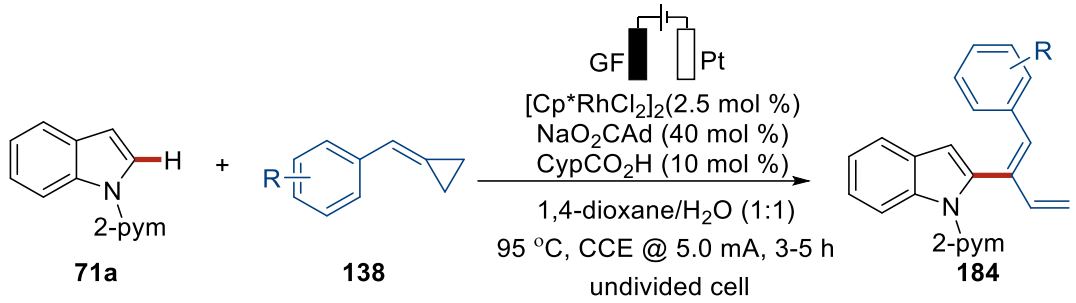
3	 **71c**	 **184ca**	95	3.3/1
4	 **71d**	 **184da**	60	2.0/1
5	 **71e**	 **184ea**	75	8.6/1
6	 **71f**	 **184fa**	71	5.0/1
7	 **71g**	 **184fga**	57	3.6/1
8	 **71h**	 **184ha**	68	6.9/1
9	 **71i**	 **184ia**	84	5.6/1

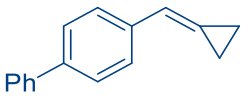
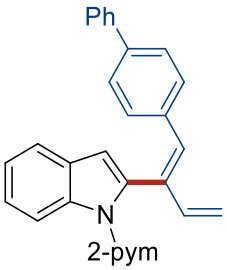
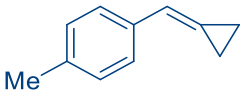
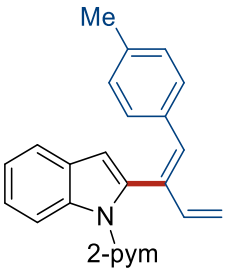
10	 **71j**	 **184ja**	66	3.2/1
11	 **71k**	 **184ka**	62	2.7/1
12	 **71l**	 **184la**	61	2.2/1
13	 **71m**	 **184ma**	61	3.6/1
14	 **71n**	 **184na**	78	3.8/1
15	 **71o**	 **184oa**	61	3.6/1
16	 **71p**	 **184pa**	85	2.0/1

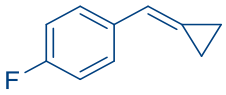
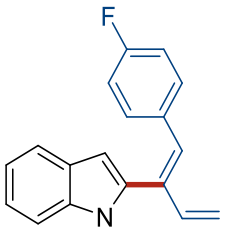
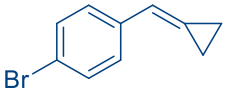
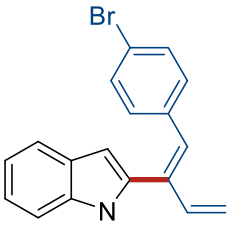
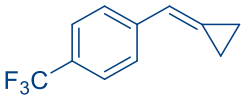
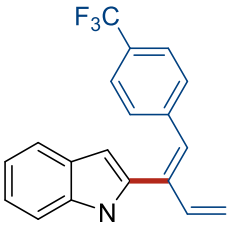
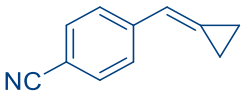
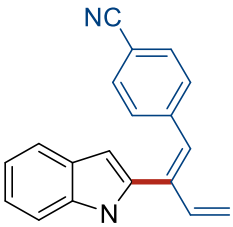
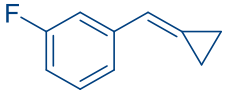
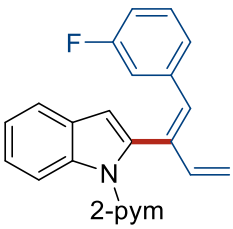
[a] Undivided cell, graphite felt anode (GF), platinum plate cathode (Pt), **71** (0.20 mmol) **138a** (0.32 mmol, 1.6 equiv), $[Cp^*RhCl_2]_2$ (2.5 mol %), NaO_2CAd (40 mol %), $CypCO_2H$ (10 mol %), 1,4-dioxane/H_2O (1:1) 8.0 mL, 95 ºC, CCE @ 5.0 mA, 3-5 h, under air, yield of isolated product, *Z/E* ratio determined by ^1H NMR.

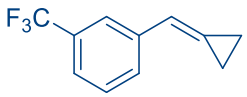
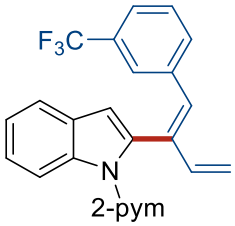
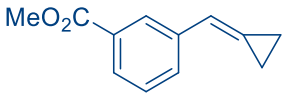
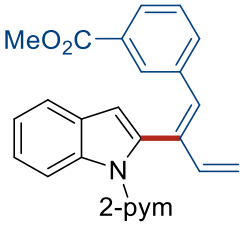
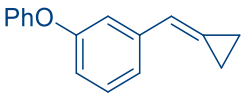
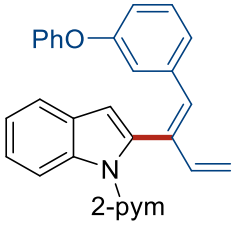
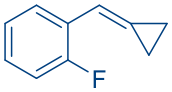
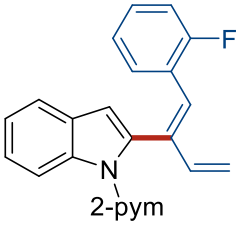
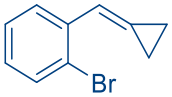
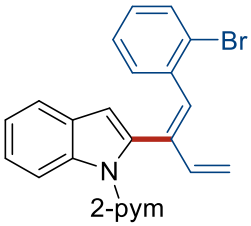
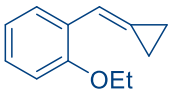
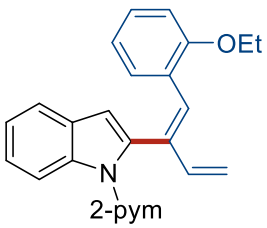
Next, the robustness of the rhodaelectro-catalyzed dienylation was evaluated with a variety of functionalized cyclopropanes **138** (Table 3.21). We found that methy- and phenyl-groups were tolerated by the electrocatalysis (**184ab, 184ac**). Substrates containing the bromo group delivered the products **184ae** and **184am** in good yields but with a lower *Z/E* ratio. Electron-deficient substrates **138i** and **138j** showed a good reactivity in this method in contrast to previous studies[144-147] and electron-rich compounds performed well in this transformation.

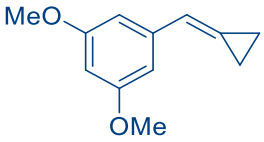
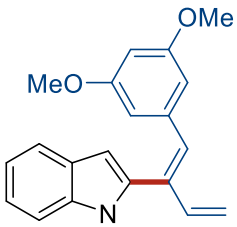
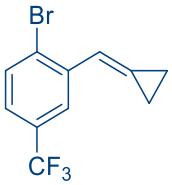
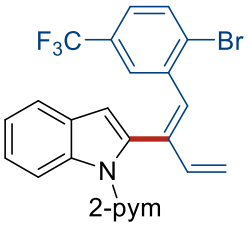
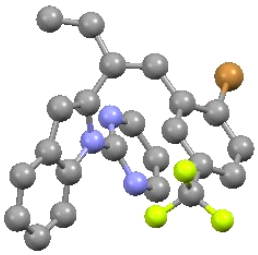
Table 3.21. Electrochemical C–H Dienylation with cyclopropane **138**.[a]



Entry	Substrate	Product	Yield [%]	*Z/E*
1	 **138b**	 **184ab**	81	3.4/1
2	 **138c**	 **184ac**	86	4.7/1

3	 **138d**	 **184ad**	76	5.1/1
4	 **138e**	 **184ae**	60	1.8/1
5	 **138f**	 **184af**	52	3.6/1
6	 **138g**	 **184ag**	90	1.4/1
7	 **138h**	 **184ah**	79	4.4/1

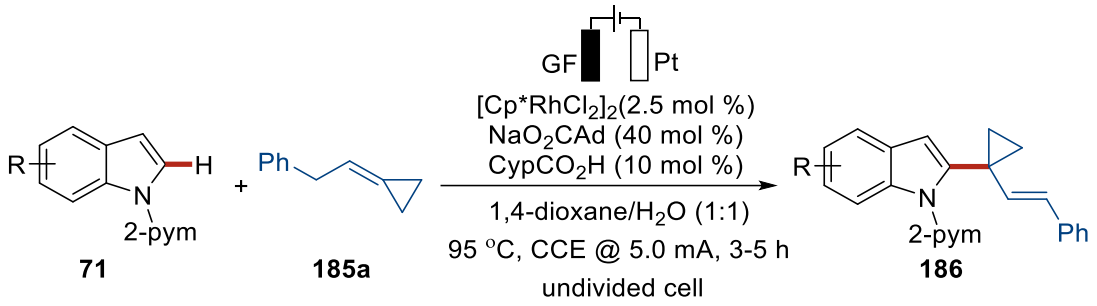
8	 **138i**	 2-pym **184ai**	82	5.7/1
9	 **138j**	 2-pym **184aj**	77	4.5/1
10	 **138k**	 2-pym **184ak**	85	7.0/1
11	 **138l**	 2-pym **184al**	75	4.8/1
12	 **138m**	 2-pym **184am**	61	1.3/1
13	 **138n**	 2-pym **184an**	78	3.0/1

14	 **138o**	 **184ao**	91	3.8/1
15	 **138p**	 **184ap**  CCDC: 2025011	51	10.5/1

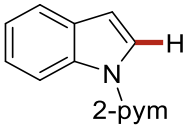
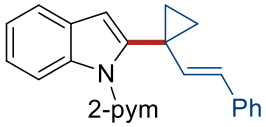
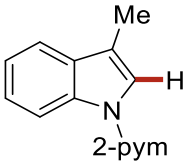
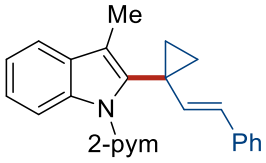
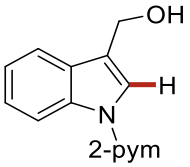
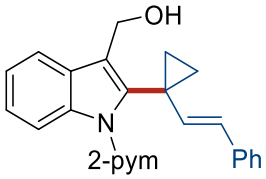
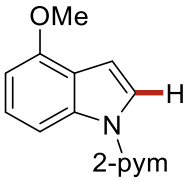
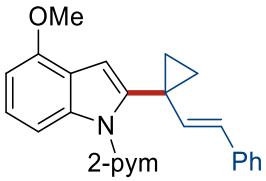
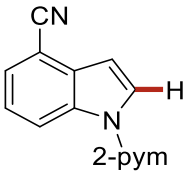
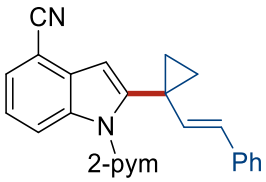
[a] Undivided cell, graphite felt anode (GF), platinum plate cathode (Pt), **71a** (0.20 mmol) **184** (0.32 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), NaO_2CAd (40 mol %), $CypCO_2H$ (10 mol %), 1,4-dioxane/H_2O (1:1) 8.0 mL, 95 ºC, CCE @ 5.0 mA, under air, yield of isolated product, *Z/E* ratio determined by ^1H NMR.

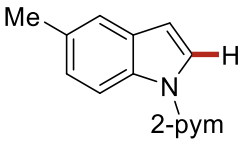
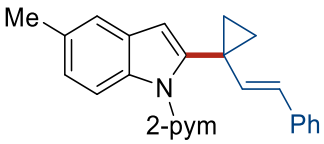
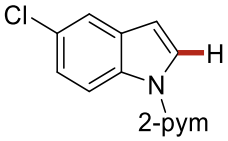
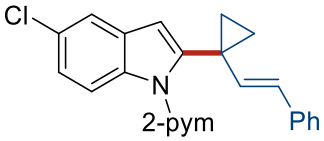
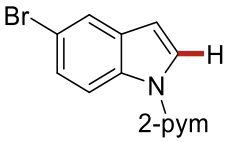
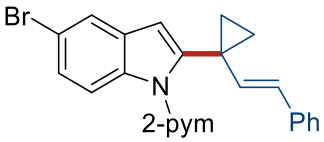
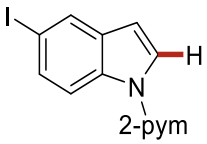
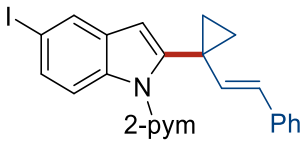
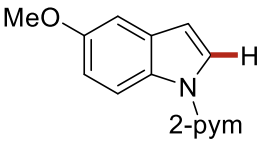
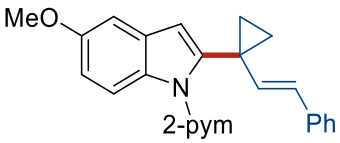
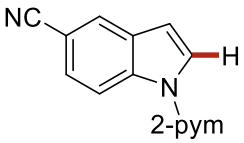
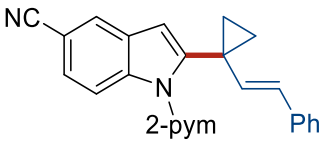
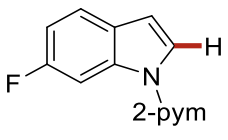
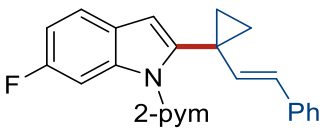
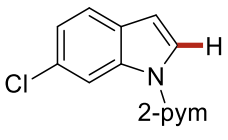
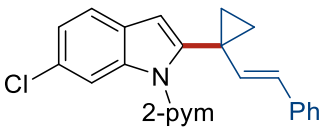
After the evaluation of the scope for the C–H dienylation, we turned to probing the versatility of the unprecedented electrochemical cyclopropylation with functionalized indoles **71** (Table 3.22). We found that a reactive hydroxyl group is tolerated despite the steric hinderance **186qa**. The halogen-containing indoles (**186ga**, **186ha** and **186ra**), even highly reactive iodo, were viable substrates. Indoles containing electron-withdrawing **71d**, **71n** or electron-donating groups **71c**, **71i** were transfered efficiently. For 7-methyl indole, the cyclopropylation showed higher efficiency compared to the dienylation (**186oa**). To our delight, 2-phenyl pyridine could also be employed under the reaction condition though with moderate yield (**186sa**). Interestingly, a tryptamine derived substrate could form the challenging ring-opening product **186ta'**.

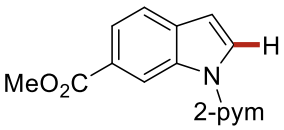
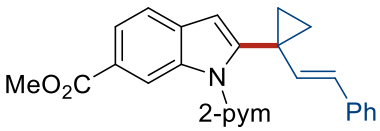
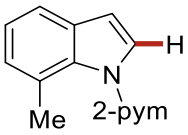
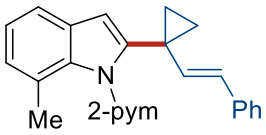
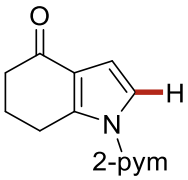
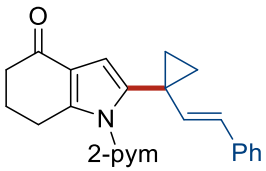
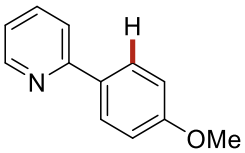
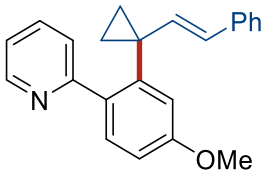
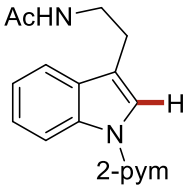
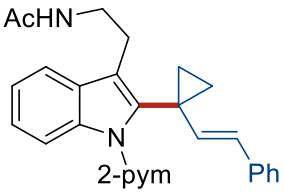
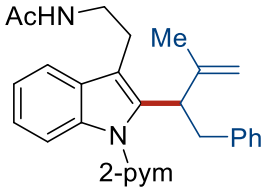
Table 3.22. Electrochemical C–H cyclopropylation of indole **71** with **185a**.



71 **185a** **186**

Entry	Substrate	Product	Yield [%]
1	 **71a**	 **186aa**	95
2	 **71b**	 **186ba**	73
3	 **71q**	 **186qa**	45
4	 **71c**	 **186ca**	75
5	 **71d**	 **186da**	55

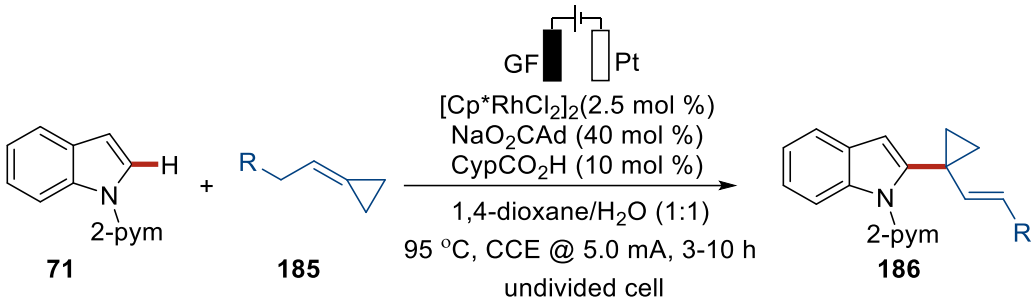
6	 **71e**	 **186ea**	81
7	 **71g**	 **186ga**	73
8	 **71h**	 **186ha**	83
9	 **71r**	 **186ra**	54
10	 **71i**	 **186ia**	84
11	 **71j**	 **186ja**	83
12	 **71k**	 **186ka**	90
13	 **71l**	 **186la**	79

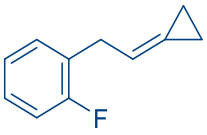
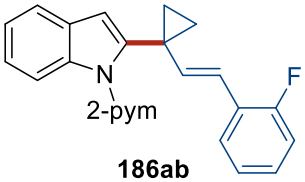
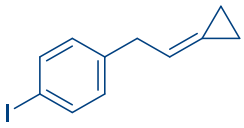
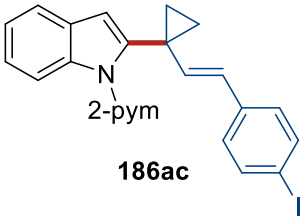
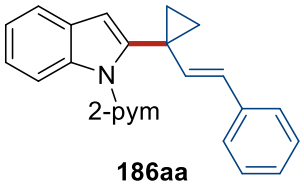
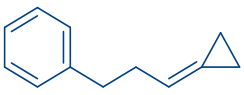
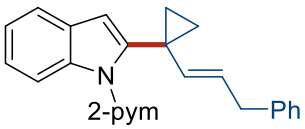
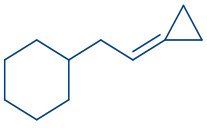
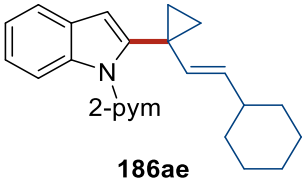
14	 **71n**	 **186na**	79
15	 **71o**	 **186oa**	75
16	 **71p**	 **186pa**	76
17	 **71s**	 **186sa**	41
18	 **71t**	 **186ta** +  **186ta'**	18 34

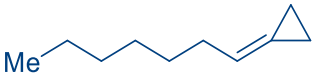
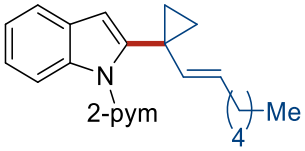
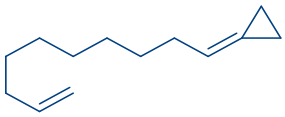
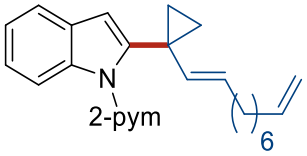
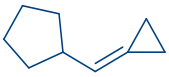
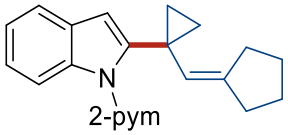
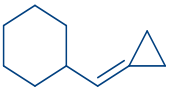
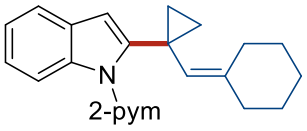
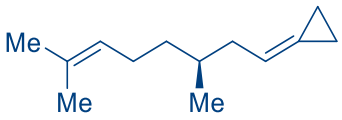
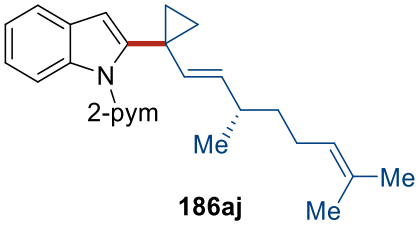
[a] Undivided cell, graphite felt anode (GF), platinum plate cathode (Pt), **71** (0.20 mmol) **185a** (0.32 mmol, 1.6 equiv), $[Cp^*RhCl_2]_2$ (2.5 mol %), NaO_2CAd (40 mol %), $CypCO_2H$ (10 mol %), 1,4-dioxane/H_2O (1:1) 8.0 mL, 95 ºC, CCE @ 5.0 mA, under air, yield of isolated product.

Subsequently a series of cyclopropanes **185** were examined for the C–H cyclopropylation reaction (Table 3.23). A substrate bearing the iodo-substituent gave the desired product **186ac** in moderate yield along with a small amount of the deiodinated product (**186aa/186ac** 1:3). The reaction conditions were compatible with linear or branched-alkyl derived cyclopropanes (**186ad-186af**). The challenging cyclopropane bearing a terminal alkene was also found to be a viable substrate, affording product **186ag** in 79% yield. The transformation was also tolerant for other changes to the backbone of the cyclic alkanes and generated the expected products in moderate yields (**186ah, 186ai**). Indeed, the structurally complex natural product Citronellol-derived starting material could be selectively converted to the desired product **186aj**.

Table 3.23. Electrochemical C–H cyclopropylation with methylenecyclopropanes **185**.[a]



Entry	Substrate	Product	Yield [%]
1	 **185b**	 **186ab**	95
2	 **185c**	 **186ac** +  **186aa**	45 + 15
3	 **185d**	 **186ad**	74
4	 **185e**	 **186ae**	77

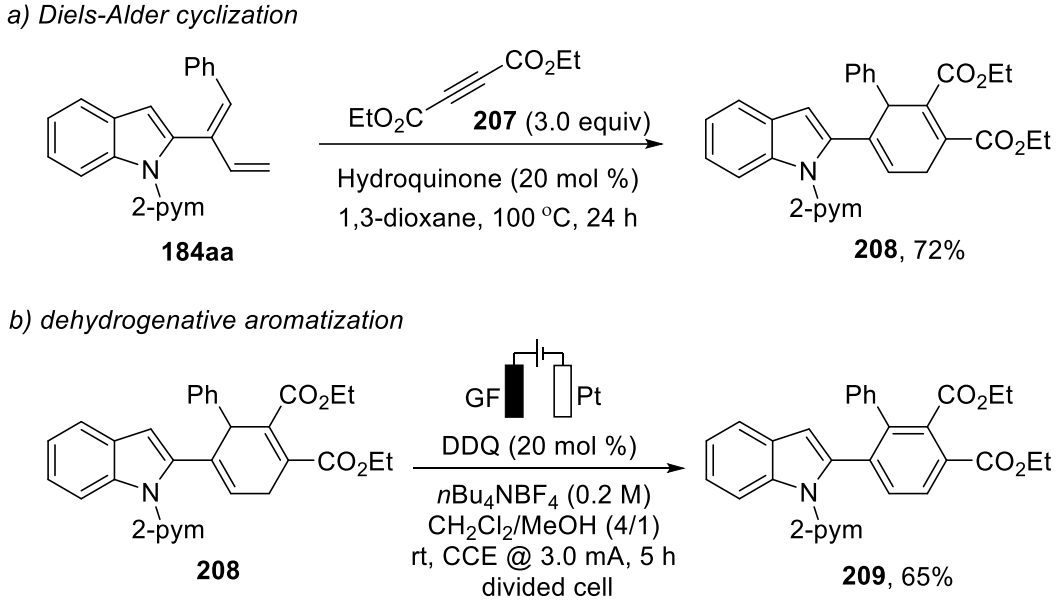
5	 **185f**	 **186af**	63
6	 **185g**	 **186ag**	79
7	 **185h**	 **186ah**	46
8	 **185i**	 **186ai**	83
9	 **185j**	 **186aj**	61

[a] Undivided cell, graphite felt anode (GF), platinum plate cathode (Pt), **71a** (0.20 mmol) **185** (0.32 mmol，1.6 equiv), $[Cp^*RhCl_2]_2$ (2.5 mol %), NaO_2CAd (40 mol %), $CypCO_2H$ (10 mol %), solvent (8.0 mL), 95 °C, CCE @ 5.0 mA, under air, yield of isolated product.

3.4.3 Derivatization of the Diene 184aa

Based on the scope evaluation of both C–H dienylation and C–H cyclopropylation, some transformations of product diene **184aa** were conducted (Scheme 3.13). Thus, a Diels-Alder reaction of dienylated product **184aa** with alkyne **207** was tried for the construction of the 1,4-cyclohexadiene skeleton (Scheme 3.13a). Hydroquinone[169] was confirmed to be a suitable catalyst to produce alkene **208** in good yield. With alkene **208** in hand, we extended the conjugation of the thus-formed product **208** through dehydrogenation of the

diene moiety. Thus, the desired product **209** was obtained in good yield using catalytic amounts of DDQ as the redox mediator at room temperature with CH_2Cl_2 and MeOH as the solvent (Scheme 3.13b).



Scheme 3.13. Derivatization of 1,3-diene **184aa**.

3.4.4 Mechanistic Investigation of Cyclopropylation and Dienylation

Based on a previously reported mechanism,[170] we propose a reasonable catalytic cycle for the C–H cyclopropylation (Figure 3.1) and C–H dienylation (Figure 3.2), respectively. The catalytic cycle is initiated by the formation of a catalytically competent mononuclear Cp*Rh(III) species **210**. As shown in Figure 3.1, coordination by the nitrogen of the pyrimidine indole **71a** to Cp*Rh(III) and the following C–H activation at the 2-position affords rhodacycle **211**. Then, insertion of alkene **185a** occurs to furnish intermediate **212,** which undergoes *β*-H elimination to generate the cyclopropylated product **186aa** along with a rhodium(I) complex.[125a] Finally the Cp*Rh(III) species **210** can be regenerated by reoxidation of rhodium(I) at the anode, generating molecular hydrogen as the byproduct produced at the cathode.

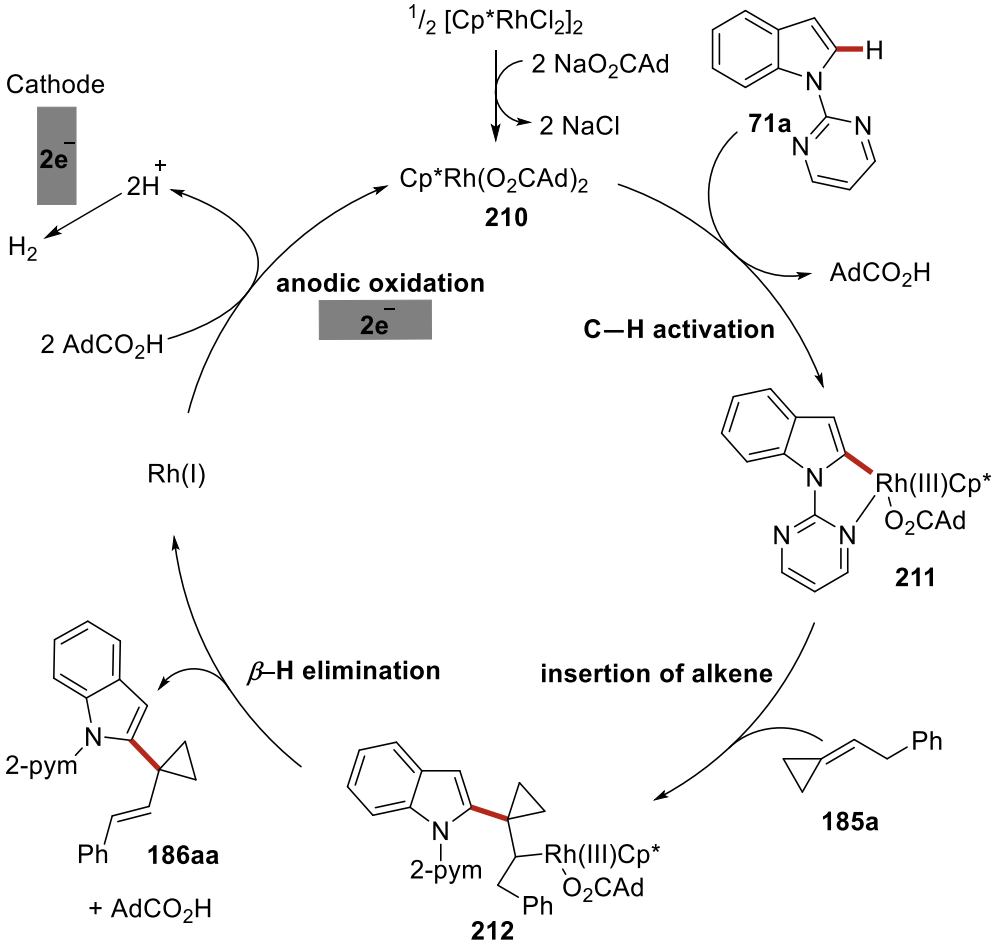


Figure 3.1. Proposed mechanism for rhodaelectro-C–H-cyclopropylation.

In terms of dienylation, the formed intermediate **213** after the insertion of alkene **138a** to rhodacycle **211** can undergo *β*-C elimination to form intermediate **214** as there are no *β*-hydrogens in intermediate **213** (Figure 3.2). The resulted intermediate **214** undergoes *β*-H elimination and delivers the dienylated indole **184aa**.

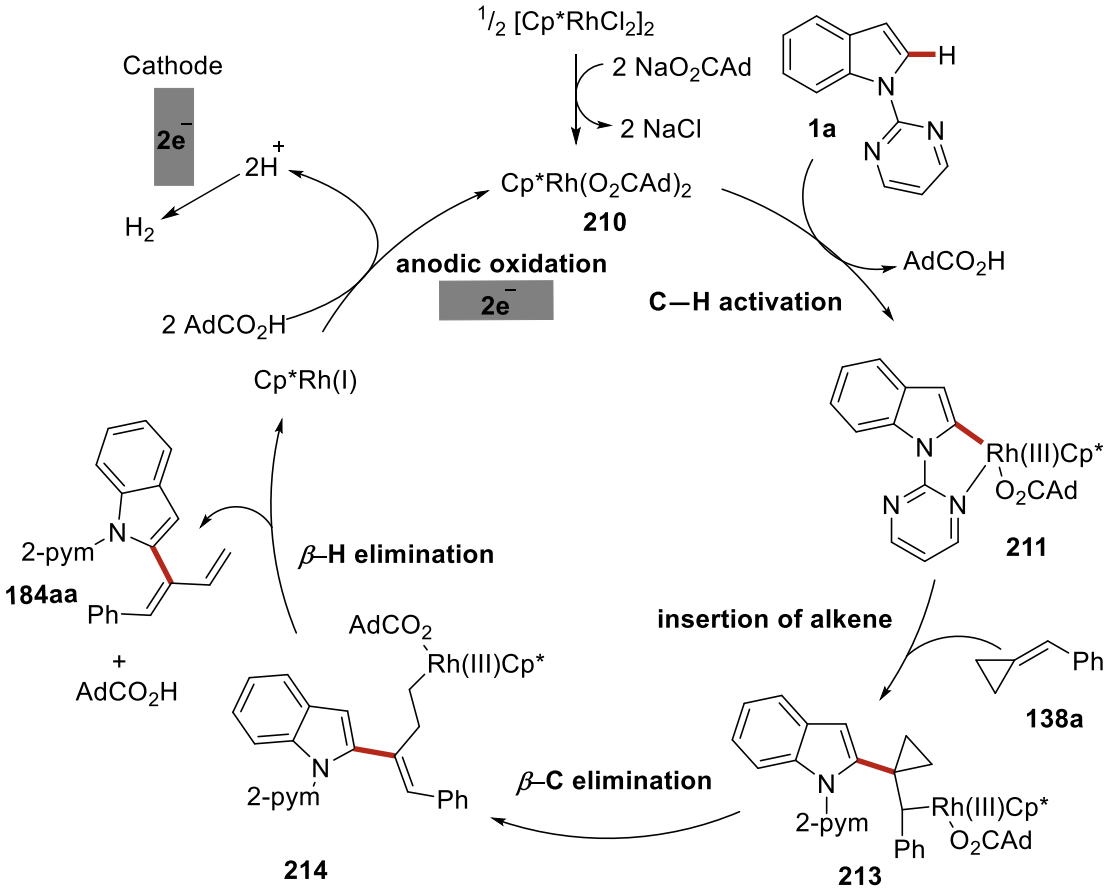
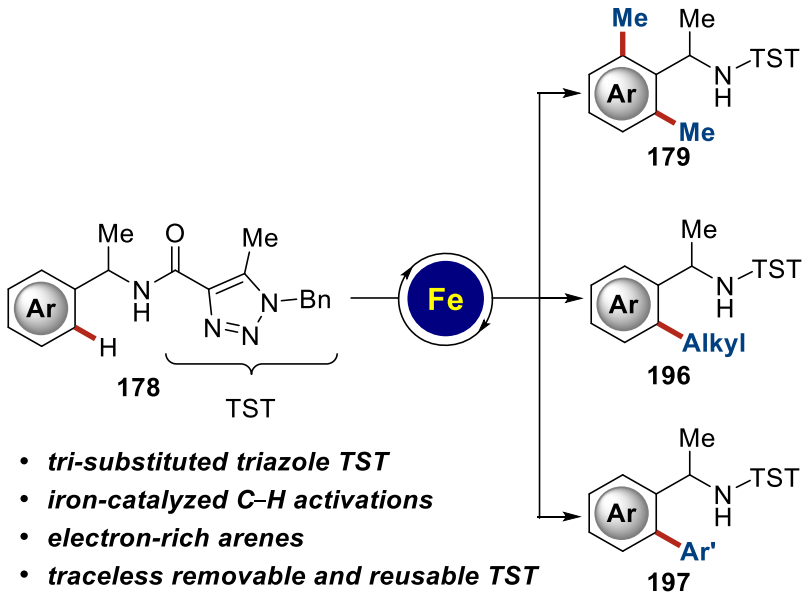


Figure 3.2. Proposed mechanism for rhodaelectro-C–H-dienylation.

4 Summary and Outlook

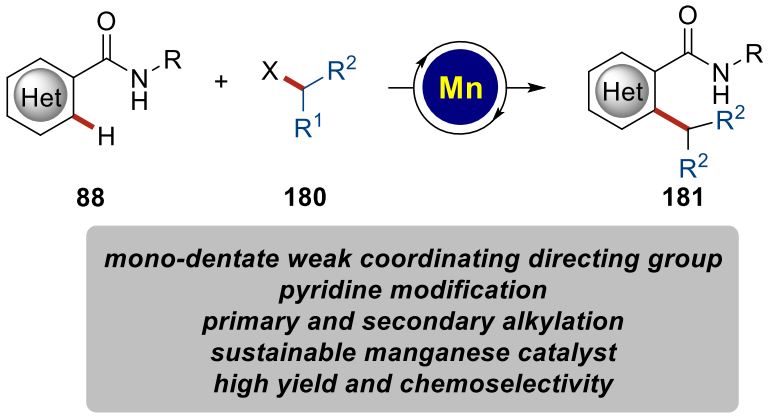
The avoidance of time- and energy-consuming prefunctionalization which generate stoichiometric amounts of waste has made direct functionalization of C–H bonds emerging as an environmentally benign alternative. While major progress was realized with noble transition metal catalysts, the employment of cost-effective and earth-abundant 3d metals has gained significant momentum during the last decade. As stoichiometric amounts of oxidants are often needed for the C–H activation, electricity has been identified as an inexpensive, economical, and environmental benign alternative for chemical redox equivalents. Thus, my projects have focused on both the earth-abundant 3d metals and resource-economic electrochemical C–H bond transformations.

In the first project, we achieved an expedient C–H functionalization of electron-rich benzyl and aryl amines by sustainable iron-catalysis with the assistance of a new fully substituted triazole TST directing group enabling C–H methylations, alkylations and arylations. This transformation featured racemization-free conditions and a newly developed reusable versatile TST group. Due to the magic contributions of methyl group to biological molecules,[149] this method may help to accelerate the discovery of new drugs.



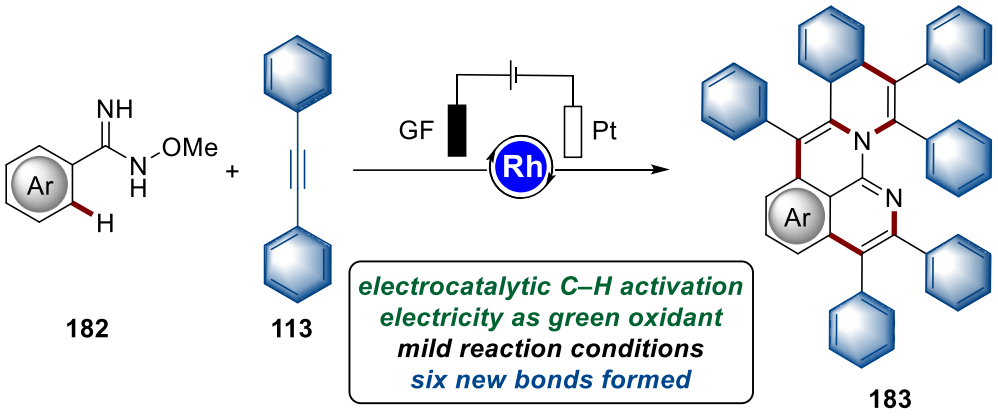
Scheme 4.1. Iron-catalyzed C–H functionalization by TST-assistance.

With the significant progresses in C–H activation, much attention has been paid to the use of weakly-coordinated directing groups and late-stage functionalization of biomolecules. In the second project, we developed a direct *ortho*-alkylation of pyridines by weak assistance of amides. A variety of alkylated pyridines were obtained *via* low-valent manganese-catalyzed alkylations. Mechanistic studies showed that SET-type C–X bond cleavage occurred during the C–H functionalization.



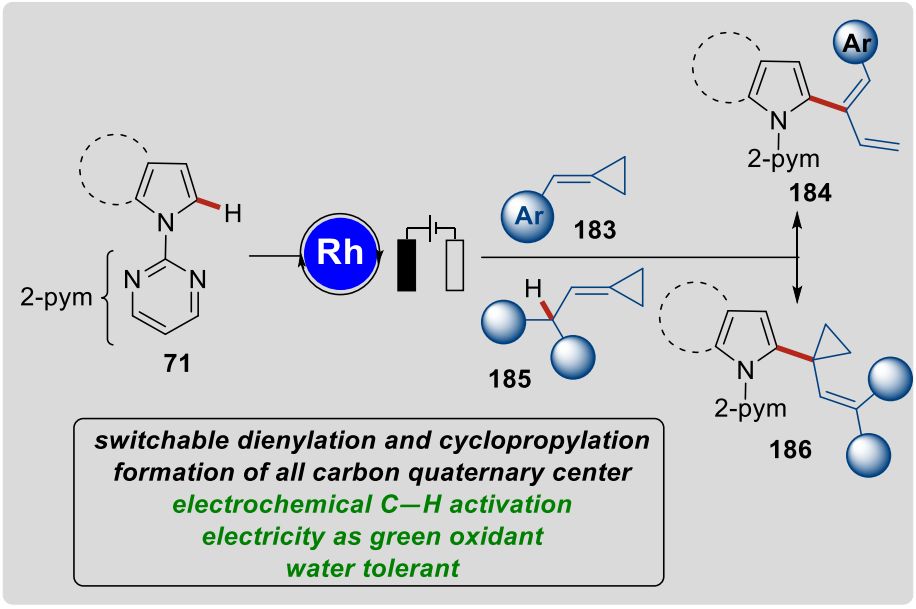
Scheme 4.2. Alkylation of pyridines catalyzed by manganese(II).

In the third project, a modular assembly of aza-PAHs enabled by rhodaelectro-catalyzed cascade C–H functionalization was developed. A multifunctional and transformable *O*-methylamidoxime was designed to guarantee the reactivity and selectivity. The isolation of two C–H-activated rhodacycles offered the proof for sequence of the cascade C–H activation. The electrosynthesis demonstrated broad substrate scope and excellent functional group tolerance, including iodo and azido groups. The practicality of this reaction was reflected by its mild conditions, most user-friendly setup, and easy scale-up.



Scheme 4.3. Rhodaelectro-catalyzed Domino C−H annulations for the assembly of aza-nanographenes.

In the last project, we have developed a bifurcated C–H cyclopropylation and dienylation of indoles by rhodaelectro-catalysis under aqueous conditions, avoiding the use of stoichiometric amounts of chemical oxidants. The reactive catalyst can be regenerated by anodic oxidation, producing hydrogen as the sole byproduct. Thereby, a wealth of indoles can be directly dienylated and cyclopropylated with good chemo-, position- and regioselectivities. Notably, electron-deficient compounds also performed well in this reaction. This method can serve as a new strategy for developing drugs containing cyclopropane motifs.



Scheme 4.4. Rhodaelectro-catalyzed bifurcated indole C−H activation with MCPS.

5 Experimental Section

5.1 General Remarks

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

Vacuum

The used Schlenk line was connected to a Vacuubrand® rotary vane pump. The following pressure was measured at the outlet of the used Schlenk line: 0.1 mbar. The values are not corrected.

Melting points

Melting points were measured by using a Stuart Melting Point Apparatus SMP3 from BarloworldScientific. The given values are not corrected.

Chromatography

Thin layer chromatography (TLC) was performed on Merck, silica gel 60 F254 aluminum TLC plates. Visualization of the substances was achieved by exposure to UV light at 254 nm or by treatment of the plates with a chemical staining agent. Purification by column chromatography refers to flash column chromatography using Merck silica gel, grade 60 (40–63 µm, 230-400 mesh ASTM) and pre-distilled solvents.

Gas Chromatography

Sample analysis and reaction monitoring was performed *via* coupled gas chromatography mass spectrometry on a 7890B GC System from Agilent Technologies coupled with either a 5977A or a 5977B mass detector from Agilent Technologies.

Nuclear Magnetic Resonance Spectroscopy (NMR)

NMR spectra were recorded on Varian VX 300, Bruker Avance 300, Bruker Avance 400 and 500 or Varian Inova 500 and 600 spectrometers in the solvent indicated. Chemical shifts are reported as δ values in ppm. ^{1}H- and ^{13}C-NMR spectra were referenced using the residual solvent signal. The coupling constants *J* are reported in Hertz (Hz).

NMR	^{1}H NMR	^{13}C NMR
CDCl3	7.26	77.16

Abbre*via*tions for the characterization of the signals are: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), m (multiplet) and sbr (broad singlet) or analogous representations. For all spectra, a baseline and phase correction were performed. Mnova 10 from Mestrelab Research was used for the processing and analysis of the spectra.

Mass Spectrometry

Electrospray ionization (ESI) and high-resolution mass spectra (HR-MS) spectra were recorded on either a time-of-flight mass spectrometer micrOTOF (ESI-TOF-MS) or a quadrupole time-of-flight maXis (ESI-QTOF-MS) spectrometer, both from Bruker Daltonic.

Infrared Spectroscopy

Infrared (IR) spectra were recorded on a Bruker Alpha-P ATR spectrometer. Liquid samples were measured as a film and solid samples were measured neat. The spectra were recorded in the range from 4000 to 400 cm⁻1. The analysis was performed using Opus 6 from Bruker. Reported are the most significant peaks and their respective wave numbers (cm^{-1}).

Electrochemistry

Pt electrodes (10 mm × 15 mm × 0.25 mm, 99.9%; obtained from ChemPur®Karlsruhe, Germany) and RVC electrodes (10 mm×15 mm×6 mm, SIGRACELL®GFA 6 EA, obtained from SGL Carbon, Wiesbaden, Germany) were connecteC using stainless steel adapters. Electrolysis was conducteC using an AXIOMET AX-3003P potentiostat in constant current

mode. Divided cells separated by a P4-glassfrit were obtained from Glasgerätebau Ochs Laborfachhandel e. K. (Bovenden, Germany).

Solvents

Solvents used for column chromatography were purified by distillation under reduced pressure prior to use. Solvents purified by a solvent purification system (SPS-800) from M. Braun: dichloromethane, toluene, diethyl ether, tetrahydrofuran, and dimethylformamide. Solvents dried and distilled over sodium with benzophenone as an indicator: toluene, xylenes, mesitylene, 1,4-dioxane, di-*n*-butyl ether, and dimethoxyethane. Solvents dried and distilled over CaH_2: 1,2-dichloroethane, dimethylacetamide, dimethylformamide, dimethylsulfoxide. Solvents dried over molecular sieves and degassed by freeze-pump-thaw cycles: acetonitrile (3 Å). Water was degassed by sparging with N_2 and simultaneous sonification for 2 h.

Reagents

Chemicals obtained from commercial suppliers (with a purity >95%) were used without further purification. The following compounds have been previously reported and were synthesized according to previously described literature protocols:

TST amide **178**,[67] *N*-(1-phenylethyl)picolinamide **178f**,[171] heterocycles azine **88**,[172] imidamides **182**,[147] alkynes **113**,[173] $[Cp^*Rh(CH_3CN)_3](SbF_6)_2$,[174] *N*-Pyrimidyl indoles **71**,[175] methylenecyclopropanes **138** and **185**.[176]

The following chemicals were kindly supplied by the following coworkers:

Karsten Rauch: $[Cp^*RhCl_2]_2$.

Dr. Cuiju Zhu: amides **88**.

5.2 General Procedures

5.2.1 General Procedure A: Iron-catalyzed C–H Methylation

To a schlenk tube charged with amide **178** (0.20 mmol), TMEDA·$ZnCl_2$ (152 mg, 0.60 mmol, 3.0 equiv) and 1.0 mL THF was added MeMgBr (457 μL, 1.4 mmol, 3.0 M in ether, 7.0 equiv) in one portion at room temperature. Five minutes later, dppen (11.9 mg, 0.03 mmol, 15 mmol %) and $FeCl_3$ (4.9 mg, 0.03 mmol, 15 mmol %) were added successively. Stirring at room temperature for another five minutes, 2,3-dichloridebutane was added and the reaction was moved to 65 °C oil bath stirring overnight. Then quenched with sat. aqueous NH_4Cl, diluted with 10 mL water. The aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine and dried over Na_2SO_4. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography on silica gel.

5.2.2 General Procedure B: Iron-catalyzed C–H Arylation

To a schlenk tube charged with amide **178** (0.20 mmol), TMEDA·$ZnCl_2$ (152 mg, 0.60 mmol, 3.0 equiv) and 1.0 mL THF was added ArMgBr (457 μL, 1.0 mmol, 2.0 M in ether, 5.0 equiv) in one portion at room temperature. Five minutes later, dppen (11.9 mg, 0.03 mmol, 15 mmol %) and $FeCl_3$ (4.9 mg, 0.03 mmol, 15 mmol %) were added successively. Stirring at room temperature for another five minutes, 2,3-dichloridebutane was added and the reaction was moved to 65 °C oil bathe stirring overnight. Then quenched with sat. aqueous NH_4Cl, diluted with 10 mL water. The aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine and dried over Na_2SO_4. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography on silica gel.

5.2.3 General Procedure C: Manganese-catalyzed Secondary Alkylation

To a Schlenk tube charged with amide **88** (0.20 mmol), TMEDA (30 µL, 0.20 mmol) $MnCl_2$ (2.7 mg, 0.02 mmol) and THF (0.60 mL), EtMgBr (0.25 mL, 0.70 mmol, 2.8 M in THF) was added dropwise at ambient temperature under N_2 atmosphere. After stirring for 5 min, alkylchloride **2** (0.60 mmol) was added and the reaction mixture stirred at 60 °C for 14 h. Then, saturated aqueous NH_4Cl (5.0 mL) and H_2O (10 mL) were subsequently added to the reaction mixture. The aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic extracts were washed with brine and dried over Na_2SO_4. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography on silica gel.

5.2.4 General Procedure D: Manganese-catalyzed Primary Alkylation

To a Schlenk tube charged with amide **88** (0.20 mmol), TMEDA (60 µL, 0.40 mmol) $MnCl_2$ (5.4 mg, 0.04 mmol) and THF (0.20 mL), *t*-$BuCH_2MgBr$ (0.47 mL, 0.7 mmol, 1.5 M in THF) was added dropwise at ambient temperature under N_2 atmosphere. After stirring for 5 min, alkylchlorides **180** (0.60 mmol) was added and the reaction mixture stirred at 60 °C for 14 h. Then, saturated aqueous NH_4Cl (5.0 mL) and H_2O (10 mL) were subsequently added to the reaction mixture. The aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic extracts were washed with brine and dried over Na_2SO_4. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography on silica gel.

5.2.5 General Procedure E: Rhodaelectro-catalyzed Domino alkyne annulation

The electrocatalysis was carried out in an undivided cell with a graphite felt anode (10 mm × 15 mm × 6 mm) and a Pt cathode (10 mm × 15 mm × 0.25 mm). The cell was charged with imidamide **182** (0.20 mmol), alkyne **113** (0.70 mmol), KOAc (74.4 mg, 0.40 mmol), 1-Adamantanecarboxylic acid ($AdCO_2H$, 3.6 mg, 10 mol %), $[Cp^*Rh(CH_3CN)_3](SbF_6)_2$

(8.4 mg, 5.0 mol %) and MeOH (4.0 mL). Electrocatalysis was performed at 35 °C with a constant current of 2.0 mA maintained for 12 h. The graphite felt anode was washed with CH_2Cl_2 (8 × 5 mL) in an ultrasonic bath. Evaporation of the solvents and subsequent column chromatography on silica gel afforded the corresponding product **183**.

5.2.6 General Procedure F: Rhodaelectro-Catalyzed Dienylation

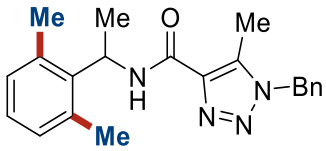
The electrolysis was carried out in an undivided cell with a GF (10 mm x 15 mm x 6 mm) and a Pt cathode (10 mm x 15 mm x 0.25 mm). $[Cp^*RhCl_2]_2$ (3.0 mg, 0.005 mmol, 2.5 mol %), NaO_2CAd (16.0 mg, 0.80 mmol, 40 mol %), cyclopentanecarboxylic acid (2.3 mg, 0.02 mmol, 10 mol %), cyclopropane **138** (0.32 mmol, 1.6 equiv) and indole **71** (0.20 mmol) were dissolved in 1,4-dioxane (4.0 mL) and then H_2O (4.0 mL) was added sequentially. At 95 °C, electrolysis was conducted with a constant current of 5.0 mA for 3 to 10 hours. Then the mixture was transferred to a flask and the electrodes were rinsed with EtOAc (3 x 5.0 mL). The combined solvent was extracted with EtOAc (3 x 10 mL) for three times, combined the organic layer, removed the solvent under reduced pressure and subsequent column chromatography on silica gel (*n*-hexane/EtOAc) yielded the desired product **184.**

5.2.7 General Procedure G: Rhodaelectro-Catalyzed Cyclopropylation

The electrolysis was carried out in an undivided cell with a GF (10 mm x 15 mm x 6 mm) and a platinum cathode (10 mm x 15 mm x 0.25 mm). $[Cp^*RhCl_2]_2$ (3.0 mg, 0.005 mmol, 2.5 mol %), NaO_2CAd (16.0 mg, 0.80 mmol, 40 mol %), cyclopentanecarboxylic acid (2.3 mg, 0.20 mmol, 10 mol %), cyclopropane **185** (0.32 mmol, 1.6 equiv) and indole **71** (0.20 mmol) were dissolved in 1,4-dioxane (4.0 mL) and then water (4.0 mL) was added sequentially. At 95 °C, electrolysis was conducted with a constant current of 4.0 mA for 3 to 10 hours. Then the mixture was transferred to a flask and the electrodes were rinsed with EtOAc (3 x 5.0 mL). The combined solvent was extracted with EtOAc (3 x 10 mL) for three times, combined the organic layer, removed the solvent under reduced pressure and subsequent column chromatography on silica gel (*n*-hexane/EtOAc) yielded the desired product **186.**

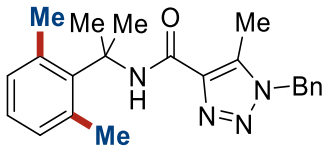
5.3 Iron Catalyzed C–H Activation

5.3.1 Experimental Procedures and Analytical Data



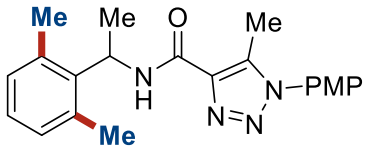
1-Benzyl-*N*-[1-(2,6-dimethylphenyl)ethyl]–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179a)

Prepared following the general procedure **A** by using **178a** (64.0 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179a** (58.9 mg, 86%) as a white solid. **M.p.** = 72–73 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.76 (d, J = 7.7 Hz, 1H), 7.37–7.30 (m, 3H), 7.15–7.12 (m, 2H), 7.06–6.97 (m, 3H), 5.70 (q, J = 7.3 Hz, 1H), 5.49 (s, 2H), 2.54 (s, 6H), 2.46 (s, 3H), 1.61 (d, J = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.2 (C_q), 139.0 (C_q), 138.7 (C_q), 135.9 (C_q), 135.3 (C_q), 134.0 (C_q), 129.4 (CH), 129.0 (CH), 128.4 (CH), 127.0 (CH), 126.7 (CH), 51.8 (CH_2), 45.2 (CH), 21.1 (CH_3), 19.8 (CH_3), 8.8 (CH_3). **IR** (ATR): 3359, 2963, 1650, 1505, 1073, 746, 402 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 371 (100) $[M+Na]^+$, 349 (30) $[M+H]^+$, 217 (10), 133 (5). **HR-MS** (ESI) *m/z* calcd for $C_{21}H_{25}N_4O$ $[M+H]^+$ 349.2028 found 349.2021.



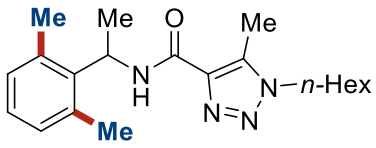
1-Benzyl-*N*-[2-(2,6-dimethylphenyl)propan–2-yl]–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179b)

Prepared following the general procedure **A** by using **178b** (66.4 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179b** (65.3 mg, 89%) as a colorless liquid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.61 (brs, 1H), 7.38–7.31 (m, 3H), 7.17–7.14 (m, 2H), 6.99–6.97 (m, 3H), 5.49 (s, 2H), 2.52 (s, 6H), 2.43 (s, 3H), 1.97 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 159.3 (C_q), 143.0 (C_q), 139.2 (C_q), 136.0 (C_q), 135.4 (C_q), 134.1 (C_q), 131.8 (CH), 129.1 (CH), 128.5 (CH), 127.2 (CH), 126.2 (CH), 58.7 (C_q), 51.8 (CH_2), 30.5 (CH_3), 25.6 (CH_3), 8.8 (CH_3). **IR** (ATR): 3342, 2983, 1657, 1503, 1257, 604, 573 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 385 (100) $[M+Na]^+$, 363 (80) $[M+H]^+$, 257 (50), 217 (55), 200 (25). **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{27}N_4O$ $[M+H]^+$ 363.2185 found 363.2180.



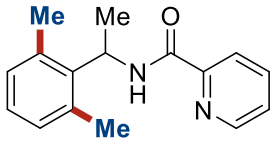
***N*-[1-(2,6-dimethylphenyl)ethyl]-1-(4-methoxyphenyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179c)**

Prepared following the general procedure **A** by using **178c** (67.2 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179c** (65.3 mg, 89%) as a yellow solid. **M.p.** = 104–106 °C.**^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.81 (d, *J* = 7.7 Hz, 1H), 7.36–7.31 (m, 2H), 7.07–6.98 (m, 5H), 5.73 (q, *J* = 7.3 Hz, 1H), 3.88 (s, 3H), 2.56 (s, 6H), 2.55 (s, 3H), 1.64 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.45 (C_q), 160.24 (C_q), 139.00 (C_q), 138.20 (C_q), 136.57 (C_q), 135.31 (C_q), 129.4 (CH), 128.4 (C_q), 126.7 (CH), 126.5 (CH), 114.6 (CH), 55.6 (CH_3), 45.3 (CH), 21.1 (CH_3), 19.8 (CH_3), 9.7 (CH_3). **IR** (ATR): 3417, 2974, 1664, 1509, 1254, 766, 589 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 387 (65) $[M+Na]^+$, 365 (100) $[M+H]^+$, 233 (70), 188 (2), 133 (65). **HR-MS** (ESI) *m/z* calcd for $C_{21}H_{25}N_4O_2$ $[M+H]^+$ 365.1978 found 365.1972.



***N*-[1-(2,6-dimethylphenyl)ethyl]-1-hexyl–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179d)**

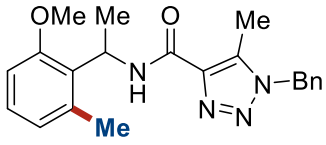
Prepared following the general procedure **A** by using **178d** (62.9 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179d** (48.1 mg, 70%) as a yellow liquid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.74 (d, *J* = 7.3 Hz, 1H), 7.05–6.96 (m, 3H), 5.70 (p, *J* = 7.3 Hz, 1H), 4.23 (t, *J* = 7.2 Hz, 2H), 2.56 (s, 3H), 2.54 (s, 6H), 1.91–1.78 (m, 2H), 1.60 (d, *J* = 7.3 Hz, 3H), 1.34–1.26 (m, 6H), 0.88 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.3 (C_q), 139.0 (C_q), 138.1 (C_q), 135.3 (C_q), 129.4 (CH), 126.7 (CH), 47.8 (CH_2), 45.2 (CH), 31.2 (CH_2), 29.7 (CH_2), 26.1 (CH_2), 22.4 (CH_2), 21.0 (CH_3), 19.7 (CH_3), 13.9 (CH_3), 8.7 (CH_3). **IR** (ATR): 3425, 2927, 1666, 1503, 1209, 772, 562 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 365 (100) $[M+Na]^+$, 343 (60) $[M+H]^+$, 211 (30), 133 (20). **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{31}N_4O$ $[M+H]^+$ 343.2498 found 343.2492.



***N*-(1-(2,6-Dimethylphenyl)ethyl)picolinamide (179f)**

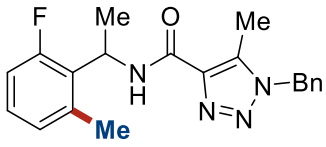
Prepared following the general procedure **A** by using **178f** (62.9 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **179f** (26.7 mg, 51%) as a colorless liquid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.57 (d, *J* = 6.4 Hz, 1H), 8.48 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 1H), 8.08 (td, *J* = 7.7, 0.9 Hz, 1H), 7.75 (td, *J* = 7.7, 1.7 Hz, 1H), 7.33 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 1H), 6.99–6.90 (m, 3H), 5.72–5.62 (m, 1H), 2.48 (s, 6H), 1.57 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 163.2 (C_q), 150.0 (C_q), 148.1 (CH), 139.5 (C_q), 137.3 (CH), 135.54 (C_q), 129.5 (CH), 126.9 (CH), 126.0 (CH), 122.2 (CH), 45.6 (CH), 21.0 (CH_3), 19.7 (CH_3). **IR** (ATR): 3402, 2997, 1679, 1497, 991, 740, 560 cm^{-1}. **MS** (ESI)

m/z (relative intensity) 277 (100) $[M+Na]^+$, 255 (40) $[M+H]^+$, 123 (30). **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{19}N_2O$ $[M+H]^+$ 255.1497 found 255.1492.



1-Benzyl-*N*-[1-(2-methoxy-6-methylphenyl)ethyl]–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179g)

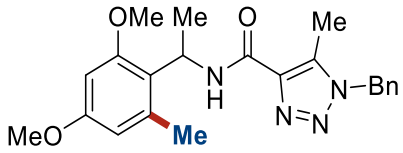
Prepared following the general procedure **A** by using **178g** (70.2 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179g** (64.3 mg, 88%) as a colorless liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.67 (d, *J* = 9.6 Hz, 1H), 7.34–7.27 (m, 3H), 7.14–7.08 (m, 3H), 6.80–6.77 (m, 2H), 5.74 (q, *J* = 7.0 Hz, 1H), 5.48 (s, 2H), 3.96 (s, 3H), 2.48 (s, 3H), 2.47 (s, 3H), 1.55 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 160.2 (C_q), 158.1 (C_q), 139.2 (C_q), 136.3 (C_q), 135.9 (C_q), 134.2 (C_q), 129.1 (C_q), 129.0 (CH), 128.4 (CH), 127.6 (CH), 127.1 (CH), 123.2 (CH), 109.3 (CH), 55.5 (CH_3), 51.7 (CH_2), 43.1 (CH), 20.2 (CH_3), 20.0 (CH_3), 8.7 (CH_3). **IR** (ATR): 3415, 2847, 1664, 1587, 1244, 7330, 581 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 387 (100) $[M+Na]^+$, 365 (40) $[M+H]^+$, 217 (15). **HR-MS** (ESI) *m/z* calcd for $C_{21}H_{25}N_4O_2$ $[M+H]^+$ 365.1978 found 365.1973.



1-Benzyl-*N*-[1-(2-fluoro-6-methylphenyl)ethyl]–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179h)

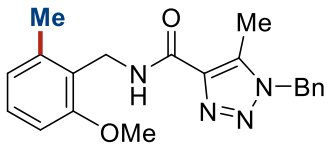
Prepared following the general procedure **A** by using **178h** (67.7 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179h** (60.8 mg, 86%) as a white solid. **M.p.** = 92–94 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.97 (d, *J* = 9.0 Hz, 1H),

7.34–7.27 (m, 3H), 7.14–7.06 (m, 3H), 6.93–6.87 (m, 2H), 5.68–5.60 (m, 1H), 5.48 (s, 2H), 2.51 (s, 3H), 2.46 (s, 3H), 1.60 (dd, *J* = 7.1, 1.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* = 162.1 (d, $^1J_{C–F}$ = 244.3 Hz, C_q),160.4 (C_q), 138.7 (C_q), 137.4 (d, ^4J = 5.0 Hz, C_q), 136.0 (C_q), 134.1 (C_q), 129.0 (CH), 128.7 (d, $^3J_{C–F}$ = 11.4 Hz, C_q),128.4 (CH), 128.0 (d, $^4J_{C–F}$ = 9.8 Hz, CH), 127.1 (CH), 126.1 (d, $^4J_{C–F}$ = 2.6 Hz, CH), 113.9 (d, $^2J_{C–F}$ = 22.6 Hz, CH), 51.7 (CH_2), 42.6 (CH), 20.5 (d, $^4J_{C–F}$ = 3.0 Hz, CH_3), 19.6 (d, $^4J_{C–F}$ = 2.5 Hz, CH_3), 8.7 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* = –116.8 (dd, *J* = 11.4, 5.6 Hz). **IR** (ATR): 3425, 2927, 1667, 1507, 1252, 730, 579 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 375 (100) $[M+Na]^+$, 353 (50) $[M+H]^+$, 217 (40), 137 (10). **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{22}FN_4O$ $[M+H]^+$ 353.1778 found 353.1772.



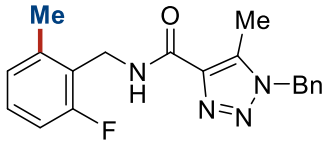
1-Benzyl-*N*-[1-(3,6-dimethoxy–2-methylphenyl)ethyl]–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179i)

Prepared following the general procedure **A** by using **178i** (76.0 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179i** (63.2 mg, 80%) as a colorless liquid. **^{1}H NMR** (300 MHz, $CDCl_3$) *δ* = 8.58 (d, *J* = 9.6 Hz, 1H), 7.33–7.28 (m, 3H), 7.13–7.10 (m, 2H), 6.34 (dd, *J* = 20.2, 2.4 Hz, 2H), 5.66 (q, *J* = 7.0 Hz, 1H), 5.47 (s, 2H), 3.93 (s, 3H), 3.76 (s, 3H), 2.47 (s, 3H), 2.44 (s, 3H), 1.52 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) *δ* = 156.0 (C_q), 159.0 (C_q), 158.9 (C_q), 139.1 (C_q), 136.9 (C_q), 135.7 (C_q), 134.1 (C_q), 128.9 (CH), 128.3 (CH), 127.0 (CH), 121.8 (C_q), 106.9 (CH), 97.1 (CH), 55.5 (CH_3), 55.2 (CH_3), 51.7 (CH_2), 42.8 (CH), 20.6 (CH_3), 20.5 (CH_3), 8.8 (CH_3). **IR** (ATR): 3416, 2934, 1661, 1503, 1262, 1153, 731, 461 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 417 (100) $[M+Na]^+$, 395 (70) $[M+H]^+$, 243 (80), 217 (10), 179 (30). **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{27}N_4O$ $[M+H]^+$ 395.2083 found 395.2078.



1-Benzyl-*N*-(2-methoxy-6-methylbenzyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179j)

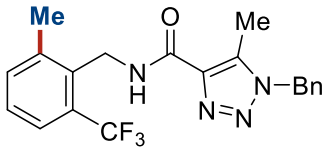
Prepared following the general procedure **A** by using **178j** (67.3 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179j** (63.2 mg, 90%) as a white solid. **M.p.** = 83–85 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.56 (t, *J* = 5.6 Hz, 1H), 7.35–7.28 (m, 3H), 7.18–7.10 (m, 3H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.75 (d, *J* = 8.3 Hz, 1H), 5.47 (s, 2H), 4.67 (d, *J* = 5.6 Hz, 2H), 3.88 (s, 3H), 2.50 (s, 3H), 2.47 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.7 (C_q), 158.2 (C_q), 138.9 (C_q), 138.1 (C_q), 135.8 (C_q), 134.0 (C_q), 128.9 (CH), 128.3 (CH), 128.2 (CH), 127.0 (CH), 124.4 (C_q), 122.7 (CH), 108.0 (CH), 55.5 (CH_3), 51.7 (CH_2), 34.6 (CH_2), 19.6 (CH_3), 8.8 (CH_3). **IR** (ATR): 3423, 2930, 1664, 1511, 1261, 731, 459 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 373 (100) $[M+Na]^+$, 351 (65) $[M+H]^+$, 211 (10). **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{23}N_4O_2$ $[M+H]^+$ 351.1821 found 351.1816.



1-Benzyl-*N*-(2-fluoro-6-methylbenzyl)-5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179k)

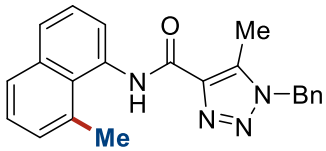
Prepared following the general procedure **A** by using **178k** (65.3 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179k** (62.3 mg, 92%) as a white solid. **M.p.** = 107–110 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.38–7.29 (m, 4H), 7.17–7.11 (m, 3H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.91 (t, *J* = 9.0 Hz, 1H), 5.48 (s, 2H), 4.67 (dd, *J* = 5.7, 1.7 Hz, 2H), 2.50 (s, 3H), 2.45 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 161.9 (d, $^1J_{C–F}$ = 245.7 Hz, C_q), 160.9 (C_q), 139.5 (d, $^4J_{C–F}$ = 3.5 Hz, C_q), 138.6 (C_q), 136.1 (C_q), 134.0 (C_q), 129.0 (CH), 128.9 (d, $^4J_{C–F}$ = 9.3 Hz, CH), 128.4 (CH), 127.1 (CH), 126.0 (d,

$^4J_{C–F}$ = 3.0 Hz, CH), 123.1 (d, $^3J_{C–F}$ = 14.3 Hz, C_q), 112.9 (d, $^2J_{C–F}$ = 22.5 Hz, CH), 51.7 (CH_2), 33.6 (d, $^4J_{C–F}$ = 5.3 Hz, CH_2), 19.1 (d, $^4J_{C–F}$ = 2.6 Hz, CH_3), 8.7 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$) δ = –118.0 (ddt, J = 9.6, 7.6, 1.7 Hz). **IR** (ATR): 3338, 2961, 1666, 1512, 1253, 730, 459 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 361 (100) $[M+Na]^+$, 339 (60) $[M+H]^+$, 205 (15), 149 (10). **HR-MS** (ESI) *m/z* calcd for $C_{19}H_{20}FN_4O$ $[M+H]^+$ 339.1621 found 339.1616.



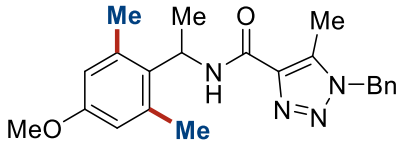
1-Benzyl–5-methyl-*N*-[2-methyl-6-(trifluoromethyl)benzyl]-1*H*-1,2,3-triazole-4-carboxamide (179l)

Prepared following the general procedure **A** by using **178l** (75.0 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179l** (62.1 mg, 80%) as a white solid. **M.p.** = 81–82 °C.**^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.54 (d, J = 7.7 Hz, 1H), 7.40 (d, J = 7.2 Hz, 1H), 7.36–7.29 (m, 4H), 7.17–7.12 (m, 3H), 5.48 (s, 2H), 4.78 (d, J = 5.3 Hz, 2H), 2.52 (s, 3H), 2.45 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 160.7 (C_q), 140.2 (C_q), 138.4 (C_q), 136.2 (C_q), 134.5 (CH), 134.0 (C_q), 133.4 (d, ^3J = 1.3 Hz, C_q), 129.9 (q, ^2J = 29.4 Hz, C_q), 129.0 (CH), 128.5 (CH), 128.0 (CH), 127.1 (CH), 124.5 (q, $^1J_{C–F}$ = 274.0 Hz, C_q), 123.8 (q, $^3J_{C–F}$ = 5.8 Hz, CH), 51.7 (CH_2), 36.7 (d, $^3J_{C–F}$ = 2.0 Hz, CH_2), 19.5 (CH_3), 8.7 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$) δ = –58.1. **IR** (ATR): 3328, 2974, 1664, 1509, 1254, 766, 589 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 411 (100) $[M+Na]^+$, 389 (50) $[M+H]^+$, 292 (10), 163 (10). **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{20}F_3N_4O$ $[M+H]^+$ 389.1589 found 389.1584.



1-Benzyl–5-methyl-*N*-(8-methylnaphthalen-1-yl)-1*H*-1,2,3-triazole-4-carboxamide (179m)

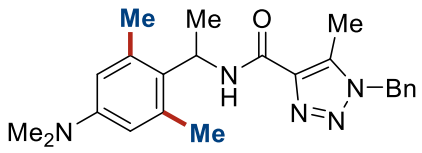
Prepared following the general procedure **A** by using **178m** (317 mg, 0.93 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179m** (226 mg, 66%) as a yellow solid. **M.p.** = 139–140 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 9.60 (brs, 1H), 7.91 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.76–7.70 (m, 2H), 7.47 (t, *J* = 8.0 Hz, 1H), 7.41–7.32 (m, 4H), 7.30–7.27 (m, 1H), 7.24–7.20 (m, 2H), 5.53 (s, 2H), 3.01 (s, 3H), 2.58 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 159.8 (C_q), 139.1 (C_q), 136.9 (C_q), 135.9 (C_q), 134.0 (C_q), 132.7 (C_q), 132.7 (C_q), 130.2 (CH), 129.2 (CH), 128.7 (CH), 128.4 (C_q), 127.7 (CH), 127.7 (CH), 127.4 (CH), 125.6 (CH), 125.2 (CH), 124.4 (CH), 52.0 (CH_2), 25.1 (CH_3), 8.9 (CH_3). **IR** (ATR): 3426, 2974, 1666, 1487, 813, 726 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 379 (100) $[M+Na]^+$, 357 (55) $[M+H]^+$, 217 (10). **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{21}N_4O$ $[M+H]^+$ 357.1715 found 357.1710.



1-Benzyl-*N*-[1-(4-methoxy–2,6-dimethylphenyl)ethyl]–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179n)

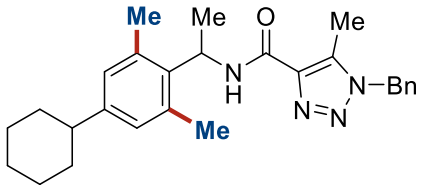
Prepared following the general procedure **A** by using **178n** (70.2 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179n** (56.4 mg, 75%) as a colorless liquid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.72 (d, *J* = 7.6 Hz, 1H), 7.36–7.29 (m, 3H), 7.14–7.11 (m, 2H), 6.55 (s, 2H), 5.62 (q, *J* = 7.3 Hz, 1H), 5.48 (s, 2H), 3.74 (s, 3H), 2.52 (s, 6H), 2.46 (s, 3H), 1.59 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.2 (C_q), 157.6 (C_q), 138.7 (C_q), 136.8 (C_q), 135.8 (C_q), 134.0 (C_q), 131.5 (C_q), 128.9 (CH), 128.4 (CH), 127.0 (CH), 114.6 (CH), 55.0 (CH_3), 51.7 (CH_2), 44.8 (CH), 21.3 (CH_3), 20.1 (CH_3), 8.8 (CH_3). **IR** (ATR): 3423, 2934, 1663, 1497, 1151, 727, 574 cm^{-1}. **MS** (ESI)

m/z (relative intensity) 401 (100) $[M+Na]^+$, 379 (50) $[M+H]^+$, 163 (10). **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{27}N_4O_2$ $[M+H]^+$ 379.2134 found 379.2128.



1-Benzyl-*N*-{1-[4-(dimethylamino)-2,6-dimethylphenyl]ethyl}–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179o)

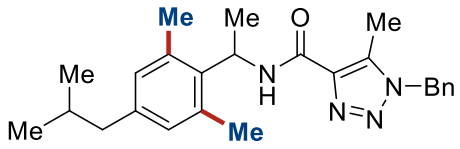
Prepared following the general procedure **A** by using **178o** (72.7 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179o** (48.5 mg, 62%) as a yellow liquid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.73 (d, *J* = 7.7 Hz, 1H), 7.37–7.29 (m, 3H), 7.14–7.11 (m, 2H), 6.42 (s, 2H), 5.63 (q, *J* = 7.2 Hz, 1H), 5.48 (s, 2H), 2.90 (s, 6H), 2.52 (s, 6H), 2.46 (s, 3H), 1.62 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.1 (C_q), 148.9 (C_q), 138.8 (C_q), 136.2 (C_q), 135.7 (C_q), 134.0 (C_q), 131.5 (C_q), 128.9 (CH), 128.3 (CH), 127.0 (CH), 113.7 (CH), 51.7 (CH_2), 44.7 (CH), 40.6 (CH_3), 21.6 (CH_3), 20.4 (CH_3), 8.8 (CH_3). **IR** (ATR): 3423, 2928, 1662, 1593, 1497, 1356, 726, 551 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 414 (100) $[M+Na]^+$, 392 (50) $[M+H]^+$, 176 (10). **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{30}N_5O$ $[M+H]^+$ 392.2450 found 392.2445.



1-Benzyl-*N*-[1-(4-cyclohexyl–2,6-dimethylphenyl)ethyl]–5-methyl-1*H*-1,2,3-triazole-4-carboxamie (179p)

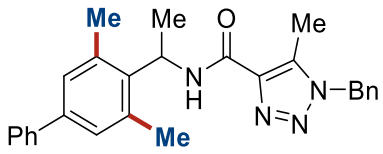
Prepared following the general procedure **A** by using **178p** (80.1 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179p** (69.4 mg, 80%)

as a yellow liquid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.76 (d, J = 7.9 Hz, 1H), 7.37–7.30 (m, 3H), 7.14–7.11 (m, 2H), 6.83 (s, 2H), 5.68 (q, J = 7.2 Hz, 1H), 5.49 (s, 2H), 2.52 (s, 6H), 2.46 (s, 3H), 2.44–2.34 (m, 1H), 1.84–1.71 (m, 5H), 1.60 (d, J = 7.2 Hz, 3H), 1.41–1.24 (m, 5H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.2 (C_q), 146.2 (C_q), 138.8 (C_q), 136.3 (C_q), 135.8 (C_q), 135.1 (C_q), 134.0 (C_q), 128.9 (CH), 128.4 (CH), 127.9 (CH), 127.0 (CH), 51.8 (CH_2), 45.0 (CH), 44.0 (CH), 34.4 (CH_2) and 34.3 (CH_2), 27.0 (CH_2), 26.2 (CH_2), 21.2 (CH_3), 20.0 (CH_3), 8.8 (CH_3). **IR** (ATR): 3431, 2921, 1670, 1501, 1246, 726, 542 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 453 (50) $[M+Na]^+$, 431 (60) $[M+H]^+$, 243 (100), 217 (20), 200 (20). **HR-MS** (ESI) *m/z* calcd for $C_{27}H_{35}N_4O$ $[M+H]^+$ 431.2811 found 431.2805.



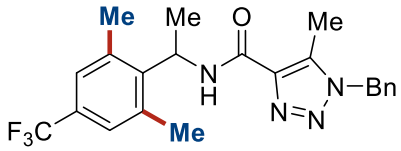
1-Benzyl-*N*-[1-(4-isobutyl–2,6-dimethylphenyl)ethyl]–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179q)

Prepared following the general procedure **A** by using **178q** (75.0 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179q** (62.3 mg, 77%) as a white solid. **M.p.** = 84–85 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.77 (d, J = 7.9 Hz, 1H), 7.37–7.28 (m, 3H), 7.15–7.12 (m, 2H), 6.78 (s, 2H), 5.69 (q, J = 7.3 Hz, 1H), 5.48 (s, 2H), 2.52 (s, 6H), 2.46 (s, 3H), 2.35 (d, J = 7.1 Hz, 2H), 1.89–1.76 (m, 1H), 1.60 (d, J = 7.3 Hz, 3H), 0.89 (d, J = 6.6 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.1 (C_q), 139.9 (C_q), 138.7 (C_q), 136.2 (C_q), 135.8 (C_q), 134.9 (C_q), 134.0 (C_q), 130.1 (CH), 128.9 (CH), 128.3 (CH), 127.0 (CH), 51.7 (CH_2), 45.0 (CH), 44.8 (CH_2), 30.0 (CH), 22.5 (CH_3), 21.0 (CH_3), 20.0 (CH_3), 8.8 (CH_3). **IR** (ATR): 3426, 2957, 1665, 1502, 1253, 729, 574 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 427 (100) $[M+Na]^+$, 405 (45) $[M+H]^+$, 243 (80), 189 (6). **HR-MS** (ESI) *m/z* calcd for $C_{25}H_{33}N_4O$ $[M+H]^+$ 405.2654 found 405.2649.



1-Benzyl-*N*-{1-[3,5-dimethyl-(1,1'-biphenyl)-4-yl]ethyl}–5-methyl-1*H*-1,2,3-triazole-4 -carboxamide (179r)

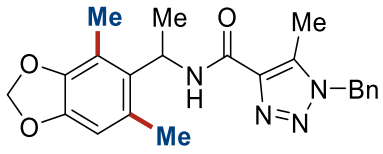
Prepared following the general procedure **A** by using **178r** (79.6 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179r** (71.2 mg, 84%) as a white solid. **M.p.** = 89–92 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.80 (d, *J* = 7.7 Hz, 1H), 7.57–7.53 (m, 2H), 7.44–7.28 (m, 6H), 7.24 (s, 2H), 7.16–7.12 (m, 2H), 5.73 (q, *J* = 7.3 Hz, 1H), 5.50 (s, 2H), 2.62 (s, 6H), 2.47 (s, 3H), 1.66 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.3 (C_q), 140.7 (C_q), 139.4 (C_q), 138.7 (C_q), 138.1 (C_q), 135.9 (C_q), 135.8 (C_q), 134.0 (C_q), 129.0 (CH), 128.5 (CH), 128.4 (CH), 128.2 (CH), 127.0 (CH), 126.9 (CH), 126.9 (CH), 51.8 (CH_2), 45.1 (CH), 21.2 (CH_3), 19.8 (CH_3), 8.8 (CH_3). **IR** (ATR): 3425, 2968, 2929, 1668, 1505, 1198, 731, 564 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 447 (100) $[M+Na]^+$, 425 (50) $[M+H]^+$, 243 (90), 209 (10). **HR-MS** (ESI) *m/z* calcd for $C_{27}H_{29}N_4O$ $[M+H]^+$ 425.2341 found 425.2336.



1-Benzyl-*N*-{1-[2,6-dimethyl-4-(trifluoromethyl)phenyl]ethyl}–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179s)

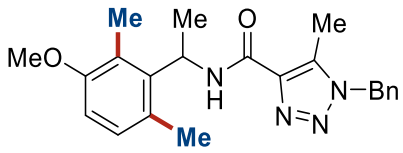
Prepared following the general procedure **A** by using **178s** (77.7 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179s** (70.3 mg, 84%) as a white solid. **M.p.** = 97–100 °C.**^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.73 (d, *J* = 7.3 Hz, 1H), 7.37–7.29 (m, 3H), 7.23 (s, 2H), 7.15–7.12 (m, 2H), 5.67 (p, *J* = 7.3 Hz, 1H), 5.49 (s, 2H), 2.58 (s, 6H), 2.45 (s, 3H), 1.61 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.3 (C_q), 142.9 (C_q), 138.4 (C_q), 136.2 (C_q), 136.0 (C_q), 133.9 (C_q), 128.9 (CH), 128.4 (CH),

127.7 (d, $^{2}J_{C–F}$ = 112.9 Hz, C_q), 127.0 (CH), 126.0 (q, $^{3}J_{C–F}$ = 3.3 Hz, CH), 124.0 (q, $^{1}J_{C–F}$ = 271.6 Hz, C_q), 51.8 (CH_2), 45.2 (CH), 21.1 (CH_3), 19.2 (CH_3), 8.7 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = -62.6. **IR** (ATR): 3373, 2983, 1647, 1581, 1513, 1323, 734, 611, 476 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 439 (100) $[M+Na]^+$, 417 (70) $[M+H]^+$, 217 (40). **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{24}F_3N_4O$ $[M+H]^+$ 417.1902 found 417.1897.



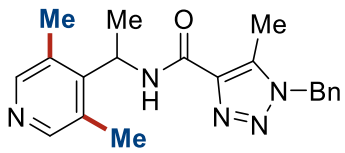
1-Benzyl-*N*-{1-(4,6-dimethylbenzo[d][1,3]dioxol–5-yl)ethyl}–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179t)

Prepared following the general procedure **A** by using **178t** (72.9 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179t** (70.8 mg, 90%) as a white solid. **M.p.** = 87–88 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.70 (d, *J* = 7.4 Hz, 1H), 7.35–7.30 (m, 3H), 7.14–7.12 (m, 2H), 6.49 (s, 1H), 5.86 (s, 2H), 5.56 (dq, *J* = 7.3, 7.4 Hz, 1H), 5.48 (s, 2H), 2.45 (s, 3H), 2.45 (s, 3H), 2.39 (s, 3H), 1.58 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 160.4 (C_q), 145.1 (C_q), 145.2 (C_q), 138.7 (C_q), 136.0 (C_q), 134.0 (C_q), 132.6 (C_q), 129.0 (CH), 128.6 (C_q), 128.5 (CH), 127.1 (CH), 117.1 (C_q), 109.0 (CH), 100.4 (CH_2), 51.7 (CH_2), 45.1 (CH), 20.94 (CH_3), 20.0 (CH_3), 12.7 (CH_3), 8.7 (CH_3). **IR** (ATR): 3311, 2883, 1647, 1512, 1247, 743, 462 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 415 (100) $[M+Na]^+$, 393 (60) $[M+H]^+$, 217 (30). **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{25}N_4O_3$ $[M+H]^+$ 393.1927 found 393.1921.



1-Benzyl-*N*-[1-(3-methoxy–2,6-dimethylphenyl)ethyl]–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179u)

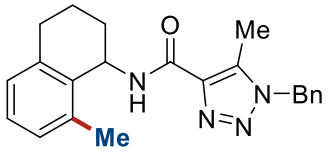
Prepared following the general procedure **A** by using **178u** (69.8 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179u** (67.5 mg, 89%) as a colorless liquid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.79 (d, *J* = 7.7 Hz, 1H), 7.36–7.29 (m, 3H), 7.14–7.11 (m, 2H), 6.96 (d, *J* = 8.3 Hz, 1H), 6.67 (d, *J* = 8.3 Hz, 1H), 5.70 (q, *J* = 7.3 Hz, 1H), 5.48 (s, 2H), 3.78 (s, 3H), 2.48 (s, 3H), 2.45 (s, 3H), 2.41 (s, 3H), 1.62 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.2 (C_q), 156.30 (C_q), 140.0 (C_q), 138.7 (C_q), 135.8 (C_q), 134.0 (C_q), 128.9 (CH), 128.4 (CH), 127.2 (C_q), 127.0 (CH), 124.1 (C_q), 109.0 (CH), 55.6 (CH_3), 51.7 (CH_2), 45.5 (CH), 20.6 (CH_3), 19.9 (CH_3), 12.5 (CH_3), 8.8 (CH_3). **IR** (ATR): 3351, 2935, 1644, 1580, 1450, 731, 472 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 401 (100) $[M+Na]^+$, 379 (50) $[M+H]^+$, 243 (10), 217 (20), 163 (25). **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{27}N_4O_2$ $[M+H]^+$ 379.2134 found 379.2129.



1-Benzyl-*N*-[1-(3,5-dimethylpyridin-4-yl)ethyl]–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (179v)

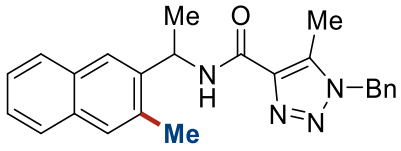
Prepared following the general procedure **A** by using **178v** (64.0 mg, 0.20 mmol). Purification by column chromatography (EtOAc/*n*-hexane 1:1 to EtOAc) yielded **179v** (36.3 mg, 52%) as a yellow liquid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.21 (s, 2H), 7.65 (d, *J* = 7.1 Hz, 1H), 7.33–7.27 (m, 3H), 7.13–7.11 (m, 2H), 5.51 (q, *J* = 7.4 Hz, 1H), 5.47 (s, 2H), 2.46 (s, 6H), 2.40 (s, 3H), 1.56 (d, *J* = 7.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.5 (C_q), 149.4 (CH), 148.9 (C_q), 138.1 (C_q), 136.2 (C_q), 133.8 (C_q), 130.6 (C_q), 129.0 (CH), 128.5 (CH), 127.1 (CH), 51.8 (CH_2), 45.0 (CH), 18.4 (CH_3), 17.3 (CH_3), 8.6 (CH_3). **IR** (ATR): 3419, 2931, 1663, 1503, 1252, 730, 596 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 372 (10) $[M+Na]^+$,

350 (100) $[M+H]^+$, 336 (10), 117 (8). **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{24}N_5O$ $[M+H]^+$ 350.1981 found 350.1975.



1-Benzyl–5-methyl-*N*-(8-methyl-1,2,3,4-tetrahydronaphthalen-1-yl)-1*H*-1,2,3-triazole-4-carboxamide (179w)

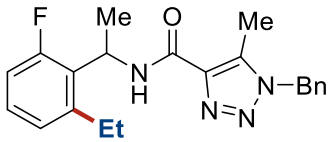
Prepared following the general procedure **A** by using **178w** (69.3 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179w** (60.3 mg, 83%) as a colorless liquid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.37–7.29 (m, 4H), 7.18–7.15 (m, 2H), 7.12 (d, *J* = 7.5 Hz, 1H), 7.01 (t, *J* = 7.1 Hz, 2H), 5.50 (s, 2H), 5.35–5.31 (m, 1H), 2.92–2.72 (m, 2H), 2.54 (s, 3H), 2.28 (s, 3H), 2.27–2.25 (m, 1H), 1.91–1.79 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 159.9 (C_q), 138.5 (C_q), 137.9 (C_q), 137.7 (C_q), 136.0 (C_q), 133.9 (C_q), 133.3 (C_q), 128.9 (CH), 128.4 (CH), 128.1 (CH), 127.4 (CH), 127.1 (CH), 51.8 (CH_2), 44.1 (CH), 29.8 (CH_2), 29.6 (CH_2), 18.8 (CH_3), 18.0 (CH_2), 8.9 (CH_3). **IR** (ATR): 3412, 2930, 1660, 1497, 1249, 774, 574 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 383 (100) $[M+Na]^+$, 361 (80) $[M+H]^+$, 217 (80), 145 (25). **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{25}N_4O$ $[M+H]^+$ 361.2028 found 361.2023.



1-Benzyl–5-methyl-*N*-[1-(3-methylnaphthalen–2-yl)ethyl]-1*H*-1,2,3-triazole-4-carbox amide (179x)

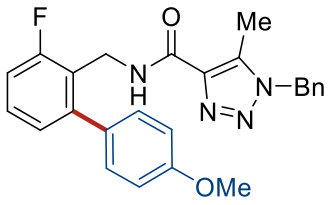
Prepared following the general procedure **A** by using **178x** (74.3 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **179x** (71.2 mg, 91%)

as a white solid. **M.p.** = 65–71 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.87 (s, 1H), 7.81–7.72 (m, 2H), 7.63 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.44–7.38 (m, 2H), 7.36–7.30 (m, 3H), 7.16–7.12 (m, 2H), 5.59 (q, *J* = 6.8 Hz, 1H), 5.47 (s, 2H), 2.6 (s, 3H), 2.48 (s, 3H), 1.68 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 160.2 (C_q), 140.2 (C_q), 138.6 (C_q), 136.1 (C_q), 133.9 (C_q), 133.7 (C_q), 132.7 (C_q), 132.1 (C_q), 128.9 (CH), 128.6 (CH), 128.4 (CH), 127.4 (CH), 127.0 (CH), 126.7 (CH), 125.7 (CH), 125.1 (CH), 123.7 (CH), 51.7 (CH_2), 45.2 (CH), 21.7 (CH_3), 19.6 (CH_3), 8.8 (CH_3). **IR** (ATR): 3410, 2974, 1662, 1504, 1251, 732, 540 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 407 (100) $[M+Na]^+$, 385 (40) $[M+H]^+$, 258 (10), 212 (20), 169 (45). **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{25}N_4O$ $[M+H]^+$ 385.2028 found 385.2023.



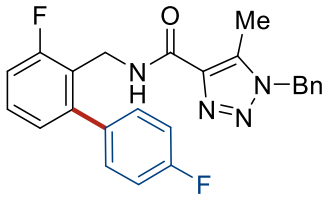
1-Benzyl-*N*-[1-(2-ethyl-6-fluorophenyl)ethyl]–5-methyl-1*H*-1,2,3-triazole-4-carbox amide (196h)

Prepared following the general procedure **B** by using **178h** (68.2 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **196h** (63.7 mg, 81%) as a colorless liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.91 (d, *J* = 8.9 Hz, 1H), 7.26–7.20 (m, 3H), 7.09–7.03 (m, 3H), 6.88–6.80 (m, 2H), 5.64–5.57 (m, 1H), 5.40 (d, *J* = 2.6 Hz, 2H), 2.88 (dq, *J* = 15.0, 7.6 Hz, 1H), 2.72 (dq, *J* = 15.0, 7.6 Hz, 1H), 2.38 (s, 3H), 1.55 (d, *J* = 6.0 Hz, 3H), 1.20 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 162.3 (d, $^1J_{C–F}$ = 244.3 Hz, C_q), 160.3 (C_q), 143.5 (d, $^4J_{C–F}$ = 4.5 Hz, C_q), 138.8 (C_q), 136.1 (C_q), 134.1 (C_q), 129.0 (CH), 128.4 (CH), 128.3 (d, $^3J_{C–F}$ = 9.8 Hz, CH), 128.2 (d, $^3J_{C–F}$ = 11.3 Hz, C_q), 127.08 (CH), 124.6 (d, $^4J_{C–F}$ = 2.6 Hz, CH), 113.8 (d, $^2J_{C–F}$ = 22.7 Hz, CH), 51.7 (CH_2), 42.1 (CH), 29.6 (CH_2), 26.4 (d, $^4J_{C–F}$ = 2.2 Hz, CH_2), 21.2 (d, $^4J_{C–F}$ = 3.4 Hz, CH_3), 15.7 (CH_3), 8.7 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$) δ = –116.1 (dd, *J* = 11.5, 5.6 Hz). **IR** (ATR): 3421, 2968, 1665, 1505, 730, 579 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 389 (100) $[M+Na]^+$, 367 (60) $[M+H]^+$, 217 (40). **HR-MS** (ESI) *m/z* calcd for $C_{21}H_{24}FN_4O$ $[M+H]^+$ 367.1934 found 367.1929.



1-Benzyl-*N*-{1-(3-fluoro-4'-methoxy-[1,1'-biphenyl]–2-yl)ethyl}–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (197a)

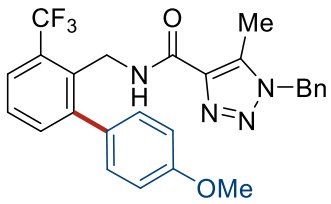
Prepared following the general procedure **B** by using **178h** (67.9 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **197a** (66.7 mg, 75%) as a colorless liquid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.83 (d, *J* = 8.9 Hz, 1H), 7.28–7.20 (m, 5H), 7.16–7.10 (m, 1H), 7.06–6.88 (m, 6H), 5.45–5.33 (m, 3H), 3.76 (s, 3H), 2.36 (s, 3H), 1.44 (dd, *J* = 7.0, 0.9 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 162.1 (d, $^{1}J_{C–F}$ = 245.2 Hz, C_q), 160.1 (C_q), 159.1 (C_q), 142.9 (d, $^{3}J_{C–F}$ = 5.2 Hz, C_q), 139.0 (C_q), 136.0 (C_q), 134.2 (C_q), 132.2 (C_q), 130.4 (CH), 129.1 (CH), 128.5 (CH), 128.3 (C_q), 128.0 (d, $^{3}J_{C–F}$ = 9.9 Hz, CH), 127.1 (CH), 126.5 (d, $^{3}J_{C–F}$ = 2.7 Hz, CH), 115.0 (d, $^{2}J_{C–F}$ = 22.7 Hz, CH), 113.8 (CH), 55.3 (CH_3), 51.8 (CH_2), 43.9 (CH), 21.6 (d, $^{3}J_{C–F}$ = 2.6 Hz, CH_3), 8.8 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = –115.9. **IR** (ATR): 3422, 2930, 1668, 1509, 1248, 730, 569 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 467 (100) $[M+Na]^+$, 445 (60) $[M+H]^+$, 288 (10), 217 (25), 177 (20). **HR-MS** (ESI) *m/z* calcd for $C_{26}H_{26}FN_4O_2$ $[M+H]^+$ 445.2040 found 445.2034.



1-Benzyl-*N*-{1-[3,4'-difluoro-(1,1'-biphenyl)-2-yl]ethyl}–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (197b)

Prepared following the general procedure **B** by using **178h** (67.9 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **197b** (72.1 mg, 83%)

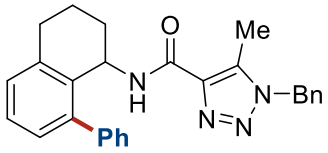
as a white solid. **M.p.** = 134–136 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.81 (d, J = 8.6 Hz, 1H), 7.33–7.18 (m, 5H), 7.16–7.11 (m, 1H), 7.07–6.95 (m, 5H), 6.90–6.87 (m, 1H), 5.38 (d, J = 3.6 Hz, 2H), 5.3–5.25 (m, 1H), 2.35 (s, 3H), 1.43 (dd, J = 7.0, 0.9 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 163.9 (d, $^1J_{C–F}$ = 25.7 Hz, C_q), 160.6 (d, $^1J_{C–F}$ = 24.8 Hz, C_q), 160.2 (C_q), 142.1 (d, $^2J_{C–F}$ = 5.2 Hz, C_q), 138.9 (C_q), 136.0 (C_q), 135.8 (t, $^2J_{C–F}$ = 3.0 Hz, C_q), 134.2 (C_q), 131.0 (d, ^2J = 8.1 Hz, CH), 129.1 (CH), 128.5 (CH), 128.4 (C_q), 128.1 (d, ^2J = 9.9 Hz, CH), 127.2 (CH), 126.3 (d, $^2J_{C–F}$ = 2.6 Hz, CH), 115.5 (d, $^1J_{C–F}$ = 22.7 Hz, CH), 115.3 (d, $^1J_{C–F}$ = 21.4 Hz, CH), 51.8 (CH_2), 43.8 (CH), 21.5 (d, ^2J = 2.6 Hz, CH_3), 8.8 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = –114.82(s,), –115.7(s,). **IR** (ATR): 3421, 2930, 1667, 1508, 1226, 729, 550 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 455 (100) $[M+Na]^+$, 433 (45) $[M+H]^+$, 217 (30), 177 (20). **HR-MS** (ESI) *m/z* calcd for $C_{25}H_{23}F_2N_4O$ $[M+H]^+$ 433.1840 found 433.1834.



1-Benzyl-*N*-{[4'-methoxy-3-(trifluoromethyl)-(1,1'-biphenyl)-2-yl]methyl}–5-methyl-1*H*-1,2,3-triazole-4-carboxamide (197c)

Prepared following the general procedure **B** by using **178l** (450 mg, 1.2 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **197c** (515 mg, 89%) as a colorless liquid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.67–7.61 (m, 1H), 7.40–7.36 (m, 2H), 7.30–7.12 (m, 5H), 7.08–7.05 (m, 2H), 6.97 (t, J = 4.4 Hz, 1H), 6.82–6.77 (m, 2H), 5.39 (s, 2H), 4.58 (d, J = 4.4 Hz, 2H), 3.70 (s, 3H), 2.36 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 159.9 (C_q), 159.0 (C_q), 145.5 (C_q), 138.4 (C_q), 135.9 (C_q), 134.5 (CH), 134.0 (C_q), 133.0 (C_q), 131.8 (C_q), 130.1 (q, $^2J_{C–F}$ = 29.8 Hz, C_q), 129.9 (CH), 129.0 (CH), 128.4 (CH), 127.7 (CH), 127.1 (CH), 125.4 (q, $^3J_{C–F}$ = 6.0 Hz, CH), 124.3 (q, $^1J_{C–F}$ = 273.8 Hz, C_q), 113.8 (CH), 55.2 (CH_3), 51.8 (CH_2), 37.7 (CH_2), 8.7 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = –58.67. **IR** (ATR): 3288, 2958, 1662, 1510, 1253, 693, 589 cm^{-1}. **MS** (ESI) *m/z* (relative intensity)

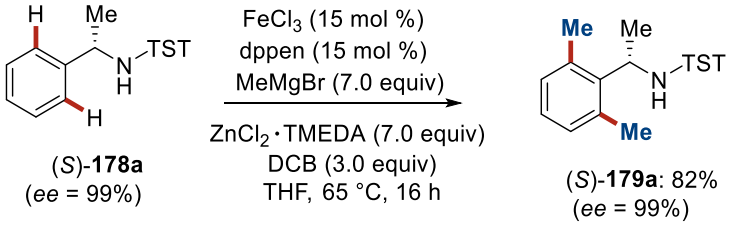
503 (100) $[M+Na]^+$, 481 (60) $[M+H]^+$, 217 (30). **HR-MS** (ESI) *m/z* calcd for $C_{26}H_{24}F_3N_4O_2$ $[M+H]^+$ 481.1851 found 481.1846.



1-Benzyl–5-methyl-*N*-(8-phenyl-1,2,3,4-tetrahydronaphthalen-1-yl)-1*H*-1,2,3-triazole -4-carboxamide (197e)

Prepared following the general procedure **B** by using **178w** (69.3 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **197d** (63.9 mg, 76%) as a colorless liquid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.31–7.23 (m, 3H), 7.17–6.99 (m, 11H), 5.37 (s, 2H), 5.17–5.12 (m, 1H), 2.89–2.71 (m, 2H), 2.24 (s, 3H), 2.08–2.00 (m, 1H), 1.83–1.72 (m, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 159.2 (C_q), 143.7 (C_q), 141.0 (C_q), 138.7 (C_q), 138.3 (C_q), 135.7 (C_q), 134.3 (C_q), 133.4 (C_q), 129.1 (CH), 128.8 (CH), 128.7 (CH), 128.5 (CH), 128.3 (CH), 127.7 (CH), 127.33 (CH), 127.1 (CH), 126.5 (CH), 51.7 (CH_2), 44.4 (CH), 29.8 (CH_2), 29.7 (CH_2), 18.3 (CH_2), 8.6 (CH_3). **IR** (ATR): 3414, 2933, 1665, 1496, 1251, 730, 541 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 445 (100) $[M+Na]^+$, 423 (60) $[M+H]^+$, 217 (40), 158 (20). **HR-MS** (ESI) *m/z* calcd for $C_{27}H_{27}N_4O$ $[M+H]^+$ 423.2185 found 423.2179.

5.3.2 Iron-catalyzed C–H methylation of chiral benzamide (S)-178a



Prepared following the general procedure **A** by using (*S*)**-1a** (64.0 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded (*S*)**-2a** (58.9 mg,

86%) as a white solid. **M.p.** = 72–73 °C. Chiral HPLC analysis (Chiralcel IC, *i*-PrOH/*n*-hexane 30:70, flow rate = 1.0 mL/min, λ = 254 nm), t_r (minor) = 8.7 min, t_r (major) = 9.8 min.

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Different Inj Volume from Sample Entry!  Actual Inj Volume : 2.000 µl
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Method Info     : Test

Additional Info : Peak(s) manually integrated
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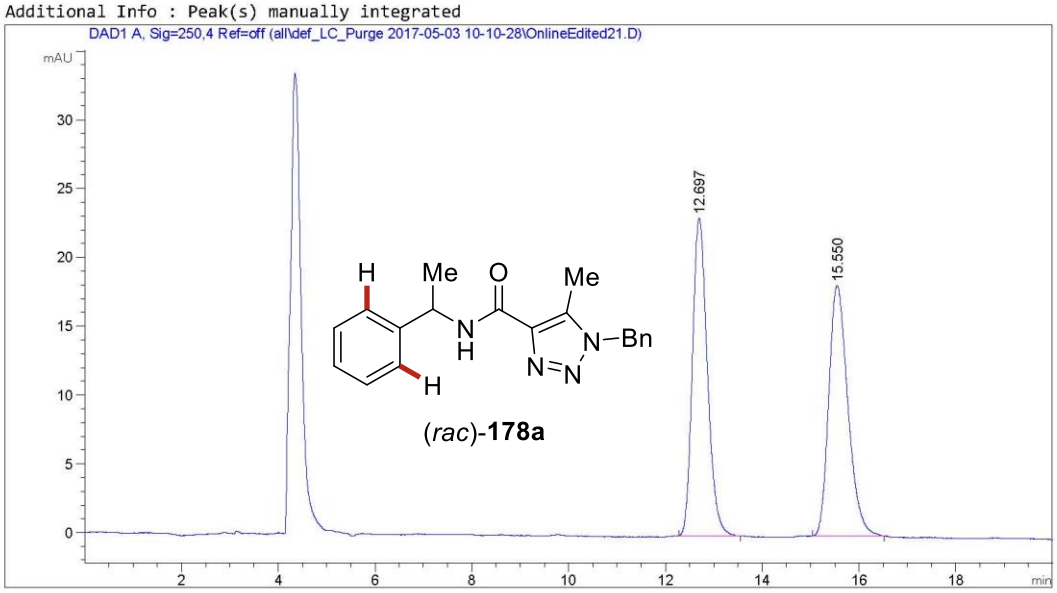

(*rac*)-**178a**

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                      Area Percent Report
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Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


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   1  12.697 BB    0.3259  494.62329   23.09455  49.7711
   2  15.550 BB    0.3999  499.17252   18.20427  50.2289

Totals :                   993.79581   41.29882

HPLC-2 5/10/2017 7:43:05 PM SYSTEM                    Page   1 of 2
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Different Inj Volume from Sample Entry!  Actual Inj Volume : 2.000 µl
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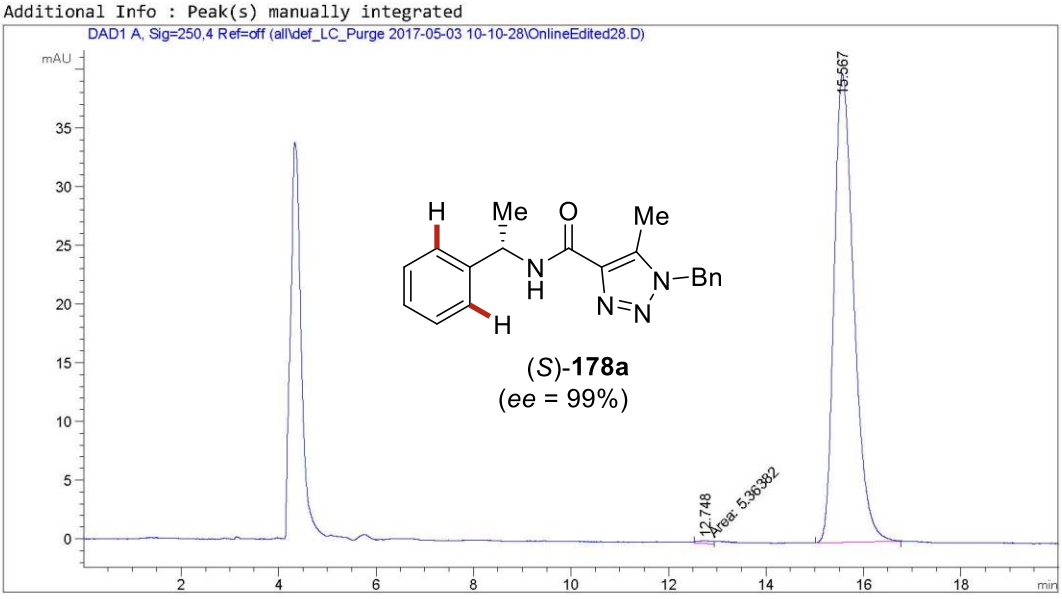

(*S*)-**178a**
(*ee* = 99%)

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======================================================================
                        Area Percent Report
======================================================================

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Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


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                                               Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry!  Actual Inj Volume : 2.000 µl
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Method Info     : Test

Additional Info : Peak(s) manually integrated
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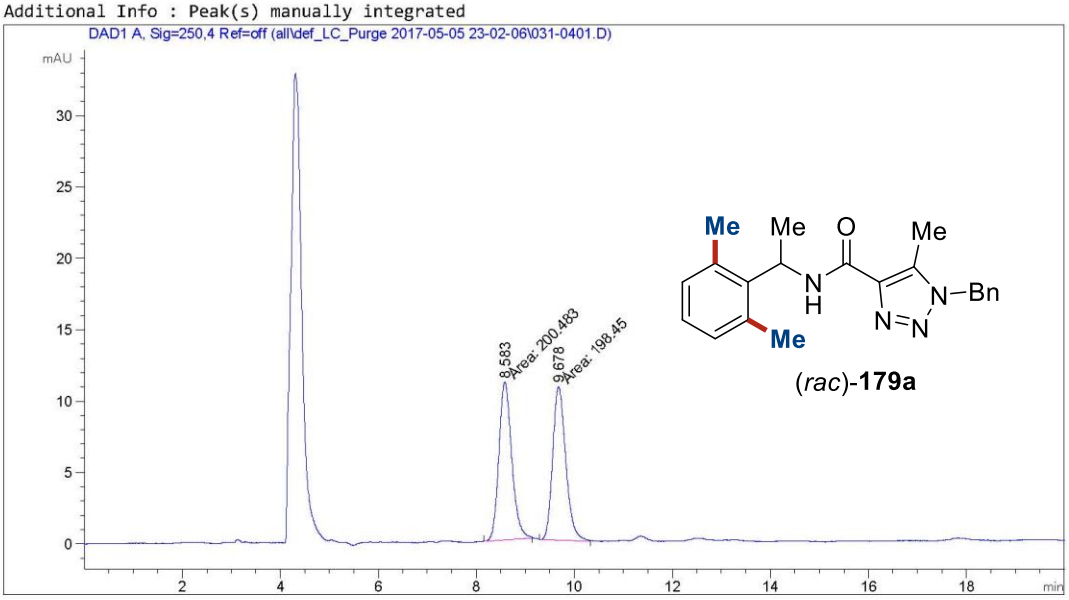

(*rac*)-**179a**

```
======================================================================
                        Area Percent Report
======================================================================

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Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
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```

```
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    Acq. Instrument : HPLC-2                         Location :  33
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                                                 Inj Volume : 5.000 µl
    Different Inj Volume from Sample Entry!  Actual Inj Volume : 2.000 µl
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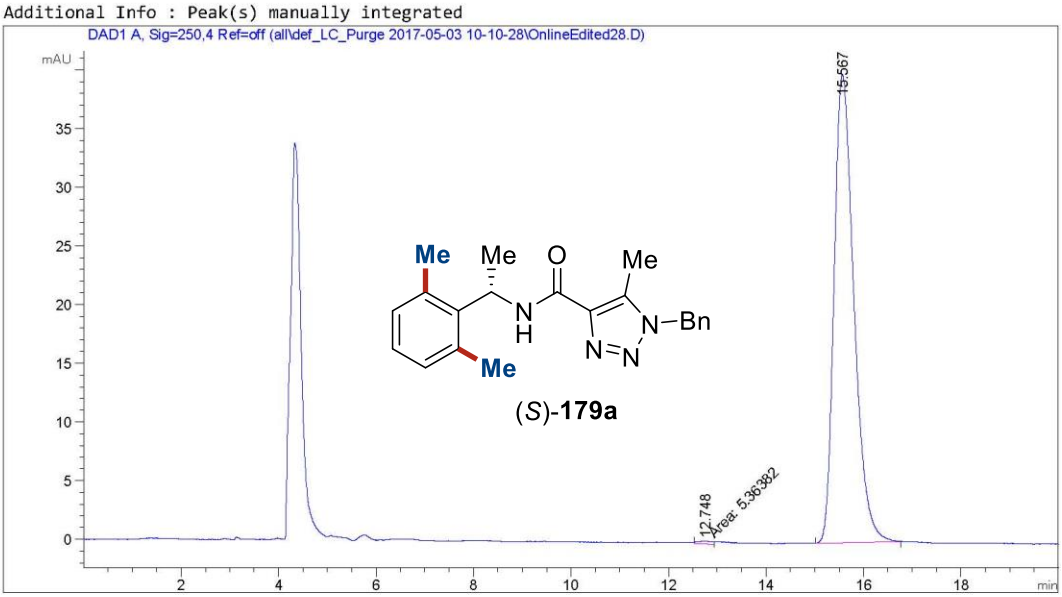

(*S*)-**179a**

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    ==================================================================
                          Area Percent Report
    ==================================================================

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    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=250,4 Ref=off

    Peak RetTime Type  Width     Area      Height     Area
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    ----|-------|----|-------|----------|----------|--------|
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       2  15.567 BB    0.4158 1120.66064   39.88580  99.5236

    Totals :                  1126.02446   40.13746
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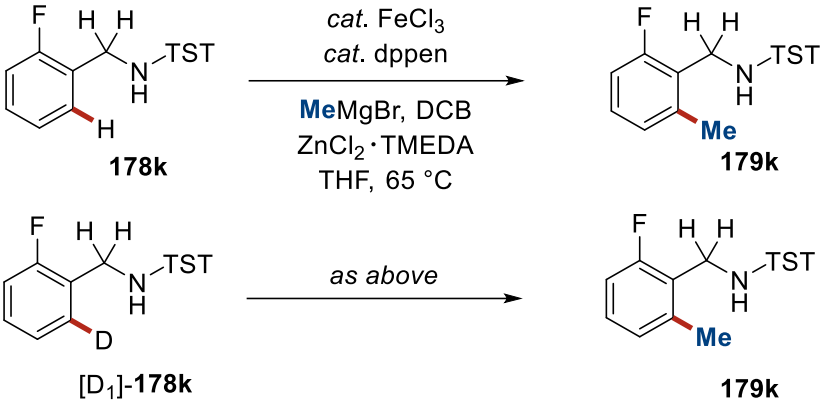
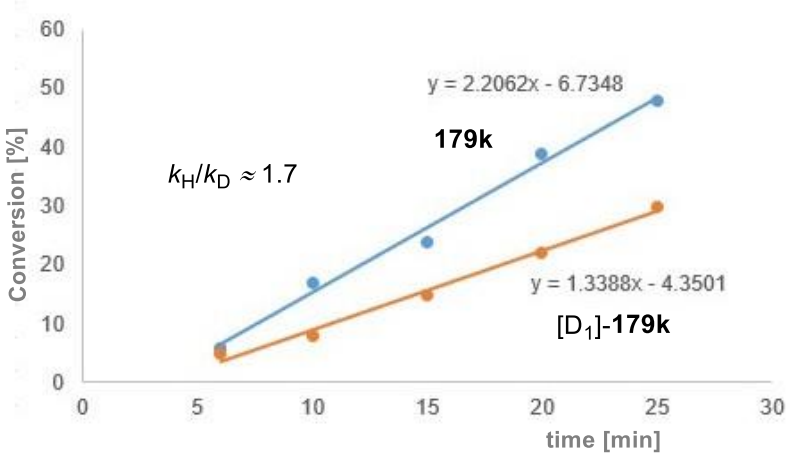
5.3.3 Parallel Experiments for KIE

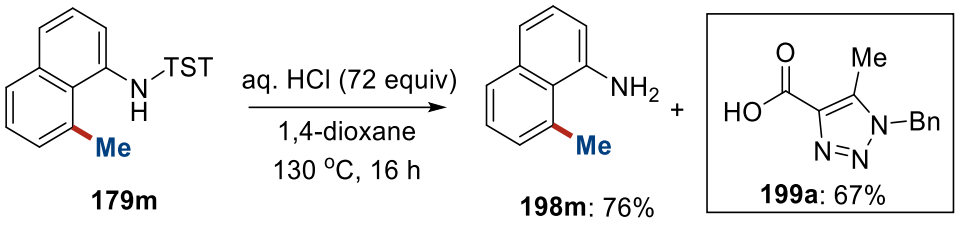




Ten independent reactions with **178k** or deuterated substrate [D_1]**-178k** under the standard conditions were performed. To a schlenk tube charged with amide (0.20 mmol), TMEDA·$ZnCl_2$ (152 mg, 0.60 mmol, 3.0 equiv) and 1.0 mL THF was added MeMgBr (457 ul, 1.4 mmol, 3.0 M in ether, 7.0 equiv) in one portion at room temperature under nitrogen gas. Five minutes later, dppen (11.9 mg, 0.030 mmol, 15 mol %) and $FeCl_3$ (4.9 mg, 0.030 mmol, 15 mol %) were added successively. Stirring at room temperature for another one minute, 2,3-dichloridebutane was added and the reaction was moved to 65 °C oil bath stirring for 5 min, 10 min, 15 min, 20 min, 25 min respectively. The yields of the products **179k** were monitored by ^{19}F NMR using benzotrifluoride as the internal standard.

t [min]	5	10	15	20	25
179k [%]	6	17	24	39	48
[D_1]-**179k** [%]	5	8	15	22	30

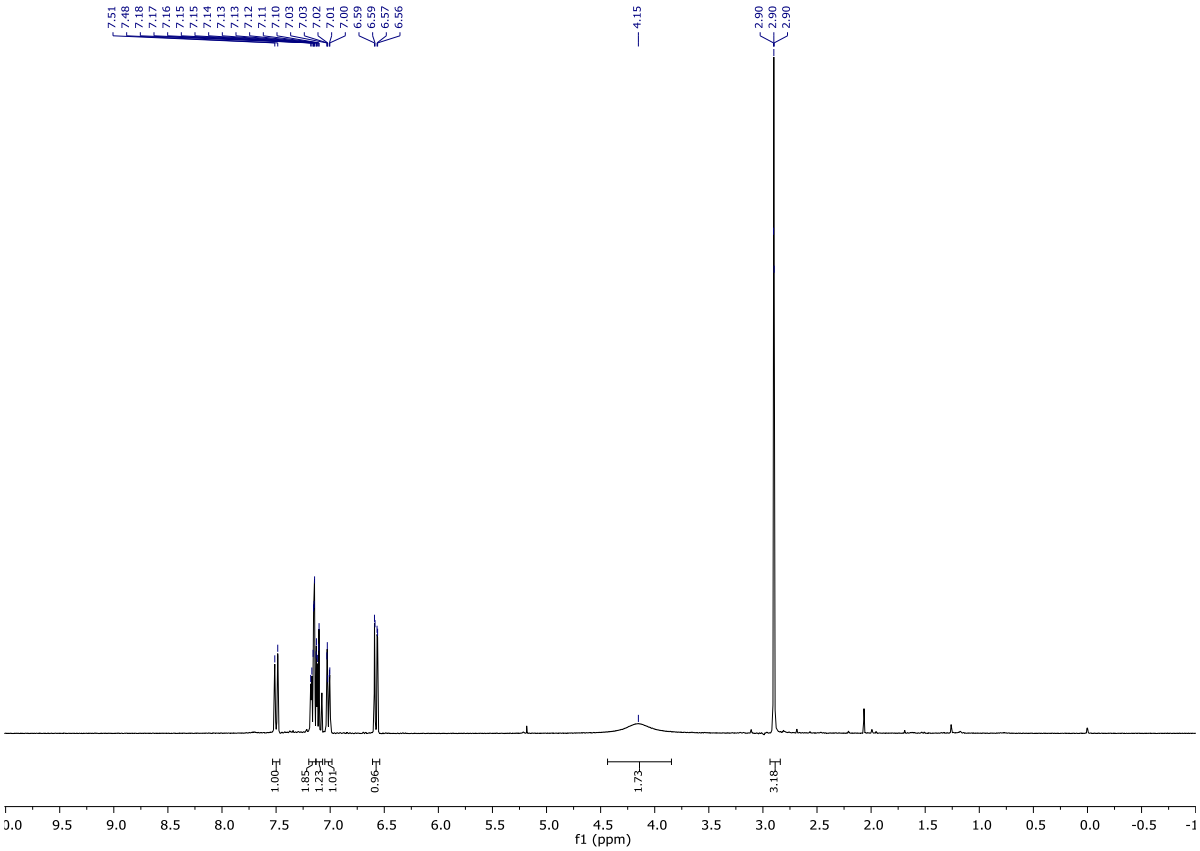
5.3.4 The Removal of Directing Group

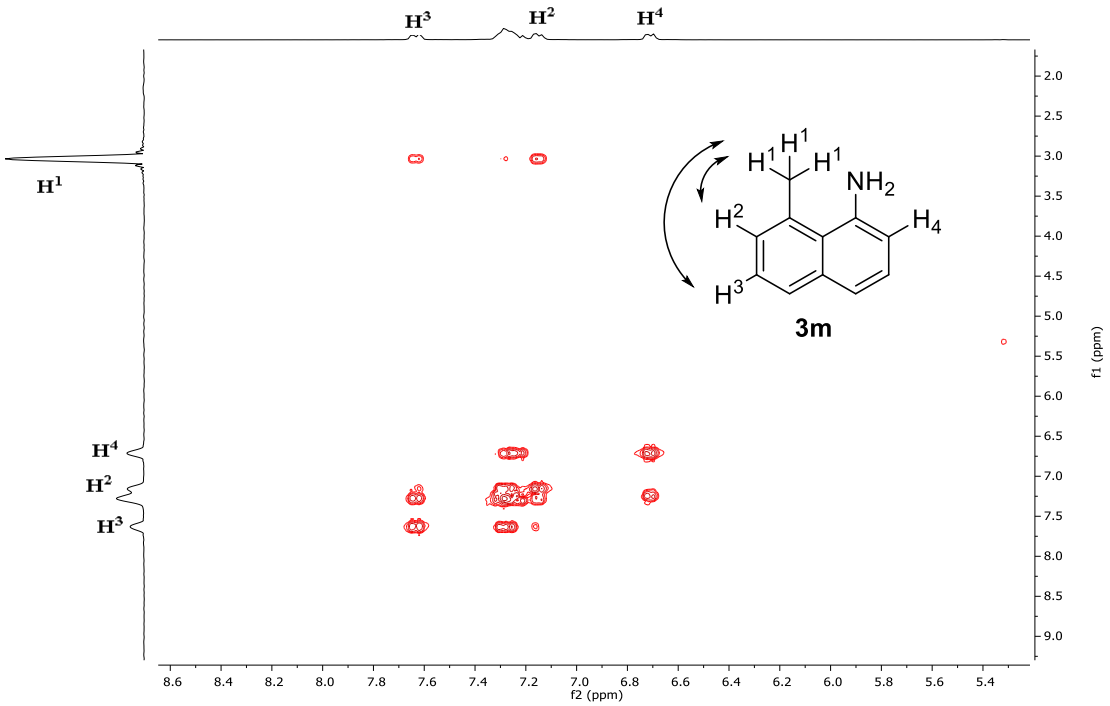


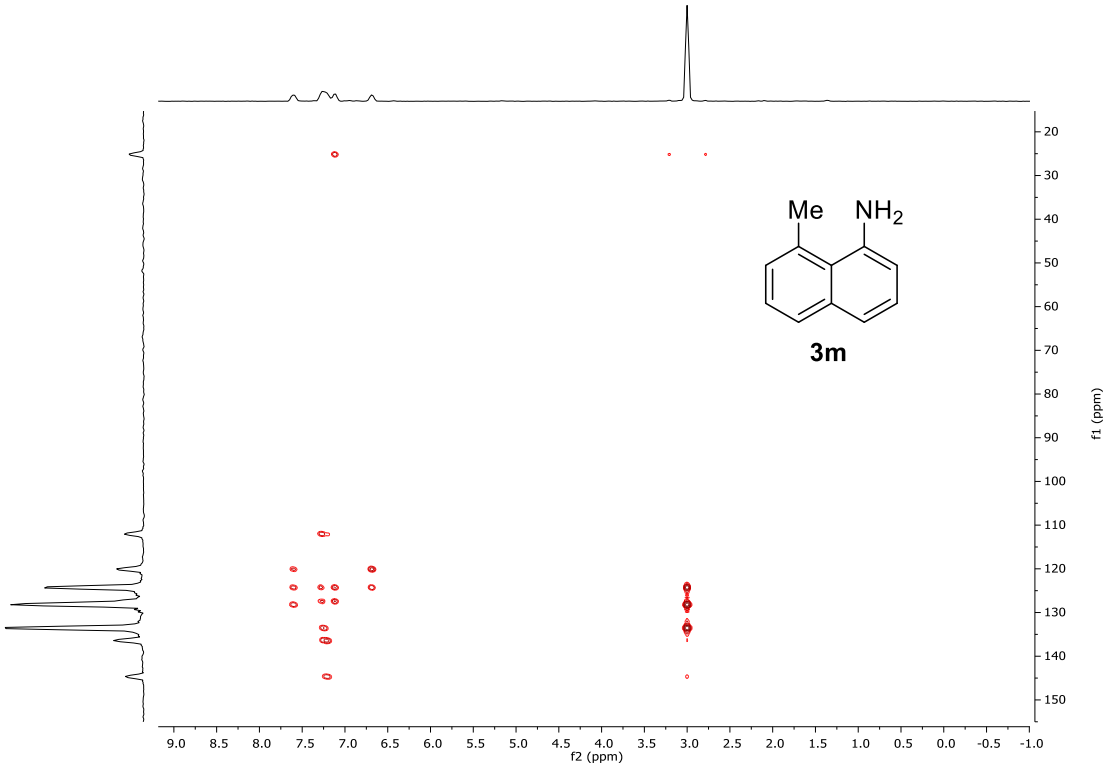
A solution of amide **179m** (178 mg, 0.50 mmol) in 3.0 ml concentrated hydrochloride and 1.5 ml 1,4-dioxane under nitrogen was stirred at 130 °C for 16 hours. Basified the mixture to pH = 12 by 3M KOH aqueous solution and extracted with mixed solvent (MeOH/DCM 1:8) for three times. Combined the organic layers, washed with brine and removed the solvent. The resulting crude material was purified by column chromatography (*n*-hexane/EtOAc 1:4) yielding amine **198m** as a brown solid (59.4 mg, 76%). **M.p.** = 68–69 °C.**^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.58 (d, J = 8.2 Hz, 1H), 7.26–7.16 (m, 3H), 7.09 (d, J = 7.0 Hz, 1H), 6.64 (dd, J = 7.2, 1.5 Hz, 1H), 4.24 (brs, 2H), 2.97 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 144.9 (C_q), 136.5 (C_q), 133.6 (C_q), 128.2 (CH), 127.5 (CH), 126.0 (CH), 125.4 (CH), 124.3 (C_q), 120.0 (CH), 111.9 (CH), 25.2 (CH_3). **IR** (ATR): 3363, 2963, 1618, 1463, 814, 759, 671 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 180 (100) $[M+Na]^+$, 158 (40) $[M+H]^+$, 141 (30). **HR-MS** (ESI) *m/z* calcd for $C_{11}H_{12}N$ $[M+H]^+$ 158.0970 found 158.0964. The ^{1}H-^{1}H COSY confirmed the structure of **198m** is 1-Amino–8-methylnaphthalene rather than reported compound 1-Amino–2-methylnaphthalene.[177]

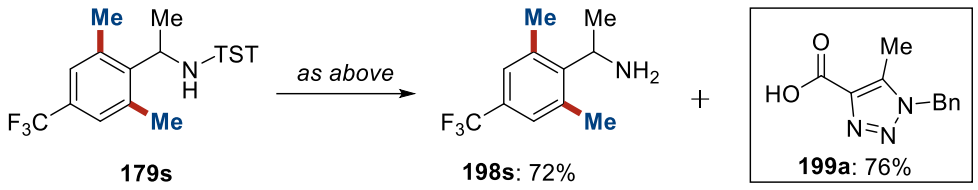
The aqueous layer was acidified to pH = 3 and extracted with mixed solvent (Methanol/DCM 1:8) for three times. Combined the organic layers, washed with brine and removed the solvent. The resulting residue was washed with very little amount of ether to afford the acid **199a** as a yellow solid (82.2 mg, 76%). **M.p.** = 133–134 °C. **^{1}H NMR** (300

MHz, D_6-acetone) δ = 7.45–7.31 (m, 3H), 7.28–7.25 (m, 2H), 5.67 (s, 2H), 2.52 (s, 3H). **^{13}C NMR** (75 MHz, D_6-acetone) δ = 167.2 (C_q), 143.8 (C_q), 141.7 (C_q), 140.5 (C_q), 134.1 (CH), 133.4 (CH), 132.6 (CH), 56.4 (CH_2), 13.4 (CH_3). **IR** (ATR): 3443, 2923, 2854, 1716, 1570, 1183, 798, 747 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 240 (100) $[M+Na]^+$, 218 (60) $[M+H]^+$, 201 (5), 91 (7). **HR-MS** (ESI) *m/z* calcd for $C_{11}H_{12}N_3O_2$ $[M+H]^+$ 218.0930 found 218.0924.




H3
H2
H4
H1
H4
H2
H3
H1
H1
H1
NH2
H2
H4
H3
3m
f2 (ppm)
f1 (ppm)


Me
NH2
3m
f2 (ppm)
f1 (ppm)



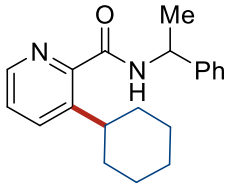
179s **198s**: 72% **199a**: 76%

A solution of amide **179s** (215 mg, 0.5 mmol) in 3.0 ml concentrated hydrochloride and 1.5 mL dioxane under nitrogen was stirred at 130 °C for 12 hours. Basified the mixture to pH = 12 by 3M KOH aqueous solution and extracted with mixed solvent (Methanol/DCM 1:8) for three times. Combined the organic layers, washed with brine and removed the solvent. The resulting crude material was purified by column chromatography (gradient elution *n*-hexane/EtOAc 1:1 to EtOAc) yielding amine **198s** as a yellow liquid (77.3 mg, 72%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.22 (s, 2H), 4.67 (q, J = 7.0 Hz, 1H), 2.51 (s, 6H), 1.53 (brs, 2H), 1.45 (d, J = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 146.2 (C_q), 136.6 (C_q), 128.2 (q, $^{2}J_{C–F}$ = 31.9 Hz, C_q), 126.0 (q, $^{3}J_{C–F}$ = 2.9 Hz, CH), 124.2 (q, $^{1}J_{C–F}$ = 271.8 Hz, C_q), 47.4 (CH), 21.8 (CH_3), 21.2 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = -62.62. **IR** (ATR): 3425, 2969, 2929, 1339, 1227, 1116, 881 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 240 (100) $[M+Na]^+$, 218 (40) $[M+H]^+$, 201 (80), 161 (6). **HR-MS** (ESI) *m/z* calcd for $C_{11}H_{15}F_3N$ $[M+H]^+$ 218.1157 found 218.1152.

The aqueous layer was acidified to pH = 3 and extracted with mixed solvent (Methanol/DCM 1:8) for three times. Combined the organic layers, washed with brine and removed the solvent. The resulting residue was washed with very little amount of ether to afford the acid **199a** as yellow solid (82.2 mg, 76%).

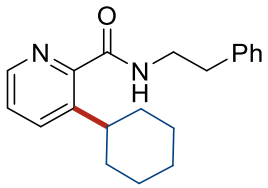
5.4 Pyridinyl C–H Alkylation Catalyzed by Manganese(II)

5.4.1 Experimental Procedure and Analytical Data



3-cyclohexyl-N-(1-phenylethyl)picolinamide (181aa)

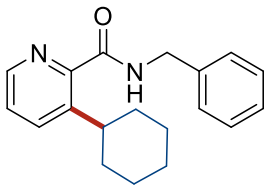
Prepared following the general procedure **C** using *N*-(1-phenylethyl)picolinamide **88a** (45.2 mg, 0.20 mmol) and cyclohexylchloride **180a** (71 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181aa** (48.7 mg, 79%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.35 (brs, 1H), 8.33 (dd, *J* = 4.5, 1.5 Hz, 1H), 7.74 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.42–7.38 (m, 2H), 7.35–7.29 (m, 3H), 7.26–7.20 (m, 1H), 5.29 (dq, *J* = 6.9, 6.4 Hz, 1H), 4.07 (tt, *J* = 11.7, 3.0 Hz, 1H), 1.93–1.72 (m, 5H), 1.59 (d, *J* = 6.9 Hz, 3H), 1.54–1.16 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.3 (C_q), 146.9 (C_q), 144.9 (CH), 144.8 (C_q), 143.6 (C_q), 136.0 (CH), 128.6 (CH), 127.1 (CH), 126.1 (CH), 125.6 (CH), 48.5 (CH), 37.7 (CH), 34.2 (CH_2), 34.0 (CH_2), 26.7 (CH_2), 26.7 (CH_2), 26.2 (CH_2), 22.3 (CH_3). **IR** (ATR): 3376, 2922, 2850, 1665, 1497, 806, 699, 625 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 331 (100) $[M+Na]^+$, 309 (30) $[M+H]^+$, 188 (30). **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{25}N_2O$ $[M+H]^+$ 309.1961 found 309.1958.



3-Cyclohexyl-*N*-phenethylpicolinamide (181ba)

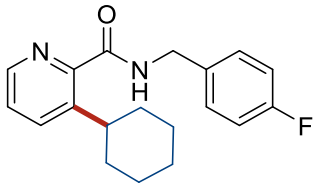
Prepared following the general procedure **C** using *N*-phenethylpicolinamide **88b** (45.2 mg, 0.20 mmol) and cyclohexylchloride **180a** (71 µL, 0.60 mmol). Purification by column

chromatography (*n*-hexane/EtOAc 8:1) yielded **181ba** (58.0 mg, 94%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.22 (dd, *J* = 4.5, 1.5 Hz, 1H), 8.01 (brs, 1H), 7.67 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.25–7.11 (m, 6H), 3.97 (tt, *J* = 11.8, 3.0 Hz, 1H), 3.69–3.54 (m, 2H), 2.86 (t, *J* = 7.2 Hz, 2H), 1.78–1.67 (m, 5H), 1.55–1.07 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.2 (C_q), 147.0 (C_q), 144.9 (CH), 144.6 (C_q), 139.1 (CH), 135.9 (CH), 128.7 (CH), 128.45 (CH), 126.3 (CH), 125.6 (CH), 40.6 (CH_2), 37.8 (CH), 35.9 (CH_2), 34.1 (CH_2), 26.7 (CH_2), 26.2 (CH_2). **IR** (ATR): 3384, 2923, 2850, 1664, 1506, 1000, 806, 698, 497 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 331 (40) $[M+Na]^+$, 309 (100) $[M+H]^+$, 284 (10), 188 (10). **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{25}N_2O$ $[M+H]^+$ 309.1965 found 309.1961.



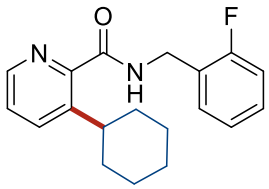
***N*-Benzyl-3-cyclohexylpicolinamide (181ca)**

Prepared following the general procedure **C** using *N*-phenethylpicolinamide **88c** (42.4 mg, 0.20 mmol) and **180a** cyclohexylchloride (71 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ca** (45.2 mg, 77%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.36 (brs, 1H), 8.31 (dd, *J* = 4.5, 1.5 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.37–7.30 (m, 5H), 7.27–7.23 (m, 1H), 4.62 (d, *J* = 6.0 Hz, 2H), 4.10 (tt, *J* = 11.8, 3.3 Hz, 1H), 1.92–1.89 (m, 2H), 1.84–1.75 (m, 3H), 1.52 (qt, *J* = 12.8, 3.3 Hz, 2H), 1.35 (qd, *J* = 12.4, 3.0 Hz, 2H), 1.24 (qt, *J* = 13.0, 3.6 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.1 (C_q), 146.8 (C_q), 145.0 (CH), 144.9 (C_q), 138.4 (C_q), 136.0 (CH), 128.6 (CH), 127.7 (CH), 127.3 (CH), 125.7 (CH), 43.3 (CH_2), 37.8 (CH), 34.1 (CH_2), 26.7 (CH_2), 26.2 (CH_2). **IR** (ATR): 3381, 2922, 2849, 1665, 1505, 805, 698 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 317 (100) $[M+Na]^+$, 295 (40) $[M+H]^+$, 188 (20), 106 (10). **HR-MS** (ESI) *m/z* calcd for $C_{19}H_{23}N_2O$ $[M+H]^+$ 295.1800 found 295.1805.



3-Cyclohexyl-*N*-(4-fluorobenzyl)picolinamide (181da)

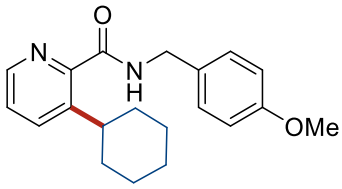
Prepared following the general procedure **C** using *N*-(4-fluorobenzyl)picolinamide **88d** (46.1 mg, 0.20 mmol) and cyclohexylchloride **180a** (71 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181da** (52.3 mg, 84%) as a white solid. **M.p.** = 72–73 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.32 (brs, 1H), 8.25 (dd, *J* = 4.5, 1.5 Hz, 1H), 7.70 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.28–7.23 (m, 3H), 6.97–6.90 (m, 2H), 4.51 (d, *J* = 6.0 Hz, 2H), 4.02 (tt, *J* = 11.8, 3.0 Hz, 1H), 1.85–1.67 (m, 5H), 1.51–1.10 (m, 5H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.0 (C_q), 161.9 (d, $^1J_{C-F}$ = 245.0 Hz, C_q), 146.6 (C_q), 144.9 (CH), 144.8 (C_q), 135.9 (CH), 134.2 (d, $^4J_{C-F}$ = 3.1 Hz, C_q), 129.2 (d, $^3J_{C-F}$ = 8.1 Hz, CH), 125.7 (CH), 115.3 (d, $^2J_{C-F}$ = 21.4 Hz, CH), 42.6 (CH_2), 37.9 (CH), 34.2 (CH_2), 26.8 (CH_2), 26.3 (CH_2). **^{19}F NMR** (275 MHz, $CDCl_3$) δ = -115.4–-115.5 (m). **IR** (ATR): 3187, 2925, 2851, 1655, 1505, 1221, 838, 728, 429 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 335 (100) $[M+Na]^+$, 313 (15) $[M+H]^+$, 244 (8). **HR-MS** (ESI) *m/z* calcd for $C_{19}H_{22}FN_2O$ $[M+H]^+$ 313.1708 found 313.1711.



3-Cyclohexyl-*N*-(2-fluorobenzyl)picolinamide (181ea)

Prepared following the general procedure **C** using *N*-(2-fluorobenzyl)picolinamide **88e** (46.0 mg, 0.20 mmol) and cyclohexylchloride **180a** (71 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ea** (51.7 mg, 83%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.38 (t, *J* = 6.4 Hz, 1H) , 8.32 (dd, *J* = 4.4, 1.6

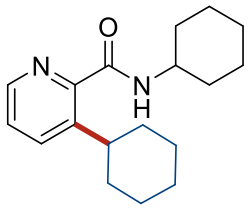
Hz, 1H), 7.75 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.40 (td, *J* = 7.6, 1.8 Hz, 1H), 7.31 (ddd, *J* = 8.0, 4.4, 0.4 Hz, 1H), 7.25–7.20 (m, 1H), 7.08 (td, *J* = 7.6, 1.2 Hz, 1H), 7.06–7.00 (m, 1H), 4.67 (d, *J* = 6.4 Hz, 2H), 4.07 (tt, *J* = 11.6, 3.0 Hz, 1H), 1.90–1.73 (m, 5H), 1.56–1.45 (m, 2H), 1.39–1.20 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.1 (C_q), 161.0 (d, $^1J_{C-F}$ = 246.0 Hz, C_q), 146.7 (C_q), 145.0 (CH), 144.9 (C_q), 136.0 (CH), 130.0 (d, $^3J_{C-F}$ = 4.3 Hz, CH), 129.0 (d, $^3J_{C-F}$ = 8.1 Hz, CH), 125.8 (CH), 125.5 (d, $^2J_{C-F}$ = 14.9 Hz, C_q), 124.2 (d, $^4J_{C-F}$ = 3.6 Hz, CH), 115.3 (d, $^2J_{C-F}$ = 21.3 Hz, CH), 37.8 (CH), 37.1 (d, $^3J_{C-F}$ = 4.2 Hz, CH_2), 34.1 (CH_2), 26.7 (CH_2), 26.2 (CH_2). **^{19}F NMR** (275 MHz, $CDCl_3$) δ = -118.7–-118.8 (m). **IR** (ATR): 3382, 2922, 2850, 1668, 1501, 1227, 805, 757, 625 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 335 (100) $[M+Na]^+$, 313 (20) $[M+H]^+$, 244 (15). **HR-MS** (ESI) *m/z* calcd for $C_{19}H_{22}FN_2O$ $[M+H]^+$ 313.1708 found 313.1709.



3-Cyclohexyl-*N*-(4-methoxybenzyl)picolinamide (181fa)

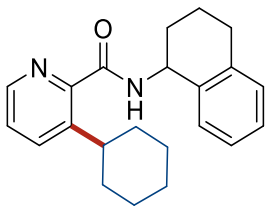
Prepared following the general procedure **C** using *N*-(4-methoxybenzyl)picolinamide **88f** (48.4 mg, 0.20 mmol) and cyclohexylchloride **181fa** (71 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181fa** (57.1 mg, 88%) as a yellow solid. **M.p.** = 107–108 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.29 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.27 (brs, 1H), 7.74 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.30 (ddd, *J* = 8.0, 4.4, 0.4 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 4.54 (d, *J* = 6.0 Hz, 2H), 4.09 (tt, *J* = 11.6, 3.1 Hz, 1H), 3.76 (s, 3H), 1.93–1.72 (m, 5H), 1.52 (qt, *J* = 12.4, 3.2 Hz, 2H), 1.34 (qd, *J* = 12.4, 3.2 Hz, 2H), 1.23 (qt, *J* = 12.8, 3.6 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.0 (C_q), 158.9 (C_q), 146.9 (C_q), 144.9 (CH), 144.8 (C_q), 136.0 (CH), 130.5 (C_q), 129.1 (CH), 125.7 (CH), 114.0 (CH), 55.2 (CH_3), 42.8 (CH_2), 37.8 (CH), 34.1 (CH_2), 26.7 (CH_2), 26.2 (CH_2). **IR** (ATR): 3306, 2925, 2848, 1652, 1513, 1242, 994, 807, 685 cm^{-1}. **MS** (ESI) *m/z* (relative intensity):

347 (100) $[M+Na]^+$, 325 (50) $[M+H]^+$, 188 (15), 121 (10). **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{25}N_2O_2$ $[M+H]^+$ 325.1905 found 325.1911.



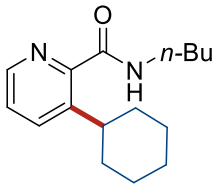
_N_,3-Dicyclohexylpicolinamide (181ga)

Prepared following the general procedure **C** using *N*-cyclohexylpicolinamide **88g** (40.8 mg, 0.20 mmol) and cyclohexylchloride **180a** (71 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ga** (45.9 mg, 80%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.30 (dd, *J* = 4.4, 1.6 Hz, 1H), 7.89 (d, *J* = 8.8 Hz, 1H), 7.72 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.28 (dd, *J* = 8.0, 4.4 Hz, 1H), 4.04 (tt, *J* = 11.6, 3.2 Hz, 1H), 3.94–3.85 (m, 1H), 2.00–1.93 (m, 9H), 1.63–1.16 (m, 11H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.3 (C_q), 147.2 (C_q), 144.8 (CH), 144.7 (C_q), 135.9 (CH), 125.5 (CH), 48.0 (CH), 37.9 (CH), 34.1 (CH_2), 33.1 (CH_2), 26.7 (CH_2), 26.2 (CH_2), 25.6 (CH_2), 24.9 (CH_2). **IR** (ATR): 3378, 2922, 2850, 1663, 1502, 805, 625 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 309 (30) $[M+Na]^+$, 287 (100) $[M+H]^+$, 202 (20), 188 (10). **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{27}N_2O$ $[M+H]^+$ 287.2119 found 287.2118.



3-Cyclohexyl-_N_-(1,2,3,4-tetrahydronaphthalen-1-yl)picolinamide (181ha)

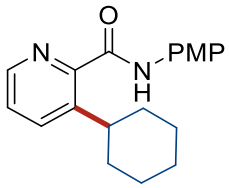
Prepared following the general procedure **C** using *N*-(1,2,3,4-tetrahydronaphthalen-1-yl)picolinamide **88h** (50.4 mg, 0.20 mmol) and cyclohexylchloride **180a** (71 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ha** (55.1 mg, 82%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.33 (d, *J* = 8.8 Hz, 1H), 8.28 (dd, *J* = 4.4, 1.6 Hz, 1H), 7.76 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.36–7.33 (m, 1H), 7.31 (ddd, *J* = 8.0, 4.4, 0.4 Hz, 1H), 7.17–7.09 (m, 3H), 5.37–5.32 (m, 1H), 4.15 (tt, *J* = 12.0, 3.2 Hz, 1H), 2.94–2.71 (m, 2H), 2.22–2.09 (m, 1H), 1.96–1.77 (m, 8H), 1.63–1.46 (m, 2H), 1.43–1.22 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.5 (C_q), 146.9 (C_q), 144.92 (CH), 144.8 (C_q), 137.5 (C_q), 137.0 (C_q), 135.9 (CH), 129.0 (CH), 128.7 (CH), 127.0 (CH), 126.1 (CH), 125.6 (CH), 47.3 (CH), 37.9 (CH), 34.2 (CH_2), 34.1 (CH_2), 30.3 (CH_2), 29.3 (CH_2), 26.8 (CH_2), 26.3 (CH_2), 20.2 (CH_2). **IR** (ATR): 3376, 2923, 2851, 1664, 1493, 1445, 805, 734, 624 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 357 (100) $[M+Na]^+$, 335 (25) $[M+H]^+$, 188 (30), 147 (10). **HR-MS** (ESI) *m/z* calcd for $C_{19}H_{22}FN_2O$ $[M+H]^+$ 335.2123 found 335.2120.



***N*-Butyl-3-cyclohexylpicolinamide (181ia)**

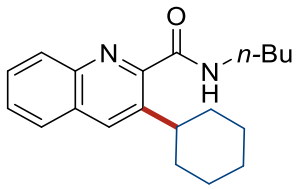
Prepared following the general procedure **C** using *N*-butylpicolinamide **88i** (35.6 mg, 0.20 mmol) and cyclohexylchloride **180a** (71 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ia** (47.7 mg, 92%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.31 (dd, *J* = 4.4, 1.6 Hz, 1H), 7.97 (brs, 1H), 7.72 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.29 (dd, *J* = 8.0, 4.4 Hz, 1H), 4.04 (tt, *J* = 12.0, 3.2 Hz, 1H), 3.39 (td, *J* = 7.2, 6.0 Hz, 2H), 1.88–1.76 (m, 5H), 1.62–1.18 (m, 9H), 0.92 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 166.2 (C_q), 147.2 (C_q), 144.9 (CH), 144.7 (C_q), 136.0 (CH), 125.5 (CH), 39.1 (CH_2), 37.8 (CH), 34.1 (CH_2), 31.7 (CH_2), 26.7 (CH_2), 26.2 (CH_2), 20.2 (CH_2), 13.8 (CH_3). **IR** (ATR): 3382, 2922, 2850, 1663, 1504, 694, 498 cm^{-1}. **MS** (ESI) *m/z* (relative

intensity): 283 (40) $[M+Na]^+$, 261 (100) $[M+H]^+$,188 (15), 160 (10). **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{25}N_2O$ $[M+H]^+$ 261.1964 found 261.1961.



3-Cyclohexyl-*N*-(4-methoxyphenyl)picolinamide (181ja)

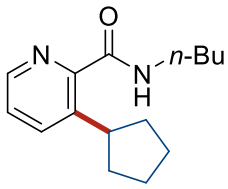
Prepared following the general procedure **C** using *N*-(4-methoxyphenyl)picolinamide **88j** (45.6 mg, 0.20 mmol) and cyclohexylchloride **180a** (71 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ja** (28.7 mg, 46%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 10.05 (brs, 1H), 8.41 (dd, *J* = 4.5, 1.5 Hz, 1H), 7.85–7.80 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.64 (d, *J* = 9.0 Hz, 2H), 7.39 (dd, *J* = 8.1, 4.5 Hz, 1H), 6.91 (d, *J* = 9.0 Hz, 2H), 4.24–4.16 (m, 1H), 3.81 (s, 3H), 1.95–1.76 (m, 5H), 1.57–1.24 (m, 5H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 163.5 (C_q), 156.1 (C_q), 146.4 (C_q), 145.4 (C_q), 144.7 (CH), 136.3 (CH), 131.3 (C_q), 125.9 (CH), 121.5 (CH), 114.1 (CH), 55.5 (CH_3), 37.9 (CH), 34.2 (CH_2), 26.8 (CH_2), 26.3 (CH_2). **IR** (ATR): 3319, 2922, 2847, 1673, 1513, 1240, 825, 689, 559 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 333 (35) $[M+Na]^+$, 211 (100) $[M+H]^+$, 188 (15), 160 (10). **HR-MS** (ESI) *m/z* calcd for $C_{19}H_{23}N_2O_2$ $[M+H]^+$ 311.1756 found 311.1754.



***N*-Butyl-3-cyclohexylquinoline–2-carboxamide (181ka)**

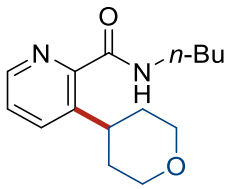
Prepared following the general procedure **C** using *N*-phenethylpicolinamide **88k** (48.4 mg, 0.20 mmol) and cyclohexylchloride **180a** (71 µL, 0.60 mmol). Purification by column

chromatography (*n*-hexane/EtOAc 8:1) yielded **181ka** (16.7 mg, 26%) as a white solid. **M.p.** = 92–93 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.28 (t, *J* = 5.6 Hz, 1H), 8.20 (brs, 1H), 8.12–8.07 (m, 2H), 7.70 (ddd, *J* = 8.4, 6.8, 1.6 Hz, 1H), 7.58 (ddd, *J* = 8.4, 6.8, 1.6 Hz, 1H), 3.51 (td, *J* = 7.1, 6.0 Hz, 2H), 3.33 (tt, *J* = 11.6, 3.0 Hz, 1H), 2.00–1.80 (m, 4H), 1.85–1.80 (m, 1H), 1.69–1.28 (m, 9H), 0.96 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 164.8 (C_q), 155.1 (C_q), 149.8 (C_q), 146.8 (C_q), 130.6 (CH), 129.3 (CH), 127.8 (C_q), 127.3 (CH), 123.1 (CH), 115.2 (CH), 39.3 (CH), 33.4 (CH_2), 31.8 (CH_2), 26.9 (CH_2), 26.2 (CH_2), 20.2 (CH_2), 13.8(CH_3). **IR** (ATR): 3322, 2928, 2855, 1669, 1529, 762 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 333 (30) $[M+Na]^+$, 311 (100) $[M+H]^+$, 238 (20). **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{27}N_2O$ $[M+H]^+$311.2119 found 311.2118.



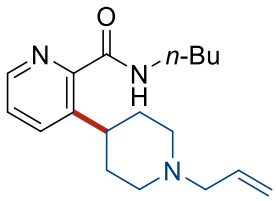
***N*-Butyl-3-cyclopentylpicolinamide (181ib)**

Prepared following the general procedure **C** using *N*-butylpicolinamide **88i** (35.6 mg, 0.20 mmol) and cyclopentylchloride **180b** (63 µL, 0.60 mmol) under stirring for 36 h. Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ib** (28.1 mg, 57%) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.31 (dd, *J* = 4.5, 1.5 Hz, 1H), 7.90 (brs, 1H), 7.74 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.30 (dd, *J* = 8.1, 4.5 Hz, 1H), 4.39 (tt, *J* = 9.6, 7.5 Hz, 1H), 3.40 (td, *J* = 7.1, 6.0 Hz, 2H), 2.17–2.07 (m, 2H), 1.77–1.70 (m, 4H), 1.62–1.36 (m, 6H), 0.93 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.3 (C_q), 147.9 (C_q), 144.8 (CH), 143.3 (C_q), 136.0 (CH), 125.5 (CH), 39.7 (CH), 39.2 (CH_2), 34.7 (CH_2), 31.8 (CH_2), 25.8 (CH_2), 20.3 (CH_2), 13.9 (CH_3). **IR** (ATR): 3385, 2947, 2859, 1660, 1508, 804, 654 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 269 (100) $[M+Na]^+$, 247 (25) $[M+H]^+$, 174 (15). **HR-MS** (ESI) *m/z* calcd for $C_{15}H_{23}N_2O$ $[M+H]^+$ 247.1803 found 247.1805.



_N_-Butyl-3-(tetrahydro–2_H_-pyran-4-yl)picolinamide (181ic)

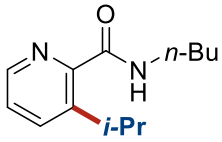
Prepared following the general procedure **C** using *N*-butylpicolinamide **88i** (35.6 mg, 0.20 mmol) and 4-chlorotetrahydro-2*H*-pyran **180c** (65 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ic** (31.5 mg, 60%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.36 (dd, *J* = 4.5, 1.5 Hz, 1H), 8.09 (brs, 1H), 7.75 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.36 (dd, *J* = 8.1, 4.5 Hz, 1H), 4.45–4.35 (m, 1H), 4.06–4.01 (m, 2H), 3.68–3,56 (m, 2H), 3.40 (td, *J* = 7.2, 6.0 Hz, 2H), 1.81–1.55 (m, 4H), 1.65–1.54 (m, 2H), 1.47–1.34 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 165.8 (C_q), 146.9 (C_q), 145.3 (CH), 142.6 (C_q), 136.0 (CH), 125.7 (CH), 68.4 (CH_2), 39.2 (CH_2), 35.4 (CH), 33.6 (CH_2), 31.7 (CH_2), 20.3 (CH_2), 13.9 (CH_3). **IR** (ATR): 3386, 2951, 2928, 2843, 1661, 1512, 1502, 1437, 1124, 630, 597 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 285 (100) $[M+Na]^+$, 263 (10) $[M+H]^+$, 224 (30), 190 (15). **HR-MS** (ESI) *m/z* calcd for $C_{15}H_{23}N_2O_2$ $[M+H]^+$ 263.1754 found 263.1754.



3-(1-Allylpiperidin-4-yl)-_N_-butylpicolinamide (181id)

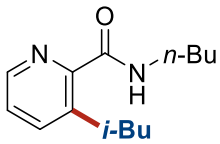
Prepared following the general procedure **C** using *N*-butylpicolinamide **88i** (35.6 mg, 0.20 mmol) and 1-allylpiperidine **180d** (94 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181id** (46.4 mg, 77%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.32 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.04 (brs, 1H), 7.76 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.30 (dd, *J* = 8.0, 4.4 Hz, 1H), 5.88 (ddt, *J* = 16.8, 10.0, 6.8 Hz, 1H), 5.19–

5.11 (m, 2H), 4.11 (tt, *J* = 12.0, 3.6 Hz, 1H), 3.37 (td, *J* = 7.2, 6.0 Hz, 2H), 3.03 (dt, *J* = 6.8, 1.2 Hz, 4H), 2.18 (td, *J* = 11.8, 2.4 Hz, 2H), 1.93–1.80 (m, 2H), 1.75 (qd, *J* = 12.4, 3.6 Hz, 2H), 1.65–1.48 (m, 2H), 1.45–1.25 (m, 2H), 0.90 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* = 166.0 (C_q), 147.1 (C_q), 145.2 (CH), 143.0 (C_q), 136.0 (CH), 134.5 (CH), 125.7 (CH), 118.4 (CH_2), 61.9 (CH_2), 53.9 (CH_2), 39.1 (CH_2), 35.9 (CH), 32.7 (CH_2), 31.6 (CH_2), 20.2 (CH_2), 13.7 (CH_3). **IR** (ATR): 3385, 2927, 2789, 1662, 1512, 1438, 994, 918, 626 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 318 (10) $[M+Na]^+$, 302 (100) $[M+H]^+$, 229 (30). **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{28}N_3O$ $[M+H]^+$ 302.2227 found 302.2224.



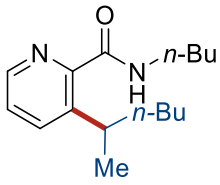
***N*-Butyl-3-isopropylpicolinamide (181ie)**

Prepared following the general procedure **C** using *N*-butylpicolinamide **88i** (35.6 mg, 0.20 mmol)and isopropylchloride **180e** (53 µL, 0.60 mmol) with stirring for 24 h. Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ie** (27.3 mg, 62%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* = 8.32 (dd, *J* = 4.4, 1.6 Hz, 1H), 7.92 (brs, 1H), 7.75 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.31 (dd, *J* = 8.0, 4.4 Hz, 1H), 4.40 (p, *J* = 6.8 Hz, 1H), 3.39 (td, *J* = 7.2, 6.0 Hz, 2H), 1.62–1.55 (m, 2H), 1.44–1.35 (m, 2H), 1.23 (d, *J* = 6.8 Hz, 6H), 0.92 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) *δ* = 166.2 (C_q), 147.2 (C_q), 145.6 (C_q), 145.0 (CH), 135.4 (CH), 125.6 (CH), 39.1 (CH_2), 31.7 (CH_2), 27.5 (CH), 23.6 (CH_3), 20.2 (CH_2), 13.8 (CH_3). **IR** (ATR): 3386, 2958, 2866, 1662, 1511, 855, 655 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 243 (100) $[M+Na]^+$, 221 (20) $[M+H]^+$, 148 (15). **HR-MS** (ESI) *m/z* calcd for $C_{13}H_{21}N_2O$ $[M+H]^+$ 221.1646 found 2212.1648.



3-(S,*ec*-Butyl)-*N*-butylpicolinamide (181if)

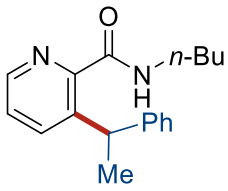
Prepared following the general procedure **C** using *N*-butylpicolinamide **88i** (35.6 mg, 0.20 mmol) and isobutylchloride **180f** (64 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181if** (35.7 mg, 75%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.28 (dd, *J* = 4.5, 1.5 Hz, 1H), 7.88 (brs, 1H), 7.66 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.27 (dd, *J* = 8.0, 4.5 Hz, 1H), 4.23–4.11 (m, 1H), 3.35 (td, *J* = 7.2, 6.0 Hz, 2H), 1.60–1.48 (m, 4H), 1.41–1.29 (m, 2H), 1.16 (d, *J* = 6.9 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H), 0.78 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.1 (C_q), 147.7 (C_q), 144.9 (CH), 144.5 (C_q), 135.8 (CH), 125.4 (CH), 39.1 (CH_2), 34.0 (CH), 31.7 (CH_2), 30.8 (CH_2), 21.4 (CH_3), 20.3 (CH_2), 13.8 (CH_3), 12.1 (CH_3). **IR** (ATR): 3394, 2958, 2865, 1669, 1514, 146, 805, 398 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 257 (100) $[M+Na]^+$, 235 (20) $[M+H]^+$, 201 (60). **HR-MS** (ESI) *m/z* calcd for $C_{14}H_{23}N_2O$ $[M+H]^+$ 235.1801 found 235.1805.



***N*-Butyl-3-(hexan–2-yl)picolinamide (181ig)**

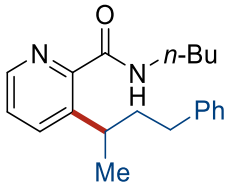
Prepared following the general procedure **C** using *N*-butylpicolinamide **88i** (35.6 mg, 0.20 mmol) and 2-chlorohexane **181g** (83 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ig** (47.6 mg, 82%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.33 (dd, *J* = 4.4, 1.6 Hz, 1H), 7.88 (brs, 1H), 7.72 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.32 (ddd, *J* = 8.0, 4.4, 0.4 Hz, 1H), 4.30 (h, *J* = 7.2 Hz, 1H), 3.43–3.39 (m, 2H), 1.63–1.48 (m, 4H), 1.45–1.35 (m, 2H), 1.30–1.19 (m, 3H), 1.21 (d, *J* = 6.8 Hz, 3H), 1.16–1.08 (m, 1H), 0.93 (t, *J* = 7.2 Hz, 3H), 0.81 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz,

$CDCl_3$) δ = 166.3 (C_q), 147.7 (C_q), 145.0 (CH), 144.9 (C_q), 136.0 (CH), 125.6 (CH), 39.1 (CH_2), 37.7 (CH_2), 32.3 (CH), 31.7 (CH_2), 29.8 (CH_2), 22.8 (CH_2), 22.0 (CH_3), 20.2 (CH_2), 14.0 (CH_3), 13.8 (CH_3). **IR** (ATR): 3387, 2955, 2925, 2863, 1665, 1511, 1457, 806, 708, 659 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 285 (30) $[M+Na]^+$, 263 (100) $[M+H]^+$, 190 (10), 162 (10). **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{29}N_2O$ $[M+H]^+$ 263.4050 found 263.4046.



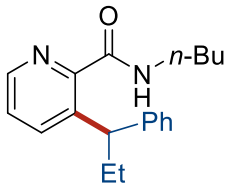
_N_-Butyl-3-(1-phenylethyl)picolinamide (181ih)

Prepared following the general procedure **C** using *N*-butylpicolinamide **88ii** (35.6 mg, 0.20 mmol) and (1-chloroethyl)benzene **180h** (80 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ih** (20.9 mg, 37%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.38 (dd, *J* = 5.2, 0.8 Hz, 1H), 8.11–8.10 (m, 1H), 8.03 (brs, 1H), 7.30–7.24 (m, 2H), 7.21–7.16 (m, 4H), 4.17 (q, *J* = 7.2 Hz, 1H), 3.44 (td, *J* = 7.2, 6.0 Hz, 2H), 1.65 (d, *J* = 7.2 Hz, 3H), 1.61–1.55 (m, 2H), 1.43–1.35 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 164.3 (C_q), 156.9 (C_q), 150.1 (C_q), 148.0 (CH), 144.0 (C_q), 128.7 (CH), 127.6 (CH), 126.7 (CH), 125.3 (CH), 121.3 (CH), 44.5 (CH), 39.1 (CH_2), 31.7 (CH_2), 20.9 (CH_3), 20.1 (CH_2), 13.8 (CH_3). **IR** (ATR): 3387, 2960, 2868, 1668, 1523, 701, 585 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 305 (100) $[M+Na]^+$, 283 (55) $[M+H]^+$, 229 (35), 207 (20). **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{23}N_2O$ $[M+H]^+$ 283.1805 found 283.1805.



_N_-Butyl-3-(4-phenylbutan–2-yl)picolinamide (181ii)

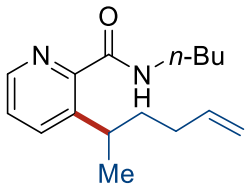
Prepared following the general procedure **C** using *N*-butylpicolinamide **88i** (35.6 mg, 0.20 mmol) and (3-chlorobutyl)benzene **180i** (101 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ii** (32.4 mg, 52%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.36 (dd, *J* = 4.5, 1.5 Hz, 1H), 7.93 (s, 1H), 7.76 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.34 (ddd, *J* = 8.1, 4.5, 0.6 Hz, 2H), 7.24–7.08 (m, 4H), 4.45 (h, *J* = 7.2 Hz, 1H), 3.42 (td, *J* = 7.2, 6.0 Hz, 2H), 2.70–2.57 (m, 1H), 2.50–2.37 (m, 1H), 1.99–1.82 (m, 2H), 1.66–1.56 (m, 2H), 1.49–1.36 (m, 2H), 1.29 (d, *J* = 6.9 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.1 (C_q), 147.7 (C_q), 145.10 (CH), 144.2 (C_q), 142.5 (C_q), 135.8 (CH), 128.1 (CH), 128.1 (CH), 125.6 (CH), 125.5 (CH), 40.1 (CH_2), 39.2 (CH_2), 34.2 (CH_2), 32.8 (CH), 31.8 (CH_2), 22.18 (CH_3), 20.3 (CH_2), 13.9 (CH_3). **IR** (ATR): 3388, 2926, 2863, 1664, 1510, 1455, 807, 700 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 333 (30) $[M+Na]^+$, 311 (100) $[M+H]^+$, 238 (10). **HR-MS** (ESI) *m/z* calcd for $C_{20}H_{27}N_2O$ $[M+H]^+$ 311.2120 found 311.2118.



***N*-Butyl-3-(1-phenylbutyl)picolinamide (181ij)**

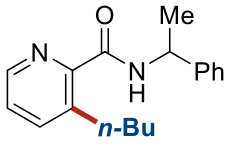
Prepared following the general procedure **C** using *N*-butylpicolinamide **88i** (35.6 mg, 0.20 mmol) and (1-chloropropyl)benzene **180j** (100 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181ij** (36.7 mg, 59%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.37 (dd, *J* = 5.1, 0.9 Hz, 1H), 8.11 (dt, *J* = 1.8, 0.6 Hz, 1H), 8.02 (brs, 1H), 7.29–7.17 (m, 6H), 3.82 (t, *J* = 7.8 Hz, 1H), 3.43 (td, *J* = 7.2, 6.3 Hz, 2H), 2.14–2.04 (m, 2H), 1.63–1.54 (m, 2H), 1.46–1.33 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H), 0.88 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 164.2 (C_q), 155.7 (C_q), 150.0 (C_q), 147.9 (CH), 142.7 (C_q), 128.6 (CH), 127.8 (CH), 126.6 (CH), 125.5 (CH), 121.5 (CH), 52.9 (CH_2), 39.2 (CH_2), 31.8 (CH_2), 27.9 (CH_2), 20.2 (CH_2), 13.8 (CH_3), 12.6 (CH_3). **IR** (ATR): 3388, 2959, 2928, 2868, 1668, 1522, 700, 593 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 319 (30)

[M+Na]$^+$, 297 (100) [M+H]$^+$, 223 (10). **HR-MS** (ESI) *m/z* calcd for $C_{19}H_{25}N_2O$ [M+H]$^+$ 297.1966 found 297.1961.



_N_-Butyl-3-(hex–5-en–2-yl)picolinamide (181k)

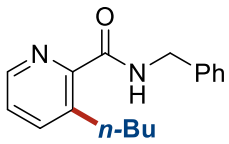
Prepared following the general procedure **C** using *N*-butylpicolinamide **88i** (35.6 mg, 0.20 mmol) and 5-chlorohex-1-ene **180k** (80 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **181k** (30.7 mg, 59%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.29 (dd, *J* = 4.5, 1.5 Hz, 1H), 7.85 (brs, 1H), 7.68 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.28 (ddd, *J* = 8.1, 4.5, 0.6 Hz, 1H), 5.72 (ddt, *J* = 16.8, 10.2, 6.6 Hz, 1H), 4.90–4.80 (m, 2H), 4.31 (h, *J* = 7.2 Hz, 1H), 3.39–3.32 (m, 2H), 2.06–1.80 (m, 2H), 1.66–1.50 (m, 4H), 1.44–1.27 (m, 2H), 1.19 (d, *J* = 6.9 Hz, 3H), 0.89 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 166.1 (C_q), 147.7 (C_q), 145.0 (CH), 144.3 (C_q), 138.6 (CH), 135.9 (CH), 125.5 (CH), 114.1 (CH_2), 39.2 (CH_2), 37.2 (CH_2), 32.2 (CH), 31.9 (CH_2), 31.8 (CH_2), 22.0 (CH_3), 20.3 (CH_2), 13.9 (CH_3). **IR** (ATR): 3385, 2924, 2864, 1664, 1512, 1373, 807, 654 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 383 (40) [M+Na]$^+$, 261 (100) [M+H]$^+$, 188 (10). **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{25}N_2O$ [M+H]$^+$ 261.1963 found 261.1961.



Butyl-_N_-(1-phenylethyl)picolinamide (200aa)

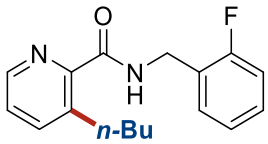
Prepared following the general procedure **D** using *N*-(1-phenylethyl)picolinamide **88a** (45.2 mg, 0.20 mmol) and *n*-butylbromide **86a** (64 µL, 0.60 mmol). Purification by column

chromatography (*n*-hexane/EtOAc 8:1) yielded **200aa** (39.0 mg, 69%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.41 (brs 1H), 8.35 (dd, *J* = 4.6, 1.7 Hz, 1H), 7.56 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.42–7.37 (m, 2H), 7.36–7.20 (m, 4H), 5.35–5.19 (m, 1H), 3.25–3.06 (m, 2H), 1.66–1.51 (m, 5H), 1.44–1.32 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 164.9 (C_q), 147.1 (C_q), 145.3 (CH), 143.7 (C_q), 140.2 (C_q), 139.9 (CH), 128.6 (CH), 127.1 (CH), 126.1 (CH), 125.5 (CH), 48.5 (CH), 33.5 (CH_2), 32.7 (CH_2), 22.7 (CH_2), 22.3 (CH_3), 14.0 (CH_3). **IR** (ATR): 2958, 2864, 1669, 1496, 1208, 698 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 305 (100) $[M+Na]^+$, 283 (50) $[M+H]^+$, 236 (10). **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{22}N_2O$ $[M+H]^+$ 283.1805, found 283.1797.



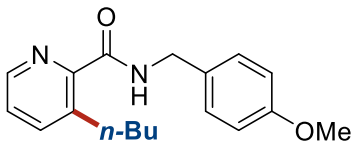
***N*-Benzyl-3-butylpicolinamide (200ba)**

Prepared following the general procedure **D** using *N*-benzylpicolinamide **88b** (42.4 mg, 0.20 mmol) and *n*-butylbromide **86a** (64 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 6:1) yielded **200ba** (34.8 mg, 65%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.44 (brs 1H), 8.34 (brs,1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.46–7.15 (m, 6H), 4.62 (d, *J* = 4.8 Hz, 2H), 3.19 (t, *J* = 7.5 Hz, 2H), 1.70–1.56 (m, 2H), 1.51–1.34 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 165.6 (C_q), 147.0 (C_q), 145.3 (CH), 140.2 (C_q), 139.9 (CH), 138.5 (C_q), 128.5 (CH), 127.7 (CH), 127.2 (CH), 125.5 (CH), 43.3 (CH_2), 33.7 (CH_2), 32.9 (CH_2), 22.9 (CH_2), 14.1 (CH_3). **IR** (ATR): 2926, 2862, 1668, 1505, 1433, 1127, 697, 602 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 291 (100) $[M+Na]^+$, 269 (30) $[M+H]^+$, 236 (10). **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{20}N_2O$ $[M+Na]^+$ 291.1468, found 291.1463.



3-Butyl-*N*-(2-fluorobenzyl)picolinamide (200ca)

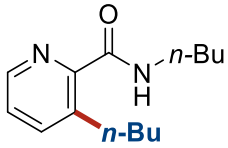
Prepared following the general procedure **D** using *N*-(2-fluorobenzyl)picolinamide **88c** (46.0 mg, 0.20 mmol) and *n*-butylbromide **86a** (64 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 6:1) yielded **200ca** (32.0 mg, 56%) as a white solid. **M.p.** = 55–57 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.45 (brs 1H), 8.34 (dd, *J* = 4.6, 1.7 Hz, 1H), 7.57 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.39 (td, *J* = 7.5, 1.8 Hz, 1H), 7.29 (dd, *J* = 7.8, 4.6 Hz, 1H), 7.26–7.16 (m, 1H), 7.13–6.96 (m, 2H), 4.67 (d, *J* = 6.3 Hz, 2H), 3.24–3.10 (m, 2H), 1.68–1.55 (m, 2H), 1.46–1.32 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 165.6 (C_q), 160.9 (d, $^1J_{C–F}$ = 243.7 Hz, C_q), 146.9 (C_q), 145.3 (CH), 140.2 (C_q), 139.9 (CH), 129.9 (d, $^3J_{C–F}$ = 3.8 Hz, CH), 128.9 (d, $^3J_{C–F}$ = 7.5 Hz, CH), 125.5 (CH), 125.4 (C_q), 124.1 (d, $^4J_{C–F}$ = 3.7 Hz, CH), 115.2 (d, $^2J_{C–F}$ = 21.3 Hz, CH), 37.2 (d, $^3J_{C–F}$ = 4.9 Hz, CH), 33.6 (CH_2), 32.8 (CH_2), 22.8 (CH_2), 14.1 (CH_3). **^{19}F NMR** (275 MHz, $CDCl_3$) δ = –118.0–117.9 (m). **IR** (ATR): 2927, 2862, 1671, 1502, 1229, 754, 607 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 309 (100) $[M+Na]^+$, 287 (30) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{17}H_{19}FN_2O$ $[M+H]^+$ 287.1554, found 287.1550.



3-Butyl-*N*-(4-methoxybenzyl)picolinamide (200da)

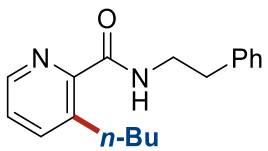
Prepared following the general procedure **D** using *N*-(4-methoxybenzyl)picolinamide **88d** (48.5 mg, 0.20 mmol) and *n*-butylbromide **86a** (64 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 6:1) yielded **200da** (41.2 mg, 69%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.35 (brs, 1H), 8.31 (dd, *J* = 4.6, 1.7 Hz, 1H), 7.57 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.30–7.25 (m, 3H), 6.85 (d, *J* = 8.8 Hz, 2H), 4.54 (d, *J* = 5.9 Hz, 2H), 3.77

(s, 3H), 3.23–3.14 (m, 2H), 1.68–1.56 (m, 2H), 1.46–1.34 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) *δ* = 165.6 (C_q), 158.8 (C_q), 147.0 (C_q), 145.3 (CH), 140.2 (C_q), 140.1 (CH), 140.0 (C_q), 130.6 (CH), 129.1 (CH), 125.5 (CH), 114.0 (CH), 113.9 (CH), 55.2 (CH_3), 42.7 (CH_2), 33.6 (CH_2), 32.8 (CH_2), 22.8 (CH_2), 14.0 (CH_3). **IR** (ATR): 2927, 2863, 1667, 1505, 1033, 813, 579 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 321 (100) $[M+Na]^+$, 299 (30) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{22}N_2O_2$ $[M+Na]^+$ 321.1573, found 321.1569.



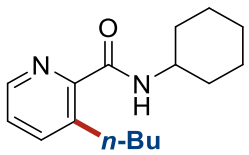
_N_,3-Dibutylpicolinamide (200ia)

Prepared following the general procedure **D** using *N*-butylpicolinamide **88i** (35.6 mg, 0.20 mmol) and *n*-butylbromide **86a** (64 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **200ia** (34.5 mg, 74%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) *δ* = 8.34 (dd, *J* = 4.6, 1.7 Hz, 1H), 8.05 (brs 1H), 7.56 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.27 (dd, *J* = 7.8, 4.6 Hz, 1H), 3.40 (td, *J* = 7.1, 6.0 Hz, 2H), 3.14 (t, *J* = 7.7 Hz, 2H), 1.64–1.54 (m, 4H), 1.45–1.34 (m, 4H), 0.92 (td, *J* = 7.3, 6.3 Hz, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) *δ* = 165.7 (C_q), 147.4 (C_q), 145.2 (CH), 139.9 (C_q), 139.8 (CH), 125.3 (CH), 39.1 (CH_2), 33.7 (CH_2), 32.9 (CH_2), 31.8 (CH_2), 22.9 (CH_2), 20.3 (CH_2), 14.1 (CH_3), 13.9 (CH_3). **IR** (ATR): 2927, 2864, 1667, 1511, 1434, 807, 605 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 257 (100) $[M+Na]^+$, 235 (40) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{14}H_{22}N_2O$ $[M+H]^+$ 235.1805, found 235.1801.



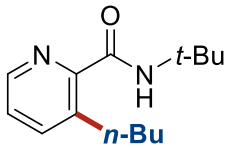
3-Butyl-_N_-phenethylpicolinamide (200fa)

Prepared following the general procedure **D** using *N*-(2-phenylethyl)picolinamide **88f** (45.2 mg, 0.20 mmol) and *n*-butylbromide **86a** (64 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **200fa** (42.3 mg, 75%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.32 (dd, *J* = 4.6, 1.7 Hz, 1H), 8.16 (brs 1H), 7.57 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.33–7.18 (m, 6H), 3.68 (td, *J* = 7.3, 6.0 Hz, 2H), 3.16 (t, *J* = 7.3 Hz, 2H), 2.92 (t, *J* = 7.3 Hz, 2H), 1.65–1.55 (m, 2H), 1.46–1.34 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.8 (C_q), 147.2 (C_q), 145.3 (CH), 140.1 (C_q), 140.0 (CH), 139.2 (C_q), 128.8 (CH), 128.5 (CH), 126.3 (CH), 125.5 (CH), 40.6 (CH_2), 36.0 (CH_2), 33.6 (CH_2), 32.8 (CH_2), 22.8 (CH_2), 14.0 (CH_3). **IR** (ATR): 2927, 2862, 1667, 1506, 1435, 745, 698 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 305 (100) $[M+Na]^+$, 283 (30) $[M+H]^+$, 236 (10). **HR-MS** (ESI) *m/z* calcd for $C_{18}H_{22}N_2O$ $[M+H]^+$ 283.1805, found 283.1798.



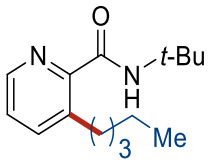
3-Butyl-*N*-cyclohexylpicolinamide (200ga)

Prepared following the general procedure **D** using *N*-cyclohexylpicolinamide **88g** (40.8 mg, 0.20 mmol) and *n*-butylbromide **86a** (64 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **200ga** (39.8 mg, 77%) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 8.33 (dd, *J* = 4.6, 1.7 Hz, 1H), 7.96 (brs 1H), 7.54 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.26 (dd, *J* = 7.8, 4.6 Hz, 1H), 3.95–3.78 (m, 1H), 3.13 (t, *J* = 7.3 Hz, 2H), 2.02–1.93 (m, 2H), 1.77–1.69 (m, 2H), 1.64–1.53 (m, 3H), 1.45–1.33 (m, 4H), 1.30–1.13 (m, 3H), 0.90 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ = 164.8 (C_q), 147.5 (C_q), 145.2 (CH), 140.1 (C_q), 140.0 (CH), 125.3 (CH), 47.9 (CH), 33.7 (CH_2), 33.1 (CH_2), 32.9 (CH_2), 25.6 (CH_2), 24.9 (CH_2), 22.8 (CH_2), 14.0 (CH_3). **IR** (ATR): 2927, 2854, 1667, 1503, 1440, 1122, 808, 590 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 283 (100) $[M+Na]^+$, 261 (50) $[M+H]^+$, 133 (5). **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{24}N_2O$ $[M+H]^+$ 261.1961, found 261.1960.



_N_-(_tert_-Butyl)-3-butylpicolinamide (200ea)

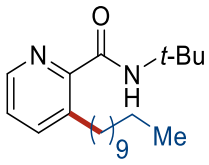
Prepared following the general procedure **D** using *N*-(*tert*-butyl)picolinamide **88e** (35.6 mg, 0.20 mmol) and *n*-butylbromide **86a** (64 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **200ea** (35.5 mg, 75%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.31 (dd, J = 4.6, 1.7 Hz, 1H), 7.83 (brs 1H), 7.54 (dd, J = 7.8, 1.7 Hz, 1H), 7.24 (dd, J = 7.8, 4.6 Hz, 1H), 3.13 (t, J = 7.3 Hz, 2H), 1.65–1.52 (m, 2H), 1.45 (s, 9H), 1.32 (d, J = 7.3 Hz, 2H), 0.90 (t, J = 7.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.4 (C_q), 148.6 (C_q), 145.0 (CH), 139.8 (CH), 139.5 (C_q), 125.1 (CH), 50.7 (C_q), 33.4 (CH_2), 32.6 (CH_2), 28.7 (CH_3), 22.6 (CH_2), 14.0 (CH_3). **IR** (ATR): 2960, 2865, 1674, 1508, 1450, 1227, 805, 603 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 257 (100) $[M+Na]^+$, 235 (80) $[M+H]^+$, 179 (10), 149 (10). **HR-MS** (ESI) *m/z* calcd for $C_{14}H_{22}N_2O$ $[M+H]^+$ 235.1805, found 235.1805.



_N_-(_tert_-Butyl)-3-pentylpicolinamide (200eb)

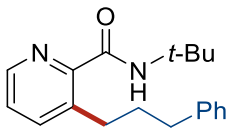
Prepared following the general procedure **D** using *N*-(*tert*-butyl)picolinamide **88e** (35.6 mg, 0.20 mmol) and *n*-pentylbromide **86b** (74 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **200eb** (35.3 mg, 71%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.32 (dd, J = 4.6, 1.6 Hz, 1H), 7.83 (brs 1H), 7.54 (dd, J = 7.8, 1.6 Hz, 1H), 7.25 (dd, J = 7.8, 4.6 Hz, 1H), 3.13 (t, J = 7.3 Hz, 2H), 1.66–1.54 (m, 2H), 1.45 (s, 9H), 1.38–1.26 (m, 4H), 0.89–0.81 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.4 (C_q), 148.6 (C_q), 145.0 (CH), 140.0 (CH), 139.5 (C_q), 125.1 (CH), 50.7 (C_q), 32.8 (CH_2), 31.8 (CH_2), 30.9 (CH_2), 28.7 (CH_3), 22.6 (CH_2), 14.0 (CH_3). **MS** (ESI) *m/z* (relative intensity)

271 (100) [M+Na]$^+$, 249 (70) [M+H]$^+$, 149 (10). **HR-MS** (ESI) *m/z* calcd for $C_{15}H_{24}N_2O$ [M+H]$^+$ 249.1961, found 249.1960.



***N*-(*tert*-Butyl)-3-undecylpicolinamide (200ec)**

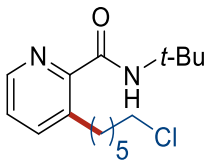
Prepared following the general procedure **D** using *N*-(*tert*-butyl)picolinamide **88e** (35.6 mg, 0.20 mmol) and 1-bromoundecane **86c** (94 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **200ec** (35.3 mg, 53%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.32 (dd, *J* = 4.6, 1.6 Hz, 1H), 7.83 (brs 1H), 7.54 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.25 (dd, *J* = 7.8, 4.6 Hz, 1H), 3.13 (t, *J* = 7.6 Hz, 2H), 1.63–1.54 (m, 2H), 1.45 (s, 9H), 1.39–1.20 (m, 16H), 0.85 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.4 (C_q), 148.6 (C_q), 145.0 (CH), 140.0 (CH), 139.6 (C_q), 125.1 (CH), 50.7 (C_q), 32.9 (CH_2), 31.9 (CH_2), 31.2 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 28.7 (CH_3), 22.7 (CH_2), 14.1 (CH_3). **IR** (ATR): 2922, 2853, 1676, 1509, 1455, 1228, 803, 604 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 355 (100) [M+Na]$^+$, 333 (60) [M+H]$^+$, 236 (10), 149 (10). **HR-MS** (ESI) *m/z* calcd for $C_{21}H_{36}N_2O$ [M+H]$^+$ 333.2900, found 333.2901.



***N*-(*tert*-Butyl)-3-(3-phenylpropyl)picolinamide (200ed)**

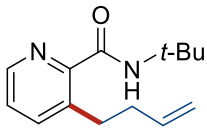
Prepared following the general procedure **D** using *N*-(*tert*-butyl)picolinamide **88e** (35.6 mg, 0.20 mmol) and (3-bromopropyl)benzene **86d** (119.4 mg, 0.60 mmol). Purification by

column chromatography (*n*-hexane/EtOAc 7:1) yielded **200ed** (43.8 mg, 74%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.33 (dd, *J* = 4.6, 1.6 Hz, 1H), 7.90 (brs 1H), 7.52 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.29–7.21 (m, 3H), 7.20–7.11 (m, 3H), 3.22 (t, *J* = 7.5 Hz, 2H), 2.70 (t, *J* = 7.3 Hz, 2H), 2.01–1.91 (m, 2H), 1.47 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.3 (C_q), 148.5 (C_q), 145.2 (CH), 142.4 (C_q), 139.9 (CH), 139.0 (C_q), 128.4 (CH), 128.2 (CH), 125.6 (CH), 125.2 (CH), 50.7 (C_q), 35.7 (CH_2), 32.8 (CH_2), 32.6 (CH_2), 28.7 (CH_3). **IR** (ATR): 2963, 1672, 1508, 1448, 1227, 1096, 745, 700, 607 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 319 (100) $[M+Na]^+$, 297 (70) $[M+H]^+$, 271 (20), 236 (15), 149 (20). **HR-MS** (ESI) *m/z* calcd for $C_{19}H_{24}N_2O$ $[M+H]^+$ 297.1961, found 297.1960.



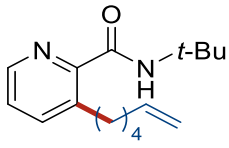
***N*-(*tert*-Butyl)-3-(6-chlorohexyl)picolinamide (200ee)**

Prepared following the general procedure **D** using *N*-(*tert*-butyl)picolinamide **88e** (35.6 mg, 0.20 mmol) and 1-bromo-6-chlorohexane **86e** (119.7 mg, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded **200ee** (43.5 mg, 73%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.33 (dd, *J* = 4.6, 1.7 Hz, 1H), 7.87 (brs 1H), 7.54 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.26 (dd, *J* = 7.8, 4.6 Hz, 1H), 3.50 (t, *J* = 6.8 Hz, 2H), 3.14 (t, *J* = 7.5 Hz, 2H), 1.78–1.70 (m, 2H), 1.66–1.57 (m, 2H), 1.45 (s, 9H), 1.49–1.32 (m, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.3 (C_q), 148.5 (C_q), 145.1 (CH), 139.9 (CH), 139.3 (C_q), 125.2 (CH), 50.7 (C_q), 45.1 (CH_2), 32.8 (CH_2), 32.5 (CH_2), 31.0 (CH_2), 28.8 (CH_2), 28.7 (CH_3), 26.7 (CH_2). **IR** (ATR): 2928, 2858, 1672, 1509, 1447, 1361, 1227, 711, 610 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 319 (100) (^{35}Cl) $[M+Na]^+$, 297 (80) (^{35}Cl) $[M+H]^+$, 249 (10), 149 (20). **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{25}{}^{35}ClN_2O$ $[M+H]^+$ 297.1728, found 297.1729.



3-(But-3-en-1-yl)-*N*-(*tert*-butyl)picolinamide (200ef)

Prepared following the general procedure **D** using *N*-(*tert*-butyl)picolinamide **88e** (35.6 mg, 0.20 mmol) and 4-bromobut-1-ene **86f** (81.0 mg, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **200ef** (24.1 mg, 52%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.33 (dd, *J* = 4.6, 1.7 Hz, 1H), 7.90 (brs 1H), 7.53 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.26 (dd, *J* = 7.8, 4.6 Hz, 1H), 5.84 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.03–4.86 (m, 2H), 3.25 (t, *J* = 6.8, Hz, 2H), 2.44–2.33 (m, 2H), 1.46 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.2 (C_q), 148.6 (C_q), 145.3 (CH), 140.2 (CH), 138.5 (C_q), 138.0 (CH), 125.1 (CH), 115.1 (CH_2), 50.8 (C_q), 35.1 (CH_2), 32.5 (CH_2), 28.8 (CH_3). **IR** (ATR): 2966, 1672, 1509, 1441, 1225, 911, 804, 601 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 255 (100) $[M+Na]^+$, 233 (50) $[M+H]^+$, 177 (10). **HR-MS** (ESI) *m/z* calcd for $C_{14}H_{20}N_2O$ $[M+H]^+$ 233.1648, found 233.1647.

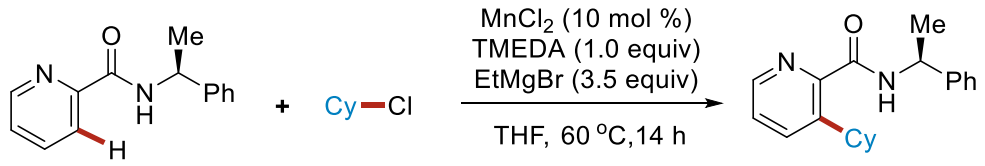


***N*-(*tert*-Butyl)-3-(hex–5-en-1-yl)picolinamide (200eh)**

Prepared following the general procedure **D** using *N*-(*tert*-butyl)picolinamide **88e** (35.6 mg, 0.20 mmol) and 6-bromohex-1-ene **86h** (97.2 mg, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **200eh** (35.6 mg, 68%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.32 (dd, *J* = 4.6, 1.7 Hz, 1H), 7.85 (brs 1H), 7.54 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.26 (dd, *J* = 7.8, 4.6 Hz, 1H), 5.78 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.00–4.86 (m, 2H), 3.15 (t, *J* = 7.3 Hz, 2H), 2.14–1.99 (m, 2H), 1.68–1.57 (m, 2H), 1.51–1.40 (m, 11H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.3 (C_q), 148.6 (C_q), 145.1 (CH), 139.9 (CH), 139.3 (C_q), 138.9 (CH), 125.2 (CH), 114.3 (CH_2), 50.8 (C_q), 33.7 (CH_2), 32.7 (CH_2), 30.7 (CH_2), 28.8 (CH_2), 28.7 (CH_3). **IR** (ATR): 2924, 2858, 1673, 1509, 1445, 1227, 910, 607 cm^{-1}.

MS (ESI) *m/z* (relative intensity) 283 (10) $[M+Na]^+$, 261 (100) $[M+H]^+$, 205 (10). **HR-MS** (ESI) *m/z* calcd for $C_{16}H_{24}N_2O$ $[M+H]^+$ 261.1961, found 261.1961.

5.4.2 Racemization Free Alkylation of 88a



(*S*)-**88a**
(*ee* = 99%)

180a

(*S*)-**181aa**: 81%
(*ee* = 99%)

Prepared following the general procedure **B** using *N*-(1-phenylethyl)picolinamide (*S*)-**88a** (45.2 mg, 0.20 mmol) and cyclohexylchloride **180a** (71 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 8:1) yielded (*S*)-**181aa** (49.8 mg, 81%) as a colorless oil. Chiral HPLC analysis (Chiralcel IC, *i*-PrOH/*n*-hexane 30:70, flow rate = 1.0 mL/min, λ = 254 nm), t_r (major) = 4.3 min, t_r (minor) = 4.9 min.

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                                                  Inj Volume : 5.000 µl
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    Additional Info : Peak(s) manually integrated
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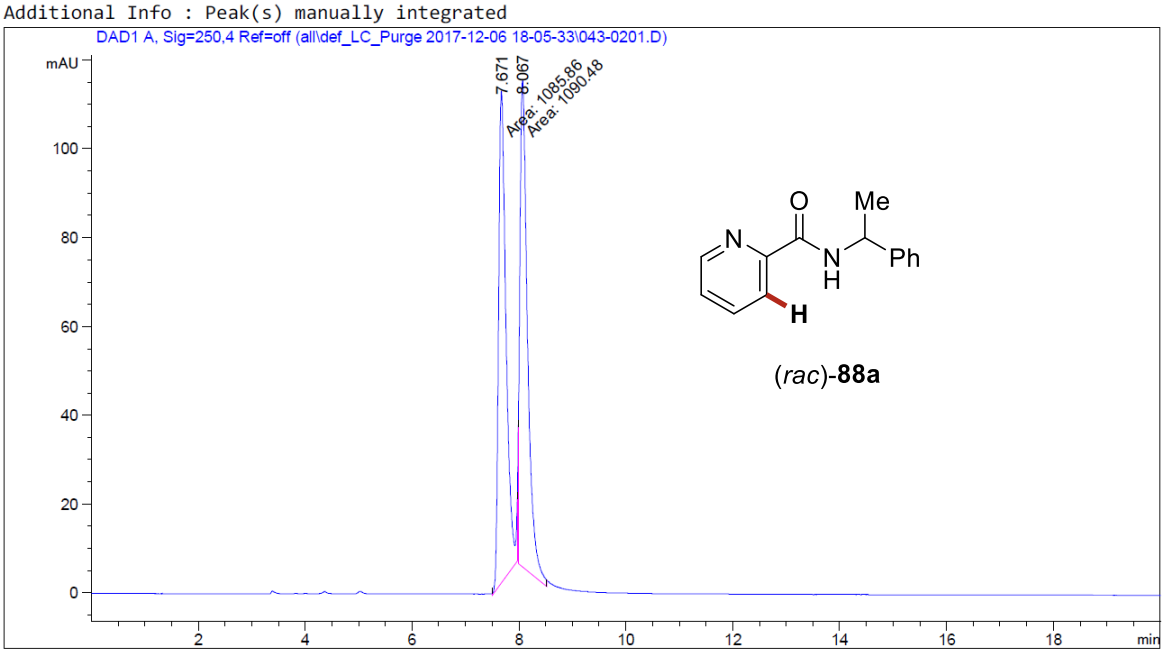

(*rac*)-**88a**

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    ======================================================================
                              Area Percent Report
    ======================================================================

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    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=250,4 Ref=off

    Peak RetTime Type  Width     Area      Height     Area
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       1   7.671 MM    0.1633 1085.86206  110.80559  49.8940
       2   8.067 MM    0.1659 1090.47510  109.54958  50.1060

    Totals :                   2176.33716  220.35517
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Data File E:\Chem32\1\Data\all\def_LC_Purge 2018-01-08 13-02-28\OnlineEdited14.D
Sample Name: zsb130-2asytm

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                                             Inj Volume : 5.000 µl
Method          : E:\Chem32\1\Data\all\def_LC_Purge 2018-01-08 13-02-28\IB_hex90_iPrOH10-1mL-
                  min-30min.M (Sequence Method)
Last changed    : 1/8/2018 7:54:28 PM by SYSTEM
Method Info     : Test

Additional Info : Peak(s) manually integrated
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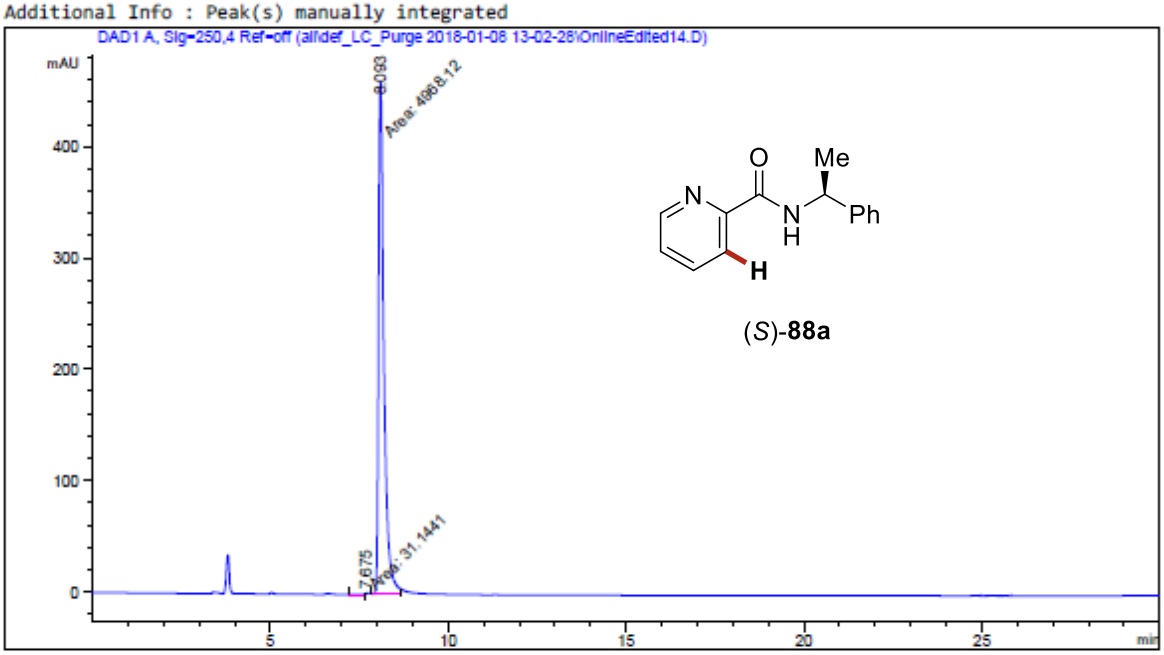

(*S*)-**88a**

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==================================================================
                        Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.675 MM    0.3221   31.14405    1.61171   0.6230
   2   8.093 MM    0.1801 4968.11621  459.88132  99.3770

Totals :                  4999.26026  461.49303

==================================================================
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Data File E:\Chem32\1\Data\all\def_LC_Purge 2017-09-18 13-41-34\OnlineEdited19.D
Sample Name: zsb130-2

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Acq. Instrument : HPLC-2                        Location :   61
Injection Date  : 9/18/2017 7:32:41 PM               Inj :   1
                                               Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry!  Actual Inj Volume : 2.000 µl
Acq. Method     : E:\Chem32\1\Data\all\def_LC_Purge 2017-09-18 13-41-34\IA_hex60_iPrOH40.M
Last changed    : 9/18/2017 5:53:09 PM by SYSTEM
Analysis Method : E:\Chem32\1\Data\all\def_LC_Purge 2017-09-18 13-41-34\IA_hex60_iPrOH40.M (
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Method Info     : Test

Additional Info : Peak(s) manually integrated
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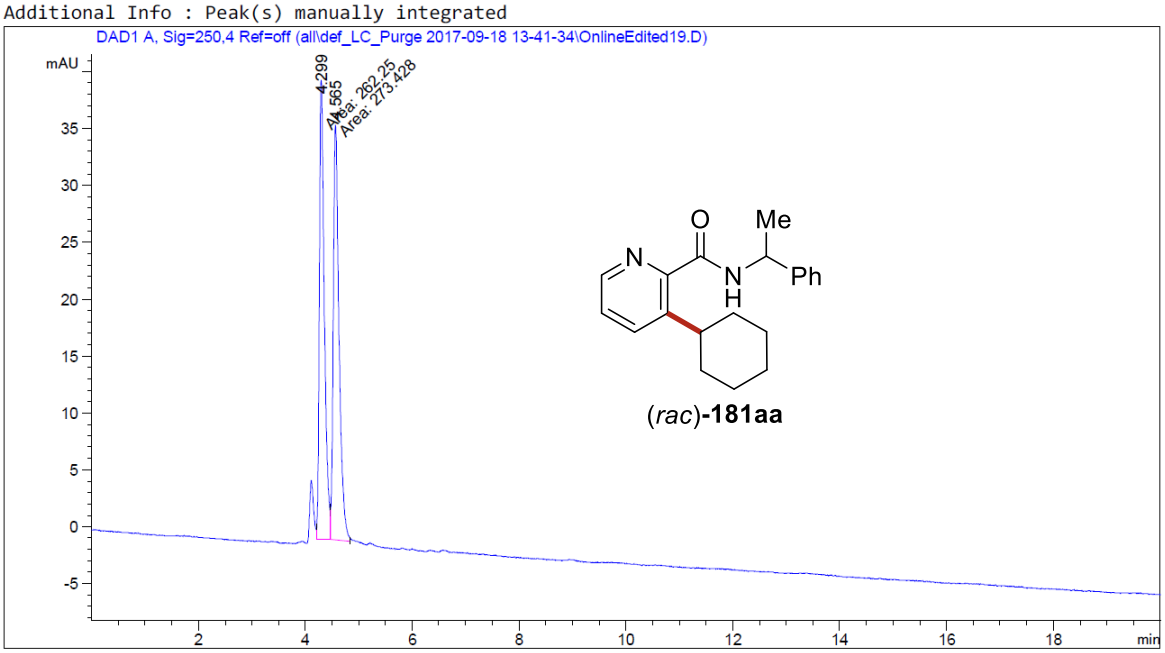


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==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
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Totals :                   535.67770   76.92252
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                                               Inj Volume : 5.000 µl
Different Inj Volume from Sample Entry!  Actual Inj Volume : 2.000 µl
Acq. Method     : E:\Chem32\1\Data\all\def_LC_Purge 2017-09-20 13-05-58\IA_hex60_iPrOH40.M
Last changed    : 9/20/2017 1:52:54 PM by SYSTEM
Analysis Method : E:\Chem32\1\Data\all\def_LC_Purge 2017-09-20 13-05-58\IA_hex60_iPrOH40.M (
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Last changed    : 9/20/2017 6:23:57 PM by SYSTEM
                  (modified after loading)
Method Info     : Test

Additional Info : Peak(s) manually integrated
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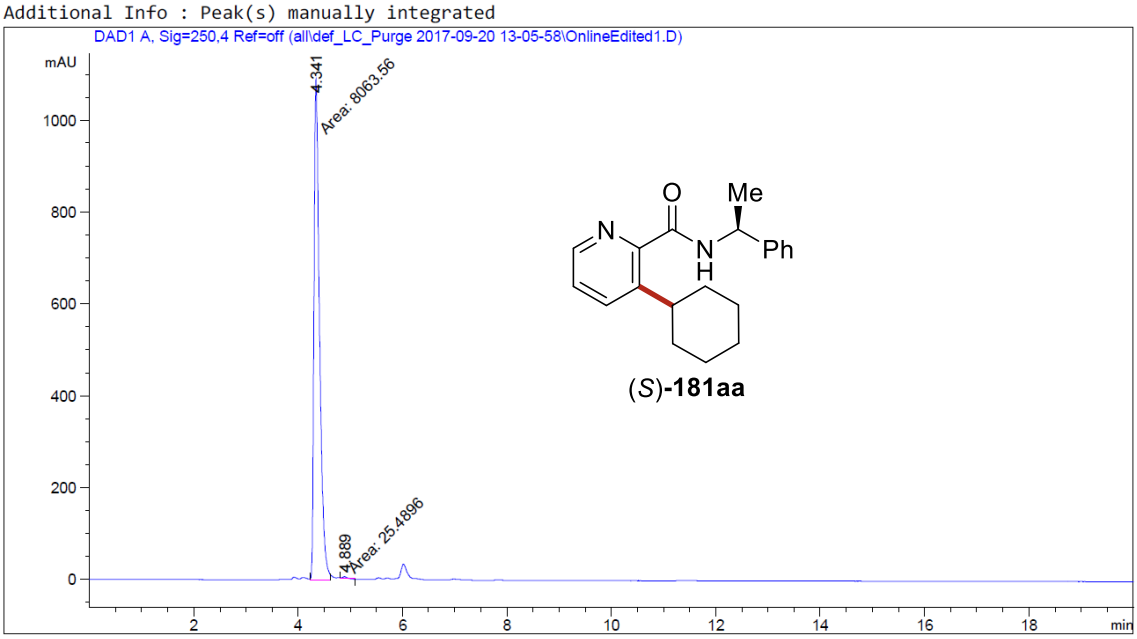


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======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=250,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   4.341 MM    0.1231 8063.56201 1091.44299  99.6849
   2   4.889 MM    0.1026   25.48958    4.14024   0.3151
```
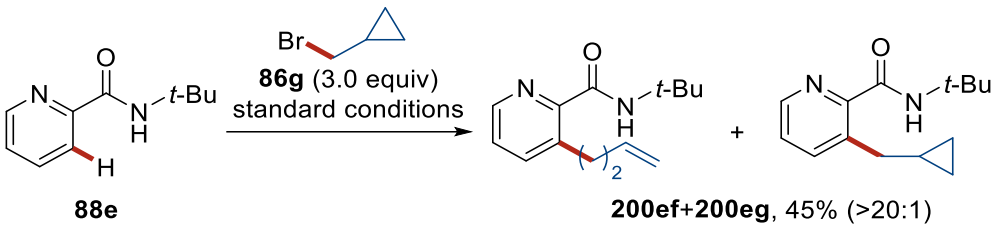
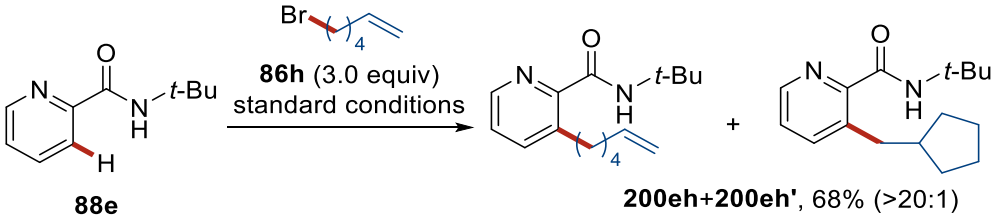

5.4.3 Mechanistic Studies

Control experiments

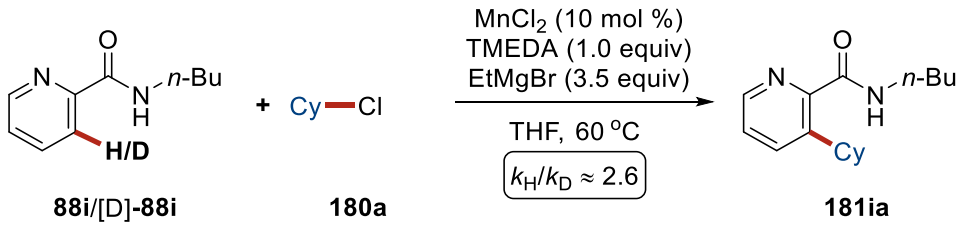


Prepared following the general procedure **D** using *N*-(*tert*-butyl)picolinamide **88e** (35.6 mg, 0.20 mmol) and (bromomethyl)cyclopropane **86g** (58 µL, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **200eg** (21.2 mg, 45%) as a colorless oil, while no cyclopropane product (**200eg'**) was detected.



Prepared following the general procedure **D** using *N*-(*tert*-butyl)picolinamide **88e** (35.6 mg, 0.20 mmol) and 6-bromohex-1-ene **86h** (97.2 mg, 0.60 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1) yielded **200eh** (35.6 mg, 68%) as a colorless oil, while no cyclopentane product (**200eh'**) was detected.

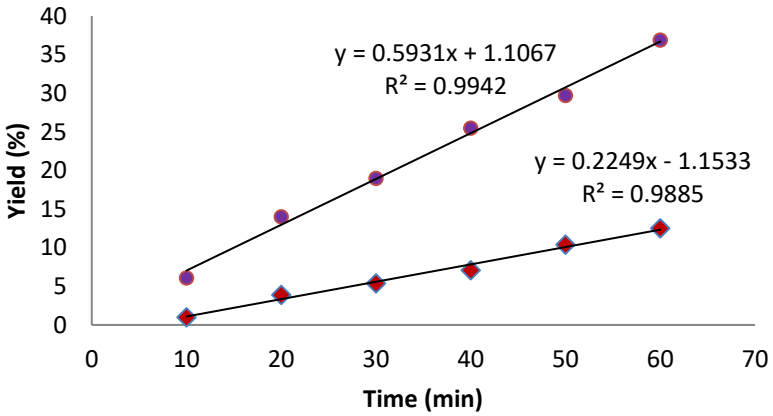
KIE Experiments



Twelve independent reactions with **88i** and deuterated substrate [D]–**88i** under the standard conditions were performed: To a schlenk tube charged with amide **88i** (45.0 mg, 0.20 mmol), TMEDA (30 µL, 0.20 mmol), $MnCl_2$ (2.7 mg, 0.02 mmol) and THF (0.6 mL),

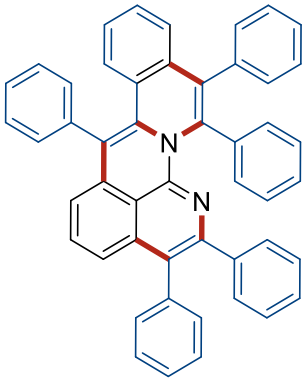
EtMgBr (250 µL, 0.70 mmol, 2.8 M in THF) was added dropwise at ambient temperature under N_2 atmosphere. After stirring for 5 min, alkyl chloride (0.60 mmol) was added and the reaction mixture stirred at 65 °C for 16 h. Then, to the reaction mixture sat. aqueous NH_4Cl (5.0 mL) and H_2O (10 mL) were subsequently added. The aqueous layer was extracted with EtOAc (3 x 15 mL). The combined organic extracts were washed with brine and dried over Na_2SO_4, and the reaction mixture stirred at 60 °C for 10 min, 20 min, 30 min, 40 min, 50 min, 60 min respectively. The conversion of the product **181ia** was monitored by **^{1}H NMR** using CH_2Br_2 as the internal standard.

T (min)	10	20	30	40	50	60
Yield [H] (%)	6.1	14.0	19.0	25.5	29.7	36.9
Yield [D] (%)	1.0	3.9	5.4	7.1	10.4	12.5



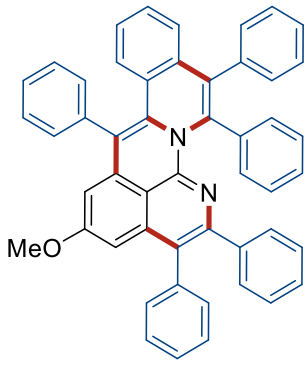
5.5 Rhodaelectro-Catalyzed Domino Alkyne Annulations to Access Aza-Polycyclic Aromatic Hydrocarbons

5.5.1 Experimental Procedure and Analytical Data



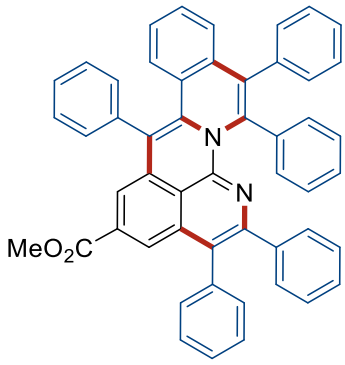
2,3,7,12,13-Pentaphenylbenzo[de]isoquinolino[2,1-a][1,8]naphthyridine (183aa)

The general procedure **E** was followed using **182a** (30.0 mg, 0.20 mmol) and **113a** (124.6 mg, 0.70 mmol) at 35 °C for 12 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 50:1) yielded **183aa** (116.6 mg, 90%) as a red solid. **M.p.** = 295–296 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.62–7.42 (m, 6H), 7.37–7.23 (m, 9H), 7.21–7.02 (m, 11H), 7.00–6.94 (m, 3H), 6.86 (ddd, *J* = 8.3, 7.1, 1.5 Hz, 1H), 6.60–6.56 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 150.1 (C_q), 149.5 (C_q), 140.7 (C_q), 138.8 (C_q), 137.9 (C_q), 137.8 (C_q), 137.5 C_q), 137.1 (C_q), 137.0 (C_q), 135.8 (C_q), 135.4 (C_q), 134.7 (C_q), 132.0 (CH), 131.9 (CH), 131.4 (CH), 131.1 (CH), 130.4 (CH, overlapped), 130.2 (CH), 129.9 (CH), 128.6 (CH, overlapped), 128.4 (CH), 128.1 (CH), 128.0 (CH), 127.5 (C_q), 127.1 (CH), 126.9 (CH, overlapped), 126.8 (CH, overlapped), 126.7 (CH), 126.0 (CH), 125.7 (C_q), 125.0 (CH), 123.3 (C_q), 122.0 (C_q), 119.1 (CH), 117.7 (CH). **IR** (ATR): 1738, 1610, 1536, 1342, 1234, 757, 699 cm^{-1}. **HR-MS** (ESI) *m/z* calcd for $C_{49}H_{33}N_2$ $[M+H]^+$ 649.2638, found 649.2635.



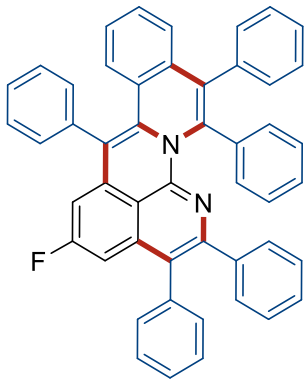
5-Methoxy–2,3,7,12,13-pentaphenylbenzo[de]isoquinolino[2,1-a][1,8] naphthyridine (183ba)

The general procedure **E** was followed using **182b** (36.0 mg, 0.20 mmol) and **113a** (124.6 mg, 0.7 mmol) at 35 °C for 12 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 50:1) yielded **183da** (103.0 mg, 76%) as a red solid. **M.p.** > 300 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.54–7.40 (m, 5H), 7.29–7.16 (m, 8H), 7.13–7.05 (m, 6H), 7.06–6.95 (m, 5H), 6.92–6.87 (m, 2H), 6.79 (ddd, *J* = 8.4, 6.6, 1.9 Hz, 1H), 6.61 (d, *J* = 2.2 Hz, 1H), 6.51–6.45 (m, 3H), 3.64 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 162.0 (C_q), 150.7 (C_q), 149.0 (C_q), 140.7 (C_q), 139.8 (C_q), 138.6 (C_q), 138.1 (C_q), 137.4 (C_q), 137.3 (C_q), 137.0 (C_q), 136.4 (C_q, overlapped, 2C 134.6 (C_q), 131.9 (CH), 131.7 (CH), 131.2 (CH), 130.3 (CH, overlapped, 2C), 130.1 (CH), 129.9 (CH), 128.6 (CH), 128.4 (CH), 128.4 (CH), 128.0 (CH), 127.9 (CH), 127.3 (C_q), 127.0 (CH), 126.7 (CH, overlapped, 2C), 126.6 (CH), 126.5 (CH), 125.9 (CH), 125.4 (C_q), 124.9 (CH), 122.8 (C_q), 118.5 (C_q), 117.8 (Cq), 107.2 (CH), 100.2 (CH), 55.1(CH_3). **IR** (ATR): 1610, 1574, 1537, 1401, 1346, 1208, 759, 701 cm^{-1}. **HR-MS** (ESI) *m/z* calcd for $C_{50}H_{35}N_2O$ $[M+H]^+$ 679.2744, found 679.2733.



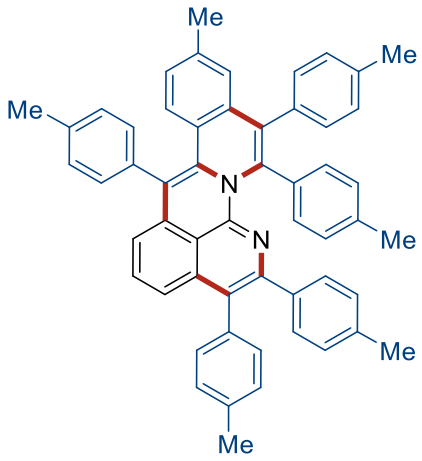
Methyl 2,3,7,12,13-pentaphenylbenzo[de]isoquinolino[2,1-a][1,8]naphthyridine-5-carboxylate (183ca)

The general procedure **E** was followed using **182c** (41.6 mg, 0.20 mmol) and **113a** (124.6 mg, 0.7 mmol) at 35 °C for 12 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 50:1) yielded **183ca** (81.0 mg, 57%) as a red solid. **M.p.** = 193–194 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.97 (d, *J* = 1.2 Hz, 1H), 7.59–7.50 (m, 6H), 7.33–7.26 (m, 8H), 7.17–6.99 (m, 11H), 6.97–6.91 (m, 2H), 6.86 (ddd, *J* = 8.4, 6.6, 1.9 Hz, 1H), 6.53 (d, *J* = 7.1 Hz, 2H), 3.84 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 167.4 (C_q), 151.1 (C_q), 149.4 (C_q), 140.4 (C_q), 138.3 (C_q), 137.6 (C_q), 137.3 (C_q), 137.3 (C_q), 136.9 (C_q), 136.8 (C_q), 136.8 (C_q), 136.6 (C_q), 135.9 (C_q), 134.7 (C_q), 132.6 (C_q), 132.0 (CH), 131.8 (CH), 131.4 (CH), 130.4 (CH), 130.3 (CH), 130.2 (CH), 128.8 (CH), 128.7 (CH), 128.7 (CH), 128.5 (CH), 128.1 (CH), 128.1 (CH), 7.4 (C_q), 127.3 (CH), 127.2 (CH), 127.0 (CH), 127.0 (CH), 126.9 (CH), 126.2 (CH), 125.2 (CH), 124.2 (C_q), 123.4 (C_q), 120.8 (CH), 119.2 (C_q), 117.5 (CH), 52.5 (CH). **IR** (ATR): 3058, 2919, 1725, 1609, 1541, 1339, 1229, 764, 669 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 707 (100) $[M+H]^+$, 739 (15) $[M+Na]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{51}H_{34}N_2O_2^+$ $[M+H]^+$ 707.2693, found 707.2695.



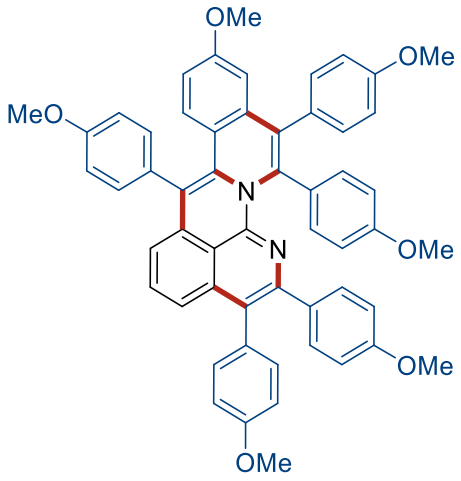
5-Fluoro–2,3,7,12,13- pentaphenylbenzo[de]isoquinolino[2,1-a][1,8]phthyridine (183da)

The general procedure **E** was followed using **182d** (33.6 mg, 0.20 mmol) and **113a** (124.6 mg, 0.7 mmol) at 35 °C for 12 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 50:1) yielded **183da** (98.0 mg, 73%) as a red solid. **M.p.** = 278–280 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.60–7.49 (s, 5H), 7.34–7.22 (m, 8H), 7.18–7.01 (m, 11H), 6.95 (t, J = 7.4 Hz, 2H), 6.89–6.82 (m, 2H), 6.62 (dd, J = 10.6, 1.9 Hz, 1H), 6.53 (d, J = 7.3 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 165.1 (C_q, $^1J_{C–F}$ = 247.1 Hz), 151.2 (C_q), 149.2 (C_q), 140.4 (C_q), 140.31 (C_q, $^3J_{C–F}$ = 11.2 Hz), 138.7 (C_q, ^3J = 11.0 Hz), 138.4 (C_q), 137.7 (C_q), 137.4 (C_q), 137.2 (C_q), 137.1 (C_q), 136.9 (C_q), 134.7 (C_q), 131.9 (CH), 131.8 (CH), 131.8 (CH), 131.2 (CH), 130.4 (CH), 130.2 (CH), 130.2 (CH), 128.8 (CH), 128.8 (CH) 128.7 (CH), 128.4 (CH), 128.1 (CH), 127.2 (CH), 127.2 (C_q), 127.1 (CH), 127.0 (CH), 127.0 (CH), 126.8 (CH), 126.2 (CH), 126.1 (C_q), 125.3 (CH), 123.32 (C_q, $^4J_{C–F}$ = 4.7 Hz), 119.2 (C_q), 118.5 (C_q), 105.9 (CH, $^2J_{C–F}$ = 27.3 Hz), 103.72 (CH, $^2J_{C–F}$ = 24.6 Hz). **^{19}F NMR** (282 MHz, $CDCl_{3)}$ δ = –105.93 (t, J = 10.7 Hz). **IR** (ATR): 3051, 2961, 2161, 1609, 1572, 1342, 1021, 696 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 649 (100), 667 (15) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{49}H_{32}FN_2$ $[M+H]^+$ 667.2544, found 667.2531.



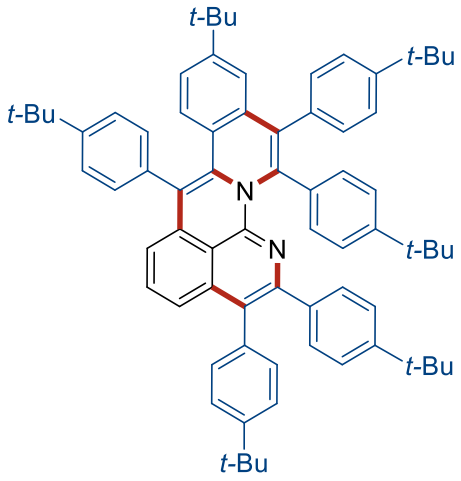
10-Methyl–2,3,7,12,13-penta-p-tolylbenzo[de]isoquinolino[2,1-a][1,8] naphthyridine (183ab)

The general procedure **E** was followed using **182a** (30.0 mg, 0.20 mmol) and **113b** (144.4 mg, 0.7 mmol) at 35 °C for 12 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 50:1) yielded **183ab** (118.6 mg, 81%) as a red solid. **M.p.** = 198–199 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.48–7.33 (m, 5H), 7.22–7.10 (m, 7H), 7.04 (d, *J* = 7.6 Hz, 4H), 7.00–6.90 (m, 3H), 6.87 (d, *J* = 8.0 Hz, 2H), 6.80 (d, *J* = 7.9 Hz, 2H), 6.69 (d, *J* = 8.3 Hz, 1H), 6.49 (d, *J* = 8.0 Hz, 2H), 2.51 (s, 3H), 2.40 (s, 3H), 2.38 (s, 3H), 2.27 (s, 3H), 2.24 (s, 3H), 2.20 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 145.0 (C_q), 149.5 (C_q), 138.10 (C_q, overlapped 3C), 138.0 (C_q), 137.6 (C_q), 137.5 (C_q), 136.1 (C_q), 136.0 (C_q), 136.0 (C_q, overlapped, 4C), 135.7 (C_q), 135.2 (C_q), 135.0 (C_q), 134.34 (C_q, overlapped, 2C), 131.8 (CH), 131.7 (CH), 131.2 (CH), 130.8 (CH), 130.6 (CH), 130.3 (CH), 130.1 (CH), 129.1 (CH), 128.6 (CH), 128.5 (CH), 127.7 (CH), 127.5 (CH) 127.0 (CH), 125.2 (C_q), 125.2 (CH), 122.8 (C_q), 121.7 (C_q), 118.7 (CH), 118.1 (C_q), 117.1 (CH), 21.5 (CH_3, overlapped, 2C), 21.4 (CH_3), 21.3 (CH_3, overlapped, 2C) 21.2 (CH_3). **IR** (ATR): 2919, 1606, 1541, 1508, 1340, 907, 815, 730 cm^{-1}. **HR-MS** (ESI) *m/z* calcd for $C_{55}H_{45}N_2$ [M+H] 733.3577, found 733.3568.



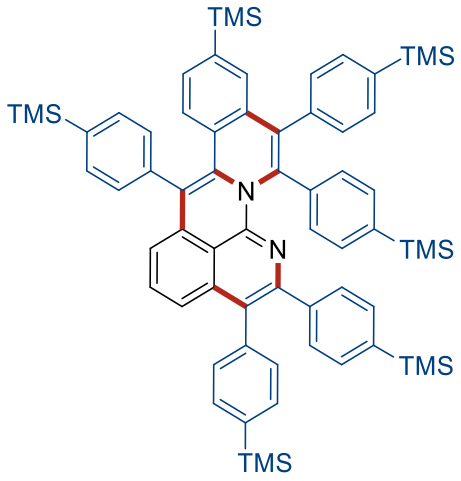
10-Methoxy–2,3,7,12,13-pentakis(4-methoxyphenyl)benzo[de]isoquinolino[2,1-a][1,8]naphthyridine (183ac)

The general procedure **E** was followed using **182a** (7.5 mg, 0.05 mmol), **113c** (49.6 mg, 0.175 mmol) and $[Cp^*Rh(CH_3CN)_3](SbF_6)_2$ (4.2 mg, 10 mol %) at 35 °C for 3 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 50:1) yielded **183ac** (38.2, 92%) as a red solid. **M.p.** = 177–178 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.45–7.39 (m, 3H), 7.22–7.14 (m, 3H), 7.11–6.97 (m, 7H), 6.91–6.82 (m, 5H), 6.64 (d, *J* = 2.7 Hz, 1H), 6.60 (dd, *J* = 8.7, 5.3 Hz, 4H), 6.52 (d, *J* = 8.8 Hz, 2H), 6.48–6.42 (m, 1H), 3.93 (s, 3H), 3.84 (s, 3H), 3.82 (s, 3H), 3.73 (s, 3H), 3.71 (s, 3H), 3.65 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 159.2 (C_q, overlapped, 2C), 158.3 (C_q, overlapped, 2C), 158.2 (C_q), 158.1 (C_q), 149.6 (C_q), 149.4 (C_q), 138.1 (C_q), 137.9 (C_q), 137.0 (C_q), 135.9 (C_q), 135.8 (C_q), 133.6 (C_q), 133.0 (CH), 132.8 (CH), 132.4 (CH), 131.6 (CH, overlapped, 2C), 131.4 (CH), 131.0 (C_q), 130.9 (CH), 130.5 (C_q), 130.1 (CH), 129.7 (C_q), 129.4 (C_q), 124.5 (C_q), 122.1 (C_q), 121.3 (C_q), 121.0 (C_q), 118.4 (CH), 116.9 (C_q), 116.8 (CH), 115.3 (CH), 113.9 (CH), 113.5 (CH), 112.5 (CH), 112.3 (CH), 109.2 (CH), 55.3 (CH_3, overlapped, 2C), 55.2 (CH_3, overlapped, 2C), 55.1 (CH_3), 55.0 (CH_3). **IR** (ATR): 2928, 1602, 1570, 1507, 1284, 1241, 1172, 1030, 826, 540 cm^{-1}. **HR-MS** (ESI) *m/z* calcd for $C_{55}H_{45}N_2O_6$ $[M+H]^+$ 829.3272, found 829.3268.



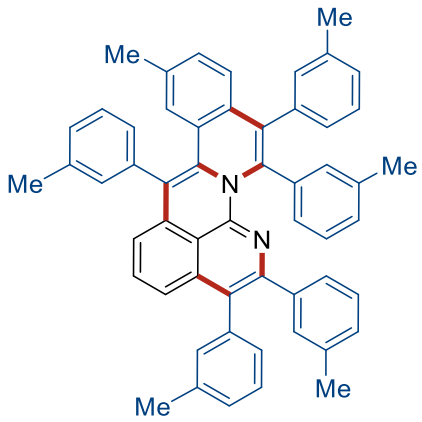
10-(*tert*-Butyl)-2,3,7,12,13-pentakis[4-(tert-butyl)phenyl]benzo[de]isoquinolino [2,1-a][1,8]naphthyridine (183ad)

The general procedure **E** was followed using **182a** (30.0 mg, 0.20 mmol) and **113d** (203.4 mg, 0.7 mmol) at 35 °C for 12 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 50:1) yielded **183ad** (88.6 mg, 45%) as a red solid. **M.p.** = 205–206 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.58 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.30 (dd, *J* = 12.8, 4.1 Hz, 6H), 7.21–7.11(m, 2H), 7.10–7.00 (m, 6H), 6.97–6.88 (m, 4H), 6.85 (dd, *J* = 8.7, 2.0 Hz, 1H), 6.47–6.45 (m, 2H), 1.48 (s, 9H), 1.37 (s, 9H), 1.35 (s, 9H), 1.26 (s, 9H), 1.22 (s, 9H), 1.18 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 151.0 (C_q), 150.8 (C_q), 150.1 (C_q), 149.5 (C_q), 149.4 (C_q), 149.3 (C_q), 149.0 (C_q), 148.9 (C_q), 138.0 (C_q), 137.9 (C_q), 137.5 (C_q), 136.0 (C_q), 135.9 (C_q), 135.8 (C_q), 135.2 (C_q), 134.5 (C_q), 134.4 (C_q), 134.3 (C_q), 131.6 (CH), 131.4 (CH), 130.9 (CH), 130.7 (CH), 130.0 (CH), 129.9 (C_q), 128.2 (CH), 126.7 (CH), 125.6 (C_q), 125.3 (C_q), 125.1 (CH), 124.4 (CH), 123.7 (CH), 123.5 (CH), 123.1 (CH), 122.6 (C_q), 121.6 (CH), 121.5 (CH), 118.5 (CH), 117.8 (C_q), 117.0 (CH), 34.8 (C_q), 34.6 (C_q), 34.5 (C_q, overlapped, 2C), 34.4 (C_q), 34.2 (C_q), 31.5 (CH_3), 31.4 (CH_3, overlapped, 2C), 31.3 (CH_3, overlapped, 2C), 31.0 (CH_3). **IR** (ATR): 2959, 2902, 1611, 1577, 1507, 1339, 1268, 1110, 1018, 823 cm^{-1}. **HR-MS** (ESI) *m/z* calcd for $C_{73}H_{81}N_2$ $[M+H]^+$ 985.6394, found 985.6379.



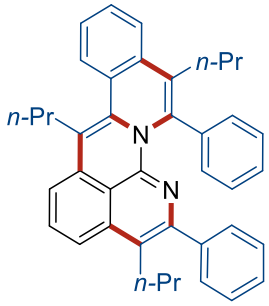
10-(Trimethylsilyl)-2,3,7,12,13-pentakis[4-(trimethylsilyl)phenyl]benzo[de]isoquinolino[2,1-a][1,8]naphthyridine (183ae)

The general procedure **E** was followed using **182a** (30.0 mg, 0.20 mmol) and **113e** (225.0 mg, 0.7 mmol) at 35 °C for 12 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 50:1) yielded **183ae** (145.0 mg, 67%) as a red solid. **M.p.** = 219–220 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.68 (d, *J* = 7.8 Hz, 2H), 7.51 (d, *J* = 7.5 Hz, 2H), 7.42–7.38 (m, 5H), 7.31 (s, 1H), 7.23–7.15 (m, 5H), 7.09–7.01 (m, 6H), 6.94 (s, 2H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.40 (d, *J* = 8.1 Hz, 2H), 0.37 (s, 9H), 0.28 (s, 9H), 0.26 (s, 9H), 0.18 (s, 9H), 0.14 (s, 9H), 0.10 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 150.1 (C_q), 149.6 (C_q), 141.1 (C_q), 140.9 (C_q), 140.2 (C_q), 139.5 (C_q), 138.6 (C_q), 138.5 (C_q), 138.5 (C_q), 138.4 (C_q), 138.2 (C_q), 137.8 (C_q), 137.6 (C_q), 137.6 (C_q), 137.5 (C_q), 135.9 (C_q), 135.6 (C_q), 134.9 (CH), 133.5 (C_q), 133.4 (CH), 132.6 (CH), 132.0 (CH), 131.9 (CH), 131.4 (CH), 131.1 (CH), 131.0 (CH), 130.8 (CH), 130.7 (CH), 130.2 (CH), 129.6 (CH), 129.6 (CH), 128.0 (C_q), 127.6 (CH), 125.9 (C_q), 123.2 (C_q), 122.0 (C_q), 119.1 (CH), 119.0 (C_q), 117.7 (CH), -0.8 (CH_3), -0.9 (CH_3), -0.9 (CH_3), –1.0 (CH_3), –1.1 (CH_3), –1.3 (CH_3). **IR** (ATR): 2954, 2203, 1548, 1342, 1249, 1108, 840 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1081 (98) $[M+H]^+$, 1082 (100) $[M(^{13}C,^{29}Si)+H]^+$, 1010 (10). **HR-MS** (ESI) *m/z* calcd for $C_{67}H_{80}N_2Si_6$ $[M+H]^+$ 1081.5010, found 1081.5017.



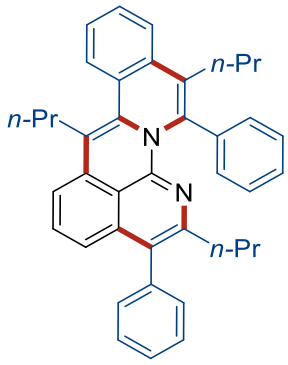
9-Methyl–2,3,7,12,13-penta-m-tolylbenzo[de]isoquinolino[2,1-a][1,8] naphthyridine (183af)

The general procedure **E** was followed using **182a** (30.0 mg, 0.20 mmol) and **113f** (144.0 mg, 0.7 mmol) at 35 °C for 12 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 50:1) yielded **183af** (104.0mg, 71%) as a red solid. **M.p.** = 153–154 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.51–7.44 (m, 2H), 7.42–7.33 (m, 3H), 7.29–7.19 (m, 3H), 7.11–7.03 (m, 7H), 7.00–6.91 (m, 6H), 6.88–6.82 (m, 3H), 6.47 (s, 2H), 2.47 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H), 2.18 (s, 3H), 2.12 (s, 3H), 2.00 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 150.1 (C_q), 149.6 (C_q), 140.7 (C_q), 139.5 (C_q), 139.1 (C_q), 138.1 (C_q), 137.8 (C_q), 137.7 (C_q), 137.3 (C_q), 137.3 (C_q), 137.0 (C_q) 136.7 (C_q), 136.4 (C_q, overlapped, 2C), 135.8 (C_q), 135.5 (C_q), 135.3 (C_q), 132.6 (CH), 132.4 (C_q, overlapped, 2C), 132.2 (CH), 131.9 (CH), 131.5 (CH), 130.9 (CH), 130.8 (CH), 129.7 (CH), 129.3 (CH), 129.3 (CH), 129.0 (CH), 128.9 (CH), 128.6 (CH), 128.5 (CH), 128.3 (CH), 128.3 (CH), 127.7 (CH), 127.7 (CH), 127.5 (CH), 127.4 (CH), 127.4 (CH), 127.2 (CH), 127.0 (CH), 126.7 (CH), 125.7 (C_q), 125.0 (CH), 123.3 (C_q), 122.0 (C_q, overlapped, 2C), 118.9 (CH), 117.5 (CH), 21.6 (CH_3), 21.5 (CH_3), 21.5 (CH_3), 21.4 (CH_3), 21.3 (CH_3), 21.3 (CH_3).. **IR** (ATR): 3023, 2914, 2091, 1997, 1606, 1538, 1337, 1289, 703 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 733 (100) $[M+H]^+$, 765 (10) $[M+Na]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{55}H_{45}N_2O^+$ $[M+H]^+$ 733.3577, found 733.3578.



2,13-Diphenyl-3,7,12-tripropylbenzo[de]isoquinolino [2,1-a][1,8]naphthyridine (183ag)

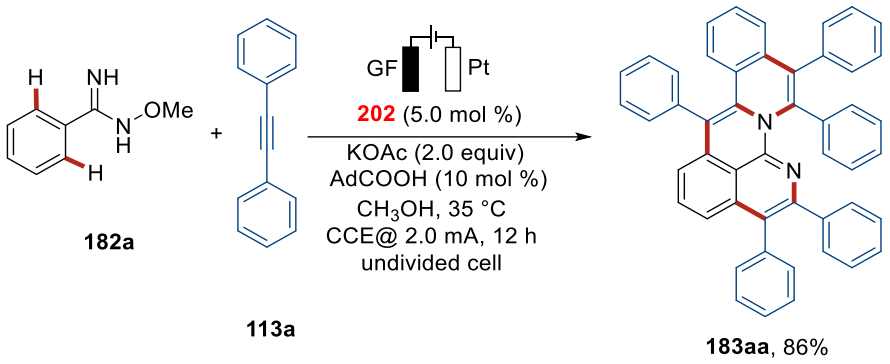
The general procedure was **G** followed using **182a** (30.0 mg, 0.20 mmol) and **113g** (101.0 mg, 0.7 mmol) at 35 °C for 12 h. Purification by column chromatography on silica gel (*n*-hexane/EtOAc 100 : 1) yielded two regioisomers **183ag** (55.5 mg) and **183ag'** (20.5 mg) (76.0 mg, 70%, **183ag**: **183ag'** = 2.7 : 1). Characterization data for **183ga**: red solid. **M.p.** = 175–176 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.70 (t, J = 8.0 Hz, 2H), 7.54 (dd, J = 8.0, 1.1 Hz, 1H), 7.47–7.41 (m, 2H), 7.37–7.31 (m, 2H), 7.28–7.10 (m, 8H), 6.77–6.72 (m, 2H), 3.08–2.96 (m, 2H), 2.67–2.55 (m, 4H), 1.96–1.84 (m, 2H), 1.56–1.43 (m, 4H), 1.18 (t, J = 7.3 Hz, 3H), 0.73 (t, J = 7.4 Hz, 3H), 0.69 (t, J = 7.3 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 150.8 (C_q), 147.7 (C_q), 141.5 (C_q), 137.9 (C_q), 137.6 (C_q), 137.4 (C_q), 136.4 (C_q), 134.5 (C_q), 134.2 (C_q), 130.8 (CH), 129.6 (CH, overlapped, 2C), 128.8 (C_q), 128.7 (CH), 127.7 (CH), 127.3 (CH, overlapped, 2C), 127.1 (CH), 126.9 (CH), 126.1 (CH), 123.2 (CH), 122.5 (C_q), 121.0 (C_q), 120.9 (C_q), 117.5 (CH), 116.7 (C_q), 115.3 (CH), 30.9 (CH_2), 30.4 (CH_2), 29.8 (CH_2), 22.8 (CH_2, overlapped, 2C), 21.2 (CH_2), 14.5 (CH_3), 14.1 (CH_3), 13.9 (CH_3). **IR** (ATR): 3065, 2957, 2866, 1611, 1547, 1334, 1281, 757 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 547 (100) $[M+H]^+$, 579 (40) $[M+Na]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{40}H_{39}N_2$ $[M+H]^+$ 547.3108, found 547.3108.



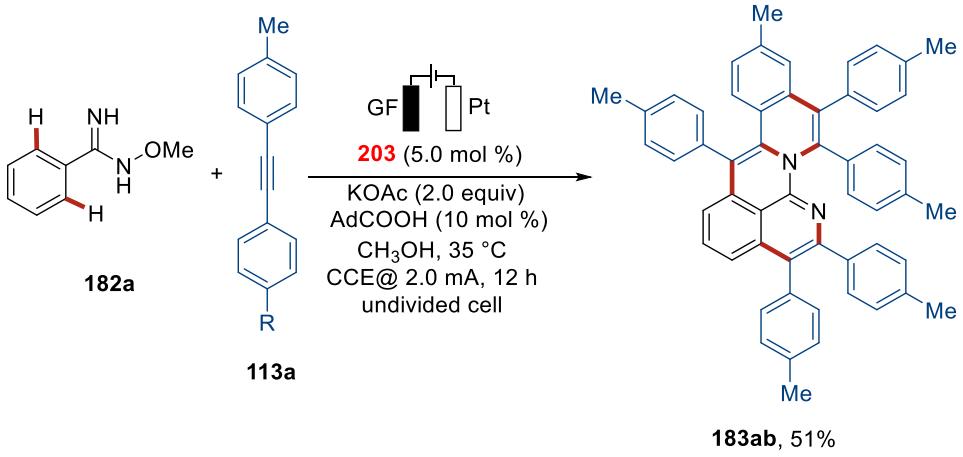
3,13-Diphenyl–2,7,12-tripropylbenzo[de]isoquinolino[2,1-a][1,8]naphthyridine (183ag')

Characterization data for **183ag'**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.74 (t, J = 7.9 Hz, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.54 (d, J = 8.3 Hz, 1H), 7.49–7.37 (m, 6H), 7.41–7.30 (m, 5H), 7.27–7.15 (m, 2H), 6.75 (dd, J = 7.6, 1.4 Hz, 1H), 3.19–3.01 (m, 2H), 3.03–2.98 (m, 2H), 2.85–2.79 (m, 2H), 1.94–1.81 (m, 2H), 1.65 (dq, J = 14.9, 7.3 Hz, 2H), 1.17 (t, J = 7.3 Hz, 3H), 0.87 (t, J = 7.3 Hz, 3H), 0.73 (p, J = 7.4 Hz, 2H), 0.45 (t, J = 7.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 151.0 (C_q), 148.0 (C_q), 142.1 (C_q), 139.6 (C_q), 138.8 (C_q), 137.5 (C_q), 136.5 (C_q), 135.5 (C_q), 133.9 (C_q), 131.5 (CH), 131.1 (CH), 129.4 (CH), 128.6 (CH), 128.6 (CH), 128.1 (CH), 127.5 (C_q), 127.4 (CH), 127.2 (CH), 126.7 (CH), 125.5 (CH), 124.9 (CH), 123.4 (C_q), 122.1 (C_q), 122.1 (C_q), 117.6 (CH), 117.6 (C_q), 115.7 (CH), 31.0 (CH_2), 30.7 (CH_2), 30.7 (CH_2), 23.1 (CH_2), 21.3 (CH_2), 20.0 (CH_2), 14.5 (CH_3), 14.3 (CH_3), 13.5 (CH_3). **IR** (ATR): 3063, 2959, 2870, 1614, 1549, 1340, 1257, 767 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 547 (100) $[M+H]^+$, 579 (20) $[M+Na]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{40}H_{39}N_2$ $[M+H]^+$ 547.3108, found 547.3110.

5.5.2 Mechanistic Studies



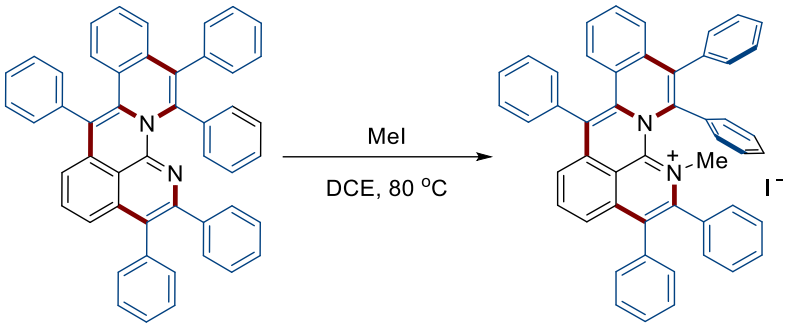
The electrocatalysis was carried out in an undivided cell with a graphite felt anode (10 mm × 15 mm × 6 mm) and a Pt cathode (10 mm × 15 mm × 0.25 mm). The cell was charged with imidate **182a** (0.20 mmol), alkyne **113a** (0.7 mmol), KOAc (39.3 mg, 0.4 mmol), AdOH (3.6 mg, 10 mol %), **202** (4.5 mg, 5.0 mol %) and MeOH (4.0 mL). Electrocatalysis was performed at 35 °C with a constant current of 2.0 mA maintained for 12 h. The graphite felt anode was washed with CH_2Cl_2 (8 × 5.0 mL) in an ultrasonic bath. Evaporation of the solvents and subsequent column chromatography on silica gel (*n*-hexane/EtOAc 50:1) afforded the corresponding product **183aa** (112.0 mg, 86%).



The electrocatalysis was carried out in an undivided cell with a graphite felt anode (10 mm × 15 mm × 6 mm) and a Pt cathode (10 mm × 15 mm × 0.25 mm). The cell was charged with imidate **182a** (0.20 mmol), alkyne **113a** (0.70 mmol), KOAc (39.3 mg, 0.40 mmol),

$AdCO_2H$ (3.6 mg, 10 mol %), **203** (6.2 mg, 5.0 mol %) and MeOH (4.0 mL). Electrocatalysis was performed at 35 °C with a constant current of 2.0 mA maintained for 12 h. The graphite felt anode was washed with CH_2Cl_2 (8 × 5.0 mL) in an ultrasonic bath. Evaporation of the solvents and subsequent column chromatography on silica gel (*n*-hexane/EtOAc 50:1) afforded the corresponding product **183ab (**75.2 mg, 51%).

5.5.3 Derivatiztion of 183aa and 183aj



183aa **204**, 93%

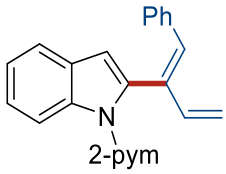
1-methyl–2,3,7,12,13-pentaphenylbenzo[de]isoquinolino[2,1-a][1,8]naphthyridin-1-ium iodide (204)

To a 25 mL Schlenk tube was added **183aa** (65.2 mg, 0.10 mmol), MeI (85 mg, 0.6 mmol, 20 µL) and 1.0 mL DCE. The reaction was stirred at 80 °C for 6 hours. Then the solvent was removed and purification of the residue by column chromatography (DCM/MeOH, 50:1) yielded the product **204** (73.4 mg, 93%) as a red solid. **M.p.** = 229–230 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.93 (t, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 7.7 Hz, 1H), 7.74 (t, *J* = 7.2 Hz, 1H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.54–7.50 (m, 3H), 7.45–7.35 (m, 7H), 7.32–7.27 (m, 3H), 7.26–6.98 (m, 13H), 6.55 (d, *J* = 7.6 Hz, 1H), 5.51 (d, *J* = 7.7 Hz, 1H), 3.63 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 151.9 (C_q), 144.3 (C_q), 136.0 (CH), 135.8 (C_q), 135.5 (C_q), 135.4 (C_q, overlapped, 2C), 135.1 (C_q), 135.0 (C_q), 134.6 (C_q), 134.1 (C_q), 133.6 (C_q), 132.5 (C_q), 132.0 (CH), 131.7 (C_q), 131.7 (C_q), 131.6 (CH), 130.9 (CH), 130.7 (CH), 130.4 (CH), 130.3 (CH), 130.0 (CH), 129.7 (CH), 129.5 (CH), 129.1 (CH), 129.0 (CH), 128.8 (CH), 128.7 (CH), 128.4 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 127.6 (C_q), 126.8 (CH), 125.4 (C_q), 123.6 (CH), 122.6 (CH), 122.6 (C_q), 46.9 (CH_3). **IR** (ATR): 3031, 3004, 1619, 1549,

1439, 1328, 1246, 758, 697 cm^{-1}. **HR-MS** (ESI) *m/z* calcd for $C_{50}H_{34}N_2$ $[M-I]^+$: 663.2795, found: 663.2799.

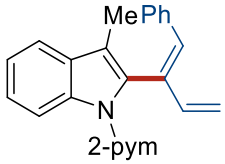
5.6 Rhodaelectro-catalyzed switchable Indole dienylation/ cyclopropylation

5.6.1 Experimental procedure and analytical data



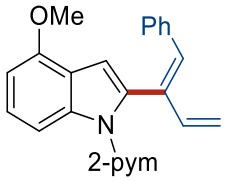
(*Z*)-2-(1-Phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184aa)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.6 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184aa** (57.6 mg, 89%, *Z/E* = 7.0/1 determined by ^{1}H NMR) as a yellow solid. **M.p.** = 137–139 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.71 (d, *J* = 4.8 Hz, 0.29H, *E* isomer), 8.62 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.33 (d, *J* = 8.3 Hz, 1H), 7.60 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.32 (td, *J* = 7.7, 1.2 Hz, 1H), 7.24 (t, *J* = 6.6 Hz, 1H), 7.08–7.06 (m, 3H), 7.03–6.99 (m, 3H), 6.69 (dd, *J* = 17.4, 10.6 Hz, 1H), 6.68 (s, 1H), 6.57 (s, 1H), 5.06 (d, *J* = 10.6 Hz, 1H), 5.02 (d, *J* = 17.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 157.9 (CH), 157.5 (C_q), 140.6 (CH), 136.7 (C_q), 136.7 (C_q), 135.4 (C_q), 134.0 (C_q), 133.0 (CH), 129.5 (C_q), 129.1 (CH), 128.1 (CH), 127.2 (CH), 123.4 (CH), 122.0 (CH), 120.8 (CH), 117.0 (CH), 115.7 (CH), 114.2 (CH), 108.7 (CH_2). **IR** (ATR): 3000, 2201, 1564, 1437, 1419, 1360, 1256, 1075, 812, 769 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 346 (80) $[M+Na]^+$, 324 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{18}N_3$ $[M+H]^+$ 324.1495, found 324.1484.$^+$



(*Z*)-3-Methyl–2-(1-phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184ba)

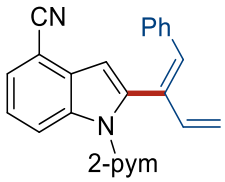
The general procedure **F** was followed using 3-methyl-1-(pyrimidin-2-yl)-1*H*-indole **71b** (41.9 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.6 mg, 0.32 mmol) for 3.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ba** (46.5 mg, 69%, *Z/E* = 9.6/1 determined by ^{1}H NMR) as a yellow solid. **M.p.** = 102–104 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.69 (d, *J* = 4.8 Hz, 0.18H, *E* isomer), 8.65 (d, *J* = 4.7 Hz, 2H, *Z* isomer), 8.44 (d, *J* = 8.1 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.39–7.24 (m, 3H), 7.17–7.10 (m, 4H), 7.01 (t, *J* = 4.8 Hz, 1H), 6.81 (s, 1H), 6.65 (ddd, *J* = 17.2, 10.4, 0.7 Hz, 1H), 4.97 (d, *J* = 10.5 Hz, 1H), 4.81 (d, *J* = 17.2 Hz, 1H), 2.00 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 157.9 (CH), 157.8 (C_q), 140.3 (CH), 137.2 (C_q), 136.5 (C_q), 133.6 (C_q), 133.5 (CH), 132.0 (C_q), 130.7 (C_q), 128.8 (CH), 128.2 (CH), 127.2 (CH), 123.6 (CH), 121.6 (CH), 119.0 (CH), 116.6 (CH), 115.2 (CH_2), 114.9 (C_q), 114.4 (CH), 9.0 (CH_3). **IR** (ATR): 3048, 2920, 1565, 1425, 1354, 1223, 1017, 988, 801, 748, 697 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 360 (68) $[M+Na]^+$, 338 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{20}N_3$ $[M+H]^+$ 338.1657, found 338.1642.



(*Z*)-4-Methoxy–2-(1-phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184ca)

The general procedure **F** was followed using 4-methoyl-1-(pyrimidin-2-yl)-1*H*-indole **71c** (45.1 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.6 mg, 0.32 mmol) for 2.8 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ca** (67.1

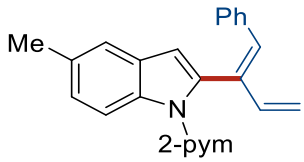
mg, 95%, *Z/E* = 3.3/1 determined by ^{1}H NMR) as a yellow solid. **M.p.** = 98–99 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 4.8 Hz, 0.6H, *E* isomer), 8.61 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 7.90 (d, *J* = 8.5 Hz, 1H), 7.25 (t, *J* = 8.1 Hz, 1H), 7.09–7.05 (m, 3H), 7.02–6.98(m, 3H), 6.73 (s, 1H), 6.71 (dd, *J* = 16.5, 10.2 Hz, 1H), 6.70 (d, *J* = 7.9 Hz, 1H), 6.66 (s, 1H), 5.09 (d, *J* = 16.5 Hz, 1H), 5.09 (d, *J* = 10.6 Hz, 1H), 3.98 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 157.8 (CH), 157.5 (C_q), 153.1 (C_q), 140.6 (CH), 138.0 (C_q), 136.7 (C_q), 133.9 (C_q), 133.8 (C_q), 133.0 (CH), 129.1 (CH), 128.0 (CH), 127.1 (CH), 124.2 (CH), 120.0 (C_q), 117.1 (CH), 115.8 (CH_2), 107.4 (CH), 105.7 (CH), 102.1 (CH), 55.5 (CH_3). **IR** (ATR): 3026, 2918, 1693, 1564, 1420, 1336, 1240, 1149, 910, 805, 740, 698 cm^{-1}**. MS** (ESI) *m/z* (relative intensity): 376 (100) $[M+Na]^+$, 354 (50) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{20}N_3O$ $[M+H]^+$ 354.1606, found 354.1601.



(*Z*)-2-(1-Phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole-4-carbonitrile (184da)

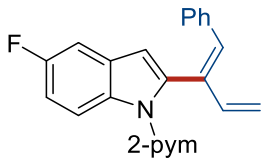
The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole-4-carbonitrile **71d** (44.1 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.6 mg, 0.32 mmol) for 5.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184da** (41.8 mg, 60%, *Z/E* = 2.0/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.76 (d, *J* = 4.8 Hz, 1H, *E* isomer), 8.65 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.49 (d, *J* = 8.5 Hz, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.45–7.43 (m, 1H), 7.35 (dd, *J* = 8.5, 7.4 Hz, 1H), 7.11 (t, *J* = 4.8 Hz, 1H), 7.09–7.04 (m, 3H), 6.94–6.92 (m, 1H), 6.82 (s, 1H), 6.73 (s, 1H), 6.71 (dd, *J* = 17.2, 10.6 Hz, 1H), 5.13 (d, *J* = 10.6 Hz, 1H), 5.02 (d, *J* = 17.2 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.0 (CH), 156.7 (C_q), 139.8 (CH), 138.4 (C_q), 136.7 (C_q), 136.1 (C_q), 133.9 (CH), 132.7 (C_q), 130.8 (C_q), 128.8 (CH), 128.1 (CH), 127.5 (CH), 126.8 (CH), 122.9 (CH), 118.7 (CH), 118.4 (C_q), 117.9 (CH), 115.9 (CH_2), 106.6 (CH), 103.1 (C_q). **IR** (ATR): 3050, 2221, 1693, 1567, 1425, 1318, 1263, 1234, 1078, 913, 813,

786, 739, 698 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 371 (40) $[M+Na]^+$, 349 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{17}N_4$ $[M+H]^+$ 349.1448, found 349.1449.



(*Z*)-5-Methyl–2-(1-phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184ea)

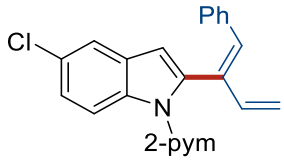
The general procedure **F** was followed using 5-methyl-1-(pyrimidin-2-yl)-1*H*-indole **71e** (45.1 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.9 mg, 0.32 mmol) for 3.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ea** (50.6 mg, 75%, *Z/E* = 8.6/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.70 (d, *J* = 4.8 Hz, 0.23H, *E* isomer), 8.61 (d, *J* = 4.8 Hz, 1.97H, *Z* isomer), 8.25 (d, *J* = 8.6 Hz, 1H), 7.40 (s, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 7.10–6.98 (m, 6H), 6.72 (d, *J* = 17.6, 10.6 Hz, 1H), 6.68 (s, 1H), 6.50 (s, 1H), 5.06 (d, *J* = 10.6 Hz, 1H), 5.01 (d, *J* = 17.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 157.8 (CH), 157.5 (C_q), 140.7 (CH), 136.8 (C_q), 135.4 (C_q), 135.0 (C_q), 134.3 (C_q), 132.8 (CH), 131.4 (CH), 129.8 (C_q), 129.1 (CH), 128.1 (CH), 127.2 (CH), 124.9 (CH), 120.6 (CH), 116.8 (CH), 115.6 (CH_2), 114.1 (CH), 108.5 (CH), 21.5 (CH_3). **IR** (ATR): 2919, 2860, 1565, 1423, 1217, 1080, 987, 806, 751, 699 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 360 (100) $[M+Na]^+$, 338 (80) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{19}N_3Na$ $[M+Na]^+$ 360.1470, found 360.1471.



(*Z*)-5-Fluoro–2-(1-phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184fa)

The general procedure **F** was followed using 5-fluoro-1-(pyrimidin-2-yl)-1*H*-indole **71f** (42.6 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.9 mg, 0.32 mmol) for 3.5

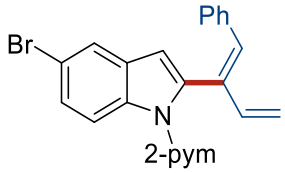
h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184fa** (48.5 mg, 71%, *Z/E* = 5.0/1 determined by ^{1}H NMR) as a yellow solid. **M.p.** = 104–106 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.67 (d, *J* = 4.8 Hz, 0.40H, *E* isomer), 8.58 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.25 (dd, *J* = 9.1, 4.7 Hz, 1H), 7.20 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.07–7.02 (m, 3H), 7.01–6.94 (m, 4H), 6.67 (dd, *J* = 17.6, 10.5 Hz, 1H), 6.65 (s, 1H), 6.48 (s, 1H), 5.03 (d, *J* = 10.5 Hz, 1H), 4.95 (d, *J* = 17.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.76 (d, *J* = 297.2 Hz, C_q), 157.9 (CH), 157.89 (d, *J* = 2.7 Hz, C_q), 140.4 (CH), 137.1 (C_q), 136.6 (C_q), 133.9 (C_q), 133.1 (CH), 132.9 (C_q), 130.16 (d, *J* = 10.0 Hz, C_q),129.1 (CH), 128.1 (CH), 127.3 (CH), 117.6 (d, *J* = 23.3 Hz), 117.2 (CH), 115.7 (CH_2), 115.3 (d, *J* = 9.1 Hz, CH), 111.3 (d, *J* = 25.3 Hz, CH), 108.4 (d, *J* = 4.1 Hz, CH), 105.8 (d, *J* = 23.5 Hz, CH). ^{19}F NMR (377 MHz, $CDCl_3$) δ = –122.3 (td, *J* = 9.1, 4.6 Hz). **IR** (ATR): 3053, 2130, 1961, 1710, 1568, 1427, 1419, 1196, 804, 698 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 364 (95) $[M+Na]^+$, 342 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}N_3F$ $[M+H]^+$ 342.1401, found 342.1403.



(*Z*)-5-chloro–2-(1-phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184ga)

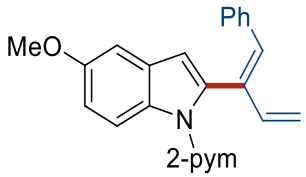
The general procedure **F** was followed using 5-chloro-1-(pyrimidin-2-yl)-1*H*-indole **71g** (45.9 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.9 mg, 0.32 mmol) for 3.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ga** (40.8 mg, 57%, *Z/E* = 3.6/1 determined by **^{1}**H NMR) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 4.8 Hz, 0.55H, *E* isomer), 8.63 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.28 (d, *J* = 8.9 Hz, 1H), 7.58 (d, *J* = 2.1 Hz, 1H), 7.28 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.15–7.04 (m, 3H), 7.05 (t, *J* = 4.8 Hz, 1H), 7.00 (dd, *J* = 6.7, 3.0 Hz, 2H), 6.71 (s, 1H), 6.70 (dd, *J* = 17.2, 10.2 Hz, 1H), 6.52 (s, 1H), 5.09 (d, *J* = 10.2 Hz, 1H), 5.00 (d, *J* = 17.2 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.0 (CH), 157.2 (C_q), 141.8 (C_q), 140.3 (CH), 136.9 (C_q), 136.5 (C_q), 135.0 (C_q), 133.7 (C_q), 133.3 (CH), 130.6 (C_q), 129.0 (CH), 128.1 (CH), 127.3 (CH), 123.5

(CH), 120.1 (CH), 117.3 (CH), 115.7 (CH_2), 115.5 (CH), 108.0 (CH). **MS** (ESI) *m/z* (relative intensity): 380 (40) (^{35}Cl) $[M+Na]^+$, 358 (100) (^{35}Cl) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}N_3{}^{35}Cl$ $[M+H]^+$ 358.1106, found 358.1104.



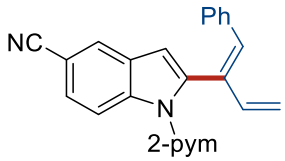
(*Z*)-5-Bromo–2-(1-phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184ha)

The general procedure **F** was followed using 5-bromo-1-(pyrimidin-2-yl)-1*H*-indole **71h** (54.8 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.9 mg, 0.32 mmol) for 3.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ha** (54.7 mg, 68%, *Z/E* = 6.9/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 4.8 Hz, 0.29H, *E* isomer), 8.63 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.23 (d, *J* = 8.9 Hz, 1H), 7.73 (d, *J* = 2.0 Hz, 1H), 7.40 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.12–7.07 (m, 3H), 7.05 (t, *J* = 4.8 Hz, 1H), 7.00–6.97 (m, 2H), 6.71 (dd, *J* = 17.3, 10.5 Hz, 1H), 6.70 (s, 1H), 6.51 (s, 1H), 5.08 (d, *J* = 10.5 Hz, 1H), 4.99 (d, *J* = 17.3 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.0, 157.2 (C_q), 140.3 (CH), 136.7 (C_q), 136.5 (C_q), 135.3 (C_q), 133.6 (C_q), 133.3 (CH), 131.2 (C_q), 129.0 (CH), 128.1 (CH), 127.4 (CH), 126.1 (CH), 123.2 (CH), 117.4 (CH), 115.9 (CH), 115.7 (CH_2), 115.2 (C_q), 107.8 (CH). **IR** (ATR): 3049, 2964, 2927, 1692, 1561, 1414, 1313, 1264, 1233, 1171, 1076, 1035, 989, 912, 808, 736, 696 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 424 (40) (^{79}Br) $[M+Na]^+$, 402 (100) (^{79}Br) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}N_3{}^{79}Br$ $[M+H]^+$ 402.0600, found 402.0594.



(*Z*)-5-Methoxy–2-(1-phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184ia)

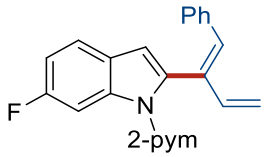
The general procedure **F** was followed using 5-methoxyl-1-(pyrimidin-2-yl)-1*H*-indole **71i** (45.1 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.9 mg, 0.32 mmol) for 2.8 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ia** (59.4 mg, 84%, *Z*/*E* = 5.7/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.70 (d, *J* = 4.8 Hz, 0.36H, *E* isomer), 8.62 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.32 (d, *J* = 9.1 Hz, 1H), 7.12–7.03 (m, 6H), 7.01–6.96 (m, 2H), 6.73 (d, *J* = 17.4, 10.5 Hz, 1H), 6.70 (s, 1H), 6.51 (s, 1H), 5.08 (d, *J* = 10.5 Hz, 1H), 5.03 (d, *J* = 17.4 Hz, 1H), 3.91 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 157.8 (CH), 157.4 (C_q), 155.5 (C_q), 140.6 (CH), 136.8 (C_q), 136.0 (C_q), 134.3 (C_q), 132.8 (CH), 131.6 (C_q), 130.3 (C_q), 129.1 (CH), 128.1 (CH), 127.2 (CH), 116.8 (CH), 115.6 (CH_2), 115.4 (CH), 112.8 (CH), 108.6 (CH), 102.7 (CH), 55.8 (CH_3). **IR** (ATR): 3044, 2950, 2249, 1717, 1565, 1421, 1280, 1202, 1106, 908, 804, 728 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 376 (80) $[M+Na]^+$, 354 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{20}N_3O$ $[M+H]^+$ 354.1601, found 354.1597.



(*Z*)-2-(1-Phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole–5-carbonitrile (184ja)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole–5-carbonitrile **71j** (44.0 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.9 mg, 0.32 mmol) for 5.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 5:1) yielded **184ja** (46.0 mg, 66%, *Z*/*E* = 3.2/1 determined by ^{1}H NMR) as a yellow solid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.76 (d, *J* = 4.8 Hz, 0.63H, *E* isomer), 8.67 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.34 (d, *J* =

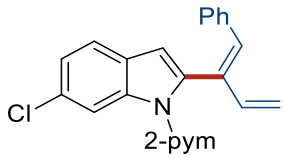
8.7 Hz, 1H), 7.95 (s, 1H), 7.55 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.43 (s, 1H), 7.13 (t, *J* = 4.8 Hz, 1H), 7.11–7.06 (m, 2H), 6.96 (dd, *J* = 7.6, 2.2 Hz, 2H), 6.73 (s, 1H), 6.69 (dd, *J* = 16.9, 10.0 Hz, 1H), 6.63 (s, 1H), 5.09 (d, *J* = 10.0 Hz, 1H), 4.97 (d, *J* = 16.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* = 158.2 (CH), 156.8 (C_q), 140.0 (CH), 138.2 (C_q), 138.1 (C_q), 136.3 (C_q), 133.9 (CH), 132.9 (C_q), 129.2 (C_q), 129.0 (CH), 128.2 (CH), 127.6 (CH) , 126.3 (CH), 125.9 (CH), 120.4 (C_q), 118.1 (CH), 115.9 (CH_2), 115.0 (CH), 108.3 (CH), 105.2 (C_q). **IR** (ATR): 3050, 2921, 2221, 1608, 1565, 1415, 1316, 1217, 1030, 986, 886, 809, 735, 698 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 371 (100) $[M+Na]^+$, 349 (90) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{17}N_4$ $[M+H]^+$ 349.1448, found 339.1440.



(*Z*)-6-Fluoro–2-(1-phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184ka)

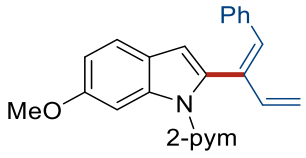
The general procedure **F** was followed using 6-fluoro-1-(pyrimidin-2-yl)-1*H*-indole **71k** (42.6 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene**138a** (41.9 mg, 0.32 mmol) for 5.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ka** (42.3 mg, 62%, *Z/E* = 2.7/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) *δ* = 8.73 (d, *J* = 4.8 Hz, 0.75H, *E* isomer), 8.64 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.12 (dd, *J* = 10.8, 2.4 Hz, 1H), 7.51 (dd, *J* = 8.6, 5.5 Hz, 1H), 7.44–7.37 (m, 1H), 7.12–7.07 (m, 3H), 7.05–6.99 (m, 4H), 6.73 (dd, *J* = 17.6, 10.8 Hz, 1H), 6.69 (s, 1H), 6.54 (s, 1H), 5.08 (d, *J* = 10.8 Hz, 1H), 5.02 (d, *J* = 17.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* = 160.6 (d, *J* = 238.2 Hz, C_q), 157.9 (CH), 157.3 (C_q), 140.5 (CH), 137.2 (C_q), 136.7 (C_q), 135.8 (d, *J* = 4.2 Hz, C_q), 133.9 (C_q), 133.0 (CH), 129.1 (CH), 128.1 (CH), 127.2 (CH), 125.9 (C_q), 121.3 (d, *J* = 10.0 Hz, CH), 117.2 (CH), 115.7 (CH_2), 110.5 (d, *J* = 24.8 Hz, CH), 108.5 (CH), 101.6 (d, *J* = 28.5 Hz, CH). ^{19}F NMR (377 MHz, $CDCl_3$) *δ* = -118.88 – -118.98 (m). **IR** (ATR): 3050, 2925, 2854, 1724, 1566, 1418, 1423, 1261, 1149, 1077, 986, 852, 808, 738, 697 cm^{-1}.

MS (ESI) *m/z* (relative intensity): 364 (20) $[M+Na]^+$, 342 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}N_3F$ $[M+H]^+$ 342.1401, found 342.1398.



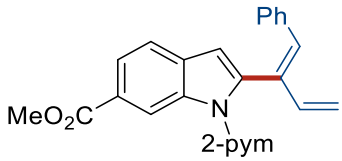
(*Z*)-6-Chloro–2-(1-phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184la)

The general procedure **F** was followed using 6-chloro-1-(pyrimidin-2-yl)-1*H*-indole **71l** (45.9 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.9 mg, 0.32 mmol) for 4.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184la** (43.7 mg, 61%, *Z/E* = 2.2/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.74 (d, *J* = 4.8 Hz, 0.91H, *E* isomer), 8.65 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.39 (s, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.23 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.12–7.07 (m, 3H), 7.06 (d, *J* = 4.8 Hz, 1H), 7.01–6.98 (m, 1H), 6.69 (s, 1H), 6.69 (dd, *J* = 17.1, 10.4 Hz, 1H), 6.53 (s, 1H), 5.07 (d, *J* = 10.4 Hz, 1H), 4.99 (d, *J* = 17.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.0 (CH), 157.2 (C_q), 140.4 (CH), 136.9 (C_q), 136.6 (C_q), 136.2 (C_q), 133.7 (C_q), 133.2 (CH), 129.3 (C_q), 129.1 (CH), 128.1 (CH), 128.0 (C_q), 127.3 (CH), 122.6 (CH), 121.5 (CH), 117.4 (CH), 115.7 (CH_2), 114.5 (CH), 108.4 (CH). **IR** (ATR): 3051, 1709, 1567, 1426, 1352, 1315, 1264, 1218, 908, 811, 748 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 380 (100) (^{35}Cl) $[M+Na]^+$, 358 (80) (^{35}Cl) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{16}N_3{}^{35}ClNa$ $[M+Na]^+$ 380.0925, found 380.0925.



(*Z*)-6-Methoxy–2-(1-phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184ma)

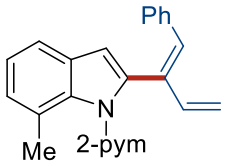
The general procedure **F** was followed using 6-methoxyl-1-(pyrimidin-2-yl)-1*H*-indole **71m** (45.1 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.9 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 10:1) yielded **184ma** (43.1 mg, 61%, *Z*/*E* = 3.6/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 4.8 Hz, 0.56H, *E* isomer), 8.63 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 7.96 (d, *J* = 2.3 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 1H), 7.12–7.06 (m, 5H), 7.02 (t, *J* = 4.8 Hz, 1H), 6.92 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.71 (d, *J* = 10.5, 17.3 Hz, 1H), 6.66 (s, 1H), 6.49 (s, 1H), 5.05 (d, *J* = 10.5 Hz, 1H), 5.02 (d, *J* = 17.3 Hz, 1H), 3.92 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 157.9 (CH), 157.6 (C_q), 157.3 (C_q), 140.8 (CH), 137.6 (C_q), 136.9 (C_q), 134.3 (C_q), 134.2 (C_q), 132.6 (CH), 129.2 (CH), 128.1 (CH), 127.1 (CH), 123.7 (C_q), 121.2 (CH), 116.9 (CH), 115.6 (CH_2), 111.3 (CH), 108.6 (CH), 98.7 (CH), 55.9 (CH_3). **IR** (ATR): 2924, 2855, 2245, 2200, 1948, 1612, 1565, 1484, 1418, 1265, 1159, 1030, 906, 808, 728 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 376 (80) $[M+Na]^+$, 354 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{20}N_3O$ $[M+H]^+$ 354.1606, found 354.1590.



Methyl (*Z*)-2-(1-phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole-6-carboxy late (184na)

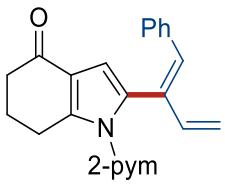
The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole-6-carboxylate **71n** (50.7 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.9 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 5:1) yielded **184na** (59.5 mg, 78%, *Z*/*E* = 3.8/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 9.00 (s, 1H), 8.77 (d, *J* = 4.8 Hz, 0.53H, *E* isomer), 8.68 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 7.96 (d, *J* = 8.3 Hz, 1H), 7.63 (d, *J* = 8.3 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.11–7.06 (m, 3H), 7.03–6.98 (m, 2H), 6.72 (s, 1H), 6.70 (dd, *J* = 17.2, 10.5 Hz, 1H), 6.61 (s, 1H), 5.08 (d, *J* = 10.5 Hz, 1H), 5.00 (d, *J* = 17.2 Hz, 1H), 3.97 (s, 3H). **^{13}C NMR** (101 MHz,

$CDCl_3$) δ = 168.2 (C_q), 158.1 (CH), 157.1 (C_q), 140.1 (CH), 138.8 (C_q), 136.4 (C_q), 136.0 (C_q), 133.6 (CH), 133.4 (C_q), 133.1 (C_q), 129.0 (CH), 128.2 (CH), 127.4 (CH), 125.1 (C_q), 123.1 (CH), 120.4 (CH), 117.6 (CH), 116.3 (CH), 115.8 (CH_2), 108.4 (CH), 52.1 (CH_3). **IR** (ATR): 3052, 2950, 2844, 1709, 1566, 1421, 1361, 1276, 1217, 1092, 990, 907, 804, 732, 696 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 404 (75) $[M+Na]^+$, 382 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{20}N_3O_2$ $[M+H]^+$ 382.1550, found 382.1543.



(*Z*)-7-Methyl–2-(1-phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184oa)

The general procedure **F** was followed using 7-methyl-1-(pyrimidin-2-yl)-1*H*-indole **71o** (41.6 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.9 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184na** (41.2 mg, 61%, *Z/E* = 3.6/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.78 (d, *J* = 4.8 Hz, 0.55H, *E* isomer), 8.64 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 7.55 (d, *J* = 7.8 Hz, 1H), 7.39–7.35 (m, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.15–7.11 (m, 5H), 7.10 (t, *J* = 4.8 Hz, 1H), 6.69 (s, 1H), 6.59 (d, *J* = 1.6 Hz, 1H), 6.58 (dd, *J* = 17.0, 10.6 Hz, 1H), 5.07 (d, *J* = 10.6 Hz, 1H), 5.00 (dd, *J* = 17.0, 1.5 Hz, 1H), 2.14 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 158.1 (C_q), 157.6 (CH), 140.2 (CH), 136.4 (C_q), 136.2 (C_q), 136.2 (C_q), 135.1 (CH), 132.7 (C_q), 129.9 (C_q), 129.3 (CH), 128.1 (CH), 127.5 (CH), 125.9 (CH), 122.7 (C_q), 121.5 (CH), 118.8 (CH), 118.5 (CH), 116.5 (CH_2), 106.6 (CH), 20.7 (CH_3). **IR** (ATR): 3051, 1691, 1567, 1422, 1309, 1208, 1058, 913, 868, 802, 733, 697 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 360 (25) $[M+Na]^+$, 338 (80) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{20}N_3$ $[M+H]^+$ 338.1652, found 338.1647.

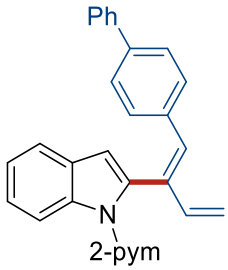


2-(1-Phenylbuta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1,5,6,7-tetrahydro-4*H*-indol-4-one (184pa)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1,5,6,7-tetrahydro-4*H*-indol-4-one **71p** (42.4 mg, 0.20 mmol) and (cyclopropylidenemethyl)benzene **138a** (41.9 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 3:1) yielded (*Z*)-**184pa** (38.7 mg, 57%) as a yellow solid and (*E*)-**184pa** (19.2 mg, 28%) as a yellow solid. (*Z*)-**184pa**: **M.p.** = 148–150 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.54 (d, *J* = 4.8 Hz, 2H), 7.13–7.05 (m, 4H), 6.88–6.82 (m, 2H), 6.64 (s, 1H), 6.60 (dd, *J* = 17.2, 10.5 Hz, 1H), 6.49 (s, 1H), 5.24 (d, *J* = 17.2 Hz, 1H), 5.14 (d, *J* = 10.5 Hz, 1H), 3.02 (t, *J* = 6.0 Hz, 2H), 2.60 (t, *J* = 6.4 Hz, 2H), 2.18 (tt, *J* = 6.0, 6.4 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 195.2 (C_q), 157.9 (CH), 156.2 (C_q), 145.6 (C_q), 140.1 (CH), 136.4 (C_q), 133.4 (CH), 132.3 (C_q), 130.1 (C_q), 128.8 (CH), 128.1 (CH), 127.3 (CH), 122.3 (C_q), 118.7 (CH), 116.1 (CH_2), 109.4 (CH), 38.1 (CH_2), 24.3 (CH_2), 24.0 (CH_2). **IR** (ATR): 3051, 2945, 1657, 1562, 1413, 1261, 1179, 996, 903, 821, 730, 695 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1048 (10), 705 (15), 683(25), 364(20) $[M+Na]^+$, 342 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{20}N_3O$ $[M+H]^+$ 342.1601, found 342.1601.

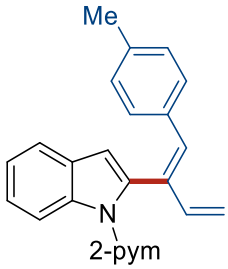
(*E*)-**184pa**: **M.p.** = 129–131 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.73 (d, *J* = 4.8 Hz, 2H), 7.35 (d, *J* = 4.4 Hz, 3H), 7.32–7.25 (m, 2H), 7.22 (t, *J* = 4.9 Hz, 1H), 6.79 (s, 1H), 6.73 (s, 1H), 6.64 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.05 (d, *J* = 17.5 Hz, 1H), 4.94 (d, *J* = 10.8 Hz, 1H), 3.02 (t, *J* = 6.1 Hz, 2H), 2.58 (t, *J* = 6.4 Hz, 2H), 2.19 (tt, *J* = 6.1, 6.4 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 194.9 (C_q), 158.5 (CH), 157.1 (C_q), 145.8 (C_q), 137.1 (C_q), 135.8 (C_q), 134.2 (CH), 132.5 (C_q), 131.4 (CH), 129.7 (CH), 128.3 (CH), 127.4 (CH), 121.9 (C_q), 119.2 (CH), 118.0 (C_q), 109.3 (CH), 38.1 (CH_2), 24.1 (CH_2), 23.9 (CH_2). **IR** (ATR): 3051, 2926, 1727, 1658, 1564, 1418, 1265, 1182, 1000, 910, 733, 700 cm^{-1}. **MS** (ESI) *m/z*

(relative intensity): 364 (70) $[M+Na]^+$, 342 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{20}N_3O$ $[M+H]^+$ 342.1601, found 342.1606.



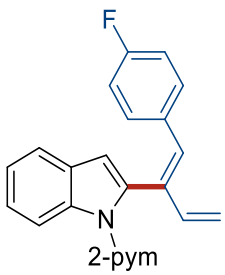
(*Z*)-2-{[1-(1,1'-Biphenyl)-4-yl]buta-1,3-dien–2-yl}-1-(pyrimidin-2-yl)-1*H*-indole (184ab)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 4-(cyclopropylidenemethyl)-1,1'-biphenyl **138b** (66.0 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ab** (64.7 mg, 81%, *Z/E* = 3.4/1 determined by ^{1}H NMR) as a yellow solid. **M.p.** = 127–128 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.74 (d, *J* = 4.8 Hz, 0.59H, *E* isomer), 8.65 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.40 (d, *J* = 8.3 Hz, 1H), 7.64 (d, *J* = 5.7 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.41–7.27 (m, 7H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.04 (t, *J* = 4.8 Hz, 1H), 6.75 (s, 1H), 6.72 (dd, *J* = 17.3, 10.6 Hz, 1H), 6.61 (s, 1H), 5.07 (d, *J* = 10.6 Hz, 1H), 5.00 (d, *J* = 17.3 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 158.0 (CH), 157.6 (C_q), 140.7 (CH), 140.6 (C_q), 139.7 (C_q), 136.7 (C_q), 135.8 (C_q), 135.5 (C_q), 134.2 (C_q), 132.7 (CH), 129.6 (CH), 129.6 (C_q), 128.8 (CH), 127.3 (CH), 126.9 (CH), 126.7 (CH), 123.4 (CH), 122.1 (CH), 120.8 (CH), 117.1 (CH), 115.7 (CH_2), 114.4 (CH), 108.6 (CH). **IR** (ATR): 3032, 2243, 1716, 1688, 1564, 1420, 1347, 1305, 1212, 904, 804, 727 cm^{-1}. **MS** (ESI) *m/z* (relative intensity):, 422 (90) $[M+Na]^+$,400 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{28}H_{22}N_3$ $[M+H]^+$ 400.1808, found 400.1806.



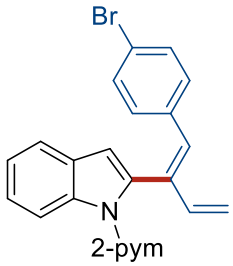
(*Z*)-1-(Pyrimidin–2-yl)-2-[1-(p-tolyl)buta-1,3-dien–2-yl]-1*H*-indole (184ac)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 1-(cyclopropylidenemethyl)-4-methylbenzene **138c** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ac** (58.0 mg, 86%, *Z*/*E* = 4.7/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.73 (d, *J* = 4.8 Hz, 0.43H, *E* isomer), 8.65 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.39 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.37–7.33 (m, 1H), 7.31–7.23 (m, 1H), 7.02 (t, *J* = 4.8 Hz, 1H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.92 (d, *J* = 8.2 Hz, 2H), 6.70 (dd, *J* = 17.2, 10.6 Hz, 1H), 6.70 (s, 1H), 6.59 (s, 1H), 5.04 (d, *J* = 10.6 Hz, 1H), 4.98 (d, *J* = 17.2 Hz, 1H), 2.26 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 157.9 (CH), 157.5 (C_q), 140.8 (CH), 137.1 (C_q), 136.6 (C_q), 135.7 (C_q), 133.9 (C_q), 133.2 (C_q), 133.2 (CH), 129.6 (CH), 129.1 (C_q), 128.9 (CH), 123.3 (CH), 122.0 (CH), 120.8 (CH), 117.0 (CH), 115.1 (CH_2), 114.2 (CH), 108.4 (CH), 21.3 (CH_3). **IR** (ATR): 3043, 2919, 1710, 1590, 1510, 1421, 1351, 1307, 1214, 1179, 985, 899, 804, 744 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 360 (100) $[M+Na]^+$, 338 (80) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{20}N_3$ $[M+H]^+$ 338.1652, found 338.1650.



(*Z*)-2-[1-(4-fluorophenyl)buta-1,3-dien-2-yl]-1-(pyrimidin-2-yl)-1*H*-indole (184ad)

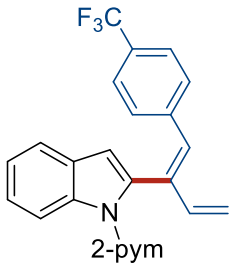
The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 1-(cyclopropylidenemethyl)-4-fluorobenzene **138c** (46.1 mg, 0.32 mmol) for 3.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ad** (51.9 mg, 76%, *Z/E* = 4.7/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.73 (d, *J* = 4.8 Hz, 0.39H, *E* isomer), 8.66 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.36 (d, *J* = 8.2, 1H), 7.64 (d, *J* = 7.2, 1H), 7.36 (dd, *J* = 8.5, 7.2 Hz, 1H), 7.28 (dd, *J* = 8.5, 6.8 Hz, 1H), 7.06–6.99 (m, 3H), 6.79 (t, *J* = 8.8 Hz, 2H), 6.69 (dd, *J* = 17.0, 10.6 Hz, 1H), 6.66 (s, 1H), 6.58 (s, 1H), 5.08 (d, *J* = 10.6 Hz, 1H), 5.03 (s, d, *J* = 17.0 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 161.9 (d, $^{1}J_{C-F}$ = 247.7 Hz, C_q), 157.9 (CH), 157.4 (C_q), 140.3 (CH), 136.7 (C_q), 135.2 (C_q), 133.85 (d, $^{4}J_{C-F}$ = 2.0 Hz, C_q), 132.9 (d, $^{4}J_{C-F}$ = 3.5 Hz, C_q), 131.7 (CH), 130.7 (d, $^{3}J_{C-F}$ = 7.9 Hz, CH), 129.4 (C_q), 123.5 (CH), 122.1 (CH), 120.8 (CH), 117.1 (CH), 115.8 (CH_2), 115.1 (d, $^{2}J_{C-F}$ = 21.3 Hz, CH), 114.2 (CH), 108.7 (CH). ^{19}F NMR (282 MHz, $CDCl_3$) δ = (-114.1) – (-114.2) (m). **IR** (ATR): 3044, 2245, 1717, 1690, 1565, 1503, 1420, 1347, 1307, 1220, 1153, 985,906, 805, 729 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 364 (70) $[M+Na]^+$, 342 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}N_3F$ $[M+H]^+$ 342.1401, found 342.1397.



(*Z*)-2-[1-(4-Bromophenyl)buta-1,3-dien–2-yl]-1-(pyrimidin-2-yl)-1*H*-indole (184ae)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 1-(cyclopropylidenemethyl)-4-bromobenzene **138e** (66.9 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ae** (48.3 mg, 60%, *Z/E* = 1.8/1 determined by ^{1}H NMR) as a yellow solid. **M.p.** = 100–102 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 4.8 Hz, 1.09H, *E* isomer), 8.66 (d, *J* = 4.8 Hz,

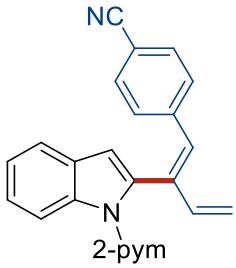
2H, *Z* isomer), 8.36 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.35–7.28 (m, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 7.05 (t, *J* = 4.8 Hz, 1H), 6.93 (d, *J* = 8.5 Hz, 2H), 6.66 (d, *J* = 17.2, 10.6 Hz, 1H), 6.62 (s, 1H), 6.54 (s, 1H), 5.08 (d, *J* = 10.6 Hz, 1H), 5.01 (d, *J* = 17.2 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 156.0 (CH), 157.5 (C_q), 140.3 (CH), 140.2 (C_q), 136.7 (C_q), 135.7 (C_q), 134.9 (C_q), 131.6 (CH), 131.2 (CH), 130.6 (CH), 129.4 (C_q), 123.6 (CH), 122.1 (CH), 121.1 (CH), 120.9 (C_q), 117.2 (CH), 116.3 (CH_2), 114.3 (CH), 108.7 (CH). **IR** (ATR): 3044, 1711, 1561, 1487, 1451, 1421, 1346, 1302, 1070, 1008, 906, 802, 727 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 364 (75) (^{79}Br) $[M+Na]^+$, 342 (75) (^{79}Br) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{14}N_3{}^{79}Br$ $[M+H]^+$ 402.0606, found 402.0604.



(*Z*)-1-(Pyrimidin–2-yl)-2-{1-[4-(trifluoromethyl)phenyl]buta-1,3-dien–2-yl}-1*H*-indole (184af)

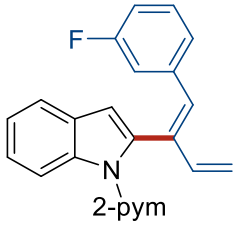
The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 1-(cyclopropylidenemethyl)-4-trifluoromethylbenzene **138f** (63.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184af** (40.7 mg, 52%, *Z/E* = 3.6/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.74 (d, *J* = 4.8 Hz, 0.56H, *E* isomer), 8.66 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.42 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.35–7.27 (m, 2H), 7.20 (d, *J* = 8.2 Hz, 2H), 7.05 (t, *J* = 4.8 Hz, 1H), 6.73 (s, 1H), 6.72 (dd, *J* = 17.3, 10.7 Hz, 1H) ,6.58 (s, 1H), 5.14 (d, *J* = 10.7 Hz, 1H), 5.07 (d, *J* = 17.3 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.0 (CH), 157.5 (C_q), 140.4 (q, *J* = 1.4 Hz, C_q), 140.1 (CH), 136.7 (C_q), 136.4 (C_q), 134.8 (C_q), 131.1 (CH), 129.4 (C_q), 129.2 (CH), 128.7 (q, *J* = 32.3 Hz, C_q), 125.0 (q, *J* = 3.9 Hz, CH), 124.3 (q, *J* = 271.9 Hz, C_q), 123.7 (CH), 122.2 (CH), 120.9 (CH), 117.2

(CH), 117.1 (CH_2), 114.4 (CH), 109.0 (CH). ^{19}F NMR (377 MHz, $CDCl_3$) δ = -62.48. **IR** (ATR): 3048, 1573, 1562, 1453, 1423, 1352, 1322, 1124, 1067, 827, 742 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 414 (100) $[M+Na]^+$, 392 (90) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{17}N_3F_3$ $[M+H]^+$ 392.1368, found 392.1362.



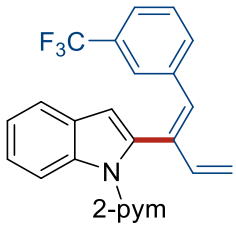
(*Z*)-4-{2-[1-(Pyrimidin–2-yl)-1*H*-indol–2-yl]buta-1,3-dien-1-yl}benzonitrile (184ag)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 4-(cyclopropylidenemethyl)benzonitrile **138g** (49.7 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ag** (62.7 mg, 90%, *Z/E* = 1.4/1 determined by ^1H NMR) as a yellow solid. **M.p.** = 140–141 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 4.8 Hz, 1.46H, *E* isomer), 8.65 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.37 (d, *J* = 8.4 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.06 (t, *J* = 4.8 Hz, 1H), 6.68 (dd, *J* = 17.3, 11.3 Hz, 1H), 6.67 (s, 1H), 6.54 (s, 1H), 5.15 (d, *J* = 11.3 Hz, 1H), 5.08 (d, *J* = 17.3 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.0 (CH), 157.4 (C_q), 141.6 (C_q), 139.8 (CH), 137.4 (C_q), 136.7 (C_q), 134.4 (C_q), 131.8 (CH), 130.2 (CH), 129.5 (CH), 129.3 (C_q), 123.9 (CH), 122.3 (CH), 120.9 (CH), 119.2 (C_q), 117.9 (CH_2), 117.2 (CH), 114.4 (CH), 110.1 (CH), 109.2 (C_q). **IR** (ATR): 2221, 2135, 2023, 1701, 1563, 1420, 1346, 1307, 905, 800, 735 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 371 (100) $[M+Na]^+$, 349 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{17}N_4$ $[M+H]^+$ 349.1448, found 349.1446.



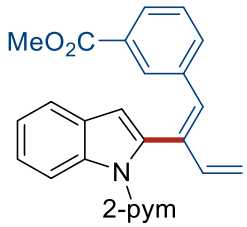
(*Z*)-2-[1-(3-Fluorophenyl)buta-1,3-dien–2-yl]-1-(pyrimidin-2-yl)-1*H*-indole (184ah)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 1-(cyclopropylidenemethyl)-3-fluorobenzene **138h** (47.4 mg, 0.32 mmol) for 3.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ah** (53.9 mg, 79%, *Z/E* = 4.4/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.73 (d, *J* = 4.8 Hz, 0.45H, *E* isomer), 8.66 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.37 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.63 (d, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 8.4 Hz, 1H), 7.33–7.21 (m, 1H), 7.05 (d, *J* = 5.0 Hz, 1H), 7.02 (t, *J* = 4.2 Hz, 1H), 6.84 (s, 1H), 6.83–6.75 (m, 2H), 6.69 (dd, *J* = 17.5, 11.2 Hz, 1H), 6.66 (s, 1H), 6.59 (s, 1H), 5.11 (d, *J* = 11.2 Hz, 1H), 5.06 (d, *J* = 17.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 162.5 (d, $^{1}J_{C–F}$ = 244.5 Hz, C_q), 157.9 (CH), 157.4 (C_q), 140.2 (CH), 139.1 (d, $^{3}J_{C–F}$ = 8.0 Hz, C_q), 136.7 (C_q), 135.4 (C_q), 134.8 (C_q), 131.4 (d, $^{4}J_{C–F}$ = 2.6 Hz, CH), 129.4, 129.1 (C_q), 124.8 (d, $^{4}J_{C–F}$ = 2.8 Hz, CH), 123.6 (CH), 122.1 (CH), 120.8 (CH), 117.1 (CH), 116.6 (CH_2), 115.7 (d, $^{2}J_{C–F}$ = 22.0 Hz), 114.3 (CH), 114.0 (d, $^{2}J_{C–F}$ = 21.4 Hz, CH), 109.0 (CH). ^{19}F NMR (282 MHz, $CDCl_3$) δ = –113.79 (td, *J* = 9.5, 6.4 Hz). **IR** (ATR): 3045, 1998, 1718, 1566, 1420, 1347, 1307, 1244, 1143, 905, 803, 729 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 364($[M+Na]^+$, 342 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}N_3F$ $[M+H]^+$ 342.1712, found 342.1400.



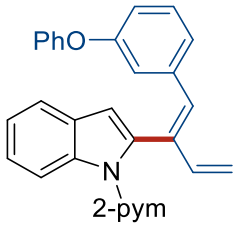
(*Z*)-1-(Pyrimidin–2-yl)-2-{1-[3-(trifluoromethyl)phenyl]buta-1,3-dien–2-yl}-1*H*-indole (184ai)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 1-(cyclopropylidenemethyl)-3-trifluoromethylbenzene **138i** (63.1 mg, 0.32 mmol) for 3.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ai** (64.2 mg, 82%, *Z/E* = 5.7/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.74 (d, *J* = 4.8 Hz, 0.35H, *E* isomer), 8.63 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.32 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.37–7.32 (m, 2H), 7.29 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.25–7.23 (m, 1H), 7.15–7.12 (m, 2H), 7.04 (t, *J* = 4.8 Hz, 1H), 6.73 (d, *J* = 16.8, 11.0 Hz, 1H), 6.69 (s, 1H), 6.61 (s, 1H), 5.18 (d, *J* = 11.0 Hz, 1H), 5.17 (d, *J* = 16.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 157.9 (CH), 157.3 (C_q), 139.9 (CH), 137.6 (C_q), 136.7 (C_q), 135.9 (C_q), 134.5 (C_q), 131.7 (CH), 130.9 (CH), 130.3 (q, $^{2}J_{C–F}$ = 32.1 Hz, C_q), 128.5 (CH), 125.9 (CH), 125.9 (q, $^{3}J_{C–F}$ = 3.8 Hz, CH), 124.1 (q, $^{1}J_{C–F}$ = 273.7 Hz, CH), 123.7 (CH), 123.6 (q, $^{3}J_{C–F}$ = 3.8 Hz, CH), 122.2 (CH), 120.8 (CH), 117.1 (CH), 117.1 (CH_2), 114.2 (CH), 109.1 (CH). ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.9. **IR** (ATR): 3045, 1720, 1594, 1420, 1347, 1224, 1090, 908, 800, 731 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 414 (80) $[M+Na]^+$, 392 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{17}N_3F_3$ $[M+H]^+$ 392.1369, found 392.1365.



Methyl (*Z*)-3-{2-[1-(pyrimidin-2-yl)-1*H*-indol–2-yl]buta-1,3-dien-1-yl}benzoate (184aj)

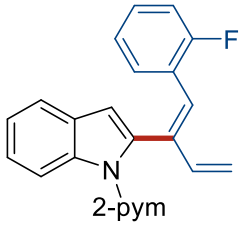
The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and methyl-3-(cyclopropylidenemethyl)benzoate **138j** (59.9 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 8:1) yielded **184aj** (58.7 mg, 77%, *Z*/*E* = 4.5/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.73 (d, *J* = 4.8 Hz, 0.44H, *E* isomer), 8.62 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.34 (d, *J* = 8.4 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.65 (s, 1H), 7.64–7.57 (m, 1H), 7.34 (t, *J* = 8.4 Hz, 1H), 7.27 (d, *J* = 7.8 Hz, 1H), 7.21–7.12 (m, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.01 (t, *J* = 4.8 Hz, 1H), 6.73 (dd, *J* = 17.2, 10.4 Hz, 1H), 6.71 (s, 1H), 6.59 (s, 1H), 5.14 (d, *J* = 10.4 Hz, 1H), 5.12 (d, *J* = 17.2 Hz, 1H), 3.75 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 167.0 (C_q), 157.9 (CH), 157.3 (C_q), 140.2 (CH), 137.0 (C_q), 136.7 (C_q), 135.2 (C_q), 134.9 (C_q), 133.0 (CH), 131.6 (CH), 130.5 (CH), 129.9 (C_q), 129.4 (C_q), 128.2 (CH), 128.1 (CH), 123.5 (CH), 122.0 (CH), 120.8 (CH), 117.1 (CH), 116.6 (CH_2), 114.3 (CH), 108.9 (CH). **IR** (ATR): 3045, 1720, 1594, 1420, 1347, 1224, 1090, 908, 800, 731 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 414 (80) $[M+Na]^+$, 392 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{20}N_3O_2$ $[M+H]^+$ 382.1556, found 382.1559.



(*Z*)-2-[1-(3-Phenoxyphenyl)buta-1,3-dien–2-yl]-1-(pyrimidin-2-yl)-1*H*-indole (184ak)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 1-(cyclopropylidenemethyl)-3-phenoxybenzene **138k** (70.8 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ak** (70.6 mg, 85%, *Z*/*E* = 7.0/1 determined by ^{1}H NMR) as a yellow solid. **M.p.** = 86–88 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 4.8 Hz, 0.28H, *E* isomer), 8.63 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.34 (d, *J* = 8.2 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.37–7.25 (m, 2H), 7.14–7.02 (m, 2H), 7.03 (t, *J* = 5.1 Hz, 2H), 6.93 (t, *J* = 7.3 Hz, 1H), 6.83–6.73 (m, 5H), 6.66 (s, 1H),

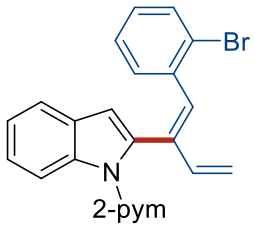
6.65 (d, *J* = 17.3, 10.8 Hz, 1H), 6.54 (s, 1H), 5.06 (d, *J* = 10.8 Hz, 1H), 5.00 (d, *J* = 17.3 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* = 157.8 (CH), 157.4 (C_q), 157.2 (C_q), 156.5 (C_q), 140.2 (CH), 138.6 (C_q), 136.7 (C_q), 135.1 (C_q), 134.9 (C_q), 132.1 (CH), 129.5 (CH), 129.4 (C_q), 129.3 (CH), 123.6 (CH), 123.4 (CH), 123.2 (CH), 122.0 (CH), 120.8 (CH), 119.2 (CH), 119.2 (CH), 118.8 (CH), 117.6 (CH), 117.0 (CH), 116.1 (CH_2), 114.3 (CH), 108.9 (CH). **IR** (ATR): 3047, 1692, 1568, 1423, 1244, 1211, 1154, 1023, 1079, 900, 800, 732, 692 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 438 (100) $[M+Na]^+$, 416 (70) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{28}H_{22}N_3O$ $[M+H]^+$ 416.1757, found 416.1744.



(*Z*)-2-(1-(2-Fluorophenyl)buta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184al)

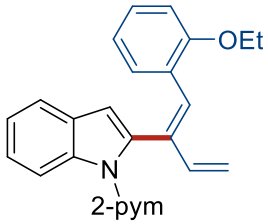
The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 1-(cyclopropylidenemethyl)-2-fluorobenzene **138l** (47.1 mg, 0.32 mmol) for 3.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184al** (51.2 mg, 75%, *Z/E* = 4.8/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) *δ* = 8.74 (d, *J* = 4.8 Hz, 0.42H, *E* isomer), 8.65 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.32 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.34 (td, *J* = 8.4, 1.5 Hz, 1H), 7.26 (td, *J* = 7.2, 1.2 Hz, 1H), 7.12–7.06 (m, 1H), 7.05 (t, *J* = 4.8 Hz, 1H), 6.97 (td, *J* = 7.8, 1.8 Hz, 1H), 6.90 (td, *J* = 8.4, 1.2 Hz, 1H), 6.85 (s, 1H), 6.75 (t, *J* = 7.1 Hz, 1H), 6.74 (dd, *J* = 18.0, 9.6 Hz, 1H), 6.61 (s, 1H), 5.13 (d, *J* = 9.6 Hz, 1H), 5.12 (d, *J* = 18.0 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* = 160.6 (d, *J* = 248.3 Hz, C_q), 157.9 (CH), 157.4 (CH), 140.2 (C_q), 136.7 (C_q), 135.5 (d, *J* = 1.6 Hz, C_q), 135.1 (C_q), 130.1 (d, *J* = 2.8 Hz, CH), 129.4 (C_q), 128.7 (d, *J* = 8.5 Hz, CH), 124.4 (d, *J* = 5.1 Hz, C_q), 123.8 (CH), 123.8 (CH), 123.6 (CH), 122.0 (CH), 120.8 (CH), 117.1 (CH), 116.5 (CH_2), 114.8 (d, *J* = 21.9 Hz, CH), 114.1 (CH), 109.0 (CH). ^{19}F NMR (282 MHz, $CDCl_3$) *δ* = –116.86—116.96 (m). **IR** (ATR): 3044, 2244, 1565, 1437,

1421, 1347, 1347, 1071, 1006, 906, 803, 727 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 414 (25) $[M+Na]^+$, 392 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}N_3F$ $[M+H]^+$ 342.1407, found 342.1401.



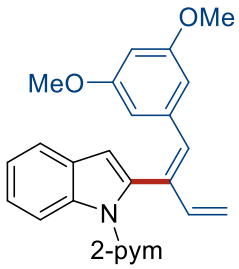
(*Z*)-2-(1-(2-Bromophenyl)buta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184am)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 1-(cyclopropylidenemethyl)-2-bromobenzene **138m** (66.6 mg, 0.32 mmol) for 4.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184am** (49.1 mg, 61%, *Z/E* = 1.3/1 determined by ^{1}H NMR) as a yellow solid. **M.p.** = 143–145 °C. ^{1}**H NMR** (400 MHz, $CDCl_3$) δ = 8.75 (d, *J* = 4.8 Hz, 1.56H, *E* isomer), 8.65 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.22 (d, *J* = 8.3 Hz, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.37–7.30 (m, 2H), 7.17 (t, *J* = 8.0 Hz, 1H), 7.05 (t, *J* = 4.8 Hz, 1H), 6.91 (t, *J* = 7.4, 1H), 6.80 (s, 1H), 6.80 (s, 1H), 6.68 (dd, *J* = 17.6, 10.6 Hz, 1H), 6.59 (s, 1H), 5.22 (d, *J* = 17.3 Hz, 1H), 5.18 (d, *J* = 10.6 Hz, 2H). ^{13}**C NMR** (101 MHz, $CDCl_3$) δ = 158.0 (CH), 157.2 (C_q), 139.8 (CH), 139.4 (C_q), 137.3 (C_q), 136.8 (C_q), 135.3 (C_q), 132.0 (CH), 131.1 (CH), 130.8 (CH), 129.2 (C_q), 128.5 (CH), 127.1 (CH), 124.3 (C_q), 123.6 (CH), 122.0 (CH), 120.8 (CH), 117.2 (CH), 116.9 (CH_2), 113.9 (CH), 109.6 (CH). **IR** (ATR): 3049, 2920, 1695, 1565, 1423, 1349, 1262, 1213, 1013, 987, 805, 741cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 424 (70) (^{79}Br) $[M+Na]^+$, 402 (100) (^{79}Br) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{17}N_3{}^{79}Br$ $[M+H]^+$ 402.0606, found 402.0534.



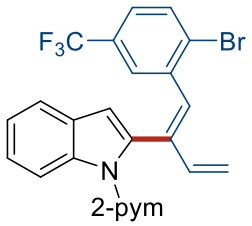
(*Z*)-2-(1-(2-Ethoxyphenyl)buta-1,3-dien–2-yl)-1-(pyrimidin-2-yl)-1*H*-indole (184an)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 1-(cyclopropylidenemethyl)-2-ethoxybenzene **138n** (66.6 mg, 0.32 mmol) for 3.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184an** (57.3 mg, 78%, *Z/E* = 3.0/1 determined by ^{1}H NMR) as a yellow solid. **M.p.** = 86–89 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.74 (d, *J* = 4.8 Hz, 0.66H, *E* isomer), 8.64 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.29 (d, *J* = 8.1 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.08–6.95 (m, 5H), 6.78 (dd, *J* = 16.4, 11.2 Hz, 1H), 6.61 (s, 1H), 6.58 (t, *J* = 7.5 Hz, 1H), 5.08 (d, *J* = 16.4 Hz, 1H), 5.07 (d, *J* = 11.2 Hz, 1H), 3.99 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 157.8 (CH), 157.4 (C_q), 156.7 (C_q), 140.8 (CH), 136.7 (C_q), 135.9 (C_q), 133.2 (C_q), 129.9 (CH), 129.5 (C_q), 128.4 (CH), 128.1 (CH), 125.7 (C_q), 123.2 (CH), 121.8 (CH), 120.7 (CH), 120.3 (CH), 116.8 (CH), 114.9 (CH_2), 113.9 (CH), 111.0 (CH), 108.7 (CH), 63.7 (CH_2), 15.1 (CH_3). **IR** (ATR): 2978, 2508, 2162, 2088, 2011, 1957, 1563, 1422, 1239, 1039, 742 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 390 (60) $[M+Na]^+$, 368 (50) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{21}N_3ONa$ $[M+H]^+$ 390.1577, found 390.1574.



(*Z*)-2-[1-(3,5-Dimethoxyphenyl)buta-1,3-dien–2-yl]-1-(pyrimidin-2-yl)-1*H*-indole (184ao)

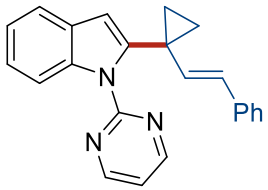
The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 1-(cyclopropylidenemethyl)-3,5-dimethoxybenzene (**138o**) (60.6 mg, 0.32 mmol) for 3.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 10:1) yielded **184ao** (69.8 mg, 91%, *Z*/*E* = 3.8/1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.73 (d, *J* = 4.8 Hz, 0.52H, *E* isomer), 8.63 (dd, *J* = 4.8 Hz, 2H, *Z* isomer), 8.33 (d, *J* = 7.8 Hz, 1H), 7.64 (dd, *J* = 7.8 Hz, 1H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.25 (t, *J* = 7.2 Hz, 1H), 7.01 (t, *J* = 4.8 Hz, 0H), 6.78 (dd, *J* = 17.2, 10.5 Hz, 1H), 6.66 (s, 1H), 6.59 (s, 1H), 6.22 (t, *J* = 2.1 Hz, 1H), 6.07 (d, *J* = 2.1 Hz, 2H), 5.25 (d, *J* = 17.2 Hz, 1H), 5.21 (d, *J* = 10.5 Hz, 1H), 3.38 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 160.2 (C_q), 157.8 (CH), 157.2 (C_q), 140.4 (CH), 138.3 (C_q), 136.6 (C_q), 135.0 (C_q), 134.5 (C_q), 132.8 (CH), 129.4 (C_q), 123.4 (CH), 122.0 (CH), 120.6 (CH), 117.0 (CH), 116.3 (CH_2), 114.3 (CH), 108.7 (CH), 106.5 (CH), 100.6 (CH), 55.0 (CH). **IR** (ATR): 3047, 2937, 2835, 1730, 1590, 1423, 1344, 1303, 1263, 1201, 1152, 1061, 985, 904, 805, 735 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 406 (100) $[M+Na]^+$, 484 (70) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{22}N_3O_2$ $[M+H]^+$ 384.1707, found 384.1705.



(*Z*)-2-{1-[2-Bromo-5-(trifluoromethyl)phenyl]buta-1,3-dien-2-yl}-1-(pyrimidin-2-yl)-1*H*-indole (184ap)

The general procedure **F** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and 1-(cyclopropylidenemethyl)-2-bromo-5-trifluoromethylbenzene **138p** (88.3 mg, 0.32 mmol) for 6.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **184ap** (48.0 mg, 78%, *Z*/*E* = 10.5/1 determined by ^{1}H NMR) as a yellow solid. **M.p.** = 71–72 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.70 (d, *J* = 4.8 Hz, 0.19H, *E* isomer), 8.60 (d, *J* = 4.8 Hz, 2H, *Z* isomer), 8.18 (dq, *J* = 8.4, 0.8 Hz, 1H), 7.54 (dd, *J* = 7.7, 1.4 Hz, 1H),

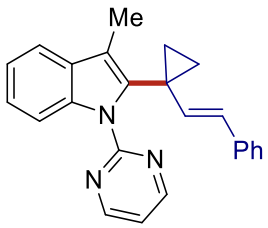
7.45 (d, *J* = 8.4 Hz, 1H), 7.28–7.23 (m, 1H), 7.19 (dd, *J* = 7.7, 2.4 Hz, 1H), 7.11 (dd, 8.4, 2.3 Hz, 1H), 7.02 (t, *J* = 4.8 Hz, 1H), 6.73 (ddd, *J* = 17.3, 10.5, 0.7 Hz, 1H), 6.72 (dd, *J* = 17.5, 10.7, 0.8 Hz, 1H), 6.71 (s, 1H), 6.56 (d, *J* = 0.8 Hz, 1H), 5.27 (dt, *J* = 17.5, 0.8 Hz, 1H), 5.21 (dt, *J* = 10.7, 0.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* = 158.0 (CH), 157.2 (C_q), 139.1 (CH), 137.9 (C_q), 137.3 (C_q), 136.9 (C_q), 133.8 (C_q), 132.4 (CH), 129.5 (q, *J* = 33.5 Hz, C_q), 129.3 (CH), 129.0 (C_q), 127.9 (q, *J* = 3.9 Hz, CH), 127.5 (C_q), 124.6 (q, *J* = 3.6 Hz, CH), 123.9 (CH), 123.5 (q, *J* = 272.5 Hz, C_q), 122.2 (CH), 120.8 (CH), 118.1 (CH_2), 117.2 (CH), 113.9 (CH), 110.1 (CH). ^{19}F NMR (376 MHz, $CDCl_3$) *δ* = -63.32. **IR** (ATR): 3048, 2922, 1701, 1566, 1423, 1324, 1263, 1166, 1123, 1079, 1025, 912, 811, 741 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 492 (100) (^{79}Br) $[M+Na]^+$, 472 (30) (^{79}Br) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{16}N_3{}^{79}BrF_3$ $[M+H]^+$ 470.0474, found 470.0459.



(*E*)-1-(Pyrimidin–2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole (**186aa**)

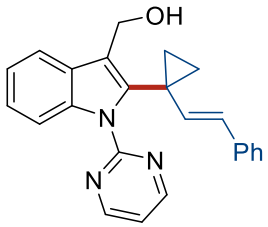
The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (39.0 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186aa** (64.1 mg, 95%) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$): *δ* = 8.77 (d, *J* = 4.7 Hz, 2H), 8.17 (d, *J* = 8.1 Hz, 1H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.37–7.30 (m, 1H), 7.30–7.26 (m, 1H), 7.25–7.14 (m, 5H), 7.09 (t, *J* = 4.8 Hz, 1H), 6.69 (s, 1H), 6.09 (d, *J* = 16.0 Hz, 1H), 6.00 (d, *J* = 16.0 Hz, 1H), 1.50 (dd, *J* = 4.6, 4.6 Hz, 2H), 1.25 (dd, *J* = 4.6, 4.6 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* = 158.3 (C_q), 158.1 (CH), 142.7 (C_q), 137.8 (C_q), 137.2 (C_q), 136.8 (CH), 128.8 (C_q), 128.4 (CH), 127.1 (CH), 126.6 (CH), 125.7 (CH), 123.1 (CH), 121.7 (CH), 120.3 (CH), 117.6 (CH), 113.4 (CH), 107.4 (CH), 22.7 (C_q), 18.4 (CH_2). **IR** (ATR): 3026, 1643, 1562, 1452, 1417, 1351, 1298, 1151, 955, 740 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 360 (100)

[M+Na]$^+$, 338 (85) [M+H]$^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{20}N_3$ [M+H]$^+$ 338.1652, found 338.1652.



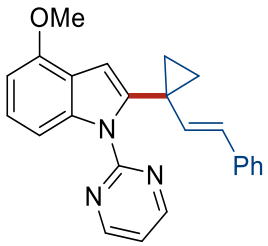
(*E*)-3-Methyl-1-(pyrimidin-2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole (186ba)

The general procedure **G** was followed using 3-methyl-1-(pyrimidin-2-yl)-1*H*-indole **71b** (41.6 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186ba** (51.3 mg, 73%) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.80 (d, *J* = 4.8 Hz, 2H), 8.23 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 1.7 Hz, 1H), 7.40–7.30 (m, 6H), 7.24–7.19 (m, 1H), 7.13 (td, *J* = 4.8, 1.6 Hz, 1H), 6.37 (d, *J* = 15.8 Hz, 1H), 6.30 (d, *J* = 15.8 Hz, 1H), 2.44 (s, 3H), 1.18 (s, 2H), 1.04 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.1 (C_q), 158.0 (CH), 138.2 (C_q), 137.2 (C_q), 136.5 (CH), 135.8 (C_q), 130.1 (C_q), 128.5 (CH), 127.2 (CH), 126.5 (CH), 125.9 (CH), 123.3 (CH), 121.5 (CH), 118.3 (CH), 117.0 (CH), 116.4 (C_q), 113.3 (CH), 21.3 (C_q), 18.1 (CH_2), 9.5 (CH_3). **IR** (ATR): 3029, 2916, 1645, 1563, 1453, 1420, 1347, 1298, 1178, 956, 736 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 374 (80) [M+Na]$^+$, 352 (100) [M+H]$^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{22}N_3$ [M+H]$^+$, 352.1808, found 352.1808.



(*E*)-(1-(Pyrimidin–2-yl)-2-(1-styrylcyclopropyl)-1*H*-indol-3-yl)methanol (**186qa**)

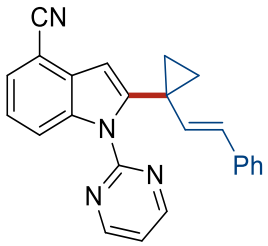
The general procedure **G** was followed using (1-(pyrimidin-2-yl)-1H-indol-3-yl)methanol **71q** (44.8 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 4.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 5:1) yielded **186qa** (33.1 mg, 45%) as a colorless solid. **M.p.** = 145–146 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.81 (d, *J* = 4.6 Hz, 2H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 7.4 Hz, 1H), 7.36–7.26 (m, 6H), 7.21–7.17 (m, 2H), 6.31 (s, 2H), 5.06 (d, *J* = 5.0 Hz, 2H), 1.56 (t, *J* = 5.0 Hz, 1H), 1.23–1.15 (m, 2H), 1.15–1.06 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.3 (CH), 158.0 (C_q), 139.4 (C_q), 137.8 (C_q), 137.0 (CH), 136.1 (C_q), 128.6 (CH), 128.3 (C_q), 127.7 (CH), 126.8 (CH), 126.0 (CH), 123.8 (CH), 122.0 (CH), 119.2 (C_q), 118.8 (CH), 117.8 (CH), 113.3 (CH), 56.4 (CH_2), 21.0 (C_q), 17.8 (CH_2). **IR** (ATR): 3492, 3023, 2858, 1562, 1455, 1423, 1358, 1298, 1100, 953, 746 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 381 (100) $[M+Na]^+$, 368 (50) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{22}N_3O$ $[M+H]^+$ 368.1755, found 368.1757.



(*E*)-4-Methoxy-1-(pyrimidin-2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole (5da)

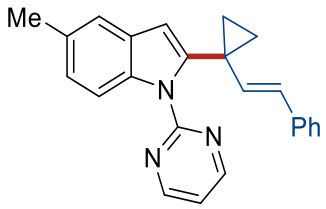
The general procedure **G** was followed using 4-methoxy-1-(pyrimidin-2-yl)-1*H*-indole **71c** (44.8 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186ca** (55.1 mg, 75%) as a colorless solid. **M.p.** = 115–116 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.76 (d, *J* = 4.8 Hz, 2H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.26–7.18 (m, 3H), 7.17–7.12 (m,, 3H), 7.08 (t, *J* = 4.8 Hz, 1H), 6.82 (s, 1H), 6.70 (d, *J* = 7.9 Hz, 1H), 6.08 (d, *J* = 16.0 Hz, 1H), 5.97 (d, *J* = 16.0 Hz, 1H), 4.03 (s, 3H), 1.53–1.48 (m, 2H), 1.25–1.20 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 158.4 (C_q), 158.1 (CH), 152.8 (C_q), 141.2 (C_q), 138.5 (C_q), 137.8 (C_q), 136.8 (CH), 128.3 (CH), 127.1 (CH), 126.5 (CH), 125.7 (CH), 123.9 (CH), 119.1 (C_q), 117.7 (CH), 106.7

(CH), 104.2 (CH), 101.8 (CH), 55.5 (CH_3), 22.6 (C_q), 18.3 (CH_2). **IR** (ATR): 3000, 2201, 1564, 1437, 1419, 1360, 1256, 1075, 812, 769 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 390 (80) $[M+Na]^+$, 368 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{22}N_3O$ $[M+H]^+$ 368.1755, found 368.1757.



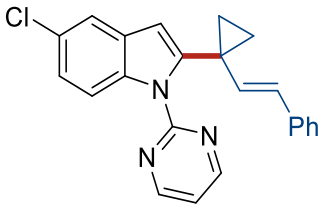
(*E*)-1-(Pyrimidin–2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole-4-carbonitrile (186da)

The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole-4-carbonitrile **71d** (43.8 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 4.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 4:1) yielded **186da** (39.9 mg, 55%) as a white solid. **M.p.** = 153–155 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.80 (d, *J* = 4.8 Hz, 2H), 8.28 (d, *J* = 8.2 Hz, 1H), 7.57 (dd, *J* = 7.4, 1.1 Hz, 1H), 7.31 (td, *J* = 8.1, 7.5, 1.4 Hz, 1H), 7.25–7.15 (m, 3H), 7.15–7.09 (m, 3H), 6.88 (s, 1H), 6.01 (d, *J* = 16.0 Hz, 1H), 5.95 (d, *J* = 16.0 Hz, 1H), 1.53–1.49 (m, 2H), 1.29–1.25 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.4 (CH), 157.7 (C_q), 145.9 (C_q), 137.4 (C_q), 137.0 (C_q), 135.6 (CH), 130.5 (C_q), 128.4 (CH), 127.7 (CH), 126.8 (CH), 126.5 (CH), 125.8 (CH), 122.8 (CH), 118.7 (C_q), 118.5 (CH), 118.0 (CH), 105.4 (CH), 102.7 (C_q), 22.6 (C_q), 18.4 (CH_2). **IR** (ATR): 3037, 2213, 1646, 1561, 1411, 1361, 1302, 1202, 928, 814, 775, 742 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 386 (100) $[M+Na]^+$, 364 (55) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{19}N_4$ $[M+H]^+$ 363.1604, found 363.1603.



(*E*)-5-Methyl-1-(pyrimidin-2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole (186ea)

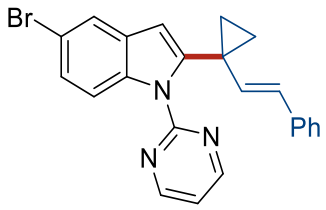
The general procedure **G** was followed using 4-methoxy-1-(pyrimidin-2-yl)-1*H*-indole **71e** (41.6 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186ea** (56.9 mg, 81%) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.72 (d, *J* = 4.8 Hz, 2H), 8.07 (d, *J* = 8.5 Hz, 1H), 7.41 (s, 2H), 7.22–7.09 (m, 6H), 7.03 (t, *J* = 4.8 Hz, 1H), 6.59 (s, 1H), 6.04 (d, *J* = 16.0 Hz, 1H), 5.98 (d, *J* = 16.0 Hz, 1H), 2.49 (s, 3H), 1.48–1.36 (m, 2H), 1.23–1.19 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.3 (C_q), 158.0, 142.7 (C_q), 137.9 (C_q), 137.0 (CH), 135.5 (C_q), 131.1 (C_q), 129.1 (C_q), 128.4 (CH), 127.0 (CH), 126.5 (CH), 125.7 (CH), 124.6 (CH), 120.1 (CH), 117.3 (CH), 113.4 (CH), 107.3 (CH), 22.9 (C_q), 21.5 (CH_3), 18.4 (CH_2). **IR** (ATR): 3023, 1644, 1564, 1418, 1336, 1215, 1151, 952, 907, 802, 731, 688 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 374 (95) $[M+Na]^+$, 352 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{22}N_3$ $[M+H]^+$ 352.1814, found 352.1808.



(*E*)-5-Chloro-1-(pyrimidin-2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole (186ga)

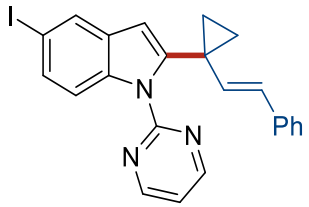
The general procedure **G** was followed using 5-chloro-1-(pyrimidin-2-yl)-1*H*-indole **71g** (45.7 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186ga** (54.3 mg, 73%) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.76 (d, *J* = 4.8 Hz, 2H), 8.07 (d,

J = 8.9 Hz, 1H), 7.58 (d, *J* = 2.1 Hz, 1H), 7.25–7.18 (m, 3H), 7.14–7.10 (m, 4H), 6.60 (s, 1H), 6.02 (d, *J* = 16.0 Hz, 1H), 5.96 (d, *J* = 16.0 Hz, 1H), 1.47–1.44 (m, 2H), 1.24–1.21 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.2 (CH), 158.0 (C_q), 144.1 (C_q), 137.7 (C_q), 136.4 (CH), 135.6 (C_q), 130.0 (C_q), 130.0 (C_q), 128.4 (CH), 127.2 (CH), 126.7 (CH), 125.8 (CH), 123.2 (CH), 119.7 (CH), 117.9 (CH), 114.7 (CH), 106.8 (CH), 22.8 (C_q), 18.4 (CH_2). **IR** (ATR): 3025, 1644, 1564, 1416, 1335, 1186, 1067, 950, 866, 800, 742, 687 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 394 (50) (^{35}Cl) $[M+Na]^+$, 372 (100) (^{35}Cl) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{19}N_3{}^{35}Cl$ $[M+H]^+$ 372.1268, found 372.1262



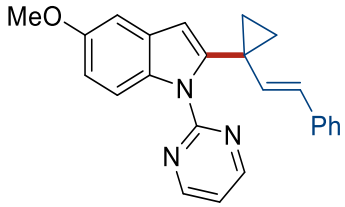
(*E*)-5-Bromo-1-(pyrimidin-2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole (186ha)

The general procedure **G** was followed using 5-bromo-1-(pyrimidin-2-yl)-1*H*-indole **71h** (54.6 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186ha** (69.1 mg, 83%) as a yellow solid. **M.p.** = 153–155 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.76 (d, *J* = 4.8 Hz, 2H), 8.03 (d, *J* = 8.8 Hz, 1H), 7.75 (d, *J* = 2.0 Hz, 1H), 7.38 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.25–7.18 (m, 2H), 7.16–7.09 (m, 4H), 6.60 (s, 1H), 6.03(d, *J* = 16.2 Hz, 1H), 5.97 (d, *J* = 16.2 Hz, 1H), 1.49–1.44 (m, 2H), 1.26–1.21 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.2 (C_q), 158.0 (CH), 144.0 (C_q), 137.6 (C_q), 136.4 (CH), 135.9 (C_q), 130.5 (C_q), 128.4 (CH), 127.2 (CH), 126.7 (CH), 125.8 (CH), 125.7 (CH), 122.8 (CH), 117.9 (CH), 115.1 (CH), 114.9 (C_q), 106.7 (CH), 22.7 (C_q), 18.4 (CH_2). **IR** (ATR): 3022, 1644, 1563, 1415, 1334, 1185, 949, 907, 866, 799, 740, 688 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 438 (60) (^{79}Br) $[M+Na]^+$, 416 (100) (^{79}Br) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{19}{}^{79}BrN_3$ $[M+H]^+$ 416.0762, found 416.0757.



(*E*)-5-Iodo-1-(pyrimidin-2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole (186ra)

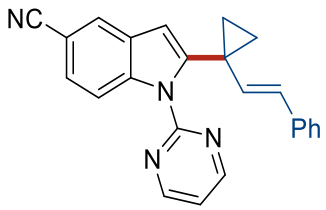
The general procedure **G** was followed using 5-iodo-1-(pyrimidin-2-yl)-1H-indole **71r** (64.0 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 4.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186ra** (50.0 mg, 54%) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.75 (d, *J* = 4.8 Hz, 2H), 7.95 (s, 1H), 7.91 (d, *J* = 8.8 Hz, 1H), 7.54 (d, *J* = 8.8 Hz, 1H), 7.24–7.17 (m, 2H), 7.15–7.08 (m, 4H), 6.57 (s, 1H), 6.00 (d, *J* = 16.2 Hz, 1H), 5.95 (d, *J* = 16.0 Hz, 1H), 1.49–1.42 (m, 2H), 1.24–1.19 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.2 (CH), 143.6 (C_q), 137.6 (C_q), 136.5 (C_q), 136.4 (C_q), 131.4 (CH), 131.3 (C_q), 129.1 (CH), 128.4 (CH), 127.2 (CH), 126.7 (CH), 125.8 (CH), 117.9 (CH), 115.6 (CH), 106.4 (CH), 85.4 (C_q), 22.6 (C_q), 18.4 (CH_2). **IR** (ATR): 3025, 2921, 2849, 1732, 1643, 1563, 1415, 1330, 1183, 1023, 947, 799, 738, 689 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 486 (60) $[M+Na]^+$, 464 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{19}N_3I$ $[M+H]^+$ 464.0624, found 464.0618.



(*E*)-5-Methoxyl-1-(pyrimidin-2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole (186ia)

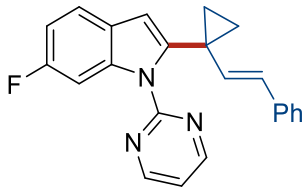
The general procedure **G** was followed using 5-methoxyl-1-(pyrimidin-2-yl)-1*H*-indole **71i** (44.8 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186ia** (61.7

mg, 54%) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.74 (d, *J* = 4.8 Hz, 2H), 8.16 (d, *J* = 9.0 Hz, 1H), 7.25–7.20 (m, 2H), 7.18–7.14 (m, 3H), 7.12 (d, *J* = 2.5 Hz, 1H), 7.05 (t, *J* = 4.8 Hz, 1H), 6.98 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.63 (s, 1H), 6.09 (d, *J* = 16.0 Hz, 1H), 6.03 (d, *J* = 16.0 Hz, 1H), 3.93 (s, 3H), 1.49–1.46 (m, 2H), 1.26–1.23 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.2 (C_q), 158.0 (CH), 155.4 (C_q), 143.2 (C_q), 137.8 (C_q), 137.0 (CH), 132.1 (C_q), 129.5 (C_q), 128.4 (CH), 126.9 (CH), 126.5 (CH), 125.7 (CH), 117.2 (CH), 114.7 (CH), 112.4 (CH), 107.6 (CH), 102.5 (CH), 55.9 (CH_3), 23.0 (C_q), 18.4 (CH_2). 3002, 1614, 1564, 1418, 1341, 1214, 1154, 1030, 951, 801, 737, 688 cm^{-1}. **MS** (ESI) *m/z* (relative intensity) 390 (25) $[M+Na]^+$, 368 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{22}N_3O$ $[M+H]^+$ 368.1757 found 368.1759.



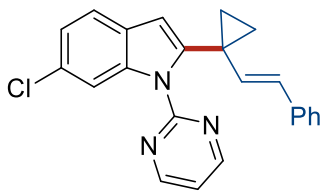
(*E*)-1-(Pyrimidin–2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole–5-carbonitrile (186ja)

The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole–5-carbonitrile **71j** (43.8 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 5:1) yielded **186ja** (60.2 mg, 83%) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.80 (d, *J* = 4.9 Hz, 2H), 8.09 (d, *J* = 8.7 Hz, 1H), 7.95 (s, 1H), 7.51 (dd, *J* = 8.6, 1.5 Hz, 1H), 7.23–7.16 (m, 3H), 7.18–7.07 (m, 3H), 6.69 (s, 1H), 5.99 (d, *J* = 16.0 Hz, 1H), 5.92 (d, *J* = 16.0 Hz, 1H), 1.49–1.46 (m, 2H), 1.26–1.23 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.4 (CH), 157.6 (C_q), 145.3 (C_q), 138.9 (C_q), 137.3 (C_q), 135.6 (CH), 128.5 (C_q), 128.4 (CH), 127.6 (CH), 126.8 (CH), 126.0 (CH), 125.7 (CH), 125.4 (CH), 120.6 (C_q), 118.6 (CH), 114.0 (CH), 106.8 (CH), 104.7 (C_q), 22.4 (C_q), 18.3 (CH_2). **IR** (ATR): 3025, 2221, 1733, 1564, 1463, 1418, 1375, 1309, 1239, 1040, 952, 808, 743, 690 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 385 (100) $[M+Na]^+$, 363 (65) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{19}N_4$ $[M+H]^+$ 363.1604, found 363.1603.



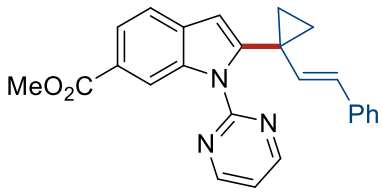
(*E*)-6-Fluoro-1-(pyrimidin-2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole (186ka)

The general procedure **G** was followed using 6-fluoro-1-(pyrimidin-2-yl)-1*H*-indole **71k** (42.4 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186ka** (64.0 mg, 90%) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.76 (d, J = 4.8 Hz, 2H), 7.96 (dd, J = 10.9, 2.4 Hz, 1H), 7.54 (dd, J = 8.6, 5.5 Hz, 1H), 7.26–7.19 (m, 2H), 7.15 –7.13 (m, 3H), 7.03 (td, J = 8.9, 2.3 Hz, 1H), 6.65 (d, J = 0.8 Hz, 1H), 6.07 (d, J = 16.0 Hz, 1H), 6.00 (d, J = 16.1 Hz, 1H), 1.51–1.46 (m, 1H), 2.28–1.22 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 160.6 (d, $^1J_{C–F}$ = 237.4 Hz, C_q), 143.2 (d, $^4J_{C–F}$ = 3.9 Hz, C_q), 137.3 (d, $^3J_{C–F}$ = 12.6 Hz, C_q), 120.8 (d, $^3J_{C–F}$ = 10.0 Hz, CH), 110.1 (d, $^2J_{C–F}$ = 24.2 Hz, CH), 100.8 (d, $^2J_{C–F}$ = 28.3 Hz, CH). 125.1 (d, $^5J_{C–F}$ = 1.4 Hz, C_q) 158.1 (CH), 158.1 (C_q), 137.7 (C_q), 136.7 (CH), 128.4 (CH), 127.1 (CH), 126.6 (CH), 125.7 (CH), 117.7 (CH), 107.3 (CH), 22.8 (C_q), 18.4 (CH_2). ^{19}F NMR (282 MHz, $CDCl_3$) δ = –119.48 (td, J = 10.1, 5.5 Hz). **IR** (ATR): 3025, 1734, 1565, 1417, 1357, 1261, 1192, 1150, 936, 813, 739, 689 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 378 (90) $[M+Na]^+$, 356 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{19}N_3F$ $[M+H]^+$ 356.1563, found 356.1558.



(*E*)-6-Chloro-1-(pyrimidin-2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole (186la)

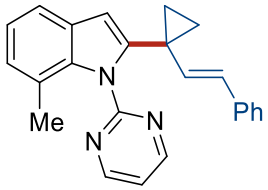
The general procedure **G** was followed using 6-chloro-1-(pyrimidin-2-yl)-1*H*-indole **71l** (45.7 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186la** (58.8 mg, 79%) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.77 (d, *J* = 4.8 Hz, 2H), 8.19 (d, *J* = 1.9 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.25–7.18 (m, 3H), 7.16–7.10 (m, 4H), 6.63 (s, 2H), 6.04 (d, *J* = 16.0 Hz, 1H), 5.96 (d, *J* = 16.0 Hz, 1H), 1.50–1.45 (m, 2H), 1.26–1.21 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.2 (CH), 157.9 (C_q), 143.5 (C_q), 137.6 (C_q), 137.5 (C_q), 136.5 (CH), 129.0 (C_q), 128.4 (CH), 127.3 (C_q), 127.2 (CH), 126.7 (CH), 125.7 (CH), 122.3 (CH), 121.0 (CH), 117.9 (CH), 113.7 (CH), 107.2 (CH), 22.7 (C_q), 18.4 (CH_2). **IR** (ATR): 3025, 2221, 1562, 1417, 1350, 1298, 958, 911, 811, 739, 688 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 394 (30) (^{35}Cl) $[M+Na]^+$, 372 (100) (^{35}Cl) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{19}N_3{}^{35}Cl$ $[M+H]^+$ 372.1262, found 372.1264.



Methyl (*E*)-1-(pyrimidin-2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole-6-carboxylate (186na)

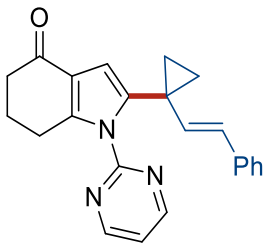
The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole-6-carboxylate **71n** (50.5 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 5:1) yielded **186na** (62.5 mg, 79%) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.80 (d, *J* = 4.8 Hz, 2H), 8.78 (s, 1H), 7.96 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.65 (dd, *J* = 8.3, 0.6 Hz, 1H), 7.24–7.17 (m, 2H), 7.16–7.10 (m, 4H), 6.70 (s, 1H), 6.04 (d, *J* = 16.2 Hz, 1H), 5.95 (d, *J* = 16.2 Hz, 1H), 3.96 (s, 3H), 1.52–1.46 (m, 2H), 1.27–1.22 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 168.2 (C_q), 158.4 (CH), 157.8 (C_q), 146.0 (C_q), 137.5 (C_q), 136.6 (C_q), 135.9 (CH), 132.5 (C_q), 128.4 (CH), 127.4 (CH), 126.7 (CH), 125.7 (CH), 124.7 (C_q), 122.8 (CH), 119.9 (CH), 118.2 (CH), 115.3 (CH), 107.0 (CH), 52.0 (CH_3), 22.6 (C_q), 18.3 (CH_2). **IR** (ATR): 3023, 2949, 1708, 1563, 1418, 1360, 1279, 1221, 1127, 1093, 956, 910, 811, 735, 688 cm^{-1}. **MS** (ESI)

m/z (relative intensity): 418 (100) $[M+Na]^+$, 396 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{25}H_{22}N_3O_3$ $[M+H]^+$ 396.1712, found 396.1707.



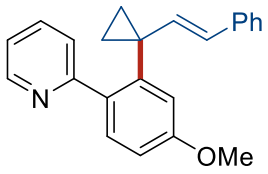
(*E*)-7-Methyl-1-(pyrimidin-2-yl)-2-(1-styrylcyclopropyl)-1*H*-indole (186oa)

The general procedure **G** was followed using 7-methyl-1-(pyrimidin-2-yl)-1*H*-indole **71o** (41.6 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186oa** (52.7 mg, 75%) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.78 (d, *J* = 4.9 Hz, 2H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.28–7.20 (m, 2H), 7.20–7.12 (m, 5H), 7.04 (d, *J* = 7.2 Hz, 1H), 6.63 (s, 1H), 6.01 (d, *J* = 16.0 Hz, 1H), 5.83 (d, *J* = 16.0 Hz, 1H), 2.00 (s, 3H), 1.45–1.39 (m, 2H), 1.08–1.01 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 159.5 (C_q), 157.9 (CH), 143.2 (C_q), 137.4 (C_q), 136.9 (C_q), 134.9 (CH), 128.9 (C_q), 128.3 (CH), 127.7 (CH), 126.6 (CH), 125.8 (CH), 125.4 (CH), 121.7 (C_q), 121.2 (CH), 119.4 (CH), 118.4 (CH), 105.3 (CH), 21.5 (C_q), 19.7 (CH_3), 16.8 (CH_2). **IR** (ATR): 3029, 1644, 1593, 1560, 1415, 1355, 1229, 955, 807, 739, 689 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 374 (95) $[M+Na]^+$, 352 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{22}N_3$ $[M+H]^+$ 352.1808, found 352.1809.



(*E*)-1-(Pyrimidin–2-yl)-2-(1-styrylcyclopropyl)-1,5,6,7-tetrahydro-4*H*-indol-4-one (186pa)

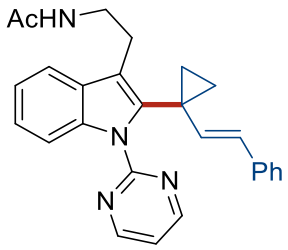
The general procedure **G** was followed using 1-(Pyrimidin–2-yl)-1,5,6,7-tetrahydro-4*H*-indol-4-one **71p** (42.5 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 2:1) yielded **186pa** (54.0 mg, 76%) as a white solid. **M.p.** = 157–159 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.75 (d, *J* = 4.8 Hz, 2H), 7.22–7.17 (m, 3H), 7.14–7.08 (m, 3H), 6.58 (s, 1H), 5.95 (d, *J* = 15.9 Hz, 1H), 5.75 (d, *J* = 15.9 Hz, 1H), 2.92 (t, *J* = 6.2 Hz, 2H), 2.55 (dd, *J* = 7.2, 5.6 Hz, 2H), 2.19–2.13 (m, 2H), 1.32 (dd, *J* = 3.5, 4.5 Hz, 2H), 1.03 (dd, *J* = 3.5, 4.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 194.9 (C_q), 158.4 (CH), 157.3 (C_q), 145.5 (C_q), 137.8 (C_q), 137.5 (C_q), 135.7 (CH), 128.4 (CH), 127.4 (CH), 126.7 (CH), 125.7 (CH), 121.0 (C_q), 119.5 (CH), 106.9 (CH), 38.0 (CH_2), 23.9 (CH_2), 23.8 (CH_2), 21.2 (C_q), 17.5 (CH_2). **IR** (ATR): 2942, 1649, 1566, 1415, 1303, 1226, 974, 940, 805, 750, 692 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 733 (100), 378 (60) $[M+Na]^+$, 356 (60) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{22}N_3O$ $[M+H]^+$ 356.1763, found 356.1768.



(*E*)-2-(4-Methoxy-2-(1-styrylcyclopropyl)phenyl)pyridine (186sa)

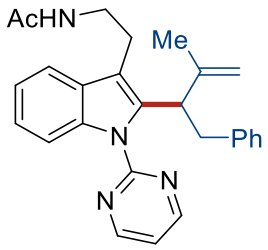
The general procedure **G** was followed using 2-(4-methoxylphenyl)pyridine **71s** (36.8 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 5.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 10:1) yielded **186sa** (26.8 mg, 41%) as a colorless solid. **M.p.** = 103–106 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.71 (dd, *J* = 5.0, 1.9 Hz, 1H), 7.64 (td, *J* = 7.7, 1.9 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 7.9 Hz, 1H), 7.29–7.17 (m, 6H), 7.14 (dd, *J* = 7.8, 1.0 Hz, 1H), 6.96 (dd, *J* = 8.3, 1.0 Hz, 1H), 5.95 (d, *J* = 15.9 Hz, 1H), 5.86 (d, *J* = 15.9 Hz, 1H), 3.77 (s, 3H), 1.02–0.97 (m, 2H), 0.76–0.70 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 157.3 (C_q), 156.8 (C_q), 148.7 (CH), 142.0 (C_q), 139.2 (CH), 137.7 (C_q), 135.5 (CH), 131.8 (C_q), 129.1 (CH), 128.4 (CH), 127.5 (CH), 126.6 (CH), 125.7 (CH), 125.6 (CH), 124.4 (CH), 121.7 (CH), 109.8 (CH), 55.9 (CH_3), 27.7 (C_q), 16.3

(CH_2). **IR** (ATR): 3004, 2937, 2837, 1640, 1574, 1459, 1426, 1352, 1254, 1056, 961, 784, 736, 694 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 350 (30) $[M+Na]^+$, 328 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{22}NO$ $[M+H]^+$ 328.1701, found 328.1696.



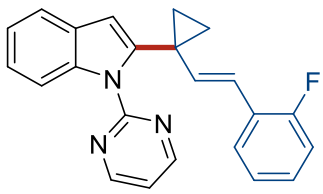
(*E*)-*N*-{2-[1-(pyrimidin-2-yl)-2-(1-styrylcyclopropyl)-1*H*-indol-3-yl]ethyl}acetamide (186ta)

The general procedure **G** was followed using *N*-(2-(1-(pyrimidin-2-yl)-1*H*-indol-3-yl)ethyl)acetamide **71t** (55.9 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 5.0 h. Isolation by column chromatography (CH_2Cl_2/EtOAc 20:1) yielded **186ta** (15.2 mg, 18%) as a yellow oil and **186ta'** (28.9 mg, 34%) as a yellow solid. **186ta**: **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.82 (d, *J* = 4.8 Hz, 2H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 6.9 Hz, 1H), 7.35–7.25 (m, 6H), 7.19 (t, *J* = 4.9 Hz, 2H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.33 (d, *J* = 15.9 Hz, 1H), 5.62 (t, *J* = 6.6 Hz, 1H), 3.68 (dt, *J* = 6.6, 6.9 Hz, 2H), 3.15 (t, *J* = 6.9 Hz, 2H), 1.74 (s, 3H), 1.22–1.09 (m, 2H), 1.04–1.09 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 170.3 (C_q), 158.3 (CH), 158.0 (C_q), 138.4 (C_q), 137.7 (C_q), 137.0 (CH), 136.1 (C_q), 129.1 (C_q), 128.7 (CH), 127.7 (CH), 127.0 (CH), 126.0 (CH), 123.6 (CH), 121.8 (CH), 118.9 (CH), 117.7 (CH), 117.0 (C_q), 113.2 (CH), 39.5 (CH_2), 25.1 (CH_2), 23.3 (CH_3), 21.0 (C_q), 18.0 (CH_2). **IR** (ATR): 3293, 3051, 2923, 1648, 1562, 1455, 1424, 1356, 1296, 1204, 963, 744, 696 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 445 (50) $[M+Na]^+$, 423 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{27}H_{27}N_4O$ $[M+H]^+$ 423.2185, found 423.2179.



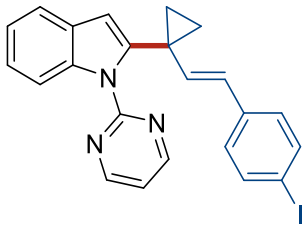
_N_-{2-[2-(3-Methyl-1-phenylbut-3-en–2-yl)-1-(pyrimidin-2-yl)-1_H_-indol-3-yl]ethyl} acetamide (186ta')

The general procedure **G** was followed using *N*-(2-(1-(pyrimidin-2-yl)-1*H*-indol-3-yl)ethyl)acetamide **71t** (55.9 mg, 0.20 mmol) and (2-cyclopropylideneethyl)benzene **185a** (46.1 mg, 0.32 mmol) for 5.0 h. Isolation by column chromatography (CH_2Cl_2/EtOAc 20:1) yielded **186ta** (15.2 mg, 18%) as a yellow oil and **186ta'** (28.9 mg, 34%) as a yellow solid. **186ta'**: **M.p.** = 74–75 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.77 (d, J = 4.8 Hz, 2H), 7.79–7.73 (m, 1H), 7.61 (dd, J = 6.3, 2.8 Hz, 1H), 7.24–7.17 (m, 3H), 7.12–7.05 (m, 3H), 7.01–6.96 (m, 2H), 5.46 (brs, 1H), 4.88 (d, J = 8.5 Hz, 2H), 4.57 (t, J = 7.7 Hz, 1H), 3.53–3.27 (m, 4H), 3.03–2.84 (m, 2H), 1.93 (s, 3H), 1.70 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 169.9 (C_q), 158.1 (CH), 158.0 (C_q), 145.8 (C_q), 140.5 (C_q), 137.0 (C_q), 136.5 (C_q), 129.4 (C_q), 128.7 (CH), 128.0 (CH), 125.9 (CH), 123.0 (CH), 121.3 (CH), 118.4 (CH), 117.8 (CH), 114.9 (C_q), 112.5 (CH), 110.7 (CH_2), 44.6 (CH), 39.5 (CH_2), 38.7 (CH_2), 24.4 (CH_2), 23.4 (CH_3), 23.1 (CH_3). **IR** (ATR): 3294, 3055, 2927, 1647, 1561, 1454, 1420, 1365, 1263, 1020, 803, 741, 698 cm−1**. MS** (ESI) *m/z* (relative intensity): 447 (100) $[M+Na]^+$, 425 (65) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{27}H_{29}N_4O$ $[M+H]^+$425.2336, found 425.2340.



(_E_)-2-[1-(2-Fluorostyryl)cyclopropyl]-1-(pyrimidin-2-yl)-1_H_-indole (**186ab**)

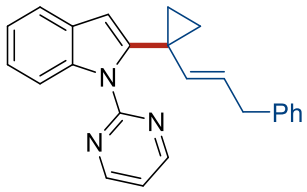
The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole (**71a**) (41.6 mg, 0.20 mmol) and 1-(2-cyclopropylideneethyl)-2-fluorobenzene **185b** (51.9 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186ab** (57.6 mg, 81%) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.77 (d, *J* = 4.8 Hz, 2H), 8.15 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.62 (d, *J* = 7.4 Hz, 1H), 7.33–7.15 (m, 3H), 7.13–7.05 (m, 2H), 7.01–6.89 (m, 2H), 6.67 (s, 1H), 6.16 (s, 2H), 1.49–1.43 (m, 2H), 1.27–1.22 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 159.84 (d, $^1J_{C-F}$ = 249 Hz, C_q), 158.3 (C_q), 158.1 (CH), 142.6 (C_q), 139.7 (d, $^4J_{C-F}$ = 5.5 Hz, CH), 137.2 (C_q), 128.1 (C_q), 127.7 (d, $^4J_{C-F}$ = 8.0 Hz, CH), 127.4 (d, $^4J_{C-F}$ = 4.2 Hz, CH), 125.6 (d, $^3J_{C-F}$ = 12 Hz, C_q), 123.9 (d, $^4J_{C-F}$ = 3.5 Hz, CH), 123.2 (CH), 121.8 (CH), 120.3 (CH), 119.8 (d, $^4J_{C-F}$ = 2.8 Hz), 117.6 (CH), 115.6 (d, $^2J_{C-F}$ = 22 Hz, CH), 113.5 (CH), 107.6 (CH), 23.1 (C_q), 18.5 (CH_2). **^{19}F NMR** (377 MHz, $CDCl_3$) δ = (-117.8) – (-117.9) (m). **IR** (ATR): 3044, 1644, 1563, 1418, 1352, 1222, 1192, 958, 803, 743, 676, 629 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 378 (90) $[M+Na]^+$, 356 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{19}N_3F$ $[M+H]^+$ 356.1563, found 356.1559.



(*E*)-2-[1-(4-Iodostyryl)cyclopropyl]-1-(pyrimidin-2-yl)-1*H*-indole (186ac)

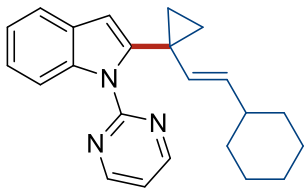
The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (41.6 mg, 0.20 mmol) and 1-(2-cyclopropylideneethyl)-4-iodobenzene **185c** (84.4 mg, 0.32 mmol) for 4.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded a mixture of **186ac** and **186aa** (51.8 mg, 45% yield for **186ac**, 15% yield for **186aa**) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.75 (d, *J* = 4.7 Hz, 2H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.62 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.24 (td, *J* = 7.5, 1.1 Hz, 1H), 7.10 (t, *J* = 4.8 Hz, 1H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.66 (s, 0.25H, **186aa**), 6.65 (s, 0.75H, **186ac**), 5.95 (s, 2H), 1.49–1.43 (m, 2H), 1.27–1.22 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.3 (C_q),

158.1 (CH), 142.3 (C_q), 137.9 (CH), 137.41 (CH), 128.8 (C_q), 128.4 (C_q), 127.6 (CH), 126.1 (C_q), 125.8 (CH), 123.2 (CH), 121.8 (CH), 120.4 (CH), 117.6 (CH), 113.5 (CH), 107.6, 91.4 (C_q), 22.8 (C_q), 18.5 (CH_2). **IR** (ATR): 3044, 2924, 1710, 1564, 1453, 1424, 1354, 1301, 1218, 1004, 959, 804, 745, 697 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 486 (45) $[M+Na]^+$, 464 (60) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{19}N_3I$ $[M+H]^+$ 464.0617, found 464.0618.



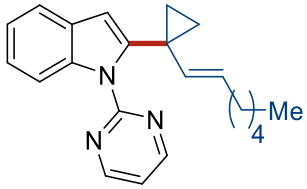
(*E*)-2-[1-(3-phenylprop-1-en-1-yl)cyclopropyl]-1-(pyrimidin-2-yl)-1*H*-indole (186ad)

The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (41.6 mg, 0.20 mmol) and (3-cyclopropylidenepropyl)benzene **185d** (50.6 mg, 0.32 mmol) for 3.5 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186ad** (52.0 mg, 74%) as a colorless solid. **M.p.** = 81–82 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.69 (d, *J* = 4.8 Hz, 2H), 8.04 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.57 (d, *J* = 6.6 Hz, 1H), 7.26–7.13 (m, 5H), 7.05 (t, *J* = 4.8 Hz, 1H), 6.91 (d, *J* = 6.4 Hz, 2H), 6.58 (s, 1H), 5.31 (d, *J* = 15.5 Hz, 1H), 5.22 (dt, *J* = 15.5, 5.9 Hz, 1H), 3.11 (d, *J* = 5.9 Hz, 2H), 1.39–1.35 (m, 2H), 1.10–1.06 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.3 (C_q), 157.9 (CH), 143.2 (C_q), 140.9 (C_q), 137.3 (C_q), 137.2 (CH), 128.7 (C_q), 128.5 (CH), 128.3 (CH), 126.5 (CH), 125.8 (CH), 123.0 (CH), 121.6 (CH), 120.2 (CH), 117.5 (CH), 113.2 (CH), 106.8 (CH), 38.8 (C_q), 22.0 (CH_2), 17.7 (CH_2). **IR** (ATR): 3026, 1728, 1562, 1418, 1352, 1302, 1198, 1024, 964, 802, 740, 693, 630 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 374 (100) $[M+Na]^+$, 352 (75) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{22}N_3$ $[M+H]^+$ 352.1814, found 352.1817.



(*E*)-2-(1-(2-Cyclohexylvinyl)cyclopropyl)-1-(pyrimidin-2-yl)-1*H*-indole (186ae)

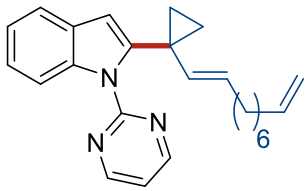
The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (41.6 mg, 0.20 mmol) and (2-cyclopropylideneethyl)cyclohexane **185e** (48.1 mg, 0.32 mmol) for 3.0 h. Isolation by column chromatography (*n*-hexane/EtOAc 15:1) yielded **186ae** (52.9 mg, 77%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.80 (d, *J* = 4.8 Hz, 2H), 8.04 (d, *J* = 8.1 Hz, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.27 (ddd, *J* = 8.4, 7.1, 1.5 Hz, 1H), 7.23–7.19 (m, 1H), 7.16 (t, *J* = 4.8 Hz, 1H), 6.56 (s, 1H), 5.07 (d, *J* = 15.6 Hz, 1H), 4.95 (dd, *J* = 15.6, 7.0 Hz, 1H), 1.67–1.54 (m, 4H), 1.44–1.39 (m, 2H), 1.35–1.29 (m, 2H), 1.18–1.00 (m, 5H), 0.73 (ddd, *J* = 12.2, 12.2, 3.3 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.4 (C_q), 158.1 (CH), 143.5 (C_q), 137.4 (C_q), 134.1 (CH), 133.0 (CH), 128.7 (C_q), 122.9 (CH), 121.5 (CH), 120.2 (CH), 117.5 (CH), 112.9 (CH), 106.2 (CH), 40.7 (CH), 33.2 (CH_2), 26.2 (CH_2), 26.1 (CH_2), 21.7 (C_q), 17.7 (CH_2). **IR** (ATR): 2925, 1561, 1421, 1351, 1324, 1206, 815, 747 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 366 (100) $[M+Na]^+$, 344 (40) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{23}H_{26}N_3$ $[M+H]^+$ 344.2127, found 344.2129.



(*E*)-2-(1-(Hept-1-en-1-yl)cyclopropyl)-1-(pyrimidin-2-yl)-1*H*-indole (186af)

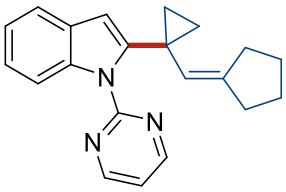
The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (41.6 mg, 0.20 mmol) and heptylidenecyclopropane **185f** (44.2 mg, 0.32 mmol) for 4.0 h. Isolation by column chromatography (*n*-hexane/DCM 8:1) yielded **186ag** (41.8 mg, 63%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.80 (d, *J* = 4.8 Hz, 2H), 8.04 (d, *J* = 8.1 Hz, 1H), 7.58

(d, *J* = 7.4 Hz, 1H), 7.26–7.14 (m, 3H), 6.56 (s, 1H), 5.14 (d, *J* = 15.5 Hz, 1H), 5.02 (dt, *J* = 15.5, 6.5 Hz, 1H), 1.72 (dt, *J* = 6.5, 6.5 Hz, 2H), 1.39–1.34 (m, 2H), 1.23–1.16 (m, 2H), 1.10–0.95 (m, 6H), 0.83 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.3 (C_q), 158.0, 143.4 (C_q), 137.2 (C_q), 135.3, 128.7 (C_q), 128.2 (CH), 122.8 (CH), 121.5 (CH), 120.1 (CH), 117.4 (CH), 112.9 (CH), 106.4 (CH), 32.3 (CH_2), 31.2 (CH_2), 29.3 (CH_2), 22.5 (CH_2), 21.7 (C_q), 17.4 (CH_2), 14.0 (CH_3). **IR** (ATR): 2923, 2853, 1564, 1454, 1424, 1354, 1301, 1200, 967, 802, 743, 679 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 354 (90) $[M+Na]^+$, 332 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{24}H_{26}N_3$ $[M+H]^+$ 332.2127, found 332.2133.



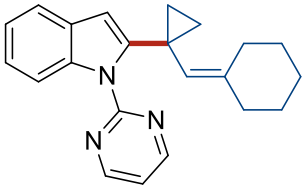
(*E*)-2-[1-(Deca-1,9-dien-1-yl)cyclopropyl]-1-(pyrimidin-2-yl)-1*H*-indole (186ag)

The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole (**71a**) (41.6 mg, 0.20 mmol) and dec–9-en-1-ylidenecyclopropane **185g** (57.1 mg, 0.32 mmol) for 4.0 h. Isolation by column chromatography (*n*-hexane/DCM 8:1) yielded **186ag** (58.7 mg, 79%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.80 (d, *J* = 4.7 Hz, 2H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.59 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.30–7.25 (m, 1H), 7.20 (td, *J* = 7.4, 1.1 Hz, 1H), 7.15 (t, *J* = 4.8 Hz, 1H), 6.57 (s, 1H), 5.83 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.15 (d, *J* = 15.5 Hz, 1H), 5.09–4.94 (m, 3H), 2.03 (dt, *J* = 7.2, 7.2 Hz, 1H), 1.74 (dt, *J* = 7.2, 7.2 Hz, 1H), 1.39–1.29 (m, 4H), 1.20 (tt, *J* = 9.9, 6.6 Hz, 2H), 1.13–0.99 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.4 (C_q), 158.1 (CH), 143.5 (C_q), 139.3 (CH), 137.3 (C_q), 135.4 (CH), 128.8 (C_q), 128.2 (CH), 122.9 (CH), 121.6 (CH), 120.2 (CH), 117.5 (CH), 114.3 (C_q), 113.1 (CH), 106.5 (CH), 33.9 (CH_2), 32.4 (CH_2), 29.7 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 28.9 (CH_2), 21.8 (C_q), 17.6 (CH_2). **IR** (ATR): 2923, 2851, 1564, 1453, 1421, 1353, 1198, 965, 908, 802, 742, 679 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 394 (18) $[M+Na]^+$, 372 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{25}H_{30}N_3$ $[M+H]^+$ 372.2434, found 372.2433.



2-[1-(Cyclopentylidenemethyl)cyclopropyl]-1-(pyrimidin-2-yl)-1*H*-indole (186ah)

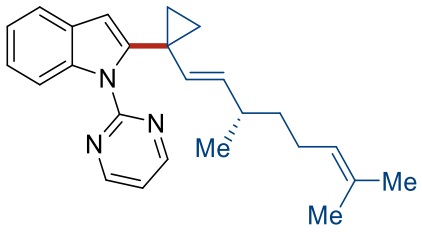
The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (41.6 mg, 0.20 mmol) and (cyclopropylidenemethyl)cyclopentane **185h** (39.1 mg, 0.32 mmol) for 5.0 h. Isolation by column chromatography (*n*-hexane/DCM 8:1) yielded **186ah** (29.0 mg, 46%) as a white solid. **M.p.** = 113–115 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.84 (d, *J* = 4.8 Hz, 2H), 7.99 (d, *J* = 7.2 Hz, 1H), 7.54 (dd, *J* = 7.1, 1.8 Hz, 1H), 7.25–7.14 (m, 3H), 6.49 (s, 1H), 5.18 (d, *J* = 2.5 Hz, 1H), 2.04–1.93 (m, 4H), 1.55–1.45 (m, 2H), 1.45–1.37 (m, 2H), 1.33–1.27 (m, 2H), 1.00–0.93 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.5 (C_q), 158.2 (CH), 146.7 (C_q), 145.4 (C_q), 137.0 (C_q), 128.9 (C_q), 124.1 (CH), 122.6 (CH), 121.5 (CH), 120.0 (CH), 117.5 (CH), 112.9 (CH), 105.0 (CH), 34.4 (CH_2), 28.6 (CH_2), 26.8 (CH_2), 26.0 (CH_2), 19.9 (C_q), 17.9 (CH_2). **IR** (ATR): 2921, 2855, 1563, 1455, 1422, 1349, 1318, 1283, 1195, 1022, 803, 744, 680 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 338 (30) $[M+Na]^+$, 316 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{21}H_{22}N_3$ $[M+H]^+$ 316.1814, found 316.1802.



2-(1-(Cyclohexylidenemethyl)cyclopropyl)-1-(pyrimidin-2-yl)-1*H*-indole (186ai)

The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (41.6 mg, 0.20 mmol) and (cyclopropylidenemethyl)cyclohexane **185i** (43.6 mg, 0.32 mmol) for 5.0 h. Isolation by column chromatography (*n*-hexane/CH_2Cl_2 8:1) yielded **186ai** (34.3 mg, 52%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.85 (d, *J* = 4.8 Hz, 2H), 7.98 (d, *J*

= 7.6 Hz, 1H), 7.59–7.49 (m, 1H), 7.25–7.13 (m, 3H), 6.49 (d, *J* = 0.8 Hz, 1H), 5.08 (s, 1H), 2.23–2.10 (m, 2H), 1.83–1.72 (m, 2H), 1.37–1.25 (m, 8H), 1.02–0.92 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.6 (C_q), 158.2 (CH), 146.5 (C_q), 144.1 (C_q), 137.0 (C_q), 129.0 (C_q), 125.5 (CH), 122.6 (CH), 121.5 (CH), 120.0 (CH), 117.5 (CH), 112.7 (CH), 104.0 (CH), 36.8 (CH_2), 29.4 (CH_2), 28.6 (CH_2), 27.0 (CH_2), 26.6 (C_q), 18.2 (CH_2). **IR** (ATR): 2921, 2849, 1559, 1454, 1420, 1352, 1262, 1196, 1024, 967, 801, 737, 681 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 354 (100) $[M+Na]^+$, 330 (25) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{22}H_{24}N_3$ $[M+H]^+$ 330.1970, found 330.1965.

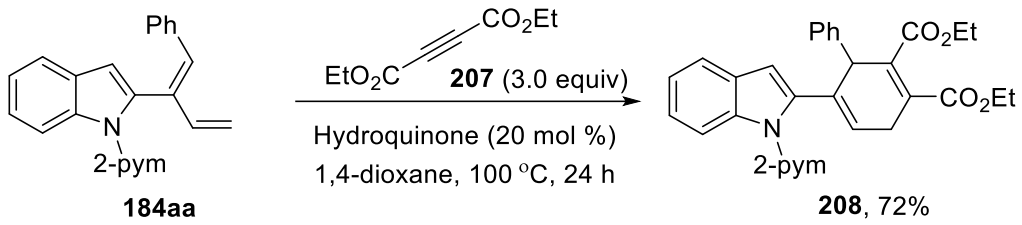


(*S*,*E*)-2-[1-(3,7-Dimethylocta-1,6-dien-1-yl)cyclopropyl]-1-(pyrimidin-2-yl)-1*H*-indole (186aj)

The general procedure **G** was followed using 1-(pyrimidin-2-yl)-1*H*-indole **71a** (41.6 mg, 0.20 mmol) and (*S*)-(3,7-dimethyloct-6-en-1-ylidene)cyclopropane **185j** (57.1 mg, 0.32 mmol) for 7.0 h. Isolation by column chromatography (*n*-hexane/DCM 8:1) yielded **186aj** (45.3 mg, 61%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.78 (d, *J* = 4.8 Hz, 2H), 8.05 (d, *J* = 8.2 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.27–7.13 (m, 3H), 6.56 (s, 1H), 5.08 (d, *J* = 15.5 Hz, 1H), 4.97 (t, *J* = 7.1 Hz, 1H), 4.87 (dd, *J* = 15.5, 8.1 Hz, 1H), 1.87–1.78 (m, 2H), 1.72–1.67 (m, 1H), 1.67 (s, 3H), 1.54 (s, 3H), 1.38–1.34 (m, 2H), 1.08–0.94 (m, 4H), 0.66 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 158.4 (C_q), 158.1 (CH), 143.6 (C_q), 137.4 (C_q), 134.1 (CH), 133.8 (CH), 131.1 (C_q), 128.8 (C_q), 125.0 (CH), 122.9 (CH), 121.6 (CH), 120.2 (CH), 117.5 (CH), 113.1 (CH), 106.5 (CH), 37.1 (CH_2), 36.2 (CH), 25.8 (CH_2), 21.8 (C_q), 21.0 (CH_3), 18.0 (CH_3), 17.8 (CH_3), 17.5 (CH_2). **IR** (ATR): 2915, 2855, 1564, 1453, 1423, 1353, 1199, 965, 803, 743, 679 cm^{-1}. **MS** (ESI) *m/z* (relative intensity):

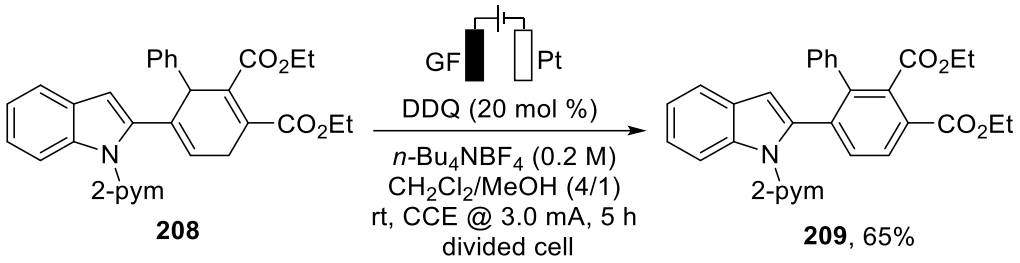
394 (80) $[M+Na]^+$, 372 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{25}H_{30}N_3$ $[M+H]^+$ 372.2440, found 372.2434.

5.6.2 Derivatization of the Diene 184aa



Diethyl-6-[1-(pyrimidin-2-yl)-1*H*-indol–2-yl]-1,4-dihydro-[1,1'-biphenyl]–2,3-dicarboxy-late (208)

To a 25 mL schlenk tube was added **184aa** (135 mg, 0.40 mmol), diethyl acetylenedicarboxylate **207** (204 mg, 1.2 mmol, 3.0 equiv), hydroquinone (8.8 mg, 0.080 mmol, 20 mol %) and 1,4-dioxane 2.0 mL. Then stirred at 100 ºC for 24 h. Removed the solvent under vacuum and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc 5:1) affording **208** (140 mg, 72%) as a yellow solid. **M.p.** = 149–150 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.83 (d, *J* = 4.8 Hz, 2H), 8.29 (dd, J = 8.3, 1.0 Hz, 1H), 7.44 (d, J = 7.7 Hz, 1H), 7.28–7.22 (m, 1H), 7.21–7.12 (m, 5H), 7.06 (dd, J = 7.8, 1.8 Hz, 2H), 6.20 (s, 1H), 6.00 (dd, *J* = 4.7, 2.7 Hz, 1H), 4.61 (t, *J* = 5.9 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.01 (dddd, *J* = 17.9, 10.8, 7.1, 3.7 Hz, 2H), 3.44 (ddd, *J* = 23.4, 6.5, 2.8 Hz, 1H), 3.23 (dt, *J* = 23.5, 5.0 Hz, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.02 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 167.8 (C_q), 167.5 (C_q), 158.4, 158.1 (C_q), 140.2 (C_q), 139.1 (C_q), 138.3 (C_q), 137.1 (C_q), 133.6 (C_q), 129.8 (C_q), 129.2 (C_q), 128.8 (CH), 128.4 (CH), 127.2 (CH), 123.5 (CH), 122.8 (CH), 122.1 (CH), 120.5 (CH), 117.3 (CH), 113.9 (CH), 109.3 (CH), 61.4 (CH_2), 60.9 (CH_2), 48.2 (CH), 28.8 (CH_2), 14.2 (CH_3), 13.9 (CH_3). **IR** (ATR): 2983, 1715, 1567, 1423, 1344, 1248, 1147, 1068, 810, 744, 705 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 516 (100) $[M+Na]^+$, 494 (90) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{30}H_{28}N_3O_4$ $[M+H]^+$ 494.2074, found 494.2072.



Diethyl 6-[1-(pyrimidin-2-yl)-1*H*-indol–2-yl]-[1,1'-biphenyl]–2,3-dicarboxylate (209)

The electrochemical dehydrogenative annulation of 3 was carried out in a divided cell (P4 glass filter as separator) with a GF anode (10 mm × 15 mm × 6 mm) and a Pt cathode (10 mm × 15 mm × 0.25 mm). The anodic cell was charged with **208** (0.1 mmol, 49.3 mg), 2,3-dichloro–5,6-dicyano-1,4-benzoquinone (DDQ) (0.02 mmol, 20 mol %, 5.5 mg), *n*-Bu_4NBF_4 (1.0 mmol, 32.9 mg), CH_2Cl_2 (4.0 mL) and MeOH (1.0 mL). The cathodic cell was charged with *n*BuN_4BF_4 (1.0 mmol, 32.9 mg), CH_2Cl_2 (4.0 mL) and MeOH (1.0 mL). Electrolysis was performed at 25 °C with a constant current of 5.0 mA maintained for 5.0 h. The anodic solution was transferred to a separating funnel charged with H_2O (50 mL) and CH_2Cl_2 (50 mL) and the GF anode was rinsed with CH_2Cl_2 (4 × 10 mL). The organic phase was collected and dried over anhydrous sodium sulfate. The evaporation of the solvent and subsequent column chromatography on silica gel (*n*-hexane/EtOAc 5:1) afforded **209** (32.1 mg, 65%) as a yellow solid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 4.8 Hz, 2H), 8.17 (d, *J* = 8.1 Hz, 1H), 8.06 (d, *J* = 8.1 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.26–7.18 (m, 2H), 7.10 (d, *J* = 7.5 Hz, 1H), 7.06–6.98 (m, 3H), 6.81 (d, *J* = 7.5 Hz, 2H), 6.60 (s, 1H), 4.40 (q, *J* = 7.2 Hz, 2H), 3.98 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 168.7 (C_q), 165.9 (C_q), 157.9 (CH), 157.2 (C_q), 139.5 (C_q), 138.5 (C_q), 137.8 (C_q), 137.2 (C_q), 137.0 (C_q), 136.3 (C_q), 130.7 (CH), 129.2 (CH), 129.1 (CH), 129.0 (C_q), 127.5 (CH), 127.5 (CH), 127.3 (C_q), 124.0 (CH), 122.2 (CH), 120.7 (CH), 117.1 (CH), 114.0 (CH), 111.3 (CH), 61.7 (CH_2), 61.3 (CH_2), 14.3 (CH_3), 13.7 (CH_3). **IR** (ATR): 2982, 2259, 1719, 1565, 1422, 1263, 1183, 1147, 1067, 1019, 911, 803, 733, 700 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 514 (100) $[M+Na]^+$, 492 (35) $[M+H]^+$, 446 (35). **HR-MS** (ESI) *m/z* calcd for $C_{30}H_{26}N_3O_4$ $[M+H]^+$ 492.1918, found 492.1912.

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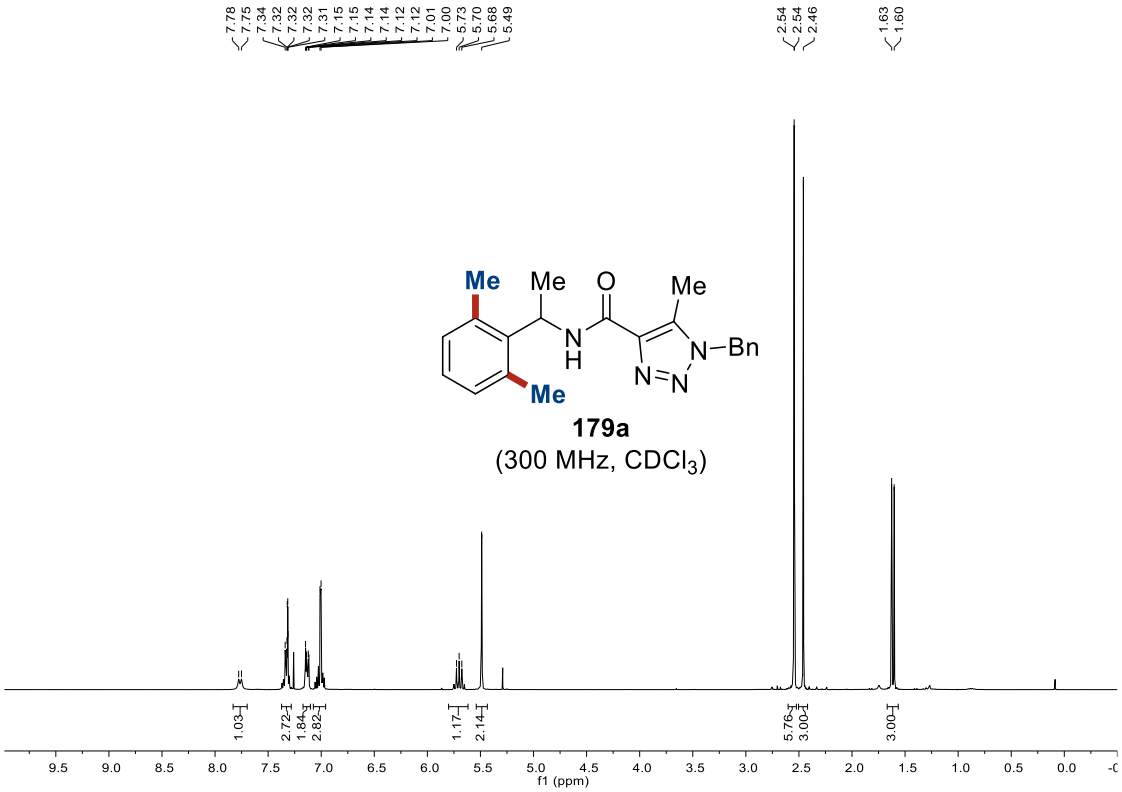
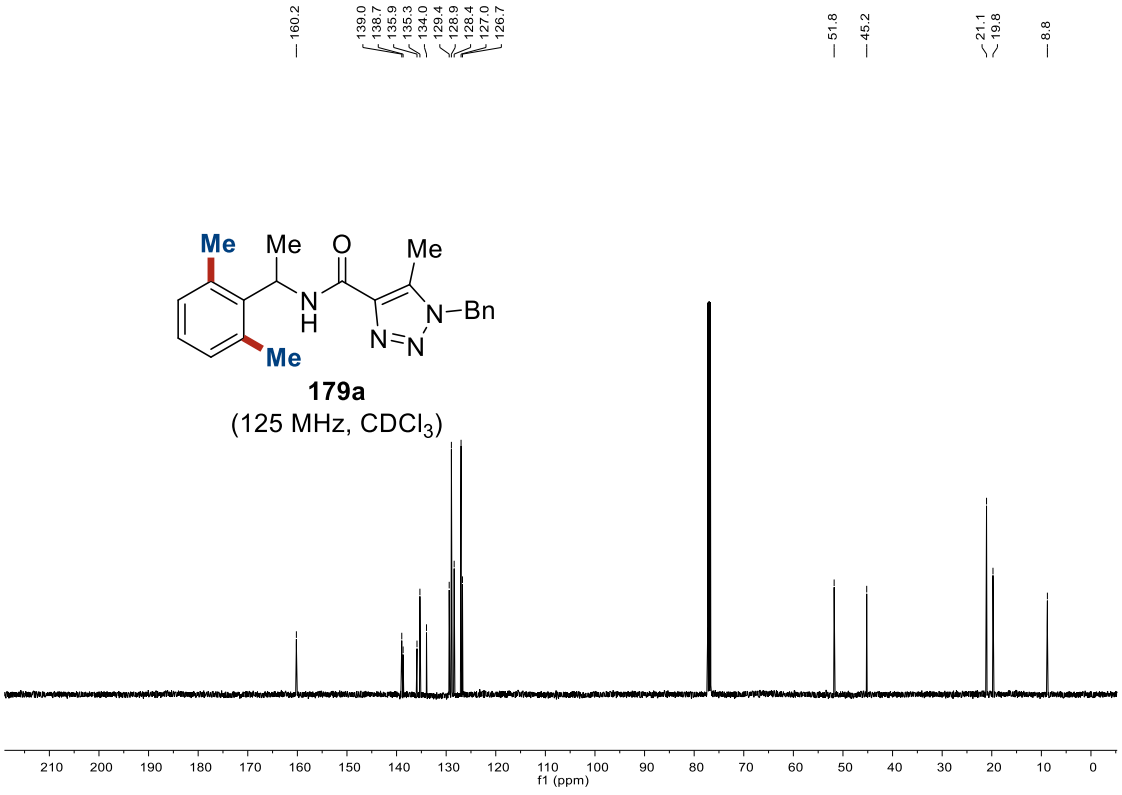
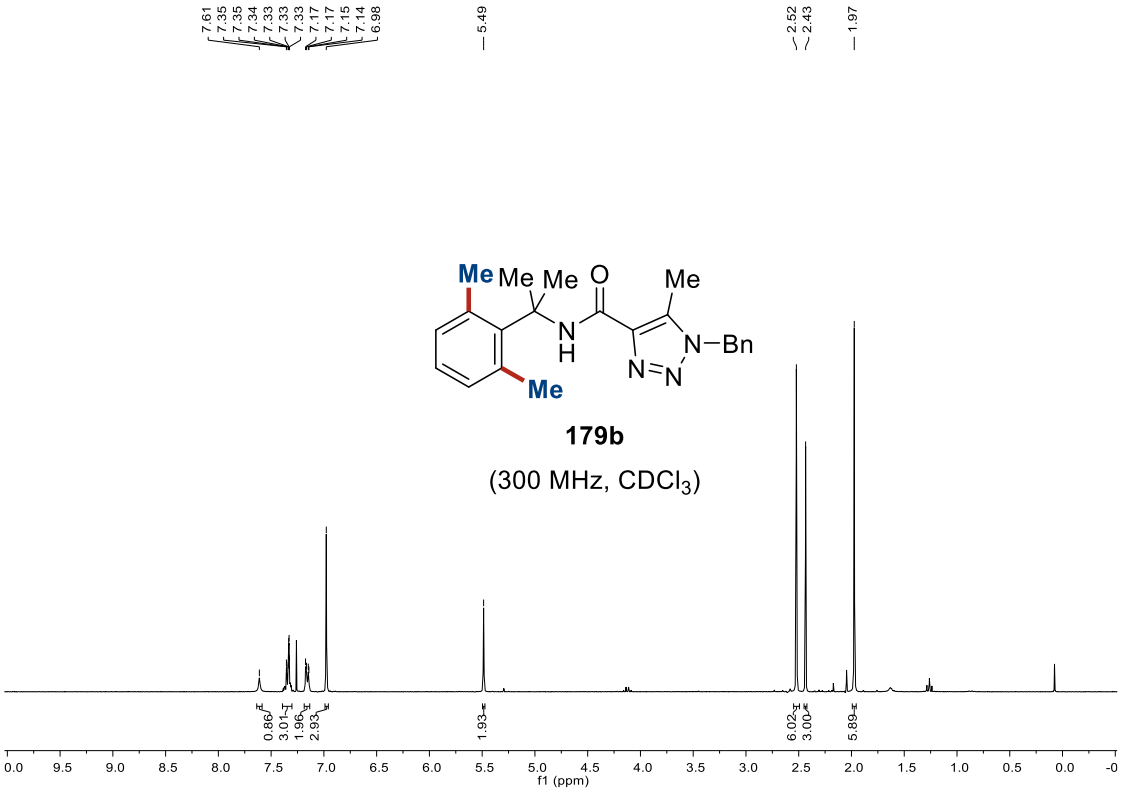
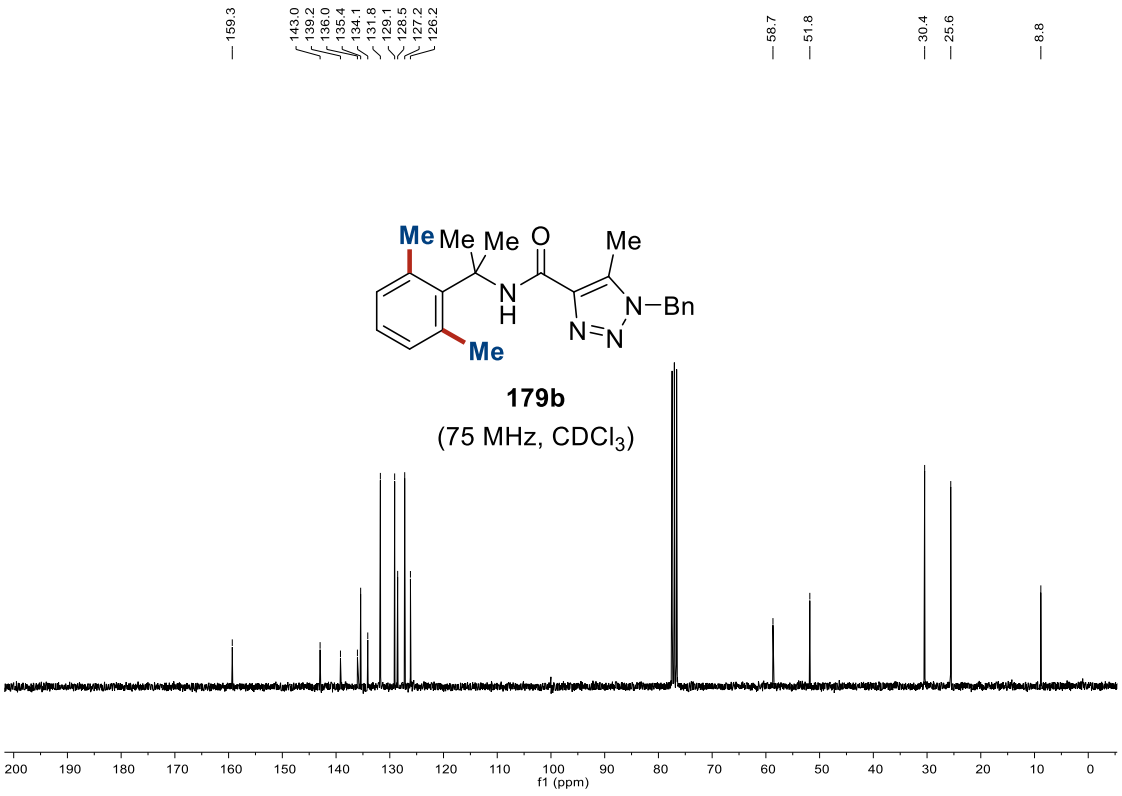
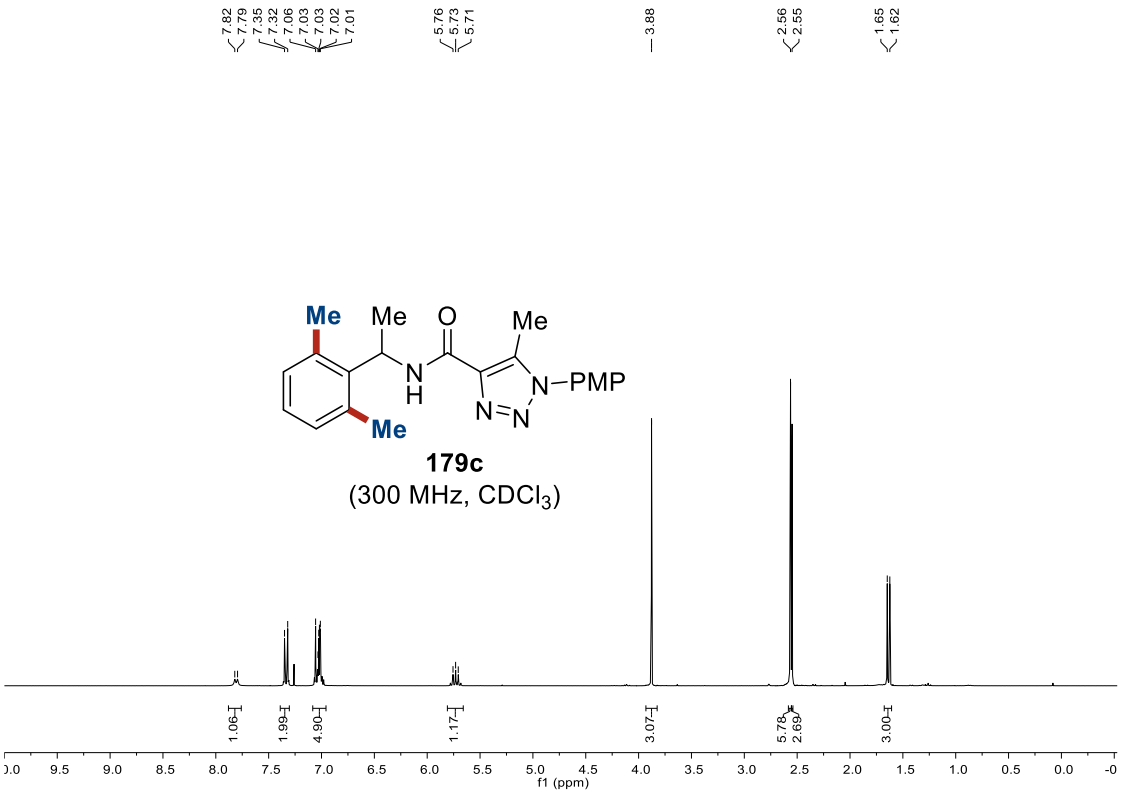
7 NMR Spectra

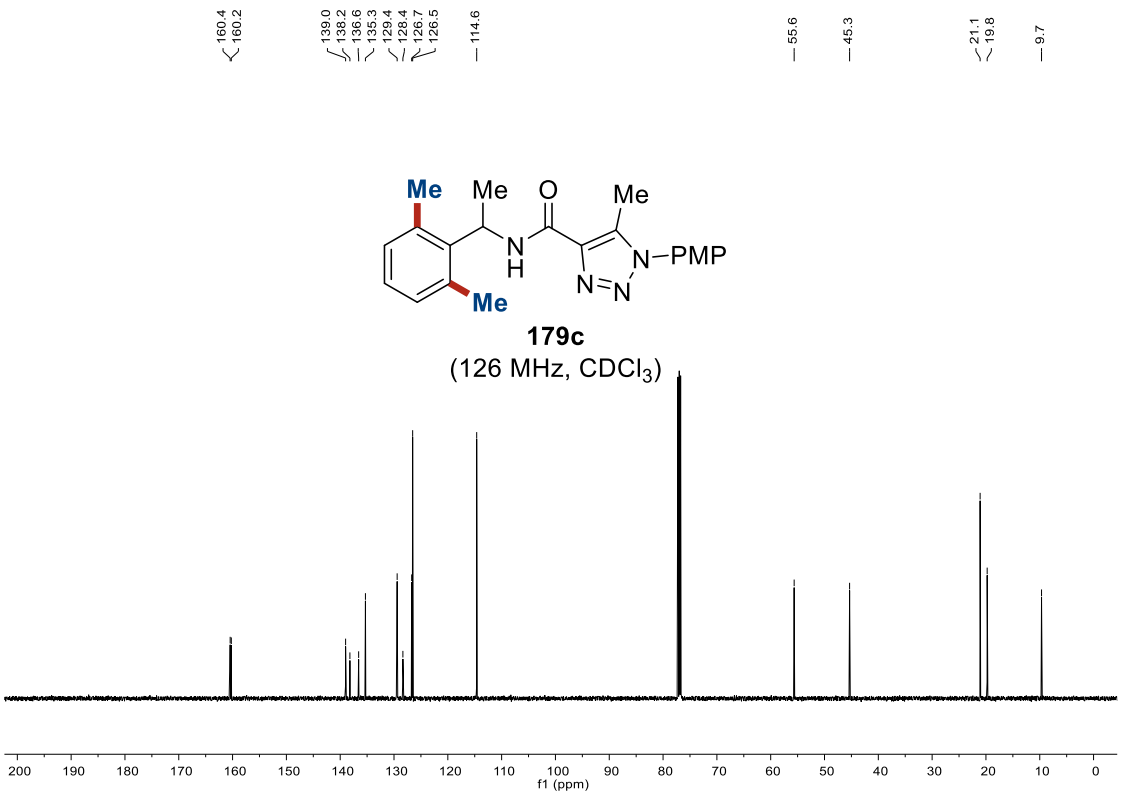


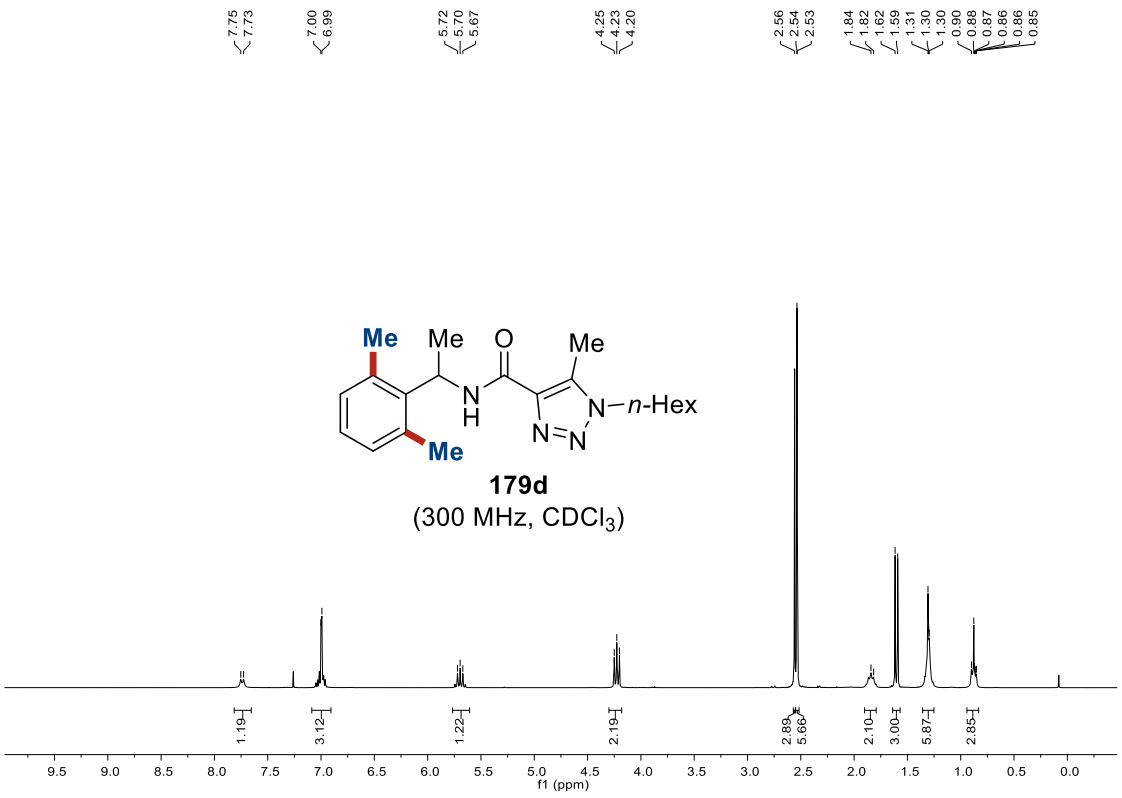


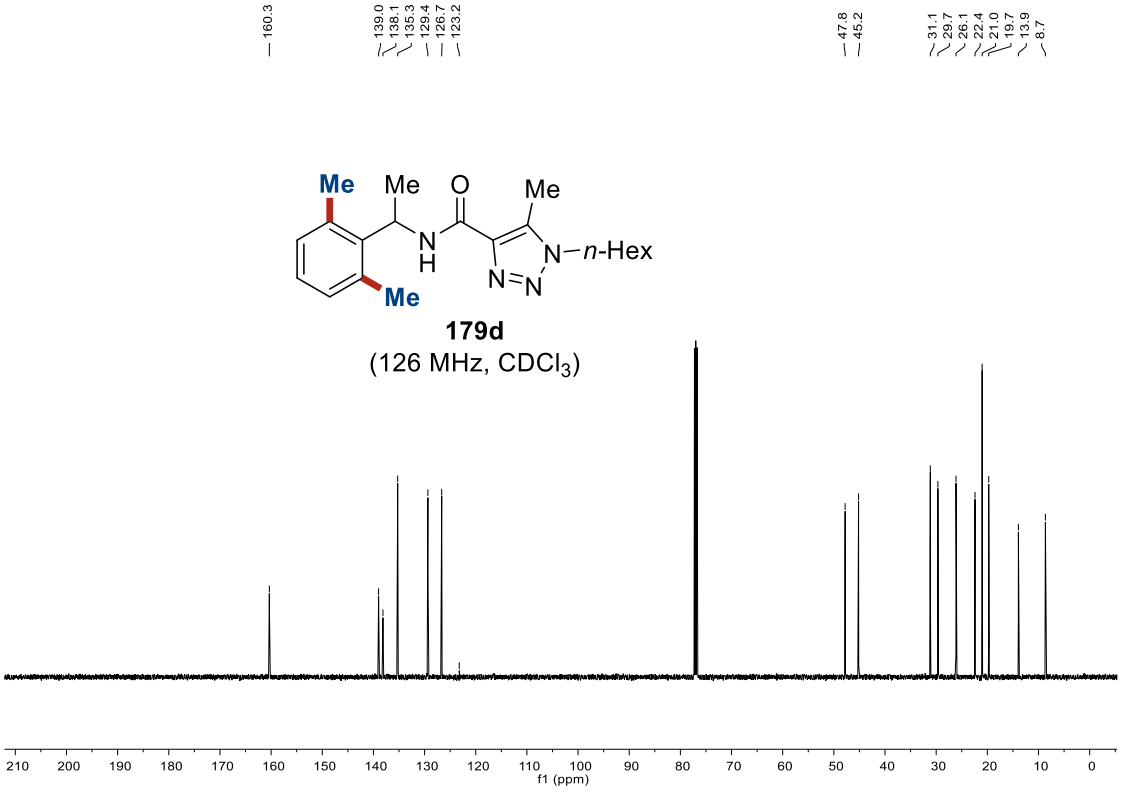

7.61
7.35
7.35
7.34
7.33
7.33
7.33
7.17
7.17
7.15
7.14
6.98
5.49
2.52
2.43
1.97
Me
Me
Me
O
Me
N
H
N–Bn
N=N
Me
179b
(300 MHz, CDCl3)
0.86
3.01
1.96
2.93
1.93
6.02
3.00
5.89
f1 (ppm)

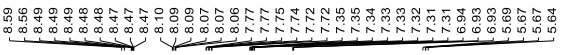

159.3
143.0
139.2
136.0
135.4
134.1
131.8
129.1
128.5
127.2
126.2
58.7
51.8
30.4
25.6
8.8
Me
Me
Me
O
Me
N
H
N–Bn
N=N
Me
179b
(75 MHz, CDCl3)
f1 (ppm)

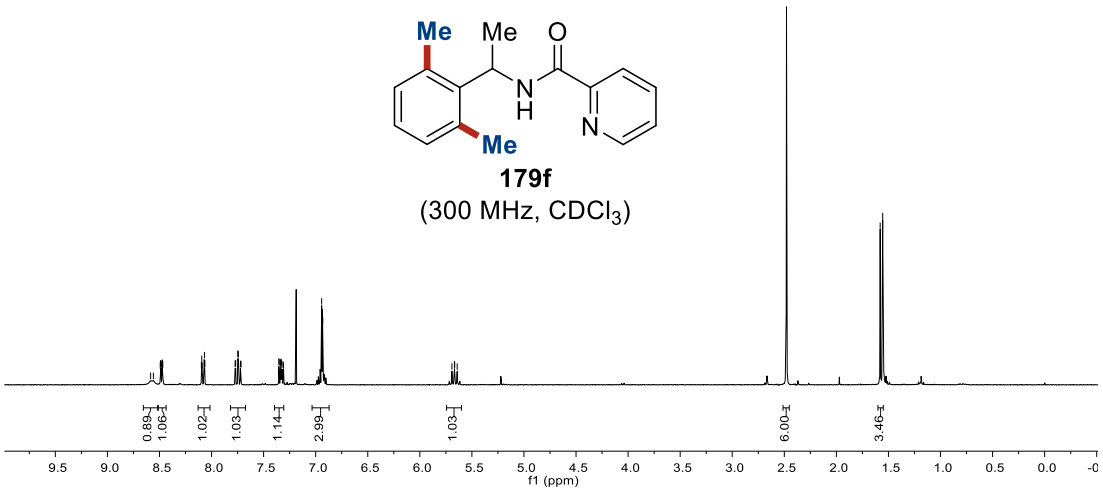

7.82
7.79
7.35
7.32
7.06
7.03
7.03
7.02
7.01
5.76
5.73
5.71
3.88
2.56
2.55
1.65
1.62
Me
Me
O
Me
N
H
N–PMP
N=N
Me
179c
(300 MHz, CDCl3)
1.06
1.99
4.90
1.17
3.07
5.78
2.69
3.00
f1 (ppm)


160.4
160.2
139.0
138.2
136.6
135.3
129.4
128.4
126.7
126.5
114.6
55.6
45.3
21.1
19.8
9.7
Me
Me
O
Me
N
H
N–PMP
N=N
Me
179c
(126 MHz, CDCl3)
f1 (ppm)

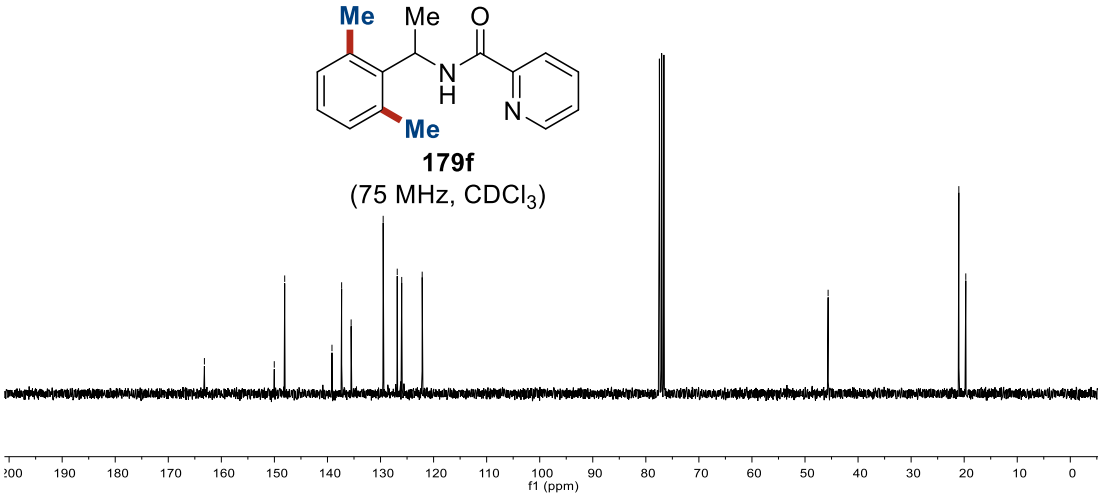

7.75
7.73
7.00
6.99
5.72
5.70
5.67
4.25
4.23
4.20
2.56
2.54
2.53
1.84
1.82
1.62
1.59
1.31
1.30
1.30
0.90
0.88
0.87
0.86
0.86
0.85
Me
Me
O
Me
N
H
N–n-Hex
N=N
Me
179d
(300 MHz, CDCl3)
1.19
3.12
1.22
2.19
2.89
5.66
2.10
3.00
5.87
2.85
f1 (ppm)

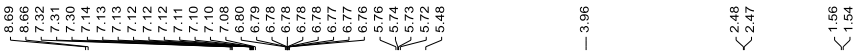

160.3
139.0
138.1
135.3
129.4
126.7
123.2
47.8
45.2
31.1
29.7
26.1
22.4
21.0
19.7
13.9
8.7
Me
Me
O
Me
N
H
N–n-Hex
N=N
Me
179d
(126 MHz, CDCl3)
f1 (ppm)

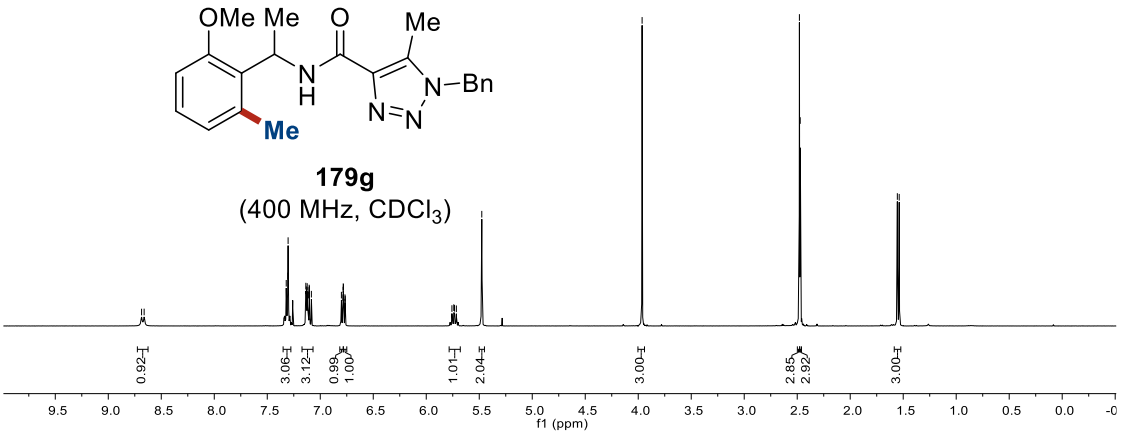

8.59
8.56
8.49
8.49
8.49
8.48
8.48
8.47
8.47
8.47
8.10
8.09
8.09
8.07
8.07
8.06
7.77
7.77
7.75
7.74
7.72
7.72
7.35
7.35
7.34
7.33
7.33
7.32
7.31
7.31
6.94
6.93
5.69
5.67
5.67
5.64
2.48
1.58
1.56


Me
Me
O
N
H
N
Me
179f
(300 MHz, CDCl3)
0.89
1.06
1.02
1.03
1.14
2.99
1.03
6.00
3.46
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
f1 (ppm)

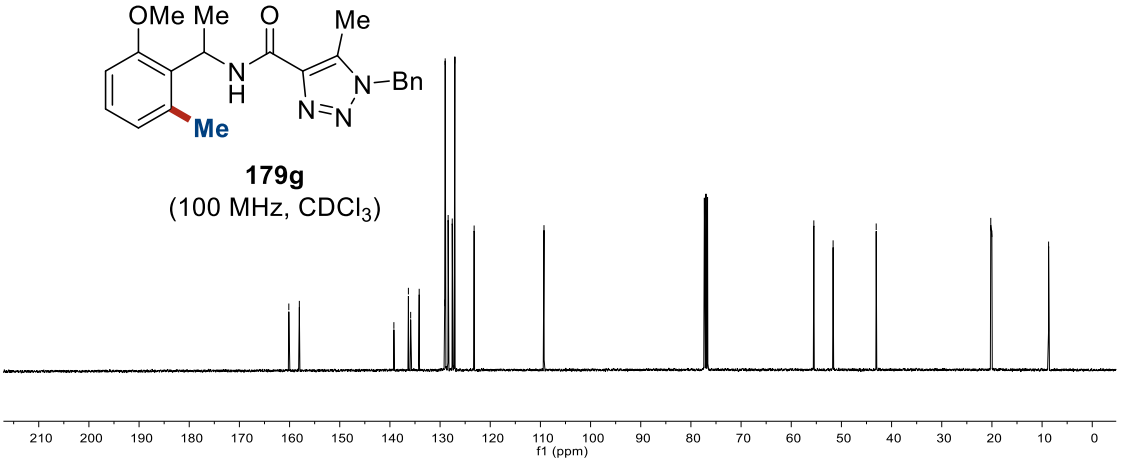

163.2
150.0
148.1
139.2
137.3
135.5
129.5
126.9
126.0
122.1
45.6
21.0
19.7

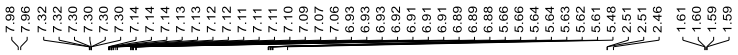

Me
Me
O
N
H
N
Me
179f
(75 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

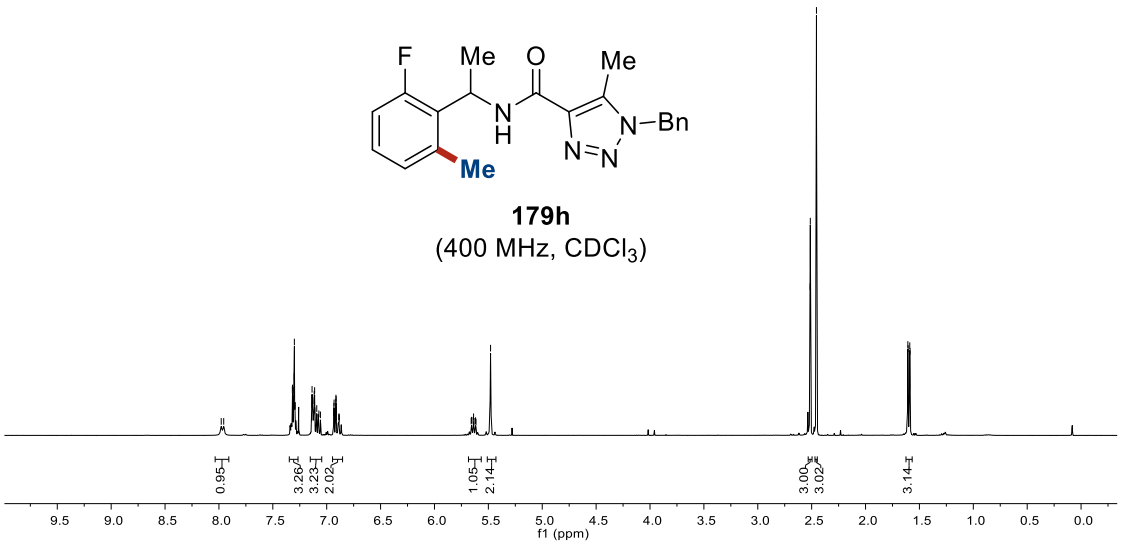

8.69
8.66
7.32
7.31
7.30
7.14
7.13
7.13
7.12
7.12
7.12
7.11
7.10
7.10
7.08
6.80
6.79
6.78
6.78
6.78
6.78
6.77
6.77
6.76
5.76
5.74
5.73
5.72
5.48
3.96
2.48
2.47
1.56
1.54

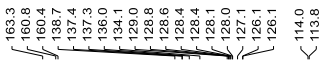

OMe
Me
O
Me
N
H
N–Bn
N=N
Me
179g
(400 MHz, CDCl3)
0.92
3.06
3.12
0.99
1.00
1.01
2.04
3.00
2.85
2.92
3.00
f1 (ppm)

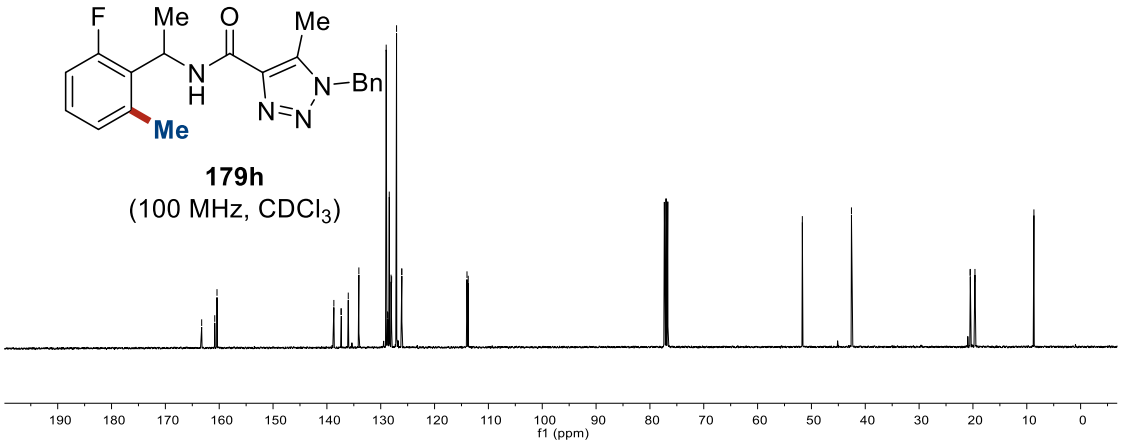

160.2
158.1
139.2
136.3
135.9
134.2
129.1
129.0
128.4
127.6
127.1
123.2
109.3
55.5
51.7
43.1
20.2
20.0
8.7

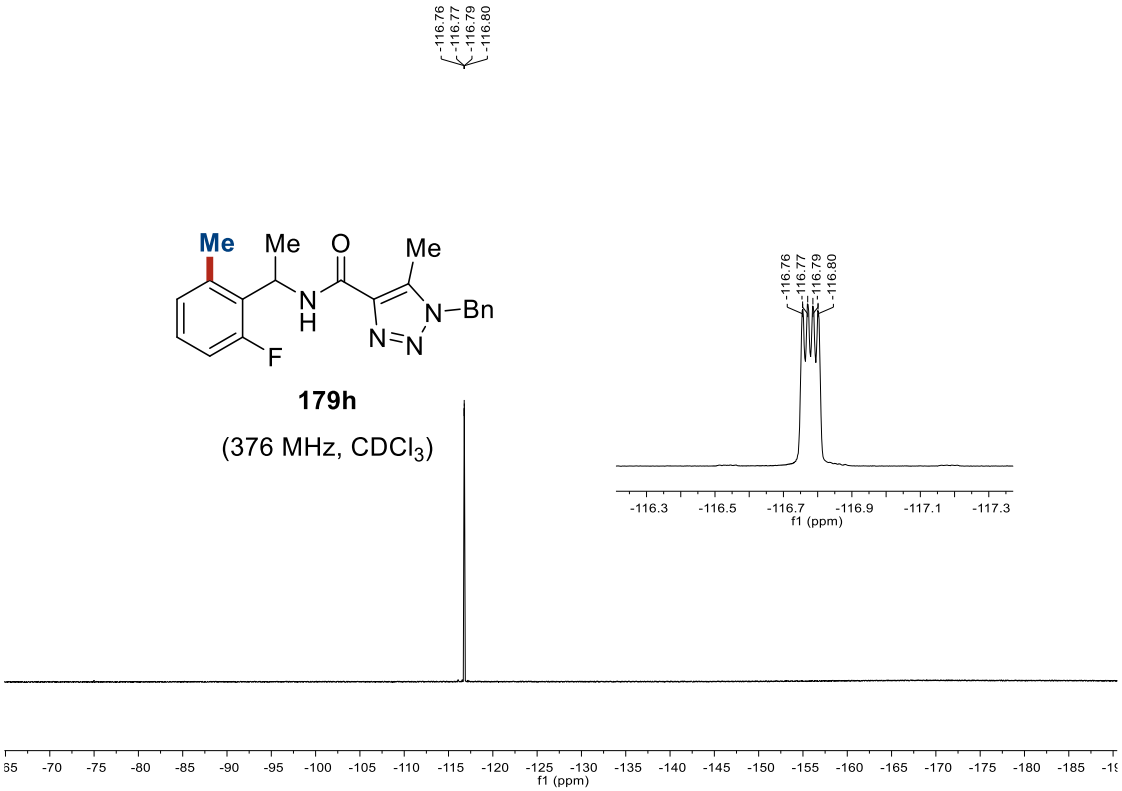

OMe
Me
O
Me
N
H
N–Bn
N=N
Me
179g
(100 MHz, CDCl3)
f1 (ppm)

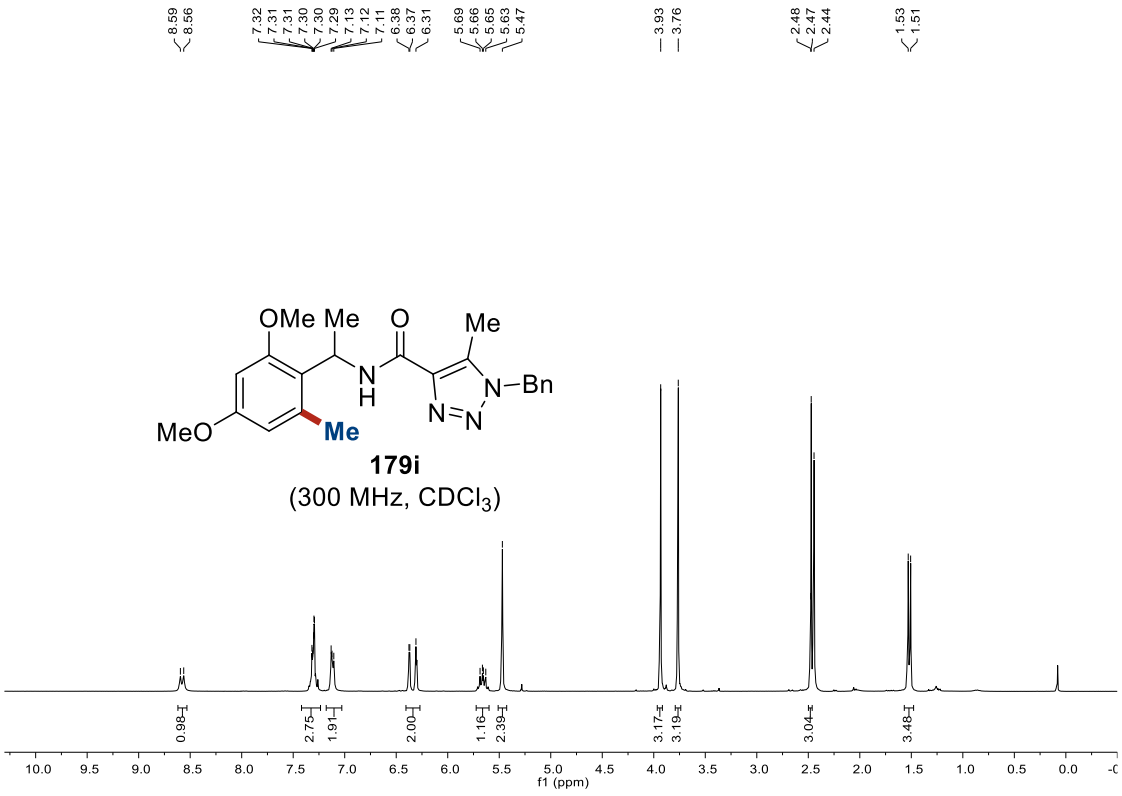

7.98
7.96
7.32
7.30
7.30
7.30
7.14
7.14
7.14
7.13
7.13
7.12
7.12
7.11
7.11
7.11
7.10
7.09
7.07
7.06
6.93
6.93
6.92
6.91
6.91
6.91
6.89
6.89
6.88
5.66
5.66
5.64
5.64
5.63
5.62
5.61
5.48
2.51
2.51
2.46
1.61
1.60
1.59
1.59

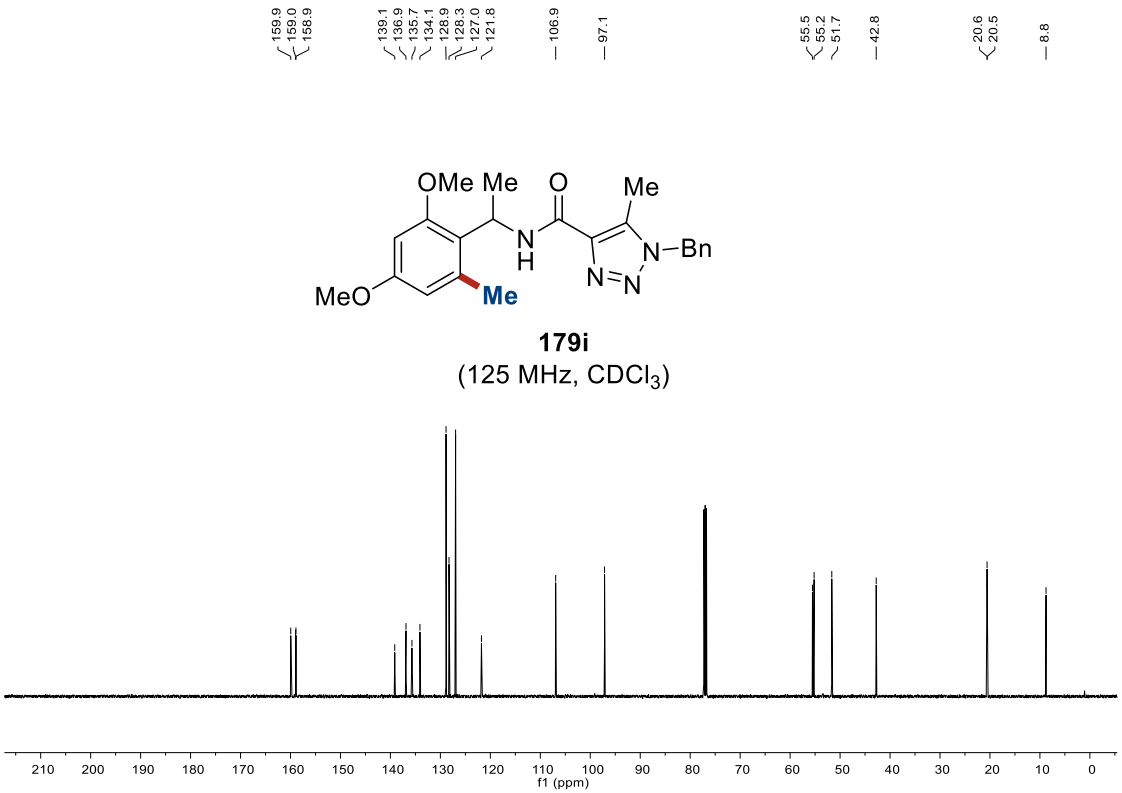

F
Me
O
Me
N
H
N–Bn
N=N
Me
179h
(400 MHz, CDCl3)
0.95
3.26
3.23
2.02
1.05
2.14
3.00
3.02
3.14
f1 (ppm)


163.3
160.8
160.4
138.7
137.4
137.3
136.0
134.1
129.0
128.8
128.6
128.4
128.4
128.1
128.0
127.1
126.1
126.1
114.0
113.8
51.7
42.6
20.5
20.5
19.7
19.6
8.7

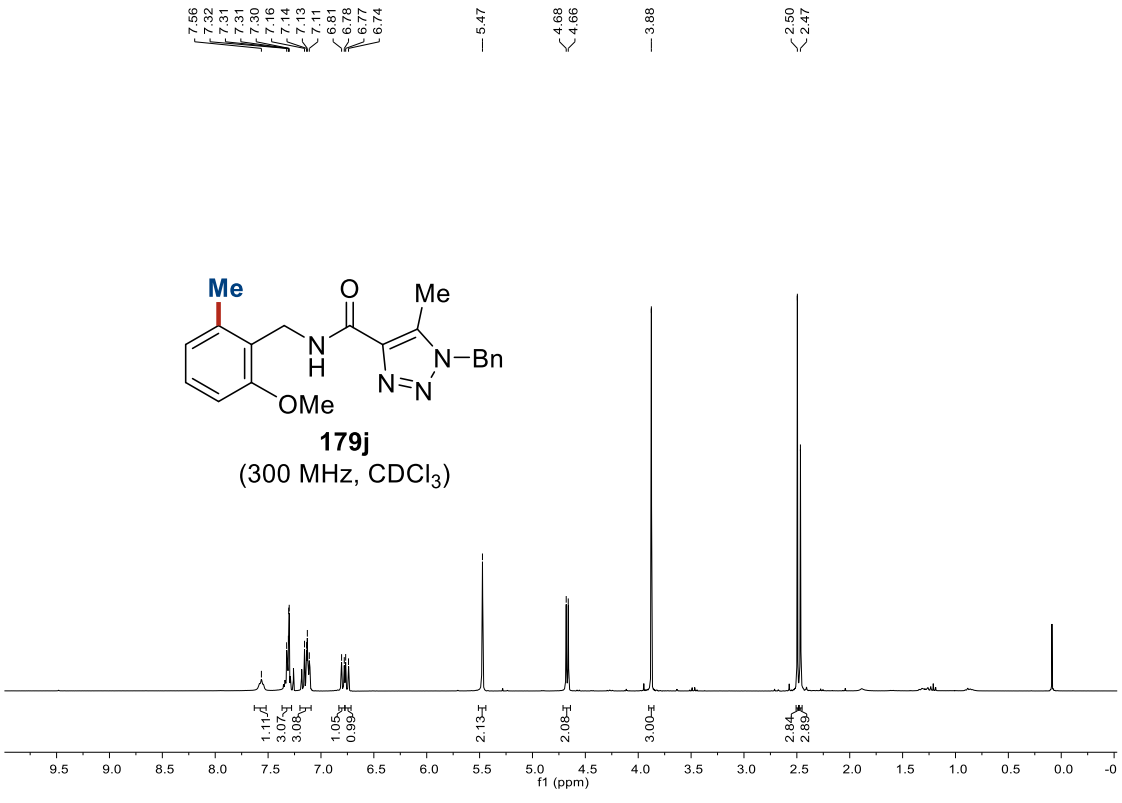

F
Me
O
Me
N
H
N–Bn
N=N
Me
179h
(100 MHz, CDCl3)
f1 (ppm)


-116.76
-116.77
-116.79
-116.80
Me
Me
O
Me
N
H
N–Bn
N=N
F
179h
(376 MHz, CDCl3)
-116.3
-116.5
-116.7
-116.9
-117.1
-117.3
f1 (ppm)
f1 (ppm)

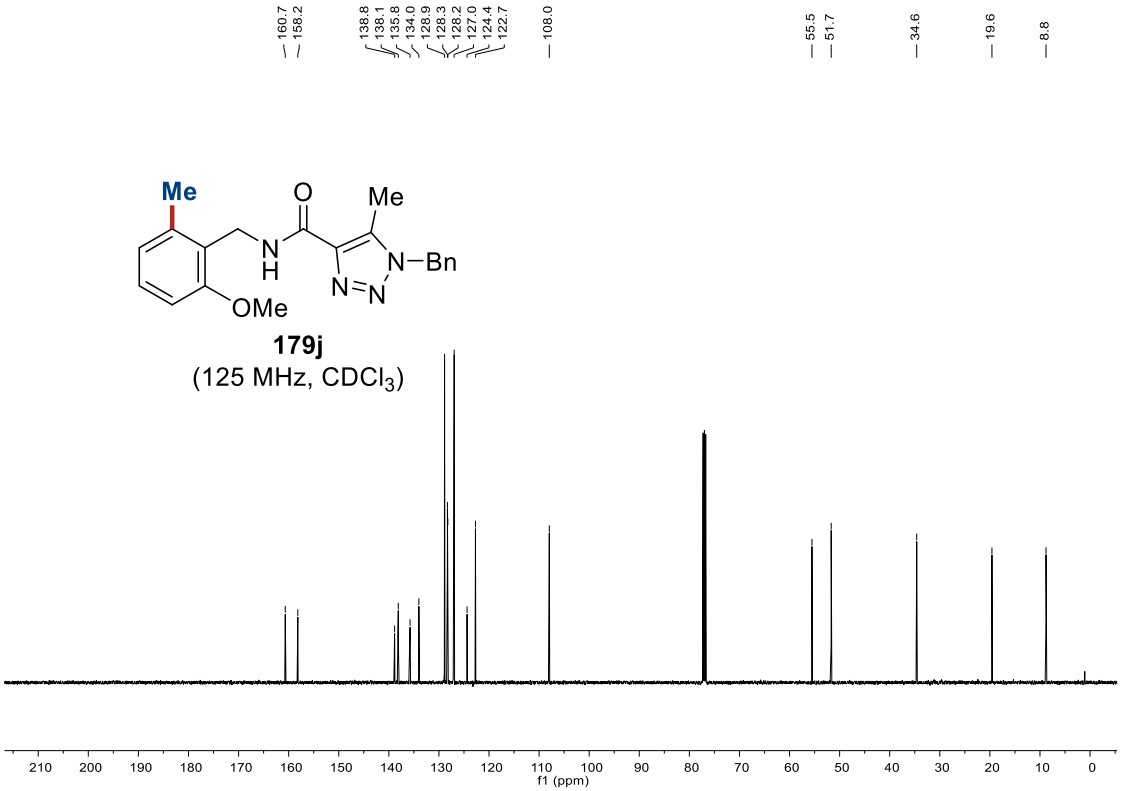

8.59
8.56
7.32
7.31
7.31
7.30
7.30
7.29
7.13
7.12
7.11
6.38
6.37
6.31
5.69
5.66
5.65
5.63
5.47
3.93
3.76
2.48
2.47
2.44
1.53
1.51
OMe
Me
O
Me
N
H
N–Bn
N=N
MeO
Me
179i
(300 MHz, CDCl3)
0.98
2.75
1.91
2.00
1.16
2.39
3.17
3.19
3.04
3.48
f1 (ppm)



179i
(125 MHz, $CDCl_3$)

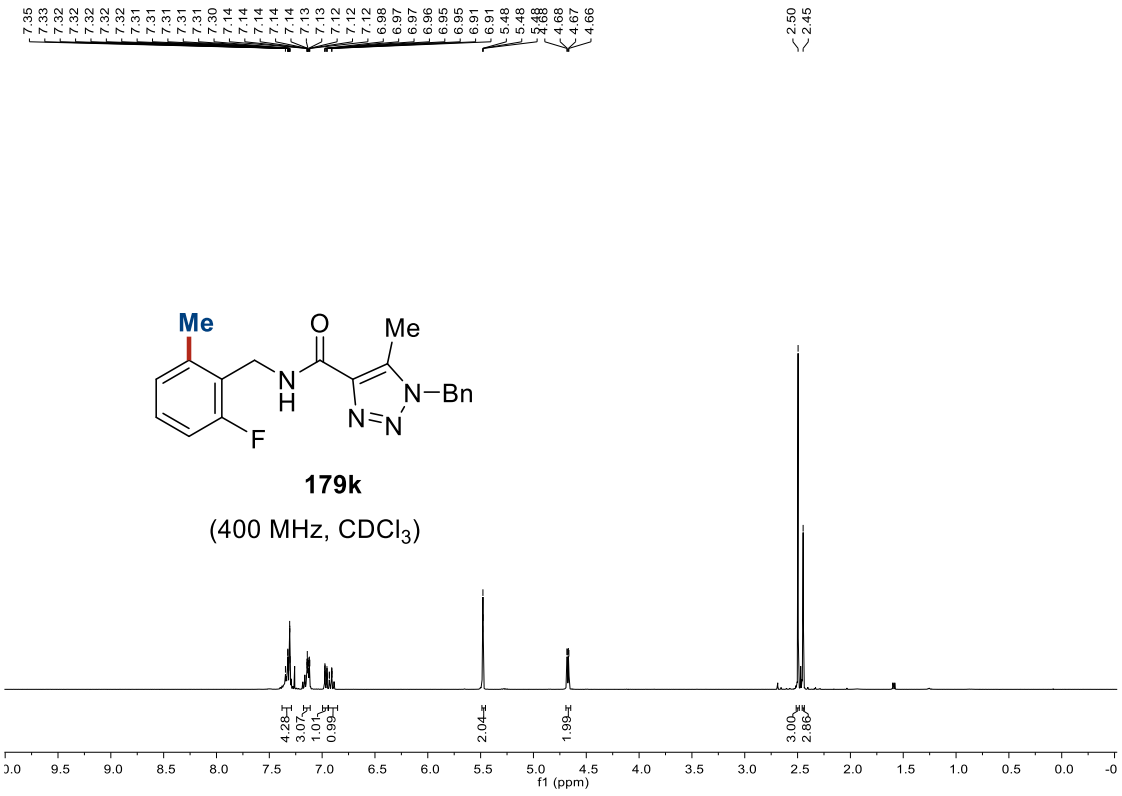


179j
(300 MHz, $CDCl_3$)



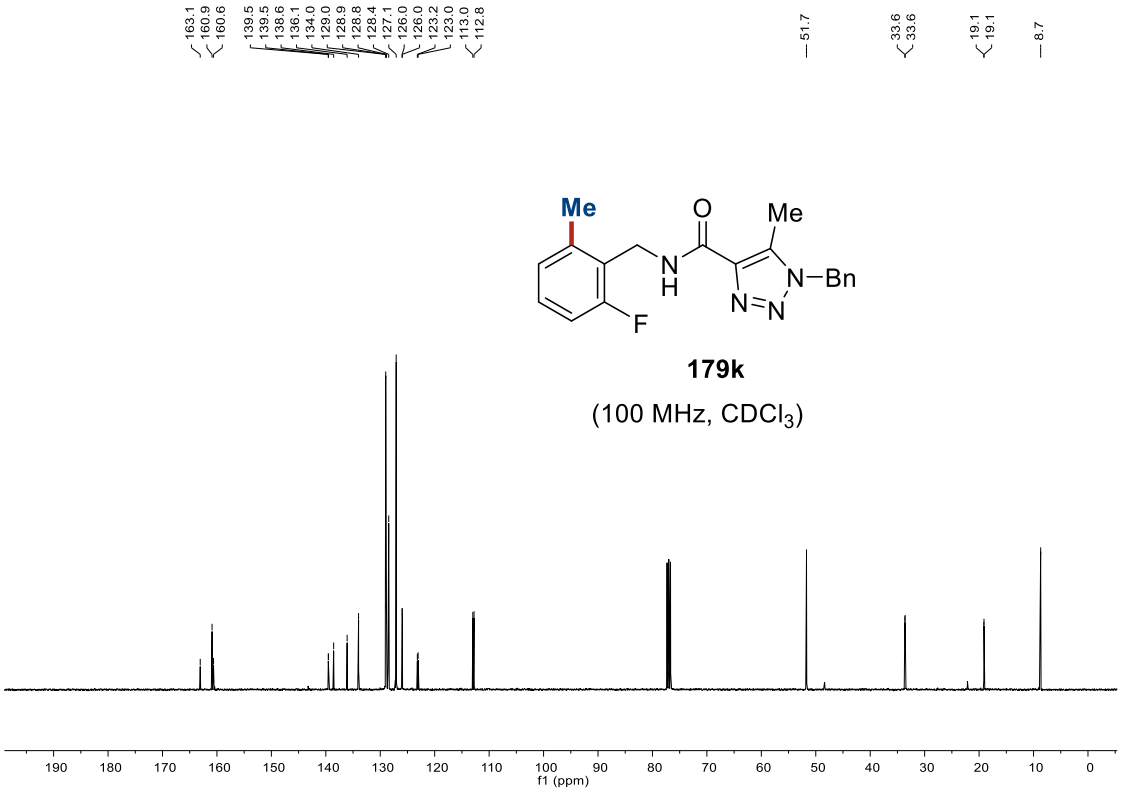
179j

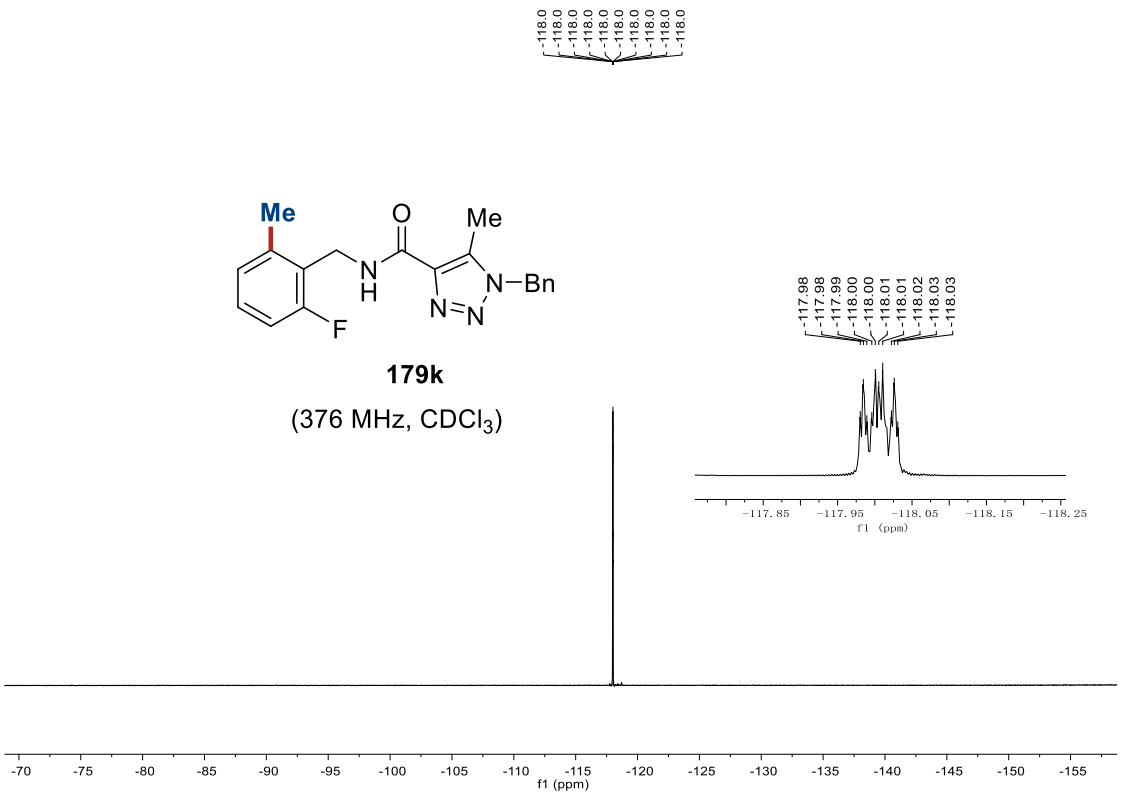
(125 MHz, $CDCl_3$)

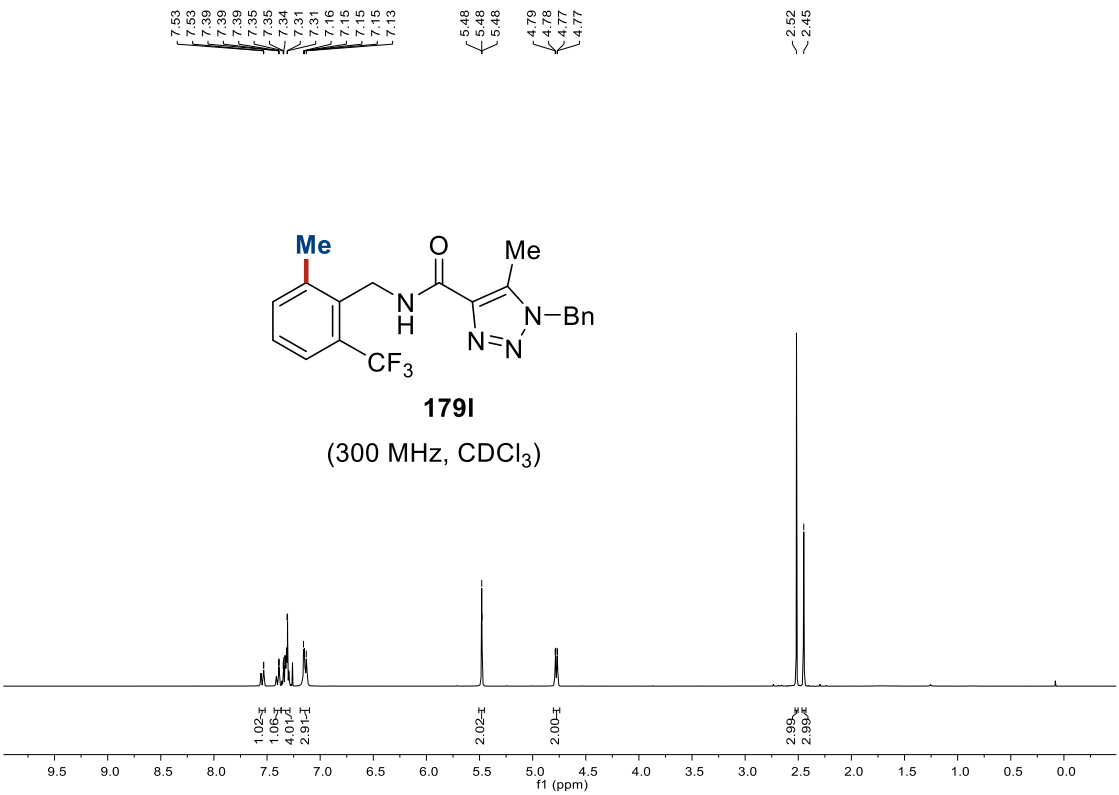


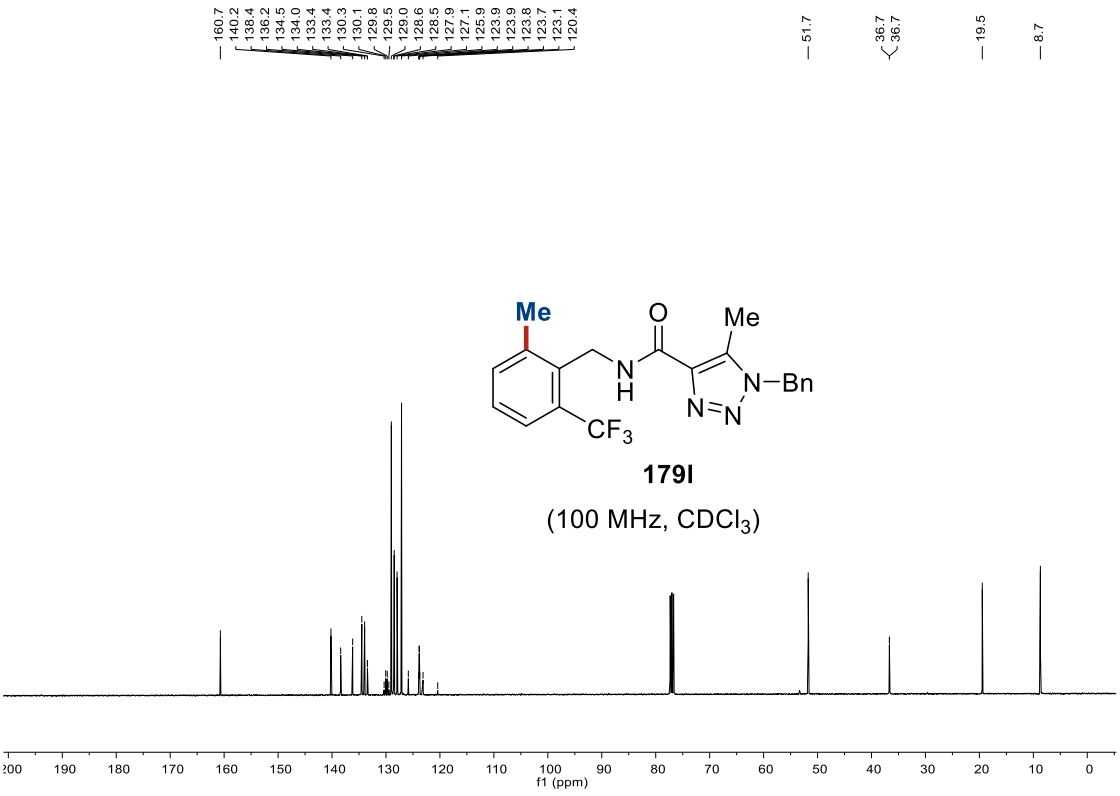
179k

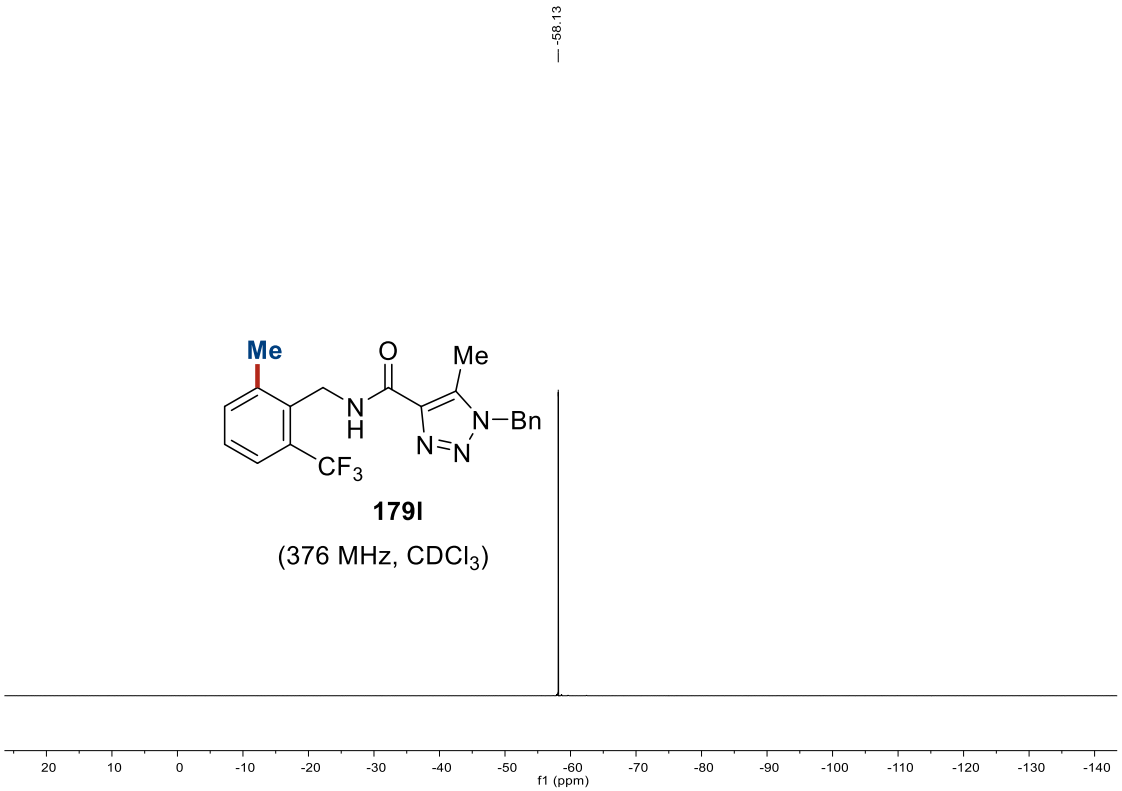
(400 MHz, $CDCl_3$)

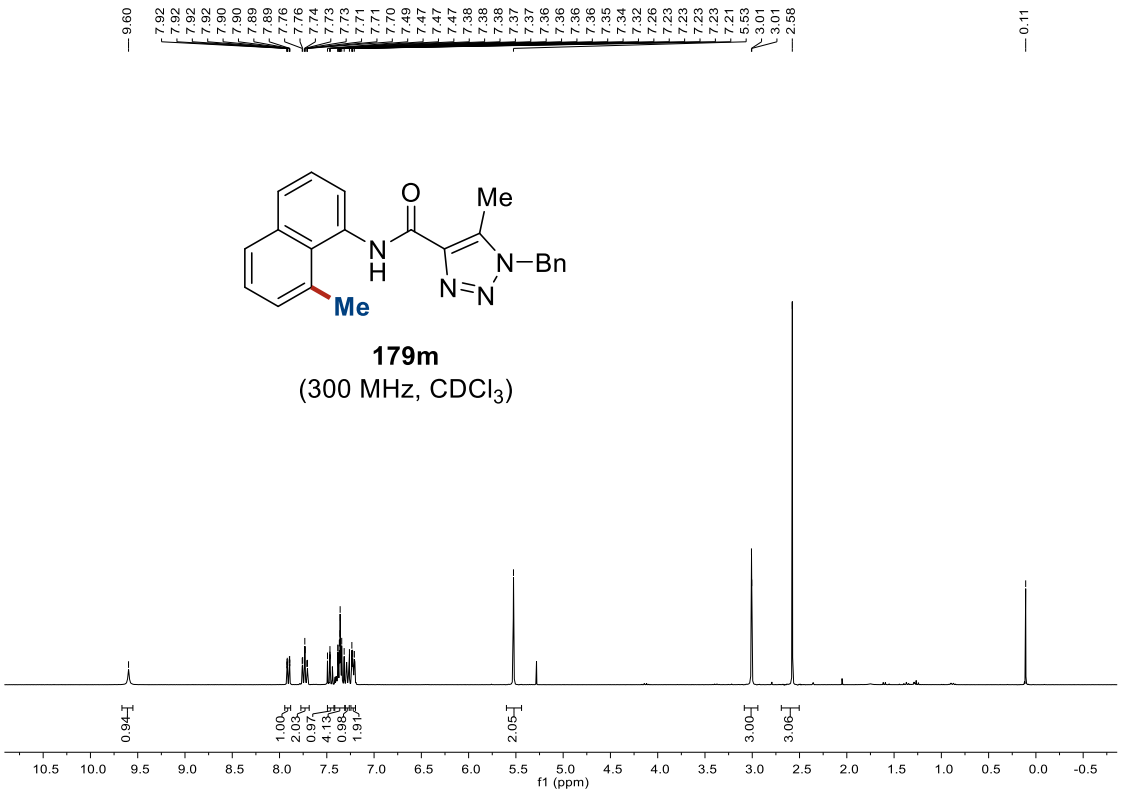

163.1
160.9
160.6
139.5
139.5
138.6
136.1
134.0
129.0
128.9
128.8
128.4
127.1
126.0
126.0
123.2
123.0
113.0
112.8
51.7
33.6
33.6
19.1
19.1
8.7
Me
O
Me
N
H
N–Bn
N=N
F
179k
(100 MHz, CDCl3)
f1 (ppm)

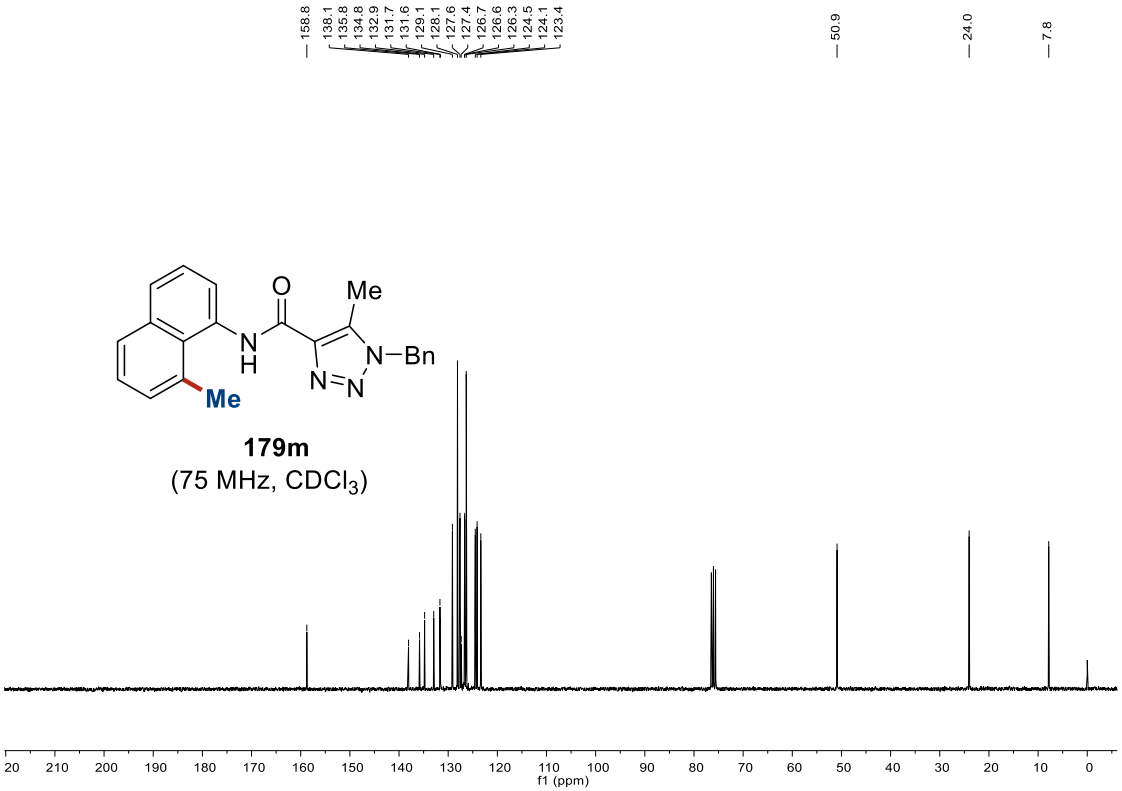

-118.0
-118.0
-118.0
-118.0
-118.0
-118.0
-118.0
-118.0
-118.0
-118.0
Me
O
Me
N
H
N–Bn
N=N
F
179k
(376 MHz, CDCl3)
-117.98
-117.98
-117.99
-118.00
-118.00
-118.01
-118.01
-118.02
-118.03
-118.03
f1 (ppm)

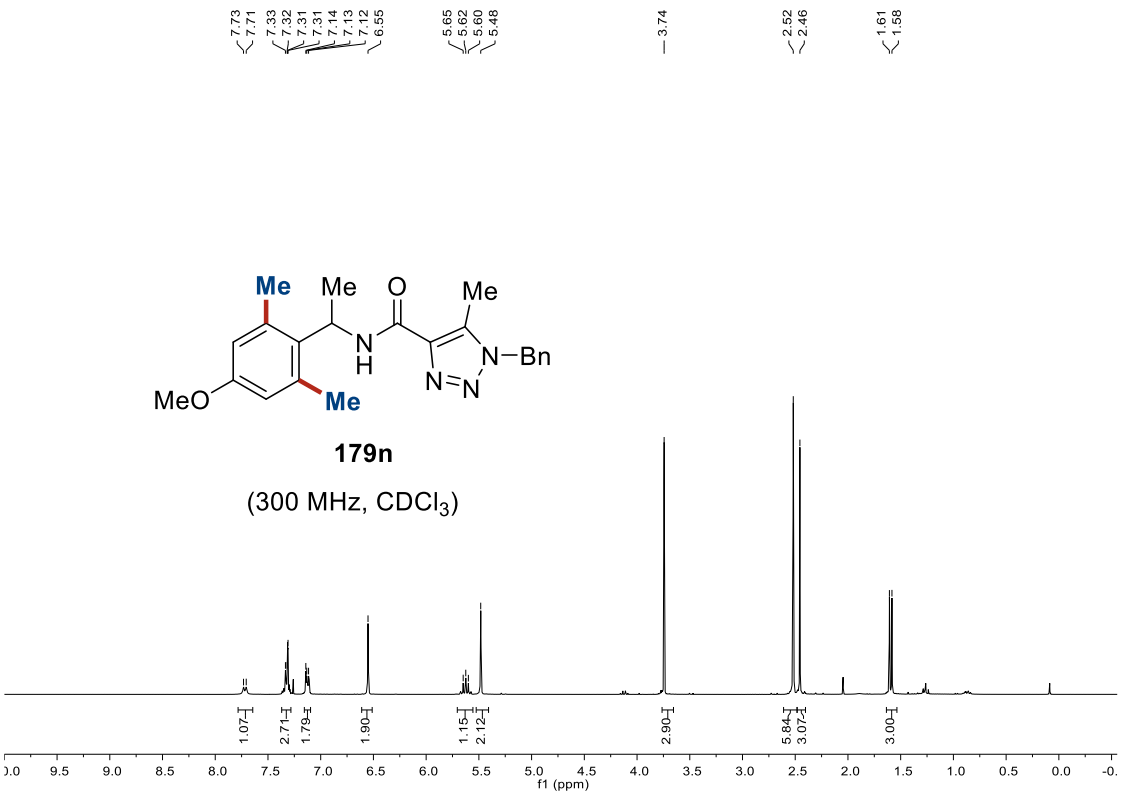

7.53
7.53
7.39
7.39
7.39
7.35
7.35
7.34
7.31
7.31
7.16
7.15
7.15
7.15
7.13
5.48
5.48
5.48
4.79
4.78
4.77
4.77
2.52
2.45
Me
O
Me
N
H
N–Bn
N=N
CF3
179l
(300 MHz, CDCl3)
1.02
1.06
4.01
2.91
2.02
2.00
2.99
2.99
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

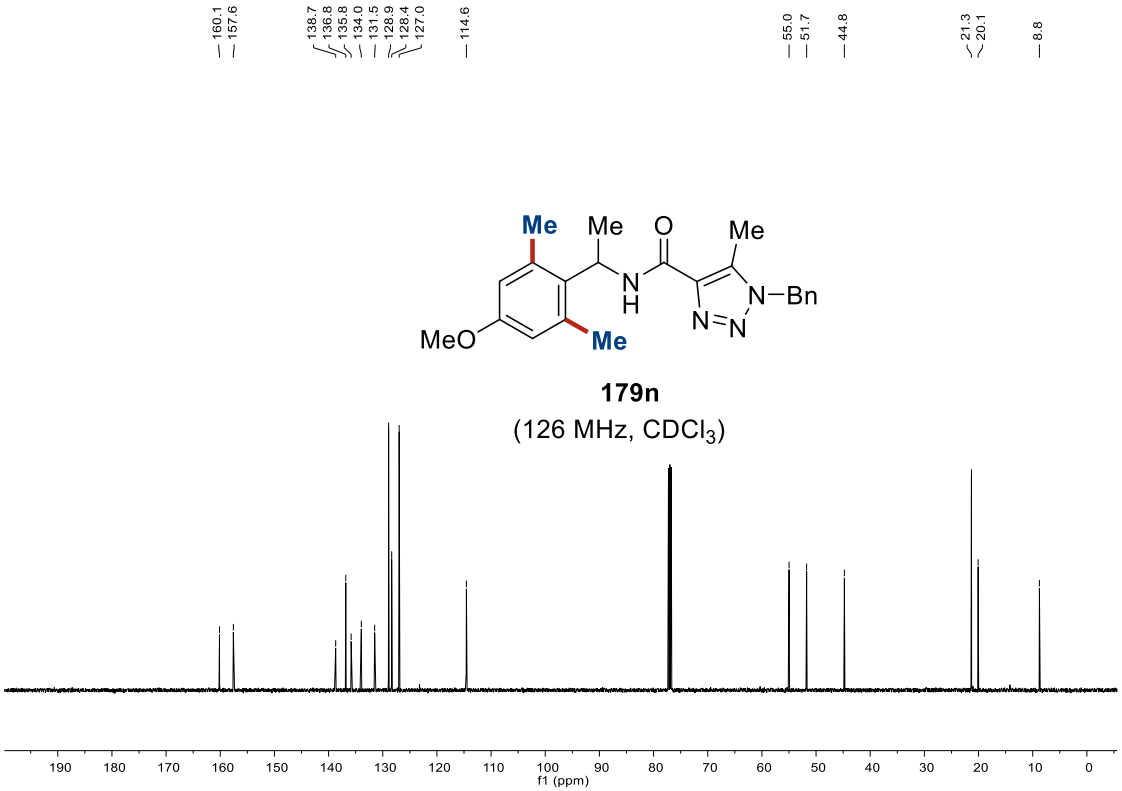

160.7
140.2
138.4
136.2
134.5
134.0
133.4
133.4
130.3
130.1
129.8
129.5
129.0
128.6
128.5
127.9
127.1
125.9
123.9
123.9
123.8
123.7
123.1
120.4
51.7
36.7
36.7
19.5
8.7
Me
O
Me
N
H
N–Bn
N=N
CF3
179l
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

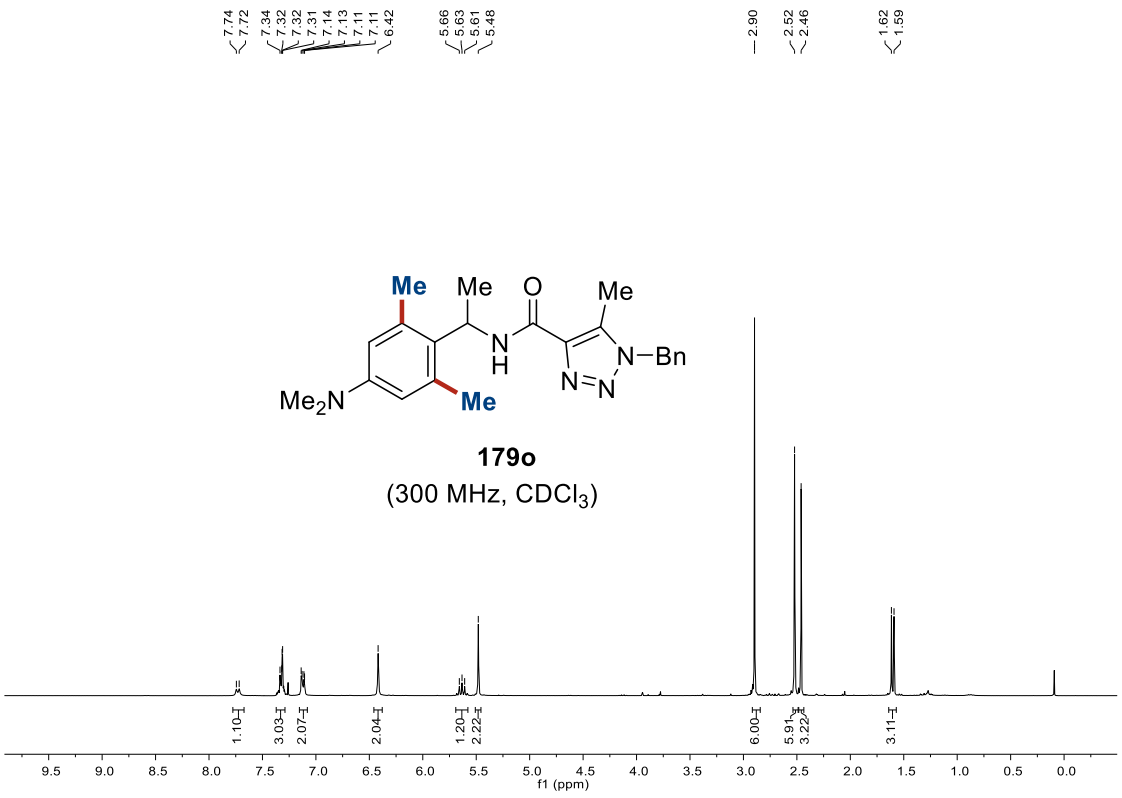

-58.13
Me
O
Me
N
H
N–Bn
N=N
CF3
179l
(376 MHz, CDCl3)
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140
f1 (ppm)

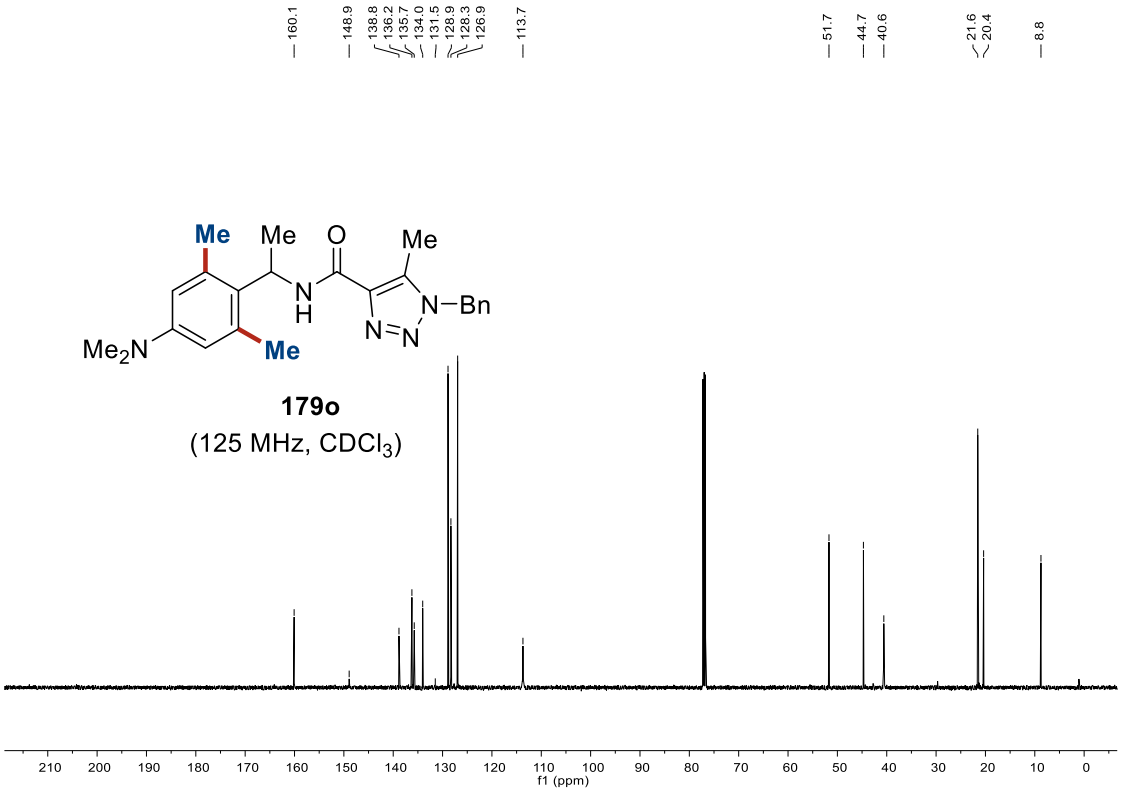

9.60
7.92 7.92 7.92 7.92 7.90 7.90 7.89 7.89 7.76 7.76 7.74 7.73 7.73 7.71 7.71 7.70 7.49 7.47 7.47 7.47 7.38 7.38 7.38 7.37 7.37 7.36 7.36 7.36 7.35 7.34 7.32 7.26 7.23 7.23 7.23 7.23 7.21
5.53
3.01
3.01
2.58
0.11
O
Me
N
H
N–Bn
N=N
Me
179m
(300 MHz, CDCl3)
0.94
1.00
2.03
0.97
4.13
0.98
1.91
2.05
3.00
3.06
10.5 10.0 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 -0.5
f1 (ppm)

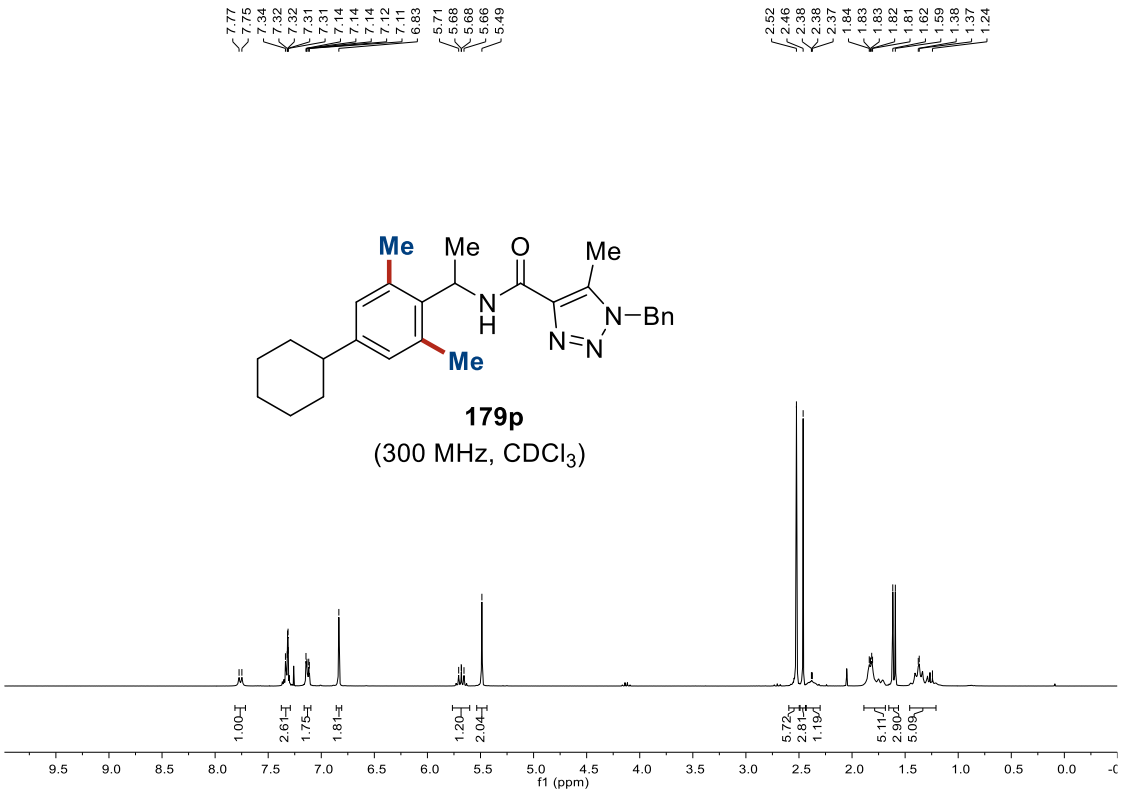

158.8
138.1
135.8
134.8
132.9
131.7
131.6
129.1
128.1
127.6
127.4
126.7
126.6
126.3
124.5
124.1
123.4
50.9
24.0
7.8
O
Me
N
H
N–Bn
N=N
Me
179m
(75 MHz, CDCl3)
f1 (ppm)

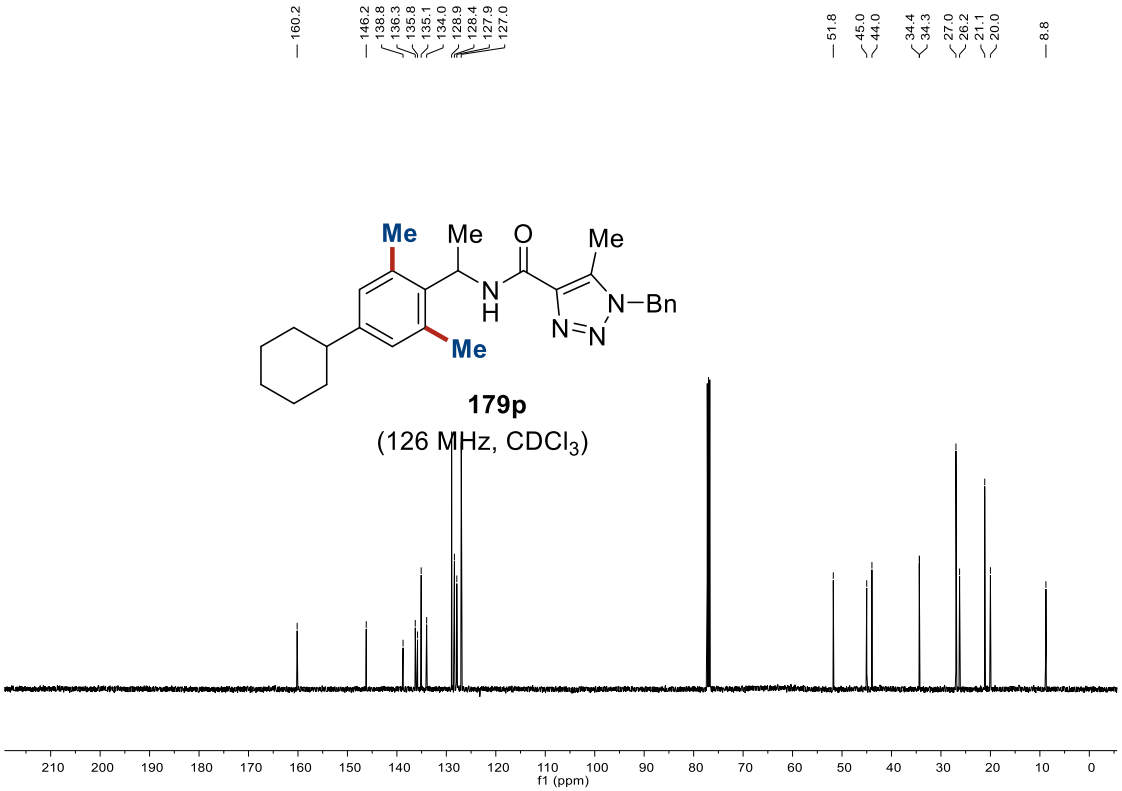

7.73
7.71
7.33
7.32
7.31
7.31
7.14
7.13
7.12
6.55
5.65
5.62
5.60
5.48
3.74
2.52
2.46
1.61
1.58
Me
Me
O
Me
N
H
N–Bn
N=N
MeO
Me
179n
(300 MHz, CDCl3)
1.07
2.71
1.79
1.90
1.15
2.12
2.90
5.84
3.07
3.00
f1 (ppm)

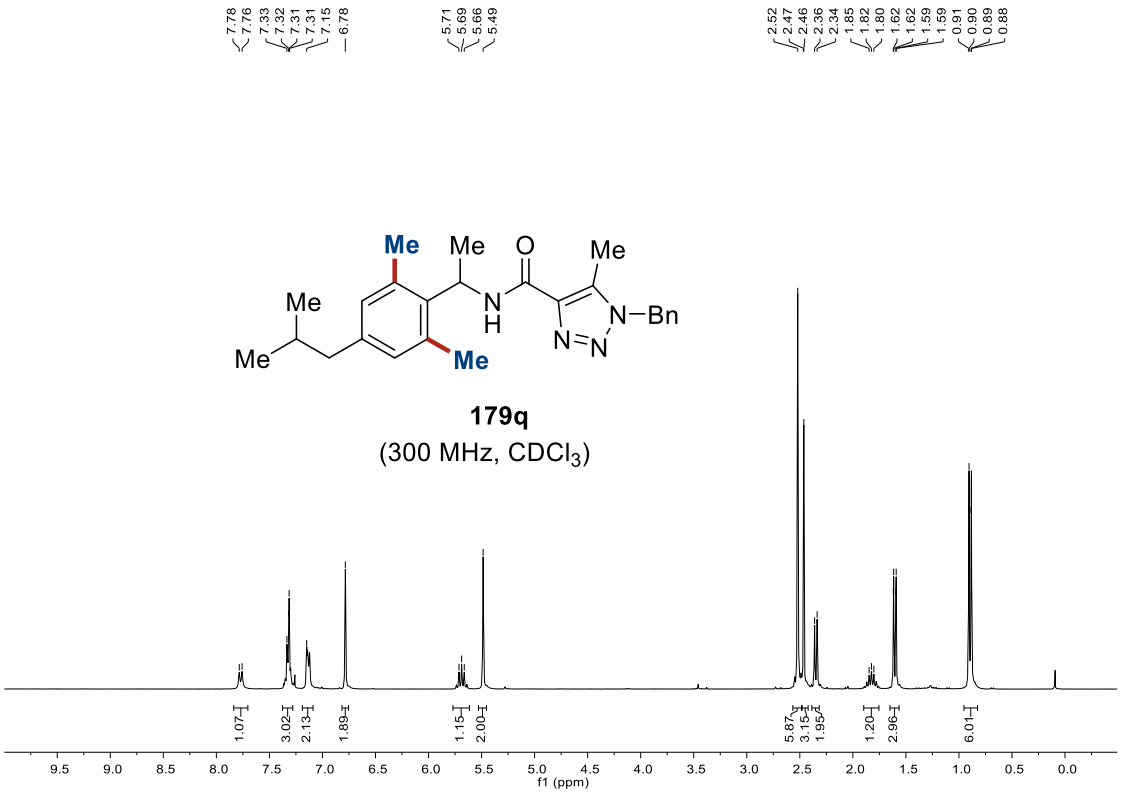

160.1
157.6
138.7
136.8
135.8
134.0
131.5
128.9
128.4
127.0
114.6
55.0
51.7
44.8
21.3
20.1
8.8
Me
Me
O
Me
N
H
N–Bn
N=N
MeO
Me
179n
(126 MHz, CDCl3)
f1 (ppm)

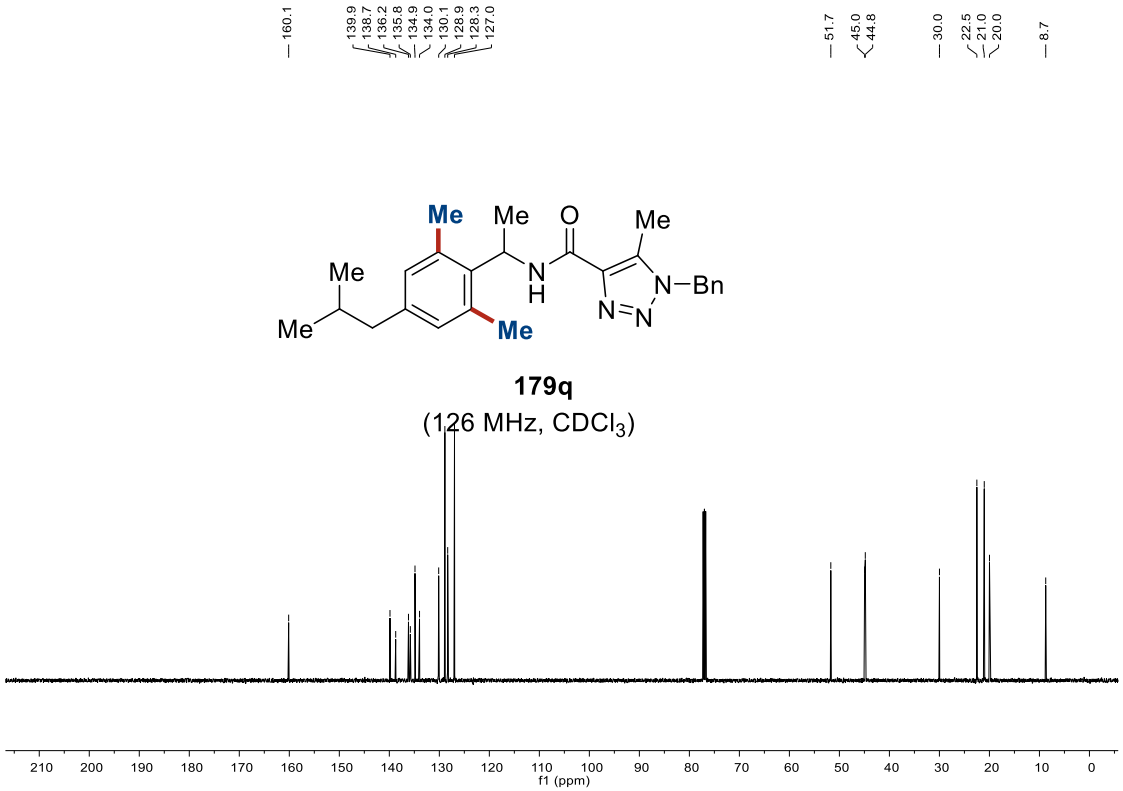

7.74
7.72
7.34
7.32
7.32
7.31
7.14
7.13
7.11
7.11
6.42
5.66
5.63
5.61
5.48
2.90
2.52
2.46
1.62
1.59
Me
Me
O
Me
N
H
N–Bn
N=N
Me2N
Me
179o
(300 MHz, CDCl3)
1.10
3.03
2.07
2.04
1.20
2.22
6.00
5.91
3.22
3.11
f1 (ppm)

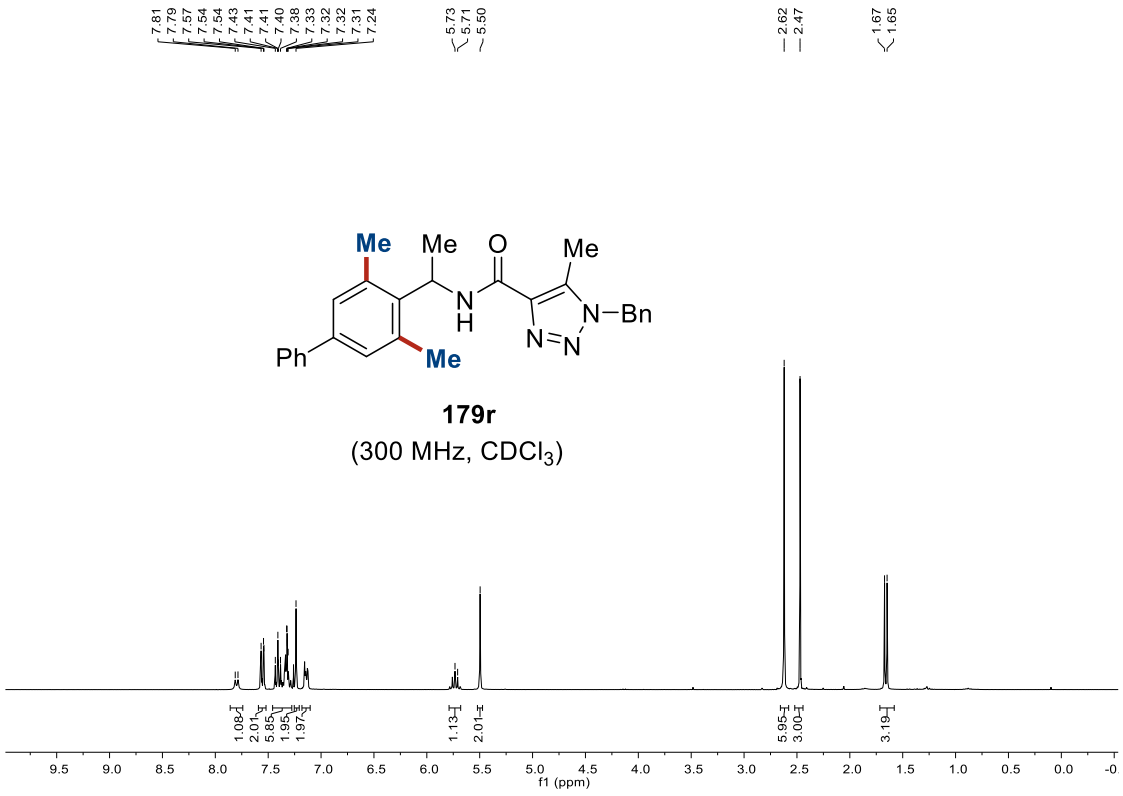

160.1
148.9
138.8
136.2
135.7
134.0
131.5
128.9
128.3
126.9
113.7
51.7
44.7
40.6
21.6
20.4
8.8
Me
Me
O
Me
N
H
N–Bn
N=N
Me
Me2N
179o
(125 MHz, CDCl3)
f1 (ppm)

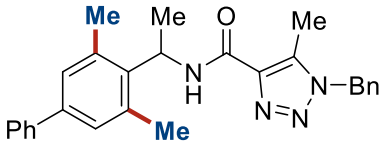

7.77
7.75
7.34
7.32
7.32
7.31
7.31
7.14
7.14
7.14
7.12
7.11
6.83
5.71
5.68
5.68
5.66
5.49
2.52
2.46
2.38
2.38
2.37
1.84
1.83
1.83
1.82
1.81
1.62
1.59
1.38
1.37
1.24
Me
Me
O
Me
N
H
N–Bn
N=N
Me
179p
(300 MHz, CDCl3)
1.00
2.61
1.75
1.81
1.20
2.04
5.72
2.81
1.19
5.11
2.90
5.09
f1 (ppm)


160.2
146.2
138.8
136.3
135.8
135.1
134.0
128.9
128.4
127.9
127.0
51.8
45.0
44.0
34.4
34.3
27.0
26.2
21.1
20.0
8.8
Me
Me
O
Me
N
H
N–Bn
N=N
Me
179p
(126 MHz, CDCl3)
f1 (ppm)


7.78
7.76
7.33
7.32
7.31
7.31
7.15
6.78
5.71
5.69
5.66
5.49
2.52
2.47
2.46
2.36
2.34
1.85
1.82
1.80
1.62
1.62
1.59
1.59
0.91
0.90
0.89
0.88
Me
Me
O
Me
Me
N
H
N–Bn
N=N
Me
Me
179q
(300 MHz, CDCl3)
1.07
3.02
2.13
1.89
1.15
2.00
5.87
3.15
1.95
1.20
2.96
6.01
f1 (ppm)

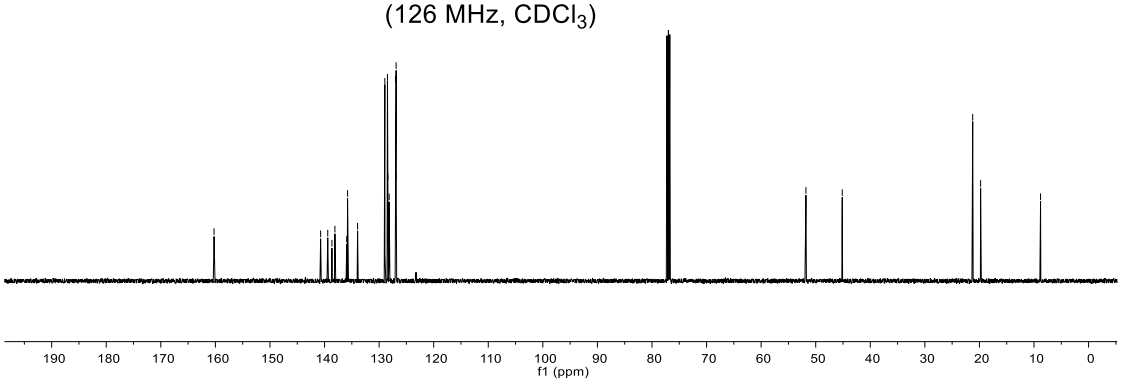

160.1
139.9
138.7
136.2
135.8
134.9
134.0
130.1
128.9
128.3
127.0
51.7
45.0
44.8
30.0
22.5
21.0
20.0
8.7
Me
Me
O
Me
Me
N
H
N–Bn
N=N
Me
Me
179q
(126 MHz, CDCl3)
f1 (ppm)

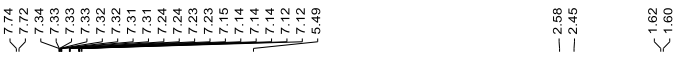

7.81
7.79
7.57
7.54
7.54
7.43
7.41
7.41
7.40
7.38
7.33
7.32
7.32
7.31
7.24
5.73
5.71
5.50
2.62
2.47
1.67
1.65
Me
Me
O
Me
N
H
N–Bn
N=N
Ph
Me
179r
(300 MHz, CDCl3)
1.08
2.01
5.85
1.95
1.97
1.13
2.01
5.95
3.00
3.19
f1 (ppm)

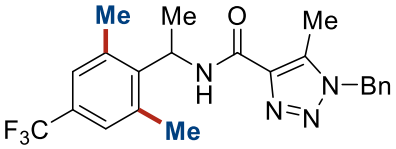


179r

(126 MHz, $CDCl_3$)

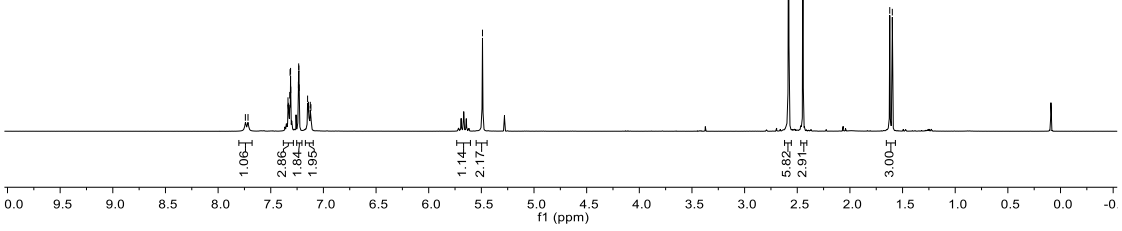


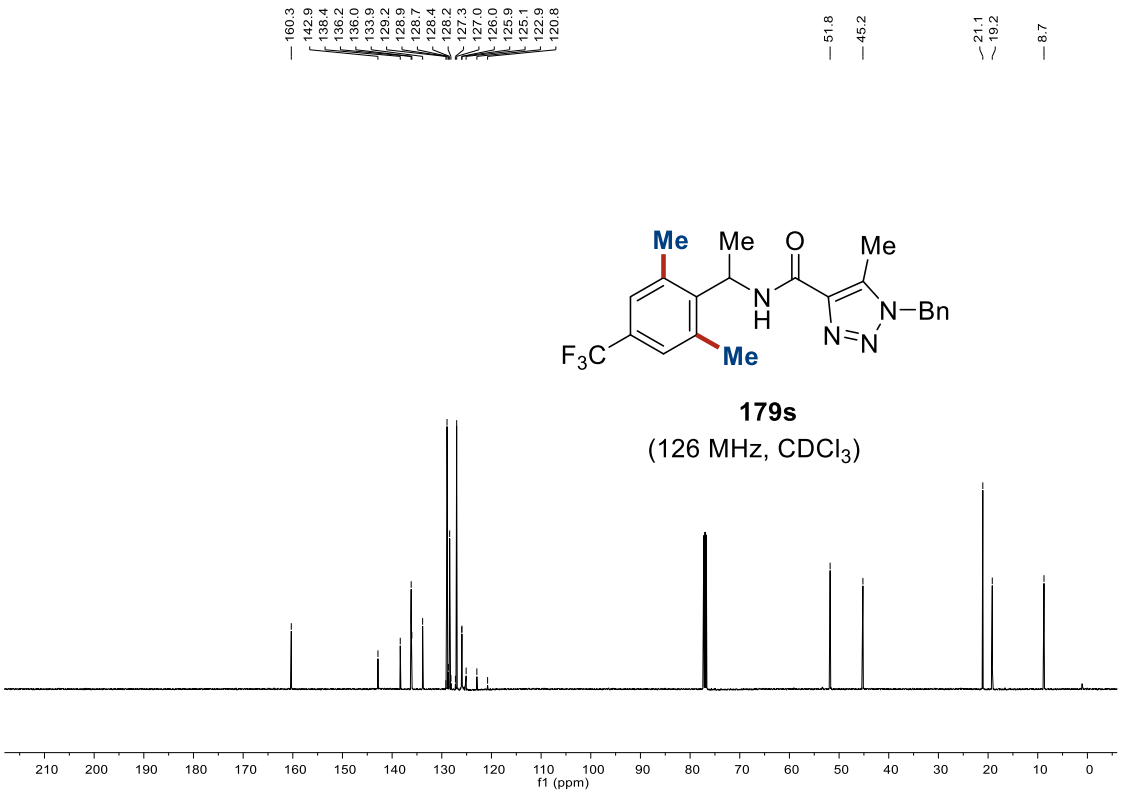


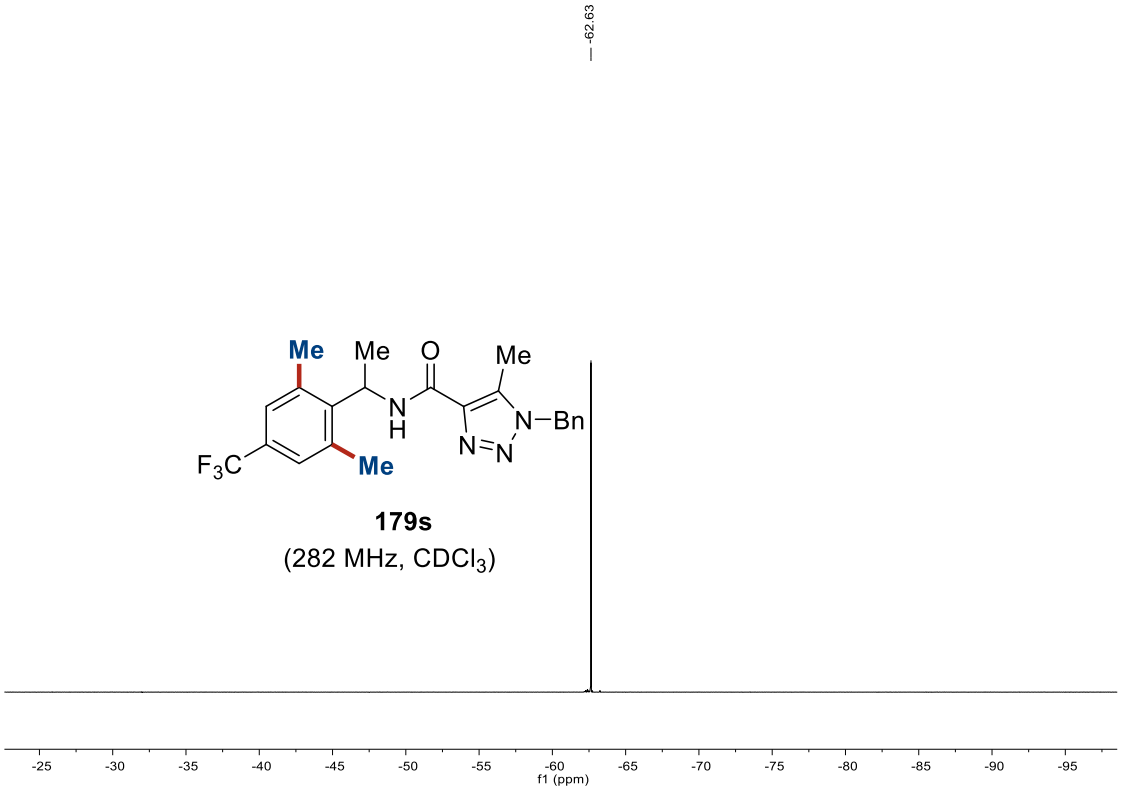


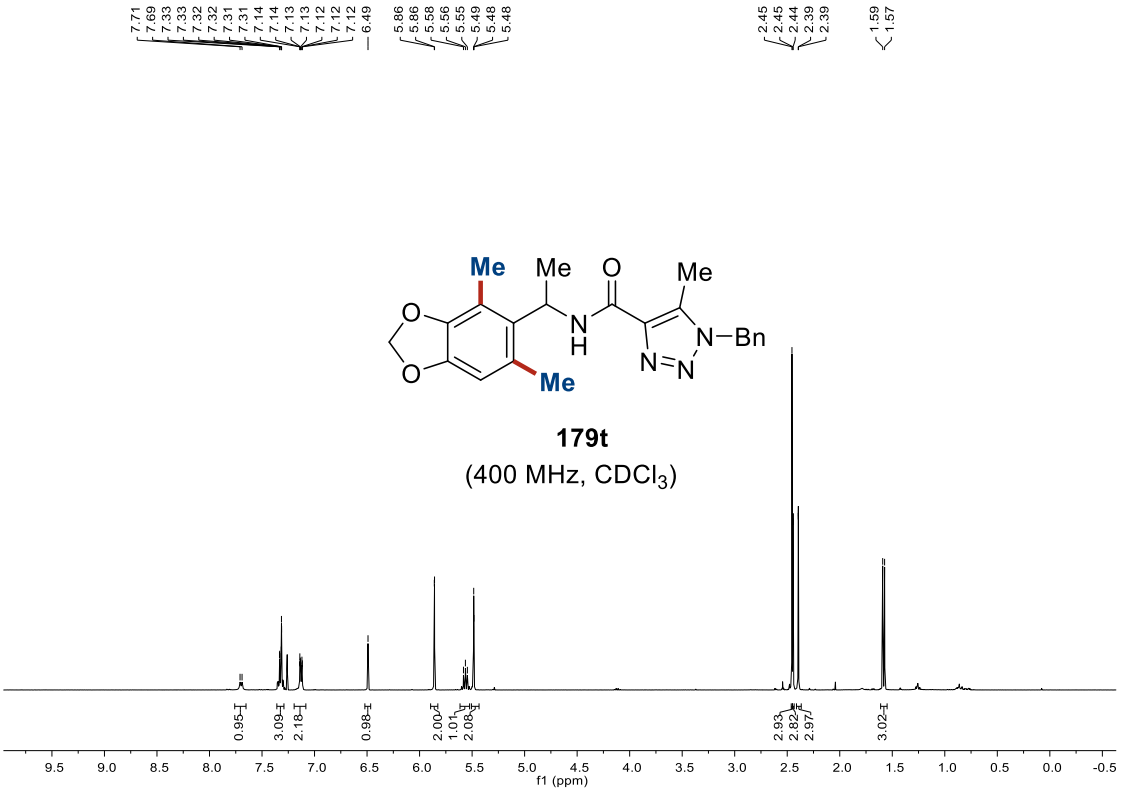
179s

(300 MHz, $CDCl_3$)



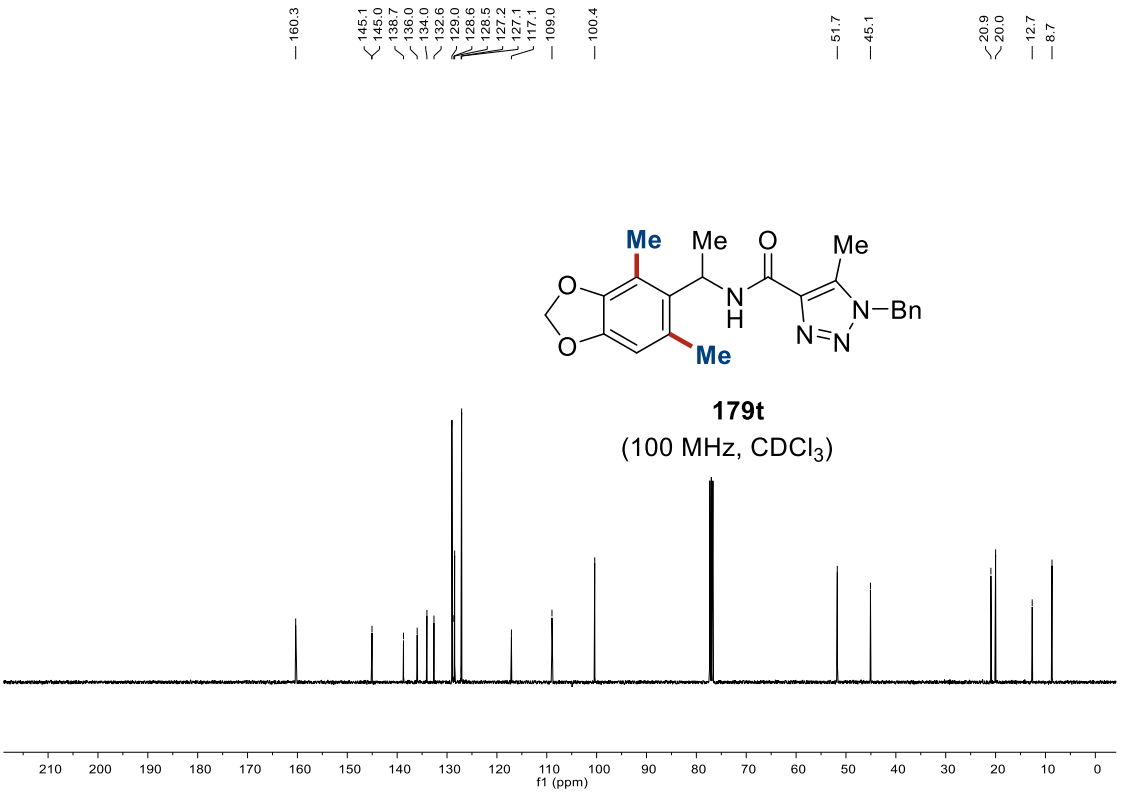

160.3
142.9
138.4
136.2
136.0
133.9
129.2
128.9
128.7
128.4
128.2
127.3
127.0
126.0
125.9
125.1
122.9
120.8
51.8
45.2
21.1
19.2
8.7
Me
Me
O
Me
N
H
N–Bn
N=N
F3C
Me
179s
(126 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-62.63
Me
Me
O
Me
N
H
N–Bn
N=N
F3C
Me
179s
(282 MHz, CDCl3)
-25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95
f1 (ppm)



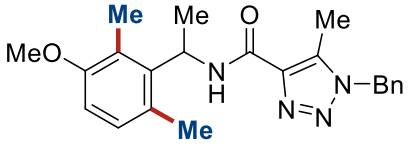
179t

(400 MHz, $CDCl_3$)



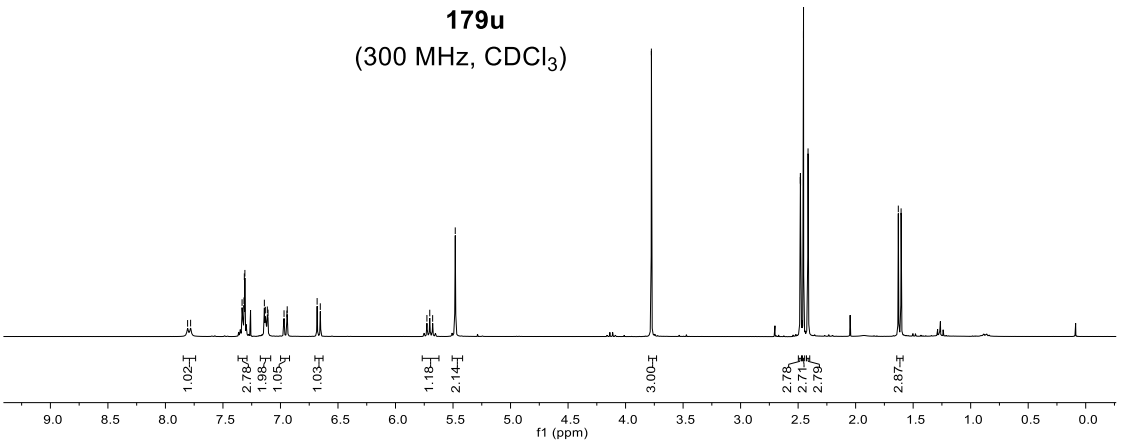
179t

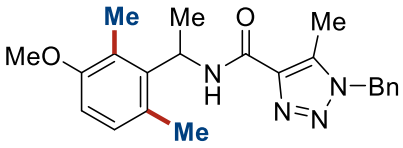
(100 MHz, $CDCl_3$)



179u

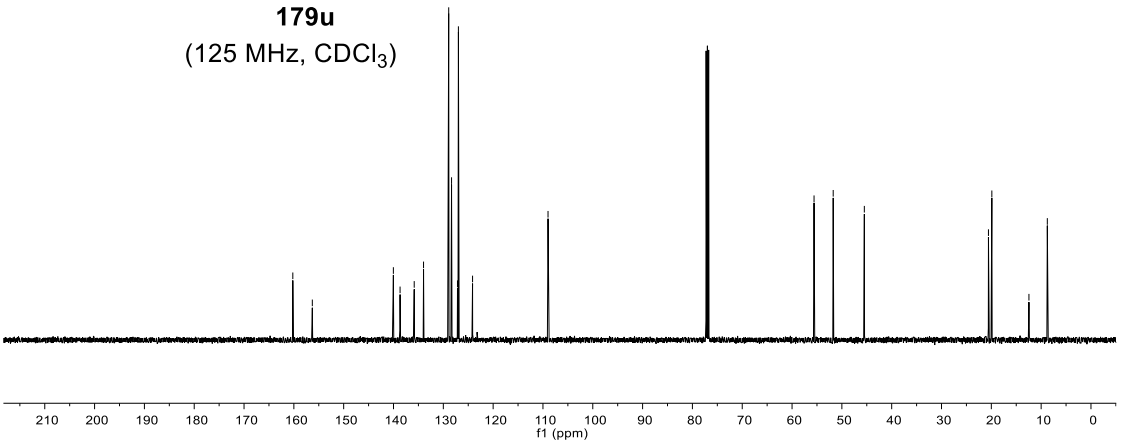
(300 MHz, $CDCl_3$)

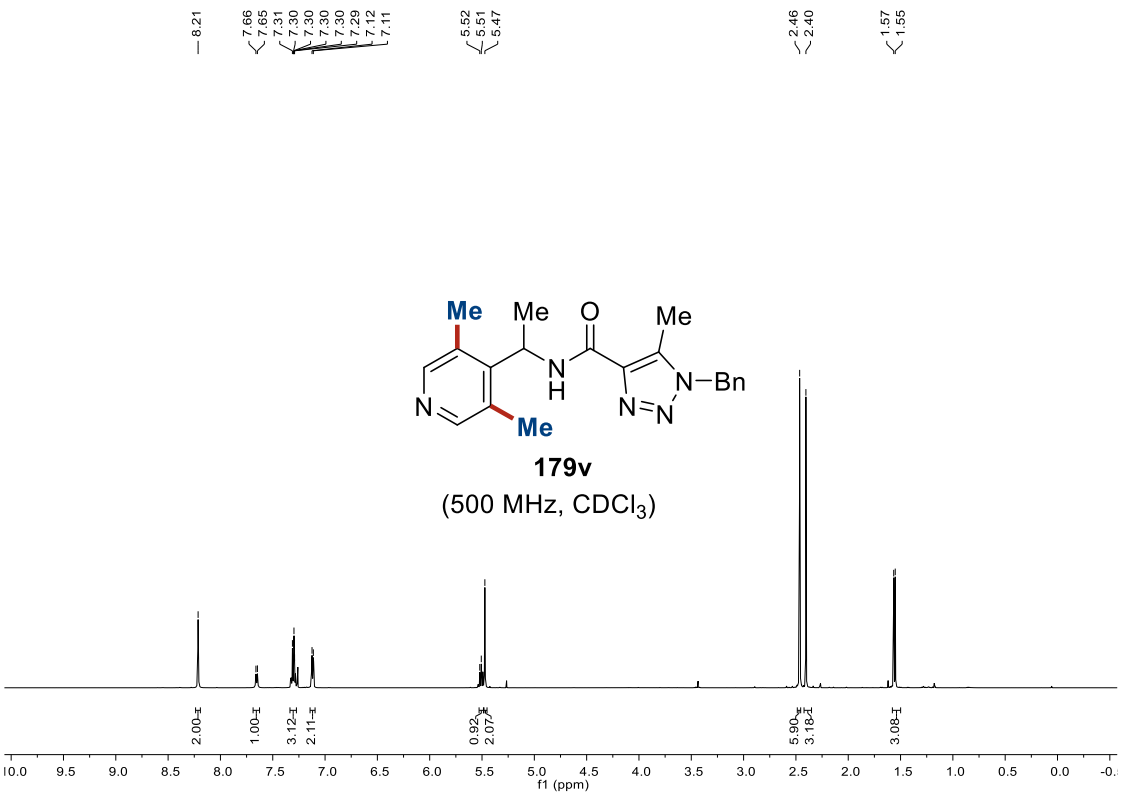


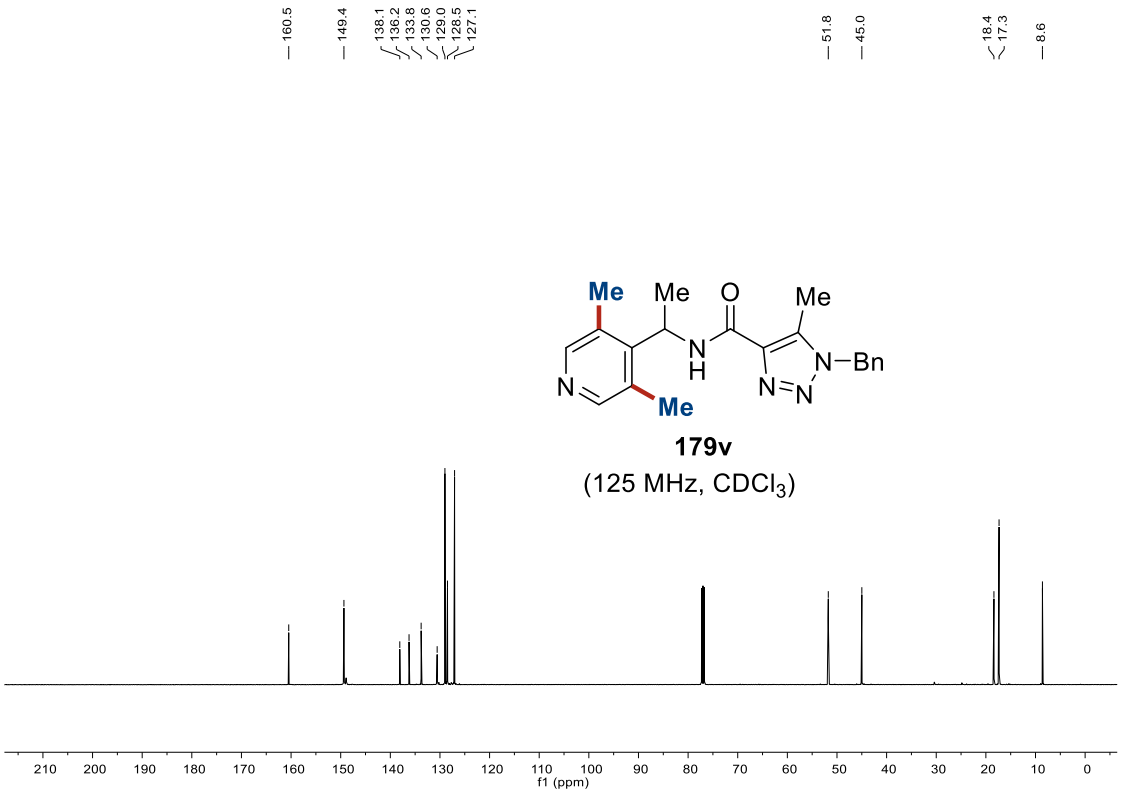


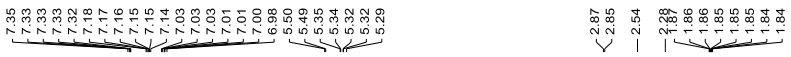
179u

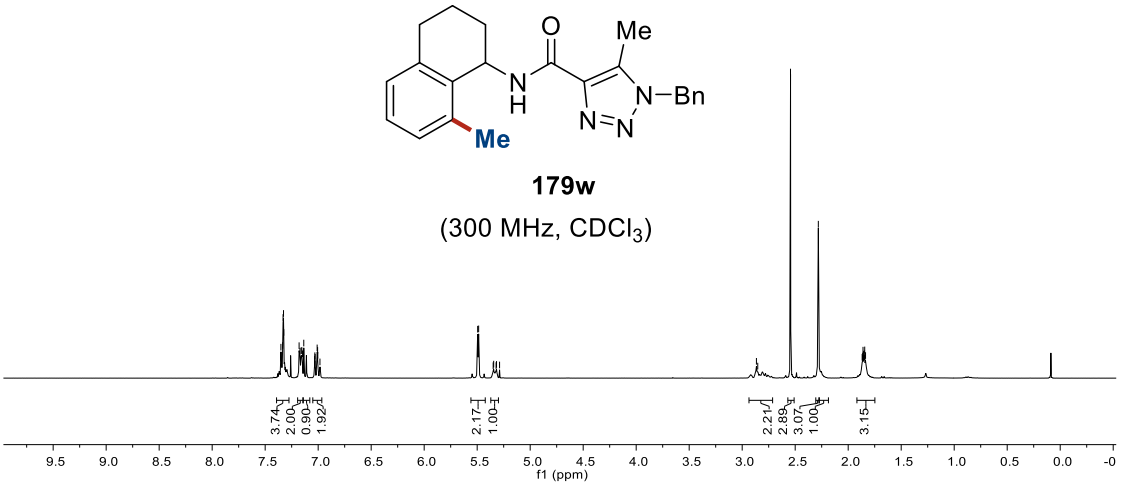
(125 MHz, $CDCl_3$)



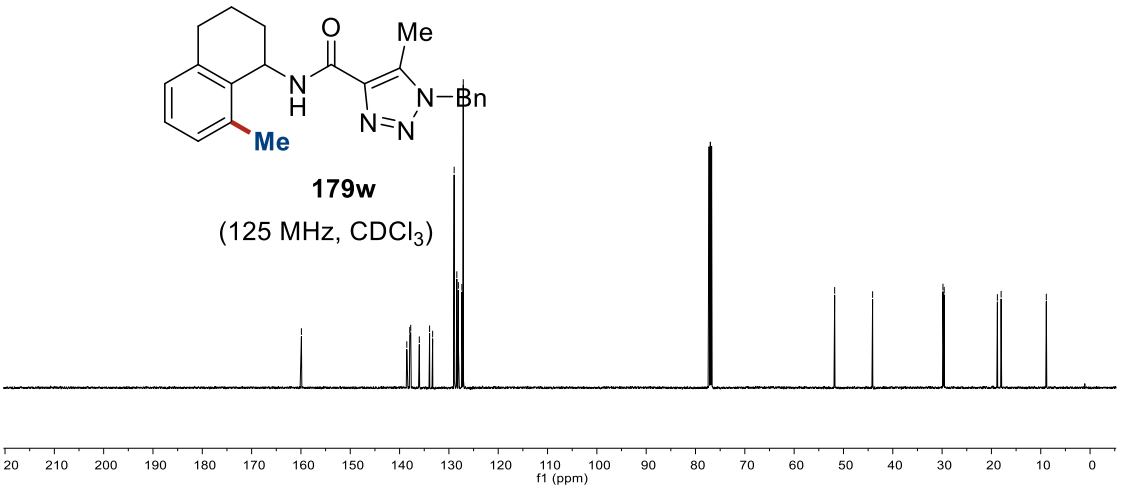

8.21
7.66
7.65
7.31
7.30
7.30
7.30
7.29
7.12
7.11
5.52
5.51
5.47
2.46
2.40
1.57
1.55
Me
Me
O
Me
N
H
N–Bn
N=N
N
Me
179v
(500 MHz, CDCl3)
2.00
1.00
3.12
2.11
0.92
2.07
5.90
3.18
3.08
f1 (ppm)

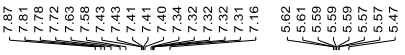

160.5
149.4
138.1
136.2
133.8
130.6
129.0
128.5
127.1
51.8
45.0
18.4
17.3
8.6
Me
Me
O
Me
N
H
N–Bn
N=N
N
Me
179v
(125 MHz, CDCl3)
f1 (ppm)

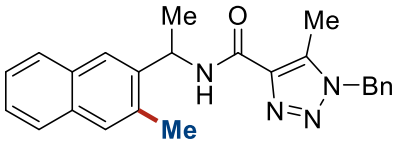

7.35
7.33
7.33
7.33
7.32
7.18
7.17
7.16
7.15
7.15
7.14
7.03
7.03
7.03
7.01
7.01
7.00
6.98
5.50
5.49
5.35
5.34
5.32
5.32
5.29
2.87
2.85
2.54
2.28
2.27
1.87
1.86
1.85
1.85
1.85
1.84
1.84


O
Me
N
H
N–Bn
N=N
Me
179w
(300 MHz, CDCl3)
3.74
2.00
0.90
1.92
2.17
1.00
2.21
2.89
3.07
1.00
3.15
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 -0
f1 (ppm)


159.9
138.5
137.9
137.7
136.0
133.9
133.3
128.9
128.4
128.1
127.4
127.1
51.8
44.1
29.8
29.6
18.8
18.0
8.9

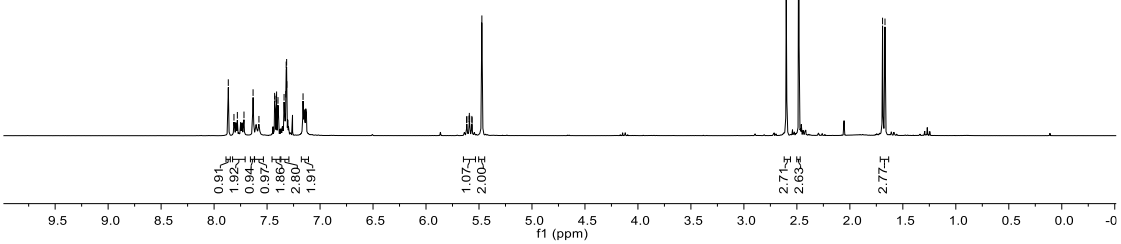

O
Me
N
H
N–Bn
N=N
Me
179w
(125 MHz, CDCl3)
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

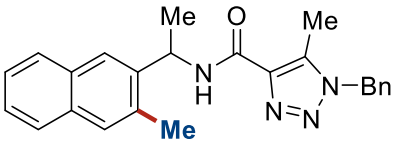




179x

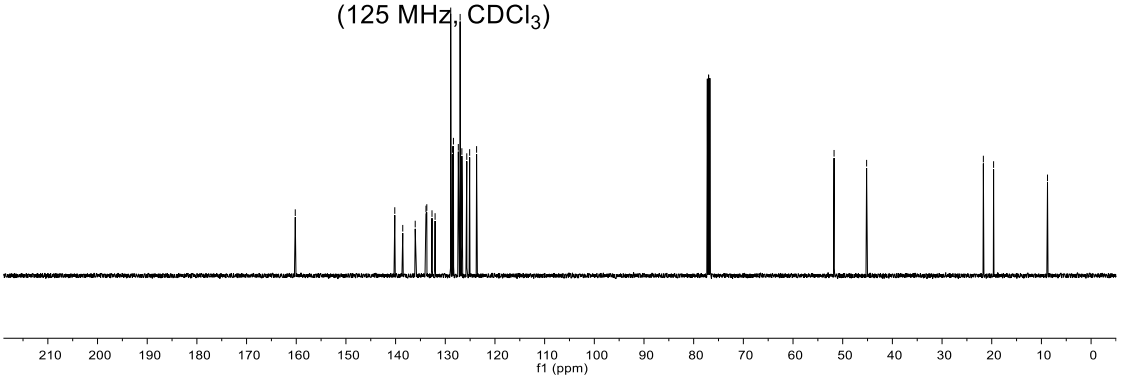
(300 MHz, $CDCl_3$)

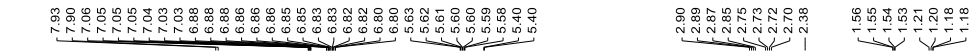


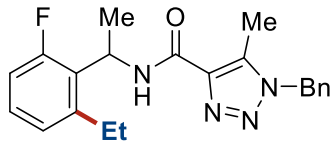


179x

(125 MHz, $CDCl_3$)

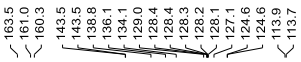


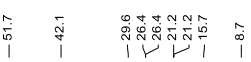


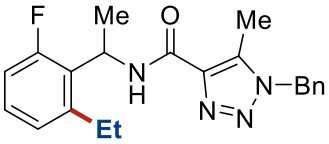


196h

(400 MHz, $CDCl_3$)

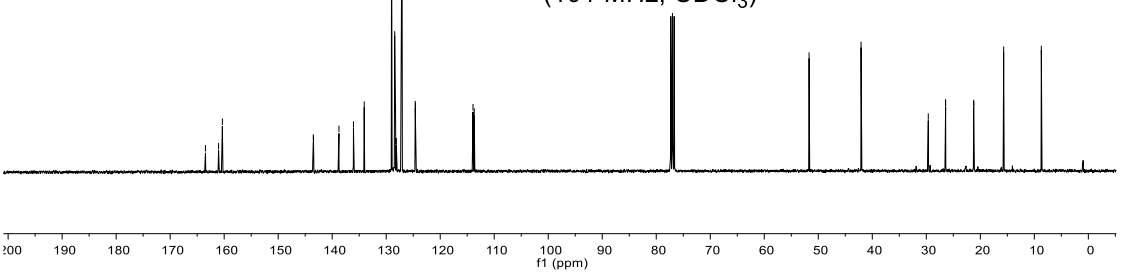


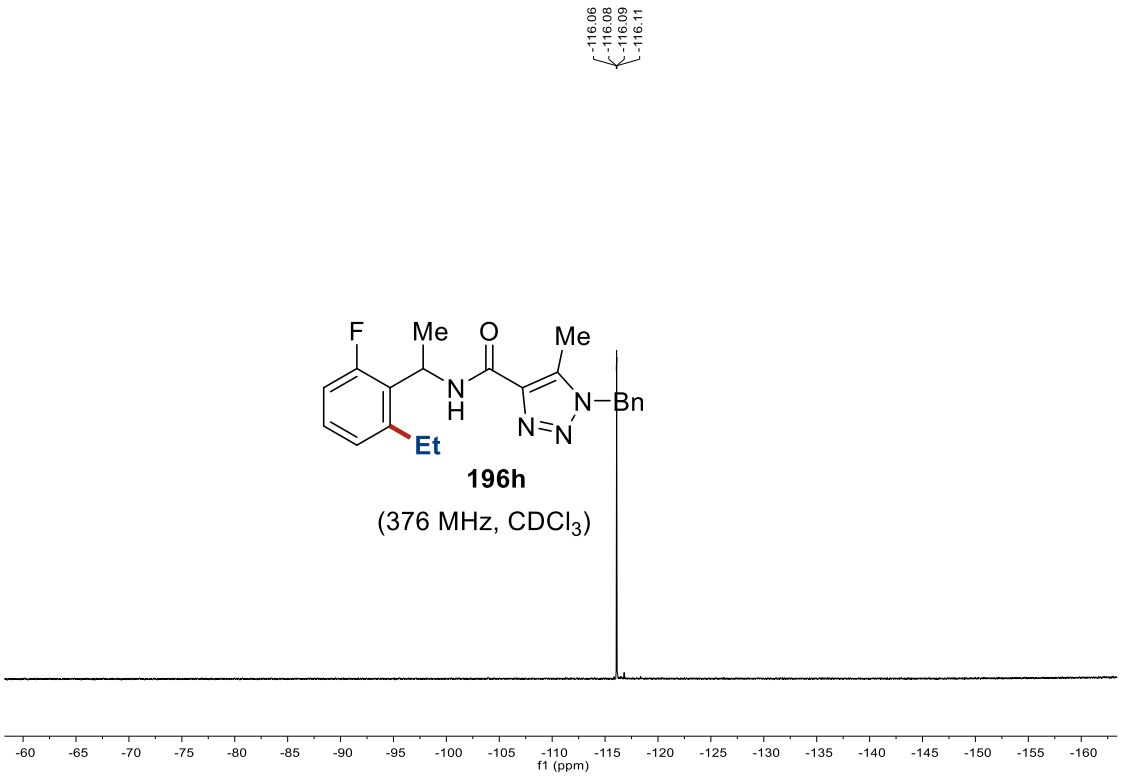


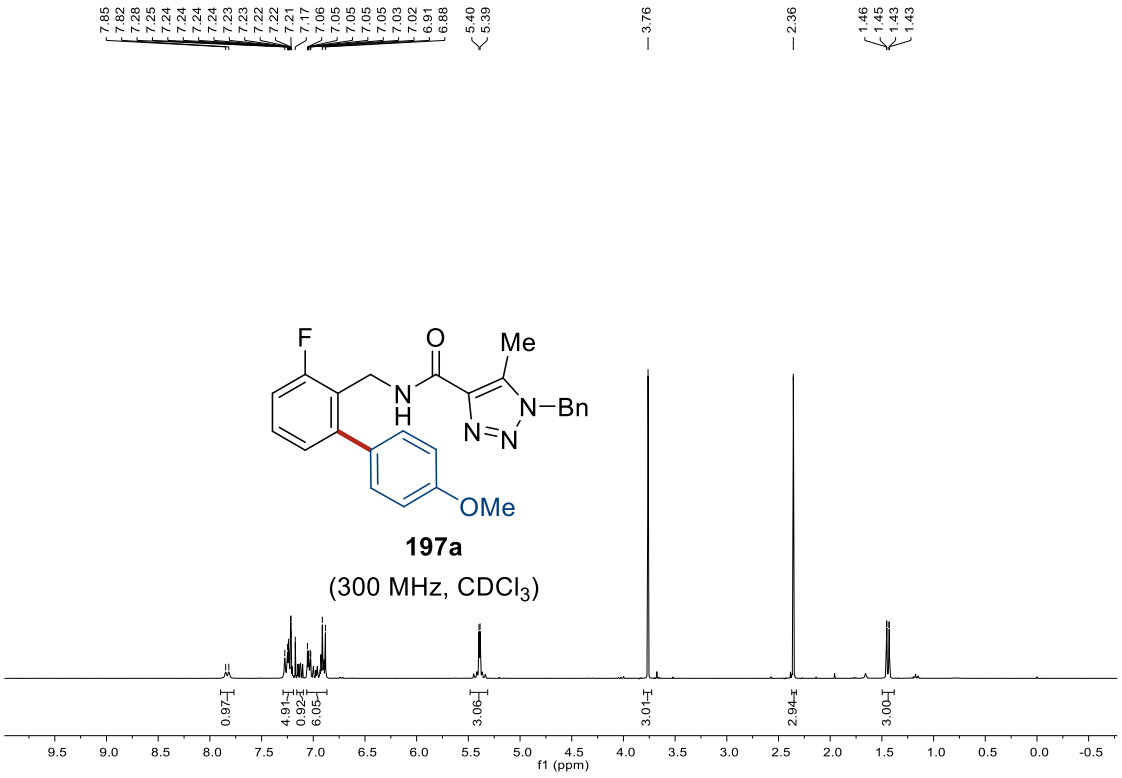


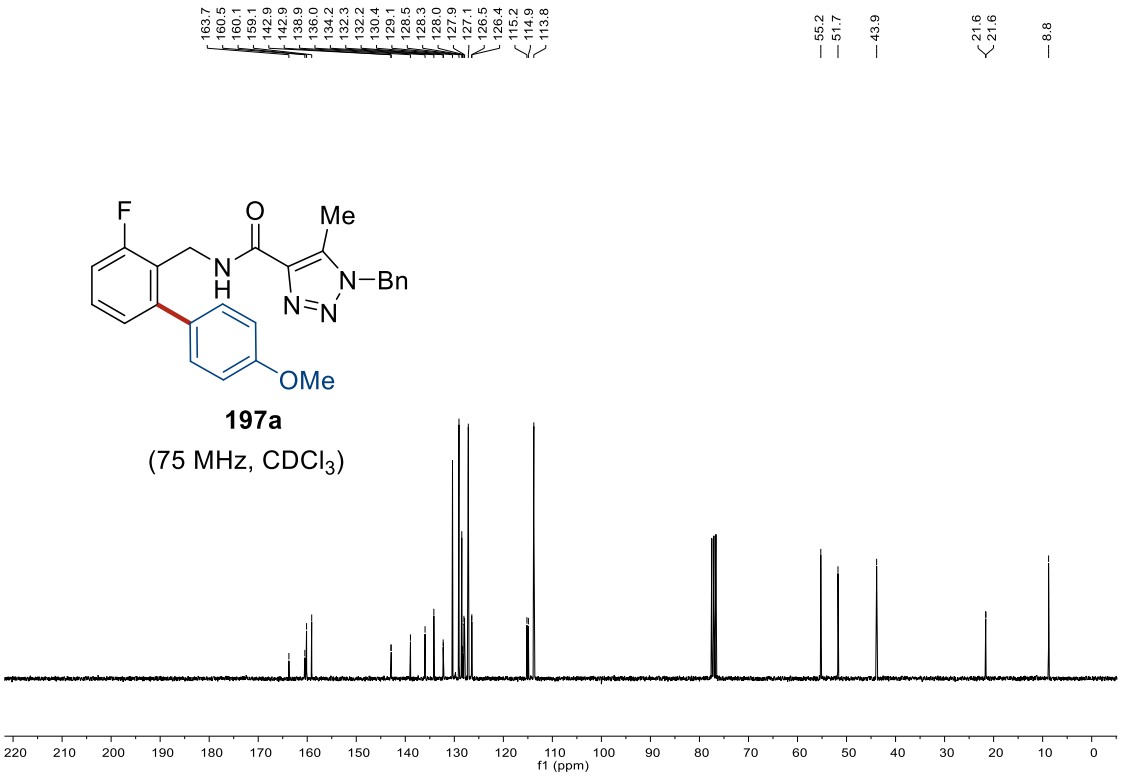
196h

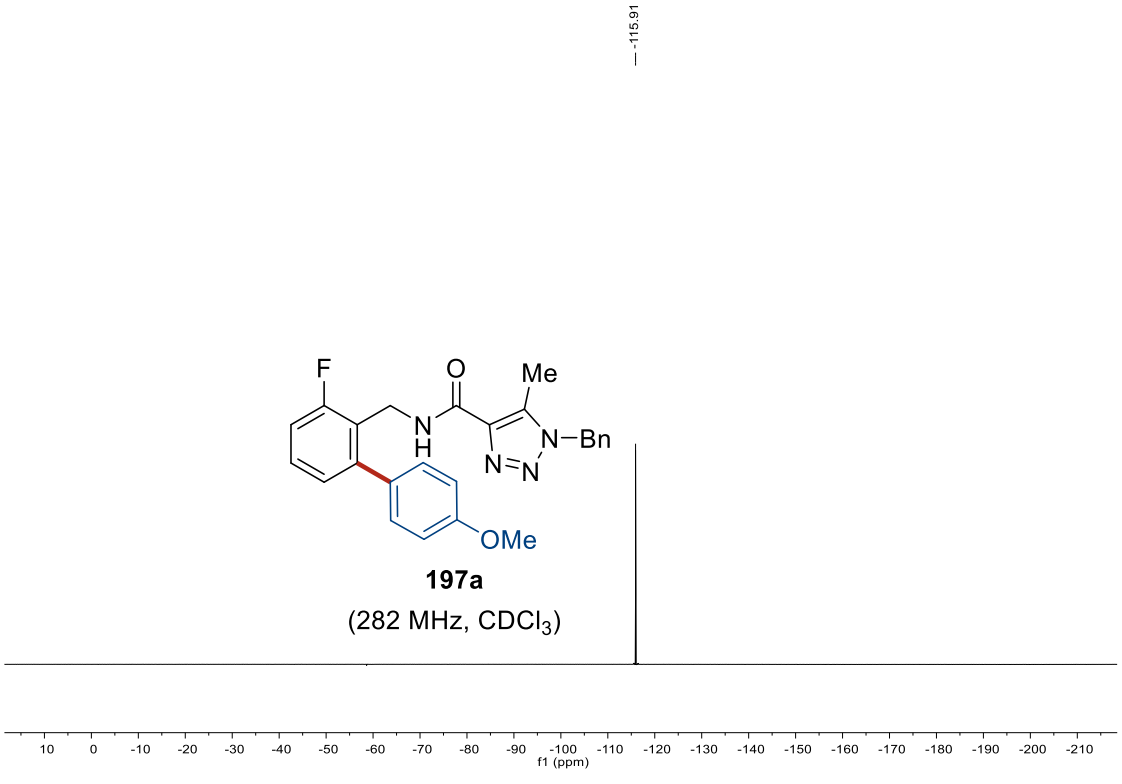
(101 MHz, $CDCl_3$)

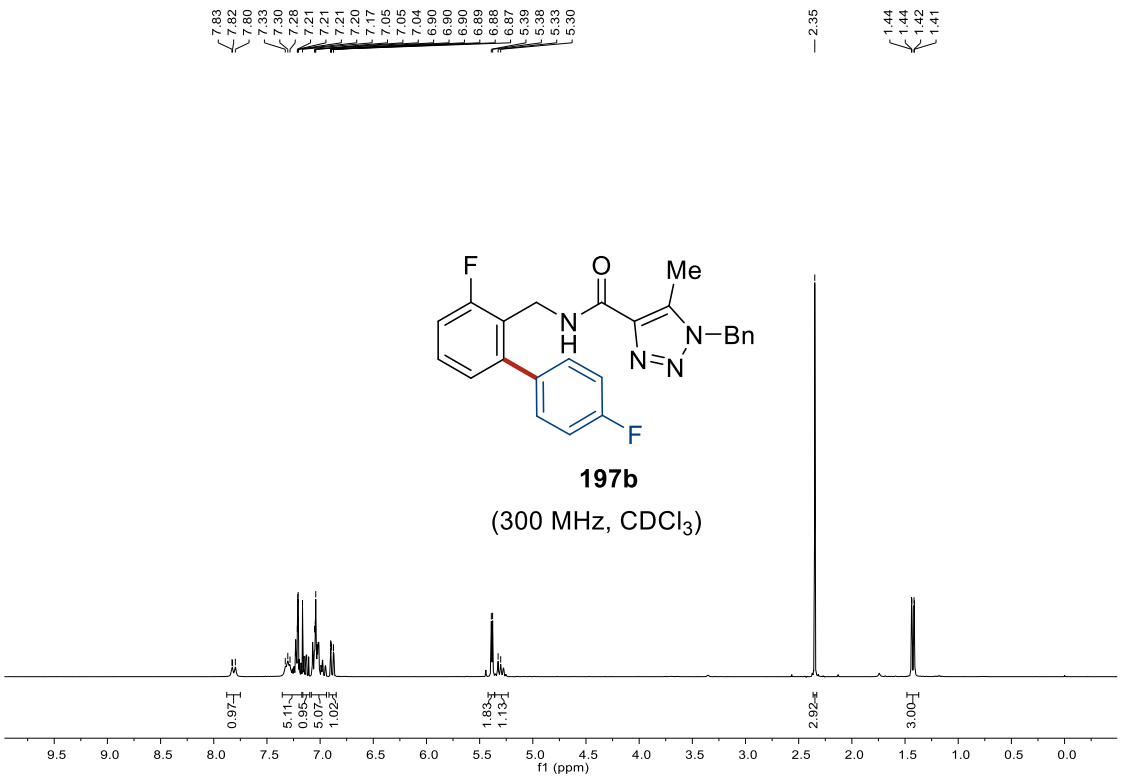



-116.06
-116.08
-116.09
-116.11
F
Me
O
Me
N
H
N–Bn
N=N
Et
196h
(376 MHz, CDCl3)
-60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160
f1 (ppm)


7.85
7.82
7.28
7.25
7.24
7.24
7.24
7.24
7.23
7.23
7.22
7.22
7.21
7.17
7.06
7.05
7.05
7.05
7.05
7.03
7.02
6.91
6.88
5.40
5.39
3.76
2.36
1.46
1.45
1.43
1.43
F
O
Me
N
H
N–Bn
N=N
OMe
197a
(300 MHz, CDCl3)
0.97
4.91
0.92
6.05
3.06
3.01
2.94
3.00
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 -0.5
f1 (ppm)

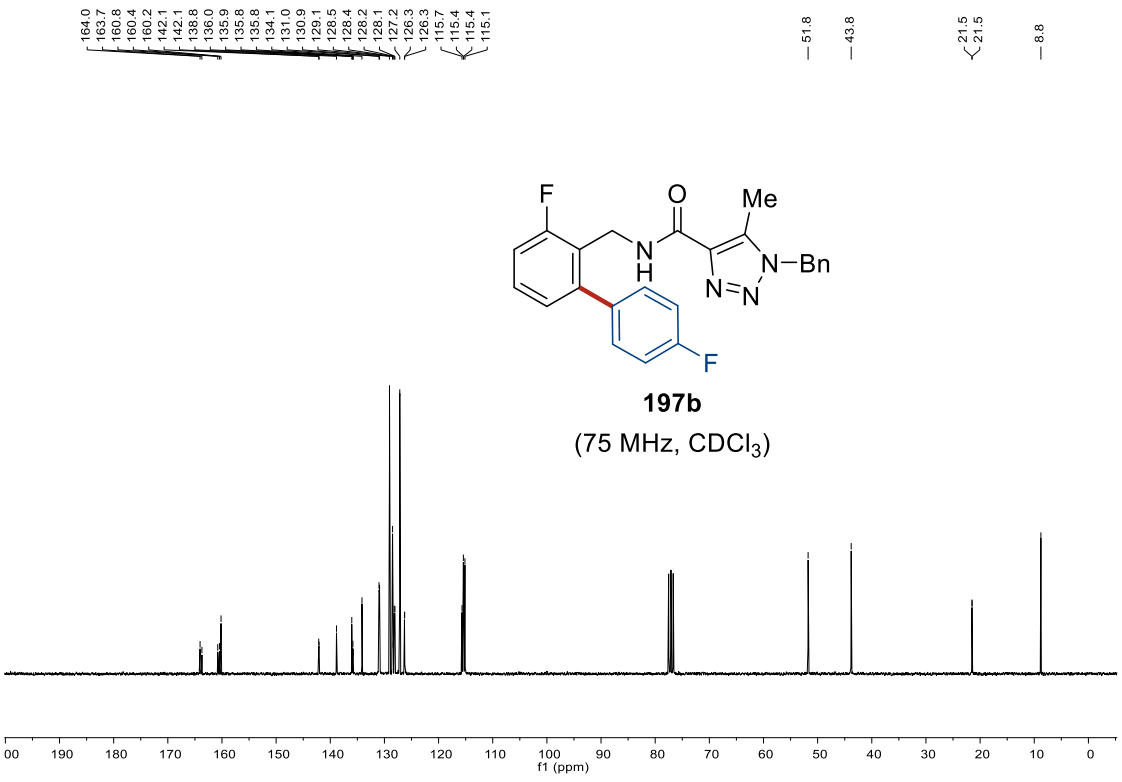

163.7
160.5
160.1
159.1
142.9
142.9
138.9
136.0
134.2
132.3
132.2
130.4
129.1
128.5
128.3
128.0
127.9
127.1
126.5
126.4
115.2
114.9
113.8
55.2
51.7
43.9
21.6
21.6
8.8
F
O
Me
N
H
N–Bn
N=N
OMe
197a
(75 MHz, CDCl3)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-115.91
F
O
Me
N
H
N–Bn
N=N
OMe
197a
(282 MHz, CDCl3)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)



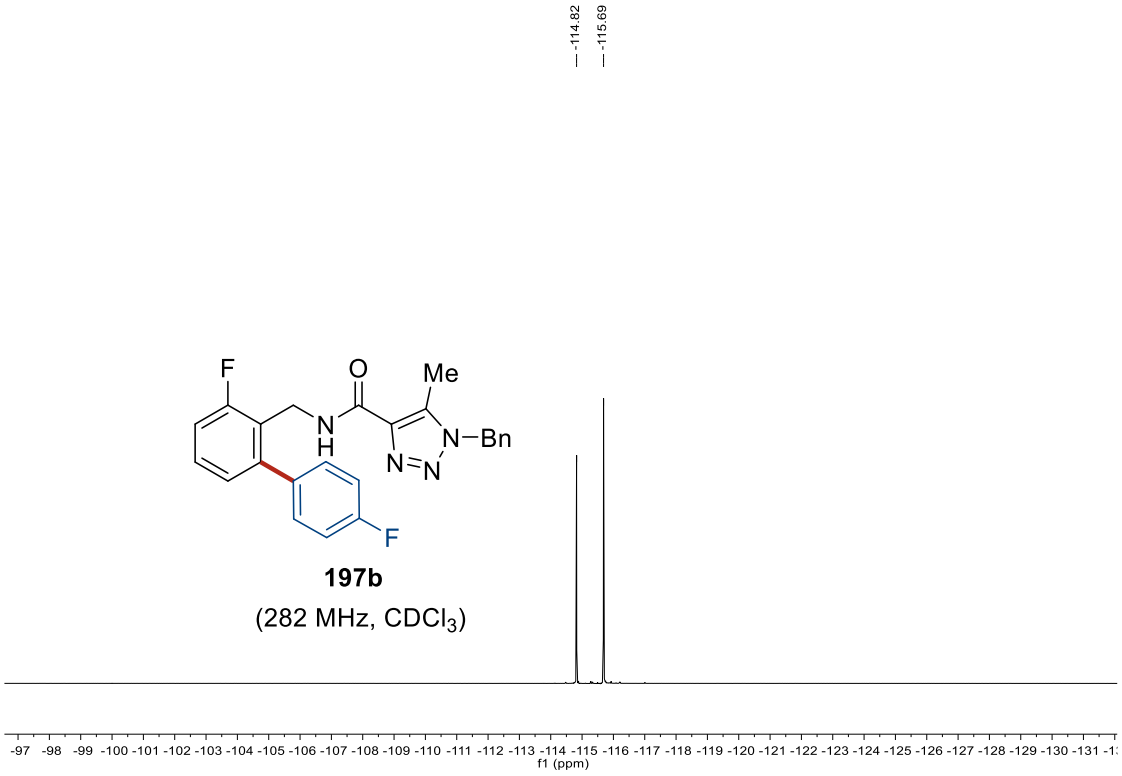
197b

(300 MHz, $CDCl_3$)



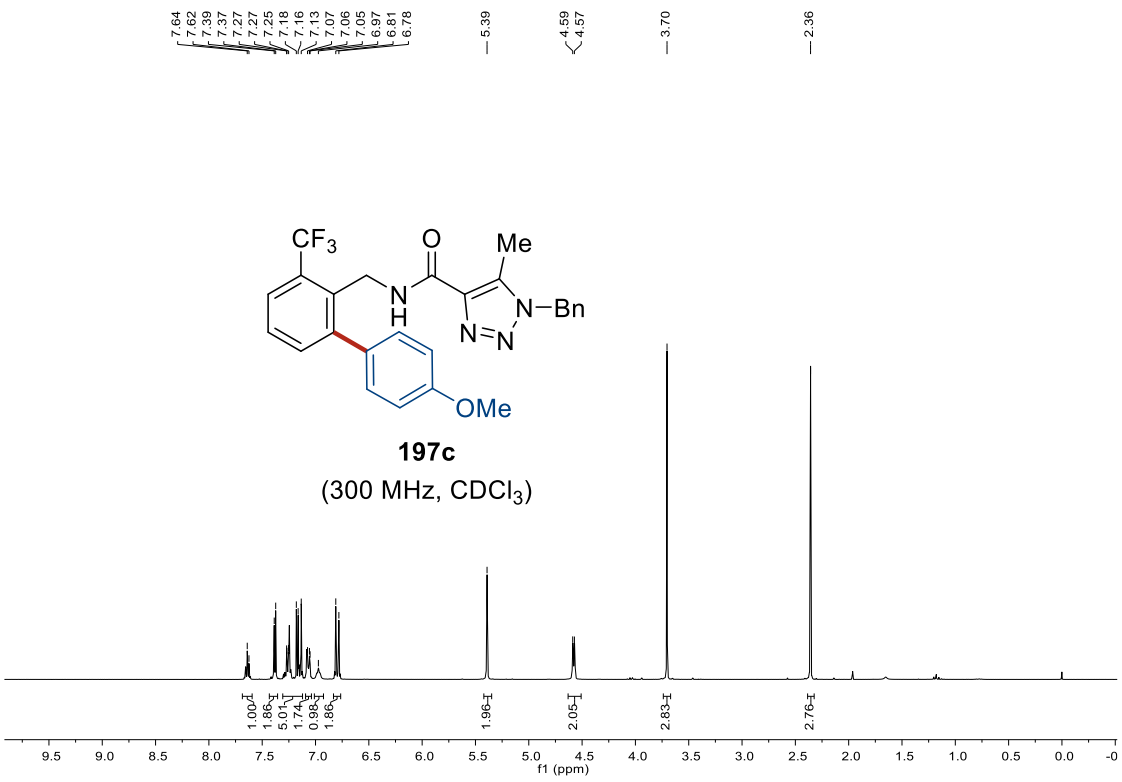
197b

(75 MHz, $CDCl_3$)



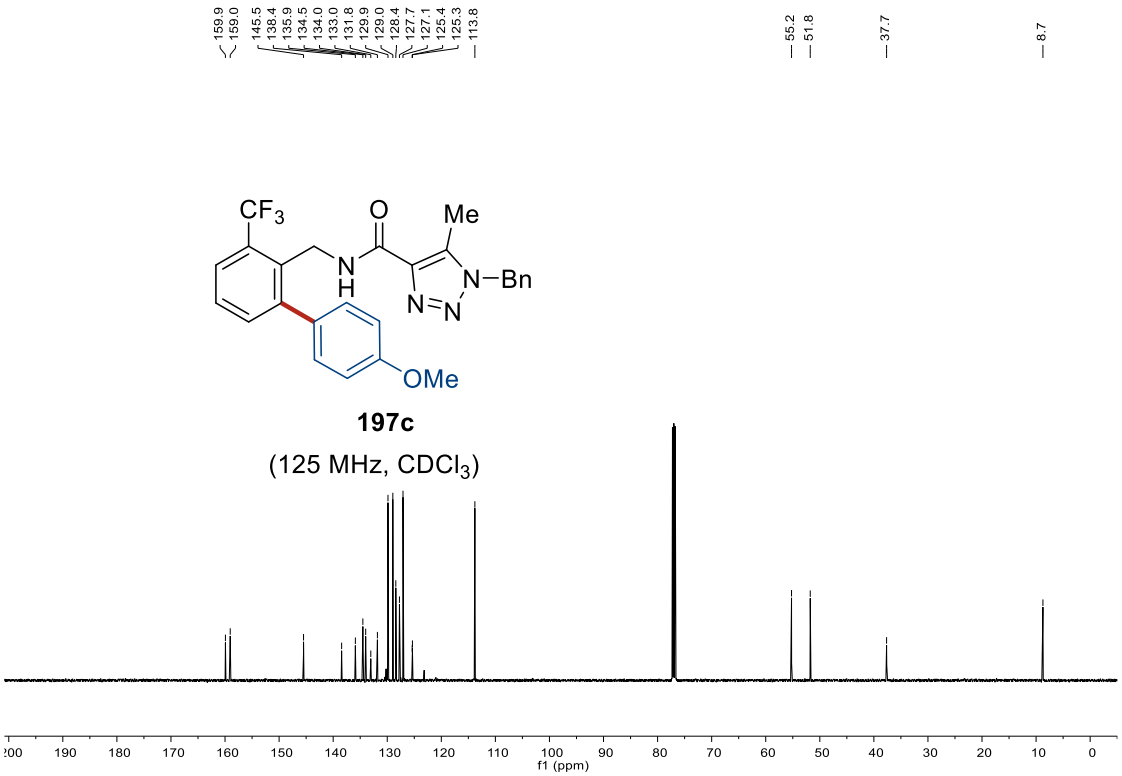
197b

(282 MHz, $CDCl_3$)



197c

(300 MHz, $CDCl_3$)

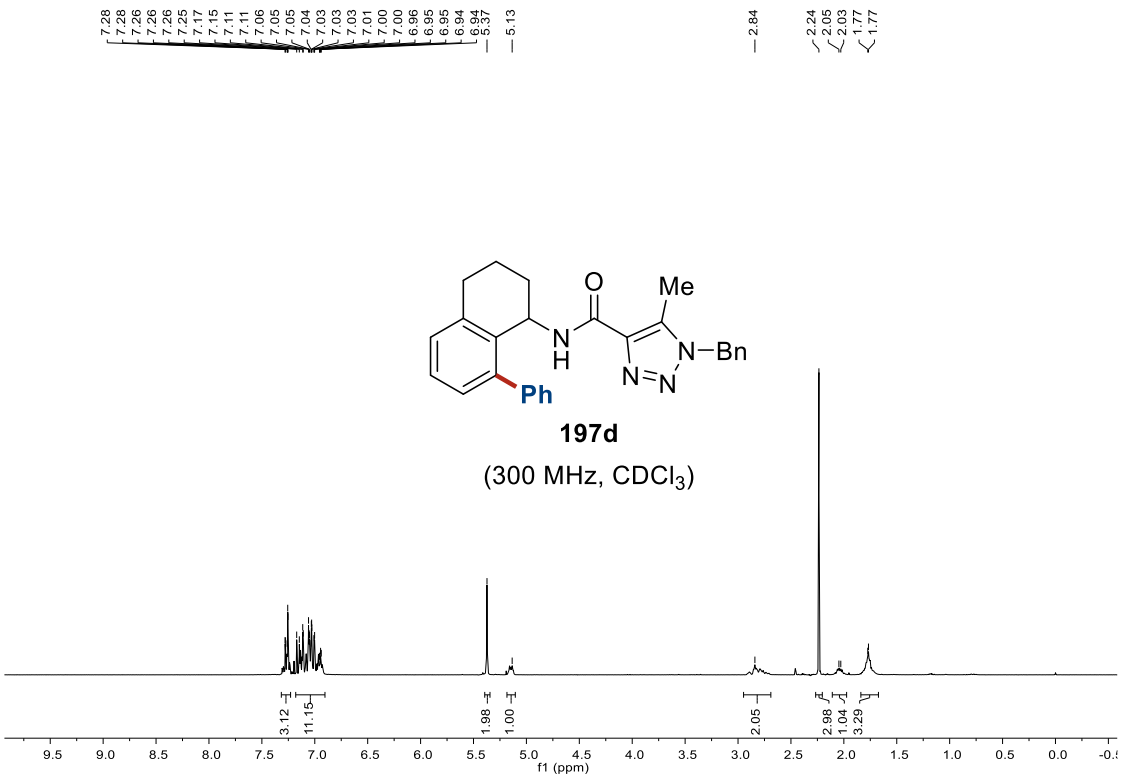


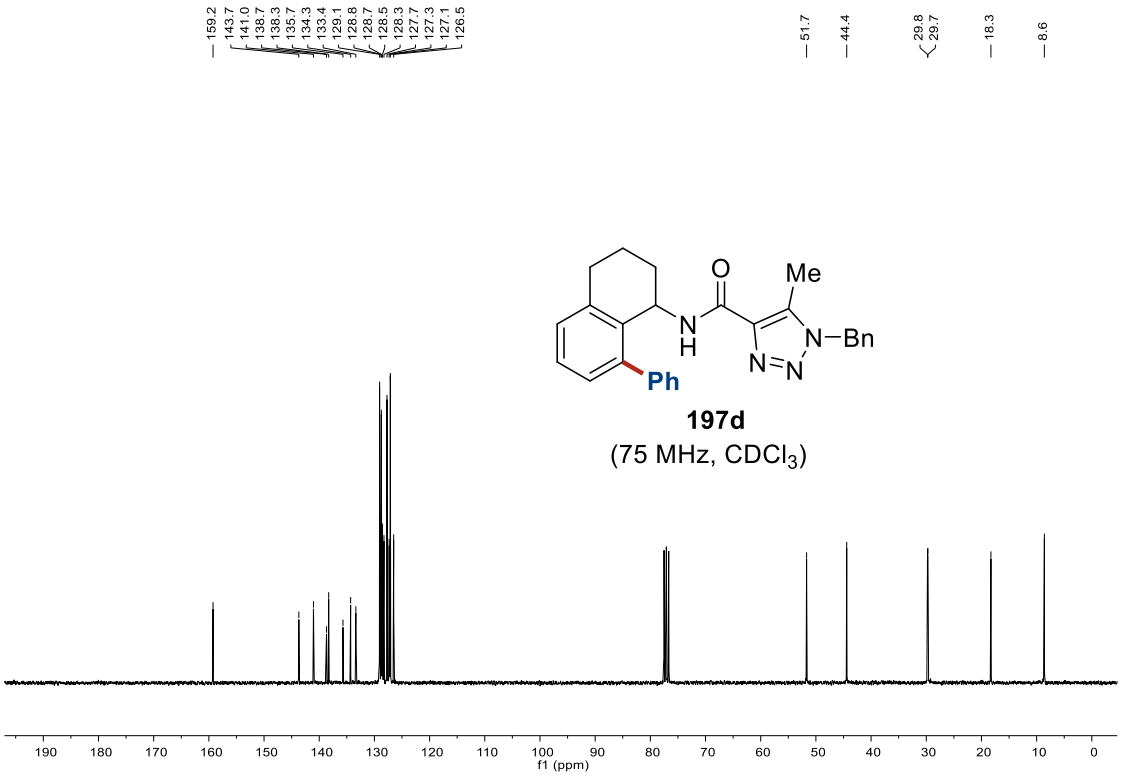
197c

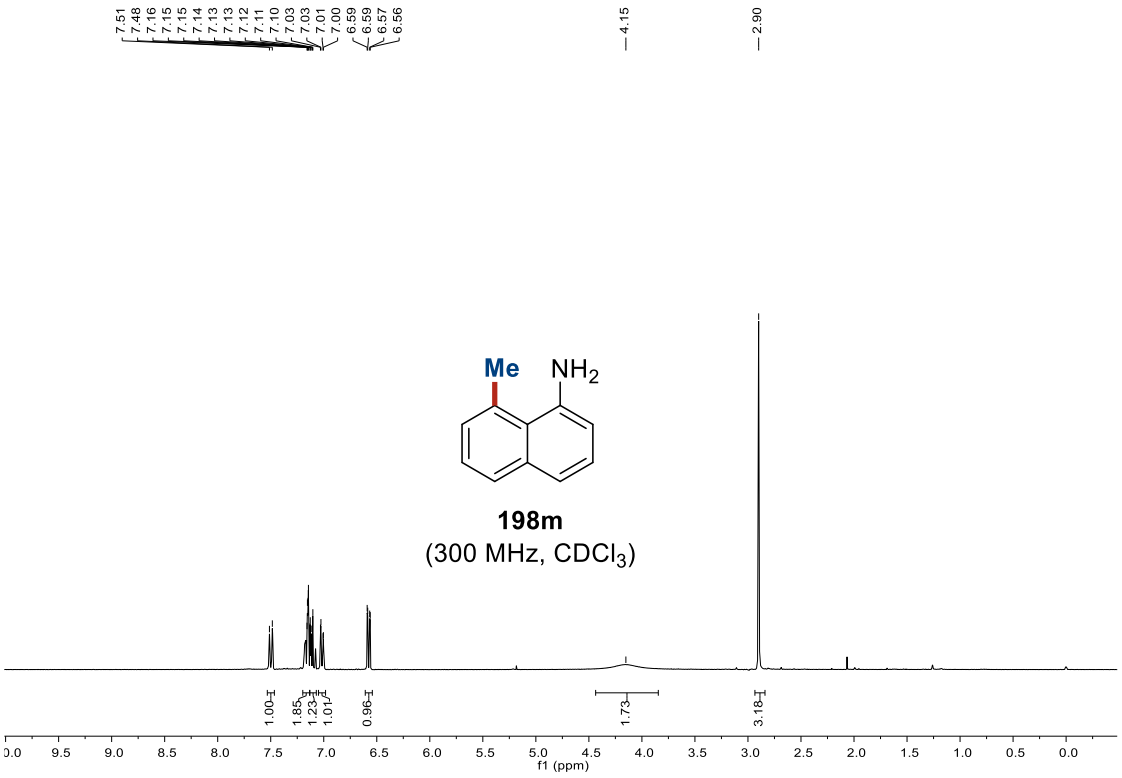
(125 MHz, $CDCl_3$)

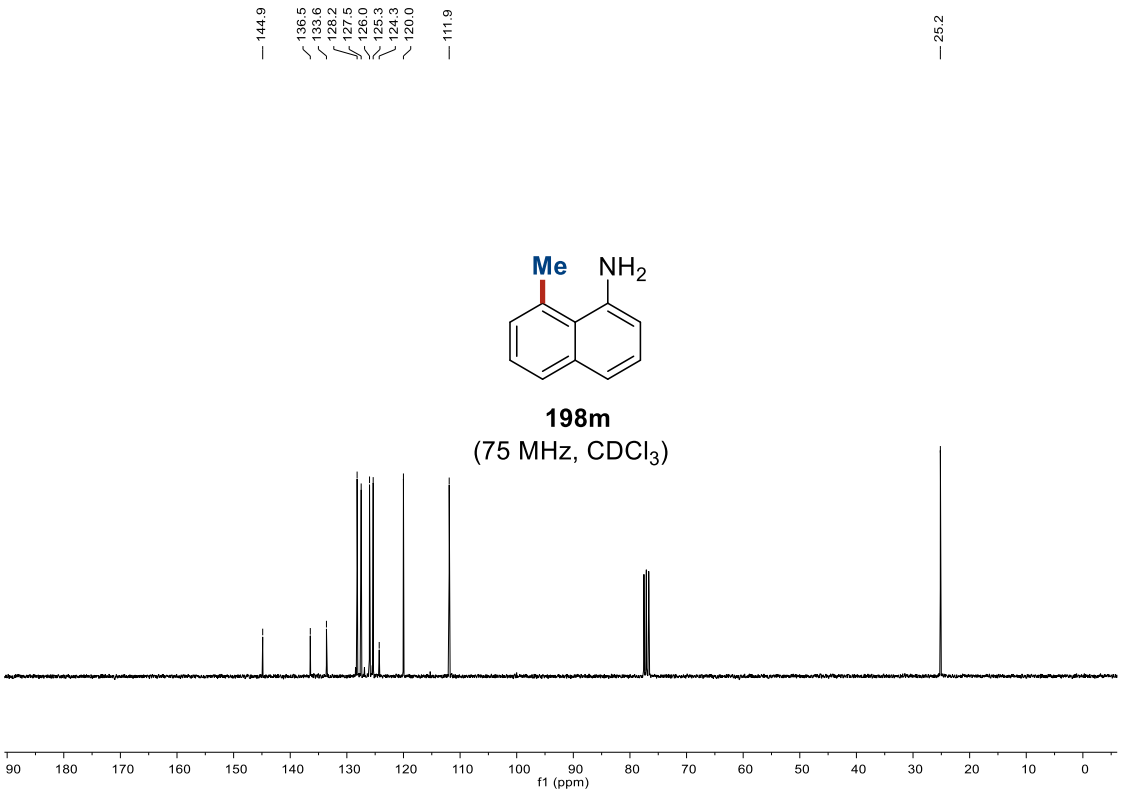
197c

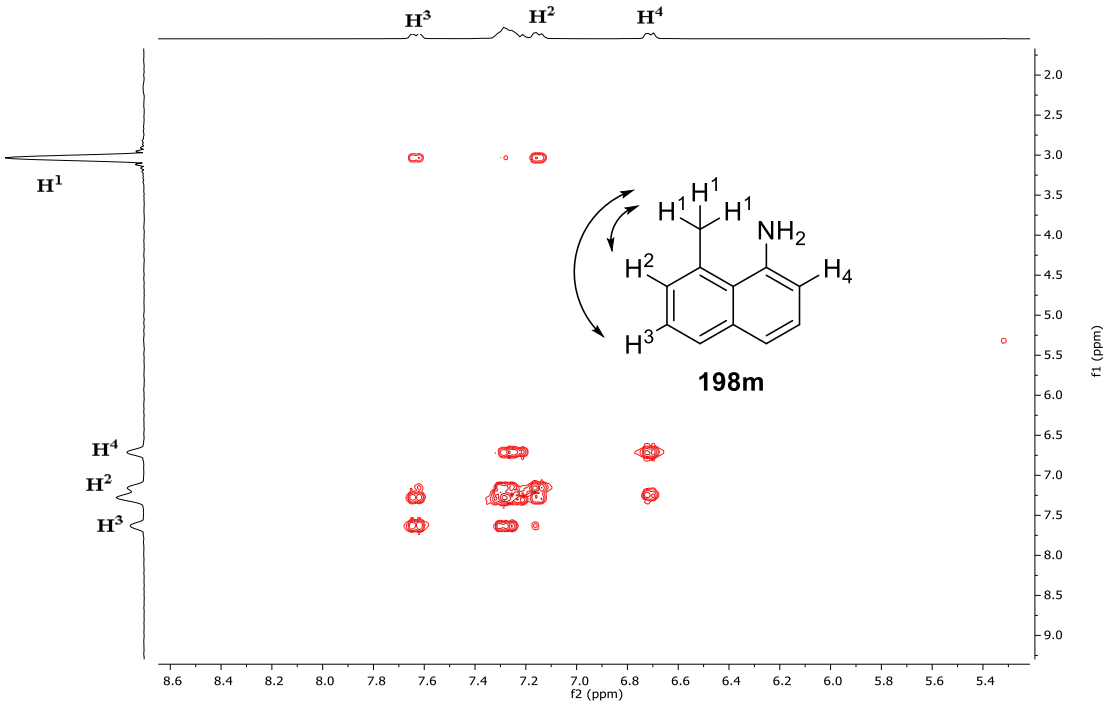
(282 MHz, $CDCl_3$)

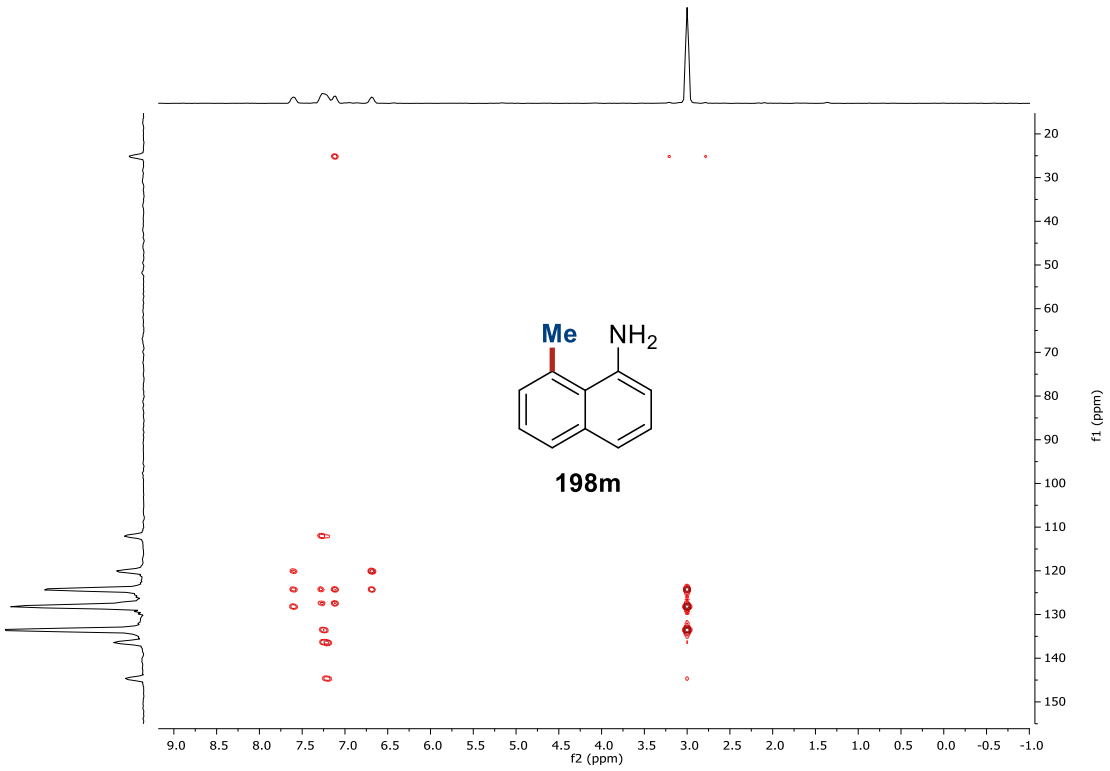

7.28
7.28
7.26
7.26
7.26
7.25
7.17
7.15
7.11
7.06
7.05
7.05
7.04
7.03
7.03
7.03
7.01
7.00
7.00
6.96
6.95
6.94
6.94
5.37
5.13
2.84
2.24
2.05
2.03
1.77
1.77
O
Me
N
H
N–Bn
N=N
Ph
197d
(300 MHz, CDCl3)
3.12
11.15
1.98
1.00
2.05
2.98
1.04
3.29
f1 (ppm)

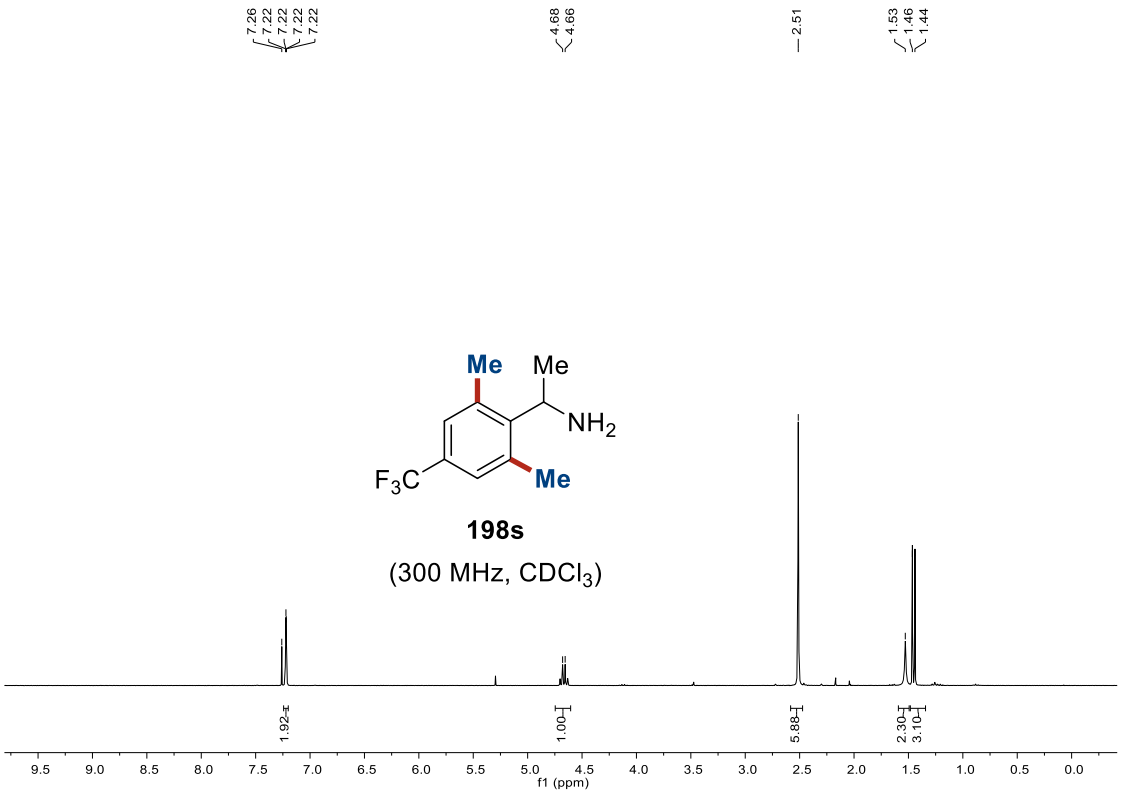

159.2
143.7
141.0
138.7
138.3
135.7
134.3
133.4
129.1
128.8
128.7
128.5
128.3
127.7
127.3
127.1
126.5
51.7
44.4
29.8
29.7
18.3
8.6
O
Me
N
H
N–Bn
N=N
Ph
197d
(75 MHz, CDCl3)
f1 (ppm)

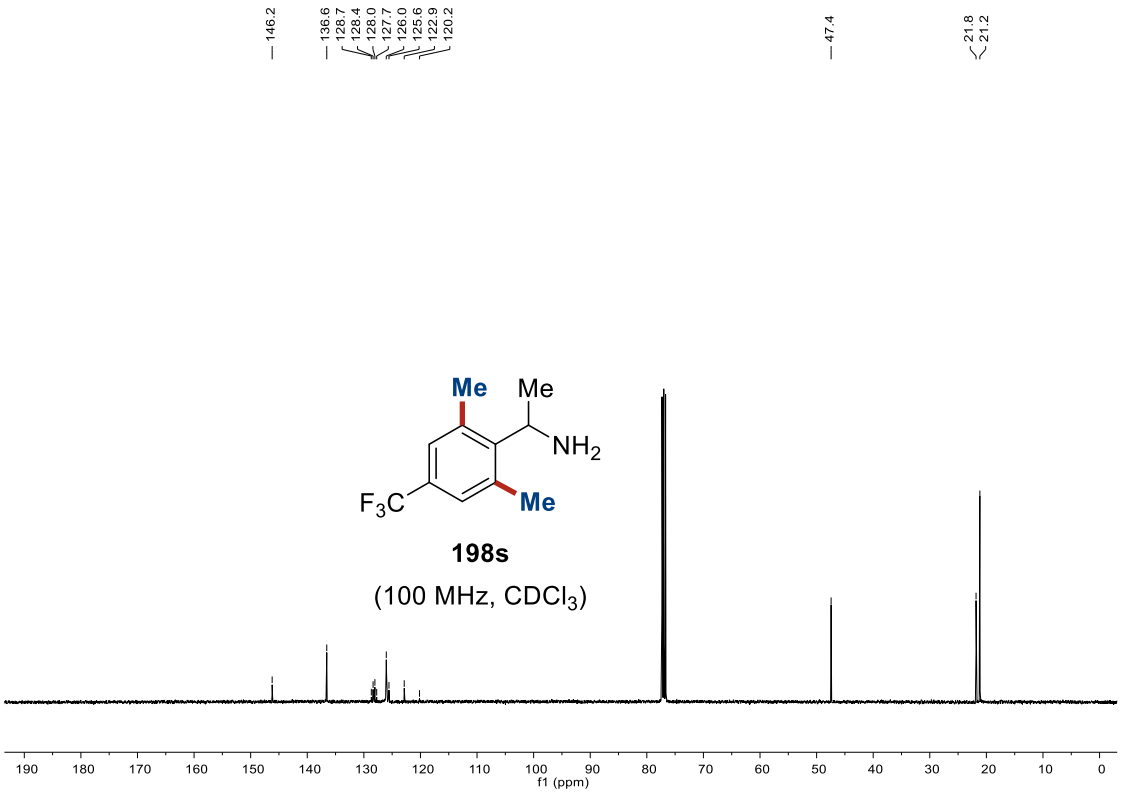

7.51
7.48
7.16
7.15
7.15
7.14
7.13
7.13
7.12
7.11
7.10
7.03
7.03
7.01
7.00
6.59
6.59
6.57
6.56
4.15
2.90
Me
NH2
198m
(300 MHz, CDCl3)
1.00
1.85
1.23
1.01
0.96
1.73
3.18
f1 (ppm)

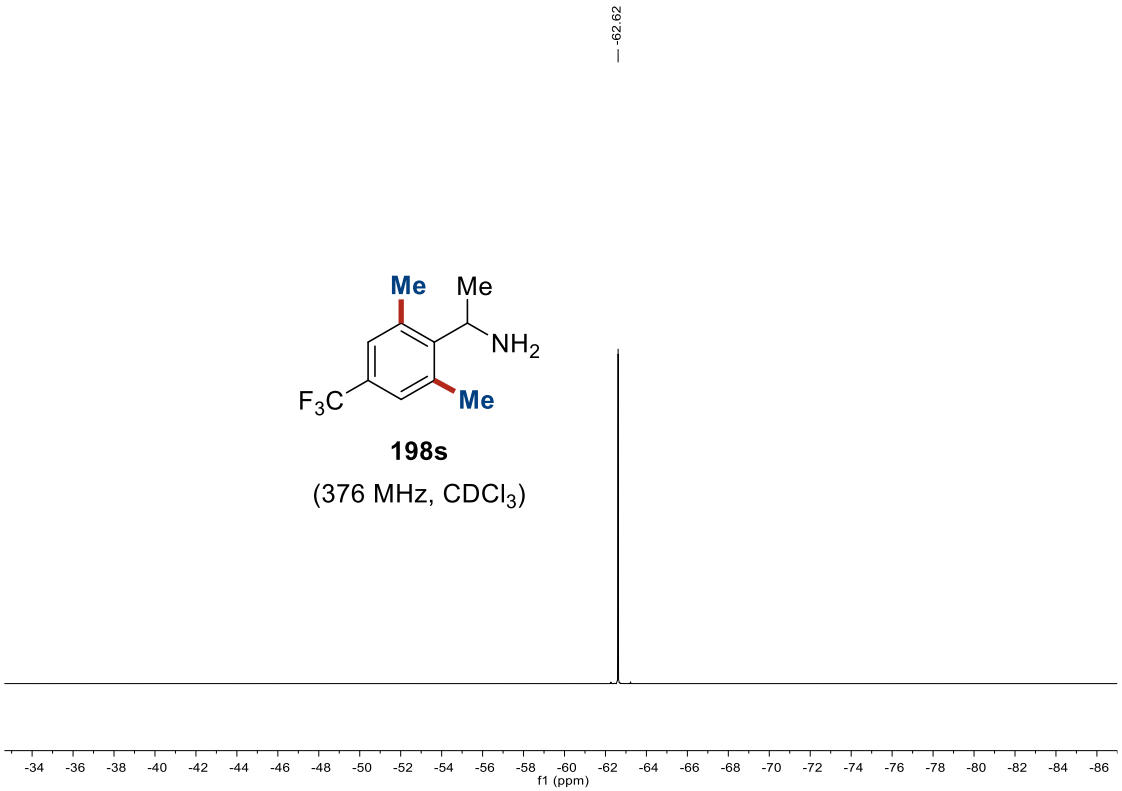

144.9
136.5
133.6
128.2
127.5
126.0
125.3
124.3
120.0
111.9
25.2
Me
NH2
198m
(75 MHz, CDCl3)
f1 (ppm)

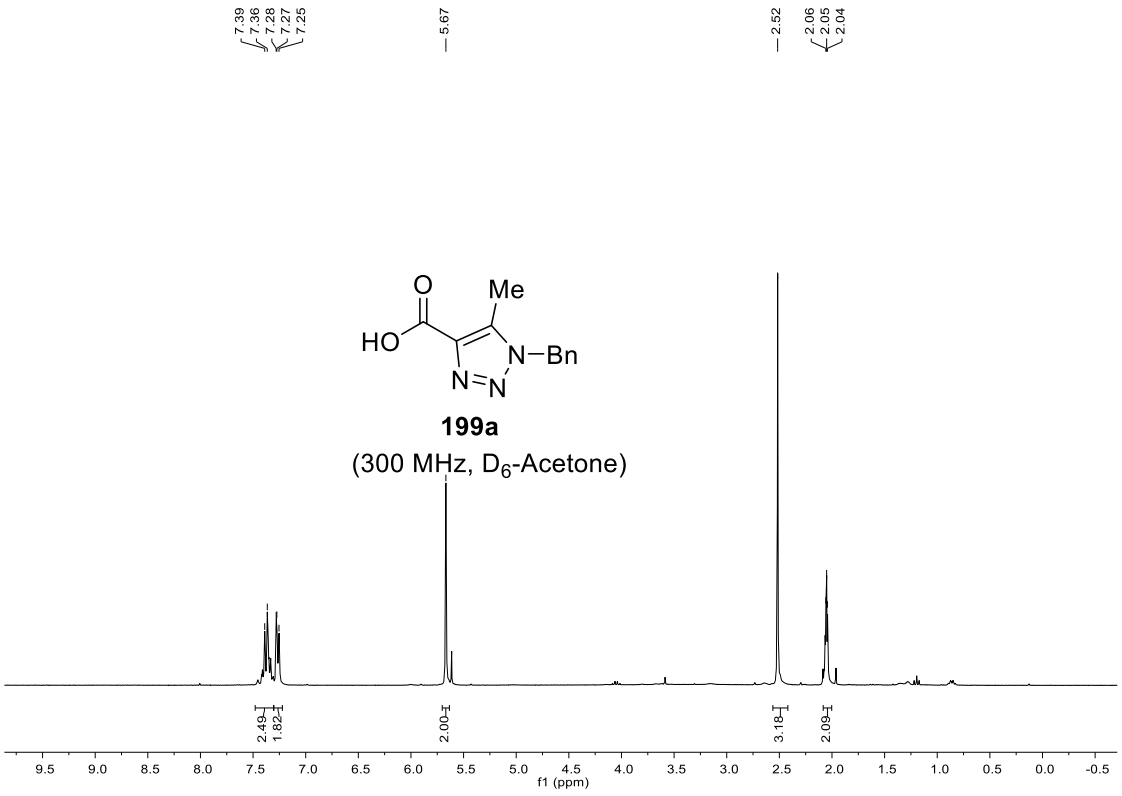

H3
H2
H4
H1
H4
H2
H3
H1
H1
H1
NH2
H2
H4
H3
198m
f2 (ppm)
f1 (ppm)

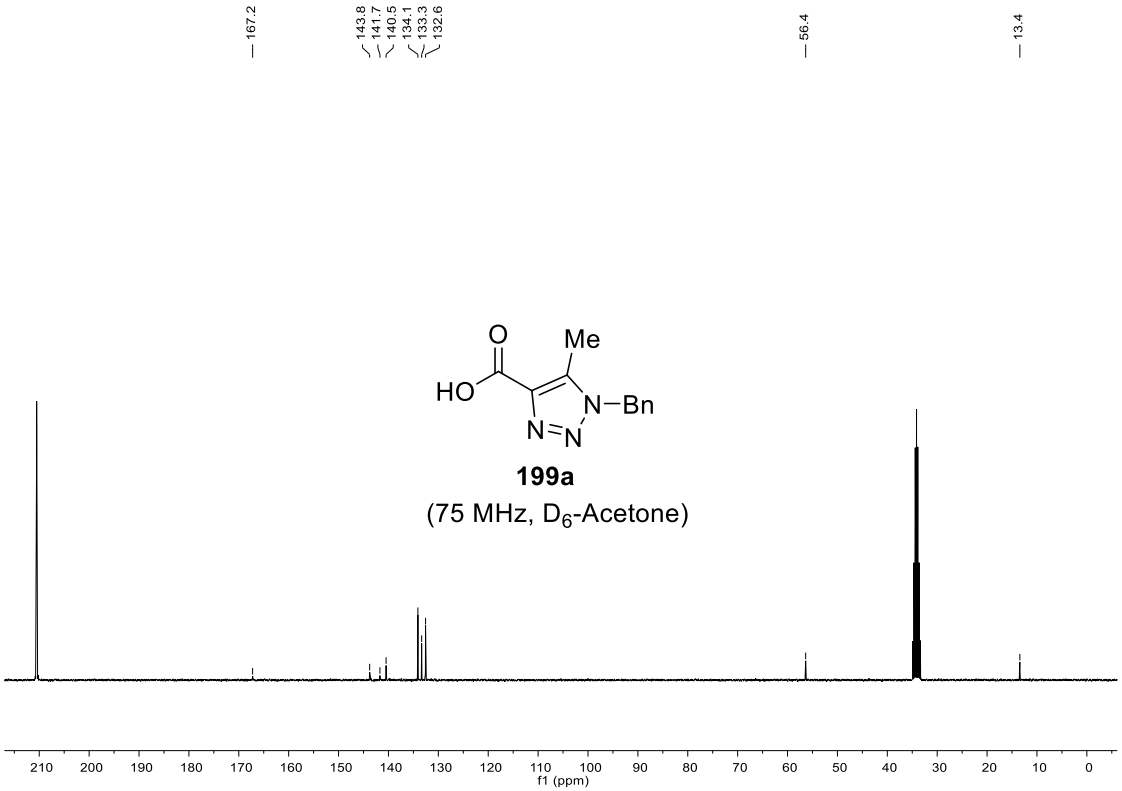

Me
NH2
198m
f2 (ppm)
f1 (ppm)

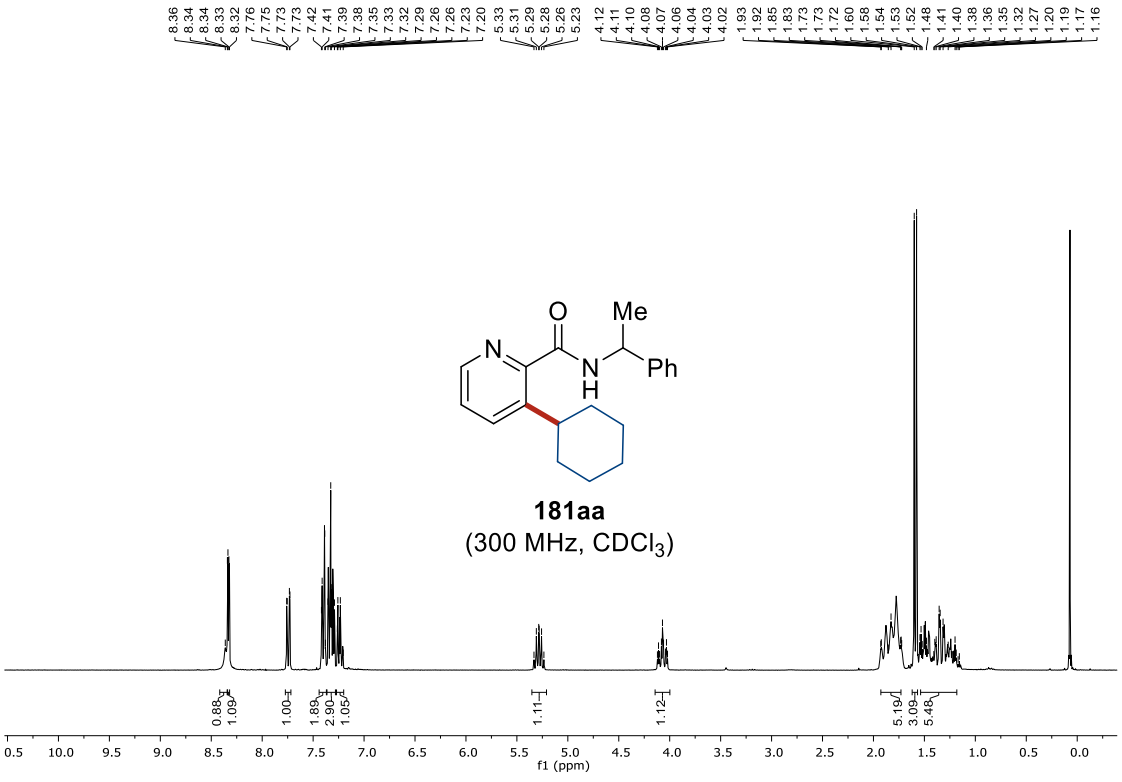

7.26
7.22
7.22
7.22
7.22
4.68
4.66
2.51
1.53
1.46
1.44
Me
Me
NH2
F3C
Me
198s
(300 MHz, CDCl3)
1.92
1.00
5.88
2.30
3.10
f1 (ppm)

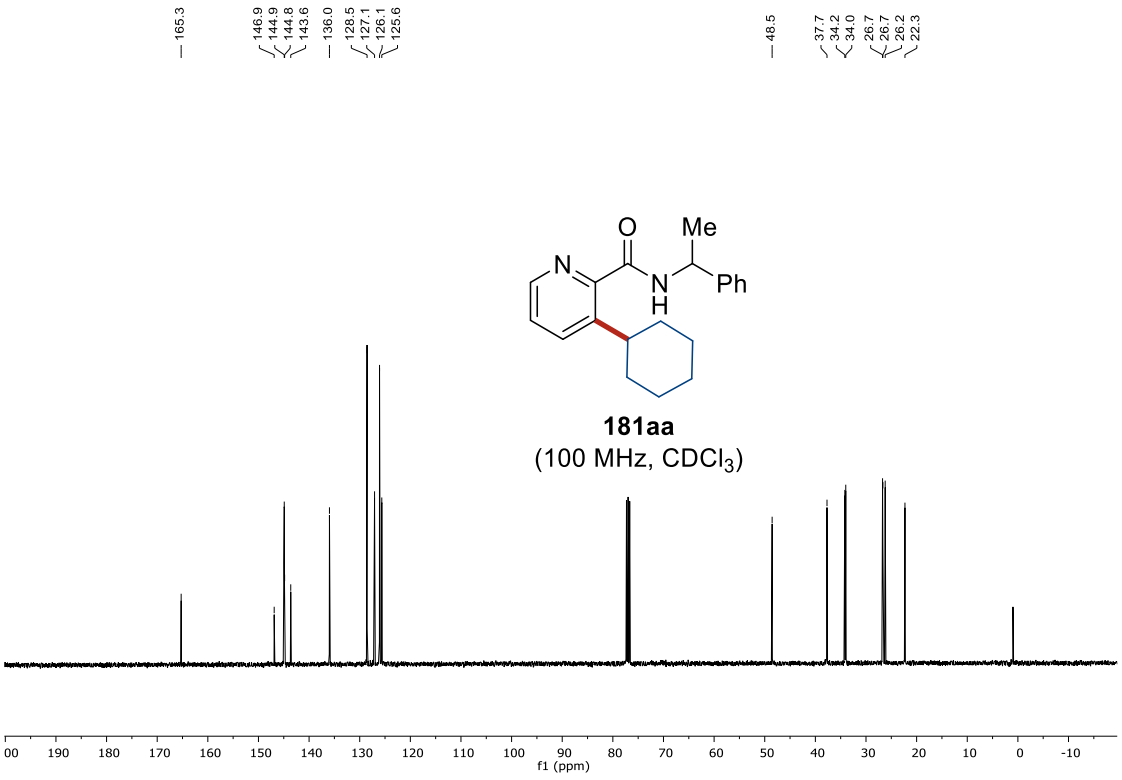

146.2
136.6
128.7
128.4
128.0
127.7
126.0
125.6
122.9
120.2
47.4
21.8
21.2
Me
Me
NH2
F3C
Me
198s
(100 MHz, CDCl3)
f1 (ppm)


-62.62
Me
Me
NH2
F3C
Me
198s
(376 MHz, CDCl3)
-34 -36 -38 -40 -42 -44 -46 -48 -50 -52 -54 -56 -58 -60 -62 -64 -66 -68 -70 -72 -74 -76 -78 -80 -82 -84 -86
f1 (ppm)

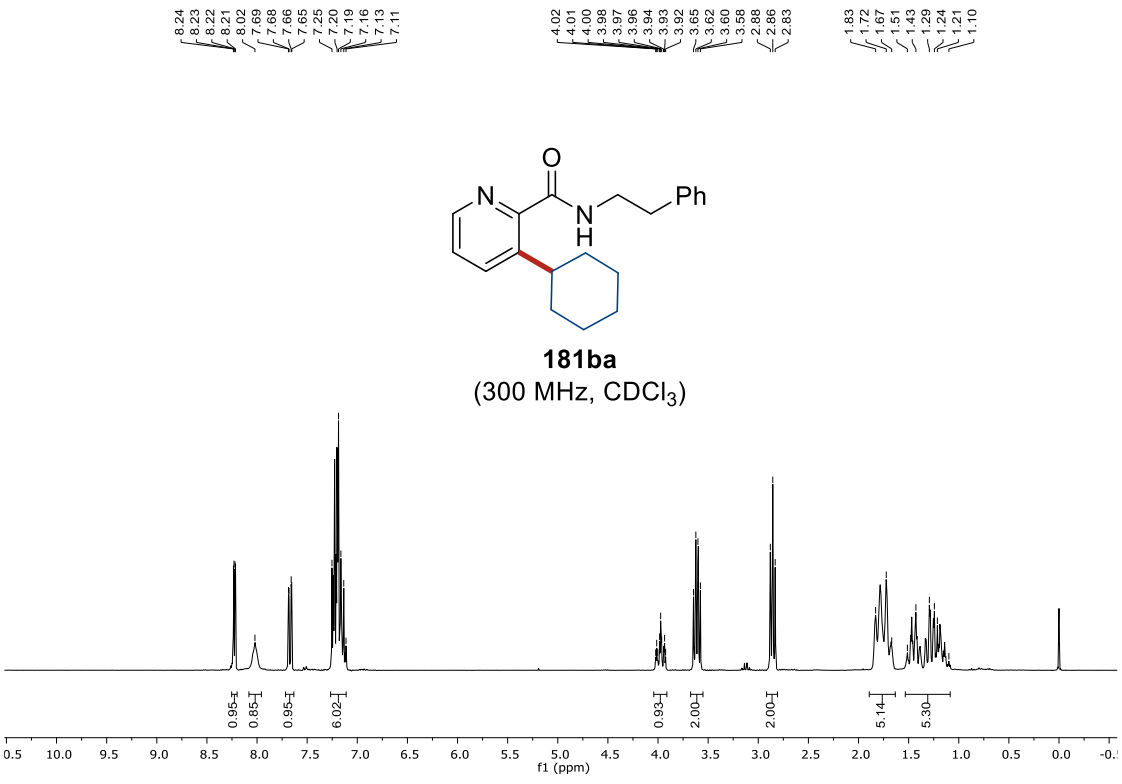

7.39
7.36
7.28
7.27
7.25
5.67
2.52
2.06
2.05
2.04
O
Me
HO
N–Bn
N=N
199a
(300 MHz, D6-Acetone)
2.49
1.82
2.00
3.18
2.09
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


167.2
143.8
141.7
140.5
134.1
133.3
132.6
56.4
13.4
O
Me
HO
N–Bn
N=N
199a
(75 MHz, D6-Acetone)
f1 (ppm)

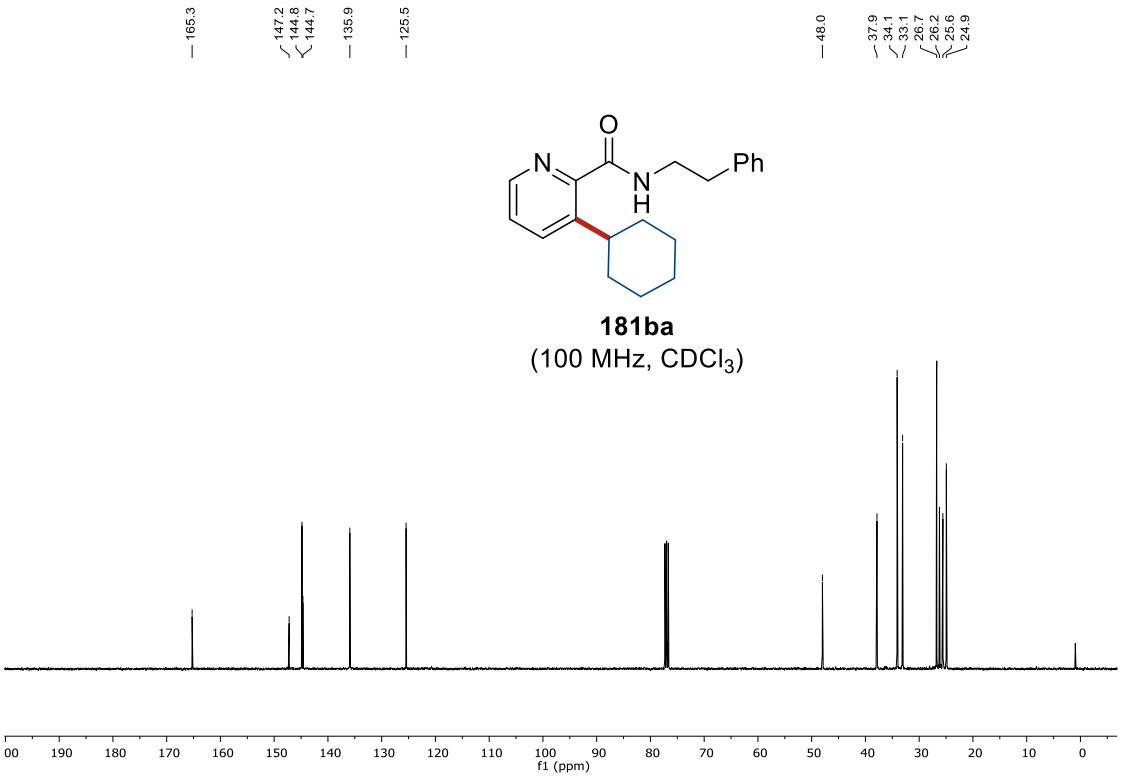

8.36
8.34
8.34
8.33
8.32
7.76
7.75
7.73
7.73
7.42
7.41
7.39
7.38
7.35
7.33
7.32
7.29
7.26
7.26
7.23
7.20
5.33
5.31
5.29
5.28
5.26
5.23
4.12
4.11
4.10
4.08
4.07
4.06
4.04
4.03
4.02
1.93
1.92
1.85
1.83
1.73
1.73
1.72
1.60
1.58
1.54
1.53
1.52
1.48
1.41
1.40
1.38
1.36
1.35
1.32
1.27
1.20
1.19
1.17
1.16
O
Me
N
N
H
Ph
181aa
(300 MHz, CDCl3)
0.88
1.09
1.00
1.89
2.90
1.05
1.11
1.12
5.19
3.09
5.48
f1 (ppm)



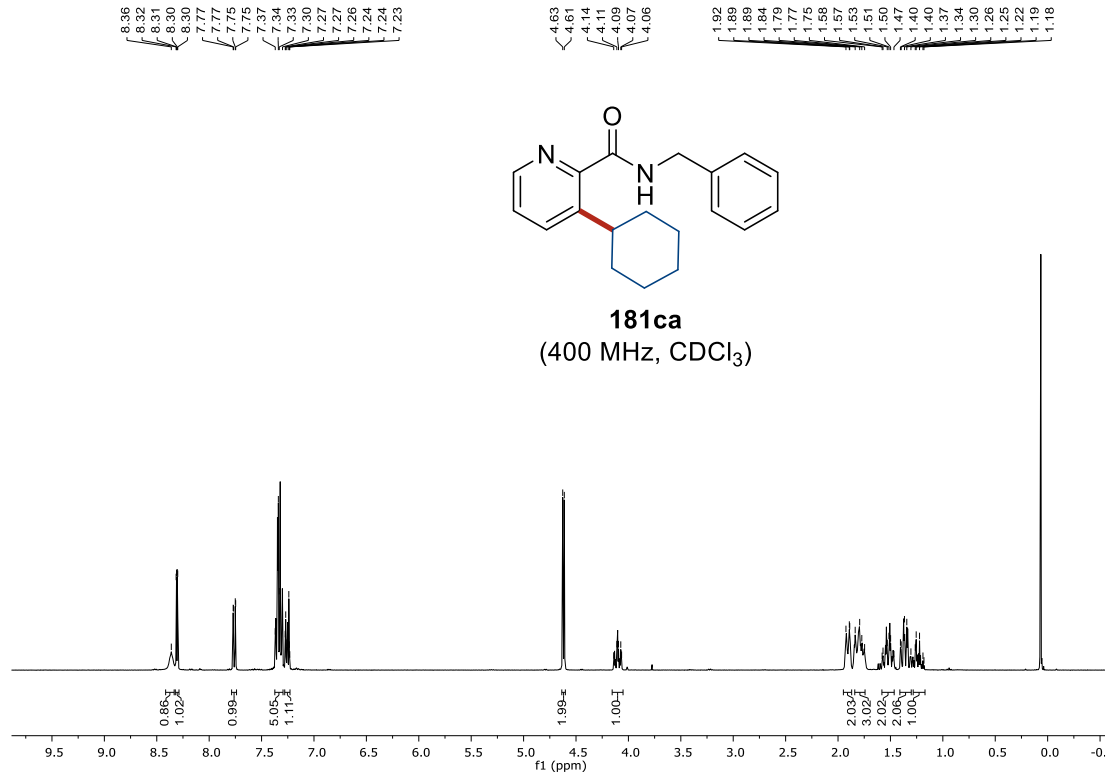
181aa
(100 MHz, $CDCl_3$)



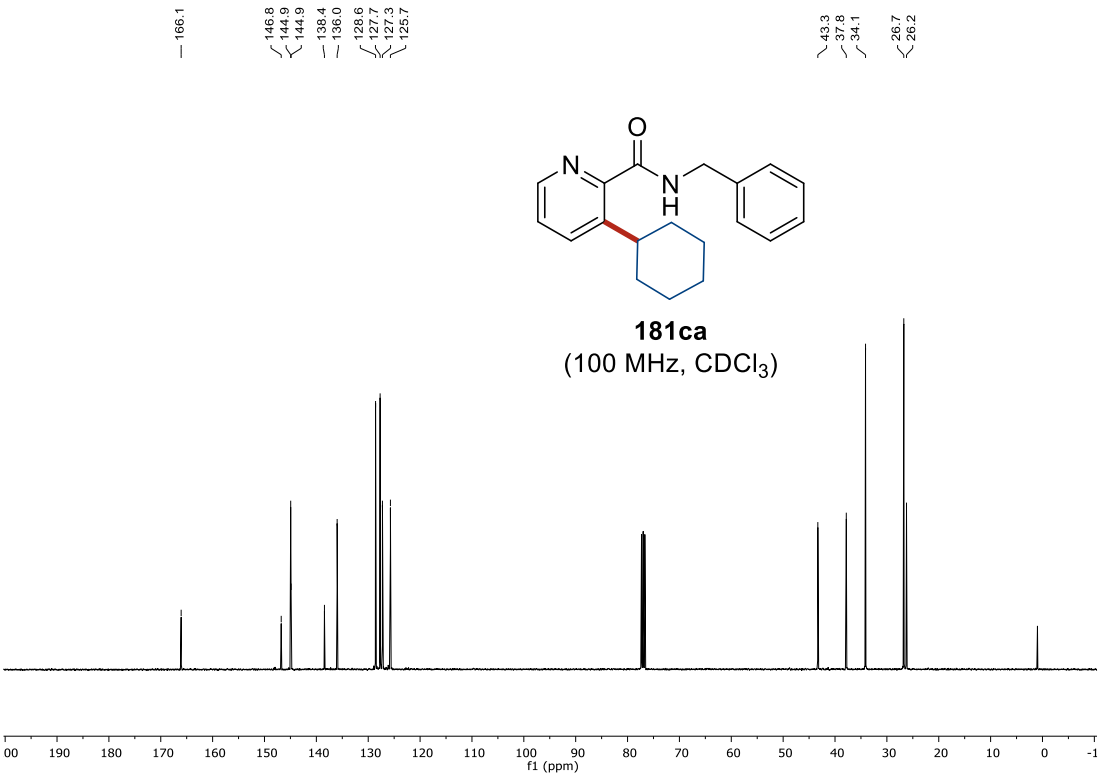
181ba
(300 MHz, $CDCl_3$)



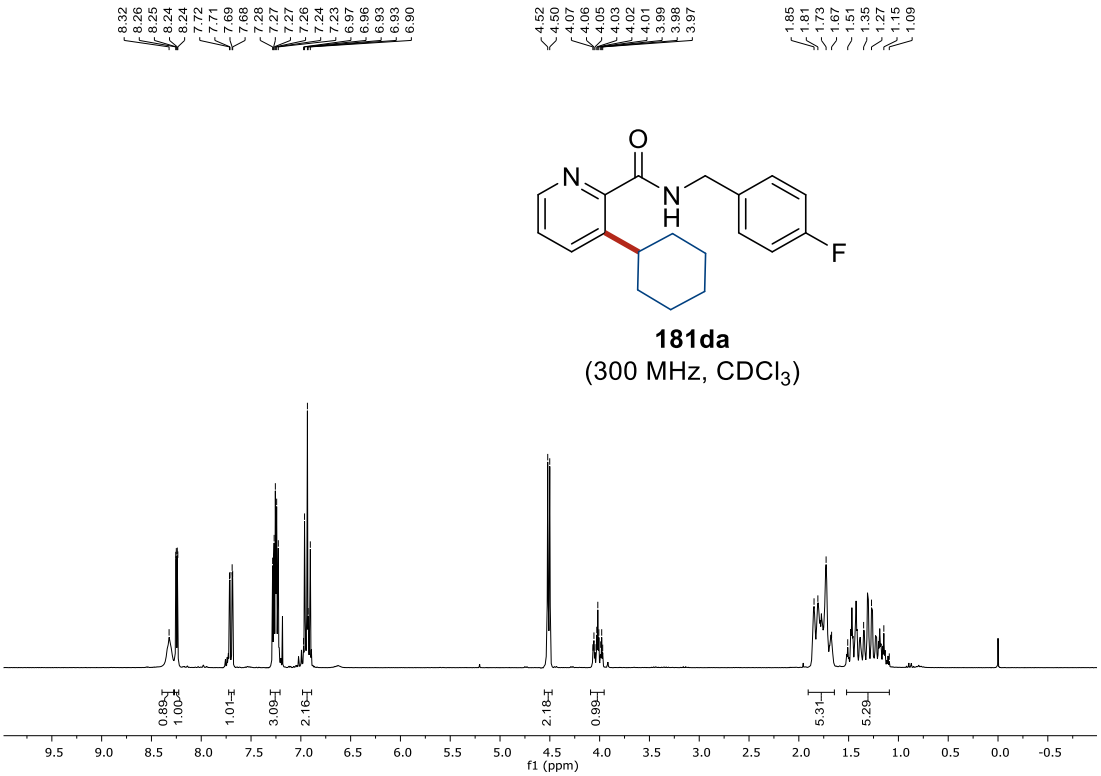
181ba
(100 MHz, $CDCl_3$)



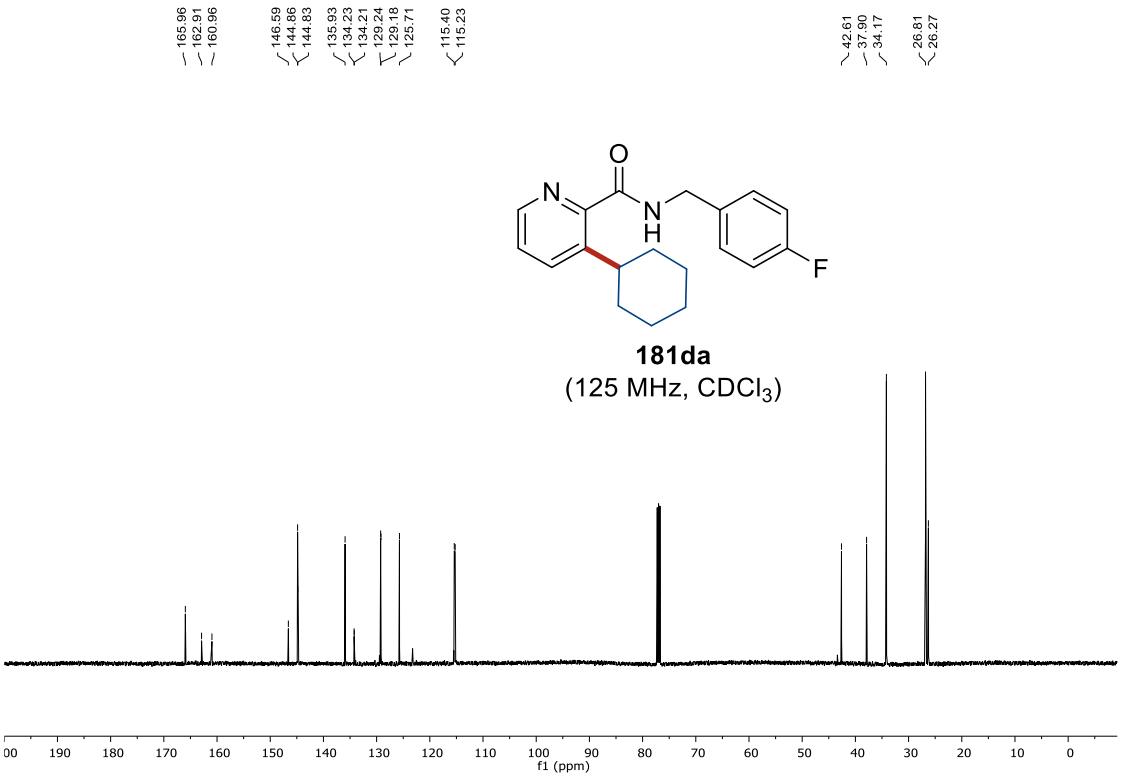
181ca
(400 MHz, $CDCl_3$)



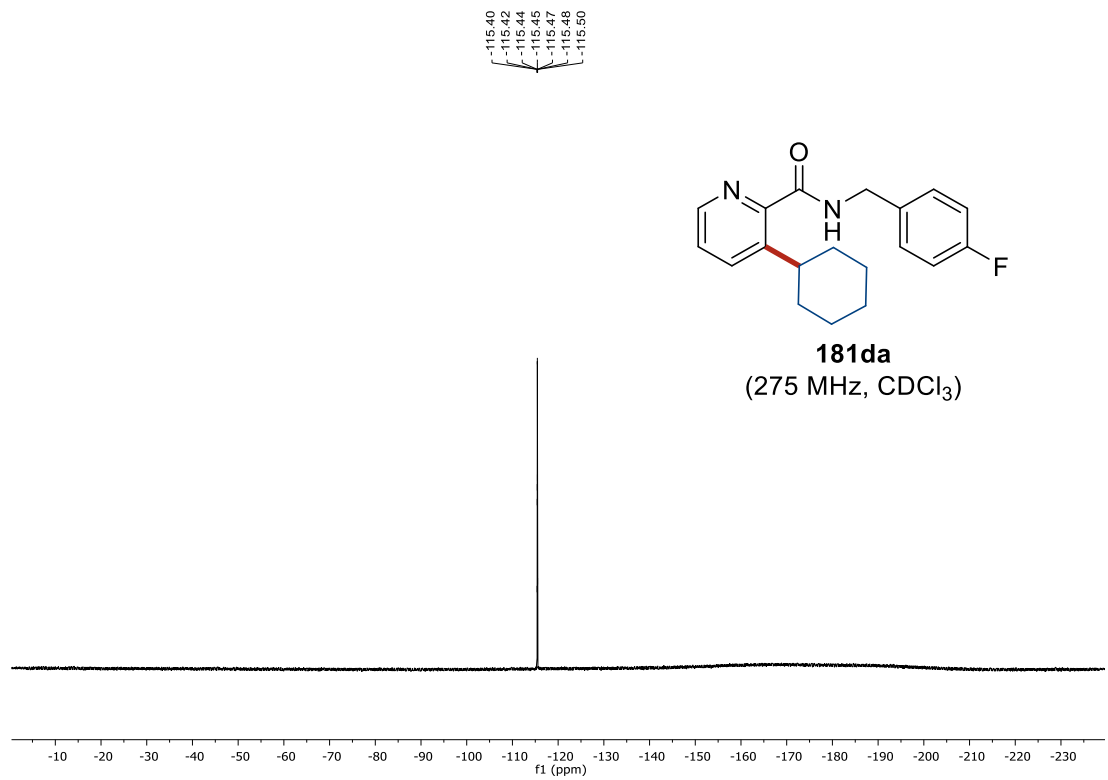
181ca
(100 MHz, $CDCl_3$)



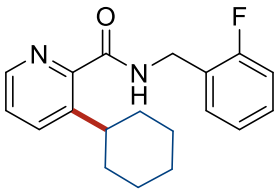
181da
(300 MHz, $CDCl_3$)



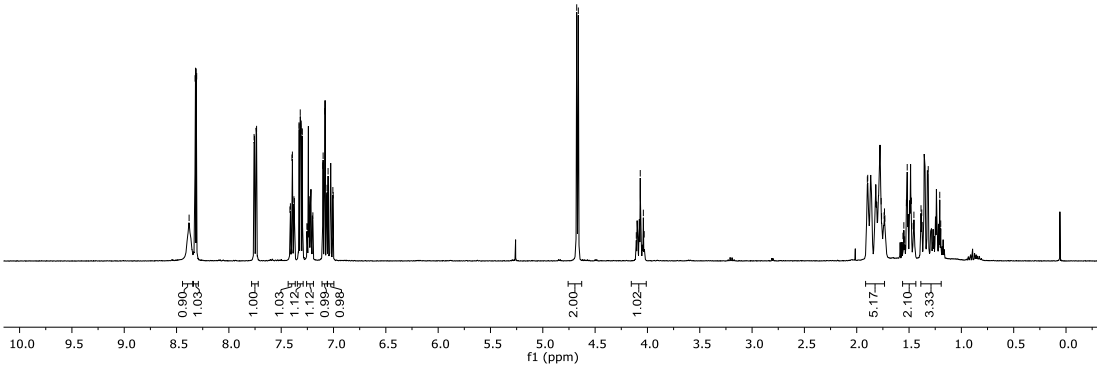
181da
(125 MHz, $CDCl_3$)

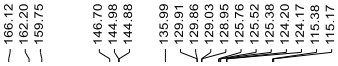


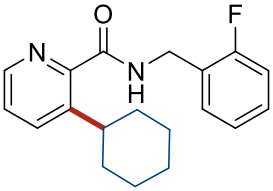
181da
(275 MHz, $CDCl_3$)



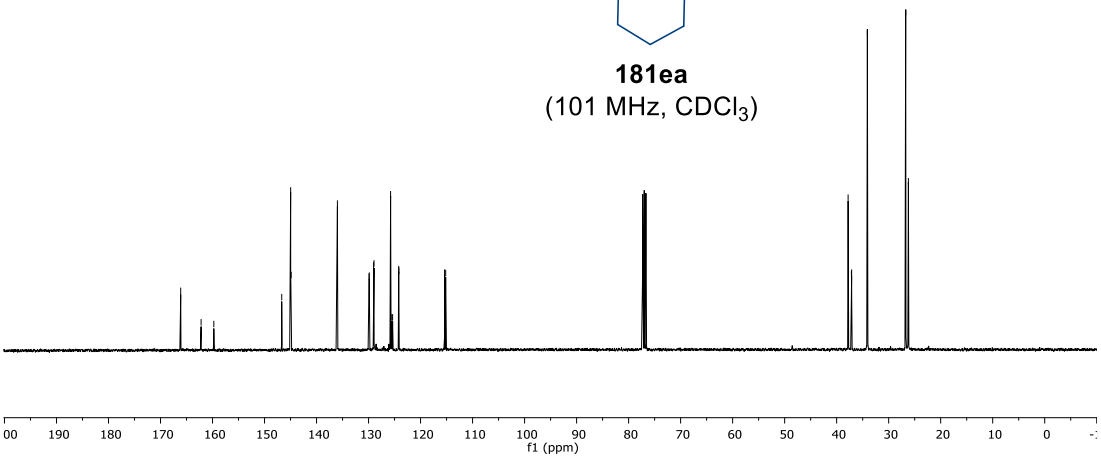
181ea
(400 MHz, $CDCl_3$)

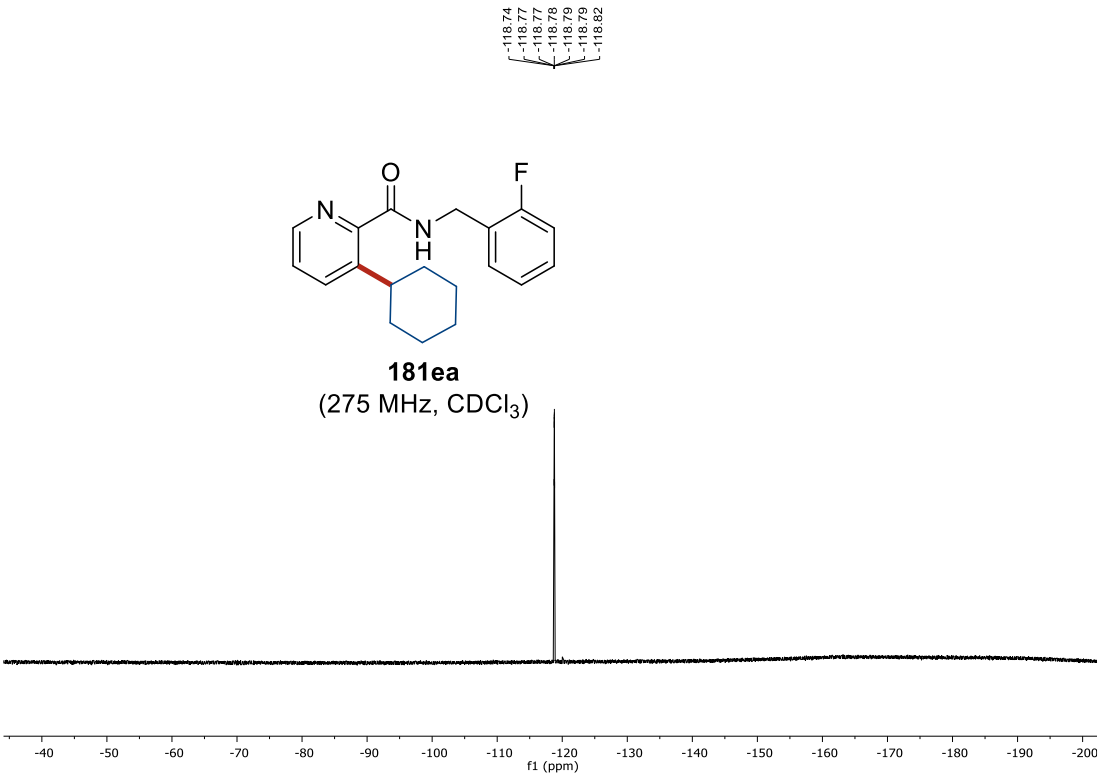


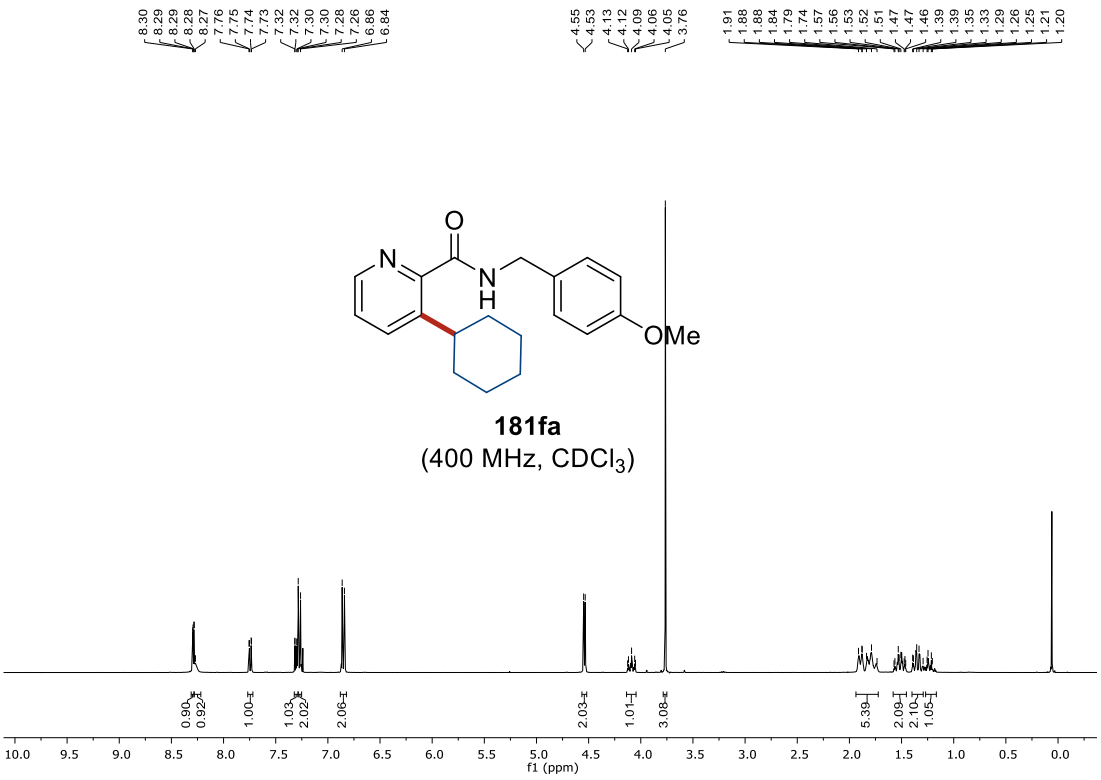


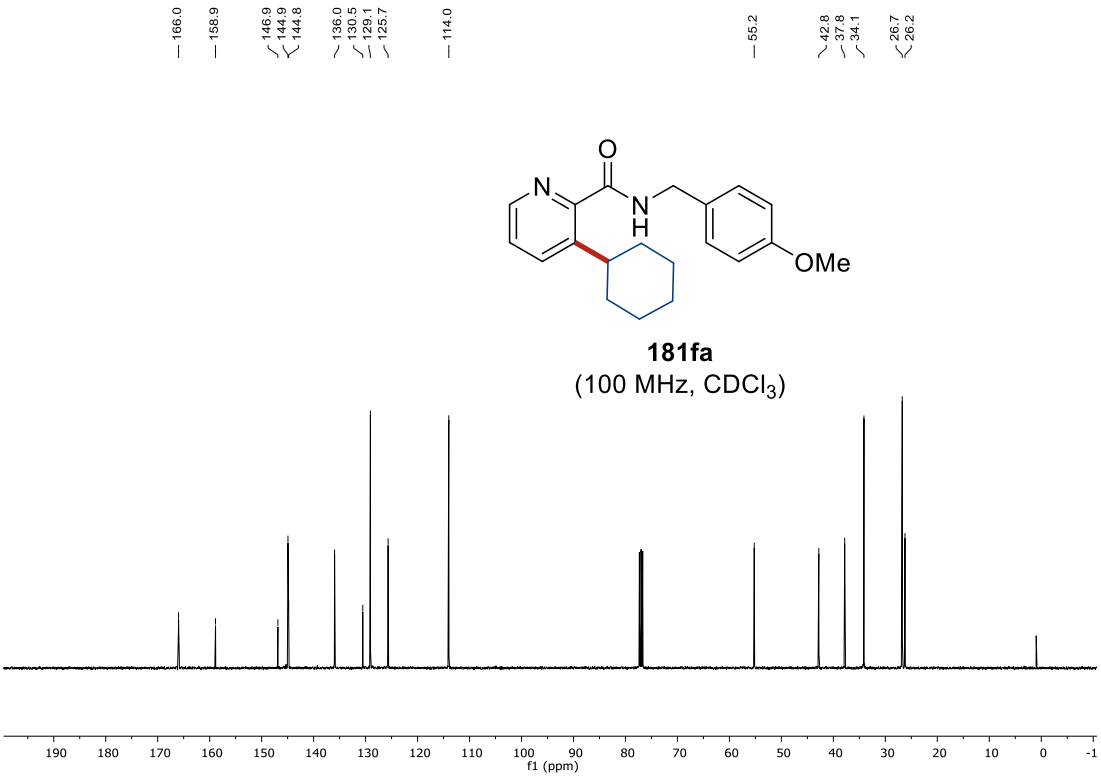


181ea
(101 MHz, $CDCl_3$)

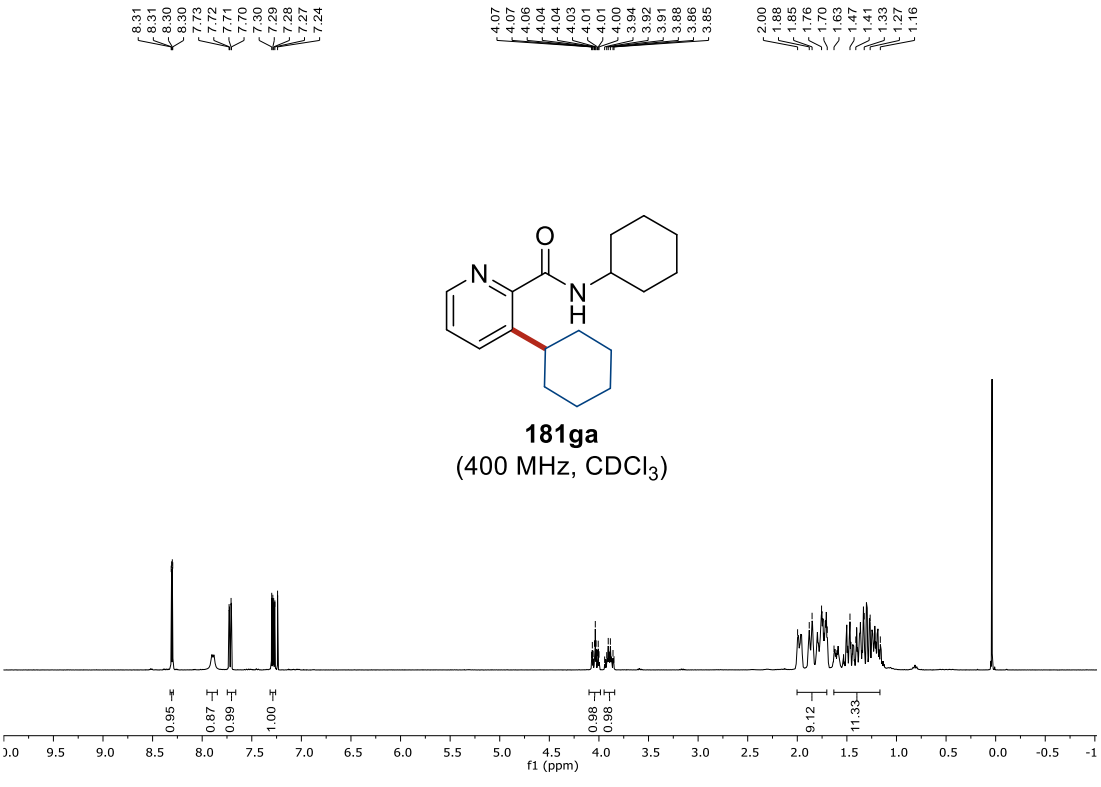



-118.74
-118.77
-118.77
-118.78
-118.79
-118.79
-118.82
O
F
N
N
H
181ea
(275 MHz, CDCl3)
-40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

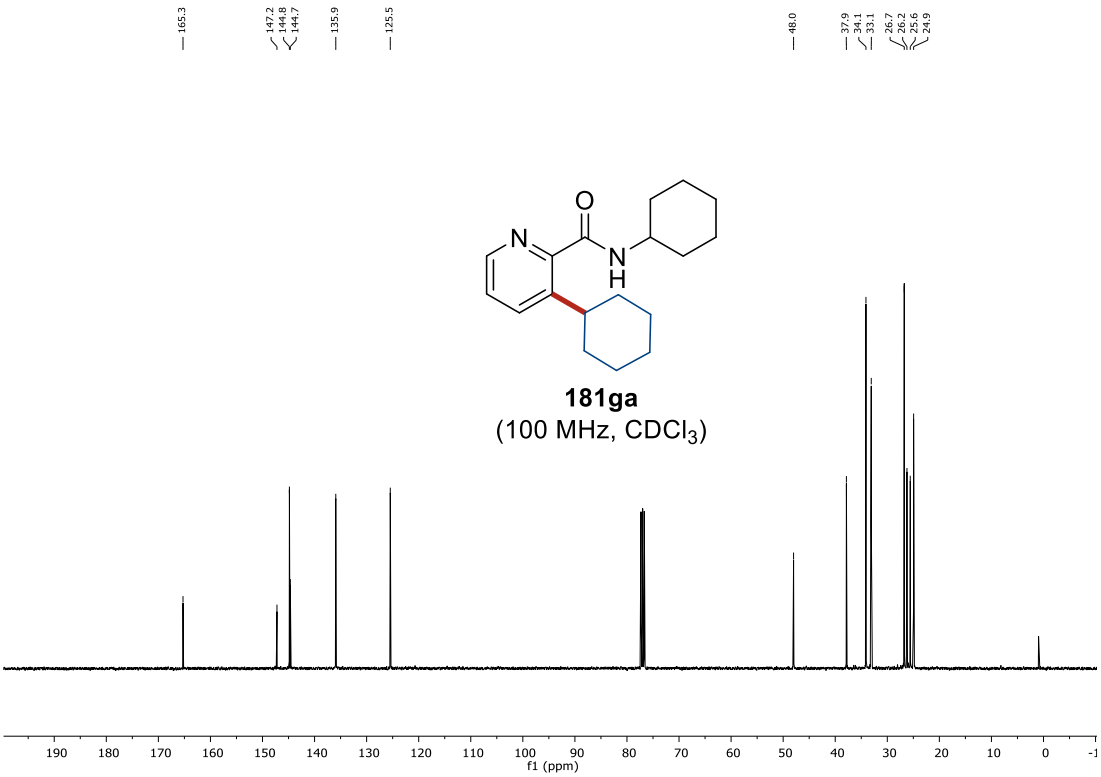

8.30
8.29
8.29
8.28
8.27
7.76
7.75
7.74
7.73
7.32
7.30
7.30
7.28
7.26
6.86
6.84
4.55
4.53
4.13
4.12
4.09
4.06
4.05
3.76
1.91
1.88
1.88
1.84
1.79
1.74
1.57
1.56
1.53
1.52
1.51
1.47
1.47
1.46
1.39
1.39
1.35
1.33
1.29
1.26
1.25
1.21
1.20
O
N
N
H
OMe
181fa
(400 MHz, CDCl3)
0.90
0.92
1.00
1.03
2.02
2.06
2.03
1.01
3.08
5.39
2.09
2.10
1.05
10.0 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
f1 (ppm)



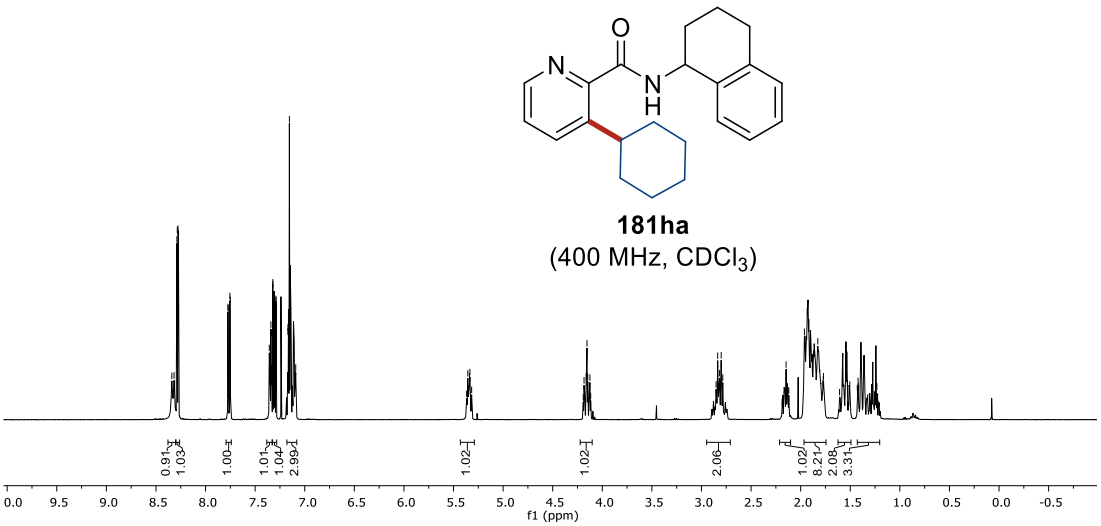
181fa
(100 MHz, $CDCl_3$)



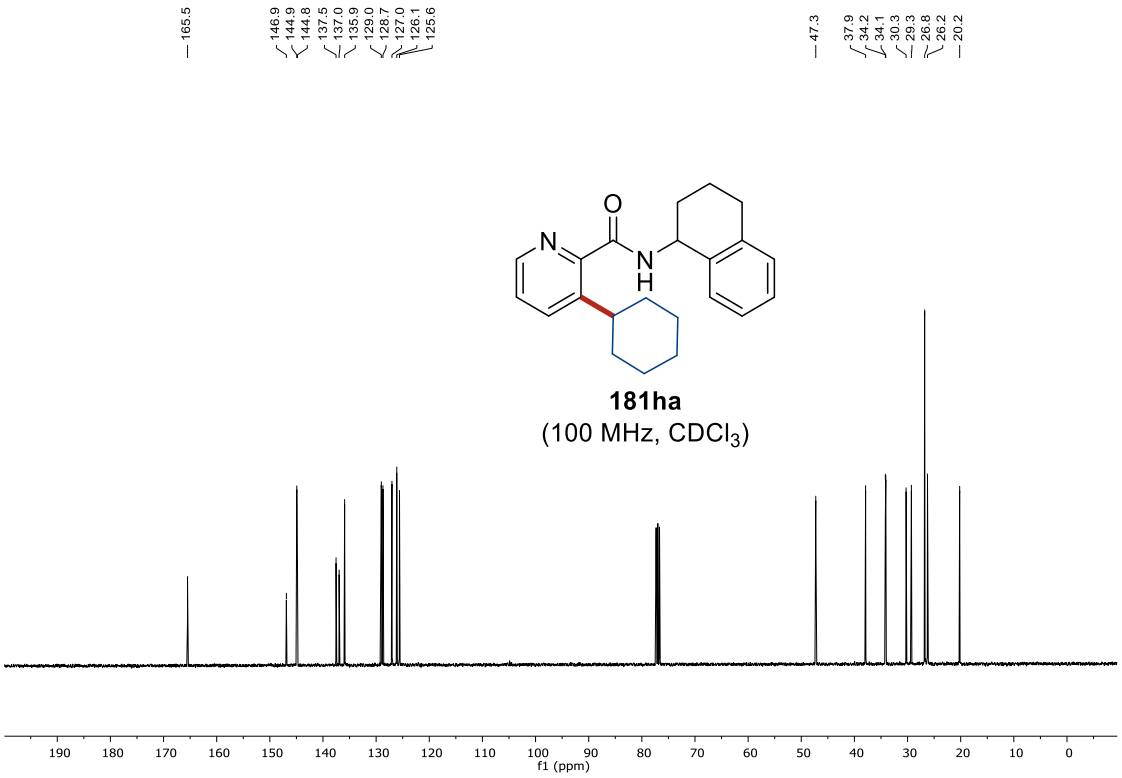
181ga
(400 MHz, $CDCl_3$)



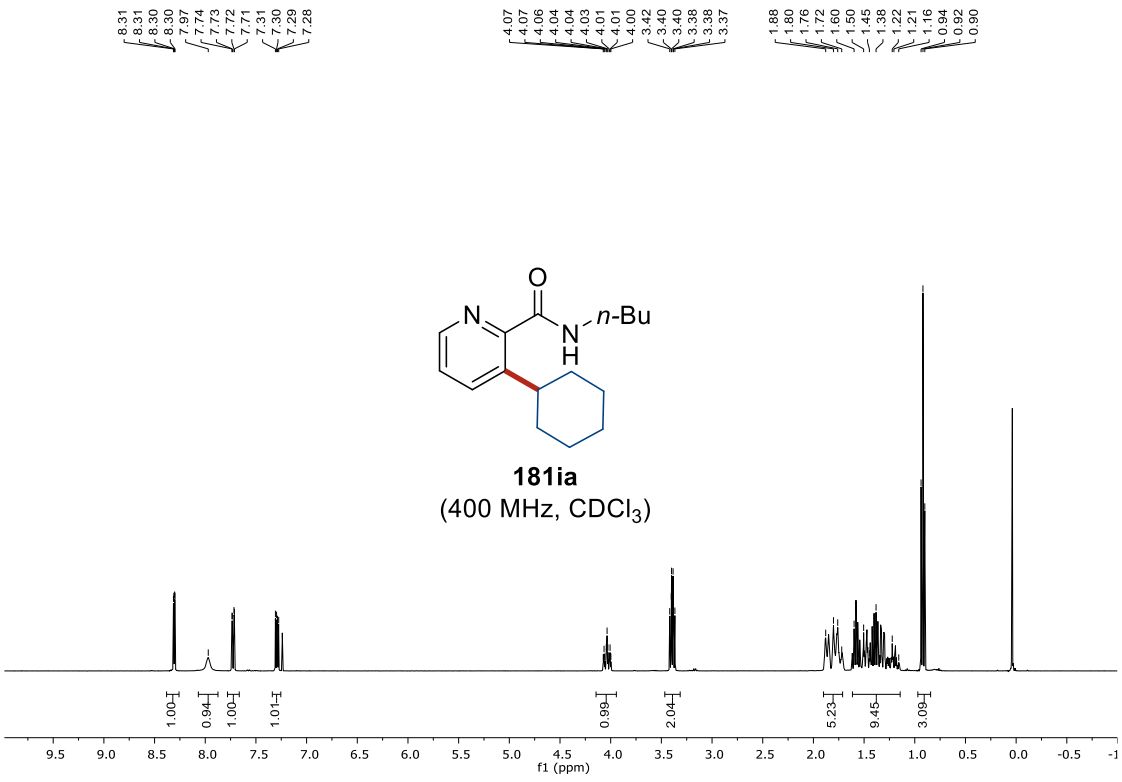
181ga
(100 MHz, $CDCl_3$)



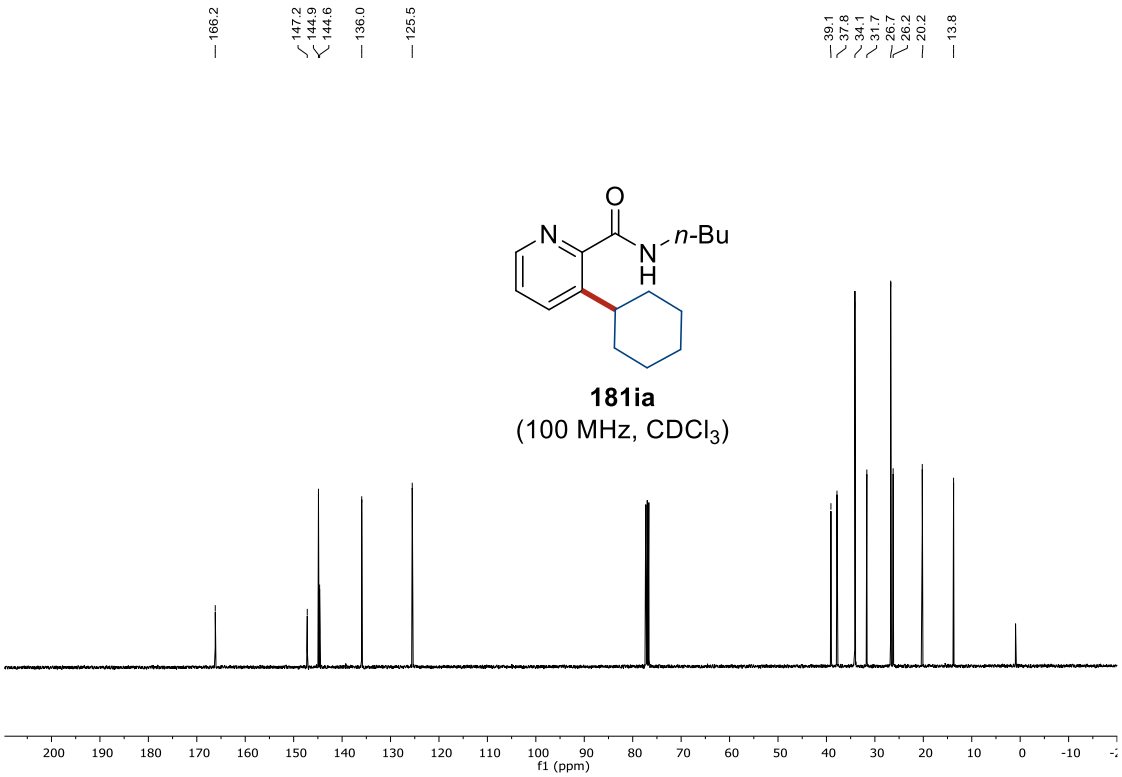
181ha
(400 MHz, $CDCl_3$)

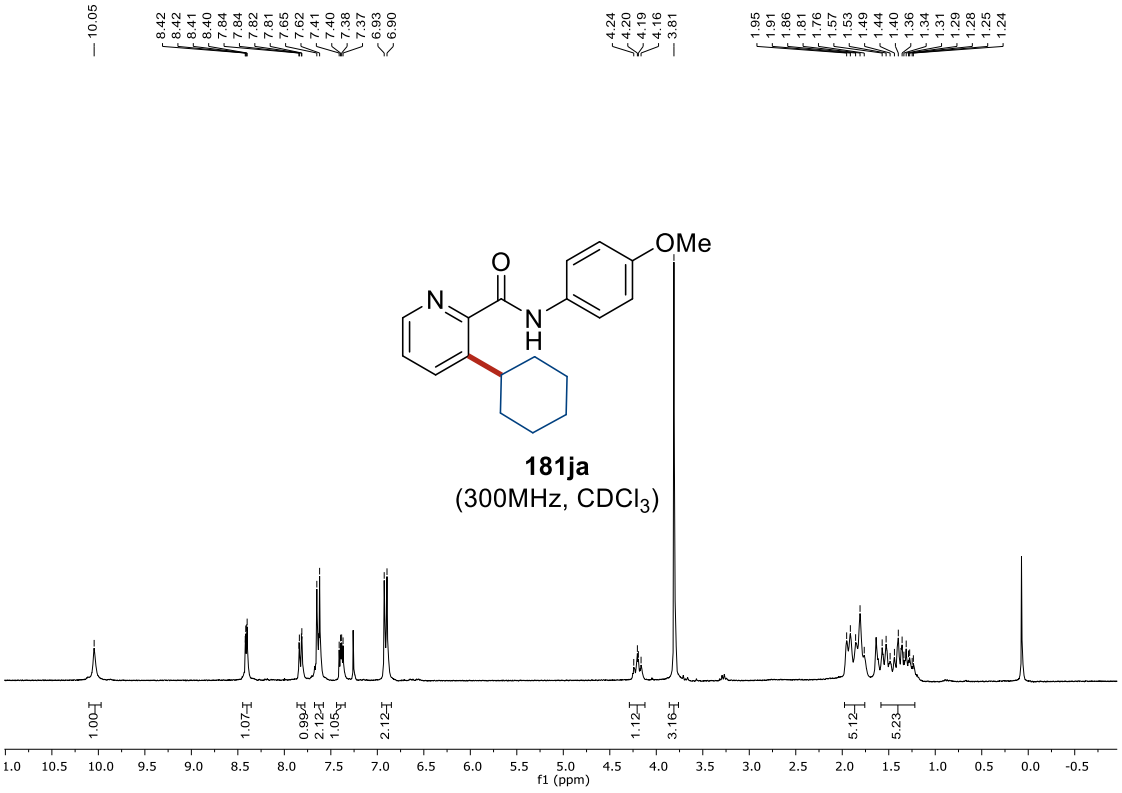


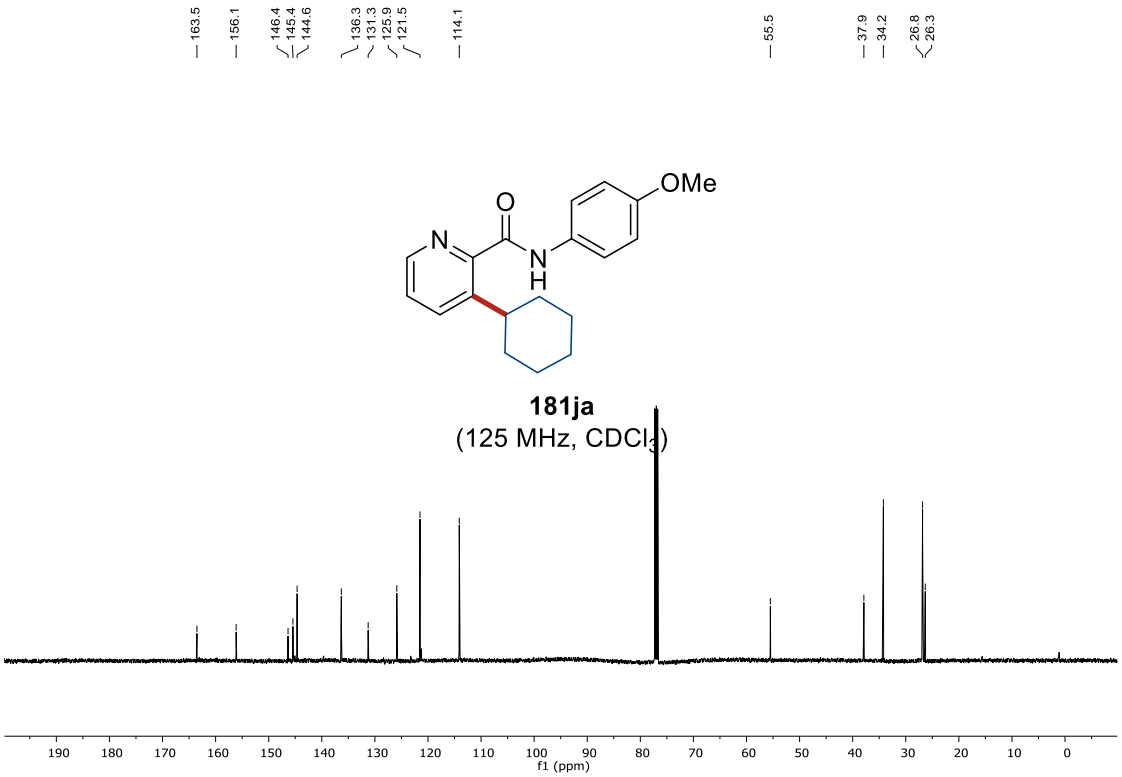
181ha
(100 MHz, $CDCl_3$)

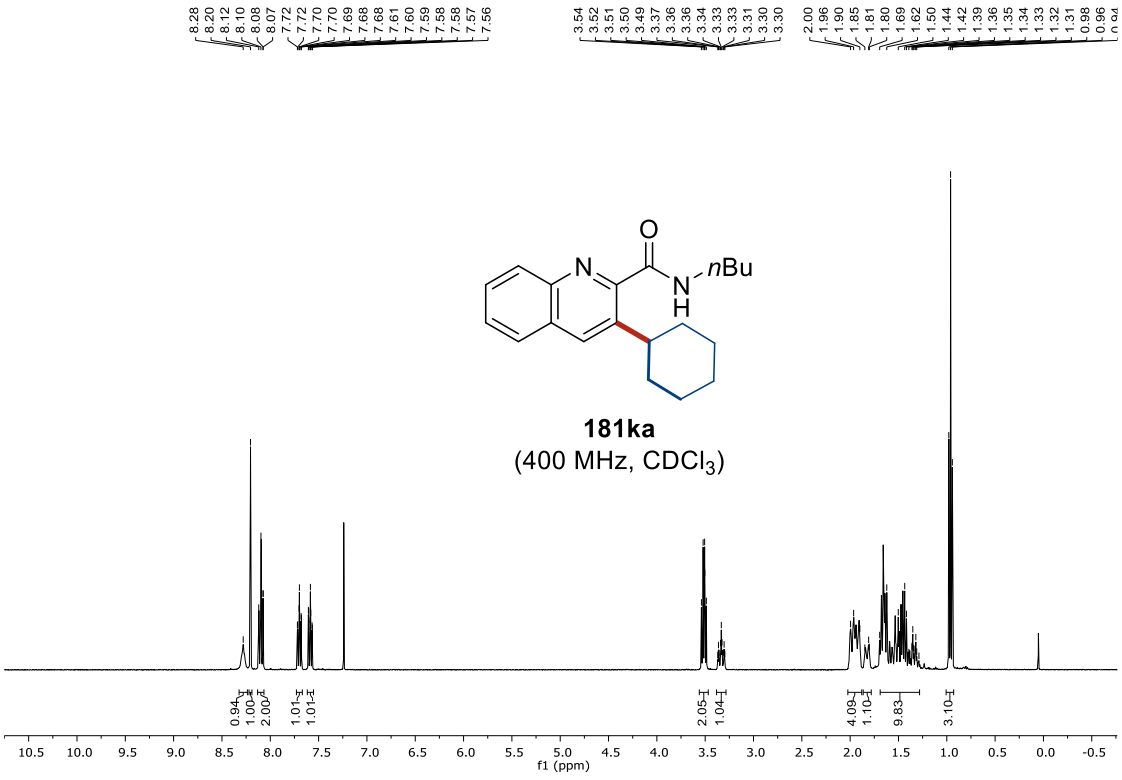


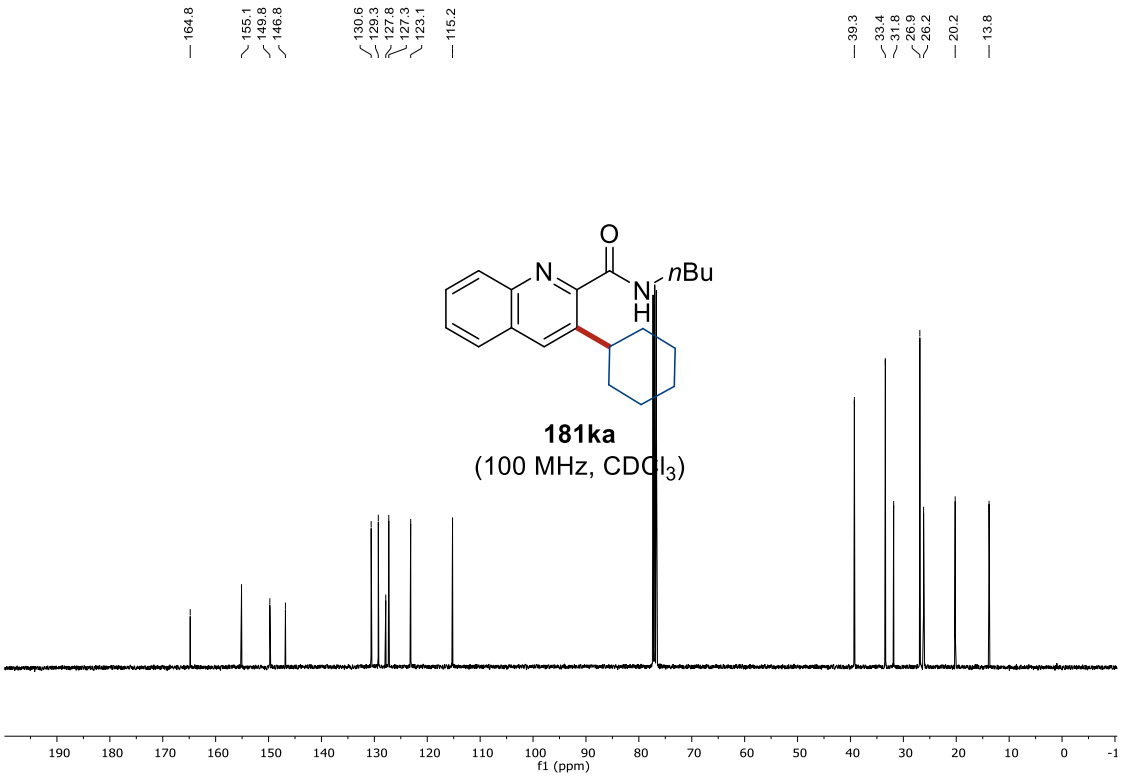
181ia
(400 MHz, $CDCl_3$)

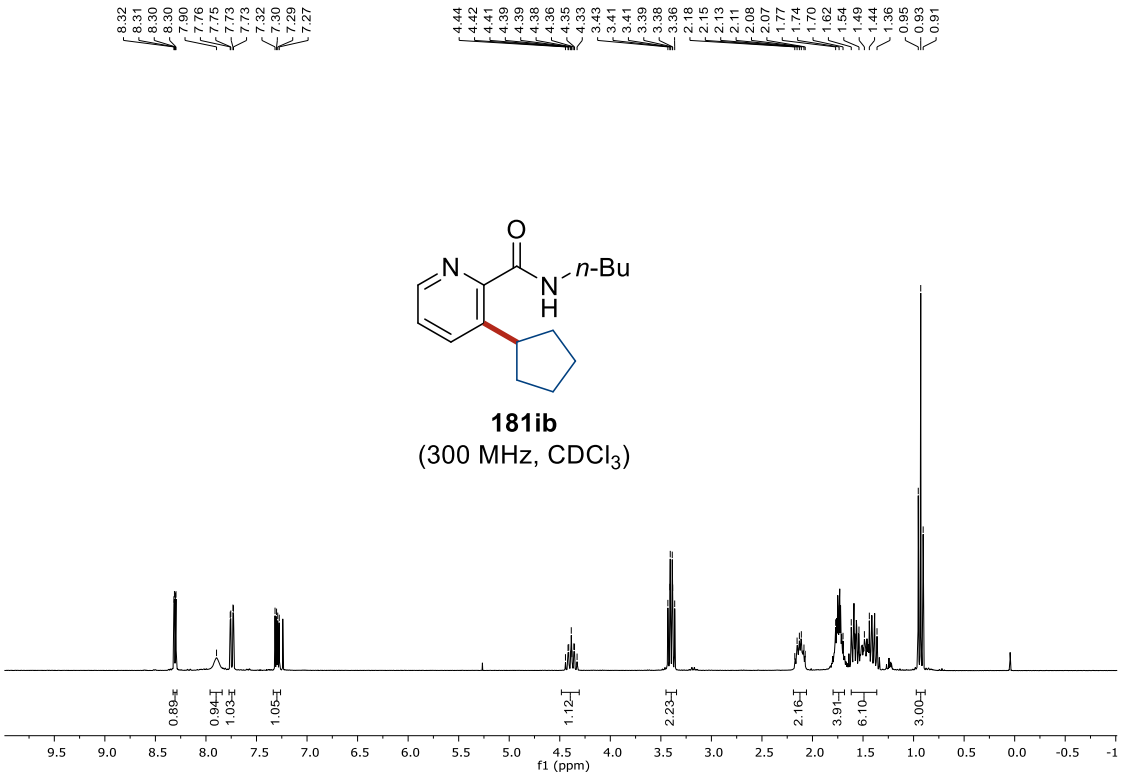

166.2
147.2
144.9
144.6
136.0
125.5
39.1
37.8
34.1
31.7
26.7
26.2
20.2
13.8
O
N
N
H
n-Bu
181ia
(100 MHz, CDCl3)
f1 (ppm)

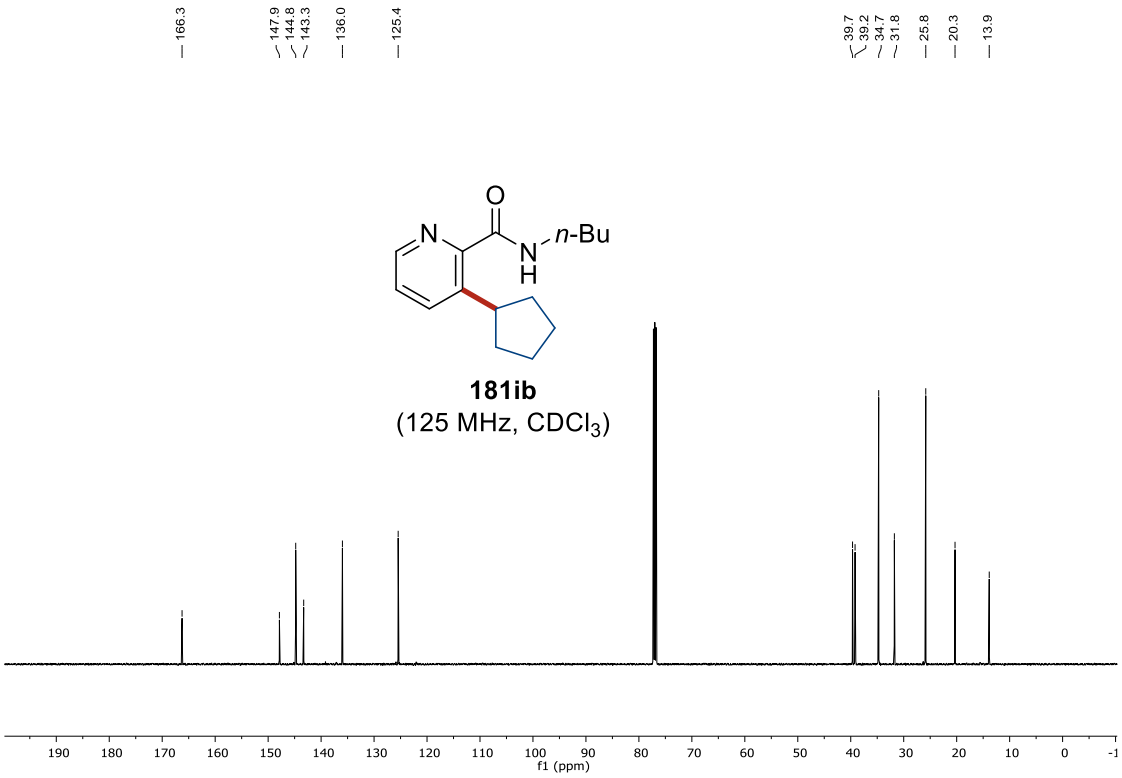

10.05
8.42
8.42
8.41
8.40
7.84
7.84
7.82
7.81
7.65
7.62
7.41
7.40
7.38
7.37
6.93
6.90
4.24
4.20
4.19
4.16
3.81
1.95
1.91
1.86
1.81
1.76
1.57
1.53
1.49
1.44
1.40
1.36
1.34
1.31
1.29
1.28
1.25
1.24
OMe
O
N
N
H
181ja
(300MHz, CDCl3)
1.00
1.07
0.99
2.12
1.05
2.12
1.12
3.16
5.12
5.23
f1 (ppm)

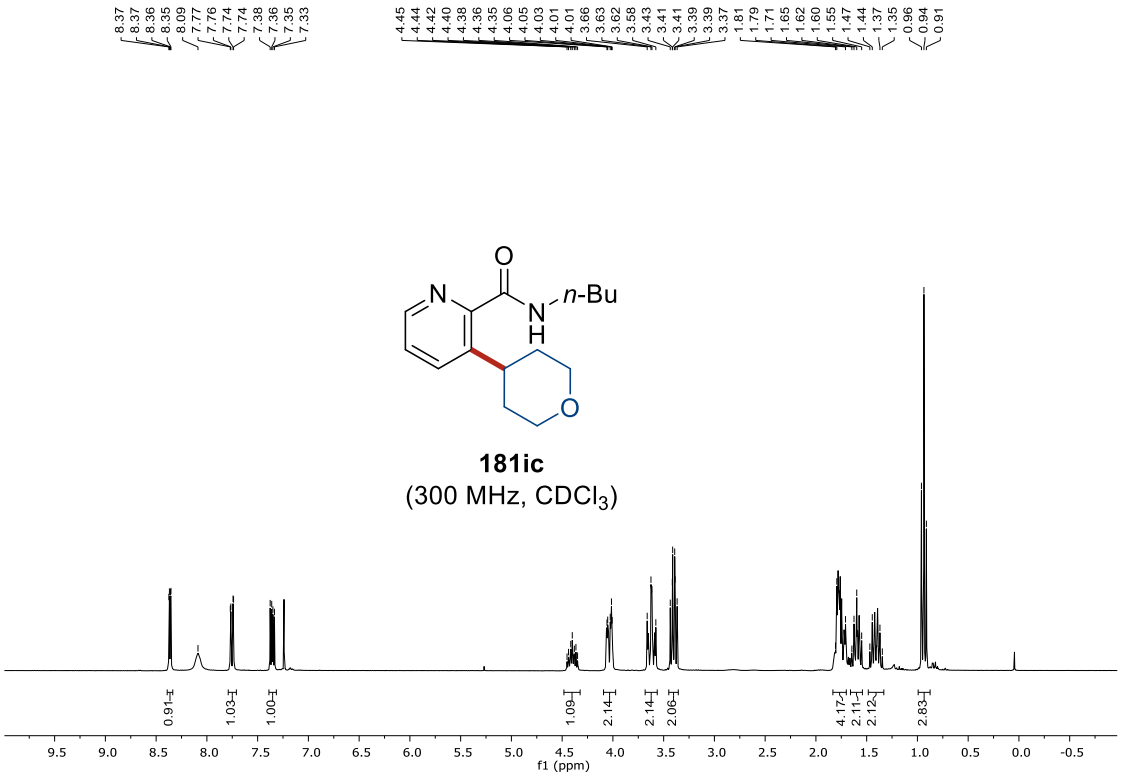

163.5
156.1
146.4
145.4
144.6
136.3
131.3
125.9
121.5
114.1
55.5
37.9
34.2
26.8
26.3
OMe
O
N
N
H
181ja
(125 MHz, CDCl3)
f1 (ppm)

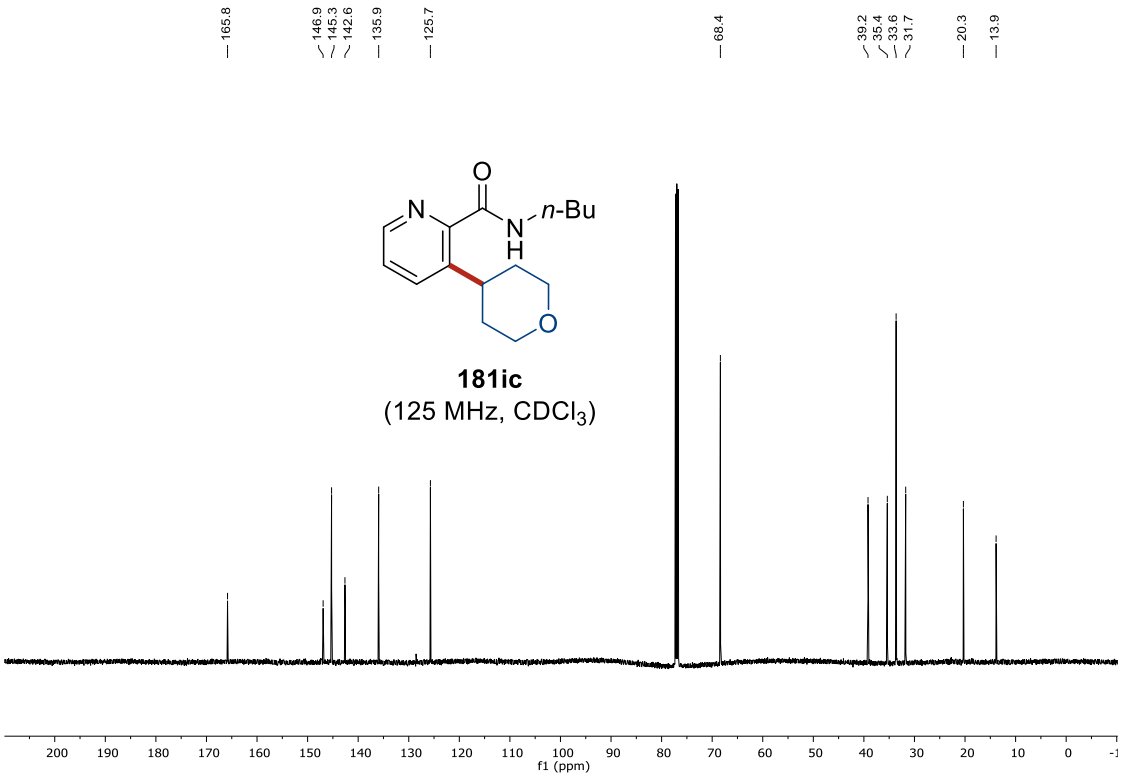

8.28
8.20
8.12
8.10
8.08
8.07
7.72
7.72
7.70
7.70
7.69
7.68
7.68
7.61
7.60
7.59
7.58
7.58
7.57
7.56
3.54
3.52
3.51
3.50
3.49
3.37
3.36
3.36
3.34
3.33
3.33
3.31
3.30
3.30
2.00
1.96
1.90
1.85
1.81
1.80
1.69
1.62
1.50
1.44
1.42
1.39
1.36
1.35
1.34
1.33
1.32
1.31
0.98
0.96
O
N
N
H
nBu
181ka
(400 MHz, CDCl3)
0.94
1.00
2.00
1.01
1.01
2.05
1.04
4.09
1.10
9.83
3.10
f1 (ppm)


164.8
155.1
149.8
146.8
130.6
129.3
127.8
127.3
123.1
115.2
39.3
33.4
31.8
26.9
26.2
20.2
13.8
O
N
N
H
nBu
181ka
(100 MHz, CDCl3)
f1 (ppm)

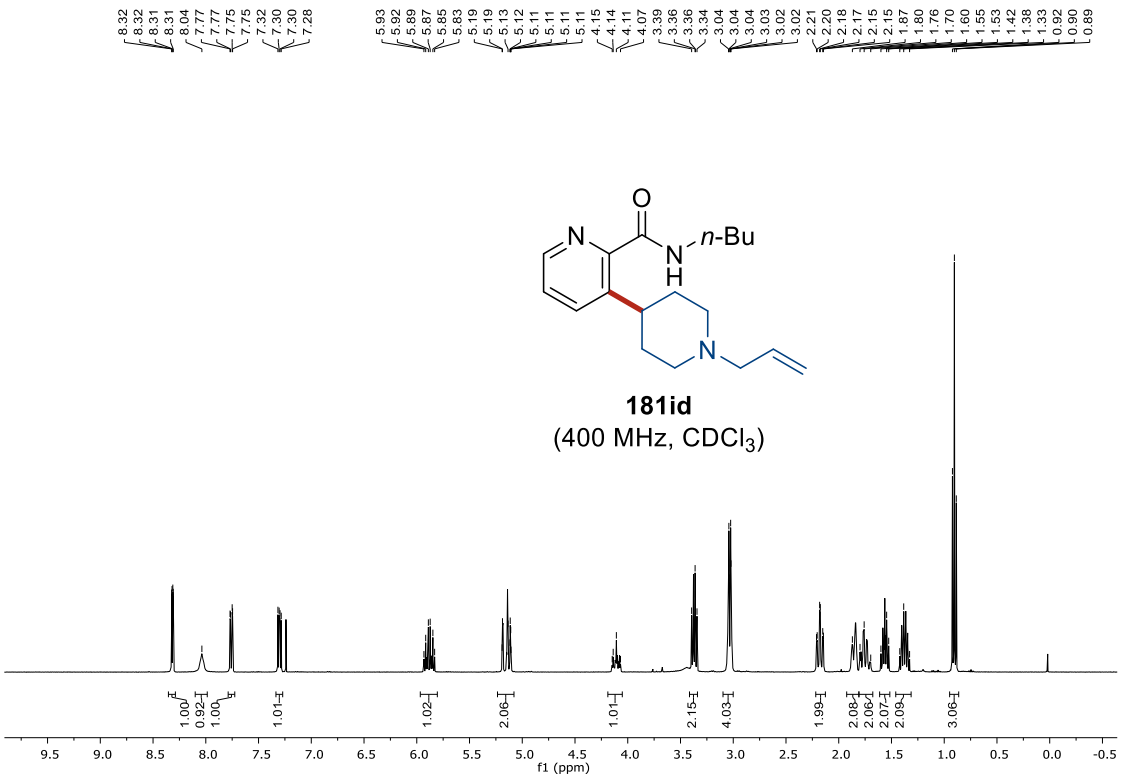

8.32
8.31
8.30
8.30
7.90
7.76
7.75
7.73
7.73
7.32
7.30
7.29
7.27
4.44
4.42
4.41
4.39
4.39
4.38
4.36
4.35
4.33
3.43
3.41
3.41
3.39
3.38
3.36
2.18
2.15
2.13
2.11
2.08
2.07
1.77
1.74
1.70
1.62
1.54
1.49
1.44
1.36
0.95
0.93
0.91
O
N
N
H
n-Bu
181ib
(300 MHz, CDCl3)
0.89
0.94
1.03
1.05
1.12
2.23
2.16
3.91
6.10
3.00
f1 (ppm)


166.3
147.9
144.8
143.3
136.0
125.4
39.7
39.2
34.7
31.8
25.8
20.3
13.9
O
N
N
H
n-Bu
181ib
(125 MHz, CDCl3)
f1 (ppm)

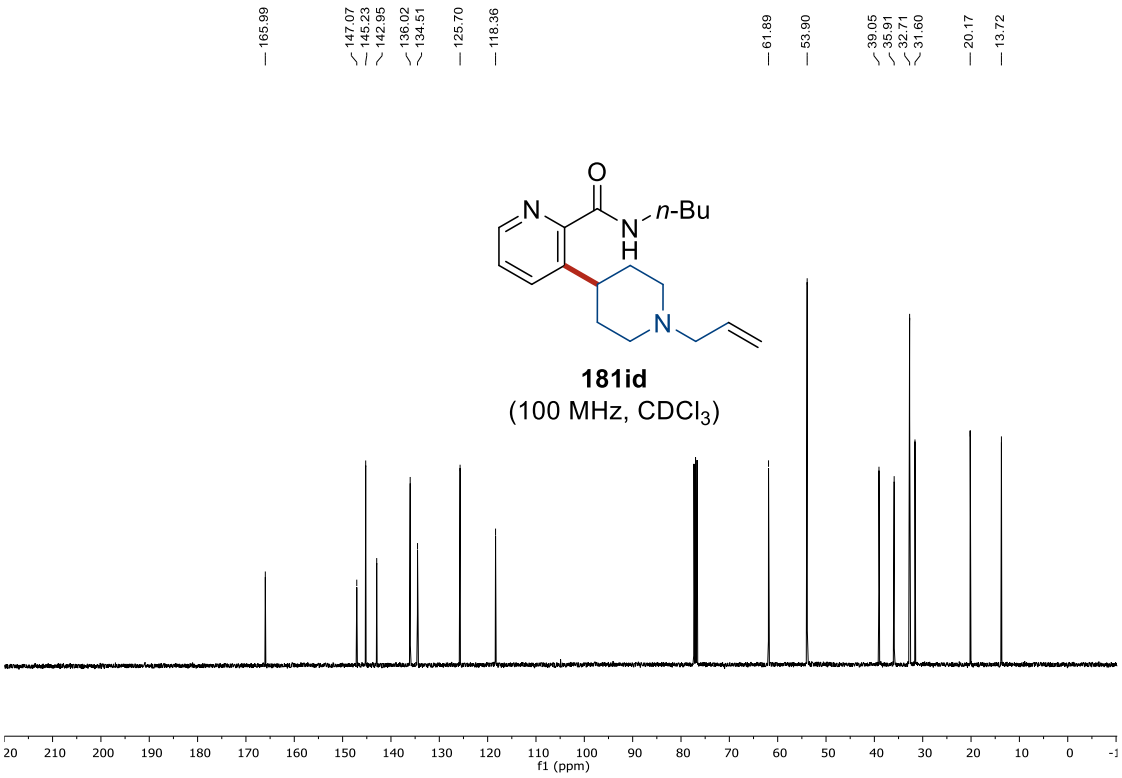

8.37
8.37
8.36
8.35
8.09
7.77
7.76
7.74
7.74
7.38
7.36
7.35
7.33
4.45
4.44
4.42
4.40
4.38
4.36
4.35
4.06
4.05
4.03
4.01
4.01
3.66
3.63
3.62
3.58
3.43
3.41
3.41
3.39
3.39
3.37
1.81
1.79
1.71
1.65
1.62
1.60
1.55
1.47
1.44
1.37
1.35
0.96
0.94
0.91
O
N
N
H
n-Bu
O
181ic
(300 MHz, CDCl3)
0.91
1.03
1.00
1.09
2.14
2.14
2.06
4.17
2.11
2.12
2.83
f1 (ppm)



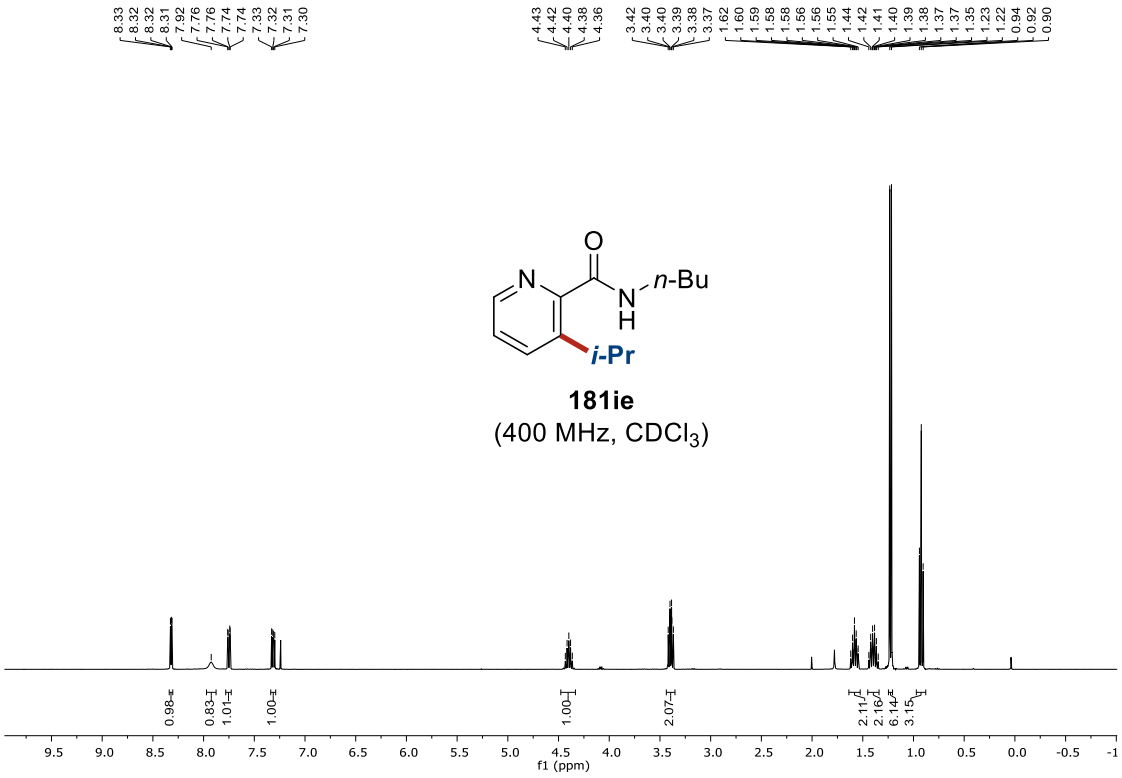
181ic
(125 MHz, $CDCl_3$)



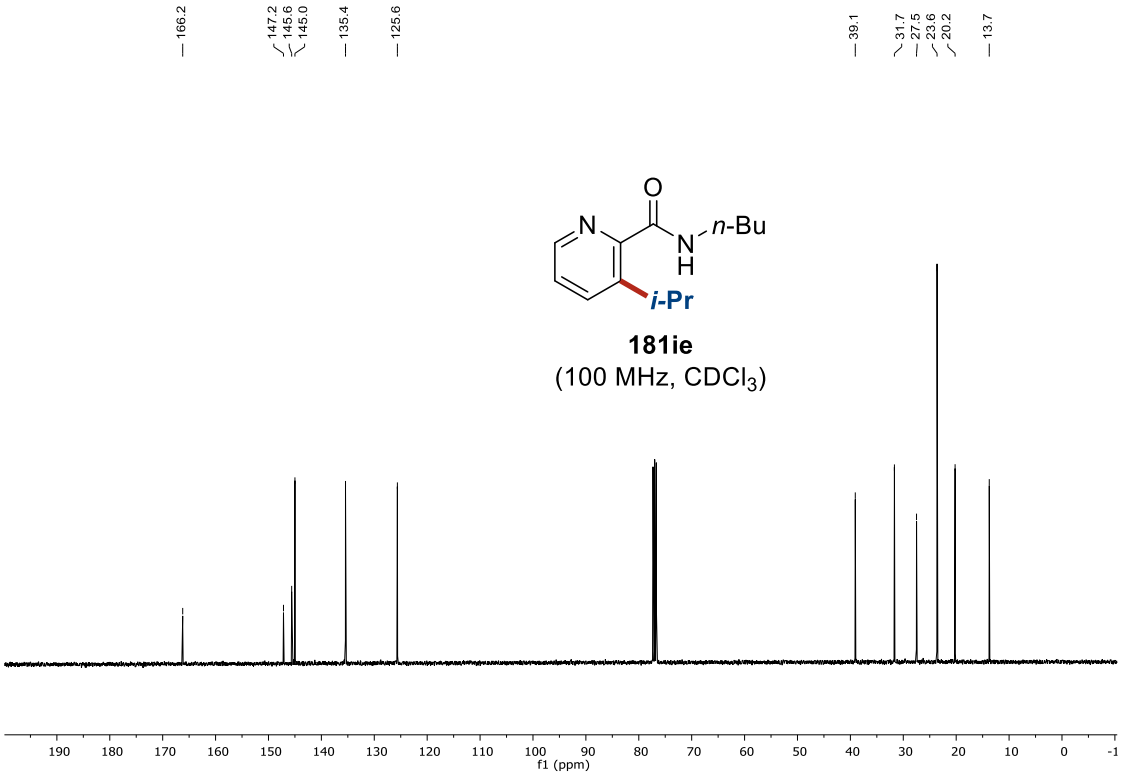
181id
(400 MHz, $CDCl_3$)



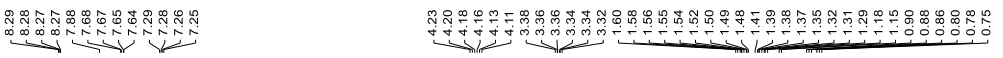
181id
(100 MHz, $CDCl_3$)

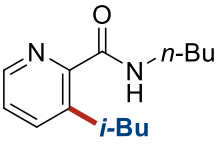


181ie
(400 MHz, $CDCl_3$)

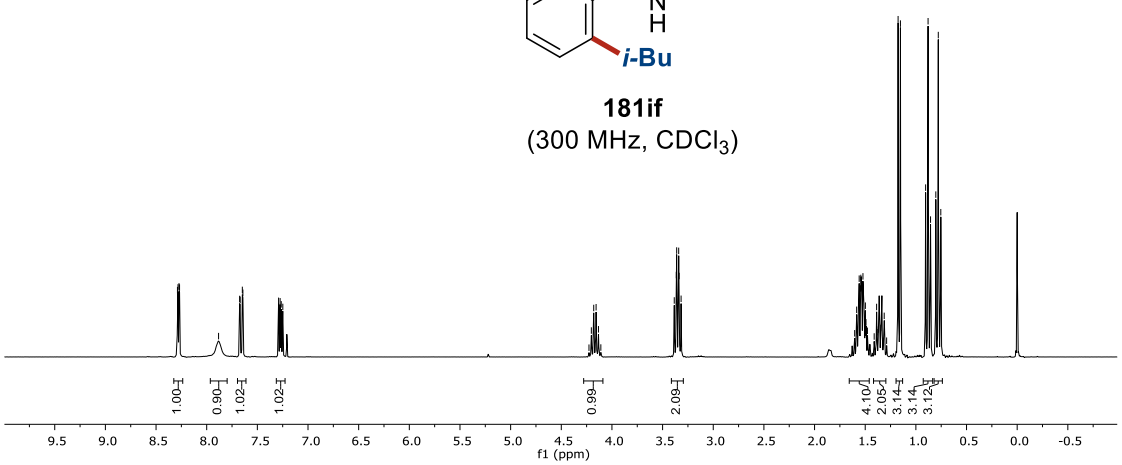


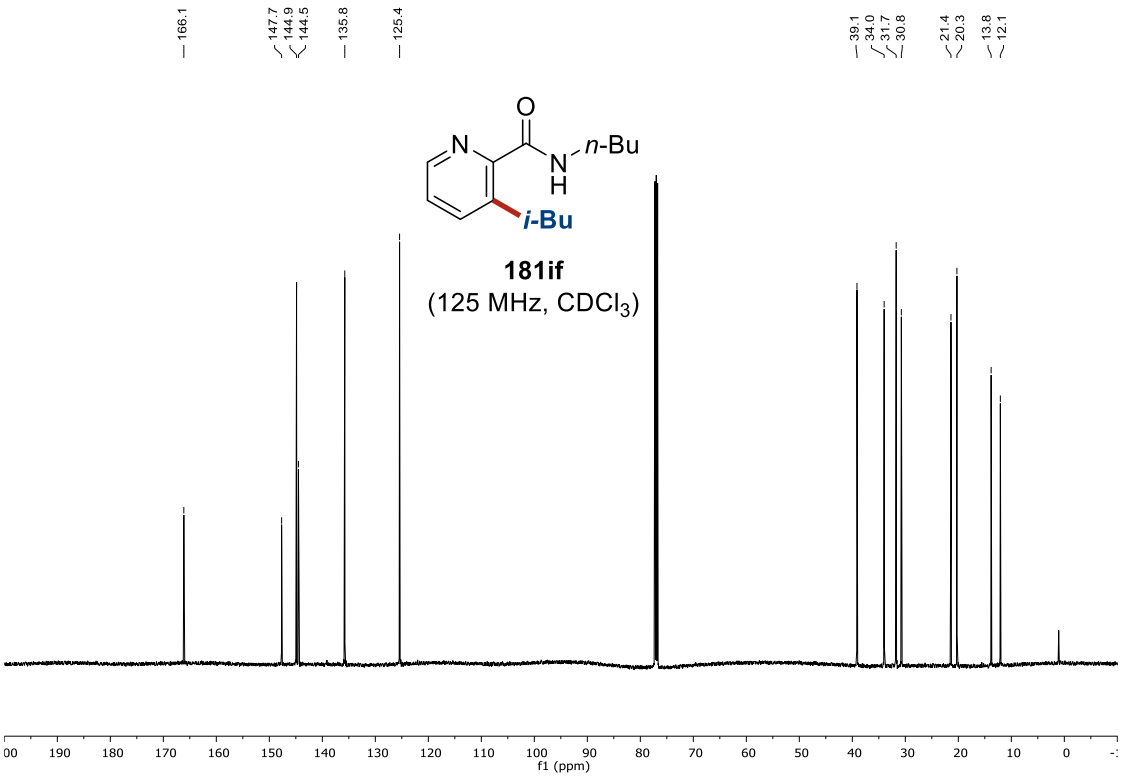
181ie
(100 MHz, $CDCl_3$)

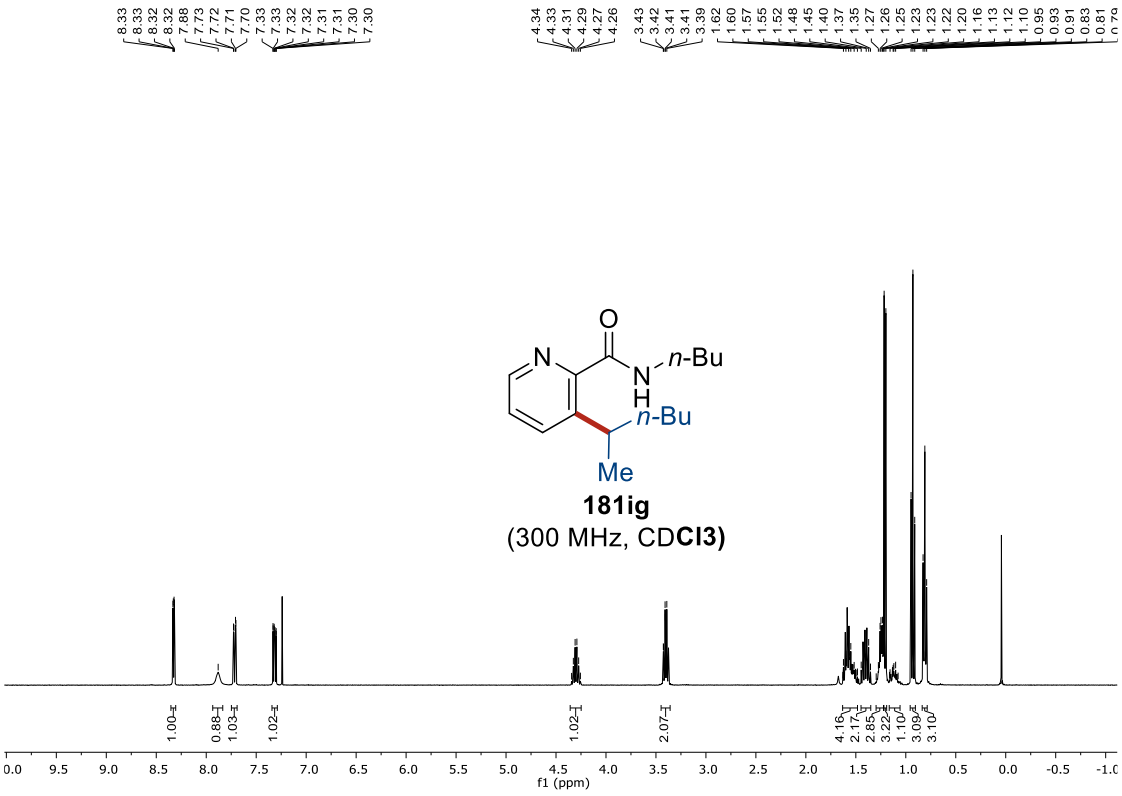


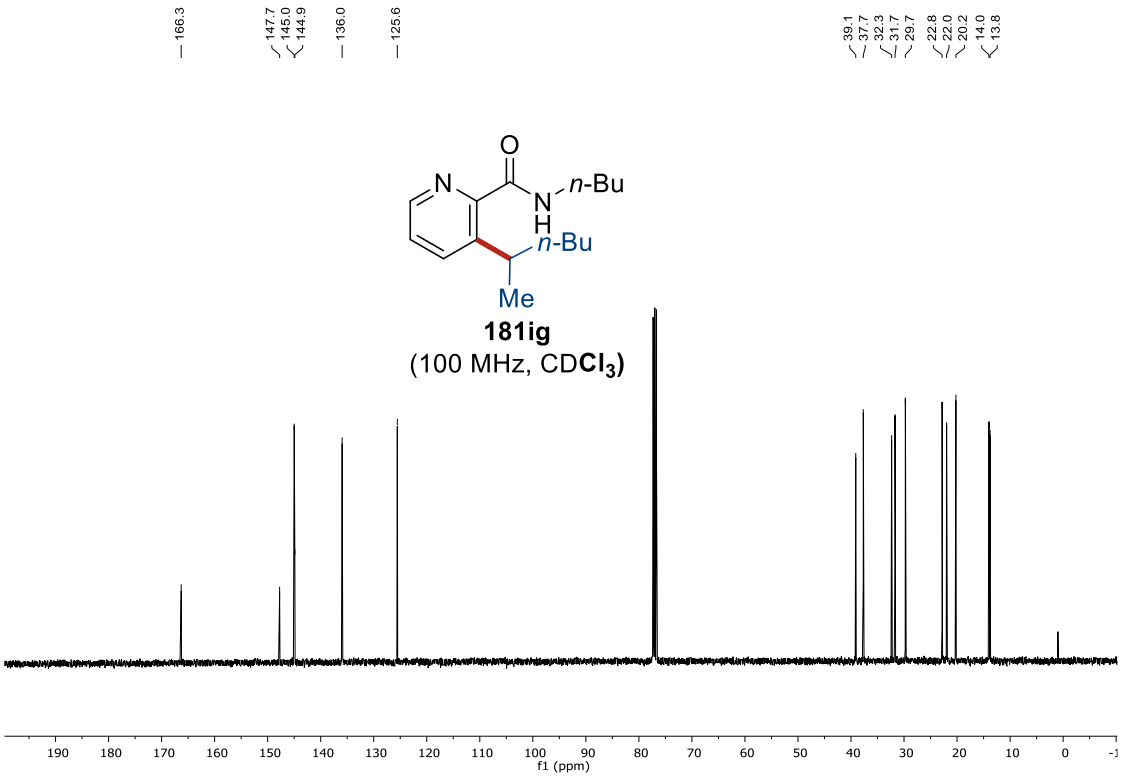


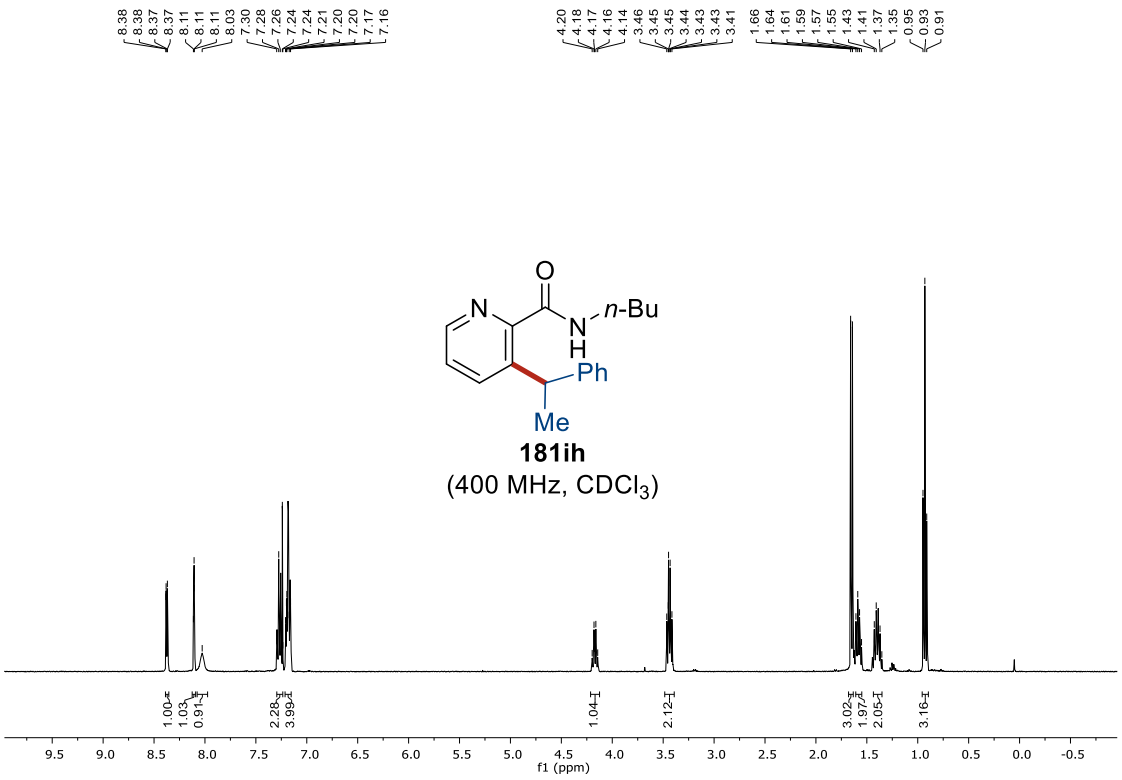
181if
(300 MHz, $CDCl_3$)

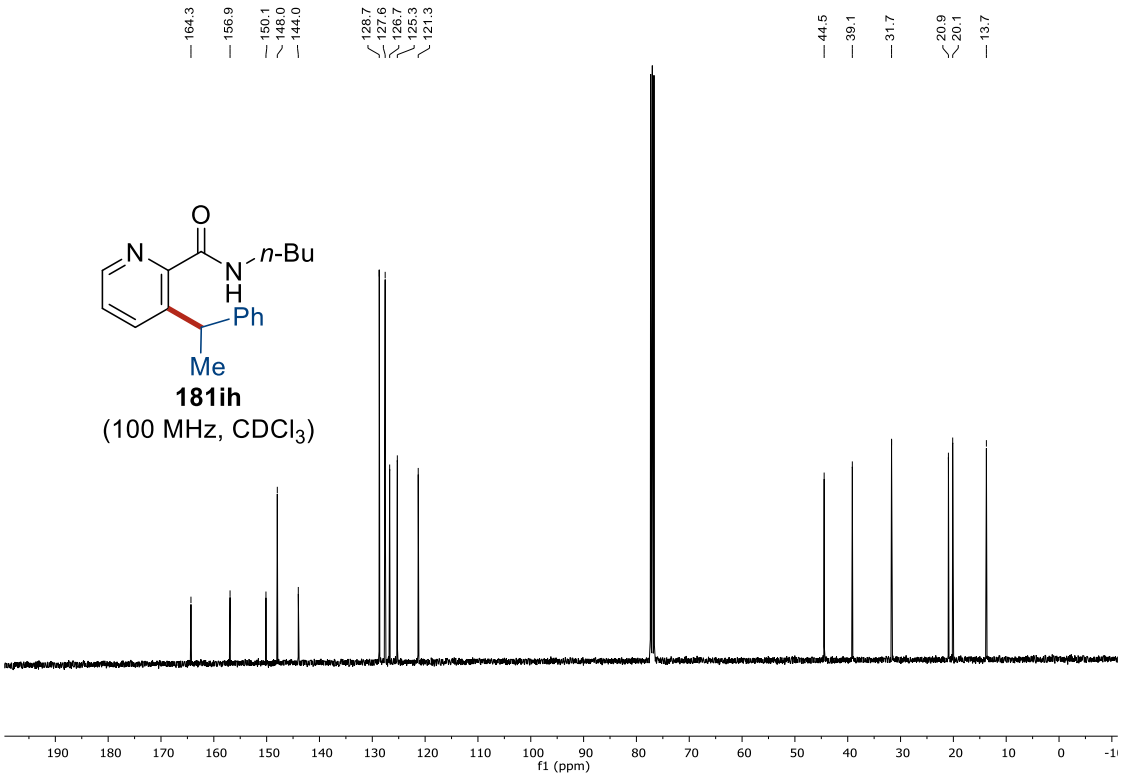


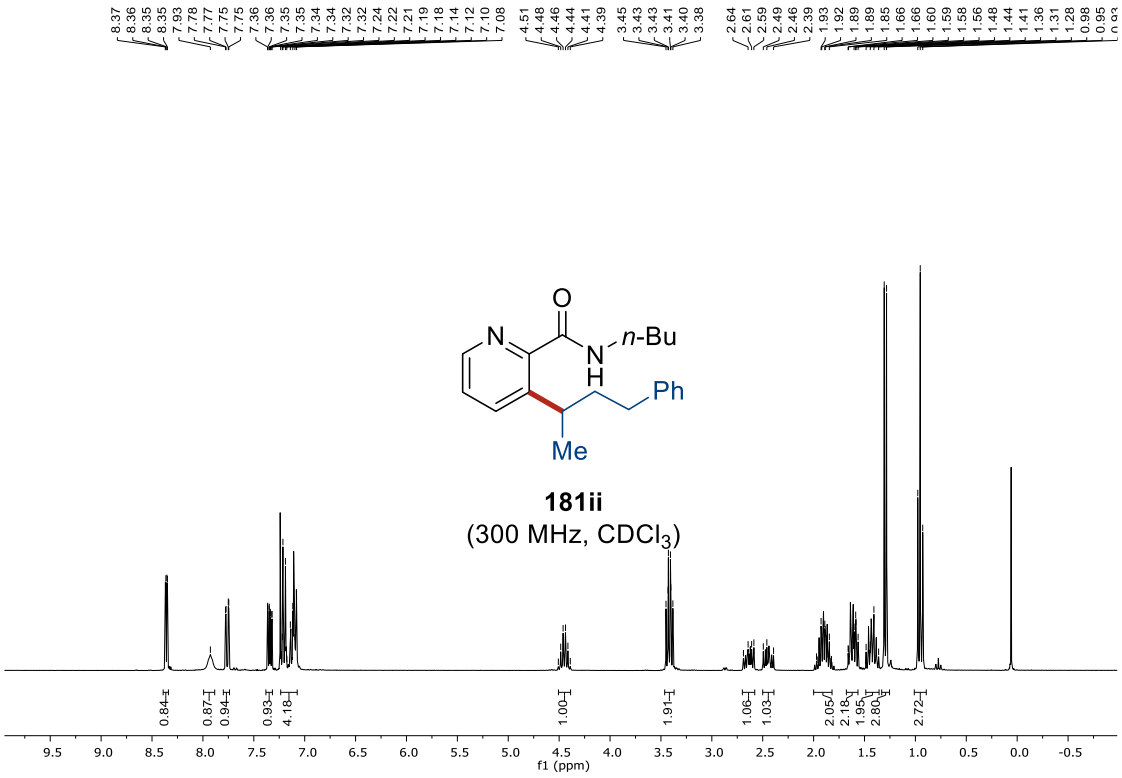

166.1
147.7
144.9
144.5
135.8
125.4
39.1
34.0
31.7
30.8
21.4
20.3
13.8
12.1
O
N
N
H
n-Bu
i-Bu
181if
(125 MHz, CDCl3)
f1 (ppm)

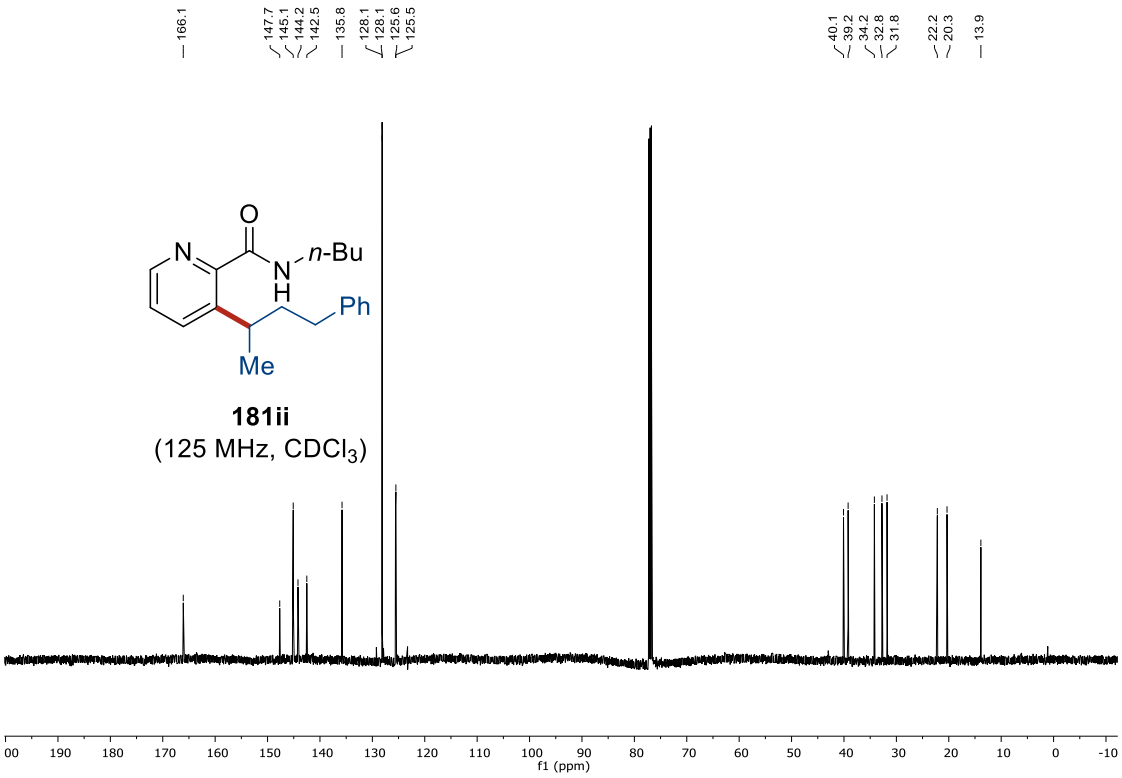

O
N
N
H
n-Bu
n-Bu
Me
181ig
(300 MHz, CDCl3)
1.00
0.88
1.03
1.02
1.02
2.07
f1 (ppm)

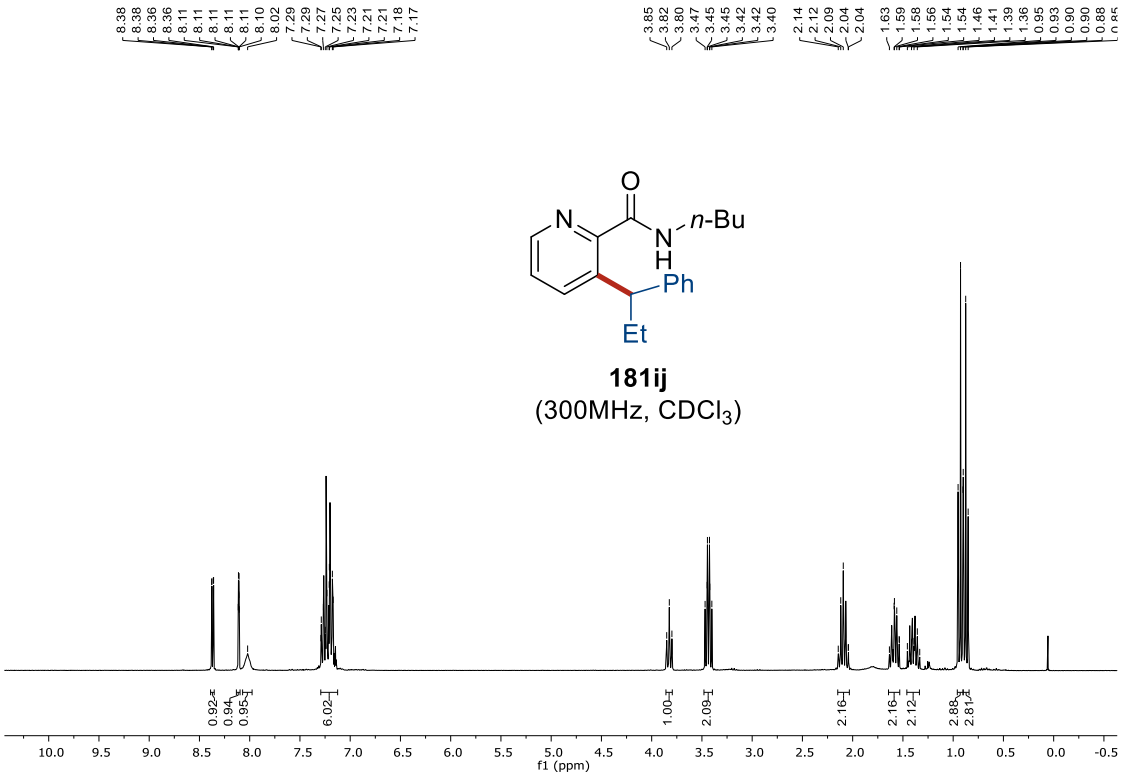

166.3
147.7
145.0
144.9
136.0
125.6
39.1
37.7
32.3
31.7
29.7
22.8
22.0
20.2
14.0
13.8
O
N
N
H
n-Bu
n-Bu
Me
181ig
(100 MHz, CDCl3)
f1 (ppm)

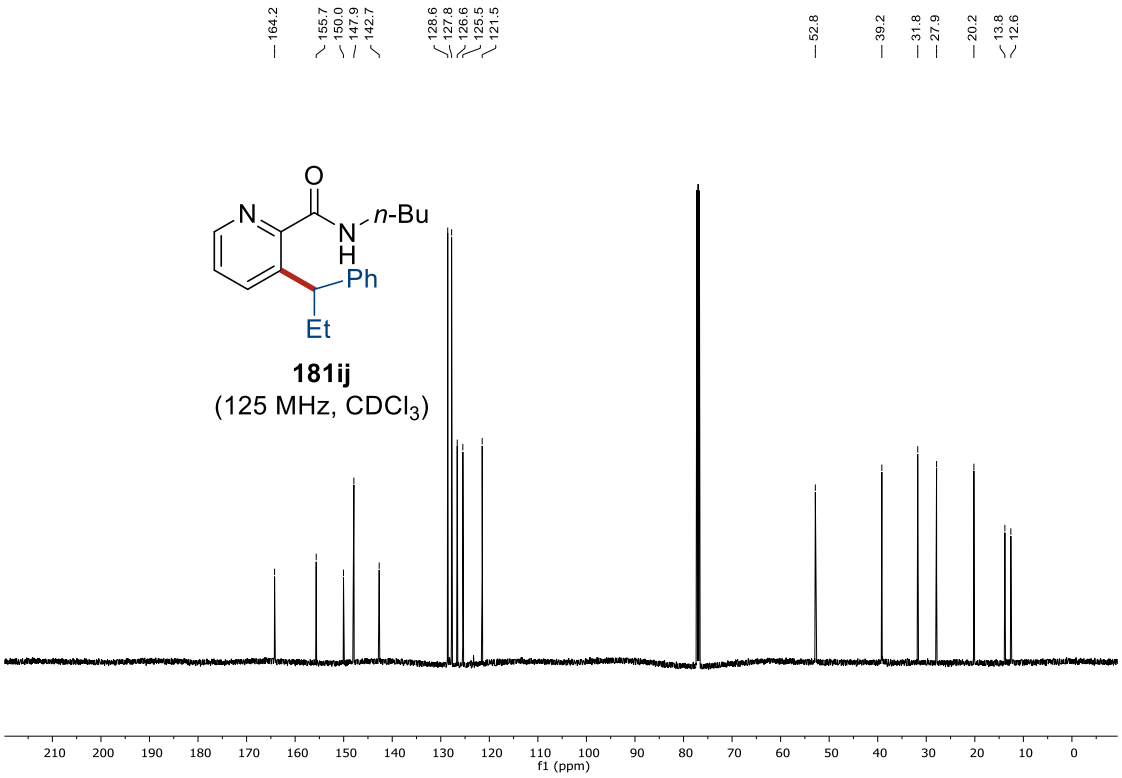

8.38
8.38
8.37
8.37
8.11
8.11
8.11
8.03
7.30
7.28
7.26
7.24
7.24
7.21
7.20
7.20
7.17
7.16
4.20
4.18
4.17
4.16
4.14
3.46
3.45
3.45
3.44
3.43
3.43
3.41
1.66
1.64
1.61
1.59
1.57
1.55
1.43
1.41
1.37
1.35
0.95
0.93
0.91
O
N
N
H
n-Bu
Ph
Me
181ih
(400 MHz, CDCl3)
1.00
1.03
0.91
2.28
3.99
1.04
2.12
3.02
1.97
2.05
3.16
f1 (ppm)


164.3
156.9
150.1
148.0
144.0
128.7
127.6
126.7
125.3
121.3
44.5
39.1
31.7
20.9
20.1
13.7
O
N
N
H
n-Bu
Ph
Me
181ih
(100 MHz, CDCl3)
f1 (ppm)

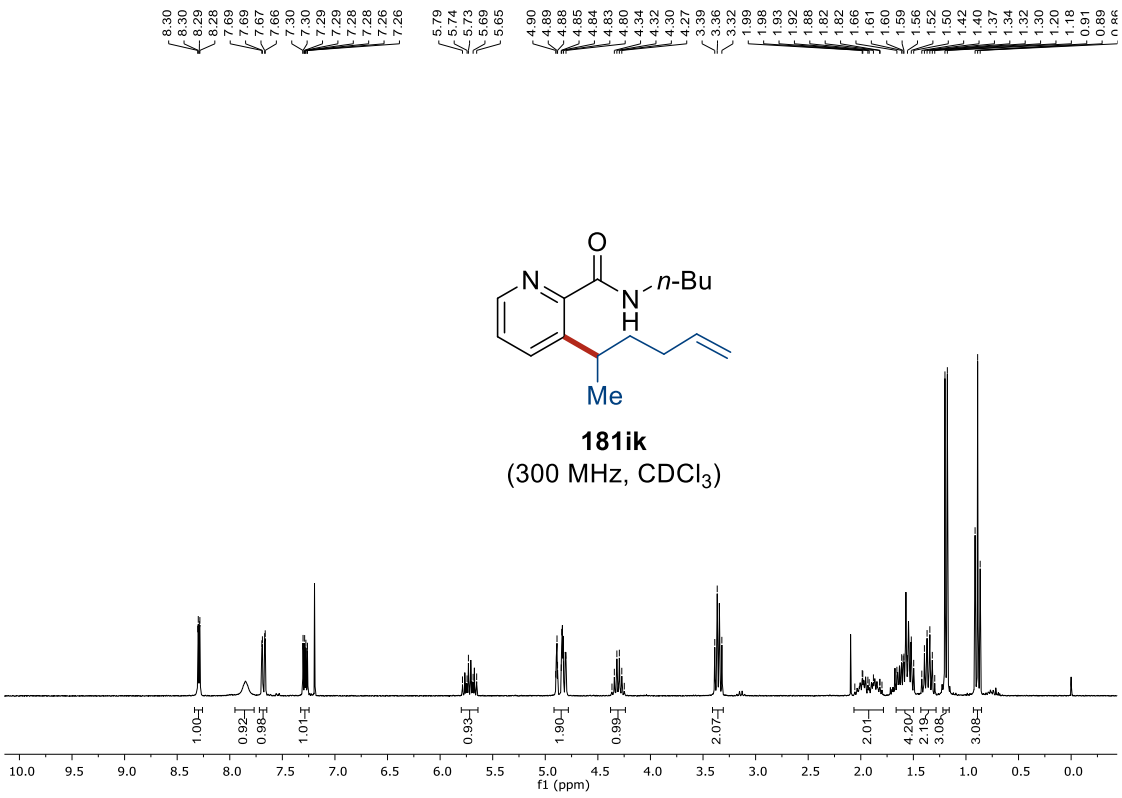

O
N
N
H
n-Bu
Ph
Me
181ii
(300 MHz, CDCl3)
0.84
0.87
0.94
0.93
4.18
1.00
1.91
1.06
1.03
2.05
2.18
1.95
2.80
2.72
f1 (ppm)


166.1
147.7
145.1
144.2
142.5
135.8
128.1
128.1
125.6
125.5
40.1
39.2
34.2
32.8
31.8
22.2
20.3
13.9
O
N
n-Bu
N
H
Ph
Me
181ii
(125 MHz, CDCl3)
f1 (ppm)

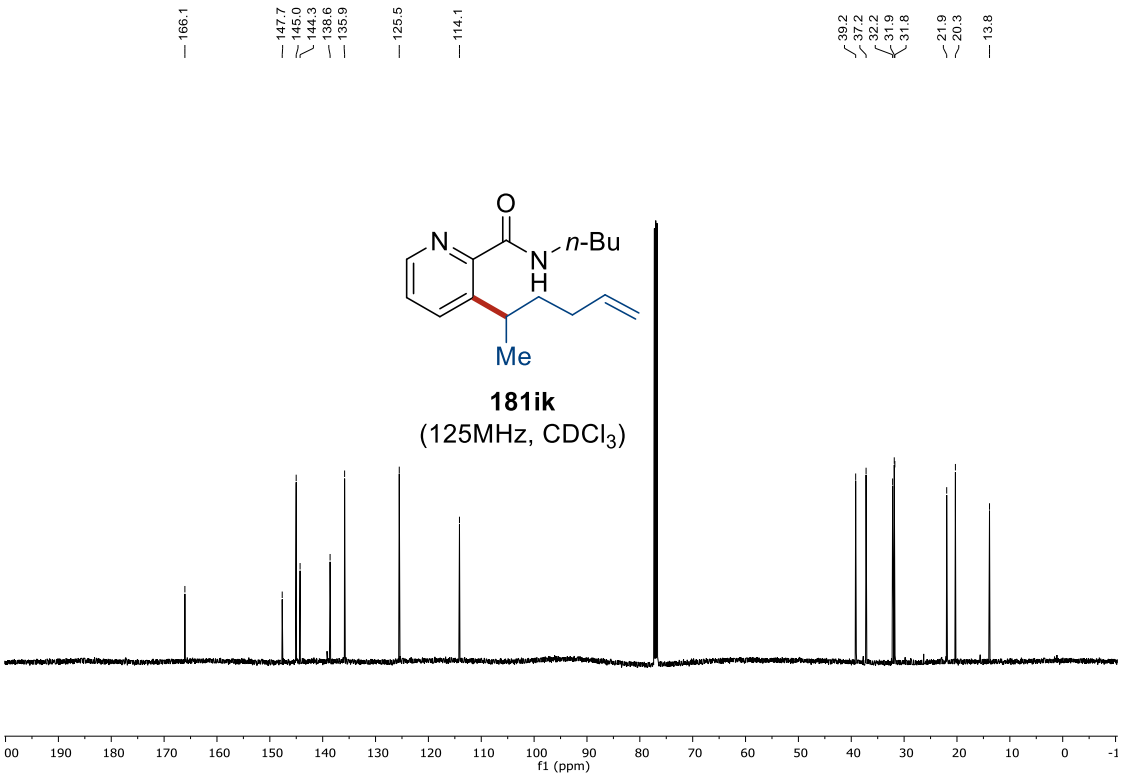

8.38
8.38
8.36
8.36
8.11
8.11
8.11
8.11
8.10
8.02
7.29
7.29
7.27
7.25
7.23
7.21
7.21
7.18
7.17
3.85
3.82
3.80
3.47
3.45
3.45
3.42
3.42
3.40
2.14
2.12
2.09
2.04
2.04
1.63
1.59
1.58
1.56
1.54
1.54
1.46
1.41
1.39
1.36
0.95
0.93
0.90
0.90
0.88
O
N
n-Bu
N
H
Ph
Et
181ij
(300MHz, CDCl3)
0.92
0.94
0.95
6.02
1.00
2.09
2.16
2.16
2.12
2.88
2.81
f1 (ppm)

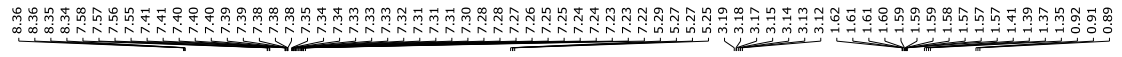


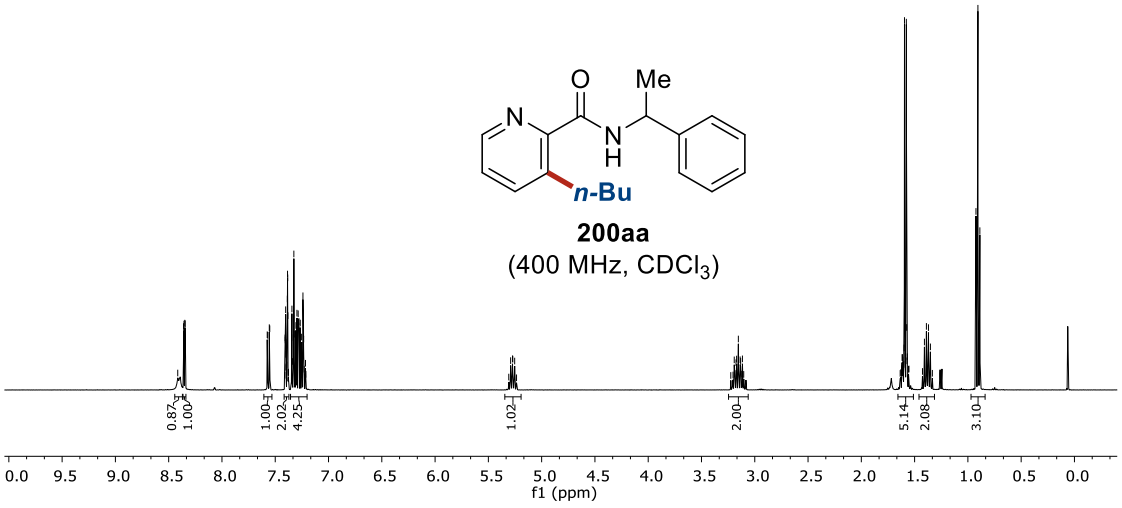
181ij
(125 MHz, $CDCl_3$)

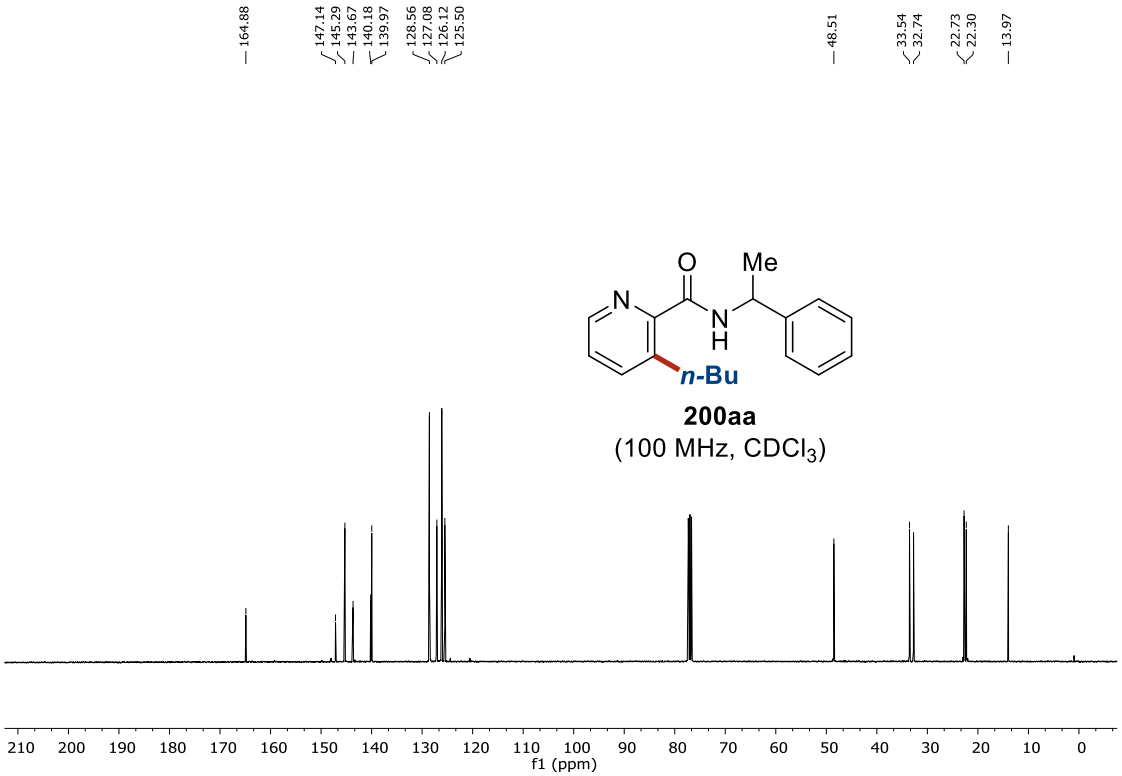


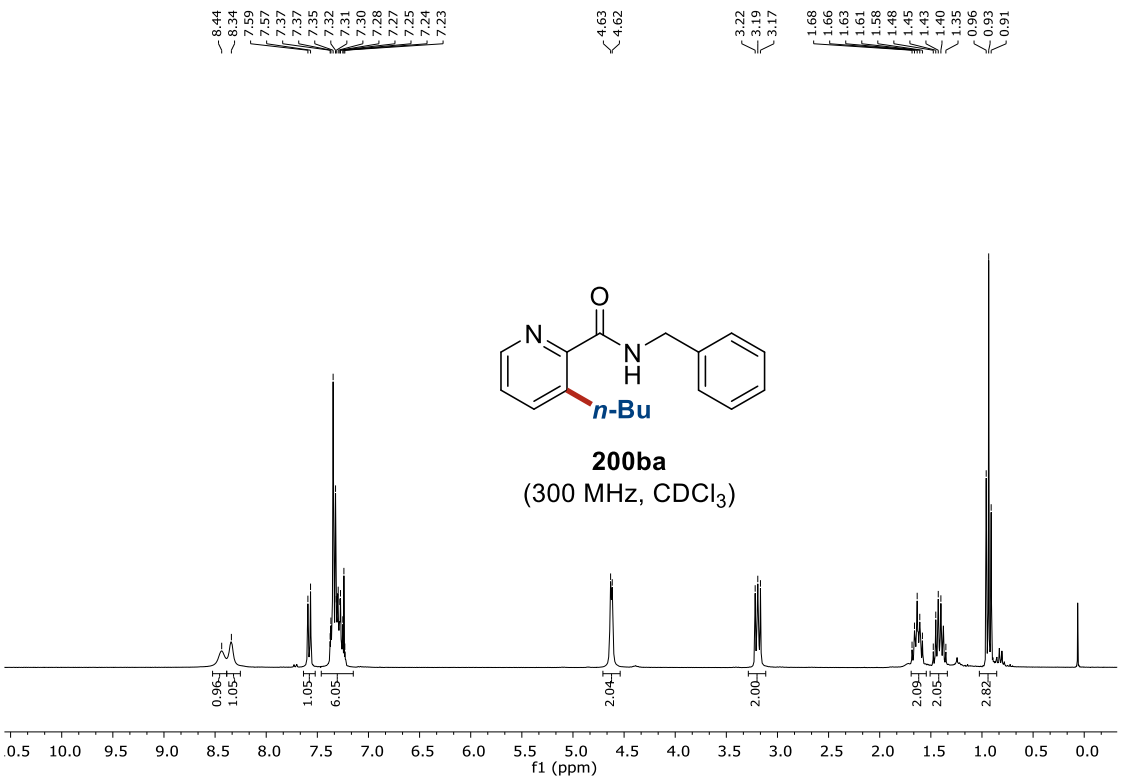
181ik
(300 MHz, $CDCl_3$)

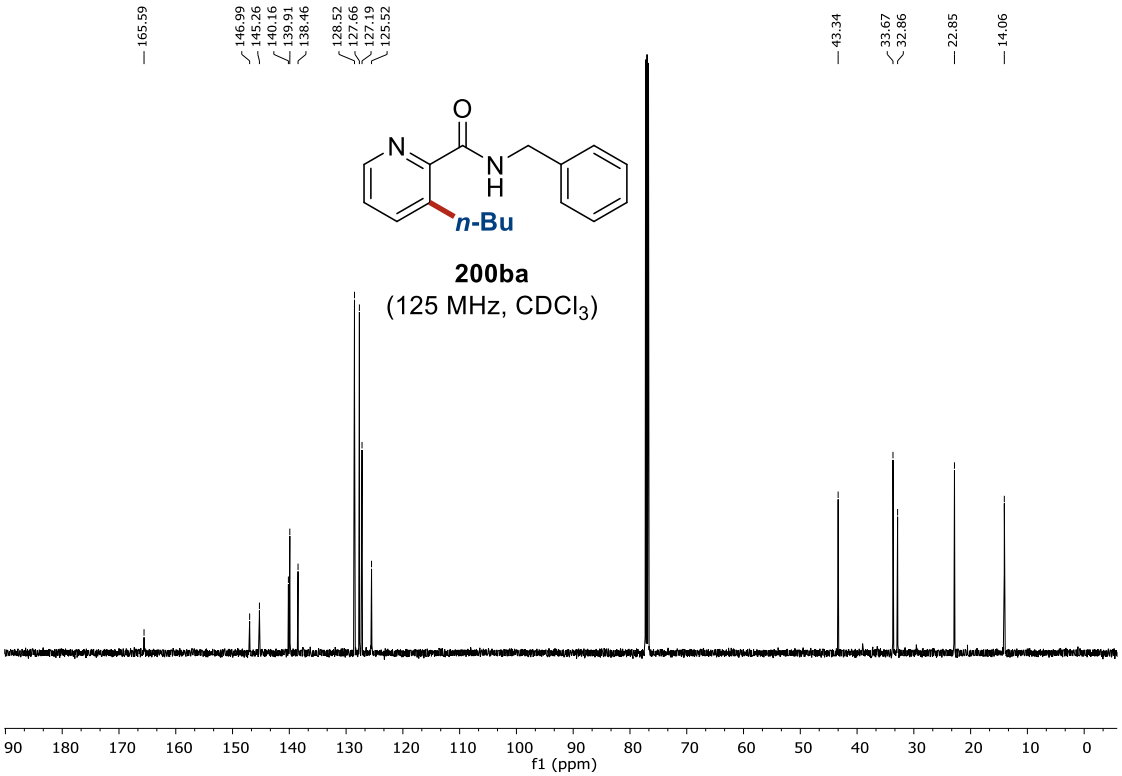

166.1
147.7
145.0
144.3
138.6
135.9
125.5
114.1
39.2
37.2
32.2
31.9
31.8
21.9
20.3
13.8
O
N
N
H
n-Bu
Me
181ik
(125MHz, CDCl3)
f1 (ppm)

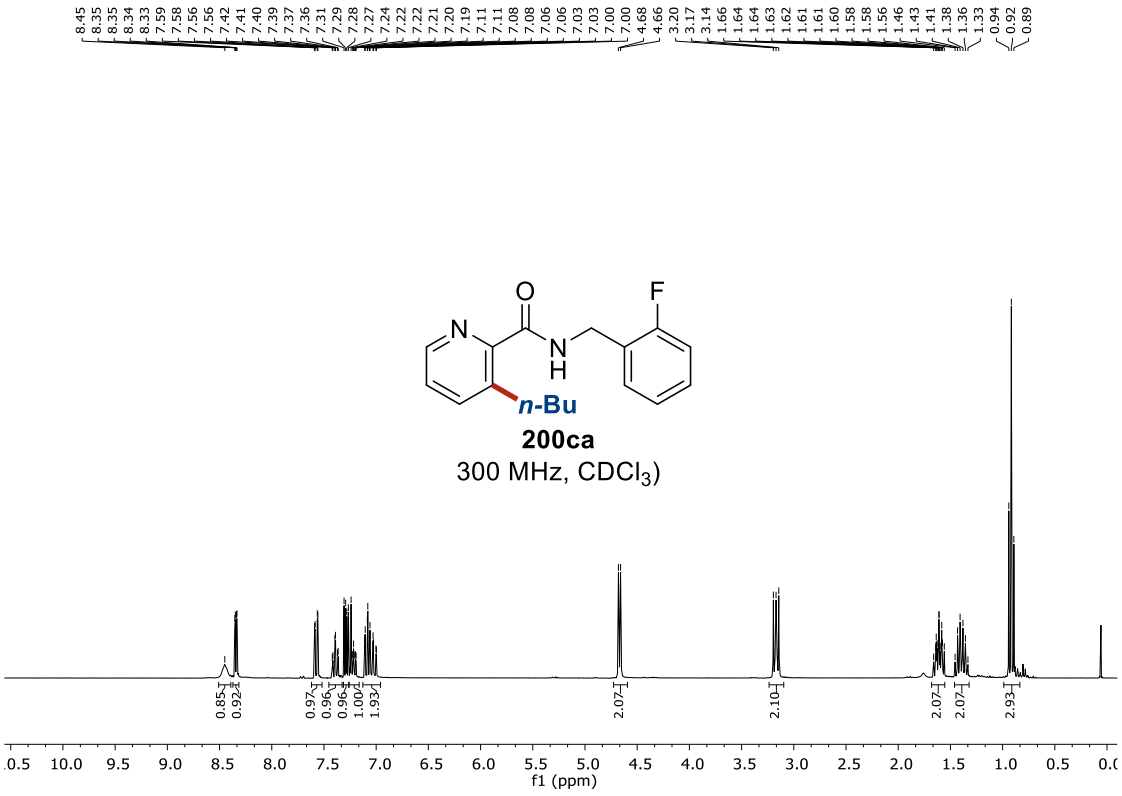

8.36
8.36
8.35
8.34
7.58
7.57
7.56
7.55
7.41
7.41
7.40
7.40
7.40
7.39
7.39
7.38
7.38
7.38
7.35
7.34
7.34
7.33
7.33
7.33
7.32
7.31
7.31
7.31
7.30
7.28
7.28
7.27
7.26
7.25
7.25
7.24
7.24
7.23
7.23
7.22
5.29
5.27
5.27
5.25
3.19
3.18
3.17
3.15
3.14
3.13
3.12
1.62
1.61
1.61
1.60
1.59
1.59
1.59
1.58
1.57
1.57
1.57
1.41
1.39
1.37
1.35
0.92
0.91
0.89

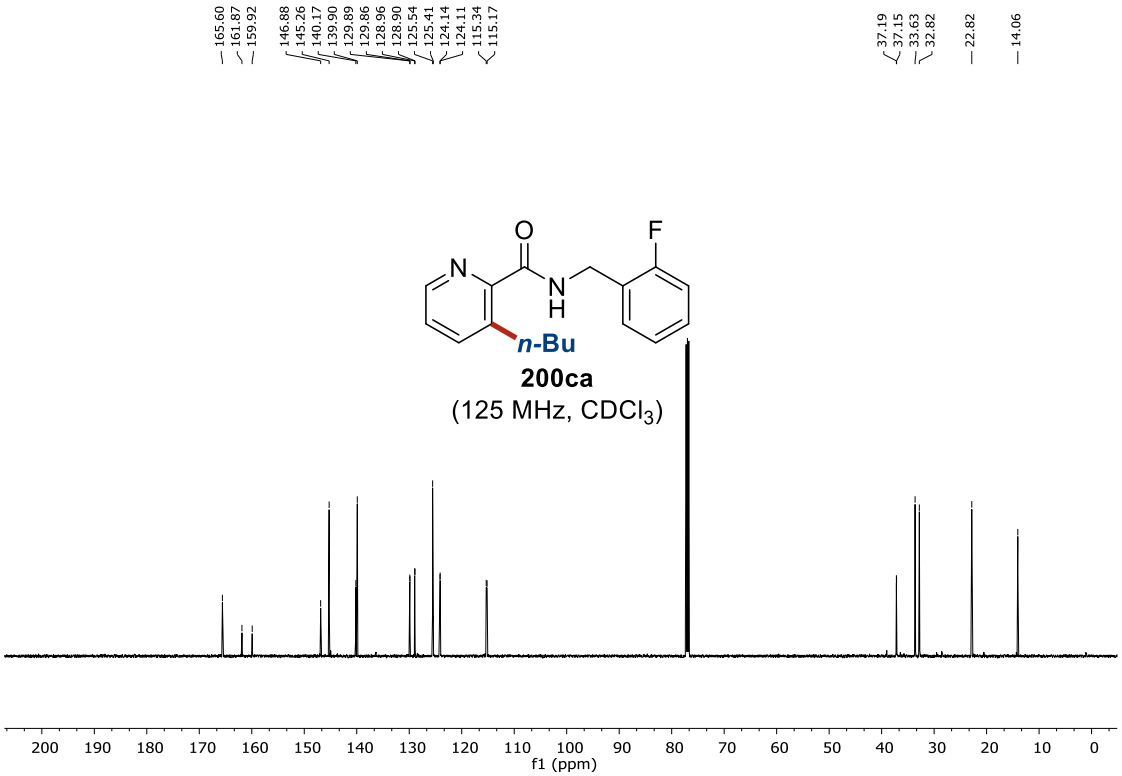

O
Me
N
N
H
n-Bu
200aa
(400 MHz, CDCl3)
0.87
1.00
1.00
2.02
4.25
1.02
2.00
5.14
2.08
3.10
f1 (ppm)

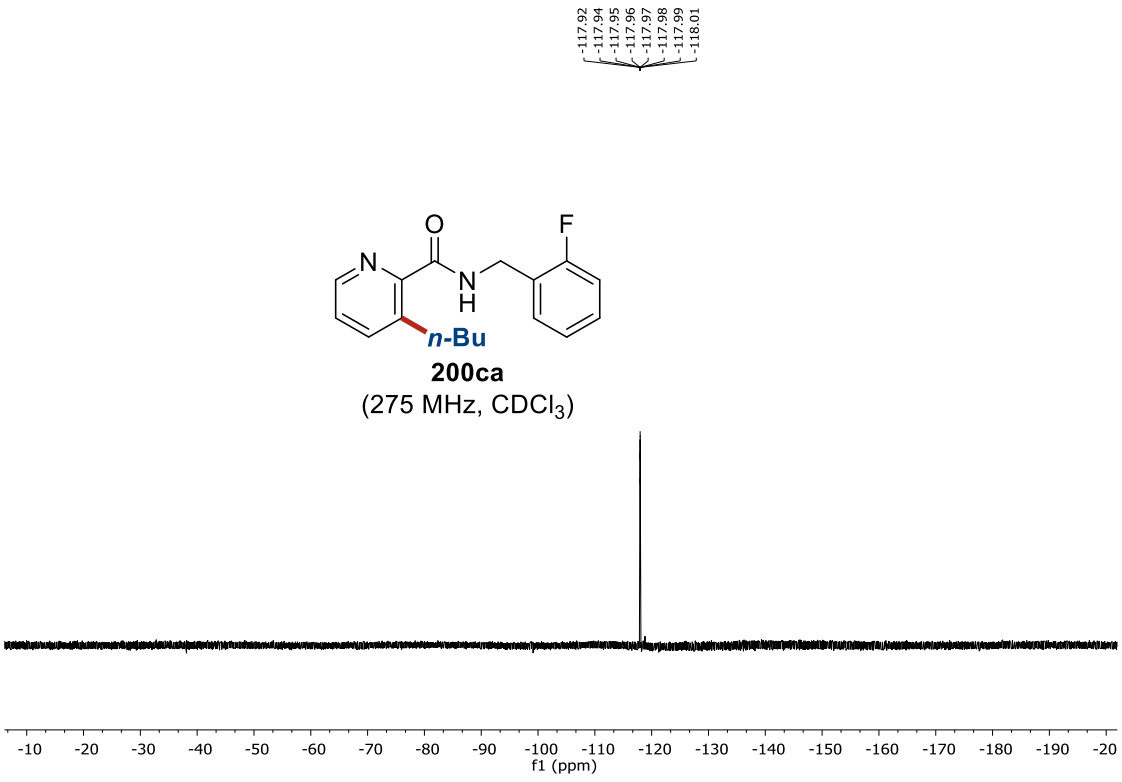

164.88
147.14
145.29
143.67
140.18
139.97
128.56
127.08
126.12
125.50
48.51
33.54
32.74
22.73
22.30
13.97
O
Me
N
N
H
n-Bu
200aa
(100 MHz, CDCl3)
f1 (ppm)

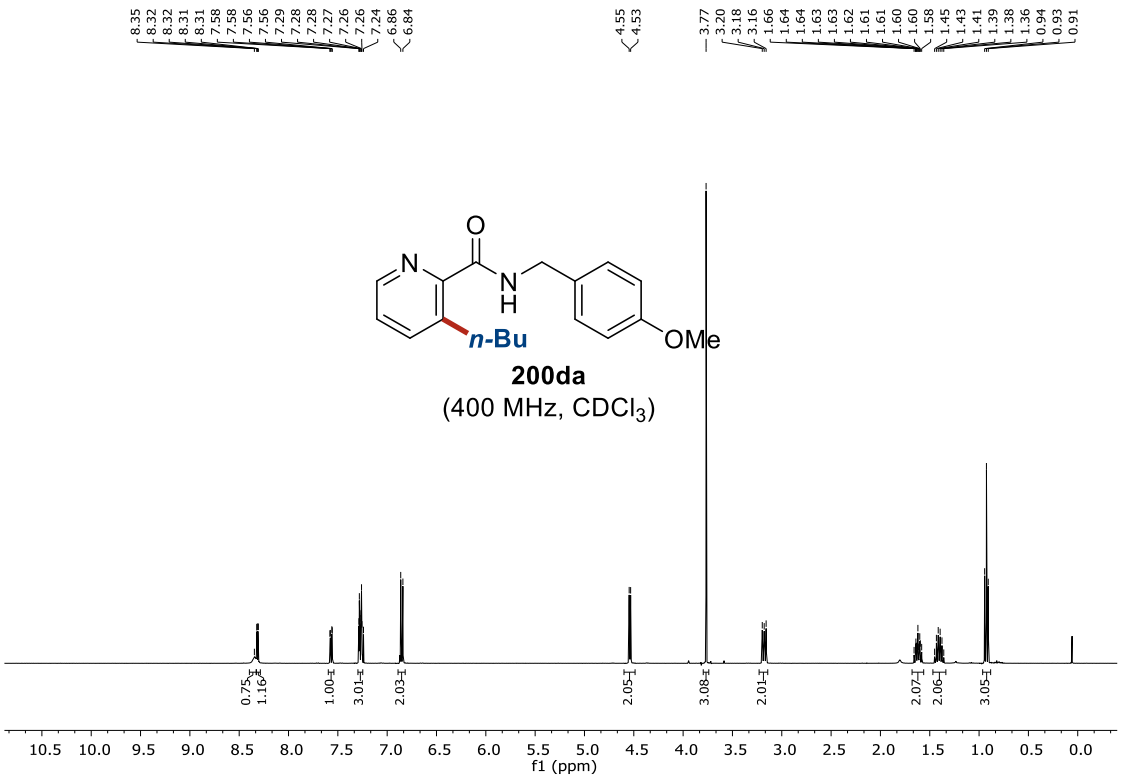

8.44
8.34
7.59
7.57
7.37
7.37
7.35
7.32
7.31
7.30
7.28
7.27
7.25
7.24
7.23
4.63
4.62
3.22
3.19
3.17
1.68
1.66
1.63
1.61
1.58
1.48
1.45
1.43
1.40
1.35
0.96
0.93
0.91
O
N
N
H
n-Bu
200ba
(300 MHz, CDCl3)
0.96
1.05
1.05
6.05
2.04
2.00
2.09
2.05
2.82
f1 (ppm)

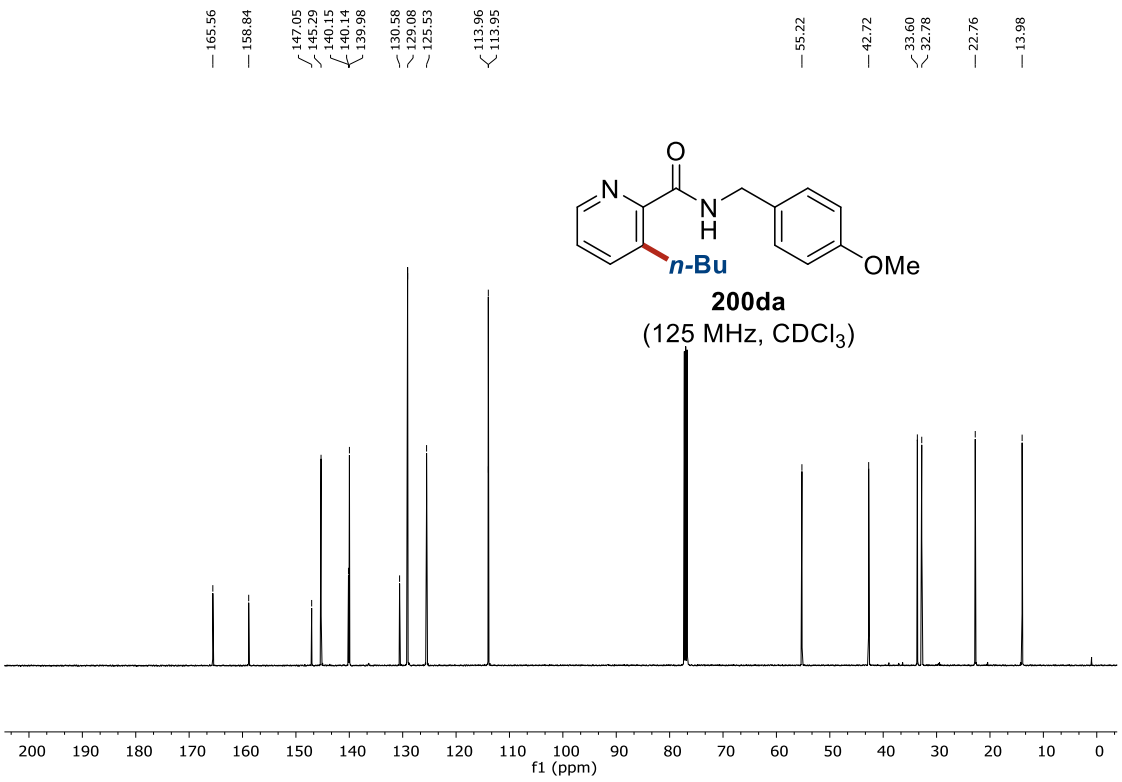

165.59
146.99
145.26
140.16
139.91
138.46
128.52
127.66
127.19
125.52
43.34
33.67
32.86
22.85
14.06
O
N
N
H
n-Bu
200ba
(125 MHz, CDCl3)
f1 (ppm)

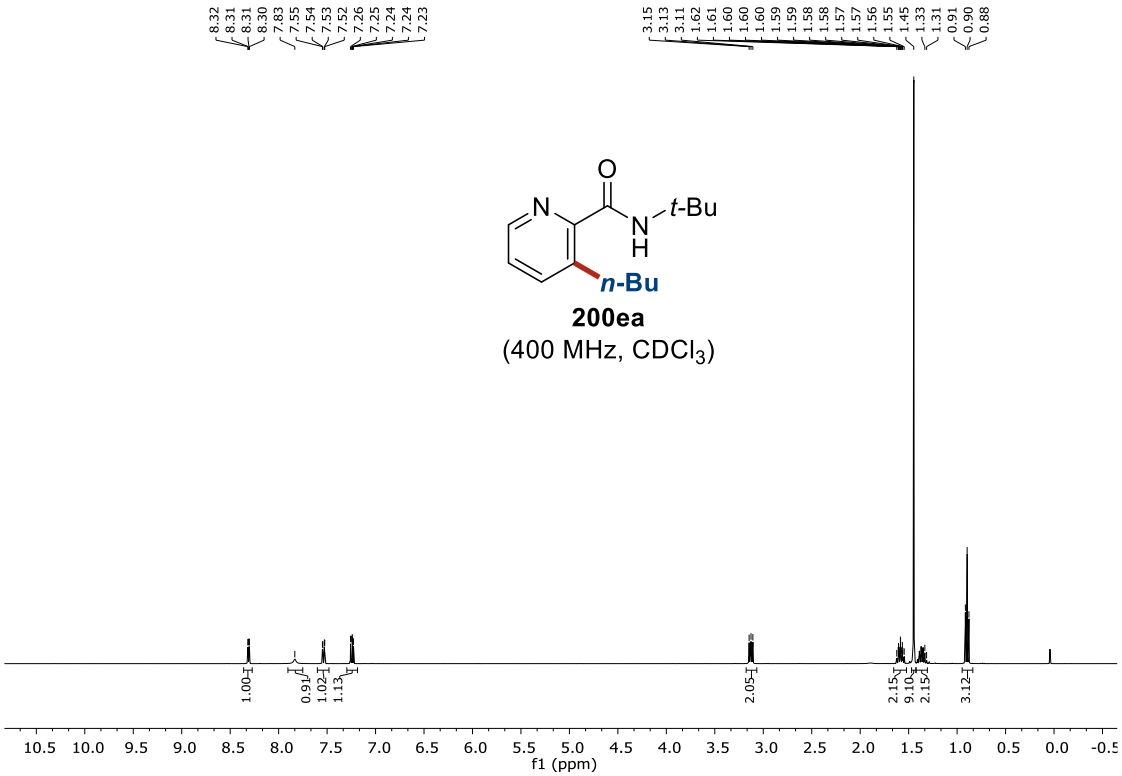

8.45
8.35
8.35
8.34
8.33
7.59
7.58
7.56
7.56
7.42
7.41
7.40
7.39
7.37
7.36
7.31
7.29
7.28
7.27
7.24
7.22
7.22
7.21
7.20
7.19
7.11
7.11
7.08
7.08
7.06
7.06
7.03
7.03
7.00
7.00
4.68
4.66
3.20
3.17
3.14
1.66
1.64
1.64
1.63
1.62
1.61
1.61
1.60
1.58
1.58
1.56
1.46
1.43
1.41
1.38
1.36
1.33
0.94
0.92
0.89
O
F
N
N
H
n-Bu
200ca
300 MHz, CDCl3)
0.85
0.92
0.97
0.96
0.96
1.00
1.93
2.07
2.10
2.07
2.07
2.93
f1 (ppm)


165.60
161.87
159.92
146.88
145.26
140.17
139.90
129.89
129.86
128.96
128.90
125.54
125.41
124.14
124.11
115.34
115.17
37.19
37.15
33.63
32.82
22.82
14.06
O
F
N
N
H
n-Bu
200ca
(125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

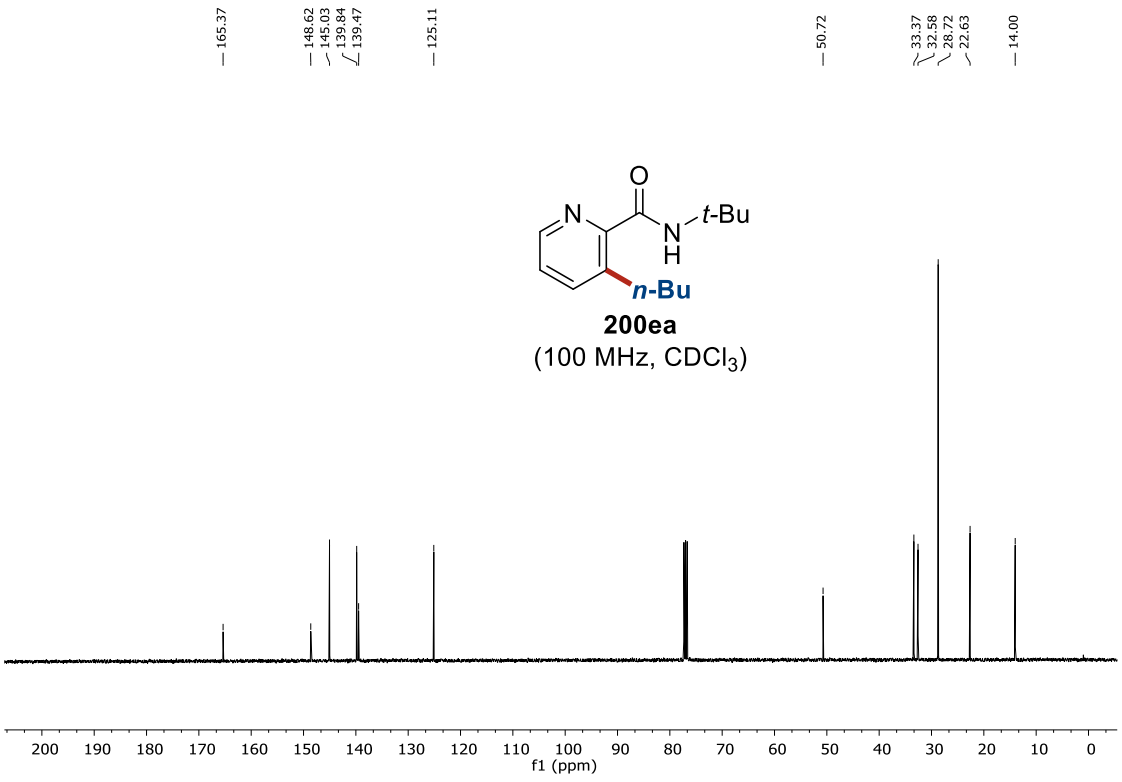

-117.92
-117.94
-117.95
-117.96
-117.97
-117.98
-117.99
-118.01
O
F
N
N
H
n-Bu
200ca
(275 MHz, CDCl3)
-10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -20
f1 (ppm)


8.35
8.32
8.32
8.31
8.31
7.58
7.58
7.56
7.56
7.29
7.28
7.28
7.27
7.26
7.26
7.24
6.86
6.84
4.55
4.53
3.77
3.20
3.18
3.16
1.66
1.64
1.64
1.63
1.63
1.62
1.61
1.61
1.60
1.60
1.58
1.45
1.43
1.41
1.39
1.38
1.36
0.94
0.93
0.91
O
N
N
H
n-Bu
OMe
200da
(400 MHz, CDCl3)
0.75
1.16
1.00
3.01
2.03
2.05
3.08
2.01
2.07
2.06
3.05
10.5 10.0 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
f1 (ppm)

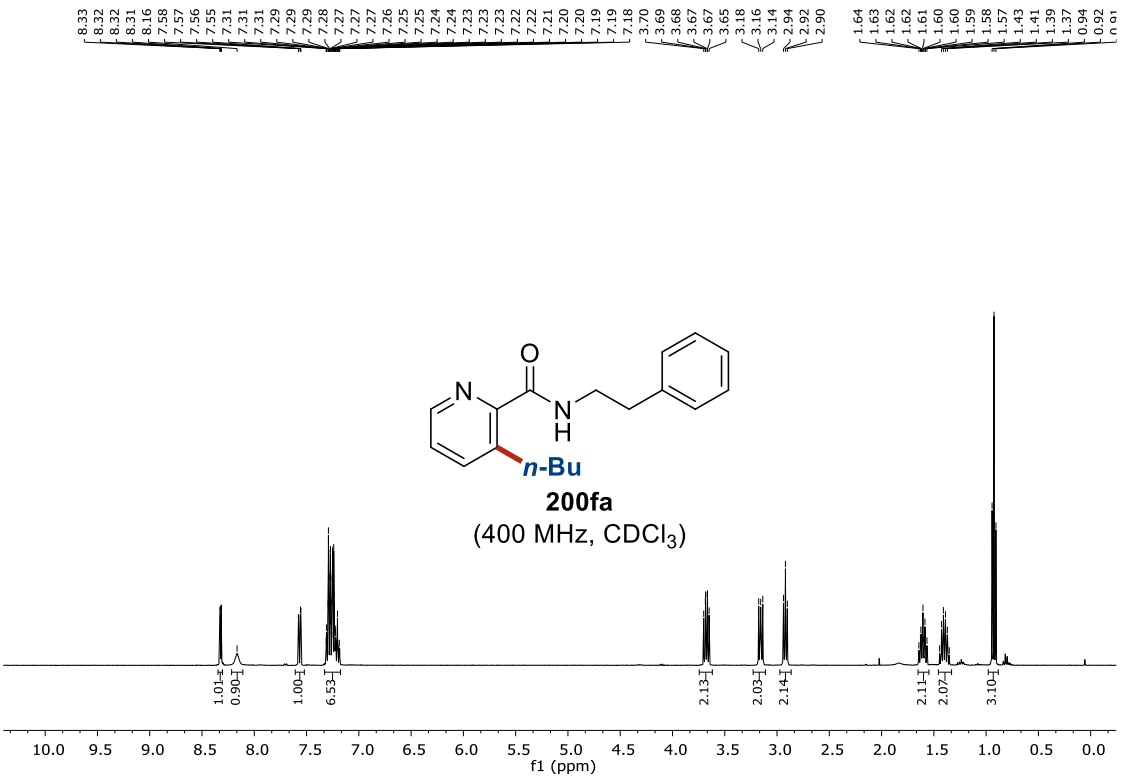

165.56
158.84
147.05
145.29
140.15
140.14
139.98
130.58
129.08
125.53
113.96
113.95
55.22
42.72
33.60
32.78
22.76
13.98
O
N
N
H
n-Bu
OMe
200da
(125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

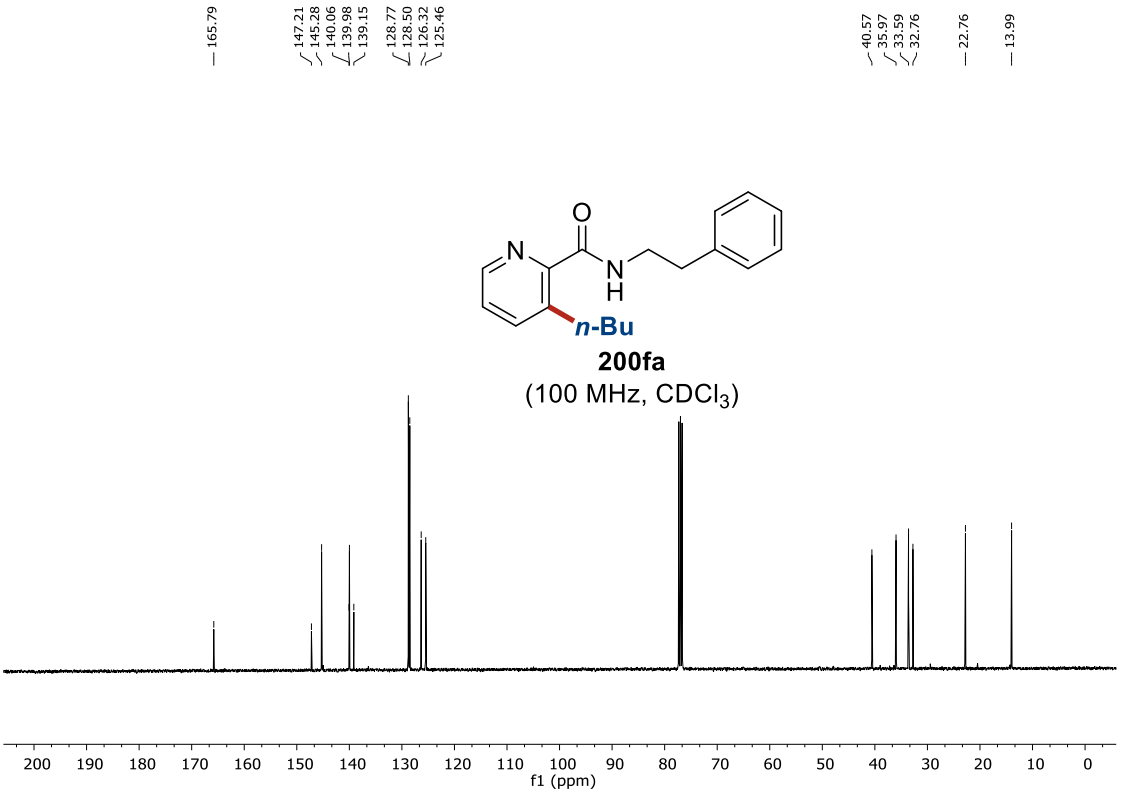


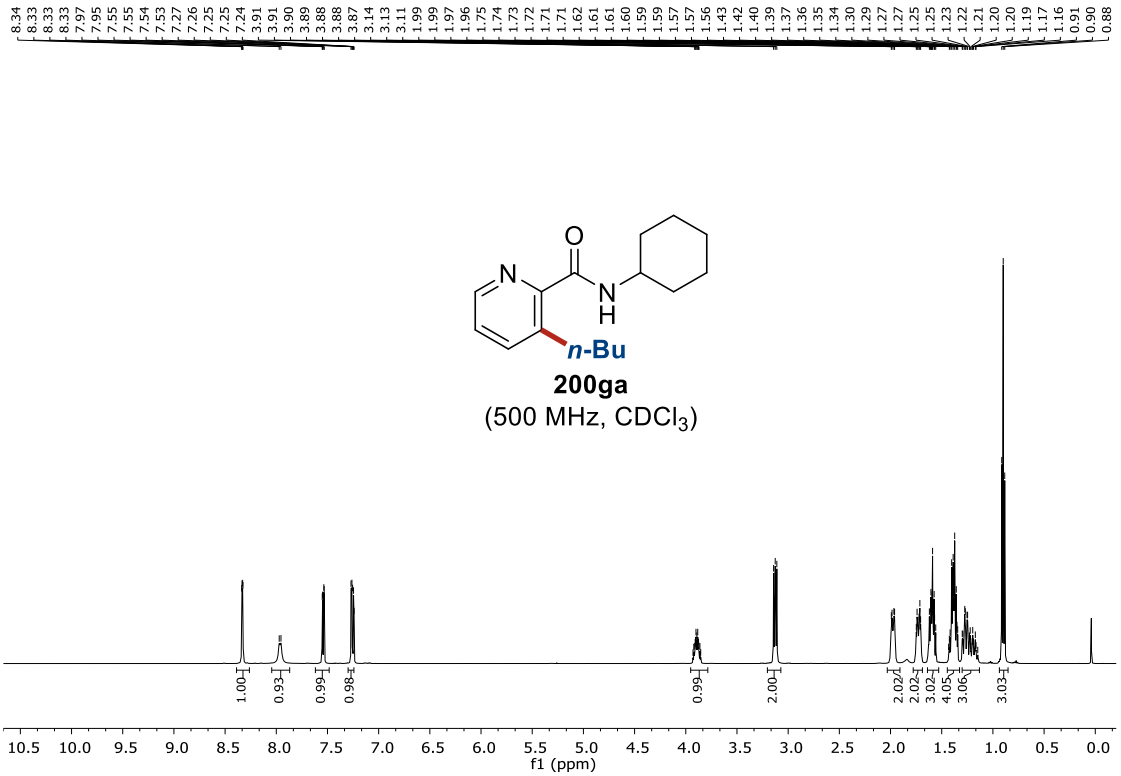
200ea
(400 MHz, $CDCl_3$)

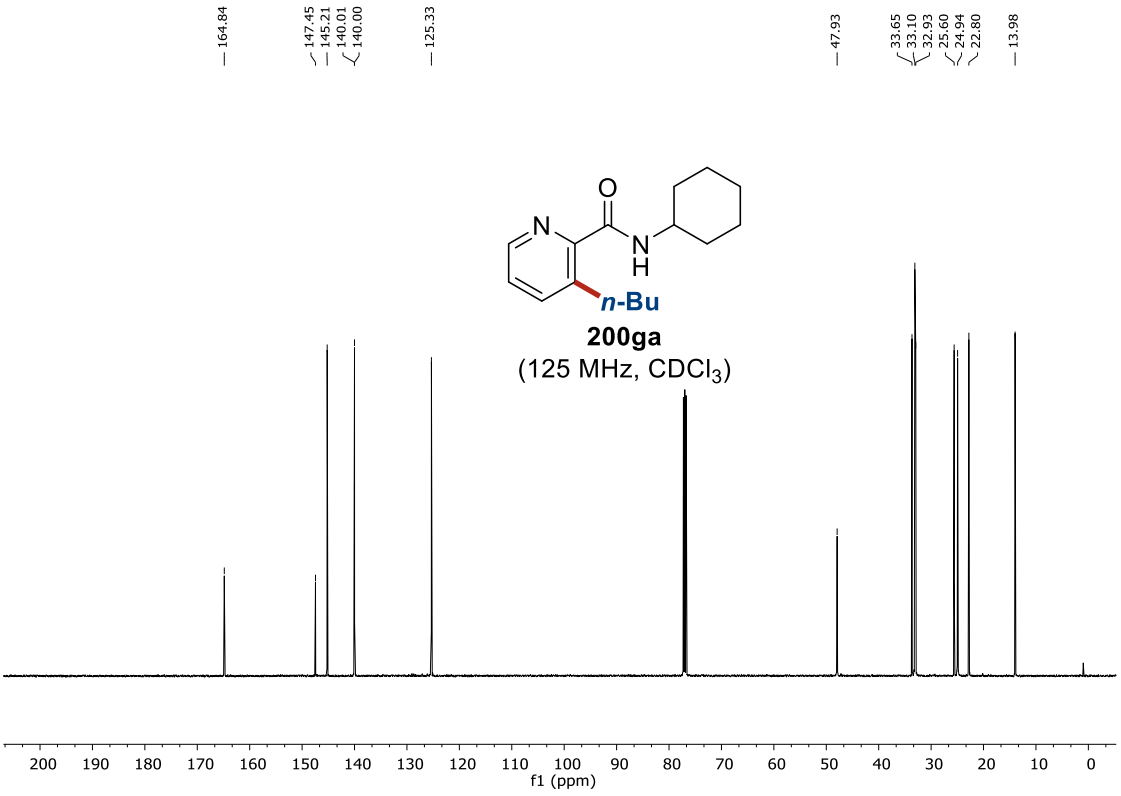


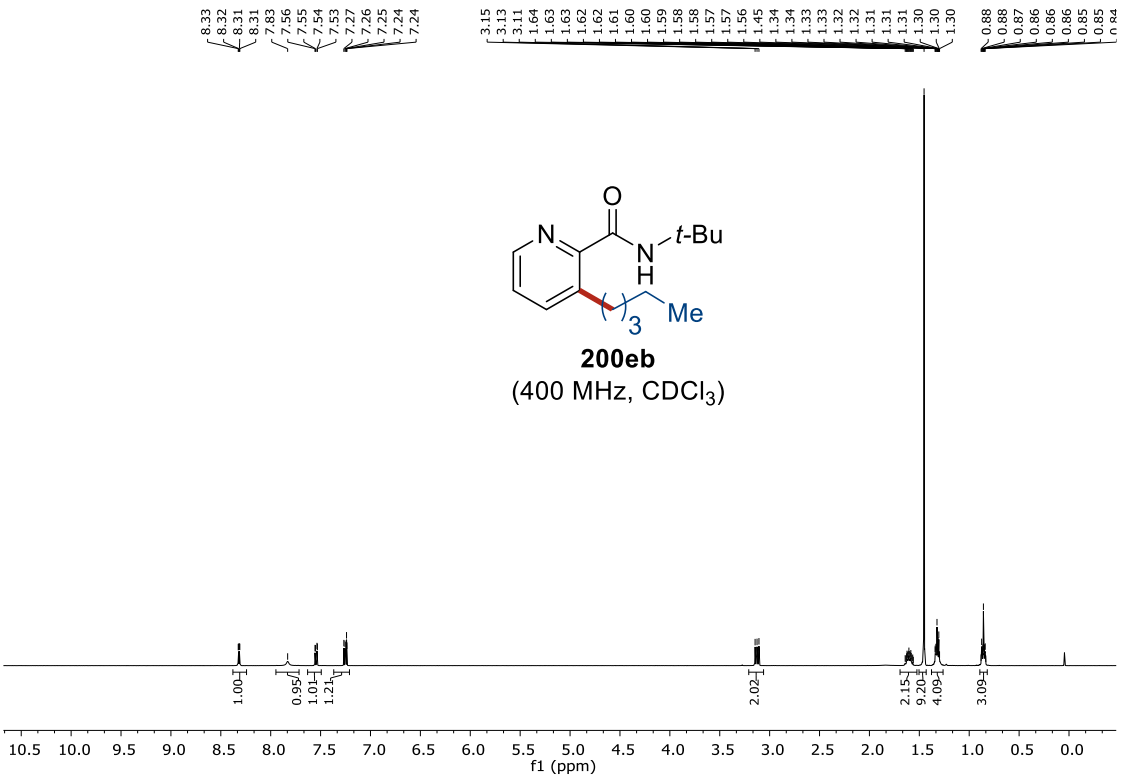
200ea
(100 MHz, $CDCl_3$)


n-Bu
200fa
(400 MHz, CDCl3)
f1 (ppm)

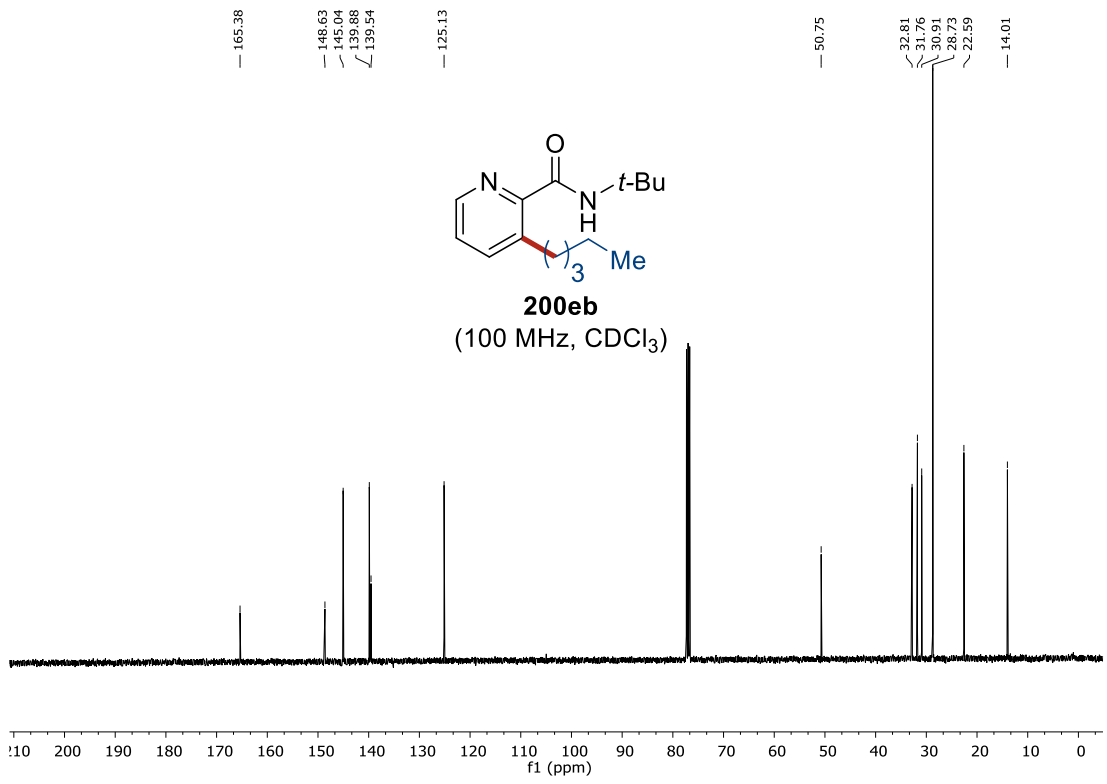

n-Bu
200fa
(100 MHz, CDCl3)
f1 (ppm)


8.34 8.33 8.33 8.33 7.97 7.95 7.55 7.55 7.54 7.53 7.27 7.26 7.25 7.25 7.24 3.91 3.91 3.90 3.89 3.88 3.88 3.87 3.14 3.13 3.11 1.99 1.99 1.97 1.96 1.75 1.74 1.73 1.72 1.71 1.71 1.62 1.61 1.61 1.60 1.59 1.59 1.57 1.57 1.56 1.43 1.42 1.40 1.39 1.37 1.36 1.35 1.34 1.30 1.29 1.27 1.27 1.25 1.25 1.23 1.22 1.21 1.20 1.20 1.19 1.17 1.16 0.91 0.90 0.88
O
N
N
H
n-Bu
200ga
(500 MHz, CDCl3)
1.00 0.93 0.99 0.98 0.99 2.00 2.02 2.02 3.02 4.05 3.06 3.03
10.5 10.0 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
f1 (ppm)

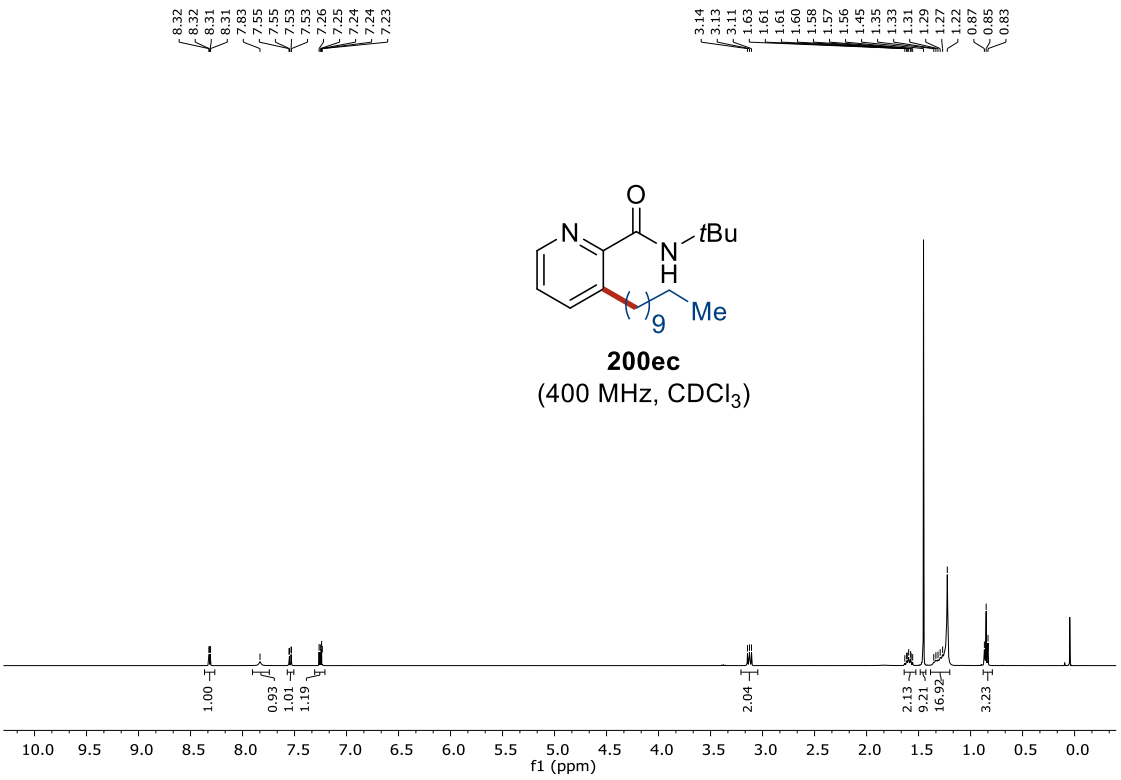

164.84 147.45 145.21 140.01 140.00 125.33 47.93 33.65 33.10 32.93 25.60 24.94 22.80 13.98
O
N
N
H
n-Bu
200ga
(125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

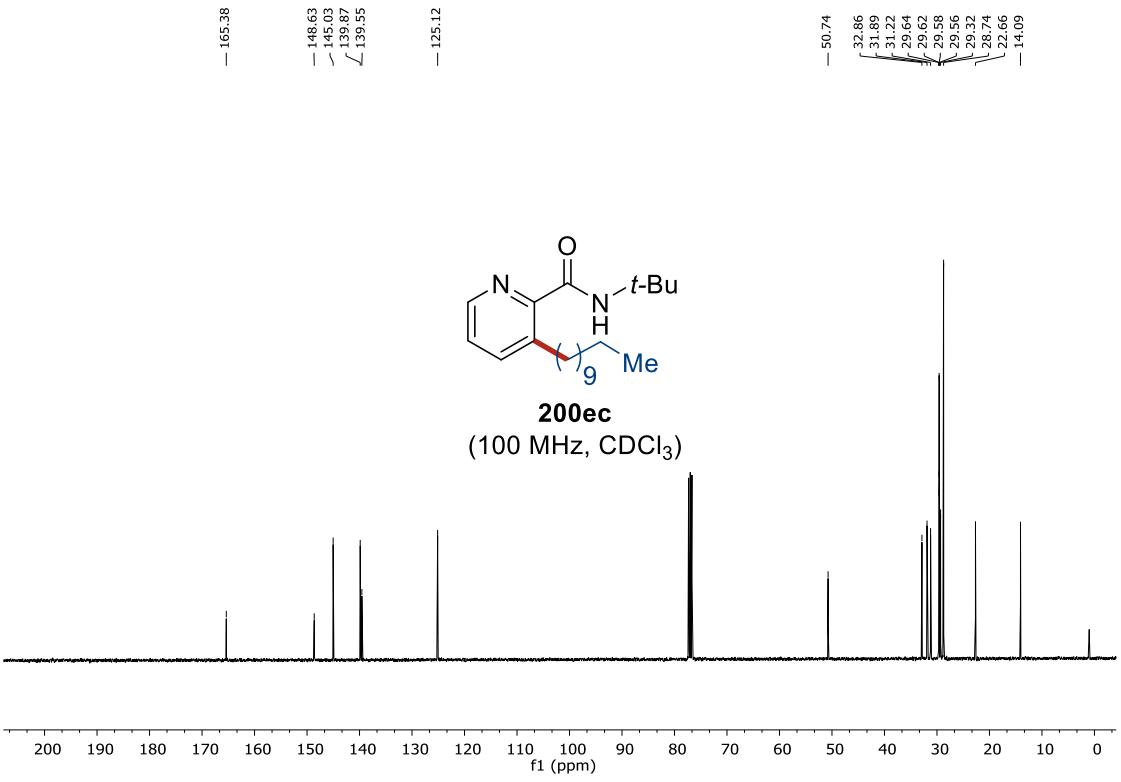


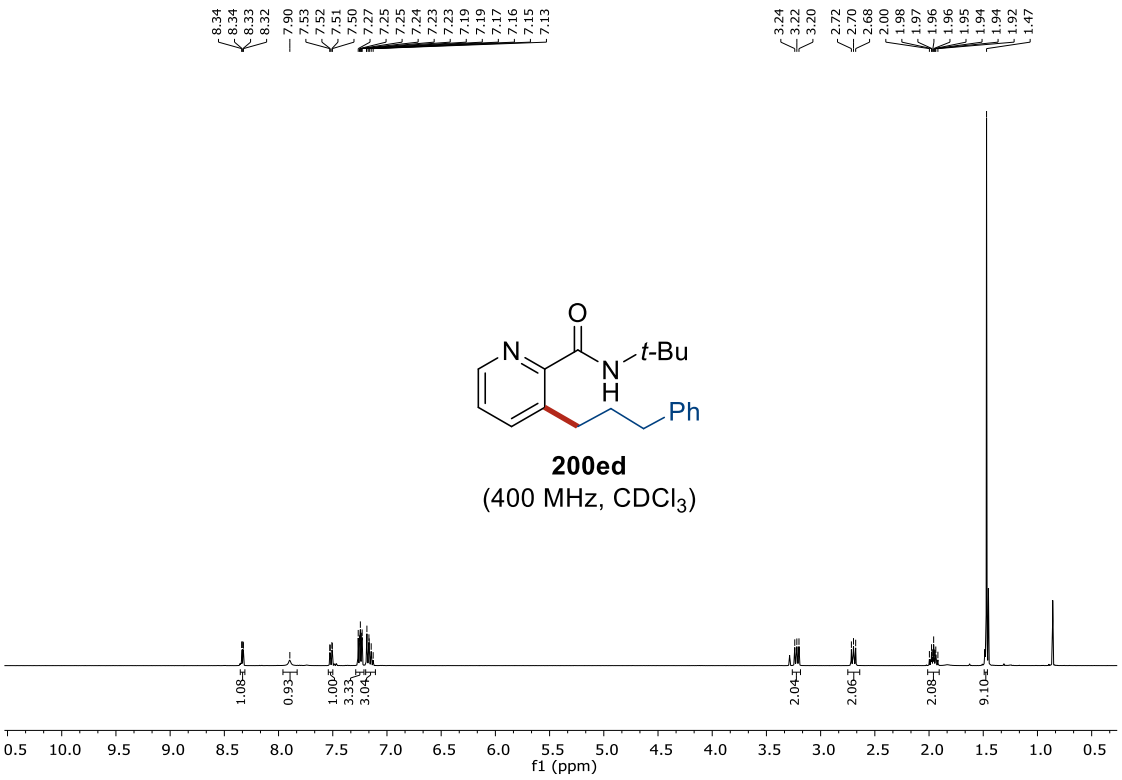
200eb
(400 MHz, $CDCl_3$)

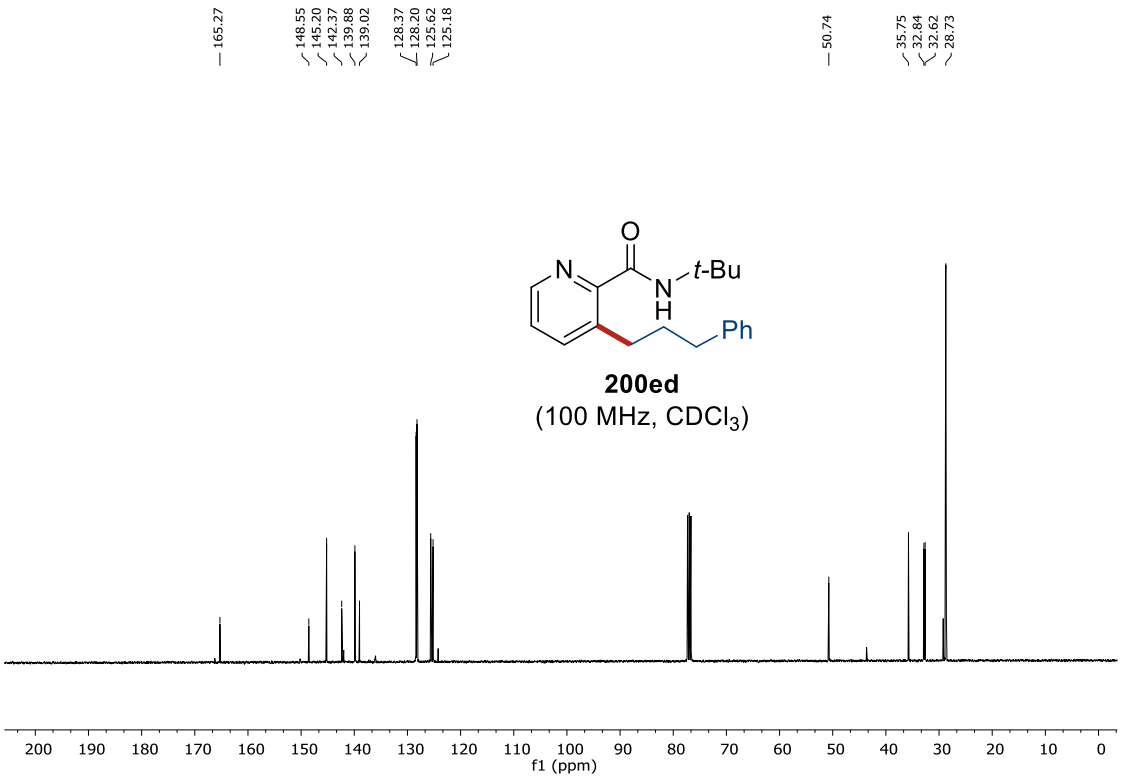


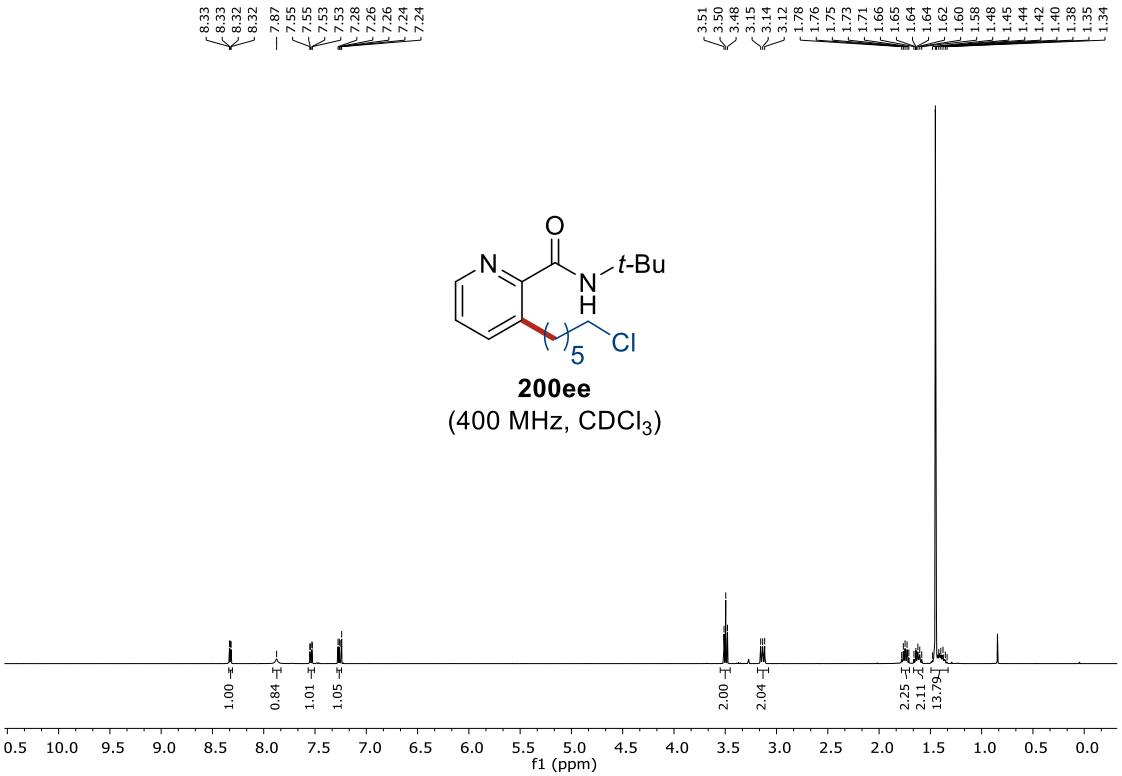
200eb
(100 MHz, $CDCl_3$)

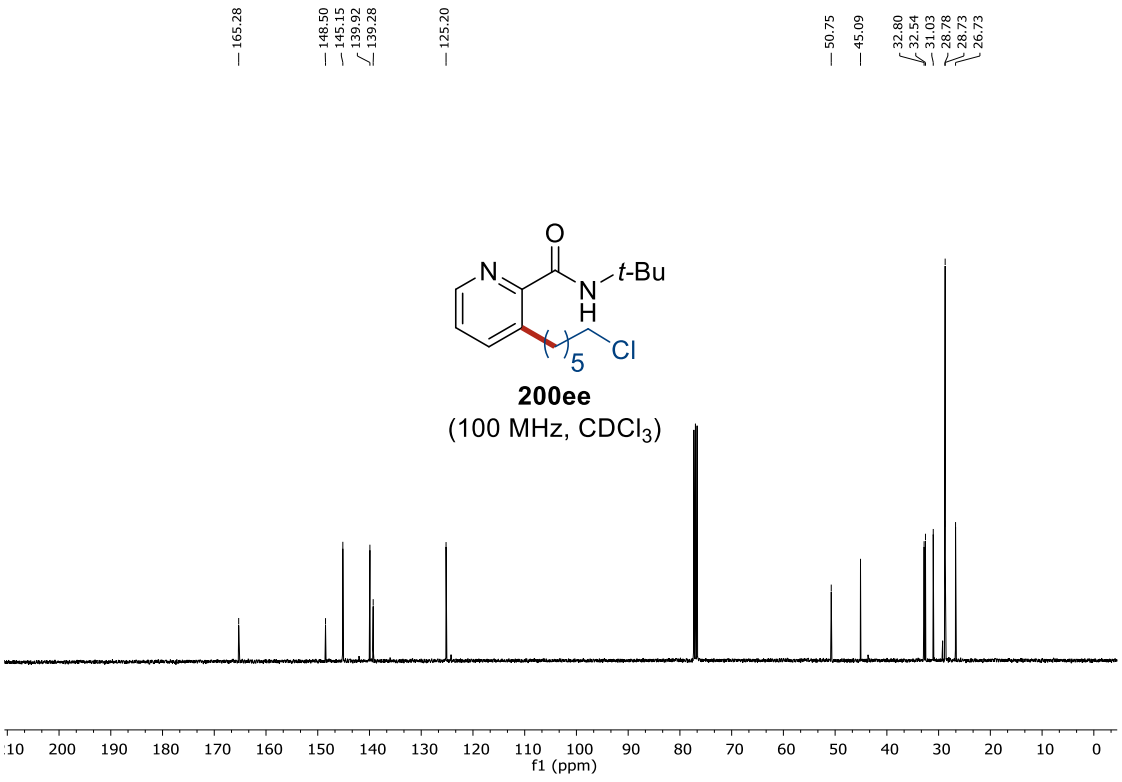

8.32
8.32
8.31
8.31
7.83
7.55
7.55
7.53
7.53
7.26
7.25
7.24
7.24
7.23
3.14
3.13
3.11
1.63
1.61
1.61
1.60
1.58
1.57
1.56
1.45
1.35
1.33
1.31
1.29
1.27
1.22
0.87
0.85
0.83
O
N
N
H
tBu
9
Me
200ec
(400 MHz, CDCl3)
1.00
0.93
1.01
1.19
2.04
2.13
9.21
16.92
3.23
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

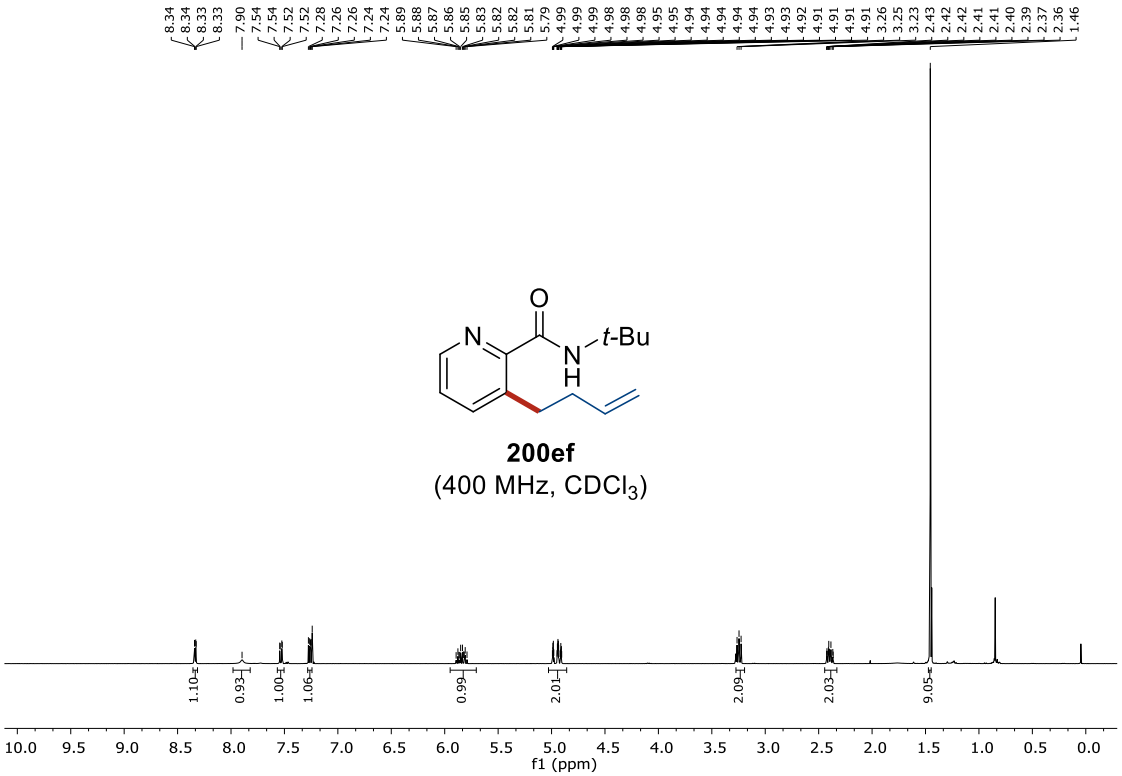

165.38
148.63
145.03
139.87
139.55
125.12
50.74
32.86
31.89
31.22
29.64
29.62
29.58
29.56
29.32
28.74
22.66
14.09
O
N
N
H
t-Bu
9
Me
200ec
(100 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.34
8.34
8.33
8.32
7.90
7.53
7.52
7.51
7.50
7.27
7.25
7.25
7.24
7.23
7.23
7.19
7.19
7.17
7.16
7.15
7.13
3.24
3.22
3.20
2.72
2.70
2.68
2.00
1.98
1.97
1.96
1.96
1.95
1.94
1.94
1.92
1.47
O
N
N
H
t-Bu
Ph
200ed
(400 MHz, CDCl3)
1.08
0.93
1.00
3.33
3.04
2.04
2.06
2.08
9.10
f1 (ppm)

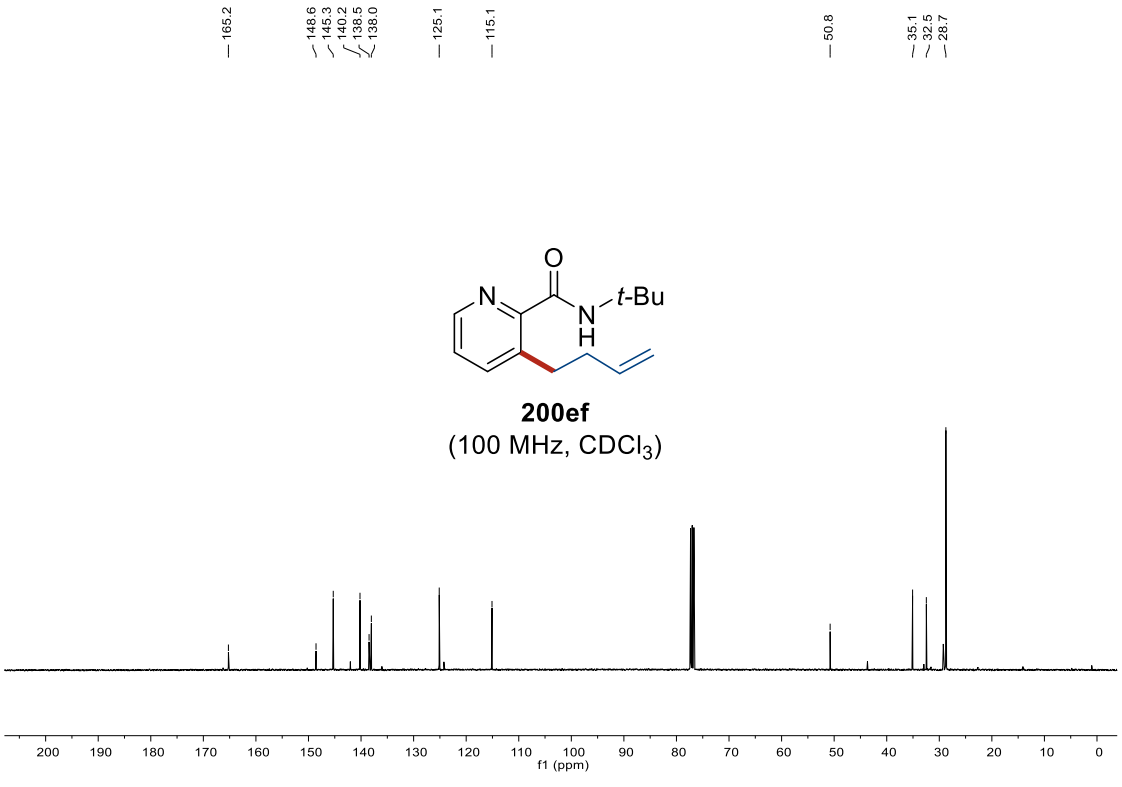

165.27
148.55
145.20
142.37
139.88
139.02
128.37
128.20
125.62
125.18
50.74
35.75
32.84
32.62
28.73
O
N
N
H
t-Bu
Ph
200ed
(100 MHz, CDCl3)
f1 (ppm)


8.33
8.33
8.32
8.32
7.87
7.55
7.55
7.53
7.53
7.28
7.26
7.26
7.24
7.24
3.51
3.50
3.48
3.15
3.14
3.12
1.78
1.76
1.75
1.73
1.71
1.66
1.65
1.64
1.64
1.62
1.60
1.58
1.48
1.45
1.44
1.42
1.40
1.38
1.35
1.34
O
N
t-Bu
N
H
5
Cl
200ee
(400 MHz, CDCl3)
1.00
0.84
1.01
1.05
2.00
2.04
2.25
2.11
13.79
f1 (ppm)

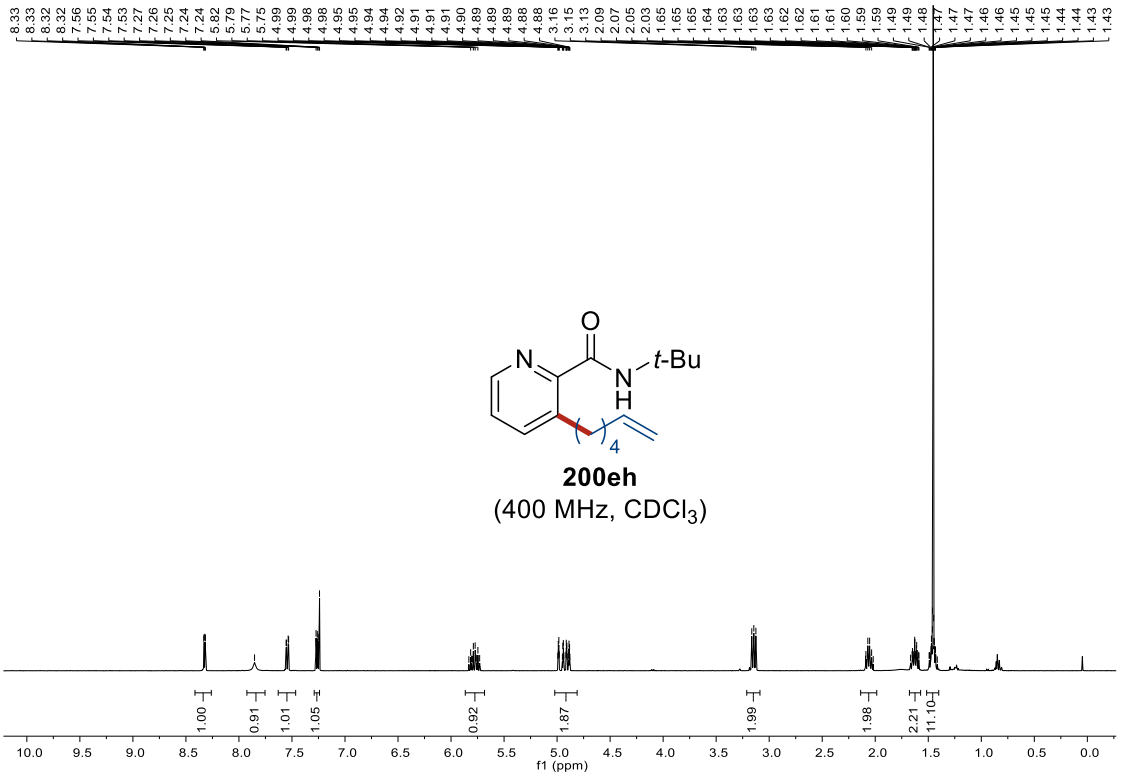

165.28
148.50
145.15
139.92
139.28
125.20
50.75
45.09
32.80
32.54
31.03
28.78
28.73
26.73
O
N
t-Bu
N
H
5
Cl
200ee
(100 MHz, CDCl3)
f1 (ppm)

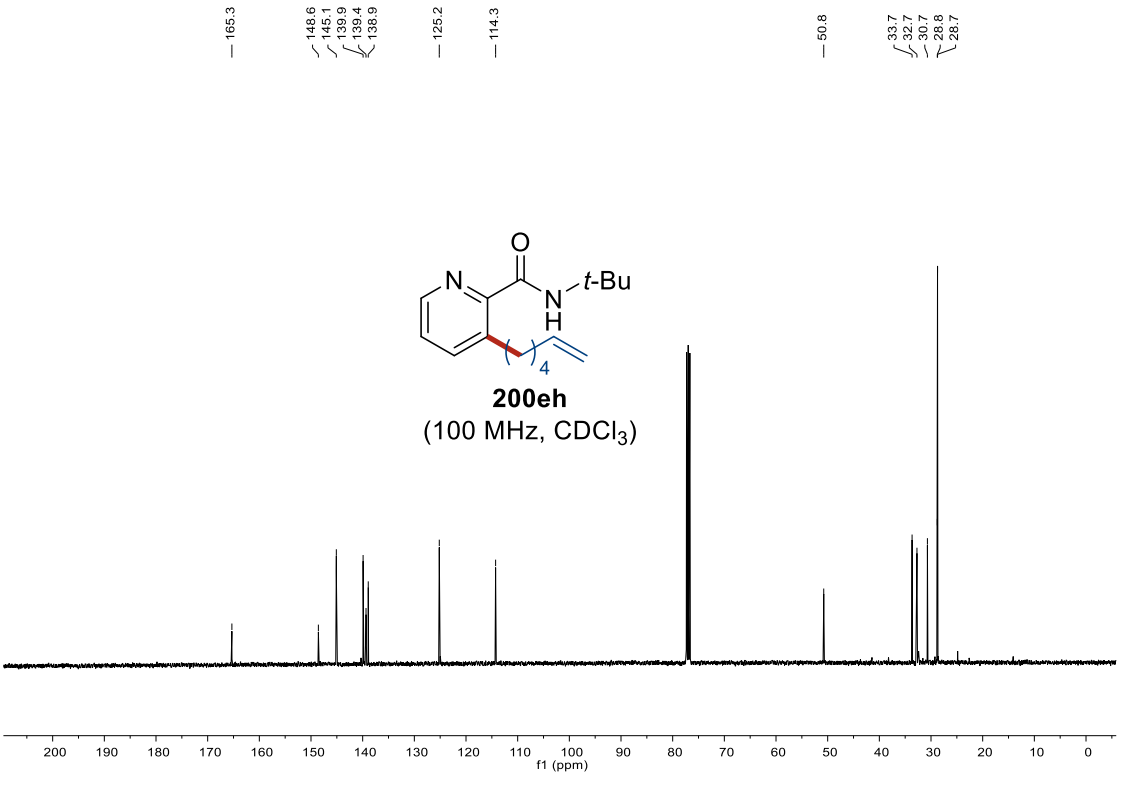


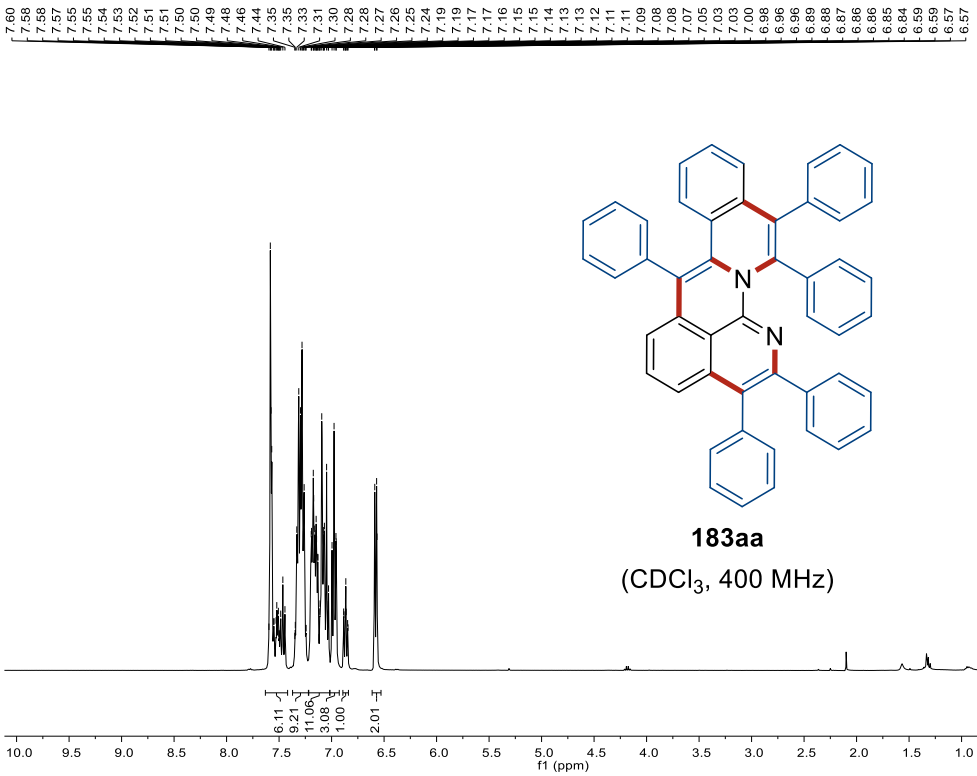
200ef
(400 MHz, $CDCl_3$)

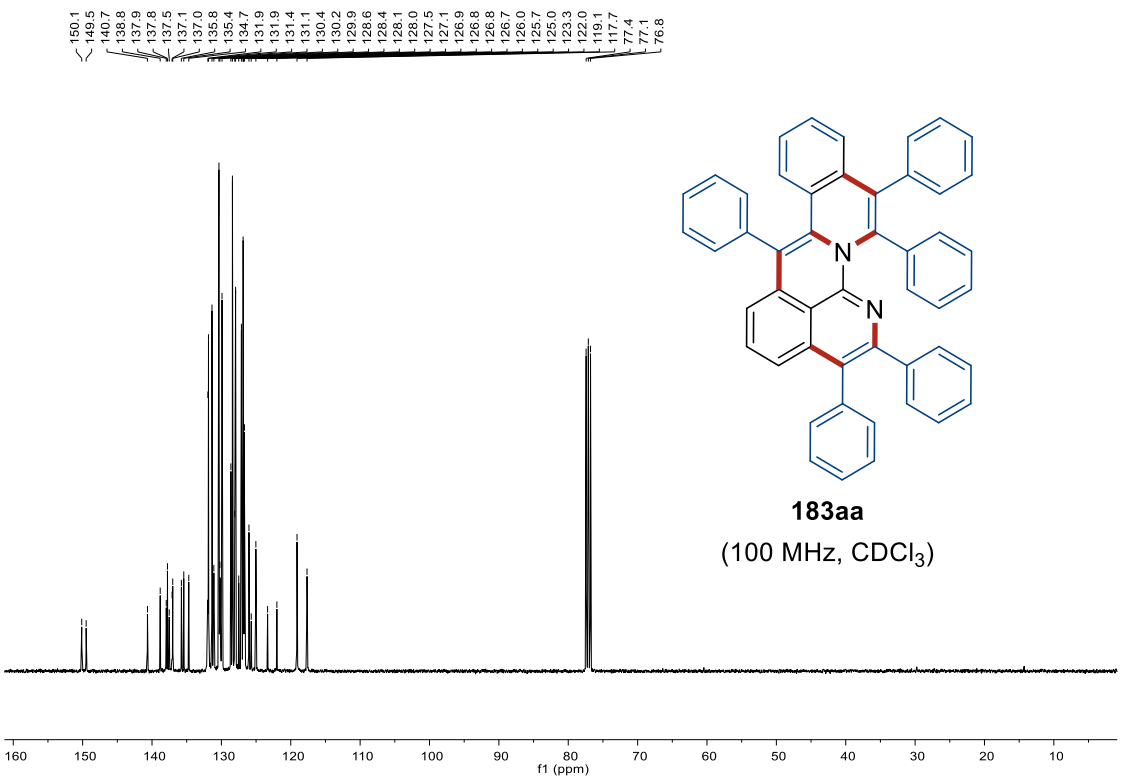


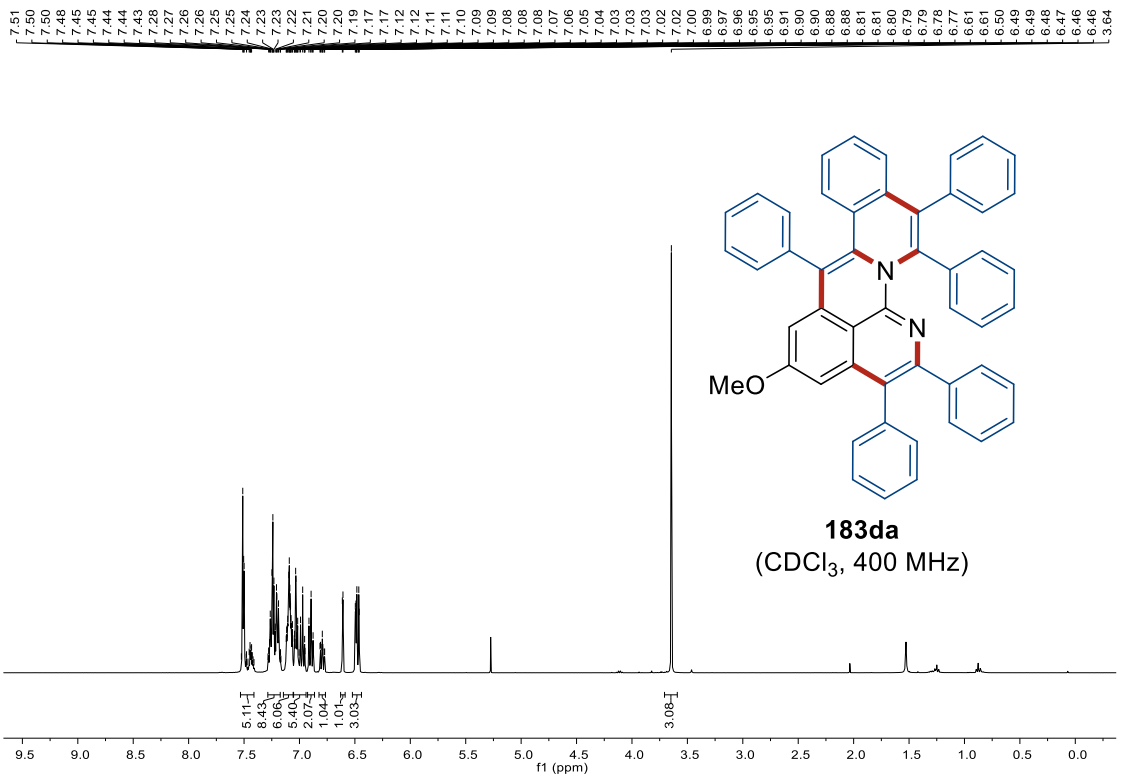
200ef
(100 MHz, $CDCl_3$)

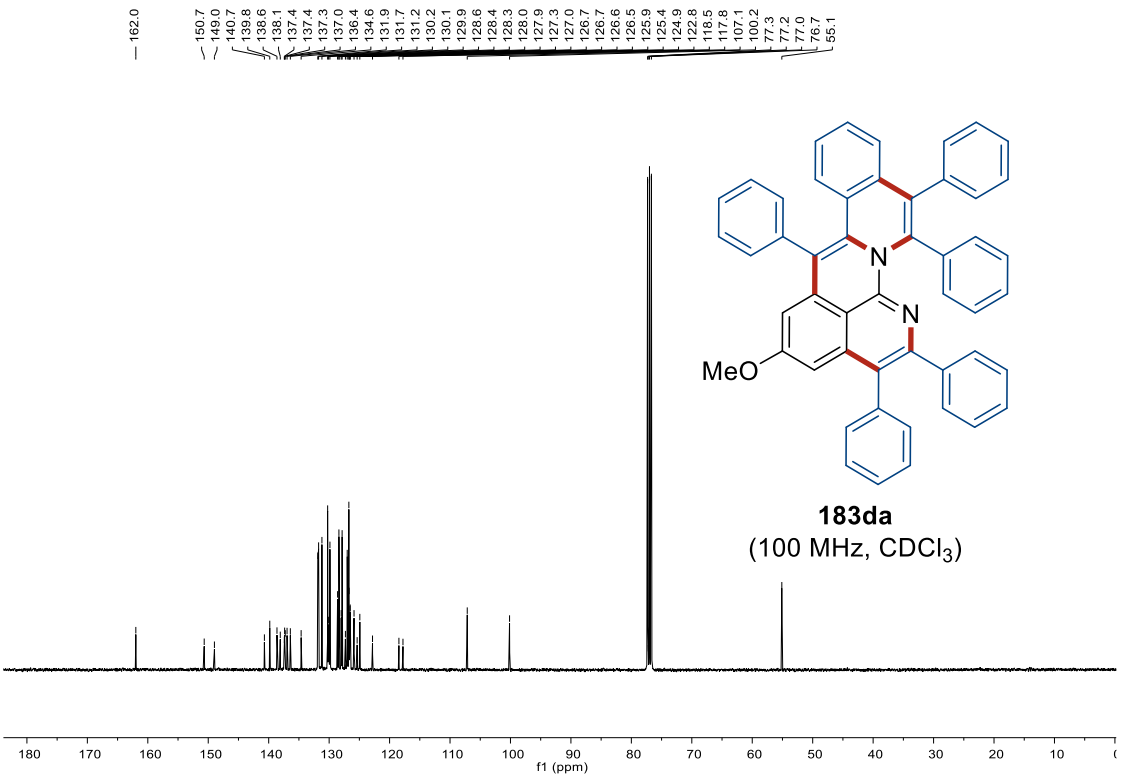

8.33
8.33
8.32
8.32
7.56
7.55
7.54
7.53
7.27
7.26
7.25
7.24
7.24
5.82
5.79
5.77
5.75
4.99
4.99
4.98
4.98
4.95
4.94
4.94
4.92
4.91
4.91
4.91
4.90
4.89
4.89
4.89
4.88
4.88
3.16
3.15
3.13
2.09
2.07
2.05
2.03
1.65
1.65
1.65
1.64
1.63
1.63
1.63
1.63
1.62
1.62
1.61
1.61
1.60
1.59
1.59
1.49
1.49
1.48
1.47
1.47
1.47
1.46
1.46
1.45
1.45
1.45
1.44
1.44
1.43
1.43
O
N
N
H
t-Bu
4
200eh
(400 MHz, CDCl3)
1.00
0.91
1.01
1.05
0.92
1.87
1.99
1.98
2.21
11.10
10.0
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
f1 (ppm)

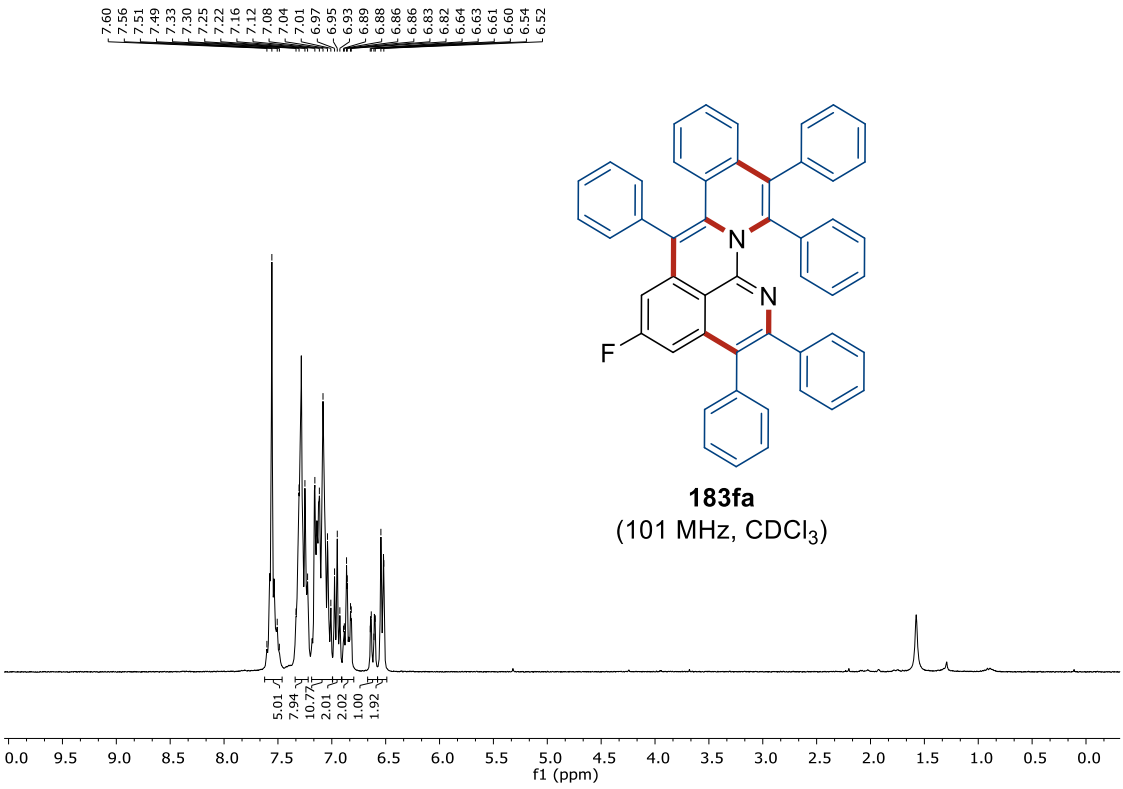

165.3
148.6
145.1
139.9
139.4
138.9
125.2
114.3
50.8
33.7
32.7
30.7
28.8
28.7
O
N
N
H
t-Bu
4
200eh
(100 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

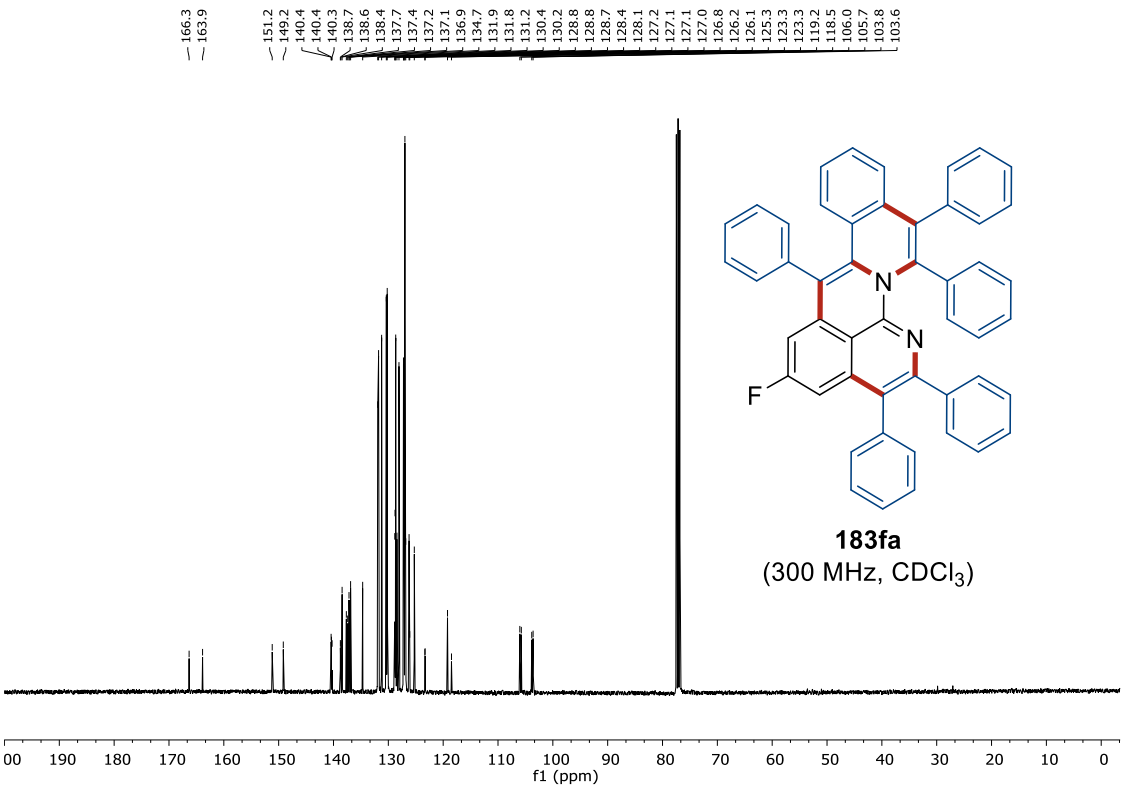

7.60 7.58 7.58 7.57 7.55 7.55 7.54 7.53 7.52 7.51 7.51 7.50 7.50 7.49 7.48 7.46 7.44 7.35 7.35 7.33 7.31 7.30 7.28 7.28 7.27 7.26 7.25 7.24 7.19 7.19 7.17 7.17 7.16 7.15 7.15 7.14 7.13 7.12 7.11 7.11 7.09 7.08 7.08 7.07 7.05 7.03 7.03 7.00 6.98 6.96 6.96 6.89 6.88 6.87 6.86 6.86 6.85 6.84 6.59 6.59 6.57 6.57
N
N
183aa
(CDCl3, 400 MHz)
6.11
9.21
11.06
3.08
1.00
2.01
10.0 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
f1 (ppm)

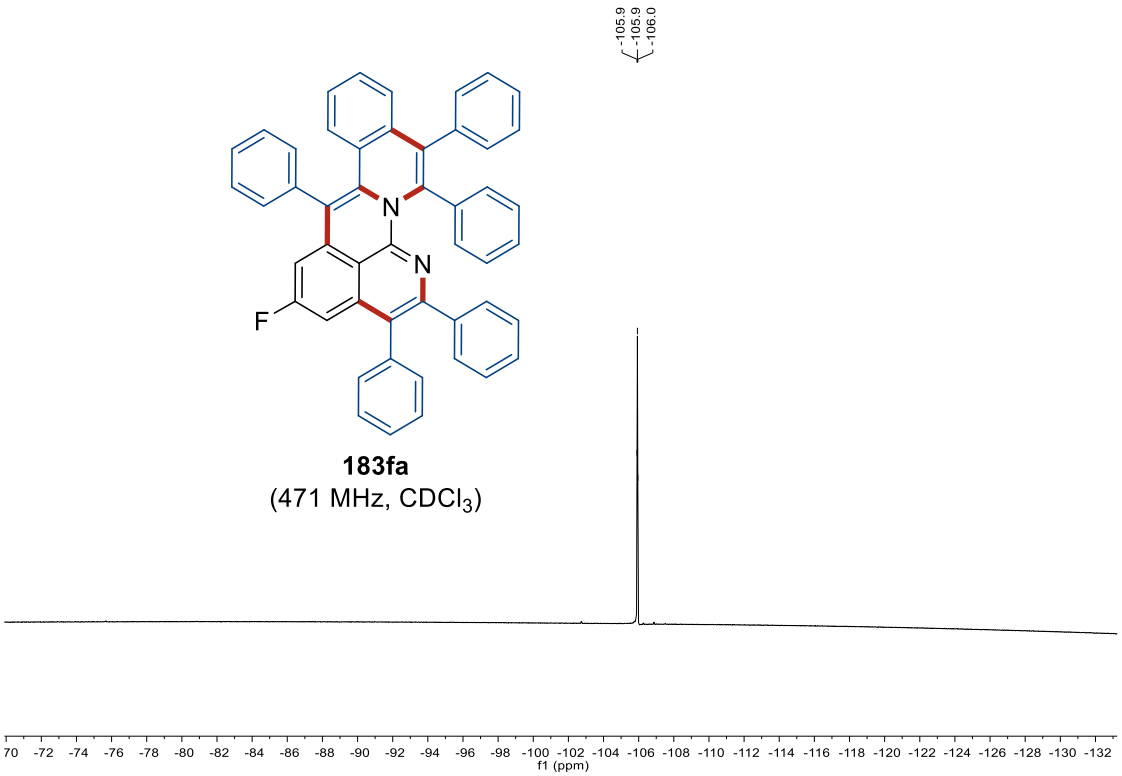

150.1 149.5 140.7 138.8 137.9 137.8 137.5 137.1 137.0 135.8 135.4 134.7 131.9 131.9 131.4 131.1 130.4 130.2 129.9 128.6 128.4 128.1 128.0 127.5 127.1 126.9 126.8 126.8 126.7 126.0 125.7 125.0 123.3 122.0 119.1 117.7 77.4 77.1 76.8
N
N
183aa
(100 MHz, CDCl3)
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

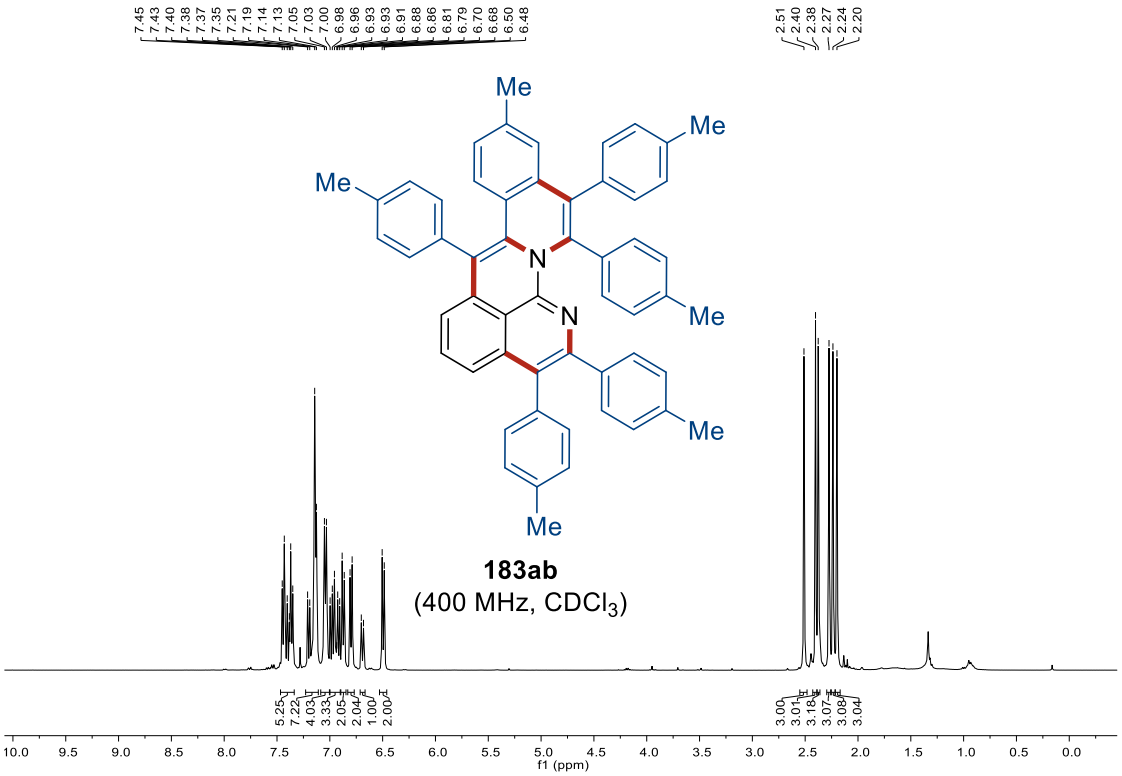

MeO
N
N
183da
(CDCl3, 400 MHz)
f1 (ppm)

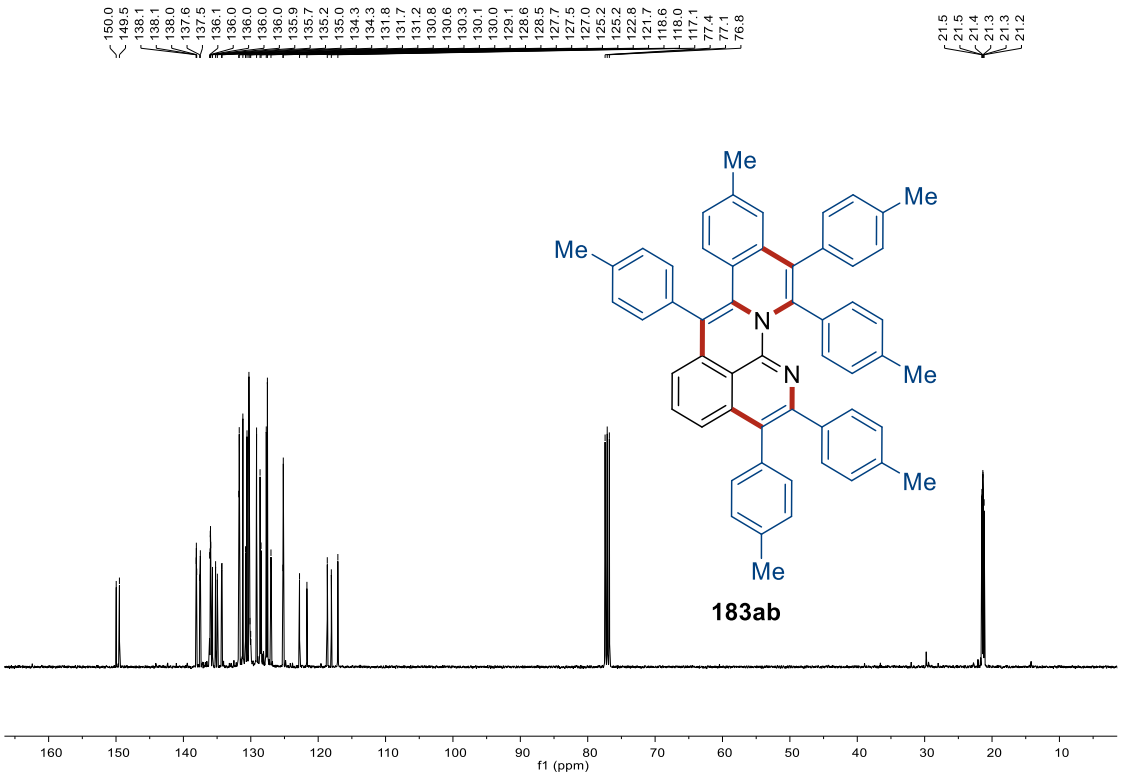

MeO
N
N
183da
(100 MHz, CDCl3)
f1 (ppm)

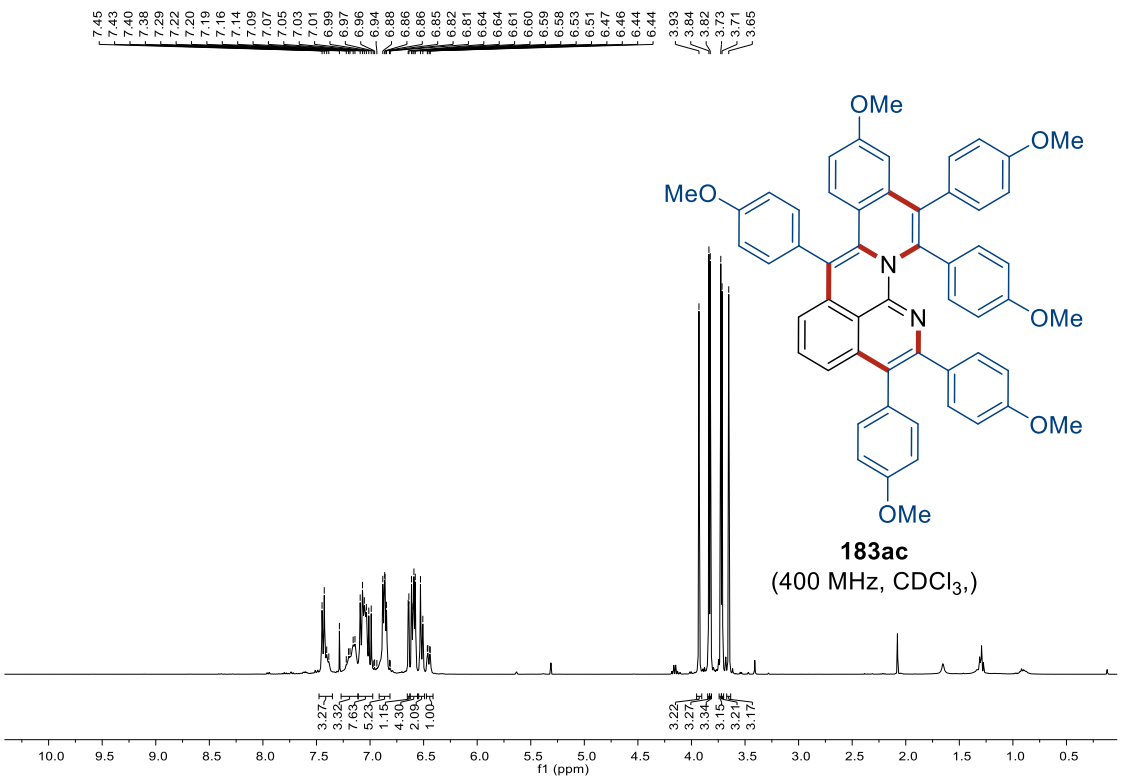

7.60
7.56
7.51
7.49
7.33
7.30
7.25
7.22
7.16
7.12
7.08
7.04
7.01
6.97
6.95
6.93
6.89
6.88
6.86
6.86
6.83
6.82
6.64
6.63
6.61
6.60
6.54
6.52
N
N
F
183fa
(101 MHz, CDCl3)
5.01
7.94
10.77
2.01
2.02
1.00
1.92
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

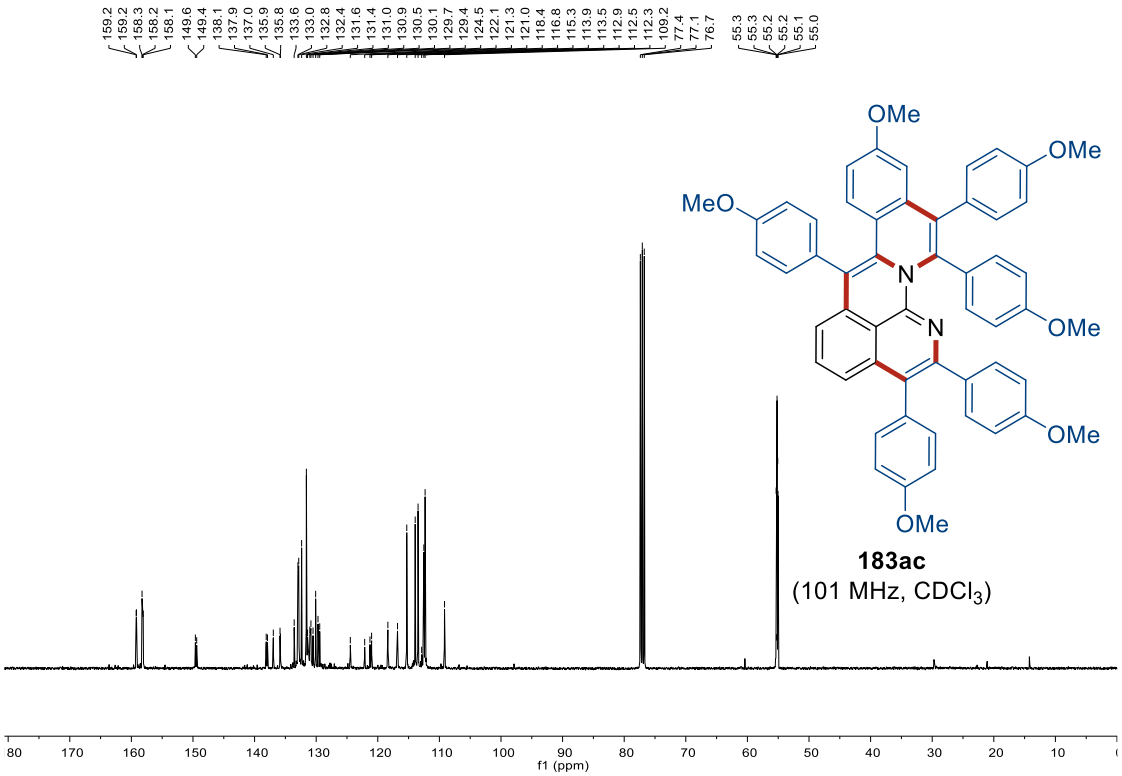

166.3
163.9
151.2
149.2
140.4
140.4
140.3
138.7
138.6
138.4
137.7
137.4
137.2
137.1
136.9
134.7
131.9
131.8
131.2
130.4
130.2
128.8
128.8
128.7
128.4
128.1
127.2
127.1
127.1
127.0
126.8
126.2
126.1
125.3
123.3
123.3
119.2
118.5
106.0
105.7
103.8
103.6
N
N
F
183fa
(300 MHz, CDCl3)
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

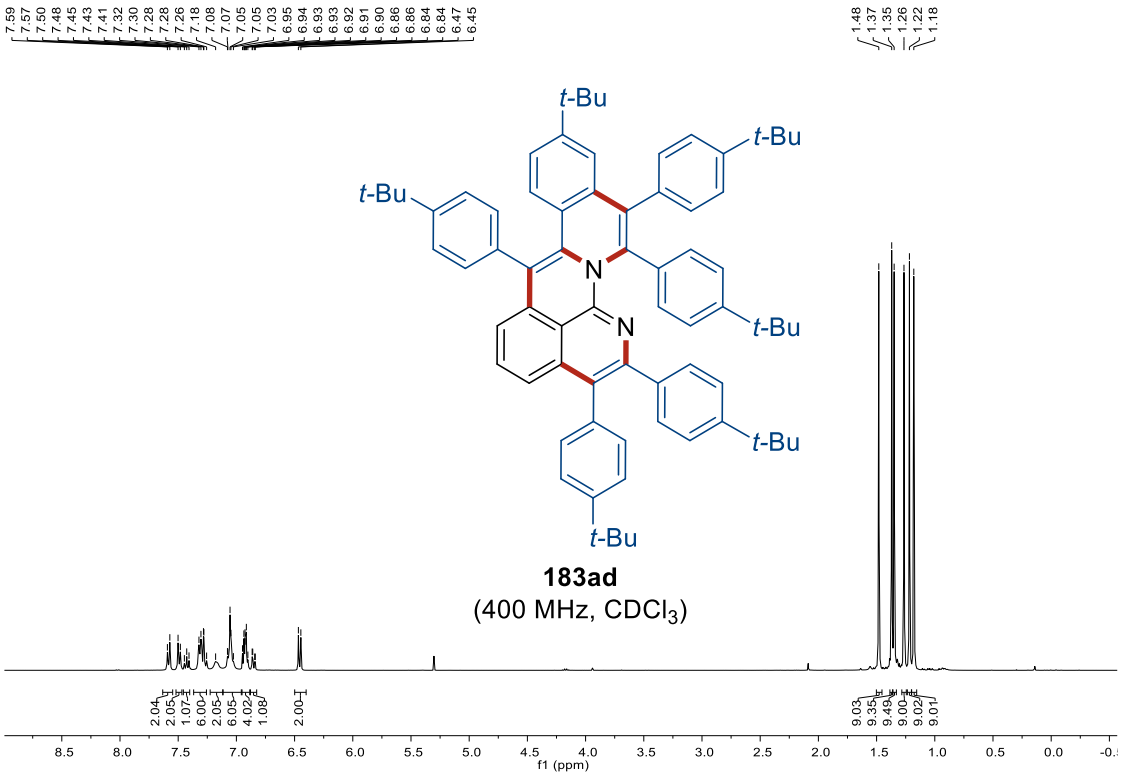

-105.9
-105.9
-106.0
N
N
F
183fa
(471 MHz, CDCl3)
70 -72 -74 -76 -78 -80 -82 -84 -86 -88 -90 -92 -94 -96 -98 -100 -102 -104 -106 -108 -110 -112 -114 -116 -118 -120 -122 -124 -126 -128 -130 -132
f1 (ppm)

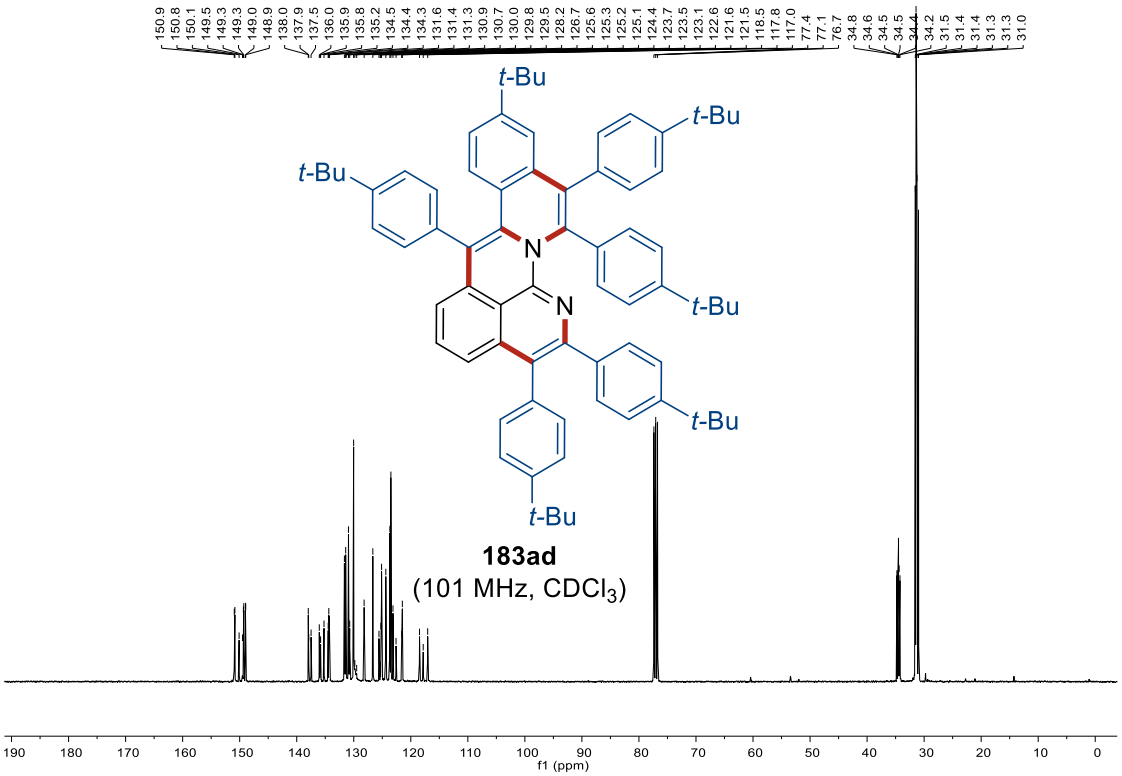

7.45
7.43
7.40
7.38
7.37
7.35
7.21
7.19
7.14
7.13
7.05
7.03
7.00
6.98
6.96
6.93
6.93
6.91
6.88
6.86
6.81
6.79
6.70
6.68
6.50
6.48
2.51
2.40
2.38
2.27
2.24
2.20
Me
Me
Me
Me
Me
Me
N
N
183ab
(400 MHz, CDCl3)
5.25
7.22
4.03
3.33
2.05
2.04
1.00
2.00
3.00
3.01
3.18
3.07
3.08
3.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 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
f1 (ppm)

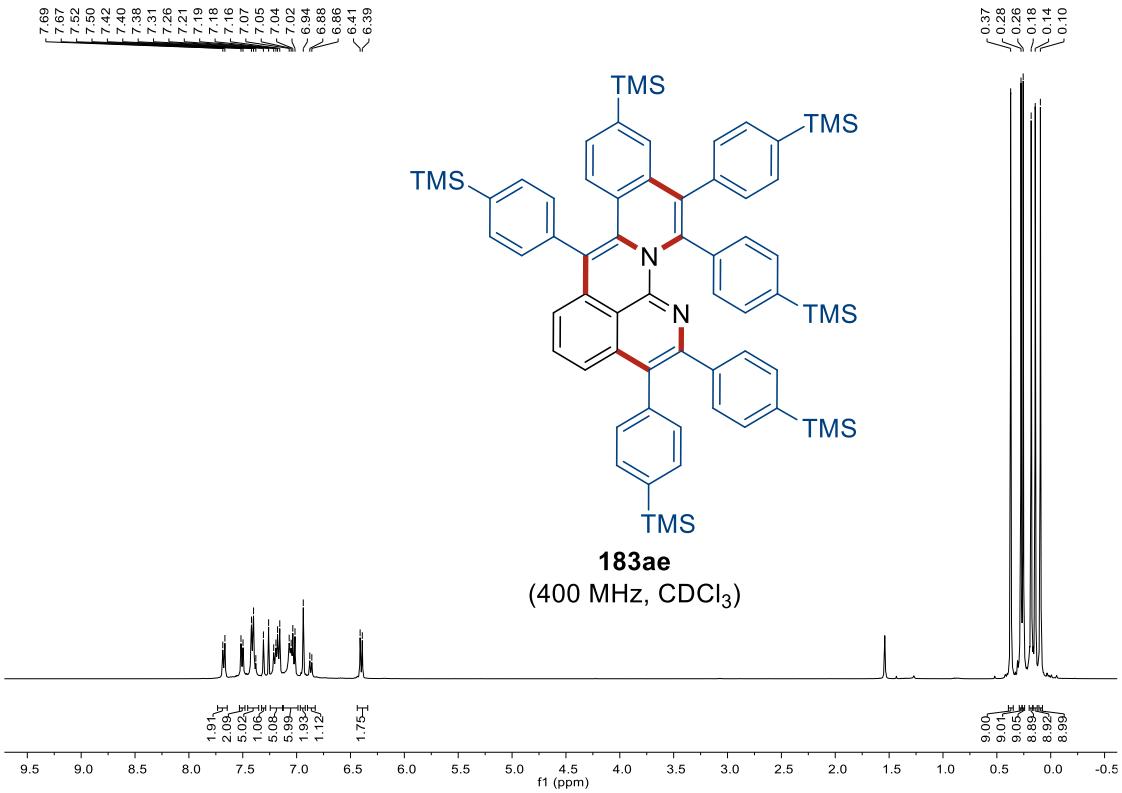

150.0
149.5
138.1
138.1
138.0
137.6
137.5
136.1
136.0
136.0
136.0
136.0
135.9
135.7
135.2
135.0
134.3
134.3
131.8
131.7
131.2
130.8
130.6
130.3
130.1
130.0
129.1
128.6
128.5
127.7
127.5
127.0
125.2
125.2
122.8
121.7
118.6
118.0
117.1
77.4
77.1
76.8
21.5
21.5
21.4
21.3
21.3
21.2
Me
Me
Me
N
N
Me
Me
Me
183ab
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

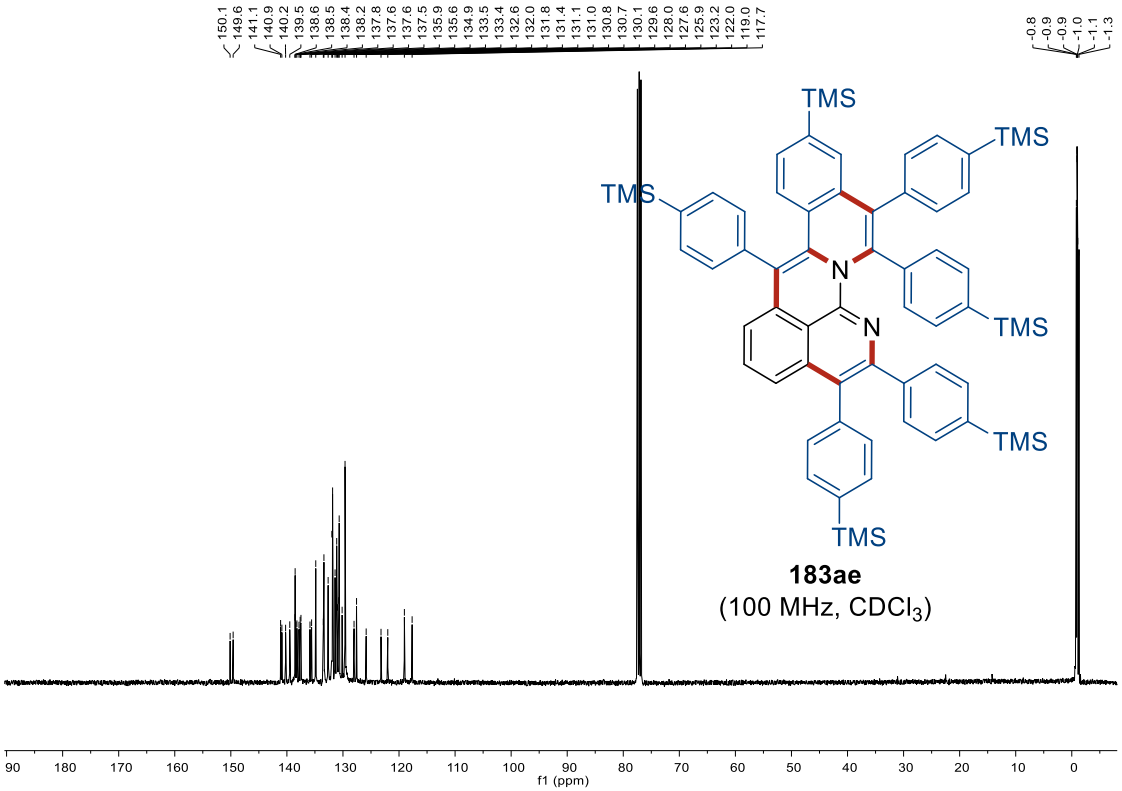

7.45
7.43
7.40
7.38
7.29
7.22
7.20
7.19
7.16
7.14
7.09
7.07
7.05
7.03
7.01
6.99
6.97
6.96
6.94
6.88
6.86
6.86
6.85
6.82
6.81
6.64
6.64
6.61
6.60
6.59
6.58
6.53
6.51
6.47
6.46
6.44
6.44
3.93
3.84
3.82
3.73
3.71
3.65
OMe
OMe
MeO
N
N
OMe
OMe
OMe
183ac
(400 MHz, CDCl3,)
3.27
3.32
7.63
5.23
1.15
4.30
2.09
1.00
3.22
3.27
3.34
3.15
3.21
3.17
10.0
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
f1 (ppm)

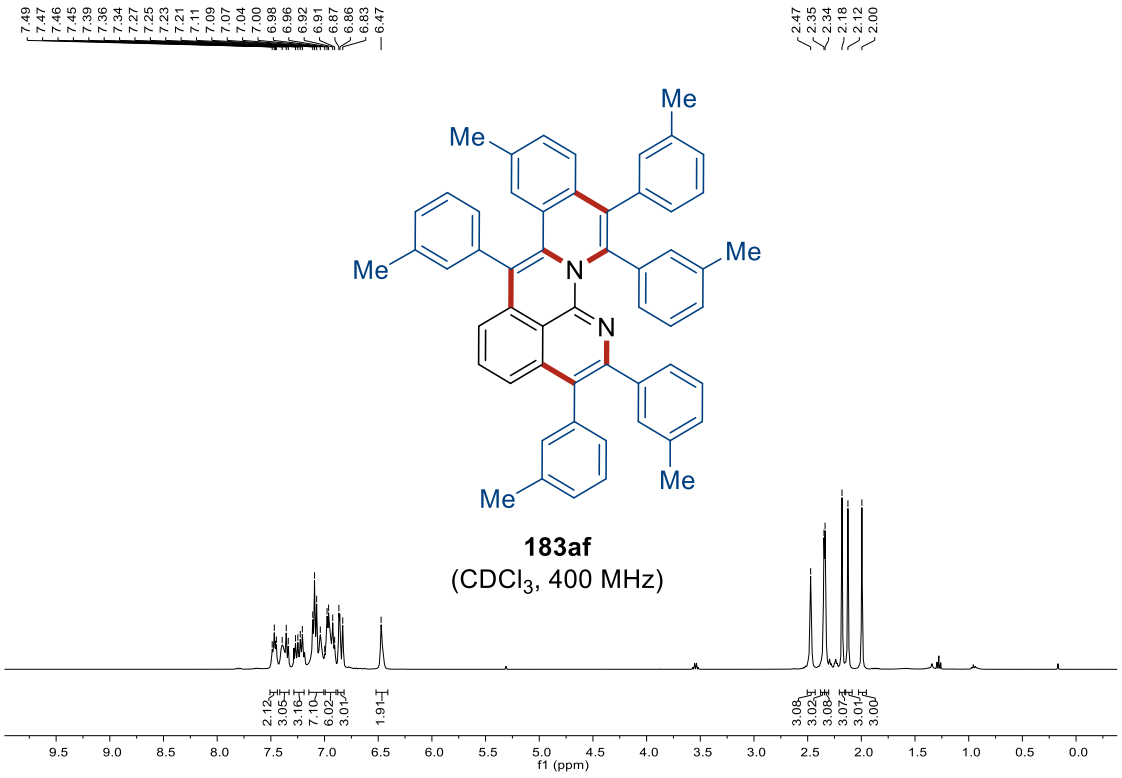

159.2
159.2
158.3
158.2
158.1
149.6
149.4
138.1
137.9
137.0
135.9
135.8
133.6
133.0
132.8
132.4
131.6
131.4
131.0
130.9
130.5
130.1
129.7
129.4
124.5
122.1
121.3
121.0
118.4
116.8
115.3
113.9
113.5
112.9
112.5
112.3
109.2
77.4
77.1
76.7
55.3
55.3
55.2
55.2
55.1
55.0
OMe
OMe
MeO
N
N
OMe
OMe
OMe
183ac
(101 MHz, CDCl3)
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

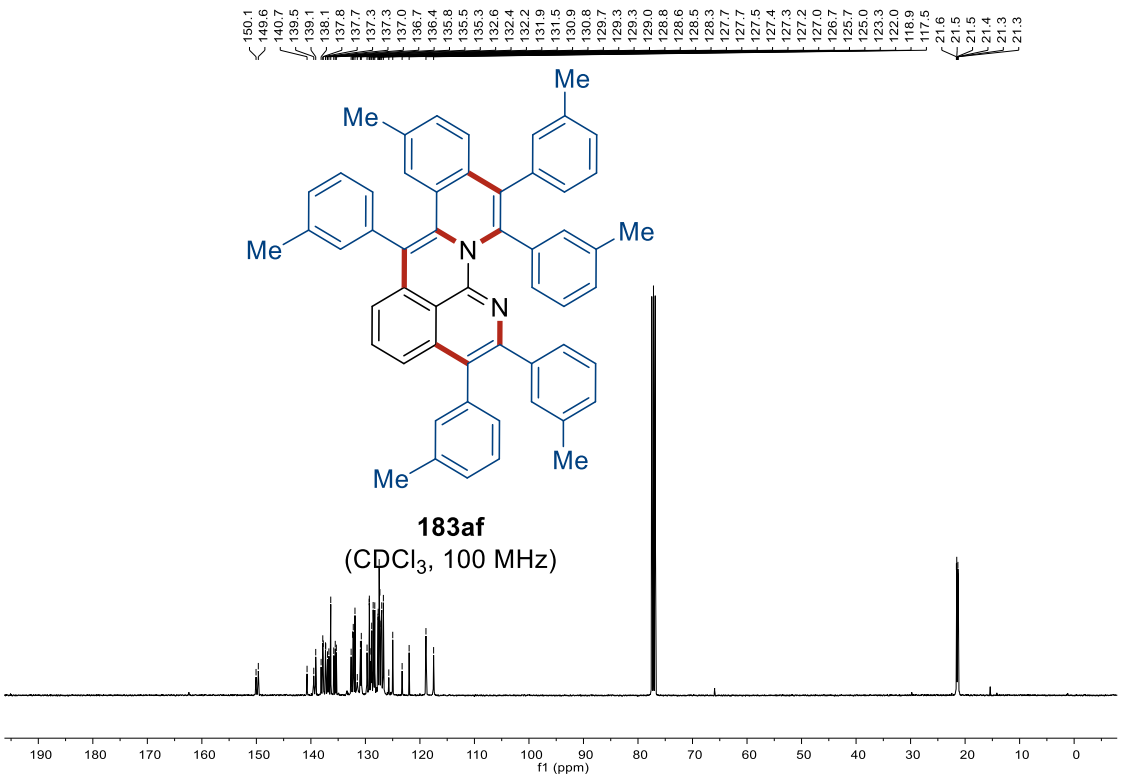

7.59
7.57
7.50
7.48
7.45
7.43
7.41
7.32
7.30
7.28
7.28
7.26
7.18
7.08
7.07
7.05
7.05
7.03
6.95
6.94
6.93
6.93
6.92
6.91
6.90
6.86
6.86
6.84
6.84
6.47
6.45
1.48
1.37
1.35
1.26
1.22
1.18
t-Bu
t-Bu
t-Bu
N
N
t-Bu
t-Bu
t-Bu
183ad
(400 MHz, CDCl3)
2.04
2.05
1.07
6.00
2.05
6.05
4.02
1.08
2.00
9.03
9.35
9.49
9.00
9.02
9.01
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
f1 (ppm)

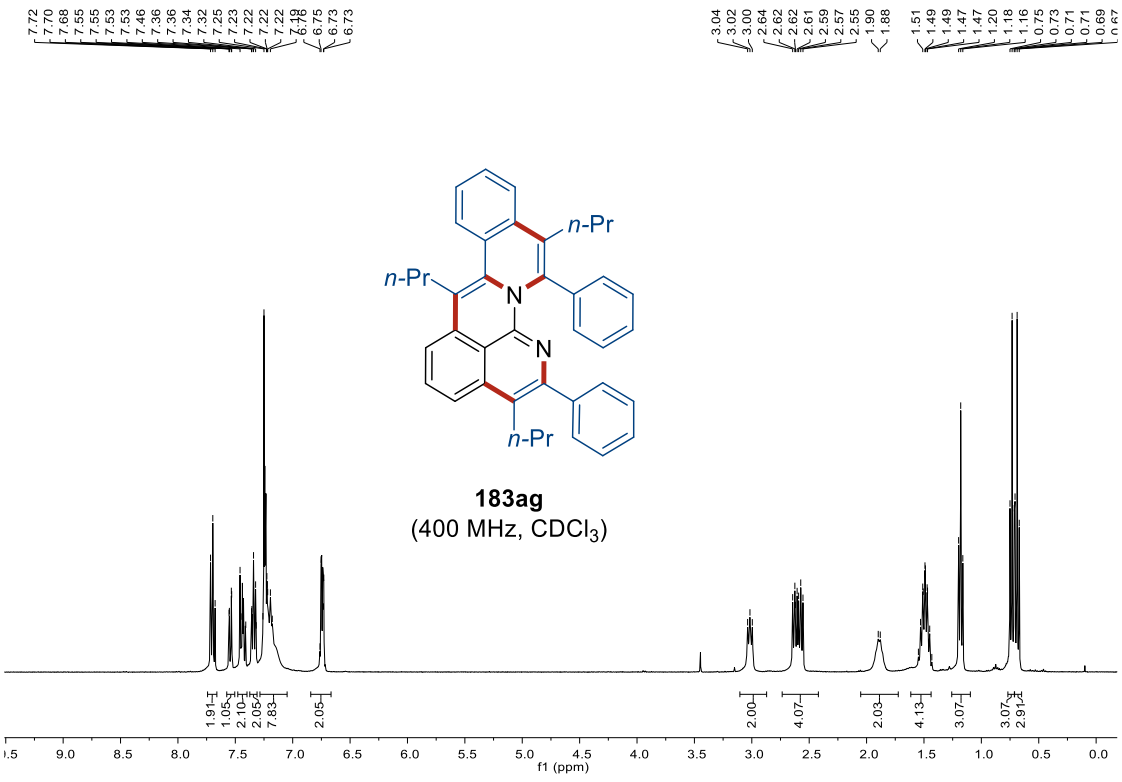

t-Bu
t-Bu
t-Bu
t-Bu
t-Bu
t-Bu
N
N
183ad
(101 MHz, CDCl3)
f1 (ppm)

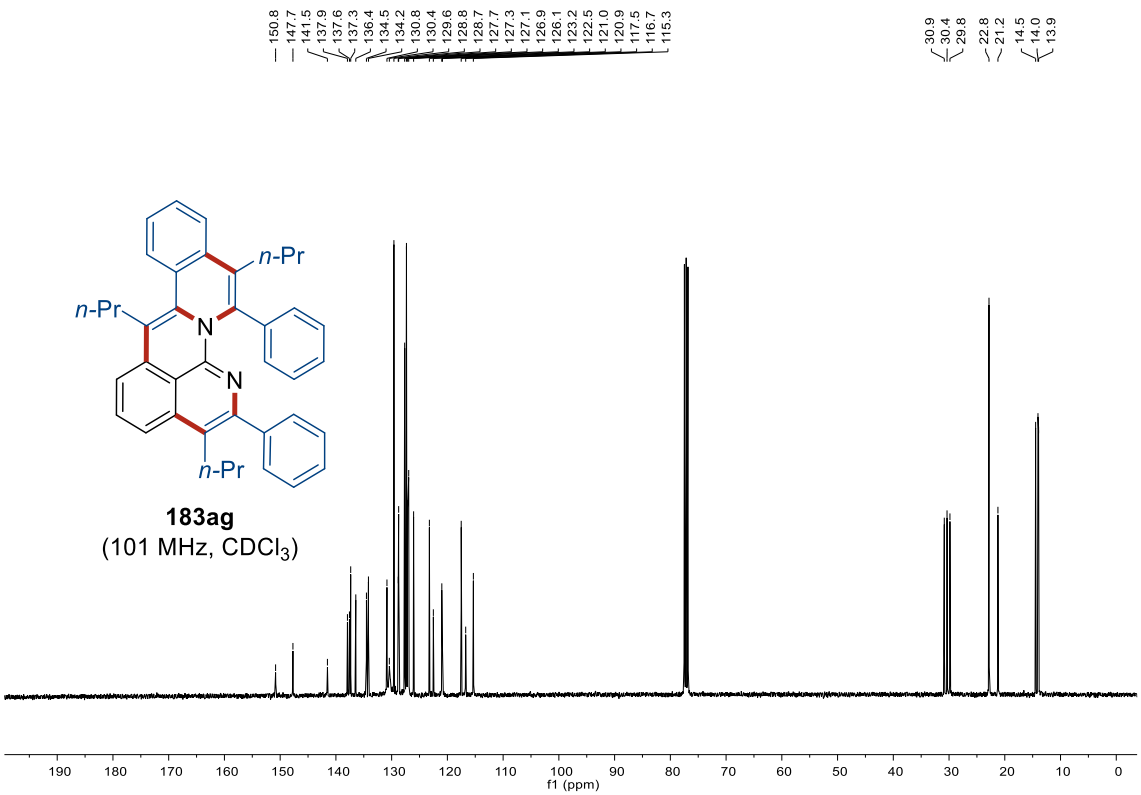

TMS
TMS
TMS
TMS
TMS
TMS
N
N
183ae
(400 MHz, CDCl3)
f1 (ppm)

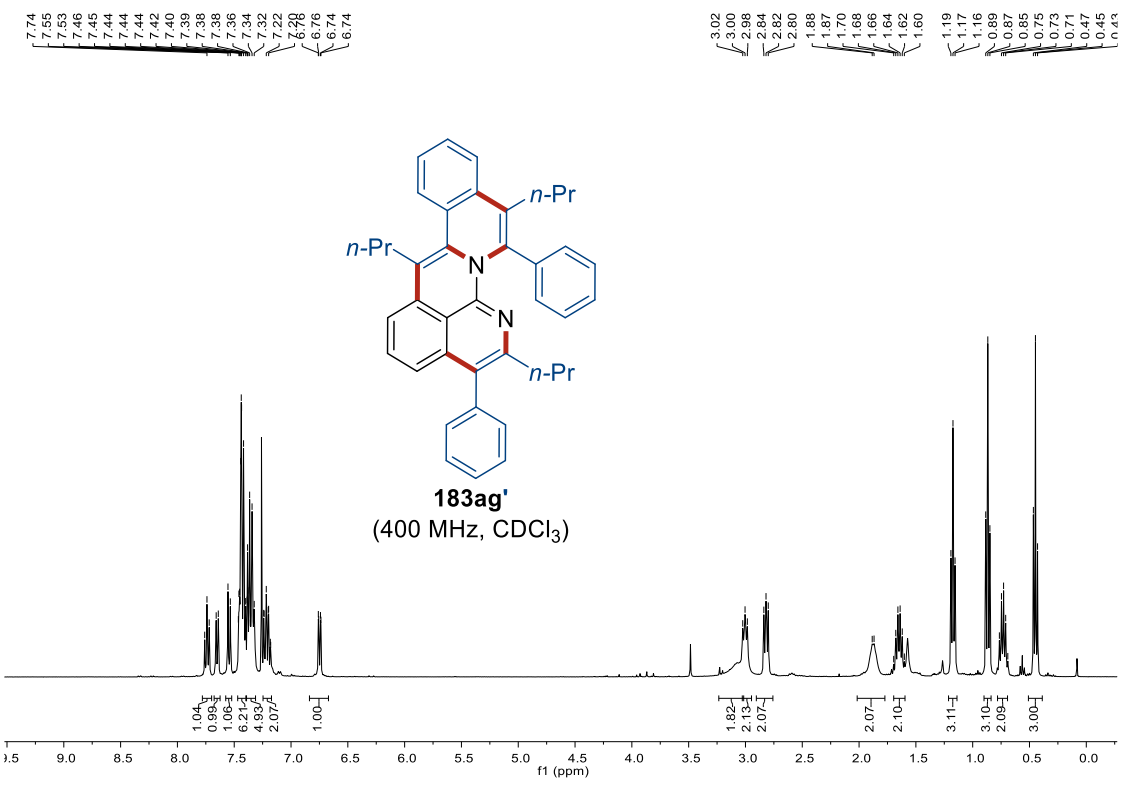

TMS
TMS
TMS
TMS
TMS
TMS
N
N
183ae
(100 MHz, CDCl3)
f1 (ppm)

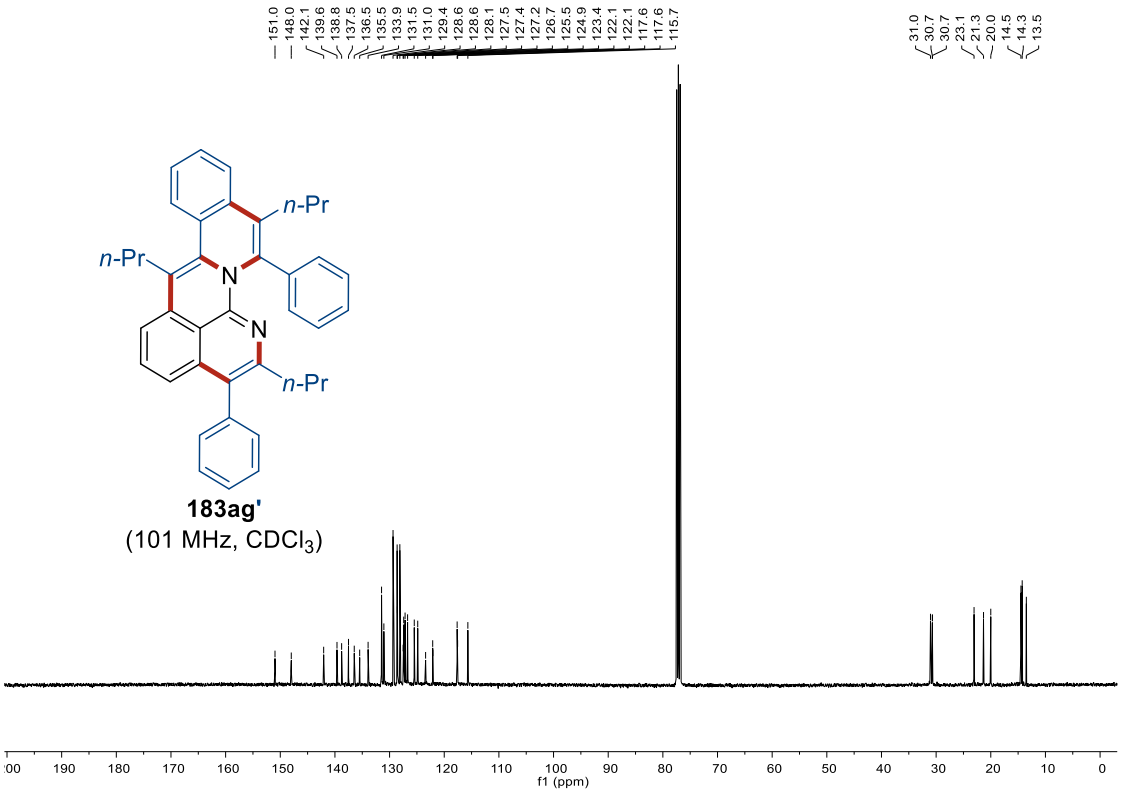

Me
Me
Me
Me
Me
Me
N
N
183af
(CDCl3, 400 MHz)
f1 (ppm)

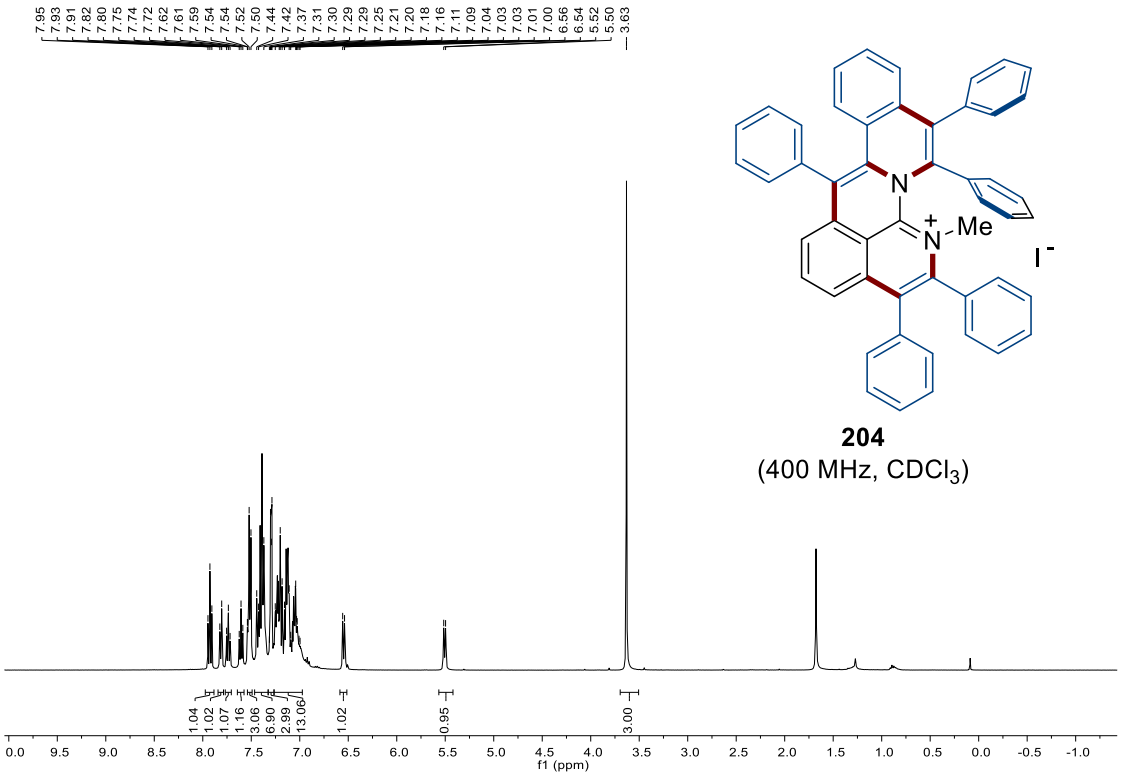

Me
Me
Me
Me
N
N
Me
Me
183af
(CDCl3, 100 MHz)
f1 (ppm)

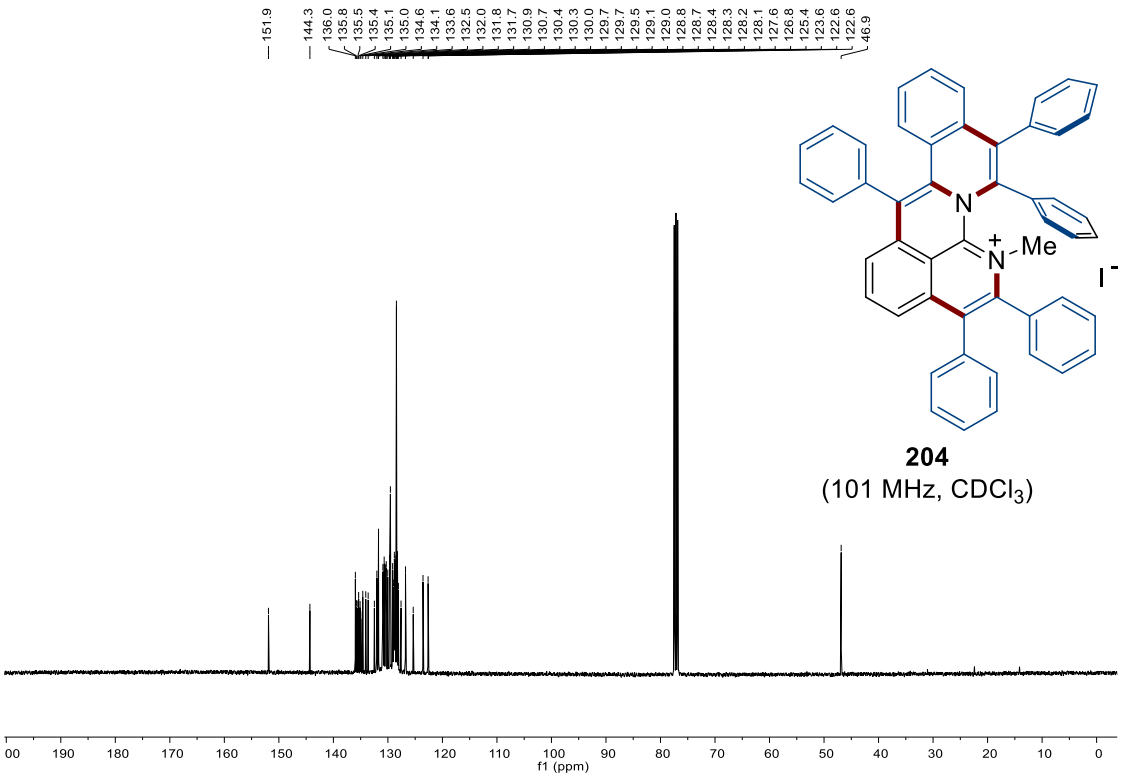

n-Pr
n-Pr
N
N
n-Pr
183ag
(400 MHz, CDCl3)
f1 (ppm)


150.8
147.7
141.5
137.9
137.6
137.3
136.4
134.5
134.2
130.8
130.4
129.6
128.8
128.7
127.7
127.3
127.1
126.9
126.1
123.2
122.5
121.0
120.9
117.5
116.7
115.3
30.9
30.4
29.8
22.8
21.2
14.5
14.0
13.9
n-Pr
n-Pr
n-Pr
N
N
183ag
(101 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

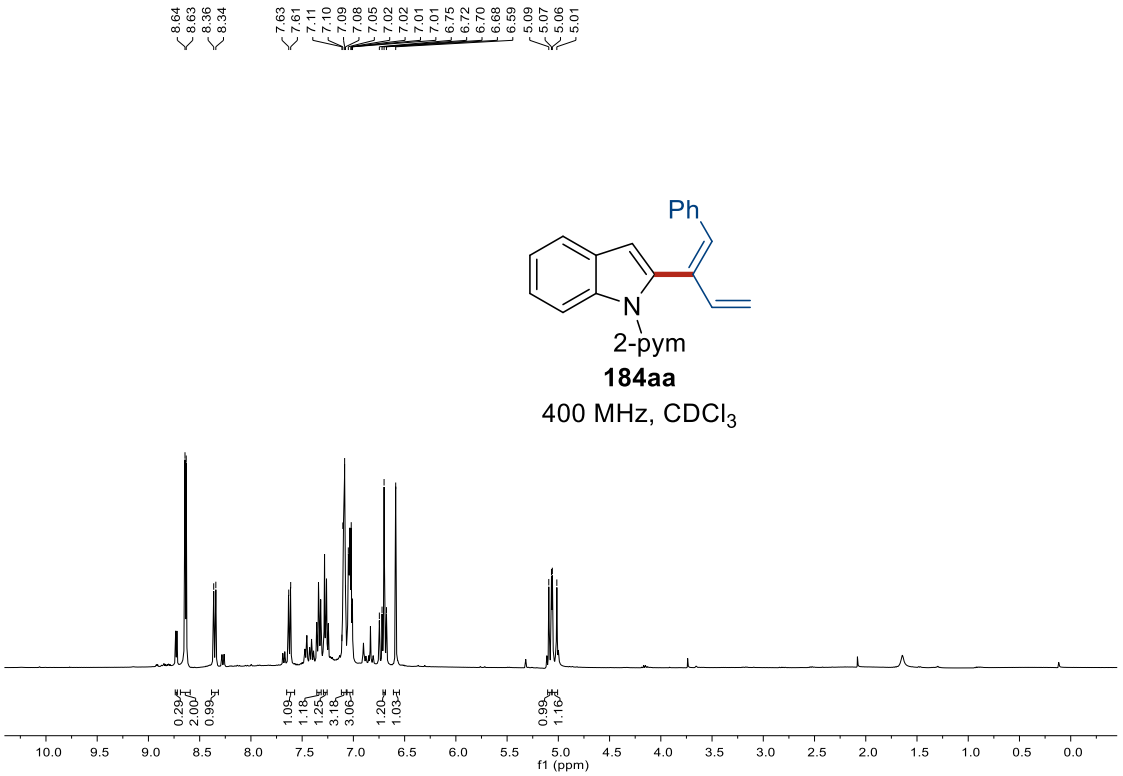

7.74
7.55
7.53
7.46
7.45
7.44
7.44
7.44
7.42
7.40
7.39
7.38
7.38
7.36
7.34
7.32
7.22
7.20
6.76
6.76
6.74
6.74
3.02
3.00
2.98
2.84
2.82
2.80
1.88
1.87
1.70
1.68
1.66
1.64
1.62
1.60
1.19
1.17
1.16
0.89
0.87
0.85
0.75
0.73
0.71
0.47
0.45
n-Pr
n-Pr
n-Pr
N
N
183ag'
(400 MHz, CDCl3)
1.04
0.99
1.06
6.21
4.93
2.07
1.00
1.82
2.13
2.07
2.07
2.10
3.11
3.10
2.09
3.00
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
f1 (ppm)


151.0
148.0
142.1
139.6
138.8
137.5
136.5
135.5
133.9
131.5
131.0
129.4
128.6
128.6
128.1
127.5
127.4
127.2
126.7
125.5
124.9
123.4
122.1
122.1
117.6
117.6
115.7
31.0
30.7
30.7
23.1
21.3
20.0
14.5
14.3
13.5
n-Pr
n-Pr
n-Pr
N
N
183ag'
(101 MHz, CDCl3)
f1 (ppm)

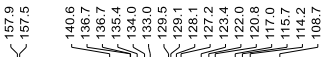

7.95
7.93
7.91
7.82
7.80
7.75
7.74
7.72
7.62
7.61
7.59
7.54
7.54
7.52
7.50
7.44
7.42
7.37
7.31
7.30
7.29
7.29
7.25
7.21
7.20
7.18
7.16
7.11
7.09
7.04
7.03
7.03
7.01
7.00
6.56
6.54
5.52
5.50
3.63
N
N
Me
I-
204
(400 MHz, CDCl3)
1.04
1.02
1.07
1.16
3.06
6.90
2.99
13.06
1.02
0.95
3.00
f1 (ppm)

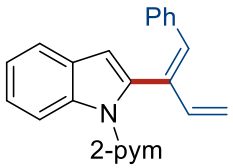


204
(101 MHz, $CDCl_3$)

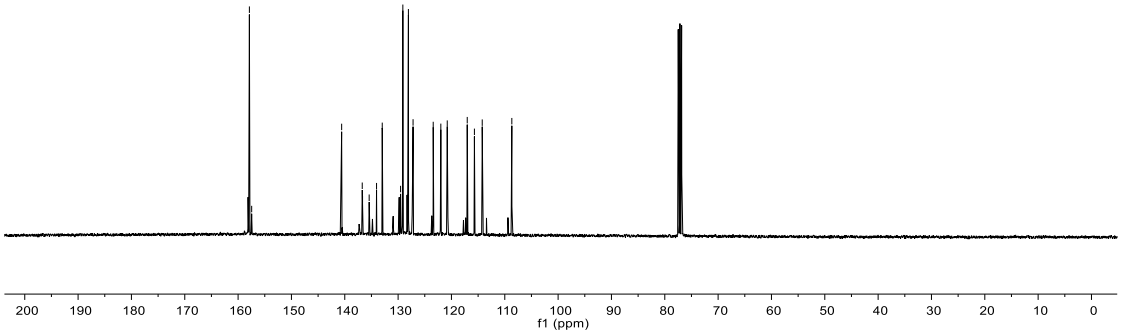


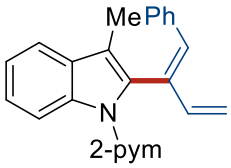
2-pym
184aa
400 MHz, $CDCl_3$



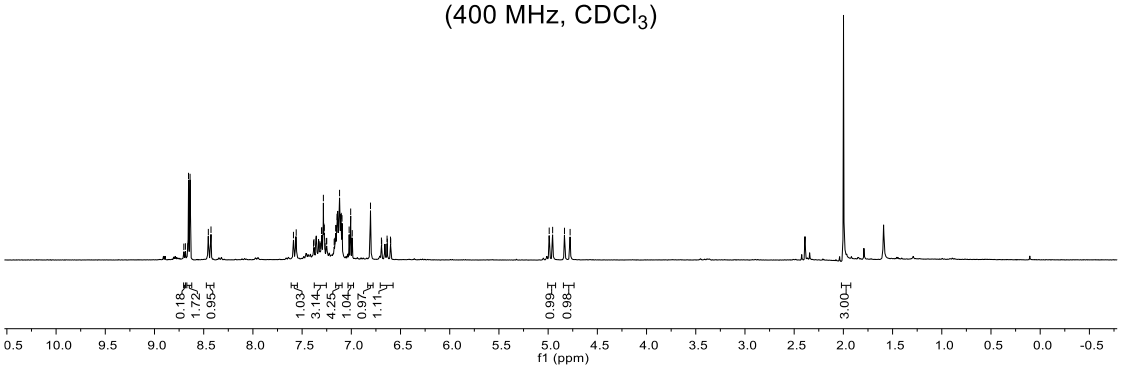


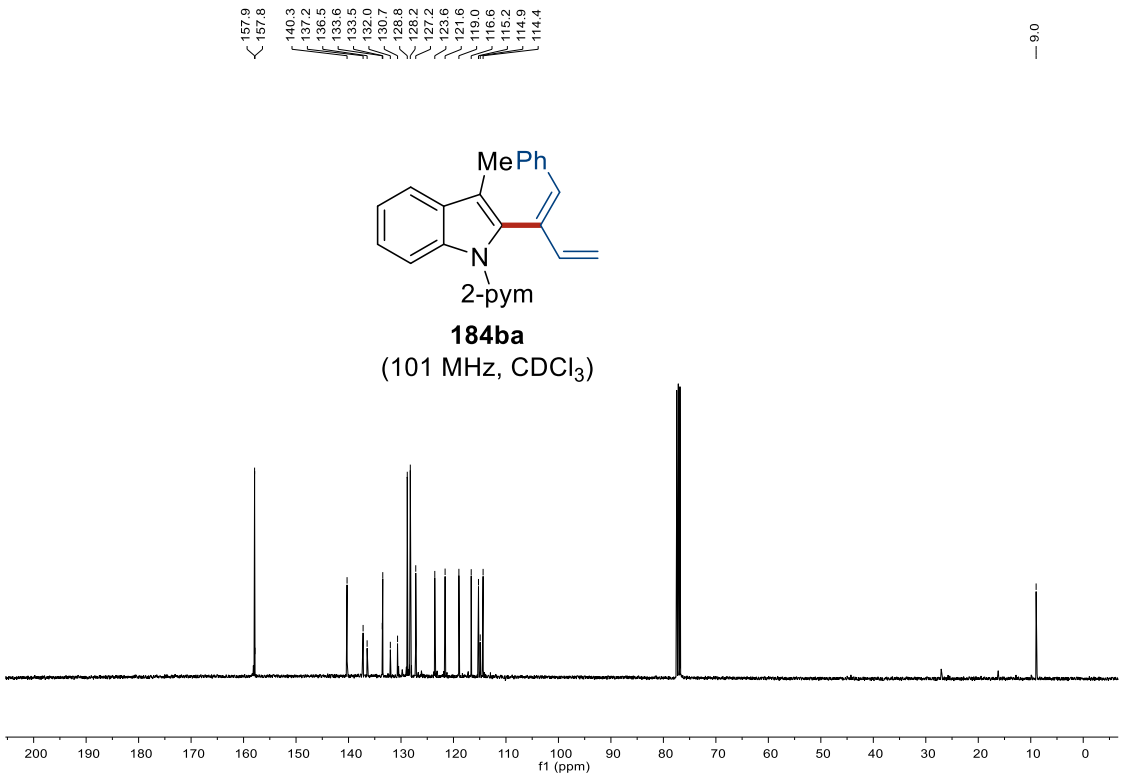
184aa
(101 MHz, CDCl**3**)



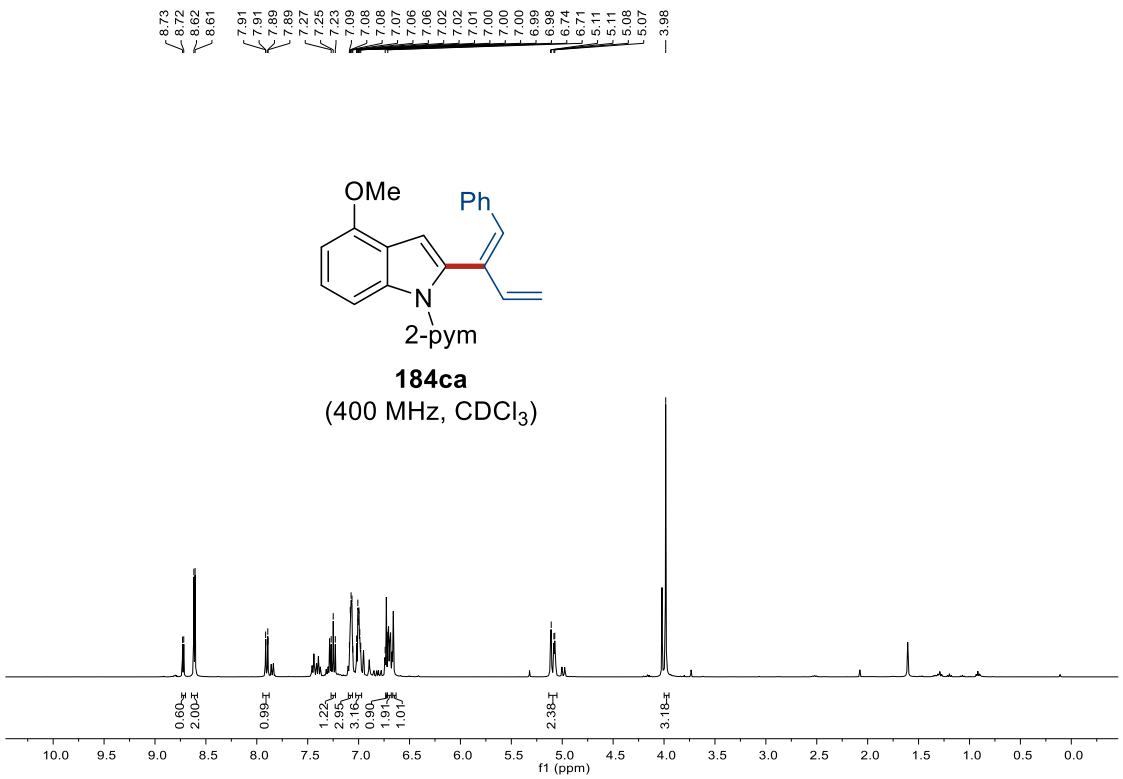


184ba
(400 MHz, $CDCl_3$)

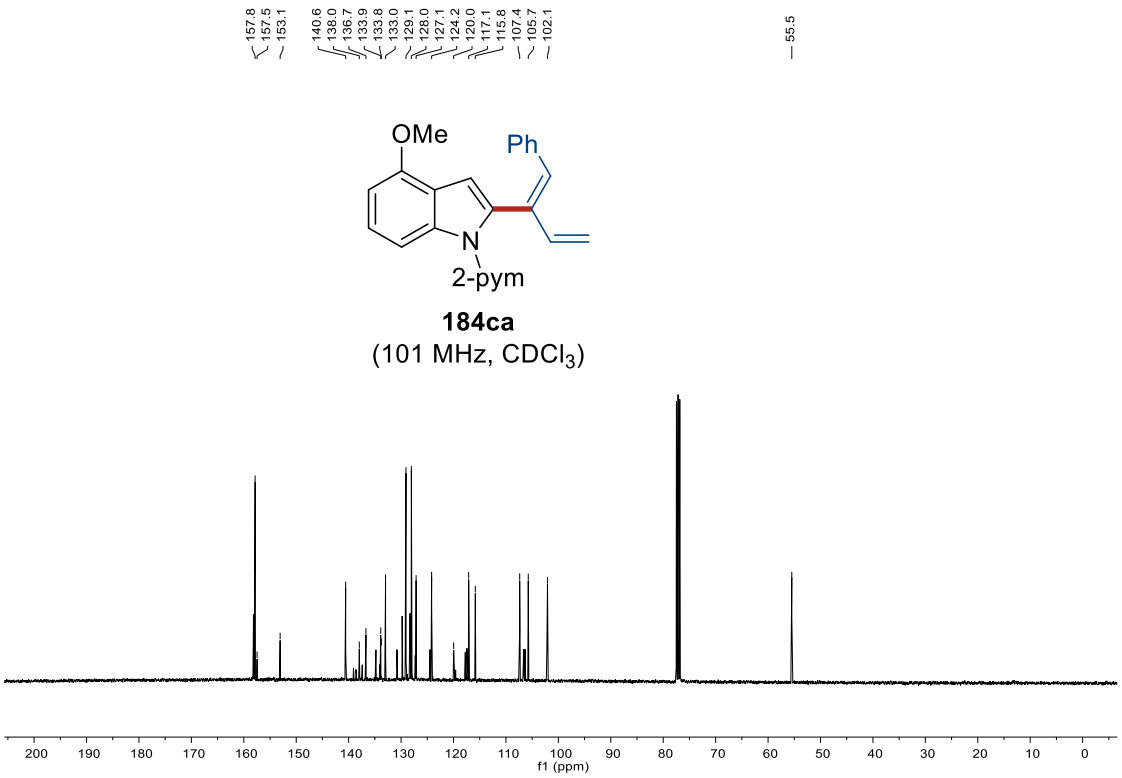




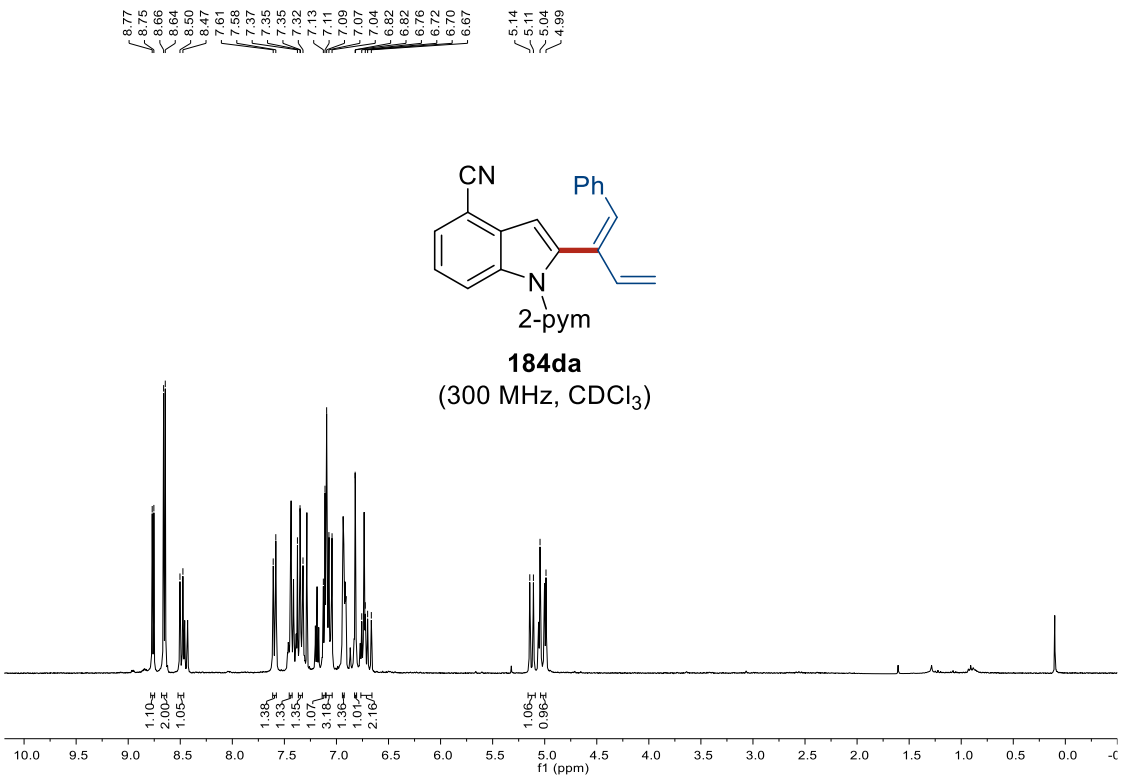
184ba
(101 MHz, $CDCl_3$)



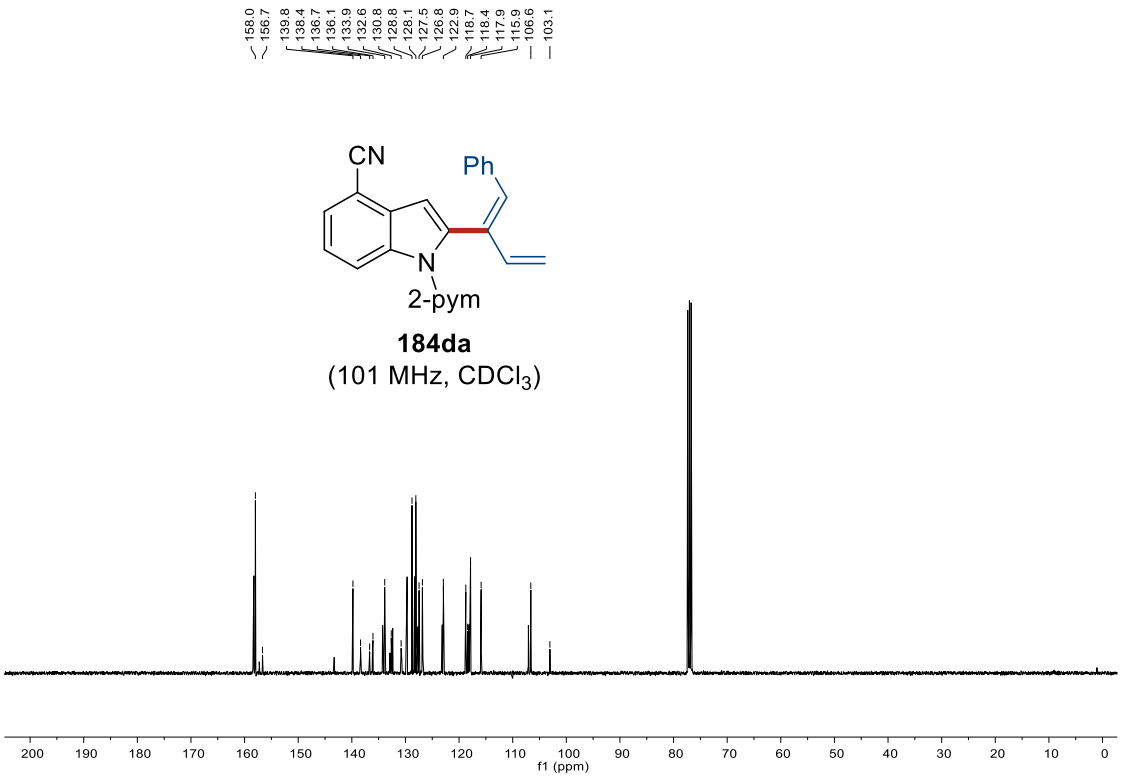
184ca
(400 MHz, $CDCl_3$)



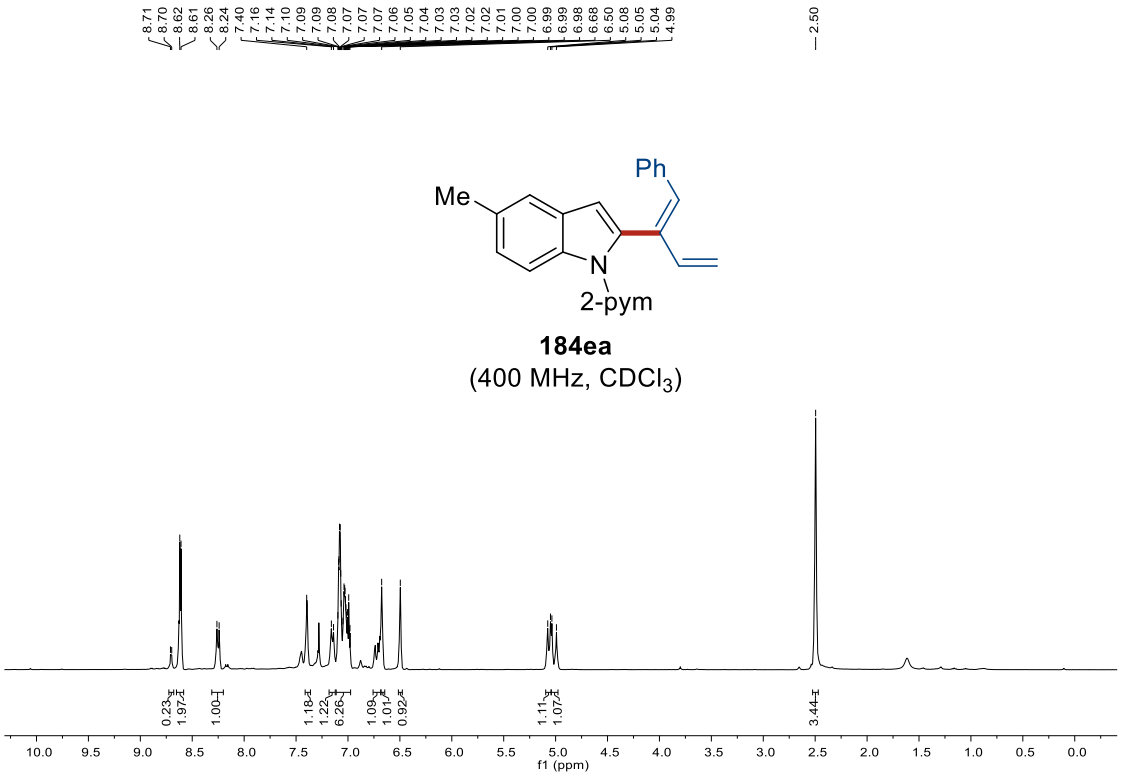
184ca
(101 MHz, $CDCl_3$)



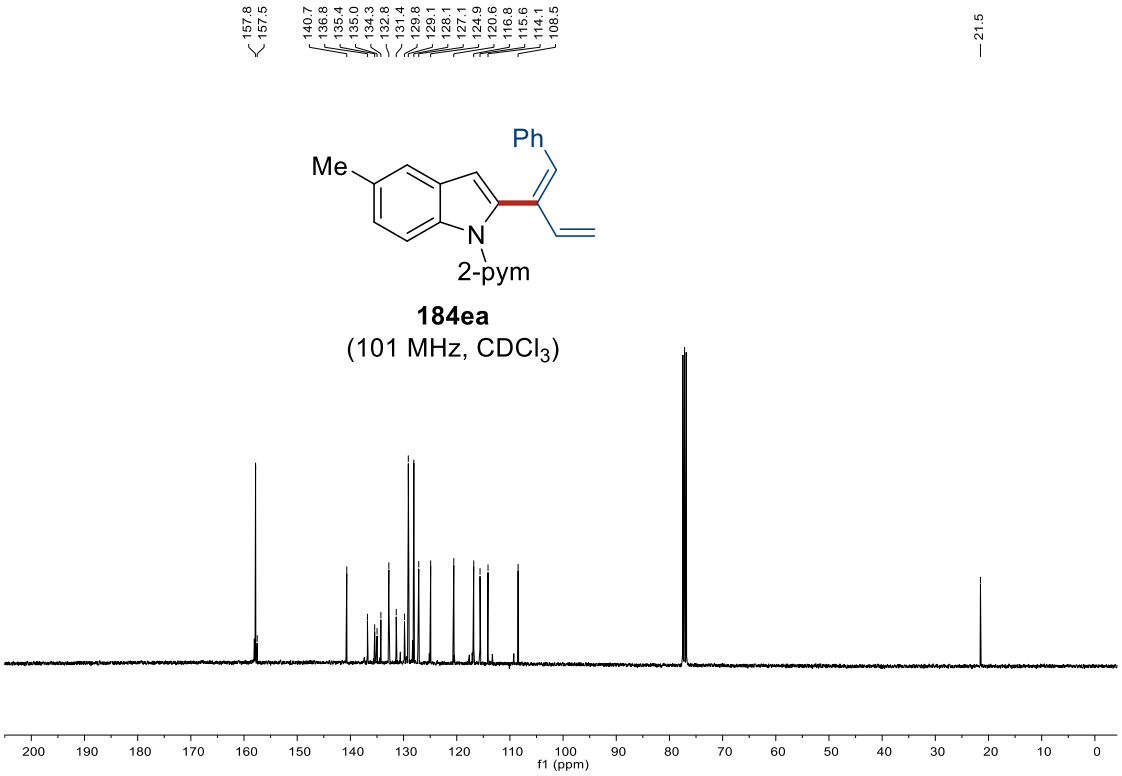
184da
(300 MHz, $CDCl_3$)



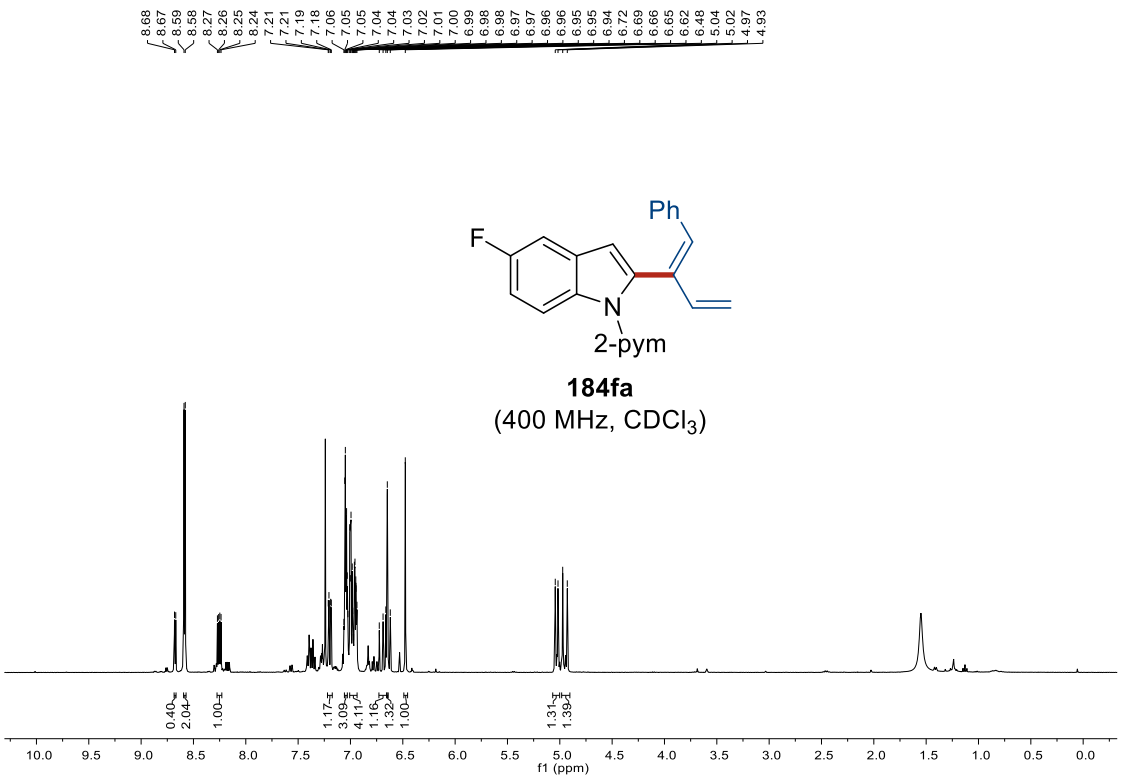
184da
(101 MHz, $CDCl_3$)



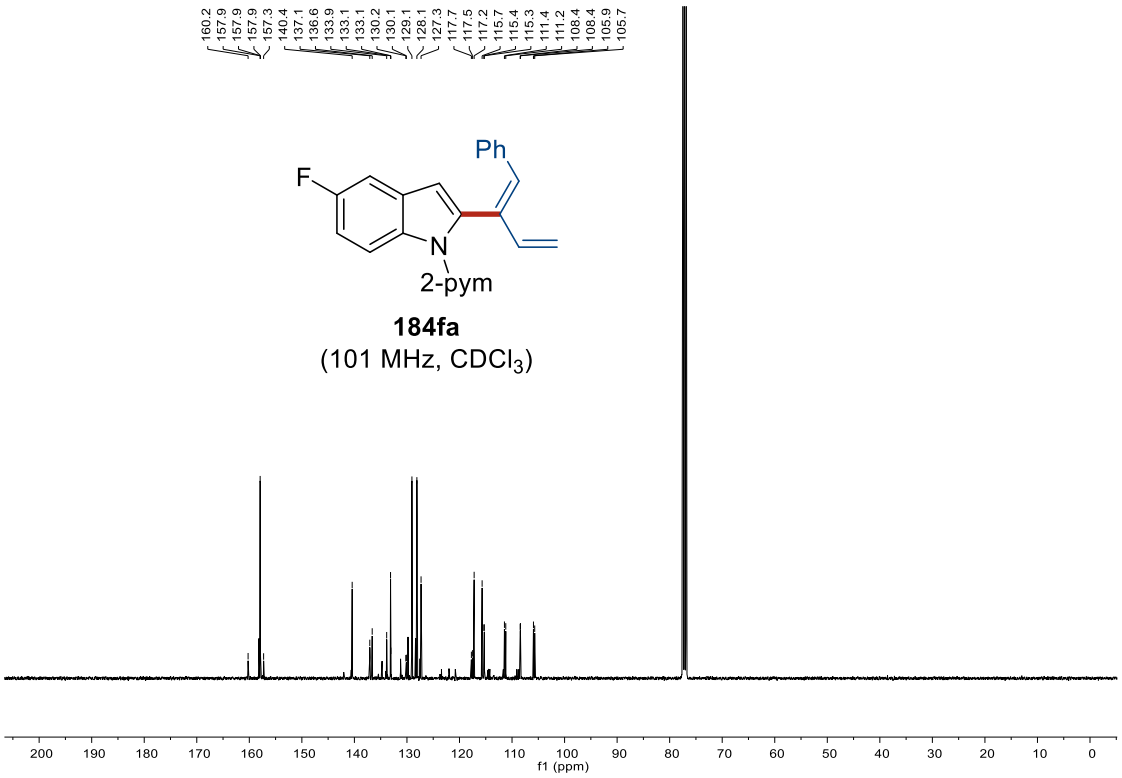
184ea
(400 MHz, $CDCl_3$)



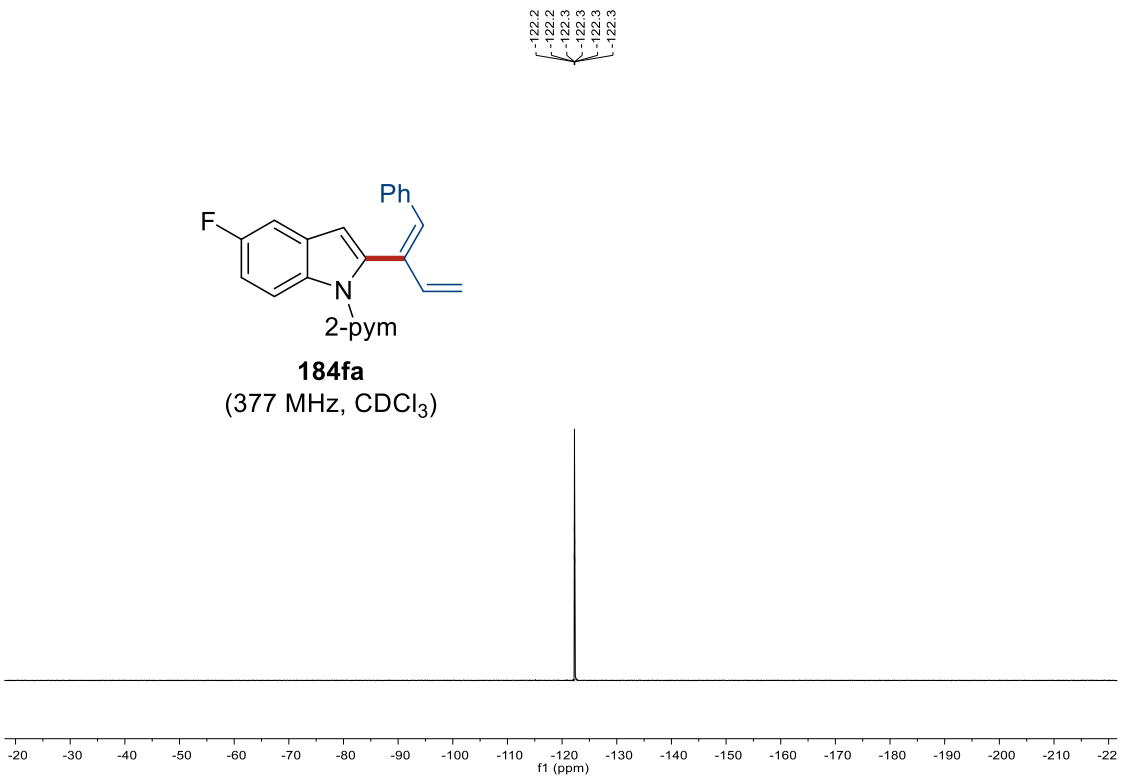
184ea
(101 MHz, $CDCl_3$)



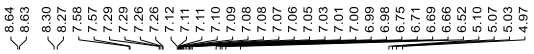
184fa
(400 MHz, $CDCl_3$)

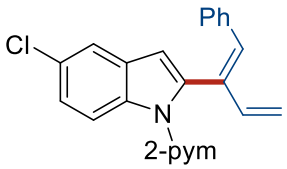


184fa
(101 MHz, $CDCl_3$)

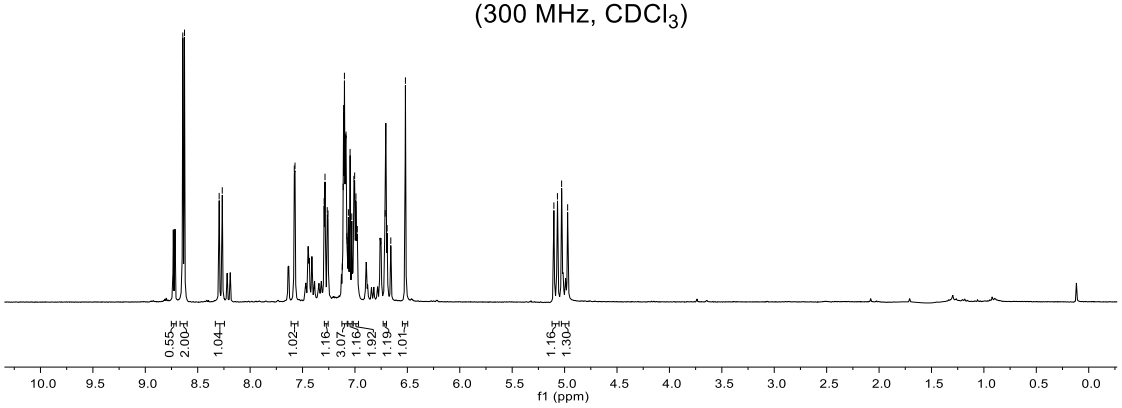


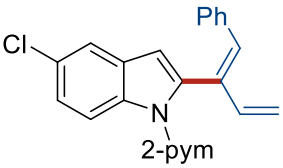
184fa
(377 MHz, $CDCl_3$)



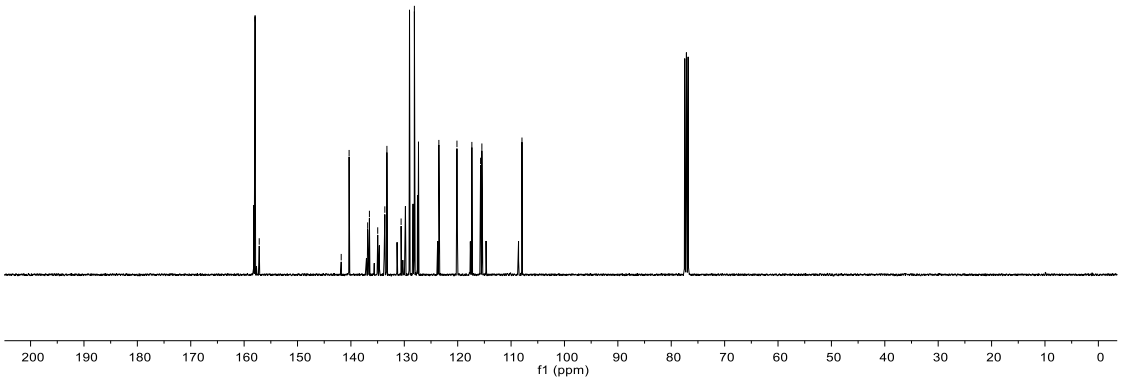


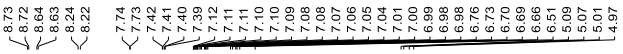
184ga
(300 MHz, $CDCl_3$)

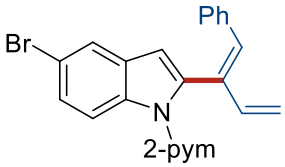




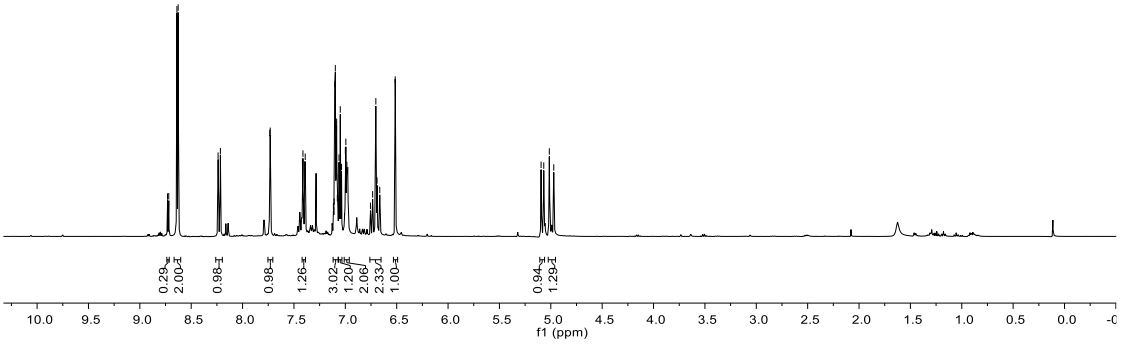
184ga
(101 MHz, $CDCl_3$)

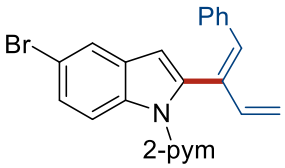




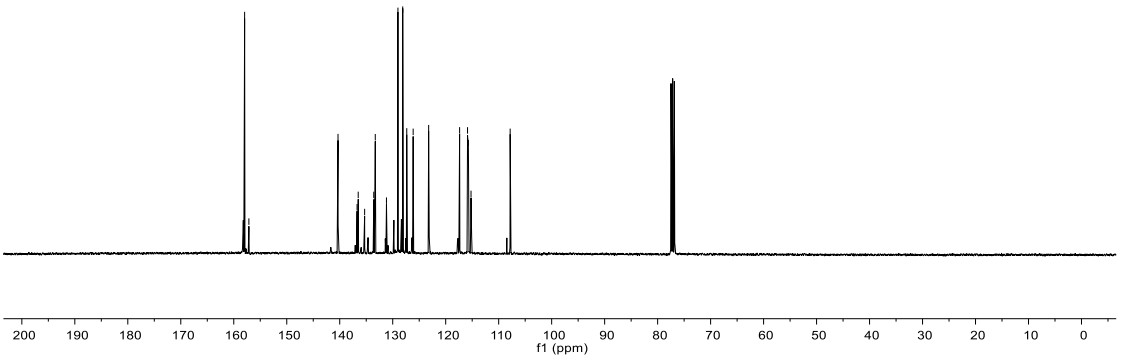


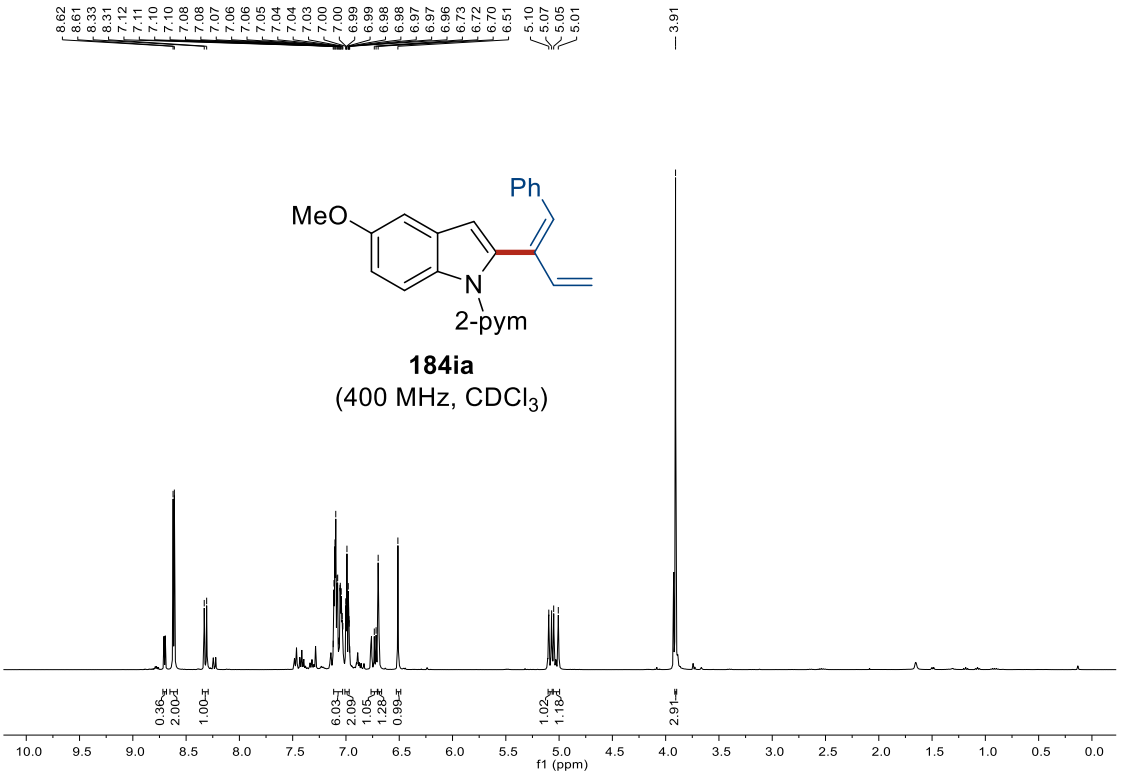
184ha
(400 MHz, $CDCl_3$)



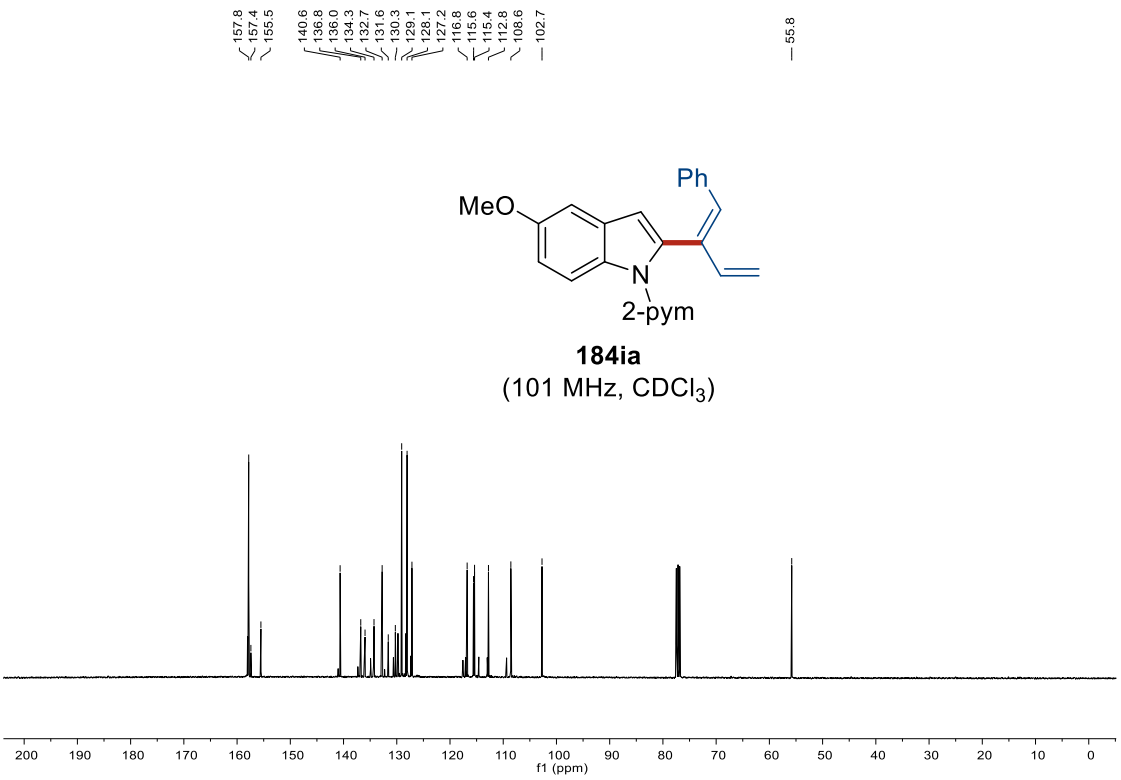


184ha
(101 MHz, $CDCl_3$)

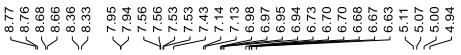


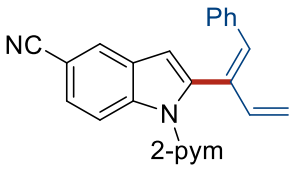


184ia
(400 MHz, $CDCl_3$)

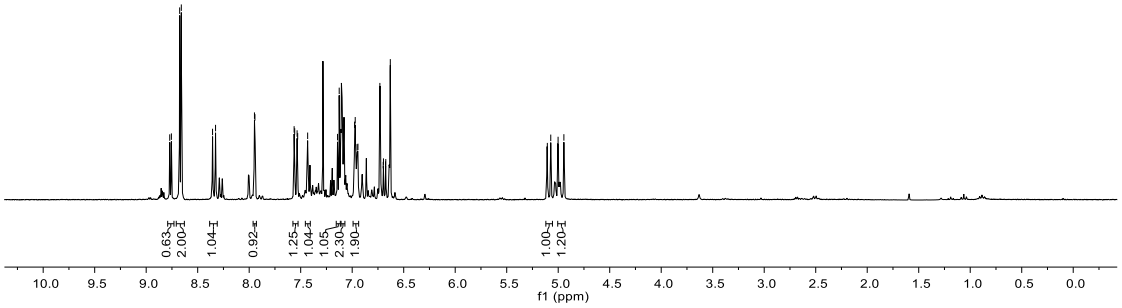


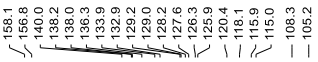
184ia
(101 MHz, $CDCl_3$)

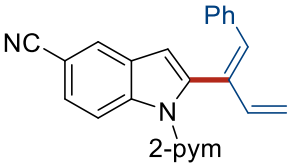




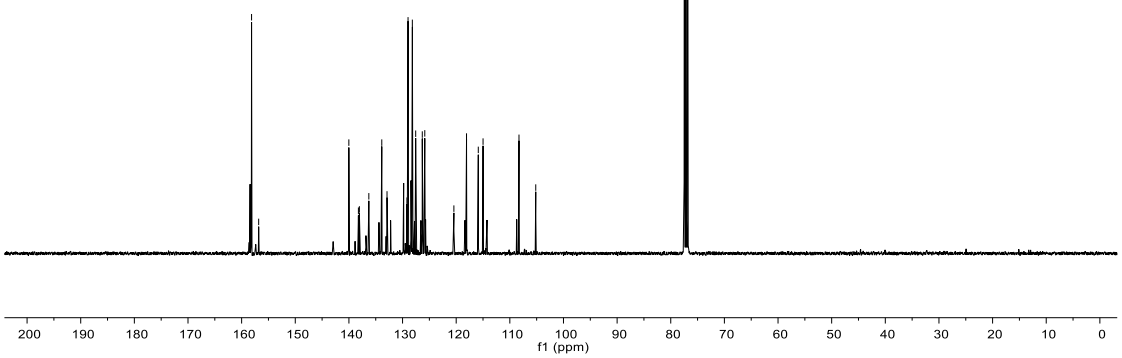
184ja
(300 MHz, $CDCl_3$)

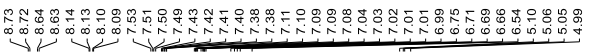


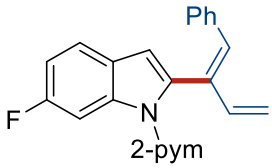




184ja
(101 MHz, $CDCl_3$)

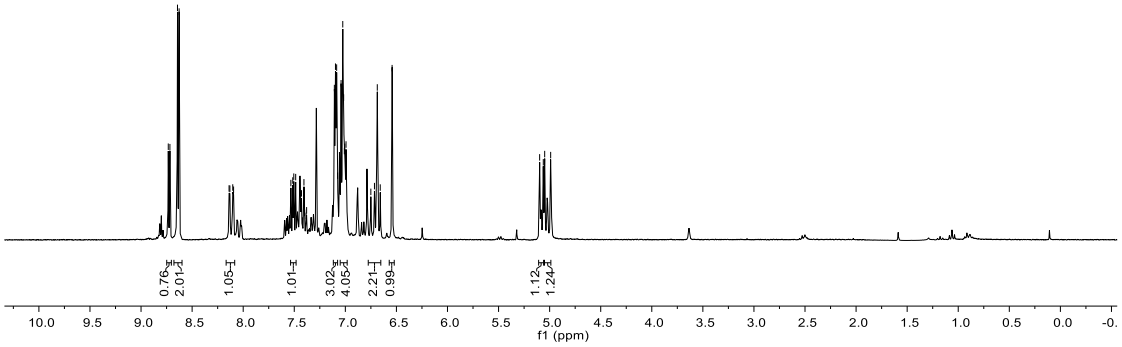


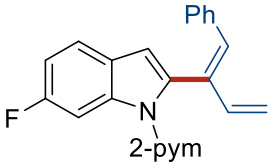




184ka

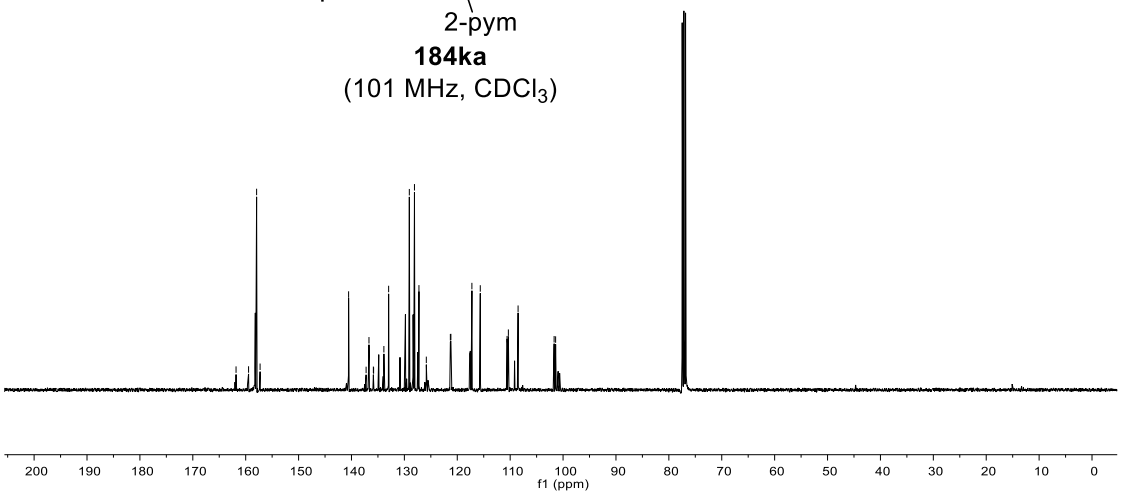
(300 MHz, $CDCl_3$)

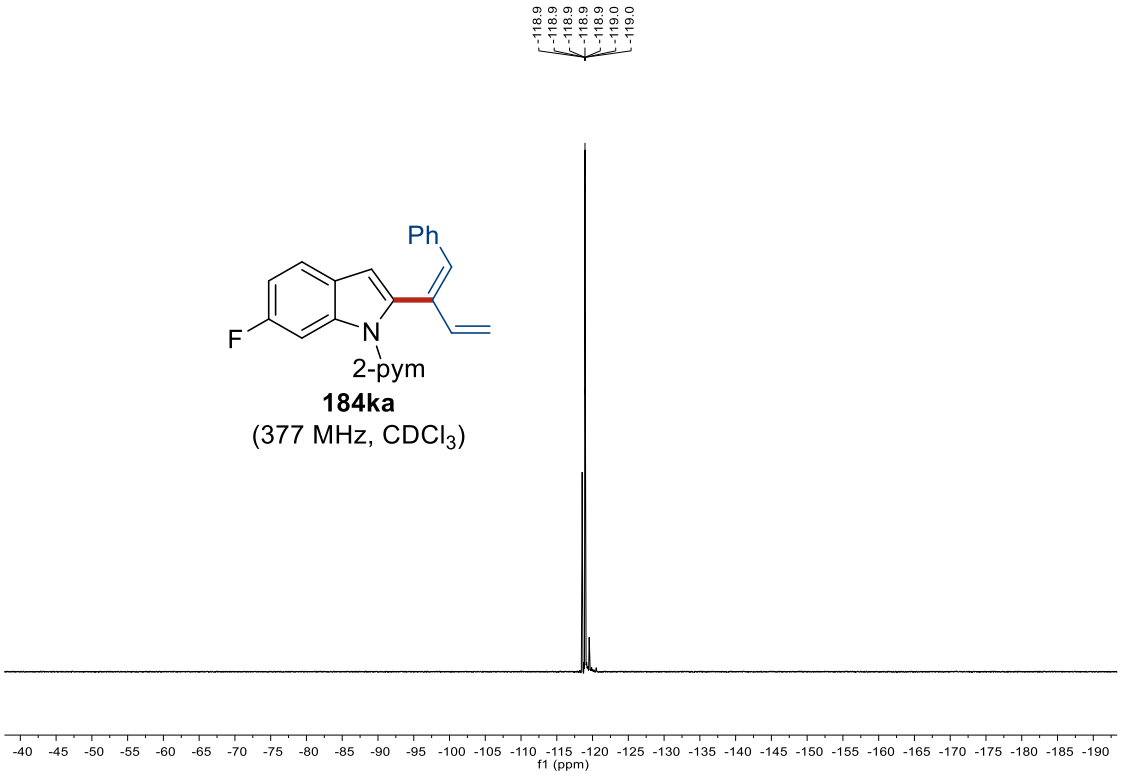




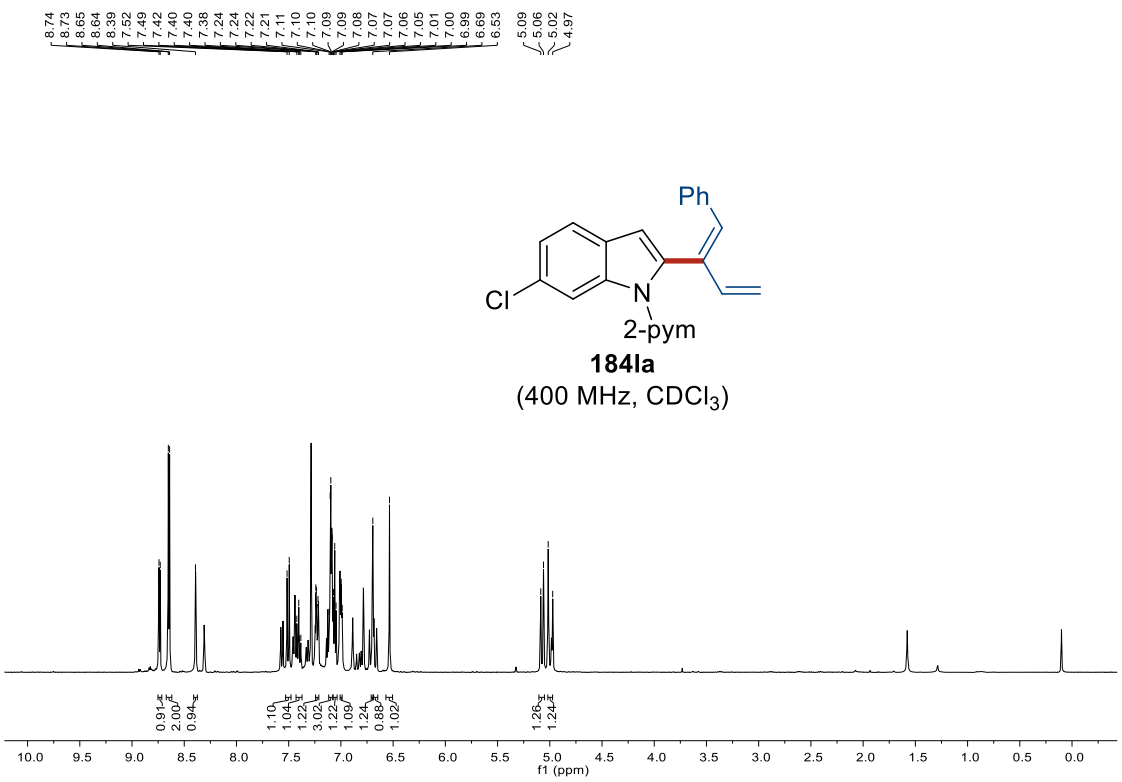
184ka

(101 MHz, $CDCl_3$)

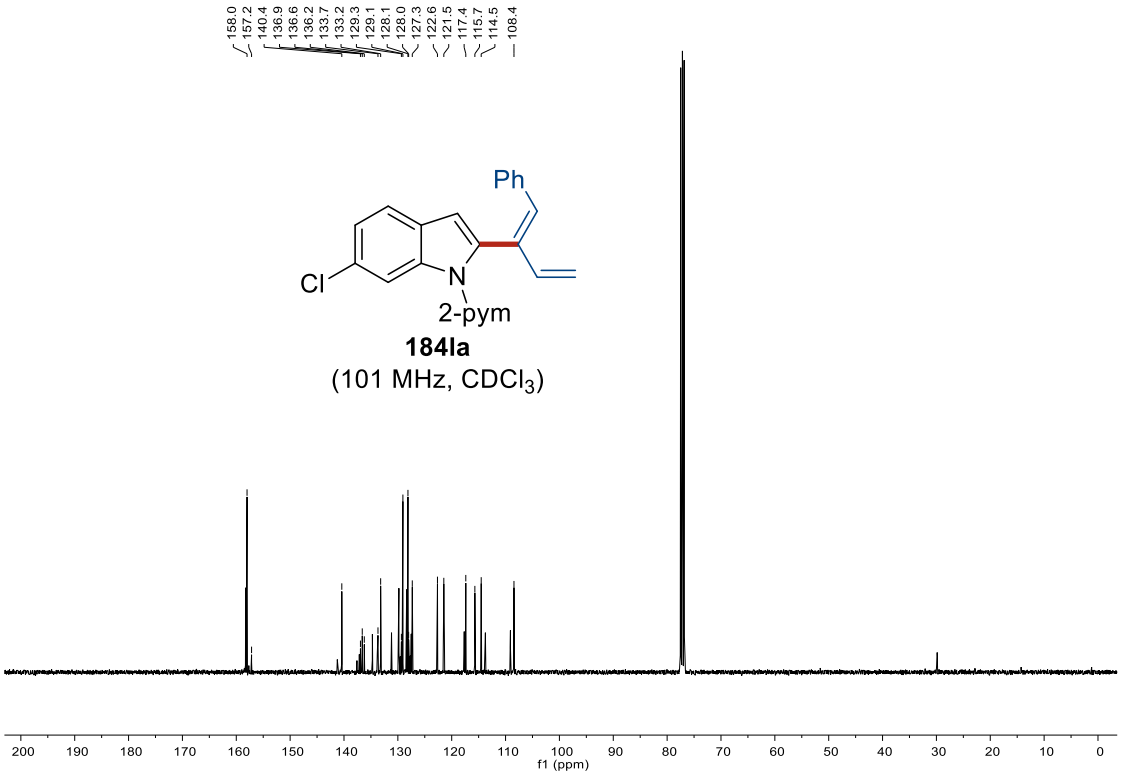




184ka
(377 MHz, $CDCl_3$)

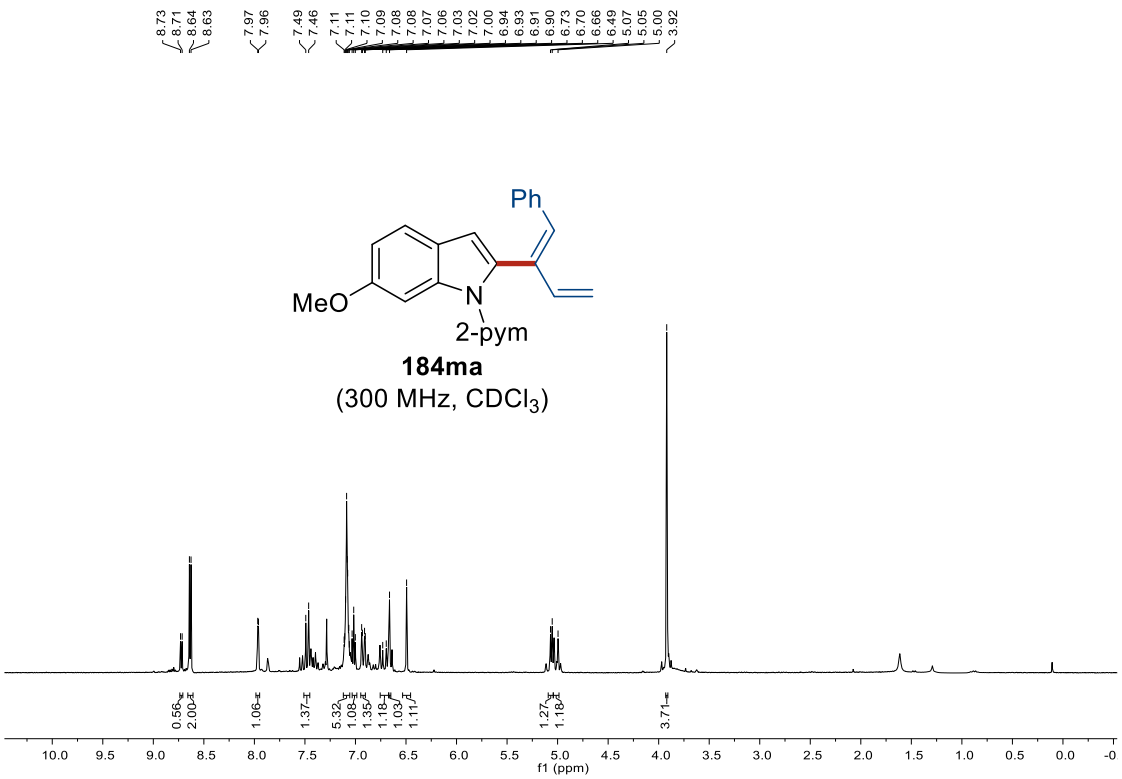


184la
(400 MHz, $CDCl_3$)



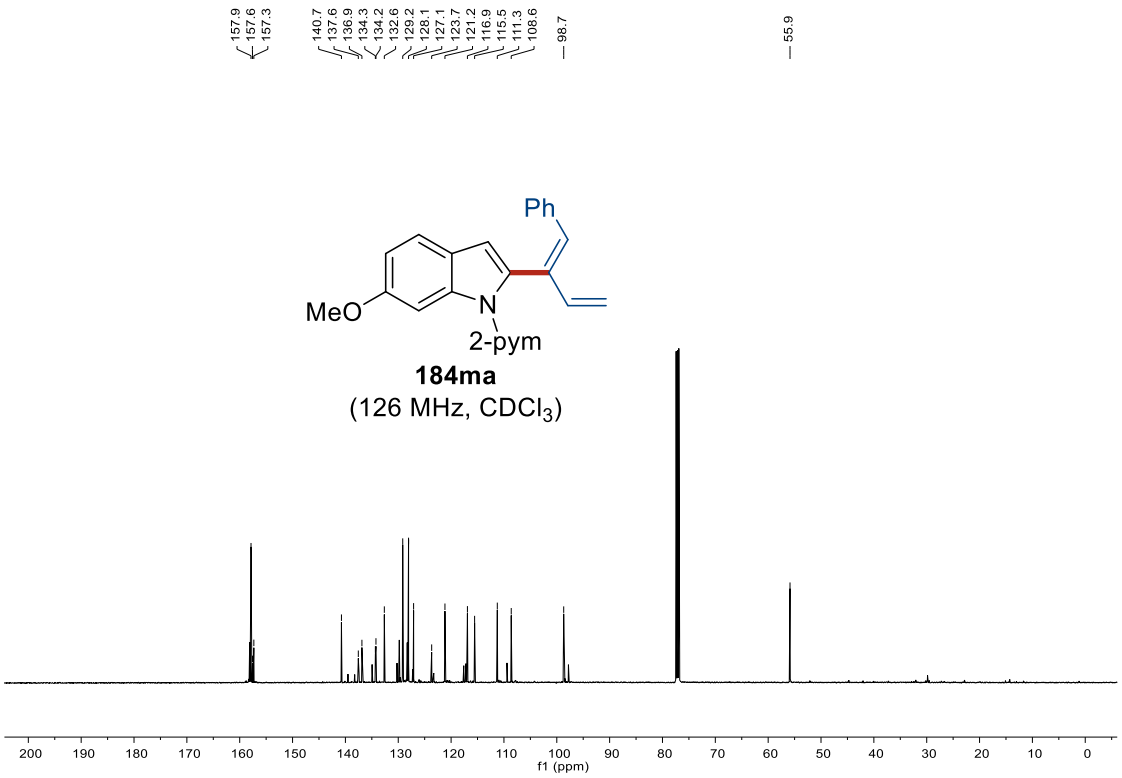
184la

(101 MHz, $CDCl_3$)

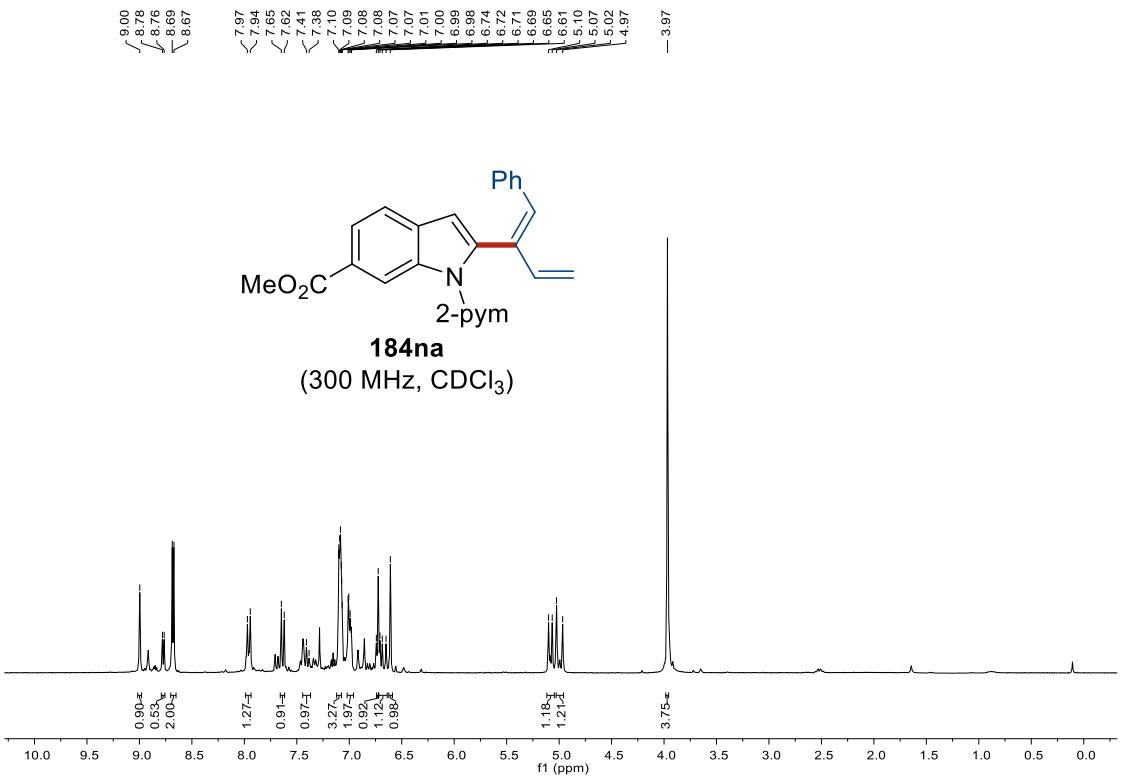


184ma

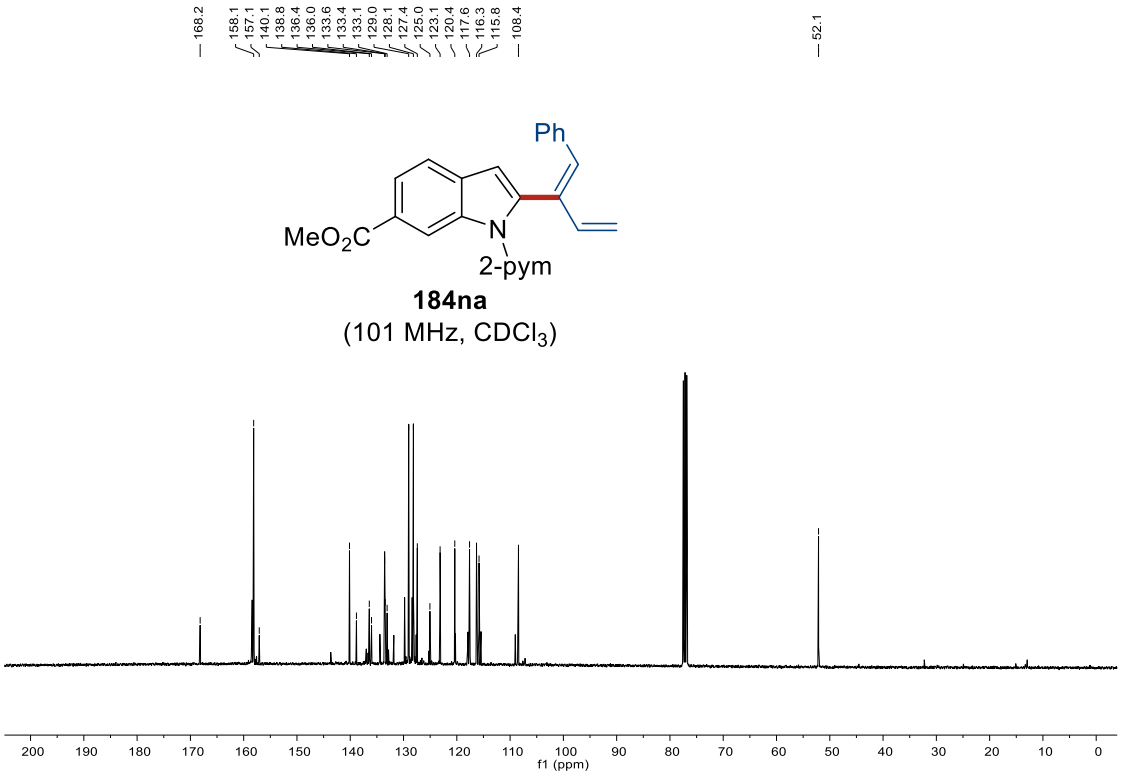
(300 MHz, $CDCl_3$)

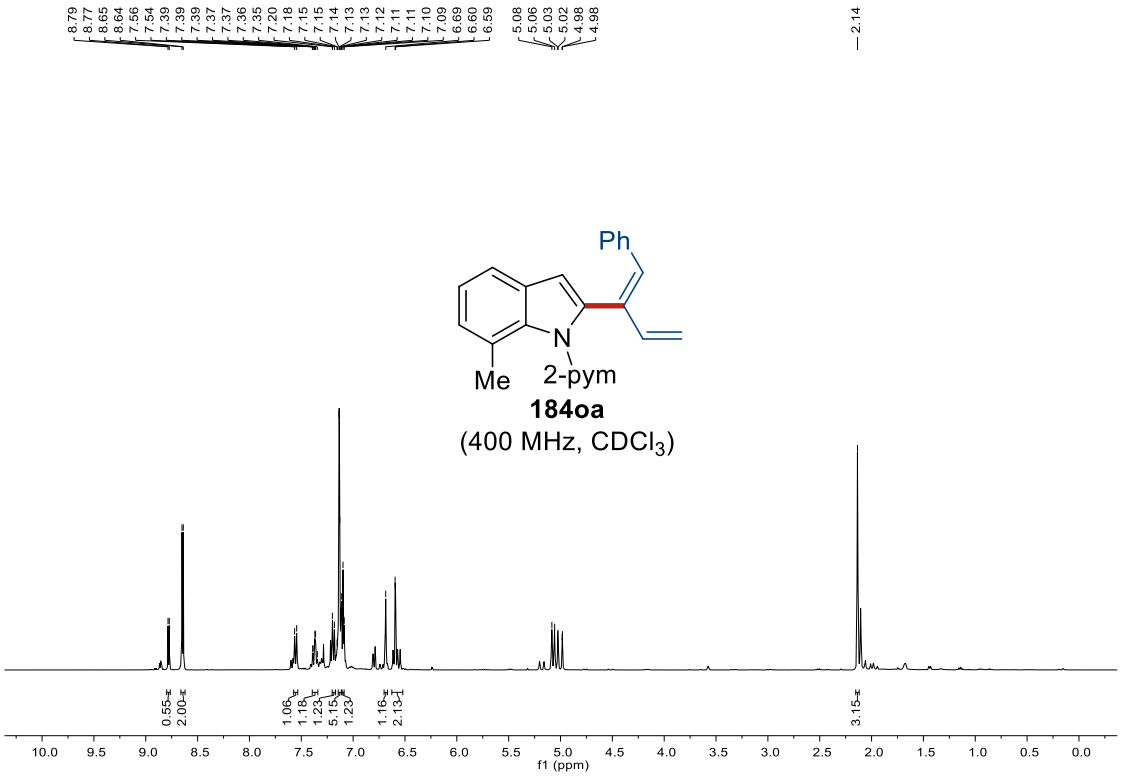


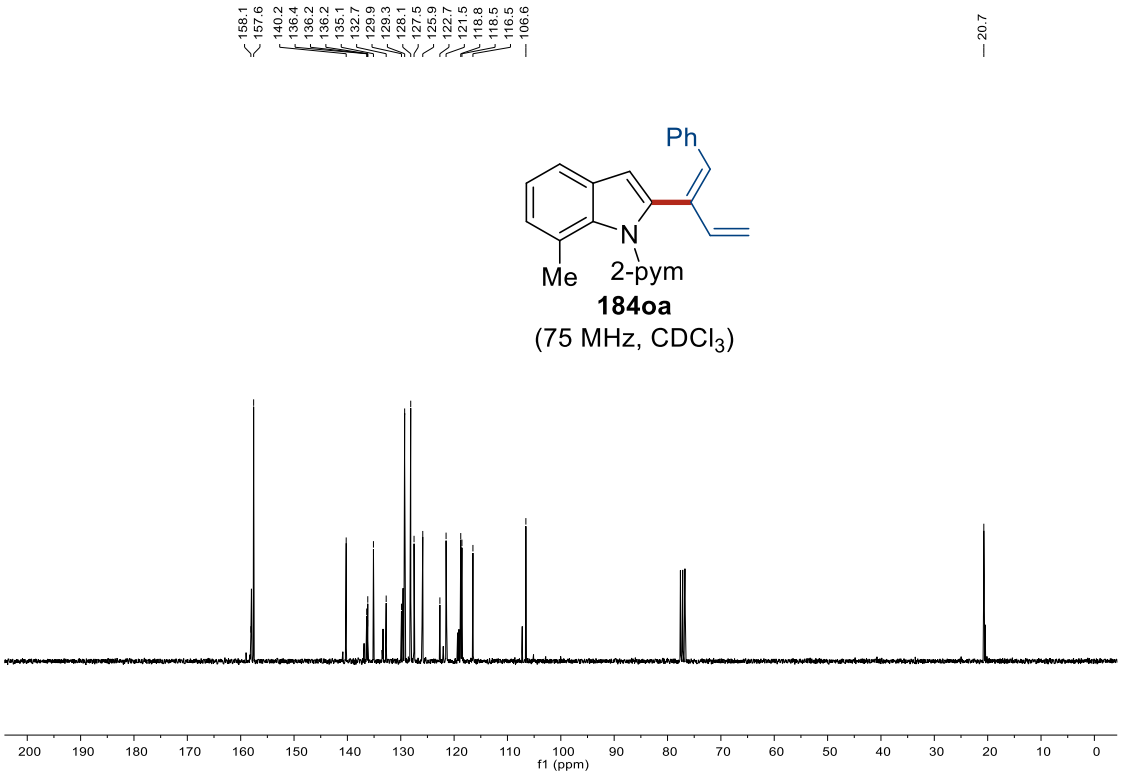
184ma
(126 MHz, $CDCl_3$)



184na
(300 MHz, $CDCl_3$)

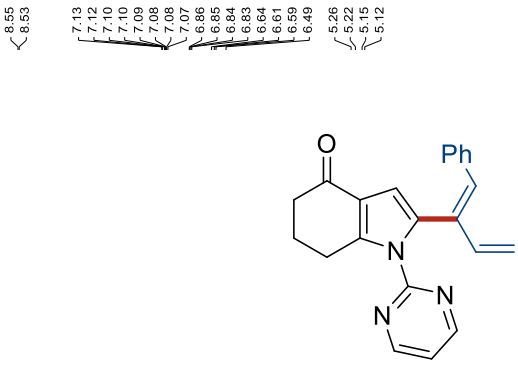

168.2
158.1
157.1
140.1
138.8
136.4
136.0
133.6
133.4
133.1
129.0
128.1
127.4
125.0
123.1
120.4
117.6
116.3
115.8
108.4
52.1
Ph
MeO2C
N
2-pym
184na
(101 MHz, CDCl3)
f1 (ppm)


8.79
8.77
8.65
8.64
7.56
7.54
7.39
7.39
7.39
7.37
7.37
7.36
7.35
7.20
7.18
7.15
7.15
7.14
7.13
7.13
7.12
7.11
7.11
7.10
7.09
6.69
6.60
6.59
5.08
5.06
5.03
5.02
4.98
4.98
2.14
Ph
N
Me
2-pym
184oa
(400 MHz, CDCl3)
0.55
2.00
1.06
1.18
1.23
5.15
1.23
1.16
2.13
3.15
f1 (ppm)



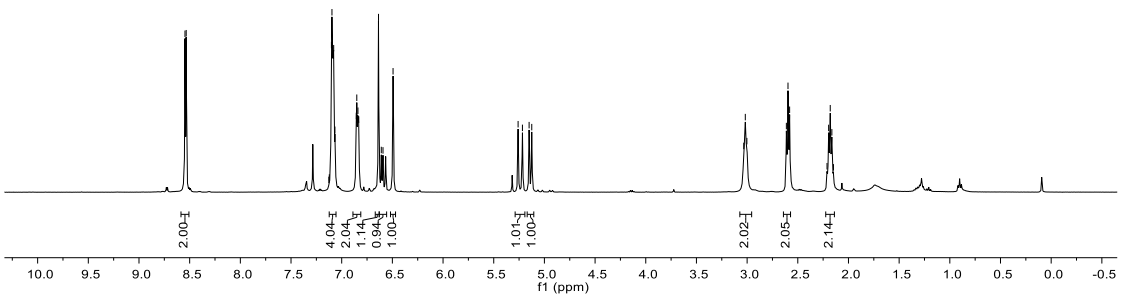
184oa

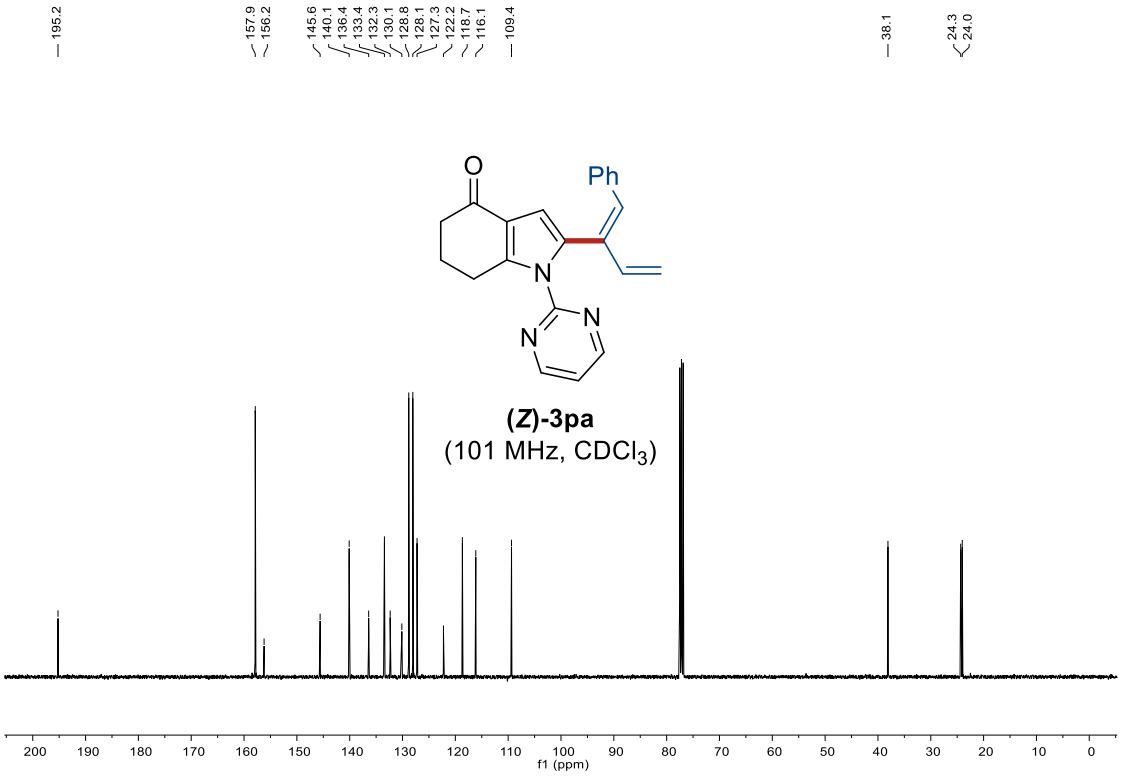
(75 MHz, $CDCl_3$)

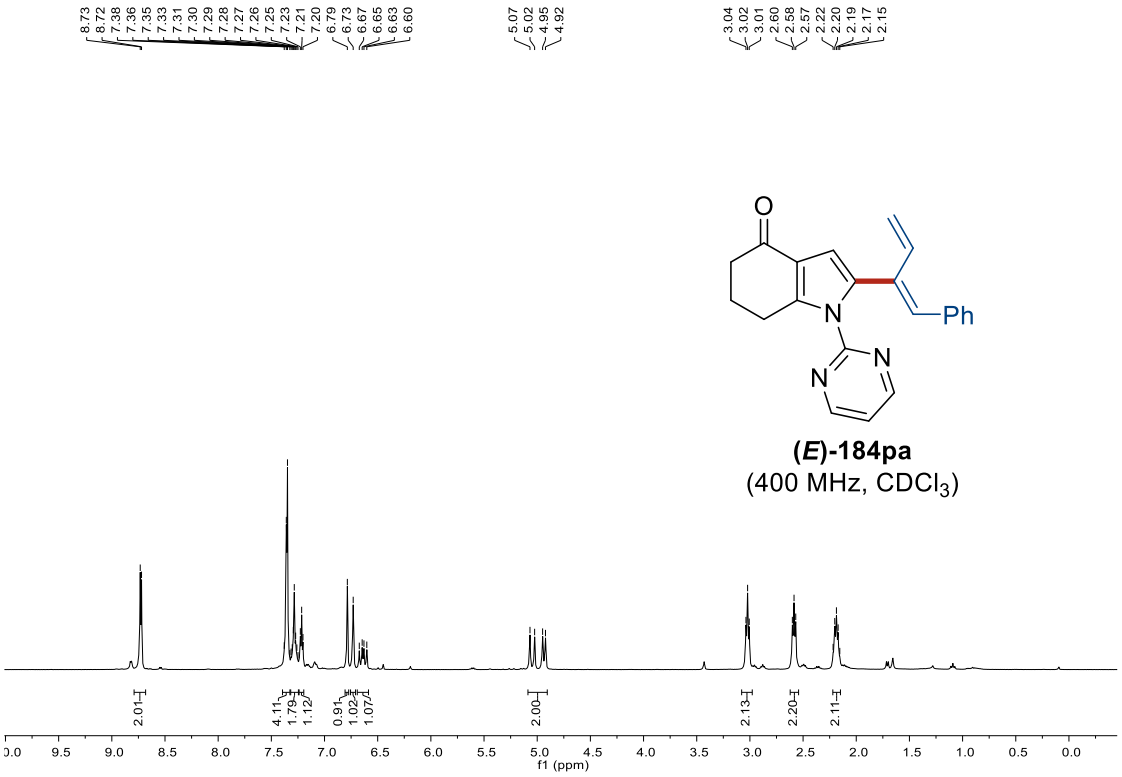


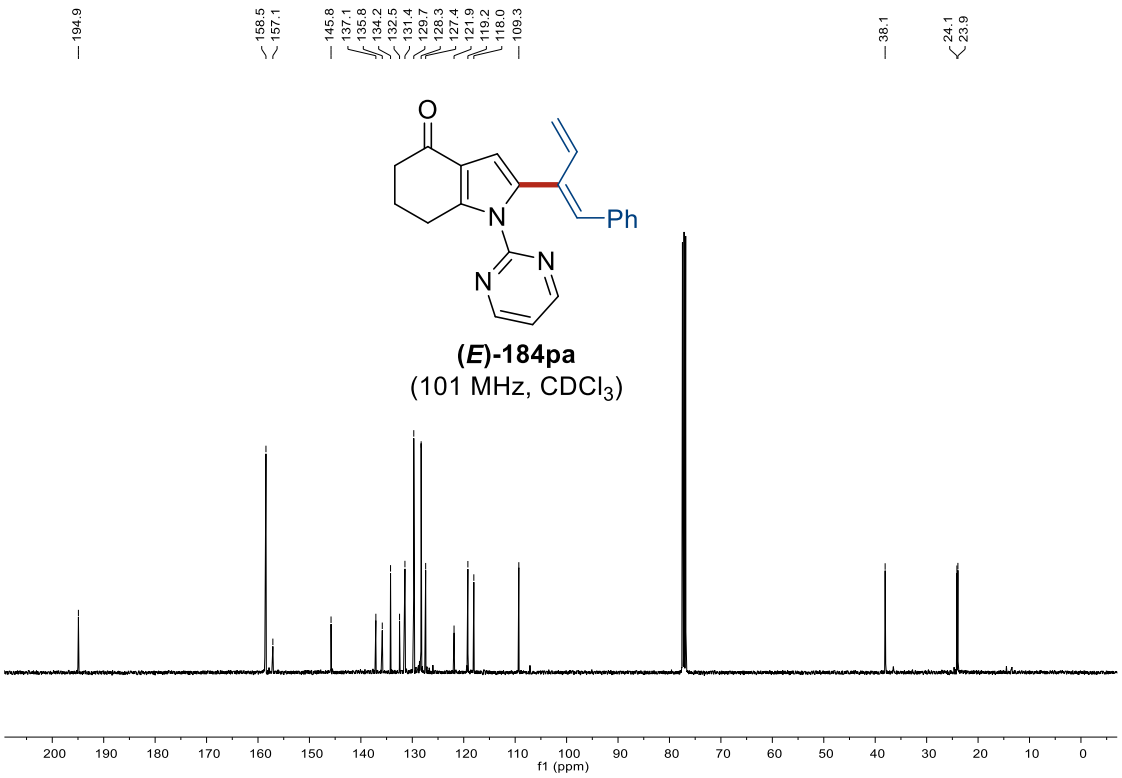
(*Z*)-3pa

(400 MHz, $CDCl_3$)

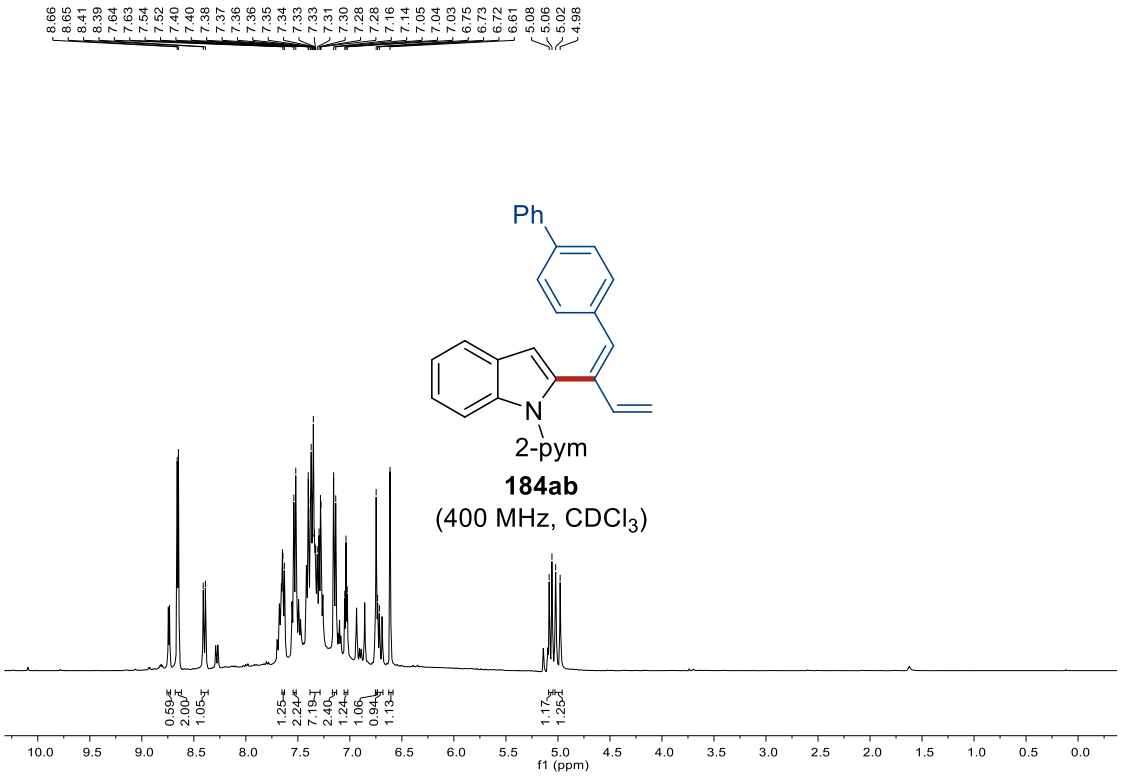



195.2
157.9
156.2
145.6
140.1
136.4
133.4
132.3
130.1
128.8
128.1
127.3
122.2
118.7
116.1
109.4
38.1
24.3
24.0
O
Ph
N
N
N
(Z)-3pa
(101 MHz, CDCl3)
f1 (ppm)

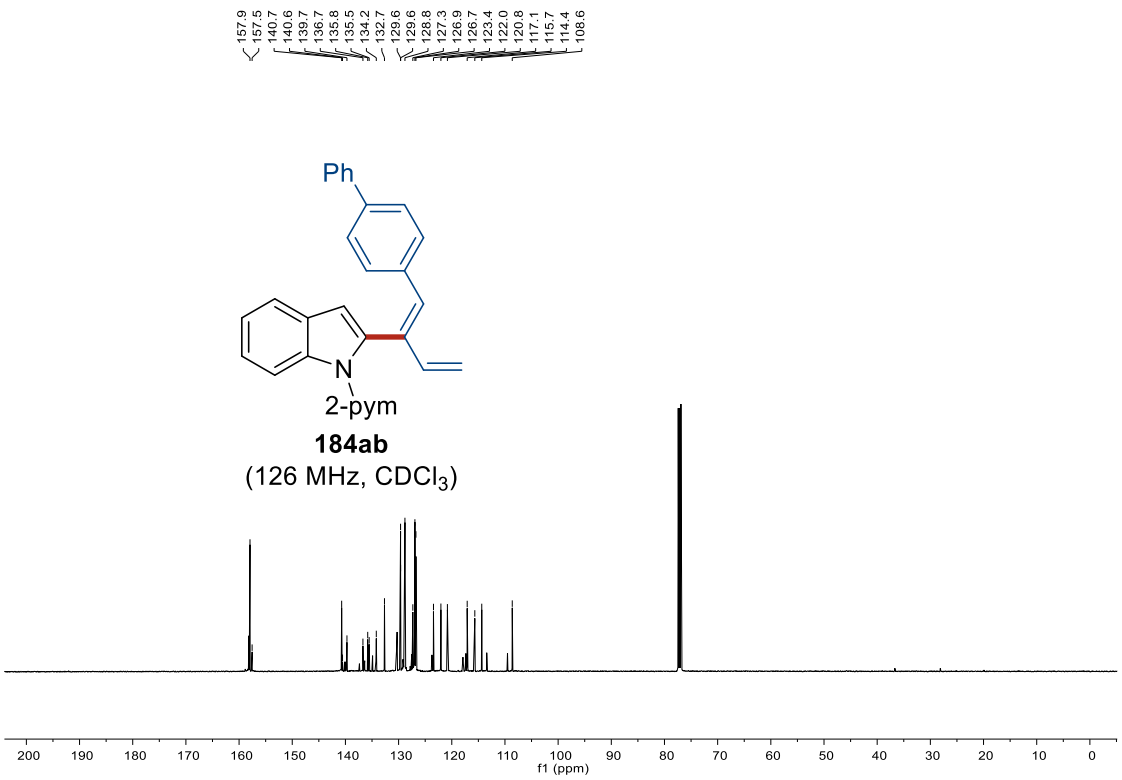

8.73
8.72
7.38
7.36
7.35
7.33
7.31
7.30
7.29
7.28
7.27
7.26
7.25
7.23
7.21
7.20
6.79
6.73
6.67
6.65
6.63
6.60
5.07
5.02
4.95
4.92
3.04
3.02
3.01
2.60
2.58
2.57
2.22
2.20
2.19
2.17
2.15
O
N
Ph
N
N
(E)-184pa
(400 MHz, CDCl3)
2.01
4.11
1.79
1.12
0.91
1.02
1.07
2.00
2.13
2.20
2.11
f1 (ppm)

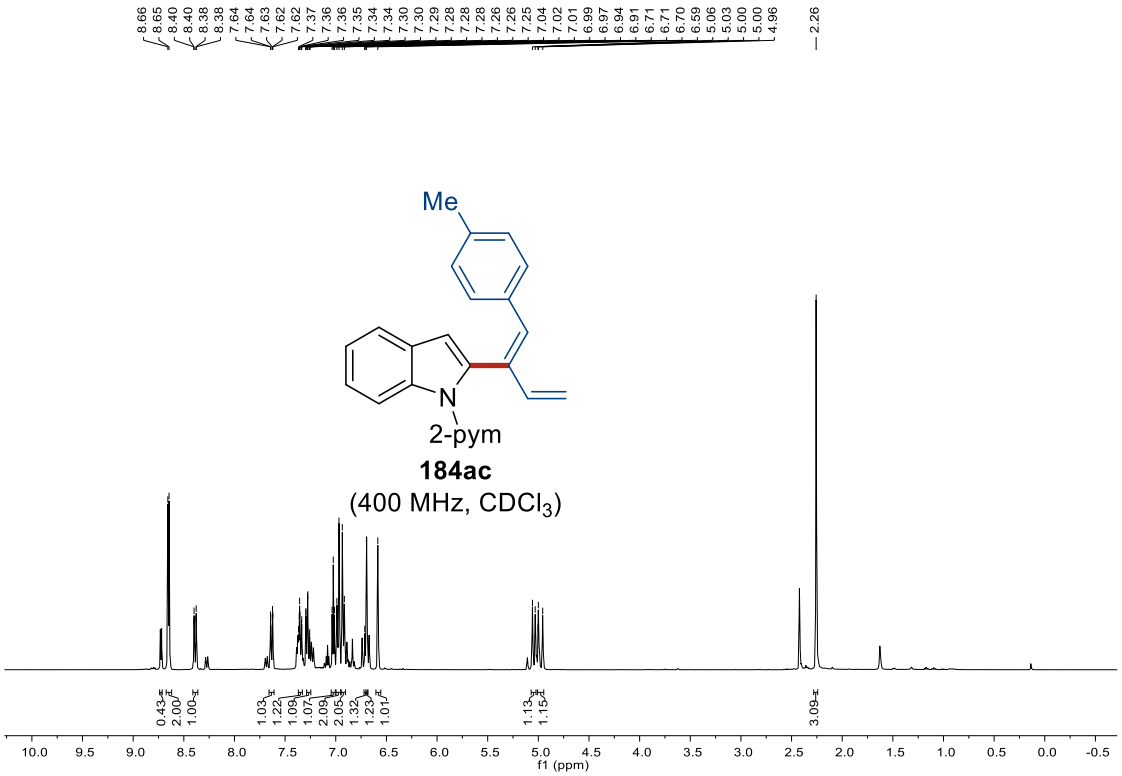


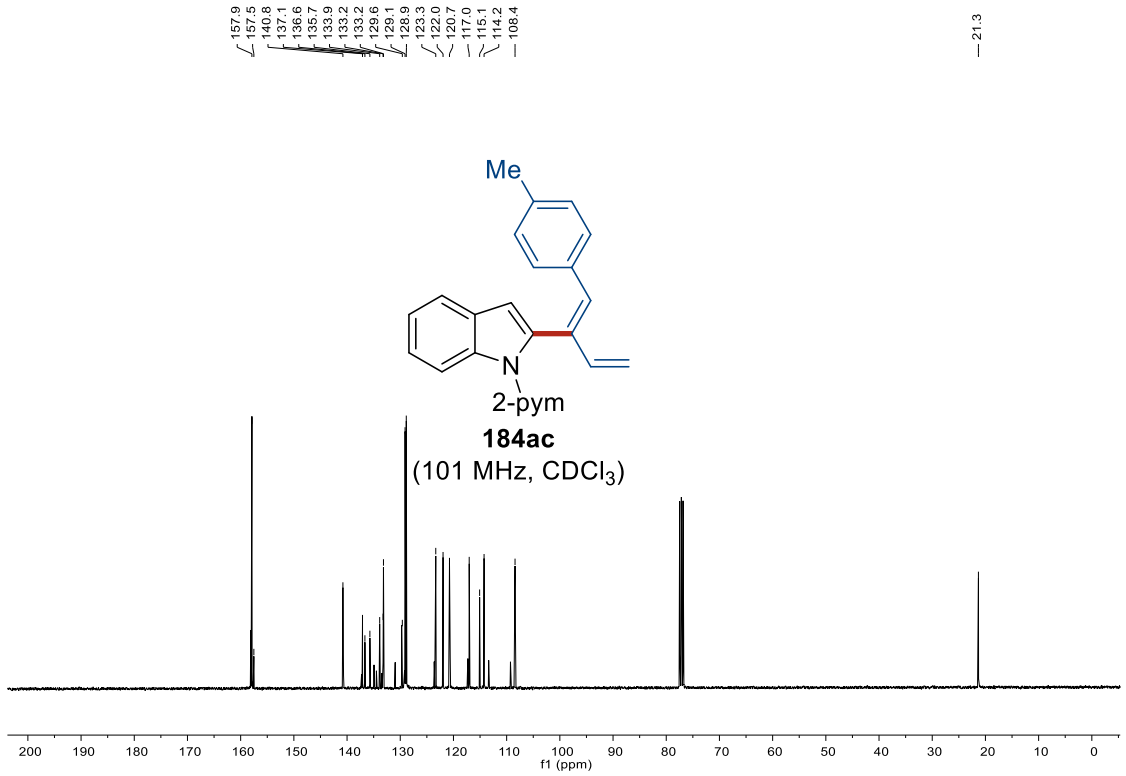
(*E*)-184pa
(101 MHz, $CDCl_3$)

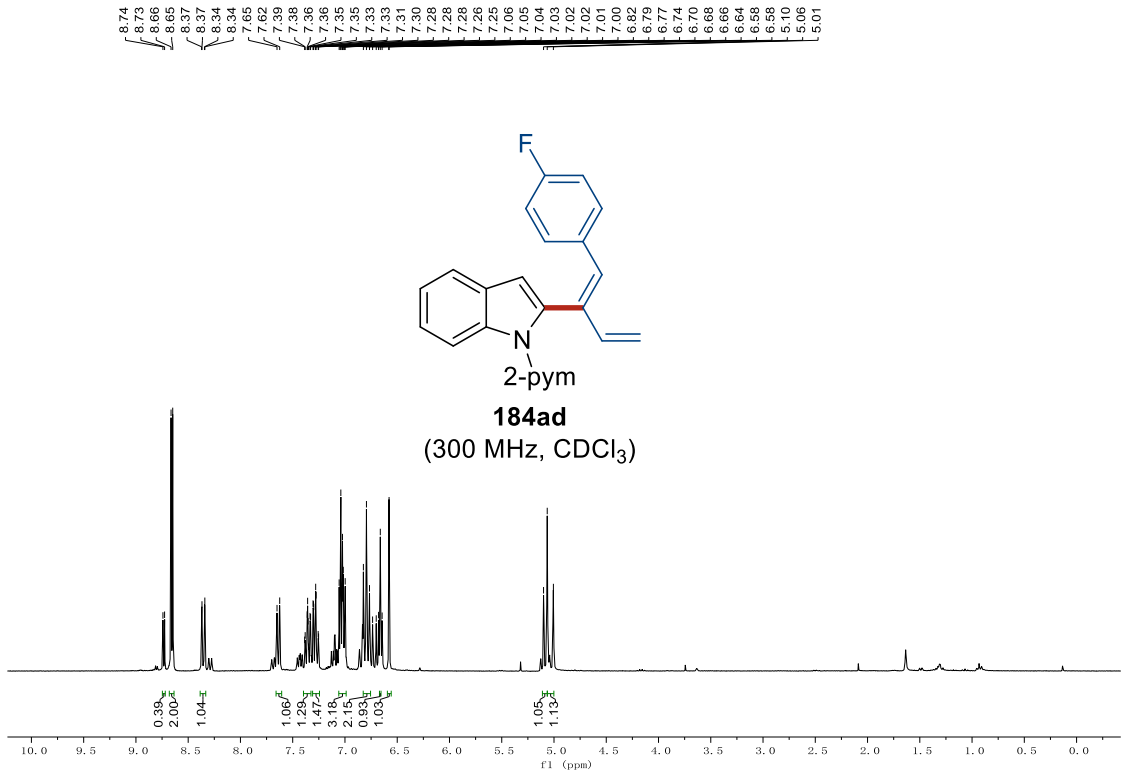


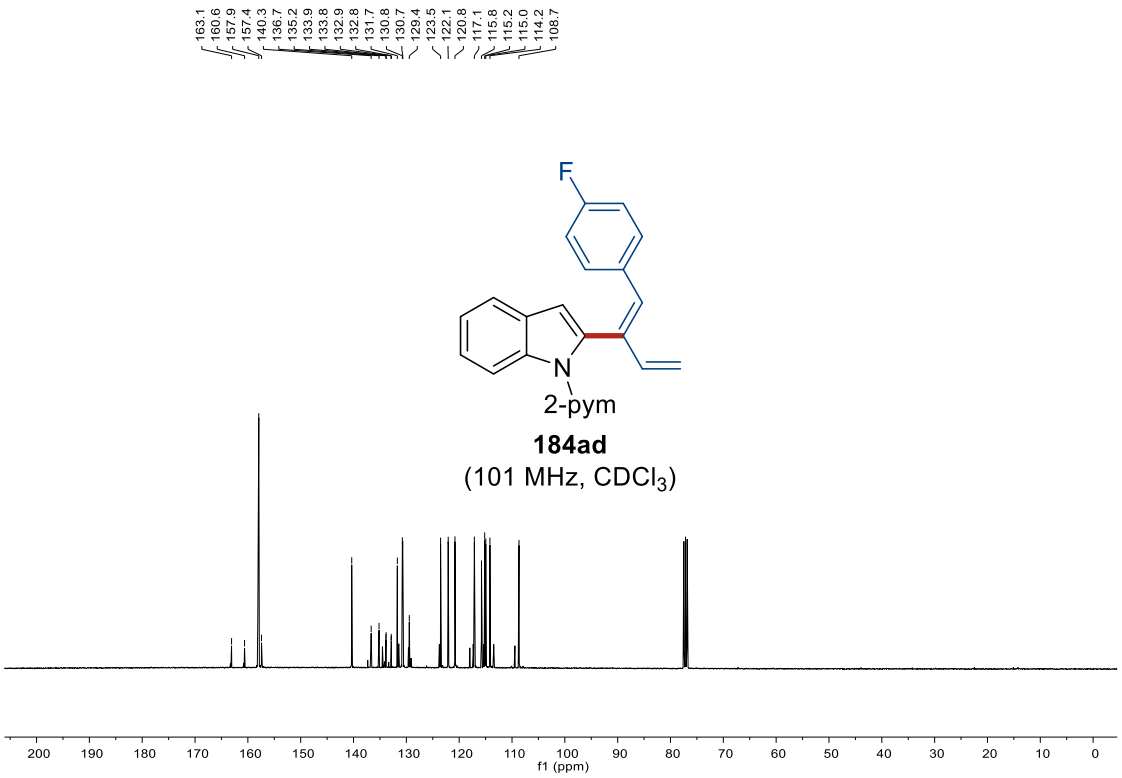
184ab
(400 MHz, $CDCl_3$)

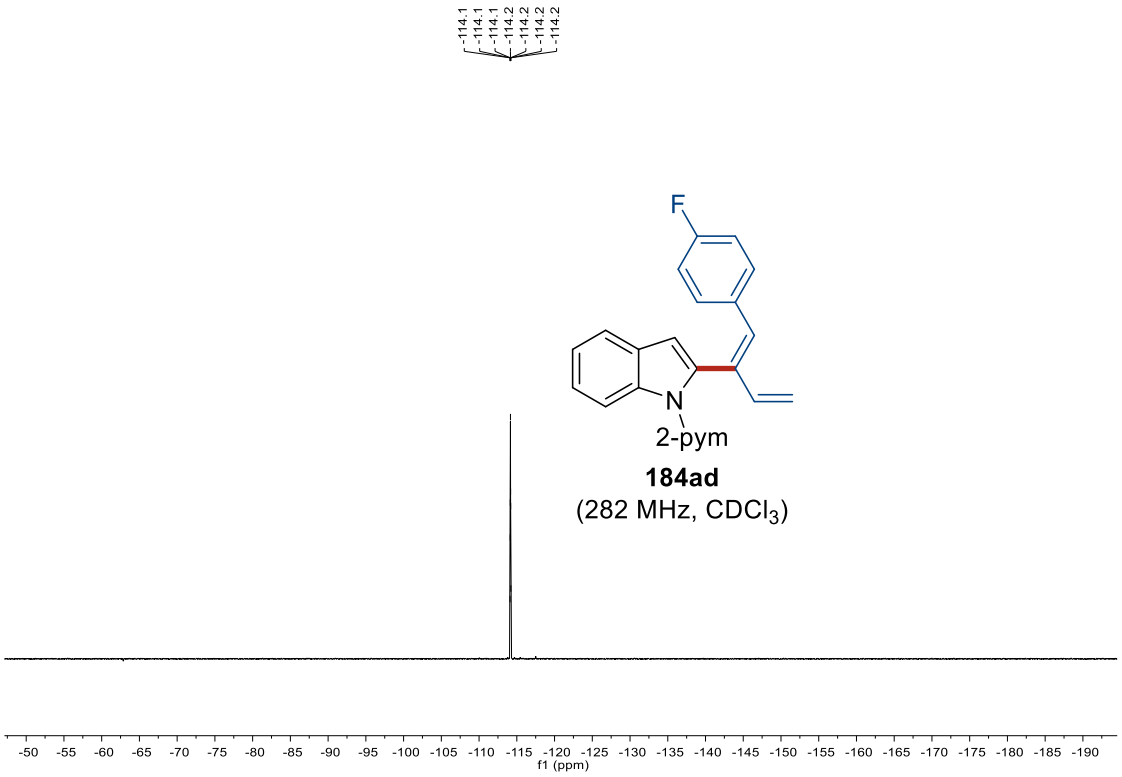

157.9
157.5
140.7
140.6
139.7
136.7
135.8
135.5
134.2
132.7
129.6
129.6
128.8
127.3
126.9
126.7
123.4
122.0
120.8
117.1
115.7
114.4
108.6
Ph
N
2-pym
184ab
(126 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

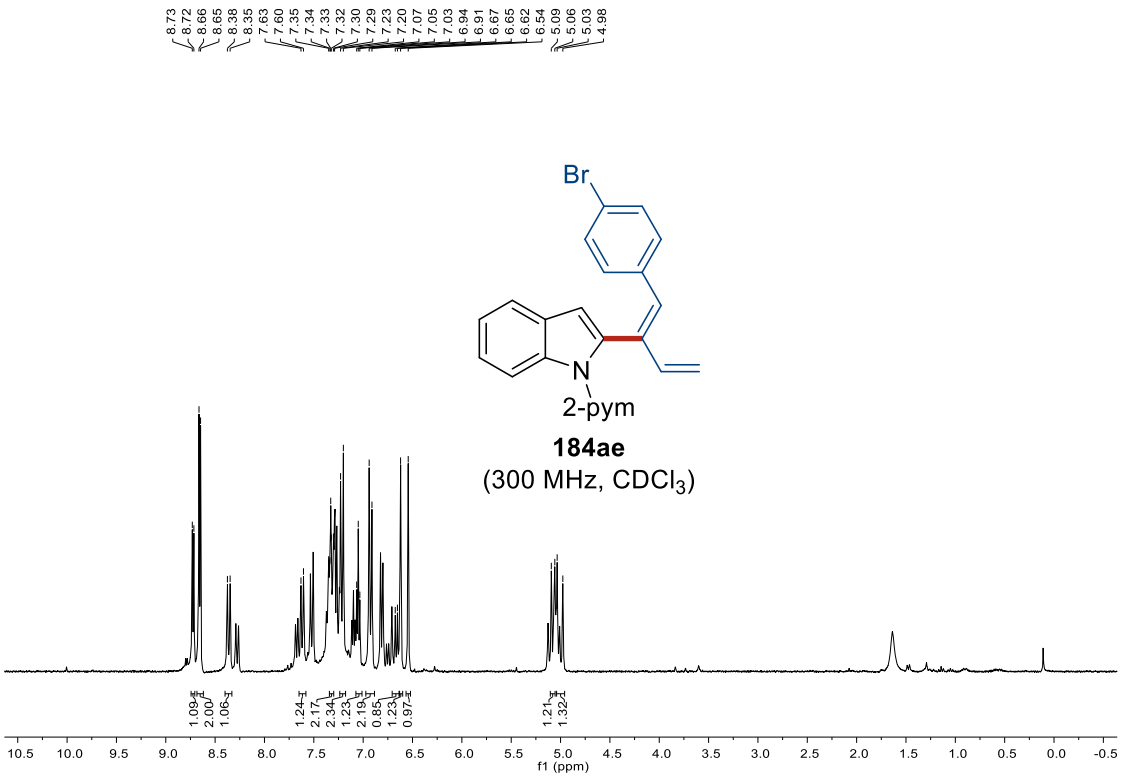

8.66
8.65
8.40
8.40
8.38
8.38
7.64
7.64
7.63
7.62
7.62
7.37
7.36
7.36
7.35
7.34
7.34
7.30
7.30
7.29
7.28
7.28
7.28
7.26
7.26
7.25
7.04
7.02
7.01
6.99
6.97
6.94
6.91
6.71
6.71
6.70
6.59
5.06
5.03
5.00
5.00
4.96
2.26
Me
N
2-pym
184ac
(400 MHz, CDCl3)
0.43
2.00
1.00
1.03
1.22
1.09
1.07
2.09
2.05
1.32
1.23
1.01
1.13
1.15
3.09
10.0 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 -0.5
f1 (ppm)

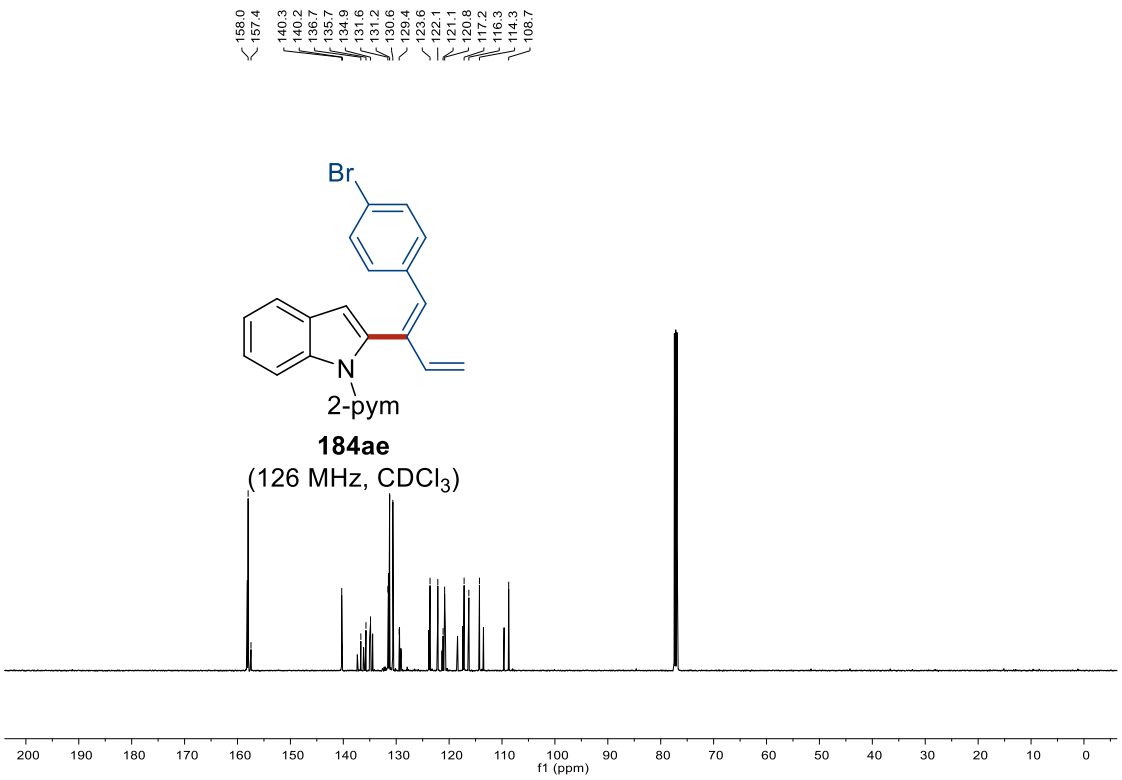

157.9
157.5
140.8
137.1
136.6
135.7
133.9
133.2
133.2
129.6
129.1
128.9
123.3
122.0
120.7
117.0
115.1
114.2
108.4
21.3
Me
N
2-pym
184ac
(101 MHz, CDCl3)
f1 (ppm)

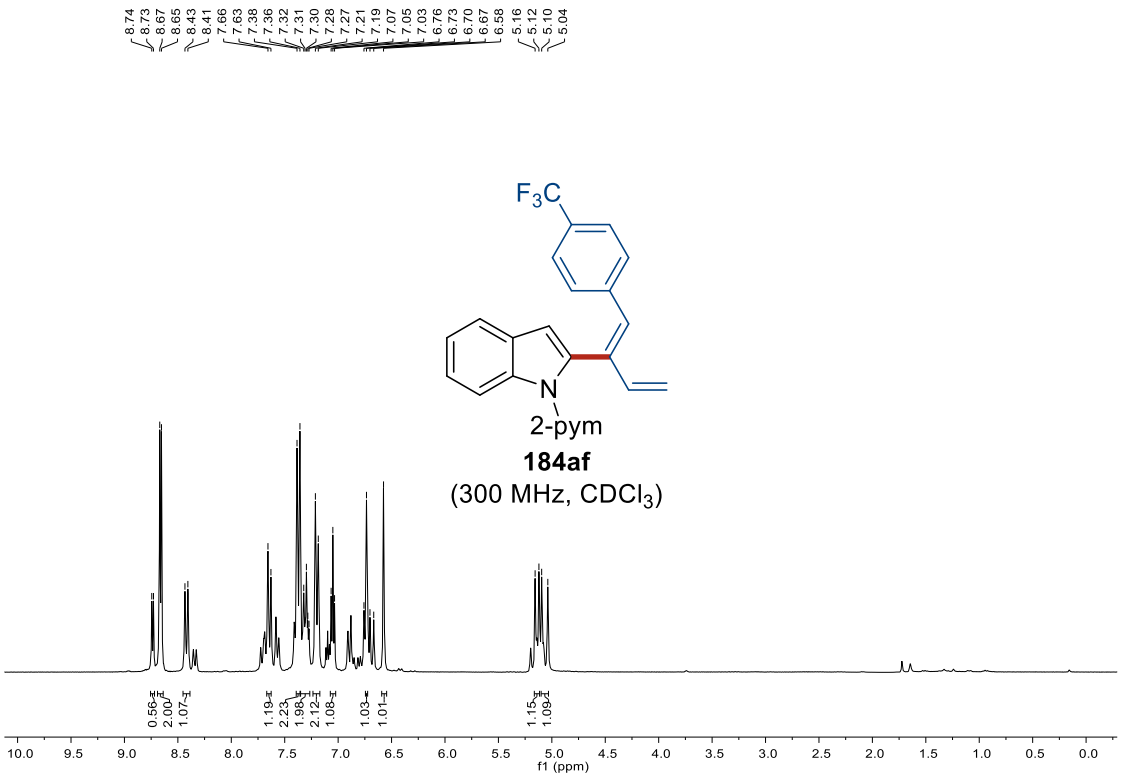

8.74
8.73
8.66
8.65
8.37
8.37
8.34
8.34
7.65
7.62
7.39
7.38
7.36
7.36
7.35
7.35
7.33
7.33
7.31
7.30
7.28
7.28
7.28
7.26
7.25
7.06
7.05
7.04
7.03
7.02
7.02
7.01
7.00
6.82
6.79
6.77
6.74
6.70
6.68
6.66
6.64
6.58
6.58
5.10
5.06
5.01
F
N
2-pym
184ad
(300 MHz, CDCl3)
0.39
2.00
1.04
1.06
1.29
1.47
3.18
2.15
0.93
1.03
1.05
1.13
f1 (ppm)

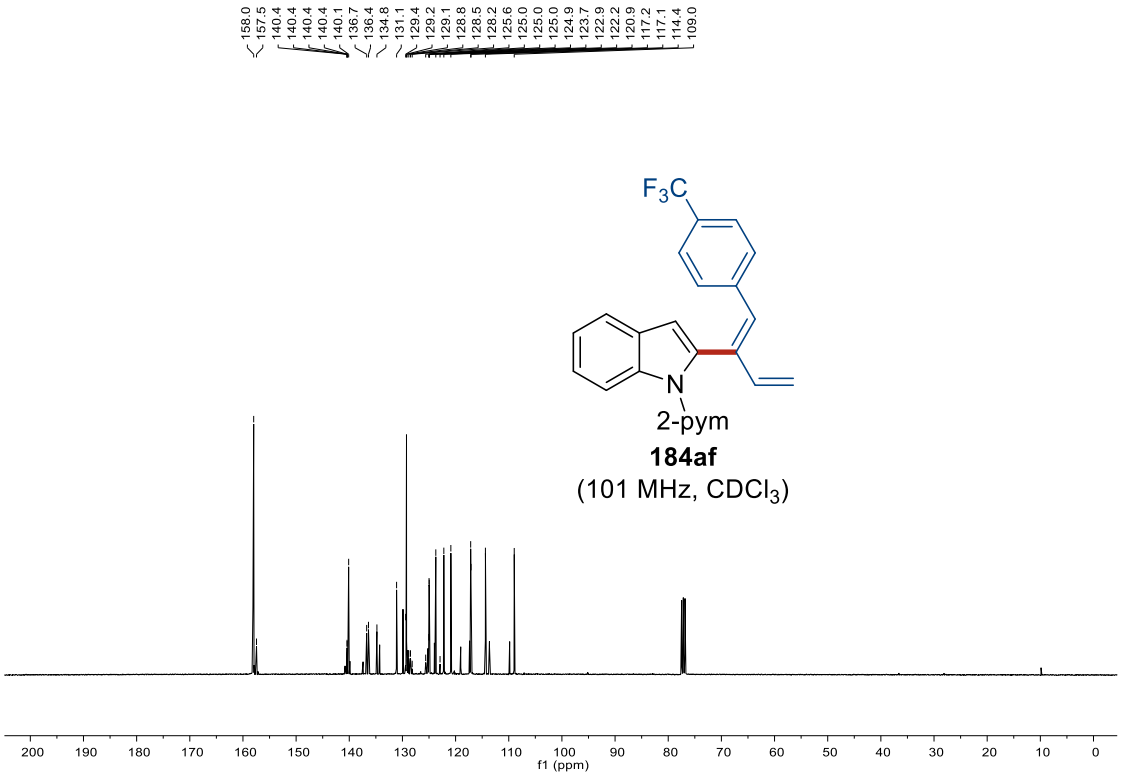

163.1
160.6
157.9
157.4
140.3
136.7
135.2
133.9
133.8
132.9
132.8
131.7
130.8
130.7
129.4
123.5
122.1
120.8
117.1
115.8
115.2
115.0
114.2
108.7
F
N
2-pym
184ad
(101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

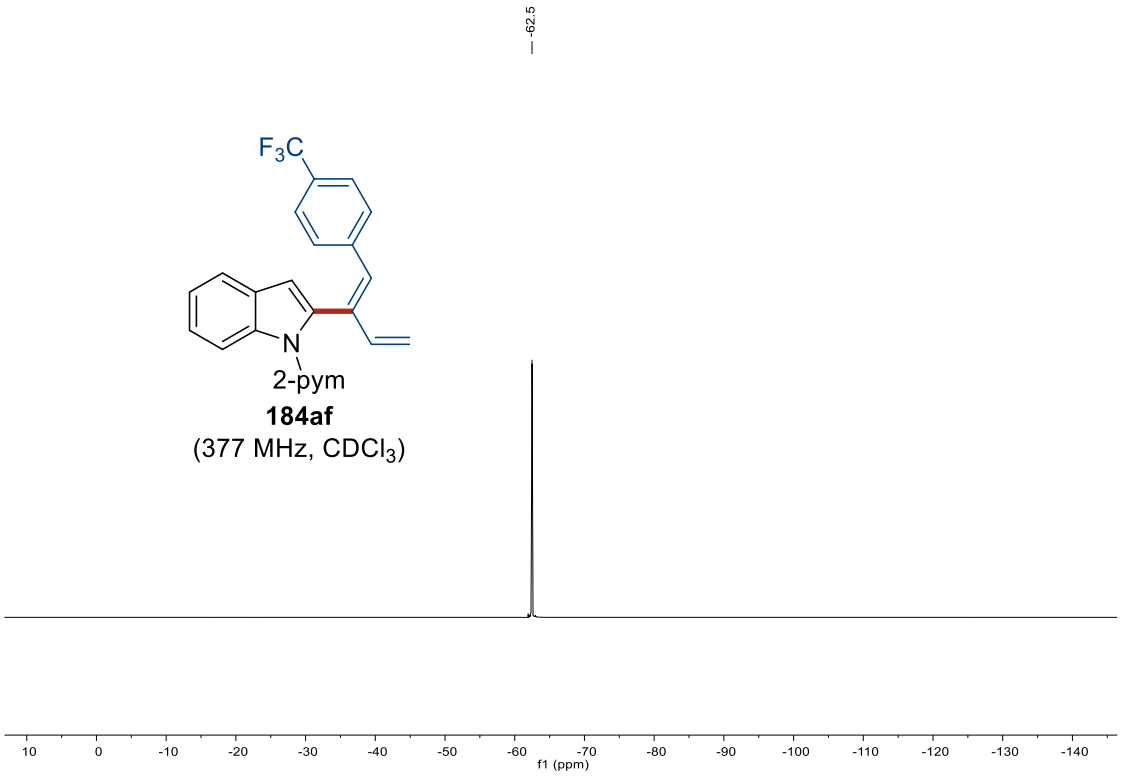

-114.1
-114.1
-114.1
-114.2
-114.2
-114.2
-114.2
F
N
2-pym
184ad
(282 MHz, CDCl3)
-50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180 -185 -190
f1 (ppm)

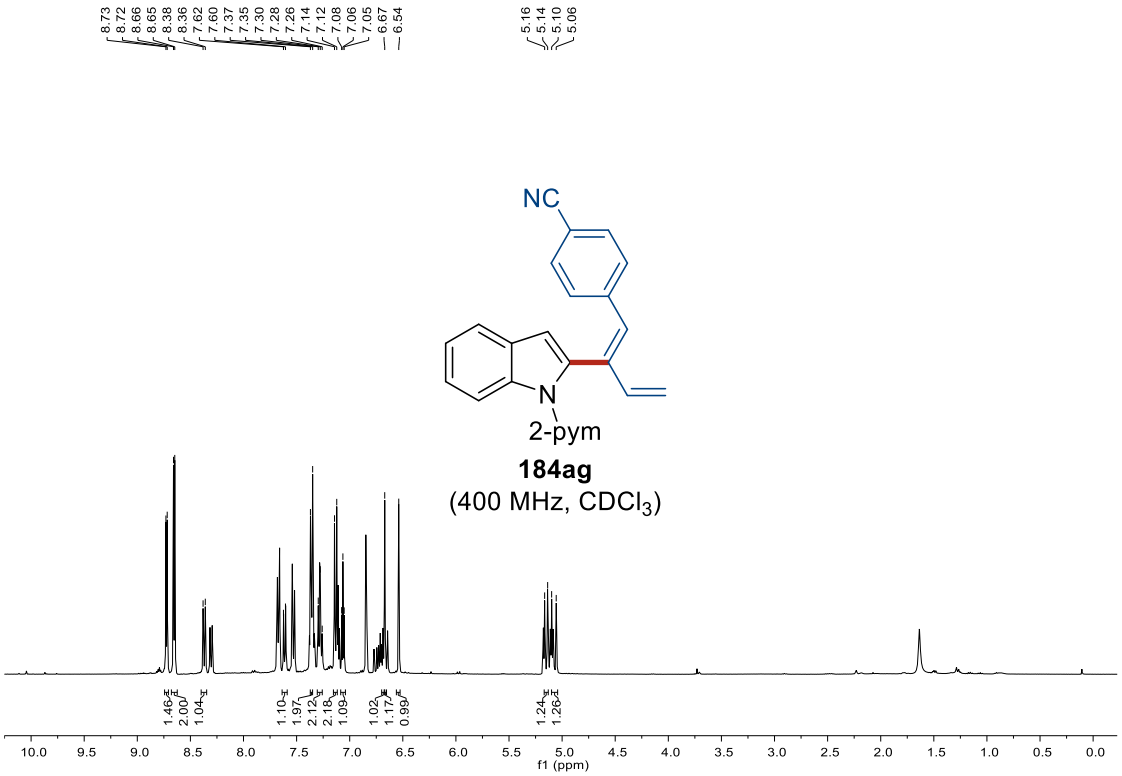

8.73
8.72
8.66
8.65
8.38
8.35
7.63
7.60
7.35
7.34
7.33
7.32
7.30
7.29
7.23
7.20
7.07
7.05
7.03
6.94
6.91
6.67
6.65
6.62
6.54
5.09
5.06
5.03
4.98
Br
N
2-pym
184ae
(300 MHz, CDCl3)
1.09
2.00
1.06
1.24
2.17
2.34
1.23
2.19
0.85
1.23
0.97
1.21
1.32
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

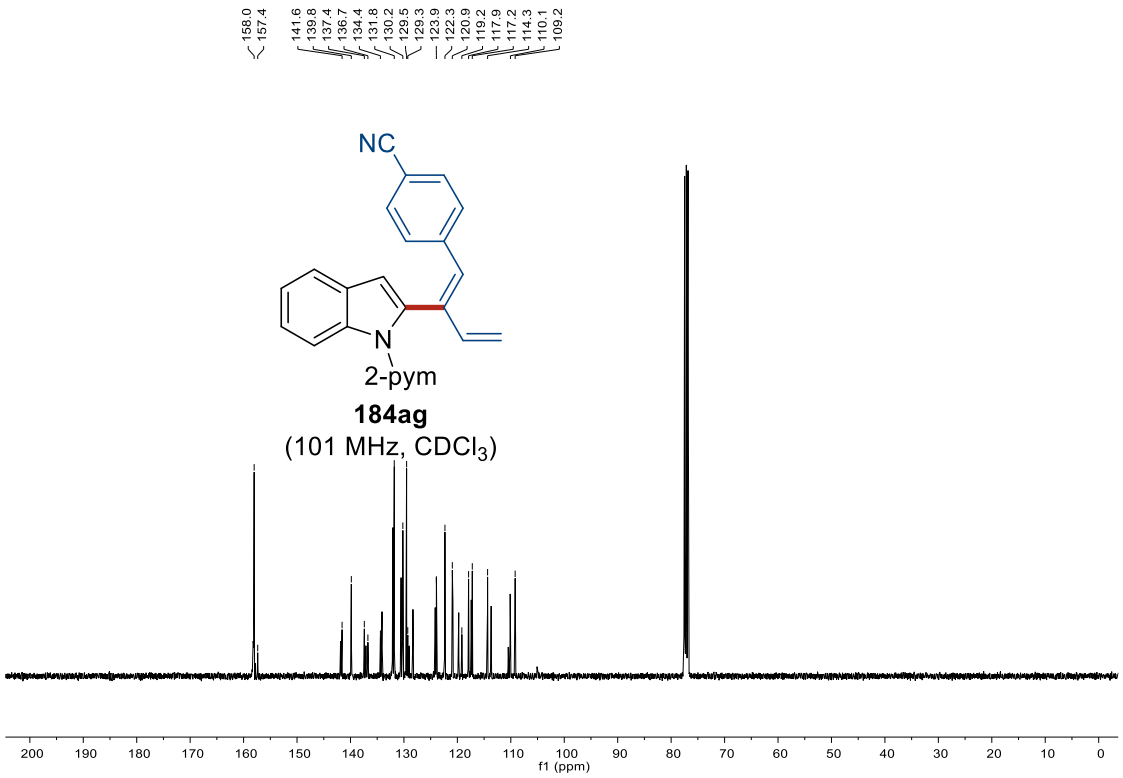

158.0
157.4
140.3
140.2
136.7
135.7
134.9
131.6
131.2
130.6
129.4
123.6
122.1
121.1
120.8
117.2
116.3
114.3
108.7
Br
N
2-pym
184ae
(126 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

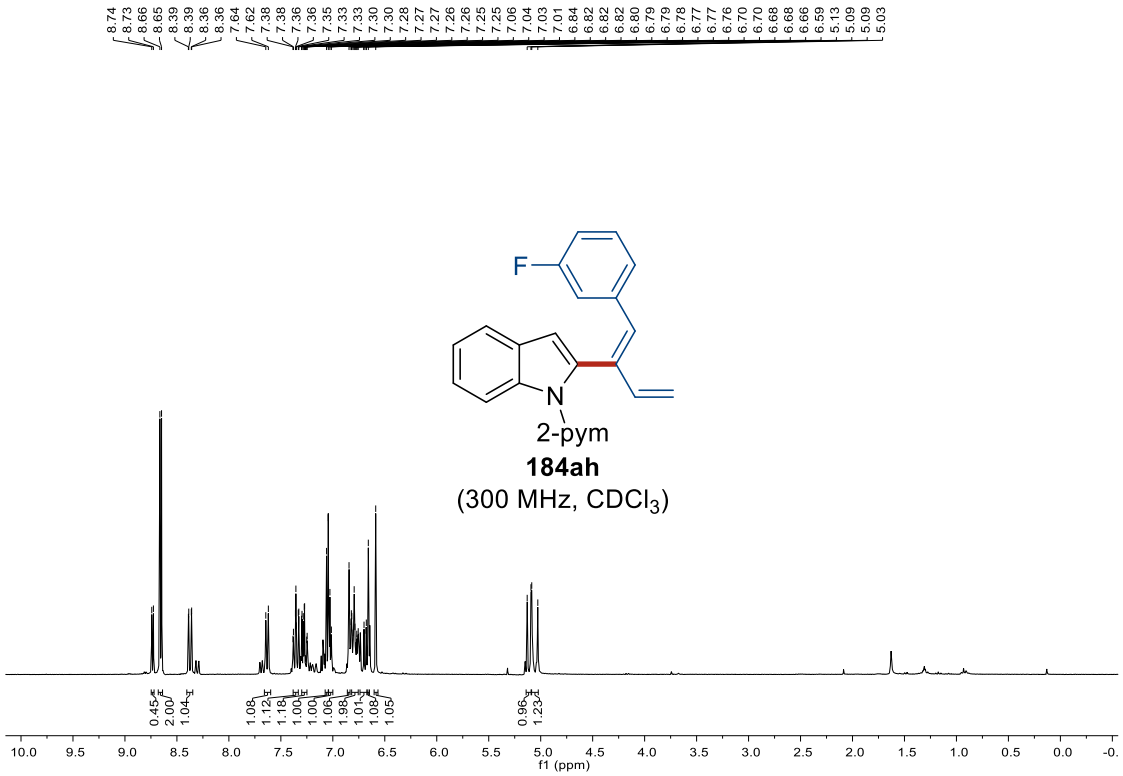

8.74
8.73
8.67
8.65
8.43
8.41
7.66
7.63
7.38
7.36
7.32
7.31
7.30
7.28
7.27
7.21
7.19
7.07
7.05
7.03
6.76
6.73
6.70
6.67
6.58
5.16
5.12
5.10
5.04
F3C
N
2-pym
184af
(300 MHz, CDCl3)
0.56
2.00
1.07
1.19
2.23
1.98
2.12
1.08
1.03
1.01
1.15
1.09
f1 (ppm)

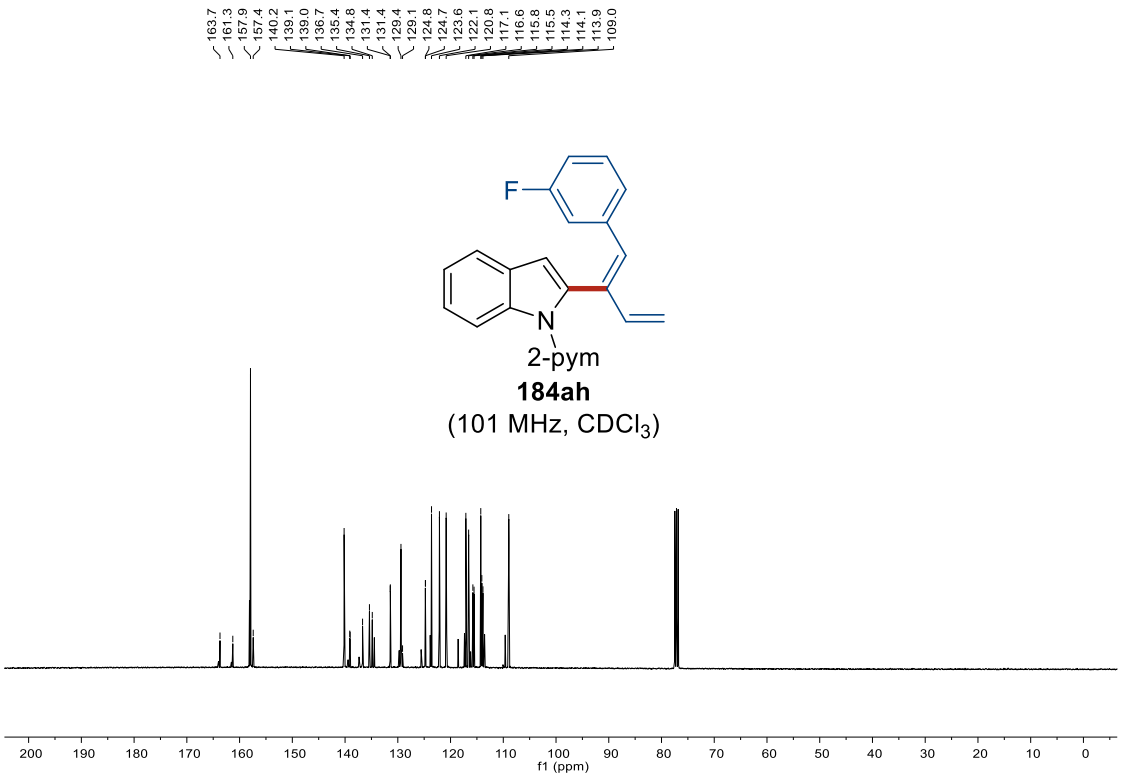

158.0
157.5
140.4
140.4
140.4
140.4
140.1
136.7
136.4
134.8
131.1
129.4
129.2
129.1
128.8
128.5
128.2
125.6
125.0
125.0
125.0
124.9
123.7
122.9
122.2
120.9
117.2
117.1
114.4
109.0
F3C
N
2-pym
184af
(101 MHz, CDCl3)
f1 (ppm)

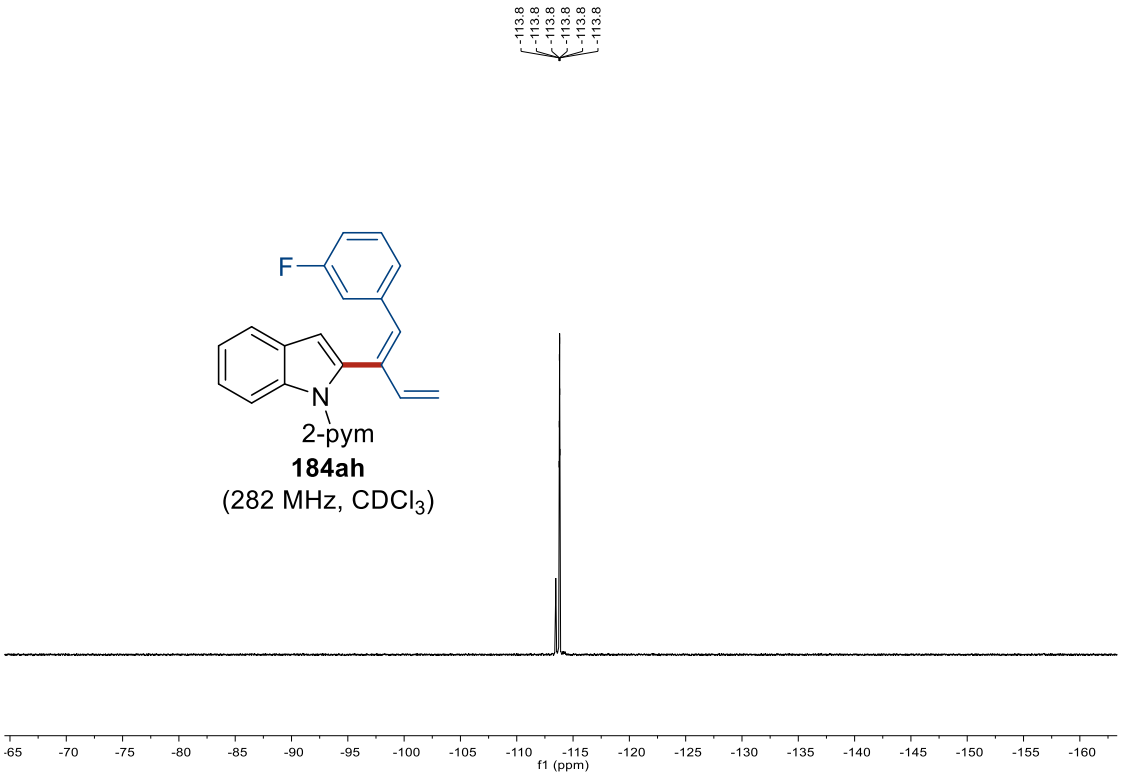

-62.5
F3C
N
2-pym
184af
(377 MHz, CDCl3)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140
f1 (ppm)

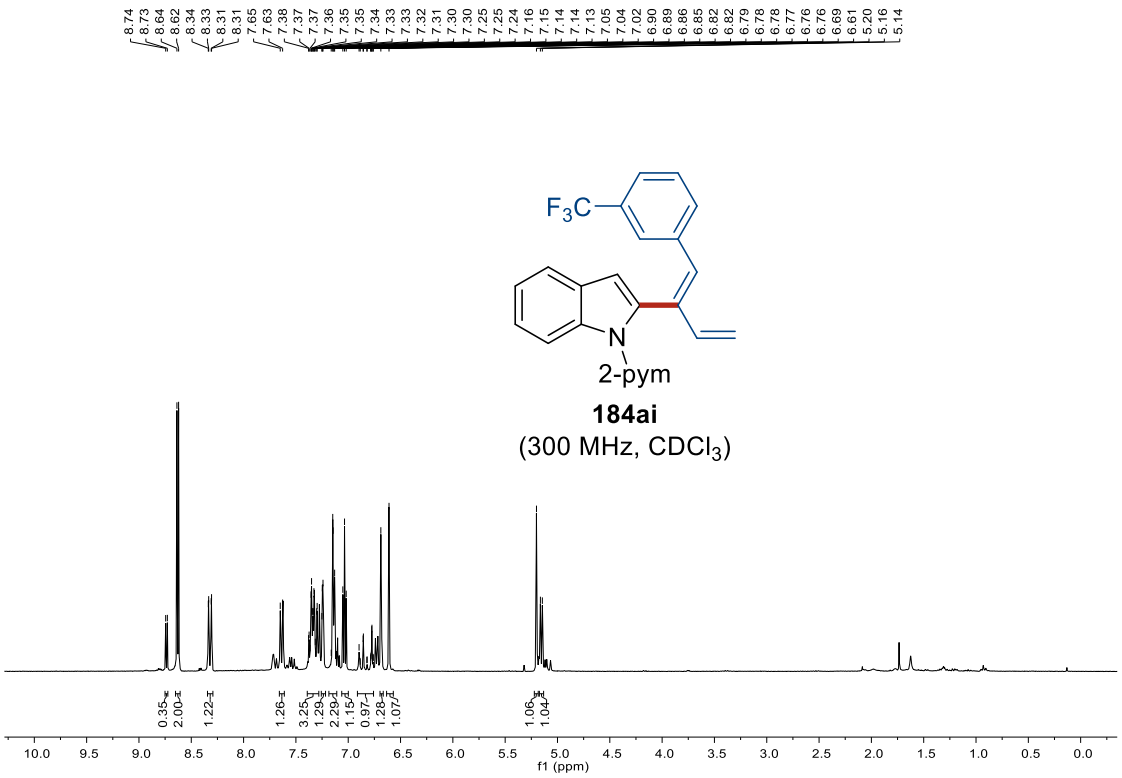

8.73 8.72 8.66 8.65 8.38 8.36 7.62 7.60 7.37 7.35 7.30 7.28 7.26 7.14 7.12 7.08 7.06 7.05 6.67 6.54
5.16 5.14 5.10 5.06
NC
N
2-pym
184ag
(400 MHz, CDCl3)
1.46 2.00 1.04 1.10 1.97 2.12 2.18 1.09 1.02 1.17 0.99 1.24 1.26
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

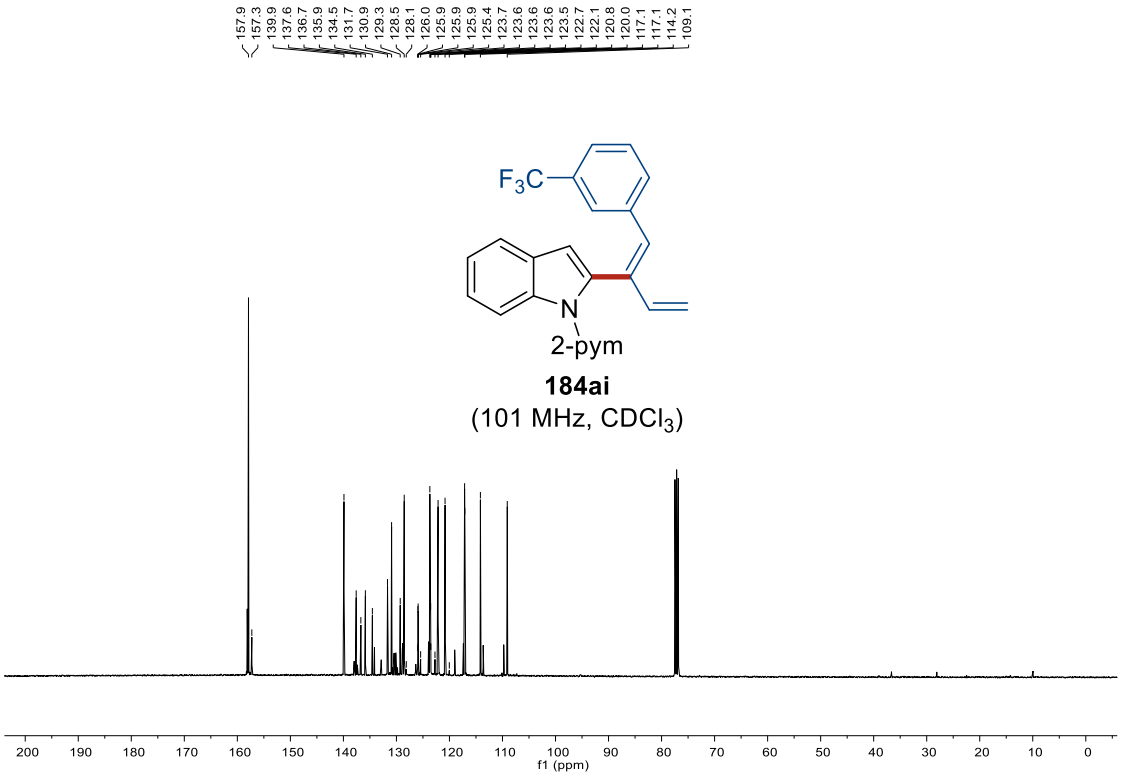

158.0
157.4
141.6
139.8
137.4
136.7
134.4
131.8
130.2
129.5
129.3
123.9
122.3
120.9
119.2
117.9
117.2
114.3
110.1
109.2
NC
N
2-pym
184ag
(101 MHz, CDCl3)
f1 (ppm)

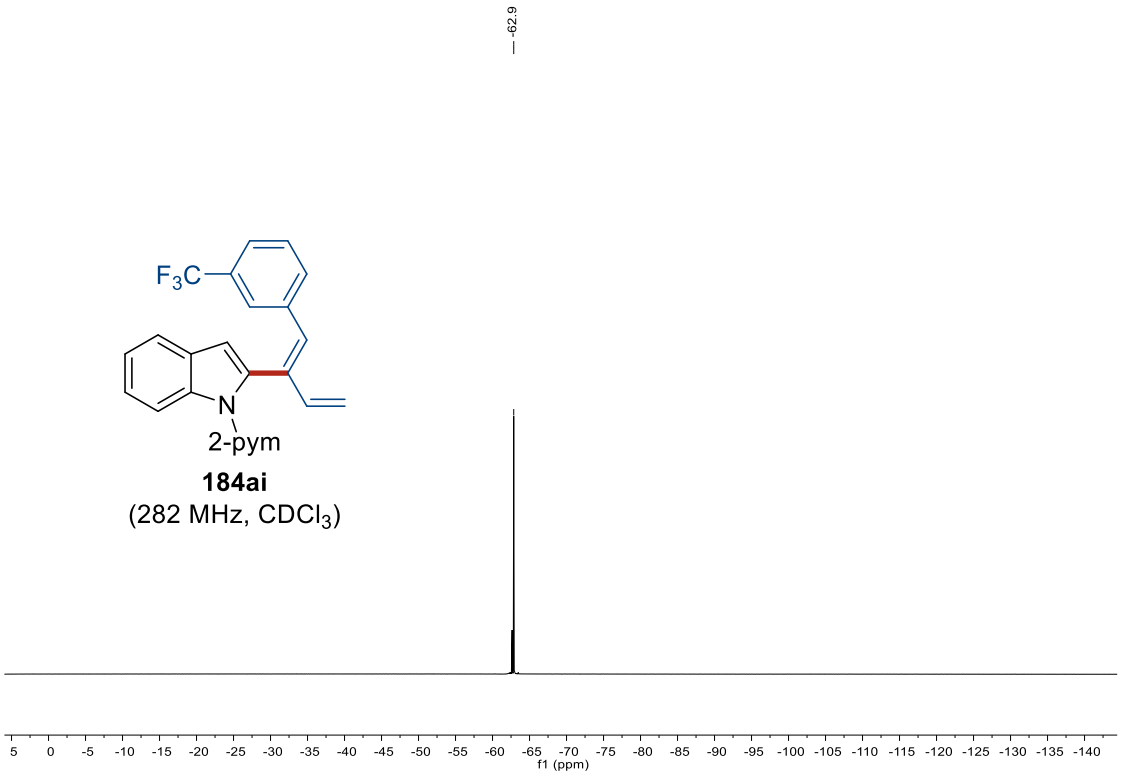

8.74
8.73
8.66
8.65
8.39
8.39
8.36
8.36
7.64
7.62
7.38
7.38
7.36
7.36
7.35
7.33
7.33
7.30
7.30
7.28
7.27
7.27
7.26
7.26
7.25
7.25
7.06
7.04
7.03
7.01
6.84
6.82
6.82
6.82
6.80
6.79
6.79
6.78
6.77
6.77
6.76
6.70
6.70
6.68
6.68
6.66
6.59
5.13
5.09
5.09
5.03
F
N
2-pym
184ah
(300 MHz, CDCl3)
0.45
2.00
1.04
1.08
1.12
1.18
1.00
1.00
1.06
1.98
1.01
1.08
1.05
0.96
1.23
f1 (ppm)

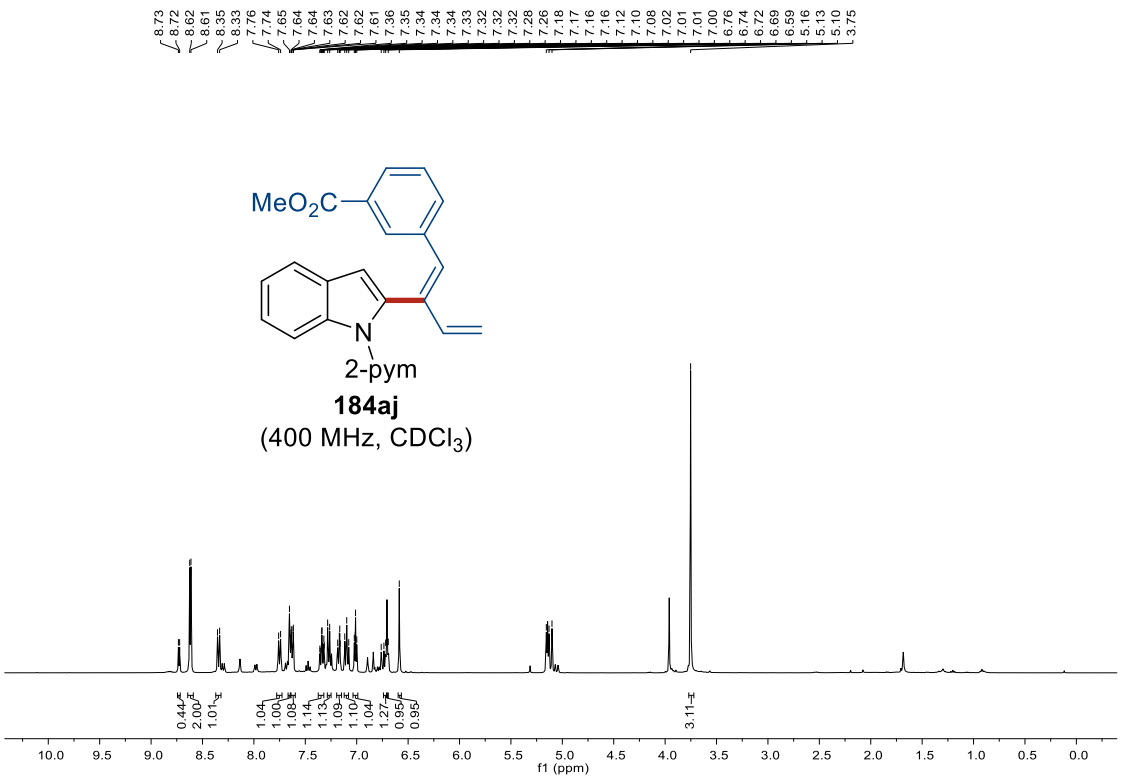

163.7
161.3
157.9
157.4
140.2
139.1
139.0
136.7
135.4
134.8
131.4
131.4
129.4
129.1
124.8
124.7
123.6
122.1
120.8
117.1
116.6
115.8
115.5
114.3
114.1
113.9
109.0
F
N
2-pym
184ah
(101 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

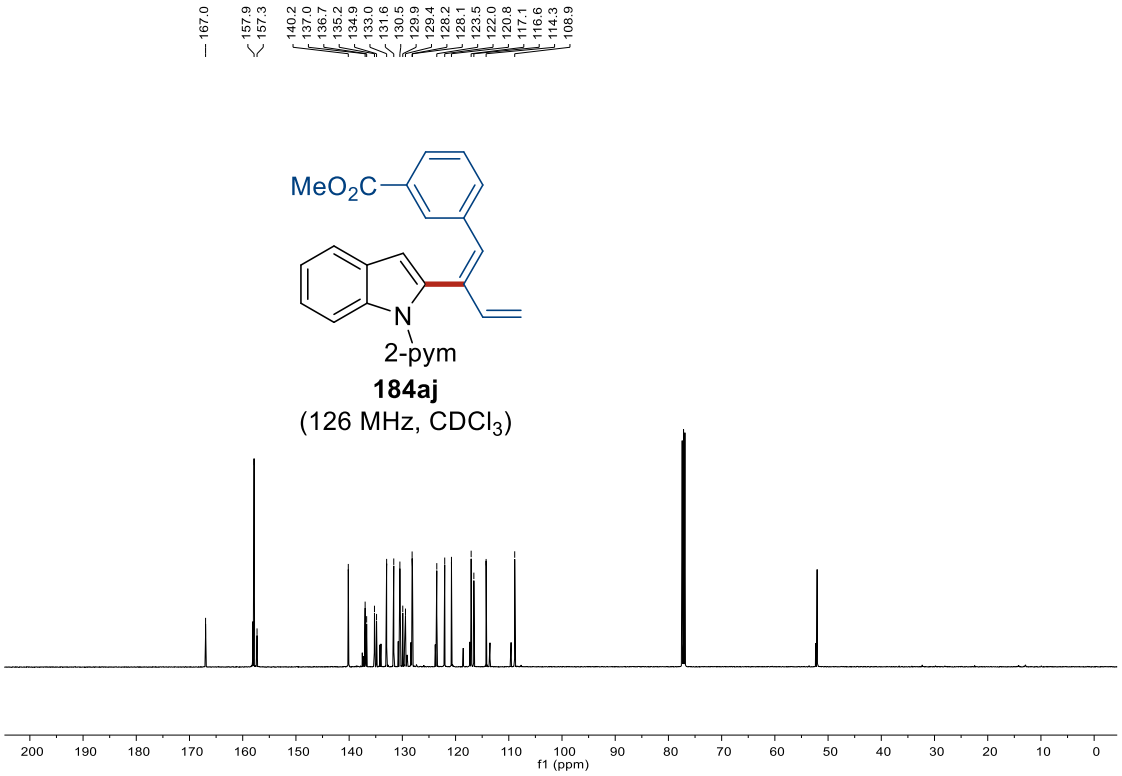

-113.8
-113.8
-113.8
-113.8
-113.8
-113.8
F
N
2-pym
184ah
(282 MHz, CDCl3)
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
f1 (ppm)


8.74 8.73 8.64 8.62 8.34 8.33 8.31 8.31 7.65 7.63 7.38 7.37 7.37 7.36 7.35 7.35 7.34 7.33 7.33 7.32 7.31 7.30 7.30 7.25 7.25 7.24 7.16 7.15 7.14 7.14 7.13 7.05 7.04 7.02 6.90 6.89 6.86 6.85 6.82 6.82 6.79 6.78 6.78 6.77 6.76 6.76 6.69 6.61 5.20 5.16 5.14
F3C
N
2-pym
184ai
(300 MHz, CDCl3)
0.35 2.00 1.22 1.26 3.25 1.29 2.29 1.15 0.97 1.28 1.07 1.06 1.04
10.0 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
f1 (ppm)


157.9 157.3 139.9 137.6 136.7 135.9 134.5 131.7 130.9 129.3 128.5 128.1 126.0 125.9 125.9 125.9 125.4 123.7 123.6 123.6 123.6 123.5 122.7 122.1 120.8 120.0 117.1 117.1 114.2 109.1
F3C
N
2-pym
184ai
(101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

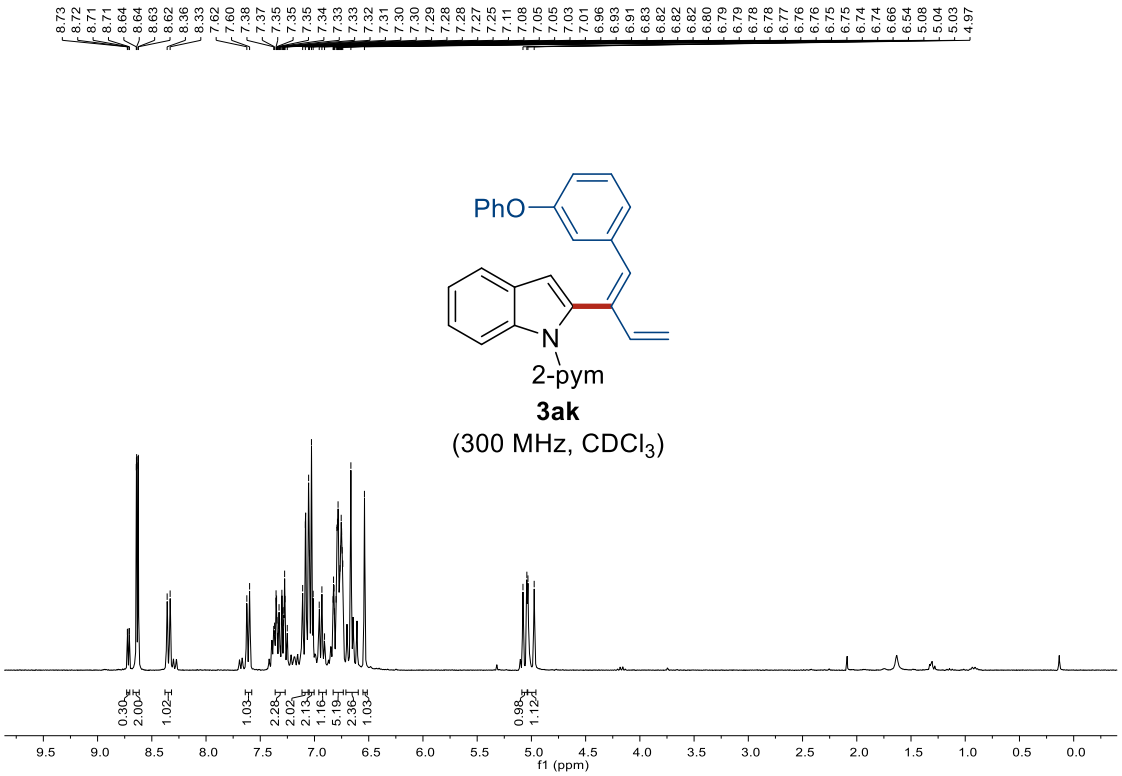

-62.9
F3C
N
2-pym
184ai
(282 MHz, CDCl3)
f1 (ppm)


MeO2C
N
2-pym
184aj
(400 MHz, CDCl3)
f1 (ppm)



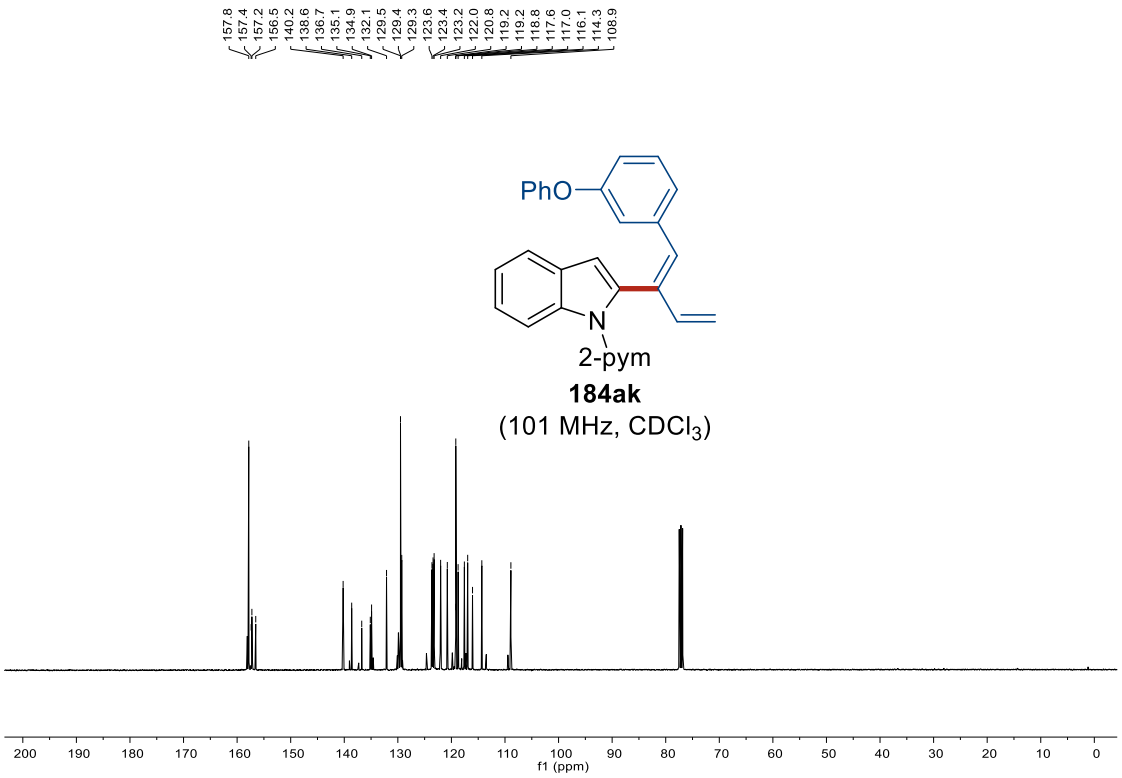
184aj

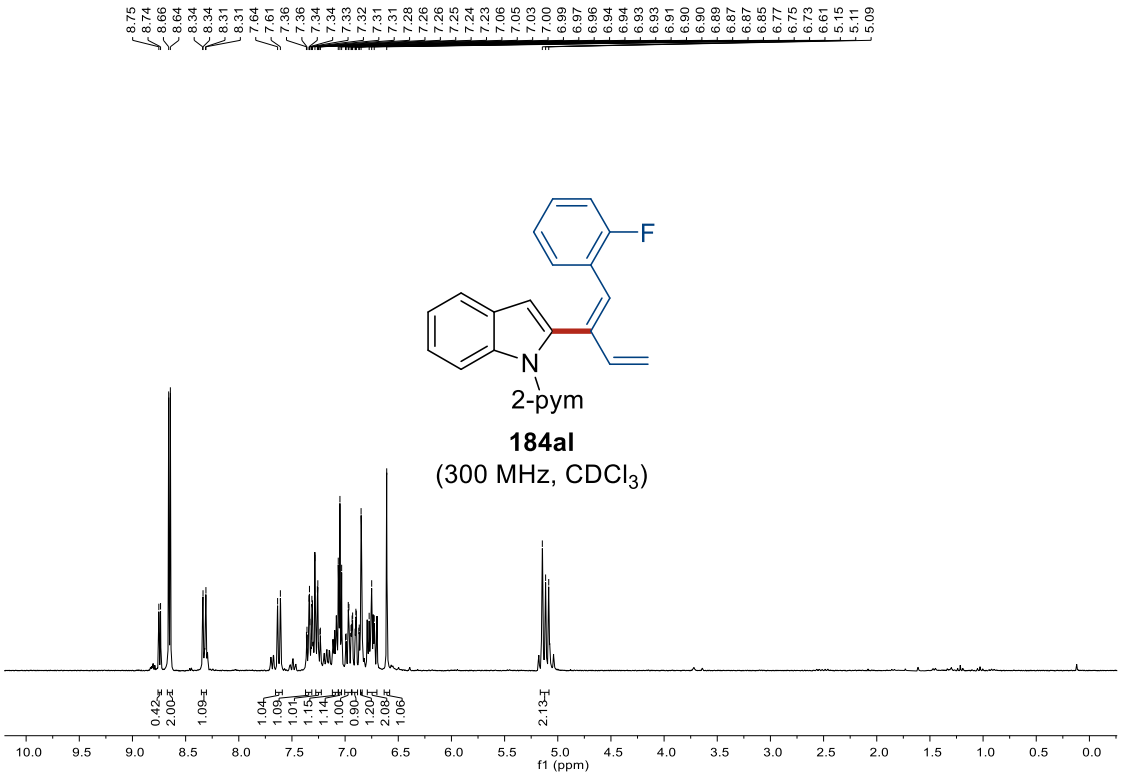
(126 MHz, $CDCl_3$)

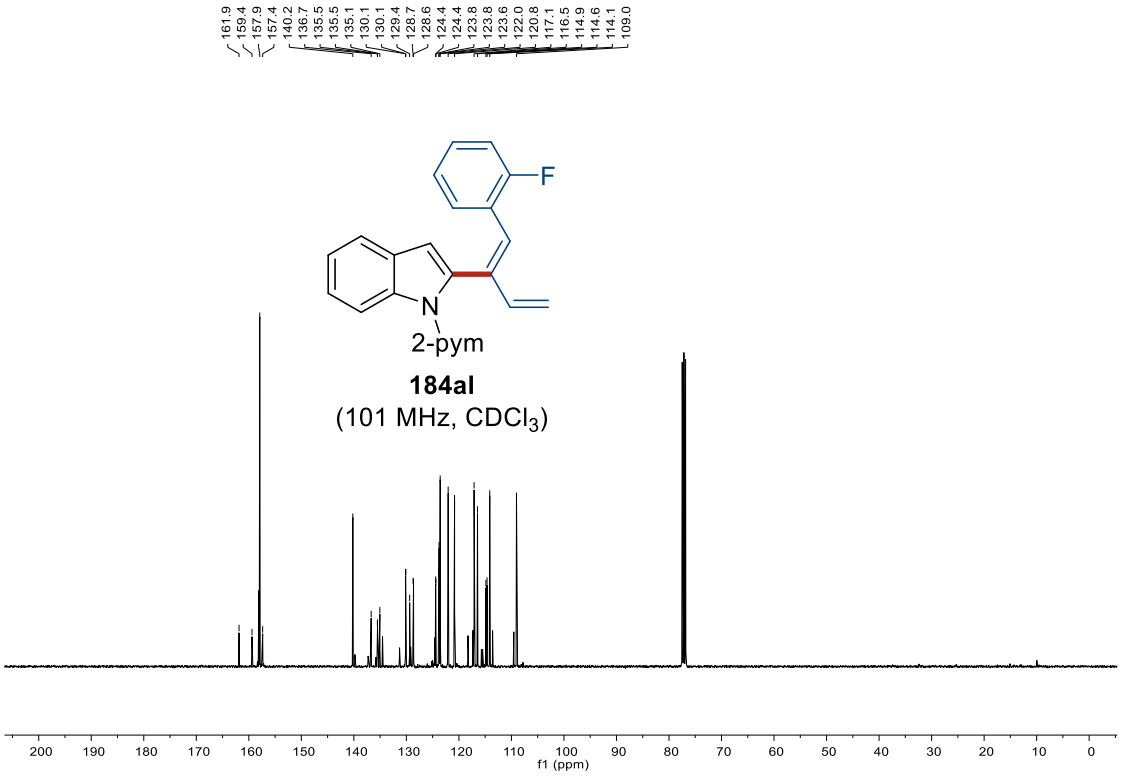


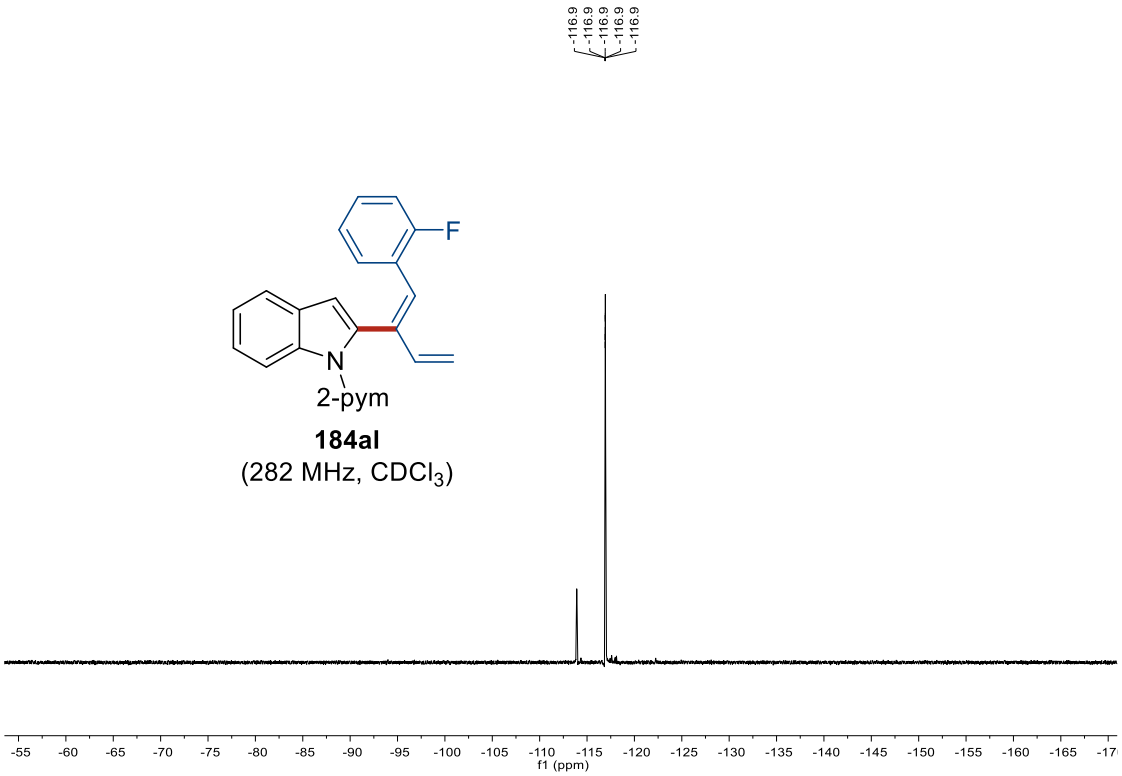
3ak

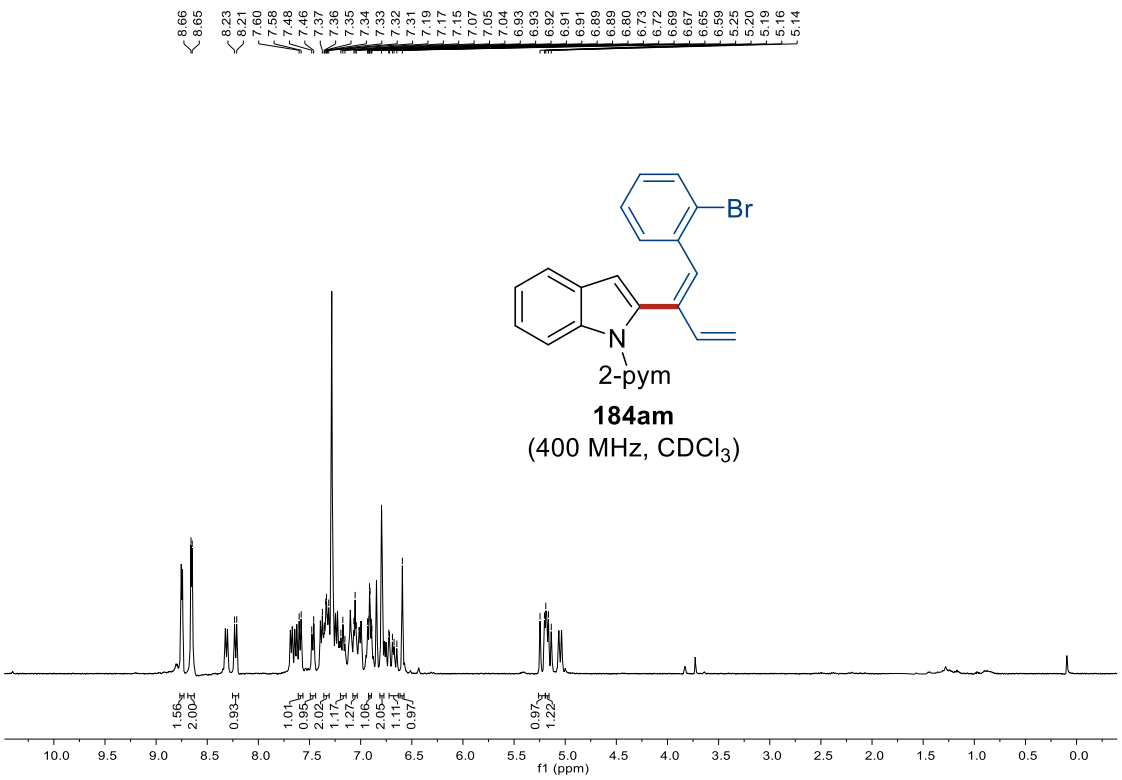
(300 MHz, $CDCl_3$)

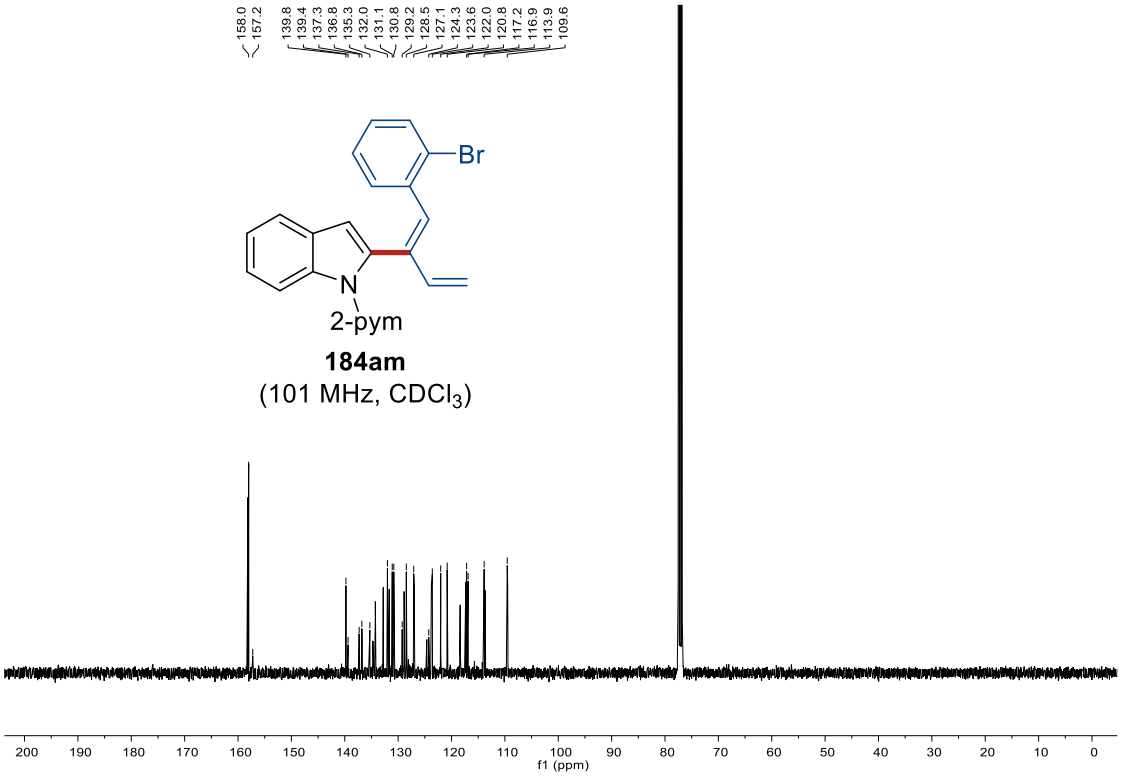

157.8
157.4
157.2
156.5
140.2
138.6
136.7
135.1
134.9
132.1
129.5
129.4
129.3
123.6
123.4
123.2
122.0
120.8
119.2
119.2
118.8
117.6
117.0
116.1
114.3
108.9
PhO
N
2-pym
184ak
(101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

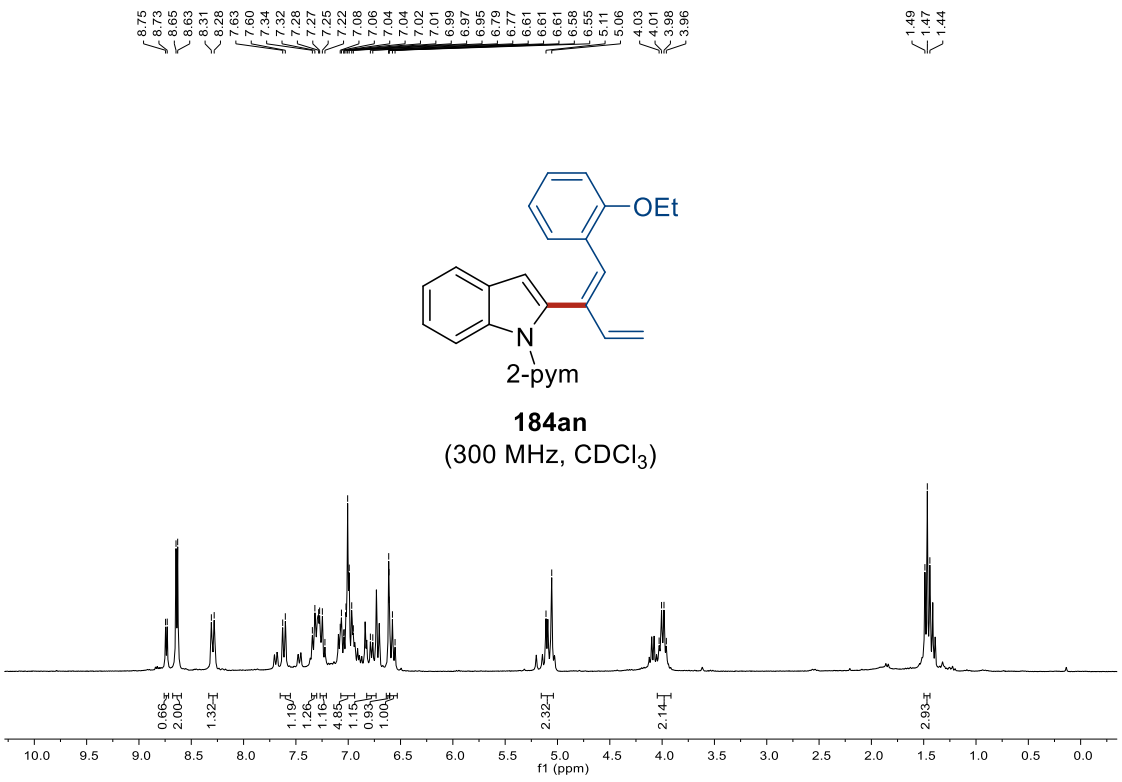

8.75
8.74
8.66
8.64
8.34
8.34
8.31
8.31
7.64
7.61
7.36
7.36
7.34
7.34
7.33
7.32
7.31
7.31
7.28
7.26
7.26
7.25
7.24
7.23
7.06
7.05
7.03
7.00
6.99
6.97
6.96
6.94
6.94
6.93
6.93
6.91
6.90
6.90
6.89
6.87
6.87
6.85
6.77
6.75
6.73
6.61
5.15
5.11
5.09
F
N
2-pym
184al
(300 MHz, CDCl3)
0.42
2.00
1.09
1.04
1.09
1.01
1.15
1.14
1.00
0.90
1.20
2.08
1.06
2.13
10.0 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
f1 (ppm)


161.9
159.4
157.9
157.4
140.2
136.7
135.5
135.5
135.1
130.1
129.4
128.7
128.6
124.4
124.4
123.8
123.8
123.6
122.0
120.8
117.1
116.5
114.9
114.6
114.1
109.0
F
N
2-pym
184al
(101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

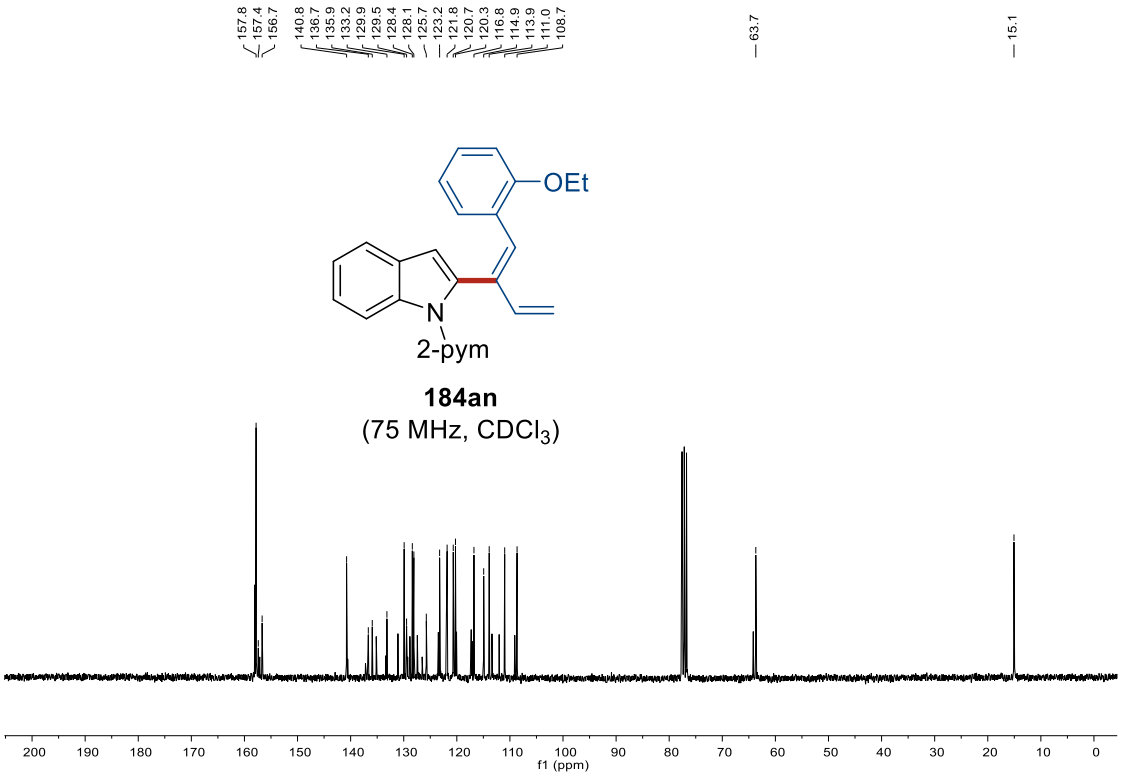

-116.9
-116.9
-116.9
-116.9
-116.9
F
N
2-pym
184al
(282 MHz, CDCl3)
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -17
f1 (ppm)


8.66
8.65
8.23
8.21
7.60
7.58
7.48
7.46
7.37
7.36
7.35
7.34
7.33
7.32
7.31
7.19
7.17
7.15
7.07
7.05
7.04
6.93
6.93
6.92
6.91
6.91
6.89
6.89
6.80
6.73
6.72
6.69
6.67
6.65
6.59
5.25
5.20
5.19
5.16
5.14
Br
N
2-pym
184am
(400 MHz, CDCl3)
1.56
2.00
0.93
1.01
0.95
2.02
1.17
1.27
1.06
2.05
1.11
0.97
0.97
1.22
10.0 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
f1 (ppm)

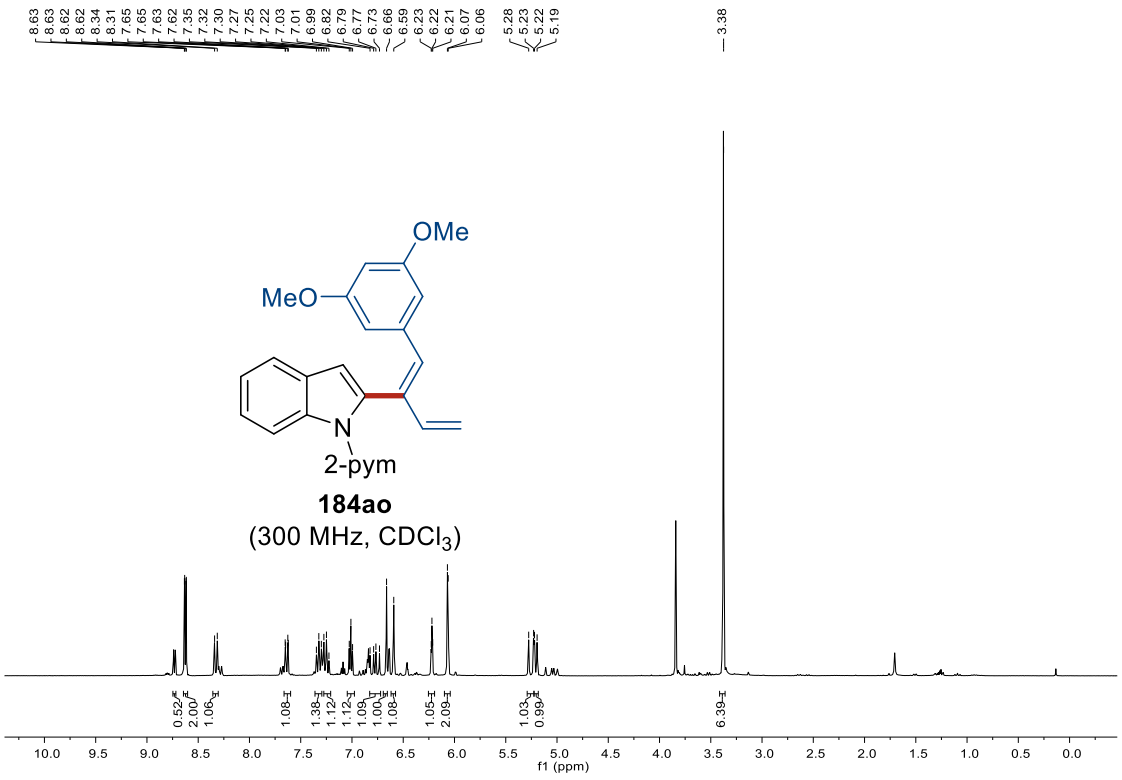

158.0
157.2
139.8
139.4
137.3
136.8
135.3
132.0
131.1
130.8
129.2
128.5
127.1
124.3
123.6
122.0
120.8
117.2
116.9
113.9
109.6
Br
N
2-pym
184am
(101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

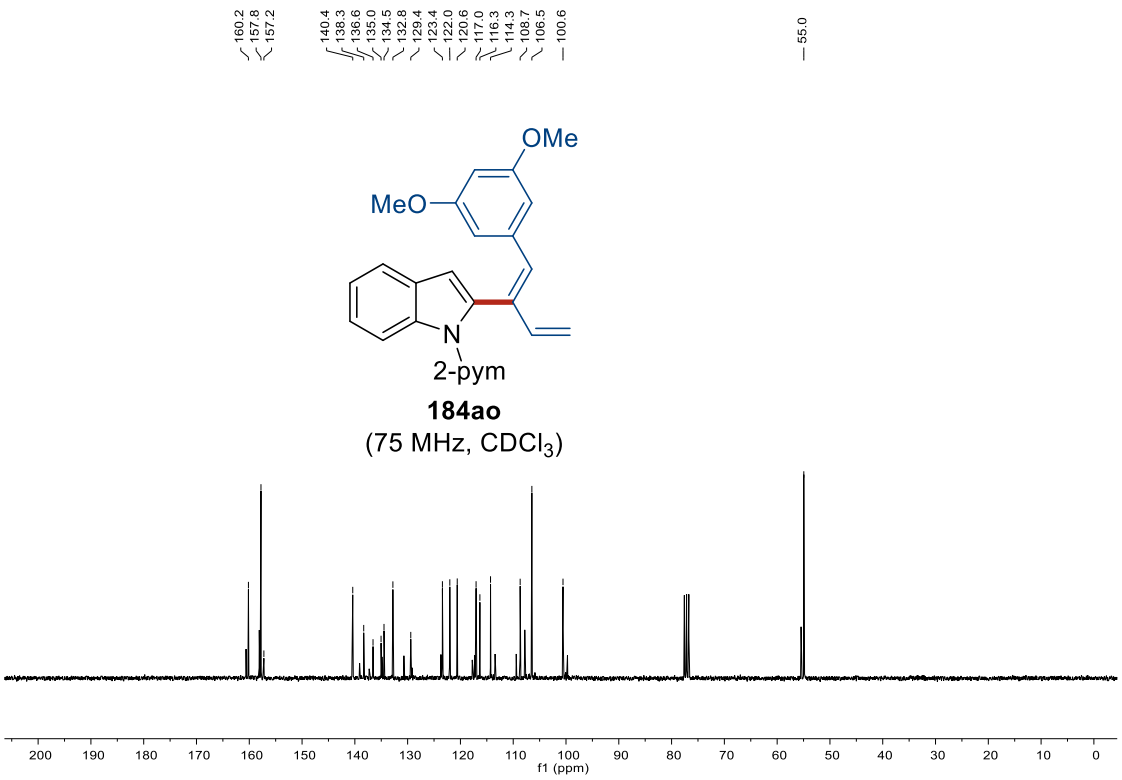


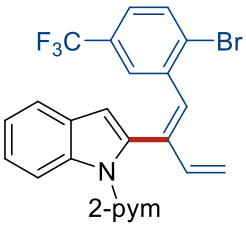
184an
(300 MHz, $CDCl_3$)



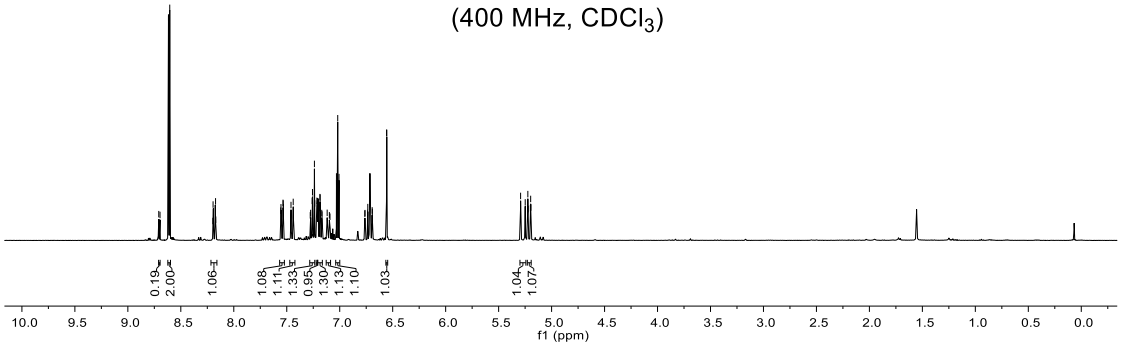
184an
(75 MHz, $CDCl_3$)

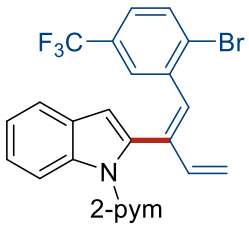

8.63
8.63
8.62
8.62
8.34
8.31
7.65
7.65
7.63
7.62
7.35
7.32
7.30
7.27
7.25
7.22
7.03
7.01
6.99
6.82
6.79
6.77
6.73
6.66
6.59
6.23
6.22
6.21
6.07
6.06
5.28
5.23
5.22
5.19
3.38
OMe
MeO
N
2-pym
184ao
(300 MHz, CDCl3)
0.52
2.00
1.06
1.08
1.38
1.12
1.12
1.09
1.00
1.08
1.05
2.09
1.03
0.99
6.39
f1 (ppm)


160.2
157.8
157.2
140.4
138.3
136.6
135.0
134.5
132.8
129.4
123.4
122.0
120.6
117.0
116.3
114.3
108.7
106.5
100.6
55.0
OMe
MeO
N
2-pym
184ao
(75 MHz, CDCl3)
f1 (ppm)

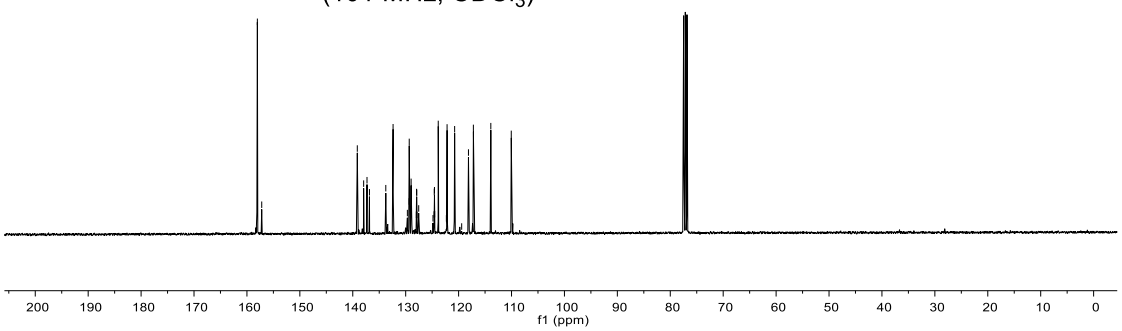


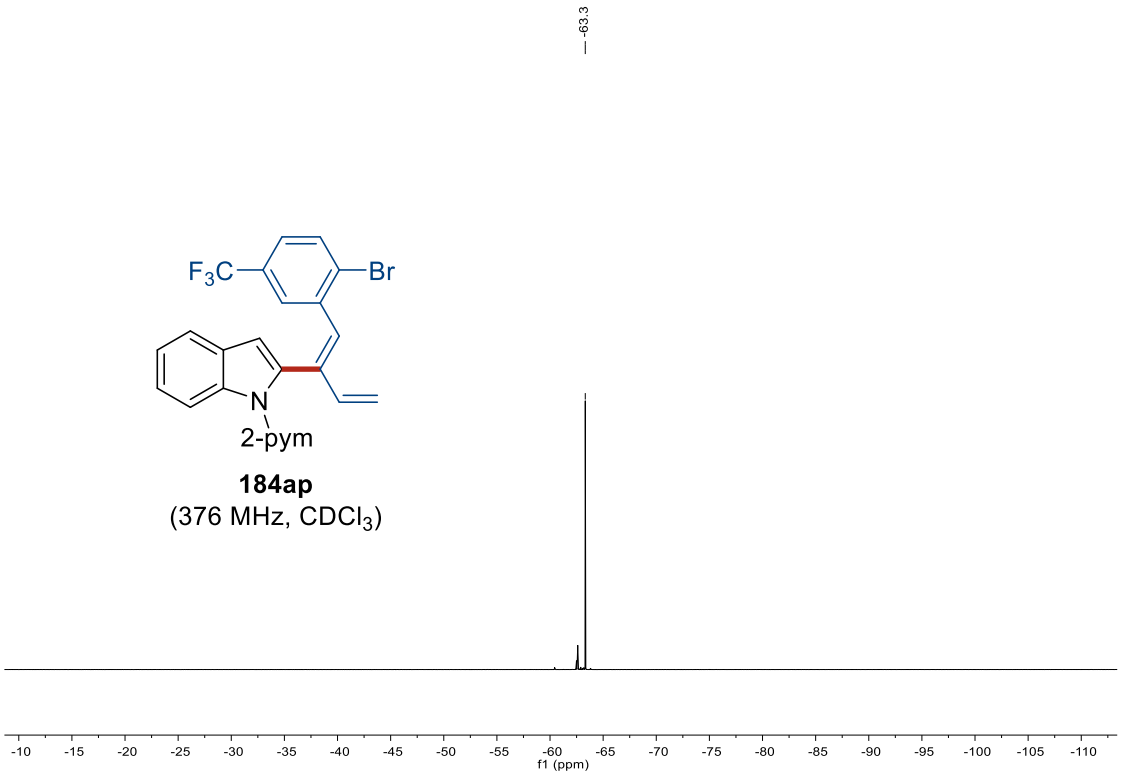
184ap
(400 MHz, $CDCl_3$)



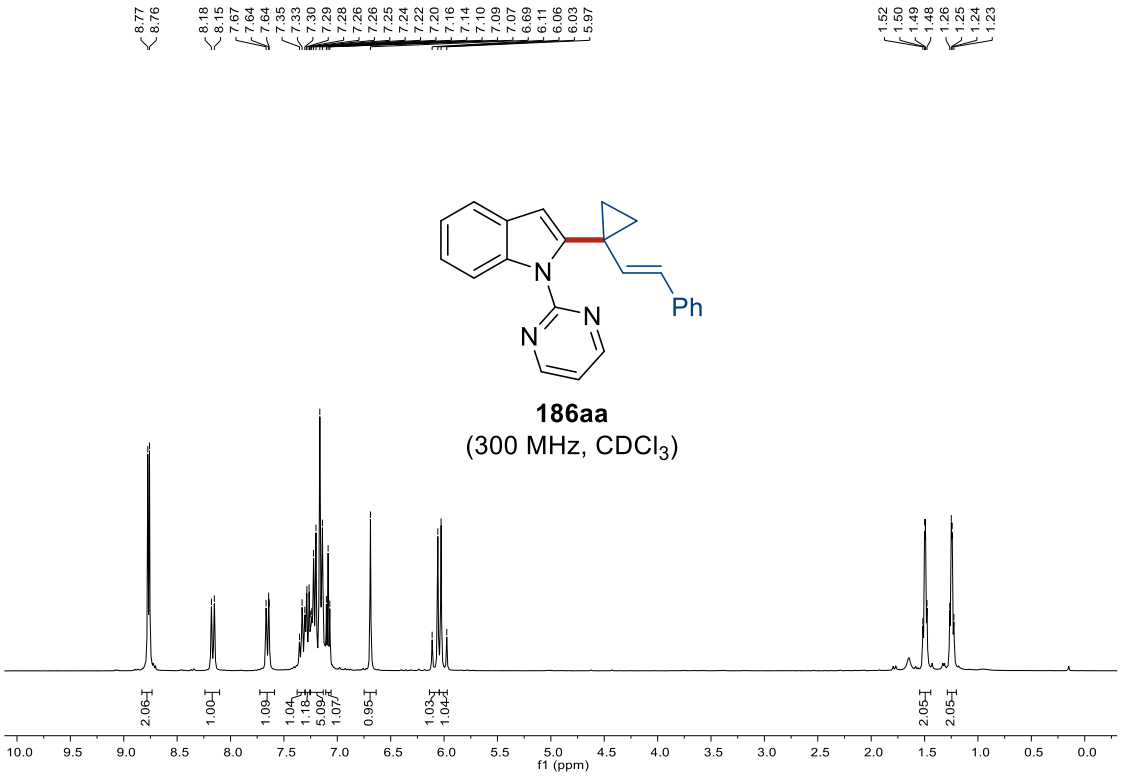


184ap
(101 MHz, $CDCl_3$)

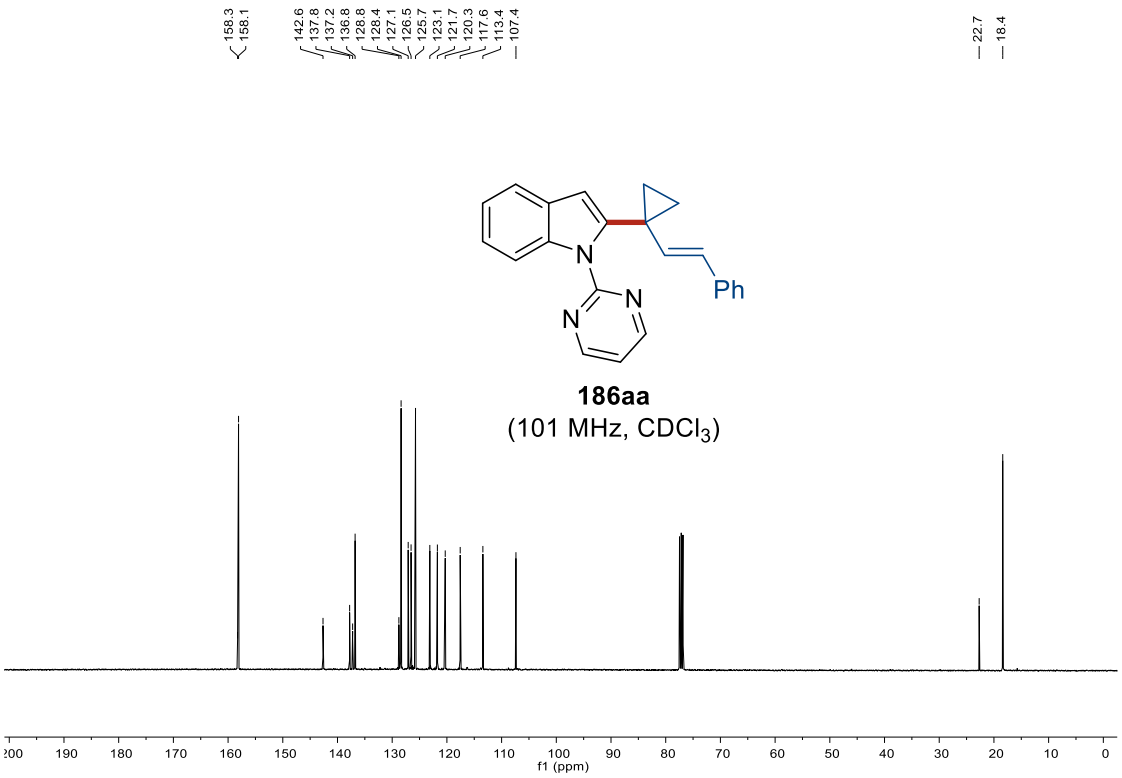




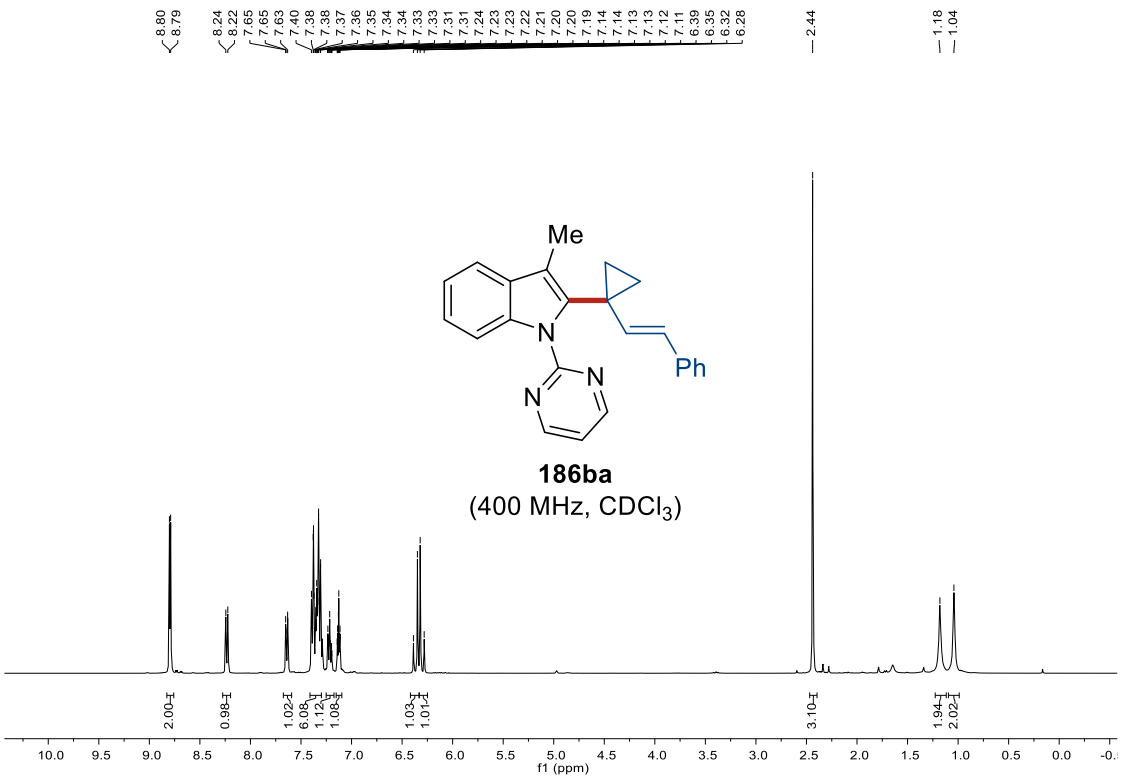
184ap
(376 MHz, $CDCl_3$)



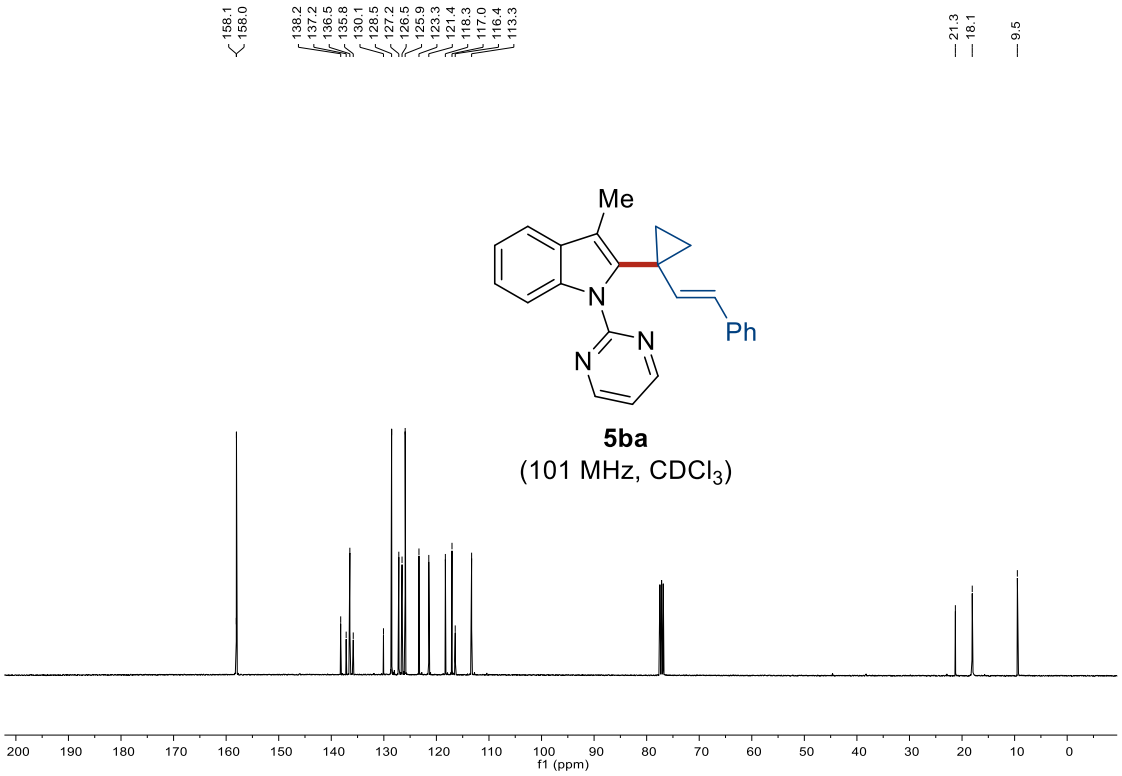
186aa
(300 MHz, $CDCl_3$)



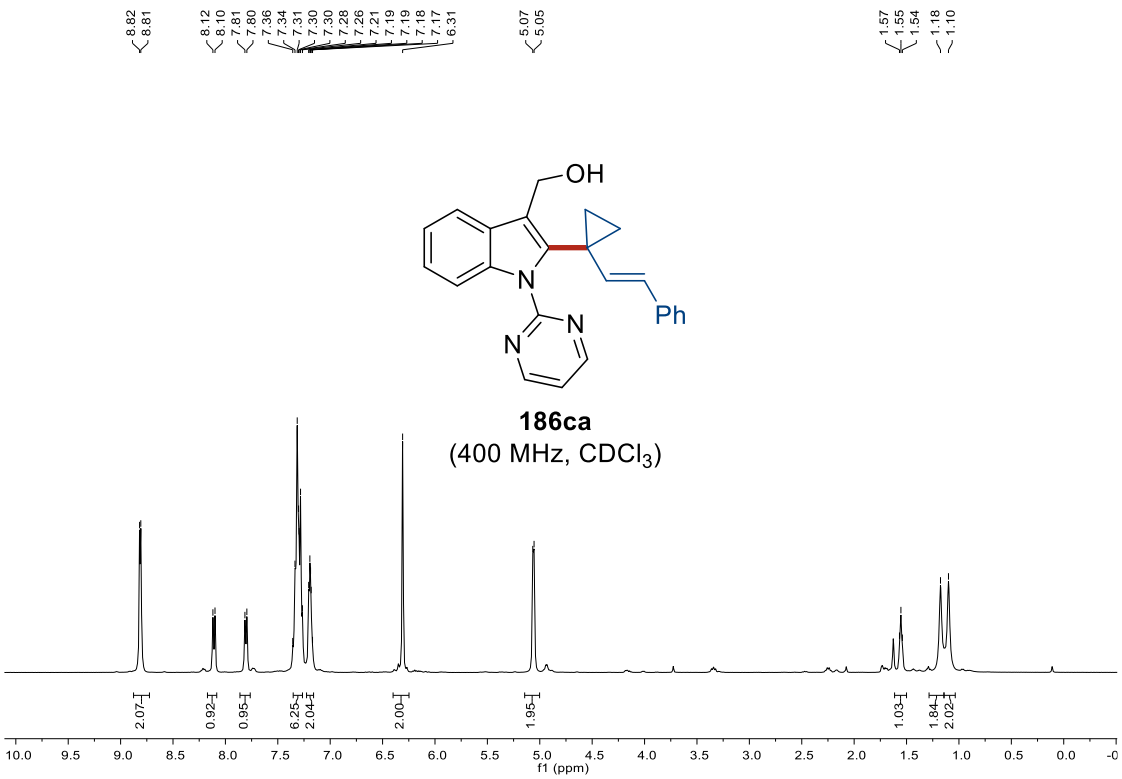
186aa
(101 MHz, $CDCl_3$)



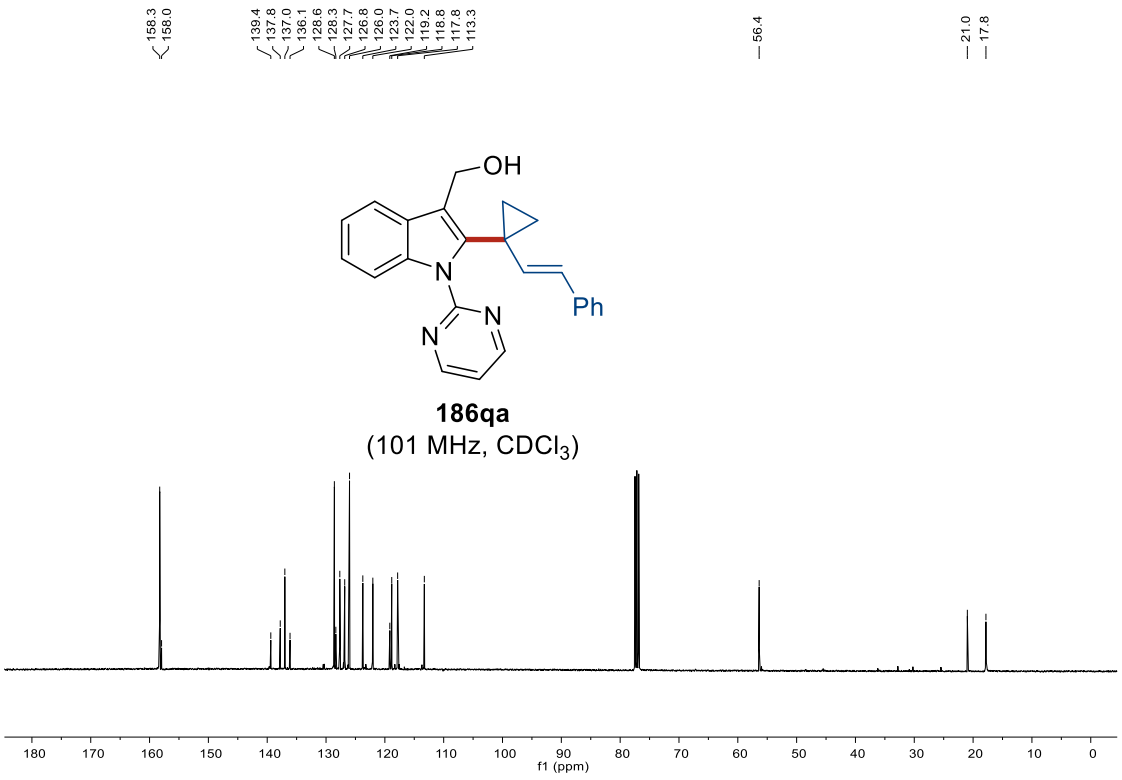
186ba
(400 MHz, $CDCl_3$)



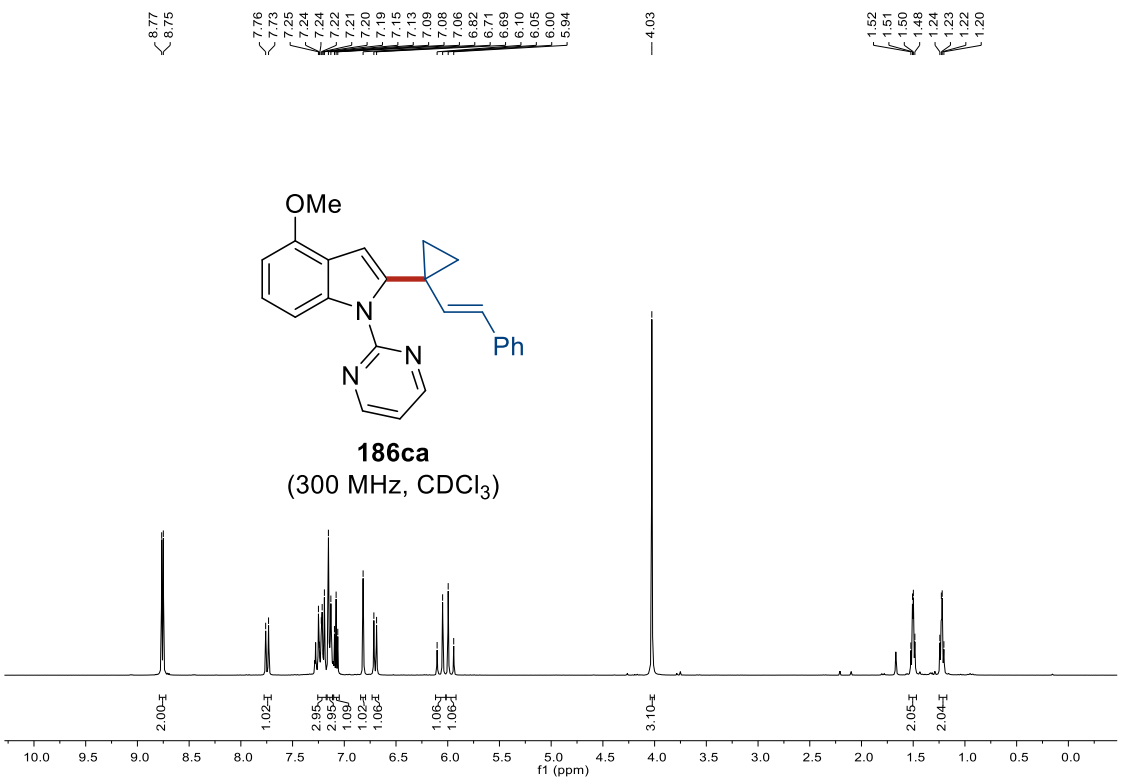
5ba
(101 MHz, $CDCl_3$)



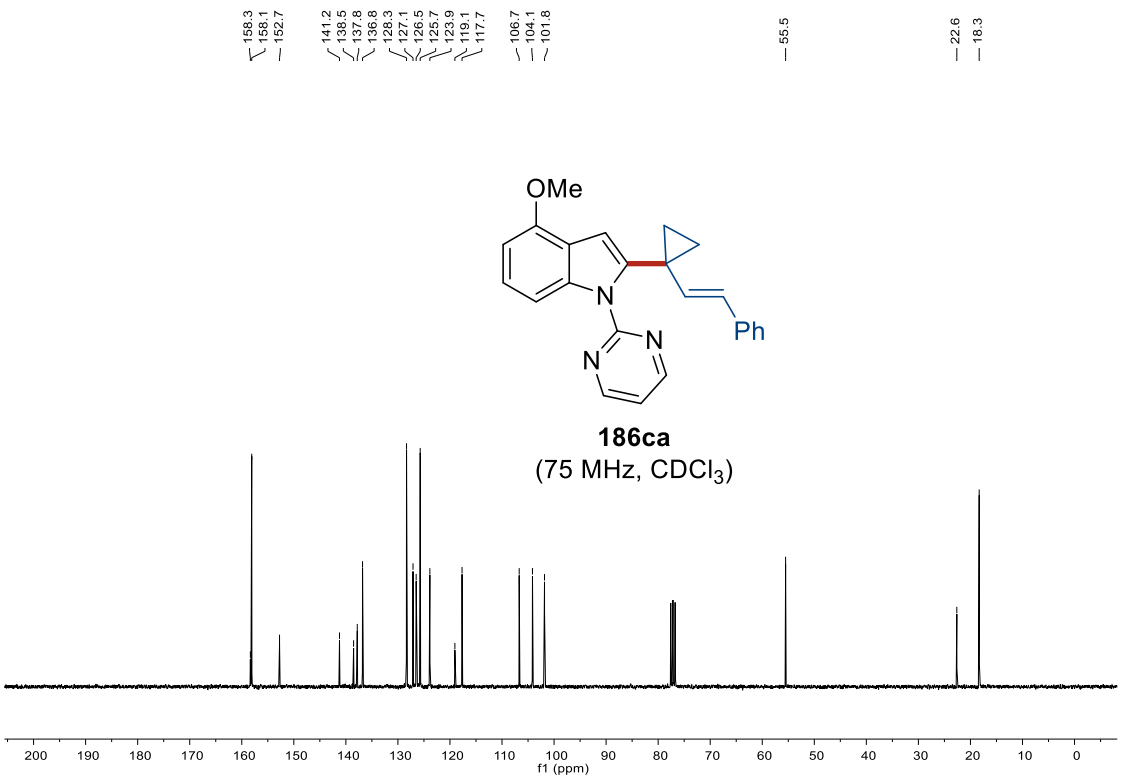
186ca
(400 MHz, $CDCl_3$)



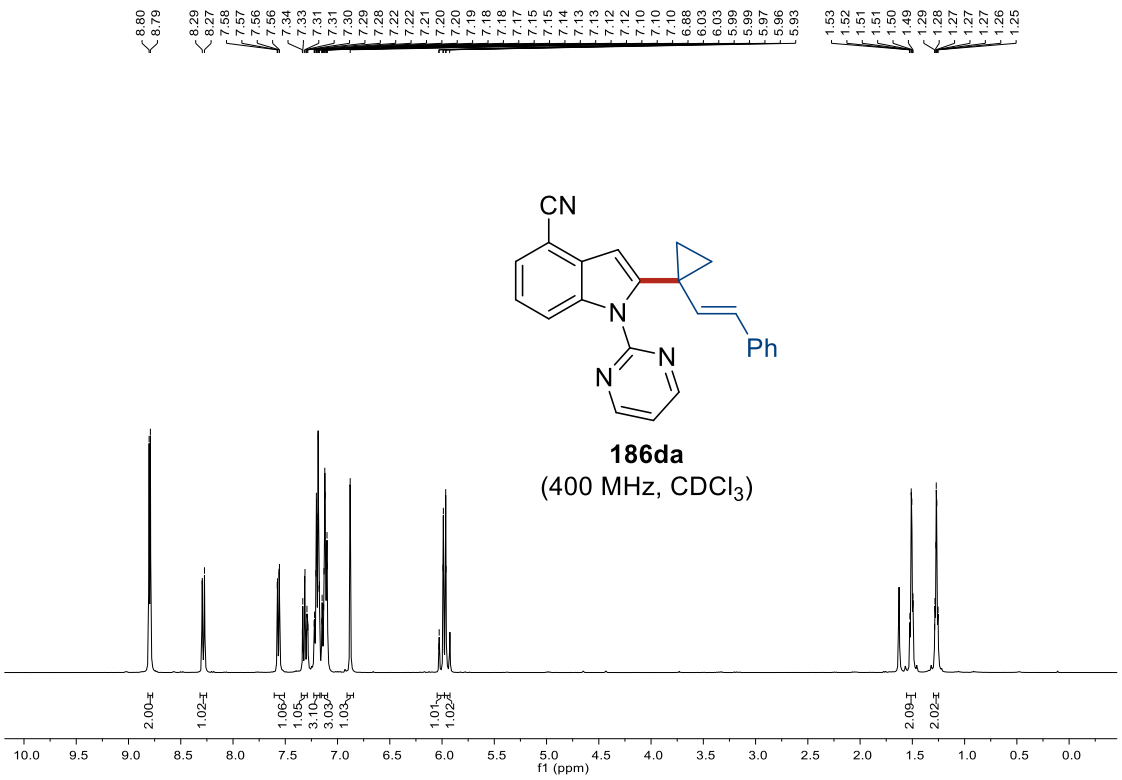
186qa
(101 MHz, $CDCl_3$)



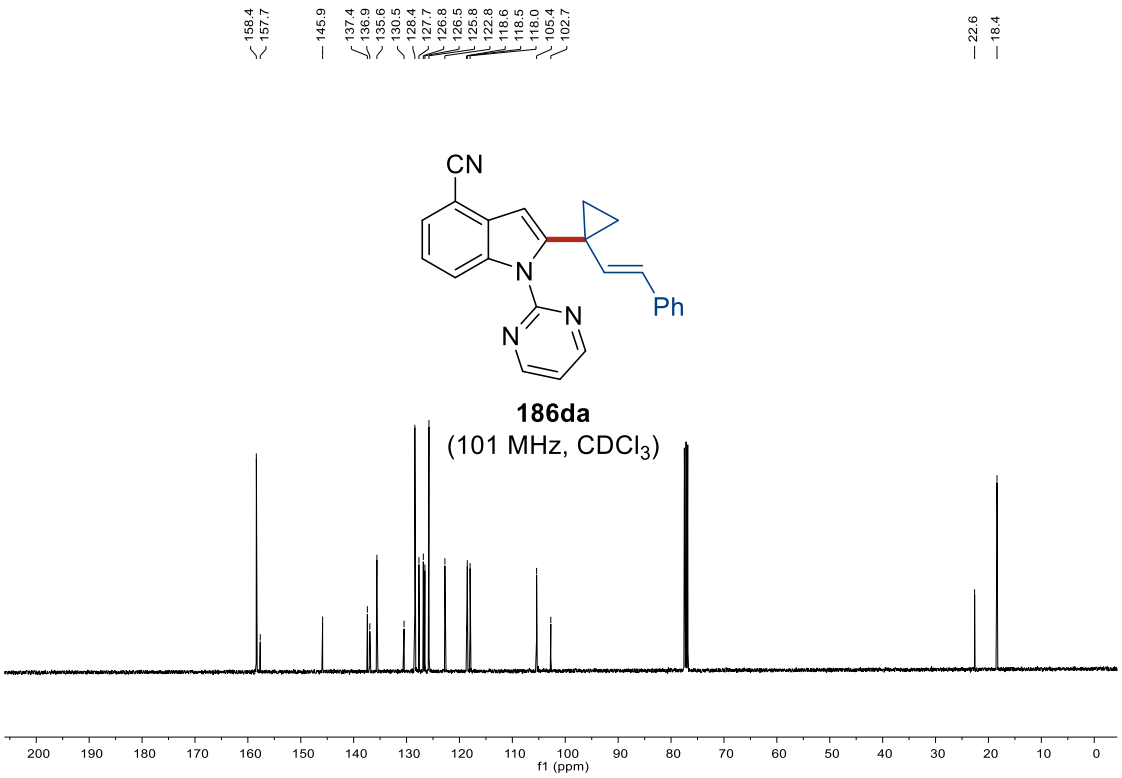
186ca
(300 MHz, $CDCl_3$)



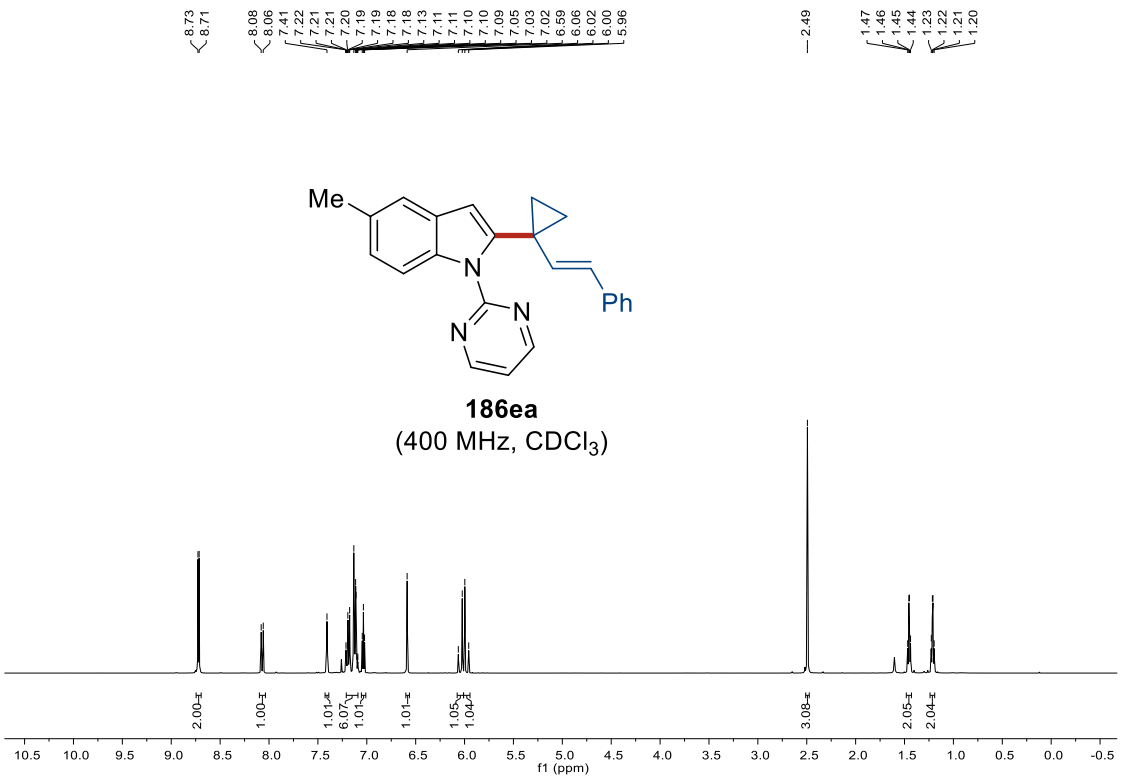
186ca
(75 MHz, $CDCl_3$)



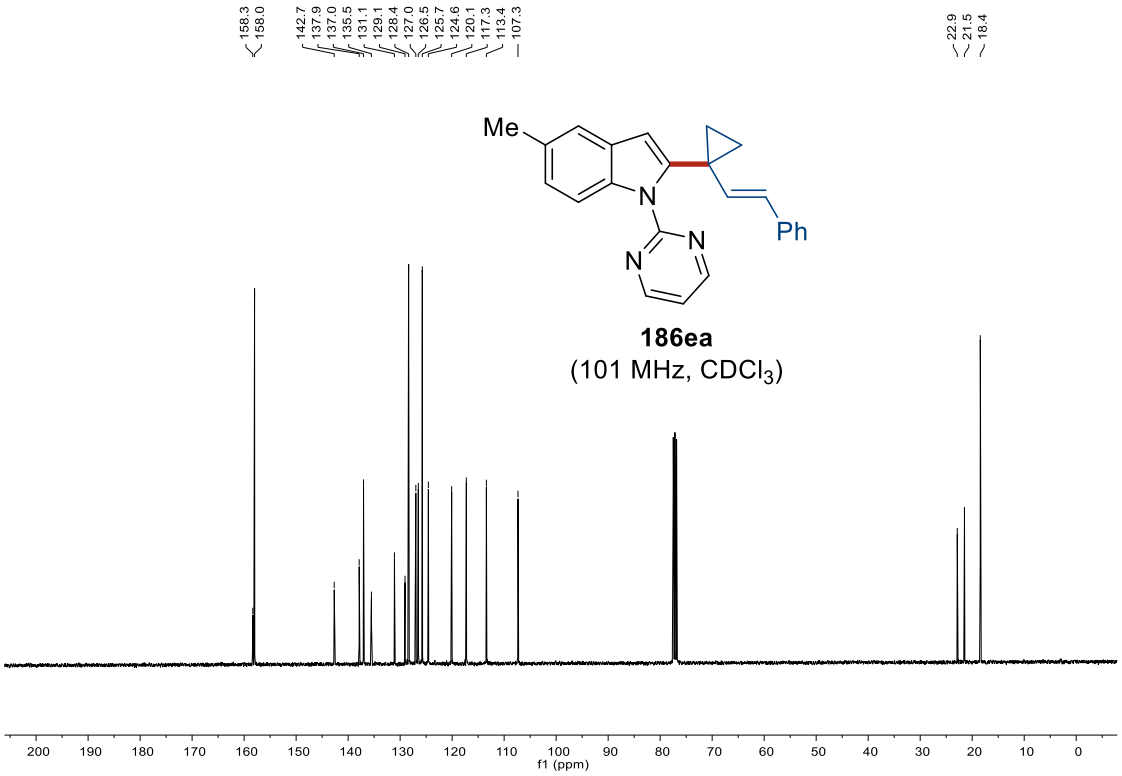
186da
(400 MHz, $CDCl_3$)



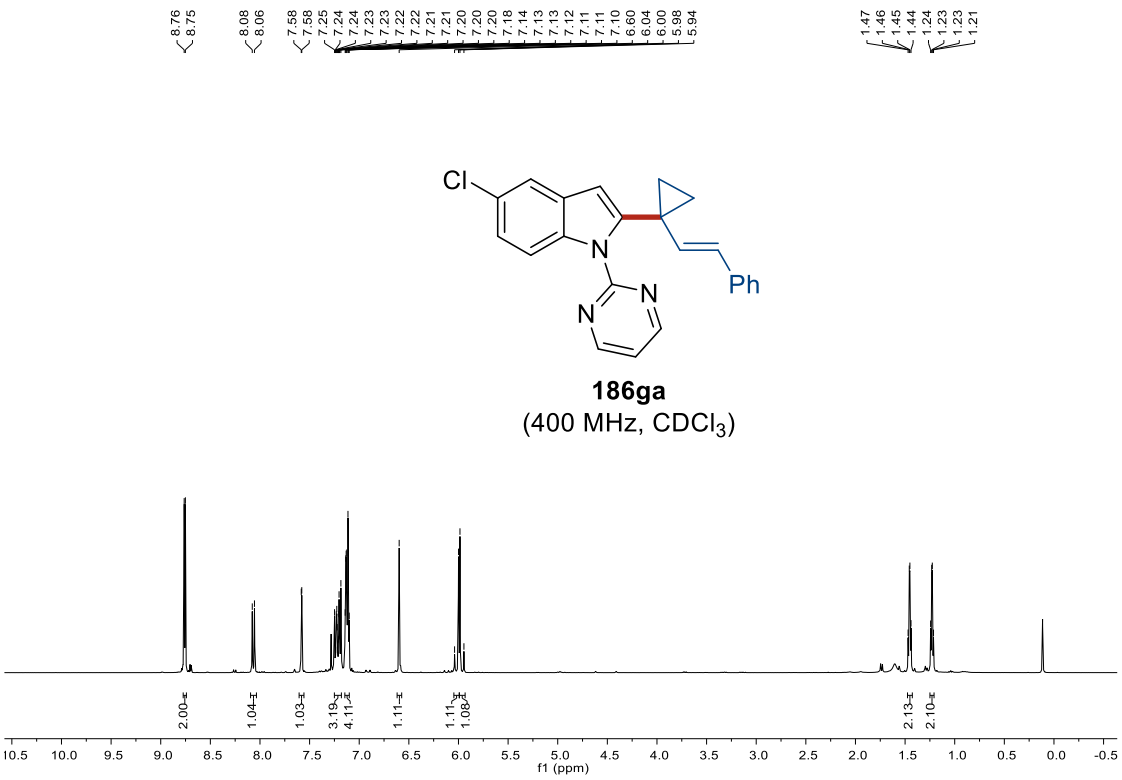
186da
(101 MHz, $CDCl_3$)



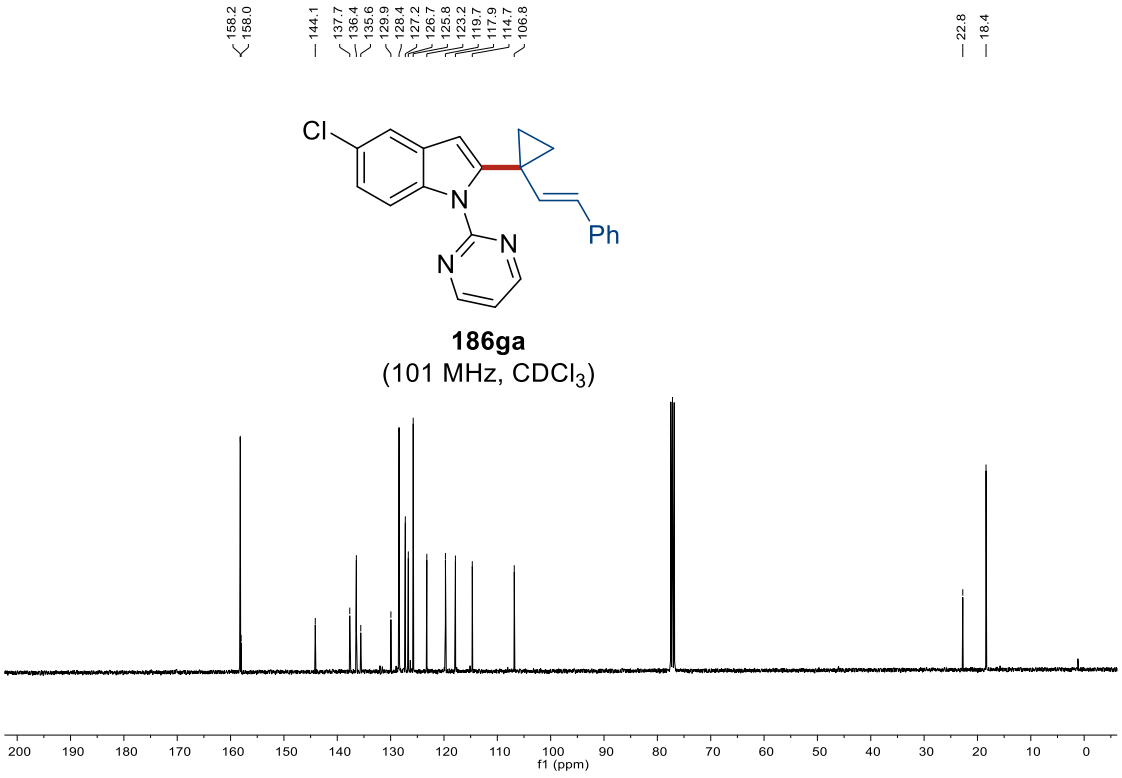
186ea
(400 MHz, $CDCl_3$)



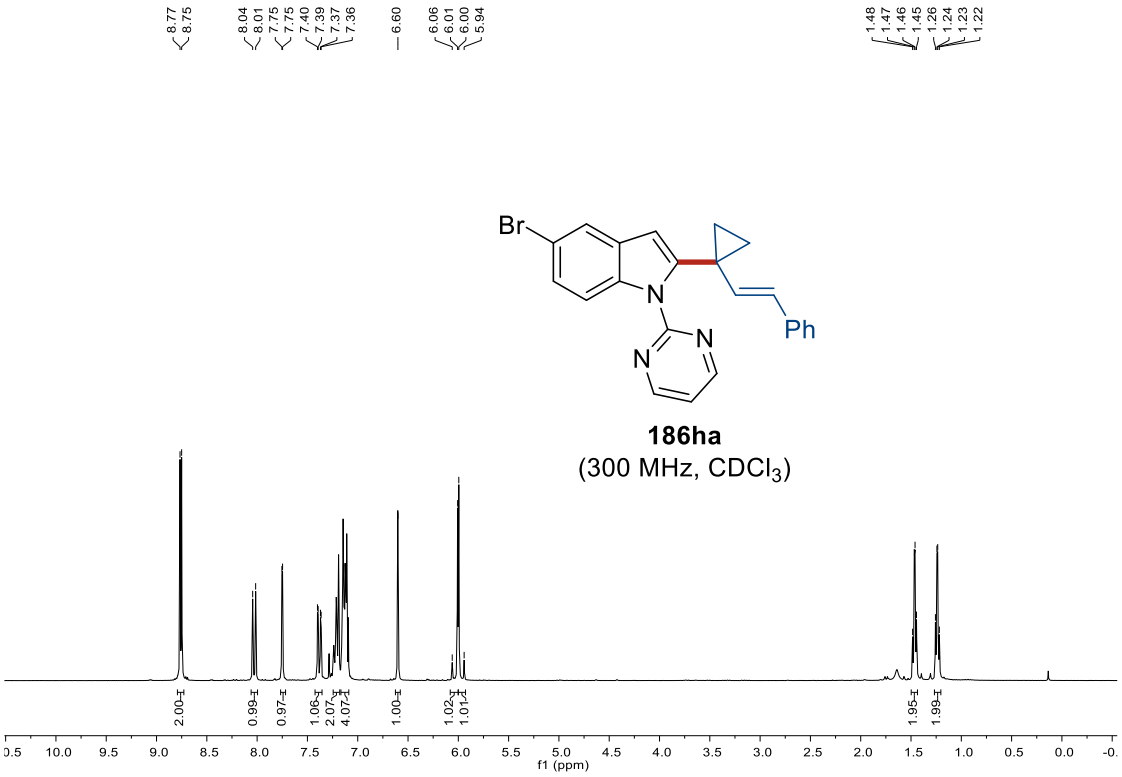
186ea
(101 MHz, $CDCl_3$)



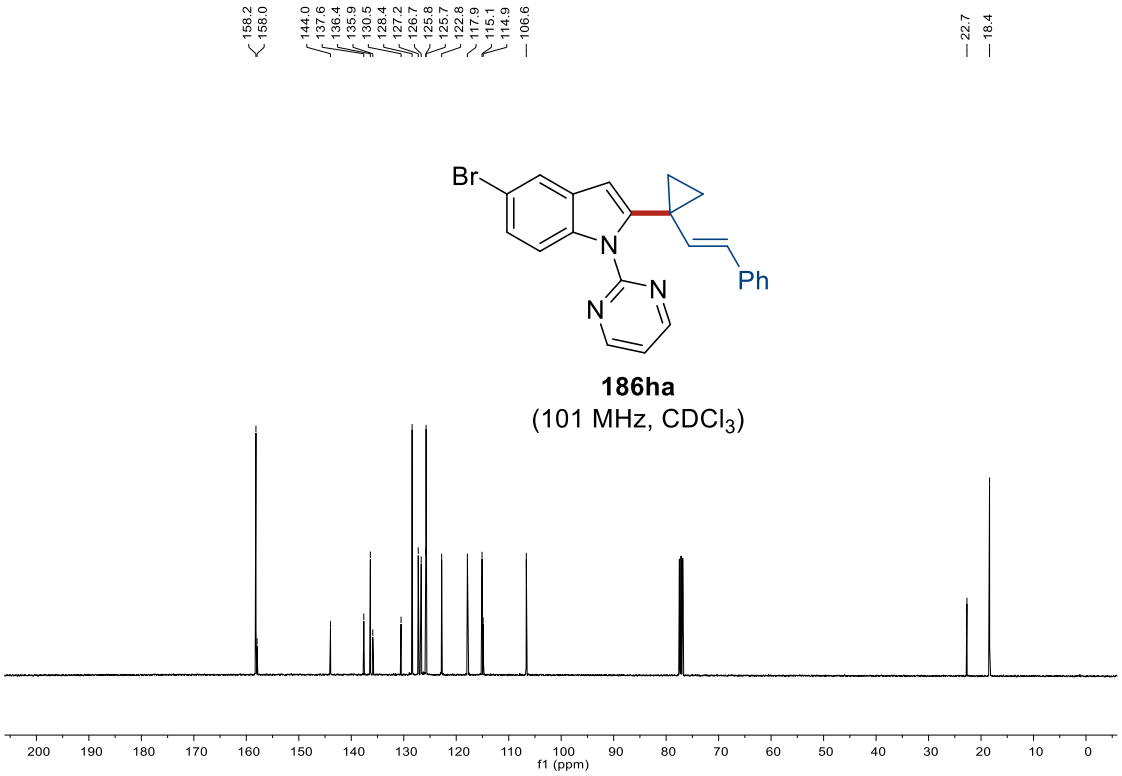
186ga
(400 MHz, $CDCl_3$)



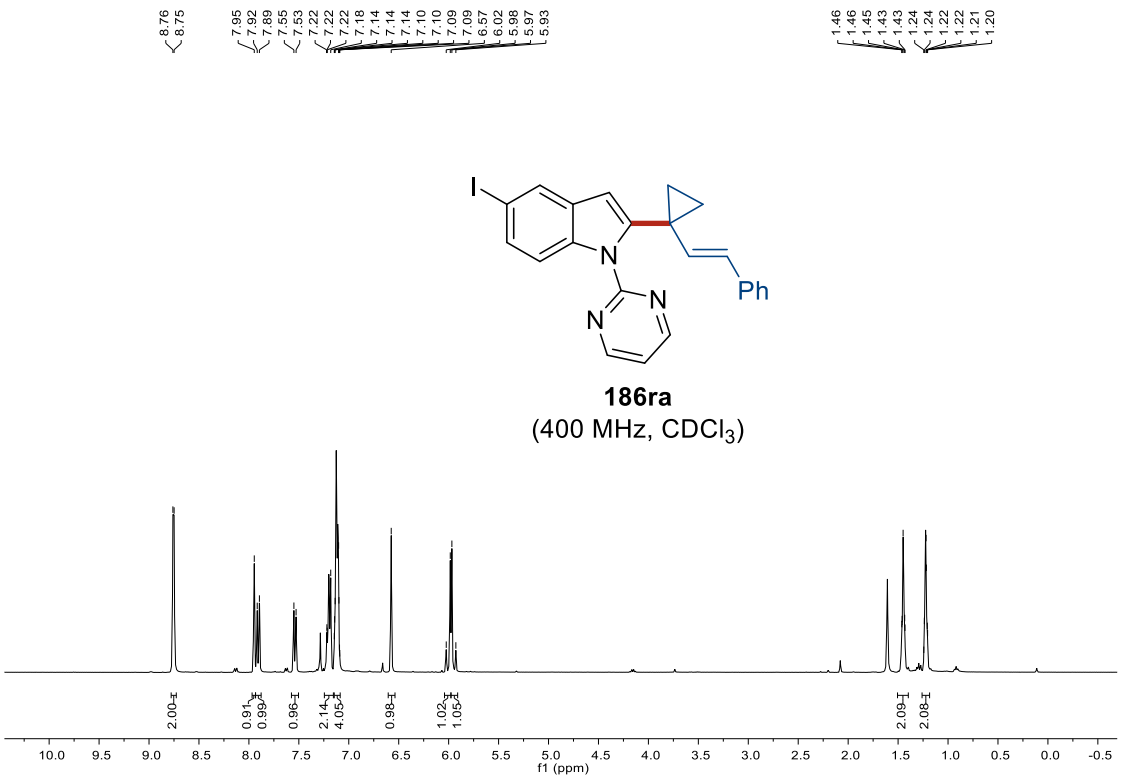
186ga
(101 MHz, $CDCl_3$)



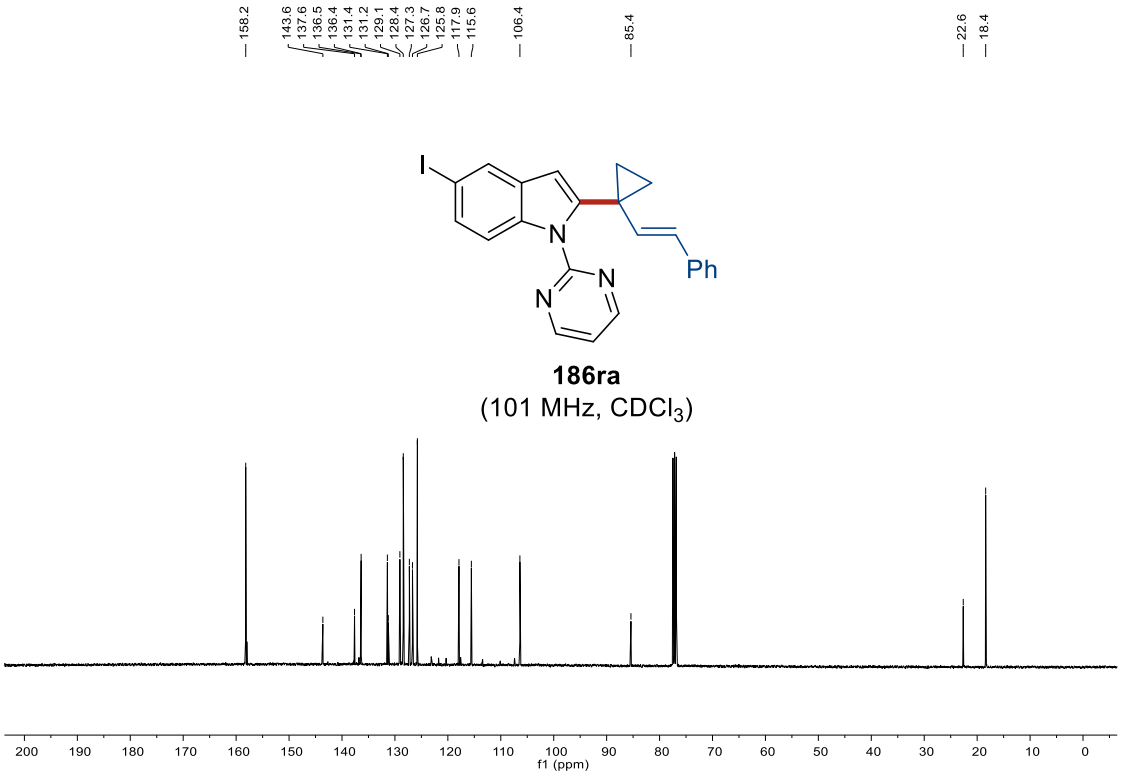
186ha
(300 MHz, $CDCl_3$)



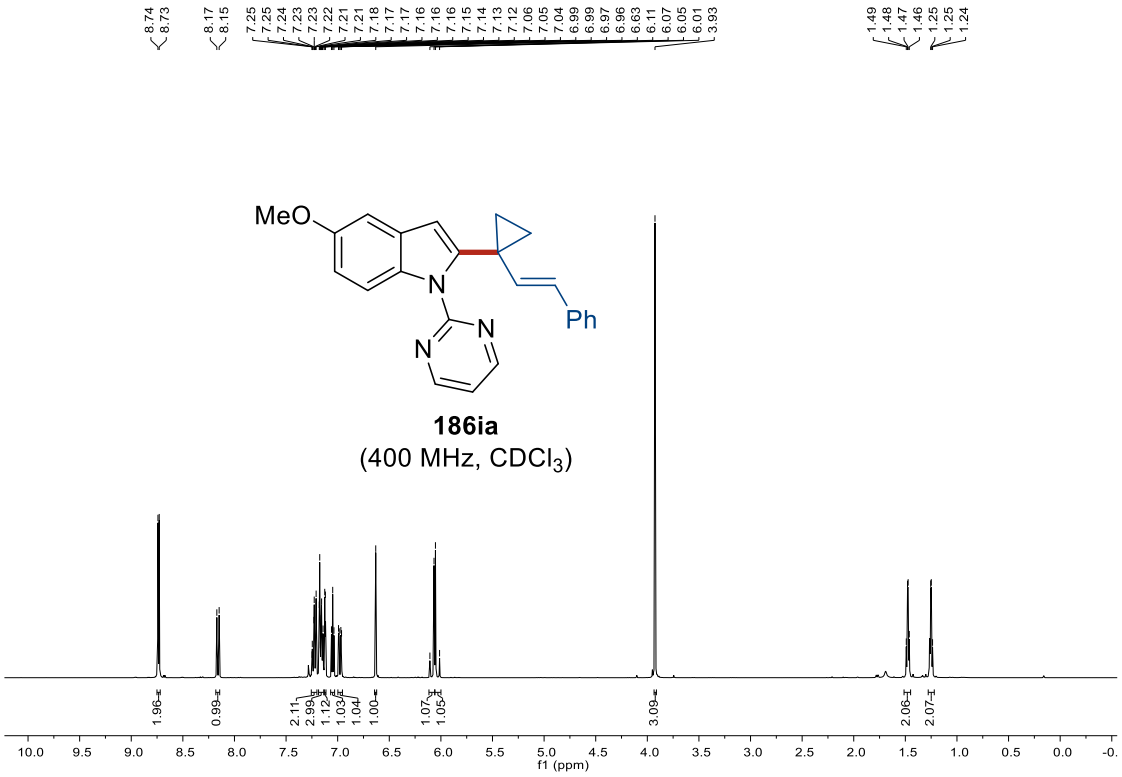
186ha
(101 MHz, $CDCl_3$)



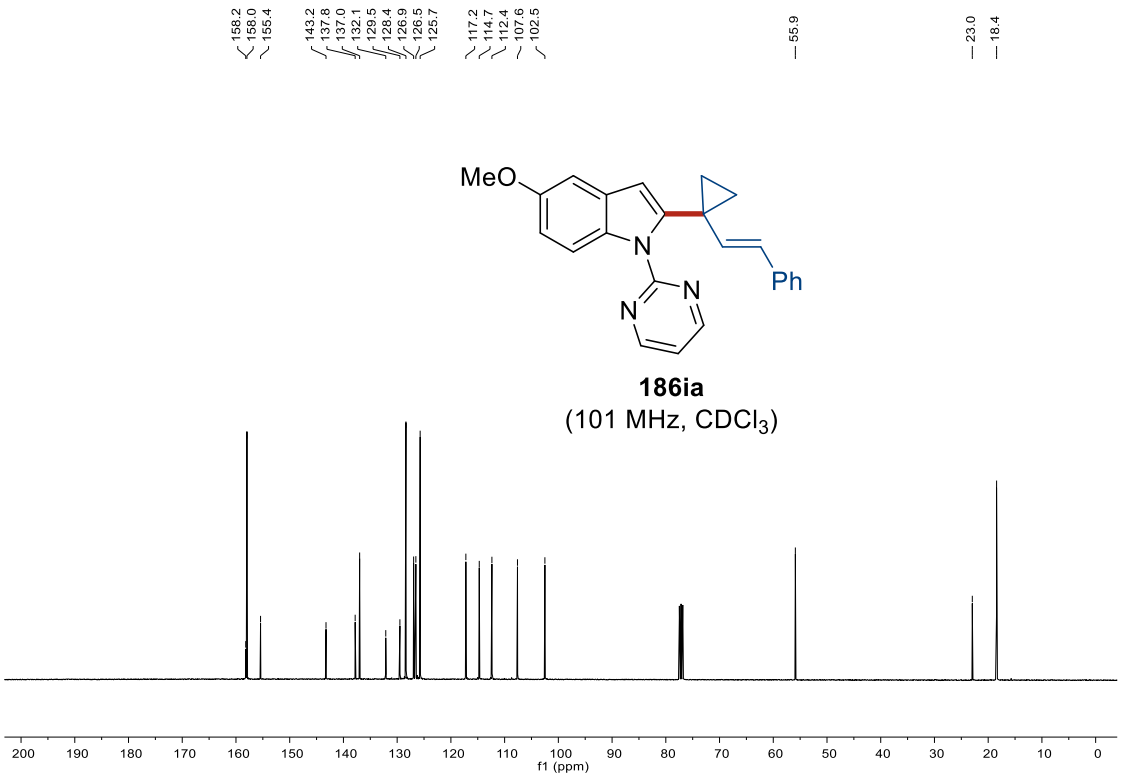
186ra
(400 MHz, $CDCl_3$)



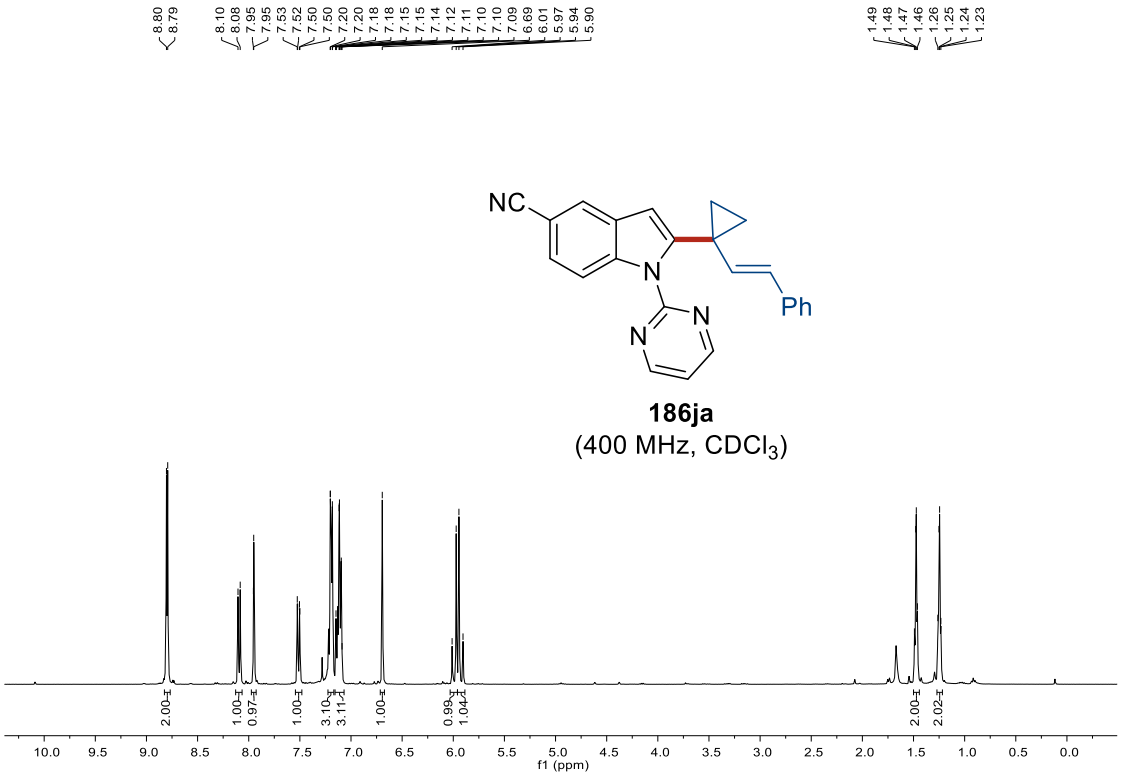
186ra
(101 MHz, $CDCl_3$)



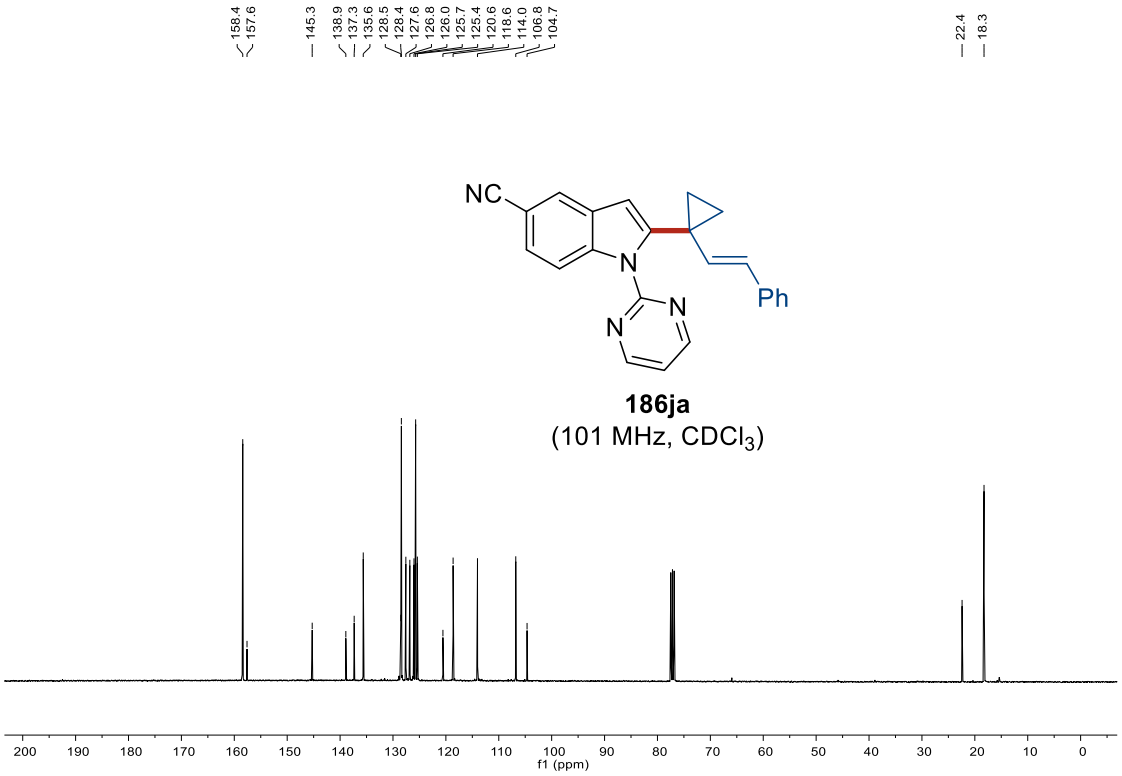
186ia
(400 MHz, $CDCl_3$)



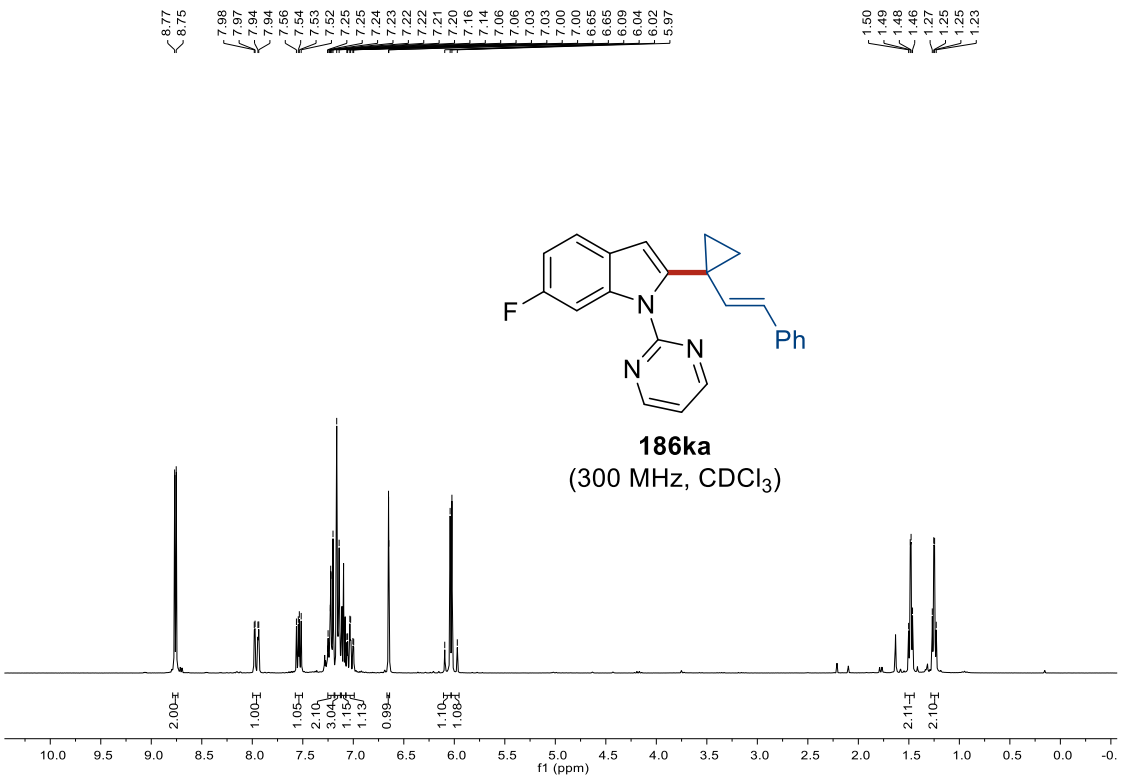
186ia
(101 MHz, $CDCl_3$)



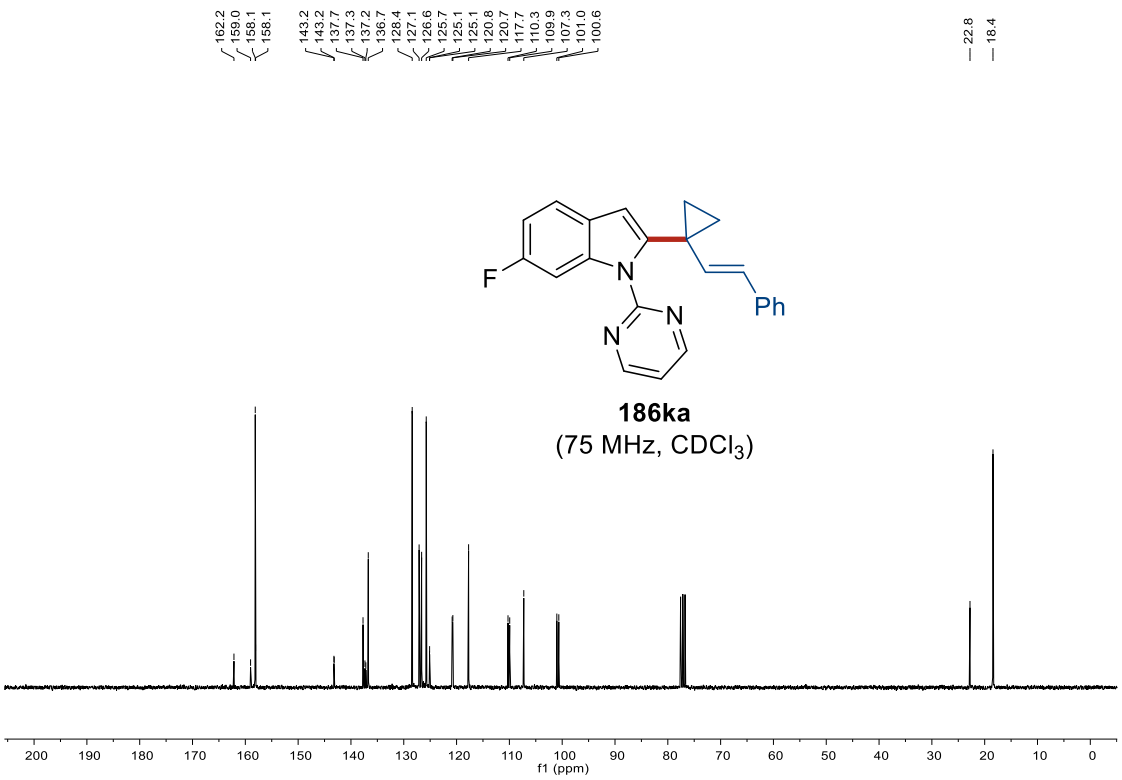
186ja
(400 MHz, $CDCl_3$)

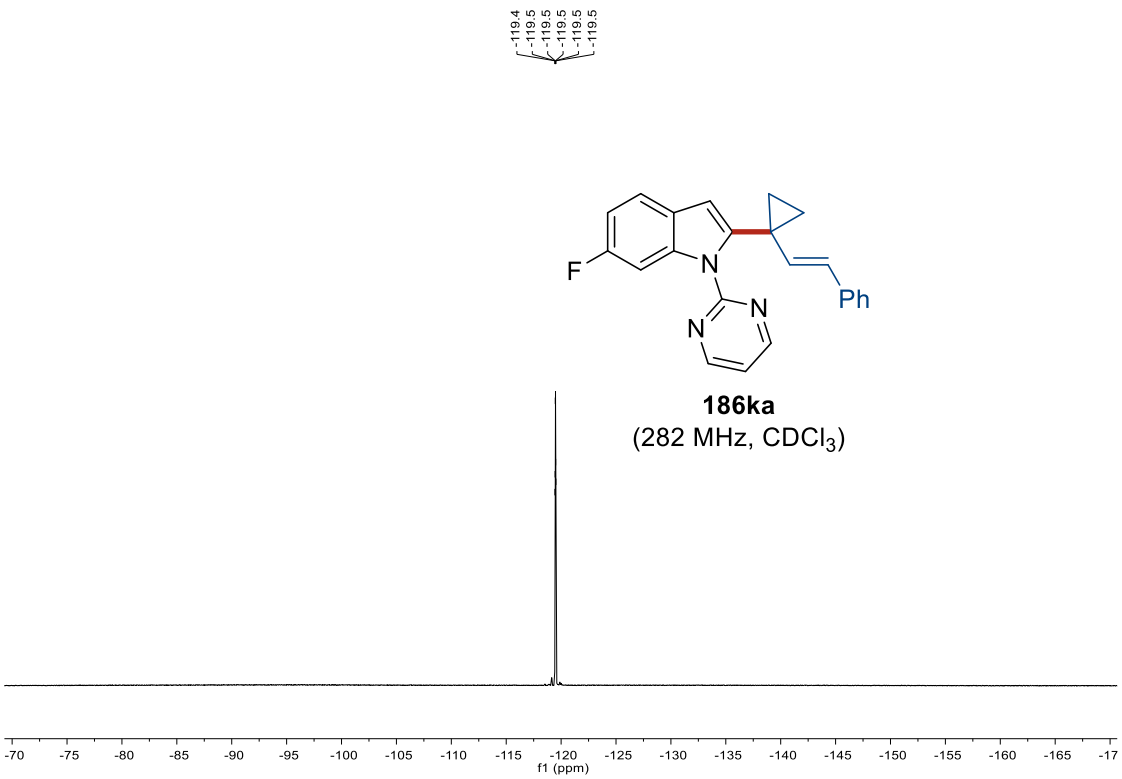


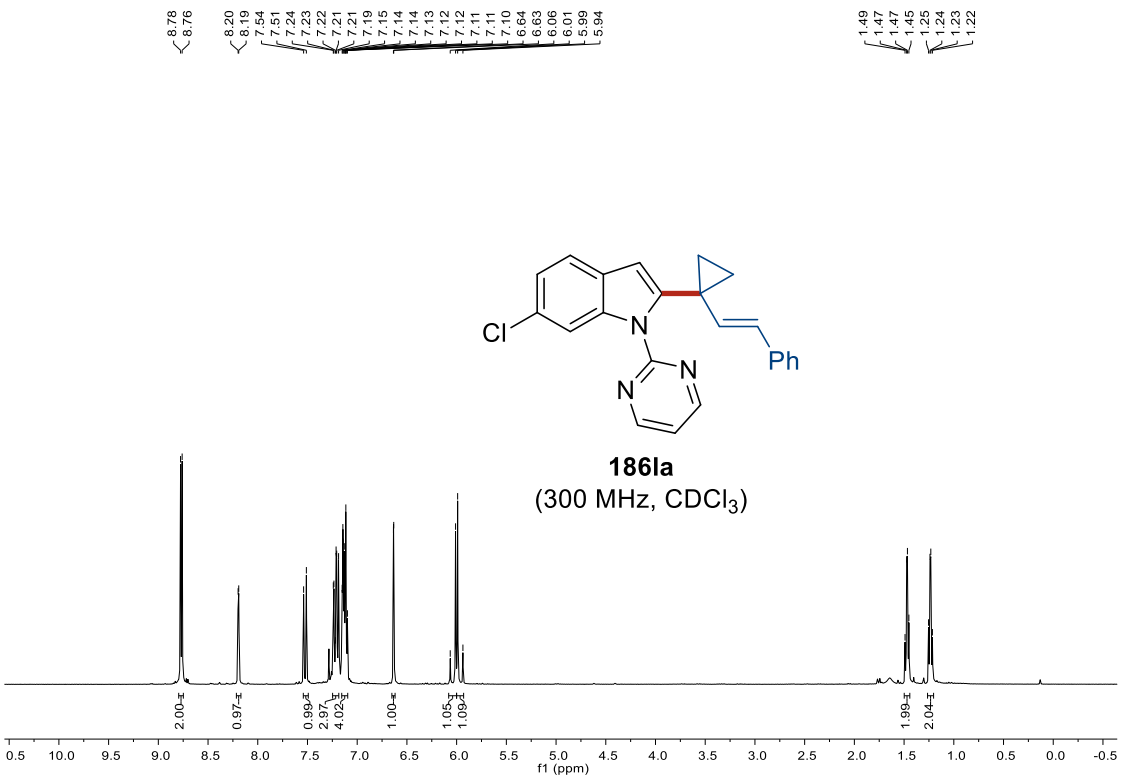
186ja
(101 MHz, $CDCl_3$)

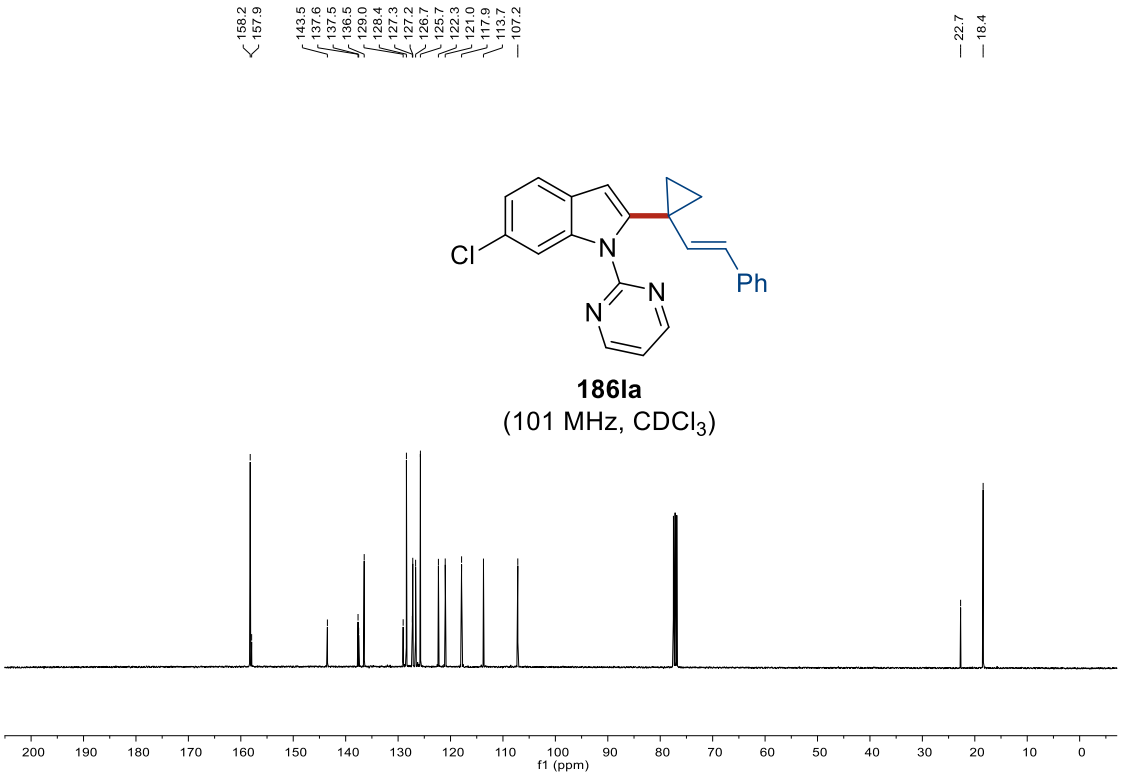


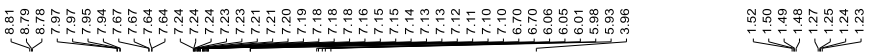
186ka
(300 MHz, $CDCl_3$)

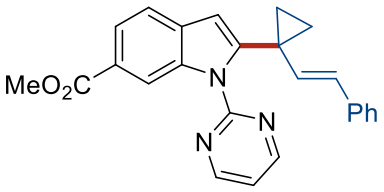

162.2
159.0
158.1
158.1
143.2
143.2
137.7
137.3
137.2
136.7
128.4
127.1
126.6
125.7
125.1
125.1
120.8
120.7
117.7
110.3
109.9
107.3
101.0
100.6
22.8
18.4
F
N
N
N
Ph
186ka
(75 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-119.4
-119.5
-119.5
-119.5
-119.5
-119.5
F
N
N
N
Ph
186ka
(282 MHz, CDCl3)
-70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -17
f1 (ppm)

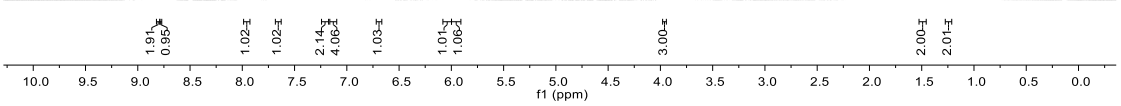

8.78
8.76
8.20
8.19
7.54
7.51
7.24
7.23
7.22
7.21
7.21
7.19
7.15
7.14
7.14
7.13
7.12
7.12
7.11
7.11
7.10
6.64
6.63
6.06
6.01
5.99
5.94
1.49
1.47
1.47
1.45
1.25
1.24
1.23
1.22
Cl
N
N
N
Ph
186la
(300 MHz, CDCl3)
2.00
0.97
0.99
2.97
4.02
1.00
1.05
1.09
1.99
2.04
f1 (ppm)

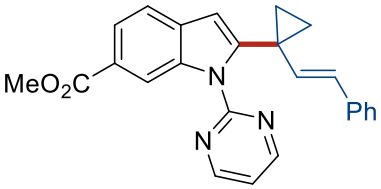

158.2
157.9
143.5
137.6
137.5
136.5
129.0
128.4
127.3
127.2
126.7
125.7
122.3
121.0
117.9
113.7
107.2
22.7
18.4
Cl
N
N
N
Ph
186la
(101 MHz, CDCl3)
f1 (ppm)



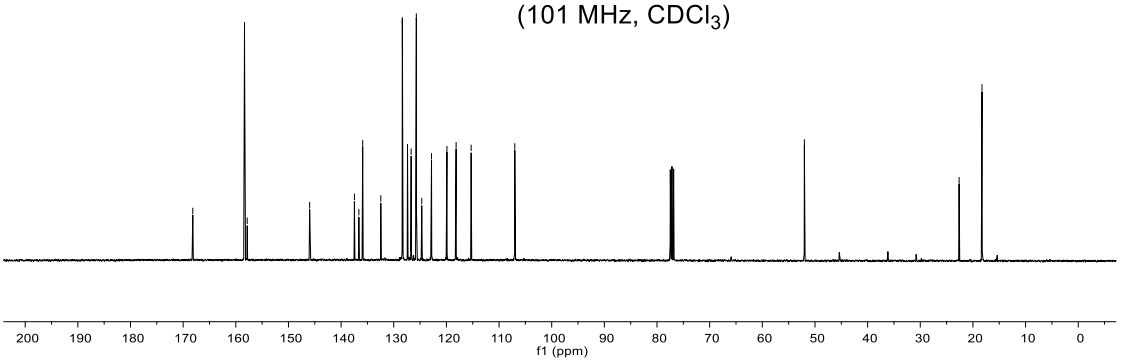


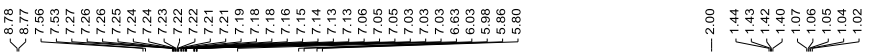
186na
(300 MHz, $CDCl_3$)

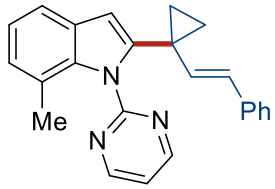




186na
(101 MHz, $CDCl_3$)

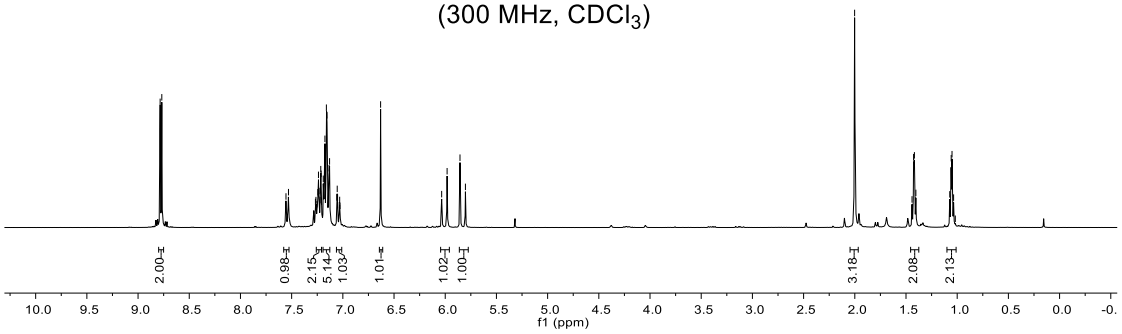


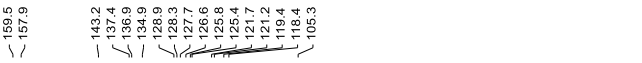


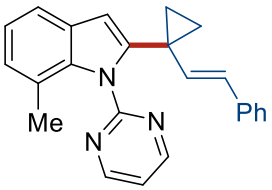


186oa

(300 MHz, $CDCl_3$)

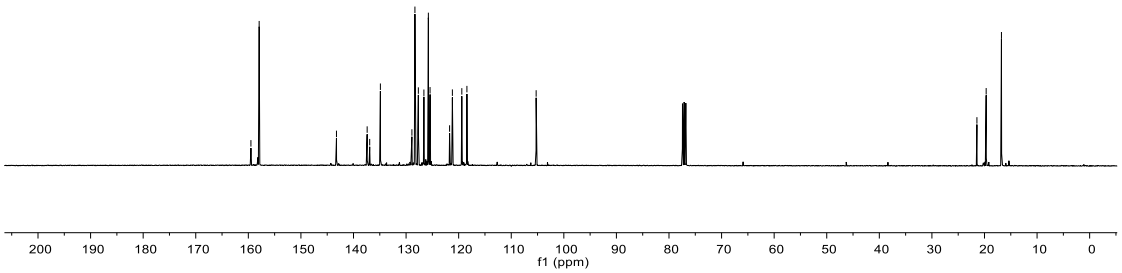


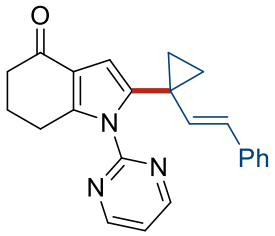




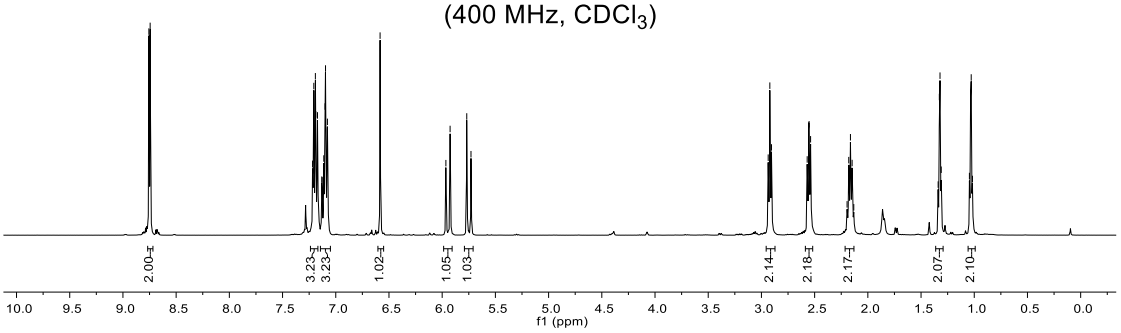
186oa

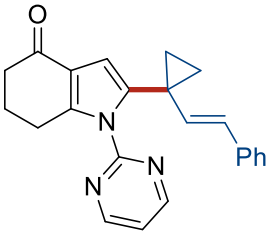
(101 MHz, $CDCl_3$)



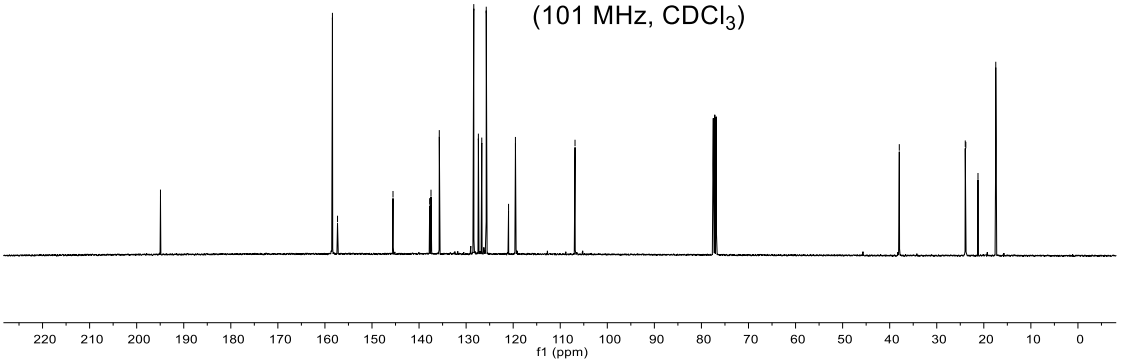


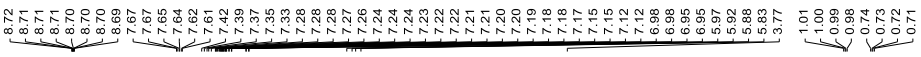
186pa
(400 MHz, $CDCl_3$)

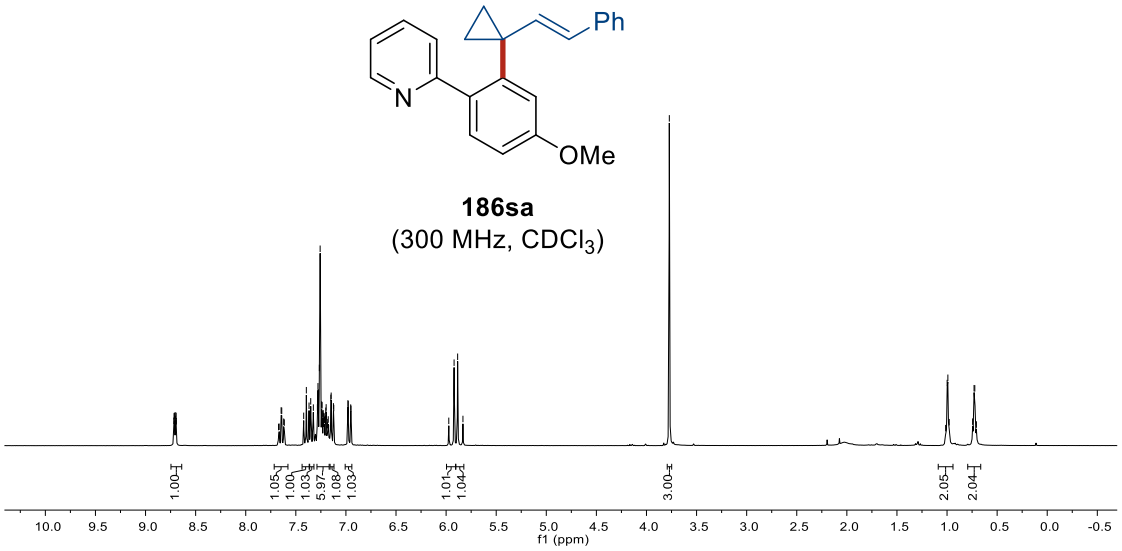




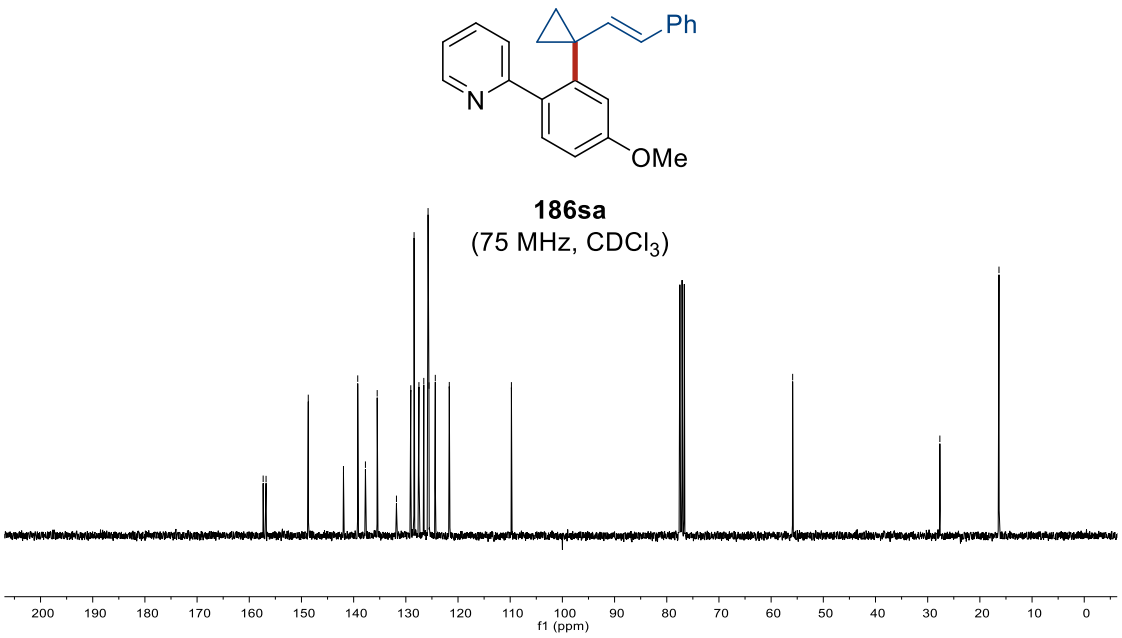
186pa
(101 MHz, $CDCl_3$)

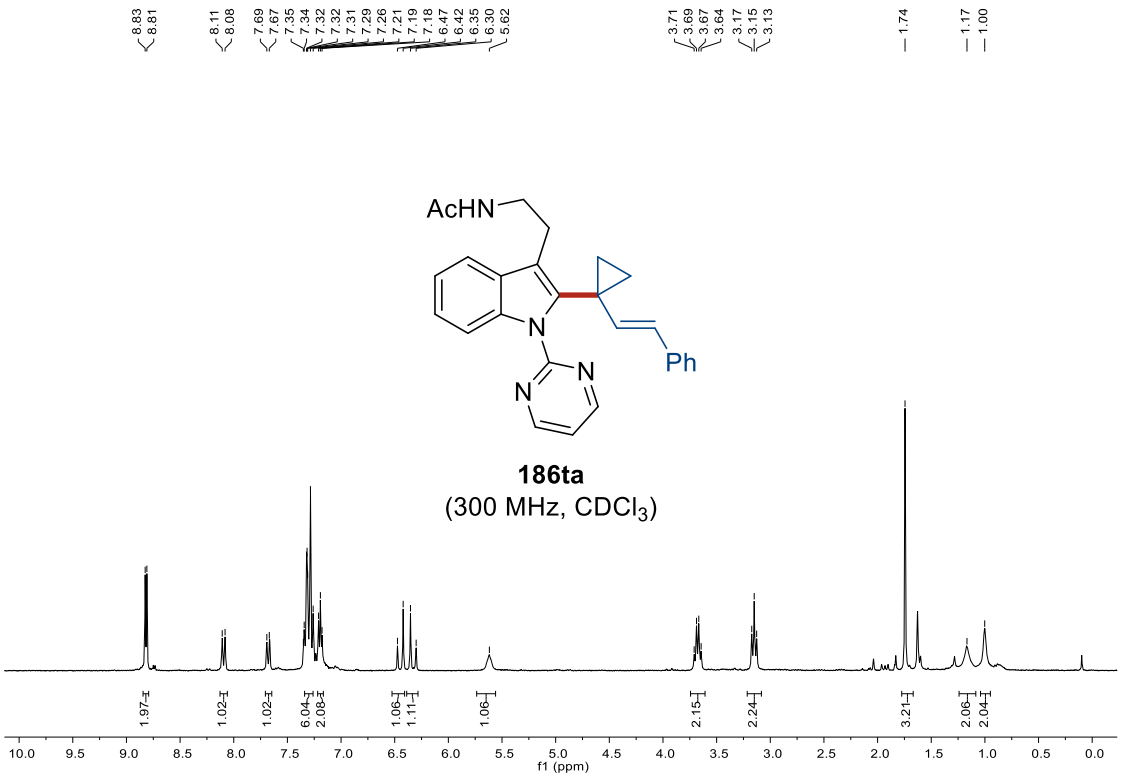



8.72 8.71 8.71 8.71 8.70 8.70 8.69 7.67 7.67 7.65 7.64 7.62 7.61 7.42 7.39 7.37 7.35 7.33 7.28 7.28 7.28 7.27 7.26 7.24 7.24 7.24 7.23 7.22 7.22 7.21 7.21 7.20 7.20 7.19 7.18 7.18 7.17 7.15 7.15 7.12 7.12 6.98 6.98 6.95 6.95 5.97 5.92 5.88 5.83 3.77 1.01 1.00 0.99 0.98 0.74 0.73 0.72 0.71

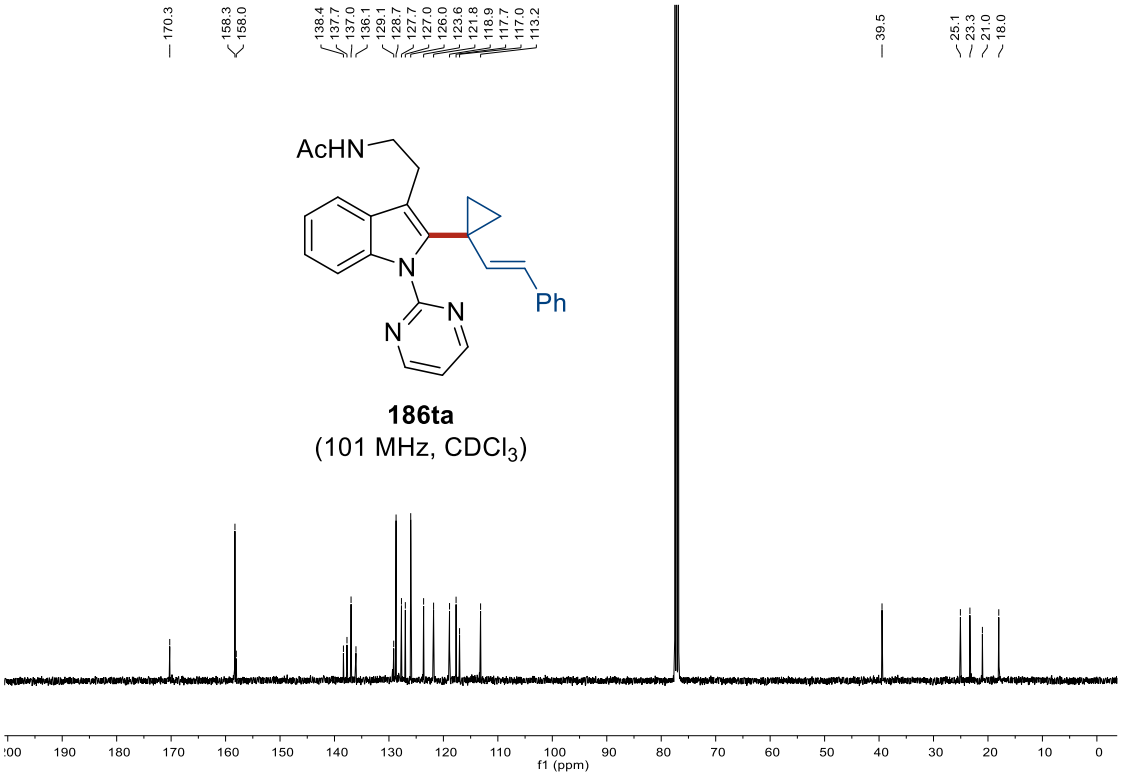

Ph
N
OMe
186sa
(300 MHz, CDCl3)
1.00 1.05 1.00 1.03 5.97 1.08 1.03 1.01 1.04 3.00 2.05 2.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


157.3 156.8 148.7 142.0 139.2 137.7 135.5 131.8 129.1 128.4 127.5 126.6 125.7 125.6 124.4 121.7 109.8 55.9 27.7 16.3

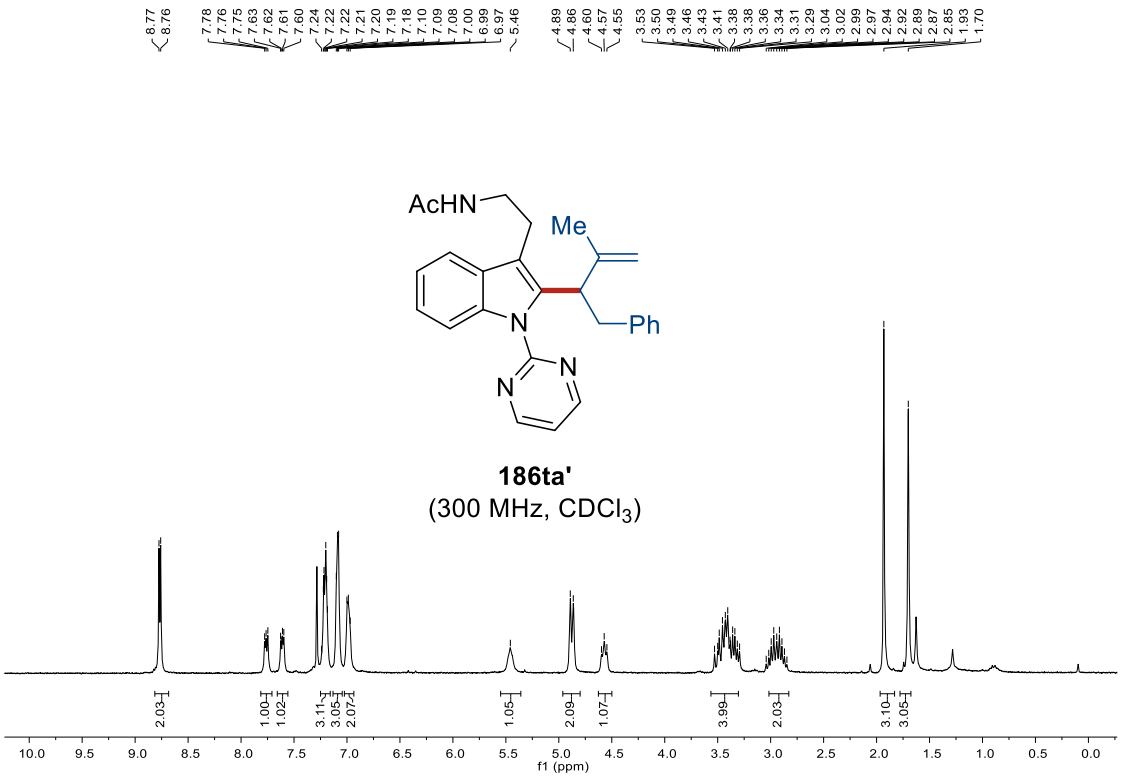

Ph
N
OMe
186sa
(75 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

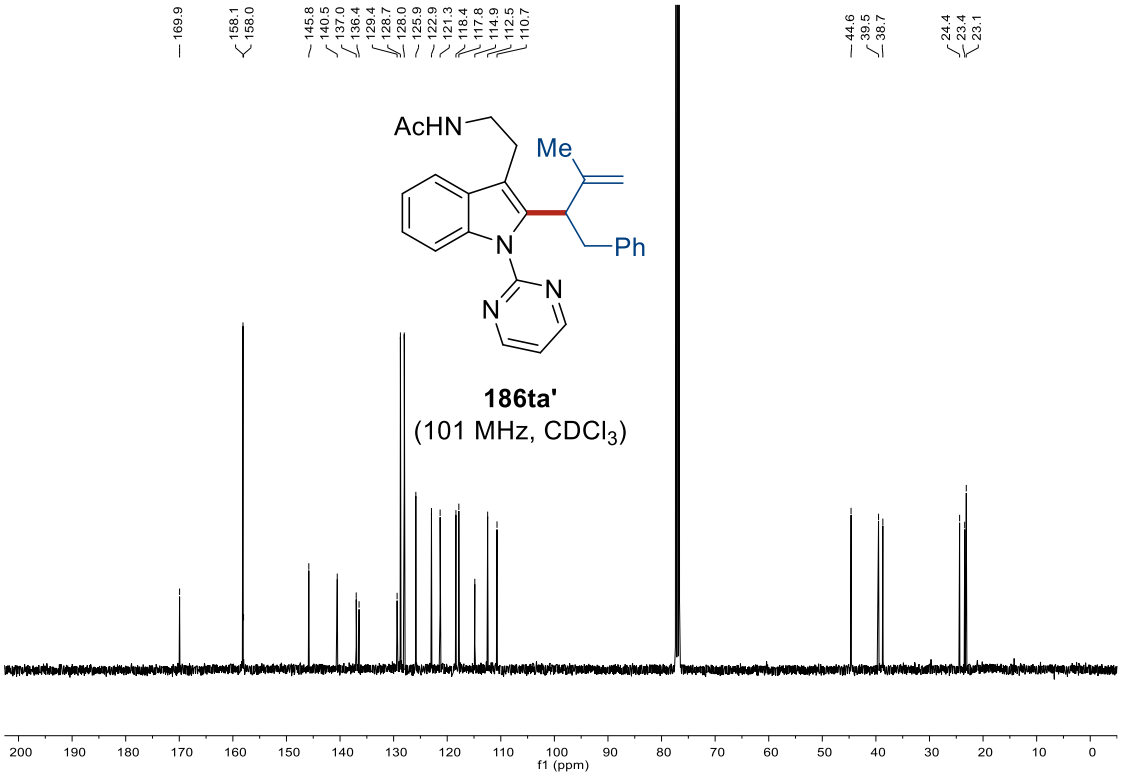


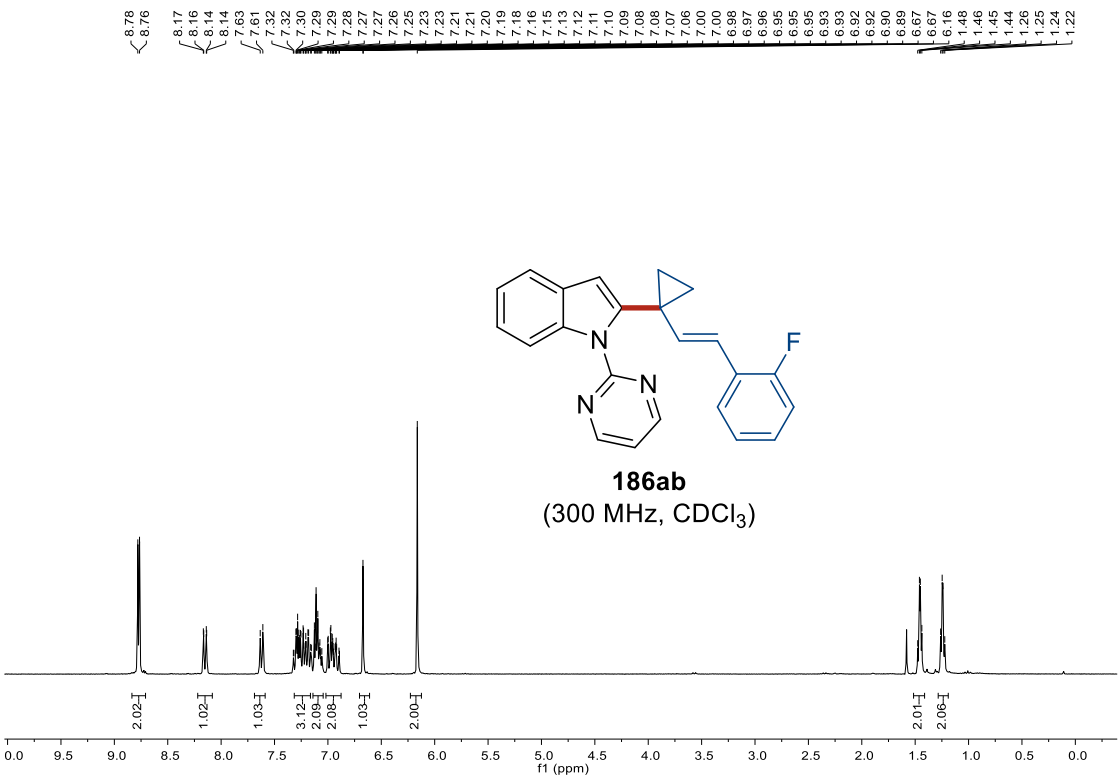
186ta
(300 MHz, $CDCl_3$)

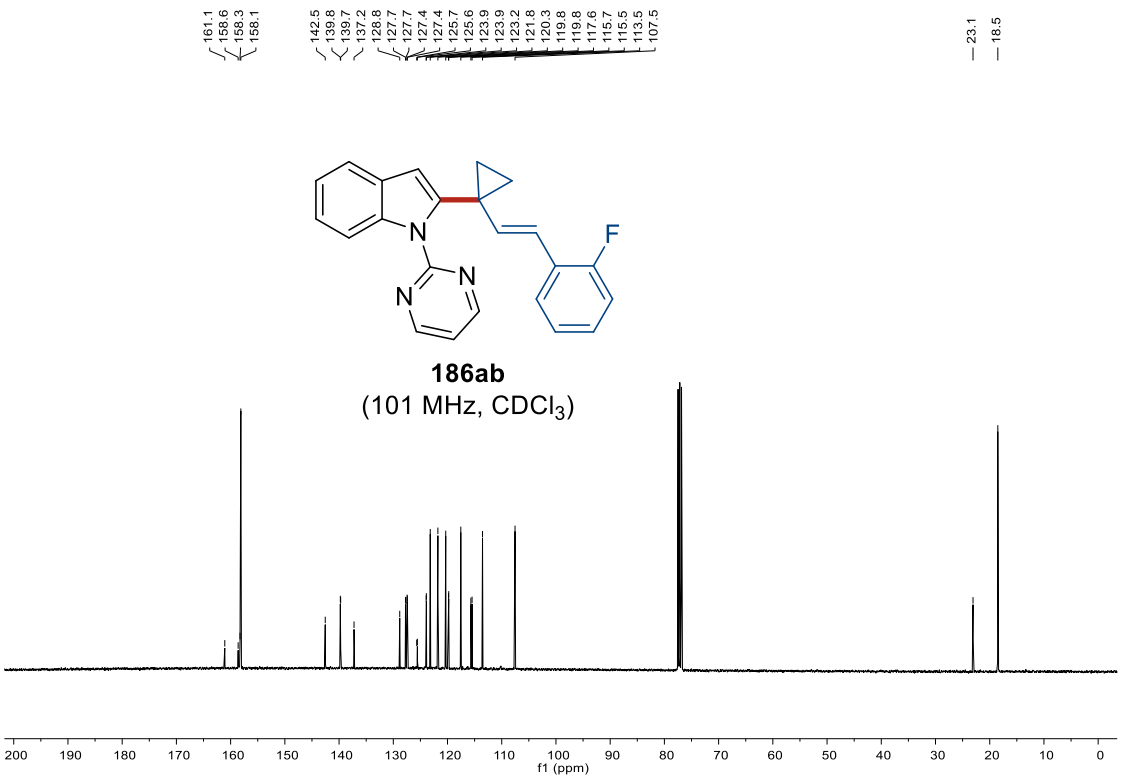


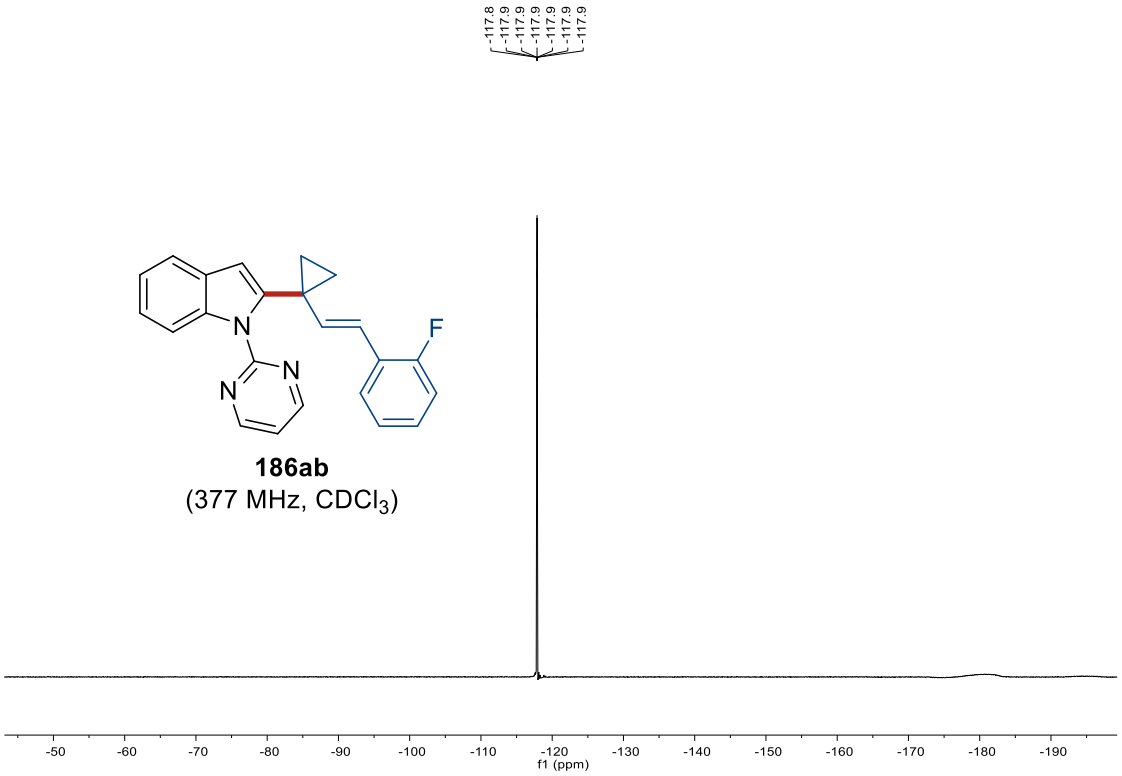
186ta
(101 MHz, $CDCl_3$)


8.77
8.76
7.78
7.76
7.75
7.63
7.62
7.61
7.60
7.24
7.22
7.22
7.21
7.20
7.19
7.18
7.10
7.09
7.08
7.00
6.99
6.97
5.46
4.89
4.86
4.60
4.57
4.55
3.53
3.50
3.49
3.46
3.43
3.41
3.38
3.38
3.36
3.34
3.31
3.29
3.04
3.02
2.99
2.97
2.94
2.92
2.89
2.87
2.85
1.93
1.70
AcHN
Me
Ph
N
N
N
186ta'
(300 MHz, CDCl3)
2.03
1.00
1.02
3.11
3.05
2.07
1.05
2.09
1.07
3.99
2.03
3.10
3.05
10.0 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
f1 (ppm)

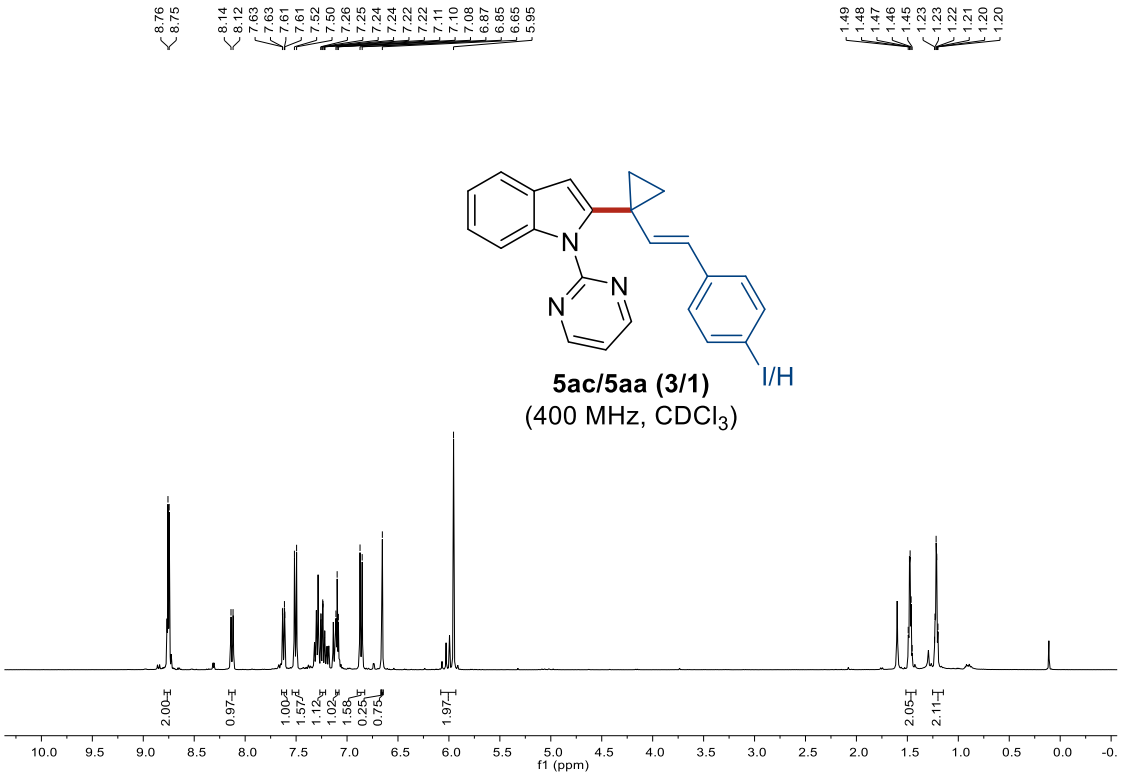

169.9
158.1
158.0
145.8
140.5
137.0
136.4
129.4
128.7
128.0
125.9
122.9
121.3
118.4
117.8
114.9
112.5
110.7
44.6
39.5
38.7
24.4
23.4
23.1
AcHN
Me
Ph
N
N
N
186ta'
(101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.78
8.76
8.17
8.16
8.14
8.14
7.63
7.61
7.32
7.32
7.30
7.29
7.29
7.28
7.27
7.27
7.26
7.25
7.23
7.23
7.21
7.21
7.20
7.19
7.18
7.16
7.15
7.13
7.12
7.11
7.10
7.09
7.08
7.08
7.07
7.06
7.00
7.00
6.98
6.97
6.96
6.95
6.95
6.95
6.93
6.93
6.92
6.92
6.90
6.89
6.67
6.67
6.16
1.48
1.46
1.45
1.44
1.26
1.25
1.24
1.22
N
N
N
F
186ab
(300 MHz, CDCl3)
2.02
1.02
1.03
3.12
2.09
2.08
1.03
2.00
2.01
2.06
0.0 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
f1 (ppm)

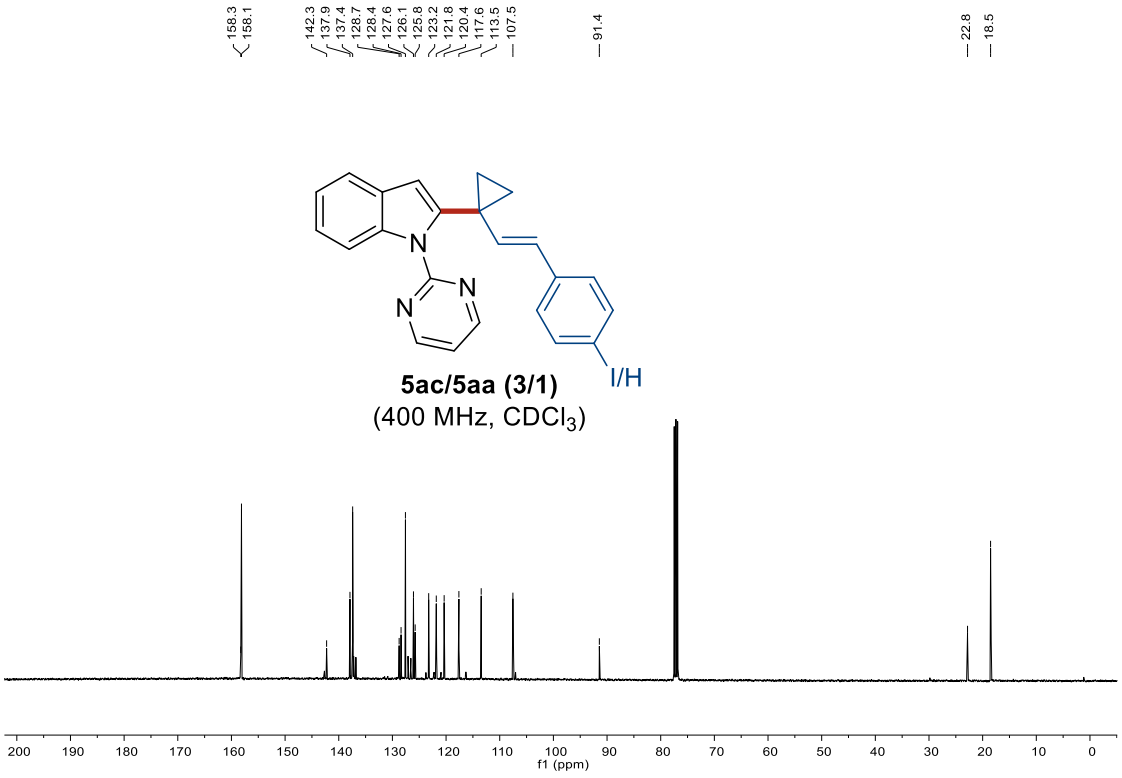

161.1
158.6
158.3
158.1
142.5
139.8
139.7
137.2
128.8
127.7
127.7
127.4
127.4
125.7
125.6
123.9
123.9
123.2
121.8
120.3
119.8
119.8
117.6
115.7
115.5
113.5
107.5
23.1
18.5
N
N
N
F
186ab
(101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



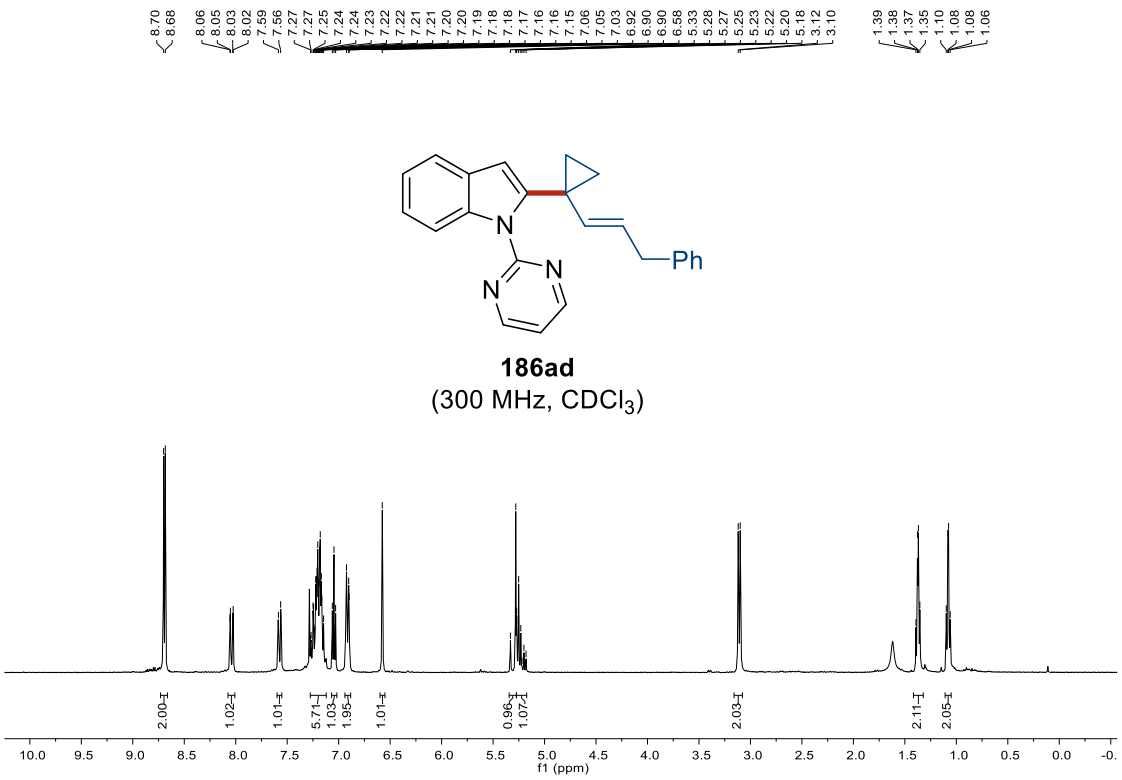
186ab
(377 MHz, $CDCl_3$)



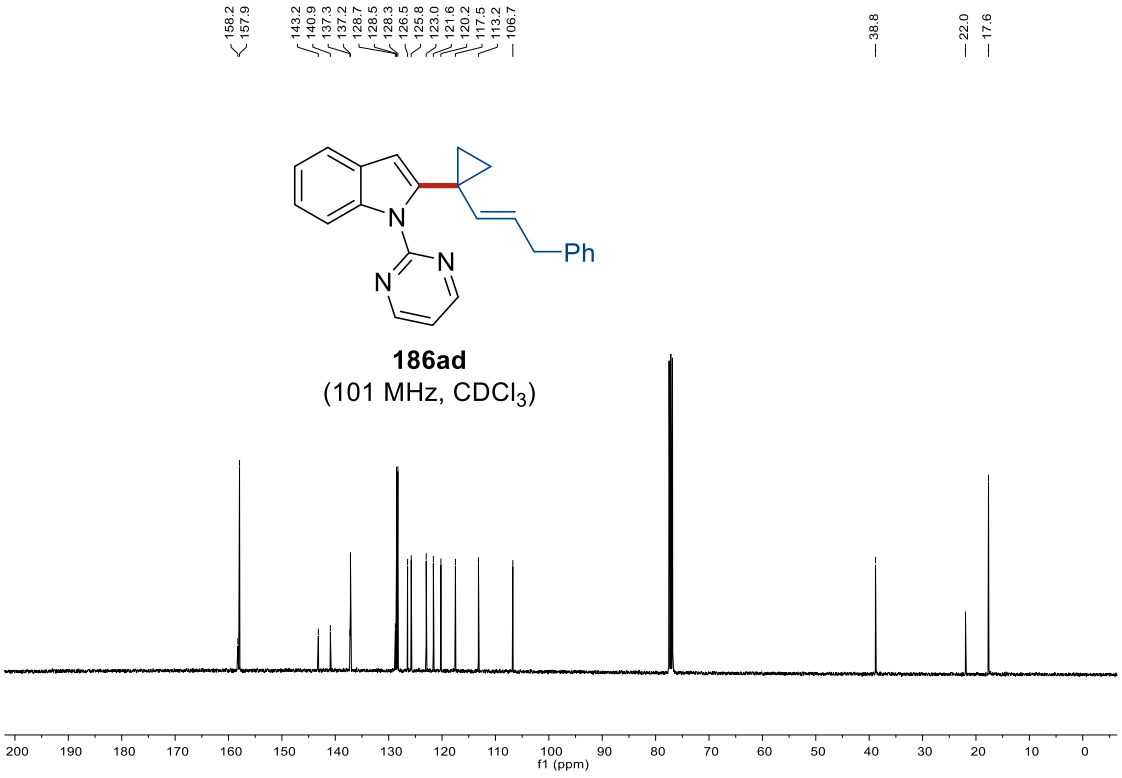
5ac/5aa (3/1)
(400 MHz, $CDCl_3$)



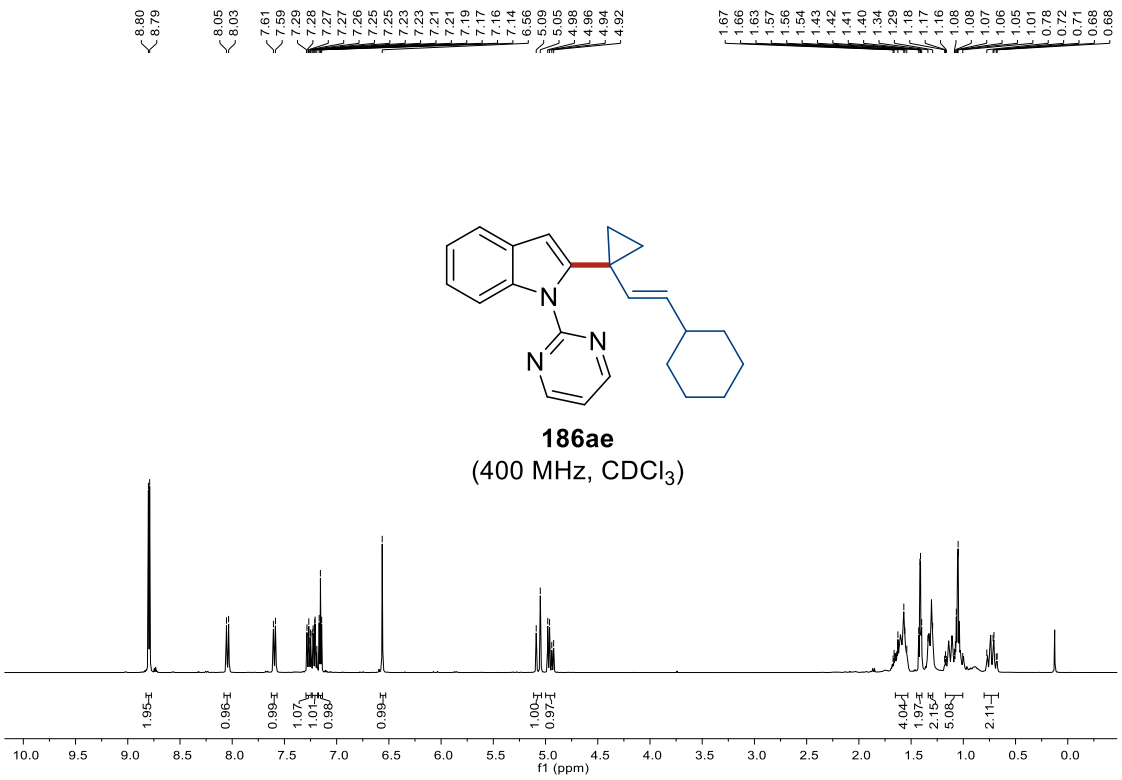
5ac/5aa (3/1)
(400 MHz, $CDCl_3$)



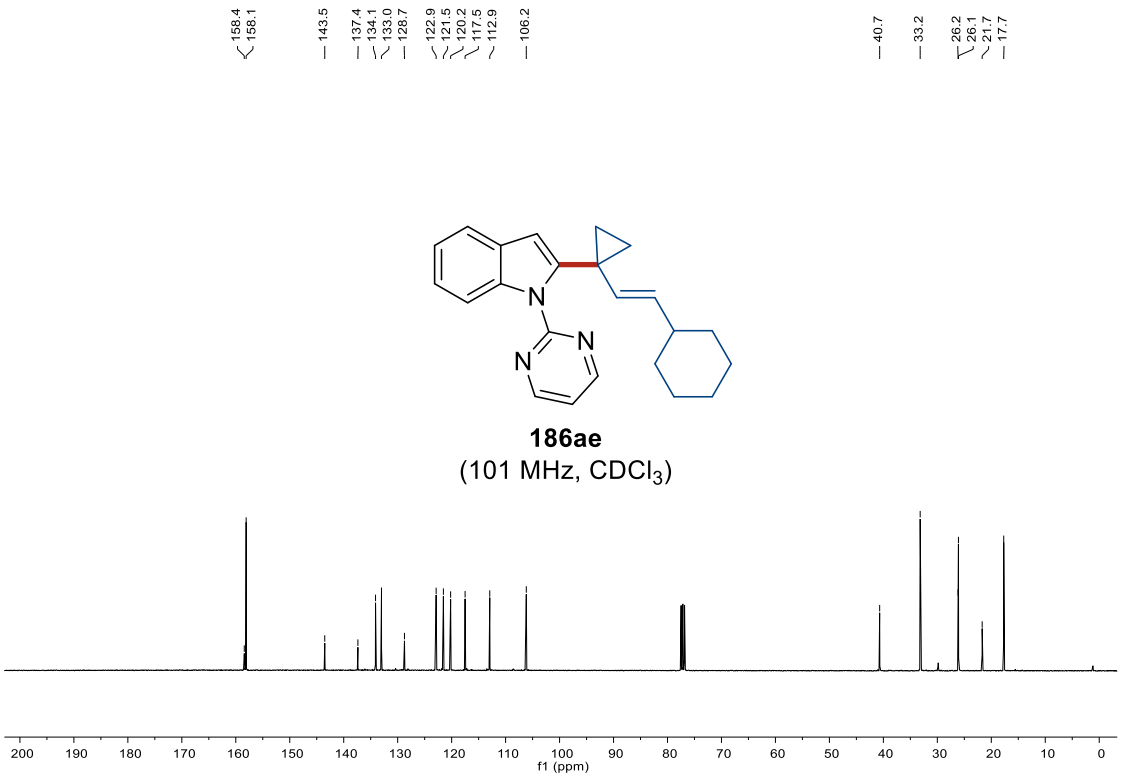
186ad
(300 MHz, $CDCl_3$)

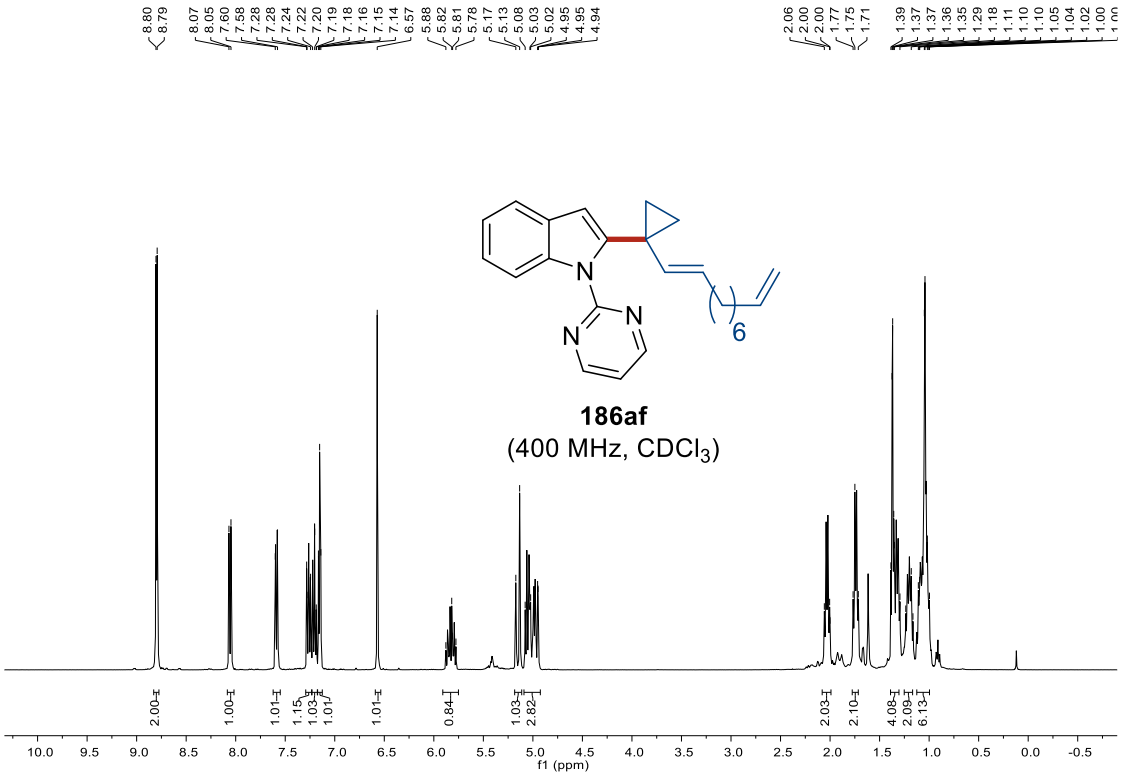


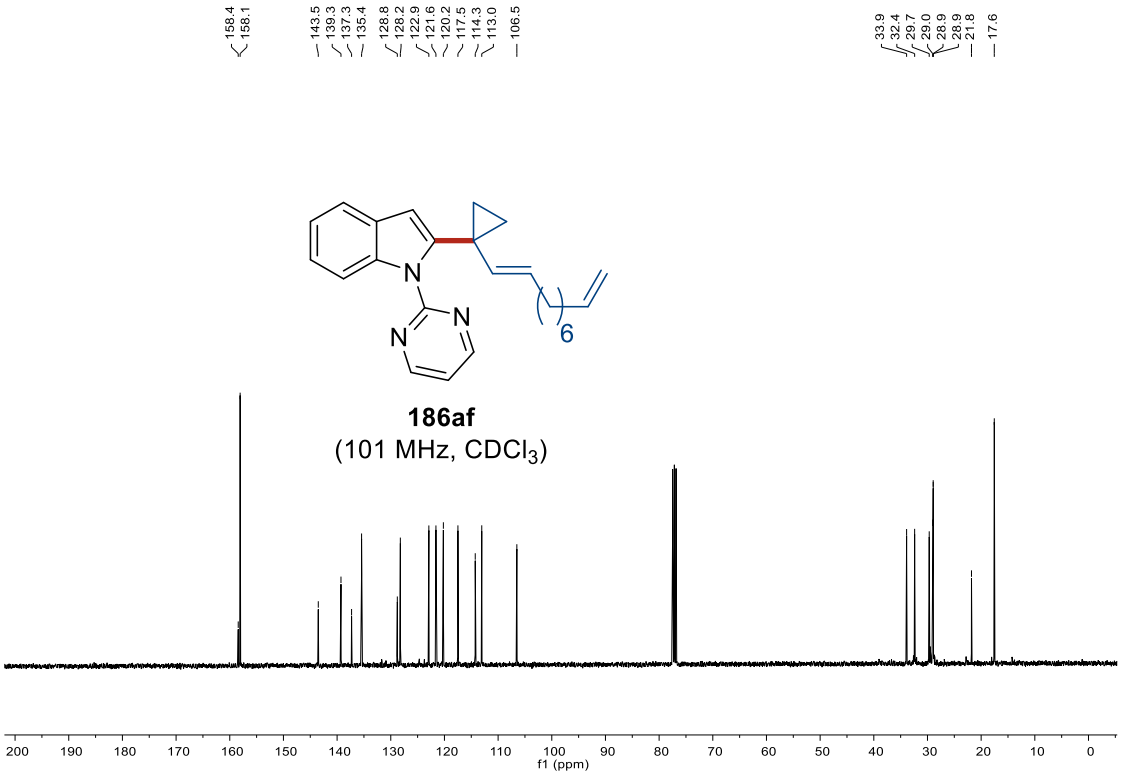
186ad
(101 MHz, $CDCl_3$)



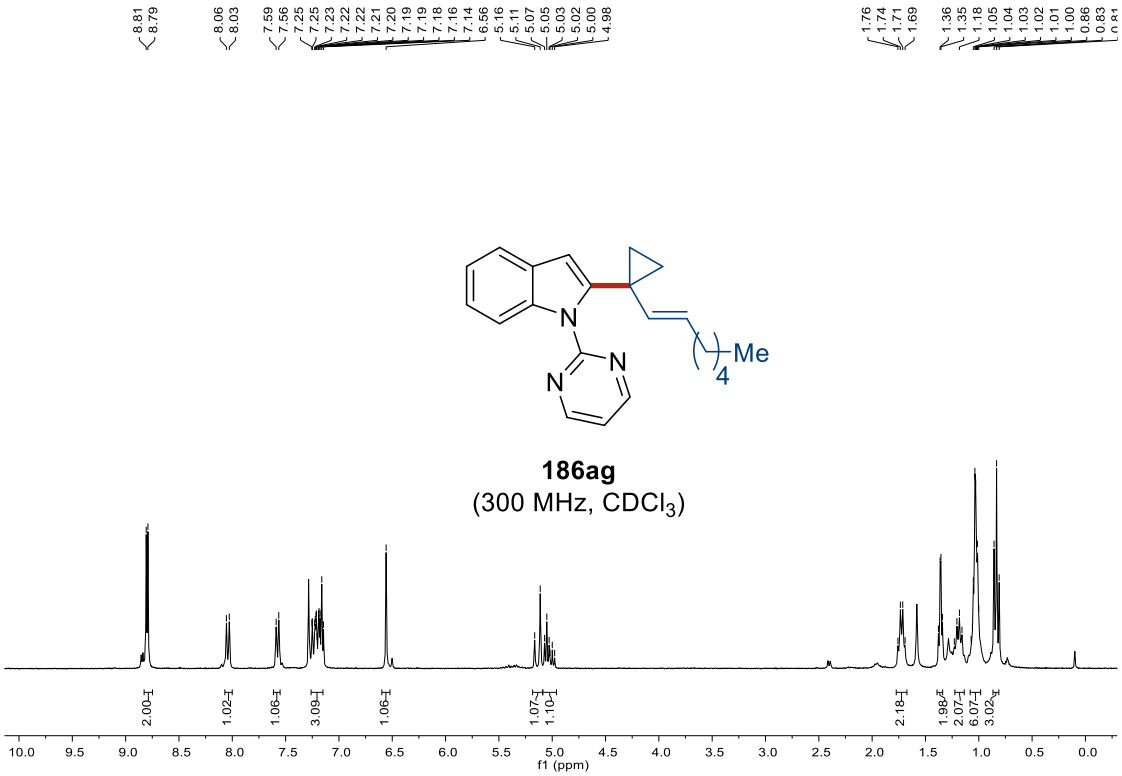
186ae
(400 MHz, $CDCl_3$)


158.4
158.1
143.5
137.4
134.1
133.0
128.7
122.9
121.5
120.2
117.5
112.9
106.2
40.7
33.2
26.2
26.1
21.7
17.7
N
N
N
186ae
(101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

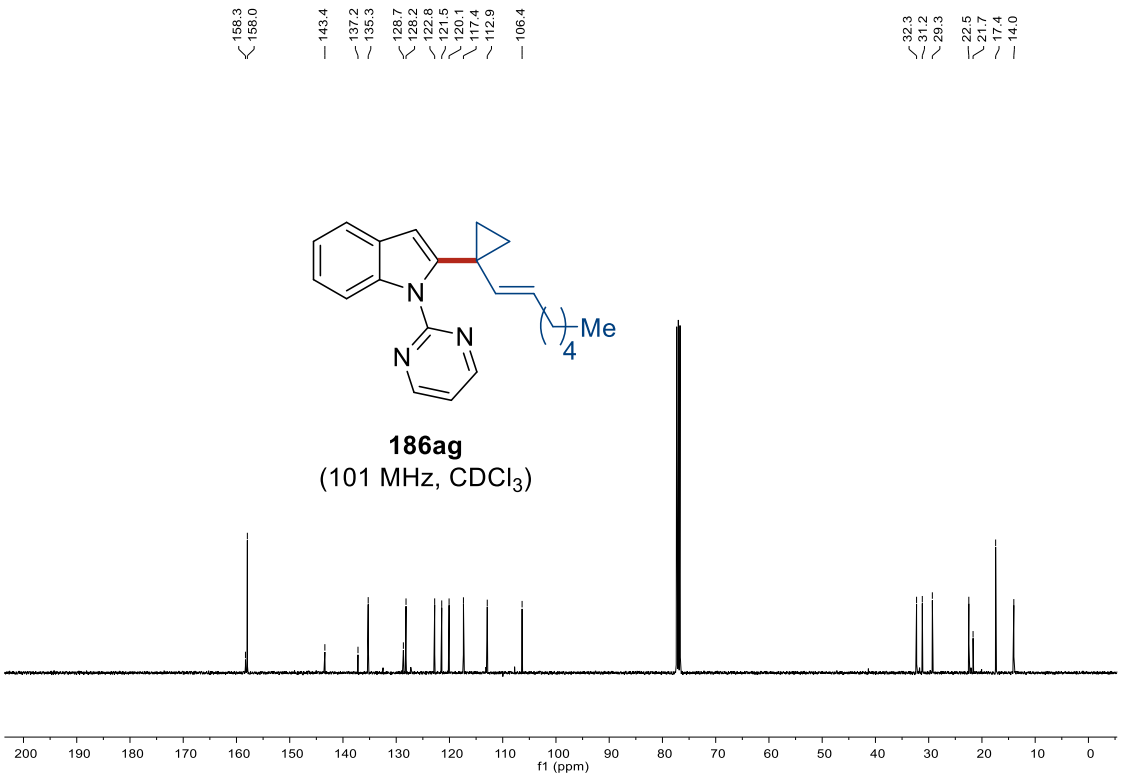

8.80
8.79
8.07
8.05
7.60
7.58
7.28
7.28
7.24
7.22
7.20
7.19
7.18
7.16
7.15
7.14
6.57
5.88
5.82
5.81
5.78
5.17
5.13
5.08
5.03
5.02
4.95
4.95
4.94
2.06
2.00
2.00
1.77
1.75
1.71
1.39
1.37
1.37
1.36
1.35
1.29
1.18
1.11
1.10
1.10
1.05
1.04
1.02
1.00
N
N
N
6
186af
(400 MHz, CDCl3)
2.00
1.00
1.01
1.15
1.03
1.01
1.01
0.84
1.03
2.82
2.03
2.10
4.08
2.09
6.13
10.0 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 -0.5
f1 (ppm)



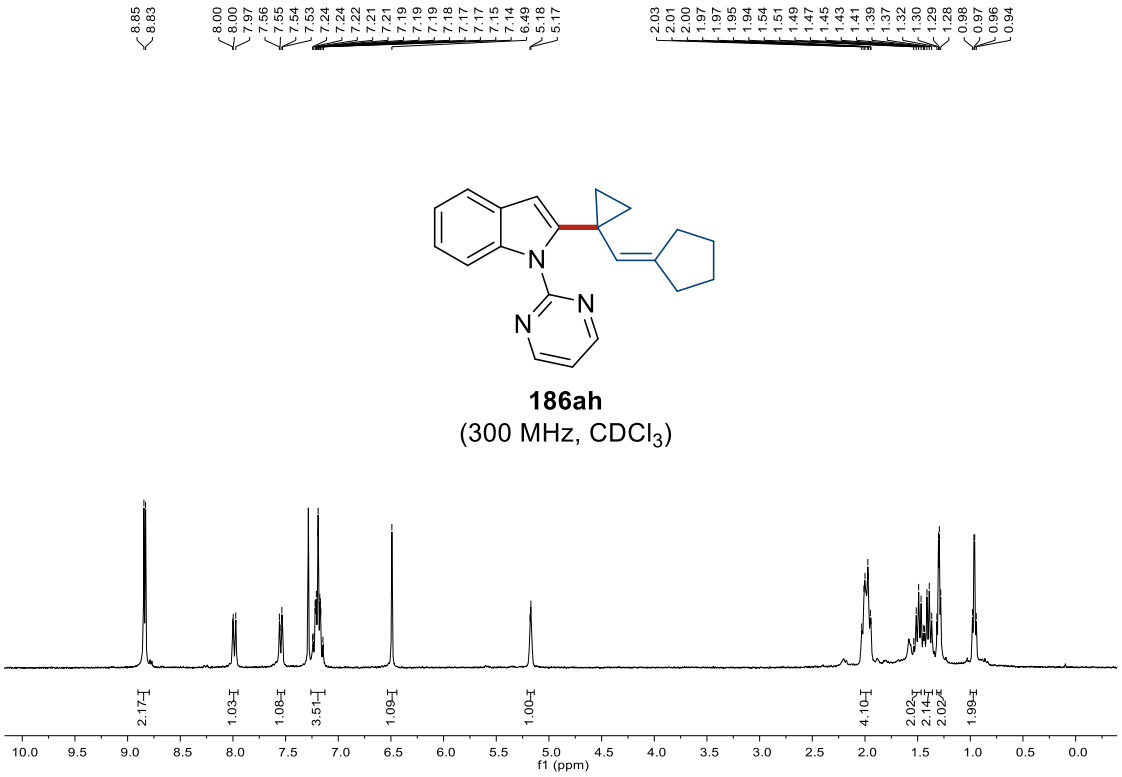
186af
(101 MHz, $CDCl_3$)



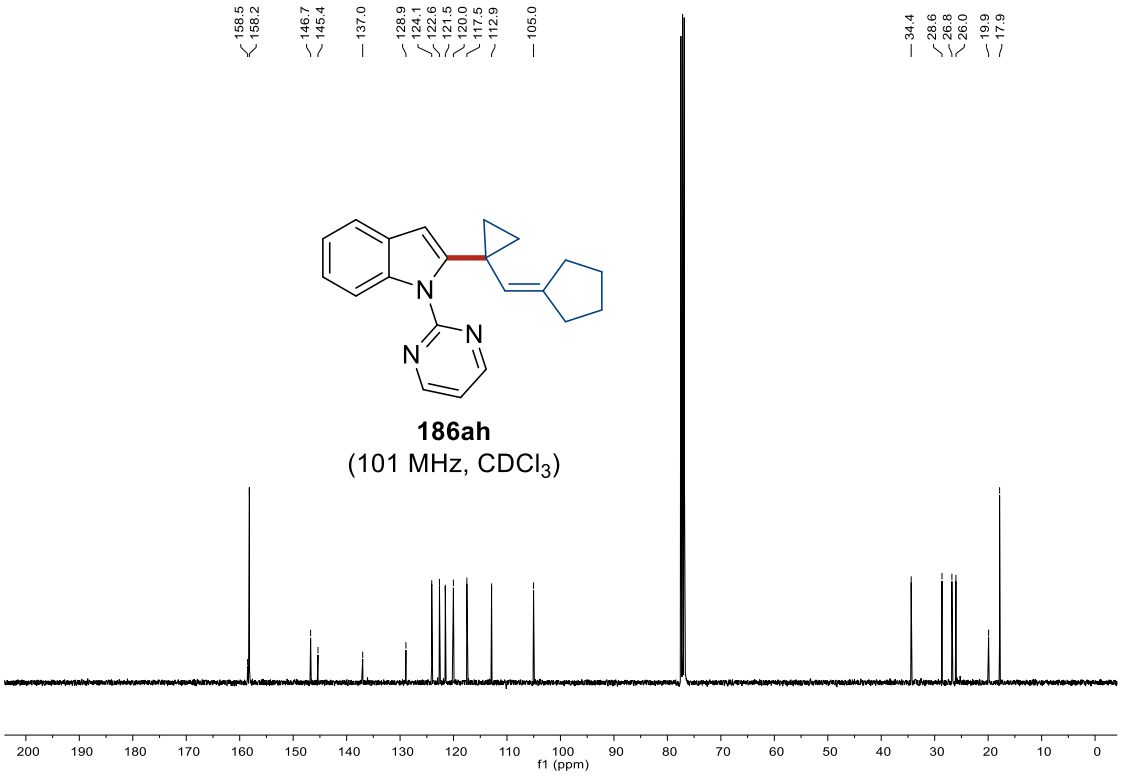
186ag
(300 MHz, $CDCl_3$)



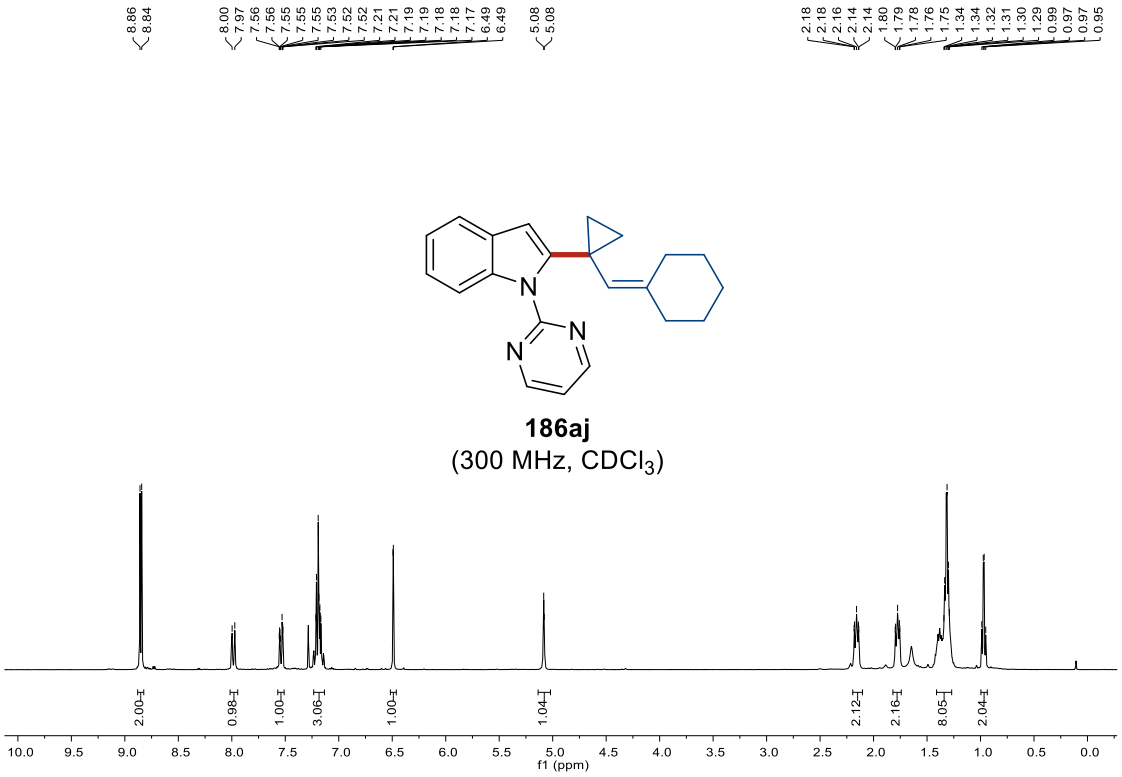
186ag
(101 MHz, $CDCl_3$)



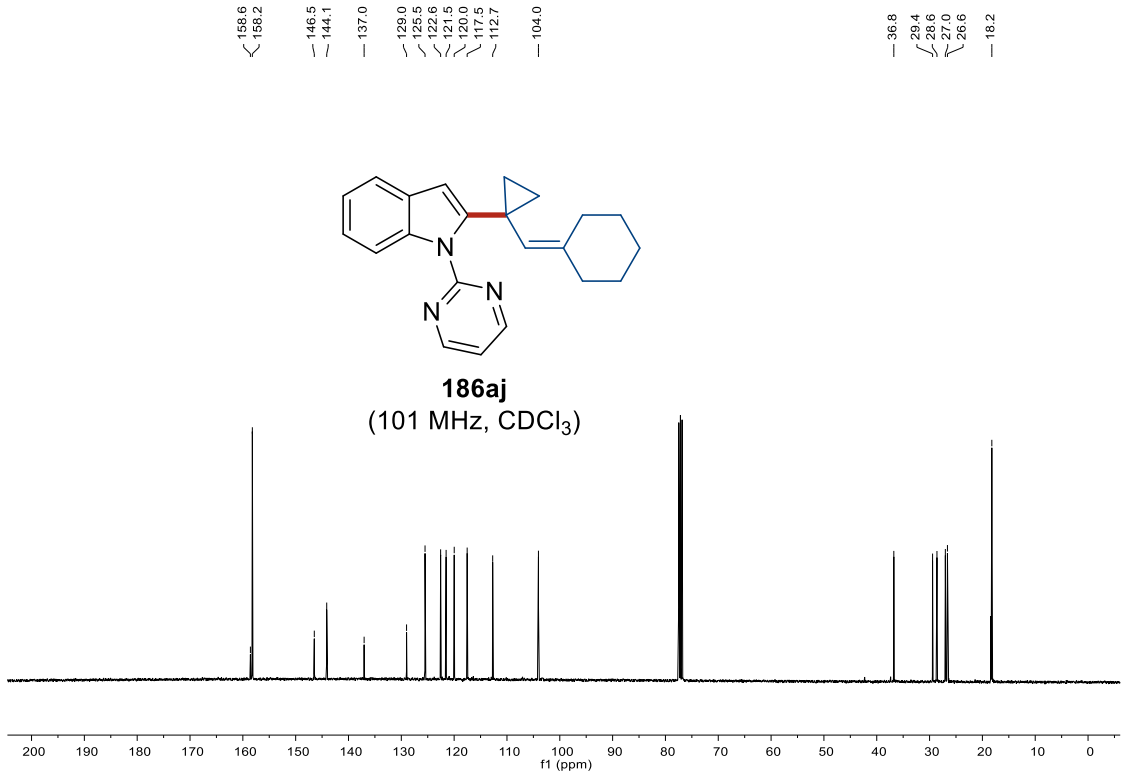
186ah
(300 MHz, $CDCl_3$)

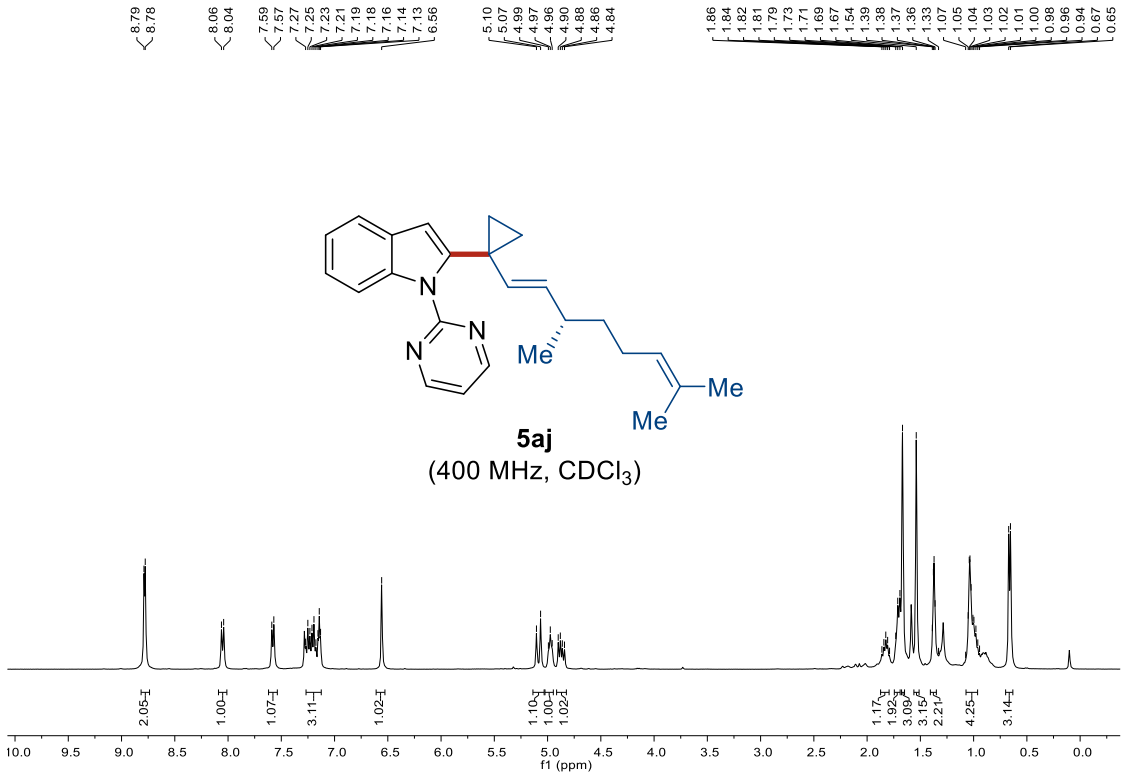


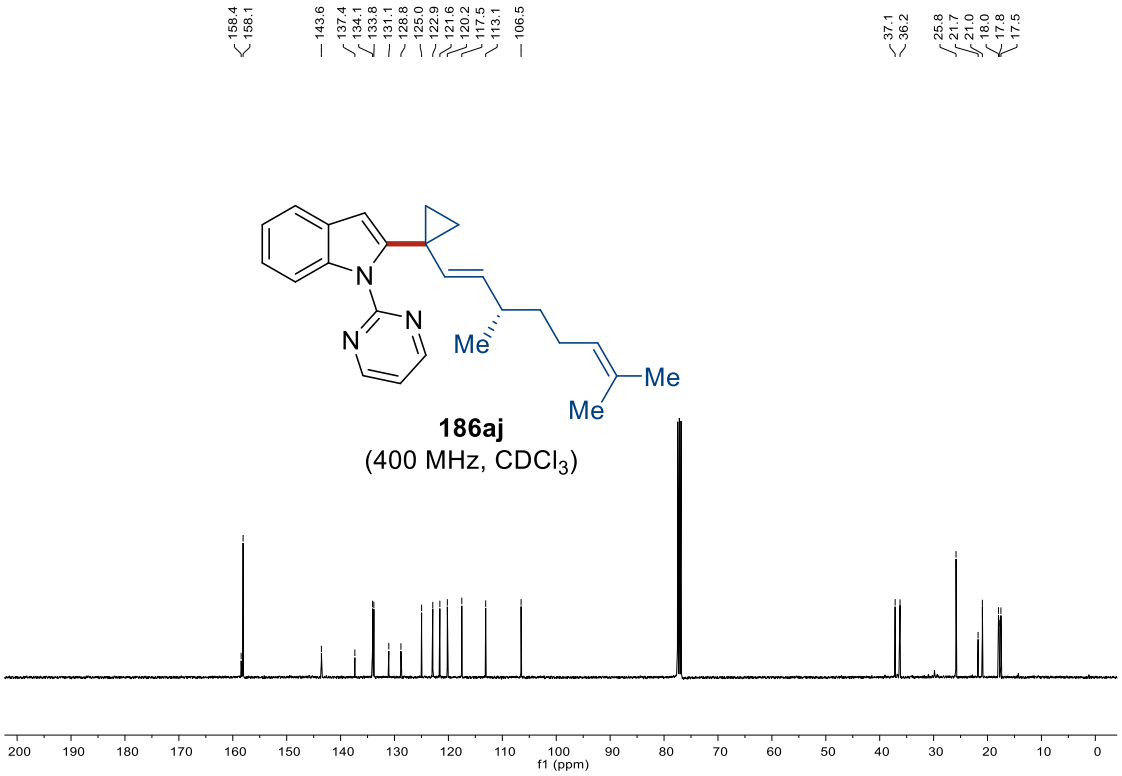
186ah
(101 MHz, $CDCl_3$)



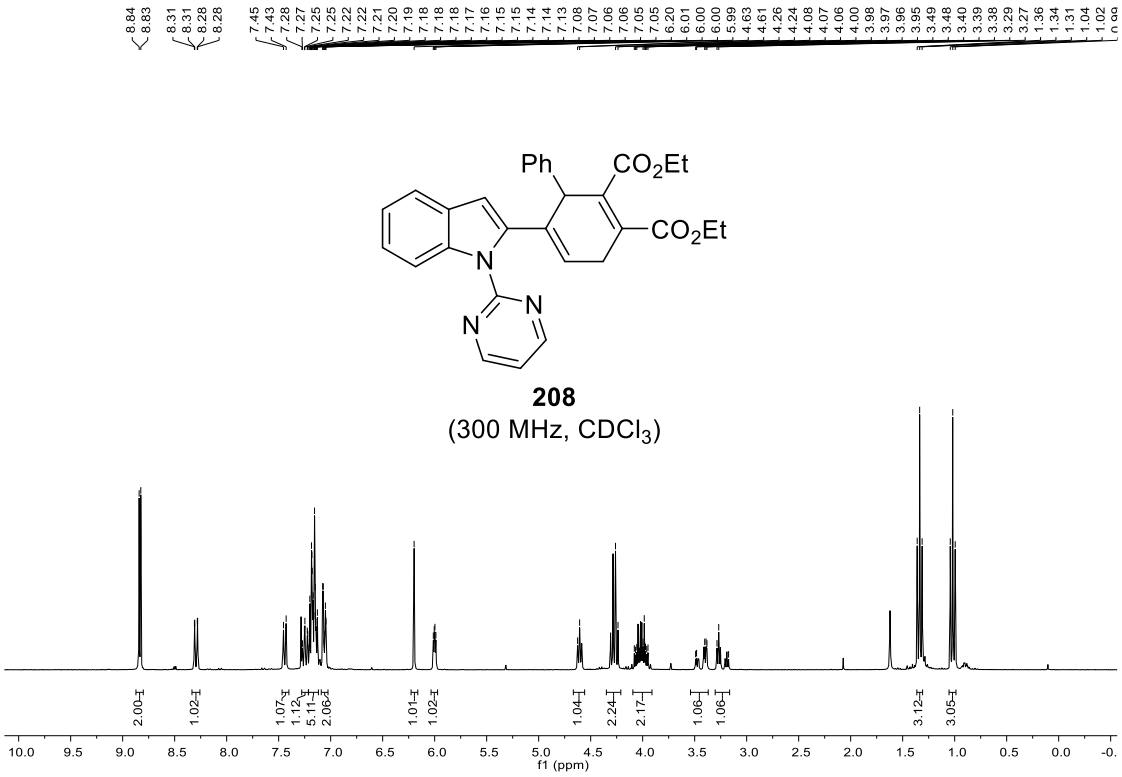
186aj
(300 MHz, $CDCl_3$)


158.6
158.2
146.5
144.1
137.0
129.0
125.5
122.6
121.5
120.0
117.5
112.7
104.0
36.8
29.4
28.6
27.0
26.6
18.2
N
N
N
186aj
(101 MHz, CDCl3)
f1 (ppm)

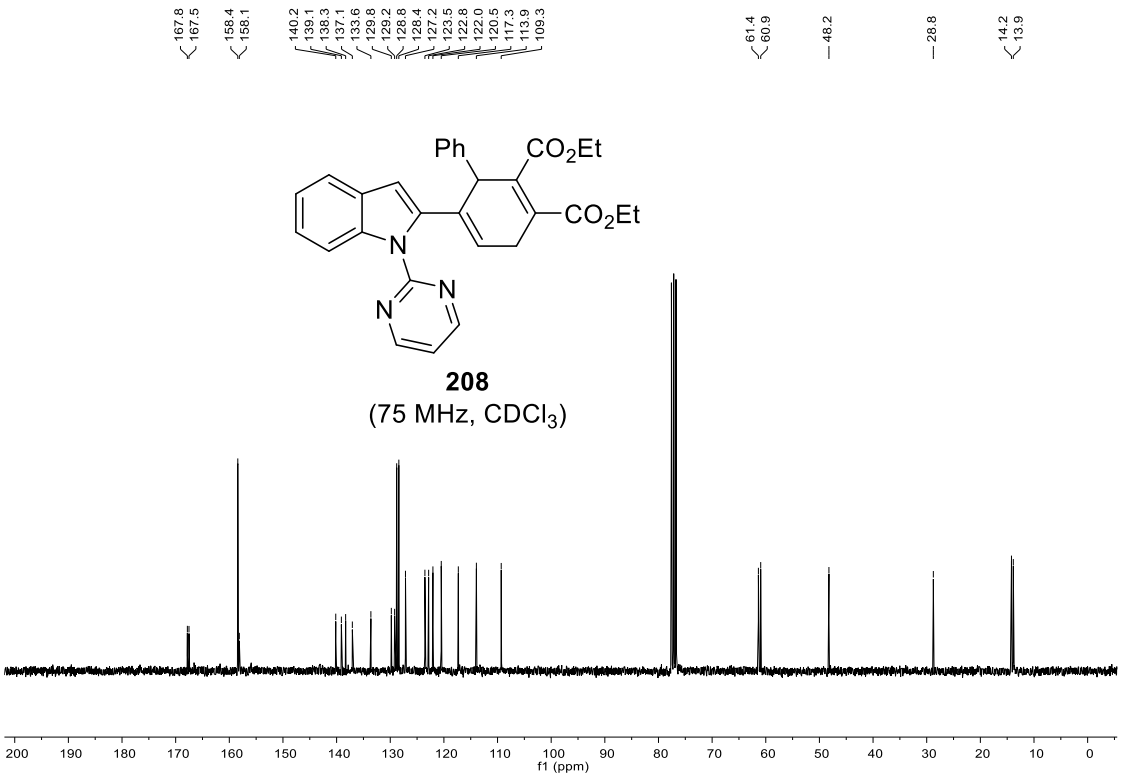

8.79
8.78
8.06
8.04
7.59
7.57
7.27
7.25
7.23
7.21
7.19
7.18
7.16
7.14
7.13
6.56
5.10
5.07
4.99
4.97
4.96
4.90
4.88
4.86
4.84
1.86
1.84
1.82
1.81
1.79
1.73
1.71
1.69
1.67
1.54
1.39
1.38
1.37
1.36
1.33
1.07
1.05
1.04
1.03
1.02
1.01
1.00
0.98
0.96
0.94
0.67
0.65
N
N
N
Me
Me
Me
5aj
(400 MHz, CDCl3)
2.05
1.00
1.07
3.11
1.02
1.10
1.00
1.02
1.17
1.92
3.09
3.15
2.21
4.25
3.14
f1 (ppm)

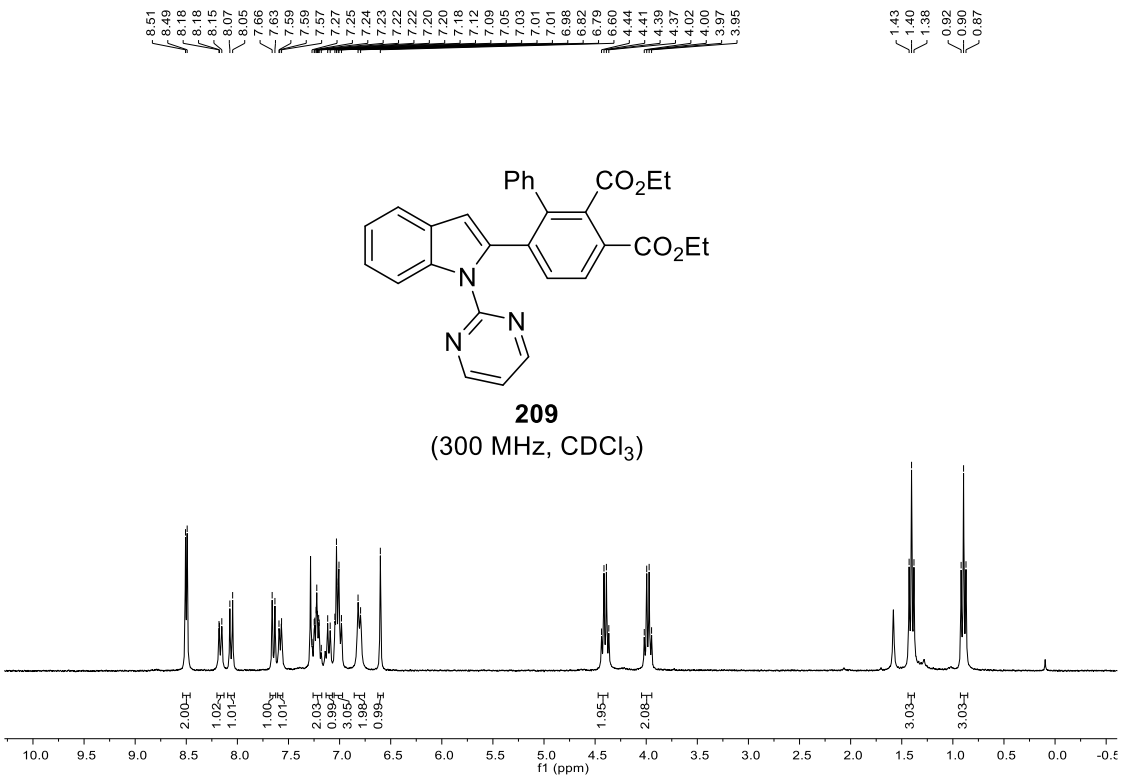


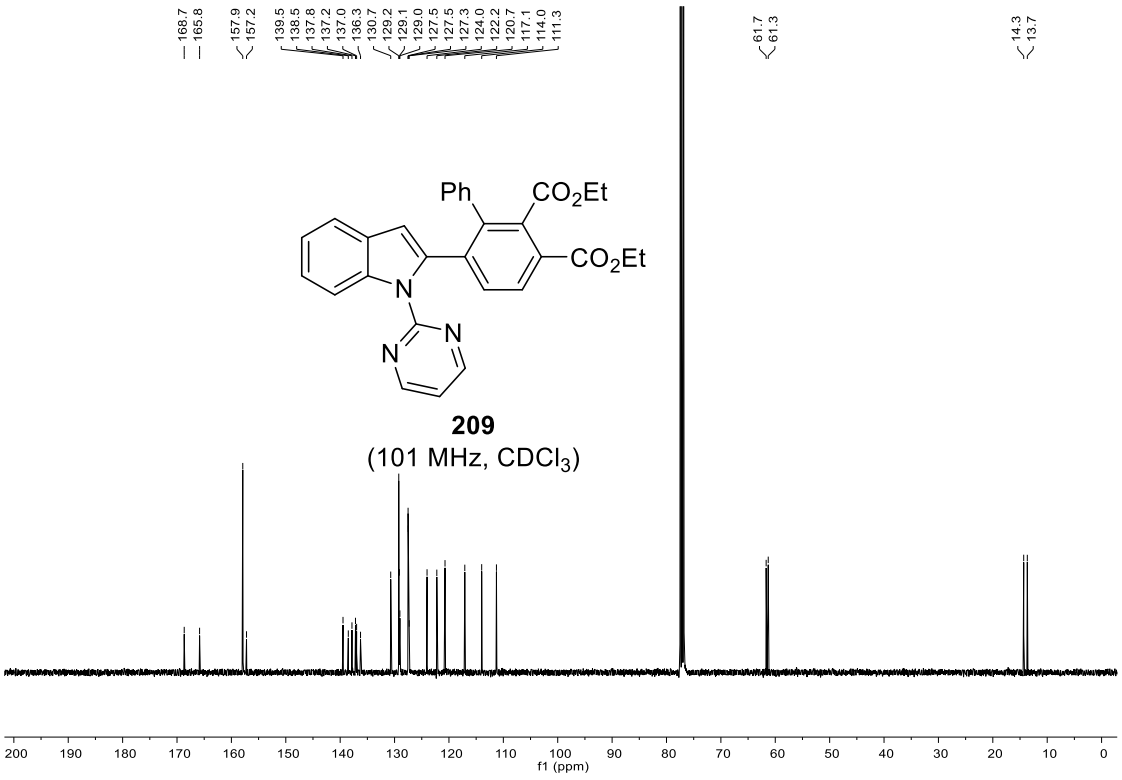
186aj
(400 MHz, $CDCl_3$)



208
(300 MHz, $CDCl_3$)


167.8
167.5
158.4
158.1
140.2
139.1
138.3
137.1
133.6
129.8
129.2
128.8
128.4
127.2
123.5
122.8
122.0
120.5
117.3
113.9
109.3
61.4
60.9
48.2
28.8
14.2
13.9
Ph
CO2Et
CO2Et
N
N
N
208
(75 MHz, CDCl3)
f1 (ppm)


8.51
8.49
8.18
8.18
8.15
8.07
8.05
7.66
7.63
7.59
7.59
7.57
7.27
7.25
7.24
7.23
7.22
7.22
7.20
7.20
7.18
7.12
7.09
7.05
7.03
7.01
7.01
6.98
6.82
6.79
6.60
4.44
4.41
4.39
4.37
4.02
4.00
3.97
3.95
1.43
1.40
1.38
0.92
0.90
0.87
Ph
CO2Et
CO2Et
N
N
N
209
(300 MHz, CDCl3)
2.00
1.02
1.01
1.00
1.01
2.03
0.99
3.05
1.98
0.99
1.95
2.08
3.03
3.03
f1 (ppm)


168.7
165.8
157.9
157.2
139.5
138.5
137.8
137.2
137.0
136.3
130.7
129.2
129.1
129.0
127.5
127.5
127.3
124.0
122.2
120.7
117.1
114.0
111.3
61.7
61.3
14.3
13.7
Ph
CO2Et
CO2Et
N
N
N
209
(101 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

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Curriculum Vitae

Personal Information

Name:	Zhigao Shen
Date of Birth:	05.02.1989
Place of Birth:	Shaodong, Hunan (P. R. China.)
Gender	Male
Nationality	Chinese

Academic Education

10/2016-11/2020	**PhD Candidate in Organic Chemistry** Institut für Organische und Biomolekulare Chemie, Georg-August-Universität Göttingen Supervisor: Prof. Dr. Lutz Ackermann Thesis: C–H Activation by Iron(III), Manganese(II) And Rhodium(III) Catalysis
09/2012-07/2015	**M. Sc. in Pharmaceutical Chemistry** China Pharmaceutical University Supervisor: Prof. Dr. Yisheng Lai Thesis: Chiral Ion-pair Organocatalyst Promotes Highly Enantioselective 3-*exo* Iodo-cycloetherification of Allyl Alcohols
09/2008-07/2012	**B.Sc. in Pharmacy** Department of Pharmacy Yanbian University

Conferences

24-29/09, 2017	Poster of the 1st Summer School on Organic Catalysis for Energy Conversion, Göttingen, Germany.
22-26/06, 2019	The Young Scholar Forum of Xiangtan University, Xiangtan, China
31/08-02/09, 2019	Poster of the 12th International School of Organometallic Chemistry (ISOC12) Collegi Universitari, Camerino, Italy.
27-31/07, 2020	ISCHA Virtual Symposium, Göttingen, Germany.
10-14/11, 2015	16th Tetrahedron Symposium Asia Edition, Shanghai, China.
08-13/09, 2013	The 24th International Society of Heterocyclic Chemistry Congress, Shanghai, China.

Publications

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3. S. R. Yetra,' **Zhigao Shen***,'* H. Wang, L. Ackermann, *Thiocarbonyl-Enabled Ferrocene C–H Nitrogenation by Cobalt(III) Catalysis: Thermal and Mechanochemical*, *Beilstein J. Org. Chem.* **2018**, *14*, 1546–1553. ('Both authors contributed equally)
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11. Z. Xia, J. Hu, **Zhigao Shen**, Q. Yao, W. Xie, *Re_2O_7 Catalyzed Dienone-phenol Rearrangement*, *RSC Adv.* **2015**, *5*, 38499–38502.

Erklärung

Ich versichere, dass ich die vorliegende Dissertation in dem Zeitraum von Oktober 2016 bis November 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 verfasst und keine anderen als die angegebenen Hilfsmittel und Quellen verwendet habe.

Göttingen, den 11.2020