Late-Stage Peptide Diversification via Transition Metal-Catalyzed C–H Activation

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Contents

List of Abbreviations

Ac	acetyl
acac	acetyl acetonate
Ala	alanine
Alk	alkyl
AMLA	ambiphilic metal-ligand activation
Arg	arginine
Asn	asparagine
Asp	Aspartic acid
aq.	aqueous
Ar	aryl
atm	atmospheric pressure
BHT	2,6-*di*-*tert*-butyl-4-methylphenol
BIES	base-assisted internal electrophilic substitution
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
Bu	butyl
Bz	benzoyl
calc.	calculated
cat.	catalytic
CMD	concerted-metalation-deprotonation
conv.	conversion
Cp*	cyclopentadienyl
Cy	cyclohexyl
Cys	cysteine
δ	chemical shift
d	doublet
DCE	1,2-dichloroethane
dd	doublet of doublet

DFT	density functional theory
DG	directing group
DME	dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone
dt	doublet of triplet
EI	electron ionization
equiv	equivalent
ES	electrophilic substitution
ESI	electronspray ionization
Et	ethyl
FG	functional group
Fmoc	fluorenylmethoxycarbonyl
g	gram
Gln	glutamine
Gly	glycine
Glu	glutamic acid
GC	gas chromatography
h	hour
Hal	halogen
Het	hetero atom
Hept	heptyl
Hex	hexyl
His	histidine
HPLC	high performance liquid chromatography
HR-MS	high resolution mass spectrometry
Hz	Hertz
i	*iso*

IR	infrared spectroscopy
IES	internal electrophilic substitution
Ile	isoleucine
J	coupling constant
KIE	kinetic isotope effect
L	ligand
Leu	leucine
Lys	lysine
m	*meta*
m	multiplet
M	molar
$[M]^+$	molecular ion peak
Me	methyl
Mes	mesityl
Met	Methionine
mg	milligram
MHz	megahertz
min	minute
mL	milliliter
mmol	millimol
M. p.	melting point
MS	mass spectrometry
m/z	mass-to-charge ratio
NCTS	*N*-cyano-4-methyl-*N*-phenyl benzenesulfonamide
NMTS	*N*-cyano-*N*-(4-methoxy)phenyl-*p*-toluenesulfonamide
NMP	*N-methylpyrrolidinone*
NMR	nuclear magnetic resonance
o	*ortho*
OPV	oil pump vacuum

p	*para*
Ph	phenyl
Phe	phenylalanine
PMP	*para*-methoxyphenyl
Piv	pivaloyl
ppm	parts per million
Pr	propyl
Pro	proline
PTSA	*p*-Toluenesulfonic acid
py	pyridyl
pym	pyrimidine
pyr	pyrazol
q	quartet
RT	room temperature
s	singlet
sat.	saturated
Ser	serine
SPS	solvent purification system
t	*tert*
t	triplet
T	temperature
TFE	2,2,2-trifluoroethanol
THF	tetrahydrofuran
Thr	threonine
TLC	thin layer chromatography
TM	transition metal
TMP	2,2,6,6-tetramethylpiperidine
TMS	trimethylsilyl
Trp	tryptophan

Ts	*para*-toluenesulfonyl
TS	transition state
Tyr	tyrosine
Val	valine
wt%	weight by volume

1. Introduction

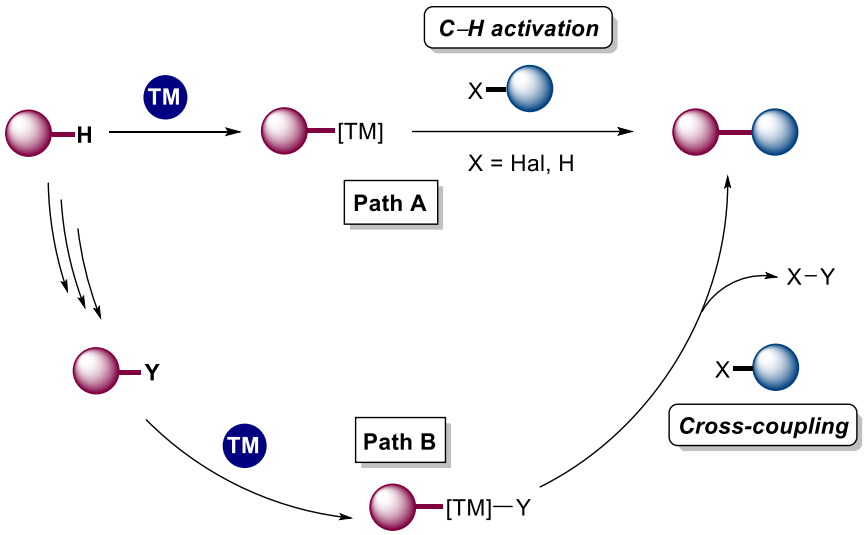
The origin of life is based on carbon, since it constitutes the framework of all biomolecules.[1] The biological events of life rely on intricate functions of these organic molecules, owing to their structural complexity. This renders organic chemistry an important discipline to study life sciences as it is highly related to organic molecule interactions. It furthermore arms chemists for creating novel organic molecules to thus interfere life activities on behalf of human health. To this end, the development of novel and efficient synthetic strategies is highly desired. A brilliant strategy to access value-added organic molecules is the direct transformation of omnipresent C–H bonds to versatile functional groups. Moreover, as one of the twelve green chemistry principles,[2] catalysis[3] has proven to be a powerful tool for performing C–H functionalization in a sustainable and efficient manner.

1.1 Transition Metal-Catalyzed C–H Functionalizations

The development of highly efficient transition metal-catalyzed organic reactions for carbon–carbon and carbon–heteroatom bond formations had a huge impact on organic synthesis. Early examples for this kind of transformations are the copper-catalyzed coupling reactions developed by Glaser,[4] Goldberg[5] and Ullman.[6] In recent decades, a variety of transition metal-catalyzed cross couplings were developed for a broad range of applications in organic syntheses, for instance, Kumada-Corriu-,[7] Mizoroki-Heck-,[8] Negishi-,[9] Stille-,[10] Hiyama-,[11] Suzuki-Miyaura-,[12] and Sonogashira-Hagihara-reactions.[13] These discoveries proved highly practical in the pharmaceutical industry and natural product synthesis.[14] These achievements featured the transition metal-catalyzed cross-couplings elegant strategy for modern organic synthesis, awarded with the Nobel Prize for Chemistry in 2010 for Professors Heck, Negishi and Suzuki.

Although cross-coupling reactions have enormously contributed to confronting problems in organic synthesis, their drawback of largely relying on lengthy substrate prefunctionalizations, such as the preparation of organic halides and organometallic reagents, remain a major limitation.[15] Many of these reagents are sensitive towards air and moisture, and difficult to synthesize, and their preparation generates often toxic byproducts. In contrast, direct C–H

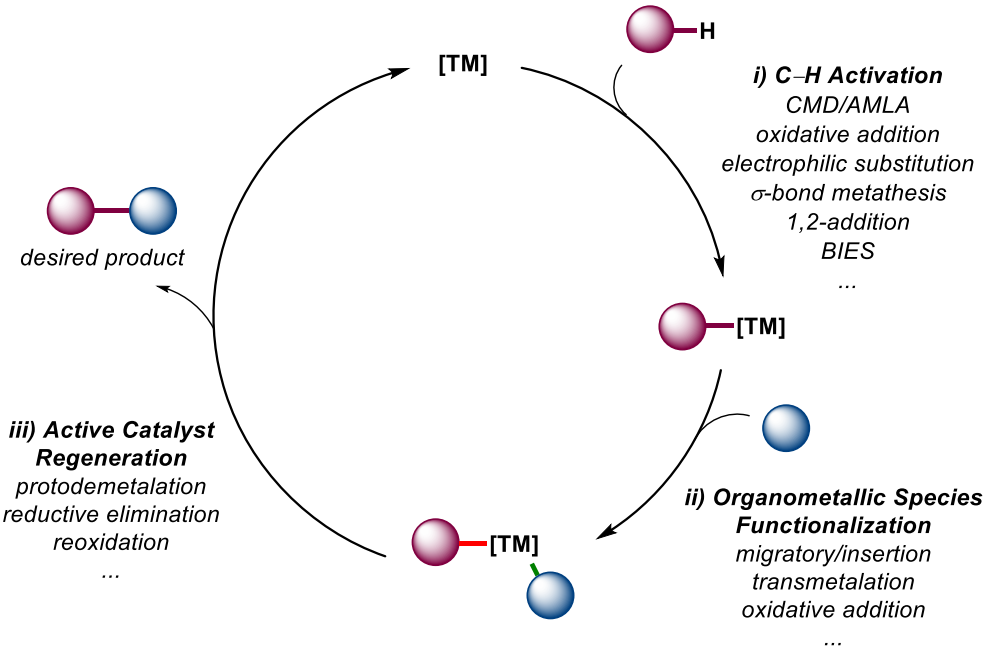
activations[16] emerged as an atom-[17] and step-economic[18] strategy for environmentally friendly organic synthesis (Scheme 1.1.1). Besides widely used 4d and 5d metal catalysis, earth-abundant 3d metal-catalyzed C–H activation[19] offers further advantages in terms of sustainability and resource-economy. Thus, the development of manganese-catalyzed C–H functionalizations[20] has made among others great contribution to sustainable organic transformations.



Scheme 1.1.1 Transition metal-catalyzed C–H functionalization *vs* cross-coupling.

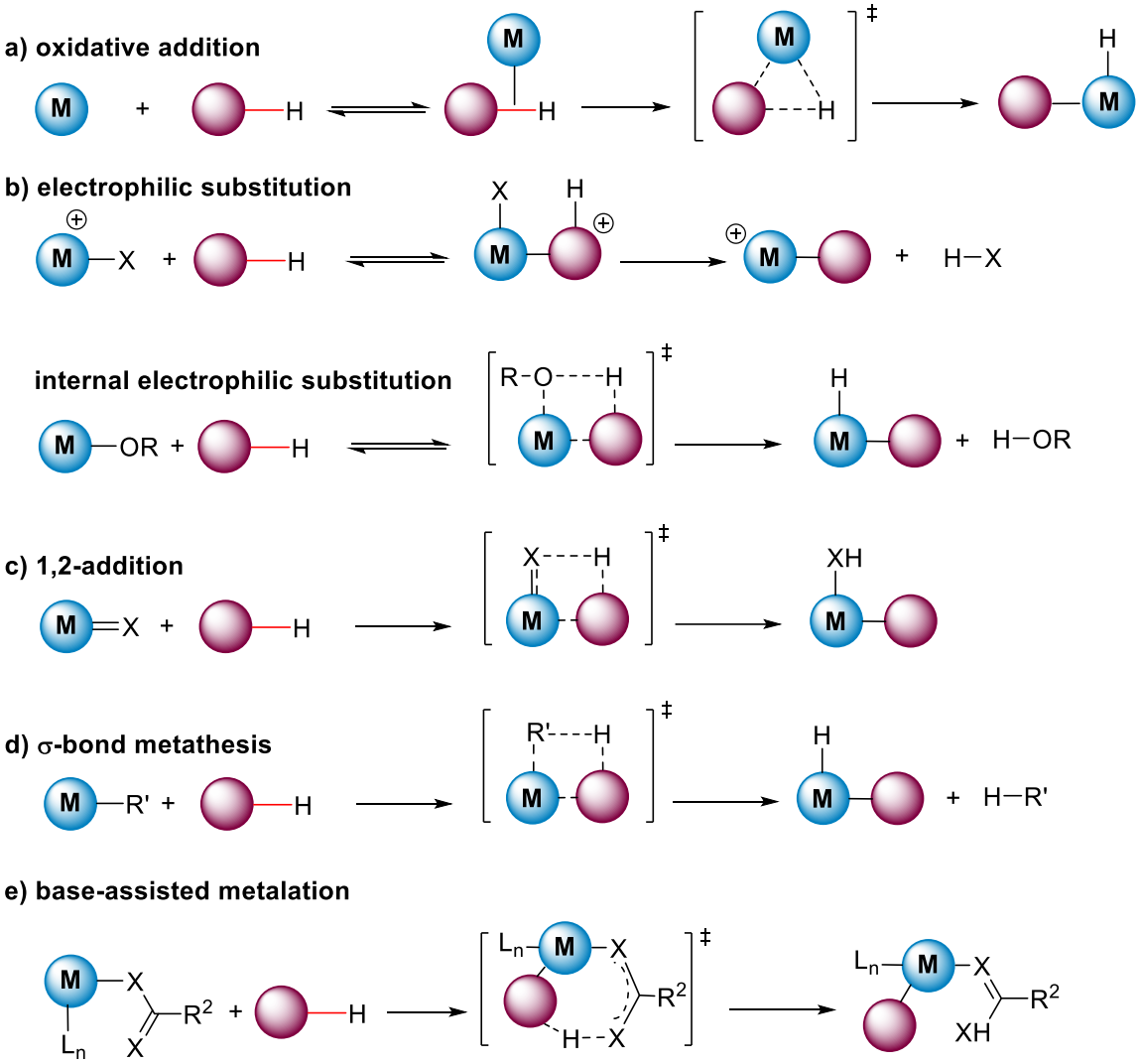
1.1.1 Mechanistic Manifolds

In general, the catalytic cycle of transition-metal catalyzed C–H functionalizations is constituted of 3 main steps: i) C–H activation; ii) organometallic species functionalization; iii) regeneration of the active catalyst (Scheme 1.1.1.1). In some cases, an oxidant is required to achieve a catalytic reaction.



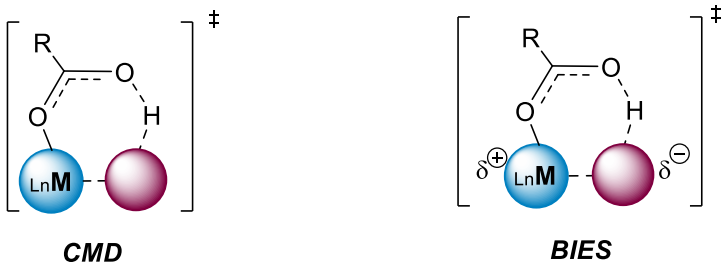
Scheme 1.1.1.1. General catalytic cycle of transition metal-catalyzed C–H activation.

For the development of novel transition-metal catalyzed C–H functionalizations, a detailed understanding of the reaction mechanism is of utmost importance. C–H activation is usually the key step of these reactions, and mechanistic insights including computational studies assisted in classifying the nature of the C–H cleavage[21] in distinct pathways: a) oxidative addition,[22] b) electrophilic substitution,[23] internal electrophilic substitution (IES),[24] c) 1,2-addition[25], d) σ-bond metathesis [26] and e) base-assisted C–H cleavage[27] (Scheme 1.1.1.2). C–H cleavage by oxidative addition generally takes place with electron-rich complexes of late transition metals in low oxidation states,[27] whereas electrophilic substitution was observed for cationic complexes of late transition metals and involves an electrophilic attack of the metal on the carbon. For alkoxide bases, internal electrophilic substitution proceeds by electrophilic attack of the metal and a deprotonation through a highly strained, four-membered transition state. 1,2-addition is a feasible pathway for early transition metals and generally occurs via a [2σ + 2π] reaction. Similarly, σ-bond metathesis is also a possible mechanism for early metals, which is a commonly proposed pathway.



Scheme 1.1.1.2. Predominant mechanistic pathways for C–H activation.

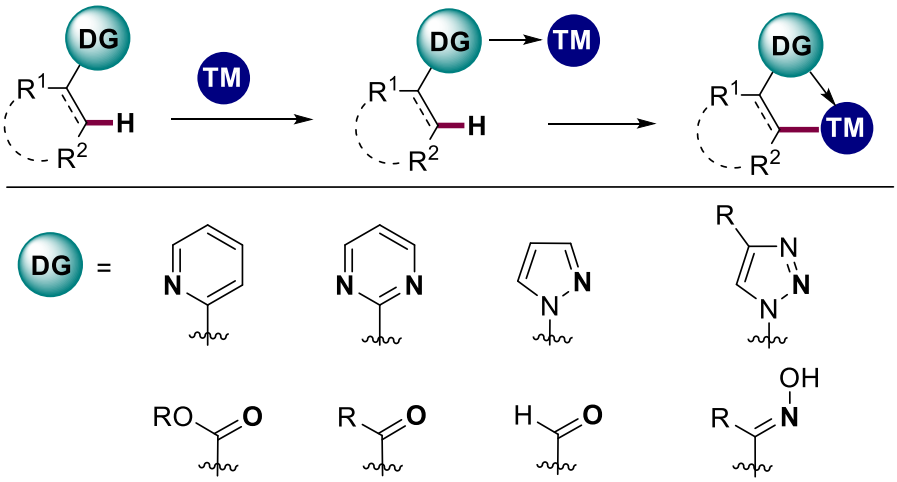
In addition to these pathways, more recent studies also revealed the existence of base-assisted C–H metalation processes (Scheme 1.1.1.3). The CMD[28] (concerted metalation deprotonation) or AMLA[29] (ambiphilic metal-ligand activation) processes take place *via* a six-membered transition state, describing the interaction of the C–H bond with the transition metal and carboxylate-ligand. This process predominantly occurs with electron-poor substrates at the kinetically most acidic C–H bond. Recently, more reports have explored an electrophilic substitution type C–H activation by carboxylate additives, which was described as base-assisted internal electrophilic substitution (BIES).[30] In contrast to CMD/AMLA mechanisms, BIES is generally more favorable for electron-rich substrates, and the selectivity of BIES-type C–H activation is not controlled by kinetic C–H acidity.[30-31]



Scheme 1.1.1.3. Comparison of transition state structures in base-assisted metalation.

1.1.2 Selectivity Control of C–H Functionalizations

Although C–H activation has enormously contributed to modern organic synthesis, it is challenged by the full control of the regioselectivity in modifications of complex molecules, especially due to the existence of many C–H bonds with similar bond dissociation energies within one compound. Weakly-coordinating[32] and removable[33] directing groups have been developed for elegantly addressing this problem by precisely controlling the site-selectivities, or directly employing internal directing groups. A Lewis basic atom of the directing group coordinates to the metal, thus activating the proximal C–H bond and further facilitating the key C–H activation step selectively (Scheme 1.1.2.1).



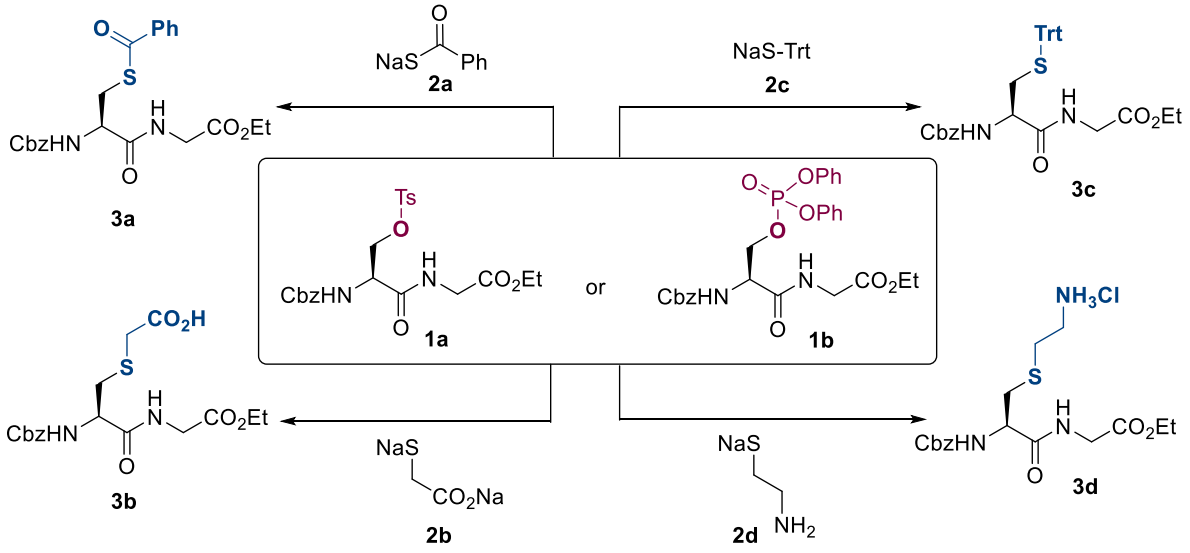
Scheme 1.1.2.1. Representative directing groups for C–H activation.

1.2 Traditional Chemical Late-Stage Peptide Modifications

As a class of important biomolecules, peptides are of key importance for various research areas, such as proteomics, diagnostics and therapeutics.[34] Novel peptides provide a useful

toolbox for exploring biological events, designing pharmaceuticals and evolving new proteins. Compared with their parental structures, unnatural peptides largely feature improved biological and pharmacokinetic properties,[35] thus making peptide modifications an important subject for interdisciplinary studies. Peptide modifications can be accomplished in a biosynthesis approach by proteins, which is referred to as post-translational modification (PTM).[36] Despite the diversity of peptides derived from PTM and the great success of solid phase peptide synthesis (SPPS) for peptide assembly,[37] peptide modifications remain to be highly restricted due to limitations of the respective chemical transformations. Valuable peptide modifications usually focus on mimicking PTM, such as acylation, methylation, phosphorylation, sulfation, ubiquitination and glycosylation. Additionally, peptide modifications should ideally be mild, efficient, non-toxic and tolerant of aqueous conditions to ensure biocompatibility.

An early example of chemical peptide modifications was demonstrated by Wilchek and coworkers (Scheme 1.2.1).[38] They performed nucleophilic substitutions of *OH*-activated serine **1** with thionucleophiles **2**, thus generating non-native cysteine derivatives **3** (Scheme 1.2.1).

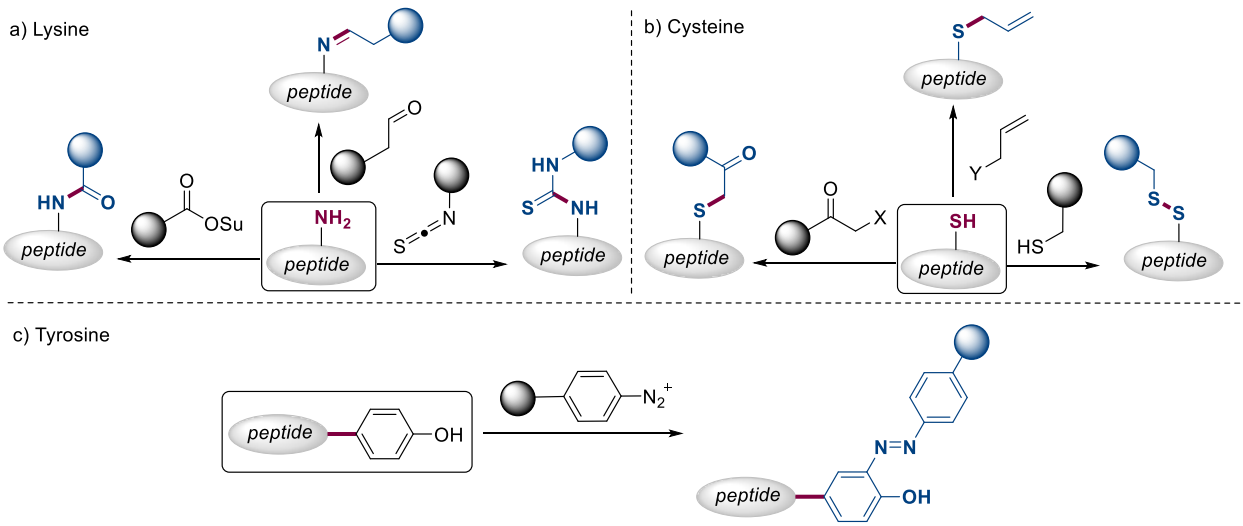


Scheme 1.2.1. Peptide modification by nucleophilic substitution.

Afterwards, numerous peptide and protein modifications were realized by site-specific chemical transformations of amino acids,[39] thereby enabling a wealth of disconnections

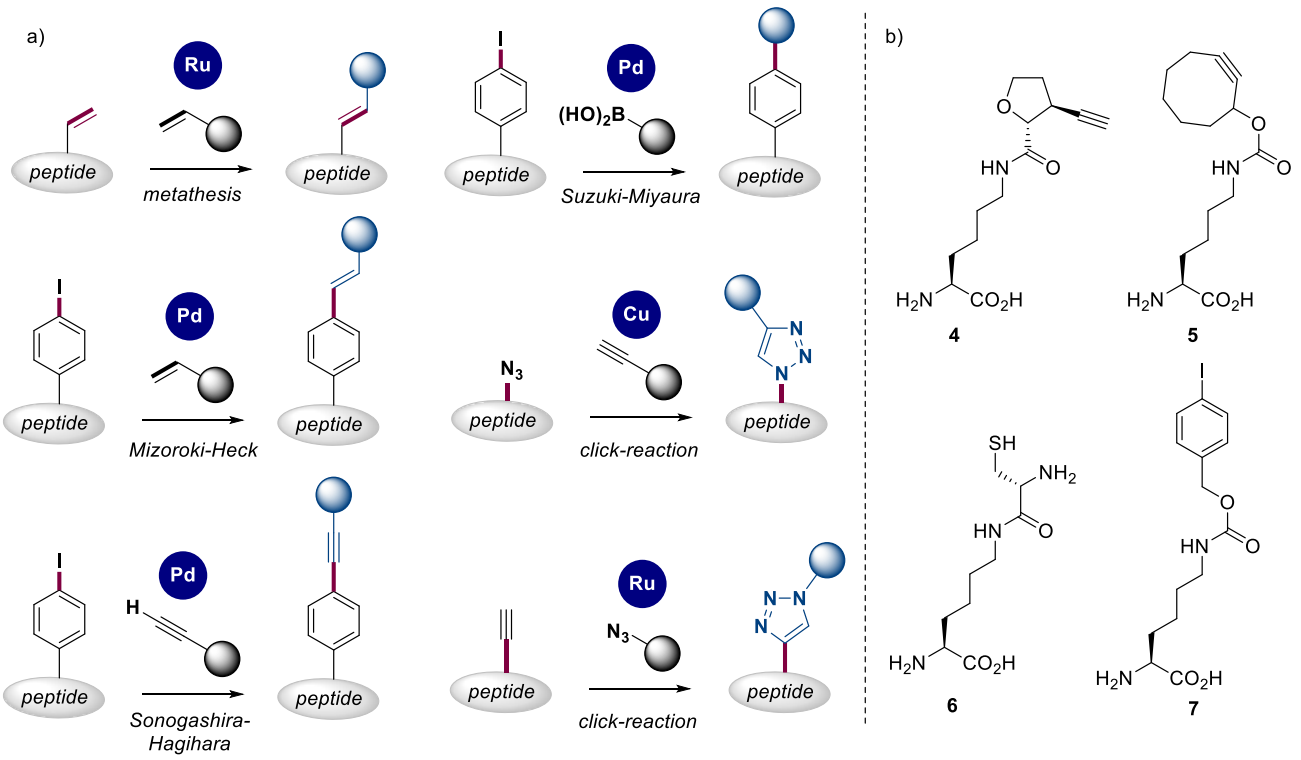
between peptides/proteins and functional groups in a positional selective fashion (Scheme 1.2.2).

Among these approaches, nucleophilic or electrophilic reactions on various amino acid residues[40] have especially contributed to this field. For example, the nucleophilic amine group of lysine can be easily reacted with electrophiles, e.g. in esterifications with activated carbonyls, condensations with carbonyls as well as Michael additions with thiocyanates (Scheme 1.2.2a). The *SH*-group of cysteine is more nucleophilic and can be transformed through nucleophilic substitutions with activated alkyl halides or through oxidations with thiols to form disulfides (Scheme 1.2.2b). Furthermore, diazonium salts are also employed for peptide modifications by electrophilic substitutions on tyrosine residues, thereby making use of the activated aromatic ring of tyrosine (Scheme 1.2.2c).



Scheme 1.2.2. Peptide modification at lysine, cysteine and tyrosine.

Besides nucleophilic and electrophilic substitution reactions for peptide modifications, transition metal catalysis has also been employed for peptide transformations in a “tag-and-modify” strategy.[41] Numerous reactions were thus employed for peptide modifications, such as click-reactions,[42] Staudinger ligations,[43] olefin metathesis[44] and cross-coupling reactions[14c, 45] (Scheme 1.2.3a). To prefunctionalize the target peptides, lysine is widely used as an anchor for the installation of reactive scaffolds, followed by the encoding of the formed unnatural lysine into transformable peptides (Scheme 1.2.3b).



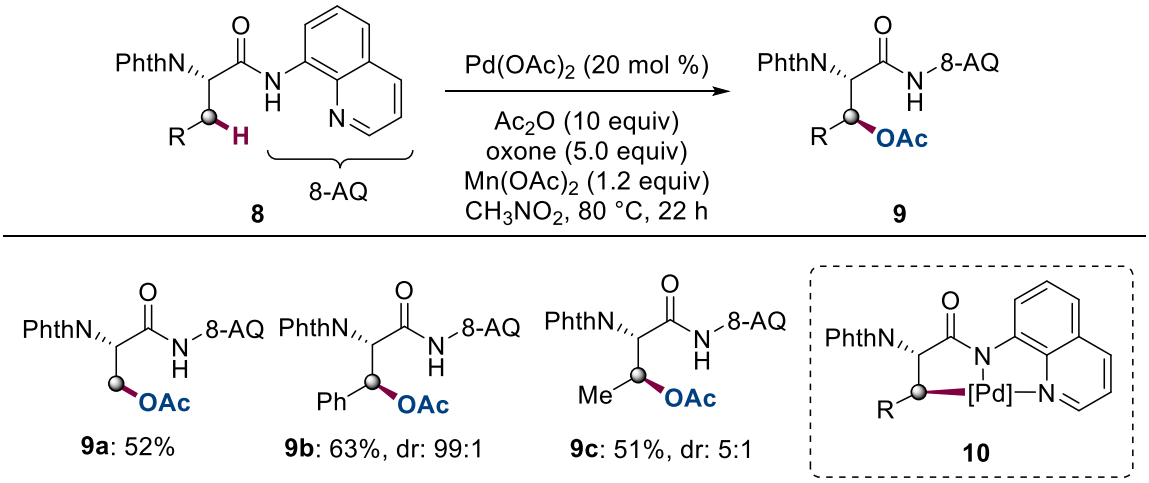
Scheme 1.2.3. a) Transition metal-catalyzed peptide modification strategies. b) Examples of genetically encoded lysine-based amino acids for biocompatible reactions.

1.3 Palladium-Catalyzed C–H Activations for Late-Stage Peptide Diversifications

Peptide modifications by classic reactions including enzymatic resolution, elaborate on asymmetric syntheses,[46] as well as transition metal-catalyzed cross-coupling reactions,[47] both of which typically require lengthy prefunctionalizations. In order to address these limitations, direct C–H activation has been successfully applied for amino acid and late-stage peptide functionalizations[48] and shows significant advantages in terms of: i) site-selectivity control, ii) racemization-free conditions, and iii) effective catalytic turnover. Therefore, C–H activation reactions for transformations of amino acids and peptides contributes productively to drug discovery and pharmaceutical industries. Until now, palladium catalysis represents the most widely used strategy for direct peptide diversifications compared to other transition metals.

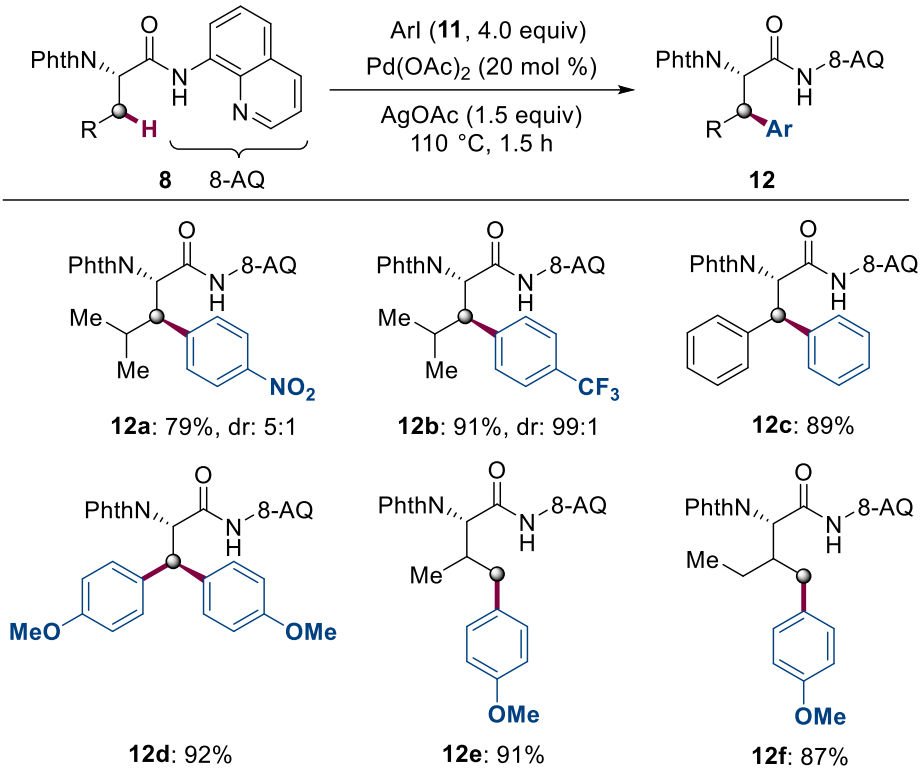
1.3.1 Early Examples of Simple Amino Acid C–H Activations

An early example of functionalizations of amino acids by C–H activation was developed by Corey and coworkers.[49] They reported on a palladium-catalyzed *β*-hydroxylation of the *N*-phthaloyl-substituted amino acids including leucine, alanine, homoalanine and phenylalanine (Scheme 1.3.1.1). The employed bidentate[50] chelation-assisted strategy was earlier developed by Daugulis.[51] Among a variety of directing groups, the 8-aminoquinoline (8-AQ) was found to be optimal for C–H oxygenations.[52] In this reaction, the oxidation of $Mn(OAc)_2$ to Lewis-acidic $Mn_3O(OAc)_7$ proved crucial for achieving the C–H activation,[49] along with $Pd(OAc)_2$ as the catalyst to give good yields and excellent *trans*-diastereoselectivities via intermediate **10**.



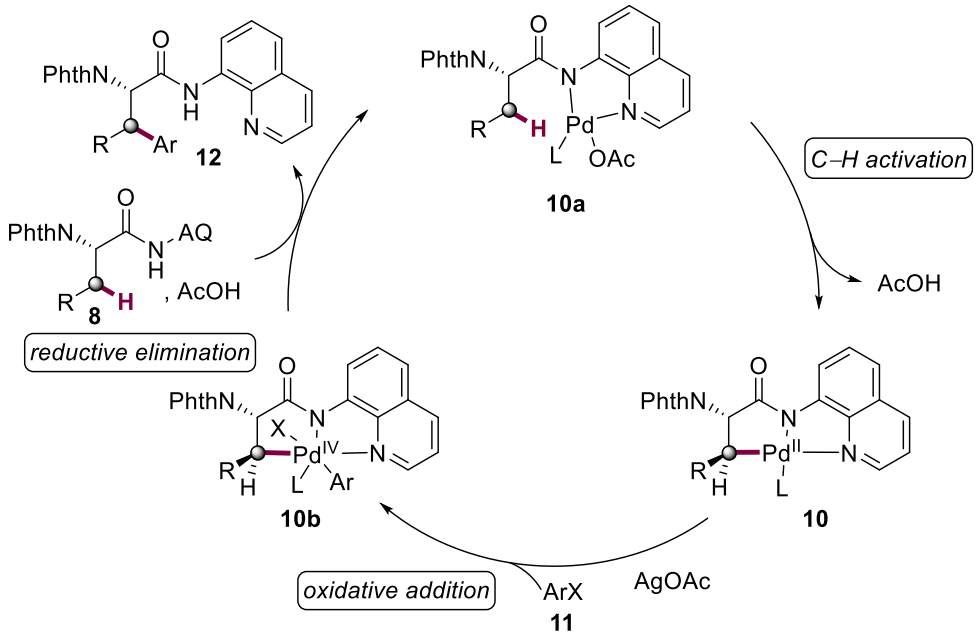
Scheme 1.3.1.1 C–H acetoxylation of amino acids **8**.

With the bidentate strategy,[51] Corey and coworkers further developed stereoselective arylation reactions of amino acid derivatives,[49] employing iodides as the arylating reagent (Scheme 1.3.1.2). The *β*-arylation was efficiently applied to the modification of leucine and phenylalanine derivatives and both electron-rich and electro-poor aryl iodides **11** were tolerated, yielding the products in high yield and diastereoselectivity. Two-fold *β*-arylation occurred for alanine derivatives with **12d** as the product, while for valine and isoleucine derivatives with a tertiary $C(sp^3)$–H bond in the *β*-position the reaction took place at the *γ*-position (**12e**, **12f**).



Scheme 1.3.1.2. Palladium-catalyzed C(sp^3)–H arylation of amino acids **1**.

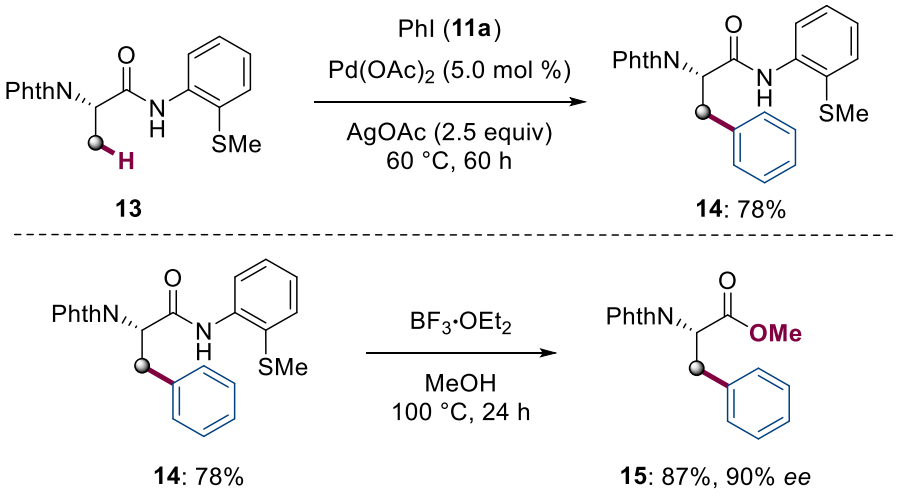
The proposed mechanism for the C(sp^3)–H arylation of alanine derivative **1** with the bidentate directing group 8-AQ generally involves a Pd(II)/Pd(IV) pathway (Scheme 1.3.1.3). Carboxylate assisted C–H palladation results in the formation of the *trans*-palladacycle **10** as the key intermediate with high diastereoselectivity.[27] Then, the oxidative addition of aryl halide **11** takes place to deliver palladium(IV)-intermediate[53] **10b**. Reductive elimination with retention of the configuration by ligand exchange follows, thus generating the arylated amino acid **12** and regenerating active catalyst **10a**.



Scheme 1.3.1.3. Proposed mechanism for palladium-catalyzed C(sp^3)–H arylation.

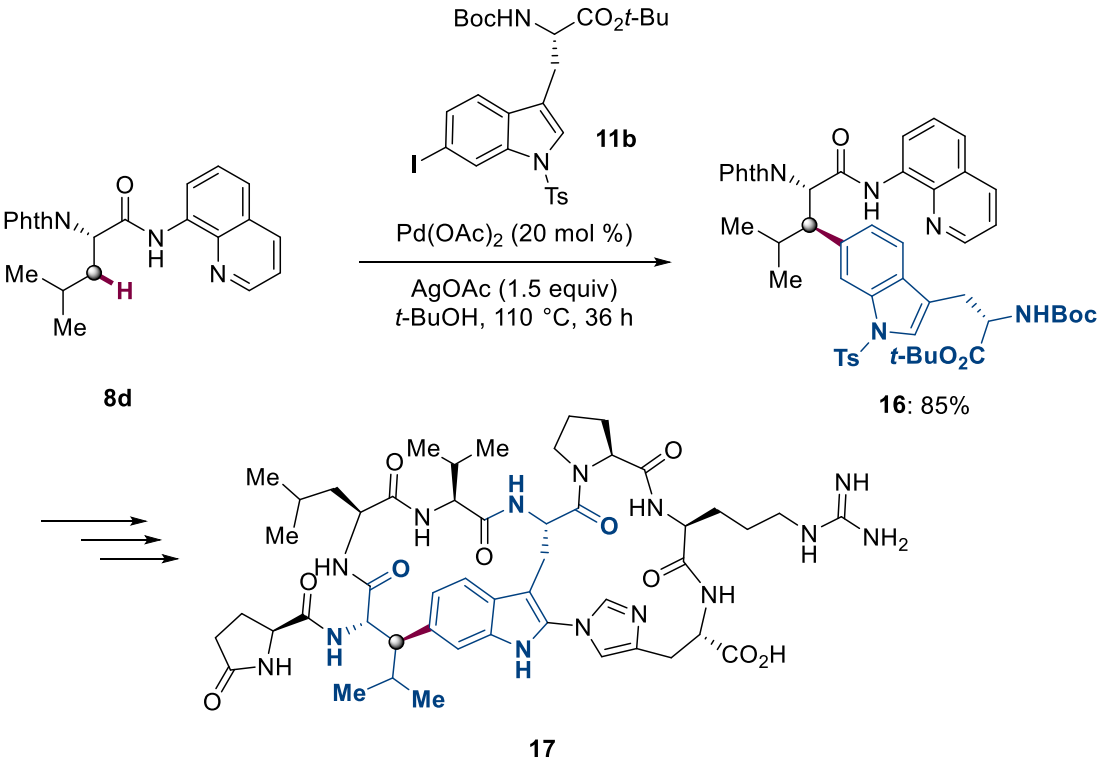
1.3.2 Simple Amino Acid C—H Activations

In addition to 8-aminoquinoline, the use of 2-thiomethylaniline as a directing group was reported by Daugulis and coworkers[54] for the mono-arylation reaction of alanine derivatives. Importantly, 2-thiomethylaniline could be removed in high yield without significant loss of the enantiomeric excess. (Scheme 1.3.2.1).



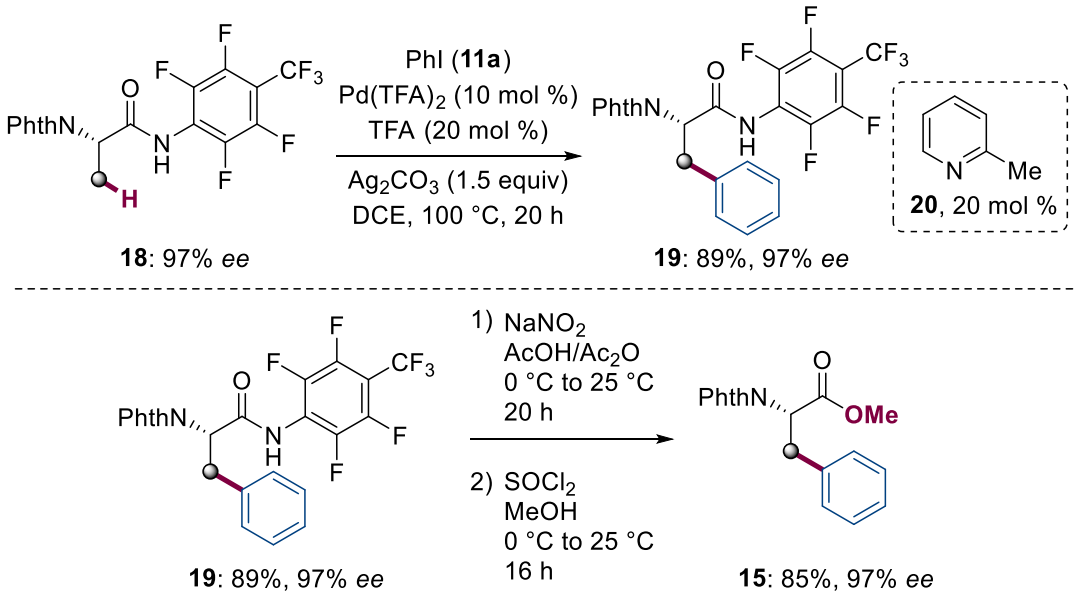
Scheme 1.3.2.1. Palladium-catalyzed C(sp^3)–H arylation of amino acid **13**.

The power of the C(sp^3)–H activation strategy was also demonstrated by Chen and coworkers with the development of a diastereoselective indolylation[55] of leucine derivatives, which formed the key intermediate in the subsequent synthesis of natural product Celogentin C (**17**) (Scheme 1.3.2.2).[56]



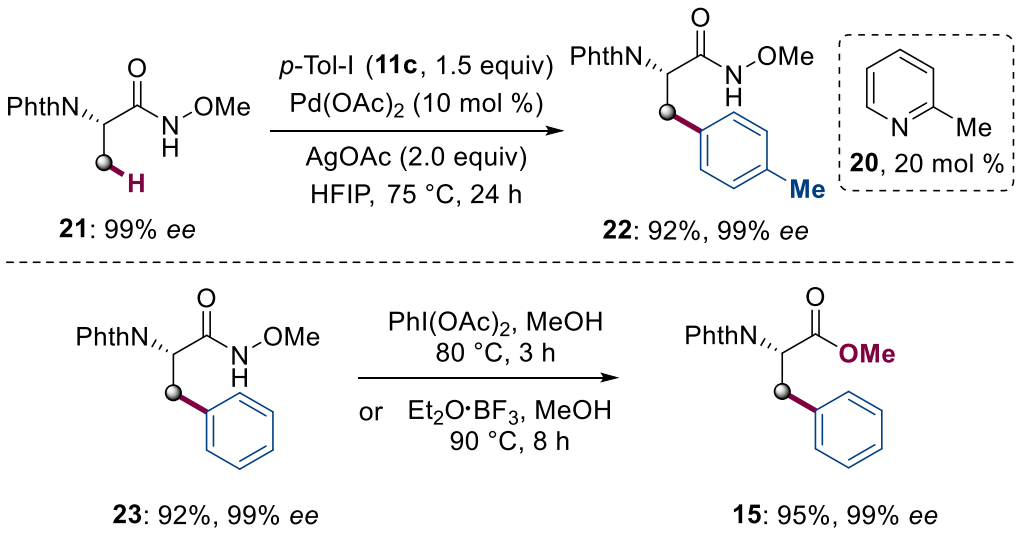
Scheme 1.3.2.2. Palladium-catalyzed C–H indolylation for the total synthesis of Celogentin C (**17**).

Yu and coworkers devised a monodentate directing group for the arylation of alanine derivatives in a racemization-free manner with 2-picoline (**20**) being employed as a crucial ligand.[57] Furthermore, traceless removal of the directing group yielded **15** as an arylated, masked amino acid (Scheme 1.3.2.3).



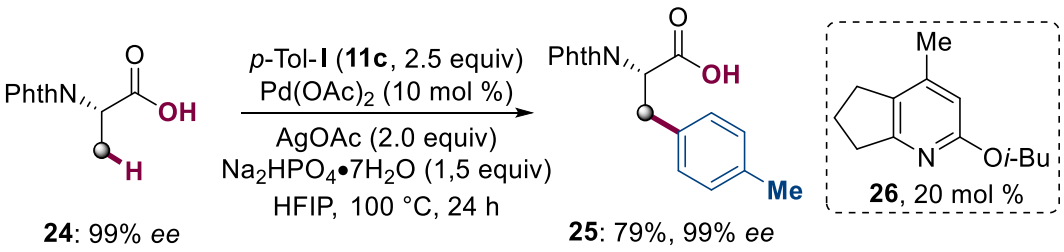
Scheme 1.3.2.3. Palladium-catalyzed C(sp^3)–H arylation of amino acid **18**.

Furthermore, Yu and coworkers explored simple and practical *N*-methoxyamide **21**, a masked ester, as the directing group.[58] Promoted by the ligand 2-picoline (**20**), the arylation reaction proceeded efficiently in a site-selective and racemization-free manner. Afterwards, the auxiliary group could be modified in high yield (Scheme 1.3.2.4).



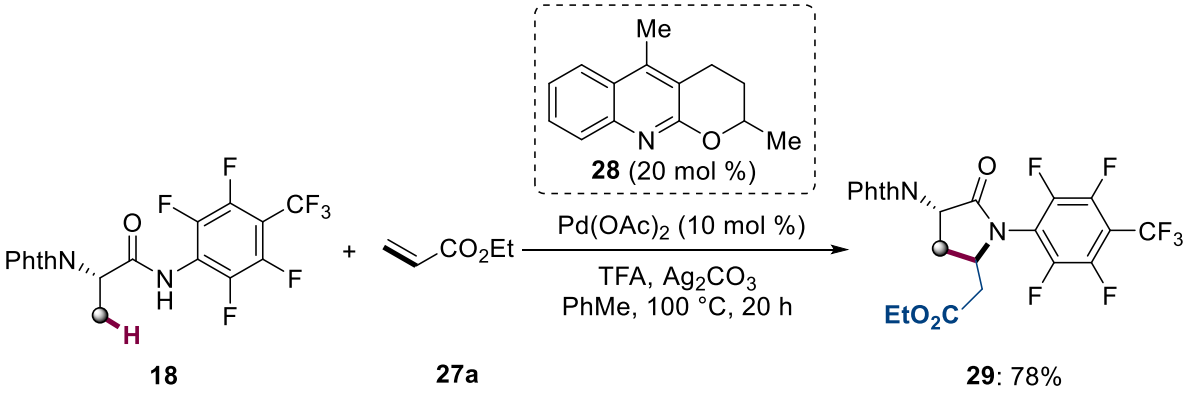
Scheme 1.3.2.4. Palladium-catalyzed C(sp^3)–H arylation by *N*-methoxyamide auxiliary.

Importantly, Yu and coworkers highlighted the power of pyridine-type ligands by developing carboxylic acid-directed arylations.[59] This strategy allowed for amino acid racemization-free arylations without installing exogenous directing groups. This transformation is more step-economical compared to other directing groups (Scheme 1.3.2.5).



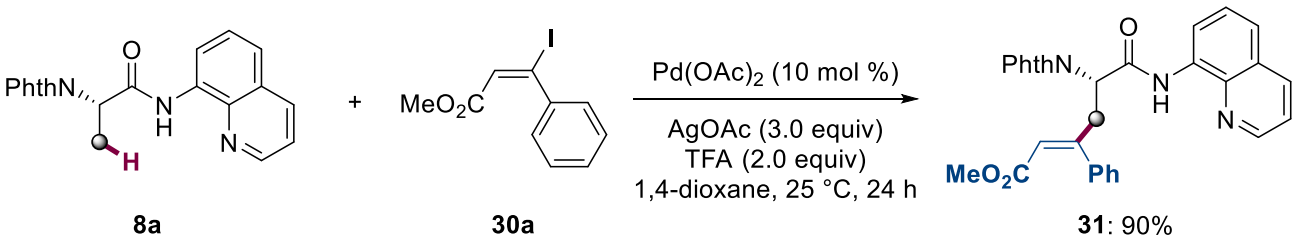
Scheme 1.3.2.5. Palladium-catalyzed C(sp^3)–H arylation directed by carboxylic acid.

In addition to the amino acid arylation approaches mentioned above, various functionalizations *via* C(sp^3)–H activations were developed. For example, employing similar conditions to the C–H arylation by Corey,[49] Yu and coworkers reported on a palladium-catalyzed, ligand controlled olefination of alanine derivative **18** and a successive intramolecular Michael addition to give *γ*-lactam **29** as the product (Scheme 1.3.2.6).[57]



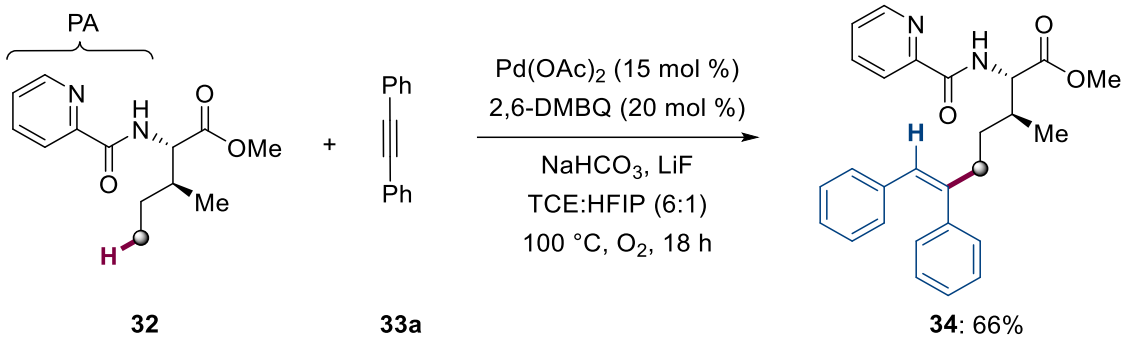
Scheme 1.3.2.6. Palladium-catalyzed one-pot C(sp^3)–H olefination and intramolecular lactamization of amino acid **18**.

Earlier, Chen and coworkers demonstrated the alkenylation of alanine derivatives at room temperature.[60] They employed various vinyl iodides, yielding the corresponding *β*-olefinated alanine derivatives in a diastereo-retentive manner (Scheme 1.3.2.7).



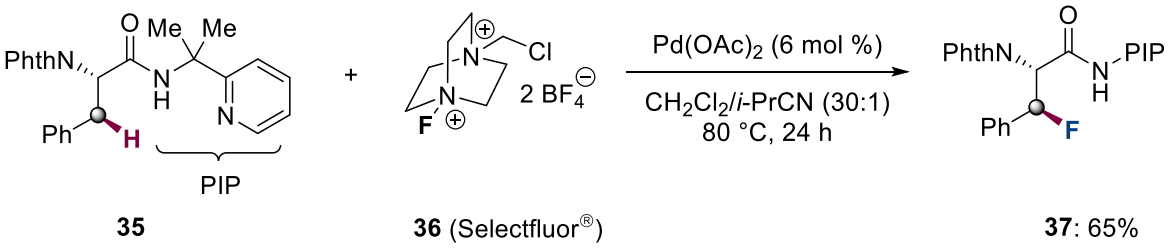
Scheme 1.3.2.7. Palladium-catalyzed C(sp^3)–H olefination.

Furthermore, Shi and coworkers developed picolinamide-directed C(sp^3)–H activations, such as unusual *δ*-C(sp^3)–H alkenylations, yielding alkenes **34** with high regioselectivity (Scheme 1.3.2.8).[61]

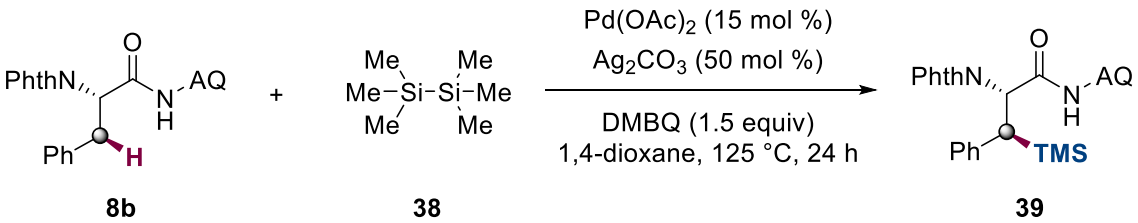


Scheme 1.3.2.8. Palladium-catalyzed *δ*-C(sp^3)–H alkenylation.

Besides the C–C bond formation strategy for amino acid modification, Shi and coworkers also developed diastereoselective C–F bond formations[62] (scheme 1.3.2.9) and C–Si bond formations[63] (scheme 1.3.2.10) for amino acid modification, thereby providing access to biological and pharmaceutically relevant fluorinated and silylated amino acids.



Scheme 1.3.2.9. Palladium-catalyzed secondary phenylalanine C(sp^3)–H fluorination.



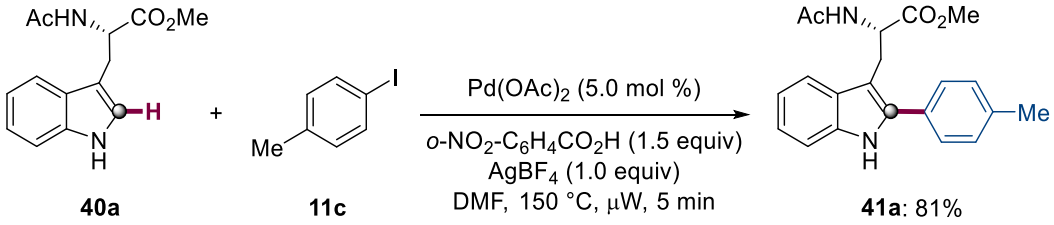
Scheme 1.3.2.10. Palladium-catalyzed secondary phenylalanine C(sp^3)–H silylation.

1.3.3 Palladium-Catalyzed C(sp^2)–H Activations for Late-Stage Peptide Diversifications

Tryptophan, an indole-based natural amino acid, is a widely studied amino acid for C(sp^2)–H activations on late-stage peptides. Tryptophan has an unique impact on biological events such as protein biosynthesis.[64] The low natural abundance, the inherent photo-electronic properties and the indole-based chemistry of tryptophan makes it an ideal and valuable C(sp^2)–H activation site for the modification of tryptophan-based peptides and proteins.[65] Studies of tryptophan modification expanded the applications of tryptophan besides its usage in protein quantification and exploration. Thus, direct C–H activation of tryptophan containing peptides is of great value.

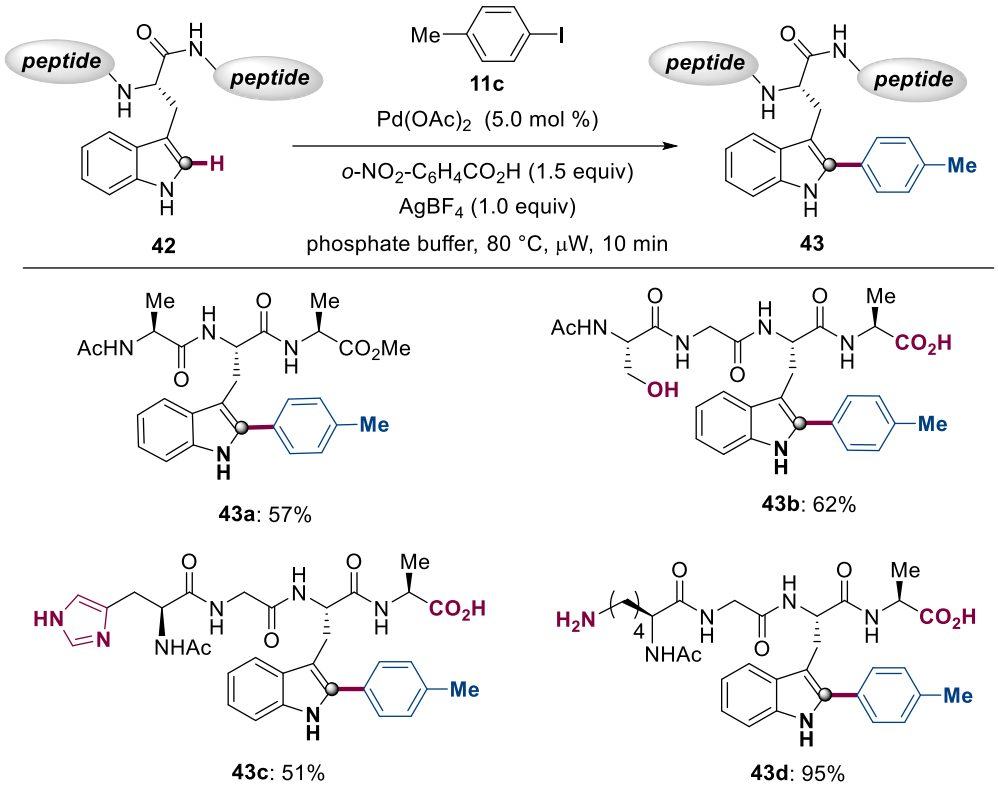
1.3.3.1 Late-Stage Peptide Diversifications *via* C(sp^2)–H Activations on Tryptophan

Palladium-catalyzed C(sp^2)–H functionalizations of indoles have seen great success in the past decades.[66] Compared to the indole moiety, the tryptophan scaffold contains the amino acid backbone on the C3 position, thus leaving the C2 position a prior activation site to be explored. Hence, palladium-catalyzed tryptophan transformations were developed by Albericio, Lavilla and coworkers for the direct arylation of *NH*-free tryptophan.[67] Here, $Pd(OAc)_2$ was found to be the optimal precatalyst along with $AgBF_4$ and 2-nitrobenzoic acid[68] as the crucial additives. Aryl iodides **11** were found to be efficient arylating reagents and microwave irradiation allowed for very short reaction times (Scheme 1.3.3.1.1).



Scheme 1.3.3.1.1. Palladium-catalyzed direct tryptophan C(sp^2)–H arylation.

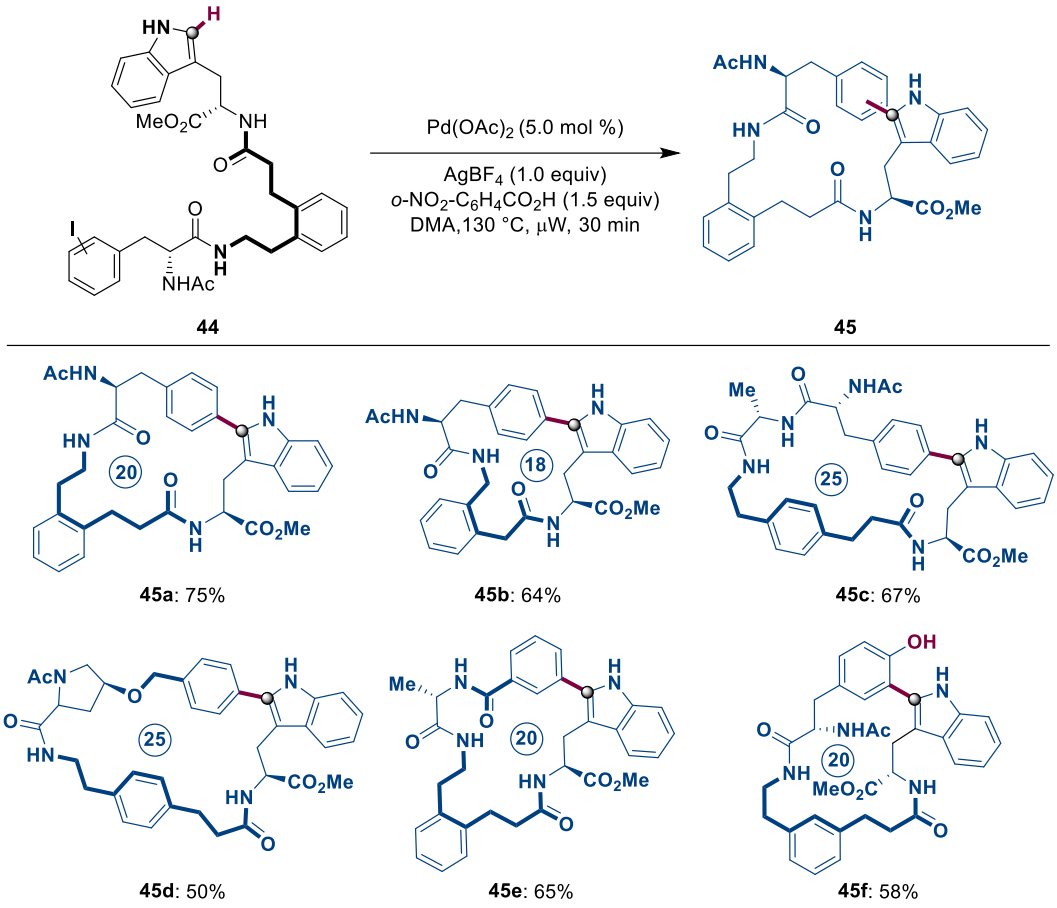
In the same publication, Albericio, Lavilla and coworkers applied the palladium catalysis to more challenging peptide C–H arylations.[67] The reactions proceeded efficiently irrespective of the position of the tryptophan in the peptide in a racemization-free manner. Importantly, the reaction tolerated aqueous media, which has the potential to be compatible with biological systems. Furthermore, the reaction was highly selective for tryptophan C–H activation and compatible with various amino acids with functional sidechains, such as Arg, Asp, His, Lys, Ser, Tyr, Gln as well as free carboxylic acids (Scheme 1.3.3.1.2).



Scheme 1.3.3.1.2. Palladium-catalyzed direct C–H arylation of tryptophan-containing peptide.

Based on this palladium-catalyzed tryptophan C–H arylation strategy, James and coworkers[69] further demonstrated the synthesis of macrocyclic peptides,[70] which were previously accessed by inter alia ring-closing olefin metathesis,[44c, 71] amide-coupling[72] or copper-catalyzed azide–alkyne cycloaddition reactions.[73] In this work, a linkage was devised for connecting the tryptophan and iodo-phenylalanie/tyrosine on the peptide substrate (Scheme 1.3.3.1.3). An evaluation of various reaction conditions showed the importance of the silver salt and the carboxylic acid additive, among which $AgBF_4$ and *o*-NO_2-$C_6H_4CO_2H$ were found to be optimal for this reaction. The cyclic peptides **45** formed by this method

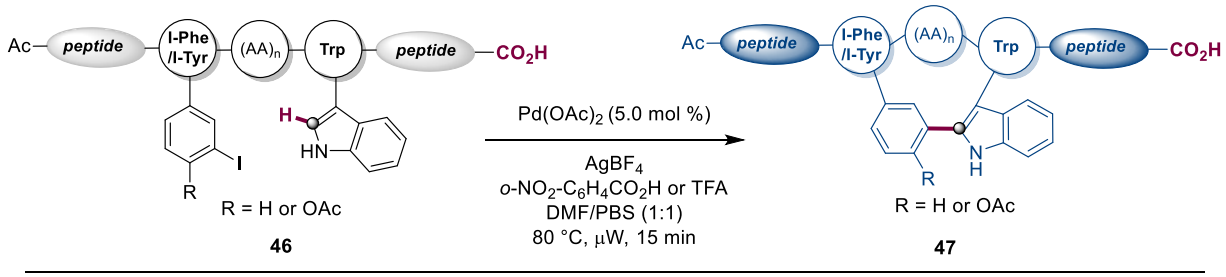
ranged in size from 15 to 25-membered rings, with different peptidic amino acid sequences of the substrates and *meta*- or *para*-aryl bridges. It is noteworthy that intermolecular cyclodimerizations were not observed.[74]



Scheme 1.3.3.1.3. Palladium-catalyzed C–H arylation for cyclic peptide synthesis.

Although the synthesis of cyclic peptidomimetics was found to be viable, the synthesis of stapled peptides through direct, linker-free C–H arylation is of great importance, since the exogenous linkers may have effects on the properties of the corresponding cyclic peptides. Lavilla, Albericio and coworkers thus developed intramolecular C–H arylations for the synthesis of stapled peptides **47** (Scheme 1.3.3.1.4).[75] The staple took place between tryptophan and iodo-phenylalanine or iodo-tyrosine, with the substituent located at the *meta*-position of the arene. *o*-Nitrobenzoic acid and trifluoroacetic acid were the optimal carboxylate additives, along with $AgBF_4$ as the silver salt of choice. Microwave irradiation enabled a fast and efficient assembly of stapled peptides in a racemization-free manner. A

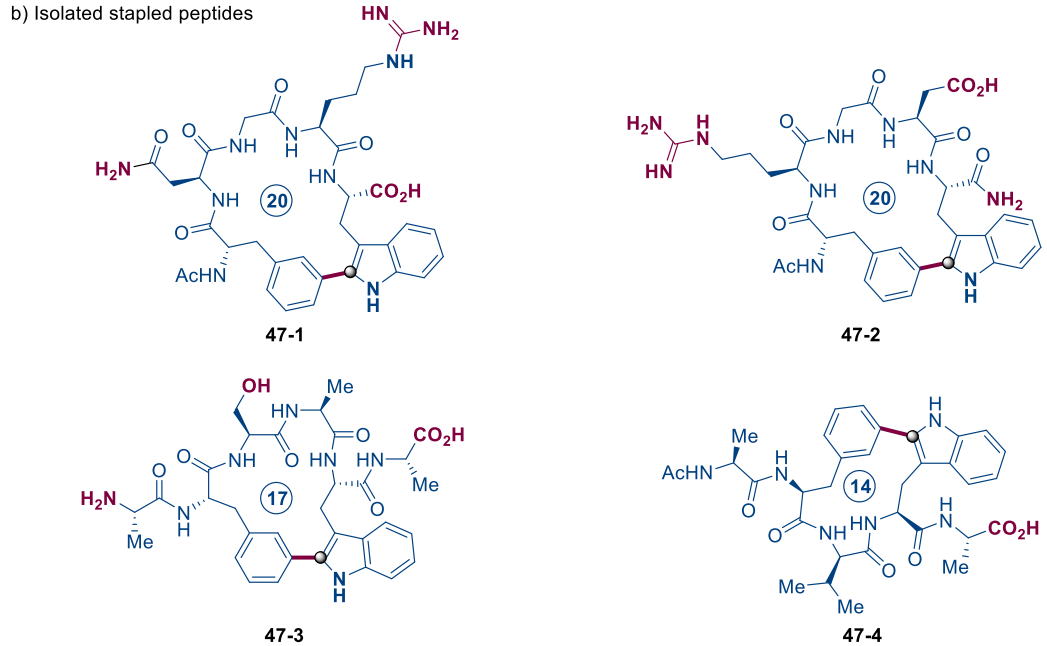
wide range of amino acid sequences was compatible, such as biologically functional NGR (-Asn-Gly-Arg-) and RGD (-Arg-Gly-Asp-) sequences as well as versatile functional groups.[76]



a) Conversion to stapled peptides from different peptide sequences

n		HPLC-MS conversion
1	Ac-Ala-***m*-l-Phe**-Ala-**Trp**-Ala-OH (**46a**)	38%
2	Ac-Ala-***m*-l-Phe**-Ala-Ala-**Trp**-Ala-OH (**46b**)	100%
3	Ac-Ala-***m*-l-Phe**-Ala-Ala-Ala-**Trp**-Ala-OH (**46c**)	100%
1	Ac-Ala-***m*-l-Ac-Tyr**-Ala-**Trp**-Ala-OH (**46d**)	100%
2	Ac-Ala-***m*-l-Ac-Tyr**-Ala-Ala-**Trp**-Ala-OH (**46e**)	100%
3	Ac-Ala-***m*-l-Ac-Tyr**-Ala-Ala-Ala-**Trp**-Ala-OH (**46f**)	100%
3	Ac-***m*-l-Phe**-Asn-Gly-Arg-**Trp**-NH_2 (**46g**)	77%
3	Ac-***m*-l-Phe**-Arg-Gly-Asp-**Trp**-NH_2 (**46h**)	70%
2	H-Ala-***m*-l-Phe**-Ser-Ala-**Trp**-Ala-OH (**46i**)	39%
1	Ac-Ala-***m*-l-Phe**-Val-**Trp**-Ala-OH (**46j**)	71%
0	Ac-Ala-***p*-l-Phe-Trp**-Ala-OH (**46k**)	60%

b) Isolated stapled peptides

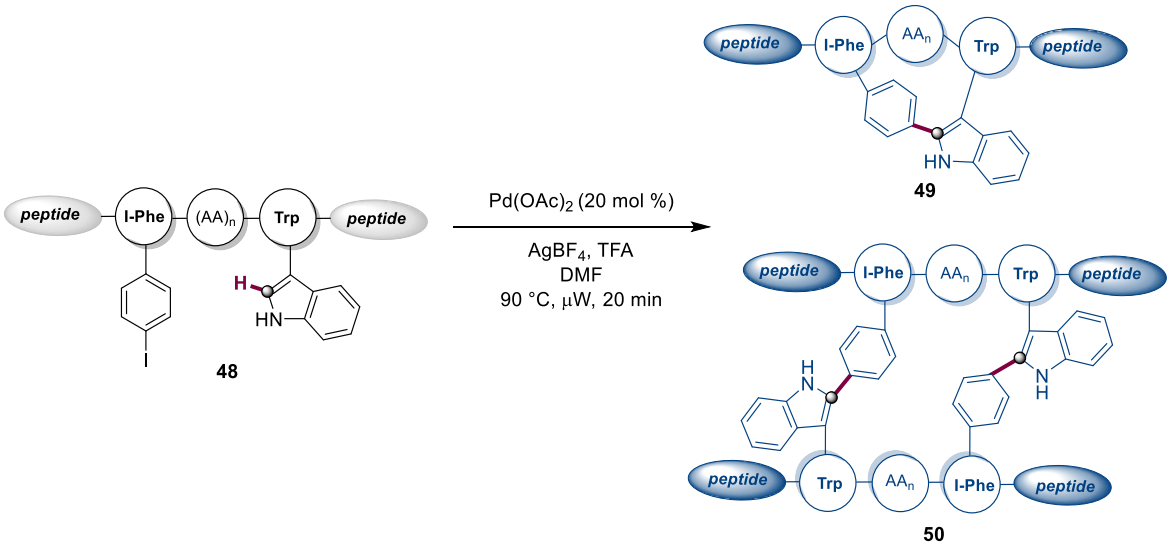


Scheme 1.3.3.1.4. Palladium-catalyzed C–H arylation for linker-free stapled peptides.

However, for synthesis of cyclic peptides through intramolecular C–H arylations the problem of dimerization cannot be ignored. Thus, Albericio, Lavilla and coworkers studied the effect of the number of amino acids between iodo-phenylalanine and tryptophan on dimerization and cyclization[74] (Table 1). With the iodo-phenylalanine adjacent to tryptophan only

dimerization took place (Entry 1). Similarly, with one amino acid between the iodo-phenylalanine and tryptophan only cyclodimeric peptide **50** was formed (Entry 2). However, with two amino acids in between both cyclodimeric and cyclomonomeric peptides were obtained, with the desired cyclomonomeric peptide **49a** as the major product (Entry 3). Notably, when the number of amino acids was increased to 3, only cyclopeptide **49b** was observed (Entry 4). These results illustrated that the structure and regiochemistry of the peptide substrate is crucial for the formation of cyclodimerization or peptide stapling, as well as the Ruggli-Ziegler high-dilution conditions.[77]

Table 1. Cyclodimerization versus cyclization effect

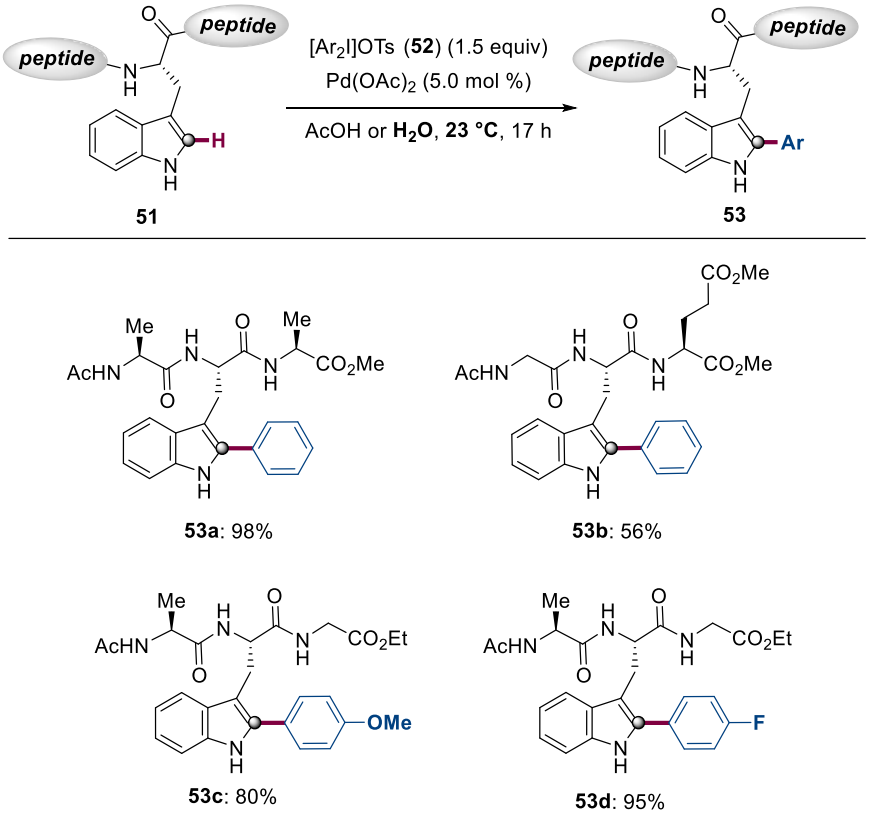


Entry	Peptide sequence	Cyclodimeric **50**	Cyclomonomeric **49**
1	Ala-(***p*-I)Phe**-**Trp**-Ala (**48l**)	**50a**: 60%	n.d.
2	(***p*-I)Phe**-Ala-**Trp**-Lys (**48m**)	**50b**: 54%	n.d.
3	Ala-(***p*-I)Phe**-Lys-Gly-**Trp**-Ala (**48n**)	**50c**: 23%	**49a**:51%
4	Ala-(***p*-I)Phe**-Arg-Lys-Gly-**Trp**-Ala (**48o**)	n.d.	**49b**: 81%

Reaction conditions: $Pd(OAc)_2$ (20 mol %), $AgBF_4$ (2.0 equiv), TFA (1.0 equiv), DMF, 90 °C, µW, 20 min.

1.3.3.2 Late-Stage Peptide Diversifications *via* C(sp^2)–H Activations on Tryptophan Under Mild Conditions

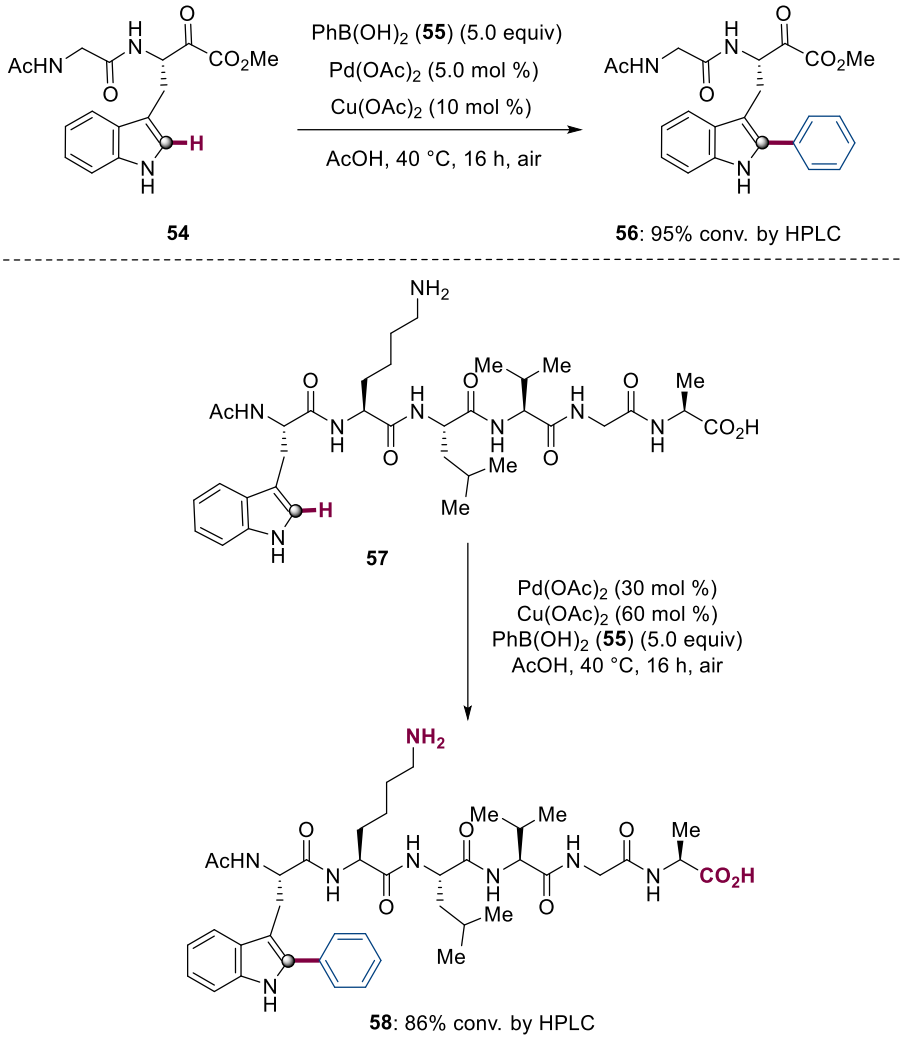
Although great contributions have been made by the palladium-catalyzed tryptophan C–H arylations, these synthetic route face major limitations, such as high catalyst loadings, use of stoichiometric amounts of silver salts, excessive use of aryl iodides and high reaction temperatures, restricting the potential for broader applications. To address these problems, Ackermann and coworkers[78] devised a peptide C–H arylation strategy employing diaryliodonium salts **52**[79] as the arylating reagents (Scheme 1.3.3.2.1). Importantly, the reaction proceeded efficiently at ambient temperature, thereby setting the stage for bioorthogonal applications. Moreover, the reaction could be conducted with a catalyst loading of only 0.5 mol % without hampering the site- and chemo-selectivity. The reaction proved its robustness with high reaction efficiency in non-toxic and bio-compatible water.[80]



Scheme 1.3.3.2.1. Palladium-catalyzed peptide C–H arylation with diaryliodonium salts **52**.

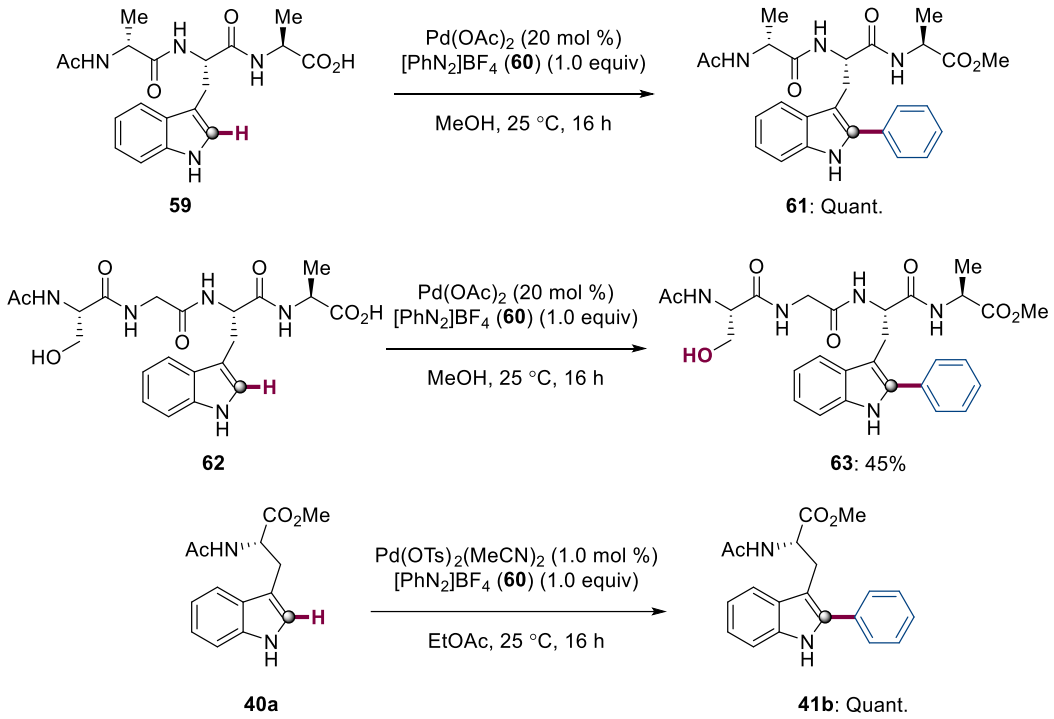
Similarly, Fairlamb and coworkers[81] reported peptide C–H arylations with aryl boronic acids **55** as the arylating reagents and $Cu(OAc)_2$ as the cocatalyst. The reaction proceeded

efficiently at a temperature of 40 °C and tolerated free NH_2 and CO_2H functional groups (Scheme 1.3.3.2.2).



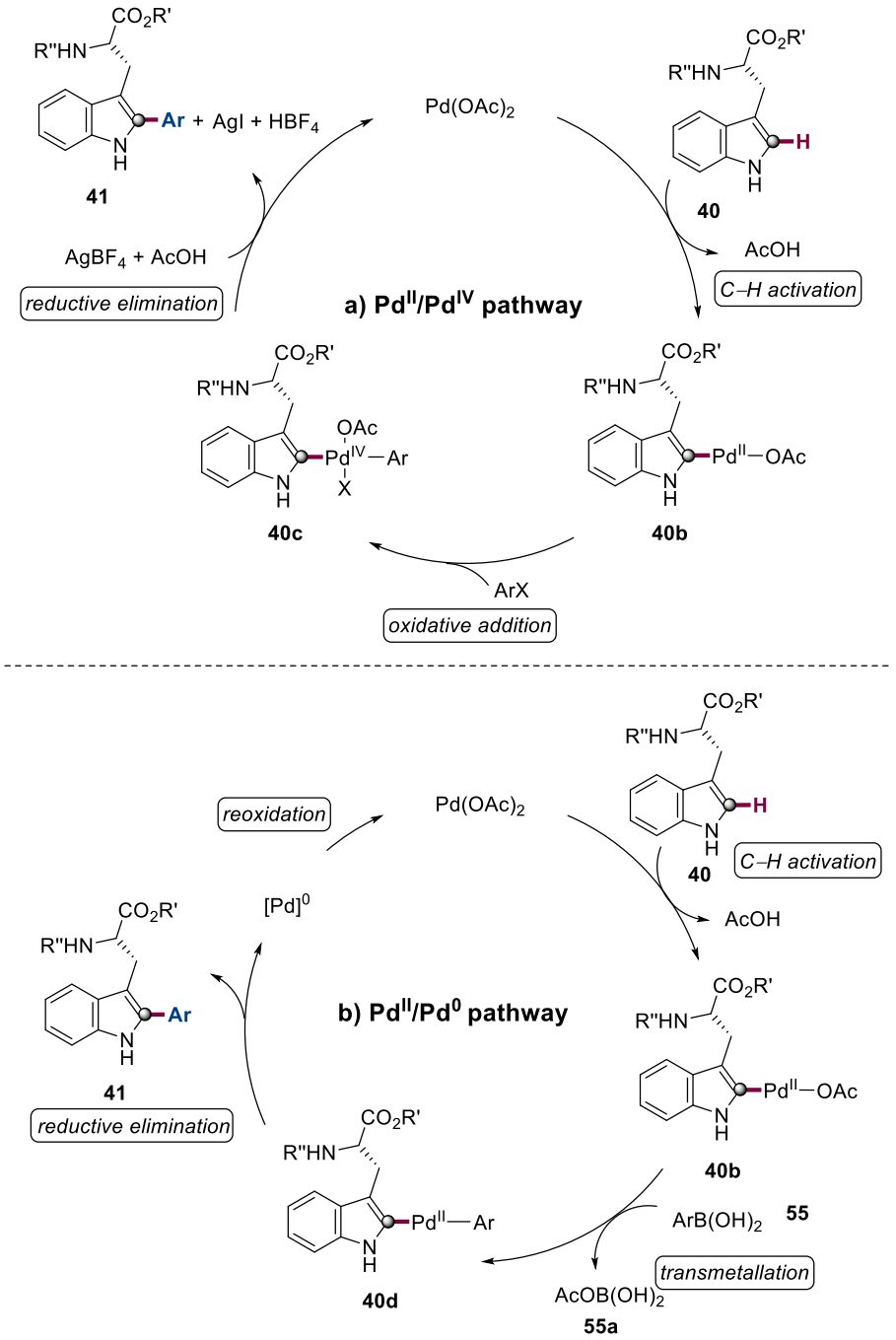
Scheme 1.3.3.2.2. Palladium-catalyzed C–H peptide arylation with aryl boronic acid **55**.

Furthermore, Fairlamb and coworkers elegantly employed aryldiazonium salt **60** for peptide arylations (Scheme 1.3.3.2.3).[82] TsOH was used as a promoter, allowing the reaction to be efficient with a catalyst loading of 1.0 mol %. Notably, this room temperature reaction required no excessive use of the arylating reagents.



Scheme 1.3.3.2.3. Palladium-catalyzed C–H peptide arylation with aryldiazonium salts

Generally, two different pathways were proposed for palladium-catalyzed tryptophan arylations (Scheme 1.3.3.2.4).[83] The Pd(II)/Pd(IV) pathway (Scheme 1.3.3.2.4a) is initiated by C–H palladation and followed by oxidative addition, delivering palladium(IV) intermediate **40c**. Subsequent reductive elimination yields the arylated product and regenerates the active palladium(II) catalyst. However, with aryl boronic acids as the arylating reagent, the palladium(II) intermediate is favored for a transmetallation process, generating Ar-Pd(II) intermediate **40d**. The reductive elimination then delivers the arylated product and a palladium(0) complex, which undergoes a reoxidation step for regenerating the active palladium(II) catalyst (Scheme 1.3.3.2.4b).

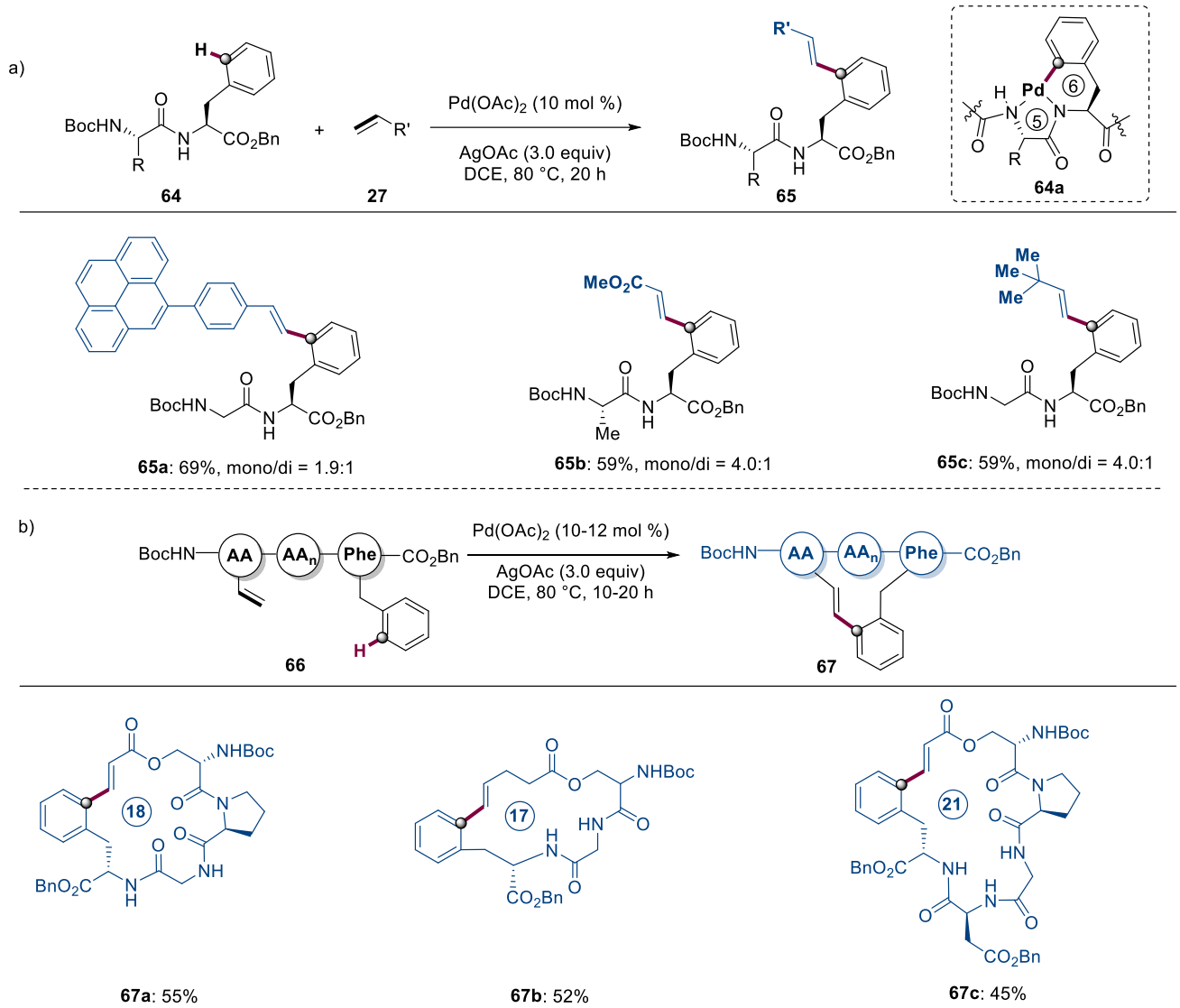


Scheme 1.3.3.2.4. Proposed mechanisms for palladium-catalyzed tryptophan C–H arylations.

1.3.3.3 Late-Stage Peptide Diversifications *via* C(sp^2)–H Activations on Phenylalanine

Other than tryptophan, phenylalanine offers potential for peptide diversifications via C–H bond activation as well. Wang and coworkers[84] reported on the *δ*-C(sp^2)–H olefination of phenylalanine, delivering both branched (Scheme 1.3.3.3.1a) and cyclic peptides (Scheme

1.3.3.3.1b). The reaction was proposed to proceed through a 6/5-bicyclic palladacycle with the assistance of the peptide backbone as an internal weakly coordinating directing group.



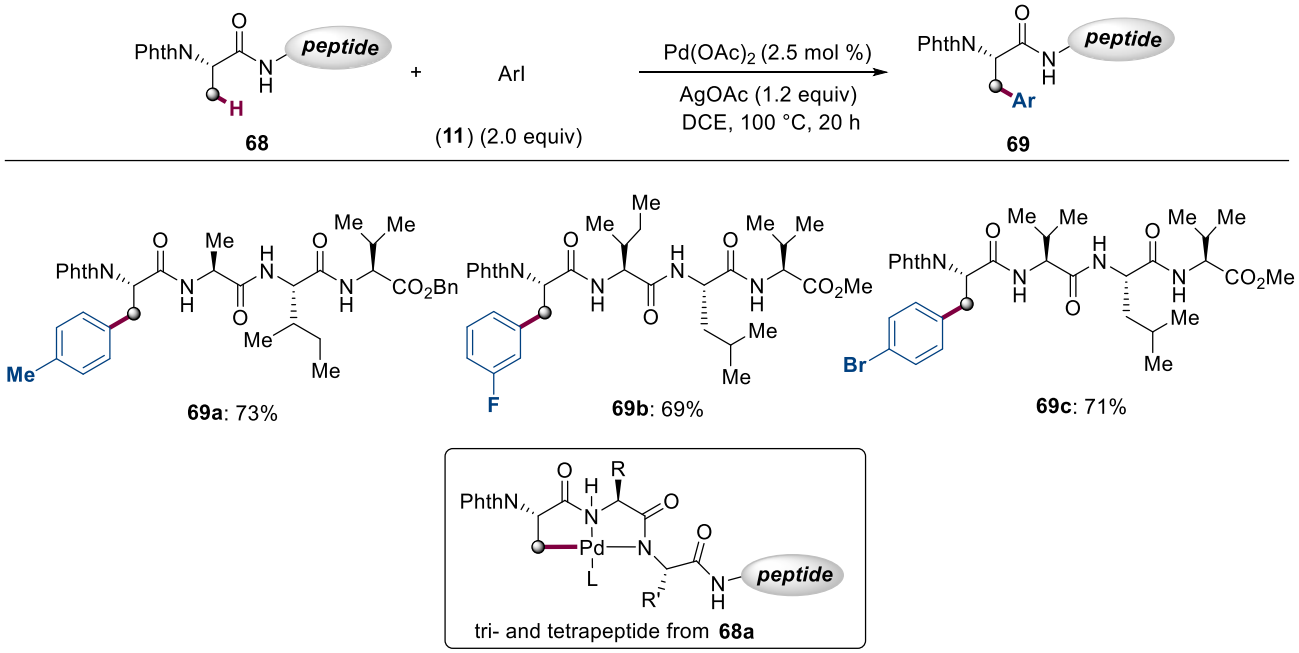
Scheme 1.3.3.3.1. Peptide modifications by phenylalanine C–H arylations.

1.3.4 Palladium-Catalyzed C(sp^3)–H Activations for Late-Stage Peptide Diversifications

In spite of major advances of late-stage peptide modifications through tryptophan C(sp^2)–H activation, challenging C(sp^3)–H activation[85] for peptide diversifications is of great importance and remains to be addressed, as C(sp^3)–H bonds are omnipresent in peptide backbones, offering the chance of utilizing the positional selectivities for late-stage peptide modifications. Ideally, this strategy should tolerate reactive functional groups.

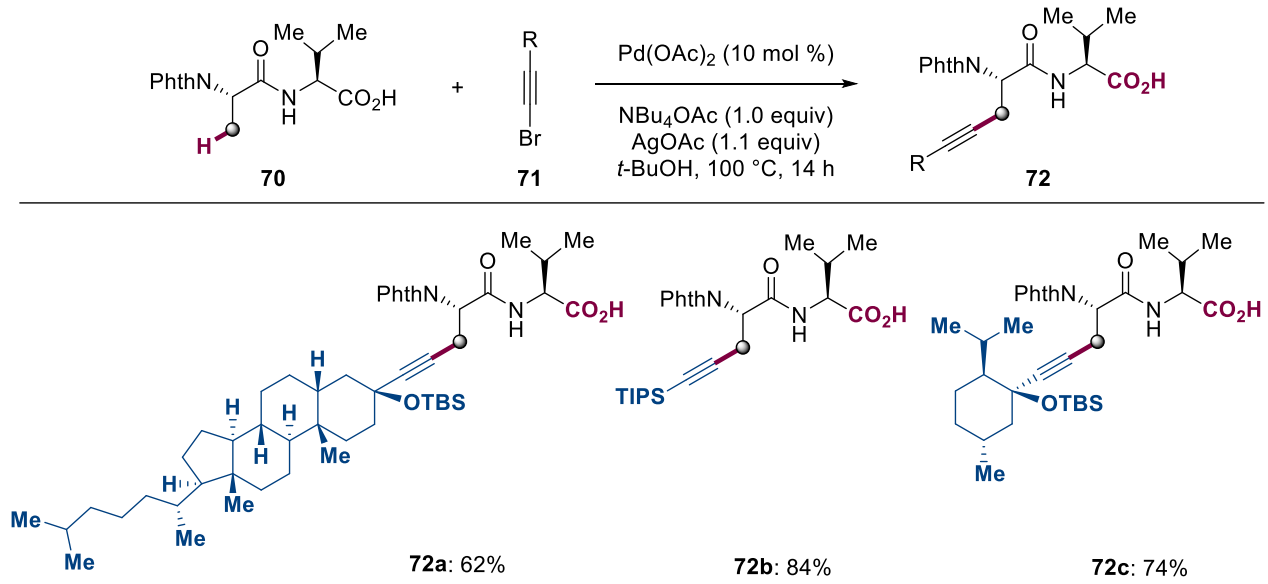
1.3.4.1 Branched Late-Stage Peptides by Palladium-Catalyzed C(sp^3)–H Activations

As one of the strategies for late-stage peptide diversification, modifications on the side chains of the parent peptides delivers unnatural branched peptides. In this context, Yu and coworkers[86] developed the *N*-terminus-selective arylation of peptides through C(sp^3)–H activations of alanine motifs (Scheme 1.3.4.1.1). Stoichiometric amounts of silver(I) were necessary for high reaction efficiencies. In this work, the peptide backbone acted as a weakly coordinating bidentate directing group, thus enabling site-selective arylations and di-, tri- and tetra-peptides were transformed in a racemization-free manner.



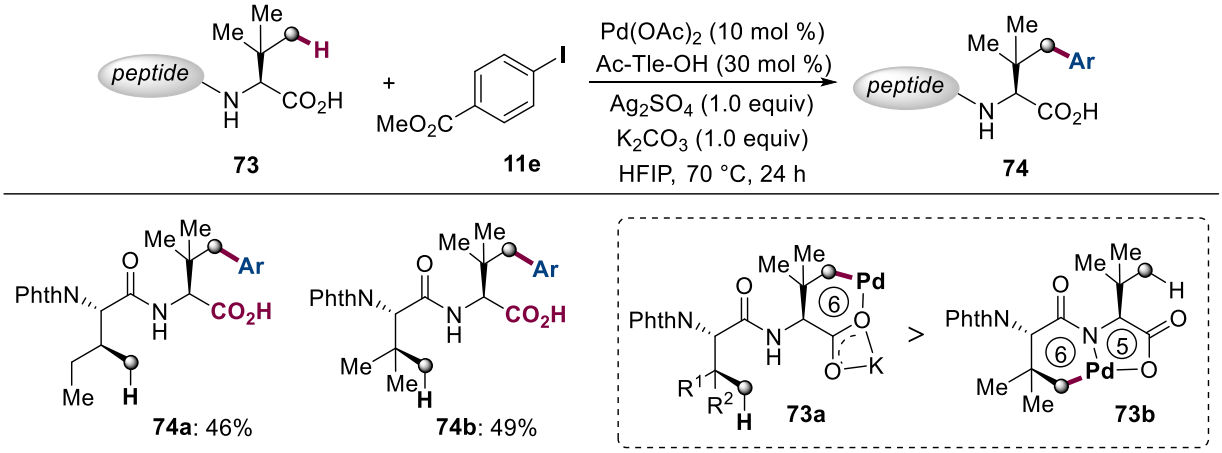
Scheme 1.3.4.1.1. *N*-terminus selective peptide C(sp^3)–H arylation.

Furthermore, an alkynylation reaction[87] was developed by Yu and coworkers for the formation of new branches with excellent site-selectivity for the *N*-terminus alanine residue. Free carboxylic acid groups were compatible in this reaction along with efficient conjugations under palladium catalysis (Scheme 1.3.4.1.2).



Scheme 1.3.4.1.2. *N*-terminus selective peptide C(sp^3)–H alkynylation

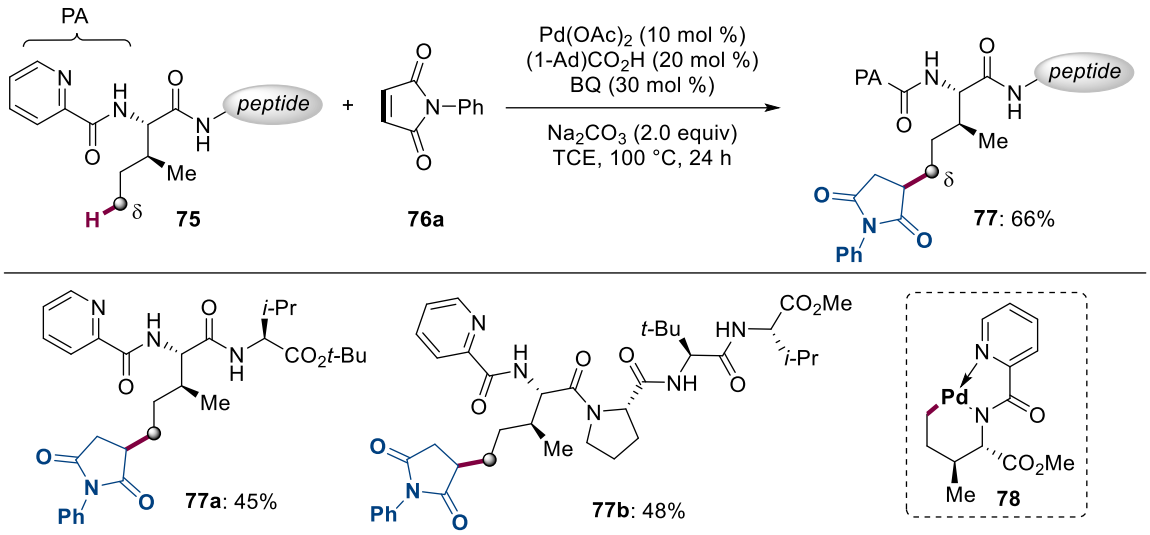
Additionally, Shi and coworkers[88] discovered that with bulky amino acid branches positioned in the *C*-terminus of *C*-free acid peptides, the *C*-terminus C(sp^3)–H bond was selectively activated by means of palladium catalysis (Scheme 1.3.4.1.3). The weakly coordinating carboxylic acid directing group formed a 6-membered palladation, outcompeting the bicyclic palladation.



Scheme 1.3.4.1.3. *C*-terminus-selective peptide C(sp^3)–H arylation.

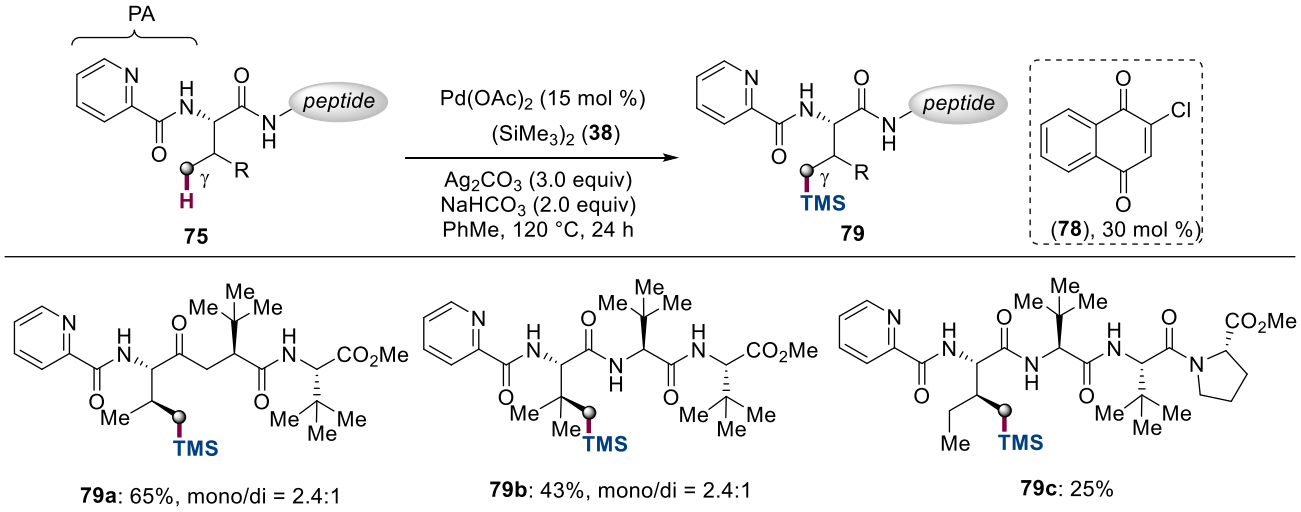
As discussed above, Shi and coworkers previously employed picolinamide (PA)[61] as an efficient directing group for amino acid C–H activations. This strategy was further employed by the same group for peptide *N*-terminus *δ*-C(sp^3)–H alkylation[89] *via* a 6-membered palladacycle, using maleimides as the alkylating reagents (Scheme 1.3.4.1.4). Here, the

benzoquinone was both used as a ligand and as the crucial cooxidant. The PA group was easily removable, enabling further *N*-terminus diversifications.



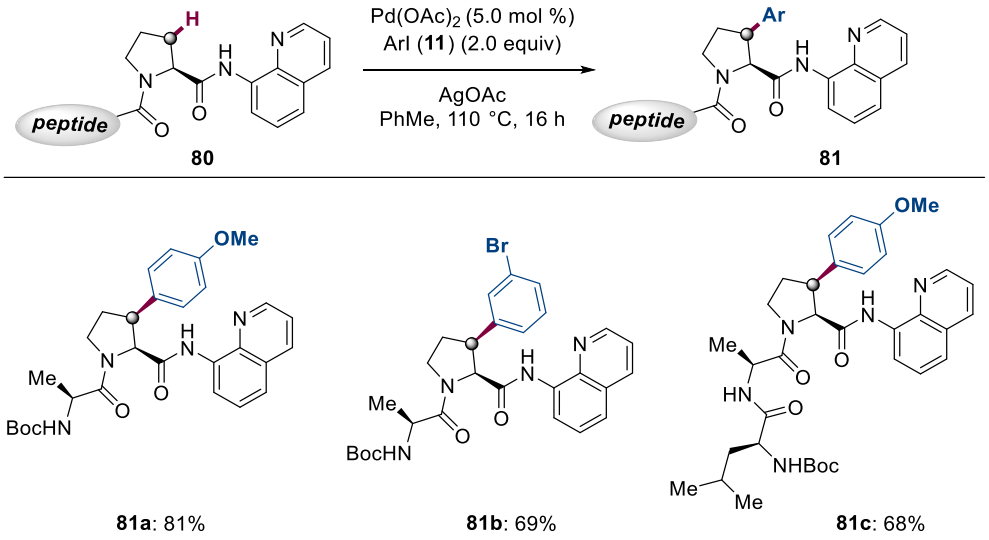
Scheme 1.3.4.1.4. *Selective peptide N-terminus δ-C(sp³)–H alkylation.*

Shi and coworkers also employed the PA group for late-stage *γ*-C(sp³)—Si bond formations[90] utilizing hexamethyldisilane (**38**) as the silylation reagent, thus synthesized a variety of silicon-containing peptides, which represent a class of peptides that have improved biological properties.[35b, 91] In this work, the quinone ligand played an important role for the selective silylation. Notably, various amino acid residues were tolerated as the *N*-terminus C—H activation site, including Val, Ile, Thr, Tle and Abu (Scheme 1.3.4.1.5).



Scheme 1.3.4.1.5. *N-terminus-selective peptide C(sp³)–H silylation*

In contrast to advances in primary C(sp^3)–H activations for peptide diversifications mainly by alanine residue modifications, secondary C(sp^3)–H activation offers new possibilities for late-stage peptide diversifications. Kazmaier and coworkers[92] established peptide functionalizations by arylation on proline secondary C(sp^3)–H bond. The reaction proved efficient for short peptides with the easily accessible and removable Boc protecting group being fully compatible with the catalyst (Scheme 1.3.4.1.6).



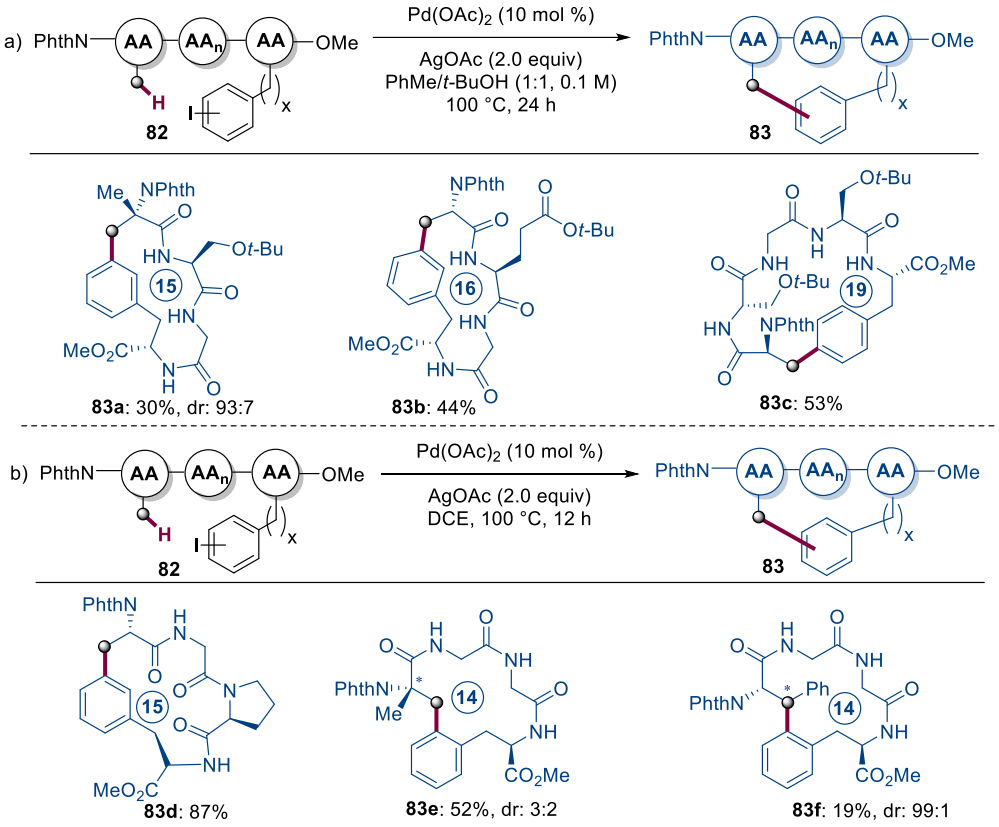
Scheme 1.3.4.1.6. Peptide diversification by proline arylations.

1.3.4.2 Cyclic Late-Stage Peptides by Palladium-Catalyzed C(sp^3)–H Activations

Besides peptide modifications for novel peptide branches, synthesis of cyclic peptides focuses on precise connections between intramolecular amino acids to deliver peptidic rings. Cyclic peptides have unique biological or material properties compared to their parent branched peptides.[70] However, the synthesis of cyclic peptides is typically lengthy and easily generates undesired byproducts such as cyclodimerized products, thus emphasizing the need for direct site-selective C–H activations to achieve a precise cyclic peptide synthesis.

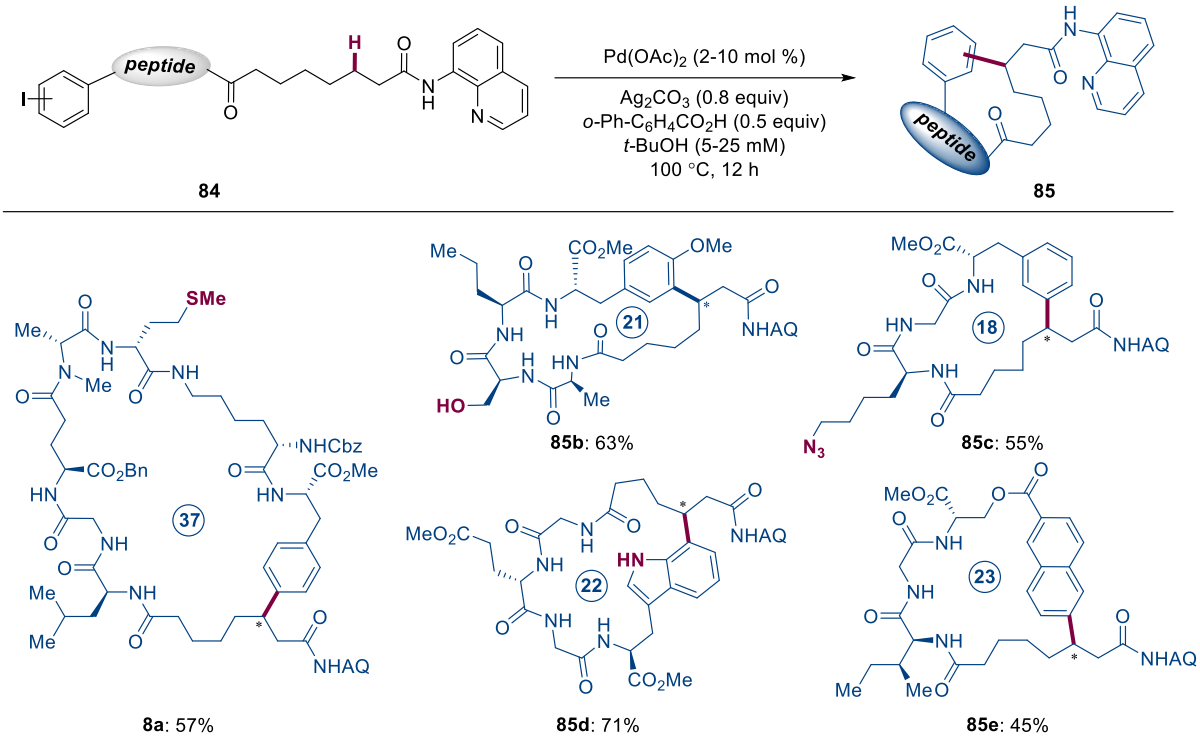
On the basis of Yu's peptide backbone-induced C(sp^3)–H arylation[86] and their own stapling strategy,[75] Albericio, Noisier and coworkers applied these strategies to the synthesis of spacer-free cyclic peptides, connecting the two amino acid residues alanine and iodo-phenylalanine[93] (Scheme 1.3.4.2.1a). The solvent was crucial in this work, since *t*-BuOH as the cosolvent prevented the formation of undesired by-products. Various amino acids were

compatible with this transformation as well as different space between the two cross-link positions. Thus, a variety of cyclic peptides were obtained, featuring different ring sizes. Similarly, Wang and coworkers[94] employed DCE as the solvent, enabling the cyclizations through both primary and secondary C(sp^3)–H arylation with excellent levels of diastereoselectivity (Scheme 1.3.4.2.1b).



Scheme 1.3.4.2.1. C(sp^3)–H arylation for stapled peptides.

As previously explored, the 8-AQ group[51] exhibits a great efficiency in promoting C(sp^3)–H activations. Thus, Chen and coworkers[95] developed an elegant C(sp^3)–H macrocyclization for cyclophane-embraced peptides (Scheme 1.3.4.2.2). The stapling took place between the aryl iodide *C*-terminus-modified amino acid residue and an alkyl chain at the *N*-terminus, bearing 8-AQ as the directing group. Various cyclophane-based stapled peptides were obtained in different ring sizes and the reaction was found to be compatible with different peptidic sequences and functional groups. A 1:1 diastereomeric ratio was predominantly observed.

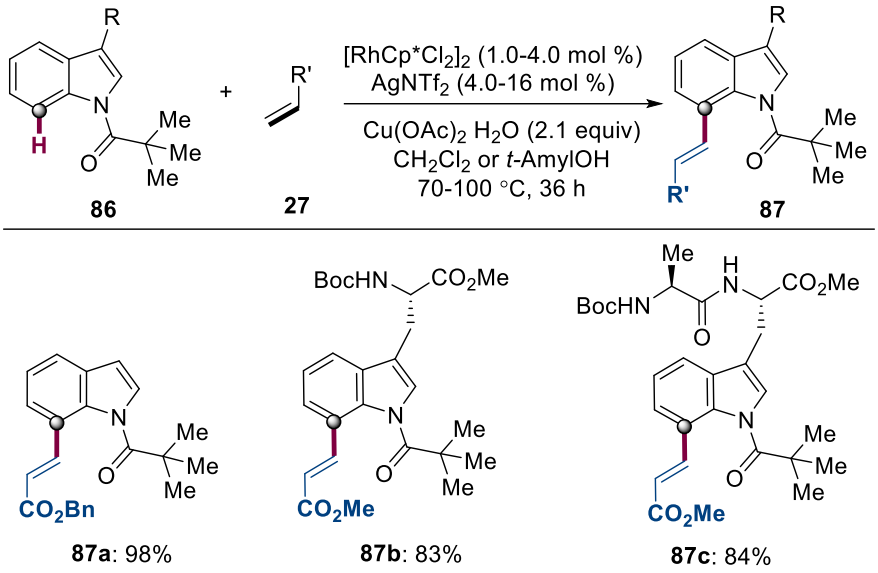


Scheme 1.3.4.2.2. C(sp^3)–H arylation for cyclophane-based cyclic peptides

1.4 Rhodium-Catalyzed C–H Activations for Late-Stage Peptide Diversifications

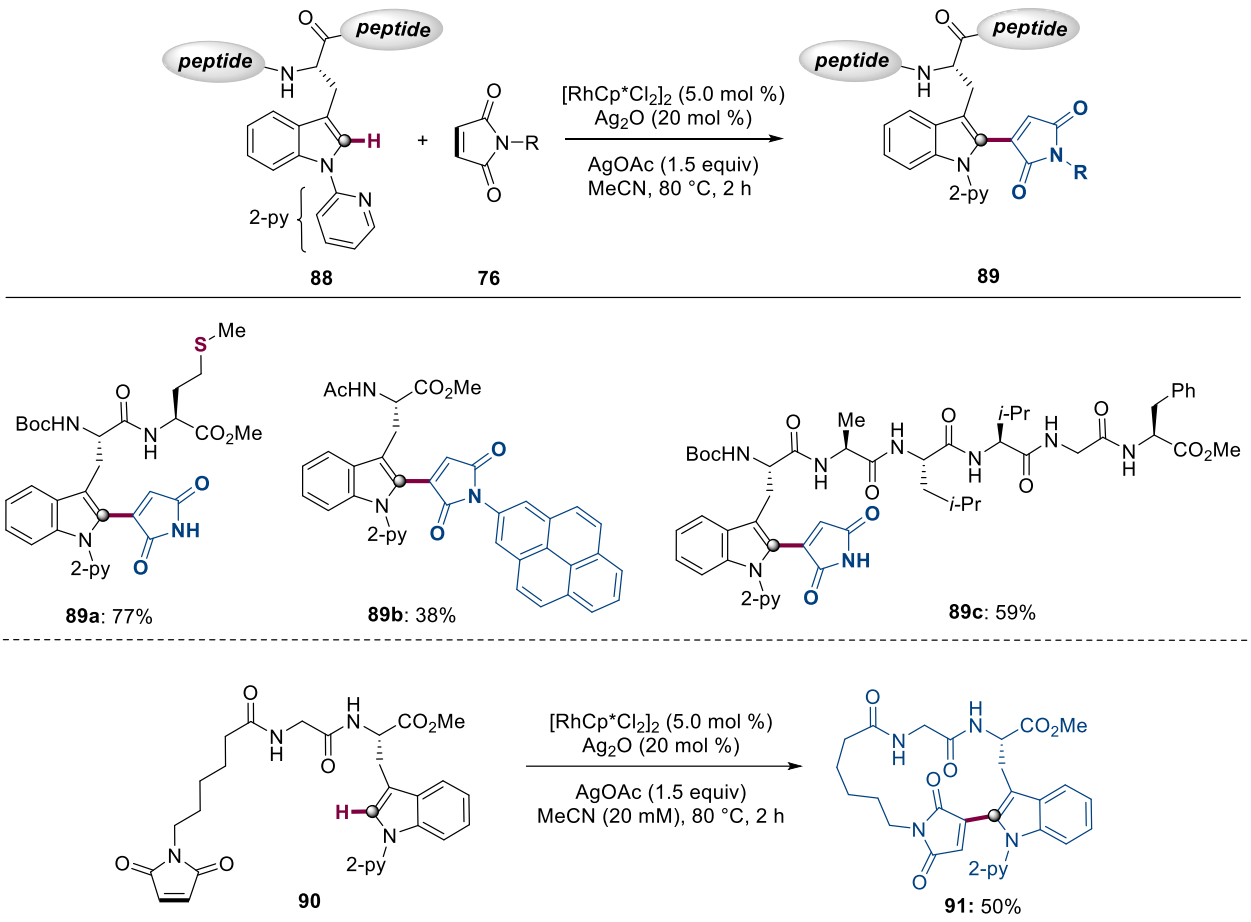
Similar to palladium, rhodium catalysis has contributed enormously to the development of catalyzed C–H activations. Although rhodium(III) catalysis[16j, 96] has been thoroughly studied for highly efficient C–H bond transformations, especially for applications in indole chemistry, rhodium(III) catalysis for amino acid and late-stage peptide diversifications is still rare.

Employing rhodium(III) catalysis, Ma and coworkers[97] employed a *N*-pivaloyl directing group for highly regioselective indole C7 C–C bond formations by C–H alkenylation and further applied this strategy to simple tryptophan and short dipeptide modifications (Scheme 1.4.1). Rhodium(III) catalysis and the *N*-pivaloyl group are pivotal for this transformation, with the directing group being easily removable, thus delivering C7-decorated native tryptophan derivatives.



Scheme 1.4.1. Rhodium-catalyzed indole/tryptophan C–H alkenylation

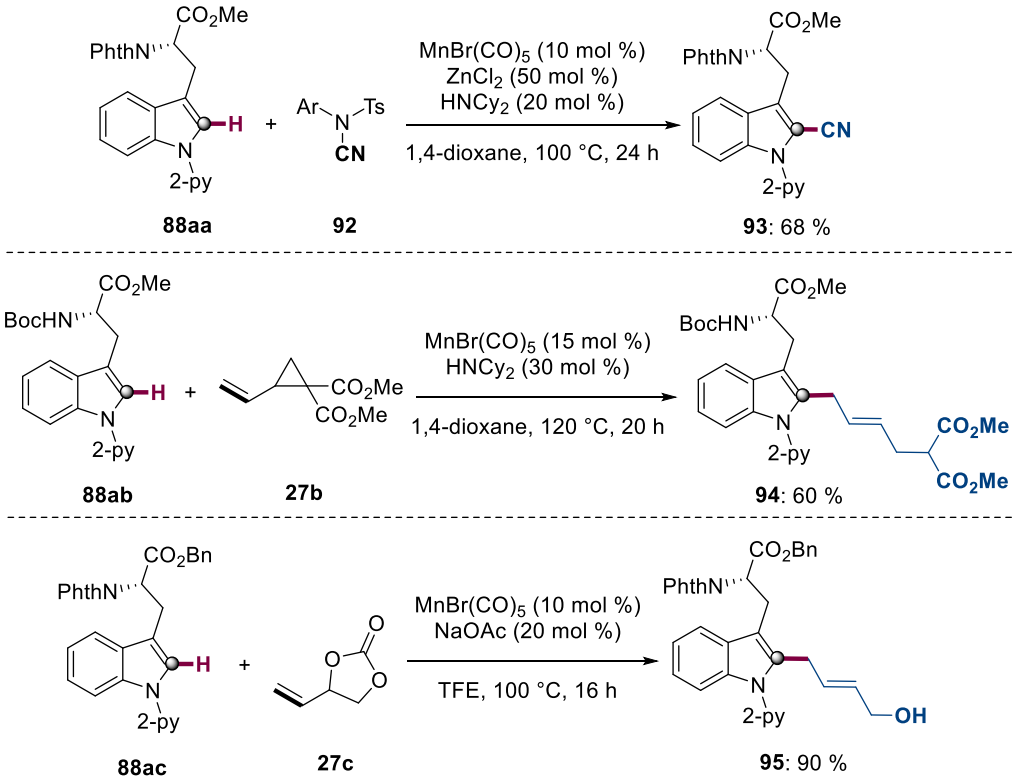
Furthermore, Liu and coworkers[98] employed a rhodium(III)-catalyzed alkenylation strategy for late-stage peptide modifications, with widely applied maleimide **76** as the alkenylating reagent in a racemization-free manner (Scheme 1.4.2). The *N*-pyridyl directing group, which was previously employed for late-stage peptide diversifications by Ackermann and coworkers[99] was employed in this transformation, allowing for tryptophan C2 site-selectivity and reaction robustness. Moreover, rhodium(III) catalysis is compatible with various functional groups and protecting groups on the peptides, thus delivering a wide range of peptide conjugates including intramolecular macrocyclizations for stapled peptides.



Scheme 1.4.2. Rhodium-catalyzed peptide C–H alkenylation.

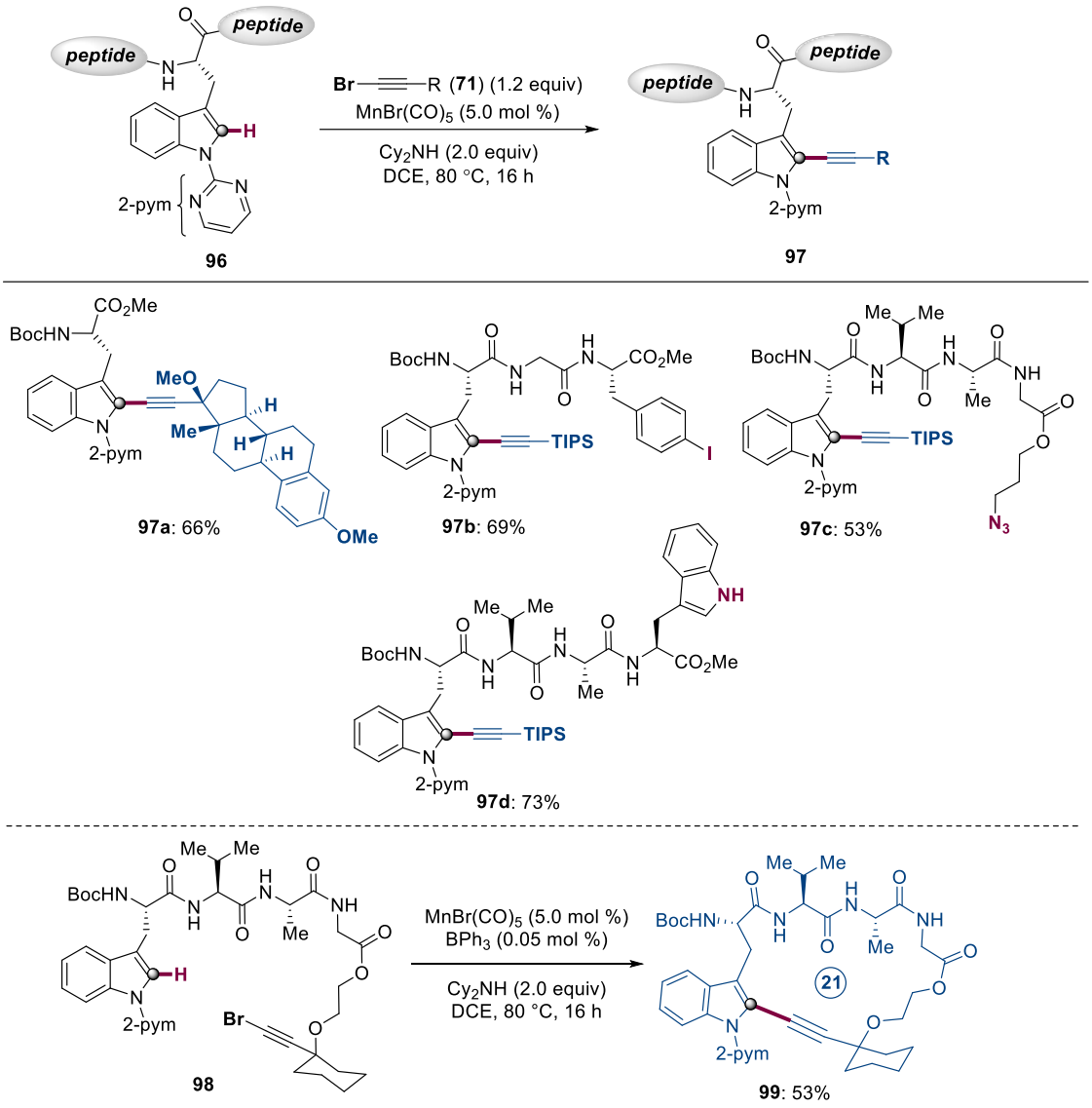
1.5 Manganese-Catalyzed C–H Activations for Late-Stage Peptide Diversifications

Precious 4d and 5d transition metals have undeniably achieved great success in the area of peptide C–H functionalizations. However, drawbacks such as the high price and toxicity of these metals limit further applications in peptide C–H functionalizations. In recent years, 3d transition metals emerged as naturally abundant, less-toxic and user-friendly catalysts,[19, 100] with considerable contributions by manganese catalysis.[20a, 101] Ackermann and coworkers pioneered the field of late-stage peptide diversifications employing manganese-catalyzed C–H activations. Early examples by Ackermann and coworkers showed tryptophan transformations by manganese(I) catalysis, such as C–H cyanations[102] and allylations[99, 103] in a racemization-free manner (Scheme 1.5.1).



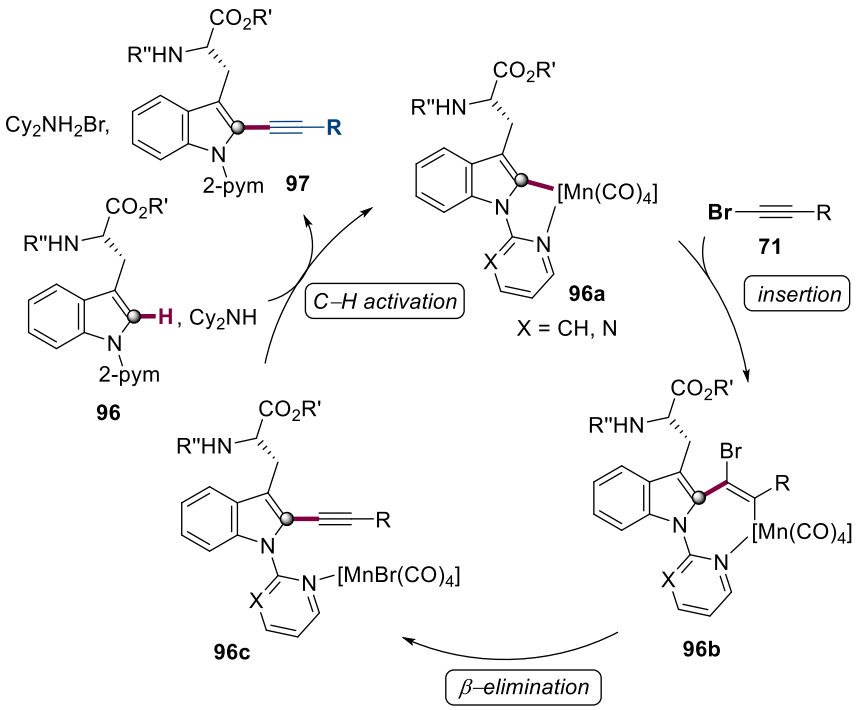
Scheme 1.5.1. Manganese-catalyzed tryptophan C–H activations.

Alkynes are synthetically useful for further transformations, such as 1,3-dipolar cycloadditions,[104] Ackermann and coworkers[105] developed manganese(I)-catalyzed chemo-selective peptide C–H alkynylations, delivering various tryptophan-based peptides bearing alkyne motifs (Scheme 1.5.2). Employing bromoalkynes as the alkynylating reagents, this late-stage peptide diversification proceeded efficiently in a racemization-free manner. Moreover, this strategy was compatible with various functional groups, such as the native *NH*-free tryptophan, azide and iodide groups, thereby outcompeting palladium catalysis. A tryptophan-natural product hybrid was efficiently delivered as well. Furthermore, an intramolecular macrocyclization was conducted, delivering a 21-membered cyclic peptide under this highly chemo-selective manganese catalysis.



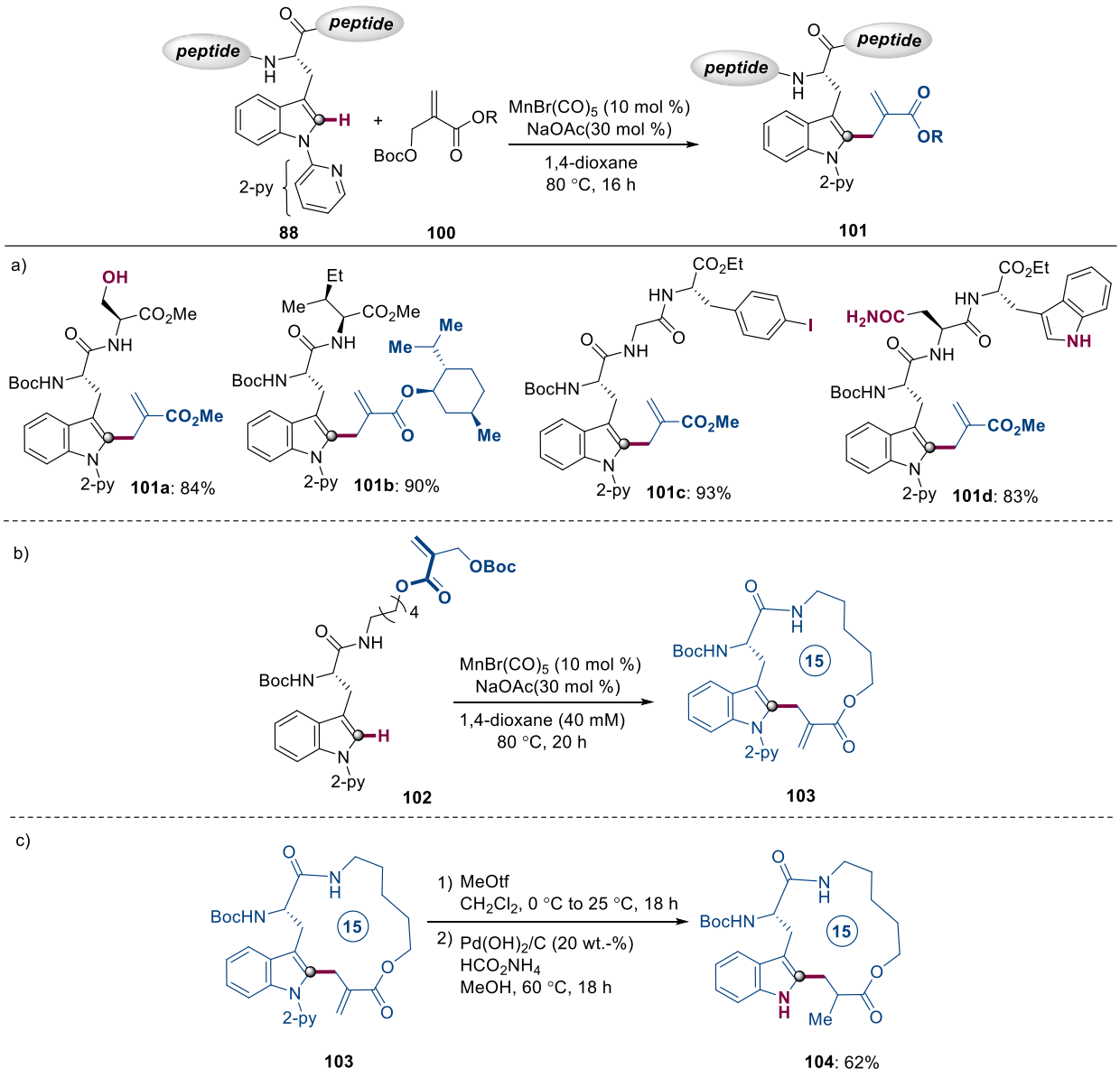
Scheme 1.5.2. Manganese-catalyzed peptide C–H alkynylations

To get mechanistic insights into the manganese catalysis, a KIE study was performed, revealing a facile C–H metalation step with $k_H/k_D \approx 1.0$. This result suggested a fast initiating C–H activation step for the C–Mn bond formation, further supported by the isolation of the key 5-membered manganacycle intermediate **96a**, which could be used as the catalyst. Migratory insertion further delivers intermediate **96b**, which yields the desired alkynylation product through *β*-elimination (Scheme 1.5.3).



Scheme 1.5.3. Proposed mechanism of manganese-catalyzed C–H alkynylations

To further explore the manganese(I)-catalyzed peptide transformations, Ackermann and coworkers[106] demonstrated a bioorthogonal C─H allylation reaction for late-stage peptide diversifications under racemization-free conditions, using easily accessible Morita-Baylis-Hillman adducts[107] as the allylating reagents (Scheme 1.5.4a). The robustness of the manganese(I) catalysis was shown by tolerating various functional groups, such as iodides, esters, amides and free hydroxyl groups.[106] Moreover, peptide-conjugates were obtained under the manganese catalysis with various steroid and drug molecules. Notably, an intramolecular allylation enabled the assembly of a 15-membered cyclic peptide (Scheme 1.5.4b), further highlighting the importance of manganese catalysis in peptide diversifications. The pyridyl group was removed in a traceless fashion under mild conditions, delivering native allylated tryptophan **104** (Scheme 1.5.4 c).

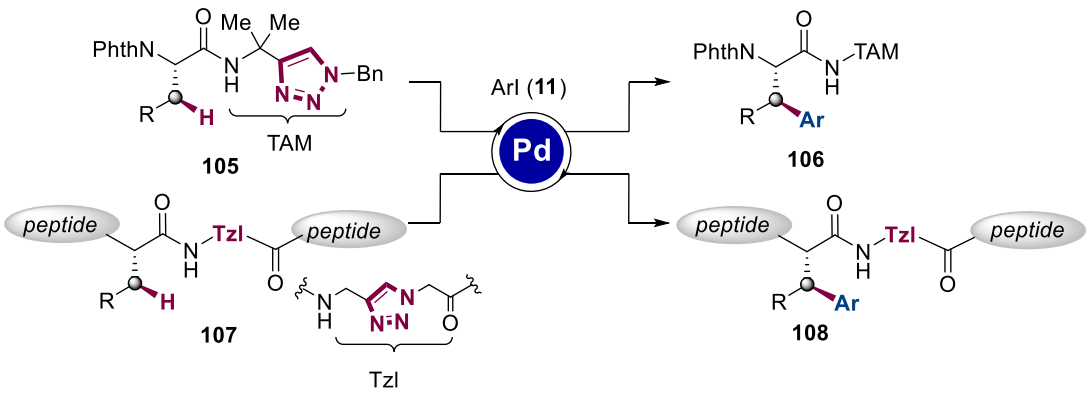


Scheme 1.5.4. Peptide diversification by manganese-catalyzed C–H allylations

2 Objectives

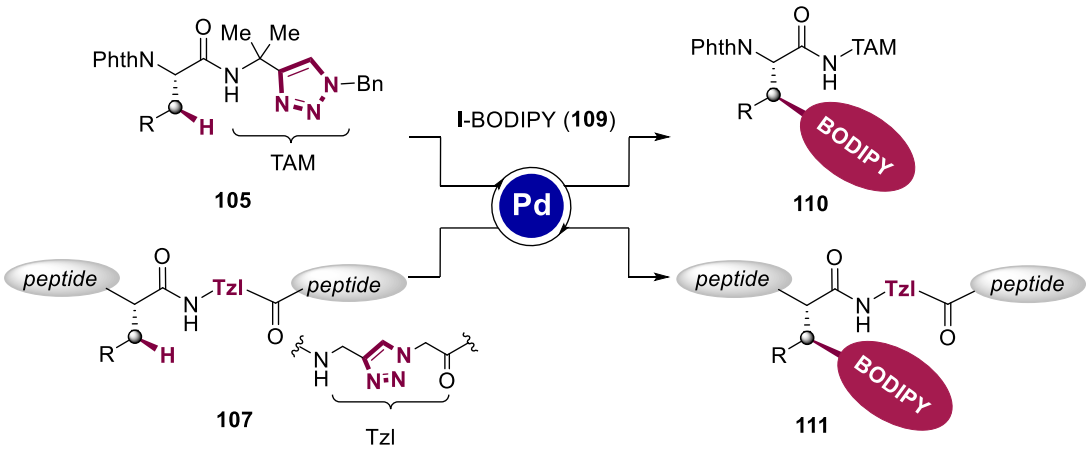
The transition metal-catalyzed C–H activations have been explored as powerful strategy for sustainable organic syntheses.[108] *Prof. Dr. Lutz Ackermann* and coworkers have achieved landmark progress in this field, focusing on establishing highly chemo- and site-selective C–H bond transformations of synthetically useful and valuable organic molecules, which further proved powerful in the applications to medicinal chemistry, material sciences, and electrochemistry.[109] In this context, major efforts were made to establish novel and highly positional selective late-stage peptide diversifications by C–H activations, under palladium, rhodium and Earth-abundant manganese catalysis.

Peptides are of great importance for medicinal chemistry and drug discovery.[34] Numerous efforts have been made in the field of peptide modifications for improved biological and pharmacokinetic properties. In the past few years, C(sp^3)–H activations have been developed as powerful tools for peptide diversifications.[48] Major advances have been limited to the alanine primary C(sp^3)–H activations at the peptide *N*-terminus. In a sharp contrast, secondary C(sp^3)–H arylations are more challenging and important due to its stereo chemistry and structural complexity. The strategy was envisioned by the assistance of peptide bond isosteric triazoles in palladium catalysis, the power of this internal triazole assistance was reflected by establishing the secondary C(sp^3)–H functionalizations on terminal peptides as well as the unprecedented positional-selective C(sp^3)–H functionalization of internal peptides (Scheme 2.1).



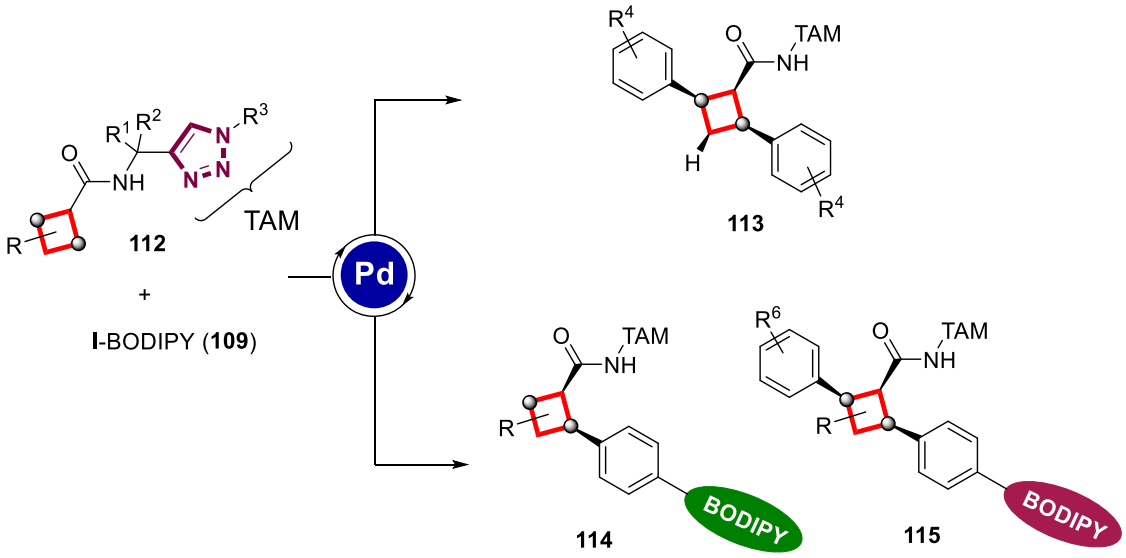
Scheme 2.1. Internal peptide diversifications by isosteric triazole.

As the late-stage peptide diversifications bears potential for drug discovery and pharmaceutical industries,[34] peptide labeling technology enabled the molecular insight into biological events and real-time therapy.[110] Although BODIPY fluorescent dyes proved biocompatible and benign optical properties,[111] BODIPY peptide labeling largely rely on lengthy prefunctionalizations. Internal peptide C–H activations offered direct functionalization strategy, thus the direct peptide BODIPY fluorescent labeling should be developed.



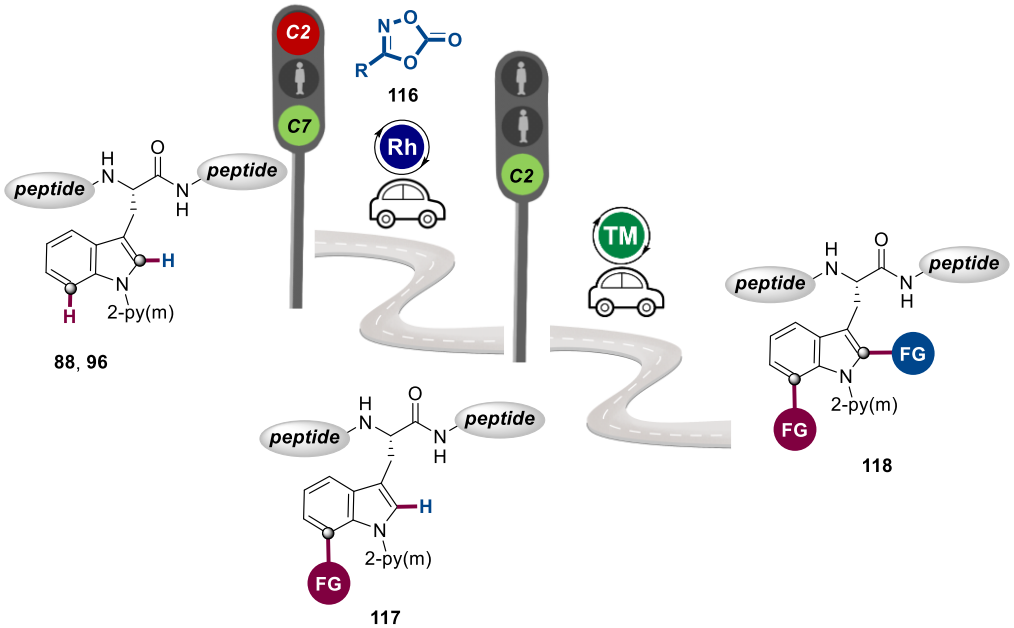
Scheme 2.2. Internal peptide BODIPY fluorescent labeling.

In the field of C(sp^3)–H functionalizations, cyclobutanes are of the great importance as well as amino acids and peptides. Because cyclobutanes represent important building blocks for complex natural molecules with relevant biological activities, and are found as common motifs in several natural products.[112] C(sp^3)–H activations of cyclobutanes enabled a direct strategy for cyclobutane derivative assembly other than [2+2] photocycloaddition[113] which is usually associated with mixtures of isomers. With the established triazole assisted C–H activations, a novel cyclobutane arylation should be established.



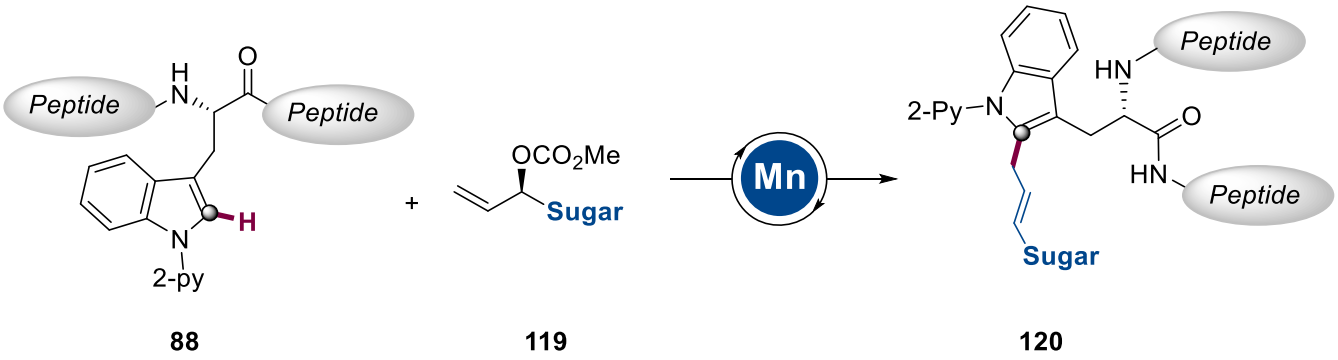
Scheme 2.3. Cyclobutane BODIPY fluorescent labeling.

C–H activation proved powerful and step-economical for peptide modifications,[48] but it is largely restricted to C–C bond formations. C–N bond formations[114] represent established strategies for medicinal chemistry and drug discovery, but rarely employed for peptide diversifications. And late-stage tryptophan containing peptide diversifications are severely restricted to the tryptophan C2 position. In sharp contrast, highly selective C7[115] amidation reaction should be explored by rhodium catalysis.



Scheme 2.4. Peptide sequential functionalizations by tryptophan C7/C2 double C–H activations

Glycopeptides and glycoproteins are largely related to key biological events.[116] Naturally and synthetic glycopeptides serve as effective therapies against infections.[117] However, glycopeptide assemblies are largely limited to lengthy prefunctionalizations. As C–H activation has seen its great success in peptide functionalizations, manganese(I)[20a, 101] catalyzed late-stage peptide C–H glycoconjugation was thus of interest, enabling unprecedented direct peptide glycoconjugation in a racemization-free manner. The manganese(I) catalyst is earth abundant and non-toxic, featuring a sustainable and user friendly peptide bioconjugation process.



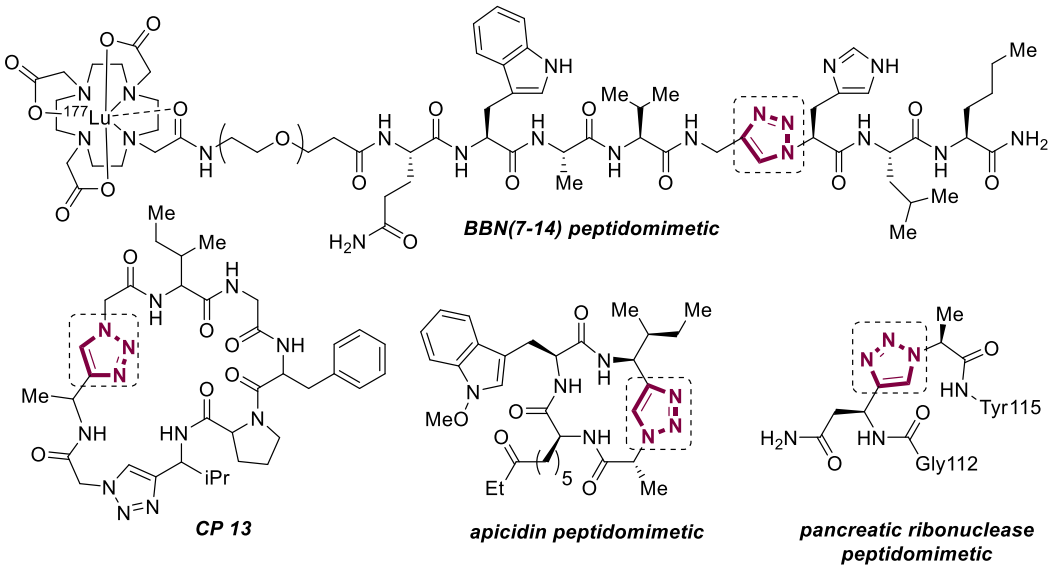
88 **119** **120**

Scheme 2.5. Direct peptide glycoconjugation by manganese(I) catalysis

3 Results and Discussion

3.1 Position-Selective C(sp^3)–H Functionalization by Internal Triazole Assistance: Access to Peptidomimetics

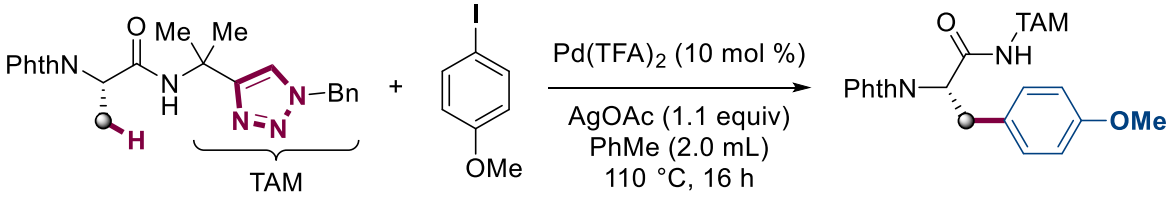
Peptides are linked to biological events, and recognized as therapeutics for the treatment of various diseases, especially unnatural peptides with enhanced biological and pharmacokinetic properties.[35b, 118] Conventional syntheses of unnatural amino acids and peptides have largely relied on biosynthesis and asymmetric synthesis, requiring lengthy prefunctionalizations.[46] C–H activations emerged as a powerful strategy for the direct peptide modifications, with pioneering studies by Correy,[49] Chen,[48c, 95, 119] Lavilla/Albericio[74-75, 93] and Yu.[57-58, 86-87, 120] The development of bidentate directing groups such as 8-aminoquinoline (8-AQ),[51] *N*-(2-pyridyl)sulfamide,[121] 2-methoxyimino acetyl (MIA)[122] and 2-(pyridine-2-yl)isopropyl (PIP)[123] enabled amino acid modification and peptide terminus modifications. In contrast, easily accessible 1,2,3-triazoles were identified as amide surrogates in bioactive peptides (Scheme 3.1.1),[73c, 124] and proved viable for C–H activations within our sustainable chemistry program.[125] We have thus developed internal triazoles for peptide modifications by palladium catalysis, featuring positional selective late-stage peptide modifications.



Scheme 3.1.1. Examples of bioactive internal triazole peptides.

3.1.1 Optimization Studies for Peptide C–H Arylations by Internal Triazole Assistance

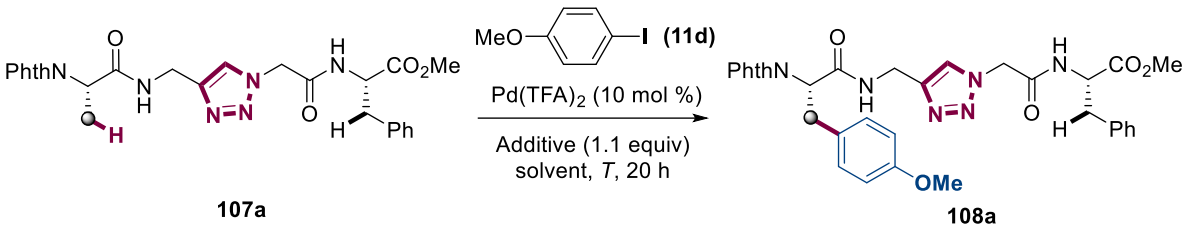
To study the triazole assisted C(sp^3)–H arylation, the previous optimization was carried on by probing reaction conditions for the alanine arylation by *Michaela Bauer* and *Chuan Dong* (Scheme 3.1.1.1).



Scheme 3.1.1.1. Standard reaction condition for alanine arylation by triazole assistance.

To further expand the versatility of this reaction, we further studied the peptide arylation by internal triazole instead of the terminal triazole amide. These optimization was initiated by employing the standard condition of alanine arylation, however, only minor conversion was observed (Table 3.1.1, entry 6), and a synthetically useful conversion was obtained only with much longer reaction time of 72 h (Table 3.1.1, entry 7), indicating a rather slow reaction rate. Decreased amounts of the aryl iodide **11d** severely decreased the yields even at high reaction temperature and irrespective of the solvents (Table 3.1.1, entries 1-5). Intriguingly, a change of the solvent from toluene to DCE led to a similar outcome at a lower reaction temperature of 80 °C, indicating DCE to be a better solvent. Thus with an increased reaction temperature of 130 °C in DCE, the reaction delivered the desired product **108a** in 80% isolated yield (Table 3.1.1, entry 9), while only 52% isolated yield was obtained at 130 °C in toluene. Changes of the silver salts diminished the reaction efficiency (Table 3.1.1.1, entries 10-15).

Table 3.1.1.1 Optimization of C(sp^3)–H arylation on Tzl-containing peptide **107a**.[a]



Entry	11d [equiv]	Additive	Solvent	T [°C]	Yield [%][b]
1	1.5	AgOAc	*o*-xylene	130	12
2	1.5	AgOAc	DMF	100	–
3	1.5	AgOAc	AcOH	100	10
4	1.5	AgOAc	DCE	80	25
5	1.5	AgOAc	PhMe	110	30
6	2.0	AgOAc	PhMe	110	40
7	2.0	AgOAc	PhMe	110	60[c]
8	2.0	AgOAc	DCE	80	57[c]
9	**2.0**	**AgOAc**	**DCE**	**130**	**80**
10	2.0	AgOAc	PhMe	130	52
11	2.0	NH_4OAc[d]	DCE	130	–
12	2.0	KOAc[d]	DCE	130	38
13	2.0	NaOAc[d]	DCE	130	–
14	2.0	KTFA[d]	DCE	130	–
15	2.0	NaTFA[d]	DCE	130	–

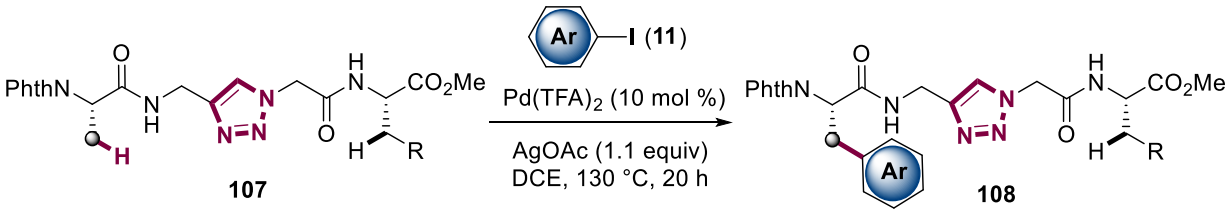
[a] Reaction conditions: **4a** (0.20 mmol), **2a** (0.40 mmol), [Pd] (10 mol %), AgOAc (0.22 mmol), solvent (2.0 mL), *T*, 20 h. [b] Yields of the isolated products. [c] 72 h. [d] 0.4 mmol.

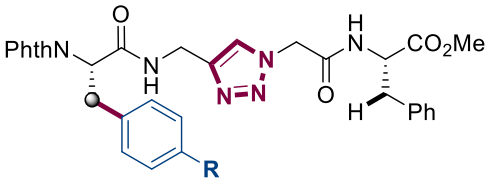
3.1.2 Scope of Peptide C(sp^3)–H Arylations by Internal Triazole Assistance

With the optimized internal peptide arylation condition in hand, we probed the scope of the reaction by palladium catalysis.

For the peptide substrates with different peptidic amino acid sequences of Phth*N*-Ala-Gly-Tzl-Gly-AA_n-OMe, the arylations occurred site-selectively at the general *N*-terminus, although C–H bonds were available at the *C*-terminus (Scheme 3.1.2.1). Both electron-withdrawing and electron-donating substituents on the aryl iodides were compatible, delivering the corresponding arylated peptide products **108** in good to excellent yields with a wealth of functional groups being tolerated, such as esters (**108c**, **108i**, **108m**), nitro (**108d**, **108p**), halides (**108h**, **108l**) and amides (**108b**, **108f**). Arylations of peptides, such as Phth*N*-Ala-Gly-Tzl-Gly-Gly-OMe and Phth*N*-Ala-Gly-Tzl-Gly-Val-OMe, were conducted in HFIP due to solubility issues of the starting materials (**108q**, **108r**). Furthermore, unprecedented internal peptide chemical ligations took place by palladium catalysis, with the alanine-integrated aryl iodide (**108s**) and iodo-phenylalanine (**108t**, **108u**), featuring novel dipeptide disconnections. Internal hexapeptide arylations were successful in HFIP with moderate yields (**108v**, **108w**).

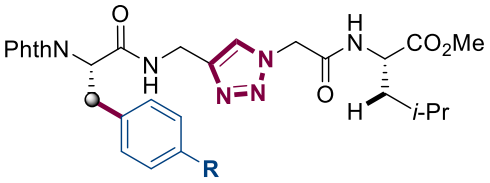
Furthermore, we envisioned the positional-selective peptide arylations controlled by the triazole moiety position. Thus, unprecedented site-selectivity was observed, differentiating the *N*-terminus peptide diversifications (Scheme 3.1.2.2). For the peptide Phth*N*-Phe-Ala-Gly-Tzl-Gly-Leu-OMe, the triazole was placed in the middle position of the peptide, with the *N*-terminus being occupied by phenylalanine. Although C–H bonds on several positions of the peptide were available, the arylation took place on the C(sp^3)–H bond according to the position of the internal triazole (Scheme 3.1.2.2a). Moreover, the dipeptide with the sequence Phth*N*-Phe-Ala-TAM was arylated at the *C*-terminus alanine by the palladium catalysis, due to the peptide *C*-terminus installed by the triazole amide (Scheme 3.1.2.2b). These results suggested a position-tunable C–H activation feature of this reaction, largely resulting from the crucial bidentate assistance from the position-flexible triazoles on the peptides. The mechanism of triazole assisted C(sp^3)–H activation was explored by DFT computational studies by *Michaela Bauer*.[126]





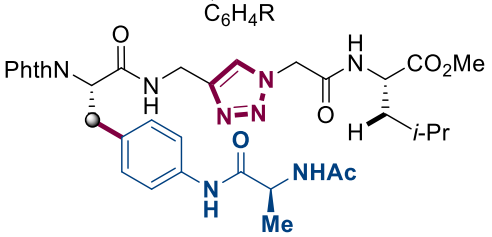
R = OMe (**108a**): 80%
R = NHFmoc (**108b**): 69%
R = CO_2Et (**108c**): 72%
R = NO_2 (**108d**): 66%
R = Ph (**108e**): 59%
R = NHAc (**108f**): 76% [a]

PhThN-Ala-Gly-Tzl-Gly-Phe-OMe
C_6H_4R

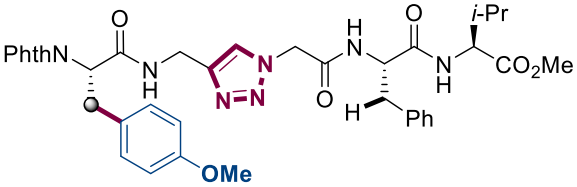


R = OMe (**108k**): 61%
R = F (**108l**): 75%
R = CO_2Et (**108m**): 51%
R = Ph (**108n**): 75%
R = H (**108o**): 65%
R = NO_2 (**108p**): 71%

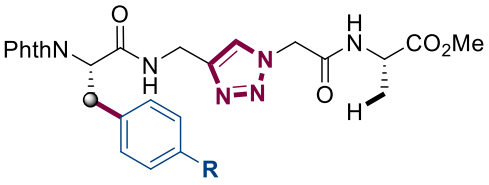
PhThN-Ala-Gly-Tzl-Gly-Leu-OMe
C_6H_4R



108s: 84%[a] PhThN-Ala-Gly-Tzl-Gly-Leu-OMe
C_6H_4-Ala-NHAc

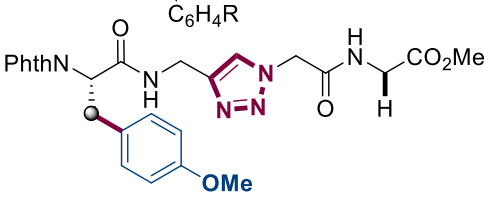


108v: 55%[a] PhThN-Ala-Gly-Tzl-Gly-Phe-Val-OMe
PMP

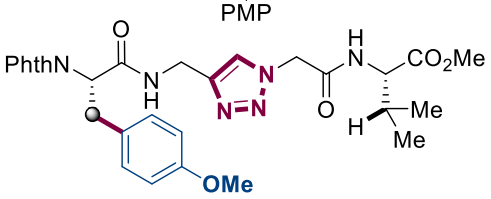


R = OMe (**108g**): 61%
R = F (**108h**): 71%
R = CO_2Et (**108i**): 55%
R = Ph (**108j**): 60%

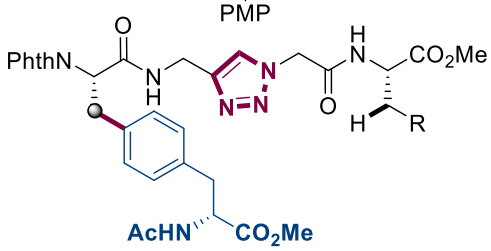
PhThN-Ala-Gly-Tzl-Gly-Ala-OMe
C_6H_4R



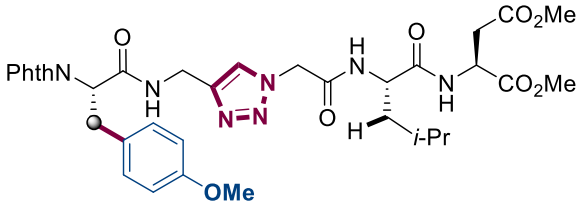
108q: 82%[a] PhThN-Ala-Gly-Tzl-Gly-Ala-OMe
PMP



108r: 79%[a] PhThN-Ala-Gly-Tzl-Gly-Val-OMe
PMP

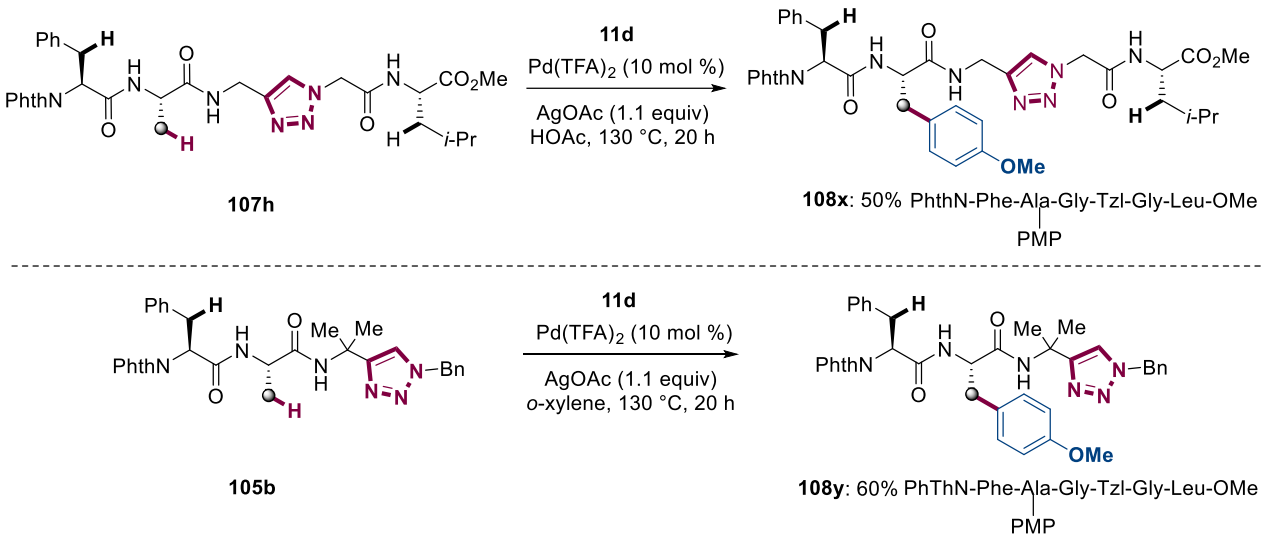


R = Ph (**108t**): 44% PhThN-Ala-Gly-Tzl-Gly-AA-OMe
R = *i*-Pr (**108u**): 82%[b] Ac-Phe-OMe



108w: 63%[a] PhThN-Ala-Gly-Tzl-Gly-Leu-Asp(OMe)-OMe
PMP

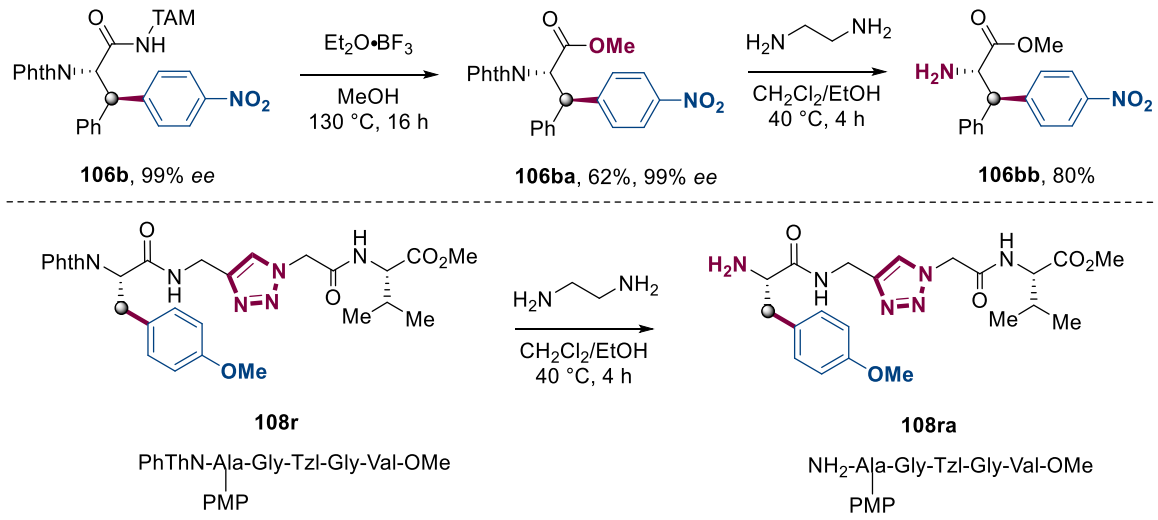
Scheme 3.1.2.1. Internal triazole assisted *N*-terminus peptide arylations. [a] HFIP as solvent. [b] AcOH as solvent.



Scheme 3.1.2.2. Triazole-assisted internal and *C*-terminal peptide C(sp^3)–H arylations.

3.1.3 Removal of TAM Directing Group and Protecting Groups

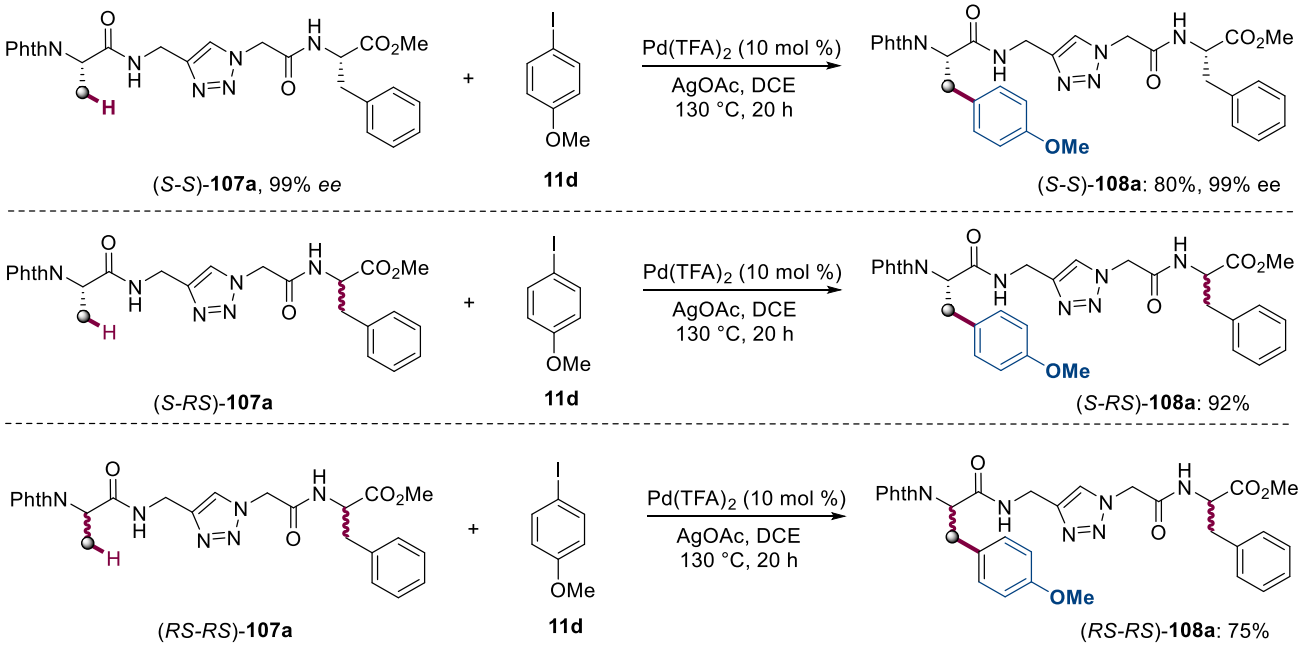
To access the unnatural amino acids, we developed a traceless[33b, 58, 127] removal strategy of the terminal TAM amide directing group. $BF_3{\cdot}Et_2O$ was employed at elevated temperature of 130 °C, giving the ester product (**106ba**) in moderate yield. Importantly, this approach did not lead to a racemization of the stereogenic center of amino acid substrate. Successively, the phthaloyl protecting group could be removed with a vicinal diamine, delivering the free amine group (**106bb**).[86] Similarly, the phthaloyl deprotection was also conducted for the internal peptide **108r**.



Scheme 3.1.3. Removal of TAM and protecting groups.

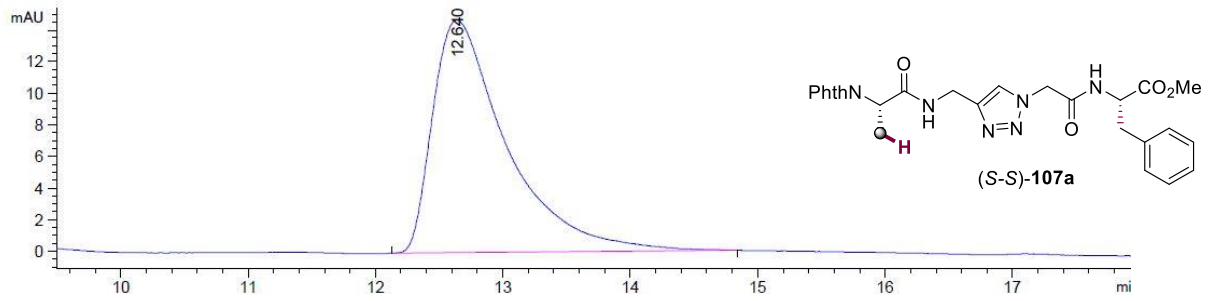
3.1.4 Studies on the Potential Racemizations of Internal Peptide Arylation

To gain insights into the potential racemization of the internal peptide arylation regime, we conducted a racemization study for the peptide C(sp^3)–H activation (Scheme 3.1.4.1).

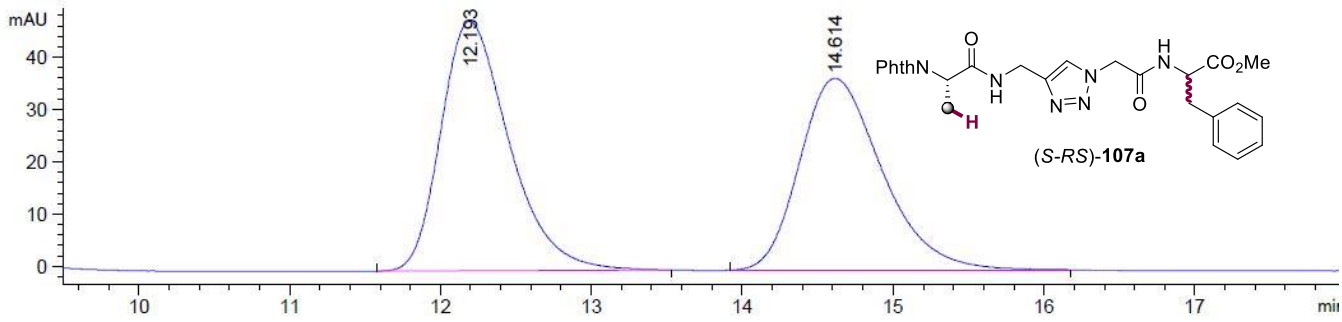


Scheme 3.1.4.1. Racemization study for peptide internal C(sp^3)–H arylation.

The enantiopure substrate were prepared from commercially available *L*-amino acids, while racemized substrates from racemized *D/L*-amino acids. The (*S*-*S*)-**107a** was identified with 99% *ee* by comparison to other racemized substrates in the HPLC studies (Scheme 3.1.4.2). Furthermore, the corresponding products were isolated from the catalytic reactions, and subjected to HPLC analyses (Scheme 3.1.4.3, Scheme 3.1.4.4, Scheme 3.1.4.5), showing the palladium catalyzed internal peptide C(sp^3)–H arylation to be racemization-free.

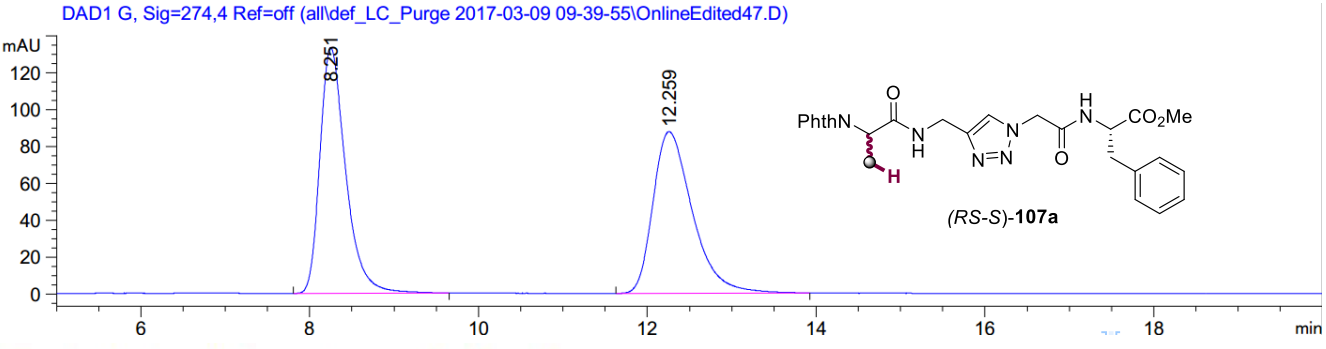


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.640	BB	0.5707	595.41803	14.72702	100.0000



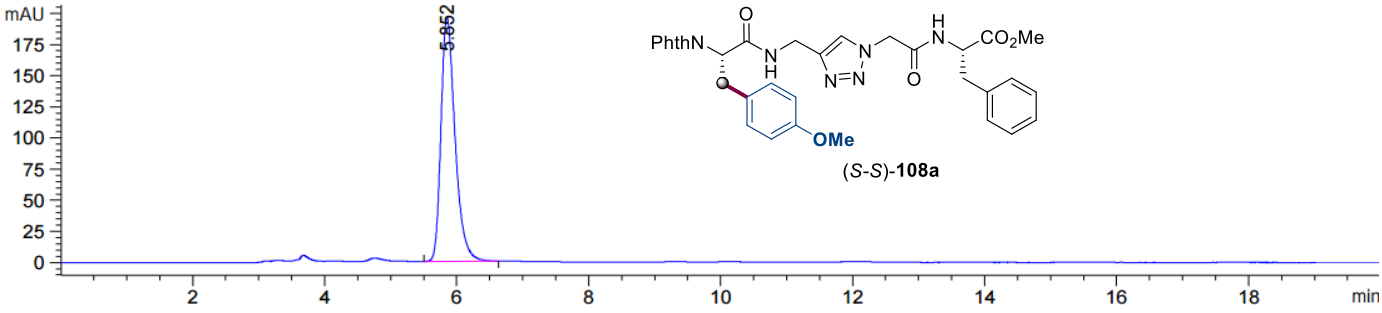
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.193	BB	0.4690	1501.34253	47.73135	51.9420
2	14.614	BB	0.5582	1389.07666	36.65165	48.0580

DAD1 G, Sig=274,4 Ref=off (all\def_LC_Purge 2017-03-09 09-39-55\OnlineEdited47.D)

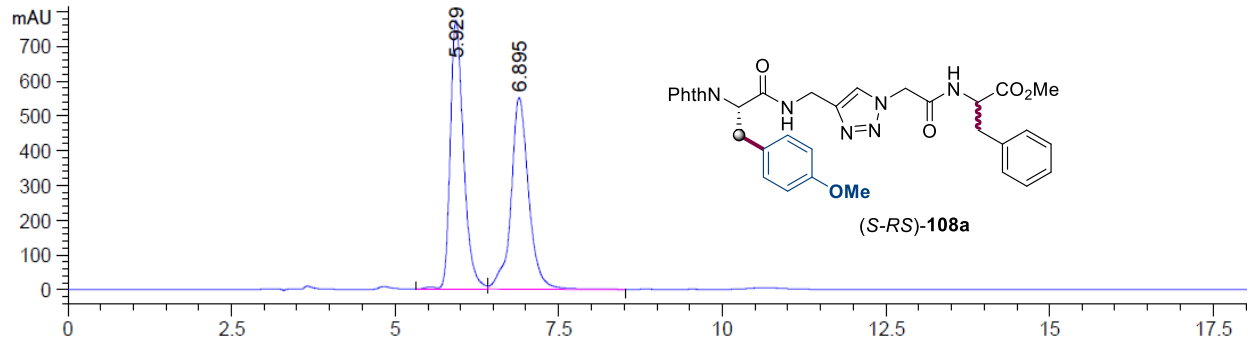


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.251	BB	0.3229	2824.91333	133.47176	49.8509
2	12.259	BB	0.4910	2841.80615	87.71259	50.1491

Scheme 3.1.4.2. HPLC analysis of the eantiopure and racemized substrates (*S-S*)-**107a**, (*S-RS*)-**107a** and (*RS-S*)-**107a**. IC-3 *n*-hexane/EtOAc 20/80 flow: 1 mL/min, 274 nm.

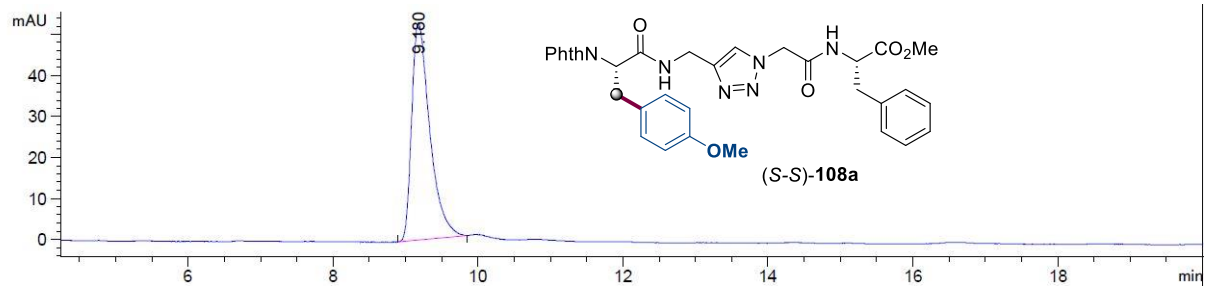


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.852	BB	0.2254	2900.43823	196.26476	100.0000

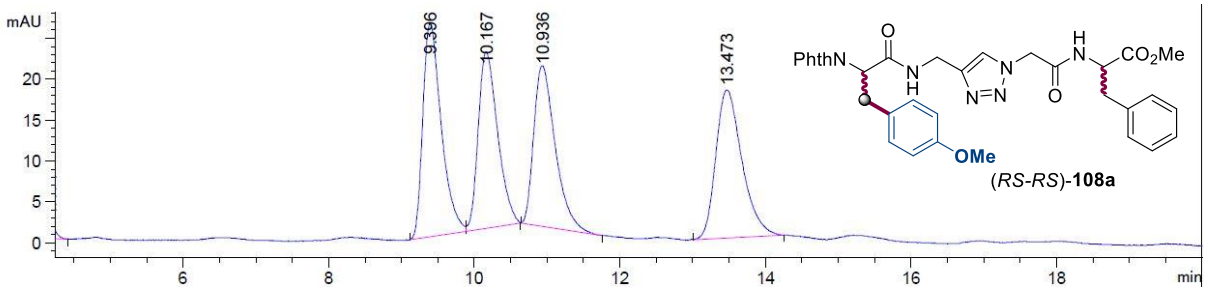


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.929	VV R	0.2154	1.09800e4	773.93903	51.4504
2	6.895	VB	0.2810	1.03609e4	551.91254	48.5496

Scheme 3.1.4.3. HPLC analysis of the eantiopure and racemized products (*S-S*)-**108a** and (*S-RS*)-**108a**. IC-3 *n*-hexane/EtOAc 20/80 flow: 1 mL/min, 274 nm.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.180	BB	0.2563	920.28894	53.06337	100.0000

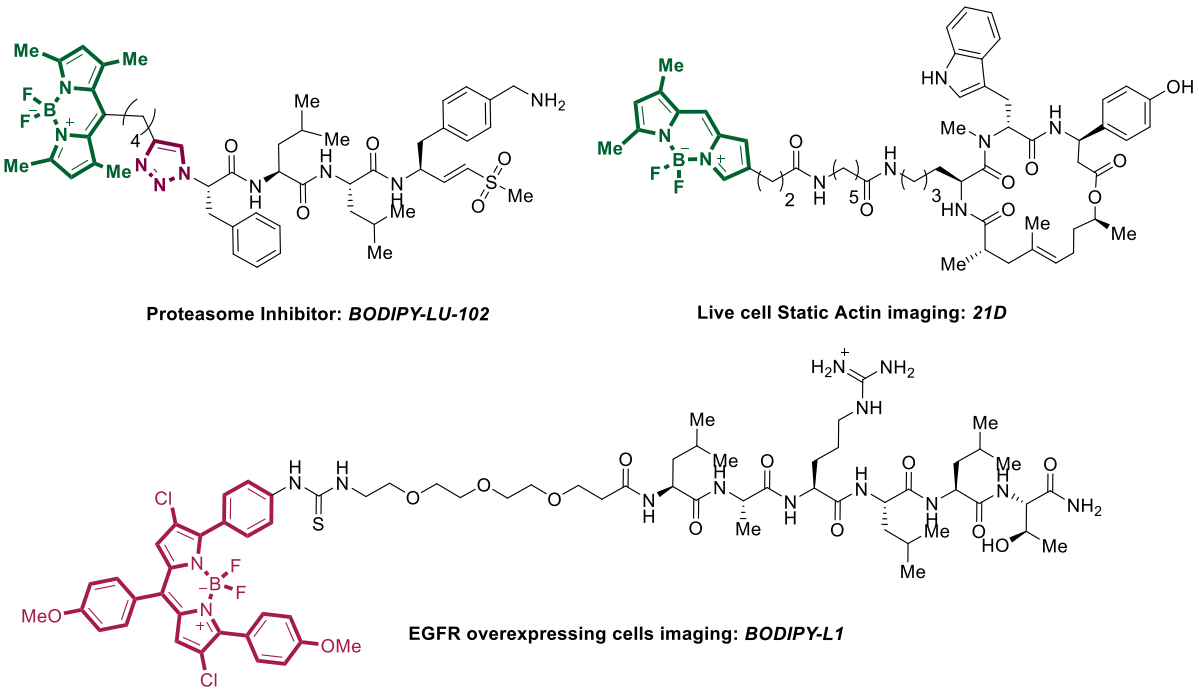


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.396	BV	0.2635	457.60428	26.10282	26.7554
2	10.167	VB	0.2699	398.56140	21.54203	23.3032
3	10.936	BB	0.3002	402.08978	19.61129	23.5095
4	13.473	BB	0.3292	452.07214	18.10910	26.4319

Scheme 3.1.4.4. HPLC analysis of the eantiopure and racemized products (*S*-*S*)-**108a** and (*RS*-*RS*)-**108a**. IF-3 *n*-hexane/EtOAc 30/70 flow: 1 mL/min, 274 nm.

3.2 BODIPY Peptide Labeling by Late-Stage C(sp^3)–H Activation

The structural complex peptides are important molecules in medicinal chemistry and pharmaceutical industries, both as therapeutics for treatment of diseases and as probes for exploring biological activities.[34] The fluorescent labeling of the peptides was recognized as a powerful strategy for visualizing the interactions of these molecules within biological systems.[110] Among various fluorescent labels, BODIPYs were found to be crucial for biochemistry and molecular biology studies.[111] BODIPYs were identified as color-tunable and biocompatible dyes, due to their structural diversity, high cell-permeability, large stock-shift, broad emission wavelength and high quantum yields.[128] BODIPYs were developed as effective biology sensors and cell imaging fluoregens, especially the advances by peptide-BODIPY conjugates (Scheme 3.2.1).[129] However, conventional labelling strategies require lengthy procedures.[130] We thus devised a direct peptide BODIPY labelling by C(sp^3)–H activation, aiming at the BODIPY fluorescent labelings for both primary and secondary C(sp^3)–H bonds with versatile BODIPY structures.

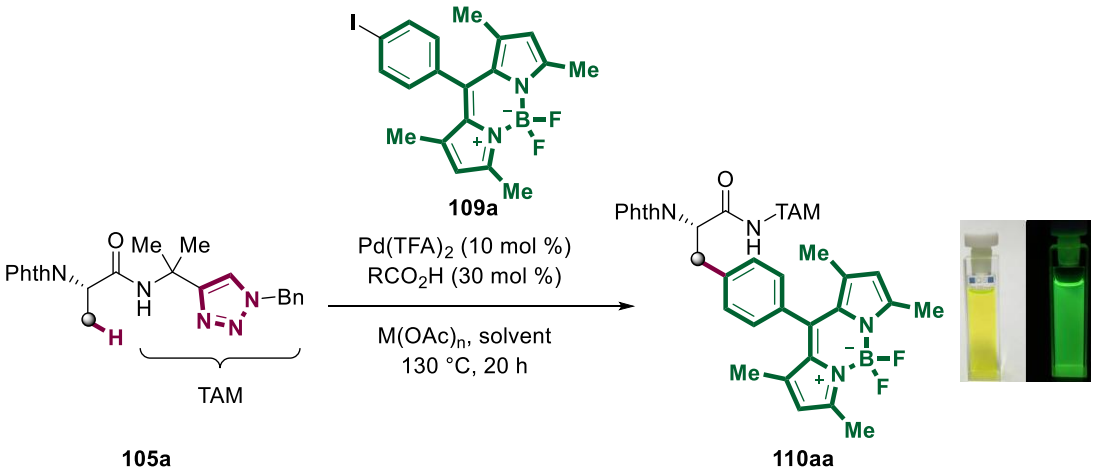


Scheme 3.2.1. Bioactive BODIPY-labeled peptide probes.

3.2.1 Optimization Studies for BODIPY Amino Acid Labeling

Based on the previously developed triazole-assisted alanine arylation reaction (Scheme 3.1.1.1), the initial studies were conducted by probing various reaction parameters for the desired C(sp^3)–H fluorescence labelling of TAM-Alanine **105a** with BODIPY **109a** (Table 3.2.1.1). Iodo-BODIPY **109a** was used as the fluorescent labeling reagent. The testing of reaction solvents identified toluene as being optimal (Table 3.2.1.1, entries 3-5), with 1,4-dioxane giving low yield, while *o*-xylene increased the efficiency. 0.2 M was found to be the concentration of choice (Table 3.2.1.1, entries 6-7). To further improve the reaction conditions, we optimized carboxylate additives[27, 125a] and obtained improved yields with (1-Ad)CO_2H, slightly outcompeting PivOH (Table 3.2.1.1, entry 1 and 8). The reaction yield dropped when shifting from silver salt to copper salts (Table 3.2.1.1, entry 9).

Table 3.2.1.1 Optimization of C(sp^3)–H labelling with BODIPY **109a**.[a]



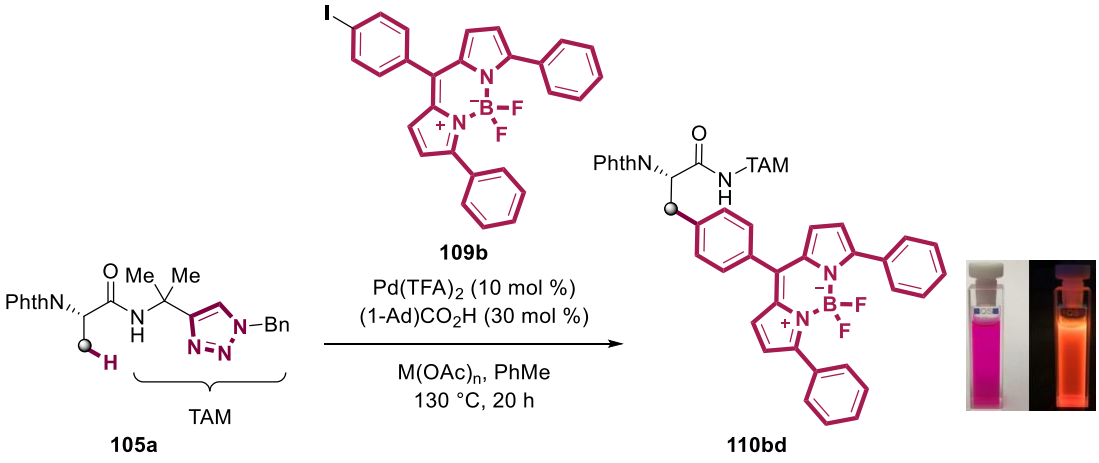
Entry	$MOAc_n$	RCO_2H	Solvent (M)	Yield [%][b]
1	**AgOAc**	**(1-Ad)CO_2H**	**toluene (0.2)**	**84**
2	AgOAc	(1-Ad)CO_2H	toluene (0.2)	69[c]
3	AgOAc	--	toluene (0.2)	75
4	AgOAc	--	1,4-dioxane (0.2)	46
5	AgOAc	--	*o*-xylene (0.2)	70
6	AgOAc	--	*o*-xylene (0.4)	67

7	AgOAc	--	*o*-xylene (0.1)	49
8	AgOAc	PivOH	toluene (0.2)	80
9	$Cu(OAc)_2$	$(1\text{-Ad})CO_2H$	toluene (0.2)	60

[a] Reaction conditions: **105a** (0.10 mmol), **109a** (0.12 mmol), $Pd(TFA)_2$ (10 mol%), $M(OAc)_n$ (0.12 mmol), solvent, N_2, 130 °C, 20 h. [b] Yields of isolated products. [c] 15 mol % $Pd(TFA)_2$ was used.

However, utilizing the optimized conditions for amino acid labeling by green label BODIPY, a decreased yield of 60% was obtained for the arylated BODIPY **109b** (Table 3.2.1.2, entry 1). Thus, identification of the best reaction conditions was further performed. Decreased amounts of the silver salt diminished the reaction yield (Table 3.2.1.2, entry 2), but with $KHCO_3$ as additive the efficiency was slightly improved (Table 3.2.1.2, entry 4). However, $AgNO_3$ almost shut down the reaction, and Ag_2CO_3 led to satisfactory yield (Table 3.2.1.2, entry 2), further emphasizing the crucial effect of the silver salts. Moreover, the use of $Cu(OAc)_2$ gave a similar outcome as the Ag_2CO_3 and was further employed as the optimal additive, considering the abundance and lower toxicity of copper (Table 3.2.1.2, entry 8).

Table 3.2.1.2 Optimization of $C(sp^3)$—H labelling with arylated BODIPY **109b**.[a]



Entry	$MOAc_n$	Additive	Yield [%][b]
1	AgOAc	--	60
2	AgOAc	--	20[c]
3	AgOAc	$KHCO_3$	59[c]
4	AgOAc	$KHCO_3$	63

5	$AgNO_3$	--	--
6	Ag_2CO_3	--	72
7	$Cu(Opiv)_2$	--	50
8	**$Cu(OAc)_2$**	**--**	**73**

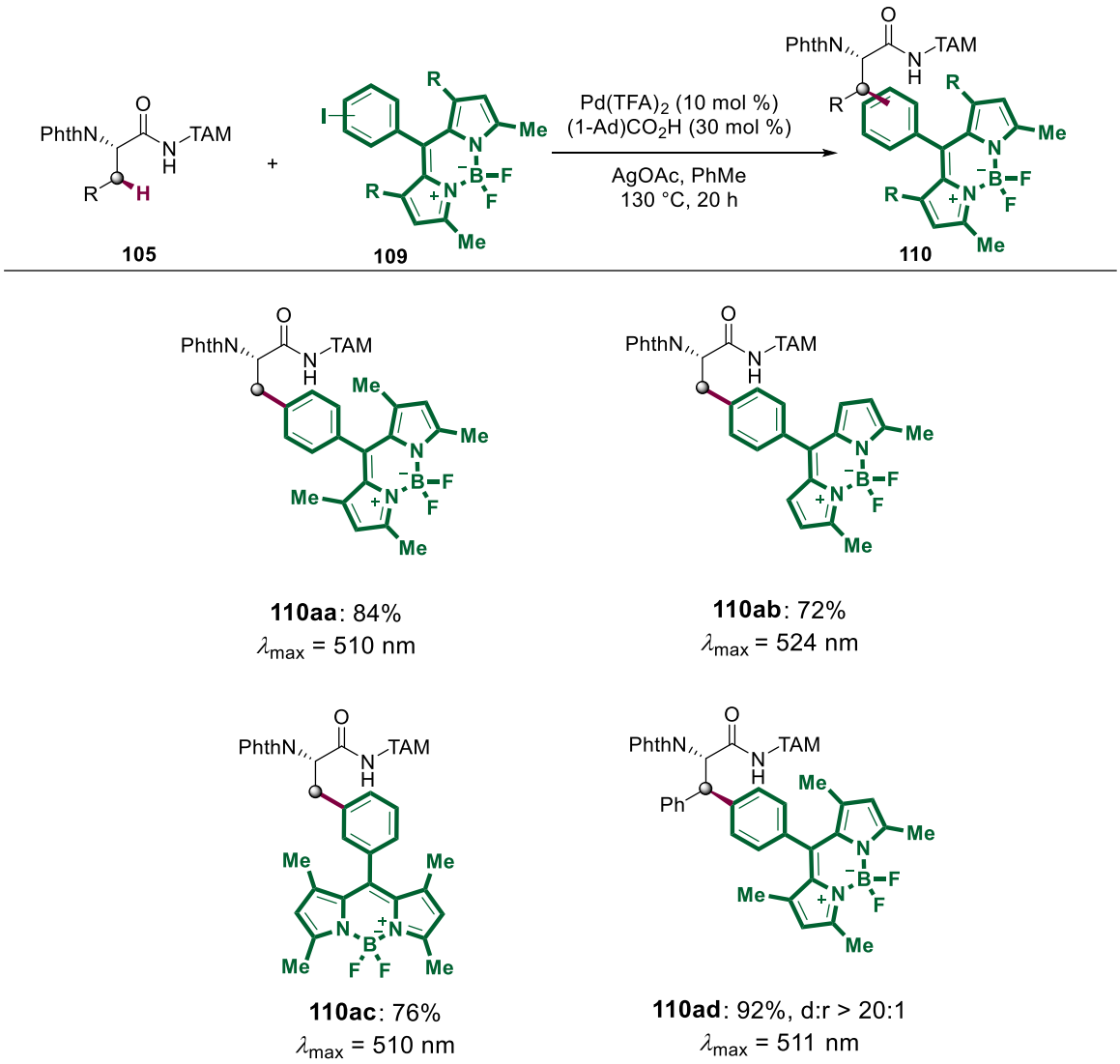
[a] Reaction conditions: **105a** (0.10 mmol), **109b** (0.12 mmol), $Pd(TFA)_2$ (10 mol %), RCO_2H (30 mol %), $M(OAc)_n$ (0.2 mmol), additive (0.12 mmol), PhMe (0.5 mL), N_2, 130 °C, 20 h. [b] Yields of isolated products. [c] AgOAc (0.12 mmol).

3.2.2 Scope of BODIPY Amino Acid Labeling

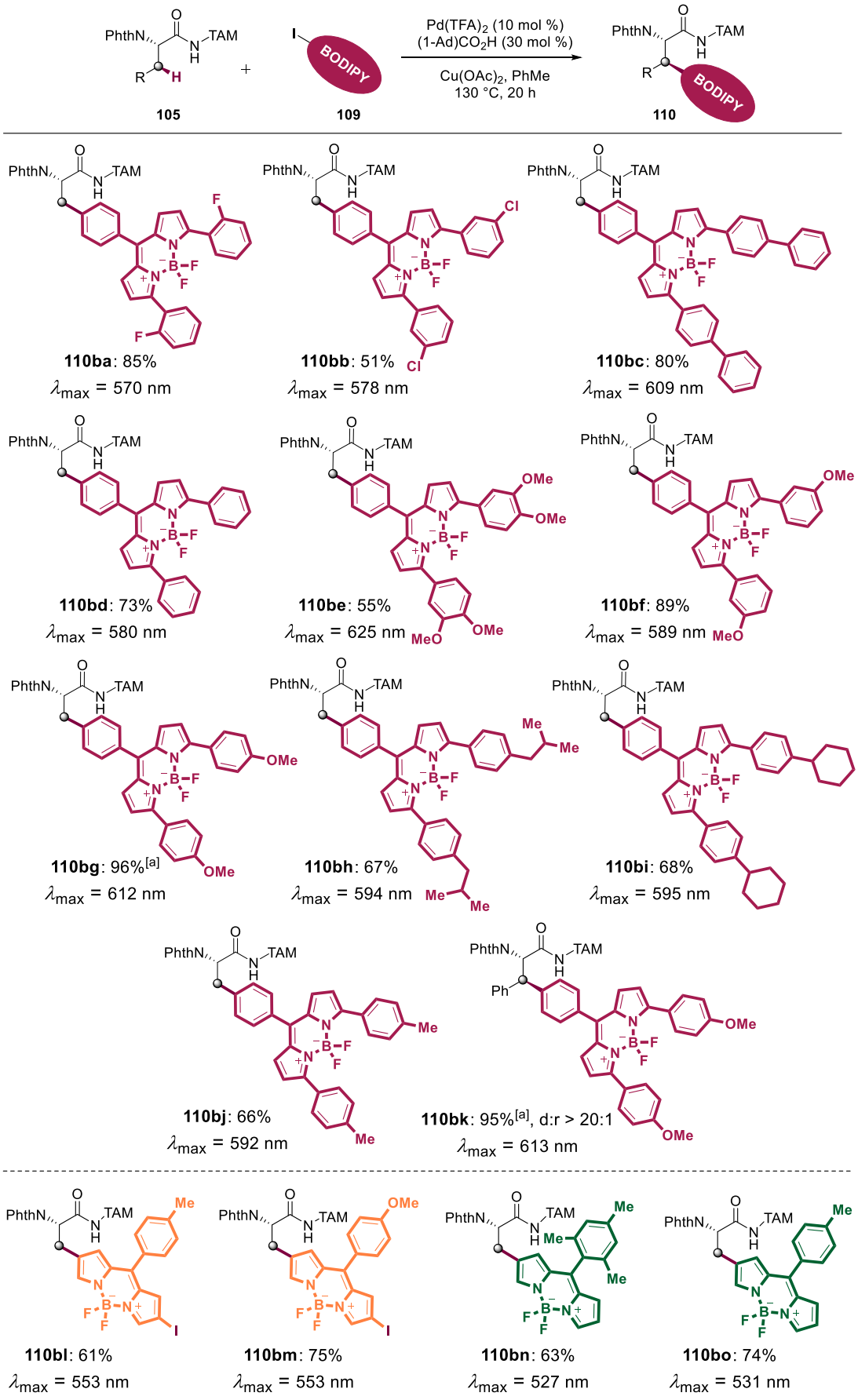
With the optimized reaction conditions in hand, we tested the product scope by the triazole-assisted alanine and phenylalanine C(sp^3)–H labeling. Excellent yield was obtained with tetramethyl iodo-BODIPY **109a**, giving the BODIPY inserted amino acid product **110aa** with an absorption maximum at λ_{max} = 510 nm. While dimethyl iodo-BODIPY led to a slightly reduced reaction efficiency (**110ab**). *meta*-Iodo-BODIPY was compatible as well (**110ac**), indicating a broad scope with various BODIPY shapes. Moreover, the labeling of phenylalanine gave an excellent yield and disastereoselectivity (**110ad**), featuring the reaction a highly precise and efficient fluorescent labeling strategy for amino acids.

Next, more BODIPY types were probed for a broader scope of BODIPY modified amino acids, employing the standard reaction conditions for arylated BODIPY labeling (Scheme 3.2.2.2). Both electron-poor and electron-rich BODIPYs were tolerated under the racemization-free conditions, with maximum emission wavelengths ranging from 570 to 625 nm. Notably, synthetically useful halides were introduced, such as fluoride (**110ba**) and chloride (**110bb**). And red-shift wavelength was observed with extended π system (**110bc**) or electron-donating substituents (**110be**-**110bk**). For secondary C(sp^3)–H labeling of phenylalanine, excellent levels of diastereo control of > 20:1 was obtained, along with excellent yields (**110bk**). Except for the iodo-BODIPY substitution at the *meso*-position of BODIPYs, the 2- and 2,6-diiodo BODIPYs were well compatible for the labeling, yielding products bearing the active BODIPY α-C–H bonds (**110bl**-**110bo**). It is noteworthy that mono-selective BODIPY labeling was viable with the 2,6-diiodo BODIPY, delivering the BODIPY labeled amino acid with functional

group iodide (**110bl**,**110bm**). Furthermore, these iodide BODIPY products bear red-shifted wavelengths as yellow fluorescence, compared to the green fluorescence of **110bn** and **110bo**.



Scheme 3.2.2.1. Primary and secondary C(sp^3)–H BODIPY labelling.

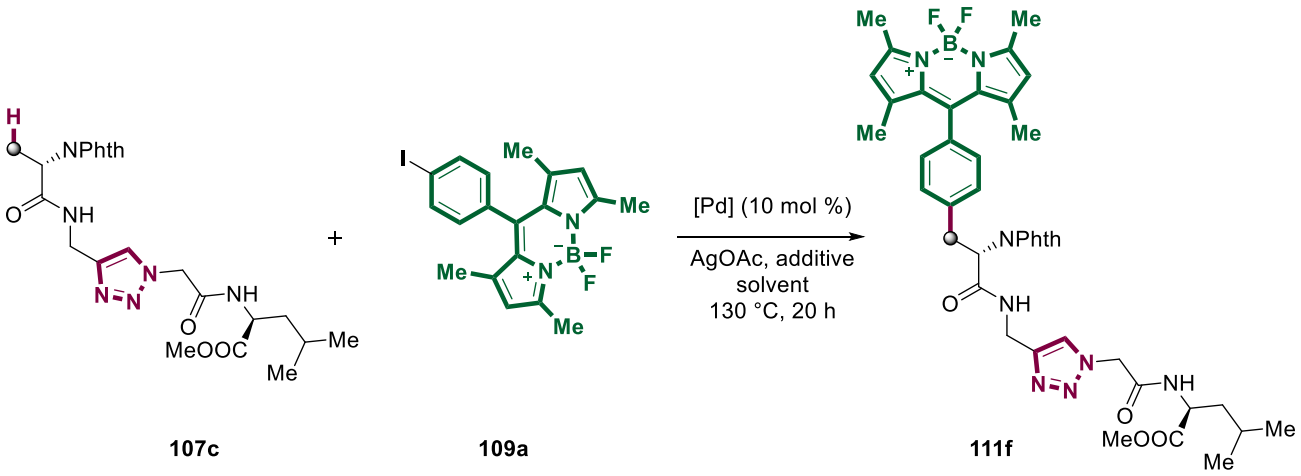


Scheme 3.2.2.2. Primary and secondary C(sp^3)–H BODIPY labelling.

3.2.3 Optimization Studies for BODIPY Peptide Labeling

Despite the success of the amino acid BODIPY labeling, standard conditions for both alkylated and arylated BODIPYs did not lead to useful yields for the internal peptides. Consequently, we conducted further optimizations for the internal peptide labeling with both green and red BODIPY labels. Utilizing of $Cu(OAc)_2$ generated more undesired byproducts. $Pd(OAc)_2$ was found to be the best catalyst (Table 3.2.3.1, entries 1-2). And toluene was found to be the solvent of choice, giving useful yields by carboxylate assistance with (1-Ad)CO_2H.

Table 3.2.3.1 Optimization of peptide C(sp^3)–H green label BODIPY labeling.[a]



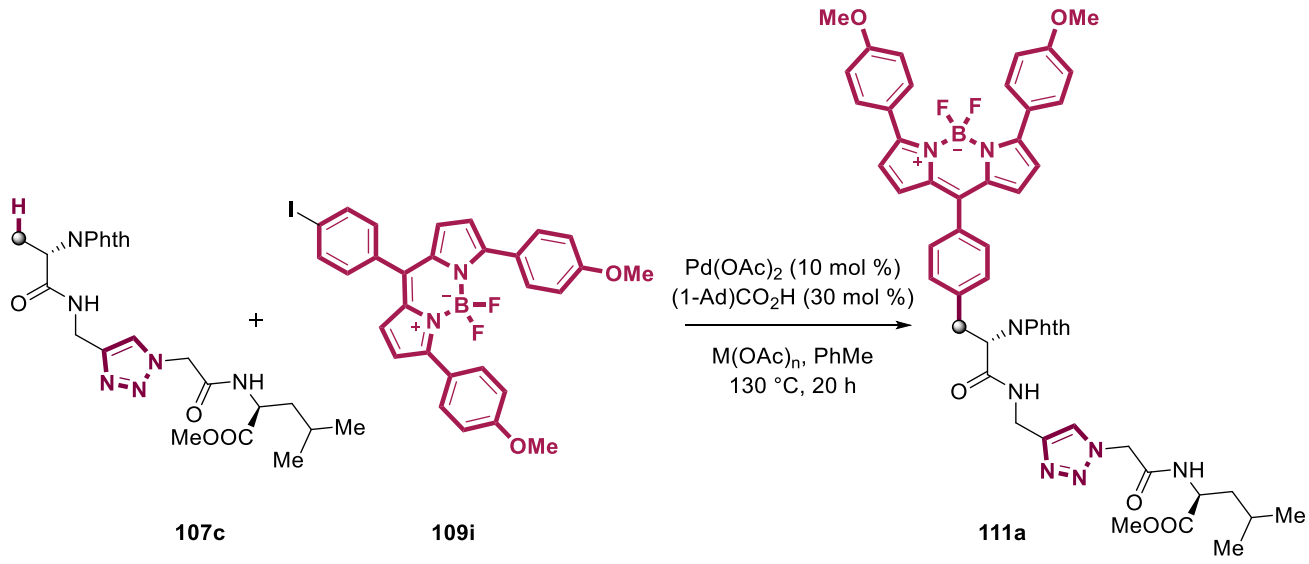
107c **109a** **111f**

Entry	[Pd]	Additive	Solvent	Yield [%][b]
1	$Pd(TFA)_2$	--	*o*-xylene	20
2	$Pd(OAc)_2$	--	*o*-xylene	40
3	**$Pd(OAc)_2$**	**(1-Ad)CO_2H**	**toluene**	**47**
4	$Pd(OAc)_2$	(1-Ad)CO_2H	*o*-xylene	33
5	$Pd(OAc)_2$	(1-Ad)CO_2H	DCE	--
6	$Pd(OAc)_2$	(1-Ad)CO_2H	DMF	--
7	$Pd(OAc)_2$	(1-Ad)CO_2H	HFIP	--

[a] Reaction conditions: **107c** (0.10 mmol), **109a** (0.12 mmol), [Pd] (10 mol %), RCO_2H (30 mol %), AgOAc (0.12 mmol), solvent (0.5 mL), N_2, 130 °C, 20 h. [b] Yields of isolated products.

Based on the above optimizations, further optimizations revealed that for the red label **109i**, a larger amount of silver salts improved the efficacy (Table 3.2.3.2, entries 1-2). AgOAc was found to be more efficient as compared with Ag_2CO_3 or $Cu(OAc)_2$ (Table 3.2.3.2, entries 3-5).

Table 3.2.3.2 Optimization of peptide C(sp^3)–H red label BODIPY labeling.[a]



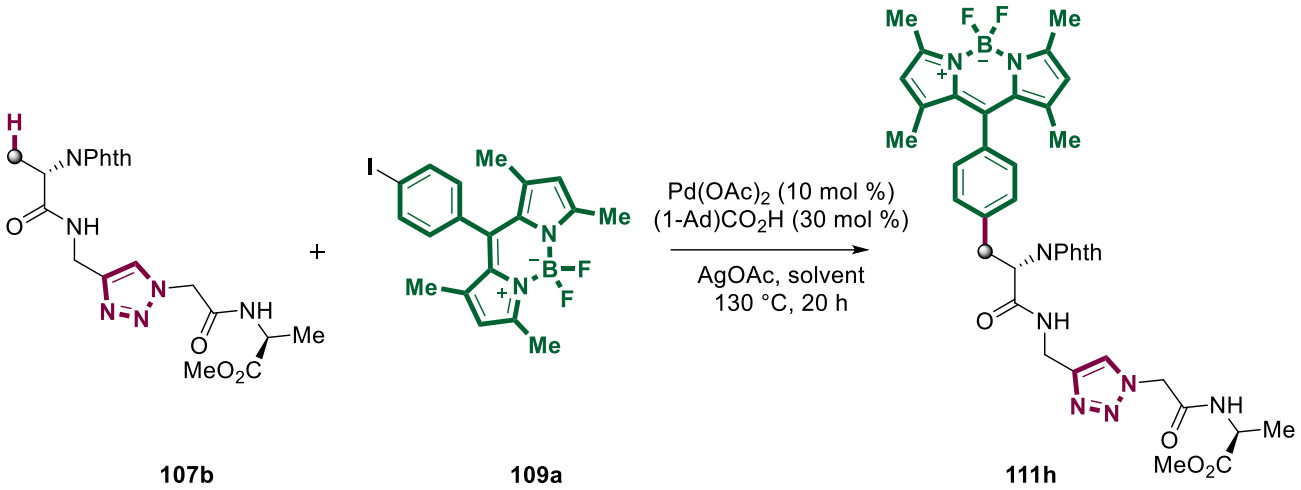
107c **109i** **111a**

Entry	$M(OAc)_n$	Yield [%][b]
1	**$Ag(OAc)_2$ (2.0 equiv)**	**74**
2	$Ag(OAc)_2$ (1.0 equiv)	36
3	Ag_2CO_3 (2.0 equiv)	40
4	Ag_2CO_3 (1.0 equiv)	46
5	$Cu(OAc)_2$ (2.0 equiv)	31

[a] Reaction conditions: **107c** (0.10 mmol), **109j** (0.12 mmol), $Pd(OAc)_2$ (10 mol %), (1-Ad)CO_2H (30 mol %), $M(OAc)_n$, PhMe (0.5 mL), N_2, 130 °C, 20 h. [b] Yields of isolated products.

However, for peptides with lower solubility levels, the C(sp^3)–H BODIPY labeling was almost shut down in toluene (Table 3.2.3.3, entries 1-3). Hence, DCE was found to be a suitable solvent (Table 3.2.3.3, entry 4). A useful yield was obtained with an increased catalyst loading (Table 3.2.3.3, entry 5).

Table 3.2.3.3 Optimization of peptide C(sp^3)–H red label BODIPY labeling.[a]

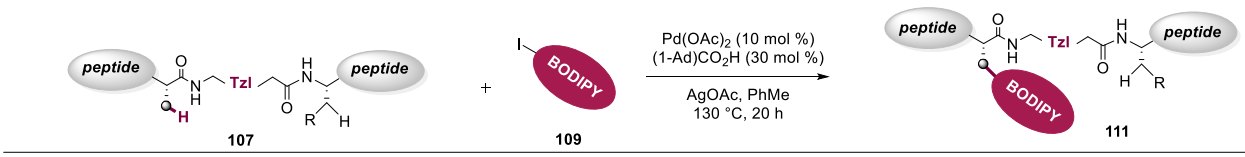


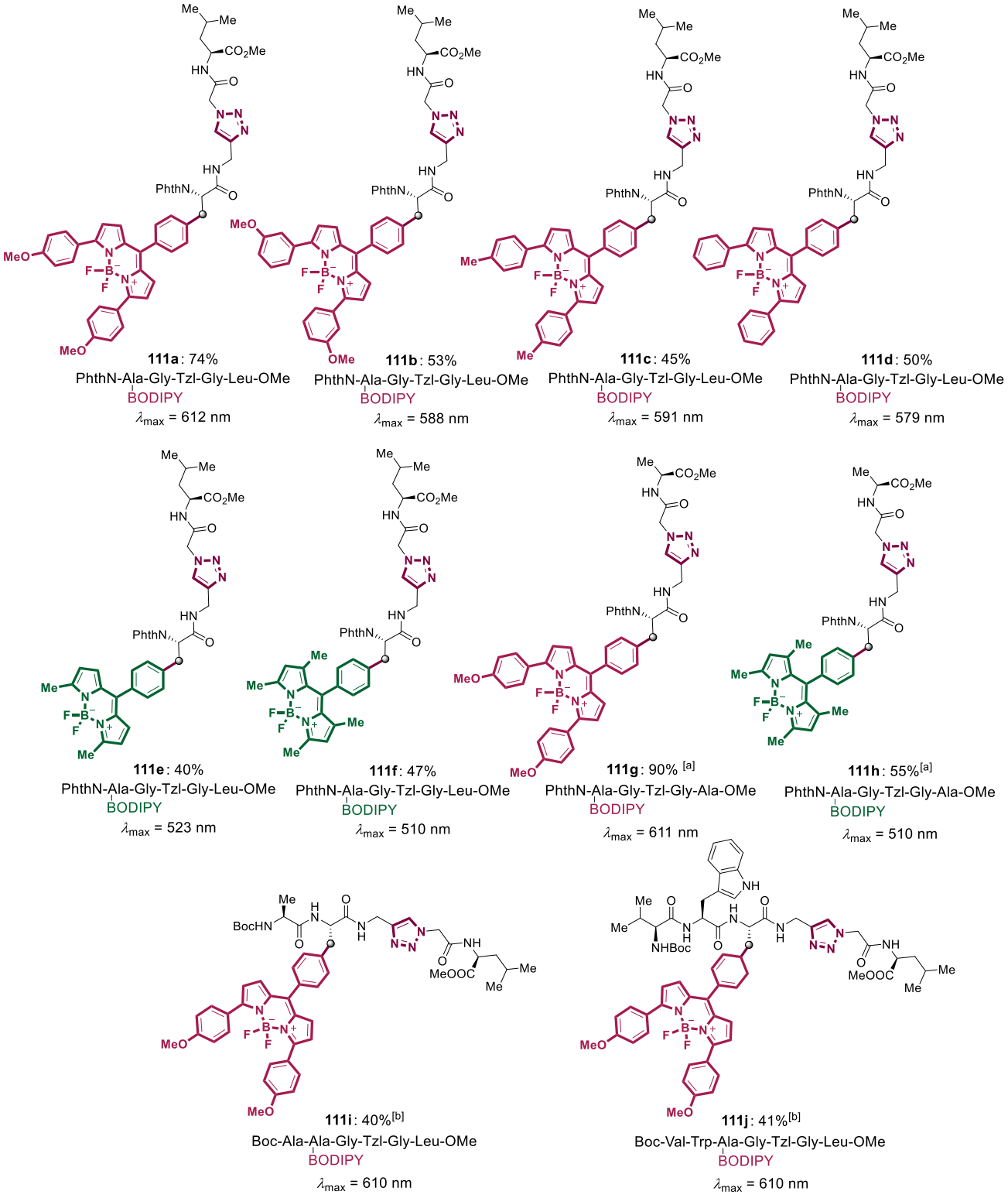
107b **109a** **111h**

Entry	Solvent	Yield [%][b]
1	*o*-xylene	<5%[c]
2	toluene	10
3	DMF	<5%[c]
4	DCE	15
5	DCE	55[d]

[a] Reaction conditions: **107b** (0.10 mmol), **109a** (0.12 mmol), $Pd(OAc)_2$ (10 mol %), $(1\text{-Ad})CO_2H$ (30 mol %), AgOAc (0.2 mmol), solvent (0.5 mL), N_2, 130 °C, 20 h. [b] Yields of isolated products. [c] Conversion determined by LC-MS analysis. [d] $Pd(OAc)_2$ (20 mol %).

With the peptide BODIPY labeling strategy established by the above optimization studies in hand, we expanded the BODIPY peptide scope by probing various peptides with green or red label BODIPYs, good to excellent yields were obtained in a racemization-free fashion, and the site-selectivity was secured by the assistance of the internal triazole moieties (Scheme 3.2.3.1). Furthermore, the *N*-terminus of peptide **111a** was deprotected, then the deprotected peptide was used for sequential peptide synthesis (**111i**, **111j**), featuring the reported BODIPY peptides stable and a unique potential for modification of structural complex peptide sensors.

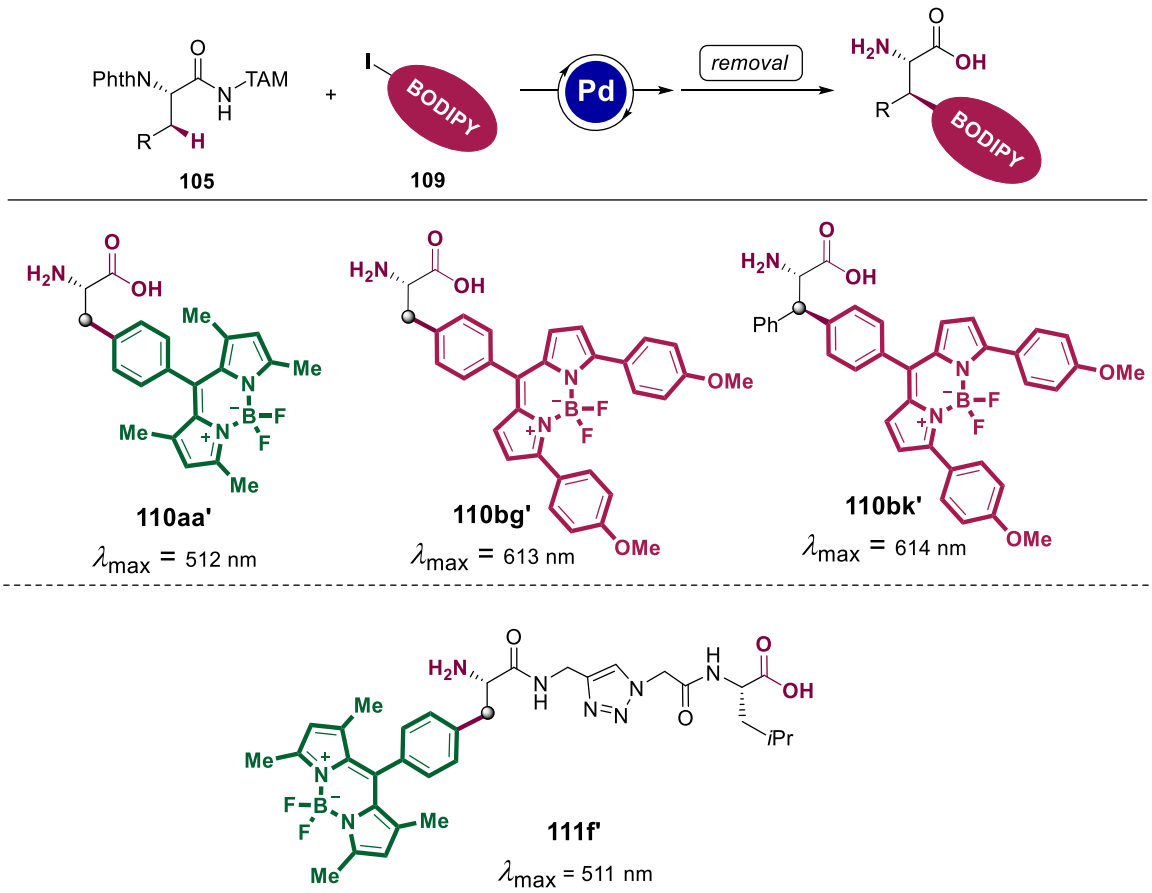




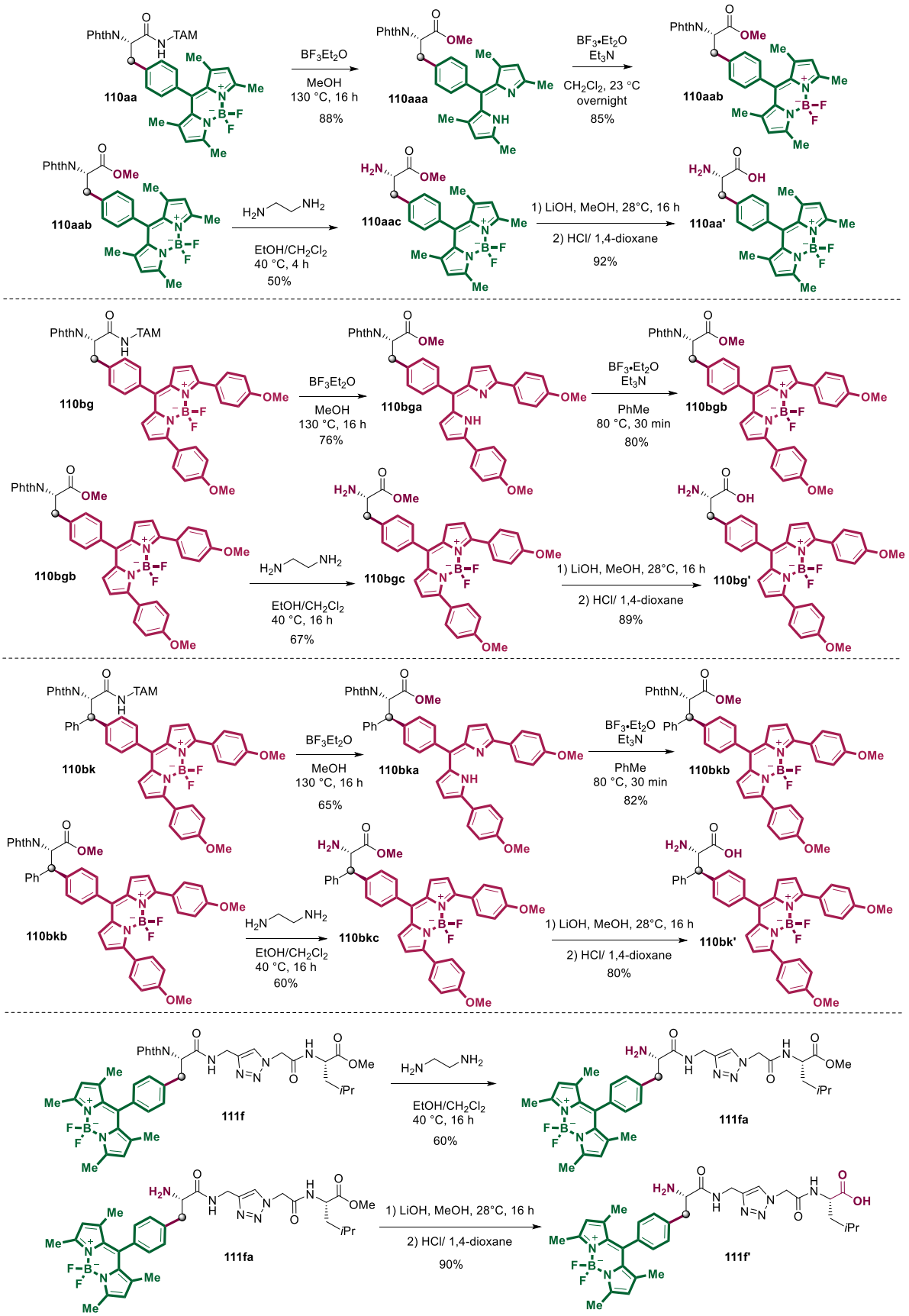
Scheme 3.2.3.1. BODIPY C(sp^3)–H labeling of internal Tzl-peptides. [a] DCE as the solvent. [b] Sequentially synthesized from **111a**.

3.2.4 Removal of TAM and Protecting Groups

Additionally, we established the traceless removal of the TAM group and the protecting groups, to gain access to free BODIPY amino acids and peptides (Scheme 3.2.4.1). To proceed the multiple removals, several steps have been conducted (Scheme 3.2.4.2). Initiating work was the removal of TAM group, with masked amino acid ester as the product. However, due to the strong acidic condition, the boron center of BODIPY was cleaved as well, which could be reinstalled by Et_3N and $BF_3{\cdot}Et_2O$ in excellent yields. Afterwards, the phthaloyl protecting group was deprotected by ethylene diamine, followed by the deprotection of ester to give the desired amino acids. For internal triazole peptide BODIPY, the phthaloyl group and ester could be sequentially removed.



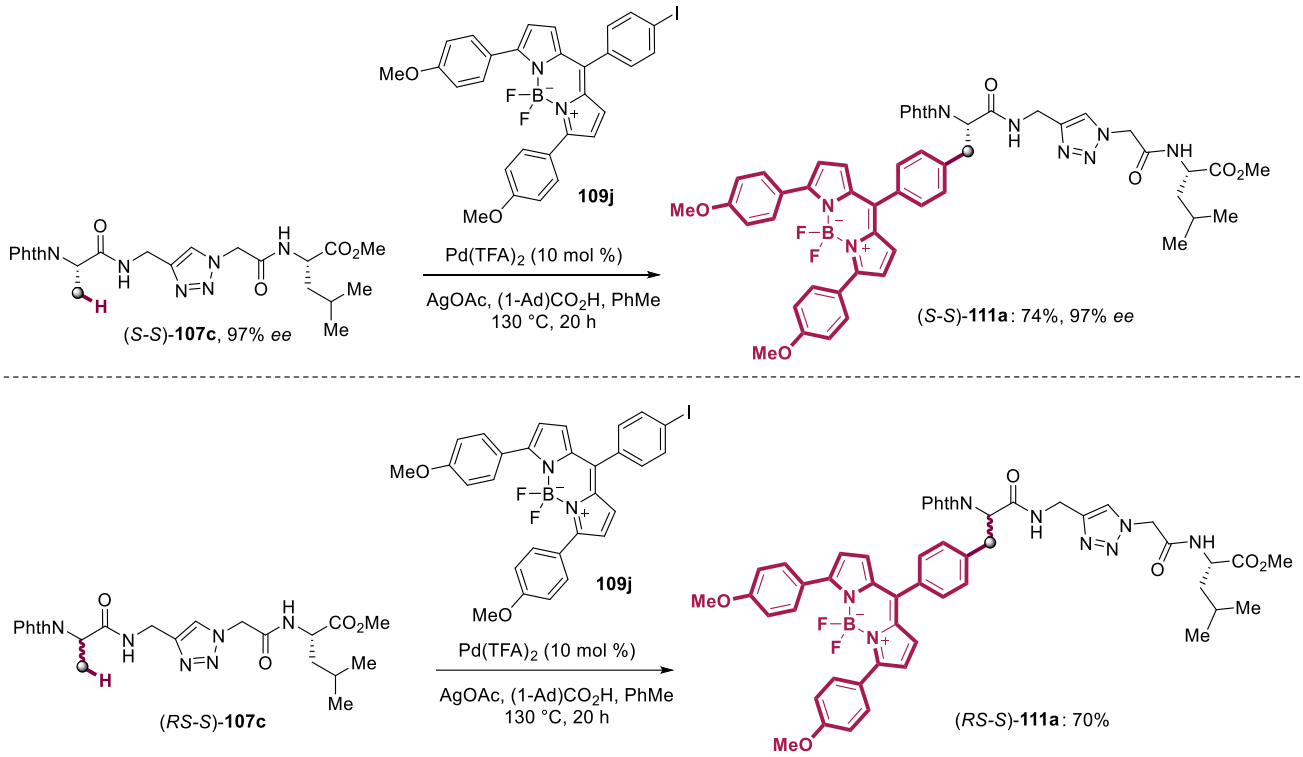
Scheme 3.2.4.1. Traceless removal towards BODIPY labeled parent amino acids **110** and peptides **111**.



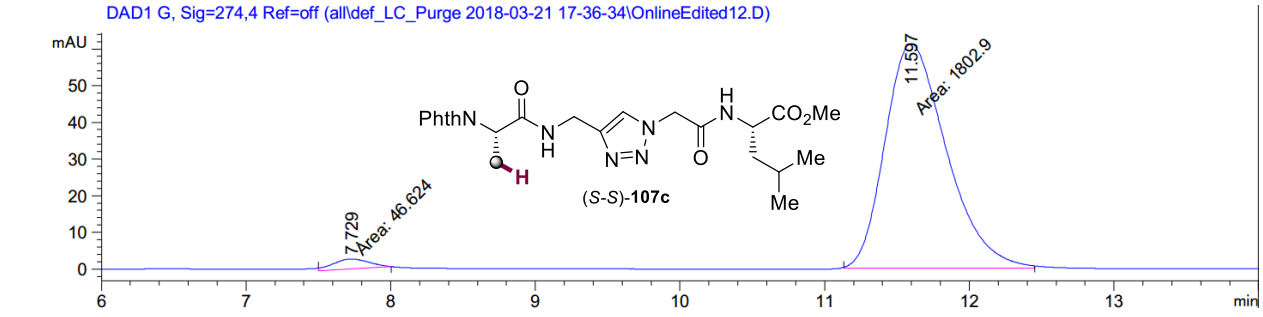
Scheme 3.2.4.2. Sequential removal towards BODIPY labeled parent amino acids **110** and peptides **111**.

3.2.5 Studies on Potential Racemizations

To explore the possible racemizations on amino acid stereogenic center during the palladium-catalyzed BODIPY labeling, we performed the C–H activation with both racemized substrates and enantiopure substrates, followed by HPLC studies. The comparison showed no loss of stereoinformation of the substrate during the reaction, for both the amino acid **105a** and the peptide **107c**.

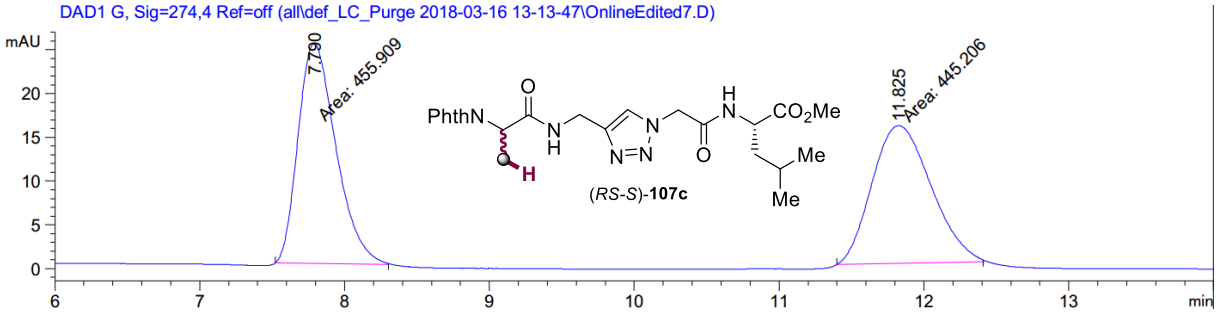


Scheme 3.2.5.1. Racemization study of peptide internal BODIPY labeling.



Signal 2: DAD1 G, Sig=274,4 Ref=off

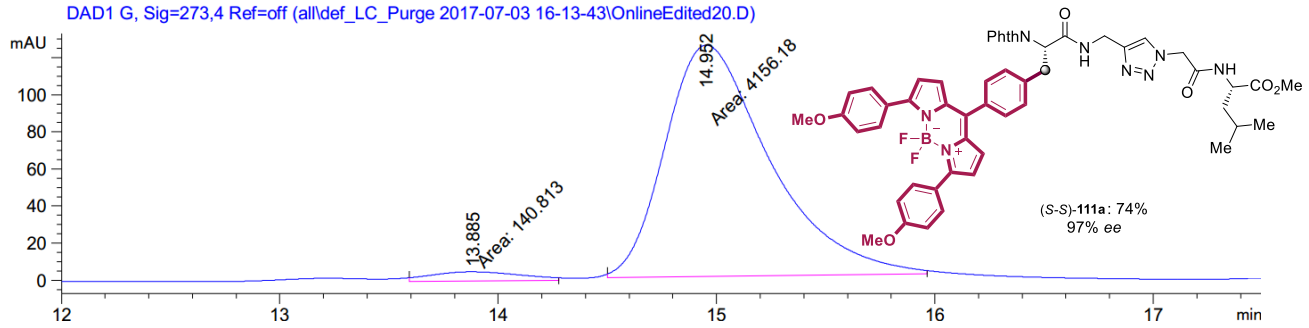
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.729	MM	0.2889	46.62395	2.68944	2.5209
2	11.597	MM	0.4916	1802.89758	61.11798	97.4791
Totals :				1849.52153	63.80742	



Signal 2: DAD1 G, Sig=274,4 Ref=off

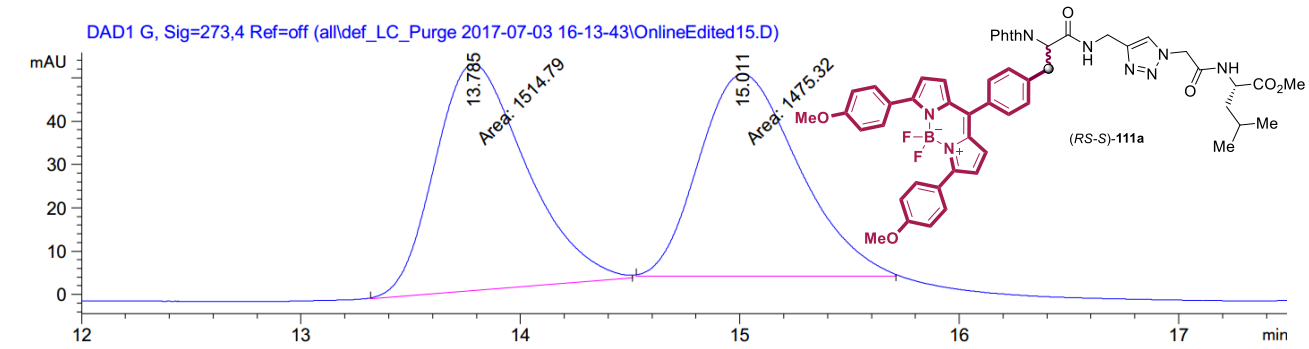
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.790	MM	0.3019	455.90894	25.17102	50.5939
2	11.825	MM	0.4723	445.20557	15.70892	49.4061
Totals :				901.11450	40.87994	

Scheme 3.2.5.2. HPLC analysis of the enantiopure and racemized substrates (*S*-*S*)-**107c** and (*RS*-*S*)-**107c**. IC *n*-hexane/EtOAc 20/80 flow: 1 mL/min, 274 nm.



Signal 2: DAD1 G, Sig=273,4 Ref=off

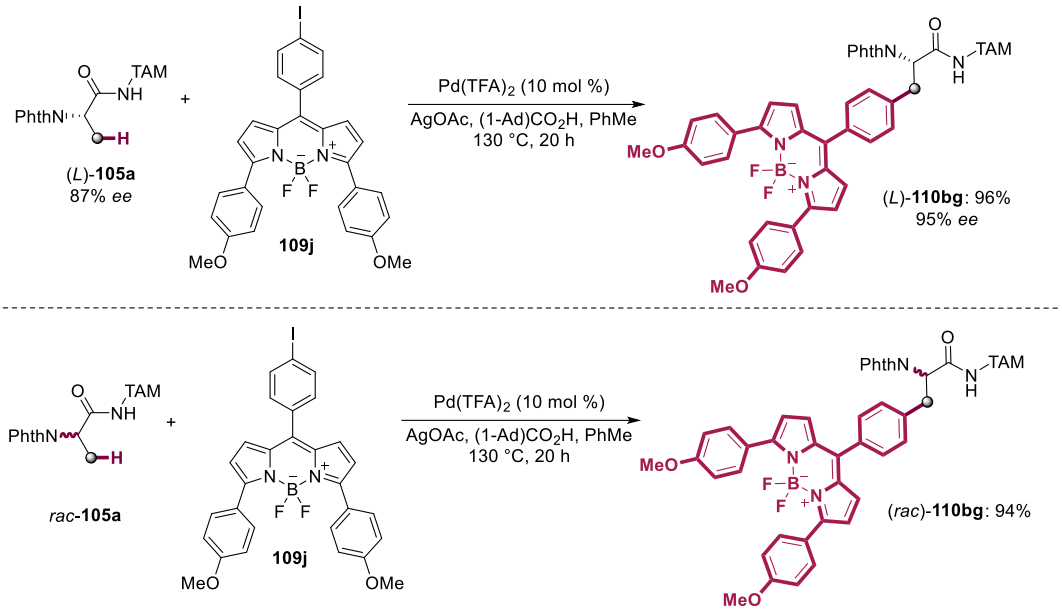
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.885	MM	0.4774	140.81349	4.91640	3.2770
2	14.952	MM	0.5555	4156.18213	124.69898	96.7230
Totals :				4296.99562	129.61538	



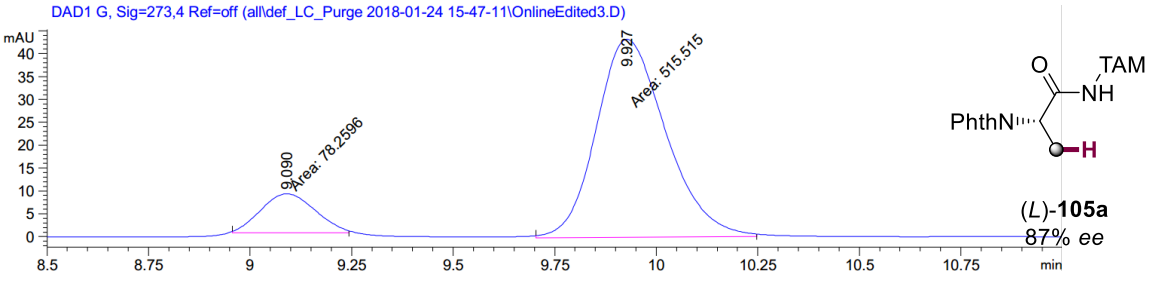
Signal 2: DAD1 G, Sig=273,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.785	MM	0.4830	1514.79065	52.27052	50.6600
2	15.011	MM	0.5268	1475.31946	46.67716	49.3400
Totals :				2990.11011	98.94768	

Scheme 3.2.5.3. HPLC analysis of the enantiopure and racemized products (*S*-*S*)-**111a** and (*RS*-*S*)-**111a**. IE *n*-hexane/EtOAc 30/70 flow: 1 mL/min, 274 nm.

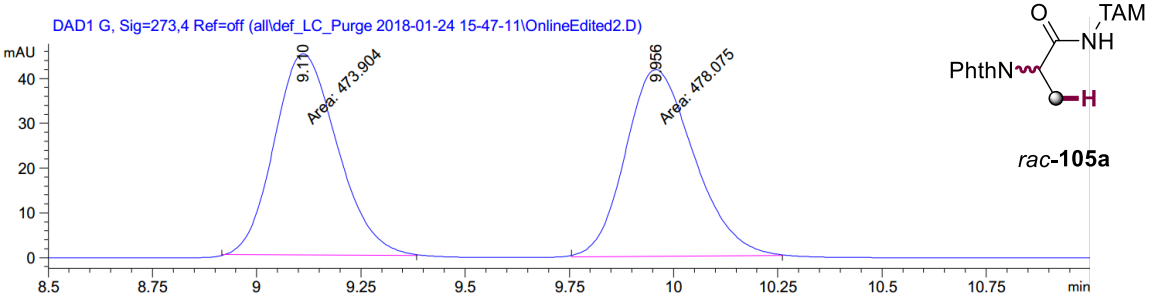


Scheme 3.2.5.4. Racemization study.



Signal 2: DAD1 G, Sig=273,4 Ref=off

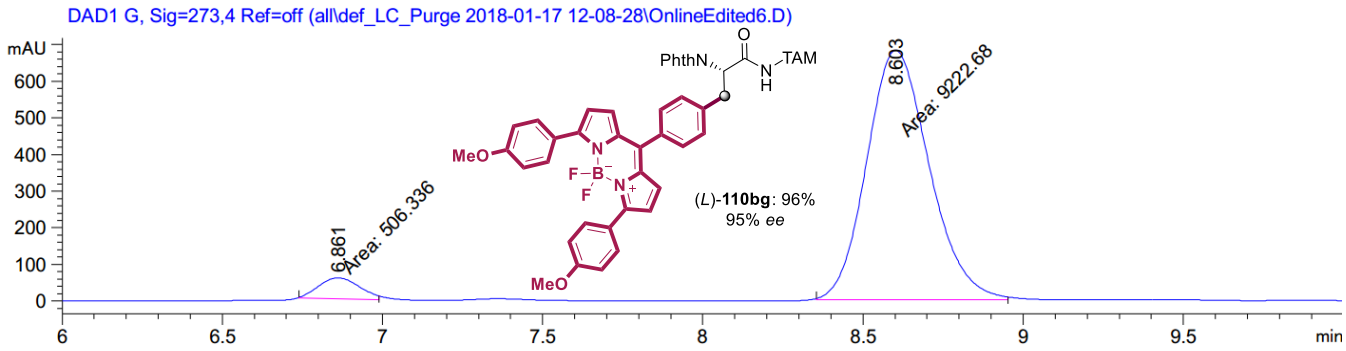
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.090	MM	0.1537	78.25957	8.48824	13.1800
2	9.927	MM	0.1985	515.51538	43.28632	86.8200
Totals :				593.77495	51.77456	



Signal 2: DAD1 G, Sig=273,4 Ref=off

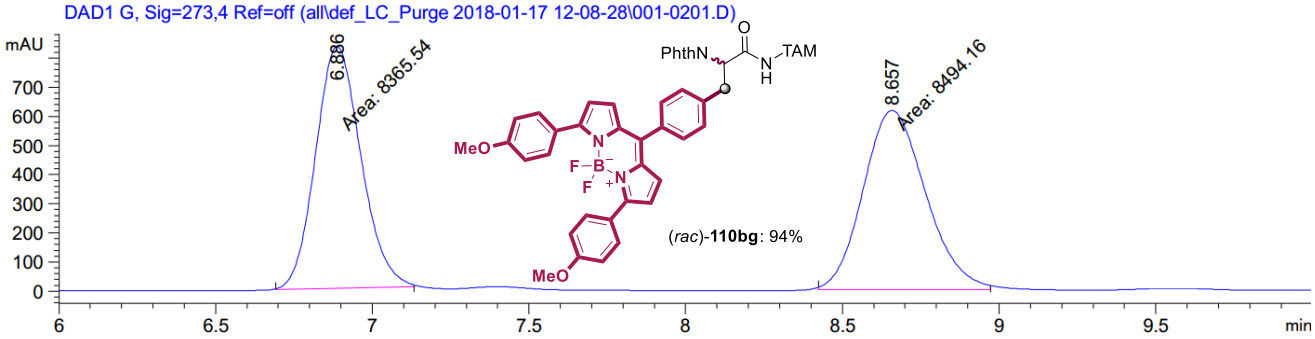
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.110	MM	0.1758	473.90439	44.91867	49.7809
2	9.956	MM	0.1912	478.07523	41.67081	50.2191
Totals :				951.97961	86.58948	

Scheme 3.2.5.5. HPLC analysis of the enantiopure and racemized amino acid substrates (*L*)-**105a** and (*rac*)-**105a**. IE n-hexane/EtOAc 30/70 flow: 1 mL/min, 274 nm.



Signal 2: DAD1 G, Sig=273,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.861	MM	0.1473	506.33603	57.29623	5.2044
2	8.603	MM	0.2257	9222.67969	681.01245	94.7956
Totals :				9729.01572	738.30868	

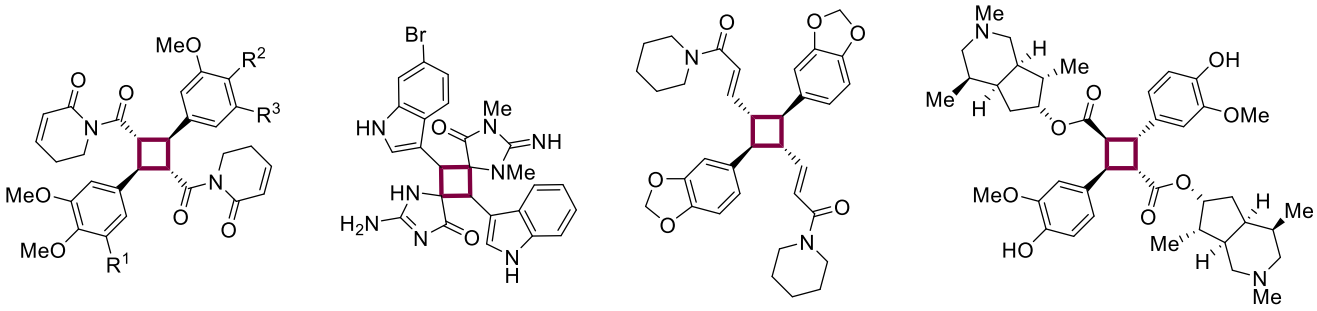


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.886	MM	0.1676	8365.53516	831.69867	49.6186
2	8.657	MM	0.2303	8494.15723	614.70007	50.3814
Totals :				1.68597e4	1446.39874	

Scheme 3.2.5.6. HPLC analysis of the enantiopure and racemized amino acid products (*L*)-**110bg** and (*rac*)-**110bg**. IE *n*-hexane/EtOAc 30/70 flow: 1 mL/min, 274 nm.

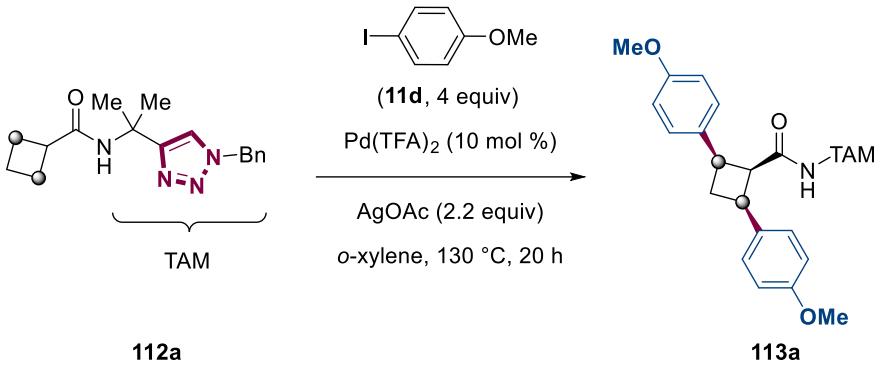
3.3 BODIPY-Labeled Cyclobutanes by Secondary C(sp^3)–H Arylations

Cyclobutanes are known as important building blocks for structural complex bioactive natural products, such as *Pipercyclobutanamides*, *Piperchabamides*, *Nigramides*, and *Dipiperamides* (Scheme 3.3.1).[131] The strained ring could be obtained by [2+2] photocycloaddition strategy.[113] Alternatively, C–H activations have met with undisputable success in sustainable and selective transformations, as employed by Baran[132] and Yu.[133] Also azetidine modifications for drug discovery was noted by Schreiber.[134] To further explore the synthetic strategy for cyclobutane derivatives synthesis, we developed palladium-catalyzed secondary C(sp^3)–H arylations of the cyclobutane and BODIPY labelings by triazole assistance. The unprecedented BODIPY cyclobutanes by this pathway were further applied for live cell imaging as an efficient probe.[135]



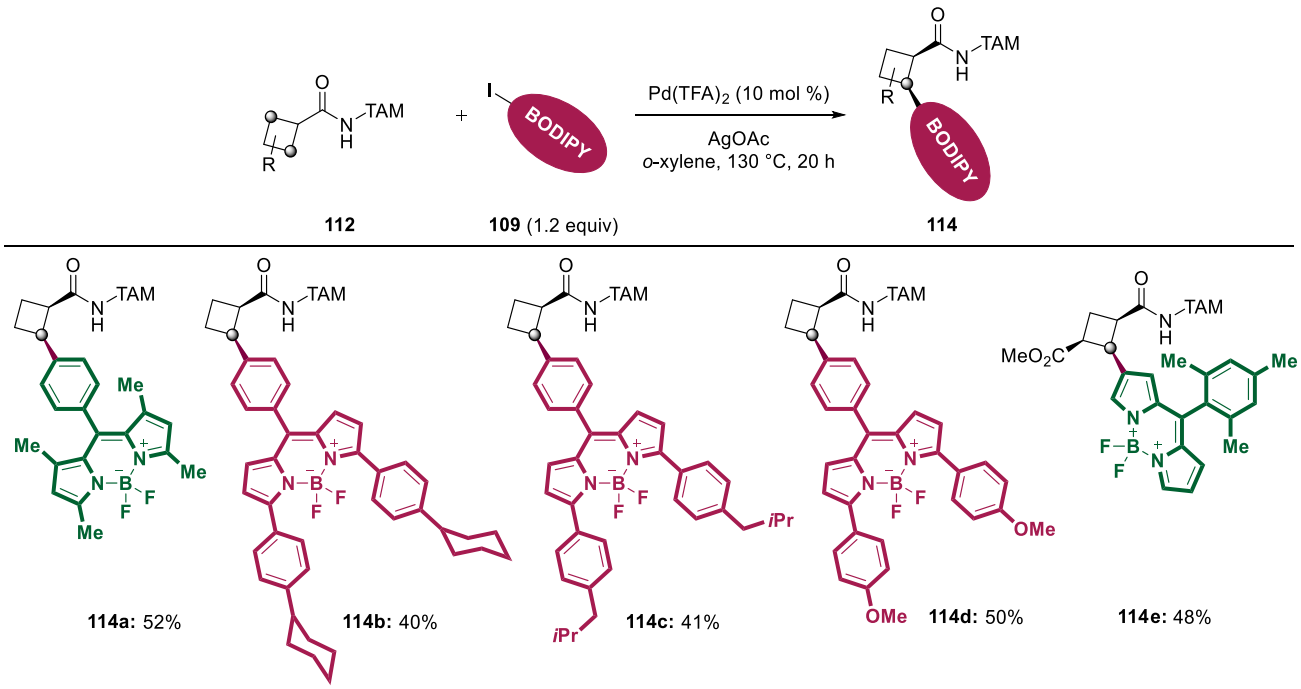
Scheme 3.3.1. Examples of bioactive cyclobutane natural products.

Preliminary studies were performed for the optimization of the TAM-cyclobutane arylation. *ortho*-Xylene was identified as the optimal solvent, and $Pd(TFA)_2$ with AgOAc as the silver salt. The desired functionalization occurred also at decreased reaction temperatures, while optimal results were achieved at 130 °C. Thus, the standard reaction condition was established by *Dr. Matteo Virelli* for the diarylations, affording the *cis*-diarylated cyclobutanes (Scheme 3.3.2).[136]



Scheme 3.3.2. Standard condition for cyclobutane arylations with TAM assistance.

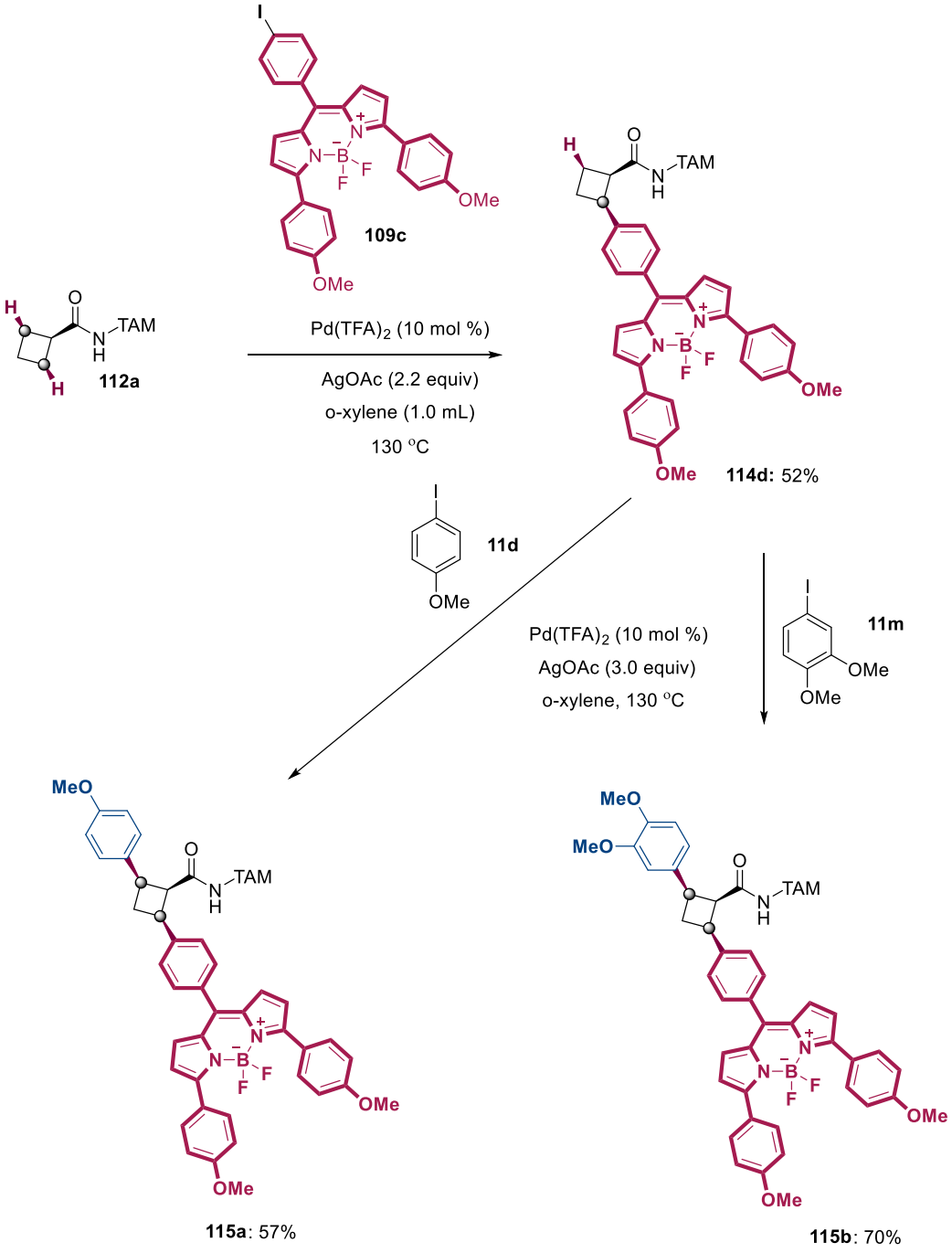
With the cyclobutane secondary C(sp^3)–H arylation in hand, we further envisioned the cyclobutane BODIPY labeling by iodo-BODIPY scaffolds. No di-substituted cyclobutane-BODIPY was observed even with 4.0 equivalents of iodo-BODIPYs **109**. The optimal outcome was obtained with 1.2 equivalent of iodo-BODIPYs **109** for the mono BODIPY labeled cyclobutanes (Scheme 3.3.3). Both green and red label BODIPYs proved to be compatible, as well as various substituents of the BODIPYs. Notably, BODIPY-labeled cyclobutane-1-carboxylate **114e**, as an unprecedented fluorescent core of natural product derivatives, was obtained.



Scheme 3.3.3. BODIPY mono-labeling of cyclobutanes assisted by TAM.

Moreover, successive modification of the mono-BODIPY labeled cyclobutane derivatives

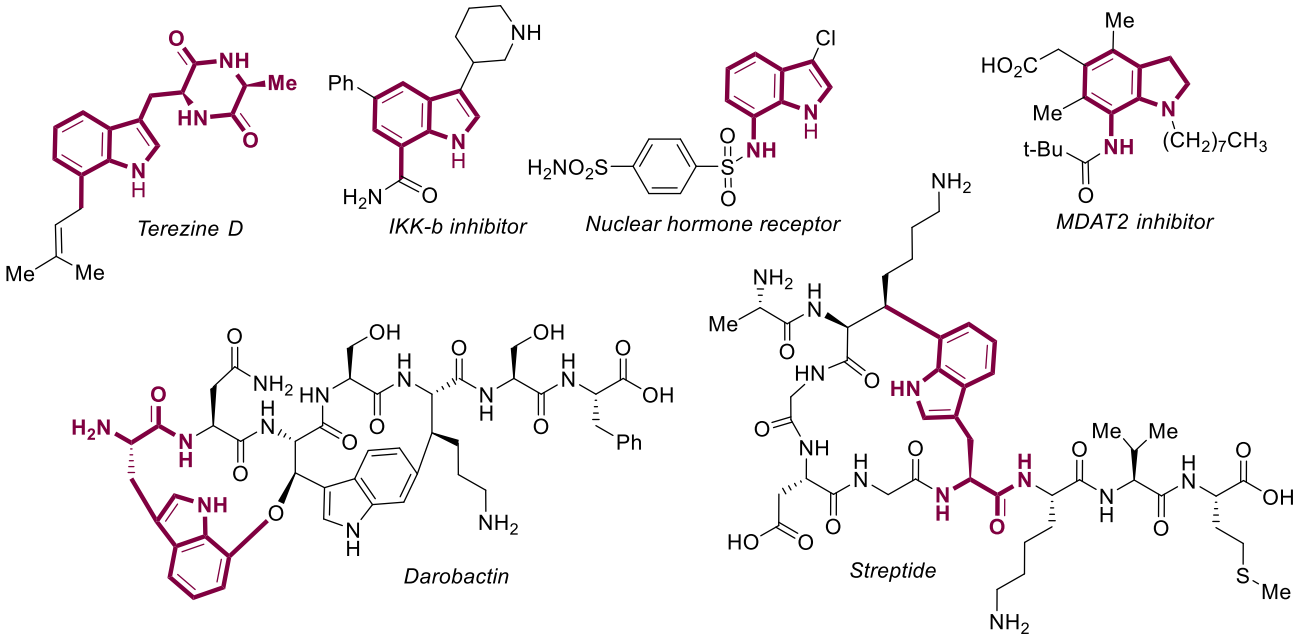
proceeded with iodoarenes **11** by a two-fold C–H activations (Scheme 3.3.4). The di-functionalized unsymmetrical cyclobutane products contain one aryl moiety and one BODIPY fluorescent dye, featuring fluorescent mimics of bio relevant natural products.



Scheme 3.3.4. Twofold C(sp^3)–H BODIPY labeling and arylation of cyclobutanes.

3.4 Peptide Late-Stage Diversifications by Rhodium-Catalyzed Tryptophan C7 Amidation

Functionalized peptides are of great importance to drug discovery. Consequently, the precise synthesis of structural complex peptides is of urgent need. Although peptide syntheses are still largely limited to classic approaches, transition metal catalyzed C–H activation[16] have contributed enormously to the late-stage peptide functionalizations, mostly by Corey,[49] Chen,[48c, 95, 119] Lavilla/Albericio,[74-75, 137] Daugulis,[50a, 54] Shi,[89, 138] Wang,[84, 94, 139] Yu,[57-58, 86-87] and Ackermann.[78, 99, 103, 105-106, 140] The efficient functionalization of peptides was established through selective tryptophan modifications, due to its low natural abundance as well as its unique impact on biological events.[141] However, all the late-stage peptide diversifications of tryptophan are restricted to the tryptophan C2 position, limiting the structural diversity of the peptides. In sharp contrast, indole/tryptophan C7 decorated products are of great importance as bioactive natural products and reagents (Scheme 3.4.1).[115]

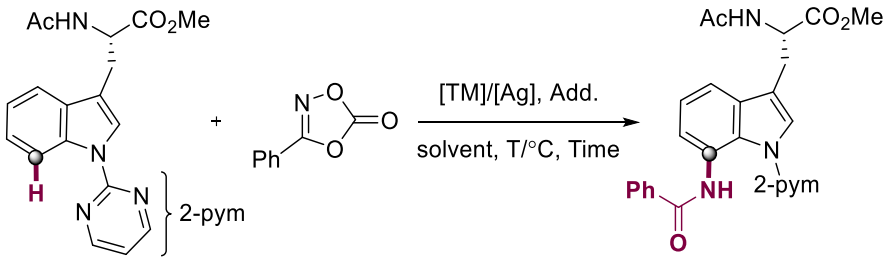


Scheme 3.4.1. Bioactive C7 decorated indole and tryptophan derivatives.

3.4.1 Optimization Studies for Tryptophan C7 Amidation

To further address the limitations of tryptophan-peptide diversifications, we initiated our exploration by C–N bond formation of peptides compared to the widely developed C–C formation of peptides. In this context, 3-phenyl-1,4,2-dioxazol-5-one was used as the efficient amidating reagent[103, 142] under rhodium(III)[16j, 96, 143] catalysis. Carboxylic acid additives[27, 125a] were found to be pivotal for the C7 amidation (Table 3.4.1.1, entries 1-8), among which $MesCO_2H$ proved to be optimal (entry 2). A change from $AgSbF_6$ to other silver salts led to diminished yields (entry 5). TFE outperformed other solvents in the reaction (entries 9-11). Excessive amount of the silver salts (entries 12, 13) or the acid additives (entry 14) gave diminished reaction yields. Decreased reaction temperatures led to a drop of the efficacy (entries 15, 16). Changing or omitting the rhodium catalyst shut down this reaction (entries 17-20). *N*-Substituents other than pyrimidyl on the indole did not lead to a superior reaction outcome (entries 21, 22).

Table 3.4.1.1. Optimization of C–H amidation of tryptophan[a]



96aa **116a** **117aa**

Entry	[TM]/[Ag]	Additives	Solvent	Time/h	T/°C	Yield [b]
1	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	--	DCE	16	110	--
2	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$MesCO_2H$ (15 mol %)	DCE	16	110	58%
3	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$(1\text{-Ad})CO_2H$ (15 mol %)	DCE	16	110	57%
4	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$C_6F_5CO_2H$ (15 mol %)	DCE	16	110	42%
5	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$C_6F_5CO_2H$ (15 mol %)	DCE	16	110	15%[c]
6	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	*m*-CF_3 $C_6H_4CO_2H$ (15 mol %)	DCE	16	110	39%

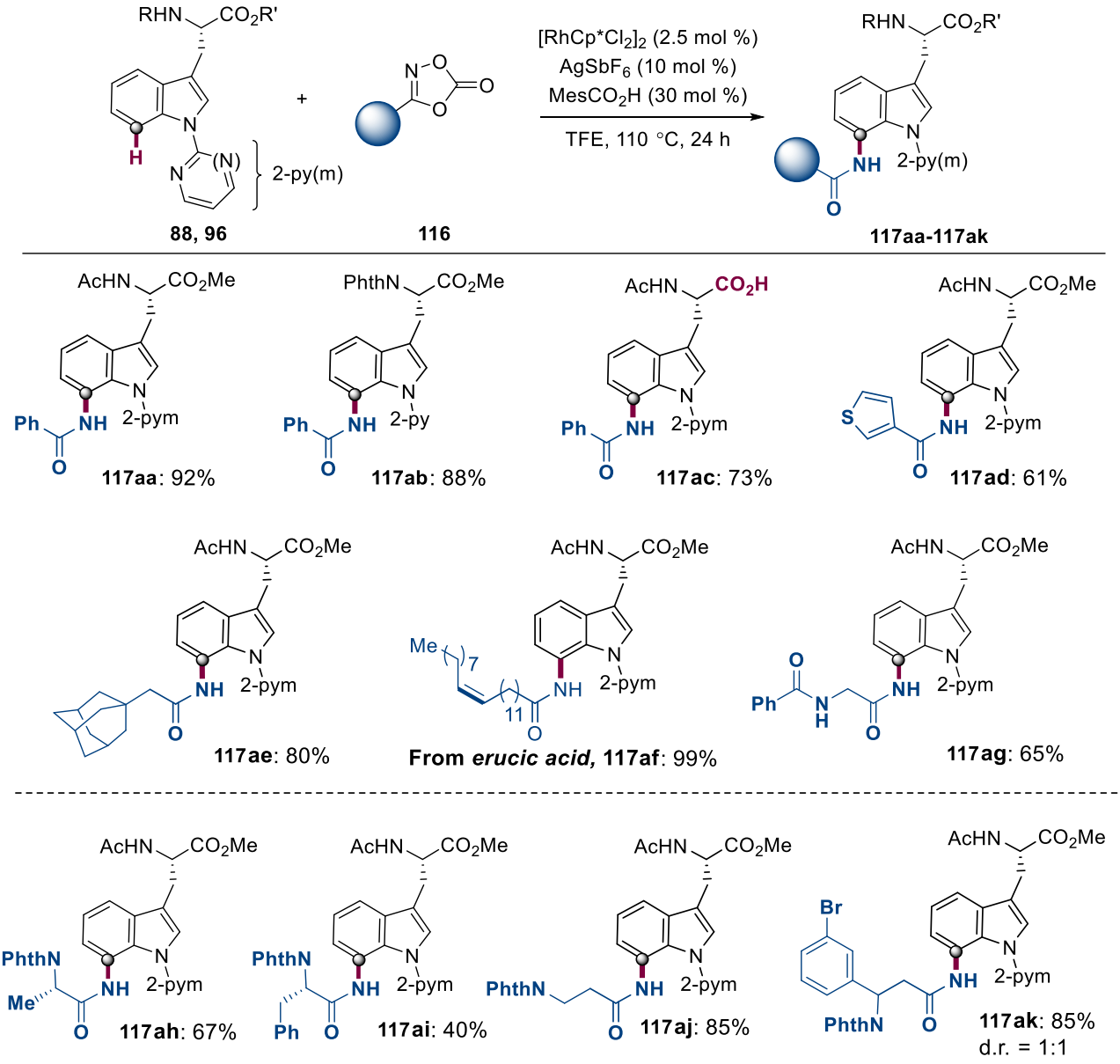
7	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	4-Toluic acid (15 mol %)	DCE	16	110	--
8	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	TFA (15 mol %)	DCE	16	110	12%
9	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$MesCO_2H$ (15 mol %)	DCE	24	110	65%
10	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$MesCO_2H$ (15 mol %)	1,4-dioxane	24	110	49%
11	**$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]**	**$MesCO_2H$ (15 mol %)**	**TFE**	**24**	**110**	**92%**
12	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$MesCO_2H$ (15 mol %)	TFE	24	110	76%[d]
13	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$MesCO_2H$ (15 mol %)	DCE	24	110	53%[d]
14	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$MesCO_2H$ (1.0 equiv)	DCE	24	110	57%
15	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$MesCO_2H$ (15 mol %)	TFE	24	90	61%
16	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$MesCO_2H$ (15 mol %)	TFE	24	26	24%
17	$CoCp^*(CO)I_2$ (10 mol %)/[Ag]	$MesCO_2H$ (30 mol %)	TFE	24	110	--
18	$MnBr(CO)_5$ (10 mol %)	$MesCO_2H$ (30 mol %)	TFE	24	110	--
19	$Pd(OAc)_2$ (10 mol %)	$MesCO_2H$ (30 mol %)	TFE	24	110	--
20	$[RhCp^*Cl_2]_2$ (--)/[Ag]	$MesCO_2H$ (15 mol %)	TFE	16	110	--
21	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$MesCO_2H$ (15 mol %)	TFE	24	110	--[e]
22	$[RhCp^*Cl_2]_2$ (2.5 mol %)/[Ag]	$MesCO_2H$ (15 mol %)	TFE	24	110	74%[f]

[a] Reaction conditions: **96aa** (0.2 mmol), **116a** (0.4 mmol), [TM] (5.0—10 mol %), [Ag] = $AgSbF_6$ (10 mol %), additives (15—30 mol %), solvent (0.4 mL), under N_2; [b] Yield of isolated products; [c] [Ag] = $AgNTf_2$ (10 mol %); [d] [Ag] = $AgSbF_6$ (20 mol %); [e] R = pivaloyl; [f] R = 2-pyridyl.

3.4.2 Scope for Tryptophan C(7)—H Amidation

With the optimized reaction conditions in hand, we explored the scope of the tryptophan diversification employing various 1,4,2-dioxazol-5-ones **116**. Both aryl and alkyl dioxazolones were thus well tolerated (Scheme 3.4.2.1). Acetyl- and phthaloyl protecting groups both gave excellent yields (**117aa**, **117ab**), and importantly, tryptophan with a free carboxylic acid selectively gave the C7 amidated product **117ac**, illustrating the robustness of this C(7)—H reaction. Besides arenes, heterocyclic thiophene was efficiently converted into the C7-modified product **117ad**. Various alkyl dioxazolones could also be introduced to give the C7-alkylated products **117ae**, **117af**. Notably, amide group was also compatible in this C7 transformation (**117ag**). Intrigued by the compatibility of alkyl groups, we employed the C—H

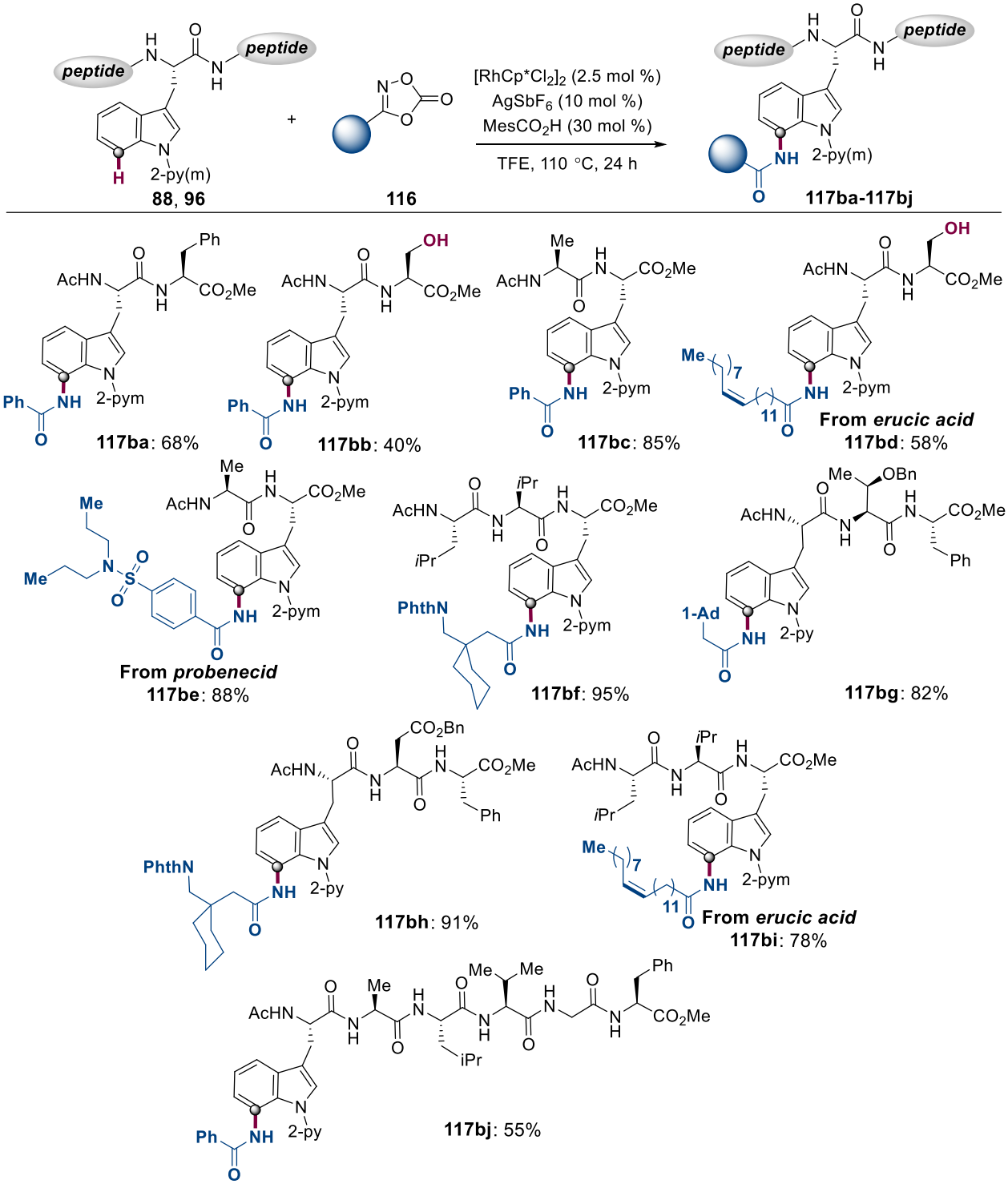
amidation for the direct chemical ligation with various amino acid-derived dioxazolones **116**, thus, enabling new disconnections towards dipeptides. Thereby, both *α*-amino acids and *β*-amino acids were introduced to the C7 position of tryptophans **117ah-117ak**.



Scheme 3.4.2.1. Tryptophan C7 amidations by various dioxazolones.

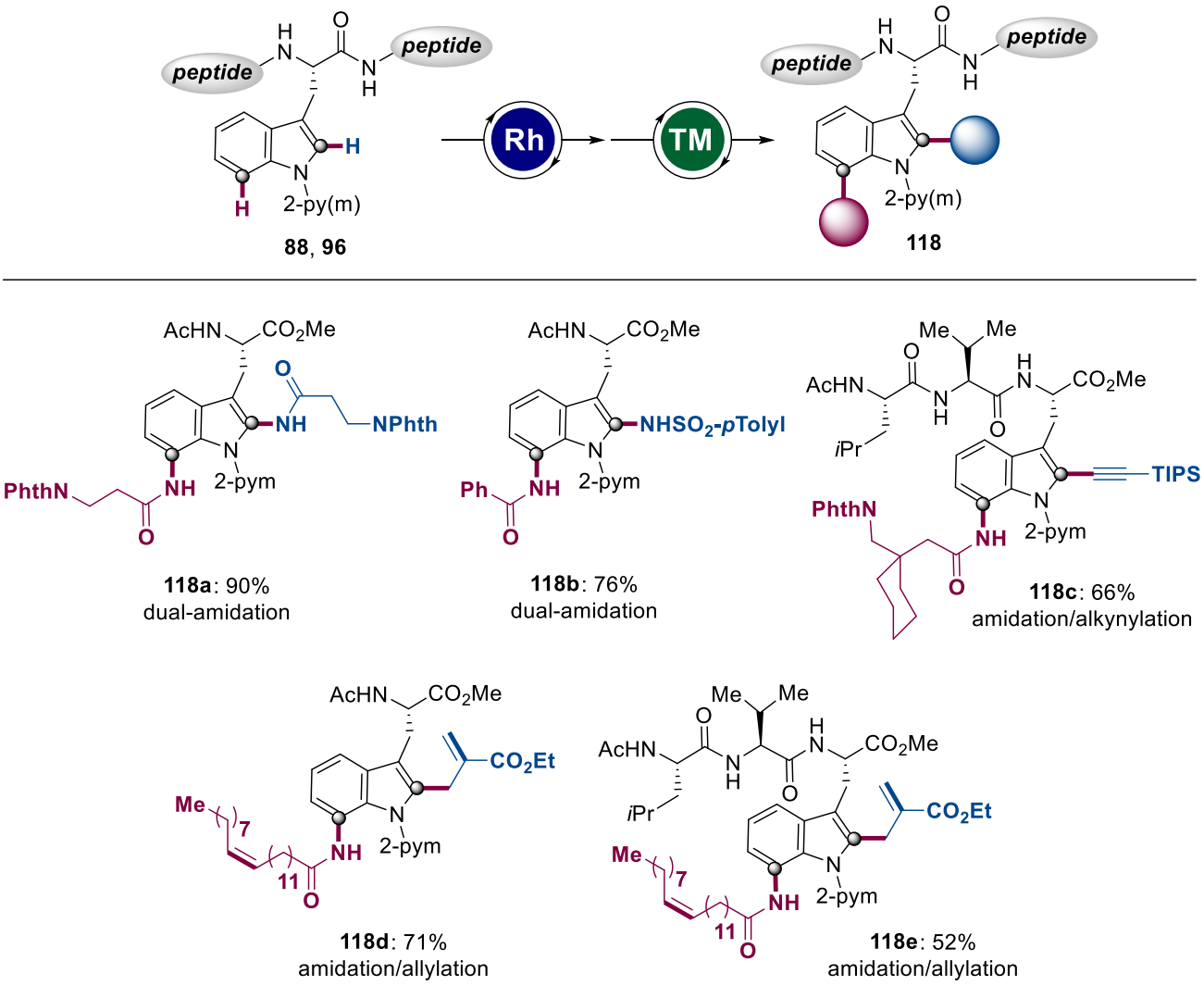
With the success on C7 amidation of tryptophan, we further probed the peptide diversifications (Scheme 3.4.2.2) with this C7 amidation strategy. Dipeptides, tripeptides and hexapeptides were all transformed into C7 amidated products in a site-selective fashion. The reaction retained the site-selectivity irrespective of the peptidic amino acid sequence. Free

hydroxyl group of serine was compatible with this reaction, thus, giving the desired products with the free *OH*-group **117bb** and **117bd**. Notably, peptide-natural product hybrids **117bd**, **117be**, **117bi** and late-stage modified peptide **117bj** were obtained by the C7 amidation, highlighting the potential to assemble structurally complex peptides.

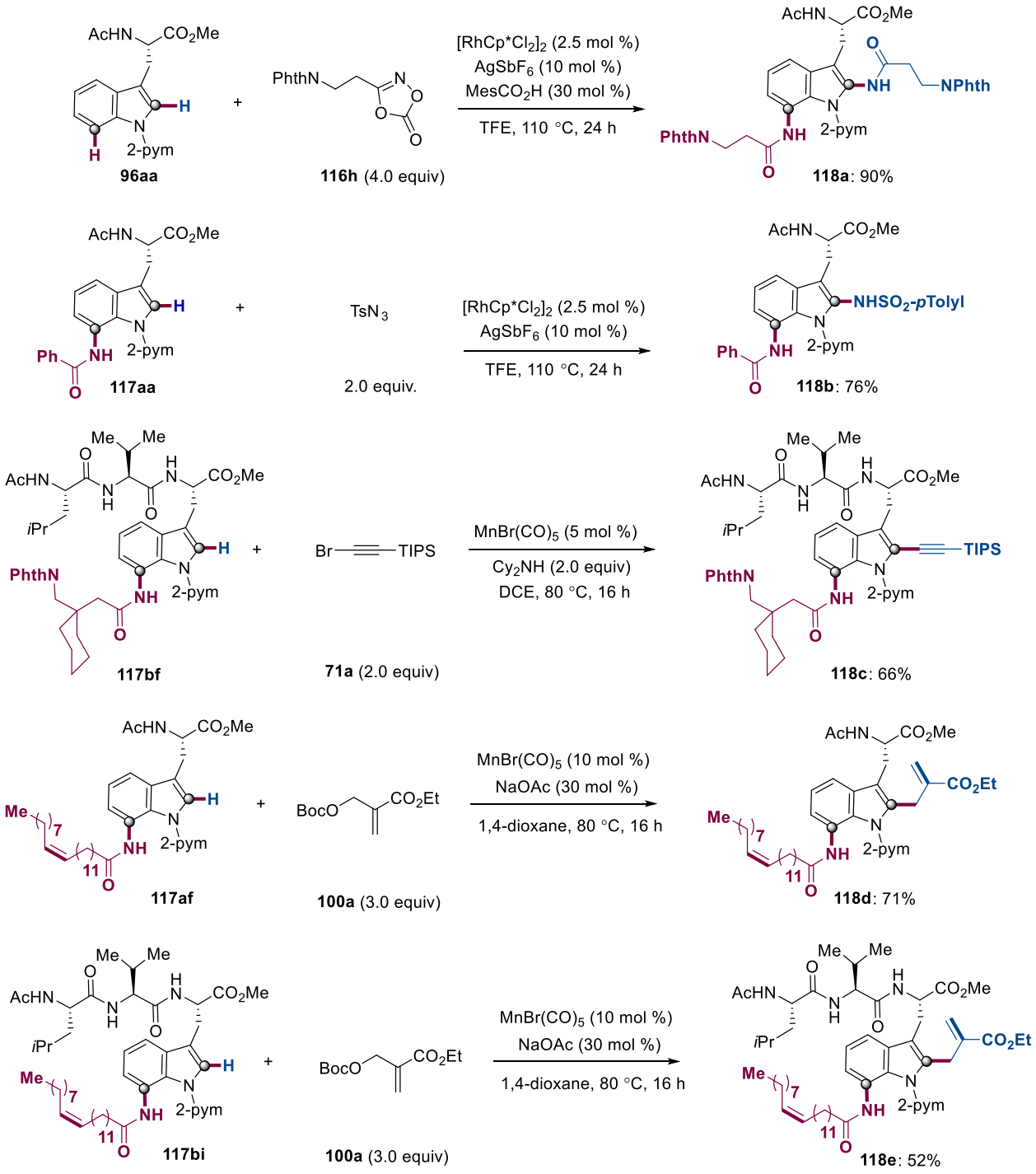


Scheme 3.4.2.2. Tryptophan C7 amidations by dioxazolones **116**.

Next, we developed the double C–H activations by tryptophan C7 amidation and then C2 position modifications, further enhancing the structural complexity (Scheme 3.4.2.3). The twofold rhodium-catalyzed amidation with dioxazolones **116** was thus conducted for di-amidated product **118a**. And another amidating reagent TsN_3 was also employed successively, delivering di-amidated products **118b**. Furthermore, manganese catalyzed C–H alkynylation[105] enabled the successive functionalization, giving di-functionalized amino acid **118c**, which should bear great potential for subsequent diversifications by click-reactions. Moreover, successive C–H allylations were also enabled by manganese catalysis,[106] furnishing peptides **118d** and **118e**, bearing erucic acid amide and allyl-tryptophan.



Scheme 3.4.2.3. Peptide sequential double C–H activations.

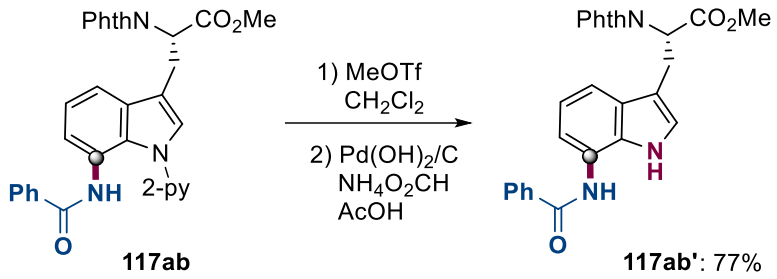


Scheme 3.4.2.4. Sequential diversifications of C7 products.

3.4.3 Traceless Removal of Pyridyl Group of C7 Amidated Product

The *N*-pyridyl group of C7 amidated products could be removed in a traceless manner. The first step was a methylation of the pyridyl group, which was followed by a palladium-catalyzed hydrogenation in the second step, thus delivering the C7 amidated native *NH*-free tryptophan

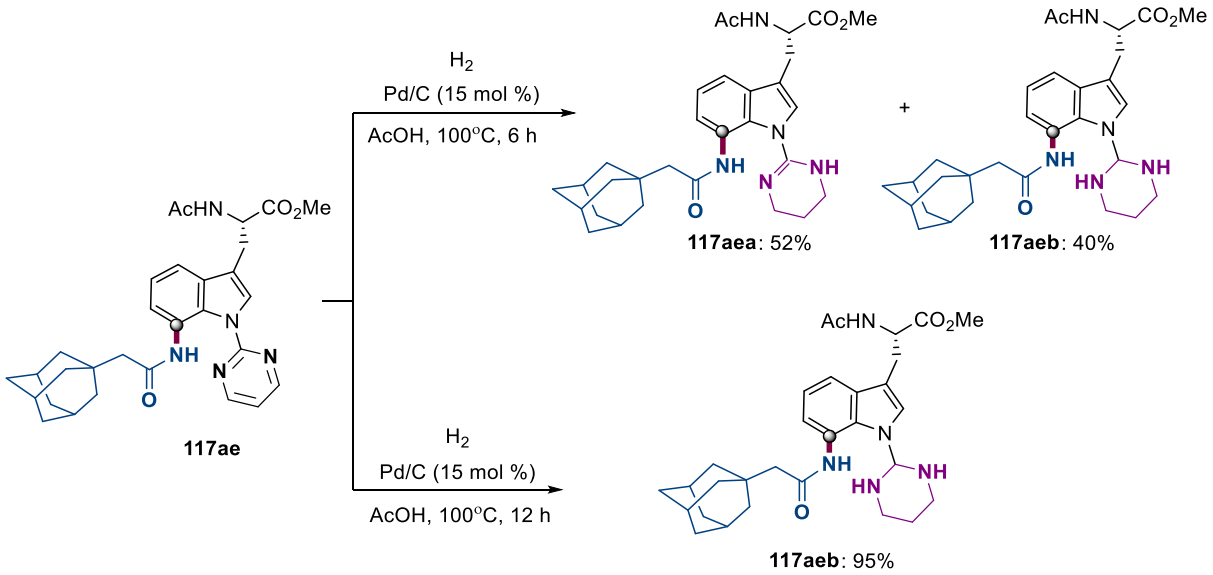
product **3c** (Scheme 3.4.3.1).[140b],[144]



Scheme 3.4.3.1. Traceless removal of the pyridyl group.

3.4.4 Pyrimidyl Transformation by Hydrogenations

Furthermore, we devised a novel hydrogenation strategy of the C7 amidated product **117ae**, which selectively took place at the *N*-pyrimidyl substituent to furnish the tetrahydropyrimidine **117aea** and hexahydropyrimidine **117aeb** by the judicious choice of the reaction time (Scheme 3.4.4.1). Thereby, the hydrogen-bond acceptor is transformed into a donor motif, which should prove instrumental for medicinal chemistry.

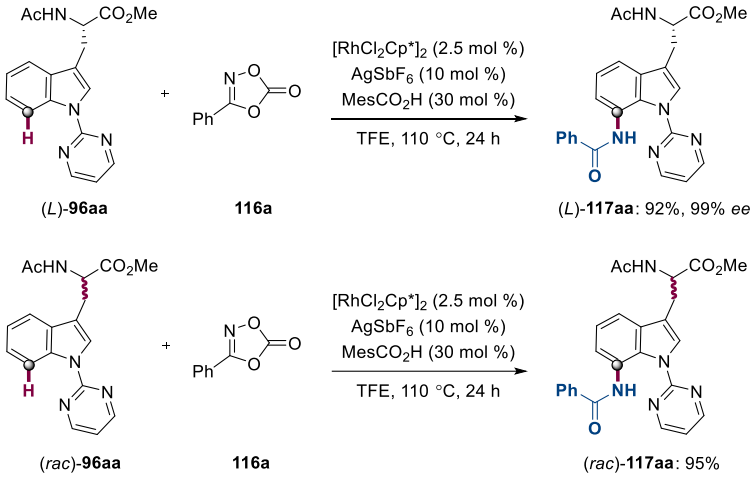


Scheme 3.4.4.1. Pyrimidyl transformation by palladium-catalyzed hydrogenation.

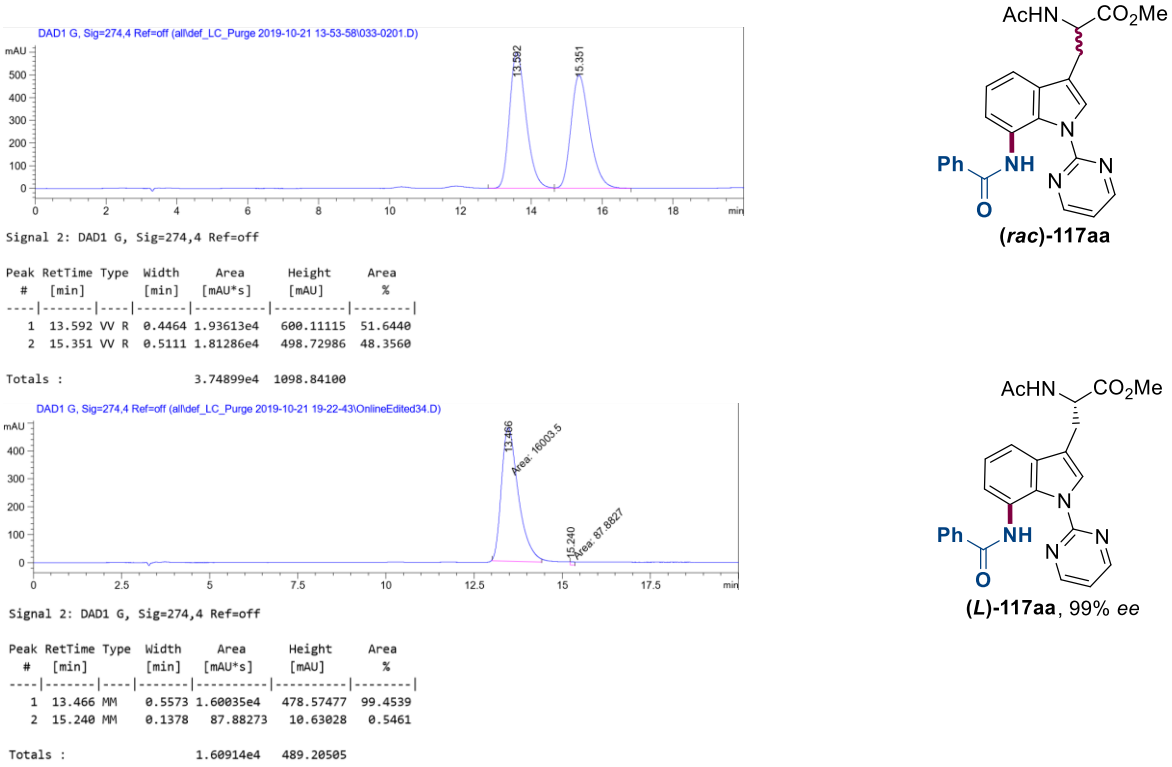
3.4.5 Studies on Potential Racemization

To explore the potential racemizations of this tryptophan C7 amidation reaction, studies were carried on the C7-amidation (Scheme 3.4.5.1). The substrates tryptophan (*L*)-**96aa** and

tryptophan (*rac*)-**96aa** were subjected to the C–H amidation under the optimized reaction conditions. A comparison between substrates and the corresponding products by HPLC analysis showed that no racemization occurred during the C–H amidation process, furnishing the site-selectively amidated products in 99% *ee* (Scheme 3.4.5.2).



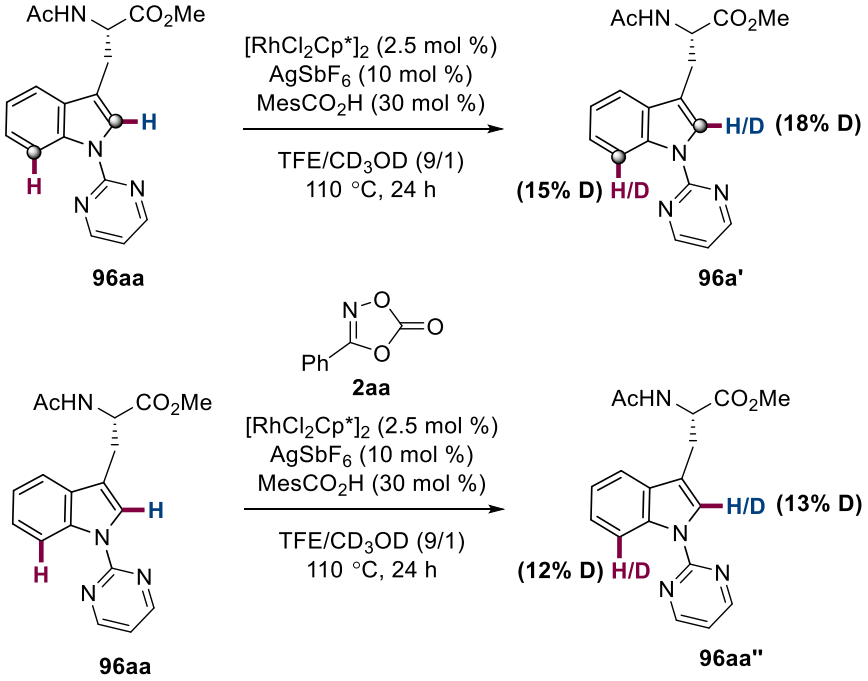
Scheme 3.4.5.1. Racemization studies on the tryptophan C7 amidation reaction.



Scheme 3.4.5.2. HPLC analysis of products (*rac*)-**117aa**, (*L*)-**117aa**. IC *n*-hexane/EtOAc 30/70 flow: 1 mL/min, 274 nm.

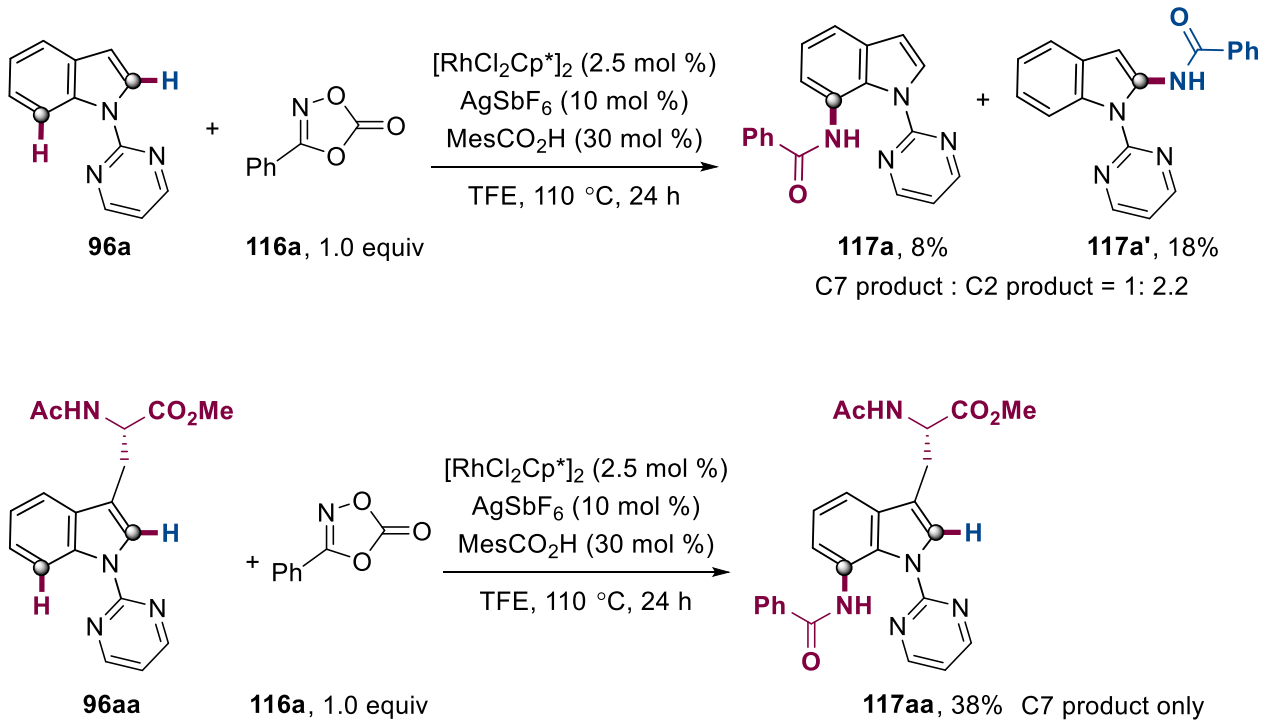
3.4.6 Mechanism Insights into C7 Positional Selectivity

To rationalize the C7 selectivity, we tested whether an H/D exchange occurred on the tryptophan **96aa** in the presence of $[D]_3$-MeOH (Scheme 3.4.6.1). Unexpectedly, a reversible C–H activation at both the C7 and the C2 position was observed.



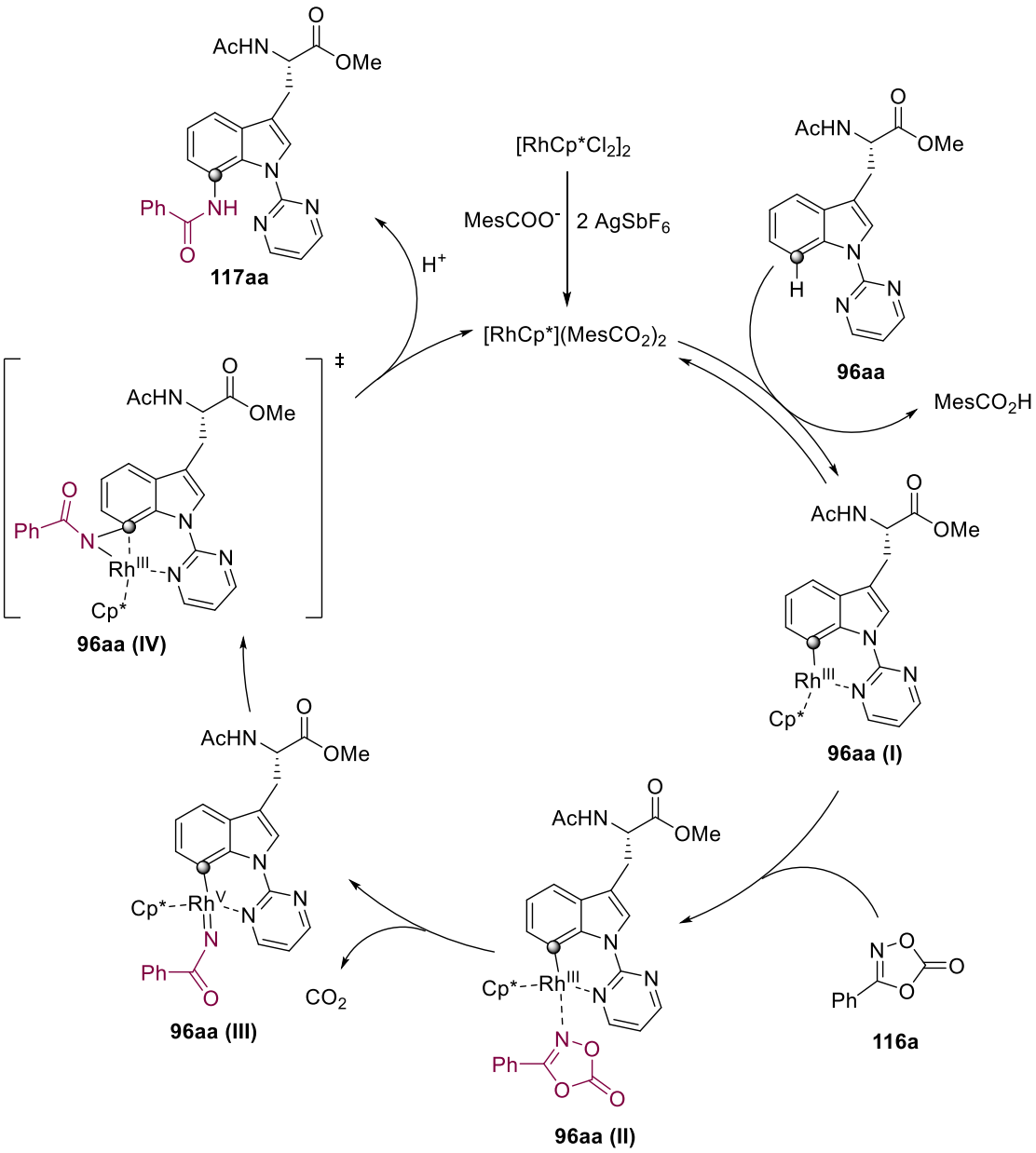
Scheme 3.4.6.1. H/D exchange experiment on substrate **96aa**.

The site-selectivity was related to the substrates (Scheme 3.4.6.2). The C–H amidation reaction with indole substrate **96a** resulted in the preferential C2 amidation, while tryptophan substrate **96aa** underwent C7 amidation with excellent site-selectivity, indicating an increased impact of the steric[145] hindrance from the substrates **96**.



Scheme 3.4.6.2. C–H amidation of substrates **96a** and **96aa**.

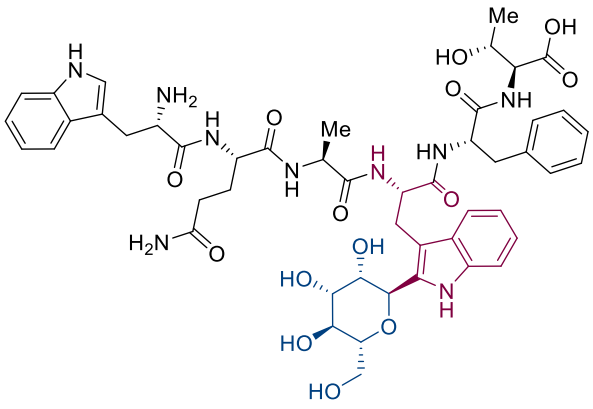
According to these experiments, the reversible C—H activation step was revealed, and according to the H/D exchange studies, both C7 and C2 position has a similar chance for the C—H activation. Furthermore, according to the DFT studies by *Dr. Rositha Kuniyil*, for the C7 position, both the decarboxylation step for **96aa(III)** and also the C—N bond formation through **96aa(IV)** went through lower energy barriers than the C2 position steps. According to all these results, we thus proposed a plausible catalytic cycle of the C7 amidation reaction shown in Scheme 3.4.6.3.



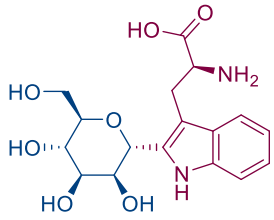
Scheme 3.4.6.3. Proposed catalytic cycle for rhodium-catalyzed tryptophan C7 amidation.

3.5 C–H Activations for Peptide-Carbohydrate Conjugation by Manganese(I)-Catalysis

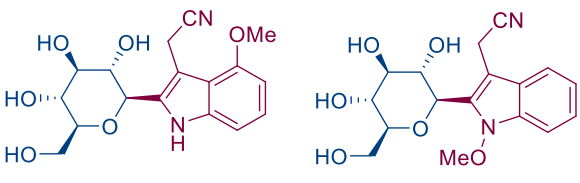
As an endogenous post-translational process, protein glycosylation is of crucial importance to glycobiology.[116] Glycopeptides and glycoproteins are highly related to key biological events, such as cell adhesion, cell growth, and cell-cell communication.[146] Structurally novel glycoproteins were developed as diagnostic tools[147] and as vaccines.[148] Moreover, glycopeptide antibiotics (GPA) are known as effective therapy for the treatment of bacterial infections.[117] For instance, the *C*-mannosyl tryptophan was identified as endogenous glycol-amino acid, and mannosyl tryptophan-containing peptides were discovered as naturally occurring alkaloids (Scheme 3.5.1).[149] These building blocks are potential for late-stage glycopeptide syntheses. Compared to the classical chemical transformations for peptide assembly with lengthy prefunctionalizations,[150] C–H activation[16] provided a step-economical and efficient strategy for late-stage peptide direct functionalizations. However, the fast assembly of glycopeptides by C–H activation remained elusive. In this context, within our sustainable chemistry program,[125] we devised the metal-catalyzed late-stage peptide C–H glycoconjugation. Manganese[19-20, 101, 151],[152],[153] was employed due to its earth-abundant, non-toxic properties and robustness. Structurally complex peptide-saccharides were thus obtained in a racemization-free manner.



Human Rnase: Trp-Gln-Ala-Trp(C-mannosylpyranosyl)-Phe-Thr



C^2-α-L-C-Mannosylpyranosyl-L-tryptophen

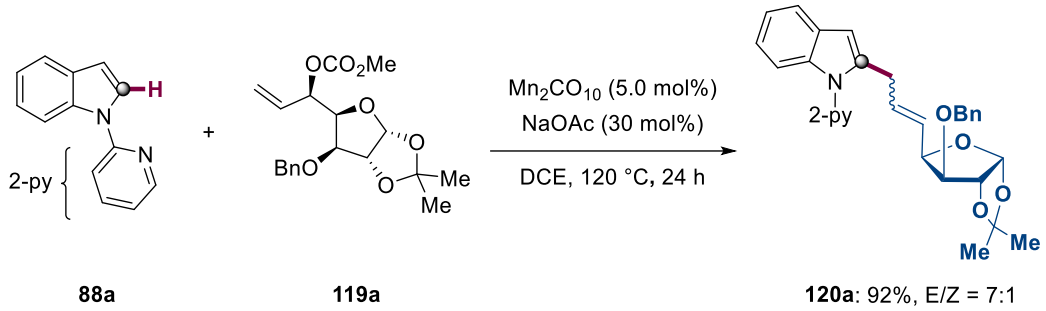


Indole-C-glucoside alkaloids from Isatis indigotica

Scheme 3.5.1. Naturally occuring glycopeptides and alkaloids.

3.5.1 Scope for Tryptophan C–H Glycoconjugation

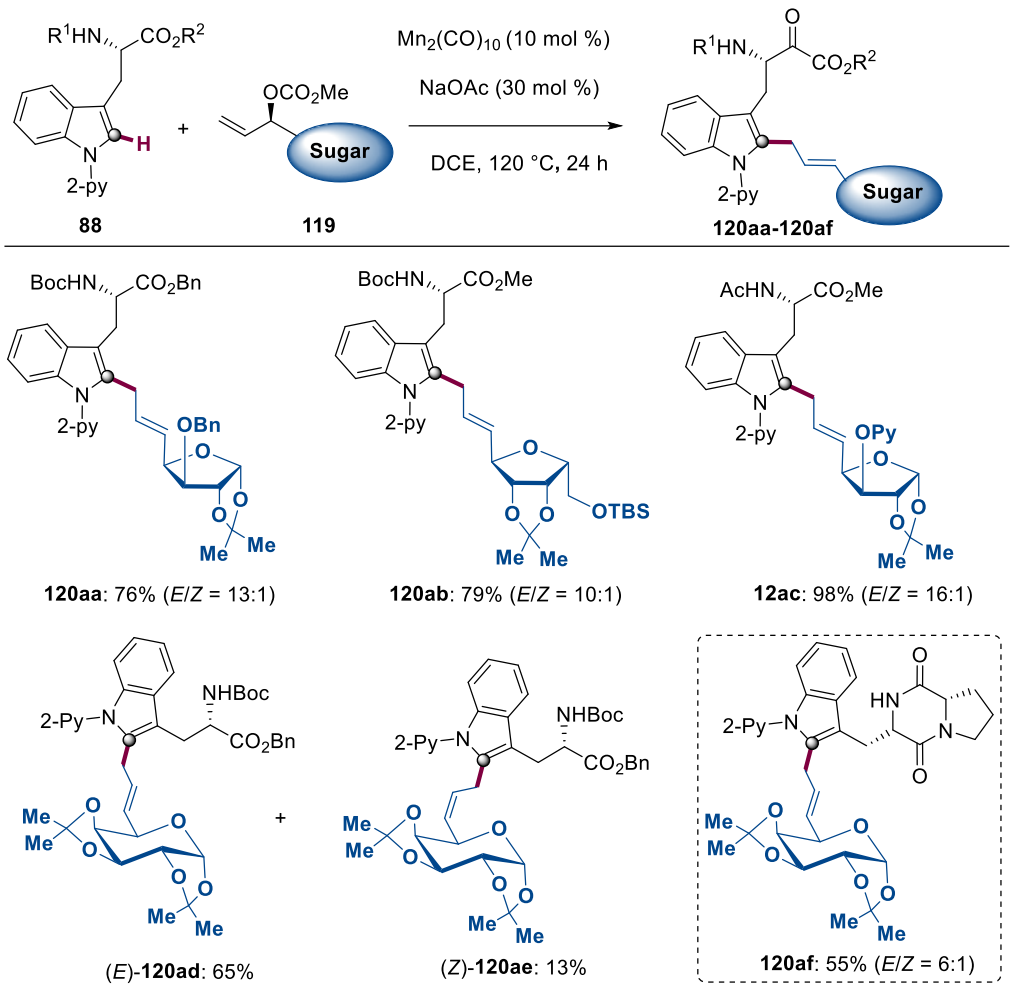
Preliminary studies were carried out by probing the indole glycosylations with glucosyl carbonate. The optimized reaction conditions of this manganese-catalyzed allylation-based glycoconjugation was established by *Dr. Parthasarathi Subramanian* (Scheme 3.5.1.1).



88a **119a** **120a**: 92%, E/Z = 7:1

Scheme 3.5.1.1. Indole glycoconjugation by manganese(I) catalysis.

Intrigued by the indole glycosylation results, we applied this reaction to enantiopure tryptophan glycosylations (Scheme 3.5.1.2). The glycosylation approach was compatible with various carbonates, delivering various glycotryptophans in a racemization-free manner, introducing furanose (**119a**, **119c**), ribose (**119b**) as well as galactose (**119d**) to the tryptophans. The *E*-/*Z*-isomers could be easily isolated separately, providing potential for structure-activity studies. Moreover, the derivative **120af** of brevianamide F,[154] a scaffold of a plethora of natural products, was efficiently transformed into the natural product-gluco hybrid. Notably, a higher *E/Z* ratio was obtained for tryptophan glycosylations.

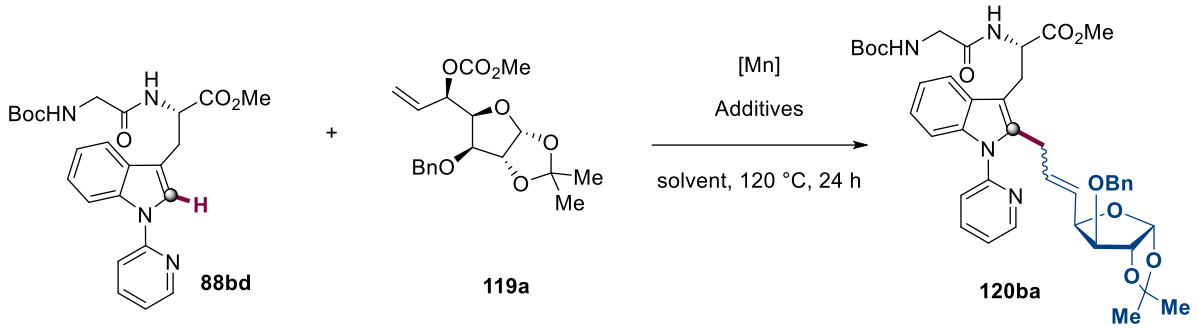


Scheme 3.5.1.2. C–H glycoconjugation of tryptophans

3.5.2 Optimization for Peptide C–H Glycoconjugation

To further explore the reaction for late-stage peptide glycosylations, orienting studies were conducted on the optimization for dipeptide glycosylations (Table 3.5.2.1). The standard conditions for tryptophan glycosylations did not lead to the best outcome (entry 3). Increased equivalents of the additive gave an improved result (entry 4). With an increased catalyst loading of $MnBr(CO)_5$, satisfactory results were noted (entry 1).

Table 3.5.2.1. Optimization of C–H glycoconjugation of dipeptide Boc-Gly-Trp^{Py}-OMe **88bd** with furanose carbonate **119a**.[a]

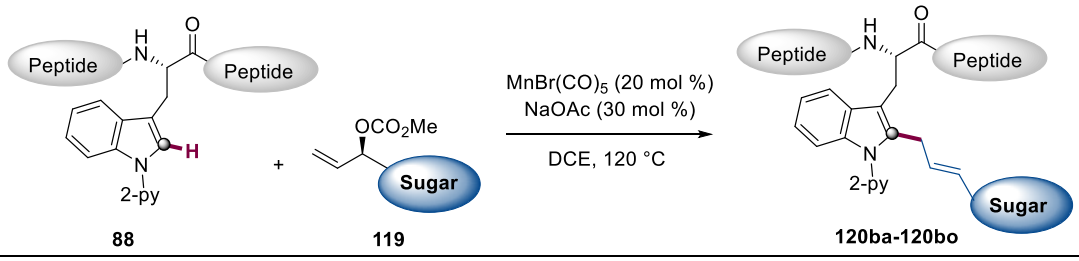


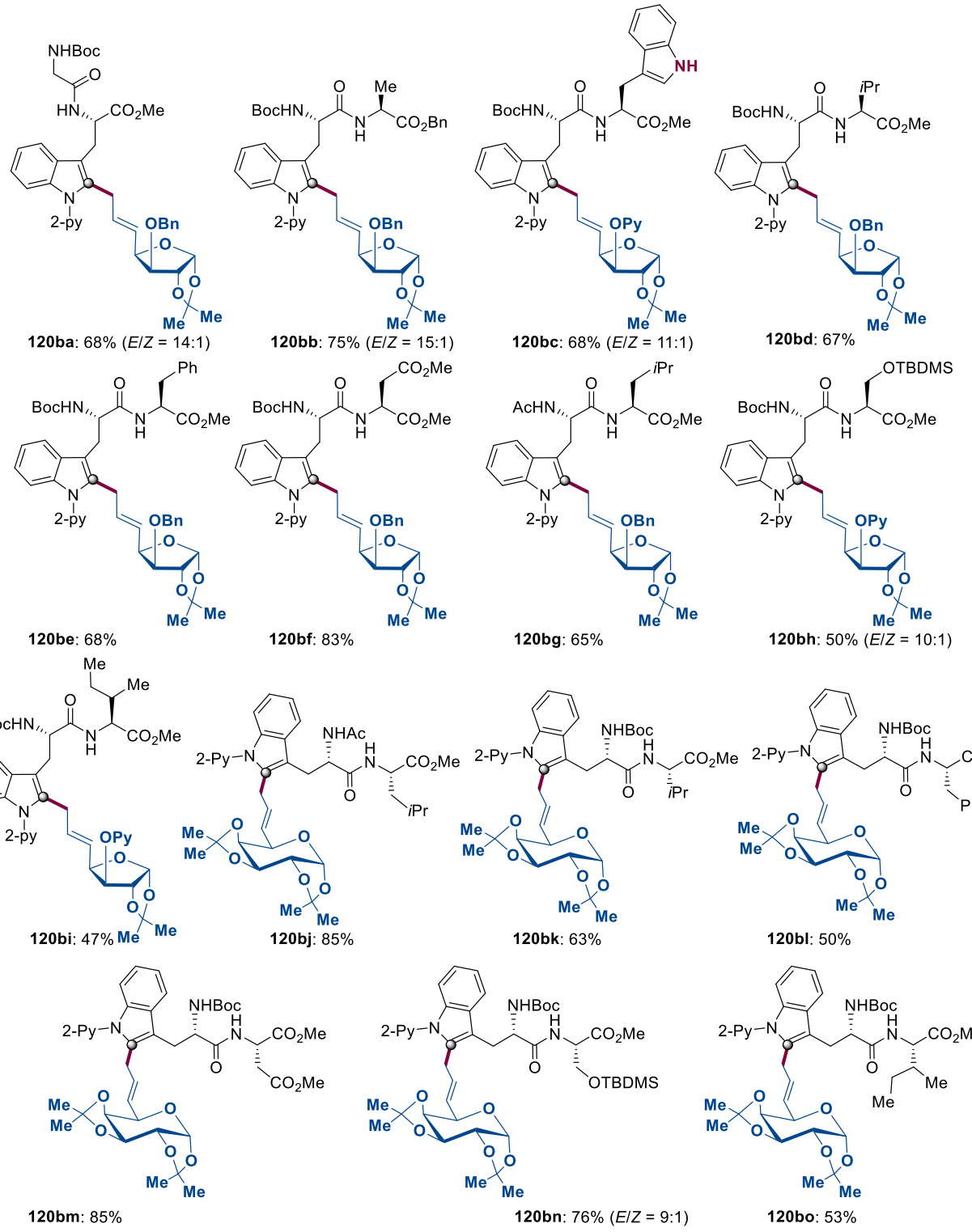
Entry	[Mn] (mol %)	Additive (mol %)	Solvent	Yield [%][b]
1	**$MnBr(CO)_5$ (20)**	**NaOAc (30)**	**DCE**	**68 (*E*/*Z* = 14:1)**
2	$Mn_2(CO)_{10}$ (20)	NaOAc (30)	DCE	20
3	$Mn_2(CO)_{10}$ (10)	NaOAc (30)	DCE	nd
4	$Mn_2(CO)_{10}$ (10)	NaOAc (200)	DCE	50 (*E*/*Z* = 10:1)
5	$Mn_2(CO)_{10}$ (10)	NaOAc (30)	DCE	nd
6	$Mn_2(CO)_{10}$ (10)	NaOAc (30)	*m*-xylene	12
7	$Mn_2(CO)_{10}$ (10)	Cy_2NH (200)	DCE	traces

[a] Reaction conditions: **88bd** (0.10 mmol), **119a** (0.20 mmol), [Mn], additive, solvent (0.5 mL), 120 °C, 24 h. [b] Yields of isolated products. *E*/*Z* ratio in parentheses was determined by ^{1}H NMR.

3.5.3 Scope for Peptide C–H Glycoconjugation

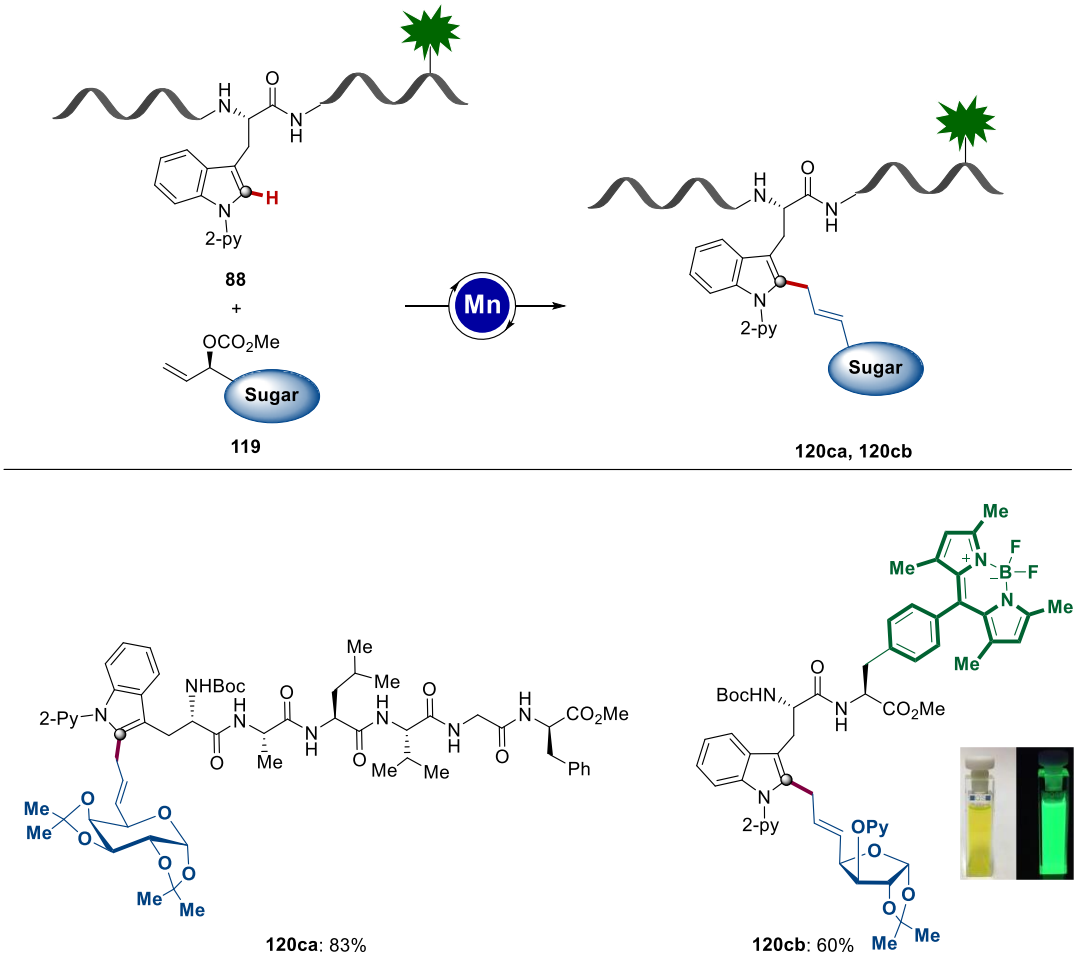
With the success of the tryptophan C–H glycoconjugations, we next employed the strategy for a broad range of structural complex glycopeptides (Scheme 3.5.3.1) with high levels of regio- and stereo-selectivities. The glycosylation on peptides provided the glycoconjugated peptide products with higher *E*/*Z* ratio than the mono tryptophan as substrates. Notably, the native tryptophan with the free *NH*-group was tolerated (**120bc**), highlighting the potential for further peptide modifications. Both furanose and galactose motifs were introduced to the peptides chemo-selectively by the manganese(I) catalysis.





Scheme 3.5.3.1. C–H glycoconjugation of tryptophan-containing peptides.

Other than the dipeptides, we further showed the unique power of the late-stage peptide glycoconjugations (Scheme 3.5.3.2). The hexapeptide was thus transformed by this manganese(I) catalysis into a glycopeptide conjugate **120ca** with a furanose scaffold, featuring as the peptide with both improved structural and functional complexity. Also, the C–H glycosylation strategy was conducted for BODPY integrated fluorescent peptide with galactose motif, unprecedentedly delivering a fluorescent glycopeptide **120cb**, which should prove invaluable for *in-vivo* fluorescent microscopy.[128c, 155]

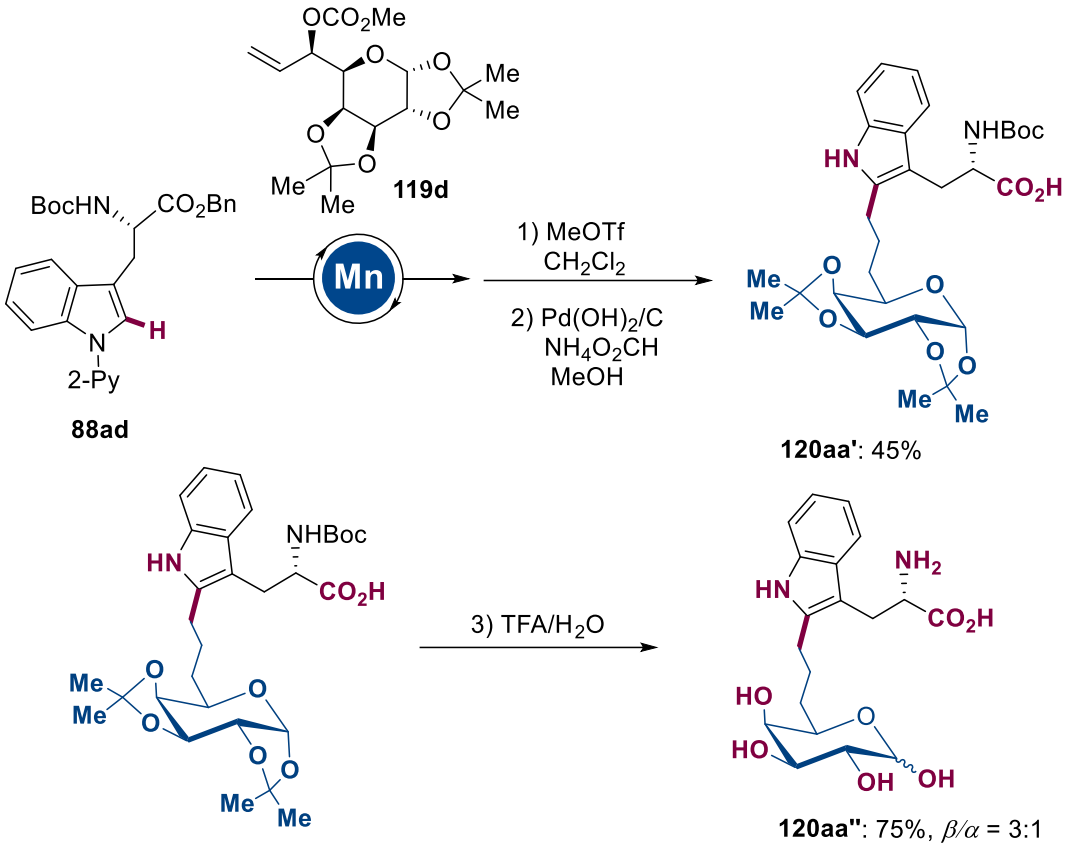


Scheme 3.5.3.2. C–H glycoconjugation of hexapeptide and fluorescent peptide

3.5.4 Traceless Removal of Glycopeptide Pyridyl and Protecting Groups

To further develop the molecular functions of the glycopeptides, we conducted the traceless removal of the pyridyl group,[140b, 144] and the protecting groups. After the removal of the pyridyl group, TFA was employed for the removal of the carbonate protecting groups. With

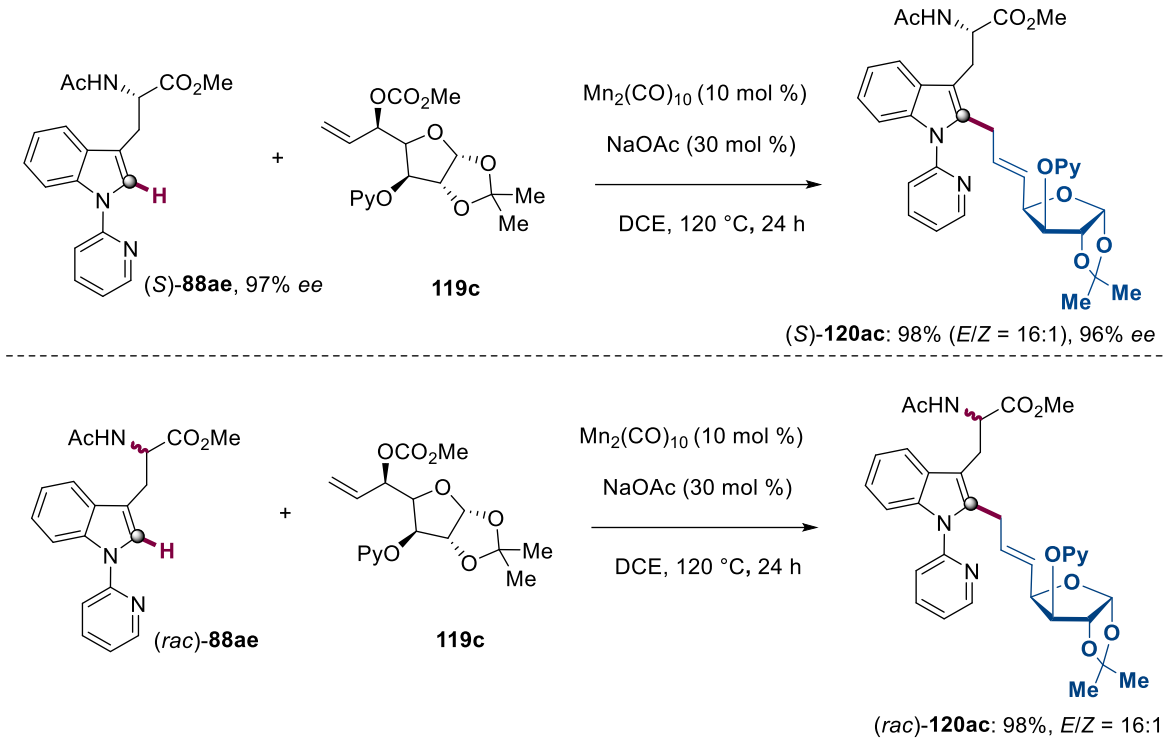
this strategy, *NH* and *OH*-free glycopeptides was delivered in a chemo-selective fashion. Thereby, we obtained **120aa'** as a novel *C*-galactosyl tryptophan[156] derivative, which is of key importance in modulating the functions of proteins in cellular processes (Scheme 3.5.4.1).



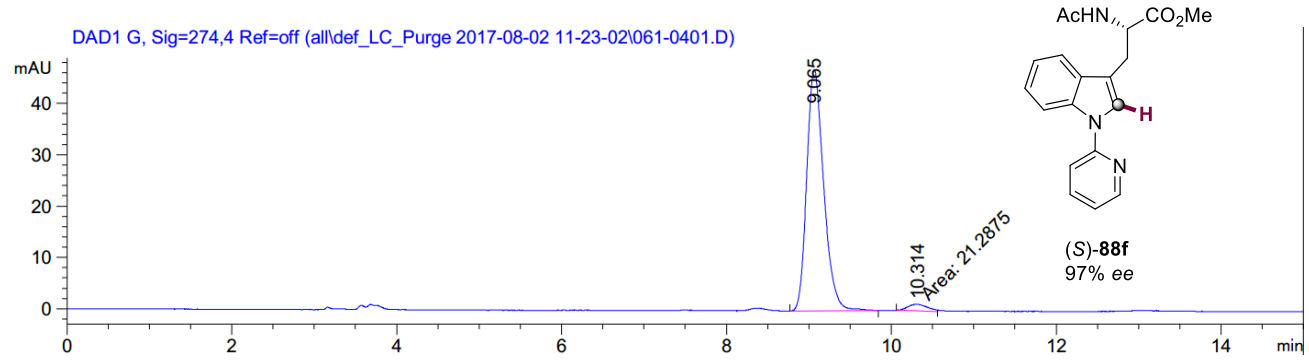
Scheme 3.5.4.1. Traceless removal for *OH* and *NH* free glycotryptophan.

3.5.5 Studies on Potential Racemization of C–H Glycoconjugation

To probe if the unprecedented C–H peptide glycosylation proceeded in a racemization-free manner, *D/L*-tryptophan and the enantiopure substrates were subjected to the glycosylation reaction (Scheme 3.5.5.1). Both the substrates and the glycoconjugated products were analyzed by HPLC comparisons (Scheme 3.5.5.2 and Scheme 3.5.5.3). The developed C–H glycosylation reaction did not cause any loss of the stereogenic integrity on the tryptophan substrates.

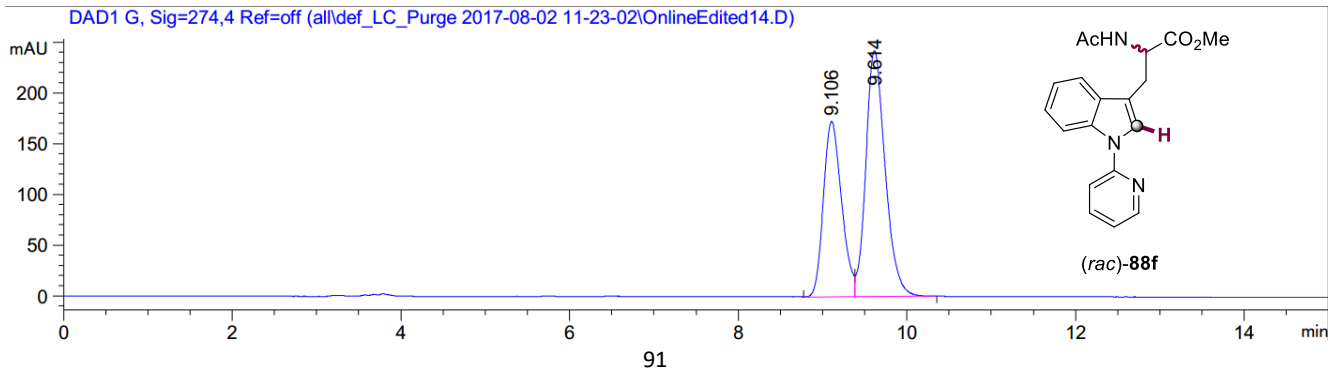


Scheme 3.5.5.1. Studies on potential racemization.



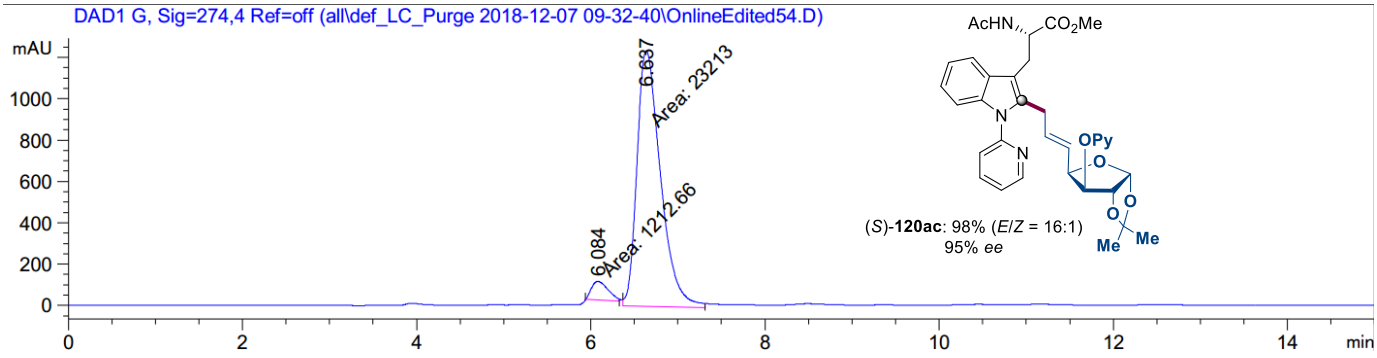
Signal 2: DAD1 G, Sig=274,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.065	BB	0.2197	671.07928	46.96846	96.9254
2	10.314	MM	0.2750	21.28746	1.29029	3.0746
Totals :				692.36674	48.25875	

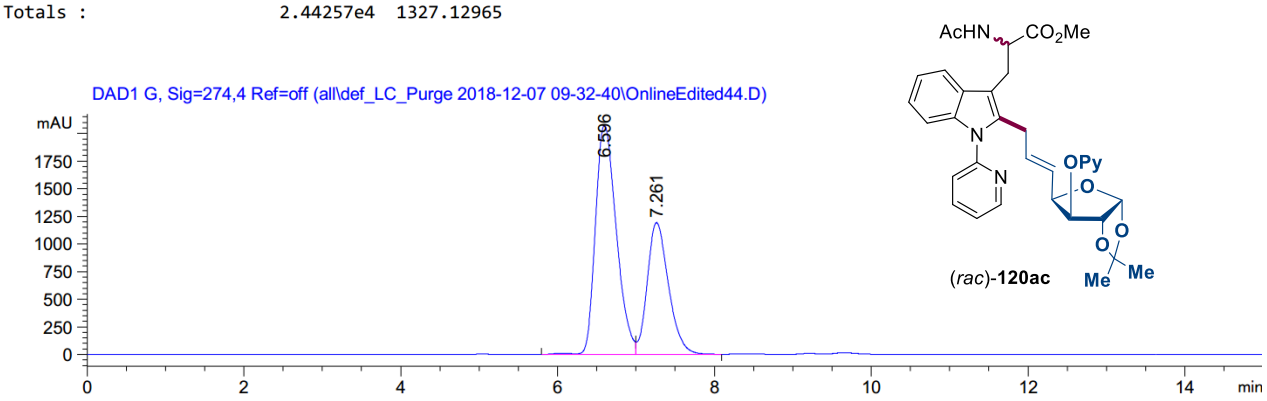


```
Signal 2: DAD1 G, Sig=274,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.106 BV    0.2318 2589.50610  172.84454  40.1506
   2   9.614 VB    0.2440 3859.98462  242.12398  59.8494

Totals :                   6449.49072  414.96852
```

Scheme 3.5.5.2. HPLC analysis of substrate (*S*)-**88ae**, (*rac*)-**88ae**. IC *n*-hexane/EtOAc 50/50 flow: 1 mL/min, 274 nm.




```
Signal 2: DAD1 G, Sig=274,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.084 MM    0.2238 1212.66467   90.31532   4.9647
   2   6.637 MM    0.3128 2.32130e4  1236.81433  95.0353

Totals :                  2.44257e4  1327.12965
```



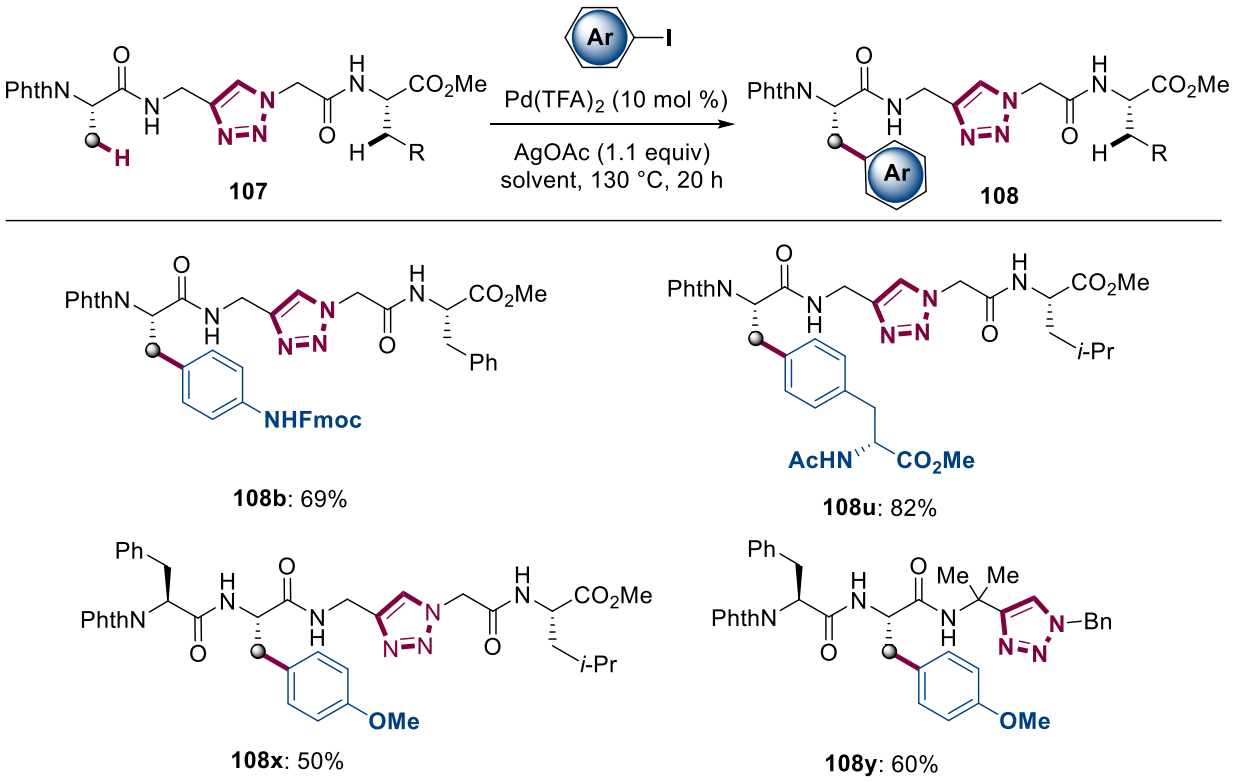

```
Signal 2: DAD1 G, Sig=274,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   6.596 VV R  0.2883 3.84361e4  2073.86426  63.1835
   2   7.261 VB    0.2893 2.23964e4  1191.38159  36.8165

Totals :                  6.08325e4  3265.24585
```

Scheme 3.5.5.3. HPLC analysis of products (*S*)-**120ac**, (*rac*)-**120ac**. IC *n*-hexane/EtOAc 50/50 flow: 1 mL/min, 274 nm.

4 Summary and Outlook

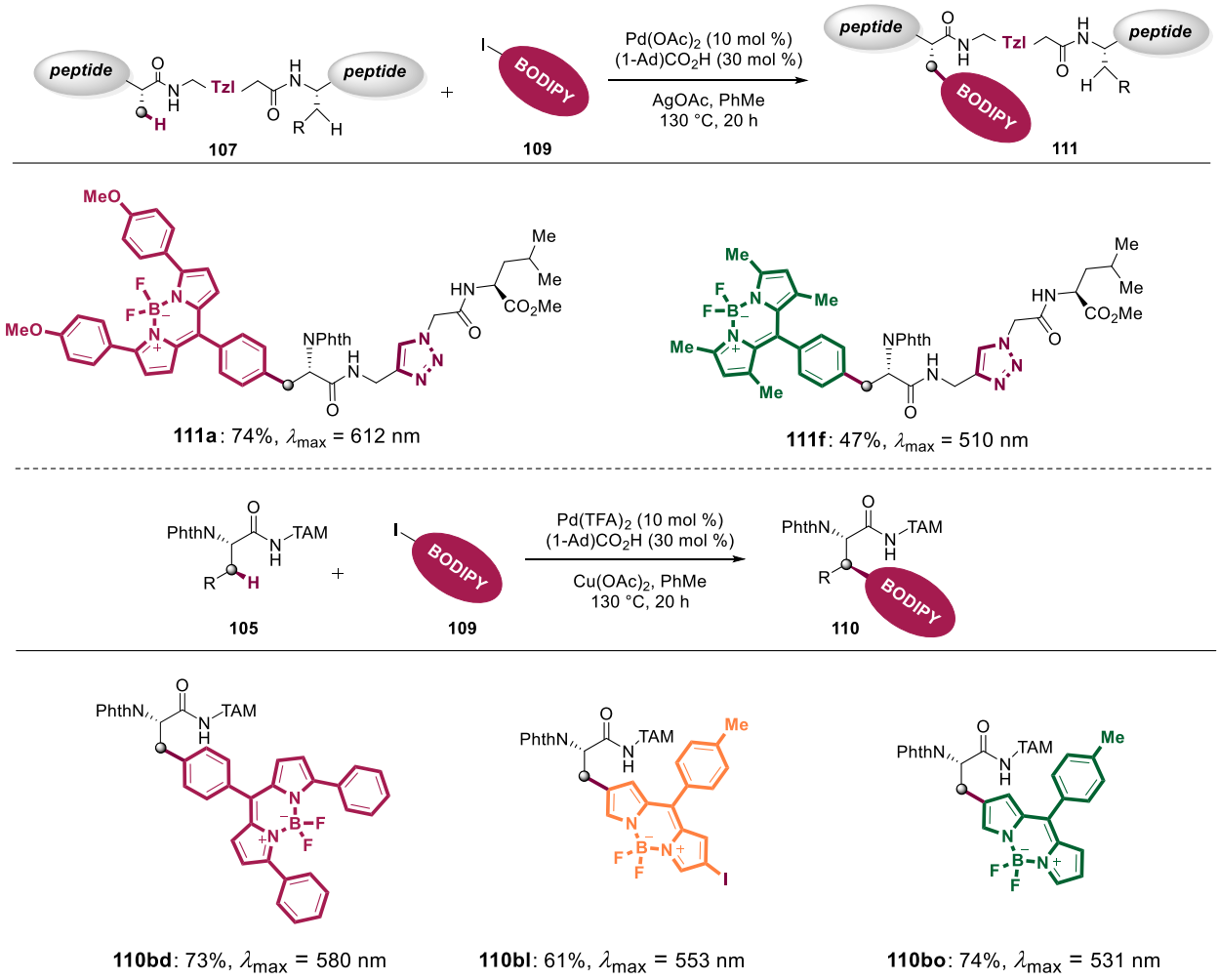
The late-stage modification of peptides is of great value to drug discovery and medicinal chemistry. Conventional syntheses of peptides are largely limited to lengthy procedures and conventional reactions. In contrast, metal catalyzed C─H activation catalysis has emerged as efficient and step-economic strategy for post-translational peptide engineering. However, a diversity of positional-selective transformation is highly desirable. Moreover, besides peptide C─C formations, C─N formation is of key importance for peptide modifications due to the pharmaceutical features and applications of C─N bond, and C─X bond formation should be studied for the diversity of novel peptide structures. Other than precious 4d and 5d metals, 3d metal manganese has recently emerged as an efficient, earth-abundant and non-toxic metal for the late-stage peptide modifications, enabling green and sustainable syntheses of structural complex peptides.

In the first project, a palladium-catalyzed internal triazole peptide C(sp^3)–H arylation was achieved (Scheme 4.1). This diversification features various functional group tolerance, and enabled the racemization-free late-stage transformation of peptides. Through this arylation reaction, a variety of functional groups was introduced to amino acids and peptides, as well as the site-selective chemical ligations through iodo-phenylalanine for new peptide disconnections. Importantly, limitations of traditional bidentate chelation strategy for challenging peptide C(sp^3)─H modifications were addressed in this work through the unprecedented internal triazole assistance. The positional control of peptide C─H functionalization was thus realized, enabling a precise late-stage peptide assembly at the *C*-terminal, *N*-terminal and internal position in a programmable fashion.



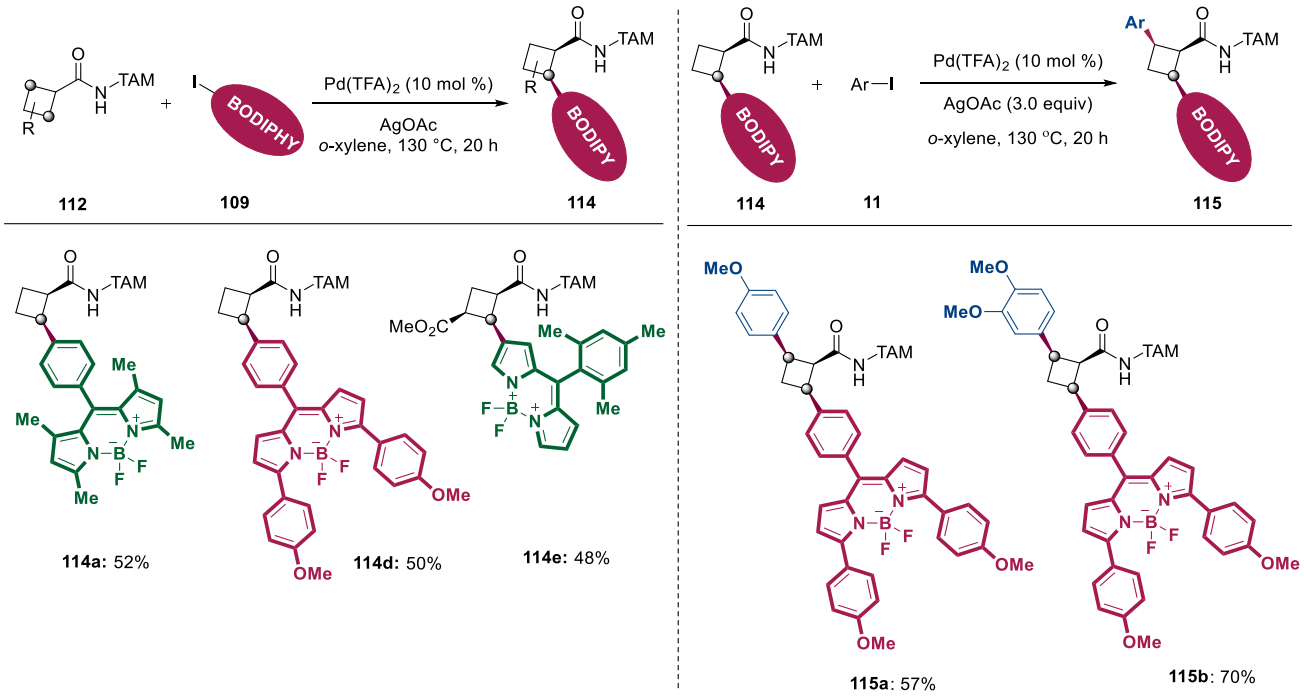
Scheme 4.1. Position-selective functionalization of C(sp^3)–H by internal triazole assistance: access to peptidomimetics.

In the second project, we reported on the first peptide BODIPY-labeling by C(sp^3)–H activation (Scheme 4.2). Through the palladium-catalyzed C(sp^3)–H BODIPY labeling, we synthesized various fluorescent BODIPY amino acids and peptides with high levels of chemo-, diastereo- and positional-selectivities. A wide range of BODIPYs with different emission wavelengths were compatible with this chemistry, delivering the BODIPY labeled amino acids and peptides with various fluorescent colors in a linker-free fashion. Notably, the isosteric triazoles were employed as the bidentate chelation assistance for this precise chemical labeling control. Furthermore, the triazole groups of BODIPY amino acid were removed in a traceless manner, giving free BODIPY-labeled amino acids as potential building blocks for the assembly of peptidic fluorescent sensors for *in-vivo* imaging studies.



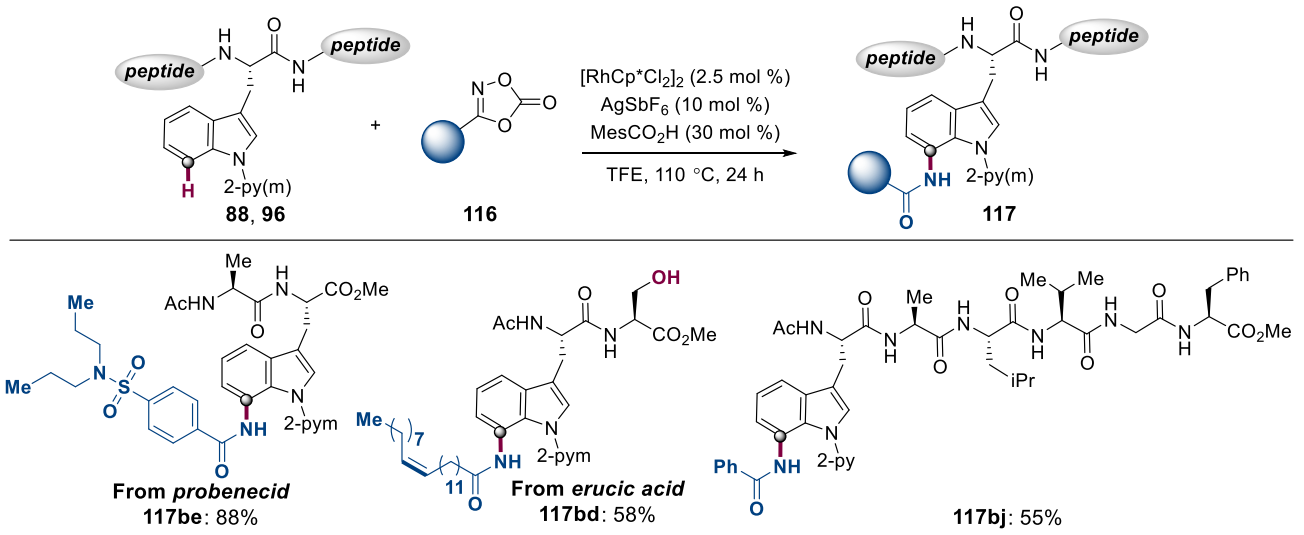
Scheme 4.2. BODIPY peptide labeling by late-stage C(sp^3)–H activation.

In the third project, the secondary C(sp^3)–H arylation was developed by triazole assistance, providing various cyclobutane natural product analogs. With our program of late-stage peptide and natural product fluorescent labeling, the unprecedented cyclobutane BODIPY labeling was thus realized (Scheme 4.3). A wide range of BODIPYs were tolerated in this work, delivering the fluorescent cyclobutane natural product derivatives. Notably, the BODIPY labeling of cyclobutanes was highly mono-selective, thus paving the way for the successive cyclobutane functionalizations, enabling synthesis of unsymmetrical fluorescent cyclobutanes, featuring a class of functional and structural complex cyclobutane derivatives.



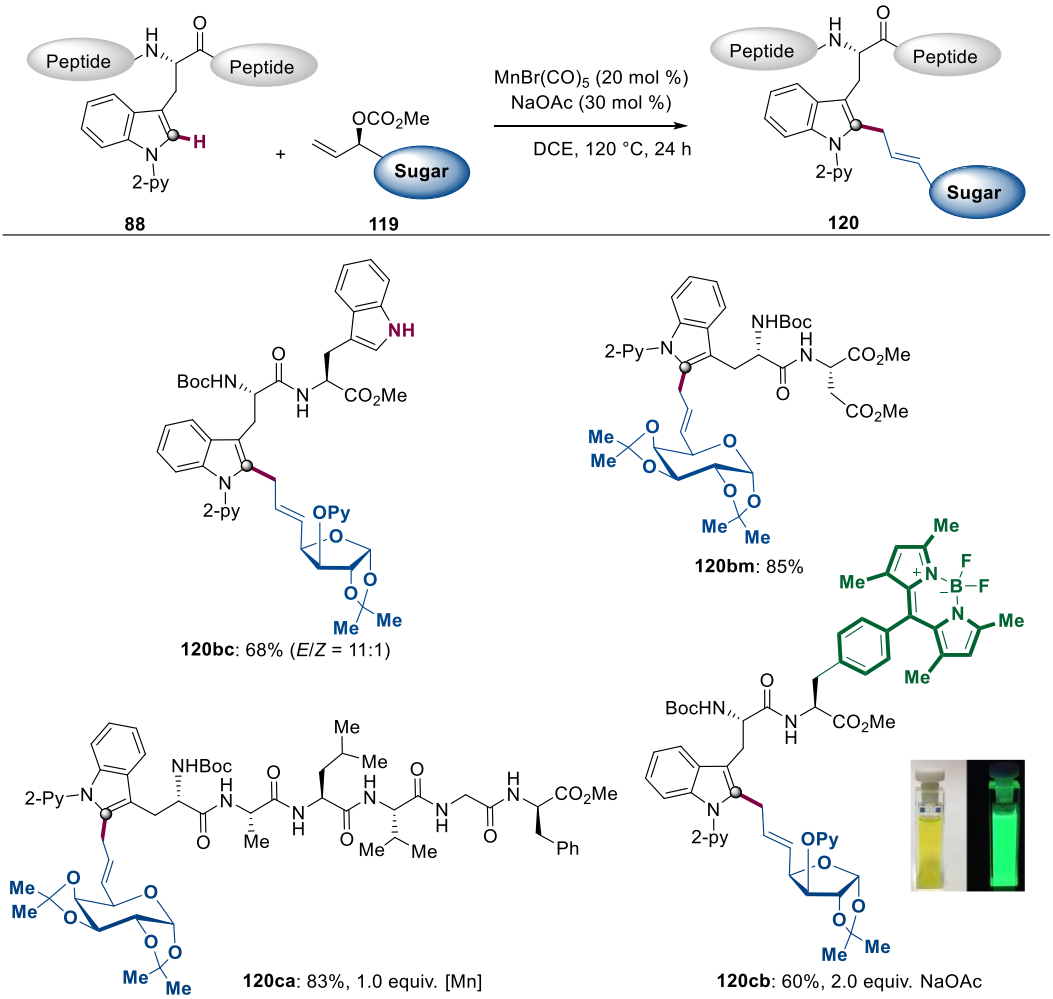
Scheme 4.3. BODIPY-labeled cyclobutanes by secondary C(sp^3)–H arylation.

In the fourth project, a robust positional-selective tryptophan C7 amidation reaction was developed by rhodium(III) catalysis (Scheme 4.4). Versatile functional groups were installed on the tryptophan containing peptides through this unprecedented C7 amidation. In contrast to all other metal-catalyzed late-stage peptide modifications, this chemistry was of significant selectivity on the unusual C7 tryptophan position as well as natural products conjugations. This enabled a sequential peptide C(2)–H activations, delivering structurally complex peptides.



Scheme 4.4. Peptide late-stage diversifications by rhodium-catalyzed tryptophan C7 amidation.

In the fifth project, the manganese(I)-catalyzed peptide allylation reaction was developed to introduce the glycol motifs (Scheme 4.5). Through this unprecedented peptide linchpin C–H glycoconjugation, various glycopeptides were assembled with high levels of chemo- and positional selectivity in a racemization-free manner. The pyridyl group was removed in a traceless manner, affording the native glycotryptophan. Notably, late-stage peptide and BODIPY labeled peptide were successfully transformed by the C–H glycoconjugation for structurally complex glycopeptides.



Scheme 4.5. Glycopeptides by linchpin C–H activation for peptide-carbohydrate conjugation by manganese(I)-catalysis.

5 Experimental Section

5.1 General Remarks

Unless otherwise noticed, all reactions were carried out under an atmosphere of N_2 using pre-dried glassware and standard Schlenk techniques. If not otherwise noted, yields refer to isolated compounds, estimated to be >95% pure as determined by ^{1}H-NMR.

Vacuum

The following pressure were measured on the used vacuum pump and were not corrected: Membrane pump vacuum (MPV): 0.5 mbar, oil pump vacuum (OPV): 0.1 mbar.

Melting Points (M.p.)

Melting points were measured using a *Stuart*® Melting Point Apparatus *SMP3* from BARLOWORLD SCIENTIFIC. The reported values are uncorrected.

Chromatography

Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel 60F-plates (MACHEREY-NAGEL) with 254 nm fluorescent indicator from MERCK. Plates were visualized under UV-light or developed by treatment with a $KMnO_4$ solution followed by carefully applying a heating gun. Chromatographic purification of products was accomplished by manual flash column chromatography on MERCK silica gel, grade 60 (0.040–0.063 mm and 0.063–0.200 mm).

Gel Permeation Chromatography (GPC)

GPC purifications were performed on a *JAI*® system (JAI-*LC-9260 II NEXT*, injection- and control-valve, UV and RI detector) connected to JAIGEL HH series columns (*JAIGEL-2HR*, gradient rate: 5.000; *JAIGEL-2.5HR*, gradient rate: 20.000; internal diameter = 20 mm; length = 600 mm; Flush rate = 10.0 mL/min). Chloroform of HPLC-grade stabilized with 0.6% EtOH was employed as the eluent.

HPLC

HPLC chromatograms were recorded on an Agilent 1290 Infinity using the column CHIRALPAK® IA, IC, IE, IF columns and *n*-hexanes/EtOAc (1 mL/min, detection at 274 nm).

LC-MS

LC-MS chromatograms were recorded on an Agilent 6100s Series Single Quad using the RP column ZORBAX SB-C18, 5 µm. The flow rate was set to 0.5 mL/min, detection at 270 and 290 nm. The methods used are as follows:

Table XX: LC-MS methods

Measuring time	*t*/min	MeCN (0.1% TFA)	H_2O (0.1% TFA)
15 min	0	60%	40%
	5	100%	0
	13	100%	0
	15	60%	40%
22 min	0	60%	40%
	5	100%	0%
	20	100%	0%
	22	60%	400%

Fluorescence Spectroscopy

Fluorescence excitation and emission data in solution were recorded on a *Jasco*® FP-8500 spectrofluorometer. The scan speed was adjusted to 200 nm/min. All compounds were measured at a concentration of 1 mg/L solution.

UV-VIS Spectroscopy

UV-Visible Spectroscopy was performed on a *Jasco*® V-770 spectrophotometer. A baseline in the appropriate solvent was obtained prior to recording spectra. All compounds were measured at a concentration of 1 mg/L solution.

Infrared Spectroscopy

Infrared spectra were recorded at a BRUKER *Alpha-P ATR FT-IR* spectrometer. Liquid samples were measured as a film, solid samples neat. The analysis of the spectra was carried out using the software from BRUKER *OPUS 6*. The absorption is given in wave numbers (cm^{-1}) and the spectra were recorded in the range of 4000–400 cm^{-1}. *in-situ*-IR studies were performed on METTLER TOLEDO *ReactIR™ 15* with an *iC IR 4.3* software.

Mass Spectrometry

Electron ionization (EI) and EI high resolution mass spectra (HR-MS) were measured on a *time-of-flight* mass spectrometer *AccuTOF* from JOEL. Electrospray ionization (ESI) mass spectra were recorded on an *Ion-Trap* mass spectrometer *LCQ* from FINNIGAN, a *quadrupole time-of-flight maXis* from BRUKER DALTONIC or on a *time-of-flight mass* spectrometer microTOF from BRUKER DALTONIC. ESI-HRMS spectra were recorded on a BRUKER *Apex IV* or a BRUKER *Daltonic 7T*, fourier transform ion cyclotron resonance (FTICR) mass spectrometer. The ratios of mass to charge (*m*/*z*) are indicated and intensities relative to the base peak (*I* = 100) are written in parentheses.

Nuclear Magnetic Resonance Spectroscopy (NMR)

Nuclear magnetic resonance (NMR) spectra were recorded on VARIAN *Inova 500*, *600*, VARIAN *Mercury 300*, *VX 300*, VARIAN *Avance 300*, VARIAN *VNMRS 300* and BRUKER *Avance III 300*, *400* and *HD 500* spectrometers. All chemical shifts are given as *δ*-values in ppm relative to the residual proton peak of the deuterated solvent or its carbon atom, respectively. ^{1}H and ^{13}C NMR spectra were referenced using the residual proton or solvent carbon peak (see table), respectively. ^{13}C and ^{19}F NMR were measured as proton-decoupled spectra.

	^{1}H-NMR	^{13}C-NMR
$CDCl_3$	7.26	77.16
$[D]_6$-DMSO	2.50	39.52

The observed resonance-multiplicities were described by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), hept (heptet), m (multiplet) or analogous representations. The coupling constants *J* are reported in Hertz (Hz). Analysis of the recorded spectra was carried out with *MestReNova 10* software.

Solvents

All solvents for reactions involving moisture-sensitive reagents were dried, distilled and stored under an inert atmosphere (Ar or N_2) according to the following standard procedures.

1,2-Dichloroethane (**DCE**) were dried over CaH_2 for 8 h, degassed and distilled under reduced pressure.

1,4-Dioxane were distilled from sodium benzophenone ketyl.

1,1,1,3,3,3-Hexafluoropropan-2-ol (**HFIP**) were distilled from 3 Å molecular sieves.

Methanol (**MeOH**) was stirred over magnesium turnings at 65 °C for 3 h prior to distillation from $Mg(OMe)_2$.

Acetonitrile (**MeCN**) was dried over P_2O_5 for 24 h degassed and distilled under reduced pressure.

Toluene (**PhMe**) was pre-dried over KH and distilled over sodium/benzophenone.

Tetrahydrofuran (**THF**), **Dichloromethane** were purified using a solvent purification system (*SPS-800*) from M. BRAUN.

***o*-Xylene** was stirred at 160 °C over sodium/benzophenone and distilled under ambient pressure.

2,2,2-Trifluoroethanol (**TFE**) was stirred over $CaSO_4$ and distilled under reduced pressure.

For synthesis grade solvents for reactions under air were used without further purification: DMF, trifluoroacetic acid, acetic acid, toluene, hexanes, aq. HCl (12 M).

Reagents

Chemicals obtained from commercial sources with purity above 95% were used without further purification.

The following compounds are known and were synthesized according to previously described methods:

TAM amide, TAM amino acids **105**, and TAM cyclobutanes **112**,[127, 157] iodo-BODIPYs **109**,[158] *N*-pyridyl/pyrimidyl tryptophans[140c, 159] and successive couplings for *N*-pyridyl/pyrimidyl tryptophan containing peptides,[160] 1,4,2-dioxazol-5-ones **116**,[142d, 142f, 161] ally carbonates **119**.[162]

The following compounds were obtained by the generous courtesy of the following persons:

M. Sc. Michaela Bauer: (*S*)-*N*-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-2-(1,3-dioxoisoindolin-2-yl)propanamide **105a**; (2*S*,3*R*)-*N*-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-2-(1,3-dioxoisoindolin-2-yl)-3-(4-nitrophenyl)-3-phenylpropanamide **106b**.

Dr. Mélanie M. Lorion:
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-[5,5-difluoro-8-iodo-10-(4-methoxyphenyl)-5*H*-5λ^4,6λ^4-dipyrrolo(1,2-c:2',1'-f)(1,3,2)diazaborinin-2-yl]-2-(1,3-dioxoisoindolin-2-yl) propanamide **110bm**.

Dr. Matteo Virelli:
N-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]cyclobutanecarboxamide **112a**, methyl (1*S*,3*S*)-3-[(2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl)carbamoyl]cyclobutane-1-carboxylate **112b**.

M. Sc. Jun Wu:
(*Z*)-3-(henicos-12-en-1-yl)-1,4,2-dioxazol-5-one **116d**, 4-(5-oxo-1,4,2-dioxazol-3-yl)-*N*,*N*-dipropylbenzenesulfonamide **116j**, 2-{{1-[(5-oxo-1,4,2-dioxazol-3-yl)methyl]cyclohexyl}methyl}isoindoline-1,3-dione **116k**:

Dr. Parthasarathi Subramanian: (*R*)-1-{(3*aR*,5*R*,6*S*,6*aR*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl}allyl methyl carbonate **119a**, (1*R*)-1-{(3a*R*,6*R*,6a*S*)-6-[((*tert*-butyldimethylsilyl)oxy)methyl]-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl}allyl methyl carbonate **119b**.

5.2 General Procedures

General Procedure A: C(sp^3)–H Arylation on Tzl-Containing Peptides

A mixture of Tzl-containing peptide **107** (0.20 mmol, 1.00 equiv), iodoarene **11** (0.40 mmol, 2.00 equiv), $Pd(TFA)_2$ (0.02 mmol, 10 mol %) and AgOAc (0.22 mmol, 1.10 equiv) in DCE (2 mL) was stirred at 130 °C for 20 h in a pressure tube. At ambient temperature, the reaction was diluted with CH_2Cl_2 (15 mL) and then filtered through a pad of Celite and washed with CH_2Cl_2 (50 mL). The solvent was removed *in vacuo* and the crude product was purified by column chromatography on silica gel or HPLC to yield the desired product **108**.

General Procedure B: BODIPY Amino Acid C(sp^3)–H Labeling

A mixture of TAM amino acid **105** (0.10 mmol, 1.0 equiv), iodo-BODIPY **109** (0.12 mmol, 1.2 equiv), $Pd(TFA)_2$ (3.3 mg, 10 mol %), (1-Ad)CO_2H (5.4 mg, 30 mol %) and M(OAc)n in PhMe (0.5 mL) was stirred at 130 °C for 20 h. At ambient temperature, the reaction was diluted with CH_2Cl_2 (10 mL), filtered through a pad of Celite and washed with CH_2Cl_2 (40 mL). The solvents were removed *in vacuo* and the crude product was purified by column chromatography on silica gel or HPLC to yield the desired product **110**.

General Procedure C: BODIPY C(sp^3)–H Labeling of Internal Tzl-Peptides

A mixture of Tzl-containing peptide **107** (0.10 mmol, 1.0 equiv), iodo-BODIPY **109** (0.12 mmol, 1.20 equiv), $Pd(OAc)_2$ (2.2 mg, 10 mol %), (1-Ad)CO_2H (5.4 mg, 30 mol %) and AgOAc (0.20 mmol, 2.0 equiv) in PhMe (0.5 mL) was stirred at 130 °C for 20 h. At ambient temperature, the reaction was diluted with CH_2Cl_2 (10 mL), filtered through a pad of Celite and washed with CH_2Cl_2 (40 mL). The solvents were removed *in vacuo* and the crude product was purified by HPLC to yield the desired product **111**.

General Procedure D: BODIPY Cyclobutanes C(sp^3)–H Labeling

A mixture of TAM cyclobutane **112** (0.10 mmol, 1.0 equiv), iodo-BODIPY **109** (0.12 mmol, 1.2 equiv), $Pd(TFA)_2$ (3.3 mg, 10 mol %) and AgOAc (37 mg, 0.22 mmol) in *o*-xylene (1.0 mL) was stirred at 130 °C for 20 h. At ambient temperature, the reaction was diluted with EtOAc (5.0 mL) and concentrated *in vacuo*. The resulting mixture was purified by column

chromatography on silica gel, giving the corresponding labeled product **114**.

General Procedure E: C–H Arylation of BODIPY Labeled Cyclobutanes

A solution of BODIPY-cyclobutanecarboxamide **114** (0.2 mmol), $Pd(TFA)_2$ (6.6 mg, 0.02 mmol, 10 mol %), iodo arenes **11** (0.8 mmol), AgOAc (73 mg, 0.44 mmol) in anhydrous *o*-xylene (2 mL) was heated at 130 °C for 20 h. After the reaction period, the reaction mixture was diluted with EtOAc (5 mL) and concentrated in vacuum and the resulting mixture was purified by column chromatography (silica gel, 100-200 mesh), furnishing the corresponding bis-arylatedcyclobutanecarboxamides.

General Procedure F: C7–H Amidation of Tryptophans and Tryptophan-Containing Peptides

Amino acid or peptide **88**/**96** (0.2 mmol), 1,4,2-dioxazol-5-one **116** (0.4 mmol), $[RhCp^*Cl_2]_2$ (3.0 mg, 2.5 mol %), $AgSbF_6$ (6.8 mg, 10 mol %) and $MesCO_2H$ (5.4 mg, 15 mol %) were placed in an oven-dried Schlenk tube. The mixture was evacuated and purged with N_2 three times. Then, TFE (0.4 mL) was added. The tube was sealed and heated at 110 °C for 24 h. After cooling to room temperature, the resulting mixture was diluted with CH_2Cl_2 (10 mL) and concentrated *in vacuo*. Purification of the residue by column chromatography on silica gel yielded the products **117**.

General procedure G: C–H Glycoconjugation of Tryptophans

Indole or tryptophan (0.10 mmol), allyl sugar carbonate **119** (0.20 mmol), $Mn_2(CO)_{10}$ (3.89 mg, 10 mol %) and NaOAc (2.5 mg, 30 mol %) were placed in an oven-dried Schlenk tube. The mixture was evacuated and purged with N_2 three times. Then, 1,2-dichloroethane (0.5 mL) was added. The mixture was stirred at 120 °C for 24 h. After cooling to room temperature, the resulting mixture was diluted with CH_2Cl_2 and concentrated *in vacuo*. Purification of the residue by column chromatography on silica gel yielded the products **120**.

General Procedure H: C–H Glycoconjugation of Tryptophan-Containing Peptides

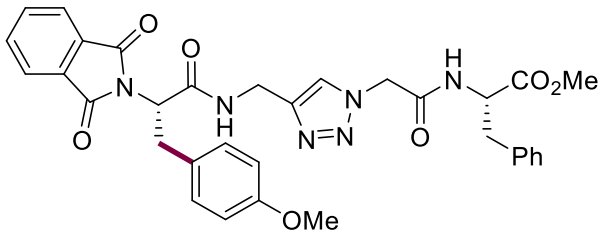
Peptide **88** (0.10 mmol), allyl sugar carbonate **119** (0.20 mmol), $MnBr(CO)_5$ (5.5 mg, 20 mol %) and NaOAc (2.5 mg, 30 mol %) were placed in an oven-dried Schlenk tube. The

mixture was evacuated and purged with N_2 three times. Then, 1,2-dichloroethane (0.5 mL) was added. The mixture was stirred at 120 °C. After 24 h, the resulting mixture was diluted with CH_2Cl_2 and concentrated *in vacuo*. Purification of the residue by column chromatography on silica gel yielded the products **120**.

5.3 Experimental and Analytical Data

5.3.1 Internal Peptide Late-Stage Diversification: Peptide-Isosteric Triazoles for C(sp^3)–H Activation

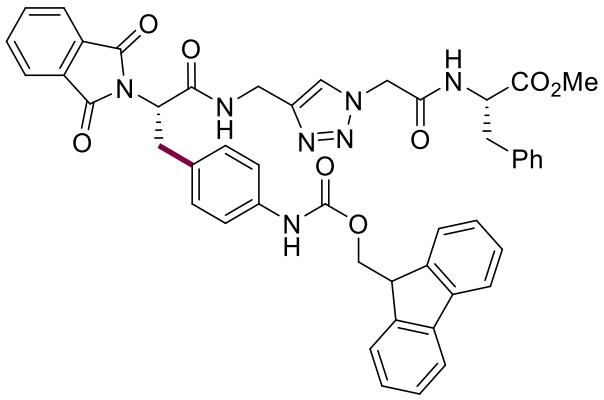
5.3.1.1 Characterization Data of Products 108



(*S*)-Methyl-2-[2-(4-{[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-3-phenylpropanoate (108a)

The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Phe-OMe (**107a**) (103.7 mg, 0.2 mmol) and 4-iodoanisole (**11d**) (93.6 mg, 0.4 mmol). After 20 h, purification by column chromatography on silica gel (EtOAc/*n*-hexane 8/1 to EtOAc/*n*-hexane 10/1. Rf (EtOAc/n-hexane 8/1): 0.25) yielded **108a** (100 mg, 80%) as a white solid (M.p.: 150–152 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.67 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.65–7.50 (m, 3H), 7.51 (brs, 1H), 7.25–7.15 (m, 4H), 7.08–7.04 (m, 2H), 6.99 (d, *J* = 8.6 Hz, 2H), 6.64 (d, *J* = 8.6 Hz, 2H), 5.03 (dd, *J* = 11.2, 5.5 Hz, 1H), 4.98 (d, *J* = 16.4 Hz, 1H), 4.85 (d, *J* = 16.4 Hz, 1H), 4.82–4.77 (m, 1H), 4.43–4.32 (m, 2H), 3.64 (s, 3H), 3.63 (s, 3H), 3.49 (dd, *J* = 14.3, 5.5 Hz, 1H), 3.41 (dd, *J* = 14.3, 11.2 Hz, 1H), 3.08 (dd, *J* = 13.9, 5.5 Hz, 1H), 2.97 (dd, *J* = 13.9, 7.2 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.5 (C_q), 168.7 (C_q), 167.8 (C_q), 164.9 (C_q), 158.3 (C_q), 144.9 (C_q), 135.6 (C_q), 134.1 (CH), 131.5 (C_q), 129.9 (CH), 129.2 (CH), 128.7 (C_q), 128.6

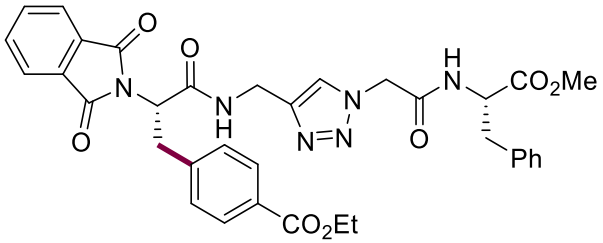
(CH), 127.2 (CH), 124.2 (CH), 123.4 (CH), 114.0 (CH), 55.5 (CH), 55.2 (CH_3), 53.7 (CH), 52.6 (CH_3) 52.5 (CH_2), 37.8 (CH_2), 35.2 (CH_2), 33.9 (CH_2). **IR** (ATR): $\tilde{\nu}$ = 2956, 1774, 1711, 1673, 1612, 1531, 1382, 1246, 1217, 1029 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1271 (45) $[2M+Na]^+$, 647 (100) $[M+Na]^+$, 625 (37) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{33}H_{33}N_6O_7$ $[M+H]^+$: 625.2405; found: 625.2403.



(*S*)-Methyl-[2-(4-{[(*S*)-3-[4-({[(9*H*-fluoren-9-yl)methoxy]carbonyl}amino)phenyl]-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetyl]-*L*-phenylalaninate (108b)

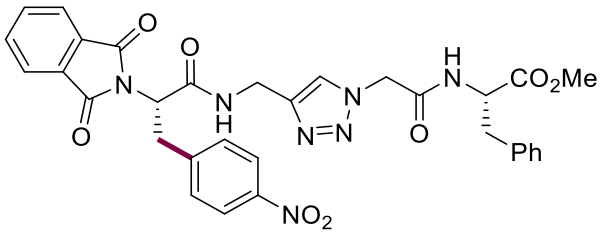
The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Phe-OMe (**107a**) (103.7 mg, 0.2 mmol) and (9*H*-fluoren-9-yl)methyl(4-iodo-phenyl)carbamate (**11e**) (176.5 mg, 0.4 mmol). After 20 h, purification by column chromatography on silica gel (EtOAc/*n*-hexane 8/1 to EtOAc/*n*-hexane 12/1. Rf (EtOAc/*n*-hexane 8/1): 0.14) yielded **108b** (114.7 mg, 69%) as a white solid (M.p.: 144–147 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 7.6 Hz, 2H), 7.67–7.55 (m, 6H), 7.54–7.50 (m, 2H), 7.37–7.33 (m, 2H), 7.25–7.08 (m, 9H), 7.04–6.99 (m, 2H), 6.98–6.96 (m, 2H), 5.04 (dd, *J* = 10.9, 5.7 Hz, 1H), 4.95 (d, *J* = 16.3 Hz, 1H), 4.84 (d, *J* = 16.3 Hz, 1H), 4.82–4.75 (m, 1H), 4.43–4.30 (m, 4H), 4.14 (dd, *J* = 6.7, 6.7 Hz, 1H), 3.60 (s, 3H), 3.50 (dd, *J* = 14.1, 5.6 Hz, 1H), 3.40 (dd, *J* = 14.1, 11.3 Hz, 1H), 3.05 (dd, *J* = 13.9, 5.5 Hz, 1H), 2.95 (dd, *J* = 13.9, 7.2 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.6 (C_q), 171.1 (C_q), 168.6 (C_q), 167.9 (C_q), 165.0 (C_q), 144.9 (C_q), 143.7 (C_q), 141.3 (C_q), 135.6 (C_q), 134.2 (CH), 131.4 (C_q), 129.5 (CH), 129.2 (CH), 128.6 (CH), 127.7 (CH), 127.6 (CH), 127.2 (CH), 127.1 (CH), 125.0 (CH), 124.2 (CH), 123.5 (CH), 120.0 (CH), 66.9 (CH_2), 60.5 (CH_2), 55.5 (CH), 53.7 (CH), 52.6 (CH_3), 52.5 (C_q), 47.2 (CH), 37.8 (CH_2), 35.2 (CH_2), 34.2 (CH_2) (*due to*

overlap, two resonances are missing). **IR** (ATR): $\tilde{\nu}$ = 3284, 1710, 1667, 1526, 1383, 1350, 1223, 1051 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1685 (5) $[2M+Na]^+$, 1267 (15), 854 (100) $[M+Na]^+$, 541 (35), 435 (45). **HR-MS** (ESI) *m/z* calcd for $C_{47}H_{41}N_7O_8Na$ $[M+Na]^+$: 854.2909; found: 854.2895.



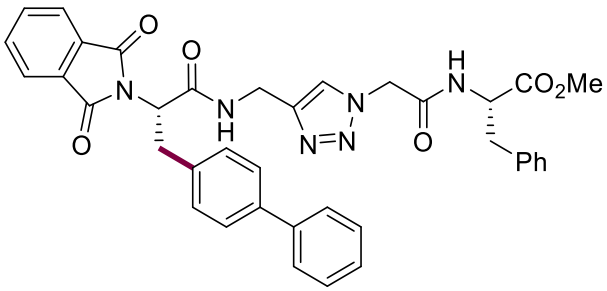
(*S*)-Ethyl-4-[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-({[1-(2-{[(*S*)-1-methoxy-1-oxo-3-phenylpropan-2-yl]amino}-2-oxoethyl)-1*H*-1,2,3-triazol-4-yl]methyl}amino)-3-oxopropyl]benzoate (108c)

The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Phe-OMe (**107a**) (103.7 mg, 0.2 mmol) and ethyl 4-iodobenzoate (**11f**) (110.4 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108c** (96.0 mg, 72%) as a white solid (M.p.: 107–108 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.3 Hz, 2H), 7.76–7.57 (m, 5H), 7.32–7.10 (m, 4H), 7.18 (d, *J* = 8.3 Hz, 2H), 7.09–6.99 (m, 2H), 6.68 (d, *J* = 8.0 Hz, 1H), 5.11 (dd, *J* = 10.5, 5.7 Hz, 1H), 5.01 (d, *J* = 16.3 Hz, 1H), 4.88 (d, *J* = 16.3 Hz, 1H), 4.87–4.77 (m, 1H), 4.44 (brs, 2H), 4.29 (ddd, *J* = 7.1, 7.1, 7.1 Hz, 2H), 3.69 (s, 3H), 3.66–3.47 (m, 2H), 3.12 (dd, *J* = 13.9, 5.4 Hz, 1H), 3.00 (dd, *J* = 13.9, 6.9 Hz, 1H), 1.33 (dd, *J* = 7.1, 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.3 (C_q), 168.3 (C_q), 167.7 (C_q), 166.3 (C_q), 164.7 (C_q), 142.1 (C_q), 135.5 (C_q), 134.4 (CH), 131.3 (C_q), 129.9 (CH), 129.2 (CH), 129.0 (CH), 128.7 (CH), 127.3 (CH), 123.7 (CH), 61.1 (CH_2), 55.1 (CH), 53.6 (CH), 52.9 (CH_2), 52.7 (CH_3), 37.8 (CH_2), 35.3 (CH_2), 34.8 (CH_2), 14.5 (CH_3) (*due to overlap, three resonances are missing*). **IR** (ATR): $\tilde{\nu}$ = 1710, 1381, 1274, 1216, 1177, 1020, 979, 871, 762, 700 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1355 (5) $[2M+Na]^+$, 1020 (15), 751 (10), 689 (100) $[M+Na]^+$, 667 (60) $[M+H]^+$, 353 (63). **HR-MS** (ESI) *m/z* calcd for $[C_{35}H_{34}N_6O_8Na]^+$: 689.2330, found: 689.2327.



(*S*)-Methyl-2-[2-(4-{[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-nitrophenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-3-phenylpropanoate (108d)

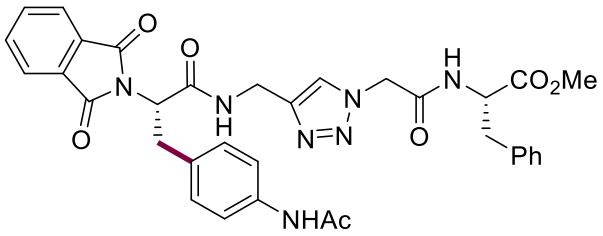
The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Phe-OMe (**107a**) (103.7 mg, 0.2 mmol) and 1-iodo-4-nitrobenzene (**11g**) (99.6 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108d** (84.4 mg, 66%) as a white solid (M.p.: 147–149 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.8 Hz, 2H), 7.73–7.67 (m, 4H), 7.63 (brs, 1H), 7.35 (brs, 1H), 7.29 (d, *J* = 8.8 Hz, 2H), 7.28–7.22 (m, 3H), 7.08–7.05 (m, 2H), 6.78 (d, *J* = 8.1 Hz, 1H), 5.13 (dd, *J* = 11.0, 5.4 Hz, 1H), 5.01 (d, *J* = 16.2 Hz, 1H), 4.87 (d, *J* = 16.2 Hz, 1H), 4.85–4.81 (m, 1H), 4.40 (brs, 2H), 3.73–3.67 (m, 5H), 3.11 (dd, *J* = 13.9, 5.5 Hz, 1H), 2.99 (dd, *J* = 13.9, 7.0 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.7 (C_q), 168.0 (C_q), 167.8 (C_q), 167.7 (C_q), 164.8 (C_q), 147.1 (C_q), 145.0 (C_q), 135.6 (C_q), 134.7 (CH), 131.3 (C_q), 130.0 (CH), 129.3 (CH), 128.8 (CH), 127.4 (CH), 124.0 (CH), 123.9 (CH), 123.8 (CH), 54.6 (CH), 53.6 (CH), 52.7 (CH_3), 37.7 (CH_2), 35.2 (CH_2), 34.6 (CH_2), 29.8 (CH_2). **IR** (ATR): $\tilde{\nu}$ = 2925, 1715, 1677, 1520, 1382, 1346, 1218, 1111, 722 cm^{-1}. MS (ESI) *m/z* (relative intensity): 1301 (8) $[2M+Na]^+$, 979 (28), 662 (100) $[M+Na]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{32}H_{29}N_7O_8Na$ $[M+Na]^+$: 662.1970; found: 662.1962.



(*S*)-Methyl-2-[2-(4-{[(*S*)-3-({1,1'-biphenyl}-4-yl)-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-3-phenylpropanoate (108e)

The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Phe-OMe (**107a**)

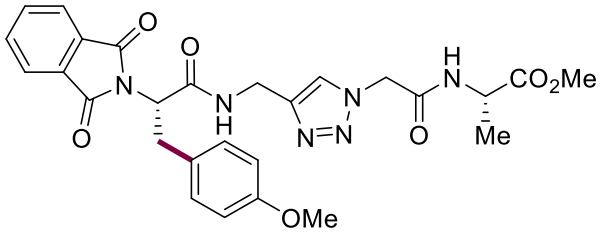
(103.7 mg, 0.2 mmol) and 4-iodobiphenyl (**11h**) (112.0 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 44.0 min) yielded **108e** (79.1 mg, 59%) as a white solid (M.p.: 149–151 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.68–7.58 (m, 3H), 7.47 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.37 (ddd, *J* = 8.3, 8.3, 1.2 Hz, 3H), 7.32–7.17 (m, 8H), 7.08–7.00 (m, 2H), 6.78–6.70 (m, 1H), 5.15 (dd, *J* = 10.6, 5.9 Hz, 1H), 5.01 (d, *J* = 16.0 Hz, 1H), 4.89 (d, *J* = 16.0 Hz, 1H), 4.86–4.80 (m, 1H), 4.46 (brs, 2H), 3.69 (s, 3H), 3.65–3.49 (m, 2H), 3.12 (dd, *J* = 13.9, 5.5 Hz, 1H), 3.00 (dd, *J* = 13.9, 7.0 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.3 (C_q), 168.6 (C_q), 167.8 (C_q), 167.7 (C_q), 164.6 (C_q), 140.5 (C_q), 139.6 (C_q), 137.8 (CH), 135.7 (C_q), 135.5 (C_q), 134.3 (CH), 131.4 (C_q), 129.5 (CH), 129.3 (CH), 129.2 (CH), 128.7 (CH), 127.3 (CH), 127.2 (CH), 126.9 (CH), 126.8 (CH), 123.5 (CH), 55.4 (CH), 53.6 (CH), 52.8 (CH_2), 52.7 (CH_3), 37.7 (CH_2), 35.2 (CH_2), 34.6 (CH_2). **IR** (ATR): $\tilde{\nu}$ = 1715, 1533, 1436, 1384, 1219, 1119, 764 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1363 (2) $[2M+Na]^+$, 693 (100) $[M+Na]^+$, 671 (35) $[M+H]^+$, 541 (43). **HR-MS** (ESI) *m/z* calcd for $[C_{38}H_{34}N_6O_6Na]^+$: 693.2432; found: 693.2429.



(*S*)-Methyl-2-[2-(4-{[(*S*)-3-(4-acetamidophenyl)-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-3-phenylpropanoate (108f)

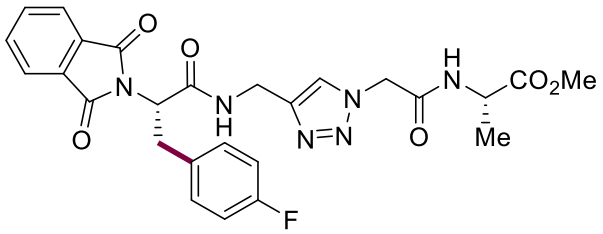
The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Phe-OMe (**107a**) (103.7 mg, 0.2 mmol) and *N*-(4-iodophenyl)acetamide (**11i**) (104.4 mg, 0.4 mmol) in HFIP. After 20 h, purification by HPLC (t_r: 43.0 min) yielded **108f** (99.1 mg, 76%) as a white solid (M.p.: 145–148 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.76 (brs, 1H), 7.70 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.63 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.47 (brs, 1H), 7.40–7.39 (m, 1H), 7.25–7.18 (m, 5H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.03 (d, *J* = 8.2 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, 2H) 5.05 (dd, *J* = 10.3, 6.3 Hz, 1H), 5.00 (d, *J* = 16.4 Hz, 1H), 4.86 (d, *J* = 16.4 Hz, 1H), 4.82–4.79 (m, 1H), 4.45 (dd, *J* = 15.2, 5.9 Hz, 1H), 4.37 (dd, *J* = 15.2, 5.9 Hz, 1H), 3.65 (s, 3H), 3.54 (dd, *J* = 14.2, 6.3 Hz, 1H), 3.39 (dd, *J* = 14.2, 10.3 Hz, 1H), 3.10 (dd, *J* = 14.0, 5.6 Hz, 1H), 3.00 (dd, *J* = 14.0, 7.2

Hz, 1H), 2.03 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.7 (C_q), 168.8 (C_q), 168.7 (C_q), 168.1 (C_q), 165.2 (C_q), 145.0 (C_q), 137.0 (C_q), 135.6 (C_q), 134.4 (CH), 132.5 (C_q), 131.5 (C_q), 129.5 (CH), 129.3 (CH), 128.8 (CH), 127.4 (CH), 124.2 (CH), 123.6 (CH), 119.9 (CH), 55.6 (CH), 53.7 (CH), 52.6 (CH_3), 52.5 (CH_2), 37.7 (CH_2), 35.2 (CH_2), 34.3 (CH_2), 24.5 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1712, 1664, 1515, 1411, 1256, 1119, 701 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 684 (53), 674 (38) $[M+Na]^+$, 652 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{34}H_{34}N_7O_7$ $[M+H]^+$: 652.2514; found: 652.2505.



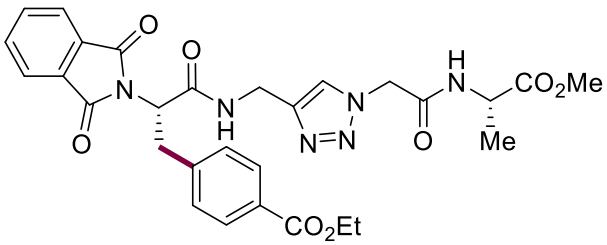
(*S*)-Methyl-2-[2-(4-{[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]propanoate (108g)

The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Ala-OMe (**107b**) (88.5 mg, 0.2 mmol) and 4-iodoanisole (**11d**) (93.6 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 44.0 min) yielded **108g** (66.9 mg, 61%) as a white solid (M.p.: 155–156 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.79–7.70 (m, 3H), 7.67 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.16 (brs, 1H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 6.9 Hz, 1H), 6.67 (d, *J* = 8.6 Hz, 2H), 5.10–5.05 (m, 3H), 4.55 (ddd, *J* = 7.2, 7.2, 6.9 Hz, 1H), 4.50–4.45 (m, 2H), 3.70 (s, 3H), 3.68 (s, 3H), 3.50 (dd, *J* = 14.2, 5.6 Hz, 1H), 3.41 (dd, *J* = 14.2, 11.1 Hz, 1H), 1.38 (d, *J* = 7.2 Hz, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.9 (C_q), 168.9 (C_q), 168.0 (C_q), 164.9 (C_q), 158.5 (C_q), 134.4 (CH), 131.6 (C_q), 130.0 (CH), 128.6 (C_q), 123.6 (CH), 114.1 (CH), 55.6 (CH), 55.3 (CH_3), 52.9 (CH_2), 52.8 (CH_3), 48.5 (CH), 35.4 (CH_2), 34.0 (CH_2), 18.1 (CH_3) (*due to overlap, two resonances are missing*). **IR** (ATR): $\tilde{\nu}$ = 1770, 1710, 1654, 1539, 1513, 1382, 1243, 722, 511 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1119 (100) $[2M+Na]^+$, 1097 (60) $[2M+H]^+$, 571 (80) $[M+Na]^+$, 549 (85) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{27}H_{28}N_6O_7Na$ $[M+Na]^+$: 571.1912; found: 571.1909.



(*S*)-Methyl-2-[2-(4-{[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-fluorophenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]propanoate (108h)

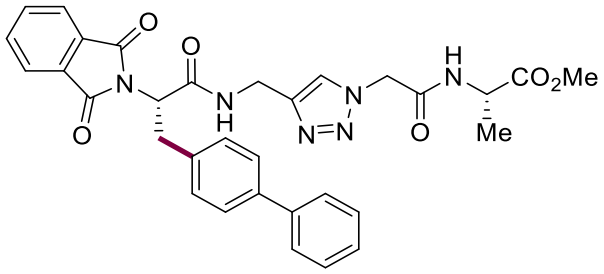
The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Ala-OMe (**107b**) (88.5 mg, 0.2 mmol) and 1-Fluoro-4-iodobenzene (**11j**) (88.8 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108h** (76.2 mg, 71%) as a white solid (M.p.: 117–118 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.72–7.68 (m, 5H), 7.21 (br s, 1H), 7.07 (dd, J = 8.4, 5.4 Hz, 2H), 6.91 (d, J = 7.3 Hz, 1H), 6.82 (dd, J = 8.7, 8.7 Hz, 2H), 5.09–5.02 (m, 2H), 4.99 (d, J = 16.4 Hz, 1H), 4.55 (dddd, J = 7.3, 7.1, 7.1, 7.1 Hz, 1H), 4.49–4.46 (m, 2H), 3.70 (s, 3H), 3.53 (dd, J = 14.2, 5.4 Hz, 1H), 3.45 (dd, J = 14.2, 11.3 Hz, 1H), 1.37 (d, J = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.8 (C_q), 168.5 (C_q), 167.8 (C_q), 164.6 (C_q), 161.8 (d, $^1J_{C\text{-}F}$ = 244.8 Hz, C_q), 134.4 (CH), 132.4 (d, $^4J_{C\text{-}F}$ = 3.3 Hz, C_q), 131.4 (C_q), 130.5 (d, $^3J_{C\text{-}F}$ = 8.0 Hz, CH), 123.6 (CH), 115.5 (d, $^2J_{C\text{-}F}$ = 21.3 Hz, CH), 55.5 (CH), 52.9 (CH_2), 52.8 (CH_3), 48.6 (CH), 35.4 (CH_2), 34.1 (CH_2), 18.2 (CH_3) (*due to overlap, two resonances are missing*). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -115.74 (tt, J = 8.7, 5.4 Hz). **IR** (ATR): $\tilde{\nu}$ = 2921, 1712, 1667, 1536, 1509, 1455, 1381, 1258, 1219, 1157, 1106, 1052, 880, 794, 719, 530, 396 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1095 (90) $[2M+Na]^+$, 559 (92) $[M+Na]^+$, 537 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{26}H_{26}FN_6O_6$ $[M+H]^+$: 537.1892; found: 537.1893.



Ethyl-4-[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-({[1-(2-{[(*S*)-1-methoxy-1-oxopropan-2-yl]amino}-2-oxoethyl)-1*H*-1,2,3-triazol-4-yl]methyl}amino)-3-oxopropyl]benzoate (108i)

The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Ala-OMe (**107b**)

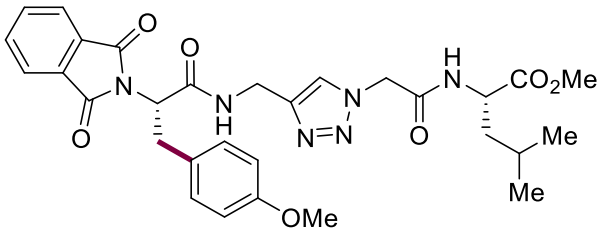
(88.5 mg, 0.2 mmol) and ethyl 4-iodobenzoate (**11f**) (110.4 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108i** (65.0 mg, 55%) as a white solid (M.p.: 105–107 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.90 (brs, 1H), 7.81 (d, *J* = 8.1 Hz, 2H), 7.73–7.63 (m, 4H), 7.35 (brs, 1H), 7.19 (d, *J* = 8.1 Hz, 2H), 6.94 (d, *J* = 7.3 Hz, 1H), 5.15–5.03 (m, 3H), 4.55 (dddd, *J* = 7.3, 7.2, 7.2, 7.2 Hz, 1H) 4.49–4.41 (m, 1H), 4.29 (ddd, *J* = 7.1, 7.1, 7.1 Hz, 2H), 3.70 (s, 3H), 3.64–3.50 (m, 2H), 1.37 (d, *J* = 7.2 Hz, 3H), 1.33 (dd, *J* = 7.1, 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.8 (Cq), 168.4 (Cq), 167.9 (Cq), 167.8 (Cq), 166.3 (Cq), 164.8 (Cq), 142.1 (Cq), 134.4 (CH), 131.4 (Cq), 129.9 (CH), 129.8 (CH), 129.2 (Cq), 128.9 (CH), 123.7 (CH), 61.1 (CH_2), 55.0 (CH), 53.1 (CH_2), 53.0 (CH_2), 52.8 (CH_3), 48.6 (CH), 34.8 (CH_2), 18.2 (CH_3), 14.5 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3065, 2926, 1774, 1713, 1535, 1382, 1277, 1054, 763 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1203 (33) $[2M+Na]^+$, 1181 (27) $[2M+H]^+$, 613 (53) $[M+Na]^+$, 591 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{31}N_6O_8$ $[M+H]^+$: 591.2198; found: 591.2194.



(*S*)-Methyl 2-[2-(4-{[(*S*)-3-[(1,1'-biphenyl)-4-yl]-2-(1,3-dioxoisoindolin-2-yl)propanamido] methyl} -1*H*-1,2,3-triazol-1-yl)acetamido]propanoate (108j)

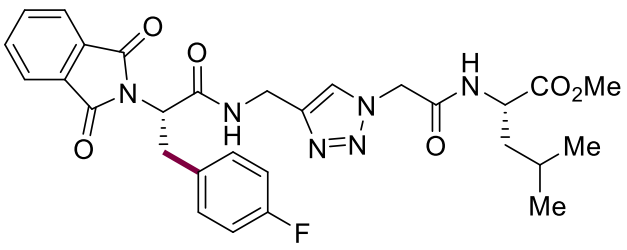
The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Ala-OMe (**107b**) (88.5 mg, 0.2 mmol) and 4-iodobiphenyl (**11h**) (112.0 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 43.0 min) yielded **108j** (71.4 mg, 60%) as a white solid (M.p.: 138–140 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.77 (brs, 1H), 7.71 (dd, *J* = 5.7, 3.1 Hz, 2H), 7.64 (dd, *J* = 5.7, 3.1 Hz, 2H), 7.47–7.44 (m, 2H), 7.39–7.24 (m, 6H), 7.18 (dd, *J* = 8.4, 1.9 Hz, 2H), 7.08 (d, *J* = 7.4 Hz, 1H), 5.15 (dd, *J* = 10.7, 5.6 Hz, 1H), 4.99 (dd, *J* = 16.6, 8.8 Hz, 2H), 4.54 (dddd, *J* = 7.4, 7.1, 7.1, 7.1 Hz, 1H), 4.51–4.45 (m, 2H), 3.68 (s, 3H), 3.66–3.44 (m, 2H), 1.37 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 173.0 (C_q), 168.8 (C_q), 168.0 (C_q), 164.9 (C_q), 140.6 (C_q), 140.1 (C_q), 139.6 (C_q), 137.9 (CH), 136.5 (C_q), 134.3 (CH), 131.5 (C_q), 129.4 (CH),

129.8 (CH), 128.7 (CH), 127.2 (CH), 127.0 (CH), 123.6 (CH), 55.4 (CH), 52.7 (CH_3), 48.5 (CH), 48.4 (CH_2), 35.2 (CH_2), 29.8 (CH_2), 18.1 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1716, 1533, 1383, 1219, 1120, 764 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1211 (7) $[2M+Na]^+$, 912 (17), 617 (100) $[M+Na]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{32}H_{30}N_6O_8Na$ $[M+Na]^+$: 617.2119; found: 617.2115.



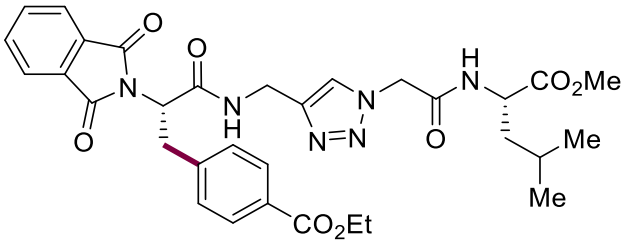
(*S*)-Methyl-2-[2-(4-{[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-4-methylpentanoate (108k)

The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (96.9 mg, 0.2 mmol) and 4-iodoanisole (**11d**) (93.6 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108k** (72.1 mg, 61%) as a white solid (M.p.: 99–100 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.81–7.62 (m, 5H), 7.16 (brs, 1H), 7.02 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 6.4 Hz, 1H), 6.67 (d, *J* = 8.5 Hz, 2H), 5.12–4.98 (m, 3H), 4.60–4.40 (m, 3H), 3.68 (s, 3H), 3.67 (s, 3H), 3.47–3.35 (m, 2H), 1.64–1.57 (m, 2H), 1.56–1.49 (m, 1H), 0.89 (d, *J* = 5.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 173.1 (C_q), 168.9 (C_q), 168.0 (C_q), 168.0 (C_q), 165.3 (C_q), 158.5 (C_q), 134.4 (CH), 131.6 (C_q), 130.0 (CH), 128.6 (C_q), 123.7 (CH), 114.1 (CH), 114.1 (CH), 55.6 (CH), 55.3 (CH_3), 52.9 (CH_2), 52.6 (CH_3) 51.2 (CH), 41.2 (CH_2), 35.3 (CH_2), 33.9 (CH_2), 25.0 (CH), 22.9 (CH_3), 21.9 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2962, 2537, 2361, 2340, 2160, 2026, 1071, 809, 668 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1203 (100) $[2M+Na]^+$, 1181 (45) $[2M+H]^+$, 613 (90) $[M+Na]^+$, 591 (85) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{30}H_{34}N_6O_7Na$ $[M+Na]^+$: 613.2381; found: 613.2369.



(*S*)-Methyl-2-[2-(4-{[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-fluorophenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-4-methylpentanoate (108l)

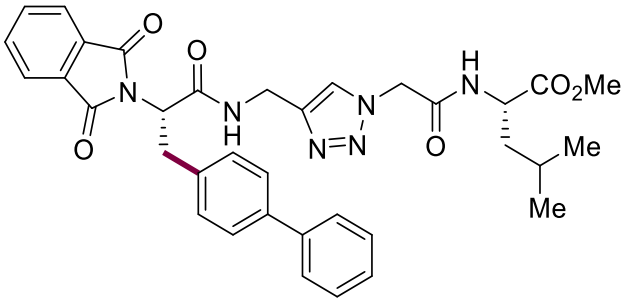
The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (96.9 mg, 0.2 mmol) and 1-Fluoro-4-iodobenzene (**11j**) (88.8 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 47.0 min) yielded **108l** (86.8 mg, 75%) as a white solid (M.p.: 101–102 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.75–7.68 (m, 3H), 7.67 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.27 (br s, 1H), 7.07 (dd, *J* = 8.5, 5.4 Hz, 2H), 6.94 (d, *J* = 8.1 Hz, 1H), 6.82 (d, *J* = 8.5, 8.5 Hz, 2H), 5.06 (d, *J* = 16.4 Hz, 1H), 5.03 (dd, *J* = 11.3, 5.5 Hz, 1H), 4.97 (d, *J* = 16.4 Hz, 1H), 4.60–4.54 (m, 1H), 4.52–4.40 (m, 2H), 3.66 (s, 3H), 3.53 (dd, *J* = 14.3, 5.5 Hz, 1H), 3.45 (dd, *J* = 14.3, 11.3 Hz, 1H), 1.63–1.49 (m, 3H), 0.89 (d, *J* = 5.9 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 173.2 (C_q), 168.6 (C_q), 167.9 (C_q), 165.1 (C_q), 161.8 (d, $^1J_{C\text{-}F}$ = 245.2 Hz, C_q), 134.5 (CH), 134.4 (CH), 132.5 (d, $^4J_{C\text{-}F}$ = 3.2 Hz, C_q), 131.9 (C_q), 131.4 (C_q), 130.5 (d, $^3J_{C\text{-}F}$ = 8.0 Hz, CH), 123.7 (CH), 115.6 (d, $^2J_{C\text{-}F}$ = 21.3 Hz, CH), 55.4 (CH), 52.8 (CH_2), 52.6 (CH_3), 51.2 (CH), 41.2 (CH_2), 35.2 (CH_2), 33.9 (CH_2), 25.0 (CH), 22.8 (CH_3), 21.9 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -115.73 (ddd, *J* = 14.0, 8.8, 5.3 Hz). **IR** (ATR): $\tilde{\nu}$ = 2955, 1666, 1533, 1509, 1382, 1221, 1156, 1106, 1052, 719 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1179 (95) $[2M+Na]^+$, 1157 (65) $[2M+H]^+$, 1085 (45), 1063 (35), 601 (85) $[M+Na]^+$, 579 (100) $[M+H]^+$, 507 (30), 485 (35). **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{32}N_6O_6F$ $[M+H]^+$: 579.2362; found: 579.2356.



(*S*)-Ethyl-4-[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-({[1-(2-{[(*S*)-1-methoxy-4-methyl-1-oxopentan-2-yl)amino]-2-oxoethyl}-1*H*-1,2,3-triazol-4-yl)methyl]amino}-3-oxopropyl]benzoate (108m)

The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (96.9 mg, 0.2 mmol) and ethyl 4-iodobenzoate (**11f**) (110.4 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108m** (64.5 mg, 51%) as a white solid (M.p.: 99–

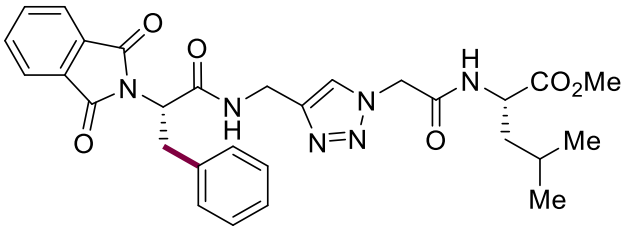
100 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.2 Hz, 2H), 7.78–7.63 (m, 5H), 7.18–7.14 (m, 3H), 6.77 (d, *J* = 8.1 Hz, 1H), 5.09 (dd, *J* = 11.1, 5.3 Hz, 1H), 5.05 (d, *J* = 16.4 Hz, 1H), 4.97 (d, *J* = 16.4 Hz, 1H), 4.60–4.56 (m, 1H), 4.46 (s, 2H), 4.27 (ddd, *J* = 7.1, 7.1, 7.1 Hz, 2H), 3.66 (s, 3H), 3.60 (dd, *J* = 14.1, 5.3 Hz, 1H), 3.53 (dd, *J* = 14.1, 11.1 Hz, 1H), 1.60–1.54 (m, 2H), 1.53–1.49 (m, 1H), 1.31 (dd, *J* = 7.1, 7.1 Hz, 3H), 0.87 (d, *J* = 6.1 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.9 (C_q), 168.3 (C_q), 167.7 (C_q), 167.7 (C_q), 166.3 (C_q), 164.9 (C_q), 142.1 (C_q), 134.4 (CH), 131.3 (C_q), 129.9 (CH), 129.2 (C_q), 129.0 (CH), 123.7 (CH), 61.1 (CH_2), 55.1 (CH), 52.9 (CH_2), 52.6 (CH_3), 51.3 (CH), 41.3 (CH_2), 35.3 (CH_2), 34.8 (CH_2), 25.1 (CH), 22.9 (CH_3), 22.0 (CH_3), 14.5 (CH_3) (*due to overlap, one resonance is missing*). **IR** (ATR): $\tilde{\nu}$ = 2956, 1711, 1381, 1274, 1178, 1105, 1052, 1021, 976, 720, 636 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1265 (30) $[2M+H]^+$, 655 (33) $[M+Na]^+$, 633 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{32}H_{37}N_6O_8$ $[M+H]^+$: 633.2667; found: 633.2670.



(*S*)-Methyl-2-[2-(4-{[(*S*)-3-{[1,1'-biphenyl]-4-yl}-2-(1,3-dioxoisoindolin-2-yl)propanamido] methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-4-methylpentanoate (108n)

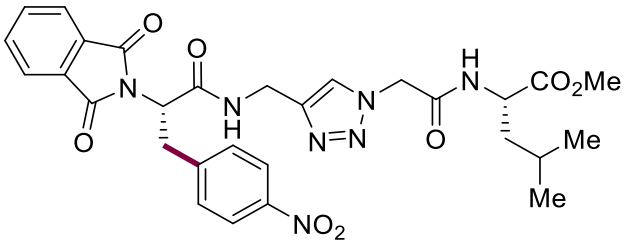
The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (96.9 mg, 0.2 mmol) and 4-iodobiphenyl (**11h**) (112.0 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 43.0 min) yielded **108n** (95.5 mg, 75%) as a white solid (M.p.: 116–117 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.79–7.63 (m, 5H), 7.48–7.46 (m, 2H), 7.39–7.35 (m, 4H), 7.28 (ddd, *J* = 7.3, 7.3, 1.0 Hz, 1H), 7.20–7.16 (m, 3H), 6.83 (d, *J* = 7.8 Hz, 1H), 5.15 (dd, *J* = 10.4, 5.2 Hz, 1H), 5.10 (d, *J* = 15.2 Hz, 1H), 5.00 (d, *J* = 15.2 Hz, 1H), 4.61–4.56 (m, 1H), 4.48 (s, 2H), 3.66 (s, 3H), 3.64–6.49 (m, 2H), 1.61–1.49 (m, 3H), 0.87 (d, *J* = 5.5 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 173.1 (C_q), 168.8 (C_q), 168.0 (C_q), 167.9 (C_q), 165.1 (C_q), 140.6 (C_q), 139.7 (C_q), 137.9 (CH), 135.8 (C_q), 134.4 (CH), 131.5 (C_q), 129.4 (CH), 128.8 (CH),

128.8 (CH), 127.3 (CH), 127.0 (CH), 123.7 (CH), 55.4 (CH), 52.9 (CH_2), 52.6 (CH_3), 51.2 (CH), 41.2 (CH_2), 35.3 (CH_2), 34.4 (CH_2), 25.0 (CH), 22.9 (CH_3), 21.9 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2953, 1712, 1667, 1100, 975, 881, 805, 760, 697, 620 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1295 (22) $[2M+Na]^+$, 974 (37), 659 (63) $[M+Na]^+$, 338 (100). **HR-MS** (ESI) *m/z* calcd for $C_{35}H_{36}N_6O_6Na$ $[M+Na]^+$: 659.2589; found: 659.2585.



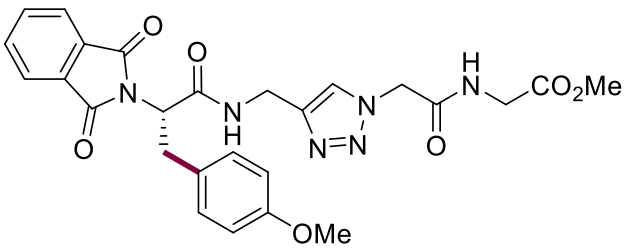
(*S*)-Methyl-2-[2-(4-{[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanamido]methyl}-1*H*-1,2,3-tri azol-1-yl)acetamido]-4-methylpentanoate (108o)

The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (96.9 mg, 0.2 mmol) and iodobenzene (**11a**) (81.6 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 47.0 min) yielded **108o** (72.9 mg, 65%) as a white solid (M.p.: 104–105 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.74–7.70 (m, 3H), 7.66 (dd, *J* = 5.7, 2.9 Hz, 2H), 7.20–7.03 (m, 6H), 6.85 (d, *J* = 8.0 Hz, 1H), 5.16–4.86 (m, 3H), 4.67–4.53 (m, 1H), 4.48 (d, *J* = 4.7 Hz, 2H), 3.68 (s, 3H), 3.57 (dd, *J* = 14.0, 5.6 Hz, 1H), 3.46 (dd, *J* = 14.0, 11.0 Hz, 1H), 1.70–1.47 (m, 3H), 0.89 (d, *J* = 5.6 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 173.1 (C_q), 168.8 (C_q), 167.9 (C_q), 165.1 (C_q), 136.8 (C_q), 134.4 (CH), 131.9 (C_q), 131.5 (C_q), 129.0 (CH), 128.7 (CH), 127.0 (CH), 124.4 (CH), 123.7 (CH), 55.5 (CH), 52.8 (CH_2), 52.6 (CH_3), 51.2 (CH), 41.2 (CH_2), 35.2 (CH_2), 34.8 (CH_2), 25.0 (CH), 22.9 (CH_3), 21.9 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2956, 1711, 1667, 1531, 1382, 1207, 719, 700, 529 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1143 (80) $[2M+Na]^+$, 1067 (44), 1045 (30), 583 (75) $[M+Na]^+$, 561 (100) $[M+H]^+$, 507 (25), 485 (30). **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{33}N_6O_6$ $[M+H]^+$: 561.2456; found: 561.2447.



(*S*)-Methyl-2-[2-(4-{[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-nitrophenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-4-methylpentanoate (108p)

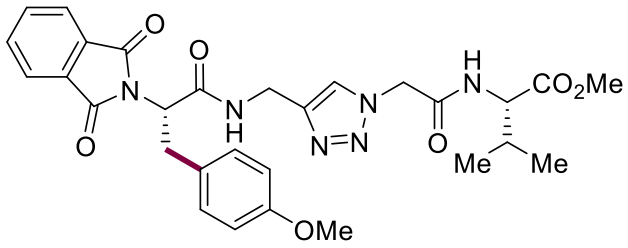
The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (96.9 mg, 0.2 mmol) and 1-iodo-4-nitrobenzene (**11g**) (99.6 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108p** (86.0 mg, 71%) as a white solid (M.p.: 100–101 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.7 Hz, 2H), 7.76–7.68 (m, 5H), 7.35–7.30 (m, 3H), 6.90 (d, *J* = 8.2 Hz, 1H), 5.13 (dd, *J* = 11.3, 5.4 Hz, 1H), 5.08 (d, *J* = 16.3 Hz, 1H), 4.99 (d, *J* = 16.3 Hz, 1H), 4.61–4.57 (m, 1H), 4.53–4.39 (m, 2H), 3.70 (dd, *J* = 14.3, 5.4 Hz, 1H), 3.66 (s, 3H), 3.64–3.57 (m, 1H), 1.64–1.58 (m, 2H), 1.55–1.50 (m, 1H),0.87 (d, *J* = 6.1 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 173.0 (C_q), 167.9 (C_q), 167.8 (C_q), 167.6 (C_q), 164.9 (C_q), 147.0 (C_q), 144.8 (C_q), 134.6 (CH), 131.2 (C_q), 129.9 (CH), 123.9 (CH), 123.8 (CH), 54.7 (CH), 52.8 (CH_2), 52.6 (CH_3), 51.3 (CH), 41.3 (CH_2), 35.3 (CH_2), 34.7 (CH_2), 25.1 (CH), 22.9 (CH_3), 22.0 (CH_3) (*due to overlap, one resonance is missing*). **IR** (ATR): $\tilde{\nu}$ = 2956, 1716, 1677, 1521, 1383, 1346, 722 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1233 (50) $[2M+Na]^+$, 1211 (55) $[2M+H]^+$, 628 (52) $[M+Na]^+$, 606 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{32}N_7O_8$ $[M+H]^+$: 606.2307; found: 606.2305.



(*S*)-Methyl-2-[2-(4-{[2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]acetate (108q)

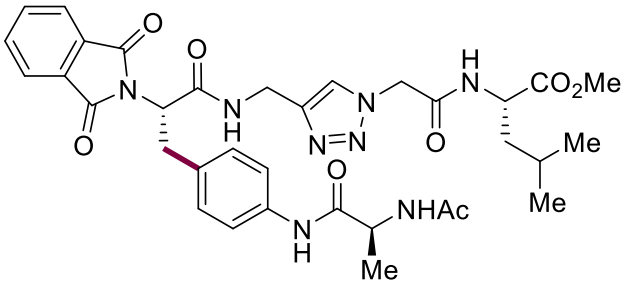
The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Gly-OMe (**107d**) (85.7 mg, 0.2 mmol) and 4-iodoanisole (**11d**) (93.6 mg, 0.4 mmol) in HFIP. After 20 h, purification by HPLC (t_r: 44.0 min) yielded **108q** (87.7 mg, 82%) as a white solid (M.p.: 103–105 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.72 (brs, 1H), 7.71–7.65 (m, 4H), 7.29 (brs, 1H), 7.01 (d, *J* = 8.6 Hz, 2H), 6.95 (dd, *J* = 5.5, 5.5 Hz, 1H), 6.67 (d, *J* = 8.6 Hz, 2H), 5.09–5.00 (m, 3H), 4.46 (dd, *J* = 15.2, 6.0 Hz, 1H), 4.38 (dd, *J* = 15.2, 6.0 Hz, 1H), 4.01 (d, *J* = 5.5 Hz,

2H), 3.70 (s, 3H), 3.68 (s, 3H), 3.49 (dd, *J* = 14.3, 5.5 Hz, 1H), 3.37 (dd, *J* = 14.3, 11.0 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): *δ* = 169.7 (C_q), 168.8 (C_q), 167.9 (C_q), 165.5 (C_q), 158.4 (C_q), 145.2 (C_q), 134.2 (CH), 131.4 (Cq), 129.8 (CH), 128.5 (C_q), 124.3 (CH), 123.4 (CH), 113.9 (CH), 59.3 (CH), 55.1 (CH_3), 52.7 (CH_2), 52.4 (CH_3), 41.2 (CH_2), 34.9 (CH_2), 33.7 (CH_2). **IR** (ATR): $\tilde{\nu}$ = 1749, 1714, 1612, 1514, 1384, 1247, 1180, 721 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1091 (47) $[2M+Na]^+$, 1069 (35) $[2M+H]^+$, 557 (47) $[M+Na]^+$, 535 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{26}H_{27}N_6O_7$ $[M+H]^+$: 535.1936; found: 535.1937.



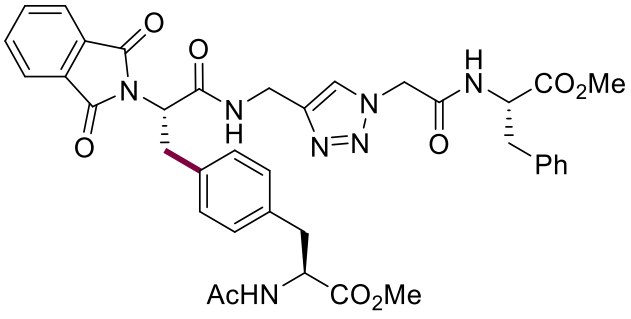
(*S*)-Methyl-2-[2-(4-{[(S)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-3-methylbutanoate (108r)

The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Val-OMe (**107e**) (94.1 mg, 0.2 mmol) and 4-iodoanisole (**11d**) (93.6 mg, 0.4 mmol) in HFIP. After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108r** (91.1 mg, 79%) as a white solid (M.p.: 136–138 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* = 7.77–7.65 (m, 5H), 7.21 (brs, 1H), 7.10 (d, *J* = 8.7 Hz, 1H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.67 (d, *J* = 8.6 Hz, 2H), 5.15 (d, *J* = 16.3 Hz, 1H), 5.07–4.99 (m, 1H), 5.01 (d, *J* = 16.3 Hz, 1H), 4.57–4.50 (m, 1H), 4.51–4.46 (m, 2H), 3.68 (s, 3H), 3.65 (s, 3H), 3.53–3.41 (m, 2H), 2.16–2.11 (m, 1H), 0.87 (dd, *J* = 15.6, 6.9 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$): *δ* = 172.2 (Cq), 168.9 (Cq), 168.1 (Cq), 168.0 (Cq), 165.3 (Cq), 158.5 (Cq), 134.3 (CH), 131.6 (Cq), 129.9 (CH), 128.7 (Cq), 124.5 (CH), 123.6 (CH), 114.1 (CH), 57.6 (CH_3), 55.8 (CH), 55.3 (CH), 52.8 (CH_2), 52.4 (CH_3), 35.3 (CH_2), 33.9 (CH_2), 31.2 (CH), 19.1 (CH_3), 17.8 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1774, 1714, 1612, 1514, 1467, 1384, 1248, 722 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1175 (52) $[2M+Na]^+$, 1153 (35) $[2M+H]^+$, 599 (51) $[M+Na]^+$, 577 (100) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{29}H_{32}N_6O_7Na$ $[M+Na]^+$: 599.2225; found: 599.2221.



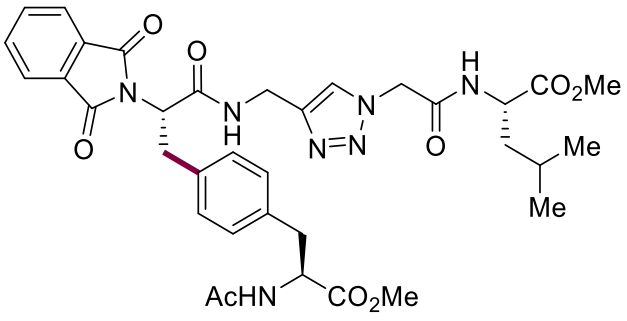
(*S*)-Methyl-2-[2-(4-{[(*S*)-3-{4-[(*S*)-2-acetamidopropanamido]phenyl}-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-4-methylpentanoate (108s)

The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (96.9 mg, 0.2 mmol) and (*S*)-2-Acetamido-*N*-(4-iodophenyl) propanamide (**11k**) (132.9 mg, 0.4 mmol) in HFIP. After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108s** (115.7 mg, 84%) as a white solid (M.p.: 127–128 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 9.26 (s, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.78 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.69 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.22–7.16 (m, 3H), 6.84–6.78 (m, 2H), 5.17–5.06 (m, 2H), 4.76 (d, *J* = 16.7 Hz, 1H), 4.63–4.56 (m, 2H), 4.51–4.36 (m, 2H), 3.76 (m, 4H), 3.33–3.25 (m, 1H), 1.99 (s, 3H), 1.72–1.57 (m, 3H), 1.42 (d, *J* = 7.1 Hz, 3H), 0.90 (dd, *J* = 6.2, 2.3 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 174.8 (C_q), 171.2 (C_q), 171.0 (C_q), 168.1 (C_q), 168.0 (C_q), 165.6 (C_q), 144.9 (C_q), 137.0 (C_q), 134.3 (CH), 132.7 (C_q), 131.6 (C_q), 129.9 (CH), 129.6 (CH), 123.6 (CH), 119.9 (CH), 55.9 (CH), 52.9 (CH_3), 52.2 (CH_2), 51.5 (CH), 50.1 (CH), 41.0 (CH_2), 35.6 (CH_2), 34.6 (CH_2), 25.1 (CH), 23.2 (CH_3), 23.1 (CH_3), 21.9 (CH_3), 18.2 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2958, 1712, 1651, 1257, 1153, 1087, 1052, 975, 879, 801, 719 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1053 (15), 711 (100) $[M+Na]^+$, 364 (55). **HR-MS** (ESI) *m/z* calcd for $C_{34}H_{40}N_8O_8Na$ $[M+Na]^+$: 711.2861; found: 711.2843.



(*S*)-Methyl-2-acetamido-3-{4-[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-[([1-(2-{[(*S*)-1-methoxy-1-oxo-3-phenylpropan-2-yl]amino}-2-oxoethyl)-1*H*-1,2,3-triazol-4-yl]methyl)amino]-3-oxopropyl]phenyl} propanoate (108t)

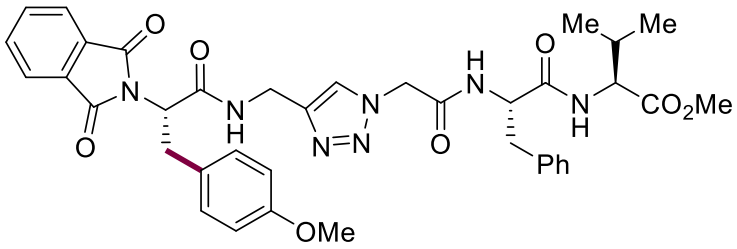
The general procedure **A** was using Phth*N*-Ala-Gly-Tzl-Gly-Phe-OMe (**107a**) (103.7 mg, 0.2 mmol) and (*S*)-methyl 2-acetamido-3-(4-iodophenyl)propanoate (**11l**) (138.9 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 47.0 min) yielded **108t** (64.9 mg, 44%) as a white solid (M.p.: 110–111 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.74 (dd, *J* = 5.7, 2.9 Hz, 2H), 7.70–7.64 (m, 2H), 7.61 (br s, 1H), 7.30–7.21 (m, 3H), 7.04 (brs, 1H), 7.06–6.98 (m, 4H), 6.87 (d, *J* = 8.0 Hz, 2H), 6.75 (d, *J* = 8.0 Hz, 1H), 5.88 (d, *J* = 7.7 Hz, 1H), 5.05 (dd, *J* = 10.6, 5.6 Hz, 1H), 4.96 (d, *J* = 17.8 Hz, 2H), 4.90–4.79 (m, 1H), 4.74 (dt, *J* = 7.7, 5.9 Hz, 1H), 4.45 (br s, 2H), 3.69 (s, 3H), 3.62 (s, 3H), 3.49–3.34 (m, 2H), 3.12 (dd, *J* = 14.0, 5.6 Hz, 1H), 3.00 (dd, *J* = 13.9, 6.5 Hz, 2H), 2.91 (dd, *J* = 13.9, 5.9 Hz, 1H), 1.89 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.9 (C_q), 171.3 (C_q), 169.5 (C_q), 168.5 (C_q), 167.9 (C_q), 167.8 (C_q), 164.7 (C_q), 135.6 (C_q), 135.5 (C_q), 134.6 (C_q), 134.3 (CH), 131.5 (C_q), 129.6 (CH), 129.5 (CH), 129.2 (CH), 129.2 (CH), 128.7 (CH), 127.3 (CH), 123.6 (CH), 55.5 (CH), 53.6 (CH), 53.2 (CH), 52.8 (CH_2), 52.7 (CH_3), 52.4 (CH_3), 37.8 (CH_2), 37.6 (CH_2), 35.4 (CH_2), 34.6 (CH_2), 23.2 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1740, 1658, 1531, 1435, 1381, 1216, 1175, 1116, 1051, 720 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1497 (20) $[2M+Na]^+$, 760 (100) $[M+Na]^+$, 738 (75) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{38}H_{39}N_7O_9Na$ $[M+Na]^+$: 760.2701; found: 760.2687.



(*S*)-methyl-2-[2-(4-{[(*S*)-3-{4-[(*S*)-2-acetamido-3-methoxy-3-oxopropyl]phenyl}-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-4-methylpentanoate (108u)

The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**)

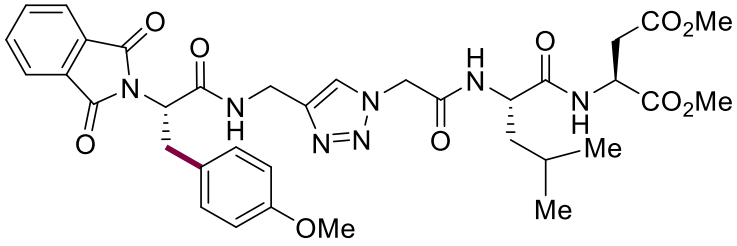
(96.9 mg, 0.2 mmol) and (*S*)-methyl 2-acetamido-3-(4-iodophenyl)propanoate (**11l**) (138.9 mg, 0.4 mmol) in HFIP. After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108u** (115.4 mg, 82%) as a white solid (M.p.: 109–110 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.75–7.67 (m, 5H), 7.16 (br s, 1H), 7.03 (d, *J* = 7.9 Hz, 2H), 6.93 (d, *J* = 7.9 Hz, 1H), 6.87 (d, *J* = 7.9 Hz, 2H), 5.91 (d, *J* = 7.8 Hz, 1H), 5.11–4.97 (m, 3H), 4.77 (dd, *J* = 13.5, 5.9 Hz, 1H), 4.59 (td, *J* = 8.5, 4.9 Hz, 1H), 4.47 (brs, 2H), 3.68 (s, 3H), 3.62 (s, 3H), 3.54 (dd, *J* = 13.9, 4.8 Hz, 1H), 3.46–3.37 (m, 1H), 3.00 (dd, *J* = 13.9, 5.8 Hz, 1H), 2.92 (dd, *J* = 13.9, 5.9 Hz, 1H), 1.90 (s, 3H), 1.66–1.57 (m, 2H), 1.56–1.47 (m, 1H), 0.89 (d, *J* = 5.2 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 173.1 (C_q), 172.1 (C_q), 169.8 (C_q), 168.7 (C_q), 168.0 (C_q), 167.9 (C_q), 165.1 (C_q), 135.7 (C_q), 134.6 (C_q), 134.4 (CH), 131.5 (C_q), 129.6 (CH), 129.6 (CH), 129.2 (CH), 123.7 (CH), 55.4 (CH), 53.2 (CH), 52.8 (CH_2), 52.6 (CH_3), 52.4 (CH_3), 51.2 (CH), 41.2 (CH_2), 37.5 (CH_2), 35.3 (CH_2), 34.5 (CH_2), 25.0 (CH), 23.2 (CH_3), 22.9 (CH_3), 21.9 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3063, 1714, 1656, 1534, 1382, 1216, 721, 530 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1075 (23), 726 (100) $[M+Na]^+$, 704 (60) $[M+H]^+$, 371 (68). **HR-MS** (ESI) *m/z* calcd for $C_{35}H_{41}N_7O_9Na$ $[M+Na]^+$: 726.2858; found: 726.2850.



(*S*)-Methyl-2-{(*S*)-2-[2-(4-{[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-3-phenylpropanamido}-3-methylbutanoate (108v)

The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Phe-Val-OMe (**107f**) (123.5 mg, 0.2 mmol) and 4-iodoanisole (**11d**) (93.6 mg, 0.4 mmol) in HFIP. After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108v** (79.5 mg, 55%) as a white solid (M.p.: 110–111 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.74–7.59 (m, 5H), 7.29–7.19 (m, 5H), 7.17–7.11 (m, 2H), 7.02 (d, *J* = 8.6 Hz, 2H), 6.66 (d, *J* = 8.6 Hz, 2H), 6.37 (d, *J* = 8.4 Hz, 1H), 5.06 (dd, *J* = 10.8, 5.4 Hz, 1H), 5.02–4.89 (m, 2H), 4.69 (dd, *J* = 7.1, 7.1Hz, 1H), 4.55–4.39 (m, 2H), 4.37 (dd, *J* = 8.4, 5.1 Hz, 1H), 3.69 (s, 3H), 3.67 (s, 3H), 3.52–3.38 (m, 2H), 3.00 (d, *J* = 7.1 Hz,

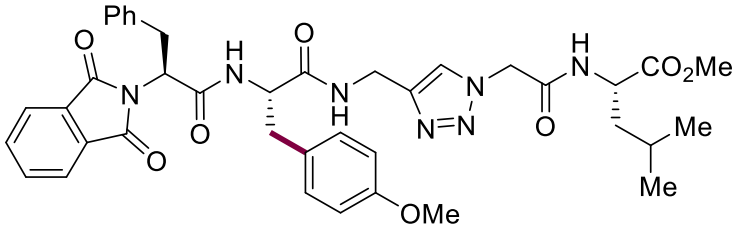
2H), 2.06 (dddd, *J* = 6.8, 6.8, 6.8, 5.1 Hz, 1H), 0.81 (dd, *J* = 17.9, 6.8 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): *δ* = 171.8 (C_q), 170.5 (C_q), 170.4 (C_q), 168.9 (C_q), 168.0 (C_q), 165.3 (C_q), 158.5 (C_q), 136.2 (C_q), 134.3 (CH), 131.6 (C_q), 130.0 (CH), 129.4 (CH), 128.8 (CH), 128.7 (C_q), 127.3 (CH), 123.6 (CH), 114.1 (CH), 114.1 (CH), 57.6 (CH), 55.6 (CH), 55.2 (CH_3), 55.1 (CH), 52.7 (CH_2), 52.3 (CH_3), 38.1 (CH_2), 35.3 (CH_2), 34.0 (CH_2), 31.1 (CH), 19.0 (CH_3), 17.9 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2957, 1713, 1647, 1535, 1512, 1382, 1245, 1205, 1178, 1152, 718 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1105 (20), 746 (100) $[M+Na]^+$, 381 (100). **HR-MS** (ESI) *m/z* calcd for $C_{38}H_{41}N_7O_8Na$ $[M+Na]^+$: 746.2909; found: 746.2897.



(*S*)-Dimethyl-2-{(*S*)-2-[2-(4-{[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetamido]-4-methylpentanamido}succinate (108w)

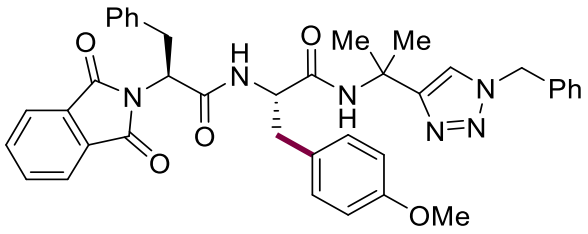
The general procedure **A** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-Asp^{OMe}-OMe (**107g**) (123.5 mg, 0.2 mmol) and 4-iodoanisole (**11d**) (93.6 mg, 0.4 mmol) in HFIP. After 20 h, purification by HPLC (t_r: 47.0 min) yielded **108w** (90.7 mg, 63%) as a white solid (M.p.: 109 – 110 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): *δ* = 7.73–7.65 (m, 5H), 7.26–7.21 (m, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.04–7.00 (m, 3H), 6.65 (d, *J* = 8.7 Hz, 2H), 5.05 (dd, *J* = 11.4, 5.7 Hz, 1H), 5.04–5.00 (m, 2H), 4.77 (ddd, *J* = 8.7, 4.7, 4.7 Hz, 1H), 4.53–4.44 (m, 2H), 4.43–4.35 (m, 1H), 3.73 (s, 3H), 3.68 (s, 3H), 3.65 (s, 3H), 3.48 (dd, *J* = 14.2, 5.7 Hz, 1H), 3.43 dd, *J* = 14.2, 11.4 Hz, 1H), 2.97 (dd, 17.1, 4.7 Hz, 1H), 2.79 (dd, *J* = 17.1, 4.7 Hz, 1H), 1.67–1.50 (m, 3H), 0.89 (dd, *J* = 8.5, 6.4 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): *δ* = 171.5 (C_q), 171.3 (C_q), 170.7 (C_q), 168.7 (C_q), 167.9 (C_q), 166.7 (C_q), 165.4 (C_q), 158.4 (C_q), 134.2 (CH), 131.6 (C_q), 129.9 (CH), 128.7 (C_q), 123.5 (CH), 114.1 (CH), 55.7 (CH), 55.3 (CH_3), 53.0 (CH_3), 52.3 (CH_3), 52.2 (CH), 48.8 (CH), 41.1 (CH_2), 36.1 (CH_2), 35.1 (CH_2), 34.0 (CH_2), 33.8 (CH_2), 24.9 (CH), 23.0 (CH_3), 22.3 (CH_3) (*due to overlap, one resonance is missing).* **IR** (ATR): $\tilde{\nu}$ = 1743, 1711, 1653, 1538, 1513, 1382, 1286, 1244, 1084, 720, 555 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1461

(25) $[2M+Na]^+$, 1439 (20) $[2M+H]^+$, 742 (100) $[M+Na]^+$, 720 (94) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{35}H_{42}N_7O_{10}$ $[M+H]^+$: 720.2988; found: 720.2985.



(*S*)-Methyl-2-(2-[4-({(*S*)-2-[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanamido]-3-(4-methoxyphenyl)propanamido}methyl)-1*H*-1,2,3-triazol-1-yl]acetamido)-4-methylpentanoate (108x)

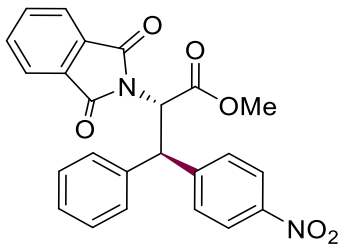
The general procedure **A** was followed using Phth*N*-Phe-Ala-Gly-Tzl-Gly-Leu-OMe (**107h**) (126.3 mg, 0.2 mmol) and 4-iodoanisole (**11d**) (93.6 mg, 0.4 mmol) in AcOH. After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108x** (73.8 mg, 50%) as a white solid. **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.72 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.66 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.55 (s, 1H), 7.14–7.11 (m, 2H), 7.10–7.05 (m, 3H), 6.99–6.92 (m, 3H), 6.86 (d, *J* = 8.2 Hz, 1H), 6.83 (d, *J* = 8.2 Hz, 1H), 6.63 (d, *J* = 8.6 Hz, 2H), 5.05 (dd, *J* = 10.3, 6.3 Hz, 1H), 5.00 (s, 2H), 4.67–4.61 (m, 1H), 4.58–4.54 (m, 1H), 4.47 (dd, *J* = 15.3, 5.8 Hz, 1H), 4.37 (dd, *J* = 15.3, 5.3 Hz, 1H), 3.68 (s, 3H), 3.63 (s, 3H), 3.41 (dd, *J* = 14.1, 6.3 Hz, 1H), 3.39 (dd, *J* = 14.1, 10.3 Hz, 1H), 2.98–2.92 (m, 2H), 1.83 (s, 1H), 1.58–1.54 (m, 2H), 0.85 (d, *J* = 6.0 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.8 (C_q), 170.5 (C_q), 168.4 (C_q), 167.5 (C_q), 164.9 (C_q), 158.4 (C_q), 136.3 (C_q), 134.1 (CH), 131.3 (C_q), 131.2 (C_q), 130.1 (CH), 128.7 (CH), 128.5 (CH), 128.0 (CH), 126.9 (C_q), 123.9 (CH), 123.4 (CH), 114.0 (CH), 55.2 (CH_3), 55.1 (CH_3), 52.7 (CH_2), 52.4 (CH), 51.1 (CH), 51.0 (CH), 41.1 (CH_2), 37.0 (CH_2), 35.2 (CH_2), 34.6 (CH_2), 24.9 (CH), 22.8 (CH_3), 21.9 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2956, 2923, 2853, 1715, 1654, 1513, 1466, 1382, 1246, 721 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1497 (10) $[2M+Na]^+$, 760 (100) $[M+Na]^+$, 737 (57) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{39}H_{43}N_7O_8Na$ $[M+Na]^+$: 760.3065; found: 760.3068.



(*S*)-N-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-2-[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl propanamido]-3-(4-methoxyphenyl)propanamide (108y)

The general procedure **A** was followed using Phth*N*-Phe-Ala-NHTAM (**105b**) (112.9 mg, 0.2 mmol) and 4-iodoanisole (**11d**) (93.6 mg, 0.4 mmol). After 20 h, purification by HPLC (t_r: 45.0 min) yielded **108y** (80.5 mg, 60%) as a yellow solid (M.p.: 118–119 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.74 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.69 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.40–7.31 (m, 4H), 7.25–7.22 (m, 2H), 7.18–7.08 (m, 5H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.68 (d, *J* = 8.6 Hz, 2H), 6.59 (d, *J* = 7.2 Hz, 1H), 6.17 (brs, 1H), 5.45 (s, 2H), 5.10–5.02 (m, 1H), 4.52–4.44 (m, 1H), 3.70 (s, 3H), 3.48–3.39 (m, 2H), 3.01 (dd, *J* = 13.6, 6.2 Hz, 1H), 2.85 (dd, *J* = 13.6, 7.6 Hz, 1H), 1.61 (s, 3H), 1.57 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 169.3 (C_q), 168.1 (C_q), 167.7 (C_q), 158.6 (C_q), 153.2 (C_q), 136.5 (C_q), 134.9 (C_q), 134.2 (CH), 131.5 (C_q), 130.4 (CH), 129.1 (CH), 129.0 (CH), 128.7 (CH), 128.7 (CH), 128.4 (C_q), 128.0 (CH), 127.0 (CH), 123.6 (CH), 120.4 (CH), 114.1 (CH), 55.6 (CH), 55.4 (CH_3), 55.4 (CH), 54.2 (CH_2), 51.9 (C_q), 37.4 (CH_2), 34.8 (CH_2), 28.3 (CH_3), 27.9 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1775, 1657, 1512, 1382, 1245, 1177, 1031, 873, 821, 719 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1363 (4) $[2M+Na]^+$, 1026 (11), 693 (69) $[M+Na]^+$, 671 (100) $[M+H]^+$, 355 (27). **HR-MS** (ESI) *m/z* calcd for $C_{39}H_{39}N_6O_5$ $[M+H]^+$: 671.2976; found: 671.2973.

5.3.1.2 Procedure and Characterization Data for TAM/PG Removal Products

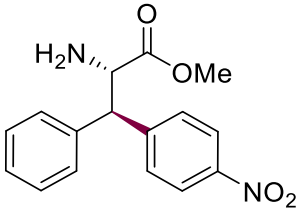


(2*S*,3*R*)-Methyl-2-(1,3-dioxoisoindolin-2-yl)-3-(4-nitrophenyl)-3-phenylpropanoate

(106ba)

In a high pressure tube, **106b** (153.6 mg, 0.25 mmol) was dissolved in dry MeOH (5.0 mL). Under N_2, BF_3.Et_2O (532.2 mg, 3.75 mmol) was then added dropwise at 0 °C. The solution was stirred at 130 °C for 16 h. At 0 °C, Et_3N (1.0 mL) was added to the solution. The solvent was removed *in vacuo* and the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc 3/1. Rf: 0.53) to yield **106ba** (66.7 mg, 62%) as a white solid. (M.p.: 70–70 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.21 (d, J = 8.8 Hz, 2H), 7.75 (dd, J = 5.6, 3.0 Hz, 2H), 7.68–7.63 (m, 4H), 7.22–7.20 (m, 2H), 7.14–7.11 (m, 2H), 7.01 (dddd, J = 8.2, 6.7, 1.3, 1.3 Hz, 1H), 5.76 (d, J = 11.9 Hz, 1H), 5.33 (d, J = 11.9 Hz, 1H), 3.61 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 168.3 (C_q), 167.1 (C_q), 149.2 (C_q), 146.7 (C_q), 138.7 (C_q), 134.2 (CH), 131.1 (C_q), 128.9 (CH), 128.5 (CH), 127.9 (CH), 127.5 (CH), 124.0 (CH), 123.5 (CH), 54.0 (CH), 52.9 (CH), 50.6 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1749, 1716, 1518, 1378, 1339, 594, 526 cm^{-1}. **MS** (ESI) m/z (relative intensity) 883 (40) $[2M+Na]^+$, 453 (100) $[M+Na]^+$. **HR-MS** (ESI): m/z calcd for $C_{24}H_{18}N_2O_6Na$ $[M+Na]^+$: 453.1057; found: 453.1051.

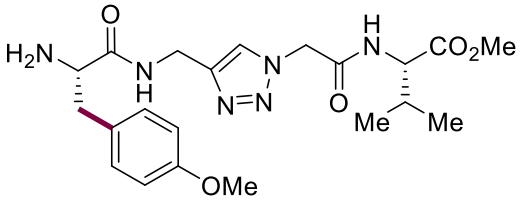
NMR and HPLC analysis showed that no racemization occurred during the TAM-removal process.



(2*S*,3*R*)-Methyl -2-amino-3-(4-nitrophenyl)-3-phenylpropanoate (106bb)

106ba (66.0 mg, 0.15 mmol) was dissolved in a 1/1 mixture of CH_2Cl_2/EtOH (4.0 mL). Ethylenediamine (45.2 mg, 0.75 mmol) was added dropwise. The solution was stirred at 40 °C for 4 h. At ambient temperature, the solvent was removed *in vacuo* and the crude product was purified by column chromatography on silica gel (CH_2Cl_2/MeOH: 40/1. Rf: 0.31) to yield **106bb** (36.2 mg, 80%) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.14 (d, J = 8.8 Hz ,2H), 7.55 (d, J = 8.8 Hz, 2H), 7.35–7.32 (m, 2H), 7.29–7.24 (m, 3H), 4.42 (d, J = 8.0 Hz, 1H), 4.24 (d, J = 8.0 Hz, 1H), 3.58 (s, 3H), 1.54 (brs, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 174.4 (C_q), 149.2 (C_q), 146.7 (C_q), 138.7 (C_q), 129.2 (CH), 129.1 (CH), 128.8 (CH), 127.7 (CH), 123.7

(CH), 58.2 (CH), 55.4 (CH_3), 52.1 (CH). **IR** (ATR): $\tilde{\nu}$ = 1737, 1595, 1517, 1498, 1440, 1251, 1173, 908, 848, 729 cm^{-1}. **MS** (ESI) m/z (relative intensity) 301 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{16}H_{16}N_2O_4$ $[M+H]^+$: 301.1183; found: 301.1183.

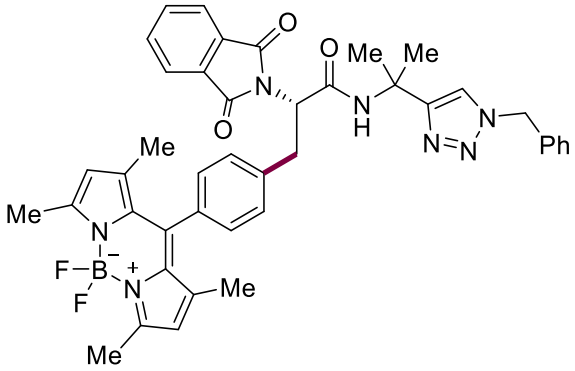


(*S*)-Methyl-2-[2-(4-{[(S)-2-amino-3-(4-methoxyphenyl)propanamido]methyl}-*1H*-1,2,3-triazol-1-yl)acetamido]-3-methylbutanoate (108ra)

108r (57.6 mg, 0.1 mmol) was dissolved in a 1/1 mixture of CH_2Cl_2/EtOH (3.0 mL). Ethylenediamine (30.1 mg, 0.5 mmol) was added dropwise. The solution was stirred at 40 °C for 4 h. At ambient, the solvent was removed *in vacuo* and the crude product was purified by column chromatography on silica gel (CH_2Cl_2/MeOH 20/1. Rf: 0.23) to yield **108ra** (27.7 mg, 62%) as a colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.86 (brs, 1H), 7.63 (s, 1H), 7.11 (d, *J* = 8.3 Hz, 2H), 6.84 (d, *J* = 8.3 Hz, 2H), 6.53 (d, *J* = 7.9 Hz, 1H), 5.06 (s, 2H), 4.55–4.49 (m, 3H), 3.79 (s, 3H), 3.72 (s, 3H), 3.63–3.59 (m, 1H), 3.18 (dd, *J* = 13.8, 4.1 Hz, 1H), 2.66 (dd, *J* = 13.8, 9.2 Hz, 1H), 2.19–2.12 (m, 1H), 1.82 (brs, 2H), 0.87 (dd, *J* = 12.8, 6.8 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 174.4 (C_q), 171.7 (C_q), 164.9 (C_q), 158.5 (C_q), 145.6 (C_q), 130.2 (CH), 129.6 (C_q), 123.8 (CH), 114.1 (CH), 57.5 (CH_3), 56.5 (CH), 55.3 (CH), 52.8 (CH_2), 52.3 (CH_3), 40.0 (CH_2), 34.6 (CH_2), 31.1 (CH), 18.9 (CH_3), 17.7 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1785, 1705, 1617, 1524, 1440, 1375, 1250, 719 cm^{-1}. **MS** (ESI) m/z (relative intensity) 447 (100) $[M+H]^+$, 469 (5) $[M+Na]^+$. **HR-MS** (ESI): m/z calcd for $C_{21}H_{30}N_6O_5$ $[M+H]^+$: 447.2350; found: 447.2354.

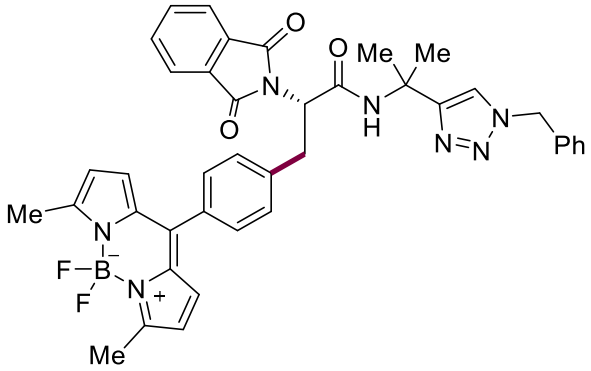
5.3.2 BODIPY Peptide Labeling by Late-Stage C(sp^3)–H Activation

5.3.2.1 Characterization Data of BODIPY Amino Acids 110



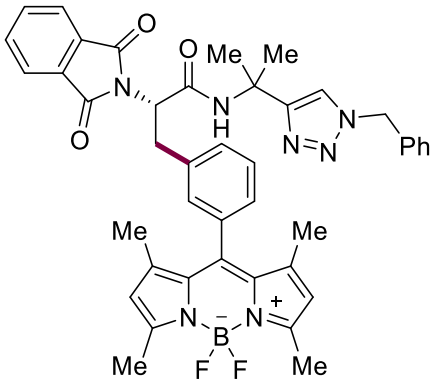
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{5,5-difluoro-1,3,7,9-tetramethyl-5H-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl) propanamide (110aa)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109a** (54 mg, 0.12 mmol) and AgOAc (20 mg, 0.12 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110aa** (62.2 mg, 84%) as a pale orange solid (M.p.: 146–147 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.78–7.67 (m, 4H), 7.43 (s, 1H), 7.42–7.32 (m, 3H), 7.29–7.24 (m, 4H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.96 (s, 1H), 5.88 (s, 2H), 5.49 (s, 2H), 5.10 (dd, *J* = 11.7, 5.5 Hz, 1H), 3.66 (dd, *J* = 13.7, 11.7 Hz, 1H), 3.55 (dd, *J* = 13.7, 5.5 Hz, 1H), 2.50 (s, 6H), 1.76 (s, 6H), 1.06 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.7 (C_q), 167.1 (C_q), 155.4 (C_q), 153.5 (C_q), 143.0 (C_q), 141.3 (C_q), 137.9 (C_q), 134.7 (C_q), 134.4 (CH), 133.7 (C_q), 131.4 (C_q), 129.8 (CH), 129.2 (CH), 128.8 (CH), 128.3 (CH), 128.1 (CH), 123.6 (CH), 121.2 (CH), 120.3 (CH), 56.2 (CH), 54.4 (CH2), 52.3 (C_q), 34.8 (CH_2), 28.2 (CH_3), 28.1 (CH_3), 14.8 (CH_3), 14.4 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = -146.40 (q, $J_{B\text{-}F}$ = 31.8 Hz). **IR** (ATR): $\tilde{\nu}$ = 1988, 1969, 1715, 1541, 1508, 531, 501, 410, 401, 389 cm^{-1}. **MS** (ESI) m/z (relative intensity): 762 (100) $[M+Na]^+$, 740 (50) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{42}H_{41}BF_2N_7O_3$ $[M+H]^+$: 740.3334; found: 740.3328. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 498 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 510 nm.



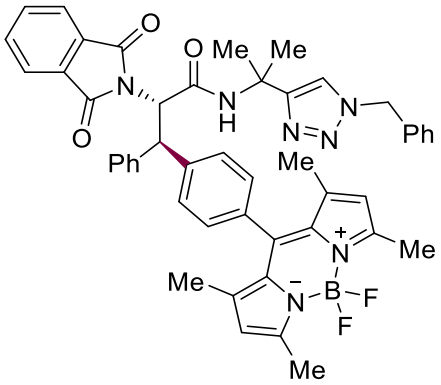
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{5,5-difluoro-3,7-dimethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl) propanamide (110ab)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109c** (51 mg, 0.12 mmol) and AgOAc (20 mg, 0.12 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110ab** (51.2 mg, 72%) as a red solid (M.p.: 152–153 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.76 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.69 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.44 (s, 1H), 7.39–7.34 (m, 3H), 7.28–7.25 (m, 3H), 7.24–7.23 (m, 3H), 6.89 (s, 1H), 6.44 (d, *J* = 4.2 Hz, 2H), 6.20 (d, *J* = 4.2 Hz, 2H), 5.48 (s, 2H), 5.08 (dd, *J* = 10.8, 6.3 Hz, 1H), 3.62 (dd, *J* = 14.1, 6.3 Hz, 1H), 3.57 (dd, *J* = 14.1, 10.8 Hz, 1H), 2.61 (s, 6H), 1.75 (s, 3H), 1.74 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.8 (C_q), 167.1 (C_q), 157.5 (C_q), 153.3 (C_q), 142.1 (C_q), 139.1 (C_q), 134.6 (C_q), 134.4 (CH), 134.3 (C_q), 132.7 (C_q), 131.4 (C_q), 130.6 (CH), 130.2 (CH), 129.2 (CH), 129.0 (CH), 128.8 (CH), 128.2 (CH), 123.6 (CH), 120.5 (CH), 119.4 (CH), 56.2 (CH), 54.4 (CH_2), 52.2 (C_q), 34.9 (CH_2), 28.2 (CH_3), 28.0 (CH_3), 15.1 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -147.69 (q, $J_{B\text{-}F}$ = 32.3 Hz). **IR** (ATR): $\tilde{\nu}$ = 1711, 1545, 1378, 1269, 1142, 1006, 985, 716, 433 cm^{-1}. **MS** (ESI) m/z (relative intensity): 1445 (10) $[2M+Na]^+$, 734 (80) $[M+Na]^+$, 712 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{40}H_{37}BF_2N_7O_3$ $[M+H]^+$: 712.3020; found: 712.3025. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 508 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 524 nm.



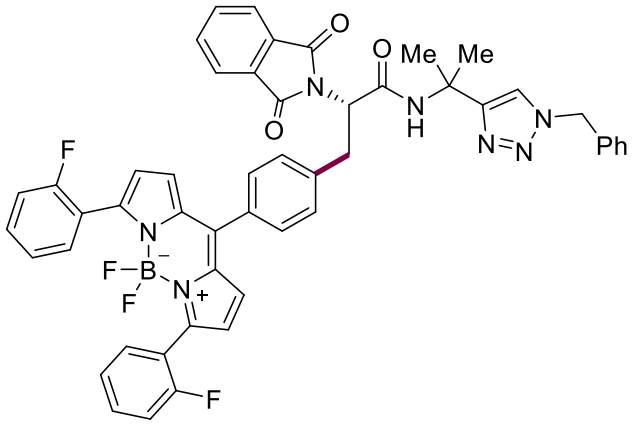
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(3-{5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl) propanamide (110ac)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109d** (54.0 mg, 0.12 mmol) and AgOAc (20.0 mg, 0.12 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110ac** (56.0 mg, 76%) as an orange solid (M.p.: 155–156 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.76–7.74 (m, 2H), 7.71–7.68 (m, 2H), 7.43 (s, 1H), 7.39–7.33 (m, 3H), 7.28–7.26 (m, 3H), 7.25 (s, 1H), 7.07–7.04 (m, 2H), 6.96 (s, 1H), 5.88 (s, 2H), 5.49 (s, 2H), 5.10 (dd, *J* = 12.0, 5.2 Hz, 1H), 3.65 (dd, *J* = 13.9, 12.0 Hz, 1H), 3.55 (dd, *J* = 13.9, 5.2 Hz, 1H), 2.50 (s, 6H), 1.76 (s, 3H), 1.75 (s, 3H), 1.06 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.7 (C_q), 167.1 (C_q), 155.4 (C_q), 153.7 (CH), 153.5 (C_q), 143.0 (C_q), 141.3 (C_q), 137.9 (C_q), 134.7 (C_q), 134.4 (CH), 133.71 (C_q), 133.66 (C_q), 131.4 (C_q), 129.8 (CH), 129.2 (CH), 128.8 (CH), 128.3 (CH), 128.2 (CH), 124.6 (CH), 123.6 (CH), 121.2 (CH), 120.3 (CH), 56.2 (CH), 54.4 (CH_2), 52.3 (C_q), 34.8 (CH_2), 28.2 (CH_3), 28.1(CH_3), 14.8 (CH_3), 14.4 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -146.40 (q, $J_{B\text{-}F}$ = 32.5 Hz). **IR** (ATR): $\tilde{\nu}$ = 1714, 1547, 1194, 499, 406, 394, 382 cm^{-1}. **MS** (ESI) m/z (relative intensity): 1501 (5) $[2M+Na]^+$, 762 (100) $[M+Na]^+$, 740 (50) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{42}H_{41}BF_2N_7O_3$ $[M+H]^+$: 740.3334; found: 740.3313. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 498 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 510 nm.



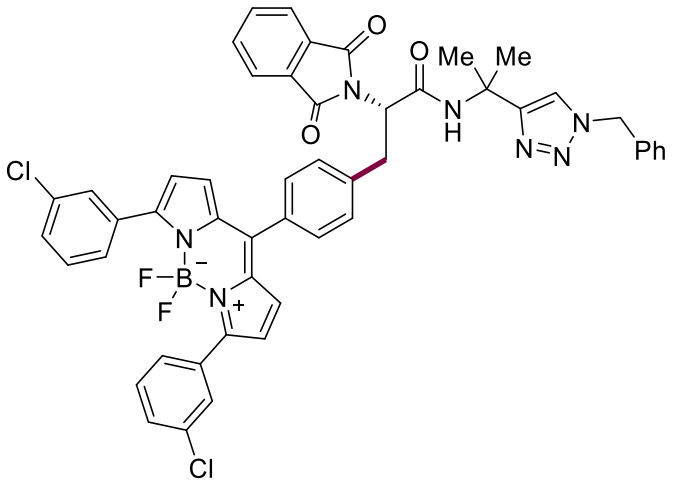
(*2S,3R*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl)3-phenylpropanamide (110ad)

The general procedure **B** was followed using Phth*N*-Phe-TAM (**105c**) (49.4 mg, 0.1 mmol), iodo-BODIPY **109a** (54 mg, 0.12 mmol) and AgOAc (20 mg, 0.12 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110ad** (75.0 mg, 92%, d:r > 20:1) as an orange solid (M.p.: 147–148 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.72 (dd, J = 5.5, 3.1 Hz, 2H), 7.65 (dd, J = 5.5, 3.1 Hz, 2H), 7.59 (d, J = 8.2 Hz, 2H), 7.35–7.30 (m, 5H), 7.23–7.19 (m, 4H), 7.15 (d, J = 8.2 Hz, 2H), 7.12–7.09 (m, 2H), 7.03–7.00 (m, 1H), 5.93 (s, 2H), 5.49 (d, J = 12.5 Hz, 1H), 5.42 (d, J = 14.7 Hz, 1H), 5.38 (d, J = 14.7 Hz, 1H), 5.35 (d, J = 12.5 Hz, 1H), 2.54 (s, 6H), 1.61 (s, 3H), 1.58 (s, 3H), 1.25 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 168.1 (C_q), 166.3 (C_q), 155.5 (C_q), 153.1 (C_q), 143.3 (C_q), 141.7 (C_q), 141.4 (C_q), 140.1 (C_q), 134.8 (C_q), 134.4 (CH), 133.9 (C_q), 131.5 (C_q), 131.2 (C_q), 129.2 (CH), 128.8 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.9 (CH), 127.3 (CH), 123.7 (CH), 121.3 (CH), 120.7 (CH), 59.6 (CH), 54.2 (CH_2), 51.9 (C_q), 50.2 (CH), 27.9 (CH_3), 27.8 (CH_3), 14.7 (CH_3), 14.6 (CH_3). **^{19}F NMR** (471 MHz, $CDCl_3$): δ = -146.31 (q, $J_{B\text{-}F}$ = 32.1 Hz). **IR** (ATR): $\tilde{\nu}$ = 2925, 1712, 1544, 1510, 1384, 1194, 1156, 716, 394 cm^{-1}. **MS** (ESI) m/z (relative intensity): 838 (100) $[M+Na]^+$, 816 (50) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{48}H_{45}BF_2N_7O_3$ $[M+H]^+$: 816.3648; found: 816.3634. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 498 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 511 nm.



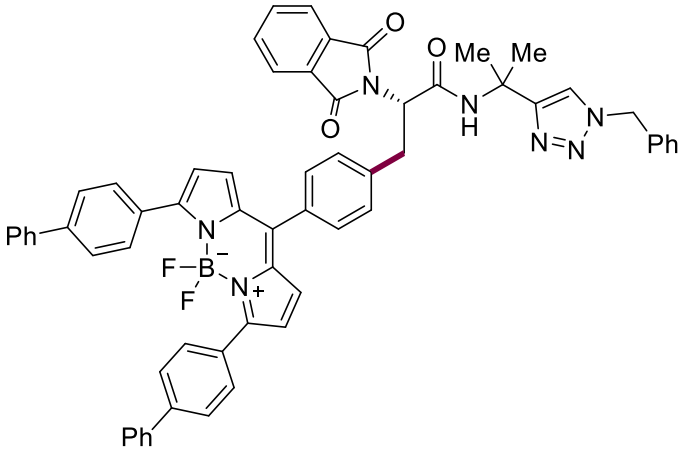
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{5,5-difluoro-3,7-bis(2-fluorophenyl)5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl) propanamide (110ba)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109e** (69.8 mg, 0.12 mmol) and $Cu(OAc)_2$ (36.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110ba** (74.0 mg, 85%) as a purple solid (M.p.: 142–143 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.85 (ddd, *J* = 7.7, 7.7, 1.7 Hz, 2H), 7.80 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.72 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.44 (s, 1H), 7.39–7.33 (m, 7H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.29–7.26 (m, 2H), 7.18 (ddd, *J* = 7.7, 7.7, 1.1 Hz, 2H), 7.10 (dd, *J* = 8.1, 1.1 Hz, 2H), 6.87 (s, 1H), 6.66 (d, *J* = 4.2 Hz, 2H), 6.59 (d, *J* = 4.2 Hz, 2H), 5.49 (s, 2H), 5.11 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.67 (dd, *J* = 13.8, 6.0 Hz, 1H), 3.61 (dd, *J* = 13.8, 10.8 Hz, 1H), 1.76 (s, 3H), 1.75 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.8 (C_q), 167.0 (C_q), 161.2 (d, $^1J_{C\text{-}F}$ = 249 Hz, C_q), 153.4 (C_q), 152.3 (C_q), 144.7 (C_q), 139.7 (C_q), 135.9 (C_q), 134.7 (C_q), 134.5 (CH), 132.8 (C_q), 132.8 (CH), 132.1 (d, $^3J_{C\text{-}F}$ = 9.0 Hz, CH), 131.4 (C_q), 131.2 (d, $^3J_{C\text{-}F}$ = 8.3 Hz, CH), 130.8 (CH), 130.6 (CH), 129.2 (d, $^4J_{C\text{-}F}$ = 3.1 Hz, CH), 128.8 (CH), 128.1 (CH), 123.9 (CH), 123.7 (CH), 122.1 (CH), 120.7 (d, $^2J_{C\text{-}F}$ = 13.5 Hz, C_q), 120.4 (CH), 115.7 (d, $^2J_{C\text{-}F}$ = 22.1 Hz, CH), 56.3 (CH), 54.4 (CH_2), 52.3 (C_q), 35.0 (CH_2), 28.2 (CH_3), 28.1 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -112.48 (m), -134.93 (q, $J_{B\text{-}F}$ = 31.0 Hz). **IR** (ATR): $\tilde{\nu}$ = 2923, 1713, 1569, 1543, 1465, 1264, 1138, 1071, 759, 721 cm^{-1}. **MS** (ESI) m/z (relative intensity): 894 (100) $[M+Na]^+$, 872 (90) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{50}H_{39}BF_4N_7O_3$ $[M+H]^+$: 872.3146; found: 872.3114. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 534 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 570 nm.



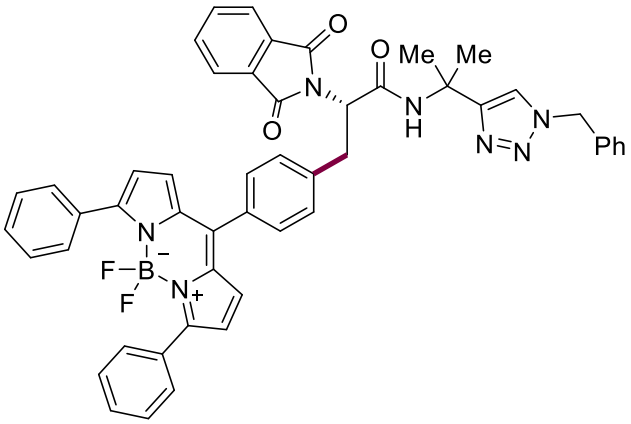
(S)-N-[2-(1-Benzyl-1H-1,2,3-triazol-4-yl)propan-2-yl]-3-[4-{3,7-bis(3-chlorophenyl)-5,5-difluoro-5H-4λ4,5λ4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl]-2-(1,3-dioxoisoindolin-2-yl) propanamide (110bb)

The general procedure B was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109f** (73.8 mg, 0.12 mmol) and $Cu(OAc)_2$ (36.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bb** (46.1 mg, 51%) as a purple solid (M.p.: 140–141 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.81–7.78 (m, 4H), 7.76–7.71 (m, 4H), 7.44 (s, 1H), 7.39–7.34 (m, 9H), 7.32–7.26 (m, 4H), 6.90 (s, 1H), 6.66 (d, J = 4.2 Hz, 2H), 6.56 (d, J = 4.2 Hz, 2H), 5.50 (s, 2H), 5.11 (dd, J = 10.8, 6.0 Hz, 1H), 3.67 (dd, J = 13.9, 6.0 Hz, 2H), 3.61 (dd, J = 13.9, 10.8 Hz, 1H), 1.77 (s, 3H). 1.76 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.8 (C_q), 167.1 (C_q), 160.4 (C_q), 157.3 (C_q), 153.4 (C_q), 144.7 (C_q), 139.8 (C_q), 136.5 (C_q), 135.7 (C_q), 134.5 (CH), 134.2 (C_q), 132.7 (C_q), 131.5 (C_q), 131.2 (CH), 130.8 (CH), 129.7 (CH), 129.6 (CH), 129.3 (CH), 129.2 (CH), 129.2 (CH), 128.8 (CH), 128.2 (CH), 127.8 (CH), 123.7 (CH), 121.0 (CH), 120.5 (CH), 56.3 (CH), 54.5 (CH_2), 52.3 (C_q), 35.0 (CH_2), 28.2 (CH_3), 28.1 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -132.44 (q, $J_{B\text{-}F}$ = 31.7). **IR** (ATR): $\tilde{\nu}$ = 2050, 1715, 1543, 558, 444, 432, 407, 393 cm^{-1}. **MS** (ESI) m/z (relative intensity): 926 (100) $[M+Na]^+$ (^{35}Cl), 903 (90) $[M+H]^+$ (^{35}Cl). **HR-MS** (ESI): m/z calcd for $C_{50}H_{39}BCl_2F_2N_7O_3$ [^{35}Cl-M+H]$^+$: 904.2555; found: 904.2563. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 548 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 578 nm.



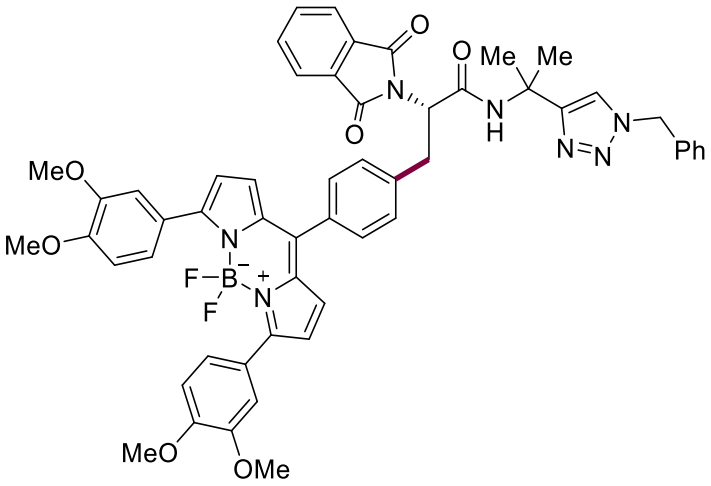
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{3,7-di([1,1'-biphenyl]-4-yl)-5,5-difluoro-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxo isoindolin-2-yl)propanamide (110bc)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109g** (83.7 mg, 0.12 mmol) and $Cu(OAc)_2$ (36.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bc** (79 mg, 80%) as a purple solid (M.p.: 158–159 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.98 (d, J = 8.4 Hz, 4H), 7.81 (dd, J = 5.5, 3.1 Hz, 2H), 7.73 (dd, J = 5.5, 3.1 Hz, 2H), 7.66 (d, J = 8.4 Hz, 4H), 7.63 (dd, J = 8.3, 1.2 Hz, 4H), 7.46–7.43 (m, 5H), 7.39–7.34 (m, 7H), 7.31 (d, J = 8.0 Hz, 2H), 7.29–7.27 (m, 2H), 6.90 (s, 1H), 6.65 (ddd, J = 4.4, 4.4, 4.4 Hz, 4H), 5.50 (s, 2H), 5.12 (dd, J = 10.8, 6.0 Hz, 1H), 3.68 (dd, J = 13.8, 6.0 Hz, 1H), 3.61 (dd, J = 13.8, 10.8 Hz, 1H), 1.77 (s, 3H), 1.76 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.9 (C_q), 167.1 (C_q), 158.4 (C_q), 153.4 (C_q), 143.2 (C_q), 142.3 (C_q), 140.5 (C_q), 139.4 (C_q), 136.5 (C_q), 134.7 (C_q), 134.5 (CH), 133.1 (C_q), 131.52 (C_q), 131.49 (C_q), 130.8 (CH), 130.7 (CH), 130.0 (CH), 129.2 (CH), 129.1 (CH), 128.85 (CH), 128.77 (CH), 128.2 (CH), 127.7 (CH), 127.2 (CH), 127.0 (CH), 123.7 (CH), 121.0 (CH), 120.4 (CH), 56.3 (CH), 54.4 (CH_2), 52.3 (C_q), 35.0 (CH_2), 28.2 (CH_3), 28.1 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$) δ = -132.46 (q, $J_{B\text{-}F}$ = 31.9 Hz). **IR** (ATR): $\tilde{\nu}$ = 2921, 1713, 1569, 1542, 1466, 1273, 1142, 1074, 764, 720, 697 cm^{-1}. **MS** (ESI) m/z (relative intensity): 1010 (80) $[M+Na]^+$, 988 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{62}H_{49}BF_2N_7O_3$ $[M+H]^+$: 988.3963; found: 988.3960. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 570 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 609 nm.



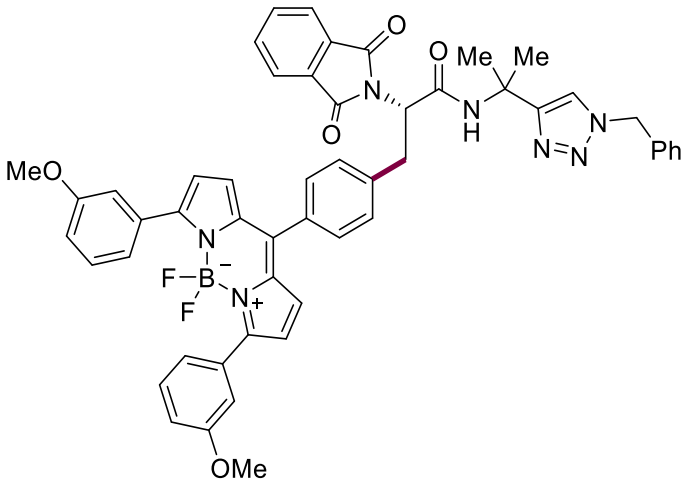
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{5,5-difluoro-3,7-diphenyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl) propanamide (110bd)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109b** (65.5 mg, 0.12 mmol) and $Cu(OAc)_2$ (36.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bd** (61.0 mg, 73%) as a purple solid (M.p.: 143–144 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.86–7.82 (m, 4H), 7.80 (dd, J = 5.4, 3.0 Hz, 2H), 7.72 (dd, J = 5.4, 3.0 Hz, 2H), 7.45 (s, 1H), 7.43–7.34 (m, 11H), 7.31–7.26 (m, 4H), 6.89 (s, 1H), 6.60 (d, J = 4.2 Hz, 2H), 6.54 (d, J = 4.2 Hz, 2H), 5.49 (s, 2H), 5.11 (dd, J = 10.8, 6.0 Hz, 1H), 3.66 (dd, J = 13.8, 6.0 Hz, 1H), 3.60 (dd, J = 13.8, 10.8 Hz, 1H), 1.77 (s, 3H), 1.75 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.8 (C_q), 167.1 (C_q), 158.9 (C_q), 153.4 (C_q), 143.7 (C_q), 139.4 (C_q), 136.3 (C_q), 134.7 (C_q), 134.5 (CH), 133.0 (C_q), 132.6 (C_q), 131.5 (C_q), 130.8 (CH), 130.7 (CH), 129.5 (CH), 129.5 (CH), 129.2 (CH), 129.1 (CH), 128.8 (CH), 128.3 (CH), 128.1 (CH), 123.6 (CH), 120.9 (CH), 120.4 (CH), 56.3 (CH), 54.4 (CH_2), 52.3 (C_q), 35.0 (CH_2), 28.2 (CH_3), 28.1 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -132.61 (q, $J_{B\text{-}F}$ = 31.8 Hz). **IR** (ATR): $\tilde{\nu}$ = 2360, 1994, 1956, 1070, 437, 411, 389 cm^{-1}. **MS** (ESI) m/z (relative intensity): 858 (90) $[M+Na]^+$, 836 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{50}H_{41}BF_2N_7O_3$ $[M+H]^+$: 836.3335; found: 836.3325. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 550 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 580 nm.



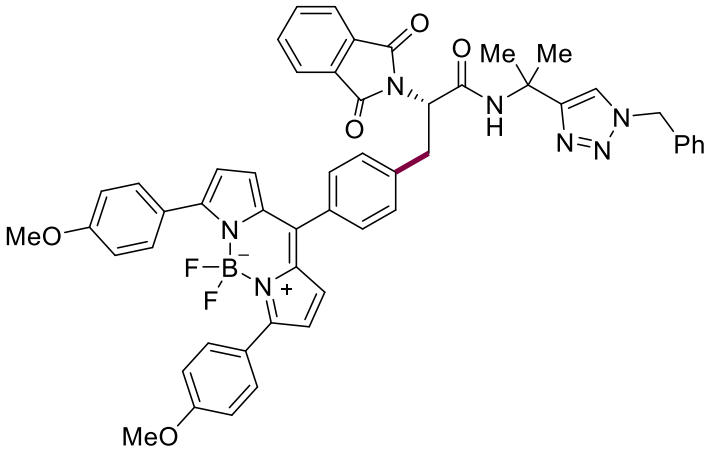
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{3,7-bis(3,4-dimethoxyphenyl)-5,5-difluoro-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoiso indolin-2-yl)propanamide (110be)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109h** (80.0 mg, 0.12 mmol) and $Cu(OAc)_2$ (36.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110be** (52.5 mg, 55%) as a purple solid (M.p.: 147–148 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.79 (dd, J = 5.4, 3.0 Hz, 2H), 7.72 (dd, J = 5.4, 3.0 Hz, 2H), 7.60 (d, J = 2.1 Hz, 2H), 7.44 (s, 1H), 7.43 (dd, J = 8.4, 2.1 Hz, 2H), 7.39–7.35 (m, 3H), 7.34–7.32 (m, 2H), 7.29–7.26 (m, 4H), 6.89 (d, J = 8.4 Hz, 2H), 6.88 (s, 1H), 6.60–6.56 (m, 4H), 5.49 (s, 2H), 5.10 (dd, J = 10.8, 6.0 Hz, 1H), 3.92 (s, 6H), 3.91 (s, 6H), 3.66 (dd, J = 13.9, 6.0 Hz, 1H), 3.59 (dd, J = 13.9, 10.8 Hz, 1H), 1.76 (s, 3H), 1.75 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.8 (C_q), 167.1 (C_q), 158.2 (C_q), 153.4 (C_q), 150.4 (C_q), 148.5 (C_q), 142.0 (C_q), 139.2 (C_q), 136.2 (C_q), 134.7 (C_q), 134.4 (CH), 133.2 (C_q), 131.5 (C_q), 130.8 (CH), 130.2 (CH), 129.2 (CH), 129.0 (CH), 128.8 (CH), 128.1 (CH), 125.4 (C_q), 123.6 (CH), 122.9 (CH), 120.4 (CH), 120.4 (CH), 112.9 (CH), 110.8 (CH), 56.3 (CH), 56.1 (CH_3), 56.1 (CH_3), 54.4 (CH_2), 52.3(C_q), 35.0 (CH_2), 28.2 (CH_3), 28.1 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -132.46 (q, $J_{B\text{-}F}$ = 32.6 Hz). **IR** (ATR): $\tilde{\nu}$ = 2926, 1714, 1548, 1470, 1258, 1148, 1075, 721 cm^{-1}. **MS** (ESI) m/z (relative intensity): 978 (25) $[M+Na]^+$, 956 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{54}H_{49}BF_2N_7O_7$ $[M+H]^+$: 956.3758; found: 956.3745. **UV-Vis λ_{max}** (1.0 mg/L in EA) = 592 nm. **Em λ_{max}** (1.0 mg/L in EA) = 625 nm.



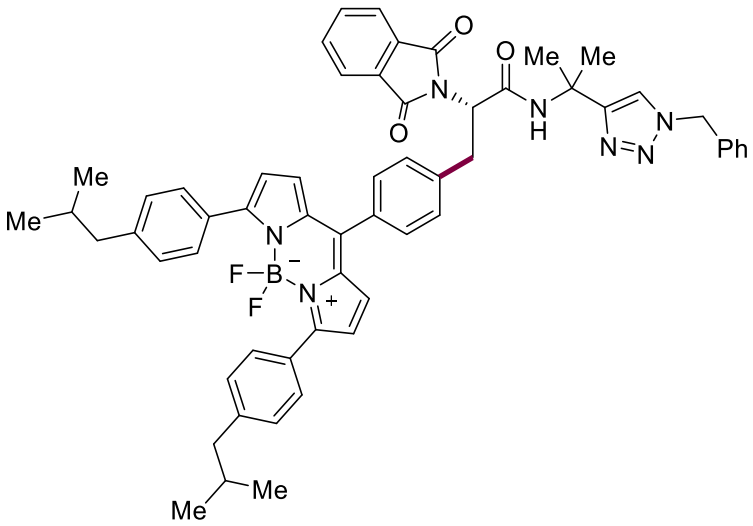
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{5,5-difluoro-3,7-bis(3-methoxyphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoiso indolin-2-yl)propanamide (110bf)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109i** (72.7 mg, 0.12 mmol) and $Cu(OAc)_2$ (36.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bf** (79.0 mg, 89%) as a purple solid (M.p.: 152–153 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.79 (dd, J = 5.5, 3.0 Hz, 2H), 7.72 (dd, J = 5.5, 3.0 Hz, 2H), 7.50 (dd, J = 2.6, 1.7 Hz, 2H), 7.44 (s, 1H), 7.41–7.33 (m, 7H), 7.32–7.27 (m, 6H), 6.94 (ddd, J = 8.3, 2.6, 0.8 Hz, 2H), 6.88 (s, 1H), 6.61 (d, J = 4.3 Hz, 2H), 6.57 (d, J = 4.3 Hz, 2H), 5.49 (s, 2H), 5.10 (dd, J = 10.8, 6.0 Hz, 1H), 3.83 (s, 6H), 3.66 (dd, J = 13.9, 6.0 Hz, 1H), 3.60 (dd, J = 13.9, 10.8 Hz, 1H), 1.76 (s, 3H), 1.75 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.8 (C_q), 167.1 (C_q), 159.2 (C_q), 158.6 (C_q), 153.4 (C_q), 143.6 (C_q), 139.4 (C_q), 136.3 (C_q), 134.7 (C_q), 134.5 (CH), 133.8 (C_q), 133.0 (C_q), 131.5 (C_q), 130.8 (CH), 130.7 (CH), 129.2 (CH), 129.1 (CH), 128.8 (CH), 128.1 (CH), 127.6 (CH), 123.6 (CH), 122.0 (CH), 120.8 (CH), 120.4 (CH), 115.9 (CH), 114.7 (CH), 56.3 (CH), 55.5 (CH_3), 54.4 (CH_2), 52.3 (C_q), 35.0 (CH_2), 28.2 (CH_3), 28.1 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -132.31 (q, $J_{B\text{-}F}$ = 32.0 Hz). **IR** (ATR): $\tilde{\nu}$ = 2925, 1713, 1570, 1546, 1468, 1241, 1138, 1069, 721 cm^{-1}. **MS** (ESI) m/z (relative intensity): 1813 (10) $[2M+Na]^+$, 918 (90) $[M+Na]^+$, 896 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{52}H_{45}BF_2N_7O_5$ $[M+H]^+$: 896.3546; found: 896.3547. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 558 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 589 nm.



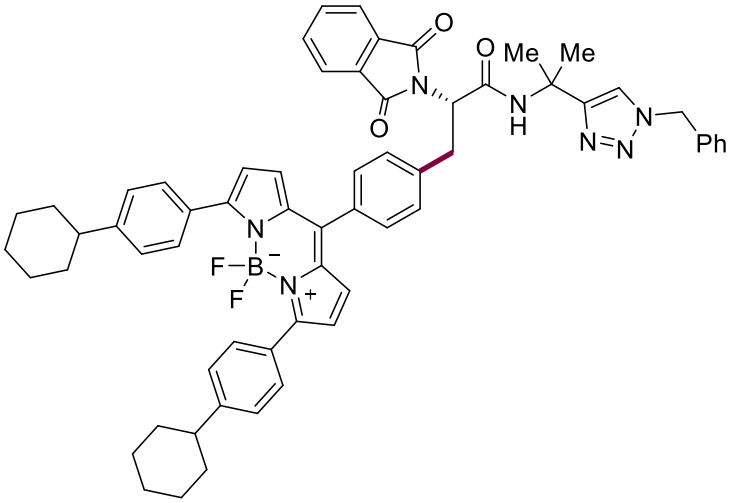
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{5,5-difluoro-3,7-bis(4-methoxyphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoiso indolin-2-yl)propanamide (110bg)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109j** (72.7 mg, 0.12 mmol) and AgOAc (20 mg, 0.12 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bg** (86.1 mg, 96%) as a purple solid (M.p.: 150–151 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 7.85 (d, J = 8.9 Hz, 4H), 7.79 (dd, J = 5.4, 3.3 Hz, 2H), 7.71 (dd, J = 5.4, 3.3 Hz, 2H), 7.44 (s, 1H), 7.39–7.26 (m, 9H), 6.94 (d, J = 8.9 Hz, 4H), 6.87 (s, 1H), 6.55 (dd, J = 9.6, 4.5 Hz, 4H), 5.49 (s, 2H), 5.10 (dd, J = 10.2, 6.4 Hz, 1H), 3.84 (s, 6H), 3.68–3.58 (m, 2H), 1.77 (s, 3H), 1.75 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.8 (C_q), 167.1 (C_q), 160.7 (C_q), 158.3 (C_q), 153.4 (C_q), 142.0 (C_q), 139.1 (C_q), 136.2 (C_q), 134.7 (C_q), 134.4 (CH), 133.3 (C_q), 131.5 (C_q), 131.1 (CH), 130.8 (CH), 130.2 (CH), 129.2 (CH), 129.0 (CH), 128.8 (CH), 128.1 (CH), 125.2 (C_q), 123.6 (CH), 120.5 (CH), 120.4 (CH), 113.9 (CH), 56.3 (CH), 55.5 (CH_3), 54.4 (CH_2), 52.3 (C_q), 35.0 (CH_2), 28.2 (CH_3), 28.1 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -133.07 (q, $J_{B\text{-}F}$ = 32.4 Hz). **IR** (ATR): $\tilde{\nu}$ = 1713, 1544, 1465, 1432, 1255, 1139, 1071, 1057, 793, 718, 386 cm^{-1}. **MS** (ESI) m/z (relative intensity): 1813 (5) $[2M+Na]^+$, 918 (100) $[M+Na]^+$, 896 (95) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{52}H_{45}BF_2N_7O_5$ $[M+H]^+$: 896.3546; found: 896.3550. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 576 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 612 nm.



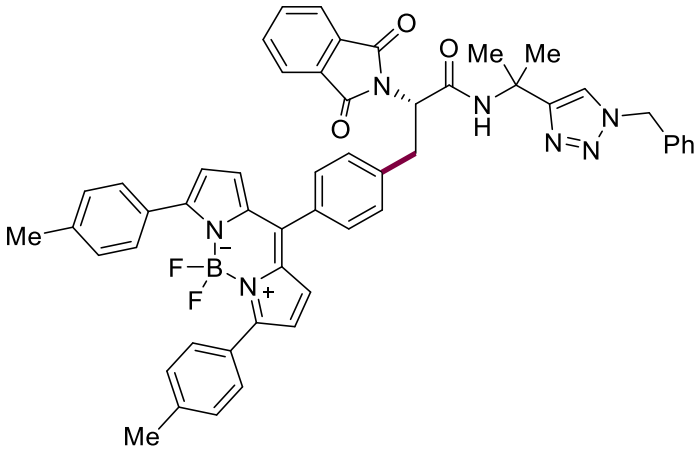
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{5,5-difluoro-3,7-bis(4-isobutylphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoiso indolin-2-yl)propanamide (110bh)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109k** (79.0 mg, 0.12 mmol) and $Cu(OAc)_2$ (36.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bh** (63.5 mg, 67%) as a purple solid (M.p.: 155–156 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.80–7.78 (m, 6H), 7.72 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.44 (s, 1H), 7.39–7.33 (m, 5H), 7.29–7.26 (m, 4H), 7.19 (d, *J* = 8.3 Hz, 4H), 6.87 (s, 1H), 6.58 (d, *J* = 4.3 Hz, 2H), 6.56 (d, *J* = 4.3 Hz, 2H), 5.49 (s, 2H), 5.10 (dd, *J* = 10.8, 6.1 Hz, 1H), 3.65 (dd, *J* = 13.9, 6.1 Hz, 1H), 3.59 (dd, *J* = 13.9, 10.8 Hz, 1H), 2.51–2.49 (m, 4H), 1.94–1.86 (m, 2H), 1.77 (s, 3H), 1.75 (s, 3H), 0.93 (s, 6H), 0.92 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.9 (C_q), 167.1 (C_q), 158.9 (C_q), 153.4 (C_q), 143.5 (C_q), 142.7 (C_q), 139.2 (C_q), 136.3 (C_q), 134.7 (C_q), 134.4 (CH), 133.2 (C_q), 131.5 (C_q), 130.8 (CH), 130.3 (CH), 130.1 (C_q), 129.3 (CH), 129.2 (CH), 129.1 (CH), 129.0 (CH), 128.8 (CH), 128.1 (CH), 123.6 (CH), 120.8 (CH), 120.4 (CH), 56.3 (CH), 54.4 (C_q), 52.3 (CH_2), 45.6 (CH_2), 30.3 (CH), 29.9 (CH_2), 28.2 (CH_3), 28.1 (CH_3), 22.7 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -132.99 (q, $J_{B\text{-}F}$ = 32.1 Hz). **IR** (ATR): $\tilde{\nu}$ = 2921, 1714, 1571, 1546, 1467, 1140, 1070, 720 cm^{-1}. **MS** (ESI) m/z (relative intensity): 970 (60) $[M+Na]^+$, 948 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{58}H_{57}BF_2N_7O_3$, $[M+H]^+$: 948.4588; found: 948.4589. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 562 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 594 nm.



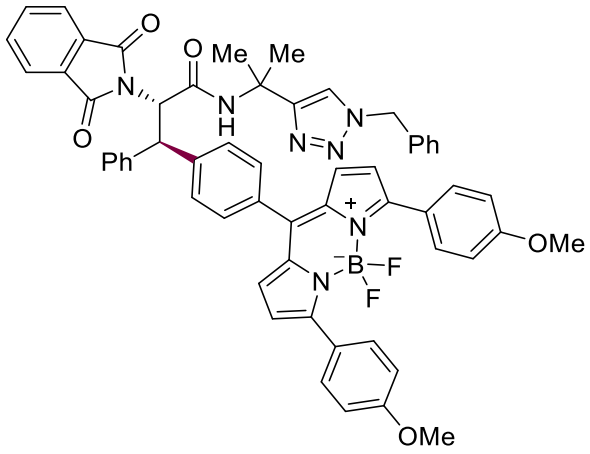
(S)-N-[2-(1-Benzyl-1H-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{3,7-bis(4-cyclohexylphenyl)-5,5-difluoro-5H-4λ4,5λ4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoiso indolin-2-yl)propanamide (110bi)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109l** (85.2 mg, 0.12 mmol) and $Cu(OAc)_2$ (36.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bi** (68.0 mg, 68%) as a purple solid (M.p.: 159–160 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.81–7.78 (m, 6H), 7.71 (dd, J = 5.4, 3.1 Hz, 2H), 7.44 (s, 1H), 7.39–7.35 (m, 3H), 7.35–7.33 (m, 2H), 7.29–7.26 (m, 4H), 7.26–7.24 (m, 4H), 6.87 (s, 1H), 6.58 (d, J = 4.3 Hz, 2H), 6.55 (d, J = 4.3 Hz, 2H), 5.49 (s, 2H), 5.10 (dd, J = 10.7, 6.1 Hz, 1H), 3.65 (dd, J = 13.8, 6.1 Hz, 1H), 3.59 (dd, J = 13.8, 10.7 Hz, 1H), 2.56–2.50 (m, 2H), 1.93–1.89 (m, 4H), 1.87–1.82 (m, 4H), 1.77–1.73 (m, 8H), 1.45–1.35 (m, 8H), 1.29–1.24 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.8 (C_q), 167.1 (C_q), 158.9 (C_q), 153.4 (C_q), 149.6 (C_q), 142.7 (C_q), 139.2 (C_q), 136.3 (C_q), 134.7 (C_q), 134.4 (CH), 133.2 (C_q), 131.5 (C_q), 130.8 (CH), 130.3 (CH), 130.2 (C_q), 129.5 (CH), 129.2 (CH), 129.0 (CH), 128.8 (CH), 128.1 (CH), 126.9 (CH), 123.6 (CH), 120.8 (CH), 120.4 (CH), 56.3 (CH), 54.4 (CH_2), 52.3 (C_q), 44.7 (CH), 35.0 (CH_2), 34.4 (CH_2), 28.2 (CH_3), 28.1 (CH_3), 27.1 (CH_2), 26.4 (CH_2). **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -132.85 (q, $J_{B\text{-}F}$ = 32.0 Hz). **IR** (ATR): $\tilde{\nu}$ = 2924, 1714, 1570, 1545, 1468, 1276, 1141, 1072, 720 cm^{-1}. **MS** (ESI) m/z (relative intensity): 1022 (40) $[M+Na]^+$, 1000 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{62}H_{61}BF_2N_7O_3$, $[M+H]^+$: 1000.4902; found: 1000.4904. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 562 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 595 nm.



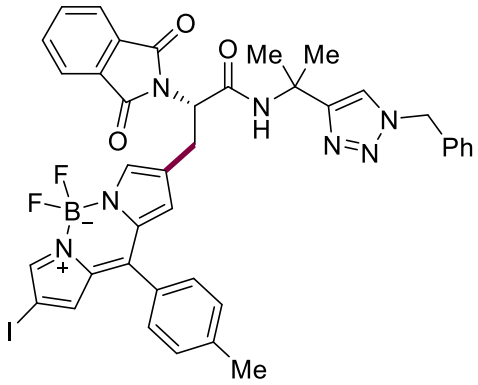
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{5,5-difluoro-3,7-di-p-tolyl-5*H*4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl) propanamide (110bj)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109m** (69.0 mg, 0.12 mmol) and $Cu(OAc)_2$ (36.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bj** (57.0 mg, 66%) as a purple solid (M.p.: 147–148 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.81–7.78 (m, 3H), 7.76 (d, J = 8.4 Hz, 4H), 7.71 (dd, J = 5.5, 3.1 Hz, 2H), 7.45 (s, 1H), 7.39–7.35 (m, 3H), 7.34–7.33 (m, 2H), 7.29–7.27 (m, 3H), 7.21 (d, J = 8.4 Hz, 4H), 6.88 (s, 1H), 6.59 (d, J = 4.2 Hz, 2H), 6.54 (d, J = 4.2 Hz, 2H), 5.49 (s, 2H), 5.10 (dd, J = 10.8, 6.0 Hz, 1H), 3.66 (dd, J = 13.8, 6.0 Hz, 1H), 3.60 (dd, J = 13.8, 10.8 Hz, 1H), 2.38 (s, 6H), 1.76 (s, 3H), 1.75 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.8 (C_q), 167.1 (C_q), 158.9 (C_q), 153.4 (C_q), 142.9 (C_q), 139.7 (C_q), 139.2 (C_q), 136.2 (C_q), 134.7 (C_q), 134.4 (CH), 133.2 (C_q), 131.5 (C_q), 130.8 (CH), 130.4 (CH), 129.9 (C_q), 129.4 (CH), 129.2 (CH), 129.1 (CH), 129.0 (CH), 128.8 (CH), 128.1 (CH), 123.6 (CH), 120.7 (CH), 120.4 (CH), 56.3 (CH), 54.4 (CH_2), 52.3 (C_q), 35.0 (CH_2), 28.2 (CH_3), 28.1 (CH_3), 21.7 (CH_3). **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -132.76 (q, $J_{B\text{-}F}$ = 32.0 Hz). **IR** (ATR): $\tilde{\nu}$ = 1715, 1571, 1546, 1468, 1141, 1072, 447, 428, 410, 379 cm^{-1}. **MS** (ESI) m/z (relative intensity): 1749 (10) $[2M+Na]^+$, 886 (100) $[M+Na]^+$, 864 (50) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{52}H_{45}BF_2N_7O_3$ $[M+H]^+$: 864.3648; found: 864.3630. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 560 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 592 nm.



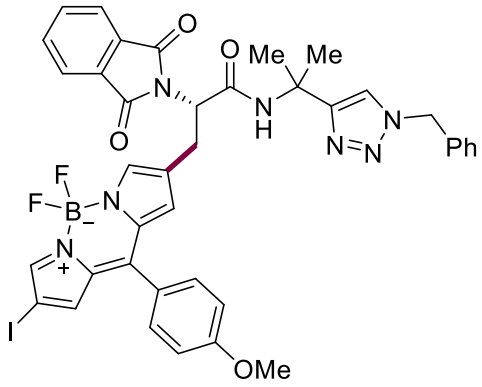
(2*S*,3*R*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-(4-{5,5-difluoro-3,7-bis(4methoxyphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3dioxoisoindolin-2-yl)-3-phenylpropanamide (110bk)

The general procedure **B** was followed using Phth*N*-Phe-TAM (**105c**) (49.4 mg, 0.1 mmol), iodo-BODIPY **109j** (72.7 mg, 0.12 mmol) and AgOAc (33.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bk** (92.0 mg, 95%, d:r > 20:1) as a purple solid (M.p.: 162–163 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.87 (d, J = 8.39 Hz, 4H), 7.75 (dd, J = 5.5, 3.0 Hz, 2H), 7.66 (dd, J = 5.5, 3.0 Hz, 2H), 7.63 (d, J = 8.2 Hz, 2H), 7.42 (d, J = 8.2 Hz, 2H), 7.36–7.33 (m, 2H), 7.31–7.27 (m, 3H), 7.23 (s, 1H), 7.21–7.14 (m, 4H), 7.11–7.07 (m, 1H), 6.98–6.94 (m, 5H), 6.80 (d, J = 4.3 Hz, 2H), 6.57 (d, J = 4.3 Hz, 2H), 5.58 (d, J = 12.6 Hz, 1H), 5.46 (d, J = 12.6 Hz, 1H), 5.37 (d, J = 2.6 Hz, 2H), 3.85 (s, 6H), 1.59 (s, 3H), 1.53 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 168.1 (C_q), 166.4 (C_q), 163.3 (C_q), 160.8 (C_q), 158.4 (C_q), 153.0 (C_q), 142.7 (C_q), 141.9 (C_q), 139.9 (C_q), 136.2 (C_q), 134.8 (C_q), 134.3 (CH), 133.7 (C_q), 131.4 (CH), 131.3 (CH), 130.6 (CH), 129.1 (CH), 129.0 (CH), 128.7 (CH), 128.3 (CH), 128.0 (CH), 127.9 (CH), 127.5 (CH), 125.3 (C_q), 123.7 (CH), 120.6 (CH), 120.5 (CH), 113.9 (CH), 59.4 (CH), 55.4 (CH), 54.1 (CH_2), 52.0 (C_q), 50.6 (CH_3), 27.8 (CH_3), 27.6 (CH_3). **^{19}F NMR** (471 MHz, $CDCl_3$): δ = -132.94 (q, $J_{B\text{-}F}$ = 32.3 Hz). **IR** (ATR): $\tilde{\nu}$ = 2051, 2033, 1992, 1715, 499, 401, 394, 380 cm^{-1}. **MS** (ESI) m/z (relative intensity): 994 (100) $[M+Na]^+$, 971 (90) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{58}H_{49}BF_2N_7O_5$ $[M+H]^+$: 972.3860; found: 972.3866. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 578 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 613 nm.



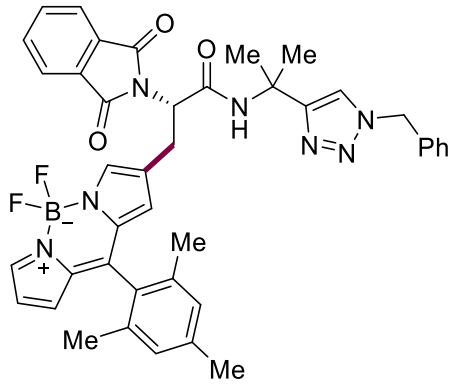
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-[5,5-difluoro-8-iodo-10-(p-tolyl)-5*H*-5λ^4,6λ^4-dipyrrolo(1,2-c:2',1'-f)(1,3,2)diazaborinin-2-yl]-2-(1,3-dioxoisoindolin-2-yl)propanamide (**110bl**)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (83.4 mg, 0.2 mmol), diiodo-BODIPY **109n** (128.4 mg, 0.24 mmol) and $Cu(OAc)_2$ (72.6 mg, 0.40 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bl** (100.5 mg, 61%) as a red solid (M.p.: 139–142 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.81 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.75 (s, 1H), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.72 (s, 1H), 7.39 (s, 1H), 7.35–7.33 (m, 3H), 7.26–7.23 (m, 6H), 6.96 (s, 1H), 6.80 (s, 1H), 6.76 (s, 1H), 5.44 (s, 2H), 4.91 (dd, *J* = 10.1, 6.3 Hz, 1H), 3.43 (dd, *J* = 15.0, 10.1 Hz, 1H), 3.37 (dd, *J* = 15.0, 6.3 Hz, 1H), 2.46 (s, 3H), 1.70 (s, 3H), 1.69 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.8 (C_q), 166.7 (C_q), 152.3 (C_q), 146.4 (C_q), 146.3 (C_q), 145.5 (CH), 141.9 (C_q), 135.9 (CH), 135.7 (C_q), 135.1 (C_q), 134.6 (C_q), 134.4 (CH), 131.5 (C_q), 130.7 (CH), 130.5 (CH), 130.4 (C_q), 130.3 (C_q), 129.3 (CH), 129.1 (CH), 128.7 (CH), 128.1 (CH), 123.7 (CH), 120.3 (CH), 120.2 (CH), 55.4 (CH), 54.2 (CH_2), 52.2 (C_q), 28.0 (CH_3), 27.9 (CH_3), 26.4 (CH_2), 21.7 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -144.9 – -145.2 (m). **IR** (ATR): $\tilde{\nu}$ = 1736, 1447, 1372, 1233, 1098, 1043, 938, 786, 634, 608 cm^{-1}. **MS** (ESI) m/z (relative intensity): 846 (100) $[M+Na]^+$, 824 (14) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{39}H_{34}BF_2IN_7O_3$ $[M+H]^+$: 824.1830; found: 824.1816. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 530 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 553 nm.



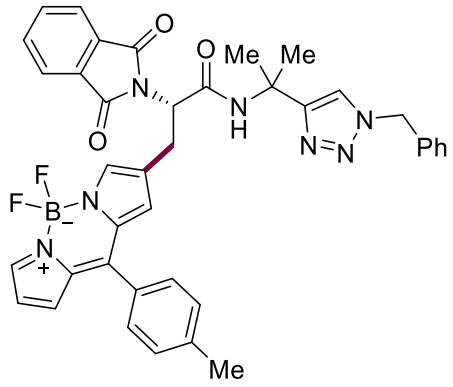
(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-[5,5-difluoro-8-iodo-10-(4-methoxyphenyl)-5*H*-5λ^4,6λ^4-dipyrrolo(1,2-c:2',1'-f)(1,3,2)diazaborinin-2-yl]-2-(1,3-dioxoisoindolin-2-yl) propanamide (110bm)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (83.4 mg, 0.2 mmol diiodo-BODIPY **109o** (132.0 mg, 0.24 mmol) and $Cu(OAc)_2$ (72.6 mg, 0.40 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bm** (125.9 mg, 75%) as a red solid (M.p.: 140–143 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.81 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.74–7.72 (m, 4H), 7.36 (s, 1H), 7.36–7.34 (m, 5H), 7.25–7.23 (m, 2H), 6.98–6.96 (m, 2H), 6.97 (s, 1H), 6.80 (s, 1H), 6.78 (s, 1H), 5.45 (s, 2H), 4.92 (dd, *J* = 10.0, 6.4 Hz, 1H), 3.91 (s, 3H), 3.43 (dd, *J* = 15.0, 10.0 Hz, 1H), 3.39 (dd, *J* = 15.0, 6.4 Hz, 1H), 1.70 (s, 3H), 1.69 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.8 (C_q), 166.8 (C_q), 162.4 (C_q), 153.3 (C_q), 146.1 (C_q), 145.9 (CH), 145.0 (CH), 135.8 (CH), 135.7 (C_q), 135.0 (C_q), 134.6 (C_q), 134.4 (CH), 132.5 (CH), 131.5 (C_q), 131.3 (CH), 130.3 (C_q), 130.2 (C_q), 129.1 (CH), 128.7 (CH), 128.1 (CH), 125.8 (C_q), 123.8 (CH), 120.4 (CH), 114.4 (CH), 55.8 (CH), 55.4 (CH_3), 52.3 (C_q), 52.3 (CH_2), 28.1 (CH_3), 28.0 (CH_3), 26.4 (CH_2). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -144.9 – -145.3 (m). **IR** (ATR): $\tilde{\nu}$ = 1733, 1446, 1373, 1238, 1044, 939, 734, 634, 608, 438 cm^{-1}. **MS** (ESI) m/z (relative intensity): 840 (35) $[M+H]^+$, 862 (100) $[M+Na]^+$. **HR-MS** (ESI): m/z calcd for $C_{39}H_{34}BF_2IN_7O_4$ $[M+H]^+$: 840.1779; found: 840.1763. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 528 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 553 nm.



(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-{5,5-difluoro-10-mesityl-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-2-yl}-2-(1,3-dioxoisoindolin-2-yl)propanamide (110bn)

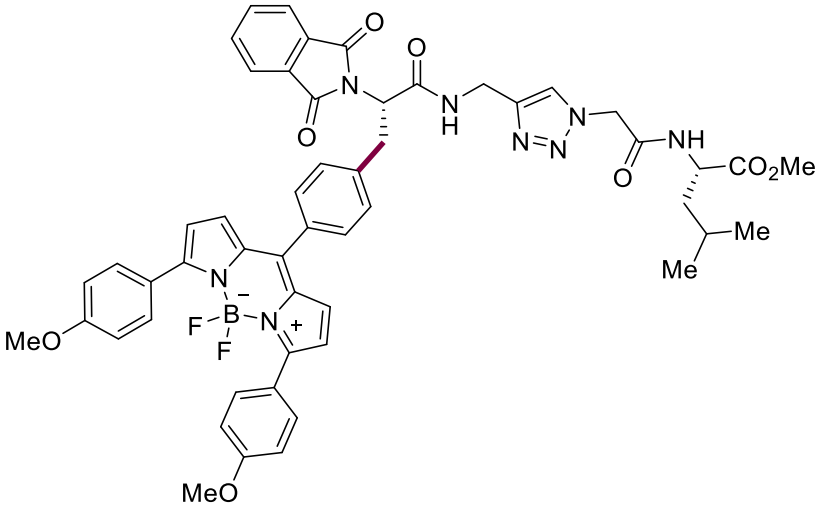
The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109p** (52.3 mg, 0.12 mmol) and $Cu(OAc)_2$ (36.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bn** (45.7 mg, 63%) as a red solid (M.p.: 136–137 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.82 (s, 1H), 7.78 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.66 (s, 1H), 7.39 (s, 1H), 7.36–7.34 (m, 2H), 7.26–7.23 (m, 2H), 6.91 (s, 1H), 6.82 (s, 1H), 6.69 (s, 1H), 6.60 (d, *J* = 4.1 Hz, 1H), 6.41 (dd, *J* = 4.1, 1.7 Hz, 1H), 6.38 (s, 1H), 5.46 (s, 2H), 4.85 (dd, *J* = 10.7, 5.9 Hz, 1H), 3.39 (dd, *J* = 15.0, 10.7 Hz, 1H), 3.29 (dd, *J* = 15.0, 5.9 Hz, 1H), 2.34 (s, 3H), 1.98 (s, 3H), 1.84 (s, 3H), 1.69 (s, 3H), 1.68 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.8 (C_q), 166.9 (C_q), 153.3 (C_q), 147.3 (C_q), 144.3 (CH), 144.0 (CH), 138.8 (C_q), 136.3 (C_q), 136.1 (C_q), 135.4 (C_q), 134.7 (C_q), 134.4 (CH), 131.5 (C_q), 130.2 (CH), 129.5 (C_q), 129.2 (C_q), 129.1 (CH), 128.7 (CH), 128.6 (CH), 128.3 (CH), 128.14 (CH), 128.08 (CH), 123.7 (CH), 120.3 (CH), 118.5 (CH), 55.5 (CH), 54.3 (CH_2), 52.3 (C_q), 28.2 (CH_3), 28.0 (CH_3), 26.3 (CH_2), 21.3 (CH_3), 20.0 (CH_3), 19.9 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -145.35 – -146.48 (m). **IR** (ATR): $\tilde{\nu}$ = 2926, 1713, 1571, 1382, 1106, 1067, 722, 436, 394 cm^{-1}. **MS** (ESI) m/z (relative intensity): 1451 (10) $[2M+H]^+$, 748 (50) $[M+Na]^+$, 726 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{41}H_{39}BF_2N_7O_3$ $[M+H]^+$: 726.3177; found: 726.3177. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 512 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 527 nm.



(*S*)-*N*-[2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-3-{5,5-difluoro-10-(p-tolyl)-5*H*-5λ^4,6λ4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-2-yl}-2-(1,3-dioxoisoindolin-2-yl)propanamide (110bo)

The general procedure **B** was followed using Phth*N*-Ala-NHTAM (**105a**) (41.7 mg, 0.1 mmol), iodo-BODIPY **109q** (48.9 mg, 0.12 mmol) and $Cu(OAc)_2$ (36.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 42.0 min) yielded **110bo** (51.6 mg, 74%) as a red solid (M.p.: 135–136 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.84 (s, 1H), 7.82 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.69 (s, 1H), 7.39 (s, 1H), 7.37–7.31 (m, 3H), 7.29–7.23 (m, 6H), 6.89 (d, *J* = 4.1 Hz, 1H), 6.73 (s, 1H), 6.69 (s, 1H), 6.49 (dd, *J* = 4.2, 1.9 Hz, 1H), 5.45 (s, 2H), 4.91 (dd, *J* = 10.1, 6.3 Hz, 1H), 3.43 (dd, *J* = 14.9, 10.1 Hz, 1H), 3.37 (dd, *J* = 14.9, 6.3 Hz, 1H), 2.46 (s, 3H), 1.70 (s, 3H), 1.69 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 168.0 (C_q), 167.0 (C_q), 153.4 (C_q), 147.4 (C_q), 143.9 (CH), 143.6 (CH), 141.6 (C_q), 135.0 (C_q), 134.8 (C_q), 134.5 (CH), 131.6 (CH), 131.9 (C_q), 131.6 (C_q), 130.9 (C_q), 130.7 (CH), 130.1 (CH), 129.3 (CH), 129.2 (CH), 129.1 (C_q), 128.8 (CH), 128.2 (CH), 123.9 (CH), 120.4 (CH), 118.4 (CH), 55.5 (CH), 54.2 (CH_2), 52.2 (C_q), 28.0 (CH_3), 27.9 (CH_3), 26.4 (CH_2), 21.6 (CH_3). **^{19}F NMR** (471 MHz, $CDCl_3$): δ = -144.8 – -145.6 (m). **IR** (ATR): $\tilde{\nu}$ = 1710, 1538, 1380, 1362, 1256, 1106, 1073, 718, 429, 405 cm^{-1}. **MS** (ESI) m/z (relative intensity): 720 (100) $[M+Na]^+$, 698 (25) $[M+H]^+$. HR-MS (ESI): m/z calcd for $C_{39}H_{35}BF_2N_7O_3$ $[M+H]^+$: 698.2864; found: 698.2859. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 510 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 531 nm.

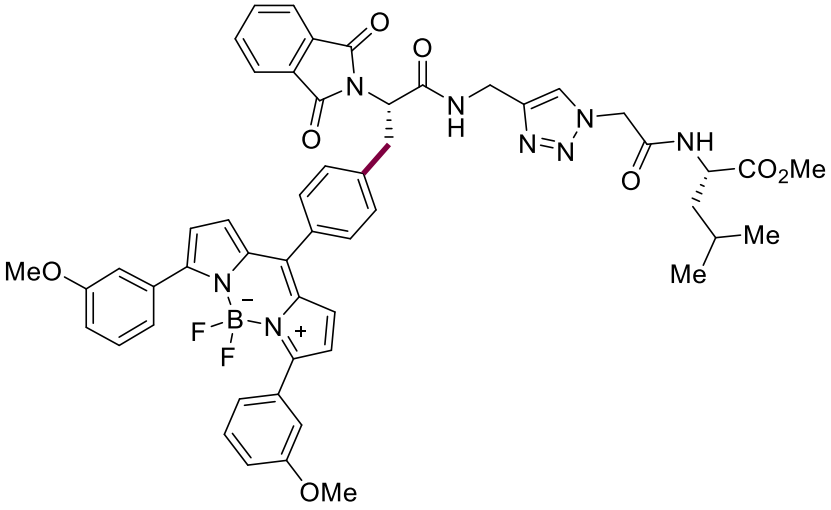
5.3.2.2 Characterization Data of BODIPY Peptides 111



Methyl[2-(4-{[(S)-3-(4-{5,5-difluoro-3,7-bis(4-methoxyphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1*H*-1,2,3triazol-1-yl)acetyl]-*L*-leucinate (111a)

The general procedure **C** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (48.4 mg, 0.1 mmol), iodo-BODIPY **109j** (72.7 mg, 0.12 mmol) and AgOAc (33.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 41.0 min) yielded 24 (71.3 mg, 74%) as a purple solid (M.p.: 158–159 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.83 (d, J = 8.9 Hz, 4H), 7.77–7.69 (m, 5H), 7.31 (d, J = 8.3 Hz, 2H), 7.26–7.19 (m, 3H), 6.93 (d, J = 8.9 Hz, 4H), 6.80 (d, J = 8.2 Hz, 1H), 6.55–6.52 (m, 4H), 5.17 (dd, J = 11.2, 5.5 Hz, 1H), 5.08 (d, J = 16.4 Hz, 1H), 5.04 (d, J = 16.4 Hz, 1H), 4.63–4.59 (m, 1H), 4.53 (d, J = 5.5 Hz, 2H), 3.83 (s, 6H), 3.71 (dd, J = 13.9, 5.5 Hz, 1H), 3.69 (s, 3H), 3.56 (dd, J = 13.9, 11.2 Hz, 1H), 1.63–1.54 (m, 2H), 1.53–1.51 (m, 1H), 0.91 (d, J = 2.5 Hz, 3H), 0.90 (d, J = 2.5 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 173.1 (C_q), 168.5 (C_q), 167.9 (C_q), 165.1 (C_q), 160.8 (C_q), 158.4 (C_q), 145.0 (C_q), 142.0 (C_q), 139.1 (C_q), 136.2 (C_q), 134.6 (CH), 133.3 (C_q), 131.4 (C_q), 131.2 (CH), 130.8 (CH), 130.2 (CH), 129.0 (CH), 125.2 (C_q), 124.4 (CH), 123.7 (CH), 120.5 (CH), 113.9 (CH), 55.4 (CH), 55.3 (CH_3), 52.8 (CH_2), 52.6 (CH), 51.2 (CH_3), 41.2 (CH_2), 35.3 (CH_2), 34.7 (CH_2), 25.0 (CH), 22.9 (CH_3), 22.0 (CH_3). **^{19}F NMR** (471 MHz, $CDCl_3$): δ = -132.98 (q, $J_{B\text{-}F}$ = 32.3 Hz). **IR** (ATR): $\tilde{\nu}$ = 1713, 1541, 1463, 1431, 1253, 1136, 1054, 717, 526, 405 cm-1. **MS** (ESI) m/z (relative intensity): 985 (100) $[M+Na]^+$, 963 (20) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{52}H_{50}BF_2N_8O_8$

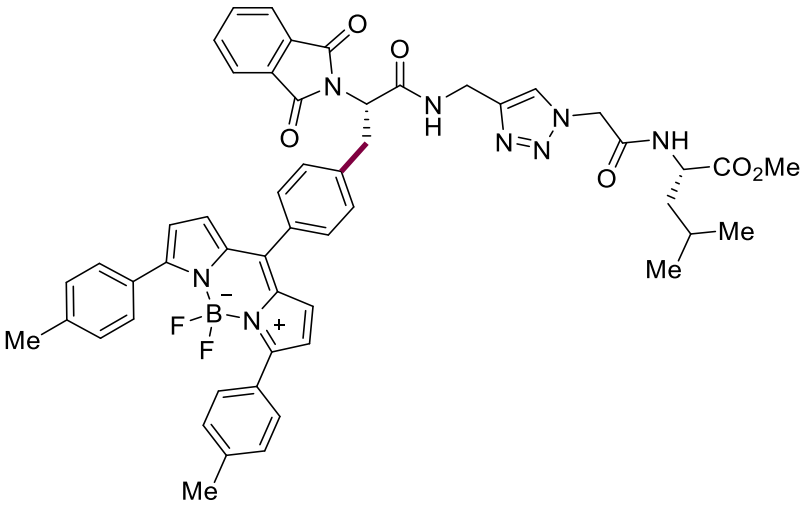
$[M+H]^+$: 963.3816; found: 963.3781. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 576 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 612 nm.



Methyl[2-(4-{[(*S*)-3-(4-{5,5-difluoro-3,7-bis(3-methoxyphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1*H*-1,2,3triazol-1-yl)acetyl]-*L*-leucinate (111b)

The general procedure **C** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (48.4 mg, 0.1 mmol), iodo-BODIPY **109i** (72.7 mg, 0.12 mmol) and AgOAc (33.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 41.0 min) yielded 25 (51 mg, 53%) as a purple solid (M.p.: 158–159 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.78–7.76 (m, 1H), 7.75 (dd, *J* = 5.6, 2.9 Hz, 2H), 7.68 (dd, *J* = 5.6, 2.9 Hz, 2H), 7.51–7.47 (m, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.34–7.26 (m, 6H), 7.15 (dd, *J* = 5.6, 5.6 Hz, 1H), 6.94 (dd, *J* = 8.0, 2.6 Hz, 2H), 6.71 (d, *J* = 8.2 Hz, 1H), 6.58 (d, *J* = 4.3 Hz, 2H), 6.56 (d, *J* = 4.3 Hz, 2H), 5.17 (dd, *J* = 11.3, 5.6 Hz, 1H), 5.08 (d, *J* = 16.4 Hz, 1H), 5.04 (d, *J* = 16.4 Hz, 1H), 4.62 (ddd, *J* = 8.2, 8.2, 4.9 Hz, 1H), 4.54 (d, *J* = 5.6 Hz, 2H), 3.83 (s, 6H), 3.73–3.67 (m, 1H), 3.70 (s, 3H), 3.57 (dd, *J* = 14.0, 11.3 Hz, 1H), 1.64–1.60 (m, 2H), 1.54–1.50 (m, 1H), 0.91 (d, *J* = 2.8 Hz, 3H), 0.90 (d, *J* = 2.8 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.8 (C_q), 168.3 (C_q), 167.7 (C_q), 164.8 (C_q), 159.2 (C_q), 158.6 (C_q), 144.9 (C_q), 143.6 (C_q), 139.3 (C_q), 136.2 (C_q), 134.6 (CH), 133.8 (C_q), 133.0 (C_q), 131.4 (C_q), 130.8 (CH), 130.6 (CH), 129.2 (CH), 129.0 (CH), 124.2 (CH), 123.7 (CH), 122.0 (CH), 120.8 (CH), 115.9 (CH), 114.7 (CH), 55.5 (CH_3), 52.9 (CH_2), 52.7 (CH), 51.3 (CH_3), 41.3 (CH_2), 35.5 (CH_2), 34.9 (CH_2), 28.1 (CH), 25.1 (CH), 23.0 (CH_3), 22.1 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$):

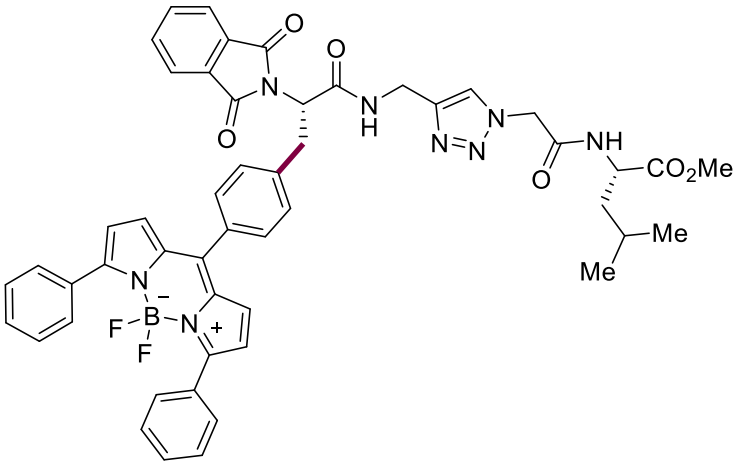
δ = -132.30 (q, $J_{B\text{-}F}$ = 31.9 Hz). **IR** (ATR): $\tilde{\nu}$ = 2927, 2160, 2034, 1543, 446, 394 cm^{-1}. **MS** (ESI) m/z (relative intensity): 985 (100) $[M+Na]^+$, 963 (30) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{52}H_{50}BF_2N_8O_8$ $[M+H]^+$: 963.3816; found: 963.3822. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 556 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 588 nm.



Methyl[2-(4-{[(*S*)-3-(4-{5,5-difluoro-3,7-di-p-tolyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl) acetyl]-*L*-leucinate (111c)

The general procedure **C** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (48.4 mg, 0.1 mmol), iodo-BODIPY **109m** (69.0 mg, 0.12 mmol) and AgOAc (33.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 41.0 min) yielded **111c** (42.0 mg, 45%) as a purple solid (M.p.: 151–152 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.77 (dd, J = 5.5, 3.0, 2H), 7.76 (d, J = 8.1 Hz, 2H), 7.75 (d, J = 8.2 Hz, 4H), 7.71 (dd, J = 5.5, 3.0 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 7.27–7.26 (m, 1H), 7.21 (d, J = 8.2Hz, 4H), 7.11 (dd, J = 5.7, 5.7 Hz, 1H), 6.66 (d, J = 8.2 Hz, 1H), 6.57 (d, J = 4.2 Hz, 2H), 6.52 (d, J = 4.2 Hz, 2H), 5.17 (dd, J = 11.2, 5.6 Hz, 1H), 5.06 (d, J = 16.4 Hz, 1H), 4.99 (d, J = 16.4 Hz, 1H), 4.65–4.59 (m, 1H), 4.55 (dd, J = 5.7, 5.7 Hz, 2H), 3.72–3.68 (m, 1H), 3.71 (s, 3H), 3.57 (dd, J = 13.9, 11.2 Hz, 1H), 2.37 (s, 6H), 1.65–1.58 (m, 2H), 1.57–1.53 (m, 1H), 0.91 (d, J = 3.4 Hz, 3H), 0.90 (d, J = 3.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.7 (C_q), 168.3 (C_q), 167.8 (C_q), 164.8 (C_q), 158.9 (C_q), 145.0 (C_q), 142.8 (C_q), 139.8 (C_q), 139.1 (C_q), 136.2 (C_q), 134.6 (CH), 133.2 (C_q), 131.4 (C_q), 130.8 (CH), 130.4 (CH), 129.8 (C_q), 129.4 (CH), 129.1 (CH), 129.0 (CH), 124.2 (CH), 123.7 (CH), 120.7 (CH),

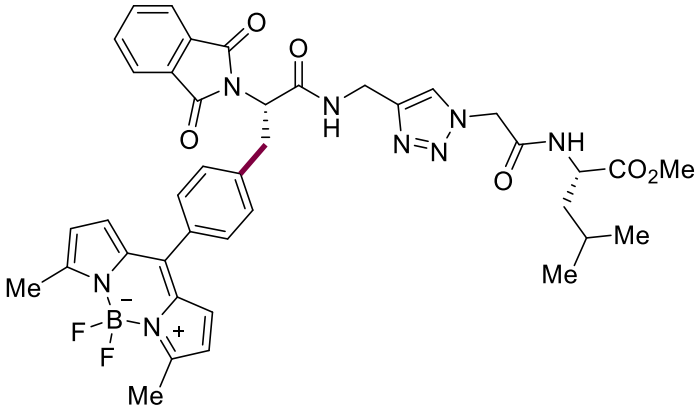
55.4 (CH), 52.9 (CH_2), 52.7 (CH), 51.3 (CH_3), 41.4 (CH_2), 35.5 (CH_2), 34.9 (CH_2), 25.1 (CH), 23.0 (CH_3), 22.1 (CH_3), 21.7 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -132.79 (q, $J_{B\text{-}F}$ = 31.9 Hz). **IR** (ATR): $\tilde{\nu}$ = 2052, 1957, 1067, 560, 526, 431, 407, 391 cm^{-1}. **MS** (ESI) m/z (relative intensity): 953 (100) $[M+Na]^+$, 931 (10) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{52}H_{50}BF_2N_8O_6$ $[M+H]^+$: 931.3918; found: 931.3929. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 560 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 591 nm.



Methyl[2-(4-{[(*S*)-3-(4-{5,5-difluoro-3,7-diphenyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl) acetyl]-*L*-leucinate (111d)

The general procedure **C** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (48.4 mg, 0.1 mmol), iodo-BODIPY **109b** (65.5 mg, 0.12 mmol) and Ag_2CO_3 (27.5 mg, 0.10 mmol). After 20 h, purification by HPLC (tr: 41.0 min) yielded **111d** (45.0 mg, 50%) as a purple solid (M.p.: 144–145 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.82 (dd, *J* = 7.7, 1.9 Hz, 4H), 7.79 (s, 1H), 7.74 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.70 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.42–7.37 (m, 6H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.24 (s, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.57 (d, *J* = 4.3 Hz, 2H), 6.52 (d, *J* = 4.3 Hz, 2H), 5.18 (dd, *J* = 11.1, 5.3 Hz, 1H), 5.06 (d, *J* = 16.4 Hz, 1H), 4.98 (d, *J* = 16.4 Hz, 1H), 4.61 (ddd, *J* = 8.4, 8.4, 4.9 Hz, 1H), 4.53–4.51 (m, 2H), 3.71 (dd, *J* = 14.0, 5.3 Hz, 1H), 3.72 (s, 3H), 3.58 (dd, *J* = 14.0, 11.1 Hz, 1H), 1.63–1.56 (m, 2H), 1.54–1.51 (m, 1H), 0.91 (d, *J* = 3.2 Hz, 3H), 0.90 (d, *J* = 3.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.9 (C_q), 168.3 (C_q), 167.7 (C_q), 164.9 (C_q), 158.9 (C_q), 144.9 (C_q), 143.6 (C_q), 139.3 (C_q), 136.3 (C_q), 134.5 (CH), 133.0 (C_q), 132.6 (C_q), 131.4 (C_q), 130.8 (CH), 130.6 (CH),

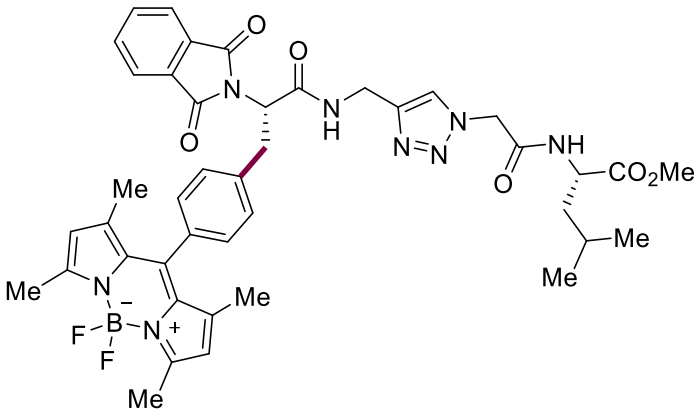
129.6 (CH), 129.5 (CH), 129.0 (CH), 128.3 (CH), 124.3 (CH), 123.6 (CH), 120.9 (CH), 55.2 (CH), 52.7 (CH_2), 52.5 (CH), 51.1 (CH_3), 41.1 (CH_2), 35.2 (CH_2), 34.7 (CH_2), 24.9 (CH), 22.8 (CH_3), 21.9 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -132.57 (q, $J_{B\text{-}F}$ = 31.7 Hz). **IR** (ATR): $\tilde{\nu}$ = 1713, 1538, 1467, 1449, 1269, 1135, 1067, 718, 693, 404 cm^{-1}. **MS** (ESI) m/z (relative intensity): 925 (100) [M+Na]+, 903 (20) [M+H]+. **HR-MS** (ESI): m/z calcd for $C_{50}H_{46}BF_2N_8O_6$ $[M+H]^+$: 903.3604; found: 903.3610. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 550 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 579 nm.



Methyl[2-(4-{[(*S*)-3-(4-{5,5-difluoro-3,7-dimethyl-5*H*-4λ4,5λ4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl) acetyl]-*L*-leucinate (111e)

The general procedure **C** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (48.4 mg, 0.1 mmol), iodo-BODIPY **109c** (51.0 mg, 0.12 mmol) and AgOAc (33.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 41.0 min) yielded **111e** (31.2 mg, 40%) as an orange solid (M.p.: 154–155 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.77 (s, 1H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.67 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.30 (brs, 1H), 7.22 (d, *J* = 8.5 Hz, 2H), 7.19 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 7.9 Hz, 1H), 6.40 (d, *J* = 4.1 Hz, 2H), 6.18 (d, *J* = 4.1 Hz, 2H), 5.14 (dd, *J* = 11.2, 5.5 Hz, 1H), 5.07 (d, *J* = 16.4 Hz, 1H), 5.00 (d, *J* = 16.4 Hz, 1H), 4.59–4.54 (m, 1H), 4.52–4.49 (m, 2H), 3.66 (s, 3H), 3.69–3.63 (m, 1H), 3.53 (dd, *J* = 13.9, 11.3 Hz, 1H), 2.60 (s, 6H), 1.63–1.60 (m, 2H), 1.59–1.53 (m, 1H), 0.90 (d, *J* = 2.6 Hz, 3H), 0.89 (d, *J* = 2.6 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 173.1 (C_q), 168.5 (C_q), 167.9 (C_q), 165.1 (C_q), 157.6 (C_q), 142.1 (C_q), 139.1 (C_q), 134.5 (CH), 134.4 (C_q), 134.0 (C_q), 132.8 (C_q), 131.4 (C_q), 130.6 (CH), 130.3 (CH), 129.1 (CH), 129.0 (CH), 123.6 (CH), 119.4 (CH), 55.2 (CH), 52.8 (CH_2), 52.6

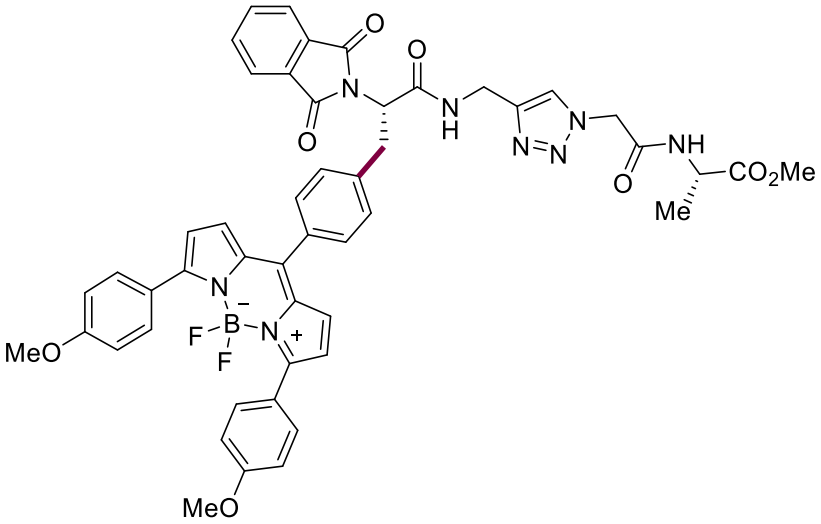
(CH_3), 51.2 (CH), 41.2 (CH_2), 35.2 (CH_2), 34.6 (CH_2), 25.0 (CH_3), 22.9 (CH), 21.9 (CH_3), 15.0 (CH_3). **^{19}F NMR** (471 MHz, $CDCl_3$): δ = -147.62 (q, $J_{B\text{-}F}$ = 32.1 Hz). **IR** (ATR): $\tilde{\nu}$ = 1979, 1971, 1715, 1676, 1541, 1271, 1148, 402, 392 cm^{-1}. **MS** (ESI) m/z (relative intensity): 801 (100) $[M+Na]^+$, 779 (20) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{40}H_{42}BF_2N_8O_6$ $[M+H]^+$: 779.3290; found: 779.3295. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 508 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 523 nm.



Methyl[2-(4-{[(*S*)-3-(4-{5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1*H*-1,2,3-triazol-1yl)acetyl]-*L*-leucinate (111f)

The general procedure **C** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Leu-OMe (**107c**) (48.4 mg, 0.1 mmol), iodo-BODIPY **109a** (54.0 mg, 0.12 mmol) and AgOAc (33.3 mg, 0.20 mmol). After 20 h, purification by HPLC (tr: 41.0 min) yielded **111f** (38.0 mg, 47%) as an orange solid (M.p.: 143–144 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.76 (s, 1H), 7.73 (dd, J = 5.5, 3.3 Hz, 2H), 7.69 (dd, J = 5.5, 3.3 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 7.13 (dd, J = 5.9, 5.6 Hz, 1H), 7.05 (d, J = 8.1 Hz, 2H), 6.72 (d, J = 8.3 Hz, 1H), 5.88 (s, 2H), 5.21–5.17 (m, 1H), 5.08 (d, J = 16.4 Hz, 1H), 5.02 (d, J = 16.4 Hz, 1H), 4.63–4.57 (m, 1H), 4.54 (dd, J = 12.2, 5.6 Hz, 1H), 4.52 (dd, J = 12.2, 5.9 Hz, 1H), 3.69 (s, 3H), 3.64–3.61 (m, 2H), 2.50 (s, 6H), 1.67–1.55 (m, 2H), 1.54–1.50 (m, 1H), 1.05 (s, 6H), 0.90 (d, J = 2.5 Hz, 3H), 0.89 (d, J = 2.5 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.8 (C_q), 168.23 (C_q), 167.6 (C_q), 164.8 (C_q), 155.5 (C_q), 144.9 (C_q), 142.9 (C_q), 141.2 (C_q), 137.8 (C_q), 134.5 (CH), 133.7 (C_q), 131.3 (C_q), 131.3 (C_q), 129.8 (CH), 128.3 (CH), 124.2 (CH), 123.6 (CH), 121.2 (CH), 55.4 (CH), 52.9 (CH_2), 52.7 (CH_3), 51.3 (CH), 41.4 (CH_2), 35.5 (CH_2), 34.6 (CH_2), 25.1 (CH), 22.9 (CH_3), 22.1 (CH_3), 14.8 (CH_3),

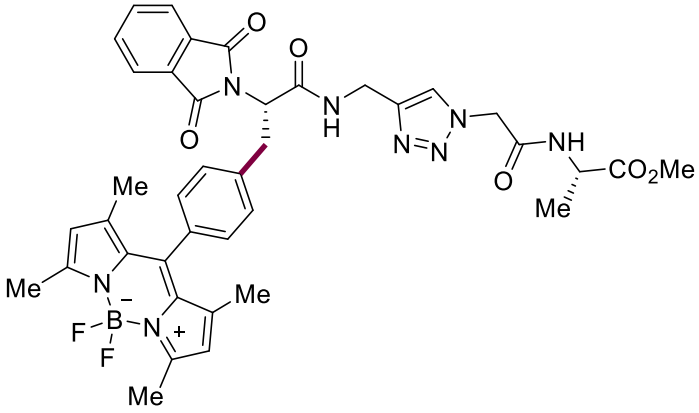
14.4 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -146.40 (q, $J_{B\text{-}F}$ = 30.6 Hz). **IR** (ATR): $\tilde{\nu}$ = 1714, 1541, 1509, 1382, 1188, 1155, 1085, 977, 717, 476 cm^{-1}. **MS** (ESI) m/z (relative intensity): 829 (100) $[M+Na]^+$, 807 (80) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{42}H_{46}BF_2N_8O_6$ $[M+H]^+$: 807.3603; found: 807.3600. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 498 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 510 nm.



Methyl[2-(4-{[(*S*)-3-(4-{5,5-difluoro-3,7-bis(4-methoxyphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1*H*-1,2,3triazol-1-yl)acetyl]-*L*-alaninate (111g)

The general procedure **C** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Ala-OMe (**107b**) (44.2 mg, 0.1 mmol), iodo-BODIPY **109j** (72.7 mg, 0.12 mmol), $Pd(OAc)_2$ (20 mol %) in DCE (0.5 mL). After 20 h, purification by HPLC (tr: 41.0 min) yielded **111g** (82.8 mg, 90%) as a purple solid (M.p.: 150–151 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.84 (d, J = 9.8 Hz, 4H), 7.77–7.69 (m, 5H), 7.31(d, J = 8.1 Hz, 2H), 7.25(d, J = 8.1 Hz, 2H), 7.19 (dd, J = 5.7, 5.7 Hz, 1H), 6.93(d, J = 9.8 Hz, 4H), 6.80 (d, J = 7.2 Hz, 1H), 6.53 (s, 4H), 5.17 (dd, J = 11.2, 5.5 Hz, 1H), 5.05 (d, J = 16.5 Hz, 1H), 5.01 (d, J = 16.5 Hz, 1H), 4.57 (dddd, J = 7.2, 7.2, 7.2, 7.2 Hz, 1H), 4.54–4.52 (m, 2H), 3.84 (s, 6H), 3.73 (s, 3H), 3.72–3.68 (m, 1H), 3.56 (dd, J = 14.0, 11.2 Hz, 1H), 1.39 (d, J = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.7 (C_q), 168.4 (C_q), 167.8 (C_q), 164.6 (C_q), 160.8 (C_q), 158.3 (C_q), 141.9 (C_q), 139.0 (C_q), 136.2 (C_q), 134.5 (CH), 133.3 (C_q), 131.4 (C_q), 131.1 (CH), 130.8 (CH), 130.1 (CH), 129.0 (CH), 125.2 (C_q), 124.3 (C_q), 123.6 (CH), 120.5 (CH), 113.9 (CH), 113.6 (CH), 55.5 (CH), 55.4 (CH), 52.9 (CH_2), 52.8 (CH_3),

48.6 (CH_3), 35.5 (CH_2), 34.9 (CH_2), 18.2 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -133.03 (q, $J_{B\text{-}F}$ = 32.5 Hz). **IR** (ATR): $\tilde{\nu}$ = 2033, 1993, 1716, 1547, 1467, 1258, 1141, 1071, 795, 490, 394 cm^{-1}. **MS** (ESI) m/z (relative intensity): 943 (100) $[M+Na]^+$, 921 (20) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{49}H_{44}BF_2N_8O_8$ $[M+H]^+$: 921.3346; found: 921.3352. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 576 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 611 nm.

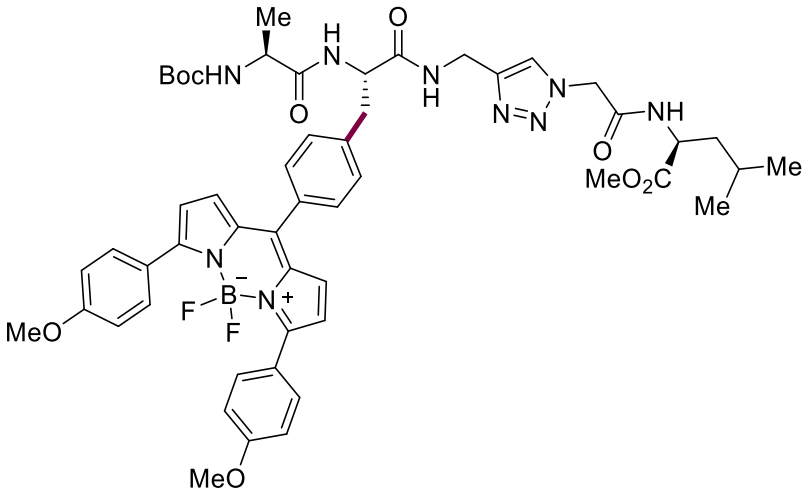


Methyl[2-(4-{[(S)-3-(4-{5,5-difluoro-1,3,7,9-tetramethyl-5H-4λ4,5λ4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl)propanamido]methyl}-1H-1,2,3triazol-1-yl)acetyl]-L-alaninate (111h)

The general procedure **C** was followed using Phth*N*-Ala-Gly-Tzl-Gly-Ala-OMe (**107b**) (44.2 mg, 0.1 mmol), iodo-BODIPY **109a** (54.0 mg, 0.12 mmol), AgOAc (33.3 mg, 0.20 mmol) and $Pd(OAc)_2$ (20 mol %) in DCE (0.5 mL) as solvent. After 20 h, purification by HPLC (tr: 41.0 min) yielded **111h** (42.0 mg, 55%) as an orange solid (M.p.: 151–152 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.76 (s, 1H), 7.72 (dd, J = 5.5, 3.0 Hz, 2H), 7.69 (dd, J = 5.5, 3.0 Hz, 2H), 7.26 (s, 1H), 7.24 (d, J = 8.1 Hz, 2H), 7.04 (d, J = 8.1 Hz, 2H), 6.90 (d, J = 7.3 Hz, 1H), 5.88 (s, 2H), 5.18 (dd, J = 10.9, 6.3 Hz, 1H), 5.06 (d, J = 16.4 Hz, 1H), 5.00 (d, J = 16.4 Hz, 1H), 4.55 (dddd, J = 7.3, 7.3, 7.3, 7.3 Hz, 1H), 4.51–4.49 (m, 2H), 3.70 (s, 3H), 3.66–3.58 (m, 2H), 2.49 (s, 6H), 1.39 (d, J = 7.3 Hz, 3H), 1.04 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.8 (C_q), 168.4 (C_q), 167.6 (C_q), 164.6 (C_q), 155.5 (C_q), 144.9 (C_q), 142.9 (C_q), 141.3 (C_q), 137.9 (C_q), 134.5 (CH), 133.7 (C_q), 131.3 (C_q), 129.8 (CH), 128.3 (CH), 124.3 (CH), 123.6 (CH), 121.2 (CH), 121.0 (C_q), 55.3 (CH), 52.9 (CH_2), 52.8 (CH), 48.6 (CH_3), 35.4 (CH_2), 34.6 (CH_2), 18.2 (CH_3), 14.8 (CH_3), 14.4 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -146.38 (q, $J_{B\text{-}F}$ = 31.5 Hz). **IR** (ATR): $\tilde{\nu}$ = 2068, 2036, 1990, 1715, 1543, 526, 424, 388 cm^{-1}. **MS** (ESI) m/z (relative intensity):

787 (100) $[M+Na]^+$, 765 (10) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{39}H_{40}BF_2N_8O_6$ $[M+H]^+$: 765.3133; found: 765.3126. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 498 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 510 nm.

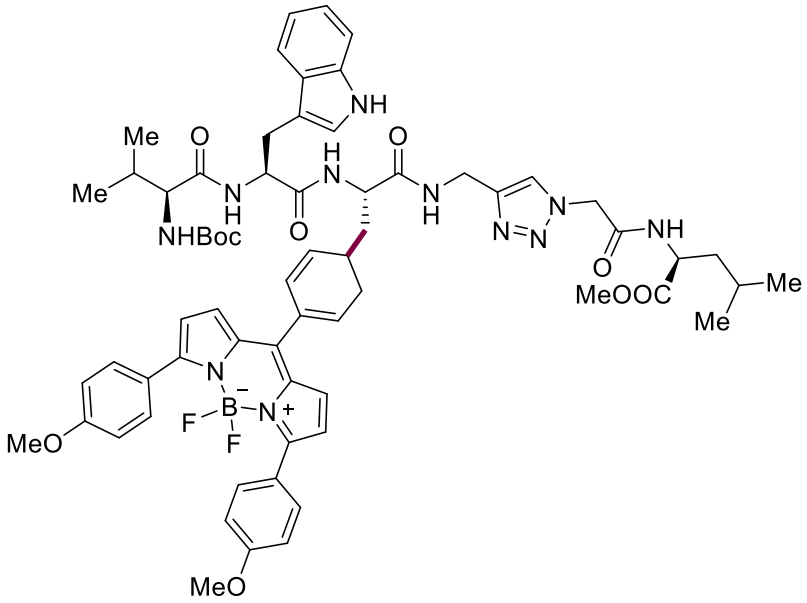
5.3.2.3 Procedure and Characterization Data of Sequentially Synthized BODIPY Peptides



Methyl-[2-(4-{[(*S*)-2-{(*S*)-2-[(tert-butoxycarbonyl)amino]propanamido}-3-(4-{5,5-difluoro-3,7bis(4-methoxyphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl) propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetyl]-*L*-leucinate (111i)

The compound **111a** (192 mg, 0.2 mmol) was dissolved in EtOH/CH_2Cl_2 (0.4 mL/ 0.4 mL). Ethylenediamine (0.1 mL) was then added dropwise. The mixture was sealed and heated at 40 °C for 4h. Then, the mixture was cooled to ambient temperature. H_2O (2.0 mL) was added, and the solution was extracted with CH_2Cl_2 (3 × 5.0 mL). The organic phase was concentrated *in vacuo*. The crude amine was then dissolved in DMF (5.0 mL). At 0 °C, Boc-Ala-OH (0.2 mmol) was added, followed by DIPEA (2.5 equiv.), HOBt (1.1 equiv.) and EDC·HCl (1.1 equiv.). The mixture was stirred for 16 h at 25 °C. Purification by column chromatography on silica gel delivered hexapeptide **111i** as a purple solid (80 mg, 40% yields for two steps) (M.p.: 165–166 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.9 Hz, 4H), 7.85 (brs, 1H), 7.70 (s, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.31(brs, 1H), 6.97 (s, 1H), 6.95 (s, 1H), 6.94 (d, *J* = 8.9 Hz, 4H), 6.78 (d, *J* = 4.3 Hz, 2H), 6.59 (d, *J* = 4.3 Hz, 2H), 5.07 (d, *J* = 5.7 Hz, 1H), 4.99 (s, 2H), 4.83 (dd, *J* = 7.5, 6.3 Hz, 1H), 4.59–4.55 (m, 1H), 4.52 (d, *J* = 5.7

Hz, 2H), 4.16–4.09 (m, 1H), 3.84 (s, 6H), 3.69 (s, 3H), 3.30 (dd, *J* = 13.9, 6.3 Hz, 1H), 3.15 (dd, *J* = 13.9, 7.5 Hz, 1H), 1.40 (s, 9H), 1.28 (d, *J* = 7.1 Hz, 3H), 1.25–1.21 (m, 2H), 0.89 (d, *J* = 2.8 Hz, 3H), 0.88 (d, *J* = 2.8 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): *δ* = 173.0 (C_q), 172.9 (C_q), 170.8 (C_q), 165.1 (C_q), 160.9 (C_q), 158.4 (C_q), 156.0 (C_q), 145.0 (C_q), 142.1 (C_q), 139.1 (C_q), 136.2 (C_q), 133.3 (C_q), 131.3 (CH), 131.0 (CH), 130.5 (CH), 129.3 (CH), 125.2 (C_q), 124.2 (CH), 120.7 (CH), 113.9 (CH), 55.6 (CH_3), 55.4 (CH_3), 54.1 (CH), 52.61 (CH), 52.59 (C_q), 51.3 (CH), 41.2 (CH_2), 37.9 (CH_2), 36.4 (CH_2), 35.3 (CH_2), 28.4 (CH_3), 27.9 (CH), 25.0 (CH_3), 22.8 (CH_3), 22.0 (CH_3). **^{19}F NMR** (471 MHz, $CDCl_3$): *δ* = -132.86 (q, $J_{B\text{-}F}$ = 32.0 Hz). **IR** (ATR): $\tilde{\nu}$ = 1640, 1541, 1463, 1432, 1253, 1137, 1070, 1054, 790, 714 cm^{-1}. **MS** (ESI) m/z (relative intensity): 1026 (100) $[M+Na]^+$, 1004 (80) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{52}H_{61}BF_2N_9O_9$ $[M+H]^+$: 1004.4657; found: 1004.4639. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 576 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 610 nm.

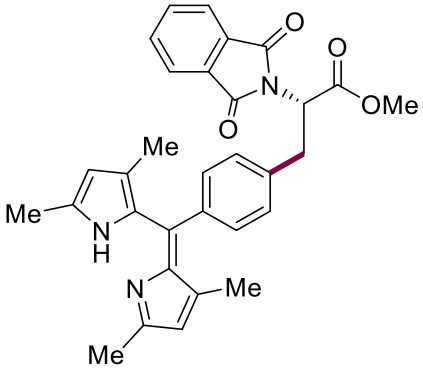


Methyl[2-(4-{[(*S*)-2-[(*S*)-2-{(*S*)-2-[(tert-butoxycarbonyl)amino]-3-methylbutanamido}-3-(1Hindol-3-yl)propanamido]-3-(4-{5,5-difluoro-3,7-bis(4-methoxyphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetyl]-*L*-leucinate (111j)

The compound **111a** (192 mg, 0.2 mmol) was dissolved in EtOH/CH_2Cl_2 (0.4 mL/ 0.4 mL). Ethylenediamine (0.1 mL) was added dropwise. The mixture was sealed and heated at 40 °C for 4h. After completion of the reaction, the mixture was cooled to ambient temperature. H_2O

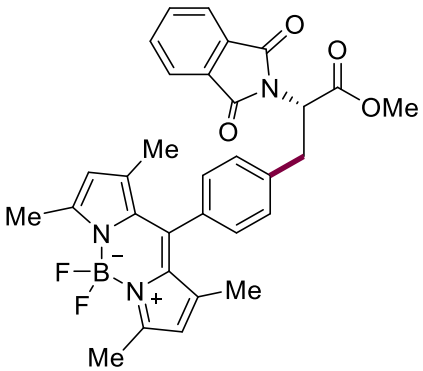
(2.0 mL) was added, and the solution was extracted with CH_2Cl_2 (3 × 5.0 mL). The organic phase was concentrated *in vacuo*. The crude amine was then dissolved in DMF (5.0 mL). At 0 °C, Boc-Val-Trp-OH (0.2 mmol) was added, followed by DIPEA (2.5 equiv.), HOBt (1.1 equiv.) and EDC·HCl (1.1 equiv.). The mixture was stirred for 16 h at 25 °C. Purification by column chromatography on silica gel delivered heptapeptide **111j** as a purple solid (97 mg, 41% yields over two steps) (M.p.: 163–164 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.86 (brs, 1H), 7.84 (d, J = 8.4 Hz, 4H), 7.69 (s, 1H), 7.63 (s, 1H), 7.43–7.41 (m, 2H), 7.30 (s, 1H), 7.24–7.20 (m, 2H), 7.16–7.14 (m, 2H), 7.10–7.00 (m, 3H), 6.94 (s, 1H), 6.93 (d, J = 8.4 Hz, 4H), 6.88 (s, 1H), 6.78 (s, 2H), 6.55 (s, 2H), 5.11–4.90 (m, 2H), 4.82–4.71 (m, 1H), 4.58–3.91 (m, 2H), 3.84 (s, 6H), 3.68 (s, 3H), 3.31–3.22 (m, 1H), 3.26–3.10 (m, 2H), 3.00–2.90 (m, 1H), 2.11–1.98 (m, 1H), 1.66–1.59 (m, 2H), 1.56–1.52 (m, 1H), 1.52–1.50 (m, 1H), 1.46–1.44 (m, 1H), 1.43–1.39 (m, 2H), 1.36 (s, 9H), 0.99–0.81 (m, 12H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.9 (C_q), 172.1 (C_q), 171.6 (C_q), 170.6 (C_q), 165.3 (C_q), 160.9 (CH), 160.7 (C_q), 158.3 (C_q), 156.4 (C_q), 145.1 (C_q), 142.2 (C_q), 139.4 (C_q), 136.3 (C_q), 136.2 (C_q), 133.0 (C_q), 131.6 (CH), 131.2 (CH), 130.8 (CH), 130.4 (CH), 129.1 (CH), 127.3 (C_q), 125.2 (C_q), 122.4 (CH), 120.6 (CH), 119.9 (CH), 118.3 (CH), 113.9 (CH), 111.9 (CH), 109.6 (C_q), 55.6 (CH), 55.5 (CH_3), 53.9 (CH_3), 52.7 (CH_3), 51.5 (CH), 46.1 (C_q), 41.2 (CH_2), 39.0 (CH_2), 38.1 (CH_2), 36.7 (CH_2), 36.5 (CH_2), 28.5 (CH), 28.1 (CH), 25.1 (CH_3), 22.9 (CH_3), 22.1 (CH_3), 19.5 (CH_3), 18.9 (CH), 17.9 (CH). **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -132.94 (q, $J_{B\text{-}F}$ = 32.0 Hz). **IR** (ATR): $\tilde{\nu}$ = 1633, 1541, 1463, 1432, 1254, 1178, 1139, 1070, 1055, 793, 739 cm^{-1}. **MS** (ESI) m/z (relative intensity): 1240 (30) $[M+Na]^+$, 1218 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{65}H_{75}BF_2N_{11}O_{10}$ $[M+H]^+$: 1218.5765; found: 1218.5753. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 576 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 610 nm.

5.3.2.4 Procedure and Characterization Data of TAM/PG Removed BODIPY Amino Acids and Peptides



Methyl(*S,Z*)-3-{4-[(3,5-dimethyl-1*H*-pyrrol-2-yl)(3,5-dimethyl-2*H*-pyrrol-2-ylidene)methyl] phenyl}-2-(1,3-dioxoisoindolin-2-yl)propanoate (110aaa)

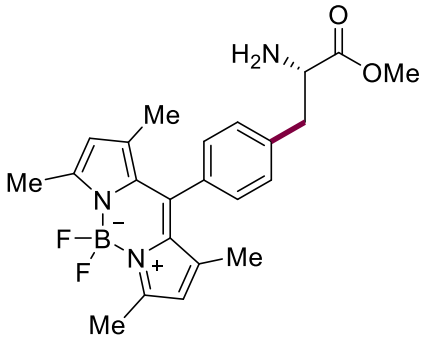
In a pressure tube, **110aa** (74 mg, 0.10 mmol) was dissolved in dry MeOH (2.0 mL). $Et_2O{\cdot}BF_3$ (15 equiv) was added dropwise at 0 °C. The solution was stirred at 130 °C for 16 h. Then, the solvent was removed in vacuo and the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc 1/2) to yield **110aaa** (45 mg, 88%) as an orange solid (M.p.: 209–210 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.69 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 5.79 (s, 2H), 5.22 (dd, *J* = 10.9, 6.5 Hz, 1H), 3.81 (s, 3H), 3.68–3.60 (m, 2H), 2.30 (s, 6H), 1.00 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 169.3 (C_q), 167.4 (C_q), 151.6 (C_q), 140.31 (C_q), 138.4 (C_q), 136.9 (C_q), 136.8 (C_q), 136.3 (C_q), 134.3 (CH), 131.6 (C_q), 129.5 (CH), 129.4 (CH), 123.6 (CH), 119.6 (CH), 53.2 (CH), 53.1 (CH_3), 34.6 (CH_2), 16.1 (CH_3), 14.4 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1740, 1711, 1386, 1366, 1274, 1096, 941, 717, 703, 530 cm^{-1}. **MS** (ESI) m/z (relative intensity): 508 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{31}H_{30}N_3O_4$ $[M+H]^+$: 508.2231; found: 508.2216. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 442 nm.



Methyl-(*S*)-3-(4-{5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-

f][1,3,2]diaza borinin-10-yl}phenyl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (110aab)

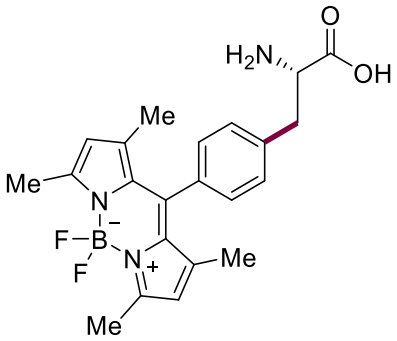
In a 100 mL flask, **110aaa** (51 mg, 0.10 mmol) was dissolved in dry CH_2Cl_2 (10 mL) at 25 °C. Et_3N (10 equiv) was then added and the solution was stirred for 10 min. $Et_2O{\cdot}BF_3$ (15 equiv) was then added dropwise. The solution was stirred at 25 °C for 4 h. The solvent was removed in vacuo and the crude product was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2 5/1) to yield **110aab** (47 mg, 85%) as an orange solid (M.p.: 296–297 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.75 (dd, *J* = 5.6, 3.0 Hz, 2H), 7.70 (dd, *J* = 5.6, 3.0 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 5.89 (s, 2H), 5.20 (dd, *J* = 11.4, 5.7 Hz, 1H), 3.81 (s, 3H), 3.66 (dd, *J* = 14.0, 5.7 Hz, 1H),3.61 (dd, *J* = 14.0, 5.7 Hz, 1H), 2.50 (s, 6H), 1.09 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 169.2 (C_q), 167.3 (C_q), 155.5 (C_q), 143.1 (C_q), 141.4 (C_q), 137.9 (C_q), 134.4 (CH), 133.8 (C_q), 131.5 (C_q), 131.4 (C_q), 129.9 (CH), 128.3 (CH), 123.6 (CH), 121.3 (CH), 53.17 (CH), 53.16 (CH_3), 34.6 (CH_2), 14.7 (CH_3), 14.3 (CH_3). **^{19}F NMR** (471 MHz, $CDCl_3$): δ = -146.39 (q, $J_{B\text{-}F}$ = 32.3 Hz). **IR** (ATR): $\tilde{\nu}$ = 1922, 1958, 1717, 1543, 1508, 510, 431, 402, 390 cm^{-1}. **MS** (ESI) m/z (relative intensity): 578 (100) $[M+Na]^+$, 556 (30) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{31}H_{29}BF_2N_3O_4$ $[M+H]^+$: 556.2219; found: 556.2227. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 498 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 510 nm.



Methyl-(*S*)-2-amino-3-(4-{5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f] [1,3,2]diazaborinin-10-yl}phenyl)propanoate (110aac)

110aab (55 mg, 0.10 mmol) was dissolved in a 1/1 mixture of CH_2Cl_2/EtOH (3.0 mL). Ethylenediamine (10 equiv) was added dropwise. The solution was stirred at 40 °C for 4 h. At ambient temperature, the solvent was removed *in vacuo* and the crude product was purified by column chromatography on silica gel (CH_2Cl_2/MeOH 50/1) to yield **110aac** (22 mg, 50%) as an orange solid (M.p.: 142–143 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 8.1

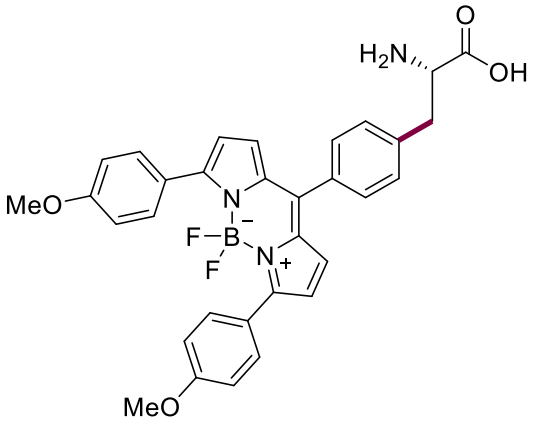
Hz, 2H), 7.21 (d, *J* = 8.1 Hz, 2H) 5.97 (s, 2H), 3.78 (dd, *J* = 6.9, 6.2 Hz, 1H), 3.67 (s, 3H), 3.10 (dd, *J* = 13.4, 6.2 Hz, 1H), 3.00 (dd, *J* = 13.4, 6.9 Hz, 1H), 2.55 (s, 6H), 1.37 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): *δ* = 175.3 (C_q), 155.6 (C_q), 143.1 (C_q), 141.6 (C_q), 138.3 (C_q), 133.7 (C_q), 131.6 (C_q), 130.2 (CH), 128.3 (CH), 121.3 (CH), 56.0 (CH), 52.1 (CH_3), 41.3 (CH_2), 14.7 (CH_3), 14.5 (CH_3). **^{19}F NMR** (471 MHz, $CDCl_3$): *δ* = -146.32 (q, $J_{B\text{-}F}$ = 32.5 Hz). **IR** (ATR): $\tilde{\nu}$ = 2036, 1968, 1543, 1508, 1193, 432, 389, 382 cm^{-1}. **MS** (ESI) m/z (relative intensity): 448 (10) $[M+Na]^+$, 426 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{23}H_{27}BF_2N_3O_2$ $[M+H]^+$: 426.2163; found: 426.2173. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 500 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 512 nm.



(*S*)-2-Amino-3-{4-(5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2] diazaborinin-10-yl)phenyl}propanoic acid (110aa')

In a 25 mL round bottom flask, NH_2-Ala-(BODIPY)-OMe **110aac** (42.5 mg, 0.10 mmol) was dissolved in dry MeOH (2.0 mL). LiOH (2N solution, 0.15 mL) was added dropwise at 0 °C. The solution was stirred at 28 °C for 16 h. HCl (4 N solution in dioxane, 75 µL) was then added dropwise at 0 °C. The resulting solution was stirred for 1 min. The solvent was removed in vacuo and the crude product was washed by *n*-hexane, ethyl acetate, suspended in 0.5 mL water, filtered and dried under vacuum to yield **110aa'** (39 mg, 92%) as an orange solid (M.p.: 280–281 °C). **^{1}H NMR** (600 MHz, CD_3OD): *δ* = 7.48 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 6.04 (s, 2H), 3.85 (dd, *J* = 7.6, 5.1 Hz, 1H), 3.33 (dd, *J* = 14.4, 5.1 Hz, 1H), 3.16 (dd, *J* = 14.4, 7.6 Hz, 1H), 2.47 (s, 6H), 1.42 (s, 6H). **^{13}C NMR** (126 MHz, CD_3OD): *δ* = 173.2 (C_q), 156.5 (C_q), 144.6 (C_q), 143.1 (C_q), 138.6 (C_q), 135.0 (C_q), 132.5 (C_q), 131.3 (CH), 129.6 (CH), 122.1 (CH), 57.1 (CH), 38.1 (CH_2), 14.9 (CH_3), 14.6 (CH_3). **^{19}F NMR** (471 MHz, CD_3OD): *δ* = -147.05 (q, $J_{B\text{-}F}$ = 32.1 Hz). **IR** (ATR): $\tilde{\nu}$ = 1629, 1540, 1505, 1469, 1303, 1153, 1080, 972,

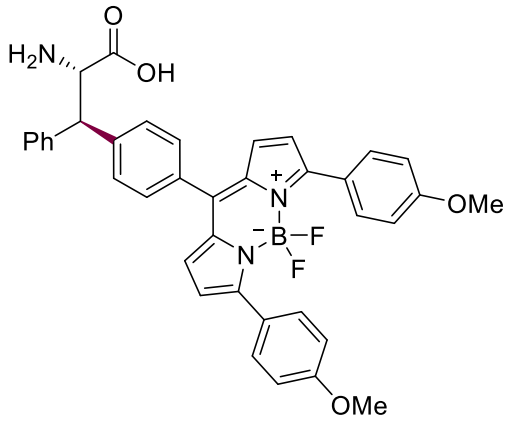
476 cm^{-1}. **MS** (ESI) m/z (relative intensity): 412 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{22}H_{25}BF_2N_3O_2$ $[M+H]^+$: 412.2006; found: 412.2004. **UV-Vis λ_{max}** (1.0 mg/L in MeOH) = 498 nm. **Em λ_{max}** (1.0 mg/L in MeOH) = 512 nm.



(*S*)-2-Amino-3-{4-(5,5-difluoro-3,7-bis(4-methoxyphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f] [1,3,2]diazaborinin-10-yl)phenyl}propanoic acid (110bg')

In a pressure tube, **110bg** (89 mg, 0.10 mmol) was dissolved in dry MeOH (2.0 mL). $Et_2O{\cdot}BF_3$ (15 equiv) was added dropwise at 0 °C. The solution was stirred at 130 °C for 16 h. Then, the solvent was removed in vacuo and the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc 1/2) to yield **110bga** (50 mg, 76%) as a red solid. In a 100 mL flask, **110bga** (66 mg, 0.10 mmol) was dissolved in dry Toluene (10 mL) at 25 °C. Et_3N (10 equiv) was then added and the solution was stirred for 10 min. $Et_2O{\cdot}BF_3$ (15 equiv) was then added dropwise. The solution was stirred at 80 °C for 30 min. The solvent was removed in vacuo and the crude product was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2 5/1) to yield **110bgb** (56 mg, 80%) as a dark purple solid. **110bgb** (71 mg, 0.10 mmol) was dissolved in a 1/1 mixture of CH_2Cl_2/EtOH (3.0 mL). Ethylenediamine (10 equiv) was added dropwise. The solution was stirred at 40 °C for 16 hours. At ambient temperature, the solvent was removed *in vacuo* and the crude product was purified by column chromatography on silica gel (CH_2Cl_2/MeOH 50/1) to yield **110bgc** (39 mg, 67%) as a purple oil. In a 25 mL round bottom flask, NH_2-Ala-(BODIPY)-OMe **110bgc** (50 mg, 0.086 mmol) was dissolved in dry MeOH (2.0 mL). LiOH (2N solution, 0.13 mL) was added dropwise at 0 °C. The solution was stirred at 28 °C for 24 h. HCl (4N solution in dioxane, 65 µL) was then

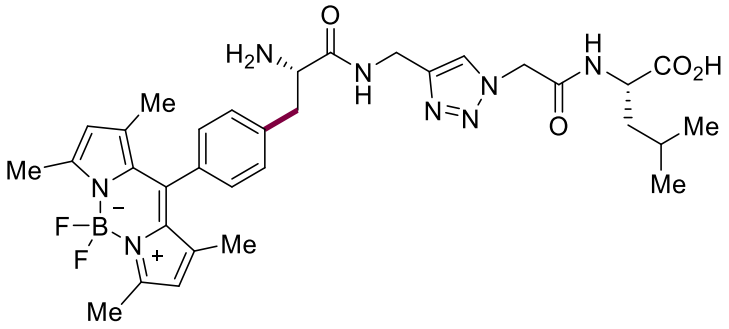
added dropwise at 0 °C. The resulting solution was stirred for 1 min. The solvent was removed *in vacuo* and the crude product was washed by *n*-hexane, ethyl acetate, suspended in 0.5 mL water, filtered and dried under vacuum to yield **110bg'** (39 mg, 89%) as a dark purple solid (M.p.: 220–221 °C). **^{1}H NMR** (400 MHz, CD_3OD): δ = 7.88 (d, J = 9.0 Hz, 4H), 7.60 (d, J = 8.1 Hz, 2H), 7.53 (d, J = 8.1 Hz, 2H), 6.98 (d, J = 9.0 Hz, 4H), 6.94 (d, J = 4.4 Hz, 2H), 6.72 (d, J = 4.4 Hz, 2H), 3.89 (dd, J = 8.2, 4.8 Hz, 1H), 3.86 (s, 6H), 3.43 (dd, J = 14.4, 4.8 Hz, 1H), 3.19 (dd, J = 14.4, 8.2 Hz, 1H). **^{13}C NMR** (126 MHz, CD_3OD): δ = 162.4 (C_q), 162.2 (C_q), 139.6 (C_q), 137.3 (C_q), 134.7 (C_q), 132.2 (CH), 132.1 (CH), 131.5 (C_q), 131.4 (CH), 130.4 (CH), 126.3 (C_q), 121.4 (CH), 114.6 (CH), 106.0 (C_q), 55.8 (CH), 38.1 (CH_2), 30.8 (CH_3). **^{19}F NMR** (375 MHz, CD_3OD): δ = -133.96 (q, $J_{B\text{-}F}$ = 32.3 Hz). **IR** (ATR): $\tilde{\nu}$ = 1605, 1570, 1545, 1466, 1433, 1259, 1142, 1073, 797 cm^{-1}. **MS** (ESI) m/z (relative intensity): 590 (100) $[M+Na]^+$, 568 (15) $[M+H]^+$, 1157 (10) $[2M+Na]^+$. **HR-MS** (ESI): m/z calcd for $C_{32}H_{29}BF_2N_3O_4$ $[M+H]^+$: 568.2219; found: 568.2215. **UV-Vis λ_{max}** (1.0 mg/L in MeOH) = 580 nm. **Em λ_{max}** (1.0 mg/L in MeOH) = 613 nm.



(2*S*,3*R*)-2-Amino-3-(4-{5,5-difluoro-3,7-bis(4-methoxyphenyl)-5H-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f] [1,3,2]diazaborinin-10-yl}phenyl)-3-phenylpropanoic acid (110bk')

In a pressure tube, **110bk** (97 mg, 0.10 mmol) was dissolved in dry MeOH (2.0 mL). $Et_2O{\cdot}BF_3$ (15 equiv) was added dropwise at 0 °C. The solution was stirred at 130 °C for 16 h. Then, the solvent was removed *in vacuo* and the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc 1/2) to yield **110bka** (48 mg, 65%) as a red solid. In a 100 mL flask, **110bka** (74 mg, 0.10 mmol) was dissolved in dry Toluene (10 mL) at 25 °C. Et_3N (10

equiv) was then added and the solution was stirred for 10 min. $Et_2O{\cdot}BF_3$ (15 equiv) was then added dropwise. The solution was stirred at 80 °C for 30 min. The solvent was removed *in vacuo* and the crude product was purified by column chromatography on silica gel (*n*-hexane/CH_2Cl_2 5/1) to yield **110bkb** (64 mg, 82%) as a purple solid. **110bkb** (79 mg, 0.10 mmol) was dissolved in a 1/1 mixture of CH_2Cl_2/EtOH (3.0 mL). Ethylenediamine (10 equiv) was added dropwise. The solution was stirred at 40 °C for 16 hours. At ambient temperature, the solvent was removed *in vacuo* and the crude product was purified by column chromatography on silica gel (CH_2Cl_2/MeOH 50/1) to yield **110bkc** (39 mg, 60%) as a purple oil. In a 10 mL round bottom flask, NH_2-Phe-(BODIPY)-OMe **110bkc** (35 mg, 0.05 mmol) was dissolved in dry MeOH (1.0 mL). LiOH (2N solution, 75 µL) was added dropwise at 0 °C. The solution was stirred at 28 °C for 24 h. HCl (4N solution in dioxane, 40 µL) was then added dropwise at 0 °C. The resulting solution was stirred for 1 min. The solvent was removed *in vacuo* and the crude product was washed by *n*-hexane, ethyl acetate, suspended in 0.5 mL water, filtered and dried under vacuum to yield **110bk'** (25 mg, 80%) as a dark purple solid (M.p.: 237–238 °C). **^{1}H NMR** (400 MHz, CD_3OD+15% DMSO-d_6): δ = 7.99–7.91 (m, 4H), 7.69–7.57 (m, 5H), 7.54–7.42 (m, 3H), 7.40 (d, J = 7.2 Hz, 1H), 7.11–7.05 (m, 4H), 7.01 (d, J = 4.4 Hz, 2H), 6.79 (d, J = 4.4 Hz, 2H), 4.50–4.37 (m, 2H), 3.92 (s, 6H). **^{13}C NMR** (126 MHz, CD_3OD): δ = 168.6 (C_q), 163.7 (C_q), 162.2 (C_q), 137.3 (C_q), 132.1 (CH), 132.0 (CH), 131.8 (C_q), 131.6 (C_q), 131.5 (C_q), 130.3 (CH), 129.8 (CH), 129.7 (CH), 129.4 (CH), 129.3 (C_q), 129.1 (CH), 127.1 (C_q), 126.2 (CH), 114.6 (CH), 55.8 (CH), 30.8 (CH), 23.8 (CH_3). **^{19}F NMR** (376 MHz, CD_3OD): δ = -133.95 (q, $J_{B\text{-}F}$ = 32.4 Hz). **IR** (ATR): $\tilde{\nu}$ = 1699, 1605, 1544, 1466, 1257, 1142, 1072, 1059, 716 cm^{-1}. **MS** (ESI) m/z (relative intensity): 666 (100) $[M+Na]^+$, 644 (10) $[M+H]^+$, 1309 (5) $[2M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{38}H_{33}BF_2N_3O_4$ $[M+H]^+$: 644.2533; found: 644.2538. **UV-Vis λ_{max}** (1.0 mg/L in MeOH) = 578 nm. **Em λ_{max}** (1.0 mg/L in MeOH) = 614 nm.



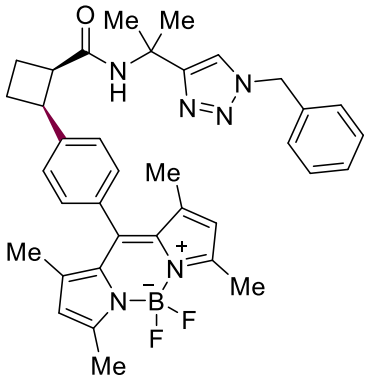
[2-(4-{[(*S*)-2-Amino-3-(4-{5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl}phenyl)propanamido]methyl}-1*H*-1,2,3-triazol-1-yl)acetyl]-*L*-leucine (111f')

Phth*N*-Ala^{BODIPY}-Gly-Tzl-Gly-Leu-OMe **111f** (0.1 mmol) was dissolved in a 1/1 mixture of CH_2Cl_2/EtOH (2.0 mL). Ethylenediamine (10 equiv) was added dropwise. The solution was stirred at 40 °C for 4 h. At ambient temperature, the solvent was removed *in vacuo* and the crude product was purified by column chromatography on silica gel (CH_2Cl_2/MeOH 50/1) to yield NH_2-Ala-(BODIPY)Gly-Tzl-Gly-Leu-OMe **111fa** (40 mg, 60%) as an orange oil. **111fa** (40 mg, 0.06 mmol) was then dissolved in dry MeOH (1.0 mL) and LiOH (2N solution, 90 µL) was added dropwise at 0 °C. The solution was stirred at 28 °C for 24 h. HCl (4N solution in dioxane, 45 µL) was then added dropwise at 0 °C. The resulting solution was stirred for 1 min. The solvent was removed *in vacuo* and the crude product was washed by *n*-hexane, ethyl acetate, dried under vacuum to yield **111fa'** (35 mg, 90%) as an orange solid (M.p.: 251–252 °C). **^{1}H NMR** (600 MHz, CD_3OD): δ = 8.03 (s, 1H), 7.39 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 6.04 (s, 2H), 5.12–5.08 (m, 2H), 4.55 (d, J = 15.4 Hz, 1H), 4.30 (dd, J = 10.4, 3.7 Hz, 1H), 4.08 (d, J = 15.4 Hz, 1H), 3.91–3.86 (m, 1H), 3.16–3.10 (m, 2H), 2.47 (s, 6H), 1.70–1.65 (m, 2H), 1.61–1.54 (m, 1H), 1.38 (s, 6H), 0.93 (d, J = 6.1 Hz, 3H), 0.91 (d, J = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, CD_3OD): δ = 179.3 (C_q), 172.1 (C_q), 166.9 (C_q), 156.5 (C_q), 145.8 (C_q), 144.4 (C_q), 143.0 (C_q), 138.2 (C_q), 135.1 (C_q), 132.4 (C_q), 131.4 (CH), 129.5 (CH), 125.7 (CH), 122.2 (CH), 56.5 (CH), 54.9 (CH_3), 53.6 (CH_2), 42.8 (CH_2), 39.8 (CH_2), 35.6 (CH_2), 26.3 (CH_3), 23.8 (CH), 22.0 (CH), 14.9 (CH_3), 14.6 (CH_3). **^{19}F NMR** (376 MHz, CD_3OD): δ = -147.01 (q, $J_{B\text{-}F}$ = 31.3 Hz). **IR** (ATR): $\tilde{\nu}$ = 1667, 1542, 1506, 1469, 1304, 1191, 1154, 973, 476 cm^{-1}. **MS** (ESI) m/z (relative intensity): 643 (100) $[M\text{-}F]^+$, 663 (40) $[M+H]^+$, 685 (30) $[M+Na]^+$. **HR-MS** (ESI): m/z calcd for $C_{33}H_{42}BF_2N_8O_4$ $[M+H]^+$: 663.3390; found: 663.3384.

UV-Vis λ_{max} (1.0 mg/L in MeOH) = 498 nm. **Em λ_{max}** (1.0 mg/L in MeOH) = 511 nm.

5.3.3 BODIPY-Labeled Cyclobutanes by Secondary C(sp^3)–H Arylations

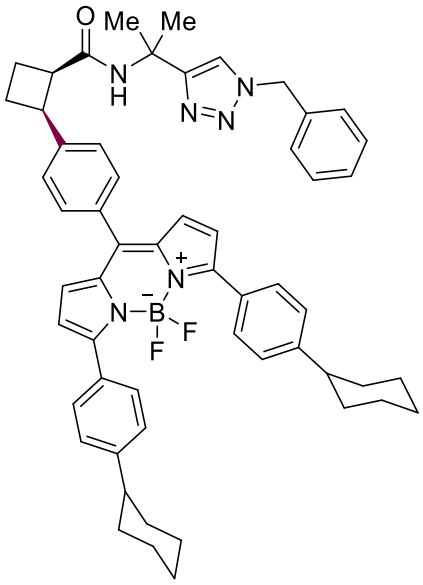
5.3.3.1 Characterization Data of Mono-BODIPY Labeled Cyclobutanes 114



(1*R*,2*S*)-*N*-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-2-[4-(5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl)phenyl]cyclobutane-1-carboxamide (114a)

The general procedure **D** was followed using *N*-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]cyclobutanecarboxamide (**112a**) (60 mg, 0.2 mmol), iodo-BODIPY **109a** (108 mg, 0.24 mmol) and AgOAc (73 mg, 0.44 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:2) yielded **114a** (65 mg, 52%) as an orange solid (M.p. = 124–125 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.35–7.30 (m, 5H), 7.28 (s, 1H), 7.22 (dd, J = 7.5, 2.0 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 6.20 (brs, 1H), 5.91 (s, 2H), 5.51–5.34 (m, 2H), 3.88 (q, J = 8.7 Hz, 1H), 3.40–3.27 (m, 1H), 2.56 (dd, J = 18.8, 9.7 Hz, 1H), 2.52 (s, 6H), 2.38–2.28 (m, 2H), 2.19 (dq, J = 11.3, 9.0, 8.5 Hz, 1H), 1.55 (s, 3H), 1.47 (s, 3H), 1.29 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.6 (C_q), 155.1 (C_q), 153.9 (C_q), 143.1 (C_q), 142.7 (C_q), 142.0 (C_q), 134.4 (C_q), 132.6 (C_q), 131.4 (C_q), 129.0 (CH), 128.7 (CH), 128.2 (CH), 128.0 (CH), 127.5 (CH), 121.0 (CH), 119.8 (CH), 54.2 (CH_2), 51.5 (C_q), 46.4 (CH), 42.5 (CH), 28.4 (CH_3), 27.7 (CH_3), 26.0 (CH_2), 21.5 (CH_2), 14.7 (CH_3), 14.6 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -146.33 (q, $J_{B\text{-}F}$ = 32.6 Hz). **IR** (ATR): $\tilde{\nu}$ = 2941, 1541, 1506, 1406, 1191, 973 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 621 (100) $[M+H]^+$, 643 (80) $[M+Na]^+$, 1264 (20) $[2M+Na]^+$. **HR-MS** (ESI) *m/z* calcd

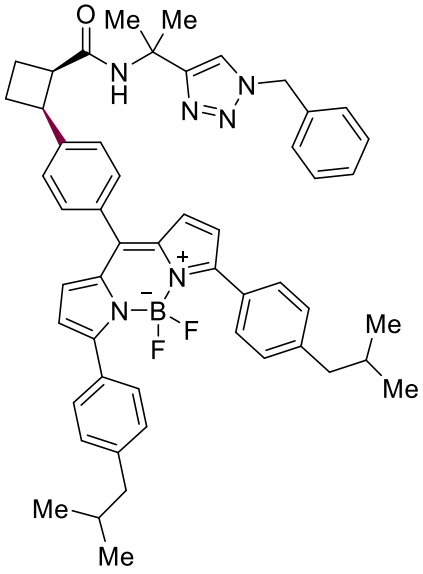
for $C_{36}H_{40}BF_2N_6O$ $[M+H]^+$ 621.3325, found 621.3306. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 495 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 510 nm.



(1*R*,2*S*)-*N*-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-2-{4-[3,7-bis(4-cyclohexylphenyl)-5,5-difluoro-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinin-10-yl]phenyl}cyclobutane-1-carboxamide (114b)

The general procedure **D** was followed using *N*-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]cyclobutanecarboxamide (**112a**) (60 mg, 0.2 mmol), iodo-BODIPY **109l** (170 mg, 0.24 mmol) and AgOAc (73 mg, 0.44 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:2) yielded **114b** (104 mg, 59%) as a purple solid (M.p. = 154–155 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.85–7.73 (m, 4H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.33–7.27 (m, 3H), 7.26–7.22 (m, 4H), 7.21–7.17 (m, 3H), 6.78 (d, *J* = 4.3 Hz, 2H), 6.55 (d, *J* = 4.3 Hz, 2H), 6.06 (brs, 1H), 5.40 (d, *J* = 1.7 Hz, 2H), 3.99 (q, *J* = 8.8 Hz, 1H), 3.38 (td, *J* = 9.0, 4.8 Hz, 1H), 2.64 (ddd, *J* = 18.5, 10.7, 8.3 Hz, 1H), 2.57-2.40 (m, 3H), 2.34 (dtdd, *J* = 10.9, 8.9, 5.0, 1.7 Hz, 1H), 2.19 (dq, *J* = 11.4, 8.3 Hz, 1H), 1.94–1.80 (m, 8H), 1.77–1.70 (m, 2H), 1.49–1.33 (m, 11H), 1.29–1.21 (m, 5H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.1 (C_q), 158.6 (C_q), 154.0 (C_q), 149.5 (C_q), 143.5 (C_q), 143.2 (C_q), 136.2 (C_q), 134.4 (C_q), 132.5 (C_q), 130.5 (CH), 130.4 (CH), 130.1 (C_q), 129.4 (CH), 129.0 (CH), 128.7 (CH), 128.0 (CH), 127.7 (CH), 126.7 (CH), 120.7 (CH), 119.8 (CH), 54.1 (CH_2), 51.2 (C_q), 46.3 (CH), 44.4 (CH), 42.6 (CH), 34.1 (CH_2), 28.0 (CH_3), 27.1 (CH_3), 26.1 (CH_2), 26.1 (CH_2), 24.2 (CH_2), 20.2 (CH_2). **^{19}F**

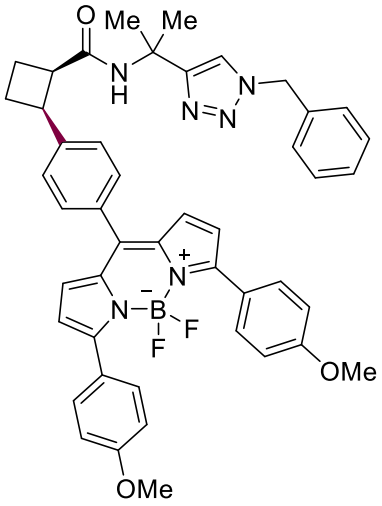
NMR (282 MHz, $CDCl_3$): δ = -132.73 (q, $J_{B\text{-}F}$ = 31.9 Hz) **IR** (ATR): $\tilde{\nu}$ = 2920, 1538, 1466, 1131, 1069, 966 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 881 (100) $[M+H]^+$, 903 (25) $[M+Na]^+$, 919 (10) $[M+K]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{56}H_{60}BF_2N_6O$ $[M+H]^+$ 881.4893, found 881.4883. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 560 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 595 nm.



(1*R*,2*S*)-*N*-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-2-{4-[5,5-difluoro-3,7-bis(4-isobutylphenyl)-5*H*-4λ⁴,5λ⁴-dipyrrolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinin-10-yl]phenyl}cyclobutane-1-carboxamide (114c)

The general procedure **D** was followed using *N*-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl)]cyclobutanecarboxamide (**112a**) (60 mg, 0.2 mmol), iodo-BODIPY **109k** (158 mg, 0.24 mmol) and AgOAc (73 mg, 0.44 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:2) yielded **114c** (68 mg, 41%) as a purple solid (M.p. = 125–126 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 8.1 Hz, 4H), 7.44 (d, *J* = 7.6 Hz, 2H), 7.39 (d, *J* = 7.8 Hz, 2H), 7.34–7.26 (m, 3H), 7.21–7.16 (m, 7H), 6.78 (d, *J* = 4.3 Hz, 2H), 6.55 (d, *J* = 4.2 Hz, 2H), 6.02 (brs, 1H), 5.41 (s, 2H), 4.01 (d, *J* = 9.1 Hz, 1H), 3.40 (s, 1H), 2.64 (p, *J* = 9.1 Hz, 1H), 2.49 (d, *J* = 7.2 Hz, 4H), 2.47–2.43 (m, 1H) 2.35 (s, 1H), 2.27–2.16 (m, 1H), 1.89 (hept, *J* = 6.8 Hz, 2H), 1.45 (s, 3H), 1.27 (s, 3H), 0.92 (d, J = 6.59 Hz, 12H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.2 (C_q), 158.6 (C_q), 154.0 (C_q), 143.5 (C_q), 143.4 (C_q), 143.2 (C_q), 136.2 (C_q), 134.4 (C_q), 132.6 (C_q), 130.6 (CH), 130.4 (CH), 130.0 (C_q), 129.2 (CH), 129.1 (CH), 129.0 (CH), 128.7 (CH), 128.0 (CH), 127.8 (CH), 120.7 (CH), 119.8 (CH), 54.2 (CH_2), 51.3

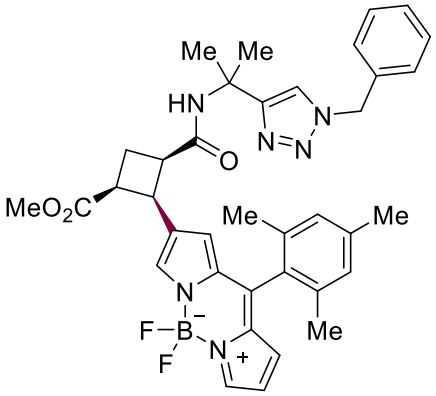
(C_q), 46.4 (CH), 45.4 (CH_2), 42.7 (CH), 30.0 (CH), 28.0 (CH_3), 27.2 (CH_3), 24.2 (CH_2), 22.5 (CH_3), 20.3 (CH_2). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -132.88 (q, $J_{B\text{-}F}$ = 32.0 Hz). **IR** (ATR): $\tilde{\nu}$ =2952, 1538, 1465, 1268, 1138, 1055, 789 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 829 (100) $[M+H]^+$, 851 (30) $[M+Na]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{52}H_{56}BF_2N_6O$ $[M+H]^+$ 829.4580, found 829.4567. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 558 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 593 nm.



(1*R*,2*S*)-*N*-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-2-{4-[5,5-difluoro-3,7-bis(4-methoxyphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-10-yl]phenyl}cyclobutane-1-carboxamide (114d)

The general procedure **D** was followed using *N*-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]cyclobutanecarboxamide (**112a**) (60 mg, 0.2 mmol), iodo-BODIPY **109j** (145 mg, 0.24 mmol) and AgOAc (73 mg, 0.44 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:2) yielded **114d** (78 mg, 50%) as a purple solid (M.p. = 147–148 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.92–7.77 (m, 4H), 7.46–7.41 (m, 2H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.32–7.27 (m, 3H), 7.21–7.18 (m, 3H), 6.99–6.89 (m, 4H), 6.77 (d, *J* = 4.3 Hz, 2H), 6.53 (d, *J* = 4.3 Hz, 2H), 6.02 (brs, 1H), 5.41 (d, *J* = 1.8 Hz, 2H), 4.00 (q, *J* = 8.8 Hz, 1H), 3.83 (s, 6H), 3.39 (td, *J* = 8.9, 4.8 Hz, 1H), 2.64 (ddd, *J* = 18.6, 10.1, 8.1 Hz, 1H), 2.51–2.41 (m, 1H), 2.35 (dddd, *J* = 17.9, 8.7, 5.2, 1.6 Hz, 1H), 2.24–2.16 (m, 1H), 1.44 (s, 3H), 1.27 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.0 (C_q), 160.5 (C_q), 158.0 (C_q), 153.9 (C_q), 143.3 (C_q), 142.4 (C_q), 136.0 (C_q), 134.4 (C_q), 132.6 (C_q), 131.0 (CH), 130.4 (CH), 130.2 (CH), 129.0 (CH), 128.6

(CH), 127.9 (CH), 127.7 (CH), 125.1 (C_q), 120.2 (CH), 119.7 (CH), 113.7 (CH), 55.3 (CH_3), 54.2 (CH_2), 51.3 (C_q), 46.4 (CH), 42.7 (CH), 28.0 (CH_3), 27.3 (CH_3), 24.3 (CH_2), 20.3 (CH_2). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -132.96 (q, $J_{B\text{-}F}$ = 32.4 Hz). **IR** (ATR): $\tilde{\nu}$ = 2938, 1543, 1466, 1142, 1072, 796 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 777 (100) $[M+H]^+$, 799 (50) $[M+Na]^+$, 1575 (10) $[2M+Na]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{46}H_{44}BF_2N_6O_3$ $[M+H]^+$ 777.3538, found 777.3524. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 580 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 620 nm.

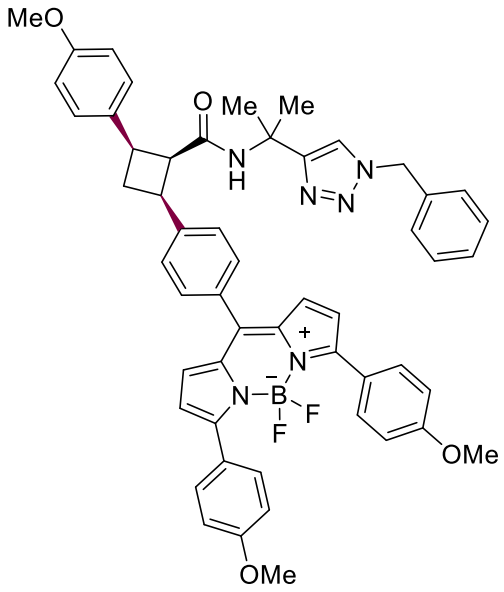


Methyl(1*S*,2*R*,3*R*)-3-{(2-[1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]carbamoyl}-2-(5,5-difluoro-10-mesityl-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-2-yl)cyclobutane-1-carboxylate (114e)

The general procedure **D** was followed using methyl (1*s*,3*s*)-3-{[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]carbamoyl}cyclobutane-1-carboxylate **112b** (71 mg, 0.2 mmol), iodo-BODIPY **109p** (174 mg, 0.4 mmol) and AgOAc (73 mg, 0.44 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:3) yielded **114e** (40 mg, 41%) as an orange solid (M.p. = 131–132 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 23.4 Hz, 2H), 7.43–7.23 (m, 6H), 6.94 (s, 2H), 6.64 (d, *J* = 4.1 Hz, 1H), 6.57 (s, 1H), 6.45 (dd, *J* = 4.2, 1.8 Hz, 1H), 6.13 (brs, 1H), 5.47 (s, 2H), 4.00 (d, *J* = 9.2 Hz, 1H), 3.67–3.36 (m, 4H), 3.30 (dd, *J* = 17.2, 7.9 Hz, 1H), 2.97 (q, *J* = 11.0 Hz, 1H), 2.37 (s, 3H), 2.18 (d, *J* = 8.0 Hz, 1H), 2.05 (d, *J* = 2.9 Hz, 6H), 1.53 (s, 3H), 1.41 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.7 (C_q), 169.3 (C_q), 153.8 (C_q), 147.3 (C_q), 145.0 (CH), 143.6 (CH), 138.8 (C_q), 136.0 (C_q), 135.2 (C_q), 135.1(C_q), 134.6 (C_q), 130.0 (C_q), 129.8 (CH), 129.3 (C_q), 129.0 (CH), 128.6 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 120.2 (CH), 118.2 (CH), 54.1 (CH_2), 51.4 (CH_3), 51.3 (C_q),

40.5 (CH), 39.7 (CH), 39.0 (CH), 27.4 (CH_3), 27.1 (CH_3), 23.4 (CH_2), 21.1 (CH_3), 19.9 (CH_3), 19.8 (CH_3). **^{19}F NMR** (377 MHz, $CDCl_3$): δ = -144.36 (dq, $J_{B\text{-}F}$ = 104.0, 29.1 Hz), -146.43 (dq, $J_{B\text{-}F}$ = 104.2, 28.5 Hz). **IR** (ATR): $\tilde{\nu}$ =2948, 1499, 1248, 1099, 1020, 705 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 687 (100) $[M+Na]^+$, 665 (60) $[M+H]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{37}H_{40}BF_2N_6O_3$ $[M+H]^+$ 665.3224, found 665.3213. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 510 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 527 nm.

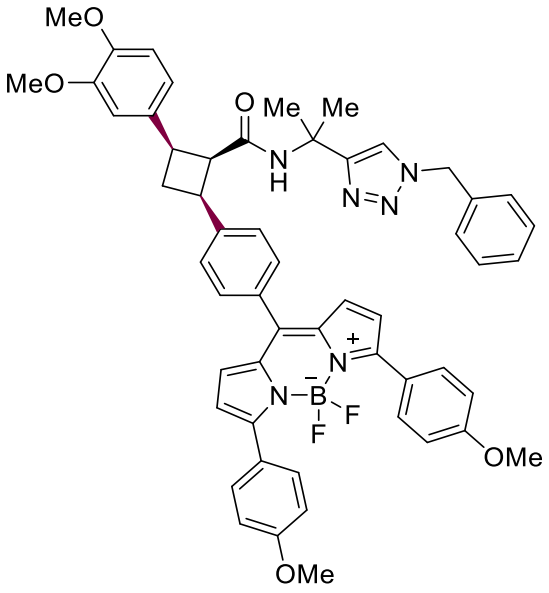
5.3.3.2 Characterization Data of Difunctionalized BODIPY Cyclobutanes 115



(1*S*,2*S*,4*R*)-*N*-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-2-{4-[5,5-difluoro-3,7-bis(4-methoxyphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinin-10-yl]phenyl}-4-(4-methoxyphenyl)cyclobutane-1-carboxamide (115a)

The general procedure **E** was followed using **114d** (155 mg, 0.2 mmol), 4-iodoanisole **11d** (93.6 mg, 0.4 mmol) and AgOAc (100 mg, 0.6 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:2) yielded **115a** (101 mg, 57%) as a purple solid (M.p. = 216–217 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.91–7.81 (m, 4H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 7.9 Hz, 2H), 7.27 (dq, *J* = 5.0, 3.6, 2.6 Hz, 3H), 7.19–7.14 (m, 2H), 7.10 (dd, *J* = 7.3, 2.3 Hz, 2H), 6.97–6.89 (m, 4H), 6.83–6.76 (m, 5H), 6.55 (d, *J* = 4.3 Hz, 2H), 6.03 (brs, 1H), 5.27 (s, 2H), 4.06–3.87 (m, 2H), 3.83 (s, 6H), 3.73 (s, 3H), 3.68 (td, *J* = 8.3, 2.9 Hz, 1H), 3.40 (q, *J* = 10.8 Hz, 1H), 2.64 (dtd, *J* = 10.6, 7.9, 2.9 Hz, 1H), 1.27 (d, *J* = 4.0 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.4 (C_q), 160.6 (C_q), 158.0 (C_q), 157.9 (C_q), 153.4 (C_q), 143.8 (C_q), 142.8 (C_q), 136.2 (C_q), 134.8 (C_q), 132.6 (C_q), 132.0 (C_q), 131.1 (CH), 130.4 (CH), 130.2 (CH), 128.9 (CH), 128.4 (CH), 128.2 (CH), 127.6 (CH), 126.7 (CH), 125.2 (C_q), 120.3 (CH), 113.8 (CH), 113.4 (CH), 55.3 (CH_3), 53.7 (CH_2), 53.4 (CH_3), 51.4 (C_q), 37.9 (CH), 37.9 (CH), 29.44 (CH_2), 28.0 (CH_3), 27.4 (CH_3). **^{19}F NMR** (377 MHz, $CDCl_3$): δ = -132.9 (q, $J_{B\text{-}F}$ = 32.3 Hz). **IR** (ATR): $\tilde{\nu}$ = 2932, 1464, 1432, 1137, 1057, 965, 792 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 883 (100) $[M+H]^+$, 905 (40) $[M+Na]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{53}H_{50}BF_2N_6O_4$ $[M+H]^+$ 883.3958, found 883.3959. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 585 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 620 nm.



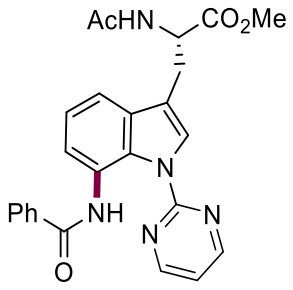
(1*S*,2*S*,4*R*)-*N*-[2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-yl]-2-{4-[5,5-difluoro-3,7-bis(4-methoxyphenyl)-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinin-10-yl]phenyl}-4-(3,4-dimethoxyphenyl)cyclobutane-1-carboxamide (115b)

The general procedure **E** was followed using **114d** (155 mg, 0.2 mmol), 4-iodo-1,2-dimethoxybenzene **11m** (106 mg, 0.4 mmol) and AgOAc (100 mg, 0.6 mmol). After 20 h, purification by column chromatography (*n*-hexane/EtOAc 1:2) yielded **115b** (128 mg, 70%) as a purple solid (M.p. = 134–135 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.91–7.79 (m, 4H), 7.45–7.39 (m, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.30–7.25 (m, 3H), 7.14–7.07 (m, 2H), 6.96–6.89 (m, 4H), 6.87 (s, 1H), 6.82–6.75 (m, 5H), 6.55 (d, *J* = 4.4 Hz, 2H), 6.15 (brs, 1H), 5.30 (d, *J* = 1.7 Hz, 2H), 3.94 (ddt, *J* = 19.3, 11.1, 8.2 Hz, 2H), 3.82 (s, 6H), 3.81 (s, 3H), 3.80 (s, 3H),

3.70 (td, *J* = 8.3, 3.0 Hz, 1H), 3.39 (q, *J* = 10.8 Hz, 1H), 2.73–2.62 (m, 1H), 1.28 (d, *J* = 9.2 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$): *δ* = 169.4 (C_q), 160.6 (C_q), 158.0 (C_q), 153.6 (C_q), 148.5 (C_q), 147.2 (C_q), 143.7 (C_q), 142.8 (C_q), 136.2 (C_q), 134.7 (C_q), 133.3 (C_q), 132.0 (C_q), 131.0 (CH), 130.4 (CH), 130.3 (CH), 128.9 (CH), 128.5 (CH), 127.7 (CH), 126.6 (CH), 125.2 (C_q), 120.3 (CH), 120.1 (CH), 119.2 (CH), 113.7 (CH), 110.9 (CH), 110.4 (CH), 55.9 (CH_3), 55.8 (CH_3), 55.2 (CH_3), 53.8 (CH_2), 53.3 (CH), 51.4 (C_q), 38.2 (CH), 37.9 (CH), 29.7 (CH_2), 27.8 (CH_3), 27.5 (CH_3). **^{19}F NMR** (377 MHz, $CDCl_3$): *δ* = -132.9 (q, J_{B-F} = 32.3 Hz). **IR** (ATR): $\tilde{\nu}$ = 2934, 1462, 1431, 1253, 1055, 1021, 794cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 913 (100) $[M+H]^+$, 935 (35) $[M+Na]^+$. **HR-MS** (ESI) *m/z* calcd for $C_{54}H_{52}BF_2N_6O_5$ $[M+H]^+$ 913.4064, found 913.4045. **UV-Vis λ_{max}** (1.0 mg/L in EtOAc) = 580 nm. **Em λ_{max}** (1.0 mg/L in EtOAc) = 619 nm.

5.3.4 Peptide Late-Stage Diversifications by Rhodium-Catalyzed Tryptophan C7 Amidation

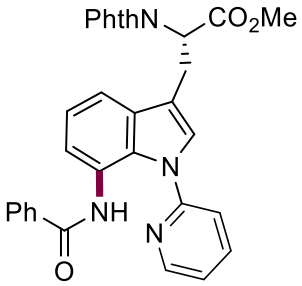
5.3.4.1 Characterization Data of C7 Functionalized Tryptophans 117aa-117ak



Methyl (*S*)-2-acetamido-3-[7-benzamido-1-(pyrimidin-2-yl)-1*H*-indol-3-yl]propanoate (117aa)

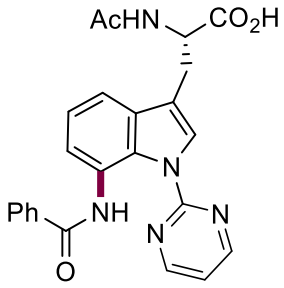
The general procedure **F** was followed using Ac-Trp^{pym}-OMe (**96aa**) (68 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one (**116a**) (66 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 1:5) yielded **117aa** (84 mg, 92%) as a white solid (M.p.: 222─223 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* = 13.00 (s, 1H), 8.49 (d, *J* = 4.9 Hz, 2H), 8.34 (dd, *J* = 7.5, 1.6 Hz, 1H), 8.11 (s, 1H), 7.94–7.91 (m, 2H), 7.57–7.46 (m, 3H), 7.36–7.27 (m, 2H), 6.99 (t, *J* = 4.9 Hz, 1H), 6.10 (d, *J* = 7.7 Hz, 1H), 4.98 (dt, *J* = 7.7, 5.4 Hz, 1H), 3.72

(s, 3H), 3.34 (ddd, *J* = 14.8, 5.4, 0.9 Hz, 1H), 3.26 (ddd, *J* = 14.8, 5.4, 0.9 Hz, 1H), 1.99 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): *δ* = 172.2 (C_q), 169.9 (C_q), 166.6 (C_q), 158.3 (CH), 156.9 (C_q), 137.2 (C_q), 134.3 (C_q), 131.6 (CH), 128.7 (CH), 127.6 (CH), 127.2 (CH), 126.6 (C_q), 126.4 (C_q), 123.6 (CH), 118.9 (CH), 116.4 (CH), 115.7 (C_q), 115.0 (CH), 52.8 (CH), 52.7 (CH_3), 27.4 (CH_2), 23.4 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3333, 1733, 1654, 1543, 1424, 1404, 1179, 791, 706, 606 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 937 (20) $[2M+Na]^+$, 480 (90) $[M+Na]^+$, 458 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{25}H_{24}N_5O_4^+$ $[M+H]^+$ 458.1823, found 458.1816.



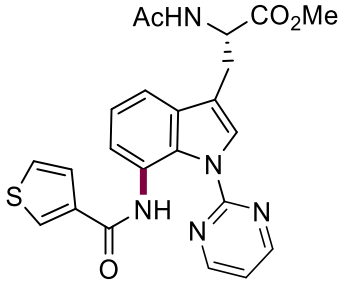
Methyl-(*S*)-3-[7-benzamido-1-(pyridin-2-yl)-1*H*-indol-3-yl]-2-(1,3-dioxoisoindolin-2-yl)propanoate (117ab)

The general procedure **F** was followed using Phth-Trp^{py}-OMe (**88aa**) (85 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one (**116a**) (66 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 3:1 to 1:1) yielded **117ab** (96 mg, 88%) as a light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* = 11.59 (s, 1H), 8.14–8.09 (m, 2H), 7.79–7.77 (m, 1H), 7.77–7.74 (m, 3H), 7.71 (ddd, *J* = 8.3, 7.4, 1.9 Hz, 1H), 7.65 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.50–7.46 (m, 1H), 7.43–7.38 (m, 3H), 7.24 (s, 1H), 7.23–7.19 (m, 2H), 7.00 (ddd, *J* = 7.4, 5.0, 0.9 Hz, 1H), 5.32 (dd, *J* = 10.1, 5.9 Hz, 1H), 3.79 (s, 3H), 3.77–3.73 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$): *δ* = 169.3 (C_q), 167.6 (C_q), 166.2 (C_q), 152.8 (C_q), 147.3 (CH), 139.7 (CH), 136.4 (C_q), 134.1 (CH), 132.0 (C_q), 131.6 (C_q), 131.3 (CH), 128.3 (CH), 127.4 (CH), 126.9 (C_q), 126.8 (CH), 125.3 (C_q), 123.5 (CH), 122.0 (CH), 120.3 (CH), 118.4 (CH), 117.4 (CH), 115.4 (C_q), 115.0 (CH), 52.9 (CH_3), 51.9 (CH), 24.6 (CH_2). **IR** (ATR): $\tilde{\nu}$ = 1744, 1711, 1575, 1471, 1435, 1386, 1364, 1220, 786, 717 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1111 (90) $[2M+Na]^+$, 567 (100) $[M+Na]^+$, 545 (80) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{32}H_{25}N_4O_5^+$ $[M+H]^+$ 545.1819, found 545.1813.



(*S*)-2-Acetamido-3-[7-benzamido-1-(pyrimidin-2-yl)-1*H*-indol-3-yl]propanoic acid (117ac)

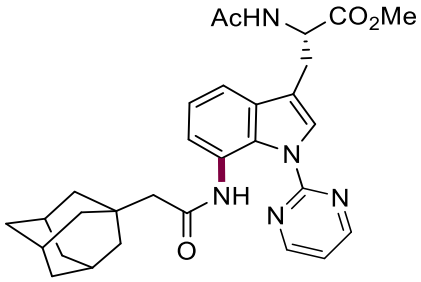
The general procedure **F** was followed using Ac-Trp^{pym}-OH (**96ab**) (65 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one (**116a**) (66 mg, 0.4 mmol). After 24 h, purification by column chromatography (EtOAc/MeOH 100:1 to 20:1) yielded **117ac** (65 mg, 73%) as a white solid (M.p.: 223─224 °C). **^{1}H NMR** (400 MHz, DMSO-*d*$_6$): δ = 12.09 (s, 1H), 8.64 (d, *J* = 4.9 Hz, 2H), 8.03 (s, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.90–7.83 (m, 3H), 7.60–7.51 (m, 3H), 7.46 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.27 (t, *J* = 7.8 Hz, 1H), 7.22 (t, *J* = 4.9 Hz, 1H), 4.42 (ddd, *J* = 7.6, 7.5, 5.0 Hz, 1H), 3.23 (dd, *J* = 14.6, 5.0 Hz, 1H), 3.02 (dd, *J* = 14.6, 7.5 Hz, 1H), 1.78 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-*d*$_6$): δ = 173.6 (C_q), 168.9 (C_q), 164.8 (C_q), 158.6 (CH), 156.2 (C_q), 135.5 (C_q), 133.8 (C_q), 131.5 (CH), 128.6 (CH), 127.2 (CH), 127.1 (CH), 126.3 (C_q), 125.4 (C_q), 122.2 (CH), 118.9 (CH), 117.0 (CH), 116.9 (C_q), 115.6 (CH), 53.4 (CH), 27.0 (CH_2), 22.7 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2925, 2161, 1653, 1576, 1566, 1540, 1422, 710, 413, 388 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 466 (100) $[M+Na]^+$, 444 (85) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{24}H_{22}N_5O_4^+$ $[M+H]^+$ 444.1666, found 444.1655.



Methyl-(*S*)-2-acetamido-3-[1-(pyrimidin-2-yl)-7-(thiophene-3-carboxamido)-1*H*-indol-3-yl]propanoate (117ad)

The general procedure **F** was followed using Ac-Trp^{pym}-OMe (**96aa**) (68 mg, 0.2 mmol) and 3-(thiophen-3-yl)-1,4,2-dioxazol-5-one (**116b**) (68 mg, 0.4 mmol). After 24 h, purification by

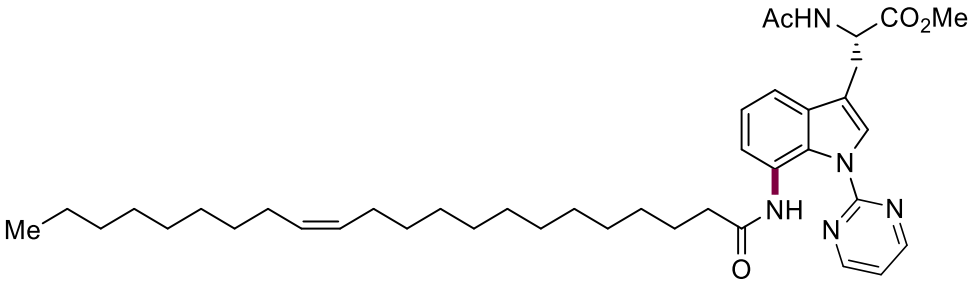
column chromatography (*n*-hexane/EtOAc 1:1 to 1:5) yielded **117ad** (56 mg, 61%) as a white solid (M.p.: 212─213 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 12.73 (s, 1H), 8.55 (d, *J* = 4.9 Hz, 2H), 8.25 (dd, *J* = 6.4, 2.7 Hz, 1H), 8.11 (s, 1H), 7.94 (dd, *J* = 3.1, 1.2 Hz, 1H), 7.53 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.40 (dd, *J* = 5.0, 3.1 Hz, 1H), 7.31–7.27 (m, 2H), 7.03 (t, *J* = 4.9 Hz, 1H), 6.26 (d, *J* = 7.7 Hz, 1H), 4.98 (dt, *J* = 7.7, 5.5 Hz, 1H), 3.73 (s, 3H), 3.32 (dd, *J* = 14.7, 5.5 Hz, 1H), 3.23 (dd, *J* = 14.7, 5.5 Hz, 1H), 2.00 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.1 (C_q), 169.8 (C_q), 161.7 (C_q), 158.0 (CH), 156.7 (C_q), 139.8 (C_q), 134.1 (C_q), 127.8 (CH), 127.1 (CH), 126.7 (CH), 126.4 (CH), 126.1 (C_q), 126.0 (C_q), 123.3 (CH), 118.8 (CH), 116.2 (CH), 115.6 (C_q), 114.8 (CH), 52.6 (CH), 52.4 (CH_3), 27.2 (CH_2), 23.1 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3330, 2919, 2850, 1732, 1652, 1541, 1420, 790, 703, 596 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 949 (50) $[2M+Na]^+$, 486 (100) $[M+Na]^+$, 464 (40) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{23}H_{22}N_5O_4S^+$ $[M+H]^+$ 464.1387, found 464.1388.



Methyl-(*S*)-2-acetamido-3-{7-[2-(adamantan-1-yl)acetamido]-1-(pyrimidin-2-yl)-1*H*-indol-3-yl}propanoate (117ae)

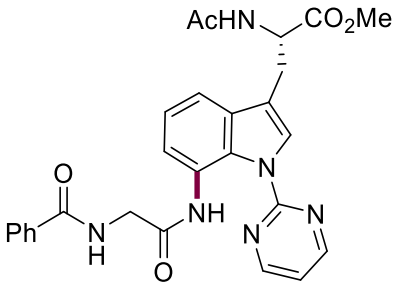
The general procedure **F** was followed using Ac-Trp^{pym}-OMe (**96aa**) (68 mg, 0.2 mmol) and 3-[((3*r*,5*r*,7*r*)-adamantan-1-yl)methyl]-1,4,2-dioxazol-5-one (**116c**) (94 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 1:5) yielded **117ae** (84 mg, 80%) as a white solid (M.p.: 245─246 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 11.99 (s, 1H), 8.71 (d, *J* = 4.9 Hz, 2H), 8.29 (dd, *J* = 6.9, 2.2 Hz, 1H), 8.08 (s, 1H), 7.32–7.22 (m, 2H), 7.16 (t, *J* = 4.9 Hz, 1H), 6.16 (d, *J* = 7.7 Hz, 1H), 4.98 (ddd, *J* = 7.7, 5.5, 5.4 Hz, 1H), 3.74 (s, 3H), 3.33 (dd, *J* = 14.8, 5.5 Hz, 1H), 3.25 (dd, *J* = 14.8, 5.4 Hz, 1H), 2.09 (s, 2H), 2.00 (s, 3H), 1.98–1.93 (m, 3H), 1.74–1.63 (m, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 172.0 (C_q), 169.7 (C_q), 168.8 (C_q), 158.0 (CH), 156.9 (C_q), 133.9 (C_q), 127.1 (CH), 126.3 (C_q), 125.9 (C_q), 123.4 (CH), 118.2 (CH), 116.3 (CH), 115.5 (C_q), 114.5 (CH), 53.8 (CH_2), 52.6 (CH), 52.4 (CH_3), 42.9

(CH_2), 36.7 (CH_2), 33.2 (C_q), 28.6 (CH), 27.2 (CH_2), 23.2 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3341, 2900, 1725, 1677, 1579, 1418, 1403, 1137, 792, 556 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 552 (100) $[M+Na]^+$, 530 (80) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{30}H_{36}N_5O_4^+$ $[M+H]^+$ 530.2762, found 530.2748.



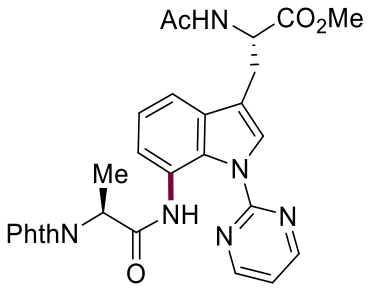
Methyl-(*S*,*Z*)-2-acetamido-3-[7-(docos-13-enamido)-1-(pyrimidin-2-yl)-1*H*-indol-3-yl]propanoate (117af)

The general procedure **F** was followed using Ac-Trp^{pym}-OMe (**96aa**) (68 mg, 0.2 mmol) and (*Z*)-3-(henicos-12-en-1-yl)-1,4,2-dioxazol-5-one (**116d**) (152 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 0:100) yielded **117af** (133 mg, 99%) as a white solid (M.p.: 138—140 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 12.12 (s, 1H), 8.66 (d, *J* = 4.8 Hz, 2H), 8.21 (d, *J* = 6.8 Hz, 1H), 8.06 (s, 1H), 7.25–7.21 (m, 2H), 7.11 (t, *J* = 4.8 Hz, 1H), 6.06 (d, *J* = 7.7 Hz, 1H), 5.48–5.13 (m, 2H), 4.94 (dt, *J* = 7.7, 5.4 Hz, 1H), 3.69 (s, 3H), 3.30 (ddd, *J* = 14.8, 5.4, 0.9 Hz, 1H), 3.22 (ddd, *J* = 14.8, 5.4, 0.9 Hz, 1H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.01–1.97 (m, 4H), 1.96 (s, 3H), 1.75–1.64 (m, 2H), 1.39–1.12 (m, 28H), 0.85 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.1 (C_q), 171.0 (C_q), 169.7 (C_q), 158.0 (CH), 157.0 (C_q), 134.0 (C_q), 129.9 (CH), 129.8 (CH), 127.0 (CH), 126.4 (C_q), 125.9 (C_q), 123.5 (CH), 118.4 (CH), 116.3 (CH), 115.6 (C_q), 114.5 (CH), 52.6 (CH), 52.5 (CH_3), 38.6 (CH_2), 31.9 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2) 29.5 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 27.3 (CH_2), 27.2 (3 × CH_2), 25.8 (2 × CH_2), 23.2 (CH_3), 22.7 (CH_2), 14.1 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3053, 1422, 1264, 896, 734, 705 cm^{-1}. **MS** (ESI) *m*/*z* (relative intensity): 696 (100) $[M+Na]^+$, 674 (13) $[M+H]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{40}H_{59}N_5NaO_4^+$ $[M+Na]^+$ 696.4459, found 696.4455.



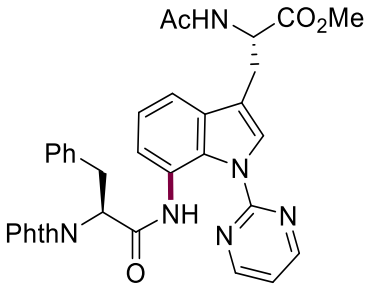
Methyl-(*S*)-2-acetamido-3-[7-(2-benzamidoacetamido)-1-(pyrimidin-2-yl)-1*H*-indol-3-yl]propanoate (117ag)

The general procedure **F** was followed using Ac-Trp^{pym}-OMe (**96aa**) (68 mg, 0.2 mmol) and *N*-[(5-oxo-1,4,2-dioxazol-3-yl)methyl]benzamide (**116e**) (88 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 0:100) yielded **117ag** (66 mg, 65%) as a white solid (M.p.: 243─244 °C). **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 11.43 (s, 1H), 8.90 (t, *J* = 5.7 Hz, 1H), 8.79 (d, *J* = 4.9 Hz, 2H), 8.41 (d, *J* = 7.5 Hz, 1H), 8.06 (s, 1H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.85–7.78 (m, 2H), 7.58–7.53 (m, 1H), 7.50–7.44 (m, 2H), 7.38 (d, *J* = 7.7 Hz, 1H), 7.27 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.13 (t, *J* = 4.9 Hz, 1H), 4.56 (ddd, *J* = 8.6, 7.5, 5.5 Hz, 1H), 4.03 (d, *J* = 5.7 Hz, 2H), 3.60 (s, 3H), 3.17 (dd, *J* = 14.8, 5.5 Hz, 1H), 3.06 (dd, *J* = 14.8, 8.6 Hz, 1H), 1.80 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 172.2 (C_q), 169.5 (C_q), 167.1 (C_q), 166.6 (C_q), 158.8 (CH), 156.1 (C_q), 133.6 (C_q), 133.0 (C_q), 131.5 (CH), 128.3 (CH), 127.4 (CH), 127.2 (CH), 126.0 (C_q), 125.3 (C_q), 122.5 (CH), 118.7 (CH), 117.1 (CH), 115.8 (C_q), 114.9 (CH), 52.2 (CH), 51.9 (CH_3), 44.2 (CH_2), 26.4 (CH_2), 22.3 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3286, 1732, 1653, 1581, 1416, 1294, 1225, 703, 690, 603 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 537 (100) [M+Na]$^+$, 515 (50) [M+H]$^+$. **HR-MS** (ESI): *m/z* calcd for $C_{27}H_{27}N_6O_5^+$ [M+H]$^+$ 515.2037, found 515.2032.



Methyl-(*S*)-2-acetamido-3-{7-[(*S*)-2-(1,3-dioxoisoindolin-2-yl)propanamido]-1-(pyrimidin-2-yl)-1*H*-indol-3-yl}propanoate (117ah)

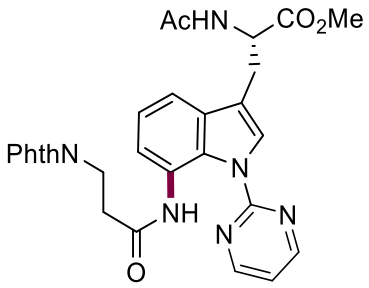
The general procedure **F** was followed using Ac-Trp^{pym}-OMe (**96aa**) (68 mg, 0.2 mmol) and (*S*)-2-[1-(5-oxo-1,4,2-dioxazol-3-yl)ethyl]isoindoline-1,3-dione (**116f**) (104 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 0:100) yielded **117ah** (74 mg, 67%) as a white solid (M.p.: 207─208 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 11.86 (s, 1H), 8.64 (d, *J* = 4.9 Hz, 2H), 8.12–8.05 (m, 1H), 8.04 (s, 1H), 7.87–7.79 (m, 2H), 7.75–7.69 (m, 2H), 7.27 (d, *J* = 4.4 Hz, 2H), 7.01 (t, *J* = 4.9 Hz, 1H), 6.12 (d, *J* = 7.7 Hz, 1H), 5.02 (q, *J* = 7.2 Hz, 1H), 4.96 (dt, *J* = 7.7, 5.5 Hz, 1H), 3.71 (s, 3H), 3.30 (dd, *J* = 14.8, 5.5 Hz, 1H), 3.22 (dd, *J* = 14.8, 5.5 Hz, 1H), 2.01 (s, 3H), 1.78 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.0 (C_q), 169.7 (C_q), 167.7 (C_q), 166.9 (C_q), 158.1 (CH), 156.8 (C_q), 134.1 (CH), 133.9 (C_q), 131.8 (C_q), 127.2 (CH), 126.4 (C_q), 125.4 (C_q), 123.4 (CH), 123.3 (CH), 119.7 (CH), 116.1 (CH), 115.7 (C_q), 115.2 (CH), 52.5 (CH), 52.4 (CH_3), 50.0 (CH), 27.2 (CH_2), 23.2 (CH_3), 15.3 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1706, 1670, 1567, 1512, 1421, 1368, 1175, 798, 720, 497 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 577 (50) $[M+Na]^+$, 555 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{29}H_{27}N_6O_6^+$ $[M+H]^+$ 555.1987, found 555.1981.



Methyl-(*S*)-2-acetamido-3-{7-[(*S*)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanamido]-1-(pyrimidin-2-yl)-1*H*-indol-3-yl}propanoate (117ai)

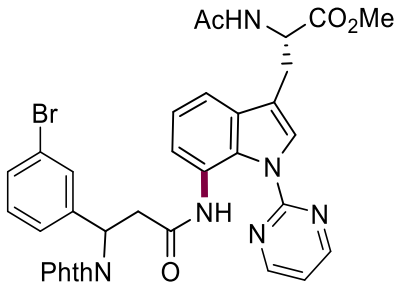
The general procedure **F** was followed using Ac-Trp^{pym}-OMe (**96aa**) (68 mg, 0.2 mmol) and (*S*)-2-[1-(5-oxo-1,4,2-dioxazol-3-yl)-2-phenylethyl]isoindoline-1,3-dione (**116g**) (134 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 0:100) yielded **117ai** (50 mg, 40%) as a white solid (M.p.: 217─218 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 11.88 (s, 1H), 8.58 (d, *J* = 4.8 Hz, 2H), 8.12–8.05 (m, 1H), 8.02 (s, 1H), 7.78–7.65 (m, 4H), 7.28–7.24 (m, 2H), 7.19–7.11 (m, 5H), 6.94 (t, *J* = 4.8 Hz, 1H), 6.10 (d, *J* = 7.7 Hz, 1H), 5.13 (dd, *J* = 9.0, 7.1 Hz, 1H), 4.95 (dt, *J* = 7.7, 5.4 Hz, 1H), 3.69 (s, 3H), 3.66–3.57 (m, 2H), 3.32–3.16 (m, 2H), 1.97 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.0 (C_q), 169.7 (C_q),

167.6 (C_q), 166.1 (C_q), 158.1 (CH), 156.7 (C_q), 137.0 (C_q), 134.1 (CH), 133.9 (C_q), 131.4 (C_q), 128.9 (CH), 128.5 (CH), 127.3 (CH), 126.8 (CH), 126.4 (C_q), 125.2 (C_q), 123.4 (CH), 123.3 (CH), 119.8 (CH), 116.1 (CH), 115.7 (C_q), 115.3 (CH), 56.2 (CH), 52.5 (CH), 52.4 (CH_3), 34.8 (CH_2), 27.2 (CH_2), 23.2 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1743, 1714, 1676, 1565, 1524, 1420, 1381, 1336, 720, 701 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 653 (100) $[M+Na]^+$, 631 (25) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{35}H_{31}N_6O_6^+$ $[M+H]^+$ 631.2300, found 631.2287.



Methyl-(*S*)-2-acetamido-3-{7-[3-(1,3-dioxoisoindolin-2-yl)propanamido]-1-(pyrimidin-2-yl)-1*H*-indol-3-yl}propanoate (117aj)

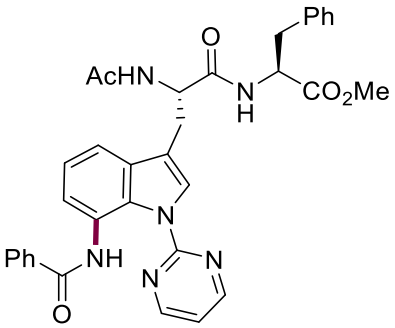
The general procedure **F** was followed using Ac-Trp^{pym}-OMe (**96aa**) (68 mg, 0.2 mmol) and 2-[2-(5-oxo-1,4,2-dioxazol-3-yl)ethyl]isoindoline-1,3-dione (**116h**) (52 mg, 0.2 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 0:100) yielded **117aj** (94 mg, 85%) as a white solid (M.p.: 214─215 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 12.53 (s, 1H), 8.70 (d, *J* = 4.9 Hz, 2H), 8.19 (dd, *J* = 6.3, 2.8 Hz, 1H), 8.05 (s, 1H), 7.80–7.75 (m, 2H), 7.67–7.64 (m, 2H), 7.24–7.18 (m, 2H), 7.11 (t, *J* = 4.9 Hz, 1H), 6.12 (d, *J* = 7.7 Hz, 1H), 4.92 (dt, *J* = 7.7, 5.6 Hz, 1H), 4.07 (t, *J* = 7.3 Hz, 2H), 3.67 (s, 3H), 3.26 (ddd, *J* = 14.8, 5.6, 0.9 Hz, 1H), 3.19 (ddd, *J* = 14.8, 5.6, 0.9 Hz, 1H), 2.75 (t, *J* = 7.3 Hz, 2H), 1.95 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.0 (C_q), 169.8 (C_q), 168.0 (C_q), 167.3 (C_q), 158.1 (CH), 156.6 (C_q), 134.0 (CH), 133.9 (C_q), 131.9 (C_q), 126.9 (CH), 126.0 (C_q), 125.7 (C_q), 123.4 (CH), 123.2 (CH), 118.2 (CH), 116.4 (CH), 115.5 (C_q), 114.7 (CH), 52.5 (CH), 52.4 (CH_3), 36.8 (CH_2), 34.8 (CH_2), 27.2 (CH_2), 23.2 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3335, 2850, 1715, 1657, 1570, 1420, 1393, 1006, 713, 506 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1131 (20) $[2M+Na]^+$, 577 (100) $[M+Na]^+$, 555 (40) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{29}H_{27}N_6O_6^+$ $[M+H]^+$ 555.1987, found 555.1983.



Methyl-(2*S*)-2-acetamido-3-{7-[3-(3-bromophenyl)-3-(1,3-dioxoisoindolin-2-yl)propanamido]-1-(pyrimidin-2-yl)-1*H*-indol-3-yl}propanoate (117ak)

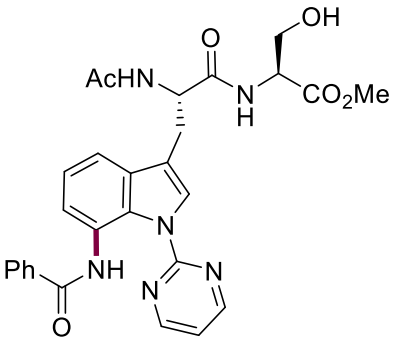
The general procedure **F** was followed using Ac-Trp^{pym}-OMe (**96aa**) (68 mg, 0.2 mmol) and 2-[1-(3-bromophenyl)-2-(5-oxo-1,4,2-dioxazol-3-yl)ethyl]isoindoline-1,3-dione (**116i**) (166 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 0:100) yielded **117ak** (120 mg, 85%) as a white solid (M.p.: 111—112 °C). d.r. = 1:1. **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 12.71–12.64 (m, 1H), 8.77 (d, *J* = 4.9 Hz, 2H), 8.11 (dd, *J* = 7.4, 1.7 Hz, 1H), 8.06 (s, 1H), 7.72–7.67 (m, 2H), 7.65–7.62 (m, 1H), 7.61–7.57 (m, 2H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.17 (t, *J* = 4.9 Hz, 1H), 7.20–7.10 (m, 3H), 6.25 (d, *J* = 7.5 Hz, 1H), 6.01–5.93 (m, 1H), 4.93–4.86 (m, 1H), 3.67–3.61 (m, 4H), 3.29 (dd, *J* = 14.8, 6.4 Hz, 1H), 3.22 (dd, *J* = 14.9, 5.3 Hz, 1H), 3.14 (dd, *J* = 14.9, 5.3 Hz, 1H), 1.92–1.90 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.0 (C_q), 169.7 (C_q), 168.0 (C_q), 166.7 (C_q), 158.1 (CH), 156.5 (C_q), 141.2 (C_q), 134.0 (CH), 133.8 (C_q), 131.4 (C_q), 131.1 (CH), 130.5 (CH), 130.2 (CH), 126.9 (CH), 126.3 (CH), 125.8 (C_q), 125.6 (C_q), 123.2 (CH), 123.2 (CH), 122.6 (C_q), 117.8 (CH), 116.5 (CH), 115.3 (C_q), 114.7 (CH), 52.4 (CH), 52.3 (CH_3), 51.0 (CH), 40.0 (CH_2), 27.1 (CH_2), 23.0 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3292, 2918, 2850, 1634, 1566, 1418, 1331, 1213, 719, 600 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 733 (100) $[M+Na]^+$ (^{81}Br), 731 (97) $[M+Na]^+$ (^{79}Br), 711 (50) $[M+H]^+$ (^{81}Br), 709 (49) $[M+H]^+$ (^{79}Br). **HR-MS** (ESI): *m/z* calcd for $C_{35}H_{30}N_6O_6{}^{79}Br^+$ $[M+H]^+$ 709.1405, found 709.1397.

5.3.4.2 Characterization Data of Tryptophan C7 Functionalized Peptides 117ba-117bj



Methyl-{(*S*)-2-acetamido-3-[7-benzamido-1-(pyrimidin-2-yl)-1*H*-indol-3-yl]propanoyl}-*L*-phenylalaninate (117ba)

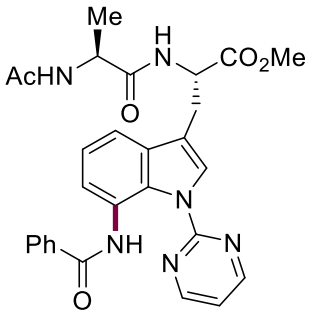
The general procedure **F** was followed using Ac-Trp^{pym}-Phe-OMe (**96ba**) (97 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one (**116a**) (66 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 0:100) yielded **117ba** (82 mg, 68%) as a white solid (M.p.: 220─221 °C). **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 12.08 (s, 1H), 8.68 (d, *J* = 4.9 Hz, 2H), 8.55 (d, *J* = 7.5 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 8.08 (s, 1H), 7.92 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.89–7.84 (m, 2H), 7.62–7.50 (m, 4H), 7.33–7.20 (m, 7H), 4.68 (dt, *J* = 8.4, 4.9 Hz, 1H), 4.51 (ddd, *J* = 8.7, 7.5, 5.9 Hz, 1H), 3.55 (s, 3H), 3.12–3.00 (m, 2H), 2.99–2.86 (m, 2H), 1.75 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 171.7 (C_q), 171.5 (C_q), 169.1 (C_q), 164.8 (C_q), 158.7 (CH), 156.2 (C_q), 137.1 (C_q), 135.5 (C_q), 133.4 (C_q), 131.5 (CH), 129.1 (CH), 128.7 (CH), 128.2 (CH), 127.5 (CH), 127.2 (CH), 126.5 (CH), 126.4 (C_q), 125.5 (C_q), 122.2 (CH), 119.1 (CH), 117.1 (CH), 116.1 (C_q), 115.7 (CH), 53.6 (CH), 52.3 (CH), 51.8 (CH_3), 36.6 (CH_2), 27.3 (CH_2), 22.5 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3279, 2927, 1750, 1637, 1538, 1418, 1315, 789, 712, 601 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1231 (20) [2M+Na]$^+$, 627 (100) [M+Na]$^+$, 605 (90) [M+H]$^+$. **HR-MS** (ESI): *m/z* calcd for $C_{34}H_{33}N_6O_5^+$ [M+H]$^+$ 605.2507, found 605.2505.



Methyl-{(*S*)-2-acetamido-3-[7-benzamido-1-(pyrimidin-2-yl)-1*H*-indol-3-yl]propanoyl}-

***L*-serinate (117bb)**

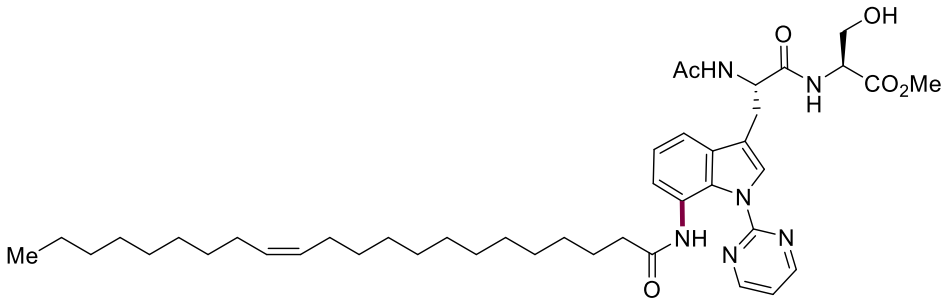
The general procedure **F** was followed using Ac-Trp^{pym}-Ser-OMe (**96bb**) (85 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one (**116a**) (66 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 0:100) yielded **117bb** (43 mg, 40%) as a white solid (M.p.: 185─186 °C). **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 12.06 (s, 1H), 8.69 (d, *J* = 4.9 Hz, 2H), 8.50 (d, *J* = 7.6 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 8.11 (s, 1H), 7.91 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.89–7.84 (m, 2H), 7.62–7.53 (m, 4H), 7.30 (t, *J* = 7.8 Hz, 1H), 7.25 (t, *J* = 4.9 Hz, 1H), 5.07 (t, *J* = 5.7 Hz, 1H), 4.76 (ddd, *J* = 9.0, 7.6, 4.3 Hz, 1H), 4.43–4.36 (m, 1H), 3.74 (dd, *J* = 10.8, 5.7 Hz, 1H), 3.64 (dd, *J* = 10.8, 5.7 Hz, 1H), 3.60 (s, 3H), 3.15 (dd, *J* = 15.0, 4.3 Hz, 1H), 2.95 (dd, *J* = 15.0, 9.0 Hz, 1H), 1.77 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 171.7 (C_q), 170.9 (C_q), 169.2 (C_q), 164.8 (C_q), 158.7 (CH), 156.2 (C_q), 135.5 (C_q), 133.5 (C_q), 131.5 (CH), 128.6 (CH), 127.6 (CH), 127.2 (CH), 126.4 (C_q), 125.4 (C_q), 122.1 (CH), 119.0 (CH), 117.1 (CH), 116.1 (C_q). 115.8 (CH), 61.2 (CH_2), 54.8 (CH), 52.4 (CH), 51.8 (CH_3), 27.5 (CH_2), 22.5 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3277, 1739, 1632, 1538, 1418, 1211, 1022, 797, 706, 600 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1111 (20) $[2M+Na]^+$, 567 (100) $[M+Na]^+$, 545 (30) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{28}H_{29}N_6O_6^+$ $[M+H]^+$ 545.2143, found 545.2134.



Methyl-(*S*)-2-((*S*)-2-acetamidopropanamido)-3-[7-benzamido-1-(pyrimidin-2-yl)-1*H*-indol-3-yl]propanoate (117bc)

The general procedure **F** was followed using Ac-Ala-Trp^{pym}-OMe (**96bc**) (82 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one (**116a**) (66 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 0:100) yielded **117bc** (89 mg, 85%) as a white solid (M.p.: 213─214 °C). **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 12.04 (s, 1H), 8.68 (d, *J* = 4.9 Hz, 2H), 8.40 (d, *J* = 7.4 Hz, 1H), 8.09 (s, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.92 (d, *J* = 7.9

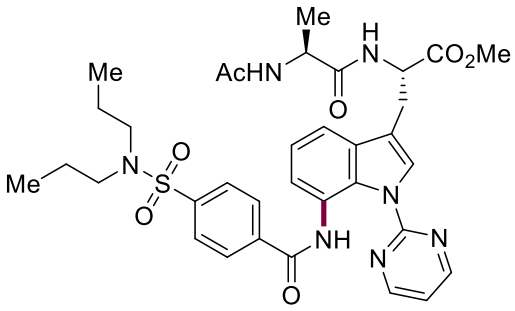
Hz, 1H), 7.87 (d, *J* = 7.4 Hz, 2H), 7.65–7.50 (m, 3H), 7.45 (d, *J* = 7.7 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.27 (t, *J* = 4.9 Hz, 1H), 4.62 (ddd, *J* = 8.5, 7.4, 5.5 Hz, 1H), 4.33 (dq, *J* = 7.8, 7.1 Hz, 1H), 3.62 (s, 3H), 3.24 (dd, *J* = 14.9, 5.5 Hz, 1H), 3.14 (dd, *J* = 14.9, 8.5 Hz, 1H), 1.75 (s, 3H), 1.16 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, DMSO-*d*$_6$): *δ* = 172.6 (C_q), 171.9 (C_q), 168.8 (C_q), 164.8 (C_q), 158.7 (CH), 156.2 (C_q), 135.4 (C_q), 133.0 (C_q), 131.5 (CH), 128.6 (CH), 127.6 (CH), 127.2 (CH), 126.5 (C_q), 125.6 (C_q), 122.3 (CH), 119.2 (CH), 117.2 (CH), 115.3 (C_q), 115.2 (CH), 52.1 (CH), 52.0 (CH_3), 47.7 (CH), 26.3 (CH_2), 22.4 (CH_3), 18.2 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3287, 2928, 1741, 1627, 1565, 1423, 1312, 1214, 790, 707 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 551 (80) $[M+Na]^+$, 529 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{28}H_{29}N_6O_5^+$ $[M+H]^+$ 529.2194, found 529.2187.



Methyl-{(*S*)-2-acetamido-3-[7-((*Z*)-docos-13-enamido)-1-(pyrimidin-2-yl)-1*H*-indol-3-yl]propanoyl}-*L*-serinate (117bd)

The general procedure **F** was followed using Ac-Trp^{pym}-Ser-OMe (**96bb**) (85 mg, 0.2 mmol) and (*Z*)-3-(henicos-12-en-1-yl)-1,4,2-dioxazol-5-one (**116d**) (76 mg, 0.2 mmol). After 24 h, purification by column chromatography (EtOAc/MeOH 100:1 to 20:1) yielded **117bd** (88 mg, 58%) as a white solid (M.p.: 184—185 °C). **^{1}H NMR** (300 MHz, DMSO-*d*$_6$): *δ* = 11.44 (s, 1H), 8.90 (d, *J* = 4.8 Hz, 2H), 8.47 (d, *J* = 7.7 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 8.08 (s, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.39 (t, *J* = 4.8 Hz, 1H), 7.22 (dd, *J* = 7.8, 7.7 Hz, 1H), 5.32–5.29 (m, 2H), 5.06 (t, *J* = 5.6 Hz, 1H), 4.73 (ddd, *J* = 9.4, 8.4, 4.6 Hz, 1H), 4.42–4.34 (m, 1H), 3.73 (dd, *J* = 11.1, 5.6 Hz, 1H), 3.67–3.62 (m, 1H), 3.60 (s, 3H), 3.12 (dd, *J* = 14.7, 4.6 Hz, 1H), 2.92 (dd, *J* = 14.7, 9.4 Hz, 1H), 2.25 (t, *J* = 7.4 Hz, 2H), 2.02–1.94 (m, 4H), 1.76 (s, 3H), 1.53–1.45 (m, 2H), 1.25–1.20 (m, 28H), 0.83 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR** (101 MHz, DMSO-*d*$_6$): *δ* = 171.7 (C_q), 170.9 (C_q), 170.1 (C_q), 169.2 (C_q), 158.8 (CH), 156.3 (C_q),

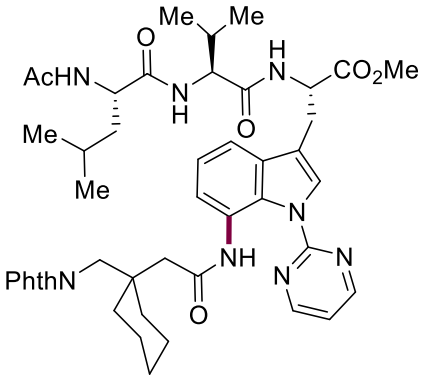
133.3 (C_q), 129.6 (2 × CH), 127.5 (CH), 125.9 (C_q), 125.6 (C_q), 122.1 (CH), 118.2 (CH), 117.3 (CH), 116.1 (C_q), 115.2 (CH), 61.2 (CH_2), 54.7 (CH), 52.3 (CH), 51.8 (CH_3), 36.9 (CH_2), 31.3 (CH_2), 29.1 (2 × CH_2), 29.0 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 28.9 (CH_2), 28.8 (CH_2), 28.8 (CH_2), 28.7 (CH_2), 28.6 (CH_2), 28.6 (CH_2), 28.5 (CH_2), 27.4 (CH_2), 26.5 (2 × CH_2), 25.0 (CH_2), 22.5 (CH_3), 22.1 (CH_2), 13.9 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3290, 2918, 2850, 1740, 1633, 1566, 1419, 1212, 779, 731 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 783 (100) $[M+Na]^+$, 761 (30) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{43}H_{65}N_6O_6^+$ $[M+H]^+$ 761.4960, found 761.4945.



Methyl-(*S*)-2-((*S*)-2-acetamidopropanamido)-3-{7-[4-(*N*,*N*-dipropylsulfamoyl)benzamido]-1-(pyrimidin-2-yl)-1*H*-indol-3-yl}propanoate (117be)

The general procedure **F** was followed using Ac-Ala-Trp^{pym}-OMe (**96bc**) (82 mg, 0.2 mmol) and 4-(5-oxo-1,4,2-dioxazol-3-yl)-*N*,*N*-dipropylbenzenesulfonamide (**116j**) (130 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 0:100) yielded **117be** (121 mg, 88%) as a white solid (M.p.: 192─193 °C). **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 12.05 (s, 1H), 8.68 (d, *J* = 4.9 Hz, 2H), 8.39 (d, *J* = 7.5 Hz, 1H), 8.07 (s, 1H), 8.06–7.94 (m, 5H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 7.7 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.24 (t, *J* = 4.9 Hz, 1H), 4.60 (ddd, *J* = 7.5, 7.0, 5.4 Hz, 1H), 4.31 (dq, *J* = 7.8, 7.0 Hz, 1H), 3.62 (s, 3H), 3.23 (dd, *J* = 15.0, 5.4 Hz, 1H), 3.19–3.12 (m, 1H), 3.08 (t, *J* = 7.5 Hz, 4H), 1.74 (s, 3H), 1.48 (qt, *J* = 7.5, 7.3 Hz, 4H), 1.15 (d, *J* = 7.0 Hz, 3H), 0.82 (t, *J* = 7.3 Hz, 6H). **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 172.6 (C_q), 171.9 (C_q), 168.8 (C_q), 163.5 (C_q), 158.6 (CH), 156.2 (C_q), 142.0 (C_q), 138.7 (C_q), 133.0 (C_q), 128.3 (CH), 127.7 (CH), 127.1 (CH), 126.6 (C_q), 125.1 (C_q), 122.3 (CH), 119.5 (CH), 117.2 (CH), 115.7 (CH), 115.2 (C_q), 52.1 (CH), 52.0 (CH_3), 49.4 (CH_2), 47.7 (CH), 26.3 (CH_2), 22.4 (CH_3), 21.4 (CH_2), 18.2 (CH_3), 11.0 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3287, 2930, 1732, 1639, 1581, 1416, 1338, 1150, 718, 600 cm^{-1}. **MS** (ESI) *m/z* (relative

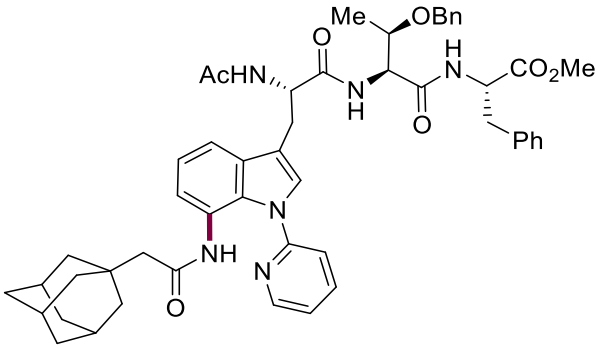
intensity): 714 (100) $[M+Na]^+$, 692 (20) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{34}H_{42}N_7O_7S^+$ $[M+H]^+$ 692.2861, found 692.2851.



Methyl-(*S*)-2-[(*S*)-2-((*S*)-2-acetamido-4-methylpentanamido)-3-methylbutanamido]-3-{7-{2-{1-[(1,3-dioxoisoindolin-2-yl)methyl]cyclohexyl}acetamido}-1-(pyrimidin-2-yl)-1*H*-indol-3-yl}propanoate (117bf)

The general procedure **F** was followed using Ac-Leu-Val-Trp^{pym}-OMe (**96bd**) (110 mg, 0.2 mmol) and 2-{{1-[(5-oxo-1,4,2-dioxazol-3-yl)methyl]cyclohexyl}methyl}isoindoline-1,3-dione (**116k**) (137 mg, 0.4 mmol). After 24 h, purification by column chromatography (EtOAc/acetone 10:1) yielded **117bf** (161 mg, 95%) as a white solid (M.p.: 178─179 °C). **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 11.34 (s, 1H), 8.88 (d, J = 4.9 Hz, 2H), 8.45 (d, J = 7.1 Hz, 1H), 8.08 (s, 1H), 7.99 (d, J = 8.1 Hz, 1H), 7.83–7.79 (m, 5H), 7.63 (d, J = 9.0 Hz, 1H), 7.39–7.34 (m, 2H), 7.25–7.18 (m, 1H), 4.58 (ddd, J = 8.3, 7.1, 5.7 Hz, 1H), 4.28 (dd, J = 9.0, 7.7 Hz, 1H), 4.19 (dd, J = 8.1, 6.6 Hz, 1H), 3.66 (s, 2H), 3.58 (s, 3H), 3.20 (dd, J = 14.9, 5.7 Hz, 1H), 3.09 (dd, J = 14.9, 8.3 Hz, 1H), 2.33 (s, 2H), 1.99–1.89 (m, 1H), 1.82 (s, 3H), 1.63–1.48 (m, 6H), 1.39–1.32 (m, 4H), 1.29–1.22 (m, 3H), 0.83–0.74 (m, 12H). **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 171.8 (C_q), 171.7 (C_q), 171.0 (C_q), 169.1 (C_q), 168.7 (C_q), 168.5 (C_q), 158.7 (CH), 156.2 (C_q), 134.2 (CH), 132.8 (C_q), 131.6 (C_q), 127.4 (CH), 126.0 (C_q), 125.6 (C_q), 122.9 (CH), 122.3 (CH), 118.5 (CH), 117.4 (CH), 115.3 (C_q), 114.6 (CH), 57.1 (CH), 54.4 (C_q), 52.1 (CH), 51.8 (CH_3), 51.0 (CH), 45.7 (CH_2), 42.6 (CH_2), 32.8 (CH_2), 32.8 (CH_2), 31.0 (CH), 26.4 (CH_2), 25.2 (CH_2), 24.1 (CH_3), 22.9 (CH_3), 22.4 (CH_3), 21.5 (CH), 21.2 (CH_2), 19.0 (CH_3), 17.8 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3276, 1629, 1530, 1418, 1218, 1048, 1023, 997, 539, 479 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 871 (100) $[M+Na]^+$, 849 (10) $[M+H]^+$. **HR-MS** (ESI): *m/z*

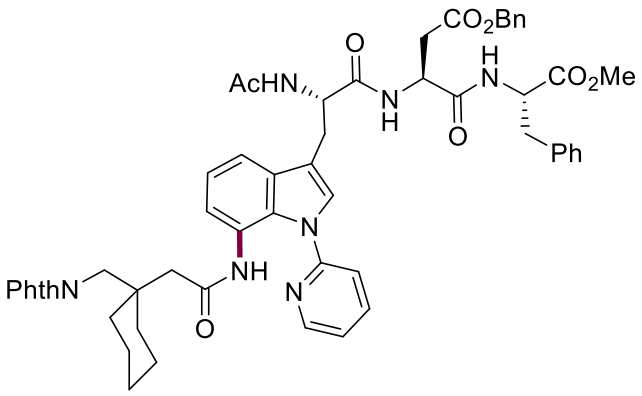
calcd for $C_{46}H_{57}N_8O_8^+$ $[M+H]^+$ 849.4294, found 849.4267.



Methyl-*N*-((*S*)-2-acetamido-3-{7-[2-(adamantan-1-yl)acetamido]-1-(pyridin-2-yl)-1*H*-indol-3-yl}propanoyl)-*O*-benzyl-*L*-threonyl-*L*-phenylalaninate (117bg)

The general procedure **F** was followed using Ac-Trp^{py}-Thr^{OBn}-Phe-OMe (**88ba**) (135 mg, 0.2 mmol) and 3-[((3*r*,5*r*,7*r*)-adamantan-1-yl)methyl]-1,4,2-dioxazol-5-one (**116c**) (94 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 1:3) yielded **117bg** (142 mg, 82%) as a white solid (M.p.: 155—156 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 10.43 (s, 1H), 8.50 (ddd, *J* = 5.0, 1.9, 0.8 Hz, 1H), 8.03 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.79 (ddd, *J* = 8.2, 7.4, 1.9 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 1H), 7.40 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.31–7.26 (m, 3H), 7.25 (s, 1H), 7.23–7.19 (m, 3H), 7.17–7.13 (m, 4H), 7.06 (d, *J* = 7.5 Hz, 1H), 6.97–6.94 (m, 2H), 6.77 (d, *J* = 6.6 Hz, 1H), 6.31 (d, *J* = 7.4 Hz, 1H), 4.78 (td, *J* = 6.9, 5.5 Hz, 1H), 4.64 (td, *J* = 7.5, 5.5 Hz, 1H), 4.50 (d, *J* = 11.6 Hz, 1H), 4.43–4.40 (m, 2H), 3.95 (dq, *J* = 6.4, 3.2 Hz, 1H), 3.61 (s, 3H), 3.26 (dd, *J* = 14.9, 5.5 Hz, 1H), 3.14 (dd, *J* = 14.9, 6.9 Hz, 1H), 3.02 (dd, *J* = 13.9, 5.5 Hz, 1H), 2.90 (dd, *J* = 13.9, 7.3 Hz, 1H), 1.93 (s, 3H), 1.90 (s, 2H), 1.86–1.84 (m, 3H), 1.62 (d, *J* = 12.1 Hz, 3H), 1.53 (d, *J* = 12.1 Hz, 3H), 1.49–1.47 (m, 6H), 0.97 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 171.4 (C_q), 171.0 (C_q), 170.1 (C_q), 169.0 (C_q), 168.6 (C_q), 153.2 (C_q), 147.2 (CH), 139.8 (CH), 137.6 (C_q), 135.7 (C_q), 132.1 (C_q), 129.0 (CH), 128.5 (CH), 128.4 (CH), 127.8 (CH), 127.7 (CH), 127.7 (CH), 127.1 (CH), 126.7 (C_q), 125.2 (C_q), 122.1 (CH), 120.7 (CH), 118.3 (CH), 117.9 (CH), 114.8 (CH), 114.5 (C_q), 73.8 (CH), 71.2 (CH_2), 55.9 (CH), 53.6 (CH), 53.6 (CH), 53.2 (CH_2), 52.1 (CH_3), 42.5 (CH_2), 37.6 (CH_2), 36.7 (CH_2), 33.0 (C_q), 28.6 (CH), 27.9 (CH_2), 23.2 (CH_3), 14.6 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3279, 2901, 1740, 1632, 1538, 1417, 1370, 1212, 780, 696 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 889 (80) $[M+Na]^+$, 867 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{51}H_{59}N_6O_7^+$

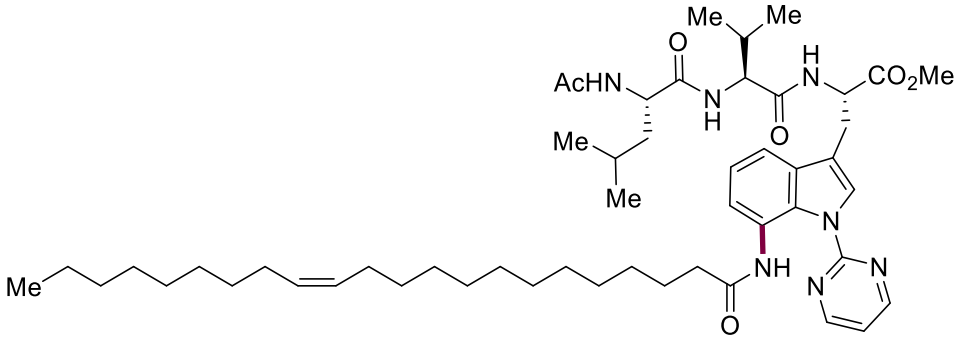
$[M+H]^+$ 867.4440, found 867.4435.



Benzyl-(*S*)-3-{(*s*)-2-acetamido-3-{7-{2-{1-[(1,3-dioxoisoindolin-2-yl)methyl]cyclohexyl}acetamido}-1-(pyridin-2-yl)-1*H*-indol-3-yl}propanamido}-4-[((*S*)-1-methoxy-1-oxo-3-phenylpropan-2-yl)amino]-4-oxobutanoate (117bh)

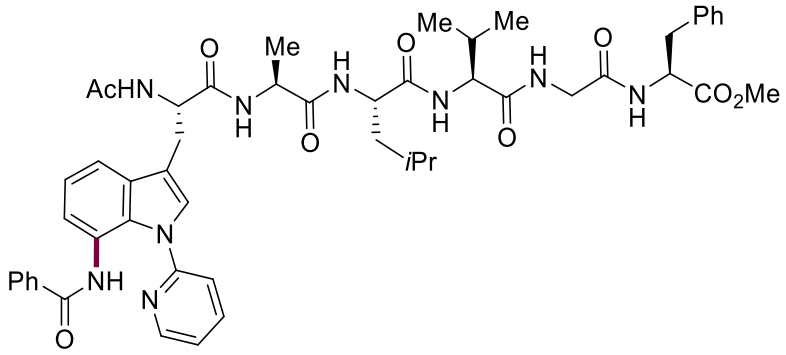
The general procedure **F** was followed using Ac-Trp^{py}-Asp^{OBn}-Phe-OMe (**88bb**) (138 mg, 0.2 mmol) and 2-{{1-[(5-oxo-1,4,2-dioxazol-3-yl)methyl]cyclohexyl}methyl}isoindoline-1,3-dione (**116k**) (137 mg, 0.4 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 1:3) yielded **117bh** (179 mg, 91%) as a white solid (M.p.: 115—116 °C). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 10.58 (s, 1H), 8.52 (dd, *J* = 5.1, 1.8 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.85 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.81–7.76 (m, 1H), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.47–7.42 (m, 2H), 7.33–7.28 (m, 5H), 7.26 (s, 1H), 7.25–7.18 (m, 5H), 7.17–7.10 (m, 3H), 7.02 (d, *J* = 7.7 Hz, 1H), 6.30 (d, *J* = 7.3 Hz, 1H), 5.03 (s, 2H), 4.81–4.66 (m, 3H), 3.79 (s, 2H), 3.66 (s, 3H), 3.24 (dd, *J* = 15.0, 6.0 Hz, 1H), 3.18–3.11 (m, 1H), 3.11–3.00 (m, 2H), 2.90 (dd, *J* = 17.2, 4.7 Hz, 1H), 2.63 (dd, *J* = 17.2, 6.8 Hz, 1H), 2.22 (s, 2H), 1.94 (s, 3H), 1.73–1.55 (m, 5H), 1.38–1.26 (m, 5H). **^{13}C NMR** (101 MHz, DMSO-*d*$_6$): δ = 171.5 (C_q), 171.4 (C_q), 170.3 (C_q), 169.8 (C_q), 169.5 (C_q), 168.7 (C_q), 168.6 (C_q), 151.9 (C_q), 147.4 (CH), 139.3 (CH), 136.9 (C_q), 135.9 (C_q), 134.3 (CH), 131.9 (C_q), 131.6 (C_q), 129.0 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 127.8 (CH), 127.2 (C_q), 126.5 (CH), 124.0 (C_q), 123.0 (CH), 122.9 (CH), 121.1 (CH), 120.6 (CH), 119.0 (CH), 118.1 (CH), 115.8 (CH), 114.3 (C_q), 65.7 (CH_2), 54.9 (C_q), 53.8 (CH), 52.8 (CH), 51.8 (CH_3), 49.3 (CH), 45.6 (CH_2), 42.1 (CH_2), 36.5 (CH_2), 36.0 (CH_2), 32.5 (CH_2), 27.2 (CH_2), 25.1 (CH_2), 22.5 (CH_3), 21.1 (CH_2). **IR** (ATR): $\tilde{\nu}$ = 3280, 2927, 1713, 1636, 1531, 1417, 1212, 713, 599, 397 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1010

(100) $[M+Na]^+$, 988 (70) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{56}H_{58}N_7O_{10}^+$ $[M+H]^+$ 988.4240, found 988.4235.



Methyl-(*S*)-2-[(*S*)-2-((*S*)-2-acetamido-4-methylpentanamido)-3-methylbutanamido]-3-[7-((*Z*)-docos-13-enamido)-1-(pyrimidin-2-yl)-1*H*-indol-3-yl]propanoate (117bi)

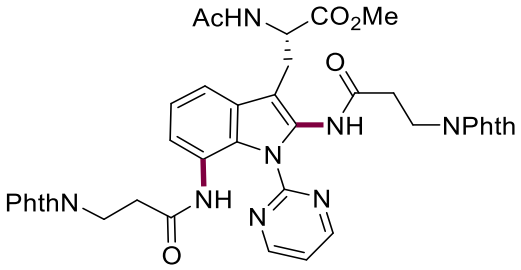
The general procedure **F** was followed using Ac-Leu-Val-Trp^{pym}-OMe (**96bd**) (110 mg, 0.2 mmol) and (*Z*)-3-(henicos-12-en-1-yl)-1,4,2-dioxazol-5-one (**116d**) (152 mg, 0.4 mmol). After 24 h, purification by column chromatography (CH_2Cl_2/acetone 3:1) yielded **117bi** (138 mg, 78%) as a white solid (M.p.: 203─204 °C). **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 11.47 (s, 1H), 8.89 (d, *J* = 4.9 Hz, 2H), 8.43 (d, *J* = 7.0 Hz, 1H), 8.08 (s, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 9.0 Hz, 1H), 7.40 (t, *J* = 4.9 Hz, 1H), 7.35 (d, *J* = 7.7 Hz, 1H), 7.22 (dd, *J* = 7.8, 7.7 Hz, 1H), 5.31–5.28 (m, 2H), 4.57 (ddd, *J* = 8.4, 7.0, 5.8 Hz, 1H), 4.27 (dt, *J* = 8.2, 7.3 Hz, 1H), 4.18 (dd, *J* = 9.0, 6.7 Hz, 1H), 3.57 (s, 3H), 3.18 (dd, *J* = 14.9, 5.8 Hz, 1H), 3.08 (dd, *J* = 14.9, 8.4 Hz, 1H), 2.25 (t, *J* = 7.3 Hz, 2H), 1.97–1.94 (m, 4H), 1.81 (s, 3H), 1.52–1.43 (m, 3H), 1.36 (t, *J* = 7.3 Hz, 2H), 1.24–1.18 (m, 28H), 0.84–0.79 (m, 7H), 0.77–0.75 (m, 9H). **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 171.8 (C_q), 171.7 (C_q), 171.0 (C_q), 170.1 (C_q), 169.1 (C_q), 158.8 (CH), 156.2 (C_q), 132.8 (C_q), 129.6 (2 × CH), 127.4 (CH), 125.9 (C_q), 125.8 (C_q), 122.4 (CH), 118.3 (CH), 117.4 (CH), 115.3 (C_q), 114.5 (CH), 57.0 (CH), 52.1 (CH), 51.8 (CH_3), 51.0 (CH), 40.3 (CH_2), 36.9 (CH_2), 31.3 (CH_2), 31.0 (CH), 29.1 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 28.9 (CH_2), 28.8 (CH_2), 28.8 (CH_2), 28.8 (CH_2), 28.7 (CH_2), 28.6 (CH_2), 28.5 (CH_2), 26.5 (3 × CH_2), 26.4 (CH_2), 25.0 (2 × CH_2), 24.1 (CH), 22.9 (CH_3), 22.4 (CH_3), 22.1 (CH_2), 21.5 (CH_3), 19.0 (CH_3), 17.8 (CH_3), 13.9 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3270, 2923, 2852, 1626, 1530, 1417, 1293, 1210, 735 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 908 (100) $[M+Na]^+$, 886 (20) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{51}H_{80}N_7O_6^+$ $[M+H]^+$ 886.6165, found 886.6152.



Methyl-{(*S*)-2-acetamido-3-[7-benzamido-1-(pyridin-2-yl)-1*H*-indol-3-yl]propanoyl}-*L*-alanyl-*L*-leucyl-*L*-valylglycyl-*L*-phenylalaninate (117bj)

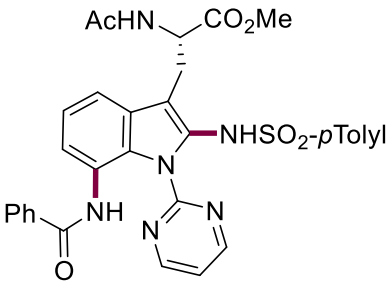
The general procedure **A** was followed using Ac-Trp^{py}-Ala-Leu-Val-Gly-Phe-OMe (**88bc**) (156 mg, 0.2 mmol) and 3-phenyl-1,4,2-dioxazol-5-one (**116a**) (66 mg, 0.4 mmol). After 24 h, purification by column chromatography (EtOAc/acetone 3:1) yielded **117bj** (104 mg, 55%) as a white solid (M.p.: 249─250 °C). **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 10.38 (s, 1H), 8.60 (dd, J = 5.0, 1.8 Hz, 1H), 8.32–8.27 (m, 2H), 8.16 (t, J = 5.8 Hz, 1H), 8.02–7.94 (m, 3H), 7.92–7.84 (m, 3H), 7.63–7.58 (m, 2H), 7.54–7.49 (m, 3H), 7.36 (dd, J = 7.5, 4.9 Hz, 1H), 7.30–7.25 (m, 3H), 7.24–7.22 (m, 1H), 7.20–7.19 (m, 2H), 7.18 (s, 1H), 7.18–7.15 (m, 1H), 4.72–4.63 (m, 1H), 4.48 (dd, J = 8.1, 5.9 Hz, 1H), 4.32–4.24 (m, 2H), 4.15 (dd, J = 8.6, 6.4 Hz, 1H), 3.73–3.68 (m, 2H), 3.58 (s, 3H), 3.12 (dd, J = 14.4, 4.7 Hz, 1H), 3.02 (dd, J = 13.7, 5.9 Hz, 1H), 2.96–2.86 (m, 2H), 1.98–1.90 (m, 1H), 1.79 (s, 3H), 1.22–1.17 (m, 3H), 0.85–0.77 (m, 12H), 0.74 (d, J = 6.4 Hz, 3H). **^{13}C NMR** (151 MHz, DMSO-d_6): δ = 172.2 (C_q), 171.8 (C_q), 171.7 (C_q), 171.5 (C_q), 170.9 (C_q), 169.5 (C_q), 168.6 (C_q), 167.7 (C_q), 149.8 (C_q), 148.9 (CH), 138.7 (CH), 137.0 (C_q), 134.1 (C_q), 133.2 (C_q), 132.1 (CH), 129.7 (C_q), 129.0 (CH), 128.5 (CH), 128.2 (CH), 127.7 (CH), 126.6 (CH), 126.5 (C_q), 122.8 (CH), 122.0 (CH), 120.5 (CH), 119.6 (CH), 119.5 (CH), 111.4 (CH), 108.4 (C_q), 59.7 (CH_2), 57.4 (CH), 53.6 (CH), 53.0 (CH), 51.8 (CH_3), 51.2 (CH), 48.4 (CH), 41.4 (CH_2), 36.8 (CH_2), 30.7 (CH), 26.5 (CH_2), 24.0 (CH), 23.0 (CH_3), 22.5 (CH_3), 21.4 (CH_3), 19.1 (CH_3), 17.9 (CH_3), 17.7 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3270, 2958, 2930, 1741, 1629, 1589, 1520, 1436, 1216, 697 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 966 (100) [M+Na]$^+$, 944 (10) [M+H]$^+$. **HR-MS** (ESI): *m/z* calcd for $C_{51}H_{62}N_9O_9^+$ [M+H]$^+$ 944.4665, found 944.4646.

5.3.4.3 Procedure and Characterization Data for Difunctionalized Amino Acids and Peptides 118a-118e



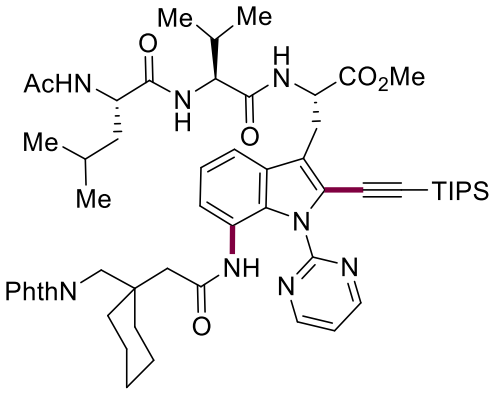
Methyl-(*S*)-2-acetamido-3-{2-{[2-(1,3-dioxoisoindolin-2-yl)ethyl]amino}-7-[3-(1,3-dioxoisoindolin-2-yl)propanamido]-1-(pyrimidin-2-yl)-1*H*-indol-3-yl}propanoate (118a)

The general procedure **F** was followed using Ac-Trp^{pym}-OMe (**96aa**) (68 mg, 0.2 mmol) and 2-[2-(5-oxo-1,4,2-dioxazol-3-yl)ethyl]isoindoline-1,3-dione (**116h**) (208 mg, 0.8 mmol). After 24 h, purification by column chromatography (*n*-hexane/EtOAc 1:1 to 0:100) yielded **118a** (133 mg, 90%) as a white solid (M.p.: 253─254 °C). **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 9.93 (s, 1H), 9.46 (s, 1H), 8.76 (d, *J* = 4.8 Hz, 2H), 8.20 (d, *J* = 6.9 Hz, 1H), 7.86–7.81 (m, 8H), 7.44 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.37 (t, *J* = 4.8 Hz, 1H), 7.17 (t, *J* = 7.7 Hz, 1H), 7.07 (dd, *J* = 7.8, 1.2 Hz, 1H), 4.50 (dt, *J* = 8.6, 6.9 Hz, 1H), 3.74 (t, *J* = 7.3 Hz, 2H), 3.59–3.53 (m, 5H), 3.11 (dd, *J* = 14.4, 6.9 Hz, 1H), 2.98 (dd, *J* = 14.4, 8.6 Hz, 1H), 2.64 (t, *J* = 7.5 Hz, 2H), 2.18 (t, *J* = 7.5 Hz, 2H), 1.75 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 172.3 (C_q), 170.6 (C_q), 169.4 (C_q), 167.6 (2 × C_q), 167.5 (C_q), 167.5 (C_q), 157.7 (CH), 155.4 (C_q), 134.3 (2 × CH), 131.6 (2 × C_q), 131.0 (C_q), 128.9 (C_q), 128.1 (C_q), 123.0 (2 × CH), 121.7 (CH), 120.8 (CH), 119.1 (CH), 116.4 (CH), 108.3 (C_q), 52.4 (CH), 51.9 (CH_3), 33.8 (CH_2), 33.7 (CH_2), 33.5 (CH_2), 33.3 (CH_2), 25.5 (CH_2), 22.2 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3290, 2919, 2850, 1634, 1566, 1419, 1373, 1213, 719, 731 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 793 (100) $[M+Na]^+$, 771 (10) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{40}H_{35}N_8O_9^+$ $[M+H]^+$ 771.2522, found 771.2508.



Methyl-(*S*)-2-acetamido-3-{7-benzamido-2-[(4-methylphenyl)sulfonamide]-1-(pyrimidin-2-yl)-1*H*-indol-3-yl}propanoate (118b)

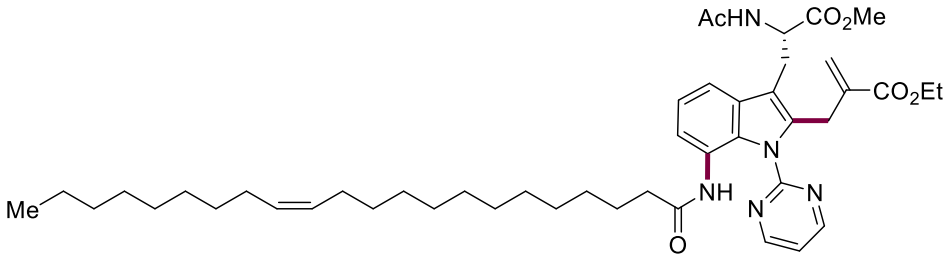
To an oven-dried Schlenk tube was added **117aa** (46 mg, 0.1 mmol), tosyl azide (40 mg, 0.2 mmol), $[RhCp^*Cl_2]_2$ (1.5 mg, 2.5 mol %) and $AgSbF_6$ (3.4 mg, 10 mol %). The tube was evacuated and purged with N_2 three times. Then, TFE (0.4 mL) was added. The tube was sealed and heated at 110 °C for 24 h. After cooling to room temperature, the resulting mixture was diluted with CH_2Cl_2 and concentrated *in vacuo*. Purification of the residue by column chromatography on silica gel (*n*-hexane/acetone 3:1) yielded **118b** (47 mg, 76%) as a white solid (M.p.: 123—124 °C). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 10.70 (s, 1H), 8.43 (s, 1H), 8.25 (d, *J* = 4.9 Hz, 2H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.71–7.68 (m, 2H), 7.51–7.48 (m, 2H), 7.44–7.39 (m, 2H), 7.30 (t, *J* = 7.8 Hz, 1H), 7.17–7.14 (m, 2H), 6.98–6.95 (m, 2H), 6.86 (t, *J* = 4.9 Hz, 1H), 6.63 (d, *J* = 7.3 Hz, 1H), 4.98 (ddd, *J* = 7.3, 7.3, 5.7 Hz, 1H), 3.77 (s, 3H), 3.41 (dd, *J* = 14.8, 7.3 Hz, 1H), 3.36 (dd, *J* = 14.8, 5.7 Hz, 1H), 2.31 (s, 3H), 1.87 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.3 (C_q), 170.2 (C_q), 165.8 (C_q), 157.6 (CH), 155.9 (C_q), 143.8 (C_q), 135.7 (C_q), 135.4 (C_q), 131.6 (CH), 129.8 (C_q), 129.6 (CH), 128.5 (CH), 127.2 (CH), 126.7 (CH), 125.8 (C_q), 124.9 (C_q), 123.1 (CH), 120.5 (CH), 117.2 (CH), 116.3 (CH), 115.2 (C_q), 109.9 (C_q), 52.5 (CH_3), 51.9 (CH), 26.0 (CH_2), 22.9 (CH_3), 21.4 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1740, 1653, 1566, 1415, 1336, 1290, 1161, 1089, 659, 535 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1275 (10) $[2M+Na]^+$, 649 (100) $[M+Na]^+$, 627 (30) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{32}H_{31}N_6O_6S^+$ $[M+H]^+$ 627.2020, found 627.2005.



Methyl-(*S*)-2-[(*S*)-2-((*S*)-2-acetamido-4-methylpentanamido)-3-methylbutanamido]-3-{7-{2-{1-[(1,3-dioxoisoindolin-2-yl)methyl]cyclohexyl}acetamido}-1-(pyrimidin-2-yl)-2-[(triisopropylsilyl)ethynyl]-1*H*-indol-3-yl}propanoate (118c)

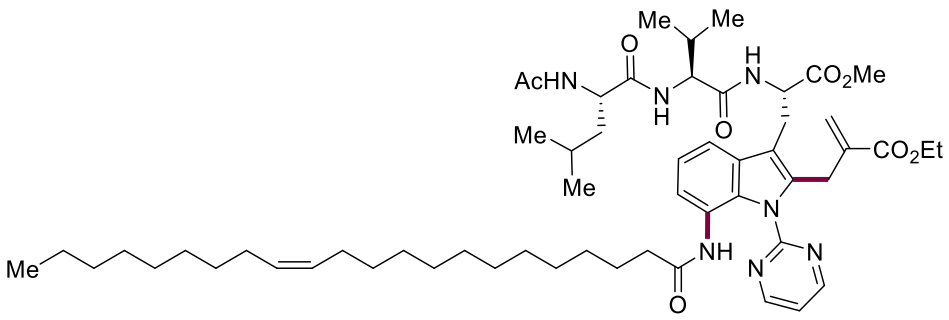
To a solution of **117bf** (85 mg, 0.1 mmol), $MnBr(CO)_5$ (1.2 mg, 5.0 mol %) and Cy_2NH (36 mg, 0.2 mmol) in DCE (0.5 mL) in the oven-dried Schlenk tube, (bromoethynyl)triisopropylsilane **71a** (52 mg, 0.2 mmol) was added. The mixture was stirred at 80 °C for 16 h. After completion of the reaction, CH_2Cl_2 (3.0 mL) was added at ambient temperature and the volatiles were removed *in vacuo*. Purification of the residue by chromatography on silica gel (*n*-hexane/EtOAc 1:2) afforded the desired product **118c** (67 mg, 66%) as a colorless oil. **^{1}H NMR** (600 MHz, DMSO-d_6): δ = 9.20 (s, 1H), 8.87 (d, J = 4.8 Hz, 2H), 8.64 (d, J = 6.4 Hz, 1H), 8.02 (d, J = 8.3 Hz, 1H), 7.89–7.87 (m, 2H), 7.85–7.83 (m, 2H), 7.65 (d, J = 9.2 Hz, 1H), 7.56 (t, J = 4.8 Hz, 1H), 7.48 (dd, J = 7.9, 1.3 Hz, 1H), 7.19–7.17 (m, 1H), 7.14 (dd, J = 7.2, 1.3 Hz, 1H), 4.46 (ddd, J = 9.8, 6.4, 6.1 Hz, 1H), 4.35–4.31 (m, 1H), 4.25 (dd, J = 9.2, 6.8 Hz, 1H), 3.53 (s, 2H), 3.36 (s, 3H), 3.28 (dd, J = 14.0, 9.8 Hz, 1H), 3.22 (dd, J = 14.0, 6.1 Hz, 1H), 1.94–1.90 (m, 1H), 1.83 (s, 3H), 1.82 (s, 2H), 1.62–1.54 (m, 2H), 1.45–1.41 (m, 4H), 1.32–1.28 (m, 3H), 1.16–1.09 (m, 4H), 1.00–0.97 (m, 21H), 0.87 (d, J = 6.6 Hz, 3H), 0.84–0.82 (m, 6H), 0.80 (d, J = 6.6 Hz, 3H). **^{13}C NMR** (151 MHz, DMSO-d_6): δ = 171.9 (C_q), 171.6 (C_q), 170.8 (C_q), 169.1 (C_q), 168.8 (C_q), 168.7 (C_q), 158.3 (CH), 156.2 (C_q), 134.3 (CH), 131.7 (C_q), 130.2 (C_q), 129.2 (C_q), 123.6 (CH), 123.2 (C_q), 123.0 (CH), 121.4 (CH), 121.1 (C_q), 120.4 (C_q), 119.8 (CH), 117.0 (CH), 100.9 (C_q), 96.3 (C_q), 65.7 (C_q), 56.8 (CH), 52.9 (CH), 51.6 (CH_3), 51.0 (CH), 45.5 (CH_2), 40.5 (CH_2), 32.6 (2 × CH_2), 31.1 (CH), 27.3 (CH_2), 24.2 (CH), 23.1 (CH_3), 22.5 (CH_3), 21.5 (CH_3), 21.1 (2 × CH_2), 19.0 (CH_3), 18.3 (CH_3), 18.0 (CH_3), 10.6 (CH).

IR (ATR): $\tilde{\nu}$ = 3275, 2926, 2864, 1713, 1638, 1561, 1419, 1292, 1026, 725 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1051 (100) $[M+Na]^+$, 1029 (10) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{57}H_{77}N_8O_8Si^+$ $[M+H]^+$ 1029.5628, found 1029.5612.



Ethyl-(*S*,*Z*)-2-{[3-(2-acetamido-3-methoxy-3-oxopropyl)-7-(docos-13-enamido)-1-(pyrimidin-2-yl)-1H-indol-2-yl]methyl}acrylate (118d)

A suspension of amino acid **117af** (67 mg, 0.1 mmol), MBH adduct ethyl 2-{[(*tert*-butoxycarbonyl)oxy]methyl}acrylate **100a** (69 mg, 0.3 mmol), $MnBr(CO)_5$ (2.8 mg, 10 mol %) and NaOAc (2.5 mg, 30 mol %) in 1,4-dioxane (0.3 mL) was stirred at 80 °C for 16 h under N_2. After cooling to ambient temperature, CH_2Cl_2 (10 mL) was added and the mixture was concentrated *in vacuo*. Purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc 1:1 to 1:4) yielded **7d** (56 mg, 71%) as a colorless oil. **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.75 (d, *J* = 4.9 Hz, 2H), 8.67 (s, 1H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.35 (d, *J* = 7.7 Hz, 1H), 7.24–7.19 (m, 2H), 6.15 (d, *J* = 7.5 Hz, 1H), 5.84 (brs, 1H), 5.34–5.31 (m, 2H), 4.91–4.86 (m, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 4.01–3.96 (m, 2H), 3.64 (s, 3H), 3.29–3.26 (m, 2H), 2.00–1.97 (m, 4H), 1.92 (s, 3H), 1.47–1.42 (m, 2H), 1.31–1.28 (m, 3H), 1.27–1.18 (m, 30H), 0.86 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 172.2 (C_q), 170.8 (C_q), 169.7 (C_q), 166.1 (C_q), 158.2 (CH), 158.1 (C_q), 138.0 (C_q), 135.8 (C_q), 131.3 (C_q), 129.9 (CH), 129.8 (CH), 128.1 (C_q), 125.2 (CH_2), 123.6 (C_q), 121.9 (CH), 120.1 (CH), 118.3 (CH), 115.5 (CH), 113.7 (C_q), 60.9 (CH_2), 52.6 (CH), 52.5 (CH_3), 37.8 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (2 × CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 27.6 (CH_2), 27.2 (CH_2), 27.0 (CH_2), 25.6 (CH_2), 23.1 (CH_3), 22.6 (CH_2), 14.2 (CH_3), 14.1 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3022, 2556, 1568, 1428, 1392, 1233, 992, 887, 712, 649 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 808 (100) $[M+Na]^+$, 786 (5) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{46}H_{67}N_5O_6Na^+$ $[M+Na]^+$ 808.4984, found 808.4984.

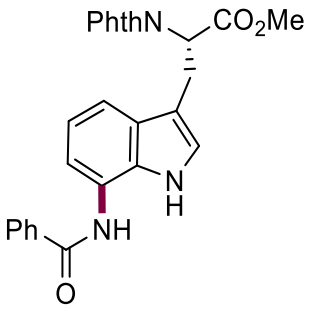


Ethyl-2-{{3-{(*S*)-2-[(*S*)-2-((*S*)-2-acetamido-4-methylpentanamido)-3-methylbutanamido]-3-methoxy-3-oxopropyl}-7-((*Z*)-docos-13-enamido)-1-(pyrimidin-2-yl)-1*H*-indol-2-yl}methyl}acrylate (118e)

A mixture of **117bi** (89 mg, 0.1 mmol), MBH adduct ethyl 2-{[(*tert*-butoxycarbonyl)oxy]methyl}acrylate **100a** (69 mg, 0.3 mmol), $MnBr(CO)_5$ (2.8 mg, 10 mol %) and NaOAc (2.5 mg, 30 mol %) in 1,4-dioxane (0.3 mL) was stirred at 80 °C for 16 h under N_2. After cooling to ambient temperature, CH_2Cl_2 (10 mL) was added and the mixture was concentrated *in vacuo*. Purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc 1:1 to 1:4) yielded **7e** (52 mg, 52%) as a white solid (M.p.: 176─177 °C). **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 9.02 (s, 1H), 8.80 (d, J = 4.8 Hz, 2H), 8.54 (d, J = 7.1 Hz, 1H), 8.04 (d, J = 8.2 Hz, 1H), 7.63 (d, J = 8.9 Hz, 1H), 7.51–7.40 (m, 2H), 7.18–7.10 (m, 1H), 7.04 (d, J = 7.6 Hz, 1H), 5.74 (brs, 1H), 5.34–5.29 (m, 2H), 4.81 (brs, 1H), 4.50 (ddd, J = 8.3, 7.1, 6.4 Hz, 1H), 4.32 (dt, J = 8.2, 7.8 Hz, 1H), 4.21 (dd, J = 8.9, 7.9 Hz, 1H), 4.08 (q, J = 7.1 Hz, 2H), 4.00 (d, J = 17.8 Hz, 1H), 3.89 (d, J = 17.7 Hz, 1H), 3.47 (s, 3H), 3.19 (dd, J = 14.6, 8.3 Hz, 1H), 3.09 (dd, J = 14.6, 6.4 Hz, 1H), 2.08–1.96 (m, 4H), 1.84 (s, 3H), 1.79–1.71 (m, 2H), 1.62–1.54 (m, 1H), 1.43 (t, J = 7.3 Hz, 2H), 1.30–1.21 (s, 30H), 0.88–0.81 (m, 19H). **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 172.4 (C_q), 172.3 (C_q), 171.4 (C_q), 170.6 (C_q), 169.6 (C_q), 166.0 (C_q), 158.7 (CH), 157.3 (C_q), 137.8 (C_q), 135.6 (C_q), 131.0 (C_q), 130.7 (C_q), 130.1 (2 × CH), 125.3 (CH_2), 123.7 (C_q), 122.1 (CH), 121.1 (CH), 119.5 (CH), 116.3 (CH), 112.4 (C_q), 60.8 (CH_2), 57.5 (CH), 53.4 (CH), 52.2 (CH_3), 51.5 (CH), 40.9 (CH_2), 35.6 (CH_2), 31.8 (CH_2), 31.4 (CH), 29.6 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 29.1 (CH_2), 27.0 (2 × CH_2), 26.8 (CH_2), 25.2 (CH_2), 24.7 (CH), 23.5 (CH_3), 22.9 (CH_3), 22.6 (CH_2), 22.0 (CH_3), 19.5 (CH_3), 18.3 (2 × CH_3), 14.5 (CH_2), 14.4 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3278, 2923, 2852, 1718, 1632, 1542, 1420, 1255, 1169,

692 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1020 (100) $[M+Na]^+$, 998 (10) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{57}H_{88}N_7O_8^+$ $[M+H]^+$ 998.6689, found 998.6670.

5.3.4.4 Characterization Data for Pyridyl Removed C7 Amidated Product 117ab'

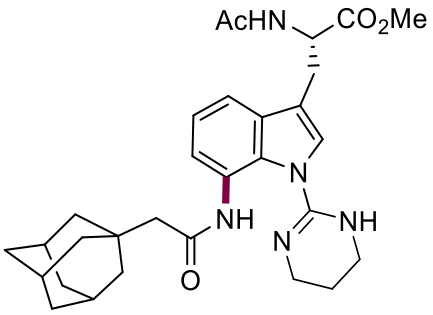


Methyl-(*S*)-3-(7-benzamido-1*H*-indol-3-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (117ab')

To a stirred solution of **117ab** (0.5 mmol, 1.0 equiv) in CH_2Cl_2 (0.5 M) was added MeOTf (2.0 equiv) at 0 °C under N_2. After 30 min, the mixture was allowed to warm to 28 °C and stirred for 18 h. The crude mixture was concentrated under reduced pressure to afford a bright yellow solid. In a sealed-tube, the crude product, $Pd(OH)_2/C$ (20 wt.-%, 10 mol %), and HCO_2NH_4 (30.0 equiv) were dissolved in AcOH (0.25 M), and stirred at 60 °C for 18 h. The mixture was filtered through a short pad of celite, concentrated under reduced pressure and purified by column chromatography to get the product **117ab'** as a light yellow oil (180 mg, 77%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 9.72 (s, 1H), 8.09 (s, 1H), 7.92–7.87 (m, 2H), 7.78 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.68 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.60–7.47 (m, 4H), 7.05 (s, 1H), 7.05–7.00 (m, 1H), 6.81 (d, *J* = 7.5 Hz, 1H), 5.34–5.27 (m, 1H), 3.82 (s, 3H), 3.81–3.70 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 169.6 (C_q), 167.6 (C_q), 165.5 (C_q), 134.2 (C_q), 134.0 (CH), 132.1 (CH), 131.7 (C_q), 130.1 (C_q), 128.9 (CH), 128.4 (C_q), 127.2 (CH), 123.6 (CH), 123.4 (CH), 122.4 (C_q), 119.2 (CH), 116.2 (CH), 113.6 (CH), 110.9 (C_q), 52.8 (CH_3), 52.5 (CH), 24.8 (CH_2). **IR** (ATR): $\tilde{\nu}$ = 3353, 2923, 1710, 1524, 1435, 1388, 1249, 1104, 718, 530 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 490 (100) $[M+Na]^+$, 468 (60) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{27}H_{22}N_3O_5^+$ $[M+H]^+$ 468.1554, found 468.1547.

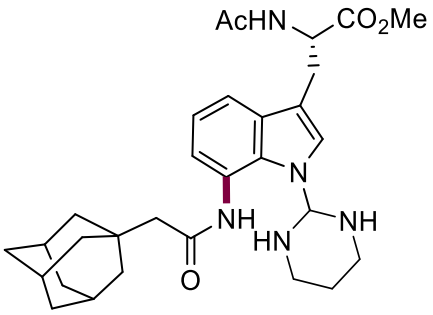
5.3.4.5 Procedure and Characterization for Hydrogenated Products by Pyrimidyl

Transformation



Methyl-(*S*)-2-acetamido-3-{7-[2-(adamantan-1-yl)acetamido]-1-(1,4,5,6-tetrahydropyrimidin-2-yl)-1*H*-indol-3-yl}propanoate (117aea)

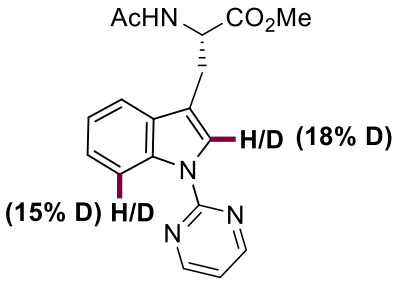
To a solution of **117ae** (52 mg, 0.1 mmol) in acetic acid (1.0 mL) in a 25 mL Schlenk tube was added Pd/C (16 mg, 15 wt.-%). Then the Schlenk tube slowly evacuated and purged with H_2 three times through a H_2-filled balloon. The mixture was stirred at 100 °C for 6 h. Then, the reaction mixture was filtered through a short pad of celite. The residue was concentrated *in vacuo*. The crude mixture was purified by flash column chromatography on silica gel (CH_2Cl_2/MeOH = 100:1 to 30:1) to yield **117aea** (28 mg, 52%) as a colorless oil. **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 11.44 (brs), 8.40 (d, J = 7.6 Hz, 1H), 7.80–7.51 (m, 1H), 7.46 (s, 1H), 7.37 (d, J = 7.9 Hz, 1H), 7.24–7.15 (m, 1H), 4.54 (ddd, J = 8.3, 7.6, 5.5 Hz, 1H), 3.62 (s, 3H), 3.54–3.44 (m, 4H), 3.13 (dd, J = 14.8, 5.5 Hz, 1H), 3.03 (dd, J = 14.8, 8.3 Hz, 1H), 2.09 (s, 2H), 1.97–1.92 (m, 3H), 1.92–1.91 (m, 2H), 1.84 (s, 3H), 1.72–1.60 (m, 12H). **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 172.1 (C_q), 172.0 (C_q), 169.5 (C_q), 168.7 (C_q), 149.0 (C_q), 131.4 (C_q), 126.0 (CH), 125.2 (C_q), 125.1 (C_q), 121.8 (CH), 114.8 (CH), 113.9 (CH), 52.3 (CH), 52.0 (CH_3), 42.1 (CH_2), 36.4 (CH_2), 32.8 (CH_2), 29.0 (C_q), 28.0 (CH), 26.4 (CH_2), 22.4 (CH_3), 21.1 (CH_2), 19.4 (CH_2). **IR** (ATR): $\tilde{\nu}$ = 3240, 2900, 1741, 1622, 1535, 1444, 1201, 920, 726, 643 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 556 (20) $[M+Na]^+$, 534 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{30}H_{40}N_5O_4^+$ $[M+H]^+$ 534.3075, found 534.3077.



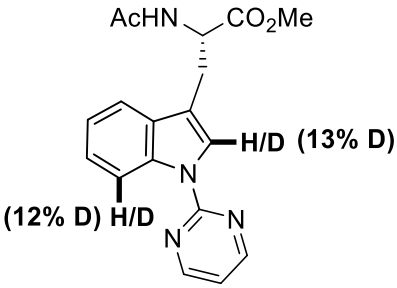
Methyl-(*S*)-2-acetamido-3-{7-[2-(adamantan-1-yl)acetamido]-1-(hexahydropyrimidin-2-yl)-1*H*-indol-3-yl}propanoate (117aeb)

To a solution of **117ae** (52 mg, 0.1 mmol) in acetic acid (1.0 mL) in a 25 mL Schlenk tube was added Pd/C (16 mg, 15 wt.-%). Then the Schlenk tube slowly evacuated and purged with H_2 three times through a H_2-filled balloon. The mixture was stirred at 100 °C for 12 h. Then, the reaction mixture was filtered through a short pad of celite. The residue was concentrated *in vacuo* under 37 °C. The crude mixture was purified by flash column chromatography on silica gel (CH_2Cl_2/MeOH/Et_3N = 100:1:1 to 100:5:1) to yield **117aeb** (51 mg, 95%) as a colorless oil. **^{1}H NMR** (300 MHz, DMSO-d_6): δ = 11.87 (s, 1H), 8.46 (d, J = 7.6 Hz, 1H), 7.66–7.58 (m, 1H), 6.92 (s, 1H), 6.91–6.87 (m, 1H), 5.36–5.29 (m, 1H), 4.31 (ddd, J = 11.3, 7.6, 4.2 Hz, 1H), 4.06–3.95 (m, 1H), 3.64 (s, 3H), 3.62–3.60 (m, 1H), 3.36–3.26 (m, 4H), 1.95–1.91 (m, 5H), 1.90 (s, 3H), 1.76–1.68 (m, 4H), 1.66–1.56 (m, 12H). **^{13}C NMR** (75 MHz, DMSO-d_6): δ = 173.0 (C_q), 170.2 (C_q), 167.8 (C_q), 151.4 (C_q), 137.0 (C_q), 135.2 (C_q), 130.5 (CH), 126.3 (C_q), 122.6 (CH), 122.4 (CH), 119.3 (CH), 63.0 (CH), 56.4 (CH_2), 52.9 (CH_2), 52.5 (CH_3), 52.4 (CH_2), 50.5 (CH), 42.8 (CH_2), 36.9 (CH_2), 33.0 (C_q), 28.5 (CH), 22.8 (CH_3), 21.3 (CH_2). **IR** (ATR): $\tilde{\nu}$ = 3432, 2899, 2249, 1660, 1032, 1024, 1012, 822, 760, 613 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 558 (10) $[M+Na]^+$, 536 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{30}H_{42}N_5O_4^+$ $[M+H]^+$ 536.3231, found 536.3234.

5.3.4.6 Characterization for H/D Exchange and Positional Selective Products

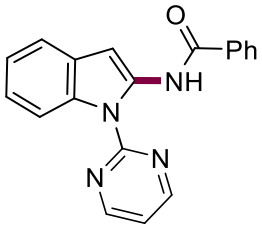


N-pyrimidyl tryptophan (**96a**) (68 mg, 0.2 mmol), $[RhCl_2Cp^*]_2$ (3.0 mg, 2.5 mol %), $AgSbF_6$ (6.8 mg, 10 mol %), $MesCO_2H$ (5.4 mg, 30 mol %), TFE (0.36 mL) and CD_3OD (0.04 mL) were placed in a 25 mL Schlenk tube under N_2 and were then stirred at 110 °C for 24 h. At ambient temperature, the reaction mixture was diluted with H_2O (5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by column chromatography (*n*-hexane/EtOAc 5:1 to 1:1) yielded **96a'** (64 mg, 95%) as a light yellow oil, The D incorporation was determined by ^1H NMR spectroscopy.



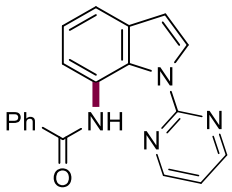
N-pyrimidyl tryptophan (**96a**) (68 mg, 0.2 mmol), 3-phenyl-1,4,2-dioxazol-5-one (**116a**) (65 mg, 0.4 mmol), $[RhCl_2Cp^*]_2$ (3.0 mg, 2.5 mol %), $AgSbF_6$ (6.8 mg, 10 mol %), $MesCO_2H$ (5.4 mg, 30 mol %), TFE (0.36 mL) and CD_3OD (0.04 mL) were placed in a 25 mL Schlenk tube under N_2 and were then stirred at 110 °C for 24 h. At ambient temperature, the reaction mixture was diluted with H_2O (5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by column chromatography (n-hexane/EtOAc 5:1 to 1:1) yielded **96a''** (45 mg, 66%) as a light yellow oil, The D incorporation was determined by ^1H NMR spectroscopy.

The general procedure **F** was followed using *N*-pyrimidyl indole (**96a**) (98 mg, 0.5 mmol) and 3-phenyl-1,4,2-dioxazol-5-one (**116a**) (82 mg, 0.5 mmol). After 24 h, purification of the residue by column chromatography on silica gel (*n*-hexane/EtOAc 5:1 to 1:1) yielded **117a** (13 mg, 8%) as a light yellow oil, and **117a'** (28 mg, 18%) as light yellow oil. The substrate **96a** was also recovered in 66%.



***N*-[1-(pyrimidin-2-yl)-1*H*-indol-2-yl]benzamide (117a')**

^{1}H NMR (600 MHz, DMSO-*d*$_6$): *δ* = 12.84 (s, 1H), 9.03 (d, *J* = 4.9 Hz, 2H), 8.60 (ddt, *J* = 6.0, 3.3, 0.7 Hz, 1H), 8.01–7.99 (m, 2H), 7.68–7.64 (m, 1H), 7.64–7.60 (m, 2H), 7.59–7.56 (m, 1H), 7.48 (t, *J* = 4.9 Hz, 1H), 7.25 (d, *J* = 0.7 Hz, 1H), 7.23–7.19 (m, 2H). **^{13}C NMR** (151 MHz, DMSO-*d*$_6$): *δ* = 163.0 (C_q), 158.7 (CH), 157.8 (C_q), 135.2 (C_q), 133.7 (C_q), 132.2 (CH), 132.1 (C_q), 129.1 (CH), 129.0 (C_q), 127.0 (CH), 122.7 (CH), 122.2 (CH), 119.6 (CH), 117.5 (CH), 115.7 (CH), 94.7 (CH). **IR** (ATR): *ṽ* = 3409, 2253, 2126, 1993, 1666, 1427, 1025, 823, 762, 539 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 651 (50) $[2M+Na]^+$, 337 (100) $[M+Na]^+$, 315 (90) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{19}H_{15}N_4O^+$ $[M+H]^+$ 315.1240, found 315.1237.



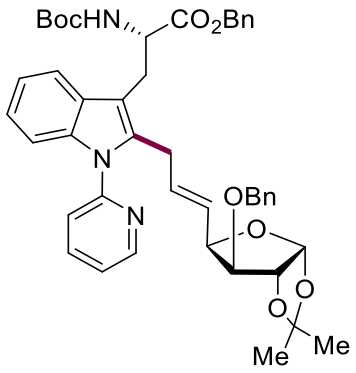
***N*-[1-(pyrimidin-2-yl)-1*H*-indol-7-yl]benzamide (117a)**

^{1}H NMR (400 MHz, DMSO-*d*$_6$): *δ* = 10.63 (s, 1H), 8.89 (d, *J* = 4.8 Hz, 2H), 8.16 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.77 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.45 (t, *J* = 4.8 Hz, 1H), 7.38 (dd, *J* = 8.3, 7.1 Hz, 1H), 7.35–7.31 (m, 2H), 7.30–7.27 (m, 2H), 7.09 (dd, *J* = 8.6, 7.1 Hz, 1H). **^{13}C NMR** (101 MHz, DMSO-*d*$_6$): *δ* = 160.1 (C_q), 158.7 (CH), 156.7 (C_q), 139.2 (C_q), 137.0 (C_q), 134.7 (C_q), 128.7 (CH), 127.3 (C_q), 125.3 (CH), 123.5 (CH), 122.4 (CH), 122.0

(CH), 119.7 (CH), 118.6 (CH), 113.2 (CH), 109.9 (CH). **IR** (ATR): $\tilde{\nu}$ = 3050, 1667, 1598, 1541, 1423, 1312, 1193, 1006, 813, 752 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 651 (70) $[2M+Na]^+$, 337 (100) $[M+Na]^+$, 315 (80) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{19}H_{15}N_4O^+$ $[M+H]^+$ 315.1240, found 315.1231.

5.3.5 C—H Activations for Peptide-Carbohydrate Conjugation by Manganese(I)-Catalysis

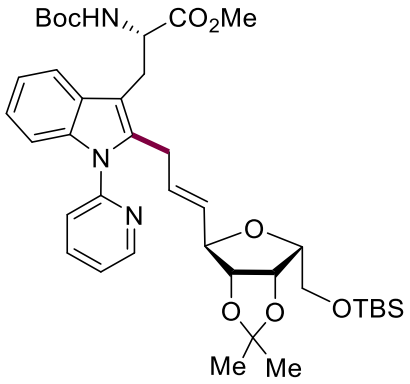
5.3.5.1 Characterization Data of Tryptophan Glycoconjugation Products 120aa-120af



(*S*)-Benzyl-3-{2-[(*E*)-3-{(3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl}allyl]-1-(pyridin-2-yl)-1*H*-indol-3-yl}-2-[(*tert*-butoxycarbonyl)amino]propanoate (120aa)

The general procedure **G** was followed using Boc-Trp^{py}-OBn **88ad** (47.1 mg, 0.1 mmol) and allyl furanose carbonate **119a** (72.8 mg, 0.2 mmol). Purification by column chromatography (*n*-pentane/EtOAc 5:1) yielded **120aa** (57.4 mg, 76%, *E/Z* = 13:1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.59 (ddd, *J* = 4.9, 2.0, 0.8 Hz, 1H), 7.76 (dd, *J* = 7.9, 2.0 Hz, 1H), 7.59–7.52 (m, 1H), 7.33–7.30 (m, 2H), 7.29–7.26 (m, 3H), 7.25–7.21 (m, 4H), 7.19–7.13 (m, 6H), 5.92 (d, *J* = 3.8 Hz, 0.07H, *Z* isomer), 5.85 (d, *J* = 3.8 Hz, 1H), 5.76 (dt, *J* = 15.6, 5.8 Hz, 1H), 5.40 (dd, *J* = 15.6, 7.4 Hz, 1H), 5.18 (d, *J* = 8.3 Hz, 1H), 5.07 (d, *J* = 12.3 Hz, 1H), 4.99 (d, *J* = 12.3 Hz, 1H), 4.68 (q, *J* = 6.9 Hz, 1H), 4.54 (d, *J* = 4.0 Hz, 1H), 4.52 (d, *J* = 12.0 Hz, 1H), 4.48–4.43 (m, 1H), 4.41 (d, *J* = 12.0 Hz, 1H), 3.70 (d, *J* = 3.1 Hz, 1H), 3.65 (d, *J* = 5.8 Hz, 2H), 3.36–3.22 (m, 2H), 1.45 (s, 3H), 1.42 (s, 9H), 1.29 (s, 3H). **^{13}C**

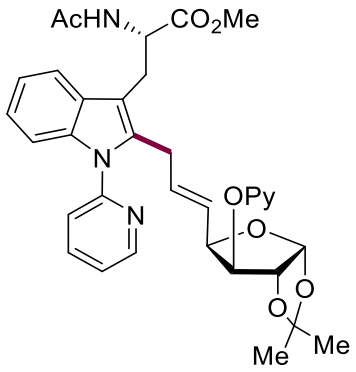
NMR (101 MHz, $CDCl_3$): δ = 172.3 (C_q), 155.2 (C_q), 151.3 (C_q), 149.5 (CH), 138.3 (CH), 137.6 (C_q), 136.9 (C_q), 135.6 (C_q), 135.3 (C_q), 132.0 (CH), 128.8 (C_q), 128.6 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 127.9 (CH), 127.5 (CH), 125.4 (CH), 122.4 (CH), 122.2 (CH), 121.4 (CH), 120.7 (CH), 118.7 (CH), 111.4 (C_q), 110.4 (CH), 109.6 (C_q), 104.7 (CH), 83.5 (CH), 82.8 (CH), 80.9 (CH), 79.9 (C_q), 72.0 (CH_2), 67.3 (CH_2), 54.3 (CH), 28.4 (CH_3), 28.0 (CH_2), 27.7 (CH_2), 26.8 (CH_3), 26.3 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2978, 2929, 1709, 1586, 1471, 1457, 1351, 1162, 1072, 1015 cm^{-1}. **MS** (ESI) *m*/*z* (relative intensity): 782 (90) $[M+Na]^+$, 760 (100) $[M+H]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{45}H_{50}N_3O_8^+$ $[M+H]^+$ 760.3592, found 760.3591.



(*S*)-Methyl2-[(*tert*-butoxycarbonyl)amino]-3-{2-[(*E*)-3-{(3a*R*,4*R*,6*R*,6a*S*)-6-{[(*tert*-butyldimethylsilyl)oxy]methyl}-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl}allyl]-1-(pyridin-2-yl)-1*H*-indol-3-yl}propanoate (120ab)

The general procedure **G** was followed using Boc-Trp^{py}-OMe **88ab** (39.5 mg, 0.1 mmol) and allyl ribose carbonate **119b** (70.2 mg, 0.2 mmol). Purification by column chromatography (*n*-pentane/EtOAc 5:1) yielded **120ab** (57.3 mg, 79%, *E*/*Z* = 10:1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.63 (ddd, *J* = 4.9, 2.0, 0.8 Hz, 1H), 7.83 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.58 – 7.52 (m, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.29 (ddd, *J* = 7.7, 4.9, 1.1 Hz, 2H), 7.18–7.05 (m, 2H), 5.58 (dt, *J* = 15.5, 6.0 Hz, 1H), 5.32 (dd, *J* = 15.5, 7.4 Hz, 1H), 5.21 (d, *J* = 8.2 Hz, 1H), 4.81 (dd, *J* = 6.0, 1.0 Hz, 0.1H, *Z* isomer), 4.74 (dd, *J* = 6.0, 1.0 Hz, 1H), 4.68–4.55 (m, 1H), 4.50–4.41 (m, 1H), 4.29 (dd, *J* = 7.4, 4.1 Hz, 1H), 3.99 (t, *J* = 3.7 Hz, 1H), 3.70–3.62 (m, 7H), 3.32 (d, *J* = 6.0 Hz, 2H), 1.42 (s, 12H), 1.31 (s, 3H), 0.85 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.8 (C_q), 155.2 (C_q), 151.3 (C_q), 149.5 (CH), 138.2 (CH), 136.8 (C_q), 135.8 (C_q), 130.7 (CH), 128.9 (C_q), 127.2 (CH), 122.2 (CH),

122.1 (CH), 121.6 (CH), 120.6 (CH), 118.6 (CH), 112.1 (C_q), 110.2 (CH), 109.6 (C_q), 84.3 (CH), 83.4 (CH), 83.3 (CH), 83.2 (CH), 79.8 (C_q), 65.0 (CH_2), 54.3 (CH), 52.4 (CH_3), 28.6 (CH_3), 28.4 (CH_2), 27.6 (CH_2), 26.6 (CH_3), 26.1 (CH_3), 25.3 (CH_3), 18.3 (C_q), –5.3 (CH_3), –5.4 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2951, 2930, 2856, 1743, 1712, 1471, 1459, 1366, 1252, 1162 cm^{-1}. **MS** (ESI) *m*/*z* (relative intensity): 744 (100) $[M+Na]^+$, 722 (50) $[M+H]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{39}H_{56}N_3O_8Si^+$ $[M+H]^+$ 722.3831, found 722.3825.

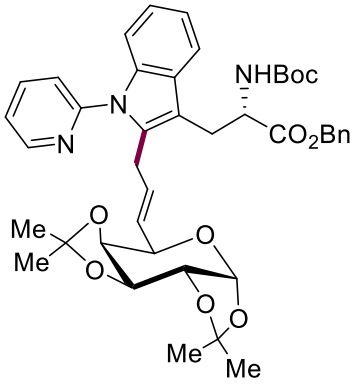


(*S*)-Methyl-2-acetamido-3-{2-[(*E*)-3-{(3a*R*,5*R*,6*S*,6a*R*)-2,2-dimethyl-6-(pyridin-2-yloxy)tetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl}allyl]-1-(pyridin-2-yl)-1*H*-indol-3-yl}propanoate (120ac)

The general procedure **G** was followed using Ac-Trp^{py}-OMe **88ae** (33.7 mg, 0.1 mmol) and allyl furanose carbonate **119c** (70.2 mg, 0.2 mmol). Purification by column chromatography (*n*-pentane/EtOAc 3:2) yielded **120ac** (60.2 mg, 98%, *E*/*Z* = 16:1 determined by ^{1}H NMR) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 8.49 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 8.17 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.63–7.53 (m, 2H), 7.52–7.44 (m, 1H), 7.26–7.21 (m, 2H), 7.15–7.09 (m, 2H), 7.00 (ddd, *J* = 7.5, 4.9, 0.9 Hz, 1H), 6.92 (ddd, *J* = 7.1, 4.9, 0.9 Hz, 1H), 6.64 (d, *J* = 8.4 Hz, 1H), 6.12 (d, *J* = 8.0 Hz, 1H), 5.95 (d, *J* = 3.9 Hz, 0.07H, *Z* isomer), 5.85 (d, *J* = 3.9 Hz, 1H), 5.75 (dt, *J* = 15.5, 5.6 Hz, 1H), 5.36 (dd, *J* = 15.5, 7.6 Hz, 1H), 5.19 (d, *J* = 3.0 Hz, 1H), 4.90 (dt, *J* = 8.0, 5.7 Hz, 1H), 4.57(dd, *J* = 8.6, 3.4 Hz, 2H), 3.65–3.61 (m, 5H), 3.21 (d, *J* = 5.6 Hz, 2H), 1.94 (s, 3H), 1.49 (s, 3H), 1.27 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.4 (C_q), 169.7 (C_q), 162.3 (C_q), 151.1 (C_q), 149.3 (CH), 146.9 (CH), 138.9 (CH), 138.1 (CH), 136.7 (C_q), 135.5 (C_q), 132.7 (CH), 128.7 (C_q), 124.7 (CH), 122.4 (CH), 122.1 (CH), 121.2 (CH), 120.7 (CH), 118.4 (CH), 117.5 (CH), 111.7 (C_q), 111.5 (CH), 110.2 (CH), 109.4 (C_q), 104.6 (CH), 83.5 (CH), 79.9 (CH), 78.8 (CH), 52.8 (CH), 52.5 (CH_3), 28.0 (CH_2), 27.1

(CH_2), 26.8 (CH_3), 26.3 (CH_3), 23.3 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2990, 1740, 1590, 1570, 1469, 1432, 1371, 1285, 1214, 1068 cm^{-1}. **MS** (ESI) *m*/*z* (relative intensity): 635 (60) $[M+Na]^+$, 613 (100) $[M+H]^+$. **HR-MS** (ESI): *m*/*z* calcd for $C_{34}H_{37}N_4O_7^+$ $[M+H]^+$ 613.2657, found 613.2654.

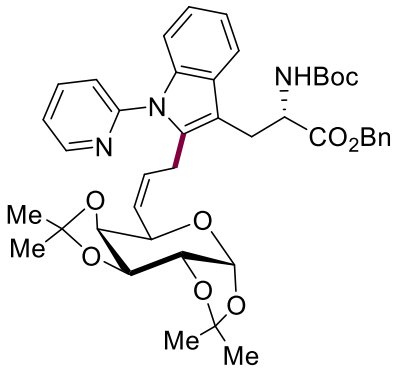
The general procedure **G** was followed using Boc-Trp^{py}-OBn **88ad** (47.1 mg, 0.1 mmol) and allyl galactose carbonate **119d** (68.8 mg, 0.2 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1 to 3:1) yielded **120ad** (48.0 mg, 65%) as a light yellow oil and **120ae** (9.6 mg, 13%) as a light yellow oil.



Benzyl-(*S*)-2-[(*tert*-butoxycarbonyl)amino]-3-{1-(pyridin-2-yl)-2-{(*E*)-3-[(3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis{[1,3]dioxolo}[4,5-b:4',5'-*d*]pyran-5-yl]allyl}-1*H*-indol-3-yl}propanoate (120ad)

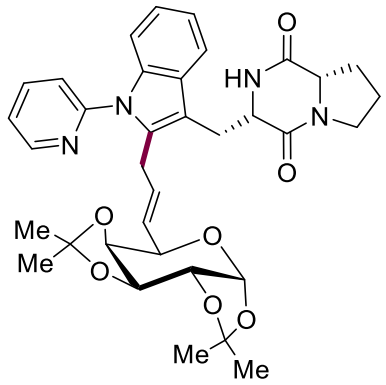
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.62 (dd, *J* = 5.0, 1.9 Hz, 1H), 7.81 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.58–7.56 (m, 1H), 7.35 (d, *J* = 7.9 Hz, 1H), 7.30–7.26 (m, 5H), 7.20–7.17 (m, 2H), 7.14–7.12 (m, 2H), 5.61 (dt, *J* = 15.6, 5.7 Hz, 1H), 5.46 (d, *J* = 5.0 Hz, 1H), 5.26 (d, *J* = 8.2 Hz, 1H), 5.21 (dd, *J* = 15.6, 5.9 Hz, 1H), 5.09 (d, *J* = 12.2 Hz, 1H), 4.99 (d, *J* = 12.2 Hz, 1H), 4.66–4.59 (m, 1H), 4.49 (dd, *J* = 7.9, 2.3 Hz, 1H), 4.22 (dd, *J* = 5.0, 2.3 Hz, 1H), 4.04–3.99 (m, 1H), 3.91 (dd, *J* = 7.9, 1.9 Hz, 1H), 3.66–3.60 (m, 2H), 3.46–3.21 (m, 2H), 1.45 (s, 3H), 1.41 (s, 9H), 1.36 (s, 3H), 1.29 (s, 3H), 1.28 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.3 (C_q), 155.2 (C_q), 151.3 (C_q), 149.5 (CH), 138.2 (CH), 136.9 (C_q), 135.7 (C_q), 135.4 (C_q), 129.8 (CH), 128.9 (C_q), 128.5 (CH), 128.3 (CH), 128.2 (CH), 127.4 (CH), 122.3 (CH), 122.2 (CH), 121.6 (CH), 120.6 (CH), 118.8 (CH), 110.2 (CH), 109.7 (C_q), 109.0 (C_q), 108.4 (C_q), 96.4 (CH), 79.8 (C_q), 73.3 (CH), 70.9 (CH), 70.6 (CH), 68.3 (CH), 67.3 (CH_2), 54.4 (CH), 28.6 (CH_3), 28.2 (CH_2), 27.6 (CH_2), 26.3 (CH_3), 26.2 (CH_3), 25.1 (CH_3), 24.5 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2979, 2025,

1711, 1587, 1437, 1369, 1164, 1064, 994, 740 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 762 (80) $[M+Na]^+$, 740 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{42}H_{50}N_3O_9$ $[M+H]^+$ 740.3542, found 740.3534.



Benzyl-(*S*)-2-[(*tert*-butoxycarbonyl)amino]-3-{1-(pyridin-2-yl)-2-{(*Z*)-3-[(3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis{[1,3]dioxolo}[4,5-b:4',5'-*d*]pyran-5-yl]allyl}-1*H*-indol-3-yl}propanoate (120ae)

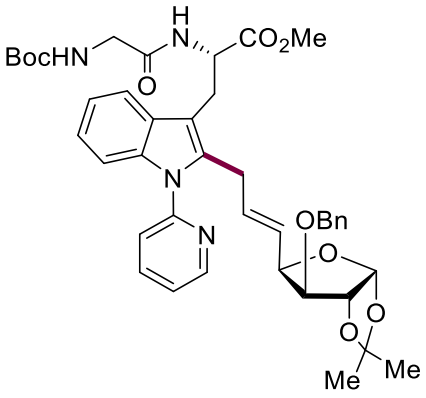
^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.65 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.84 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.60–7.56 (m, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.31–7.27 (m, 5H), 7.25–7.17 (m, 2H), 7.15–7.12 (m, 2H), 5.54 (d, *J* = 5.2 Hz, 1H), 5.49–5.39 (m, 2H), 5.35 (d, *J* = 8.5 Hz, 1H), 5.13 (d, *J* = 12.4 Hz, 1H), 5.05 (d, *J* = 12.4 Hz, 1H), 4.71 (q, *J* = 7.1 Hz, 1H), 4.57 (dd, *J* = 7.9, 2.4 Hz, 1H), 4.55 (dd, *J* = 6.3, 1.9 Hz, 1H), 4.29 (dd, *J* = 5.2, 2.4 Hz, 1H), 3.95 (d, *J* = 7.9 Hz, 1H), 3.88–3.72 (m, 2H), 3.35–3.26 (m, 2H), 1.67 (s, 3H), 1.43 (s, 3H), 1.40 (s, 9H), 1.36 (s, 3H), 1.31 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.4 (C_q), 155.3 (C_q), 154.6 (CH), 151.3 (C_q), 149.9 (CH), 138.3 (CH), 136.7 (C_q), 136.5 (C_q), 135.5 (C_q), 131.7 (CH), 128.7 (C_q), 128.5 (CH), 128.2 (CH), 125.4 (CH), 122.4 (CH), 121.9 (CH), 121.1 (CH), 120.8 (CH), 118.7 (CH), 110.1 (CH), 109.6 (C_q), 109.2 (C_q), 108.5 (C_q), 96.7 (CH), 79.8 (C_q), 73.0 (CH), 71.0 (CH), 70.3 (CH), 67.2 (CH_2), 63.7 (CH), 54.4 (CH), 28.6 (CH_3), 28.1 (CH_2), 27.7 (CH_2), 26.3 (CH_3), 26.2 (CH_3), 25.1 (CH_3), 24.6 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3354, 2980, 1712, 1472, 1458, 1368, 1255, 1066, 995, 742 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 762 (30) $[M+Na]^+$, 740 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{42}H_{50}N_3O_9$ $[M+H]^+$ 740.3542, found 740.3535.



(3*S*,8a*S*)-3-[(1-(Pyridin-2-yl)-2-{(*E*)-3-(3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis{[1,3]dioxolo}[4,5-b:4',5'-d]pyran-5-yl}allyl)-1*H*-indol-3-yl]methyl)hexahydropyrrolo[1,2-*a*]pyrazine-1,4-dione (120af)

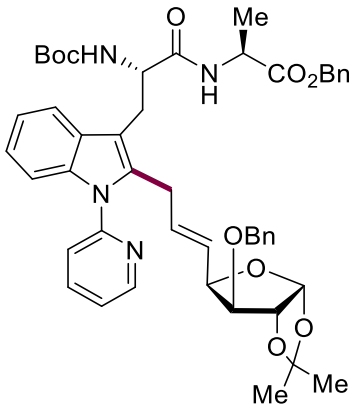
The general procedure **G** was followed using Brevianamide F^{py} **88af** (36.0 mg, 0.1 mmol) and allyl galactose carbonate **119d** (68.8 mg, 0.2 mmol). Purification by column chromatography (*n*-hexane/EtOAc 10:1 to 3:1) yielded **120af** (34.5 mg, 55%, *E/Z* = 6:1 determined by ^{1}H NMR) as a light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.63 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.86 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.58–7.55 (m, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.35–7.30 (m, 2H), 7.19–7.15 (m, 2H), 5.74–5.72 (m, 1H), 5.45 (d, *J* = 5.0 Hz, 1H), 5.31 (dd, *J* = 16.2, 6.3 Hz, 1H), 4.50 (dd, *J* = 7.8, 2.0 Hz, 1H), 4.46–4.38 (m, 1H), 4.22 (dd, *J* = 5.0, 2.3 Hz, 1H), 4.09–4.04 (m, 2H), 3.98 (dd, *J* = 7.8, 2.0 Hz, 1H), 3.72–3.66 (m, 3H), 3.61–3.54 (m, 1H), 3.06 (dd, *J* = 15.1, 11.3 Hz, 1H), 2.35–2.26 (m, 1H), 2.17–2.16 (m, 1H), 2.08–1.78 (m, 4H), 1.46 (s, 3H), 1.38 (s, 3H), 1.28 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 169.3 (C_q), 165.7 (C_q), 151.0 (C_q), 149.6 (CH), 138.4 (CH), 137.1 (C_q), 136.2 (C_q), 130.1 (CH), 128.1 (C_q), 127.7 (CH), 122.8 (CH), 122.5 (CH), 121.7 (CH), 121.1 (CH), 118.1 (CH), 110.7 (CH), 109.1 (C_q), 108.7 (C_q), 108.5 (C_q), 96.5 (CH), 73.4 (CH), 71.0 (CH), 70.5 (CH), 68.3 (CH), 59.3 (CH), 55.1 (CH), 45.6 (CH_2), 28.5 (CH_2), 28.3 (CH_2), 26.3 (CH_3), 26.3 (CH_3), 25.9 (CH_2), 25.1 (CH_3), 24.7 (CH_3), 22.9 (CH_2). **IR** (ATR): $\tilde{\nu}$ = 2985, 1667, 1588, 1471, 1371, 1256, 1167, 1066, 994, 745 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 651 (100) $[M+Na]^+$, 629 (90) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{35}H_{41}N_4O_7$ $[M+H]^+$ 629.2970, found 629.2967.

5.3.5.2 Characterization Data of Peptide Glycoconjugates 120ba-120bo



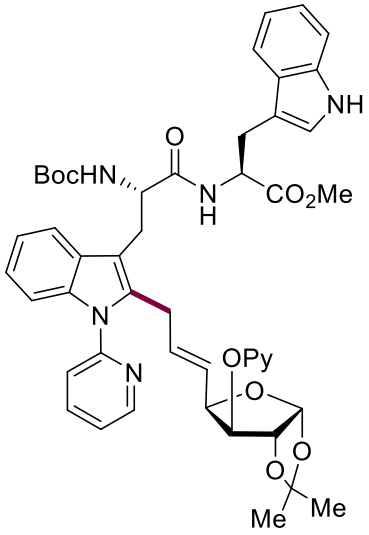
Methyl-(*S*)-3-{2-[(*E*)-3-{(3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl)allyl}-1-(pyridin-2-yl)-1*H*-indol-3-yl]-2-{2-[(*tert*-butoxycarbonyl)amino]acetamido}propanoate (120ba)

The general procedure **H** was followed using Boc-Gly-Trp^{py}-OMe **88bd** (45.3 mg, 0.1 mmol), allyl furanose carbonate **119a** (72.8 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120ba** (50.0 mg, 68 %, *E/Z* = 14:1 determined by ^{1}H NMR) as a light yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.56 (dd, *J* = 5.0, 1.4 Hz, 1H), 7.79 (dd, *J* = 7.8, 2.1 Hz, 1H), 7.52 (d, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.29–7.26 (m, 2H), 7.26–7.22 (m, 2H), 7.21–7.18 (m, 2H), 7.16–7.14 (m, 3H), 6.55 (d, *J* = 7.7 Hz, 1H), 5.95 (d, *J* = 3.8 Hz, 0.07H, *Z* isomer), 5.88 (d, *J* = 3.8 Hz, 1H), 5.81 (d, *J* = 15.5, 5.1 Hz, 1H), 5.45 (dd, *J* = 15.5, 6.0 Hz, 1H), 5.33–5.15 (m, 1H), 4.92 (q, *J* = 6.5 Hz, 1H), 4.59–4.55 (m, 2H), 4.47–4.40 (m, 2H), 3.74–3.68 (m, 4H), 3.64 (s, 3H), 3.37–3.25 (m, 2H), 1.44 (s, 3H), 1.39 (s, 9H), 1.28 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.0 (C_q), 169.1 (C_q), 155.1 (C_q), 151.0 (C_q), 149.3 (CH), 138.2 (CH), 137.3 (C_q), 136.7 (C_q), 135.5 (C_q), 128.4 (C_q), 128.3 (CH), 127.7 (CH), 127.4 (CH), 125.1 (CH), 122.4 (CH), 122.1 (CH), 121.2 (CH), 120.7 (CH), 118.2 (CH), 114.5 (CH), 111.4 (C_q), 110.2 (CH), 109.4 (C_q), 104.5 (CH), 83.1 (CH), 82.5 (CH), 80.5 (CH), 79.8 (C_q), 71.8 (CH_2), 52.8 (CH), 52.4 (CH_3), 44.0 (CH_2), 28.3 (CH_3), 27.9 (CH_2), 27.1 (CH_2), 26.7 (CH_3), 26.2 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3356, 2979, 2023, 1716, 1519, 1472, 1369, 1165, 1020, 468 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1503 (40) $[2M+Na]^+$, 763 (100) $[M+Na]^+$, 741 (60) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{41}H_{49}N_4O_9^+$ $[M+H]^+$ 741.3494, found 741.3490.



Benzyl-{(*S*)-3-[2-{(*E*)-3-[(3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl]allyl}-1-(pyridin-2-yl)-1*H*-indol-3-yl]-2-[(*tert*-butoxycarbonyl)amino]propanoyl}-*L*-alaninate (120bb)

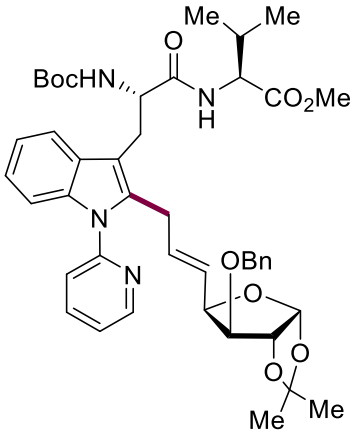
The general procedure **H** was followed using Boc-Trp^{py}-Ala-OBn **88be** (54.2 mg, 0.1 mmol), allyl furanose carbonate **119a** (72.8 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bb** (62.3 mg, 75%, *E/Z* = 15:1 determined by ^{1}H NMR) as a yellow solid (M.p. = 83–84 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.54 (dd, *J* = 4.9, 1.9 Hz, 0.06H, *Z* isomer), 8.59 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.78 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.65 (d, *J* = 6.5 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.35–7.27 (m, 5H), 7.26–7.23 (m, 5H), 7.19–7.16 (m, 2H), 7.15–7.12 (m, 2H), 6.32 (d, *J* = 5.9 Hz, 1H), 5.84 (d, *J* = 3.8 Hz, 1H), 5.80 (dt, *J* = 15.5, 5.2 Hz, 1H), 5.47 (dt, *J* = 15.5, 7.5 Hz, 1H), 5.00 (s, 2H), 4.53 (s, 1H), 4.52 (d, *J* = 6.8 Hz, 1H), 4.49–4.42 (m, 4H), 3.73 (d, *J* = 2.9 Hz, 1H), 3.69 (d, *J* = 5.2 Hz, 2H), 3.37–3.26 (m, 1H), 3.19–3.09 (m, 1H), 1.43 (s, 3H), 1.41 (s, 9H), 1.27 (s, 3H), 1.26 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.7 (C_q), 170.9 (C_q), 151.2 (C_q), 149.3 (CH), 138.1 (CH), 137.4 (C_q), 136.8 (C_q), 135.4 (C_q), 135.3 (C_q), 132.2 (CH), 128.5 (CH), 128.4 (CH), 128.3 (C_q), 128.2 (CH), 127.9 (CH), 127.7 (CH), 127.4 (CH), 125.3 (CH), 122.3 (CH), 122.0 (CH), 121.3 (CH), 120.7 (CH), 118.7 (CH), 111.3 (C_q), 110.3 (CH), 109.8 (2C_q), 104.6 (CH), 83.4 (CH), 82.8 (CH), 80.9 (CH), 79.8 (C_q), 72.0 (CH_2), 66.9 (CH_2), 54.9 (CH), 48.3 (CH), 28.4 (CH_3), 29.8 (CH_2), 28.0 (CH_2), 26.8 (CH_3), 26.3 (CH_3), 18.4 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1668, 1471, 1438, 1367, 1161, 1072, 1016, 739, 797 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 853 (80) $[M+Na]^+$, 831 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{48}H_{55}N_4O_9^+$ $[M+H]^+$ 831.3964, found 831.3959.



Methyl-[(*S*)-2-[(*tert*-butoxycarbonyl)amino]-3-(2-{(*E*)-3-[(3a*R*,5*R*,6*S*,6a*R*)-2,2-dimethyl-6-(pyridin-2-yloxy)tetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl]allyl}-1-(pyridin-2-yl)-1*H*-indol-3-yl)propanoyl]-*L*-tryptophanate (120bc)

The general procedure **H** was followed using Boc-Trp^{py}-Trp-OMe **88bf** (58.1 mg, 0.1 mmol), allyl furanose carbonate **119c** (70.3 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bc** (58.3 mg, 68%, *E*/*Z* = 11:1 determined by ^{1}H NMR) as a white solid (M.p. = 118–119 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.78 (s, 1H), 8.58 (dd, *J* = 5.0, 1.3 Hz, 1H), 8.15 (ddd, *J* = 5.0, 2.0, 0.7 Hz, 1H), 7.68–7.63 (m, 2H), 7.56 (ddd, *J* = 8.4, 7.0, 2.0 Hz, 1H), 7.31 (d, *J* = 7.0 Hz, 1H), 7.25–7.18 (m, 3H), 7.17–7.12 (m, 3H), 7.09–7.05 (m, 1H), 7.00–6.95 (m, 1H), 6.90 (dd, *J* = 7.1, 5.0 Hz, 1H), 6.64 (d, *J* = 8.3 Hz, 1H), 6.44–6.35 (m, 1H), 6.20–6.10 (m, 1H), 5.90 (dd, *J* = 3.7 Hz, 0.1H, *Z* isomer), 5.85 (dd, *J* = 3.7 Hz, 1H), 5.77 (dt, *J* = 15.3, 5.9 Hz, 1H), 5.38 (dd, *J* = 15.3, 7.5 Hz, 1H), 5.27 (d, *J* = 2.4 Hz, 1H), 5.12–5.06 (m, 1H), 4.70–4.62 (m, 2H), 4.59 (d, *J* = 3.7 Hz, 1H), 4.51–4.43 (m, 1H), 3.69–3.58 (m, 2H), 3.53 (s, 3H), 3.37–3.20 (m, 1H), 3.07 (d, *J* = 5.9 Hz, 2H), 3.02–2.91 (m, 1H), 1.53 (s, 3H), 1.41 (s, 9H), 1.30 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.3 (C_q), 170.8 (C_q), 162.2 (C_q), 155.0 (C_q), 151.0 (C_q), 149.1 (CH), 146.8 (CH), 138.9 (CH), 138.3 (CH), 136.8 (C_q), 135.9 (C_q), 135.5 (C_q), 132.4 (CH), 128.3 (C_q), 127.2 (C_q), 124.7 (CH), 122.9 (CH), 122.3 (CH), 122.2 (CH), 121.7 (CH), 121.5 (CH), 120.8 (CH), 119.2 (CH), 119.1 (CH), 118.2 (CH), 117.4 (CH), 111.6 (C_q), 111.3 (CH), 111.1 (CH), 110.1 (CH), 109.8 (C_q), 109.1 (C_q), 104.5 (CH), 83.5 (CH), 79.9 (CH), 79.8 (C_q), 78.7 (CH), 52.7 (CH), 52.5 (CH), 52.2

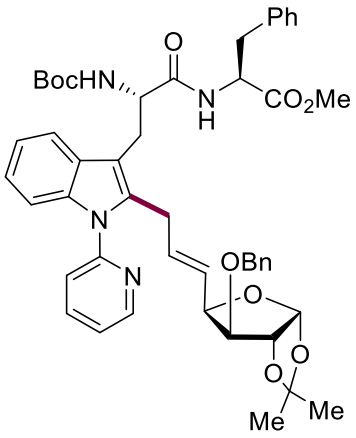
(CH_3), 45.9 (CH_2), 28.4 (CH_3), 27.9 (CH_2), 27.3 (CH_2), 26.7 (CH_3), 26.2 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1671, 1588, 1471, 1367, 1163, 1014, 854, 781, 740, 698 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 879 (80) $[M+Na]^+$, 857 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{48}H_{53}N_6O_9^+$ $[M+H]^+$ 857.3869, found 857.3872.



Methyl-[(*S*)-3-{2-[(*E*)-3-[(3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl]allyl]-1-(pyridin-2-yl)-1*H*-indol-3-yl}-2-[(*tert*-butoxycarbonyl)amino]propanoyl]-*L*-valinate (120bd)

The general procedure **H** was followed using Boc-Trp^{py}-Val-OMe **88bg** (49.5 mg, 0.1 mmol), allyl furanose carbonate **119a** (72.8 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bd** (52.5 mg, 67%, only traces of *Z* isomer observed by ^{1}H NMR) as a white solid (M.p. = 86–87 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.59 (ddd, *J* = 4.9, 1.9, 0.7 Hz, 1H), 7.78 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.64 (d, *J* = 6.4 Hz, 1H), 7.43 (m, 1H), 7.31–7.28 (m, 1H), 7.26–7.24 (m, 3H), 7.24–7.23 (m, 1H), 7.19–7.16 (m, 2H), 7.16–7.13 (m, 2H), 6.16 (d, *J* = 8.3 Hz, 1H), 5.84 (d, *J* = 3.8 Hz, 1H), 5.78 (dt, *J* = 15.6, 5.1 Hz, 1H), 5.46 (dd, *J* = 15.6, 7.5 Hz, 1H), 5.31–5.22 (m, 1H), 4.53 (dd, *J* = 7.9, 4.1 Hz, 2H), 4.48–4.46 (m, 1H), 4.46–4.42 (m, 2H), 4.34 (dd, *J* = 8.3, 5.1 Hz, 1H), 3.73 (d, *J* = 3.1 Hz, 1H), 3.72–3.68 (m, 2H), 3.52 (s, 3H), 3.33–3.25 (m, 1H), 3.20–3.12 (m, 1H), 2.03–1.97 (m, 1H), 1.43 (s, 3H), 1.42 (s, 9H), 1.27 (s, 3H), 0.79 (d, *J* = 6.9 Hz, 3H), 0.77 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.2 (C_q), 171.1 (C_q), 155.2 (C_q), 151.1 (C_q), 149.3 (CH), 138.1 (CH), 137.4 (C_q), 136.8 (C_q), 135.4 (C_q), 132.1 (CH), 128.3 (CH), 128.2 (C_q), 127.7 (CH), 127.4 (CH), 125.3 (CH), 122.2 (CH), 122.0 (CH), 121.3 (CH), 120.7 (CH), 118.5 (CH), 111.3

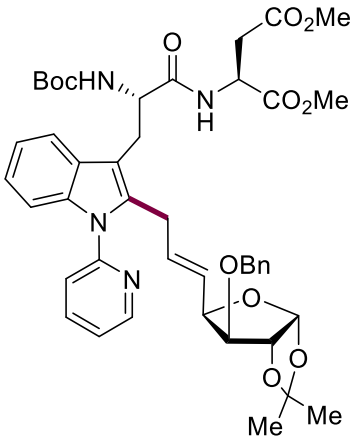
(C_q), 110.2 (CH), 109.8 (C_q), 104.6 (CH), 83.4 (CH), 82.7 (CH), 80.8 (CH), 79.8 (C_q), 72.0 (CH_2), 57.3 (CH), 55.2 (CH), 52.0 (CH_3), 31.9 (CH_2), 31.6 (CH), 28.4 (CH_3), 28.0 (CH_2), 26.8 (CH_3), 26.2 (CH_3), 18.7 (CH_3), 18.0 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2977, 1674, 1437, 1211, 1069, 994, 861, 741, 699, 507 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 805 (100) $[M+Na]^+$, 783 (80) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{44}H_{55}N_4O_9^+$ $[M+H]^+$ 783.3964, found 783.3956.



Methyl-[(*S*)-3-(2-{(*E*)-3-[(3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl]allyl}-1-(pyridin-2-yl)-1*H*-indol-3-yl)-2-[(*tert*-butoxycarbonyl)amino]propanoyl]-*L*-phenylalaninate (120be)

The general procedure **H** was followed using Boc-Trp^{py}-Phe-OMe **88bh** (54.2 mg, 0.1 mmol), allyl furanose carbonate **119a** (72.8 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120be** (56.5 mg, 68%, only traces of *Z* isomer observed by ^{1}H NMR) as a yellow solid (M.p. = 86–87 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.58 (ddd, *J* = 4.9, 2.0, 0.6 Hz, 1H), 7.77 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.65 (d, *J* = 6.1 Hz, 1H), 7.40 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.29 (dd, *J* = 6.8, 1.7 Hz, 1H), 7.26–7.23 (m, 4H), 7.19–7.15 (m, 3H), 7.15 (dd, *J* = 2.2, 1.3 Hz, 1H), 7.14–7.12 (m, 3H), 6.87 (d, *J* = 3.0 Hz, 2H), 6.15–6.04 (m, 1H), 5.84 (d, *J* = 3.8 Hz, 1H), 5.79 (dt, *J* = 15.5, 5.9 Hz, 1H), 5.45 (dd, *J* = 15.6, 7.6 Hz, 1H), 5.30–5.19 (m, 1H), 4.66–4.59 (m, 1H), 4.54 (d, *J* = 1.9 Hz, 1H), 4.53 (d, *J* = 10.0 Hz, 1H), 4.48–4.45 (m, 3H), 3.74–3.68 (m, 3H), 3.50 (s, 3H), 3.32–3.23 (m, 1H), 3.14–3.06 (m, 1H), 3.00–2.88 (m, 2H), 1.43 (s, 3H), 1.41 (s, 9H), 1.27 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 170.9 (C_q), 170.8 (C_q), 155.0 (C_q), 151.0 (C_q), 149.3 (CH), 138.1 (CH), 137.4 (C_q), 136.8 (C_q), 135.7 (C_q), 135.5 (C_q), 132.1 (CH), 129.1 (CH), 128.3 (CH), 128.3 (CH), 128.2 (C_q),

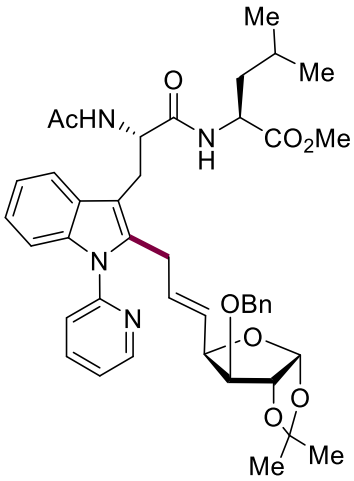
127.7 (CH), 127.4 (CH), 126.8 (CH), 125.3 (CH), 122.3 (CH), 122.1 (CH), 121.3 (CH), 120.8 (CH), 118.7 (CH), 111.3 (C_q), 110.2 (CH), 109.7 (C_q), 104.5 (CH), 83.4 (CH), 82.7 (CH), 80.8 (CH), 79.8 (C_q), 72.0 (CH_2), 54.9 (CH), 53.5 (CH), 52.1 (CH_3), 52.0 (CH_2), 38.1 (CH_2), 28.3 (CH_3), 28.0 (CH_2), 26.8 (CH_3), 26.2 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1711, 1471, 1212, 1164, 1067, 994, 899, 741, 700, 508 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 853 (100) $[M+Na]^+$, 831 (70) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{48}H_{55}N_4O_9^+$ $[M+H]^+$ 831.3964, found 831.3956.



Dimethyl-[(*S*)-3-(2-{(*E*)-3-[(3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl]allyl}-1-(pyridin-2-yl)-1*H*-indol-3-yl)-2-[(*tert*-butoxycarbonyl)amino]propanoyl]-*L*-aspartate (120bf)

The general procedure **H** was followed using Boc-Trp^{py}-Asp^{OMe}-OMe **88bi** (52.5 mg, 0.1 mmol), allyl furanose carbonate **119a** (72.8 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bf** (67.5 mg, 83%, only traces of *Z* isomer observed by ^{1}H NMR) as a white solid. M.p. = 92–93 °C. **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.58 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.78 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.66–7.60 (m, 1H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.28 (dd, *J* = 6.6, 2.6 Hz, 1H), 7.25–7.23 (m, H), 7.15–7.12 (m, 2H), 7.16–7.11 (m, 2H), 6.63 (d, *J* = 7.4 Hz, 1H), 5.84 (d, *J* = 3.8 Hz, 1H), 5.79 (dt, *J* = 15.6, 6.0 Hz, 1H), 5.45 (dd, *J* = 15.6, 7.5 Hz, 1H), 5.27–5.17 (m, 1H), 4.65 (dt, *J* = 7.5, 4.8 Hz, 1H), 4.54 (s, 1H), 4.52 (d, *J* = 8.5 Hz, 1H), 4.48 – 4.45 (m, 1H), 4.43 (d, *J* = 12.0 Hz, 1H), 3.72 (d, *J* = 3.1 Hz, 1H), 3.70 (d, *J* = 6.0 Hz, 2H), 3.57 (s, 3H), 3.56 (s, 3H), 3.34–3.23 (m, 1H), 3.22–3.14 (m, 1H), 2.85 (dd, *J* = 17.0, 4.5 Hz, 1H), 2.77 (dd, *J* = 17.0, 5.1 Hz, 1H), 1.43 (s, 3H), 1.41 (s, 9H), 1.27 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.3 (C_q), 170.8 (C_q), 170.2 (C_q), 151.1

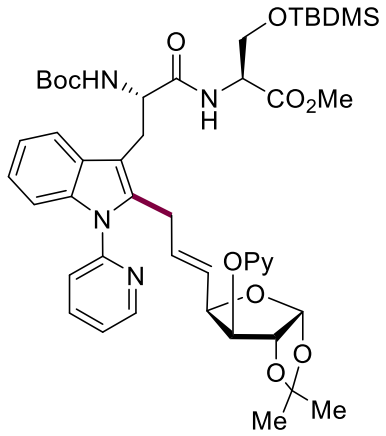
(C_q), 149.3 (CH), 138.1 (CH), 137.4 (C_q), 136.8 (C_q), 135.5 ($2C_q$), 132.0 (CH), 128.3 (CH), 128.3 (C_q), 127.7 (CH), 127.4 (CH), 125.3 (CH), 122.2 (CH), 122.1 (CH), 121.3 (CH), 120.7 (CH), 118.5 (CH), 111.3 (C_q), 110.2 (CH), 109.6 (C_q), 104.5 (CH), 83.3 (CH), 82.7 (CH), 80.8 (CH), 79.9 (C_q), 72.0 (CH_2), 52.7 (CH), 51.9 ($2CH_3$), 48.9 (CH), 36.1 (CH_2), 28.3 (CH_3), 28.0 (CH_2), 27.8 (CH_2), 26.8 (CH_3), 26.2 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2162, 1739, 1437, 1367, 1213, 1164, 1072, 1014, 740, 415 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 835 (100) $[M+Na]^+$, 813 (80) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{44}H_{53}N_4O_{11}^+$ $[M+H]^+$ 813.3705, found 813.3713.



Methyl-[(*S*)-2-acetamido-3-[2-{(*E*)-3-[(3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl]allyl}-1-(pyridin-2-yl)-1*H*-indol-3-yl)propanoyl]-*L*-leucinate (120bg)

The general procedure **H** was followed using Ac-Trp^{py}-Leu-OMe **88bj** (45.1 mg, 0.1 mmol), allyl furanose carbonate **119a** (72.8 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bg** (48.0 mg, 65%, only traces of *Z* isomer observed by ^{1}H NMR) as a yellow solid (M.p. = 96–97 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.59 (ddd, *J* = 4.9, 1.9, 0.7 Hz, 1H), 7.80 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.72–7.69 (m, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.31–7.30 (m, 1H), 7.27–7.24 (m, 4H), 7.21–7.18 (m, 2H), 7.17–7.13 (m, 2H), 6.34 (d, *J* = 7.4 Hz, 1H), 6.21 (d, *J* = 7.9 Hz, 1H), 5.85 (dt, *J* = 15.6, 5.1 Hz, 1H), 5.84 (d, *J* = 3.7 Hz, 1H), 5.55 (dd, *J* = 15.6, 7.7 Hz, 1H), 4.78 (dt, *J* = 7.6, 7.0 Hz, 1H), 4.54 (dd, *J* = 8.0, 4.1 Hz, 2H), 4.50–4.41 (m, 3H), 3.75 (d, *J* = 3.1 Hz, 1H), 3.73–3.68 (m, 2H), 3.54 (s, 3H), 3.28 (dd, *J* = 14.4, 6.2 Hz, 1H), 3.14 (dd, *J* = 14.4, 8.7 Hz, 1H), 1.95 (s, 3H), 1.52–1.44 (m, 2H), 1.43 (s, 3H), 1.41–1.37 (m, 1H), 1.27 (s, 3H), 0.85 (d, *J* = 6.2 Hz, 3H), 0.82 (d, *J* = 6.2

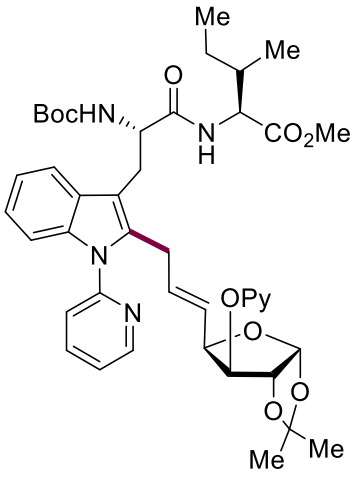
Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.1 (C_q), 170.8 (C_q), 169.8 (C_q), 151.1 (C_q), 149.3 (CH), 138.1 (CH), 137.4 (C_q), 136.7 (C_q), 135.4 (C_q), 132.6 (CH), 128.3 (CH), 128.2 (C_q), 127.7 (CH), 127.4 (CH), 125.3 (CH), 122.3 (CH), 122.0 (CH), 121.3 (CH), 120.8 (CH), 118.6 (CH), 111.3 (C_q), 110.2 (CH), 109.9 (C_q), 104.5 (CH), 83.3 (CH), 82.7 (CH), 80.9 (CH), 72.0 (CH_2), 53.6 (CH), 52.2 (CH_3), 50.9 (CH), 41.7 (CH_2), 28.2 (CH_2), 27.8 (CH_2), 26.7 (CH), 26.2 (CH_3), 24.7 (CH_3), 23.2 (CH_3), 22.6 (CH_3), 22.1 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1710, 1652, 1437, 1215, 1163, 1073, 1016, 861, 740, 698 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 761 (100) $[M+Na]^+$, 739 (80) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{42}H_{51}N_4O_8^+$ $[M+H]^+$ 739.3701, found 739.3691.



Methyl-*N*-[(*S*)-2-[(tert-butoxycarbonyl)amino]-3-[2-{(*E*)-3-[(3a*R*,5*R*,6*S*,6a*R*)-2,2-dimethyl-6-(pyridin-2-yloxy)tetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl]allyl}-1-(pyridin-2-yl)-1*H*-indol-3-yl]propanoyl)-*O*-(*tert*-butyldimethylsilyl)-*L*-serinate (120bh)

The general procedure **H** was followed using Boc-Trp^{py}-Ser^{OTBDMS}-OMe **88bk** (59.7 mg, 0.1 mmol), allyl furanose carbonate derivative **119c** (70.3 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bh** (43.6 mg, 50%, *E/Z* = 10:1 determined by ^{1}H NMR) as a yellow solid (M.p. = 91–92 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.50 (dd, *J* = 4.8, 1.2 Hz, 1H), 8.16 (dd, *J* = 5.0, 1.9 Hz, 1H), 7.65–7.55 (m, 3H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.25–7.22 (m, 1H), 7.13–7.08 (m, 2H), 7.03–7.00 (m, 1H), 6.91 (dd, *J* = 7.1, 5.0 Hz, 1H), 6.65 (d, *J* = 8.3 Hz, 1H), 6.41 (d, *J* = 7.8 Hz, 1H), 5.84 (d, *J* = 3.7 Hz, 1H), 5.74 (dt, *J* = 15.1, 5.9 Hz, 1H), 5.36 (dd, *J* = 15.3, 7.5 Hz, 1H), 5.21 (d, *J* = 2.9 Hz, 1H), 5.20–5.16 (m, 1H), 4.59 (d, *J* = 5.9 Hz, 1H), 4.56 (d, *J* = 3.8 Hz, 1H), 4.49–4.41 (m, 2H), 3.89 (dd, *J* = 10.1, 2.6 Hz, 1H), 3.85 (dd, *J* = 10.1, 2.6 Hz, 0.09H, *Z* isomer), 3.73–3.62 (m, 3H), 3.57 (s, 3H),

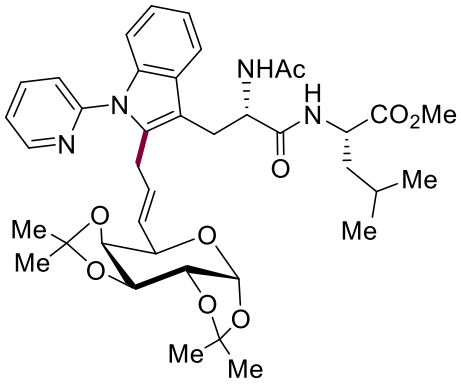
3.26–3.14 (m, 1H), 3.11–3.02 (m, 1H), 1.49 (s, 3H), 1.42 (s, 9H), 1.27 (s, 3H), 0.76 (s, 9H), –0.08 (s, 3H), –0.10 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.2 (C_q), 171.1 (C_q), 169.9 (CH), 162.3 (C_q), 151.1 (C_q), 149.2 (CH), 146.8 (CH), 138.8 (CH), 137.9 (CH), 136.7 (C_q), 135.4 (C_q), 132.5 (CH), 128.3 (C_q), 124.5 (CH), 122.2 (CH), 121.9 (CH), 121.2 (CH), 120.6 (CH), 117.3 (CH), 111.5 (2C_q), 111.4 (CH), 110.0 (CH), 109.6 (C_q), 104.4 (CH), 83.4 (CH), 79.8 (CH), 79.7 (C_q), 78.7 (CH), 63.4 (CH_2), 54.5 (2CH), 52.2 (CH_3), 28.4 (CH_3), 28.0 (CH_2), 27.9 (CH_2), 26.7 (CH_3), 26.3 (CH_3), 25.7 (CH_3), 18.1 (C_q), –5.5 (CH_3), –5.6 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2928, 1681, 1592, 1471, 1434, 1368, 1252, 1164, 1069, 1015, 835, 778, 740 cm^{-1}. **MS** (ESI) m/z (relative intensity): 895 (80) $[M+Na]^+$, 872 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{46}H_{62}N_5O_{10}Si^+$ $[M+H]^+$ 872.4260, found 872.4271.



Methyl-{(*S*)-2-[(tert-butoxycarbonyl)amino]-3-[2-{(*E*)-3-[(3a*R*,5*R*,6*S*,6a*R*)-2,2-dimethyl-6-(pyridin-2-yloxy)tetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl]allyl}-1-(pyridin-2-yl)-1*H*-indol-3-yl]propanoyl}-*L*-isoleucinate (120bi)

The general procedure **H** was followed using Boc-Trp^{py}-Ile-OMe **88bl** (50.9 mg, 0.1 mmol), allyl furanose carbonate **119c** (70.3 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bi** (34.7 mg, 47%, only traces of *Z* isomer observed by ^{1}H NMR) as a light yellow solid (M.p. = 99–100 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.51 (dd, *J* = 5.0, 1.8 Hz, 1H), 8.16 (dd, *J* = 5.2, 1.9 Hz, 1H), 7.67–7.54 (m, 3H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.27–7.22 (m, 1H), 7.15–7.08 (m, 2H), 7.08–7.02 (m, 1H), 6.91 (dd, *J* = 7.1, 5.1 Hz, 1H), 6.64 (d, *J* = 8.3 Hz, 1H), 6.18 (d, *J* = 8.2 Hz, 1H), 5.85 (d, *J* = 3.8 Hz, 1H), 5.78 (dt, *J* = 15.6, 5.9 Hz, 1H), 5.39 (dd, *J* = 15.6, 7.6 Hz, 1H), 5.28–5.25 (m, 1H), 5.24 (d, *J* = 3.1

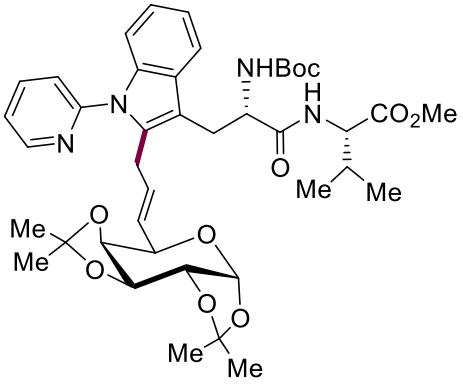
Hz, 1H), 4.64–4.59 (m, 1H), 4.57 (d, *J* = 3.8 Hz, 1H), 4.43–4.38 (m, 1H), 4.36 (dd, *J* = 8.1, 5.0 Hz, 1H), 3.66 (d, *J* = 5.9 Hz, 2H), 3.51 (s, 3H), 3.21–3.12 (m, 1H), 3.08–2.97 (m, 1H), 1.77–1.67 (m, 1H), 1.49 (s, 3H), 1.43 (s, 9H), 1.34–1.28 (m, 1H), 1.27 (s, 3H), 1.06–0.98 (m, 1H), 0.82 (t, *J* = 7.4 Hz, 3H), 0.71 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): *δ* = 171.1 (C_q), 171.0 (C_q), 162.3 (C_q), 151.1 (C_q), 149.2 (CH), 146.8 (CH), 138.8 (CH), 137.9 (CH), 136.7 (C_q), 135.3 (C_q), 132.6 (CH), 128.2 (C_q), 124.6 (CH), 122.2 (CH), 121.9 (CH), 121.2 (CH), 120.6 (CH), 118.5 (CH), 117.3 (CH), 111.5 (2C_q), 111.4 (CH), 110.0 (CH), 109.8 (C_q), 104.5 (CH), 83.4 (CH), 79.9 (CH), 79.7 (C_q), 78.7 (CH), 56.6 (CH), 55.1 (CH), 51.9 (CH_3), 38.1 (CH), 28.4 (CH_3), 28.0 (CH_2), 27.7 (CH_2), 26.7 (CH_3), 26.3 (CH_3), 25.2 (CH_2), 15.1 (CH_3), 11.6 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2963, 1656, 1470, 1368, 1254, 1068, 1015, 859, 779, 739 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 806 (60) $[M+Na]^+$, 784 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{43}H_{54}N_5O_9^+$ $[M+H]^+$ 784.3916, found 784.3912.



Methyl-[(*S*)-2-acetamido-3-[1-(pyridin-2-yl)-2-[(*E*)-3-{(3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-b:4',5'-*d*]pyran-5-yl]allyl}-1*H*-indol-3-yl]propanoyl]-*L*-leucinate (120bj)

The general procedure **H** was followed using Ac-Trp^{py}-Leu-OMe **88bj** (45.1 mg, 0.1 mmol), allyl galactose carbonate **119d** (68.9 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bj** (61.1 mg, 85%, only traces of *Z* isomer observed by ^{1}H NMR) as a light yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$): *δ* = 8.62 (ddd, *J* = 5.0, 2.0, 0.8 Hz, 1H), 7.83 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.72–7.69 (m, 1H), 7.48 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.32–7.27 (m, 2H), 7.16–7.11 (m, 2H), 6.36 (d, *J* = 7.4 Hz, 1H), 6.18 (d, *J* = 7.8 Hz, 1H), 5.70 (dt, *J* = 15.6, 6.1 Hz, 1H), 5.45 (d, *J* = 5.1 Hz, 1H), 5.37 (dd, *J* = 15.6, 6.6 Hz, 1H), 4.74

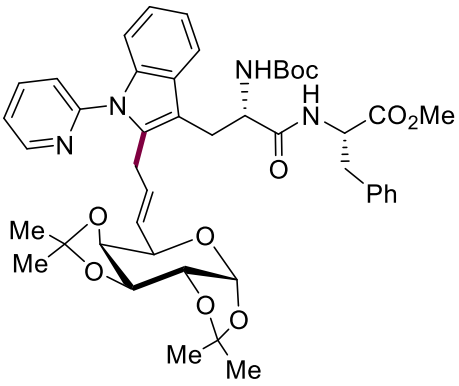
(ddd, *J* = 8.6, 7.4, 6.0 Hz, 1H), 4.51 (dd, *J* = 7.9, 2.3 Hz, 1H), 4.42 (td, *J* = 8.1, 5.3 Hz, 1H), 4.24–4.19 (m, 1H), 4.06 (d, *J* = 6.6 Hz, 1H), 4.00 (dd, *J* = 7.9, 1.9 Hz, 1H), 3.70–3.64 (m, 2H), 3.55 (s, 3H), 3.34 (dd, *J* = 14.5, 6.1 Hz, 1H), 3.15 (dd, *J* = 14.5, 8.7 Hz, 1H), 1.98 (s, 3H), 1.52–1.46 (m, 2H), 1.44 (s, 3H), 1.43–1.40 (m, 1H), 1.39 (s, 3H), 1.29 (s, 3H), 1.28 (s, 3H), 0.85 (d, *J* = 6.2 Hz, 3H), 0.83 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 172.1 (C_q), 170.9 (C_q), 169.8 (C_q), 151.2 (C_q), 149.3 (CH), 138.0 (CH), 136.7 (C_q), 135.7 (C_q), 130.4 (CH), 128.2 (C_q), 127.4 (CH), 122.2 (CH), 122.0 (CH), 121.5 (CH), 120.7 (CH), 118.6 (CH), 110.2 (CH), 109.7 (C_q), 108.9 (C_q), 108.2 (C_q), 96.3 (CH), 73.3 (CH), 70.7 (CH), 70.4 (CH), 68.4 (CH), 53.8 (CH), 52.2 (CH_3), 51.0 (CH), 41.8 (CH_2), 28.2 (CH_2), 27.7 (CH_2), 26.1 (CH_3), 26.1 (CH_3), 24.9 (CH_3), 24.7 (CH), 24.4 (CH_3), 23.4 (CH_3), 22.7 (CH_3), 22.1 (CH_3). **IR (ATR)**: $\tilde{\nu}$ = 3277, 2957, 1743, 1644, 1471, 1370, 1165, 993, 781, 741 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 741 (100) $[M+Na]^+$, 719 (60) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{39}H_{51}N_4O_9^+$ $[M+H]^+$ 719.3651, found 719.3660.



Methyl-[(*S*)-2-[(*tert*-butoxycarbonyl)amino]-3-[1-(pyridin-2-yl)-2-{(*E*)-3-[(3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-b:4',5'-*d*]pyran-5-yl]allyl}-1*H*-indol-3-yl]propanoyl)-*L*-valinate (120bk)

The general procedure **H** was followed using Boc-Trp^{py}-Val-OMe **88bg** (49.5 mg, 0.1 mmol), allyl galactose carbonate **119d** (68.9 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bk** (48.1 mg, 63%, only traces of *Z* isomer observed by ^{1}H NMR) as a white solid (M.p. = 101–102 °C). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.62 (ddd, *J* = 4.9, 2.0, 0.8 Hz, 1H), 7.83 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.69–7.61 (m, 1H), 7.46 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.31–7.27 (m, 2H), 7.15–7.11 (m, 2H), 6.26 (d, *J* = 8.3 Hz, 1H), 5.66

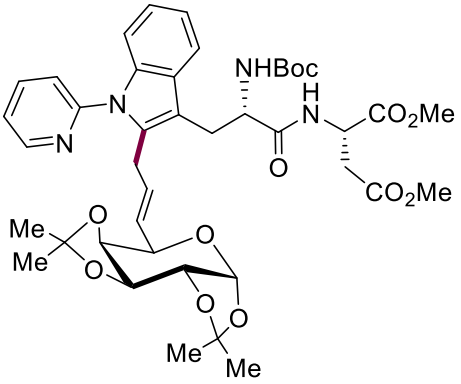
(dt, *J* = 15.5, 6.1 Hz, 1H), 5.46 (d, *J* = 5.0 Hz, 1H), 5.42–5.33 (m, 1H), 5.30 (dd, *J* = 15.5, 5.5 Hz, 1H), 4.51 (dd, *J* = 7.9, 2.3 Hz, 1H), 4.41 (q, *J* = 7.5 Hz, 1H), 4.35 (dd, *J* = 8.3, 5.1 Hz, 1H), 4.22 (dd, *J* = 5.1, 2.3 Hz, 1H), 4.11–4.03 (m, 1H), 3.99 (dd, *J* = 7.9, 1.9 Hz, 1H), 3.66 (d, *J* = 6.1 Hz, 2H), 3.54 (s, 3H), 3.42–3.30 (m, 1H), 3.26–3.15 (m, 1H), 2.01 (pq, *J* = 6.9, 5.0 Hz, 1H), 1.45 (s, 3H), 1.42 (s, 9H), 1.39 (s, 3H), 1.30 (s, 3H), 1.29 (s, 3H), 0.81 (d, *J* = 6.9 Hz, 3H), 0.78 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): *δ* = 171.5 (C_q), 171.3 (C_q), 151.3 (C_q), 149.4 (CH), 138.1 (CH), 136.8 (C_q), 135.6 (C_q), 129.9 (CH), 128.4 (C_q), 127.3 (CH), 122.2 (CH), 122.1 (CH), 121.5 (CH), 120.7 (CH), 118.6 (CH), 110.2 (CH), 109.8 (C_q), 108.9 ($2C_q$), 108.3 (C_q), 96.3 (CH), 79.8 (C_q), 73.2 (CH), 70.7 (CH), 70.3 (CH), 68.2 (CH), 57.3 (CH), 55.3 (CH), 51.9 (CH_3), 31.4 (CH), 28.3 (CH_3), 28.0 (CH_2), 27.4 (CH_2), 26.1 (CH_3), 26.0 (CH_3), 24.9 (CH_3), 24.3 (CH_3), 18.7 (CH_3), 17.8 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2974, 1658, 1368, 1253, 1165, 1068, 860, 780, 741, 412 cm^{-1}. **MS** (ESI) m/z (relative intensity): 785 (95) $[M+Na]^+$, 763 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{41}H_{55}N_4O_{10}^+$ $[M+H]^+$ 763.3913, found 763.3926.



Methyl-{(*S*)-2-[(*tert*-butoxycarbonyl)amino]-3-[1-(pyridin-2-yl)-2-{(*E*)-3-[(3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-b:4',5'-*d*]pyran-5-yl]allyl}-1*H*-indol-3-yl]propanoyl}-*L*-phenylalaninate (120bl)

The general procedure **H** was followed using Boc-Trp^{py}-Phe-OMe **88bh** (54.3 mg, 0.1 mmol), allyl galactose carbonate **119d** (68.9 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bl** (40.5 mg, 50%, only traces of *Z* isomer observed by ^{1}H NMR) as a yellow solid (M.p. = 100–101 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): *δ* = 8.61 (dd, *J* = 4.8, 0.9 Hz, 1H), 7.86–7.79 (m, 1H), 7.70–7.62 (m, 1H), 7.44 (d, *J* = 7.9 Hz,

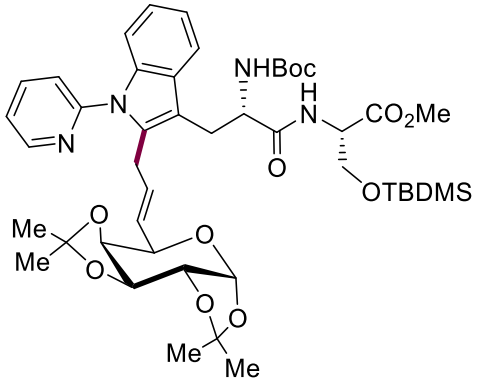
1H), 7.30–7.27 (m, 2H), 7.19–7.10 (m, 5H), 6.92–6.87 (m, 2H), 6.26–6.11 (m, 1H), 5.66 (dt, *J* = 16.3, 5.8 Hz, 1H), 5.45 (d, *J* = 5.0 Hz, 1H), 5.36–5.22 (m, 2H), 4.68–4.60 (m, 1H), 4.50 (d, *J* = 7.8 Hz, 1H), 4.45–4.37 (m, 1H), 4.25–4.20 (m, 1H), 4.09–4.03 (m, 1H), 3.97 (d, *J* = 7.8 Hz, 1H), 3.67 (d, *J* = 5.8 Hz, 2H), 3.52 (s, 3H), 3.39–3.29 (m, 1H), 3.19–3.12 (m, 1H), 2.99–2.89 (m, 2H), 1.46 (s, 3H), 1.41 (s, 9H), 1.39 (s, 3H), 1.29 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.0 (C_q), 170.9 (C_q), 151.1 (C_q), 149.3 (CH), 138.0 (CH), 136.8 (C_q), 135.7 ($2C_q$), 129.9 (CH), 129.1 (CH), 128.3 (CH), 128.2 (C_q), 127.4 (CH), 126.8 (CH), 122.2 (CH), 122.1 (CH), 121.5 (CH), 120.7 (CH), 118.7 (CH), 110.1 (CH), 109.7 (C_q), 108.9 ($2C_q$), 108.2 (C_q), 96.3 (CH), 79.8 (C_q), 73.2 (CH), 70.7 (CH), 70.4 (CH), 68.2 (CH), 55.0 (CH), 53.5 (CH), 52.1 (CH_3), 38.0 (CH_2), 28.3 (CH_3), 28.2 (CH_2), 27.9 (CH_2), 26.2 (CH_3), 26.0 (CH_3), 25.0 (CH_3), 24.4 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1674, 1471, 1253, 1210, 1065, 993, 899, 701, 508, 413 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 833 (100) $[M+Na]^+$, 811 (75) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{45}H_{55}N_4O_{10}^+$ $[M+H]^+$ 811.3913, found 811.3917.



Dimethyl-{(S)-2-[(*tert*-butoxycarbonyl)amino]-3-[1-(pyridin-2-yl)-2-{(*E*)-3-[(3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-b:4',5'-*d*]pyran-5-yl]allyl)-1*H*-indol-3-yl}propanoyl]-*L*-aspartate (120bm)

The general procedure **H** was followed using Boc-Trp^{py}-Asp^{OMe}-OMe **88bi** (52.5 mg, 0.1 mmol), allyl galactose carbonate **119d** (68.9 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bm** (67.4 mg, 85%, *Z* traces determined by ^{1}H NMR) as a white solid (M.p. = 92–93 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.61 (dd, *J* = 5.0, 2.0 Hz, 1H), 7.83 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.66–7.59 (m, 1H), 7.46 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.30–7.27 (m, 2H), 7.16–7.09 (m, 2H), 6.68 (d, *J* = 7.5 Hz, 1H), 5.66 (dt,

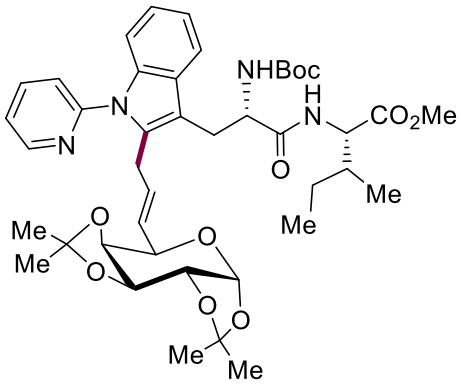
J = 15.3, 6.3 Hz, 1H), 5.46 (d, *J* = 5.0 Hz, 1H), 5.37–5.23 (m, 1H), 4.66 (dt, *J* = 7.5, 4.7 Hz, 1H), 4.50 (dd, *J* = 7.9, 2.2 Hz, 1H), 4.46–4.36 (m, 1H), 4.22 (dd, *J* = 5.0, 2.2 Hz, 1H), 4.12–4.03 (m, 1H), 3.99 (dd, *J* = 7.9, 1.9 Hz, 1H), 3.66 (d, *J* = 6.3 Hz, 2H), 3.58 (s, 6H), 3.42–3.30 (m, 1H), 3.25–3.16 (m, 1H), 2.86 (dd, *J* = 17.0, 4.5 Hz, 1H), 2.77 (dd, *J* = 17.0, 5.1 Hz, 1H), 1.45 (s, 3H), 1.41 (s, 9H), 1.39 (s, 3H), 1.30 (s, 3H), 1.28 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.4 (C_q), 170.8 (C_q), 170.3 (C_q), 155.0 (C_q), 151.2 (C_q), 149.3 (CH), 138.0 (CH), 136.8 (C_q), 135.6 (C_q), 129.9 (CH), 128.4 (C_q), 127.3 (CH), 122.1 (CH), 122.0 (CH), 121.5 (CH), 120.6 (CH), 110.1 (CH), 109.6 (CH), 108.9 ($2C_q$), 108.2 (C_q), 96.3 (CH), 79.8 (C_q), 73.2 (CH), 70.7 (CH), 70.4 (CH), 68.2 (CH), 55.0 (CH), 52.6 (CH_3), 51.9 (CH_3), 48.9 (CH), 36.1 (CH_2), 28.3 (CH_3), 28.2 (CH_2), 27.9 (CH_2), 26.1 (CH_3), 26.0 (CH_3), 24.9 (CH_3), 24.4 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 1672, 1471, 1437, 1368, 1210, 1164, 1066, 994, 897, 742 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 815 (100) $[M+Na]^+$, 793 (50) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{41}H_{53}N_4O_{12}^+$ $[M+H]^+$ 793.3654, found 793.3658.



Methyl-*N*-{(*S*)-2-[(*tert*-butoxycarbonyl)amino]-3-[1-(pyridin-2-yl)-2-{(*E*)-3-[(3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-b:4',5'-*d*]pyran-5-yl]allyl}-1*H*-indol-3-yl]propanoyl}-*O*-(*tert*-butyldimethylsilyl)-*L*-serinate (120bn)

The general procedure **H** was followed using Boc-Trp^{py}-Ser^{OTBDMS}-OMe **88bk** (59.7 mg, 0.1 mmol), allyl galactose carbonate **119d** (68.9 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bn** (65.7 mg, 76%, *E/Z* = 9:1 determined by ^{1}H NMR) as a white solid. M.p. = 90–91 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.61 (ddd, *J* = 4.9, 2.0, 0.9 Hz, 1H), 7.82 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.64 (d, *J* = 3.8 Hz, 1H),

7.49–7.42 (m, 1H), 7.31–7.27 (m, 2H), 7.14–7.10 (m, 2H), 6.50 (d, *J* = 7.8 Hz, 1H), 6.43 (d, *J* = 7.8 Hz, 0.09H, *Z* isomer), 5.63 (dt, *J* = 15.5, 6.2 Hz, 1H), 5.45 (d, *J* = 5.0 Hz, 1H), 5.28 (dd, *J* = 15.5, 5.9 Hz, 2H), 4.52–4.46 (m, 3H), 4.21 (dd, *J* = 5.1, 2.3 Hz, 1H), 4.04 (d, *J* = 6.2 Hz, 1H), 3.97 (dd, *J* = 7.9, 1.8 Hz, 1H), 3.92 (dd, *J* = 10.0, 2.9 Hz, 1H), 3.70–3.64 (m, 3H), 3.58 (s, 3H), 3.43–3.30 (m, 1H), 3.27–3.17 (m, 1H), 1.45 (s, 3H), 1.41 (s, 9H), 1.39 (s, 3H), 1.29 (d, *J* = 3.9 Hz, 6H), 0.78 (s, 9H), -0.08 (s, 3H), -0.06 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.3 (C_q), 169.9 (C_q), 151.2 (C_q), 149.3 (CH), 138.0 (CH), 136.8 (C_q), 135.7 (C_q), 129.8 (CH), 128.4 (C_q), 127.3 (CH), 122.1 (CH), 122.0 (CH), 121.5 (CH), 120.5 (CH), 118.6 (CH), 110.1 (CH), 109.6 (C_q), 108.9 ($2C_q$), 108.2 (C_q), 96.3 (CH), 79.7 (C_q), 73.3 (CH), 70.8 (CH), 70.4 (CH), 68.2 (CH), 63.4 (CH_2), 54.5 (CH), 54.2 (CH), 52.2 (CH_3), 28.3 (CH_3), 28.1 (CH_2), 26.2 (CH_3), 26.1 (CH_3), 25.7 (CH_3), 25.0 (CH_3), 24.4 (CH_3), 18.1 (CH_2), –5.5 (CH_3), –5.6 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2931, 1712, 1438, 1212, 1150, 1103, 1067, 994, 779, 742 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 887 (75) $[M+Na]^+$, 865 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{52}H_{50}BF_2N_8O_8$ $[M+H]^+$ 865.4446, found 865.4436.

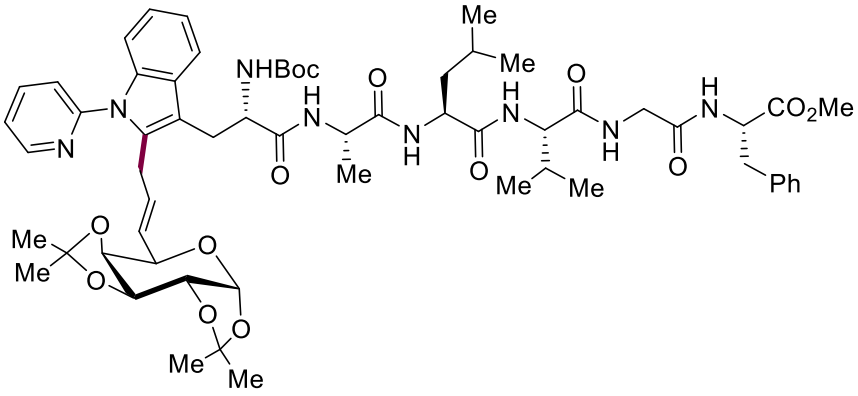


Methyl-{(*S*)-2-[(*tert*-butoxycarbonyl)amino]-3-[1-(pyridin-2-yl)-2-{(*E*)-3-[(3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl]allyl}-1*H*-indol-3-yl]propanoyl}-*L*-isoleucinate (120bo)

The general procedure **H** was followed using Boc-Trp^{py}-Ile-OMe **88bl** (50.9 mg, 0.1 mmol), allyl galactose carbonate **119d** (68.9 mg, 0.20 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **120bo** (41.2 mg, 53%, only traces of *Z* isomer observed by ^{1}H NMR) as a yellow solid (M.p. = 93–94 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.62 (ddd, *J* = 4.9, 2.0, 0.6 Hz, 2H), 7.83 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.65 (d, *J* = 3.6 Hz, 1H),

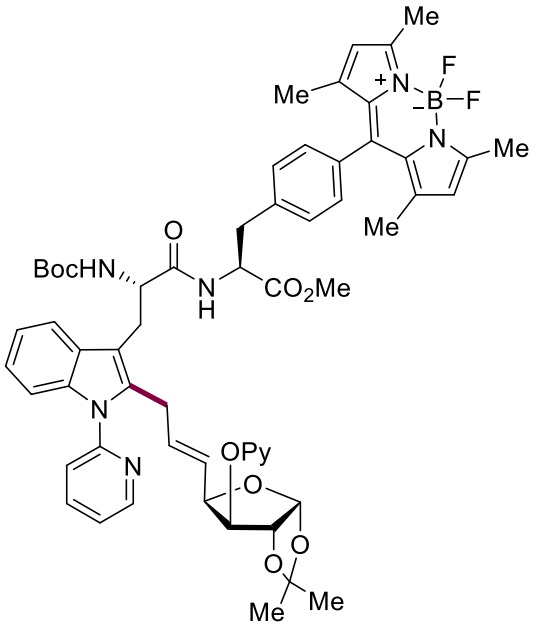
7.46 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.31–7.27 (m, 2H), 7.15–7.10 (m, 2H), 6.28 (d, *J* = 8.2 Hz, 1H), 5.67 (dt, *J* = 15.6, 6.1 Hz, 1H), 5.46 (d, *J* = 5.0 Hz, 1H), 5.39 – 5.34 (m, 1H), 5.30 (dd, *J* = 15.6, 5.8 Hz, 1H), 4.50 (dd, *J* = 8.0, 2.3 Hz, 1H), 4.45–4.41 (m, 1H), 4.40 (dd, *J* = 8.0, 5.0 Hz, 1H), 4.22 (dd, *J* = 5.0, 2.3 Hz, 1H), 4.08–4.01 (m, 1H), 3.99 (dd, *J* = 7.9, 1.9 Hz, 1H), 3.66 (d, *J* = 6.1 Hz, 2H), 3.53 (s, 3H), 3.47–3.12 (m, 2H), 1.78–1.70 (m, 1H), 1.45 (s, 3H), 1.45–1.42 (m, 9H), 1.39 (s, 3H), 1.30 (s, 3H), 1.29 (s, 3H), 1.08 – 0.99 (m, 1H), 0.84 (t, *J* = 7.4 Hz, 3H), 0.74 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.1 (C_q), 151.2 (C_q), 149.3 (CH), 138.0 (CH), 136.8 (C_q), 135.6 (C_q), 129.9 (CH), 128.3 (C_q), 127.9 (C_q), 127.3 (CH), 122.1 (CH), 122.0 (CH), 121.5 (CH), 120.6 (CH), 118.6 (CH), 110.1 (CH), 109.8 (C_q), 108.9 ($2C_q$), 108.2 (C_q), 96.3 (CH), 79.8 (C_q), 73.3 (CH), 70.8 (CH), 70.4 (CH), 68.2 (CH), 56.6 (CH), 51.9 (CH_3), 38.1 (CH), 28.4 (CH_3), 28.1 (CH_2), 27.6 (CH_2), 26.2 (CH_3), 26.1 (CH_3), 25.2 (CH_2), 25.0 (CH), 24.4 (CH_3), 15.2 ($2CH_3$), 11.6 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2975, 1674, 1437, 1209, 1165, 1065, 993, 899, 741, 512 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 799 (100) $[M+Na]^+$, 777 (100) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{42}H_{57}N_4O_{10}^+$ $[M+H]^+$ 777.4069, found 777.4073.

5.3.5.3 Characterization Data of Hexapeptide and BODIPY-Peptide Glycoconjugates 120ca and 120cb



Methyl-{(*S*)-2-[(*tert*-butoxycarbonyl)amino]-3-[1-(pyridin-2-yl)-2-{(*E*)-3-[(3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl]allyl}-1*H*-indol-3-yl)propanoyl]-*L*-alanyl-*L*-leucyl-*L*-valylglycyl-*L*-phenylalaninate (120ca)

The general procedure **H** was followed using hexapeptide Boc-Trp^{py}-Ala-Leu-Val-Gly-Phe-OMe **88bm** (88.3 mg, 0.1 mmol), allyl galactose carbonate **119d** (68.9 mg, 0.20 mmol) and $MnBr(CO)_5$ (27.4 mg, 0.1 mmol). Purification by column chromatography (EtOAc/MeOH 100:1 to 10:1) yielded **120ca** (95.6 mg, 83%) as a white solid (M.p. = 206–208 °C). **^{1}H NMR** (500 MHz, DMSO-*d*$_6$): δ = 8.62–8.14 (m, 1H), 8.31 (d, *J* = 7.7 Hz, 1H), 8.22–8.13 (m, 2H), 8.05–7.90 (m, 2H), 7.69–7.55 (m, 2H), 7.53–7.42 (m, 2H), 7.32–7.24 (m, 2H), 7.22–7.19 (m, 3H), 7.15–7.04 (m, 2H), 7.02–6.87 (m, 1H), 5.59–5.41 (m, 1H), 5.39–5.28 (m, 1H), 5.09 (dd, *J* = 15.5, 6.5 Hz, 1H), 4.40–4.29 (m, 2H), 4.27–4.18 (m, 2H), 4.16 (dd, *J* = 8.6, 6.5 Hz, 1H), 3.93–3.82 (m, 2H), 3.75–3.59 (m, 4H), 3.58 (s, 3H), 3.20–3.09 (m, 1H), 3.06–2.94 (m, 2H), 2.94–2.88 (m, 1H), 1.98–1.90 (m, 1H), 1.61–1.55 (m, 1H), 1.46 (t, *J* = 7.4 Hz, 2H), 1.41–1.33 (m, 3H), 1.32–1.17 (m, 19H), 1.14 (s, 2H), 1.02–0.91 (m, 2H), 0.90–0.76 (m, 13H). **^{13}C NMR** (126 MHz, DMSO-*d*$_6$): δ = 171.9 (C_q), 171.7 (C_q), 171.6 (C_q), 171.0 (C_q), 170.9 (C_q), 168.6 (C_q), 155.0 (C_q), 150.5 (C_q), 149.2 (CH), 138.8 (CH), 136.9 (C_q), 136.2 (C_q), 135.5 (C_q), 129.1 (CH), 129.0 (CH), 128.2 (CH), 128.1 (C_q), 127.4 (CH), 126.5 (CH), 122.5 (CH), 121.7 (CH), 121.2 (CH), 119.9 (CH), 118.5 (CH), 110.1 (C_q), 109.8 (CH), 107.9 (C_q), 107.4 (C_q), 95.5 (CH), 78.2 (C_q), 72.5 (CH), 70.0 (CH), 69.6 (CH), 68.5 (CH_2), 67.7 (CH), 57.4 (CH), 55.8 (CH_2), 53.6 (CH), 51.8 (CH_3), 51.1 (CH), 47.9 (CH), 41.4 (CH_2), 36.9 (CH_2), 30.7 (CH), 29.6 (CH), 28.0 (CH), 26.9 (CH_2), 25.9 (CH_3), 24.8 (CH_3), 24.1 (CH_3), 24.0 (CH_3), 23.0 (CH_3), 21.5 (CH_3), 19.1 (CH_3), 17.9 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 3297, 2165, 1992, 1633, 1369, 1166, 739, 696, 580, 413 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 1173 (100) $[M+Na]^+$, 1151 (40) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{61}H_{83}N_8O_{14}^+$ $[M+H]^+$ 1151.6023, found 1151.6000.

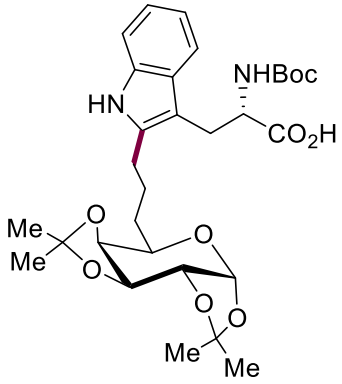


Methyl-(*S*)-2-[(*S*)-2-[(*tert*-butoxycarbonyl)amino]-3-{2-[(*E*)-3-[(3a*R*,5*R*,6*S*,6a*R*)-2,2-dimethyl-6-(pyridin-2-yloxy)tetrahydrofuro[2,3-*d*][1,3]dioxol-5-yl]allyl]-1-(pyridin-2-yl)-1*H*-indol-3-yl}propanamido]-3-[4-(5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinin-10-yl)phenyl]propanoate (120cb)

The general procedure **H** was followed using BODIPY peptide Boc-Trp^{py}-Phe^{BODIPY}-OMe **88bn** (78.9 mg, 0.1 mmol), allyl furanose carbonate **119c** (70.3 mg, 0.20 mmol) and NaOAc (16.4 mg, 0.2 mmol). Purification by column chromatography (*n*-hexane/Acetone 10:1 to 3:1) yielded **10b** (63.8 mg, 60%, *Z* traces determined by ^{1}H NMR) as an orange solid (M.p. = 136–138 °C). **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.42 (dd, *J* = 5.0, 2.0 Hz, 1H), 8.14 (dd, *J* = 5.0, 2.0 Hz, 1H), 7.66–7.63 (m, 1H), 7.61 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.54 (ddd, *J* = 8.9, 7.3, 2.0 Hz, 1H), 7.27 (d, *J* = 7.9 Hz, 1H), 7.22 (d, *J* = 7.9 Hz, 1H), 7.14–7.07 (m, 2H), 7.08–6.96 (m, 4H), 6.90–6.86 (m, 4H), 6.60 (d, *J* = 8.3 Hz, 1H), 6.10 (d, *J* = 7.3 Hz, 1H), 5.95–5.93 (m, 1H), 5.83 (d, *J* = 3.8 Hz, 1H), 5.75 (dt, *J* = 15.6, 6.0 Hz, 1H), 5.37 (dd, *J* = 15.6, 7.7 Hz, 1H), 5.23 (d, *J* = 3.1 Hz, 1H), 5.21–5.07 (m, 1H), 4.66 (q, *J* = 6.4 Hz, 1H), 4.65–4.61 (m, 1H), 4.55 (d, *J* = 3.8 Hz, 1H), 4.47–4.32 (m, 1H), 3.71–3.59 (m, 2H), 3.48 (s, 3H), 3.32–3.20 (m, 1H), 3.01–2.87 (m, 2H), 2.52 (s, 6H), 1.47 (s, 3H), 1.41 (s, 9H), 1.25 (s, 3H), 1.22 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 170.8 (C_q), 170.6 (C_q), 162.2 (C_q), 155.2 (2C_q), 150.9 (C_q), 149.3 (CH), 146.8 (CH), 143.0 (C_q), 141.4 (C_q), 138.8 (CH), 138.0 (CH), 136.8 (C_q), 136.7 (C_q), 135.5

(C_q), 133.4 (C_q), 132.4 (CH), 131.3 (C_q), 129.8 (CH), 128.1 (C_q), 128.0 (CH), 124.7 (CH), 122.4 (CH), 122.0 (CH), 121.1 (CH), 121.0 (CH), 120.8 (CH), 118.8 (CH), 117.4 (CH), 111.6 (C_q), 111.4 (CH), 110.1 (CH), 109.8 (C_q), 109.6 (C_q), 104.5 (CH), 83.4 (CH), 80.0 (C_q), 79.9 (CH), 78.7 (CH), 54.7 (CH), 53.4 (CH), 52.2 (CH_3), 38.1 (CH_2), 28.4 (CH_3), 28.1 (CH_2), 27.7 (CH_2), 26.7 (CH_3), 26.2 (CH_3), 14.6 (CH_3), 14.4 (CH_3). **^{19}F NMR** (282 MHz, $CDCl_3$): δ = –146.27. **IR** (ATR): $\tilde{\nu}$ = 2221, 1682, 1508, 1470, 1366, 1192, 1068, 975, 778, 414 cm^{-1}. **MS** (ESI) m/z (relative intensity): 1086 (75) $[M+Na]^+$, 1064 (100) $[M+H]^+$. **HR-MS** (ESI): m/z calcd for $C_{59}H_{65}BF_2N_7O_9^+$ $[M+H]^+$ 1064.4909, found 1064.4892. **UV-Vis Absorption λ_{max}** (1.0 mg/L in EtOAc) = 498 nm. **E_m λ_{max}** (1.0 mg/L in EtOAc) = 510 nm.

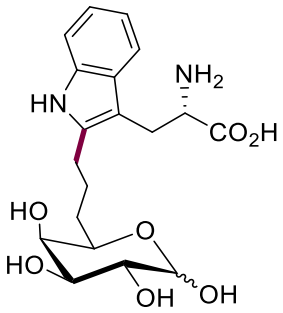
5.3.5.4 Characterization Data of Unprotected Glycotryptophans



(*S*)-2-[(*tert*-butoxycarbonyl)amino]-3-{2-[3-[(3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl]propyl]-1*H*-indol-3-yl}propanoic acid (120aa')

To a stirred solution of **120ad** and **120ae** mixture (0.2 mmol, 1.0 equiv) in CH_2Cl_2 (0.25 M) was added MeOTf (1.0 equiv) at 0 °C under N_2. After 30 min, the mixture was allowed to warm to 27 °C and stirred for 18 h. The crude mixture was concentrated under reduced pressure to afford a bright yellow solid. In a sealed-tube, the crude product, $Pd(OH)_2$/C (20 wt.-%, 10 mol %), and NH_4O_2CH (20.0 equiv) were dissolved in MeOH (0.5 M), and stirred at 60 °C for 16 h. The mixture was filtered through a short pad of celite, concentrated under reduced pressure and purified by column chromatography to get the product **120aa'** as a light yellow oil (52 mg, 45%). NMR analysis showed that no racemization occurred during the

pyridyl removal process. **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 8.12 (s, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.25 (d, *J* = 7.8 Hz, 1H), 7.11 (t, *J* = 7.0 Hz, 1H), 7.06 (t, *J* = 7.2 Hz, 1H), 5.59 (d, *J* = 5.1 Hz, 1H), 4.60 (dd, *J* = 7.9, 2.3 Hz, 1H), 4.33 (dd, *J* = 5.1, 2.3 Hz, 1H), 4.15 (d, *J* = 7.8 Hz, 1H), 3.83–3.75 (m, 1H), 3.30–3.19 (m, 2H), 2.75–2.68 (m, 2H), 1.80–1.75 (m, 2H), 1.54 (s, 3H), 1.53–1.51 (m, 2H), 1.47 (s, 3H), 1.46–1.45 (m, 2H), 1.43 (s, 9H), 1.35 (s, 3H), 1.34 (3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 174.3 (C_q), 155.2 (C_q), 137.1 (C_q), 135.2 (C_q), 128.9 (C_q), 121.2 (CH), 119.4 (CH), 118.4 (CH), 110.2 (CH), 109.2 (C_q), 108.6 (C_q), 105.5 (C_q), 96.5 (CH), 79.8 (C_q), 73.0 (CH), 70.9 (CH), 70.4 (CH), 67.6 (CH), 54.1 (CH_3), 29.6 (CH_2), 28.4 (CH_3), 28.0 (CH), 27.4 (CH_2), 26.2 (CH_2), 26.1 (CH_3), 25.8 (CH_2), 24.9 (CH_3), 24.5 (CH_3). **IR** (ATR): $\tilde{\nu}$ = 2985, 1745, 1382, 1210, 1167, 1066, 999, 898, 742, 511 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 597 (100) $[M+Na]^+$, 575 (80) $[M+H]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{30}H_{43}N_2O_9$ $[M+H]^+$ 575.2963, found 575.2959.



(*S*)-2-Amino-3-{2-{3-[(2*R*,3*R*,4*S*,5*R,6R*)-3,4,5,6-tetrahydroxytetrahydro-2*H*-pyran-2-yl]propyl}-1*H*-indol-3-yl}propanoic acid (120aa'')

To the solution of TFA/H_2O (0.5 mL/0.5 mL) was added **120aa'** (0.1 mmol) at 0 °C. The mixture was allowed to warm to 27 °C and stirred for 24 h. The crude mixture was concentrated under reduced pressure to afford a yellow oil. The product **120aa''** was recrystallized from a solution of MeOH/Et_2O = 1:5 to give a white solid (29 mg, 75%, β/α = 3:1). M.p. = 240–242 °C. **^{1}H NMR** (400 MHz, D_2O): δ = 7.52 (d, *J* = 7.7 Hz, 1H), 7.38–7.31 (m, 1H), 7.09 (dd, *J* = 16.3, 8.3 Hz, 2H), 5.10 (d, *J* = 3.0 Hz, 0.27 H, α anomer), 4.34 (d, *J* = 7.3 Hz, 1H, β anomer), 3.96–3.86 (m, 1H), 3.69–3.65 (m, 1H), 3.59 (d, *J* = 3.1 Hz, 1H), 3.38–3.29 (m, 2H), 3.26 (s, 1H), 3.10 (dd, *J* = 15.4, 8.7 Hz, 1H), 2.77–2.59 (m, 2H), 1.67–1.41 (m, 4H). **^{13}C NMR** (101 MHz, D_2O): β anomer δ = 174.1 (C_q), 138.9 (C_q), 135.4 (C_q), 127.6 (C_q), 121.3 (CH), 119.3 (CH),

117.6 (CH), 111.1 (CH), 103.4 (C_q), 96.3 (CH), 74.3 (CH), 73.0 (CH), 71.8 (CH), 70.2 (CH), 68.3 (CH), 29.4 (CH_2), 25.6 (CH_2), 25.1 (CH_2), 25.0 (CH_2). **^{13}C NMR** (101 MHz, D_2O): *α* anomer *δ* = 170.4 (C_q), 139.1 (C_q), 135.6 (C_q), 127.5 (C_q), 121.5 (CH), 119.4 (CH), 117.3 (CH), 111.2 (CH), 103.5 (C_q), 94.8 (CH), 92.1 (CH), 70.7 (CH), 69.5 (CH), 69.4 (CH), 66.0 (CH), 29.3 (CH_2), 25.1 (CH_2), 25.0 (CH_2), 24.8 (CH_2). **IR** (ATR): $\tilde{\nu}$ = 3586, 2276, 2209, 2015, 2000, 1625,1052, 742, 499, 463 cm^{-1}. **MS** (ESI) *m/z* (relative intensity): 395 (100) $[M+H]^+$, 417 (15) $[M+Na]^+$. **HR-MS** (ESI): *m/z* calcd for $C_{19}H_{27}N_2O_7$ $[M+H]^+$ 395.1813, found 395.1815.

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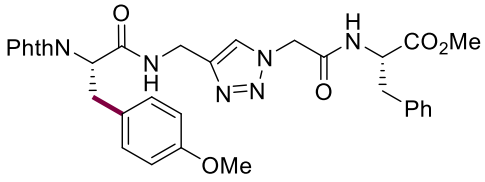
7. NMR Spectra



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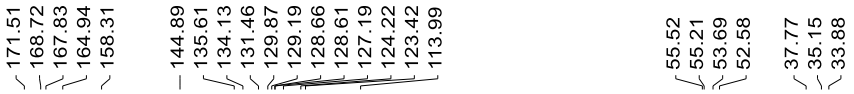

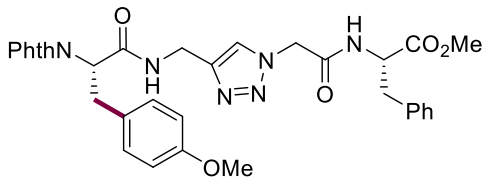

108a
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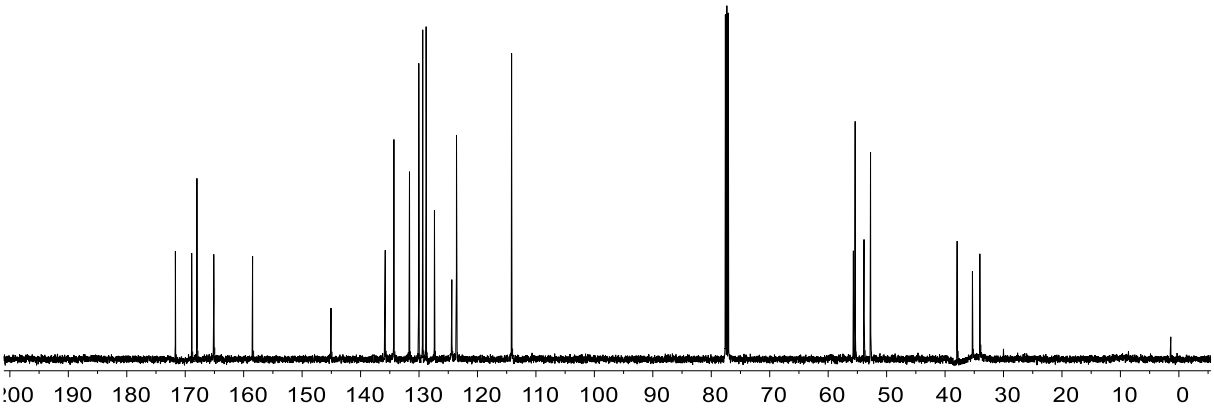

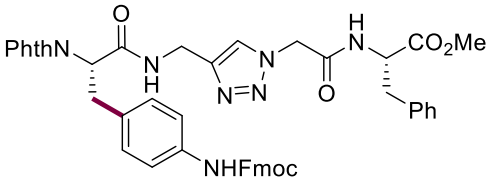

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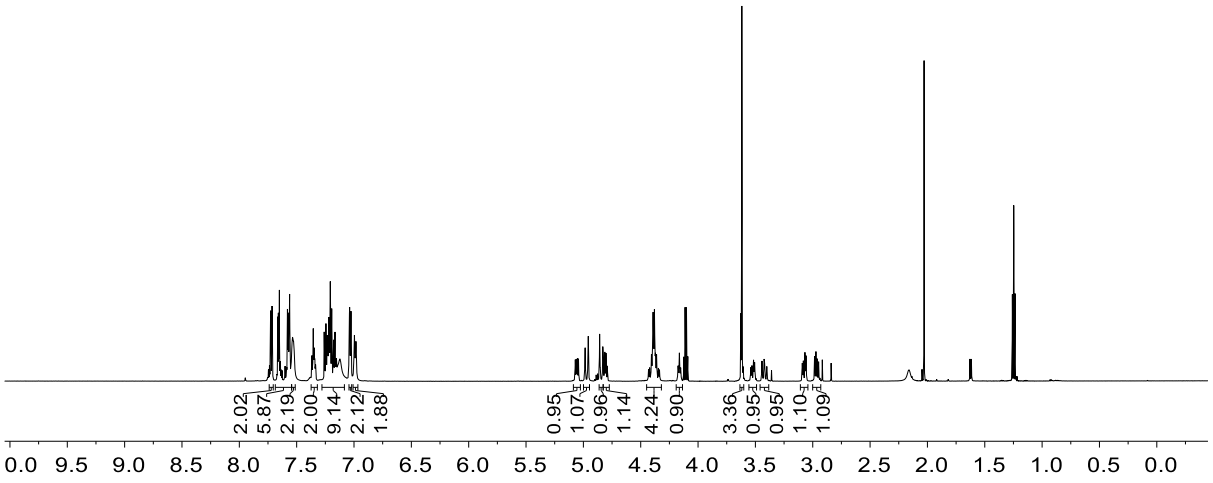

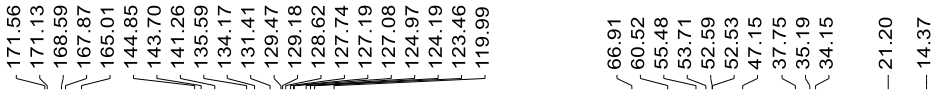

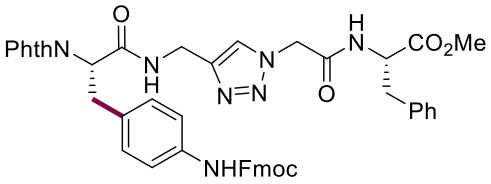

108b

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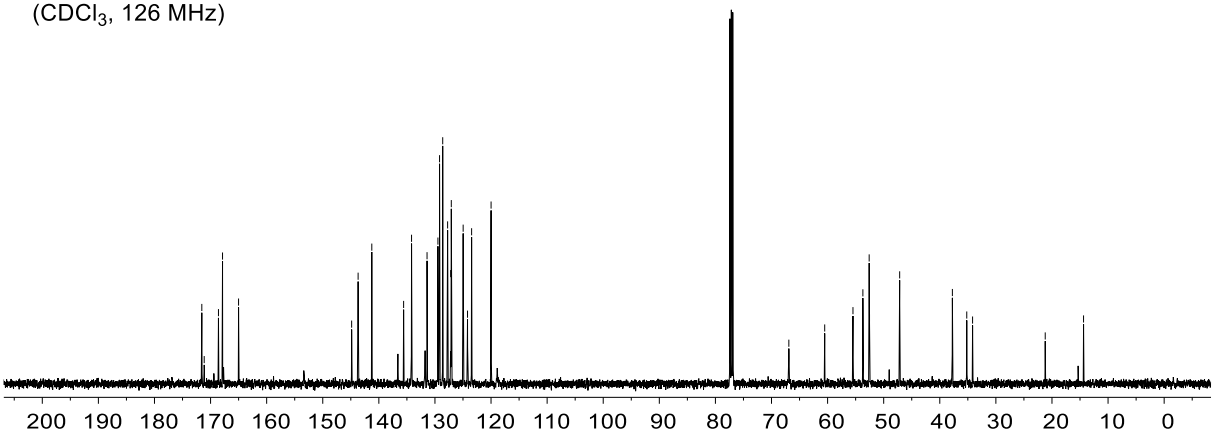

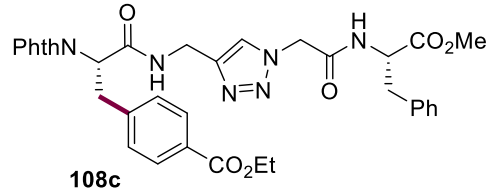

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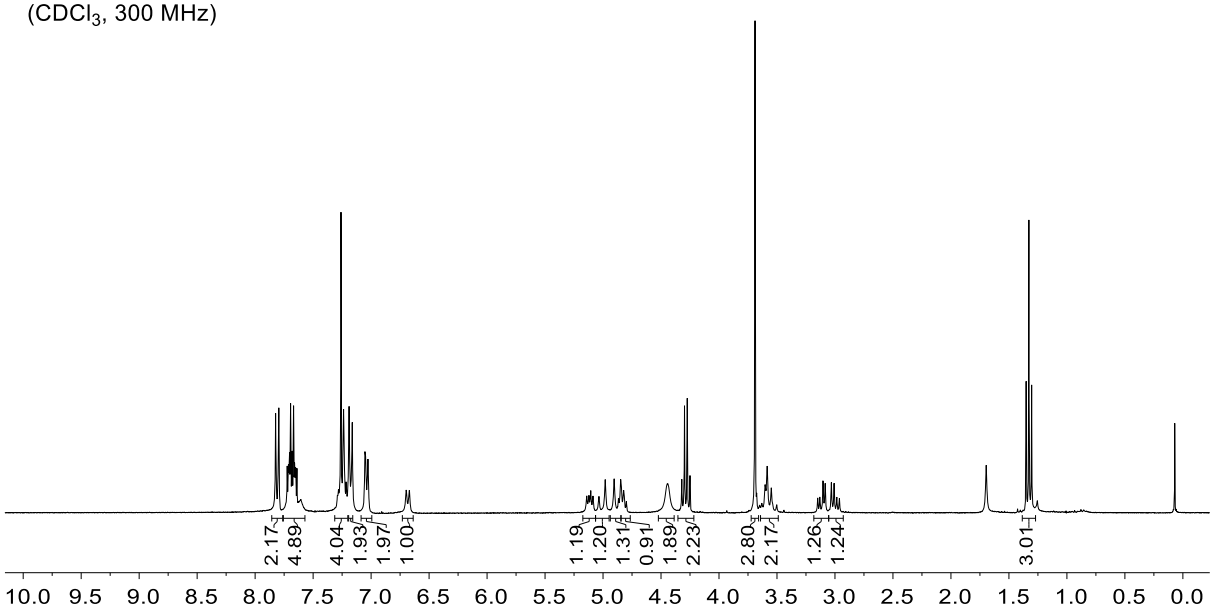

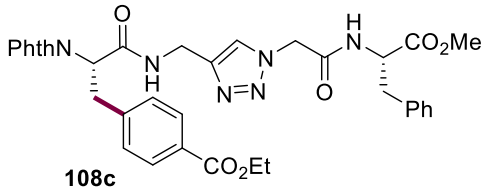

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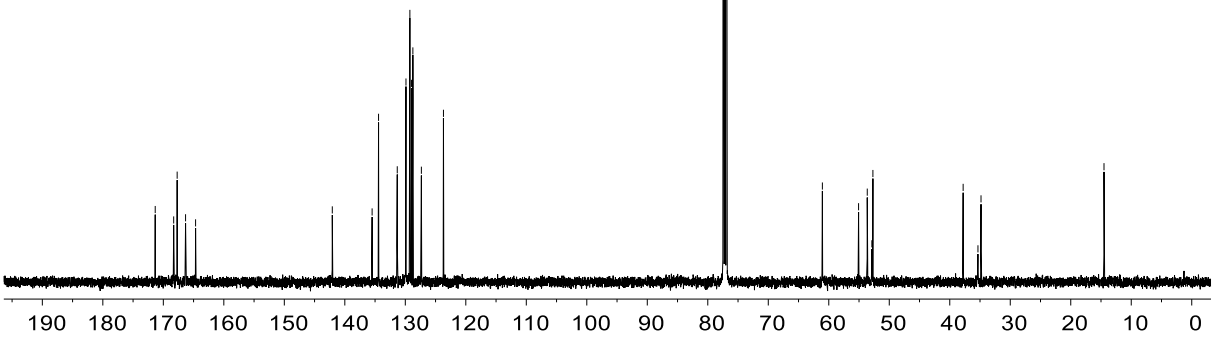

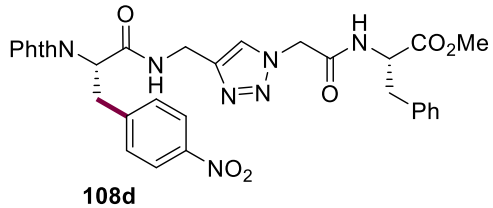

108d
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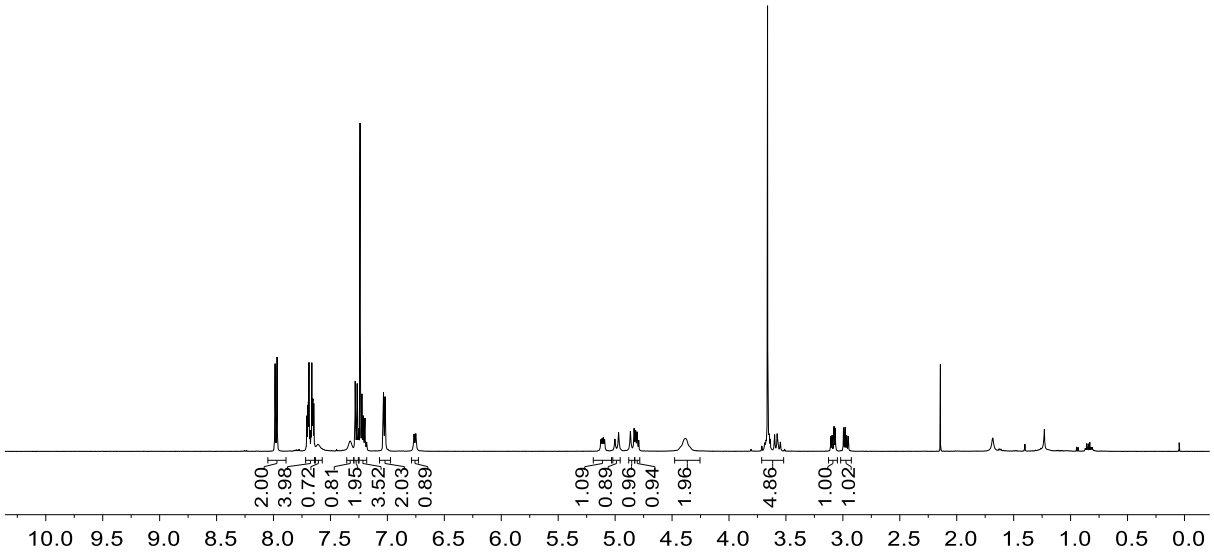

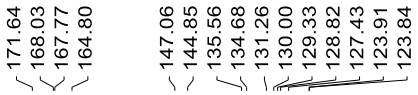

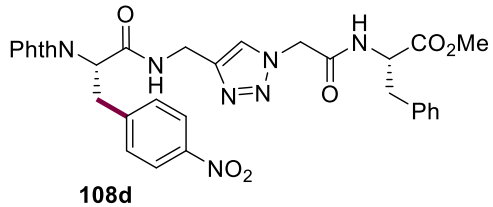

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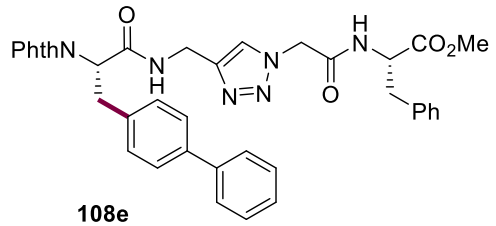

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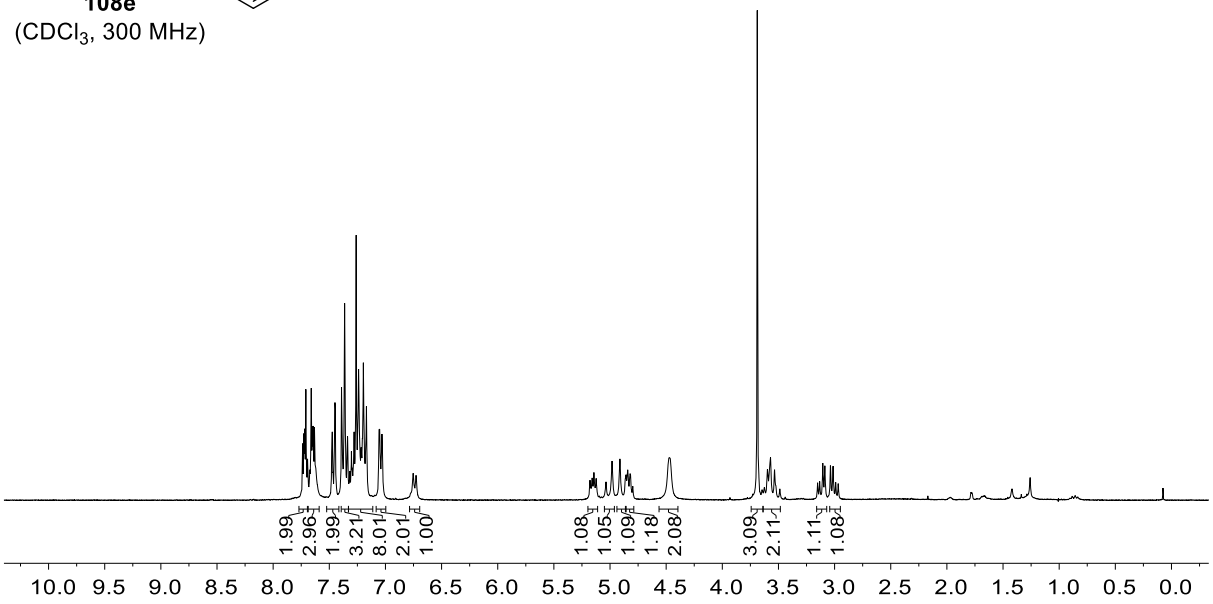

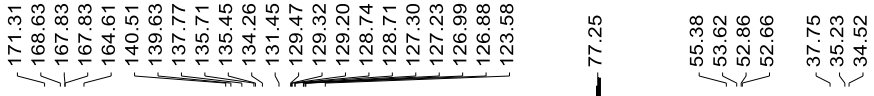

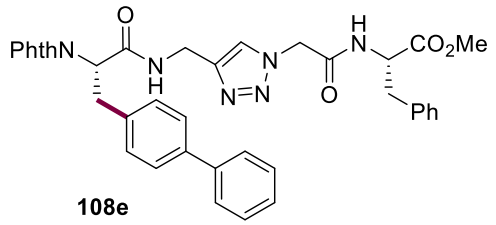

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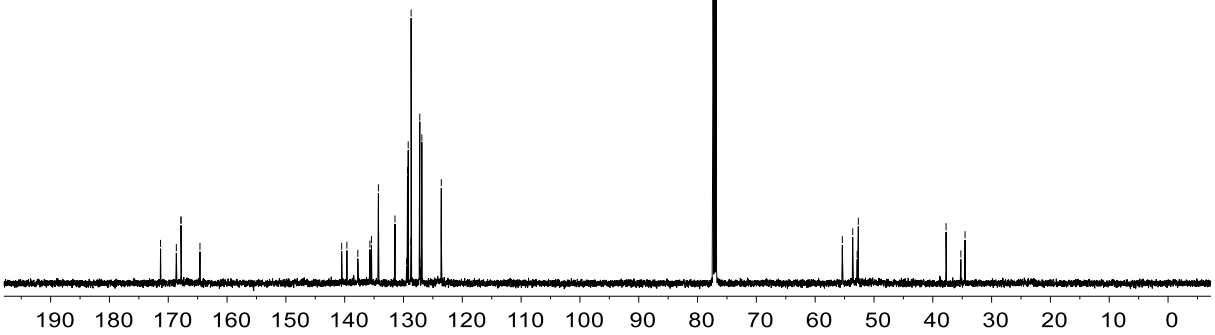

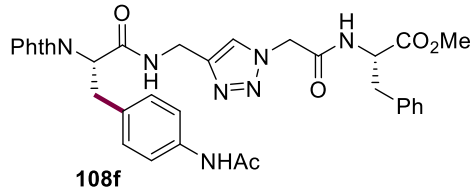

108f
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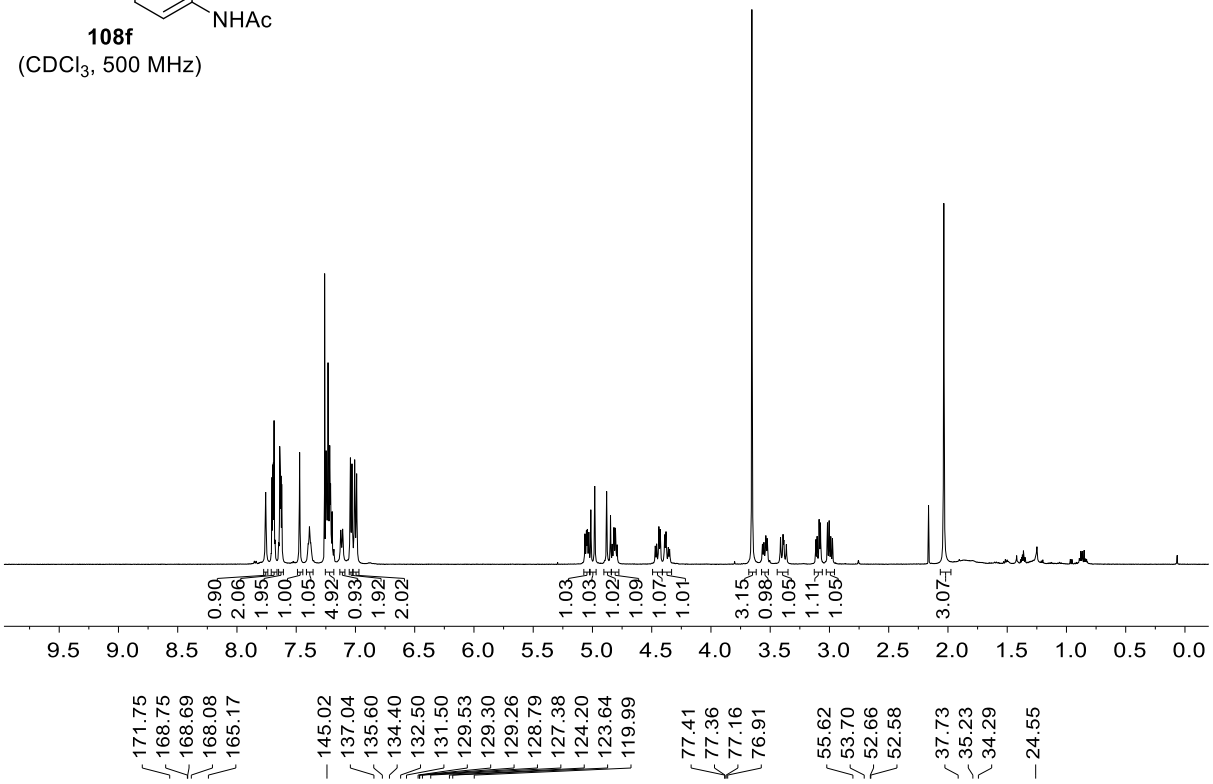

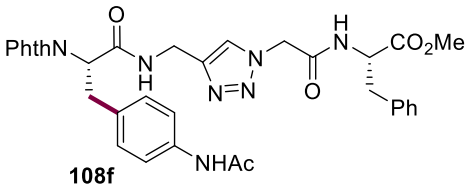

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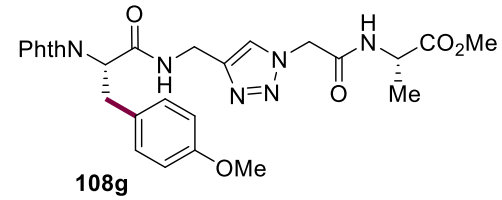

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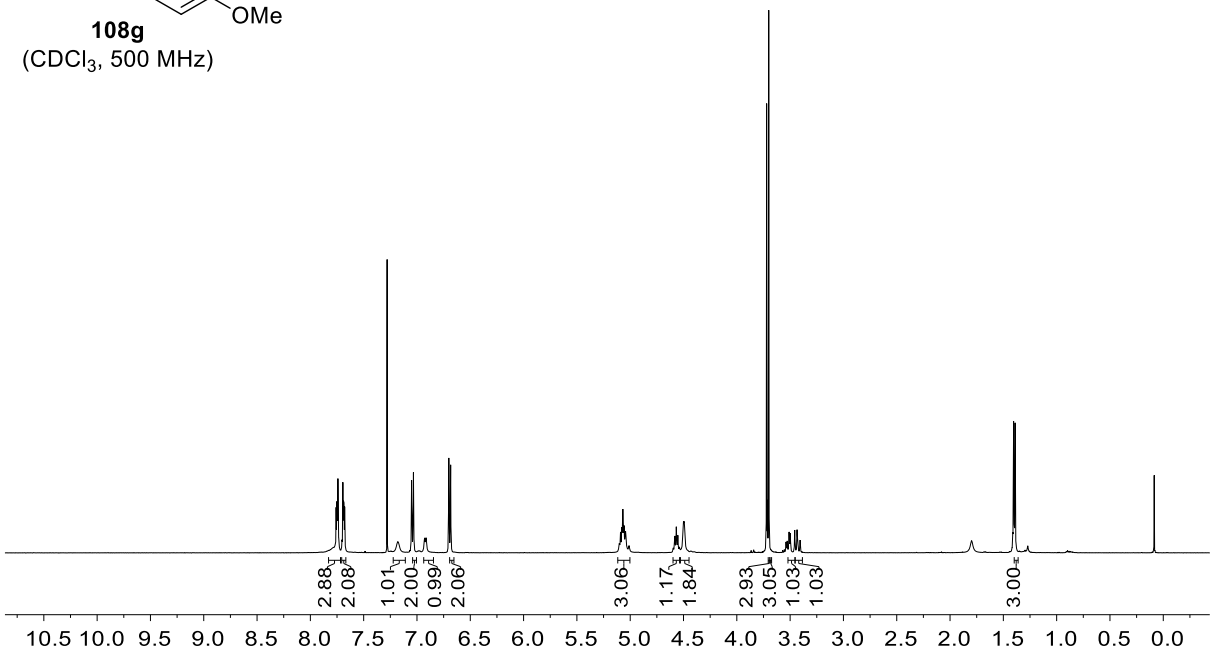
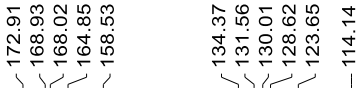
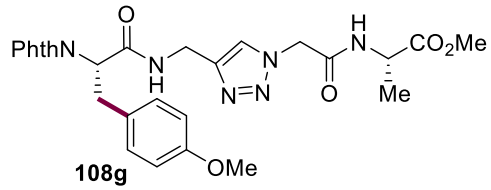
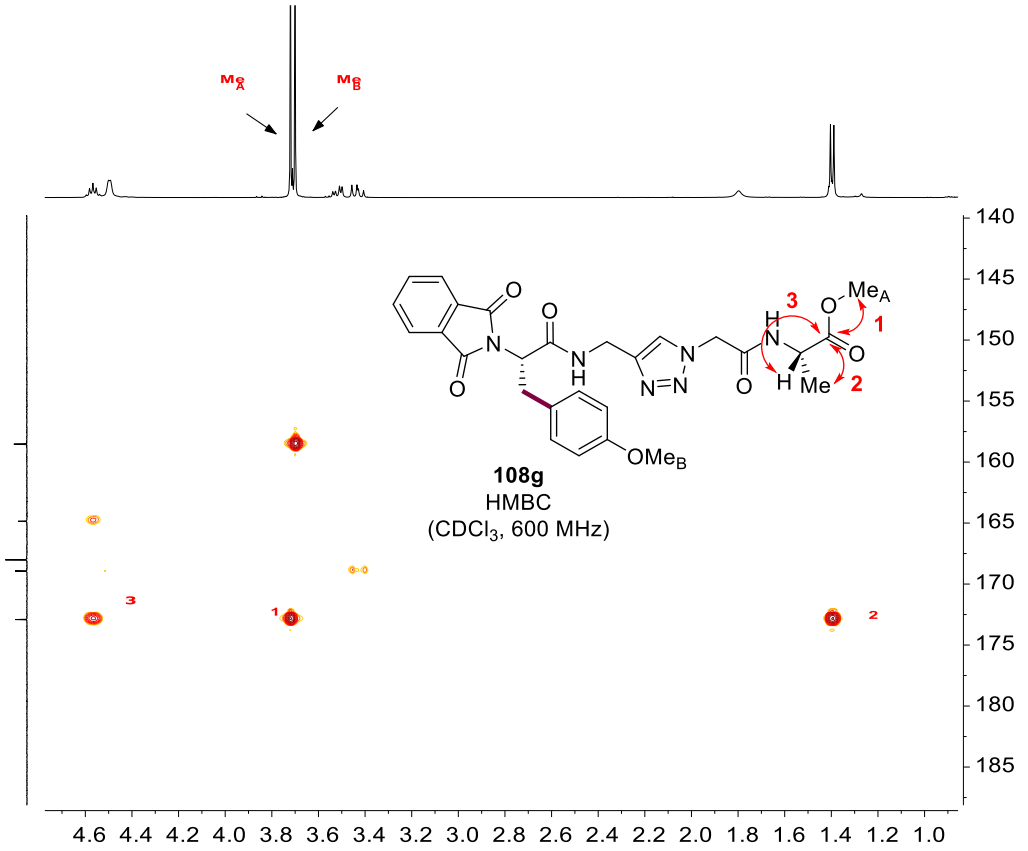


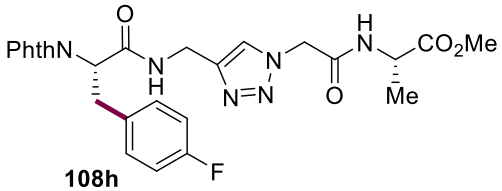




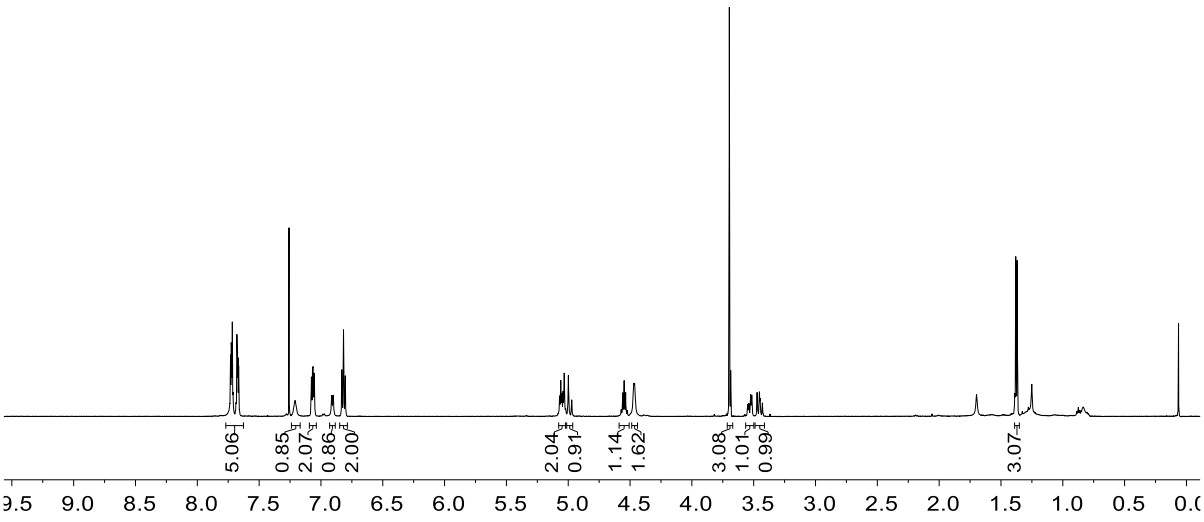
108g
($CDCl_3$, 126 MHz)

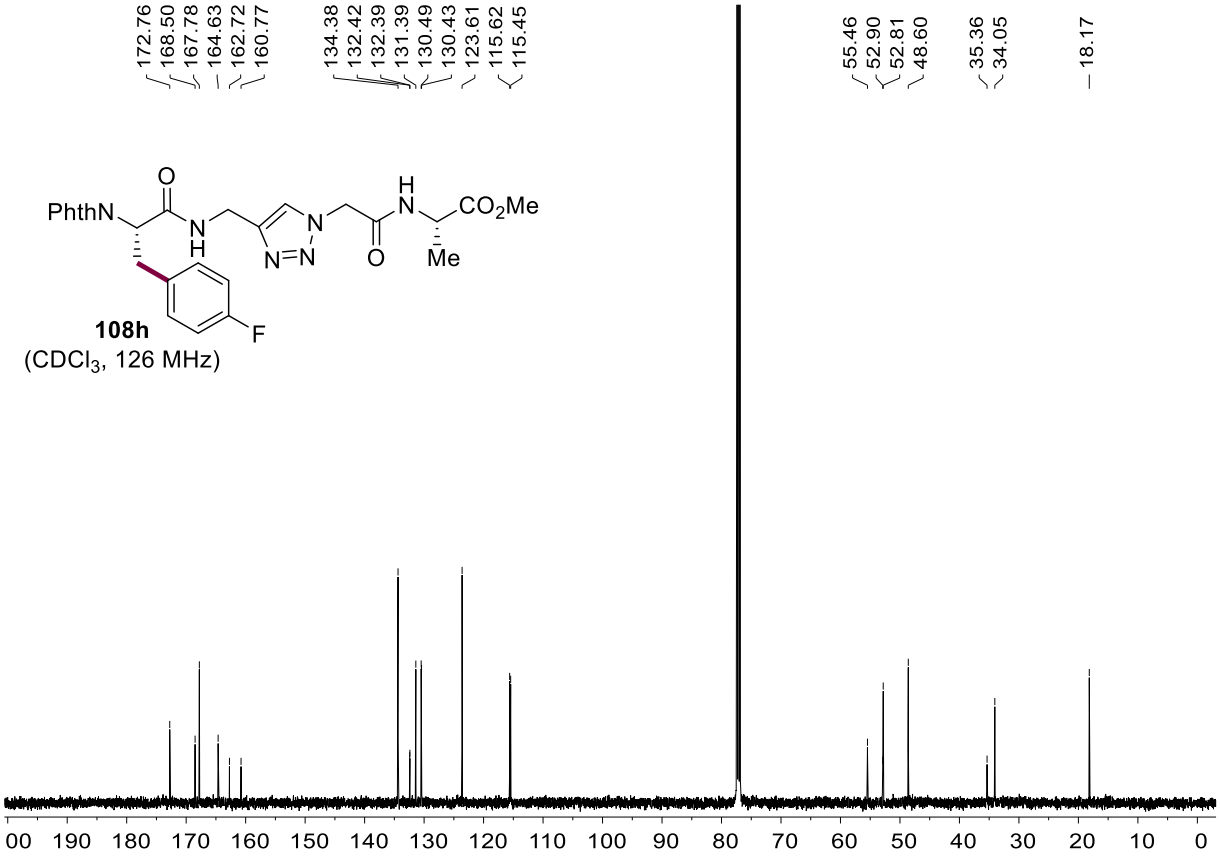


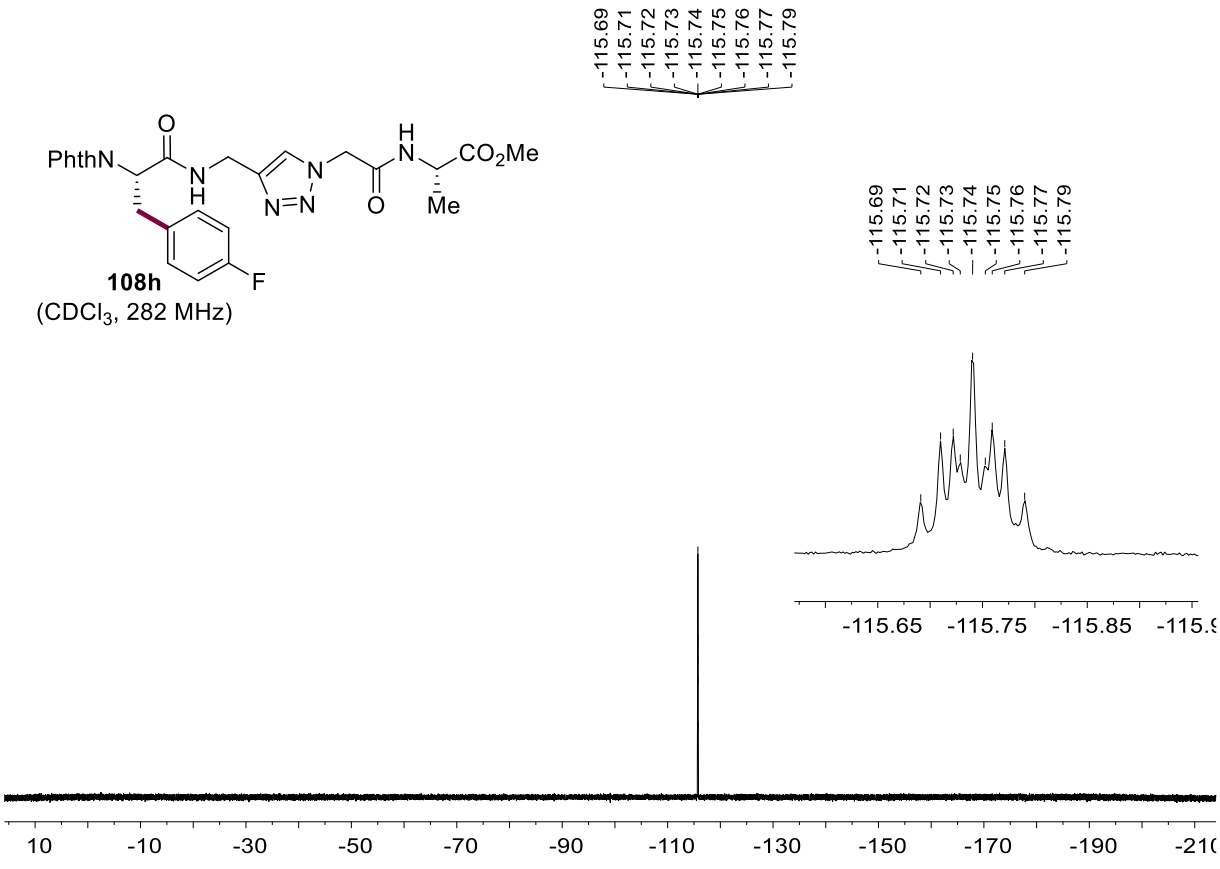
108g
HMBC
($CDCl_3$, 600 MHz)

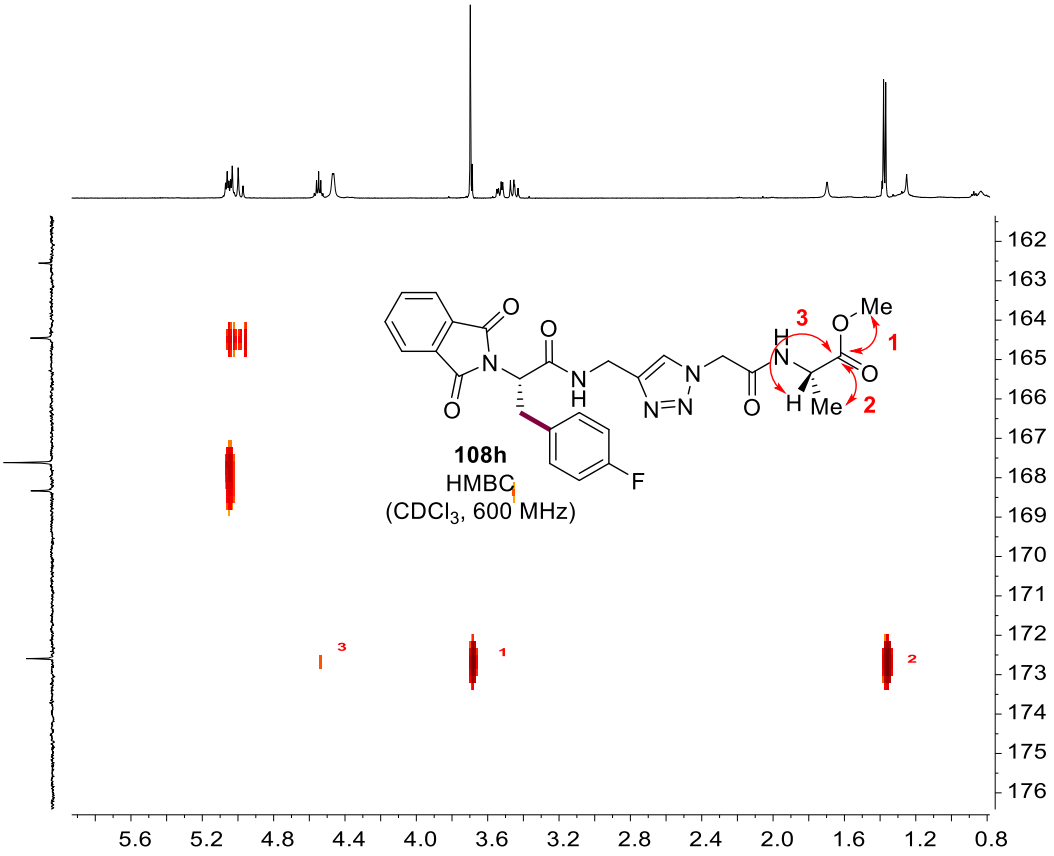


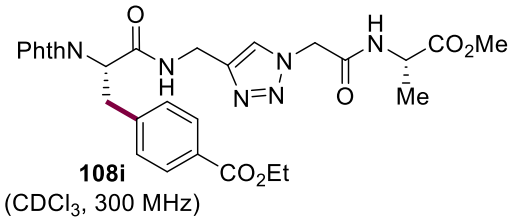
108h
($CDCl_3$, 600 MHz)

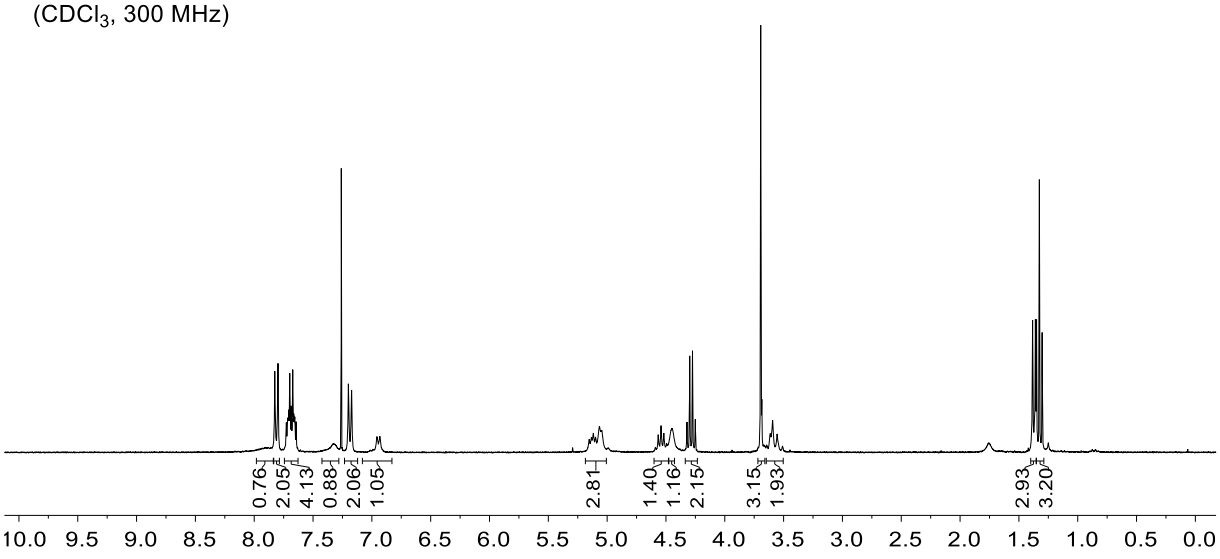


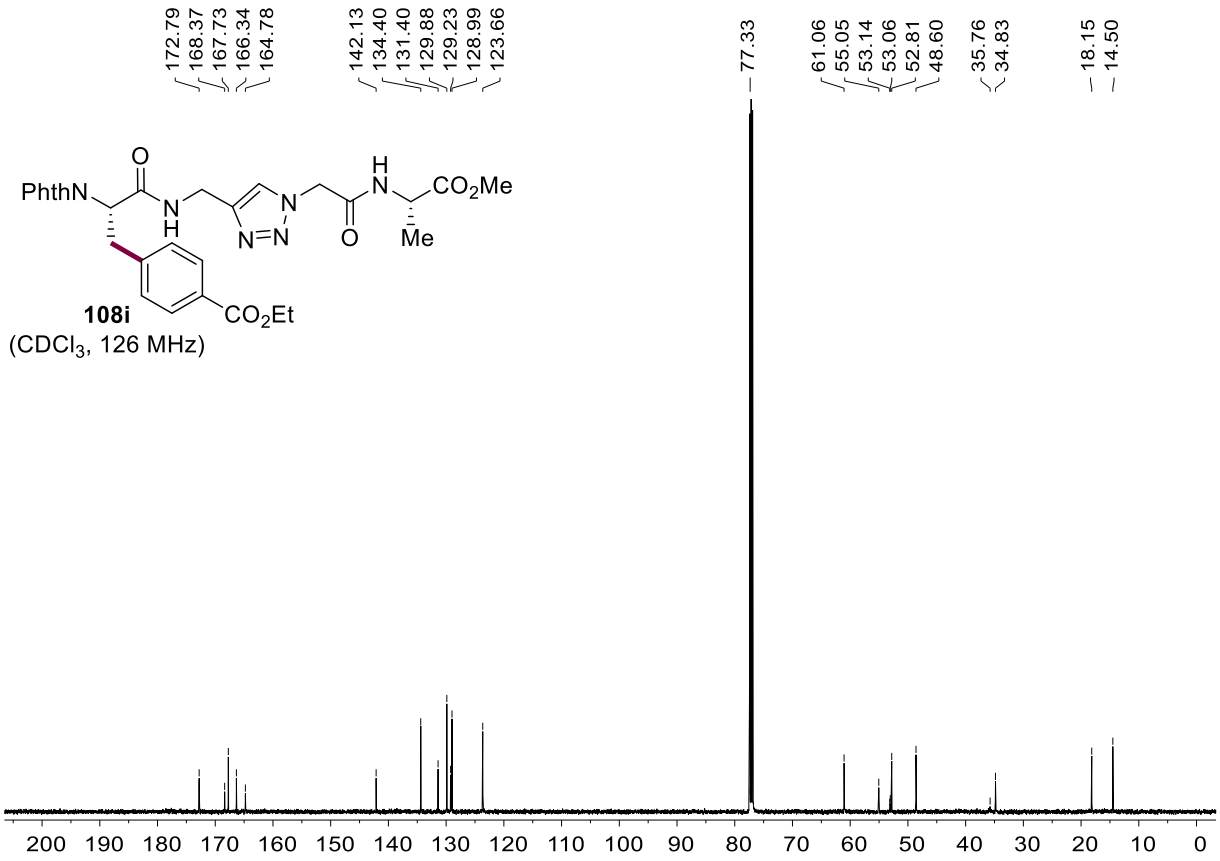

172.76
168.50
167.78
164.63
162.72
160.77
134.38
132.42
132.39
131.39
130.49
130.43
123.61
115.62
115.45
55.46
52.90
52.81
48.60
35.36
34.05
18.17
PhthN
O
N
H
N
N
H
N
O
CO2Me
Me
F
108h
(CDCl3, 126 MHz)
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

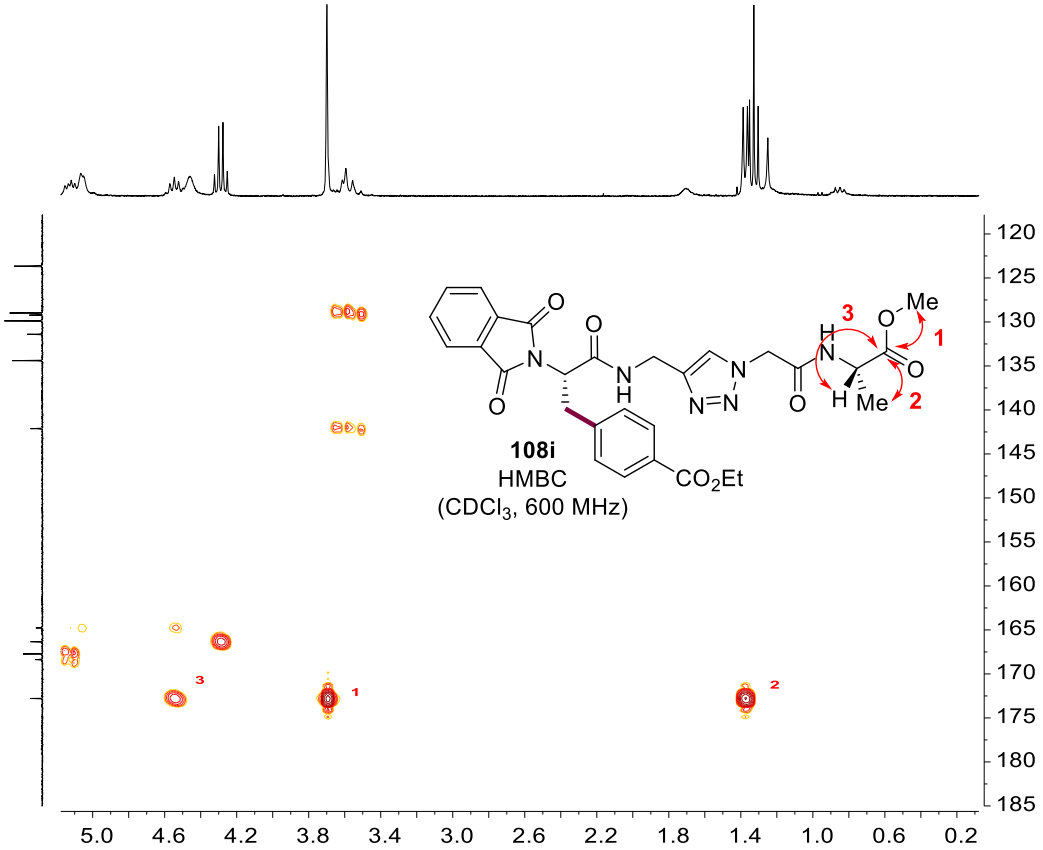

-115.69
-115.71
-115.72
-115.73
-115.74
-115.75
-115.76
-115.77
-115.79
PhthN
O
N
H
N
N
H
N
O
CO2Me
Me
F
108h
(CDCl3, 282 MHz)
-115.65
-115.75
-115.85
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190

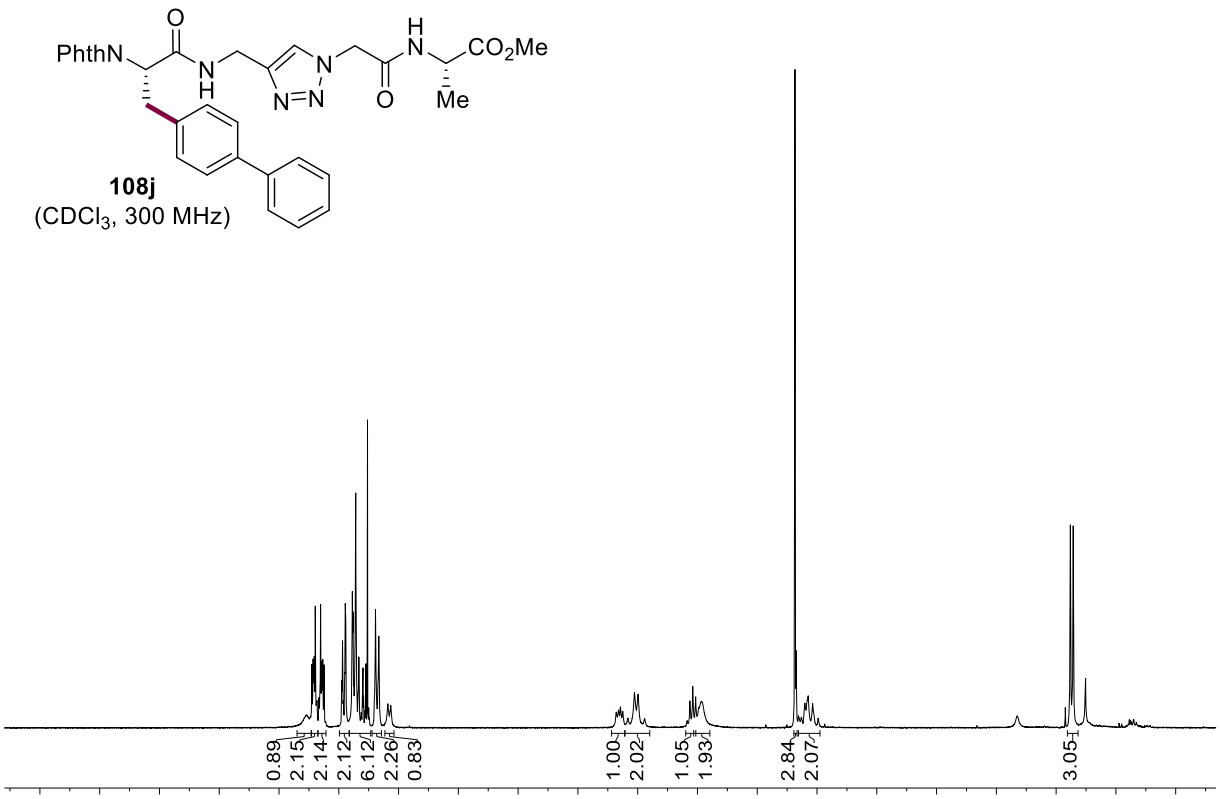

108h
HMBC
(CDCl3, 600 MHz)
F
Me
H Me
1
2
3
162
163
164
165
166
167
168
169
170
171
172
173
174
175
176
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8

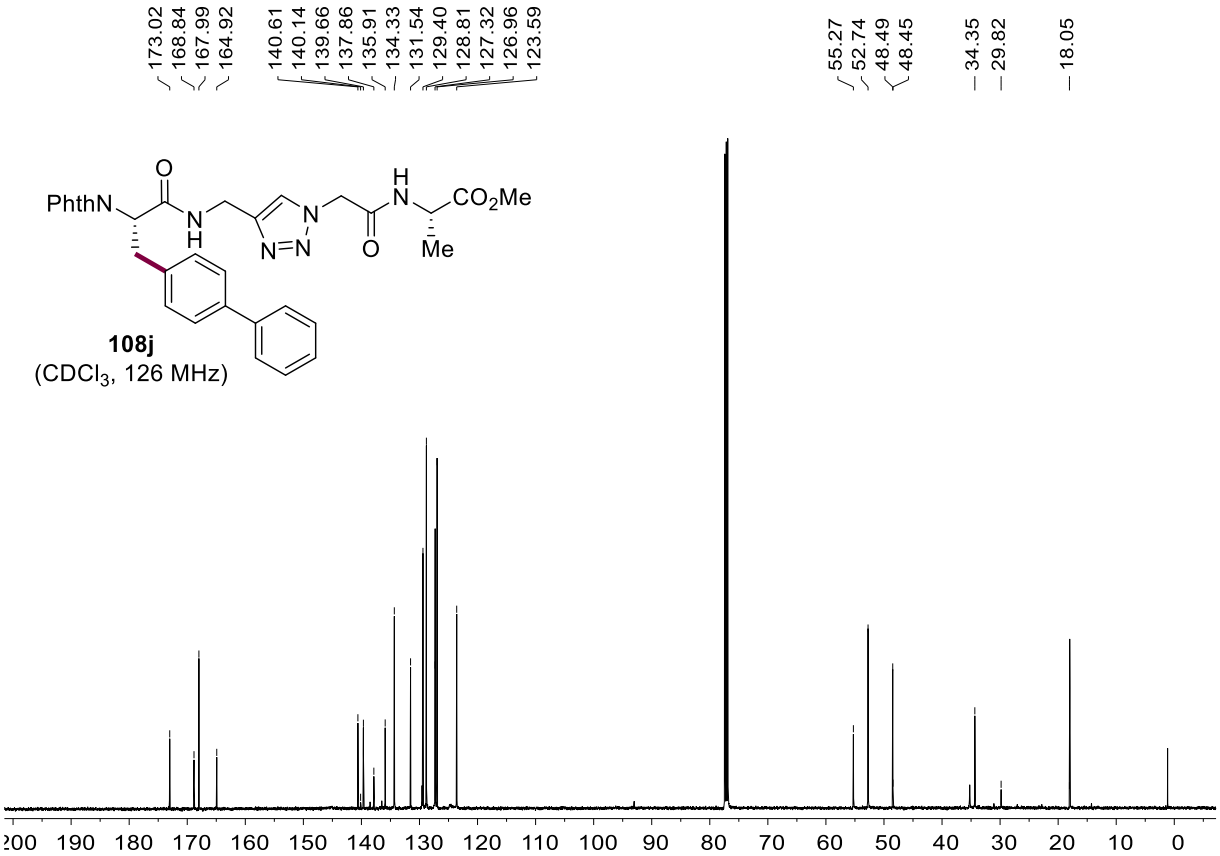

PhthN
CO2Me
Me
CO2Et
108i
(CDCl3, 300 MHz)

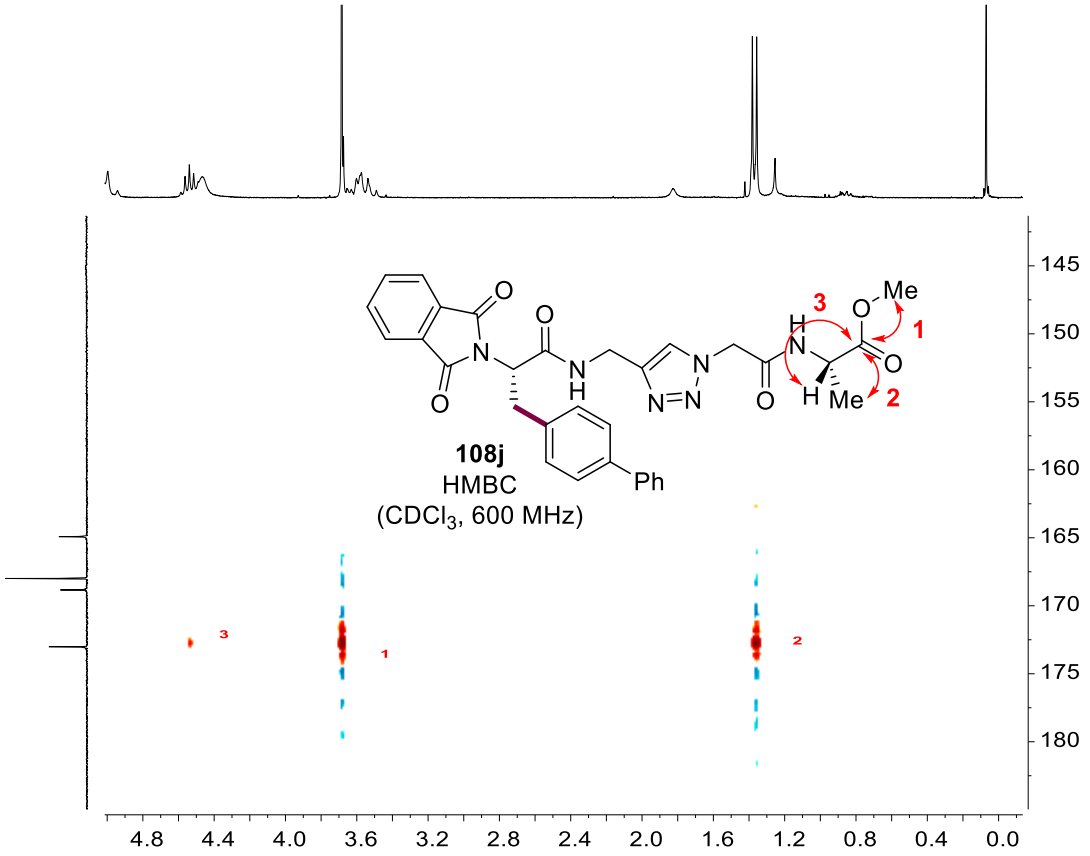

0.76
2.05
4.13
0.88
2.06
1.05
2.81
1.40
1.16
2.15
3.15
1.93
2.93
3.20
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

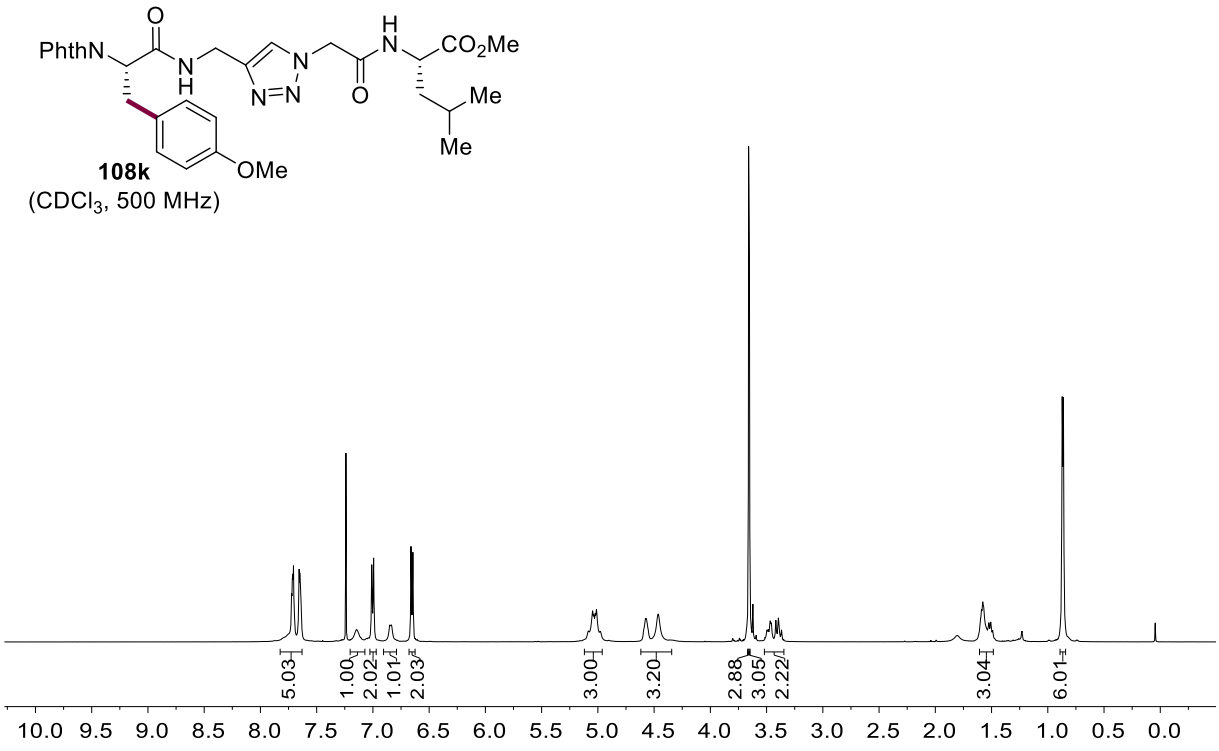

172.79
168.37
167.73
166.34
164.78
142.13
134.40
131.40
129.88
129.23
128.99
123.66
77.33
61.06
55.05
53.14
53.06
52.81
48.60
35.76
34.83
18.15
14.50
PhthN
CO2Me
Me
CO2Et
108i
(CDCl3, 126 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

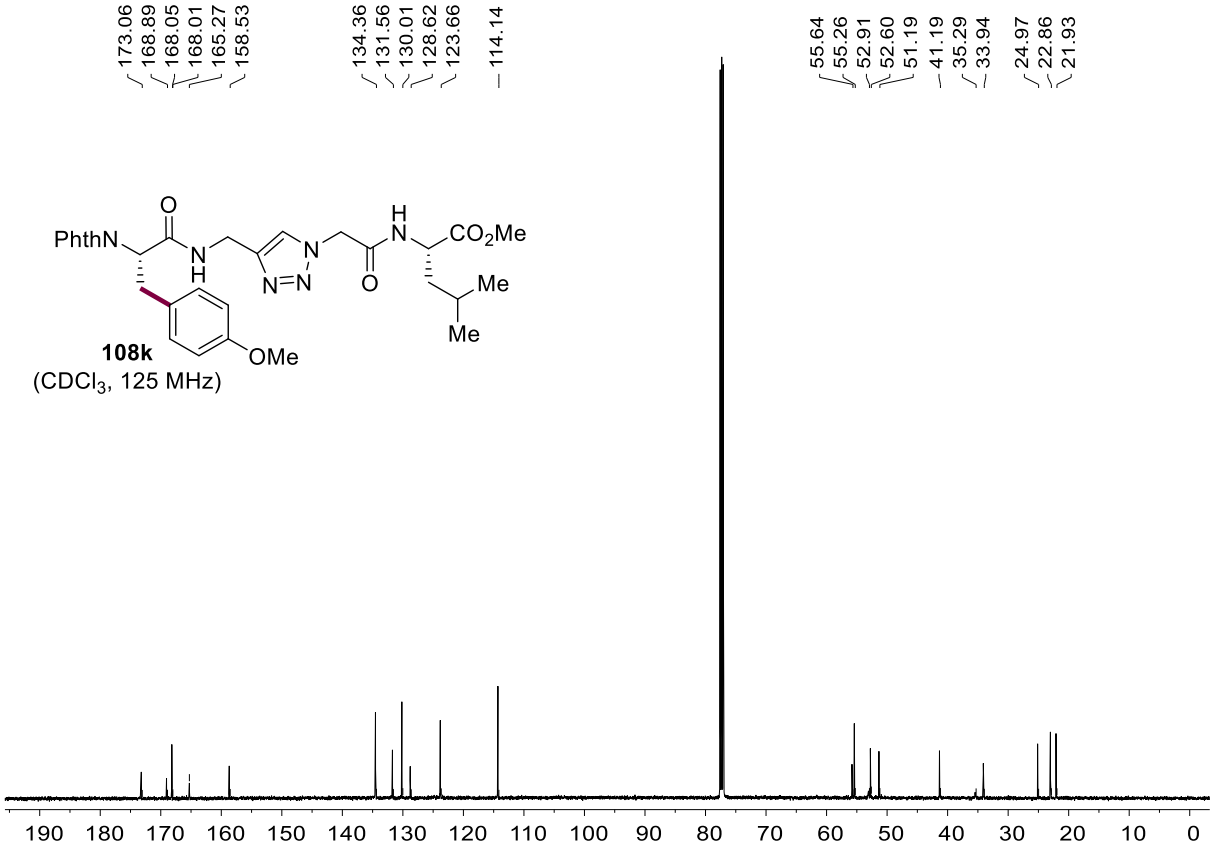

108i
HMBC
(CDCl3, 600 MHz)
CO2Et
Me
Me
1
2
3
120 125 130 135 140 145 150 155 160 165 170 175 180 185
5.0 4.6 4.2 3.8 3.4 3.0 2.6 2.2 1.8 1.4 1.0 0.6 0.2

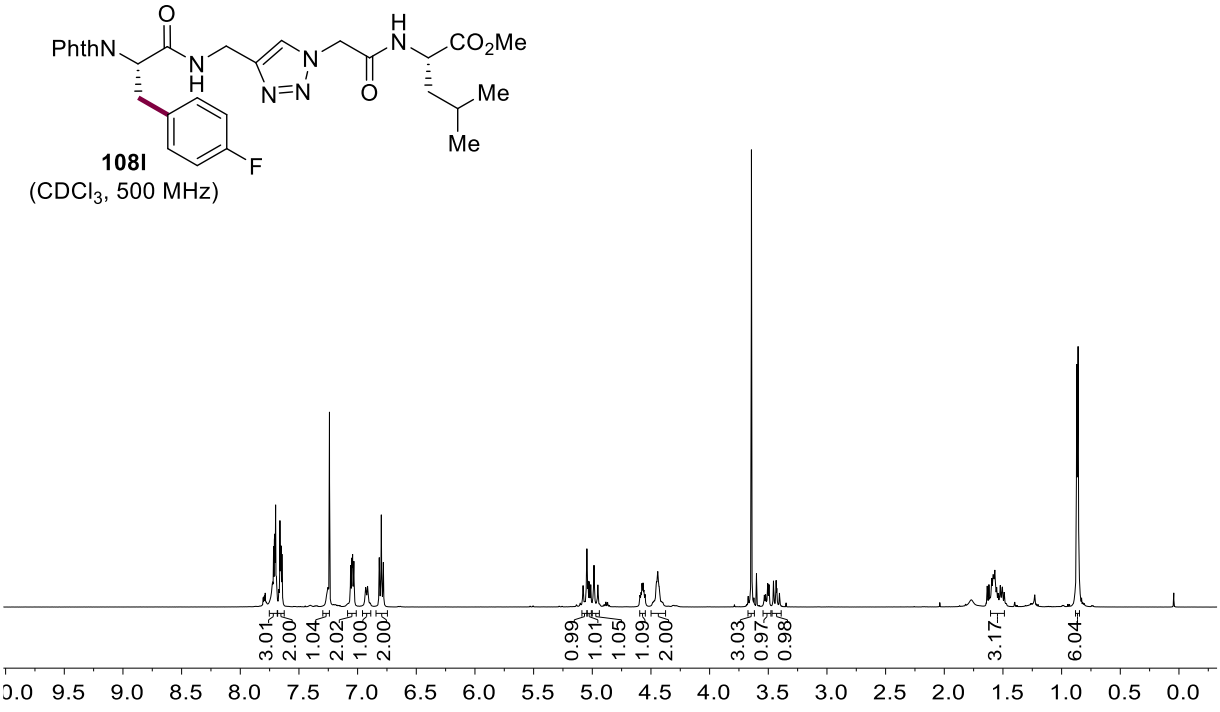

PhthN
O
N
H
N
N=N
O
H
N
CO2Me
Me
108j
(CDCl3, 300 MHz)
0.89
2.15
2.14
2.12
6.12
2.26
0.83
1.00
2.02
1.05
1.93
2.84
2.07
3.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

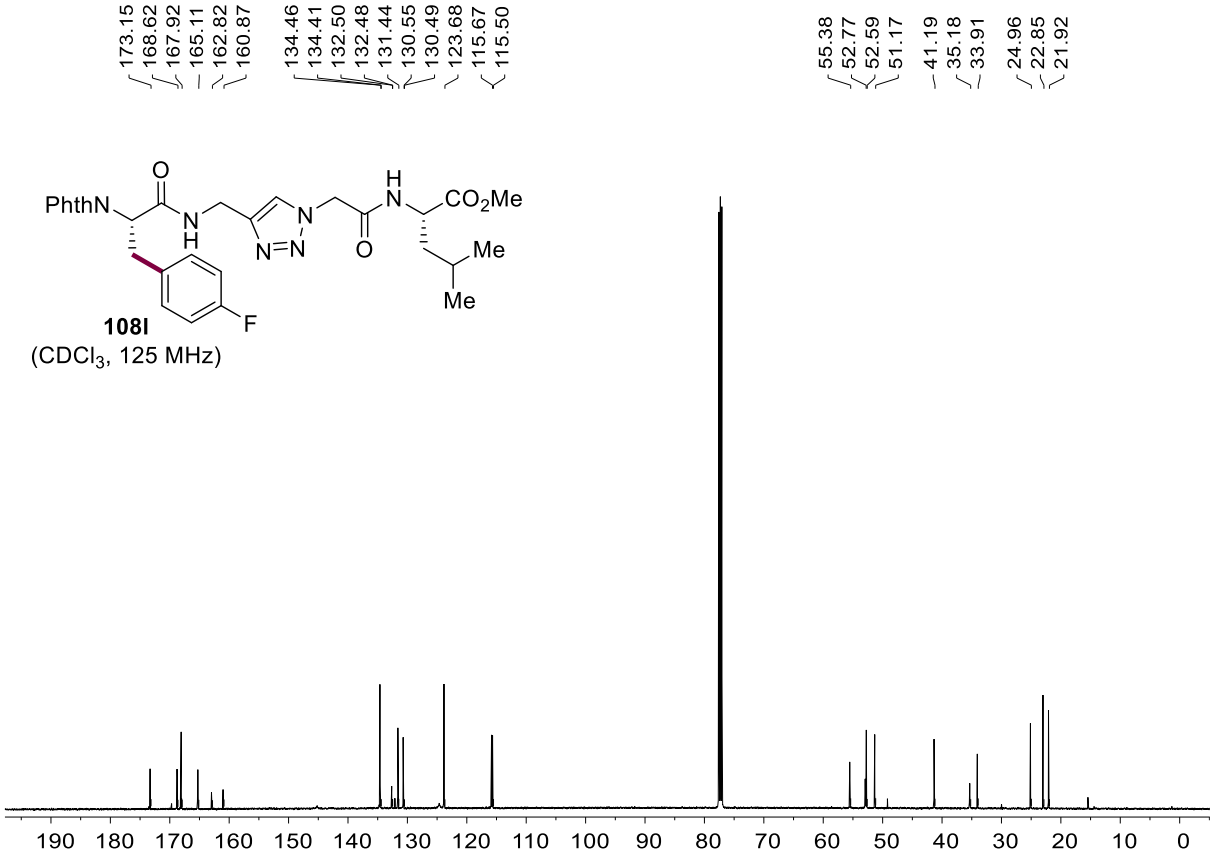

173.02
168.84
167.99
164.92
140.61
140.14
139.66
137.86
135.91
134.33
131.54
129.40
128.81
127.32
126.96
123.59
55.27
52.74
48.49
48.45
34.35
29.82
18.05
PhthN
O
N
H
N
N=N
O
H
N
CO2Me
Me
108j
(CDCl3, 126 MHz)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


108j
HMBC
(CDCl3, 600 MHz)
Ph
Me
Me
1
2
3
145
150
155
160
165
170
175
180
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0

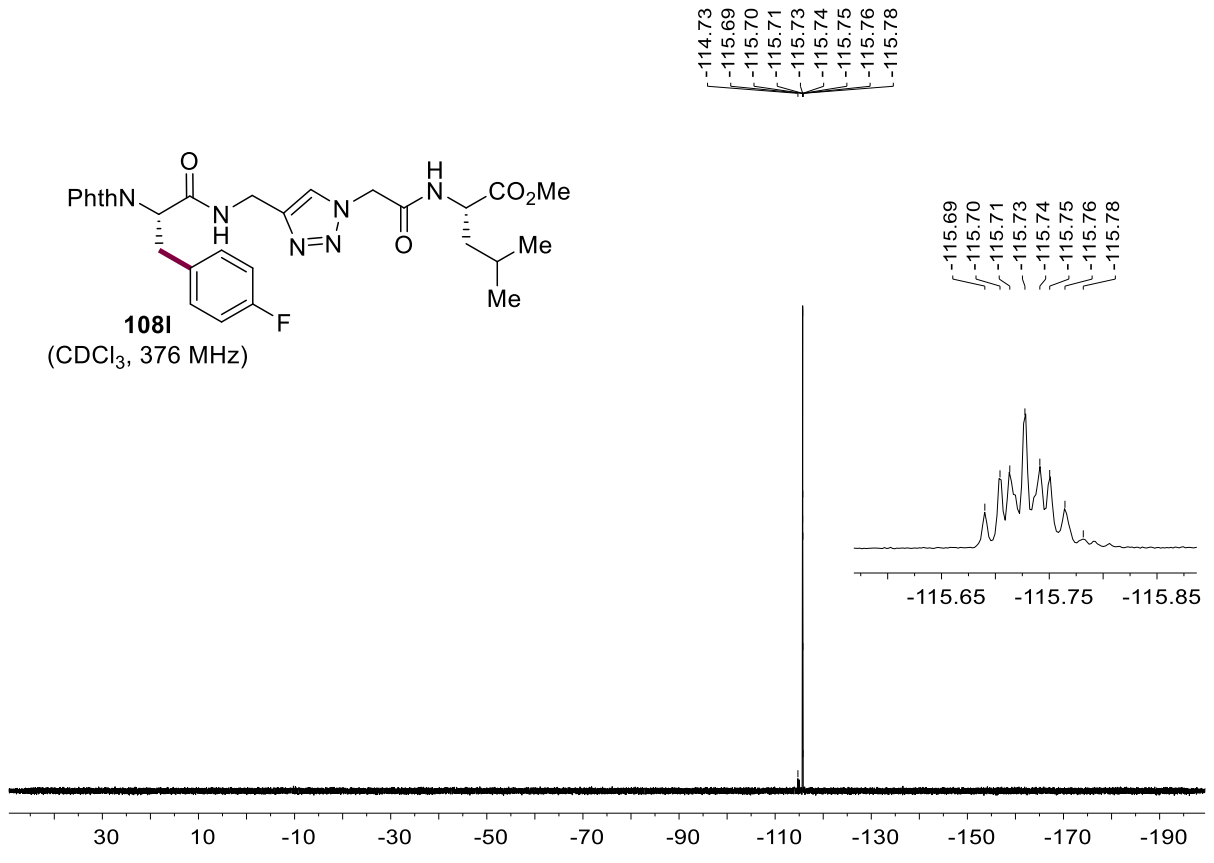

PhthN
CO2Me
Me
Me
OMe
108k
(CDCl3, 500 MHz)
5.03
1.00
2.02
1.01
2.03
3.00
3.20
2.88
3.05
2.22
3.04
6.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


173.06
168.89
168.05
168.01
165.27
158.53
134.36
131.56
130.01
128.62
123.66
114.14
55.64
55.26
52.91
52.60
51.19
41.19
35.29
33.94
24.97
22.86
21.93
PhthN
O
N
H
N
N=N
O
H
N
CO2Me
Me
Me
OMe
108k
(CDCl3, 125 MHz)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

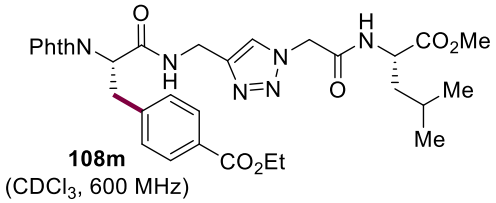

PhthN
O
N
H
N
N=N
O
H
N
CO2Me
Me
Me
F
108l
(CDCl3, 500 MHz)
3.01
2.00
1.04
2.02
1.00
2.00
0.99
1.01
1.05
1.09
2.00
3.03
0.97
0.98
3.17
6.04
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0



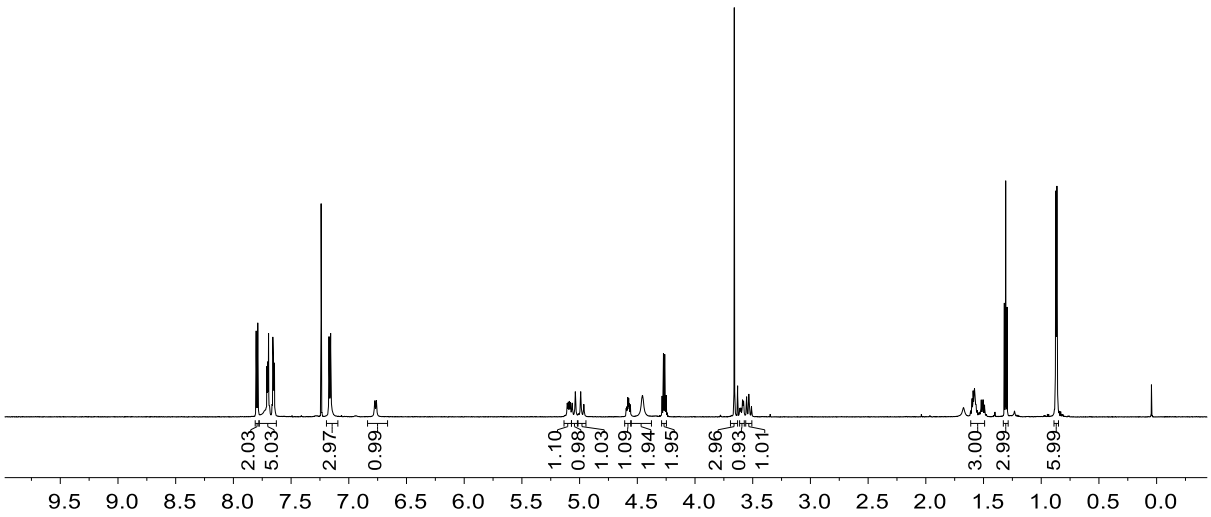
108l
($CDCl_3$, 125 MHz)

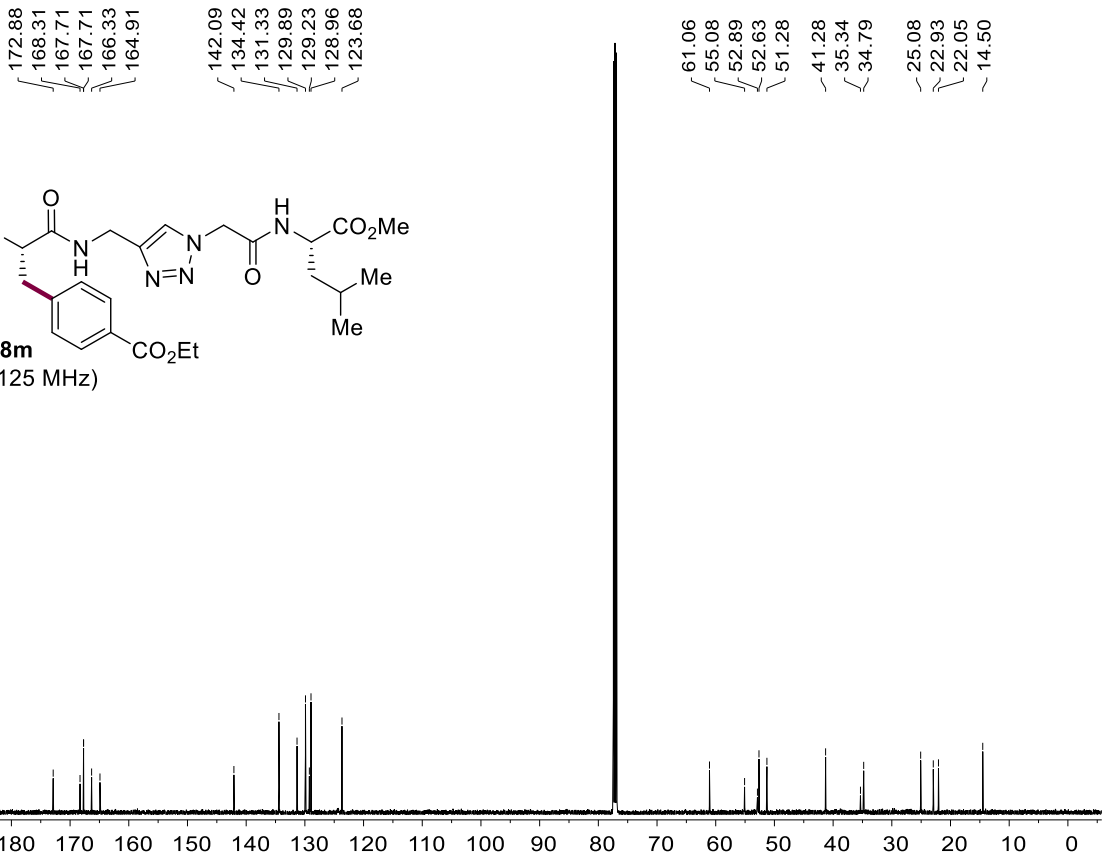


108l
($CDCl_3$, 376 MHz)

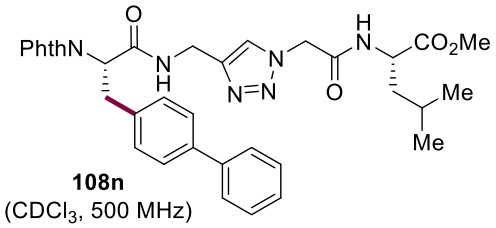


108m
($CDCl_3$, 600 MHz)

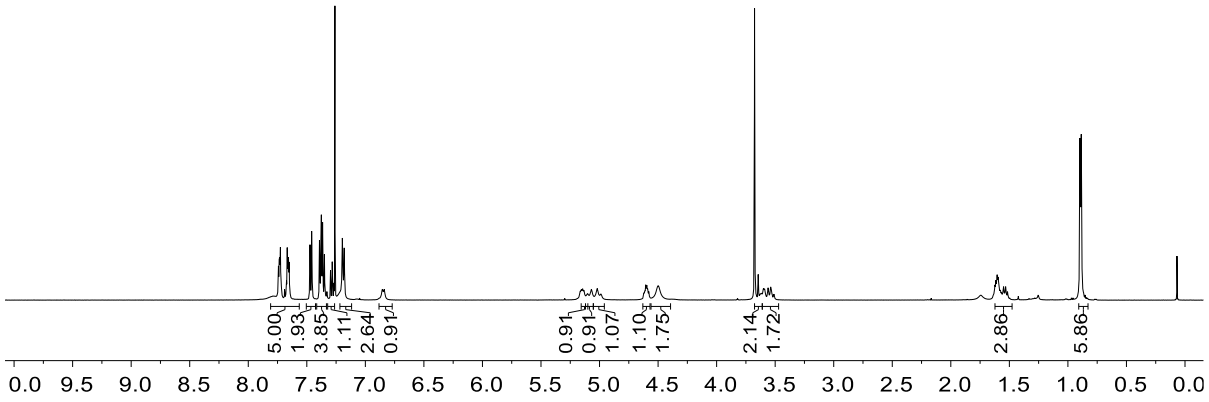


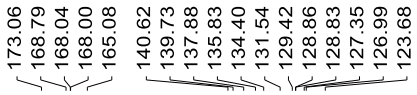


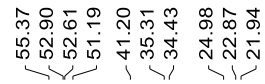
108m
($CDCl_3$, 125 MHz)

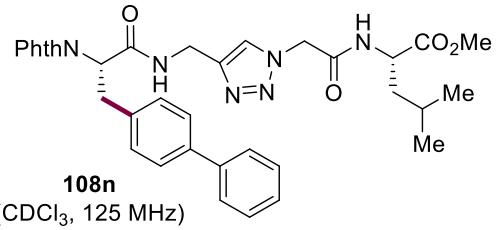


108n
($CDCl_3$, 500 MHz)

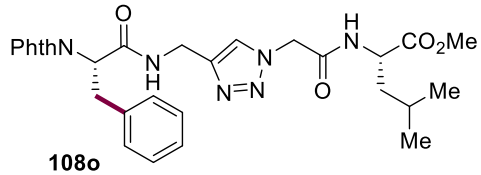




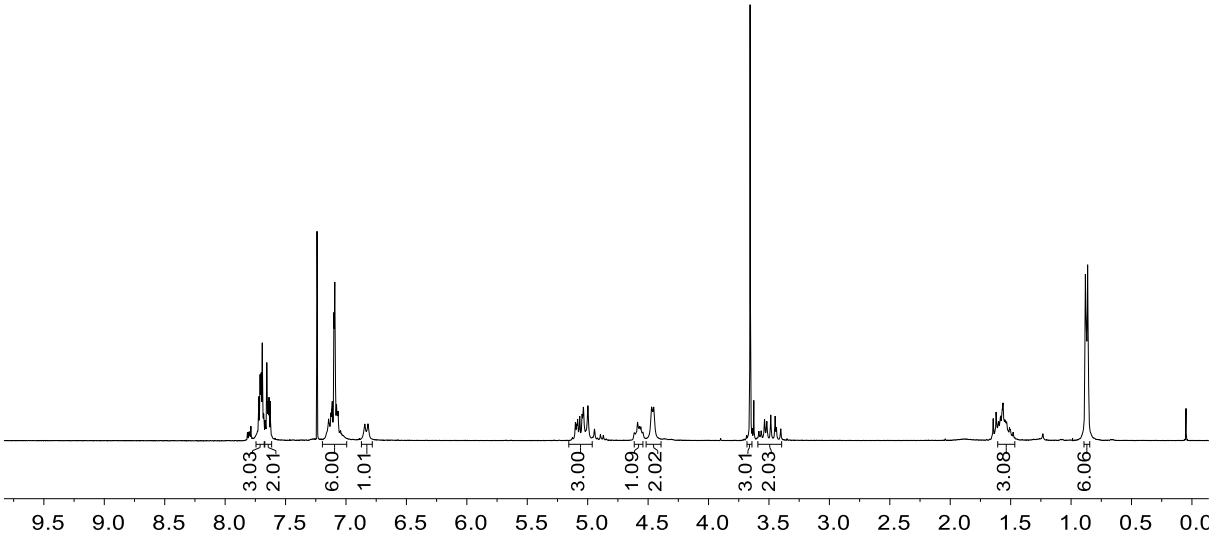


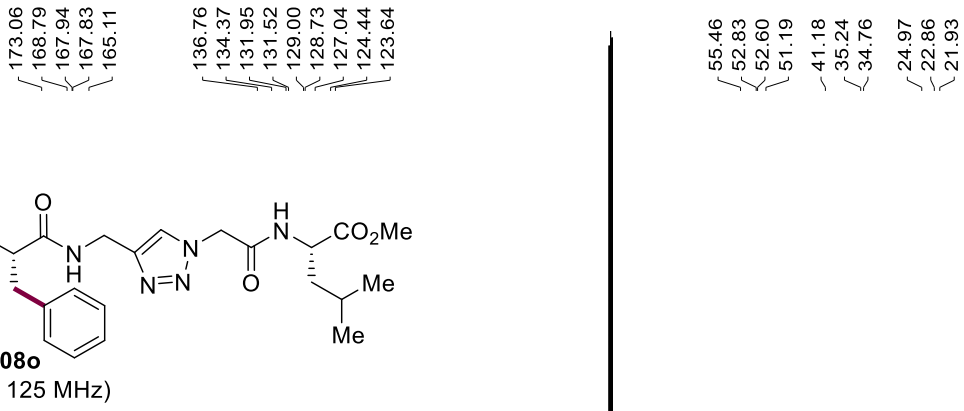


108n
($CDCl_3$, 125 MHz)

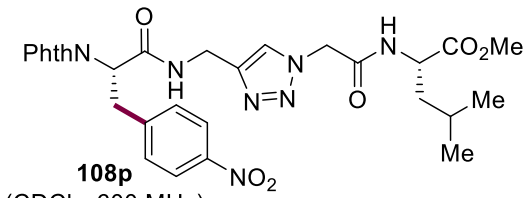


108o
($CDCl_3$, 300 MHz)

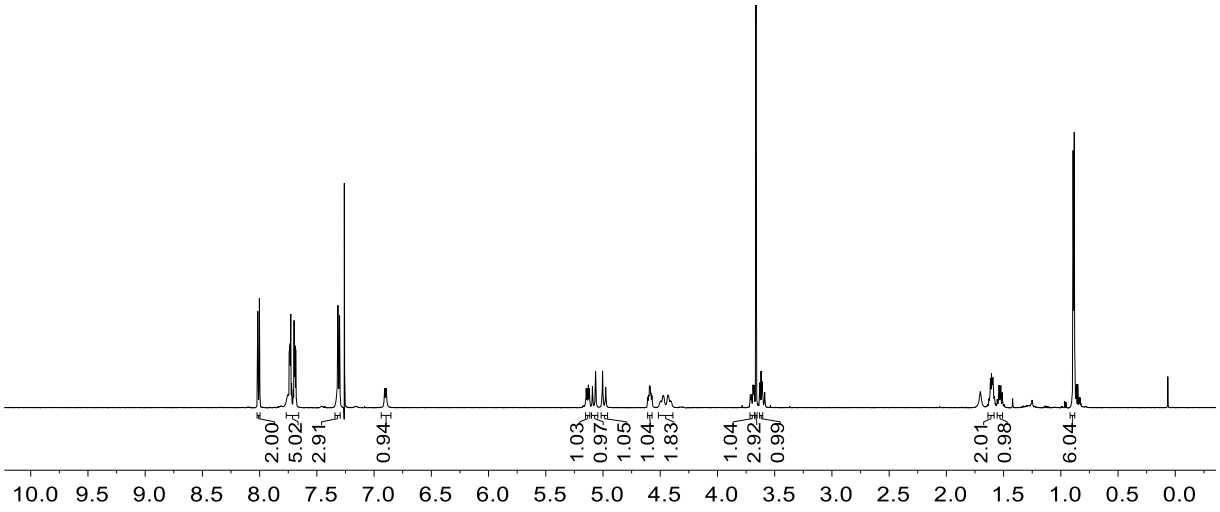


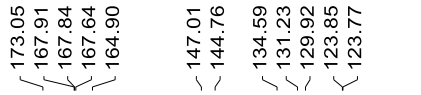


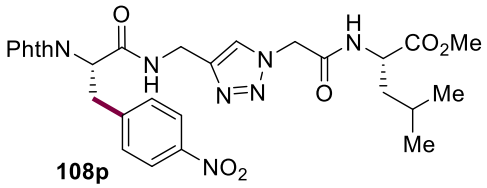
108o
($CDCl_3$, 125 MHz)



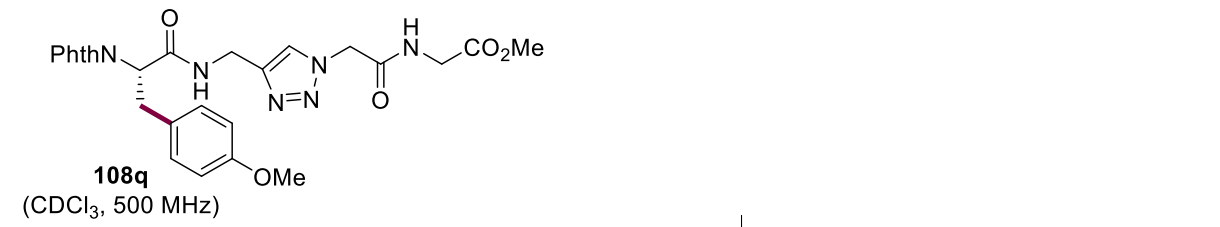
108p
($CDCl_3$, 600 MHz)



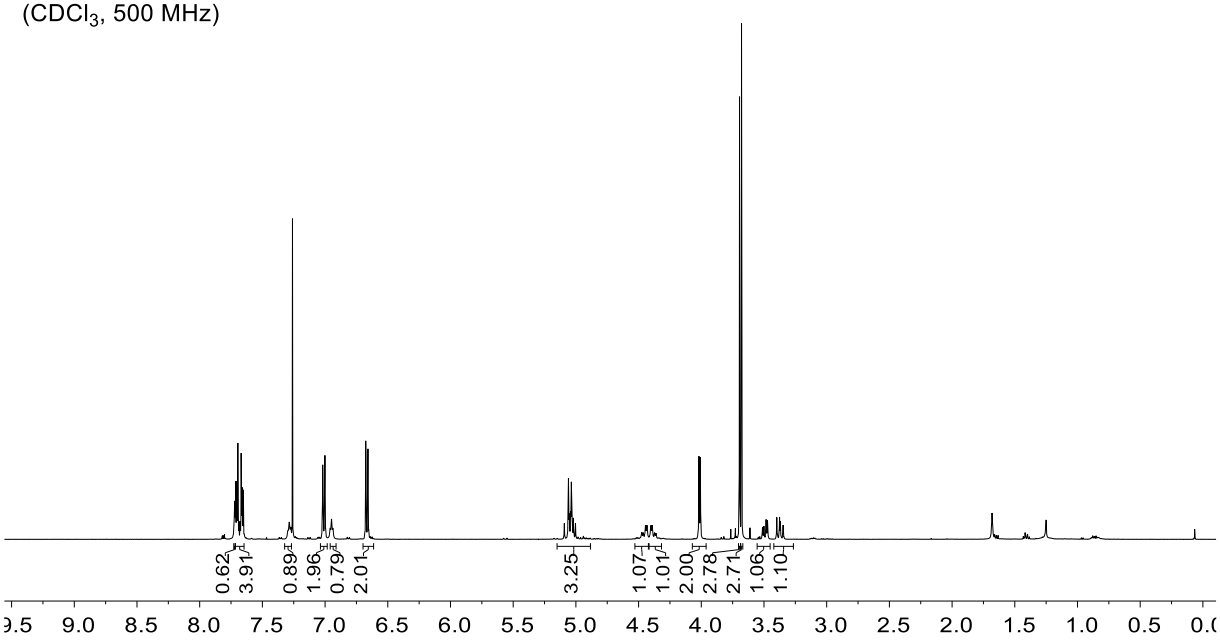


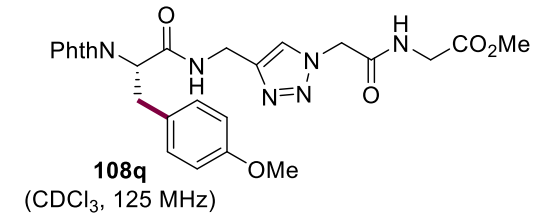


108p
($CDCl_3$, 126 MHz)

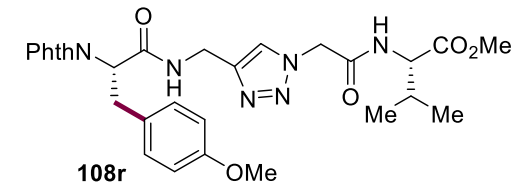


108q
($CDCl_3$, 500 MHz)

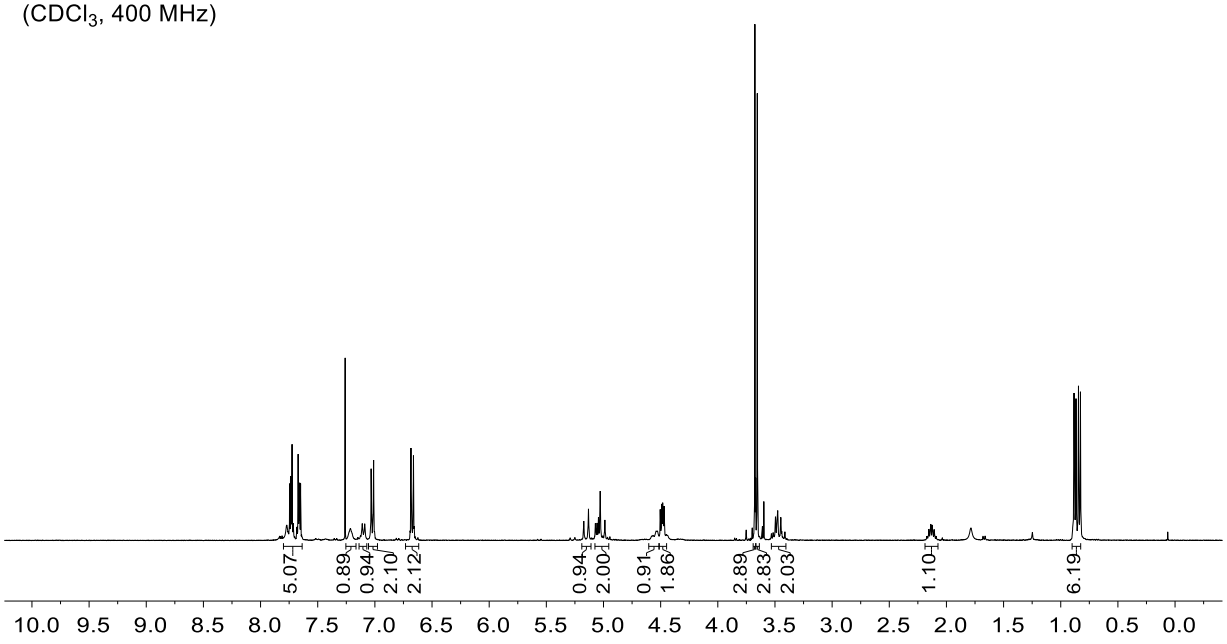


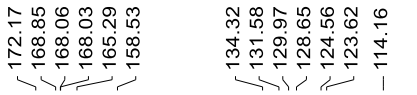


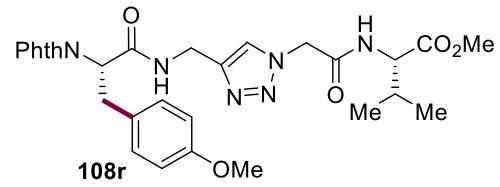
108q
($CDCl_3$, 125 MHz)



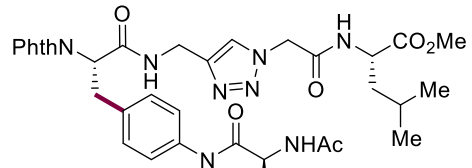
108r
($CDCl_3$, 400 MHz)



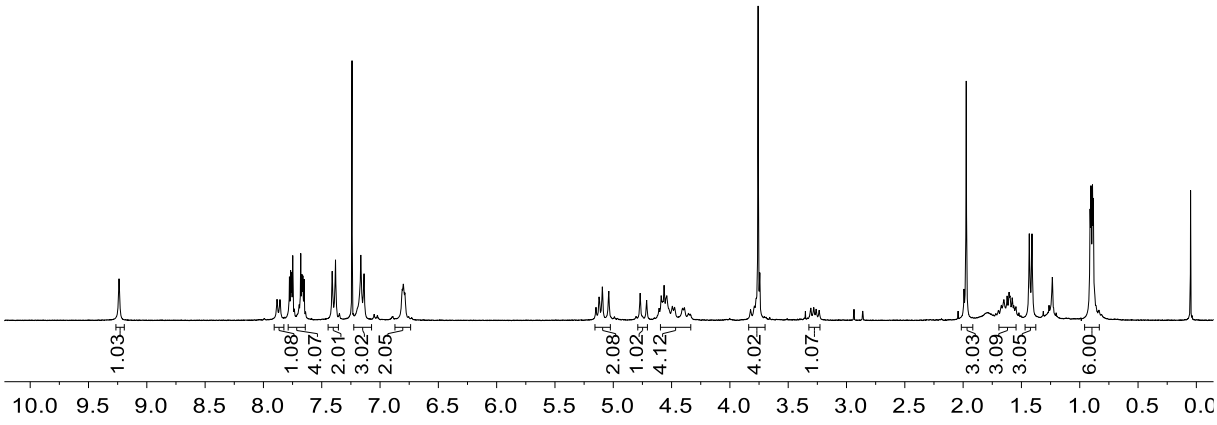


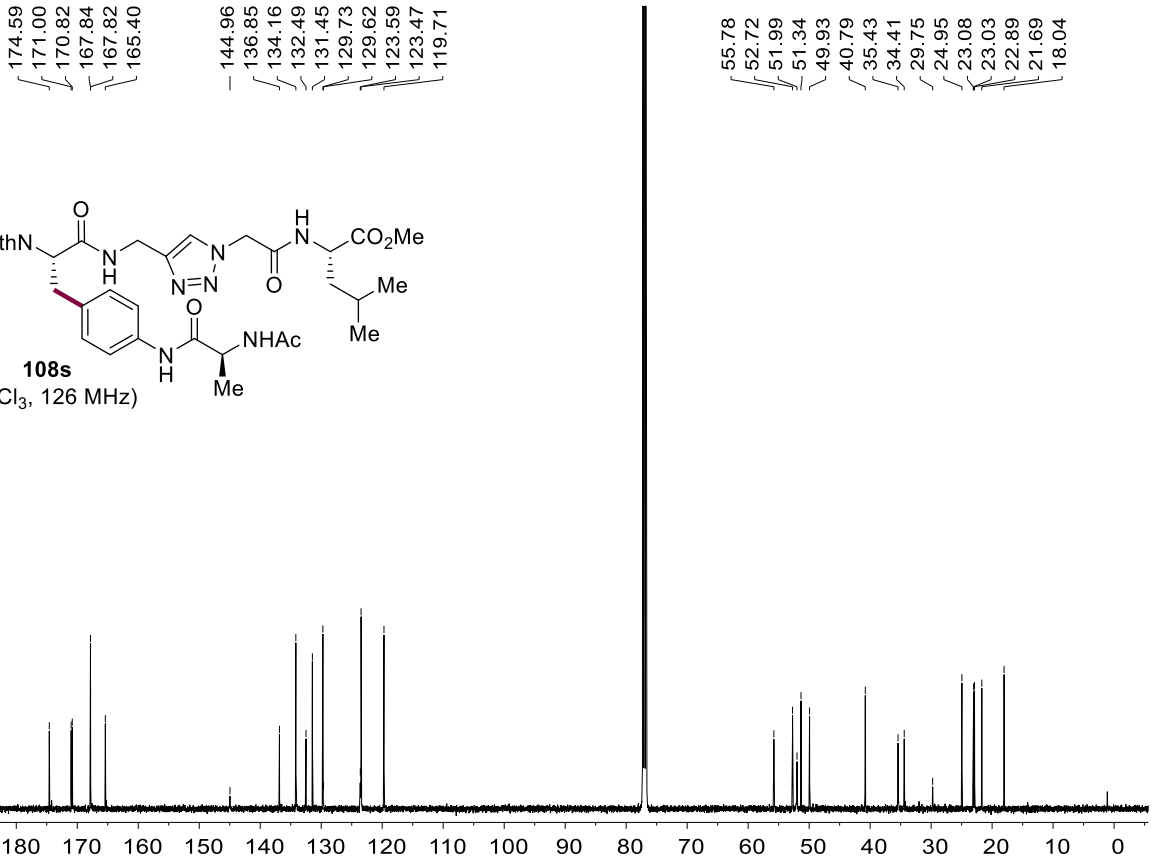


108r
($CDCl_3$, 101 MHz)

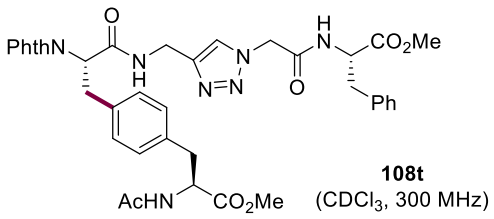


108s
($CDCl_3$, 300 MHz)

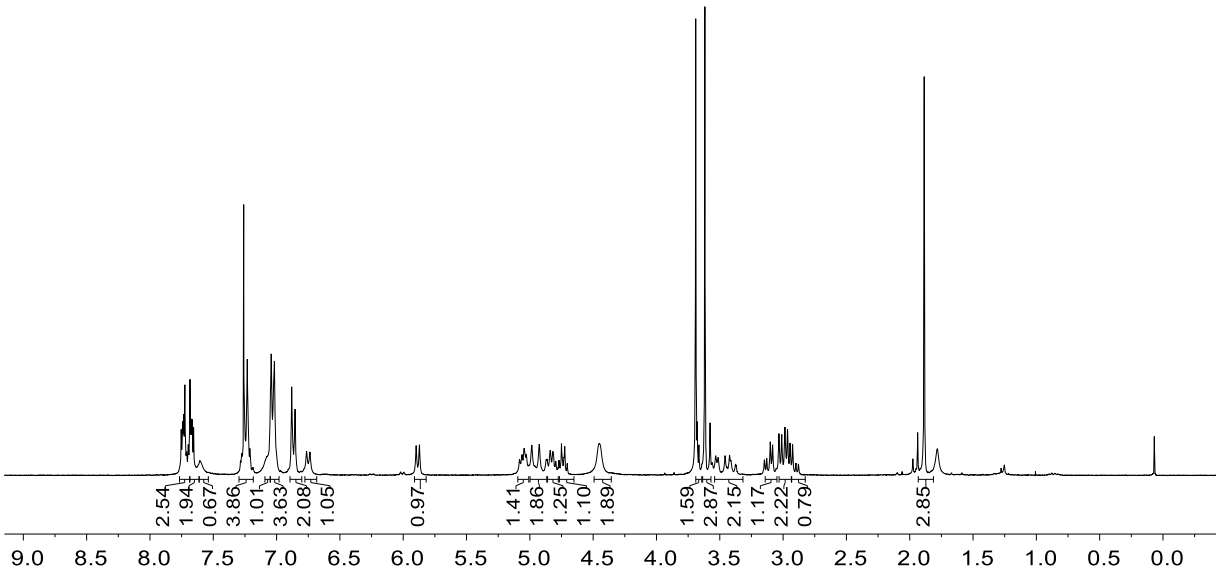


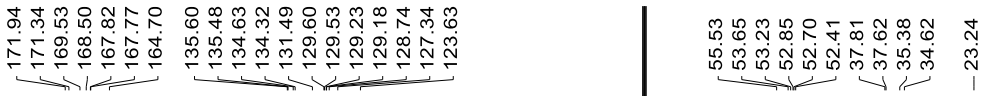


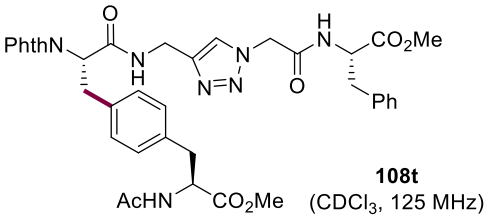
108s
($CDCl_3$, 126 MHz)



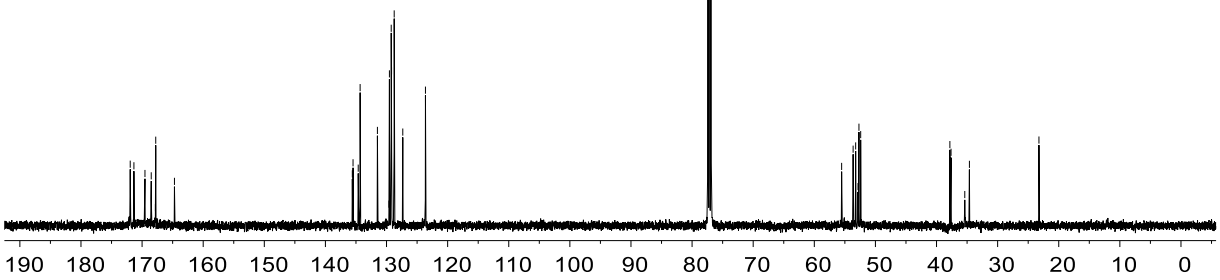
108t
($CDCl_3$, 300 MHz)

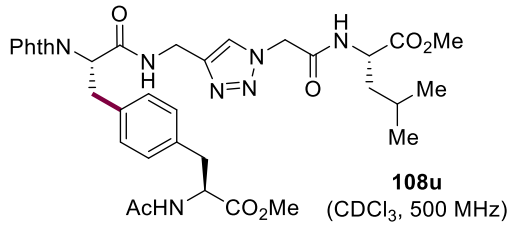




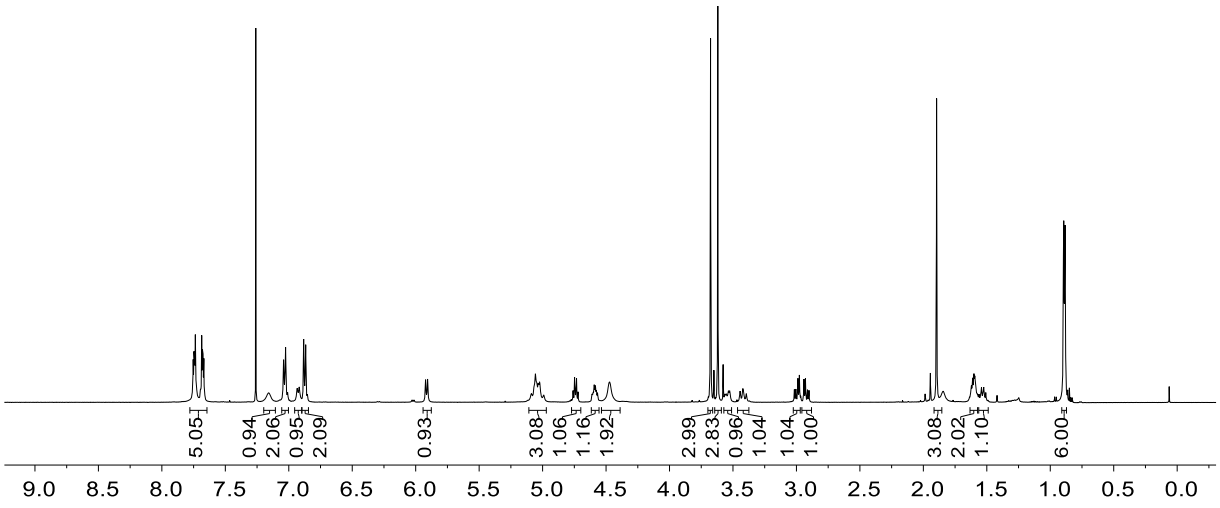


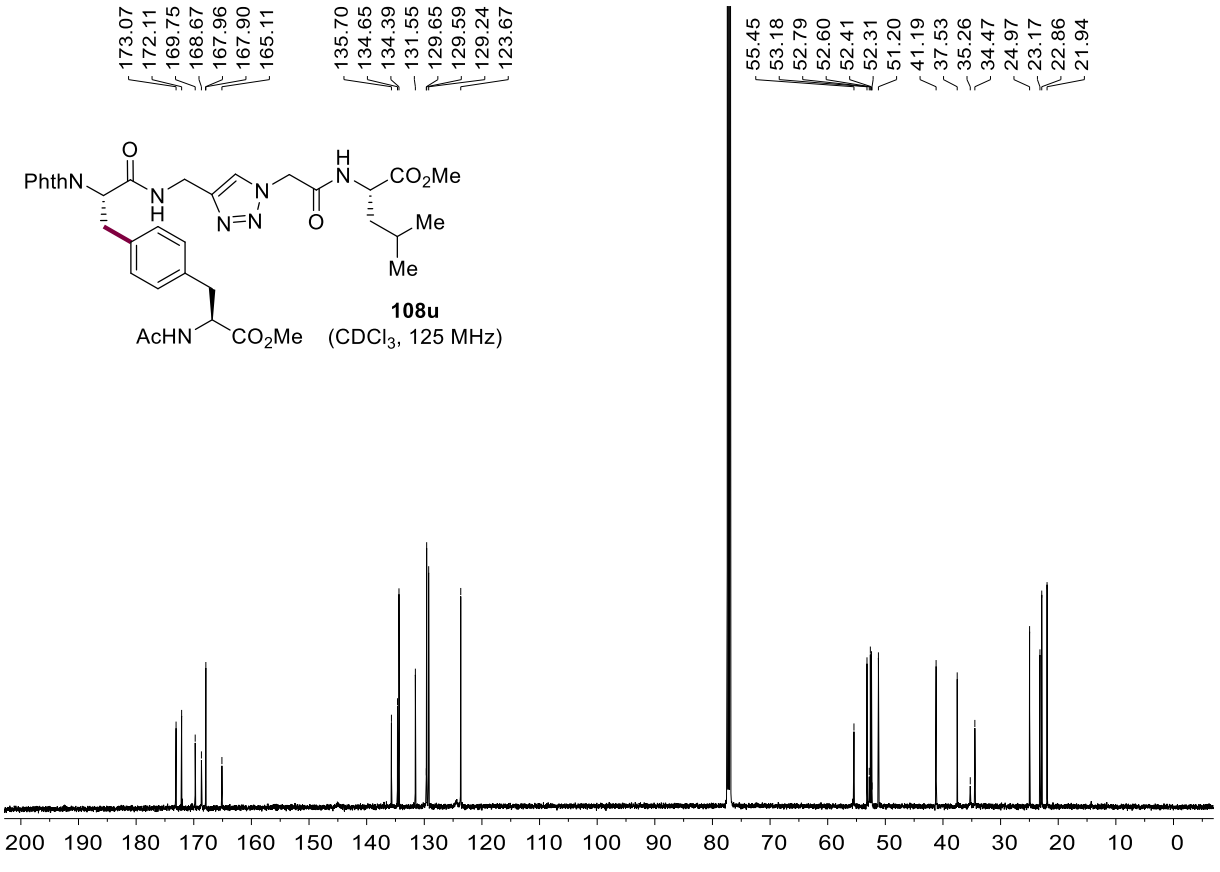
108t
($CDCl_3$, 125 MHz)



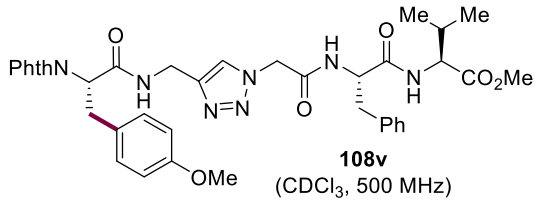


108u ($CDCl_3$, 500 MHz)

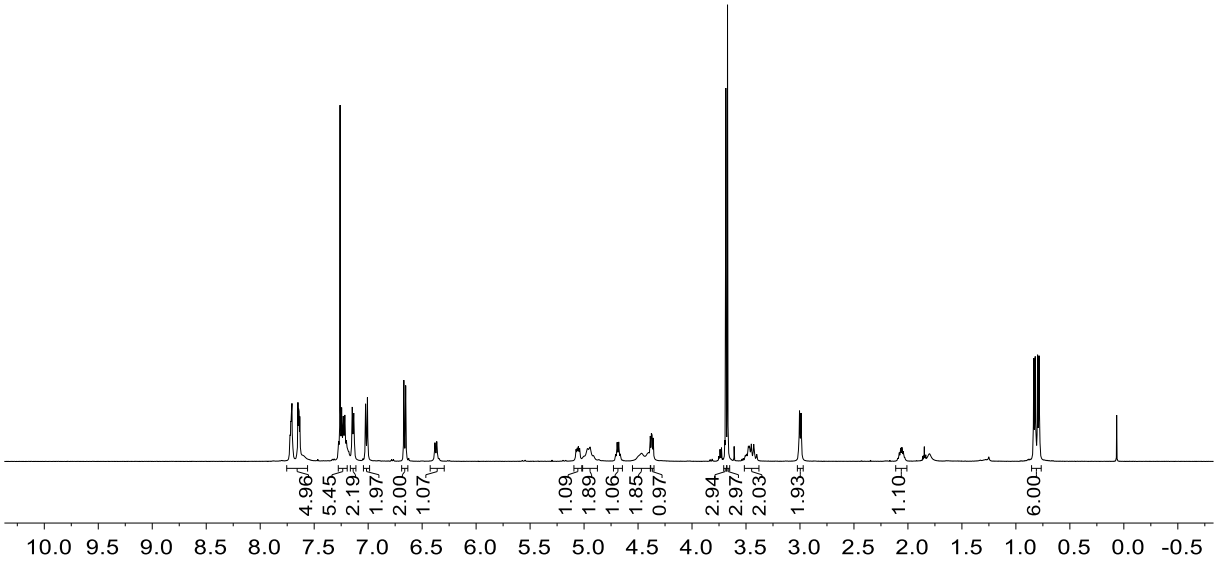


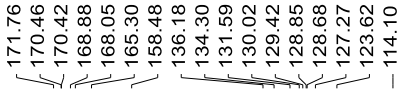


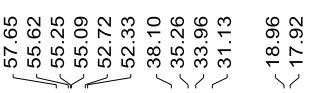
108u ($CDCl_3$, 125 MHz)

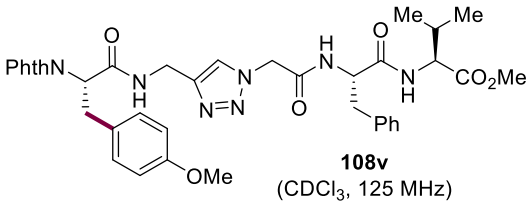


108v
($CDCl_3$, 500 MHz)

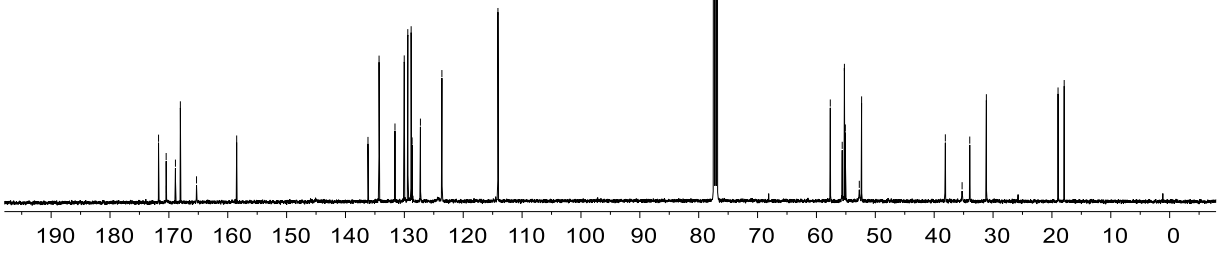


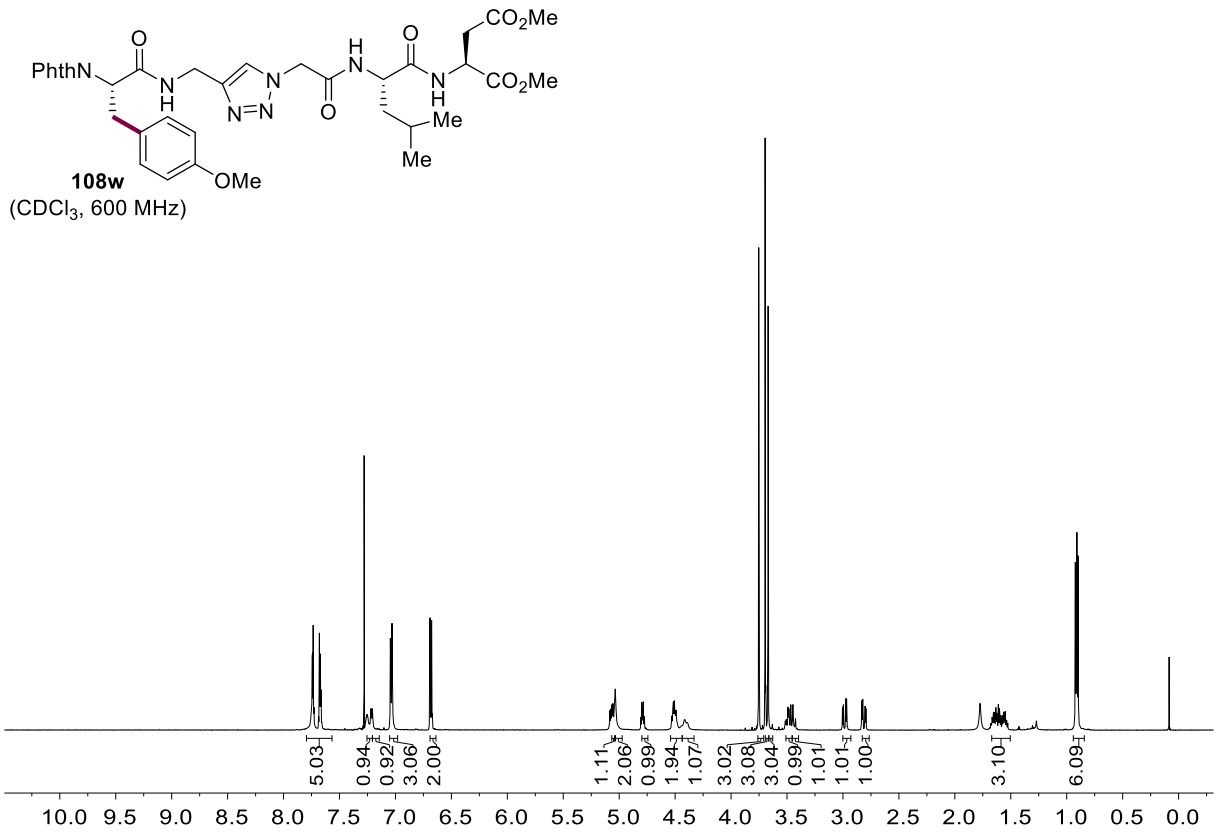


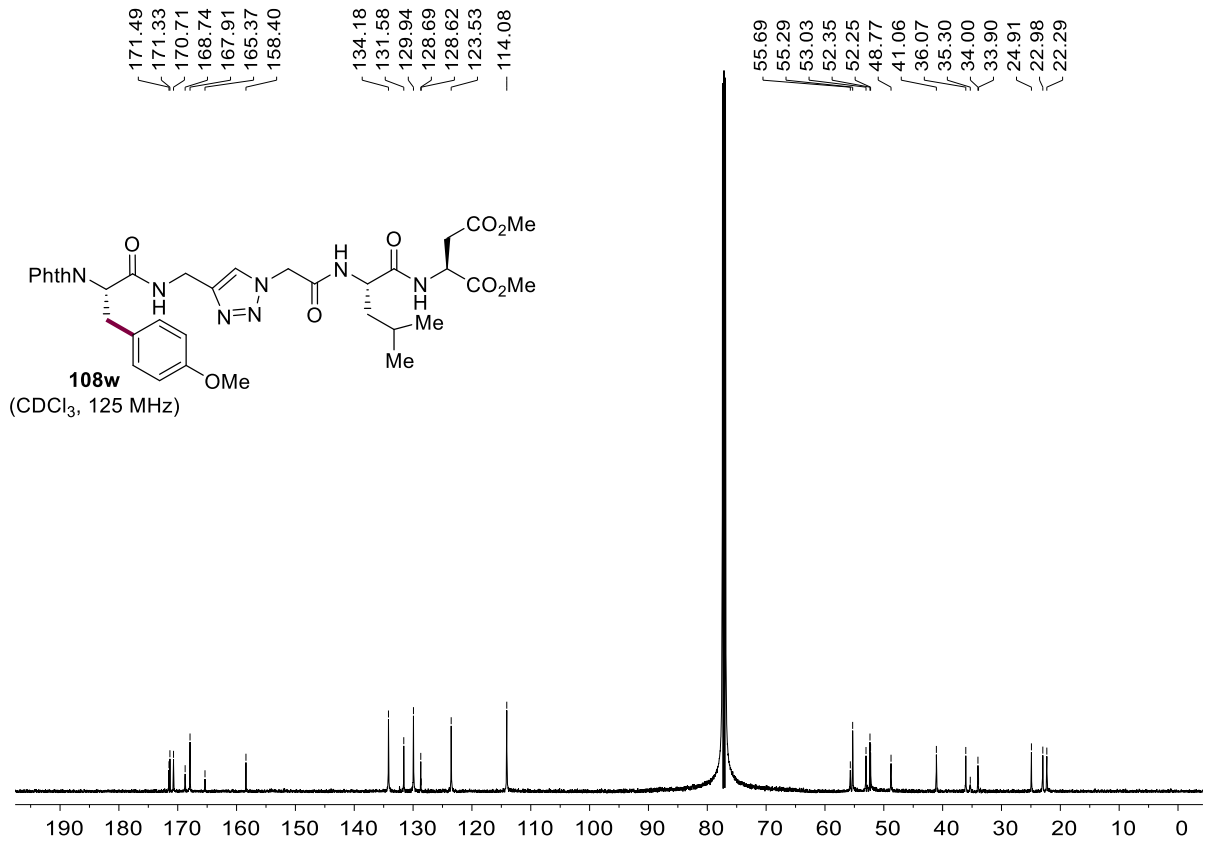


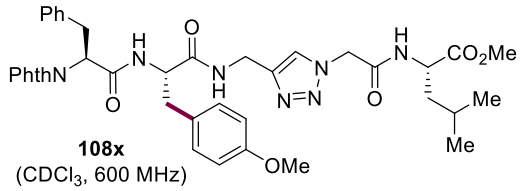


108v
($CDCl_3$, 125 MHz)

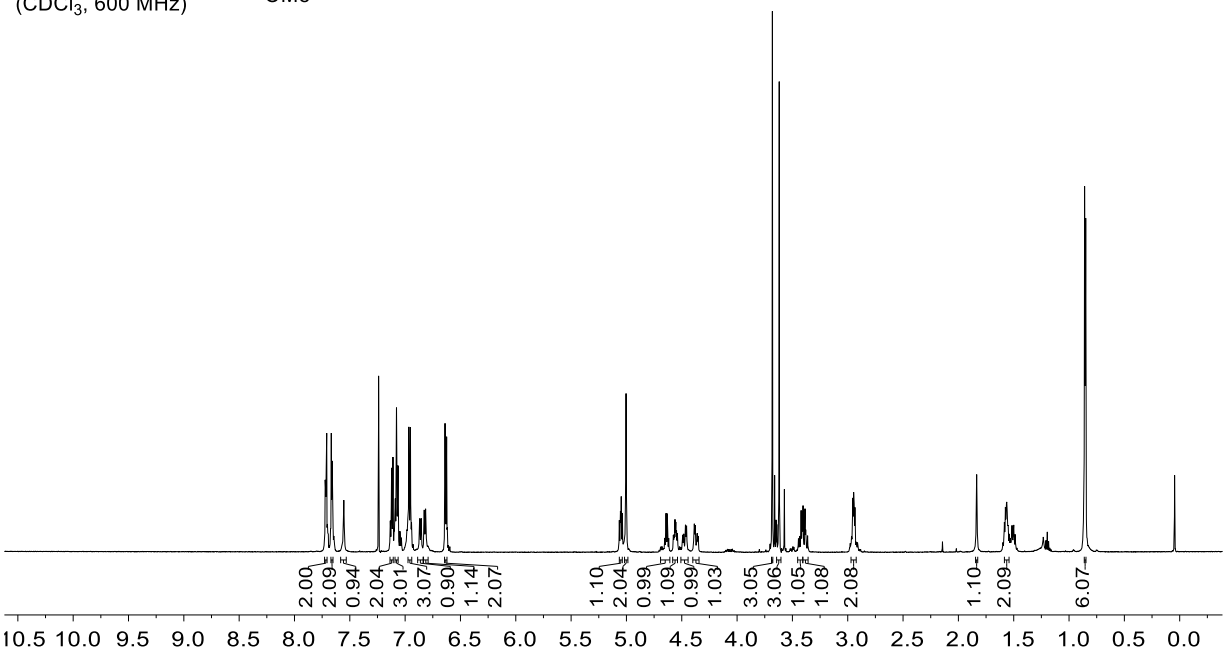


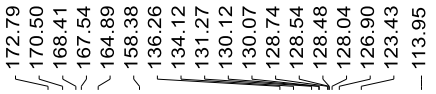

PhthN
O
N
H
N
N=N
O
H
N
O
N
H
CO2Me
CO2Me
Me
Me
OMe
108w
(CDCl3, 600 MHz)
5.03
0.94
0.92
3.06
2.00
1.11
2.06
0.99
1.94
1.07
3.02
3.08
3.04
0.99
1.01
1.01
1.00
3.10
6.09
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

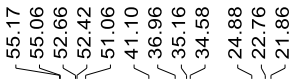

171.49
171.33
170.71
168.74
167.91
165.37
158.40
134.18
131.58
129.94
128.69
128.62
123.53
114.08
55.69
55.29
53.03
52.35
52.25
48.77
41.06
36.07
35.30
34.00
33.90
24.91
22.98
22.29
PhthN
O
N
H
N
N=N
O
H
N
O
N
H
CO2Me
CO2Me
Me
Me
OMe
108w
(CDCl3, 125 MHz)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

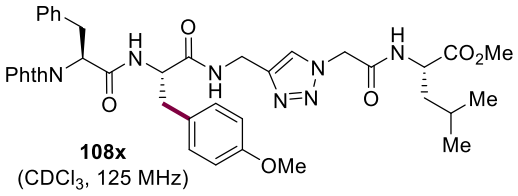


108x
($CDCl_3$, 600 MHz)

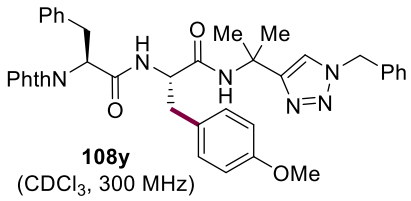




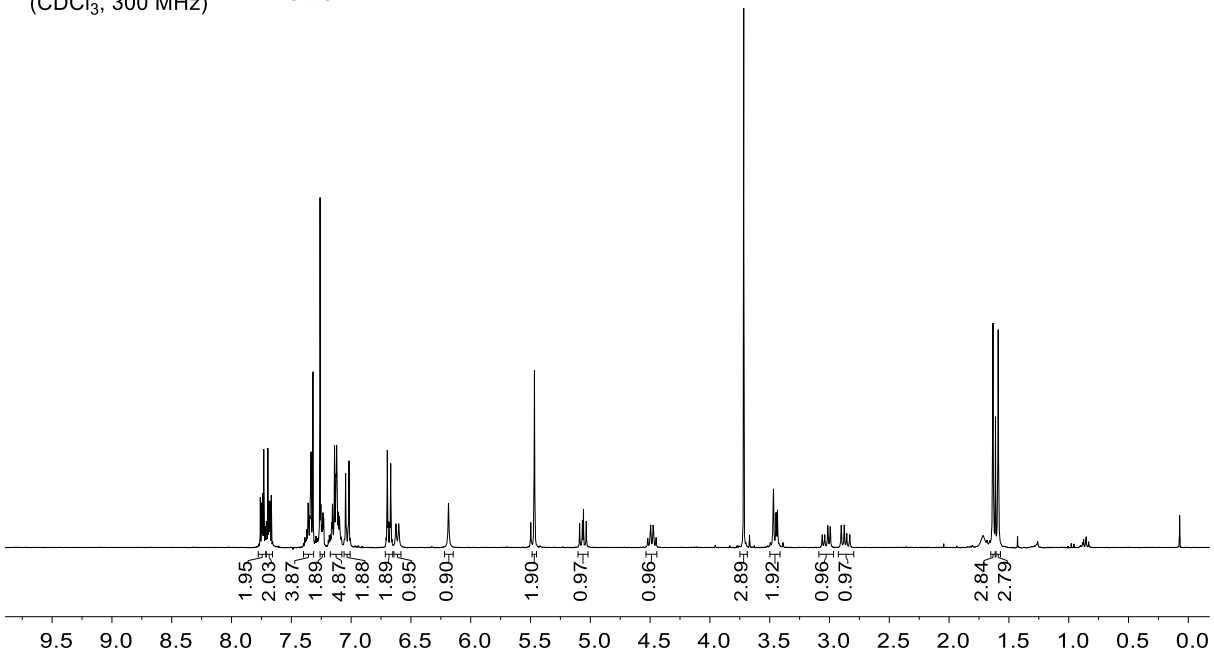


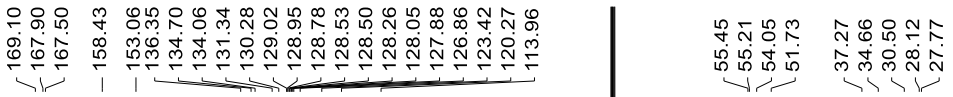


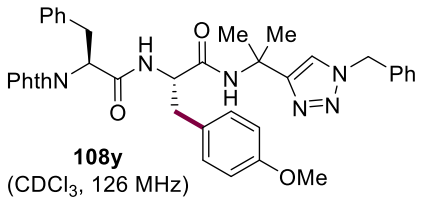
108x
($CDCl_3$, 125 MHz)



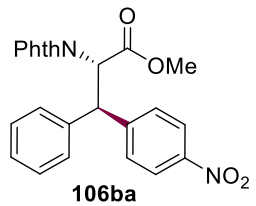
108y
($CDCl_3$, 300 MHz)



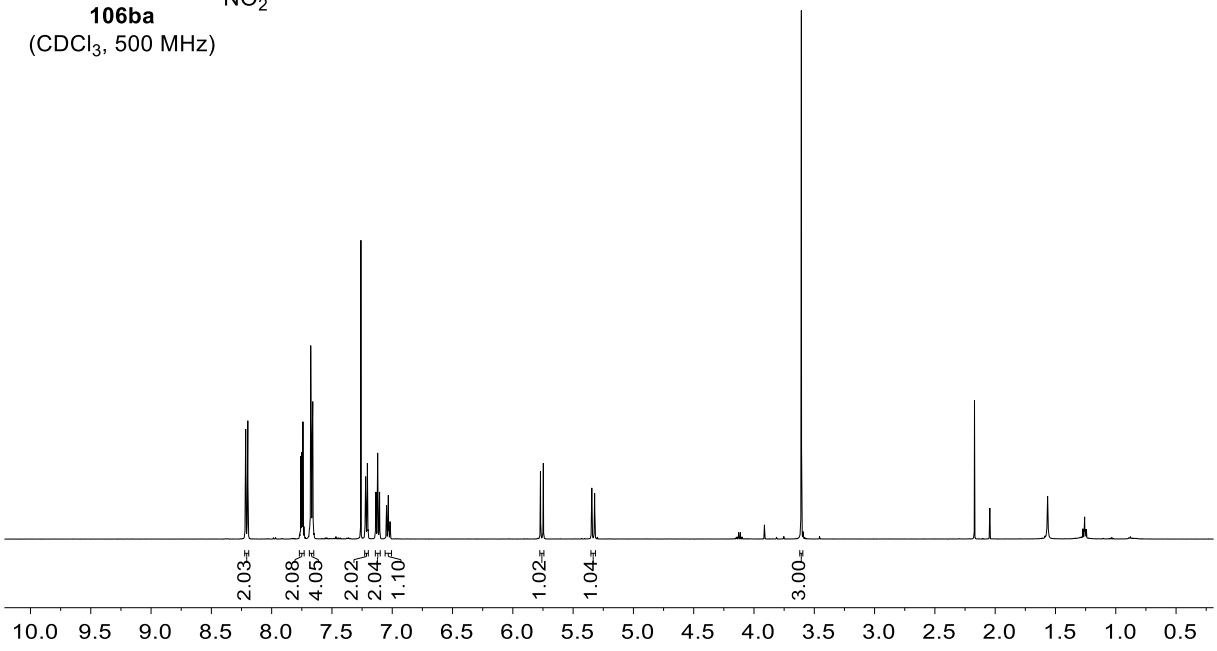


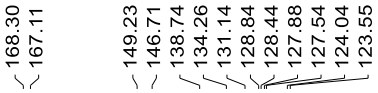


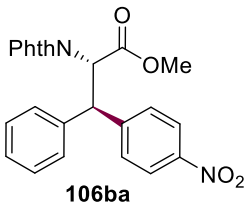
108y
($CDCl_3$, 126 MHz)



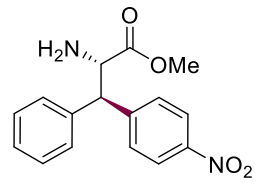
106ba
($CDCl_3$, 500 MHz)



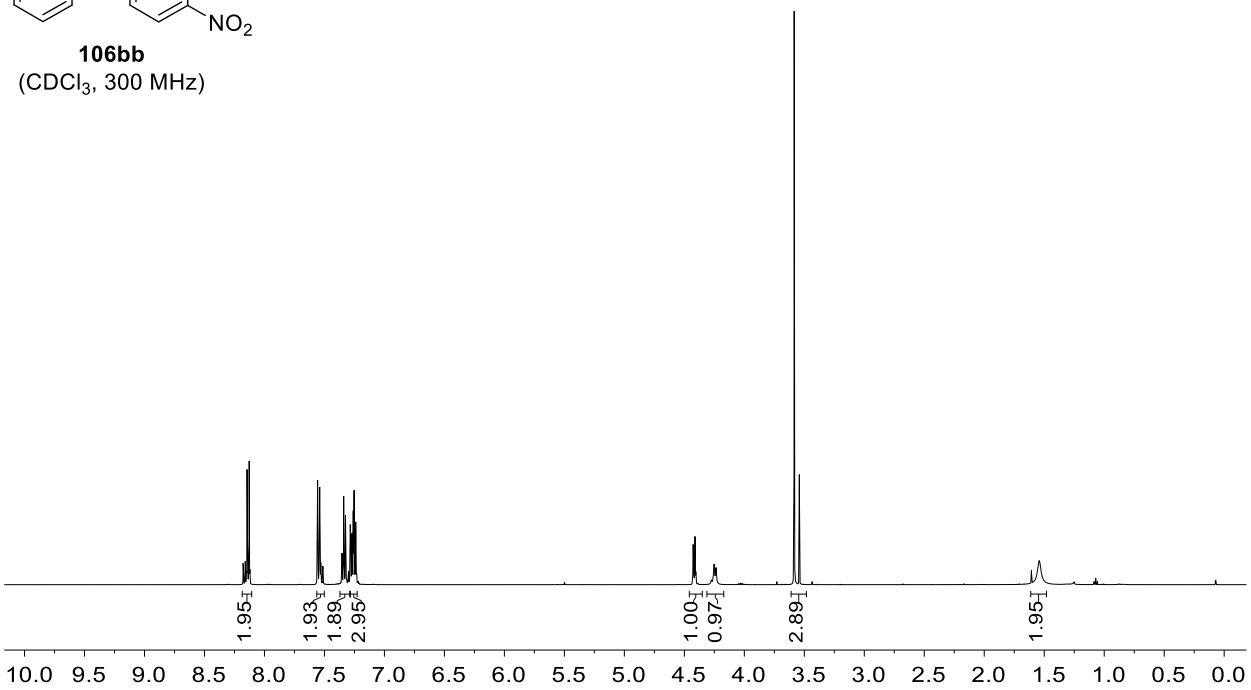


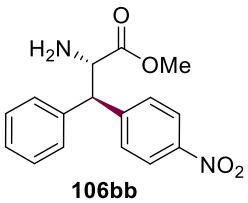


106ba
($CDCl_3$, 126 MHz)

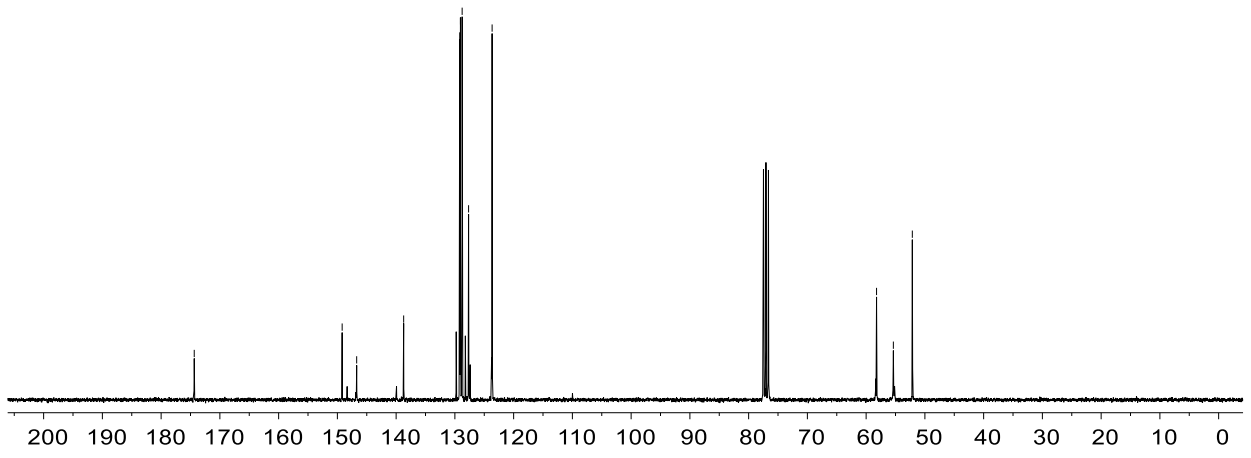


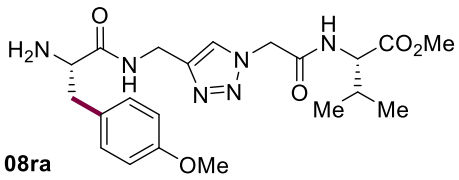
106bb
($CDCl_3$, 300 MHz)



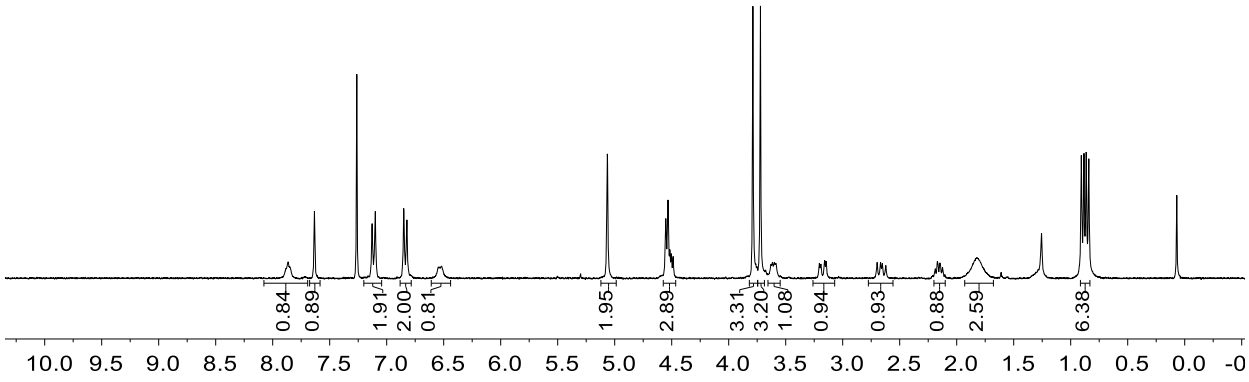


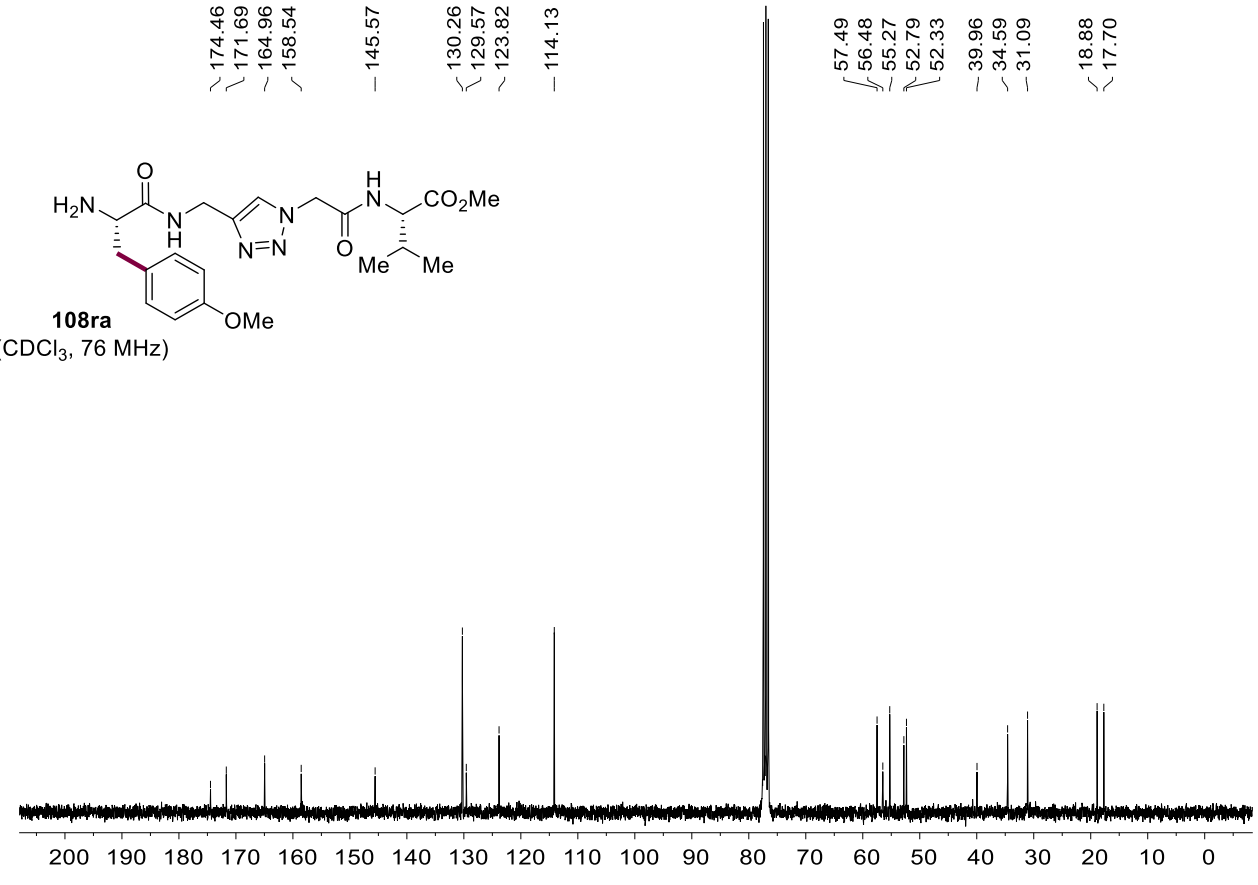
106bb
($CDCl_3$, 76 MHz)



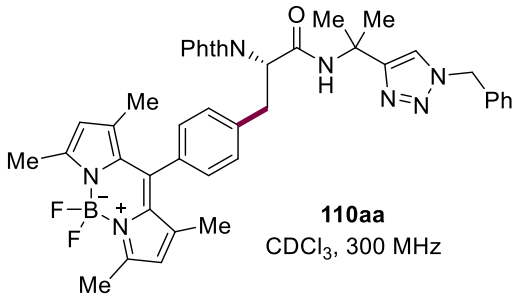


108ra
($CDCl_3$, 300 MHz)

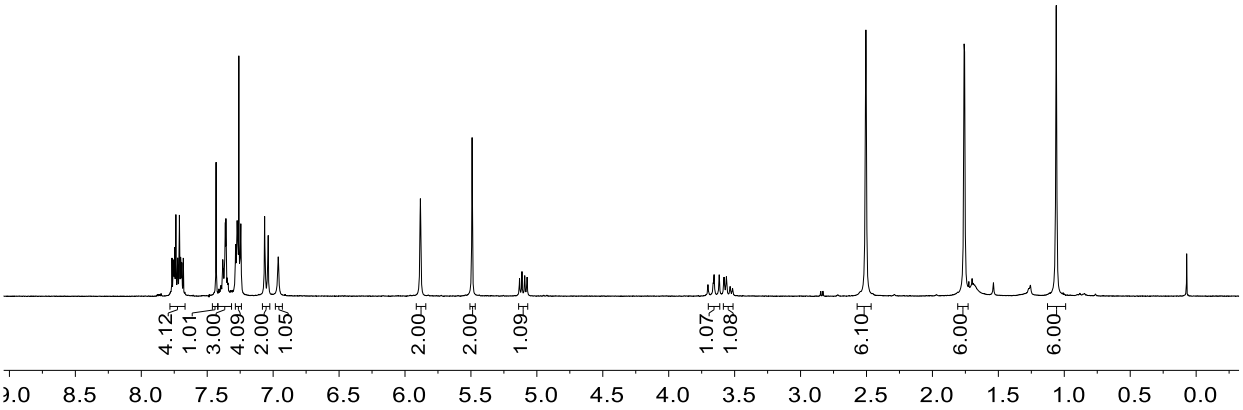


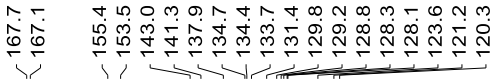


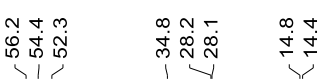
108ra
($CDCl_3$, 76 MHz)

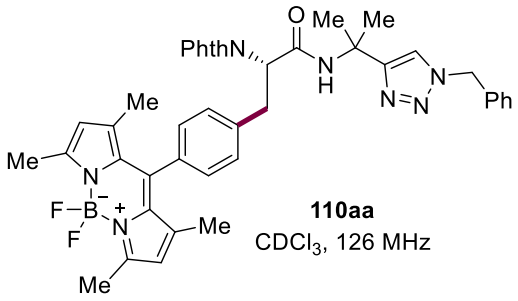


110aa
$CDCl_3$, 300 MHz

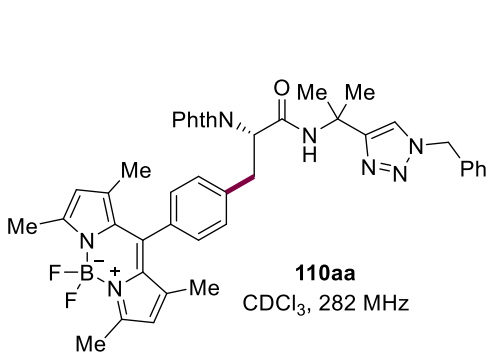






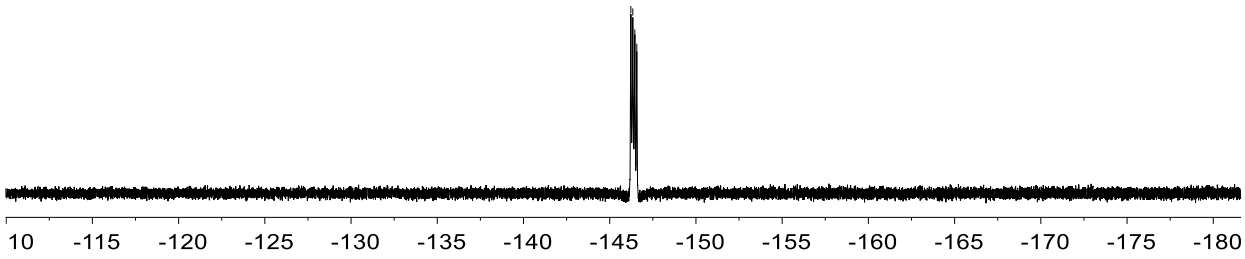


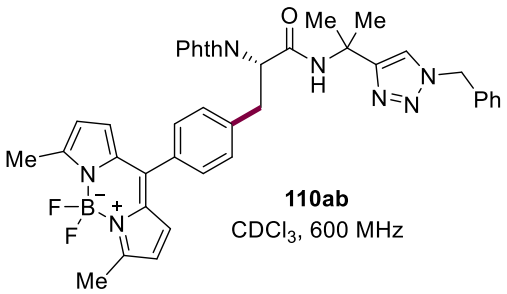
110aa
$CDCl_3$, 126 MHz



110aa

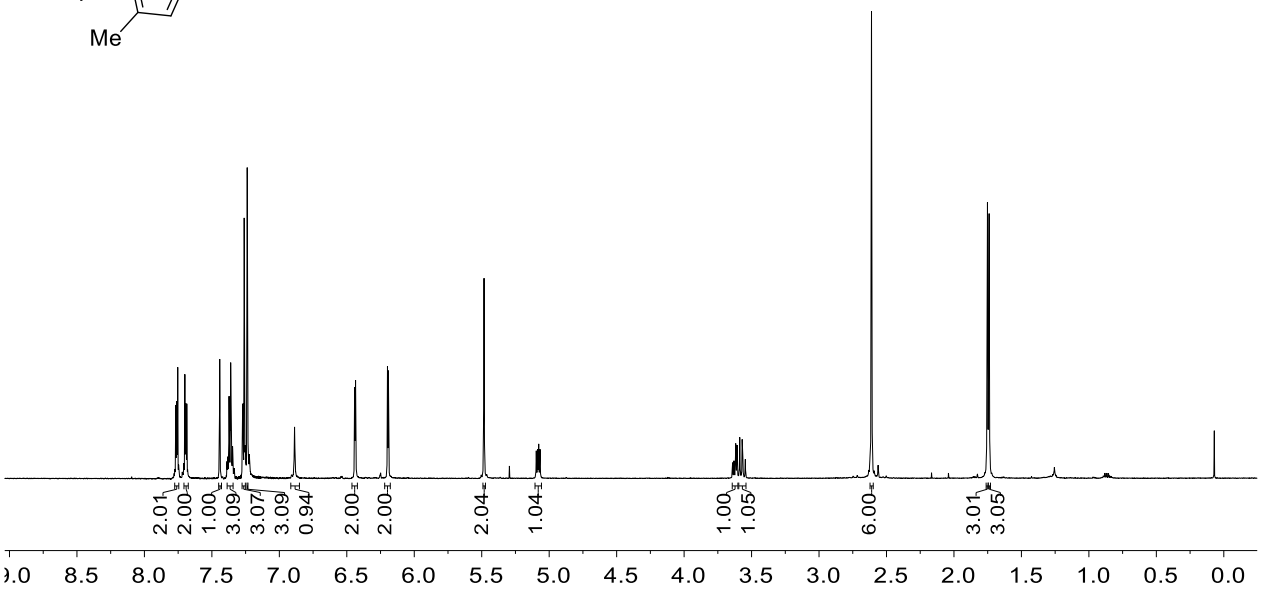
$CDCl_3$, 282 MHz

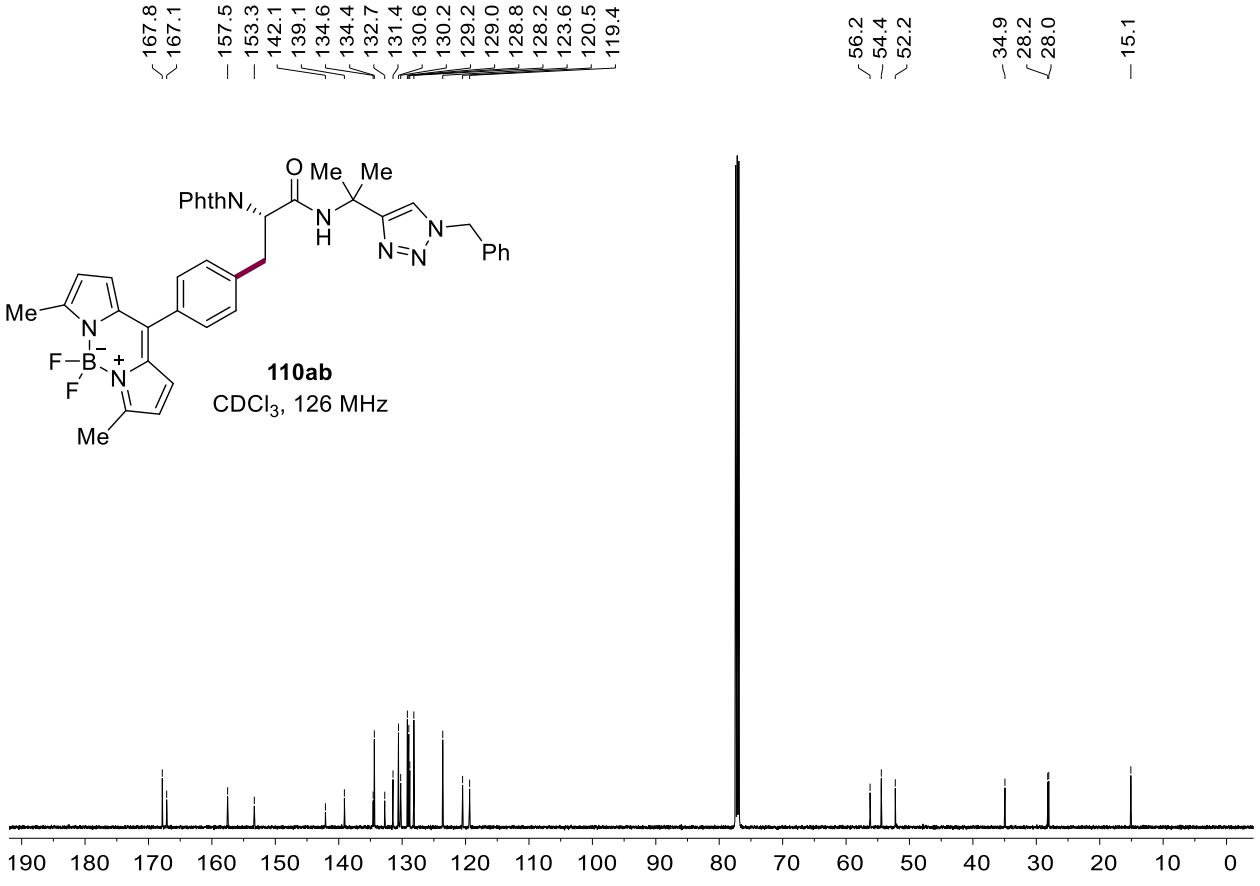


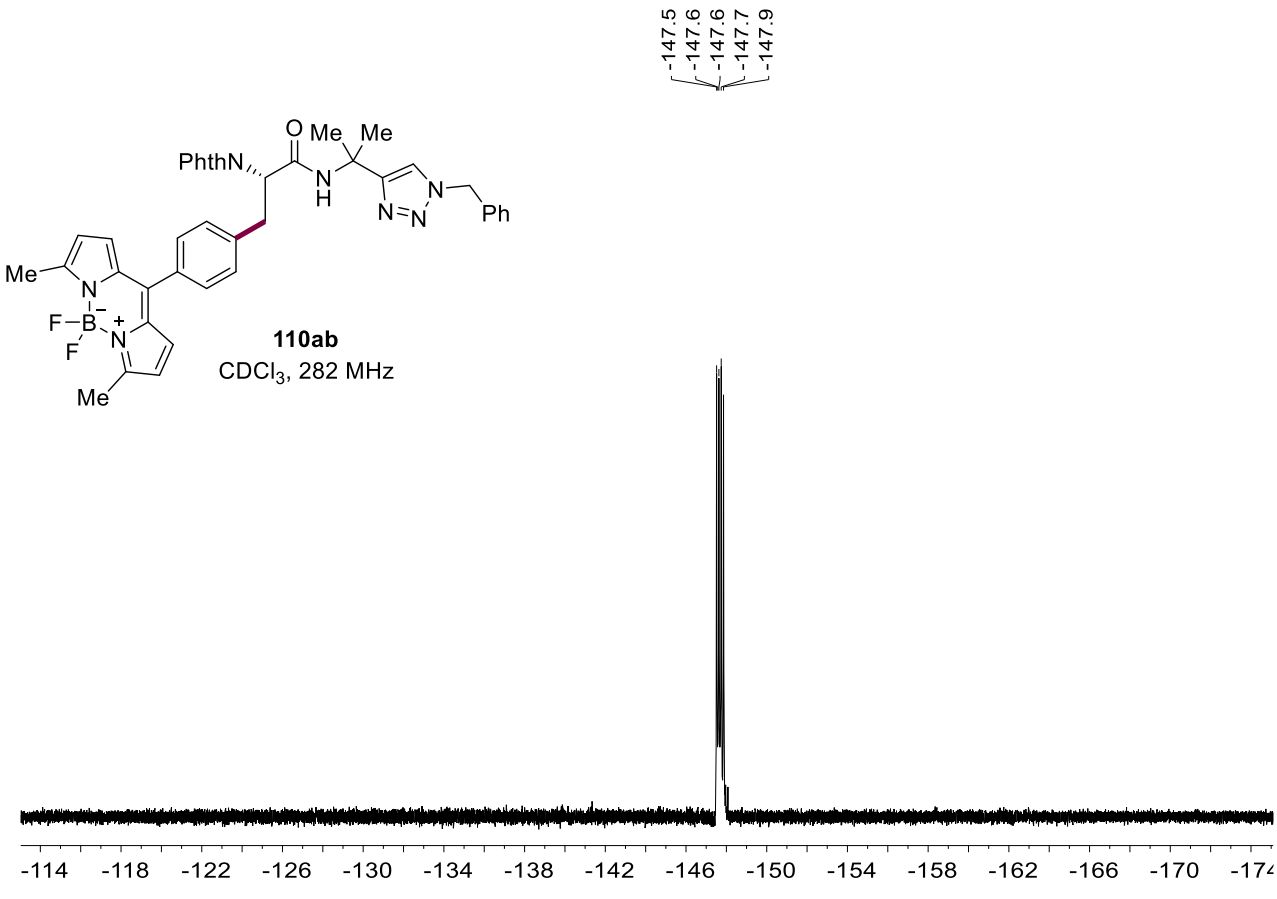


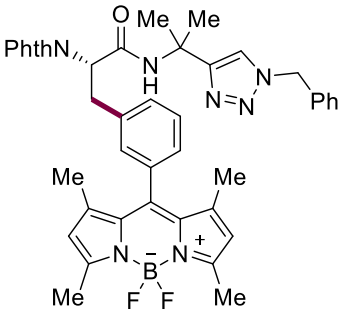
110ab

$CDCl_3$, 600 MHz



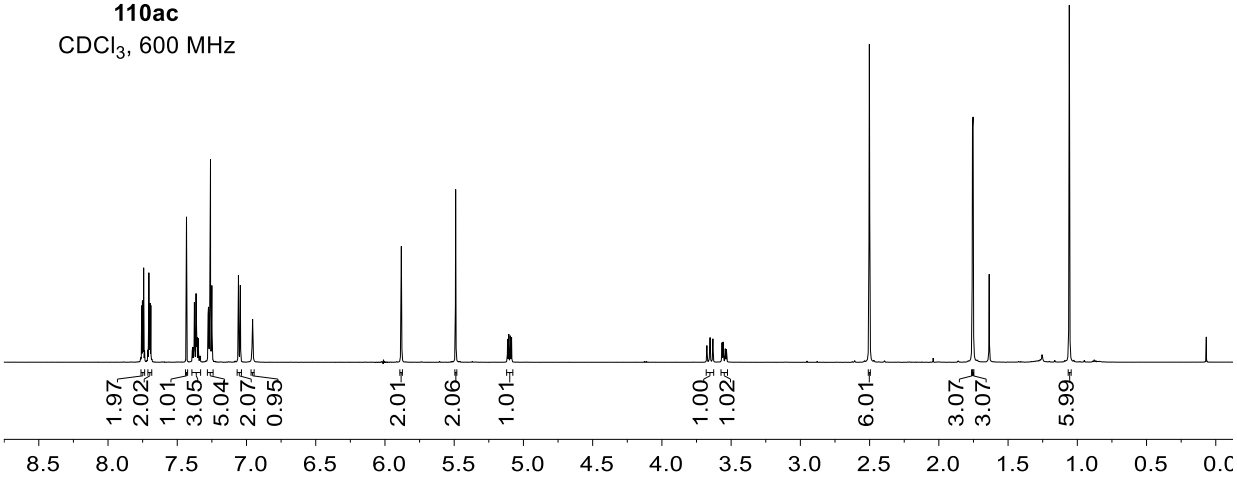

167.8
167.1
157.5
153.3
142.1
139.1
134.6
134.4
132.7
131.4
130.6
130.2
129.2
129.0
128.8
128.2
123.6
120.5
119.4
56.2
54.4
52.2
34.9
28.2
28.0
15.1
PhthN
O
Me
Me
N
H
N
N=N
Ph
Me
N
F−B
F
N
Me
110ab
CDCl3, 126 MHz
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

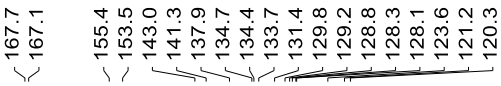

-147.5
-147.6
-147.6
-147.7
-147.9
PhthN
O
Me
Me
N
H
N
N=N
Ph
Me
N
F−B
F
N
Me
110ab
CDCl3, 282 MHz
-114 -118 -122 -126 -130 -134 -138 -142 -146 -150 -154 -158 -162 -166 -170 -174

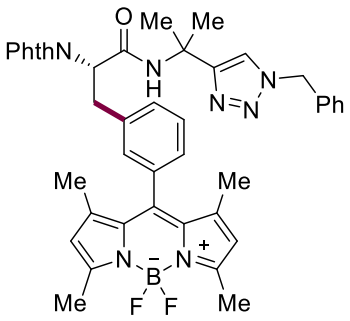


110ac

$CDCl_3$, 600 MHz

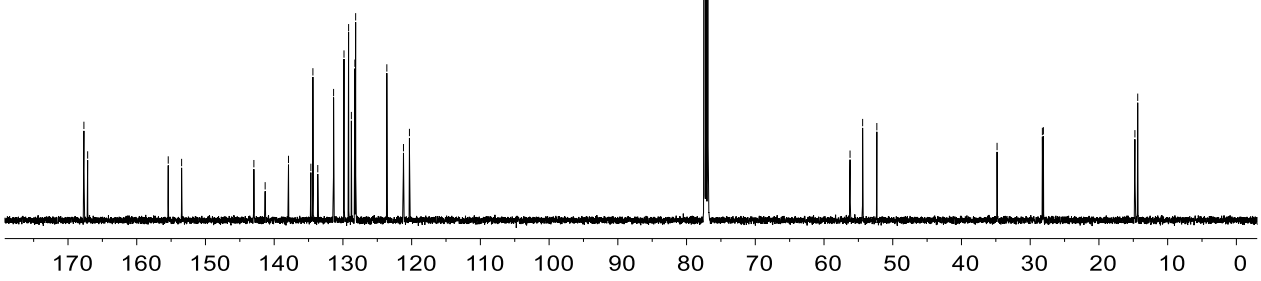


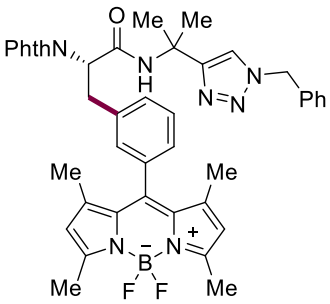




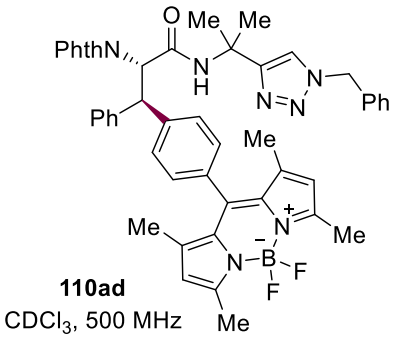
110ac

$CDCl_3$, 126 MHz

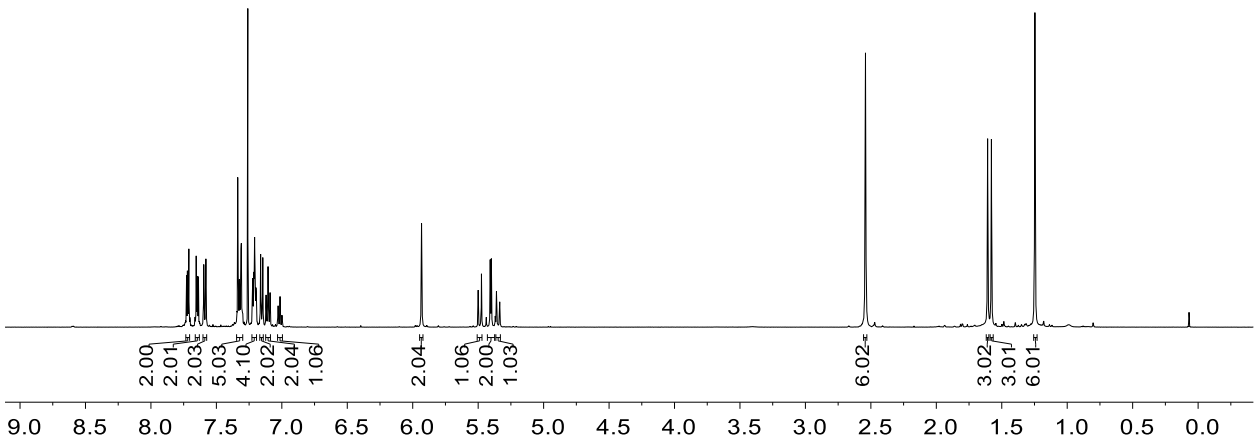


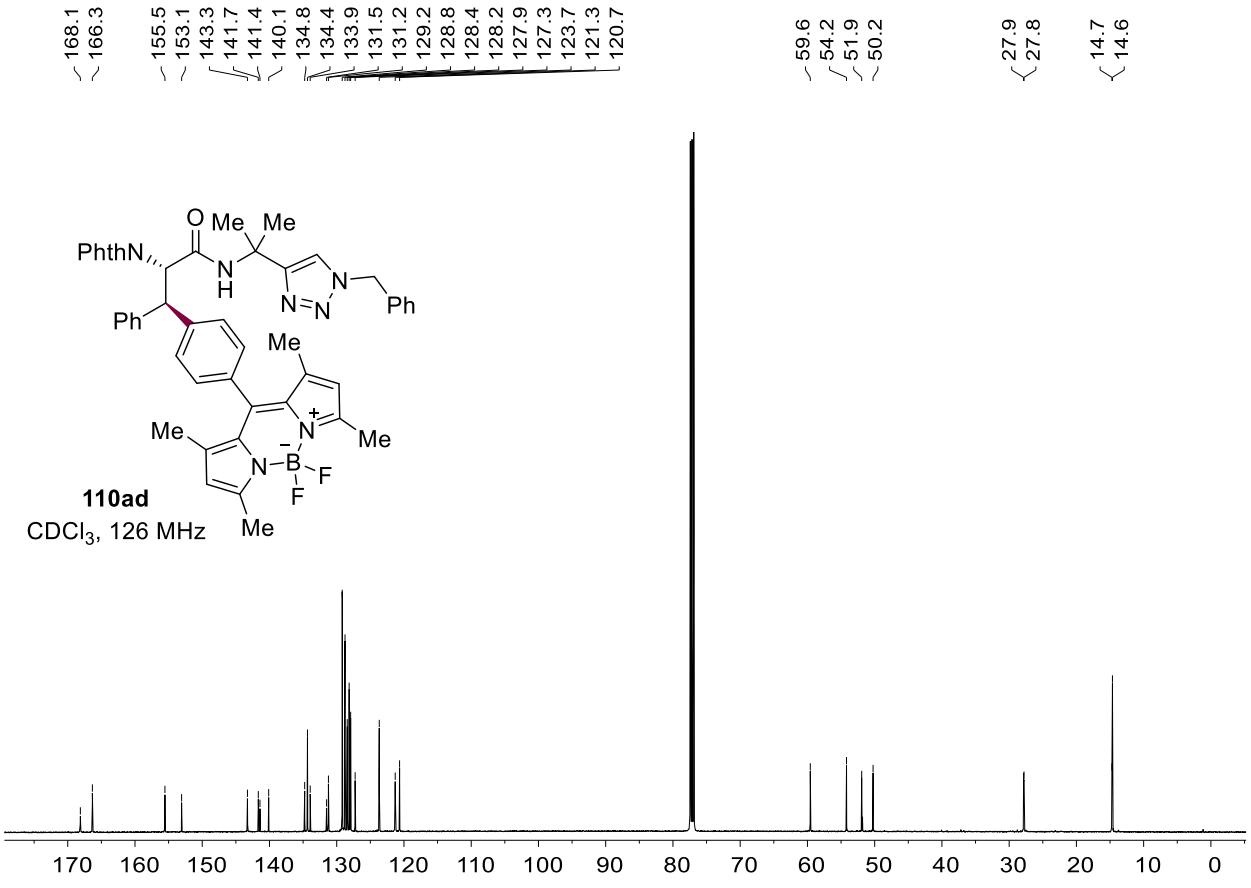


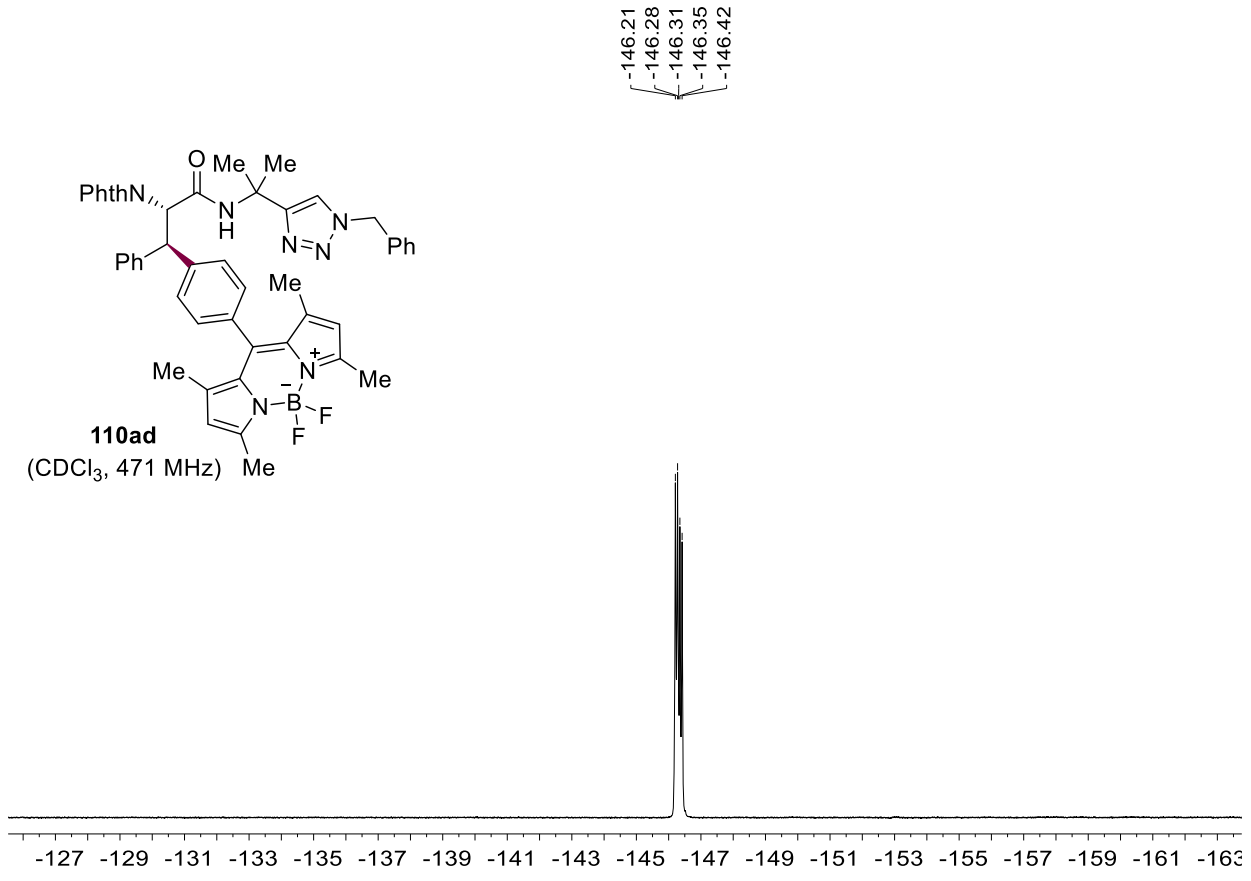
110ac
$CDCl_3$, 282 MHz

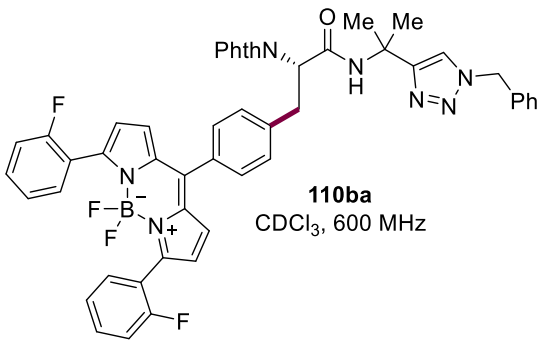


110ad
$CDCl_3$, 500 MHz

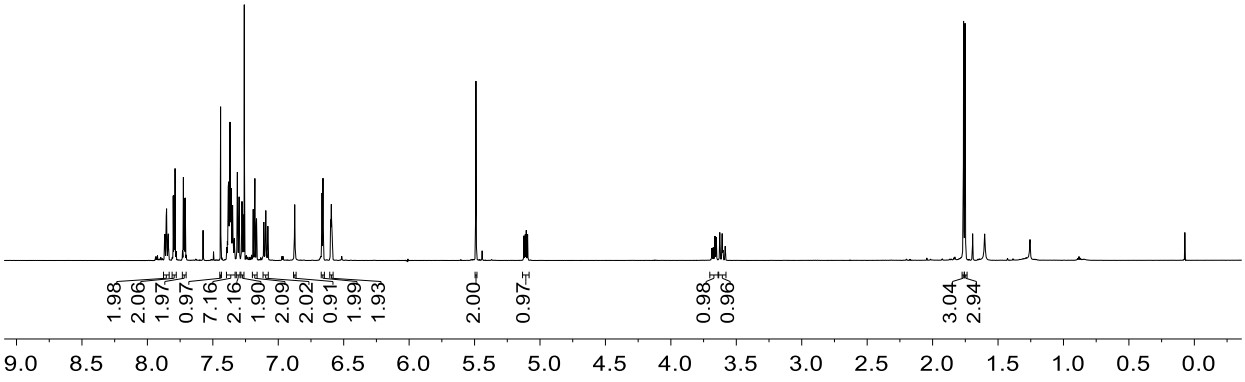


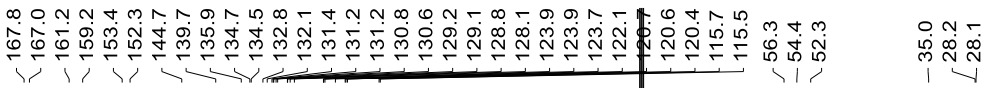

168.1
166.3
155.5
153.1
143.3
141.7
141.4
140.1
134.8
134.4
133.9
131.5
131.2
129.2
128.8
128.4
128.2
127.9
127.3
123.7
121.3
120.7
59.6
54.2
51.9
50.2
27.9
27.8
14.7
14.6
110ad
CDCl3, 126 MHz
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

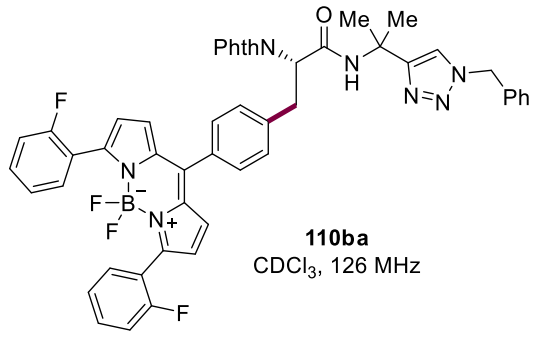

-146.21
-146.28
-146.31
-146.35
-146.42
110ad
(CDCl3, 471 MHz)
-127 -129 -131 -133 -135 -137 -139 -141 -143 -145 -147 -149 -151 -153 -155 -157 -159 -161 -163



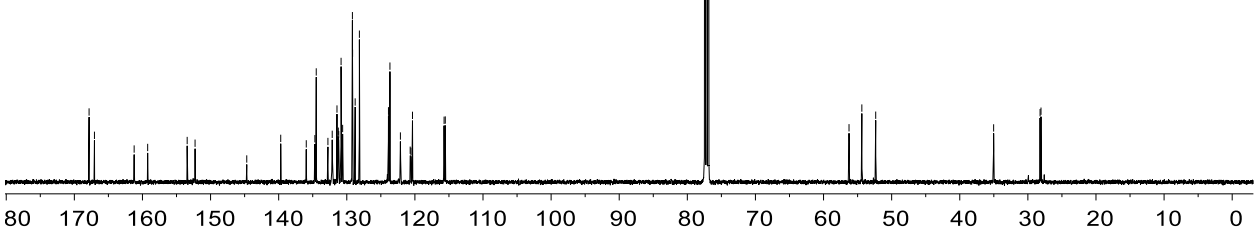
110ba
$CDCl_3$, 600 MHz

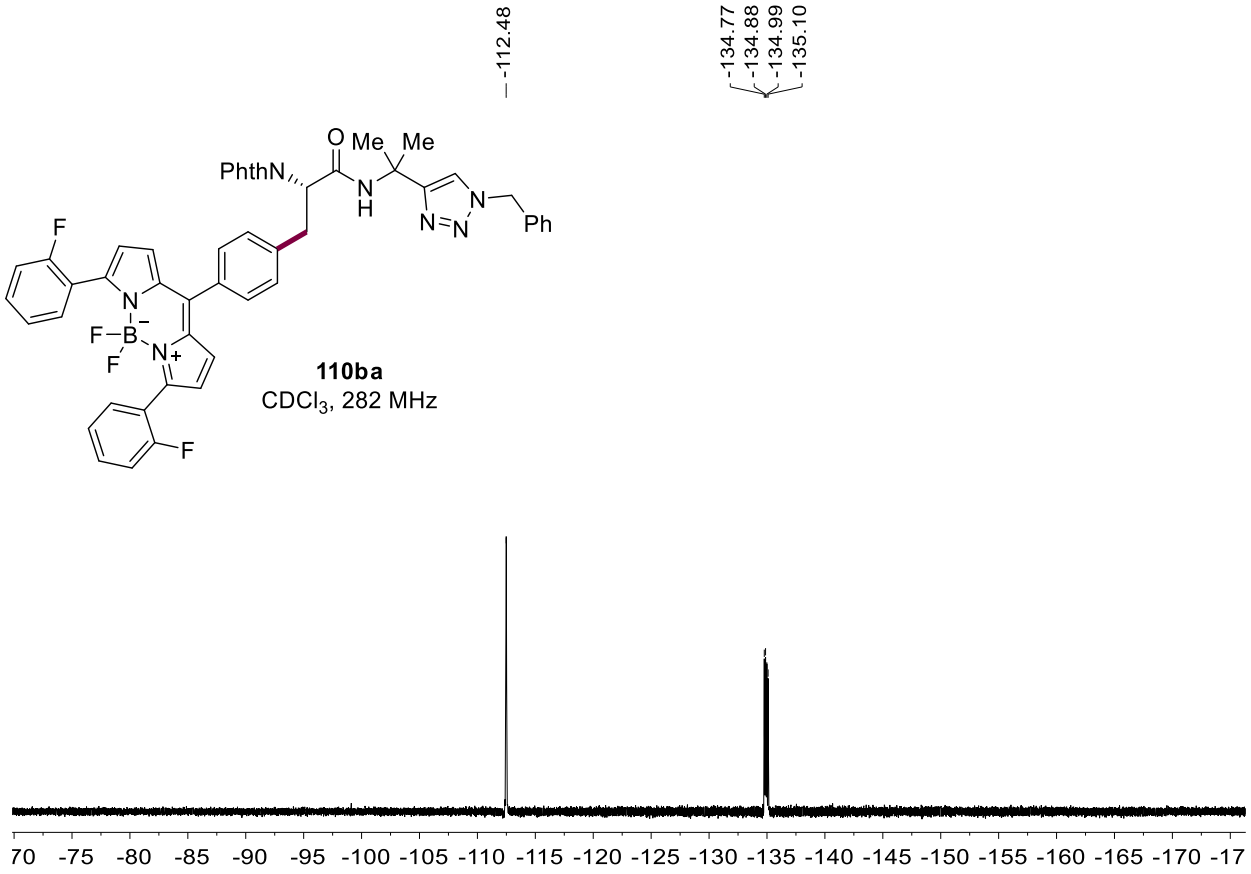


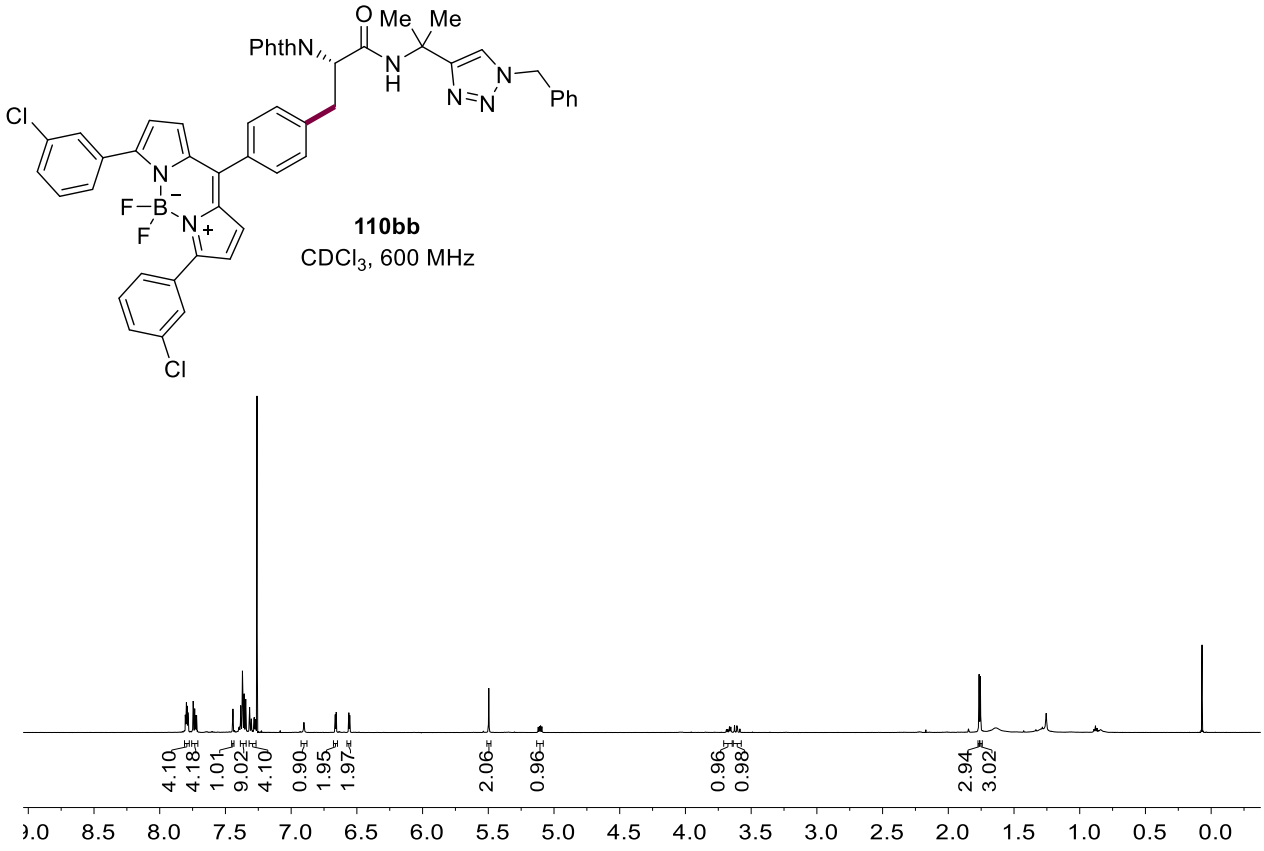


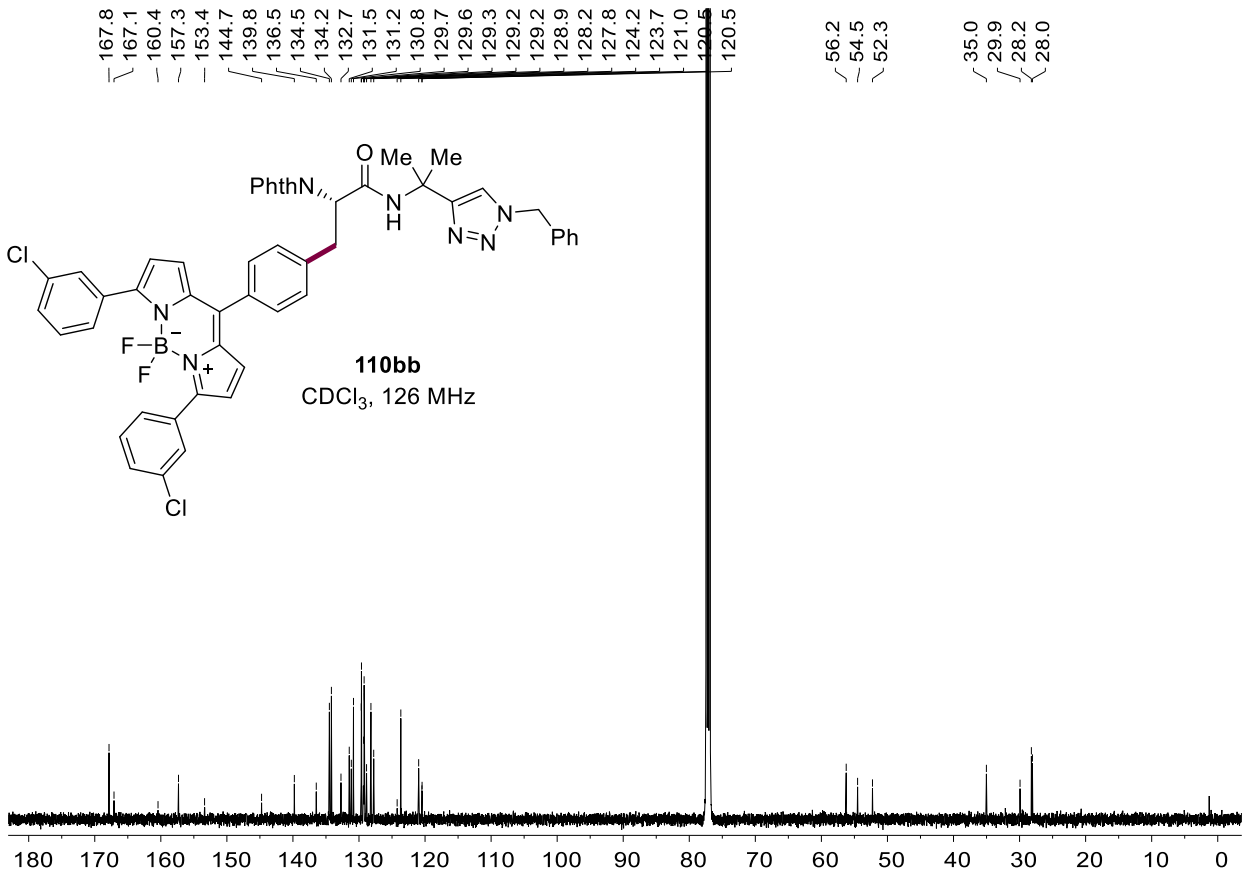


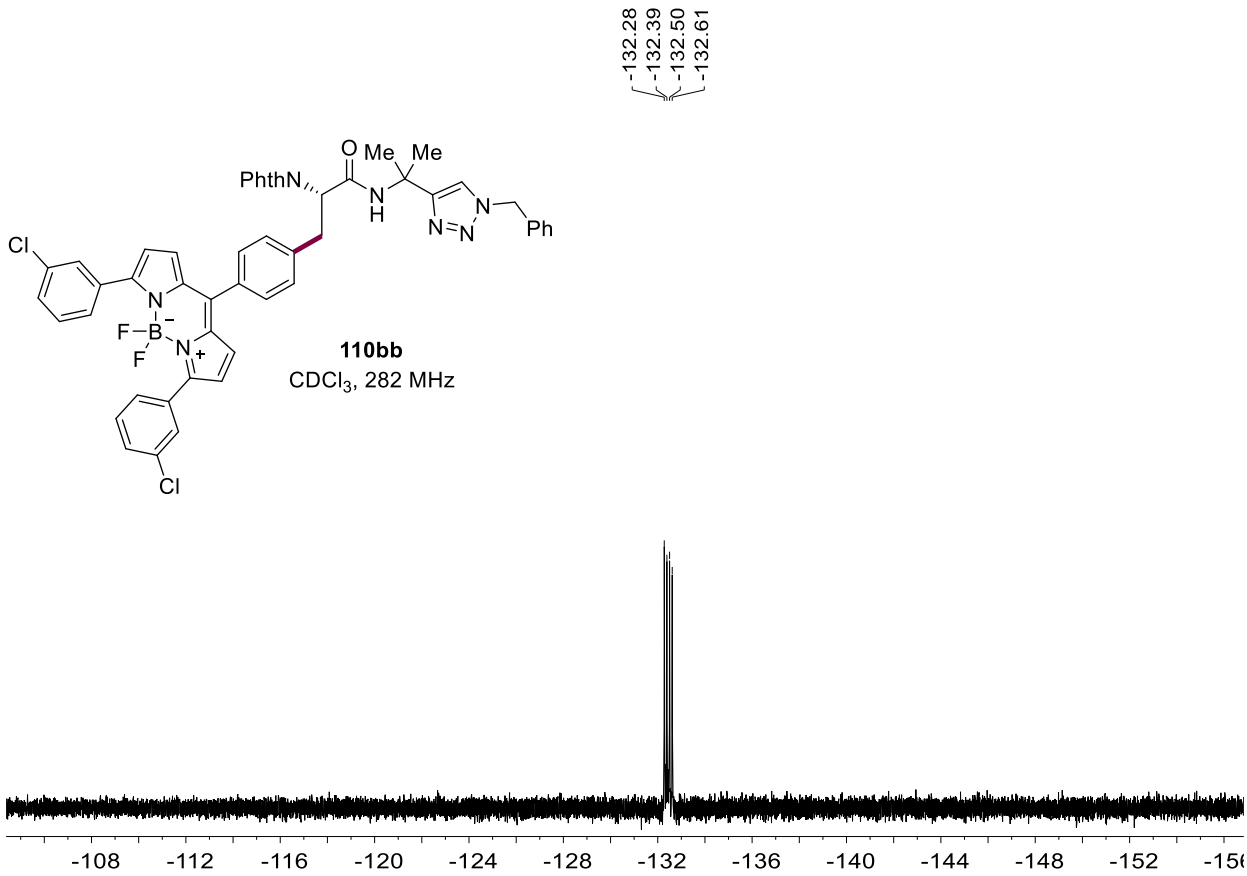
110ba
$CDCl_3$, 126 MHz

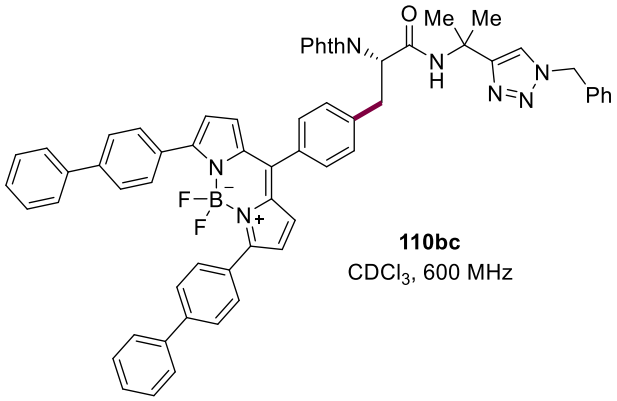



-112.48
-134.77
-134.88
-134.99
-135.10
O Me Me
PhthN
N
H
N
N=N
Ph
F
N
F–B–
F
N+
F
110ba
CDCl3, 282 MHz
70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -17

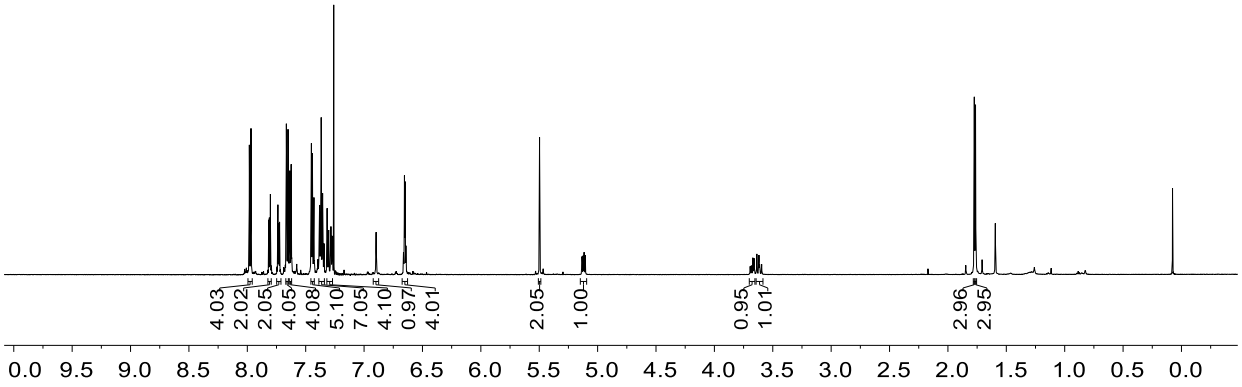

O Me Me
PhthN
N
H
N
N=N
Ph
Cl
N
F–B–
F
N+
Cl
110bb
CDCl3, 600 MHz
4.10
4.18
1.01
9.02
4.10
0.90
1.95
1.97
2.06
0.96
0.96
0.98
2.94
3.02
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

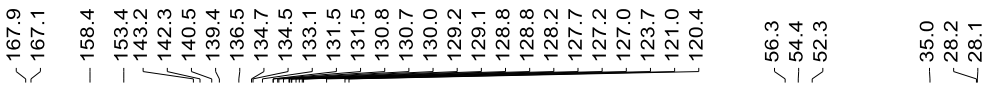

167.8
167.1
160.4
157.3
153.4
144.7
139.8
136.5
134.5
134.2
132.7
131.5
131.2
130.8
129.7
129.6
129.3
129.2
129.2
128.9
128.2
127.8
124.2
123.7
121.0
120.6
120.5
56.2
54.5
52.3
35.0
29.9
28.2
28.0
O
Me
Me
PhthN
N
H
N
N=N
Ph
Cl
N
F–B
F
N+
Cl
110bb
CDCl3, 126 MHz
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

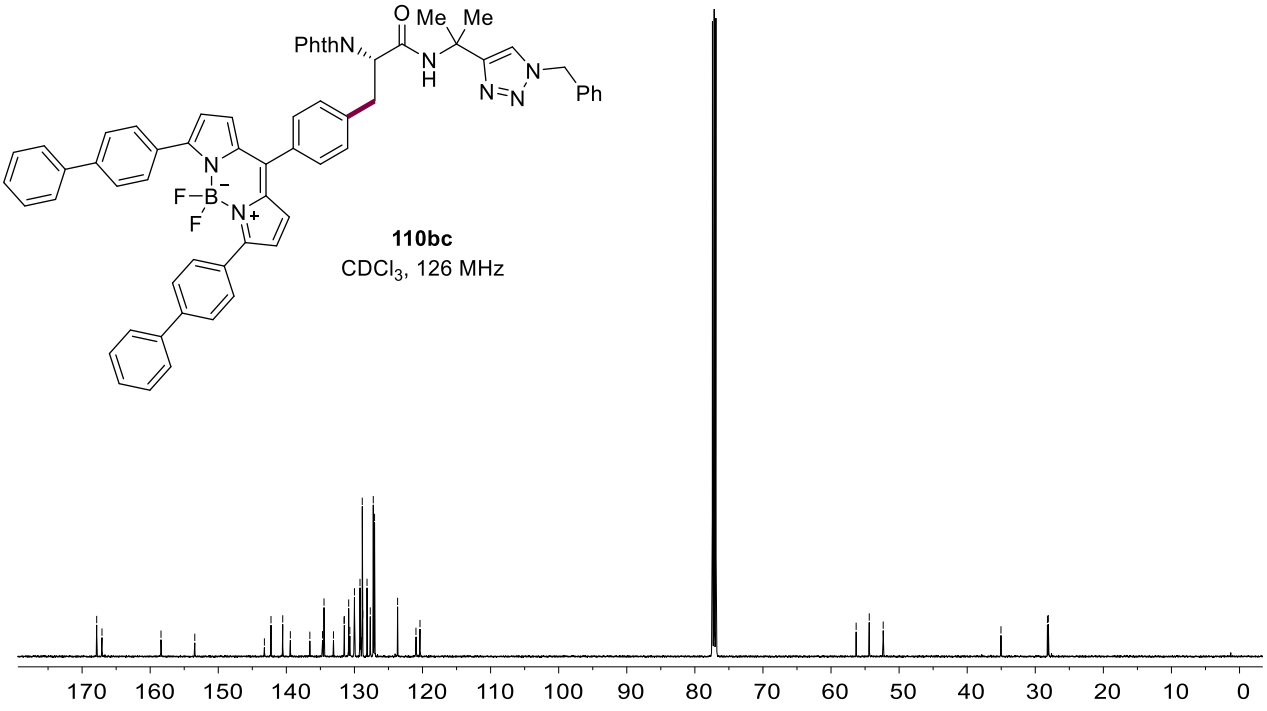

-132.28
-132.39
-132.50
-132.61
O
Me
Me
PhthN
N
H
N
N=N
Ph
Cl
N
F–B
F
N+
Cl
110bb
CDCl3, 282 MHz
-108
-112
-116
-120
-124
-128
-132
-136
-140
-144
-148
-152



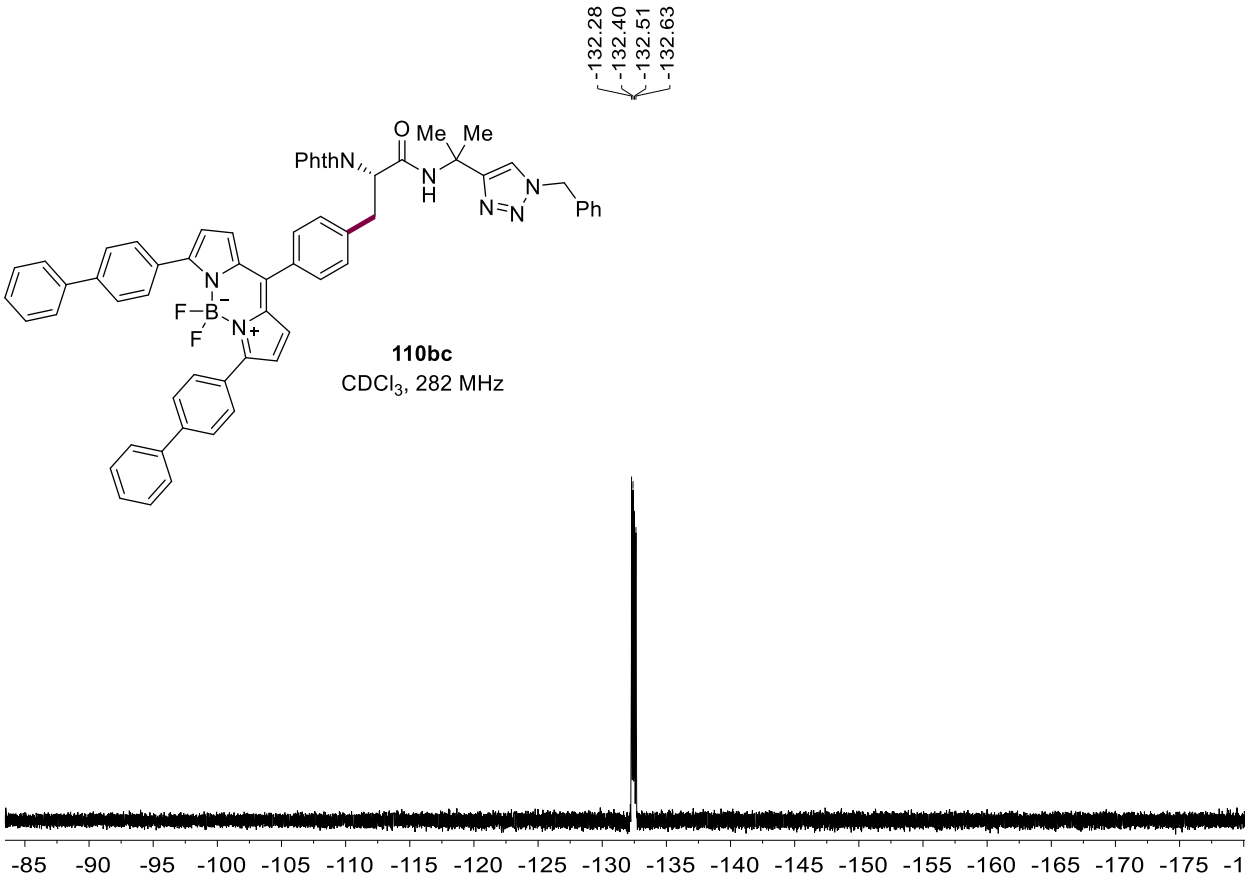
110bc
$CDCl_3$, 600 MHz

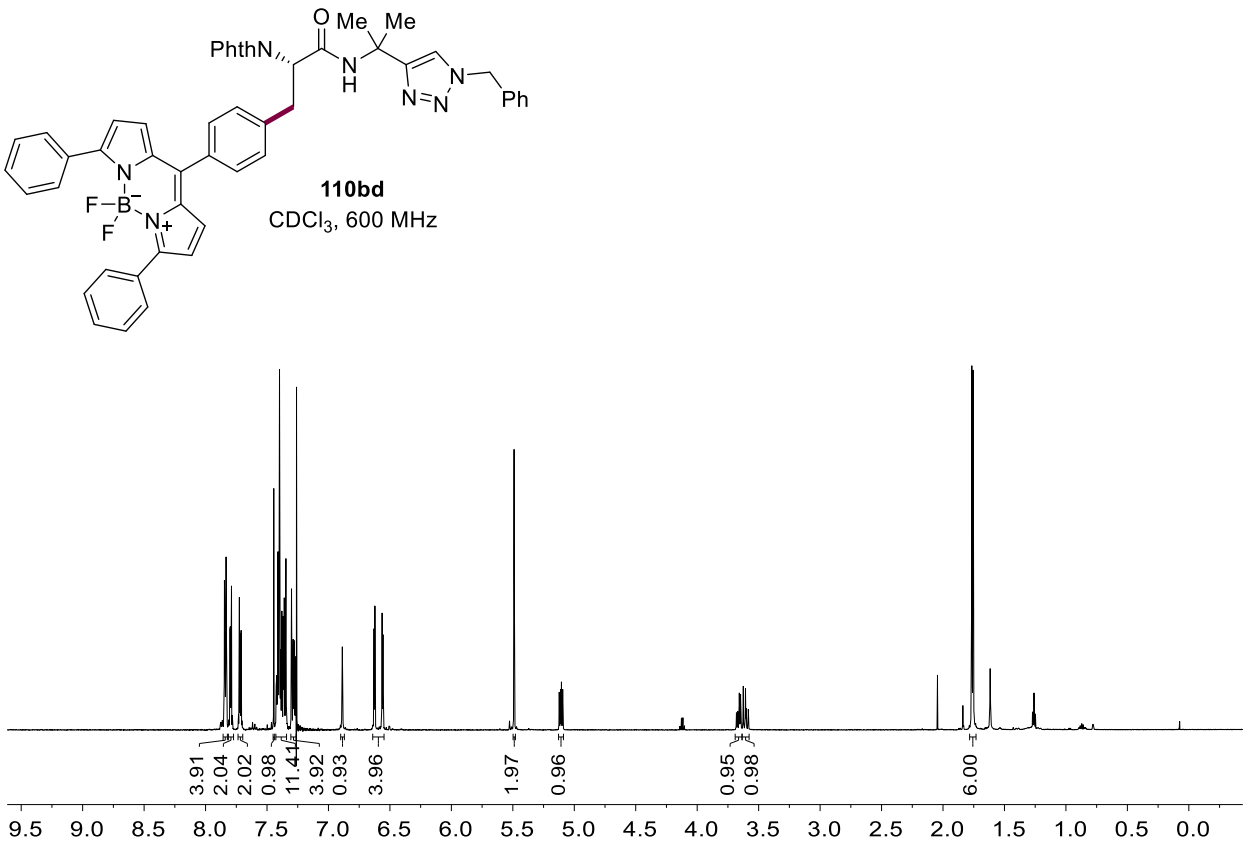


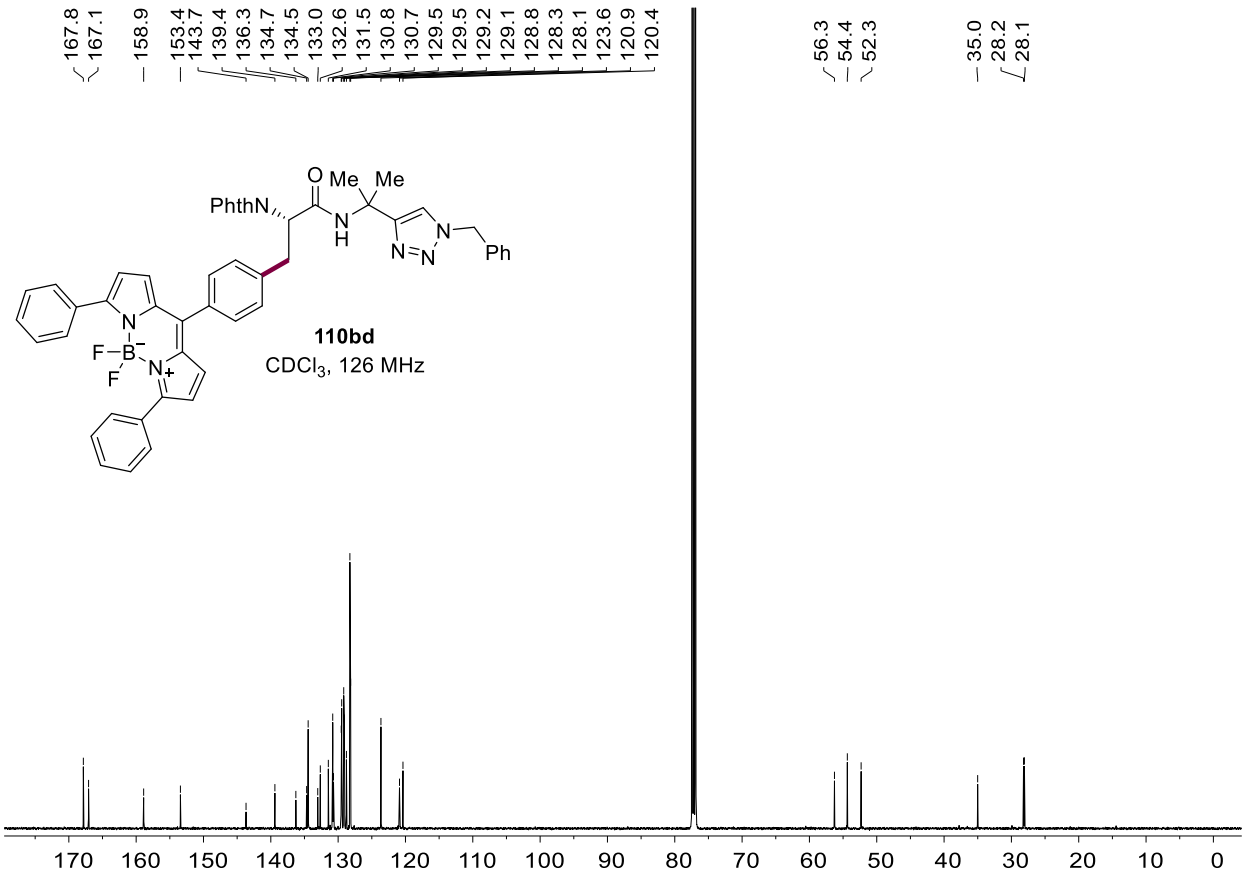


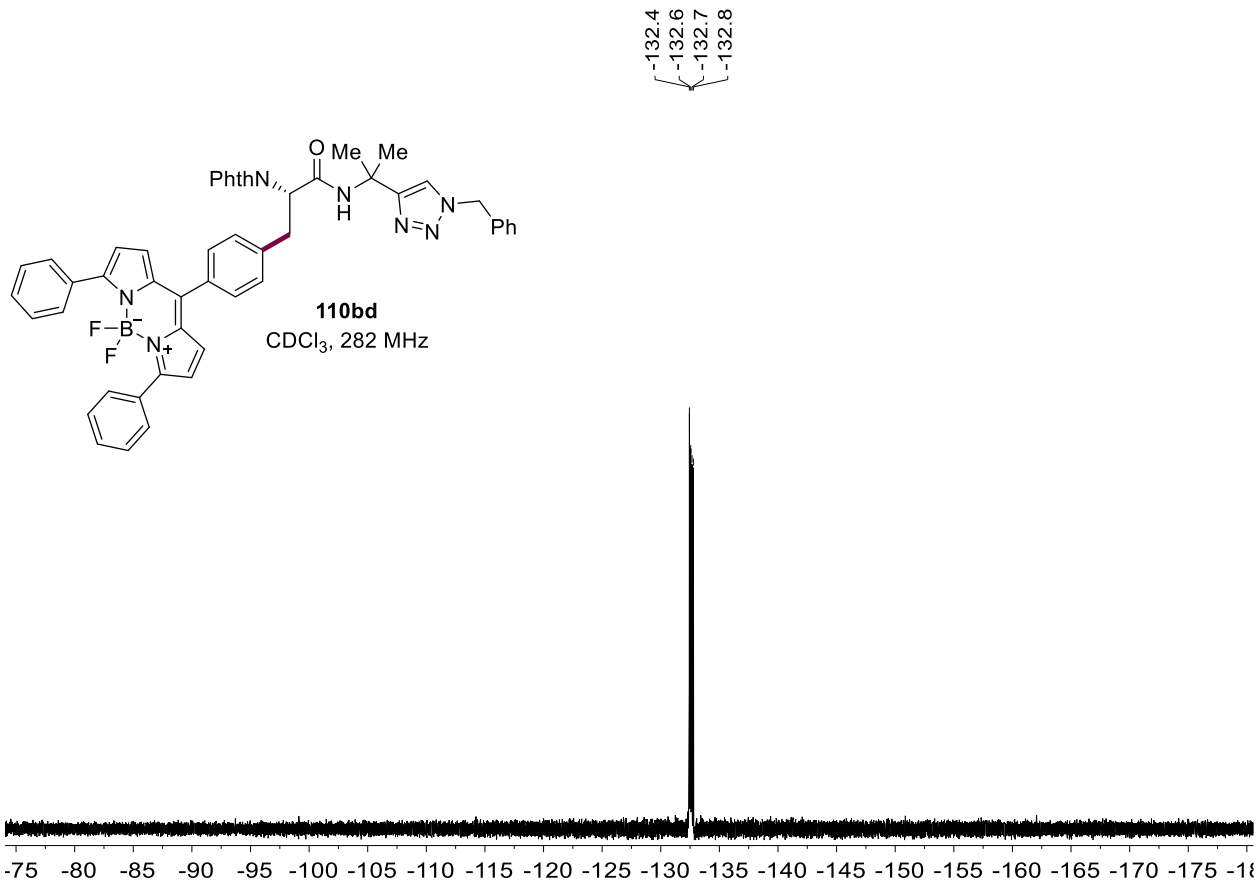


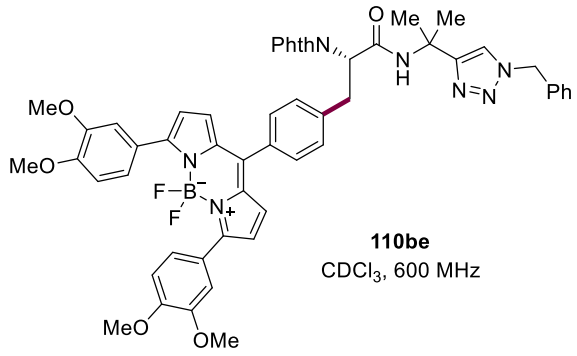
110bc
$CDCl_3$, 126 MHz


-132.28
-132.40
-132.51
-132.63
PhthN
O
Me
Me
N
H
N
N
N
Ph
N
F
B
F
N
110bc
CDCl3, 282 MHz
-85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -1


PhthN
O
Me
Me
N
H
N
N
N
Ph
N
F
B
F
N
110bd
CDCl3, 600 MHz
3.91
2.04
2.02
0.98
11.41
3.92
0.93
3.96
1.97
0.96
0.95
0.98
6.00
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

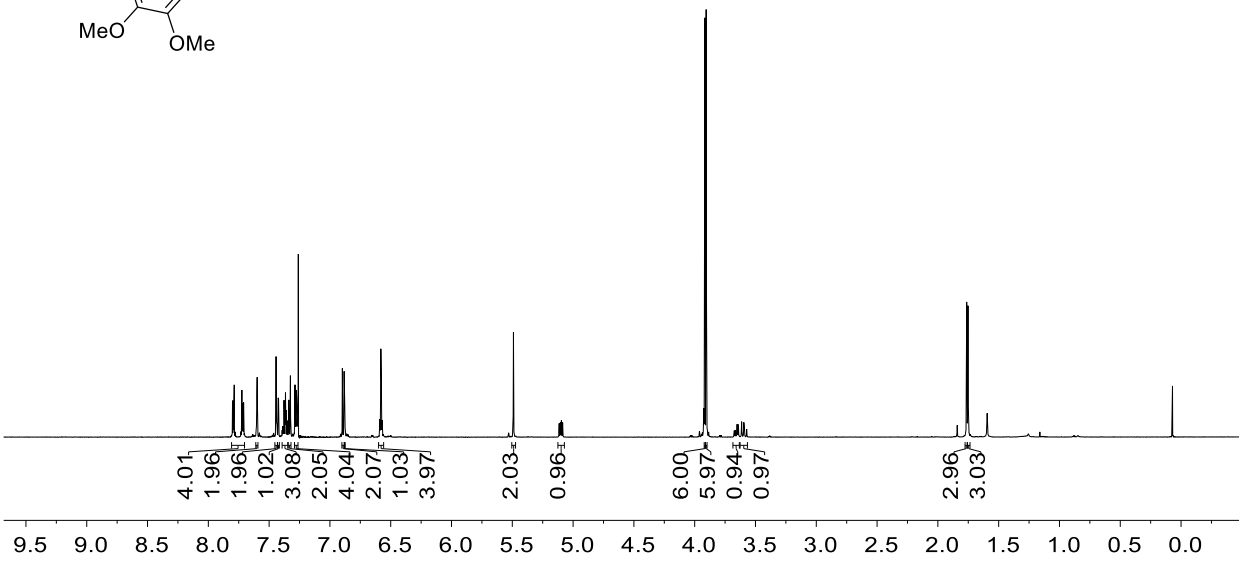

167.8
167.1
158.9
153.4
143.7
139.4
136.3
134.7
134.5
133.0
132.6
131.5
130.8
130.7
129.5
129.5
129.2
129.1
128.8
128.3
128.1
123.6
120.9
120.4
56.3
54.4
52.3
35.0
28.2
28.1
PhthN
O
Me
Me
N
H
N
N=N
N
Ph
N
F−B−F
N+
110bd
CDCl3, 126 MHz
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

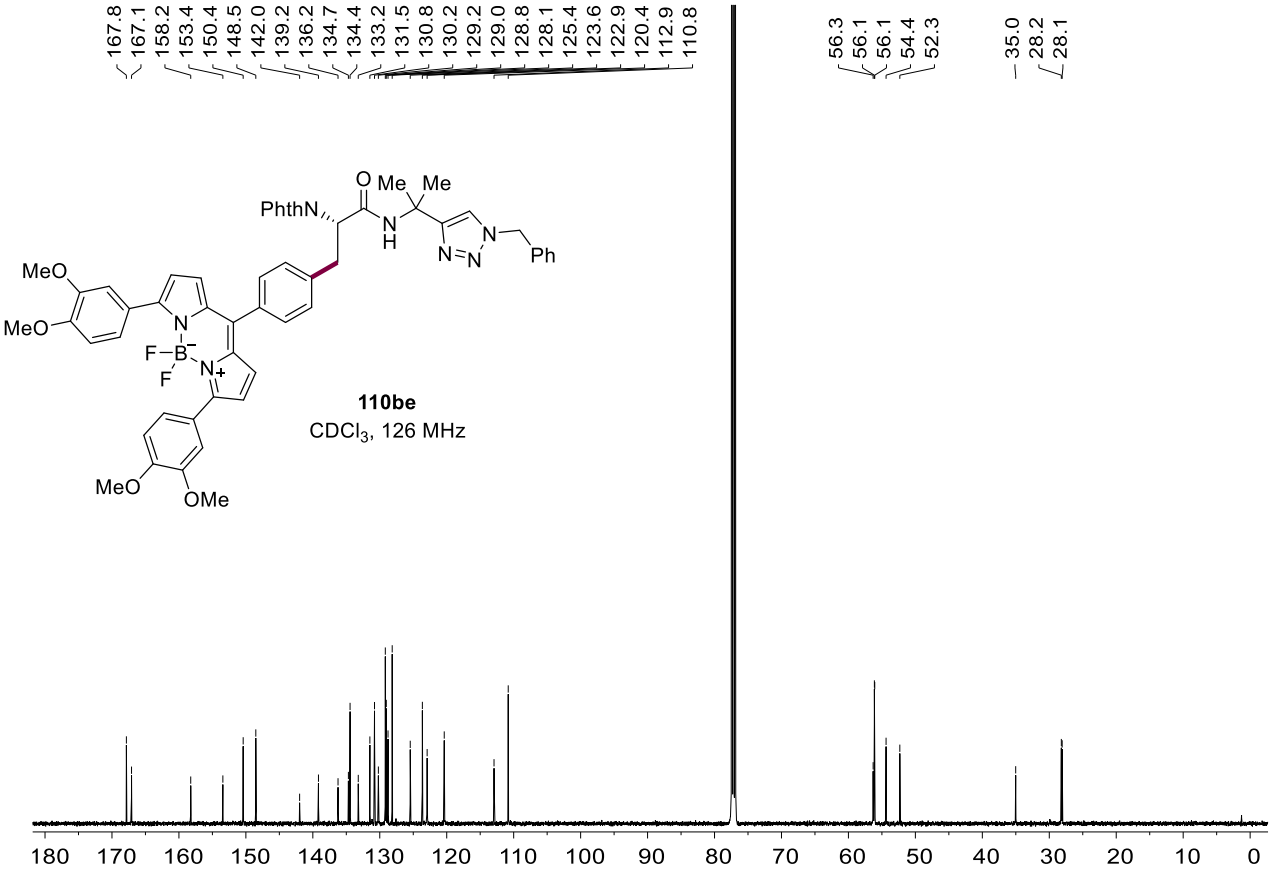

-132.4
-132.6
-132.7
-132.8
PhthN
O
Me
Me
N
H
N
N=N
N
Ph
N
F−B−F
N+
110bd
CDCl3, 282 MHz
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
-165
-170
-175



110be

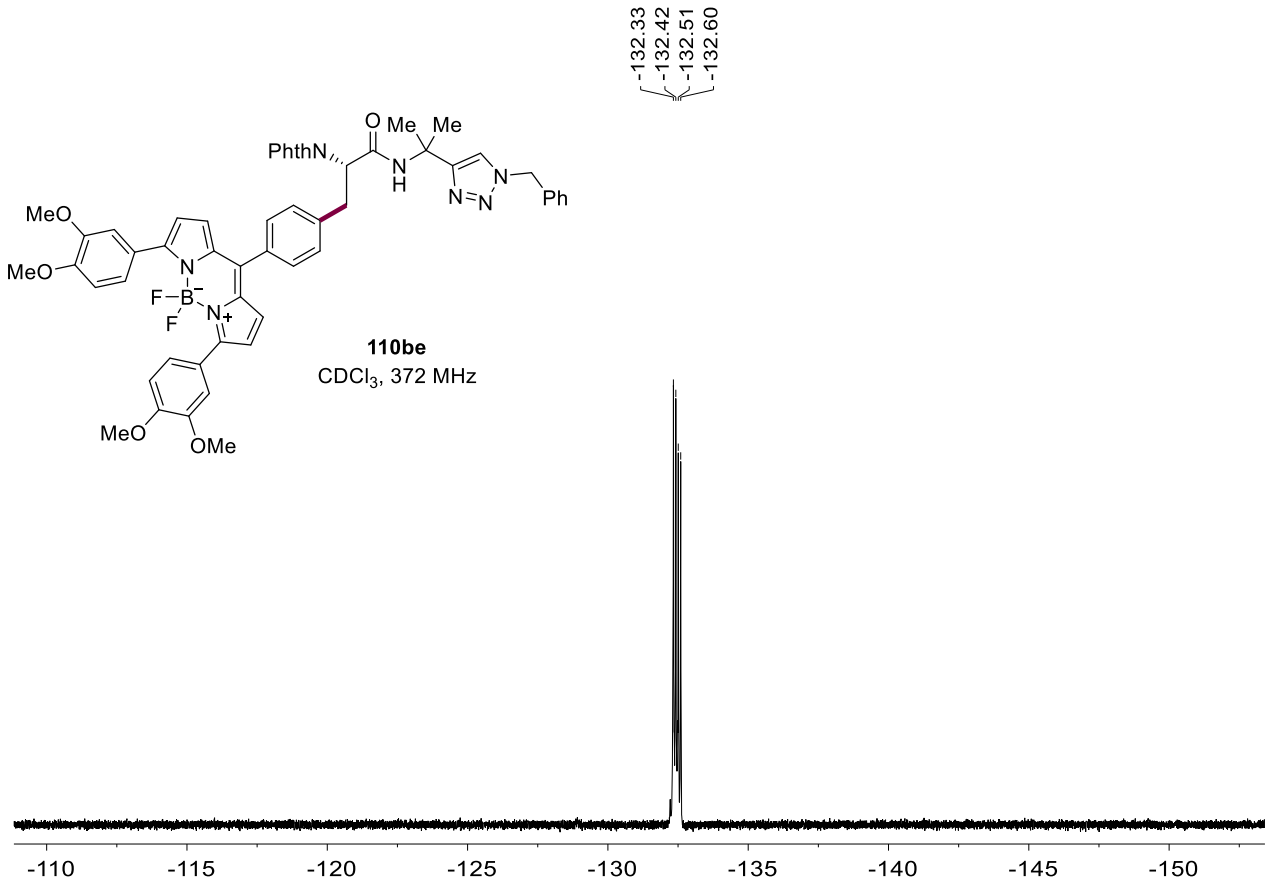
$CDCl_3$, 600 MHz

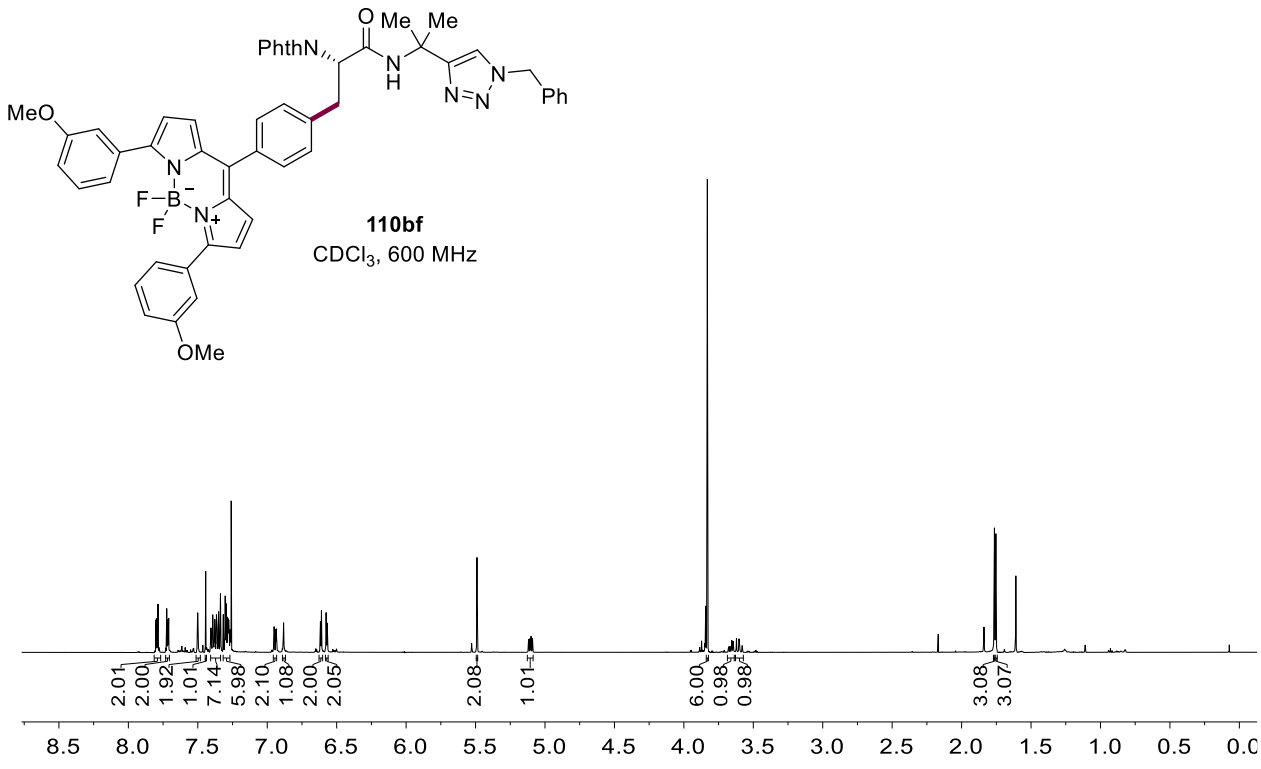


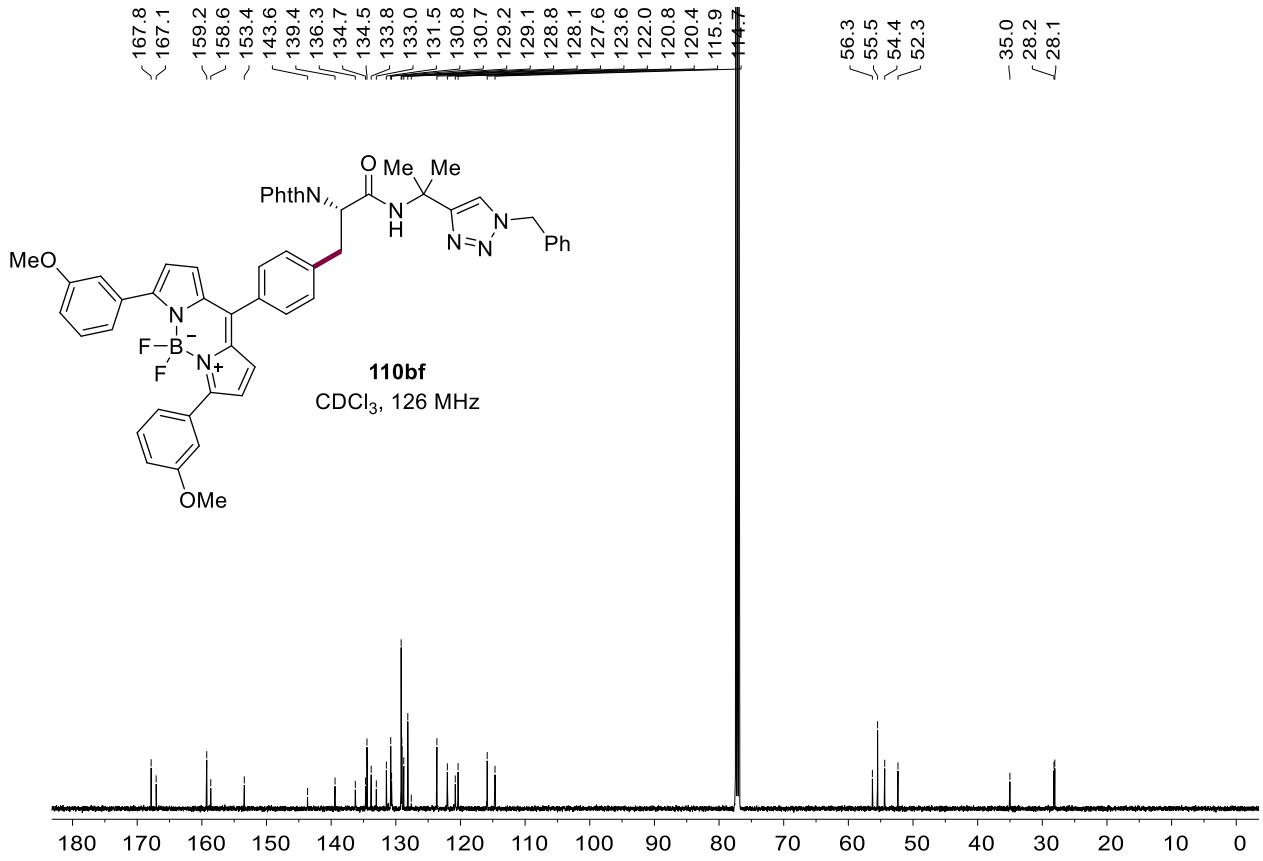


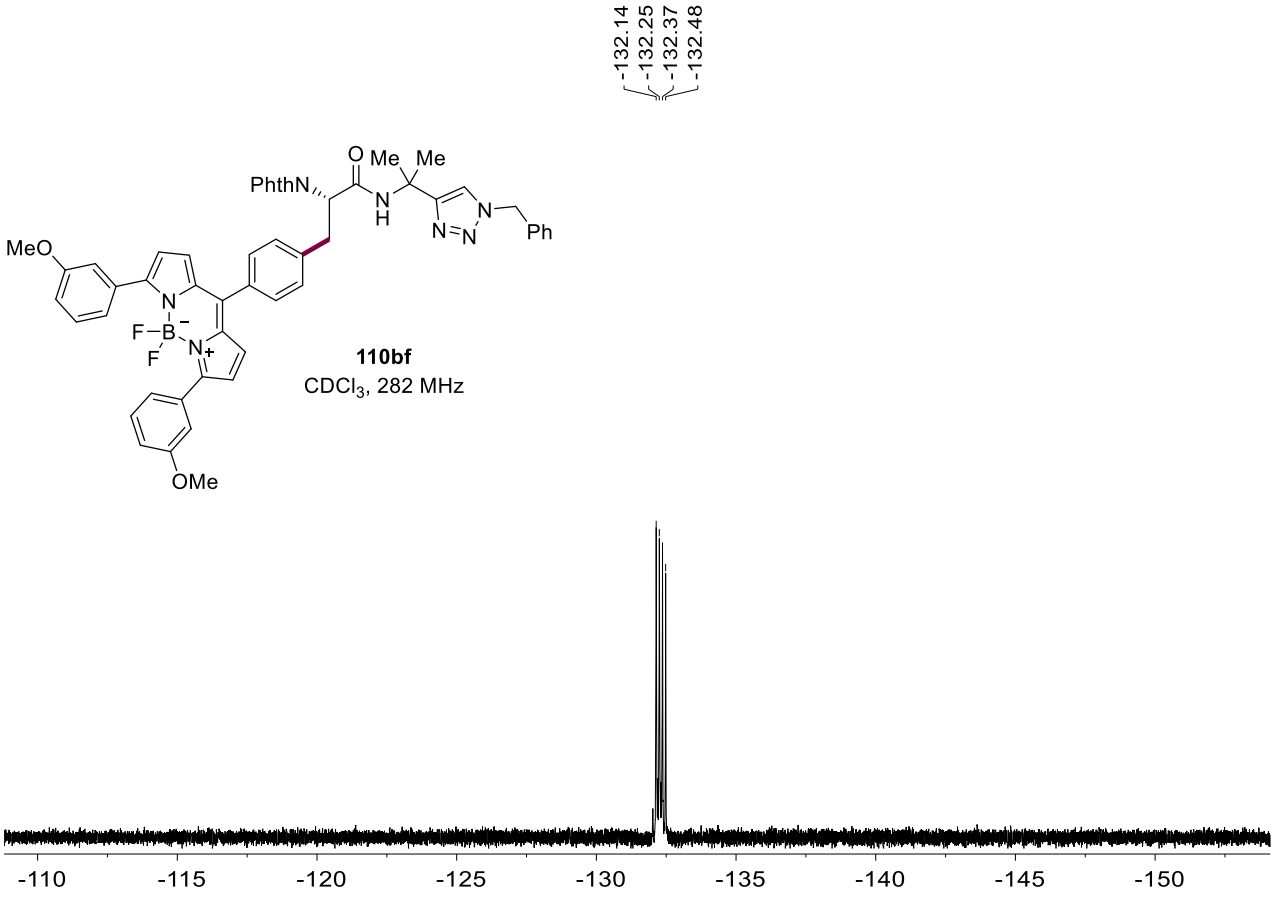
110be

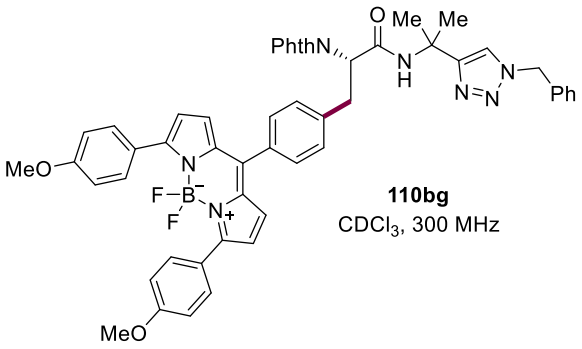
$CDCl_3$, 126 MHz


-132.33
-132.42
-132.51
-132.60
110be
CDCl3, 372 MHz
-110
-115
-120
-125
-130
-135
-140
-145
-150

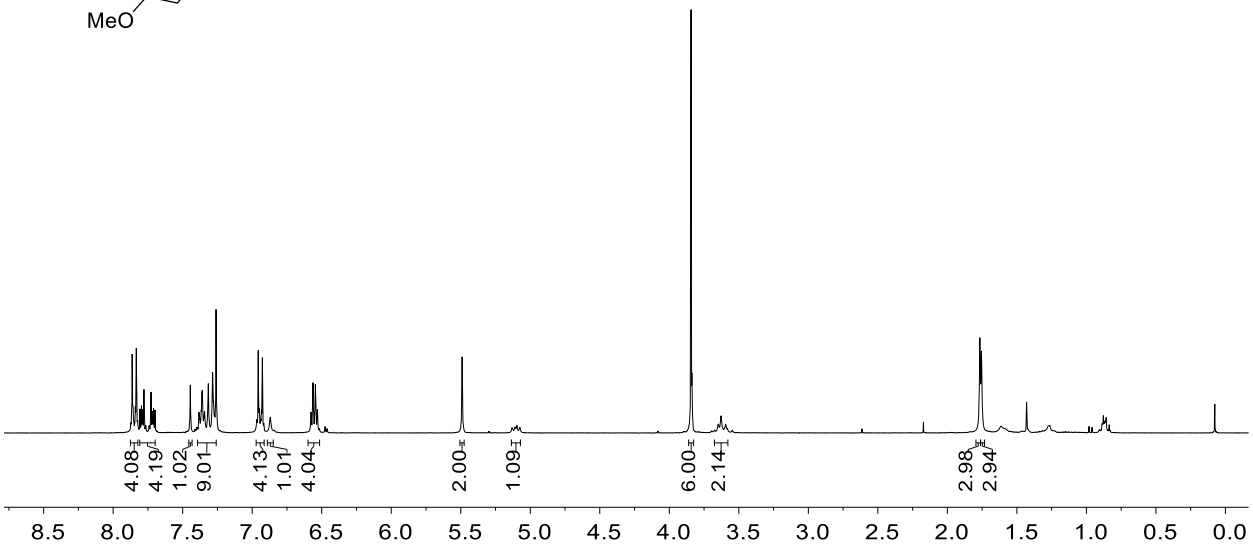

110bf
CDCl3, 600 MHz
2.01
2.00
1.92
1.01
7.14
5.98
2.10
1.08
2.00
2.05
2.08
1.01
6.00
0.98
0.98
3.08
3.07
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

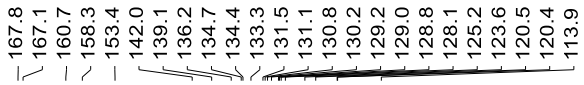

167.8
167.1
159.2
158.6
153.4
143.6
139.4
136.3
134.7
134.5
133.8
133.0
131.5
130.8
130.7
129.2
129.1
128.8
128.1
127.6
123.6
122.0
120.8
120.4
115.9
114.7
56.3
55.5
54.4
52.3
35.0
28.2
28.1
O
Me
Me
PhthN
N
H
N
N=N
N
Ph
MeO
N
F–B
F
N+
OMe
110bf
CDCl3, 126 MHz
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

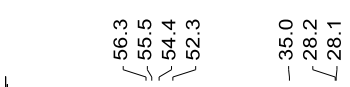

-132.14
-132.25
-132.37
-132.48
O
Me
Me
PhthN
N
H
N
N=N
N
Ph
MeO
N
F–B
F
N+
OMe
110bf
CDCl3, 282 MHz
-110
-115
-120
-125
-130
-135
-140
-145
-150

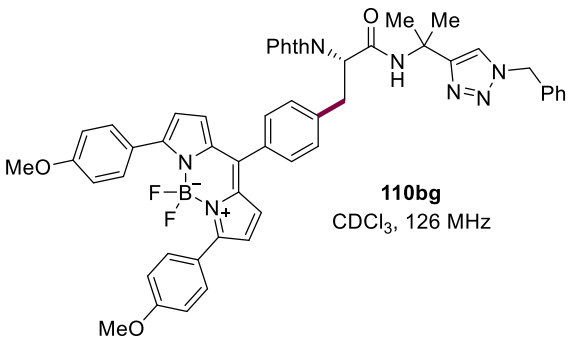


110bg
$CDCl_3$, 300 MHz

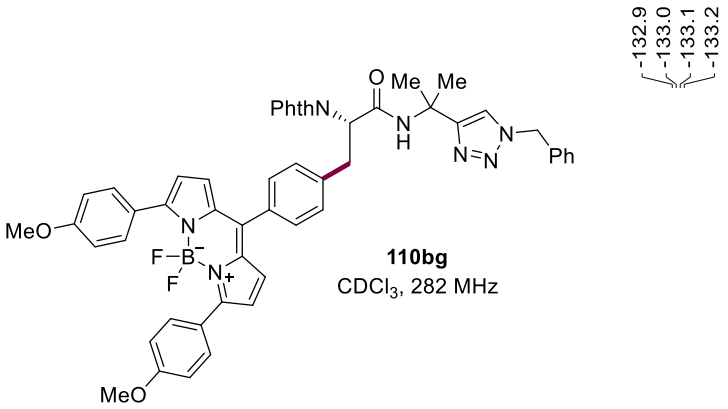




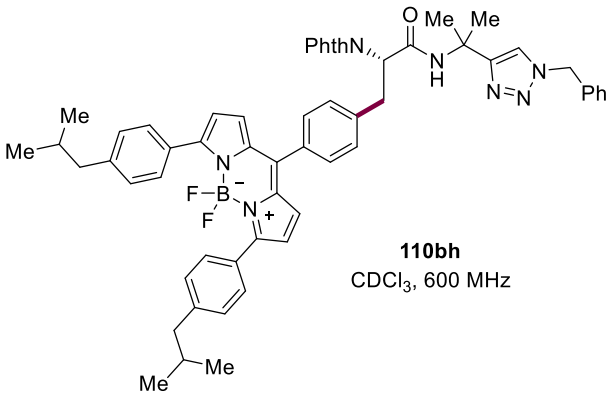




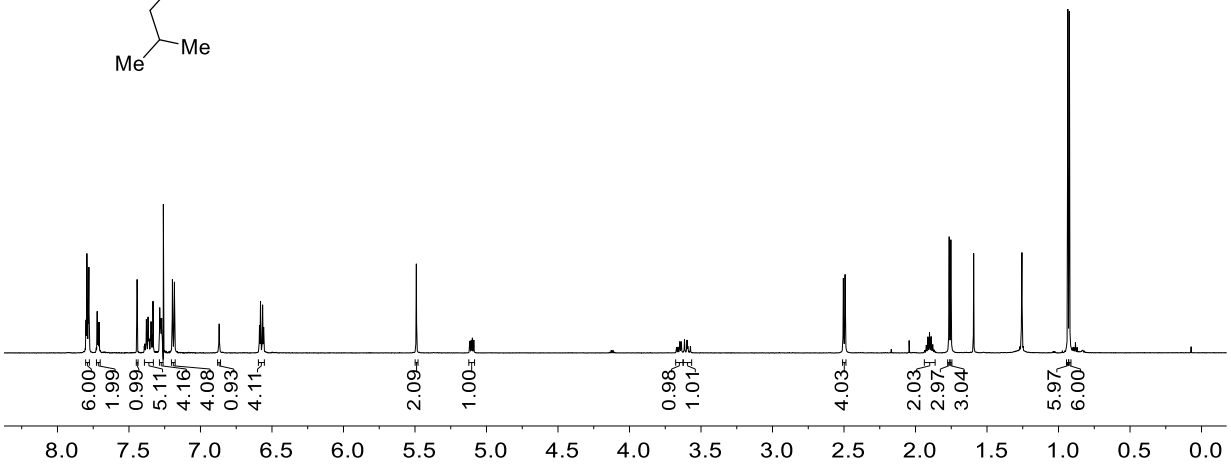
110bg
$CDCl_3$, 126 MHz

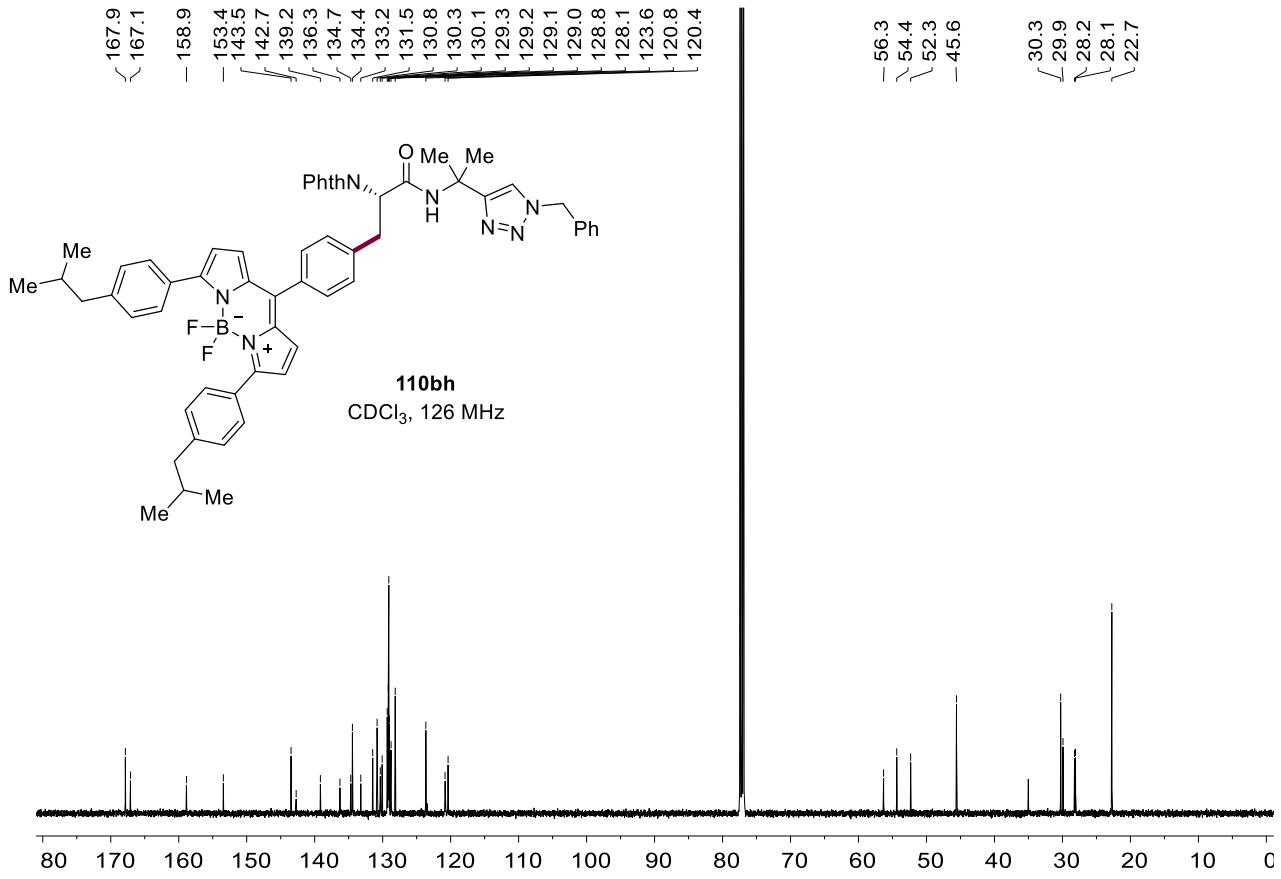


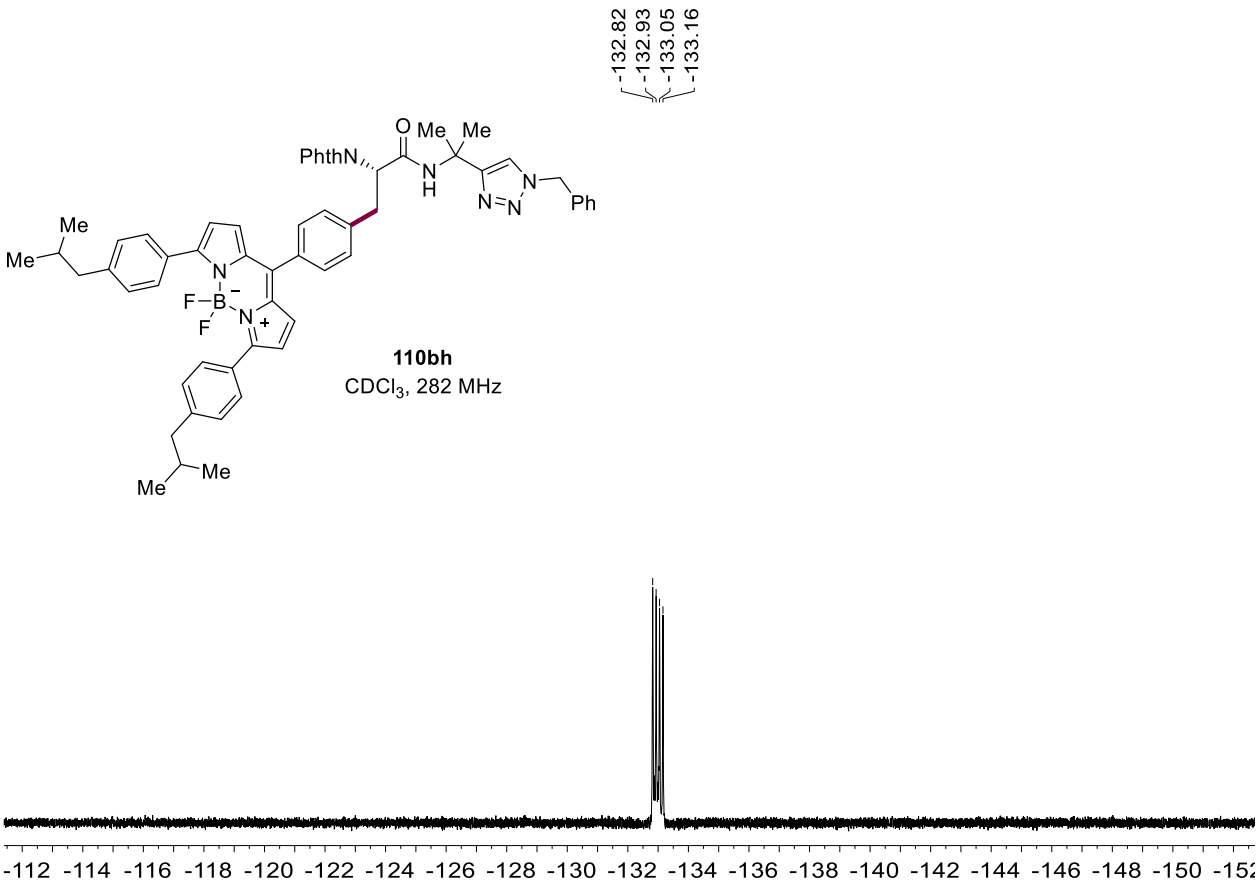
110bg
$CDCl_3$, 282 MHz

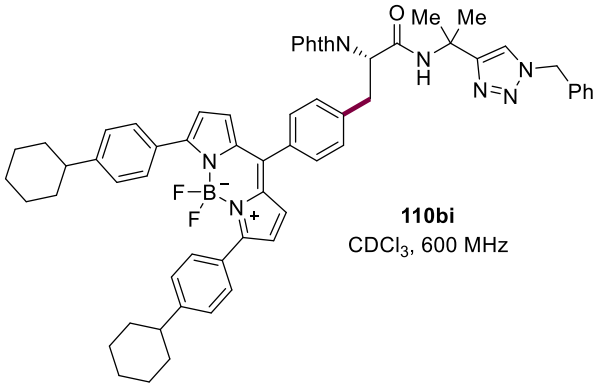


110bh
$CDCl_3$, 600 MHz

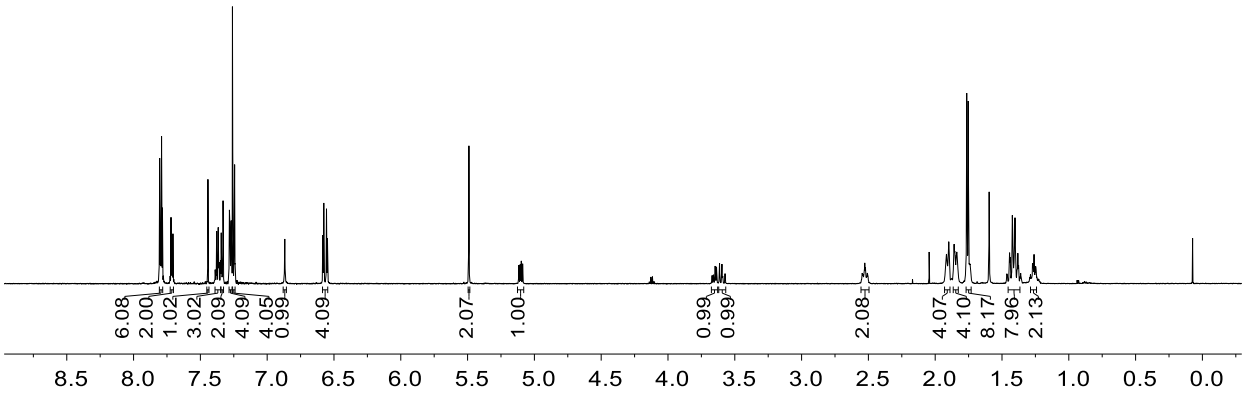


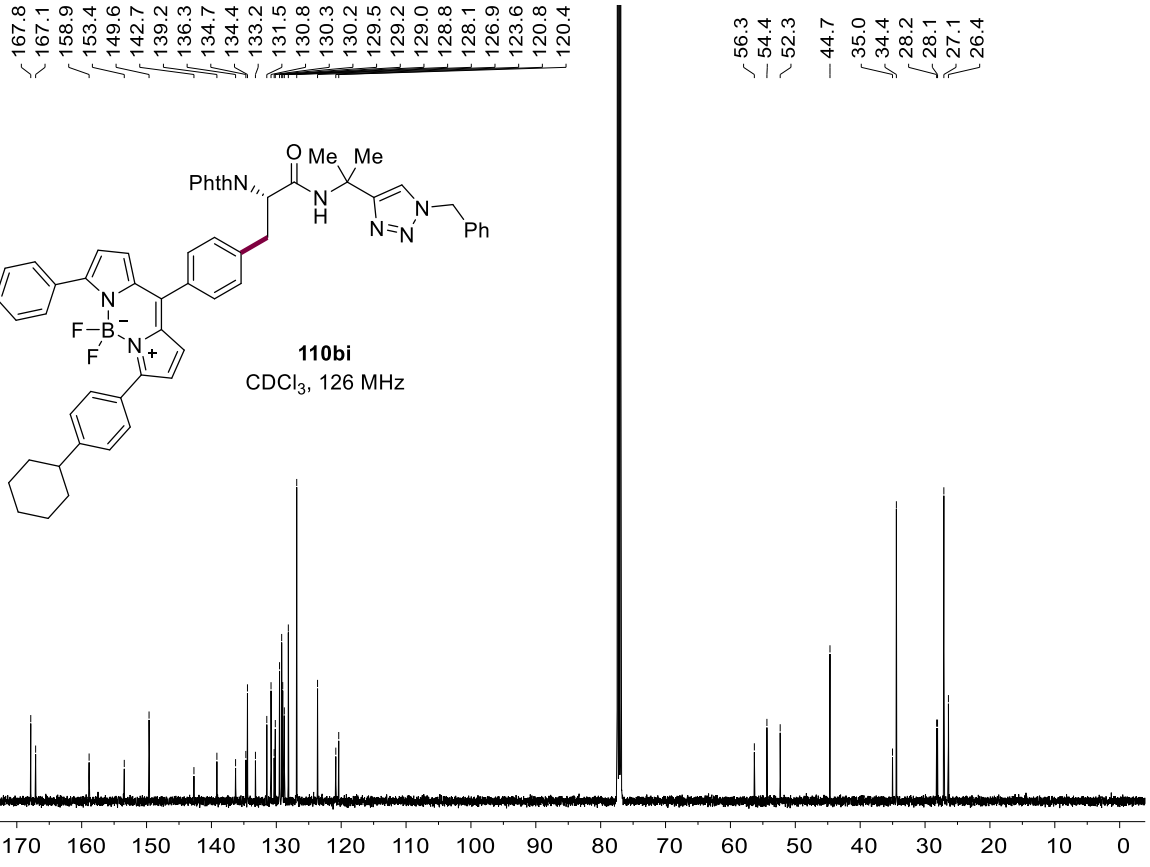

167.9
167.1
158.9
153.4
143.5
142.7
139.2
136.3
134.7
134.4
133.2
131.5
130.8
130.3
130.1
129.3
129.2
129.1
129.0
128.8
128.1
123.6
120.8
120.4
56.3
54.4
52.3
45.6
30.3
29.9
28.2
28.1
22.7
PhthN
O Me Me
N
H
N
N=N
Ph
Me
Me
F–B
F
N+
Me
Me
110bh
CDCl3, 126 MHz
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


-132.82
-132.93
-133.05
-133.16
PhthN
O Me Me
N
H
N
N=N
Ph
Me
Me
F–B
F
N+
Me
Me
110bh
CDCl3, 282 MHz
-112 -114 -116 -118 -120 -122 -124 -126 -128 -130 -132 -134 -136 -138 -140 -142 -144 -146 -148 -150 -152

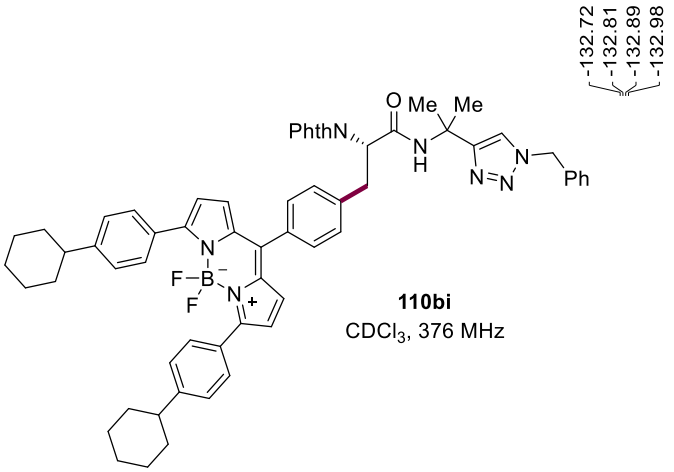


110bi
$CDCl_3$, 600 MHz

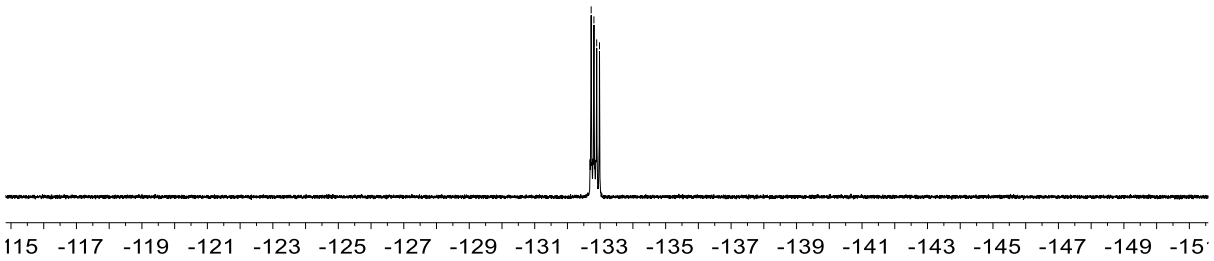


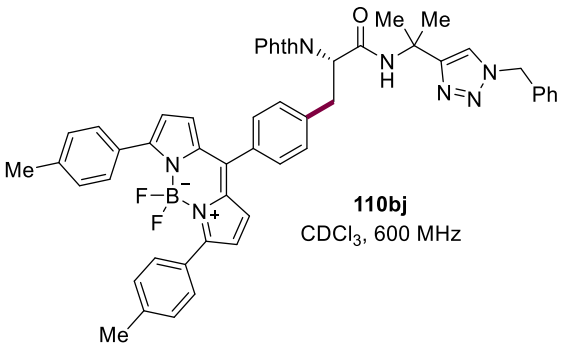


110bi
$CDCl_3$, 126 MHz

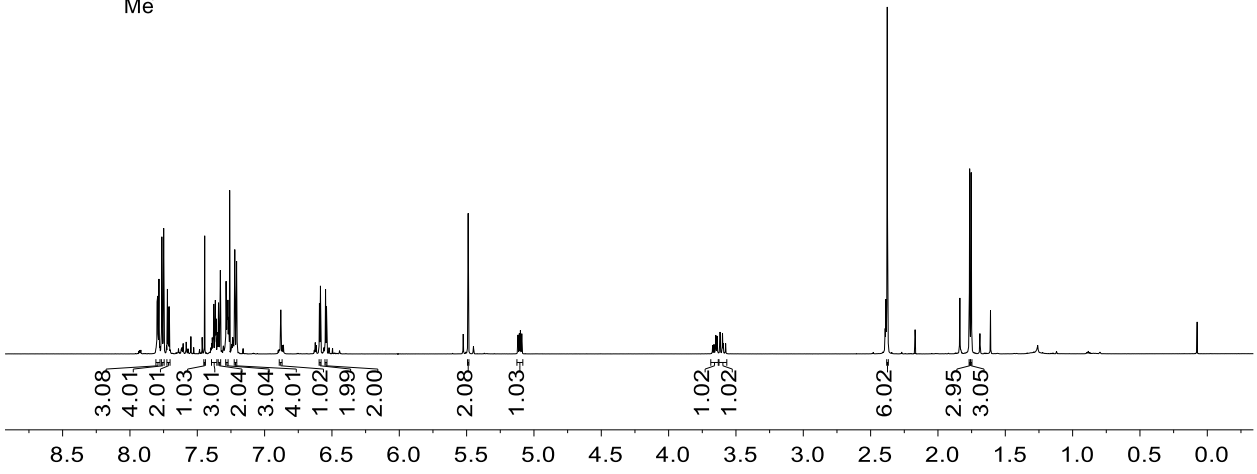


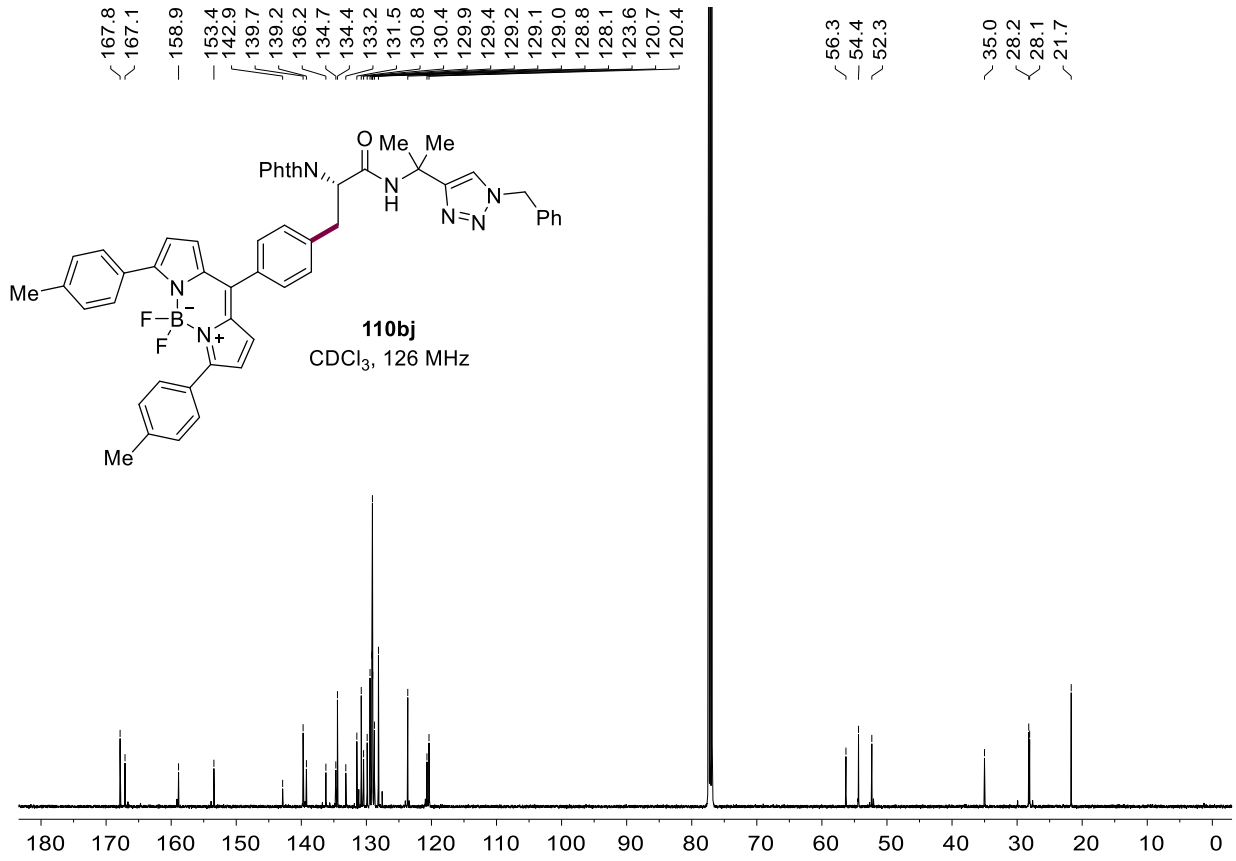
110bi
$CDCl_3$, 376 MHz

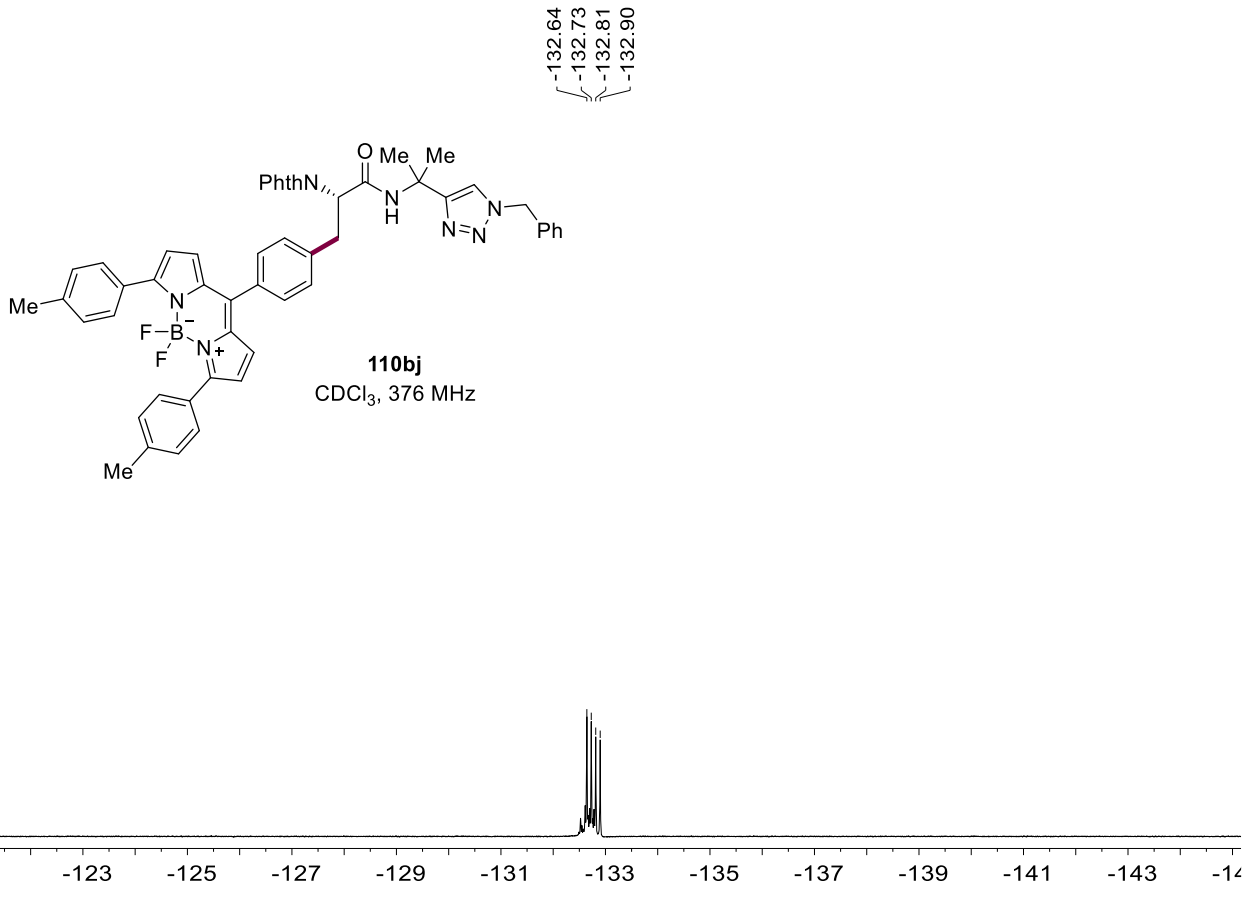


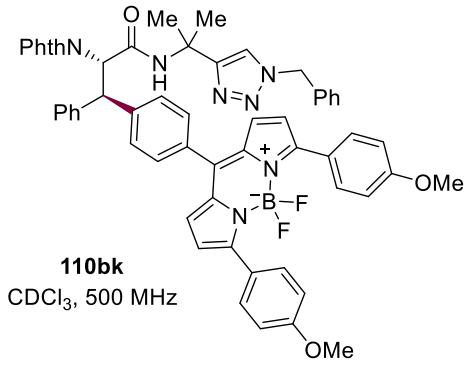


110bj
$CDCl_3$, 600 MHz

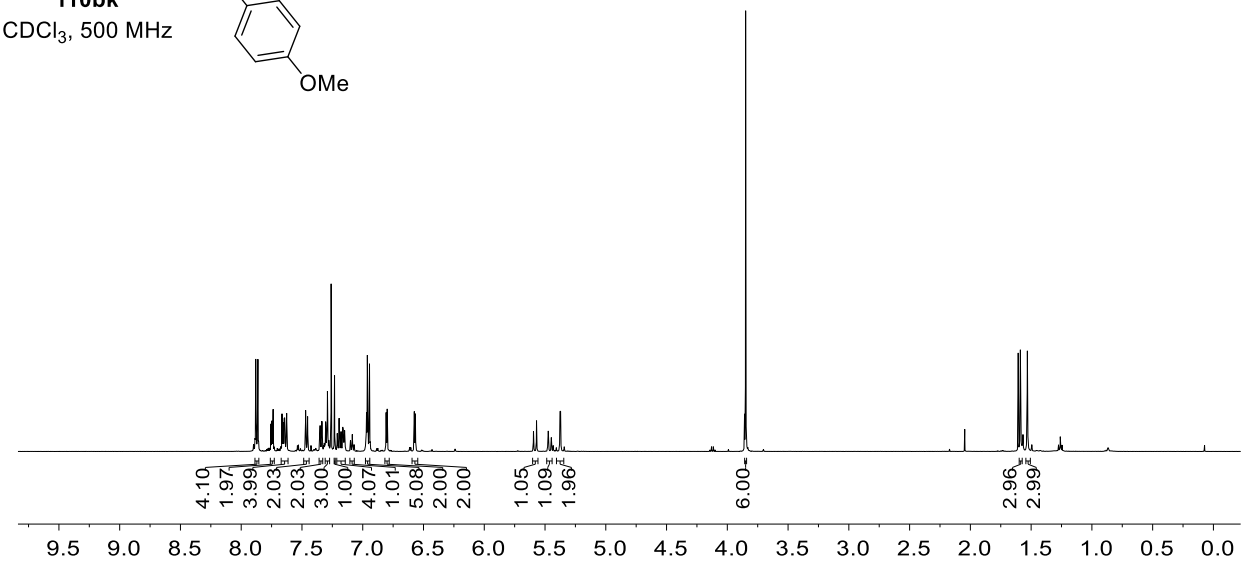


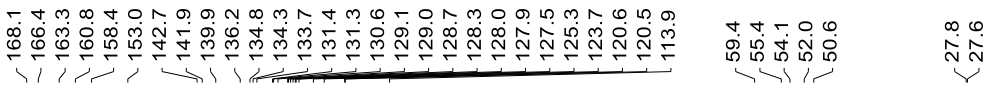

167.8
167.1
158.9
153.4
142.9
139.7
139.2
136.2
134.7
134.4
133.2
131.5
130.8
130.4
129.9
129.4
129.2
129.1
129.0
128.8
128.1
123.6
120.7
120.4
56.3
54.4
52.3
35.0
28.2
28.1
21.7
O Me Me
PhthN
N
H
N
N=N
Ph
Me
F–B–F
N+
Me
110bj
CDCl3, 126 MHz
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

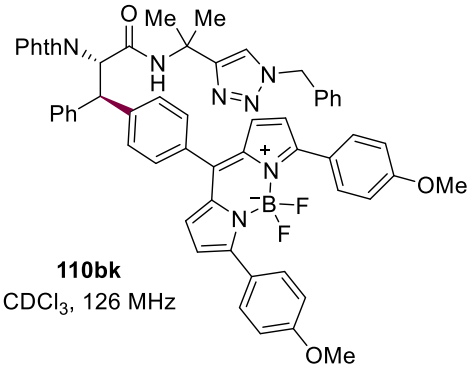

-132.64
-132.73
-132.81
-132.90
O Me Me
PhthN
N
H
N
N=N
Ph
Me
F–B–F
N+
Me
110bj
CDCl3, 376 MHz
-123 -125 -127 -129 -131 -133 -135 -137 -139 -141 -143



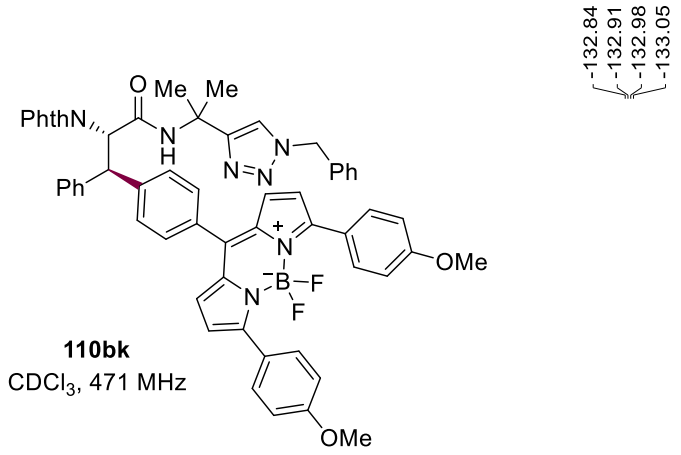
110bk
$CDCl_3$, 500 MHz

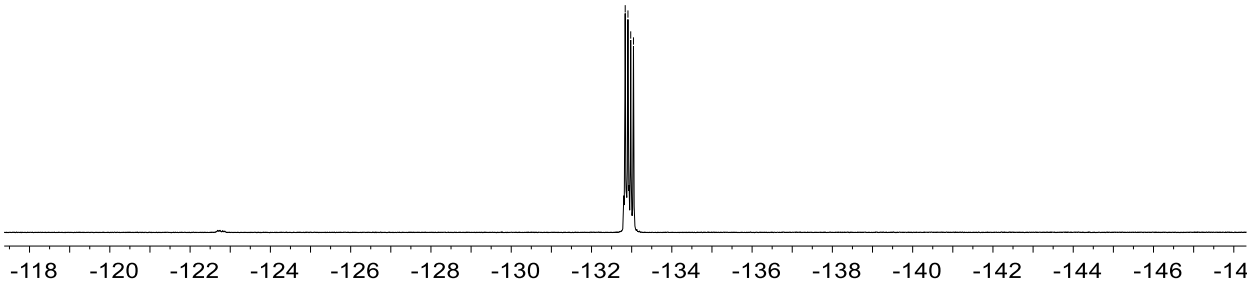


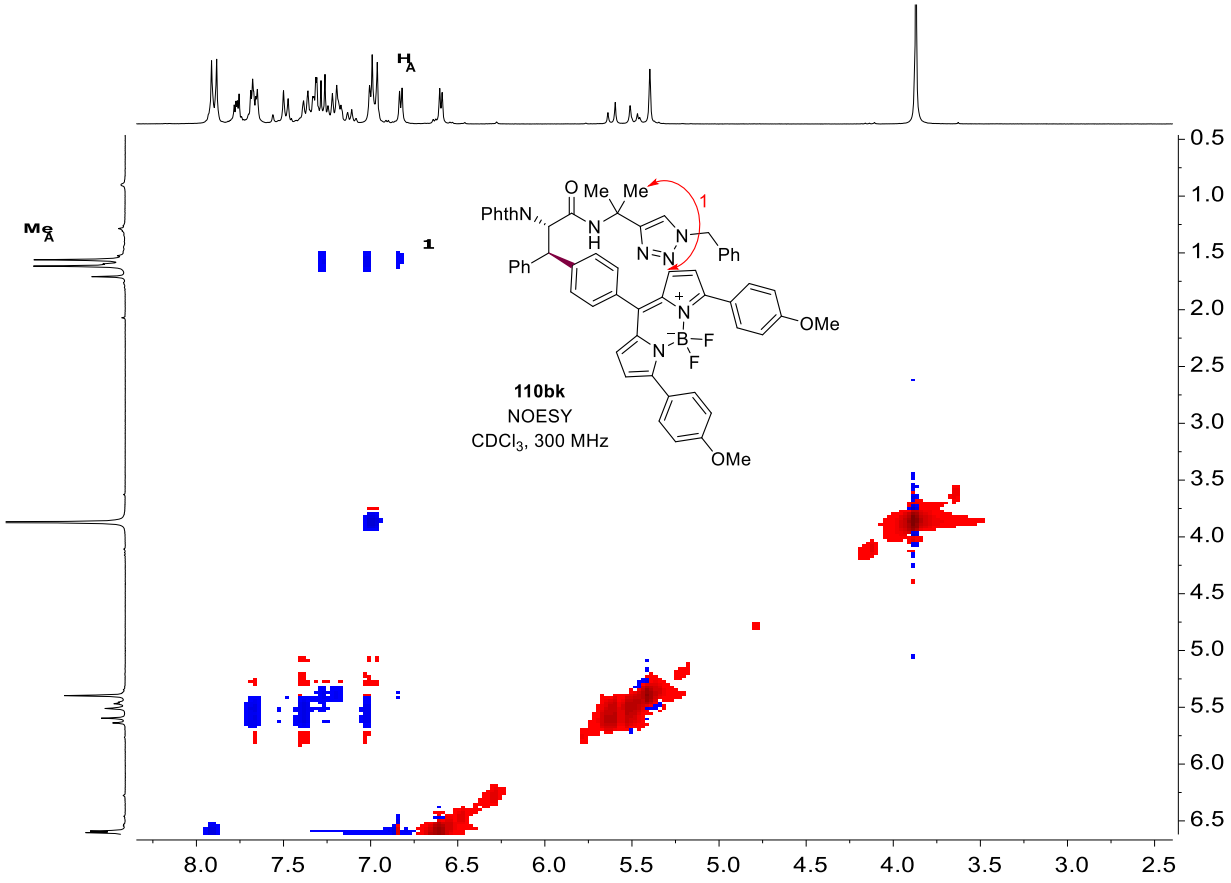


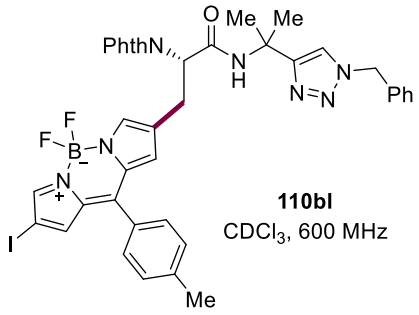


110bk
$CDCl_3$, 126 MHz

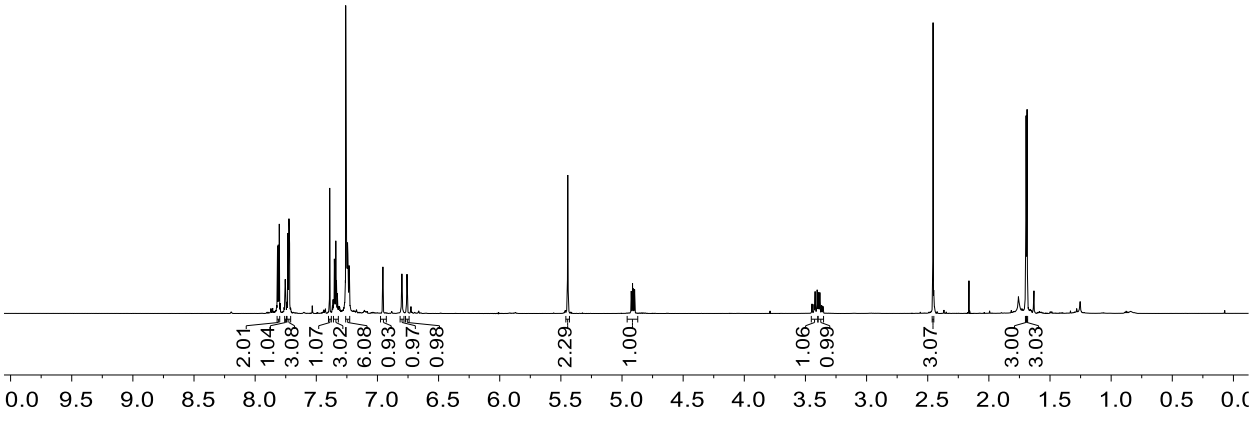

-132.84
-132.91
-132.98
-133.05
PhthN
O
Me
Me
N
H
Ph
N
N
N
Ph
N
B
F
F
OMe
OMe
110bk
CDCl3, 471 MHz

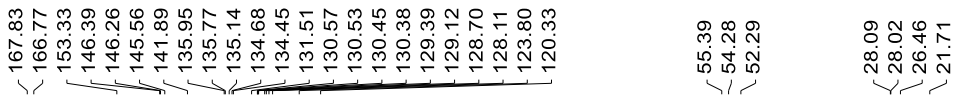

-118
-120
-122
-124
-126
-128
-130
-132
-134
-136
-138
-140
-142
-144
-146
-14

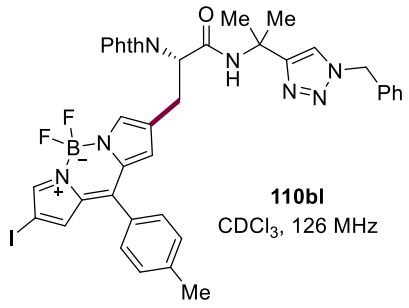

HA
MeA
1
PhthN
O
Me
Me
N
H
Ph
N
N
N
Ph
1
N
B
F
F
OMe
OMe
110bk
NOESY
CDCl3, 300 MHz
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5



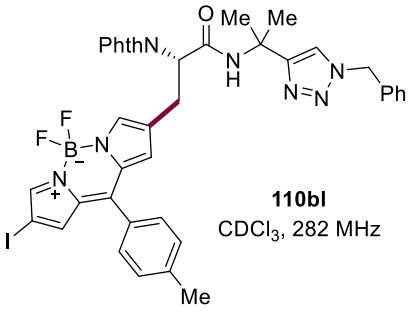
110bl
$CDCl_3$, 600 MHz



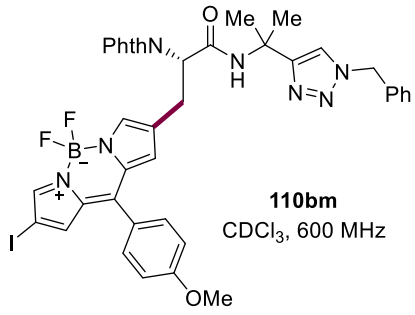




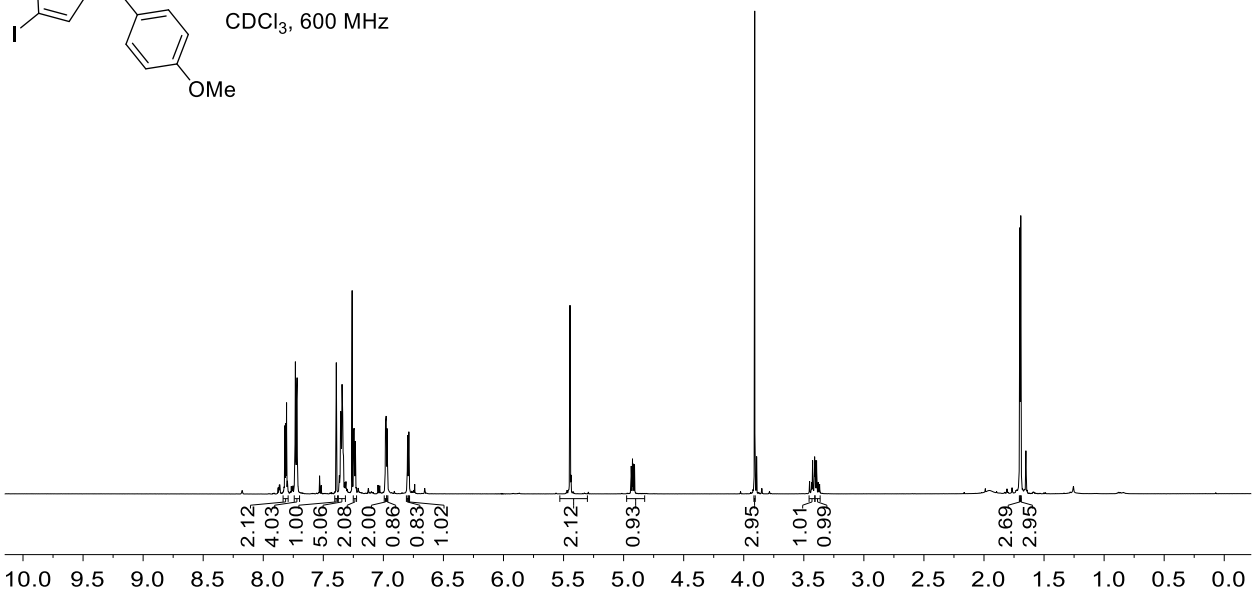
110bl
$CDCl_3$, 126 MHz

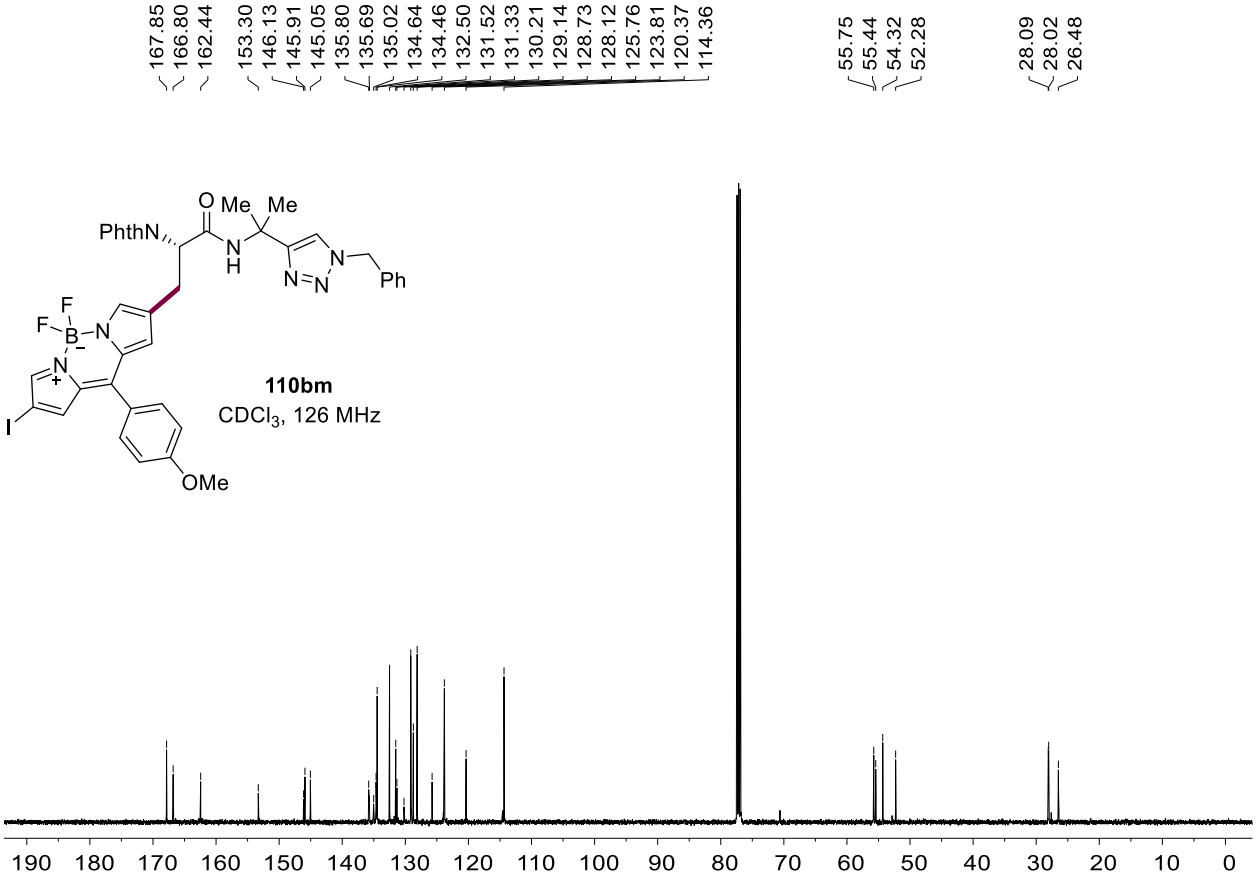


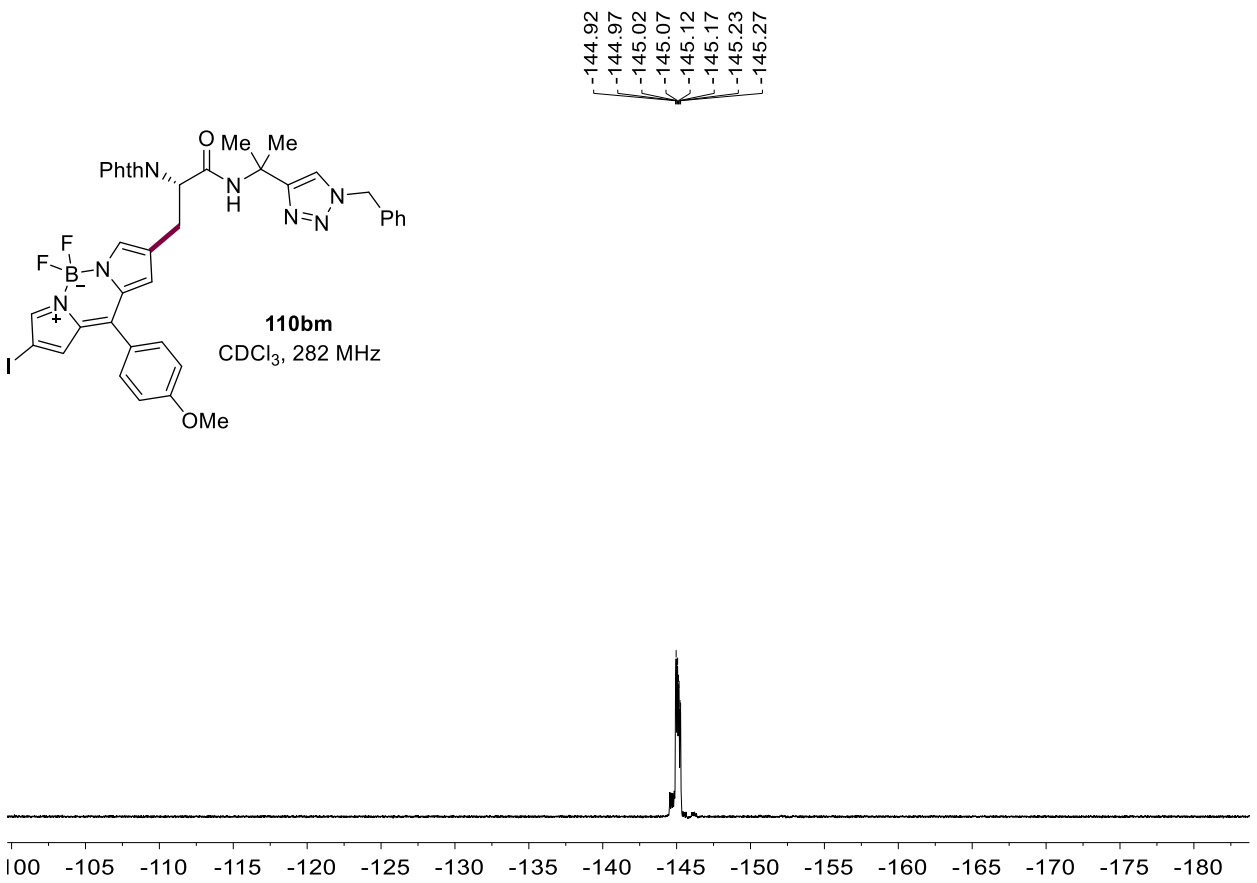
110bl
$CDCl_3$, 282 MHz



110bm
$CDCl_3$, 600 MHz




167.85
166.80
162.44
153.30
146.13
145.91
145.05
135.80
135.69
135.02
134.64
134.46
132.50
131.52
131.33
130.21
129.14
128.73
128.12
125.76
123.81
120.37
114.36
55.75
55.44
54.32
52.28
28.09
28.02
26.48
PhthN
O
Me
Me
N
H
N
N=N
N
Ph
F
F
B
N
N
I
OMe
110bm
CDCl3, 126 MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


-144.92
-144.97
-145.02
-145.07
-145.12
-145.17
-145.23
-145.27
PhthN
O
Me
Me
N
H
N
N=N
N
Ph
F
F
B
N
N
I
OMe
110bm
CDCl3, 282 MHz
100
-105
-110
-115
-120
-125
-130
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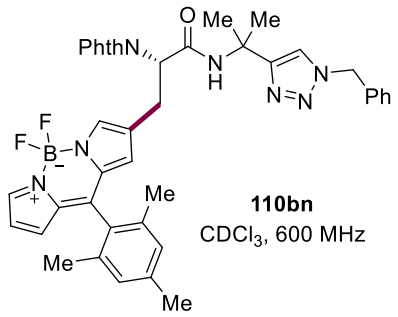
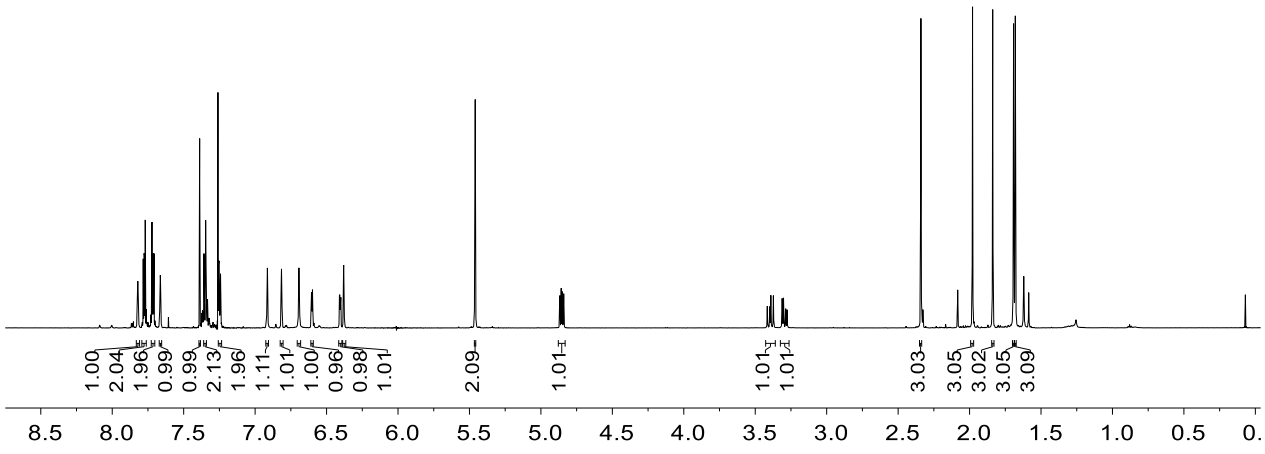
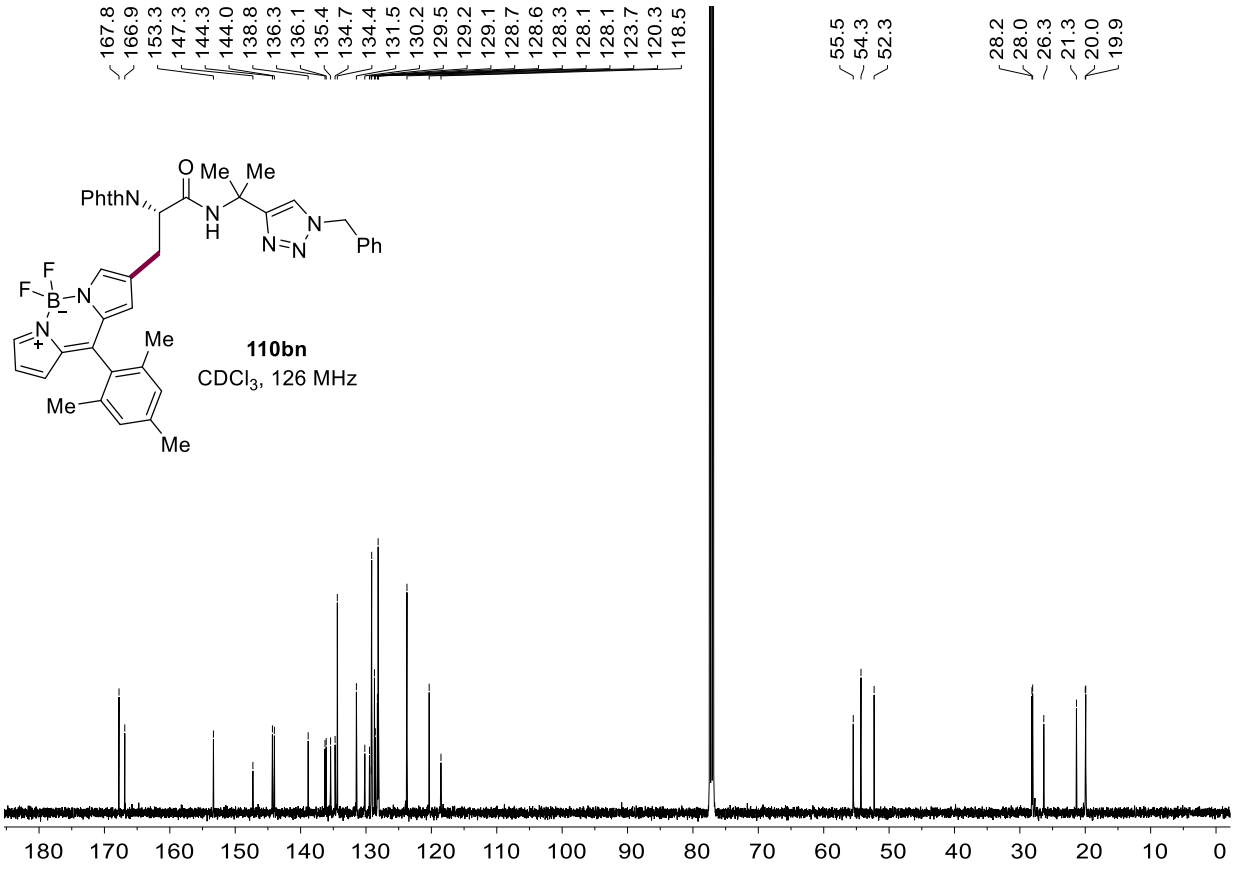
-140
-145
-150
-155
-160
-165
-170
-175
-180

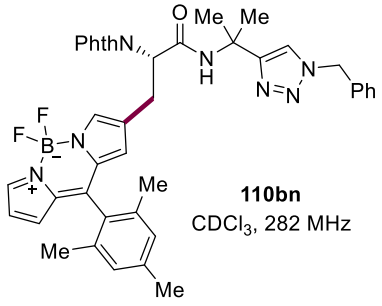


110bn
$CDCl_3$, 600 MHz

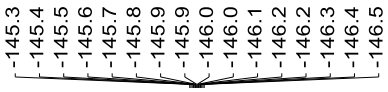


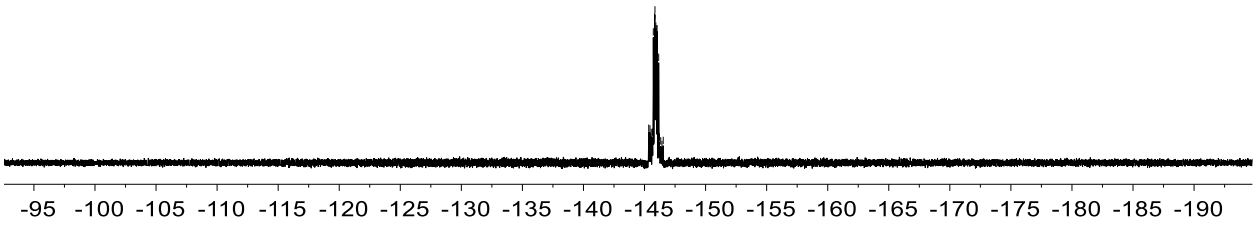


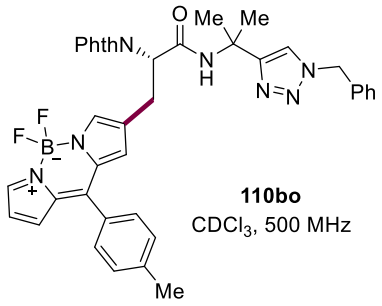
110bn
$CDCl_3$, 126 MHz



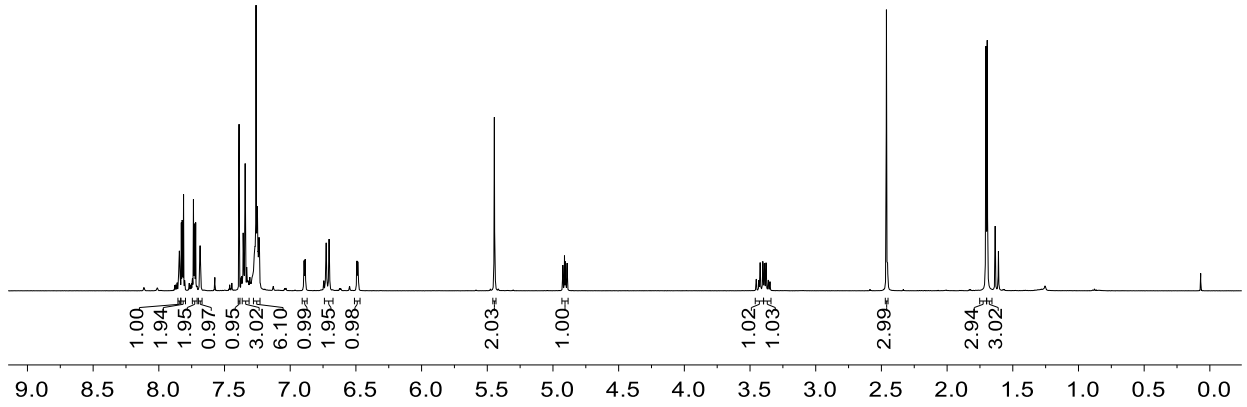
110bn
$CDCl_3$, 282 MHz

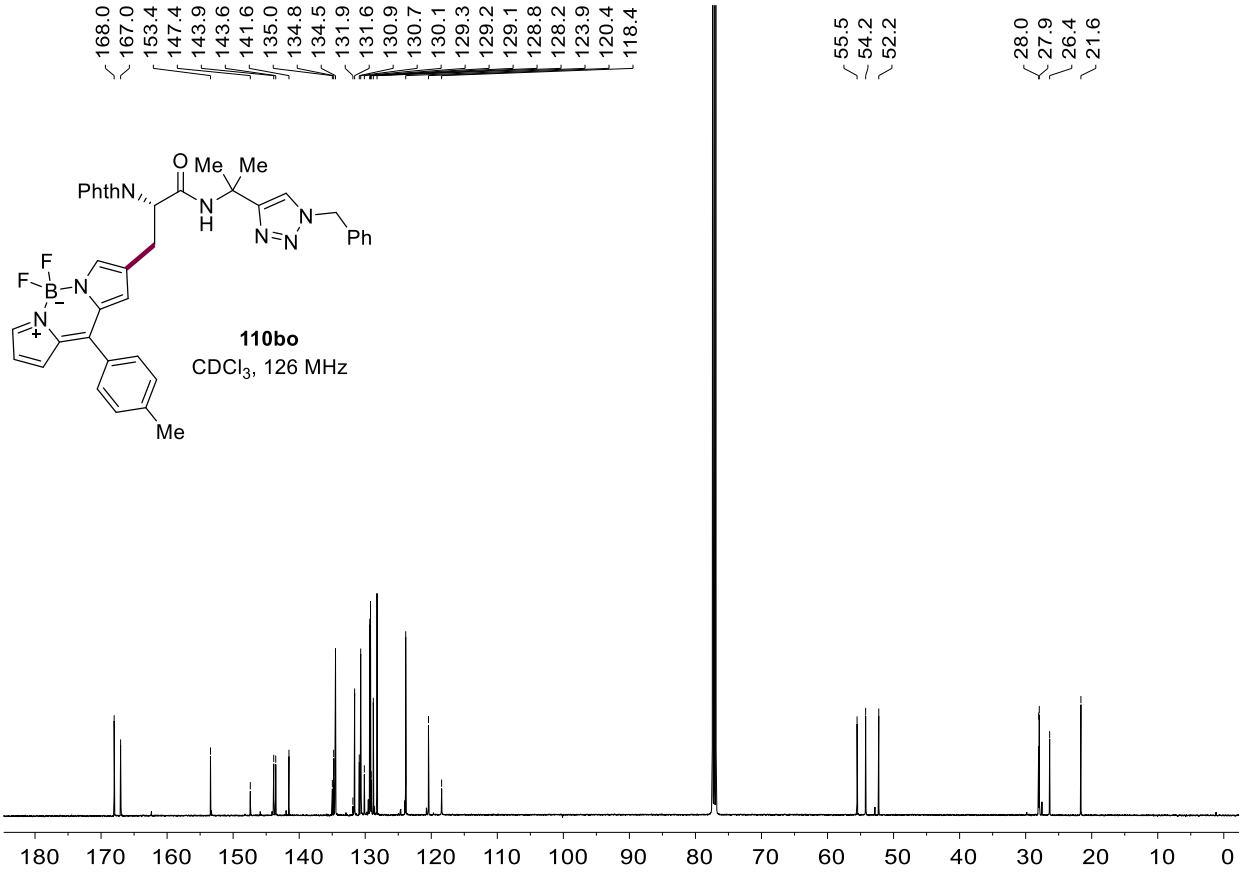


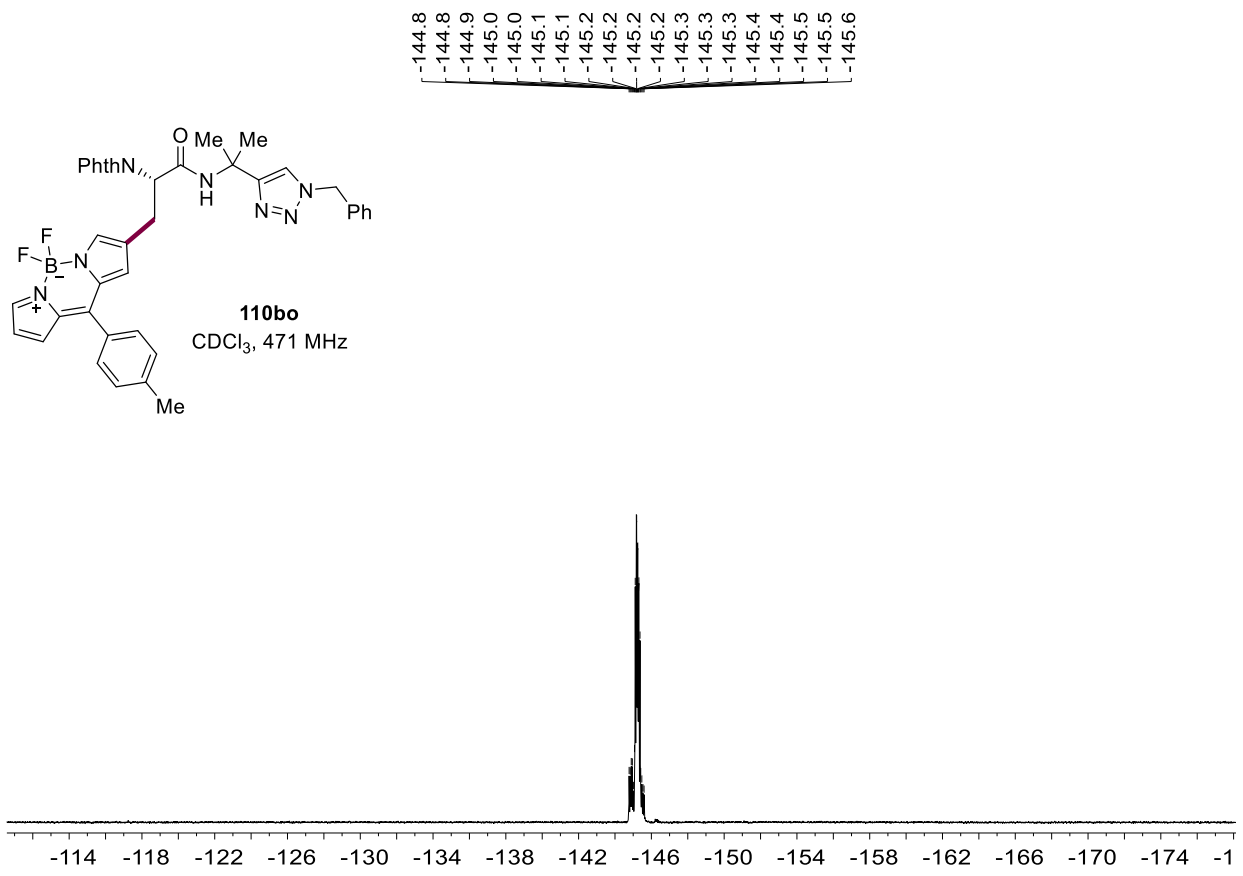


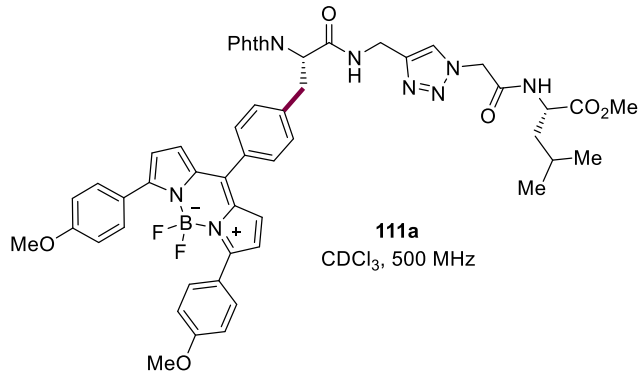


110bo
$CDCl_3$, 500 MHz

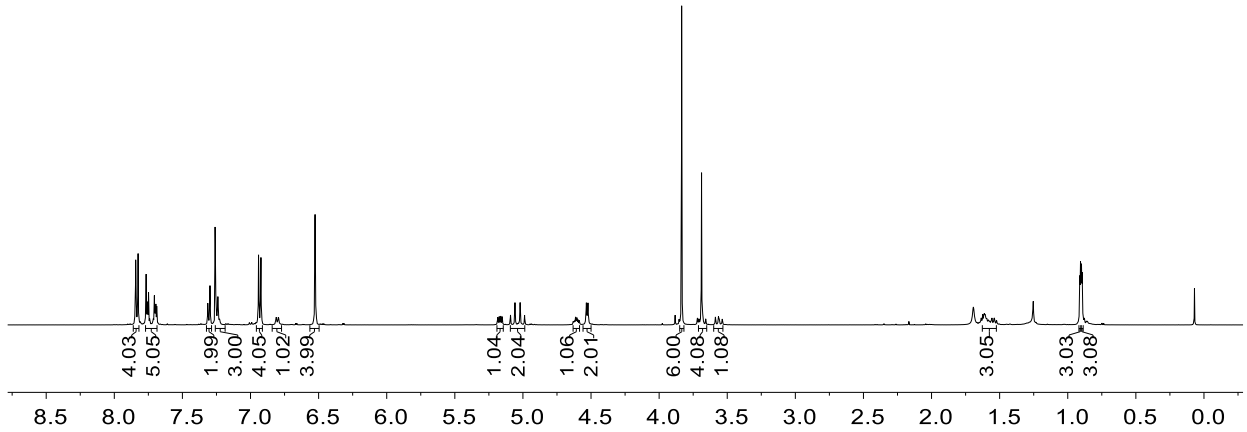


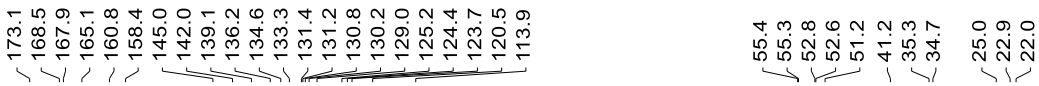

168.0
167.0
153.4
147.4
143.9
143.6
141.6
135.0
134.8
134.5
131.9
131.6
130.9
130.7
130.1
129.3
129.2
129.1
128.8
128.2
123.9
120.4
118.4
55.5
54.2
52.2
28.0
27.9
26.4
21.6
PhthN
O
Me
Me
N
H
N
N=N
N
Ph
F
F
B
N
N
Me
110bo
CDCl3, 126 MHz
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

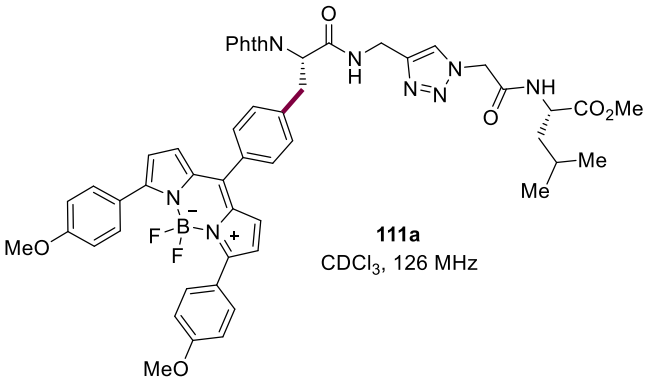

-144.8
-144.8
-144.9
-145.0
-145.0
-145.1
-145.1
-145.2
-145.2
-145.2
-145.2
-145.3
-145.3
-145.3
-145.4
-145.4
-145.5
-145.5
-145.6
PhthN
O
Me
Me
N
H
N
N=N
N
Ph
F
F
B
N
N
Me
110bo
CDCl3, 471 MHz
-114
-118
-122
-126
-130
-134
-138
-142
-146
-150
-154
-158
-162
-166
-170
-174
-1



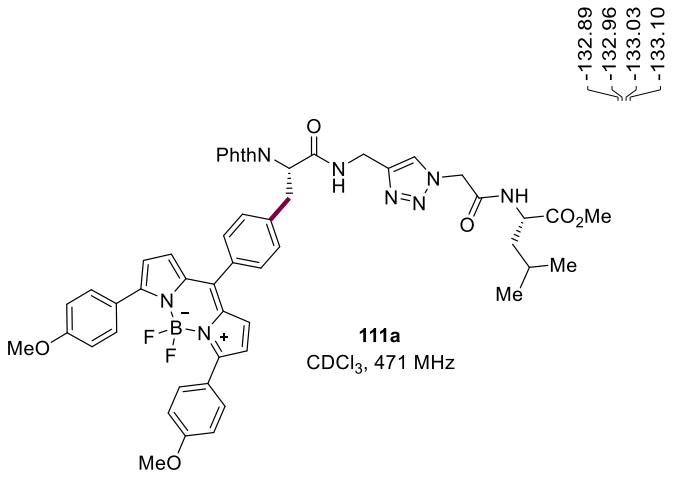
111a
$CDCl_3$, 500 MHz



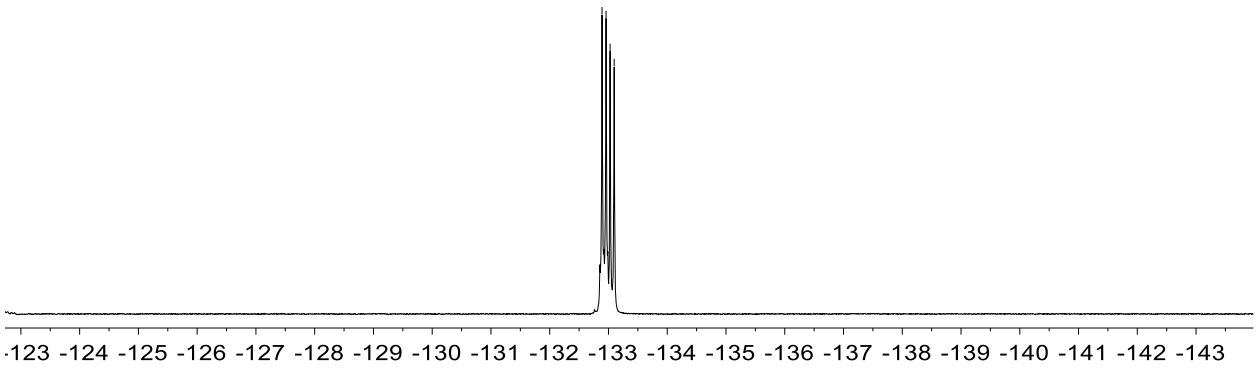


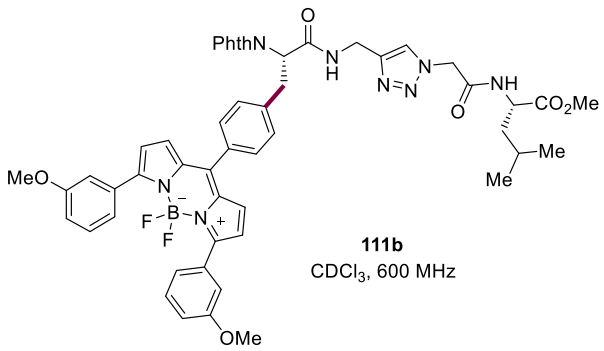


111a
$CDCl_3$, 126 MHz

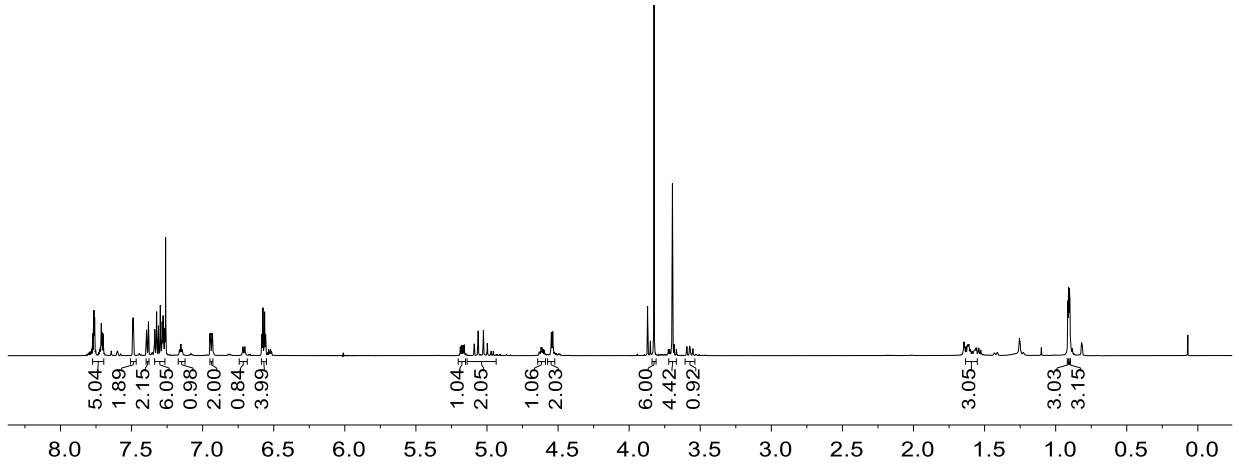


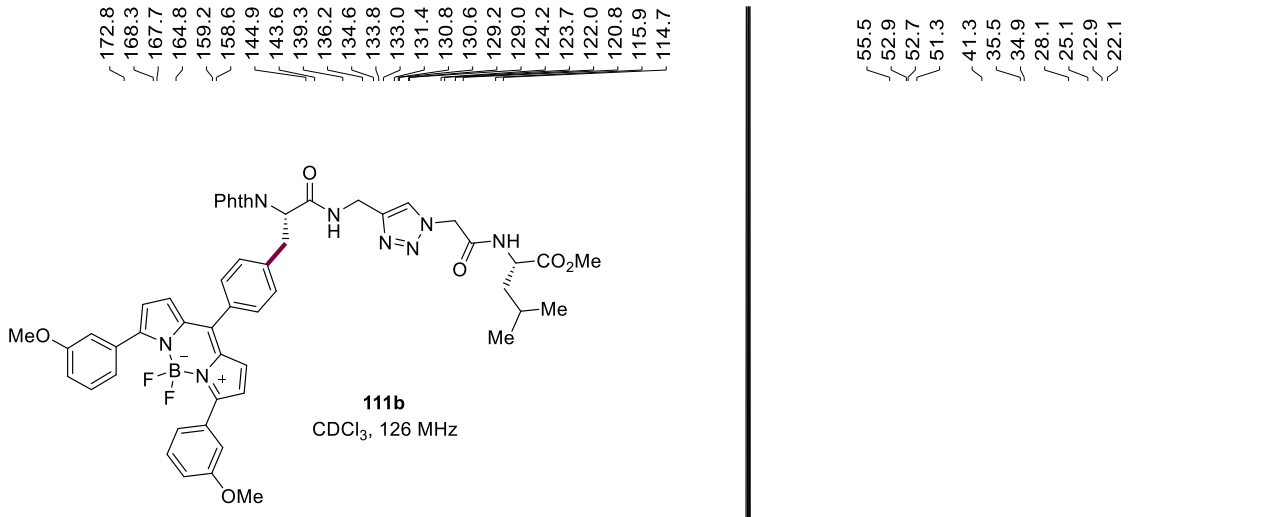
111a
$CDCl_3$, 471 MHz



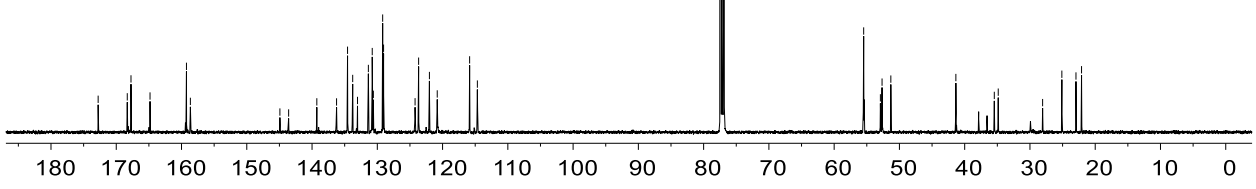


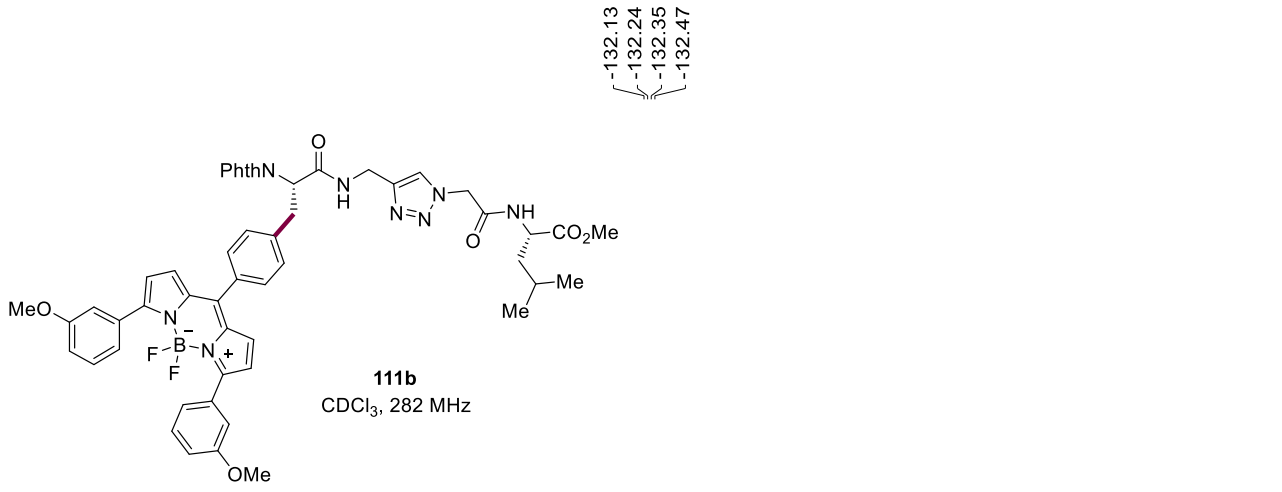
111b
$CDCl_3$, 600 MHz



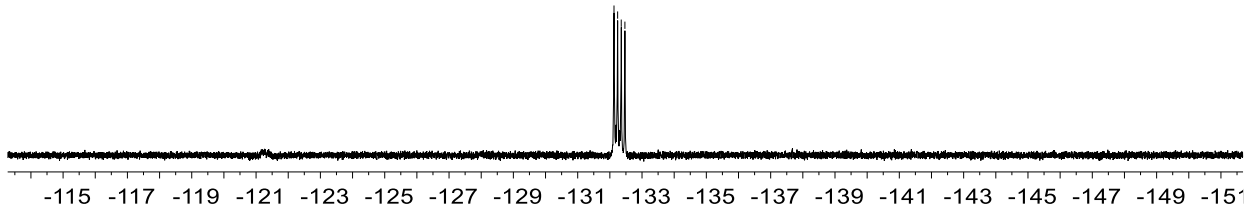


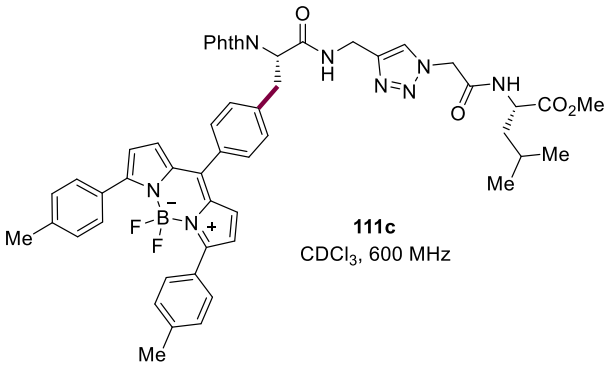
111b
$CDCl_3$, 126 MHz



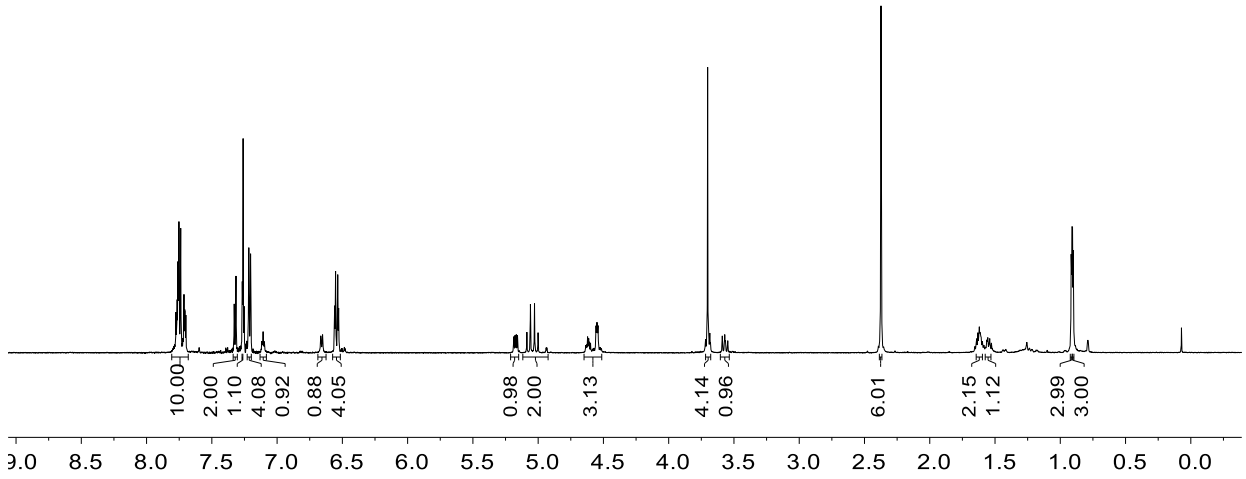


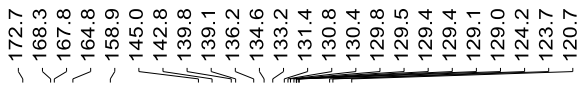
111b
$CDCl_3$, 282 MHz

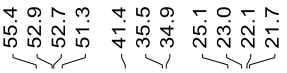


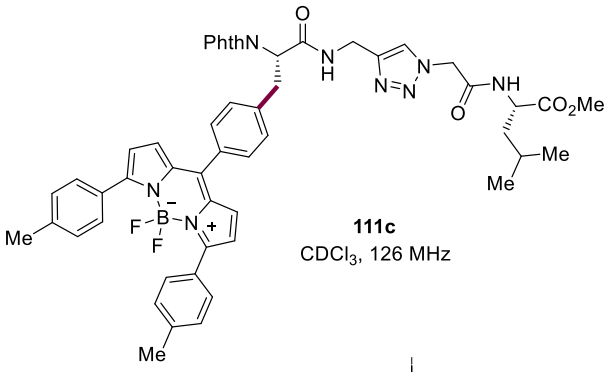


111c
$CDCl_3$, 600 MHz

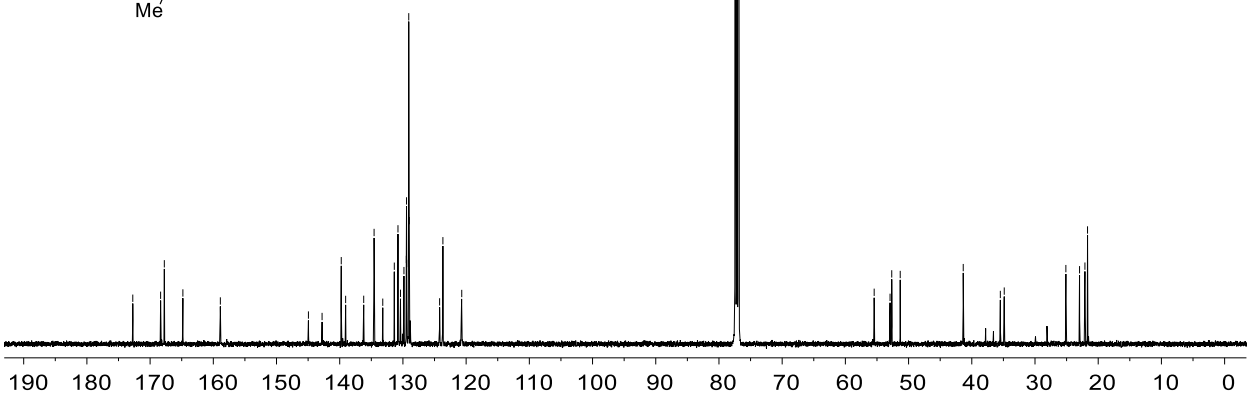


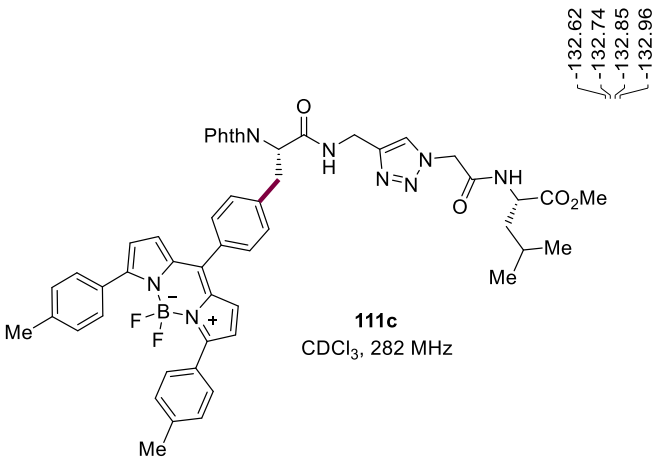




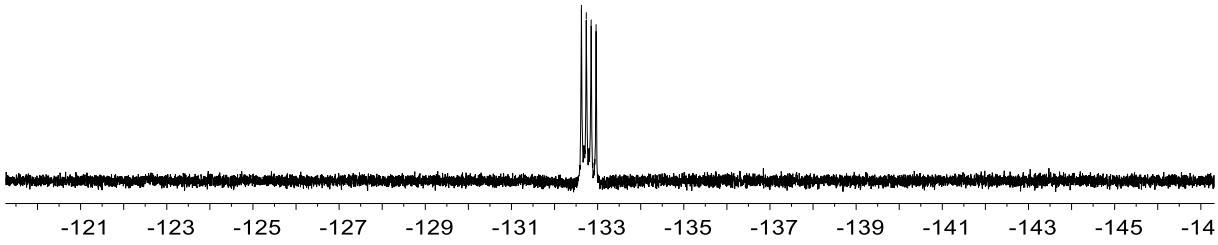


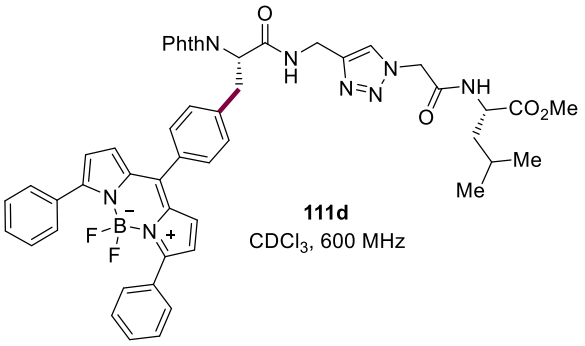
111c
$CDCl_3$, 126 MHz



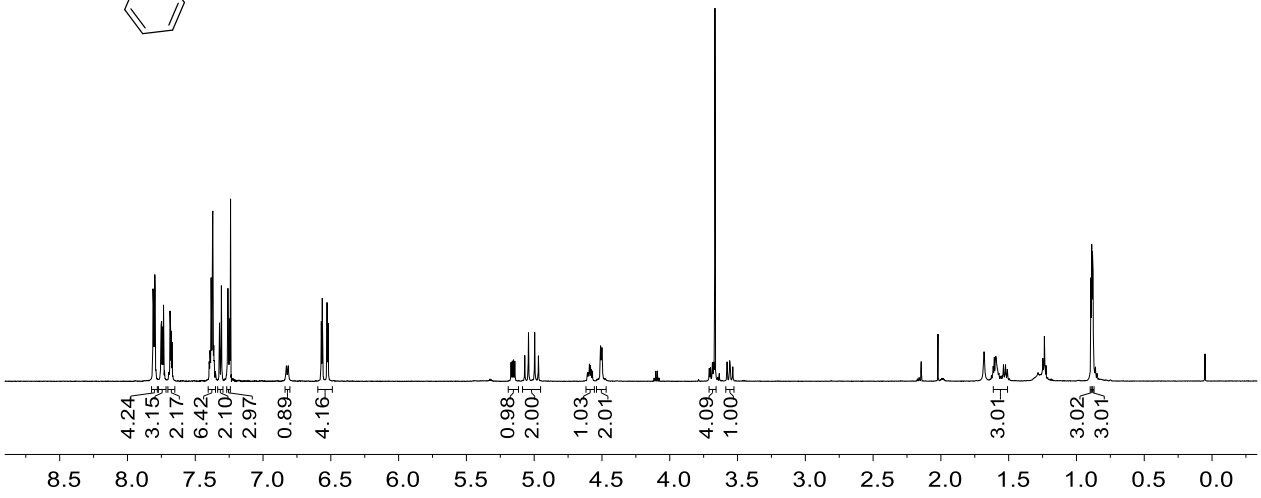


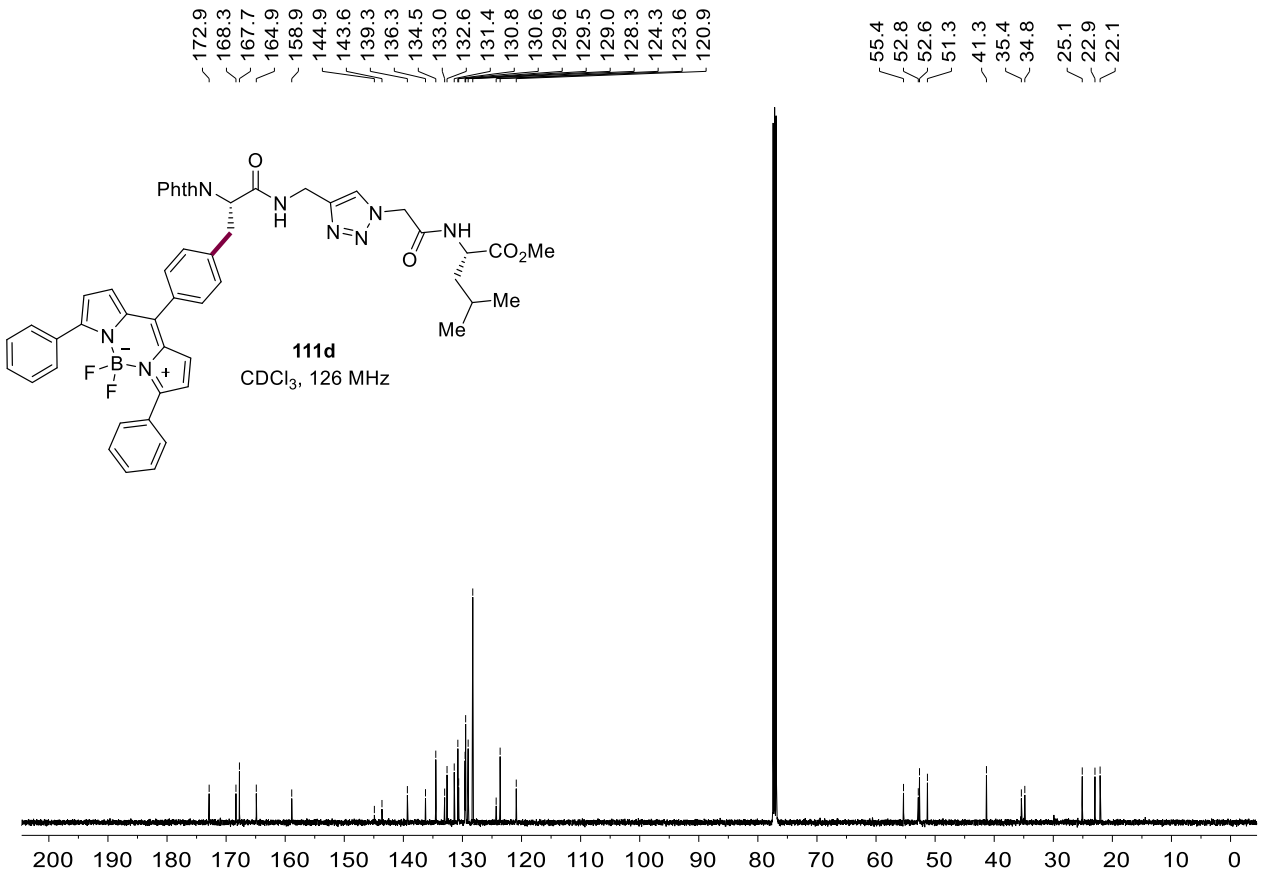
111c
$CDCl_3$, 282 MHz

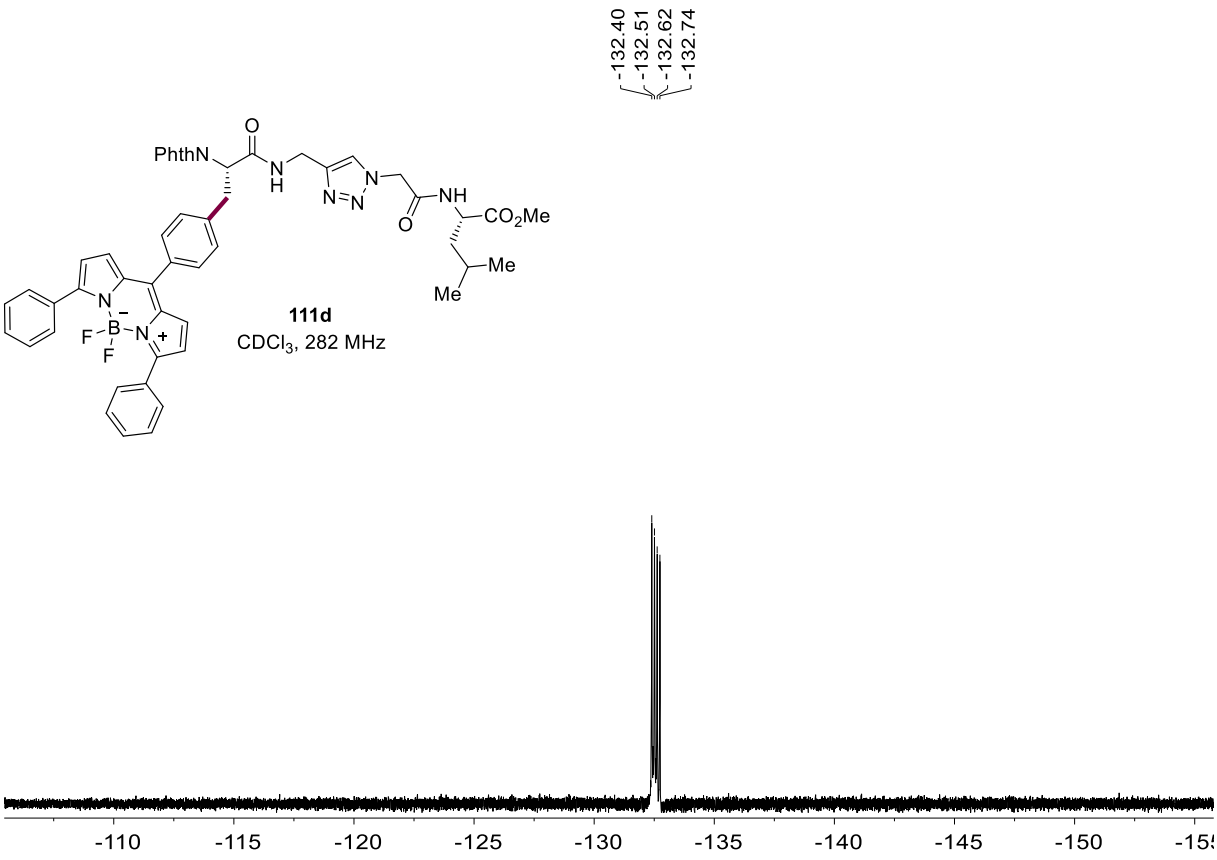


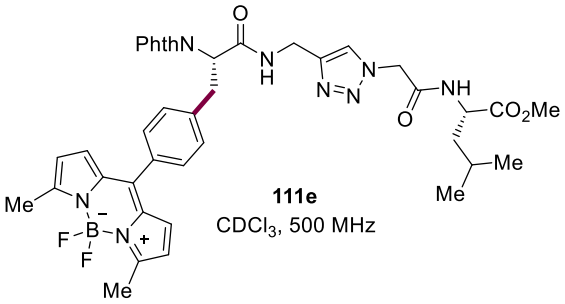


111d
$CDCl_3$, 600 MHz

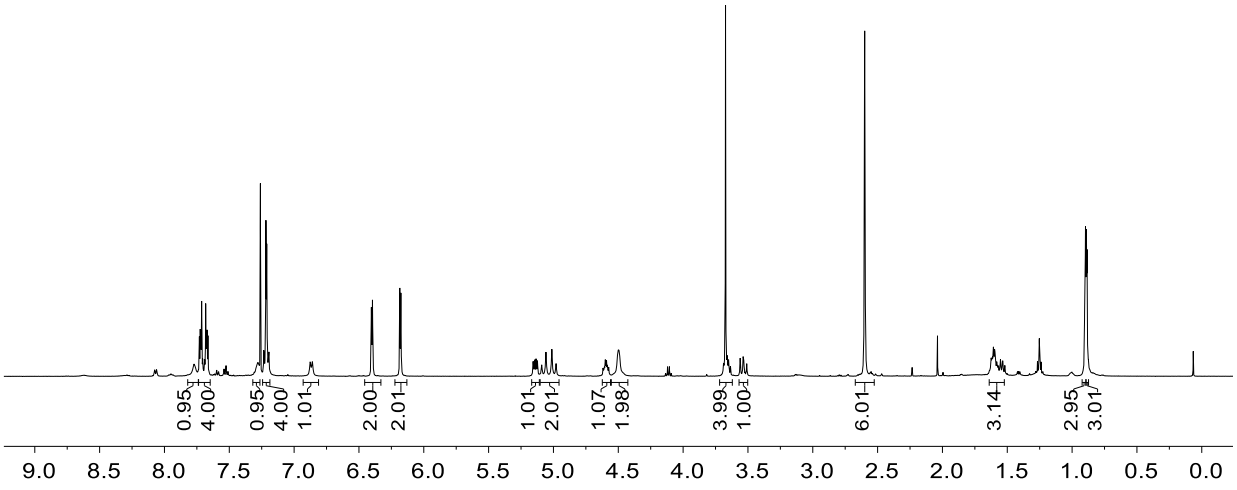


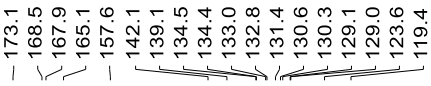

172.9
168.3
167.7
164.9
158.9
144.9
143.6
139.3
136.3
134.5
133.0
132.6
131.4
130.8
130.6
129.6
129.5
129.0
128.3
124.3
123.6
120.9
55.4
52.8
52.6
51.3
41.3
35.4
34.8
25.1
22.9
22.1
PhthN
O
N
H
N
N
N
NH
O
CO2Me
Me
Me
F
B
F
111d
CDCl3, 126 MHz
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

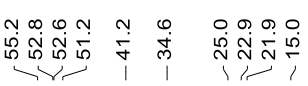

-132.40
-132.51
-132.62
-132.74
PhthN
O
N
H
N
N
N
NH
O
CO2Me
Me
Me
F
B
F
111d
CDCl3, 282 MHz
-110 -115 -120 -125 -130 -135 -140 -145 -150 -15

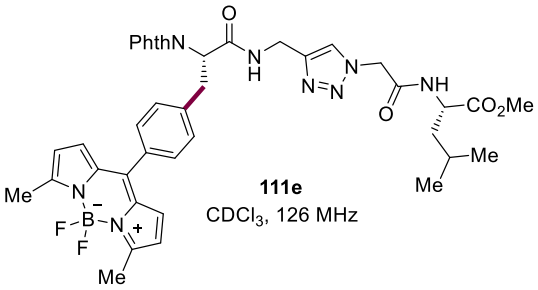


111e
$CDCl_3$, 500 MHz

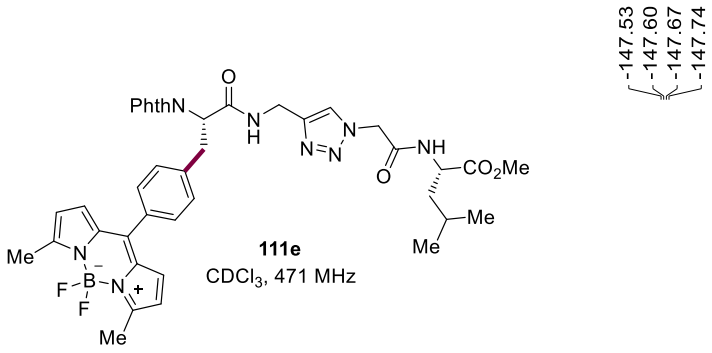


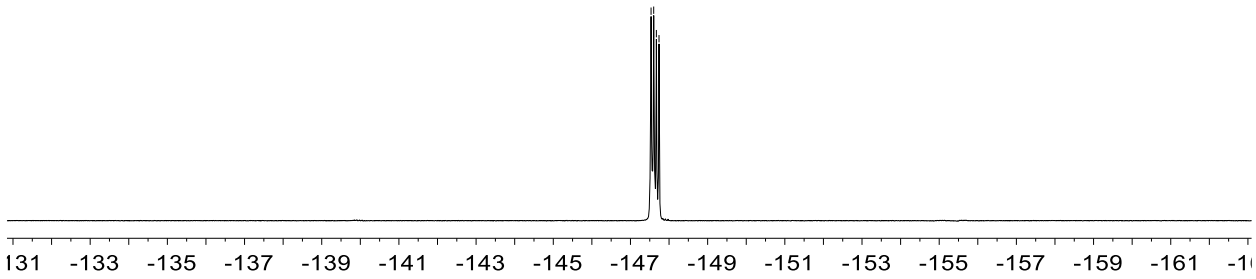


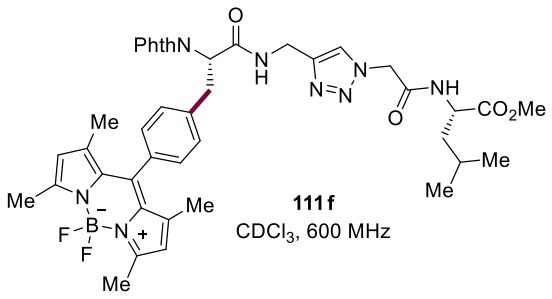


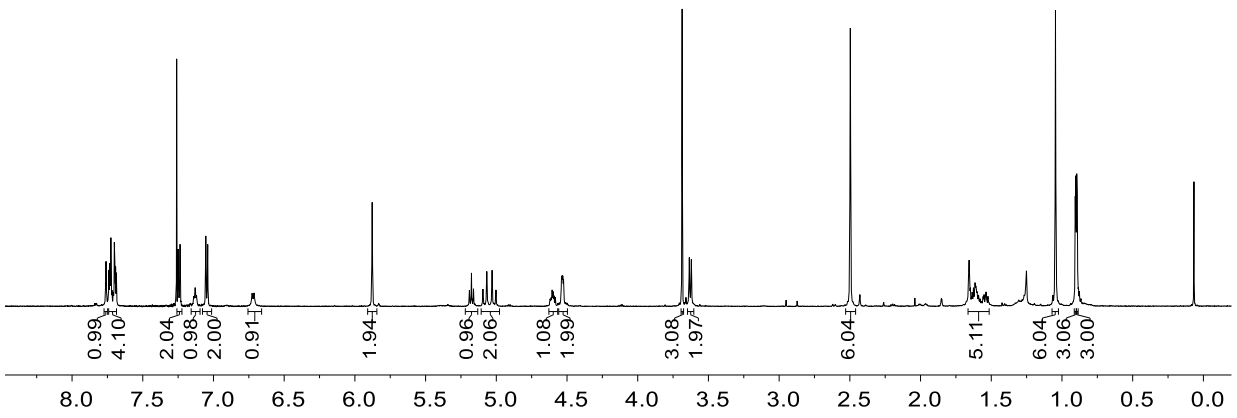


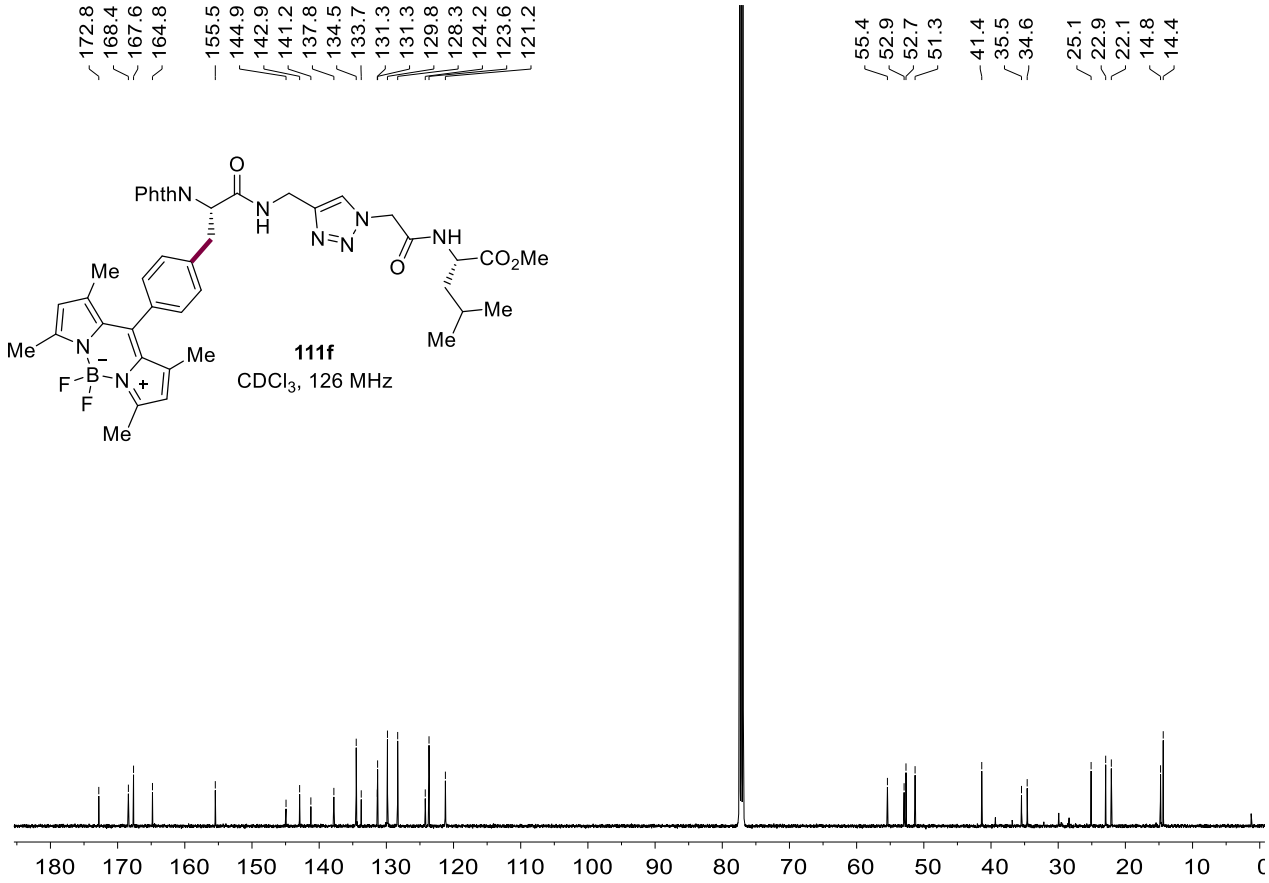
111e
$CDCl_3$, 126 MHz

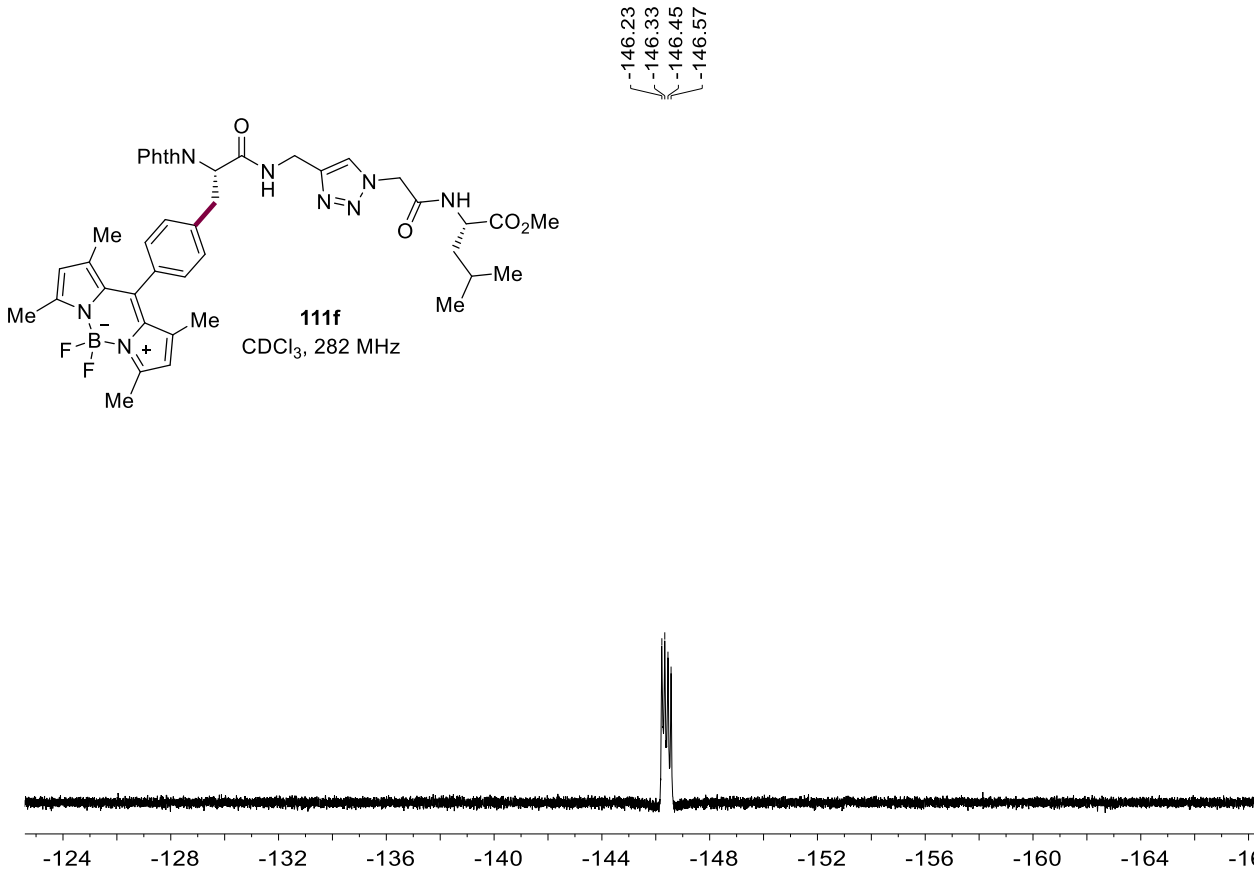

-147.53
-147.60
-147.67
-147.74
PhthN
O
N
H
N
N=N
O
NH
CO2Me
Me
Me
Me
N
F
B
F
N
Me
111e
CDCl3, 471 MHz

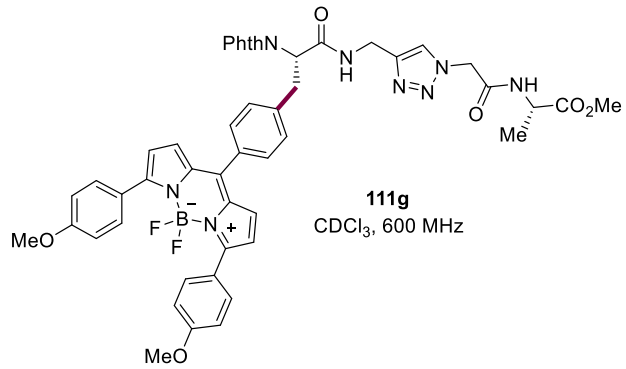

131 -133 -135 -137 -139 -141 -143 -145 -147 -149 -151 -153 -155 -157 -159 -161


PhthN
O
N
H
N
N=N
O
NH
CO2Me
Me
Me
Me
Me
Me
N
F
B
F
N
Me
111f
CDCl3, 600 MHz


0.99
4.10
2.04
0.98
2.00
0.91
1.94
0.96
2.06
1.08
1.99
3.08
1.97
6.04
5.11
6.04
3.06
3.00
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

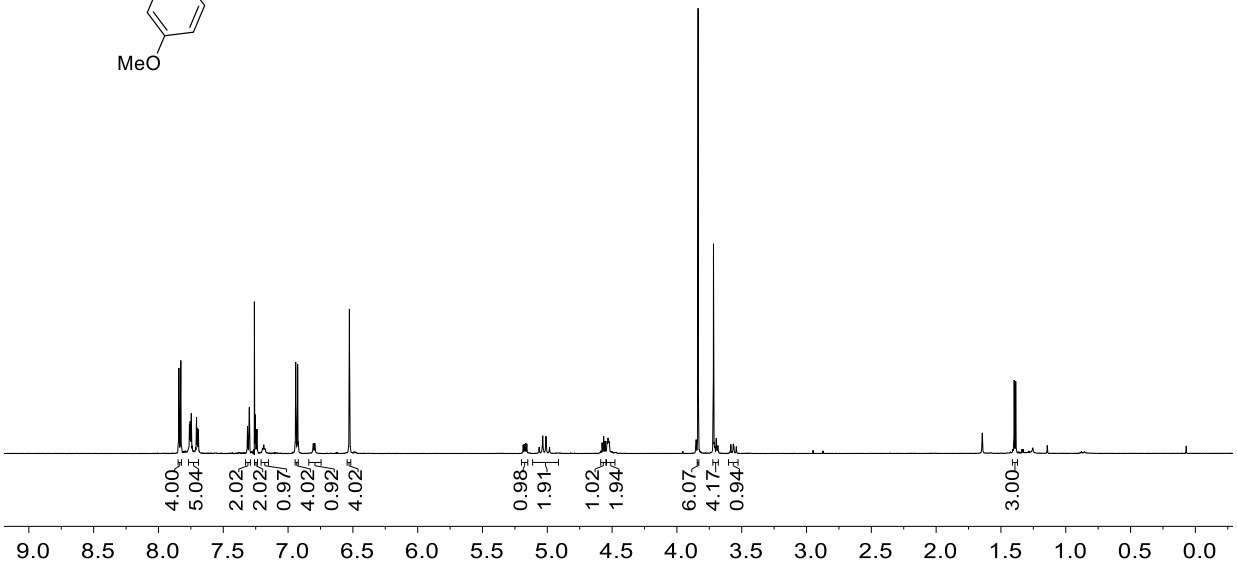

172.8
168.4
167.6
164.8
155.5
144.9
142.9
141.2
137.8
134.5
133.7
131.3
131.3
129.8
128.3
124.2
123.6
121.2
55.4
52.9
52.7
51.3
41.4
35.5
34.6
25.1
22.9
22.1
14.8
14.4
PhthN
O
N
H
N
N=N
O
NH
CO2Me
Me
Me
Me
Me
Me
N
B
F
F
N+
Me
111f
CDCl3, 126 MHz
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

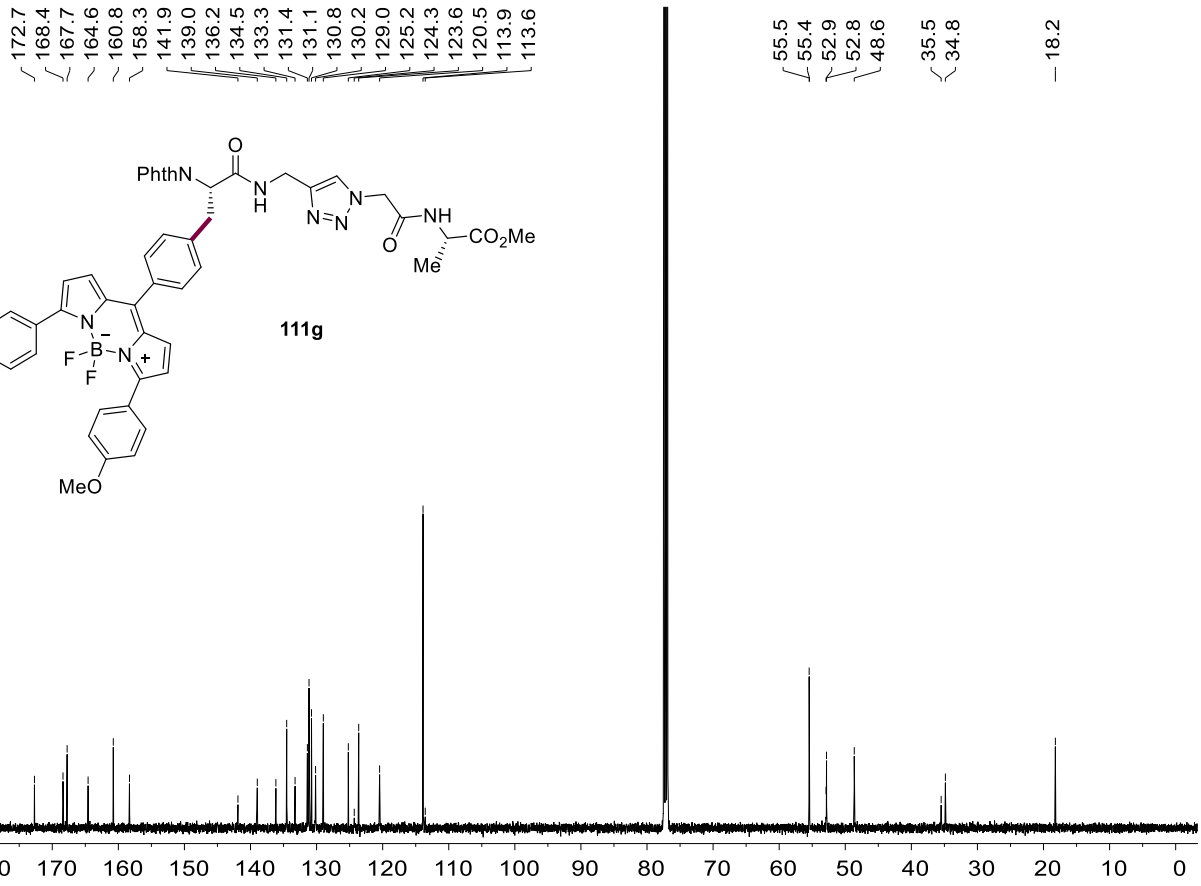

-146.23
-146.33
-146.45
-146.57
PhthN
O
N
H
N
N=N
O
NH
CO2Me
Me
Me
Me
Me
Me
N
B
F
F
N+
Me
111f
CDCl3, 282 MHz
-124
-128
-132
-136
-140
-144
-148
-152
-156
-160
-164



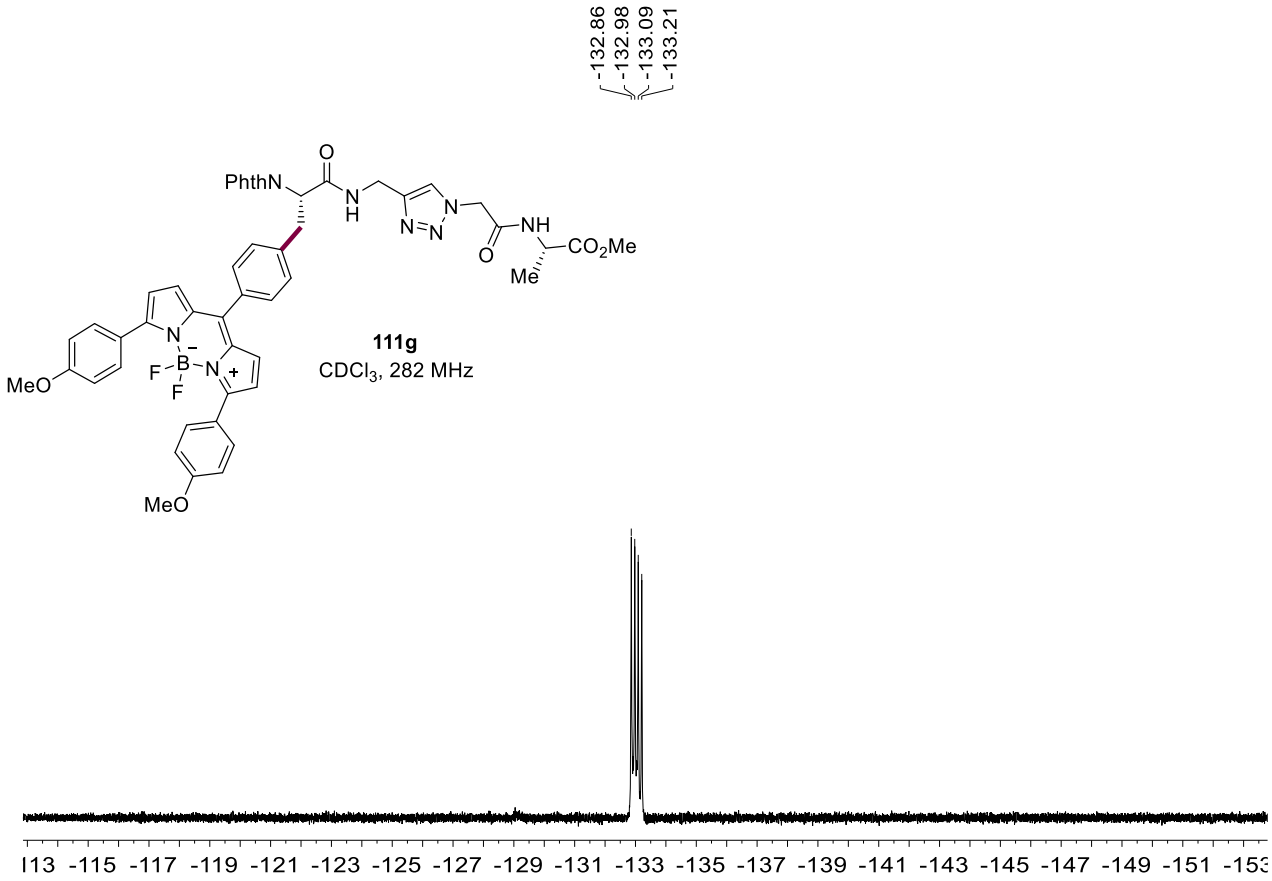
111g

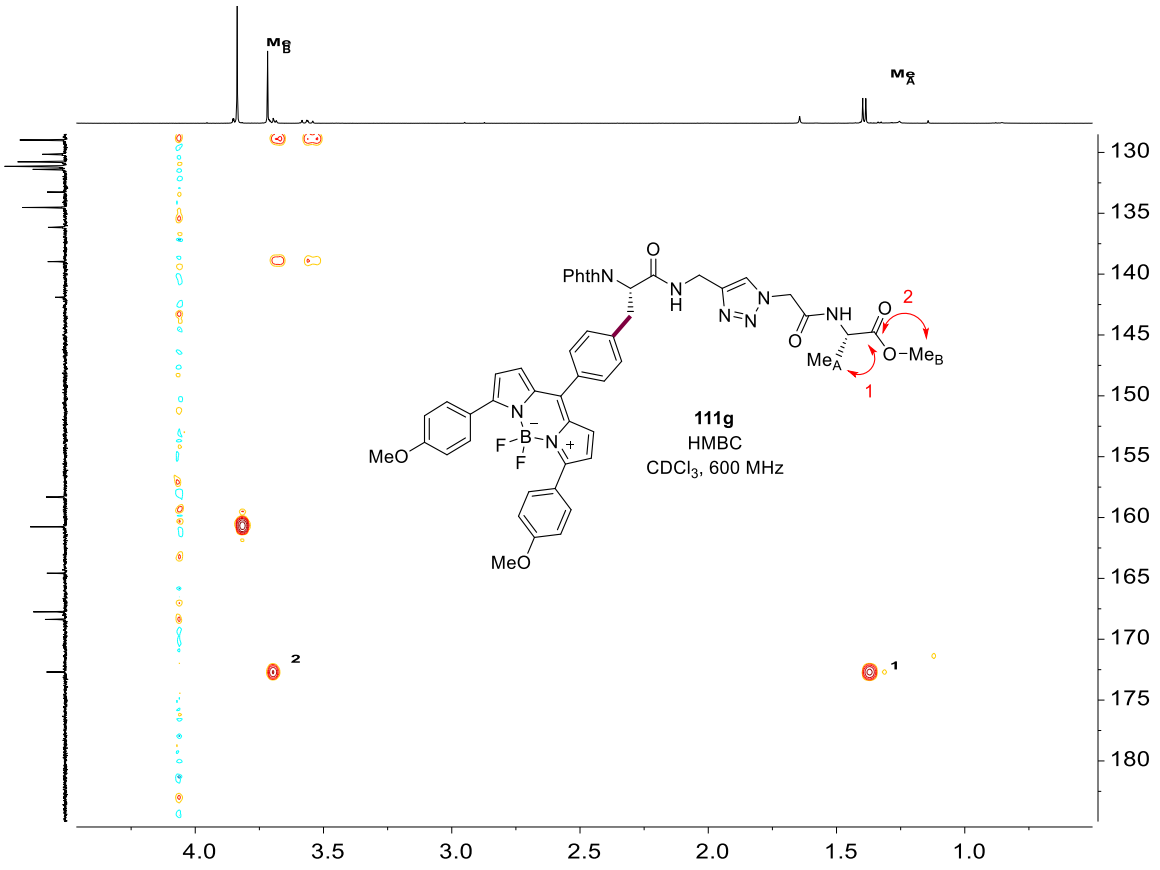
$CDCl_3$, 600 MHz

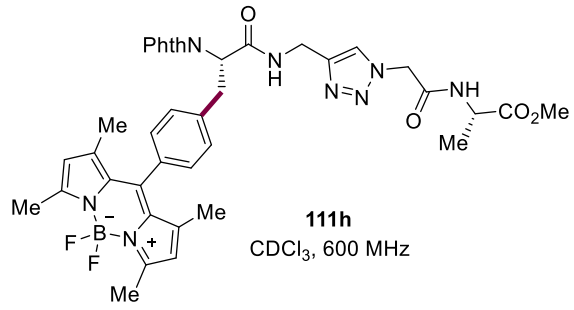




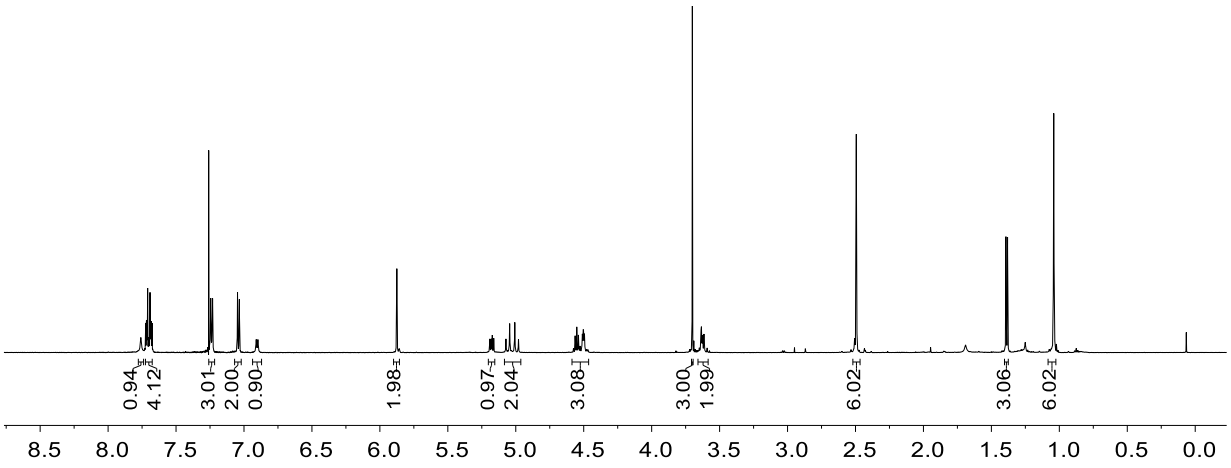
111g

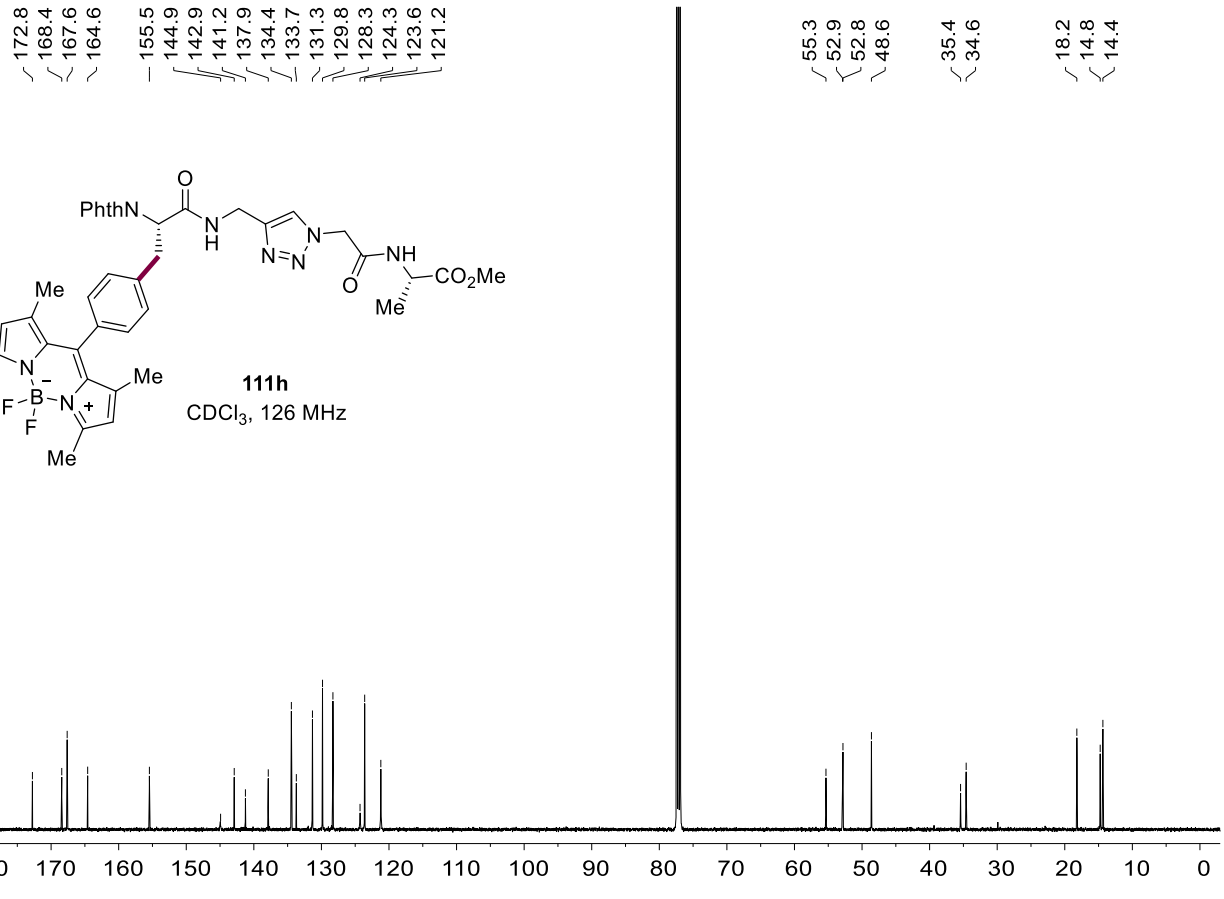

-132.86
-132.98
-133.09
-133.21
PhthN
O
N
H
N
N=N
N
NH
O
CO2Me
Me
MeO
F
B
F
N
N
+
MeO
111g
CDCl3, 282 MHz
-113 -115 -117 -119 -121 -123 -125 -127 -129 -131 -133 -135 -137 -139 -141 -143 -145 -147 -149 -151 -153


MeB
MeA
130
135
140
145
150
155
160
165
170
175
180
PhthN
O
N
H
N
N=N
N
NH
O
MeA
O
2
1
O-MeB
MeO
F
B
F
N
N
+
MeO
111g
HMBC
CDCl3, 600 MHz
2
1
4.0
3.5
3.0
2.5
2.0
1.5
1.0

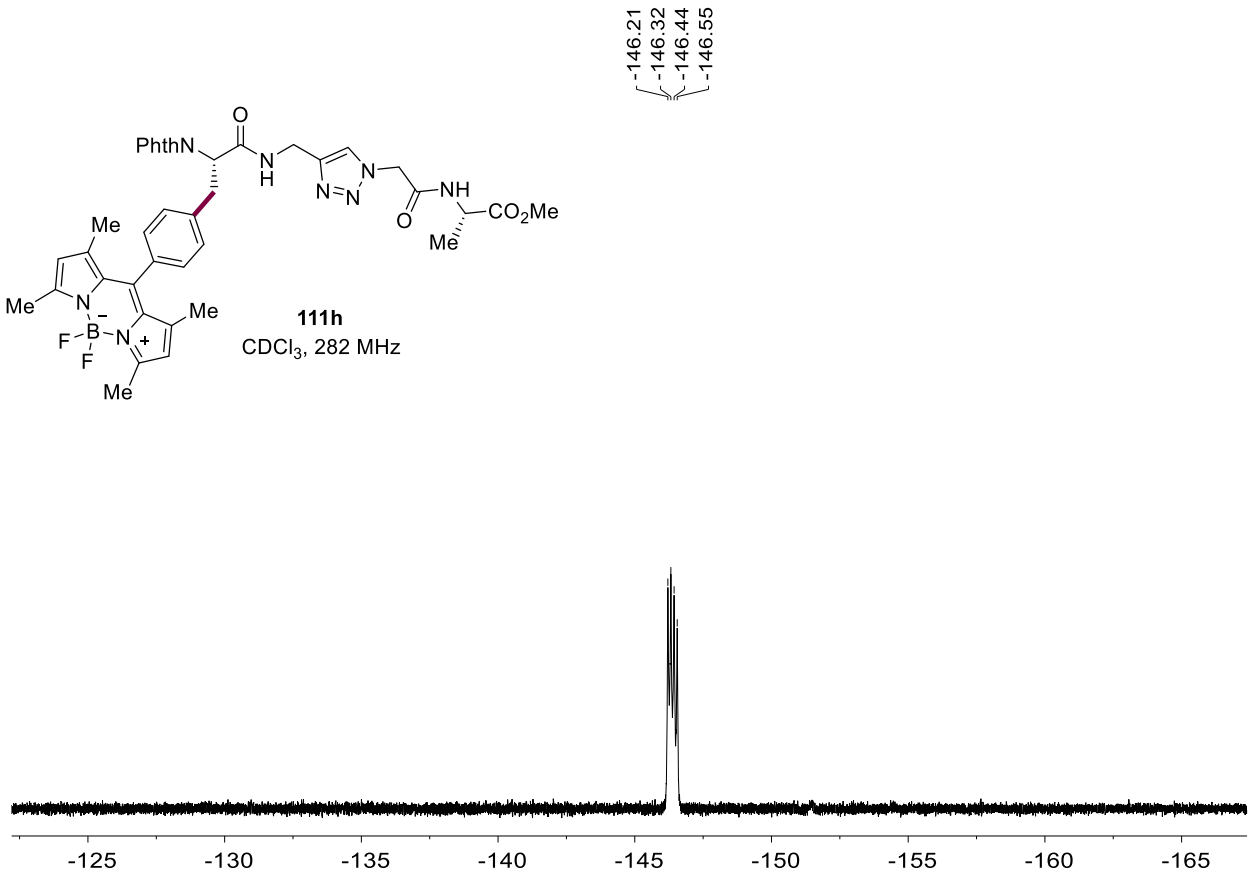


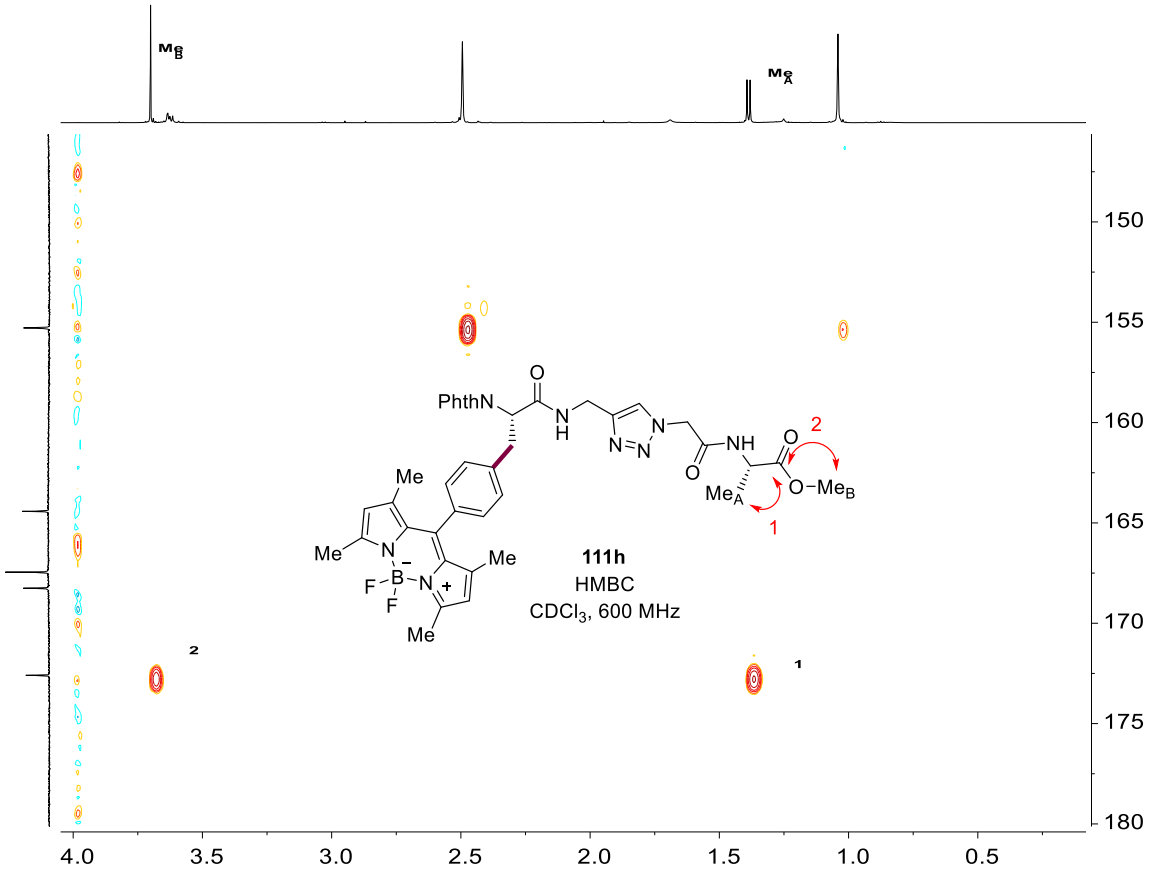
111h
$CDCl_3$, 600 MHz

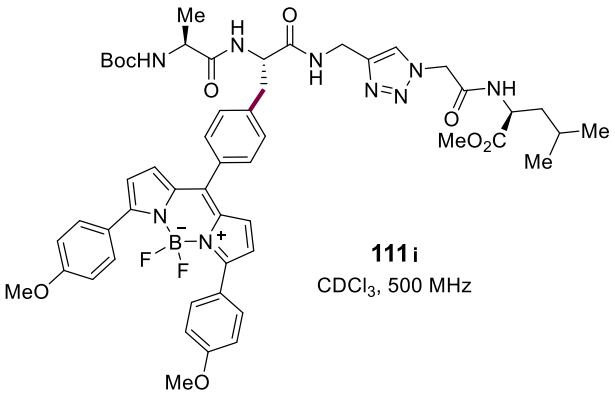




111h
$CDCl_3$, 126 MHz

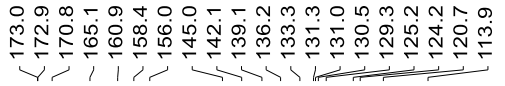

-146.21
-146.32
-146.44
-146.55
111h
CDCl3, 282 MHz
-125
-130
-135
-140
-145
-150
-155
-160
-165

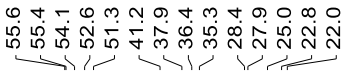

111h
HMBC
CDCl3, 600 MHz
150
155
160
165
170
175
180
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

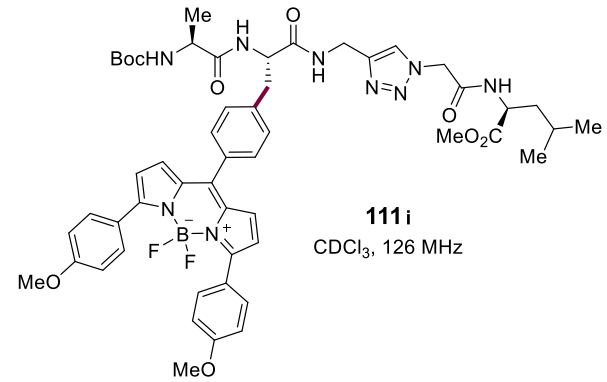


111i

$CDCl_3$, 500 MHz

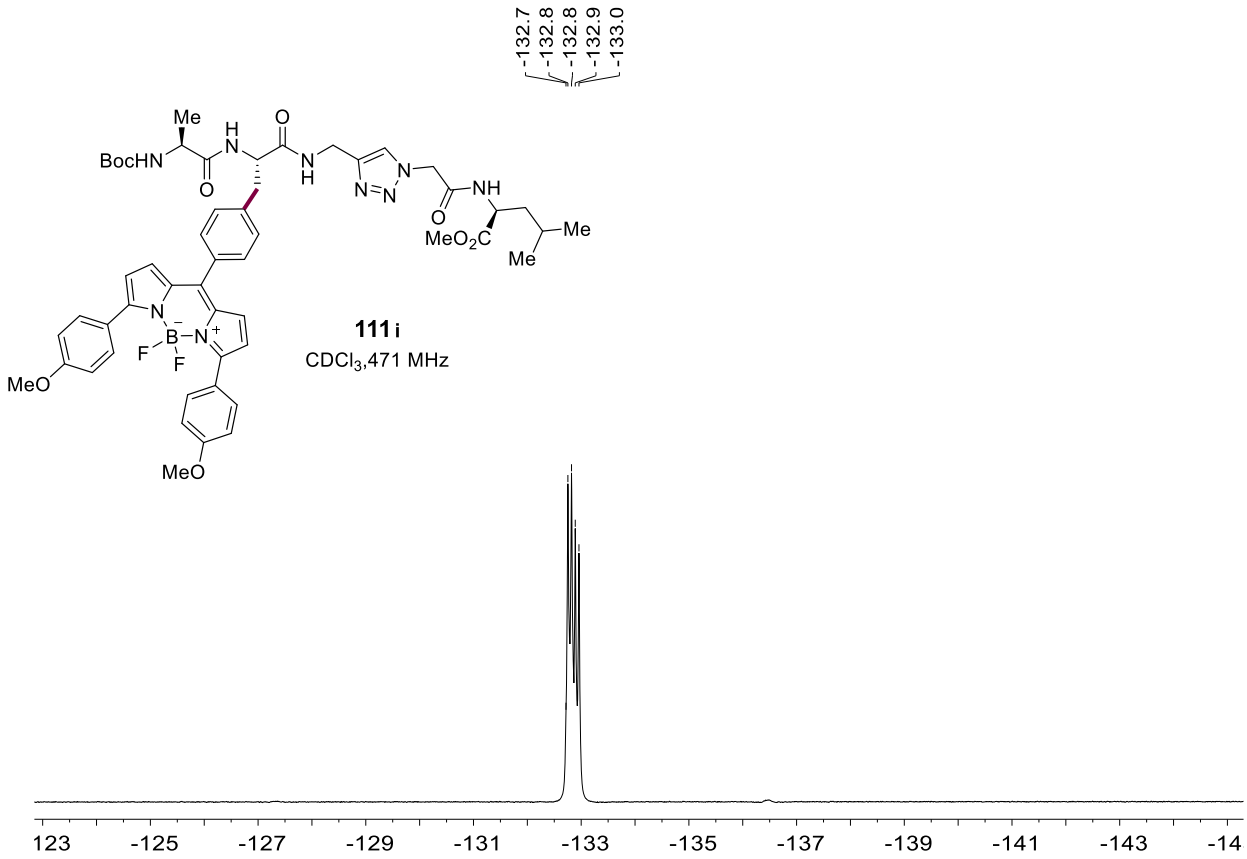


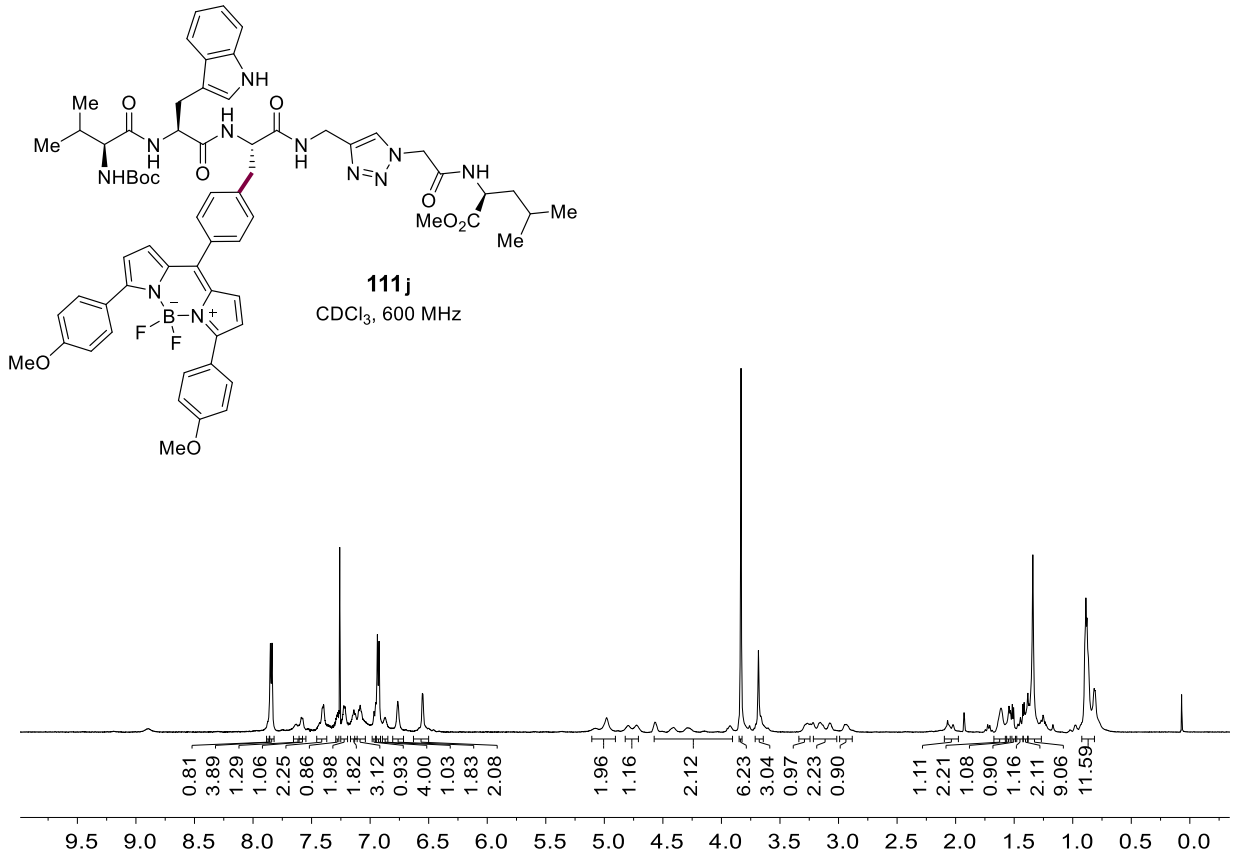


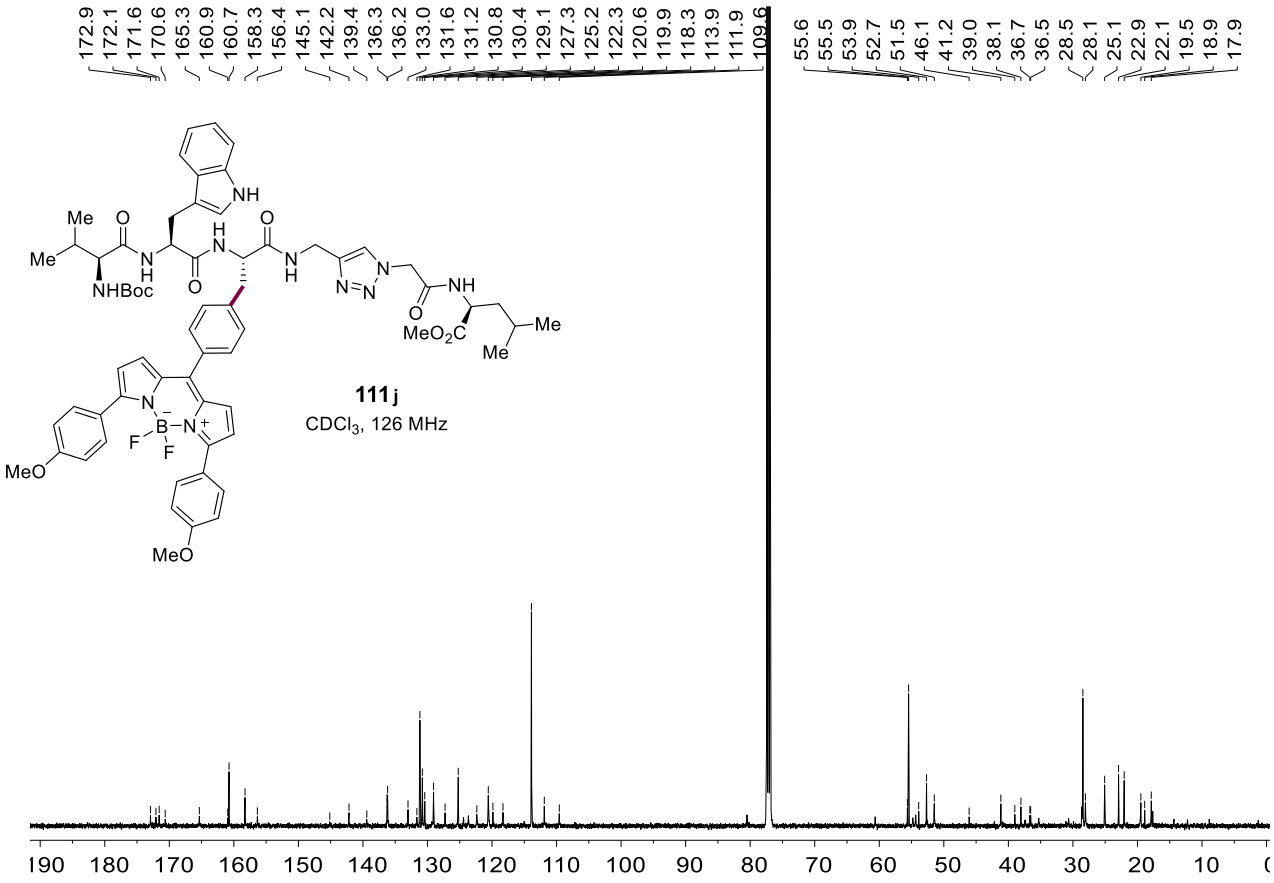


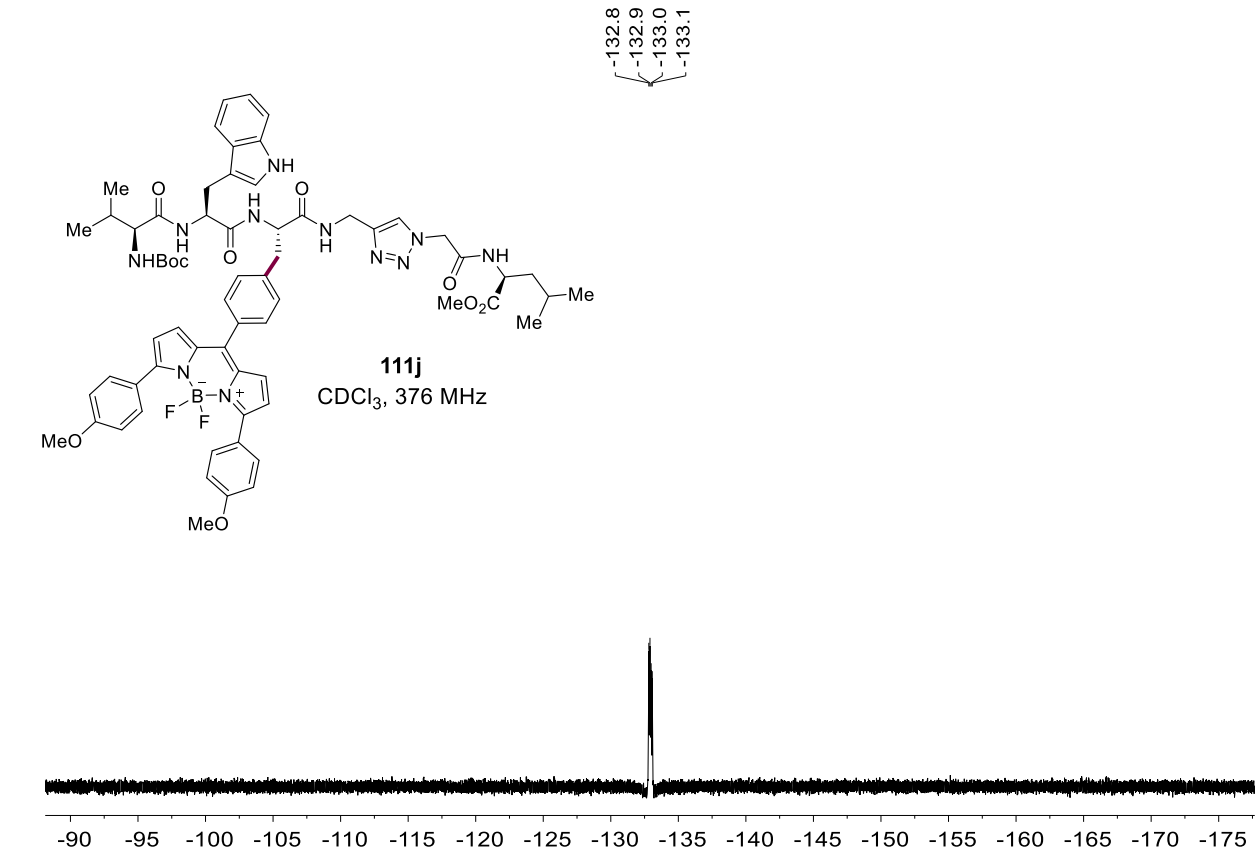
111i

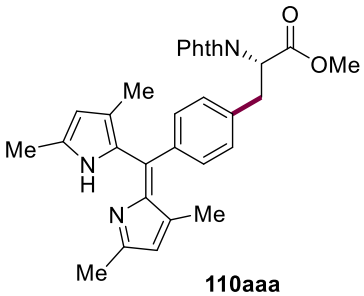
$CDCl_3$, 126 MHz


-132.7
-132.8
-132.8
-132.9
-133.0
111i
CDCl3,471 MHz
123
-125
-127
-129
-131
-133
-135
-137
-139
-141
-143
-14

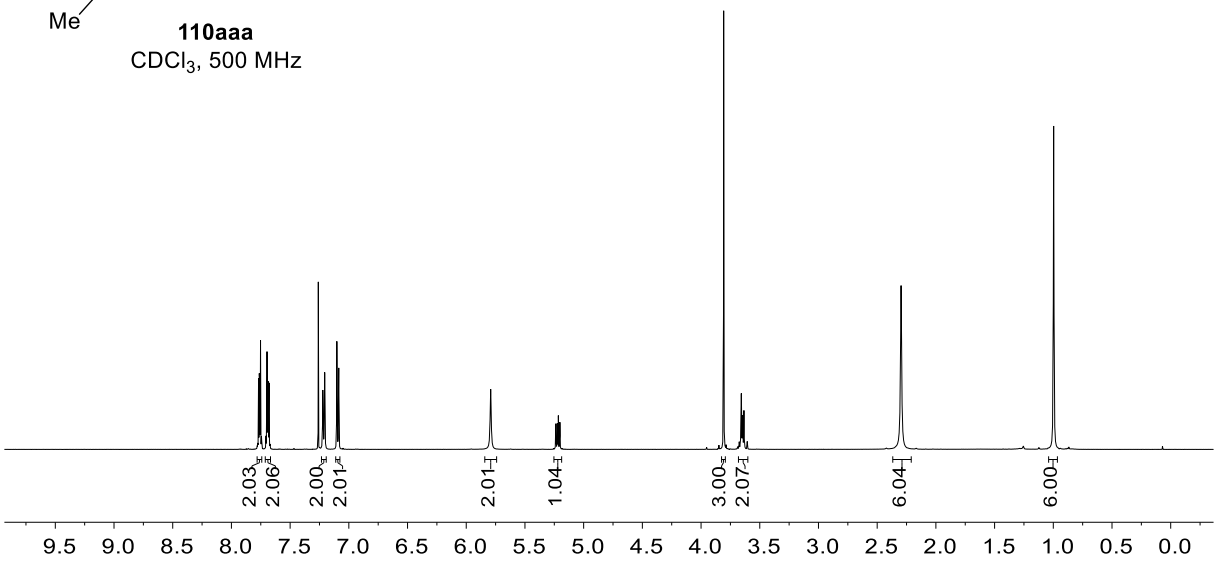

111j
CDCl3, 600 MHz
0.81
3.89
1.29
1.06
2.25
0.86
1.98
1.82
3.12
0.93
4.00
1.03
1.83
2.08
1.96
1.16
2.12
6.23
3.04
0.97
2.23
0.90
1.11
2.21
1.08
0.90
1.16
2.11
9.06
11.59
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

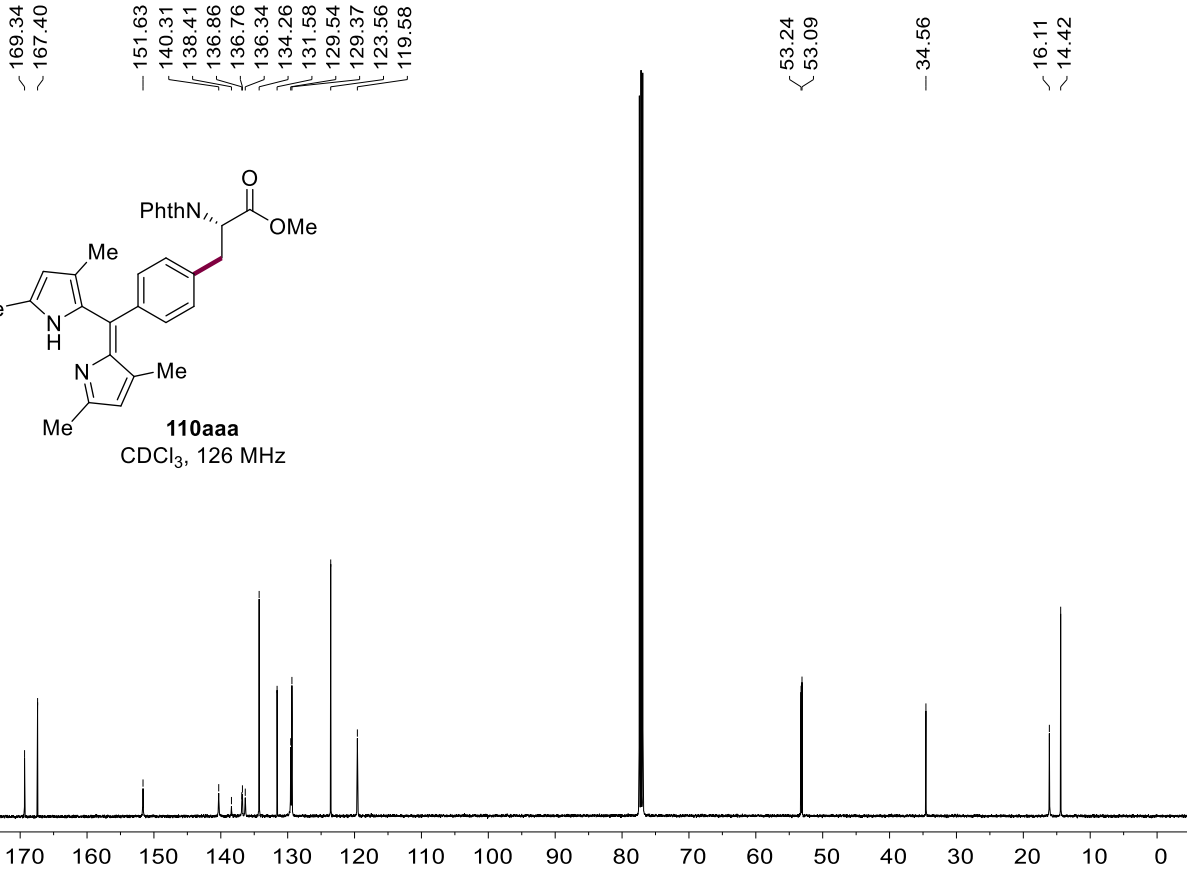

172.9
172.1
171.6
170.6
165.3
160.9
160.7
158.3
156.4
145.1
142.2
139.4
136.3
136.2
133.0
131.6
131.2
130.8
130.4
129.1
127.3
125.2
122.3
120.6
119.9
118.3
113.9
111.9
109.6
55.6
55.5
53.9
52.7
51.5
46.1
41.2
39.0
38.1
36.7
36.5
28.5
28.1
25.1
22.9
22.1
19.5
18.9
17.9
111j
CDCl3, 126 MHz
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10


-132.8
-132.9
-133.0
-133.1
111j
CDCl3, 376 MHz
-90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175

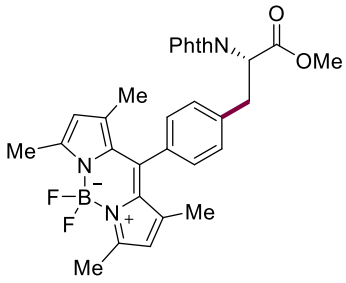


110aaa
$CDCl_3$, 500 MHz

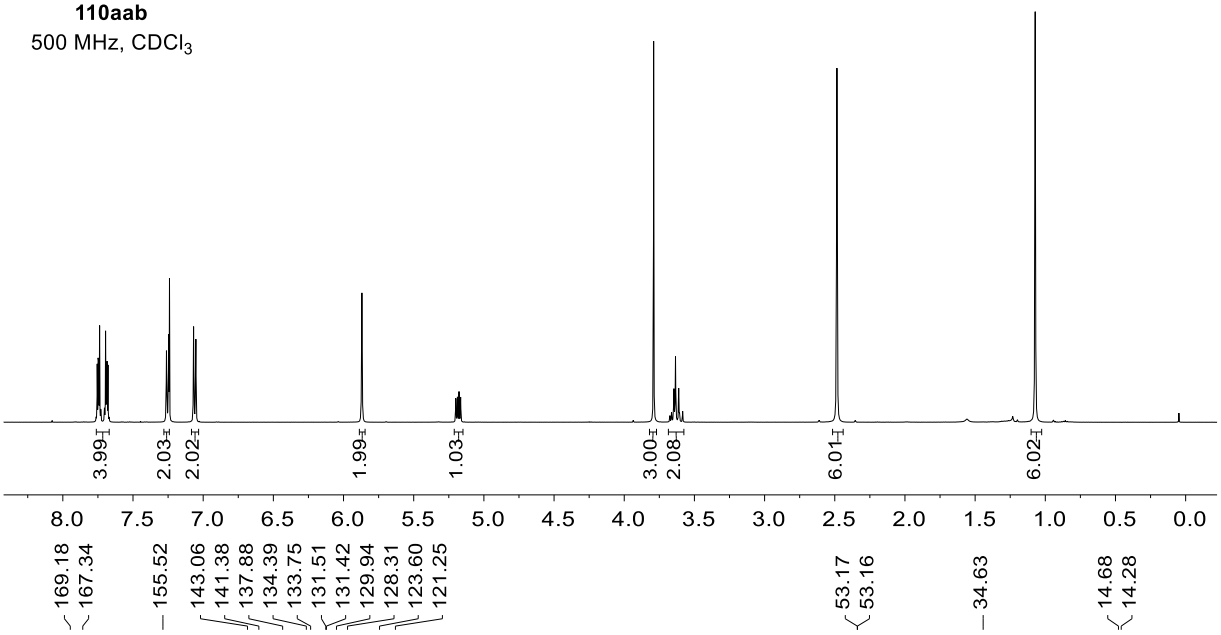


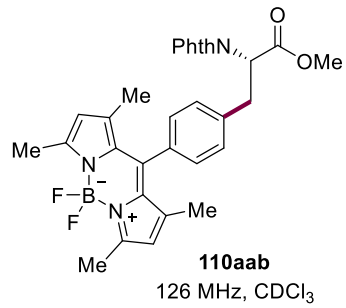


110aaa
$CDCl_3$, 126 MHz

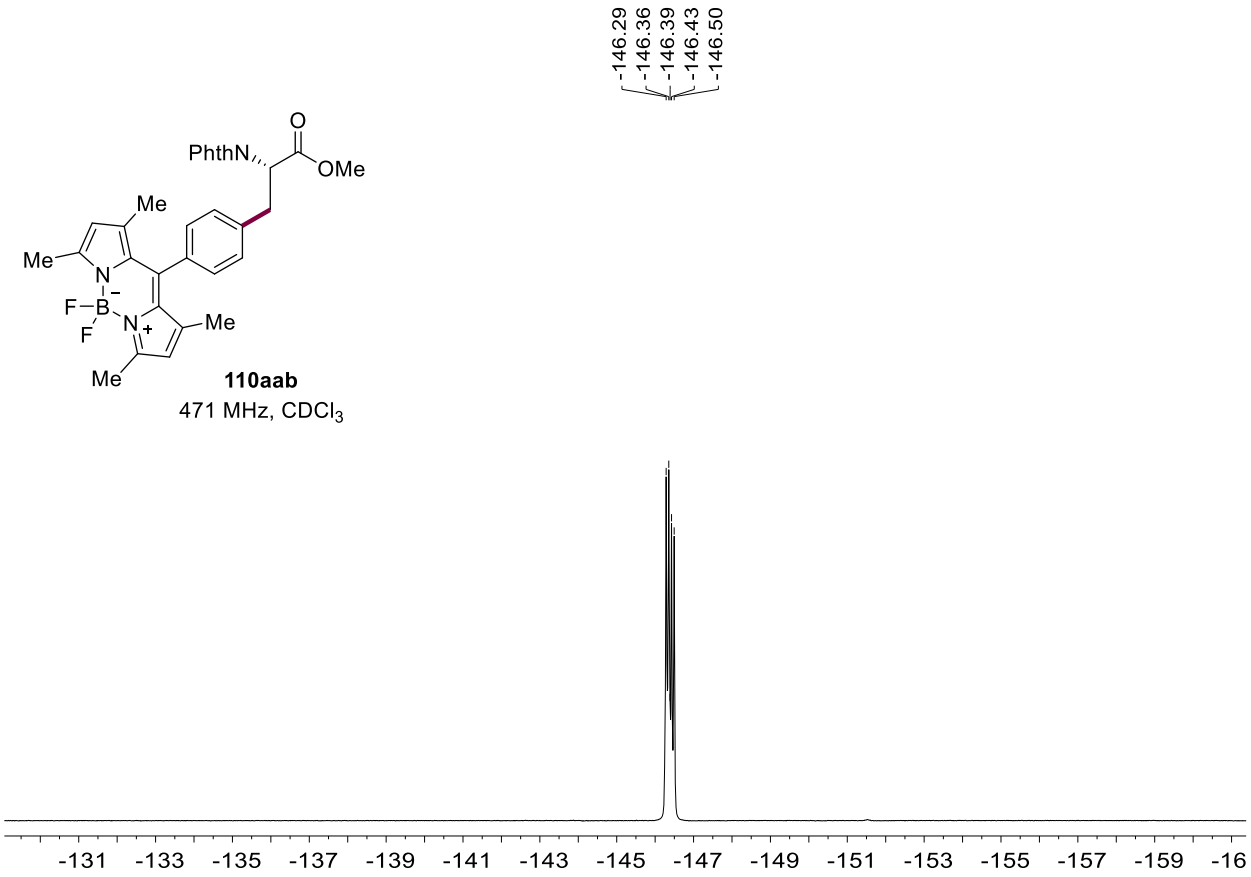


110aab
500 MHz, $CDCl_3$

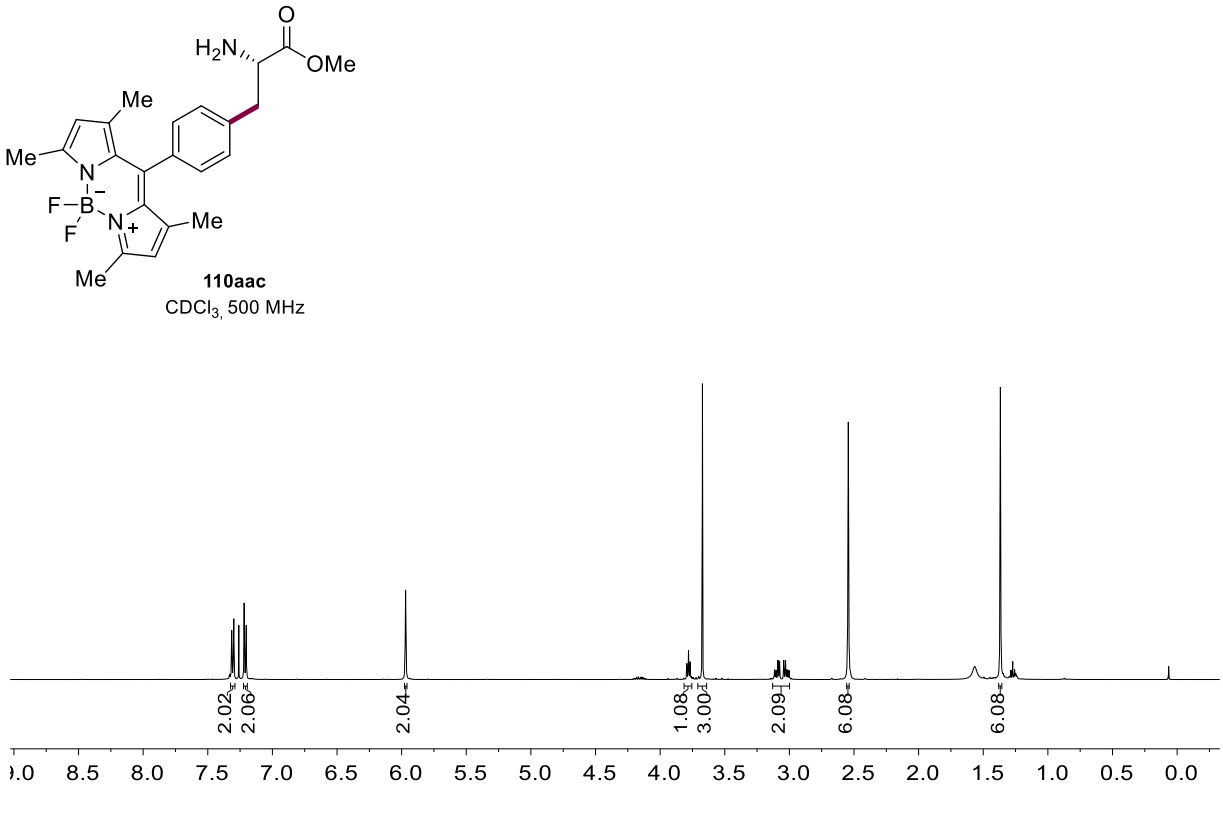




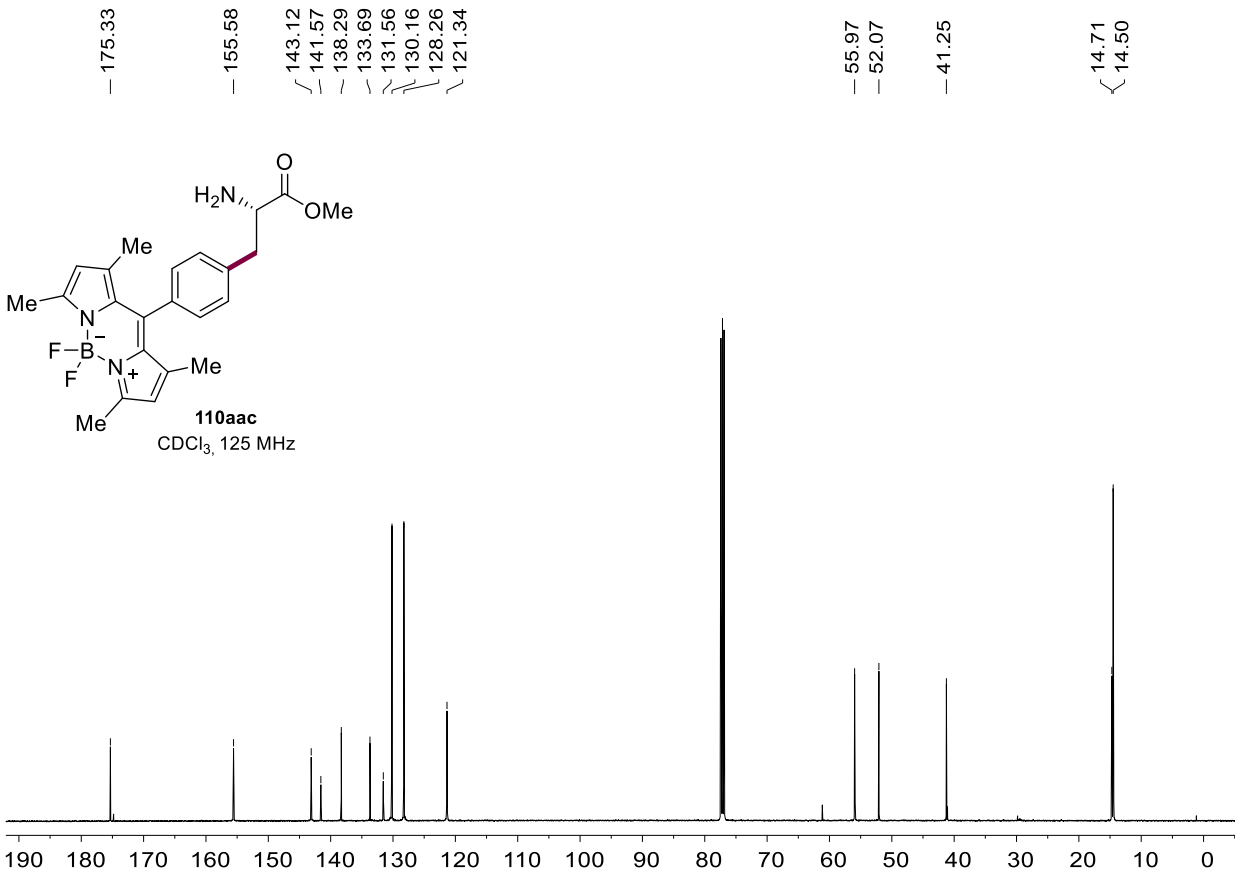
110aab
126 MHz, $CDCl_3$

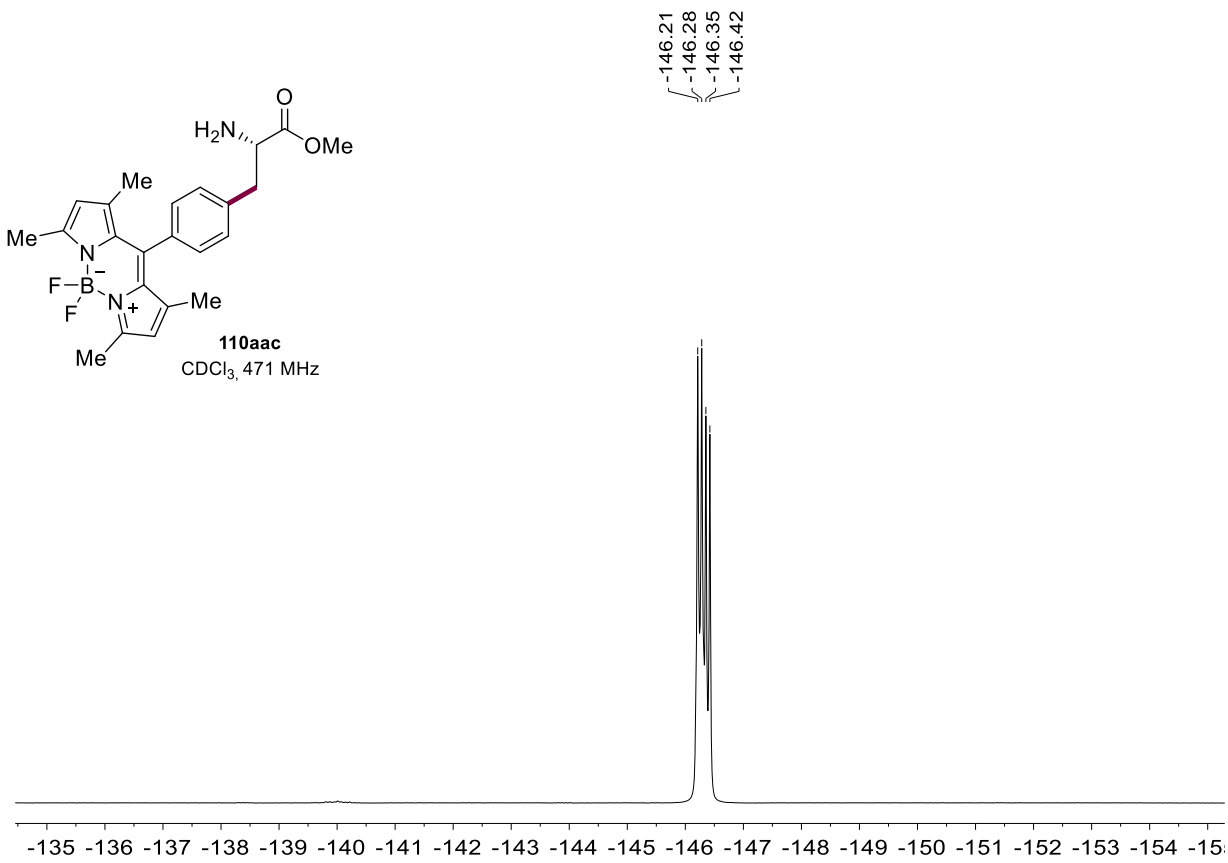


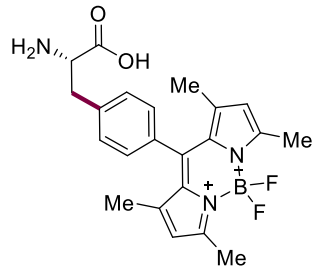
110aab
471 MHz, $CDCl_3$



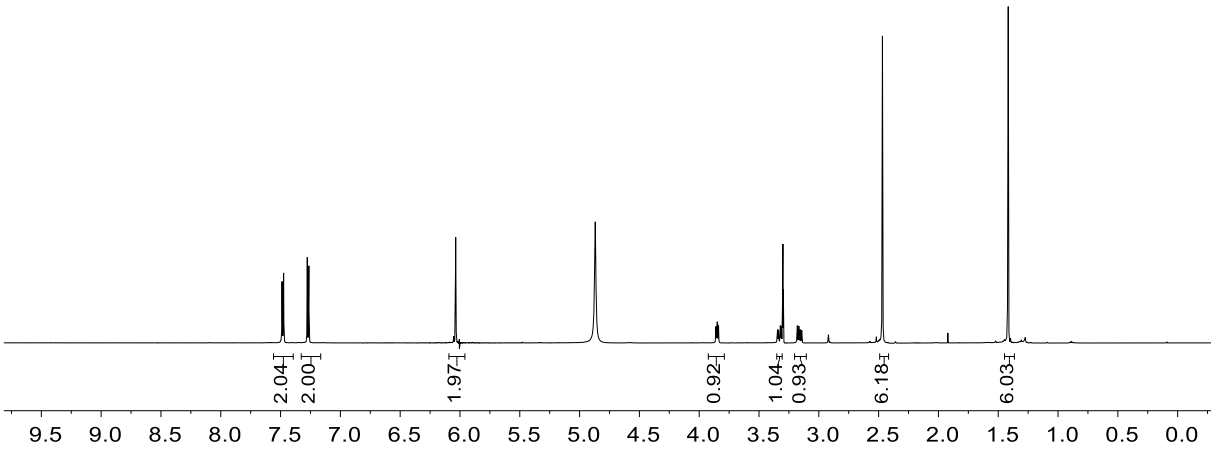
110aac
$CDCl_3$, 500 MHz

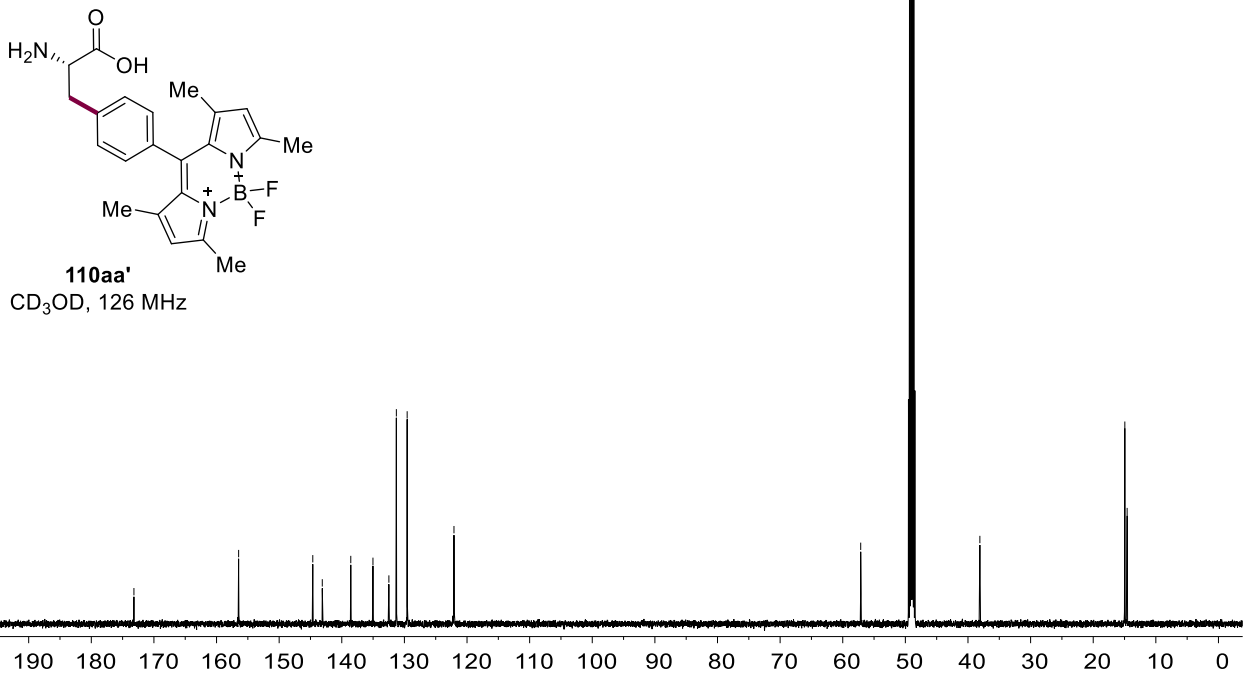

175.33
155.58
143.12
141.57
138.29
133.69
131.56
130.16
128.26
121.34
55.97
52.07
41.25
14.71
14.50
110aac
CDCl3, 125 MHz
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


-146.21
-146.28
-146.35
-146.42
110aac
CDCl3, 471 MHz
-135 -136 -137 -138 -139 -140 -141 -142 -143 -144 -145 -146 -147 -148 -149 -150 -151 -152 -153 -154 -15

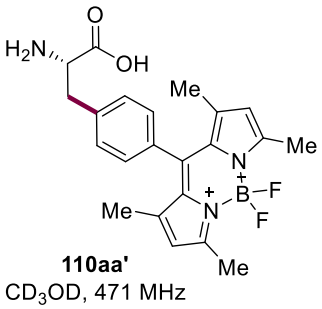


110aa'
CD_3OD, 600 MHz

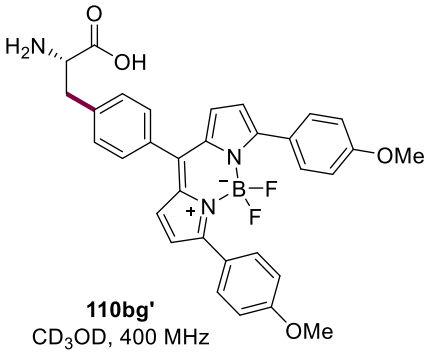




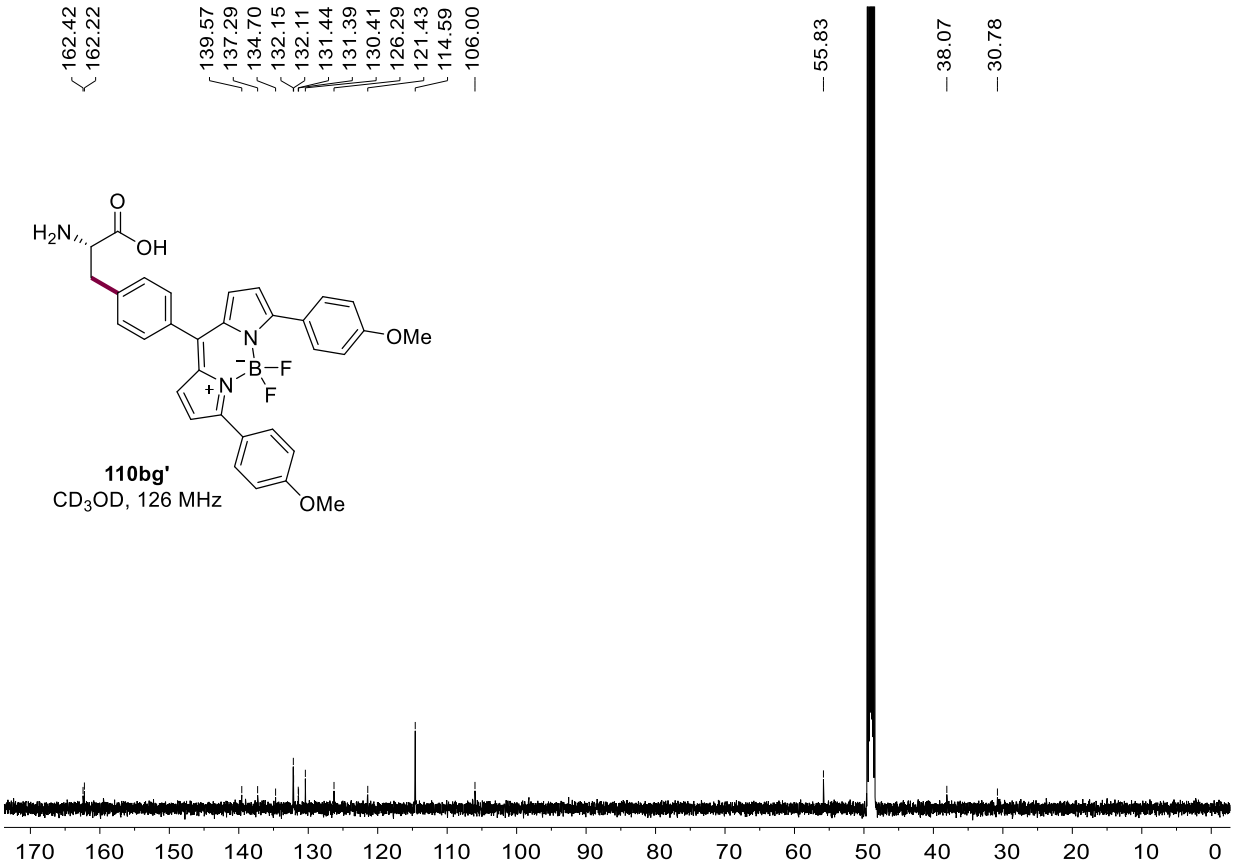
110aa'
CD_3OD, 126 MHz

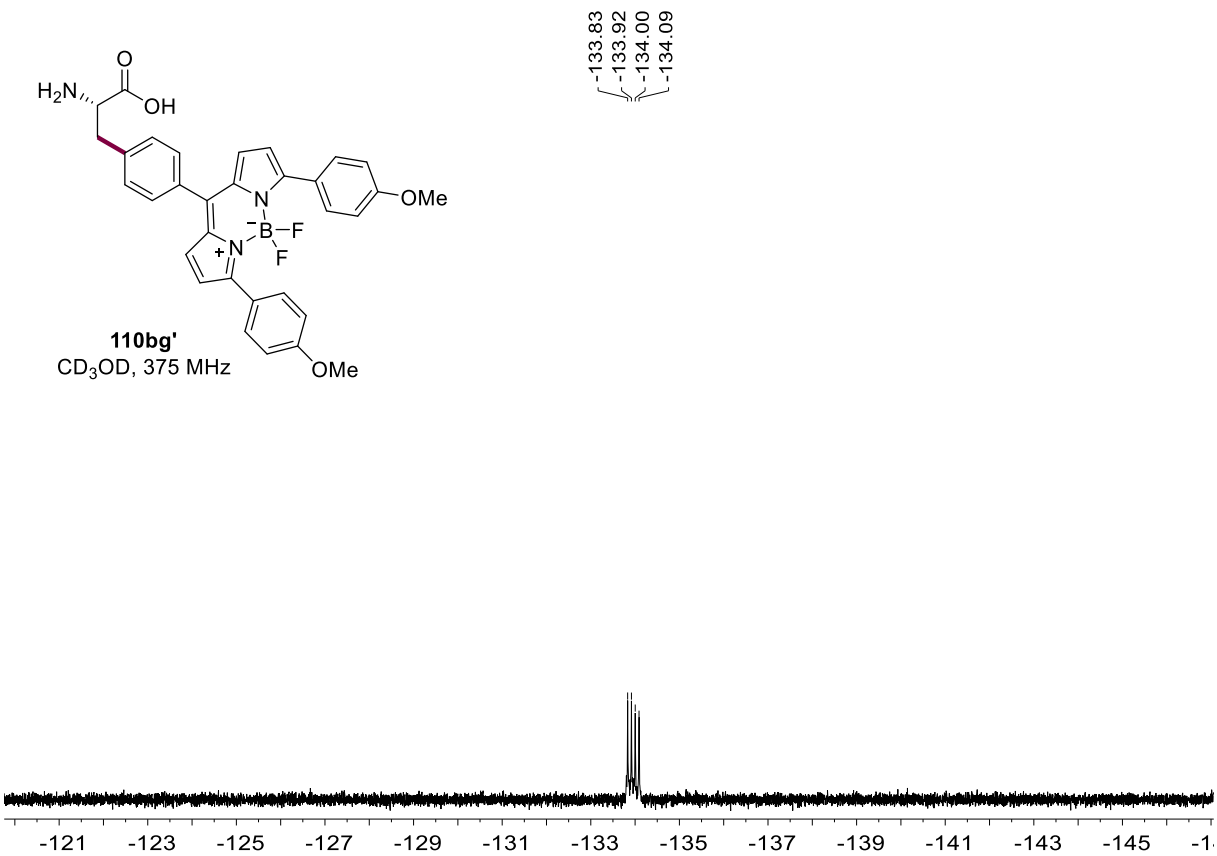


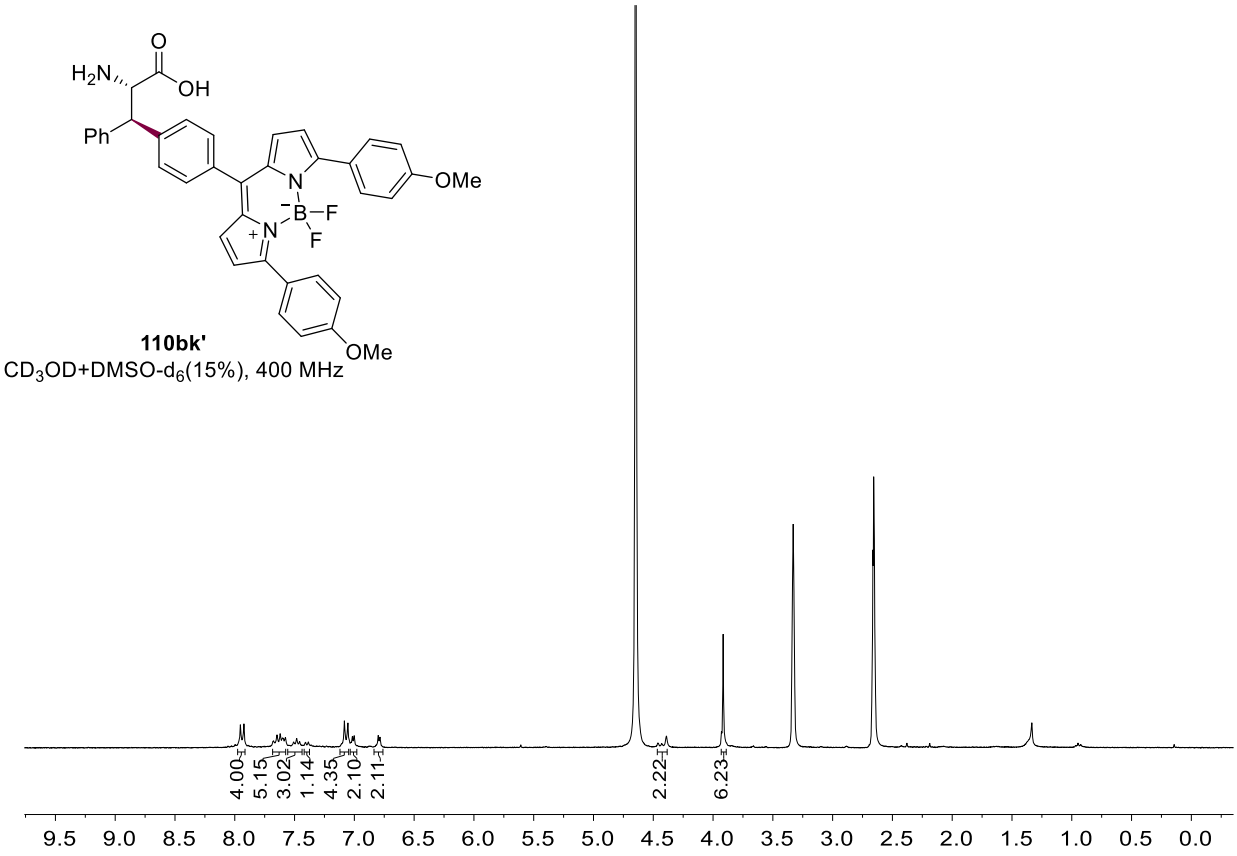
110aa'
CD_3OD, 471 MHz

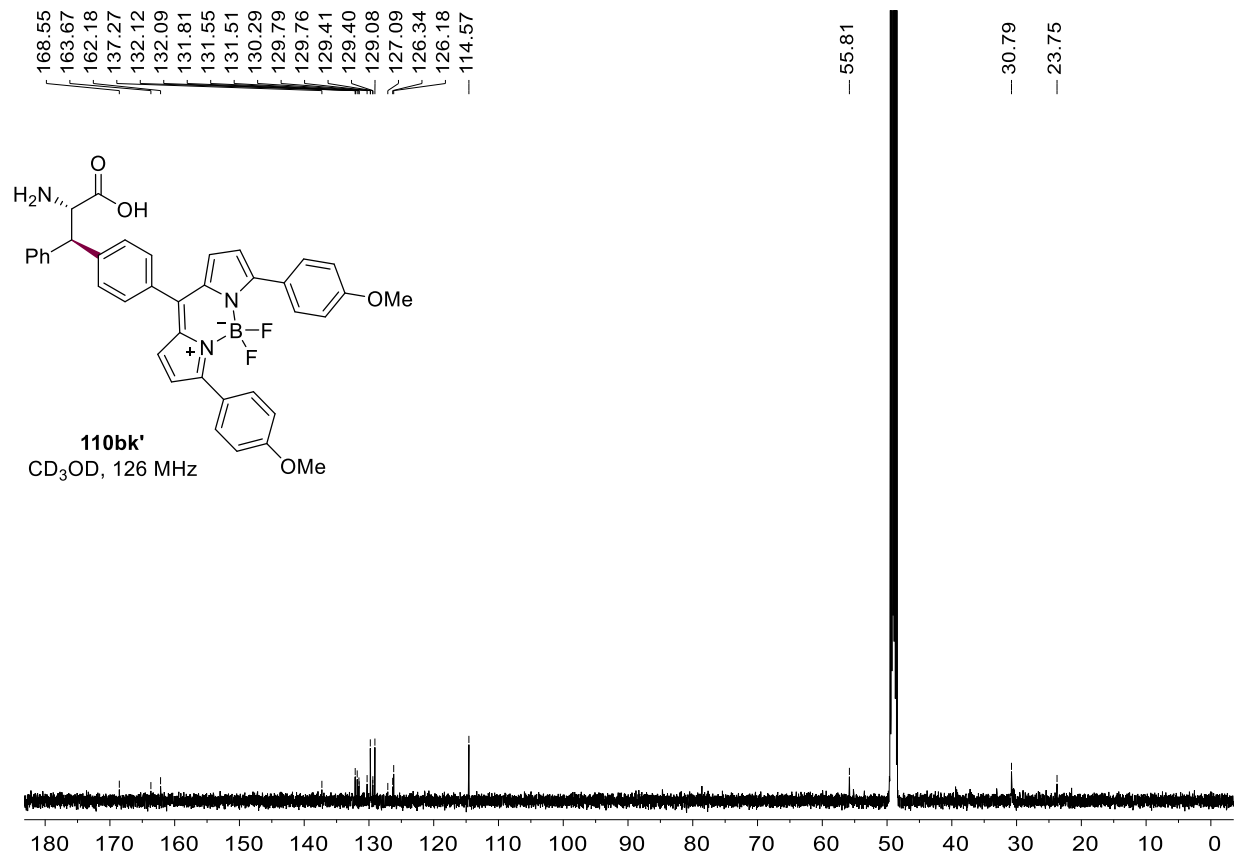


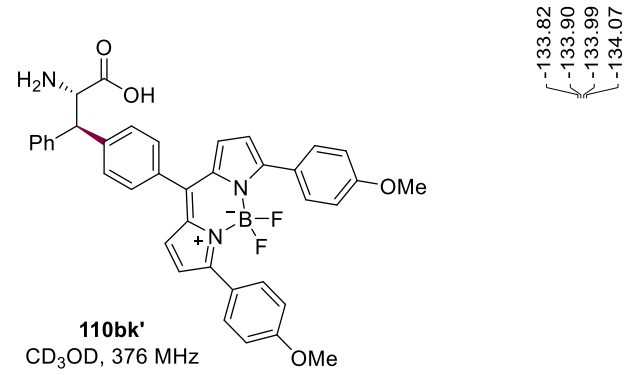
110bg'
CD_3OD, 400 MHz

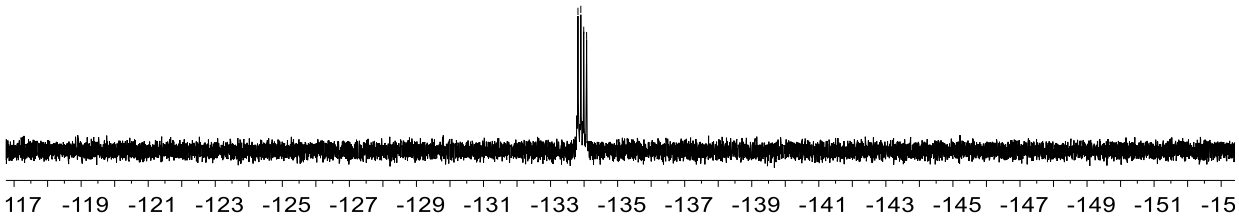

162.42
162.22
139.57
137.29
134.70
132.15
132.11
131.44
131.39
130.41
126.29
121.43
114.59
106.00
55.83
38.07
30.78
OMe
OMe
110bg'
CD3OD, 126 MHz
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

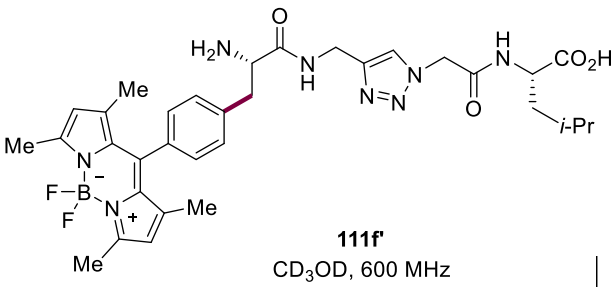

-133.83
-133.92
-134.00
-134.09
OMe
OMe
110bg'
CD3OD, 375 MHz
-121 -123 -125 -127 -129 -131 -133 -135 -137 -139 -141 -143 -145

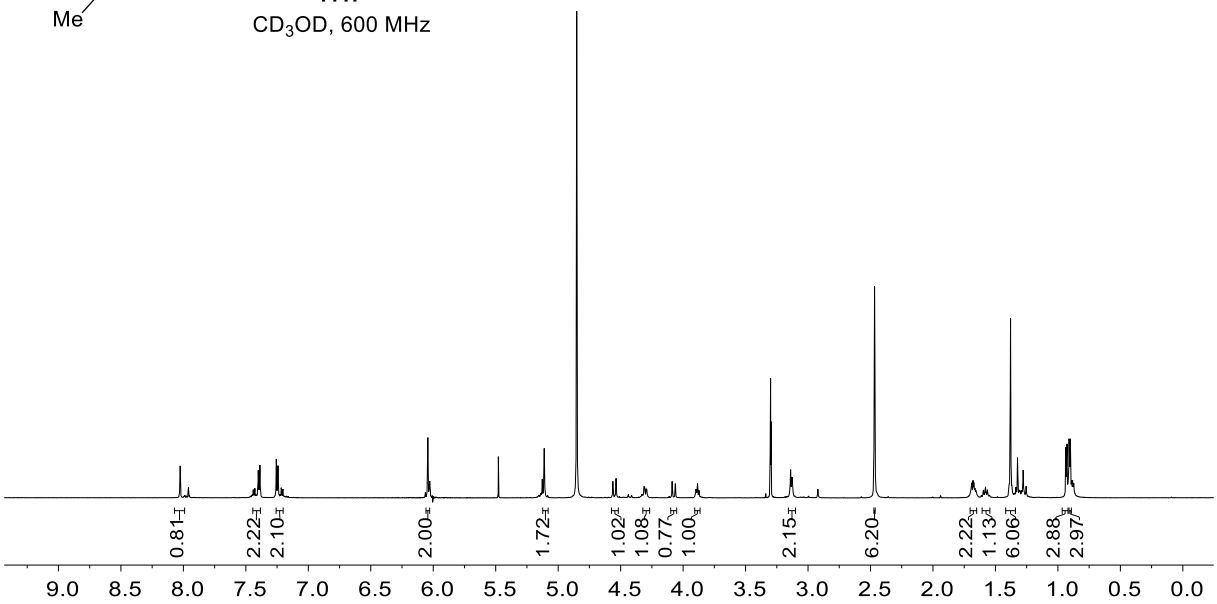

110bk'
CD3OD+DMSO-d6(15%), 400 MHz
4.00
5.15
3.02
1.14
4.35
2.10
2.11
2.22
6.23
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

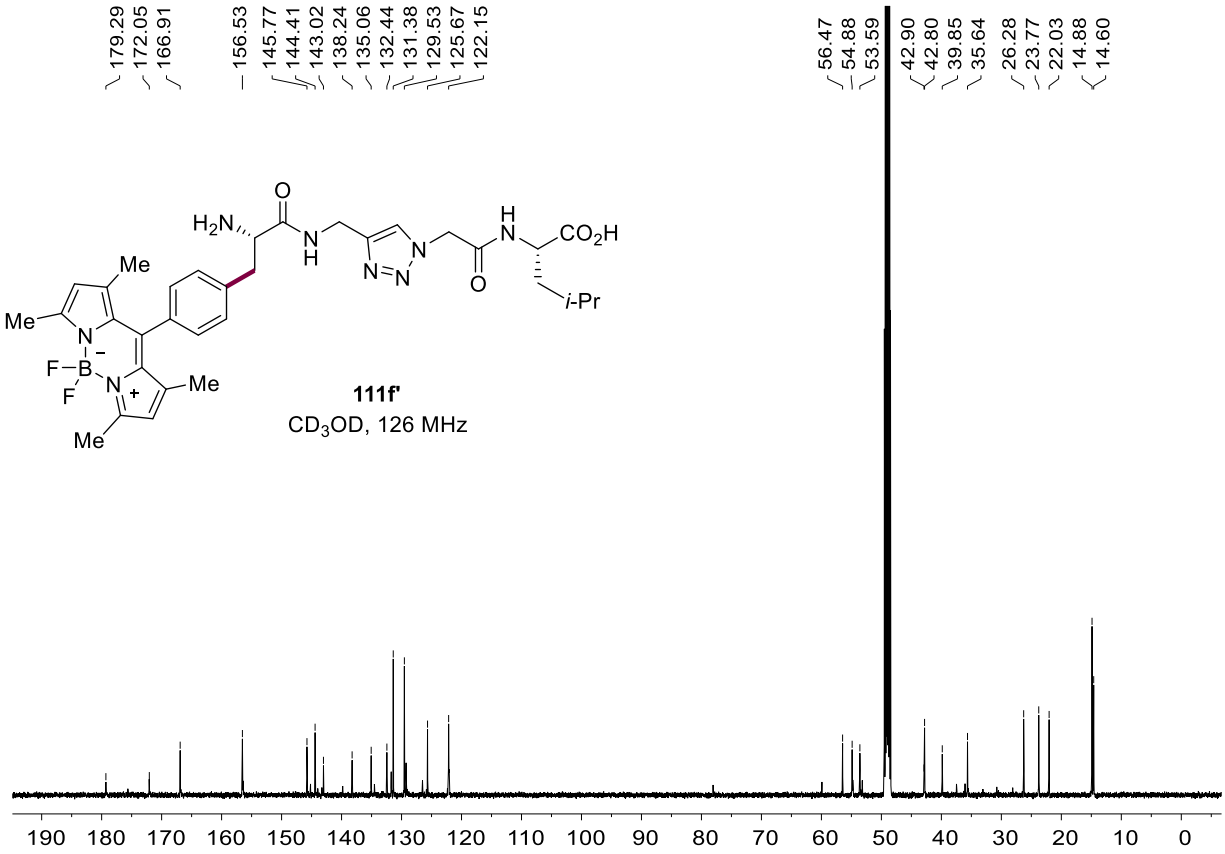

168.55
163.67
162.18
137.27
132.12
132.09
131.81
131.55
131.51
130.29
129.79
129.76
129.41
129.40
129.08
127.09
126.34
126.18
114.57
55.81
30.79
23.75
110bk'
CD3OD, 126 MHz
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

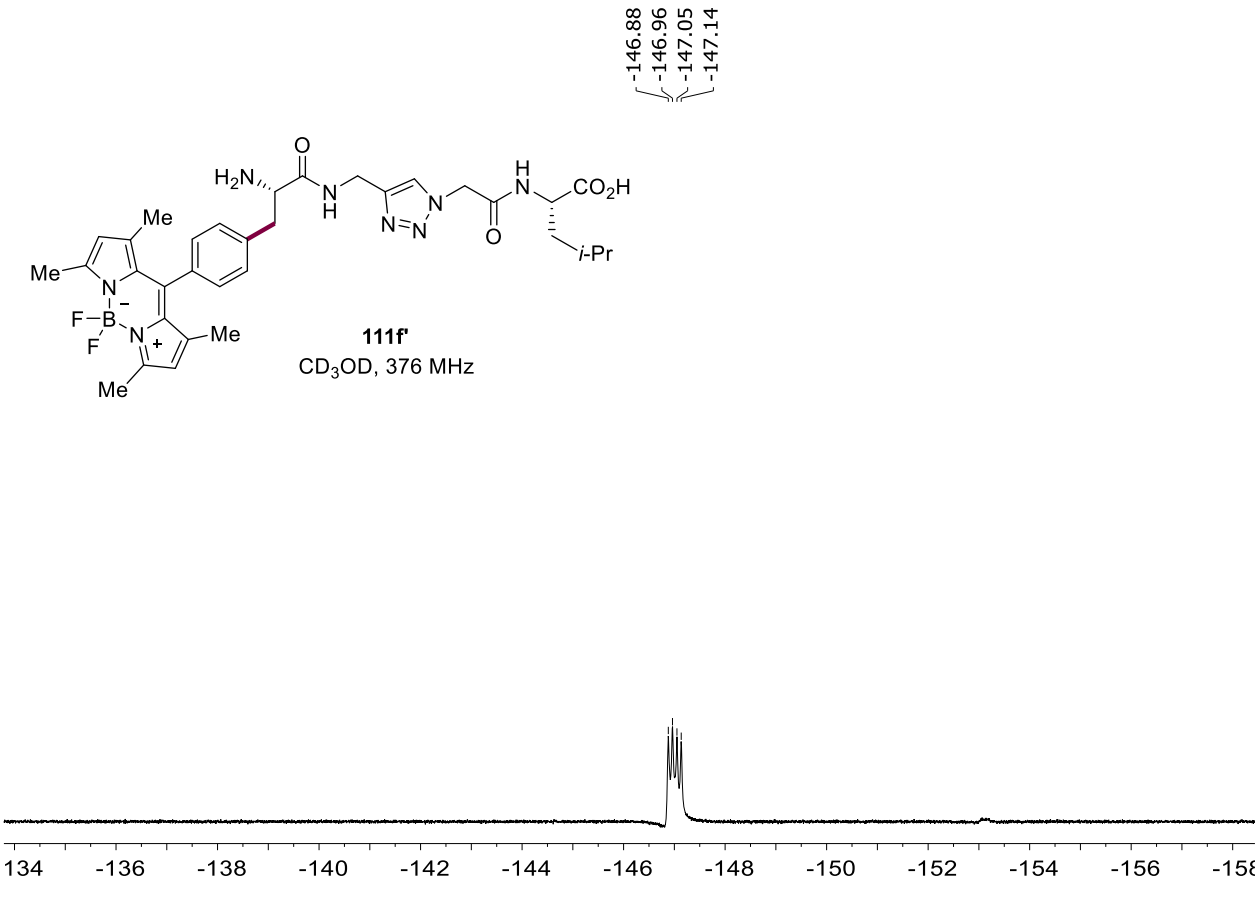

-133.82
-133.90
-133.99
-134.07
110bk'
CD3OD, 376 MHz

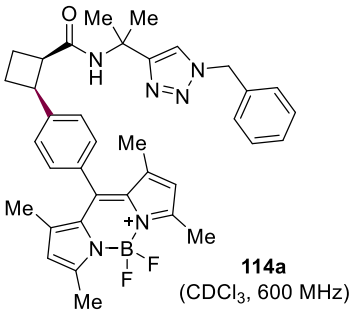

117 -119 -121 -123 -125 -127 -129 -131 -133 -135 -137 -139 -141 -143 -145 -147 -149 -151 -15


111f'
CD3OD, 600 MHz

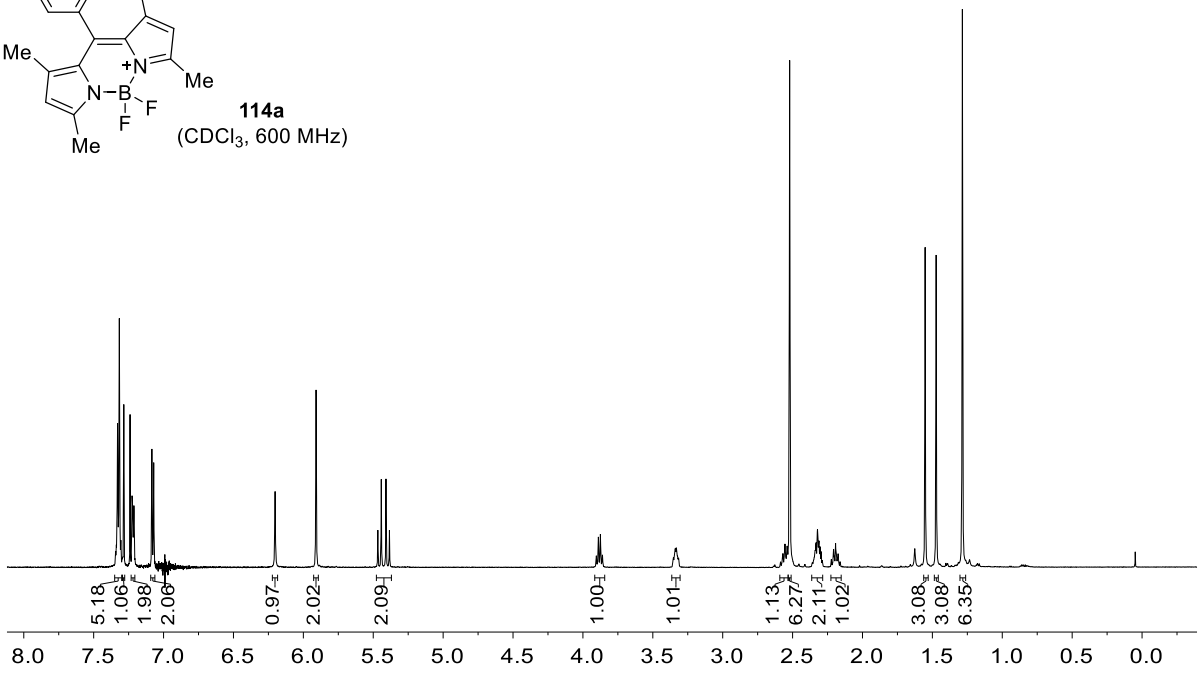

0.81
2.22
2.10
2.00
1.72
1.02
1.08
0.77
1.00
2.15
6.20
2.22
1.13
6.06
2.88
2.97
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

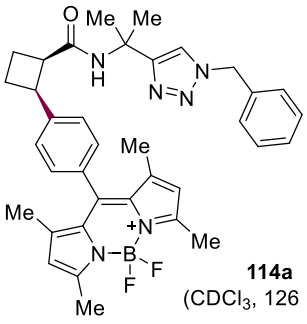

179.29
172.05
166.91
156.53
145.77
144.41
143.02
138.24
135.06
132.44
131.38
129.53
125.67
122.15
56.47
54.88
53.59
42.90
42.80
39.85
35.64
26.28
23.77
22.03
14.88
14.60
111f'
CD3OD, 126 MHz
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


-146.88
-146.96
-147.05
-147.14
111f'
CD3OD, 376 MHz
134 -136 -138 -140 -142 -144 -146 -148 -150 -152 -154 -156 -158

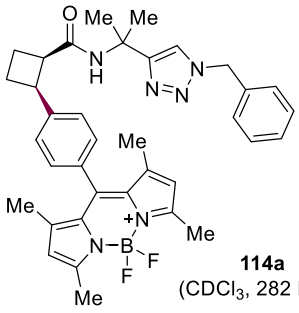


114a
($CDCl_3$, 600 MHz)

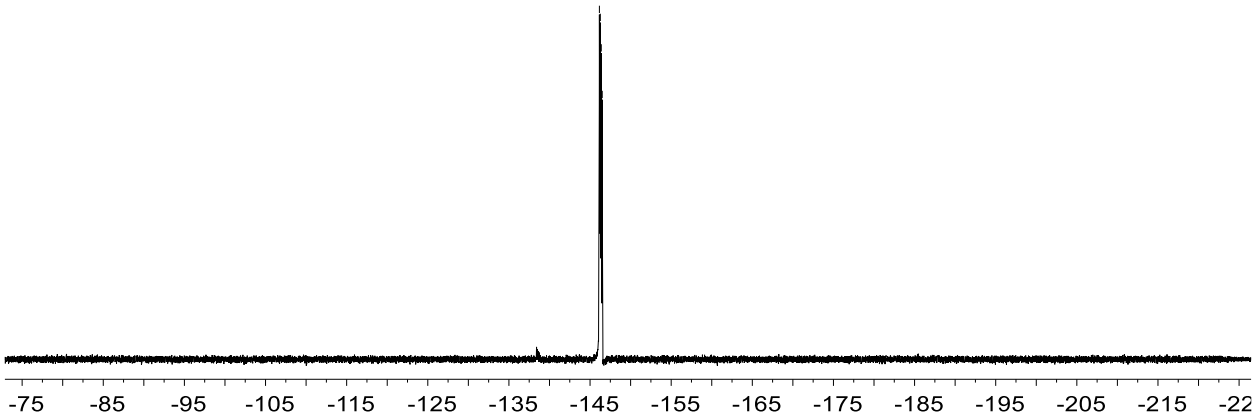


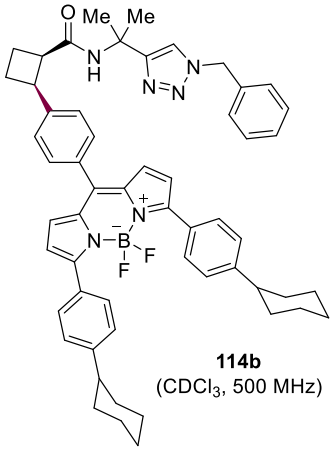


114a
($CDCl_3$, 126 MHz)

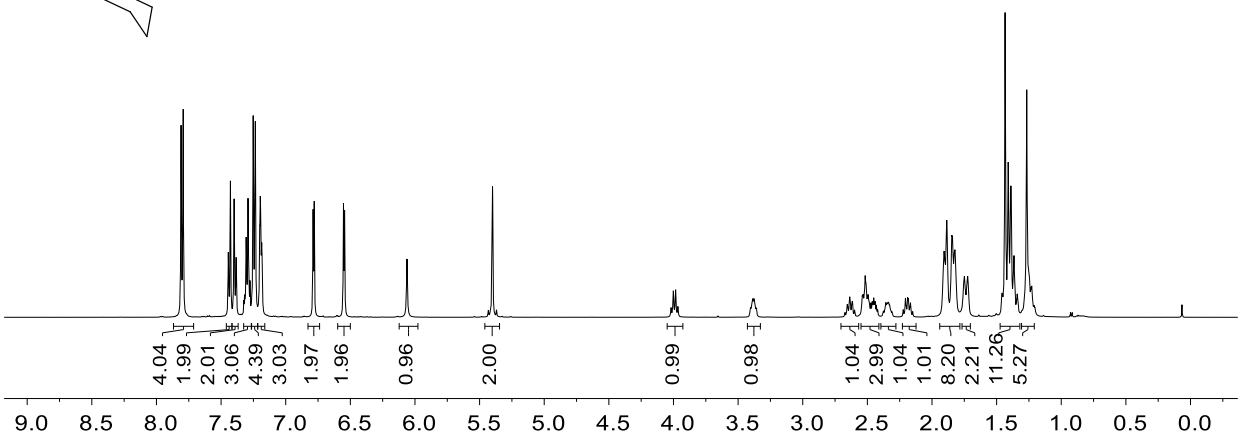


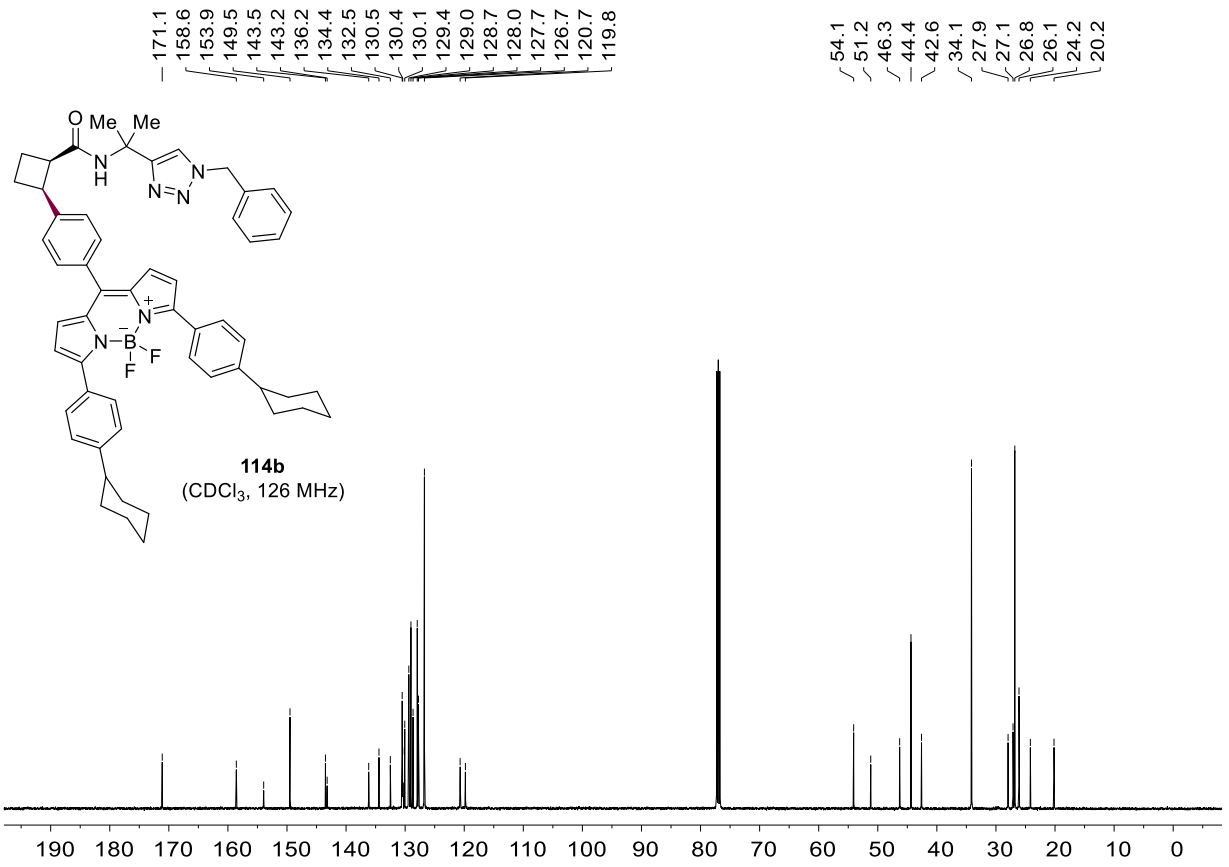
114a
($CDCl_3$, 282 MHz)



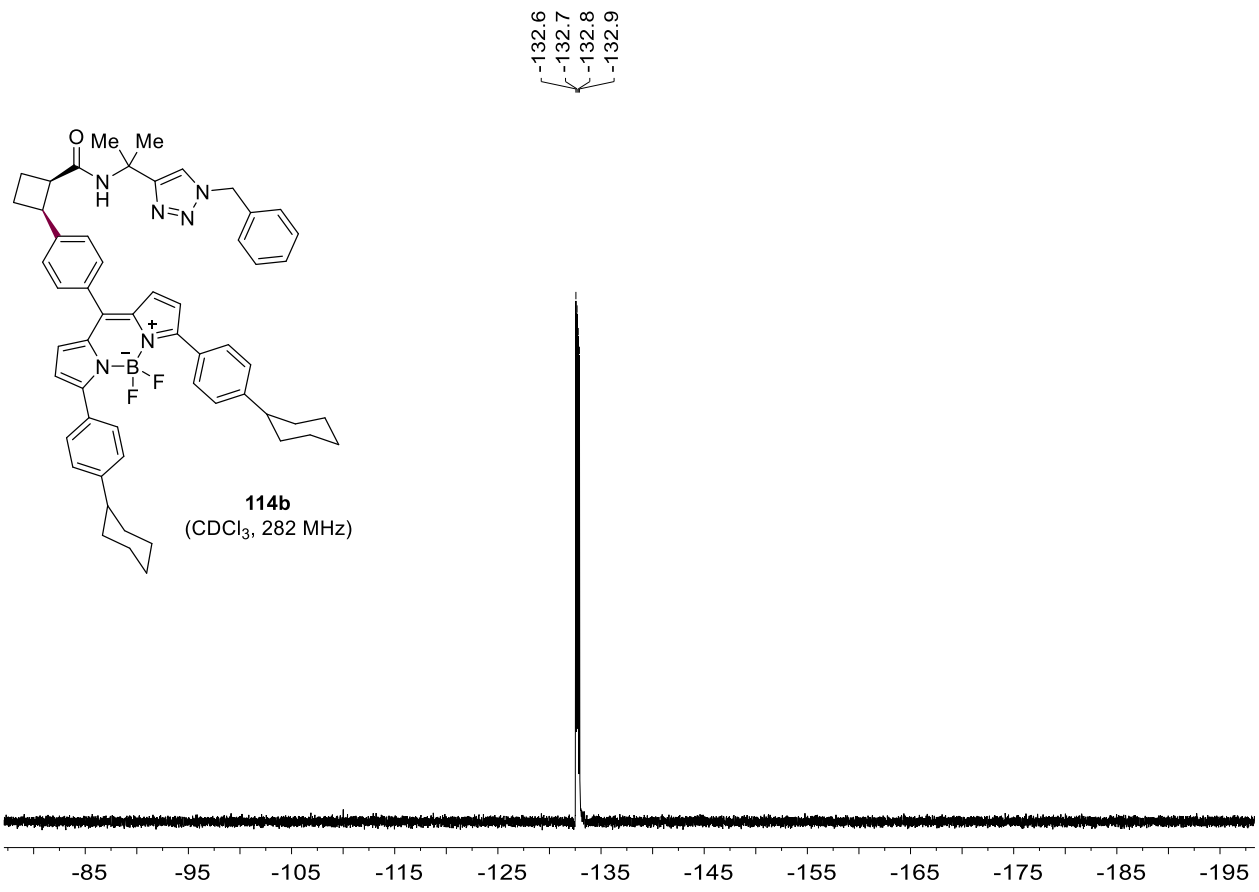


114b
($CDCl_3$, 500 MHz)

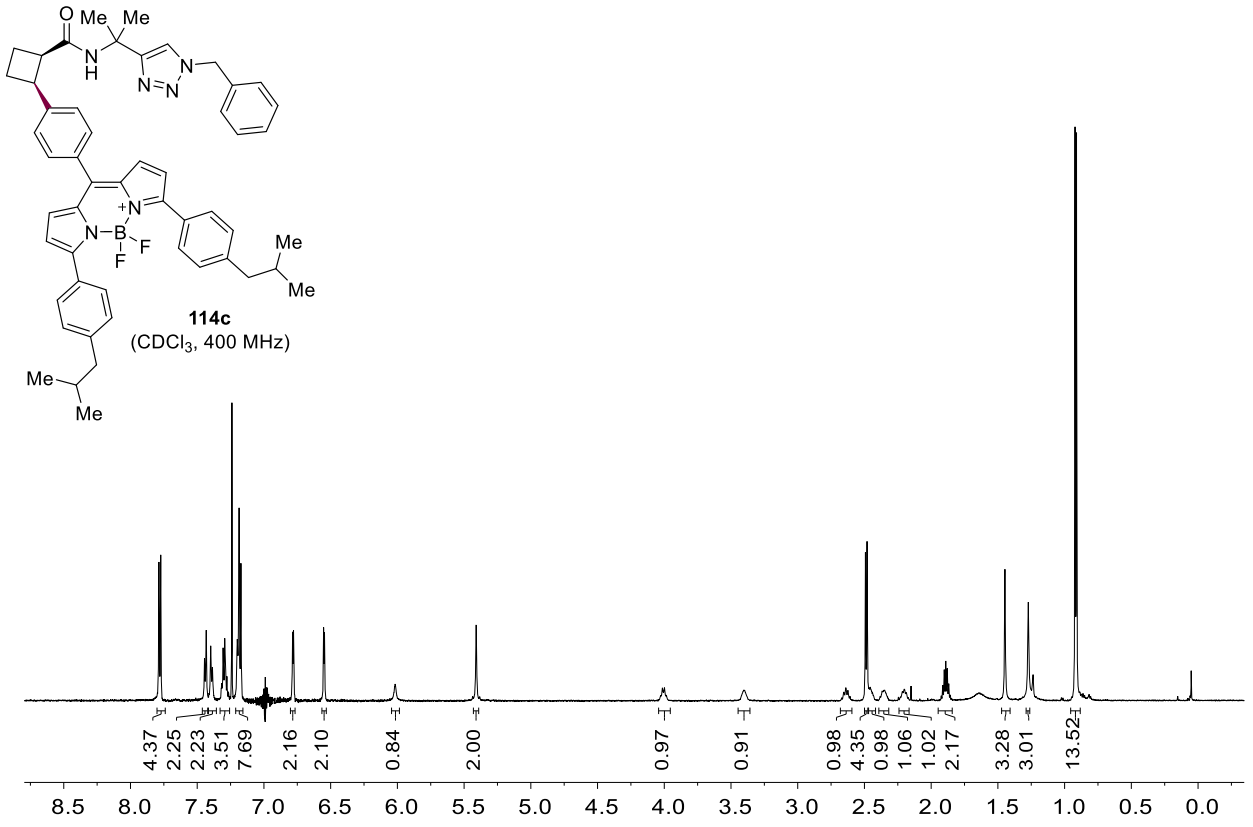


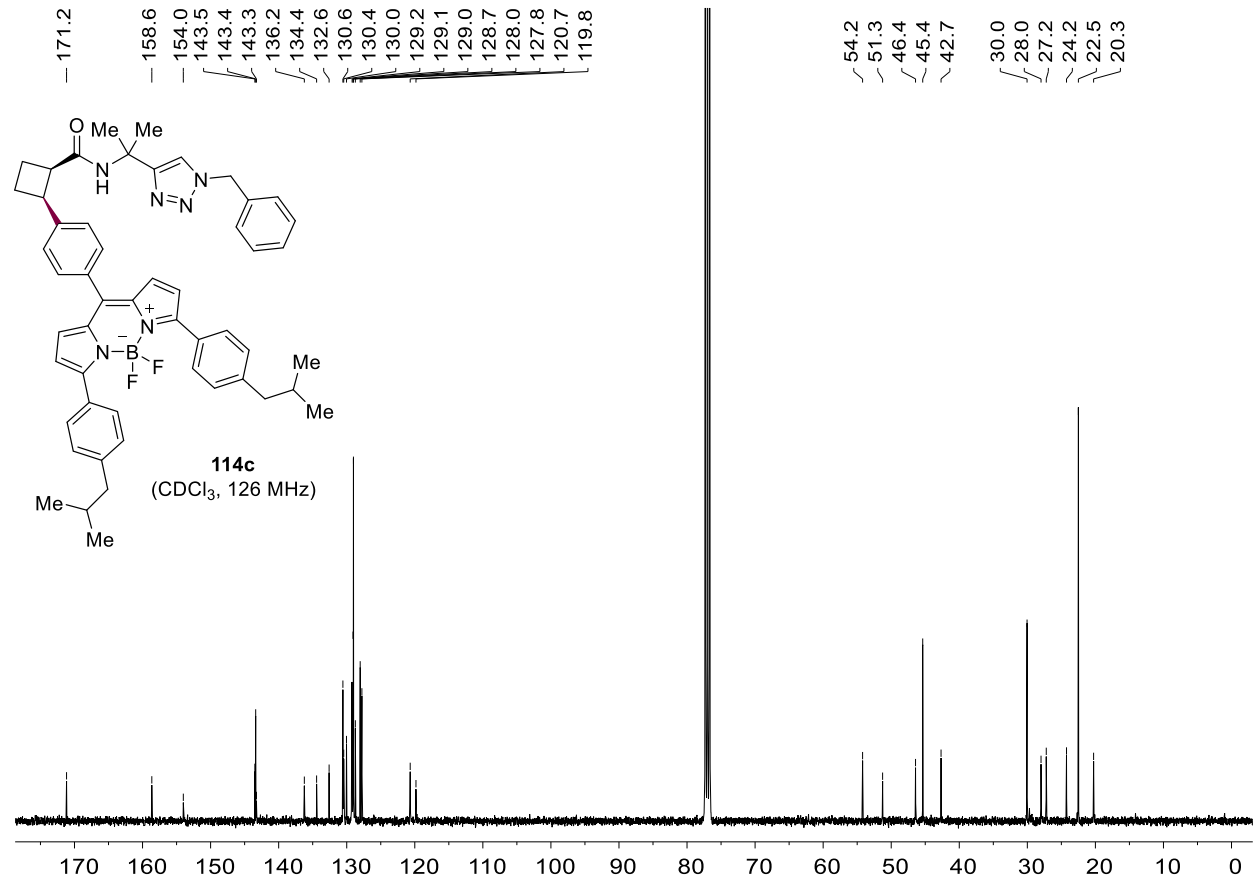


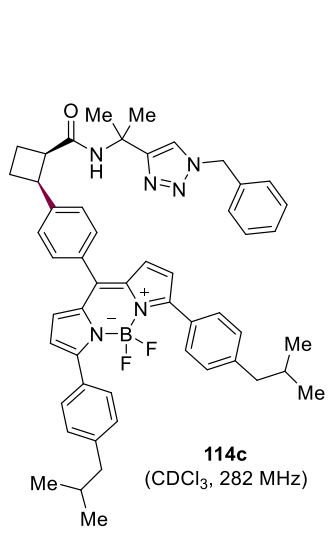
114b
($CDCl_3$, 126 MHz)



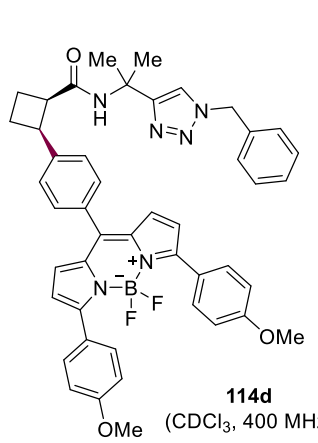
114b
($CDCl_3$, 282 MHz)


114c
(CDCl3, 400 MHz)
4.37
2.25
2.23
3.51
7.69
2.16
2.10
0.84
2.00
0.97
0.91
0.98
4.35
0.98
1.06
1.02
2.17
3.28
3.01
13.52

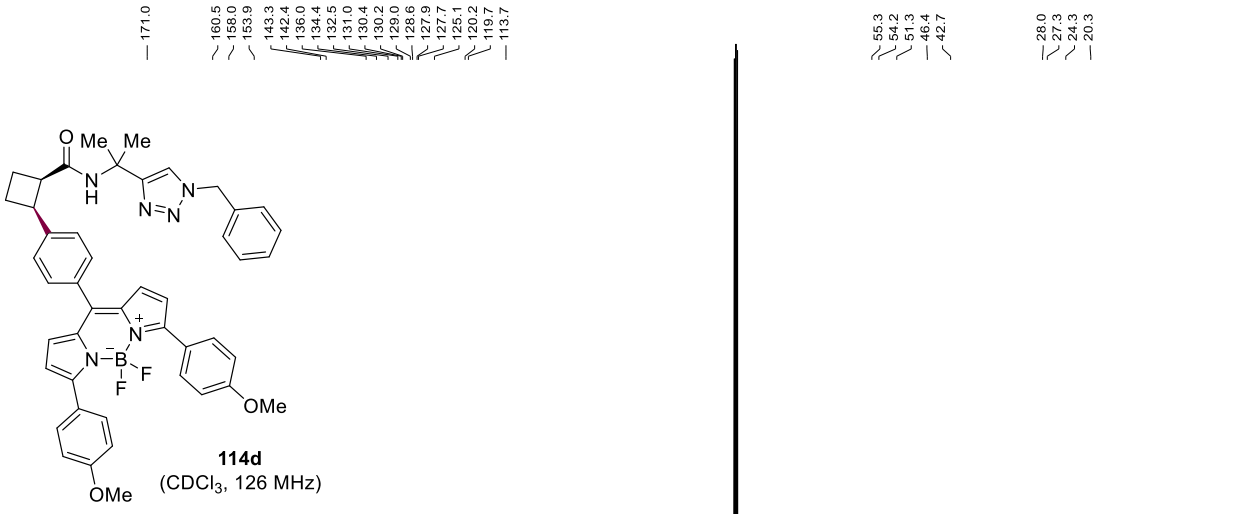

171.2
158.6
154.0
143.5
143.4
143.3
136.2
134.4
132.6
130.6
130.4
130.0
129.2
129.1
129.0
128.7
128.0
127.8
120.7
119.8
54.2
51.3
46.4
45.4
42.7
30.0
28.0
27.2
24.2
22.5
20.3
114c
(CDCl3, 126 MHz)



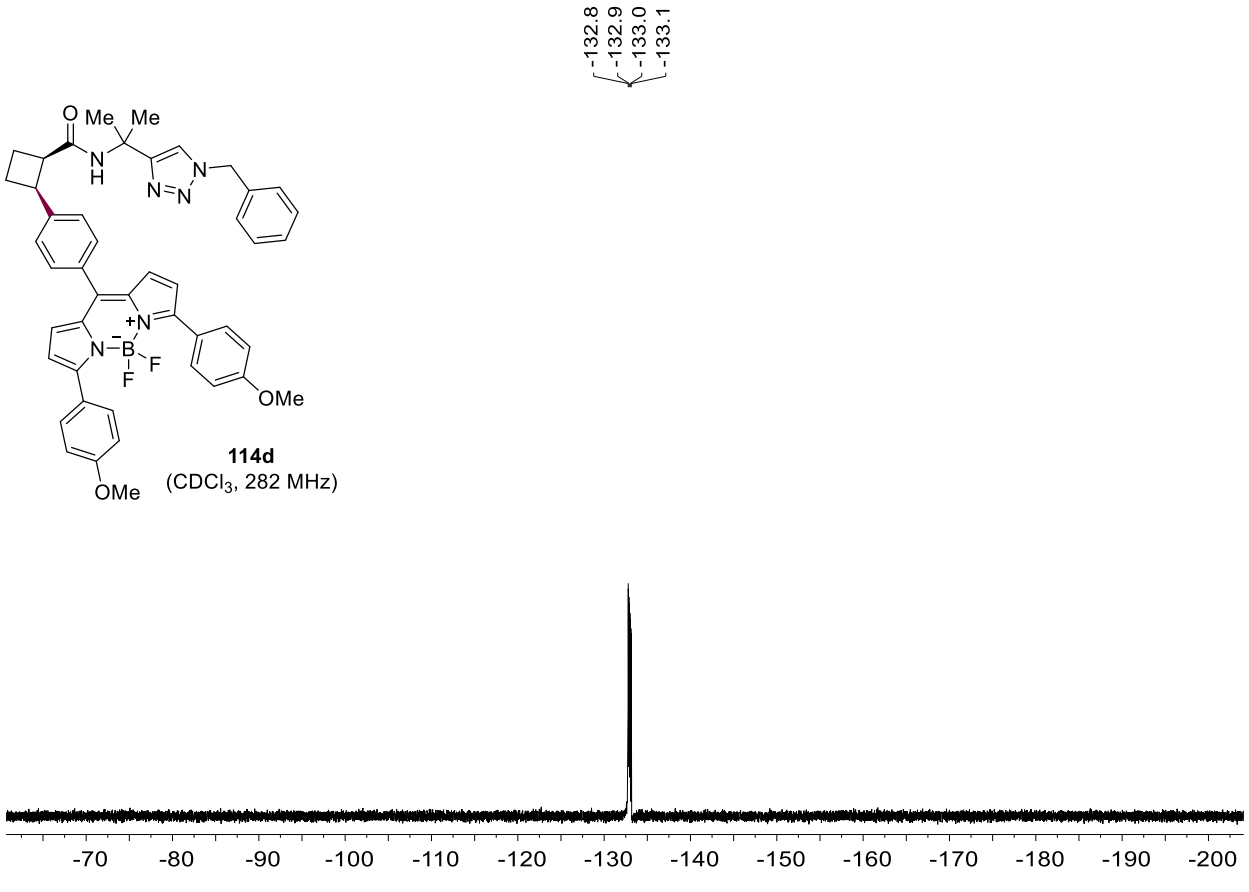
114c
($CDCl_3$, 282 MHz)



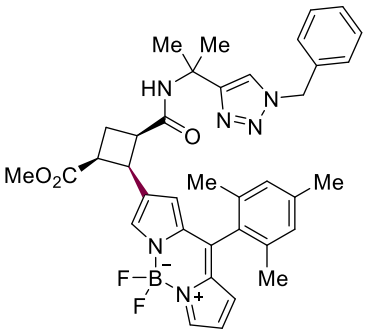
114d
($CDCl_3$, 400 MHz)



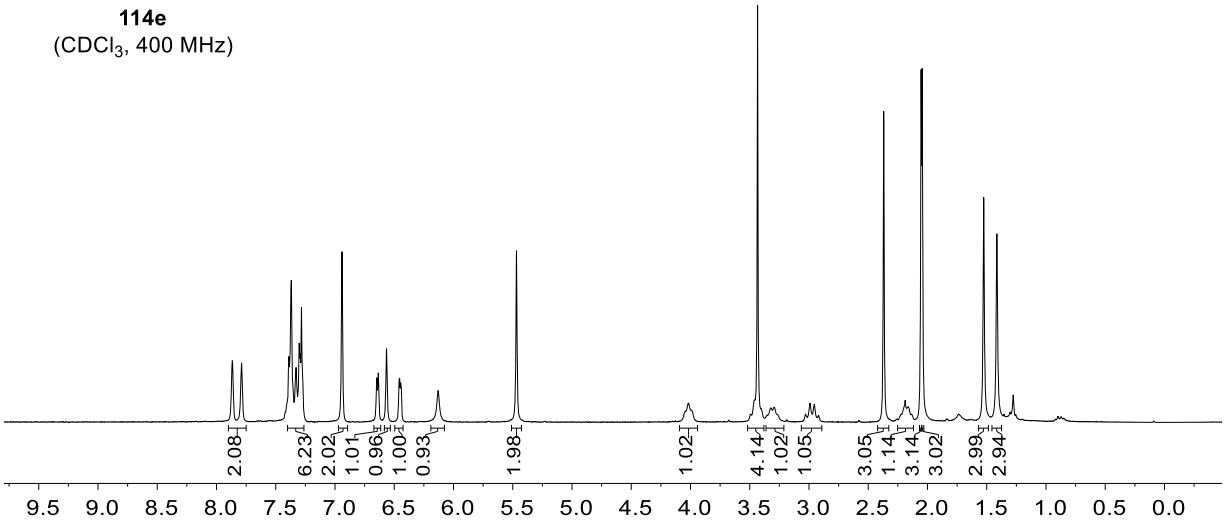
114d
($CDCl_3$, 126 MHz)

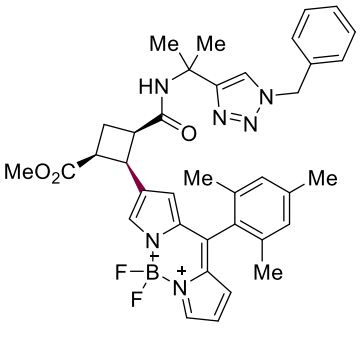


114d
($CDCl_3$, 282 MHz)

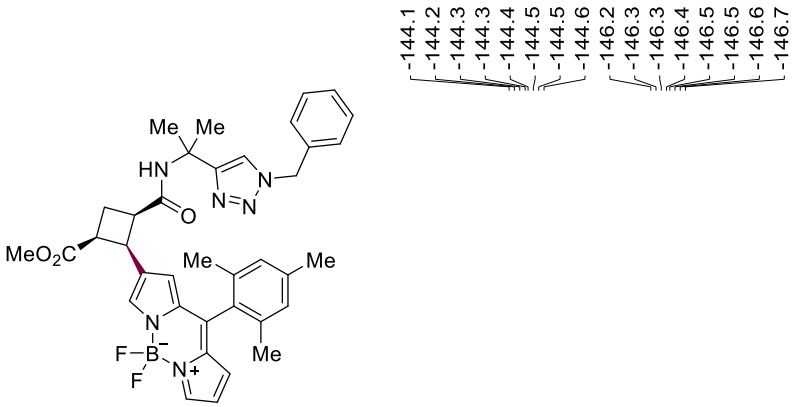


114e
($CDCl_3$, 400 MHz)

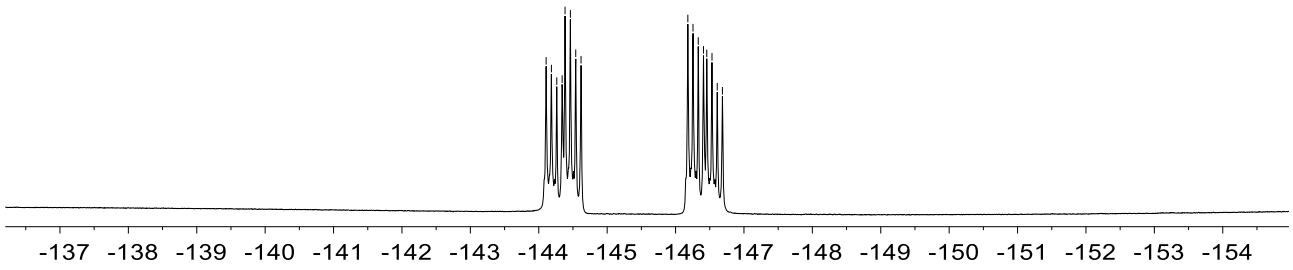


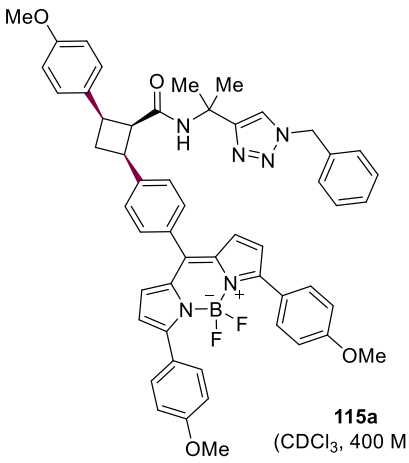


114e
($CDCl_3$, 101 MHz)

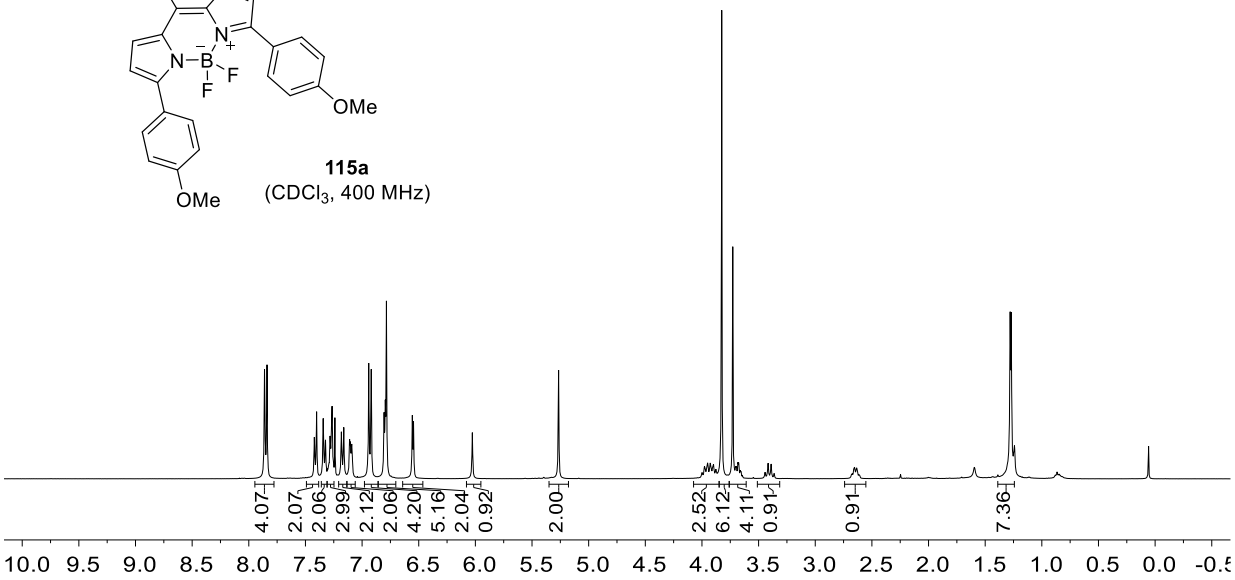


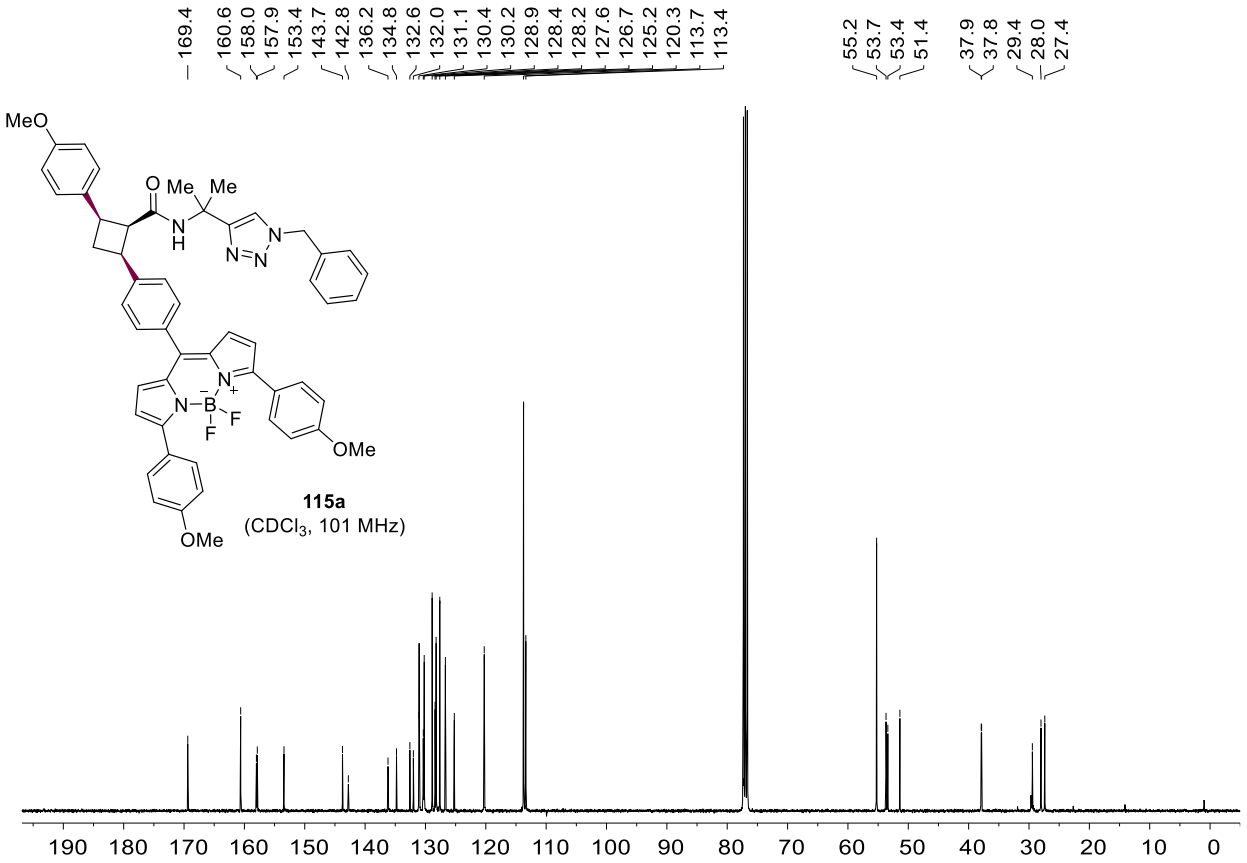
114e
($CDCl_3$, 282 MHz)

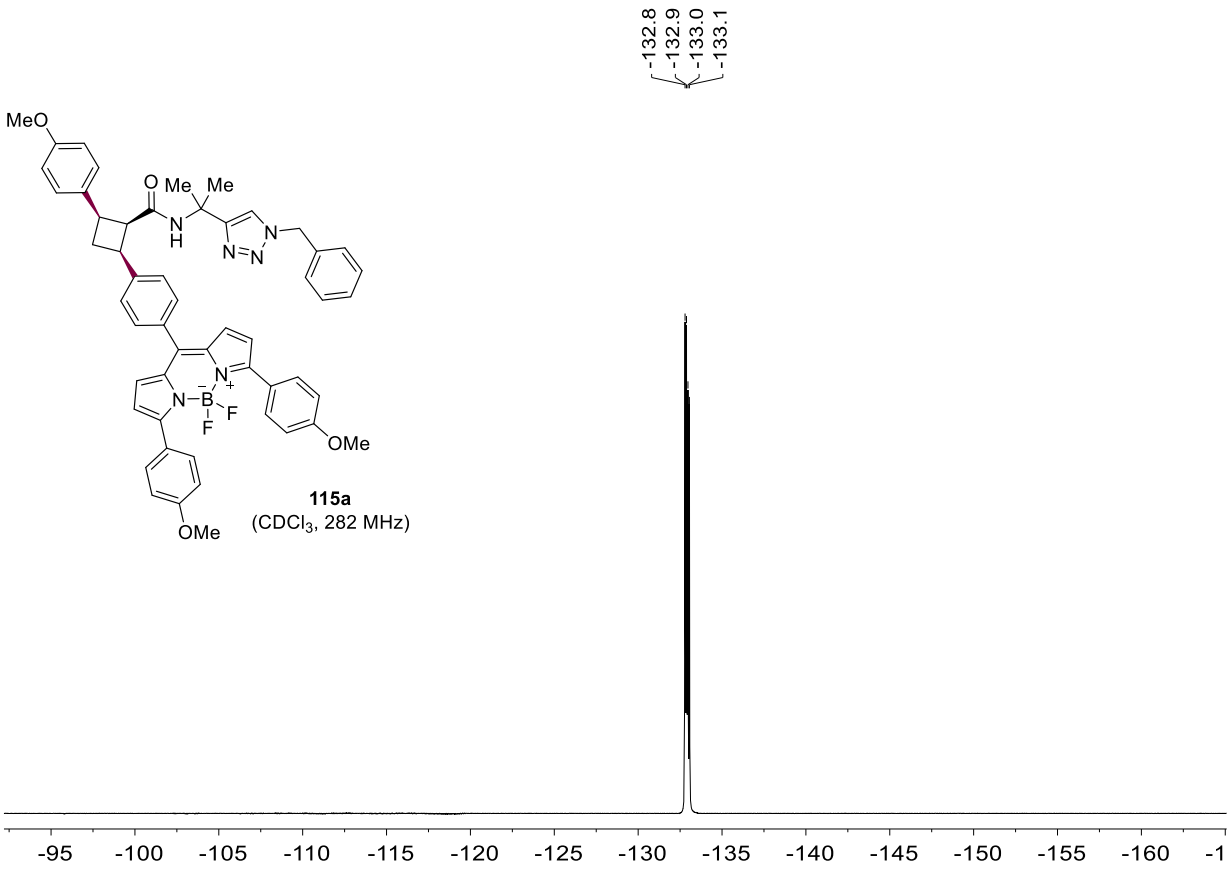


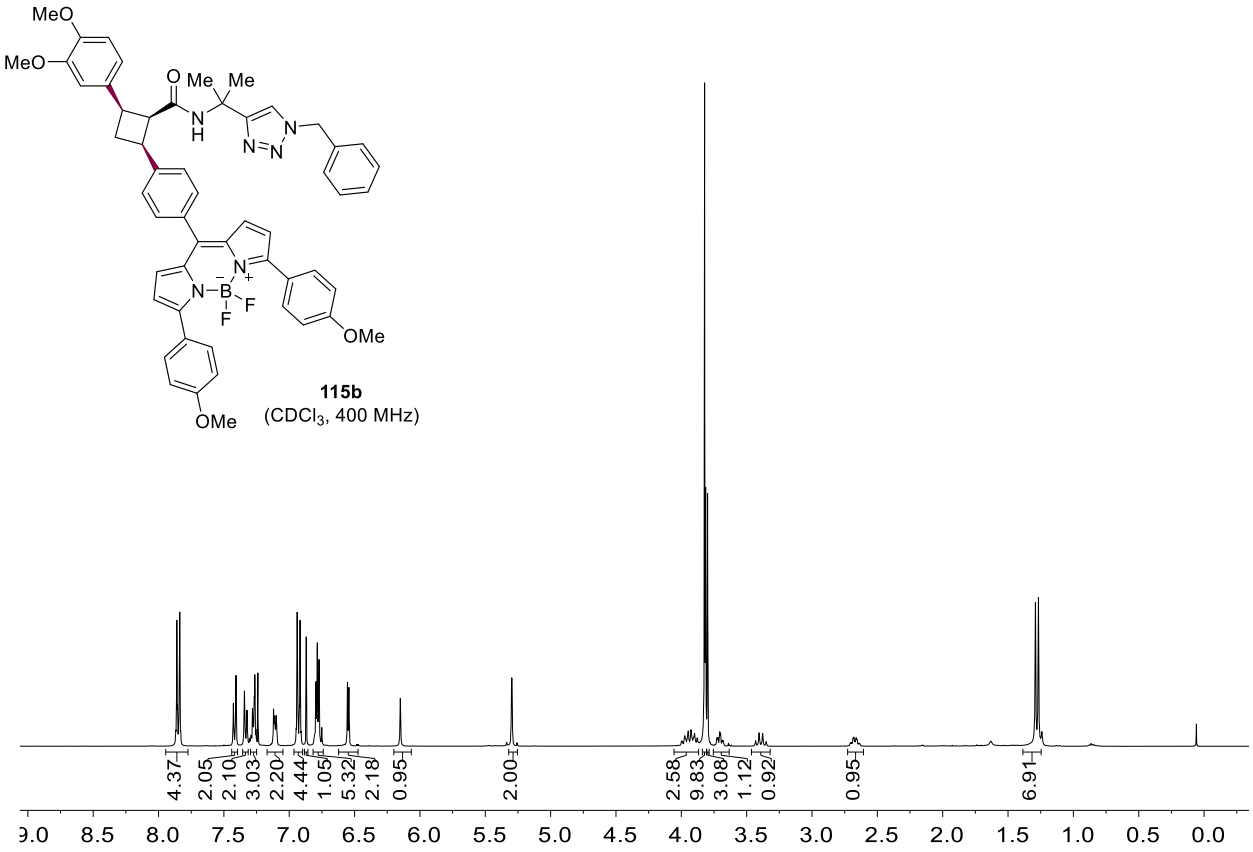


115a
($CDCl_3$, 400 MHz)

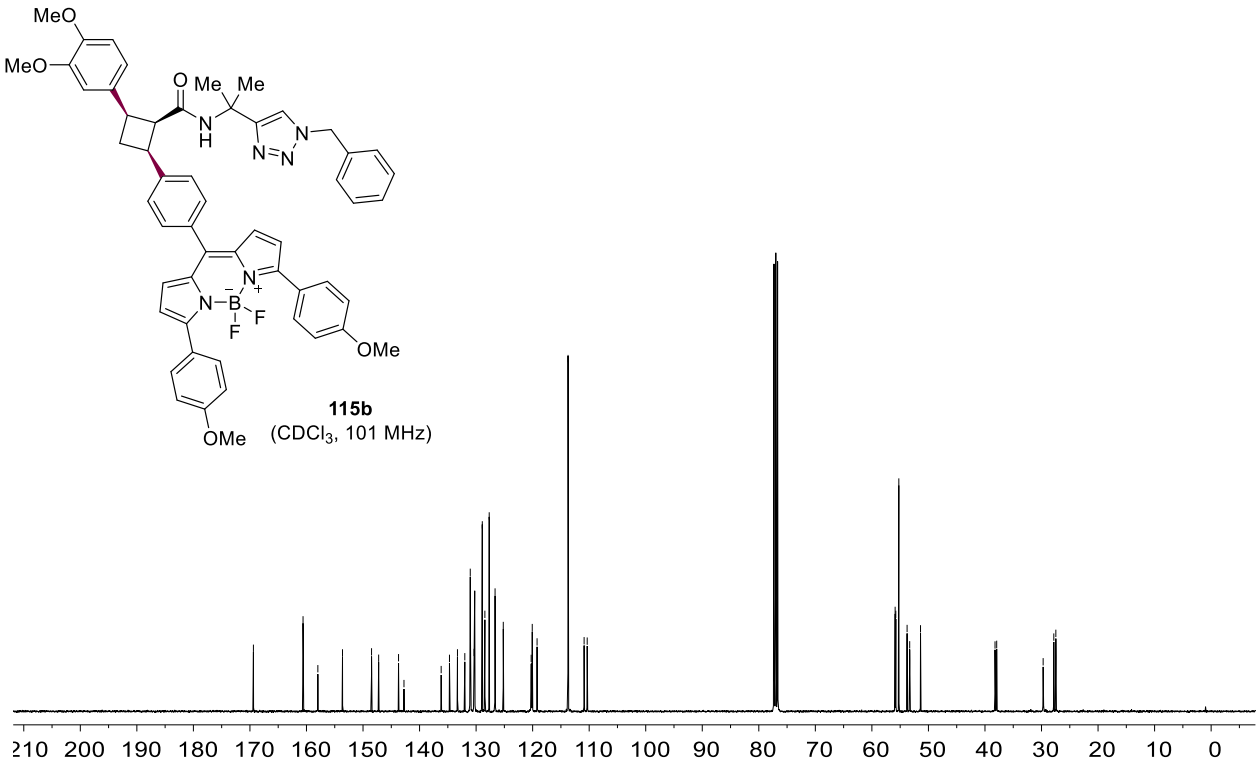



169.4
160.6
158.0
157.9
153.4
143.7
142.8
136.2
134.8
132.6
132.0
131.1
130.4
130.2
128.9
128.4
128.2
127.6
126.7
125.2
120.3
113.7
113.4
55.2
53.7
53.4
51.4
37.9
37.8
29.4
28.0
27.4
MeO
O
Me
Me
N
H
N
N=N
N
B
F
F
OMe
OMe
115a
(CDCl3, 101 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

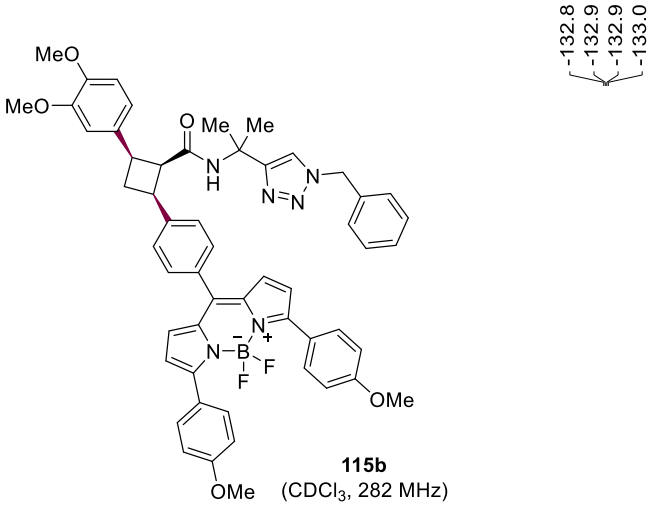

-132.8
-132.9
-133.0
-133.1
MeO
O
Me
Me
N
H
N
N=N
N
B
F
F
OMe
OMe
115a
(CDCl3, 282 MHz)
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
-1



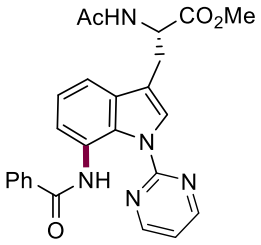
115b
($CDCl_3$, 400 MHz)



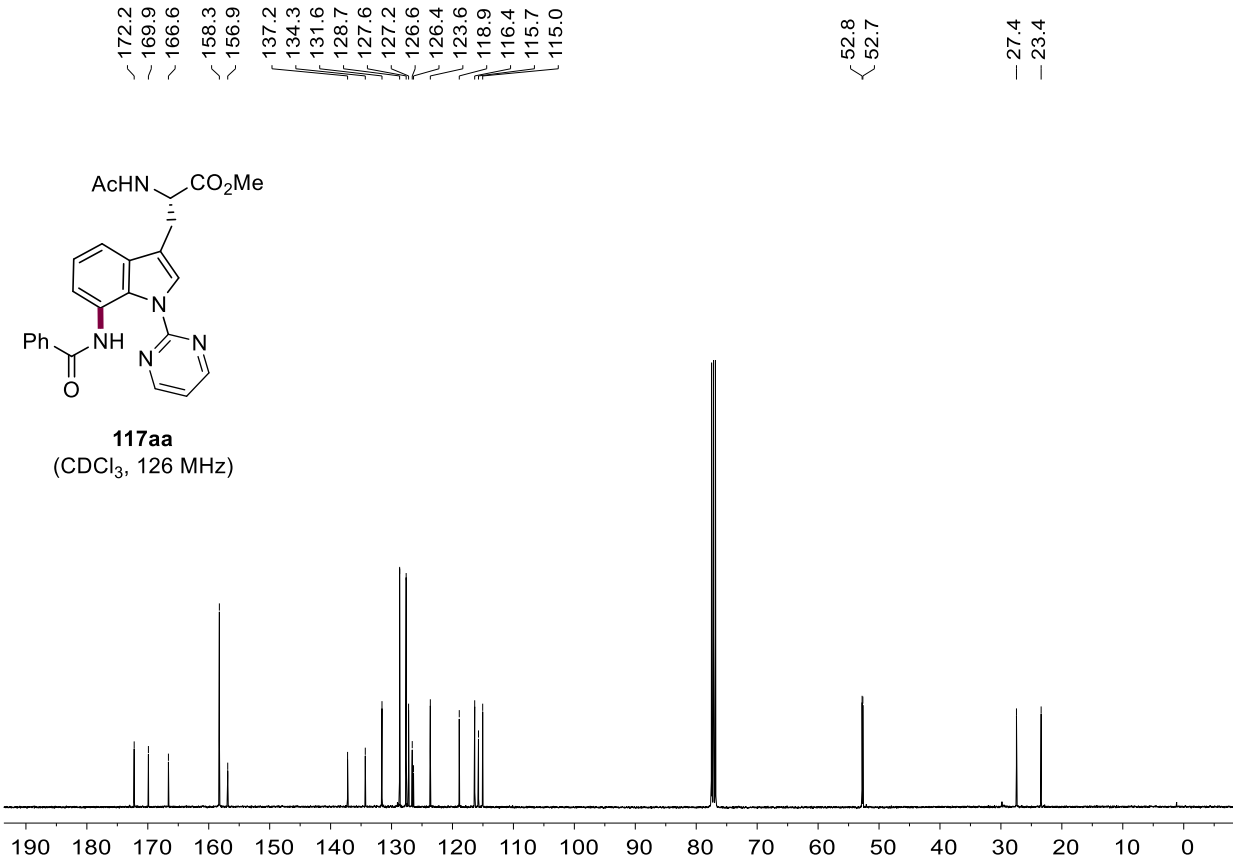
115b
($CDCl_3$, 101 MHz)

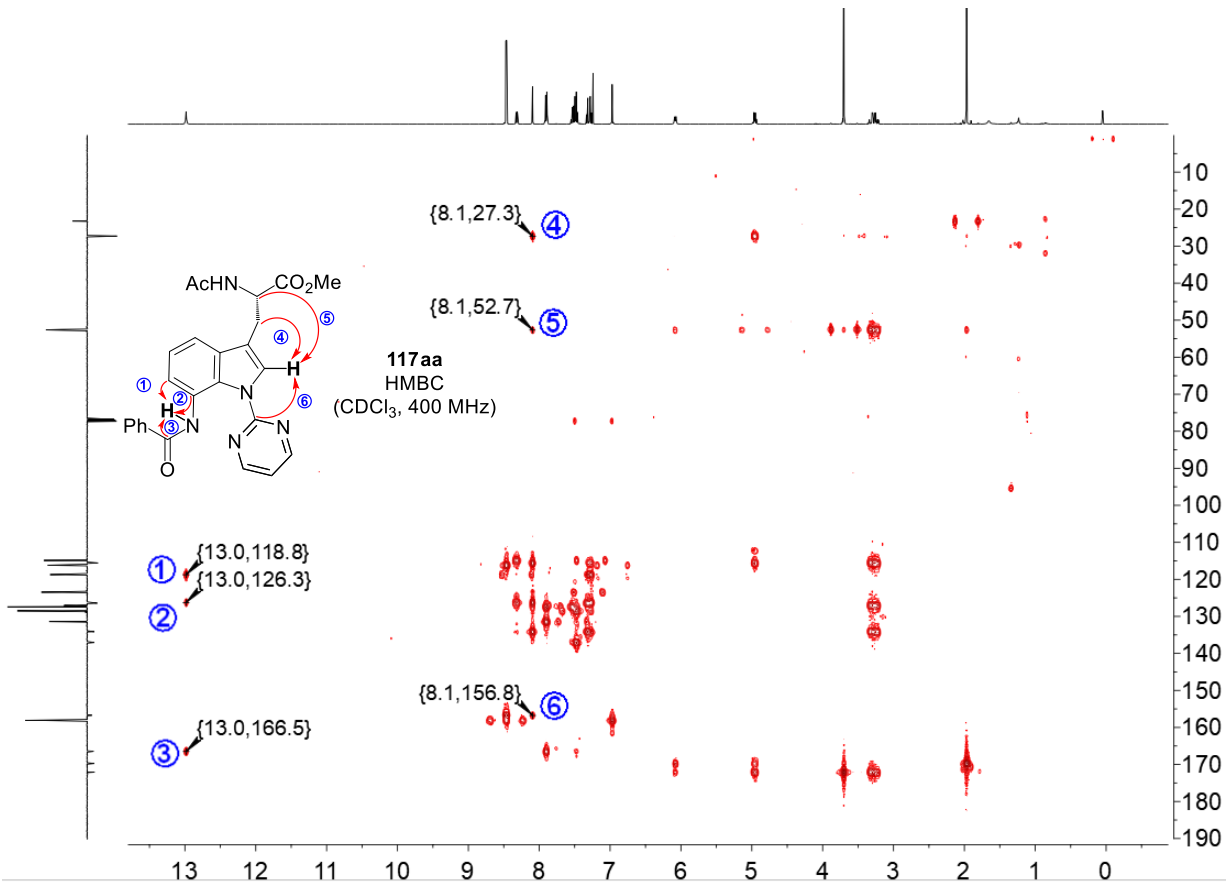


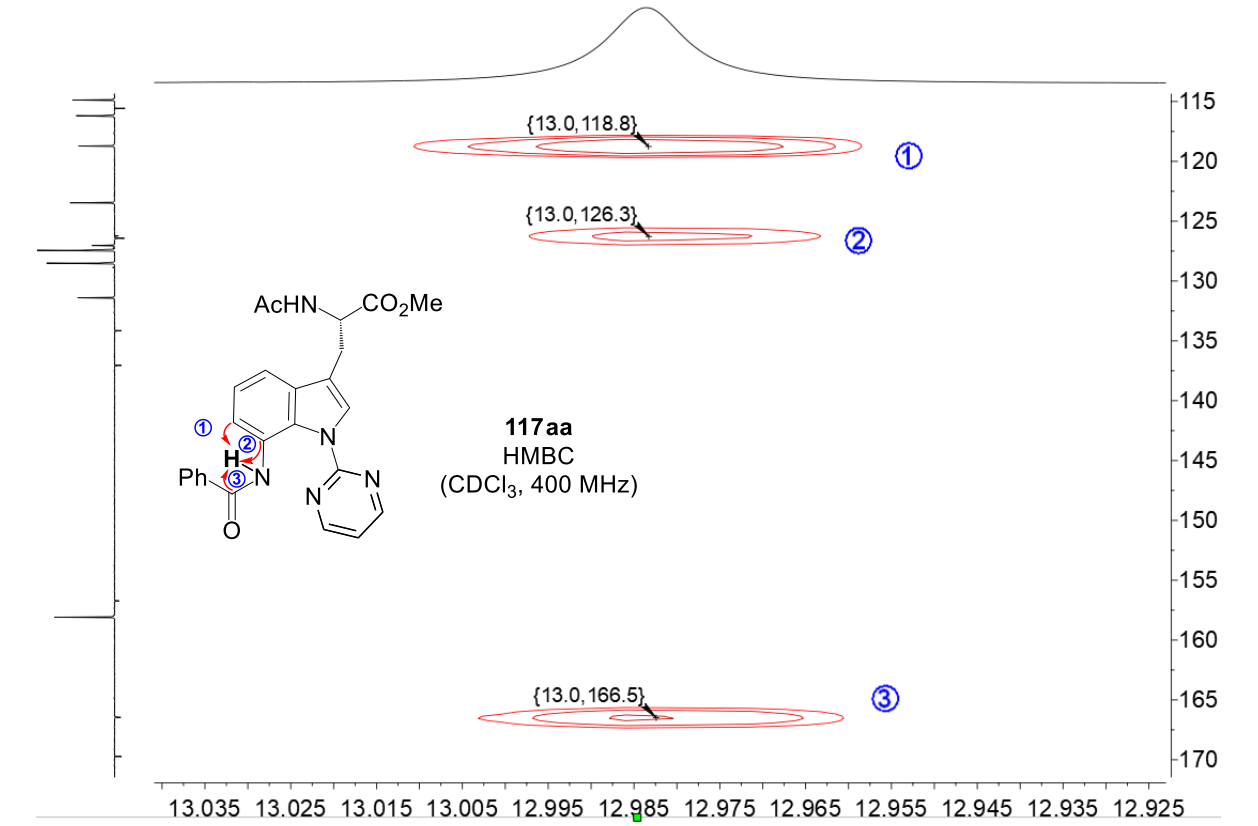
115b
($CDCl_3$, 282 MHz)

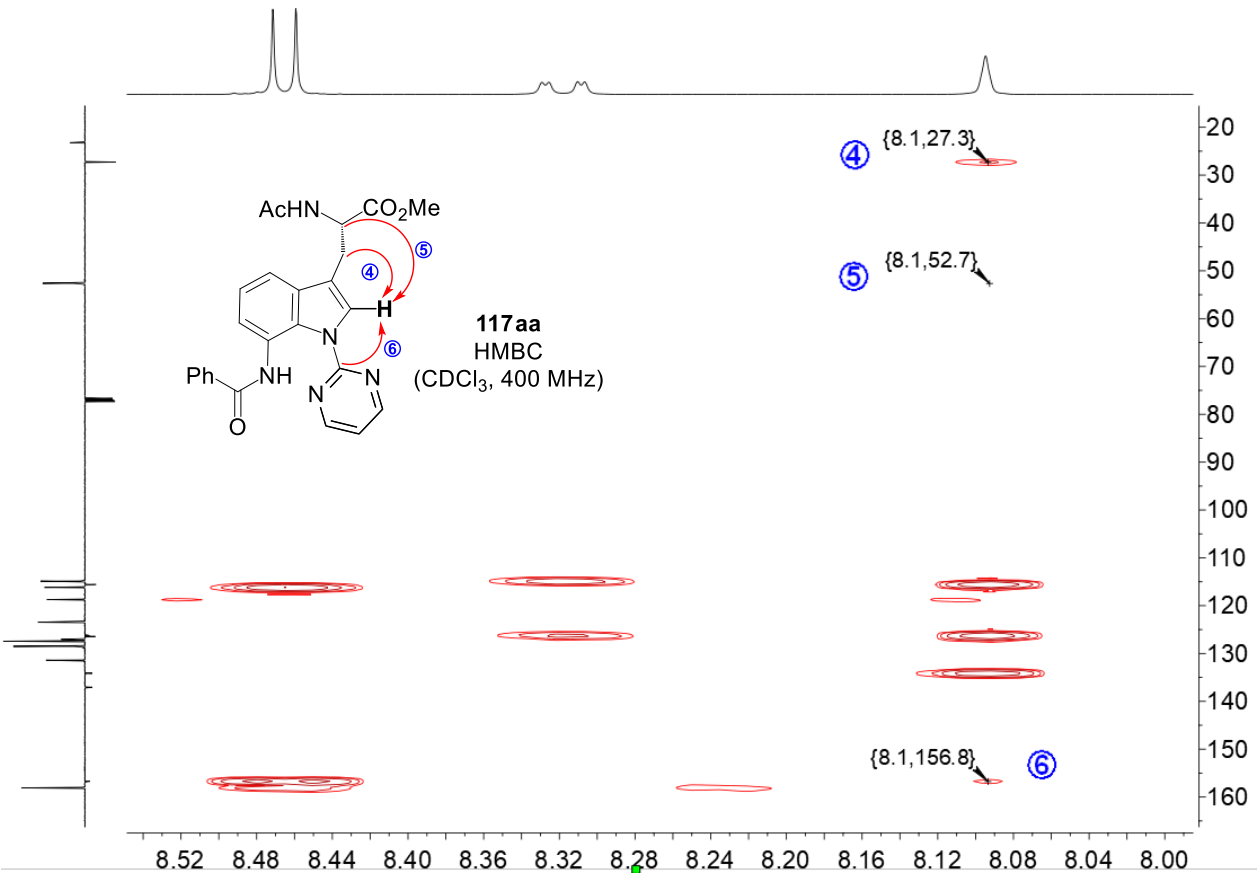


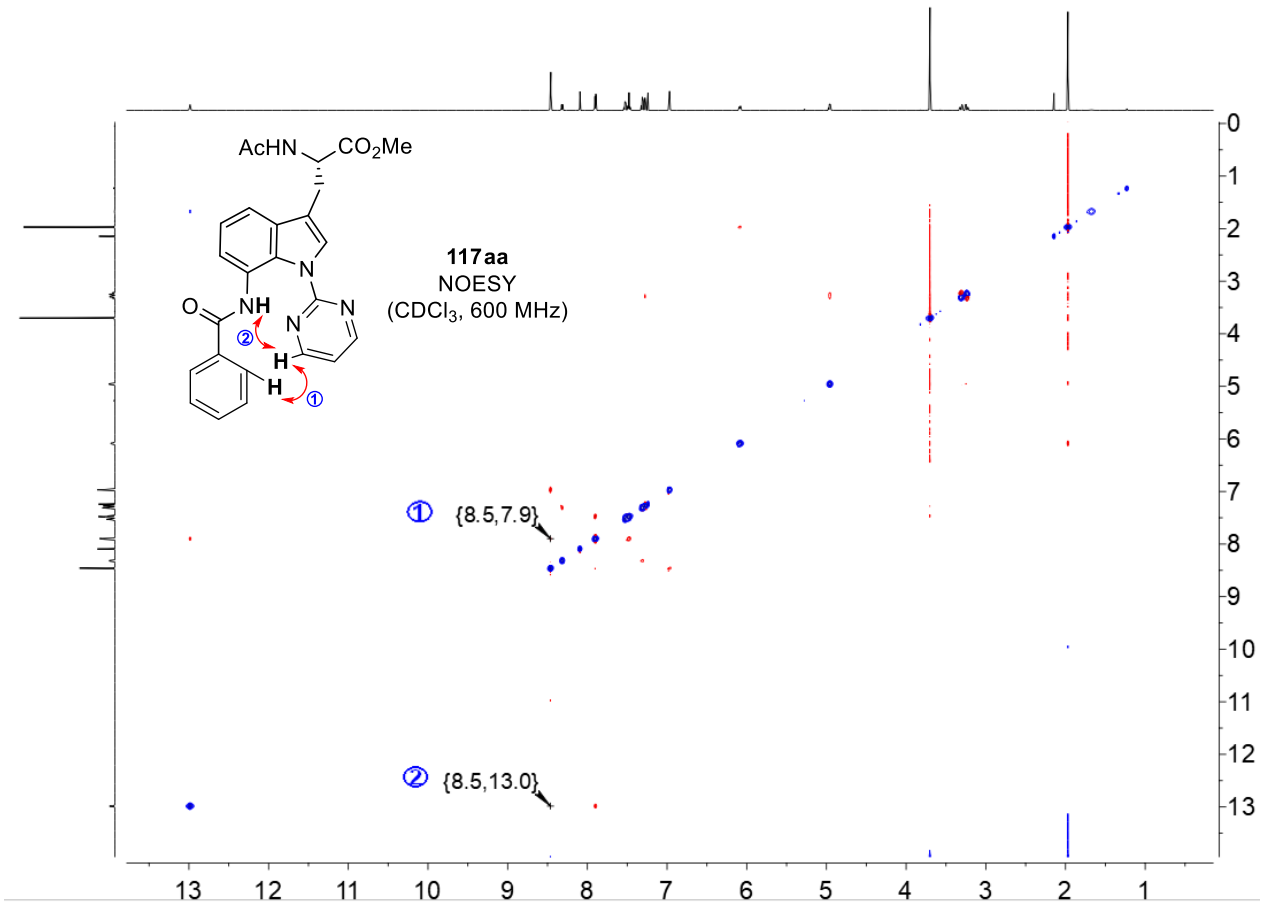
117aa
($CDCl_3$, 400 MHz)

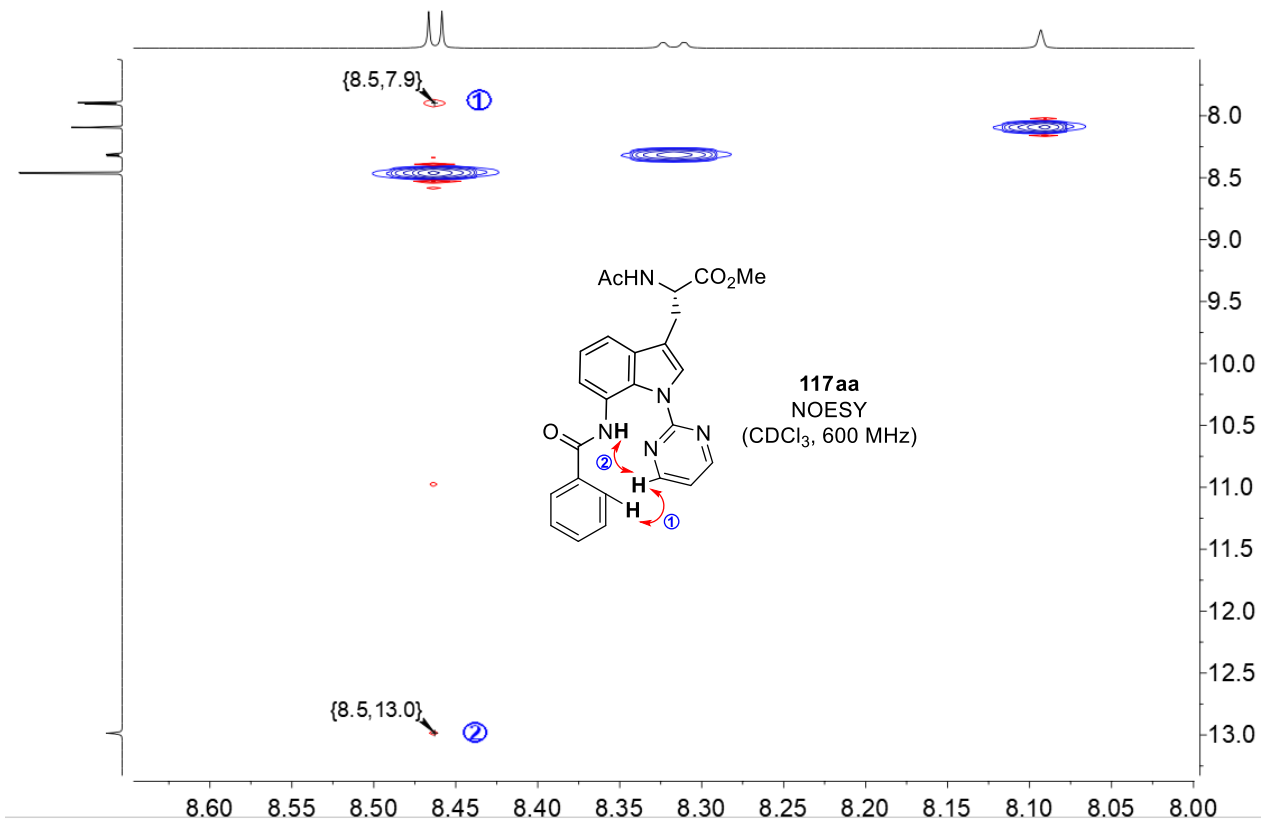

172.2
169.9
166.6
158.3
156.9
137.2
134.3
131.6
128.7
127.6
127.2
126.6
126.4
123.6
118.9
116.4
115.7
115.0
52.8
52.7
27.4
23.4
AcHN
CO2Me
Ph
NH
O
N
N
N
117aa
(CDCl3, 126 MHz)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

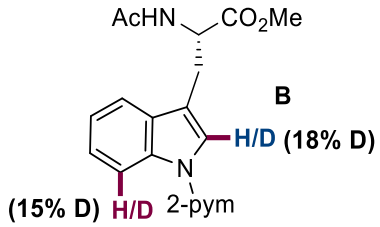

{8.1,27.3}
④
{8.1,52.7}
⑤
AcHN
CO2Me
117aa
HMBC
(CDCl3, 400 MHz)
{13.0,118.8}
{13.0,126.3}
①
②
{8.1,156.8}
⑥
{13.0,166.5}
③
13 12 11 10 9 8 7 6 5 4 3 2 1 0
10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190


{13.0,118.8}
{13.0,126.3}
{13.0,166.5}
AcHN
CO2Me
Ph
NH
O
N
H
117aa
HMBC
(CDCl3, 400 MHz)
13.035 13.025 13.015 13.005 12.995 12.985 12.975 12.965 12.955 12.945 12.935 12.925
115 120 125 130 135 140 145 150 155 160 165 170


{8.1,27.3}
{8.1,52.7}
{8.1,156.8}
AcHN
CO2Me
Ph
NH
O
N
H
117aa
HMBC
(CDCl3, 400 MHz)
8.52 8.48 8.44 8.40 8.36 8.32 8.28 8.24 8.20 8.16 8.12 8.08 8.04 8.00
20 30 40 50 60 70 80 90 100 110 120 130 140 150 160

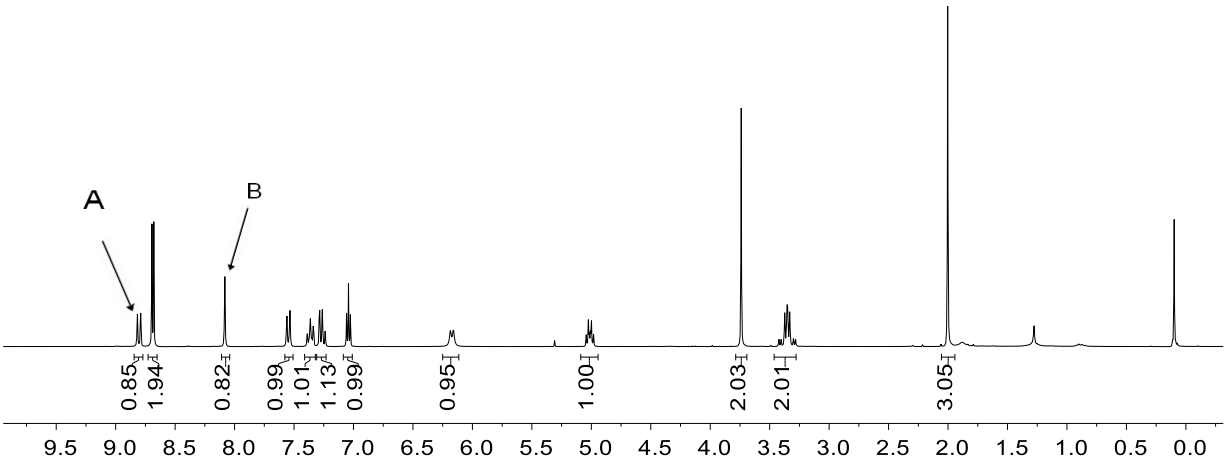

AcHN
CO2Me
117aa
NOESY
(CDCl3, 600 MHz)
{8.5,7.9}
{8.5,13.0}

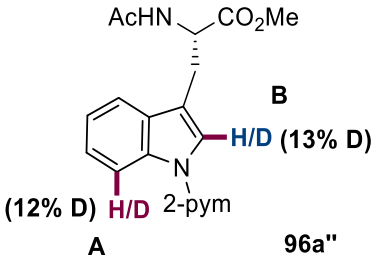

{8.5,7.9}
{8.5,13.0}
AcHN
CO2Me
117aa
NOESY
(CDCl3, 600 MHz)



96a'

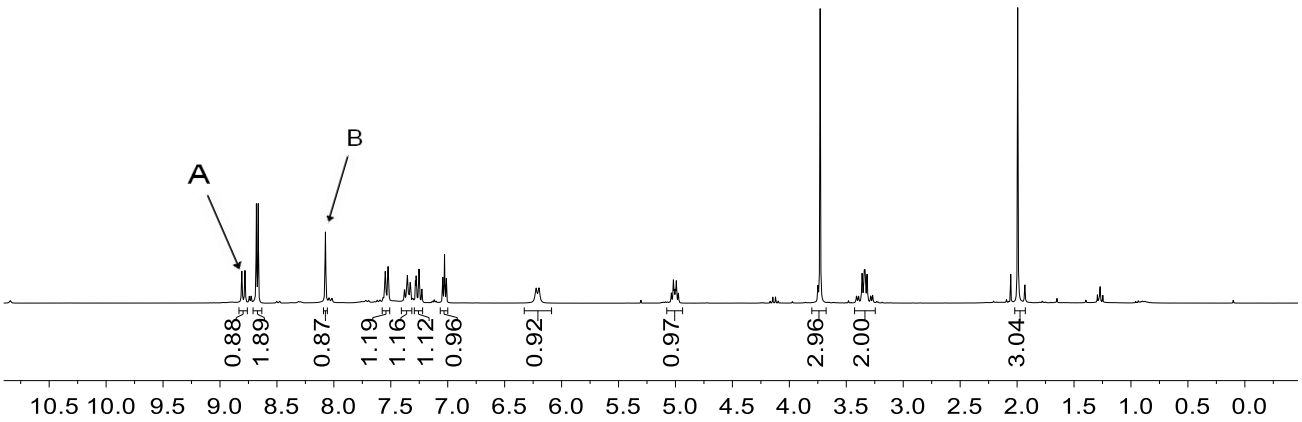
($CDCl_3$, 300 MHz)

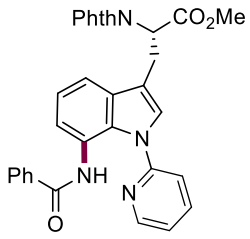




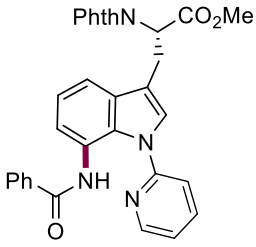
96a''

($CDCl_3$, 300 MHz)

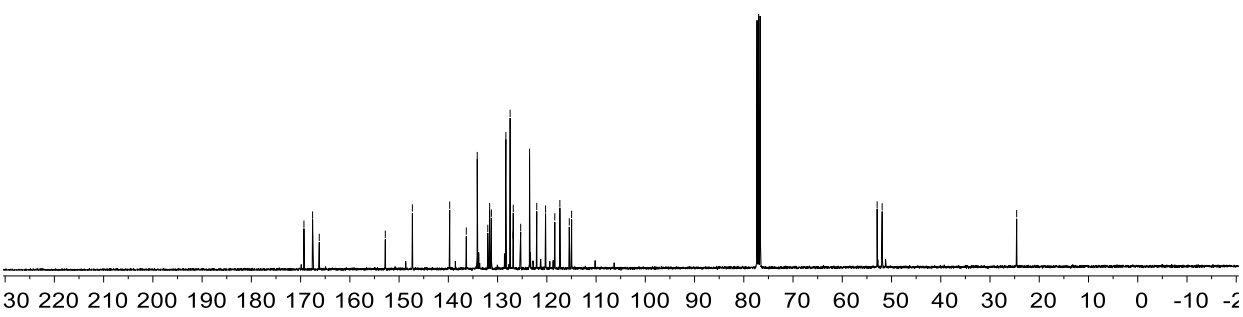


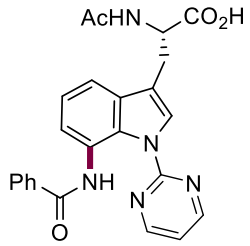


117ab
($CDCl_3$, 400 MHz)

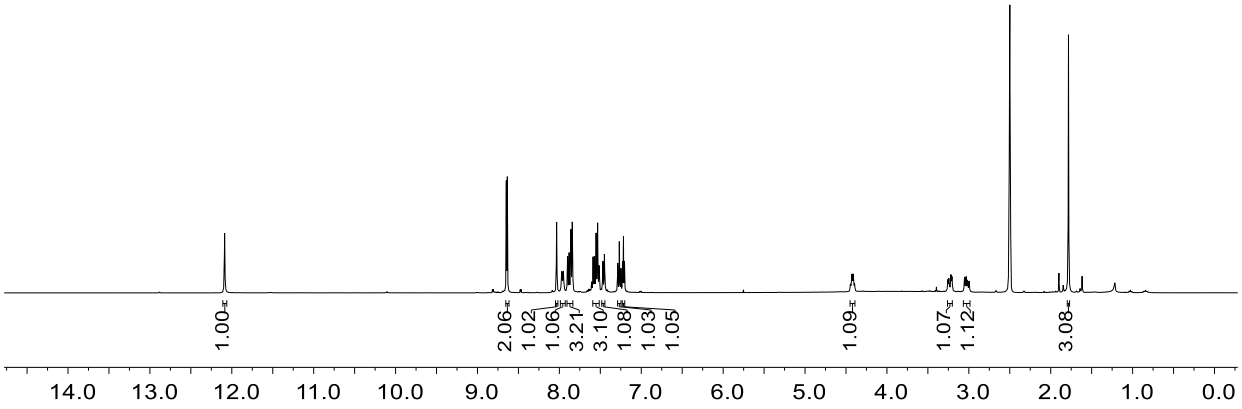


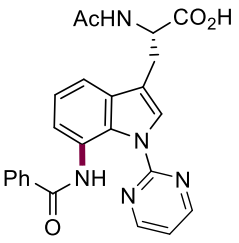
117ab
($CDCl_3$, 101 MHz)



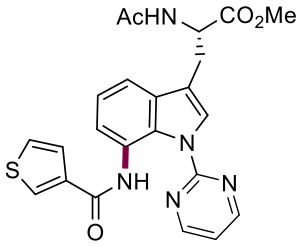


117ac
(DMSO-d_6, 400 MHz)

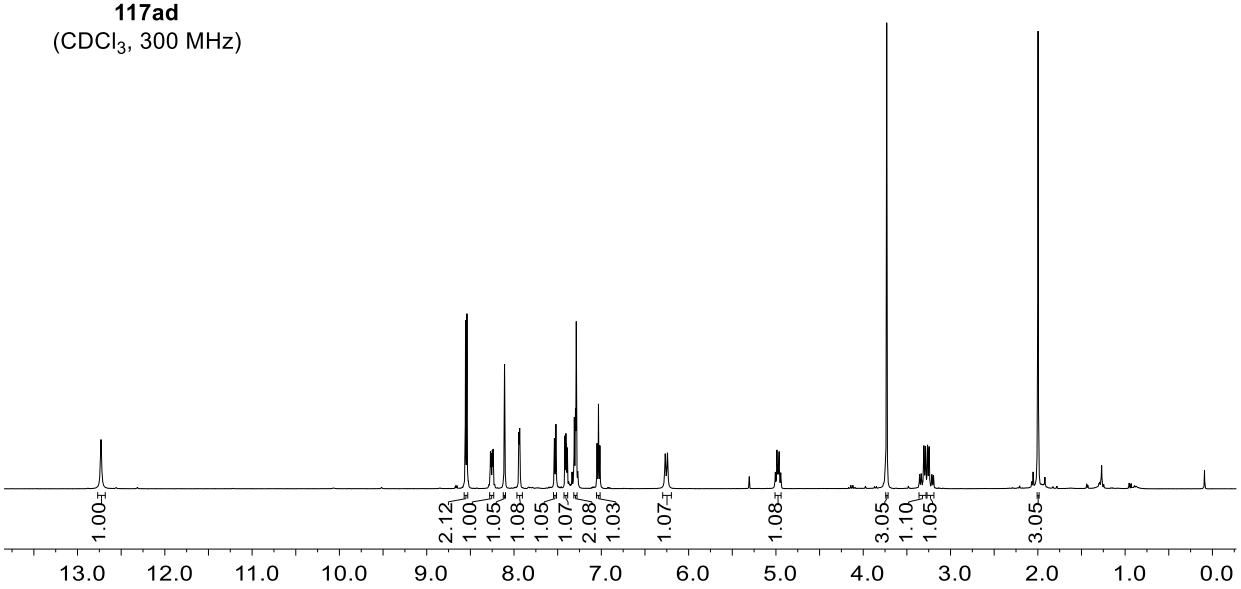


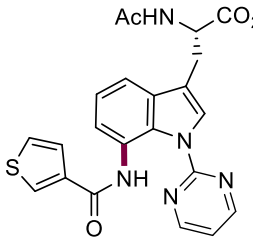


117ac
(DMSO-d_6, 101 MHz)

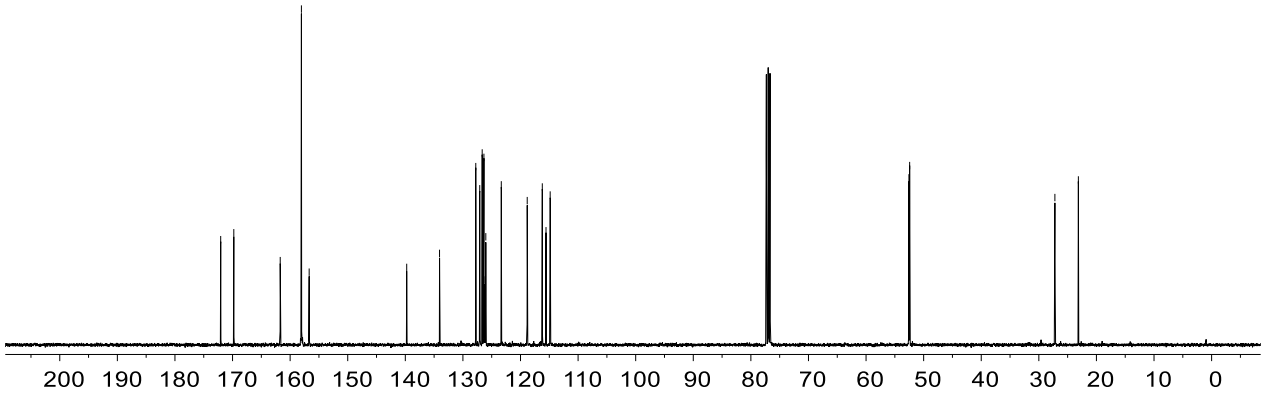


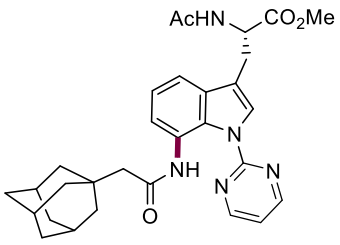
117ad
($CDCl_3$, 300 MHz)



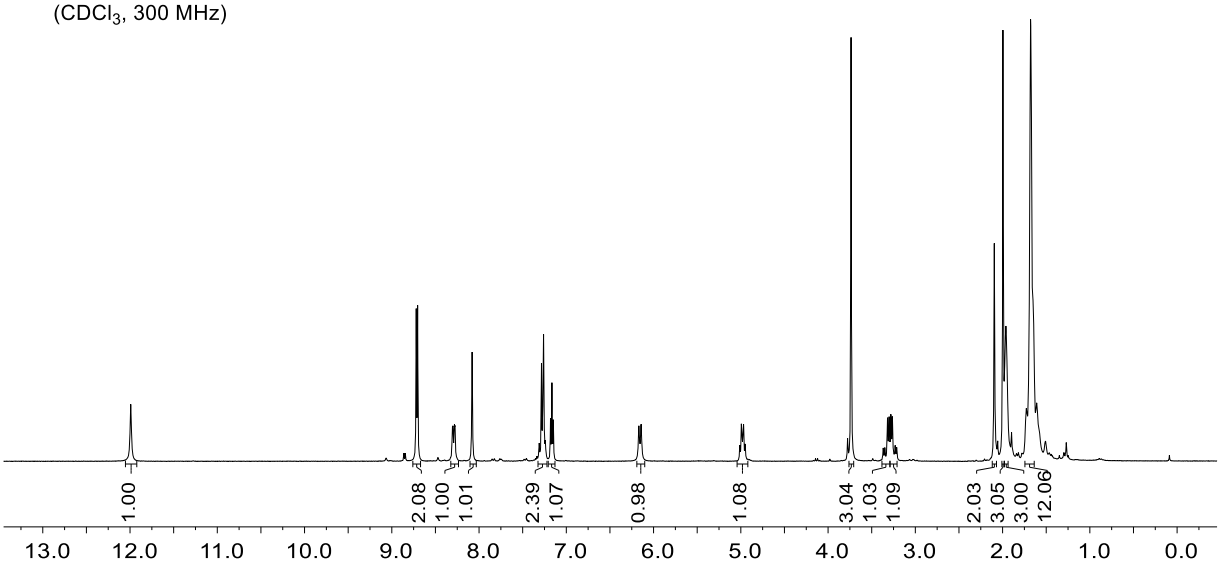


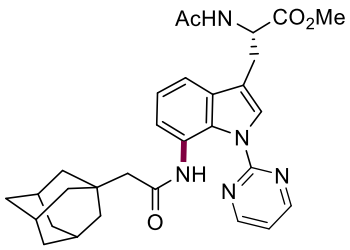
117ad



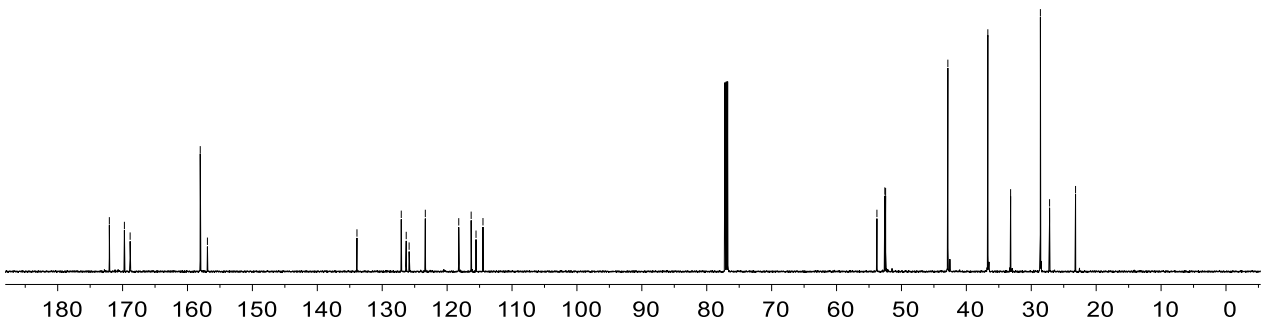


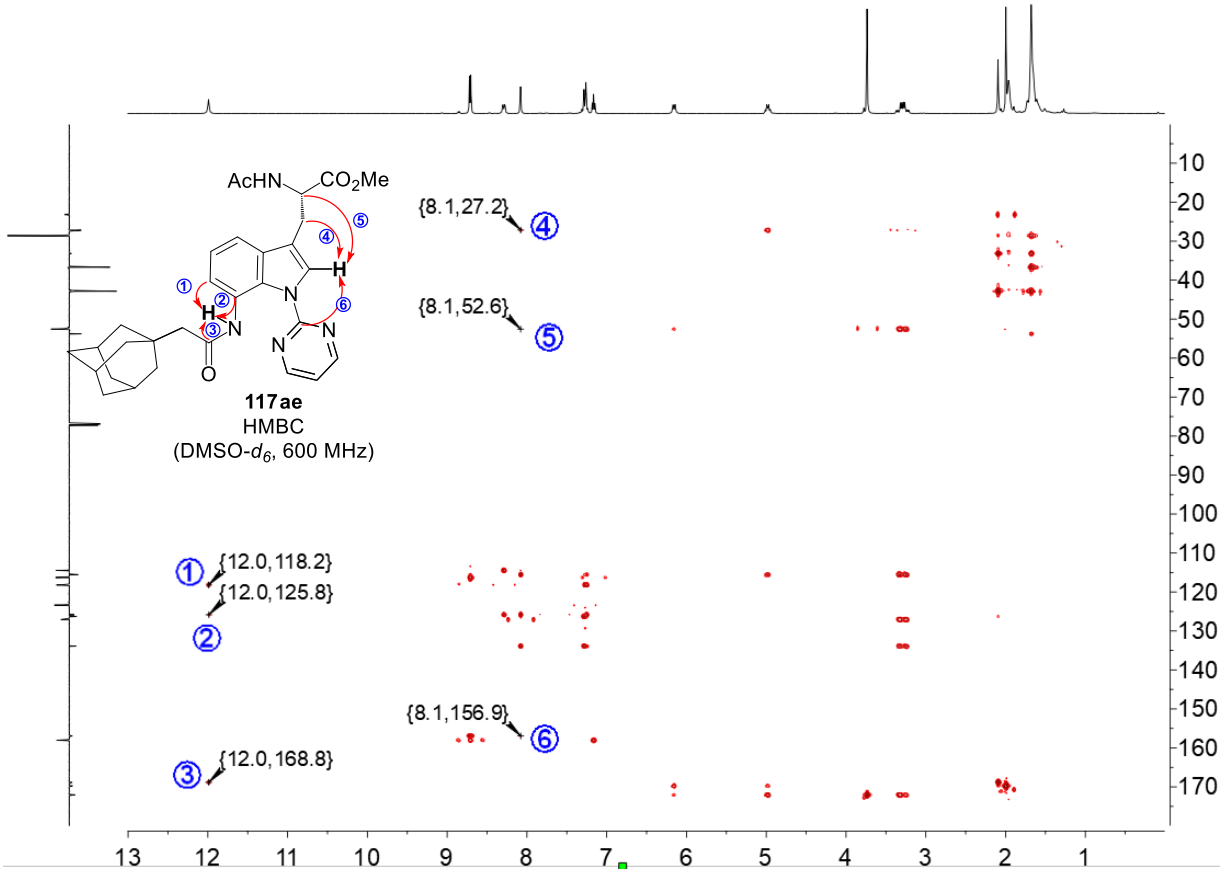
117ae
($CDCl_3$, 300 MHz)

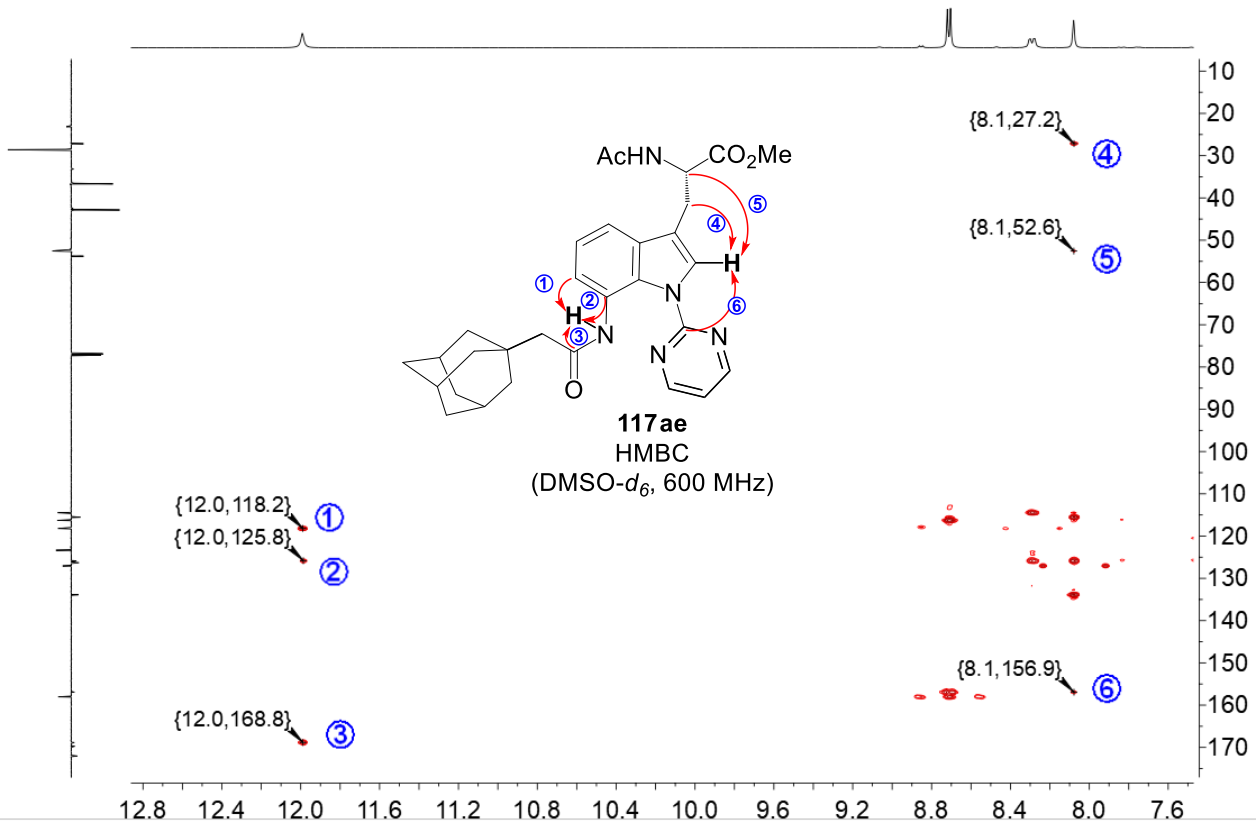


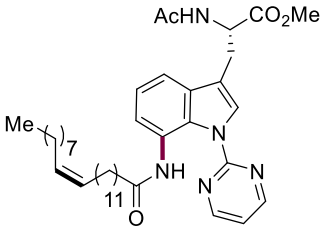


117ae
($CDCl_3$, 151 MHz)

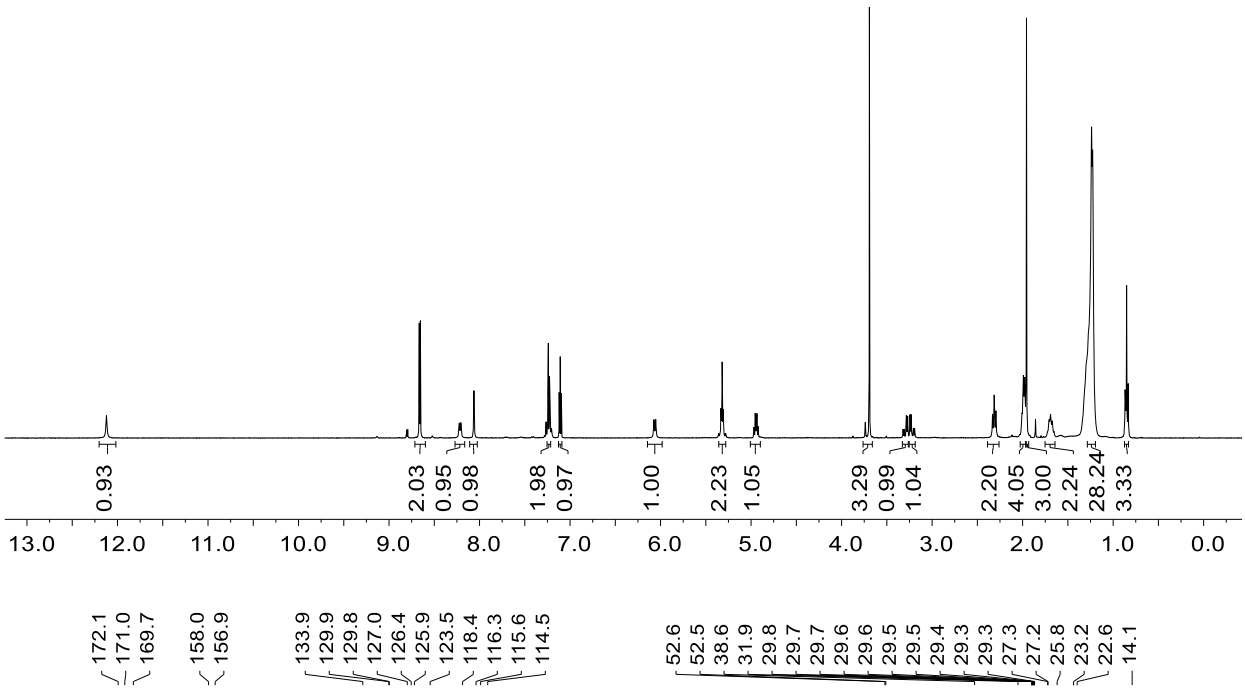


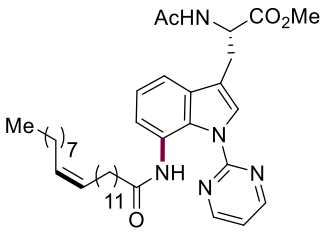

AcHN
CO2Me
{8.1,27.2}
{8.1,52.6}
{12.0,118.2}
{12.0,125.8}
{8.1,156.9}
{12.0,168.8}
117ae
HMBC
(DMSO-d6, 600 MHz)


AcHN
CO2Me
{8.1,27.2}
{8.1,52.6}
{12.0,118.2}
{12.0,125.8}
{8.1,156.9}
{12.0,168.8}
117ae
HMBC
(DMSO-d6, 600 MHz)

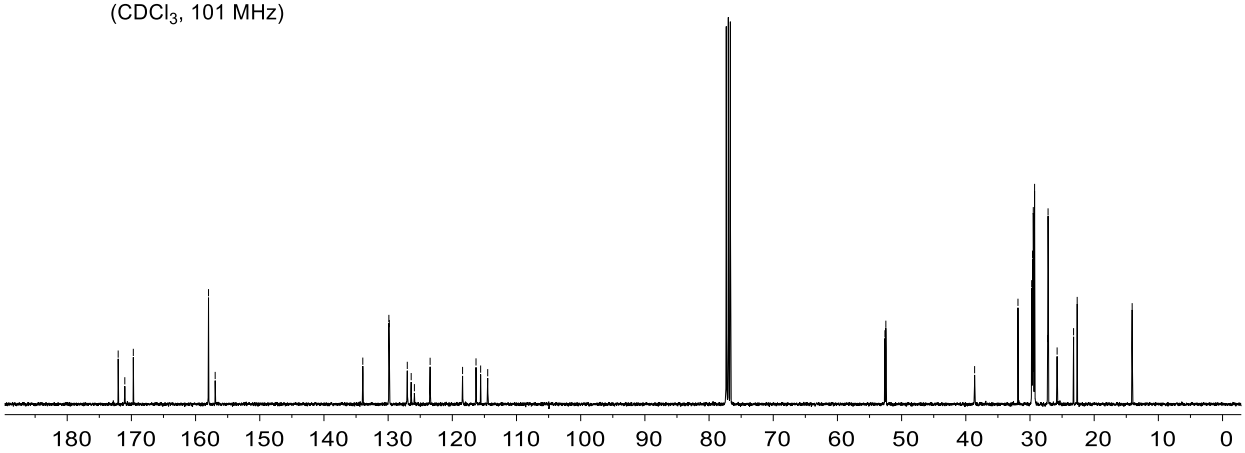


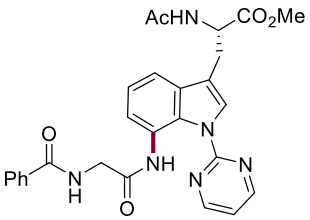
117af
($CDCl_3$, 400 MHz)



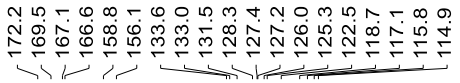


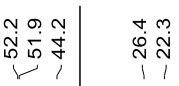
117af
($CDCl_3$, 101 MHz)

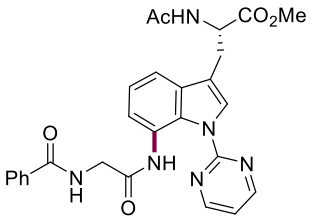




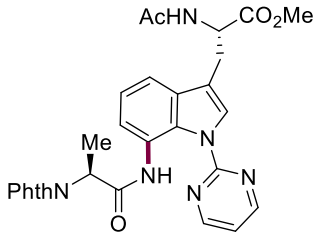
117ag
(DMSO-d_6, 400 MHz)



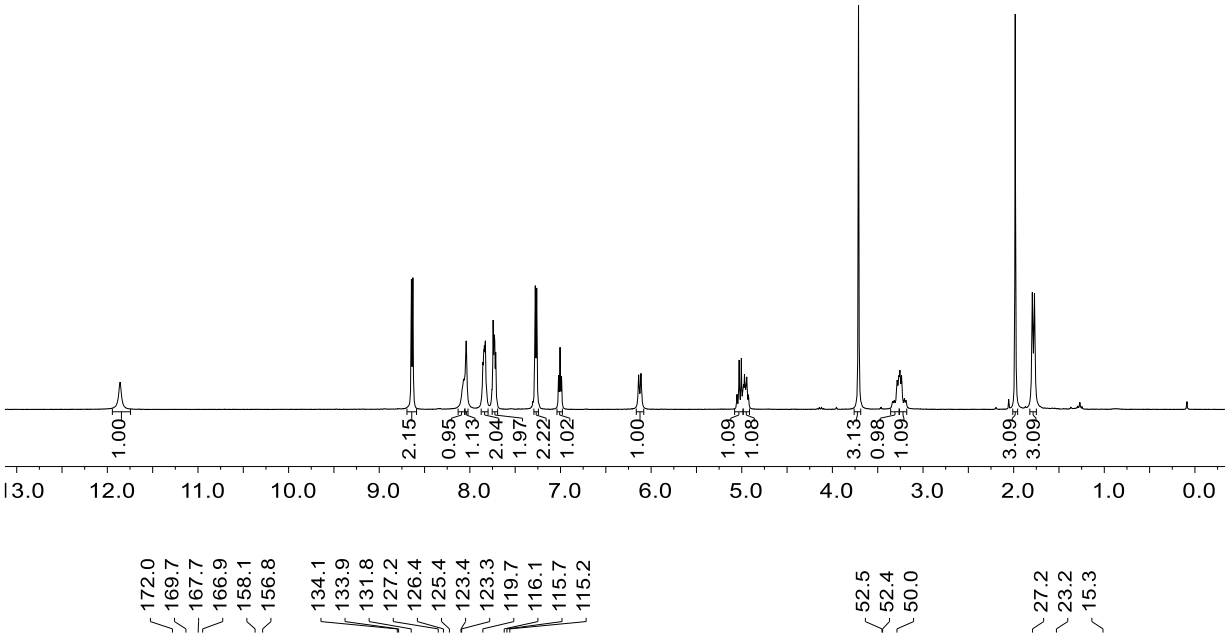


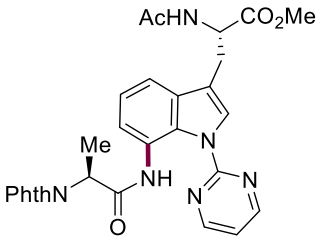


117ag
(DMSO-d_6, 101 MHz)

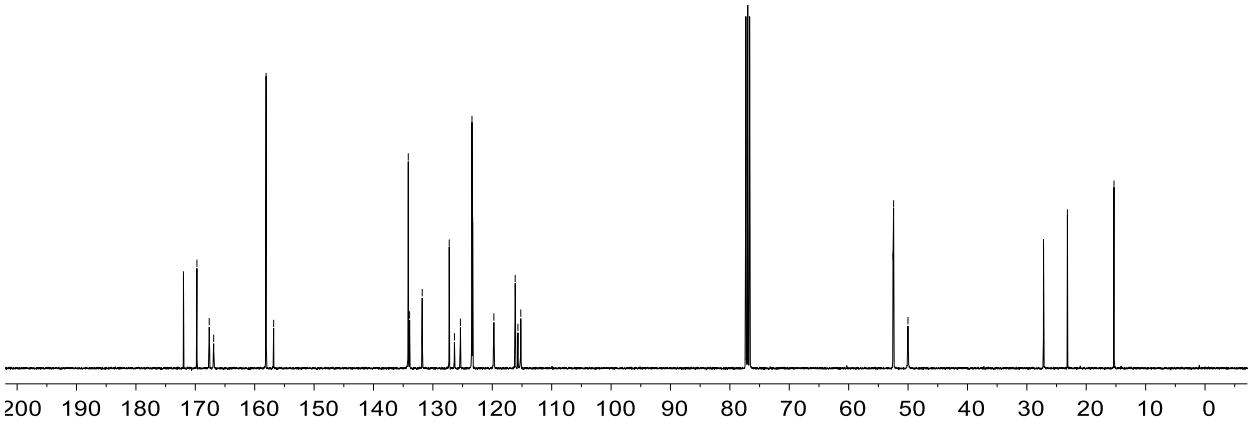


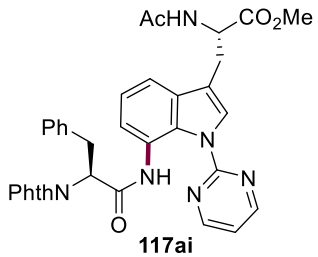
117ah
($CDCl_3$, 300 MHz)



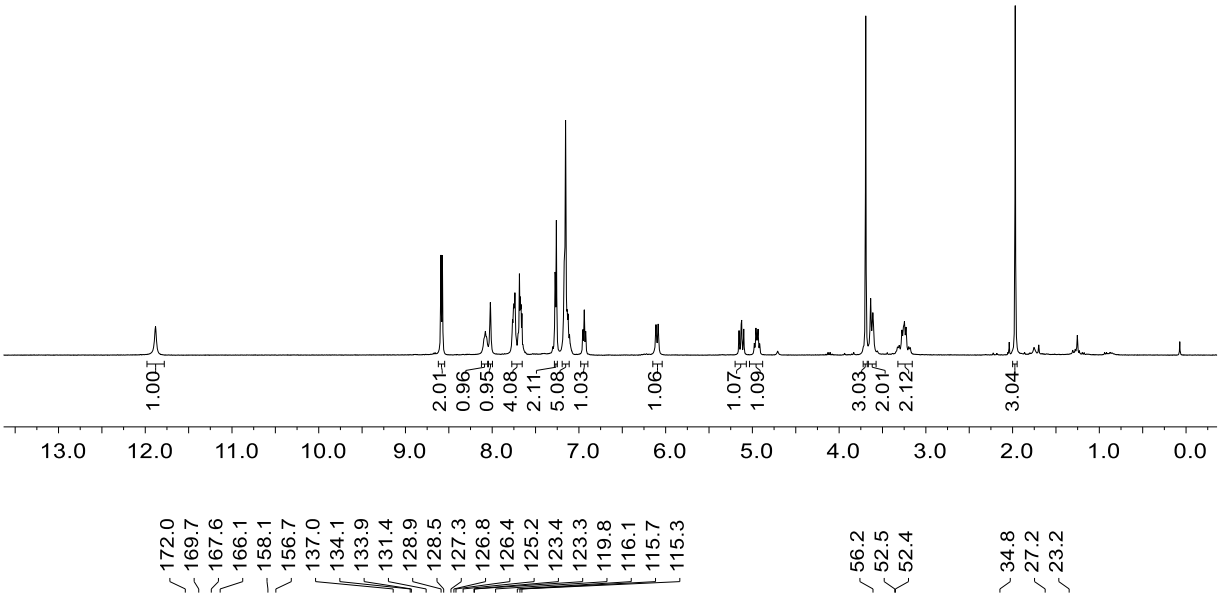


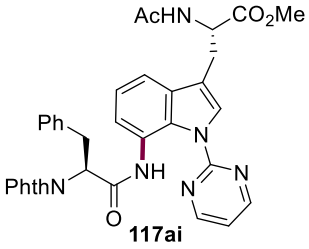
117ah
($CDCl_3$, 101 MHz)



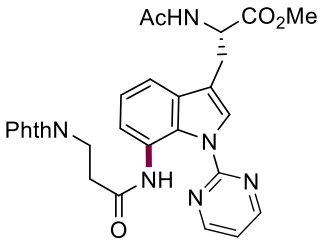


117ai
($CDCl_3$, 300 MHz)

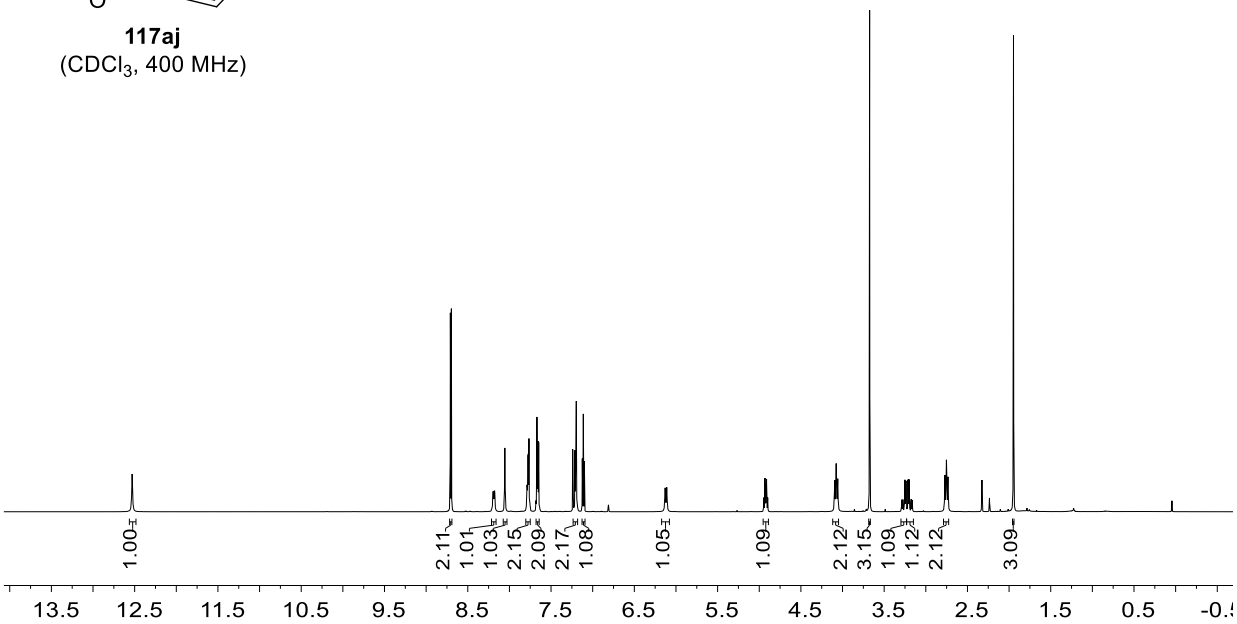


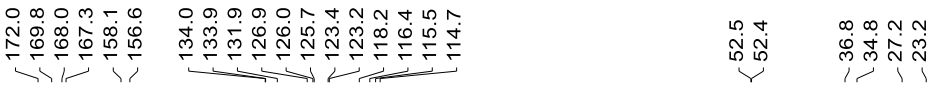


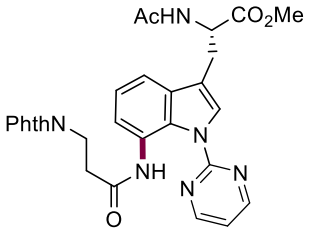
117ai
($CDCl_3$, 101 MHz)



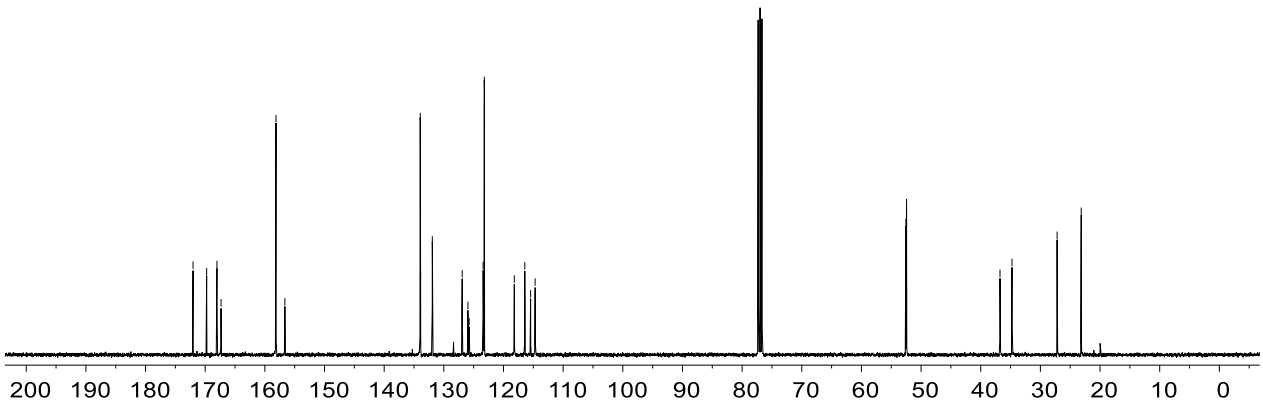
117aj
($CDCl_3$, 400 MHz)

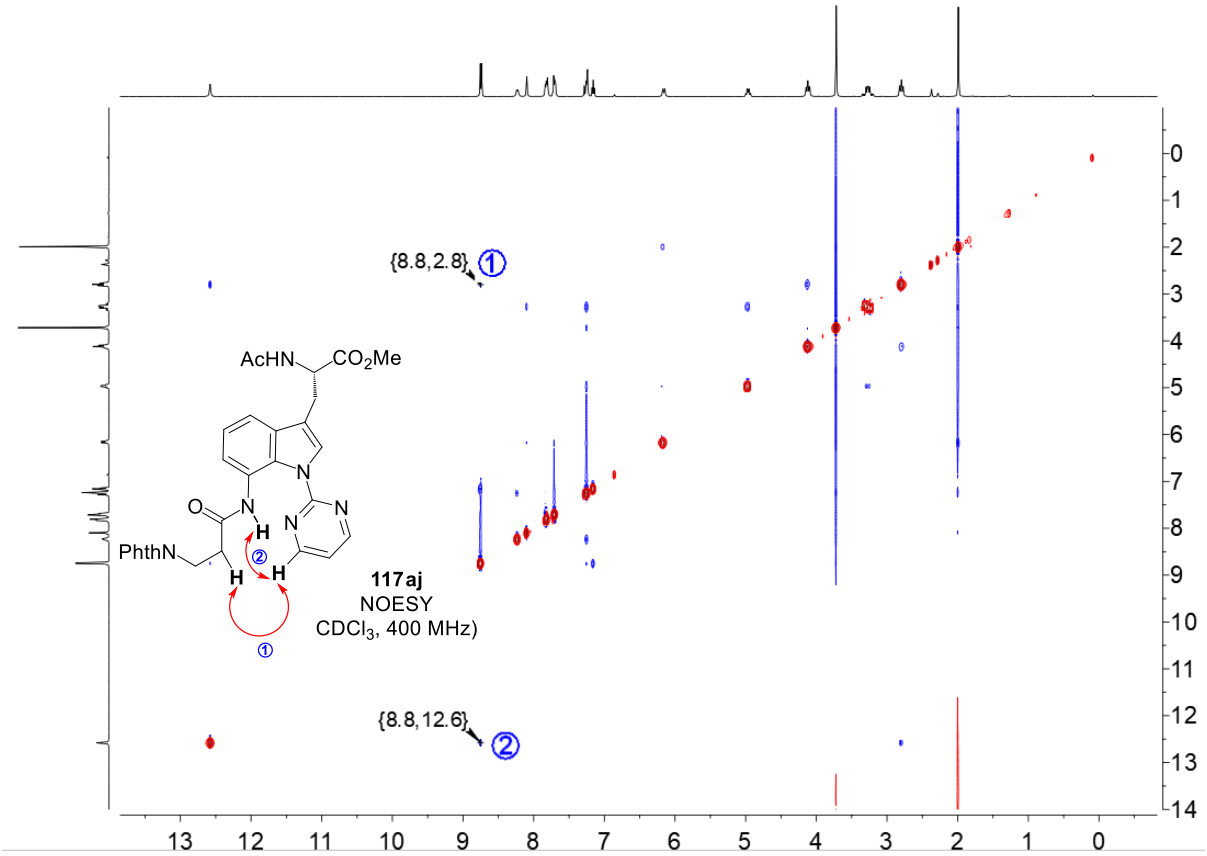


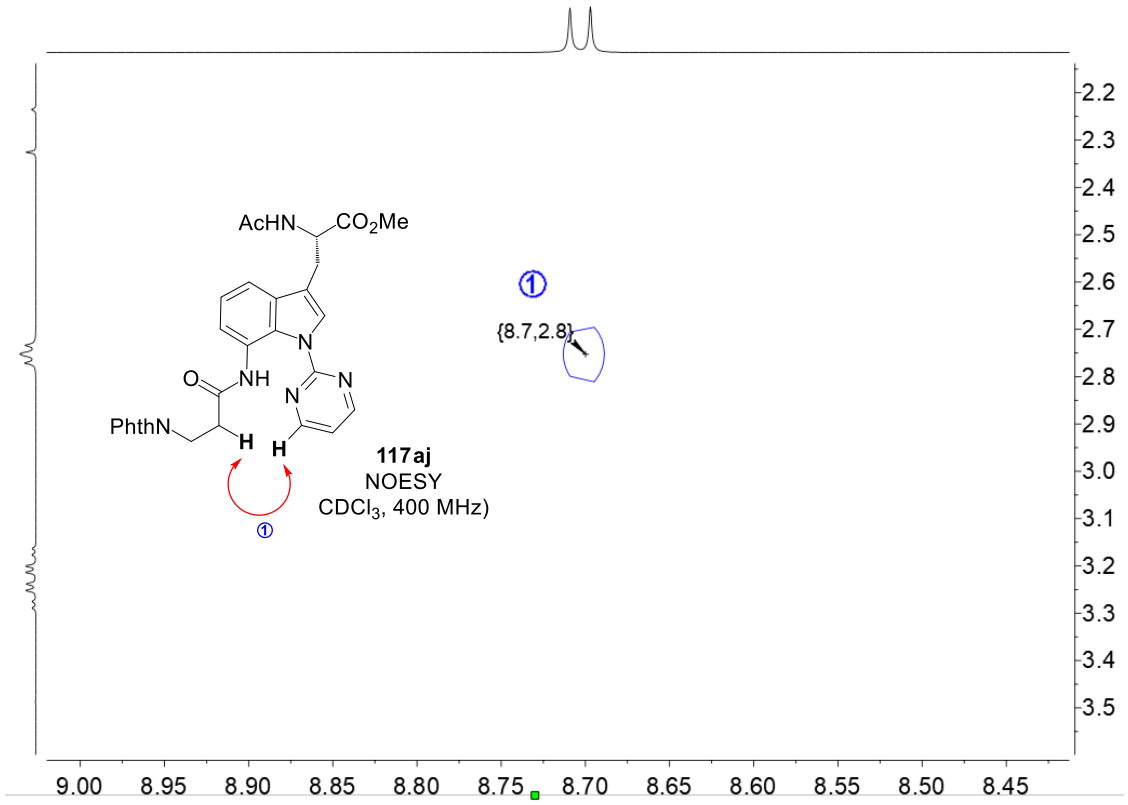


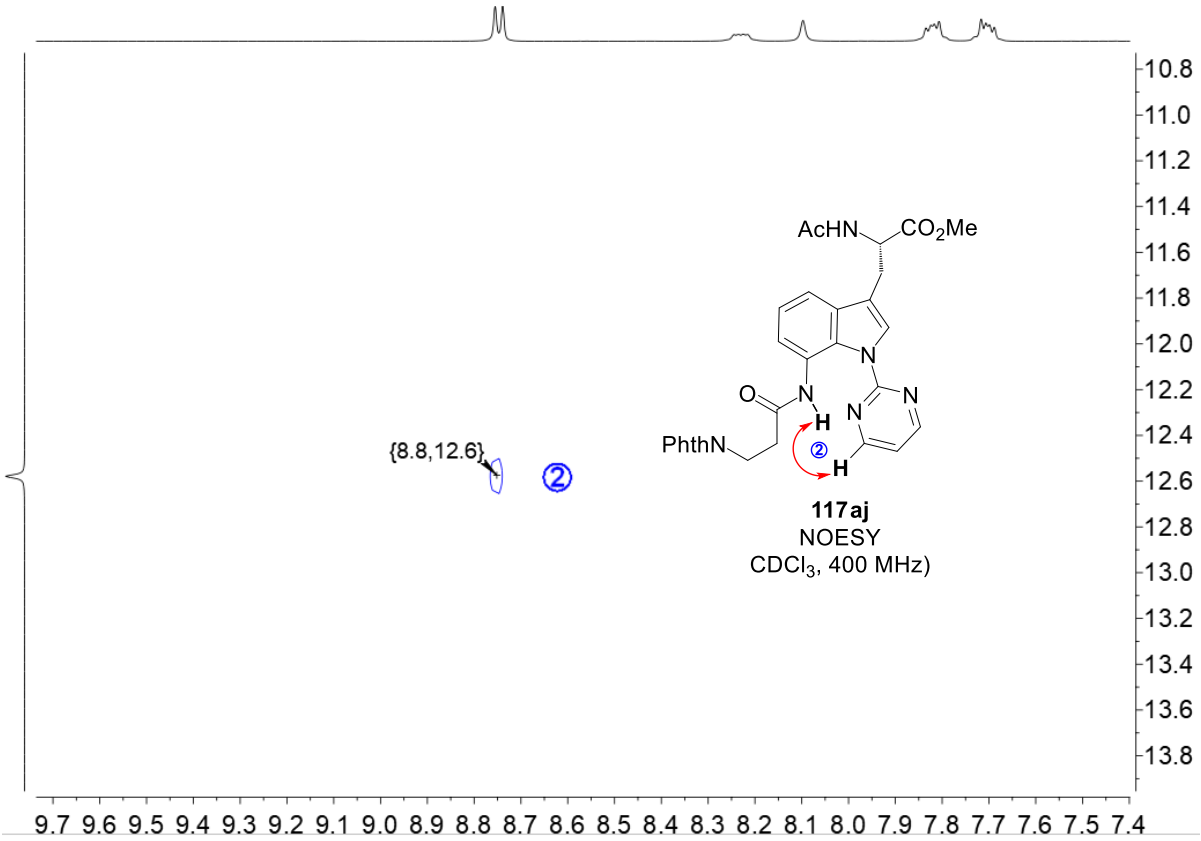


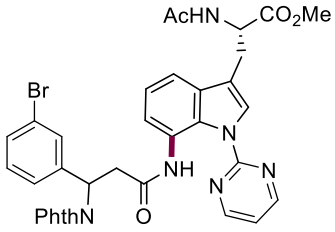
117aj
($CDCl_3$, 101 MHz)



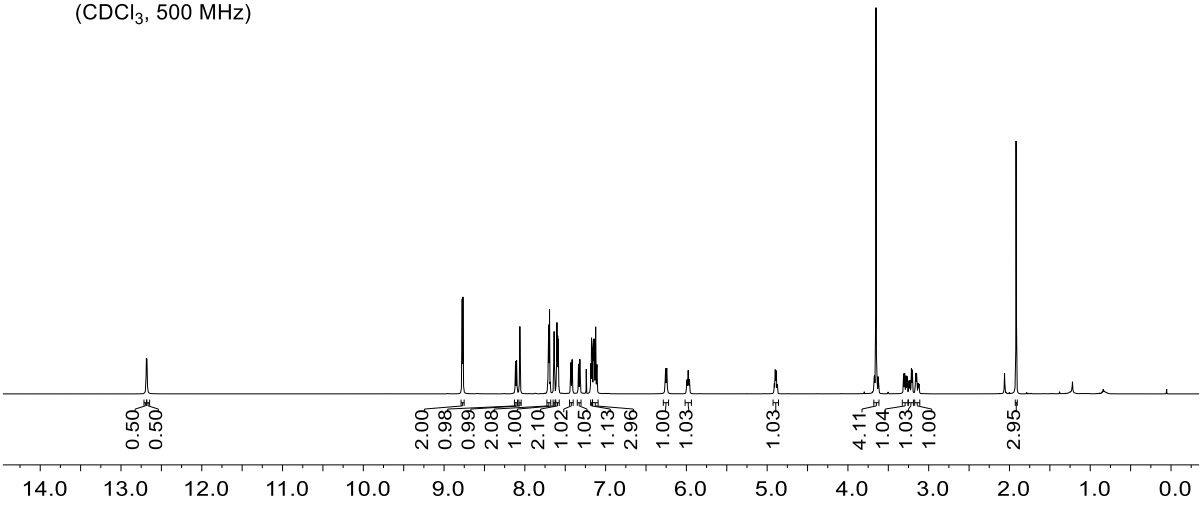

{8.8,2.8}
①
AcHN
CO2Me
PhthN
O
N
H
②
H
N
N
N
①
117aj
NOESY
CDCl3, 400 MHz)
{8.8,12.6}
②
13 12 11 10 9 8 7 6 5 4 3 2 1 0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14

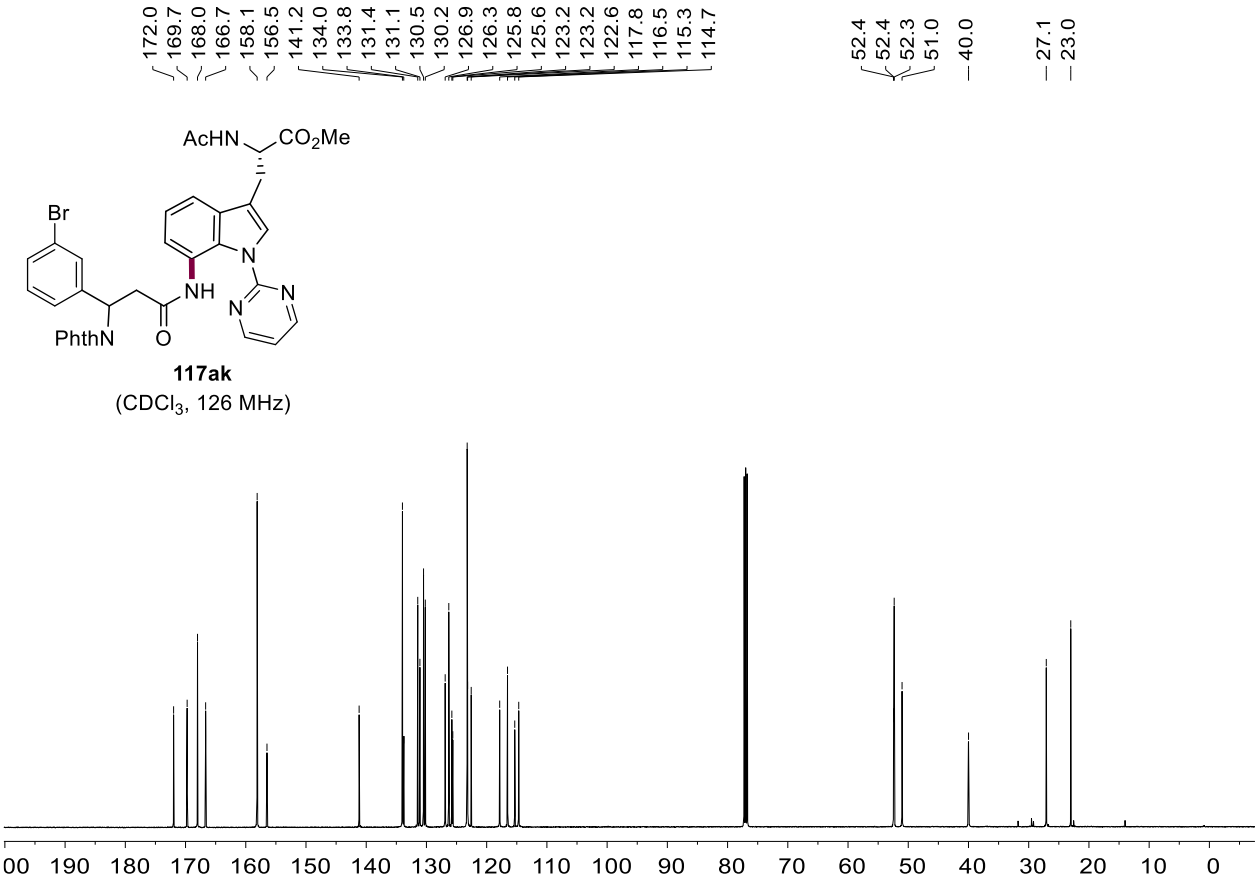

AcHN
CO2Me
①
{8.7,2.8}
PhthN
O
NH
N
N
H
H
①
117aj
NOESY
CDCl3, 400 MHz)
9.00 8.95 8.90 8.85 8.80 8.75 8.70 8.65 8.60 8.55 8.50 8.45
2.2 2.3 2.4 2.5 2.6 2.7 2.8 2.9 3.0 3.1 3.2 3.3 3.4 3.5

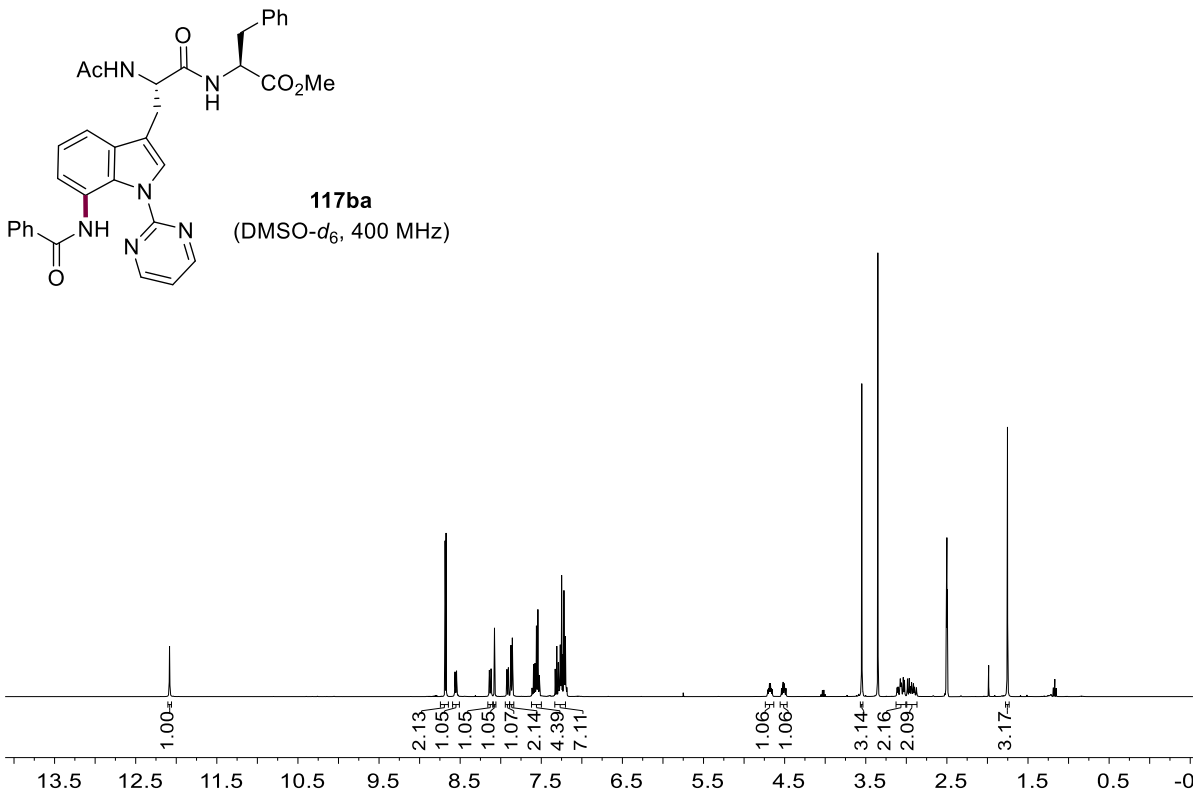


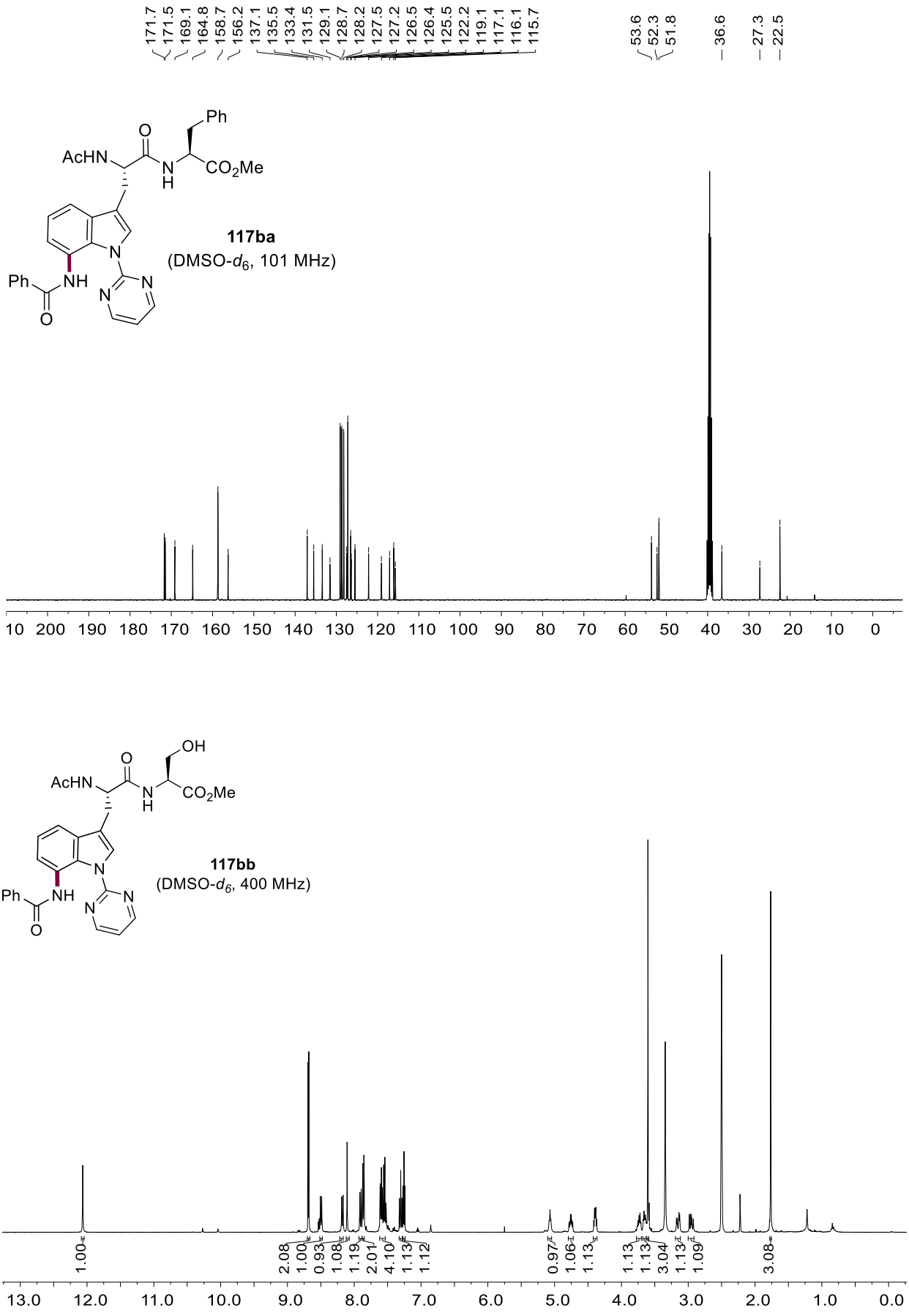


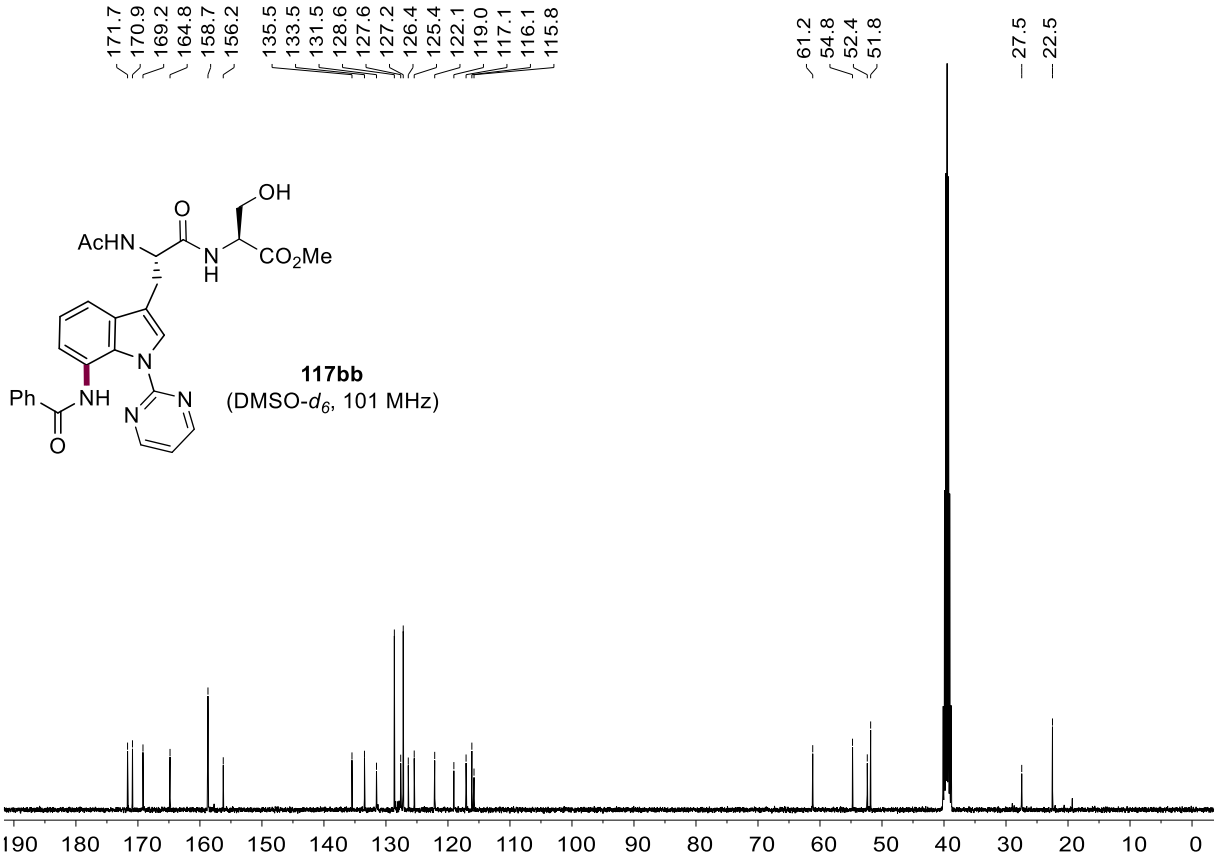
117ak
($CDCl_3$, 500 MHz)

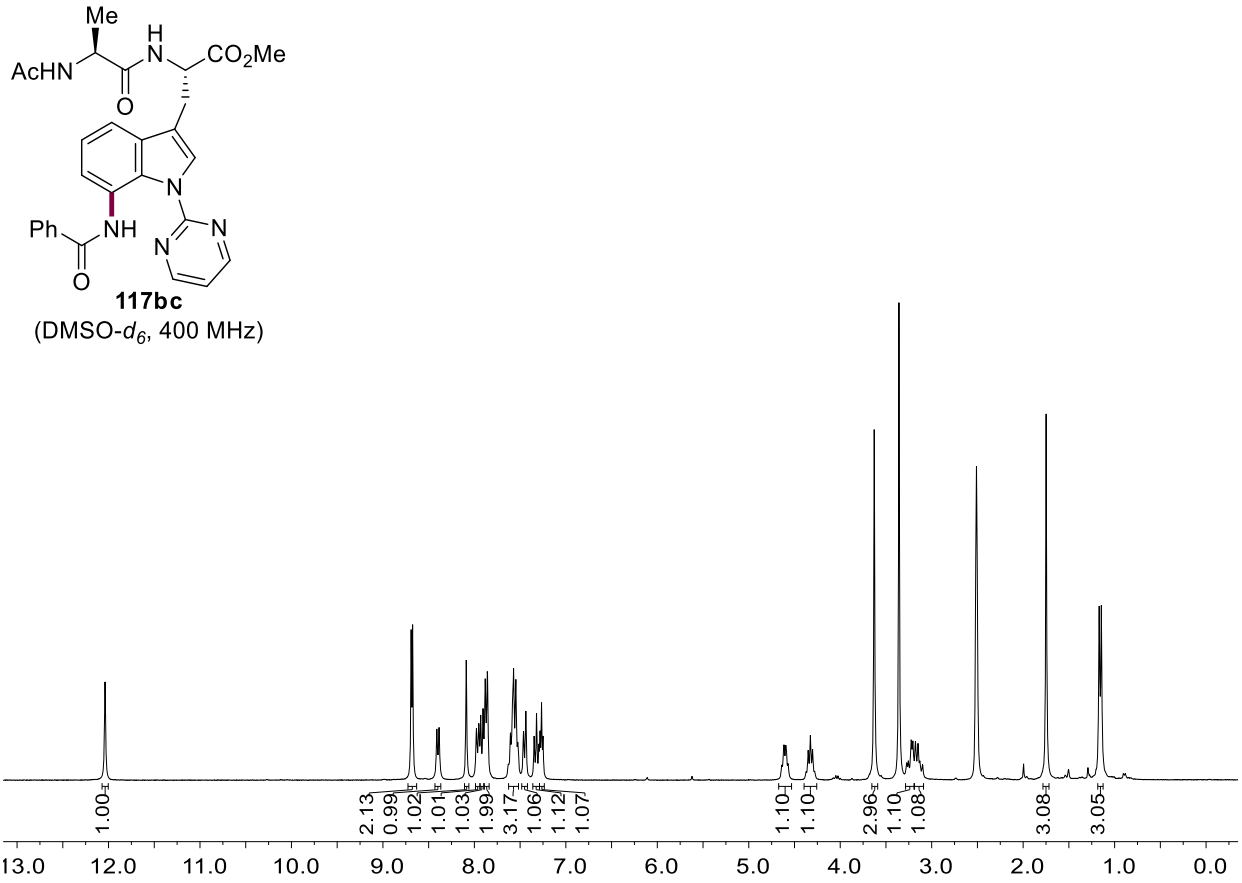


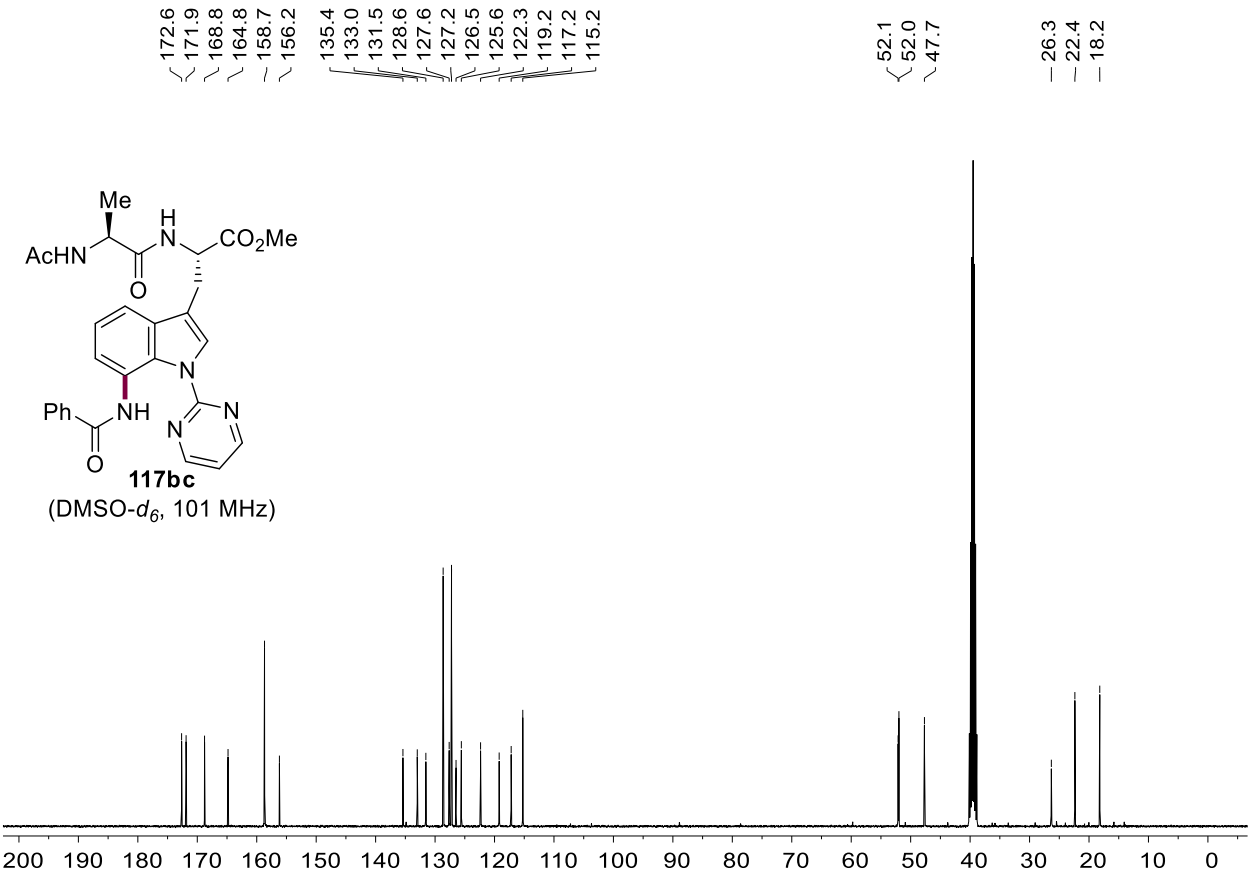

172.0
169.7
168.0
166.7
158.1
156.5
141.2
134.0
133.8
131.4
131.1
130.5
130.2
126.9
126.3
125.8
125.6
123.2
123.2
122.6
117.8
116.5
115.3
114.7
52.4
52.4
52.3
51.0
40.0
27.1
23.0
AcHN
CO2Me
Br
NH
PhthN
O
N
N
117ak
(CDCl3, 126 MHz)
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


Ph
AcHN
O
N
H
CO2Me
Ph
NH
O
N
N
117ba
(DMSO-d6, 400 MHz)
1.00
2.13
1.05
1.05
1.05
1.07
2.14
4.39
7.11
1.06
1.06
3.14
2.16
2.09
3.17
13.5 12.5 11.5 10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0

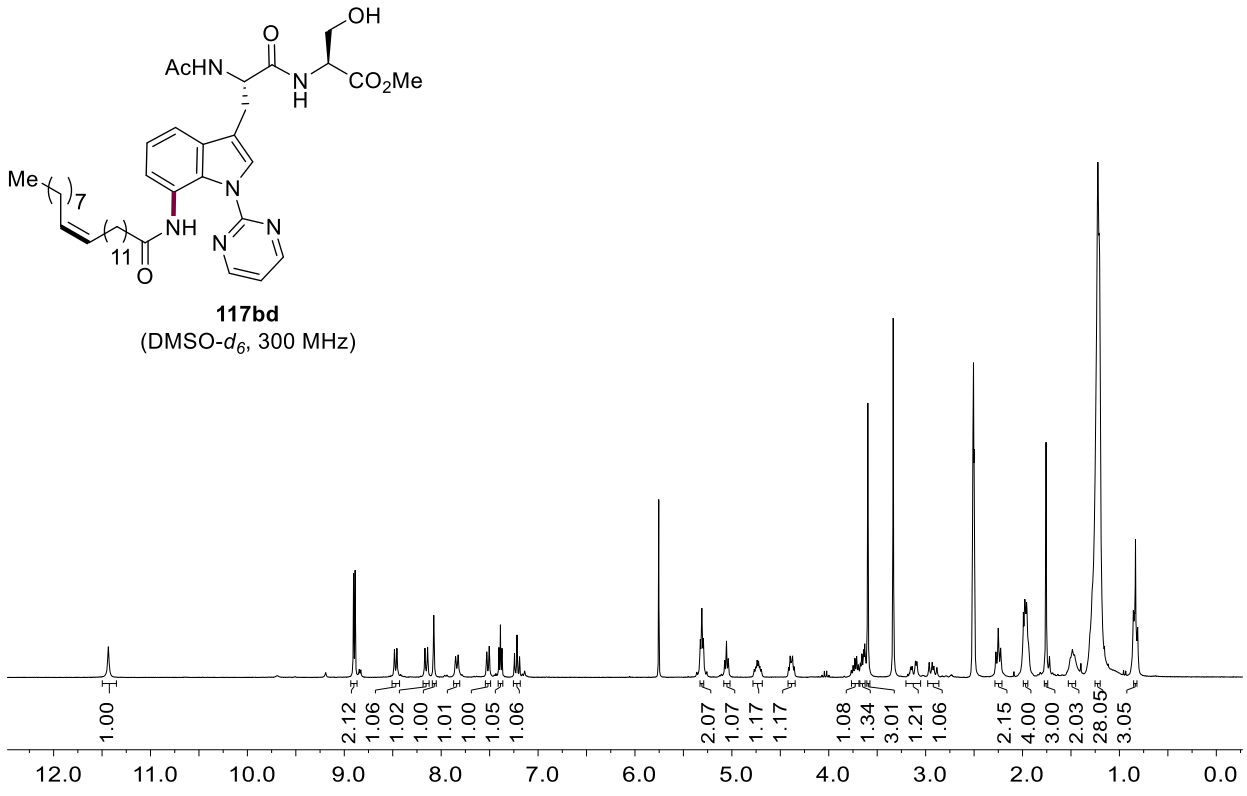

171.7
171.5
169.1
164.8
158.7
156.2
137.1
135.5
133.4
131.5
129.1
128.7
128.2
127.5
127.2
126.5
126.4
125.5
122.2
119.1
117.1
116.1
115.7
53.6
52.3
51.8
36.6
27.3
22.5
AcHN
O
N
H
Ph
CO2Me
N
Ph
NH
O
N
N
117ba
(DMSO-d6, 101 MHz)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
OH
AcHN
O
N
H
CO2Me
N
Ph
NH
O
N
N
117bb
(DMSO-d6, 400 MHz)
1.00
2.08
1.00
0.93
1.08
1.19
2.01
4.10
1.13
1.12
0.97
1.06
1.13
1.13
1.13
3.04
1.13
1.09
3.08
13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0


171.7
170.9
169.2
164.8
158.7
156.2
135.5
133.5
131.5
128.6
127.6
127.2
126.4
125.4
122.1
119.0
117.1
116.1
115.8
61.2
54.8
52.4
51.8
27.5
22.5
AcHN
O
N
H
OH
CO2Me
Ph
NH
O
N
N
117bb
(DMSO-d6, 101 MHz)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

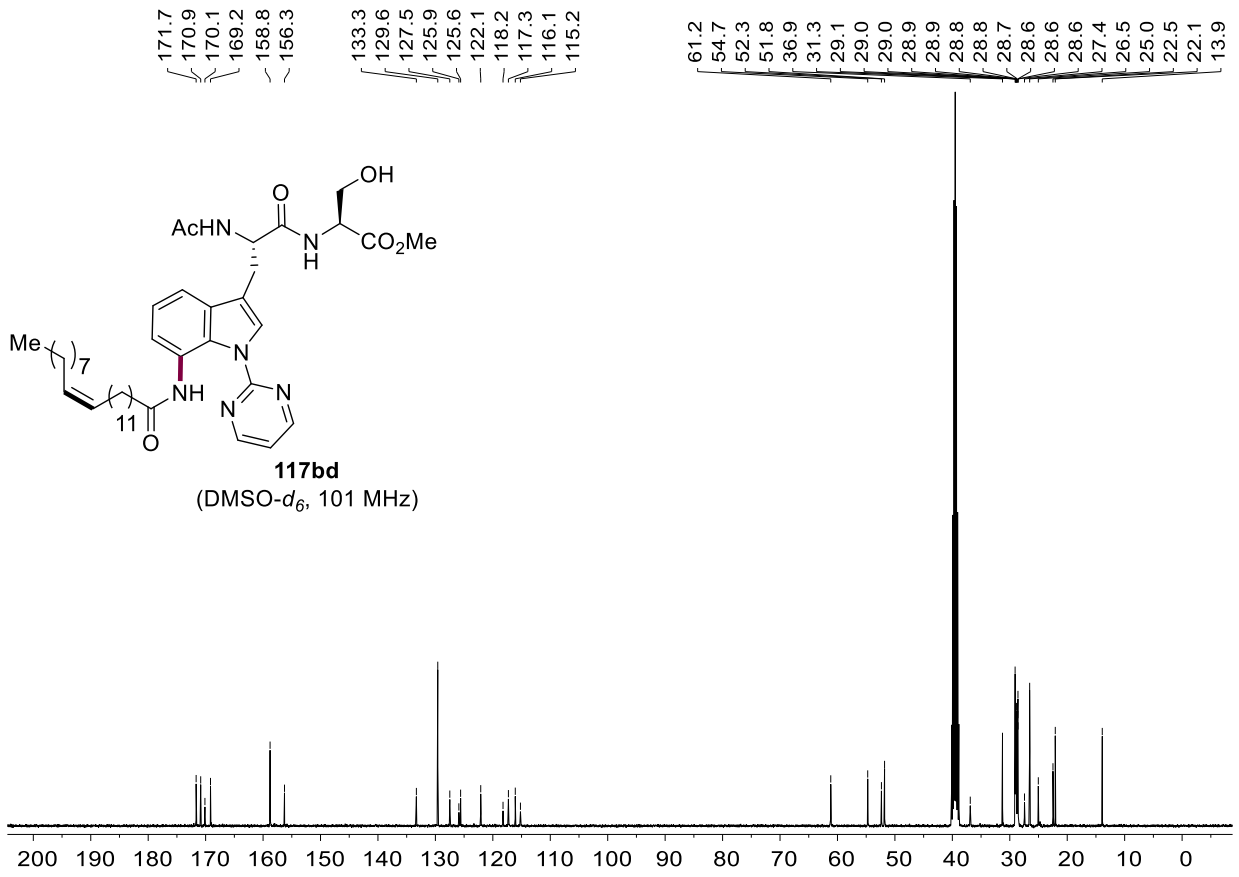

Me
AcHN
O
H
N
CO2Me
Ph
NH
O
N
N
117bc
(DMSO-d6, 400 MHz)
1.00
2.13
0.99
1.02
1.01
1.03
1.99
3.17
1.06
1.12
1.07
1.10
1.10
2.96
1.10
1.08
3.08
3.05
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0



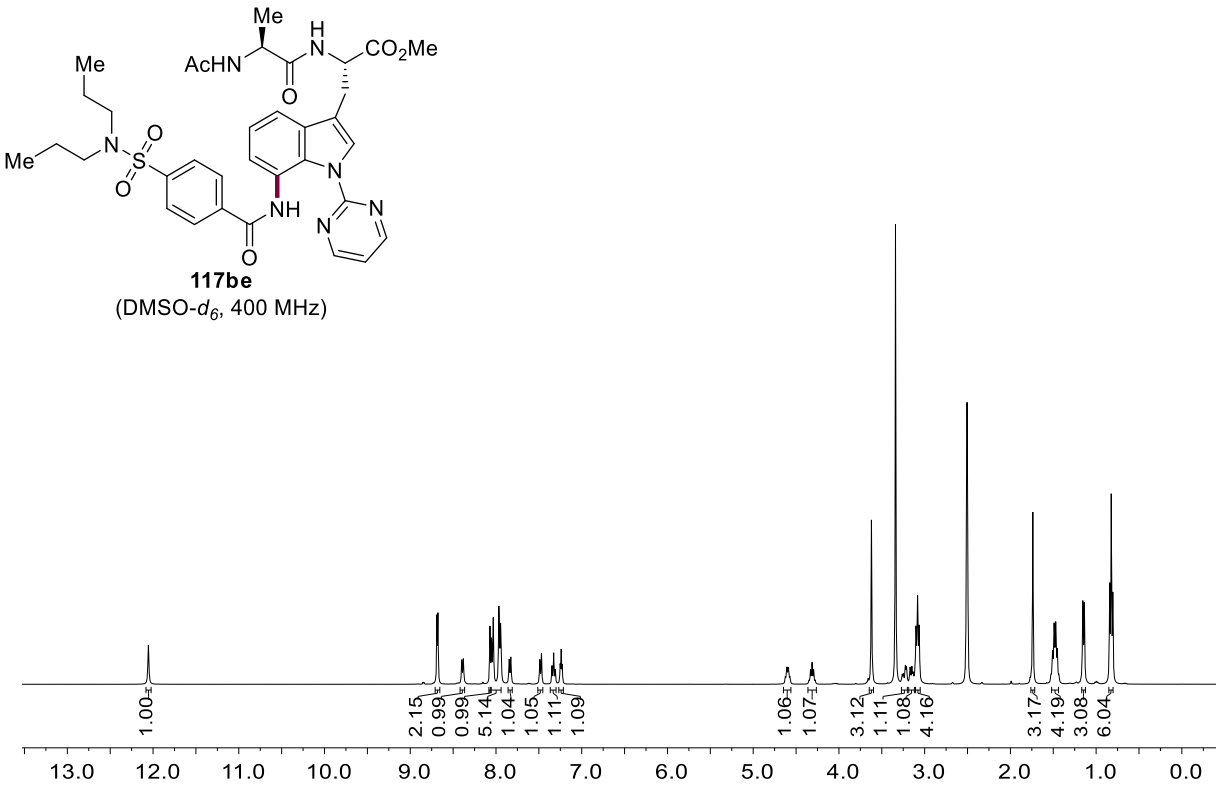
117bc
(DMSO-d_6, 101 MHz)



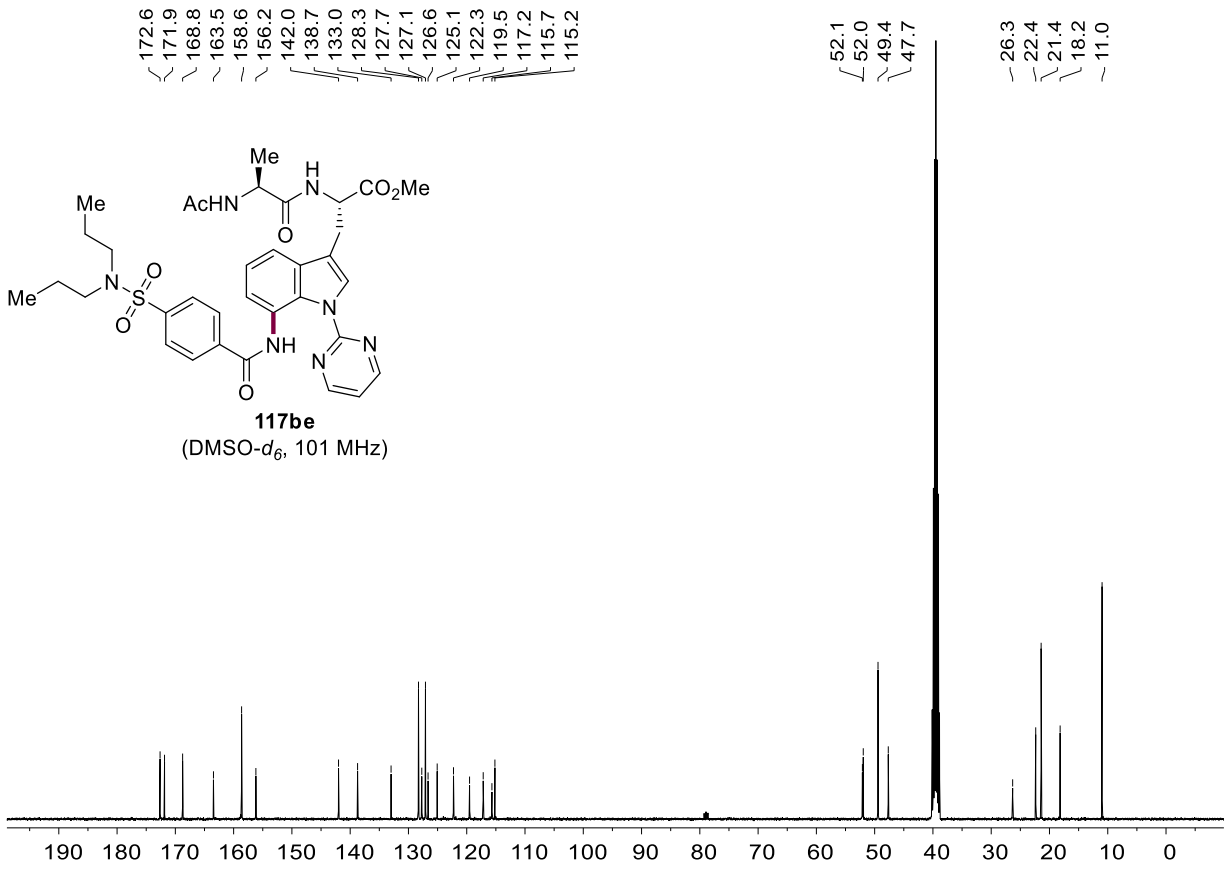
117bd
(DMSO-d_6, 300 MHz)



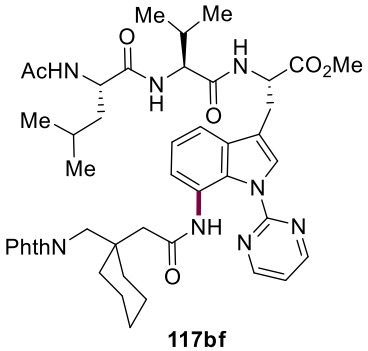
117bd
(DMSO-d_6, 101 MHz)



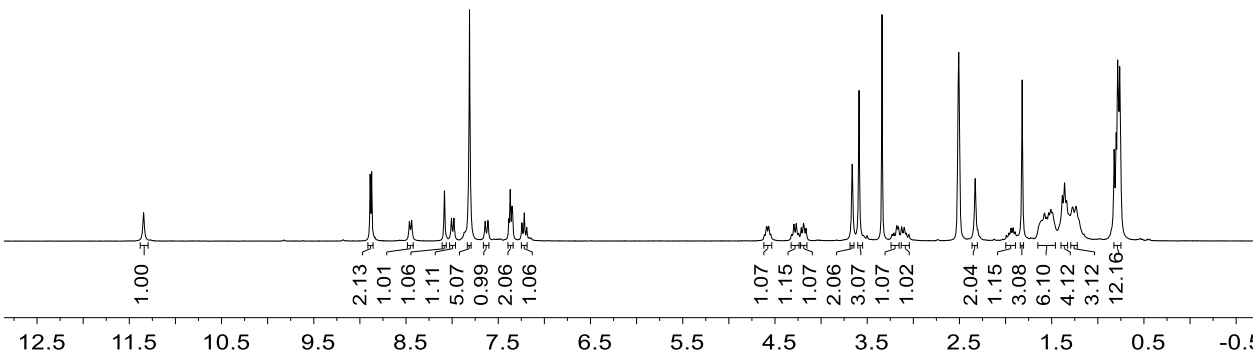
117be
(DMSO-d_6, 400 MHz)

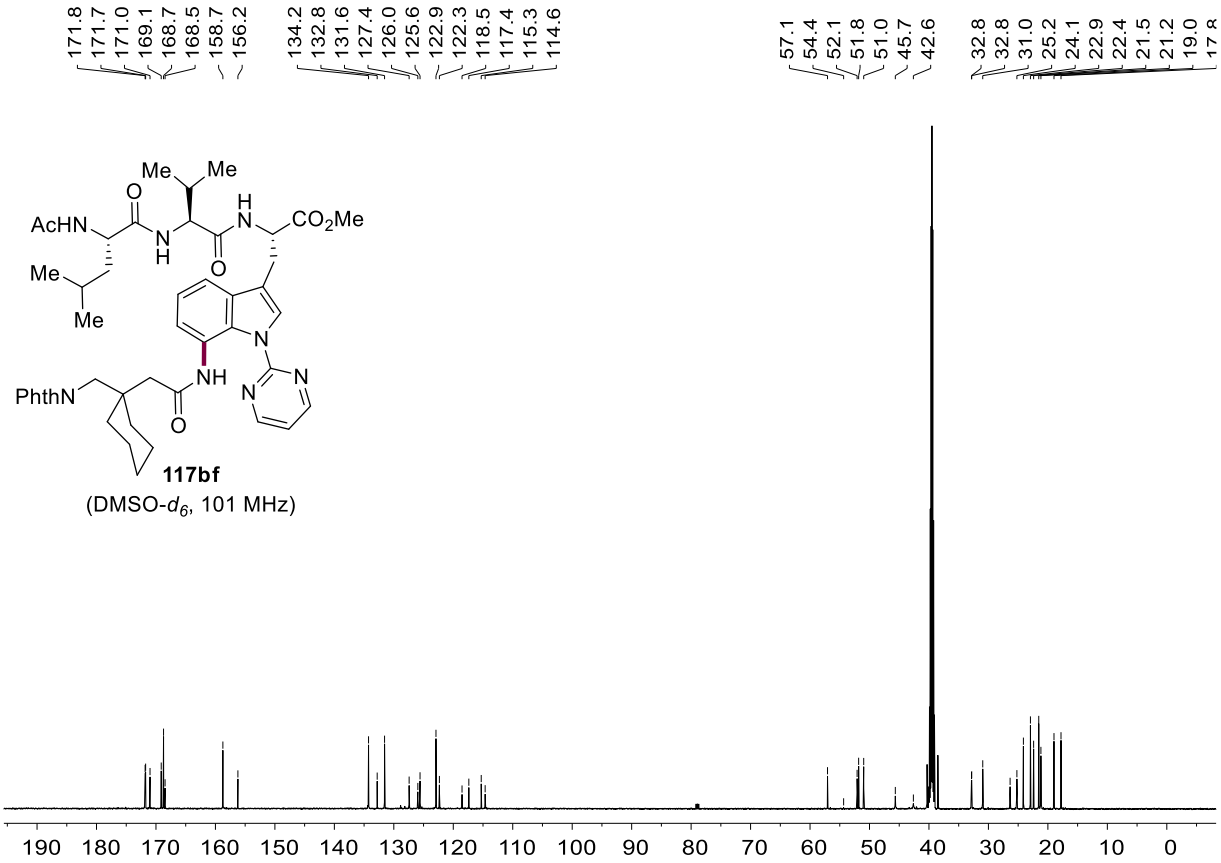


117be
(DMSO-d_6, 101 MHz)

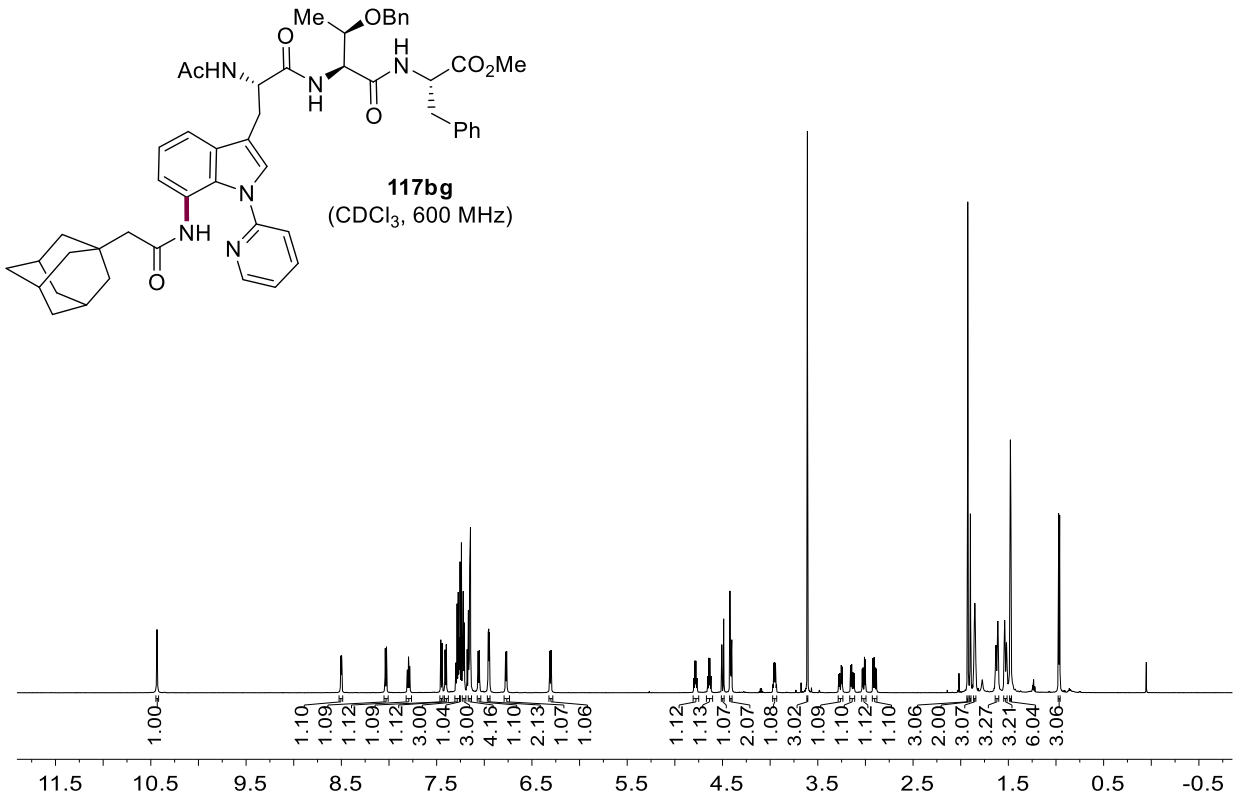


117bf
(DMSO-d_6, 300 MHz)

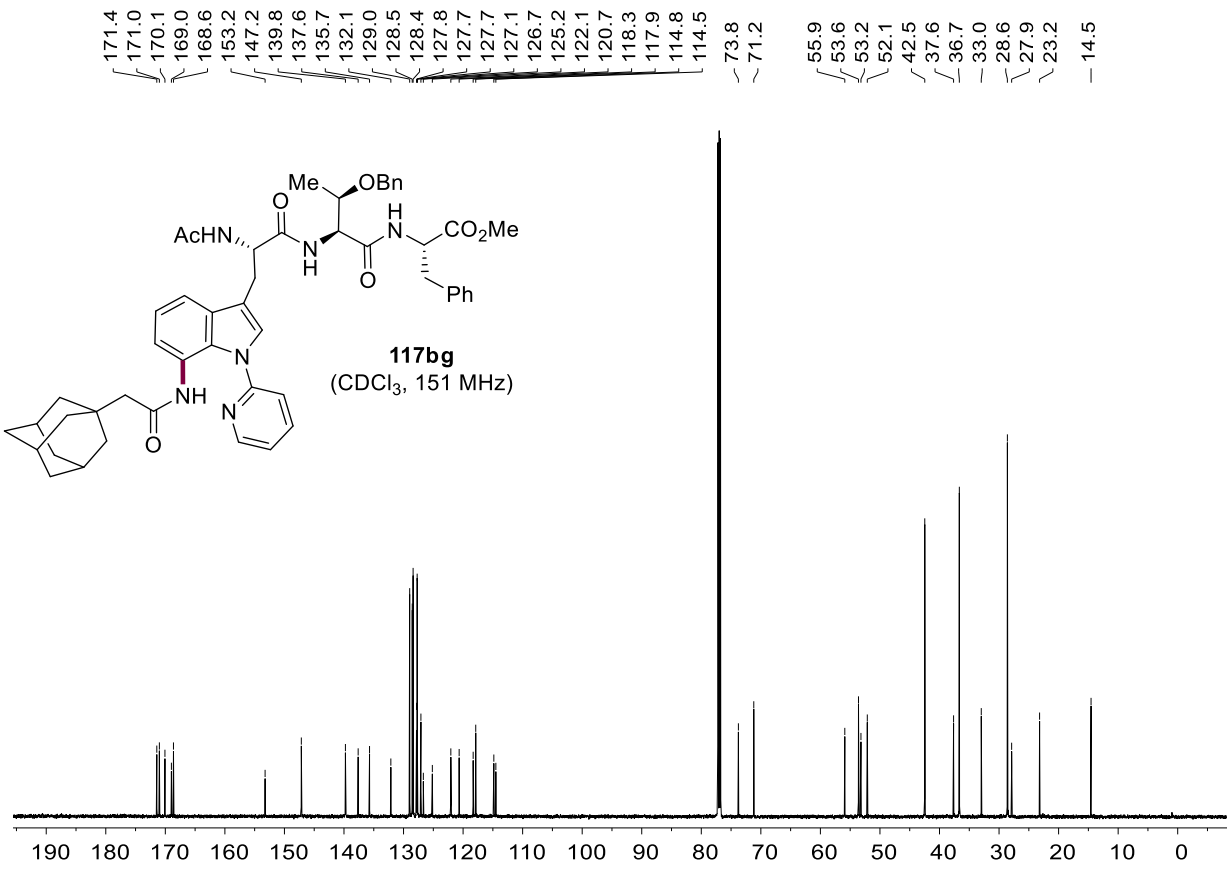


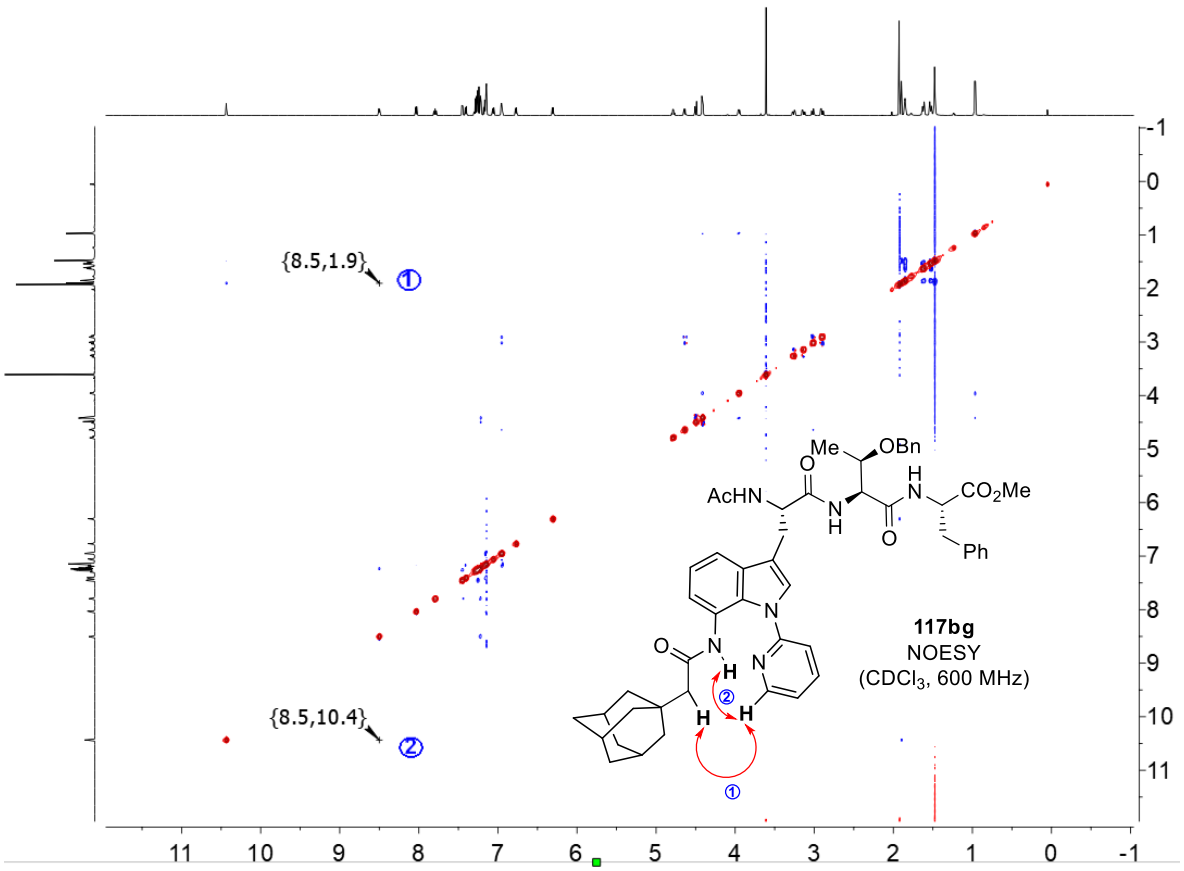


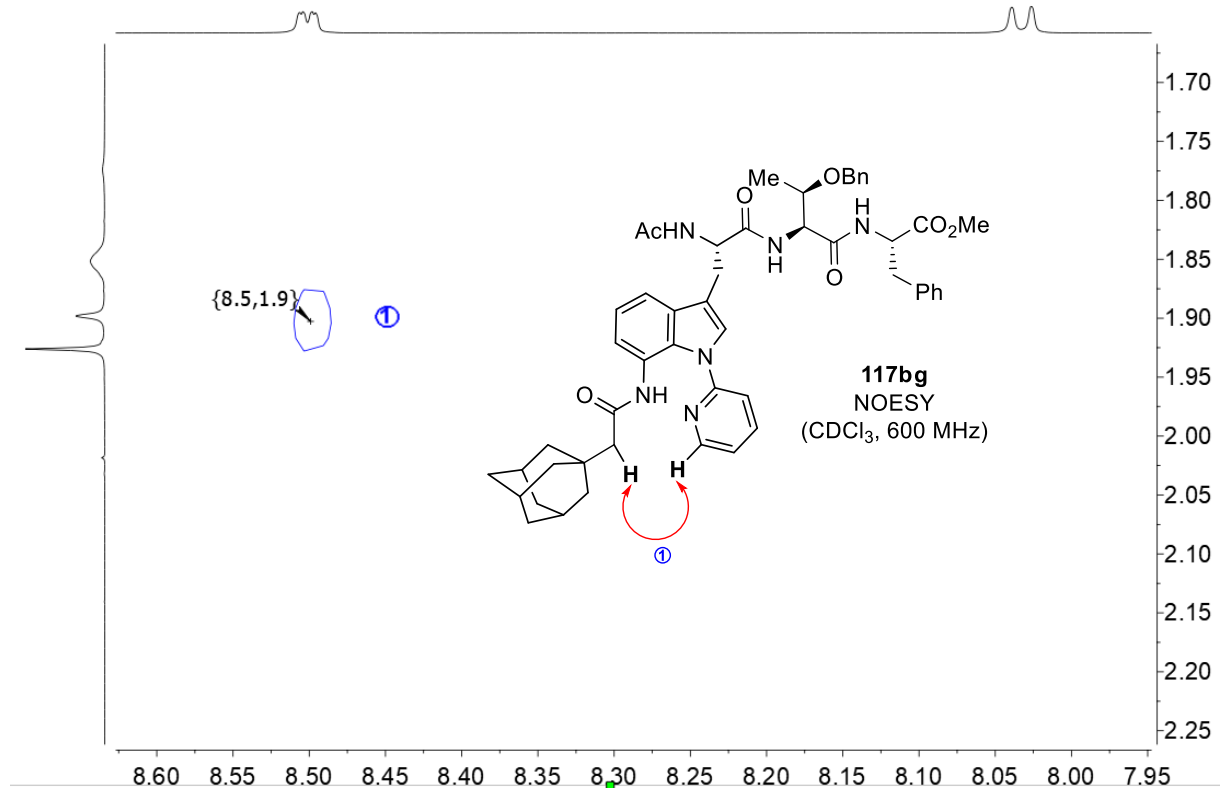
117bf
(DMSO-d_6, 101 MHz)

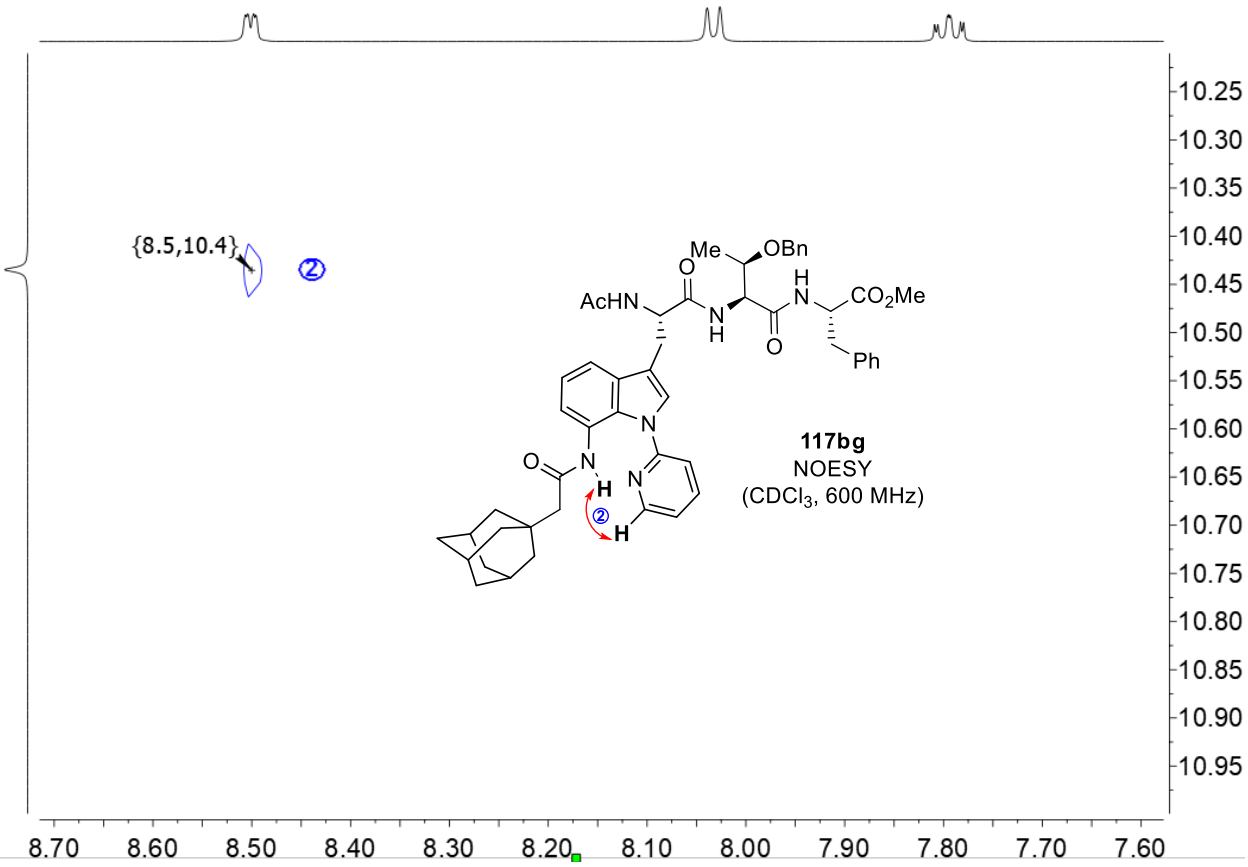


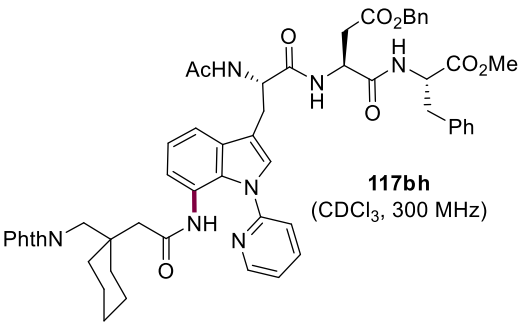
117bg
($CDCl_3$, 600 MHz)


171.4
171.0
170.1
169.0
168.6
153.2
147.2
139.8
137.6
135.7
132.1
129.0
128.5
128.4
127.8
127.7
127.7
127.1
126.7
125.2
122.1
120.7
118.3
117.9
114.8
114.5
73.8
71.2
55.9
53.6
53.2
52.1
42.5
37.6
36.7
33.0
28.6
27.9
23.2
14.5
Me
OBn
AcHN
CO2Me
Ph
117bg
(CDCl3, 151 MHz)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

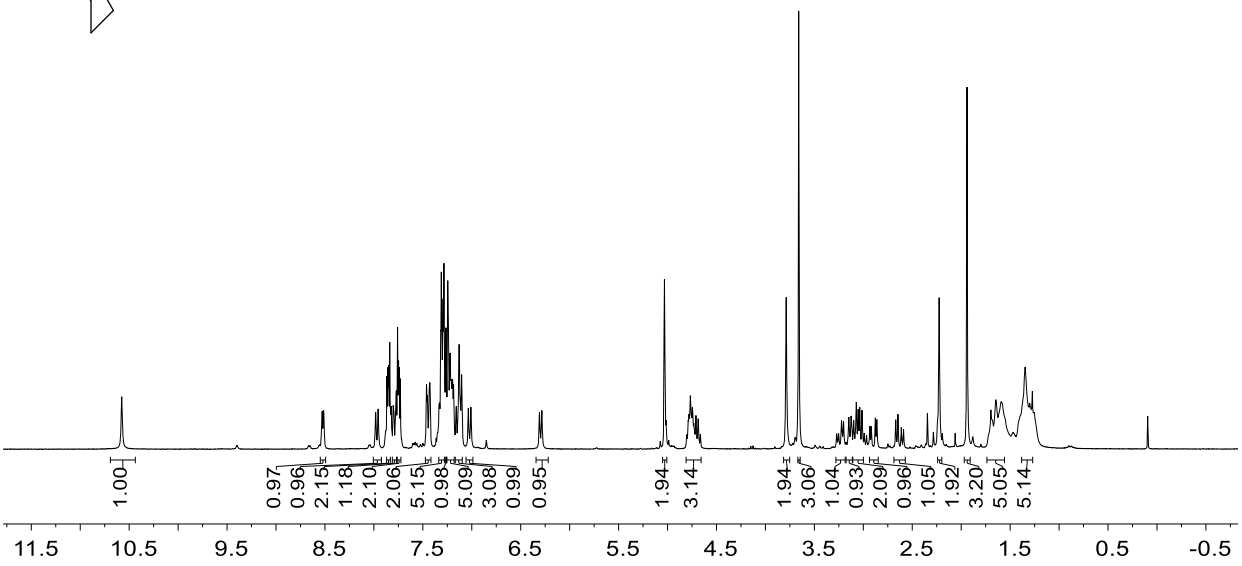

{8.5,1.9}
{8.5,10.4}
Me
OBn
AcHN
CO2Me
Ph
117bg
NOESY
(CDCl3, 600 MHz)
11 10 9 8 7 6 5 4 3 2 1 0 -1

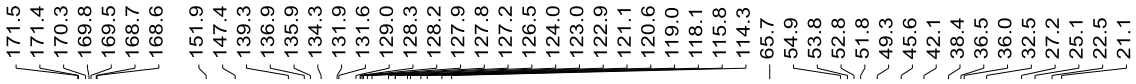

{8.5,1.9}
①
Me
OBn
AcHN
O
N
H
H
N
CO2Me
O
Ph
N
O
NH
N
H
H
①
117bg
NOESY
(CDCl3, 600 MHz)
1.70
1.75
1.80
1.85
1.90
1.95
2.00
2.05
2.10
2.15
2.20
2.25
8.60
8.55
8.50
8.45
8.40
8.35
8.30
8.25
8.20
8.15
8.10
8.05
8.00
7.95

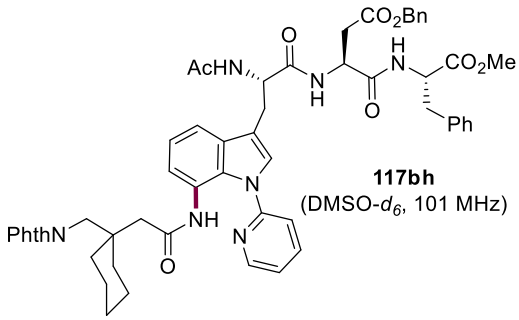

{8.5,10.4}
②
Me
OBn
AcHN
O
N
H
H
N
CO2Me
O
Ph
N
O
N
H
N
②
H
117bg
NOESY
(CDCl3, 600 MHz)
10.25
10.30
10.35
10.40
10.45
10.50
10.55
10.60
10.65
10.70
10.75
10.80
10.85
10.90
10.95
8.70
8.60
8.50
8.40
8.30
8.20
8.10
8.00
7.90
7.80
7.70
7.60



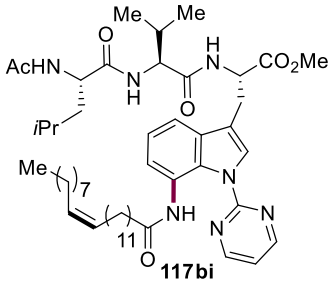
117bh
($CDCl_3$, 300 MHz)





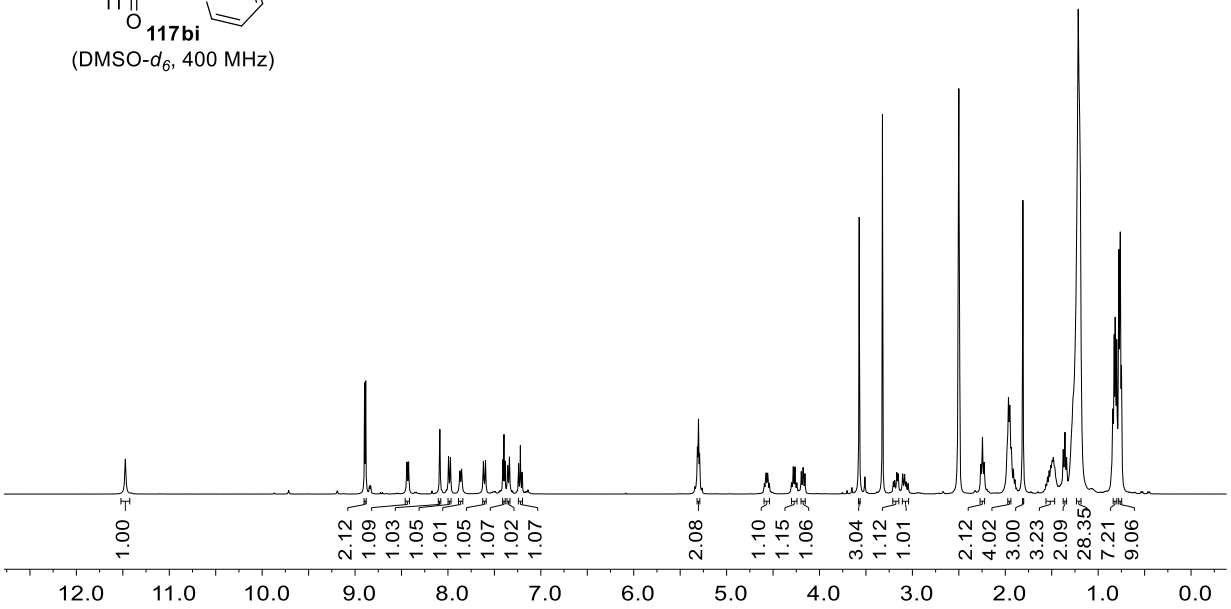


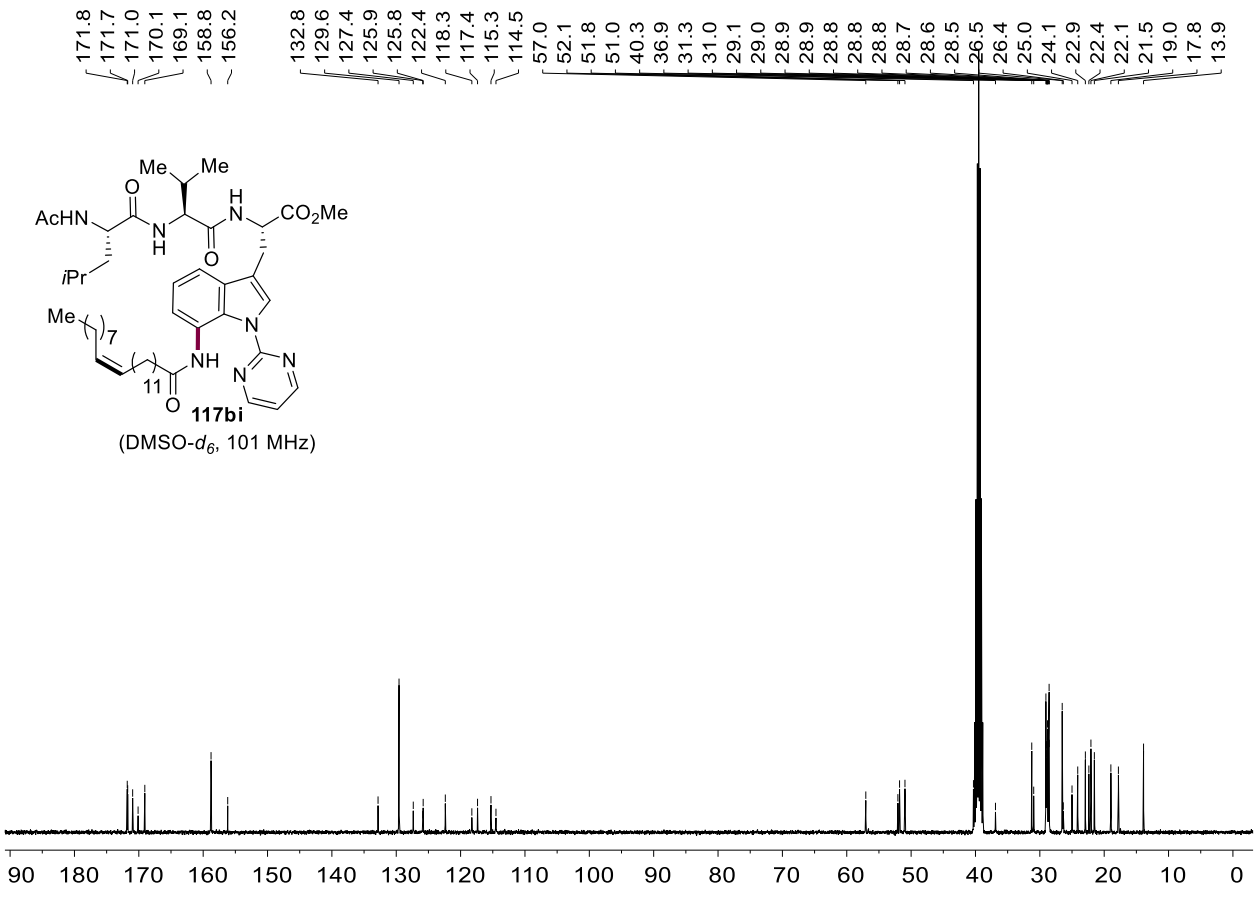
117bh
(DMSO-d_6, 101 MHz)



117bi

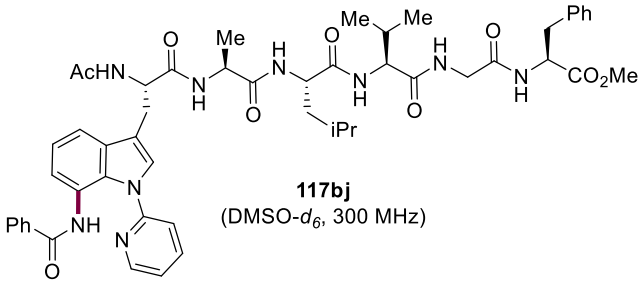
(DMSO-d_6, 400 MHz)



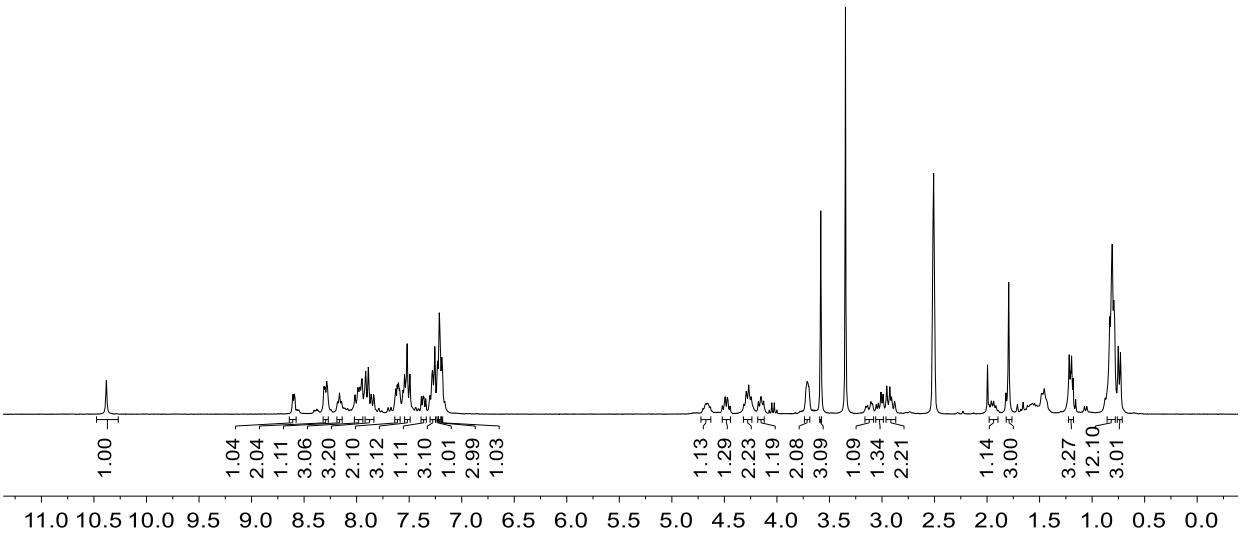


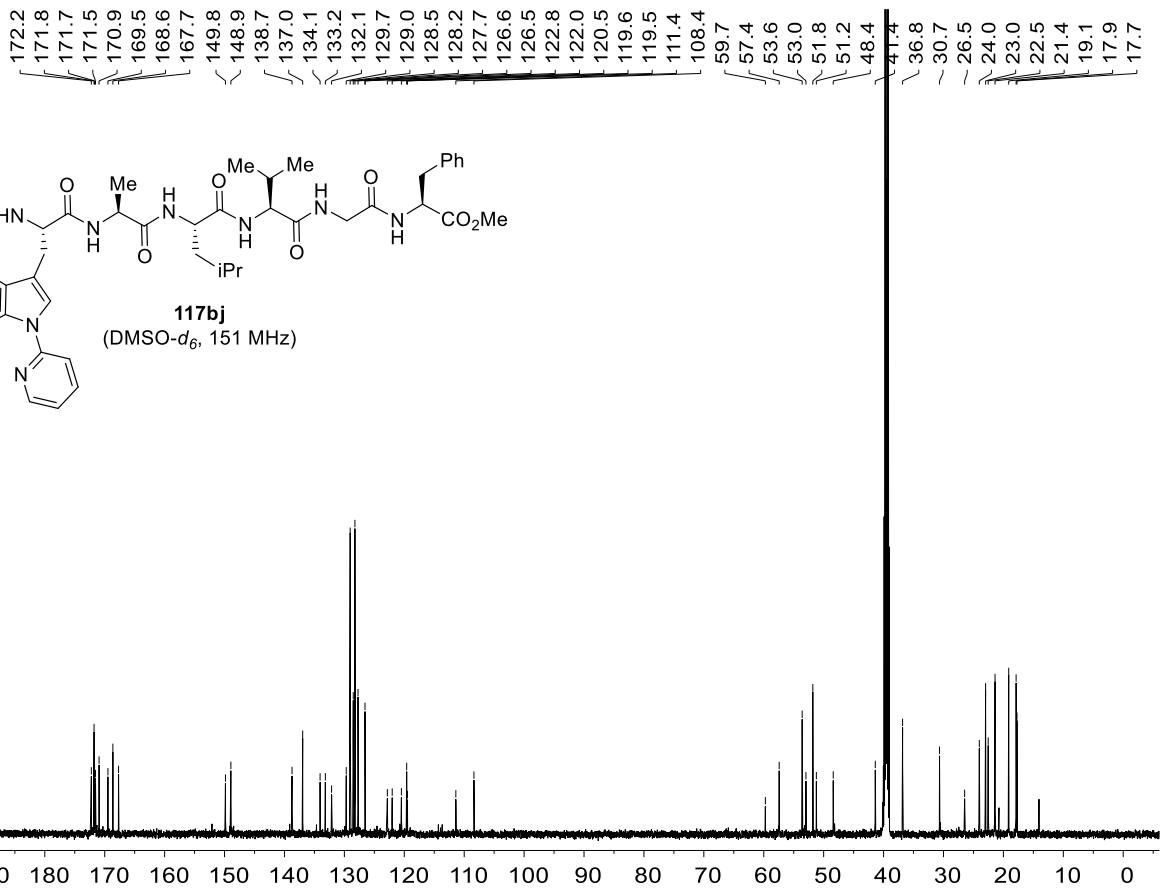
117bi

(DMSO-d_6, 101 MHz)

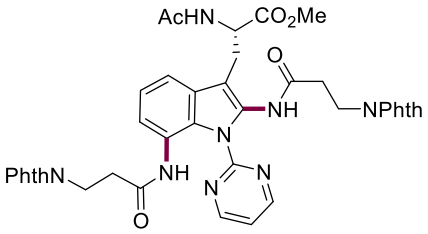


117bj
(DMSO-d_6, 300 MHz)

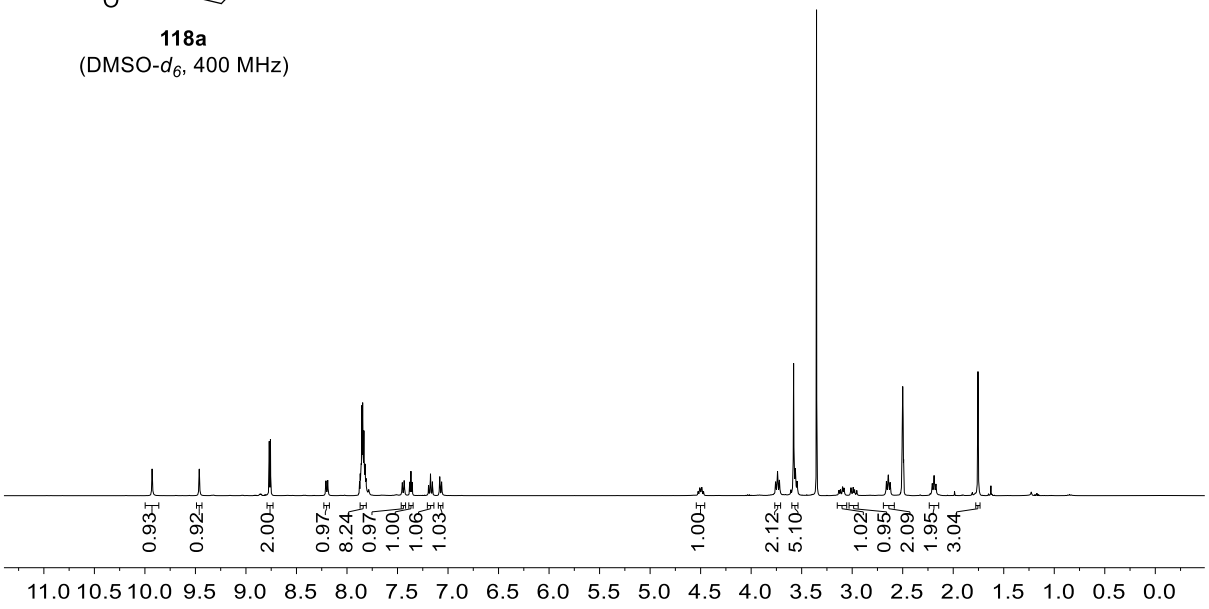


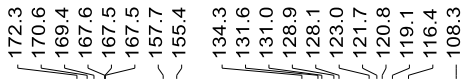


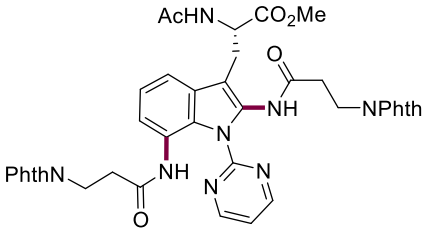
117bj
(DMSO-d_6, 151 MHz)



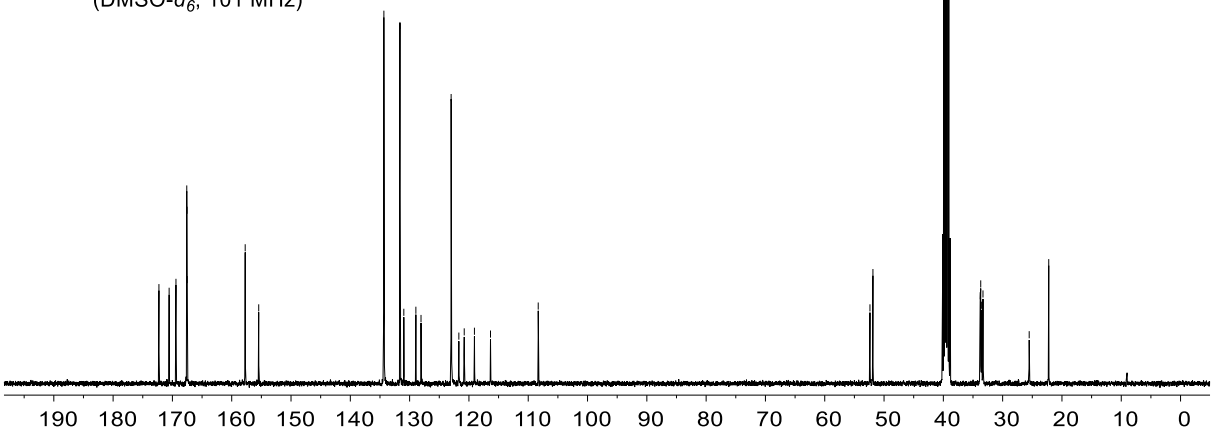
118a
(DMSO-d_6, 400 MHz)

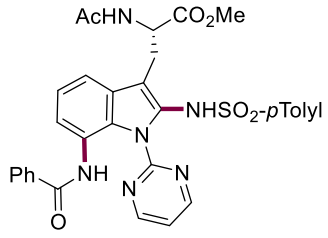




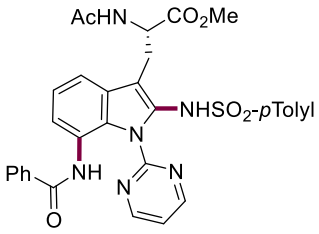


118a
(DMSO-d_6, 101 MHz)

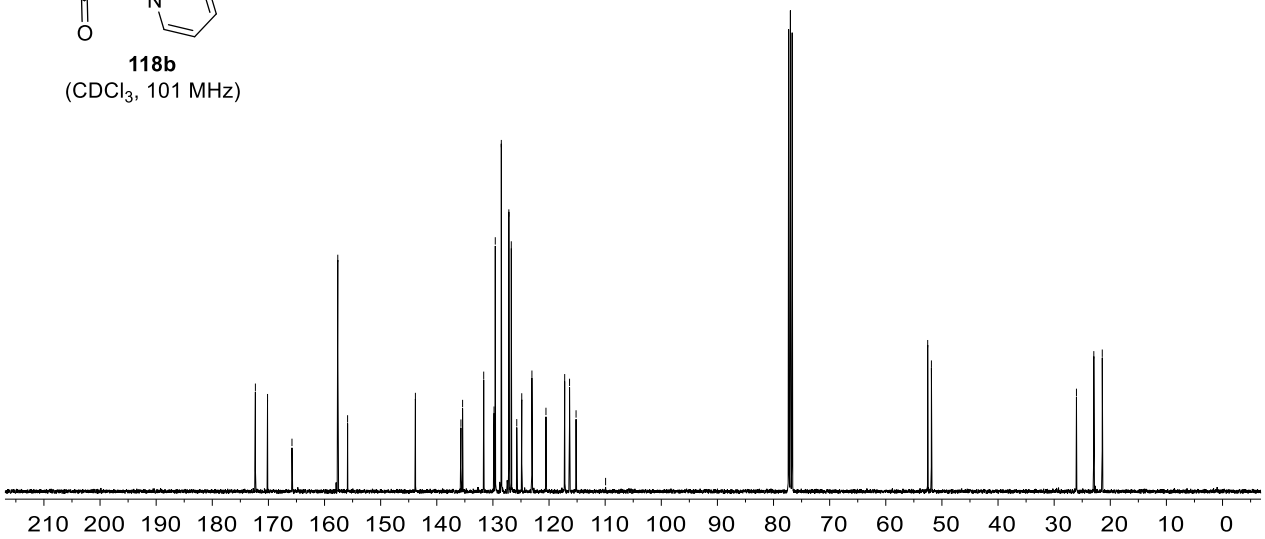


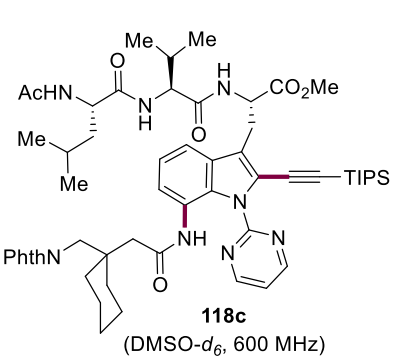


118b
($CDCl_3$, 400 MHz)

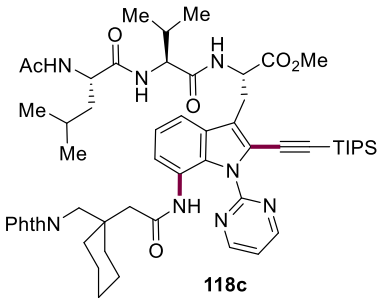


118b
($CDCl_3$, 101 MHz)

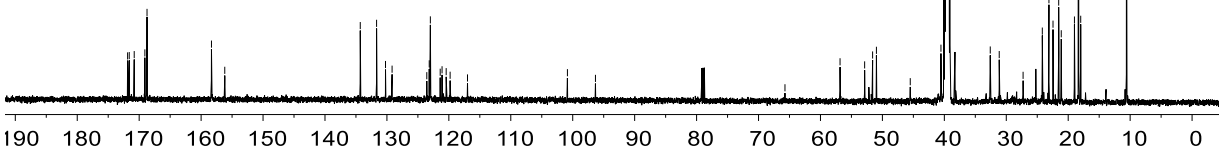


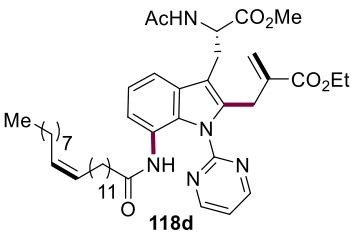


118c
(DMSO-d_6, 600 MHz)

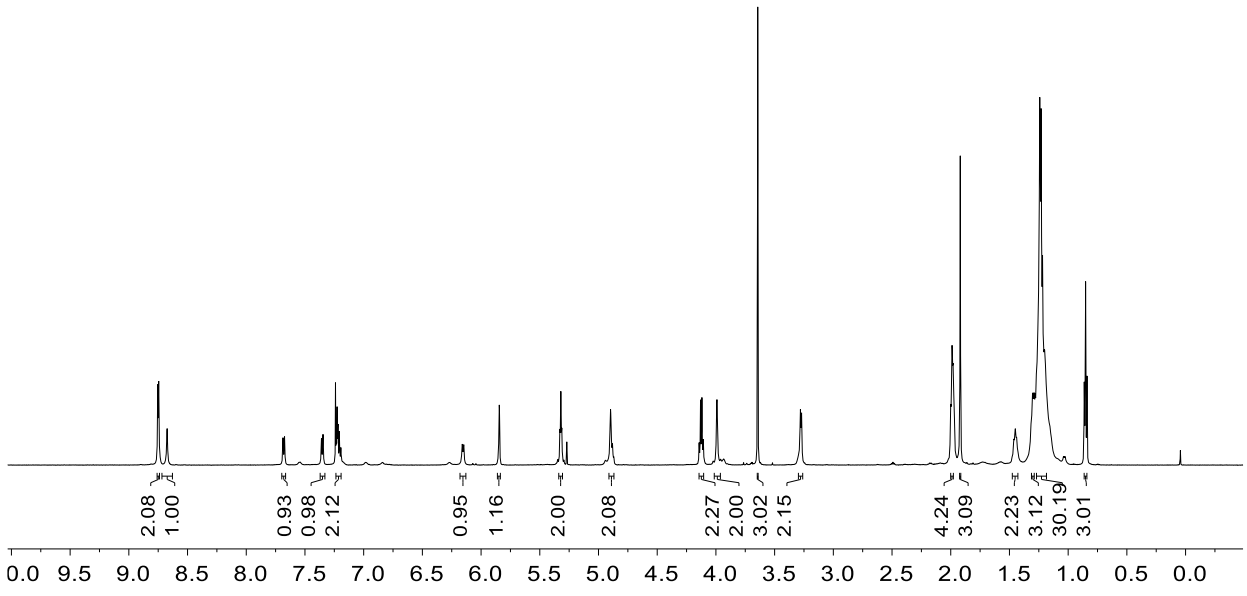


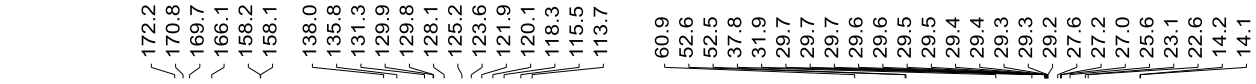
118c
(DMSO-d_6, 151 MHz)

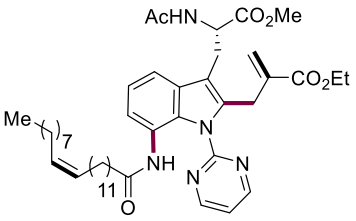




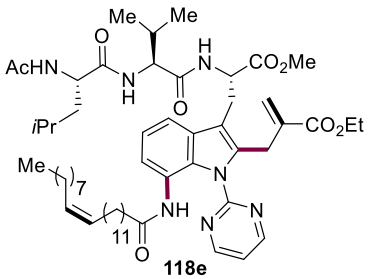
118d
($CDCl_3$, 600 MHz)



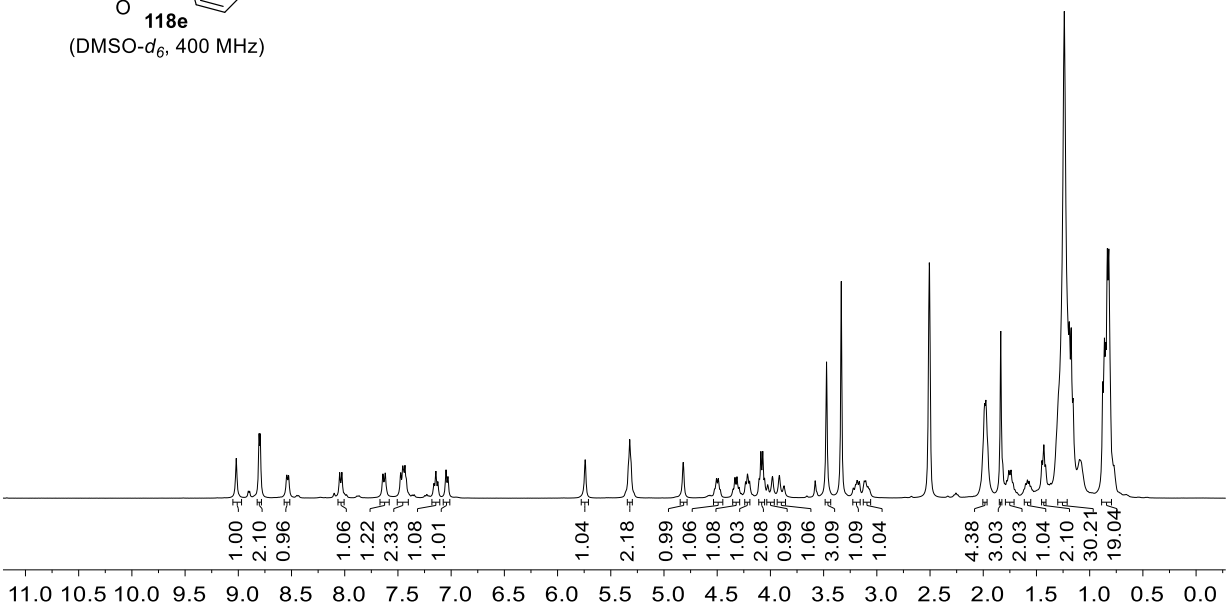


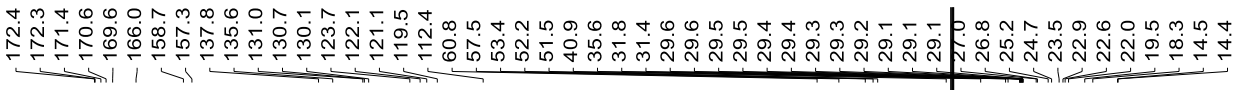


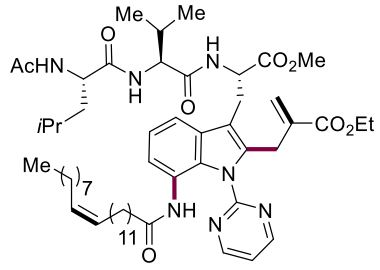
118d
($CDCl_3$, 151 MHz)



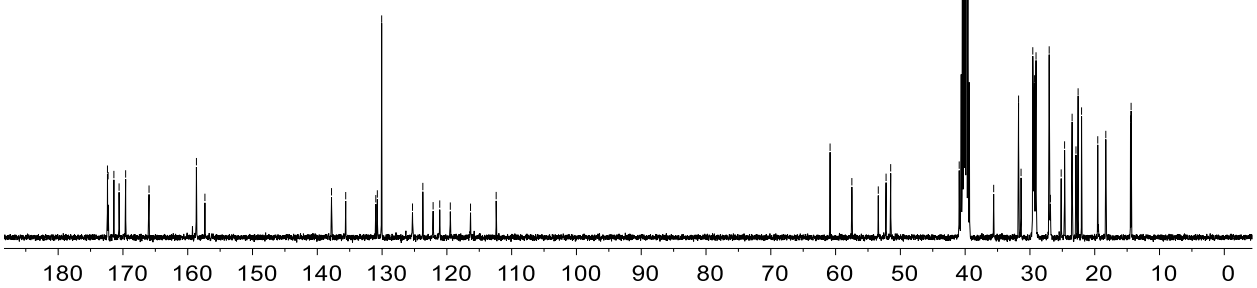
118e
(DMSO-d_6, 400 MHz)

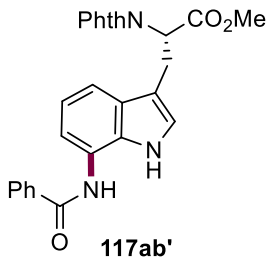




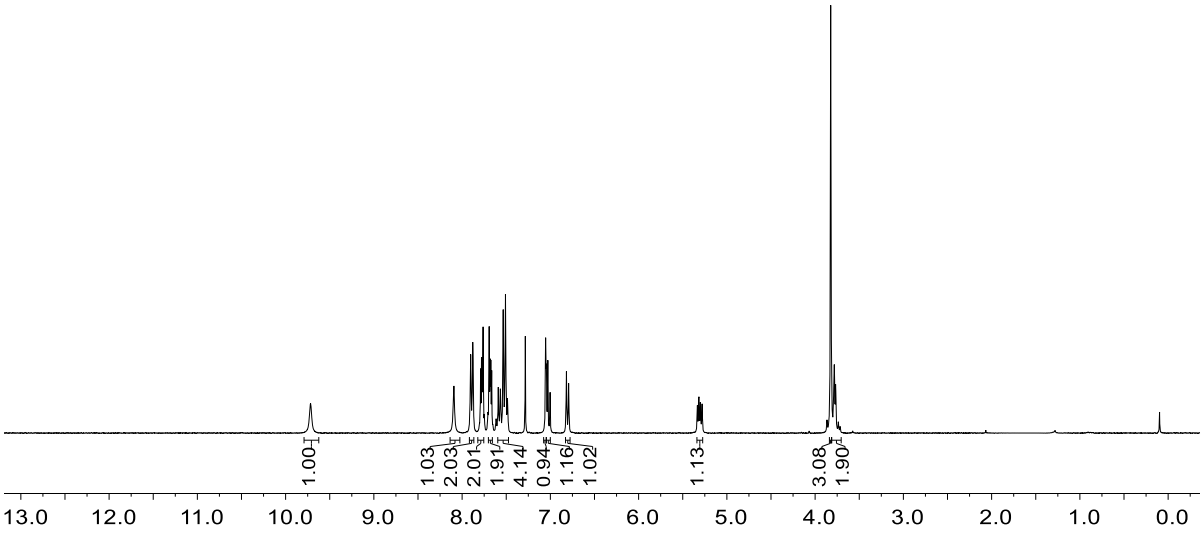


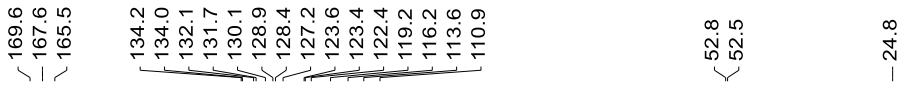
118e
(DMSO-d_6, 101 MHz)

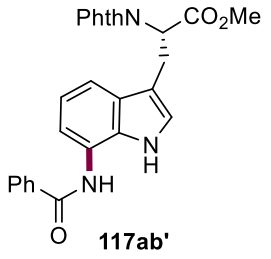




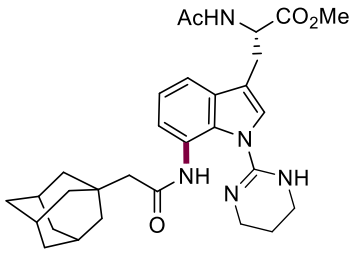
117ab'
($CDCl_3$, 300 MHz)



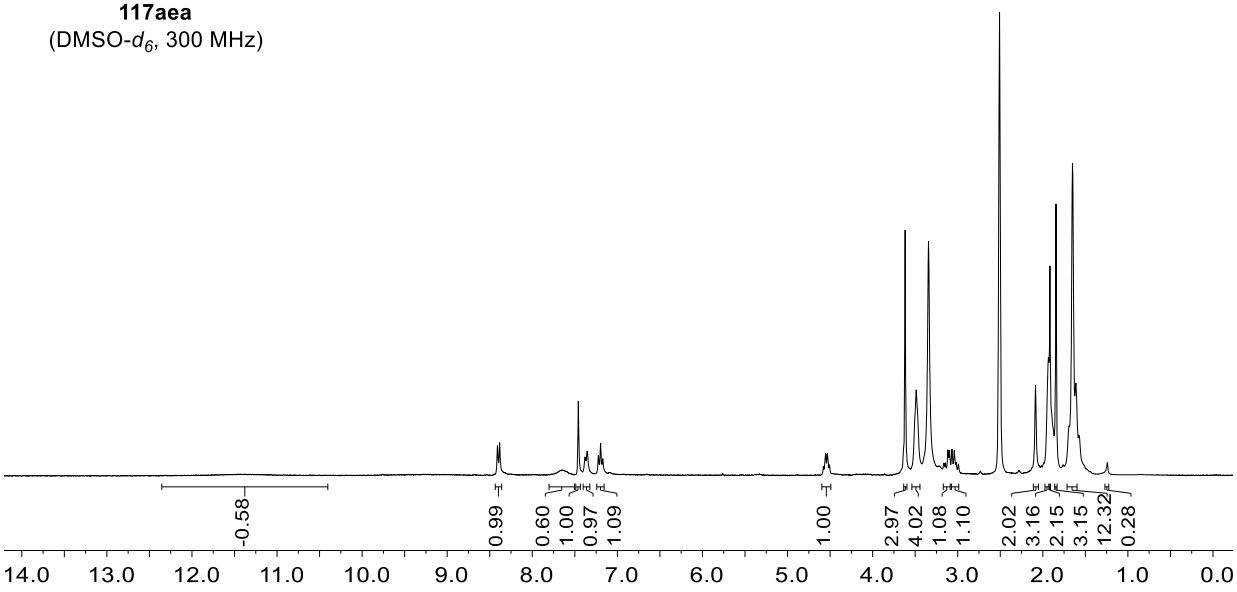


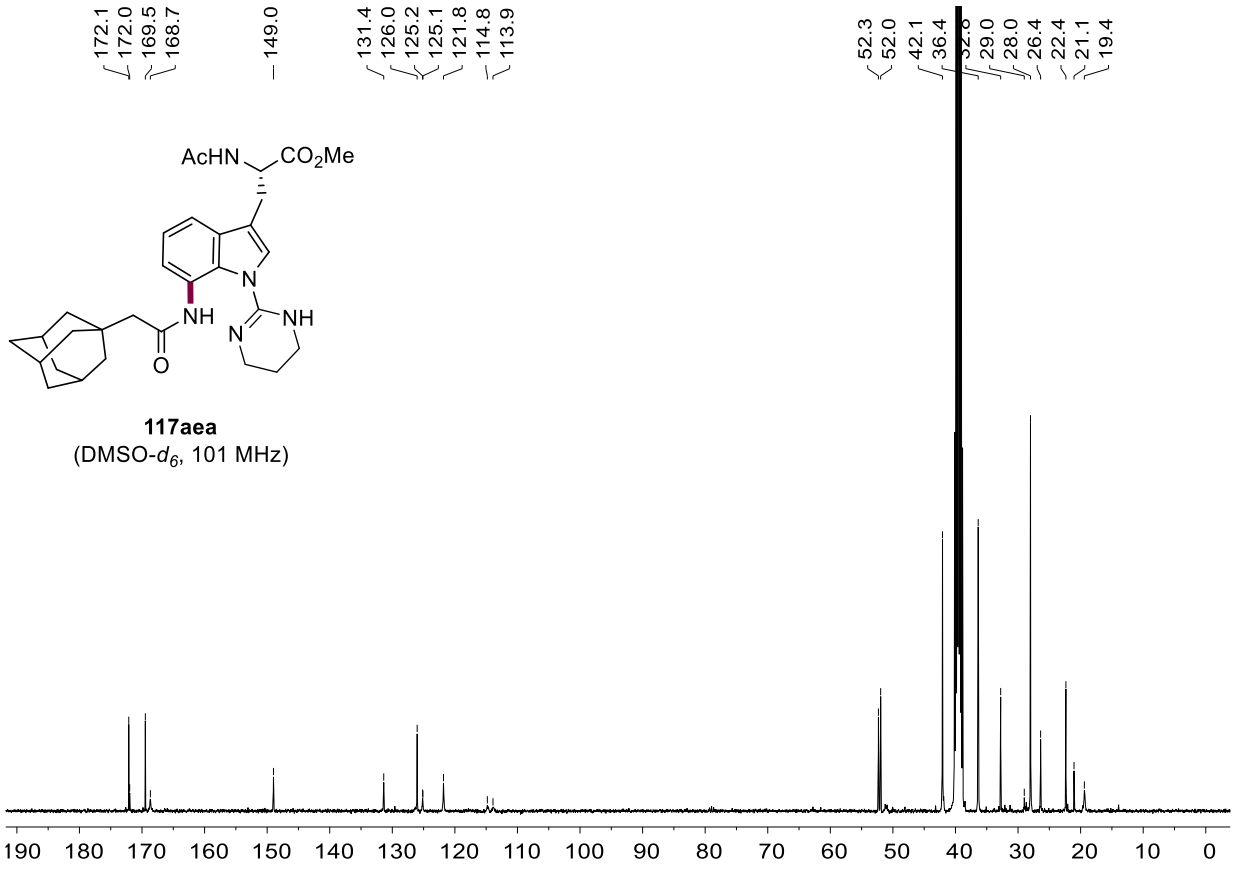


117ab'
($CDCl_3$, 151 MHz)

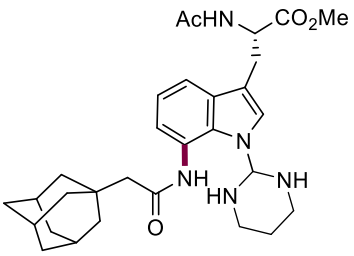


117aea
(DMSO-d_6, 300 MHz)

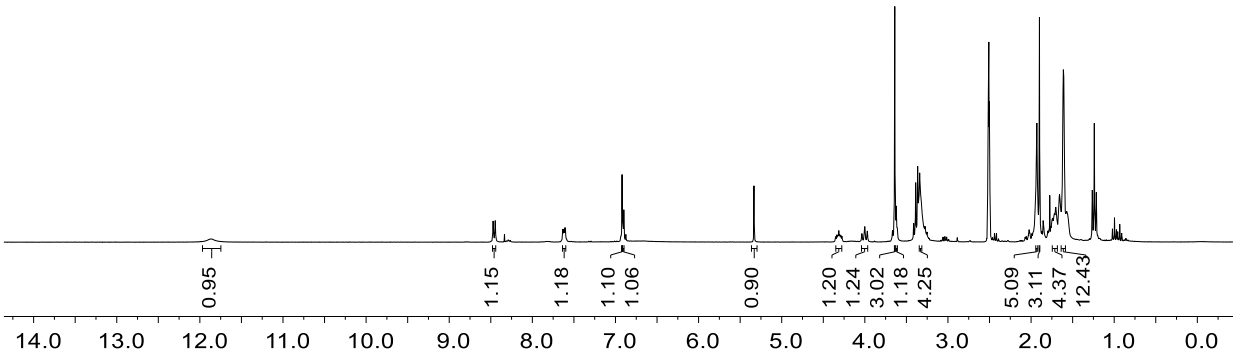


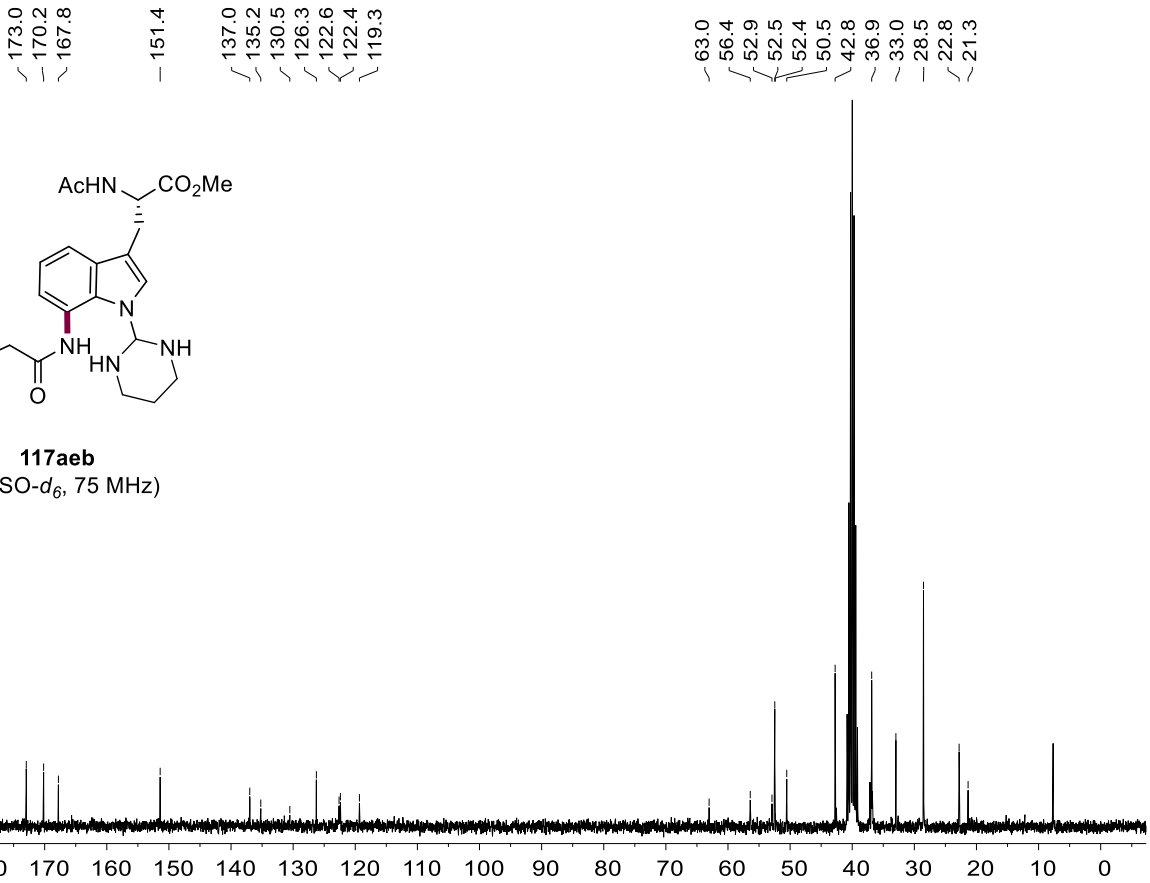


117aea
(DMSO-d_6, 101 MHz)

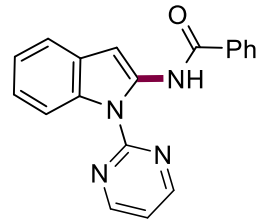


117aeb
(DMSO-d_6, 300 MHz)

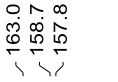


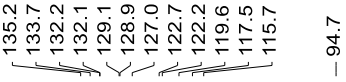


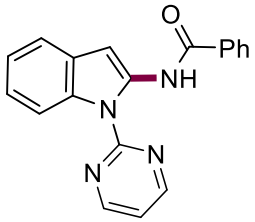
117aeb
(DMSO-d_6, 75 MHz)



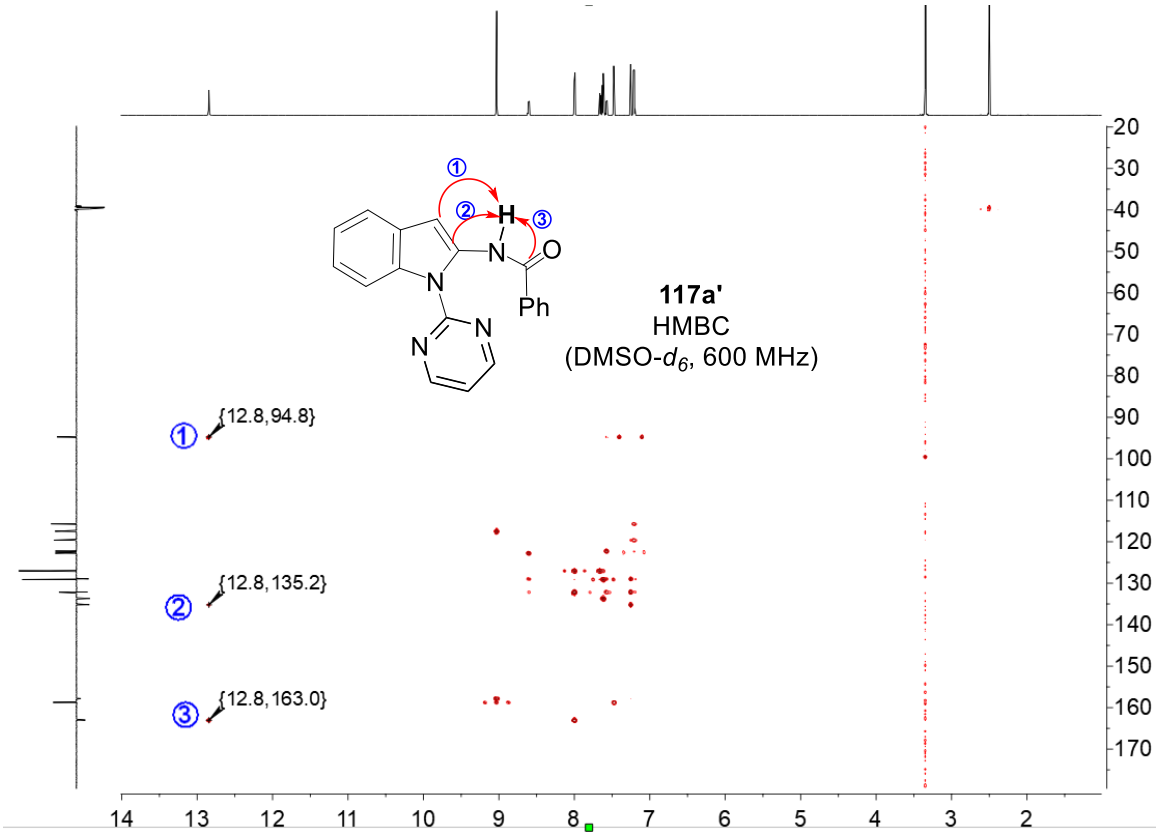
117a'
(DMSO-d_6, 600 MHz)

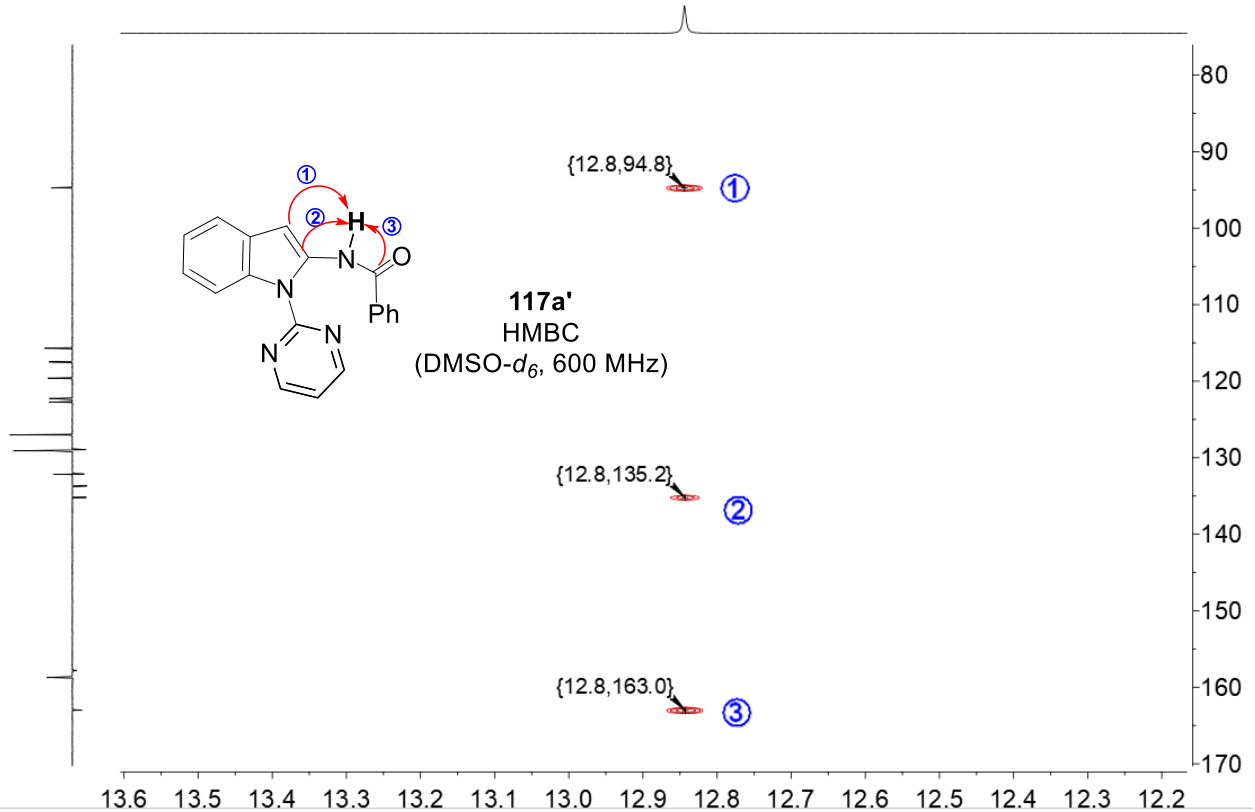


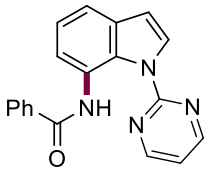




117a'
(DMSO-d_6, 151 MHz)

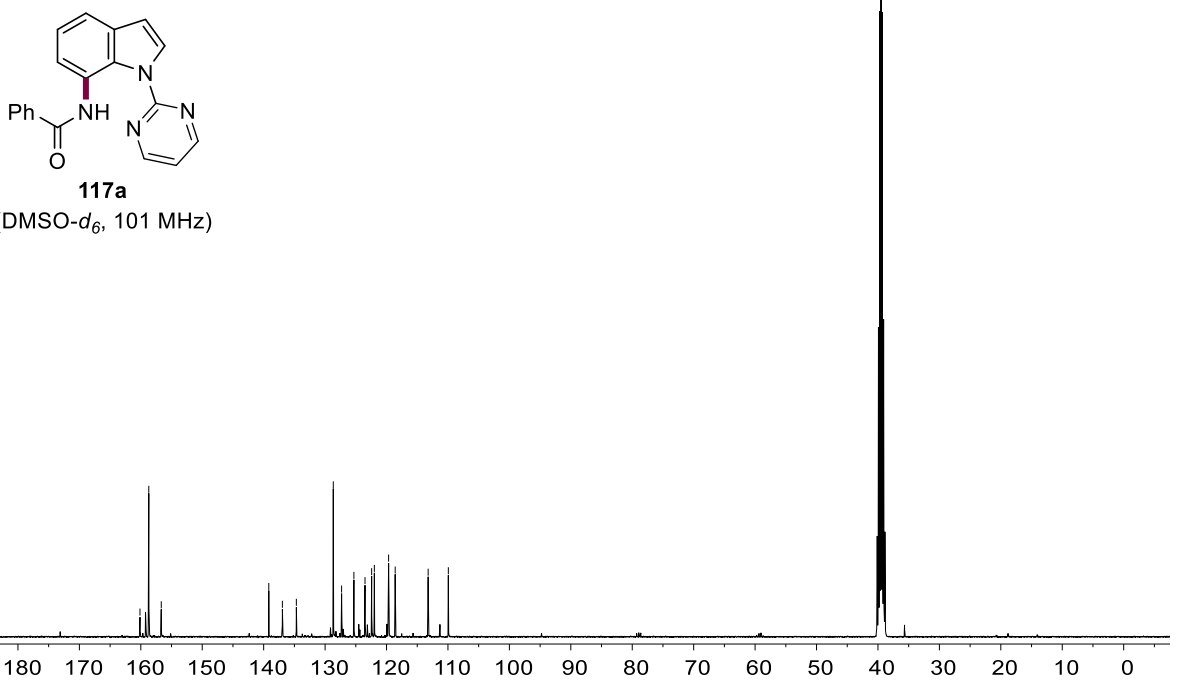

117a'
HMBC
(DMSO-d_6, 600 MHz)
{12.8,94.8}
{12.8,135.2}
{12.8,163.0}


117a'
HMBC
(DMSO-d_6, 600 MHz)
{12.8,94.8}
{12.8,135.2}
{12.8,163.0}



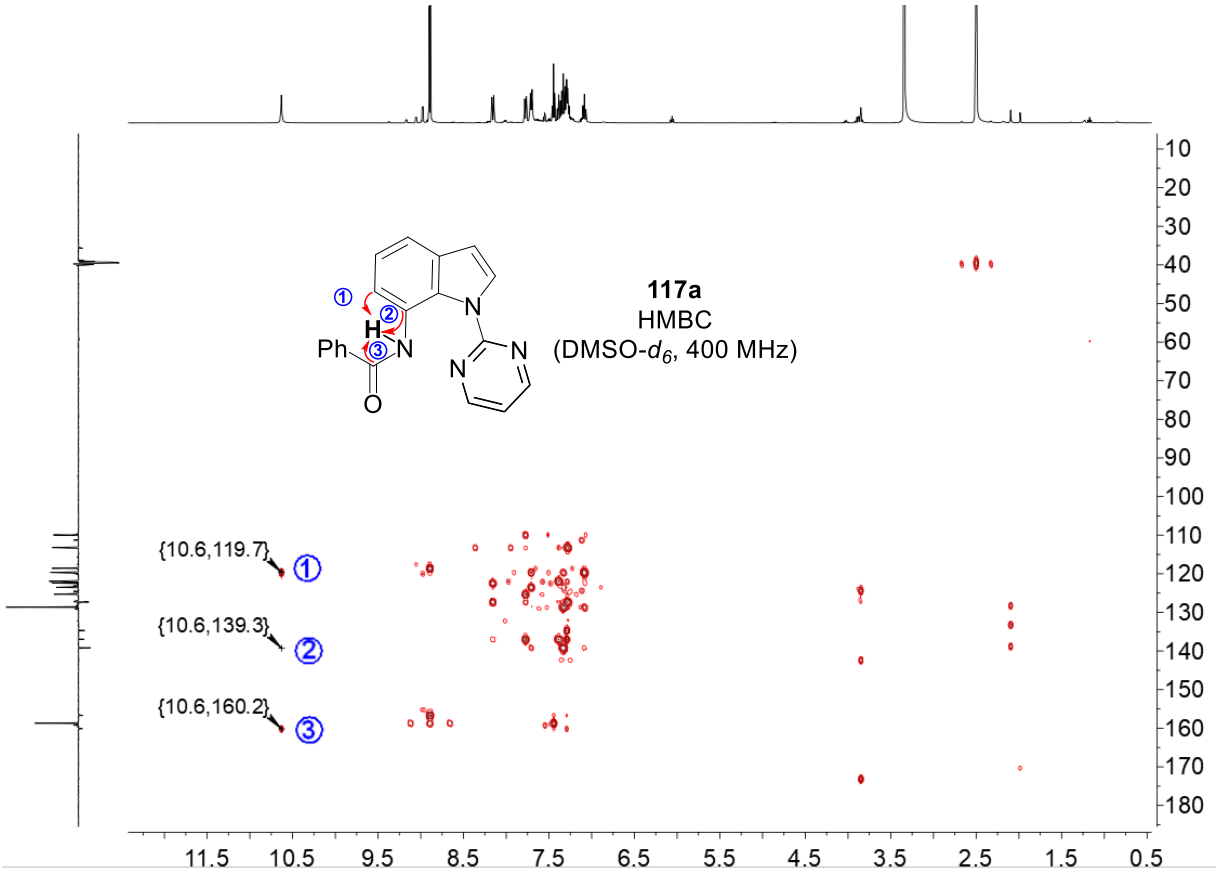
117a

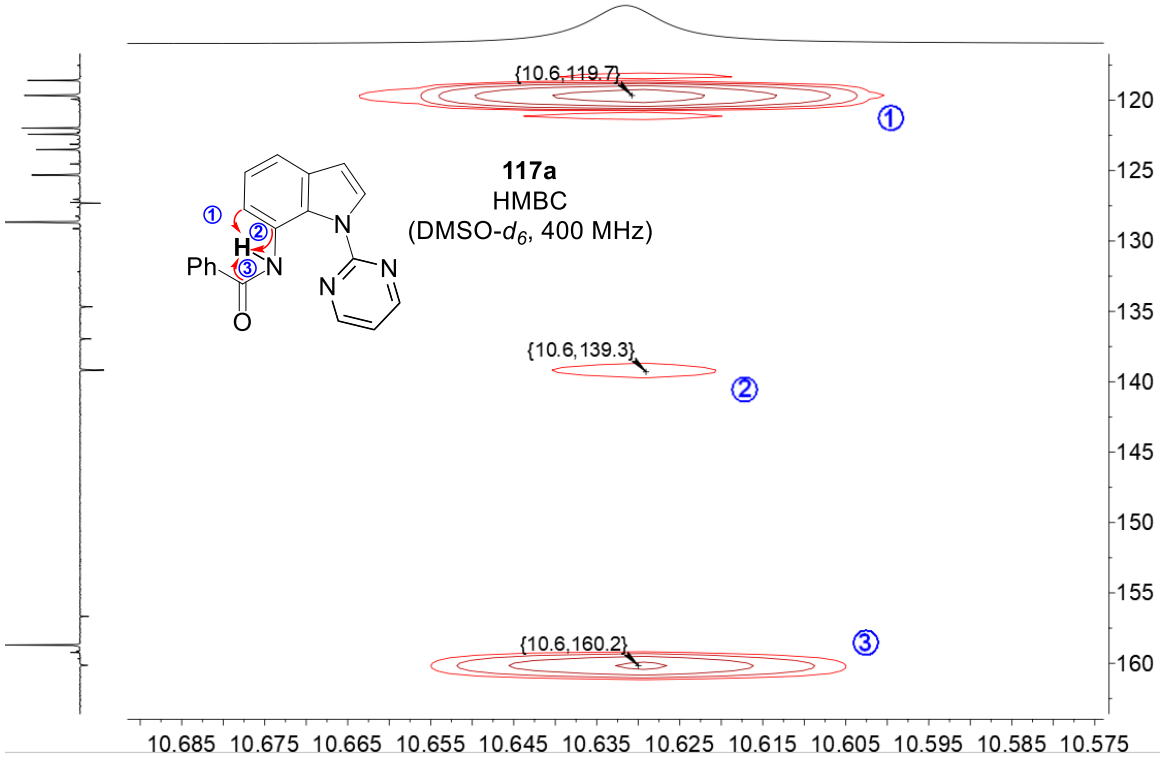
(DMSO-d_6, 400 MHz)

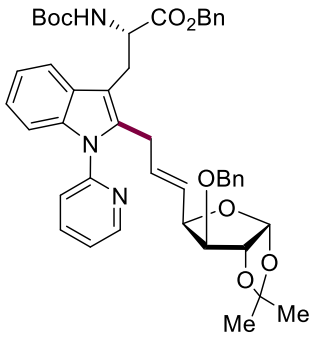


117a

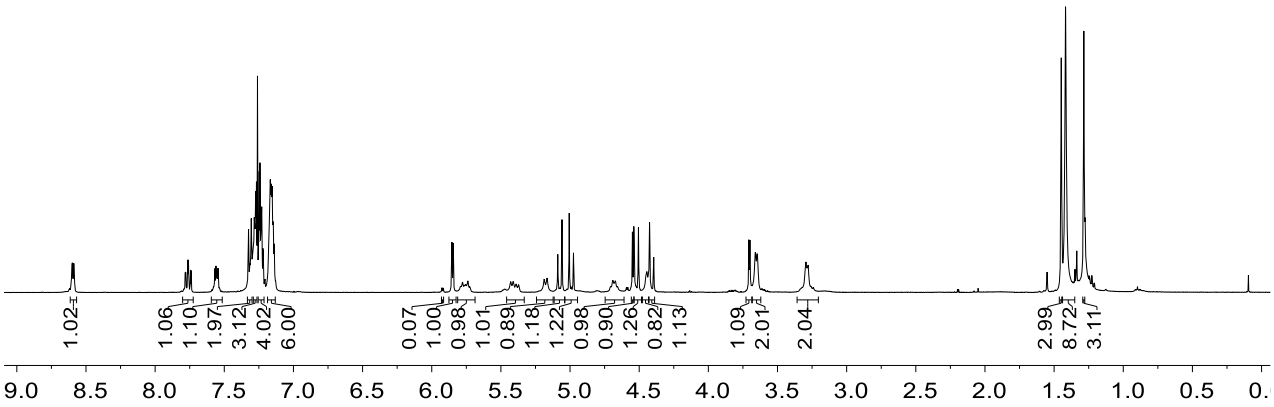
(DMSO-d_6, 101 MHz)

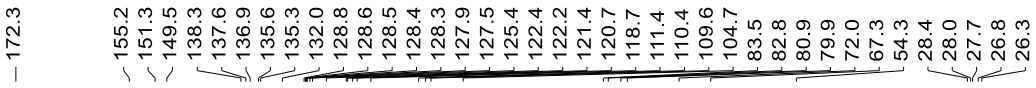

117a
HMBC
(DMSO-d_6, 400 MHz)
{10.6,119.7}
{10.6,139.3}
{10.6,160.2}
11.5 10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5
10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180

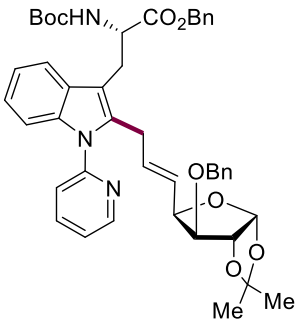

117a
HMBC
(DMSO-d_6, 400 MHz)
{10.6,119.7}
{10.6,139.3}
{10.6,160.2}
10.685 10.675 10.665 10.655 10.645 10.635 10.625 10.615 10.605 10.595 10.585 10.575
120 125 130 135 140 145 150 155 160



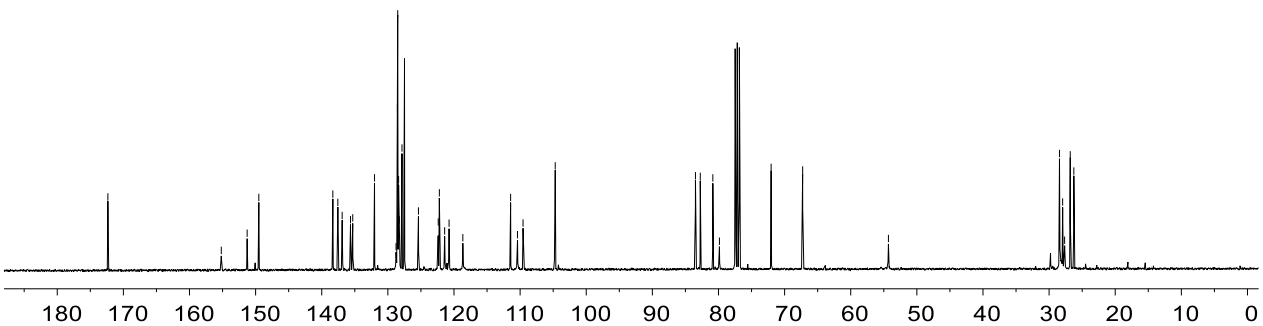
120aa
($CDCl_3$, 400 MHz)

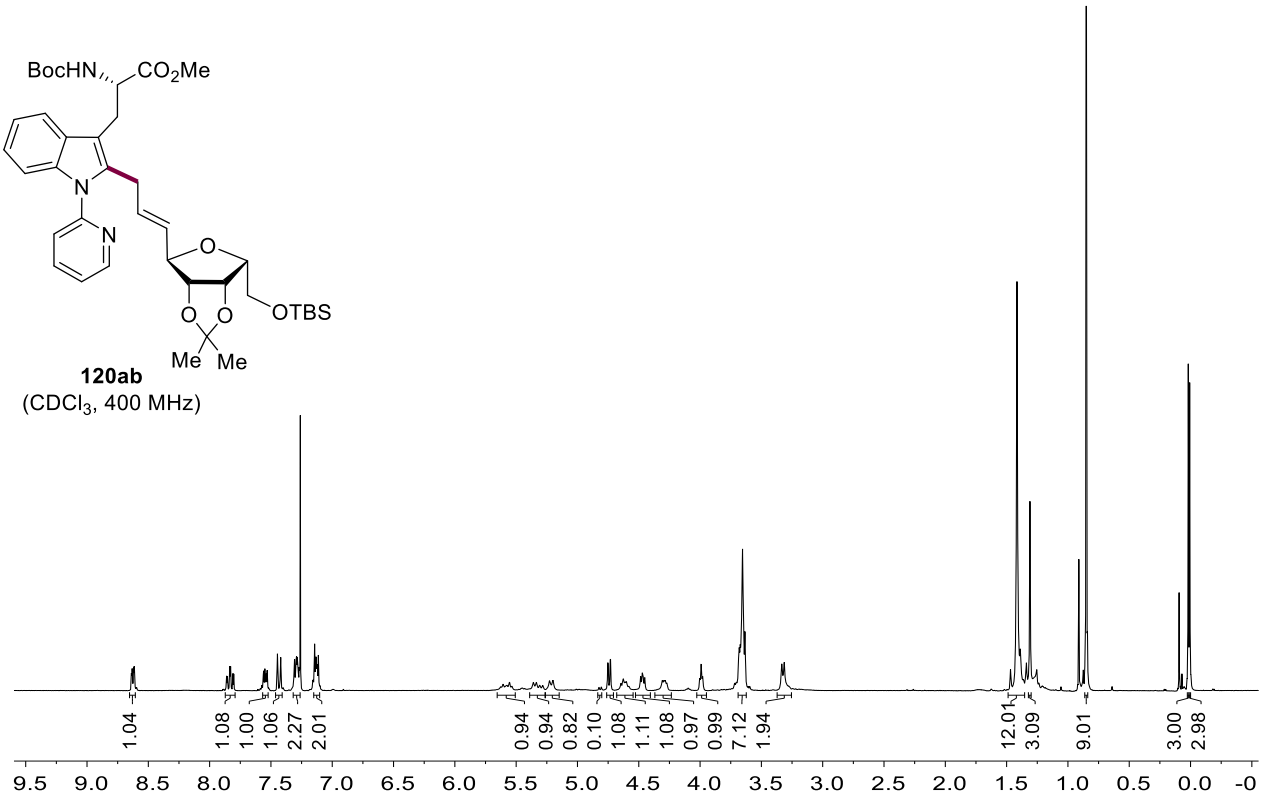


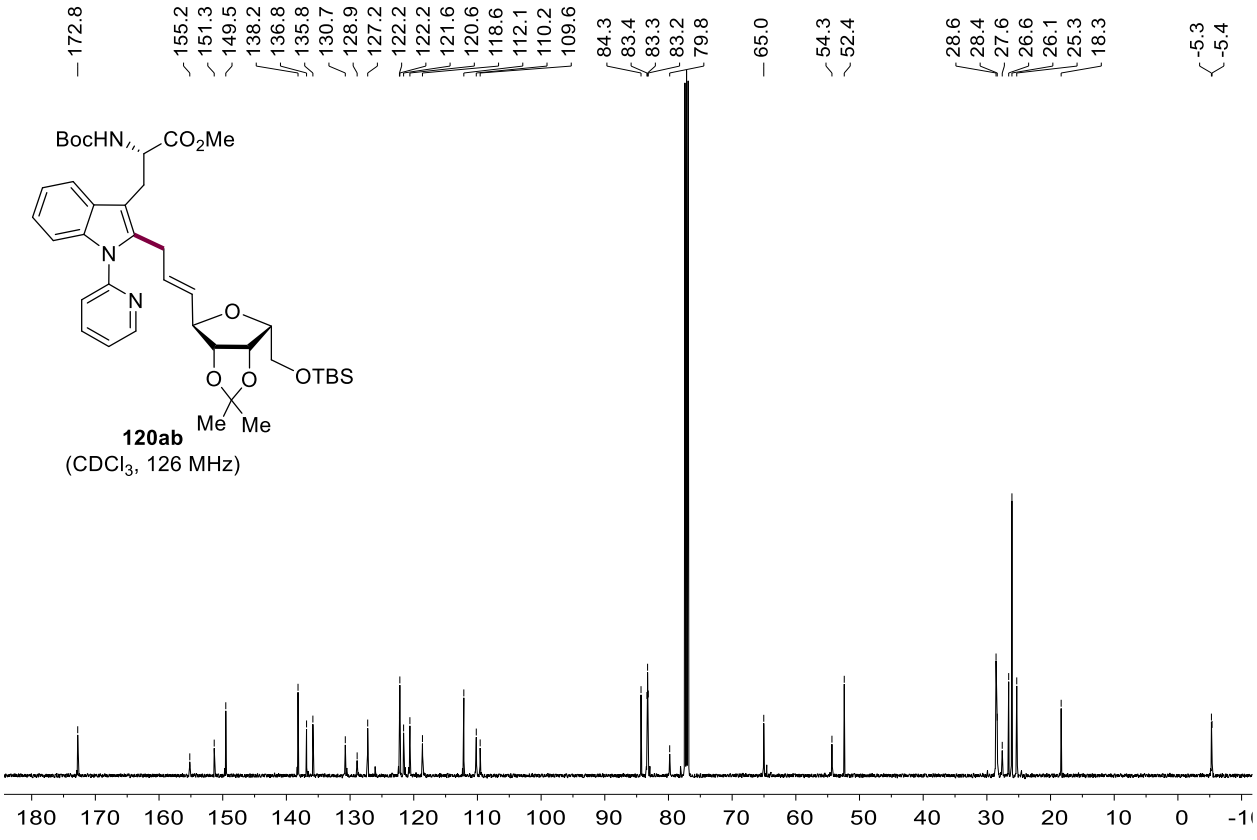


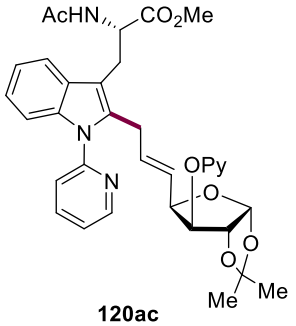


120aa
($CDCl_3$, 101 MHz)

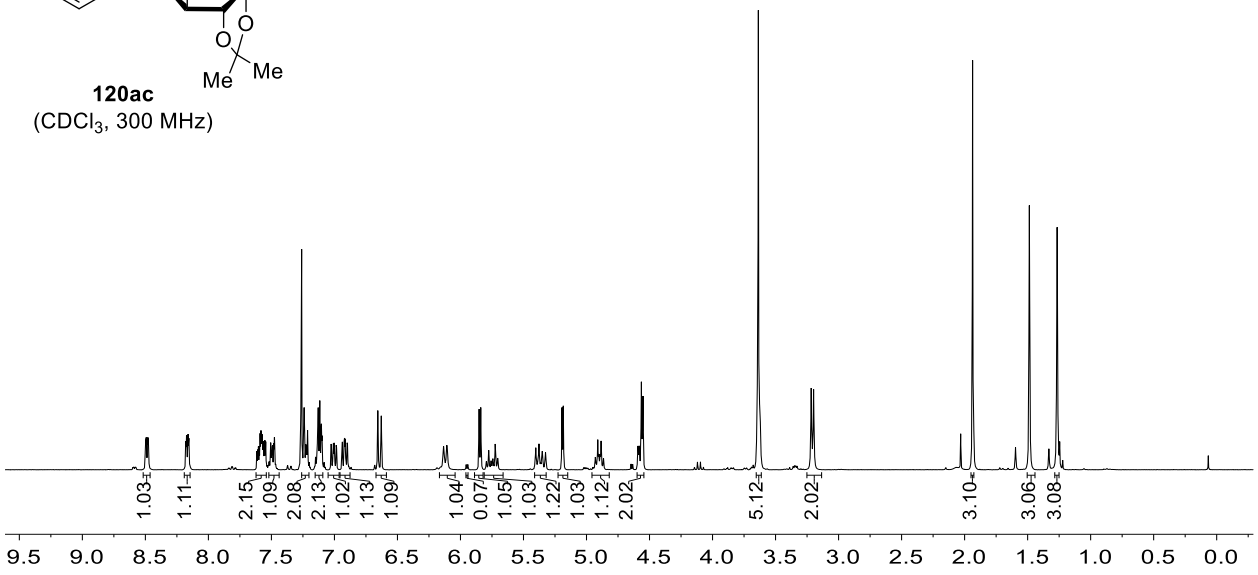


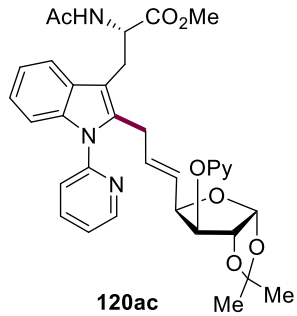

BocHN
CO2Me
N
N
O
O
O
OTBS
Me
Me
120ab
(CDCl3, 400 MHz)
1.04
1.08
1.00
1.06
2.27
2.01
0.94
0.94
0.82
0.10
1.08
1.11
1.08
0.97
0.99
7.12
1.94
12.01
3.09
9.01
3.00
2.98
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0


172.8
155.2
151.3
149.5
138.2
136.8
135.8
130.7
128.9
127.2
122.2
122.2
121.6
120.6
118.6
112.1
110.2
109.6
84.3
83.4
83.3
83.2
79.8
65.0
54.3
52.4
28.6
28.4
27.6
26.6
26.1
25.3
18.3
-5.3
-5.4
BocHN
CO2Me
N
N
O
O
O
OTBS
Me
Me
120ab
(CDCl3, 126 MHz)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1

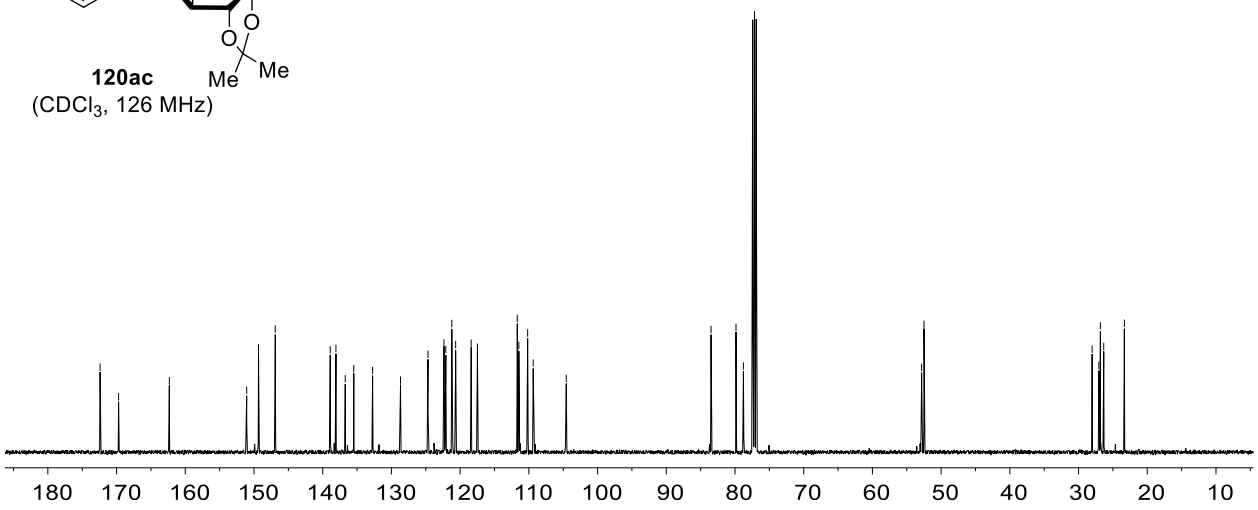


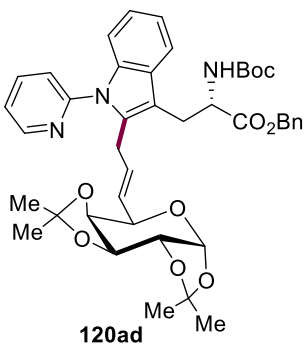
120ac
($CDCl_3$, 300 MHz)



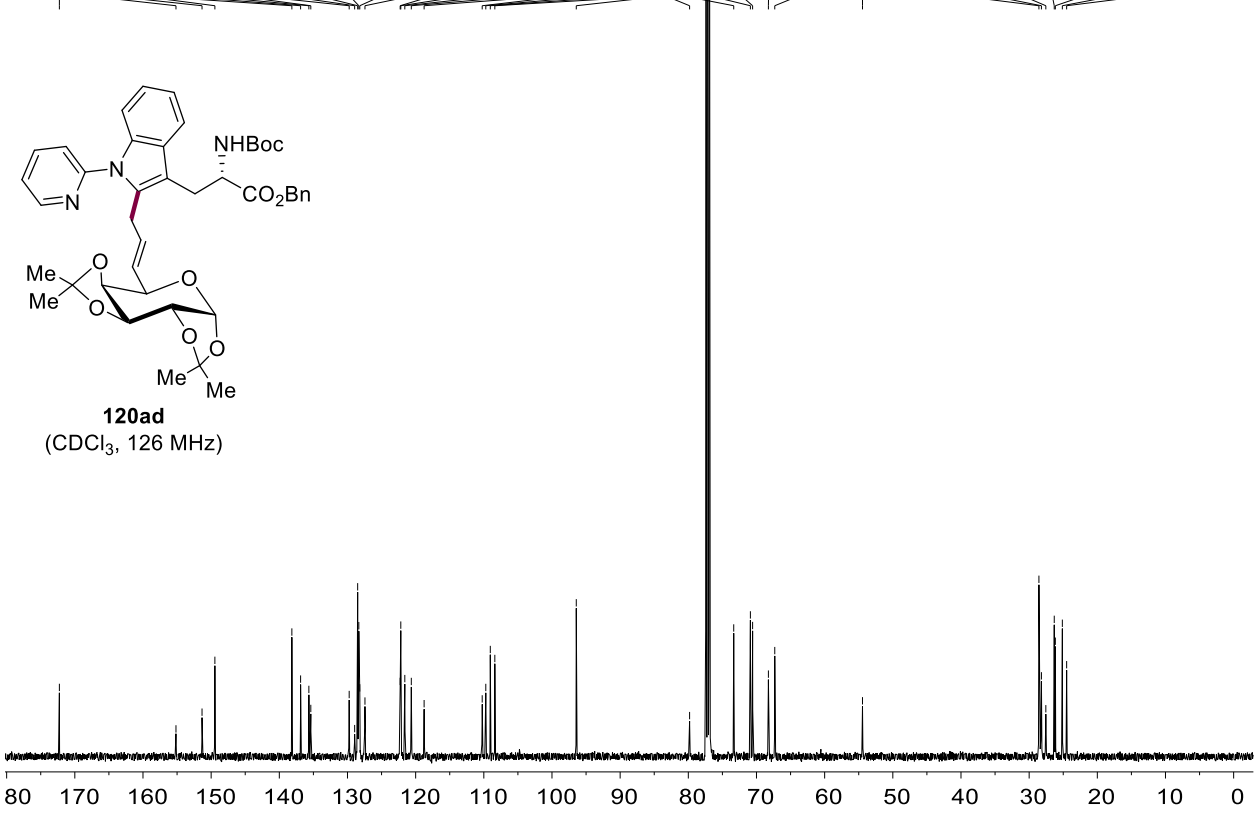


120ac
($CDCl_3$, 126 MHz)

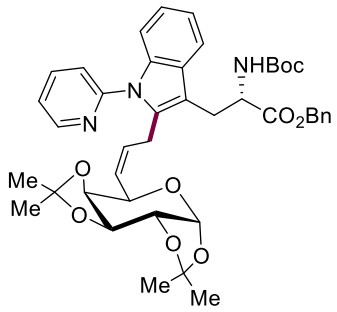




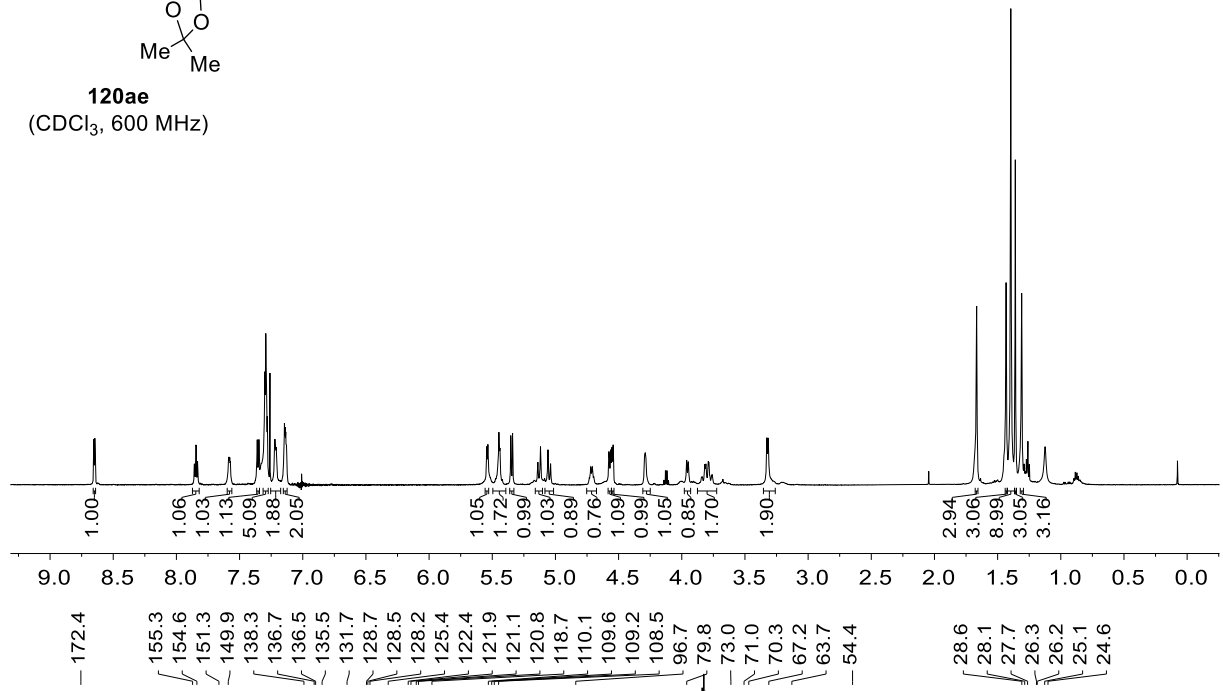
120ad
($CDCl_3$, 600 MHz)

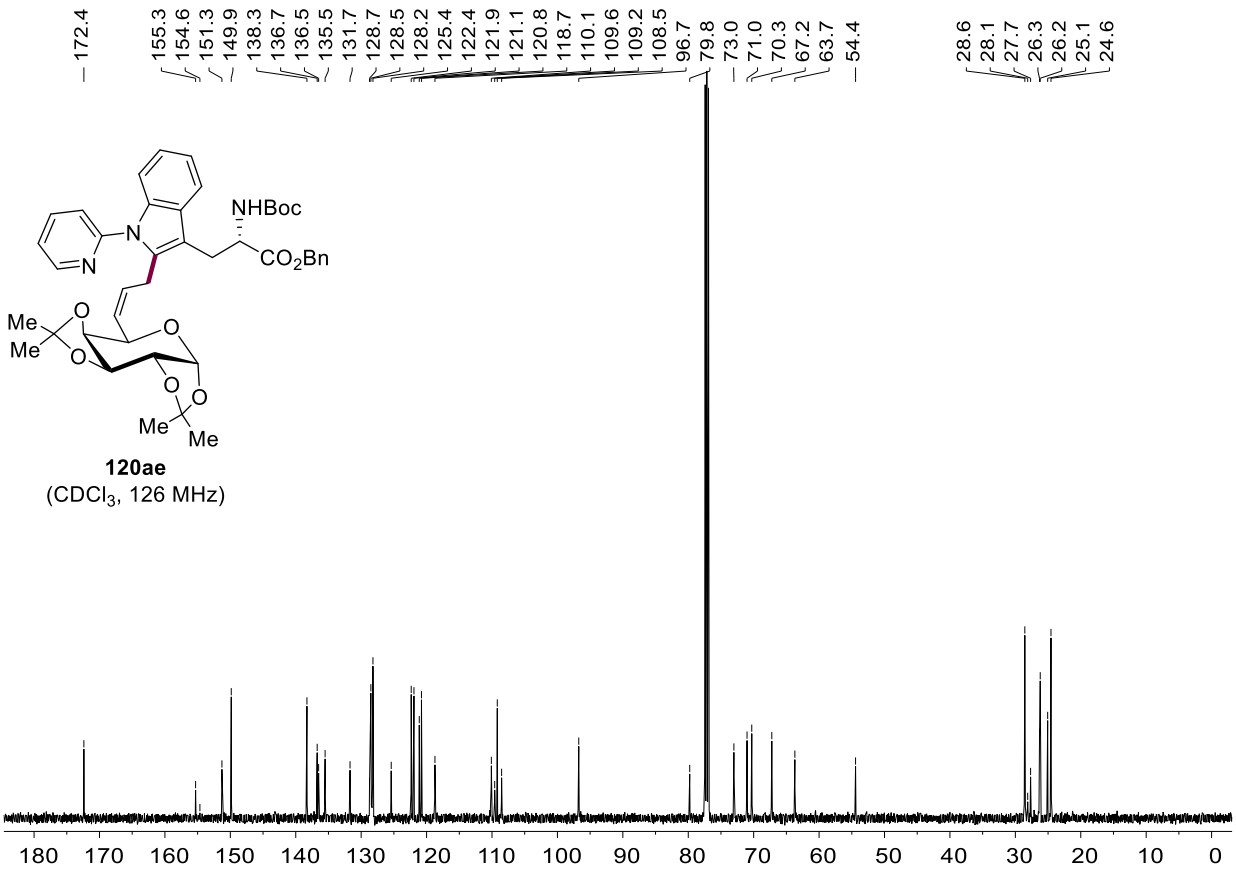


120ad
($CDCl_3$, 126 MHz)

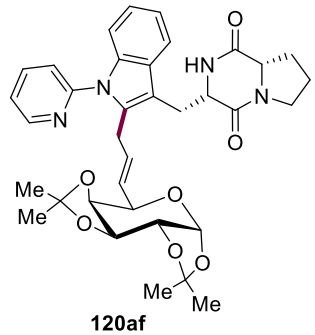


120ae
($CDCl_3$, 600 MHz)

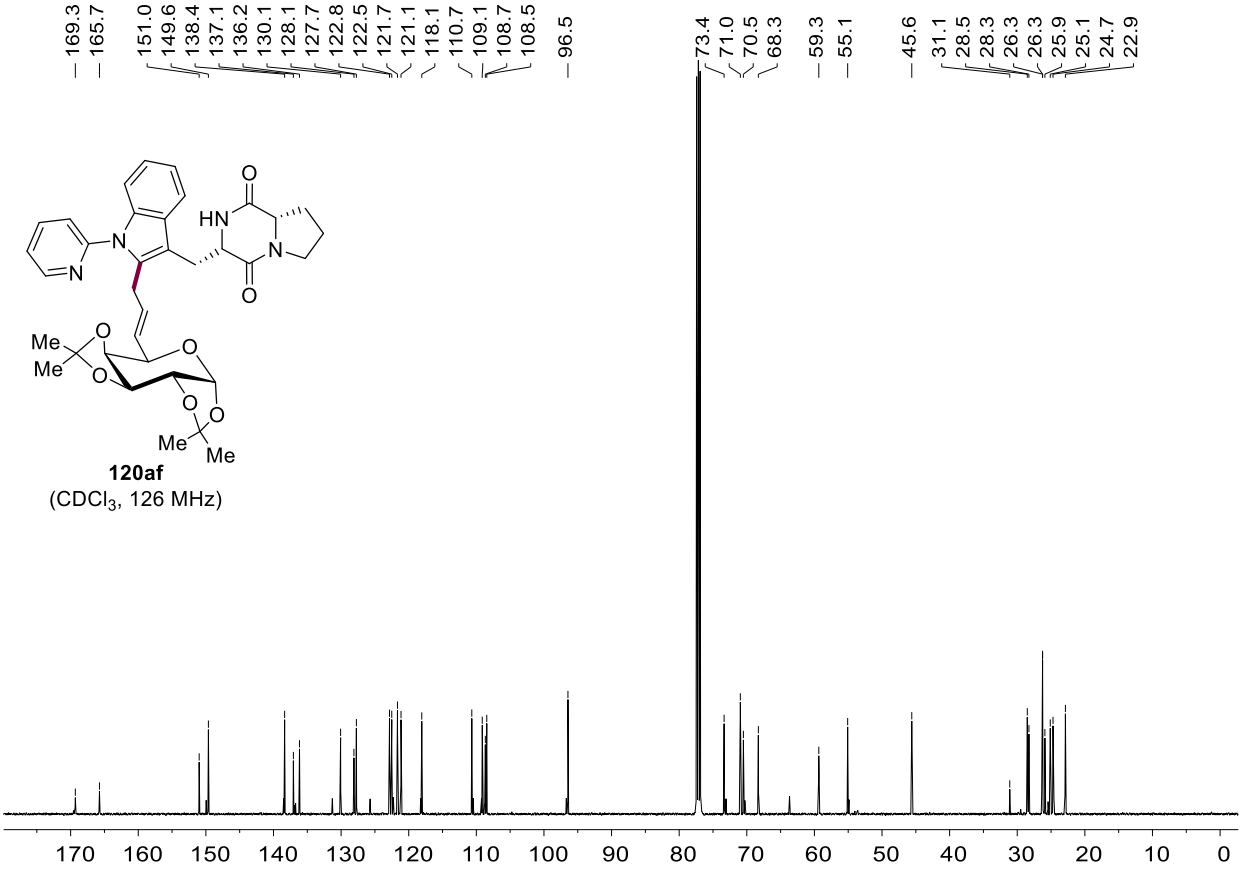




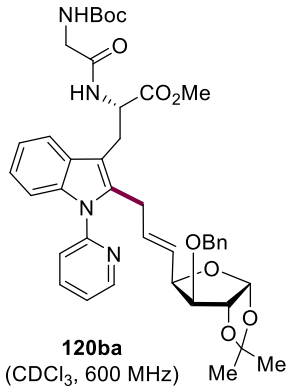
120ae
($CDCl_3$, 126 MHz)



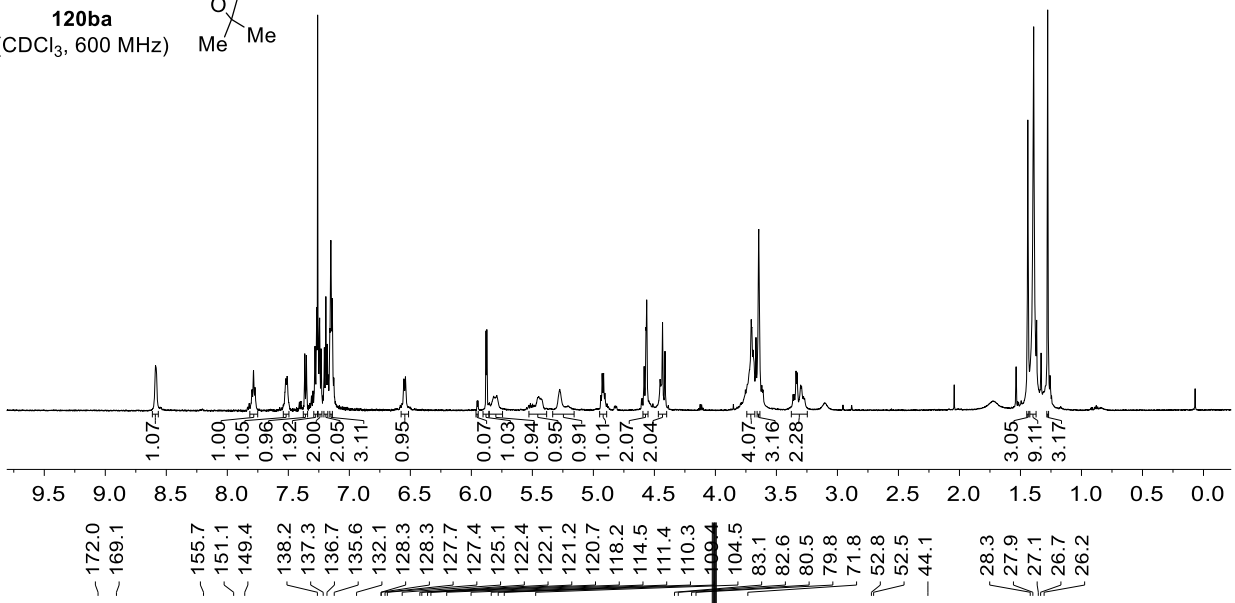
120af
($CDCl_3$, 400 MHz)

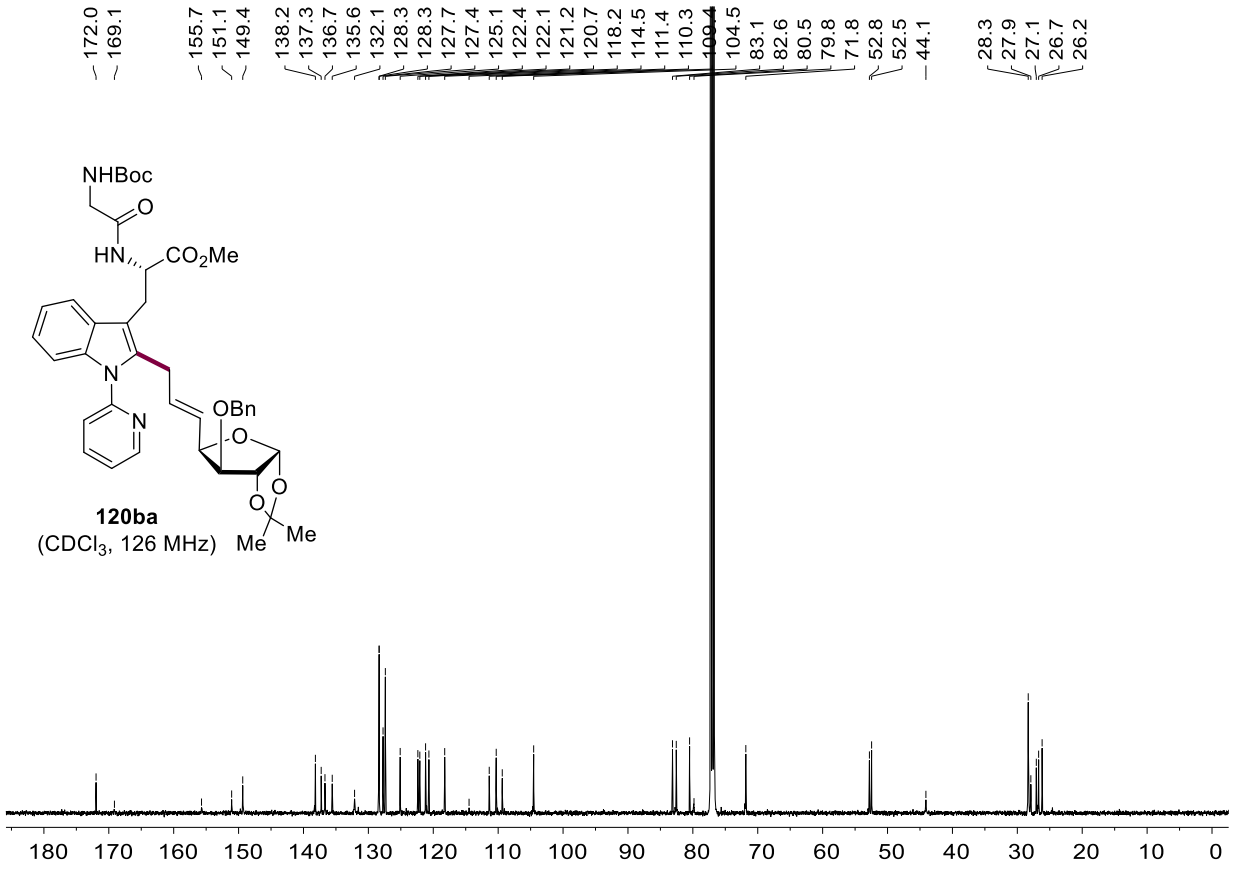


120af
($CDCl_3$, 126 MHz)

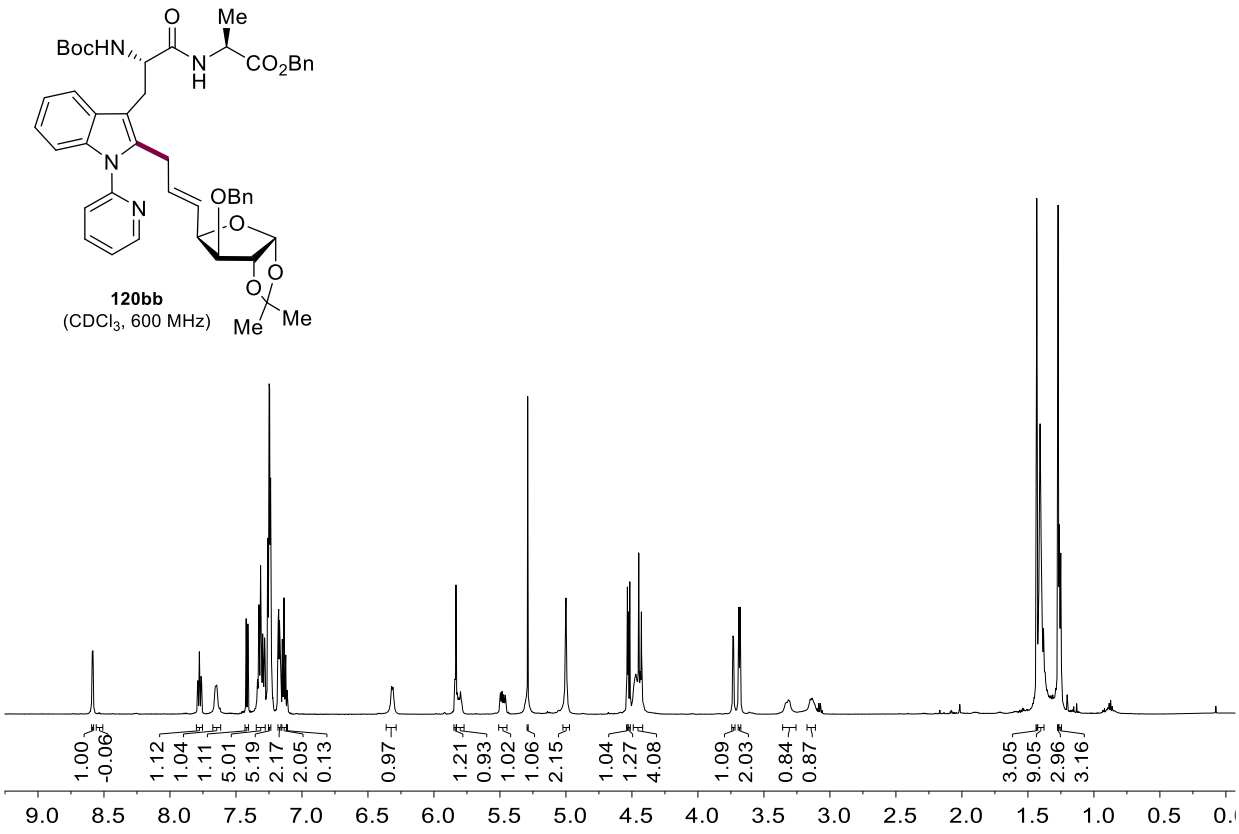


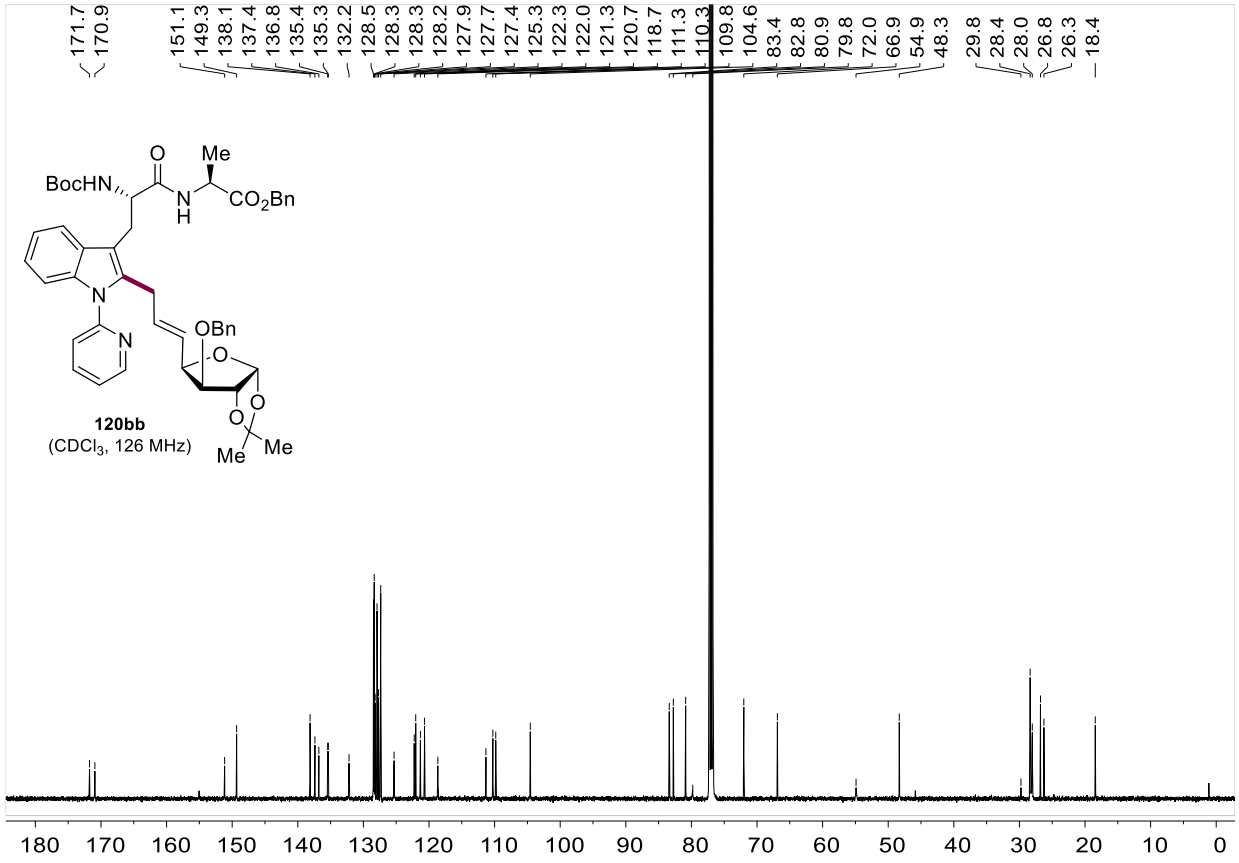
120ba
($CDCl_3$, 600 MHz)

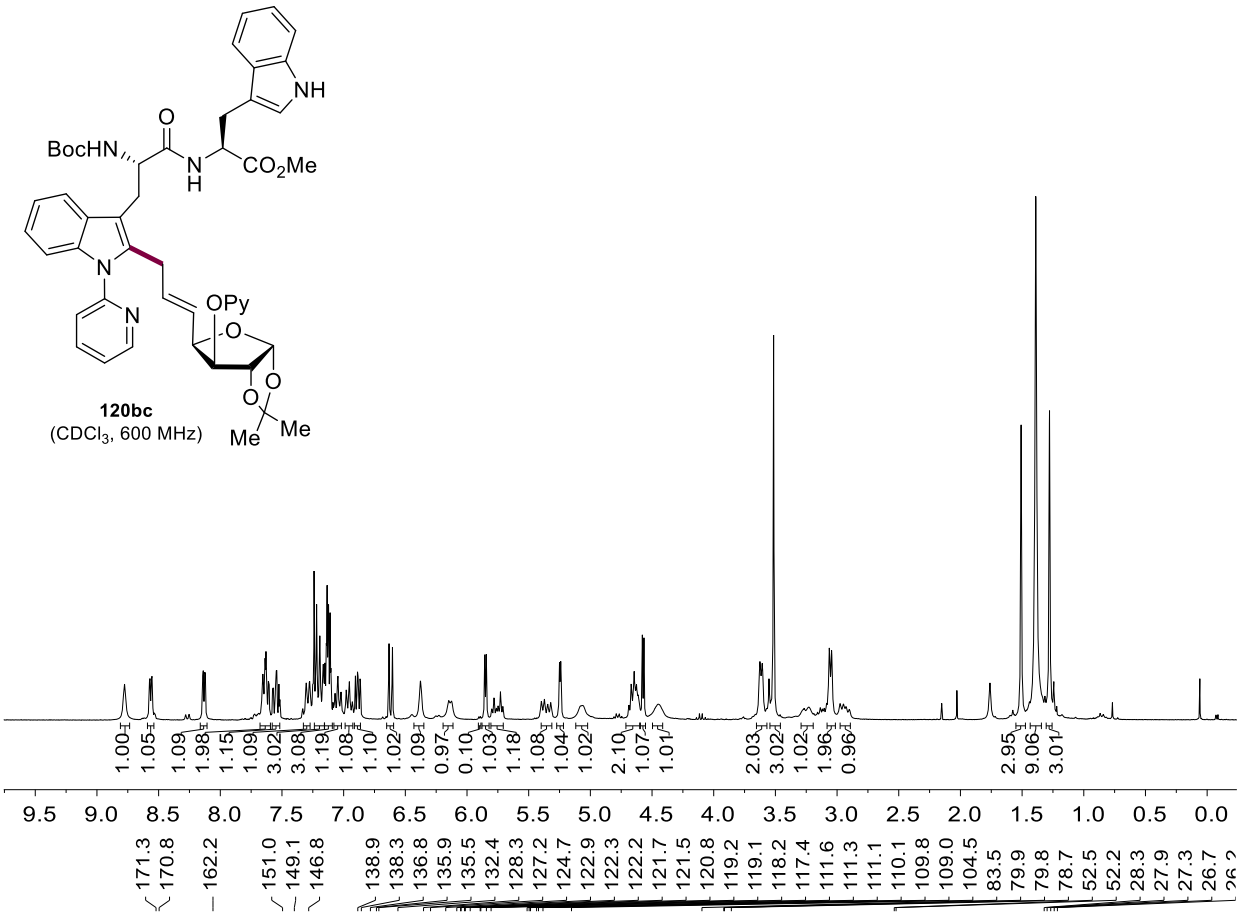


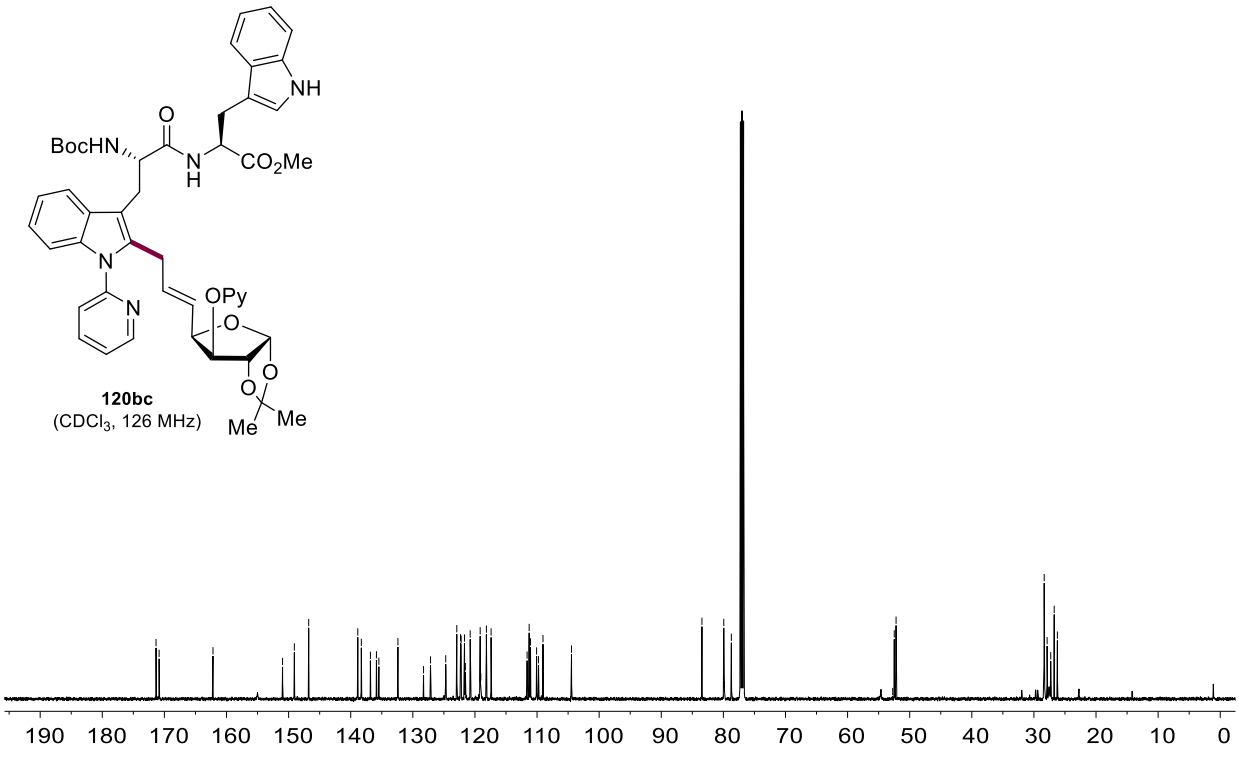


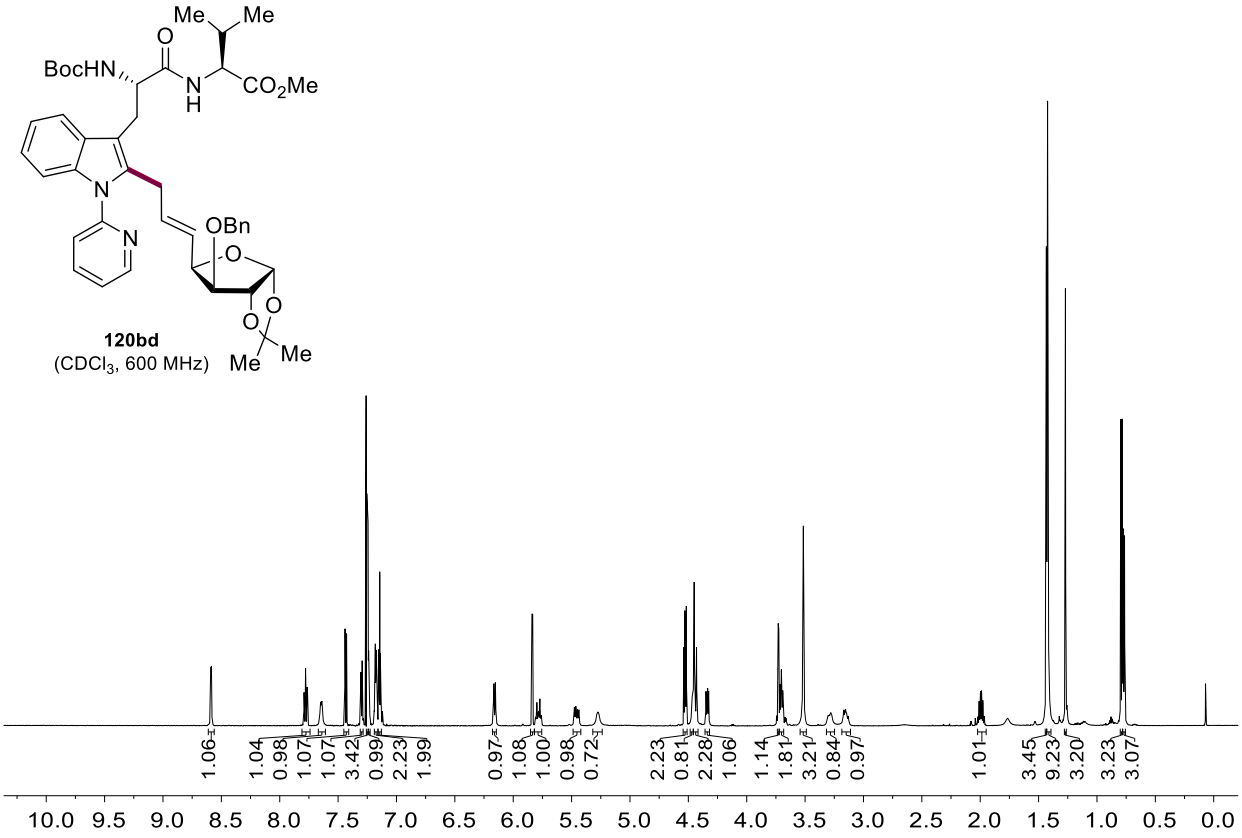
120ba
($CDCl_3$, 126 MHz)

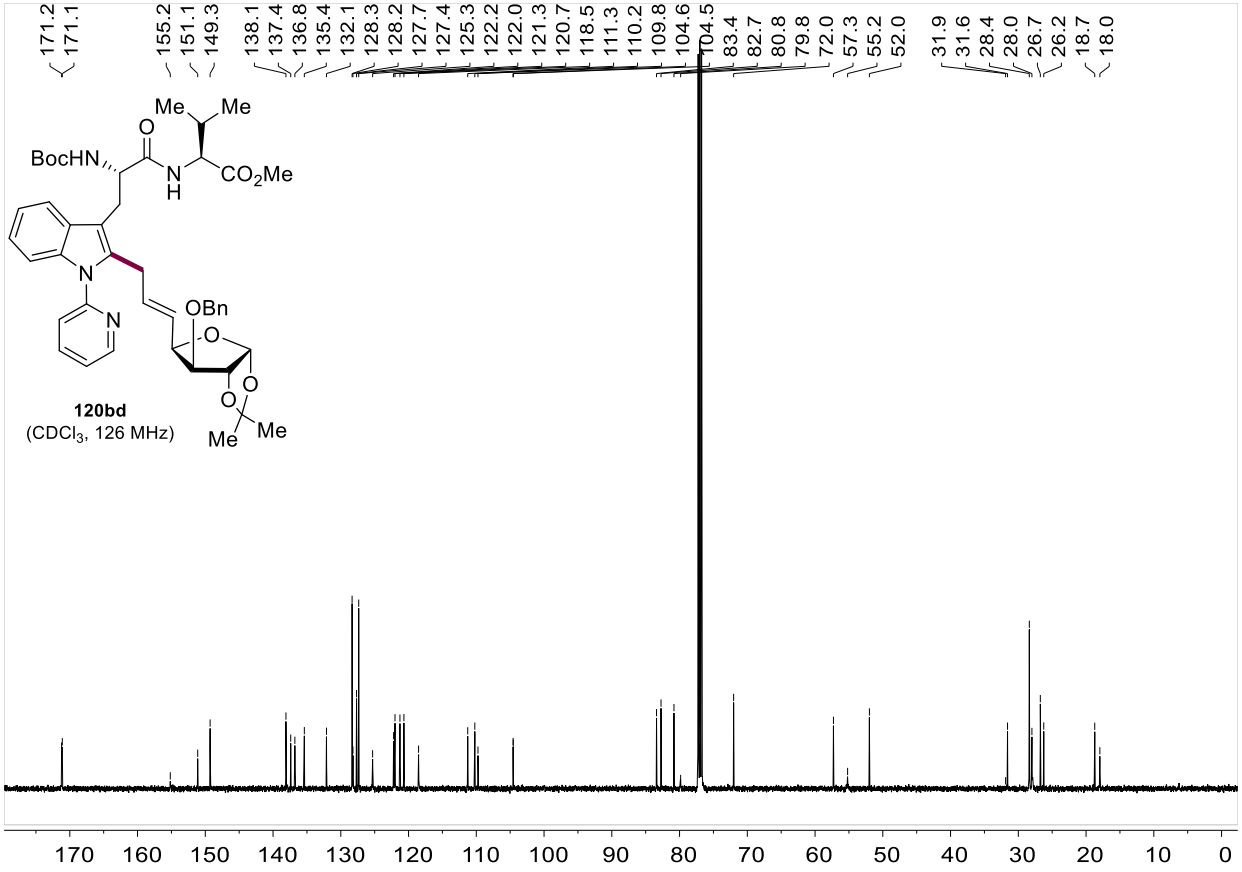

BocHN
O
Me
N
H
CO2Bn
N
N
OBn
O
O
O
Me
Me
120bb
(CDCl3, 600 MHz)
1.00
-0.06
1.12
1.04
1.11
5.01
5.19
2.17
2.05
0.13
0.97
1.21
0.93
1.02
1.06
2.15
1.04
1.27
4.08
1.09
2.03
0.84
0.87
3.05
9.05
2.96
3.16
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

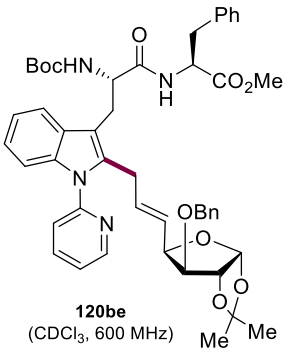

171.7
170.9
151.1
149.3
138.1
137.4
136.8
135.4
135.3
132.2
128.5
128.3
128.3
128.2
127.9
127.7
127.4
125.3
122.3
122.0
121.3
120.7
118.7
111.3
110.3
109.8
104.6
83.4
82.8
80.9
79.8
72.0
66.9
54.9
48.3
29.8
28.4
28.0
26.8
26.3
18.4
BocHN
O
Me
N
H
CO2Bn
N
N
OBn
O
O
O
Me
Me
120bb
(CDCl3, 126 MHz)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


BocHN
O
N
H
NH
CO2Me
N
N
OPy
O
O
O
Me
Me
120bc
(CDCl3, 600 MHz)
1.00 1.05 1.09 1.98 1.15 1.09 3.02 3.08 1.19 1.08 1.10 1.02 1.09 0.97 0.10 1.03 1.18 1.08 1.04 1.02 2.10 1.07 1.01 2.03 3.02 1.02 1.96 0.96 2.95 9.06 3.01
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
171.3 170.8 162.2 151.0 149.1 146.8 138.9 138.3 136.8 135.9 135.5 132.4 128.3 127.2 124.7 122.9 122.3 122.2 121.7 121.5 120.8 119.2 119.1 118.2 117.4 111.6 111.3 111.1 110.1 109.8 109.0 104.5 83.5 79.9 79.8 78.7 52.5 52.2 28.3 27.9 27.3 26.7

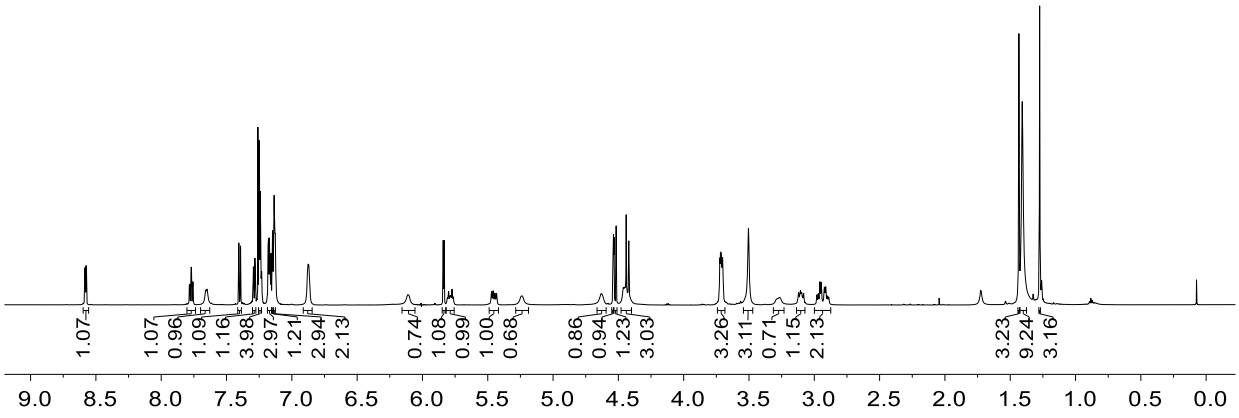

BocHN
O
N
H
NH
CO2Me
N
N
OPy
O
O
O
Me
Me
120bc
(CDCl3, 126 MHz)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

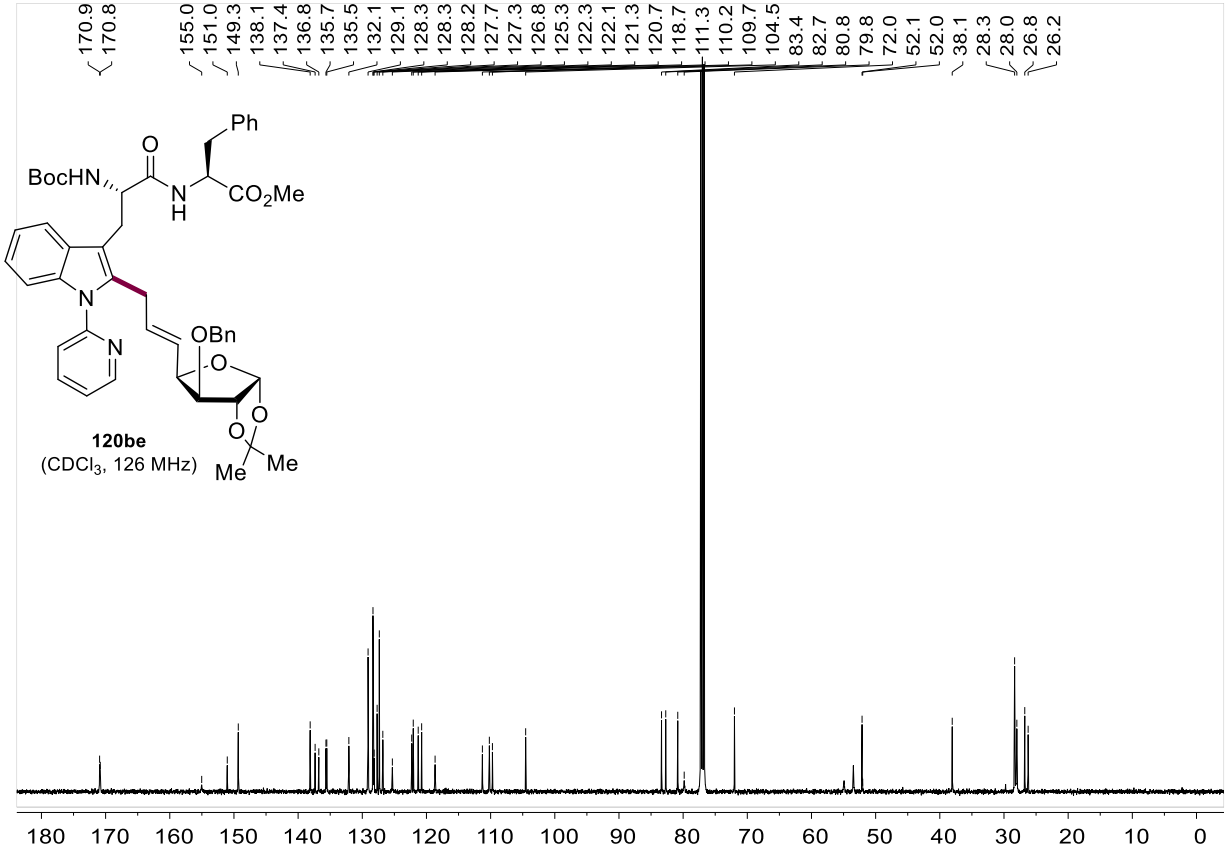

Me
Me
O
BocHN
N
H
CO2Me
N
OBn
O
O
O
Me
Me
120bd
(CDCl3, 600 MHz)
1.06
1.04
0.98
1.07
1.07
3.42
0.99
2.23
1.99
0.97
1.08
1.00
0.98
0.72
2.23
0.81
2.28
1.06
1.14
1.81
3.21
0.84
0.97
1.01
3.45
9.23
3.20
3.23
3.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0


171.2
171.1
155.2
151.1
149.3
138.1
137.4
136.8
135.4
132.1
128.3
128.2
127.7
127.4
125.3
122.2
122.0
121.3
120.7
118.5
111.3
110.2
109.8
104.6
104.5
83.4
82.7
80.8
79.8
72.0
57.3
55.2
52.0
31.9
31.6
28.4
28.0
26.7
26.2
18.7
18.0
Me
Me
O
BocHN
N
H
CO2Me
N
OBn
O
O
O
Me
Me
120bd
(CDCl3, 126 MHz)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

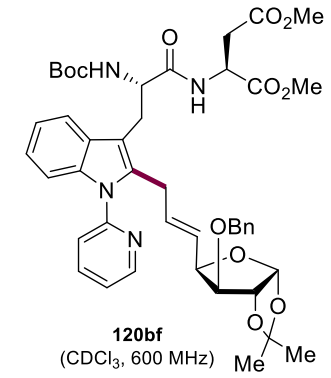


120be
($CDCl_3$, 600 MHz)

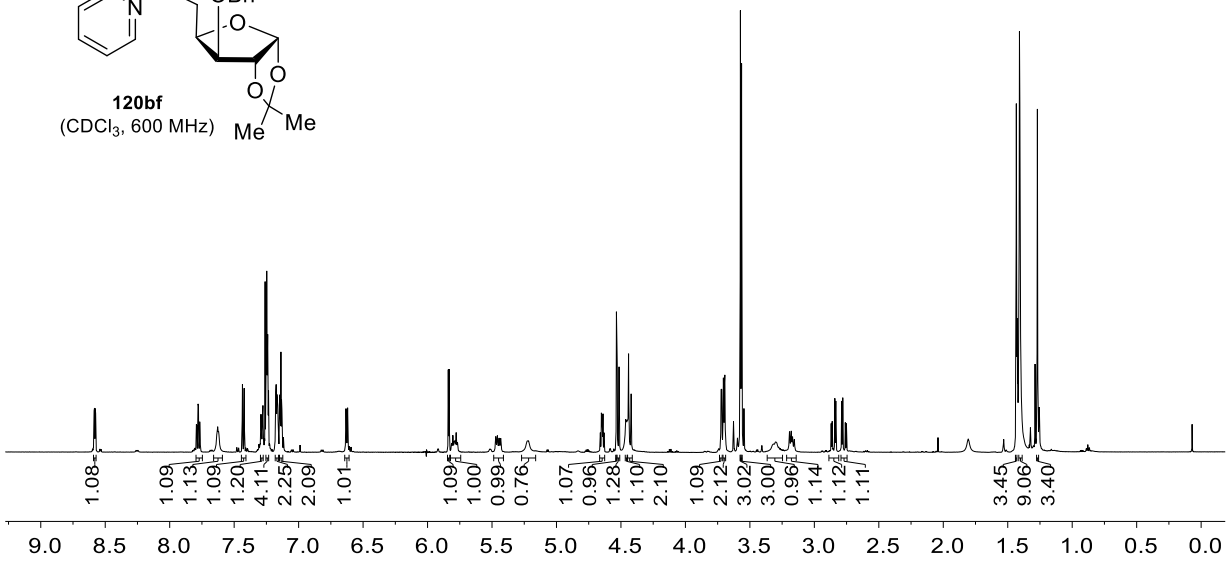


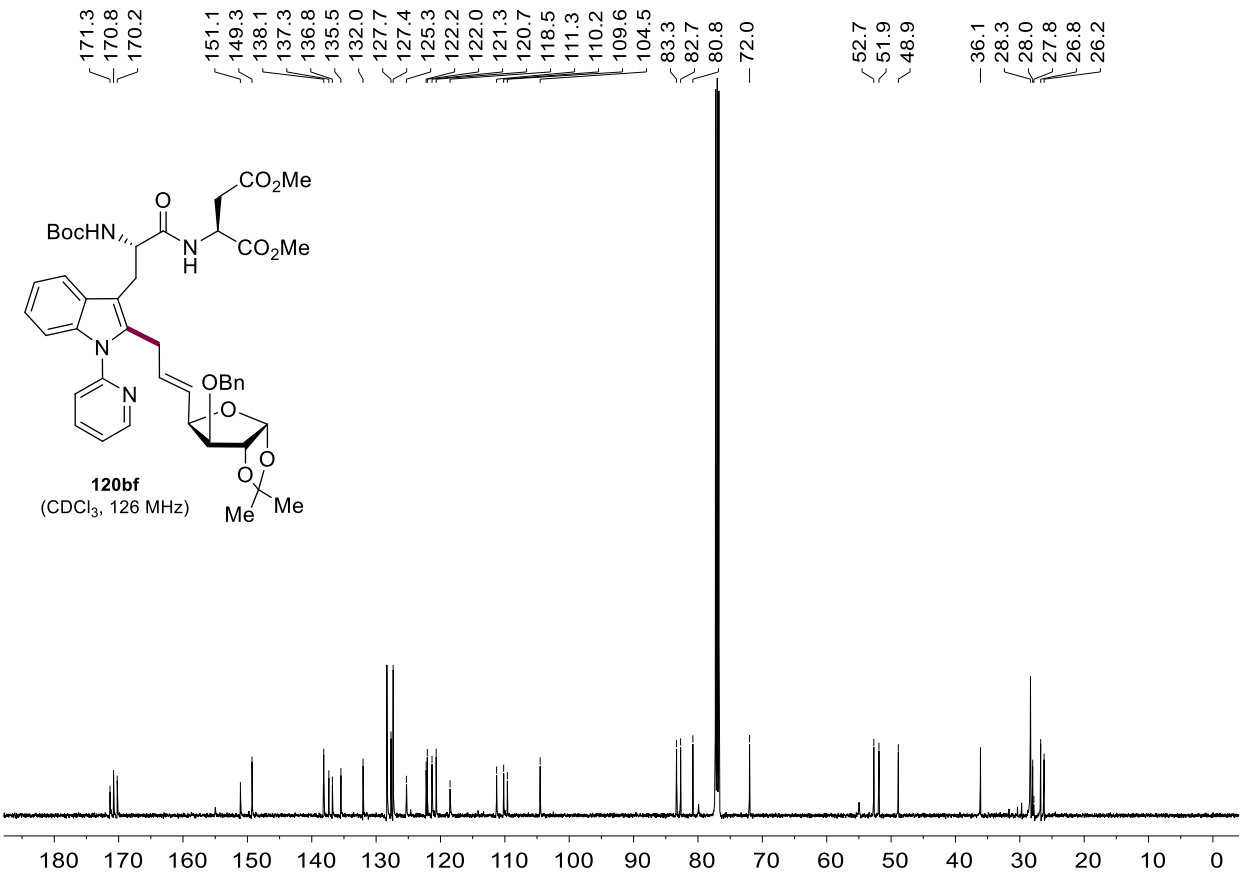


120be
($CDCl_3$, 126 MHz)

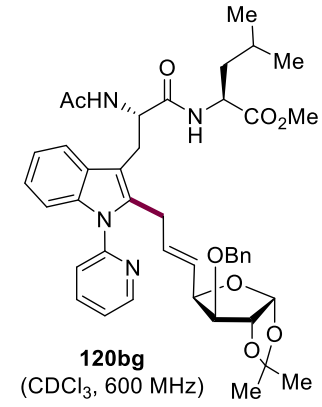


120bf
($CDCl_3$, 600 MHz)

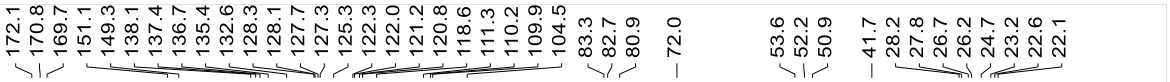


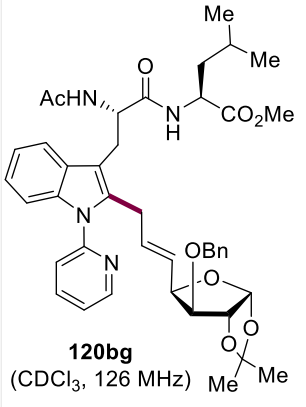


120bf
($CDCl_3$, 126 MHz)

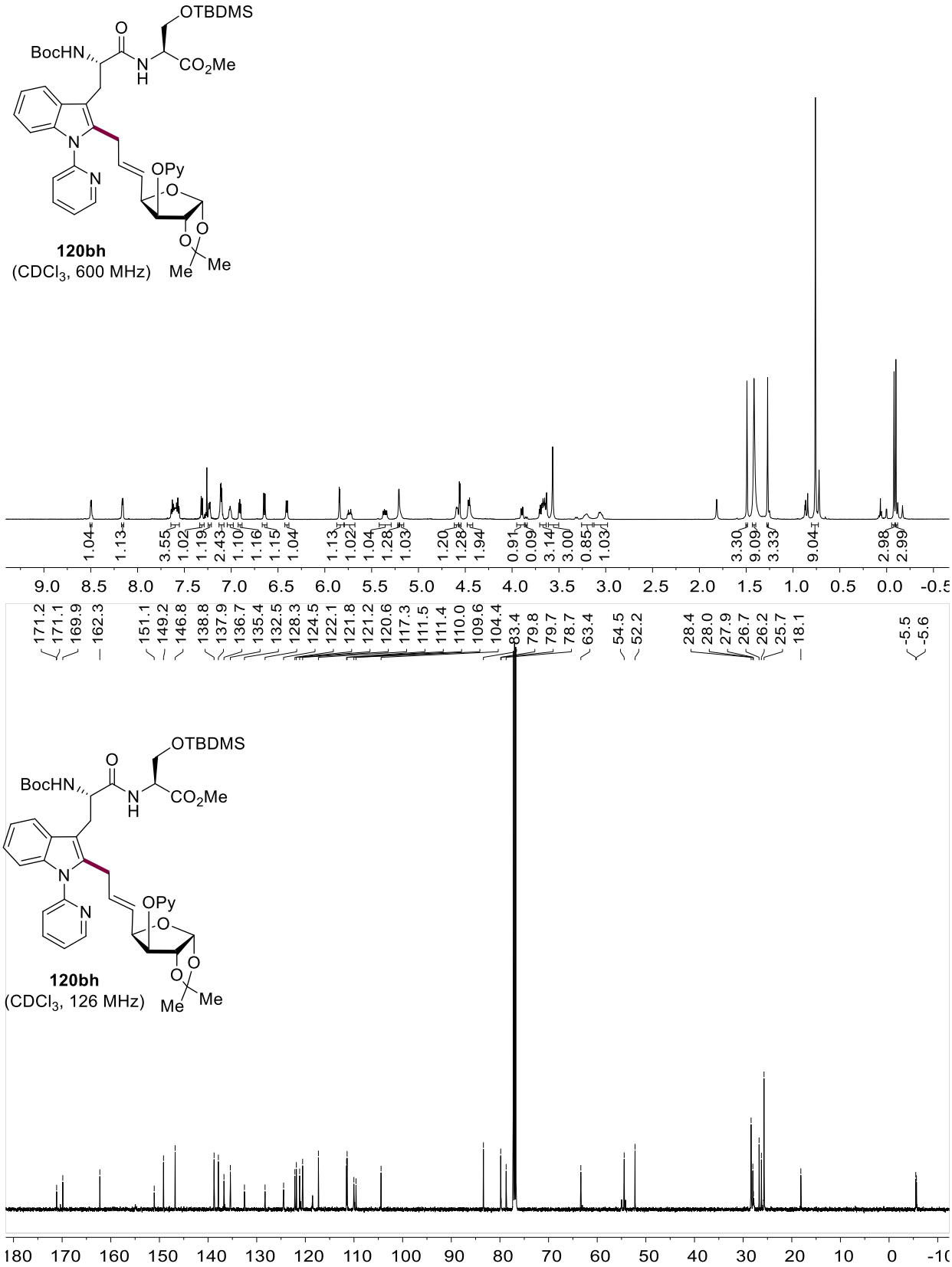


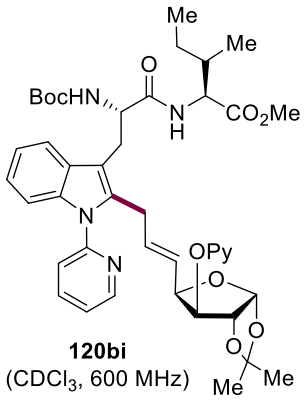
120bg
($CDCl_3$, 600 MHz)



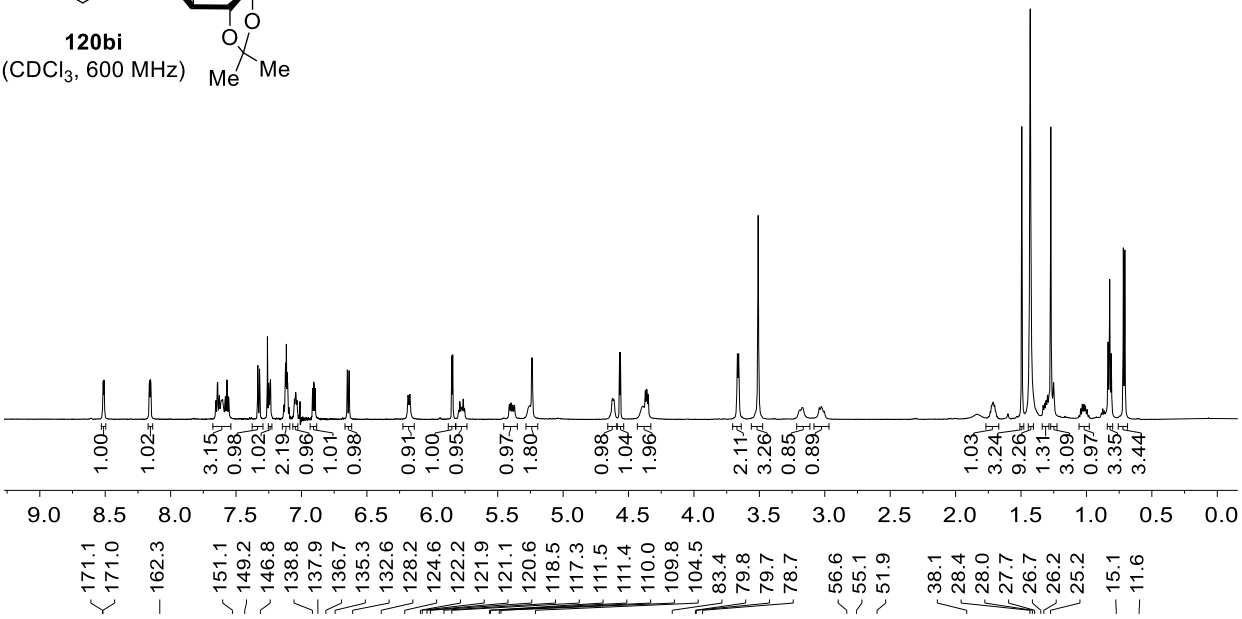


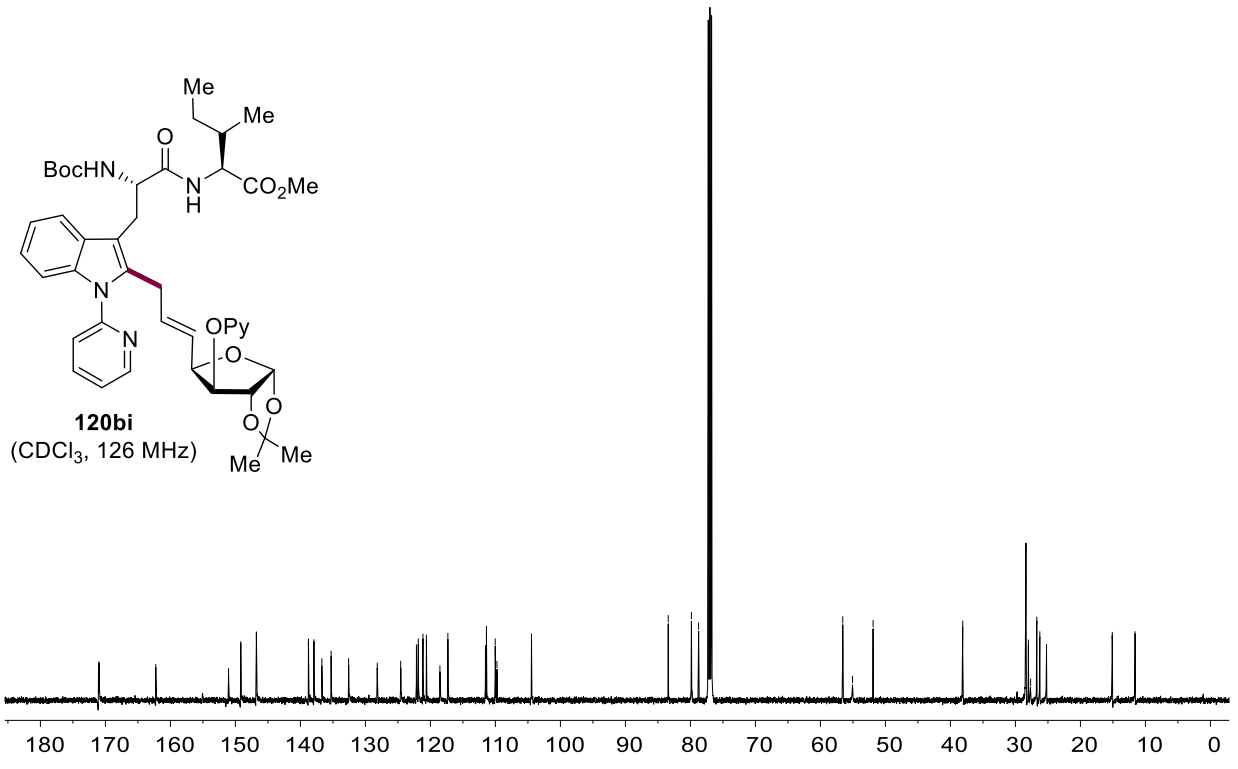
120bg
($CDCl_3$, 126 MHz)


OTBDMS
BocHN
O
N
H
CO2Me
N
N
OPy
O
O
O
Me
Me
120bh
(CDCl3, 600 MHz)
1.04 1.13 3.55 1.02 1.19 2.43 1.10 1.16 1.15 1.04 1.13 1.02 1.04 1.28 1.03 1.20 1.28 1.94 0.91 0.09 3.14 3.00 0.85 1.03 3.30 9.09 3.33 9.04 2.98 2.99
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
171.2 171.1 169.9 162.3 151.1 149.2 146.8 138.8 137.9 136.7 135.4 132.5 128.3 124.5 122.1 121.8 121.2 120.6 117.3 111.5 111.4 110.0 109.6 104.4 83.4 79.8 79.7 78.7 63.4 54.5 52.2 28.4 28.0 27.9 26.7 26.2 25.7 18.1 -5.5 -5.6
OTBDMS
BocHN
O
N
H
CO2Me
N
N
OPy
O
O
O
Me
Me
120bh
(CDCl3, 126 MHz)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

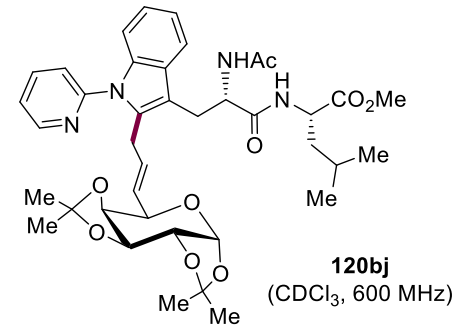


120bi
($CDCl_3$, 600 MHz)

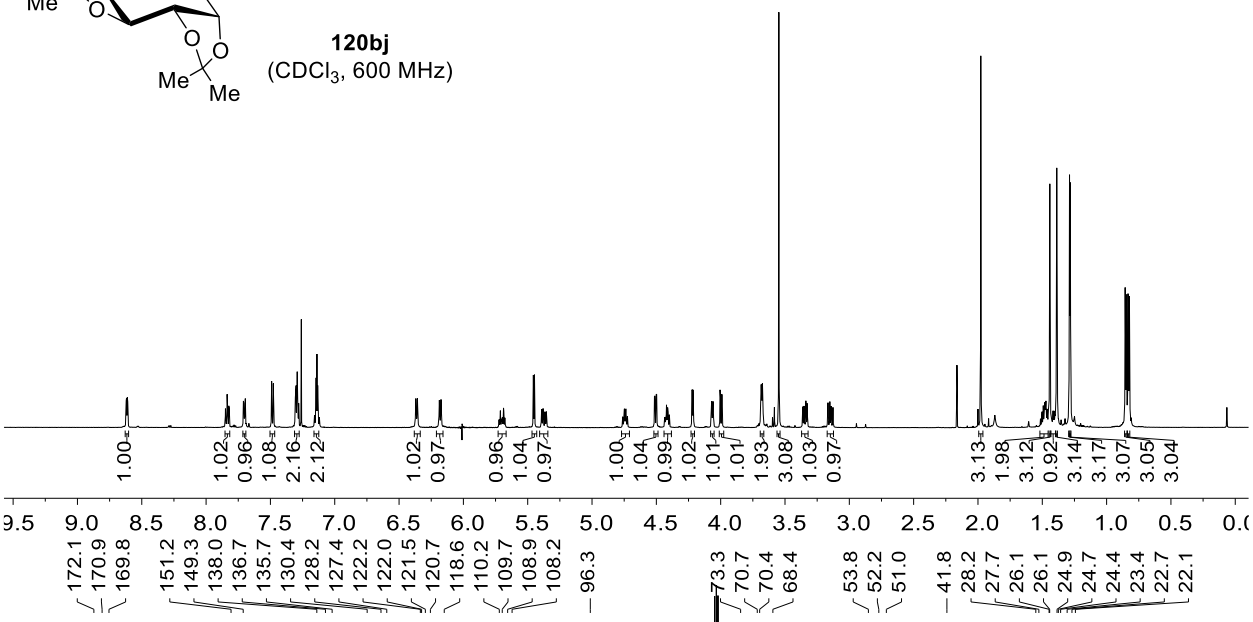


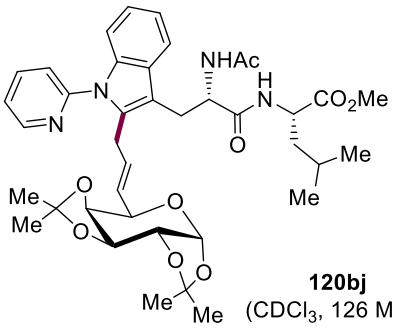


120bi
($CDCl_3$, 126 MHz)

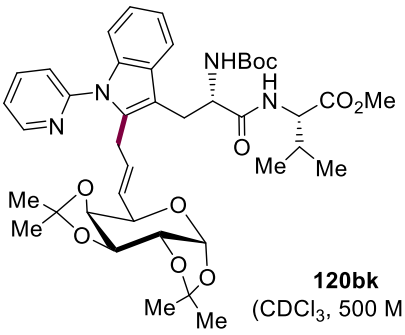


120bj
($CDCl_3$, 600 MHz)

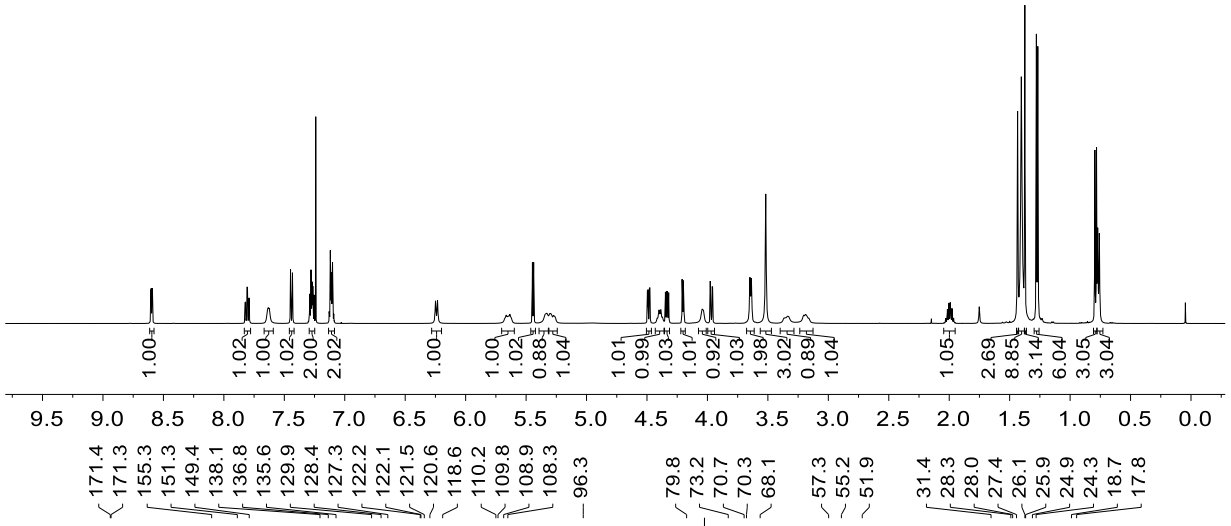


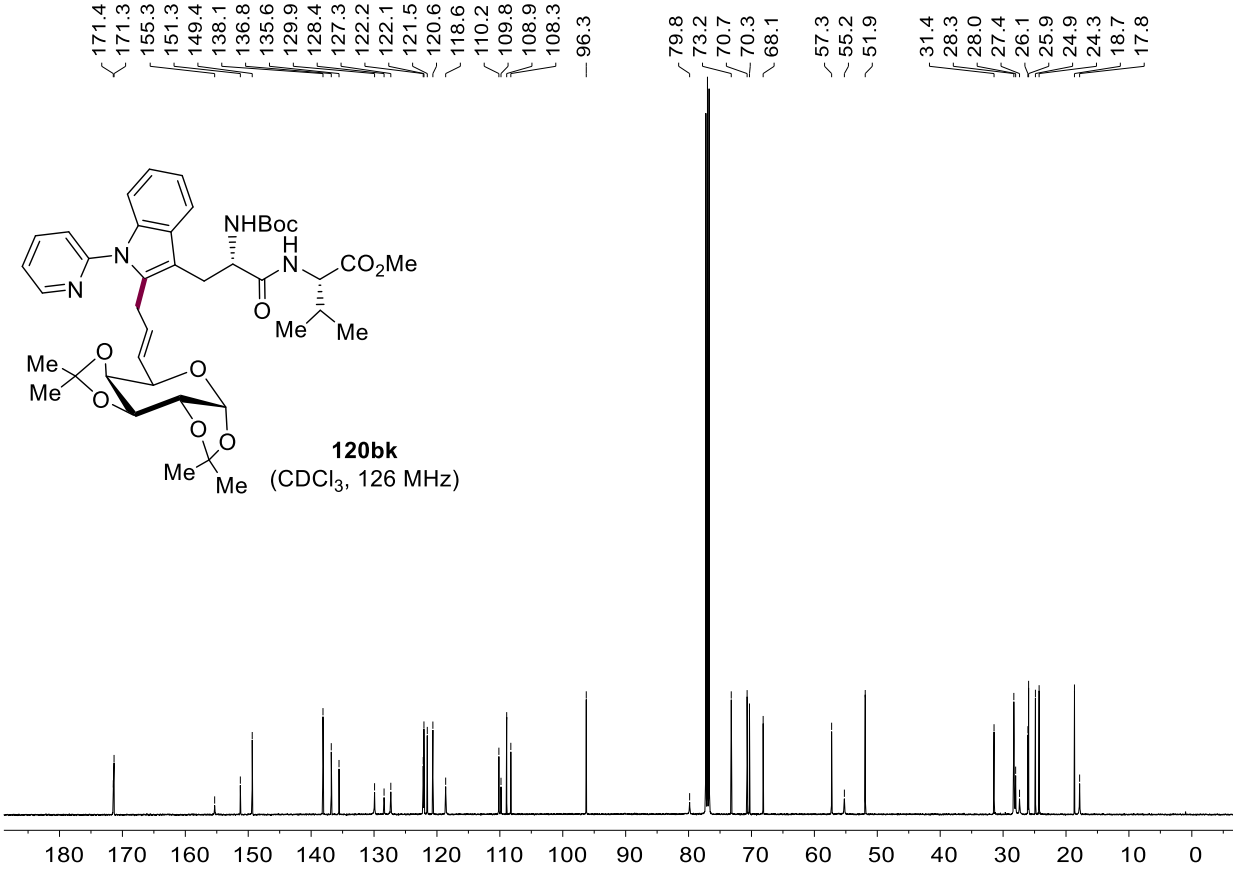


120bj
($CDCl_3$, 126 MHz)

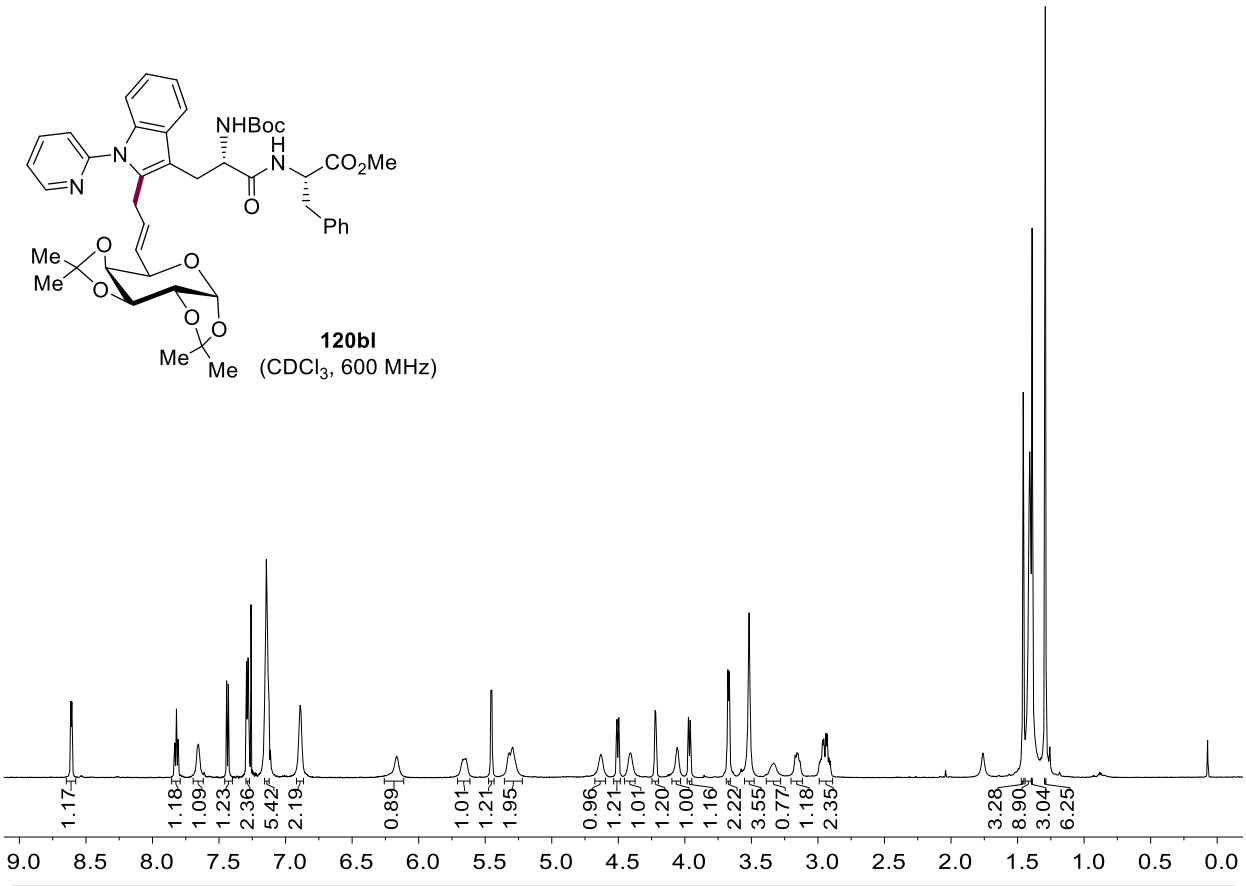


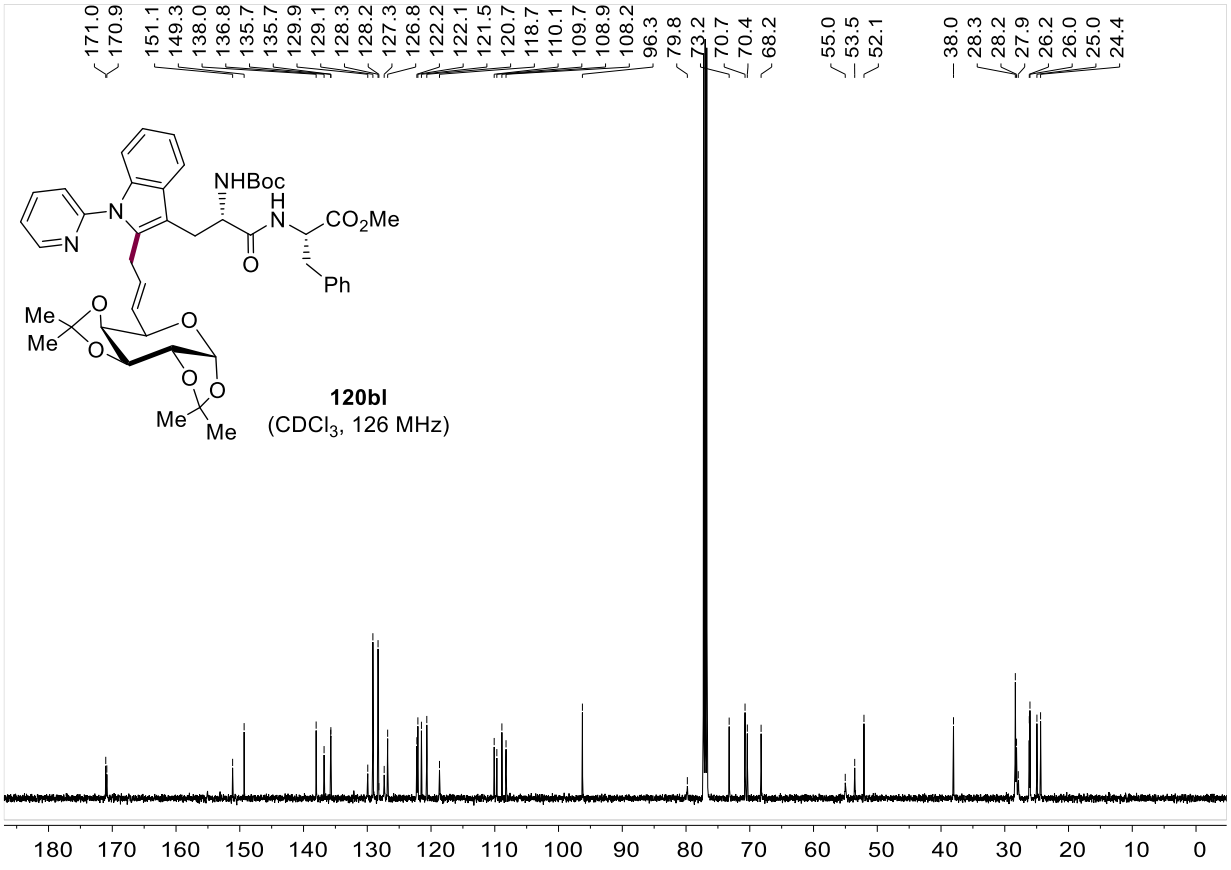
120bk
($CDCl_3$, 500 MHz)

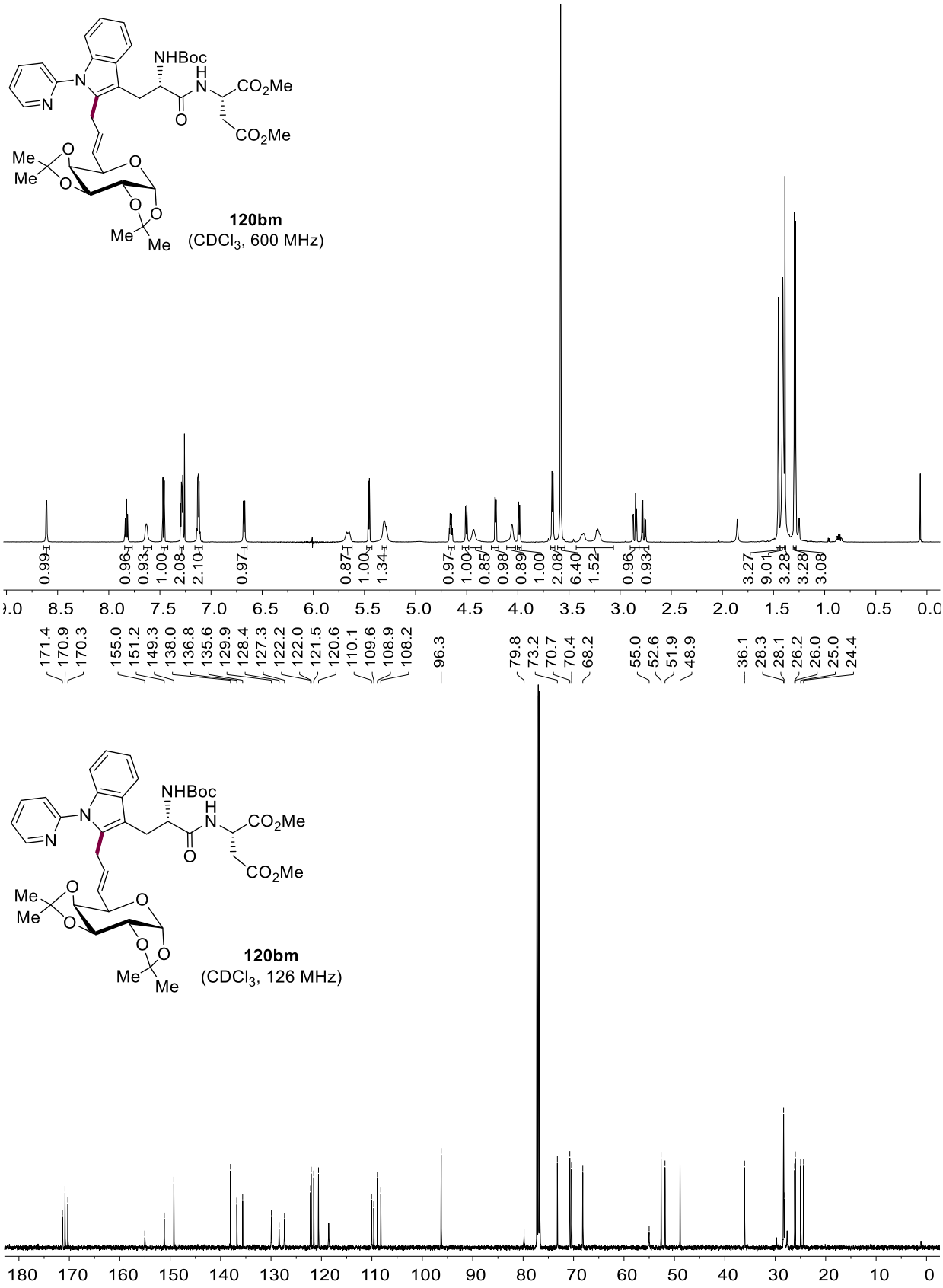


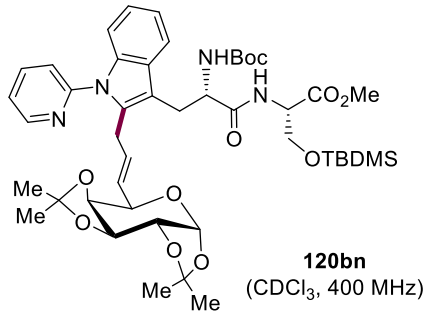


120bk
($CDCl_3$, 126 MHz)

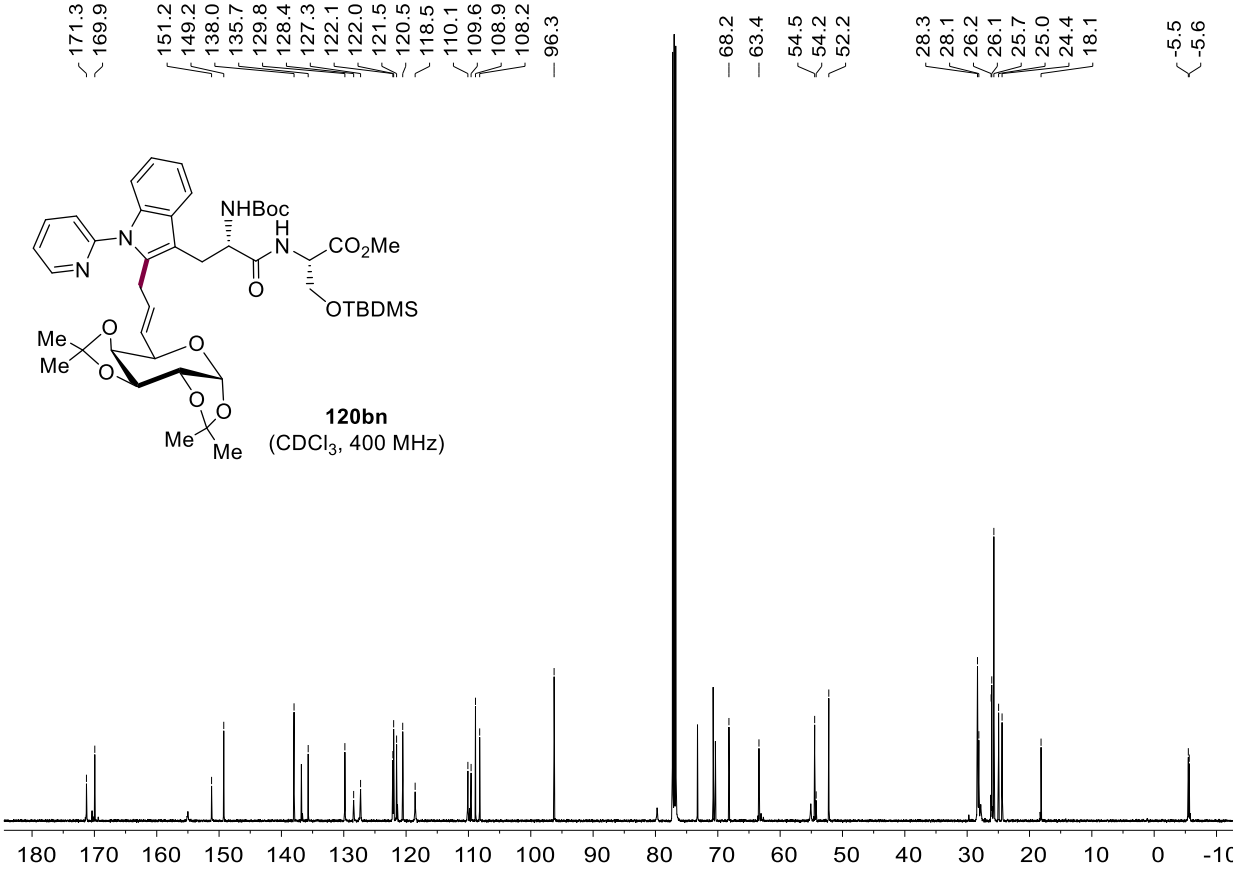

NHBoc
H
N
CO2Me
Ph
Me
Me
Me
Me
120bl
(CDCl3, 600 MHz)
1.17
1.18
1.09
1.23
2.36
5.42
2.19
0.89
1.01
1.21
1.95
0.96
1.21
1.01
1.20
1.00
1.16
2.22
3.55
0.77
1.18
2.35
3.28
8.90
3.04
6.25
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0


171.0
170.9
151.1
149.3
138.0
136.8
135.7
135.7
129.9
129.1
128.3
128.2
127.3
126.8
122.2
122.1
121.5
120.7
118.7
110.1
109.7
108.9
108.2
96.3
79.8
73.2
70.7
70.4
68.2
55.0
53.5
52.1
38.0
28.3
28.2
27.9
26.2
26.0
25.0
24.4
NHBoc
H
N
CO2Me
Ph
Me
Me
Me
Me
120bl
(CDCl3, 126 MHz)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

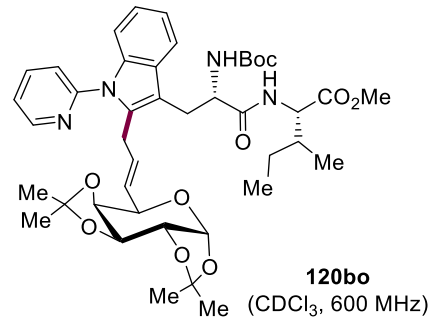

NHBoc
H
N
CO2Me
O
CO2Me
N
N
Me
Me
O
O
O
O
O
Me
Me
120bm
(CDCl3, 600 MHz)
0.99
0.96
0.93
1.00
2.08
2.10
0.97
0.87
1.00
1.34
0.97
1.00
0.85
0.98
0.89
1.00
2.08
6.40
1.52
0.96
0.93
3.27
9.01
3.28
3.28
3.08
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
171.4
170.9
170.3
155.0
151.2
149.3
138.0
136.8
135.6
129.9
128.4
127.3
122.2
122.0
121.5
120.6
110.1
109.6
108.9
108.2
96.3
79.8
73.2
70.7
70.4
68.2
55.0
52.6
51.9
48.9
36.1
28.3
28.1
26.2
26.0
25.0
24.4
NHBoc
H
N
CO2Me
O
CO2Me
N
N
Me
Me
O
O
O
O
O
Me
Me
120bm
(CDCl3, 126 MHz)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



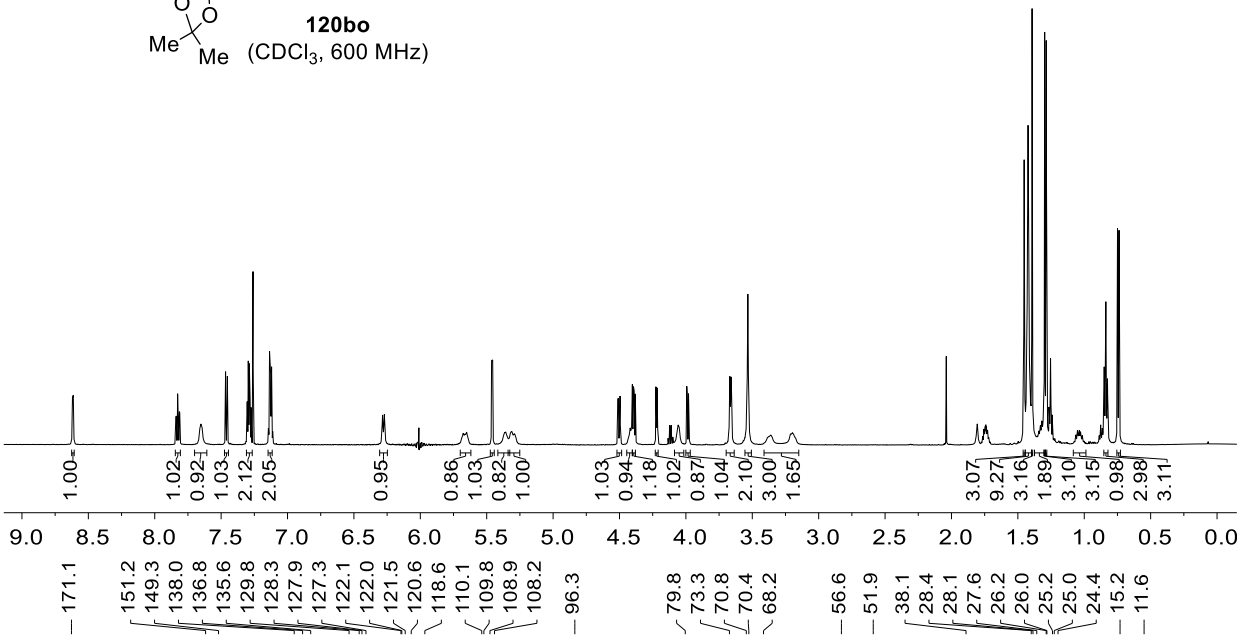
120bn
($CDCl_3$, 400 MHz)

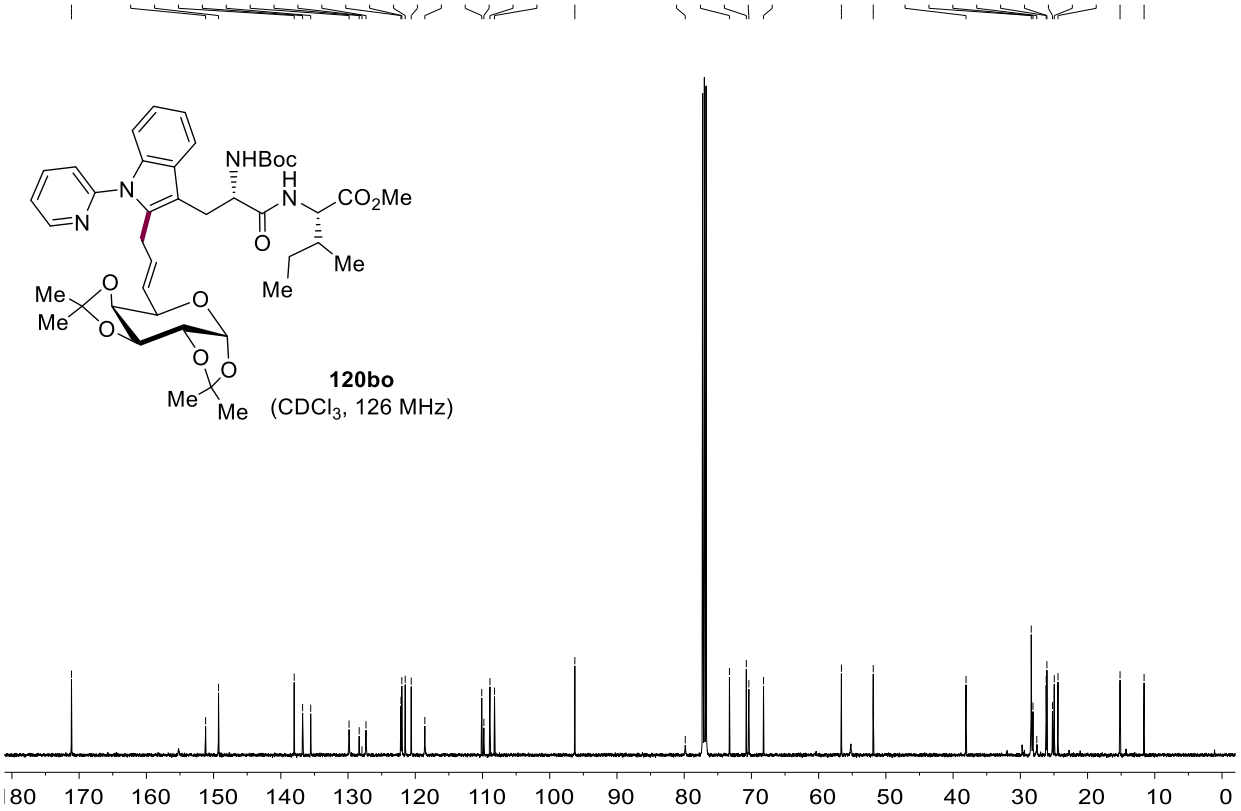


120bn
($CDCl_3$, 400 MHz)

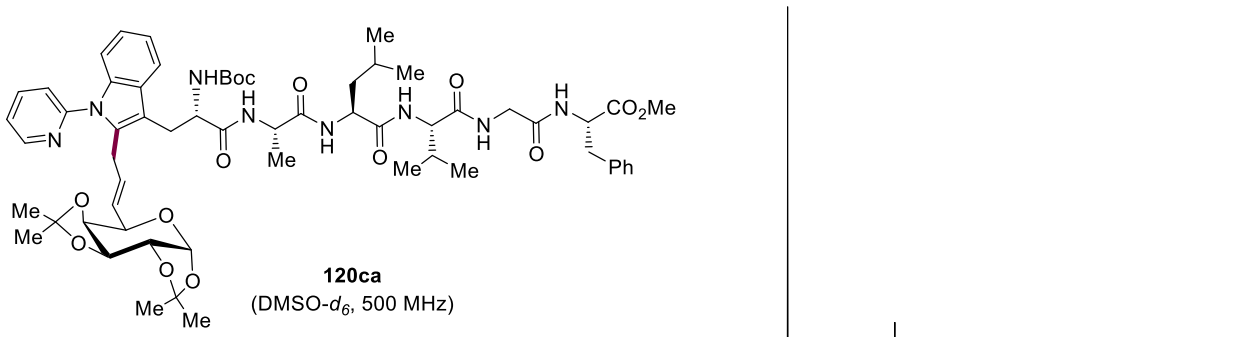


120bo
($CDCl_3$, 600 MHz)

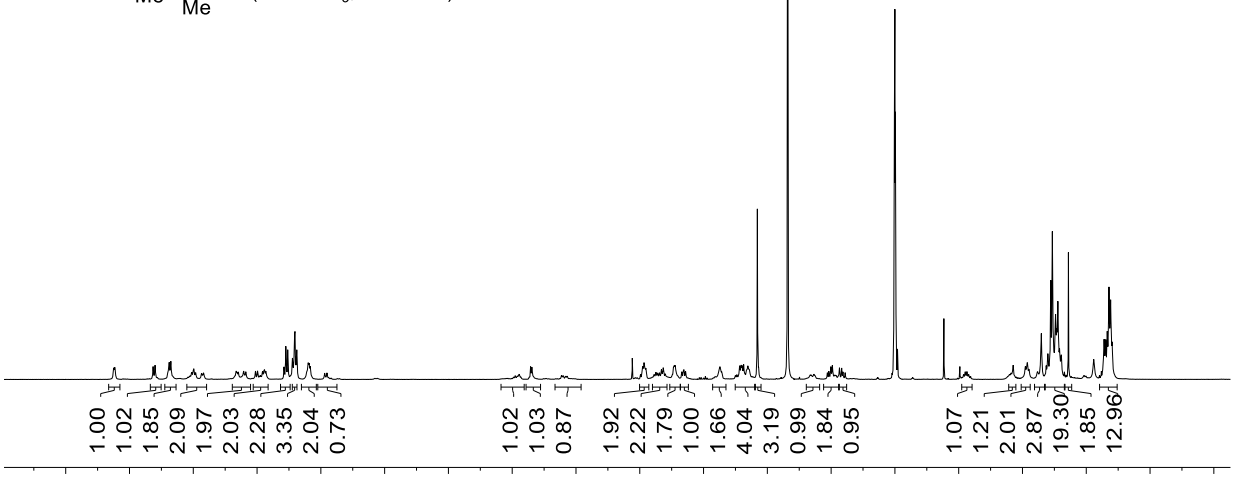


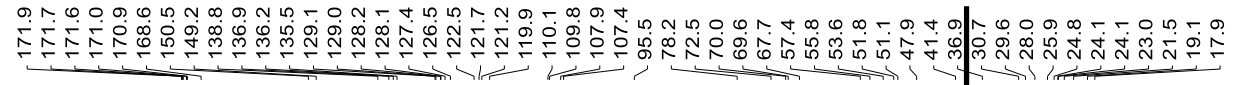


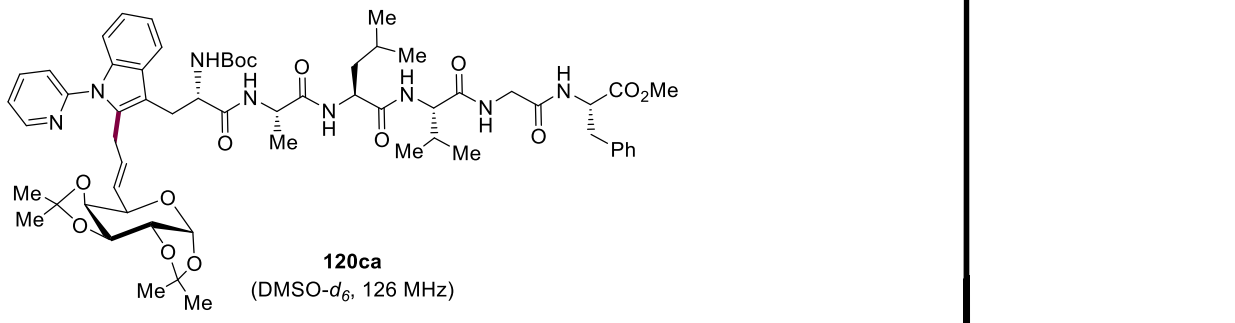
120bo
($CDCl_3$, 126 MHz)



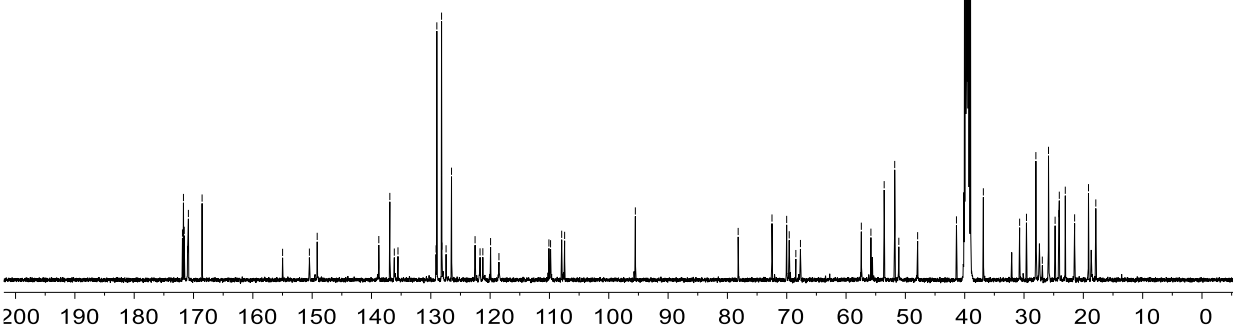
120ca
(DMSO-d_6, 500 MHz)

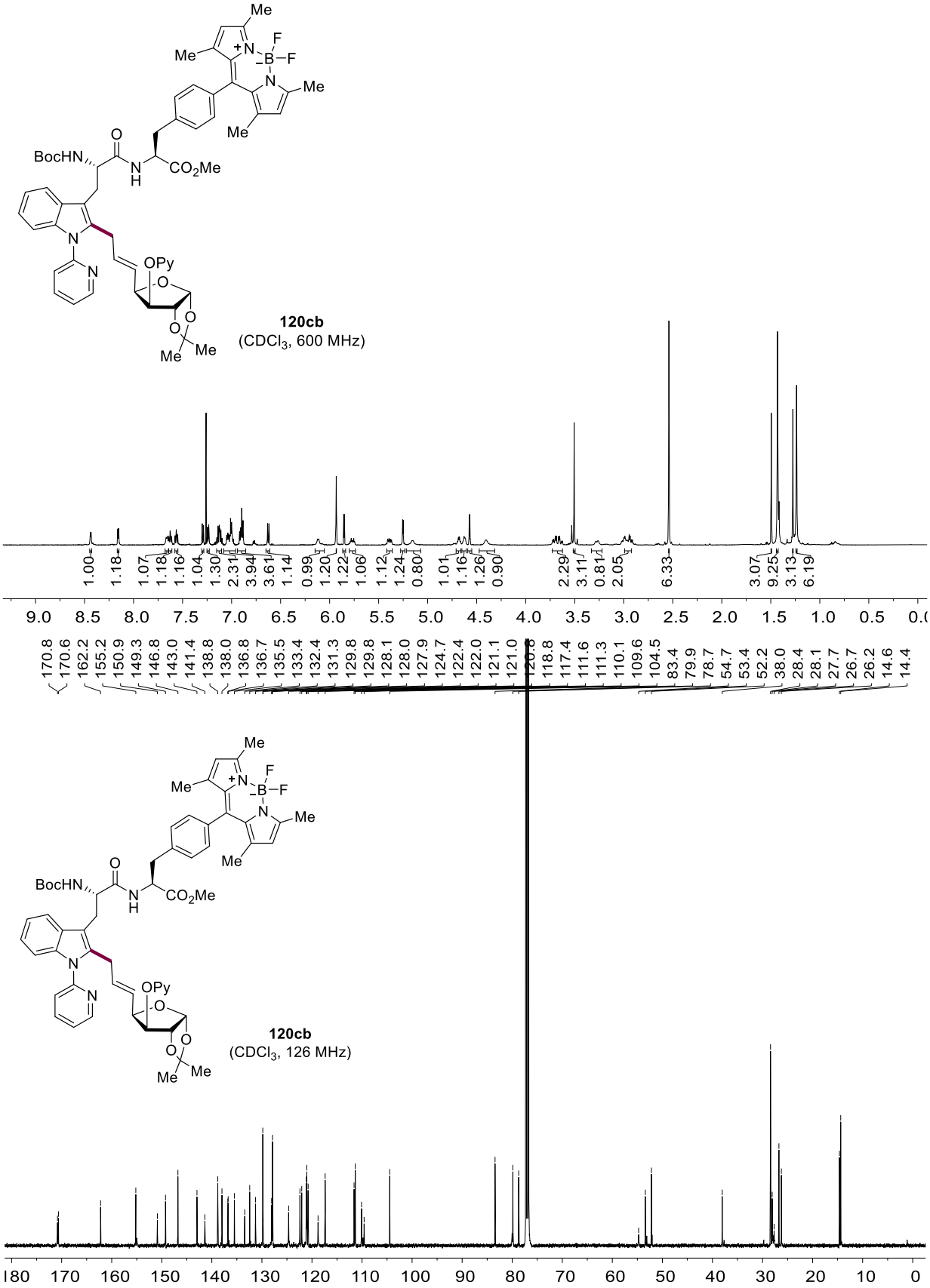


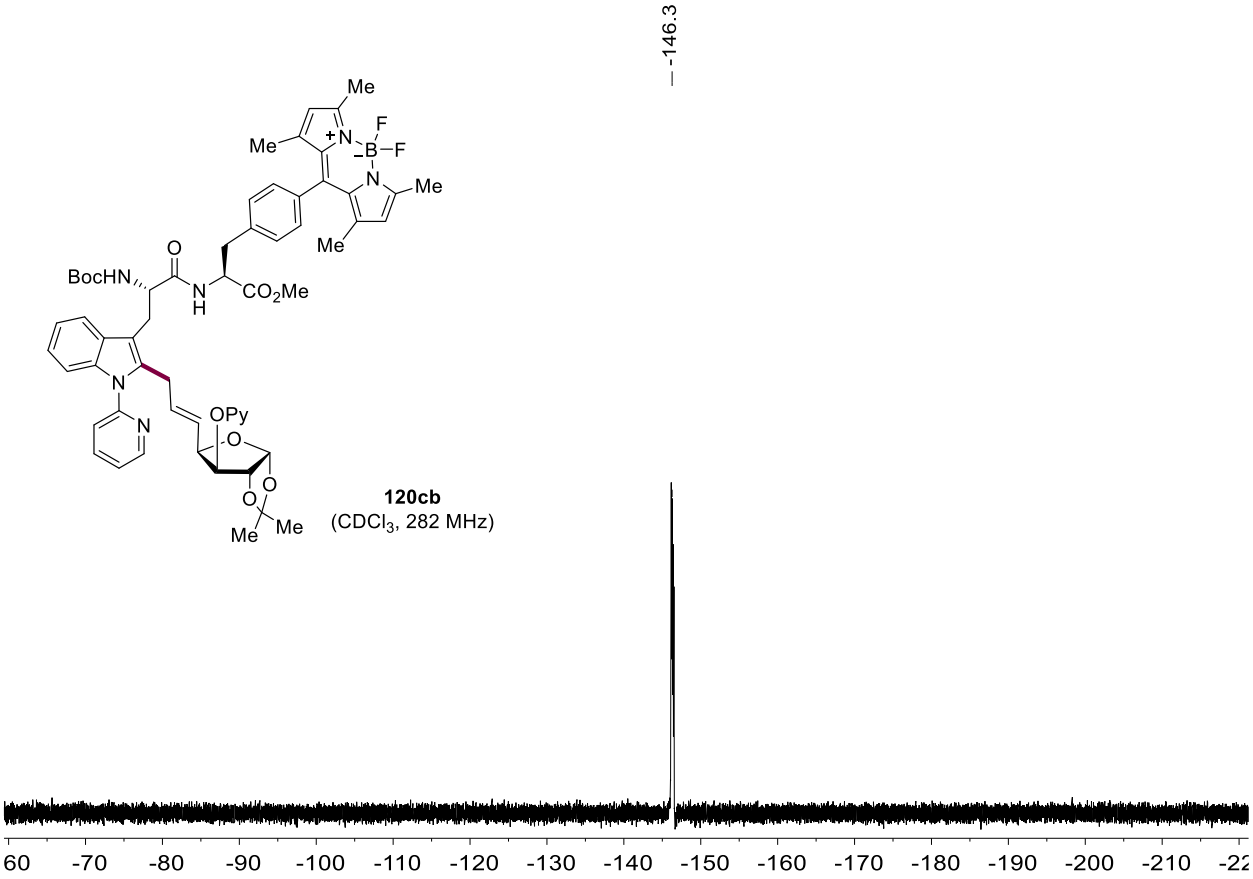


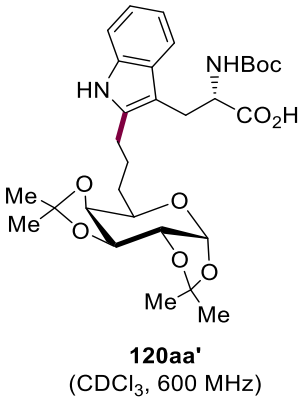


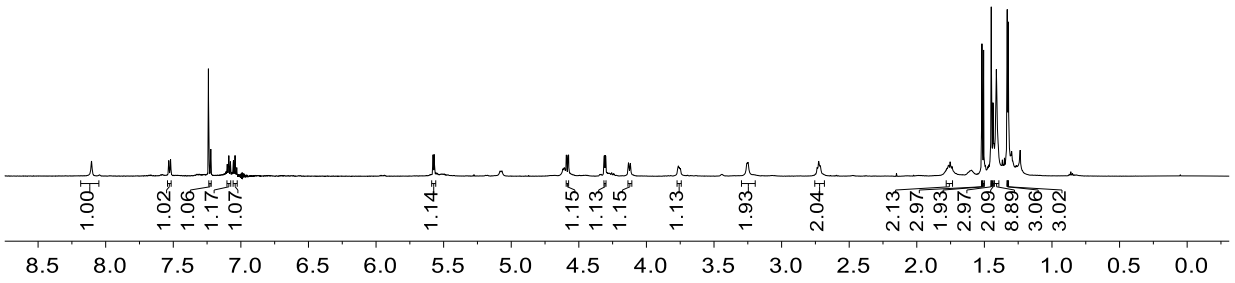
120ca
(DMSO-d_6, 126 MHz)

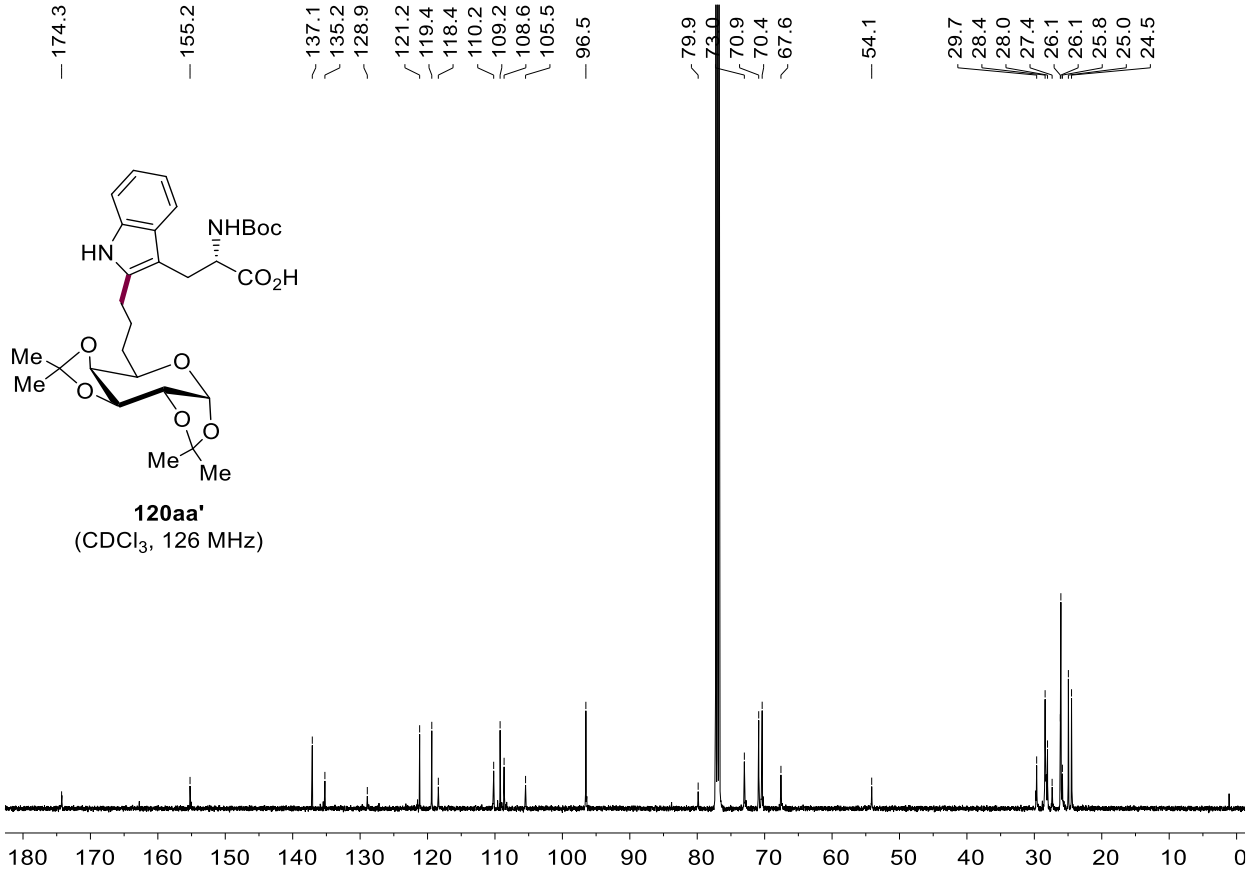



120cb
(CDCl3, 600 MHz)
120cb
(CDCl3, 126 MHz)

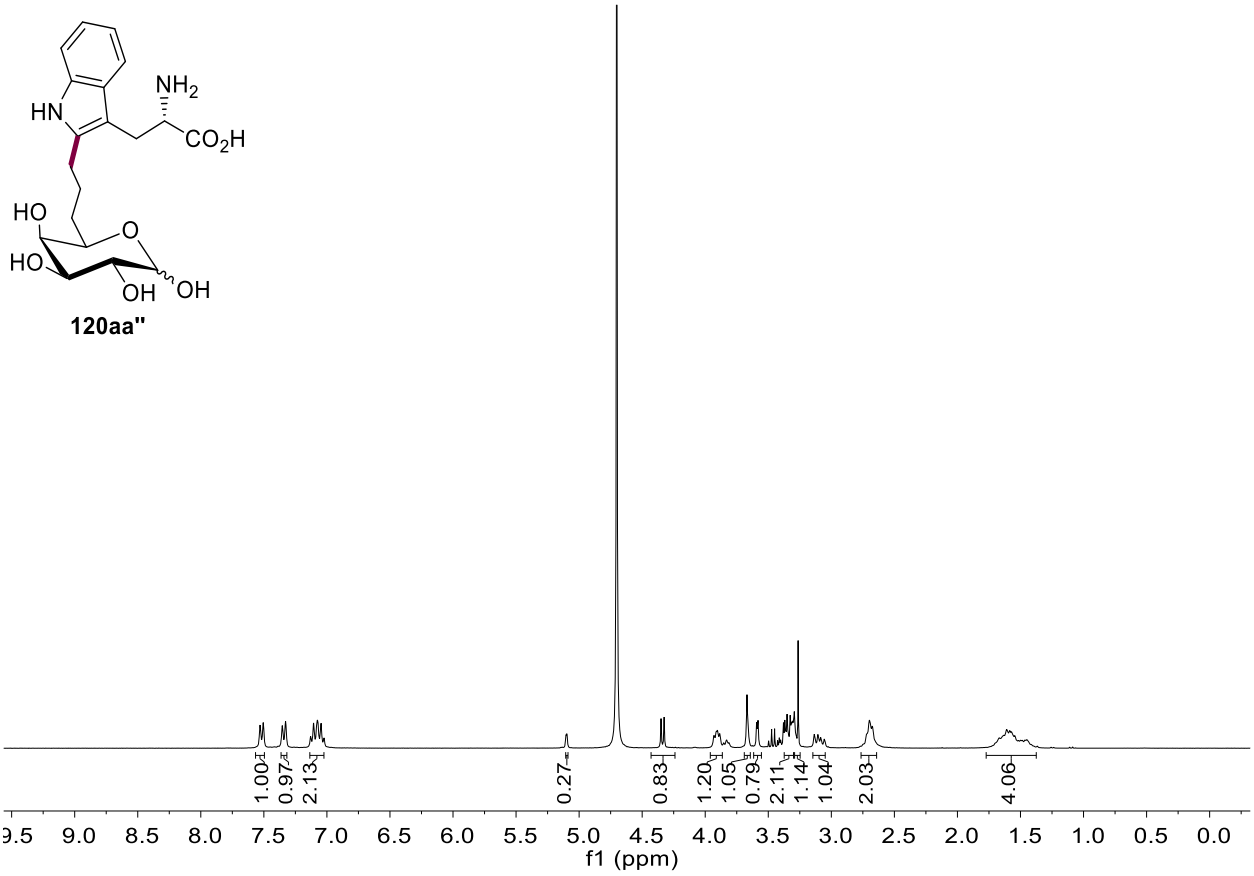

-146.3
120cb
(CDCl3, 282 MHz)
60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210


120aa'
(CDCl3, 600 MHz)

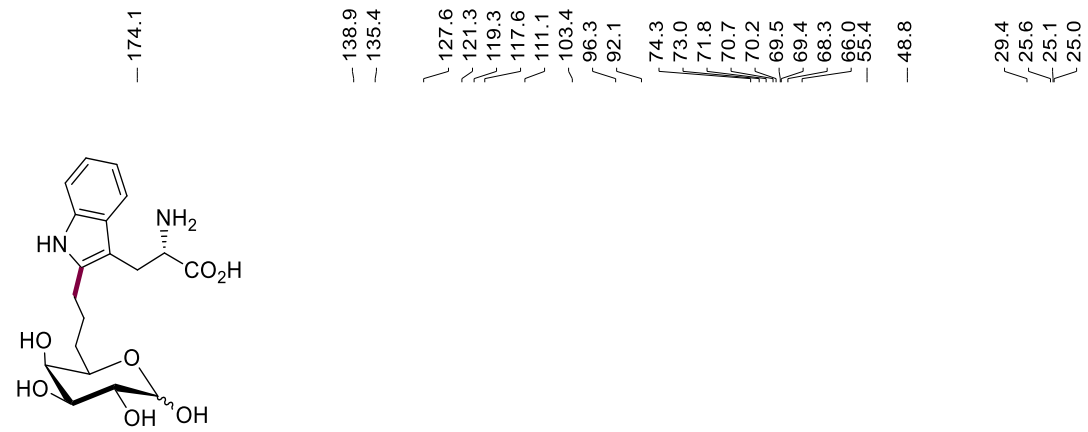

1.00 1.02 1.06 1.17 1.07 1.14 1.15 1.13 1.15 1.13 1.93 2.04 2.13 2.97 1.93 2.97 2.09 8.89 3.06 3.02
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0



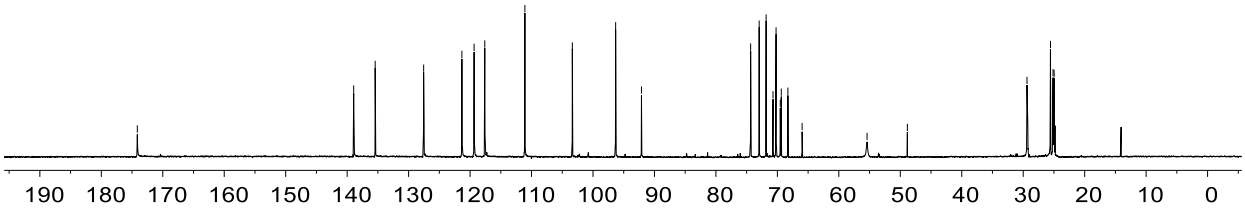
120aa'
($CDCl_3$, 126 MHz)



120aa''



120aa''
(D_2O, 101 MHz)



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24-28.09.2017	Poster of the Summer School on Organic Catalysis For Energy Conversion, Goettingen, Germany
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Publications

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7. L. Yang, **W. Wang**, Q. Sun, F. Xu, Y. Niu, C. Wang, L. Liang, P. Xu. "Development of novel proteasome inhibitors based on phthalazinone scaffold": *Bioorg. Med. Chem. Lett.*, **2016**, *26*, 2801-2805;

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10. **W. Wang**, L. Liang, F. Xu, W. Huang, Y. Niu, Q. Sun, P. Xu. "Ruthenium-Catalyzed Switchable N–H/C–H Alkenylation of 6 Phenyl(dihydro)pyridazinones with Alkynes": *Eur. J. Org. Chem.*, **2014**, 6863–6867;

11. L. Liang, **W. Wang**, F. Xu, Y. Niu, Q. Sun, P. Xu. "Relay Catalysis by a Multifunctional Cu Catalyst in a Tandem Dehydro-/Dehalogenation Sequence along with N-Arylation". *Org. Lett.*, **2013**, 15, 2770–2773;

12. L. Liang, **W. Wang**, J. Wu, F. Xu, Y. Niu, B. Xu, P. Xu. "Rational Design, Green Synthesis, and Initial Evaluation of a Series of Full Color Tunable Fluorescent Dyes Enabled by the Copper-Catalyzed N-Arylation of 6-Phenyl Pyridazinones and Their Application in Cell Imaging": *Chem. Eur. J.*, **2013**, 19, 13774-13782;

13. L. Liang, G. Yang, **W. Wang**, F. Xu, Y. Niu, Q. Sun, P. Xu. "A Copper-Catalyzed Aerobic Cascade Dehydrogenative-Dehalogenative Reaction": *Adv. Synth. Catal.*, **2013**, *355*, 1284-1290;