ENANTIOSELECTIVE SYNTHESIS AND STEREOSPECIFIC TRANSFORMATION OF ALKYLBORONATES

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Abstract: This dissertation will present three projects focusing on the enantioselective synthesis and stereospecific transformation of alkylboronates. The first project describes the development of a nickel-catalyzed enantioselective dicarbofunctionalization of alkenylboronates, which provides a modular route to secondary alkylboronic esters. Intramolecular reaction leads to enantioselective synthesis of exocyclic boronates. The second project depicts a new method for the synthesis of azetidines, pyrrolidines and piperidines *via* an intramolecular amination of alkylboronic esters. Regioselective amination of vicinal bis(boronates) allows the synthesis of saturated azacycles bearing boronic ester substitutions that can serve as useful synthetic handles. As the transformation is stereospecific, stereodefined cyclic amines can be synthesized from the enantioenriched boronic esters. The method is applied to the synthesis of an intermediate towards a Kras G12C inhibitor. The third project describes the development of a new chiral auxiliary on boron that can be easily synthesized from inexpensive starting materials. The auxiliary is applied to a diastereoselective radical ring-opening/closing [3+2] cycloaddition of cyclopropylanilines with alkenylboron species.

Dedicated to

My parents, Jiahong Xu and Fang Deng.

For their love and support.

ACKNOWLEDGMENTS

I would like to thank my advisor, Professor James. P. Morken, for his guidance in the past five years. Jim's vast knowledge of chemistry continues to amaze me till today, and inspires me to always keep learning. I am grateful to him for his commitment to educating his students and for cultivating a motivating environment in the lab, which is what allowed me to grow into the best scientist I could be.

Although some may agree that graduate school is a lonely endeavor, none of the work in this dissertation would be possible without the help of my fellow Morken group members. First, I would like to thank Dr. Matteo Chierchia for mentoring me when I joined the lab, both in chemistry and in American pop culture. Next, I would like to thank all the group members that have contributed to the work in this thesis – Dr. Matteo Chierchia, Dr. Gabriel Lovinger, Mingkai Zhang, Dr. Bryan Ingoglia and Dr. Alex Vendola. I would also like to thank Dr. Christophe Allais, Dr. Anne-Marie Dechert-Schmitt and Dr. Robert Singer for their intellectual contribution during the Pfizer collaboration. I also want to thank Dr. Chenlong Zhang and Mingkai Zhang for taking time to help proofread my dissertation. I also want to thank Hao Liang for conducting the DFT computational studies in this dissertation. I would also like to thank Dr. Yan Meng, Dr. Chenlong Zhang, Weipeng Hu, Ziyin Kong, Mingkai Zhang, Chenpeng Gao, Hao Liang and other group members for filling my time in (and out of) the lab with joy and company.

Finally, I would like to thank my parents for their unconditional love and support throughout the years.

LIST OF ABBREVIATIONS

Ac: acetyl

acac: acetylacetonyl

ACN: acetylnitrile

Ad: adamantyl

aq.: aqueous

Ar: aryl

atm: atmosphere

$B_2(cat)_2$: bis(catecholato)diboron

$B_2(pin)_2$: bis(pinacolato)diboron

BBN: 9-borabicyclo[3.3.1]nonane

BHT: 2,6-di-*tert*-butyl-4-methylphenol

BINAP: 2,2'-bis(diohenylphosohino)-1,1'-binaphthyl

Bn: benzyl

Boc: *tert*-butyloxycarbonyl

BOX: bisoxazoline

Bz: benzoyl

cat.: catalyst or catalytic amount

cat: catechol

Cb: *N*, *N*-diisopropylcarbamoyl

Cbz: benzyloxycarbonyl

cod: 1,5-cyclooctadiene

conv.: conversion

Cp: cyclopentadienyl

Cy: cyclohexyl

d: day(s)

dan: 1,8-diaminoaphthalene

DART: direct analysis in real time

dba: dibenzylideneacetone

DCC: *N, N'*-dicyclohexylcarbodiimide

DCE: dichloroethane

DCM: dichloromethane

DEAD: Diethyl azodicarboxylate

DFT: density functional theory

DG: directing group

DIAD: diisopropyl azodicarboxylate

DMA: dimethylacetamide

DMAP: 4-dimethylaminopyridine

DME: dimethoxyethane

DMF: *N, N*-dimethylformamide

DMP: Dess-Martin periodinane

dmpd: 2,4-dimethylpenane-2,4-diol

DMPU: 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone

DMSO: dimethyl sulfoxide

DPED: 1,2-diphenylethylene-1,2-diamine

dppbz: 1,2-bis(diphenylphosphino)benzene

dppf: 1,1'-bis(diphenylphosphino)ferrocene

dppp: 1,1'-bis(diphenylphosphino)propane

dr: diastereomeric ratio

dtbpy: 4,4'-di-*tert*-butyl-2,2'-dipyridyl

EAS: enantioselective allylic substitution

EDC: 1-ethyl-3-carbodiimide

EDTA: ethylenediaminetetraacetic acid

ee: enantiomeric excess

ent: enantiomeric

EPR: electron paramagnetic resonance

eq: equation(s)

equiv: equivalent

er: enantiomeric ratio

Et: ethyl

EtOAc: ethyl acetate

glyme: dimethoxyethane

h: hour(s)

H-bond: hydrogen bond

HG2: Hoveyda-Grubbs II Catalyst

HMPA: hexamethylphosphoramide

HOBt: hydroxybenzotriazole

HRMS: high resolution mass spectrometry

Hz: hertz

^{i}Bu: isobutyl

IPA: isopropanol

Ipc: isopinocamphenyl

IPO: iminopyridine-oxazoline

^{i}Pr: isopropyl

IR: infrared spectroscopy

LAH: lithium aluminum hydride

LDA: lithium diisopropylamine

LiTMP: lithium 2,2,6,6-tetramethylpiperidide

M: molar

mac: methylated acenaphthoquinone

mCPBA: meta-chloroperoxybenzoic acid

Me: methyl

MeCN: acetylnitrile

mes: mesityl

min: minute(s)

MOM: methoxymethyl

MOP: 2-(dipenylphosphino)-2'-methoxy-1,1'-binaphthyl

MS: molecular sieves

MTBE: methyl *tert*-butyl ether

MVK: methyl vinyl ketone

N/A: not available

NBS: *N*-bromosuccinimide

^{n}Bu: *n*-butyl

NCS: *N*-chlorosuccinimide

neo: neopentylglycol

NHC: *N*-heterocyclic carbene

*n*Hex: *n*-hexyl

NIS: *N*-iodosuccinimide

NMO: *N*-methylmorpholine N-oxide

NMR: nuclear magnetic resonance

PCC: pyridinium chlorochromate

PDI: pyridine(diimine)

Ph: phenyl

Piv: pivaloyl

PMB: *para*-methoxybenzyl

PMDTA: *N,N,N′,N″,N‴*-pentamethyldiethylenetriammine

PMHS: polymethylhydrosiloxane

PMP: *para*-methoxyphenyl

PPFA: 2-(1-(dimethylamino)ethyl)-1-(diphenylphophino)ferrocene

ppm: parts per million

PyBOX: pyridine bis(oxazoline)

quant: quantatitive

Quinap: 1-(2-diphenylphosphino-1-naphthyl)isoquinoline

rac: racemic

rr: regioisomeric ratio

rt: room temperature

^{s}Bu: *sec*-butyl

SFC: supercritical fluid chromatography

TADDOL: 2,2-dimethyl-α, α, α', α'-tetraaryl-1,3-dioxolane-4,5-dimethanol

TBAB: tetrabutylamonium bromide

TBAF: tetrabutylamonium fluoride

TBDPS: *tert*-butyldiphenylsilyl

TBHP: *tert*-butyl hydroperoxide

TBS: *tert*-butyldimethylsilyl

^{t}Bu: *tert*-butyl

TCCA: trichloroisocyanuric acid

TEA: triethylamine

temp: temperature

TES: triethylsilyl

Tf: trifluoromethanesulfonyl

TFA: trifluoroacetic acid

THF: tetrahydrofuran

THP: tetrahydropyran

TIB: 2,4,6-triisopropylbenzoyl

TIPS: triisopropylsilyl

TLC: thin layer chromatography

TMDSO: 1,1,3,3-tetramethyldisiloxane

TMEDA: *N, N, N', N'*-tetramethylethylenediamine

TMS: trimethylsilyl

TRIP: 3,3'-bis(2,4,6-triisopropylphenyl-2,2'-binaphtholate

Ts: p-toluenesulfonyl

UV: ultraviolet

xylyl: dimethylphenyl

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Chapter 1

Enantioselective Radical Addition/Cross-Coupling of Organozinc Reagents, Alkyl Iodides, and Alkenylboron Reagents

1.1. Introduction

Organoboron compounds are widely used in modern organic synthesis as intermediates due to their stability, non-toxicity and versatility in transformations. In particular, stereodefined secondary alkyl organoboronates can undergo a variety of stereospecific transformations to construct carbon-carbon or carbon-heteroatom bonds (where the heteroatom can be, for example, nitrogen, oxygen or a halogen).[1] Combined with these transformations, the enantioselective construction of secondary organoboronates arises as a modular strategy for asymmetric synthesis.

Apart from their role as useful synthetic handles, sp^2 hybridized alkylboronic esters also stabilize adjacent carbon-centered radicals.[2] This feature renders vinyl boronates good radical acceptors that will regioselectively form stabilized α-boryl radicals when treated with an alkyl radical species. Radical addition followed by capturing the resulting radical with a transition metal that can undergo reductive elimination enables the dicarbofunctionalization of an alkene. This chapter will describe the development of the first enantioselective dicarbofunctionalization of alkenyl boronates via a radical addition/cross-coupling cascade. This transformation can be carried out both inter- and intramolecularly, leading to the modular buildup of stereodefined secondary boronates from simple starting materials.

(1) Sandford, C.; Aggarwal, V. K. *Chem. Commun.* **2017**, *53*, 5481–5494.
(2) Walton, J. C.; McCarroll, A. J.; Chen, Q.; Carboni, B.; Nziengui, R. *J. Am. Chem. Soc.* **2000**, *122*, 5455–5463.

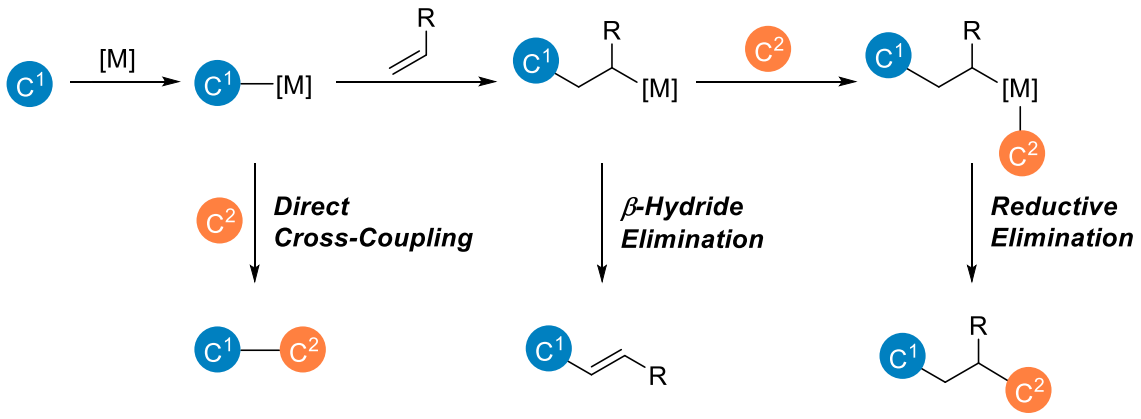
1.2 Background

1.2.1. Transition Metal-Catalyzed 1,2-Dicarbofunctionalization of Alkenes

Recently, dicarbofunctionalization of alkenes that installs two carbon-based moieties in one single operation has gained considerable attention.[3] As depicted in Scheme 1.1, these reactions typically start with the catalytic activation of electrophile C1, by a transition metal catalyst, followed by the addition of the carbon-centered fragment C1 and the transition metal across an alkene. The C(sp^3)-[M] intermediate could then be intercepted by a second carbon moiety C2, and subsequent reductive elimination will yield the dicarbofunctionalization product.

Despite being an efficient and modular synthetic strategy by design, the cascade reaction mode suffers from several potential side reactions along the pathway. The three-component reaction needs to outcompete direct cross-coupling between the two carbon-centered entities. In addition, the C(sp^3)-[M] intermediate could undergo β-hydride elimination.

Scheme 1.1. Transition Metal-Catalyzed Dicarbofuntionalization: Demonstration of Reaction Pathway and Possible Side Reactions

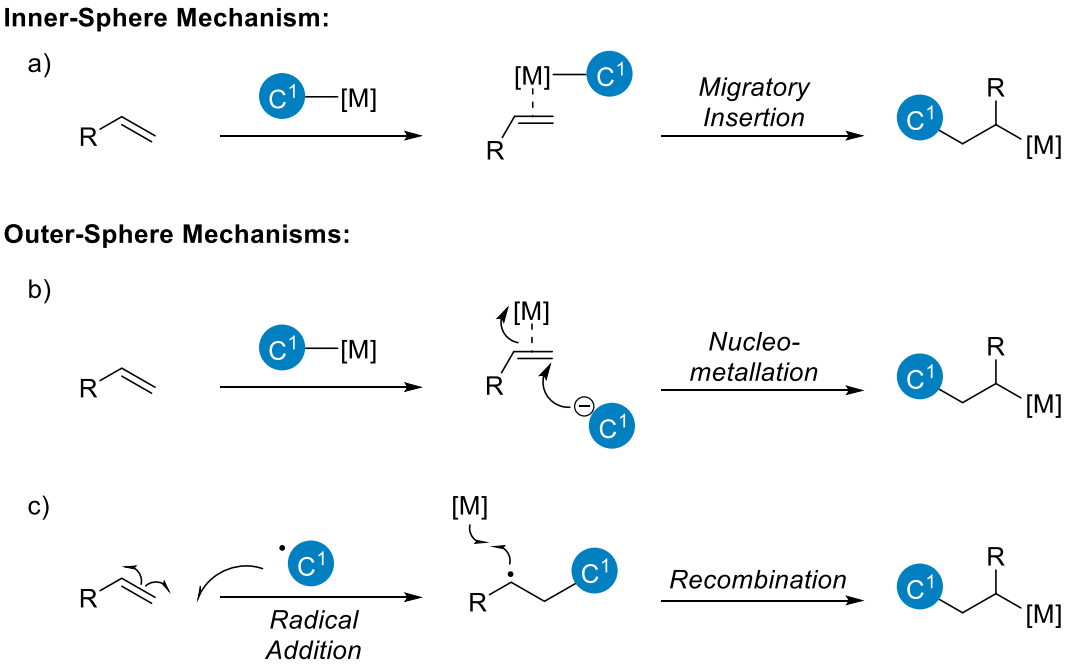


(3) For a review: Dhungana, R. K.; Shekhar, K. C.; Basnet, P.; Giri, R. *Chem. Rec.* **2018**, *18*, 1314–1340.

In the past decades, these challenges have been overcome by judicious choice of catalytic systems. In particular, first-row late transition metal complexes (Fe, Co, Ni and Cu) received the most attention because of their low tendency to undergo *β*-hydride elimination compared to organometallic complexes involving Pd.[4]

The dicarbofunctionalization of olefins can proceed through several different pathways (Scheme 1.2). Carbometallation can occur through inner-sphere migratory insertion (Scheme 1.2a), with the carbon-centered moiety and transition metal adding *syn* to the alkene. Alternatively, an outer-sphere nucleometallation can operate *via trans*-1,2-addition (Scheme 1.2b).

Scheme 1.2. Different Mechanisms for Dicarbofunctionalization of Olefins



Apart from two-electron pathways, an outer-sphere carbometallation can go through addition of an alkyl radical to the alkene, followed by recombination of the intermediate

(4) Menezes Da Silva, V. H.; Braga, A. A. C.; Cundari, T. R. *Organometallics* **2016**, *35*, 3170–3181.

radical with a transition metal that has the capacity to undergo single electron oxidation/reduction (Scheme 1.2c). This pathway is referred to as radical addition/cross-coupling cascade.

1.2.2. Nickel-Catalyzed 1,2-Dicarbofunctionalization of Alkenes via Radical Addition/Cross-Coupling Cascade

Because of their low tendency to undergo β-hydride elimination and versatile reactivity to access either two-electron[5] and single-electron pathways, nickel complexes are widely employed in the dicarbofunctionalization of alkenes. In particular, carbometallations going through radical addition/cross-coupling mechanism can occur with distinct regioselectivity. Moreover, the presence of radical intermediates opens unique pathways for enantioselective reactions.

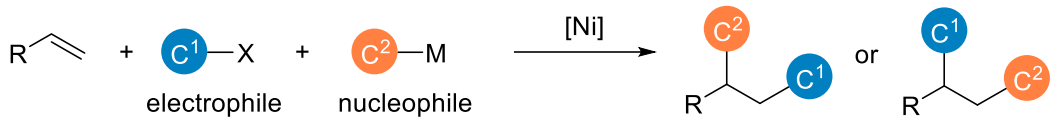
Similar to cross-coupling, redox-neutral dicarbofunctionalization with a nucleophile and an electrophile (Scheme 1.3a) can provide good regioselectivity, owing to the inherent difference in reactivity of the two substrates. Alternatively, reductive dicarbofunctionalization employing two electrophiles has also been developed (Scheme 1.3b). The two electrophiles need to be distinct in terms of steric and/or electronic properties to allow control of regioselectivity. Although reductive dicarbofunctionalization requires stoichiometric reductant to regenerate the catalyst, it avoids the use of air-sensitive

(5) Selected examples of Ni-catalyzed 1,2-dicarbofunctionalizations *via* two-electron pathways: (a) Solé, D.; Cancho, Y.; Llebaria, A.; Moretó, J. M.; Delgado, A. *J. Org. Chem.* **1996**, *61*, 5895–5904. (b) Walker, J. A.; Vickerman, K. L.; Humke, J. N.; Stanley, L. M. *J. Am. Chem. Soc.* **2017**, *139*, 10228–10231. (c) Shrestha, B.; Basnet, P.; Dhungana, R. K.; Kc, S.; Thapa, S.; Sears, J. M.; Giri, R. *J. Am. Chem. Soc.* **2017**, *139*, 10653–10656. (d) Derosa, J.; Tran, V. T.; Boulous, M. N.; Chen, J. S.; Engle, K. M. *J. Am. Chem. Soc.* **2017**, *139*, 10657–10660. (e) Li, W.; Boon, J. K.; Zhao, Y. *Chem. Sci.* **2018**, *9*, 600–607. (f) Zheng, Y. L.; Newman, S. G. *Angew. Chem. Int. Ed.* **2019**, *58*, 18159–18164.

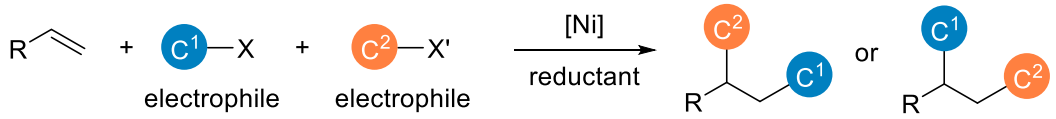
organometallic reagents. This section will describe the development of both modes of nickel-catalyzed dicarbofunctionalization of alkenes *via* radical addition/cross-coupling cascades.

Scheme 1.3. Different Reaction Modes of Nickel-Catalyzed Dicarbofunctionalization

a) **Redox-neutral:**



b) **Reductive:**



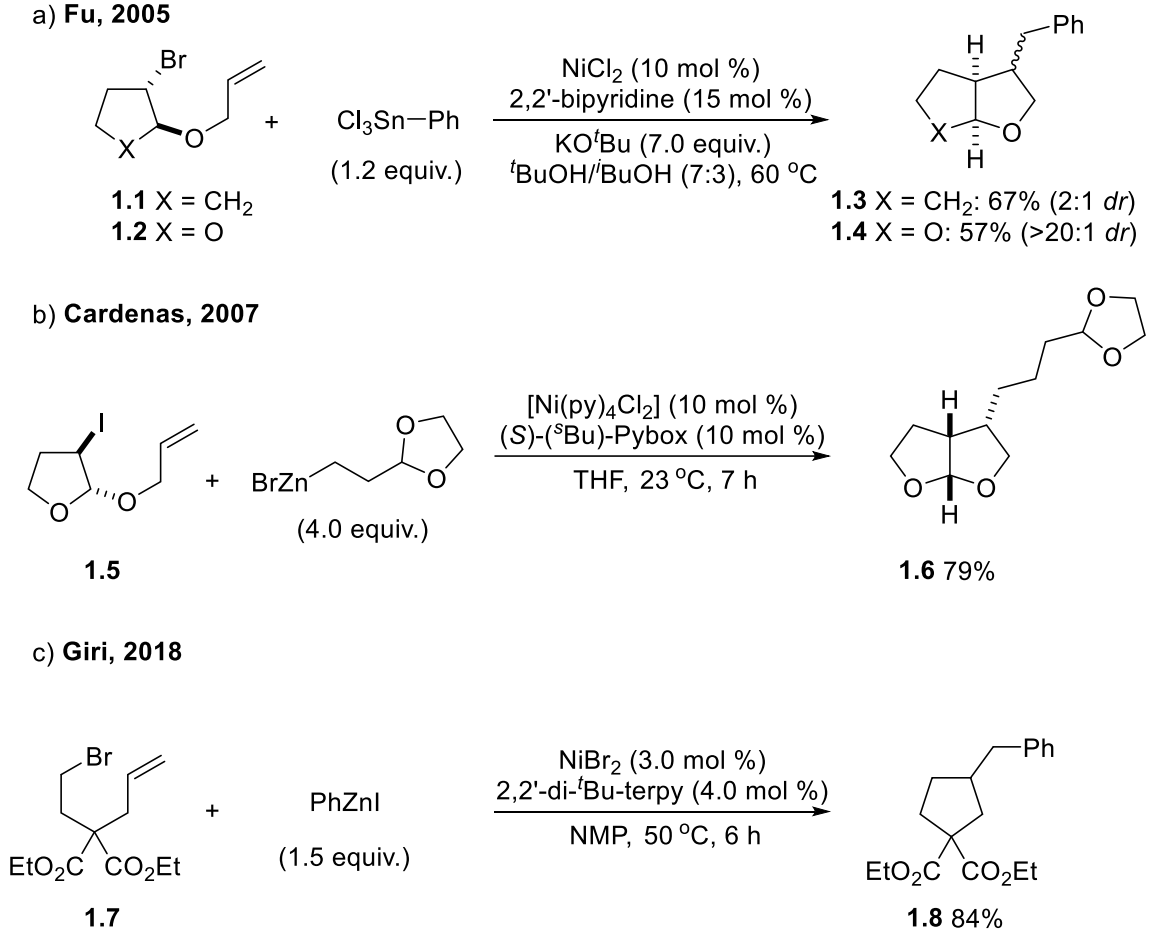
X/X' = Cl, Br, I, OTf M = Mg, Zn, Si, B

1.2.2.1. Redox-Neutral 1,2-Dicarbofunctionalization

The earliest Ni-catalyzed dicarbofunctionalizations via radical pathways involved a series of intramolecular reactions occurring through radical cyclization followed by recombination with a nickel catalyst. In 2005, Fu reported a case of intramolecular radical cyclization/cross-coupling reaction (Scheme 1.4a) as a radical probe experiment in a Stille cross-coupling of secondary alkyl halide with organotin reagents.[6] Later, Cárdenas utilized this reactivity to develop an intramolecular dicarbofunctionalization by alkyl iodides and

(6) Powell, D. A.; Maki, T.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 510–511.

Scheme 1.4. Selected Examples of Ni-catalyzed Intramolecular Dicarbofunctionalization

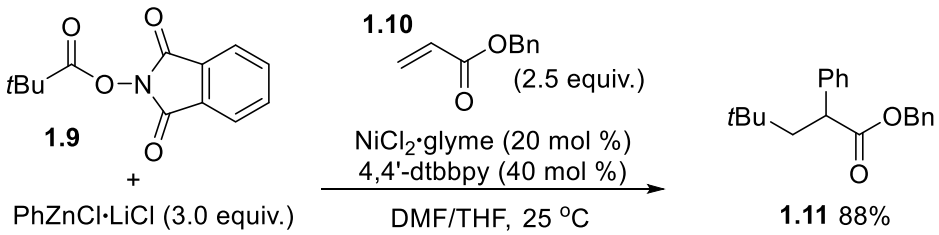


alkylzinc reagents (Scheme 1.4b).[7] Computational studies suggested that the reduction of the primary iodide to the carbon-centered radical by a Ni(I)-terpyridine complex had a low activation free energy of 5.3 kcal/mol. Radical clock experiments revealed that the direct cross-coupling step was a fast process that could even compete with cyclization of alkyl radicals. Recently, Giri reported a related work using aryl zinc reagents as nucleophile (Scheme 1.4c).[8]

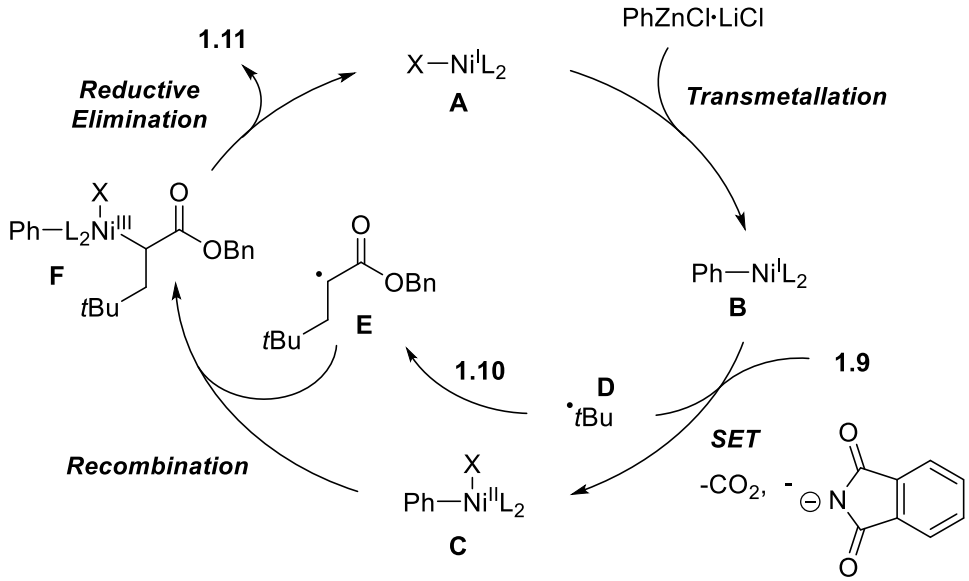
(7) Phapale, V. B.; Buñuel, E.; García-Iglesias, M.; Cárdenas, D. J. *Angew. Chem. Int. Ed.* **2007**, *46*, 8790–8795.
(8) KC, S.; Basnet, P.; Thapa, S.; Shrestha, B.; Giri, R. *J. Org. Chem.* **2018**, *83*, 2920–2936.

The first intermolecular dicarbofunctionalization was developed by the Baran group in 2016.[9] Tertiary redox-active esters were employed as radical precursors, which cross-coupled with α,β-unsaturated esters and phenyl zinc reagents (Scheme 1.5). The reaction started with the transmetallation of Ni(I) species **A** with phenyl zinc reagent to form **B**, which could reduce redox active ester **1.9** into tertiary radical **D** *via* single electron transfer (SET). Then, the radical **D** could add to the unsaturated ester **1.10** to form stabilized α-carbonyl radical **E**, which could recombine with Ni(II) species **C** generated during the

Scheme 1.5. Baran's Ni-Catalyzed Three-Component Cross-Coupling of Redox-Active Esters



Proposed Catalytic Cycle:

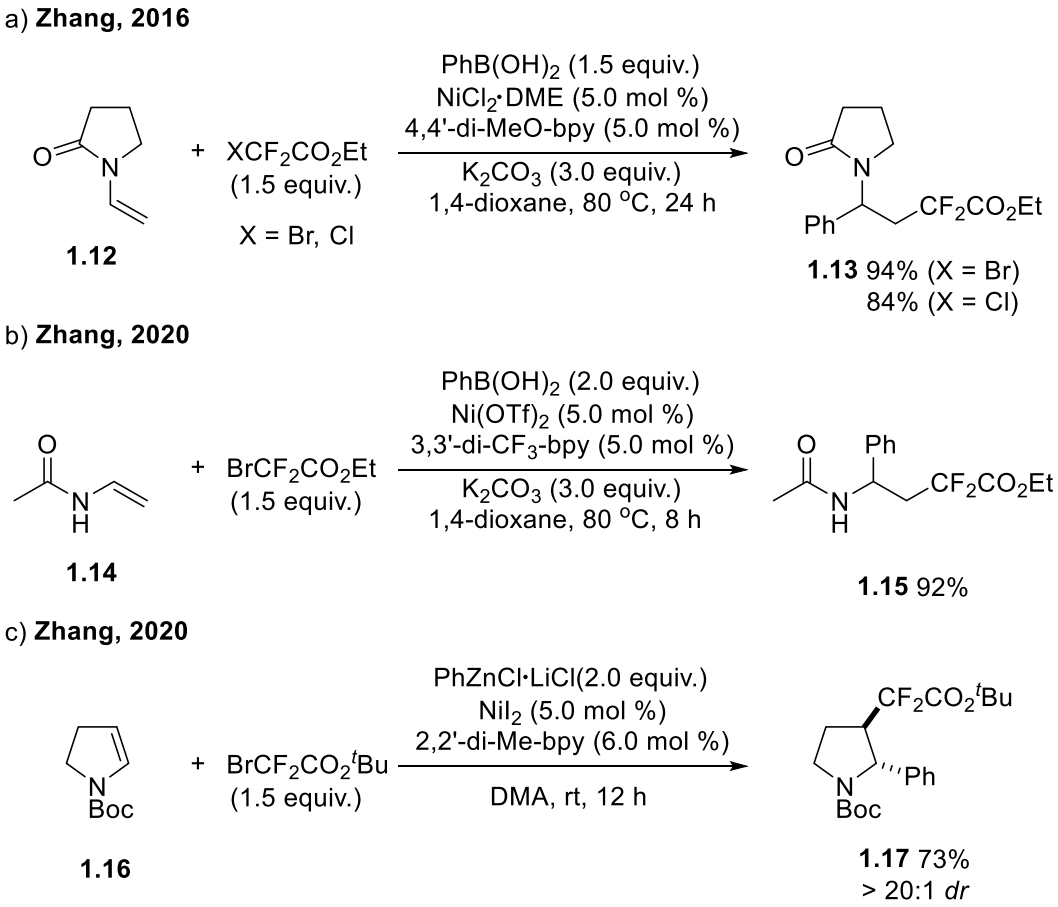


(9) Qin, T.; Cornella, J.; Li, C.; Malins, L. R.; Edwards, J. T.; Kawamura, S.; Maxwell, B. D.; Eastgate, M. D.; Baran, P. S. *Science.* **2016**, *352*, 801–805.

course of SET to form Ni(III) complex **F**. The dicarbofunctionalization product **1.11** will form after reductive elimination.

In the same year, Zhang group reported a dicarbofunctionalization of an enamide (**1.12**, Scheme 1.6a).[10] Electron-poor radicals, generated from difluoroalkyl halide electrophiles, would undergo radical addition with the electron-rich enamide double bonds to form *α*-nitrogen radicals. The *α*-nitrogen radicals could then participate in nickel-catalyzed coupling reactions with aryl boronic acids to produce **1.13**. The amide oxygen lone-pairs were proposed to bind to the nickel after recombination .

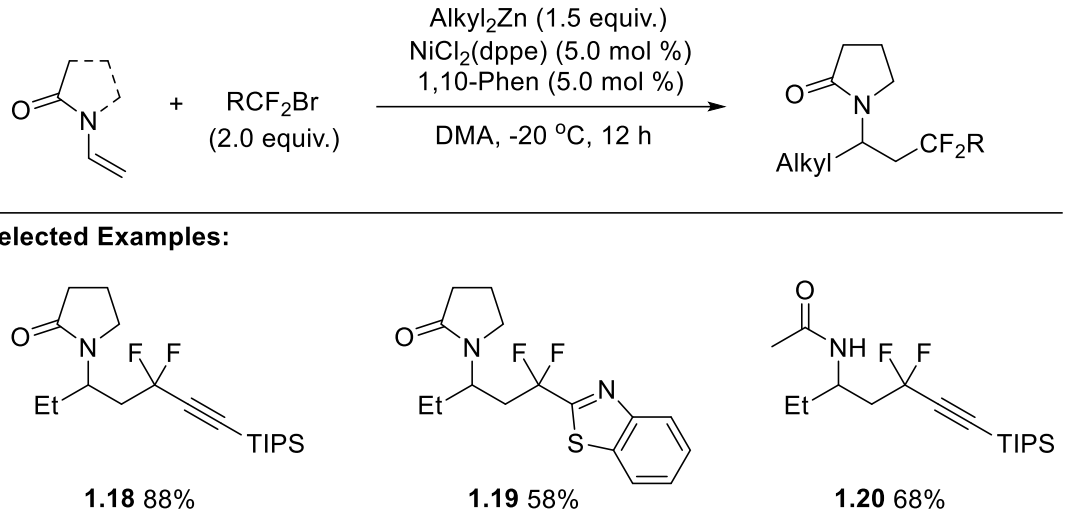
Scheme 1.6. Zhang's Difluoroalkylaltion-Arylation of Enamides



(10) Gu, J. W.; Min, Q. Q.; Yu, L. C.; Zhang, X. *Angew. Chem. Int. Ed.* **2016**, *55*, 12270–12274.

The methodology was later extended to acyclic amides (**1.14**, Scheme 1.6b) with cleavable acetal groups, making it more synthetically useful. Difluoroalkylaltion-arylation of endocyclic enamides (**1.16**, Scheme 1.6c) was enabled by using arylzinc reagents as nucleophile, leading to a series of useful *N*-heterocycles in excellent *trans* diastereoselectivity.[11] In another work by Zhang, dialkylzinc reagents were employed as nucleophiles to conduct difluoroalkylation-alkylation of enamides (Scheme 1.7). [12] Propargyl or α-aryl difluorobromides were activated by nickel catalysts to form radicals and participated in the radical cascade in moderate to high yields.

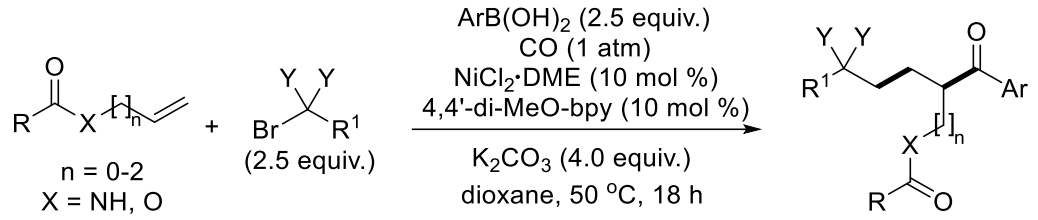
Scheme 1.7. Zhang's Difluoroalkylaltion-Alkylation of Enamides



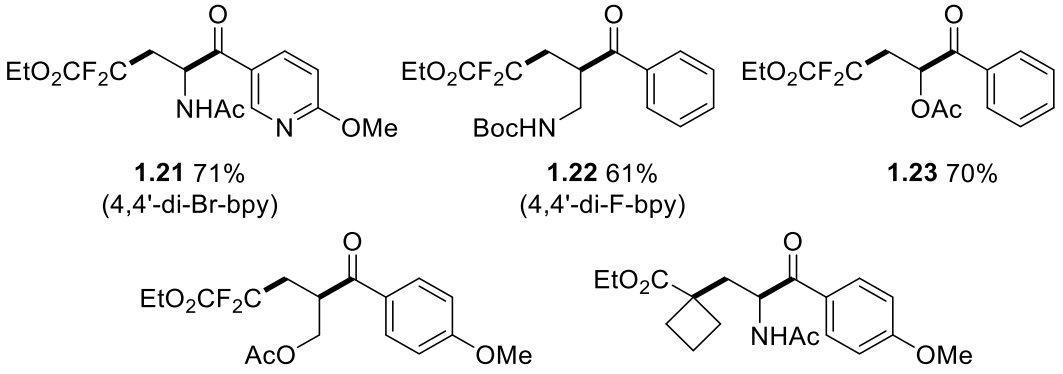
Based on the three-component cross-coupling reactions, Zhang group developed a four-component carbocarbonylation of alkenes under 1 atm of CO, allowing for the rapid construction of a wide array of complex fluorinated carbonyl compounds (Scheme 1.8).[13] The scope of alkene was expanded to include enol esters (**1.23**), allylic esters (**1.24**) /amides

(11) Yang, Z. F.; Xu, C.; Zheng, X.; Zhang, X. *Chem. Commun.* **2020**, *56*, 2642–2645.
(12) Xu, C.; Yang, Z. F.; An, L.; Zhang, X. *ACS Catal.* **2019**, *9*, 8224–8229.
(13) Zhou, M.; Zhao, H. Y.; Zhang, S.; Zhang, Y.; Zhang, X. *J. Am. Chem. Soc.* **2020**, *142*, 18191–18199.

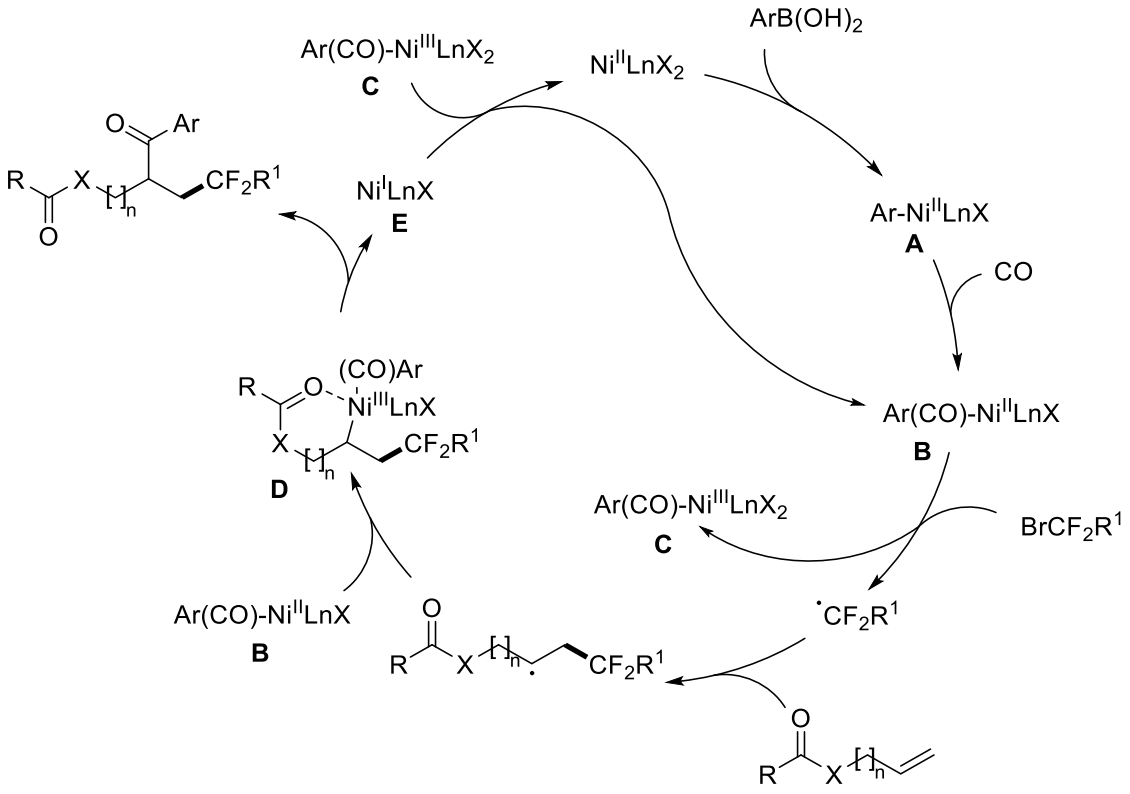
Scheme 1.8. Zhang's Four-Component Carbocarbonylation of Alkenes under 1 atm of CO



Selected Examples:



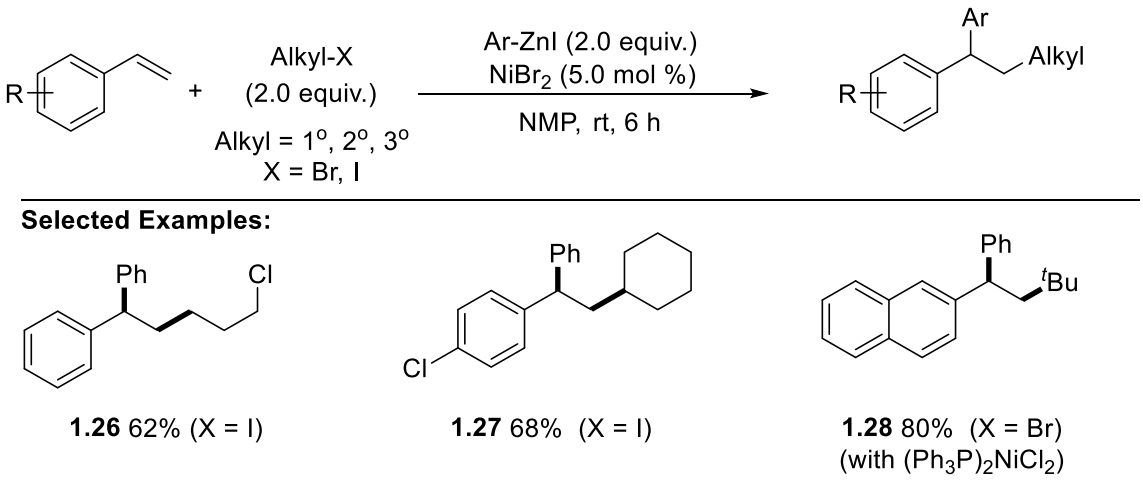
Proposed Catalytic Cycle:



(**1.22**), and homoallylic amides. Non-fluorinated tertiary alkyl electrophiles (**1.25**) could be incorporated as well. Detailed mechanistic studies suggested that carbonylated Ni(II) species **B** was responsible for the SET reduction of electrophile.

In 2018, Giri reported the first dicarbofunctionalization of unactivated olefins (Scheme 1.9).[14] Alkyl bromides or iodides and arylzinc reagents were coupled with aryl alkenes under the catalysis of nickel. A wide range of primary (**1.26**), secondary (**1.27**) or tertiary (**1.28**) alkyl electrophiles could be incorporated. Direct competition experiments revealed that the reaction rates of different alkyl halides followed the relationship of $3^{\circ} > 2^{\circ} > 1^{\circ}$ and R-I >R-Br >R-Cl. The authors proposed that halogen atom abstraction by the Ni catalyst was the rate-limiting step.

Scheme 1.9. Giri's Alkylarylation of Vinylarenes

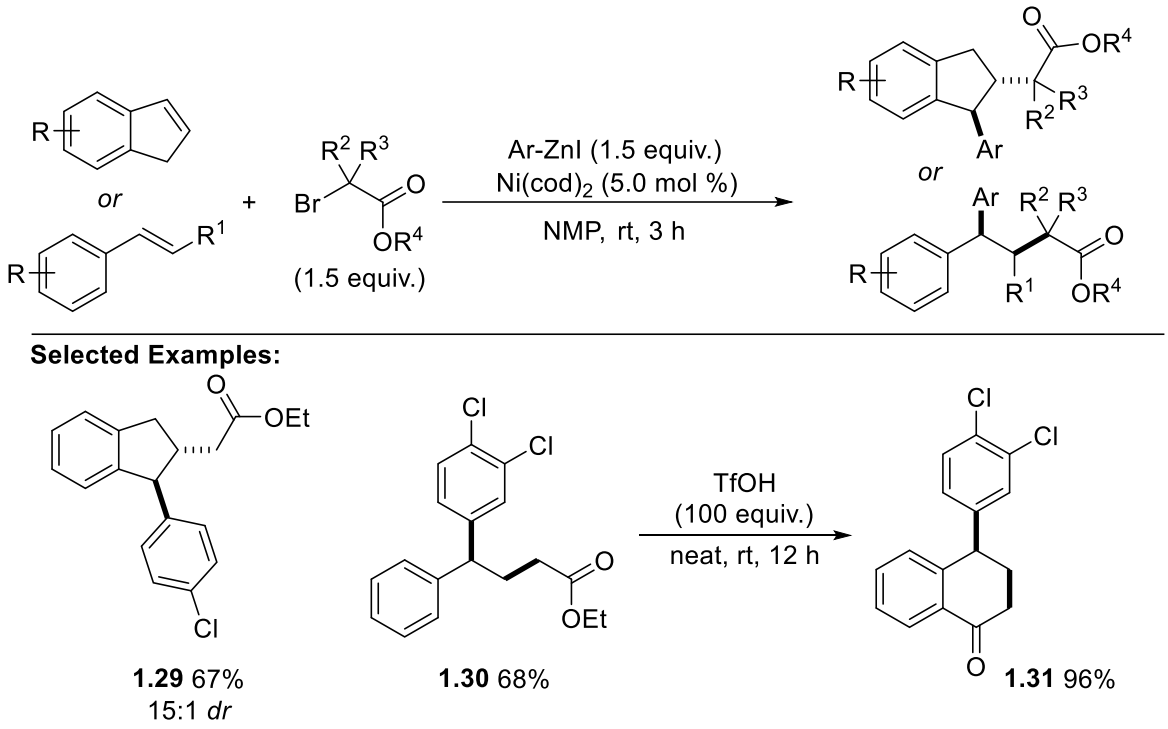


Incorporating α-haloesters as electrophiles, α-carbonylalkylarylation of aryl alkenes was realized by Giri and coworkers in a subsequent publication (Scheme 1.10).[15] When indenes were employed as the reactant, the *trans* dicarbofunctionalization products (**1.29**)

(14) KC, S.; Dhungana, R. K.; Shrestha, B.; Thapa, S.; Khanal, N.; Basnet, P.; Lebrun, R. W.; Giri, R. *J. Am. Chem. Soc.* **2018**, *140*, 9801–9805.
(15) KC, S.; Dhungana, R. K.; Khanal, N.; Giri, R. *Angew. Chem. Int. Ed.* **2020**, *59*, 8047–8051.

were formed in good to high *dr*. The cross-coupling product (**1.30**) from acyclic arylarenes was set up to undergo intramolecular Friedel-Crafts acylation, forming a cyclic structure (**1.31**).

Scheme 1.10. Giri's α-Carbonylalkylarylation of Vinylarenes

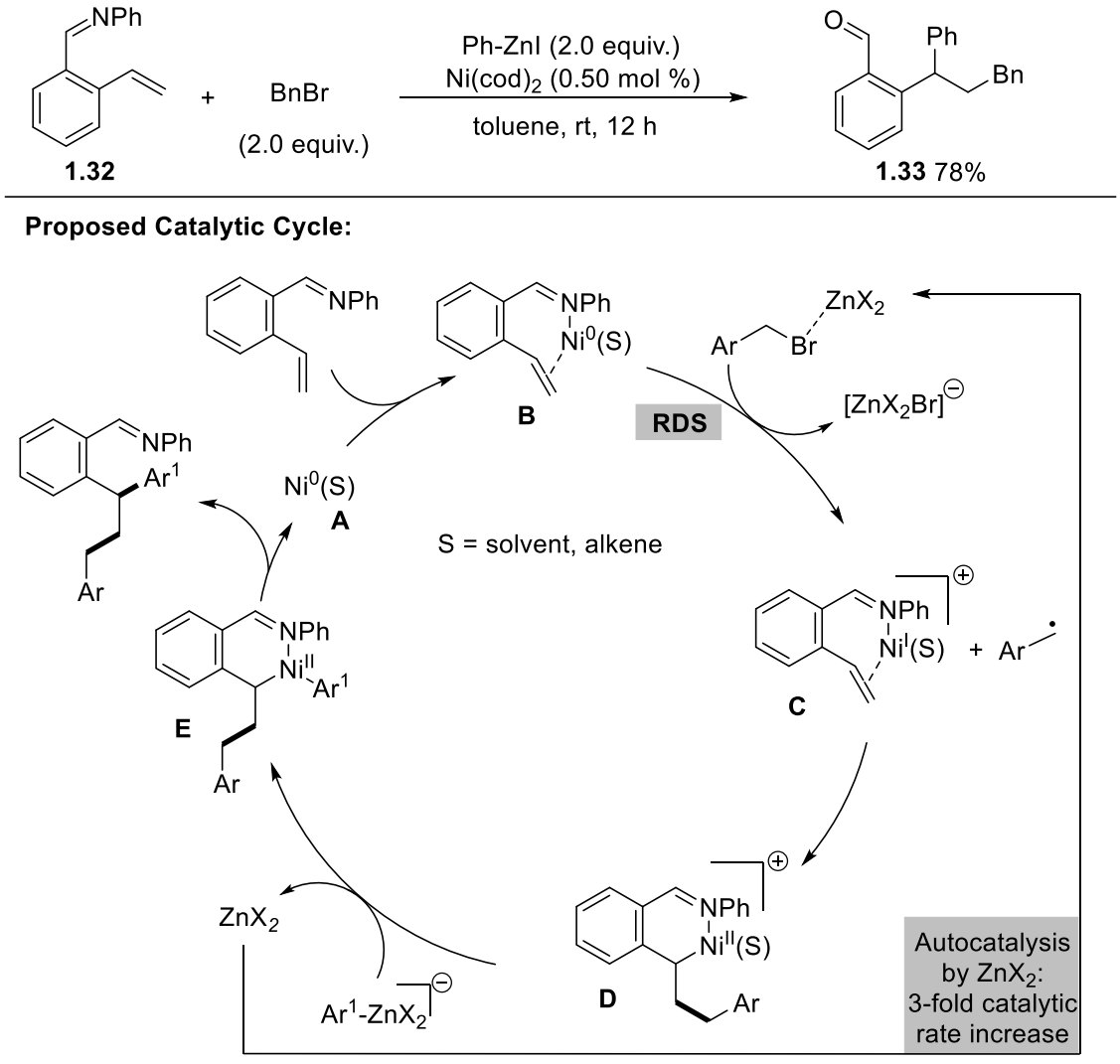


In a later study, Giri group reported a benzylarylation of alkenylarenes directed by an imine group (Scheme 1.11).[16] After detailed kinetic studies, an unusual Ni(0)/Ni(I)/Ni(II) mechanism was proposed. The zinc salt generated as by-product from the nucleophile served as an autocatalyst that helped promote the rate-determining halogen abstraction step. Around the same time, imine-directed benzylalkylation of the same motif was reported by

(16) Dhungana, R. K.; Sapkota, R. R.; Wickham, L. M.; Niroula, D.; Shrestha, B.; Giri, R. *Angew. Chem. Int. Ed.* **2021**, *60*, 22977–22982.

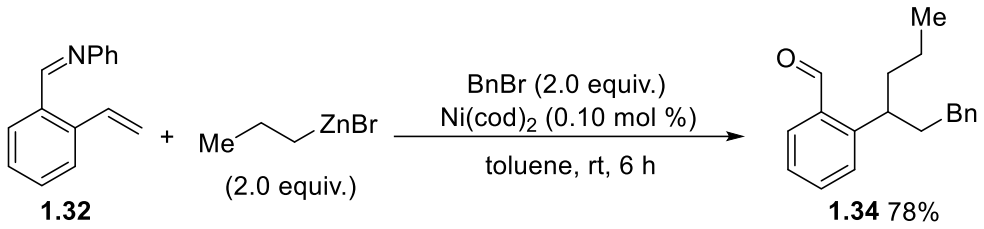
the same group (Scheme 1.12), which further expanded the synthetic utility of the catalytic system.[17]

Scheme 1.11. Giri's Benzylarylation of Alkenylarenes



(17) Dhungana, R. K.; Sapkota, R. R.; Wickham, L. M.; Niroula, D.; Giri, R. *J. Am. Chem. Soc.* **2020**, *142*, 20930–20936.

Scheme 1.12. Giri's Dialkylation of Alkenylarenes



1.32 **1.34** 78%

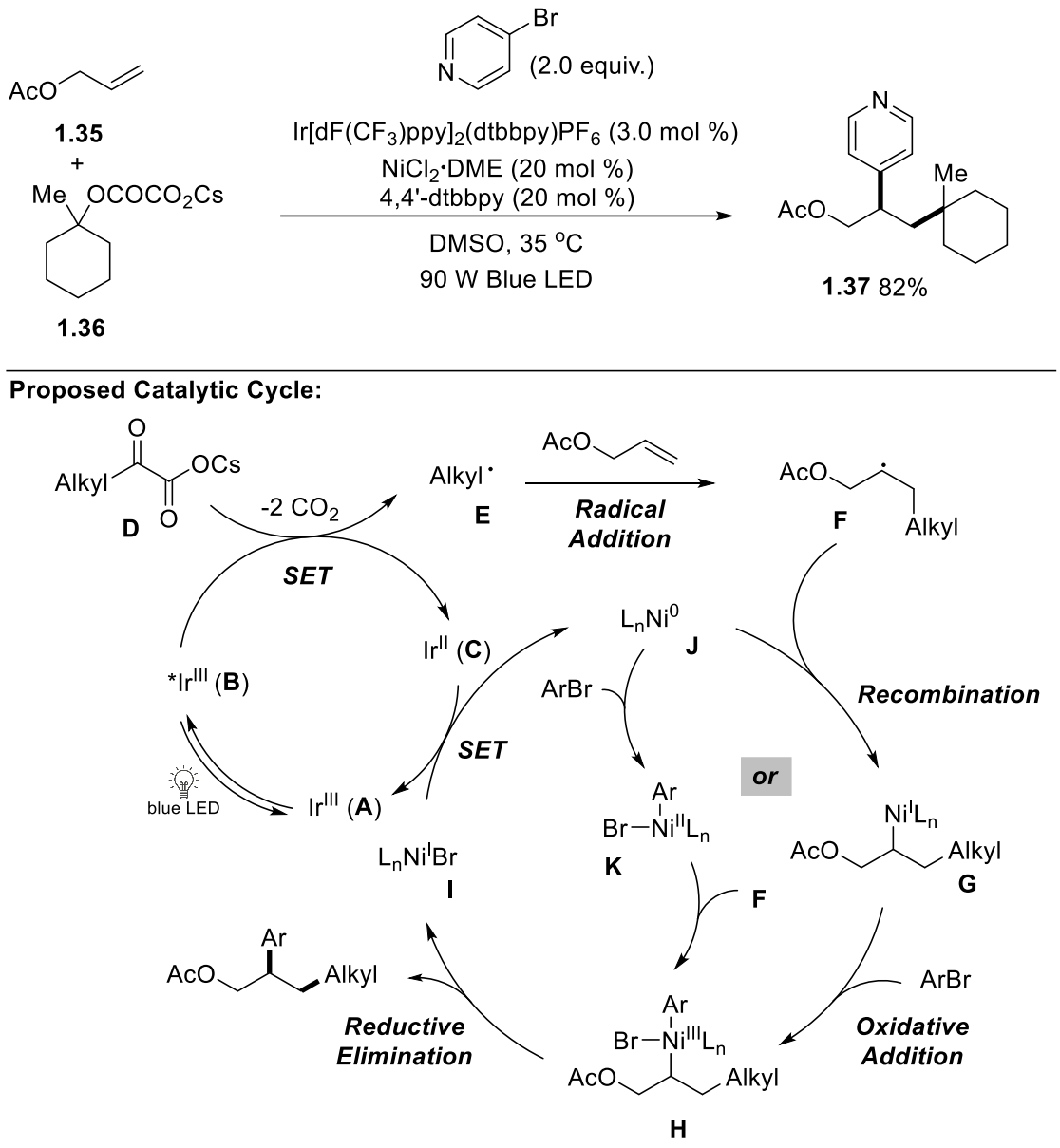
1.2.2.2 Photoredox/Nickel Dual Catalysis

With nickel as the sole catalyst, the alkyl radical precursors incorporated in dicarbofunctionalization reactions were limited to alkyl halides and, in rare cases, redox active esters[9] that underwent single electron reduction by nickel to produce alkyl radicals. Alternatively, generation of the carbon-centered radical could be accomplished *via* single electron oxidation of nucleophiles by photocatalysis, and dicarbofunctionalization could be accomplished in combination with nickel as the cross-coupling catalyst.

The first example of photoredox/Ni-catalyzed three-component alkylarylation was introduced by Chu group in 2019, using 3°-alkyl oxalates (**1.36**, Scheme 1.13) as radical precursors to cross-couple with allylic esters (**1.35**) and aryl bromides.[18] In the reported catalytic cycle, an alkyl oxalate **D** was oxidized by visible-light activated iridium complex **B**, generating alkyl radical and releasing CO_2. The radical would add to the alkene and form a secondary radical **F**, which would recombine with Ni(0) catalyst to form Ni(I) species **G**. Oxidative addition to an aryl bromide electrophile and subsequent reductive elimination would yield the desired product. The resulting Ni(I) catalyst **I** would undergo SET with Ir(II) species **C** to regenerate Ni(0) and Ir (III) complexes, respectively.

(18) Guo, L.; Tu, H. Y.; Zhu, S.; Chu, L. *Org. Lett.* **2019**, *21*, 4771–4776.

Scheme 1.13. Chu's Photocatalyzed Alkylarylation via Ir/Ni Dual Catalysis

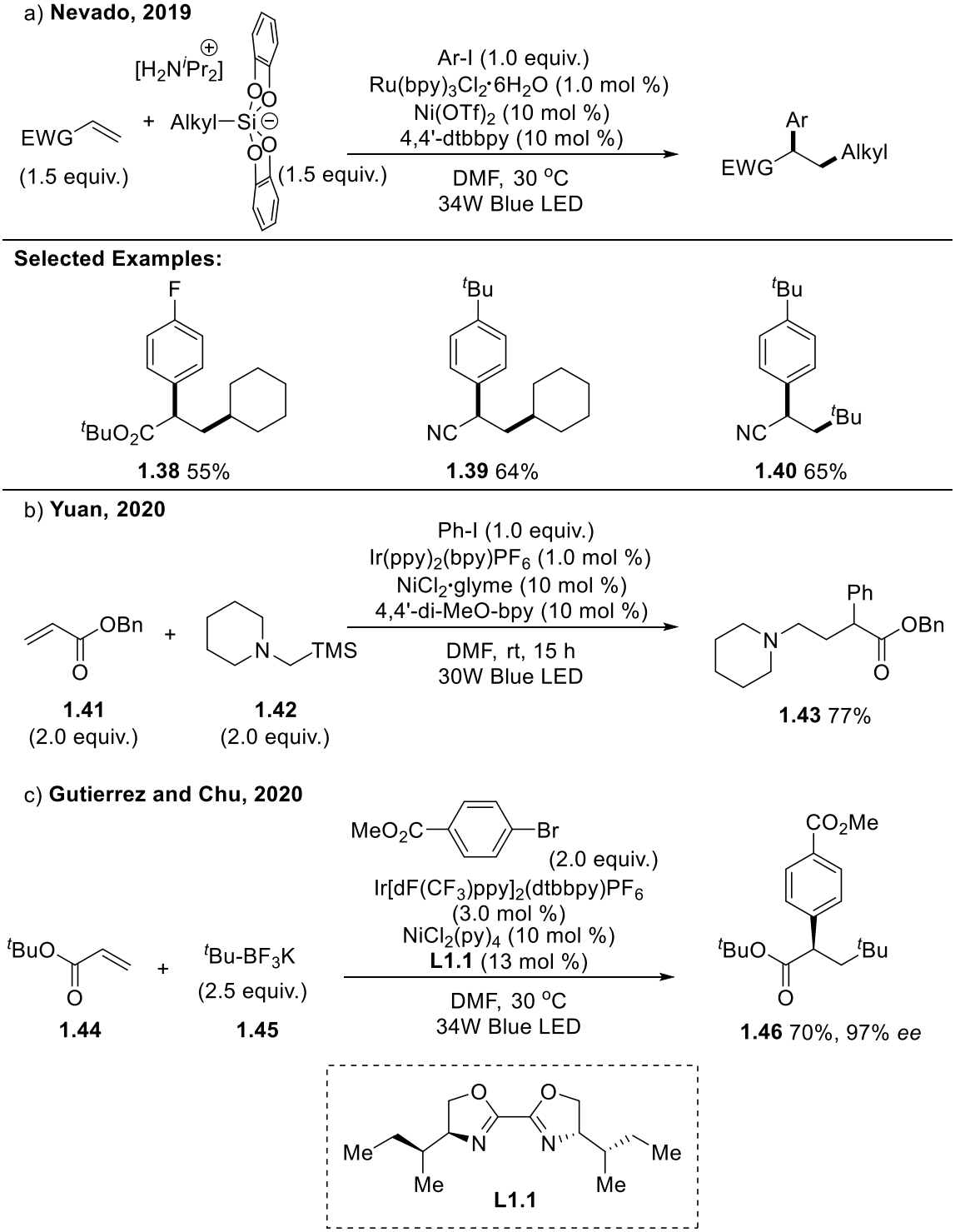


In the same year, Nevado reported a similar reaction employing alkylsilicates as radical precursors (Scheme 1.14a).[19] Secondary (**1.38**, **1.39**) or tertiary alkylsilicates (**1.40**) could be oxidized to alkyl radicals and undergo radical addition/cross-coupling cascade on

(19) García-Domínguez, A.; Mondal, R.; Nevado, C. *Angew. Chem. Int. Ed.* **2019**, *58*, 12286–12290.

electron-deficient alkenes. Following this report, Yuan expanded the scope of nucleophile to include α-aminylmethyl groups by incorporating trimethylsilane as the redox-active

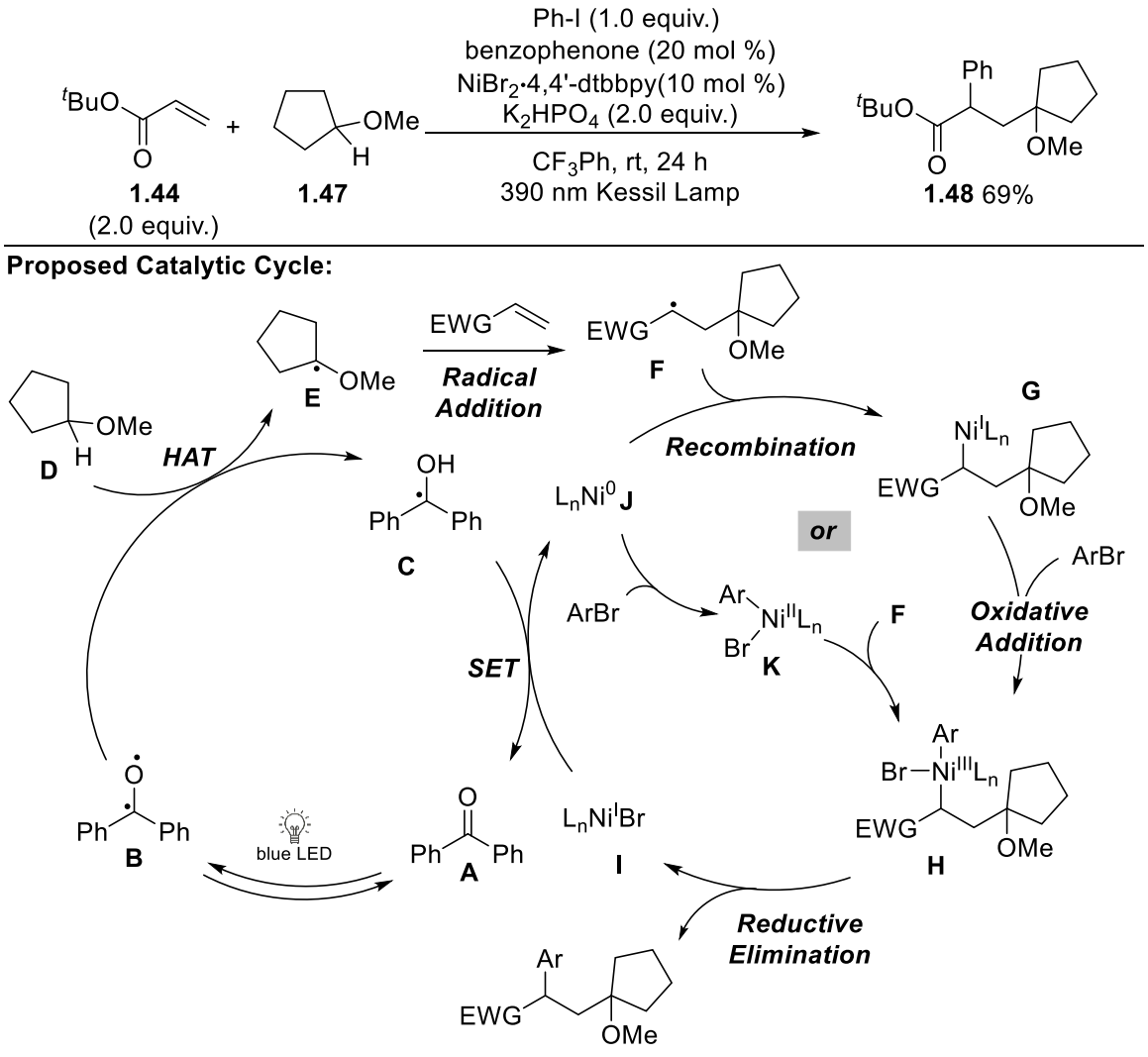
Scheme 1.14. Photoredox/Ni Duel-Catalyzed Dicarbofunctionalizations



group (Scheme 1.14b). [20] Gutierrez and Chu accomplished an enantioselective carboalkylation using a chiral bioxazoline ligand **L1.1** on nickel in combination with iridium photocatalyst (Scheme 1.14c). [21] Tertiary trifluoroborate salts (**1.45**) were employed as radical precursors.

In 2021, Gutierrez and Molander merged the power of photochemical C-H activation

Scheme 1.15. Gutirrez and Molander's C-H Activation/Nickel Alkylarylation



(20) Zheng, S.; Chen, Z.; Hu, Y.; Xi, X.; Liao, Z.; Li, W.; Yuan, W. *Angew. Chem. Int. Ed.* **2020**, *59*, 17910–17916.

(21) Guo, L.; Yuan, M.; Zhang, Y.; Wang, F.; Zhu, S.; Gutierrez, O.; Chu, L. *J. Am. Chem. Soc.* **2020**, *142*, 20390–20399.

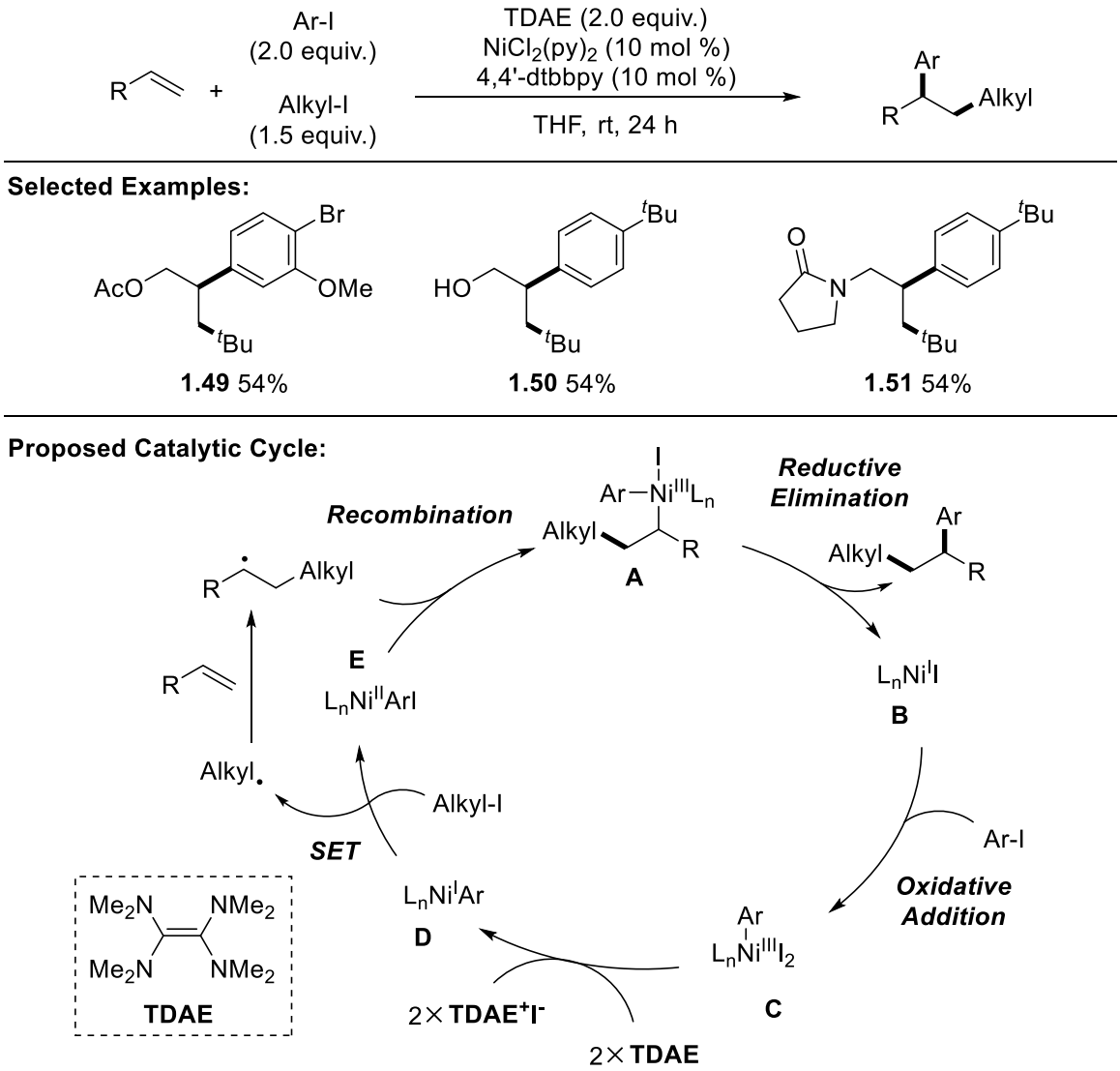
and nickel catalysis, and successfully employed ethers (**1.47**, Scheme 1.15) as radical precursors in the dicarbofunctionalization of alkenes.[22] Benzophenone **A** was employed as the photocatalyst, which, upon irradiation, could be activated to triplet state diradical **B** The newly formed diradical **B** could abstract an α-alkoxy hydrogen atom from ether **D**. α-Oxygen radical **E** generated in this process could then participate in a nickel-based catalytic cycle, which was silimar to Chu's proposal[18] in Scheme 1.13, to furnish dicarbofunctionalization product **1.48**.

1.2.2.3. Reductive Dicarbofunctionalization

Reductive dicarbofunctionalization of alkenes using two electrophiles is an emerging area in recent years. The first case was developed by Nevado in 2017, where a tertiary alkyl iodide and an aryl iodide were coupled regioselectively across an electron-deficient alkene (Scheme 1.16).[23] In a follow-up research, computational and experimental studies pointed to an unconventional mechanism.[24] In the catalytic cycle proposed, Ni(I) species **B** would oxidatively add to aryl iodide to form Ni(III) complex **C**, which would be reduced by two molecules of TDAE into aryl-bound Ni(I) complex **D**. After that, a SET/radical addition/recombination sequence would form Ni(III) **A**, which could undergo reductive elimination to deliver the product.

(22) Campbell, M. W.; Yuan, M.; Polites, V. C.; Gutierrez, O.; Molander, G. A. *J. Am. Chem. Soc.* **2021**, *143*, 3901–3910.
(23) García-Domínguez, A.; Li, Z.; Nevado, C. *J. Am. Chem. Soc.* **2017**, *139*, 6835–6838.
(24) Shu, W.; García-Domínguez, A.; Quirós, M. T.; Mondal, R.; Cárdenas, D. J.; Nevado, C. *J. Am. Chem. Soc.* **2019**, *141*, 13812–13821.

Scheme 1.16. Nevado's Reductive Alkylarylation

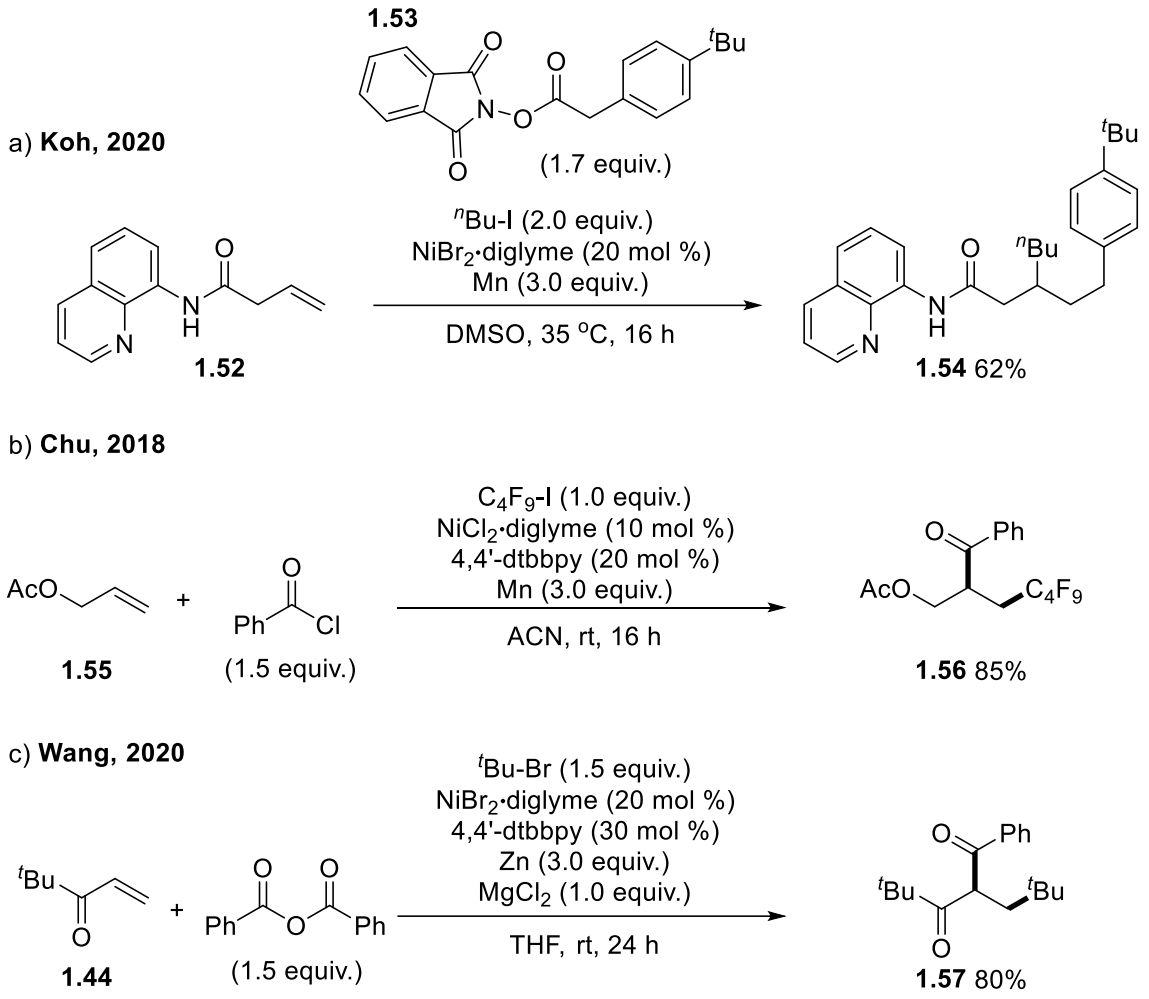


Following Nevado's pioneering report, a series of three-component reductive dicarbofunctionalizations were developed. Commonly used reductants included Mn and Zn metal. Koh incorporated benzylic redox active esters (**1.53**, Scheme 1.17a) as radical precursors and primary iodides as the other electrophile, accomplishing a chemo- and regioselective dialkylation of alkene **1.52** with quinoline derivative as a directing group.[25]

(25) Yang, T.; Jiang, Y.; Luo, Y.; Lim, J. J. H.; Lan, Y.; Koh, M. J. *J. Am. Chem. Soc.* **2020**, *142*, 21410–21419.

Reactions using acyl electrophiles were first reported by Chu in 2018 (Scheme 1.17b).[26]

Scheme 1.17. Reductive Dicarbofunctionalizations of Alkenes

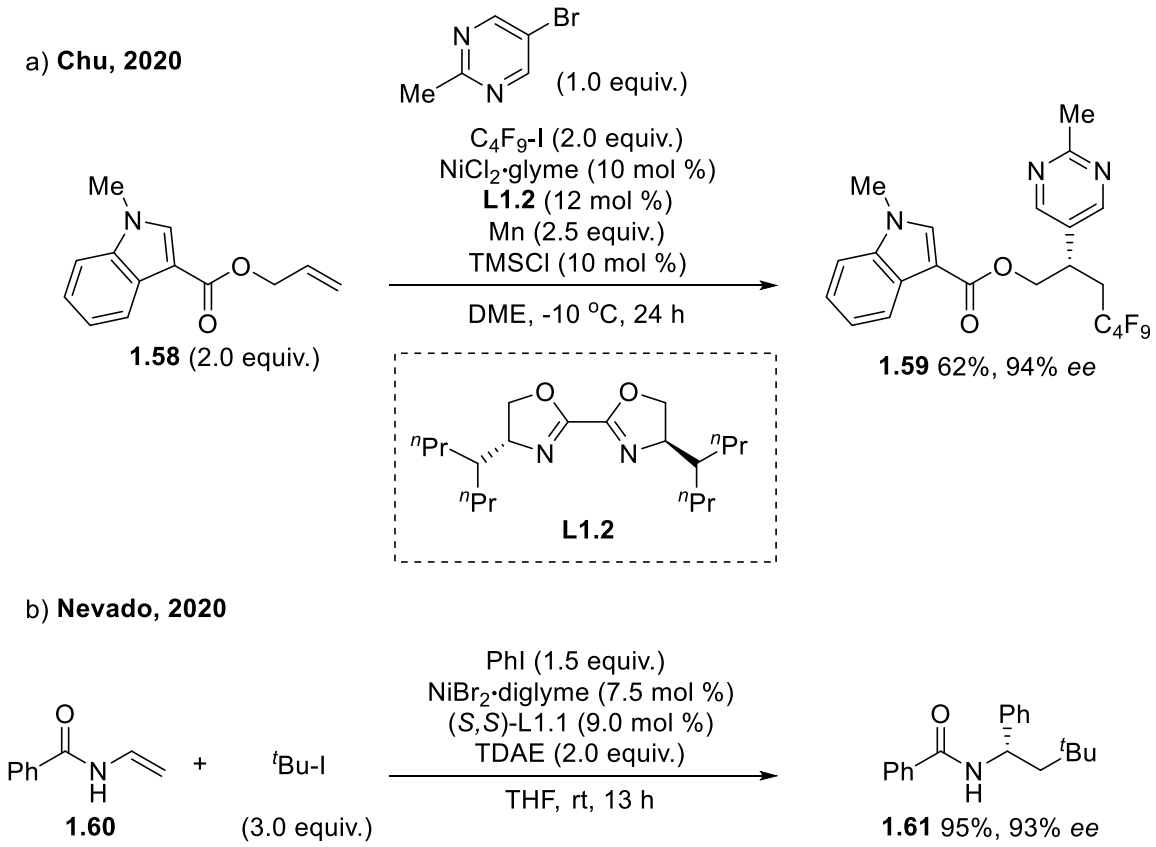


Electron-deficient radicals were generated from perfluoroalkyl iodides, and the product was formed after radical addition and recombination with an acyl-bound Ni(II) species. Wang reported a related work using anhydrides as acyl eletrophiles (Scheme 1.17c).[27] Tertiary alkyl bromides served as precursors to electron-rich tertiary radicals, which added regioselectively to conjugated esters.

(26) Zhao, X.; Tu, H. Y.; Guo, L.; Zhu, S.; Qing, F. L.; Chu, L. *Nat. Commun.* **2018**, *9*, 3488.
(27) Wang, L.; Wang, C. *Org. Lett.* **2020**, *22*, 8829–8835.

Enantioselective reductive dicarbofunctionalizations *via* a radical addition/cross-coupling cascade were accomplished by employing chiral ligands on nickel catalyst. Chu reported an enantioselective perfluoroalkylarylation of allyl esters (**1.58**, Scheme 1.18a)

Scheme 1.18. Enantioselective Reductive Dicarbofunctionalizations of Alkenes



utilizing a chiral bioxazoline ligand (**L1.2**).[28] The ester group was found to have a chelating effect that provided enantioinduction. In a later publication, Nevado achieved an enantioselective alkylarylation of enamides (**1.60**, Scheme 1.18b), leading to a large scope of stereodefined benzylic amines in high enantioselectivity.[29]

(28) Tu, H. Y.; Wang, F.; Huo, L.; Li, Y.; Zhu, S.; Zhao, X.; Li, H.; Qing, F. L.; Chu, L. *J. Am. Chem. Soc.* **2020**, *142*, 9604–9611.

(29) Wei, X.; Shu, W.; García-Domínguez, A.; Merino, E.; Nevado, C. *J. Am. Chem. Soc.* **2020**, *142*, 13515–13522.

1.2.3. Dicarbofunctionalization of Alkenylborons: Stability of *α*-Boryl Radicals

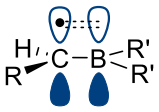
The radical-based dicarbofunctionalization reactions listed in the last section relied on substitutions on the alkene to provide stabilization for the generated radical and to achieve regioselective radical addition. Common substitutions on activated alkenes include amide, carbonyl, and ester groups, while aryl and alkyl substitutions on non-activated alkenes could also dictate the regioselectivity of radical addition by providing stabilization to *α*-radicals and creating steric bias.

Another genre of functional groups that provide stabilization to *α*-radicals are boron moieties. The effect of three-coordinate boron atoms on neighboring carbon-centered radicals has been well studied over the past decades.[30] The stabilizing effect can be attributed to the conjugation between the SOMO of the radical and the empty p-orbital on a three-coordinate boron atom (Scheme 1.19). The strength of such stablization varies with different substituents R'. Substituents such as O and N that bear lone-pairs can donate into the empty p-orbital on boron, thus diminishing the stabilizing effect to *α*-radicals. Radical stability is known to follow the trend of boranes> borinates> boronates, as carbon substituents are replaced by oxygen ligands.

(30) (a) Grotewold, J.; Lissi, E. A.; Scaiano, J. C. *J. Organomet. Chem.* **1969**, *19*, 431–434. (b) Matteson, D. S. *Prog. Boron Chem*. **1970**, *3*, 117. (c) Lane, C. F.; Brown. H. C. *J. Am. Chem. Soc.* **1970**, *92*, 7212–7213. (d) Grotewold, J. E.; Lissi, E. A.; Scaiano, J. C. *J. Chem. Soc. B* **1971**, 1187–1191. (e) Pasto, D. J. *J. Am. Chem. Soc.* **1988**, *110*, 8164–8175. (f) Coolidge, M. B.; Borden, W. T. *J. Am. Chem. Soc.* **1988**, *110*, 2298–2299. (g) Henry, D. J.; Parkinson, C. J.; Mayer, P. M.; Radom, L. J. *Phys. Chem. A* **2001**, 105, 6750–6756. (h) Walton, J. C.; McCarroll, A. J.; Chen, Q.; Carboni, B.; Nziengui, R. *J. Am. Chem. Soc.* **2000,** *122,* 5455–5463.

Scheme 1.19. Stablization of Three-Coordinate Boron on α-Radicals

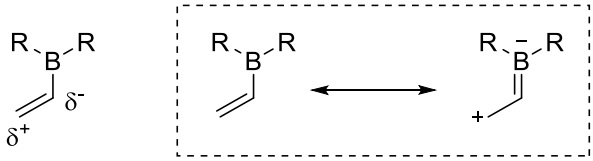
C-H Bond Type	BDE (kcal/mol)
H_3C–H	104
$H_2C(B(OMe)_2)$–H	98
$H_2C(BMe_2)$–H	94



Stablization by p-orbital on B

The stabilizing effect can be quantitatively measured by the bond dissociation energy (BDE) of the adjacent C-H bond. Scaiano estimated the BDE of α-borane C-H bond to be 80±3 kcal/mol based on kinetic studies of photochemical gas phase bromination of triethylborane.[30a] Computational studies by Pasto[30e], Borden[30f] and Radom[30g] showed that the radical stabilizing energy (RSE) of BH_2 group to α-radicals was around 9-11 kcal/mol. Lastly, the BDE of *α*-boronic ester C–H bonds was determined to be around 98 kcal/mol by Carboni.[30h] The stabilizing effect was comparable to that provided by an alkyl substitution. It was also noted that the resonance structure resulting from the donation of π-electron on alkene to the vacant p-orbital on boron had a polarizing effect on the alkene.

Scheme 1.20. Polarization of Boron-Substituted Olefin



1.2.4. Dicarbofunctionalization of Alkenyl Boron Compounds *via* Radical Addition

The dicarbofunctionalization of alkenyl boron compounds can lead to modular construction of secondary or tertiary alkyl boron motifs that possess great synthetic versatility to be transformed into various functional groups. Moreover, depending on the

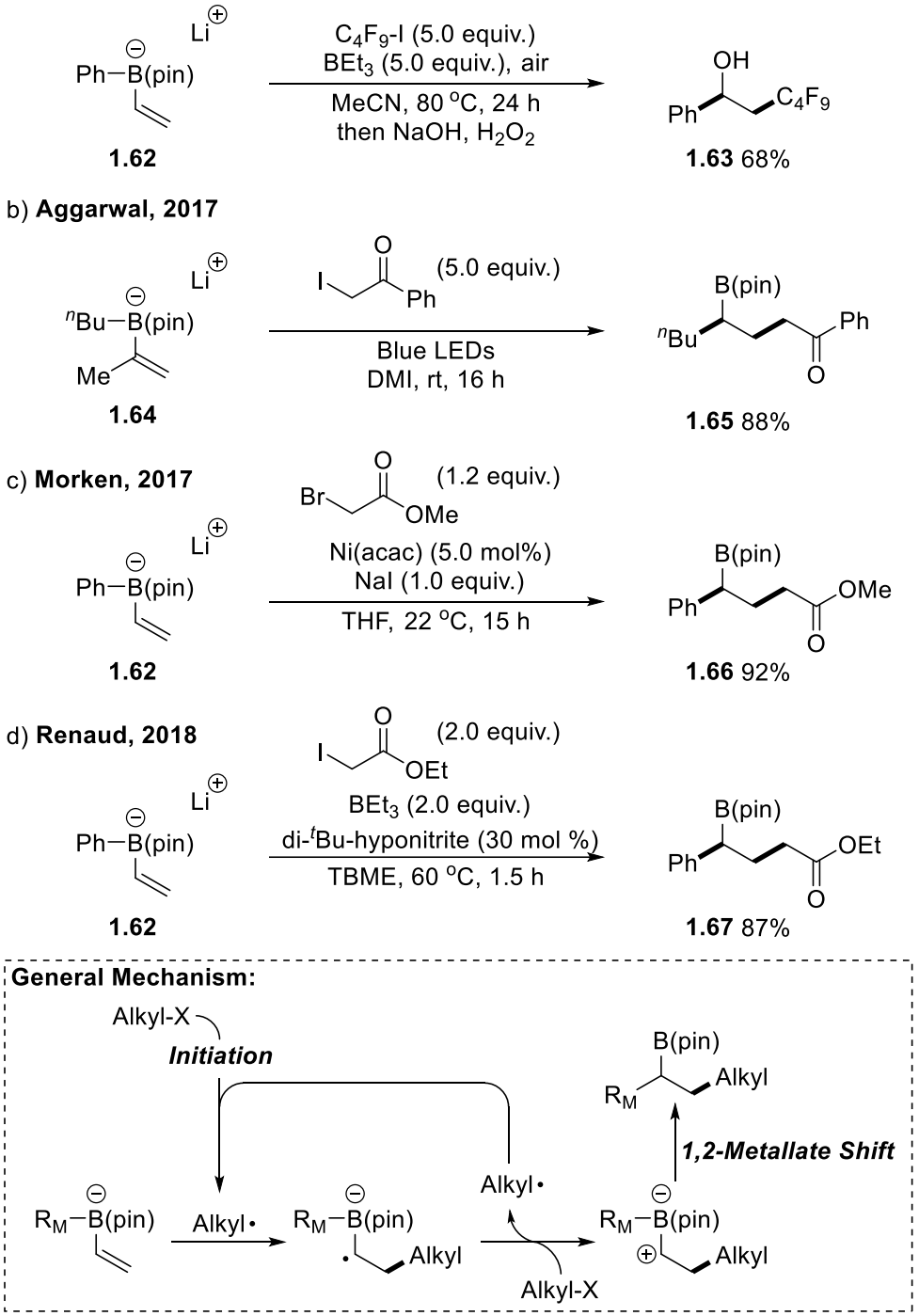
ligands on boron, three- or four-coordinate boron groups can modulate the reactivity of α-radicals in different ways, providing chemists with an extra handle for the design of reactions.

1.2.4.1. Radical-Polar Crossover: Radical Addition/1,2-Metallate Shift Cascade

The first dicarbofunctionalizations of alkenyl boron compounds were a series of reactions that exploited the special properties of four-coordinate boron 'ate' complexes. In 2017, Studer[31] and Aggarwal[32] discovered the radical-polar crossover reactivity, in which an electron-deficient radical species added to an vinyl boron 'ate' complex (prepared by pre-mixing an organolithium reagent with organoboron species), generating a radical adjacent to an electron-rich four-coordinate boron (Scheme 1.21, dashed box). The SOMO energy level of the radical would be elevated by the HOMO of the boron 'ate' complex, rendering the former prone to undergo single electron oxidation to give an α-boryl cation, and triggering an 1,2-metallate shift to form dicarbofunctionalized product. In the first report by Studer,[31a] a perfluoroalkyl radical was generated from the iodide by triethylborane/O_2[33] as the initiator (Scheme 1.21a). The radical formed after addition to the vinyl boron 'ate' (**1.62**) was postulated to reduce the perfluoroalkyl iodide and propagate the radical chain. Renaud conducted mechanistic studies on a similar system (Scheme 1.21d) in 2018 and supported the radical-polar crossover mechanism.[34] Closely following

(31) (a) Kischkewitz, M.; Okamoto, K.; Mück-Lichtenfeld, C.; Studer, A. *Science.* **2017**, *355*, 936–938. (b) Gerleve, C.; Kischkewitz, M.; Studer, A. *Angew. Chem. Int. Ed*. **2018**, *57*, 2441–2444. (c) Kischkewitz, M.; Gerleve, C.; Studer, A. *Org. Lett.* **2018**, *20*, 3666–3669.
(32) Silvi, M.; Sandford, C.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2017**, *139*, 5736–5739.
(33) Et_3B/O_2 as radical initiator: Uematsu, R.; Saka, C.; Sumiya, Y.; Ichino, T.; Taketsugu, T.; Maeda, S. *Chem. Commun.* **2017**, *53*, 7302–7305.
(34) Tappin, N. D. C.; Gnägi-Lux, M.; Renaud, P. *Chem. Eur. J.* **2018**, *24*, 11498–11502.

Scheme 1.21. Dicarbofunctionalizations of Alkenyl Boron 'Ate' Complexes via Radical-Polar Crossover



Studer's publication, Aggarwal reported that a similar process could be initiated by

irradiation with blue LED (Scheme 1.21b).[32] The reaction could also be carried out in the absence of a photocatalyst.

Our group encountered the same radical-polar crossover reactivity in the course of investigating a nickel-catalyzed conjunctive cross-coupling with alkyl iodide electrophiles (Scheme 1.21c).[35] In this work, when non-activated alkyl iodides were employed as electrophiles, an asymmetric 1,2-metallate shift triggered by Ni/Pybox catalyst occurred and led to alkylarylation of vinylB(pin) in high enantioselectivity. However, when an activated electron-deficient alkyl halide was used, racemic products formed, even when chiral ligands on nickel were employed. Mechanistic studies showed that a radical-polar crossover took place in the case of an activated electrophile.

1.2.4.2. Radical Addition/Cross-coupling Cascade

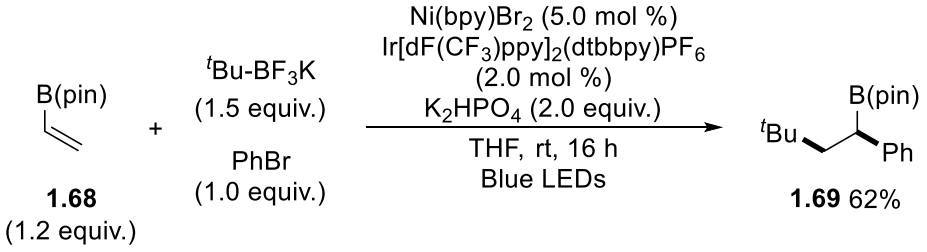
Dicarbofunctionalizations of alkenylboron species *via* radical addition/cross-coupling cascade have drawn considerable attention. Different from the radical-polar crossover cascade that relies on the SOMO-enhancement of the α-boryl radical by an adjacent four-coordinate alkenyl boron 'ate' complex, the α-boryl radical requires stabilization until it undergoes recombination with a transition metal catalyst. For this reason, the boron species have to be three-coordinate to prevent oxidation of the α-boryl radical that leads to potential side reactions.

In 2019, Molander achieved the alkylarylation of vinylB(pin) **1.68** with Ni/Ir duel catalysis under photoredox conditions (Scheme 1.22).[36] Tertiary trifluoroborate salt was

(35) Lovinger, G. J.; Morken, J. P. *J. Am. Chem. Soc.* **2017**, *139*, 17293–17296.
(36) Campbell, M. W.; Compton, J. S.; Kelly, C. B.; Molander, G. A. *J. Am. Chem. Soc.* **2019**, *141*, 20069–20078.

utilized as the radical precursor. The proposed catalytic cycle was similar to Gutirrez and Chu's Ni/Ir catalyzed alkylarylation of conjugated esters.[21] VinylB(pin) was found to be a competent electron-deficient radical acceptor, and has strong affinity for electron-rich tertiary alkyl radicals. Competition experiments showed that the rate of dicarbofunctionalization was 16 times faster than direct cross-coupling between the electrophile and nucleophile.

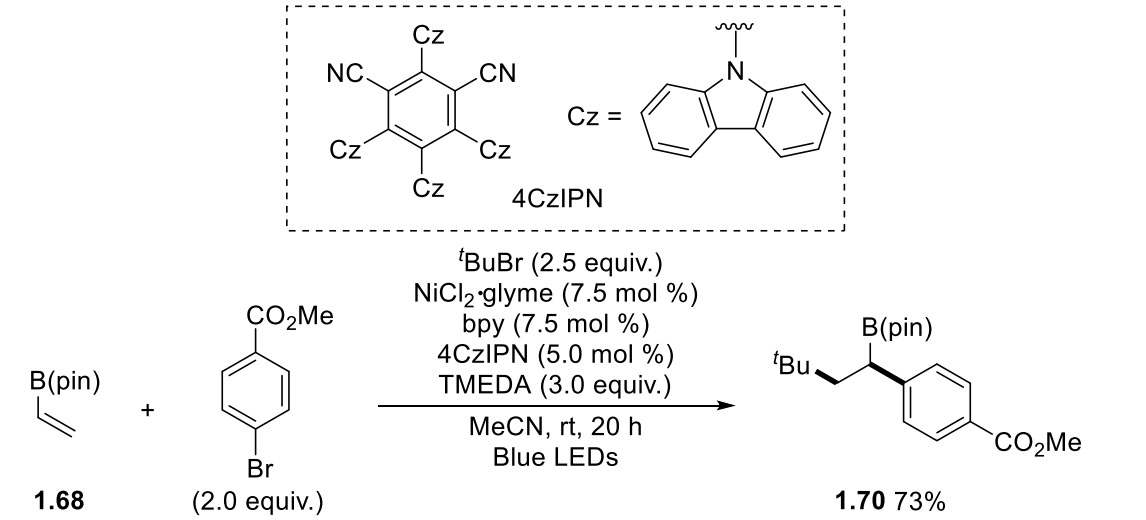
Scheme 1.22. Molander's Alkylarylation Enabled by Nickel/Photoredox Duel Catalysis



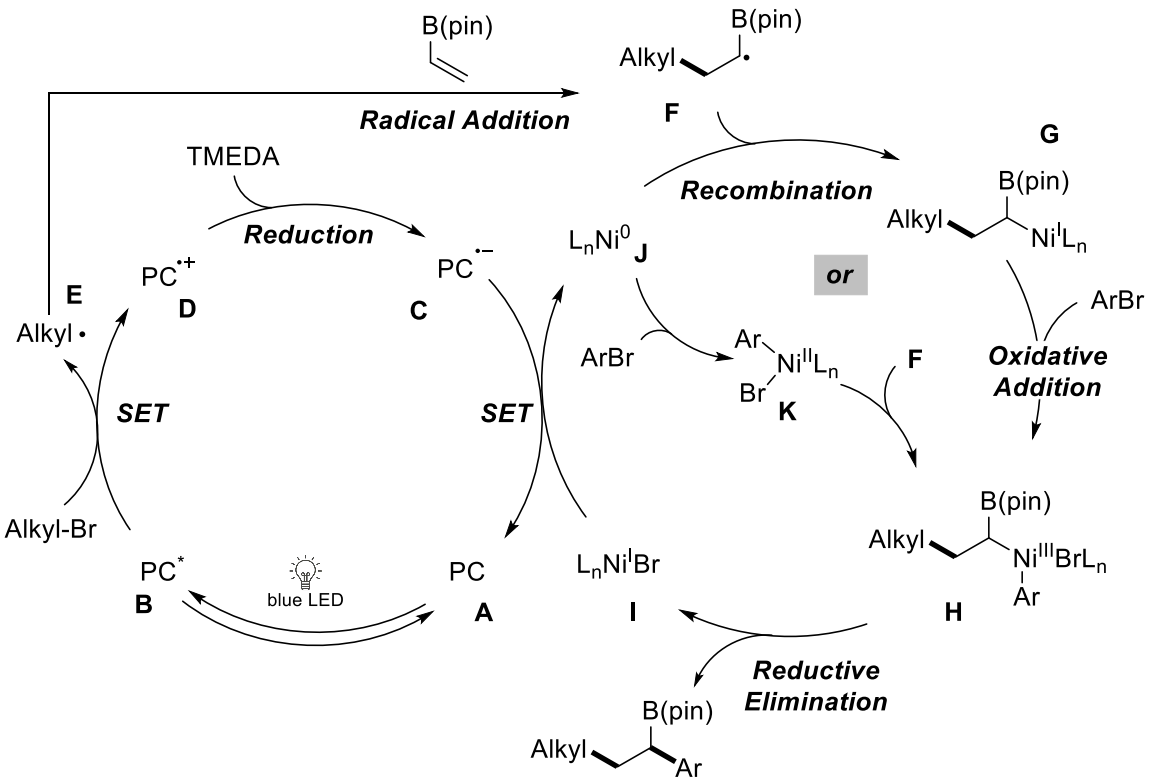
Similar products were synthesized by photoinduced reductive dicarbofunctionalization of vinylB(pin) reported by Martin (Scheme 1.23), where a tertiary alkyl bromide electrophile and an aryl electrophile were coupled regioselectively across the double bond.[37] According to the postulated mechanism, alkyl radical **E** was generated *via* single electron reduction by photo-excited organophotocatalyst 4CzIPN **B**. Radical **E** could undergo radical addition to vinylB(pin) to form α-boryl radical **F** that could recombine with Ni(0) catalyst **J** to generate Ni(I) complex **G**. Oxidative addition of the aryl electrophile followed by reductive elimination furnished the cross-coupling product. The oxidized photocatalyst **D** was reduced by TMEDA into its radical anion form **C**, which served as a reductant to regenerate Ni(0) catalyst **J**.

(37) Sun, S. Z.; Duan, Y.; Mega, R. S.; Somerville, R. J.; Martin, R. *Angew. Chem. Int. Ed.* **2020**, *59*, 4370–4374.

Scheme 1.23. Martin's Reductive Alkylarylation enabled by Nickel/Photoredox Duel Catalysis



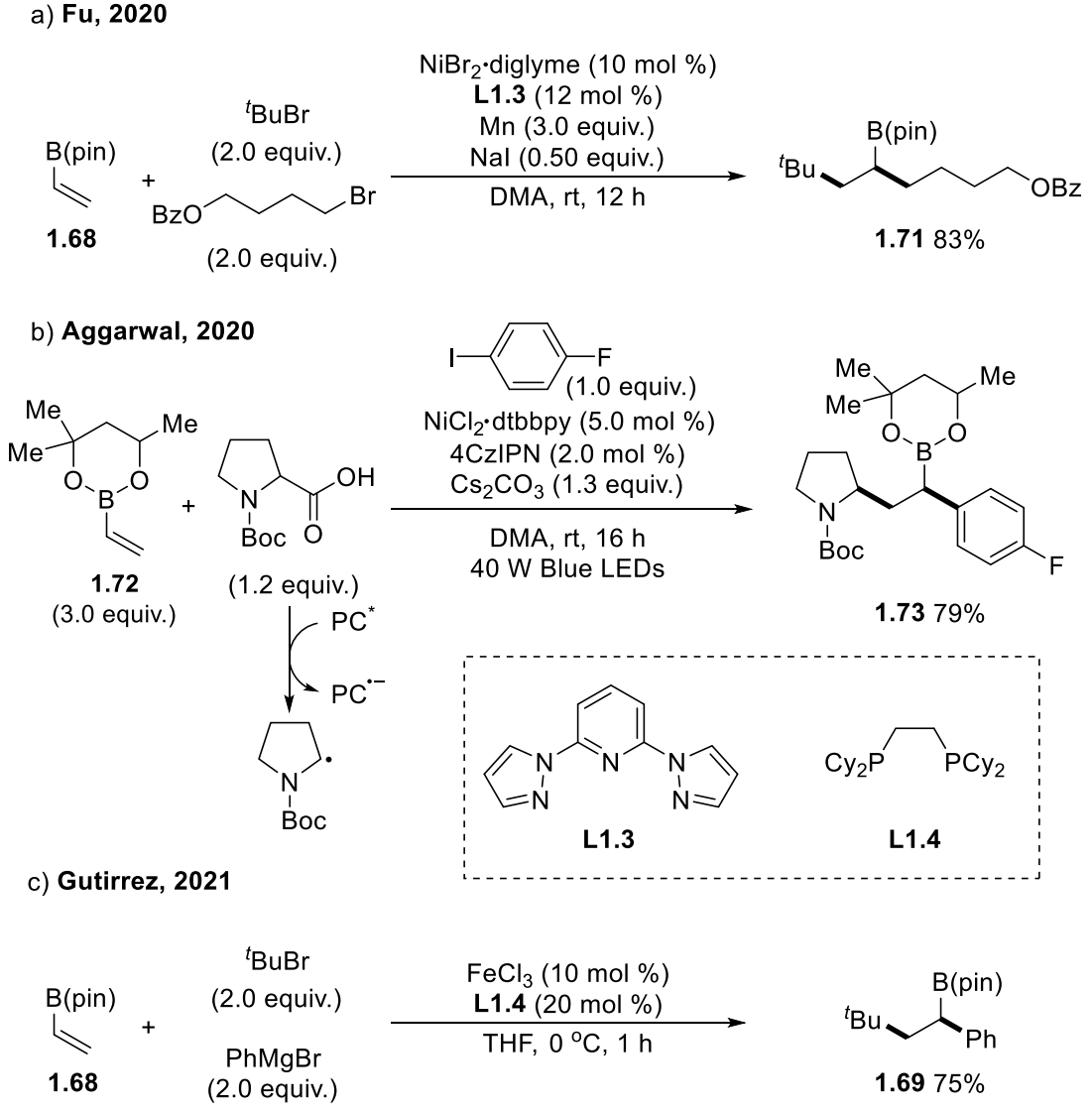
Proposed Catalytic Cycle:



Yao Fu reported a reductive dialkylation of vinylB(pin), successfully differentiating a tertiary electrophile from a primary one, and achieved high chemo- and regioselectivity

(Scheme 1.24a).[38] The high level of selectivity hypothetically came from the tendency for tertiary alkyl bromide to undergo facile halogen atom abstraction, and the primary bromide presumably went through an S_n2 type oxidative addition with Ni(0) species. An electron-rich tridentate nitrogen-based ligand **L1.3** containing two pyrazole rings was found to give the highest yield.

Scheme 1.24. Dicarbofunctionalizations of Alkenyl Boronates via Radical Addition/Cross-Coupling Cascade



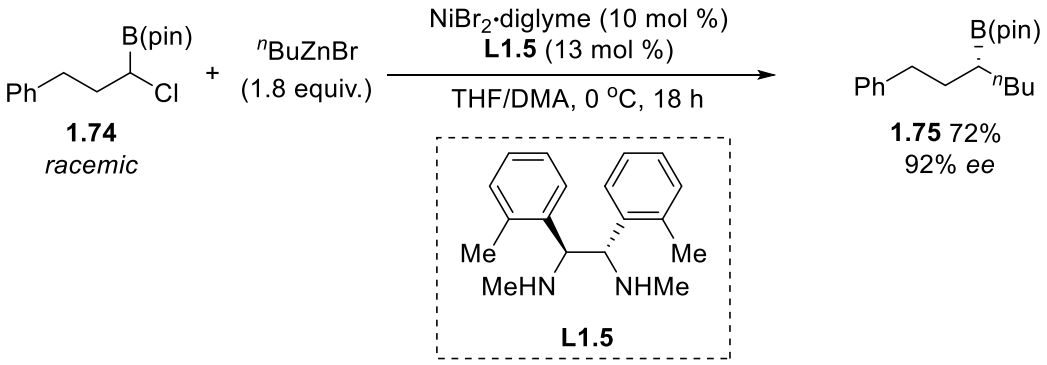
(38) Wang, X. X.; Lu, X.; He, S. J.; Fu, Y. *Chem. Sci.* **2020**, *11*, 7950–7956.

Naturally abundant carboxylic acids were directly employed as radical precursors by Aggarwal. Using photoredox/nickel duel catalysis (Scheme 1.24b),[39] vinyl boronate **1.72** was found to give moderately better yields than vinylB(pin) in conversion to **1.73**.

In 2021, Gutirrez discovered that iron performed as well as, if not better than nickel in dicarbofunctionalization of vinyl boronates (Scheme 1.24c).[40] Aryl Grignard reagents were utilized as nucleophile when using a catalyst derived from iron equipped with a diphosphine ligand **L1.4**. Mechanistic and computational studies suggested that the reaction occurred *via* a Fe(I)/Fe(II)/Fe(III) catalytic cycle, similar to that of a nickel catalyzed redox-neutral dicarbofunctionalization.

α-Boryl radicals could be trapped by a chiral nickel catalyst to afford enantioenriched cross-coupling product, as exemplified in G. C. Fu's stereoconvergent Negishi cross-coupling of α-boryl halides (Scheme 1.25).[41] An enantioselective reductive alkylarylation

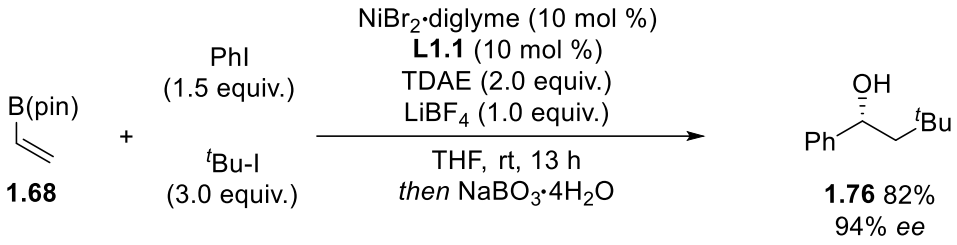
Scheme 1.25. Fu's Stereoconvergent Negishi Cross-Coupling of α-Boryl Halides



(39) Mega, R. S.; Duong, V. K.; Noble, A.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2020**, *59*, 4375–4379.
(40) Liu, L.; Aguilera, M. C.; Lee, W.; Youshaw, C. R.; Neidig, M. L.; Gutierrez, O. *Science.* **2021**, *374*, 432–439.
(41) Schmidt, J.; Choi, J.; Liu, A. T.; Slusarczyk, M.; Fu, G. C. *Science*, **2016**, *354*, 1265–1269.

of vinylB(pin) was achieved by Nevado (Scheme 1.26) with minor modifications to the conditions from the reaction mentioned above in section **1.2.2.2** (Scheme 1.18b).[29]

Scheme 1.26. Nevado's Asymmetric Dicarbofunctionalization of Alkenyl B(pin)

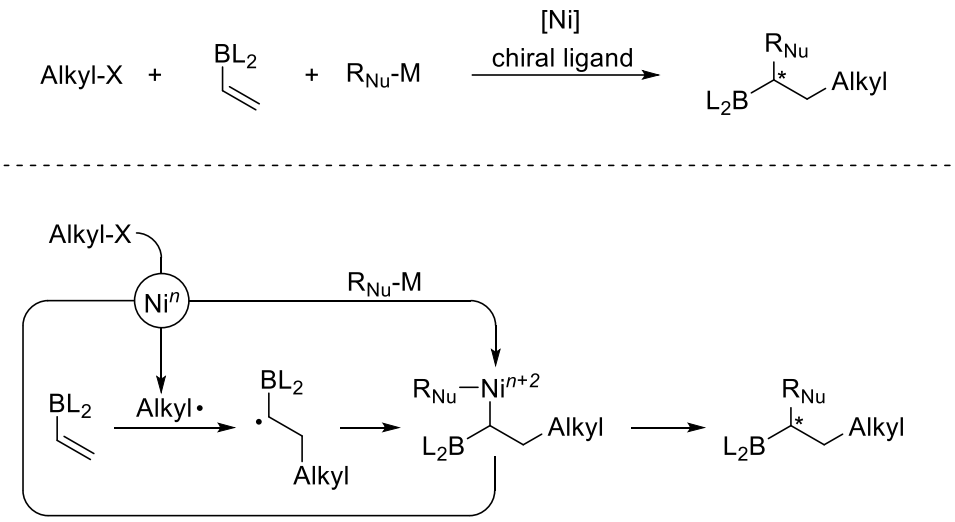


1.3. Enantioselective Radical Addition/Cross-Coupling of Organozinc Reagents, Alkyl Iodides, and Alkenylboron Reagents[42]

1.3.1. Reaction Development

Inspired by the literature results on nickel-catalyzed dicarbofunctionalization *via* radical addition/cross-coupling cascade, we envisioned that the same reactivity could be applied to vinyl boron species, and by incorporating a chiral ligand on the nickel catalyst, it could lead to the modular enantioselective synthesis of chiral organoboron compounds (Scheme 1.27).

Scheme 1.27. Reaction Design



Previous reports on radical-polar crossover reactions alerted us that an α-boryl radical adjacent to a four-coordinate boron would be susceptible to single electron oxidation into a carbocation. If the carbocation reacted with the organometallic reagent, the background

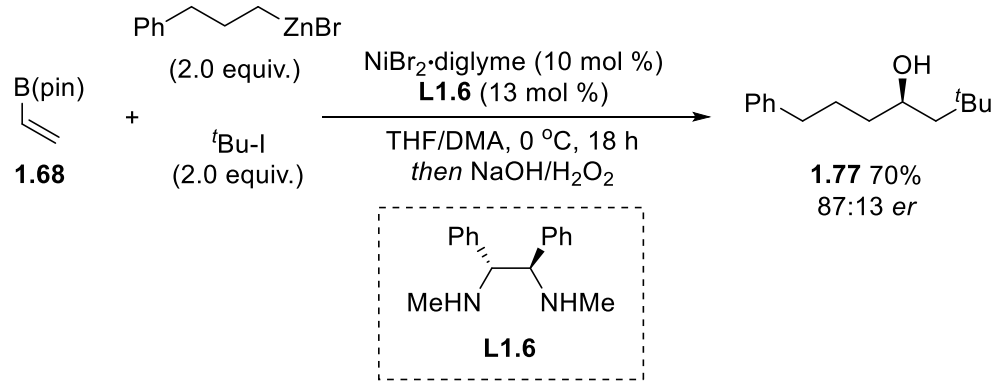
(42) Chierchia, M.; Xu, P.; Lovinger, G. J.; Morken, J. P. *Angew. Chem. Int. Ed.* **2019**, *58*, 14245-14248.

reaction would lower enantioselectivity. In terms of reaction design, if a three-coordinate vinylboronate was employed as the starting material, the nucleophile would need to be a weak Lewis base so that it would not ligate to the Lewis acidic boronic ester. For this reason, organozinc reagents were selected as nucleophile, since 'ate' complexes were not observed by ^{11}B NMR when organozinc reagents were mixed with organoboron species.

Alkenyl boronic esters are electron-deficient and the addition by electron-rich radicals would be favored.[30h] We reasoned that tertiary alkyl iodides as radical precursors would form electron-rich radicals that would match the polarity of the radical acceptors. Based on the observations by Giri[14], tertiary alkyl iodides would be more prone to radical formation than secondary and primary iodides *via* halogen atom abstraction by nickel.

We adapted the nickel-based catalytic system from Fu's stereoconvergent Negishi cross-coupling of α-boryl halides[41] since it demonstrated good levels of stereocontrol in a catalytic cycle that involved recombination of an α-boryl radical with nickel catalyst. Initial test reactions with vinylB(pin), primary zinc reagents and *tert*-butyl iodide as starting material yielded the dicarbofunctionalization product **1.77** in 70% yield after

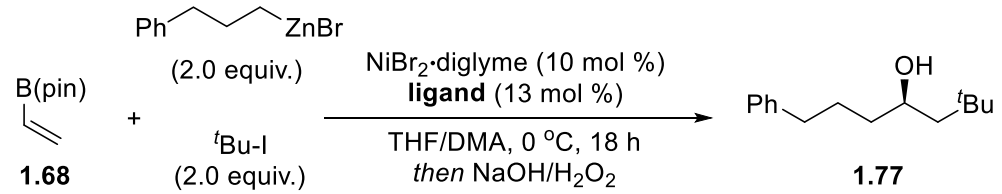
Scheme 1.28. Initial Results with Dicarbofunctionalization of VinylB(pin)

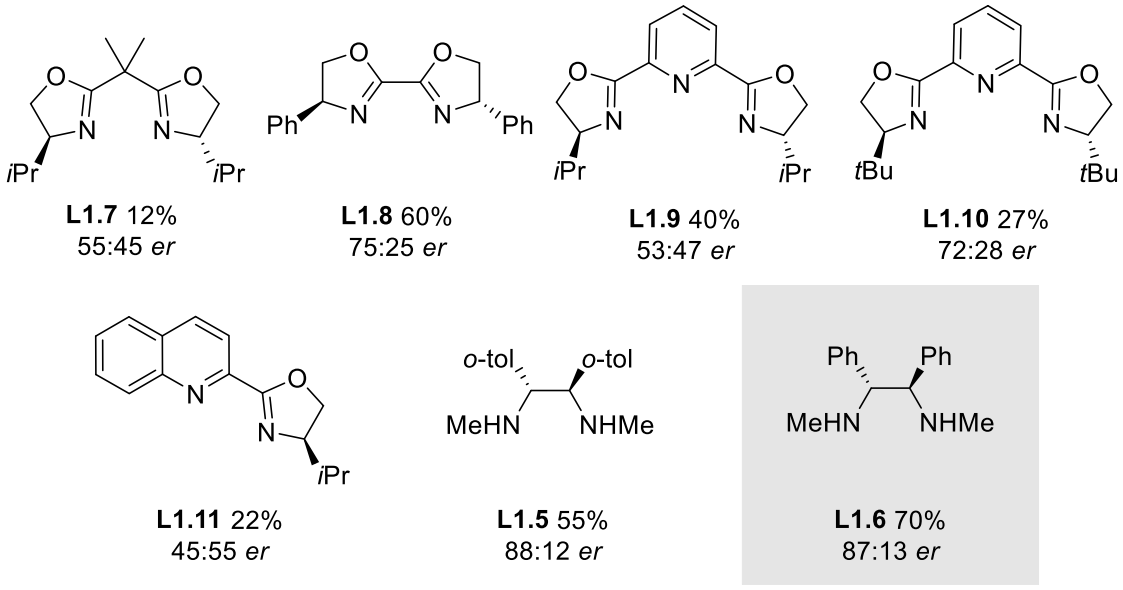


oxidation with H_2O_2 (Scheme 1.28). Moderate enantioselectivity of 87:13 *er* was achieved with diamine ligand **L1.6**.

With a functioning prototype reaction in hand, we set out to optimize the reaction to improve the enantioselectivity (Scheme 1.29). First, the effect of ligand on nickel was investigated. Reaction in the presence of a range of bidentate (**L1.7**, **L1.8**, **L1.11**) and

Scheme 1.29. Optimization of Ligands on Nickel

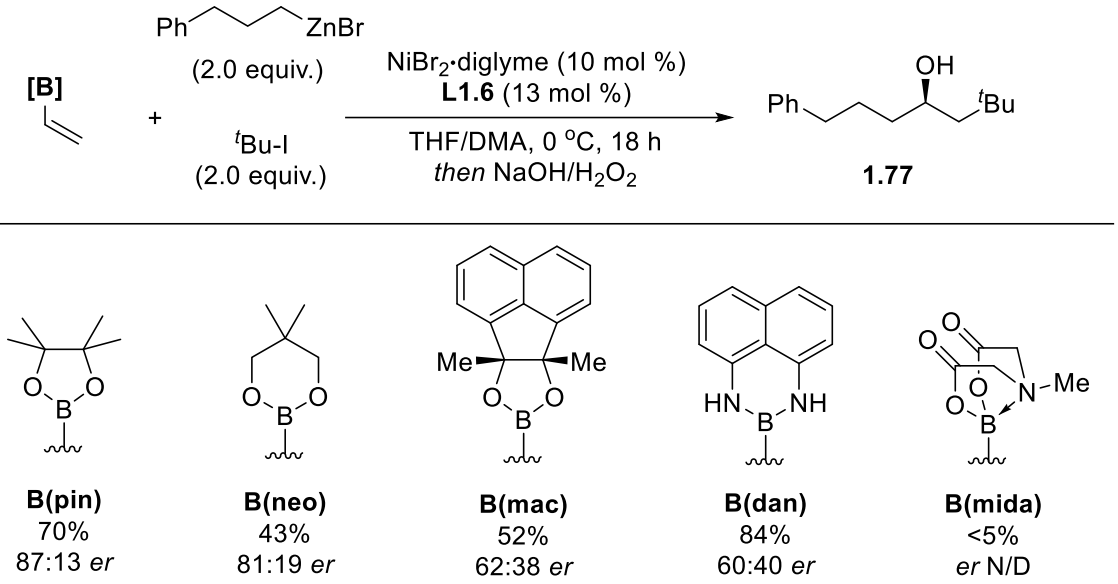




tridentate (**L1.9**, **L1.10**) ligands yielded the desired product, but none of them provided comparable enantioselectivity provided by diamine ligand **L1.6**. *o*-Tolyl diamine ligand **L1.5** used by Fu in stereoconvergent Negishi cross-coupling of α-boryl halides[41] didn't have a significant effect on the enantioselectivity but resulted in a lower yield.

To further improve the reaction, we studied the effect of boron species (Scheme 1.30). Vinyl boronates equipped with diol ligands such as neopentyl glycol (**B(neo)**) and mac-diol (**B(mac)**) developed by our group[43] resulted in low yields and enantioselectivities, suggesting the important effect of the steric profile of the ligand on the reaction. The electron-rich nitrogen-based vinyl**B(dan)** provided much higher yield but low enantioselectivity. When a four-coordinate vinyl**B(mida)** was used, we observed full

Scheme 1.30. Effect of Ligands on Boron



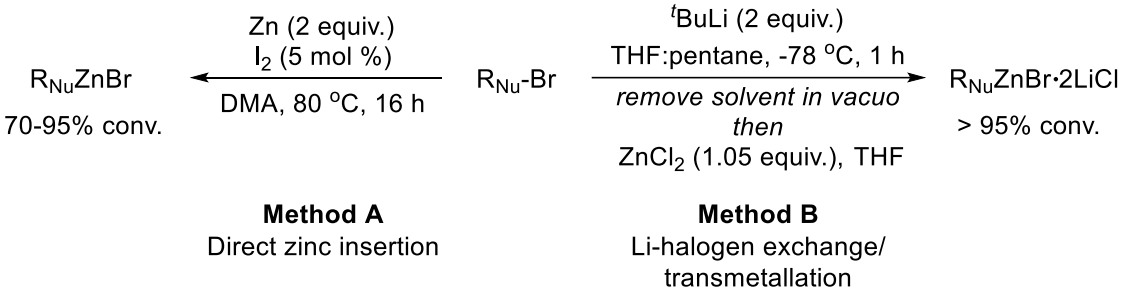
recovery of the vinyl boron after quenching, which suggested that the radical addition was suppressed. This observation indicated the importance of an empty p-orbital on boron which provides reactivity by stabilizing the α-boryl radical.

(43) (a) Myhill, J. A.; Wilhelmsen, C. A.; Zhang, L.; Morken, J. P. *J. Am. Chem. Soc.* **2018**, *140*, 15181–15185. (b) Meng, Y.; Kong, Z.; Morken, J. P. *Angew. Chem. Int. Ed.* **2020**, *59*, 8456–8459. (c) Koo, S. M.; Vendola, A. J.; Momm, S. N.; Morken, J. P. *Org. Lett.* **2020**, *22*, 666–669. (d) Zhang, C.; Hu, W.; Lovinger, G. J.; Jin, J.; Chen, J.; Morken, J. P. *J. Am. Chem. Soc.* **2021**, *143*, 14189–14195. (e) Wilhelmsen, C. A.; Zhang, X.; Myhill, J. A.; Morken, J. P. *Angew. Chem. Int. Ed.* **2022**, *61*, 1–5.

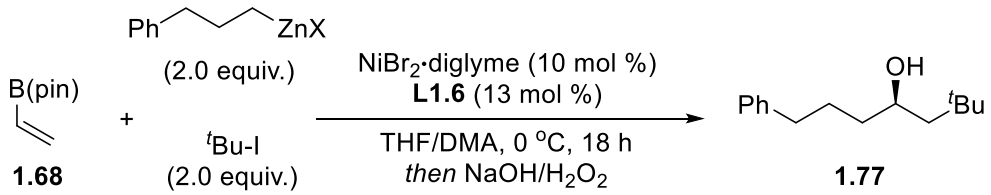
We also considered that the source of organozinc reagent might also have an effect on the reactivity. Alkylzinc reagents could be synthesized from the corresponding alkyl bromide by two distinct methods (Scheme 1.31a). Vacuum-dried and ground zinc powder when activated by iodine, could directly insert into alkyl bromide upon heating in DMA (**Method A**), yielding alkylzinc reagent solution with 70-95% conversion (determined by

Scheme 1.31. Effect of Composition of Zinc Reagents and Additives

a) **Methods to generate zinc reagents:**



b) **Effect of composition of zinc reagent and additives**



Entry	Zinc reagent	Yield(%)	*er*
1	$Ph(CH_2)_3ZnBr$ **(Method A)**	70	87:13
2	$Ph(CH_2)_3ZnBr{\cdot}2LiCl$ **(Method B)**	53	95:5
3	$Ph(CH_2)_3ZnBr$ **(Method A)**+ 2LiCl	52	94:6

titration with iodine[44]). Alternatively, organozinc reagents could be synthesized via lithium halogen exchange and subsequent transmetallation with zinc chloride (**Method B**). Organozinc reagents generated from **Method B** provided diminished yield but significantly

(44) Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, *5*, 890–891.

higher enantioselectivity (Scheme 1.31b, entry 2). The effect might stem from the different salt composition of the zinc reagent. To probe this hypothesis, a control experiment was conducted by pre-mixing lithium chloride and the organozinc reagent generated *via* **Method A** (entry 3). A similar result to the reaction in entry 2 was obtained.

The results above pointed to the effect of lithium chloride salt in enhancing the enantioselectivity of the dicarbofunctionalization reaction, but the reason behind this effect was unclear. It is known that lithium chloride salt increases the nucleophilicity of organozinc reagents by forming organozinc 'ate' complexes $[R_{Nu}ZnX_2]Li$.[45] However, this effect should only influence the transmetallation step, which is proposed to occur before the generally accepted stereodetermining reductive elimination step.[46] Alternatively, the lithium chloride additive could affect the enantioselectivity in other ways. For example, during the stereodetermining step, the lithium cation could bind to the oxygen on boronate, or the chloride anion could ligate to the nickel catalyst, changing the steric profile around the organonickel complex thereby leading to a different stereochemical outcome.

1.3.2. Scope of three-component radical addition/cross-coupling cascade

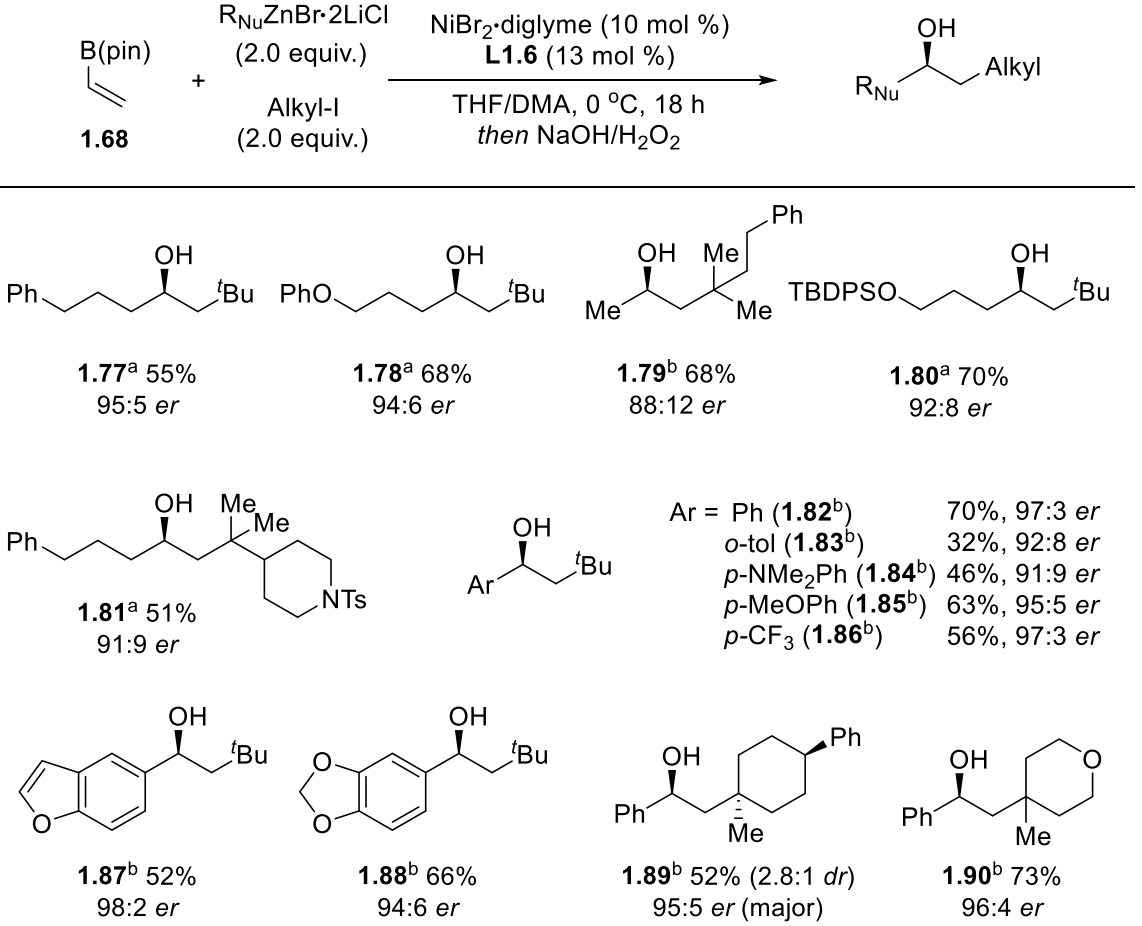
With optimized conditions in hand, we investigated the scope of the dicarbofunctionalization of vinylB(pin) with tertiary iodide electrophiles and organozinc reagents in the presence of lithium chloride salt (Scheme 1.32). Alkylzinc reagents bearing

(45) (a) Fleckenstein, J. E.; Koszinowski, K. *Organometallics* **2011**, *30*, 5018–5026. (b) Zhang, G.; Li, J.; Deng, Y.; Miller, J. T.; Kropf, A. J.; Bunel, E. E.; Lei, A. *Chem. Commun.* **2014**, *50*, 8709–8711. (c) Jess, K.; Kitagawa, K.; Tagawa, T. K. S.; Blum, S. A. *J. Am. Chem. Soc.* **2019**, *141*, 9879–9884. (d) Huang, L.; Ackerman, L. K. G.; Kang, K.; Parsons, A. M.; Weix, D. J. *J. Am. Chem. Soc.* **2019**, *141*, 10978–10983.

(46) Diccianni, J.; Lin, Q.; Diao, T. *Acc. Chem. Res.* **2020**, *53*, 906–919.

phenoxy (**1.78**) and silyl ether (**1.80**) could be incorporated as nucleophiles, and a simple methylzinc reagent could be used (**1.79**). In terms of aryl nucleophiles, phenyl zinc reagent was prepared from commercially available phenyllithium solution, and the other aryl zinc reagents (**1.82–1.86**) were made from aryl bromides via lithium halogen exchange. Arenes

Scheme 1.32. Scope of Three-Component Radical Addition/Cross-Coupling Cascade

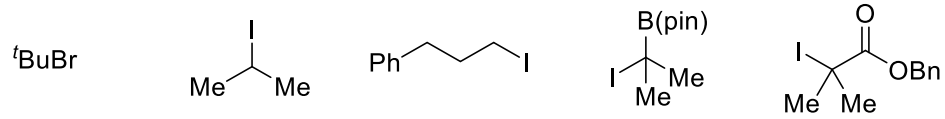


a) Zinc reagent obtained from direct zinc insertion and adding LiCl (2 equiv.);
b) Zinc reagent obtained from addition of RLi to $ZnCl_2$.

bearing either electron-withdrawing (**1.86**) or electron-donating groups (**1.84**, **1.85**, **1.87**, **1.88**) could be incorporated in the reaction. Different tertiary iodides work in the reaction, including those bearing protected amine (**1.81**) and ether (**1.90**) functional groups. The

diastereoselective production of **1.89** showed the possibility for a diastereoselective radical addition *via* substrate control.

Scheme 1.33. Ineffective Electrophiles



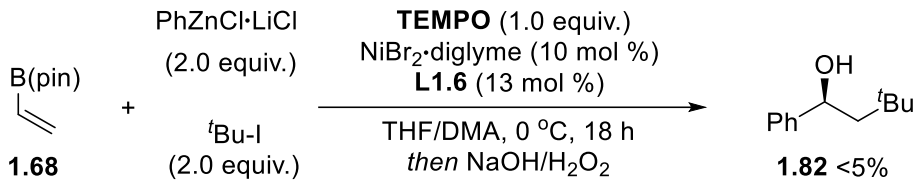
1.91	**1.92**	**1.93**	**1.94**	**1.95**
< 5%	20%	< 5%	< 5%	< 5%

A range of electrophiles other than non-activated tertiary iodides were examined, but those resulted in low reactivity. Tertiary bromide **1.91** did not participate in the reaction, presumably due to its lower tendency to undergo halogen atom abstraction.[14] Use of secondary electrophile **1.92** resulted in greatly diminished yield, and when primary iodide **1.93** was employed, no product was detected. Tertiary iodides bearing electron-withdrawing groups such as boronic ester (**1.94**) and carbonyl (**1.95**) failed to participate in the reaction, suggesting that radical polar mismatching between electron-poor vinylB(pin) with electron-poor radicals was detrimental to the reaction.

1.3.3. Mechanistic studies

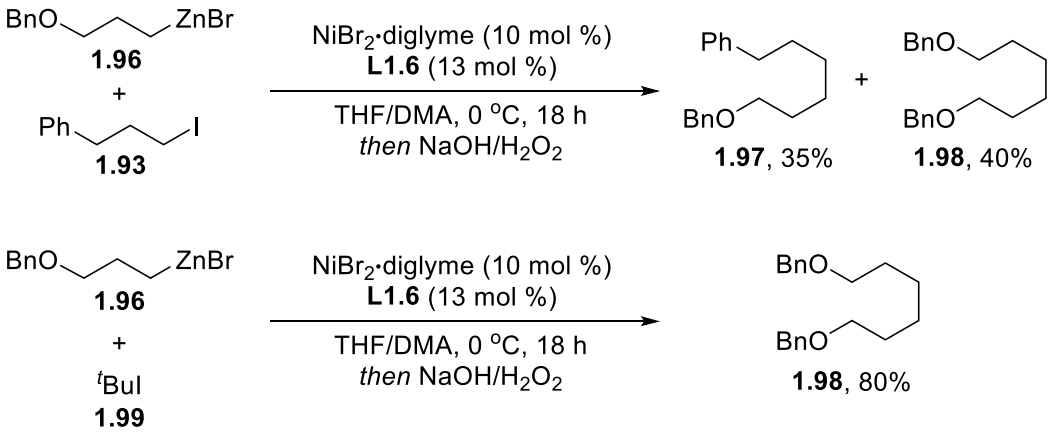
After investigation of the scope of the tandem cross-coupling, we were interested in unraveling the mechanism of the reaction. First, we found that adding a radical scavenger TEMPO to a standard reaction resulted in complete inhibition of the reaction, suggesting the existence of a radical intermediate.

Scheme 1.34. Radical Scavenger Experiment



We were intrigued by the difference in reactivity between primary and tertiary iodides. The inefficient reaction using primary iodides could stem from a slow radical generation *via* SET, or it could arise from unproductive side reactions. To investigate this, we studied the background reaction in the absence of vinylB(pin) (Scheme 1.35). When primary iodide **1.93** was subjected to the reaction with alkylzinc bromide **1.96**, we observed direct Negishi cross-coupling product **1.97** in 35% yield, as well as the homocoupling product of the nucleophile (**1.98**). On the other hand, when tertiary iodide **1.99** was subjected to the same reaction, only homocoupling product **1.98** was observed, and the tertiary iodide only served as the oxidant to regenerate the nickel catalyst.

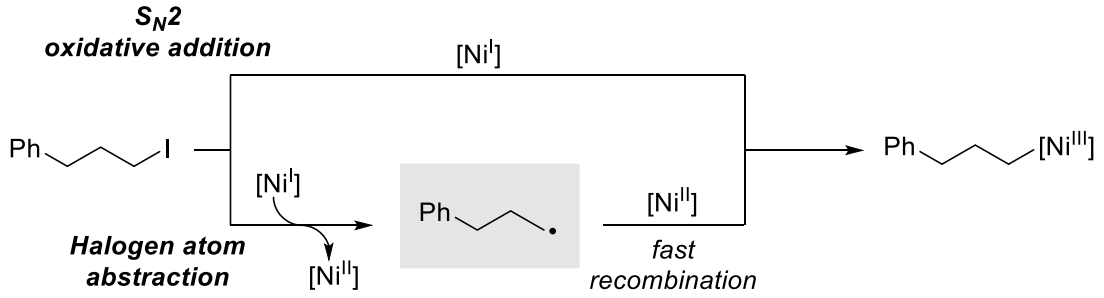
Scheme 1.35. Background Reaction Studies



These results indicate that primary iodides could undergo oxidative addition to form alkylnickel complexes that lead to direct cross-coupling product, while tertiary iodides do

not. This outcome may arise from the different steric profile of the two electrophiles. The oxidative addition could occur *via* two pathways (Scheme 1.36), either a S_N2 mechanism, or a halogen atom abstraction by the Ni(I) complex, where a primary radical will form first and then swiftly recombines with the Ni(II) catalyst to form the oxidative addition product. The key difference between these two mechanisms is whether a radical intermediate is present.

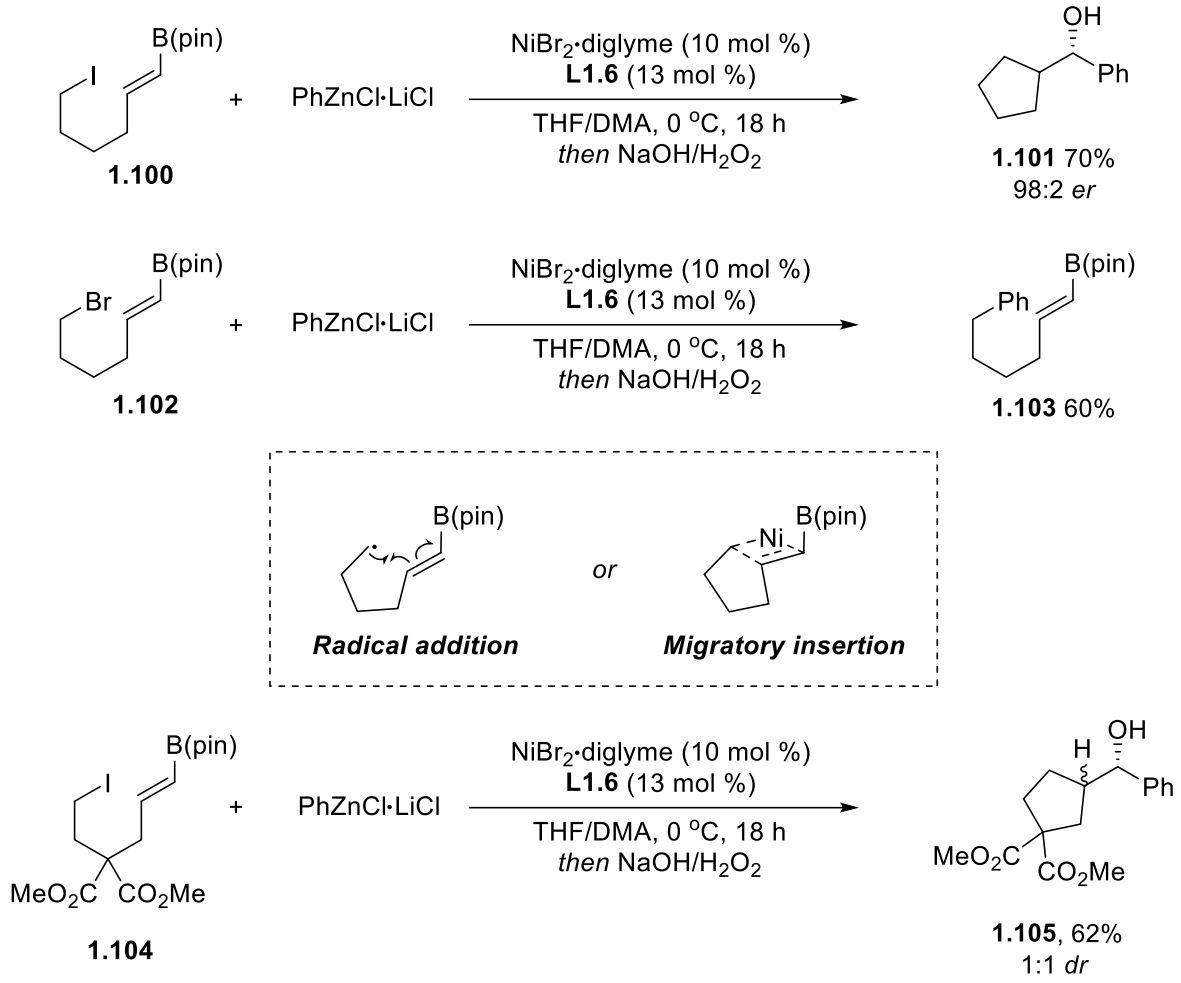
Scheme 1.36. Pathways for Oxidative Addition of Primary Radicals



In order to probe this, we synthesized a radical clock molecule **1.100** with tethered alkenyl B(pin) and primary iodide, and subjected it to the reaction conditions (Scheme 1.37). Cyclization product **1.101** formed in good yield and enantioselectivity after the reaction. Interestingly, probe molecule **1.102** with an alkyl bromide resulted in direct Negishi cross-coupling product **1.103** instead of cyclization. The cyclization could go through 2 pathways: an outer-sphere radical 5-exo-trig cyclization to form α-boryl radical or an inner-sphere migratory insertion by an alkylnickel complex. To distinguish between these two mechanisms, probe molecule **1.104** was subjected to the reaction conditions, and the cyclization step happened with no diastereomeric control. We reasoned that the involvement of a nickel catalyst bearing a chiral ligand was unlikely, and a radical intermediate could be present in the oxidative addition of a primary iodide. The rate of the

intramolecular cyclization was higher so that it happened before recombination of the radical with Ni.

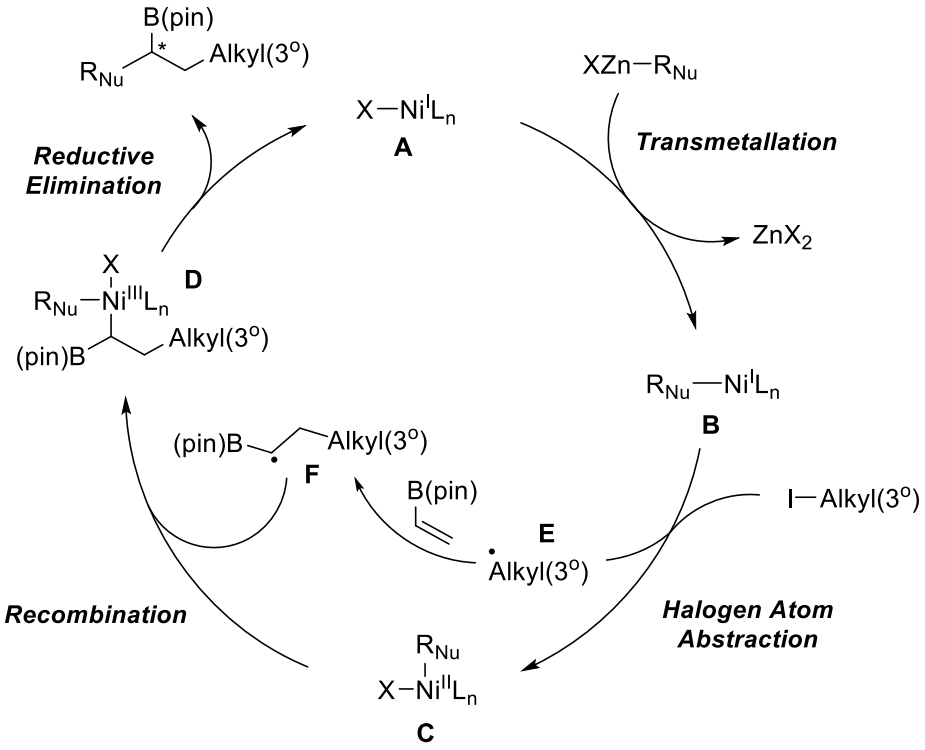
Scheme 1.37. Cyclizing Probe Experiment



Based on the mechanism studies above and literature reports[9,41], we proposed a catalytic cycle as shown in Scheme 1.38. Ni(I) species **A** would undergo transmetallation with an organozinc reagents to form organonickel complex **B**, which could generate tertiary radical **E** through halogen atom abstraction and be oxidized to Ni(II) complex **C**. The radical **E**

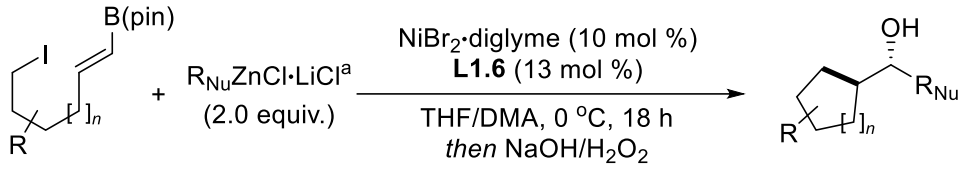
would add to vinylB(pin) and form α-boryl radical **F**. Recombination with Ni(II) complex **C** followed by reductive elimination would yield the three-component tandem cross-coupling product. Of note, the order of basic steps in the proposed mechanism could be exchanged, and Ni(I) complex **A** bearing a halide ligand had a chance to undergo SET before transmetallation with the organozinc reagent. Also, the possibility could not be excluded that α-boryl radical **F** could directly undergo radical substitution with Ni(II) species **C** to form the product and regenerate Ni(I) complex **A**, without going through Ni(III) complex **D**. Further studies were required to further elucidate the mechanistic details.

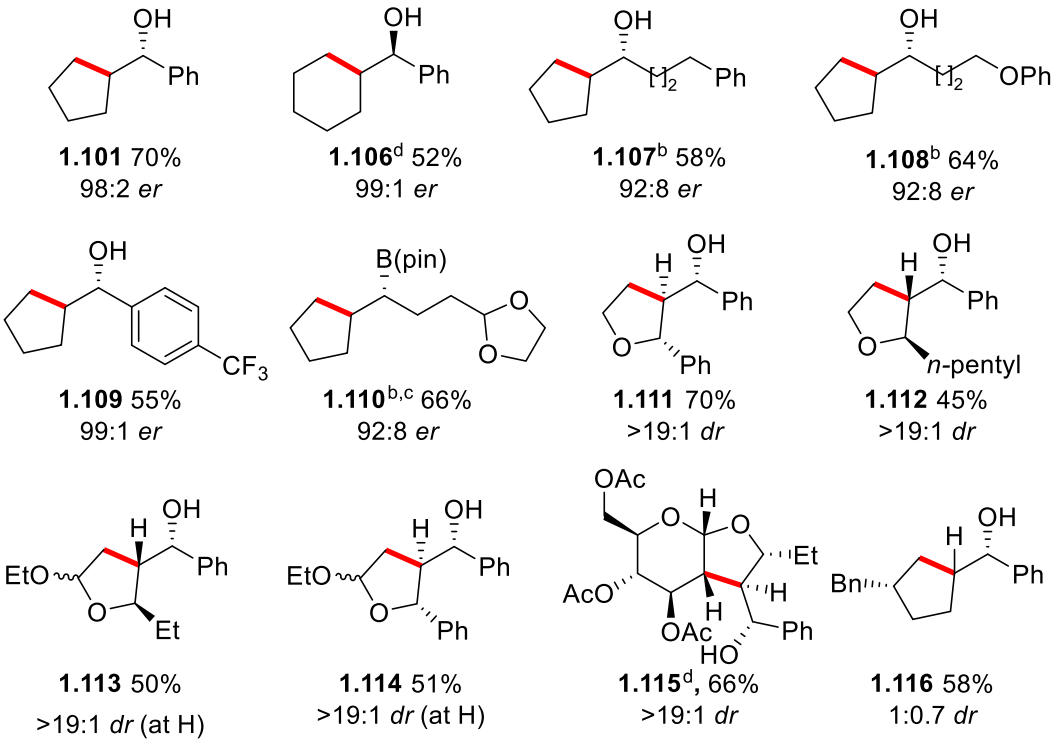
Scheme 1.38. Proposed Mechanism



1.3.4. Scope of Intramolecular Cyclization/Cross-Coupling Reaction

Scheme 1.39. Scope of Intramolecular Cyclization/Cross-Coupling Reaction





1.101 70%
98:2 *er*

1.106[d] 52%
99:1 *er*

1.107[b] 58%
92:8 *er*

1.108[b] 64%
92:8 *er*

1.109 55%
99:1 *er*

1.110[b,c] 66%
92:8 *er*

1.111 70%
>19:1 *dr*

1.112 45%
>19:1 *dr*

1.113 50%
>19:1 *dr* (at H)

1.114 51%
>19:1 *dr* (at H)

1.115[d], 66%
>19:1 *dr*

1.116 58%
1:0.7 *dr*

a) Unless otherwise noted, zinc reagent were obtained from addition of RLi to $ZnCl_2$;
b) Zinc reagent obtained from direct zinc insertion of alkyl bromide;
c) Boronic ester isolated because alcohol deriviative was unstable;
d) Reaction conducted using *R,R*-**L1.6** ligand.

The intramolecular radical cyclization reaction uncovered through the mechanistic studies expanded the utility of the tandem cross-coupling reaction. Using this process, we can synthesize 5- or 6-membered rings (**1.101**, **1.106**) bearing an exocyclic boronic ester in good enantioselectivity. A variety of aryl- (**1.109**) or alkylzinc (**1.107**, **1.108**, **1.110**) reagents could be employed. To further exploit the synthetic utility of this method, we

synthesized a series of enantiomerically enriched compounds that could potentially lead to diastereoselective radical cyclization. Intramolecular tandem cross-coupling reactions resulted in a range of complex structures (**1.111**-**1.116**) with multiple defined stereogenic centers *via* a combination of substrate and ligand control.

1.3.5. Conclusion

In this chapter, a new method for the enantioselective synthesis of secondary alkyl boronic esters was discussed, which was accomplished by dicarbofunctionalization of alkenyl boronates *via* a nickel-catalyzed radical addition/cross-coupling cascade. Intermolecular reaction between tertiary iodides, vinylB(pin) and organozinc reagents provided a modular method for the construction of linear alkyl boronate motifs, and intramolecular reaction allowed the rapid buildup of cyclic scaffolds with cyclic boron-containing stereogenic centers. Mechanistic studies revealed the existence of a radical intermediate, and a catalytic cycle was proposed involving radical addition to alkenyl boron followed by recombination with nickel catalyst.

1.4 Experimental

1.4.1. General Information

1H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, app = apparent), and coupling constants (Hz). 13C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), Varian Gemini-600 (150 MHz) or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). 11B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) spectrometer. Chemical shifts are reported in ppm using boron trifluoride diethyl etherate as the external standard ($BF_3{\bullet}O(C_2H_5)_2$: 0.0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm-1) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 x 450 Mesh) purchased from Silicycle, or with a Biotage Isolera One equipped with full wavelength scan. Thin layer chromatography (TLC) was performed on 25 μm silica gel aluminum backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm),

ceric ammonium molybdate in water/sulfuric acid (CAM), phosphomolybdic acid in ethanol (PMA), phosphomolybdic acid and cerium sulfate in water/sulfuric acid (Seebach), or potassium permanganate ($KMnO_4$). Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol as the modifier.

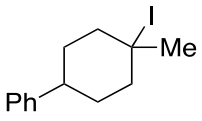
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. N, N-dimethyl acetamide (DMA) was purchased from Sigma Aldrich, distilled over 4Å molecular sieves under reduced pressure and stored under argon atmosphere. Nickel(II) dibromide glyme was purchased from STREM. (*S*,*S*)-N,N′-dimethyl-1,2-diphenylethane-1,2-diamine **L1.6** (as well as (*R*,*R*)-**L1.6** and racemic **L1.6**) was synthesized from the corresponding commercially available (S,S)-1,2-diphenylethylenediamine (Oakwood Chemicals) following literature methods.[47] All other reagents were purchased from Sigma Aldrich, Alfa Aesar, Oakwood Chemicals, Combi-Blocks, or Acros Organics and used without further purification.

(47) Kuznetsov, V. F.; Jefferson, G. R.; Yap, G. P. A.; Alper, H. *Organometallics* **2002**, *21*, 4241–4248.

1.4.2. Experimental Procedures

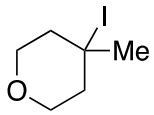
1.4.2.1. Procedure for Preparation of Tertiary Alkyl Iodides

The corresponding tertiary alcohol (1.0 equiv.) and sodium iodide (2.0 equiv.) were dissolved in acetonitrile and cooled to 0º C. Methanesulfonic acid (2 equiv.) was added dropwise to the reaction mixture, which was then warmed to room temperature and stirred for an additional 30 minutes. Minimizing light exposure, the mixture was then concentrated on a rotary evaporator, re-dissolved in diethyl ether and washed with aqueous saturated $NaHCO_3$ solution followed by a wash with saturated $Na_2S_2O_3$. The organic layer was dried over $MgSO_4$ and concentrated. Purification by silica gel column chromatography was generally carried out rapidly (prolonged residence on the stationary phase resulted in H-I elimination). The compounds were stored in a freezer in the dark under N_2 atmosphere.

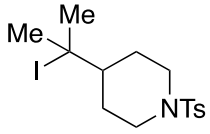


(4-iodo-4-methylcyclohexyl)benzene (SI-1). The title compound was obtained through the general procedure from the corresponding alcohol 1-methyl-4-phenylcyclohexan-1-ol (1.08 g, 5.7mmol). The product was isolated by silica gel chromatography (pentane, stain in CAM) to afford a white solid (1.4 g, 82% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.42-7.17 (m, 5H), 2.51 (tt, *J* = 12.4, 3.8 Hz, 1H), 2.29-2.23 (m, 2H), 2.19 (s, 3H), 2.10-1.98 (m, 2H), 1.88 (dd, *J* = 14.2, 3.7 Hz, 2H), 1.07 (ddd, *J* = 15.4, 12.4, 3.6 Hz, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 146.7, 128.6, 127.1, 126.3, 58.6, 46.1, 43.7, 39.6, 32.8. **IR** (neat) ν_{max} 2952.20 (m), 2905.07 (m), 2853.6 (m), 1463.3 (w),

1441.3 (w), 1102.4 (s), 1013.6 (s), 979.7 (s), 775.6 (s), 614.3 (s), 476.6 (s). **HRMS** (DART) for $C_{13}H_{17}$ $(M+H-HI)^+$: Calc'd: 173.1325, found: 173.1318.

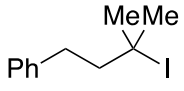


4-iodo-4-methyltetrahydro-2*H*-pyran (SI-2). The title compound was obtained through the general procedure from the corresponding alcohol 1-methyl-4-phenylcyclohexan-1-ol (780 mg, 6.7 mmol). The product was isolated by silica gel chromatography (1% ethyl acetate in pentane, stain in CAM) to afford a clear yellow oil (986 mg, 67% yield). Clear yellow liquid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.95-3.88 (m, 2H), 3.77-3.69 (m, 2H), 2.15 (s, 3H), 2.03 (dd, *J* = 14.7, 2.3 Hz, 2H), 1.31 (ddd, *J* = 15.1, 10.8, 4.4 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 66.4, 52.9, 44.9, 39.1. **IR** (neat) ν_{max} 2952.2 (m), 2905.0 (m), 2853.6 (m), 1463.3 (w), 1441.3 (w), 1102.4 (s), 1013.6 (s), 979.7 (s), 775.6 (s), 614.3 (s), 476.6 (s). **HRMS** (DART) for $C_6H_{22}OI$ $(M+H)^+$: Calc'd: 226.9922, found: 226.9927.



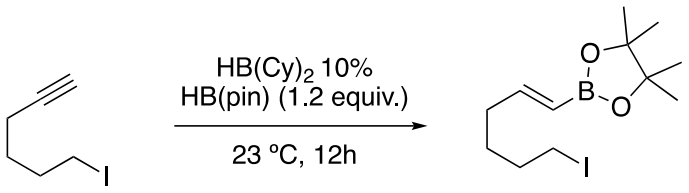
4-(2-iodopropan-2-yl)-1-tosylpiperidine (SI-3). The title compound was synthesized from the corresponding alcohol (2-(1-tosylpiperidin-4-yl)propan-2-ol) which was obtained in turn through standard procedures starting from commercially available ethyl isonipecotate. All spectral data was in accordance with the literature.[48]

(48) Soulard, V.; Villa, G.; Vollmar, D. P. *J. Am. Chem. Soc.* **2018**, *140*, 155–158.



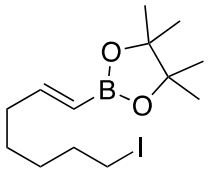
(3-iodo-3-methylbutyl)benzene (SI-4). The title compound was synthesized from the corresponding alcohol 2-methyl-4-phenylbutan-2-ol. All spectral data was in accordance with the literature.[49]

1.4.2.2 Procedure for Preparation of Cyclizing Substrates

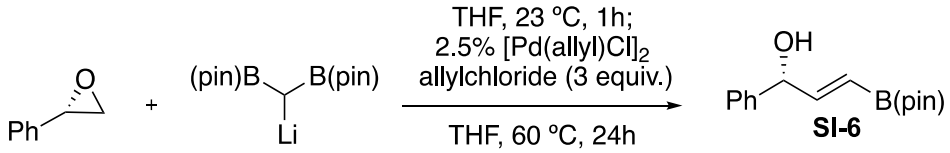


(*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.100). In the glovebox, a 2-dram vial was charged with neat 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.88 g, 22.5 mmol, 1.2 equiv.) and dicyclohexylborane (333.9 mg, 1.87 mmol, 0.10 equiv.). The vial was cooled inside the glovebox freezer for 30 min and 6-iodohex-1-yne (3.90 g, 18.8 mmol, 1.0 equiv.) was added to the cold mixture. The vial was sealed and the mixture was stirred for 12 hours at room temperature. The reaction mixture was quenched by bubbling air through the solution for 2 h at room temperature. to oxidize the dicyclohexylborane. The resulting mixture was diluted with hexanes, washed with water, dried over Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel with 2% ethyl acetate in hexanes as eluent (5.32 g, 84% yield). All spectra for the isolated product was in accordance with the literature.[50]

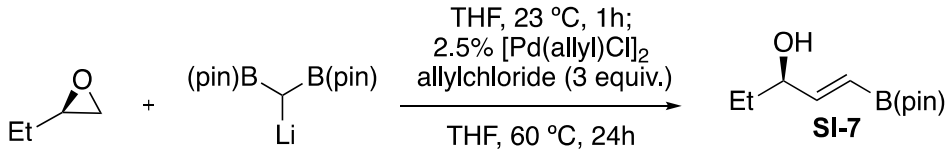
(49) Zhao, S.; Mankad, N. P. *Angew. Chem. Int. Ed.* **2018**, *57*, 5867–5870.
(50) Guennouni, N.; Lhermitte, F.; Cochard, S.; Carboni, B. *Tetrahedron* **1995**, *51,* 6999–7018.



(*E*)-2-(7-iodohept-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SI-5) was synthesized using the same procedure as for substrate **1.100** from 7-Iodohept-1-yne. The crude product was isolated by silica gel chromatography (2% ethyl acetate in hexanes, stain in CAM), as a colorless oil (78% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.59 (dt, *J* = 17.9, 6.4 Hz, 1H), 5.42 (dt, *J* = 17.9, 1.4 Hz, 1H), 3.16 (t, *J* = 7.1 Hz, 2H), 2.15 (q, *J* = 6.6 Hz, 2H), 1.81 (p, *J* = 7.1 Hz, 2H), 1.47-1.34 (m, 4H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.0, 83.2, 35.6, 33.5, 30.2, 27.2, 24.9, 6.9. **IR** (neat) ν_{max} 2974.1 (w), 2926.4 (w), 2853.3 (w), 1636.4 (m), 1359.4 (s), 1317.2 (s), 1143.0 (s), 994.9 (w), 969.2 (w), 848.5 (w). **HRMS** (DART) for $C_{13}H_{25}BO_2I$ $(M+H)^+$: Calc'd: 351.0987, found: 351.0967.

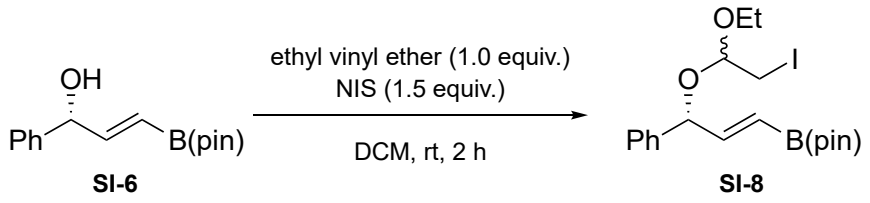


(*R*,*E*)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-ol (SI-6) was generated from commercial (*S*)-styrene oxide following the method reported by Meek.[51] All spectral data matched previously published results.



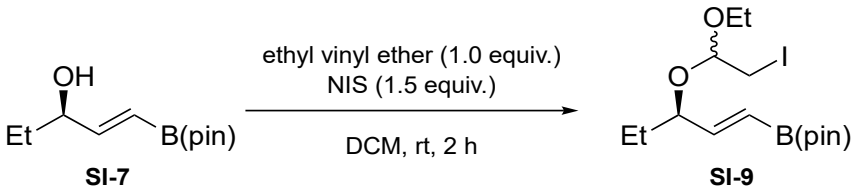
(51) Murray, S. A.; Luc, E. C. M.; Meek, S. J. *Org. Lett.* **2018**, *20*, 469–472.

(*R,E*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-3-ol (SI-7) was generated from commercial (*R*)-1,2-epoxybutanestyrene (434 mg, 6.00 mmol, 1.0 equiv.) following the method reported by Meek.[5] The product was isolated by silica gel column chromatography (15% ethyl acetate in hexanes, stain in CAM) as a colorless oil (1.27 g, 77 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.59 (dd, *J* = 18.1, 5.3 Hz, 1H), 5.60 (d, *J* = 18.1 Hz, 1H), 4.06 (brs, 1H), 1.77 (brs, 1H), 1.55 (dt, *J* = 21.1, 14.3, 7.4 Hz, 2H), 1.25 (s, 12H), 0.92 (t, *J* = 7.5 Hz, 3H).**^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.1, 117.7, 83.4, 75.1, 29.5, 24.8, 9.7. **IR** (neat) ν_{max} 3432.2 (br), 2974.1 (w), 2928.7 (w), 2874.5 (w), 1640.5(m), 1356.0 (s), 1317.8 (s), 1142.4 (s), 997.0 (m), 965.7 (m), 898.8 (m), 647.3 (w). **HRMS** (DART) for $C_{11}H_{25}BNO_3$ $(M+NH_4)^+$: Calc'd: 230.1922, found: 230.1926. **$[\alpha]_D^{20}$** = -12.40 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).



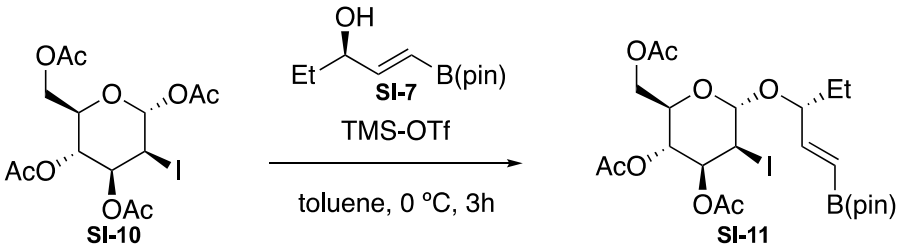
2-((*3R,E*)-3-(1-ethoxy-2-iodoethoxy)-3-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SI-8). A mixture of **SI-6** (156.1 mg, 0.6 mmol) and ethyl vinyl ether (43.3 mg, 0.6 mmol) in CH_2Cl_2 (10 mL) was added to a suspension of N-iodosuccinimide (202.5 mg, 0.9 mmol) in CH_2Cl_2 (10 mL) at 0 °C over 5 minutes. After stirring at room temperature for 2 hours, water (10 mL) was added, and the stirring was continued for one additional hour. The layers were separated, and the aqueous layer was extracted with

CH_2Cl_2 (2×15 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (10% ethyl acetate in hexanes, stain in CAM) afforded **SI-8** as a 1:1 mixture of diastereomers (clear yellow oil, 0.21 g, 77% yield).**^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36-7.26 (m, 10H), 6.66 (ddd, *J* = 39.0, 18.0, 5.8 Hz, 2H), 5.69 (t, *J* = 19.2, 19.2 Hz, 2H), 5.14 (dd, *J* = 18.9, 5.8 Hz, 2H), 4.78 (t, *J* = 5.5, 5.5 Hz, 1H), 4.56 (t, 1H), 3.79-3.69 (m, 2H), 3.60-3.52 (m, 3H), 3.43 (dq, *J* = 9.0, 7.1, 7.1, 6.9 Hz, 1H), 3.23-3.18 (m, 4H), 1.86-1.84 (m, 2H), 1.25 (d, *J* = 6.7 Hz, 24H), 1.20 (t, *J* = 7.0, 7.0 Hz, 3H), 1.13 (t, *J* = 7.0, 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 152.0, 151.6, 140.4, 139.5, 128.6, 128.5, 128.2, 127.9, 127.7, 127.1, 100.2, 99.4, 83.5, 83.4, 80.1, 79.8, 68.0, 61.7, 61.2, 25.7, 24.9, 24.9, 24.9, 15.2, 15.1, 5.9, 5.6. **IR** (neat) ν_{max} 2973.5 (m), 2925.1 (w), 1636.7 (m), 1352.8 (s), 1323.0 (s), 1266.5 (w), 1141.2 (s), 1107.9 (m), 1055.3 (m), 994.4 (s), 968.5 (s), 847.3 (m), 759.1 (m), 698.2 (m), 658.9 (w). **HRMS** (DART) for $C_{19}H_{32}BNO_4I$ $(M+NH_4)^+$: Calc'd: 476.1464, found: 476.1463.



2-((*3R,E*)-3-(1-ethoxy-2-iodoethoxy)pent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3-dioxolane (SI-9) was synthesized using the same procedure for the synthesis of **SI-8** using **SI-7** (200 mg, 0.94 mmol, 1 equiv**.)** as starting material. The product consisting of a 1:1 inseparable mixture of diastereomers was isolated by silica gel chromatography (10% ethyl

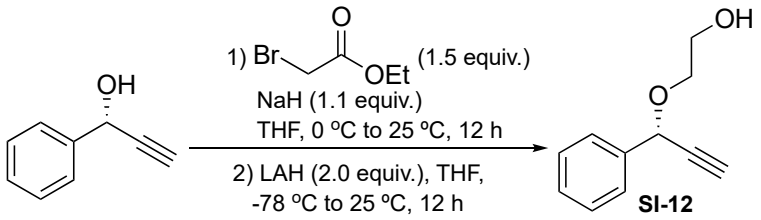
acetate in hexanes, stain in CAM) as a clear yellow oil (240 mg, 62% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.46 (ddd, *J* = 45.5, 18.1, 7.1 Hz, 2H), 5.58 (dd, *J* = 18.2, 2.9 Hz, 2H), 4.59 (dt, *J* = 14.7, 5.6, 5.6 Hz, 2H), 3.99 (q, *J* = 6.7, 6.7, 6.7 Hz, 1H), 3.88 (q, *J* = 6.5, 6.5, 6.5 Hz, 1H), 3.69-3.44 (m, 4H), 3.20 (dt, *J* = 5.0, 2.9, 2.9 Hz, 4H), 1.70-1.50 (m, 5H), 1.32-1.24 (m, 24H), 1.22 (t, *J* = 7.0, 7.0 Hz, 3H), 1.17 (t, *J* = 7.0, 7.0 Hz, 3H), 0.92 (t, *J* = 7.5, 7.5 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.1, 152.4, 100.9, 99.6, 83.5, 83.4, 81.2, 80.5, 62.2, 61.5, 28.2, 27.8, 25.0, 24.9, 24.9, 24.8, 15.3, 15.0, 9.8, 9.7, 6.3, 6.3. **IR** (neat) ν_{max} 2972.9 (m), 2927.8 (w), 2874.6 (w), 1639.6 (m), 1365.7 (s), 1323.9 (s), 1141.9 (s), 1101.4 (s), 1047.4 (s), 998.4 (s), 968.6 (s), 847.9 (m), 648.5 (w), 577.4 (w). **HRMS** (DART) for $C_{15}H_{32}BNO_4I$ $(M+NH_4)^+$: Calc'd: 428.1464, found: 428.1467.



(2*R*,3*R*,4*S*,5*S*,6*S*)-2-(acetoxymethyl)-5-iodo-6-(((*R*,*E*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-3-yl)oxy)tetrahydro-2*H*-pyran-3,4-diyl diacetate (SI-11) was synthesized starting from (2*R*,3*S*,4*S*,5*R*,6*R*)-6-(acetoxymethyl)-3-iodotetrahydro-2*H*-pyran-2,4,5-triyl triacetate (**SI-10**) (1.07 g, 2.34 mmol, 1.1 equiv.) and **SI-7** (452 mg, 2.13 mmol, 1.0 equiv.) following the method described by Wan.[52] The crude product was

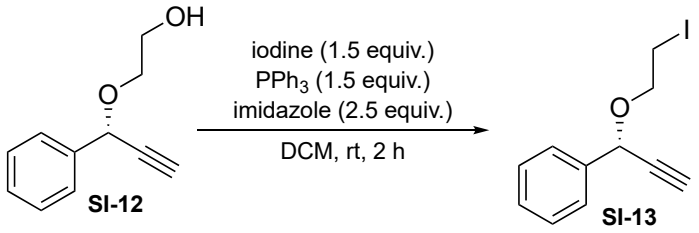
(52)Wang, H.; Tao, J.; Cai, X.; Chen, W.; Zhao, Y.; Xu, Y.; Yao, W.; Zeng, J.; Wan, Q. *Chem. Eur. J.* **2014**, *20*, 17319–17323.

isolated by silica gel chromatography (30% ethyl acetate in hexanes, UV) to afford a white a solid (1.12 g, 86% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.33 (dd, *J* = 18.1, 7.2 Hz, 1H), 5.59 (d, *J* = 18.1 Hz, 1H), 5.37 (t, *J* = 9.8 Hz, 1H), 5.16 (s, 1H), 4.66 (dd, *J* = 9.5, 4.3 Hz, 1H), 4.50 (d, *J* = 4.3 Hz, 1H), 4.21 (dd, *J* = 12.2, 5.0 Hz, 1H), 4.16-4.12 (m, 1H), 4.08-4.05 (m, 1H), 3.99 (q, *J* = 6.8 Hz, 1H), 2.11 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 1.72-1.50 (m, 4H), 1.28 (d, *J* = 2.5 Hz, 13H), 0.93 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.8, 169.9, 169.7, 150.4, 98.7, 98.6, 83.6, 80.8, 69.4, 69.2, 67.9, 62.5, 30.4, 28.1, 25.0, 24.9, 24.8, 21.1, 20.9, 20.8, 10.2. **IR** (neat) ν_{max} 2973.9 (m), 2933.1 (m), 1744.3 (s), 1641.1 (m), 1453.5 (w), 1366.3 (m), 1328.9 (w), 1222.2 (s), 1142.9 (s), 1114.6 (s), 1030.7 (s). **HRMS** (DART) for $C_{23}H_{40}BNOI$ $(M+NH_4)^+$: Calc'd: 628.1785, found: 628.1779. **$[\alpha]_D^{20}$** = 47.39 (*c* =1.0, $CHCl_3$, *l* = 50 mm).



(*R*)-2-((1-phenylprop-2-yn-1-yl)oxy)ethan-1-ol (SI-12). Commercial (*R*)-1-phenylprop-2-yn-1-ol (981.0 mg, 7.42 mmol, 1.0 equiv.) was added dropwise to a suspension of sodium hydride (217.6 mg, 8.16 mmol, 90% purity, 1.1 equiv.) in THF (6 mL) at 0 °C. The mixture was warmed to room temperature and stirred for 1 h. After the mixture was cooled to 0 °C, ethyl 2-bromoacetate (1.86 g, 11.13 mmol, 1.5 equiv.) was added dropwise to the mixture. The mixture was warmed to room temperature and stirred for 12 h. The reaction mixture

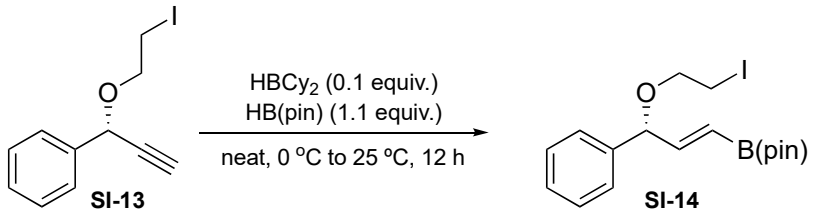
was quenched by saturated NH_4Cl aq. solution (10 mL) and extracted with Et_2O (3 x 20 mL). The combined organic layer was then dried over anhydrous Na_2SO_4. After filtration, the material was concentrated under reduced pressure. The corresponding crude ether was dissolved in THF (20 mL) and added dropwise to a solution of LAH in THF (1 M, 15.0 mL) at −78 °C under a nitrogen atmosphere. The reaction was allowed to warm to room temperature and stir for 12 h, after which it was cooled to 0ºC and quenched by careful addition of H_2O (1.0 mL) and then aqueous NaOH (3 M, 3.0 mL). After stirring at room temperature for 20 min $MgSO_4$ was added to the reaction mixture and the suspension was filtered through celite. The solvent was removed in vacuo and the crude product was purified by flash column chromatography (20% ethyl acetate in hexanes) to obtain **SI-12** (0.78 g, 44% yield over two steps) as a colorless oil. All spectral data is in accordance with the literature.[53]



(*R*)-(1-(2-iodoethoxy)prop-2-yn-1-yl)benzene (SI-13). A solution of triphenylphosphine (1.03 g, 3.92 mmol) and iodine (0.99 g, 3.92 mmol) in dichloromethane (20 mL) was allowed to stir for 10 min at ambient temperature. Imidazole (0.44 g, 6.53 mmol) was added to the resulting mixture. After a 10 min stir, **SI-12** (0.46 g, 2.61 mmol) was added and the resulting mixture was stirred for 2 h. The mixture was quenched by the addition of saturated

(53) Bucher, J.; Wurm, T.; Nalivela, K. S.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Angew. Chem. Int. Ed.* **2014**, *53*, 3854–3858.

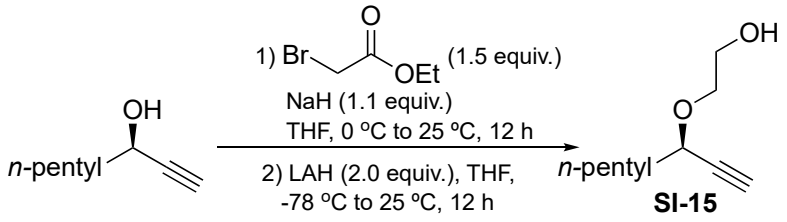
sodium metabisulfite (10 mL). The aqueous and organic layers were separated followed by extraction of the aqueous with dichloromethane (3 x 20 mL). The combined organic extracts were dried (anhydrous Na_2SO_4) and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (5% ethyl acetate in hexanes) to afford the **SI-13** (0.45 g, 60% yield) as a light-yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56-7.54 (m, 2H), 7.44-7.32 (m, 3H), 5.28 (d, *J* = 2.2 Hz, 1H), 3.95-3.89 (m, 1H), 3.84-3.77 (m, 1H), 3.31-3.28 (m, 2H), 2.69 (d, *J* = 2.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 137.7, 128.8, 128.7, 127.5, 81.1, 76.4, 71.4, 68.9, 2.5. **IR** (neat) ν_{max} 3284.2 (m), 3059.1 (w), 3027.0 (w), 2914.6 (w), 2850.9 (w), 1491.4 (w), 1451.3 (m), 1261.2 (m), 1189.5 (w), 1170.2 (w), 1094.3 (s), 1054.1 (s), 1027.2 (m), 990.3 (m), 740.0 (m), 696.4 (s), 652.8 (s). **HRMS** (DART) for $C_{11}H_{12}OI$ $(M+H)^+$: Calc'd: 286.9927, found: 286.9929.



SI-13 SI-14

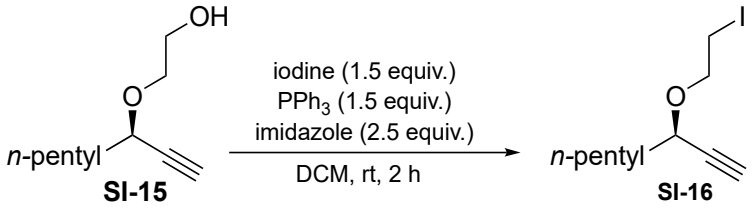
(*R,E*)-2-(3-(2-iodoethoxy)-3-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SI-14). In the glovebox a 2-dram vial is charged with neat dicyclohexylborane (19.1 mg, 0.11 mmol), 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (164.5 mg, 1.30 mmol) and **SI-13** (306.4 mg, 1.1 mmol) was added at 0 °C and the mixture was stirred for a 12 hours at room temperature. The reaction mixture was quenched by bubbling air through the solution with tube pump for 2 hours at room temperature to oxidize the dicyclohexylboryl group. The resulting mixture was diluted with hexane, washed with

water, dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (5% ethyl acetate in hexanes, stain in CAM) to afford the title compound (0.25 g, 56% yield) as a clear yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H, 6.66 (dd, *J* = 18.0, 5.8 Hz, 1H), 5.70 (d, *J* = 17.8 Hz, 1H), 4.86 (d, *J* = 5.7 Hz, 1H), 3.79-3.71 (m, 2H), 3.67-3.63 (m, 1H), 3.28-3.24 (m, 2H), 1.87-1.84 (m, 1H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 151.9, 140.1, 128.7, 128.0, 127.2, 84.0, 83.5, 69.5, 24.9, 3.0. **IR** (neat) ν_{max} 2974.2 (w), 1637.3 (m), 1355.7 (s), 1355.7 (s), 1265.3 (w), 1142.6 (s), 1106.9 (w), 995.4 (w), 969.3 (w), 847.8 (m), 669.2 (m). **HRMS** (DART) for $C_{17}H_{23}BO_3I$ $(M+H)^+$: Calc'd: 413.0779, found: 413.0788. **$[\alpha]_D^{20}$**= 19.11 (*c* =1.0, $CHCl_3$, *l* = 50 mm).

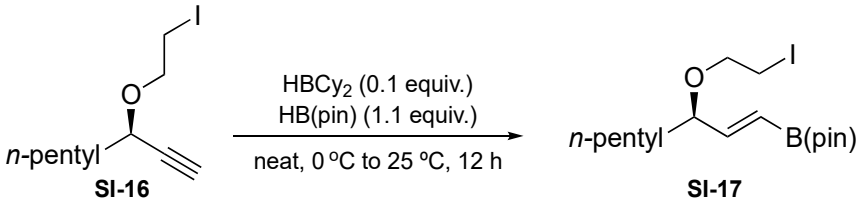


(*R*)-2-(oct-1-yn-3-yloxy)ethan-1-ol (SI-15) was synthesized using the same procedure for the synthesis of **SI-13**, using commercially available (*R*)-oct-1-yn-3-ol. The product was isolated by silica gel chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford a colorless oil (37% yield over two steps). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.08 (td, *J* = 6.7, 6.6, 2.0 Hz, 1H), 3.88-3.83 (m, 1H), 3.80-3.75 (m, 2H), 3.56-3.51 (m, 1H), 2.45 (t, *J* = 1.9, 1.9 Hz, 1H), 1.93 (t, *J* = 6.3, 6.3 Hz, 1H), 1.81-1.69 (m, 2H), 1.50-1.44 (m, 2H), 1.36-1.31 (m, 4H), 0.91 (t, *J* = 7.0, 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 83.0, 74.0,

70.2, 70.1, 62.1, 35.7, 31.6, 25.0, 22.7, 14.1. **IR** (neat) ν_{max} 3423.7 (br), 3306.2 (m), 2950.9 (s), 2927.2 (s), 2858.8 (m), 1460.8 (w), 1333.3 (w), 1105.5 (s), 1070.6 (m), 657.9 (w), 629.3 (w). **HRMS** (DART) for $C_{10}H_{19}O_2$ $(M+H)^+$: Calc'd: 171.1380, found: 171.1376.



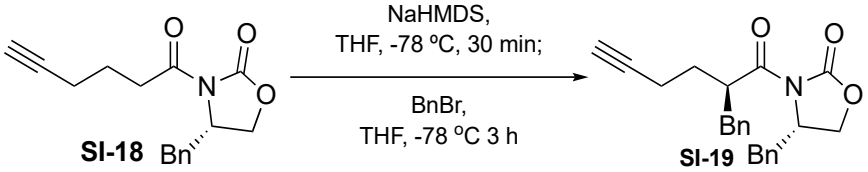
(*R*)-3-(2-iodoethoxy)oct-1-yne was synthesized using the same procedure for the synthesis of **SI-13**. All spectral data is in accordance with the literature.[54]



2-((*R*,*E*)-3-(2-iodoethoxy)oct-1-en-1-yl)-4,4,5-trimethyl-1,3,2-dioxaborolane (SI-17) was synthesized using the same procedure for the synthesis of **SI-14**. Isolated by silica gel chromatography (10% ethyl acetate in hexanes, stain CAM) to afford the product as a clear yellow oil (60% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.42 (dd, *J* = 18.1, 6.6 Hz, 1H), 5.57 (d, *J* = 18.1 Hz, 1H), 3.77-3.71 (m, 2H), 3.58-3.46 (m, 1H), 3.21 (t, *J* = 7.0, 7.0 Hz, 2H), 1.59-1.38 (m, 4H), 1.33-1.22 (d, 16H), 0.87 (t, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ

(54) Iwamoto, H.; Ozawa, Y.; Kubota, K.; Ito, H. *J. Org. Chem.* **2017**, *82*, 10563–10573.

153.2, 83.4, 82.5, 69.7, 35.2, 31.9, 25.2, 24.9, 22.7, 14.2, 3.4. **IR** (neat) ν_{max} 2973.9 (w), 2953.2 (w), 2926.2 (m), 2855.6 (w), 1639.1 (m), 1464.4 (w), 1356.5 (s), 1327.2 (s), 1265.6 (m), 1142.9 (s), 1107.2 (m), 1107.2 (m), 998.2 (m), 968.8 (m), 848.5 (m). **HRMS** (DART) for $C_{16}H_{34}BNO_3I$ $(M+NH_4)^+$: Calc'd: 426.1671, found: 426.1669. $\mathbf{[\alpha]_D^{20}}$ = 26.05 (*c* =1.0, $CHCl_3$, *l* = 50 mm)

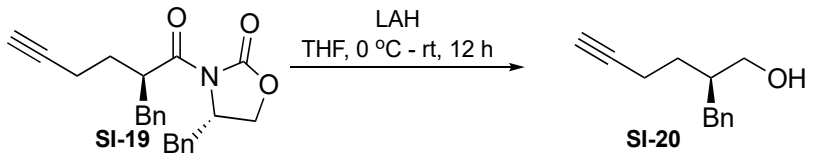


(*S*)-4-benzyl-3-(hex-5-ynoyl)oxazolidin-2-one (SI-18) was synthesized using reported method. All spectral data is in accordance with the literature.[55]

(*S*)-4-benzyl-3-((*R*)-2-benzylhex-5-ynoyl)oxazolidin-2-one (SI-19). In a flame-dried round bottom flask, under an atmosphere of N_2, a solution of sodium bis(trimethylsilyl)amide (11.6 mL, 1.00 M in THF, 11.6 mmol) was further diluted with THF (20 mL) and cooled to -78 °C. To it was added a solution of (4S)-4-benzyl-3-hex-5-ynoyl-oxazolidin-2-one (**SI-18**) (1.8 g, 6.63 mmol) in THF (10 mL) by syringe over 10 min. After stirring for 30 min, benzylbromide (3.40 g, 19.9 mmol) was added neat. The solution was then stirred at -78 ℃ temperature for 2.5 h at which point the reaction was

(55) Moyes, C. R.; Berger, R.; Goble, S. D.; Harper, B.; Shen, D.; Wang, L.; Bansal, A.; Brown, P. N.; Chen, A. S.; Dingley, K. H.; Salvo, J. Di; Fitzmaurice, A.; Gichuru, L. N.; Hurley, A. L.; Jochnowitz, N.; Miller, R. R.; Mistry, S.; Nagabukuro, H.; Salituro, G. M.; San, A.; Stevenson, A. S.; Villa, K.; Zamlynny, B.; Struthers, M.; Weber, A. E.; Edmondson, S. D. *J. Med. Chem.* **2014**, *57*, 1437–1453.

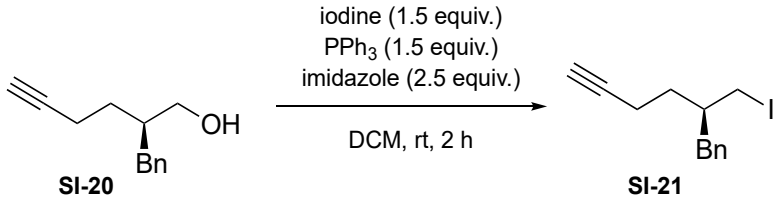
quenched with 100 mL of 0.5 M HCl (aq.). The mixture was extracted with ethyl acetate (50 mL x 2) and the combined organic extracts were washed with water (100 mL), brine (100 mL) and dried over anhydrous Na_2SO_4. The solution was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (15% ethyl acetate in hexanes, UV active) to afford the product as a colorless oil (1.41 g, 59% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34-7.16 (m, 8H), 7.12-7.03 (m, 2H), 4.66-4.62 (m, 1H), 4.39-4.30 (m, 1H), 4.13 (t, *J* = 8.4 Hz, 1H), 4.07 (dd, *J* = 9.0, 2.6 Hz, 1H), 3.13-3.00 (m, 2H), 2.79 (dd, *J* = 13.4, 7.5 Hz, 1H), 2.46 (dd, *J* = 13.4, 9.6 Hz, 1H), 2.25-2.22 (m, 2H), 2.06-1.99 (m, 1H), 1.94-1.93 (m, 1H), 1.78-1.70 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.4, 153.1, 138.6, 135.3, 129.5, 129.5, 129.0, 128.5, 127.4, 126.7, 83.4, 69.2, 66.0, 55.3, 43.8, 38.8, 37.8, 30.1, 16.6. **IR** (neat) ν_{max} 3284.2 (m), 3059.2 (w), 3025.4 (w), 2921.6 (m), 2856.9 (w), 1772.4 (s), 1691.1 (s), 1385.3 (s), 1348.1 (s), 1239.9 (s), 1210.1 (s), 1193.1 (s), 739.9 (s). **HRMS** (DART) for $C_{23}H_{24}NO3$ $(M+H)^+$: Calc'd: 362.1751, found: 362.1761. **$[\alpha]_D^{20}$** = 18.20 (*c* =1.0, $CHCl_3$, *l* = 50 mm).



SI-19 **SI-20**

(*R*)-2-benzylhex-5-yn-1-ol (SI-20). To a solution of LAH (220.5 mg, 5.8 mmol) in THF (30 mL) was added a solution of **SI-19** (0.70 g, 1.94 mmol) in 20 mL THF at -78 °C. The mixture was allowed to warm to room temperature over the course of a several hours and stirred for 12 hours. The mixture was cooled to 0 ºC and H_2O (0.6 mL) was carefully added, followed by 3 M NaOH (0.6 mL). The suspension was stirred at room temperature for 20

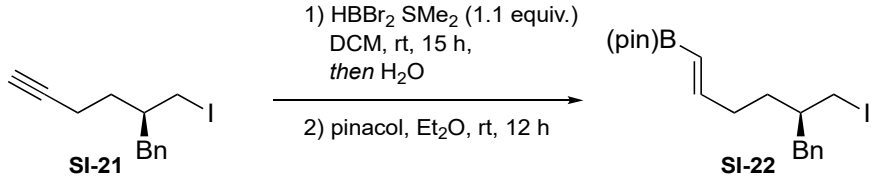
min after which $MgSO_4$ was added. The resulting mixture was filtered through a pad of celite and concentrated in vacuo. The crude product was purified by silica gel column chromatography (15% ethyl acetate in hexanes) to afford **SI-20** (0.25 g, 68% yield) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32-7.27 (m, 2H), 7.23-7.21 (m, 3H), 3.63-3.53 (m, 2H), 2.67 (d, *J* = 7.3 Hz, 2H), 2.30-2.27 (m, 2H), 2.02-1.97 (m, 2H), 1.72-1.57 (m, 2H), 1.31 (td, *J* = 5.6, 5.6, 2.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.4, 129.3, 128.5, 126.2, 84.5, 68.8, 64.3, 41.6, 37.5, 29.7, 16.4. **IR** (neat) ν_{max} 3288.6 (m), 3023.4 (w), 3025.4 (w), 2921.3 (m), 1600.8 (w), 1493.5 (m), 1451.5 (m), 1029.0 (s), 981.9 (s), 736.3 (s), 699.3 (s), 631.8 (s), 493.4 (w). **HRMS** (DART) for $C_{13}H_{17}O$ $(M+H)^+$: Calc'd:189.1274, found: 189.1268. **$[\alpha]_D^{20}$** = 1.19 (*c* =1.0, $CHCl_3$, *l* = 50 mm).



SI-20 SI-21

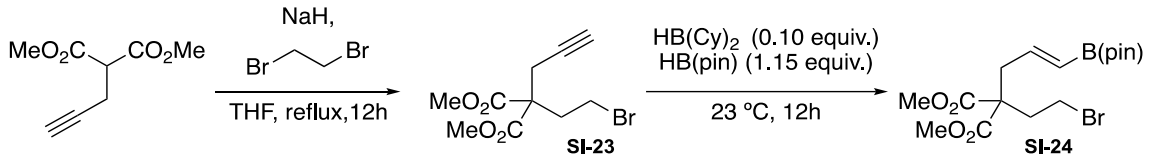
(*R*)-(2-(iodomethyl)hex-5-yn-1-yl)benzene (SI-21). A solution of triphenylphosphine (0.53 g, 2.0 mmol) and iodine (0.51 g, 2.0 mmol) in dichloromethane (5 mL) was allowed to stir for 10 min at ambient temperature. Imidazole (0.23 g, 3.3 mmol) was added to the resulting mixture. After stirring for 10 min, **SI-20** (.25 g, 1.3 mmol) was added and the resulting mixture was stirred for 2 h. The mixture was quenched by the addition of saturated sodium metabisulfite aq. solution (5 mL). The aqueous and organic layers were separated and the aqueous layer was extracted with dichloromethane (3 x 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The

resulting residue was purified by flash chromatography (5% ethyl acetate in hexane, stain in CAM) to afford the title compound (0.3 g, 75%) as a light-yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34-7.31 (m, 2H), 7.28-7.24 (m, 3H), 3.27 (dd, *J* = 10.3, 3.1 Hz, 1H), 3.16 (dd, *J* = 10.2, 2.9 Hz, 1H), 2.71 (dd, *J* = 13.8, 4.1 Hz, 1H), 2.56 (dd, *J* = 13.8, 7.6 Hz, 1H), 2.37-2.19 (m, 2H), 2.00 (t, *J* = 2.6, 2.6 Hz, 1H), 1.71-1.56 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.5, 129.3, 128.6, 126.5, 83.4, 69.3, 40.2, 39.1, 33.1, 15.9, 15.5. **IR** (neat) ν_{max} 3290.6 (m), 3058.8 (w), 2920.0 (m), 2851.4 (w), 1601.0 (w), 1493.7 (m), 1451.2 (m), 1220.8 (m), 735.9 (s), 699.1 (s), 634.9 (s), 491.3 (w). **HRMS** (DART) for $C_{13}H_{16}I$ $(M+H)^+$: Calc'd: 299.0291, found: 299.0292. **$[\alpha]_D^{20}$** = -45.02 (*c* =1.0, $CHCl_3$, *l* = 50 mm).



(*R*,*E*)-2-(5-benzyl-6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SI-22). To a solution of **SI-21** (0.30 g, 1.0 mmol) in 10 mL of anhydrous dichloromethane was added 1.1 mL of a 1.0 M solution of $HBBr_2$•SMe_2 (1.1 mmol) in dichloromethane. After 15 h at room temperature, the mixture was cooled to 0 ºC and water (5 mL) was slowly added. The aqueous phase was extracted with 2 x 20 mL of ether. Addition of pinacol (0.12 g, 1.0 mmol) to the combined organic phases was followed by stirring for 12 hours at room temperature. The reaction mixture is concentrated under reduced pressure, and purified by flash chromatography (5% ethyl acetate in hexane, stain in CAM) to afford **SI-22** (0.35 g, 82%) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33-7.26 (m, 2H), 7.24-7.19 (m, 3H), 6.63 (dt, *J* = 17.9, 6.4, 6.4 Hz, 1H), 5.49 (d, *J* = 17.9 Hz, 1H), 3.23 (dd, *J* = 10.0, 4.2 Hz, 1H), 3.13 (dd, *J* = 10.0, 3.7 Hz, 1H), 2.67 (dd, *J* = 13.8, 5.5 Hz, 1H), 2.55

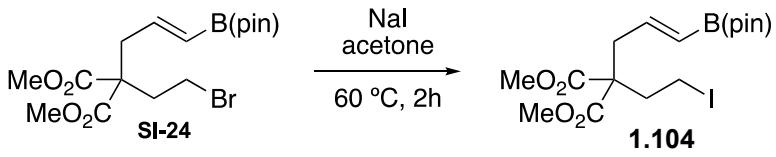
(dd, J = 13.8, 8.4 Hz, 1H), 2.30-2.21 (m, 1H), 2.18-2.11 (m, 1H), 1.59-1.46 (m, 2H), 1.46-1.37 (m, 1H), 1.29 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.4, 139.7, 129.2, 128.5, 126.4, 83.2, 40.4, 39.9, 33.1, 32.8, 24.9, 15.9. **IR** (neat) ν_{max} 3022.6 (m), 2974.1 (m), 2923.5 (w), 1636.3 (m), 1452.0 (w), 1396.3 (m), 1360.6 (s), 1320.1 (s), 1143.0 (s), 999.4 (w), 969.5 (w), 848.7 (w), 738.3 (w), 699.7 (m). **HRMS** (DART) for $C_{19}H_{29}BO_2I$ $(M+H)^+$: Calc'd: 427.1300, found: 427.1315. **$[\alpha]_D^{20}$** = -18.64 (c = 1.0, $CHCl_3$, l = 50 mm).



Dimethyl(E)-2-(2-bromoethyl)-2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)malonate (SI-24). Sodium hydride (260 mg, 10.75 mmol, 1.15 equiv.) was placed in a flame dried round bottom flask under Ar atmosphere and dissolved in 10 mL of THF. The flask was cooled to 0 ºC and a solution of dimethyl 2-prop-2-ynylpropanedioate (1.59 g, 9.34 mmol, 1.0 equiv.) in 10 mL of THF was added dropwise. The mixture was stirred for 20 min at 0 ºC after which time neat 1,2-dibromoethane (5.27 g, 28.03 mmol, 3.0 equiv.) was added. The mixture was then heated to reflux for 12 hours. The suspension was then cooled to 0 ºC and the reaction was quenched with 10 mL of saturated NH_4Cl aq. solution. The organic layer was extracted with ethyl acetate three times, washed with brine, dried over sodium sulfate and concentrated under reduced pressure. The crude material was filtered through a silica plug with 20% ethyl acetate in hexanes and carried to the next step.

Inside an argon filled glovebox a 4 dram vial was charged with neat 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (637.32 mg, 5.00 mmol, 1.15 equiv.) and dicyclohexylborane (77.13

mg, 0.43 mmol, 0.10 equiv.). The vial was placed inside the glove box freezer to cool for 30 minutes. Dimethyl-2-(2-bromoethyl)-2-prop-2-ynyl-propanedioate **(SI-23)** (1.20 g, 4.33 mmol, 1.0 equiv.) was added to the cool suspension and the vial was then sealed and stirred for 12 hours at room temperature. Finally, the reaction mixture was quenched by bubbling air through the solution for 2 hours at room temperature to oxidize the dicyclohexylborane. The resulting mixture was diluted with diethyl ether, washed with water, dried over Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (10% ethyl acetate in hexanes, stain in $KMnO_4$) to afford the product **SI-24** as a colorless oil (862 mg, 49% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.35 (dt, *J* = 17.7, 7.2 Hz, 1H), 5.53 (dt, *J* = 17.7, 1.2 Hz, 1H), 3.74 (s, 6H), 3.34 (t, 2H), 2.76 (dd, *J* = 7.2, 1.3 Hz, 2H), 2.45 (t, 2H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.7, 146.1, 121.9, 83.5, 57.5, 52.9, 40.1, 36.4, 27.2, 24.9. **IR** (neat) ν_{max} 2975.4 (w), 1732.4 (s), 1637.6 (w), 1436.1 (w), 1390.7 (m), 1362.6 (m), 1268.9 (m), 1166.2 (m), 998.4 (w), 970.4 (w), 643.0 (w). **HRMS** (DART) for $C_{16}H_{26}BIO_6$ $(M+H)^+$: Calc'd: 405.1079, found: 405.1075.



Dimethyl(E)-2-(2-iodoethyl)-2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)malonate (1.104). To a round bottom flask containing **SI-24** (400 mg, 0.99 mmol, 1.0 equiv.) was added a solution of sodium iodide (592.04 mg, 3.95 mmol, 4.0 equiv.) in acetone (22 mL). The reaction mixture was heated to reflux for 2 hours. The mixture was

cooled to room temperature, diluted with diethyl ether (100 mL), and washed with water and brine. The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The product was isolated after silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) as a clear yellow oil (395 mg, 89% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.34 (dt, *J* = 17.7, 7.2 Hz, 1H), 5.52 (d, *J* = 17.7 Hz, 1H), 3.73 (s, 6H), 3.14-3.00 (m, 2H), 2.73 (d, *J* = 7.2 Hz, 2H), 2.52-2.38 (m, 2H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.47, 146.12, 83.43, 59.05, 52.85, 39.82, 37.97, 24.88, 2.42. **IR** (neat) ν_{max} 2975.24 (br), 1732.1 (s), 1637.31 (w), 1436.06 (w), 1390.18 (m), 1324.55 (m), 1143.48 (m), 997.73 (w), 970.29 (w), 848.74 (w). **HRMS** (DART) for $C_{16}H_{26}BIO_6$ $(M+H)^+$: Calc'd: 453.0940, found: 453.0949.

1.4.2.3. Procedures for the Preparation of Organozinc Reagents

Alkyl zinc bromide synthesis by zinc insertion into C-Br bond.

A 20 mL vial was charged with zinc powder (1.26 g, 19.31 mmol, 2.50 equiv.) and a stir bar. The vial was capped with a PTFE-lined pierceable screwcap and he system was heated at 80 °C under high vacuum for 2 hours with stirring. The vial is then cooled to room temperature and backfilled with N_2. At this point the vial is brought into an Ar filled glove box, a solution of iodine (95.84 mg, 0.38 mmol, 0.02 equiv.) in DMA (1 mL) and the suspension was stirred until the red color subsided. In turn, alkyl bromide (7.60 mmol, 1.00 equiv.) and an additional 4 mL of DMA were added. The vial was capped with a Teflon screwcap, taped and the suspension was heated at 80 °C for 12 hours. Next, the mixture was cooled to room temperature, brought inside the glovebox and filtered through a syringe filter (pore-size: 0.45 μM, PTFE). The resulting organo-zinc solution was titrated following the Knochel method (I_2 in a 0.5 M THF solution of LiCl).[44]

The solutions could be stored in a freezer under inert atmosphere for several weeks without deleterious effects.

Note: for the three-component cross-coupling reactions (**Procedure A**, see below) the alkyl zinc bromide solution (0.4 mmol, 2.0 equiv.) was transferred under inert atmosphere into a flame dried vial containing LiCl (35.6 mg, 0.84 mmol, 4.20 equiv.) in 0.5 mL of THF. The mixture was stirred vigorously for 1 hour at room temperature prior to being used in the cross-coupling reaction.

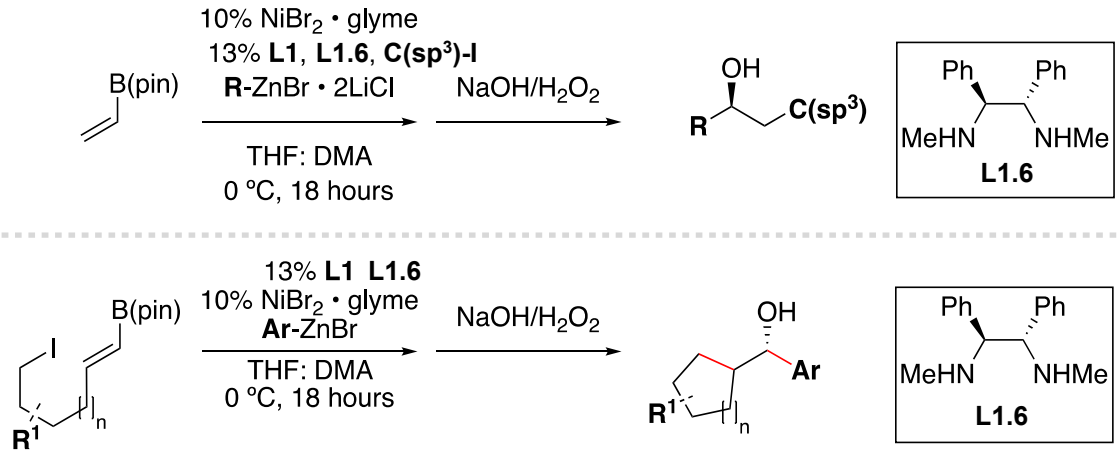
Organozinc Chloride synthesis by addition of organolithium reagents to $ZnCl_2$.

Organolithium reagents were generated by lithium-halogen exchange with *tert*-butyllithium using the following procedure: an aryl bromide or alkyl iodide (1.0 mmol) was placed in a flame-dried 20 mL vial under N_2 atmosphere and dissolved 5 mL of dry diethyl ether. The vial was sealed with a pierceable PTFE-lined cap and a septum was taped over it (this second septum was backfilled with N_2 and creates a buffer zone to prevent air from entering the vial). The solution was cooled to -78 ºC and *tert*-butyllithium (1.18 mL, 1.7 M, 2.0 equiv.) was added dropwise. The solution was stirred at -78°C for 30-40 min after which a solution of $ZnCl_2$ in THF was added (2.4 mL, 0.5 M, 1.2 equiv.). The mixture was warmed to room temperature and stirred for 45 minutes after which time the solvent was carefully removed under vacuum through the Schlenck line. The concentrated residue was brought inside an argon filled glovebox and re-dissolved in 2 mL of THF. The resulting solution was titrated following the Knochel method.[10]

Note: phenyllithium and methyllithium solutions purchased from commercial sources (Sigma Aldrich) were added to $ZnCl_2$ solutions in THF (0.5 M, 1.2 equiv.) at 0 ºC, stirred for 45 min, and used directly in the reaction.

1.4.2.4. Representative Procedure for Cross-Coupling

Procedure A, for the three component cross-coupling (alkyl or aryl ZnX) and two-component cyclization/cross-coupling with aryl ZnX reagents.

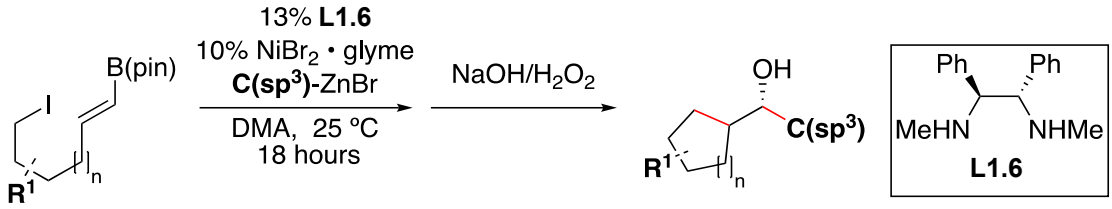


In an argon-filled glovebox, an oven-dried 2 dram vial equipped with a magnetic stirrer was charged with **$NiBr_2$·glyme** (6.17 mg, 0.02 mmol), (*S*,*S*)-N,N-dimethyl-1,2-diphenyl-ethane-1,2-diamine **L1.6** (6.25 mg, 0.026 mmol) and dissolved in 1.0 mL of THF. The catalyst solution was stirred for 1 hour at ambient temperature. **Vinylboronic acid pinacol ester** (30.80 mg, 0.20 mmol, 1.00 equiv.) and **alkyl iodide** (0.40 mmol, 2.00 equiv.), or **cyclizing alkenyl boron** substrate (0.20 mmol, 1.00 equiv.) were added to the catalyst solution (alternatively, the reactants could be weighed out in a separate vial and the catalyst solution added to the latter). At this point, THF and DMA were added so as to reach a final volume (taking into account the volume of the organozinc solution) of 2.00 mL of THF and 0.40 mL DMA. The vial was sealed with a PTFE-lined pierceable cap, taped, and brought outside the glovebox where it was placed in a CryoCool set at 0 ºC. The vial was

cooled for 20-30 minutes before addition of the **organozinc** solution (0.40 mmol, 2.00 equiv.) (***Note:*** for the three component reactions with alkyl-ZnBr reagents, the organozinc reagent was stirred with LiCl (35.6 mg, 0.84 mmol, 4.20 equiv.), in 0.50 mL of THF for 1 hour at room temperature before addition). The puncture hole was taped over and the reaction mixture was stirred at 0 ºC for 18 hours. Oxidation was then carried out by adding 0.50 mL of 30% H_2O_2 and 0.50 mL of 3.0 M aqueous NaOH solution to the cold reaction mixture (the vial was vented to prevent pressure build-up). The mixture was stirred vigorously for 2-3 hours and allowed to slowly warm to room temperature. At this point the reaction mixture was cooled to 0 ºC once more and the oxidation was quenched by addition of 0.50 mL of saturated aqueous $Na_2S_2O_3$.The organic layer was extracted four times with ethyl acetate, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel chromatography.

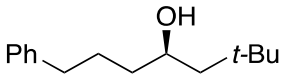
Note: In order to isolate the boronic ester product prior to oxidation, the work-up was carried out by adding 0.30 mL of saturated aqueous NH_4Cl solution to the reaction mixture at 0 ºC. The mixture was then transferred to a separatory funnel using ethyl acetate, and the organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The crude product was then purified by silica gel chromatography.

Procedure B, for intramolecular cyclization/cross-coupling reactions using alkyl-ZnBr.



In an argon-filled glovebox, an oven-dried 2 dram vial equipped with a magnetic stirrer was charged with **$NiBr_2$·glyme** (6.17 mg, 0.02 mmol), (*S,S*)-N,N-dimethyl-1,2-diphenyl-ethane-1,2-diamine **L1.6** (6.25 mg, 0.026 mmol) and dissolved in 1.0 mL of DMA. The catalyst solution was stirred for 1 hour at ambient temperature. The **cyclizing alkenyl-boron** substrate (0.20 mmol, 1.00 equiv.) was added to the catalyst solution (alternatively, the substrated could be weighed out in a separate vial and the catalyst solution added to the latter). DMA was added so as to reach a final volume (taking into account the volume of the organozinc solution) of 2.00 mL. The vial was sealed with a PTFE-lined pierceable cap, taped, and brought outside the glovebox where it was placed in an ice-bath. The vial was cooled for a few minutes before addition of the organozinc solution (0.40 mmol, 0.20 equiv.). The puncture hole was taped over and the reaction mixture was taken off the ice bath and stirred at room temperature for 18 hours. Finally, the mixture was cooled to 0 ºC and 0.30 mL of saturated aqueous NH_4Cl solution were added. The mixture was then transferred to a separatory funnel using ethyl acetate and the organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The crude product could then be isolated as the boronic ester by silica gel chromatography, or re-dissolved in 1.0 mL of THF and oxidized following the method outlined in **procedure B**.

1.4.2.5. Procedures and Characterization for Cross-Coupling Product



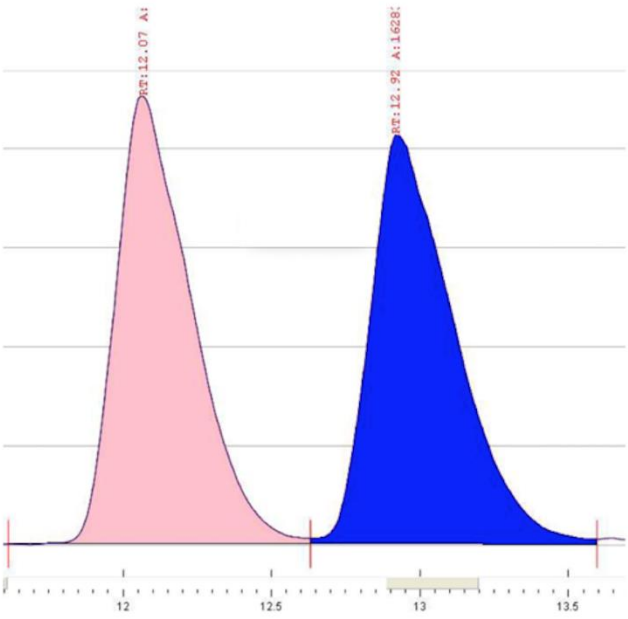
(*R*)-6,6-dimethyl-1-phenylheptan-4-ol (**1.77**) The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (3-phenylpropyl)zinc bromide·2LiCl solution in DMA (0.24 mL, 1.68 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (24.3 mg, 55% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29-7.26 (m, 3H), 7.19-7.18 (m, 2H), 3.80-3.75 (m, 1H), 2.67-2.60 (m, 2H), 1.82-1.69 (m, 1H), 1.7-1.60 (m, 1H), 1.52-1.42 (m, 2H), 1.38-1.30 (m, 2H), 0.95 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.56, 128.55, 128.44, 125.87, 69.64, 51.49, 39.33, 36.04, 30.41, 30.30, 27.59. **IR** (neat) ν_{max} 3358.9 (br), 3023.7 (w), 2945.4 (s), 2931.7 (s), 2859.3 (m), 1602.2 (w), 1494.4 (m), 1452.2 (m), 1362.2 (m),1089.6 (m), 746.89 (m), 697.6 (s). **HRMS** (DART) for $C_{15}H_{28}NO$ $(M+NH_4)^+$: Calc'd: 238.2165, found: 238.2166. **$[\alpha]_D^{20}$** = 8.60 (*c* =1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel AD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-6,6-dimethyl-1-phenylheptan-4-ol**.

Racemic Material



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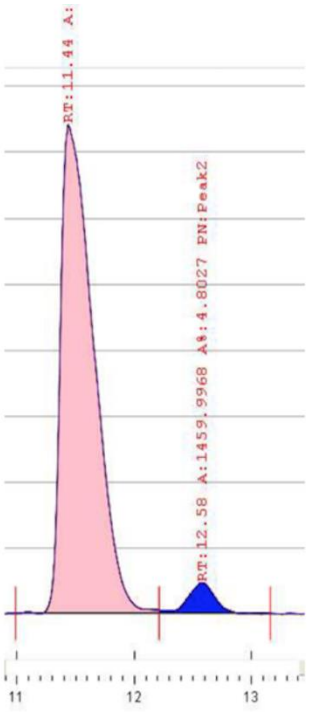
Enantioenriched Material



Peak Info			
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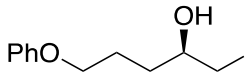


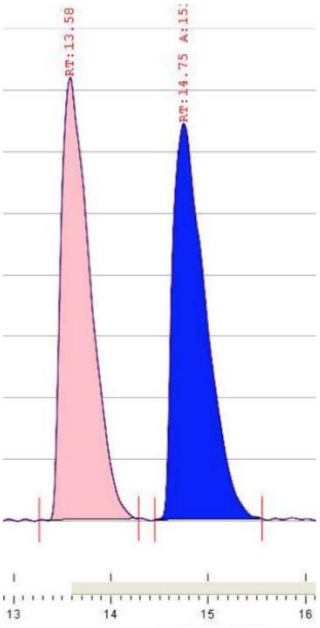
(*R*)-6,6-dimethyl-1-phenoxyheptan-4-ol (1.78). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (3-phenoxypropyl)zinc bromide·2LiCl solution in DMA (0.360 mL, 1.1 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (33.1 mg,70% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32-7.21 (m, 2H), 6.99-6.84 (m, 3H), 4.08-3.91 (m, 2H), 3.91-3.75 (m, 1H), 2.00-1.76 (m, 2H), 1.71-1.55 (m, 2H), 1.40 (d, *J* = 5.1 Hz, 2H), 0.98 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.0, 129.6, 120.8, 114.6, 69.2, 68.1, 51.5, 36.4, 30.4, 30.3, 25.7. **IR** (neat) ν_{max} 3394.5 (br), 2947.5 (m), 1598.8 (m), 1495.5 (m), 1471.1 (m), 1360.4 (w), 1247.9 (s), 1034.4 (w), 757.1 (m), 690.7 (m). **HRMS** (DART) for $C_{15}H_{25}O_2$ $(M+H)^+$: Calc'd: 237.18491, found: 237.18571. **$[\alpha]_D^{20}$** = -6.898 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(R)-6,6-dimethyl-1-phenoxyheptan-4-ol.**

Racemic Material



Peak No	% Area	Area	RT (min)
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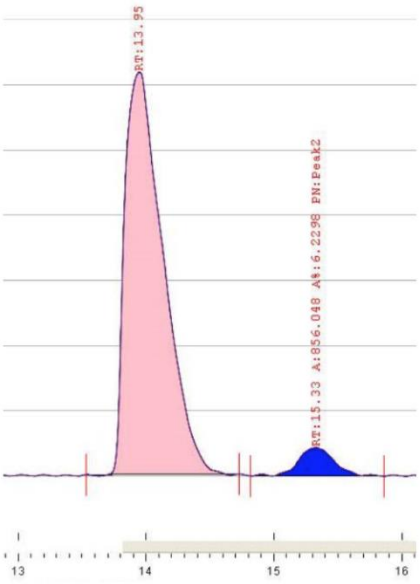
Total:	100	30067.1482	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
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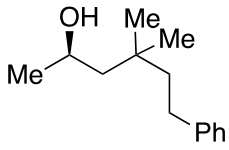
Total:	100	13741.2181	



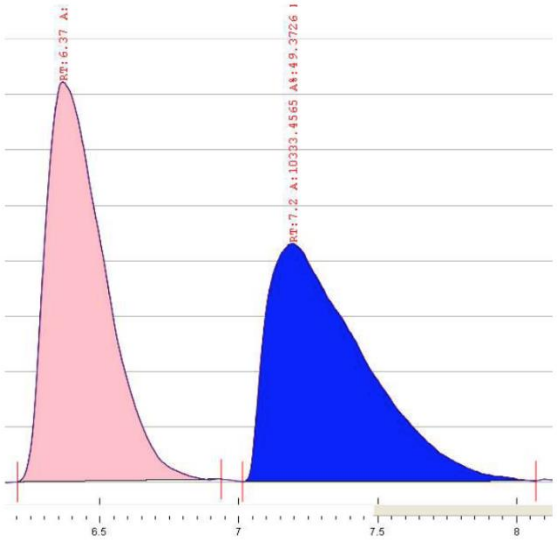
(*R*)-4,4-dimethyl-6-phenylhexan-2-ol (1.79). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), (3-iodo-3-methylbutyl)benzene (109.7 mg, 0.40 mmol, 2.0 equiv.), and methylzinc chloride·2LiCl solution in THF (1.01 mL, 0.40 M, 0.40 mmol, 2.0 equiv.) (**note:** the organozinc reagent was obtained by addition of commercial MeLi (130 µL, 3.1 M in DME, 0.4 mmol, 2.0 equiv.) to $ZnCl_2$ in THF (880 µL, 0.5 M, 0.44 mmol, 2.2 equiv.). After stirring for 30 min at room temperature additional LiCl (18.7 mg, 0.44 mmol, 2.2 equiv.) was added to improve yield and selectivity of the reaction), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (48.9 mg, 55% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30-7.23 (m, 2H), 7.21-7.14 (m, 3H), 4.03-4.00 (m, 1H), 2.65-2.50 (m, 2H), 1.65-1.52 (m, 2H), 1.50 (dd, *J* = 14.5, 7.9 Hz, 1H), 1.41 (dd, *J* = 14.6, 2.9 Hz, 1H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.02 (s, 3H), 1.01 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.5, 128.5, 125.7, 65.7, 51.0, 45.3, 33.1, 30.9, 27.9, 27.8, 26.3. **IR** (neat) ν_{max} 3363.6 (br), 3023.3 (w), 2955.9 (s), 2924.5 (s), 2863.2 (m), 1494.9 (m), 1467.25 (m), 1259.0 (m), 1072.9 (s), 1051.5 (s), 1029.7 (s), 737.7 (s) 697.4 (s). **HRMS** (DART) for $C_{14}H_{26}NO$ $(M+NH_4)^+$: Calc'd: 224.2007, found: 224.2009. $\mathbf{[\alpha]_D^{20}}$ = 11.80 (*c* =1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel AS-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(R)-4,4-dimethyl-6-phenylhexan-2-ol.**

Racemic Material



Peak Info

Peak No	% Area	Area	RT (min)
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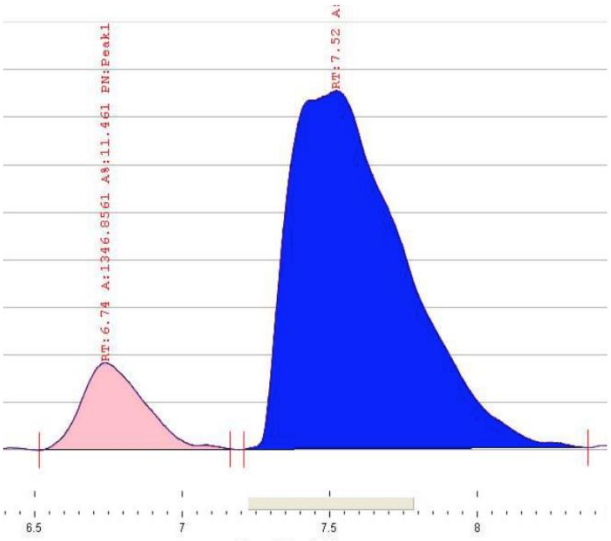
Total:	100	20929.526	

Enantioenriched Material



Peak Info

Peak No	% Area	Area	RT (min)
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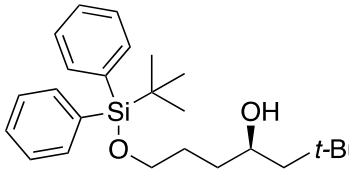
Total:	100	11751.6019	



(*R*)-1-((*tert*-butyldiphenylsilyl)oxy)-6,6-dimethylheptan-4-ol (1.80). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (3-((*tert*-butyldiphenylsilyl)oxy)propyl)zinc bromide• 2LiCl solution in DMA (0.425 mL, 0.94 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (56 mg, 70% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.69-7.67 (m, 3H), 7.48-7.36 (m, 5H), 3.82-3.76 (m, 1H), 3.71-3.68 (m, 2H), 1.83 (s, 1H), 1.73-1.61 (m, 2H), 1.60-1.47 (m, 2H), 1.42 -1.32 (m, 2H), 1.06 (s, 9H), 0.97 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 135.7, 135.7, 133.9, 133.9, 129.8, 127.8, 69.3, 64.3, 51.4, 36.6, 30.4, 30.3, 28.9, 27.0, 19.3. **IR** (neat) ν_{max} 3385.9 (br), 3067.8 (w), 3047.8 (w), 2948.0 (s), 2928.7 (s), 2856.3 (s), 1471.1 (m), 1426.3 (m), 1388.8 (m), 1108.8 (s), 700.3 (s), 613.0 (m), 504.4 (s). **HRMS** (DART) for $C_{25}H_{39}O_2Si$ $(M+H)^+$: Calc'd: 399.2714, found: 399.2723. **$[\alpha]_D^{20}$** = -3.60 (*c* =1.0, $CHCl_3$, *l* = 50 mm).

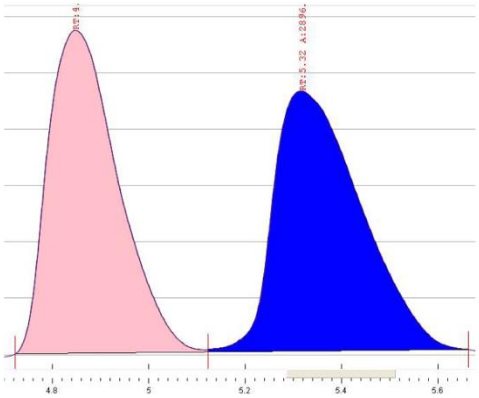
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of

(R)-1-((tert-butyldiphenylsilyl)oxy)-6,6-dimethylheptan-4-ol.

Racemic Material



Peak Info

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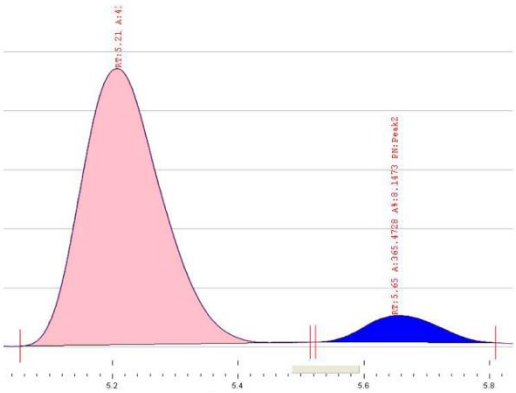
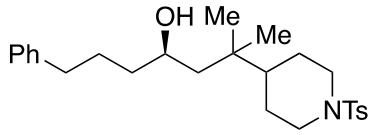
Total:	100	5779.3152	

Enantioenriched Material



Peak Info

Peak No	% Area	Area	RT (min)
1	91.8527	4120.3358	5.21
2	8.1473	365.4728	5.65
Total:	100	4485.8086	



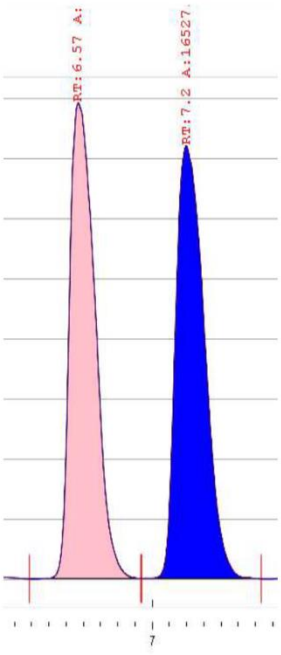
(*R*)-6-methyl-1-phenyl-6-(1-tosylpiperidin-4-yl)heptan-4-ol (1.81). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), 4-(2-iodopropan-2-yl)-1-tosylpiperidine *(*162.92 mg, 0.40 mmol, 2.0 equiv.), and (3-phenylpropyl)zinc bromide·2LiCl solution in DMA (0.24 mL, 1.68 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as white solid (48.9 mg, 55% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65-7.63(m, 2H), 7.33-7.26 (m, 4H), 7.19-7.17 (m, 3H), 3.84 (apparent d, *J* = 11.2 Hz, 2H), 3.70-3.67 (m, 1H), 2.69-2.55 (m, 2H), 2.43 (s, 3H), 2.20-1.99 (m, 2H), 1.79-1.58 (m, 4H), 1.45-1.25 (m, 6H), 1.11-1.07 (m, 2H), 0.87 (s, 3H), 0.84 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.5, 142.3, 133.2, 129.6, 128.5, 128.4, 127.9, 125.9, 69.0, 47.3, 47.2, 44.7, 39.6, 35.9, 34.7, 27.5, 26.1, 25.3, 25.1, 21.6. **IR** (neat) ν_{max} 3541.5 (br), 3023.0 (m), 2926.1 (s), 2850.8 (m), 1715.6 (w), 1596.4 (w), 1493.2 (m),1464.6 (s), 1450.4 (s), 1353.5 (s), 1334.5 (s), 1303.2 (s), 1054.5 (s), 930.8 (s), 862.3 (s), 813.0 (s), 724.1 (s), 698.9 (s), 649.2 (s), 573.8 (s). **HRMS** (DART) for $C_{26}H_{38}NO_3S$ $(M+H)^+$: Calc'd: 444.2565, found: 444.2567. **$[\alpha]_D^{20}$** = 4.60 (*c* =1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel OJ-H, 15% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(R)-6-methyl-1-phenyl-6-(1-tosylpiperidin-4-yl)heptan-4-ol**.

Racemic Material



Peak Info

Peak No	% Area	Area	RT (min)
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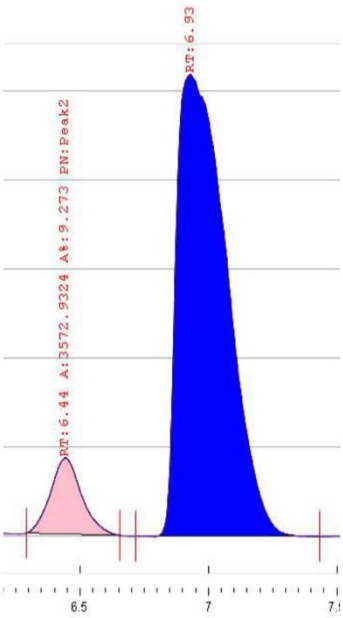
2	50.6156	16527.6547	7.2
Total:	100	32653.2625	

Enantioenriched Material



Peak Info

Peak No	% Area	Area	RT (min)
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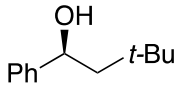
2	90.727	34957.4911	6.93
Total:	100	38530.4235	



(*S*)-3,3-dimethyl-1-phenylbutan-1-ol (1.82). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and phenylzinc chloride solution in THF (1.0 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (25.1 mg, 70% yield). **HRMS** (DART) for $C_{26}H_{38}NO3S$ $(M+H-H_2O)^+$: Calc'd: 161.1321, found: 161.1325. $[\alpha]_D^{20}$ = -52.39 (*c* = 0.5, $CHCl_3$, *l* = 50 mm). (lit: $[\alpha]_D^{20}$ = -71.2 (*c* = 1.9, THF, *l* = 100mm, ≤ 99% *ee*, (*S*)-enantiomer)). All spectral data was in accordance with the literature.[56]

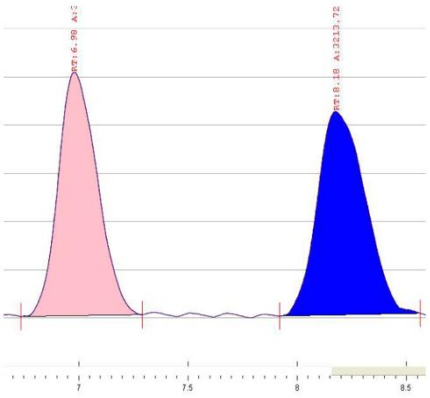
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was determined from the X-ray crystal structure of the unoxidized boronic ester product obtained using **L1.6** as ligand.

Chiral SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-3,3-dimethyl-1-phenylbutan-1-ol.**

Racemic Material Enantioenriched Material

(56) Ishikawa, H.; Suzuki, T.; Orita, H.; Uchimaru, T.; Hayashi, Y. *Chem. Eur. J.* **2010**, *16*, 12616–12626.



Peak Info

Peak No	% Area	Area	RT (min)
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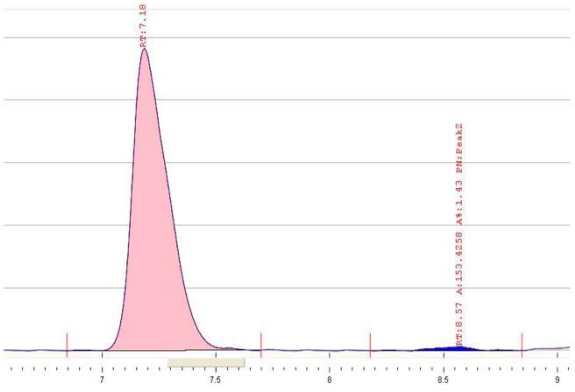
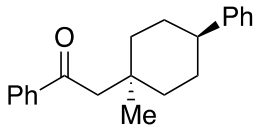
2	50.6564	3213.7248	8.18
Total:	100	6344.1668	



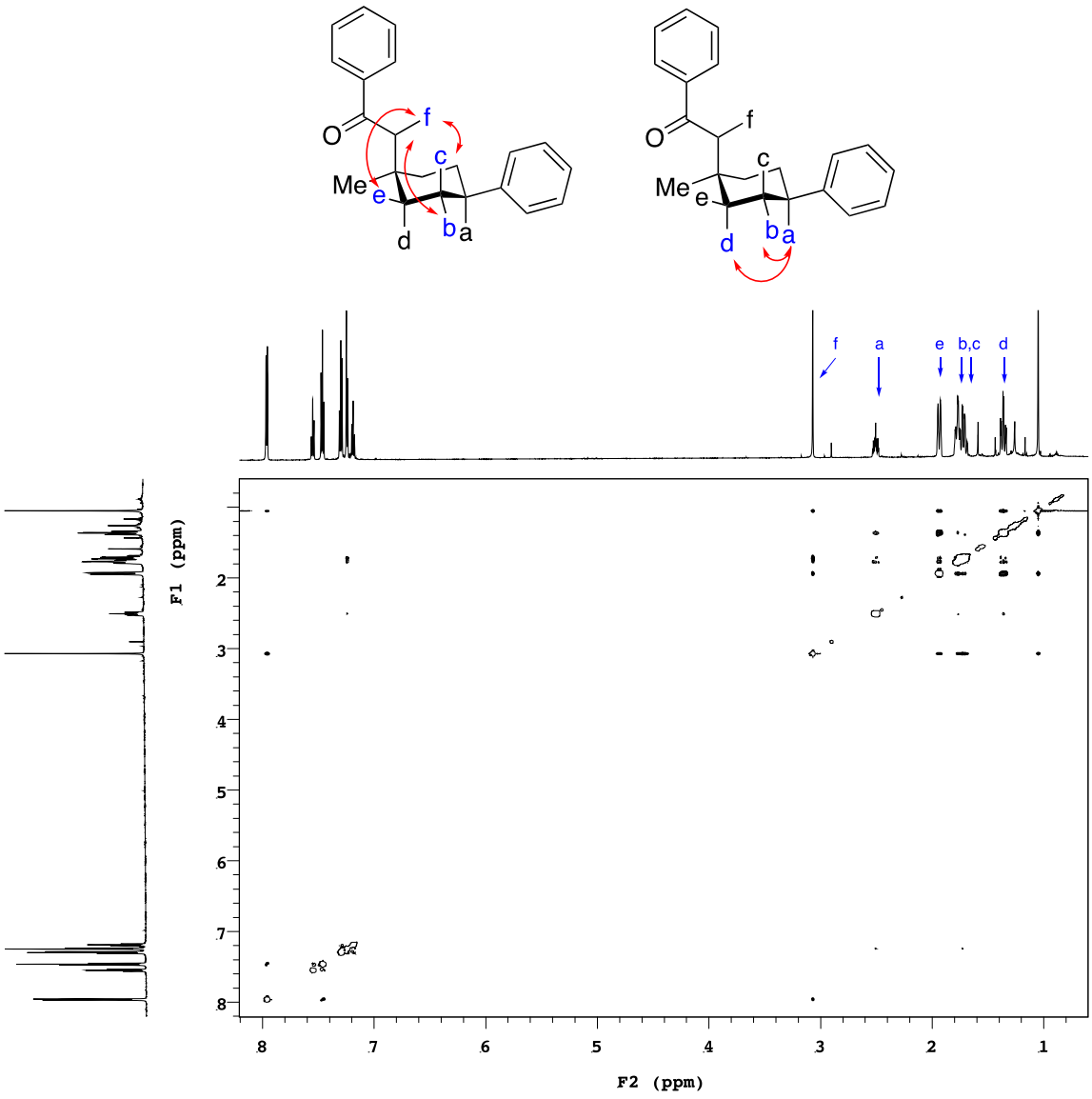
Peak Info

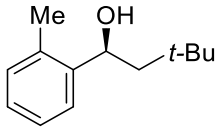
Peak No	% Area	Area	RT (min)
1	98.57	10575.7422	7.18
2	1.43	153.4258	8.57
Total:	100	10729.168	



2-((1*s*,4*s*)-1-methyl-4-phenylcyclohexyl)-1-phenylethan-1-one (SI-25) Diastereomeric mixture **1.89** (40.7 mg, 0.14 mmol, 1.0 equiv.) was placed in a scintillation vial equipped with a stirr-barr, and dissolved in 5 mL of dichloromethane. Sodium bicarbonate (47 mg, 0.56 mmol, 4.0 equiv.) was added to the solution followed by Dess-Martin periodinane (88.0 mg, 0.21 mmol, 1.5 equiv.) and the mixture was stirred at room temperature for 2 hours. The reaction was quenched with 2 mL of 10% sodium thiosulfate aq. solution followed by 2 mL of sat. sodium bicarbonate aq. solution. The organic layer was extracted twice with dichloromethane and twice with diethyl ether, the combined organic layers were dried over MgSO4 and concentrated in vacuo. The major diastereomer was isolated by silica gel chromatography (1-5% ethyl acetate in pentanes, UV) as a colorless oil (22 mg, 55% yield). **^{1}H NMR** (600 MHz, $CDCl_3$(600 MHz, Chloroform-*d*) δ 7.99-7.94 (m, 2H), 7.58-7.52 (m, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.26-7.23 (m, 2H), 7.21-7.17 (m, 1H), 3.07 (s, 2H), 2.51 (tt, *J* = 12.0, 4.1 Hz, 1H), 1.94 (app. d, *J* = 11.3 Hz, 2H), 1.82 – 1.66 (m, 4H), 1.36 (td, *J* = 13.4, 4.1 Hz, 2H), 1.05 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 201.1, 147.2, 139.0, 132.7, 128.5, 128.3, 128.3, 128.2, 128.1, 126.8, 125.9, 44.1, 42.6, 38.6, 33.6, 29.9, 29.8. **IR** (neat) ν_{max} 3056.3 (w), 3023.3 (w), 2921.7 (s), 2858.7 (s), 1686.2 (s), 1671.2 (s), 1596.3 (w), 1447.0 (m), 1375.0 (m), 1252.8 (m), 750.0 (s), 728.2 (s). **HRMS** (DART) for $C_{13}H_{19}$ $(M+H-H_2O)^+$: Calc'd: 175.1481, found: 175.1473

Relevant NOESY correlations are illustrated below.


O
f
c
Me
e
d
b
a
f
a
e
b,c
d
F1 (ppm)
F2 (ppm)



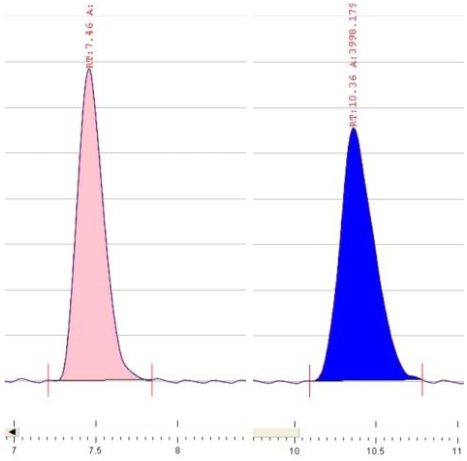
(*S*)-3,3-dimethyl-1-(o-tolyl)butan-1-ol (1.83) The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (o-tolyl) zinc chloride (0.89 mL, 0.45 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (27.6 mg, 56% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.7, 1.5 Hz, 1H), 7.23 (t, *J* = 7.4, 7.4 Hz, 1H), 7.17-7.11 (m, 2H), 5.10 (dt, *J* = 9.3, 2.9, 2.9 Hz, 1H), 2.34 (s, 3H), 1.68 (dd, *J* = 14.9, 9.1 Hz, 1H), 1.58 (dt, *J* = 3.5, 1.2 Hz, 1H), 1.51 (dd, *J* = 14.8, 1.4 Hz, 1H), 1.04 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.8, 133.8, 130.5, 127.1, 126.5, 125.3, 68.8, 52.1, 30.9, 30.4, 19.3. **IR** (neat) ν_{max} 2953.0 (m), 2922.3 (s), 2850.9 (w), 1462.4 (w), 1363.0 (w), 1337.35 (w), 1079.7 (w), 1026.27 (w), 425.5 (w). **HRMS** (DART) for $C_{13}H_{19}$ $(M+H-H_2O)^+$: Calc'd: 175.1481, found: 175.1473. **$[\alpha]_D^{20}$** = 17.00 (*c* = 0.20, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-1-(4-methoxyphenyl)-3,3-dimethylbutan-1-ol.**

Racemic Material



Peak No	% Area	Area	RT (min)
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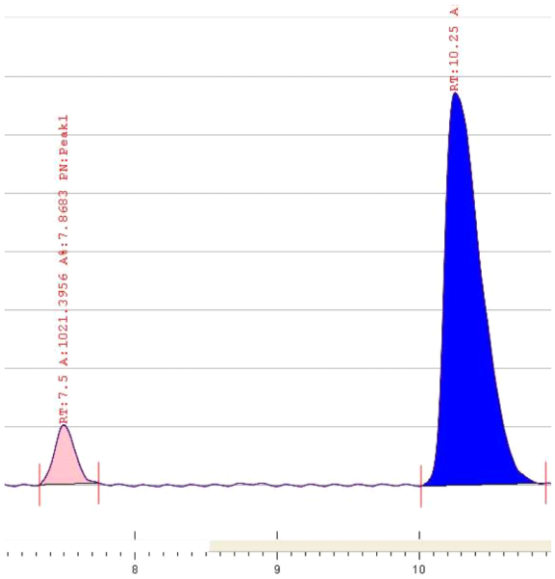
2	50.9823	3998.1798	10.36
Total:	100	7842.2974	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
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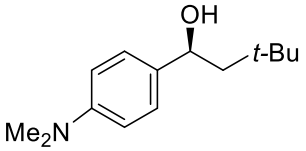
2	92.1317	11959.7606	10.25
Total:	100	12981.1562	



(*S*)-1-(4-(dimethylamino)phenyl)-3,3-dimethylbutan-1-ol

(1.84) The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (4-(dimethylamino)phenyl) zinc chloride (1.11 mL, 0.36 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using NiBr2·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (20.4 mg, 46% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, 2H), 6.72 (d, 2H), 4.74 (dd, J = 8.3, 4.1 Hz, 1H), 2.95 (s, 6H), 1.82-1.74 (m, 1H), 1.63-1.54 (m, 2H), 0.97 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.3, 134.6, 127.0, 112.8, 72.4, 52.5, 40.8, 30.5, 30.4. **IR** (neat) ν_{max} 3256.4 (br), 2947.6 (m), 2915.3 (w), 2882.2 (w), 2027.4 (w), 1614.0 (m), 1521.8 (m), 1468.3 (w), 1360.7 (w), 1348.2 (w), 1224.4 (w), 1059.5 (w), 1018.6 (w), 988.7 (w), 819.1 (w). **HRMS** (DART) for $C_{14}H_{22}N$ $(M+H-H_2O)^+$: Calc'd: 204.1747, found: 204.1743. $[\alpha]_D^{20}$ = 28.98 (c = 0.35, $CHCl_3$, l = 50 mm).

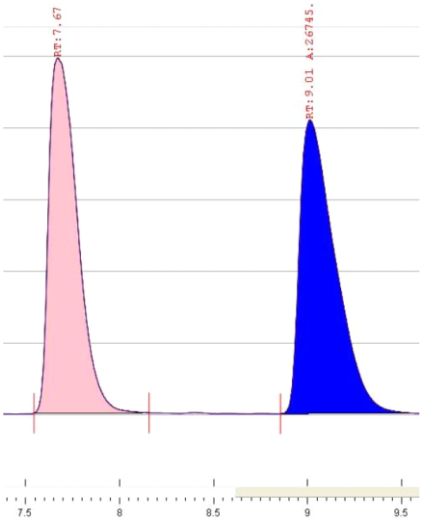
Analysis of Stereochemistry:

Racemic compound was prepared according to the **general procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of

(*S*)-1-(4-(dimethylamino)phenyl)-3,3-dimethylbutan-1-ol.

Racemic Material



Peak No	% Area	Area	RT (min)
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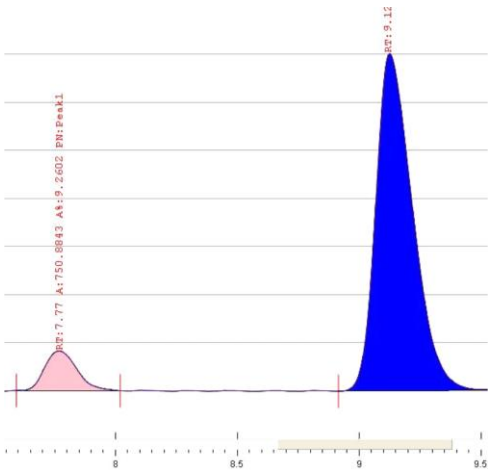
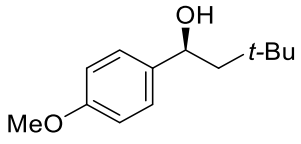
2	50.6972	26745.8883	9.01
Total:	100	52756.1957	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	9.2602	750.8843	7.77
2	90.7398	7357.8656	9.12
Total:	100	8108.7499	



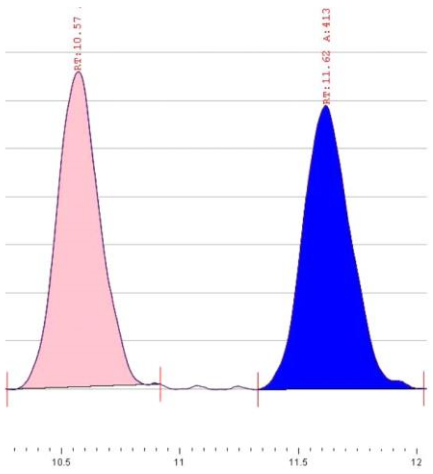
(*S*)-1-(4-methoxyphenyl)-3,3-dimethylbutan-1-ol (1.85). The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (4-methoxyphenyl)zinc chloride (0.23 mL, 1.74 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (26.2 mg, 63% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.28-7.26 (m, 2H), 6.90-6.83 (d, J = 8.6 Hz, 2H), 4.79 (dt, J = 7.9, 3.8 Hz, 1H), 3.80 (s, 3H), 1.77 (dd, J = 14.3, 8.1 Hz, 1H), 1.60 (dd, 2H), 0.97 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.1, 138.8, 127.2, 114.0, 72.2, 55.4, 52.9, 30.6, 30.3. **IR** (neat) ν_{max} 3408.8 (br), 2948.4 (m), 2864.8 (w), 2833.9 (w), 1610.5 (w), 1510.3 (s), 1244.4 (s), 1173 (m), 1035.3 (m), 830.6 (m), 587.3 (w). **HRMS** (DART) for $C_{13}H_{19}O$ $(M+H-H_2O)^+$: Calc'd: 191.1430, found: 191.1420. **$[\alpha]_D^{20}$** = 39.72 (c =0.59, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(S)-1-(4-methoxyphenyl)-3,3-dimethylbutan-1-ol.**

Racemic Material



Peak No	% Area	Area	RT (min)
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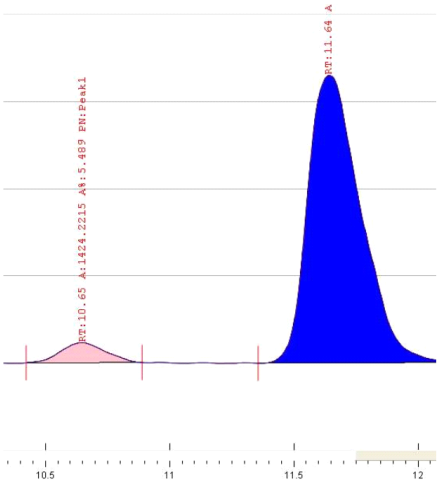
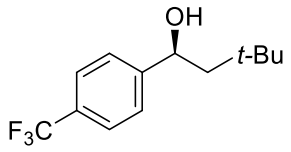
2	50.0172	4131.6767	11.62
Total:	100	8260.5137	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	5.489	1424.2215	10.65
2	94.511	24522.3855	11.64
Total:	100	25946.607	



(*S*)-3,3-dimethyl-1-(4-(trifluoromethyl)phenyl)butan-1-ol (1.86). The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and 4-(trifluoromethyl)phenylzinc chloride (0.52 mL, 0.77 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (27.6 mg, 56% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 2H), 4.91 (d, *J* = 8.0 Hz, 1H), 1.77– 1.71 (m, 2H), 1.56 (dd, *J* = 14.7, 3.1 Hz, 1H), 1.02 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.5, 126.1, 125.6, 125.6, 125.6, 125.6, 72.1, 53.3, 30.8, 30.3. **IR** (neat) ν_{max} 3396.7 (br), 2952.3 (m), 2866.9 (w), 1324.8 (s), 1164.2 (m), 1126.6 (m), 1067.7 (m), 1016.6 (w), 843.7 (w). **HRMS** (DART) for $C_{13}H_{16}F_3$ $(M+H-H_2O)^+$: Calc'd: 229.1199, found: 229.1204. **$[\alpha]_D^{20}$** = 28.66 (*c* = 0.30, $CHCl_3$, *l* = 50 mm).

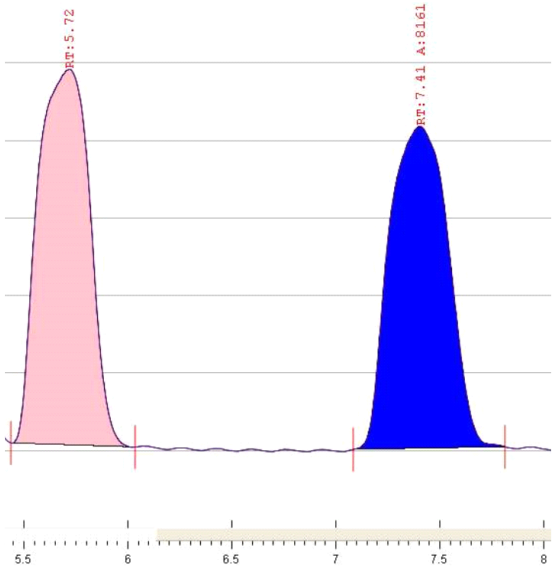
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of

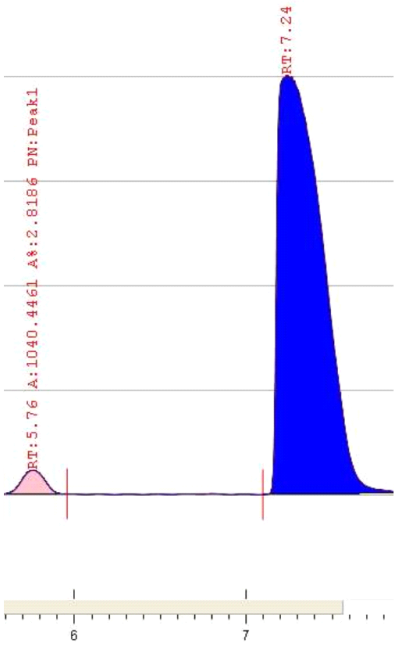
(S)-3,3-dimethyl-1-(4-(trifluoromethyl)phenyl)butan-1-ol

Racemic Material

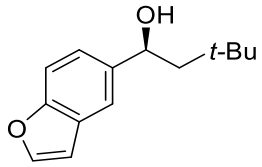


Peak No	% Area	Area	RT (min)
1	50.6036	8360.4958	5.72
2	49.3964	8161.0401	7.41
Total:	100	16521.5359	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	2.8186	1040.4461	5.76
2	97.1814	35873.3607	7.24
Total:	100	36913.8068	



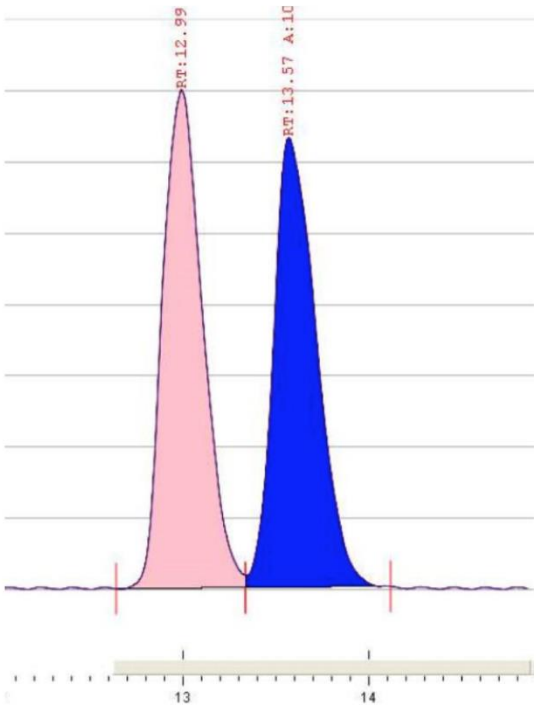
(S)-1-(benzofuran-5-yl)-3,3-dimethylbutan-1-ol (1.87). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (3- benzofuran-5-ylzinc chloride solution in THF (1.0 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, UV active) to afford the product as a colorless oil (23.1 mg, 52% yield).**^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 2.1 Hz, 1H), 7.59 (s, 1H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.29 (dd, *J* = 8.5, 1.5 Hz, 1H), 6.75 (d, *J* = 2.2 Hz, 1H), 4.93 (dd, *J* = 8.9, 3.3 Hz, 1H), 1.82 (dd, *J* = 14.5, 8.3 Hz, 1H), 1.74 (s, 1H), 1.66 (dd, *J* = 14.5, 3.7 Hz, 1H), 1.00 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.5, 145.6, 141.4, 127.6, 122.54, 118.5, 111.5, 106.8, 72.8, 53.4, 30.7, 30.4. **IR** (neat) ν_{max} 3377.6 (br), 2948.9 (s), 2864.0 (m), 1466.2 (m), 1362.9 (m), 1158.8 (m), 1106.2 (m), 767.5 (m), 747.2 (m), 734.3 (m), 699.5 (m). **HRMS** (DART) for $C_{14}H_{17}O$ $(M+H-H_2O)^+$: Calc'd: 201.1274, found: 201.1268. **$[\alpha]_D^{20}$** = -47.687 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

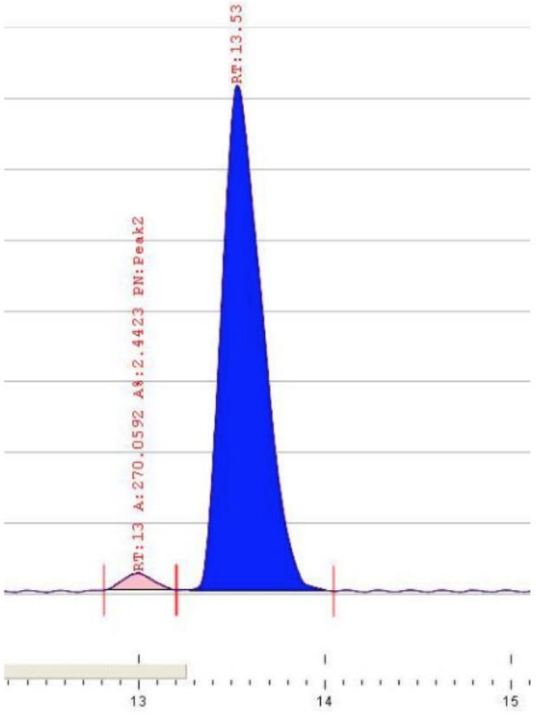
Chiral SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(S)-1-(benzofuran-5-yl)-3,3-dimethylbutan-1-ol**.

Racemic Material

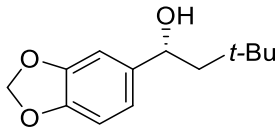


Peak No	% Area	Area	RT (min)
1	50.839	10492.7555	12.99
2	49.161	10146.4396	13.57
Total:	100	20639.1951	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	2.4423	270.0592	13
2	97.5577	10787.3117	13.53
Total:	100	11057.3709	



(S)-1-(benzo[d][1,3]dioxol-5-yl)-3,3-dimethylbutan-1-ol (1.88).

The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (benzo[d][1,3]dioxol-5-yl) zinc bromide·2LiCl (1.11 mL, 0.36 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using NiBr2·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **(*R*,*R*)-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (29.3 mg, 66% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.93-6.86 (s, 1H), 6.80-6.74(m, 2H), 5.94 (s, 2H), 4.74 (dd, *J* = 8.2, 3.9 Hz, 1H), 1.74 (dd, *J* = 14.4, 8.2 Hz, 1H), 1.64 (s, 1H), 1.57 (dd, *J* = 14.4, 3.9 Hz, 1H), 0.97 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.9, 146.9, 140.8, 119.2, 108.2, 106.5, 101.1, 72.5, 53.0, 30.6, 30.5, 30.3. **IR** (neat) ν_{max} 3378.6 (br), 2948.8 (s), 2901.2 (m), 1502.1 (m), 1485.9 (s), 1440.4 (m), 1363.4 (w), 1243.2 (s), 1039.5 (s), 934.0 (w), 810.7 (w). **HRMS** (DART) for $C_{13}H_{17}O_2$ $(M+H-H_2O)^+$: Calc'd: 205.1223, found: 205.1219. **$[\alpha]_D^{20}$** = 31.17 (*c* = 0.34, $CHCl_3$, *l* = 50 mm).

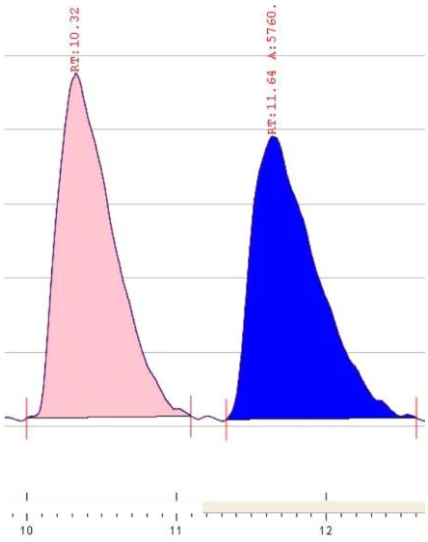
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel AS-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of

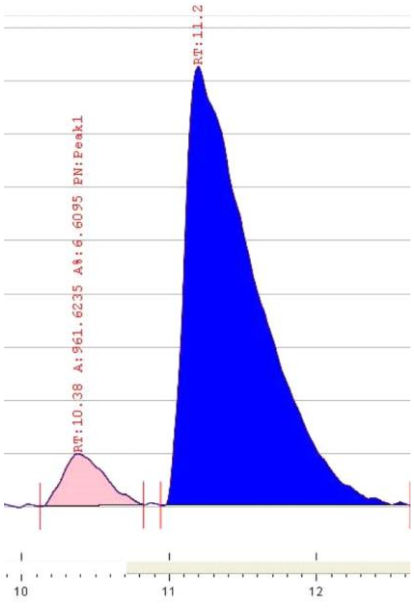
(*S*)-1-(benzo[d][1,3]dioxol-5-yl)-3,3-dimethylbutan-1-ol.

Racemic Material

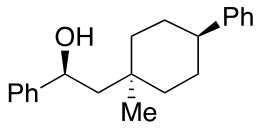


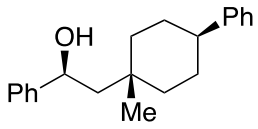
Peak No	% Area	Area	RT (min)
1	50.8722	5964.8104	10.32
2	49.1278	5760.2832	11.64
Total:	100	11725.0936	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	6.6095	961.6235	10.38
2	93.3905	13587.4501	11.2
Total:	100	14549.0736	



and


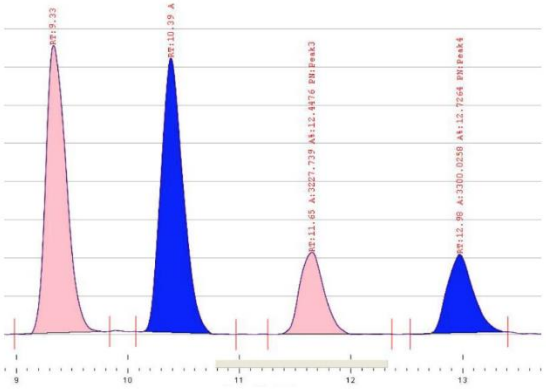
(*S*)-2-((1*s*,4*R*)-1-methyl-4-phenylcyclohexyl)-1-phenylethan-1-ol (1.89 and **1.89')**. The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), (4-iodo-4-methylcyclohexyl)benzene (120.1 mg, 0.40 mmol, 2.0 equiv.), and phenylzinc chloride solution in THF (1.0 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil consisting of a 1:2.7 mixture of diastereomers (30.6 mg, 52% yield). The diastereomeric ratio was determined by ^{1}H NMR integration. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44-7.34 (m, 13H), 7.34-7.26 (m, 12H), 7.26-7.16 (m, 11H), 4.97 (dd, *J* = 8.4, 2.9 Hz, 1H, minor diastereomer), 4.88 (dd, *J* = 8.2, 3.2 Hz, 3H, major diastereomer), 2.55-2.37 (m, 5H), 2.00 (m, 4H), 1.94-1.85 (m, 4H), 1.84-1.52 (m, 32H), 1.39-1.24 (m, 9H), 1.14 (s, 3H), 1.09 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.7, 147.6, 146.8, 146.8, 128.7, 128.7, 128.4, 128.4, 127.6, 127.5, 127.0, 126.9, 126.0, 126.0, 125.9, 72.4, 71.8, 55.4, 45.2, 44.7, 44.4, 39.1, 38.7, 38.7, 38.6, 32.8, 32.4, 30.5, 29.9, 29.8, 29.8, 29.7, 22.3. **IR** (neat) ν_{max} 412.6 (br), 2919.3 (m), 2857.4 (w), 1491.2 (w), 1053.4 (w), 718.5 (m), 697.2 (s), 533.78 (w). **HRMS** (DART) for $C_{15}H_{25}O_2$ $(M+H-H_2O)^+$: Calc'd: 277.1951, found: 277.1951.

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

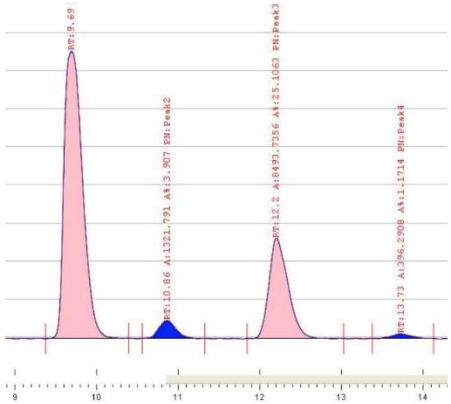
Chiral SFC (Chiracel OJ-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-2-(1-methyl-4-phenylcyclohexyl)-1-phenylethan-1-ol**.

Racemic Material



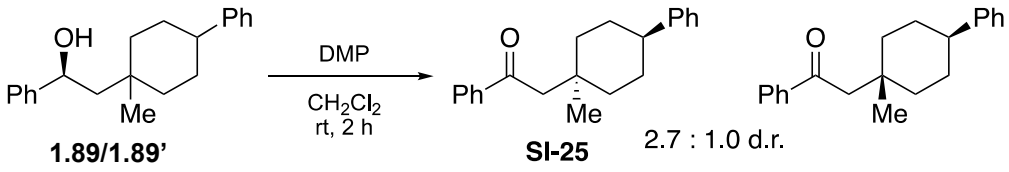
Peak No	% Area	Area	RT (min)
1	36.764	9533.1123	9.33
2	38.062	9869.7005	10.39
3	12.4476	3227.739	11.65
4	12.7264	3300.0258	12.98
Total:	100	25930.5776	

Enantioenriched Material

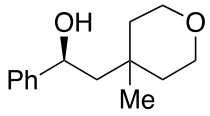


Peak No	% Area	Area	RT (min)
1	69.8153	23619.2332	9.69
2	3.907	1321.791	10.86
3	25.1063	8493.7356	12.2
4	1.1714	396.2908	13.73
Total:	100	33831.0506	

The stereochemical configuration was determined by COSY and NOESY analysis of compound **SI-25** which was isolated as a single stereoisomer from the mixture obtained after oxidation of product **1.89**.



1.89/1.89' **SI-25** 2.7 : 1.0 d.r.



(*S*)-2-(4-methyltetrahydro-2*H*-pyran-4-yl)-1-phenylethan-1-ol (1.90).

The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), 4-iodo-4-methyltetrahydro-2*H*-pyran (90.0 mg, 0.40 mmol, 2.0 equiv.), and phenylzinc chloride solution in THF (1.0 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (32.2 mg, 73% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36-7.35 (m, 3H), 7.29-7.26 (m, 2H), 4.90 (dd, *J* = 8.8, 3.5 Hz, 1H), 3.84-3.70 (m, 1H), 3.71-3.59 (m, 2H), 1.91 (dd, *J* = 14.7, 8.7 Hz, 1H), 1.75-1.58 (m, 3H), 1.56-1.44 (m, 2H), 1.37-1.30 (m, 1H), 1.26 (s, 1H), 1.14 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 146.4, 128.8, 127.7, 125.8, 71.8, 64.1, 64.0, 51.5, 38.5, 38.4, 31.0, 24.5. **IR** (neat) ν_{max} 3410.3 (br), 2950.7 (s), 2919.2 (s), 2853.8 (s), 1452.7 (m), 1102.3 (s), 1060.0 (m), 1036.0 (m), 1017.1 (m), 699.3 (m). **HRMS** (DART) for $C_{14}H_{19}O$ $(M+H-H_2O)^+$: Calc'd: 203.1424, found: 203.1430. **$[\alpha]_D^{20}$** = 40.78 (*c* = 0.5, $CHCl_3$, *l* = 50 mm).

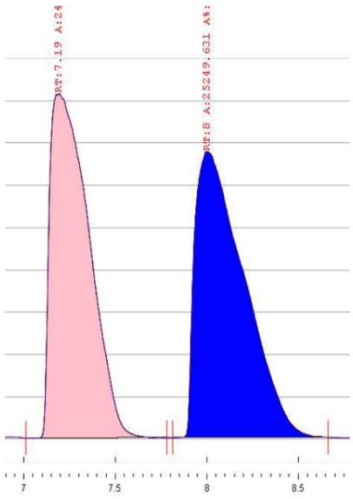
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of

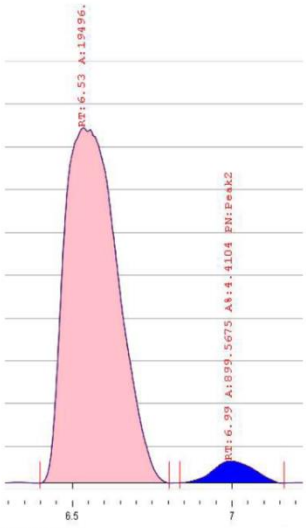
(*S*)-2-(4-methyltetrahydro-2*H*-pyran-4-yl)-1-phenylethan-1-ol.

Racemic Material

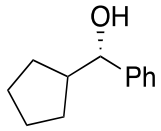


Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	48.9012	24163.7375	7.19
2	51.0988	25249.631	8
Total:	100	49413.3685	

Enantioenriched Material



Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	95.5896	19496.8917	6.53
2	4.4104	899.5675	6.99
Total:	100	20396.4592	



(*S*)-cyclopentyl(phenyl)methanol (1.101). The reaction was performed according to general **procedure A** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (24.6 mg, 70% yield). **HRMS** (DART) for $C_{12}H_{15}$ $(M+H-H_2O)^+$: Calc'd: 159.1166, found: 151.1168. $\mathbf{[\alpha]_D^{20}}$ = -51.03 (*c* = 1.0, $CHCl_3$, *l* = 50 mm (lit: $\mathbf{[\alpha]_D^{20}}$ = - 40.08 (*c* = 0.8, $CHCl_3$, 78% *ee*, (*S*)-enantiomer)). All spectral data was in accordance with the literature.[57]

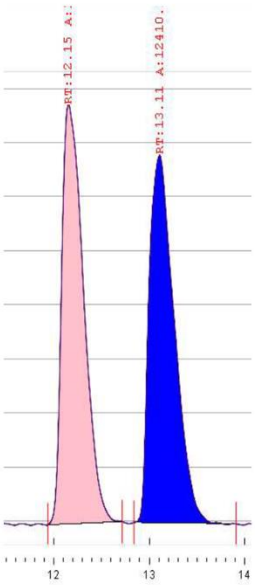
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by comparison with the optical rotation reported in the literature for the same compound.[12] The stereochemical assignment was found to be in accordance with product **1.82** (determined through X-ray crystallography).

Chiral SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-cyclopentyl(phenyl)methanol.**

(57) Morris, D. J.; Hayes, A. M.; Wills, M. *J. Org. Chem.* **2006**, *71*, 7035–7044.

Racemic Material



Peak Info

Peak No	% Area	Area	RT (min)
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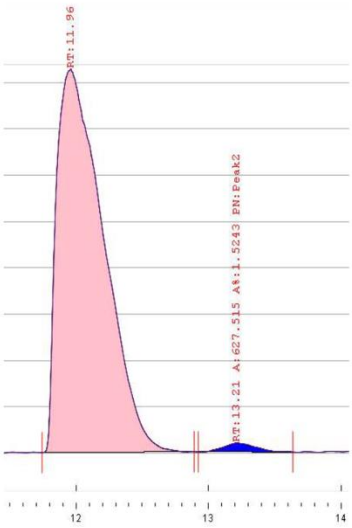
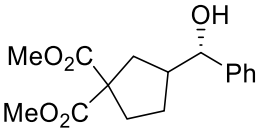
2	50.1865	12410.1565	13.11
Total:	100	24728.0733	

Enantioenriched Material



Peak Info

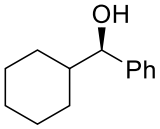
Peak No	% Area	Area	RT (min)
1	98.4757	40539.7235	11.96
2	1.5243	627.515	13.21
Total:	100	41167.2385	



dimethyl 3-((S)-hydroxy(phenyl)methyl)cyclopentane-1,1-dicarboxylate (1.105). The reaction was performed according to general **procedure A** dimethyl (*E*)-2-(2-iodoethyl)-2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)malonate (90.4 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. **Note** the oxidation was carried out under buffered conditions by using pH7 phosphate buffer solution (0.50 mL) in place of 3M NaOH solution, and carrying out the oxidation for 12 hours. The crude mixture was purified by silica gel column chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (36.0 mg, 62% yield).

^{1}H NMR (600 MHz, C_6D_6) δ 7.15-7.12 (m, 2H), 7.10-7.04 (m, 6H), 7.04-6.99 (m, 2H), 4.18 (d, *J* = 7.1 Hz, 1H), 4.11 (d, *J* = 6.7 Hz, 1H), 3.27 (s, 3H), 3.24 (s, 3H), 3.22 (s, 3H), 3.19 (s, 3H), 2.70-2.62 (m, 1H), 2.41-2.36 (m, 1H), 2.35-2.29 (m, 3H), 2.25-2.19 (m, 2H), 2.19-2.12 (m, 1H), 2.12-2.05 (m, 1H), 1.83-1.73 (m, 1H), 1.73-1.63 (m, 1H), 1.35 (s, 1H), 1.35-1.29 (m, 3H), 0.39 (s, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.3, 173.1, 172.9, 172.8, 144.0, 143.8, 128.6, 128.5, 127.80, 127.8, 126.4, 126.3, 77.9, 77.7, 60.2, 60.1, 52.9, 52.8, 52.8, 52.8, 46.9, 46.8, 37.2, 37.2, 34.2, 34.0, 28.8, 28.3. **IR** (neat) ν_{max} 3522.2 (br), 3026.2 (w), 1726.3 (s), 1492.2 (w), 1267.0 (m), 1197.0 (w), 1158.7 (w), 1102.6 (w), 763.8 (w), 702.4 (w). **HRMS** (DART) for $C_{16}H_{19}O_5$ $(M+H)^+$: Calc'd: 291.1227, found: 291.1226. **Note**: the product was obtained as a mixture of diastereomers and an optical rotation was

not obtained. The diastereomeric ratio was determined by the integration of the ^{1}H NMR in C_6D_6.



(*R*)-cyclohexyl(phenyl)methanol (1.106). The reaction was performed according to general **procedure A** with (*E*)-2-(7-iodohept-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (70.0 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(R,R)*-L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (19.0 mg, 52% yield). **HRMS** (DART) for $C_{13}H_{17}$ $(M+H-H_2O)^+$: Calc'd: 173.1325, found: 173.1329. $\mathbf{[\alpha]_D^{20}}$ = 28.27 (*c* = 0.29, $CHCl_3$, *l* = 50 mm (lit: $\mathbf{[\alpha]_D^{20}}$ = -21.4 (*c* = 1.01, $CHCl_3$, 91% *ee*, (*S*)-enantiomer)). All spectral data was in accordance with the literature.[58]

Analysis of Stereochemistry:

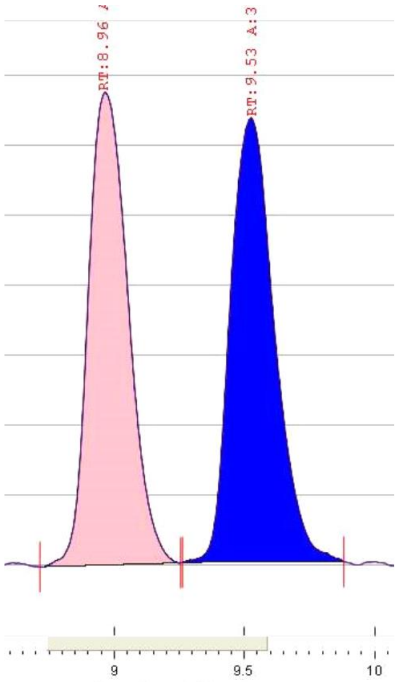
Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**) and comparison of optical rotation reported in the literature for the same compound.[13]

(58) Arenas, I.; Boutureira, O.; Matheu, M. I.; Díaz, Y.; Castillón, S. *European J. Org. Chem.* **2015**, *2015*, 3666–3669.

Chiral SFC (Chiracel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of

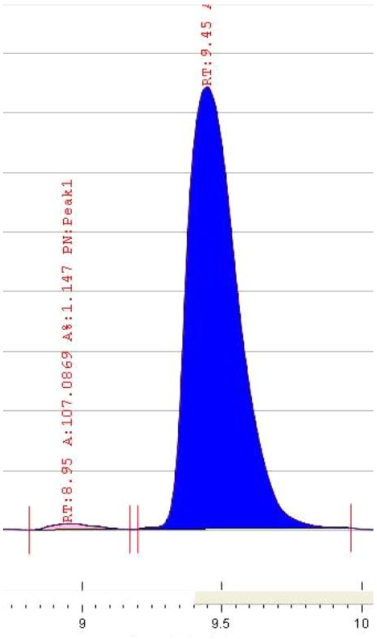
(*S*)-cyclohexyl(phenyl)methanol.

Racemic Material

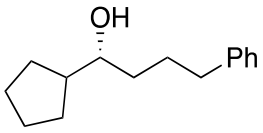


Peak No	% Area	Area	RT (min)
1	49.1136	3580.9512	8.96
2	50.8864	3710.2034	9.53
Total:	100	7291.1546	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	1.147	107.0869	8.95
2	98.853	9229.2502	9.45
Total:	100	9336.3371	



(*R*)-1-cyclopentyl-4-phenylbutan-1-ol (1.107). The reaction was performed according to general **procedure B** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv.), and (3-phenylpropyl)zinc bromide solution in DMA (0.24 mL, 1.68 M, 0.4 mmol, 2.0 equiv.), with (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) in DMA (2.40 mL). The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (25.3 mg, 58% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29-7.26 m, 2H), 7.20-7.18(m, 3H), 3.43 (td, *J* = 8.0, 3.2 Hz, 1H), 2.72-2.53 (m, 2H), 1.89-1.50 (m, 10H), 1.46-1.28 (m, 2H), 1.29 -1.15 (m, 1H).**^{13}C NMR** (151 MHz, $CDClz_3$) δ 142.6, 128.5, 128.4, 125.8, 75.9, 46.5, 36.1, 35.9, 29.3, 28.6, 27.7, 25.8, 25.7. **IR** (neat) ν_{max} 3357.1 (br), 3082.2 (w), 3057. 3022.8 (w), 2938.7 (s), 2861.2 (s), 1494.2 (m), 1450.8 (m), 1094.4 (m), 1053.8 (m), 1028.9 (m), 920.6 (m), 800.8 (s), 746.5 (s). **HRMS** (DART) for $C_{15}H_{21}$ $(M+H-H_2O)^+$: Calc'd: 201.1634, found: 201.1638. **$[\alpha]_D^{20}$** = -5.66 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).

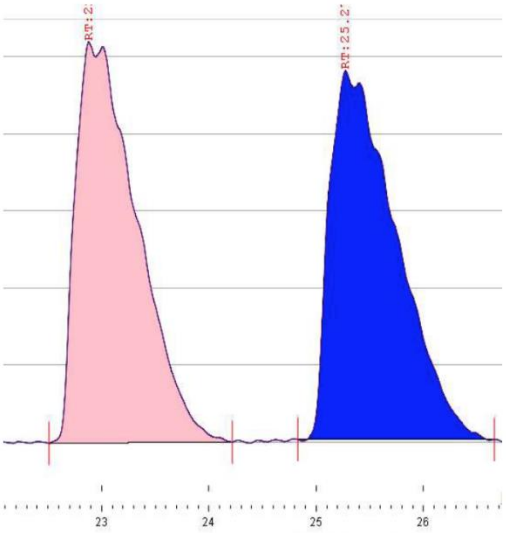
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of

(*R*)-1-cyclopentyl-4-phenylbutan-1-ol.

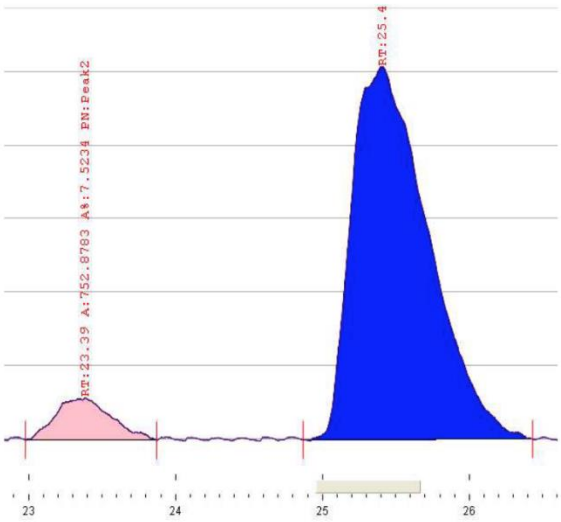
Racemic Material



Peak Info

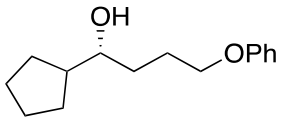
Peak No	% Area	Area	RT (min)
1	50.074	20889.2315	22.88
2	49.926	20827.4806	25.27
Total:	100	41716.7121	

Enantioenriched Material



Peak Info

Peak No	% Area	Area	RT (min)
1	7.5234	752.8783	23.39
2	92.4766	9254.2799	25.41
Total:	100	10007.1582	



(*R*)-1-cyclopentyl-4-phenoxybutan-1-ol (1.108). The reaction was performed according to general **procedure B** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv.), and (3-phenoxypropyl)zinc bromide solution in DMA (0.360 mL, 1.1 M, 0.4 mmol, 2.0 equiv.), with (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) in DMA (2.40 mL). The crude mixture was purified by silica gel column chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (30.1 mg, 64% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39-7.18 (m, 2H), 7.05-6.76 (m, 3H), 4.00 (ddd, *J* = 5.8, 3.0 Hz, 2H), 3.59-3.35 (m, 1H), 2.14-1.43 (m, 12H), 1.43-1.30 (m, 1H), 1.27-1.17 (m, 1H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.1, 129.6, 120.8, 114.7, 75.8, 68.1, 46.7, 33.0, 29.3, 28.8, 25.9, 25.8 (one diastereotopic carbon peak not observed). **IR** (neat) ν_{max} 3408.7 (Br), 2946.9 (m), 2865.0 (m), 1598.1 (w), 1495.6 (m), 1299.5 (w), 1244.0 (s), 1040.7 (w), 1012.4 (w), 752.3 (m), 690.7 (m). **HRMS** (DART) for $C_{15}H_{23}O_2$ $(M+H)^+$: Calc'd: 235.1694, found: 235.1704. **$[\alpha]_D^{20}$** = 4.159 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).

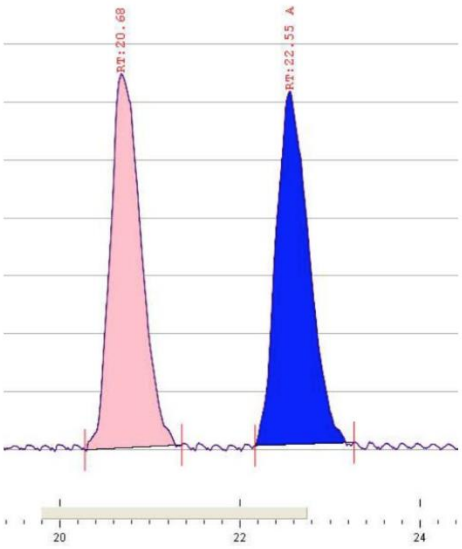
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel OJ-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of

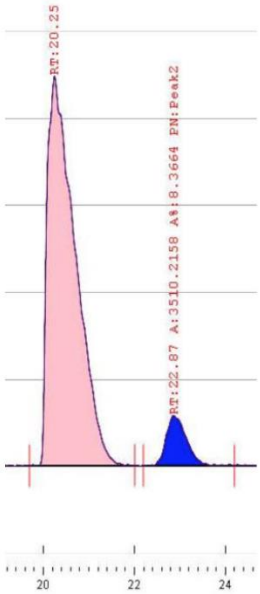
(*R*)-1-cyclopentyl-4-phenoxybutan-1-ol.

Racemic Material

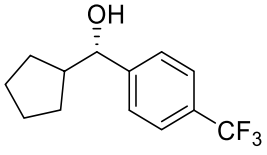


Peak No	% Area	Area	RT (min)
1	49.9026	3070.2661	20.68
2	50.0974	3082.2568	22.55
Total:	100	6152.5229	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	91.6336	38445.685	20.25
2	8.3664	3510.2158	22.87
Total:	100	41955.9008	



(*S*)-cyclopentyl(4-(trifluoromethyl)phenyl)methanol (1.109). The reaction was performed according to general **procedure A** with (E)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv.), and 4-(trifluoromethyl)phenyl zinc chloride solution in THF (0.52 mL, 0.77 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (27.0 mg, 55% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.9 Hz, 2H), 7.46 (d, *J* = 7.8 Hz, 2H), 4.50 (d, *J* = 8.2 Hz, 1H), 2.18 (h, *J* = 8.9, 8.9, 8.9, 8.3, 8.3 Hz, 1H), 1.93 (dd, *J* = 3.3, 1.2 Hz, 1H), 1.85 (h, td, *J* = 12.4, 12.2, 7.3 Hz, 1H), 1.71-1.55 (m, 3H), 1.55-1.45 (m, 2H), 1.43-1.36 (m, 1H), 1.22-1.14 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 148.5, 126.9, 125.4, 125.4, 125.4, 125.4, 78.4, 47.9, 29.5, 29.2, 25.6, 25.5. **IR** (neat) ν_{max} 3374.5 (br), 2953.1 (w), 2867.0 (w), 1618.6 (w), 1417.4 (w), 1323.9 (s), 1162.2 (m), 1123.4 (s), 1065.9 (s), 1016.1 (w), 836.9 (w), 758.6 (w). **HRMS** (DART) for $C_{13}H_{14}F_3$ $(M+H-H_2O)^+$: Calc'd: 227.1042, found: 227.1048. **$[\alpha]_D^{20}$** = -29.83 (*c* = 1.00, $CHCl_3$, *l* = 50 mm).

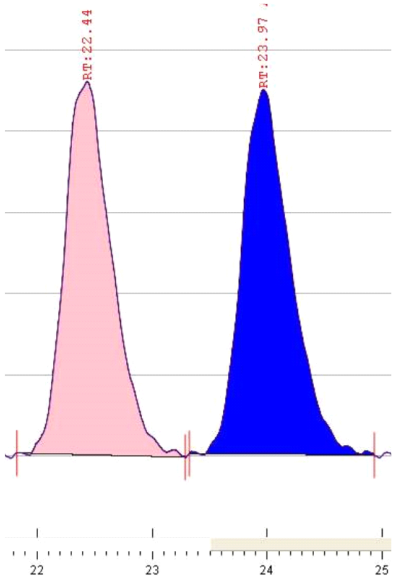
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Chiral SFC (Chiracel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of

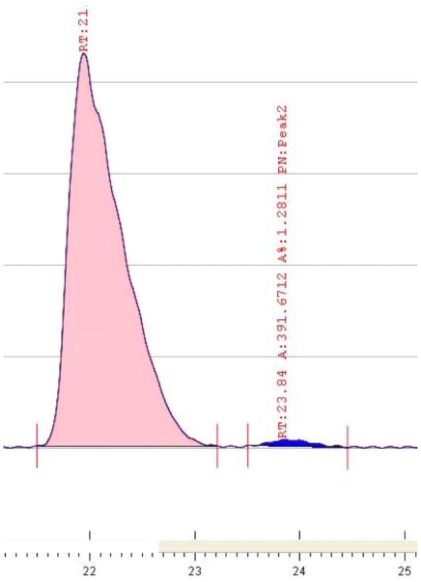
(*S*)-cyclopentyl(4-(trifluoromethyl)phenyl)methanol.

Racemic Material

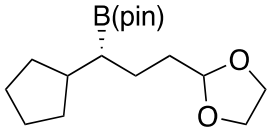


Peak No	% Area	Area	RT (min)
1	49.6834	6573.1351	22.44
2	50.3166	6656.9053	23.97
Total:	100	13230.0404	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	98.7189	30182.1448	21.94
2	1.2811	391.6712	23.84
Total:	100	30573.816	



(*R*)-2-(1-cyclopentyl-3-(1,3-dioxolan-2-yl)propyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.110). The reaction was performed according to general **procedure B** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv.), and (2-(1,3-dioxolan-2-yl)ethyl)zinc bromide solution in DMA (0.330 mL, 1.23 M, 0.4 mmol, 2.0 equiv.), with (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) in DMA (2.40 mL). ***Note:*** product was isolated and characterized as the boronic ester prior to oxidation since the corresponding alcohol was prone to decomposition. The crude mixture was purified by silica gel column chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (40.8 mg, 66% yield). **^{1}H NMR** (600 MHz, $CDCl_3$)) δ 4.83 (t, *J* = 4.8 Hz, 1H), 3.99-3.91 (m, 2H), 3.87-3.78 (m, 2H), 1.88-1.77 (m, 2H), 1.77-1.64 (m, 2H), 1.62-1.54 (m, 4H), 1.53-1.40 (m, 3H), 1.24 (s, 12H), 1.17-1.05 (m, 2H), 0.96-0.85 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 104.9, 83.0, 65.0, 42.0, 33.9, 32.6, 32.2, 25.4, 25.3, 25.1, 25.0. **IR** (neat) ν_{max} 2974.1 (m), 2943.9 (m), 2864.7 (m), 1455.5 (w), 1378.4 (m), 1316.5 (m), 1213.3 (w), 1143.8 (s), 1033.6 (w), 966.8 (w), 842.5 (w). **HRMS** (DART) for $C_{17}H_{32}BO_4$ $(M+H)^+$: Calc'd:311.2388, found: 311.2386. **$[\alpha]_D^{20}$** = 6.67 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).

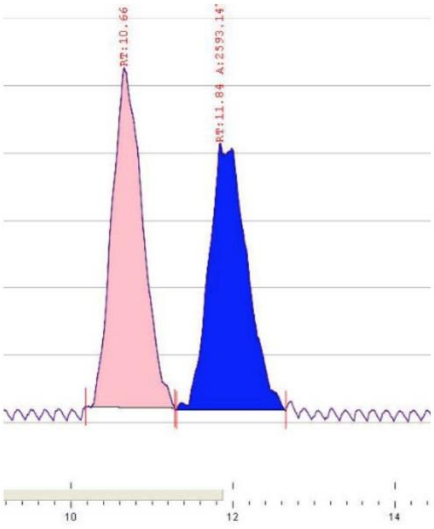
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1.6** as ligand. Absolute stereochemistry was assigned by analogy (see product **1.82** and **1.101**).

Note: the analysis of stereochemistry was performed on the corresponding TBDPS protected silyl ether. The boronic ester (both the enriched sample and the racemate) was oxidized under standard conditions and the crude alcohol was promptly protected with TBDPS-Cl following standard procedures.

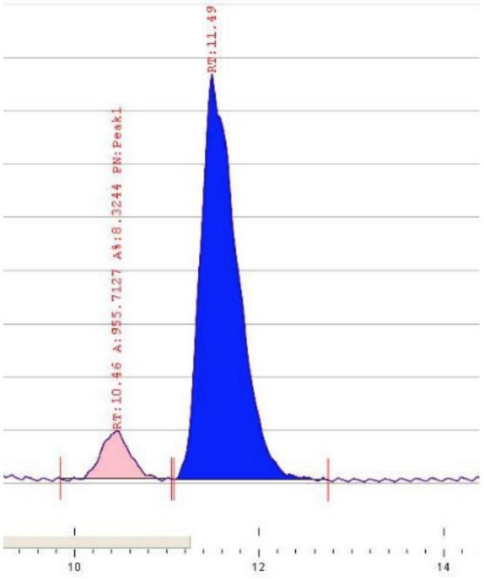
Chiral SFC (Chiracel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-1-cyclopentyl-3-(1,3-dioxolan-2-yl)propan-1-ol**.

Racemic Material



Peak No	% Area	Area	RT (min)
1	50.5782	2653.8255	10.66
2	49.4218	2593.1472	11.84
Total:	100	5246.9727	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
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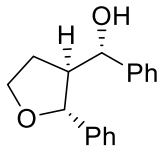
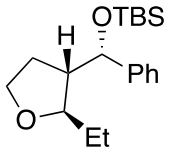
2	91.6756	10525.088	11.49
Total:	100	11480.8007	



(*S*)-phenyl((*2R*,*3R*)-2-phenyltetrahydrofuran-3-yl)methanol (1.111). The reaction was performed according to the general **procedure A** with (*R,E*)-2-(3-(2-iodoethoxy)-3-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (82.8 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using NiBr2·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel /column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (35.8 mg, 70% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33-7.22 (m, 8H), 7.10 (d, *J* = 6.8 Hz, 2H), 4.72 (d, *J* = 6.6 Hz, 2H), 4.11 (q, *J* = 8.1, 8.1, 8.1 Hz, 1H), 4.00 (q, *J* = 8.0, 8.1, 8.1 Hz, 1H), 2.53-2.48 (m, 1H), 2.26 (m, 2H), 2.05-1.95 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.4, 142.6, 128.6, 128.4, 127.9, 127.4, 126.4, 126.1, 82.6, 74.0, 68.3, 55.3, 27.5. **IR** (neat) ν_{max} 3400.0 (br), 3081.8 (w), 3058.3 (w), 2921.4 (w), 2872.1 (w), 1600.9 (w), 1491.9 (m), 1452.0 (m), 1059.6 (m), 1040.6 (m), 1024.8 (m), 756.3 (m), 699.3 (s). **HRMS** (DART) for $C_{17}H_{19}O_2$ $(M+H)^+$: Calc'd: 255.1380, found: 255.1383 **$[\alpha]_D^{20}$** = 23.05 (*c* = 0.85, $CHCl_3$, *l* = 50 mm).

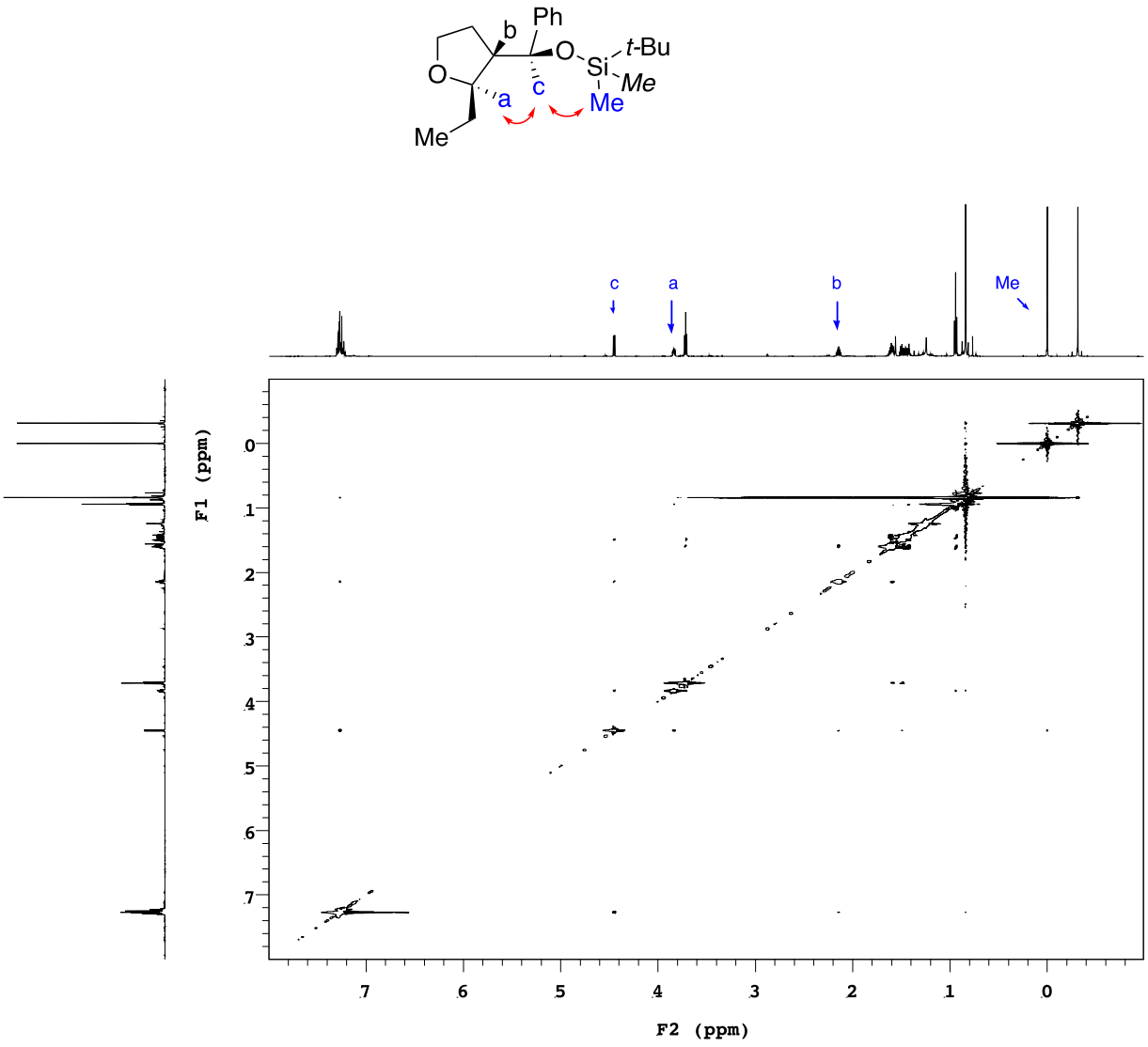
Analysis of Stereochemistry:

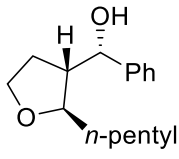
In order to assign the stereochemical configuration of the title compound, the substrate was first protected with TBSCl through standard methods. All spectra for the resulting TBS-ether was found to match that obtained for compound **SI-26** for which the stereochemical configuration has been determined through NOESY correlation **(**see below).



***Tert*-butyl((*S*)-((*2R,3S*)-2-ethyltetrahydrofuran-3-yl)(phenyl)methoxy)dimethylsilane (SI-26)**. Compound **1.113** (12 mg, 0.048 mmol) was dissolved in anhydrous DMF (4 mL), followed by addition of imidazole (9.8 mg, 0.14 mmol), and TBSCl (5.9 mg, 0.072 mmol). The resulting mixture was stirred overnight at room temperature, diluted with diethyl ether, washed twice with water and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture is filtered through silica gel (3% ethyl in hexanes). The resulting mixture was dissolved in CH_2Cl_2 (5 mL) and triethylsilane (17.5 µL, 0.1 mmol) was added, followed by dropwise addition of BF_3•Et_2O (6.8 µL, 0.055 mmol) at 0 ℃ . The reaction mixture was stirred for 10 min at the same temperature, then saturated aqueous sodium bicarbonate solution (5 mL) was added, and the mixture was extracted with CH_2Cl_2 (3×10 mL). The combined extracts were dried over anhydrous sodium sulfate and concentrated in vacuo. Purification by flash column chromatography provided **SI-25** (8.2 mg, 93% over two steps) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31-7.19 (m, 5H), 4.45 (d, J = 8.5 Hz, 1H), 3.84 (ddd, J = 8.3, 5.8, 3.7 Hz, 1H), 3.72 (t, J = 6.7, 6.7 Hz, 2H), 2.17-2.12 (m, 1H), 1.65-1.55 (m, 2H), 1.53-1.39 (m, 2H), 0.95 (t, J = 7.4, 7.4 Hz, 3H), 0.84 (s, 9H), 0.00 (s, 3H), -0.31 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.4, 128.2, 127.5, 126.9, 84.0, 78.4, 67.0, 52.7, 30.2, 29.0, 25.9, 18.2, 10.8, -4.4, -4.8. **IR** (neat) ν_{max} 2953.9 (s), 2926.3 (s), 2853.9 (s), 1460.2 (w), 1251.7 (m), 1107.9 (m), 1080.2 (m), 851.6 (s), 836.2 (s), 775.0 (s). **HRMS** (DART) for $C_{19}H_{33}O_2Si$ $(M+H)^+$: Calc'd: 321.2244, found: 321.2232. **$[\alpha]_D^{20}$** = -42.66 (c = 0.38, $CHCl_3$, l = 50 mm).

Relevant NOESY correlations are illustrated below.



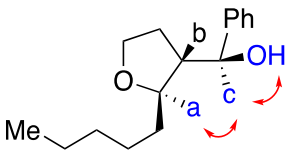


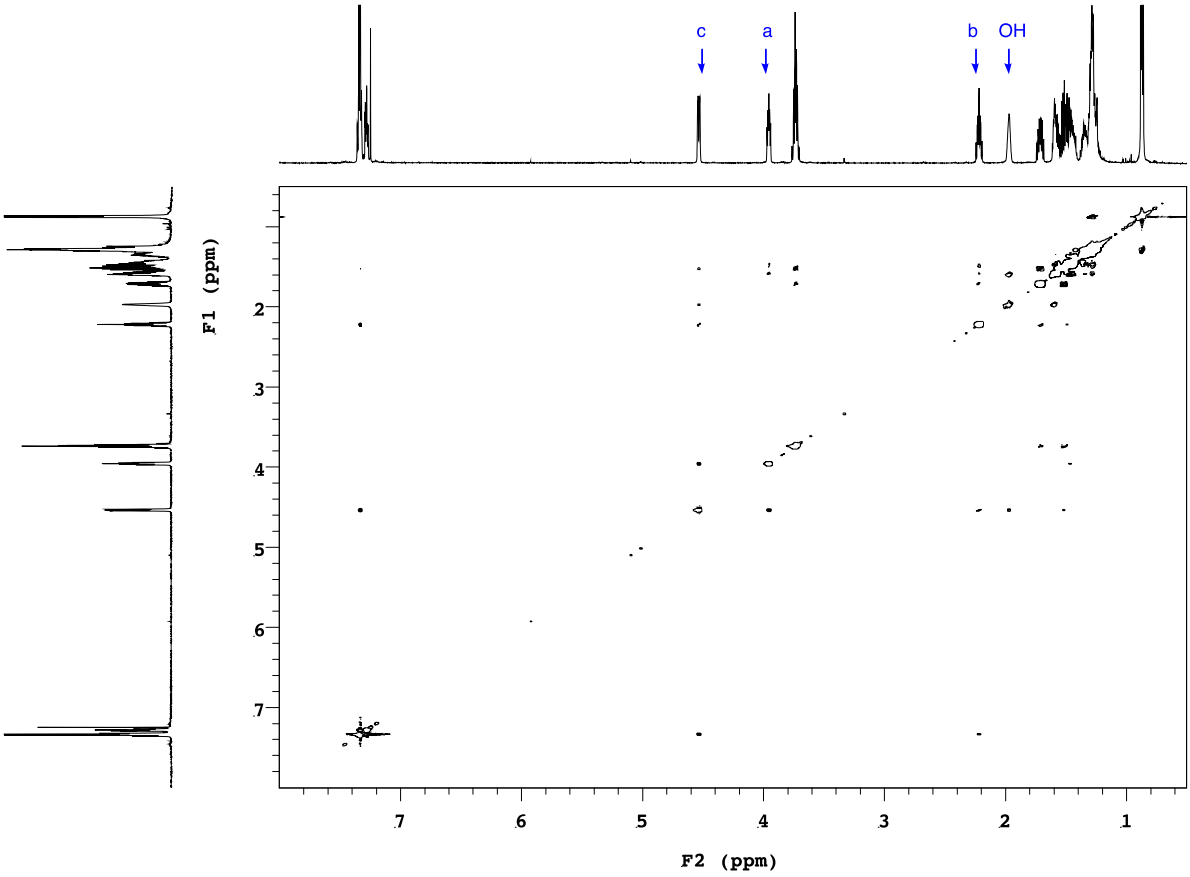
(*S*)-((*2R*,*3R*)-2-pentyltetrahydrofuran-3-yl)(phenyl)methanol (1.112).

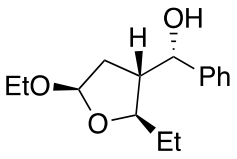
The reaction was performed according to the general **procedure A** with (*R*,*E*)-2-(3-(2-iodoethoxy)oct-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (81.6 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using NiBr2·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (17.6 mg, 45% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33-7.23 (m, 5H), 4.52 (dd, 1H), 3.96-3.92 (m, 1H), 3.74-3.70 (m, 2H), 2.23-2.17 (m, 1H), 1.94 (d, J = 3.4 Hz, 1H), 1.73-1.63 (m, 1H), 1.60-1.36 (m, 4H), 1.32-1.12 (m, 5H), 0.86 (t, J = 6.5, 6.5 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.9, 128.7, 128.0, 126.7, 82.6, 77.5, 66.7, 51.4, 36.0, 32.1, 30.1, 26.2, 22.8, 14.2. **IR** (neat) ν_{max} 3407.6 (br), 3061.1 (w), 3027.4 (w), 2951.6 (s), 2925.5 (s), 2855.4 (s), 1452.7 (w), 1074.5 (m), 1034.4 (m), 904.6 (w), 761.9 (m), 700.8 (s). **HRMS** (DART) for $C_{16}H_{25}O_2$ $(M+H)^+$: Calc'd: 249.1849, found: 249.1848 **$[\alpha]_D^{20}$** = 31.80 (c = 0.64, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

The stereochemistry of the carbon skeleton was assigned through NOESY correlation analysis. The absolute configuration at the B(pin)/OH containing stereocenter was assigned by analogy (see substrates: **1.82** and **1.101**). Relevant NOESY correlations are illustrated below.


Ph
b
OH
O
c
a
Me


c
a
b
OH
F1 (ppm)
2
3
4
5
6
7
7
6
5
4
3
2
1
F2 (ppm)



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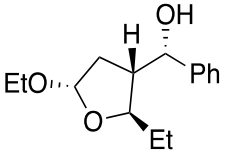
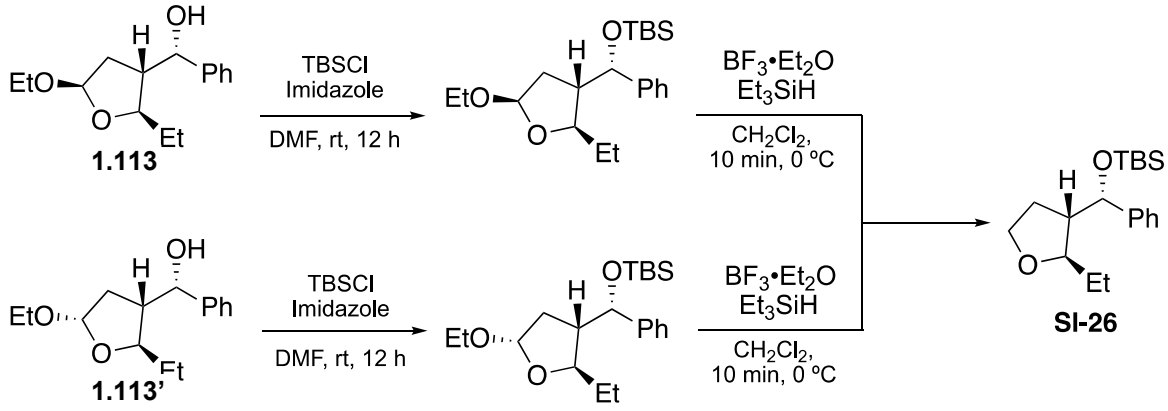


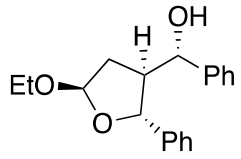
(*1S*)-((*2R*,*3R*)-5-ethoxy-2-ethyltetrahydrofuran-3-yl)(phenyl)methanol (1.113 and 1.113'). The reaction was performed according to the general **procedure A** with 2-((3*R,E*)-3-(1-ethoxy-2-iodoethoxy)pent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (82.0 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using NiBr2·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel /column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (25.0 mg, 50% yield). The product was obtained as a pair of separable diastereomers. *Diastereomer 1:* **^{1}H NMR** (500 MHz, $CDCl_3$) 7.37-7.36 (m, 2H), 7.33-7.30 (m, 2H), 7.23-7.19 (m, 1H), 5.12 (d, *J* = 4.6 Hz, 1H), 4.90 (d, *J* = 4.3 Hz, 1H), 4.12 (q, *J* = 5.1, 5.1, 4.9 Hz,1H), 4.05 (s, 1H), 3.82 (dq, *J* = 9.3, 7.2, 7.2, 7.1 Hz, 1H), 3.50 (dq, *J* = 9.2, 9.2, 6.1, 6.1 Hz, 1H), 2.28-2.25 (m, 1H), 2.20 (ddd, *J* = 13.3, 11.1, 4.9 Hz, 1H), 1.88 (dd, *J* = 13.5, 2.2 Hz, 1H), 1.26-1.21 (m, 5H), 0.66 (t, *J* = 7.4, 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.6, 128.4, 127.3, 126.1, 102.7, 79.9, 75.4, 62.2, 49.4, 37.7, 28.9, 15.2, 9.5. **IR** (neat) ν_{max} 3423.0 (br), 3059.3 (w), 3026.7 (w), 2968.8 (m), 2920.7 (s), 2873.5 (m), 1492.0 (w), 1452.3 (m), 1202.9 (w), 1082.4 (s), 1072.3 (s), 979.0 (s), 758.2 (w), 701.0 (s). **HRMS** (DART) for $C_{15}H_{21}O_3$ $(M+H)^+$: Calc'd: 249.1485, found: 249.1483. **$[\alpha]_D^{20}$** = 22.40 (*c* =1.00, $CHCl_3$, *l* = 50 mm). *Diastereomer 2:* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33-7.25 (m, 5H), 4.99 (d, *J* = 2.9 Hz, 1H), 4.51 (dd, *J* = 8.5, 3.0 Hz, 1H), 4.03 (ddd, *J* = 9.5, 6.3, 3.7 Hz, 1H), 3.72 (dq, *J* = 9.4, 7.1, 7.1, 7.0 Hz, 1H), 3.36 (dq, *J* = 9.6, 7.2, 7.1, 7.1 Hz, 1H), 2.55-2.46

(m, 1H), 1.90 (d, J = 3.4 Hz, 1H), 1.74-1.63 (m, 3H), 1.57 (ddd, J = 13.5, 8.6, 6.9 Hz, 1H), 1.14 (t, J = 7.1, 7.1 Hz, 3H), 0.99 (t, J = 7.4, 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.6, 128.7, 128.1, 126.5, 103.2, 103.2, 85.2, 77.9, 62.4, 49.5, 37.3, 31.1, 15.3, 11.1. **IR** (neat) ν_{max} 3433.0 (br), 2968.7 (m), 2927.1 (m), 2872.2 (m), 1452.9 (m), 1372.2 (w), 1343.9 (w), 1309.5 (w), 1190.3 (w), 1092.5 (s), 1064.9 (s), 1023.0 (s), 971.8 (s), 760.1 (w), 701.4 (s), 624.9 (w). **HRMS** (DART) for $C_{15}H_{21}O_3$ $(M+H)^+$: Calc'd: 249.1485, found: 249.1490. **$[\alpha]_D^{20}$**= -108.38 (c = 1.00, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

The transformations below were carried out on the isolated compounds **1.113** and **1.113'** separately in order to assess the stereochemistry of the isolated compounds. Upon reduction all spectral data of the two separate products was found to be identical. The stereochemical assignment was determined through NOESY correlation analysis of the resulting products. The absolute configuration at the B(pin)/silyl ether containing stereo center was assigned by analogy (see substrates **1.82** and **1.101**).





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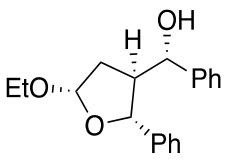
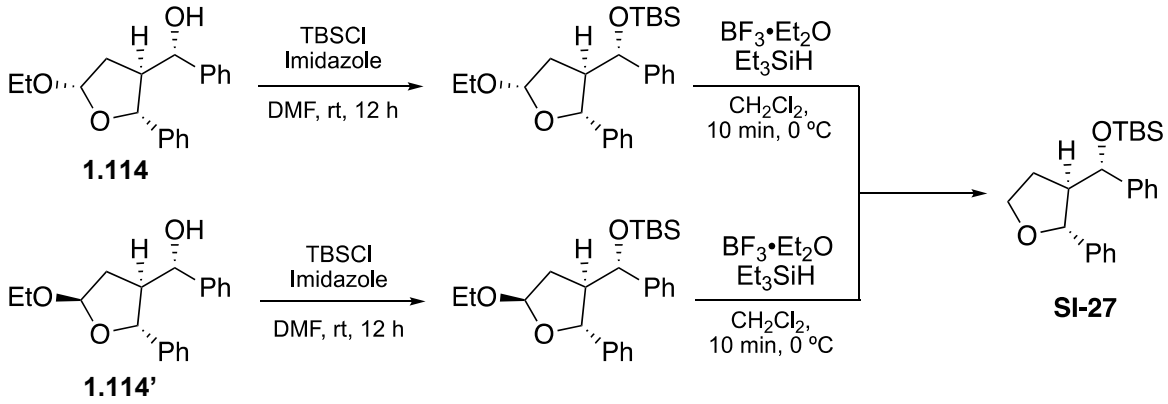


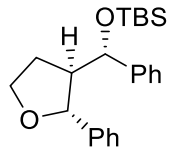
(*1S*)-((*2R*,*3S*)-5-ethoxy-2-phenyltetrahydrofuran-3-yl)(phenyl)methanol (1.114 and 1.114') . The reaction was performed according to the general **procedure A** with 2-((*3R*,*E*)-3-(1-ethoxy-2-iodoethoxy)-3-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (91.6 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using NiBr2·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (30.4 mg, 51% yield). The product is a pair of separable diastereomers. *Diastereomer 1 (up):* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36-7.23 (m, 9H), 7.23-7.18 (m, 1H), 5.34 (d, *J* = 4.9 Hz, 1H), 5.12 (d, *J* = 5.8 Hz, 1H), 4.94 (t, *J* = 4.9, 4.9 Hz, 1H), 3.99 (d, *J* = 5.8 Hz, 1H), 3.93-3.86 (m, 1H), 3.61-3.58 (m, 1H), 2.58-2.54 (m, 1H), 2.12-2.07 (m, 1H), 2.01 (dd, *J* = 14.0, 3.2 Hz, 1H), 1.30 (td, *J* = 7.1, 7.1, 1.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.1, 142.3, 128.7, 128.4, 127.8, 127.2, 126.0, 126.0, 103.3, 103.3, 82.1, 82.1, 73.3, 62.6, 54.1, 33.3, 15.2. **IR** (neat) ν_{max} 3424.6 (br), 3060.1 (w), 3029.2 (w), 2971.0 (w), 2923.0 (w), 1492.5 (w), 1452.4 (w), 1197.7 (w), 1097.0 (m), 1046.2 (s), 1022.8 (s), 759.1 (w), 699.6 (s). **HRMS** (DART) for $C_{19}H_{26}NO_3$ $(M+NH_4)^+$: Calc'd: 316.1907, found: 316.1906. $[\alpha]_D^{20}$ = 72.04 (*c* =1.00, $CHCl_3$, *l* = 50 mm). *Diastereomer 2 (down):* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.27-7.15 (m, 10H), 5.18 (d, *J* = 5.2 Hz, 1H), 4.91 (d, *J* = 8.9 Hz, 1H), 4.69 (s, 1H), 3.84 (dq, *J* = 9.8, 7.2, 7.1, 7.1 Hz, 1H), 3.47 (dq, *J* = 9.8, 7.1, 7.1, 7.1 Hz, 1H), 2.74-2.69 (m, 1H), 2.32 (ddd, *J* = 12.9, 11.4, 5.3 Hz, 1H), 1.99-1.94 (m, 2H), 1.23 (t, *J* =

7.1, 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.1, 142.3, 128.4, 128.2, 127.7, 127.4, 127.2, 125.9, 103.7, 84.1, 77.3, 77.0, 76.8, 72.7, 62.8, 53.4, 34.3, 15.1. **IR** (neat) ν_{max} 3434.9 (br), 3059.9 (w), 3027.7 (w), 2972.1 (w), 2923.4 (w), 1492.4 (w), 1453.4 (w), 1190.9 (w), 1094.9 (m), 1041.2 (m), 974.1 (m), 908.4 (w), 754.9 (w), 700.6 (s). **HRMS** (DART) for $C_{19}H_{26}NO_3$ $(M+NH_4)^+$: Calc'd: 316.1907, found: 316.1894. **$[\alpha]_D^{20}$** = 57.75 (*c* =1.00, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

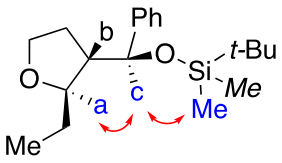
The transformations below were carried out on the isolated compounds **1.114** and **1.114'** separately in order to assess the stereochemistry of the isolated compounds. Upon reduction all spectral data of the two separate products was found to be identical. The stereochemical assignment was determined through NOESY correlation analysis of the resulting products. The absolute configuration at the B(pin)/silyl ether containing stereocenter was assigned by analogy (see substrates **1.82** and **1.101**).

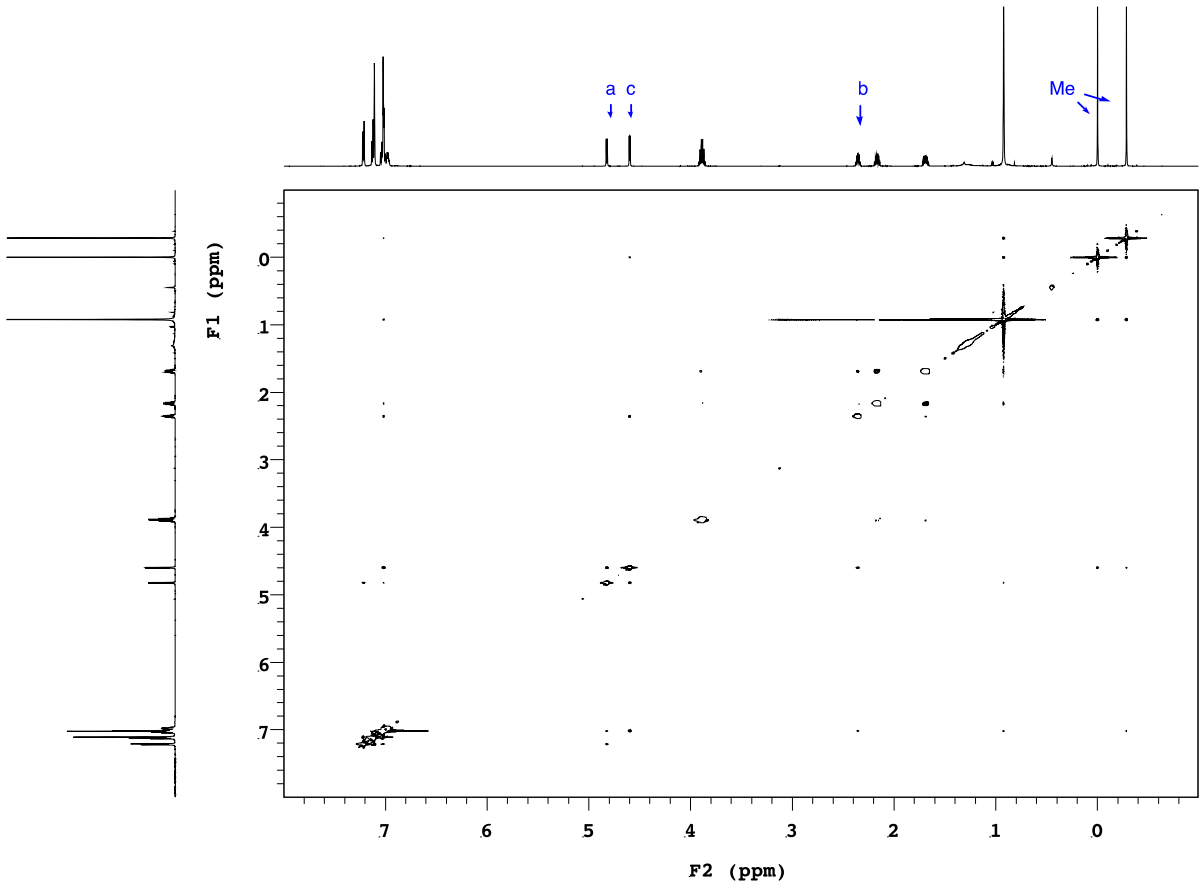


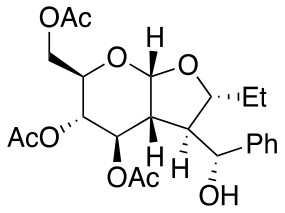


***tert*-butyldimethyl((*S*)-phenyl((*2R,3R*)-2-phenyltetrahydrofuran-3-yl)methoxy)silane (SI-27).** The title compound was generated through the same procedure used to synthesize **SI-25** and isolated by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (17.0 mg, 81% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.28-7.21 (m, 8H), 7.15-7.14 (m, 2H), 4.68 (dd, *J* = 15.2, 5.9 Hz, 2H), 4.08 (td, *J* = 7.8, 7.7, 6.1 Hz, 1H), 3.97 (td, *J* = 8.0, 7.9, 6.4 Hz, 1H), 2.43-2.40 (m, 1H), 2.33-2.27 (m, 1H), 1.95-1.89 (m, 1H), 0.93 (s, 9H), 0.08 (s, 3H), -0.25 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.2, 143.0, 128.4, 128.2, 127.4, 127.4, 126.6, 126.3, 82.5, 82.4, 74.3, 74.3, 68.5, 57.0, 27.4, 26.0, 18.3, -4.1, -4.2, -4.8, -4.8. **IR** (neat) ν_{max} 3026.5 (w), 2880.3 (w), 2853.3 (w), 1452.1 (w), 1250.7 (w), 1060.6 (m), 1003.2 (w), 834.1(s), 773.9 (m), 698.4 (s). **HRMS** (DART) for $C_{23}H_{33}O_2Si$ $(M+NH_4)^+$: Calc'd: 386.2515, found: 386.2510. **$[\alpha]_D^{20}$** = -49.60 (*c* = 0.90, $CHCl_3$, *l* = 50 mm).

NOESY was carried out in C_6D_6. Relevant NOESY correlations are illustrated below.





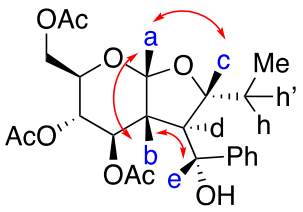


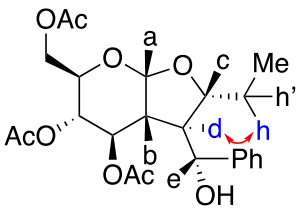
(2*R*,3*R*,3a*R*,4*R*,5*S*,6*R*,7a*S*)-6-(acetoxymethyl)-2-ethyl-3-((*R*)-hydroxy(phenyl)methyl)hexahydro-4*H*-furo[2,3-*b*]pyran-4,5-diyl diacetate (1.115). The reaction was performed according to general **procedure A** with (2*R*,3*R*,4*S*,5*S*,6*S*)-2-(acetoxymethyl)-5-iodo-6-(((*R*,*E*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-3-yl)oxy)tetrahydro-2*H*-pyran-3,4-diyl diacetate (122.1 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(R,R)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. ^{1}H NMR of the boronic ester isolated prior to oxidation indicated a 5:1 diastereomeric ratio in the reaction product. ***Note:*** the oxidation was carried out under buffered conditions by using pH7 phosphate buffer solution (0.50 mL) in place of 3M NaOH solution, and carrying out the oxidation for 12 hours. The crude mixture was purified by silica gel column chromatography (30% ethyl acetate in hexanes, stain in CAM) to afford the product as a single diastereomer. White solid (59.6 mg, 66% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37-7.30 (m, 2H), 7.27-7.22 (m, 3H), 5.44 (d, *J* = 4.6 Hz, 1H), 5.00-4.88 (m, 2H), 4.64-4.63 (m, 1H), 4.33 (dd, *J* = 12.3, 4.2 Hz, 1H), 4.11 (ddd, *J* = 9.6, 4.3, 2.2 Hz, 1H), 4.03 (dd, *J* = 12.3, 2.2 Hz, 1H), 3.88 (q, *J* = 6.1 Hz, 1H), 2.42 (ddd, *J* = 9.0, 4.6, 1.8 Hz, 1H), 2.17-2.09 (m, 2H), 2.05 (s, 3H), 1.93 (s, 3H), 1.75-1.56 (m, 2H), 1.53 (s, 3H), 1.00 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_{z3}$) δ 171.0, 170.8, 169.7, 143.0, 128.7, 127.7, 125.6, 100.8, 79.4, 74.3, 73.7, 69.5, 68.2, 62.2, 54.5, 43.1, 28.8, 20 .9, 20.7, 20.5, 10.3. **IR** (neat) ν_{max} 3506.0 (br), 2960.8 (m), 2931.6 (m), 2876.70 (w), 1744.4 (s), 1451.8 (m), 1230.9 (s),

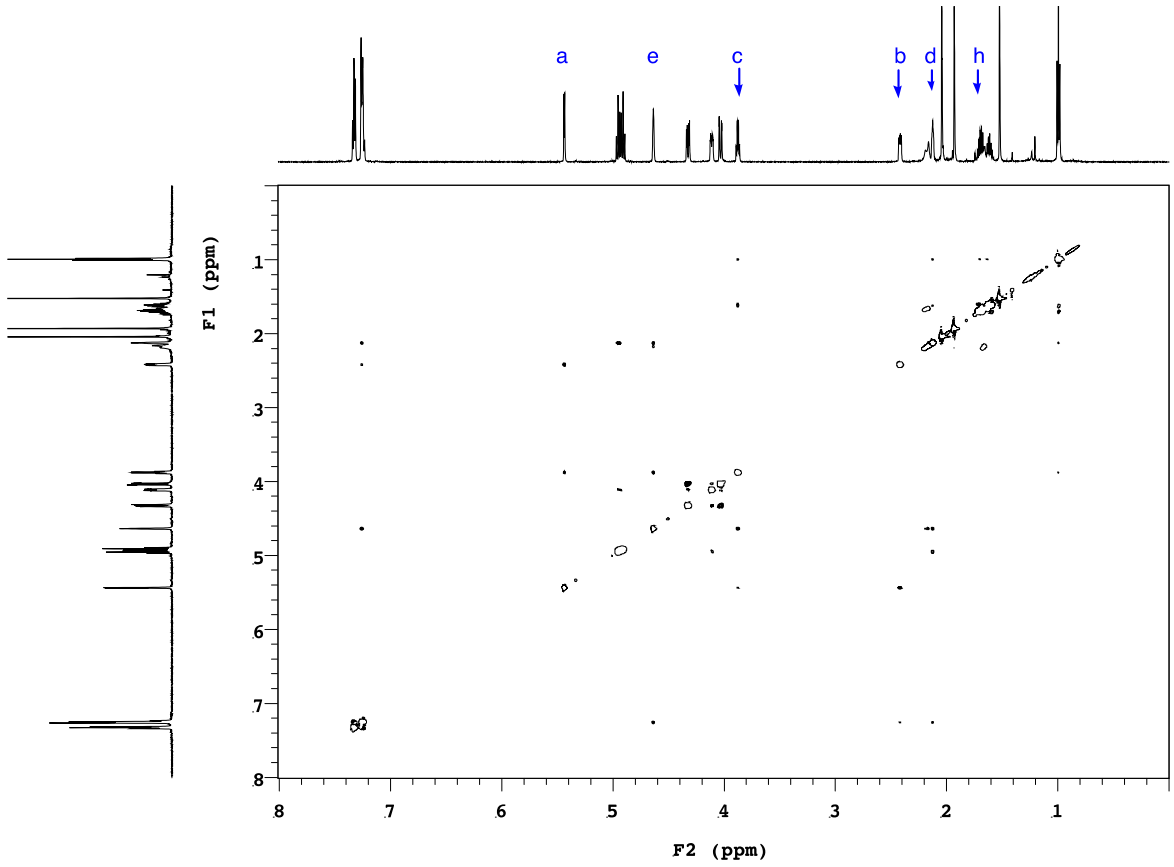
1036.4 (s), 795.2 (w) 763.7 (w). **HRMS** (DART) for $C_{23}H_{34}NO_9$ $(M+NH_4)^+$: Calc'd 468.2228:, found: 468.2248. $[\alpha]_D^{20}$ = 78.38 (*c* = 0.5, $CHCl_3$, *l* = 50 mm).

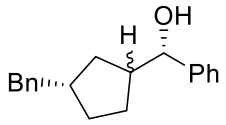
Analysis of Stereochemistry:

The stereochemistry of the carbon skeleton was assigned through NOESY correlation analysis. The absolute configuration at the B(pin)/OH containing stereocenter was assigned by analogy (see substrates **1.82** and **1.101**). Relevant NOESY correlations are illustrated below (assignment of the ^{1}H NMR shifts was aided by COSY analysis. The COSY spectrum is included along with the other spectral data).



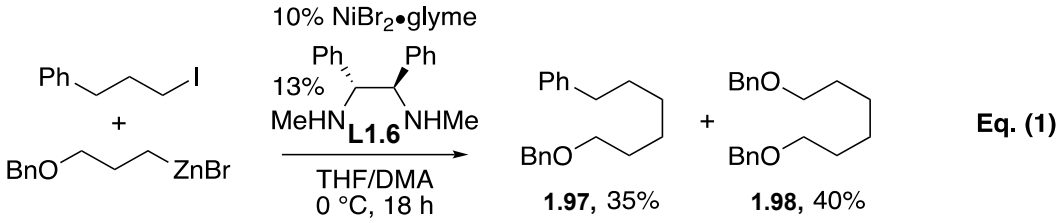



a
e
c
b
d
h
F1 (ppm)
F2 (ppm)
1
2
3
4
5
6
7
8

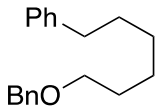


(*1S*)-((*3S*)-3-benzylcyclopentyl)(phenyl)methanol (1.116). The reaction was performed according to the general **procedure A** with (*R*,*E*)-2-(5-benzyl-6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (85.2 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using NiBr2·glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **L1.6** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel /column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (30.9 mg, 58% yield). The product is a diastereomeric mixture (d.r. = 1.2:1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (m, 8H), 7.30-7.24 (m, 7H), 7.19-7.12 (m, 7H), 4.43 (d, *J* = 8.2 Hz, 1H), 4.38 (d, *J* = 8.5 Hz, 1H), 2.68-2.56 (m, 5H), 2.43-2.38 (m, 2H), 2.32-2.23 (m, 2H), 2.14-2.08 (m, 1H), 1.88-1.66 (m, 8H), 1.63-1.43 (m, 5H), 1.39-1.14 (m, 5H), 0.97 (q, *J* = 11.1, 11.1, 11.1 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.3, 144.3, 142.1, 142.0, 128.9, 128.8, 128.5, 128.3, 128.3, 127.7, 127.7, 126.7, 126.6, 125.8, 125.8, 79.3, 79.2, 47.4, 46.3, 42.4, 42.3, 42.1, 41.3, 37.0, 35.1, 32.9, 31.7, 29.6, 28.1. **IR** (neat) ν_{max} 3022.8 (w), 2922.3 (w), 2852.0 (w), 1492.5 (m), 1450.5 (m), 1028.6 (w), 741.5 (m), 697.0 (s), 599.3 (w), 542.1 (w), 479.9 (m). **HRMS** (DART) for $C_{19}H_{21}$ $(M+H-H_2O)^+$: Calc'd: 249.1638, found: 249.1627. **Note**: the product was obtained as a mixture of diastereomers and an optical rotation was not obtained.

1.4.2.6. Background Reaction Experiments

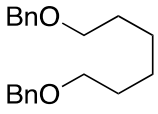


Equation (1). In an argon-filled glovebox, an oven-dried 2 dram vial equipped with a magnetic stirrer was charged with **$NiBr_2$·glyme** (6.17 mg, 0.02 mmol), (*S,S*)-N,N-dimethyl-1,2-diphenyl-ethane-1,2-diamine **L1.6** (6.25 mg, 0.026 mmol) and dissolved in 2.0 mL of THF. The catalyst solution was stirred for 1 hour at ambient temperature. **(3-iodopropyl)benzene** (98.4 mg, 0.40 mmol, 1.0 equiv.) was added to the catalyst solution. The vial was sealed with a PTFE-lined pierceable cap, taped, and brought outside the glovebox where it was placed in a CryoCool set at 0 ºC. The vial was cooled for 30 minutes before addition of **(3-(benzyloxy)propyl)zinc bromide** solution (0.410 mL, 0.97M 0.40 mmol, 1.0 equiv.). The puncture hole was taped over and the reaction mixture was stirred at 0 ºC for 18 hours. The reaction was quenched with 0.40 mL of saturated NH_4Cl aq. solution, diluted with diethyl ether and washed with water and brine sequentially. The organic layer was dried over magnesium sulfate and concentrated. The crude material was then submitted to silica gel chromatography.

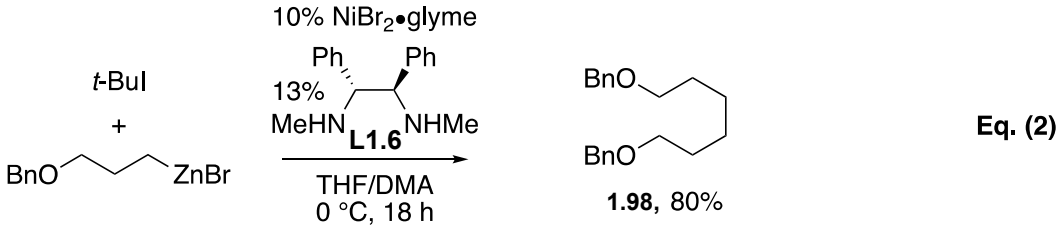


(6-(benzyloxy)hexyl)benzene (1.97). The product of the reaction was isolated by silica gel column chromatography (25% CH_2Cl_2 in hexane, stain in CAM) as a

colorless oil (37.8 mg, 35% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36-7.34 (m, 4H), 7.32-7.23 (m, 3H), 7.20-7.13 (m, 3H), 4.50 (s, 2H), 3.46 (t, J = 6.6 Hz, 2H), 2.84-2.53 (m, 2H), 1.69-1.55 (m, 4H), 1.45-1.34 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.9, 138.8, 128.5, 128.5, 128.4, 127.7, 127.6, 125.7, 73.0, 70.6, 36.0, 31.6, 29.8, 29.3, 26.2. **IR** (neat) ν_{max} 3082.6 (w), 3060.2 (w), 3024.1 (w), 2925.8 (s), 2851.7 (s), 1494.1 (m), 1452.2 (m), 1360.8 (m), 1202.6 (s), 734.2 (s), 696.4 (s). **HRMS** (DART) for $C_{19}H_{25}O$ $(M+H)^+$: Calc'd: 269.1900 , found: 269.1901.



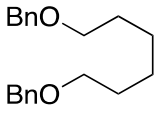
1,6-bis(benzyloxy)hexane (1.98) was isolated by silica gel column chromatography (40% CH_2Cl_2 in hexane, stain in CAM) as a colorless oil (24.1 mg, 40% yield based on 0.50 equiv. of starting material). All spectral data were in accordance with the literature.[59]



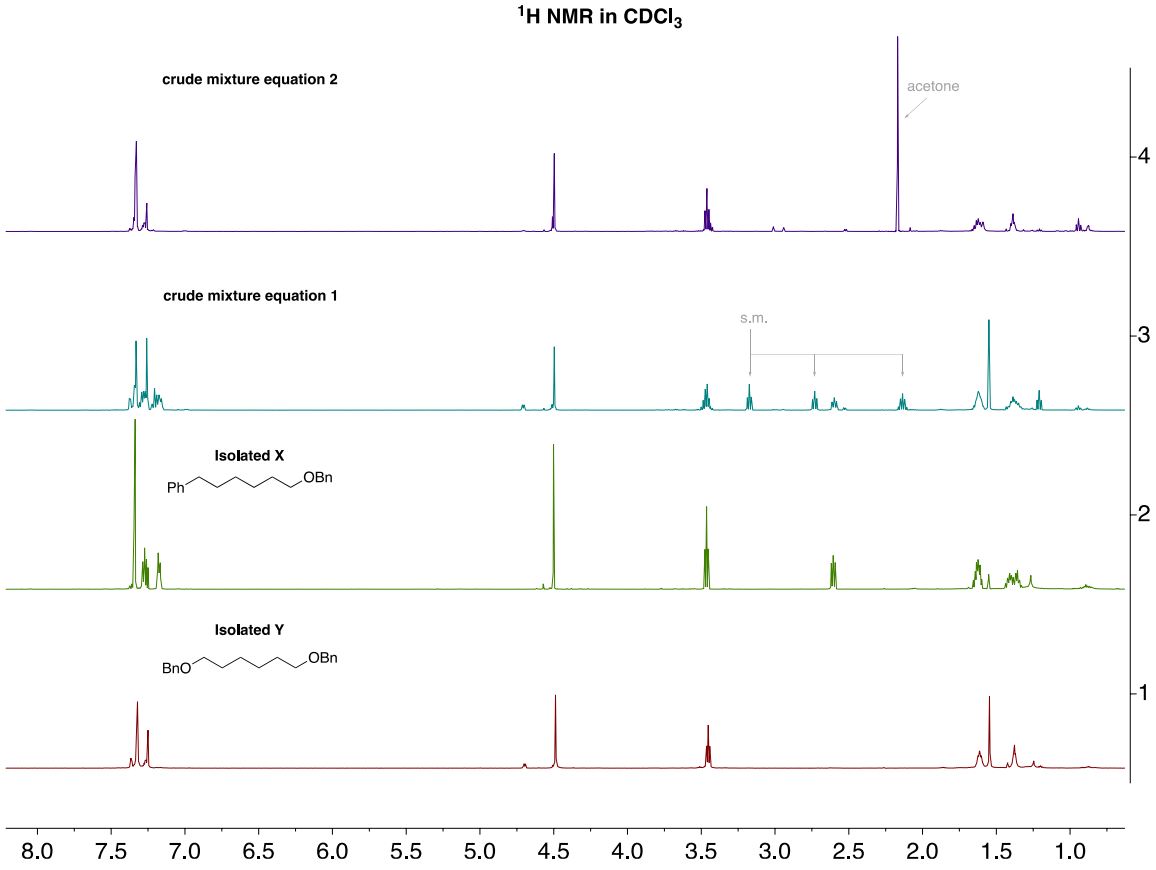
Eq. (2)

Equation (2). The experiment was carried out following the same procedure as for equation (1) by replacing **(3-iodopropyl)benzene** with ***t*-butyl iodide** (73.6 mg, 0.40 mmol, 1.00 equiv.).

(59) Mash, E. A.; Kantor, L. T. A.; Waller, S. C. *Synth. Commun.* **1997**, *27*, 507–514.



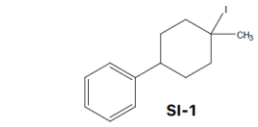
1,6-bis(benzyloxy)hexane (1.98) was isolated by silica gel column chromatography (40% CH_2Cl_2 in hexane, stain in CAM) as a colourless oil (47.8 mg 80% yield based on 0.50 equiv. of starting material) All spectral data were in accordance with the literature.[58]



Comparison of the ^{1}H NMR for the crude mixtures from **eq. (1)** and **eq. (2)** with the corresponding isolated products ^{1}H NMR spectra for reference. The starting material (s. m.) corresponds to unreacted (3-iodopropyl)benzene.

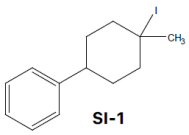
1.4.3. NMR Spectra

^{1}H NMR (500 MHz, $CDCl_3$)



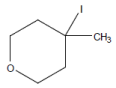
SI-1

^{13}C NMR (151 MHz, $CDCl_3$)



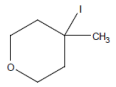
SI-1

^{1}H NMR (500 MHz, $CDCl_3$)



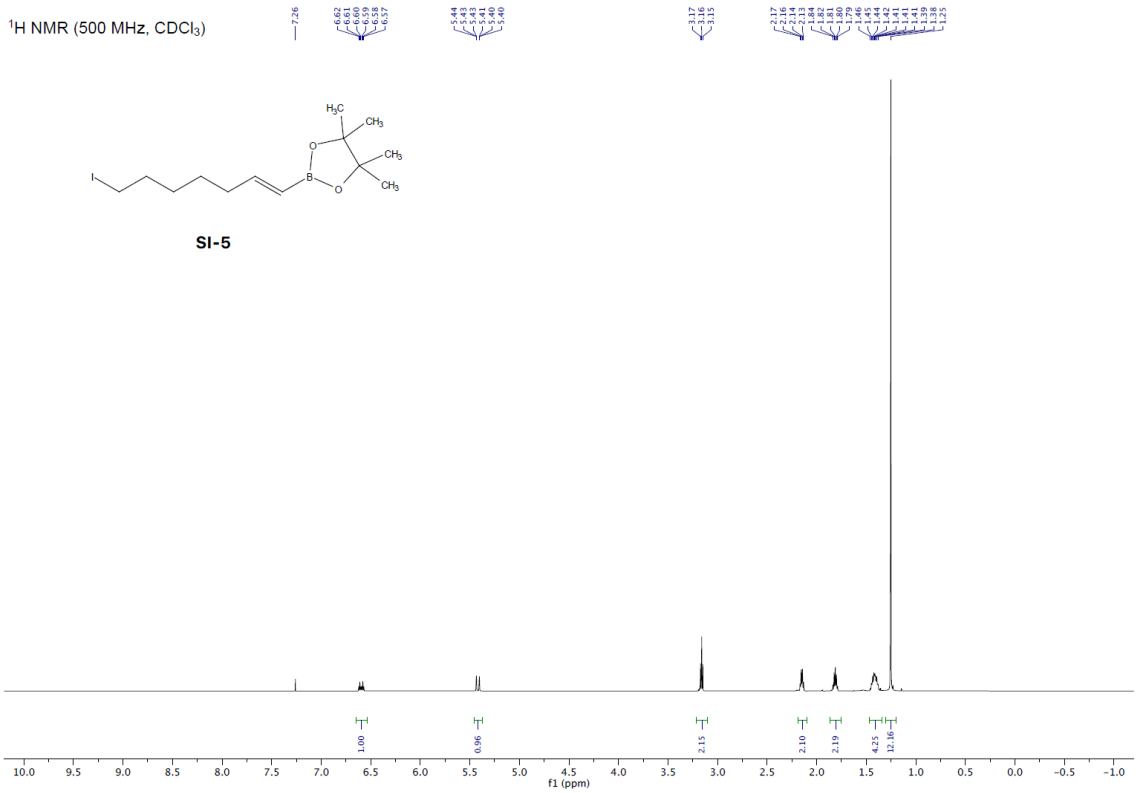
SI-2

^{13}C NMR (151 MHz, $CDCl_3$)



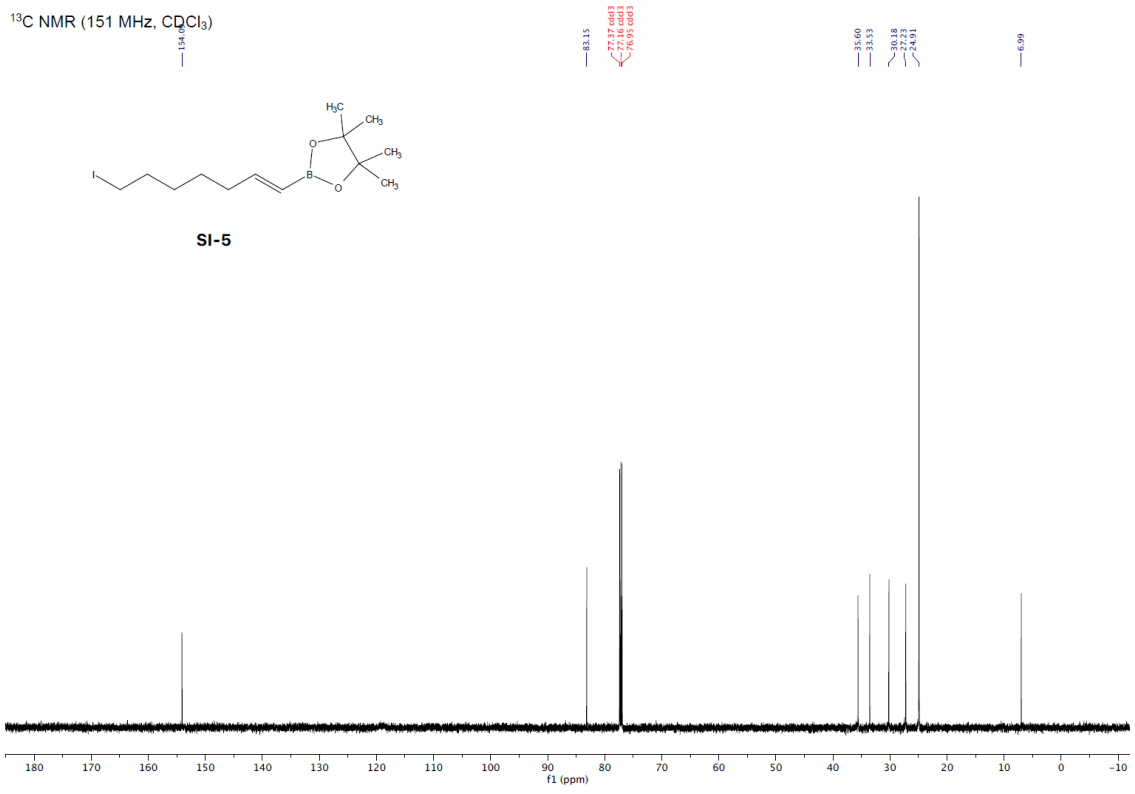
SI-2

^{1}H NMR (500 MHz, $CDCl_3$)



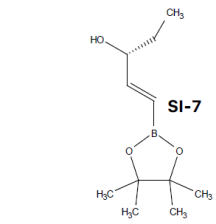
SI-5

^{13}C NMR (151 MHz, $CDCl_3$)

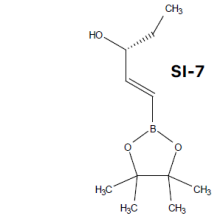


SI-5

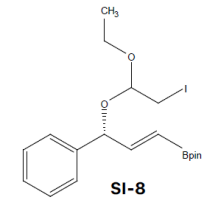
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (151 MHz, $CDCl_3$)

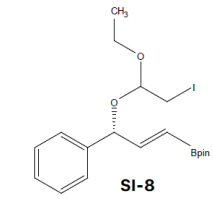


^{1}H NMR (500 MHz, $CDCl_3$)



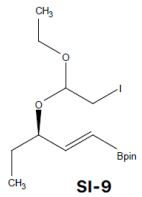
SI-8

^{13}C NMR (151 MHz, $CDCl_3$)



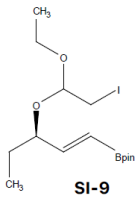
SI-8

^{1}H NMR (500 MHz, $CDCl_3$)



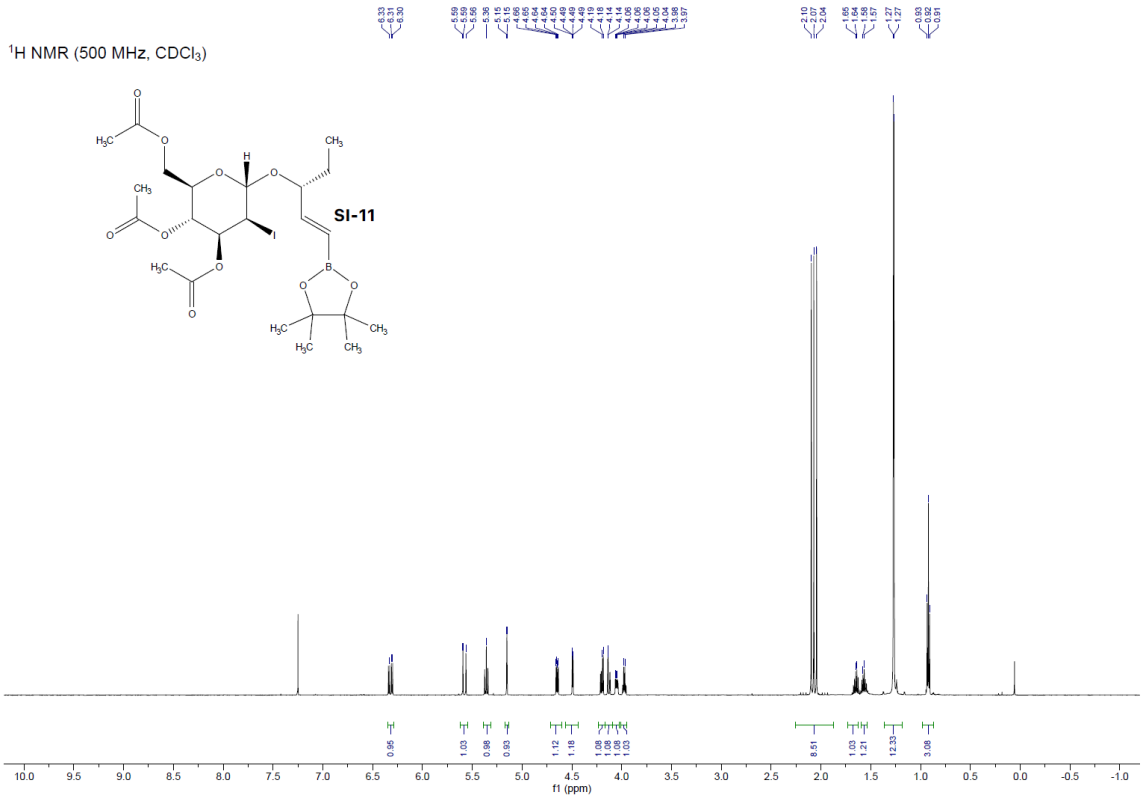
SI-9

^{13}C NMR (151 MHz, $CDCl_3$)

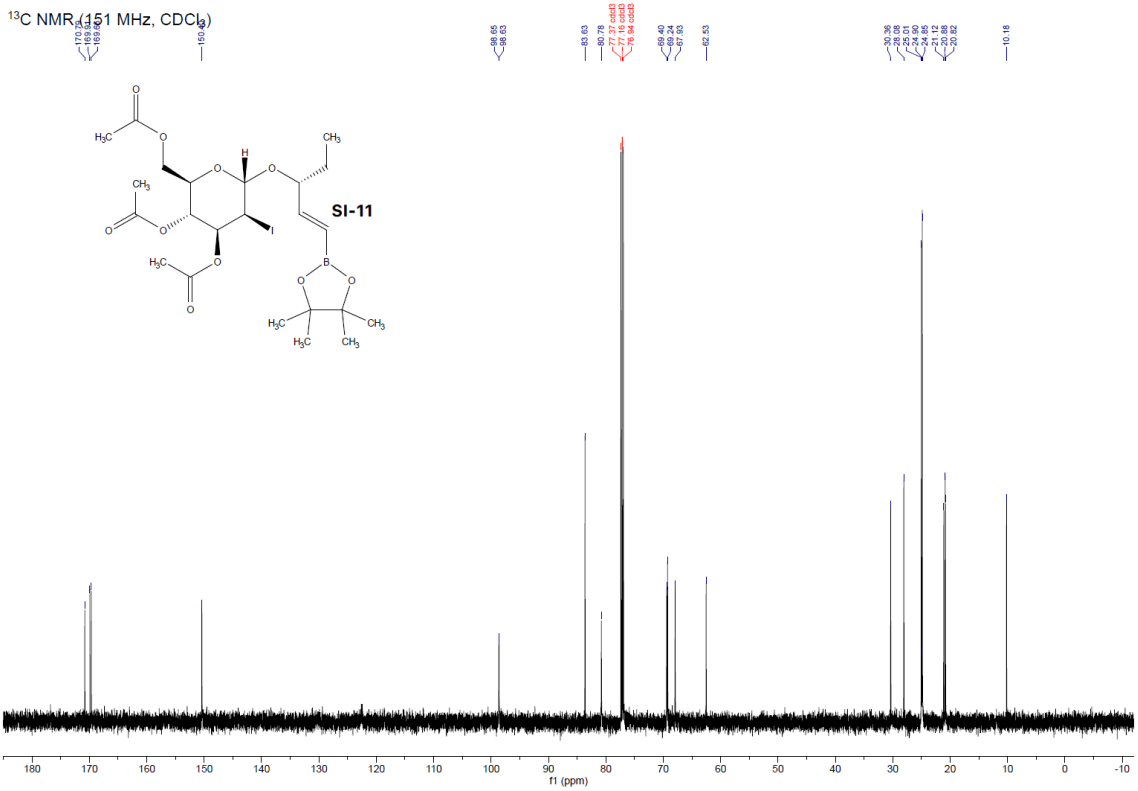


SI-9

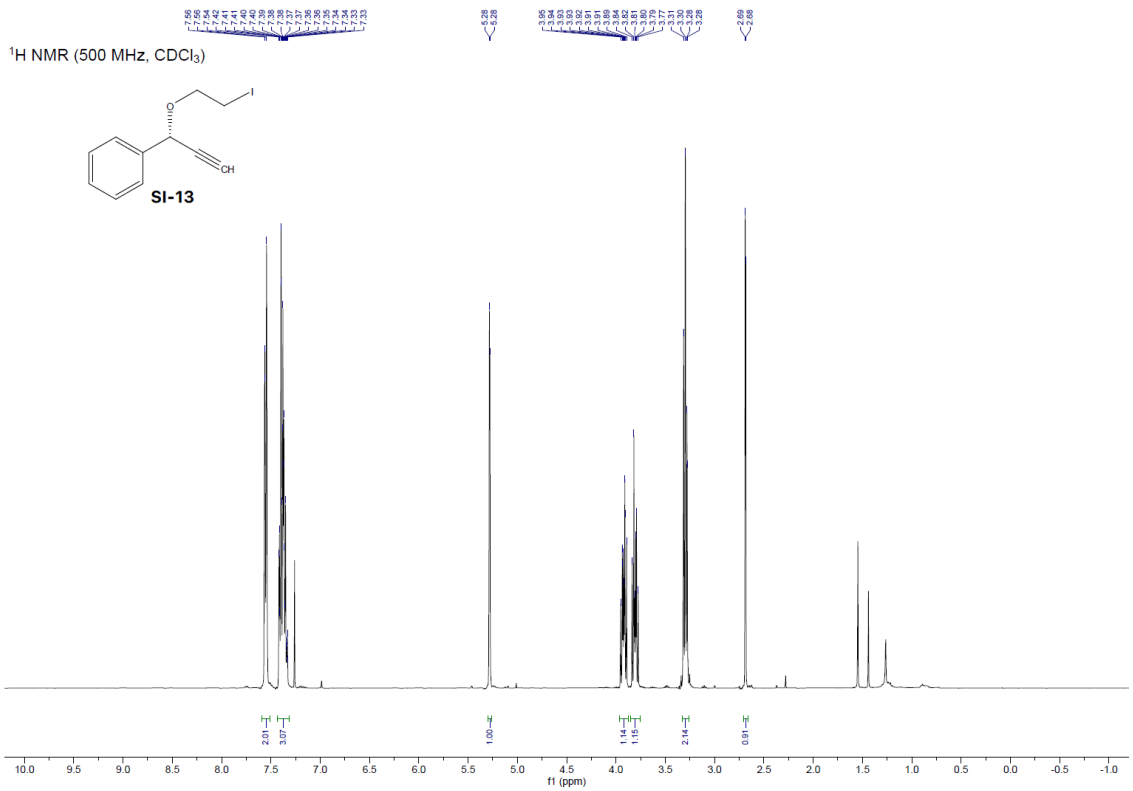
^{1}H NMR (500 MHz, $CDCl_3$)



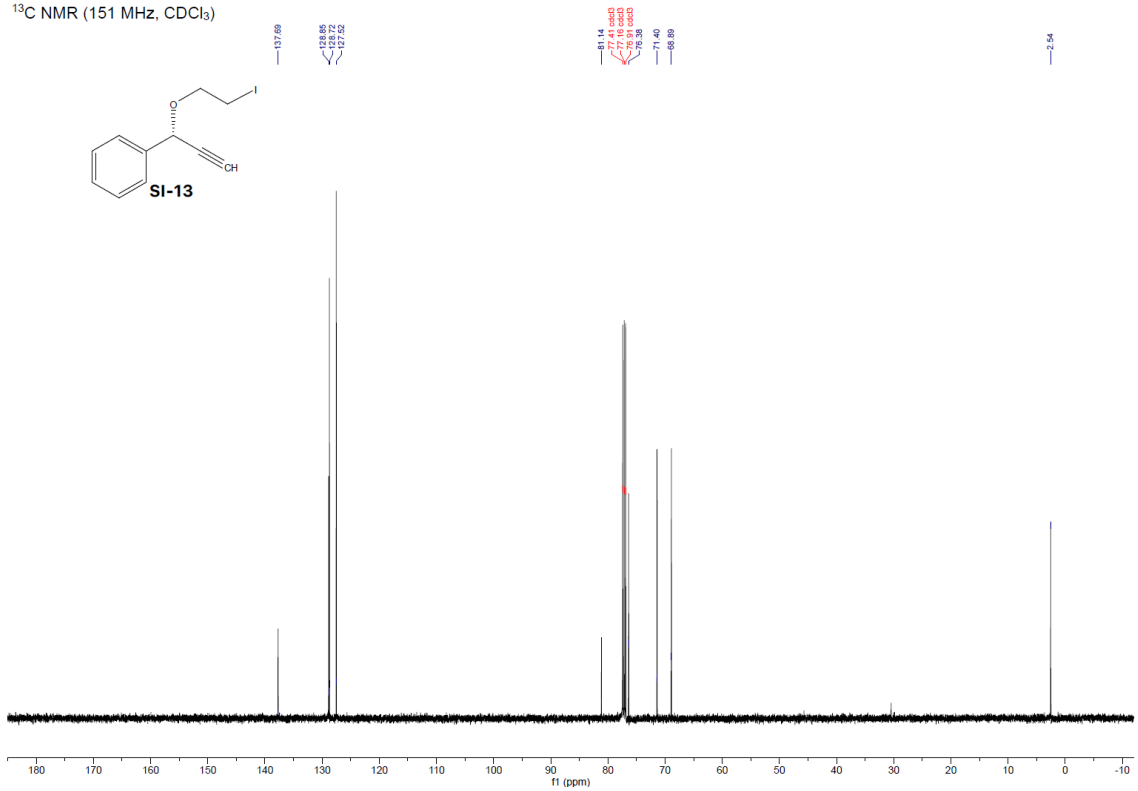
^{13}C NMR (151 MHz, $CDCl_3$)



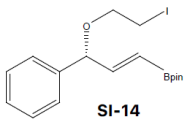
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (151 MHz, $CDCl_3$)

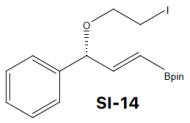


^{1}H NMR (500 MHz, $CDCl_3$)



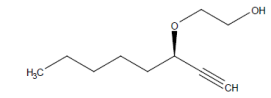
SI-14

^{13}C NMR (151 MHz, $CDCl_3$)



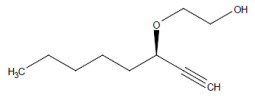
SI-14

^{1}H NMR (500 MHz, $CDCl_3$)



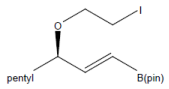
SI-15

^{13}C NMR (151 MHz, $CDCl_3$)



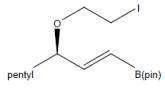
SI-15

^{1}H NMR (500 MHz, $CDCl_3$)



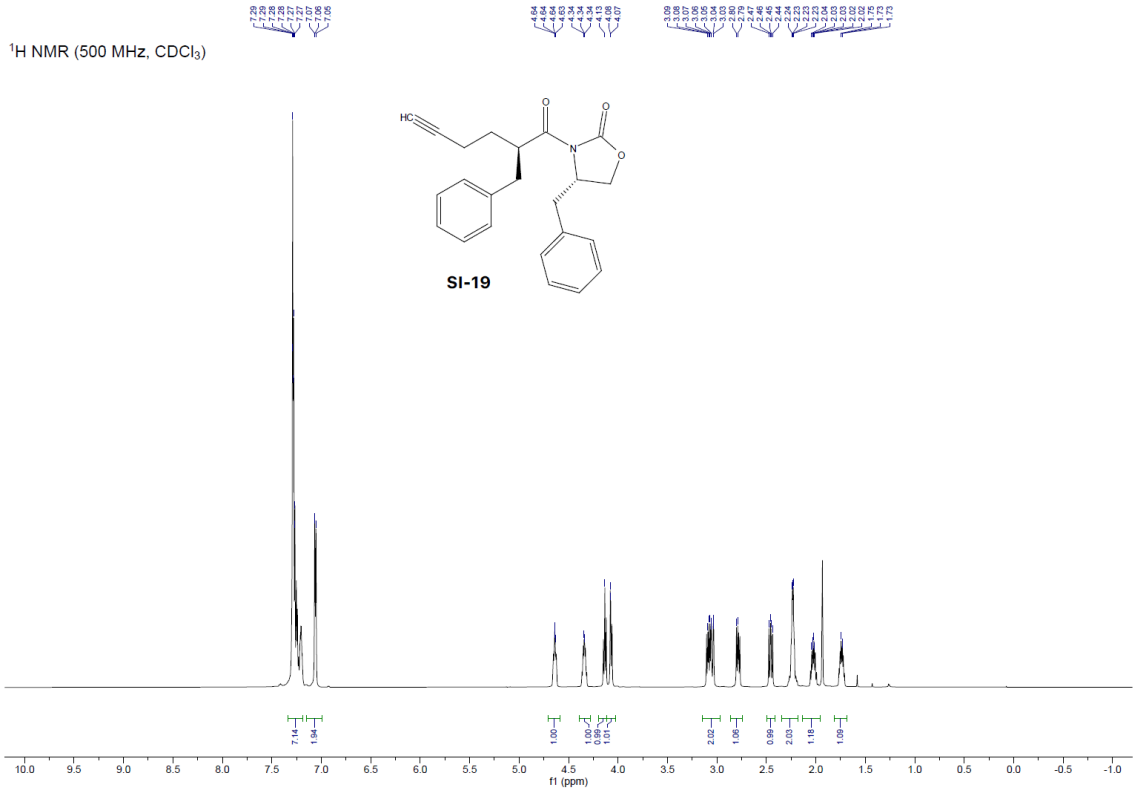
SI-17

^{13}C NMR (151 MHz, $CDCl_3$)

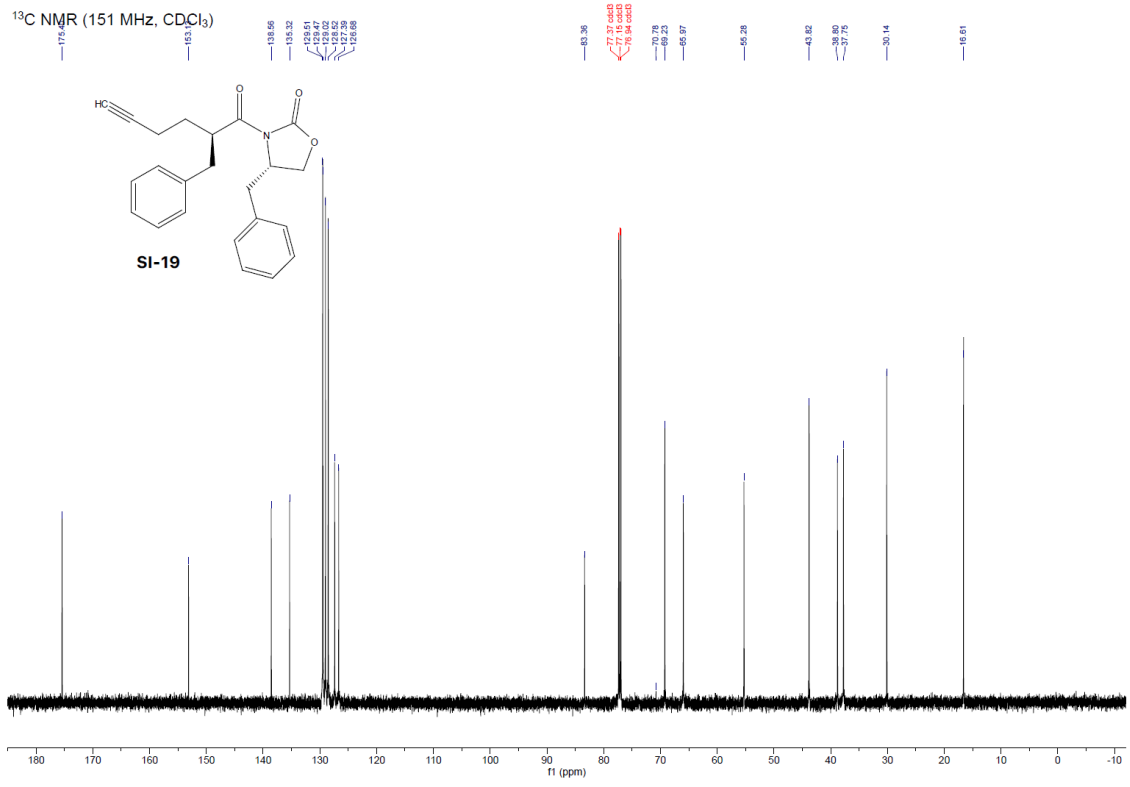


SI-17

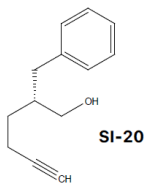
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (151 MHz, $CDCl_3$)

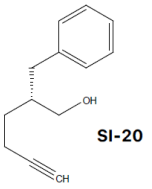


^{1}H NMR (500 MHz, $CDCl_3$)



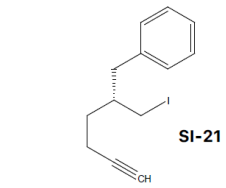
SI-20

^{13}C NMR (151 MHz, $CDCl_3$)



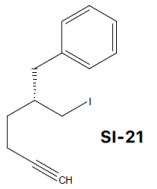
SI-20

^{1}H NMR (500 MHz, $CDCl_3$)



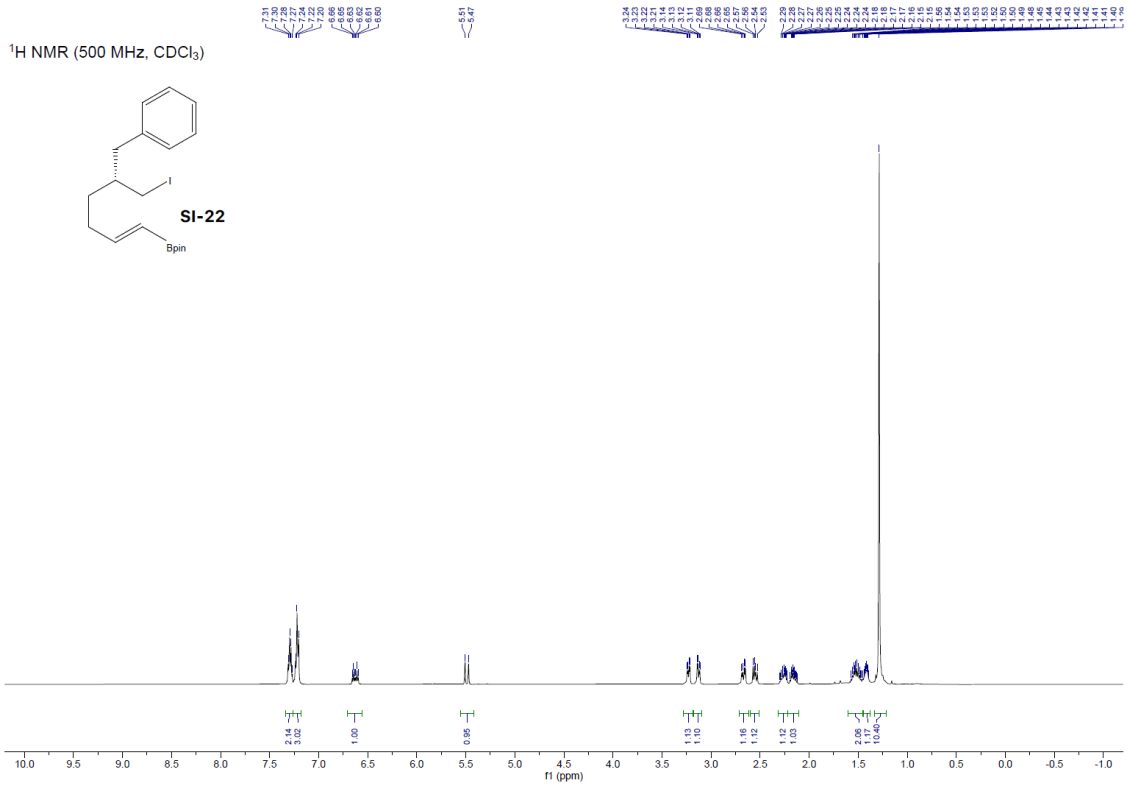
SI-21

^{13}C NMR (151 MHz, $CDCl_3$)

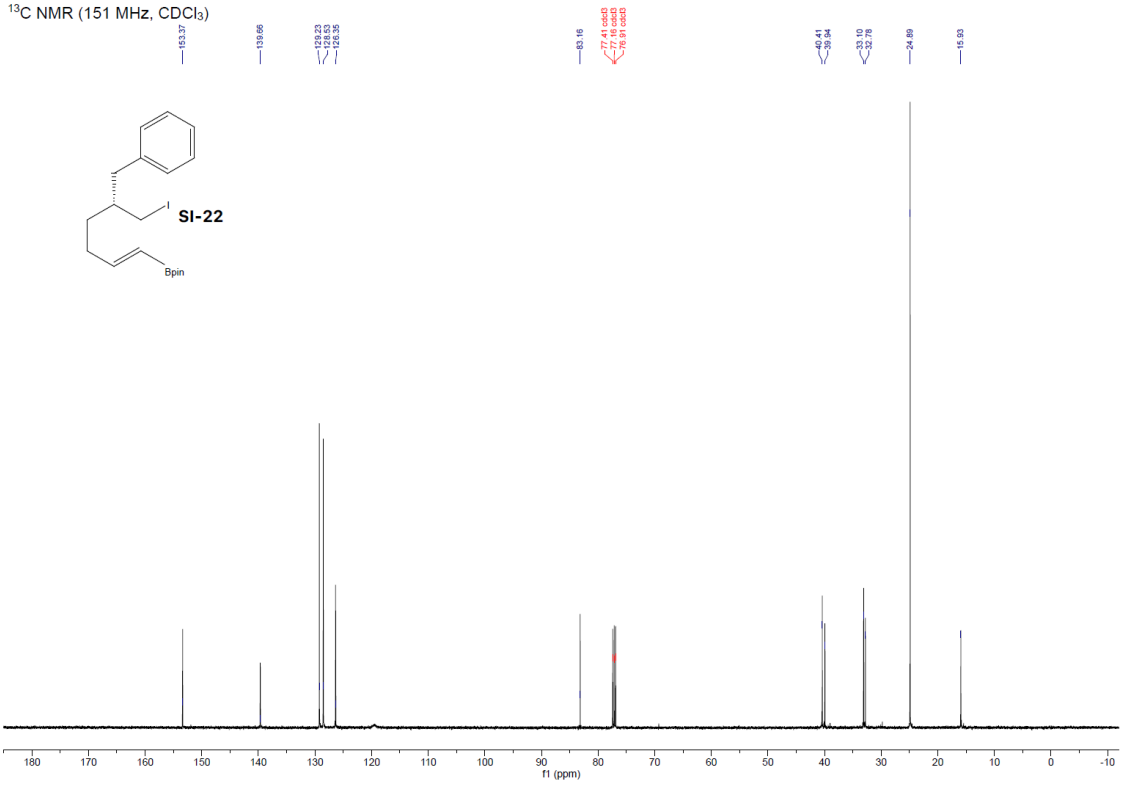


SI-21

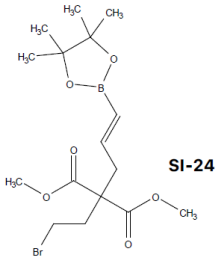
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (151 MHz, $CDCl_3$)

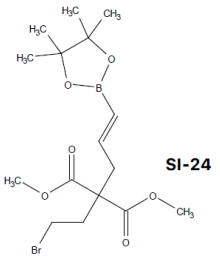


^{1}H NMR (500 MHz, $CDCl_3$)



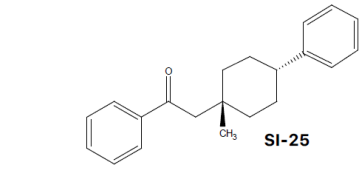
SI-24

^{13}C NMR (151 MHz, $CDCl_3$)



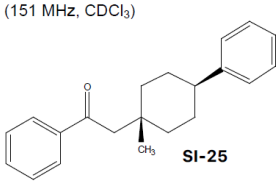
SI-24

^{1}H NMR (500 MHz, $CDCl_3$)



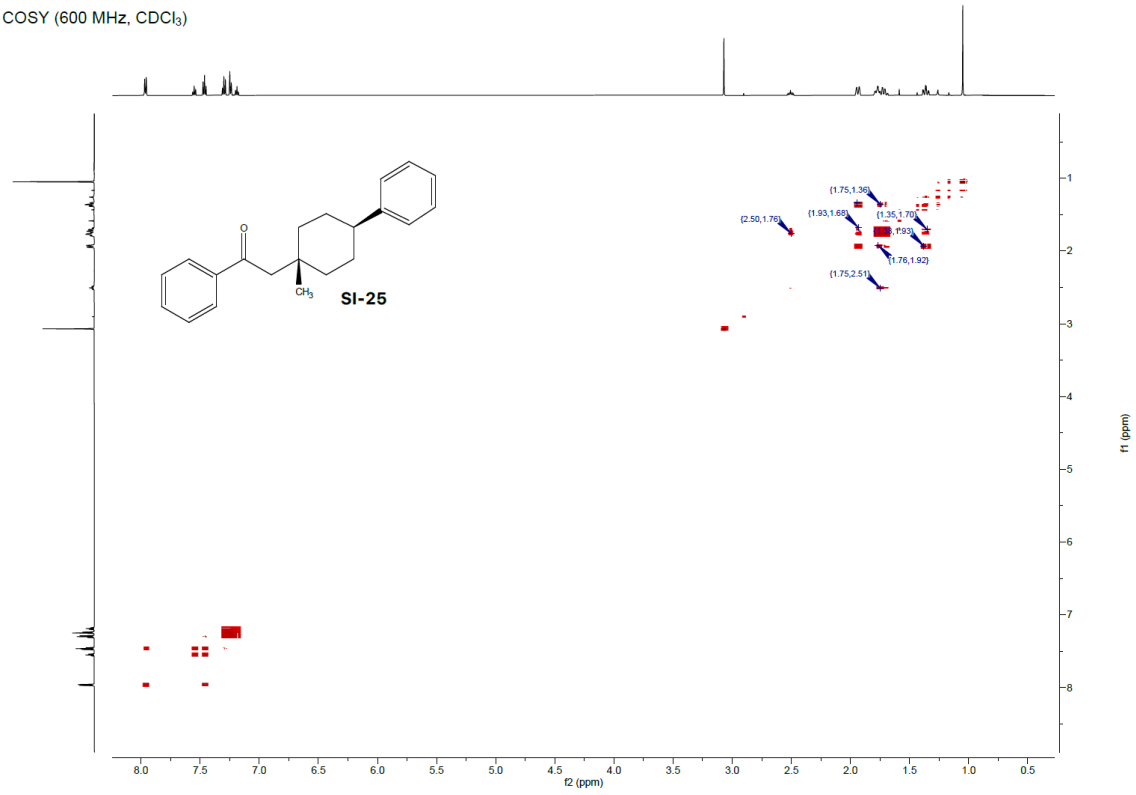
SI-25

^{13}C NMR (151 MHz, $CDCl_3$)

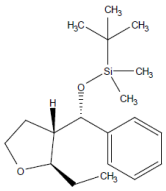


SI-25

COSY (600 MHz, $CDCl_3$)

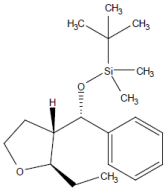


^{1}H NMR (500 MHz, $CDCl_3$)



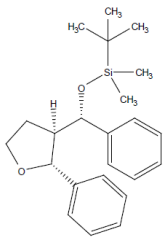
SI-26

^{13}C NMR (151 MHz, $CDCl_3$)



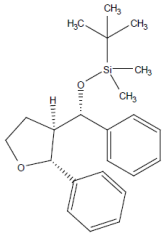
SI-26

^{1}H NMR (500 MHz,



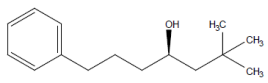
SI-27

^{13}C NMR (151 MHz, $CDCl_3$)



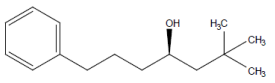
SI-27

^{1}H NMR (500 MHz, $CDCl_3$)



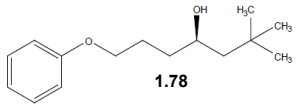
1.77

^{13}C NMR (151 MHz, $CDCl_3$)



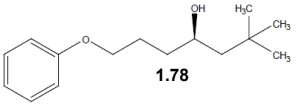
1.77

^{1}H NMR (500 MHz, $CDCl_3$)



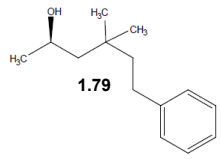
1.78

^{13}C NMR (151 MHz, $CDCl_3$)



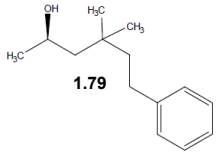
1.78

^{1}H NMR (500 MHz, $CDCl_3$)



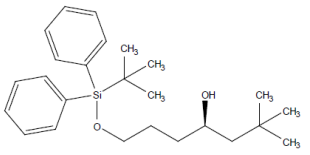
1.79

^{13}C NMR (151 MHz, $CDCl_3$)



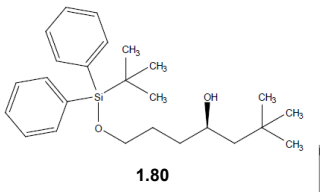
1.79

^{1}H NMR (500 MHz, $CDCl_3$)



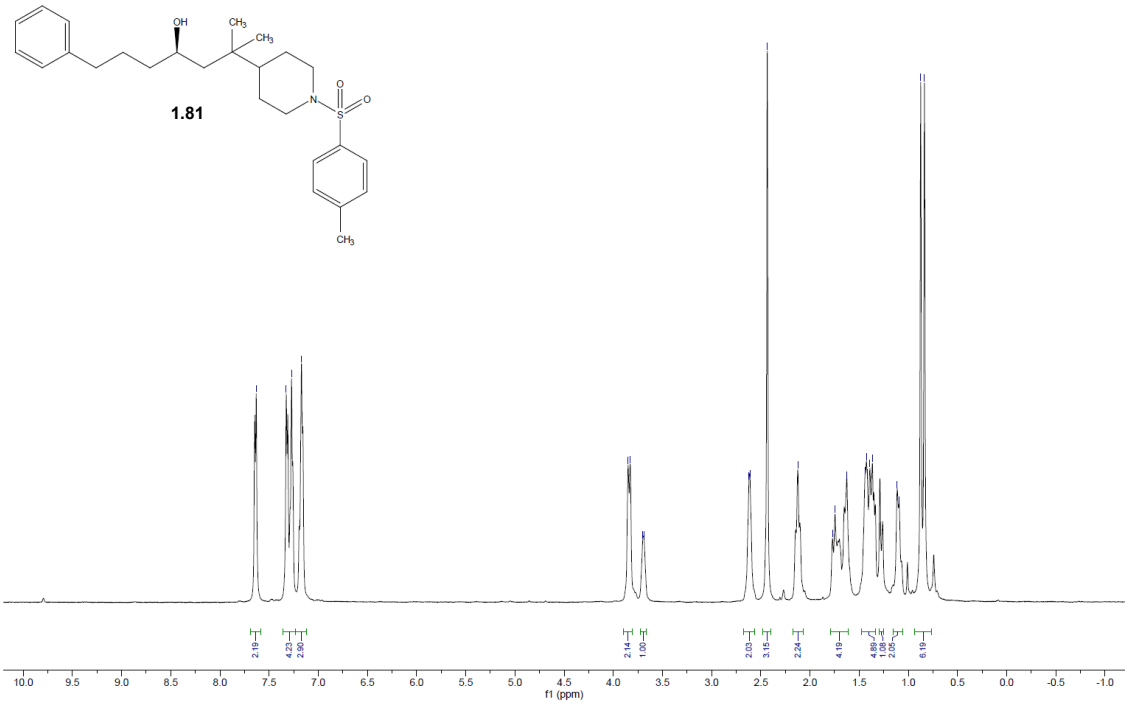
1.80

^{13}C NMR (151 MHz, $CDCl_3$)

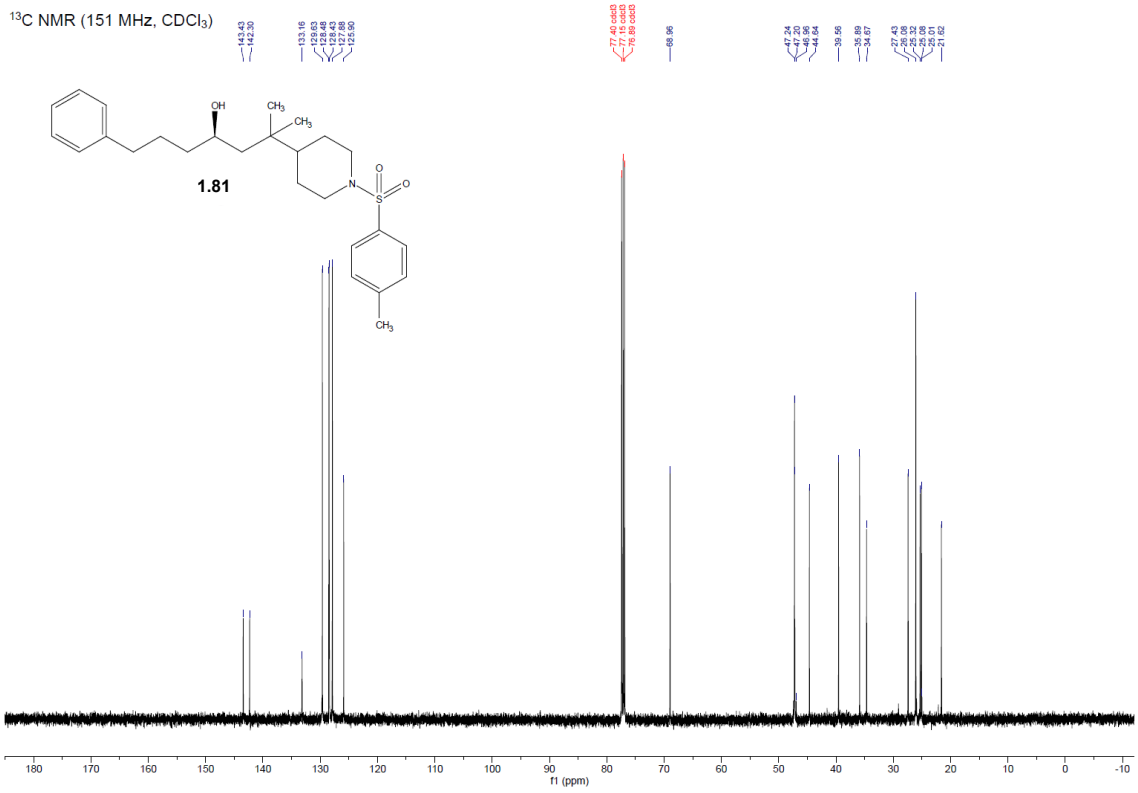


1.80

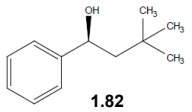
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (151 MHz, $CDCl_3$)

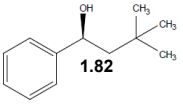


^{1}H NMR (500 MHz, $CDCl_3$)



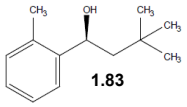
1.82

^{13}C NMR (151 MHz, $CDCl_3$)



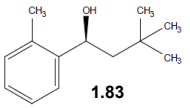
1.82

^{1}H NMR (500 MHz, $CDCl_3$)



1.83

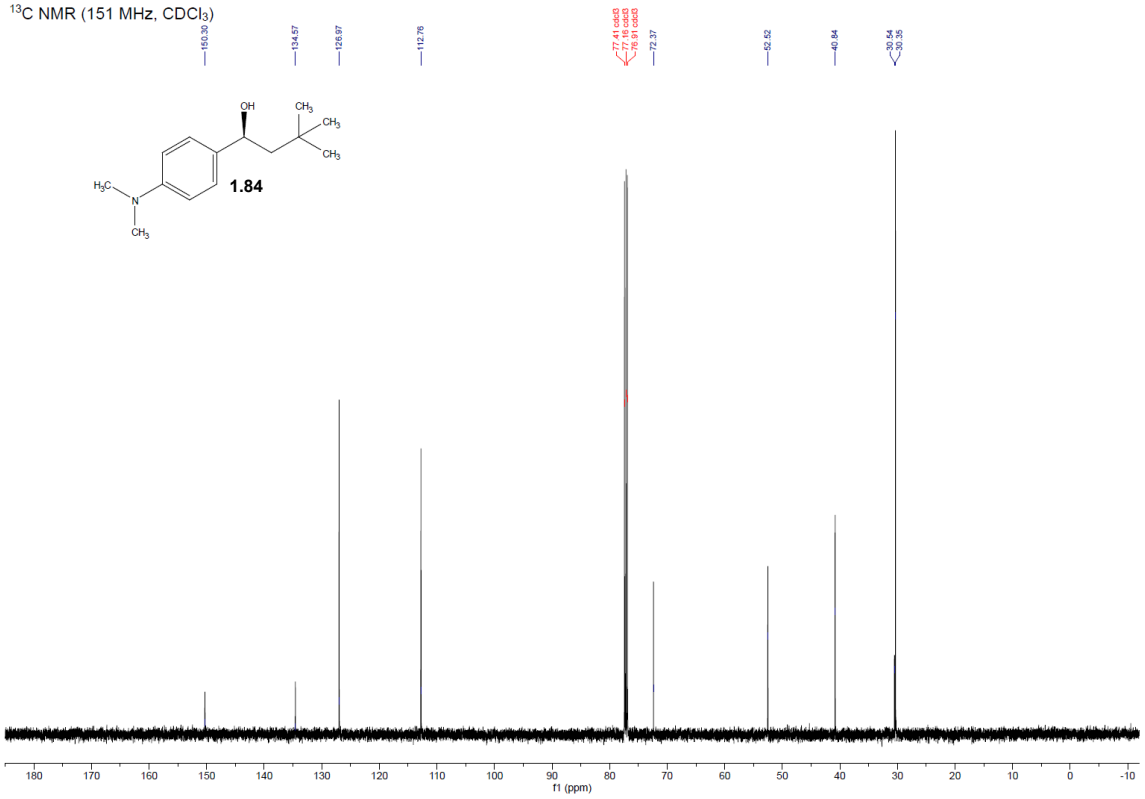
^{13}C NMR (151 MHz, $CDCl_3$)



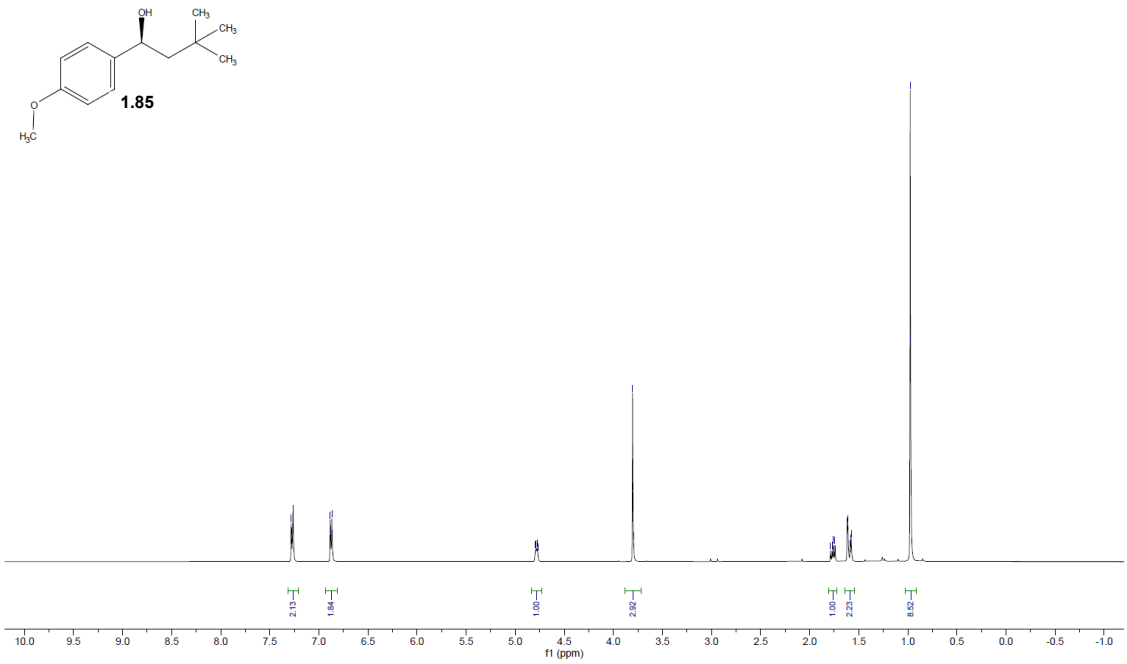
1.83

^{1}H NMR (500 MHz, $CDCl_3$)

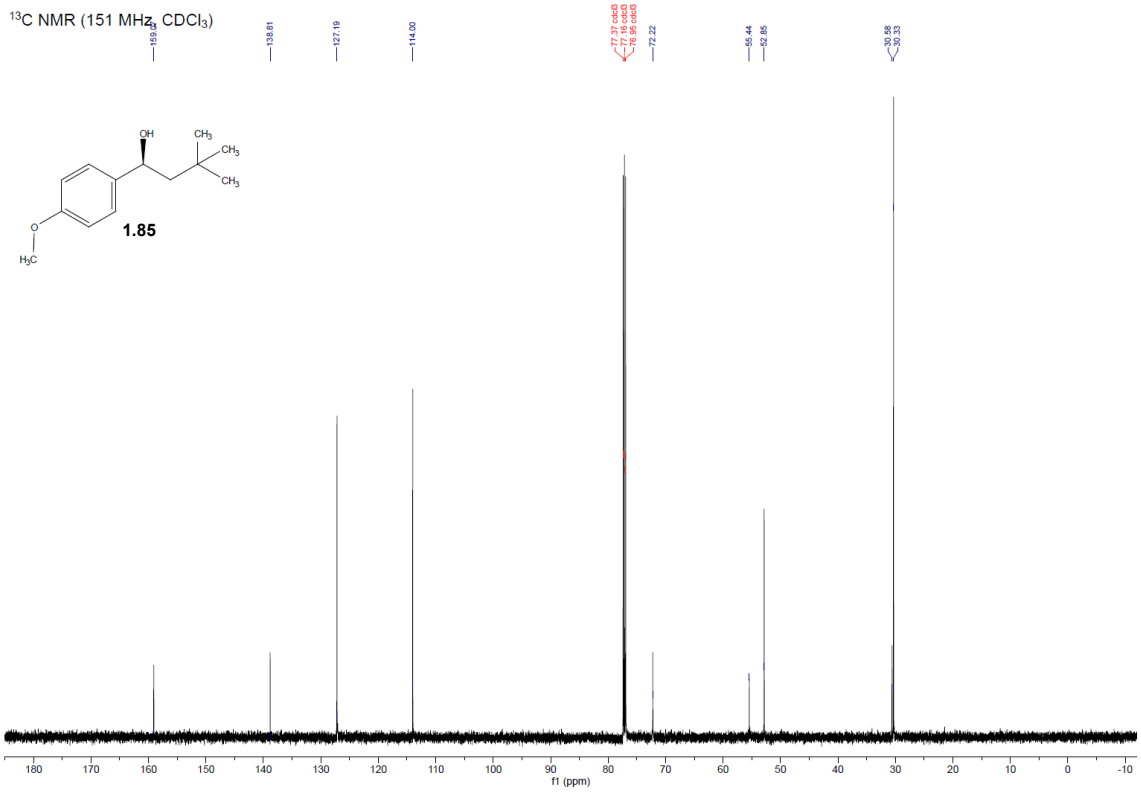
^{13}C NMR (151 MHz, $CDCl_3$)



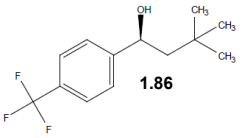
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (151 MHz_3 $CDCl_3$)

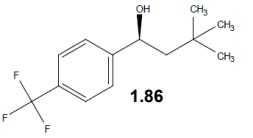


^{1}H NMR (500 MHz, $CDCl_3$)



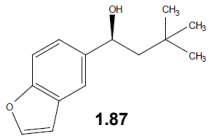
1.86

^{13}C NMR (151 MHz, $CDCl_3$)



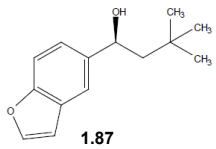
1.86

^{1}H NMR (500 MHz, $CDCl_3$)



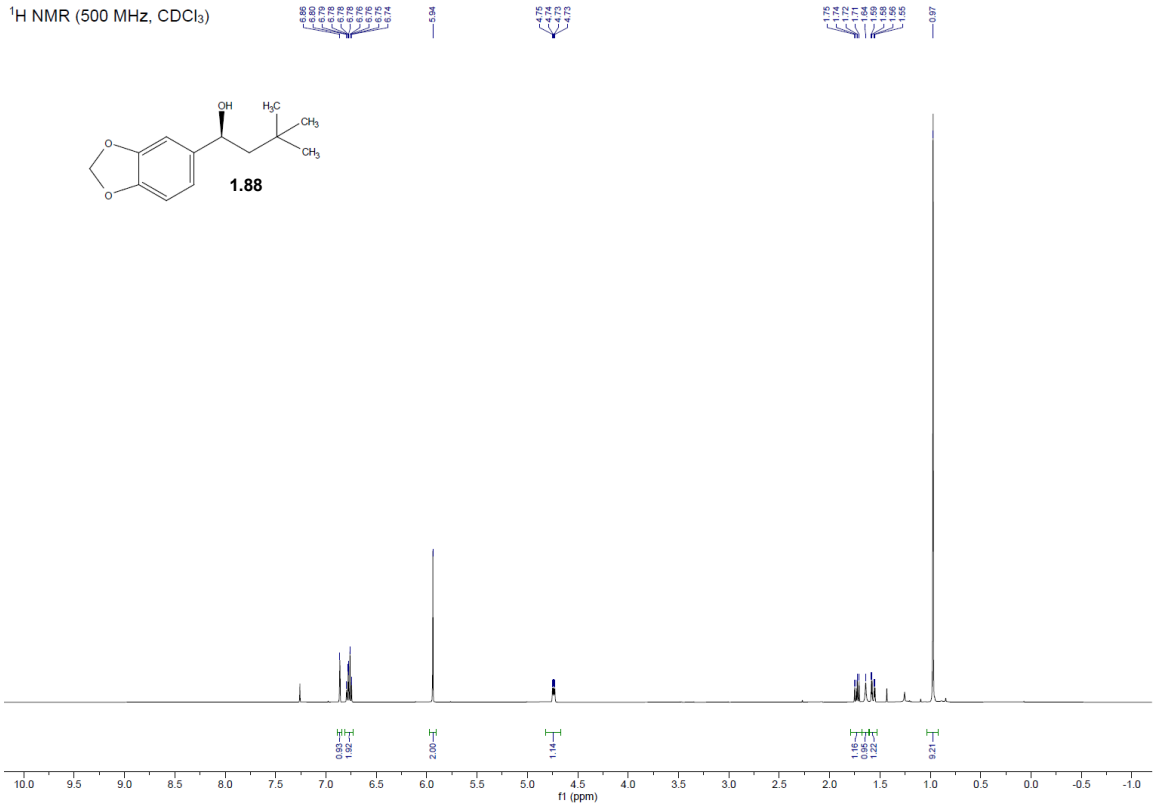
1.87

^{13}C NMR (151 MHz, $CDCl_3$)

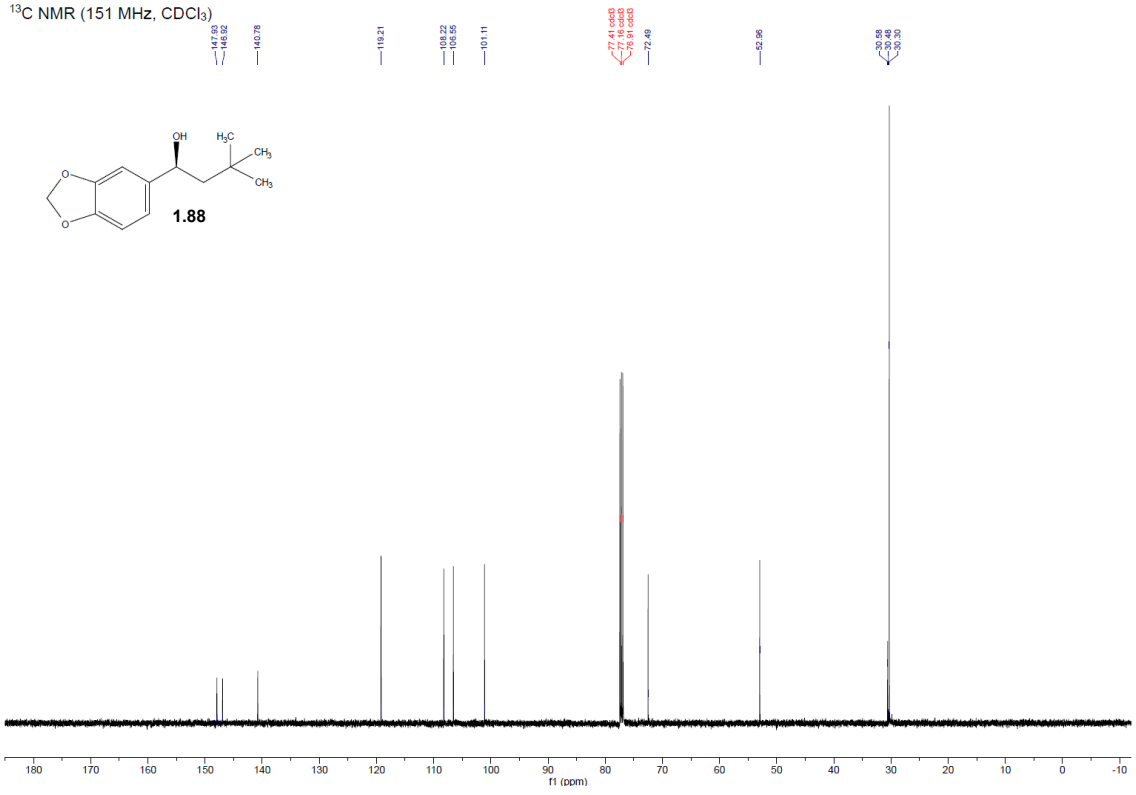


1.87

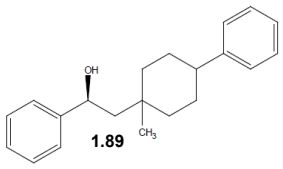
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (151 MHz, $CDCl_3$)

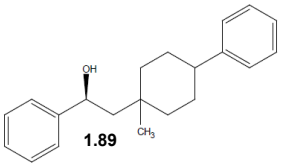


^{1}H NMR (500 MHz, $CDCl_3$)



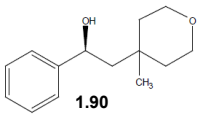
1.89

^{13}C NMR (151 MHz, $CDCl_3$)



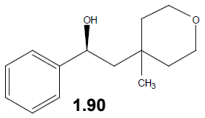
1.89

^{1}H NMR (500 MHz, $CDCl_3$)



1.90

^{13}C NMR (151 MHz, $CDCl_3$)



1.90

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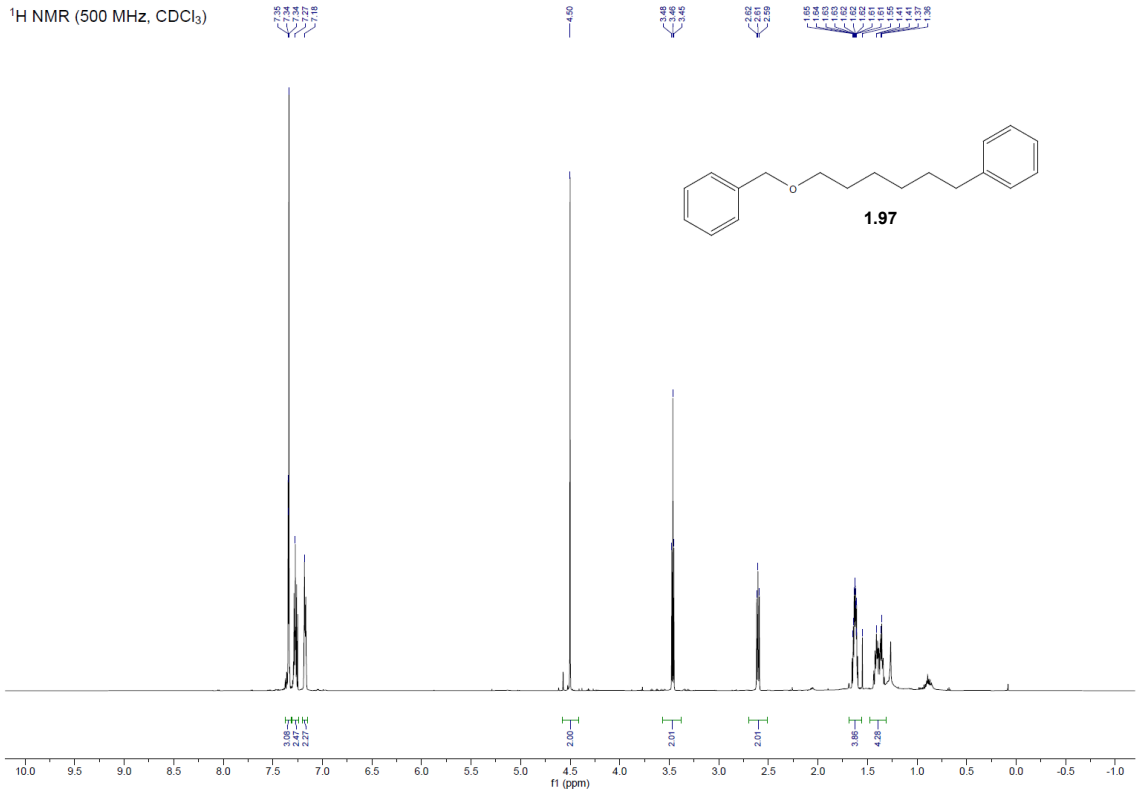

1.97

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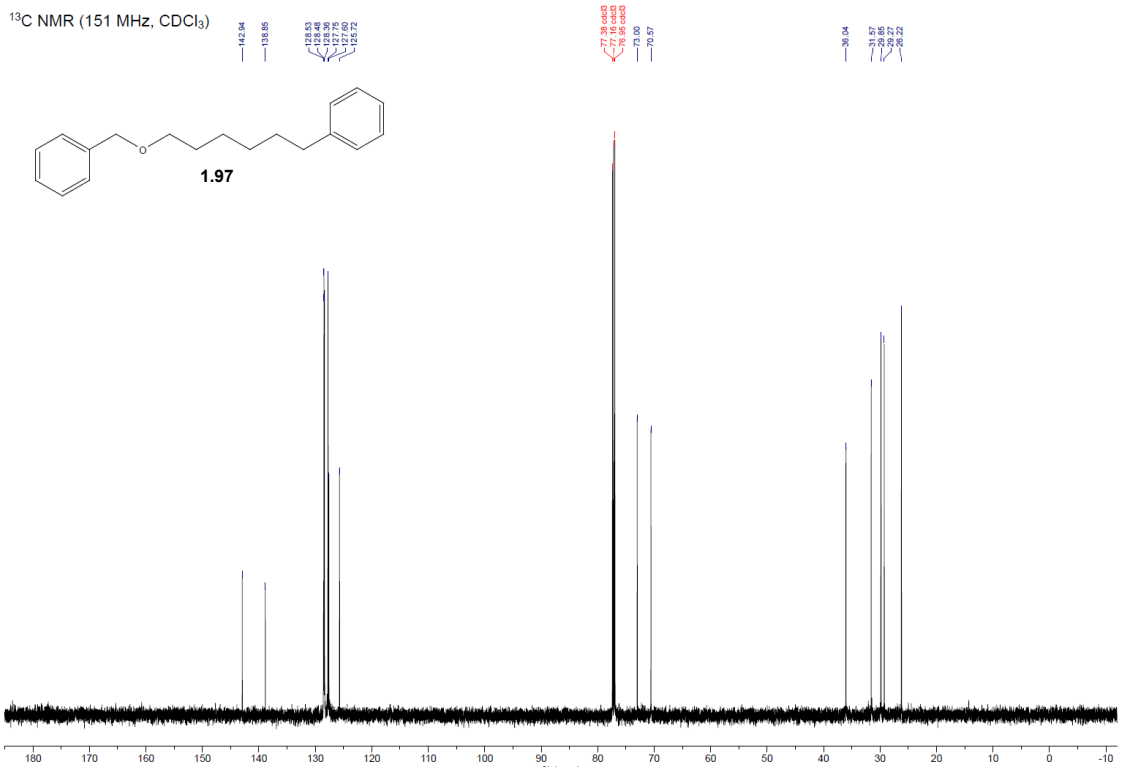

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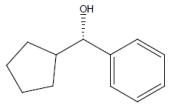

1.101

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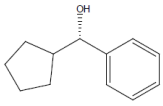

1.101

1.84

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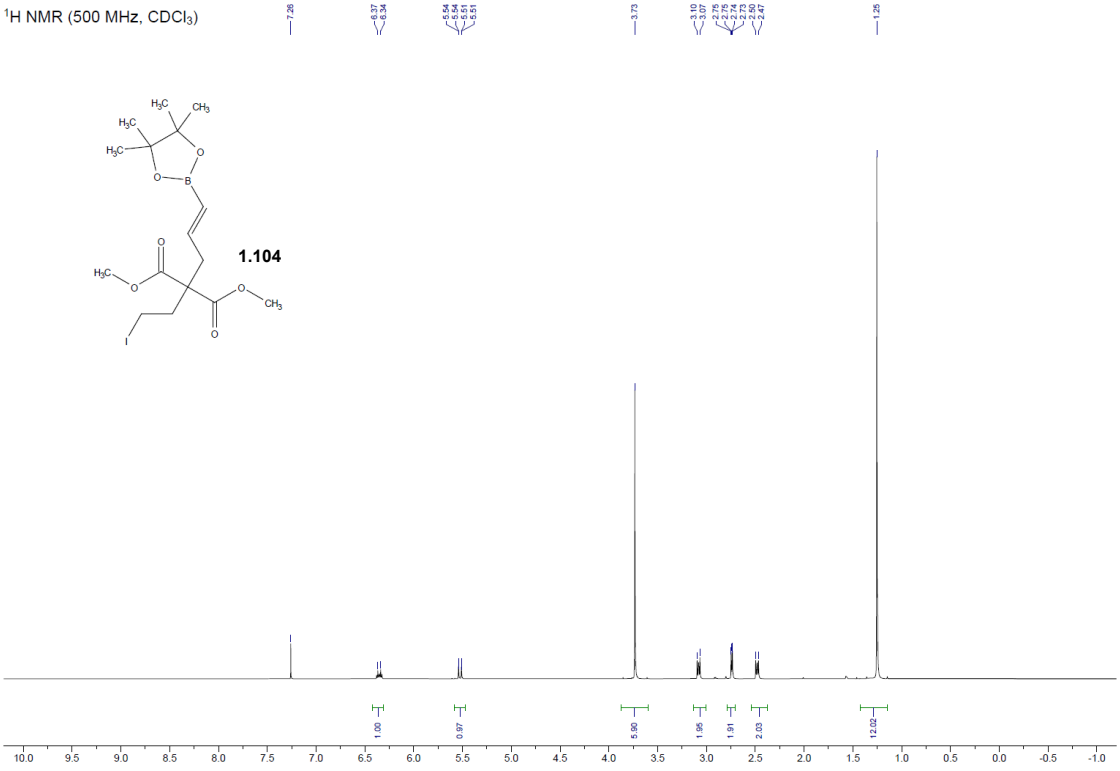

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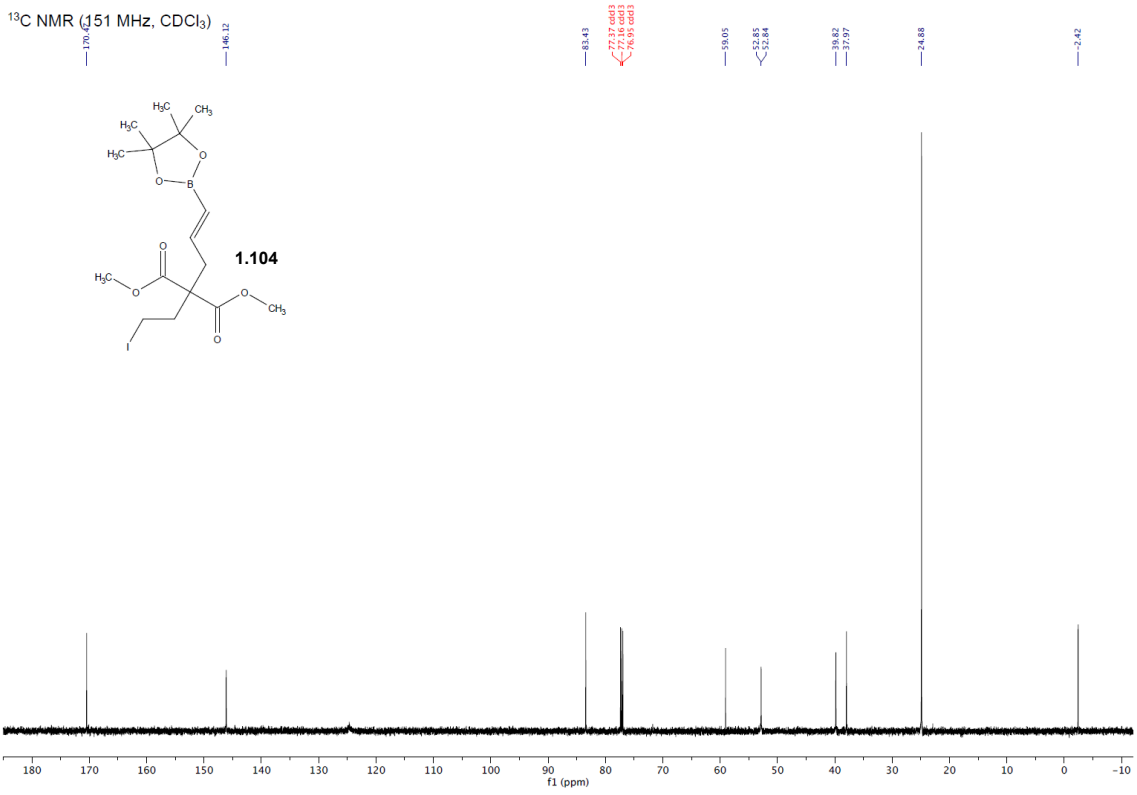

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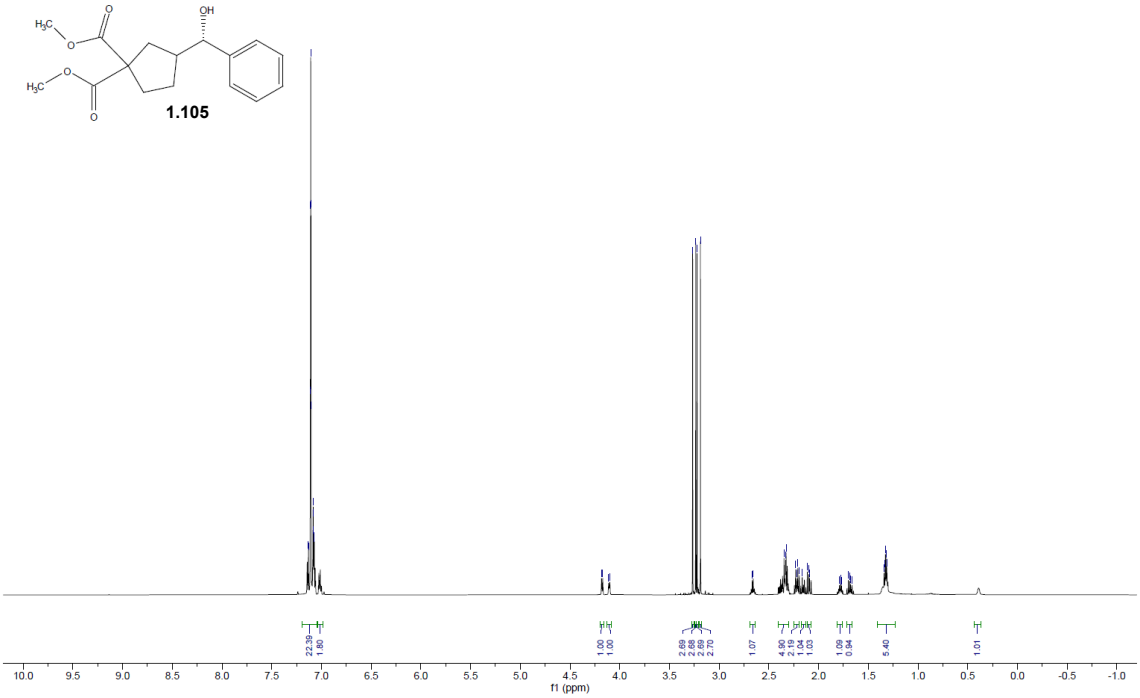

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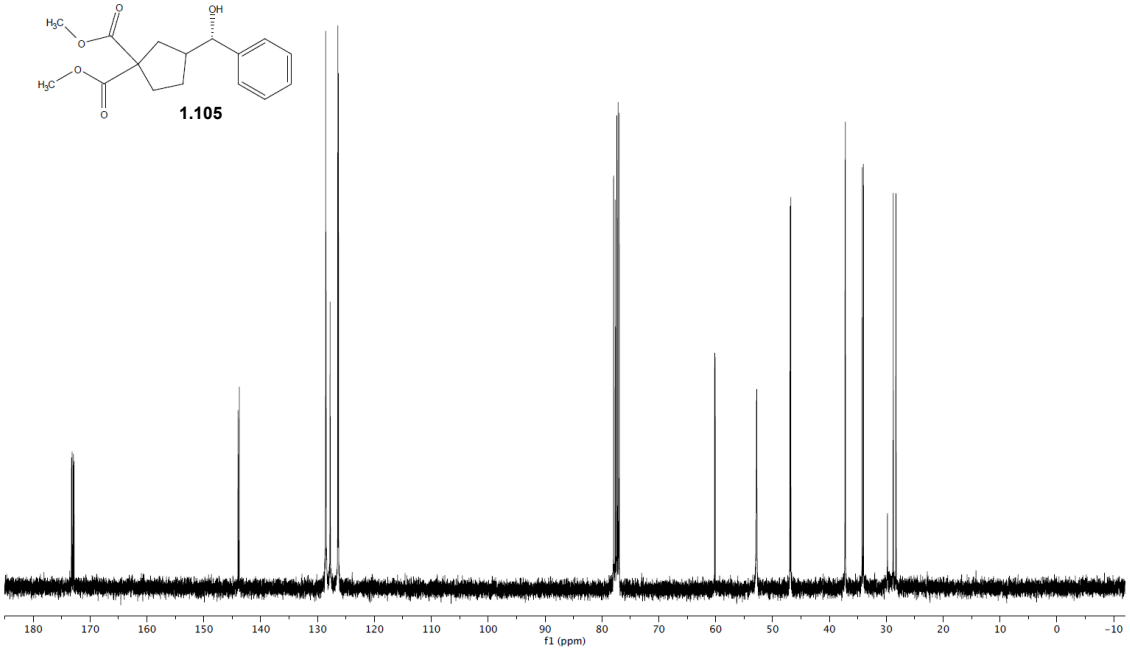

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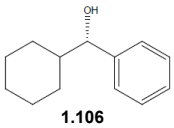

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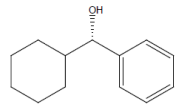

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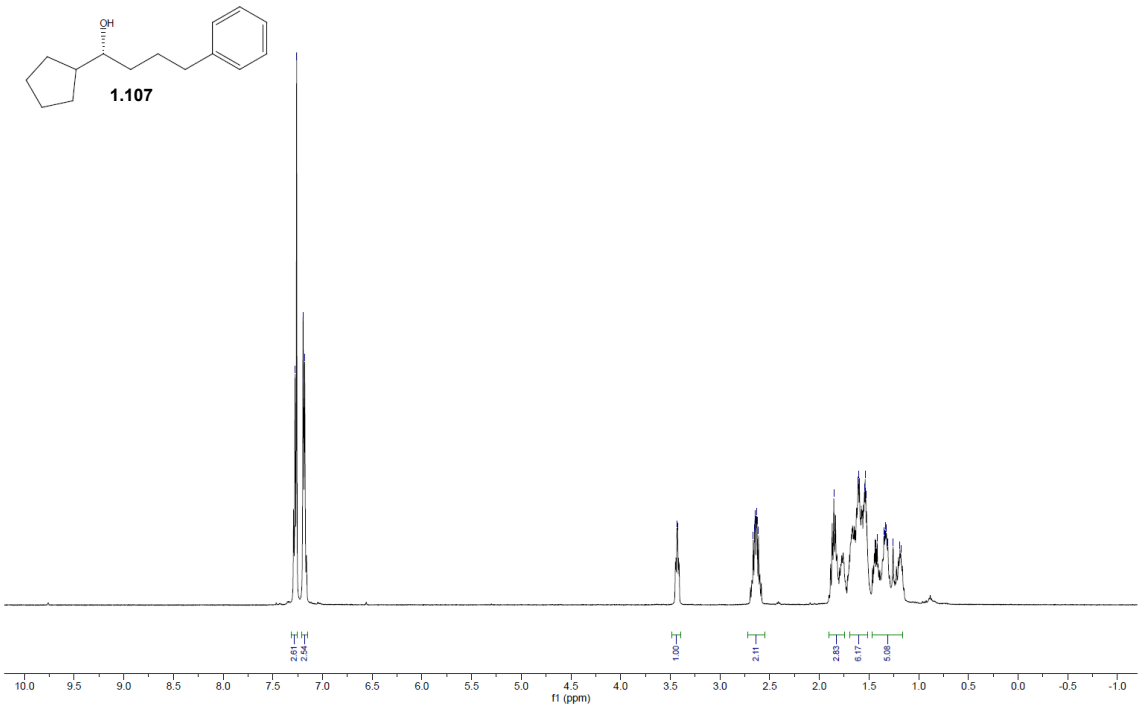

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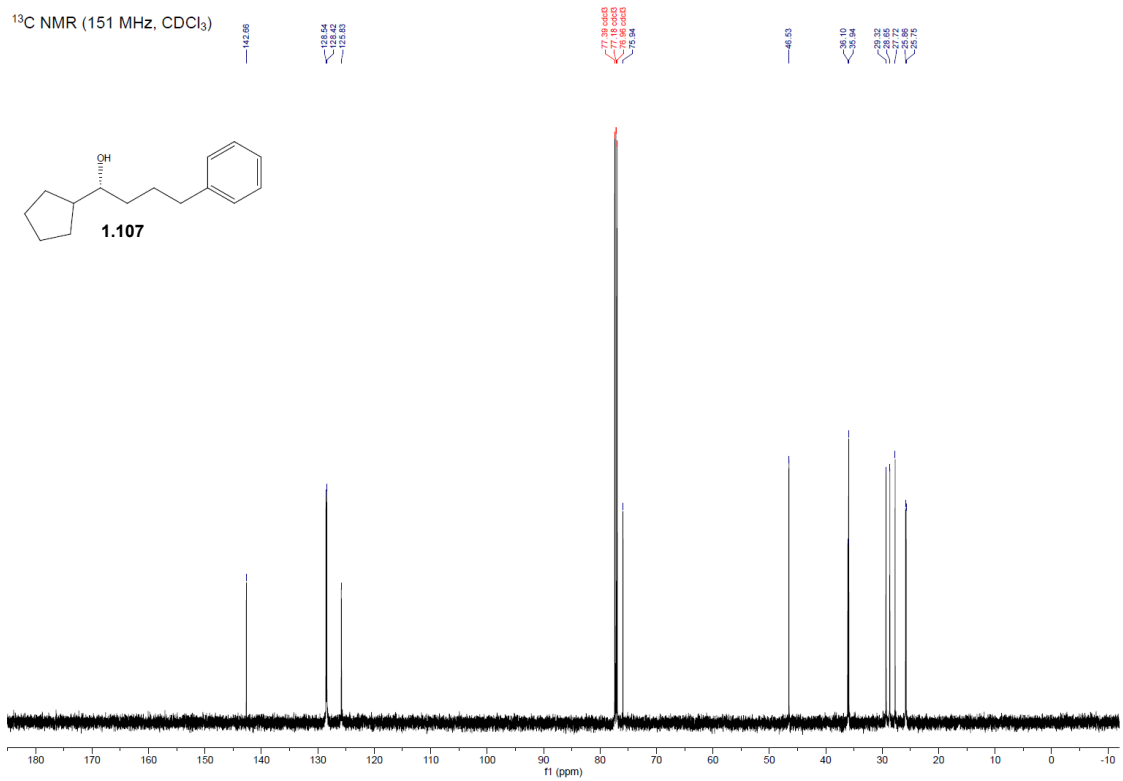

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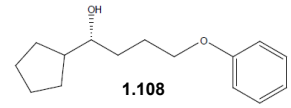

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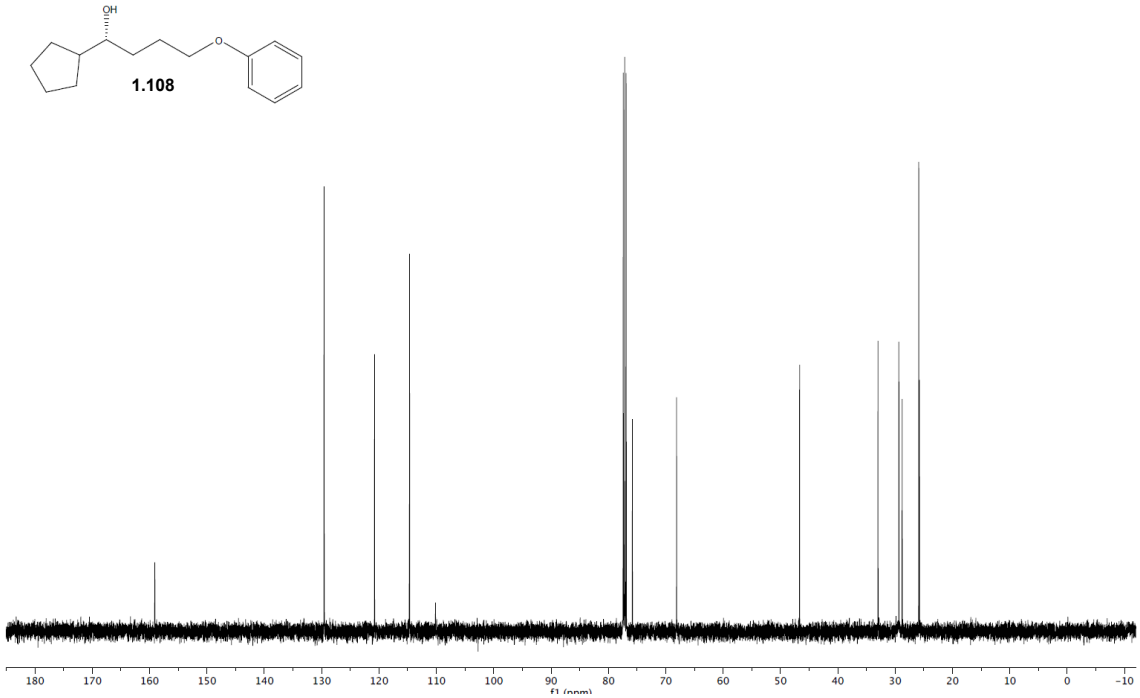

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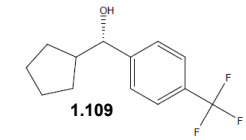

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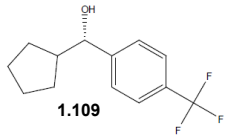

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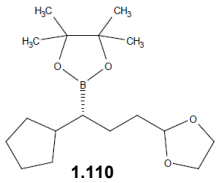

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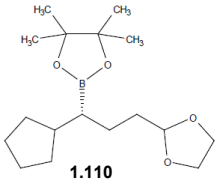

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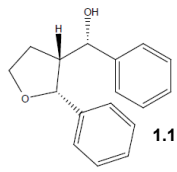

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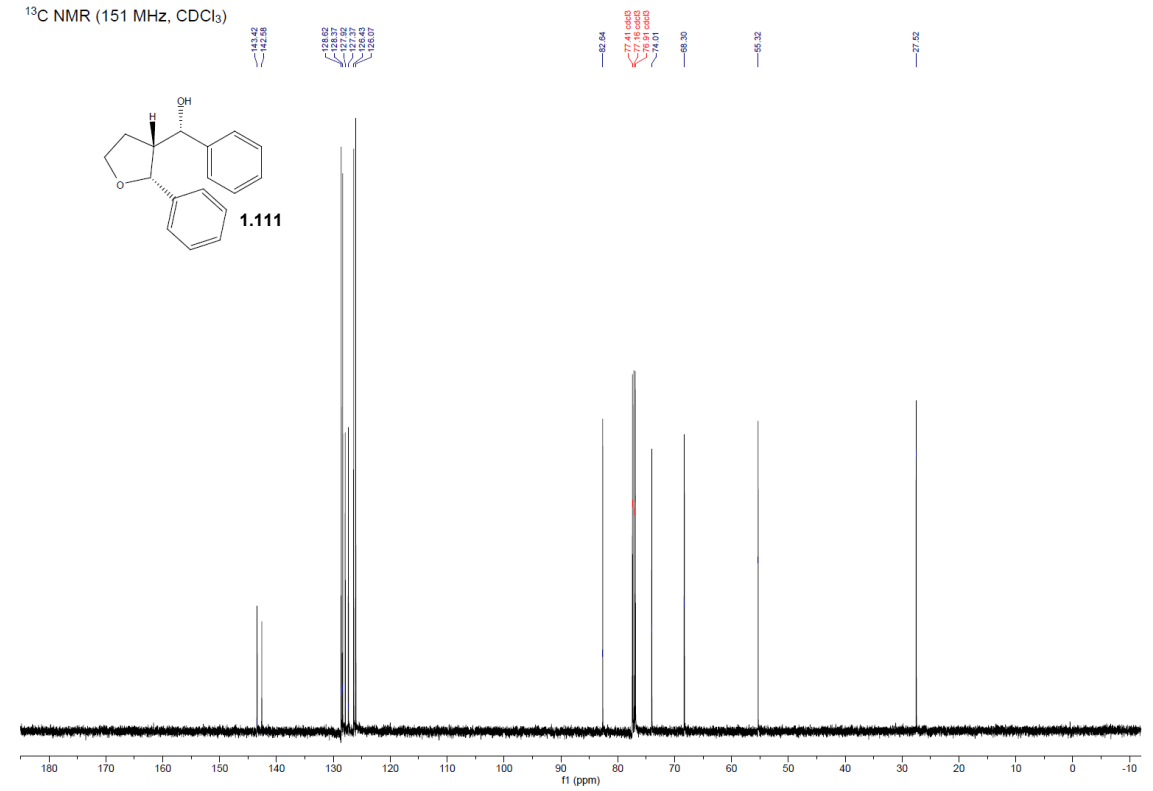

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1.111

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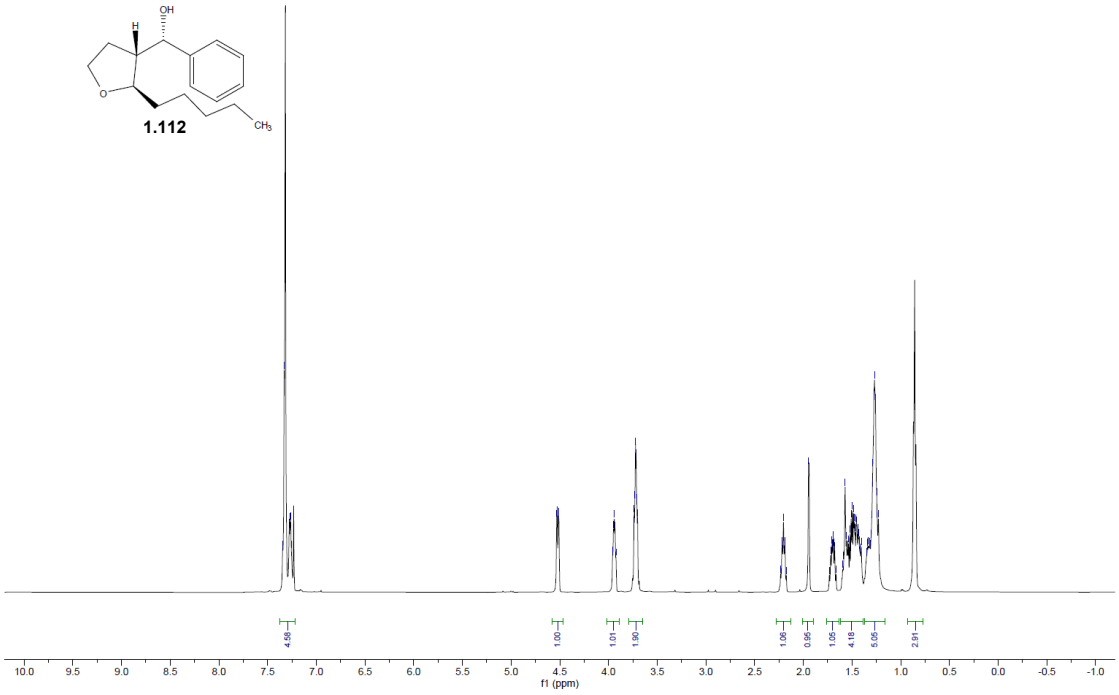

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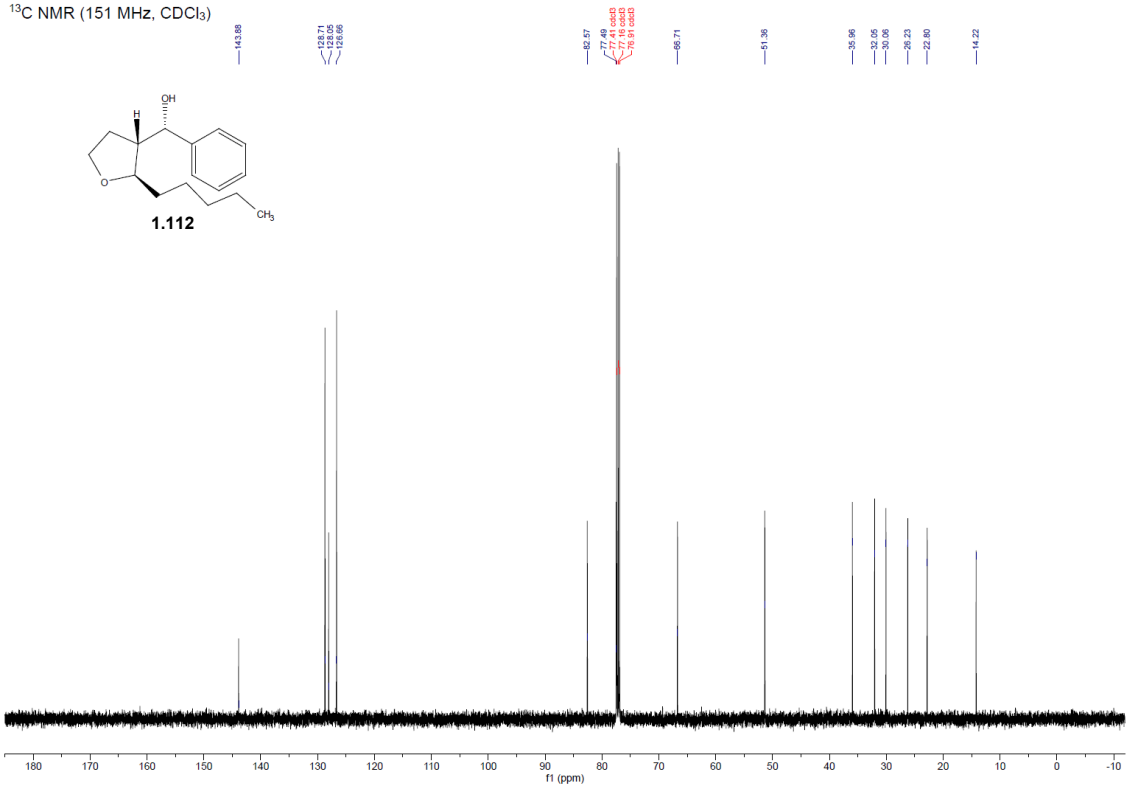

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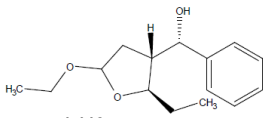

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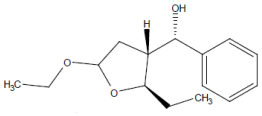

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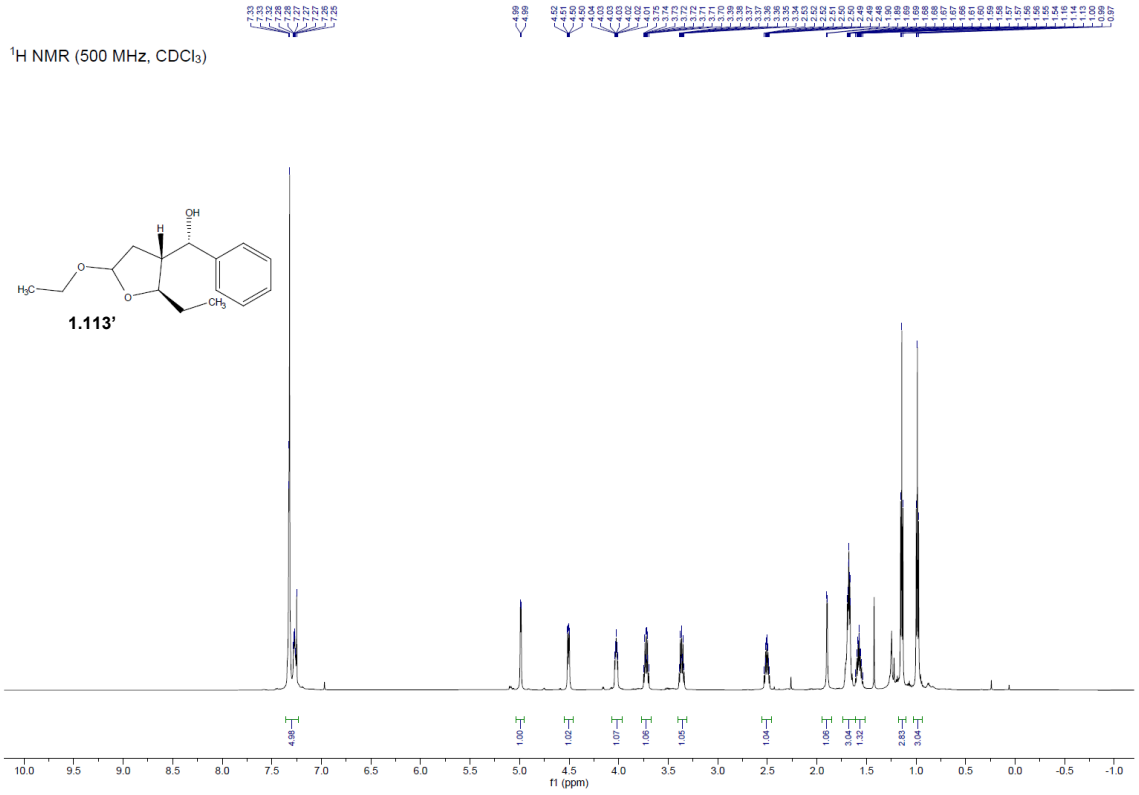

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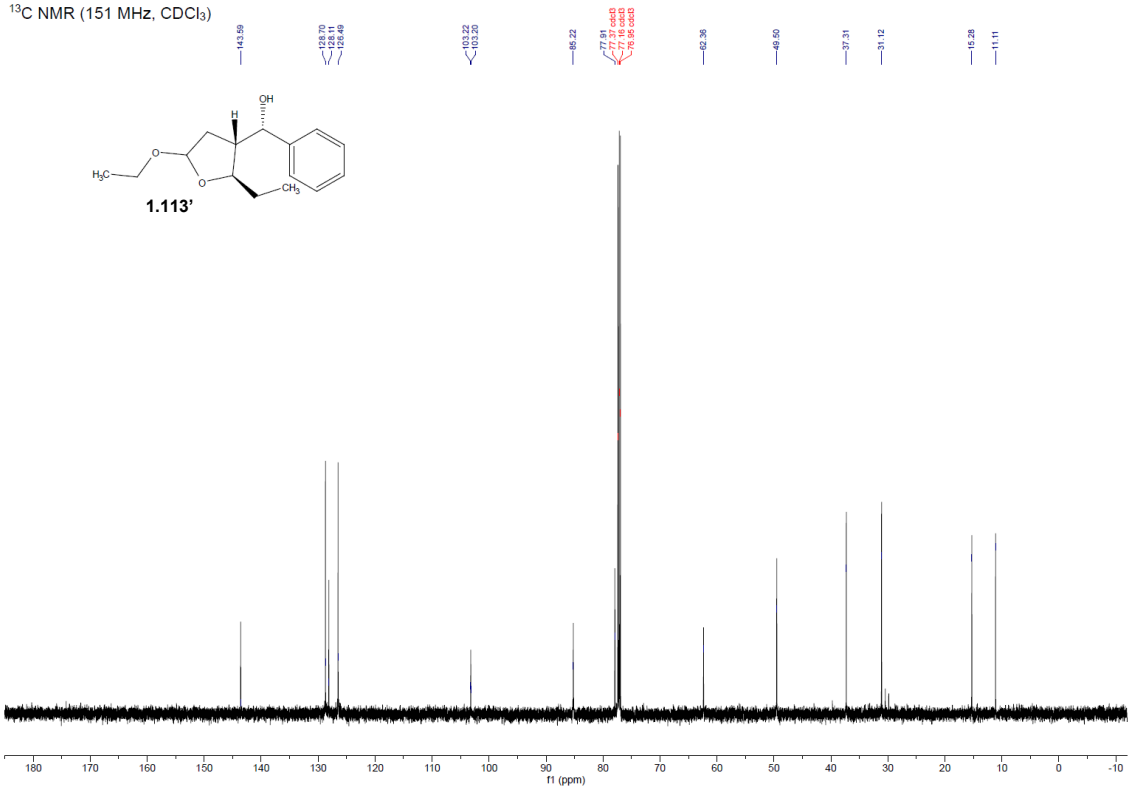

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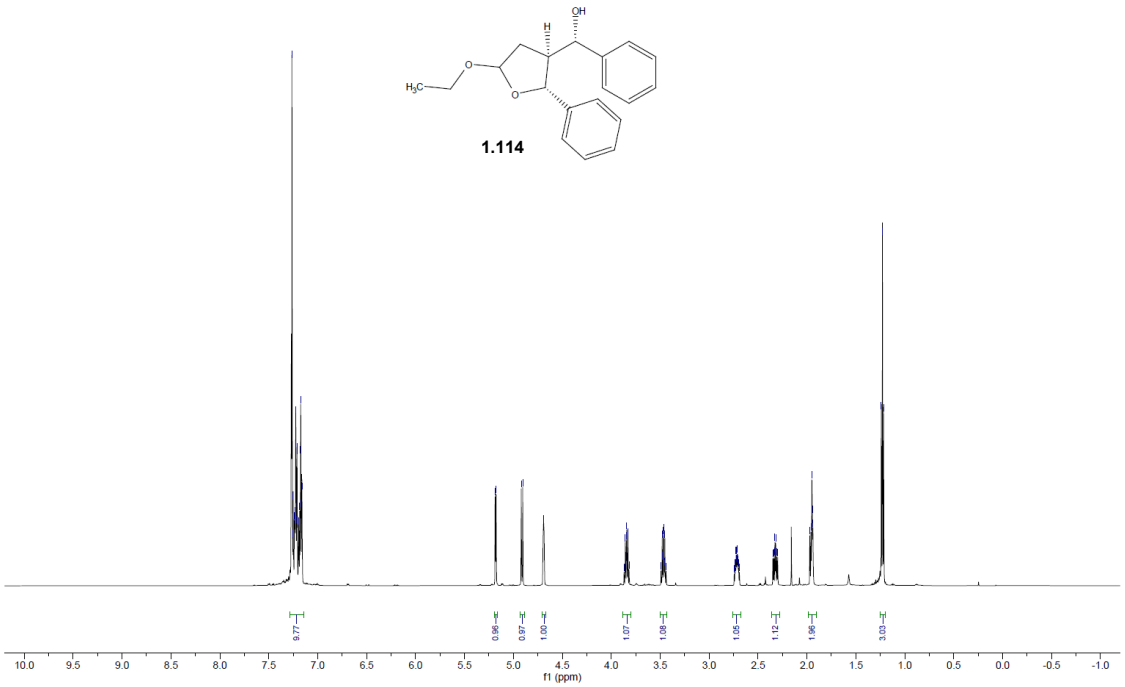

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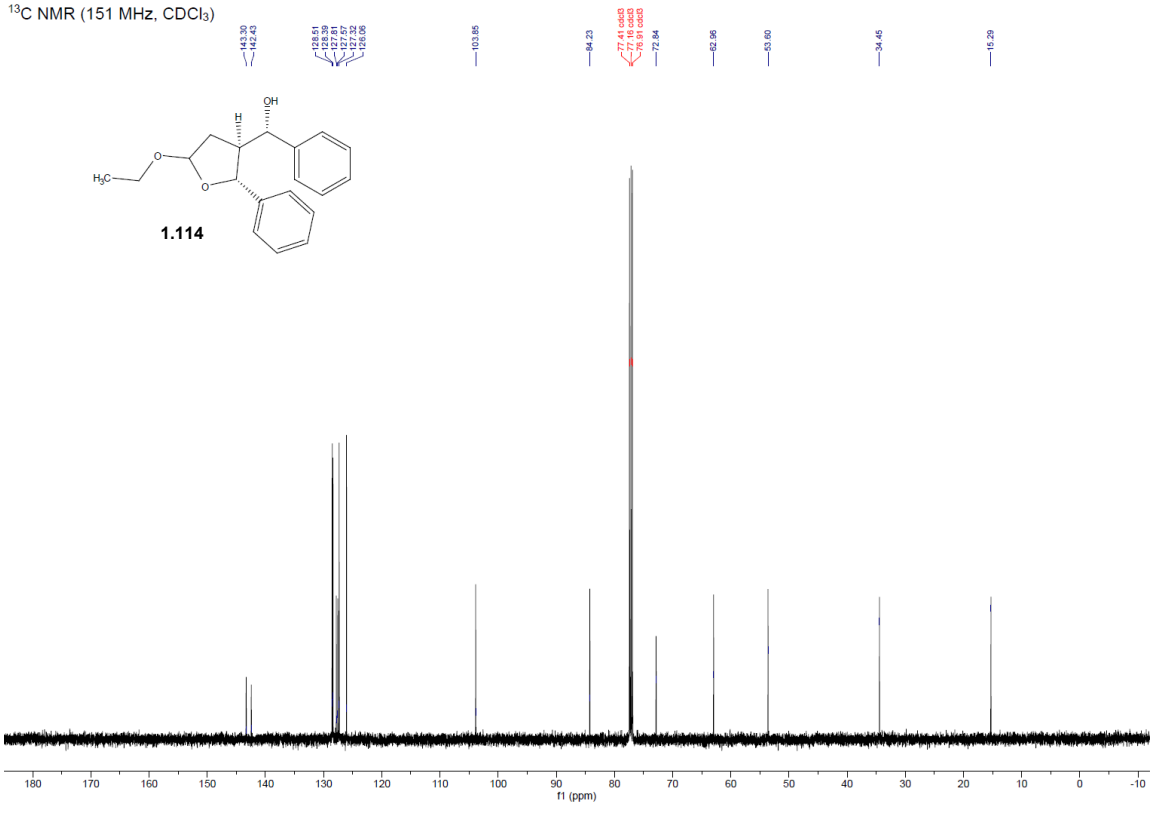

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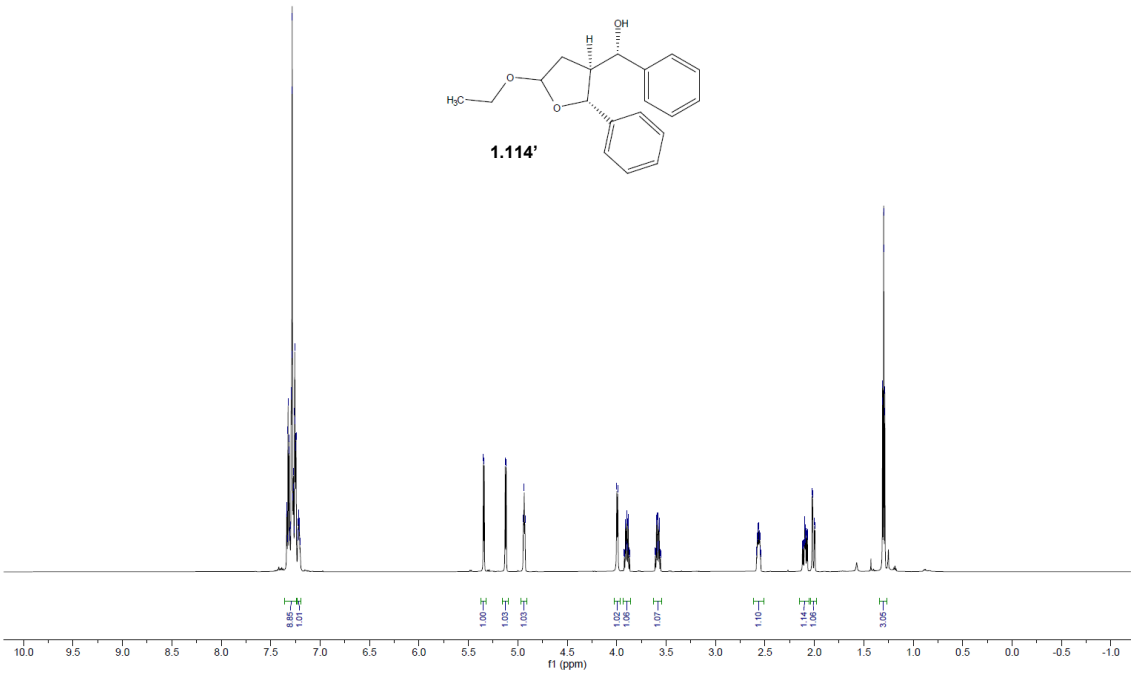

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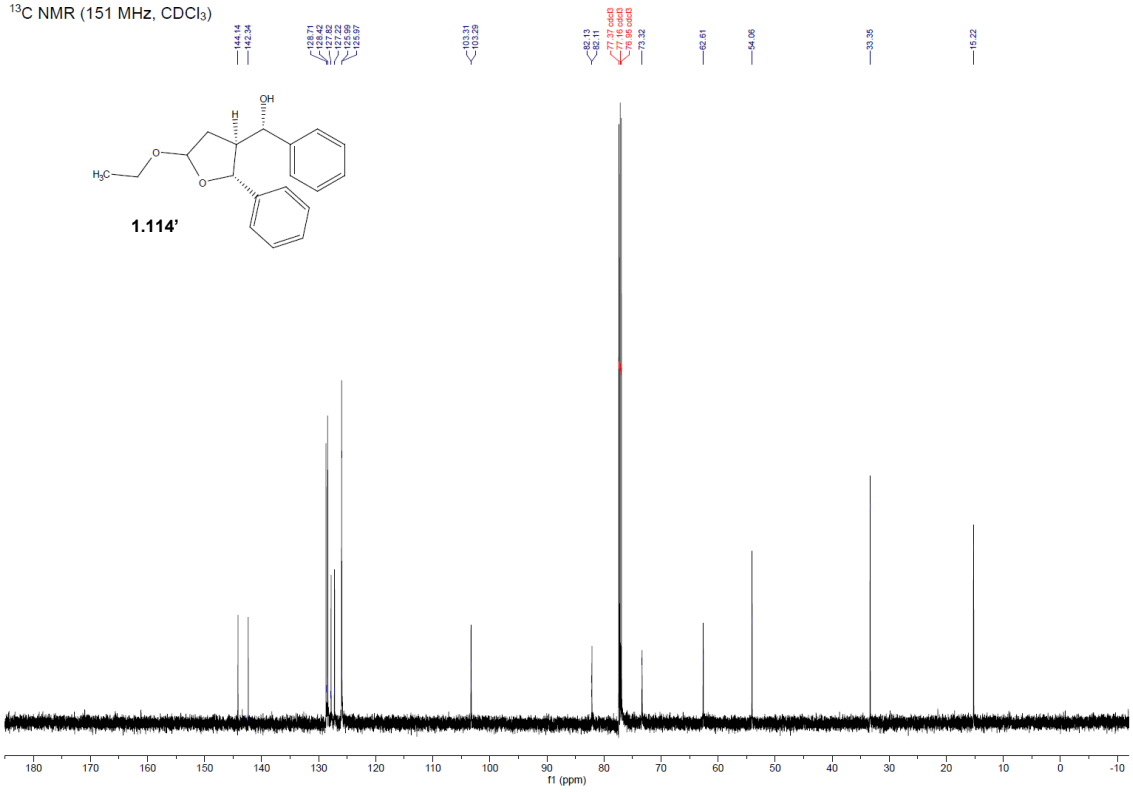

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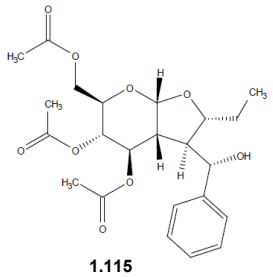

1.115

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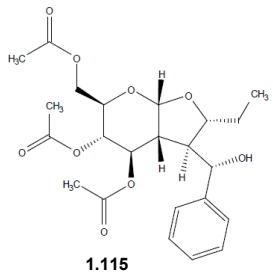

1.115

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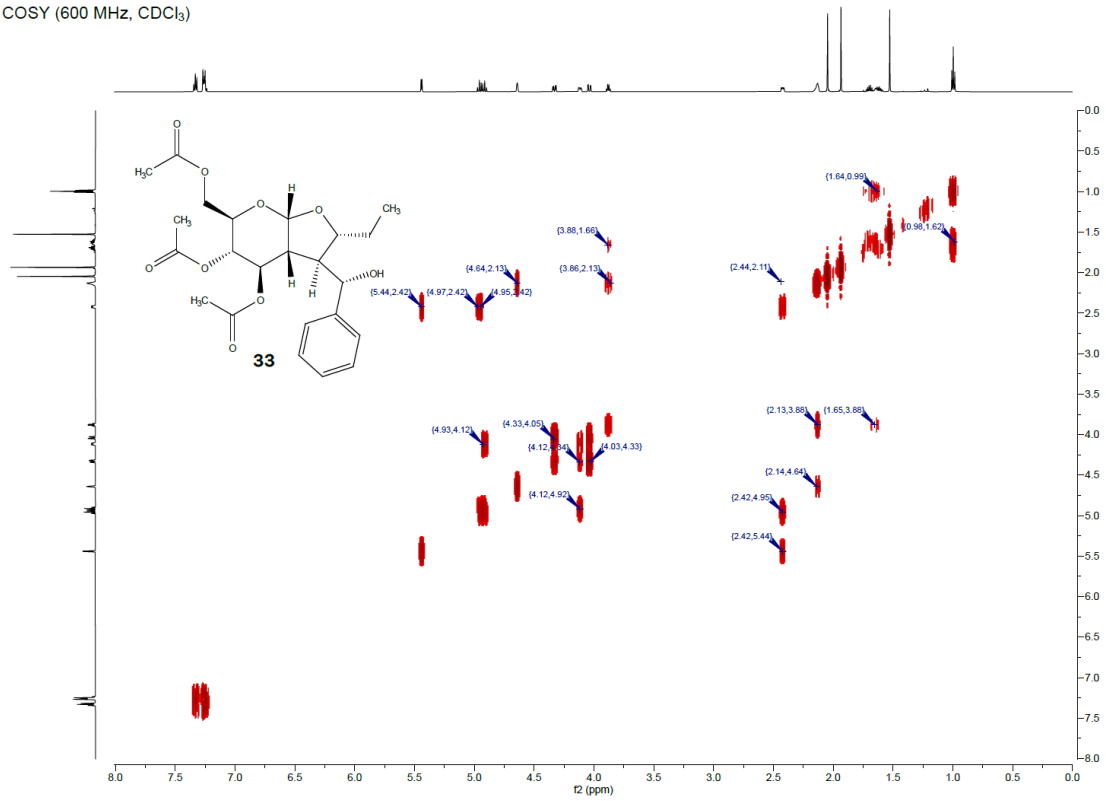

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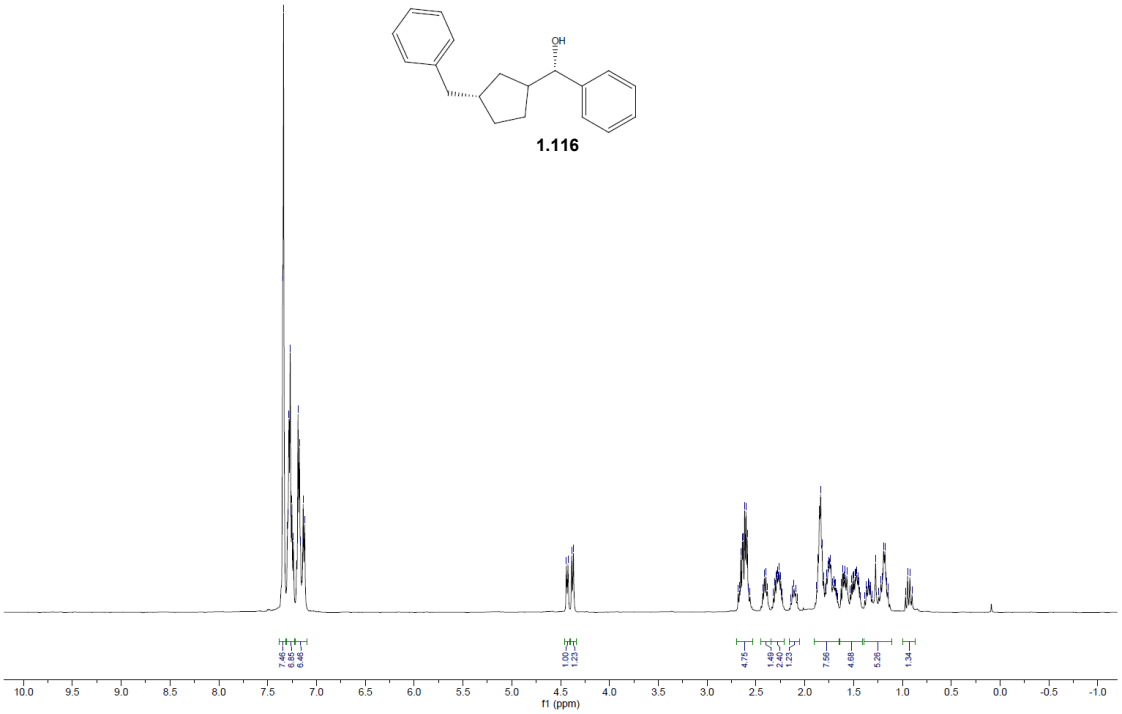
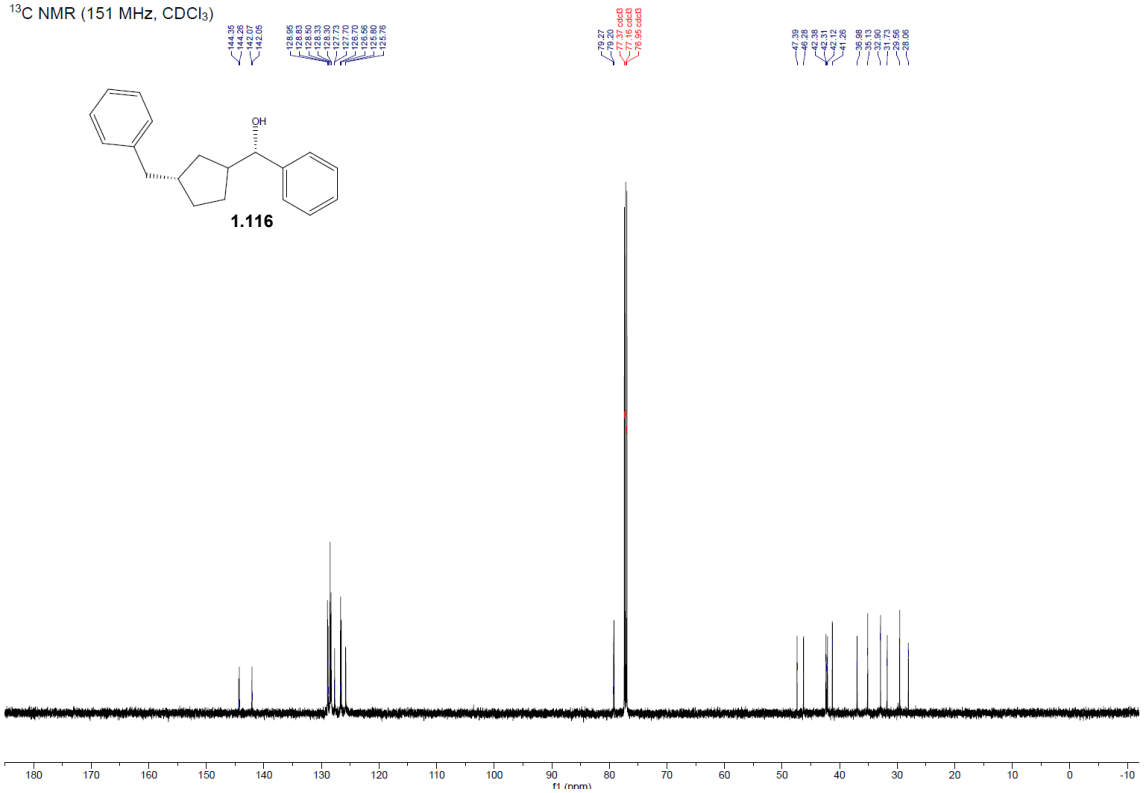


^{13}C NMR (151 MHz, $CDCl_3$)



Chapter 2

Construction of Azacycles by Intramolecular Amination of Organoboronates and Organobis(boronates)

2.1. Introduction

Saturated azacycles, such as azetidines, pyrrolidines and piperidines, are prevalent structures in natural products[1] and pharmaceutically relevant molecules.[2] From a retro-synthetic perspective, one of the most common strategies for the *de novo* synthesis of saturated azacycles is the construction of the C-N bond *via* processes like S_N2 displacement of a leaving group[3], C-H amination[4] and intramolecular aminofunctionalization of alkenes[5].

---

(1) Selected reviews of azacyclic natural products: (a) Pinder, A. R. *Nat. Prod. Rep.* **1992**, *9*, 491−504. (b) O'Hagan, D. *Nat. Prod. Rep.* 2000, *17*, 435−446.

(2) (a) Vitaku, E.; Smith, D. T.; Njardarson, J. T. *J. Med. Chem.* **2014**, *57*, 10257−10274. (b) Ho, S. J.; Brighton, T. A. *Vasc. Health Risk Manag.* **2006**, *2*, 49−58. (c) Akizawa, T.; Ikejiri, K.; Kondo, Y.; Endo, Y.; Fukagawa, M. *Ther. Apheresis Dial.* **2020**, *24*, 248−257. (d) Pinder, R. M.; Brogden, R. N.; Speight, T. M.; Avery, G. S. *Drugs* **1977**, *14*, 81−104.

(3) (a) Concellón, J. M.; Bernad, P. L.; Pérez-Andrés, J. A. *Tetrahedron Lett.* **2000**, *41*, 1231–1234. (b) Brandi, A.; Cicchi, S.; Cordero, F. M. *Chem. Rev.* **2008**, *108*, 3988–4035. (c) Burkett, B. A.; Ting, S. Z.; Gan, G. C. S.; Chai, C. L. L. *Tetrahedron Lett.* **2009**, *50*, 6590–6592. (d) Zhang, H.; Muñiz, K. *ACS Catal.* **2017**, *7*, 4122–4125. (e) Betz, K. N.; Chiappini, N. D.; Du Bois, J. *Org. Lett.* **2020**, *22*, 1687–1691.

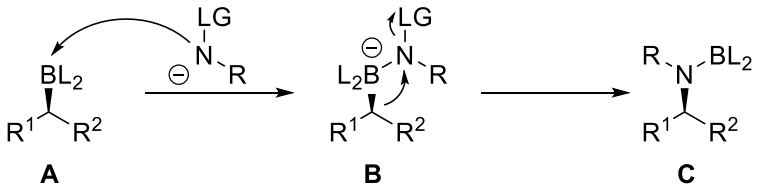
(4) For a review of intramolecular C-H aminations, see: (a) Jeffrey, J. L.; Sarpong, R. *Chem. Sci.* **2013**, *4*, 4092–4106. Selected examples: (b) Fan, R.; Pu, D.; Wen, F.; Wu, J. *J. Org. Chem.* **2007**, *72*, 8994-8997. (c) Hennessy, E. T.; Betley, T. A. *Science* **2013**, *340*, 591–596. (d) Shing, K.-P.; Liu, Y.; Cao, B.; Chang, X.-Y.; You, T.; Che, C.-M. *Angew. Chem. Int. Ed.* **2018**, *57*, 11947–11951. (e) Qin, J.; Zhou, Z.; Cui, T.; Hemming, M.; Meggers, E. *Chem. Sci.* **2019**, *10*, 3202–3207. (f) Wen, X.; Li, X.; Luo, X.; Wang, W.; Song, S.; Jiao, N. *Chem. Sci.* **2020**, *11*, 4482–4487.

(5) For a review of intramolecular hydroaminations: (a) Huo, J.; He, G.; Chen, W.; Hu, X.; Deng, Q.; Chen, D. *BMC Chem.* **2019**, *13*, 1–12. Selected examples of intramolecular carboaminations: (b) Zeng, W.; Chemler, S. R. *J. Am. Chem. Soc.* **2007**, *129*, 12948–12949. (c) Rosewall, C. F.; Sibbald, P. A.; Liskin, D. V.; Michael, F. E. *J. Am. Chem. Soc.* **2009**, *131*, 9488–9489. (d) Mai, D. N.; Wolfe, J. P. *J. Am. Chem. Soc.* **2010**, *132*, 12157–12159. (e) Zhang, G.; Cui, L.; Wang, Y.; Zhang, L. *J. Am. Chem. Soc.* **2010**, *132*, 1474–1475. (f) Liwosz, T. W.; Chemler, S. R. *J. Am. Chem. Soc.* **2012**, *134*, 2020–2023. (g) Wdowik, T.; Galster, S. L.; Carmo, R. L. L.; Chemler, S. R. *ACS Catal.* **2020**, *10*, 8535–8541. Selected examples of intramolecular

The synthesis of azetidines remains a challenge due to the strained nature of the four-membered ring compounds.

One way to access C-N bonds is the amination of organoboron compounds. Four-coordinate boron 'ate' complexes can undergo stereospecific 1,2-metallate shift. This process can take place through the displacement of a leaving group connected to boron. When a three-coordinate alkyl boron motif **A** is treated with a nitrogen Lewis base bearing a leaving group, a boron 'ate' complex **B** will form. Subsequent 1,2-metallate shift will generate the desired alkylamine **C** stereoretentively (Scheme 2.1).

Scheme 2.1. Amination of Alkyl Boron via 1,2-Metallate Shift



This process has been extensively studied and applied to the metal-free construction of carbon-nitrogen bonds, both inter- and intramolecularly. Three classes of aminating reagents have been developed so far, which are chloroamines, azides and hydroxylamine derivatives. The transformation has been reported to work on trialkylboranes, boronic acids, borinic esters, boroxines, and dichloroboranes. Considering that alkylboronic esters are stable, nontoxic and readily available in high enantiopurity, amination of these compounds is important. The intermolecular amination of alkylboronic esters was accomplished by our group using hydroxylamines.

heteroaminations: (h) Wu, T.; Yin, G.; Liu, G. *J. Am. Chem. Soc.* **2009**, *131*, 16354–16355. (i) Qi, X.; Chen, C.; Hou, C.; Fu, L.; Chen, P.; Liu, G. *J. Am. Chem. Soc.* **2018**, *140*, 7415–7419.

Multiple isolated cases of intramolecular amination of alkylboron species *via* 1,2-metallate shift has been employed to form pyrrolidines and piperidines (*vide infra*). However, the formation of strained rings like azetidines has not been addressed. Moreover, the selective amination of vicinal bis(boronate) species, which are easily accessible through diboration of alkenes, can lead to azacycles retaining boronic esters as useful synthetic handles. In this chapter, we will describe the development of the intramolecular amination of alkylboronates and alkylbis(boronates) for the construction of cyclic amines.

2.2. Background

2.2.1. Construction of C-N Bonds *via* 1,2-Metallate Shift

2.2.1.1. Amination of Trialkylboranes

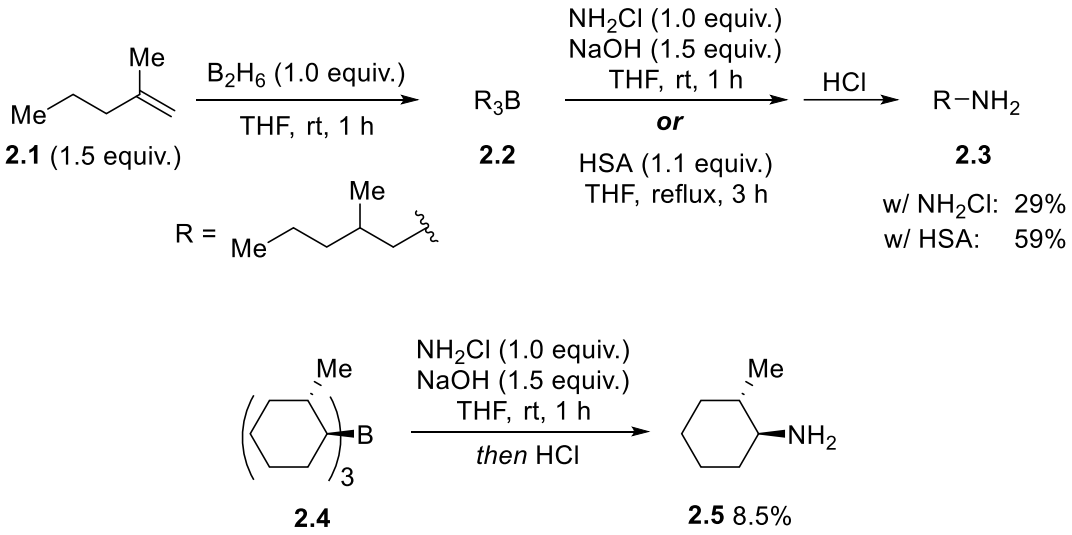
In 1964, Brown reported the first amination of organoboron groups by treating strongly Lewis acidic primary trialkylboranes with chloroamine or hydroxylamine-O-sulfonic acid (HSA) (Scheme 2.2).[6] Trialkylboranes were prepared from hydroboration of alkenes with diborane solution in THF. As for the aminating reagents, chloroamine was prepared fresh by treating aqueous ammonia with sodium hypochlorite and used as a solution, while HSA was a commercially available solid, making it preferable for practical reasons. Reactions with chloroamine were carried out at room temperature and in the presence of base, while the more stable hydroxylamine-O-sulfonic acid required heating at reflux. After the

(6) Brown, H. C.; Heydkamp, W. R.; Breuer, E.; Murphy, W. S. *J. Am. Chem. Soc.* **1964**, *86*, 3565-3566.

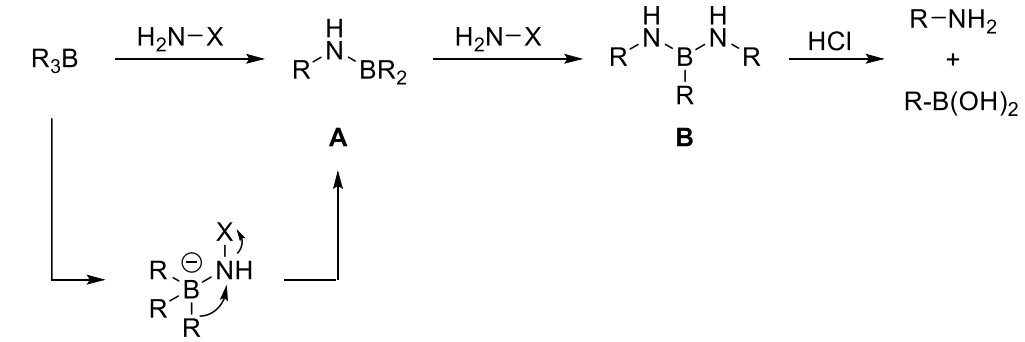
amination reaction, the crude solution was acidified with HCl to yield primary amines in generally 50-60% yield (based on reaction of one alkyl group).

The side product isolated from these reactions was monoalkylboronic acid, which suggested that trialkylborane would undergo amination twice, and the reaction would stop at intermediate **B**, due to its reduced Lewis acidity. When trialkylborane **2.4** synthesized from 1-methylcyclohexene was subjected to the reaction conditions, only *trans* product **2.5** was observed, suggesting that a stereoretentive 1,2-metallate shift took place. Secondary alkylboranes reacted with much lower yield. In a following study in 1966, Brown reported

Scheme 2.2. Brown's Amination of Trialkylboranes with Chloroamine or HSA.



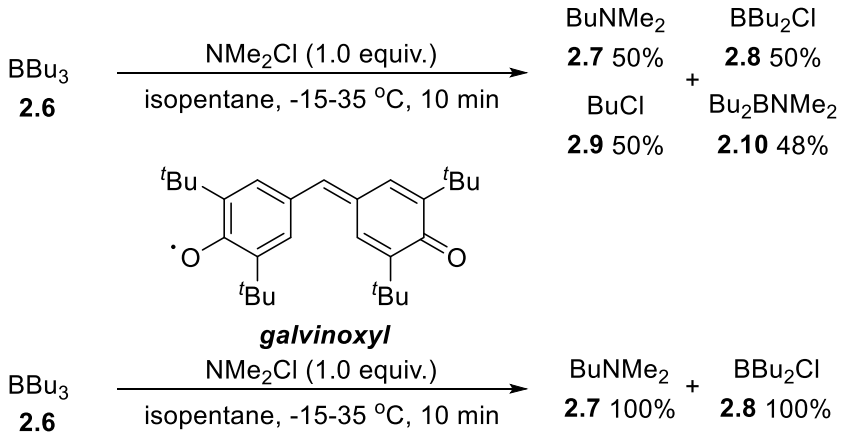
Proposed Mechanism:



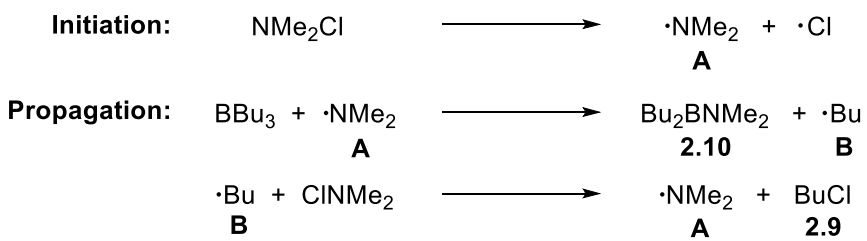
that efficient amination of secondary hindered alkylboranes could be accomplished by treating them with hydroxylamine-O-sulfonic acid in diglyme as the solvent.[7]

Davies later reported that when dimethylchloroamine was used to aminate tributylborane, an unexpected side reaction generated BuCl (**2.9**, Scheme 2.3) and aminoborane **2.10**, in addition to the usual amination products **2.7** and **2.8**.[8] In the presence of a radical scavenger galvinoxyl, only **2.7** and **2.8** were observed. The author proposed that dimethylchloroamine could homolyze into dimethylaminyl radical **A**, which underwent radical substitution with tributylborane to form **2.10** and butyl radical **B**. **B**

Scheme 2.3 Davies' Amination of Trialkylboranes with Dimethylchloroamine Involving Radical Mechanism.



Proposed Radical Chain Pathway:

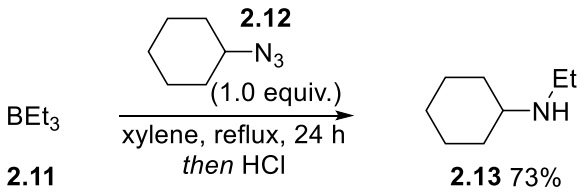


(7) Rathke, M. W.; Inoue, N.; Varma, K. R.; Brown, H. C. *J. Am. Chem. Soc.* **1966**, *88*, 2870-2871.
(8) Davies, A. G.; Hook, S. C. W.; Roberts, B. P. *J. Organomet. Chem.* **1970**, *23*, C11.

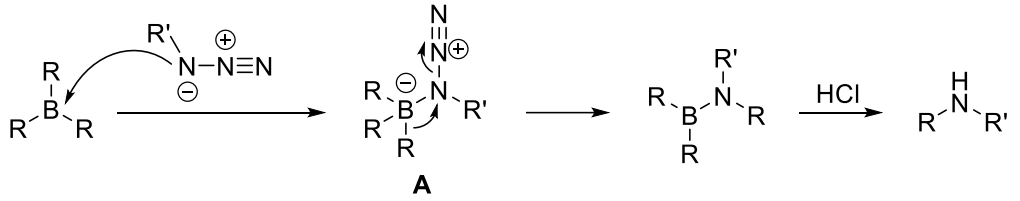
would react with dimethylchloroamine to form **2.9** and dimethylaminyl radical **A**, propagating the radical chain.

In 1971, Brown reported that organoazides react readily with trialkylboranes in refluxing xylene to form the corresponding secondary amine in good yields (Scheme 2.4).[9] In the proposed mechanism, the organoazide coordinates to trialkylborane to form 'ate' complex **A**. 1,2-metallate shift was triggered, with N_2 serving as the leaving group. Organoazides were found to be stable under the reaction temperature, so the mechanism involving pre-formation of nitrene was ruled out.

Scheme 2.4. Brown's Amination of Trialkylboranes with Organoazides.



Proposed Mechanism:

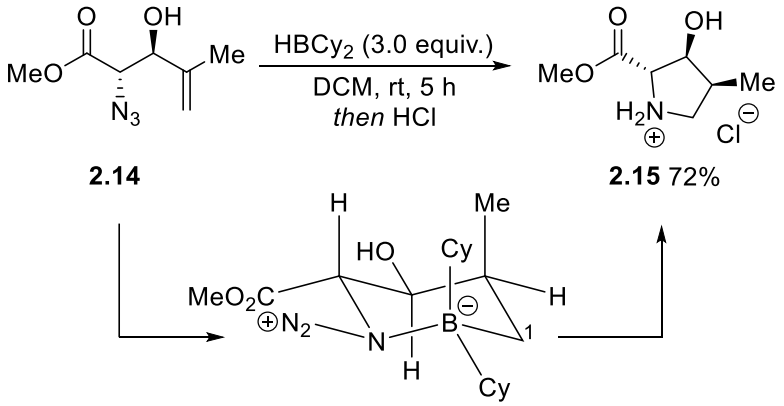


Evans pioneered in applying this method to an intramolecular reaction (Scheme 2.5).[10] During the synthesis of cyclic hexapeptide echinocandin D, azido olefin **2.14** was treated with dicyclohexylborane, and an intramolecular amination reaction led to the desired pyrrolidine ring **2.15** in 72% yield, presumably through a six-membered intermediate. The C1-B bond migrated, being anti-periplanar to the N-N_2^+ bond in a chair-like transition state.

(9) Suzuki, A.; Sono, S.; Itoh, M.; Brown, H. C.; Midland, M. *J. Am. Chem. Soc.* **1971**, *93*, 4329-4330.

(10) Evans, D. A.; Weber, A. E. *J. Am. Chem. Soc.* **1987**, *109*, 7151–7157.

Scheme 2.5. Evans's Intramolecular Amination of Trialkylboranes with Organoazides

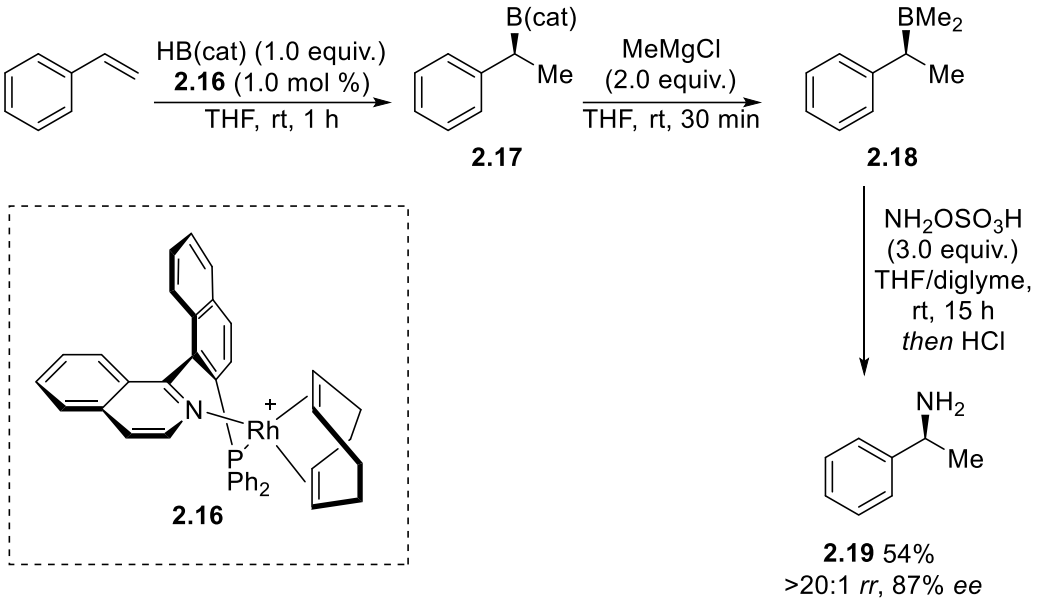


Due to their low Lewis acidity, boronic esters were transformed into trialkylboranes before undergoing amination reactions using the early protocols. In 1997, J. M. Brown reported an enantioselective hydroboration/amination of vinyl arenes to construct chiral benzylic amines (Scheme 2.6).[11] In one example, styrene was hydroborated with catechol borane under the catalysis of chiral Rh complex **2.16**. The resulting boronic ester **2.17** was treated with 2 equivalents of methylmagnesium chloride reagent to form trialkylborane **2.18**, which underwent amination with HSA to form benzylic amine **2.19** in good yield and selectivity. Of note, migration of the methyl group is slower than the secondary alkyl group. In a following study, Brown reported the synthesis of secondary and tertiary amines using substituted aminating reagents and the borane intermediates mentioned above.[12]

(11) Fernandez, E.; Hooper, M. W.; Knight, F. I.; Brown, J. M. *Chem. Commun.* **1997**, *21*, 173–174.

(12) Fernandez, E.; Maeda, K.; Hooper, M. W.; Brown, J. M. *Chem. Eur. J.* **2000**, 10, 1840–1846.

Scheme 2.6. J. M. Brown's Amination of Catechol Boronic Acids via in situ Generation of Boranes



2.2.1.2. Amination of Alkylchloroboranes

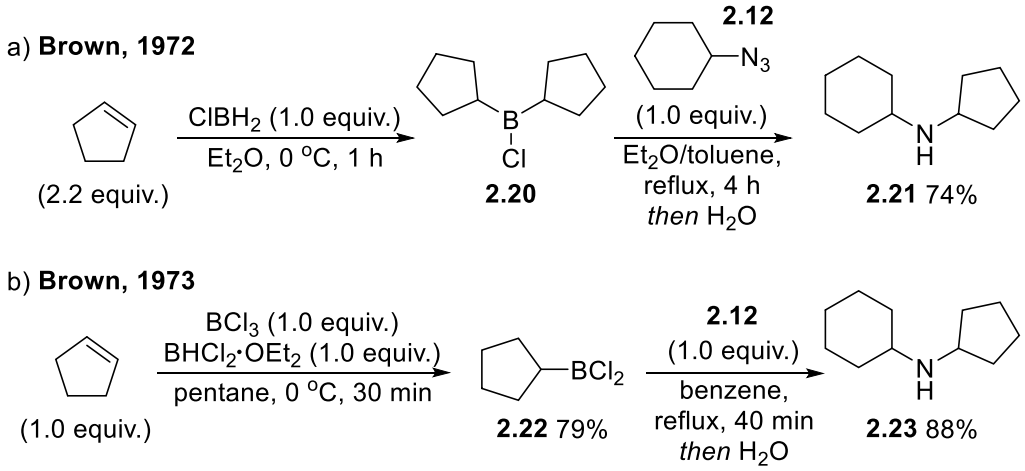
Similar to trialkylboranes, alkyldichloroboranes and dialkylchloroboranes are highly Lewis acidic organoboron species and readily interact with aminating reagents. They can be synthesized *via* hydroboration of alkenes with dichloro- or chloroborane.

In 1972, H. C. Brown reported that dialkylchloroboranes, synthesized from hydroboration of alkenes with chloroborane, could be aminated with alkylazides (Scheme 2.7a).[13] The amination of dialkylchloroboranes, possibly due to their higher Lewis acidity, were found to be faster and less sensitive to steric requirements than that of trialkylboranes. Secondary dicyclopentylchloroborane (**2.20**) reacted with secondary azide **2.12** in good yield in refluxing toluene. However, only one of the two alkyl groups on boron was utilized in the synthesis. Brown improved this reaction by employing alkyldichloroboranes with

(13) Brown, H. C.; Midland, M. M. *J. Am. Chem. Soc.* **1972**, *94*, 2114-2115.

only one alkyl group connected to the boron atom (Scheme 2.7b).[14] Dichloroborane etherate, generated from reduction of trichloroborane by lithium borohydride, could react with alkenes in the presence of Lewis acidic trichloroborane to form alkyldichloroboranes that were isolable by distillation. Reaction with alkylazides in refluxing benzene yielded secondary amines. Vaultier thoroughly studied the scope of the reaction, and explored the synthetic utility of this method.[15]

Scheme 2.7. Brown's Amination of Alkylchloroboranes



Apart from hydroboration of alkenes, dichloroboranes could also be generated by treating boronic esters with trichloroborane. Historically, this method was applied for the transformation of boronic esters to alkyl amines. In 1987, Vaultier achieved the synthesis of simple pyrrolidines and piperidines *via* intramolecular amination (Scheme 2.8).[16] Azido boronic ester **2.24** was treated with trichloroborane, forming alkyldichloroborane intermediate *in situ*, which rapidly reacted with azido group intramolecularly and produced

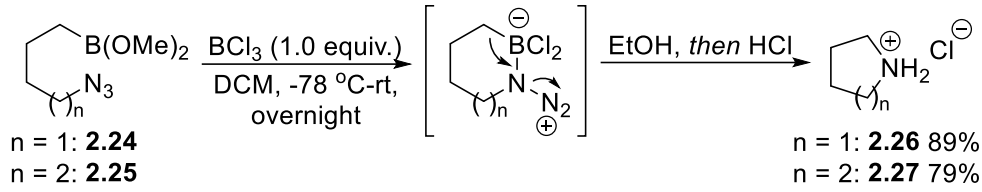
(14) (a) Brown, H. C.; Midland, M. M.; Levy, A. B. *J. Am. Chem. Soc.* **1973**, *95*, 2394-2396. (b) Brown, H. C.; Ravindran, N. *J. Am. Chem. Soc.* **1973**, *95*, 2396-2397.

(15) (a) Carboni, B.; Vaultier, M.; Carrié, R. *Tetrahedron* **1987**, *43*, 1799–1810. (b) Carboni, B.; Vaultier, M.; Carrié, R. *Tetrahedron Lett.* **1988**, *29*, 1279–1282.

[16] Jego, J. M.; Carboni, B.; Vaultier, M.; Carrie, R. *J. Chem. Soc. Chem. Commun.* **1989**, 142–143.

pyrrolidine hydrochloride (**2.26**) in high yield after workup. Piperidines were also synthesized efficiently using this method.

Scheme 2.8. Vaultier's Intramolecular Amination of Dichloroboranes



Intermolecular amination of alkyl boronic esters were also achieved through dichloroborane intermediates. In 2002, Knochel showed that secondary amine **2.30** could be synthesized from alkyl boronic ester **2.28** by first converting into alkyldichloroborane **2.29** using trichloroborane followed by amination with benzyl azide (Scheme 2.9a).[17] The reaction proved to be highly stereoretentive. Morken synthesized enantioenriched secondary alkylamine **2.33** using a similar procedure from boronic ester **2.32** generated *via* rhodium-catalyzed enantioselective hydrogenation of alkenylboronic ester **2.31** (Scheme 2.9b).[18]

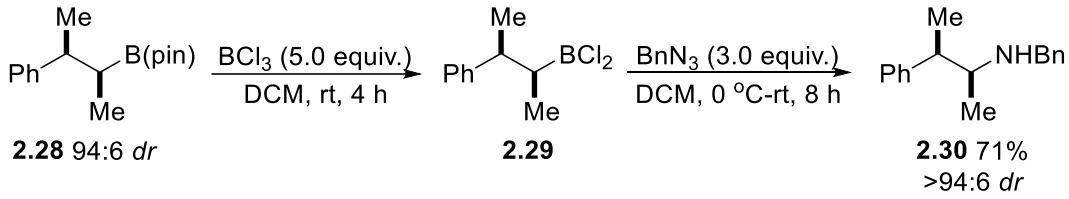
Diaminoboranes were also used as precursors to dichloroboranes. Vaultier discovered that bis(diisopropylamino)borane **2.34**, synthesized from addition of alkyl Grignard reagent to bis(diisopropylamino)chloroborane, could be transformed into alkyldichloroborane **2.35** and subsequently be aminated by alkylazide (Scheme 2.10).[19]

Although the amination of potassium trifluoroborate salts were found to go through dichloroboranes as intermediates, it will be discussed separately below.

(17) Hupe, E.; Marek, I.; Knochel, P. *Org. Lett.* **2002**, *4*, 2861–2863.
(18) Moran, W. J.; Morken, J. P. *Org. Lett.* **2006**, *8*, 2413–2415.
(19) Chavant, P. Y.; Lhermitte, Vaultier, M. *Synlett*, **1993**, 519–521.

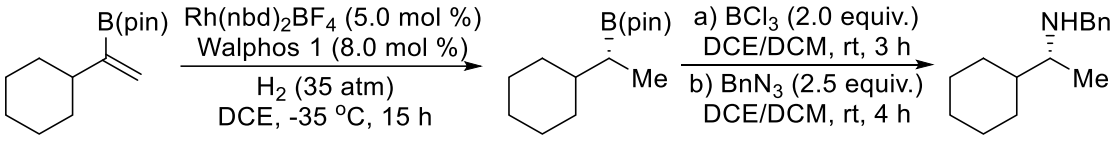
Scheme 2.9. Examples of Amination of Boronic Esters through Dichloroborane Intermediates

a) **Knochel, 2002**

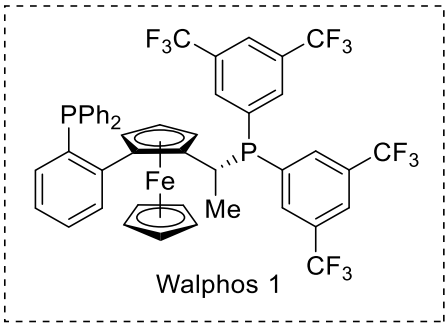


2.28 94:6 *dr* **2.29** **2.30** 71% >94:6 *dr*

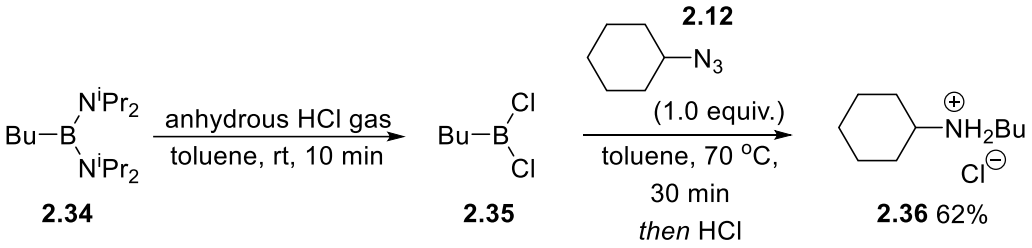
b) **Morken, 2006**



2.31 **2.32** **2.33** 81% >95% *ee*



Scheme 2.10. Vaultier's Amination of Bis(diisopropylamino)boranes through Dichloroborane Intermediates

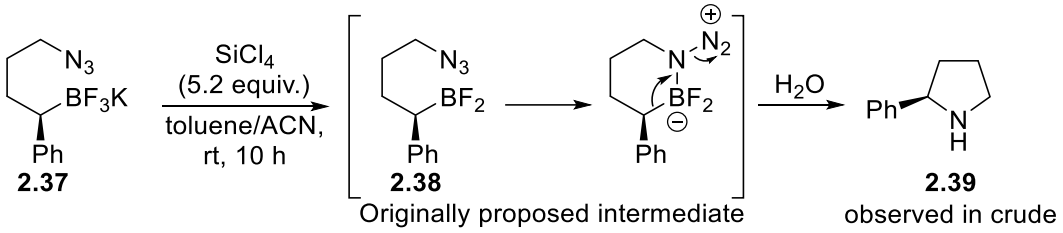


2.34 **2.35** **2.36** 62%

2.2.1.3. Amination of Potassium Trifluoroborate Salts

Potassium trifluoroborate salts are readily available and stable organoboron reagents.[20] In 2002, Matteson accomplished the amination of potassium organotrifluoroborate salts by treating them with alkylazides in the presence of tetrachlorosilane.[21] An intramolecular example was reported (Scheme 2.11). The author proposed that potassium trifluoroborate salt **2.37** could be defluorinated by tetrachlorosilane into difluoroborane **2.38**, which served as the intermediate towards amination. However, in a following study, the author carefully examined the reaction of potassium trifluoroborate salts with tetrachlorosilane using ^{11}B and ^{19}F NMR, and discovered that organodichloroborane was produced, accompanied by the emission of tetrafluorosilane gas.[22] Thus the intermediate in the amination of potassium trifluoroborate salts were identified to be dichloroboranes.

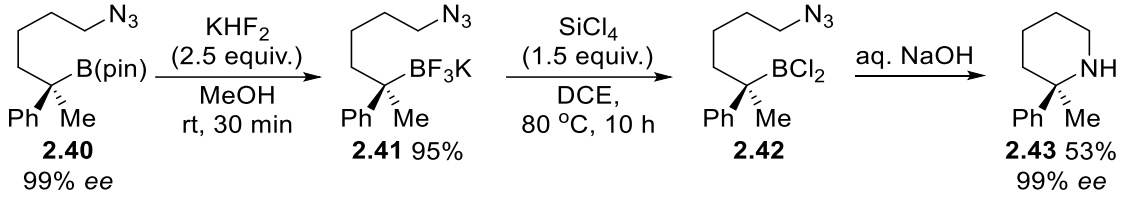
Scheme 2.11. Matteson's Amination of Trifluoroborate Salts



In 2011, Aggarwal reported that similar conditions could be applied to the synthesis of enantioenriched tertiary benzylic amines from the corresponding stereodefined boronic esters.[23] In an intramolecular example, a substituted piperidine **2.43** was synthesized stereospecifically from tertiary boronic ester **2.40** by first converting the latter into potassium trifluoroborate salt **2.41**.

(20) Molander, G. A.; Sandrock, D. L. *Curr. Opin. Drug Discov. Dev.* **2009**, *12*, 811–823.
(21) Matteson, D. S.; Kim, G. Y. *Org. Lett.* **2002**, *4*, 2153–2155.
(22) Kim, B. J.; Matteson, D. S. *Angew. Chem. Int. Ed.* **2004**, *43*, 3056–3058.
(23) Bagutski, V.; Elford, T. G.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2011**, *50*, 1080–1083.

Scheme 2.12. Aggarwal's Amination of Tertiary Trifluoroborate Salts

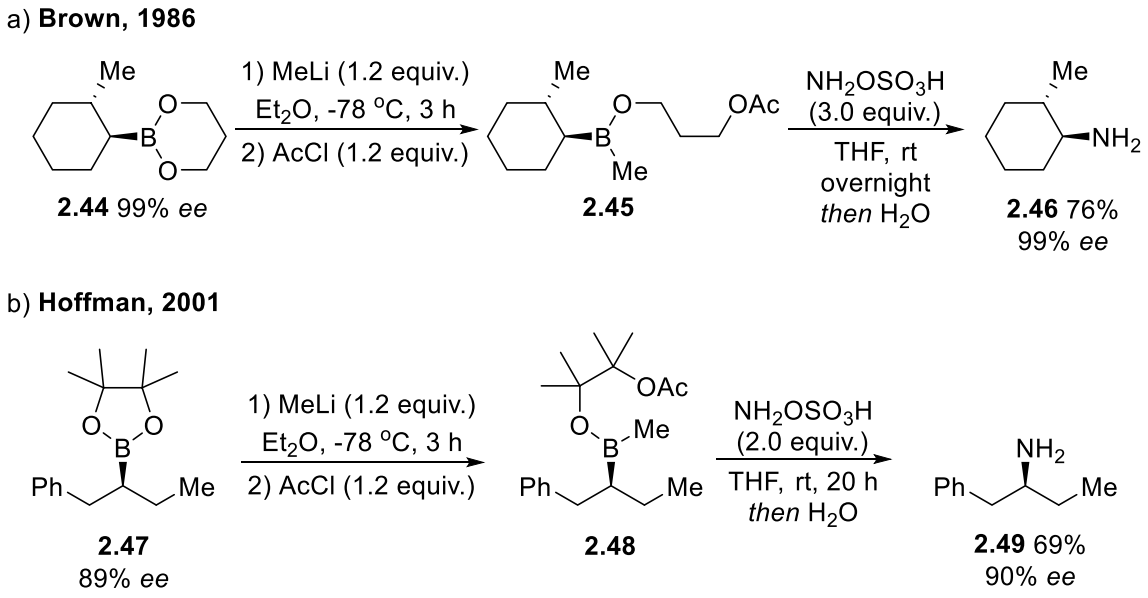


2.2.1.4. Amination of Borinic Esters

Borinic acids, with two alkyl ligands and one oxygen ligand, are more Lewis acidic than boronic esters and are thus more reactive in interaction with aminating reagents. Methods have been developed to aminate boronic esters by first converting them into borinic esters.

In 1986, Brown treated boronic ester **2.44** with methyllithium solution followed by acyl chloride, and converted it into borinic ester **2.45**, which was Lewis acidic enough to be aminated by HSA at room temperature (Scheme 2.13a).[24] The secondary cyclohexyl group was found to migrate much faster than methyl group, and the desired amination product

Scheme 2.13. Amination of Boronic Esters through Borinic Ester Intermediates



(24) Brown, H. C.; Kim, K.-W.; Cole, T. E.; Singaram, B. *J. Am. Chem. Soc.* **1986**, *108*, 6761.

2.46 formed with good yield and perfect stereospecificity. The same reactivity was applied to the amination of pinacol boronic ester by Hoffman in 2001 (Scheme 2.13b).[25]

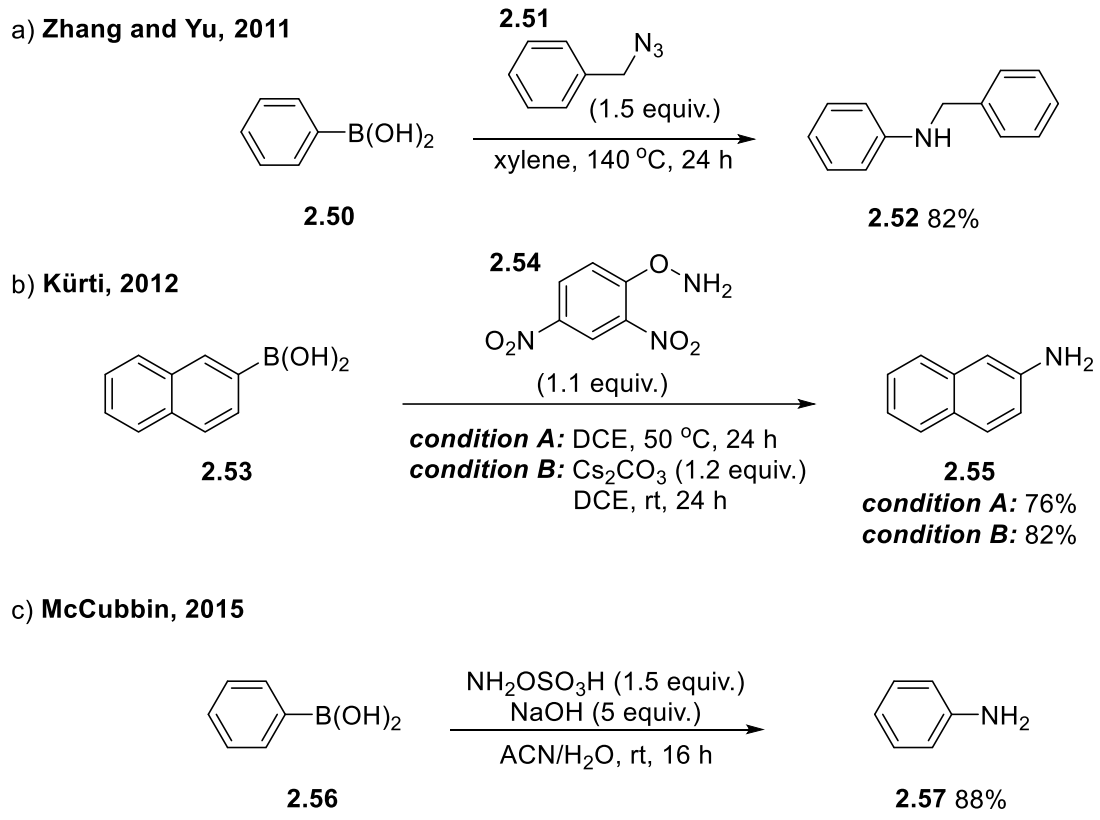
2.2.1.5. Amination of Boronic Acids

Boronic acids, with two oxygen ligands donating lone pairs to the boron's empty p-orbital, are lower in Lewis acidity than trialkylboranes and borinic esters. Aminating reagents with higher nucleophilicity are required, and usually harsher conditions like heating and promotion by base are employed for the conversion of boronic acids to amines.

In 2011, Zhang and Yu accomplished the amination of arylboronic acids using organoazides (phenyl or benzyl) as aminating reagents (Scheme 2.14a).[26] However, organoazides were not Lewis basic enough to interact with boronic acids. Very high temperature (140 ℃) was required, and electron-rich arylboronic acids (2-thienyl) were unreactive under the condition. Kürti screened a series of aminating reagents and found that **2.54** was effective for the amination of arylboronic acids under mild conditions (Scheme 2.14b).[27] A wide range of electron-rich and electron-poor arylboronic acids were tolerated. It was worth noting that the addition of cesium carbonate as base allowed the reaction to be carried out at room temperature. Later, McCubbin applied the base activation strategy and used HSA as the aminating reagent under aqueous basic conditions (Scheme 2.14c).[28]

(25) Hoffmann, R. W.; Hölzer, B.; Knopff, O. *Org. Lett.* **2001**, *3*, 1945–1947.
(26) Ou, L.; Shao, J.; Zhang, G.; Yu, Y. *Tetrahedron Lett.* **2011**, *52*, 1430–1431.
(27) Zhu, C.; Li, G.; Ess, D. H.; Falck, J. R.; Kürti, L. *J. Am. Chem. Soc.* **2012**, *134*, 18253–18256.
(28) Voth, S.; Hollett, J. W.; Mccubbin, J. A. *J. Org. Chem.* **2015**, *80*, 2545–2553.

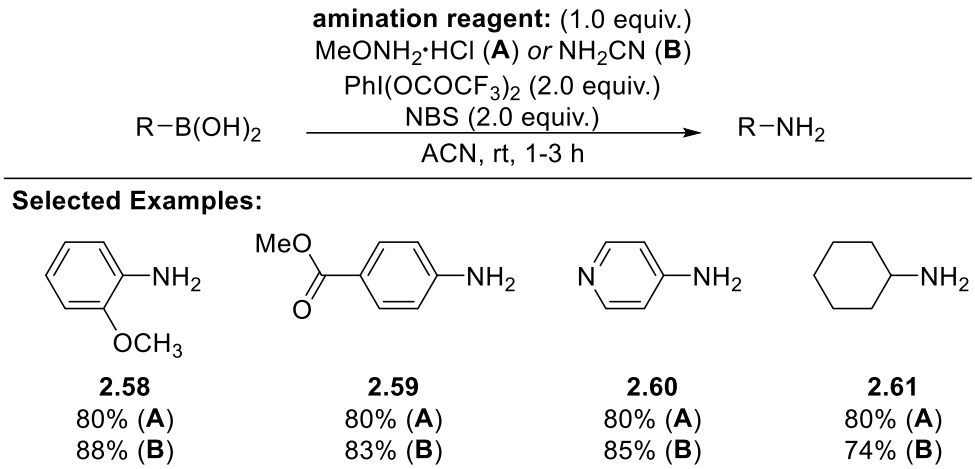
Scheme 2.14. Amination of Aryl Boronic Acids



Goswami developed an amination reaction that was applicable to a wide range of boronic acids (Scheme 2.15).[29] Methoxyamine hydrochloride (**A**)[29a] or cyanamide (**B**)[29b] were employed as the aminating reagents, and PIFA and NBS, as was claimed by the authors, were used to activate the aminating reagents *via* a radical mechanism. Anilines bearing electron-donating (**2.58**) and electron-withdrawing groups (**2.59**) were synthesized from corresponding boronic acids, as well as heteroarylamines (**2.60**) and alkylamines (**2.61**).

(29) (a) Chatterjee, N.; Goswami, A. *Org. Biomol. Chem.* **2015**, *13*, 7940–7945. (b) Chatterjee, N.; Arfeen, M.; Bharatam, P. V.; Goswami, A. *J. Org. Chem.* **2016**, *81*, 5120–5127.

Scheme 2.15. Goswami's Amination of Boronic Acids

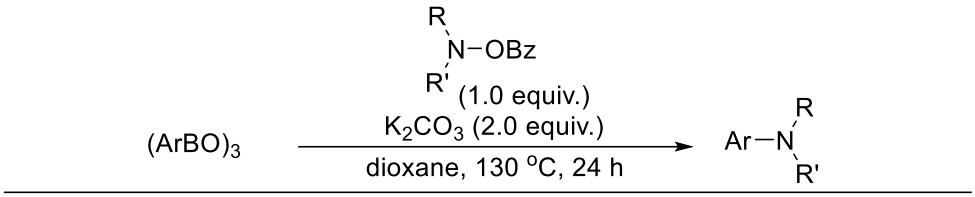


2.2.1.6. Amination of Boroxines

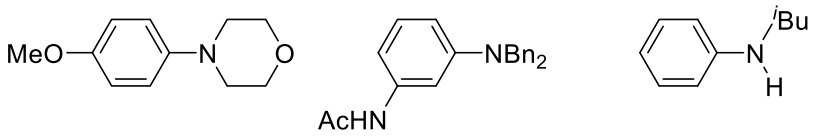
Boroxines, or boronic acid anhydrides, are dehydration products of boronic acids, and are chemically stable reagents that are widely applied in organic synthesis and material science.[30] In 2012, Wang accomplished the amination of arylboroxines using benzoyl hydroxylamine derivatives (Scheme 2.16).[31] A range of tertiary (**2.62**, **2.63**) and secondary anilines (**2.64**) were synthesized in good to excellent yields. Since the aminating reagents employed were rather sterically hindered around the nitrogen atom, it was unlikely that the formation of a N-B 'ate' complex was involved. After ruling out radical mechanisms by radical scavenger experiments, the author proposed that the benzoyl oxygen group was bonding to the boron, and the amination reaction went through a six-membered transition state **A**.

(30) For a review: Tokunaga, Y. *Heterocycles* **2013**, *87*, 991–1021.
(31) Xiao, Q.; Tian, L.; Tan, R.; Xia, Y.; Qiu, D.; Zhang, Y.; Wang, J. *Org. Lett.* **2012**, *14*, 4230–4233.

Scheme 2.16. Wang's Amination of Aryl Boroxines

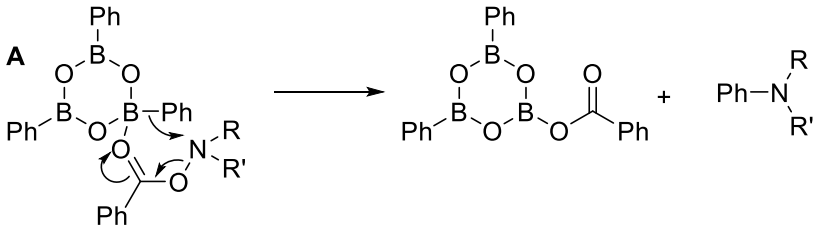


Selected Examples:



2.62 99% **2.63** 99% **2.64** 79%

Proposed Mechanism:



2.2.2.7. Amination of Boronic Esters

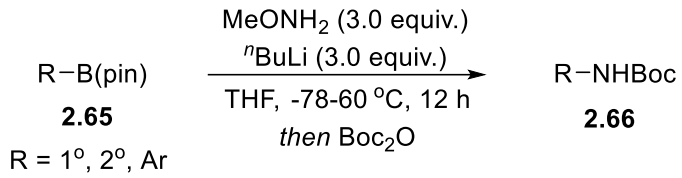
Boronic esters are low in Lewis acidity due to the two oxygen ligands on boron and high steric hinderance around the boron center. As a result, to generate a reactive 'ate' complex, reagents of high nucleophilicity are required for the amination of these compounds. In 2012, Morken reported the first direct amination of pinacol boronic esters using methoxyamine deprotonated in advance with *n*-butyllithium (Scheme 2.17a).[32] Primary, secondary and aryl pinacol boronic esters were successfully converted to the corresponding primary amines, However, tertiary pinacol boronates failed to participate in the reaction and resulted in recovery of the starting material. In 2018, Morken group solved this limitation by activating methoxy amine using a weak base potassium tert-butoxide (Scheme 2.17b).[33]

(32) Mlynarski, S. N.; Karns, A. S.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 16449–16451.
(33) Edelstein, E. K.; Grote, A. C.; Palkowitz, M. D.; Morken, J. P. *Synlett* **2018**, *29*, 1749–1752.

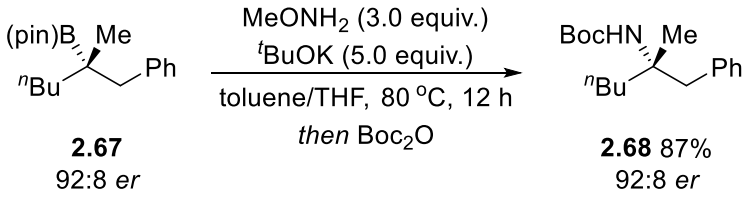
The amination reaction was found to be perfectly stereoretentive. This method was later employed in intramolecular amination of alkylboronic esters to construct pyrrolidine[34] and piperidine rings[35]. In 2020, Jin and Liu developed a new amination reagent H_2N-DABCO (**2.70**, Scheme 2.17c) that could aminate a wide range of alkyl or aryl boronic esters.[36]

Scheme 2.17. Direct Aminations of Boronic Esters

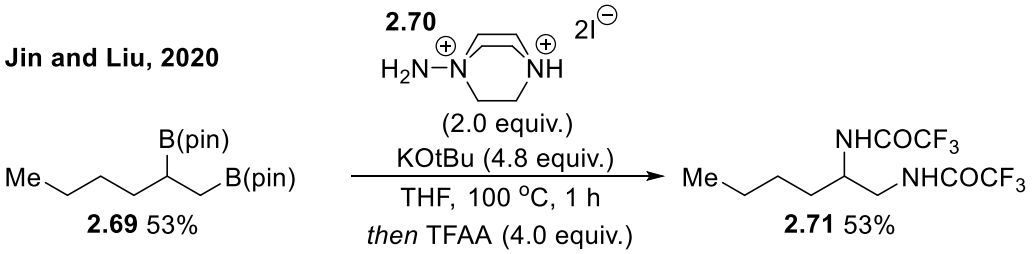
a) **Morken, 2012**



b) **Morken, 2018**



c) **Jin and Liu, 2020**

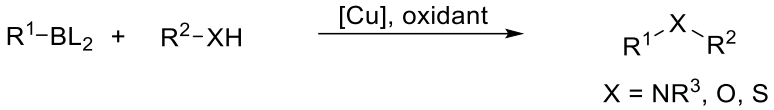


Importantly, vicinal bis(boronate) **2.69** was successfully converted to 1,2-diamine **2.71** using **2.70**.

(34) Zhang, C.; Hu, W.; Lovinger, G. J.; Jin, J.; Chen, J.; Morken, J. P. *J. Am. Chem. Soc.* **2021**, *143*, 14189–14195.
(35) Koo, S. M.; Vendola, A. J.; Momm, S. N.; Morken, J. P. *Org. Lett.* **2020**, *22*, 666–669.
(36) Liu, X.; Zhu, Q.; Chen, D.; Wang, L.; Jin, L.; Liu, C. *Angew. Chem. Int. Ed.* **2020**, *59*, 2745–2749.

2.2.2. Construction of C-N Bond *via* Chan-Lam-Evans Cross-Coupling

Scheme 2.18. Chan-Lam Cross-Coupling



Apart from conducting amination by a 1,2-metallate shift, the construction of C-N bonds from organoboron species has been accomplished using Chan-Lam-Evans cross-coupling, an oxidative copper-catalyzed reaction between organoboron compounds and amines (Scheme 2.18).[37] In 1998, Chan and Lam, both scientists at DuPont at the time, published the pioneering reports of this transformation concurrently, and around the same time, Evans reported a related C-O bond forming reaction.[38] Over the past two decades, continuous development of this transformation greatly expanded its scope and synthetic utility. Boronic acids readily undergo Chan-Lam cross-coupling, and reactions with potassium organotrifluoroborate salts[39] have also been reported. Boronic esters suffer from low reactivity and there can be catatlyst inhibition by the pinacol released.[40] For this reason, reports using organoboronates as starting materials are less common, and typically aryl

(37) For a review: (a) West, M. J.; Fyfe, J. W. B.; Vantourout, J. C.; Watson, A. J. B. *Chem. Rev.* **2019**, *119*, 12491–12523. (b) Munir, I.; Zahoor, A. F.; Rasool, N.; Naqvi, S. A. R.; Zia, K. M.; Ahmad, R. *Mol. Divers.* **2019**, *23*, 215–259.

(38) (a) Chan, D. M. T.; Monaco, K. L.; Wang, R. P.; Winters, M. P. *Tetrahedron Lett.* **1998**, *39*, 2933–2936. (b) Lam, P. Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Winters, M. P.; Chan, D. M. T.; Combs, A. *Tetrahedron Lett.* **1998**, *39*, 2941–2944. (c) Evans, D. A.; Katz, J. L.; West, T. R. *Tetrahedron Lett.* **1998**, *39*, 2937–2940.

(39) Selected examples of Chan-Lam-Evans cross-coupling with potassium organotrifluoroborate salts: (a) Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 4397–4400. (b) Bolshan, Y.; Batey, R. A. *Angew. Chem. Int. Ed.* **2008**, *47*, 2109–2112. (c) Huang, F.; Quach, T. D.; Batey, R. A. *Org. Lett.* **2013**, *15*, 3150–3153.

(40) Vantourout, J. C.; Miras, H. N.; Isidro-Llobet, A.; Sproules, S.; Watson, A. J. B. *J. Am. Chem. Soc.* **2017**, *139*, 4769–4779.

substrates are employed.[41] Reactions with alkylboronic esters have been developed,[42] but there has been no report of stereoselective or stereospecific reactions, therefore this topic will not be discussed further.

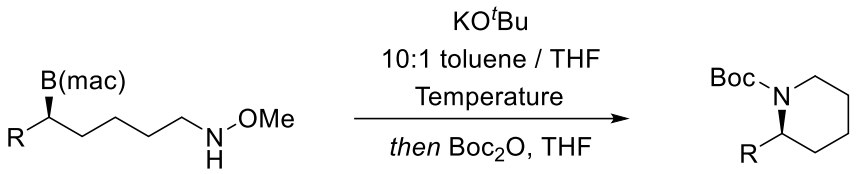
(41) Selected examples with arylB(pin): (a) Tzschucke, C. C.; Murphy, J. M.; Hartwig, J. F. *Org. Lett.* **2007**, *9*, 761–764. (b) McGarry, K. A.; Duenas, A. A.; Clark, T. B. *J. Org. Chem.* **2015**, *80*, 7193–7204. (c) Vantourout, J. C.; Li, L.; Bendito-Moll, E.; Chabbra, S.; Arrington, K.; Bode, B. E.; Isidro-Llobet, A.; Kowalski, J. A.; Nilson, M. G.; Wheelhouse, K. M. P.; Woodard, J. L.; Xie, S.; Leitch, D. C.; Watson, A. J. B. *ACS Catal.* **2018**, *8*, 9560–9566.

(42) (a) Sueki, S.; Kuninobu, Y. *Org. Lett.* **2013**, *15*, 1544–1547. (b) Racine, E.; Monnier, F.; Vors, J. P.; Taillefer, M. *Chem. Commun.* **2013**, *49*, 7412–7414. (c) Mori-Quiroz, L. M.; Shimkin, K. W.; Rezazadeh, S.; Kozlowski, R. A.; Watson, D. A. *Chem. Eur. J.* **2016**, *22*, 15654–15658. (d) Grayson, J. D.; Dennis, F. M.; Robertson, C. C.; Partridge, B. M. *J. Org. Chem.* **2021**, *86*, 9883–9897.

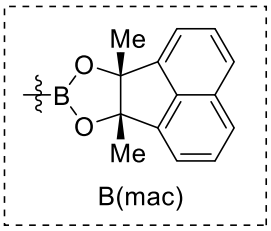
2.3. Development of Intramolecular Amination of Organoboronates and Organobis(boronates)[43]

2.3.1. Previous Results

Table 2.1. Optimization of Reaction Conditions in the Previous Work



Entry	R	KO^{t}Bu (equiv.)	Temperature (^{o}C)	Isolated Yield (%)
1	^{n}Bu	1.5	110	68
2	^{n}Bu	1.5	100	<5
3	^{n}Bu	1.5	120	50[a)]
4	^{n}Bu	4	110	25
5	^{n}Bu	6	110	<5
6	**^{n}Pr**	**1.1**	**110**	**90**
7	^{n}Pr	1.5	110	79
8	^{n}Pr	2.0	110	64



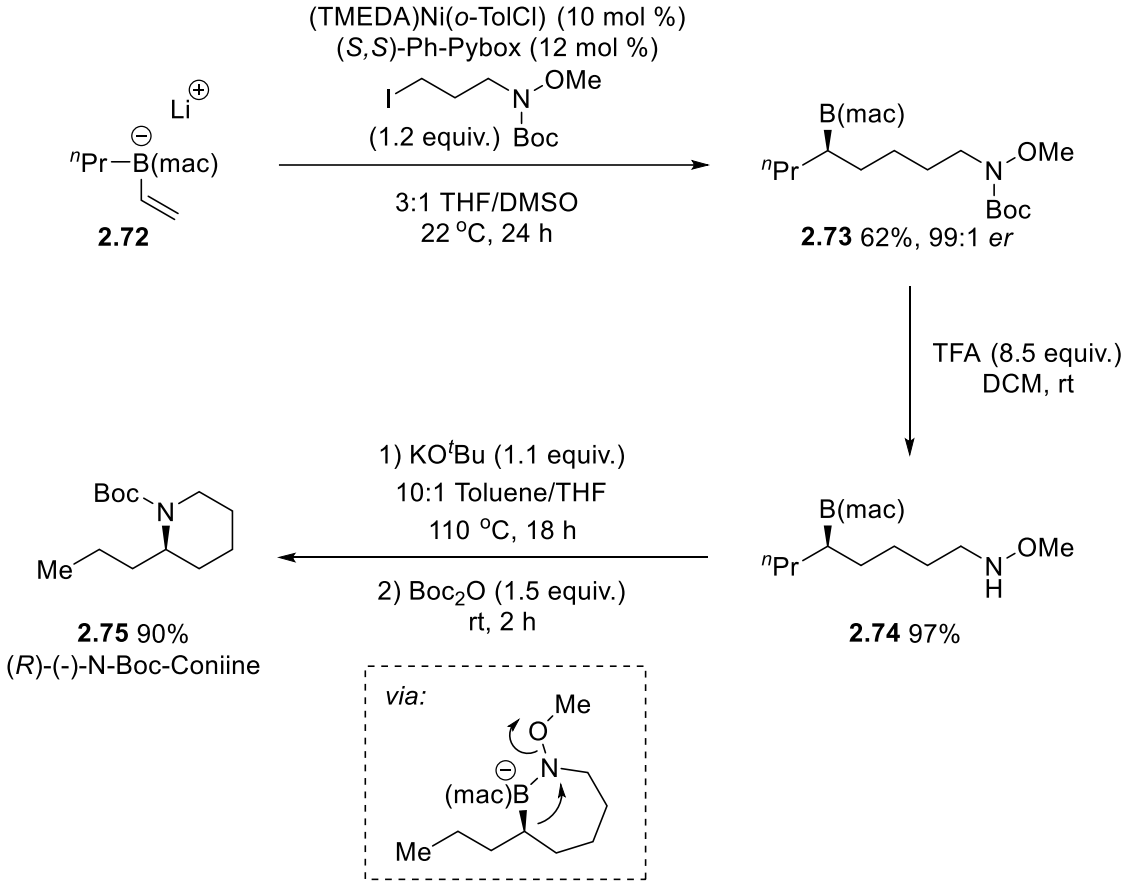
a) Yield determined by NMR

An instance of intramolecular amination reaction of alkylboronic esters was reported by our group.[35] An alkyl chain bearing a methoxyamine group at the end was installed using nickel-catalyzed conjunctive cross-coupling, forming a secondary boronate enantioselectively. The structure was set up for an intramolecular amination reaction to form a piperidine ring via a 7-membered-ring 'ate' complex upon soft deprotonation with KO^{t}Bu (Table 2.1). Optimization of the reaction was carried out, and 110 °C was identified as the optimal reaction temperature (entry 1). Increased equivalents of base was found to

(43) Xu, P.; Zhang, M.; Ingoglia, B.; Allais, C.; Dechert-Schmitt, A. M. R.; Singer, R. A.; Morken, J. P. *Org. Lett.* **2021**, *23*, 3379–3383.

be detrimental to reactivity (entry 4,5). Further fine tuning of the reaction conditions revealed that 1.1 equiv. of KO^{t}Bu (entry 6) is optimal. The reaction delivered (*R*)-(-)-N-Boc-Coniine in 90% yield after heating the aminoboronate at 110 °C for 18 hours followed by *in situ* Boc protection.

Scheme 2.19. Synthesis of (R)-(-)-N-Boc-Coniine In Previous Work

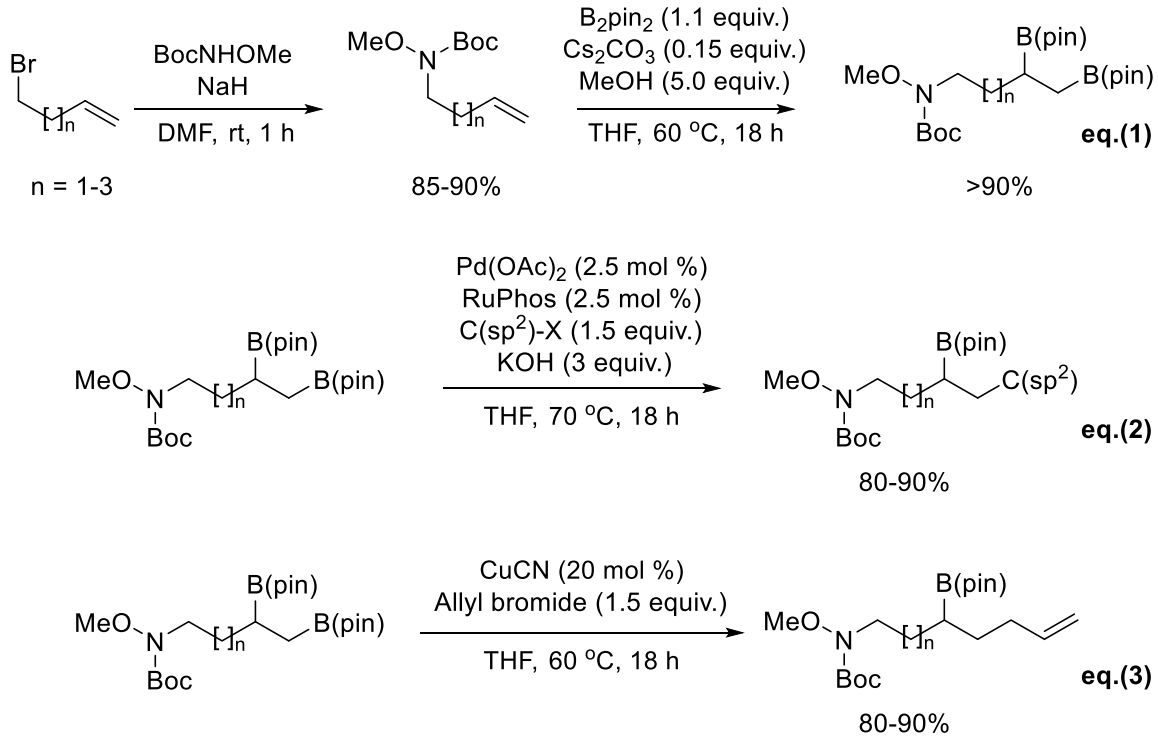


This result inspired us to consider whether this reactivity can be employed on 1,3- or 1,4-aminoboronates to generate azetidines or pyrrolidines. The synthesis of substrates for the intramolecular amination, however, is not trivial.

2.3.2. Synthesis of Substrates for Intramolecular Amination

A modular method to construct secondary boronates with methoxyamine substitutions was designed (Scheme 2.20). The methoxyamino group could be installed by substitution of alkyl bromide with deprotonated BocNHOMe as the nucleophile in good yield (**eq. 1**). Diboration of terminal alkenes using a procedure developed by Fernandez group [44] delivered the 1,2-bis(boronate)s. Substitution on the side chain of the aminoboronate could be installed using regioselective cross-couplings developed by our group. Aryl and alkenyl groups could be installed using palladium-catalyzed Suzuki-Miyaura cross-coupling[45] (**eq.**

Scheme 2.20. Synthesis of Substrates via Diboration/Cross-Coupling

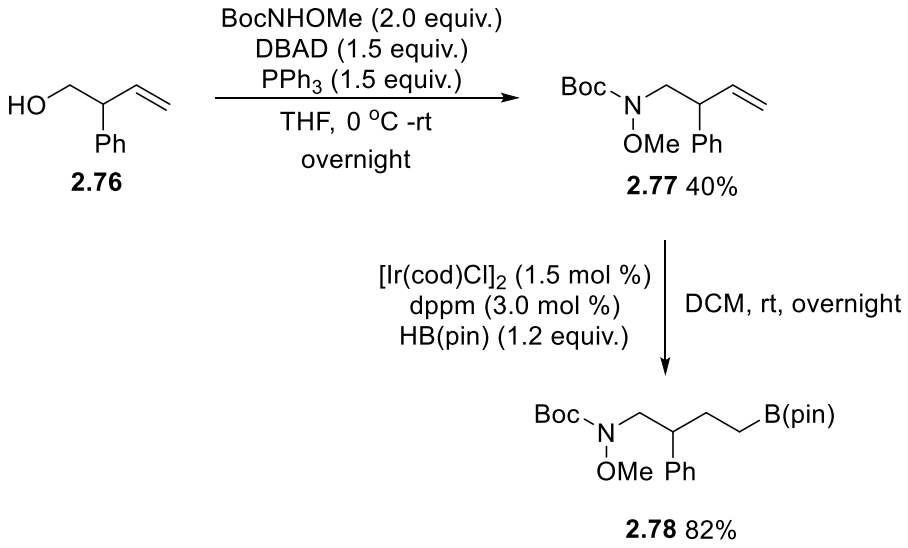


(44) Bonet, A.; Pubill-Ulldemolins, C.; Bo, C.; Gulyás, H.; Fernández, E. *Angew. Chem. Int. Ed.* **2011**, *50*, 7158–7161.
(45) Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2014**, *505*, 386–390.

2), while copper-catalyzed allylation reaction[46] installed a terminal alkene (**eq. 3**), which could be further functionalized.

We also envisioned that substrates containing primary boronic esters could be synthesized through hydroboration of terminal alkenes. Mitsunobu reaction with BocNHOMe was developed to install methoxyamino group from primary alcohol **2.76** in one step. DBAD/PPh_3 was found to be a viable reaction system to enable this reaction. Iridium-catalyzed anti-Markovnikov hydroboration[47] installed the primary boronic ester and delivered substrate **2.78** for intramolecular amination.

Scheme 2.21. Synthesis of Substrates via Hydroboration of Terminal Alkenes



2.3.3. Substrate Scope of Intramolecular Amination

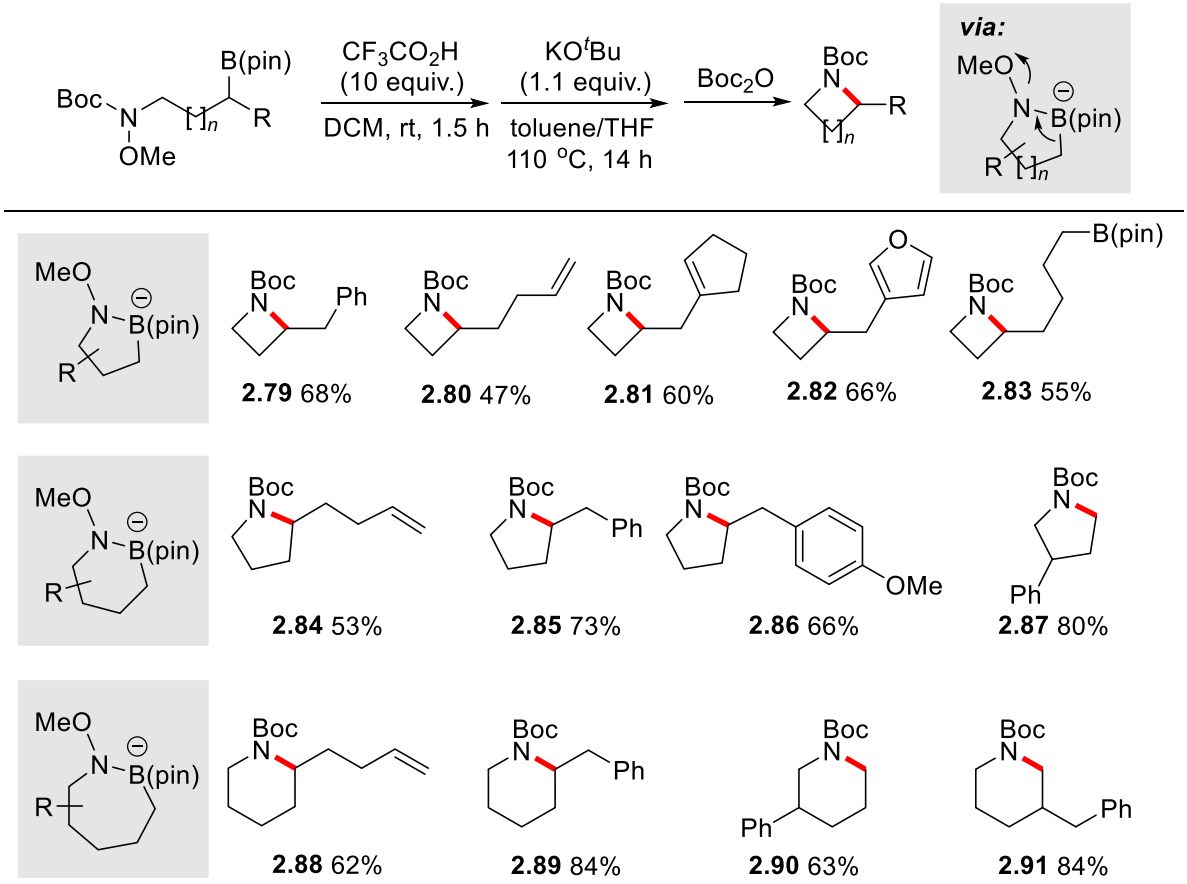
We synthesized a series of aminoboronate substrates using the methods described above, and tested the reactivity. Prior to the amination reaction, the Boc protecting group was

(46) Xu, N.; Kong, Z.; Kativhu, E. T.; Wang, J.; Morken, J. P., *Unpublished Result.*
(47) Yamamoto, Y.; Fujikawa, R.; Umemoto, T.; Miyaura, N. *Tetrahedron* **2004**, *60*, 10695–10700.

removed by stirring with CF_3CO_2H in DCM. After the deprotection was complete, the crude material was washed with saturated sodium bicarbonate solution to remove residual CF_3CO_2H. It was found that the complete removal of CF_3CO_2H was crucial to the success of intramolecular amination reaction. The content of CF_3CO_2H in the crude amine could be examined using ^{19}F NMR. After washing and removal of solvent, the unpurified deprotected amine could be used directly in the intramolecular amination, or it could be purified by silica gel column chromatography if necessary.

Following the previously developed conditions, the deprotected intermediate was heated in toluene/THF (10:1) mixed solvent and 1.1 equiv. of potassium *tert*-butoxide at

Scheme 2.22. Synthesis of Azetidine, Pyrrolidine, and Piperidine Rings by Intramolecular Amination of Boronic Esters



110 ºC. After the reaction was complete, Boc_2O solution in THF was added to protect the forming azacycle *in situ*.

The synthesis of a range of substituted azetidines (**2.79**-**2.83**, Scheme 3.4) was realized using intramolecular reaction of γ-aminoboronates. Functional groups on the side chain such as alkene (**2.80**, **2.81**), furan ring (**2.82**) and a distal boronic ester (**2.83**) were tolerated.

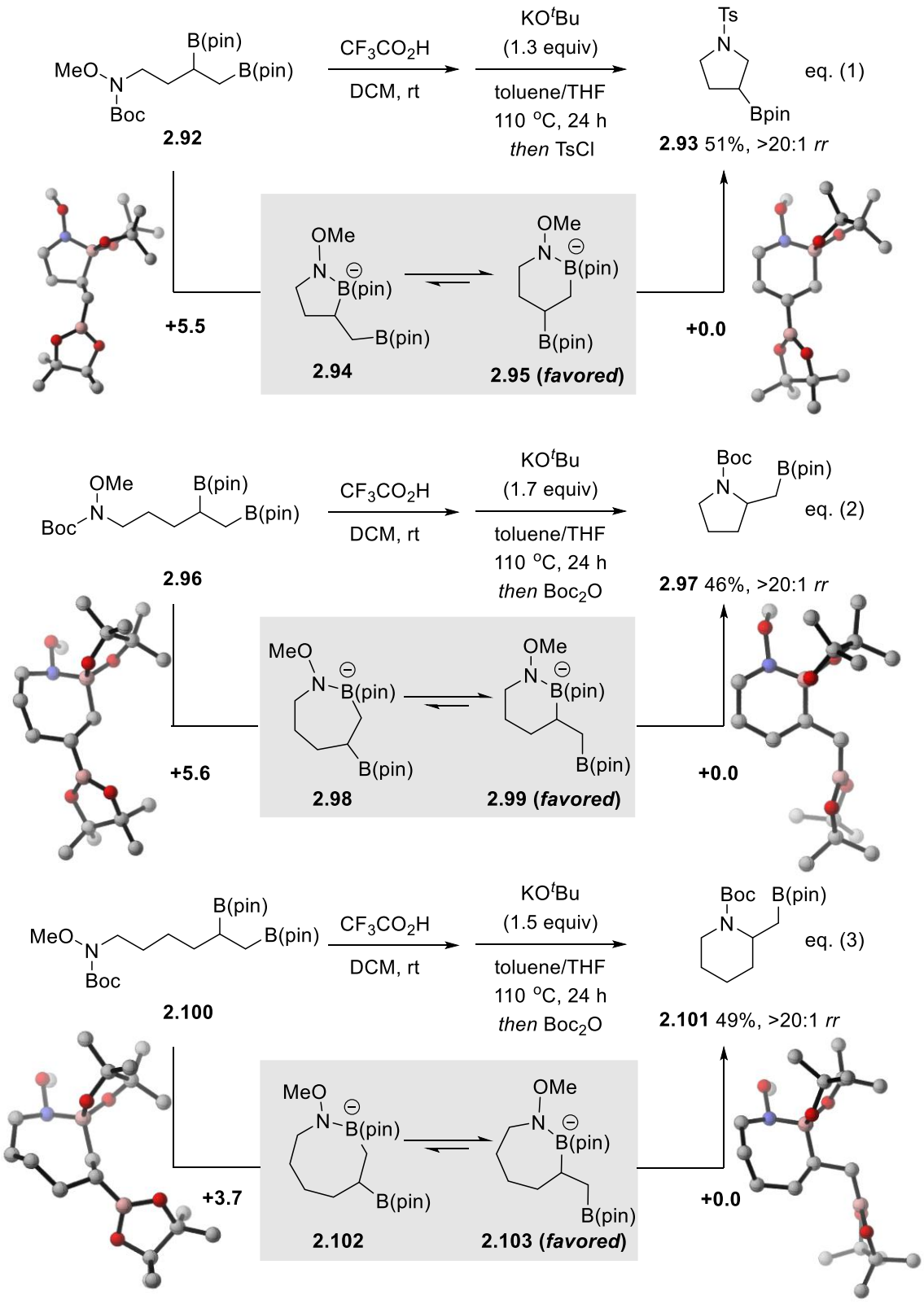
Pyrrolidines (**2.84**-**2.87**) and piperidines (**2.88**-**2.91**) were also synthesized using this method from the appropriate precursor 1,4- or 1,5-aminoboronic esters. A series of azacycles bearing substitutents at the 2- or 3-position could be prepared from the corresponding aminoboronates.

2.3.4. Chemoselectivity in Intramolecular Amination of Vicinal Bis(boronic) Esters

Vicinal bis(boronic) esters can be readily prepared *via* diboration of terminal alkenes. Intramolecular amination reactions of bis(boronates), if site-selectivity were achieved, could potentially deliver azacycles bearing boronic esters as a useful synthetic intermediate for the preparation of a diverse library of heterocyclic building blocks.

We synthesized 1,2-bis(boronates) with methoxyamine substitution using the method described in Scheme 2.20. As depicted in Scheme 2.23 (eq. 1), while both of the alkyl boronates in **2.92** had a chance to react, the intramolecular amination happened with very good regioselectivity, giving tosyl-protected pyrrolidine **2.93** in 51% yield. No regioisomer was observed. Computational studies suggested that the 6-membered 'ate' complex **2.95** generated from the ligation of methoxyamine to the primary B(pin) was favored by 5.5 kcal/mol. The lower energy presumably stemmed from the smaller steric encumbrance around the primary boronate.

Scheme 2.23. Chemoselectivity in Intramolecular Amination of Vicinal Bis(boronic) Esters. Intermediate Energy ΔG (kcal/mol): B3LYP(D3BJ)/6-31g*



High chemoselectivity was also observed when compound **2.96** and **2.100** were subjected to the conditions, yielding pyrrolidine **2.97** and piperidine **2.101** respectively (Scheme 2.23, eq. 2, 3). The experimental observations were in line with the computational result that the 'ate' complexes (**2.99**, **2.103**) with the smaller ring sizes were lower in energy by 5.6 and 3.7 kcal/mol respectively. The smaller ring intermediates were favored probably because of their relatively lower ring strains.

Reaction of vicinal bis(boronic) esters were found to be less efficient than mono(boronates), and increased equivalents of potassium *tert*-butoxide (1.3-1.7 equiv.) and a longer reaction time (24 h) were required to increase the conversion.

2.3.5. Diastereoselective Synthesis of an Intermediate towards a Kras G12C Inhibitor

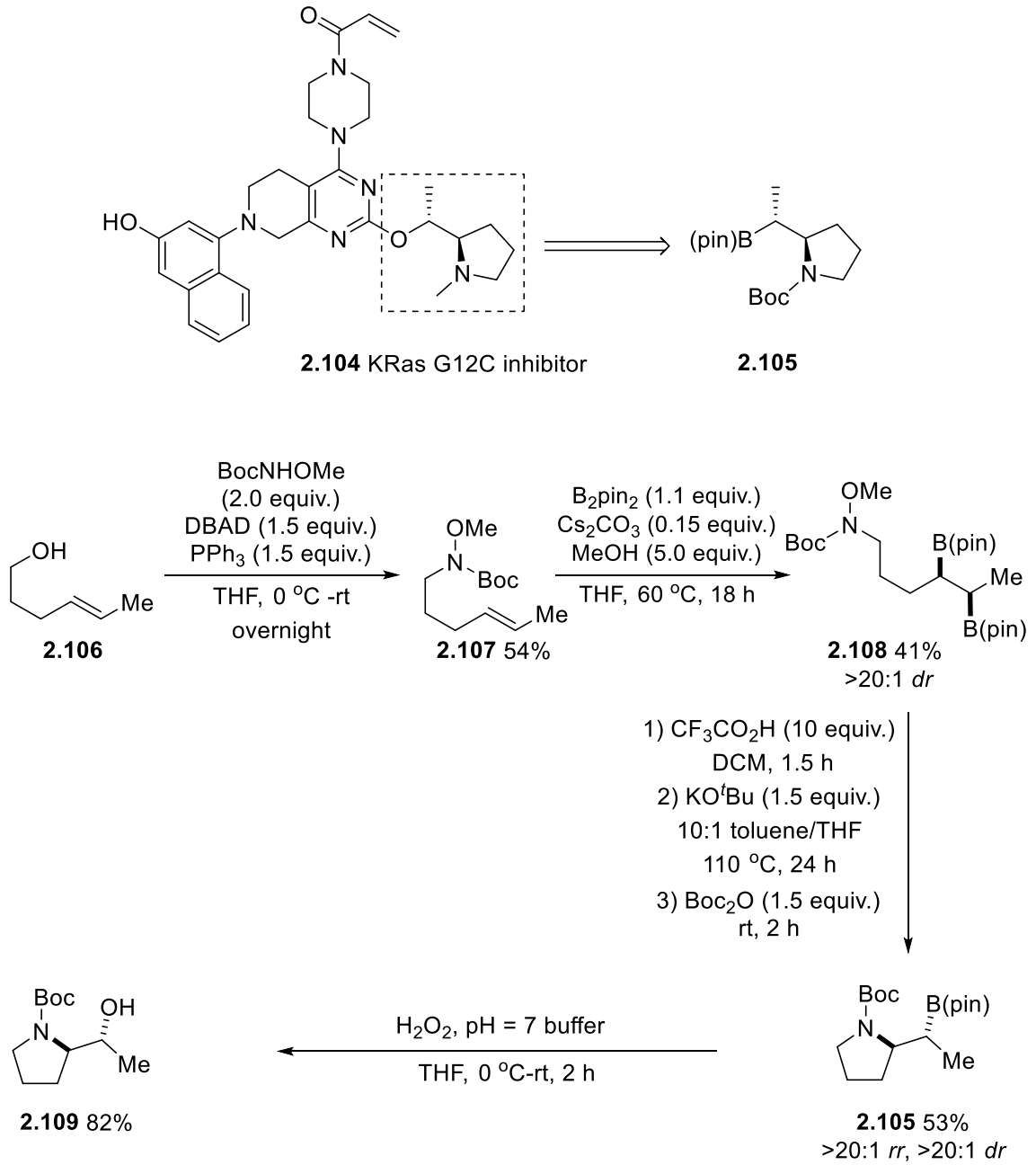
To demonstrate the synthetic utility of the regioselective amination, we sought to synthesize an intermediate **2.110** reported in the route towards a Kras G12C inhibitor (**2.104**, Scheme 2.24).[48] Compound **2.110** was a pyrrolidine ring with a hydroxyethyl substituent, and we envisioned that it could arise from the product (**2.105**) of a regioselective intramolecular amination. The success of this reaction would require two secondary boronates to be differentiated.

Installation of methoxyamine group by Mitsunobu reaction, followed by *syn* diboration of internal alkene **2.107**, delivered aminobis(boronate) **2.108** as a single diastereomer. Deprotection of the Boc group followed by intramolecular amination using 1.5 equiv. of

(48) Fischer, J. P.; Fell, J. B.; Blake, J. F.; Hinklin, R. J.; Mejia, M. J.; Hicken, E. J.; Chicarelli, M. J.; Gaudino, J. J.; Vigers, G. P. A.; Burgess, L. E.; Marx, M. A.; Christensen, J. G.; Lee, M. R.; Savechenkov, P.; Zecca, H. J. WO2017201161 (A1), **2017**.

base successfully generated the pyrroline motif with high regioselectivity and diastereoselectivity. Oxidation of secondary boronic ester **2.105** using hydrogen peroxide under neutral conditions yielded the target intermediate **2.109**, and the synthesis was completed in 4 steps.

Scheme 2.24. Synthesis of an an Intermediate towards a Kras G12C Inhibitor



2.3.6. Synthesis of Enantiomerically Enriched Azacycles

The 1,2-metallate shift mechanism results in stereoretention in the amination of alkylboronic esters. We would like to examine whether the intramolecular amination could occur with stereospecificity for the construction of strained ring systems and on vicinal bis(boronates).

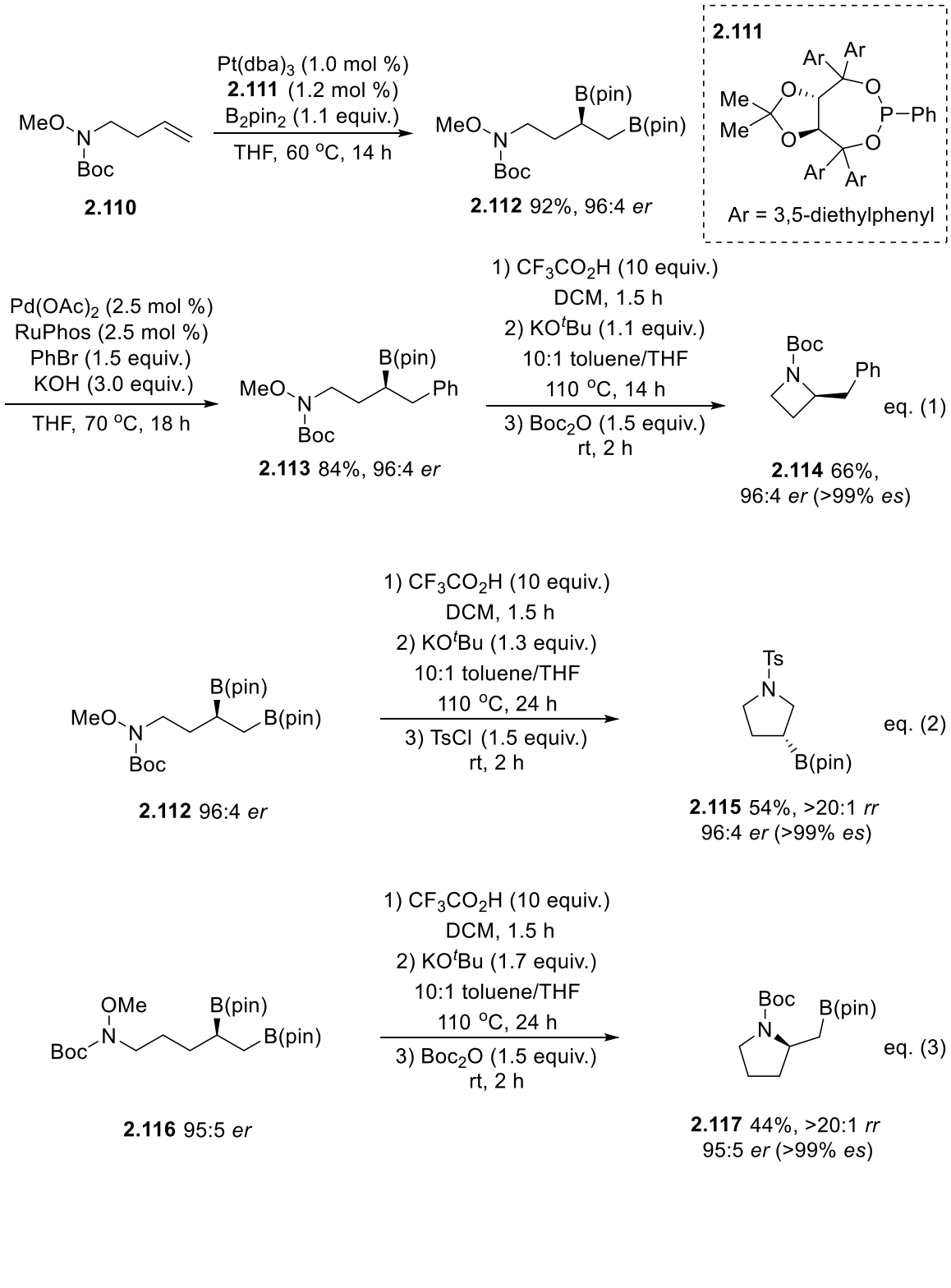
Platinum-catalyzed enantioselective diboration of terminal alkenes developed by our group[49] can lead to the synthesis of highly enantiomerically enriched vicinal bis(boronates), and this reaction enabled the enantioselective construction of substrates with only a slight modification of the route used to prepare racemic materials (as in Scheme 2.20). As depicted in Scheme 2.25, 1,2-bis(boronic) ester **2.112** was obtained in good yield and enantioselectivity (eq. 1). Subsequent chemoselective Suzuki-Miyuara cross-coupling installed the phenyl group without racemization of the unreacted secondary boronate. Intramolecular amination of **2.113** led to benzyl substituted azetidine (**2.114**) with perfect stereospecificity. It is worth noting that **2.114**, in its Boc-free form, was reported to have affinity to TAAR1 receptor[50].

Enantiomerically enriched vicinal bis(boronates) were also subjected to intramolecular amination conditions. Pyrrolidine **2.115** bearing an boronic ester with defined stereochemistry was synthesized with complete preservation of enantiomeric purity (eq. 2). Lastly, vicinal bis(boronic) ester **2.116** underwent intramolecular amination to yield pyrrolidine **2.117**, and the C-N bond formed with full stereoretention (eq. 3).

(49) (a) Kliman, L. T.; Mlynarski, S. N.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 13210−13211. (b) Coombs, J. R.; Haeffner, F.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2013**, **135**, 11222− 11231.

(50) Cecere, G.; Galley, G.; Norcross, R.; Pflieger, P.; Rauber, E. WO2016030310 (A1), **2016**.

Scheme 2.25. Synthesis of Enantiomerically Enriched Azacycles



2.3.7. Conclusion

In this chapter, we described the development of an intramolecular amination reaction of alkyl boronic esters. Azetidines, pyrrolidines and piperidines bearing a variety of substitutions were synthesized using this method. The reaction was found to proceed with high chemoselectivity on vicinal bisboronates, generating azacycles bearing boronic ester substitutions as useful synthetic handles. Intramolecular amination was also carried out on stereodefined alkyl boronic esters synthesized *via* enantioselective diboration of terminal alkenes, and the reaction occurred with complete stereoretention. Bioactive intermediates were constructed, including a TAAR1 receptor antagonist and an intermediate towards a KRAS G12C inhibitor, demonstrating the synthetic utility of this methodology.

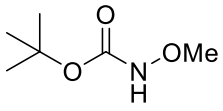
2.4. Experimental

2.4.1.General Information

^{1}H NMR spectra were recorded on either a Varian Gemini-600 (600 MHz), Inova-400 (400 MHz) or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-600 (150 MHz) or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) spectrometer. Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART+) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Purification was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel aluminum backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol, basic potassium permanganate or ninhydrin and acetic acid in ethanol.

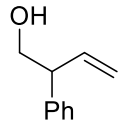
Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol as the modifier. HPLC measurements were carried out on a Shimadzu HPLC system.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon unless otherwise specified. Heated reactions are conducted in a mineral oil bath on a hot plate equipped with a temperature probe. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with nitrogen. Potassium *tert*-butoxide was purchased from Oakwood Chemicals. Tris(dibenzylidineacetone)platinum(0) ($Pt(dba)_3$) was synthesized following literature methods.[49b] (*3aS,8aS*)-(+)-4,4,8,8-tetrakis(3,5-diethylphenyl)tetrahydro-2,2-dimethyl-6-phenyl-1,3-dioxolo[4,5-e]dioxaphosphepine (**2.111**) was synthesized from D-(-)-tartaric acid (obtained from Sigma Aldrich) following literature methods.[49a] All other reagents were purchased from Sigma Aldrich, Alfa Aesar, Oakwood Chemicals, Combi-Blocks, or Acros Organics and used without further purification.

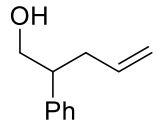


***tert*-butyl methoxycarbamate (SI-1)** The title compound was prepared according to the procedure reported in the patent literature.[51] All spectral data was in accordance with previously published results.

(51) Array Biopharma, Inc.; Ahrendt, K.; Delisle, R.; Hans, J.; Lyssikatos, J. P.; Robinson, J. E.; Wallace, E. M.; Zhao, Q. WO2008/42928, **2008**.



2-phenylbut-3-en-1-ol (2.76) The title compound was prepared according to the procedure reported in the literature.[52] All spectral data was in accordance with previously published results.



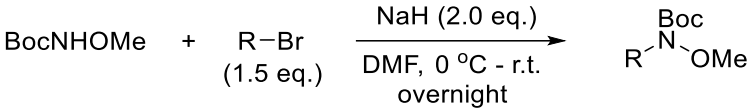
2-phenylpent-4-en-1-ol (SI-2) The title compound was prepared according to the procedure reported in the literature.[53] All spectral data was in accordance with previously published results.

(52) Joe, C. L.; Blaisdell, T. P.; Geoghan, A. F.; Tan, K. L. *J. Am. Chem. Soc.* **2014**, 136, 8556–8559.

(53) Yakura, T.; Horiuchi, Y.; Nishimura, Y.; Yamada, A.; Nambu, H.; Fujiwara, T. *Adv. Synth. Catal.* **2016**, *358*, 869 –873.

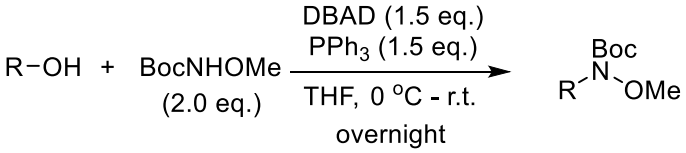
2.4.2. Representative Procedures for Preparation of Starting Materials

General procedure A: S_N2 substitution with tert-butyl methoxycarbamate



In a round bottom flask, *tert*-butyl methoxycarbamate (**SI-1**) (20 mmol, 1.0 equiv.) was added dropwise carefully to a suspension of sodium hydride (40 mmol, 2.0 equiv.) in DMF (50 mL) at 0 °C. After addition was complete, the reaction was allowed to warm up to room temperature and stirred for 1 hour. The reaction was cooled down to 0 °C, and the corresponding alkyl bromide (30 mmol, 1.5 equiv.) was added to the reaction mixture, which was then warmed to room temperature and allowed to stir overnight. The reaction was quenched carefully with saturated ammonium chloride solution (20 mL), diluted with diethyl ether (100 mL), and transferred to a separatory funnel. The organic phase was washed with DI water (4 x 10 mL) and then with brine (10 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The pure products were isolated with SiO_2 chromatography.

General procedure B: Mitsunobu reaction with tert-butyl methoxycarbamate

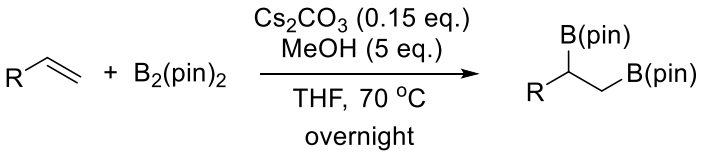


This procedure is adapted from literature.[54] In a round bottom flask, the corresponding alcohol (10 mmol, 1.0 equiv.), triphenyl phosphine (15 mmol, 1.5 equiv.) and *tert*-butyl methoxycarbamate (**SI-1**) (20 mmol, 2.0 equiv) were dissolved in THF (20 mL). The

(54) Chen, Y.; Bilban, M.; Foster, C. A.; Boger, D. L. *J. Am. Chem. Soc.* **2002**, *124*, 5431–5440

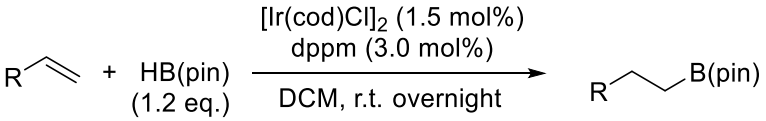
reaction mixture was cooled to 0 °C, and di-*tert*-butyl azodicarboxylate (15 mmol, 1.5 equiv.) in THF (15 mL) was added to the reaction mixture, which was then warmed to room temperature and stirred overnight. At this time, the reaction mixture was opened to the air and the solvent was removed under reduced pressure. The pure products were isolated with SiO_2 chromatography.

General procedure C: Diboration of alkenes



This procedure is adapted from literature.[44] A round bottom flask was charged with cesium carbonate (1.5 mmol, 0.15 equiv.) and bis(pinacolato)diboron (11 mmol, 1.1 equiv.). THF (30 mL) and methanol (50 mmol, 5.0 equiv.) was added, followed by the corresponding alkene (10 mmol, 1.0 equiv.). The reaction was heated at 70 °C overnight. At this time, the reaction mixture was opened to the air and the solvent was removed under reduced pressure. The pure products were isolated with SiO_2 chromatography.

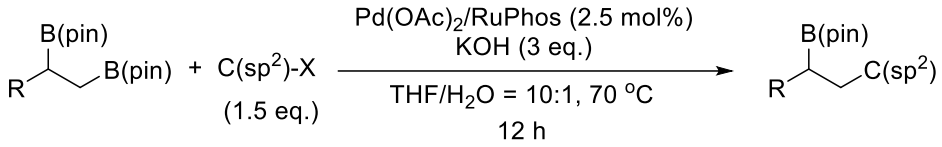
General procedure D: Hydroboration of alkenes.



This procedure is adapted from literature.[47] An oven-dried vial was loaded with $[Ir(cod)Cl]_2$ (0.015 mmol, 1.5 mol%) and bis(diphenylphosphino)methane (0.03 mmol, 3 mol%). Anhydrous DCM (4 mL) was added, followed by the corresponding alkene (1.0 mmol, 1.0 equiv.) and pinacol borane (1.2 mmol, 1.2 equiv.). The mixture was stirred at room temperature overnight, then quenched with water (2 mL), extracted with diethyl ether

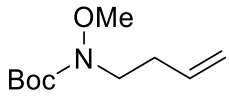
(3 x 10 mL) and dried over anhydrous sodium sulfate. After removal of solvent under reduced pressure, the pure products were isolated with SiO_2 chromatography.

General procedure E: Suzuki-Miyaura cross-coupling of 1,2-bisboronates



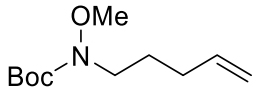
This procedure is adapted from literature.[45] In the glovebox, an oven dried vial was charged with the corresponding 1,2-bisboronate (1.0 mmol, 1.0 equiv.), solid potassium hydroxide (3 mmol, 3 equiv.), $Pd(OAc)_2$/RuPhos (0.025 mmol, 2.5 mol%) as a 1:1 solution in THF (1 mL), THF (9 mL) and electrophile (1.5 mmol, 1.5 equiv.). The vial was sealed, removed from the glovebox, and H_2O (sparged with N_2 for 30 min, 1.0 mL) was added through the teflon septum cap. The vial was heated to 70 ºC and stirred for 12 h. At this time, the vial was cooled down to room temperature and opened to air, and the reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL) and the combined organics were dried over anhydrous sodium sulfate. After removal of solvent under reduced pressure, the pure products were isolated with SiO_2 chromatography.

2.4.3. Procedures for Preparation of Substrates



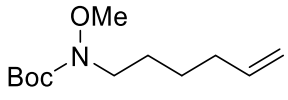
***tert*-butyl but-3-en-1-yl(methoxy)carbamate (2.110)** The reaction was performed according to *General procedure A* with 4-bromobut-1-ene (3.05 mL, 30 mmol, 1.5 equiv.), *tert*-butyl methoxycarbamate (**SI-1**) (2.94 g, 20 mmol, 1.0 equiv.), sodium hydride (1.07 g, 90% purity, 40 mmol, 2 equiv.) in DMF (50 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain in $KMnO_4$) as a colorless oil (3.41 g, 85%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.82 – 5.73 (m, 1H), 5.09 (dd, *J* = 17.1, 1.7 Hz, 1H), 5.03 (dd, *J* = 10.3, 1.7 Hz, 1H), 3.66 (s, 3H), 3.51 – 3.46 (m, 2H), 2.35 (q, *J* = 7.1, 7.0, 7.0 Hz, 2H), 1.47 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.4, 135.4, 116.8, 81.3, 62.3, 48.7, 31.6, 28.4. **IR** (neat) ν_{max} 2977 (w), 2934 (w), 1727 (m), 1700 (s), 1642 (w), 1467 (w), 1436 (w), 1366 (s), 1320 (w), 1287 (w), 1252 (m), 1220 (w), 1147 (s), 1074 (m), 1034 (w), 993 (m), 914 (m), 858 (w), 837 (w), 766 (m), 630 (w), 564 (w) cm^{-1}. **HRMS** (DART+) for $C_{10}H_{20}NO_3$ $[M+H]^+$: Calc'd: 202.1438, found: 202.1440.



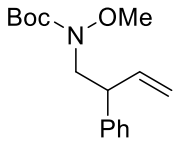
***tert*-butyl methoxy(pent-4-en-1-yl)carbamate (SI-3)** The reaction was performed according to *General procedure A* with 5-bromopent-1-ene (3.55 mL, 30 mmol, 1.5 equiv.), *tert*-butyl methoxycarbamate (**SI-1**) (2.94 g, 20 mmol, 1.0 equiv.), sodium hydride (1.07 g, 90% purity, 40 mmol, 2 equiv.) in DMF (50 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain in $KMnO_4$) as a colorless oil (3.15 g, 73%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.82 – 5.72 (m, 1H), 4.99 (dq, *J* = 17.2, 1.7, 1.7, 1.7 Hz, 1H), 4.97 – 4.91 (m, 1H), 3.63 (s, 3H), 3.42 – 3.36 (m, 2H), 2.09 – 2.00 (m, 2H), 1.70 – 1.64 (m, 2H), 1.46 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.3, 137.9, 115.0, 81.1, 62.2, 48.5, 30.9, 28.4, 26.3. **IR** (neat) ν_{max} 2977 (w), 2934 (w), 1725 (m), 1701 (s), 1641 (w), 1456 (w), 1438 (w), 1391 (m), 1366 (s), 1282 (m), 1253 (m), 1158 (s), 1080 (m), 992 (w), 911 (w), 852 (w), 825 (w), 765 (w), 627 (w) cm^{-1}. **HRMS** (DART+) for $C_{11}H_{22}NO_3$ $[M+H]^+$: Calc'd: 216.1594, found: 216.1604.



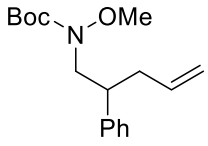
***tert*-butyl hex-5-en-1-yl(methoxy)carbamate (SI-4)** The reaction was performed according to *General procedure A* with 6-bromohex-1-ene (4.02 mL, 30 mmol, 1.5 equiv.), *tert*-butyl methoxycarbamate (**SI-1**) (2.94 g, 20 mmol, 1.0 equiv.), sodium hydride (1.07 g, 90% purity, 40 mmol, 2 equiv.) in DMF (50 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain in $KMnO_4$) as a colorless oil (4.44 g, 97%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 5.77 – 5.67 (m, 1H), 4.94 (d, *J* = 17.2 Hz, 1H), 4.88 (d, *J* = 10.1 Hz, 1H), 3.60 (s, 3H), 3.36 (t, *J* = 7.2 Hz, 2H), 2.01 (q, *J* = 6.5 Hz, 2H), 1.59 – 1.52 (m, 2H), 1.43 (s, 9H), 1.38 – 1.30 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.3, 138.5, 114.6, 81.0, 62.1, 48.8, 33.4, 28.3, 26.6, 26.0. **IR** (neat) ν_{max} 3076 (w), 2976 (w), 2933 (w), 2861 (w), 2816 (w), 1700 (s), 1640 (w), 1456 (w), 1437 (w), 1391 (m), 1366 (s), 1294 (w), 1253 (m), 1095 (w), 1060 (w), 992 (m), 909 (m), 859 (w), 765 (m), 632 (w) cm^{-1}. **HRMS** (DART+) for $C_{12}H_{24}NO_3$ $[M+H]^+$: Calc'd: 230.1751, found: 230.1753.



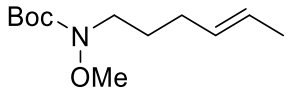
***tert*-butyl methoxy(2-phenylbut-3-en-1-yl)carbamate (2.77)** The reaction was performed according to *General procedure B* with 2-phenylbut-3-en-1-ol (**2.76**) (1.48 g, 10 mmol, 1.0 equiv.), *tert*-butyl methoxycarbamate (**S-1**) (2.95 g, 20 mmol, 2.0 equiv), triphenyl phosphine (3.92 g, 15 mmol, 1.5 equiv.) and di-*tert*-butyl azodicarboxylate (3.45 g, 15 mmol, 1.5 equiv.) in THF (35 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain in $KMnO_4$) as a colorless oil (1.10 g, 40%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.25 – 7.20 (m, 3H), 6.07 – 5.98 (m, 1H), 5.15 – 5.10 (m, 2H), 3.84 – 3.75 (m, 2H), 3.74 – 3.67 (m, 1H), 3.61 (s, 3H), 1.41 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 155.9, 141.6, 139.2, 128.7, 128.2, 126.8, 116.5, 81.3, 62.1, 53.8, 47.8, 28.4. **IR** (neat) ν_{max} 2977 (w), 2932 (w), 1722 (s), 1701 (s), 1638 (w), 1601 (w), 1493 (w), 1476 (w), 1454 (w), 1391 (w), 1366 (s), 1304 (w), 1228 (w), 1165 (s), 1140 (w), 1087 (w), 1075 (w), 1032 (w), 997 (w), 917 (w), 860 (w), 754 (w), 700 (s), 542 (w) cm^{-1}. **HRMS** (DART+) for $C_{16}H_{24}NO_3$ $[M+H]^+$: Calc'd:278.1751, found: 278.1755.



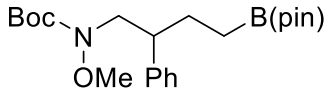
***tert*-butyl methoxy(2-phenylpent-4-en-1-yl)carbamate (SI-5)** The reaction was performed according to *General procedure B* with 2-phenylpent-4-en-1-ol (**SI-3**) (1.62 g, 10 mmol, 1.0 equiv.), *tert*-butyl methoxycarbamate (**S-1**) (2.95 g, 20 mmol,

2.0 equiv), triphenyl phosphine (3.92 g, 15 mmol, 1.5 equiv.) and di-*tert*-butyl azodicarboxylate (3.45 g, 15 mmol, 1.5 equiv.) in THF (35 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain in $KMnO_4$) as a colorless oil (1.45 g, 50%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 7.22 – 7.18 (m, 3H), 5.69 – 5.61 (m, 1H), 5.01 – 4.96 (m, 1H), 4.95 – 4.91 (m, 1H), 3.72 – 3.61 (m, 2H), 3.56 (s, 3H), 3.14 – 3.09 (m, 1H), 2.49 – 2.36 (m, 2H), 1.39 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 155.8, 142.3, 136.2, 128.4, 128.2, 126.6, 116.5, 81.1, 61.9, 54.1, 43.6, 37.9, 28.3. **IR** (neat) ν_{max} 2976 (w), 2931 (w), 1720 (s), 1700 (s), 1640 (w), 1603 (s), 1494 (s), 1476 (s), 1453 (m), 1438 (m), 1391 (m), 1366 (s), 1228 (m), 1162 (s), 1127 (m), 1076 (m), 1033 (w), 994 (w), 912 (m), 855 (w), 757 (m), 699 (s) cm^{-1}. **HRMS** (DART+) for $C_{17}H_{26}NO_3$ $[M+H]^+$: Calc'd: 292.1907, found: 292.1911.

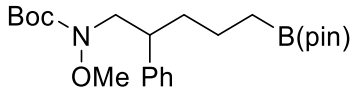


***tert*-butyl *(E)*-hex-4-en-1-yl(methoxy)carbamate (2.107)** The reaction was performed according to *General procedure B* with (*E*)-hex-4-en-1-ol (1.00 g, 10 mmol, 1.0 equiv.), *tert*-butyl methoxycarbamate (**SI-1**) (3.93 g, 30 mmol, 3.0 equiv), triphenyl phosphine (5.23 g, 20 mmol, 2.0 equiv.) and di-*tert*-butyl azodicarboxylate (4.60 g, 20 mmol, 2.0 equiv.) in THF (35 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain in $KMnO_4$) as a colorless oil (1.26 g, 54%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.49 – 5.32 (m, 2H), 3.65 (s, 3H), 3.44 – 3.35 (m, 2H), 2.06 – 1.91 (m, 2H), 1.71 – 1.57 (m, 5H), 1.47 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 156.4, 130.4, 125.6, 81.1, 62.3, 48.7, 29.8, 28.4, 27.0, 18.0. **IR** (neat) ν_{max} 2977 (w), 2935 (w), 2162 (w), 1724 (m), 1703 (s), 1456 (w), 1438 (w), 1392 (m), 1367 (s), 1280 (w), 1256

(w), 1166 (s), 966 (w) cm^{-1}. **HRMS** (DART+) for $C_{12}H_{24}NO_3$ $[M+H]^+$: Calc'd: 230.1751, found: 230.1761.

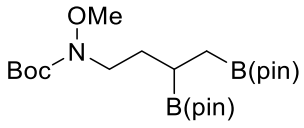


***tert*-butyl methoxy(2-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)carbamate (2.78)** The reaction was performed according to *General procedure D* with *tert*-butyl methoxy(2-phenylbut-3-en-1-yl)carbamate (**2.77**) (0.28 g, 1.0 mmol, 1.0 equiv.), $[Ir(cod)Cl]_2$ (10.1 mg, 0.015 mmol, 1.5 mol%), bis(diphenylphosphino)methane (11.5 mg, 0.03 mmol, 3 mol%), pinacol borane (0.17 mL, 1.2 mmol, 1.2 equiv.) in DCM (4 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.33 g, 82%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.28 – 7.22 (m, 2H), 7.20 – 7.13 (m, 3H), 3.63 (d, *J* = 7.5 Hz, 2H), 3.54 (s, 3H), 2.99 – 2.90 (m, 1H), 1.85 – 1.77 (m, 1H), 1.69 – 1.58 (m, 1H), 1.36 (s, 9H), 1.18 (s, 12H), 0.67 – 0.56 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 155.8, 142.6, 128.3, 128.3, 126.4, 82.9, 80.9, 61.8, 54.6, 46.0, 28.2, 28.1, 27.8, 24.9, 24.8, 9.1. **IR** (neat) ν_{max} 2976 (w), 2931 (w), 1720 (w), 1702 (w), 1453 (w), 1366 (s), 1318 (m), 1236 (w), 1169 (m), 1145 (s), 1093 (w), 968 (w), 859 (w), 847 (w), 757 (w), 700 (w) cm^{-1}. **HRMS** (DART+) for $C_{22}H_{37}BNO_5$ $[M+H]^+$: Calc'd: 406.2759, found: 406.2756.



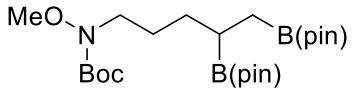
***tert*-butyl methoxy(2-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)carbamate (SI-6)** The reaction was performed according to

General procedure D with *tert*-butyl methoxy(2-phenylpent-4-en-1-yl)carbamate **(SI-5)** (0.29 g, 1.0 mmol, 1.0 equiv.), $[Ir(cod)Cl]_2$ (10.1 mg, 0.015 mmol, 1.5 mol%), bis(diphenylphosphino)methane (11.5 mg, 0.03 mmol, 3 mol%), pinacol borane (0.17 mL, 1.2 mmol, 1.2 equiv.) in DCM (4 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.30 g, 71%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 2H), 7.21 – 7.12 (m, 3H), 3.62 – 3.55 (m, 2H), 3.54 (s, 3H), 3.03 – 2.93 (m, 1H), 1.71 – 1.55 (m, 2H), 1.36 (s, 9H), 1.31 – 1.24 (m, 2H), 1.19 (s, 12H), 0.77 – 0.66 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.9, 143.0, 128.4, 128.3, 126.4, 83.0, 81.0, 61.9, 55.1, 43.9, 36.1, 28.3, 24.9, 21.9, 11.3. **IR** (neat) ν_{max} 2976 (w), 2931 (w), 1721 (m), 1701 (m), 1453 (w), 1366 (s), 1320 (m), 1227 (m), 1161 (m), 1143 (s), 1093 (m), 1074 (m), 1030 (w), 992 (w), 968 (m), 846 (m), 756 (m), 700 (s), 543 (w) cm^{-1}. **HRMS** (DART+) for $C_{23}H_{39}BNO_5$ $[M+H]^+$: Calc'd: 420.2916, found: 420.2938.

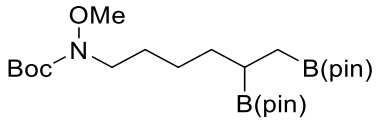


***tert*-butyl (3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (2.92)** The reaction was performed according to *General procedure C* with *tert*-butyl but-3-en-1-yl(methoxy)carbamate (**2.110**) (2.02 g, 10 mmol, 1.0 equiv.), bis(pinacolato)diboron (2.78 g, 11 mmol, 1.1 equiv.), cesium carbonate (0.49 g, 1.5 mmol, 0.15 equiv.), methanol (2.0 mL, 50 mmol, 5.0 equiv.) in THF (30 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a white solid (3.87 g, 85%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.63 (s, 3H), 3.46 –

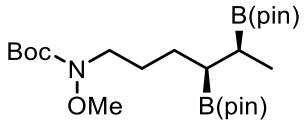
3.35 (m, 2H), 1.80 – 1.70 (m, 1H), 1.62 – 1.53 (m, 1H), 1.45 (s, 9H), 1.20 (s, 12H), 1.19 (s, 12H), 1.13 – 1.07 (m, 1H), 0.90 – 0.77 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.3, 83.0, 83.0, 80.9, 62.2, 48.8, 30.8, 28.4, 25.1, 25.0, 24.9, 24.9, 24.8, 15.9, 12.6. **IR** (neat) ν_{max} 2976 (m), 2931 (w), 1701 (m), 1366 (s), 1313 (s), 1235 (m), 1214 (w), 1143 (s), 1109 (w), 1087 (w), 967 (m), 860 (w), 846 (m), 765 (w), 671 (w), 578 (w) cm^{-1}. **HRMS** (DART+) for $C_{22}H_{44}B_2NO_7$ $[M+H]^+$: Calc'd: 456.3298, found: 456. 3300. **Melting point**: 71-74 ºC.



***tert*-butyl (4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)(methoxy)carbamate (2.96)** The reaction was performed according to *General procedure C* with *tert*-butyl methoxy(pent-4-en-1-yl)carbamate (**SI-3**) (2.15 g, 10 mmol, 1.0 equiv.), bis(pinacolato)diboron (2.78 g, 11 mmol, 1.1 equiv.), cesium carbonate (0.49 g, 1.5 mmol, 0.15 equiv.), methanol (2.0 mL, 50 mmol, 5.0 equiv.) in THF (30 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (3.80 g, 81%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.61 (s, 3H), 3.38 – 3.26 (m, 2H), 1.61 – 1.52 (m, 2H), 1.46 – 1.37 (m, 10H), 1.34 – 1.23 (m, 1H), 1.17 (s, 12H), 1.17 (s, 12H), 1.12 – 1.04 (m, 1H), 0.86 – 0.72 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.4, 82.9, 80.9, 62.3, 49.7, 30.9, 28.4, 26.5, 25.1, 24.9, 24.9, 24.8, 24.8, 18.2, 12.7. **IR** (neat) ν_{max} 2976 (m), 2932 (w), 1702 (m), 1458 (w), 1366 (s), 1312 (s), 1274 (m), 1248 (m), 1214 (m), 1140 (s), 967 (m), 883 (w), 846 (m), 766 (w), 671 (w), 578 (w) cm^{-1}. **HRMS** (DART+) for $C_{23}H_{49}B_2N_2O_7$ $[M+NH_4]^+$: Calc'd: 487.3720, found: 487.3726.

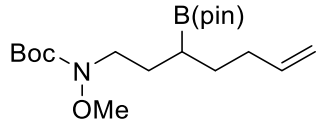


***tert*-butyl (5,6-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)(methoxy)carbamate (2.100)** The reaction was performed according to *General procedure C* with *tert*-butyl hex-5-en-1-yl(methoxy)carbamate (**SI-4**) (2.29 g, 10 mmol, 1.0 equiv.), bis(pinacolato)diboron (2.78 g, 11 mmol, 1.1 equiv.), cesium carbonate (0.49 g, 1.5 mmol, 0.15 equiv.), methanol (2.0 mL, 50 mmol, 5.0 equiv.) in THF (30 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (3.2 g, 67%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.63 (s, 3H), 3.39 – 3.32 (m, 2H), 1.59 – 1.52 (m, 2H), 1.46 (s, 10H), 1.33 – 1.25 (m, 3H), 1.20 (s, 24H), 1.13 – 1.04 (m, 1H), 0.87 – 0.73 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.5, 82.9, 82.9, 81.0, 62.4, 49.5, 33.6, 28.4, 27.5, 26.2, 25.1, 25.0, 24.9, 24.9, 24.8, 18.5, 12.7. **IR** (neat) ν_{max} 2976 (w), 2931 (w), 2864 (w), 1702 (m), 1366 (m), 1311 (m), 1269 (w), 1214 (w), 1140 (s), 1109 (w), 994 (w), 967 (w), 859 (w), 846 (m), 766 (w), 735 (w), 703 (w), 671 (w), 577 (w) cm^{-1}. **HRMS** (DART+) for $C_{24}H_{51}B_2N_2O_7$ $[M+NH_4]^+$: Calc'd: 501.3877, found: 501.3886.



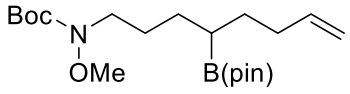
***tert*-butyl (*rac*-(*4S*,*5S*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)(methoxy)carbamate (2.107)** The reaction was performed according to *General procedure C* with *tert*-butyl *(E)*-hex-4-en-1-yl(methoxy)carbamate (**2.106**) (0.23 g, 1.0 mmol, 1.0 equiv.), bis(pinacolato)diboron (0.278 g, 11 mmol, 1.1 equiv.), cesium carbonate (0.98 g, 0.3 mmol, 0.15 equiv.), methanol (0.2 mL, 5.0 mmol,

5.0 equiv.) in THF (1.5 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.20 g, 41%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.62 (s, 3H), 3.35 (t, *J* = 7.0 Hz, 2H), 1.66 – 1.55 (m, 1H), 1.53 – 1.46 (m, 2H), 1.44 (s, 9H), 1.35 – 1.27 (m, 1H), 1.21 – 1.15 (m, 24H), 1.14 – 1.09 (m, 1H), 1.06 – 0.99 (m, 1H), 0.92 (d, *J* = 7.5 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 156.4, 82.9, 82.8, 80.9, 62.3, 49.9, 28.4, 27.0, 26.8, 26.0, 25.1, 25.0, 24.8, 24.7, 17.9, 14.5, 13.9. **IR** (neat) ν_{max} 2976 (w), 2932 (w), 1703 (w), 1459 (w), 1368 (s), 1311 (m), 1215 (w), 1142 (s), 969 (w), 858 (w) cm^{-1}. **HRMS** (DART+) for $C_{24}H_{51}B_2N_2O_7$ $[M+NH_4]^+$: Calc'd: 501.3877, found: 501.3897.

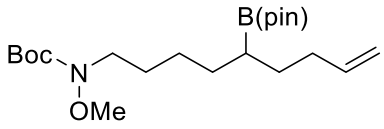


***tert*-butyl methoxy(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-6-en-1-yl)carbamate (SI-7)** The reaction was performed using a method under development in the group from *tert*-butyl (3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (**2.92**) (0.46 g, 1 mmol) and this method will be reported separately. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.25 g, 68%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.84 – 5.73 (m, 1H), 5.01 – 4.95 (m, 1H), 4.94 – 4.88 (m, 1H), 3.65 (s, 3H), 3.48 – 3.35 (m, 2H), 2.13 – 1.98 (m, 1H), 1.77 – 1.69 (m, 1H), 1.69 – 1.61 (m, 1H), 1.59 – 1.50 (m, 1H), 1.48 (s, 10H), 1.23 (s, 12H), 1.04 – 0.94 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.4, 139.1, 114.5, 83.2, 81.1, 62.3, 48.9, 33.4, 30.4, 28.5, 28.4, 25.0, 24.9. **IR** (neat) ν_{max} 2977 (w), 2931 (w), 1726 (m), 1701 (m), 1640 (w), 1457 (w), 1380 (m), 1367 (m),

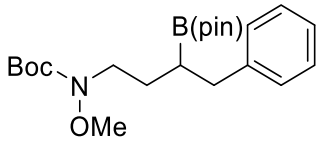
1318 (m), 1239 (m), 1160 (s), 1143 (s), 1085 (w), 995 (w), 967 (w), 909 (w), 859 (w), 765 (w), 693 (w), 670 (w), 578 (w) cm^{-1}. **HRMS** (DART+) for $C_{19}H_{37}BNO_5$ $[M+H]^+$: Calc'd: 370.2759, found: 370.2763.



***tert*-butyl methoxy(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-7-en-1-yl)carbamate (SI-8)** The reaction was performed using a method under development in the group from *tert*-butyl (4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)(methoxy)carbamate (**2.96**) (0.47 g, 1 mmol) and this method will be reported separately. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.24 g, 62%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.83 – 5.69 (m, 1H), 4.98 – 4.91 (m, 1H), 4.90 – 4.86 (m, 1H), 3.63 (s, 3H), 3.38 – 3.33 (m, 2H), 2.08 – 1.95 (m, 2H), 1.61 – 1.53 (m, 2H), 1.54 – 1.41 (m, 10H), 1.43 – 1.28 (m, 3H), 1.20 (s, 12H), 1.02 – 0.91 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 156.4, 139.2, 114.4, 83.0, 81.0, 62.3, 49.5, 33.4, 30.6, 28.4, 26.8, 24.9, 23.2. **IR** (neat) ν_{max} 2977 (w), 2931 (w), 2857 (w), 1725 (w), 1703 (m), 1640 (w), 1458 (w), 1380 (m), 1367 (s), 1316 (m), 1254 (w), 1214 (w), 1152 (s), 1144 (s), 1083 (w), 994 (w), 967 (w), 908 (w), 856 (w), 766 (w), 690 (w), 670 (w) cm^{-1}. **HRMS** (DART+) for $C_{20}H_{42}BN_2O_5$ $[M+NH_4]^+$: Calc'd: 401.3181, found: 401.3196.

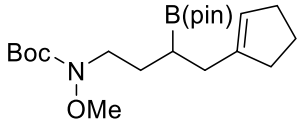


***tert*-butyl methoxy(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)non-8-en-1-yl)carbamate (SI-9)** The reaction was performed using a method under development in the group from *tert*-butyl (5,6-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)(methoxy)carbamate (**2.100**) (0.48 g, 1 mmol) and this method will be reported separately. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.26 g, 65%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.82 – 5.73 (m, 1H), 4.96 (dd, *J* = 17.1, 1.9 Hz, 1H), 4.89 (dd, *J* = 10.2, 1.2 Hz, 1H), 3.64 (s, 3H), 3.37 (t, *J* = 7.3 Hz, 2H), 2.08 – 1.95 (m, 2H), 1.61 – 1.54 (m, 2H), 1.53 – 1.37 (m, 12H), 1.37 – 1.25 (m, 3H), 1.21 (s, 12H), 1.00 – 0.92 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.5, 139.3, 114.3, 83.0, 81.1, 62.4, 49.3, 33.5, 31.0, 30.7, 28.4, 27.6, 26.5, 24.9. **IR** (neat) ν_{max} 2976 (w), 2930 (w), 2856 (w), 1727 (w), 1702 (m), 1640 (w), 1458 (w), 1387 (m), 1367 (m), 1315 (w), 1234 (w), 1143 (s), 994 (w), 967 (w), 908 (w), 859 (w), 766 (w), 689 (w), 670 (w) cm^{-1}. **HRMS** (DART+) for $C_{21}H_{44}BN_2O_5$ $[M+NH_4]^+$: Calc'd: 415.3338, found: 415.3326.



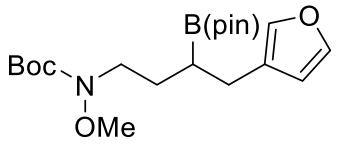
***tert*-butyl methoxy(4-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)carbamate (SI-10)** The reaction was performed according to *General procedure E* with *tert*-butyl (3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (**2.92**) (0.46 g, 1 mmol, 1.0 equiv.), solid potassium hydroxide (0.17 g, 3 mmol, 3 equiv.), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 2.5 mol%), RuPhos

(11.7 mg, 0.025 mmol, 2.5 mol%) and bromobenzene (0.24 g, 1.5 mmol, 1.5 equiv.) in THF (10 mL) and H_2O (1 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.24 g, 60%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.24 – 7.17 (m, 4H), 7.16 – 7.10 (m, 1H), 3.61 (s, 3H), 3.50 – 3.37 (m, 2H), 2.78 – 2.64 (m, 2H), 1.79 – 1.63 (m, 2H), 1.46 (s, 9H), 1.39 – 1.32 (m, 1H), 1.16 (s, 6H), 1.14 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.4, 142.0, 129.0, 128.2, 125.8, 83.3, 81.1, 62.4, 48.9, 37.1, 28.5, 28.3, 24.9, 24.8. **IR** (neat) ν_{max} 2976 (w), 2931 (w), 1724 (w), 1700 (m), 1454 (w), 1380 (m), 1366 (s), 1321 (m), 1242 (m), 1142 (s), 1111 (w), 967 (w), 880 (w), 747 (w), 699 (w) cm^{-1}. **HRMS** (DART+) for $C_{22}H_{37}BNO_5$ $[M+H]^+$: Calc'd: 406.2759, found: 406.2761.



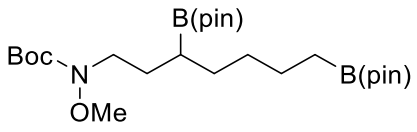
***tert*-butyl (4-(cyclopent-1-en-1-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (SI-11)** The reaction was performed according to *General procedure E* with *tert*-butyl (3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (**2.92**) (0.46 g, 1 mmol, 1.0 equiv.), solid potassium hydroxide (0.17 g, 3 mmol, 3 equiv.), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 2.5 mol%), RuPhos (11.7 mg, 0.025 mmol, 2.5 mol%) and 1-chlorocyclopentene (0.15 g, 1.5 mmol, 1.5 equiv.) in THF (10 mL) and H_2O (1 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.35 g, 89%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.35 (s, 1H), 3.66 (s, 3H), 3.46 – 3.37 (m, 2H), 2.28 – 2.17 (m, 5H), 2.17 – 2.11 (m, 1H), 1.86 – 1.79 (m, 2H), 1.75 – 1.61 (m, 2H), 1.48 (s, 9H),

1.26 – 1.17 (m, 13H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.4, 144.4, 124.3, 83.2, 81.1, 62.3, 49.0, 35.2, 32.6, 32.5, 28.6, 28.5, 25.0, 24.9, 23.7. **IR** (neat) ν_{max} 2976 (w), 2931 (w), 2843 (w), 1725 (w), 1701 (m), 1438 (w), 1379 (m), 1366 (m), 1321 (m), 1241 (m), 1142 (s), 1091 (w), 1061 (w), 1034 (w), 967 (w), 860 (w), 835 (w), 766 (w), 669 (w) cm^{-1}. **HRMS** (DART+) for $C_{21}H_{39}BNO_5$ $[M+H]^+$: Calc'd: 396.2916, found: 396.2913.

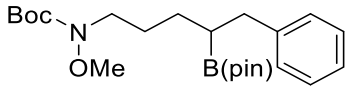


***tert*-butyl (4-(furan-3-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (SI-12)** The reaction was performed according to *General procedure E* with *tert*-butyl (3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (**2.92**) (0.46 g, 1 mmol, 1.0 equiv.), solid potassium hydroxide (0.17 g, 3 mmol, 3 equiv.), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 2.5 mol%), RuPhos (11.7 mg, 0.025 mmol, 2.5 mol%), 3-bromofuran (0.22 g, 1.5 mmol, 1.5 equiv.) and LiCl (42 mg, 1.0 mmol, 1.0 equiv.) in THF (10 mL) and H_2O (1 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.20 g, 50%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.26 (s, 1H), 7.18 (s, 1H), 6.24 (s, 1H), 3.60 (s, 3H), 3.46 – 3.35 (m, 2H), 2.57 – 2.41 (m, 2H), 1.76 – 1.61 (m, 2H), 1.44 (s, 9H), 1.26 – 1.18 (m, 1H), 1.14 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.3, 142.5, 139.4, 124.4, 111.4, 83.2, 81.0, 62.2, 48.7, 28.4, 28.2, 25.9, 24.8, 24.8. **IR** (neat) ν_{max} 2976 (w), 2931 (w), 1698 (m), 1456 (w), 1366 (m), 1319 (m), 1241 (m), 1151 (m), 1141 (s), 1093 (w), 1063 (w), 1023 (m), 967 (w), 872 (m), 860 (w), 774 (w), 737 (w),

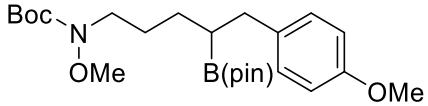
670 (w), 599 (m) cm^{-1}. **HRMS** (DART+) for $C_{20}H_{35}BNO_6$ $[M+H]^+$: Calc'd: 396.2552, found: 396.2550.



***tert*-butyl (3,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)heptyl)(methoxy)carbamate (SI-13)** The reaction was performed according to *General procedure D* with *tert*-butyl methoxy(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-6-en-1-yl)carbamate (**SI-7**) (0.37 g, 1.0 mmol, 1.0 equiv.), $[Ir(cod)Cl]_2$ (10.1 mg, 0.015 mmol, 1.5 mol%), bis(diphenylphosphino)methane (11.5 mg, 0.03 mmol, 3 mol%), pinacol borane (0.17 mL, 1.2 mmol, 1.2 equiv.) in DCM (4 mL). The compound was purified with SiO_2 chromatography (15% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.42 g, 85%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.63 (s, 3H), 3.43 – 3.31 (m, 2H), 1.73 – 1.56 (m, 2H), 1.45 (s, 9H), 1.42 – 1.30 (m, 4H), 1.30 – 1.23 (m, 2H), 1.20 (s, 24H), 0.96 – 0.89 (m, 1H), 0.75 – 0.69 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 156.4, 83.0, 82.9, 81.0, 62.3, 49.1, 32.0, 31.0, 28.5, 28.4, 24.9, 24.9, 24.9, 24.4. **IR** (neat) ν_{max} 2976 (w), 2929 (w), 2860 (w), 1742 (w), 1701 (m), 1459 (w), 1367 (s), 1315 (s), 1242 (m), 1414 (m), 1144 (s), 1111 (m), 1089 (w), 1031 (w), 967 (m), 859 (w), 846 (m), 766 (w), 671 (w), 578 (w) cm^{-1}. **HRMS** (DART+) for $C_{25}H_{50}B_2NO_7$ $[M+H]^+$: Calc'd: 498.3768, found: 498.3785.

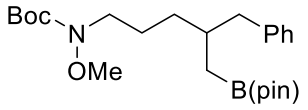


***tert*-butyl methoxy(5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)carbamate (SI-14)** The reaction was performed according to *General procedure E* with *tert*-butyl (4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)(methoxy)carbamate (**2.96**) (0.47 g, 1 mmol, 1.0 equiv.), solid potassium hydroxide (0.17 g, 3 mmol, 3 equiv.), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 2.5 mol%), RuPhos (11.7 mg, 0.025 mmol, 2.5 mol%) and bromobenzene (0.24 g, 1.5 mmol, 1.5 equiv.) in THF (10 mL) and H_2O (1 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.25 g, 60%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.24 – 7.16 (m, 4H), 7.15 – 7.10 (m, 1H), 3.63 (s, 3H), 3.37 (t, J = 7.3, 2H), 2.75 – 2.61 (m, 2H), 1.69 – 1.55 (m, 2H), 1.47 (s, 9H), 1.45 – 1.33 (m, 3H), 1.15 (s, 6H), 1.12 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.5, 142.2, 129.0, 128.2, 125.8, 83.2, 81.1, 62.3, 49.6, 37.4, 28.5, 28.4, 26.8, 24.9, 24.9. **IR** (neat) ν_{max} 2976 (w), 2931 (w), 2857 (w), 1701 (m), 1603 (w), 1454 (w), 1380 (m), 1367 (m), 1320 (m), 1270 (w), 1250 (w), 1141 (s), 1112 (w), 1033 (w), 989 (w), 968 (w), 857 (w), 748 (w), 699 (w), 579 (w) cm^{-1}. **HRMS** (DART+) for $C_{23}H_{42}BN_2O_5$ $[M+NH_4]^+$: Calc'd: 437.3181, found: 437.3176.



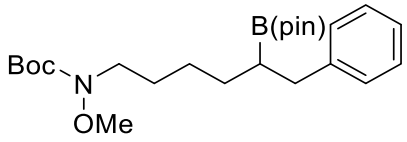
***tert*-butyl methoxy(5-(4-methoxyphenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)carbamate (SI-15)** The reaction was performed according to *General procedure E* with *tert*-butyl (4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)(methoxy)carbamate (**2.96**) (0.47 g, 1 mmol, 1.0 equiv.), solid potassium hydroxide (0.17 g, 3 mmol, 3 equiv.), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 2.5

mol%), RuPhos (11.7 mg, 0.025 mmol, 2.5 mol%) and 1-bromo-4-methoxybenzene (0.28 g, 1.5 mmol, 1.5 equiv.) in THF (10 mL) and H_2O (1 mL). The compound was purified with SiO_2 chromatography (12% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.35 g, 79%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.09 (d, J = 8.2 Hz, 2H), 6.77 (d, J = 8.2 Hz, 2H), 3.75 (s, 3H), 3.63 (s, 3H), 3.37 (t, J = 7.3, 2H), 2.70 – 2.55 (m, 2H), 1.68 – 1.54 (m, 2H), 1.47 (s, 9H), 1.43 – 1.28 (m, 3H), 1.15 (s, 6H), 1.13 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 157.8, 156.4, 134.3, 129.8, 113.6, 83.1, 81.0, 62.3, 55.3, 49.5, 36.4, 28.4, 28.3, 26.8, 26.0, 24.9, 24.8. **IR** (neat) ν_{max} 2976 (w), 2931 (w), 2857 (w), 1700 (m), 1611 (w), 1511 (m), 1458 (w), 1366 (s), 1319 (m), 1299 (m), 1245 (s), 1140 (s), 1112 (m), 1061 (w), 1036 (m), 967 (w), 854 (m), 839 (m), 762 (w), 686 (w), 670 (w) cm^{-1}. **HRMS** (DART+) for $C_{24}H_{44}BN_2O_6$ $[M+NH_4]^+$: Calc'd: 467.3287, found: 467.3293.



***tert*-butyl (4-benzyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)(methoxy)carbamate (SI-16)** In an oven-dried 20 mL vial, *tert*-butyl methoxy(5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)carbamate (**SI-14**) (0.42 g, 1.0 mmol, 1.0 equiv.) and bromochloromethane (0.20 mL, 3.0 mmol, 3.0 equiv.) were dissolved in anhydrous THF (7.5 mL). After the solution was cooled to -78 °C, *n*-butyllithium in hexane (1.6 M, 1.56 mL, 2.5 mmol, 2.5 equiv.) was added dropwise, and the reaction mixture was stirred at this temperature for 20 mins before the cooling bath was removed. The mixture was allowed to warm up to r.t. and stirred for 2 h. The reaction mixture was quenched by the addition of saturated ammonium chloride

solution, extracted with ethyl acetate (3 x 20 mL), dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure. compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.35 g, 81%). The isolated compound contained 9% of unreacted starting material (**S-23**) and was used without further purification. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.19 (m, 2H), 7.18 – 7.11 (m, 3H), 3.62 (s, 3H), 3.33 (t, *J* = 7.3 Hz, 2H), 2.55 (d, *J* = 7.7 Hz, 2H), 1.96 – 1.85 (m, 1H), 1.72 – 1.51 (m, 2H), 1.46 (s, 9H), 1.38 – 1.26 (m, 1H), 1.21 (s, 12H), 0.76 (d, *J* = 6.0 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.5, 141.5, 129.5, 128.2, 128.2, 125.7, 83.0, 81.1, 62.4, 49.6, 43.1, 36.4, 33.1, 28.5, 25.0, 24.7. **IR** (neat) ν_{max} 2976 (w), 2930 (w), 1701 (m), 1454 (w), 1366 (s), 1317 (m), 1248 (m), 1142 (s), 1113 (m), 1032 (w), 968 (m), 847 (m), 740 (m), 700 (m), 577 (w) cm^{-1}. **HRMS** (DART+) for $C_{24}H_{41}BNO_5$ $[M+H]^+$: Calc'd: 434.3072, found: 434.3079.



***tert*-butyl methoxy(6-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)carbamate (SI-17)** The reaction was performed according to *General procedure E* with *tert*-butyl (5,6-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)(methoxy)carbamate (**2.100**) (0.48 g, 1.0 mmol, 1.0 equiv.), solid potassium hydroxide (0.17 g, 3 mmol, 3 equiv.), $Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 2.5 mol%), RuPhos (11.7 mg, 0.025 mmol, 2.5 mol%) and bromobenzene (0.24 g, 1.5 mmol, 1.5 equiv.) in THF (10 mL) and H_2O (1 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.34 g, 79%). **^{1}H NMR**

(600 MHz, $CDCl_3$) δ 7.26 – 7.16 (m, 4H), 7.16 – 7.10 (m, 1H), 3.65 (s, 3H), 3.41 – 3.35 (m, 2H), 2.74 – 2.62 (m, 2H), 1.63 – 1.54 (m, 2H), 1.48 (s, 9H), 1.46 – 1.30 (m, 5H), 1.15 (s, 6H), 1.12 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.5, 142.3, 129.0, 128.2, 125.7, 83.1, 81.1, 62.4, 49.3, 37.4, 31.0, 28.5, 27.6, 26.5, 24.9, 24.8. **IR** (neat) ν_{max} 2976 (w), 2930 (w), 2856 (w), 1723 (w), 1701 (m), 1454 (w), 1380 (m), 1366 (m), 1319 (m), 1252 (w), 1239 (w), 1214 (w), 1142 (s), 1111 (w), 1074 (w), 1031 (w), 966 (w), 861 (m), 749 (w), 699 (m), 670 (w), 578 (w) cm^{-1}. **HRMS** (DART+) for $C_{24}H_{44}BN_2O_5$ $[M+NH_4]^+$: Calc'd: 451.3338, found: 451.3351.

2.4.4. Representative Procedure of Intramolecular Amination

Intramolecular amination followed by Boc protection (Method A):

The corresponding *tert*-butyl(methoxy)carbamate substrate (0.2 mmol) was dissolved in dichloromethane (2 mL). Trifluoroacetic acid (2.0 mmol, 0.15 mL) was added dropwise. The mixture was allowed to stir at r.t. for 90 min and monitored by TLC. The mixture was quenched carefully with saturated sodium bicarbonate solution, extracted with ethyl acetate, and dried over anhydrous sodium sulfate and concentrated. The product was used without further purification.

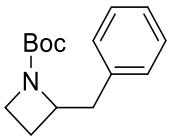
The deprotected methoxy amine substrate was transferred into an oven-dried 20 mL vial loaded with a stir bar, and brought into the glovebox. Potassium *tert*-butoxide (0.22 mmol, 24.5 mg) was added, followed by toluene (3.6 mL) and THF (0.36 mL). The vial was sealed with a PTFE screw-cap, removed from the glovebox, and heated at 110 °C (reaction time: 24 hours for azetidines, and 14 hours for pyrrolidines and piperidines). After the reaction was cooled to r.t., a solution of di-*tert*-butyl dicarbonate (0.3 mmol, 35mg) in THF (1.5 mL) was added and the mixture was allowed to stir for 3 hours. The mixture was washed with water, extracted with ethyl acetate, dried over anhydrous sodium sulfate and concentrated. The crude mixture was then purified using SiO_2 chromatography.

Intramolecular amination followed by Ts protection (Method B):

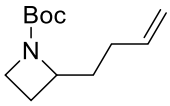
The corresponding *tert*-butyl(methoxy)carbamate substrate (0.2 mmol) was dissolved in dichloromethane (2 mL). Trifluoroacetic acid (2.0 mmol, 0.15 mL) was added dropwise. The mixture was allowed to stir at r.t. for 90 min and monitored by TLC. The mixture was quenched carefully with saturated sodium bicarbonate solution, extracted with ethyl acetate, and dried over anhydrous sodium sulfate and concentrated. The product was used without further purification.

The deprotected methoxy amine substrate was transferred into an oven-dried 20 mL vial loaded with a stir bar, and brought into the glovebox. Potassium *tert*-butoxide (0.22 mmol, 24.5 mg) was added, followed by toluene (3.6 mL) and THF (0.36 mL). The vial was sealed with a PTFE screw-cap, removed from the glovebox, and heated at 110 °C (reaction time: 24 hours for azetidines, and 14 hours for pyrrolidines and piperidines). After the reaction was cooled to r.t., a solution of tosyl chloride (0.4 mmol, 28 mg) in THF (2 mL) was added, followed by triethylamine (0.5 mmol, 0.07 mL) and the mixture was allowed to stir for 3 hours. The mixture was washed with water, extracted with ethyl acetate, dried over anhydrous sodium sulfate and concentrated. The crude mixture was then purified using SiO_2 chromatography.

2.4.5. Procedures and Characterization for Intramolecular Amination Products



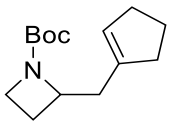
tert*-butyl 2-benzylazetidine-1-carboxylate (2.79)** The reaction was performed according to the general procedure above (Method A***) with *tert*-butyl methoxy(4-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)carbamate (**SI-10**) (83.9 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 24 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with Ninhydrin) as a colorless oil (33.6 mg, 68%). All spectral data was in accordance with previously published results.[55]



tert*-butyl 2-(but-3-en-1-yl)azetidine-1-carboxylate (2.80)** The reaction was performed according to the general procedure above (Method A***) with *tert*-butyl methoxy(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-6-en-1-yl)carbamate (**SI-7**) (73.9 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 24 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with $KMnO_4$) as a colorless oil (19.8 mg, 47%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.90 – 5.74 (m, 1H), 5.02 (d, J = 17.1 Hz, 1H), 4.95 (d, J = 10.3 Hz, 1H), 4.26 – 4.15 (m, 1H), 3.88 – 3.73 (m, 2H), 2.29

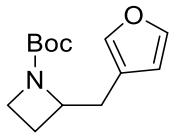
(55) Qiu, Z.; Zhu, M.; Zheng, L.; Li, J.; Zou, D.; Wu, Y.; Wu, Y. *Tetrahedron. Lett.*, **2019**, *60*, 1321-1324.

– 2.19 (m, 1H), 2.13 – 2.04 (m, 2H), 2.03 – 1.93 (m, 1H), 1.88 – 1.78 (m, 1H), 1.74 – 1.64 (m, 1H), 1.43 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 156.8, 138.3, 114.7, 79.2, 61.8, 46.3, 34.8, 30.4, 29.1, 28.6, 22.1. **IR** (neat) ν_{max} 2928 (w), 2891 (w), 2861 (w), 2160 (m), 1701 (s), 1391 (w), 1365 (w), 1183 (w), 1135 (w), 908 (w) cm^{-1}. **HRMS** (DART+) for $C_{12}H_{22}NO_2$ $[M+H]^+$: Calc'd: 212.1645, found: 212.1643.

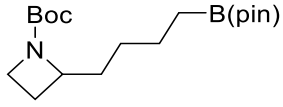


***tert*-butyl 2-(cyclopent-1-en-1-ylmethyl)azetidine-1-carboxylate (2.81)**

The reaction was performed according to the general procedure above (***Method A***) with *tert*-butyl (4-(cyclopent-1-en-1-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (**SI-11**) (79.0 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 24 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with $KMnO_4$) as a colorless oil (28.5 mg, 60%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.32 (s, 1H), 4.34 – 4.24 (m, 1H), 3.85 – 3.72 (m, 2H), 2.72 (d, J = 14.6 Hz, 1H), 2.36 (dd, J = 14.0, 9.3 Hz, 1H), 2.31 – 2.25 (m, 2H), 2.25 – 2.19 (m, 3H), 1.89 – 1.79 (m, 3H), 1.43 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 156.5, 140.2, 125.7, 79.2, 60.9, 37.0, 35.9, 32.6, 28.6, 23.5, 22.4. **IR** (neat) ν_{max} 2929 (w), 2890 (w), 2845 (w), 1698 (s), 1478 (w), 1455 (w), 1388 (s), 1363 (s), 1254 (w), 1181 (w), 1131 (s), 1082 (w), 864 (w), 777 (w), 564 (w) cm^{-1}. **HRMS** (DART+) for $C_{14}H_{24}NO_2$ $[M+H]^+$: Calc'd: 238.1802, found: 238.1815.

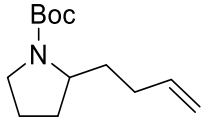


tert*-butyl 2-(furan-3-ylmethyl)azetidine-1-carboxylate (2.82)** The reaction was performed according to the general procedure above (Method A***) with *tert*-butyl (4-(furan-3-yl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (**SI-12**) (79.1 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 24 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (31.0 mg, 66%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36 (s, 1H), 7.25 (s, 1H), 6.28 (s, 1H), 4.39 – 4.33 (m, 1H), 3.82 – 3.75 (m, 1H), 3.69 – 3.62 (m, 1H), 2.91 (dd, *J* = 14.3, 3.6 Hz, 1H), 2.80 (dd, *J* = 14.5, 8.2 Hz, 1H), 2.24 – 2.09 (m, 1H), 1.90 – 1.78 (m, 1H), 1.45 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.4, 143.0, 140.1, 120.0, 111.7, 79.4, 61.4, 46.3, 30.0, 28.6, 21.2. **IR** (neat) ν_{max} 2973 (w), 2927 (w), 1692 (s), 1500 (w), 1478 (w), 1455 (w), 1389 (s), 1364 (s), 1306 (w), 1254 (w), 1182 (m), 1133 (s), 1069 (w), 1022 (m), 972 (w), 947 (w), 872 (m), 770 (m), 727 (w), 600 (m), 564 (w) cm^{-1}. **HRMS** (DART+) for $C_{13}H_{20}NO_3$ $[M+H]^+$: Calc'd: 238.1438, found: 238.1430.



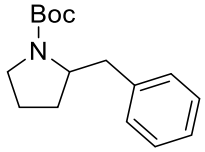
tert*-butyl 2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)azetidine-1-carboxylate (2.83)** The reaction was performed according to the general procedure above (Method A***) with *tert*-butyl (3,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)heptyl)(methoxy)carbamate (**SI-13**) (99.5 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36

mL, 0.05 M) for 24 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (37.3 mg, 55%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.20 – 4.10 (m, 1H), 3.84 – 3.72 (m, 2H), 2.29 – 2.14 (m, 1H), 1.92 – 1.73 (m, 2H), 1.63 – 1.52 (m, 1H), 1.46 – 1.37 (m, 11H), 1.32 – 1.25 (m, 2H), 1.23 (s, 12H), 0.77 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.7, 83.0, 79.1, 62.3, 35.3, 30.5, 28.6, 27.4, 24.9, 24.2, 22.1. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.9. **IR** (neat) ν_{max} 2976 (w), 2930 (w), 2890 (w), 2860 (w), 1698 (s), 1456 (w), 1364 (s), 1317 (m), 1255 (w), 1142 (s), 968 (w), 881 (w), 846 (w), 777 (w) cm^{-1}. **HRMS** (DART+) for $C_{18}H_{35}BNO_4$ $[M+H]^+$: Calc'd: 340.2654, found: 340.2658.

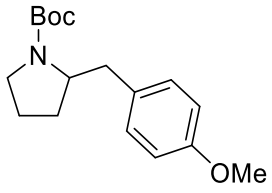


tert*-butyl 2-(but-3-en-1-yl)pyrrolidine-1-carboxylate (2.84)** The reaction was performed according to the general procedure above (Method A***) with *tert*-butyl methoxy(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-7-en-1-yl)carbamate (**SI-8**) (76.7 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 14 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with $KMnO_4$) as a colorless oil (24.0 mg, 53%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.87 – 5.77 (m, 1H), 5.06 – 4.98 (m, 1H), 4.97 – 4.91 (m, 1H), 3.76 (br, 1H), 3.36 (br, 1H), 3.33 – 3.26 (m, 1H), 2.11 – 1.96 (m, 2H), 1.96 – 1.73 (m, 4H), 1.69 – 1.60 (m, 1H), 1.46 (s, 9H), 1.41 – 1.33 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$, rotamers) δ 154.8, 138.5, 114.6, 79.1&79.0, 57.0&56.9, 46.6&46.2, 34.0&33.4, 30.8, 29.9&29.8, 28.7, 23.9&23.2. **IR** (neat) ν_{max} 2972 (w), 2928

(w), 2873 (w), 1694 (s), 1641 (w), 1478 (w), 1454 (w), 1392 (m), 1365 (w), 1250 (w), 1171 (w), 1107 (w), 909 (w), 868 (w), 771 (w) cm^{-1}. **HRMS** (DART+) for $C_{13}H_{24}NO_2$ $[M+H]^+$: Calc'd: 226.1802, found: 226.1805.



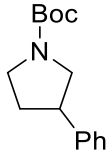
tert*-butyl 2-benzylpyrrolidine-1-carboxylate (2.85)** The reaction was performed according to the general procedure above (Method A***) with *tert*-butyl methoxy(5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)carbamate (**SI-14**) (83.9 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 14 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with Ninhydrin) as a colorless oil (38.1 mg, 73%). All spectral data was in accordance with previously published results.[56]



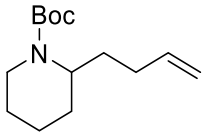
tert*-butyl 2-(4-methoxybenzyl)pyrrolidine-1-carboxylate (2.86)** The reaction was performed according to the general procedure above (Method A***) with *tert*-butyl methoxy(5-(4-methoxyphenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-

(56) Angelini, L.; Davies, J.; Simonetti, M.; Sanz, L. M.; Sheikh, N. S.; Leonori, D. *Angew. Chem. Int. Ed.* **2019**, *58*, 5003-5007.

yl)pentyl)carbamate (**SI-14**) (89.9 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 14 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with Ninhydrin) as a colorless oil (38.4 mg, 66%). All spectral data was in accordance with previously published results.[56]



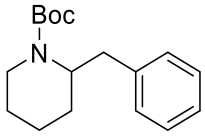
tert*-butyl 3-phenylpyrrolidine-1-carboxylate (2.87)** The reaction was performed according to the general procedure above (Method A***) with *tert*-butyl methoxy(2-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)carbamate (**2.78**) (81.6 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 14 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with Ninhydrin) as a colorless oil (39.5 mg, 80%). All spectral data was in accordance with previously published results.[57]



tert*-butyl 2-(but-3-en-1-yl)piperidine-1-carboxylate (2.88)** The reaction was performed according to the general procedure above (Method A***) with *tert*-

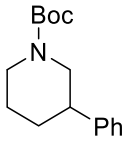
(57) Barré, B.; Gonnard, L.; Campagne, R.; Reymond, S.; Marin, J.; Ciapetti, P.; Brellier, M.; Guérinot, A.; Cossy, J. *Org. Lett.* **2014**, 16, 6160–6163.

butyl methoxy(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)non-8-en-1-yl)carbamate (**SI-9**) (79.5 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 14 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with $KMnO_4$) as a colorless oil (29.7 mg, 62%). All spectral data was in accordance with previously published results.[58]

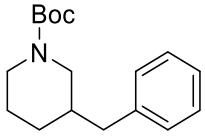


tert*-butyl 2-benzylpiperidine-1-carboxylate (2.89)** The reaction was performed according to the general procedure above (Method A***) with *tert*-butyl methoxy(6-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)carbamate (**SI-17**) (86.7 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 14 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with Ninhydrin) as a colorless oil (39.5 mg, 84%). **IR** (neat) ν_{max} 2974 (w), 2931 (w), 2858 (w), 1686 (s), 1454 (w), 1411 (m), 1363 (m), 1270 (m), 1160 (s), 1034 (w), 871 (w), 742 (w), 700 (w) cm^{-1}. All other spectral data was in accordance with previously published results.[59]

(58) Cheng, J.; Zheng, X.; Huang, P. *Tetrahedron*, **2019**, *75*, 1612-1623.
(59) Sun, Z.; Tang, B.; Liu, K.; Zhu, H. Y. *Chem. Commun.* **2020**, *56*, 1294-1297.

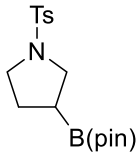


tert*-butyl 3-phenylpiperidine-1-carboxylate (2.90)** The reaction was performed according to the general procedure above (Method A***) with *tert*-butyl methoxy(2-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)carbamate (**SI-6**) (83.9 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 14 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with Ninhydrin) as a colorless oil (33.2 mg, 63%). All spectral data was in accordance with previously published results.[57]



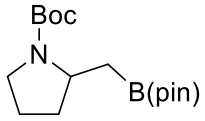
tert*-butyl 3-benzylpiperidine-1-carboxylate (2.91)** The reaction was performed according to the general procedure above (Method A***) with *tert*-butyl (4-benzyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)(methoxy)carbamate (**SI-16**) (86.7 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 14 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with Ninhydrin) as a colorless oil (46.2 mg, 84%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.30 – 7.24 (m, 2H), 7.21 – 7.12 (m, 3H), 4.17 – 3.66 (brm, 2H), 2.78 (brs, 1H), 2.68 – 2.37 (brm, 3H), 1.79 – 1.69 (m, 2H), 1.68 – 1.57 (brm, 1H), 1.42 (s, 10H), 1.13 (brs, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 155.0, 140.1, 129.2, 128.4, 126.1, 79.3, 49.7, 44.6, 40.3, 37.8, 30.8, 28.6, 25.0. **IR** (neat) ν_{max} 2975 (w), 2929 (w), 2851 (w), 1688 (s), 1419 (m), 1364 (m), 1266 (m), 1240 (m), 1167

(m), 1130 (m), 886 (w), 745 (w), 700 (m) cm^{-1}. **HRMS** (DART+) for $C_{17}H_{26}NO_2$ $[M+H]^+$: Calc'd: 276.1958, found: 276.1971.



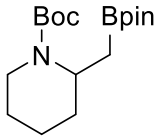
3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-tosylpyrrolidine (2.93)

The reaction was performed according to the general procedure above (***Method B***) with *tert*-butyl (3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (**2.92**) (91.0 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (29.2 mg, 0.26 mmol, 1.3 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 24 hours. The compound was purified with SiO_2 chromatography (15% ethyl acetate in hexane, stain with CAM) as a white solid (35.8 mg, 51%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71 (d, J = 7.9 Hz, 2H), 7.30 (d, J = 7.9 Hz, 2H), 3.47 (t, J = 9.2 Hz, 1H), 3.37 – 3.27 (m, 1H), 3.19 – 3.09 (m, 2H), 2.42 (s, 3H), 1.97 – 1.87 (m, 1H), 1.75 – 1.63 (m, 1H), 1.48 – 1.38 (m, 1H), 1.18 (s, 12H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.2, 134.5, 129.7, 127.7, 83.8, 50.1, 48.7, 28.0, 24.8, 24.8, 21.6. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.9. **IR** (neat) ν_{max} 2976 (w), 2929 (w), 2883 (w), 1597 (w), 1452 (w), 1382 (m), 1326 (s), 1230 (w), 1158 (s), 1142 (s), 1098 (m), 1026 (w), 1015 (w), 972 (w), 855 (w), 816 (w), 775 (w), 709 (w), 661 (s), 591 (s), 548 (s) cm^{-1}. **HRMS** (DART+) for $C_{17}H_{27}BNO_4S$ $[M+H]^+$: Calc'd: 352.1748, found: 352.1750. **Melting point**: 73-74 ºC.



***tert*-butyl 2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)pyrrolidine-1-carboxylate (2.97)**

The reaction was performed according to the general procedure above (***Method A***) with *tert*-butyl (4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)(methoxy)carbamate (**2.96**) (93.9 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (38.2 mg, 0.34 mmol, 1.7 equiv.) in toluene and THF (0.9/0.09 mL, 0.2 M) for 24 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a white solid (28.6 mg, 46%). **Melting point**:63-66 ºC. All spectral data was in accordance with previously published results.[60]

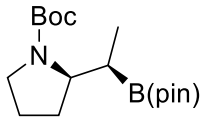


tert-butyl 2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)piperidine-1-carboxylate (2.101)

The reaction was performed according to the general procedure above (***Method A***) with *tert*-butyl (5,6-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)(methoxy)carbamate (**2.100)** (96.7 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (33.7 mg, 0.30 mmol, 1.5 equiv.) in toluene and THF (0.9/0.09 mL, 0.2 M)

(60) Georgiou, I.; Whiting, A. *Eur. J. Org. Chem.* **2012**, *22*, 4110–4113.

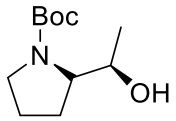
for 24 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (32.0 mg, 49%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 4.49 (brs, 1H), 3.88 (brd, *J* = 12.2 Hz, 1H), 2.81 (t, *J* = 13.3, 13.3 Hz, 1H), 1.63 – 1.48 (m, 5H), 1.44 (s, 9H), 1.39 – 1.30 (m, 1H), 1.29 – 1.22 (m, 1H), 1.22 (s, 6H), 1.22 (s, 6H), 1.00 (dd, *J* = 15.3, 5.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.9, 83.2, 79.0, 47.8, 38.8, 30.1, 28.7, 25.9, 25.0, 24.9, 18.8. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 34.0. **IR** (neat) ν_{max} 2975 (w), 2930 (w), 2856 (w), 1687 (s), 1470 (w), 1447 (w), 1363 (s), 1322 (s), 1269 (m), 1253 (m), 1150 (s), 1141 (s), 1097 (w), 1068 (w), 1039 (w), 1003 (w), 968 (m), 927 (w), 872 (m), 847 (m), 769 (w) cm^{-1}. **HRMS** (DART+) for $C_{17}H_{33}BNO_4$ $[M+H]^+$: Calc'd: 326.2497, found: 326.2501.



***tert*-butyl *rac*-(*R*)-2-((*R*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)pyrrolidine-1-carboxylate (2.105)**

The reaction was performed according to the general procedure above (***Method A***) with *tert*-butyl (*rac*-(*4S*,*5S*)-4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)(methoxy)carbamate (**2.108**) (96.7 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (33.7 mg, 0.30 mmol, 1.5 equiv.) in toluene and THF (0.9/0.09 mL, 0.2 M) for 24 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (34.2 mg, 53%). **^{1}H NMR** (500 MHz, $CDCl_3$, rotamers) δ 3.98 (brs, 1H), 3.57 (brs, 0.5 H), 3.42 (brs, 0.5 H), 3.26 – 3.12 (m, 1H), 2.06 – 1.92 (m, 1H), 1.91 – 1.73 (m, 2H), 1.73 – 1.53 (m, 2H), 1.44 (s, 9H), 1.21 (s, 12H), 0.84

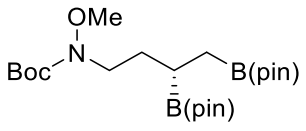
(d, J = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$, rotamers) δ 155.0&154.7, 83.1&82.6, 79.0, 59.3&58.4, 47.6, 29.4, 28.7, 24.9, 24.4&24.2, 21.1, 9.7, 8.5. ^{11}B NMR (160 MHz, $cdcl_3$) δ 33.9. **IR** (neat) ν_{max} 2975 (w), 2931 (w), 2876 (w), 1692 (s), 1458 (w), 1392 (s), 1366 (s), 1317 (w), 1269 (w), 1168 (m), 1145 (m), 1107 (m), 868 (w) cm^{-1}. **HRMS** (DART+) for $C_{17}H_{33}BNO_4$ $[M+H]^+$: Calc'd: 326.2497, found: 326.2505.



***tert*-butyl *rac*-(*R*)-2-((*R*)-1-hydroxyethyl)pyrrolidine-1-carboxylate (2.109)** *Tert*-butyl *rac*-(*R*)-2-((*R*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)pyrrolidine-1-carboxylate (**2.105**) (34.2 mg, 0.105 mmol, 1.0 equiv.) was dissolved in THF (1 mL). At 0 ºC, the solution was treated carefully with 3M NaOH (0.4 mL), pH 7.00 buffer solution (0.4 mL) and 30% H_2O_2 (0.2 mL). The cooling bath was removed, and the reaction was allowed to stir at r.t. for 2 hours. At this time the reaction was again cooled down to 0 ºC and carefully quenched with saturated aqueous sodium thiosulfate (0.5 mL). The aqueous phase was extracted with ethyl acetate (3 x 4 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, concentrated under reduced pressure. The compound was purified with SiO_2 chromatography (40% ethyl acetate in hexane, stain with ninhydrin) as a colorless oil (18.6 mg, 82%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.76 – 3.69 (m, 1H), 3.69 – 3.62 (m, 1H), 3.54 – 3.46 (m, 1H), 3.31 – 3.23 (m, 1H), 2.01 – 1.91 (m, 1H), 1.86 – 1.78 (m, 1H), 1.78 – 1.71 (m, 1H), 1.62 (s, 1H), 1.47 (s, 9H), 1.16 – 1.13 (m, 3H). **IR** (neat) ν_{max} 3420 (br), 2974 (w), 2929 (w), 1683 (s),

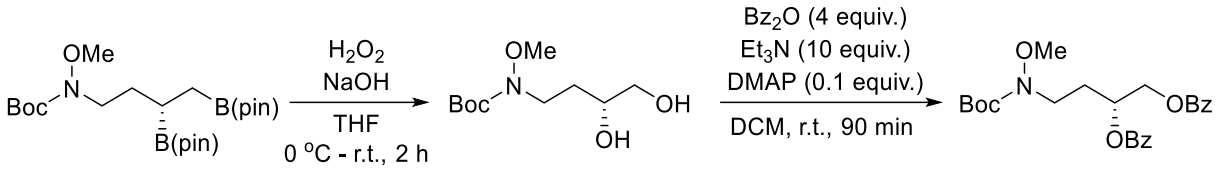
1668 (s), 1456 (w), 1401 (s), 1366 (w), 1168 (m), 1106 (w). **HRMS** (DART+) for $C_{11}H_{22}NO_3$ $[M+H]^+$: Calc'd: 216.1594, found: 216.1600.

2.4.6. Synthesis of Enantiomerically Enriched Compounds and Testing of Stereospecificity



***tert*-butyl (*S*)-(3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (2.112)** The reaction was performed according to a procedure reported in the literature[1] with slight modification. In the glovebox, an oven-dried 20 mL vial was loaded with bis(pinacolato)diboron (0.28 g, 1.1 mmol, 1.1 equiv.), $Pt(dba)_3$ (9.0 mg, 0.01 mmol, 1.0 mol%), **2.111** (9.6 mg, 0.012 mmol, 1.2 mol%) and anhydrous THF (5 mL). The vial was sealed with a pierceable PTFE cap, taken out of the glovebox and heated at 80 °C for 20 mins. After the reaction was removed from the oil bath and cooled down to r.t., *tert*-butyl but-3-en-1-yl(methoxy)carbamate (**2.110**) (0.20 g, 1.0 mmol, 1.0 equiv) was added via syringe and the reaction was heated at 60 °C for 14 hours. The vial was cooled down to r.t. and opened to air. The solvent was removed under reduced pressure. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a yellow oil (0.42 g, 92%). $[\alpha]_D^{20}$: +2.2 (*c* = 0.89, $CHCl_3$, *l* = 50 mm). All other spectral data are in accordance with the racemic compound reported above (**2.92**).

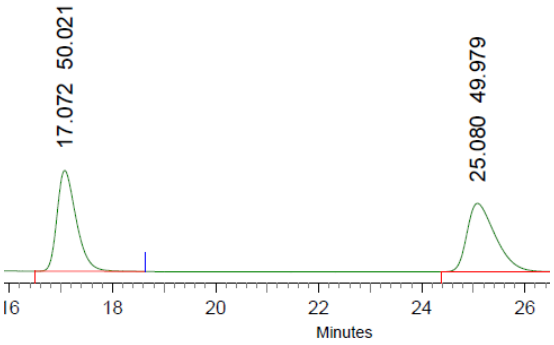
Analysis of Stereochemistry:



The compound was oxidized with hydrogen peroxide and sodium hydroxide, and the resulting diol was treated with benzoic anhydride, triethylamine and 4-dimethylaminopyridine. The resulting protected diol was compared with the racemic compound prepared using the same method from **2.92**.

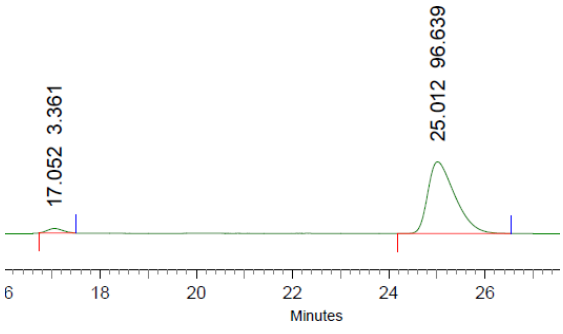
Chiral HPLC (Chiracel IF, 10% isopropanol in hexanes, 0.8 mL/min, 35 °C, 210-290 nm), analysis of tert-butyl (S)-(3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate

Racemic Material

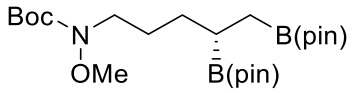


Pk #	Retention Time	Area Percent
1	17.072	50.021
2	25.080	49.979
Totals		100.000

Enantioenriched Material



Pk #	Retention Time	Area Percent
1	17.052	3.361
2	25.012	96.639
Totals		100.000



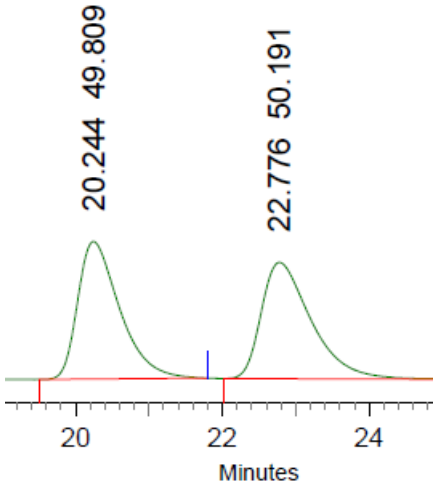
***tert*-butyl (*S*)-(4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)(methoxy)carbamate (2.116)** The reaction was performed using the same method as (**2.112**) with *tert*-butyl methoxy(pent-4-en-1-yl)carbamate (**SI-3**) (0.22 g, 1.0 mmol, 1.0 equiv), bis(pinacolato)diboron (0.28 g, 1.1 mmol, 1.1 equiv.), $Pt(dba)_3$ (9.0 mg, 0.01 mmol, 1.0 mol%), **2.111** (9.6 mg, 0.012 mmol, 1.2 mol%) and anhydrous THF (5 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a yellow oil (0.45 g, 96%). $[\alpha]_D^{20}$: +2.3 (*c* = 1.05, $CHCl_3$, *l* = 50 mm). All other spectral data are in accordance with the racemic compound reported above (**2.96**).

Analysis of Stereochemistry:

The compound was converted to the protected diol using the same method as (**2.112**). The resulting protected diol was compared with the racemic compound prepared using the same method from **2.96**.

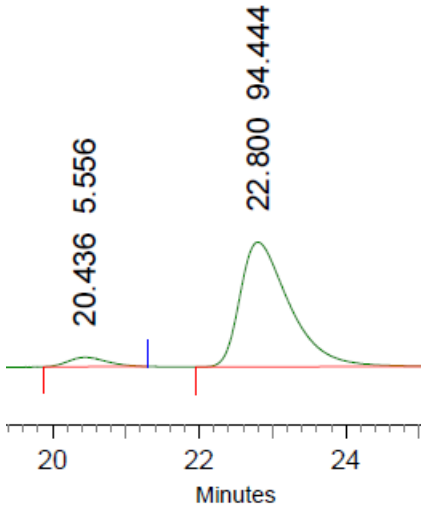
Chiral HPLC (Chiracel IF, 10% isopropanol in hexanes, 0.8 mL/min, 35 °C, 210-290 nm), analysis of tert-butyl (S)-(4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)(methoxy)carbamate

Racemic Material

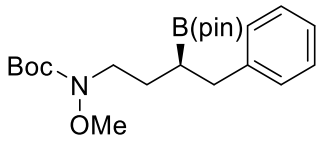


Pk #	Retention Time	Area Percent
1	20.244	49.809
2	22.776	50.191
Totals		100.000

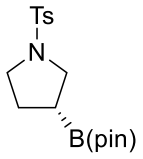
Enantioenriched Material



Pk #	Retention Time	Area Percent
1	20.436	5.556
2	22.800	94.444
Totals		100.000



***tert*-butyl (*S*)-methoxy(4-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)carbamate (2.113)** The reaction was performed according to *General procedure E* with *tert*-butyl (*S*)-(3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (**2.112**) (0.32 g, 0.7 mmol, 1.0 equiv.), solid potassium hydroxide (0.12 g, 2.1 mmol, 3 equiv.), $Pd(OAc)_2$ (3.9 mg, 0.018 mmol, 2.5 mol%), RuPhos (8.2 mg, 0.018 mmol, 2.5 mol%) and bromobenzene (0.16 g, 1.5 mmol, 1.5 equiv.) in THF (6 mL) and H_2O (0.6 mL). The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (0.24 g, 84%). $[\alpha]_D^{20}$: +5.4 (c = 1.00, $CHCl_3$, l = 50 mm). All other spectral data are in accordance with the racemic compound reported above (**SI-10**).



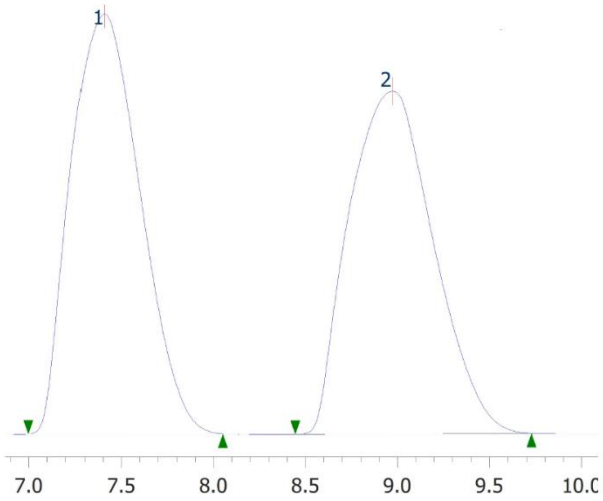
(*R*)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-tosylpyrrolidine (2.115) The reaction was performed according to the general procedure above (***Method B***) with *tert*-butyl (*S*)-(3,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)(methoxy)carbamate (**2.112**) (91.0 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (29.2 mg, 0.26 mmol, 1.3 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 24 hours. The compound was purified with SiO_2 chromatography (15% ethyl acetate in hexane, stain with CAM) as a colorless oil (37.0 mg, 54%). **[α]$_D^{20}$**: -9.3 (*c* = 0.50, $CHCl_3$, *l* = 50 mm). All other spectral data are in accordance with the racemic compound reported above (**2.93**).

Analysis of Stereochemistry:

Enantiomeric ratio was determined in comparison to the racemic compound (**2.93**).

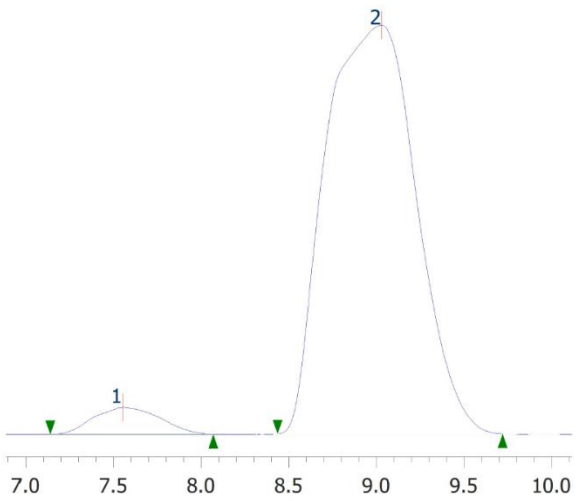
Chiral SFC (Chiracel OJ-H, 3% isopropanol, 3.0 mL/min, 35 °C, 210-290 nm), analysis of (R)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-tosylpyrrolidine

Racemic Material

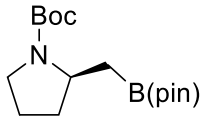


#	tR [min]	Area [μV·sec]	Area%
1	7.407	9294435	50.025
2	8.970	9285128	49.975

Enantioenriched Material



#	tR [min]	Area [μV·sec]	Area%
1	7.553	269854	4.652
2	9.030	5531094	95.348



***tert*-butyl (*S*)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)pyrrolidine-1-carboxylate (2.115)**

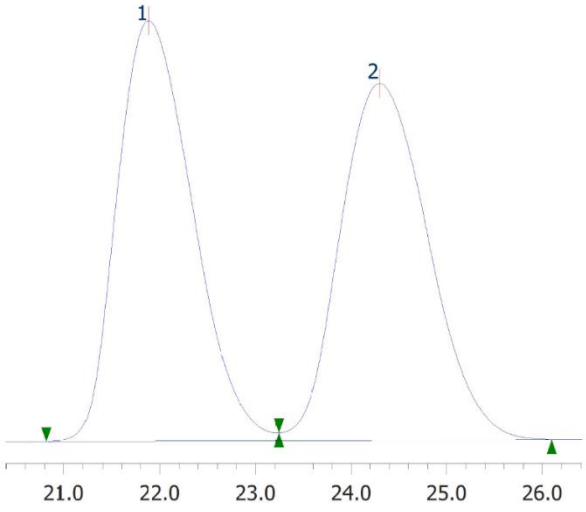
The reaction was performed according to the general procedure above (***Method A***) with *tert*-butyl (*S*)-(4,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)(methoxy)carbamate (**2.116**) (93.9 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (38.2 mg, 0.34 mmol, 1.7 equiv.) in toluene and THF (0.9/0.09 mL, 0.2 M) for 24 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with CAM) as a colorless oil (27.2 mg, 44%). $[\alpha]_D^{20}$: +18.4 (*c* = 0.79, $CHCl_3$, *l* = 50 mm). All other spectral data are in accordance with the racemic compound reported above (**2.97**).

Analysis of Stereochemistry:

Enantiomeric ratio was determined using the tosyl-protected pyrrolidine synthesized following ***Method B***. Racemic compound was prepared using the same method from **2.97**.

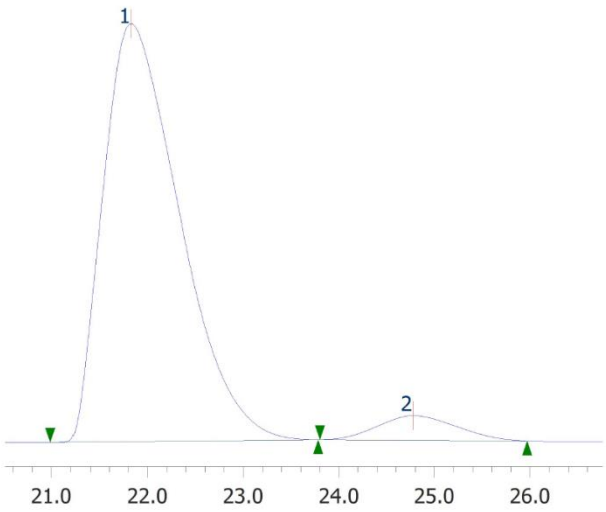
Chiral SFC (Chiracel OJ-H, 3% isopropanol, 3.0 mL/min, 35 °C, 210-290 nm), analysis of (S)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)pyrrolidine-1-carboxylate

Racemic Material

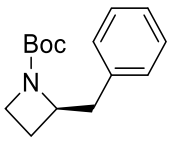


#	tR [min]	Area [µV·sec]	Area%
1	21.880	28256627	50.141
2	24.293	28097273	49.859

Enantioenriched Material



#	tR [min]	Area [µV·sec]	Area%
1	21.827	42863810	94.320
2	24.773	2581138	5.680



tert*-butyl (*S*)-2-benzylazetidine-1-carboxylate (2.114)** The reaction was performed according to the general procedure above (Method A***) with *tert*-butyl (*S*)-methoxy(4-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)carbamate

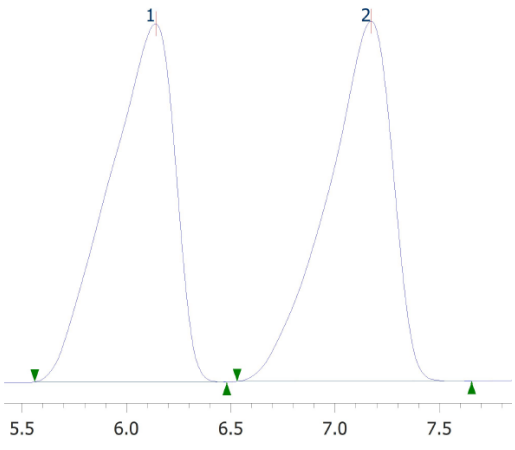
(**2.113**) (83.9 mg, 0.20 mmol, 1.0 equiv.), and potassium *tert*-butoxide (24.7 mg, 0.22 mmol, 1.1 equiv.) in toluene and THF (3.6/0.36 mL, 0.05 M) for 24 hours. The compound was purified with SiO_2 chromatography (10% ethyl acetate in hexane, stain with Ninhydrin) as a colorless oil (32.4 mg, 66%). $[\alpha]_D^{20}$: +90.0 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Enantiomeric ratio was determined in comparison to the racemic compound (**2.79**).

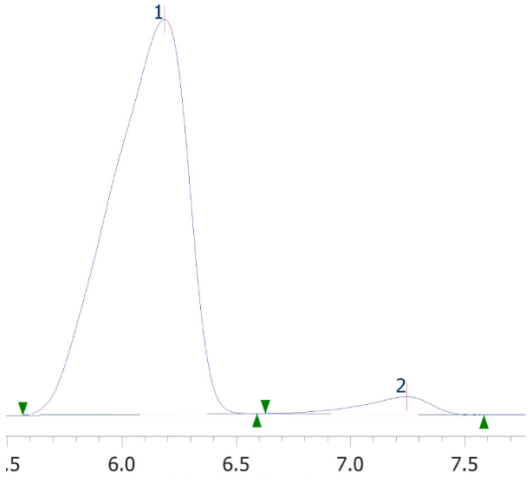
Chiral SFC (Chiracel OJ-H, 5% isopropanol, 1.0 mL/min, 35 °C, 210-290 nm), analysis of tert-butyl (S)-2-benzylazetidine-1-carboxylate

Racemic Material



#	tR [min]	Area [μV·sec]	Area%
1	6.140	5295752	50.213
2	7.173	5250840	49.787

Enantioenriched Material

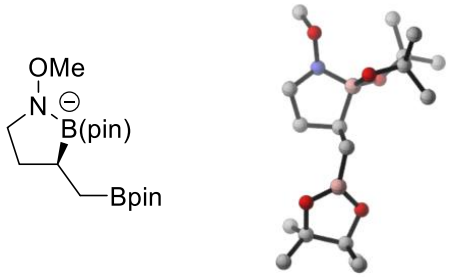


#	tR [min]	Area [μV·sec]	Area%
1	6.187	24282680	96.087
2	7.247	988770	3.913

2.4.7. Computational Data for Scheme 2.23

All calculations were conducted using density functional theory (DFT) implemented in Gaussian 16 suite of program. All molecular structures were optimized by B3LYP-D3 functional with 6-31G* basis sets. Frequency calculations were performed at the same level of theory to characterize the stationary points (no imaginary frequencies for local minima), and transition states (single imaginary frequency).

Intermediate 2.94



IEFPCM (PhMe)

Sum of electronic and thermal Free Energies= -1148.712780

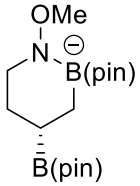
-1 1

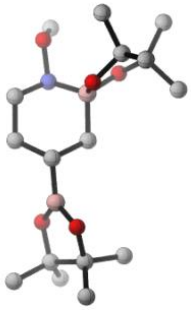
C	0.94027000	2.63088000	-0.36956100
C	0.03245400	0.46866900	0.29970300
C	-0.24769500	1.99328100	0.35925100
H	1.02931100	3.71208400	-0.16534200
H	0.83601900	2.51602000	-1.46665600
H	-0.30121300	-0.01510400	1.22897400
H	-1.20613200	2.29467600	-0.08459000
H	-0.24056200	2.33824300	1.40175800
C	3.36161100	-1.20166500	0.75878200
C	2.88077400	-1.50416500	-0.70990000
C	3.53095300	-2.43987600	1.64687600
H	4.27755300	-3.13404300	1.23759500

H	3.86665900	-2.13039100	2.64420700
H	2.58344300	-2.97200600	1.76504700
C	4.67237800	-0.39045600	0.77901700
H	4.83135600	-0.01891000	1.79816500
H	5.54491300	-0.99236800	0.48945100
H	4.58476800	0.46771400	0.10990800
C	4.01142100	-1.72009000	-1.72229500
H	4.65514600	-2.56510900	-1.44154200
H	3.58433500	-1.93134700	-2.71044000
H	4.62395700	-0.81982600	-1.80921800
C	1.92822100	-2.71617700	-0.75747800
H	1.45327600	-2.74953700	-1.74440000
H	2.44781900	-3.66940600	-0.59080600
H	1.14224900	-2.60979500	-0.00435100
B	1.69447500	0.35255700	0.15977100
O	2.31081200	-0.41544900	1.27226000
O	2.17148100	-0.33996400	-1.06446600
O	3.26241400	2.23333200	-0.55568200
C	3.97768300	3.14375800	0.24153300
H	4.89321000	3.39726000	-0.31249300
H	3.41023100	4.07198200	0.42597800
H	4.24831800	2.70945900	1.21453400
N	2.05380500	1.87453900	0.16791900
C	-0.72262500	-0.19650200	-0.89705600
H	-0.33071600	-1.20540900	-1.05191400
H	-0.50394200	0.36465600	-1.81360700
C	-4.31670300	0.59258400	-0.06836500
C	-4.25240500	-0.93906300	0.26666000
C	-4.76904800	-1.31921000	1.65140900
H	-5.82878300	-1.05837600	1.76109700

H	-4.66565000	-2.39941500	1.79798400
H	-4.19968800	-0.81783600	2.43665200
C	-4.91971400	-1.81412300	-0.80231000
H	-4.64806800	-2.85856200	-0.62058500
H	-6.01207100	-1.72809800	-0.77978400
H	-4.56656400	-1.54181600	-1.80150900
C	-4.12316500	1.48162600	1.16677400
H	-3.97002300	2.51328900	0.83667200
H	-4.99341400	1.45151200	1.83225700
H	-3.23547600	1.17739400	1.72866500
C	-5.55231400	1.03519700	-0.84611000
H	-6.46606400	0.85050000	-0.26830500
H	-5.48984800	2.10872700	-1.05214300
H	-5.63057100	0.51270700	-1.80220400
B	-2.23813400	-0.22342100	-0.56763800
O	-2.83904200	-1.20673200	0.21023700
O	-3.15250100	0.77076900	-0.90069000

Intermediate 2.95





IEFPCM (PhMe)

Sum of electronic and thermal Free Energies= -1148.721479

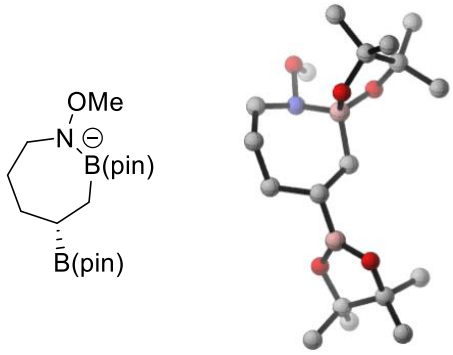
-1 1

C	0.81019500	0.67218800	-0.75785100
C	0.50922400	2.17944100	-0.79096300

C	-0.98858600	2.47572200	-0.93332400
C	-0.02097900	-0.00040400	0.38424900
H	-1.15270000	3.56438900	-0.91280100
H	0.87187300	2.63799400	0.13880500
H	1.04906300	2.66576600	-1.61833400
H	0.46869800	0.21778200	-1.69842600
H	0.32488000	0.37851000	1.35892600
H	0.15952300	-1.08519200	0.37729900
H	-1.34319900	2.11278100	-1.91789300
C	-3.25639300	-1.08988900	-0.83980700
C	-3.21428200	-1.34109200	0.71958900
C	4.07126400	-1.06949800	-0.08784500
C	4.42384300	0.39492000	0.35260700
C	-3.54157500	2.74482000	1.27420700
H	-2.92717100	3.57282500	1.66601400
H	-4.57685600	3.09391900	1.14320000
H	-3.52077100	1.91835100	1.99440600
C	-4.46878300	-0.24365000	-1.27377000
H	-4.34389400	0.01167900	-2.33290900
H	-5.42215300	-0.77778100	-1.15849400
H	-4.48871200	0.69178300	-0.71195700
C	-3.22971300	-2.37318400	-1.68248700
H	-4.09776500	-3.01501800	-1.47767100
H	-3.24789400	-2.10768300	-2.74628400
H	-2.31738100	-2.94650000	-1.49898400
C	-4.59180200	-1.40019100	1.38956900
H	-5.20479500	-2.21837000	0.98801800
H	-4.46917300	-1.56334000	2.46746000
H	-5.12820000	-0.45850500	1.25065600
C	-2.43073200	-2.61943400	1.08585700

H	-2.25471700	-2.61692400	2.16761100
H	-2.96989500	-3.53906800	0.82206400
H	-1.45808500	-2.62898300	0.58731200
C	5.14233800	-1.77245100	-0.91612200
H	6.07148800	-1.88211700	-0.34373700
H	4.79269800	-2.77210300	-1.19406000
H	5.35951200	-1.22405900	-1.83557200
C	3.64119600	-1.95857500	1.08613200
H	3.21498400	-2.88367100	0.68646400
H	4.48404200	-2.21396700	1.73835700
H	2.86684900	-1.46598400	1.68144900
C	5.29615200	1.13390900	-0.67027400
H	5.31391300	2.19746000	-0.41287000
H	6.32594000	0.75893300	-0.67865000
H	4.87856200	1.03644200	-1.67691300
C	5.02988400	0.52149400	1.74735200
H	5.98120200	-0.02048800	1.81323500
H	5.22104200	1.57639300	1.97048500
H	4.35056400	0.13455500	2.50962100
O	-2.51706000	-0.22542100	1.22439400
O	-2.07325500	-0.36633700	-1.08337300
O	2.90333000	-0.86712600	-0.90805300
O	3.13416400	1.03525600	0.34823000
B	-1.62347000	0.31398700	0.17324500
B	2.28889700	0.30362100	-0.47785200
N	-1.71479000	1.86225400	0.16411400
O	-3.10000300	2.32383000	0.00701200

Intermediate 2.98



IEFPCM (PhMe)

Sum of electronic and thermal Free Energies= -1188.005694

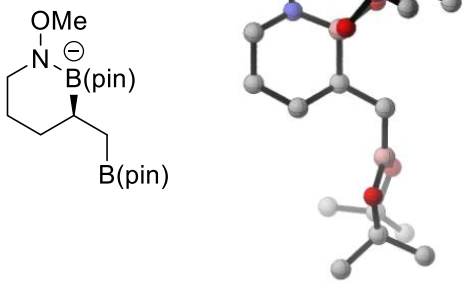
-1 1

C	0.91274500	0.58721500	-0.96050600
C	-1.80475500	2.69319300	-0.63218900
C	0.03901400	-0.03408700	0.17388600
H	-1.66035400	3.70904700	-0.22016800
H	0.63504400	0.07306200	-1.89242300
H	0.39578400	0.34077300	1.14671900
H	0.21394900	-1.12078000	0.17813700
H	-2.78035100	2.70864400	-1.15292500
C	-3.34052200	-0.98591400	-0.90228100
C	-3.06218900	-1.58565900	0.52773400
C	4.09989100	-1.15001100	0.01681900
C	4.45072500	0.33556100	0.38099200
C	-2.88357300	2.01574900	2.50306100
H	-2.12461800	2.76347200	2.78546300
H	-3.84685500	2.28235200	2.96308000
H	-2.56831200	1.03018900	2.86459600
C	-4.54601000	-0.02614500	-0.90960700
H	-4.55555600	0.50259900	-1.87038200
H	-5.50308600	-0.55486600	-0.79919000

H	-4.44305900	0.71610800	-0.11458600
C	-3.53263800	-2.03419300	-2.00438300
H	-4.39055500	-2.68843200	-1.79769500
H	-3.71494600	-1.52795000	-2.96002300
H	-2.63867800	-2.65240600	-2.12017700
C	-4.31835900	-1.82083600	1.37331100
H	-5.00870800	-2.52550800	0.88994000
H	-4.03371900	-2.23754200	2.34746200
H	-4.84096400	-0.87802400	1.55059900
C	-2.24878500	-2.89422600	0.45529600
H	-1.88877400	-3.13316200	1.46241000
H	-2.83988900	-3.74279300	0.08543200
H	-1.37815800	-2.76296500	-0.19286800
C	5.20647000	-1.92037300	-0.69676600
H	6.09758800	-2.00369600	-0.06281200
H	4.85727000	-2.93175900	-0.92909500
H	5.48785600	-1.43721300	-1.63523900
C	3.58425800	-1.95342500	1.21770000
H	3.16812700	-2.89779000	0.85411400
H	4.38165700	-2.17514400	1.93604200
H	2.78275100	-1.41348400	1.73014800
C	5.39565400	0.99348100	-0.63261600
H	5.41586700	2.07147500	-0.44486700
H	6.41759300	0.60551800	-0.55319200
H	5.03804400	0.83467300	-1.65445600
C	4.97313800	0.54618600	1.79915700
H	5.90854100	-0.00385600	1.95928800
H	5.16967800	1.61076300	1.96403000
H	4.24146400	0.22068500	2.54135000
O	-2.27328900	-0.60059400	1.15604300

O	-2.15893200	-0.26203700	-1.16978400
O	2.98698100	-0.98680400	-0.88526400
O	3.17487500	0.99162800	0.25559600
B	-1.58770900	0.21902900	0.12740300
B	2.36703300	0.21634100	-0.56709300
N	-1.81686500	1.73625100	0.45591500
O	-3.09995600	2.00325800	1.11415400
C	-0.72936400	2.42217000	-1.69149900
H	-0.68541900	3.31733500	-2.32986600
H	-1.06696000	1.59336100	-2.32247200
C	0.67975900	2.09607900	-1.16253600
H	1.42479900	2.47618600	-1.87902000
H	0.86420500	2.62832600	-0.21969200

Intermediate 2.99



IEFPCM (PhMe)

Sum of electronic and thermal Free Energies= -1188.014614

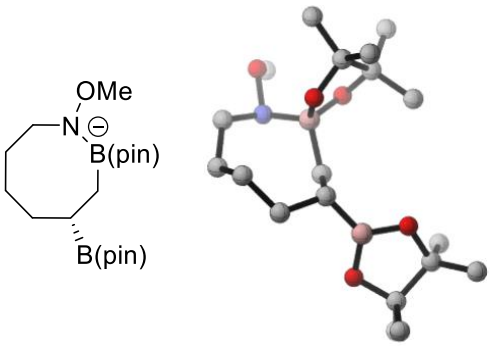
-1 1

C	-0.30335700	2.82062900	-1.02561100
C	-1.82808000	2.69240900	-0.92461200
C	-0.00061200	0.55422900	0.06910300
H	-2.27780200	3.68897100	-0.79506800
H	0.05931200	3.35018100	-0.13250000

H	-0.04928300	3.44201100	-1.89798400
H	0.30930600	1.05841500	0.99865400
H	-2.22441800	2.27527800	-1.87087000
C	-3.07907800	-1.24594500	-0.88169500
C	-2.95570700	-1.50547200	0.68686500
C	4.45422200	-0.45293200	-0.56558300
C	4.25641100	0.12640100	0.88041000
C	-3.90406500	2.22591300	1.68268600
H	-3.48463800	3.20222400	1.97798400
H	-5.00041600	2.26298400	1.76807500
H	-3.50987100	1.45492100	2.35527000
C	-4.43444700	-0.64244500	-1.30260900
H	-4.38353700	-0.40740200	-2.37274800
H	-5.27318100	-1.33422100	-1.14428800
H	-4.61303900	0.28894900	-0.76335100
C	-2.83018700	-2.49468200	-1.74336900
H	-3.57802600	-3.27805700	-1.56049700
H	-2.88602900	-2.21163500	-2.80103200
H	-1.83547900	-2.91027300	-1.56402300
C	-4.30650800	-1.52371600	1.41985600
H	-4.95042400	-2.34470900	1.07646900
H	-4.13000200	-1.65568300	2.49431000
H	-4.83456400	-0.57918900	1.27777300
C	-2.21189200	-2.81151900	1.03038100
H	-2.03536800	-2.83238200	2.11207200
H	-2.78273500	-3.70827300	0.75539100
H	-1.23958900	-2.85014900	0.53494000
C	5.21410900	0.45690600	-1.52658900
H	6.23304700	0.64500400	-1.16675200
H	5.28113100	-0.02108000	-2.50950100

H	4.70240500	1.41316400	-1.65220700
C	5.07167900	-1.85710200	-0.57048000
H	4.97879200	-2.27793100	-1.57649000
H	6.13245700	-1.84002200	-0.29562800
H	4.54008100	-2.51653200	0.12215700
C	4.14398000	1.65640500	0.90507700
H	3.80032900	1.96512600	1.89686800
H	5.10549800	2.14090100	0.70027000
H	3.40816500	2.00576800	0.17503700
C	5.28354100	-0.33844500	1.90896600
H	6.29353800	-0.01619200	1.62794100
H	5.04572800	0.09641800	2.88520200
H	5.27894600	-1.42561700	2.01478700
O	-2.19266200	-0.42636600	1.18114100
O	-2.05933100	-0.31659400	-1.15721600
O	3.09774300	-0.58864100	-1.03265100
O	2.96333500	-0.39374300	1.24421800
B	-1.64243000	0.39343900	0.08488900
B	2.25749100	-0.63837000	0.07169700
N	-2.15516700	1.86162400	0.21895400
O	-3.61693200	1.92173000	0.34008800
C	0.71836400	-0.82581500	0.01718000
H	0.37168600	-1.40842500	0.87904700
H	0.39683700	-1.35369000	-0.88919100
C	0.38933200	1.45537700	-1.11564400
H	0.07909800	0.95560300	-2.04477200
H	1.47946000	1.60655700	-1.20158000

Intermediate 2.102



IEFPCM (PhMe)

Sum of electronic and thermal Free Energies= -1227.292567

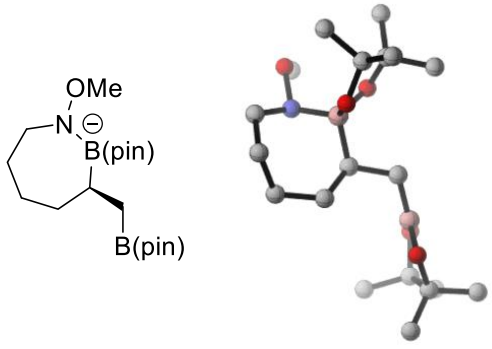
-1 1

C	0.78253900	0.92702800	-0.78765700
C	-0.03204200	0.67904800	0.52316600
H	0.34746100	0.26886900	-1.55047600
H	0.12853800	1.52021300	1.21175800
H	0.38383100	-0.19540700	1.04787000
C	-2.58949400	-1.29322400	-1.16623800
C	-2.11894700	-2.02144800	0.15053000
C	3.78970400	-1.06489500	0.22814500
C	4.36840000	0.39038500	0.33560900
C	-3.94443800	0.68029000	2.61709700
H	-3.70803000	1.56573200	3.23057400
H	-4.98270900	0.37251500	2.81156100
H	-3.26508700	-0.13574100	2.88795100
C	-4.11199600	-1.06582400	-1.20615100
H	-4.33664600	-0.40694400	-2.05368400
H	-4.67415100	-2.00036900	-1.33940100
H	-4.43566100	-0.56091800	-0.29348500
C	-2.15539600	-1.98849900	-2.46231900
H	-2.57974600	-2.99861000	-2.54237800

H	-2.50503400	-1.40487300	-3.32244700
H	-1.06663000	-2.05924100	-2.52679600
C	-3.13376200	-3.02192500	0.71483300
H	-3.34974800	-3.82881800	0.00157100
H	-2.73234500	-3.47481100	1.62975600
H	-4.06820400	-2.51724500	0.97116900
C	-0.76198900	-2.73713500	-0.03033100
H	-0.40041000	-3.03912200	0.95974800
H	-0.83896200	-3.63454300	-0.65860500
H	-0.01494000	-2.06904300	-0.46649200
C	4.71525200	-2.08410800	-0.42873800
H	5.63743100	-2.20816800	0.15192500
H	4.21071400	-3.05431700	-0.48037700
H	4.97859500	-1.78680500	-1.44642000
C	3.27317100	-1.60498000	1.56769800
H	2.69116400	-2.51157800	1.37743500
H	4.09174900	-1.84816100	2.25468900
H	2.60800500	-0.88165500	2.04800500
C	5.30241300	0.75019300	-0.82661100
H	5.48671000	1.82892400	-0.80849100
H	6.26448700	0.23009200	-0.75588000
H	4.83876500	0.50184800	-1.78605100
C	5.03521300	0.72211600	1.66731700
H	5.89887600	0.07033700	1.84703100
H	5.38633700	1.75939400	1.65488100
H	4.33414400	0.61373300	2.49733400
O	-1.96289400	-0.97073700	1.07444900
O	-1.93726500	-0.04447200	-1.08409500
O	2.63816700	-0.86884100	-0.61592400
O	3.18645800	1.20352400	0.19448400

B	-1.64087200	0.28547100	0.34597700
B	2.21311400	0.44368800	-0.44295600
N	-2.50059600	1.43452400	0.95926000
O	-3.86885500	0.96771500	1.24351700
C	-0.74685800	2.87661300	-1.52860900
H	-0.70811900	3.69447400	-2.26310200
H	-1.33001400	2.06908600	-1.98403800
C	0.68953800	2.37206900	-1.29943400
H	1.24088600	2.44383700	-2.25061800
H	1.20835000	3.04830900	-0.60283300
C	-2.74762100	2.61596100	0.14718600
H	-3.38790200	3.28950100	0.73749800
H	-3.31877000	2.36751000	-0.76812300
C	-1.48531300	3.38948900	-0.26478400
H	-0.80243100	3.43370000	0.59163200
H	-1.80267500	4.42639900	-0.44630200

Intermediate 2.103



IEFPCM (PhMe)

Sum of electronic and thermal Free Energies= -1227.298474

-1 1

C	2.63272600	2.64642800	0.33865600
C	-0.02987100	0.51636600	0.02598100

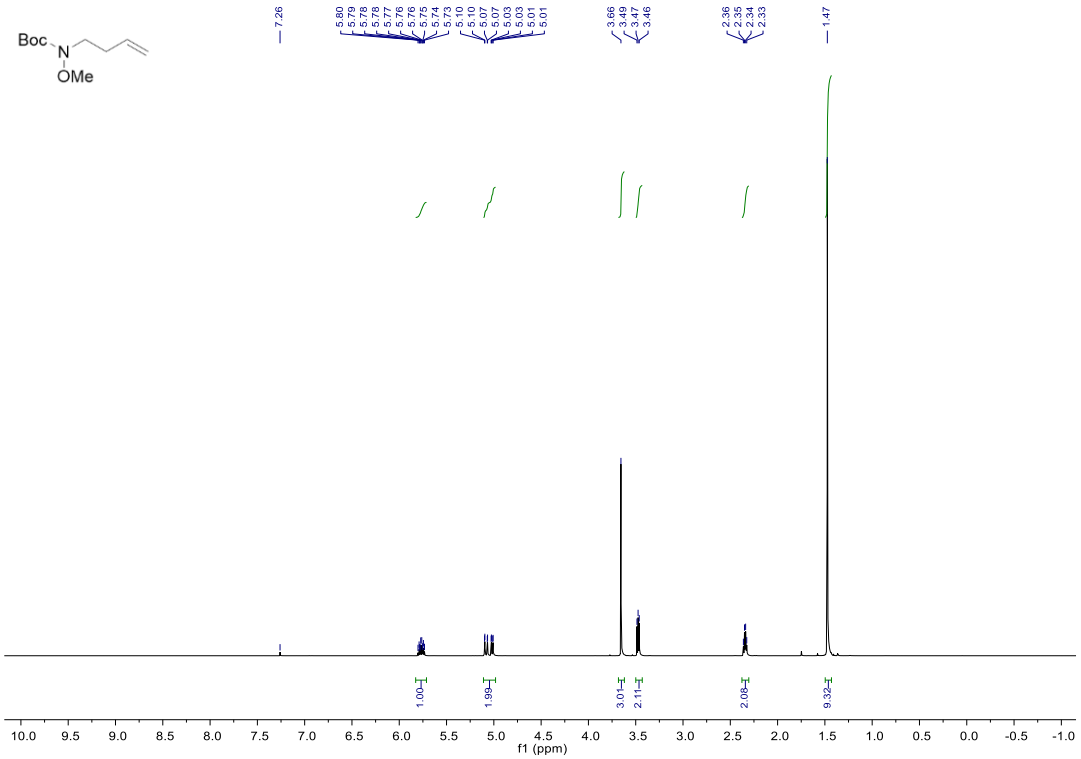
H	2.72725600	3.60934600	-0.19753300
H	-0.32475000	0.95989600	-0.93865100
H	3.63323200	2.43353800	0.75972200
C	3.17295800	-1.15160600	0.96632600
C	2.77416100	-1.77290600	-0.44028800
C	-4.55107800	-0.49155700	0.55679100
C	-4.29183700	0.05445100	-0.89266900
C	2.98404000	1.42443100	-2.78101000
H	2.44112100	2.34730600	-3.04149800
H	3.89644700	1.35202000	-3.39141700
H	2.34162400	0.55971200	-2.98362000
C	4.52475300	-0.41002000	0.93382500
H	4.63662100	0.13646300	1.87785900
H	5.37415100	-1.09964700	0.83429600
H	4.55343000	0.30973500	0.11451500
C	3.21122600	-2.16506700	2.11806200
H	3.95642100	-2.95308800	1.94600200
H	3.47631300	-1.64365700	3.04559800
H	2.23387200	-2.63097300	2.26628200
C	3.96728100	-2.02035700	-1.37544200
H	4.69097500	-2.72490900	-0.94309700
H	3.60366700	-2.44445400	-2.31959500
H	4.47185700	-1.07941200	-1.60091100
C	1.98008000	-3.08663100	-0.30648300
H	1.58757200	-3.35450300	-1.29426900
H	2.59958300	-3.91752400	0.05621600
H	1.12953600	-2.96140200	0.36726000
C	-5.37425300	0.42773800	1.45466000
H	-6.37727700	0.58676800	1.04028600
H	-5.48150800	-0.02604700	2.44548100

H	-4.88707000	1.39683000	1.57972100
C	-5.14312900	-1.90663500	0.56843700
H	-5.09446200	-2.29919600	1.58890700
H	-6.18856000	-1.91709200	0.23977800
H	-4.56514800	-2.57380000	-0.07808100
C	-4.21263500	1.58547300	-0.95470700
H	-3.82423000	1.87512600	-1.93565100
H	-5.19426900	2.05220500	-0.81399800
H	-3.52438700	1.97246700	-0.19782500
C	-5.25464300	-0.46080400	-1.95896400
H	-6.28455300	-0.15482700	-1.73853200
H	-4.97631100	-0.04622900	-2.93328400
H	-5.22072500	-1.54992200	-2.03486000
O	1.92942500	-0.80812300	-1.03168400
O	2.13529200	-0.23241000	1.22689800
O	-3.21761600	-0.58994700	1.09419300
O	-2.97151400	-0.44545300	-1.17673900
B	1.59919800	0.26609900	-0.07082500
B	-2.32191300	-0.65379600	0.03431200
N	2.22134400	1.62077400	-0.59531300
O	3.40511900	1.43891800	-1.43930500
C	1.66669000	2.82089100	1.51486900
H	1.95016200	3.75271500	2.02650900
H	1.82729200	2.00073000	2.22242700
C	0.17465700	2.86324400	1.14299300
H	-0.35717400	3.49213400	1.87385100
H	0.04645600	3.34596000	0.16338900
C	-0.78692400	-0.84181700	0.16349500
H	-0.41364500	-1.49947000	-0.62920300
H	-0.51540600	-1.30088600	1.12332800

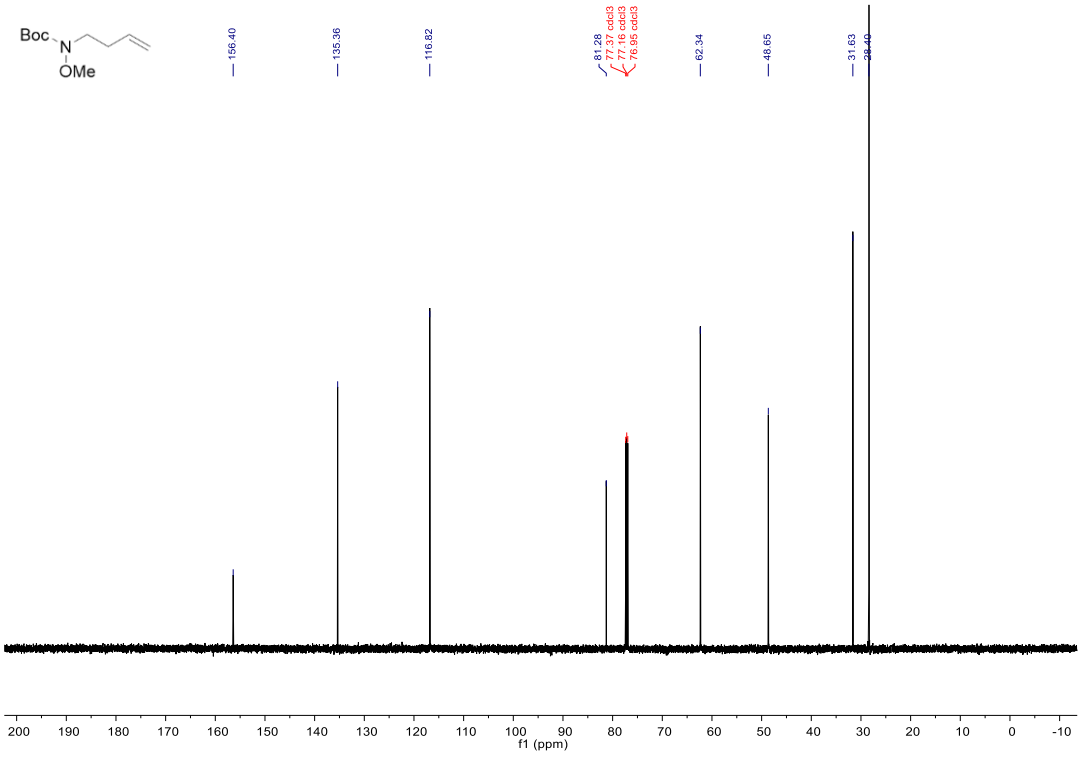
C	-0.48704400	1.47767800	1.13483600
H	-0.29176600	1.00331900	2.10900600
H	-1.58079000	1.62415300	1.09825000

2.4.8. NMR Spectral Data

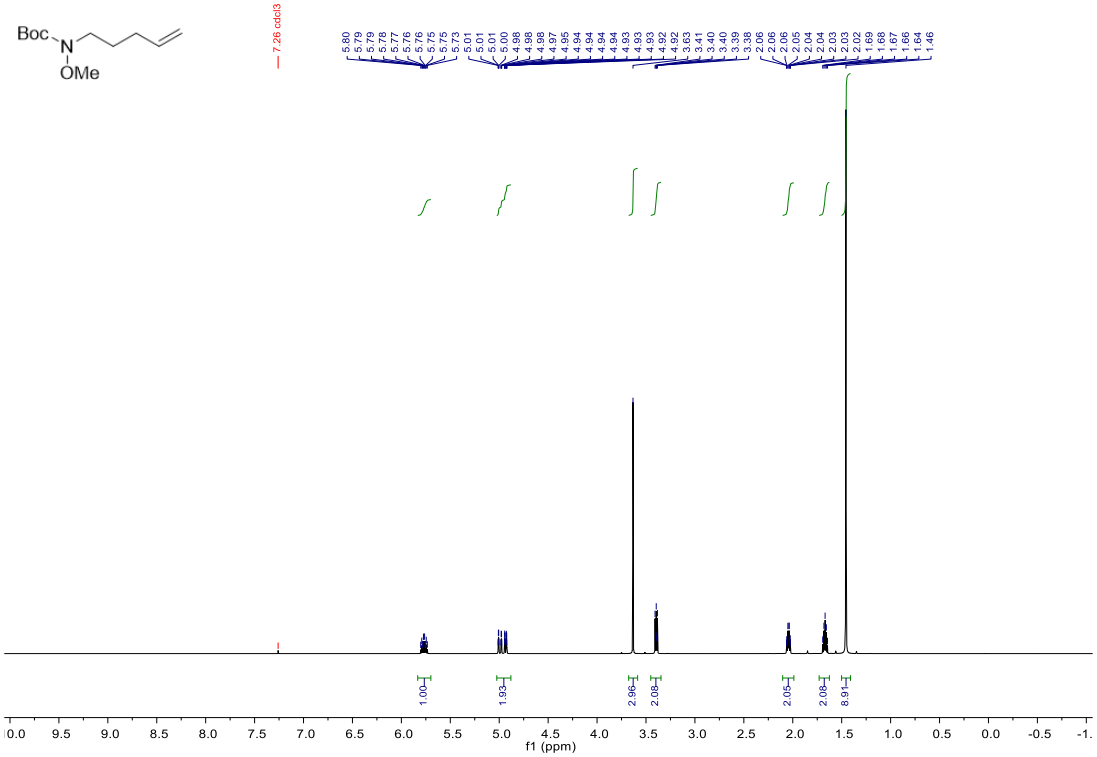
^{1}H NMR (600 MHz, $CDCl_3$) (**2.110**)



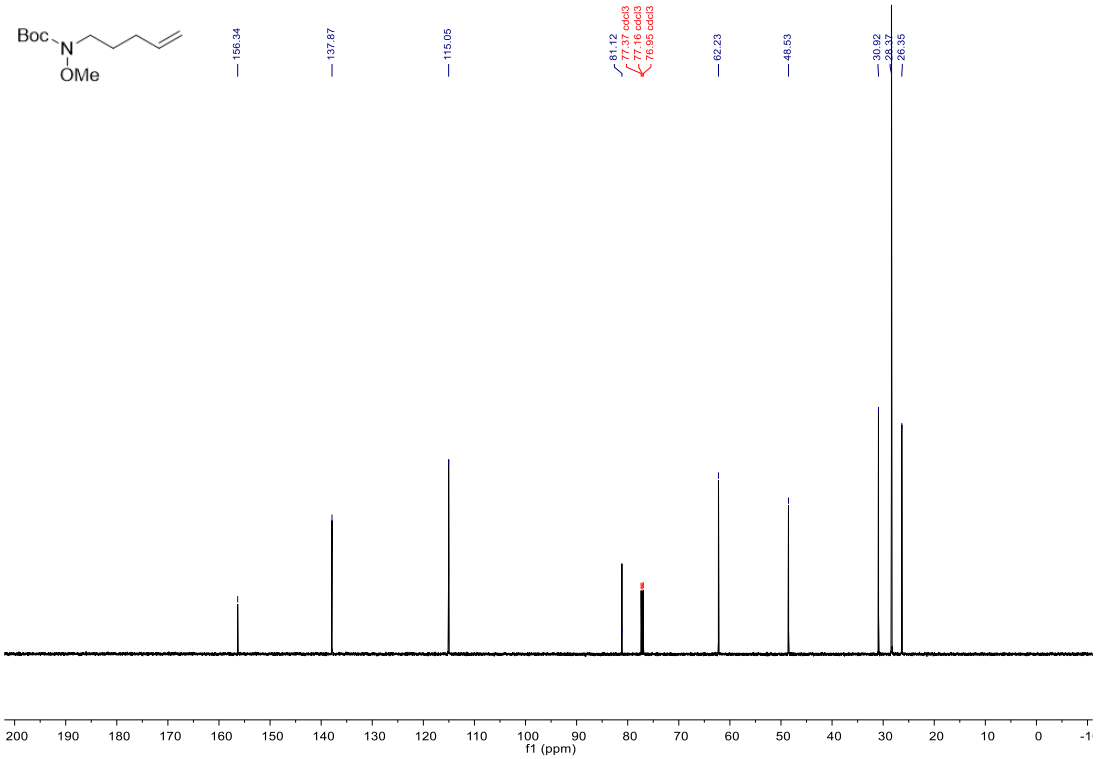
^{13}C NMR (151 MHz, $CDCl_3$) (**2.110**)



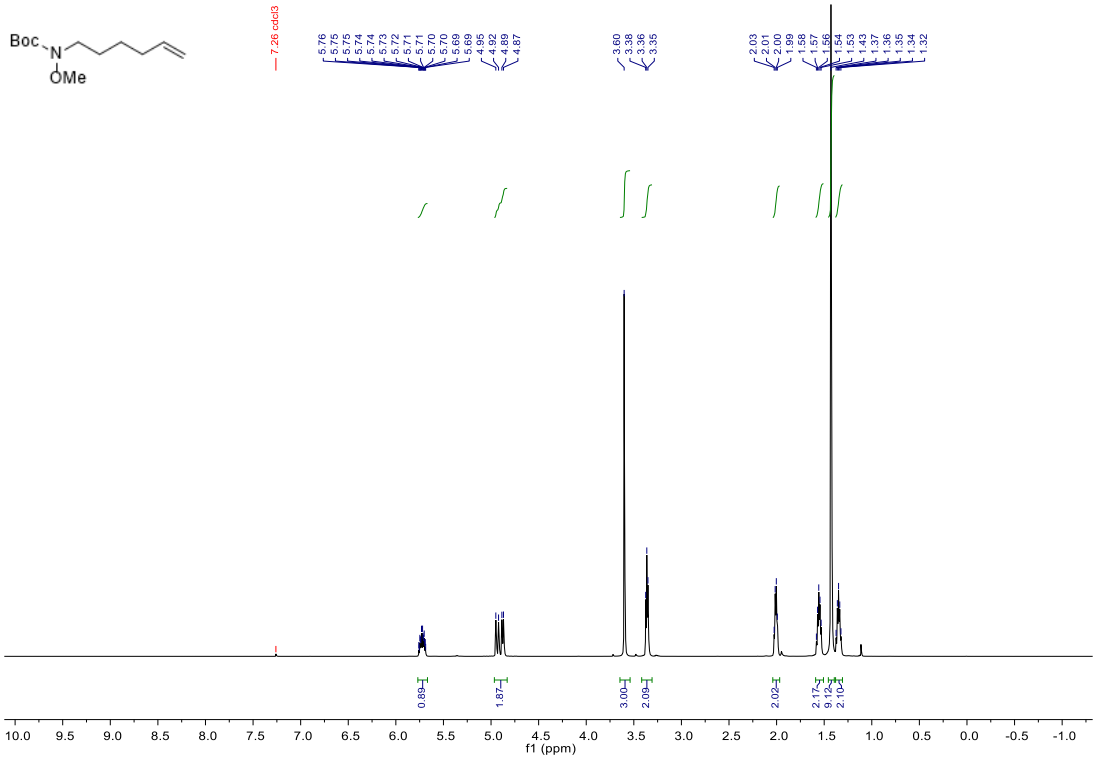
^{1}H NMR (600 MHz, $CDCl_3$) (**SI-3**)



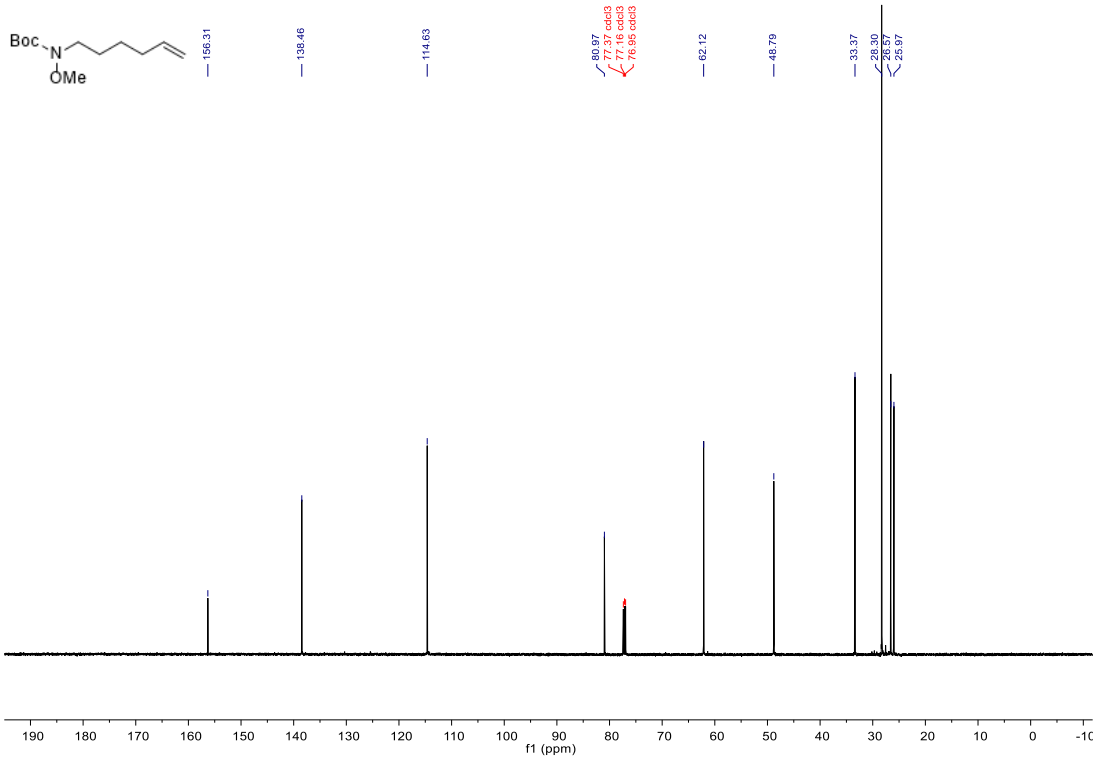
^{13}C NMR (151 MHz, $CDCl_3$) (**SI-3**)



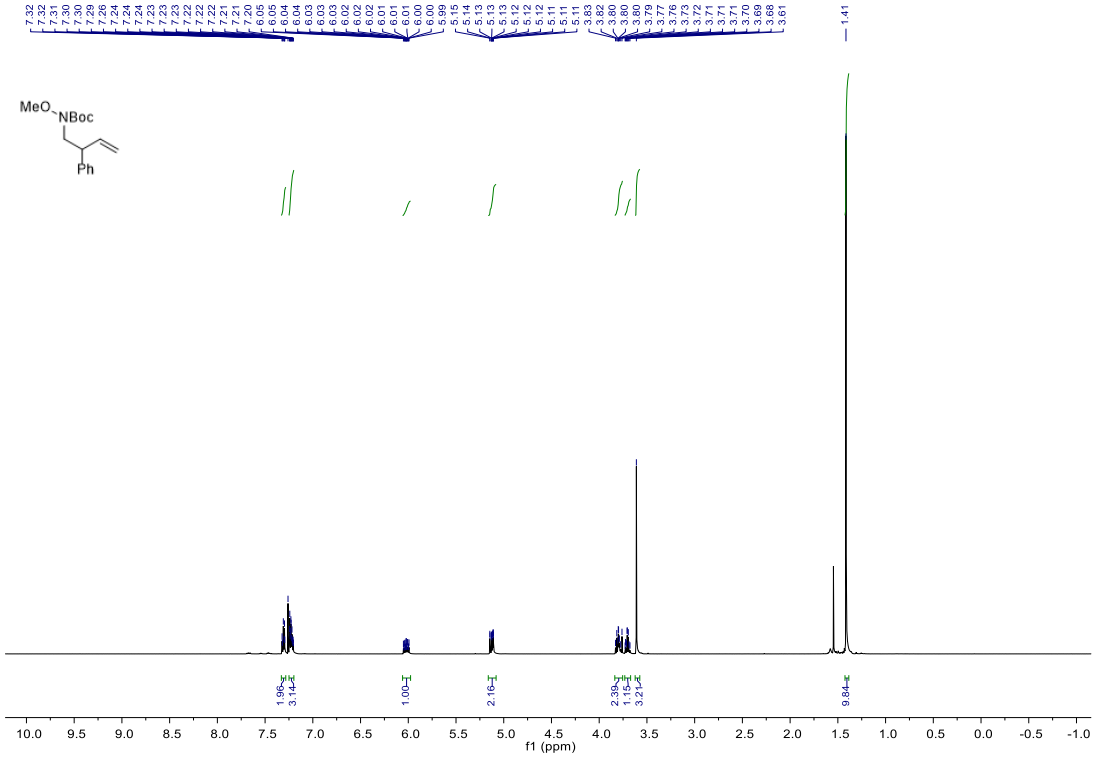
^{1}H NMR (600 MHz, $CDCl_3$) (**SI-4**)



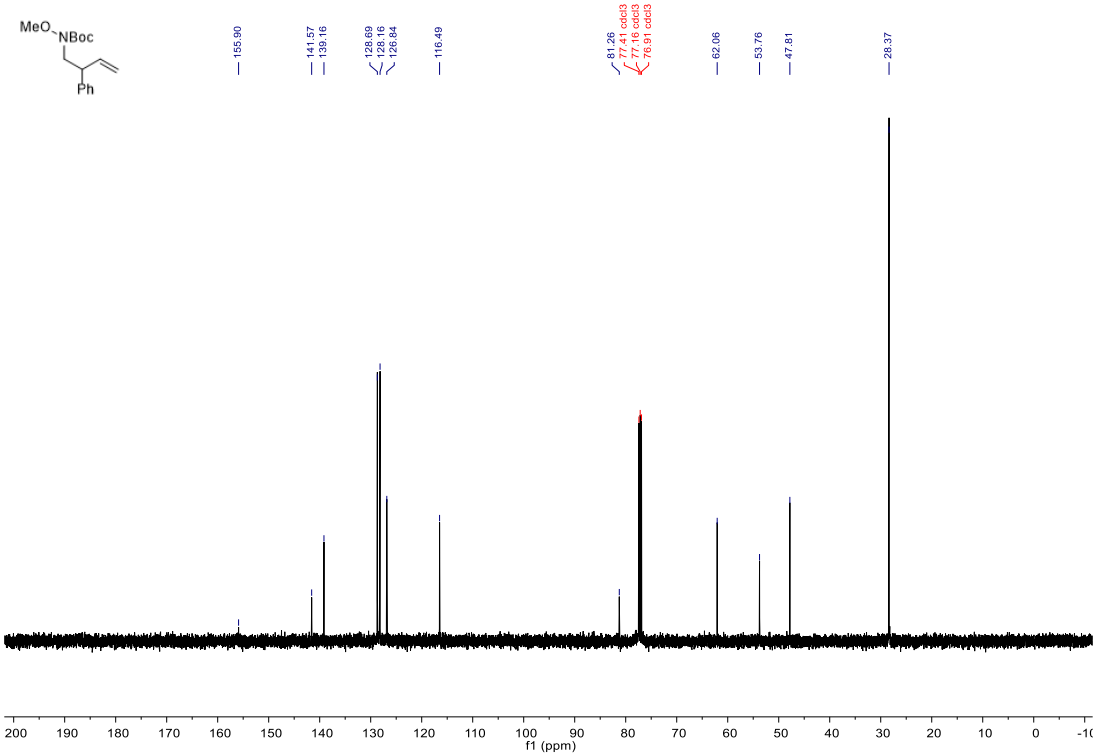
^{13}C NMR (151 MHz, $CDCl_3$) (**SI-4**)



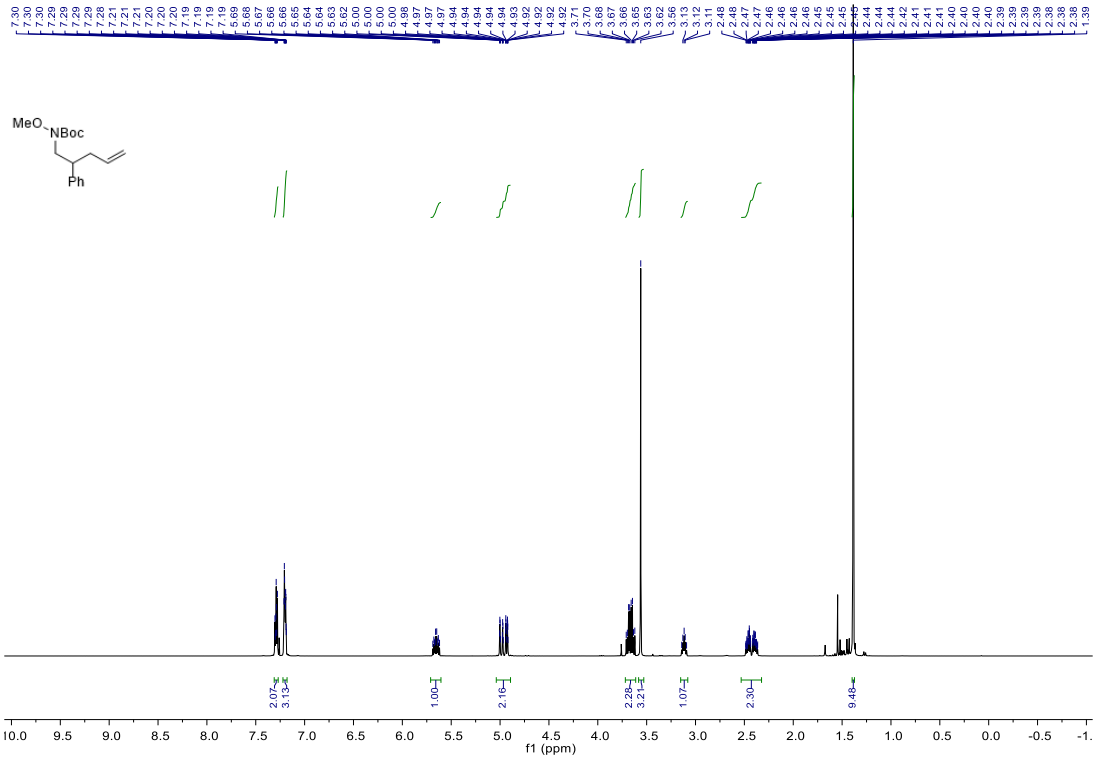
^{1}H NMR (600 MHz, $CDCl_3$) (**2.77**)



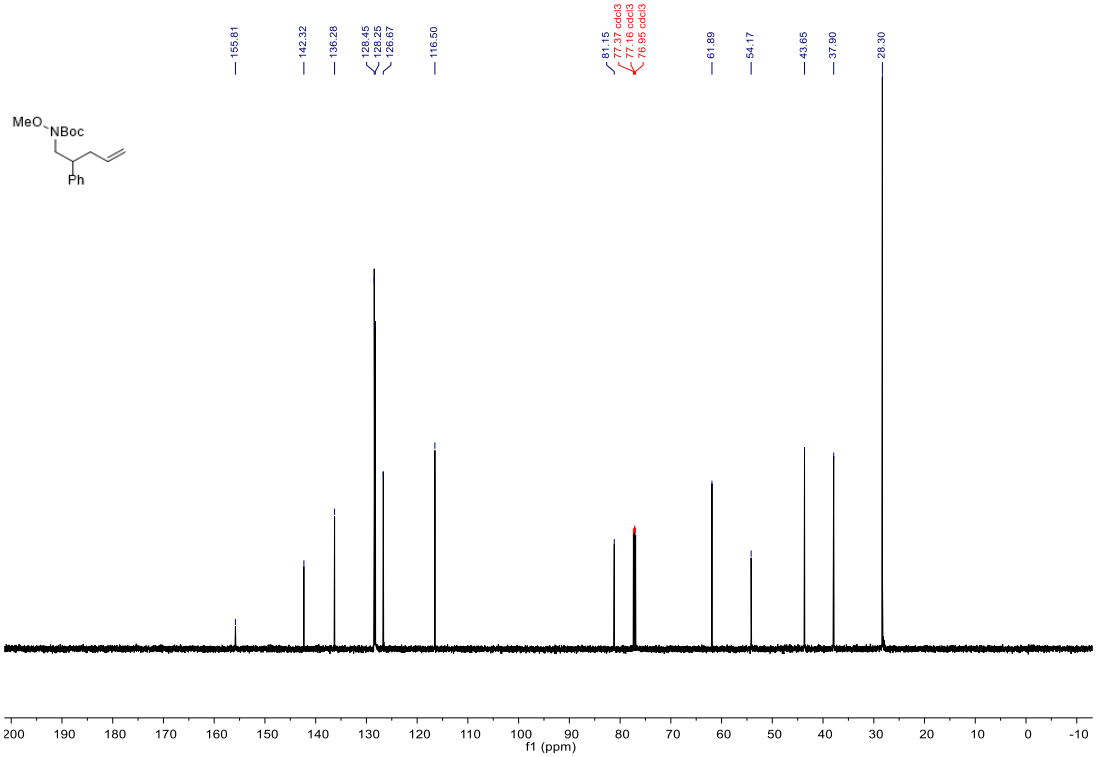
^{13}C NMR (126 MHz, $CDCl_3$) (**2.77**)



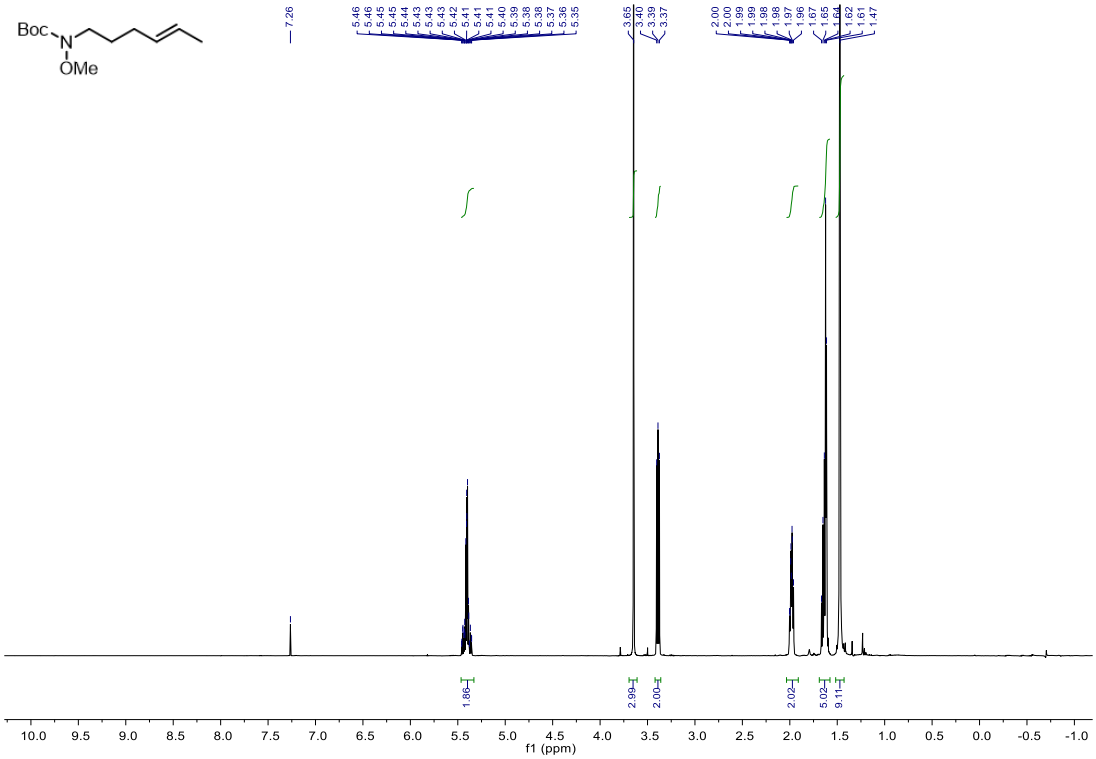
^{1}H NMR (600 MHz, $CDCl_3$) (**SI-5**)



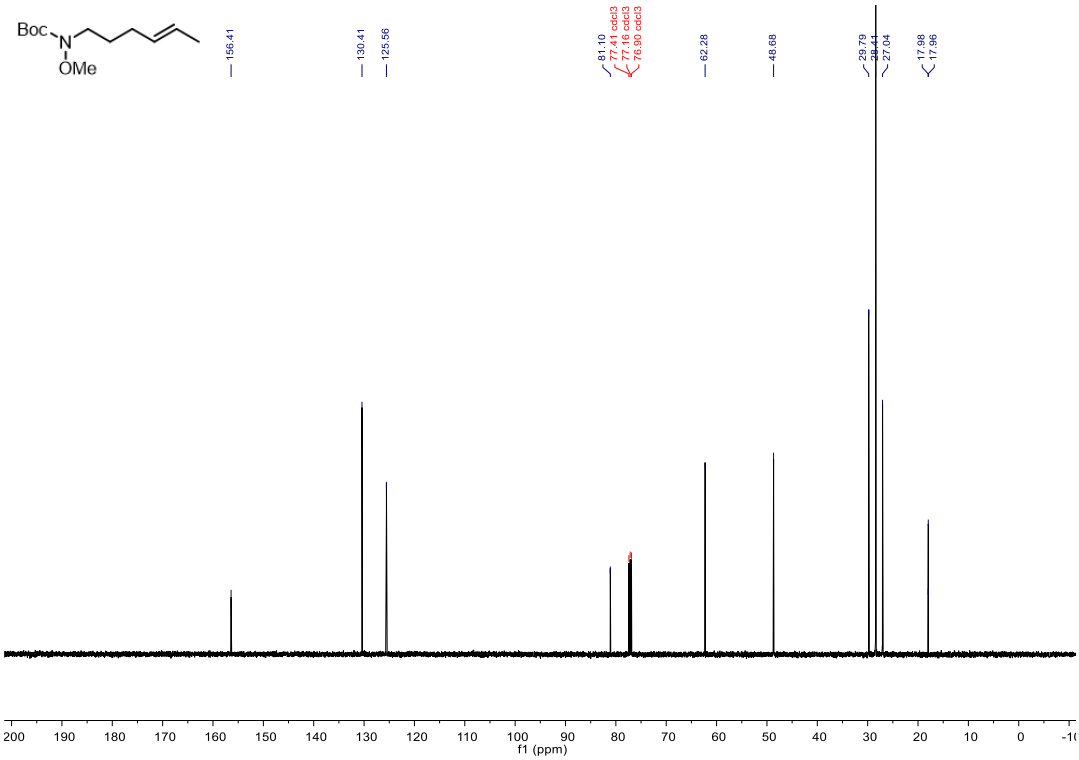
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-5**)



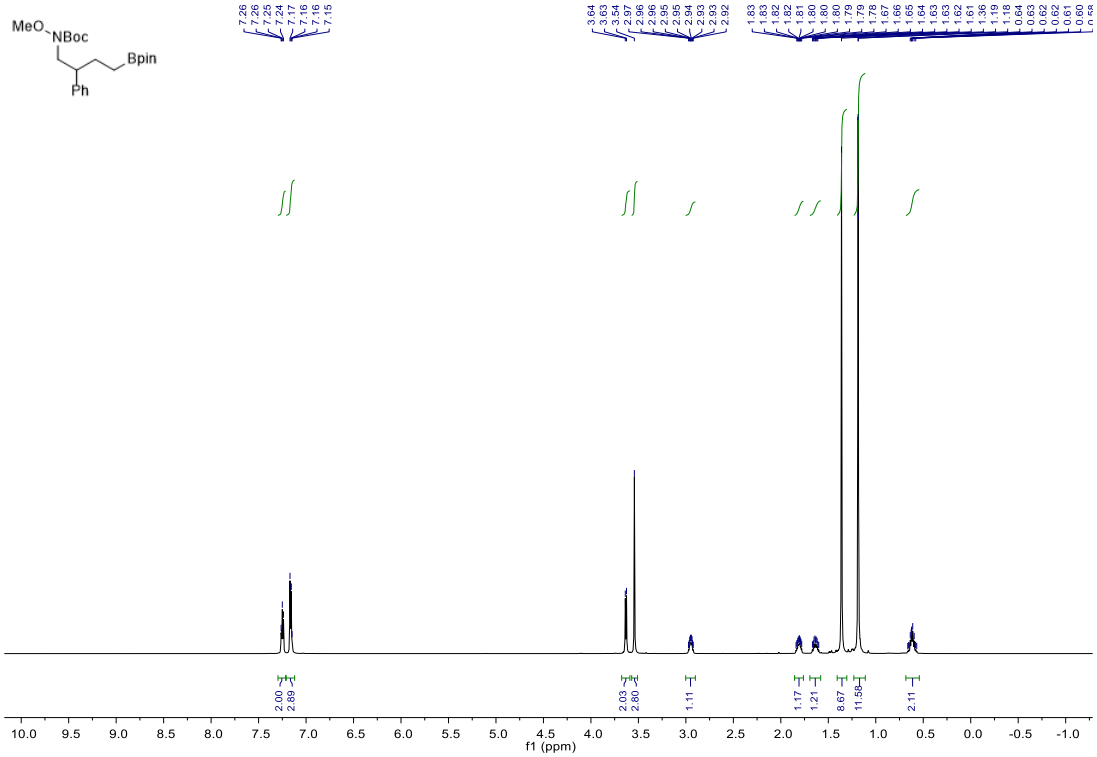
^{1}H NMR (500 MHz, $CDCl_3$) (**2.107**)



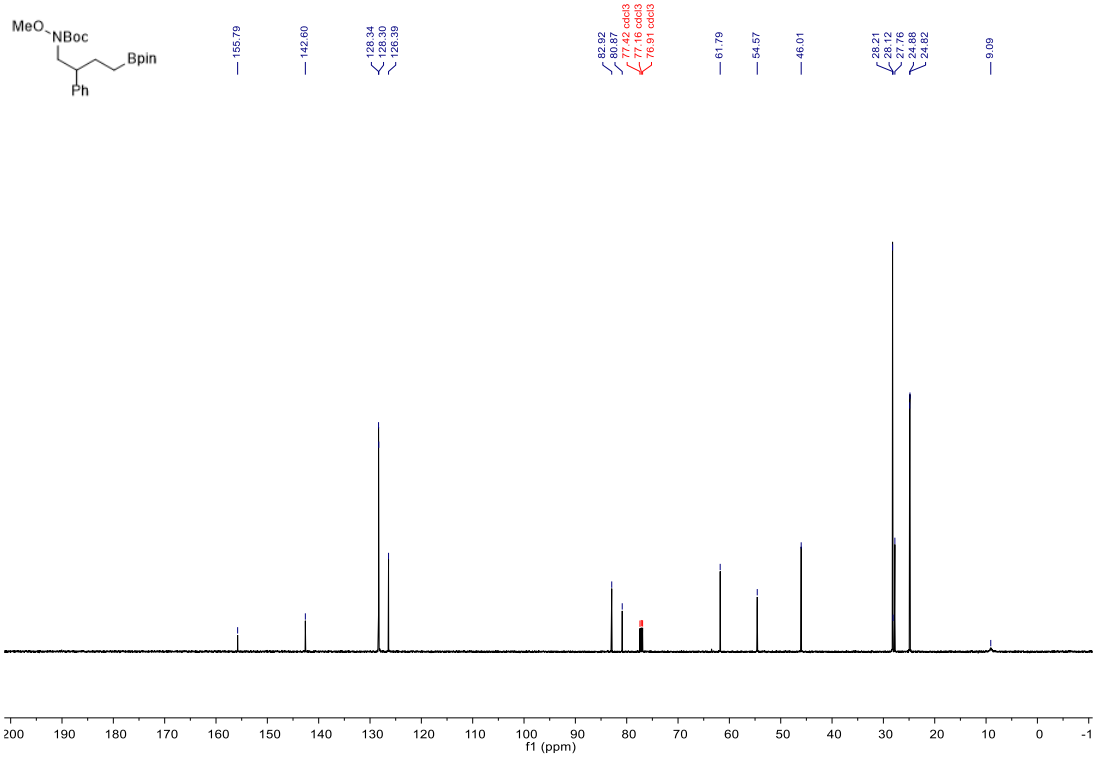
^{13}C NMR (126 MHz, $CDCl_3$) (**2.107**)



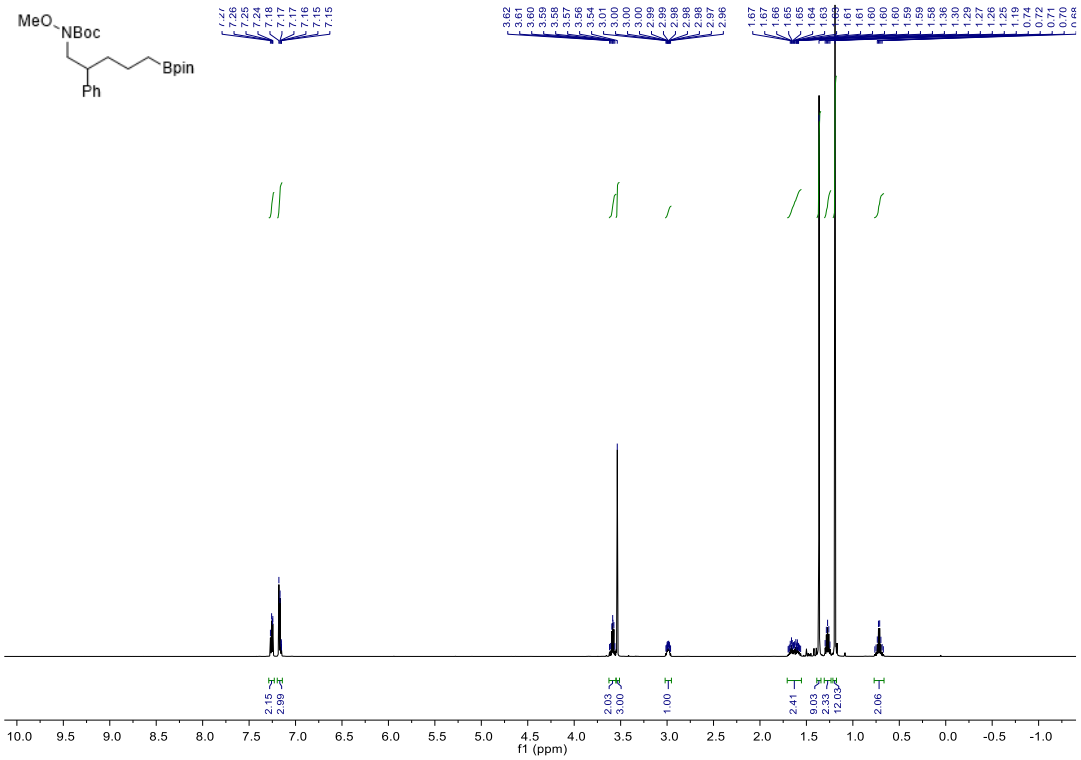
^{1}H NMR (600 MHz, $CDCl_3$) (**2.78**)



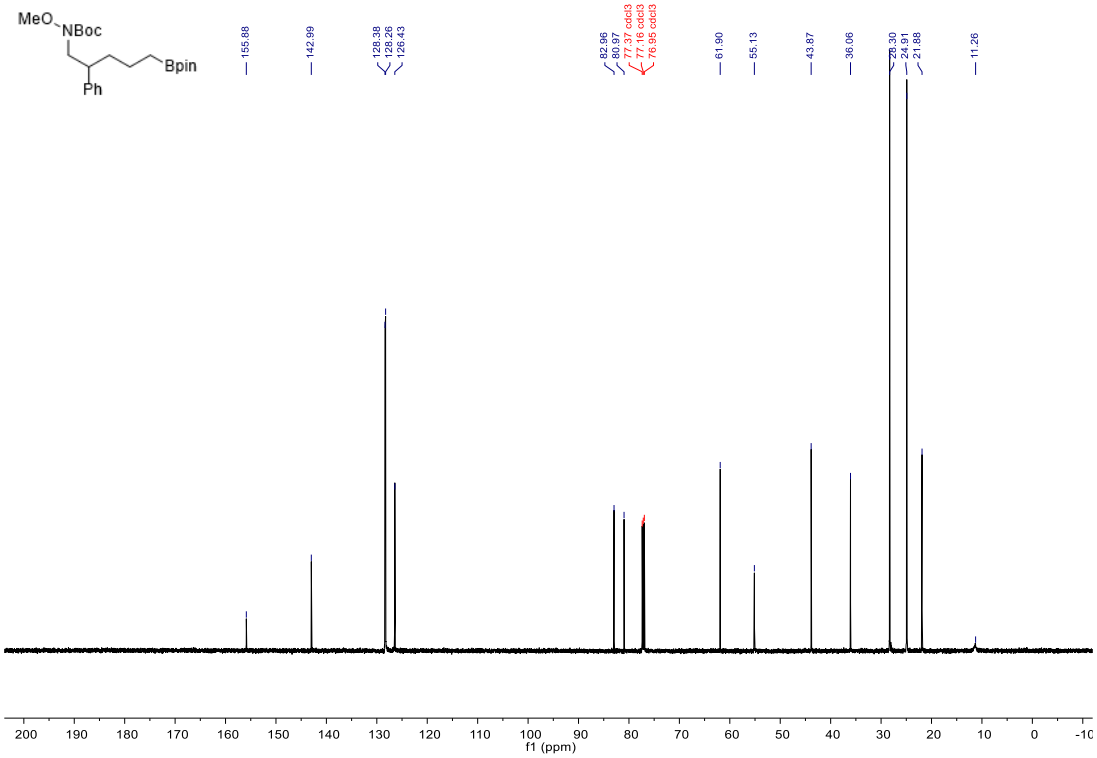
^{13}C NMR (126 MHz, $CDCl_3$) (**2.78**)



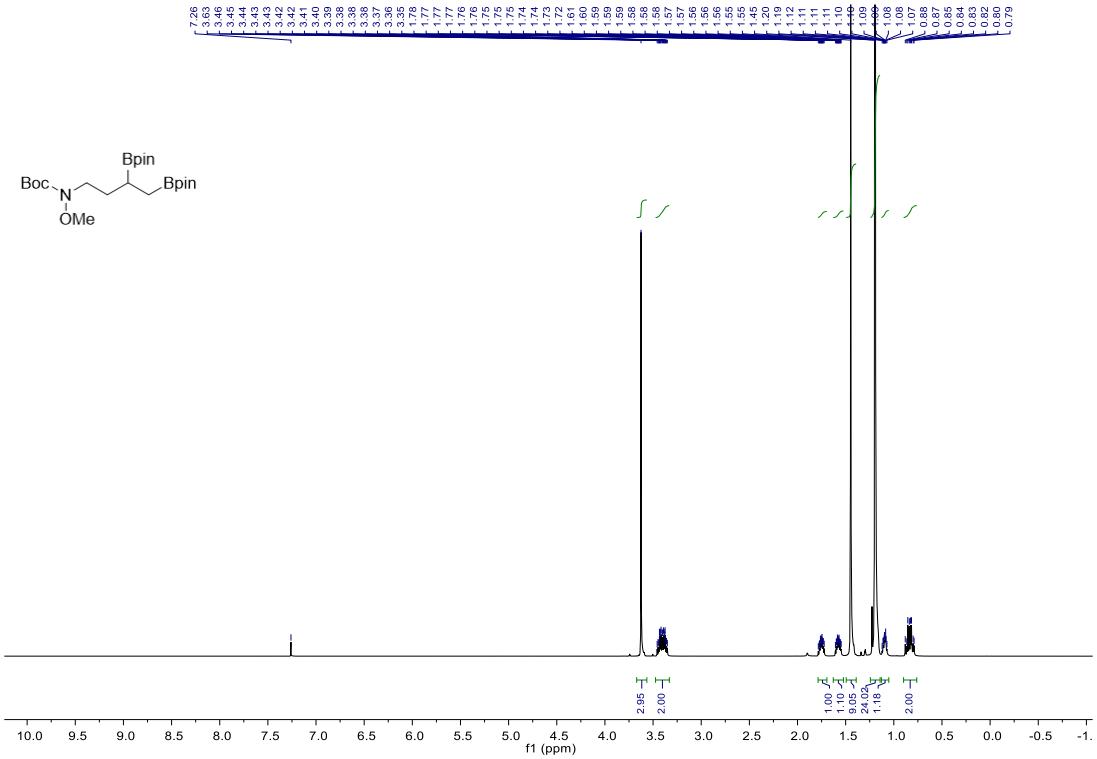
^{1}H NMR (600 MHz, $CDCl_3$) (**SI-6**)



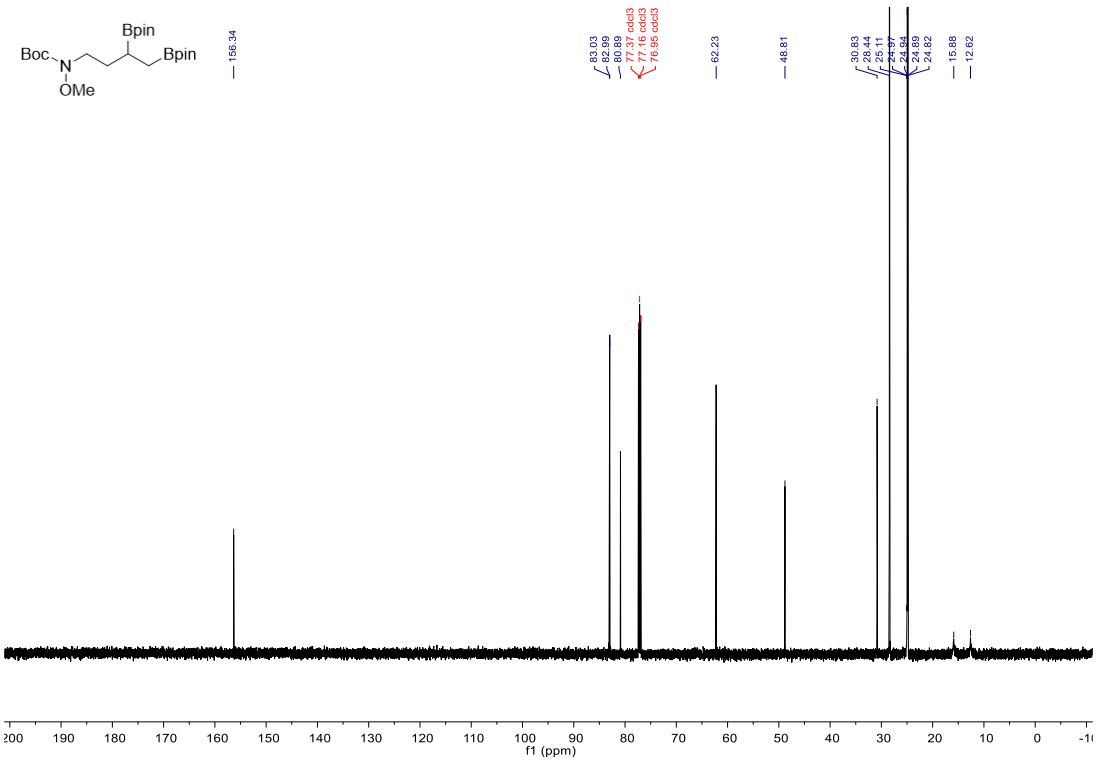
^{13}C NMR (151 MHz, $CDCl_3$) (**SI-6**)



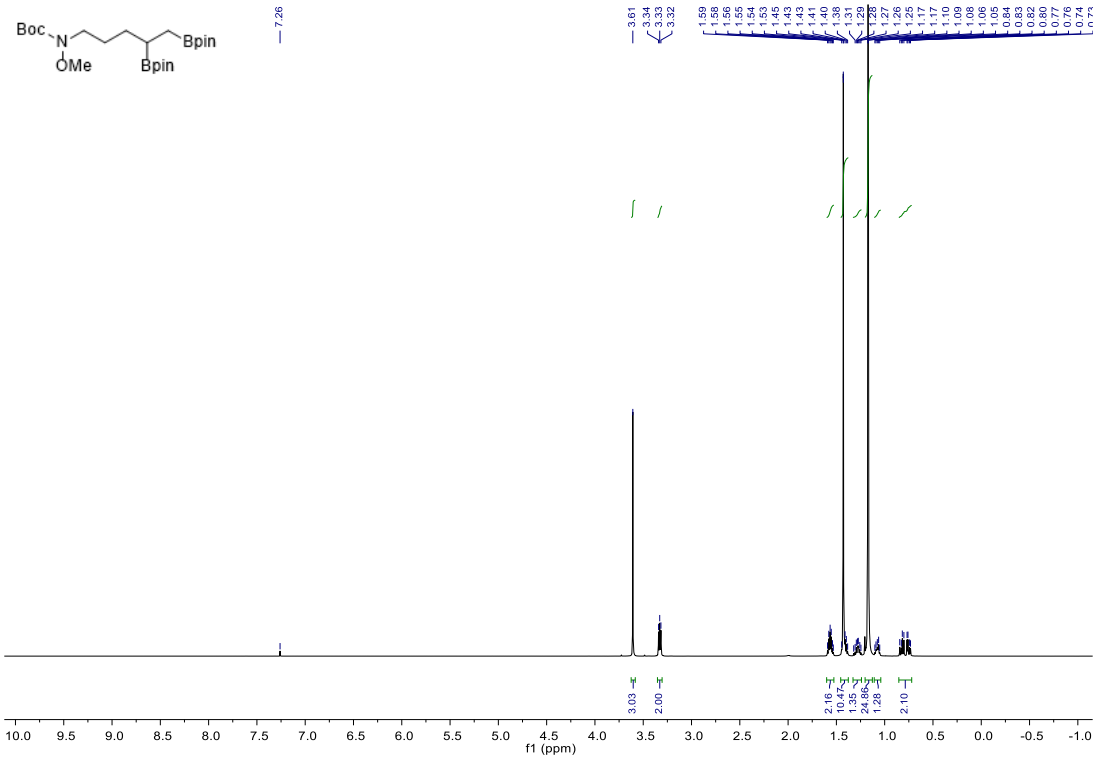
^{1}H NMR (600 MHz, $CDCl_3$) (**2.92**)



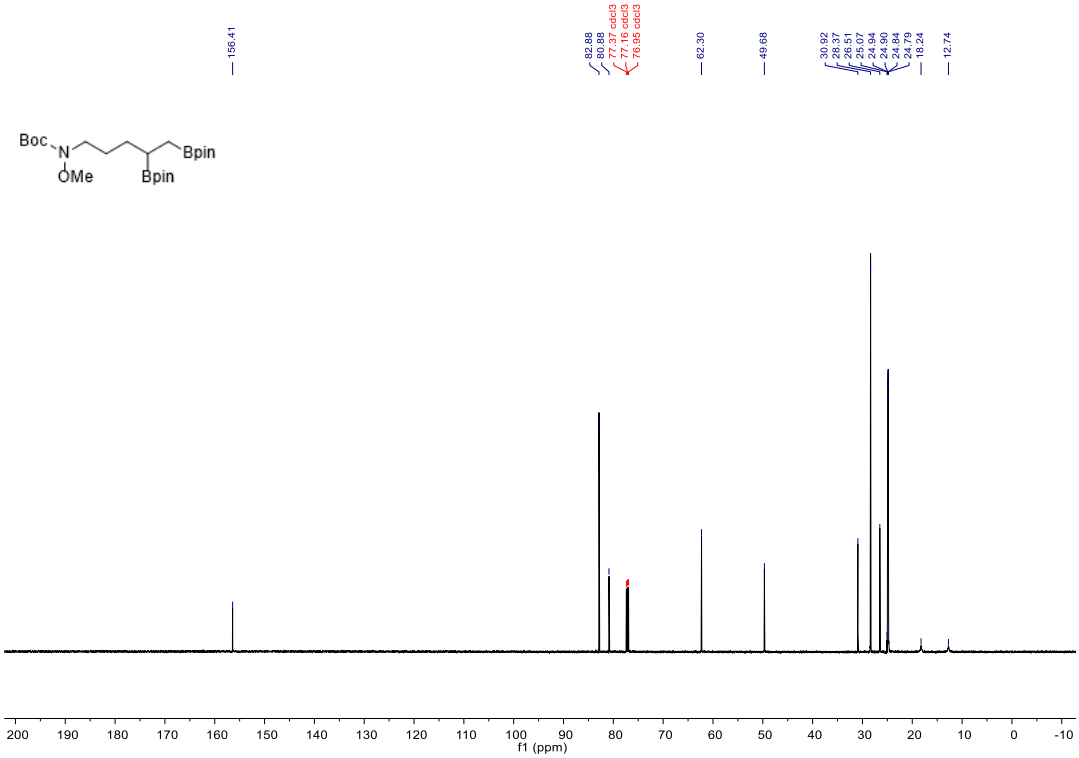
^{13}C NMR (151 MHz, $CDCl_3$) (**2.92**)



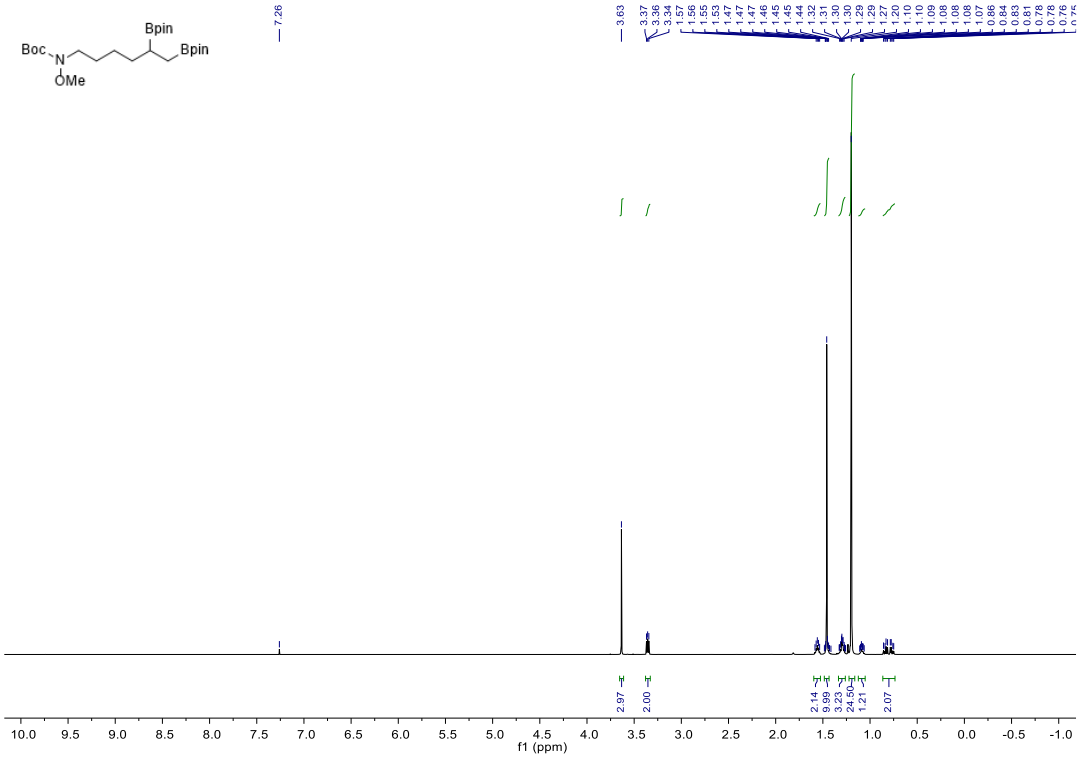
^{1}H NMR (600 MHz, $CDCl_3$) (**2.96**)



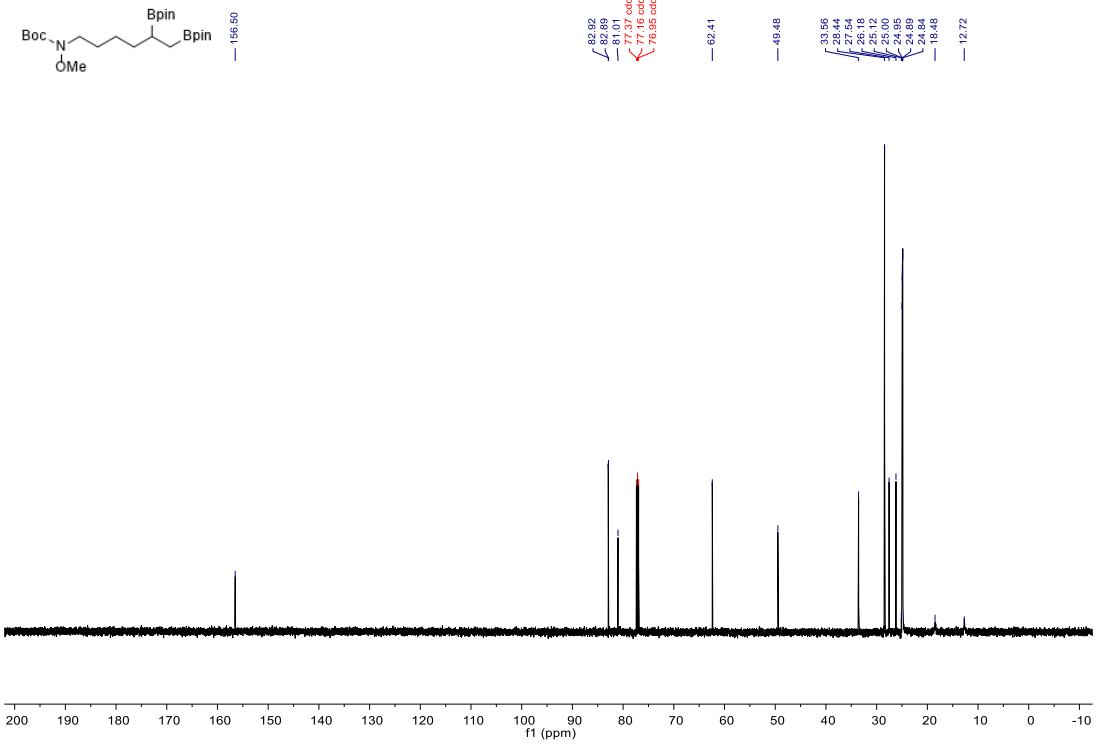
^{13}C NMR (151 MHz, $CDCl_3$) (**2.96**)



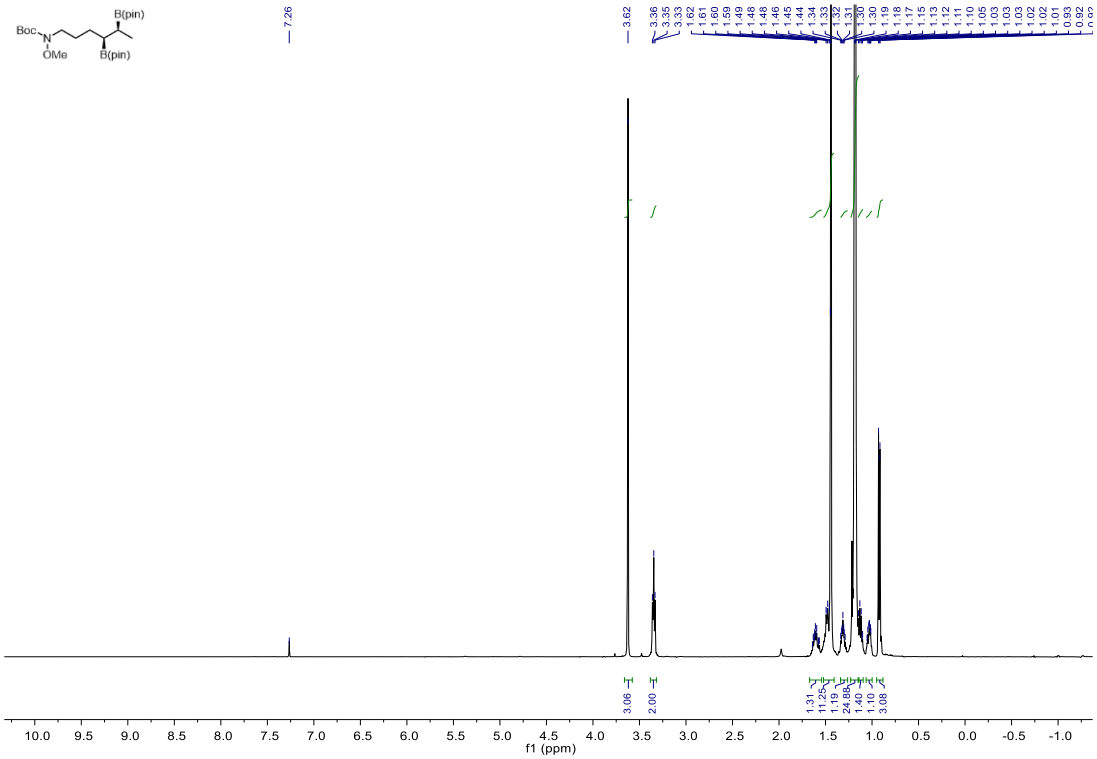
^{1}H NMR (600 MHz, $CDCl_3$) (**2.100**)



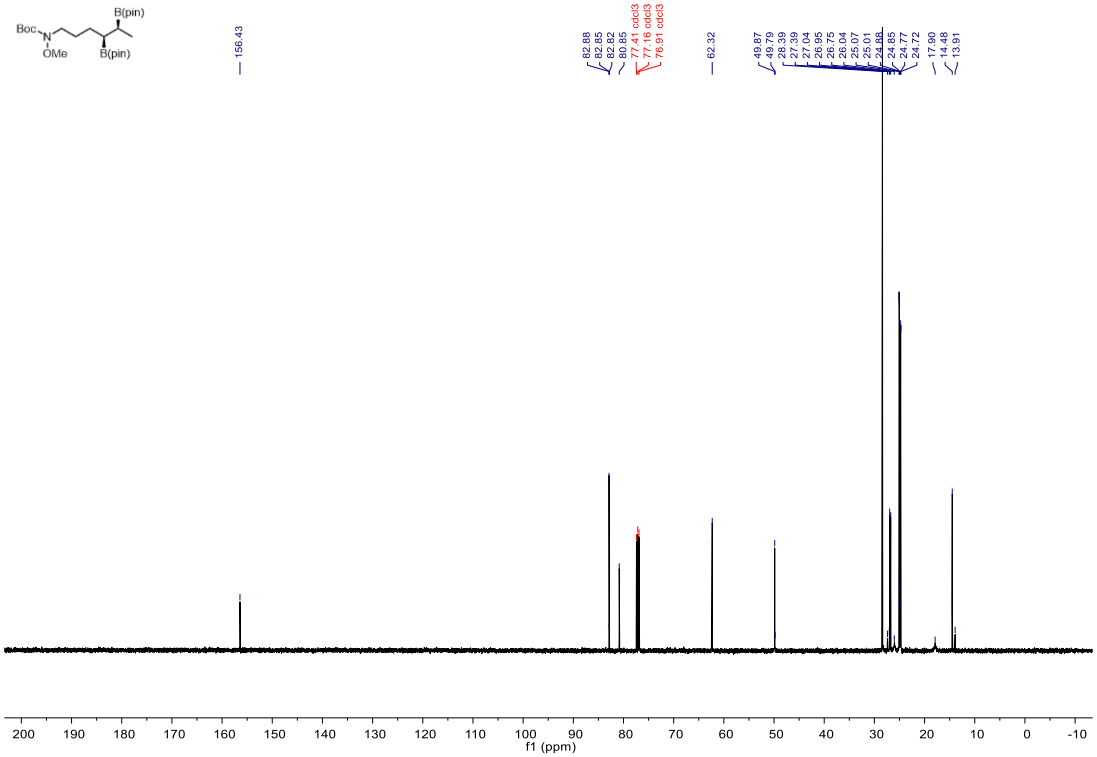
^{13}C NMR (151 MHz, $CDCl_3$) (**2.100**)



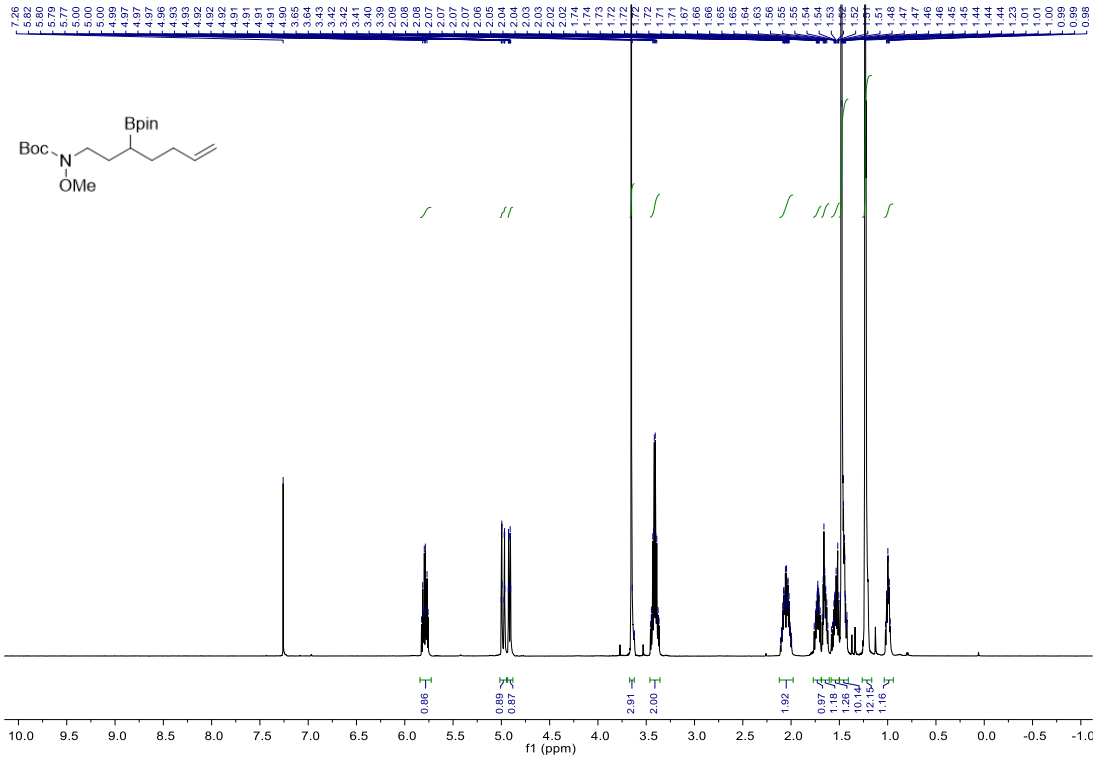
^{1}H NMR (500 MHz, $CDCl_3$) (**2.107**)



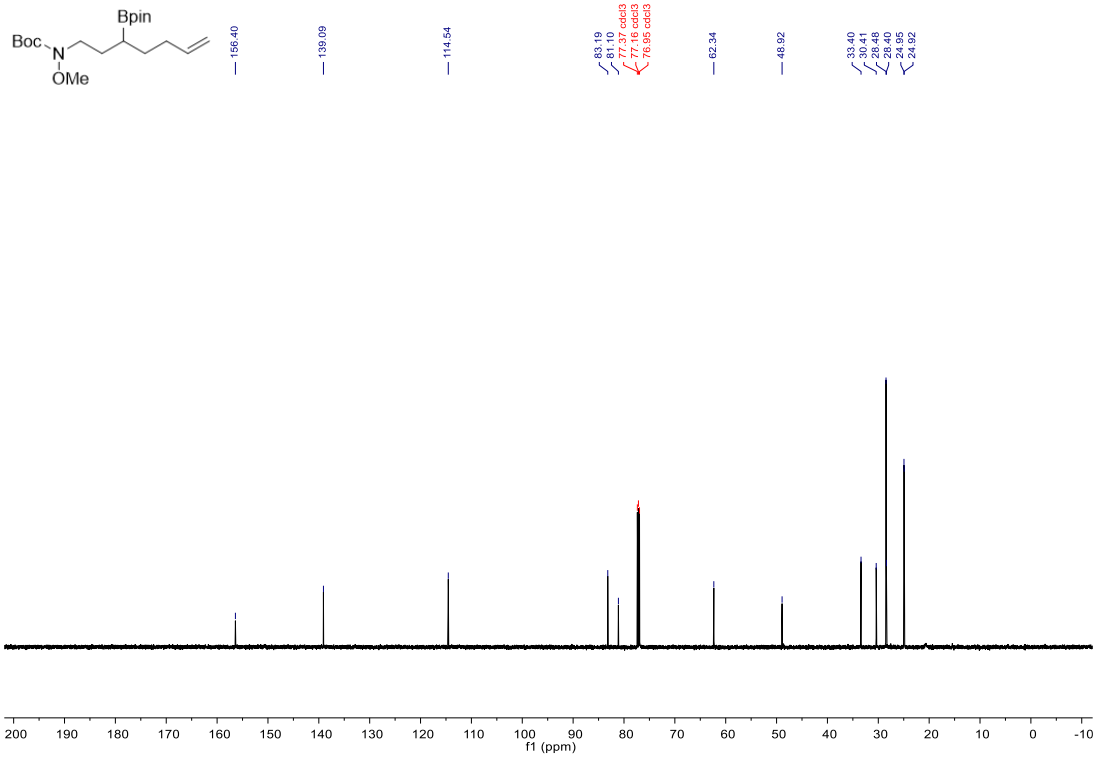
^{13}C NMR (126 MHz, $CDCl_3$) (**2.107**)



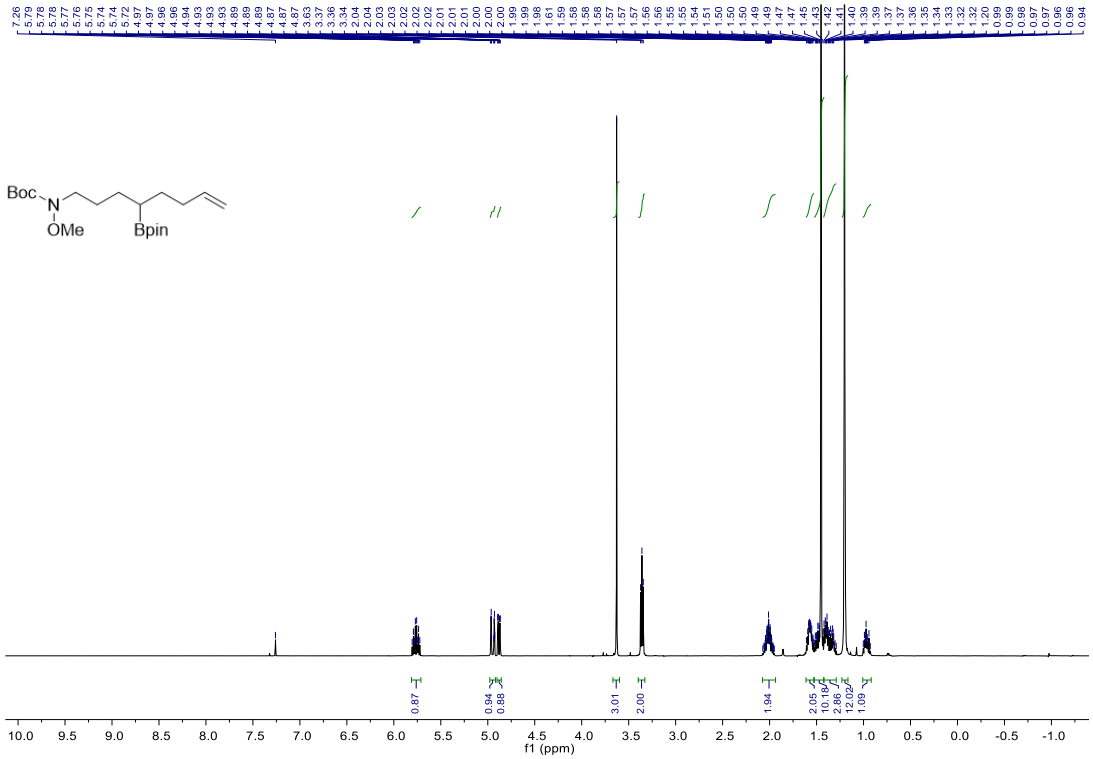
^{1}H NMR (600 MHz, $CDCl_3$) (**SI-7**)



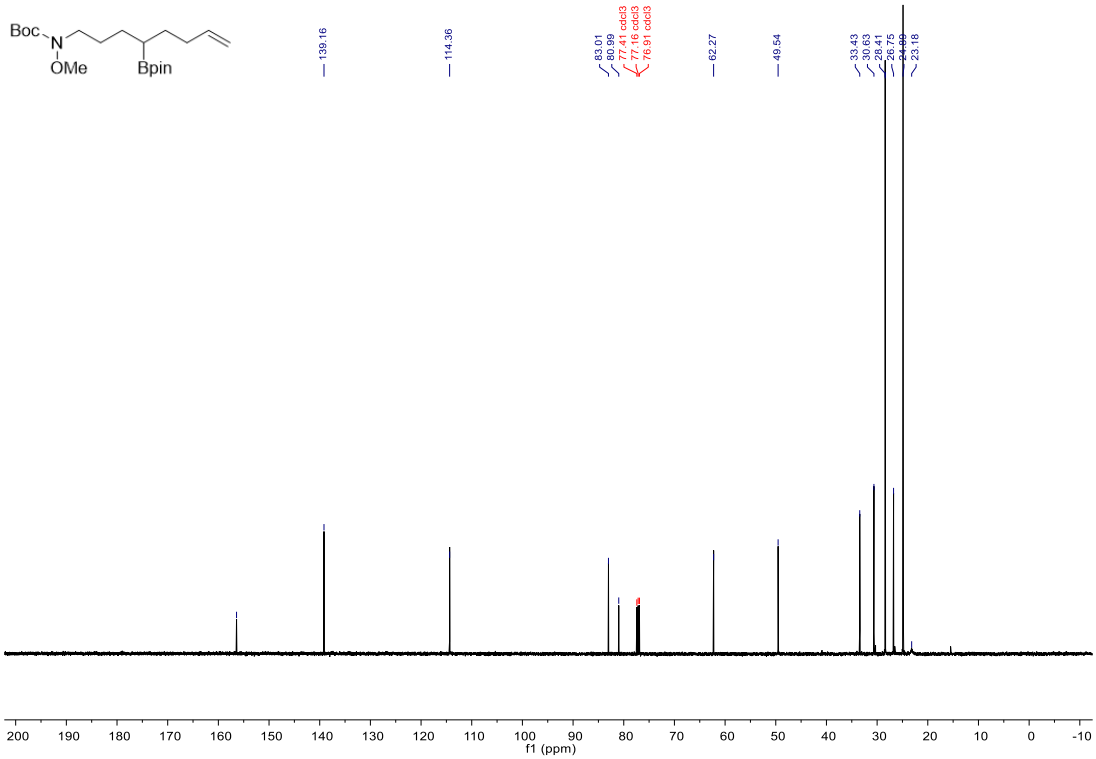
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-7**)



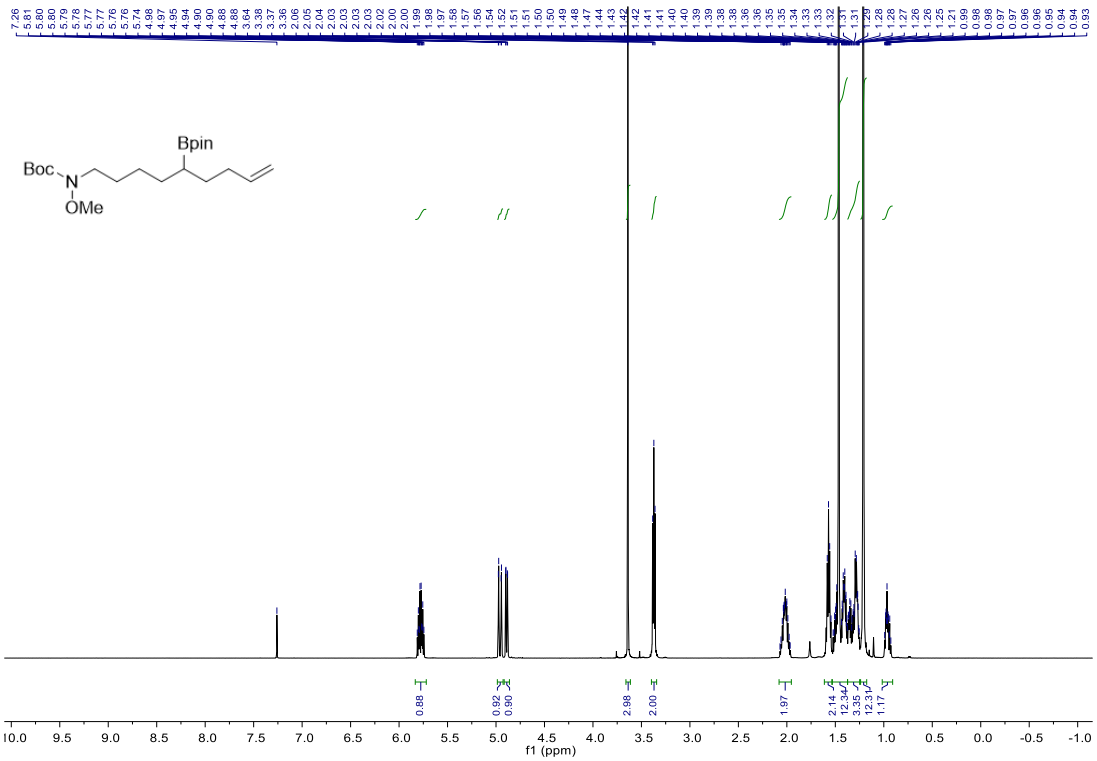
^{1}H NMR (500 MHz, $CDCl_3$) (**SI-8**)



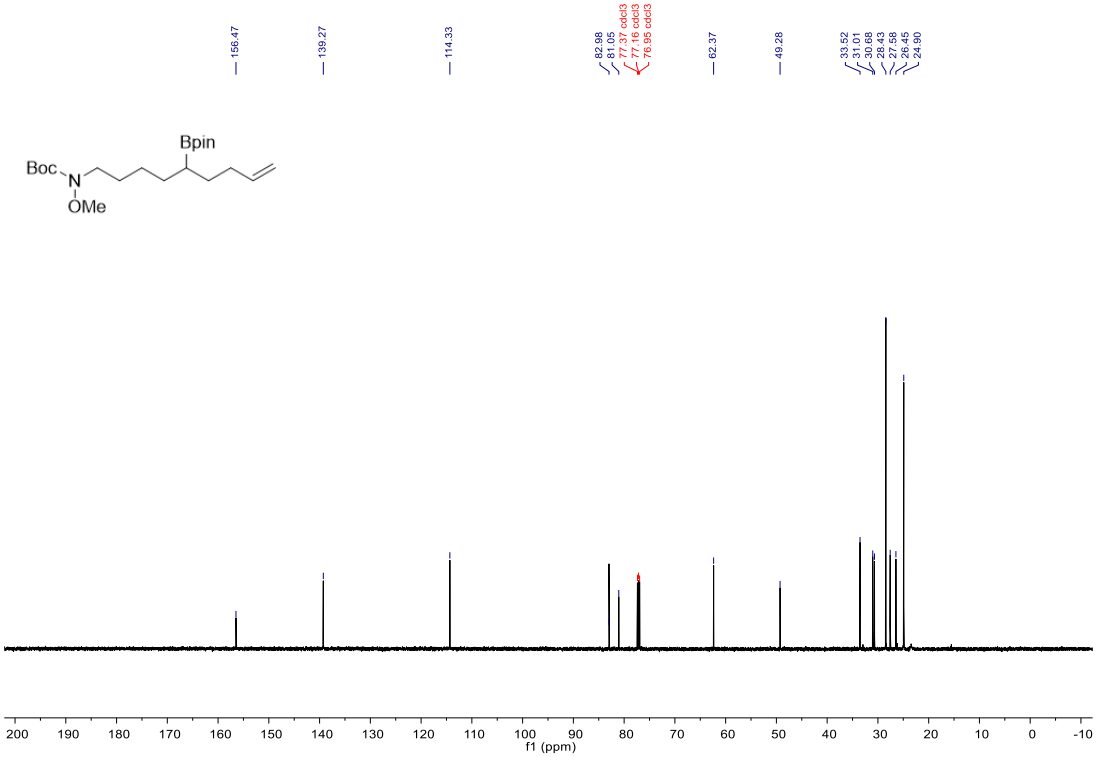
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-8**)



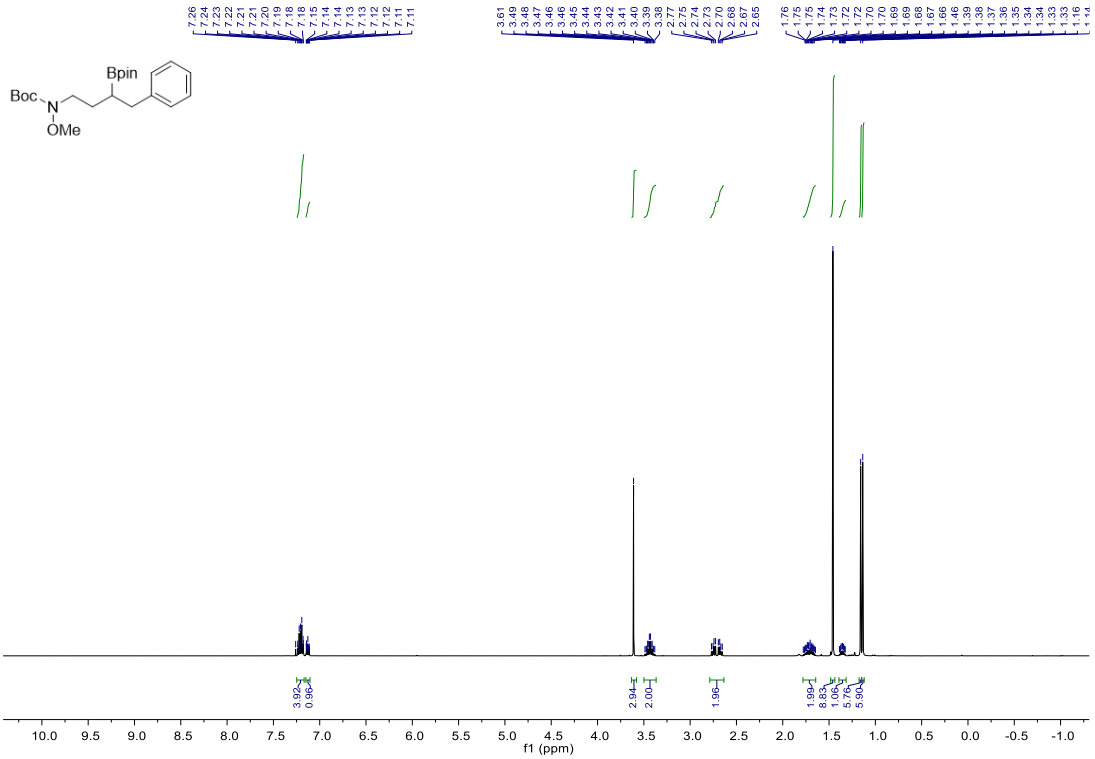
^{1}H NMR (600 MHz, $CDCl_3$) (**SI-9**)



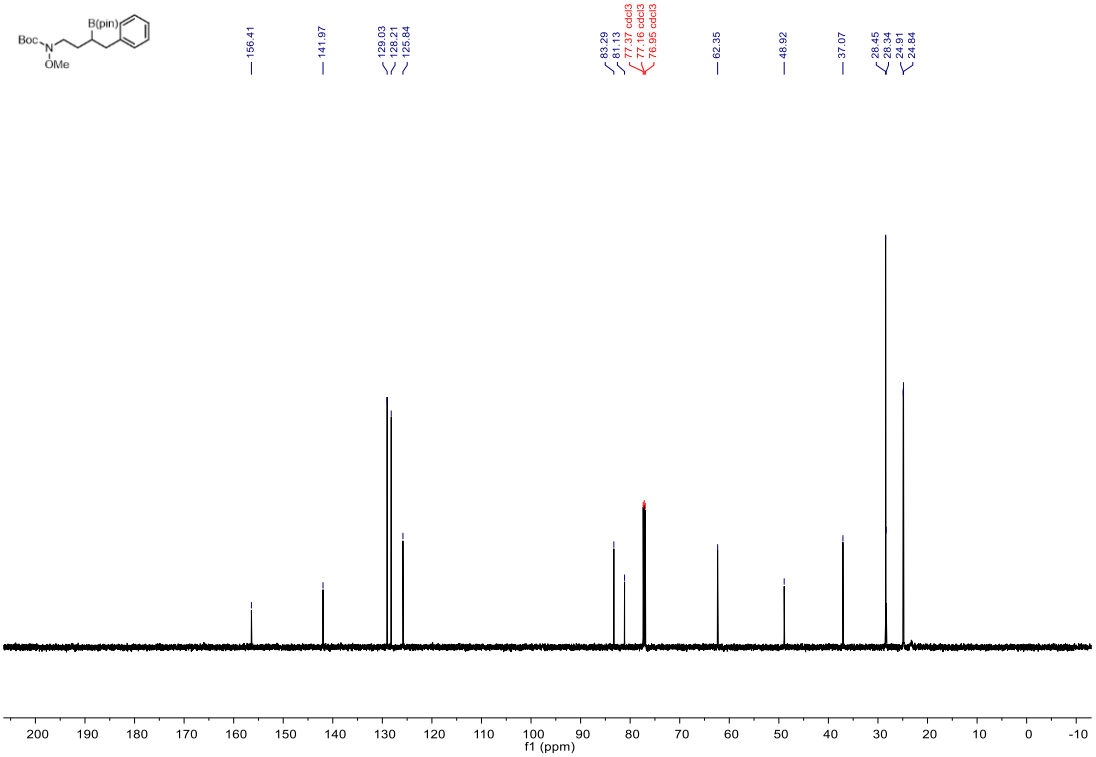
^{13}C NMR (151 MHz, $CDCl_3$) (**SI-9**)



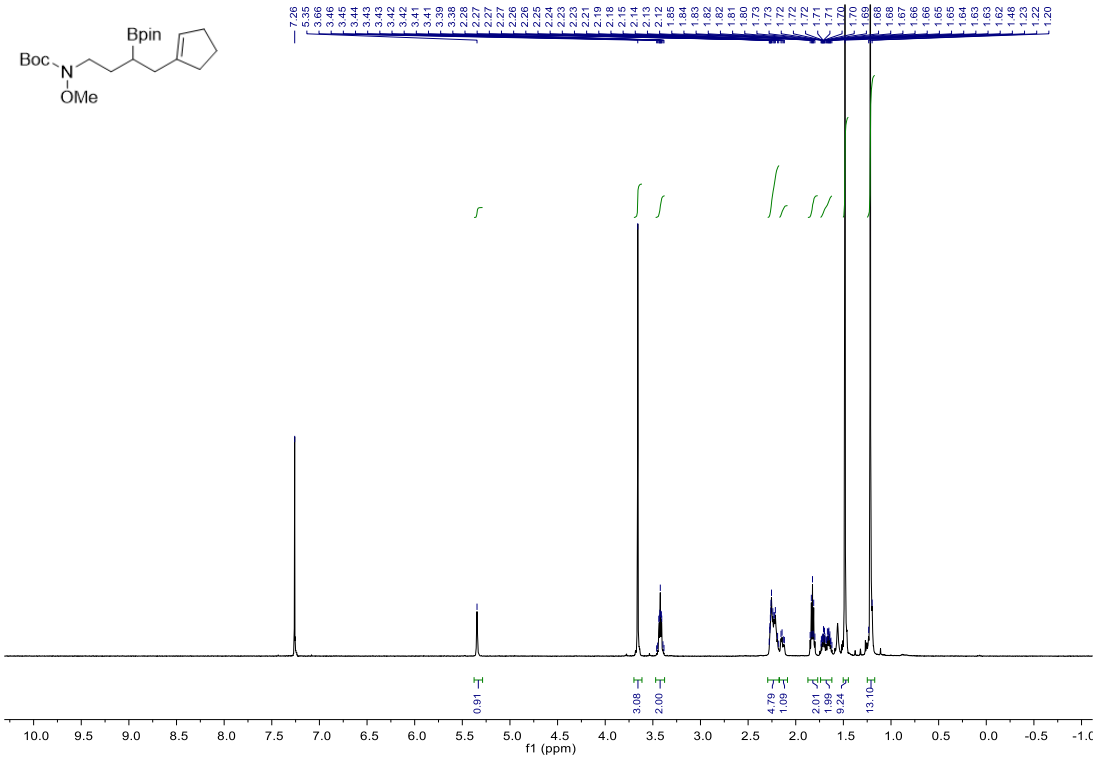
^{1}H NMR (500 MHz, $CDCl_3$) (**SI-10**)



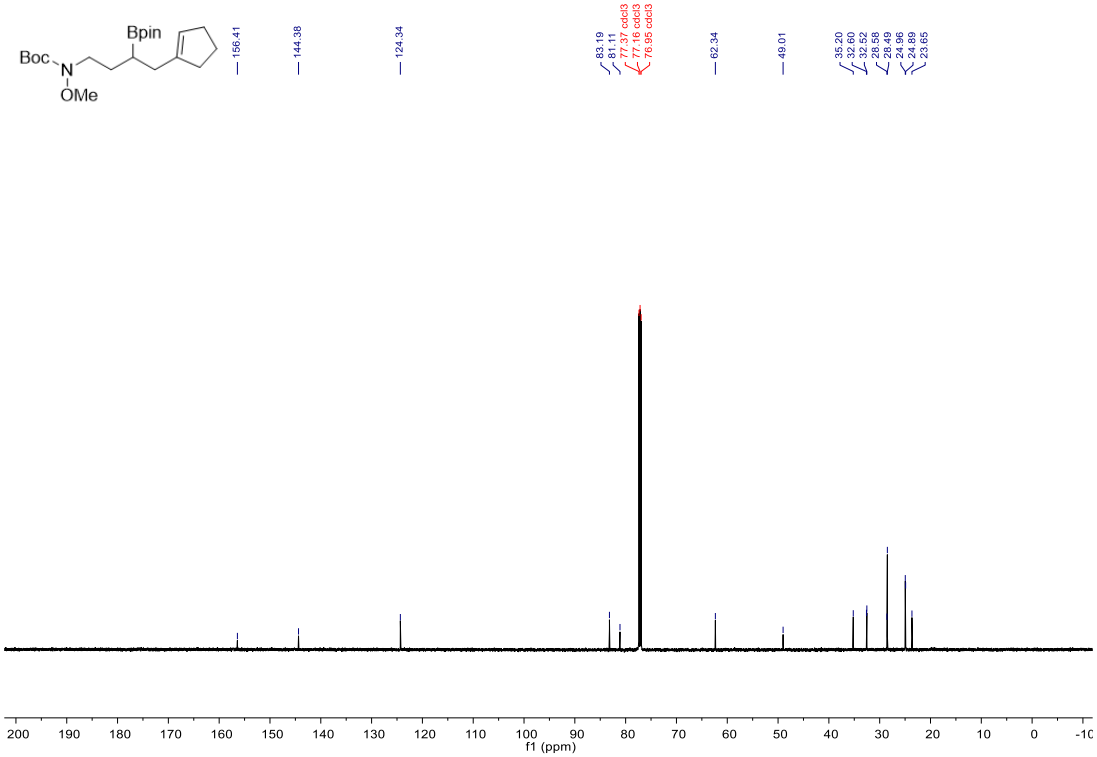
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-10**)



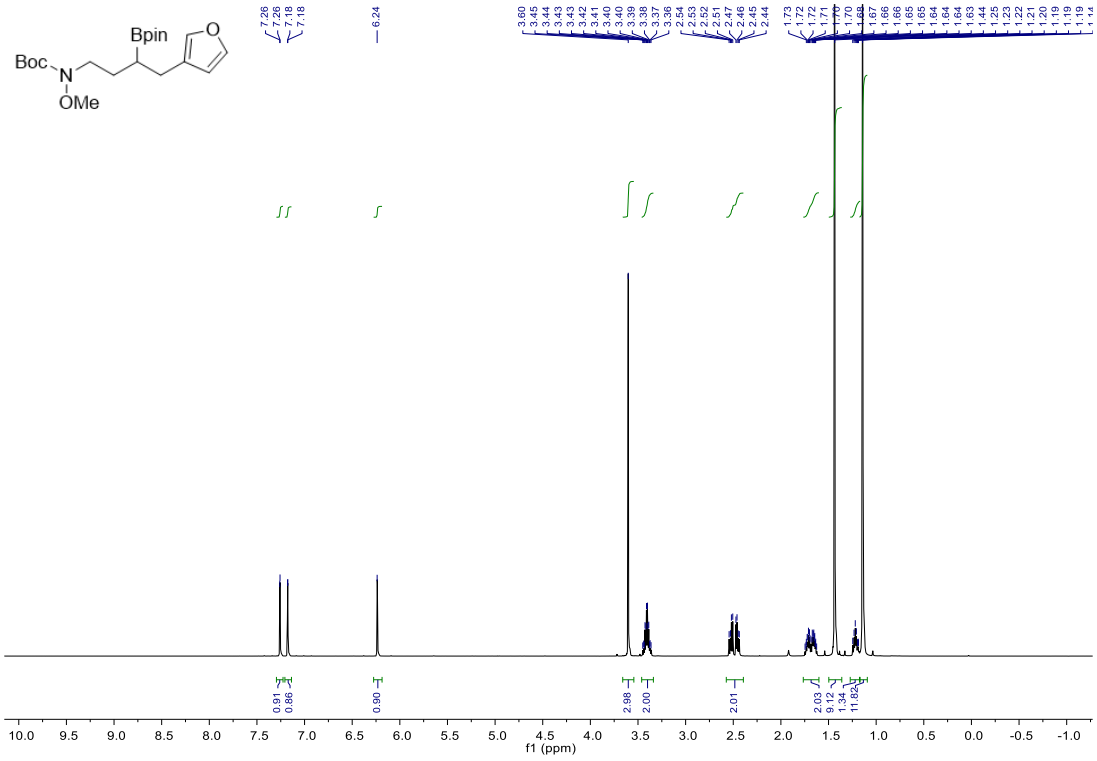
^{1}H NMR (600 MHz, $CDCl_3$) (**SI-11**)



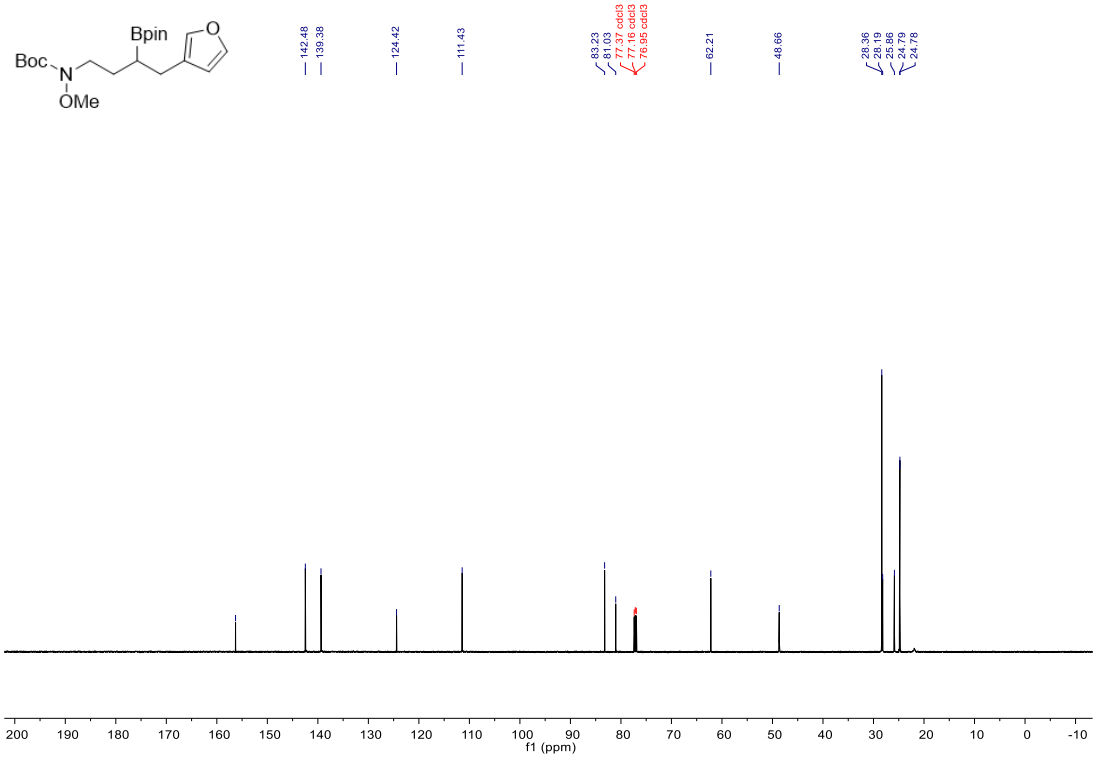
^{13}C NMR (151 MHz, $CDCl_3$) (**SI-11**)



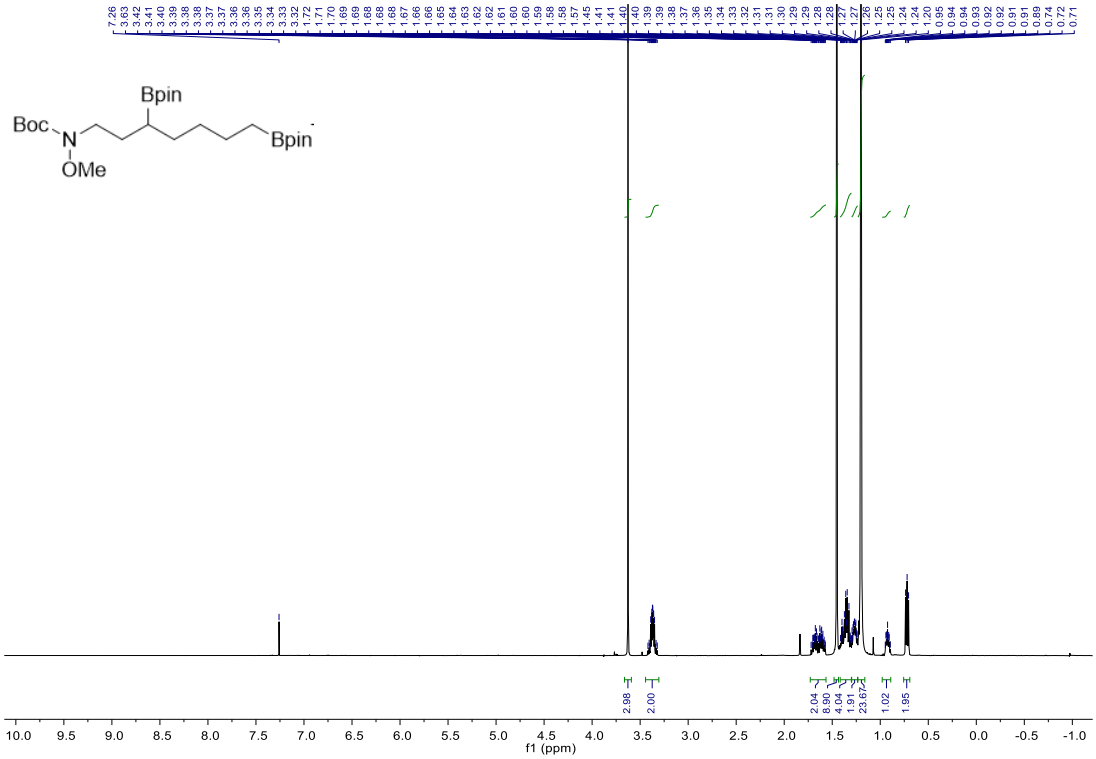
^{1}H NMR (600 MHz, $CDCl_3$) (**SI-12**)



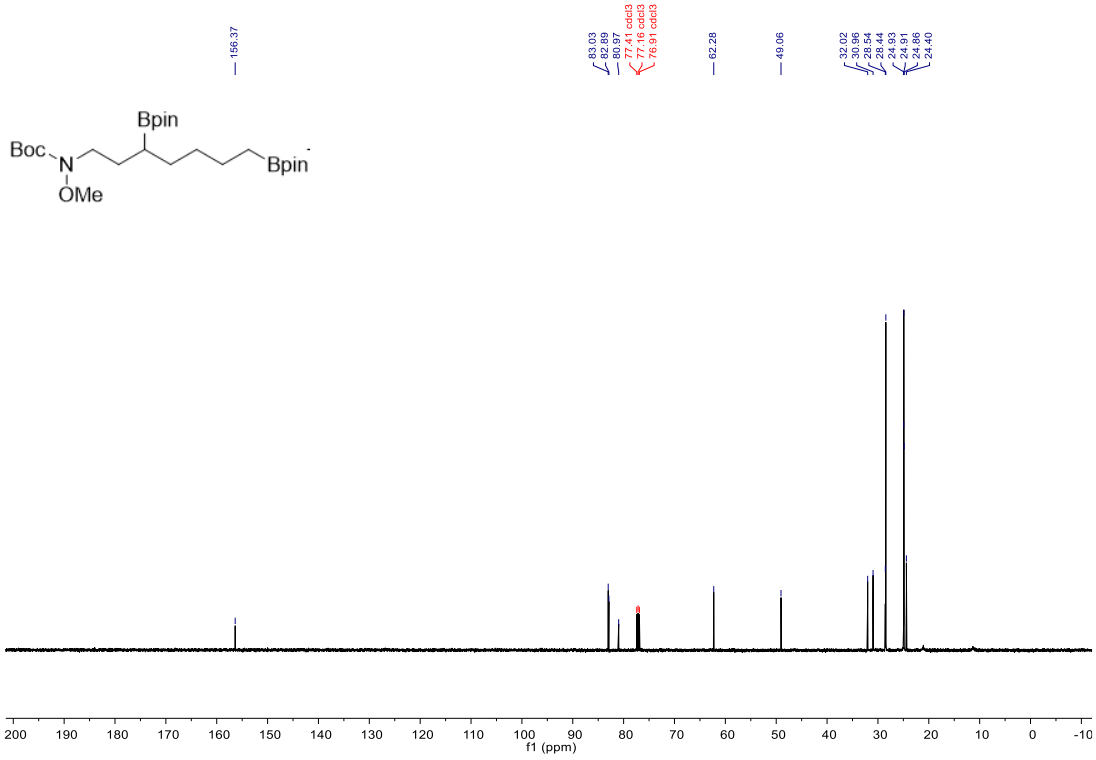
^{13}C NMR (151 MHz, $CDCl_3$) (**SI-12**)



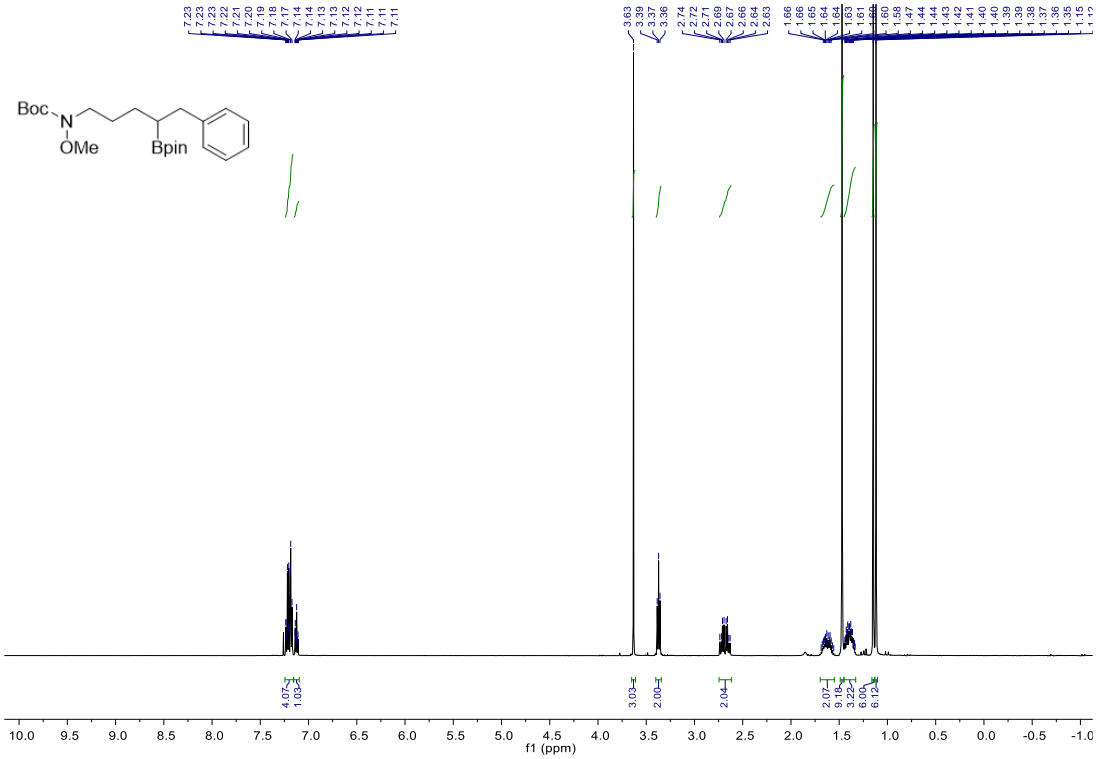
^{1}H NMR (500 MHz, $CDCl_3$) (**SI-13**)



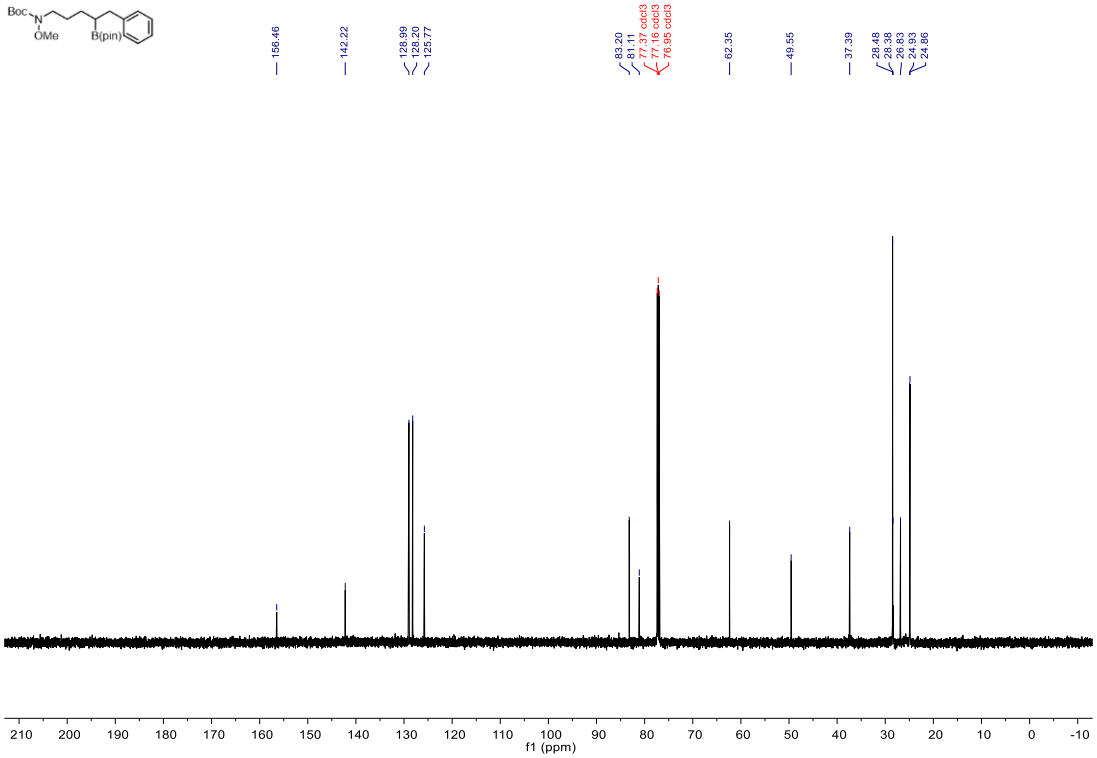
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-13**)



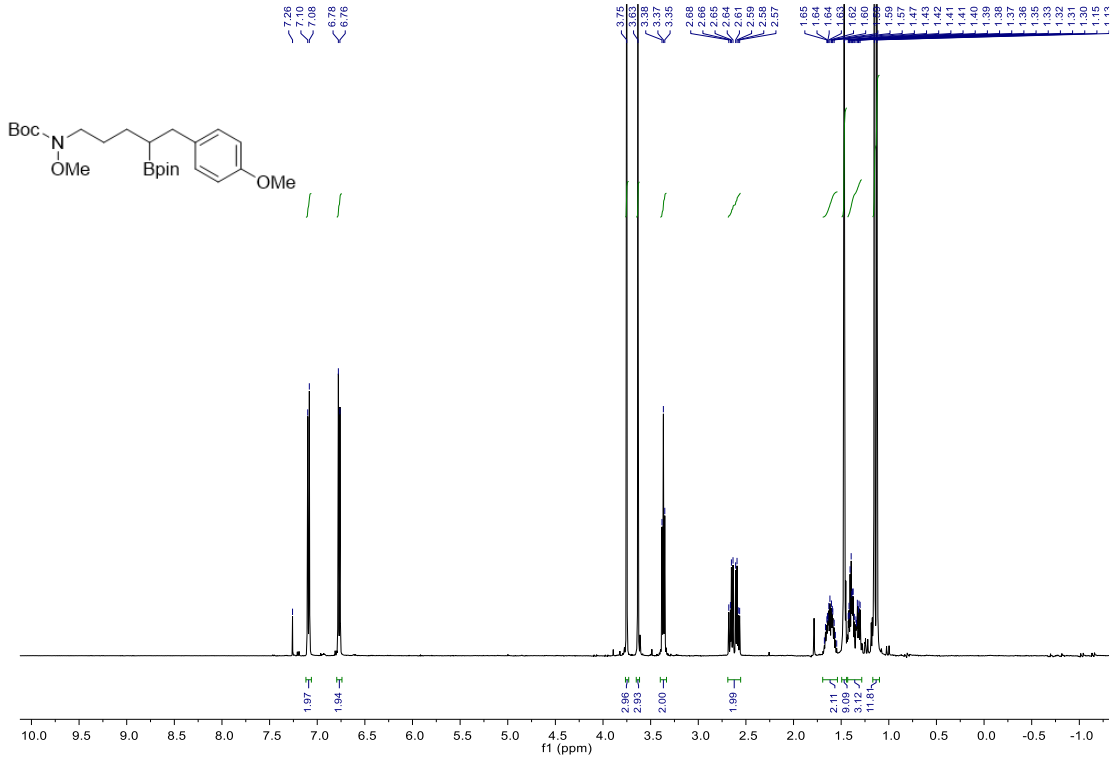
^{1}H NMR (500 MHz, $CDCl_3$) (**SI-14**)



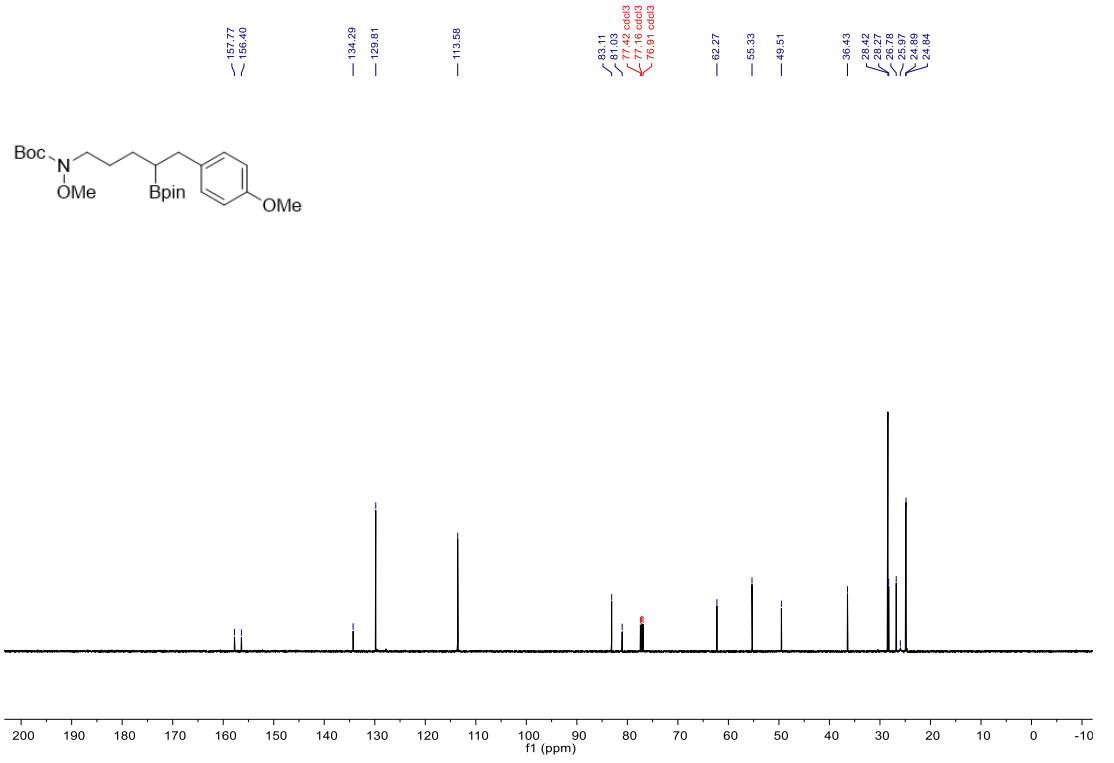
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-14**)



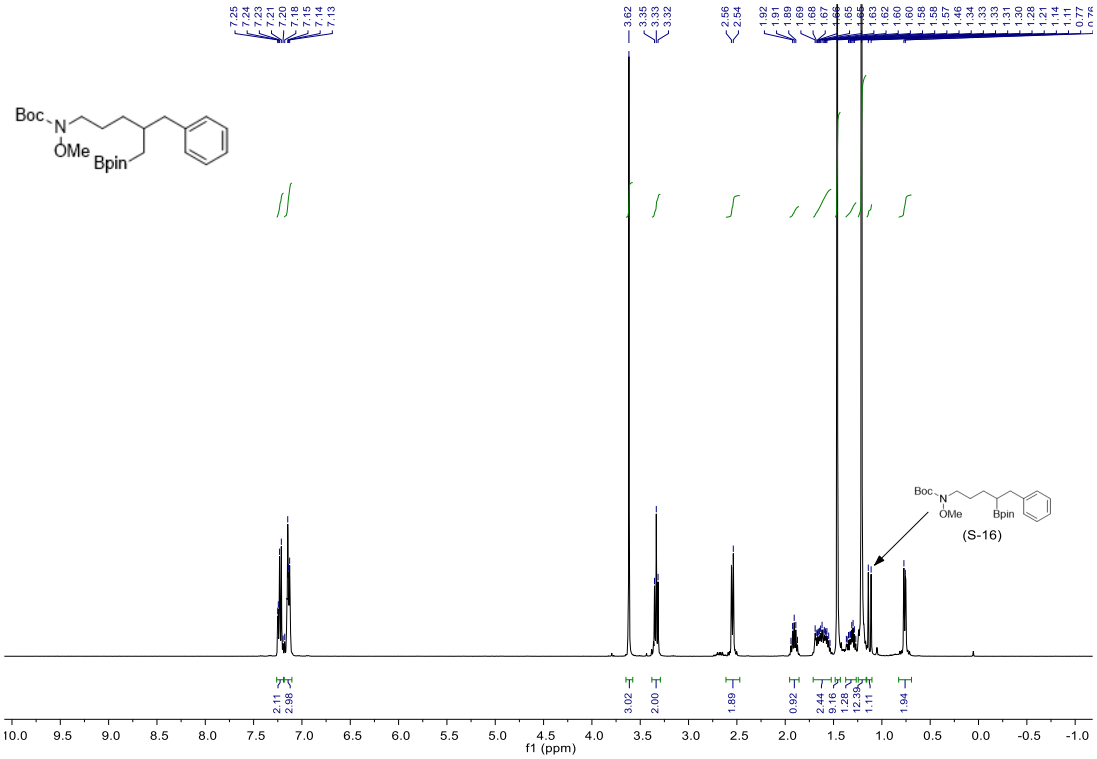
^{1}H NMR (500 MHz, $CDCl_3$) (**SI-15**)



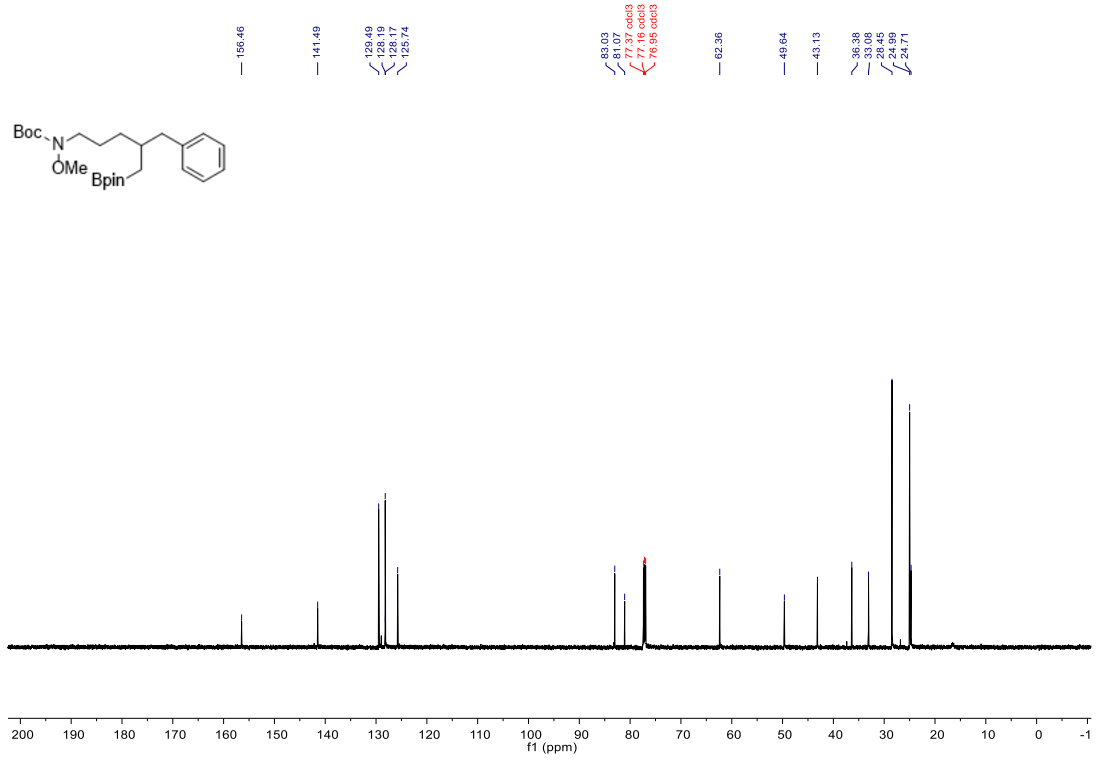
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-15**)



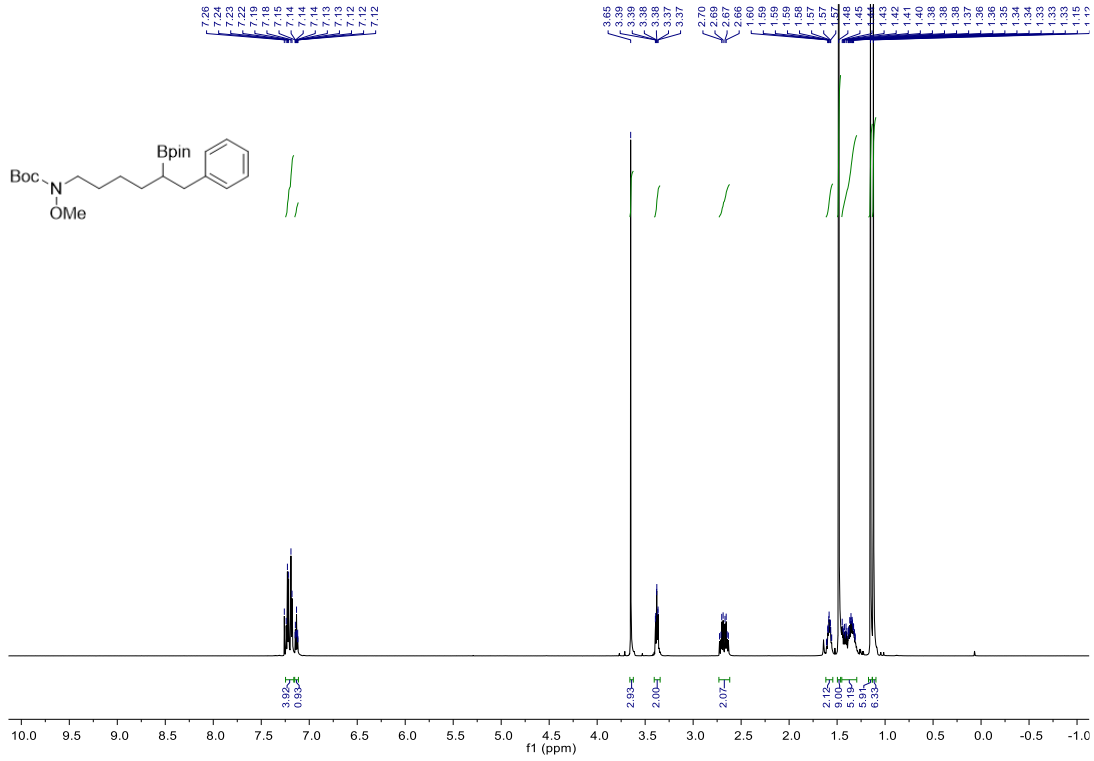
^{1}H NMR (400 MHz, $CDCl_3$) (**SI-16**)



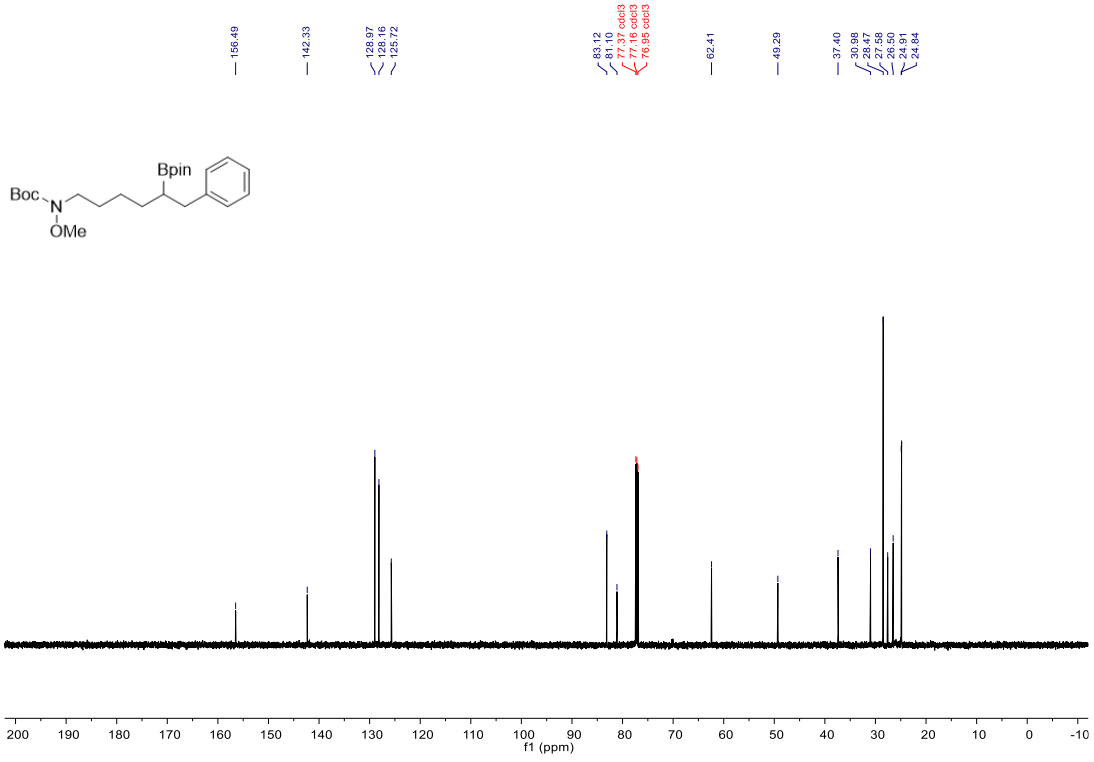
^{13}C NMR (151 MHz, $CDCl_3$) (**SI-16**)



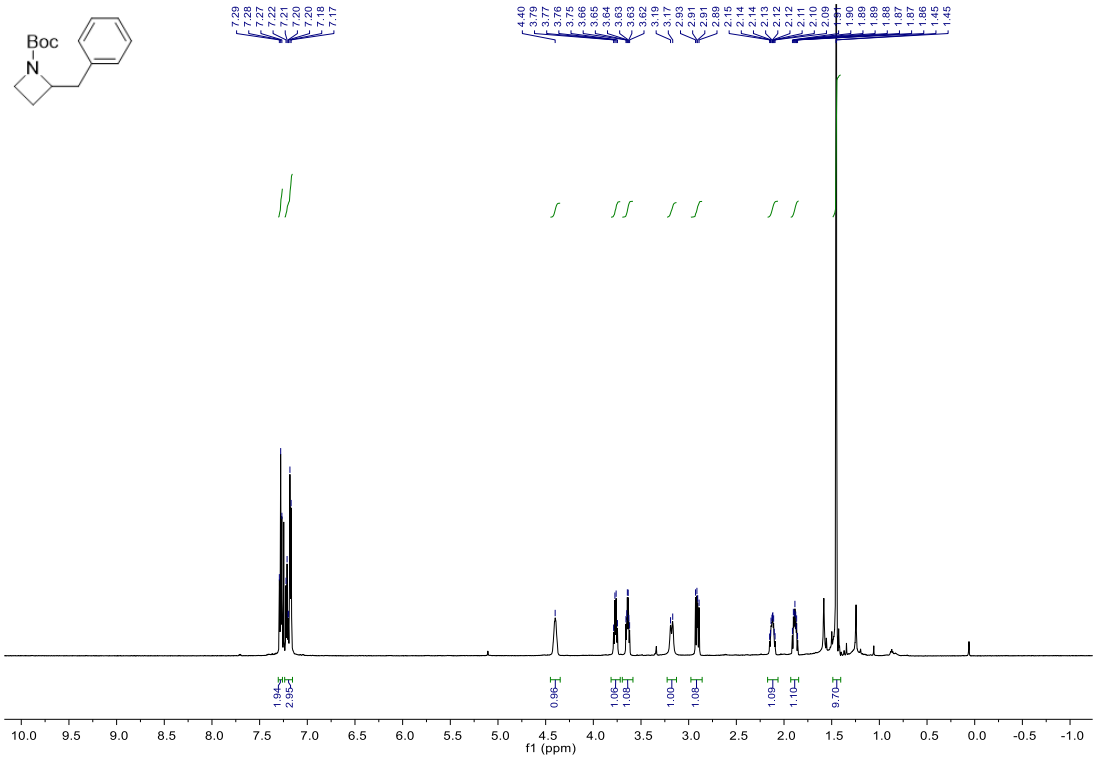
^{1}H NMR (600 MHz, $CDCl_3$) (**SI-17**)



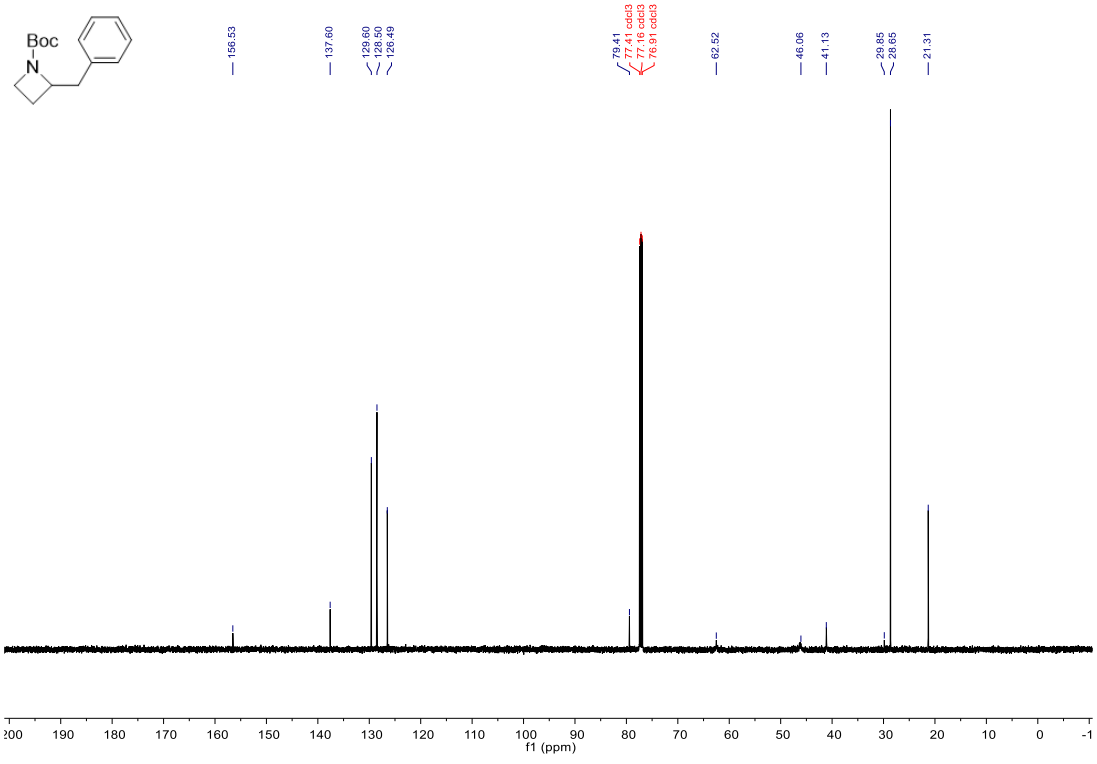
^{13}C NMR (151 MHz, $CDCl_3$) (**SI-17**)



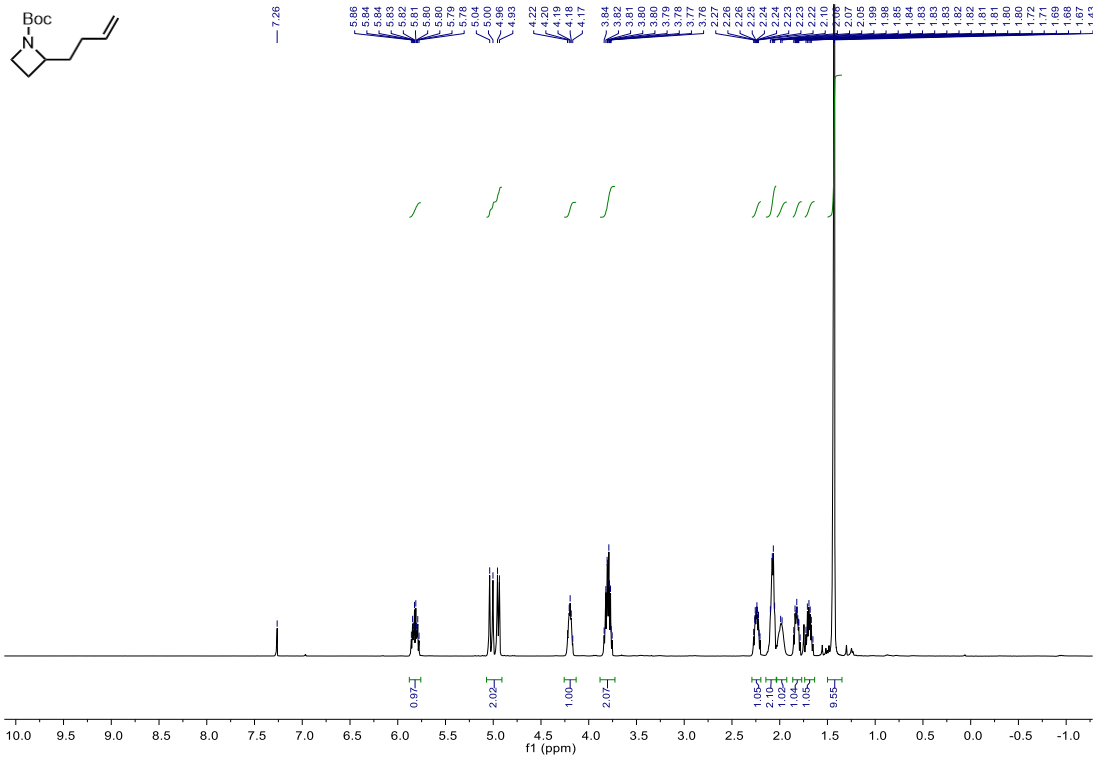
^{1}H NMR (600 MHz, $CDCl_3$) (**2.79**)



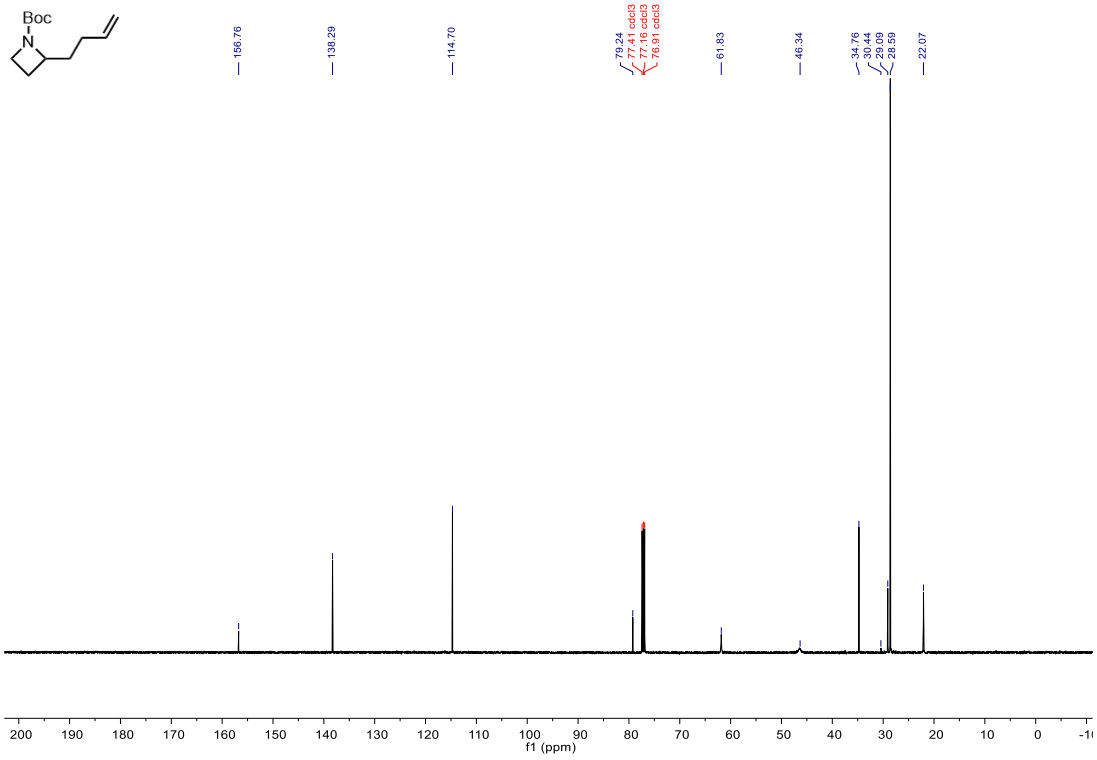
^{13}C NMR (151 MHz, $CDCl_3$) (**2.79**)



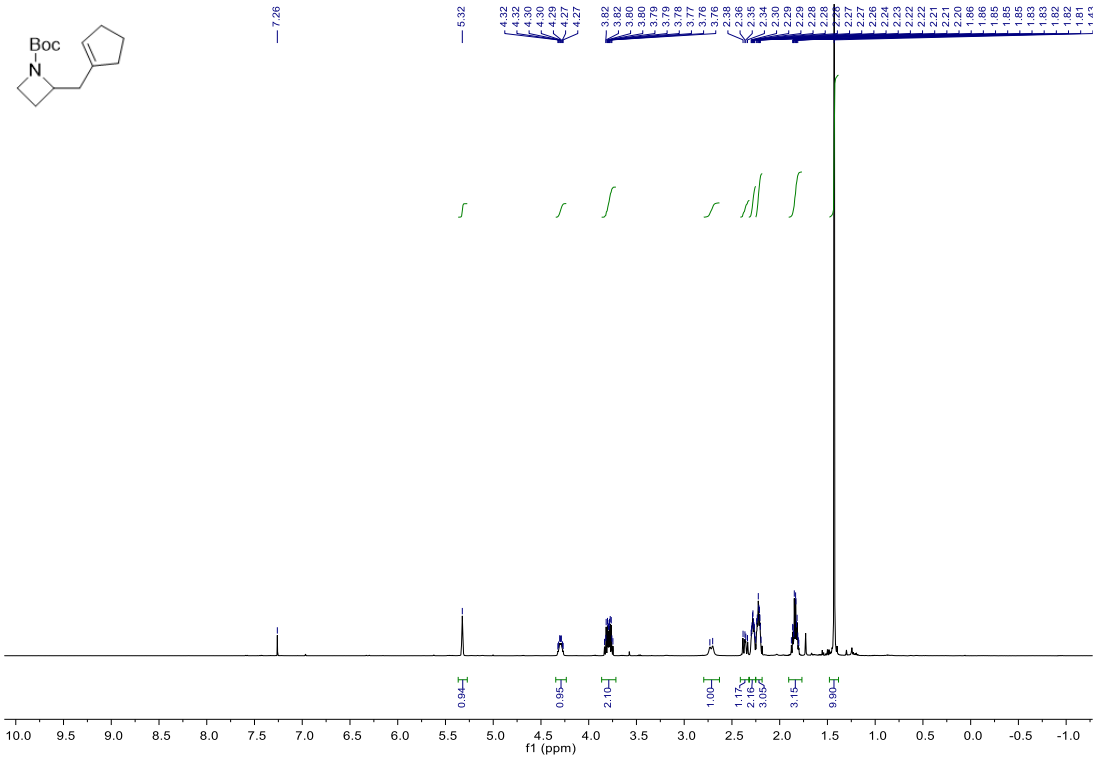
^{1}H NMR (500 MHz, $CDCl_3$) (**2.80**)



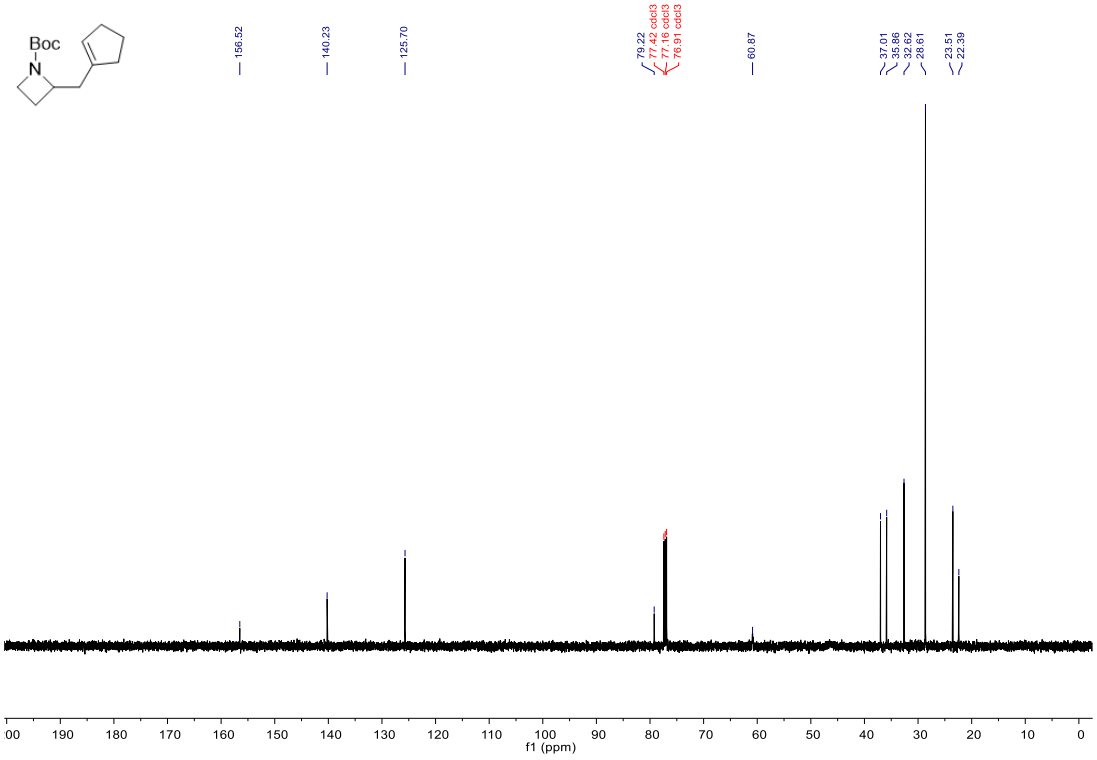
^{13}C NMR (126 MHz, $CDCl_3$) (**2.80**)



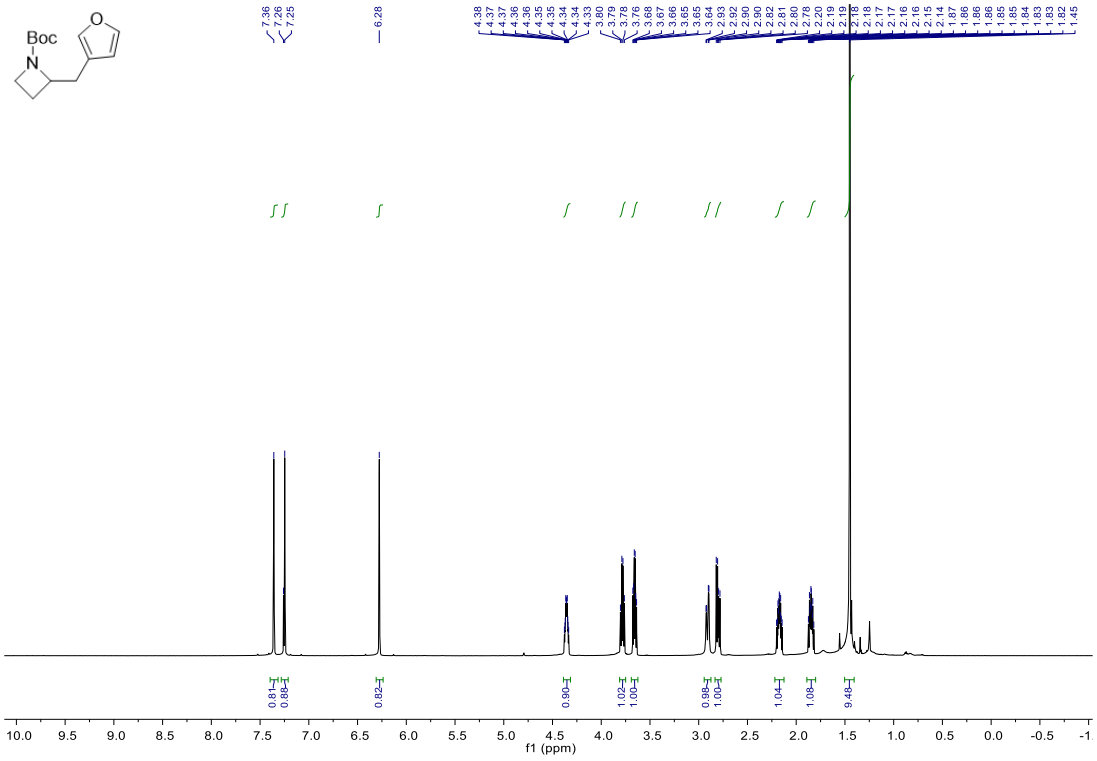
^{1}H NMR (500 MHz, $CDCl_3$) (**2.81**)



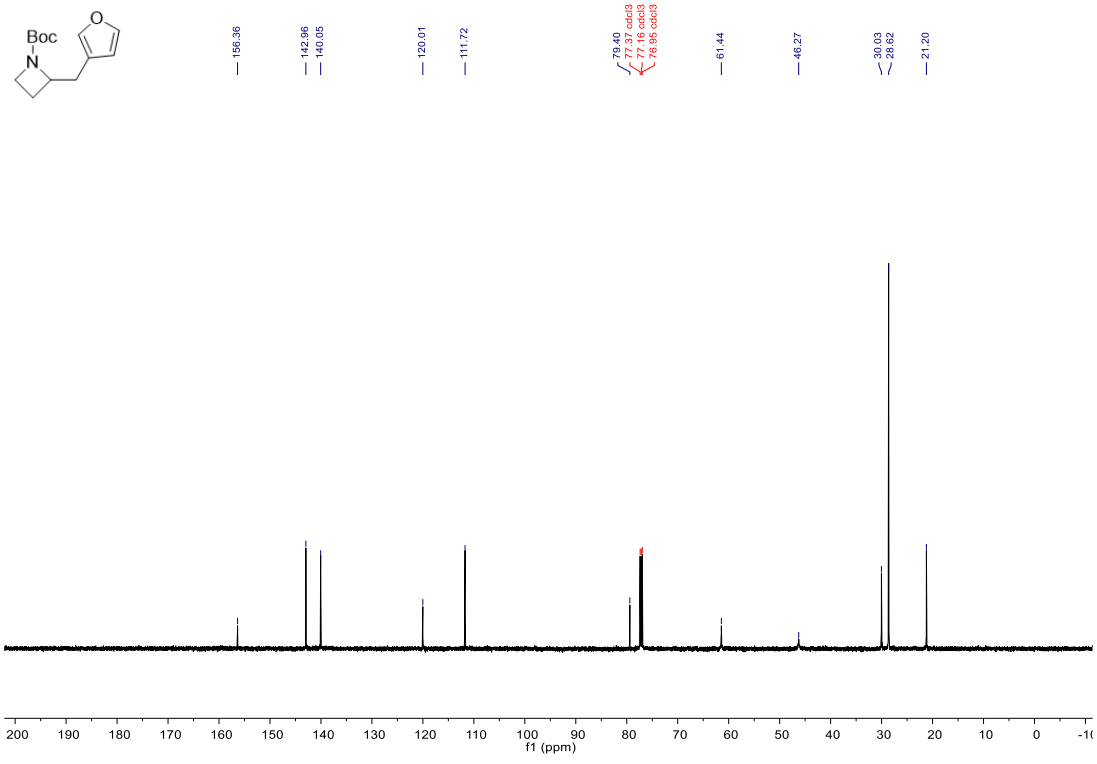
^{13}C NMR (126 MHz, $CDCl_3$) (**2.81**)



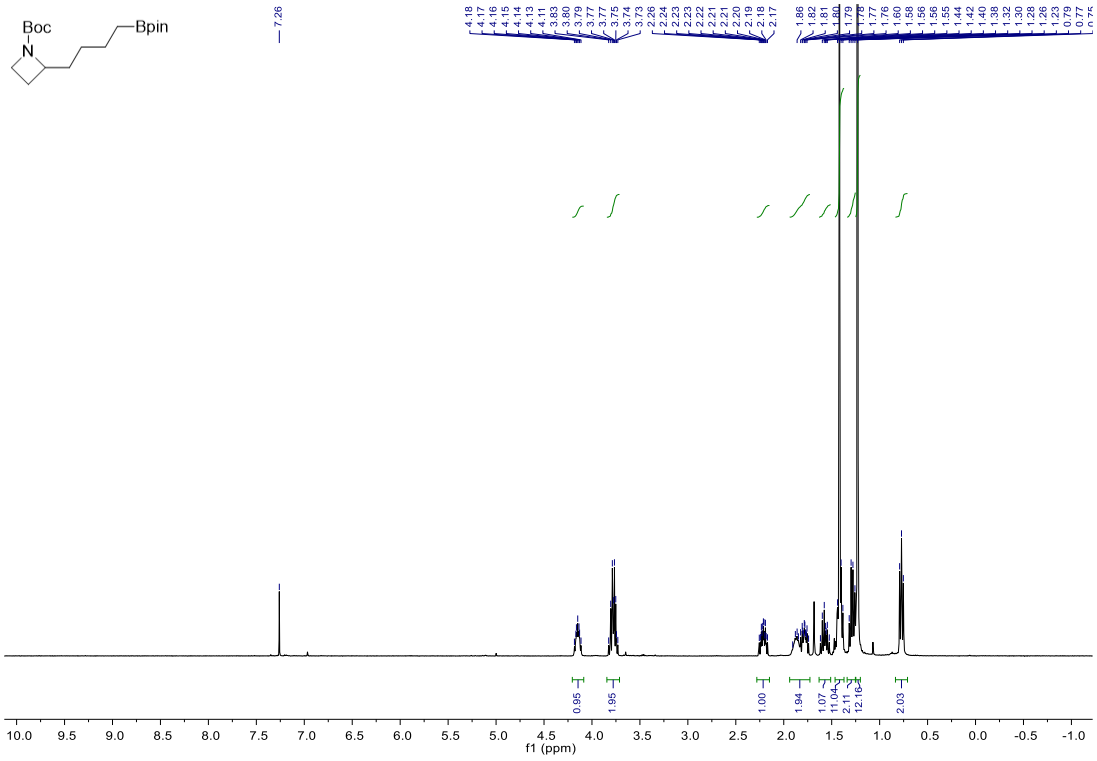
^{1}H NMR (600 MHz, $CDCl_3$) (**2.82**)



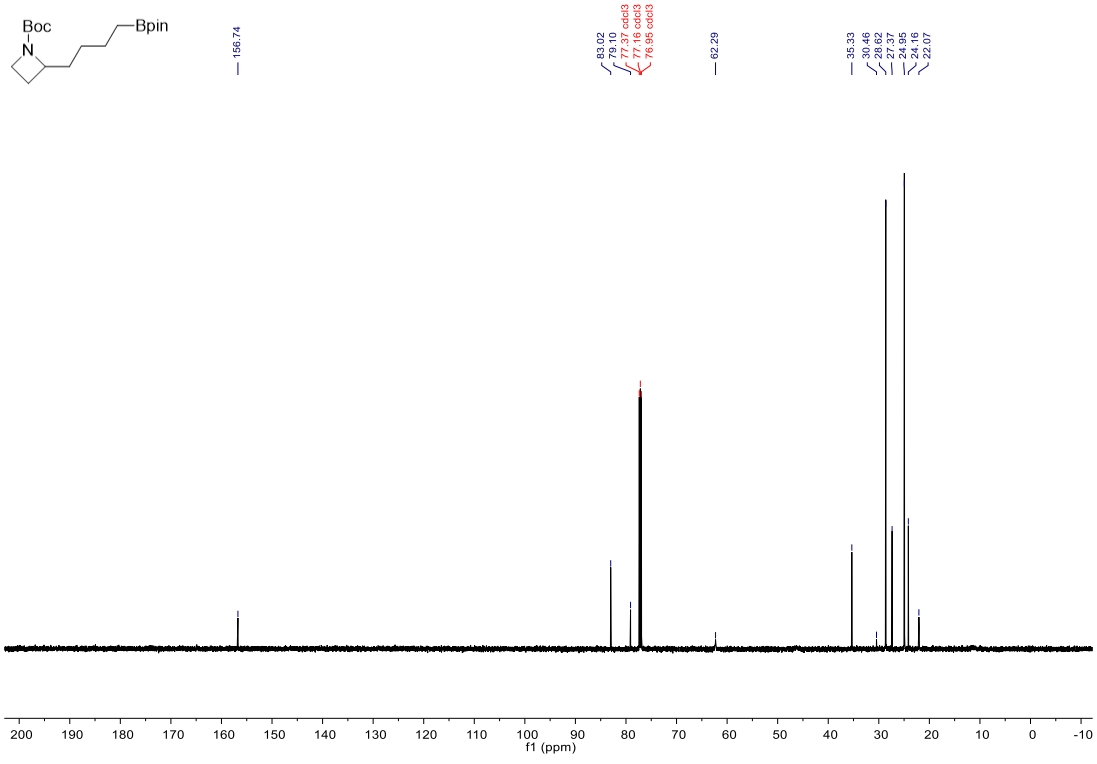
^{13}C NMR (151 MHz, $CDCl_3$) (**2.82**)



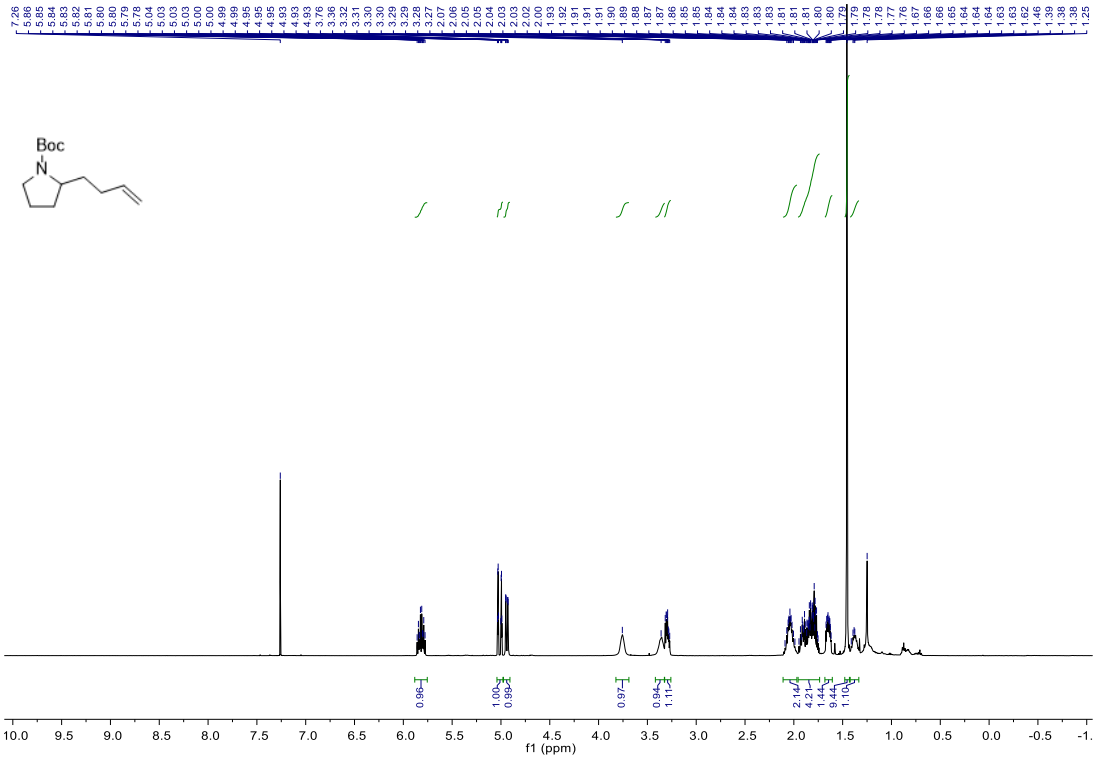
^{1}H NMR (400 MHz, $CDCl_3$) (**2.83**)



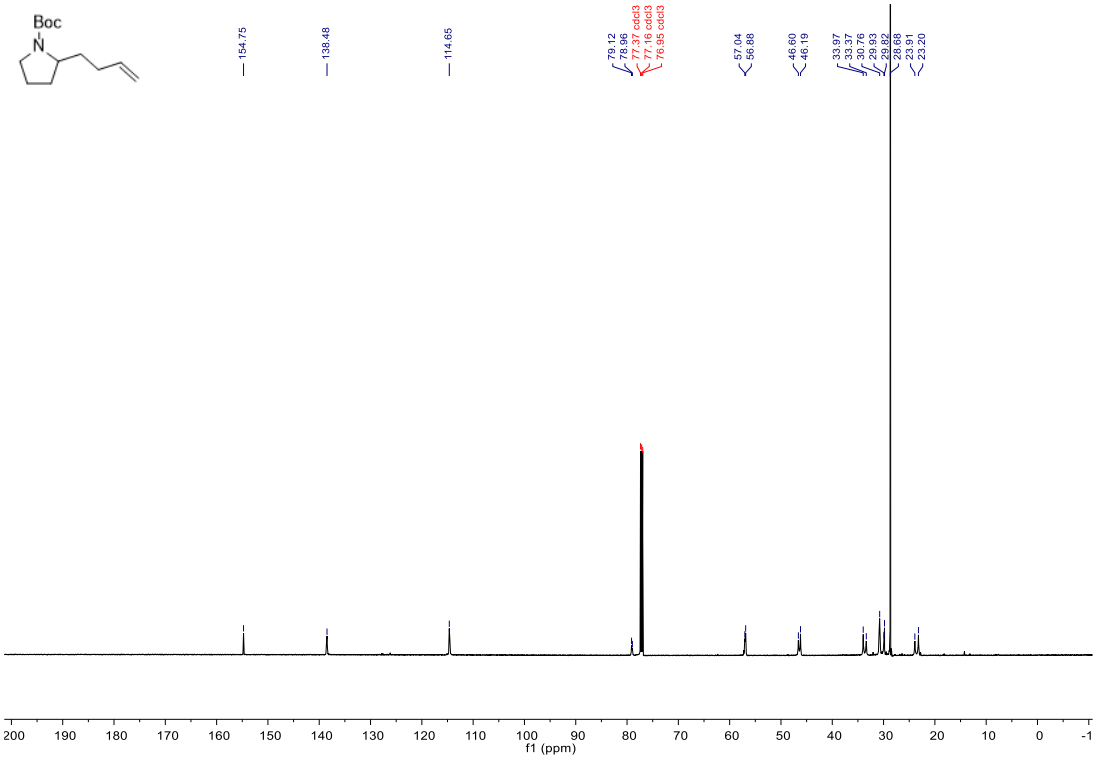
^{13}C NMR (151 MHz, $CDCl_3$) (**2.83**)



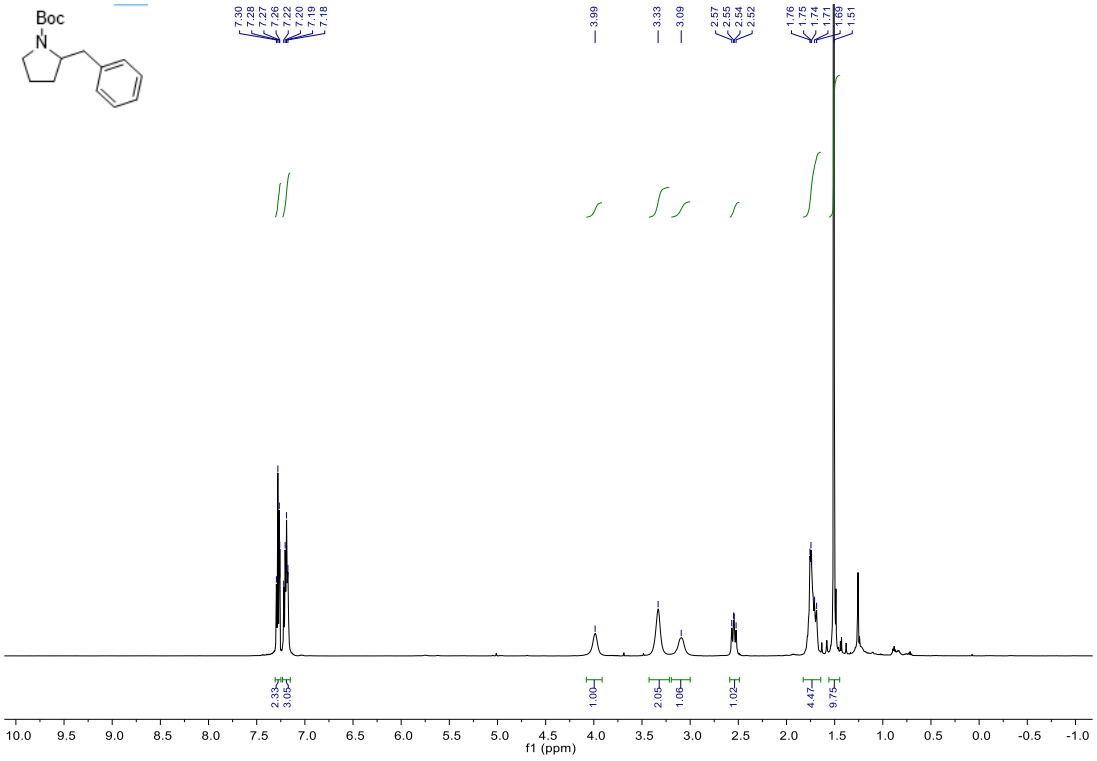
^{1}H NMR (500 MHz, $CDCl_3$) (**2.84**)



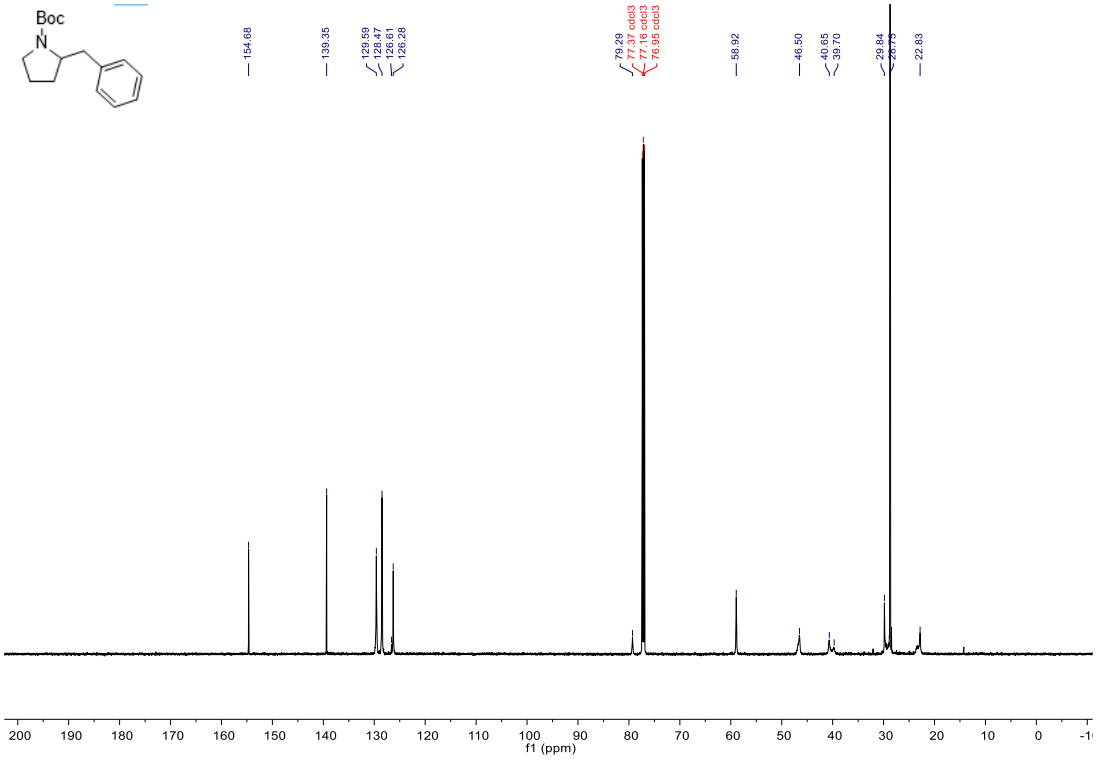
^{13}C NMR (151 MHz, $CDCl_3$) (**2.84**)



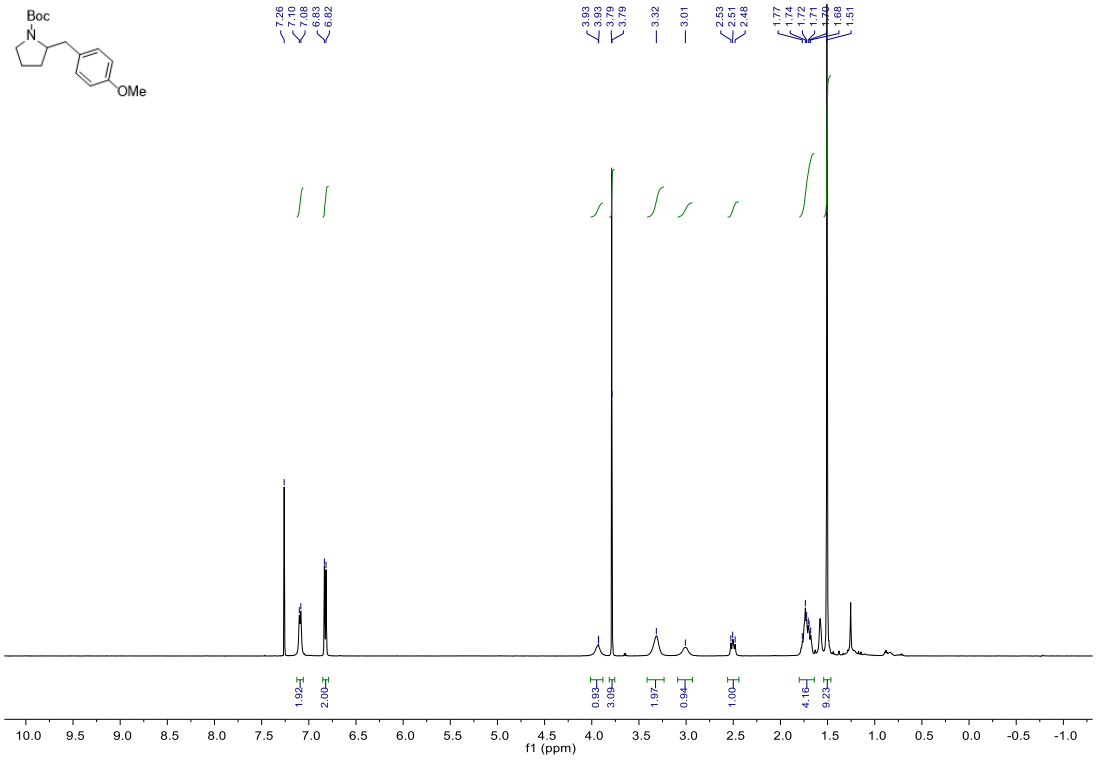
^{1}H NMR (500 MHz, $CDCl_3$) (**2.85**)



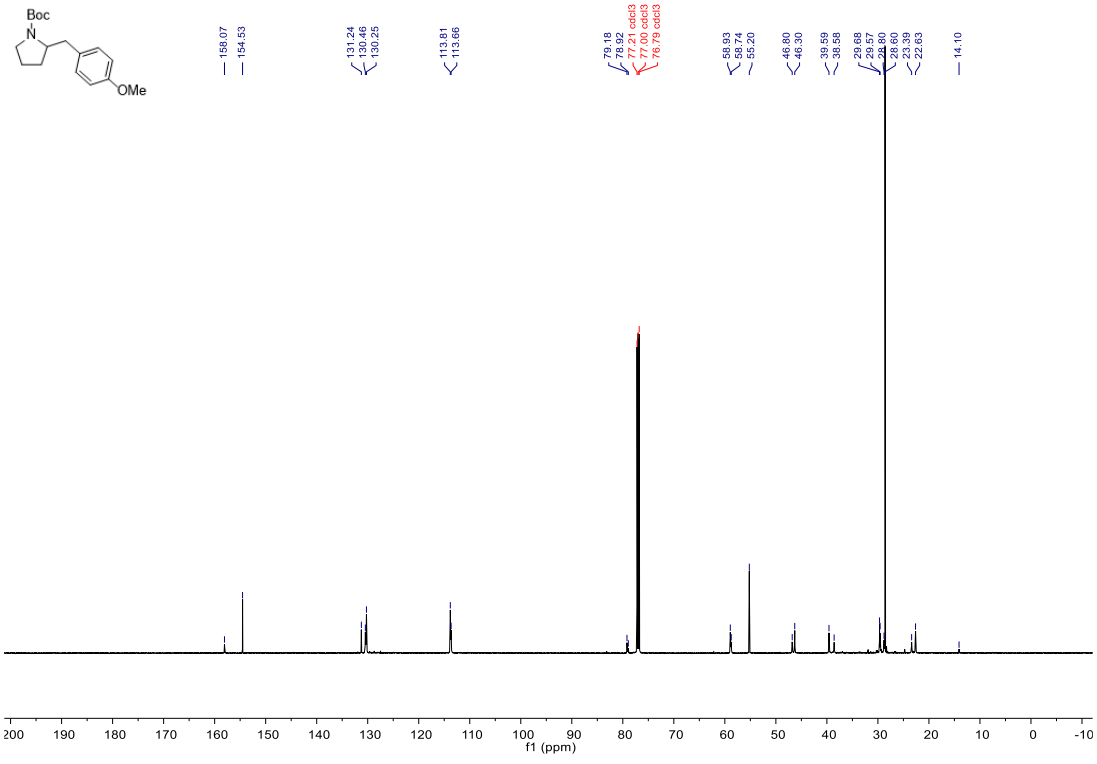
^{13}C NMR (151 MHz, $CDCl_3$) (**2.85**)



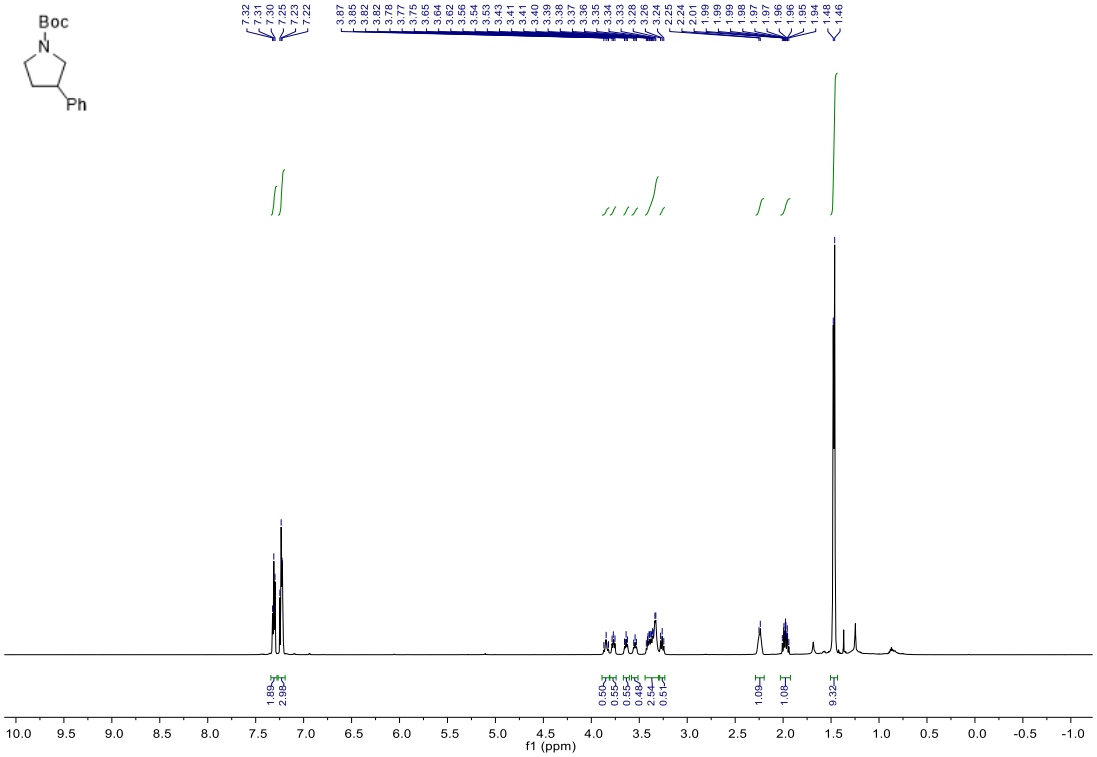
^{1}H NMR (500 MHz, $CDCl_3$) (**2.86**)



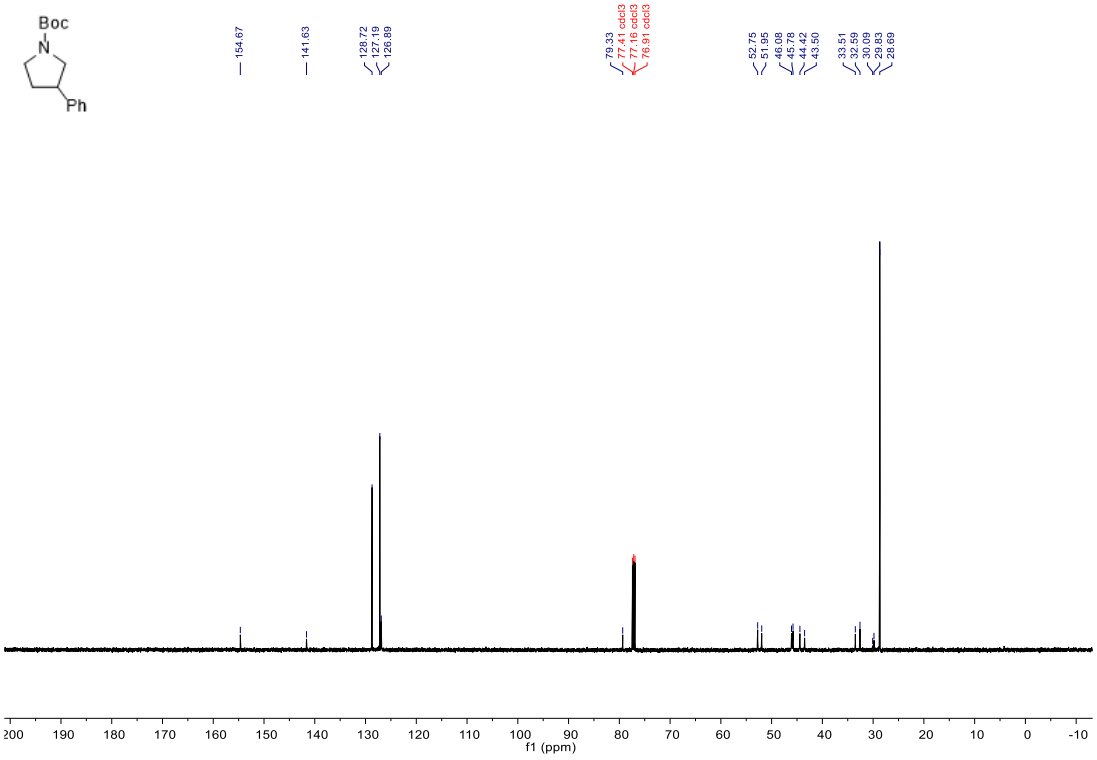
^{13}C NMR (151 MHz, $CDCl_3$) (**2.86**)



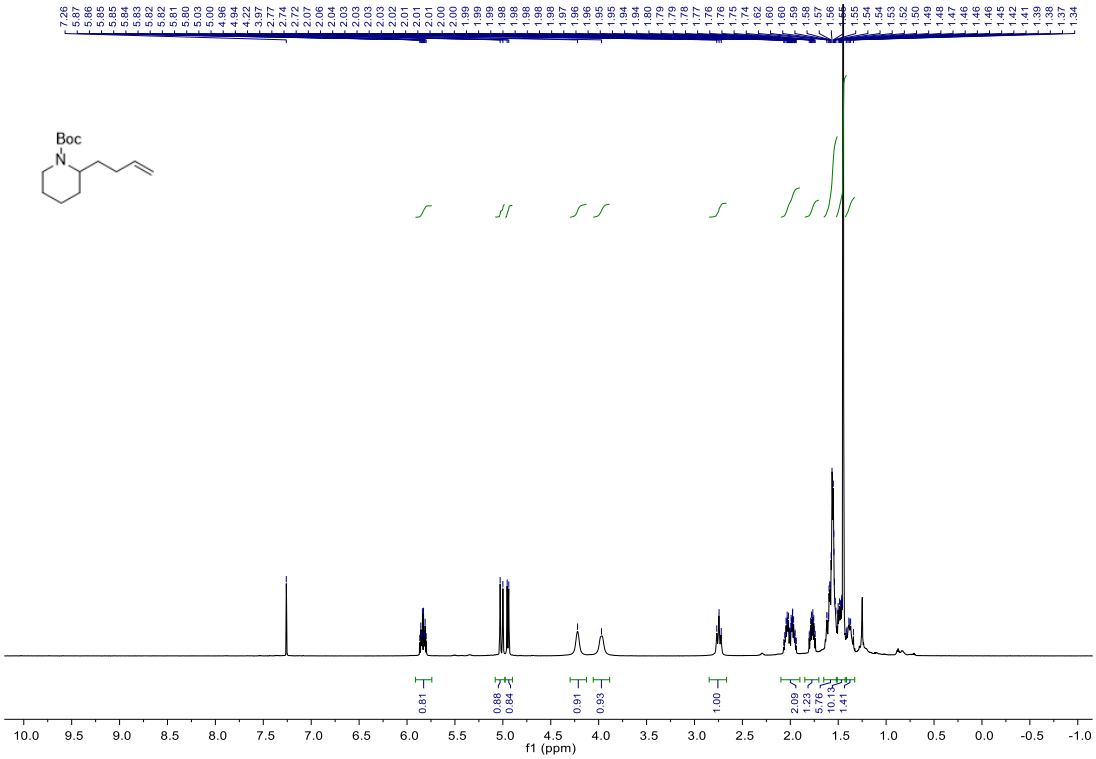
^{1}H NMR (500 MHz, $CDCl_3$) (**2.87**)



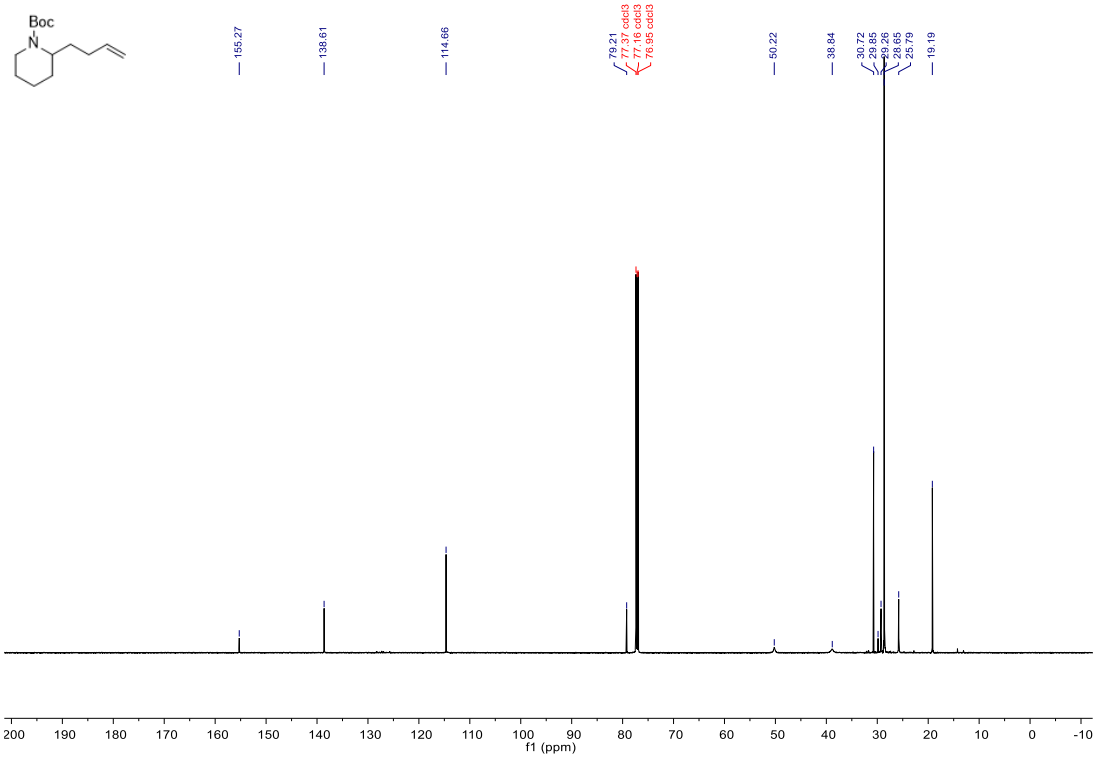
^{13}C NMR (151 MHz, $CDCl_3$) (**2.87**)



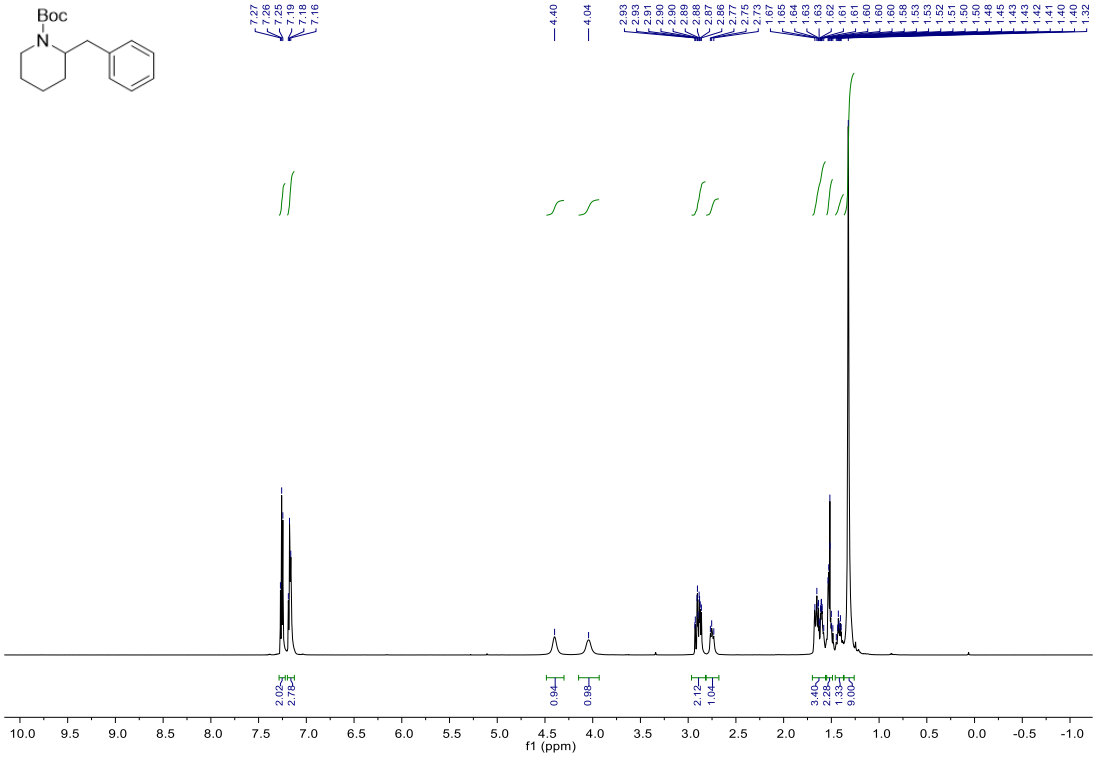
^{1}H NMR (500 MHz, $CDCl_3$) (**2.88**)



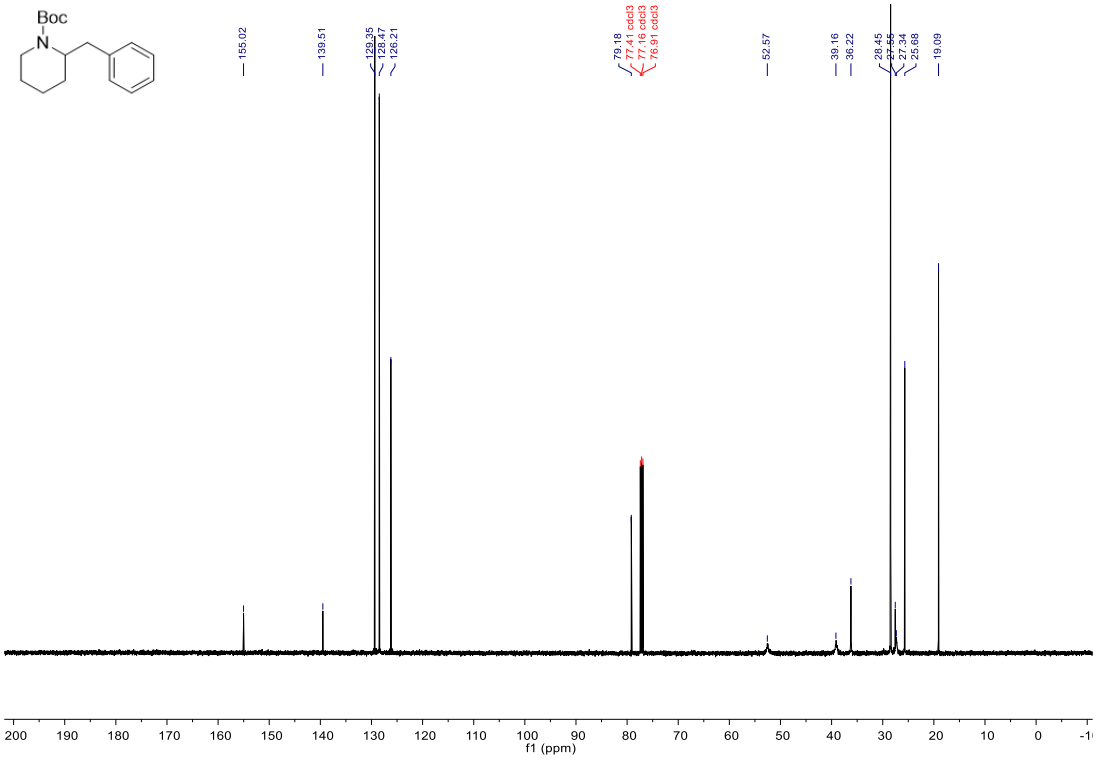
^{13}C NMR (151 MHz, $CDCl_3$) (**2.88**)



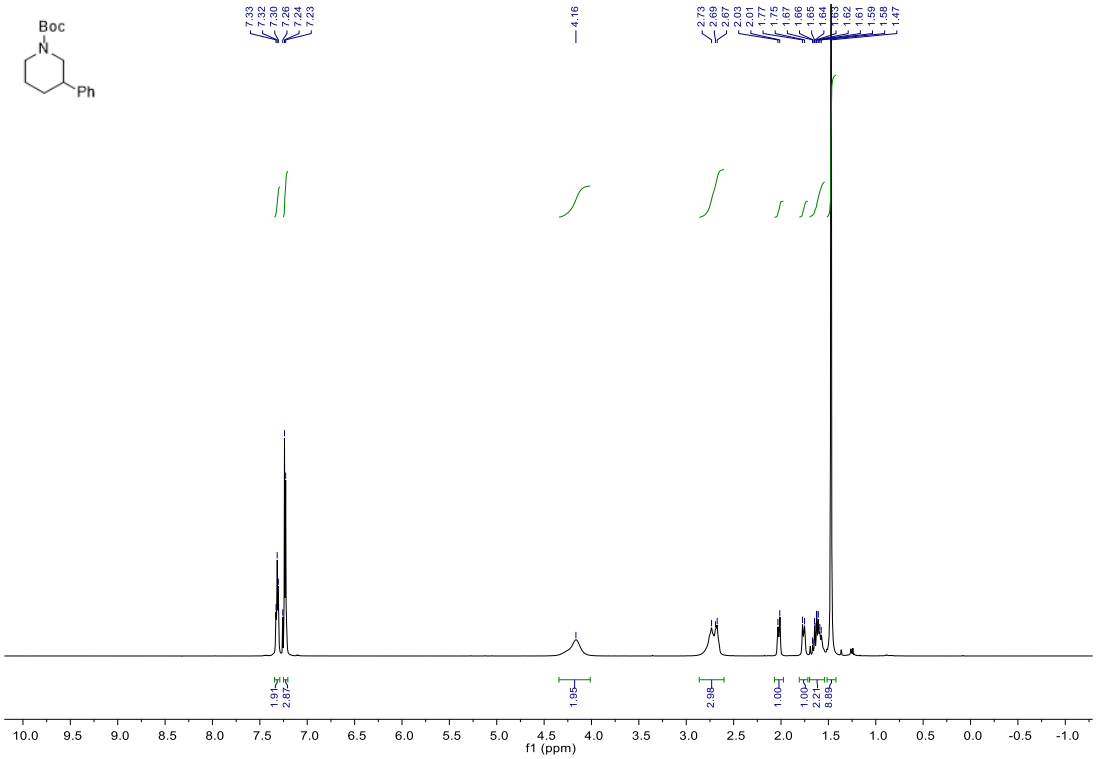
^{1}H NMR (500 MHz, $CDCl_3$) (**2.89**)



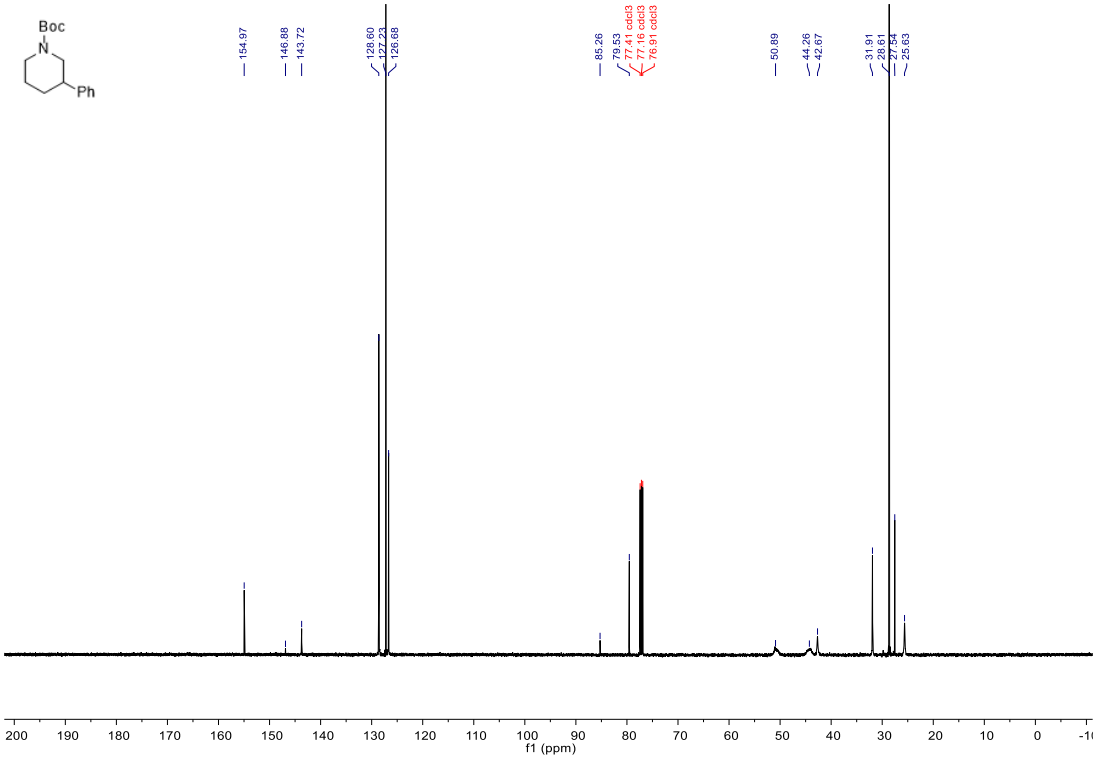
^{13}C NMR (151 MHz, $CDCl_3$) (**2.89**)



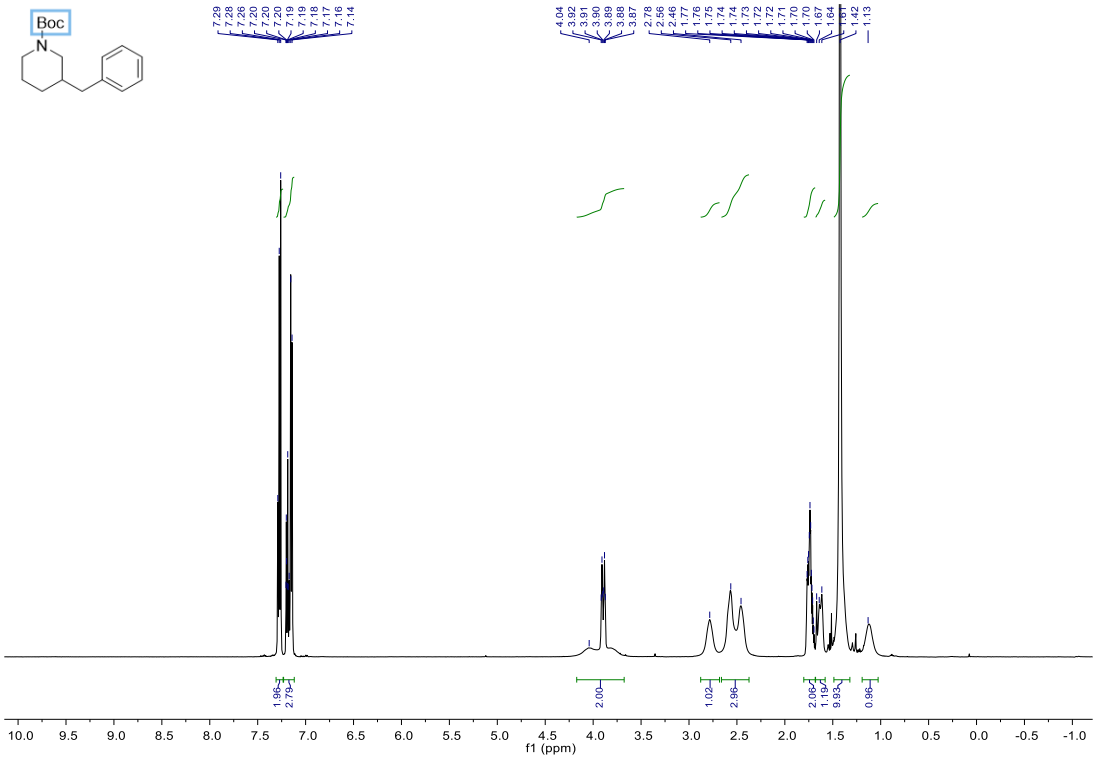
^{1}H NMR (500 MHz, $CDCl_3$) (**2.90**)



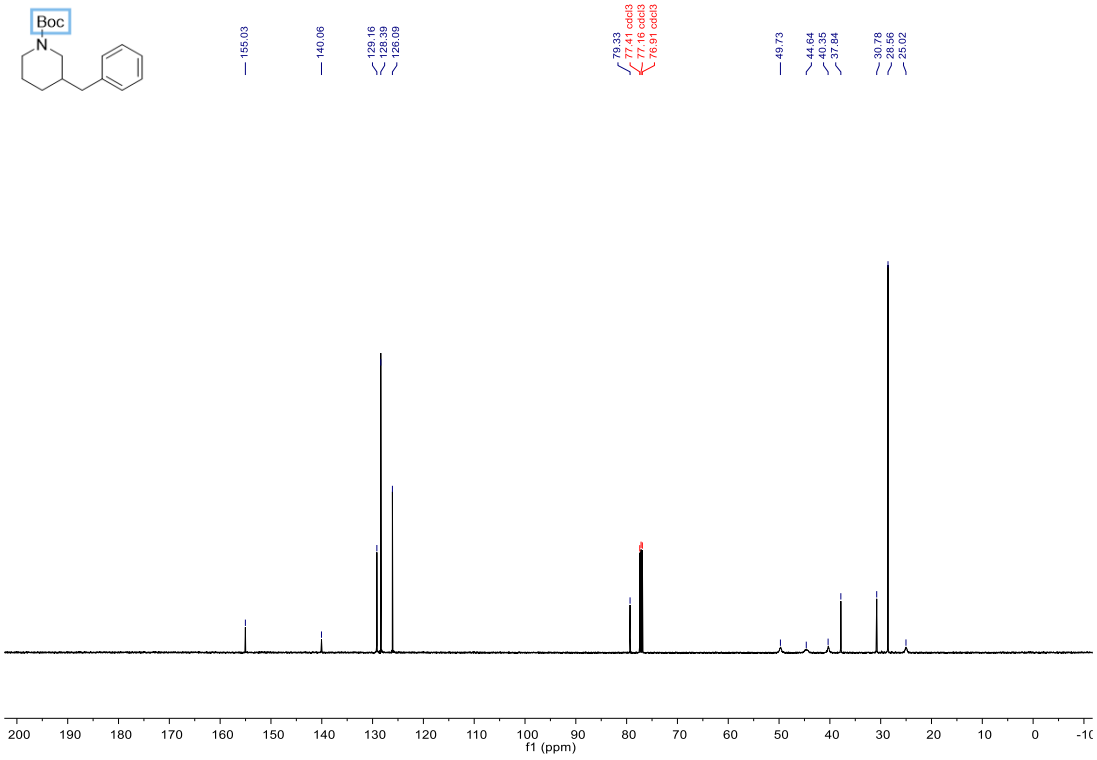
^{13}C NMR (151 MHz, $CDCl_3$) (**2.90**)



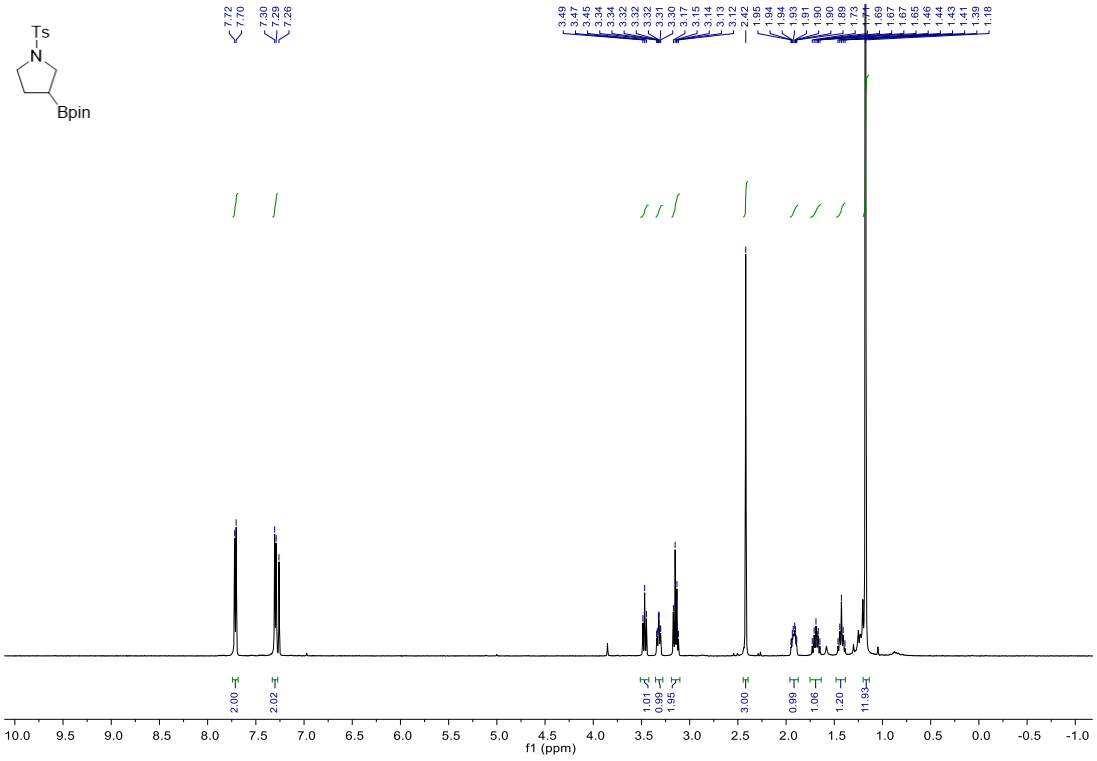
^{1}H NMR (500 MHz, $CDCl_3$) (**2.91**)



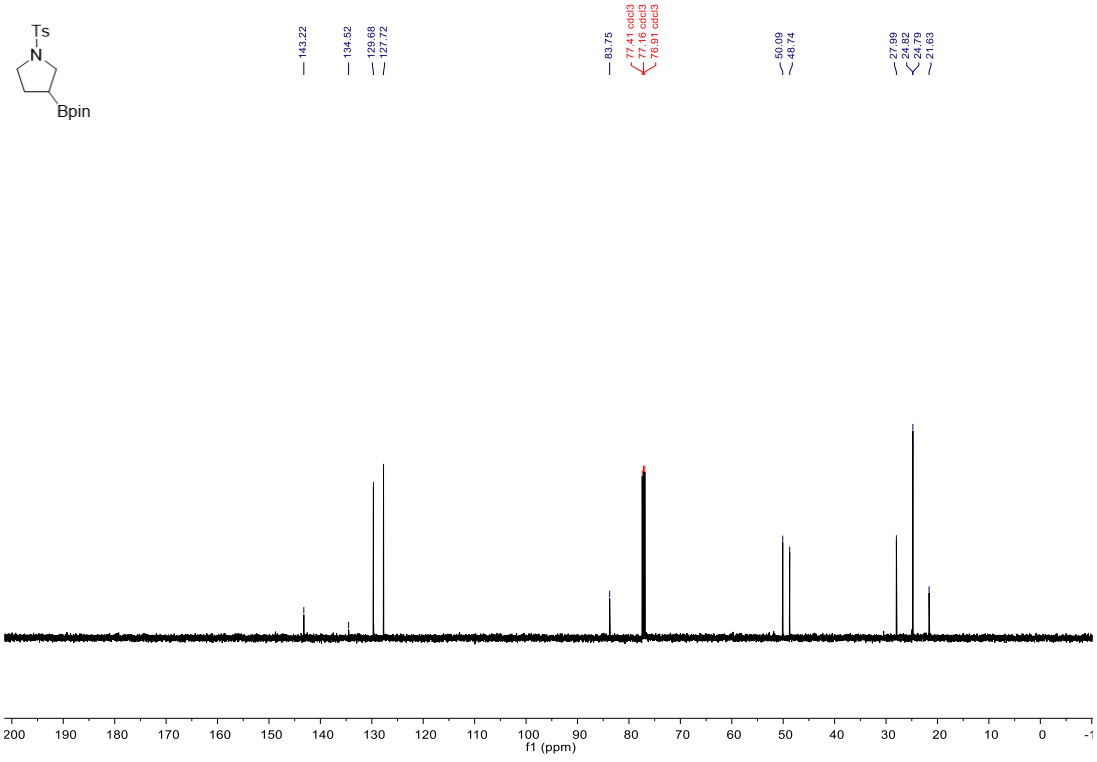
^{13}C NMR (151 MHz, $CDCl_3$) (**2.91**)



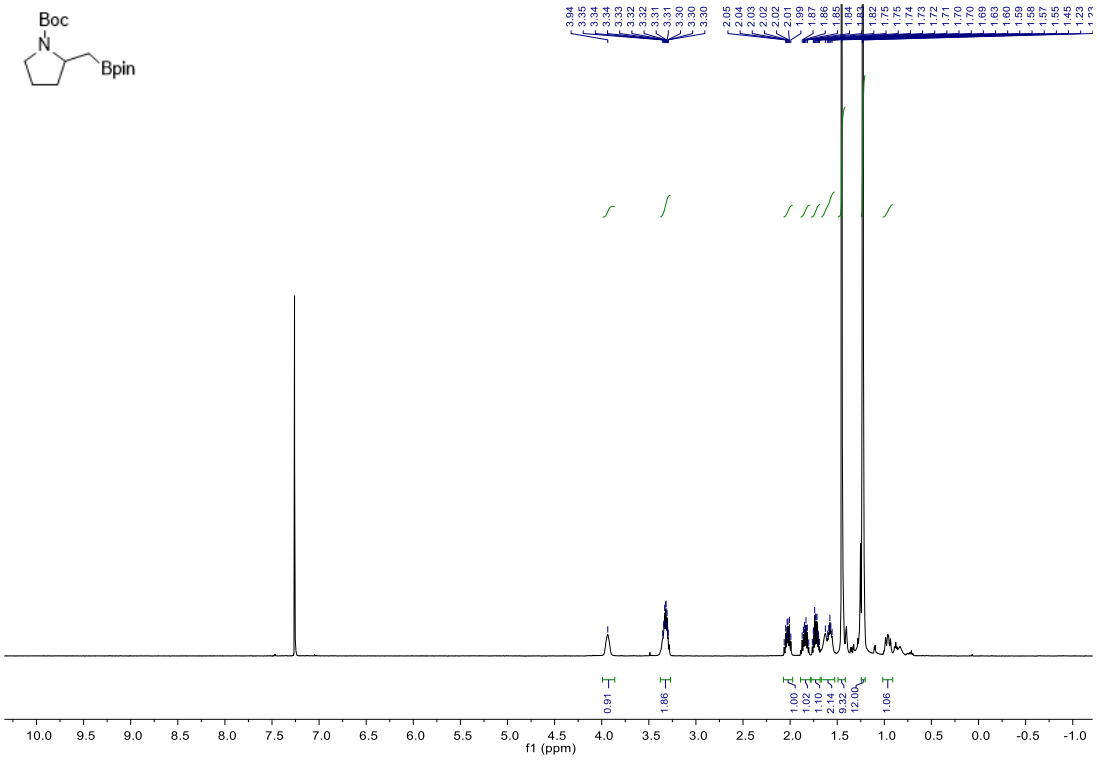
^{1}H NMR (500 MHz, $CDCl_3$) (**2.93**)



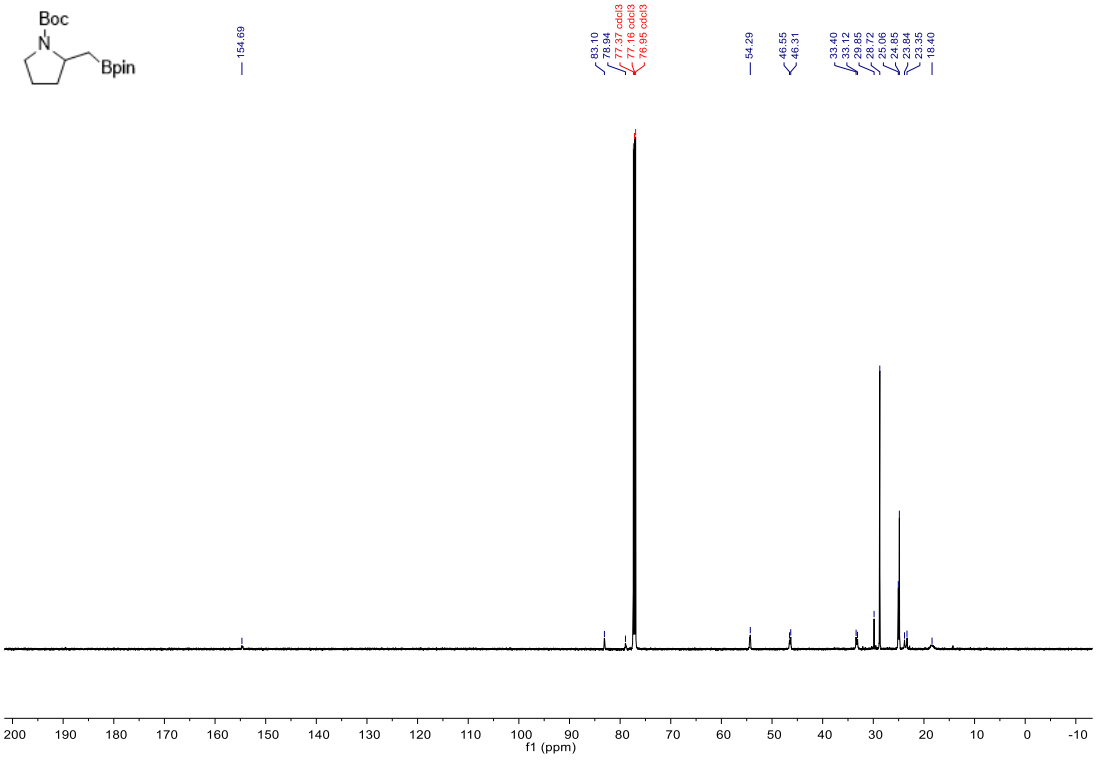
^{13}C NMR (126 MHz, $CDCl_3$) (**2.93**)



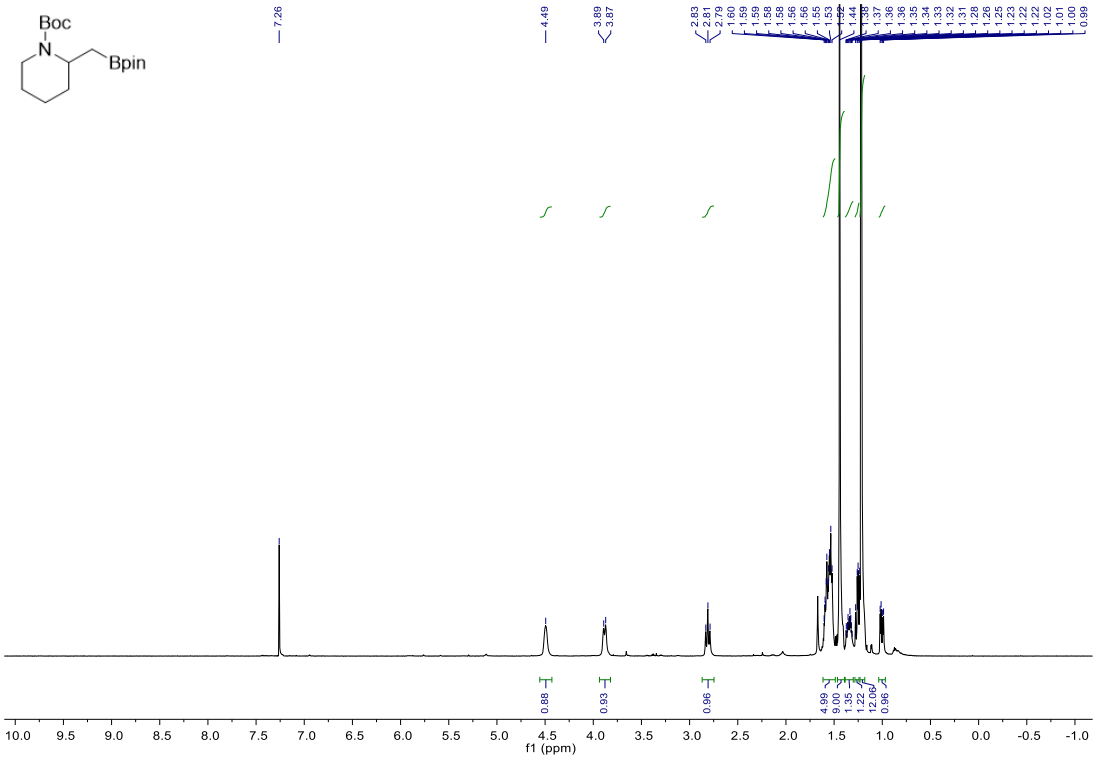
^{1}H NMR (500 MHz, $CDCl_3$) (**2.97**)



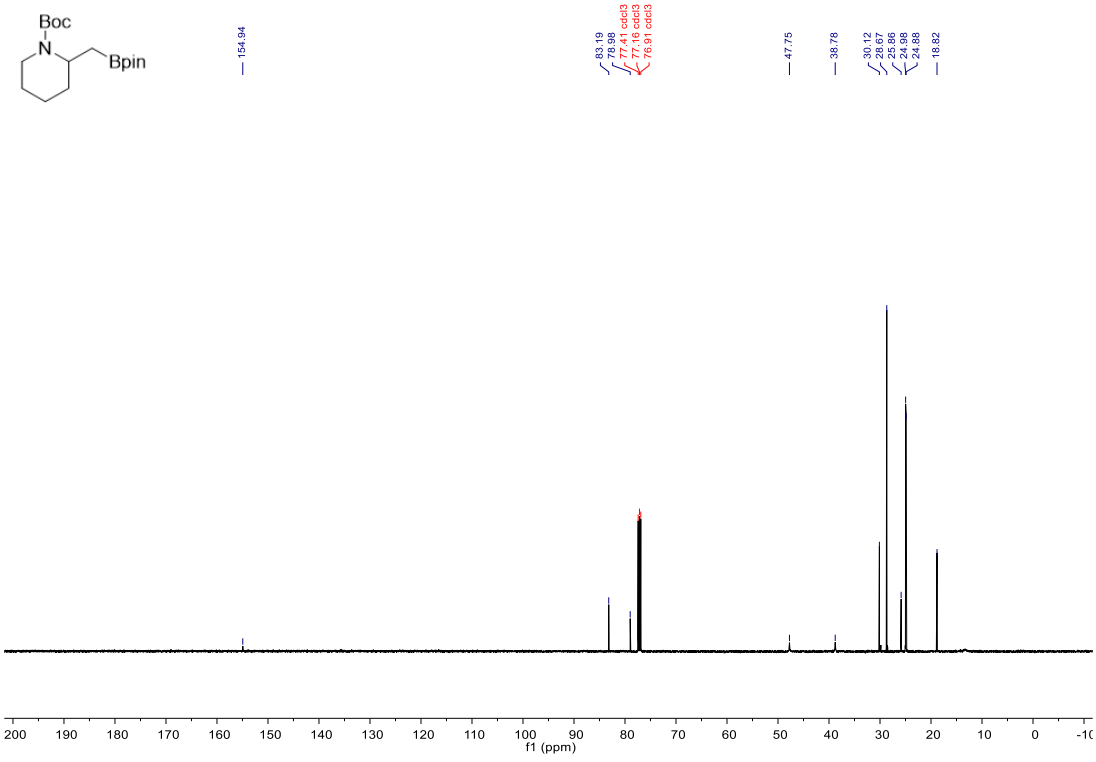
^{13}C NMR (151 MHz, $CDCl_3$) (**2.97**)



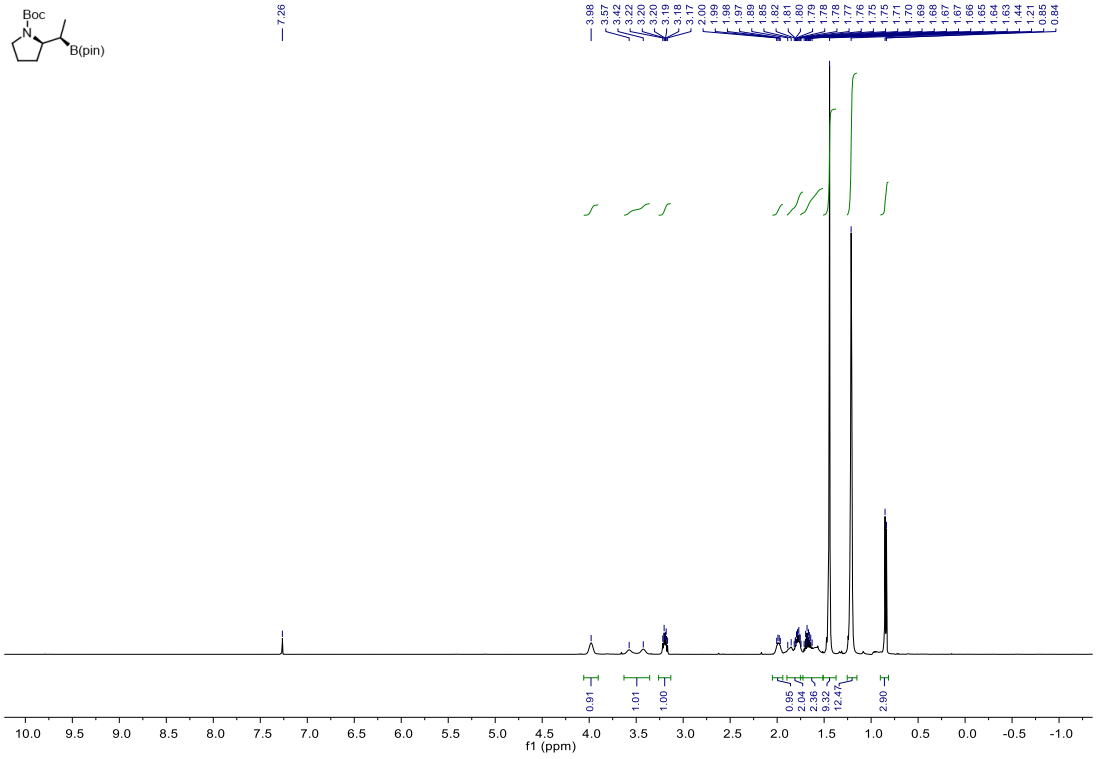
^{1}H NMR (600 MHz, $CDCl_3$) (**2.101**)



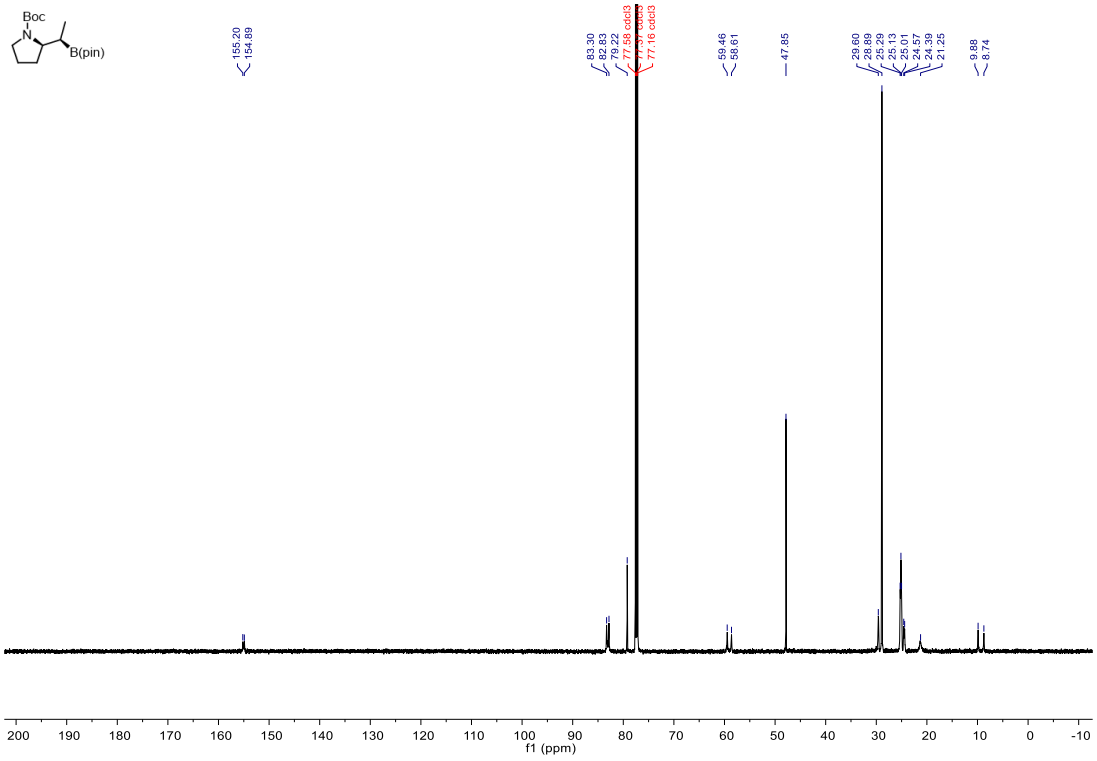
^{13}C NMR (126 MHz, $CDCl_3$) (**2.101**)



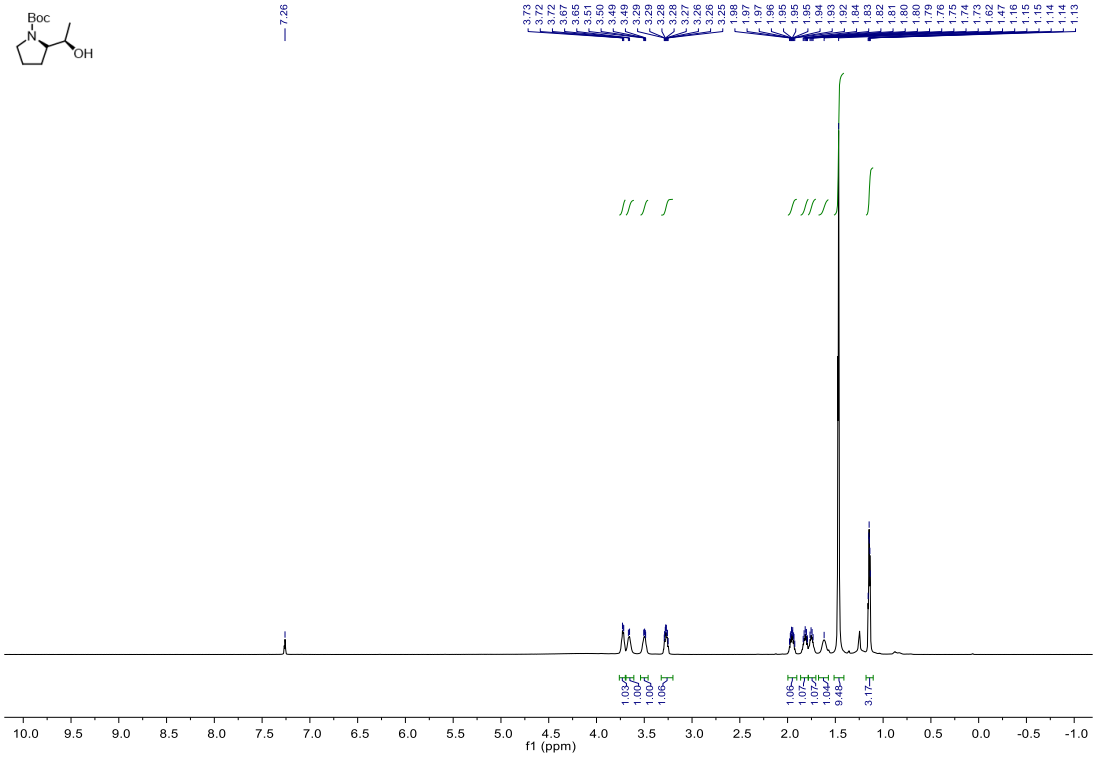
^{1}H NMR (500 MHz, $CDCl_3$) (**2.105**)



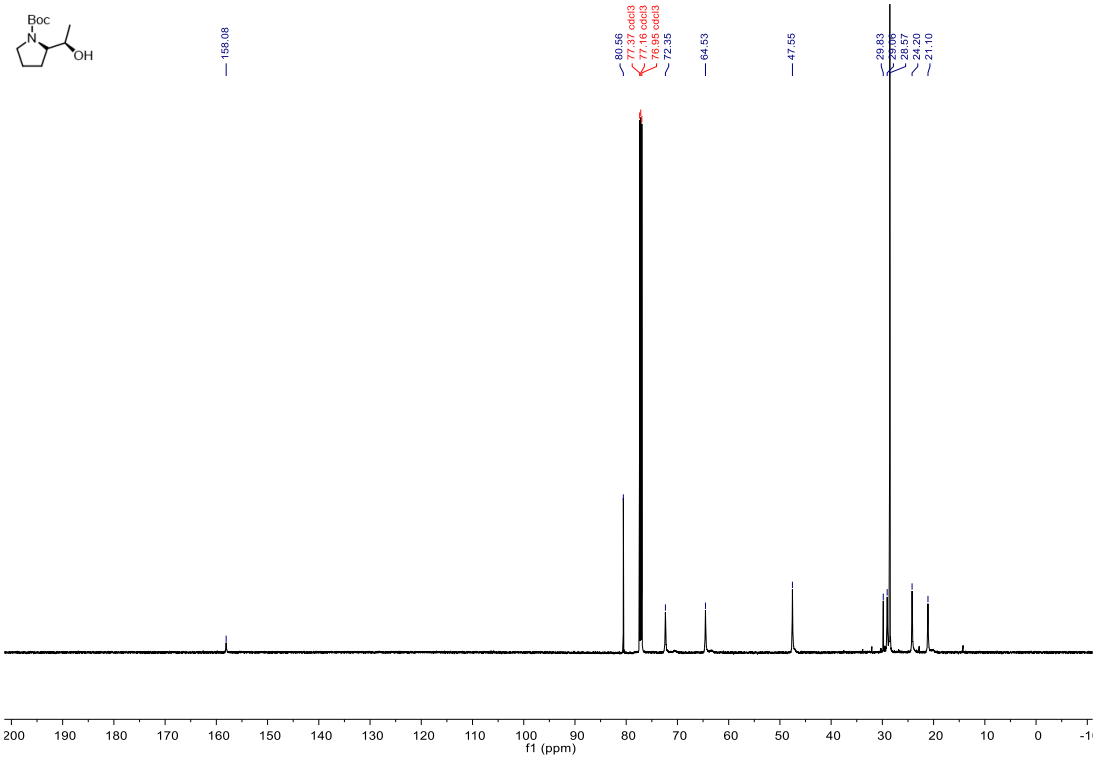
^{13}C NMR (151 MHz, $CDCl_3$) (**2.105**)



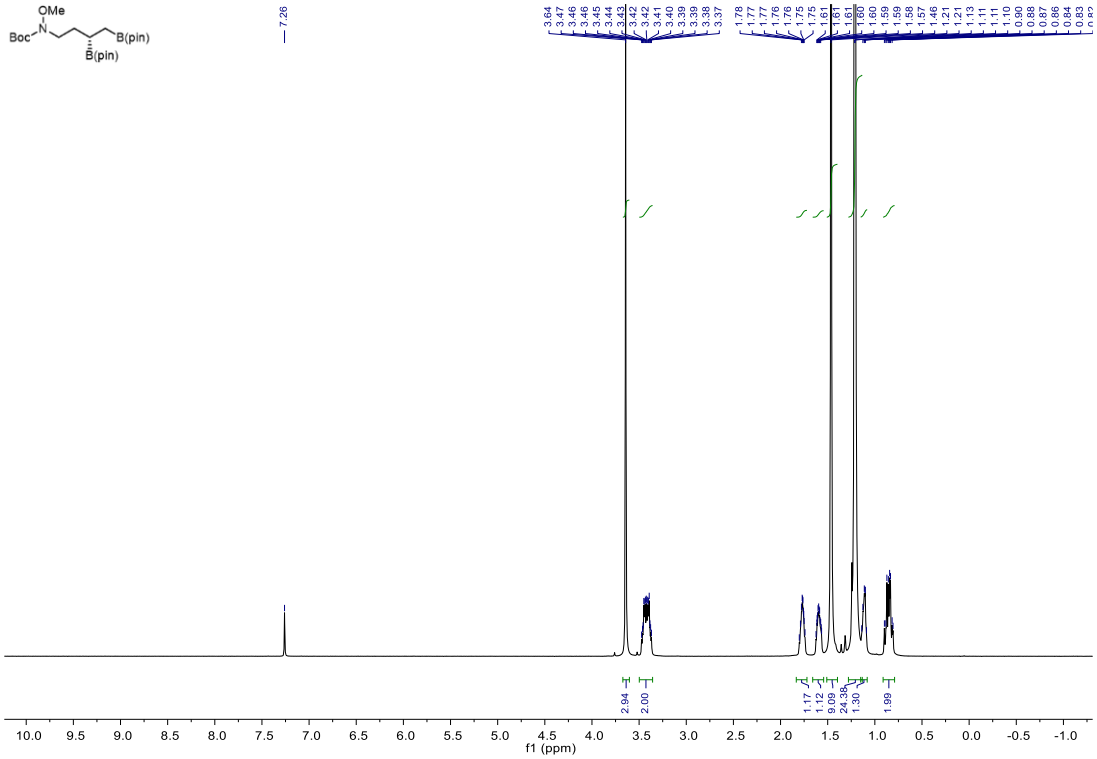
^{1}H NMR (600 MHz, $CDCl_3$) (**2.109**)



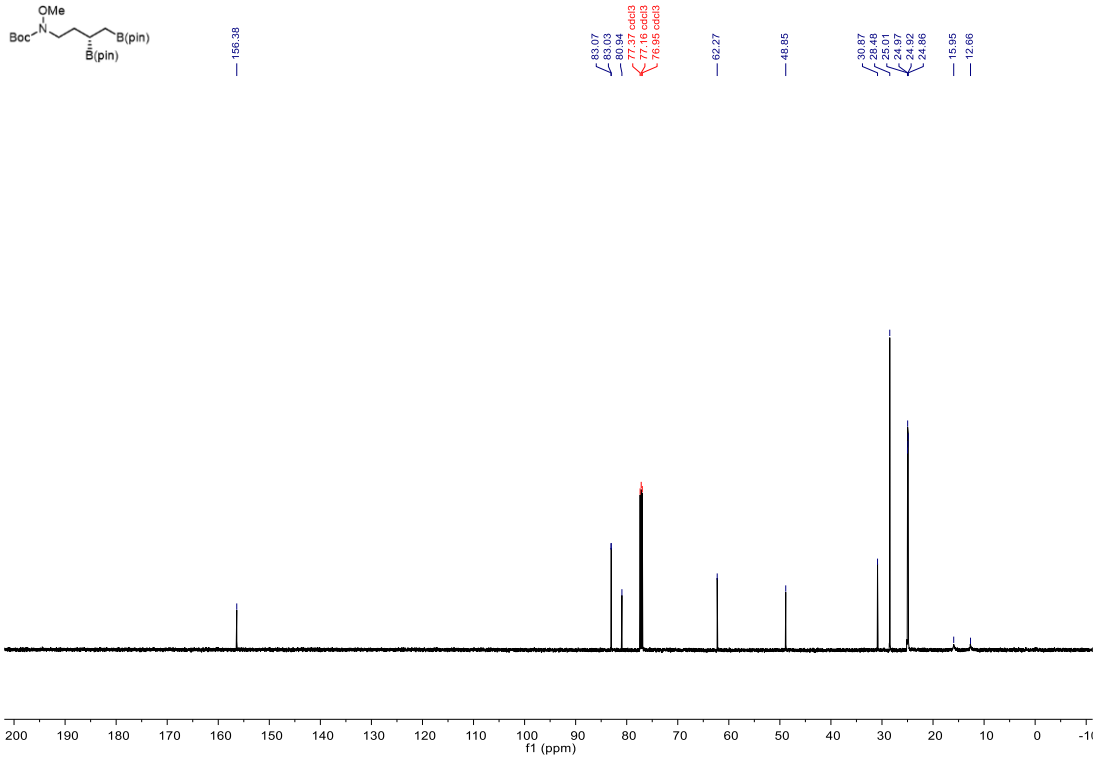
^{13}C NMR (151 MHz, $CDCl_3$) (**2.109**)



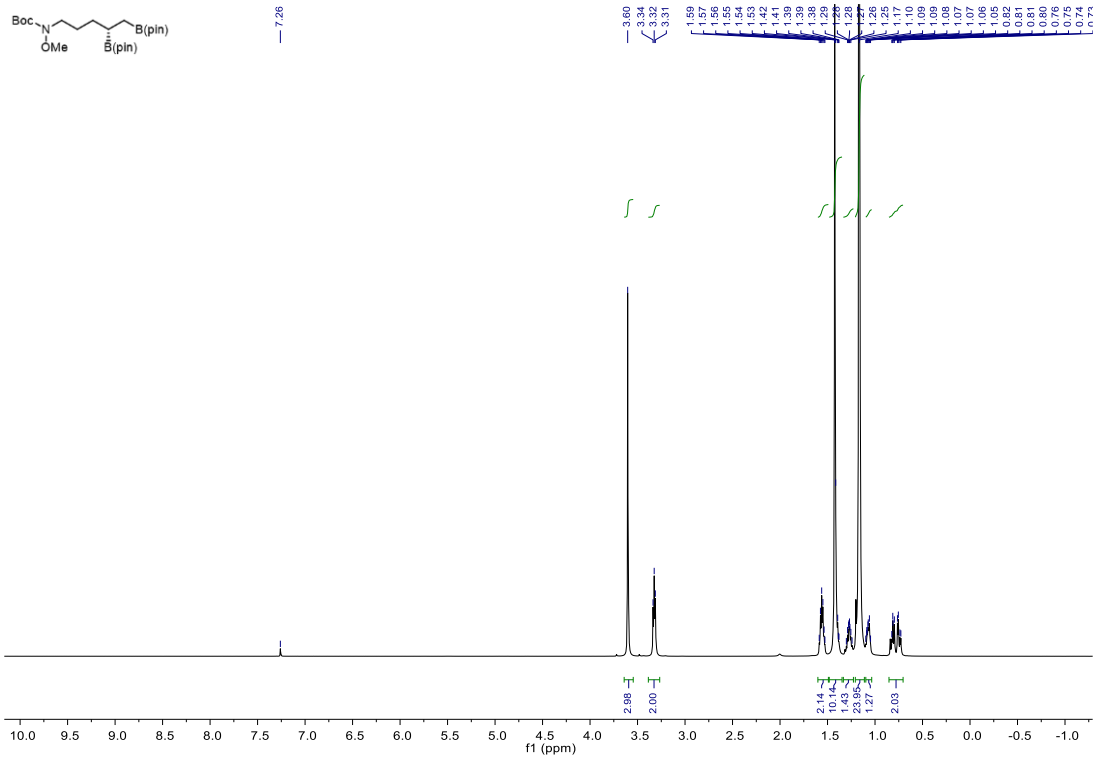
^{1}H NMR (600 MHz, $CDCl_3$) (**2.112**)



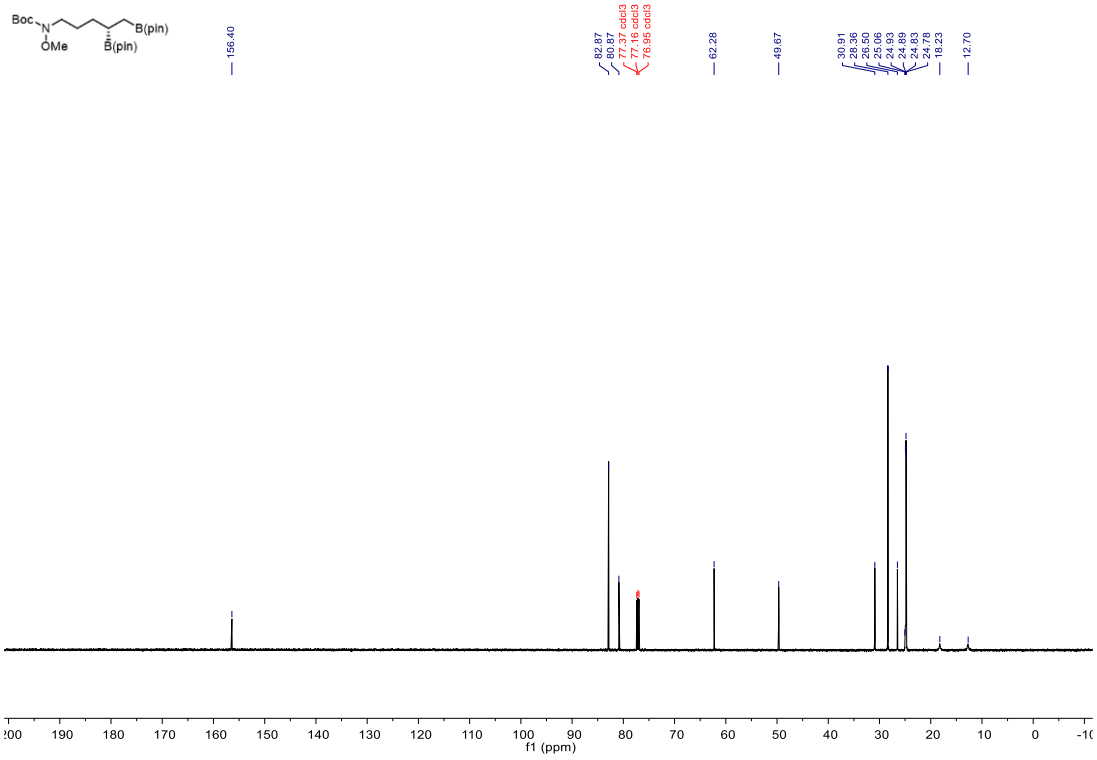
^{13}C NMR (151 MHz, $CDCl_3$) (**2.112**)



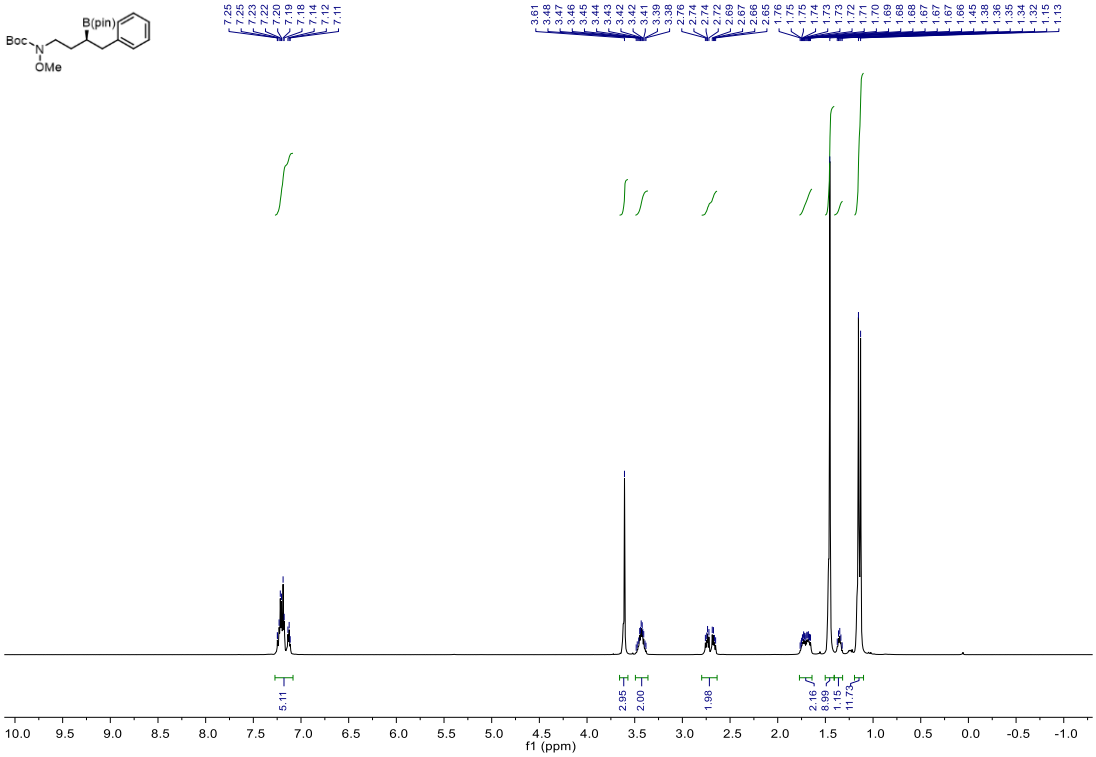
^{1}H NMR (600 MHz, $CDCl_3$) (**2.116**)



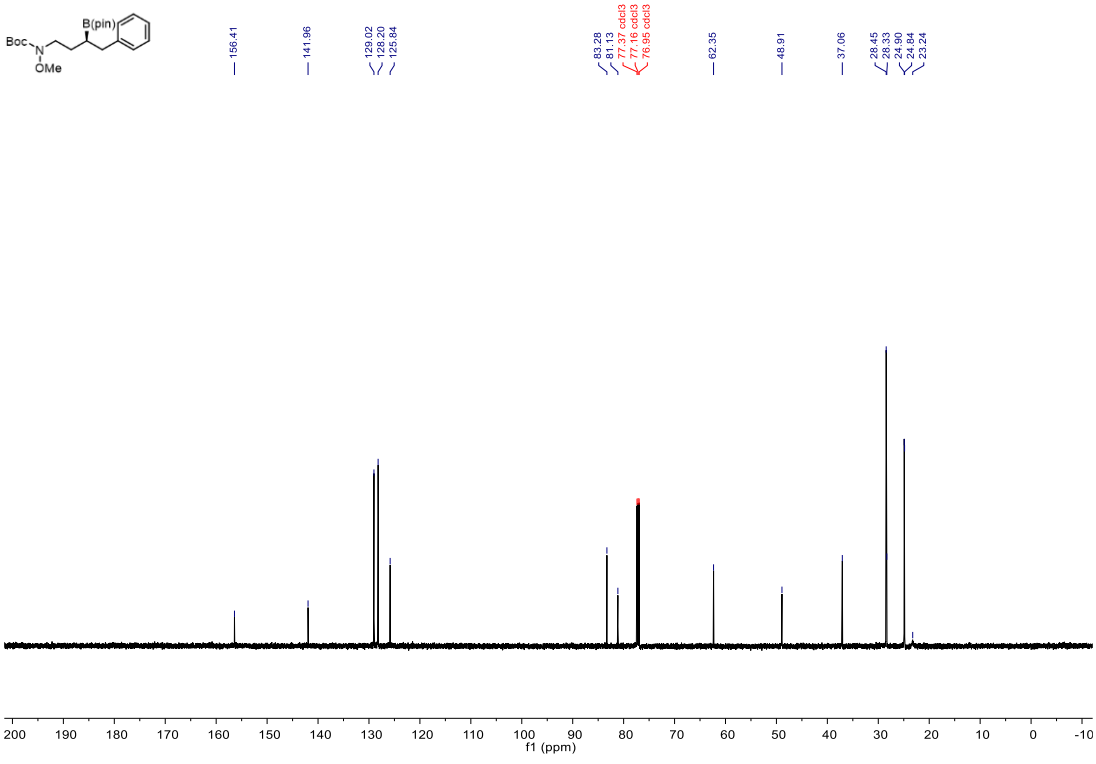
^{13}C NMR (151 MHz, $CDCl_3$) (**2.116**)



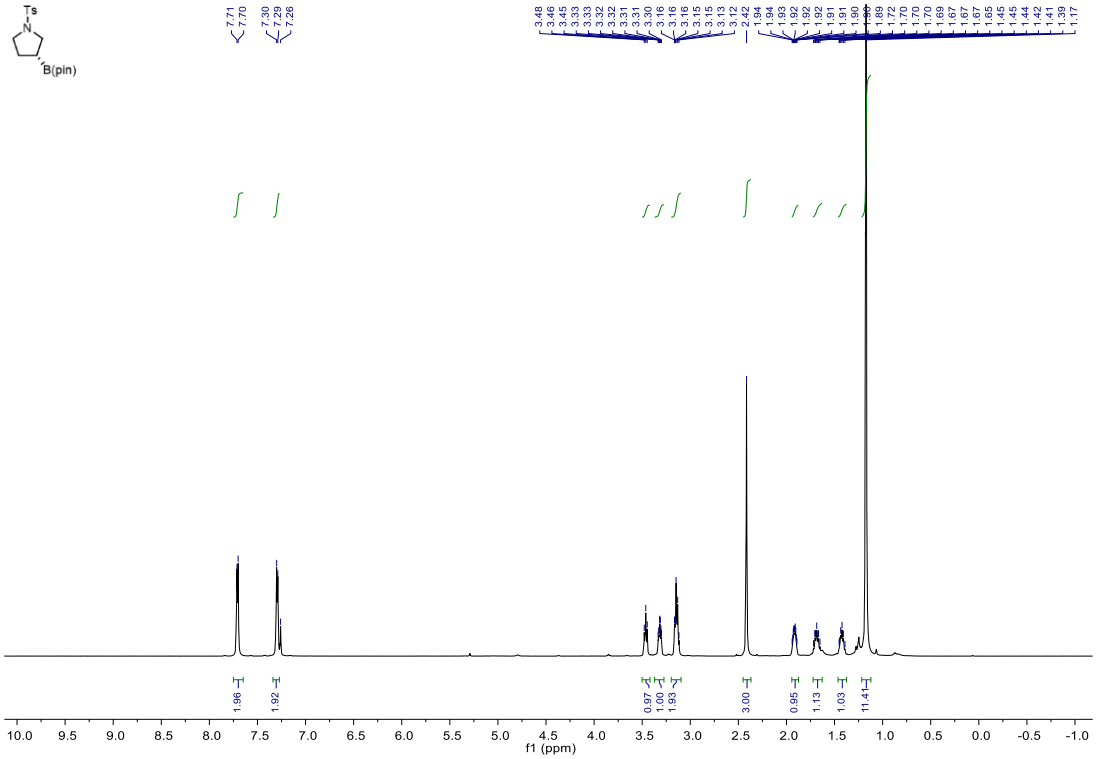
^{1}H NMR (600 MHz, $CDCl_3$) (**2.113**)



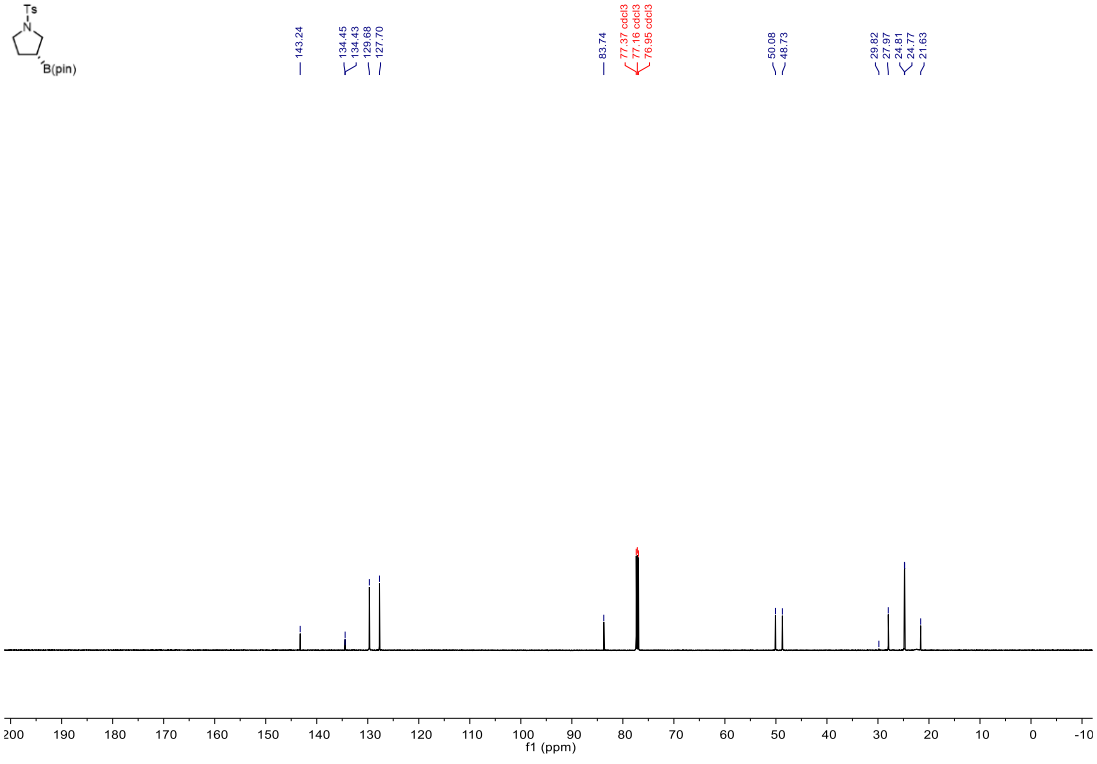
^{13}C NMR (151 MHz, $CDCl_3$) (**2.113**)



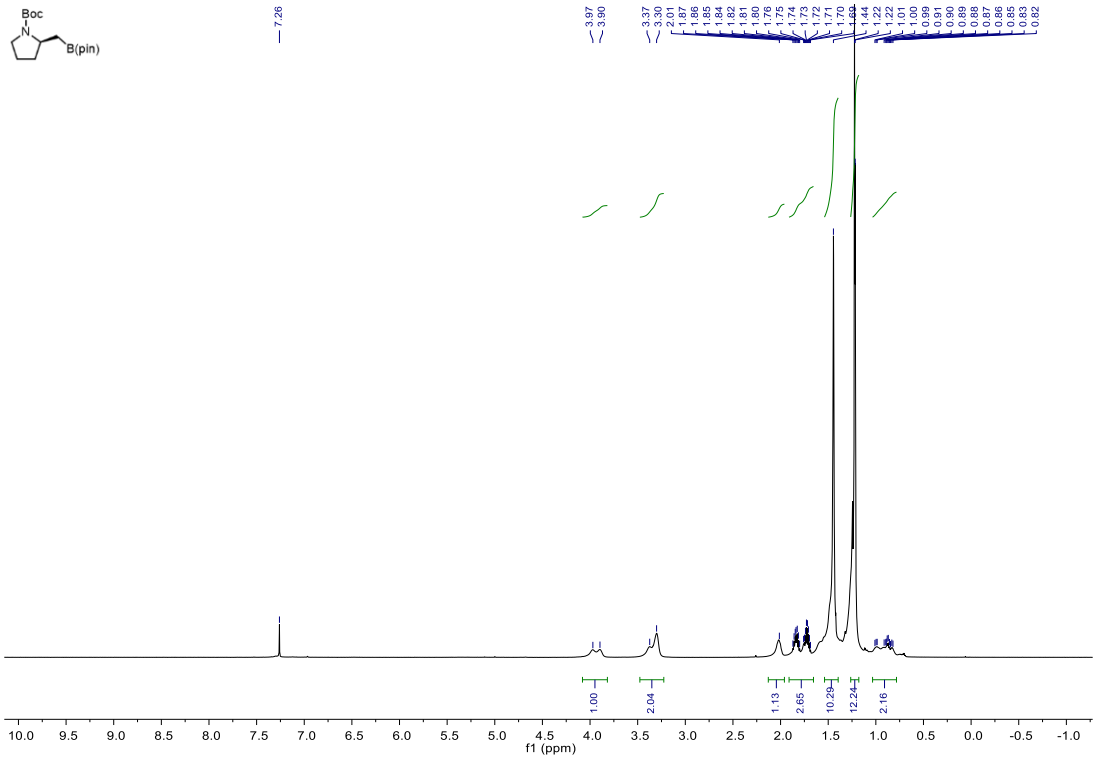
^{1}H NMR (600 MHz, $CDCl_3$) (**2.115**)



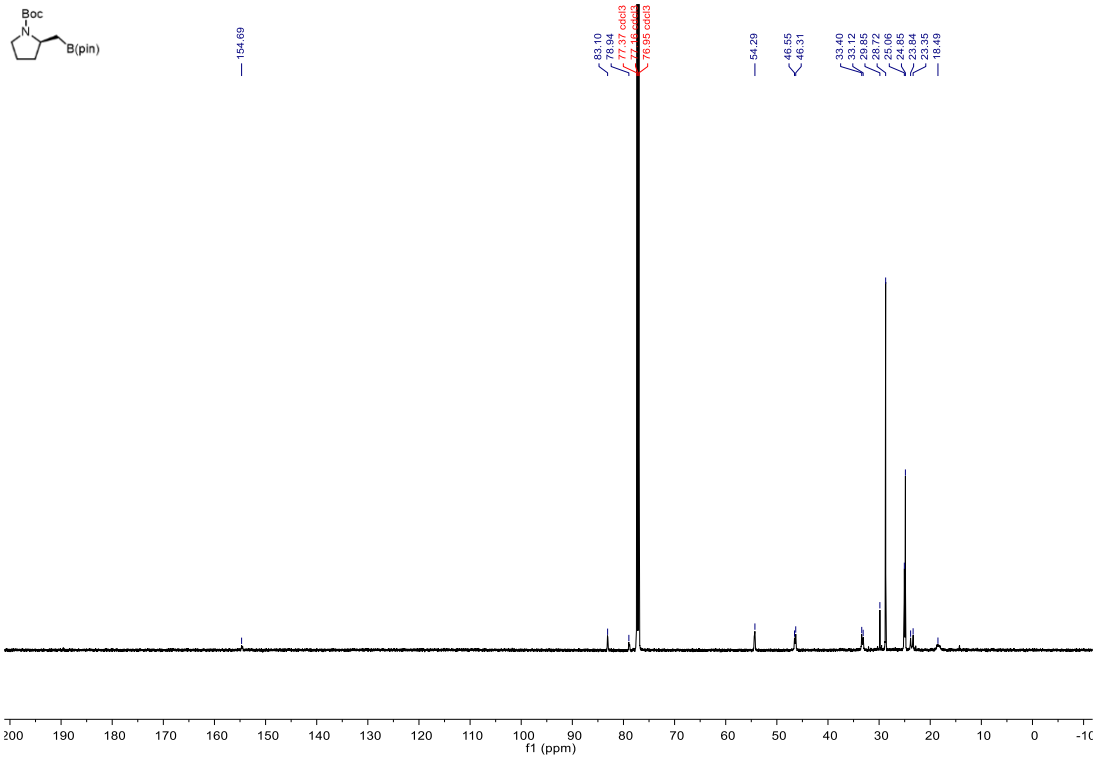
^{13}C NMR (151 MHz, $CDCl_3$) (**2.115**)



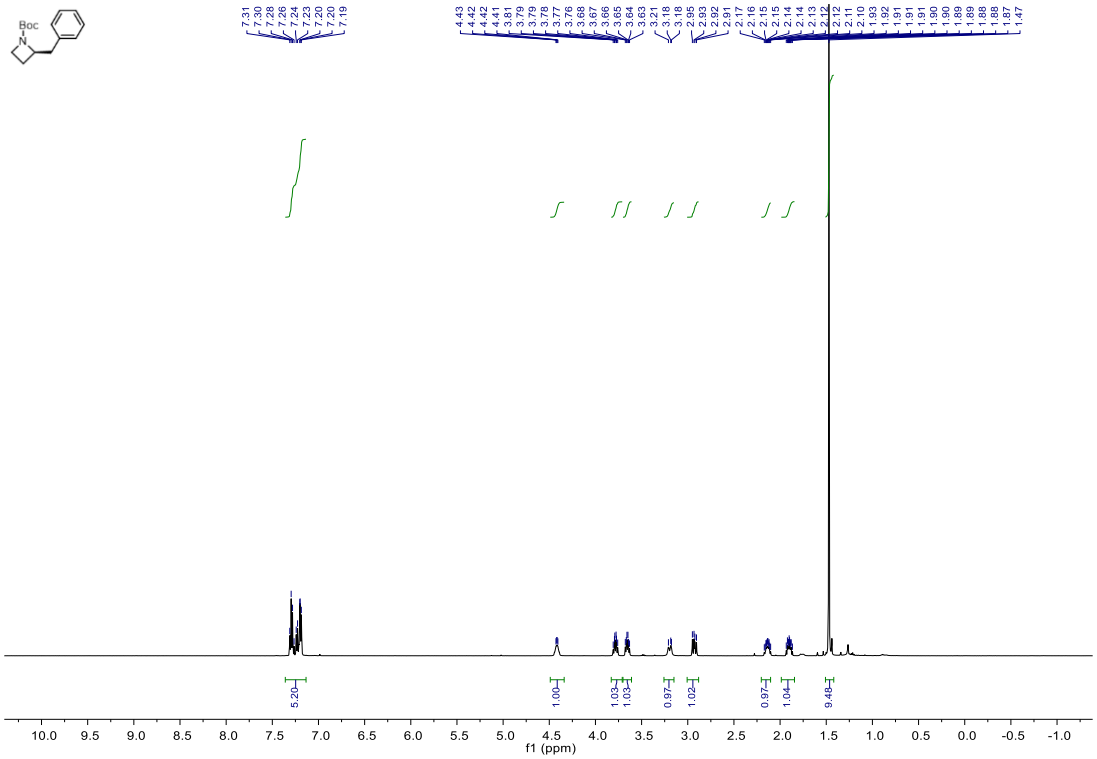
^{1}H NMR (600 MHz, $CDCl_3$) (**2.117**)



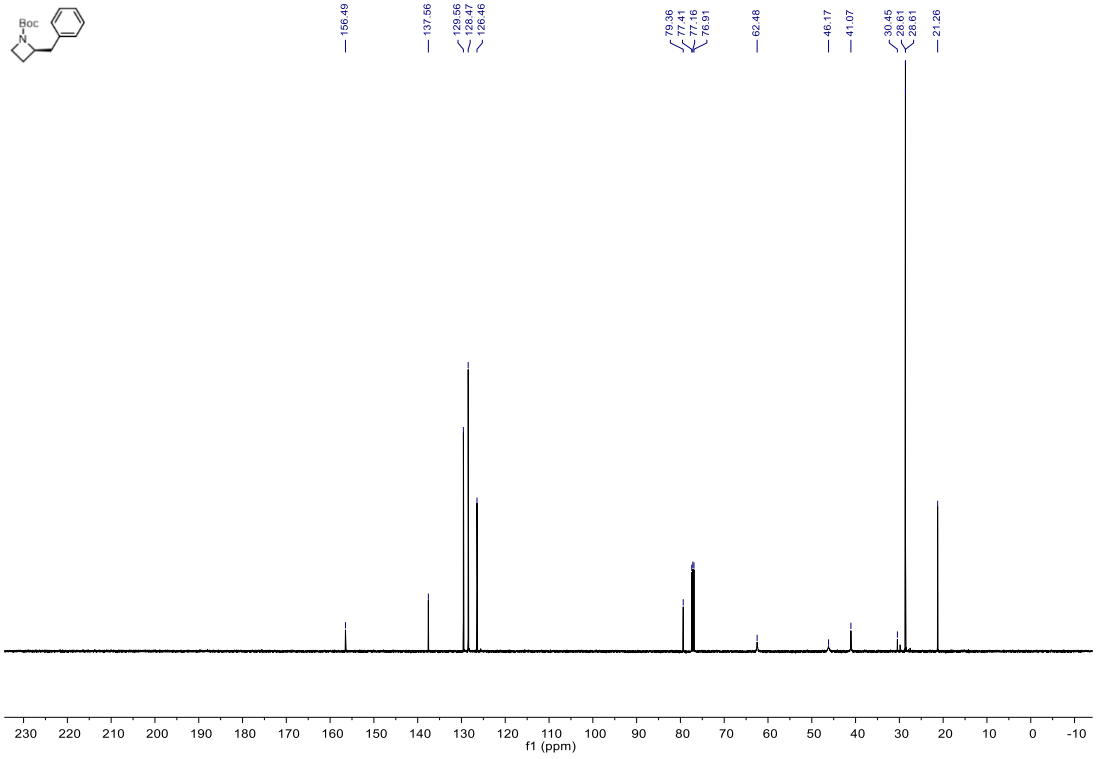
^{13}C NMR (151 MHz, $CDCl_3$) (**2.117**)



^{1}H NMR (600 MHz, $CDCl_3$) (**2.114**)



^{13}C NMR (151 MHz, $CDCl_3$) (**2.114**)



Chapter 3

Development of a Novel Boron-Based Chiral Auxiliary and its Use in Enantioselecitive Radical [3+2] Cycloaddition of Cyclopropylaniline and Alkenyl Diazaborolidines

3.1. Introduction

Saturated, boron-containing cyclic compounds possess potential therapeutic value due to their chameleonic coordination modes.[1] Moreover, the boron motif can serve as a versatile synthetic handle, allowing the modular construction of functionalized cyclic structures. This strategy is especially useful when chemists are equipped with strategies for control over the boron-containing stereocenters. In this connection, the boron-containing cyclic structures can be produced with high efficiency by cycloaddition reactions of simple acyclic alkenyl boron compounds.[2] In such reactions, multiple stereogenic centers can be produced in one step, allowing the rapid buildup of structural complexity. However, a large portion of these reactions take place with high reaction rates without a catalyst, rendering stereocontrol using external catalysts difficult. An alternative solution is the use of a chiral auxiliary attached to the boron center. While the use of chiral auxiliaries on boron has been well documented,[2, 3] stereocontrol over pericyclic cycloaddition reactions, in which the boron center or the auxiliary is not directly involved in the reaction, prove to be more

(1) Diaz, D. B.; Yudin, A. K. *Nat. Chem.* **2017**, *9*, 731–742.
(2) Reviews: (a) Grygorenko, O. O.; Moskvina, V. S.; Hryshchuk, O. V.; Tymtsunik, A. V. *Synth.* **2020**, *52*, 2761–2780. (b) Kanti Das, K.; Kumar, P.; Ghorai, D.; Mondal, B.; Panda, S. *Asian J. Org. Chem.* **2022**, *11*, e2021000.
(3) Review: "Boron-Containing Chiral Auxiliaries": Mantel, M.; Brauns, M.; Pietruszka J.; H*etero-cycles as Chiral Auxiliaries in Asymmetric Synthesis*, Springer, Cham, **2017**, pp. 73–112.

challenging. We hope to give a solution to these challenges by developing a new auxiliary that is generally effective and is readily prepared from inexpensive starting materials.

In this chapter, we will describe the development of a novel boronic ester-based auxiliary. Its powerful ability to control stereoselectivity will be exemplified by a stereoselective radical [3+2] cycloaddition of cyclopropylaniline and alkenylboron equipped with the auxiliary.

3.2. Background

3.2.1. Stereoselective Cycloaddition Reactions of Alkenyl Boron Compounds using Chiral Auxiliaries

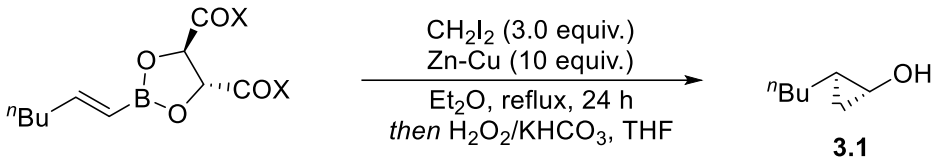
3.2.1.1. [2+1] Cycloaddition

Cyclopropanation. In 1990, Imai published the first stereoselective Simmons-Smith cyclopropanation of a *β*-substituted alkenyl boronate enabled by chiral auxiliaries on boron (Scheme 3.1).[4] A series of tartaric acid-derived diols were tested, and it was found that the auxiliary with X = NMe_2 (Entry 3, Scheme 3.1) provided the highest enantioselectivity (93% *ee*) for the derived cyclopropanol, although the yield was moderate. The observed facial selectivity was proposed to be controlled by bidentate chelation of the Simmons-Smith reagent with both the oxygen atom on the boronic ester and the carbonyl group on the backbone. Pietruszka modified the reaction by employing palladium-catalyzed

(4) Imai, T.; Mineta, H.; Nishida, S. *J. Org. Chem.* **1990**, *55*, 4986–4988.

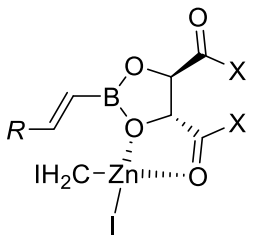
cyclopropanation[5] (Scheme 3.2).[6] Alkenyl boronate **3.2** was converted quantitatively to the cyclopropyl boronic ester **3.3** in 93:7 *dr.* Slow addition of the diazomethane solution was critical to achieving high diastereoselectivity.

Scheme 3.1. Imai's Stereoselective Cyclopropanation of Alkenyl Boronic Esters



Entry	X	Yield of **3.1** (%)	*ee* (%)
1	OMe	41	73
2	O^{i}Pr	44	86
3	NMe_2	48	93

Model of Stereocontrol:

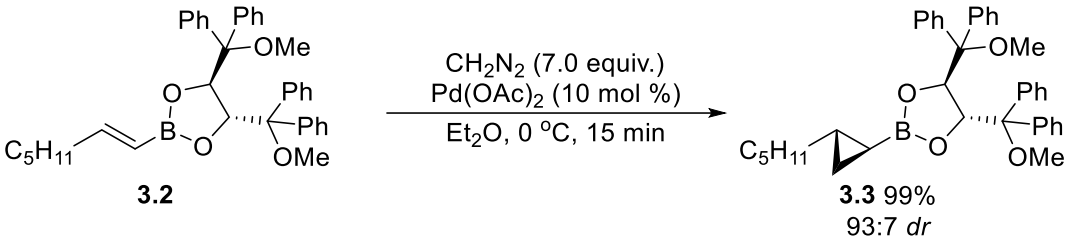


X = OMe, O^{i}Pr, or NMe_2

Epoxidation. Although epoxidation is usually categorized as oxidation and is rarely regarded as [2+1] cycloaddition, it is worth discussing in this section. Pietruszka evaluated the stereoselective epoxidation of alkenyl boronates bearing the auxiliary as in compound **3.2.** Using a range of oxidants, the diastereoselectivity was between 14% to 27% *de* (Scheme 3.2).[7]

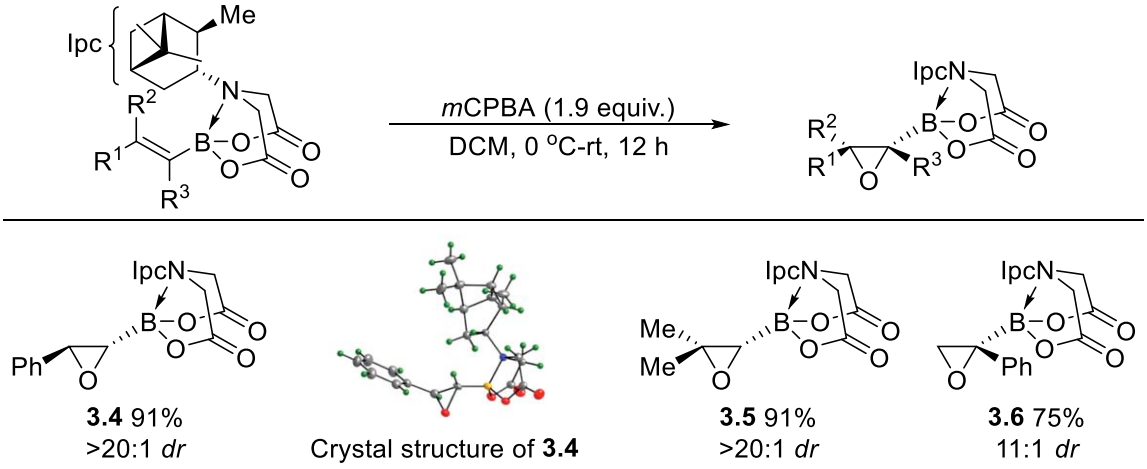
(5) Fontani, P.; Carboni, B.; Vaultier, M.; Carrié, R. *Tetrahedron Lett.* **1989**, *30*, 4815–4818.
(6) Luithle, J. E. A.; Pietruszka, J.; Witt, A. *Chem. Commun.* **1998**, 2651–2652.
(7) Fernández, E.; Frey, W.; Pietruszka, J. *Synlett,* **2010**, *9*, 1386–1388.

Scheme 3.2. Pietruszka's Stereoselective Cyclopropanation of Alkenyl Boronic Esters



In 2011, Burke published a diastereoselective epoxidation of alkenyl boronates using a newly designed pinene-derived iminodiacetic acid (PIDA) auxiliary (Scheme 3.3).[8] With *m*CPBA as the oxidant, alkenyl boronates of various substitution patterns were converted to epoxides in high yield and diastereoselectivity. Crystal structure of epoxidation product **3.4** showed that the isopinocampheyl group (Ipc) was in close proximity to the newly formed epoxide. Moreover, variable-temperature NMR analysis showed that the PIDA auxiliary was a conformationally rigid framework in both the starting material and the product. These features allowed the highly effective transfer of stereochemical information. The B(PIDA) auxiliary was synthesized from inexpensive α-pinene, and was stable on silica gel column chromatography, making it a practical chiral auxiliary on boron.

Scheme 3.3. Burke's Diastereoselective Epoxidation of Alkenyl Boronates



(8) Li, J.; Burke, M. D. *J. Am. Chem. Soc.* **2011**, *133*, 13774–13777.

3.2.1.2. [3+2] Cycloaddition

[3+2] Cycloaddition reactions between 1,3-dipolar compounds and alkenyl boronates has been extensively studied.[9] However, attempts for diastereoselective cycloadditions using chiral auxiliaries on boron generally resulted in moderate selectivity.

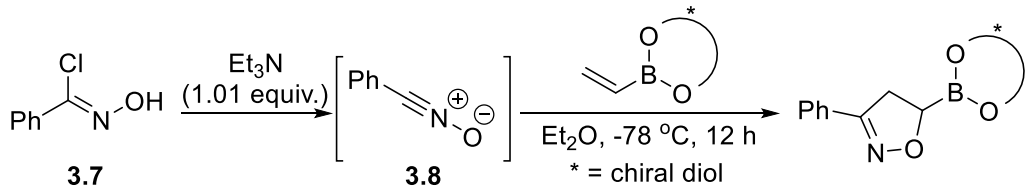
In 1999, Wallace examined a range of chiral diols as auxiliaries on boron in the [3+2] cycloaddition of alkenyl boronates with benzonitrile oxide (**3.8**). 1,3-Dipolar intermediate **3.8** was generated by treating phenylhydroximic acid chloride (**3.7**) with triethylamine (Scheme 3.4). Among the diol ligands tested, 1,2-diols, including pinane diol (**3.9**), tartaric acid-derived diol (**3.10**) and dihydrobenzoin (**3.11**), resulted in high yield but very low diastereoselectivity. The author then examined a few 1,4-diols and found that binaphthol (**3.12**) and TADDOL derivative **3.13** delivered the cycloaddition product in 2:1 *dr* and 2.8:1 *dr*, respectively.

Marsden developed a diethanolamine auxiliary that contained two stereogenic centers on the [3.3.0]-bicyclic framework of the boron derivative (Scheme 3.5a).[10] [3+2] Cycloaddition of *β*-ester alkenyl boronate **3.14** with benzonitrile oxide formed cycloadduct **3.16**, which after 1,3-boratropic shift, protonolysis and tautomerisation delivered isoxazoline **3.18** in 33% *ee*. The regioselectivity was different from Wallace's example (as in Scheme 3.4), possibly due to the inverted charge distribution on the alkene. In a later report, Marsden successfully improved the stereoselectivity by modification of the N-benzyl substituent (Scheme 3.5a).[11] Adding a methyl group (**3.15**) led to a significantly higher enantiomeric excess (70%). The author proposed a model for stereoselectivity. The

(9) Hilt, G.; Bolze, P. *Synthesis* **2005**, *13*, 2091–2115.
(10) Davies, C. D.; Marsden, S. P.; Stokes, E. S. E. *Tetrahedron Lett.* **1998**, *39*, 8513–8516.
(11) Davies, C. D.; Marsden, S. P.; Stokes, E. S. E. *Tetrahedron Lett.* **2000**, *41*, 4229–4233.

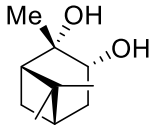
conformation of [3.3.0]-bicycle was fixed by the two α-oxygen phenyl substituents, and the alkyl substituent on nitrogen was forced to rotate to the depicted position. In order to avoid the steric repulsion shown in **A**, the alkene would point to the right (**B**), thus determining the face selectivity of the cycloaddition. The author also evaluated the auxiliary in the cycloaddition with a nitrone dipole (**3.20**, Scheme 3.5b) generated from benzaldoxime (**3.19**). After oxidation of the boronate, the hydroxylated isoxazolidine (**3.21**) was isolated in 65% *ee.*

Scheme 3.4. Wallace's Attempts for Diastereoselective [3+2] Cycloaddition of Alkenyl Boronates

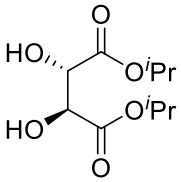


3.7 **3.8**

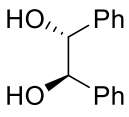
Chiral Diol Auxiliaries:



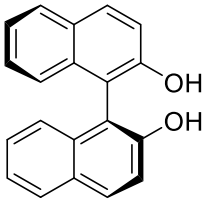
3.9
1:1 *dr*



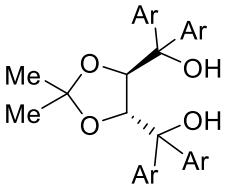
3.10
1:1 *dr*



3.11
1:1 *dr*



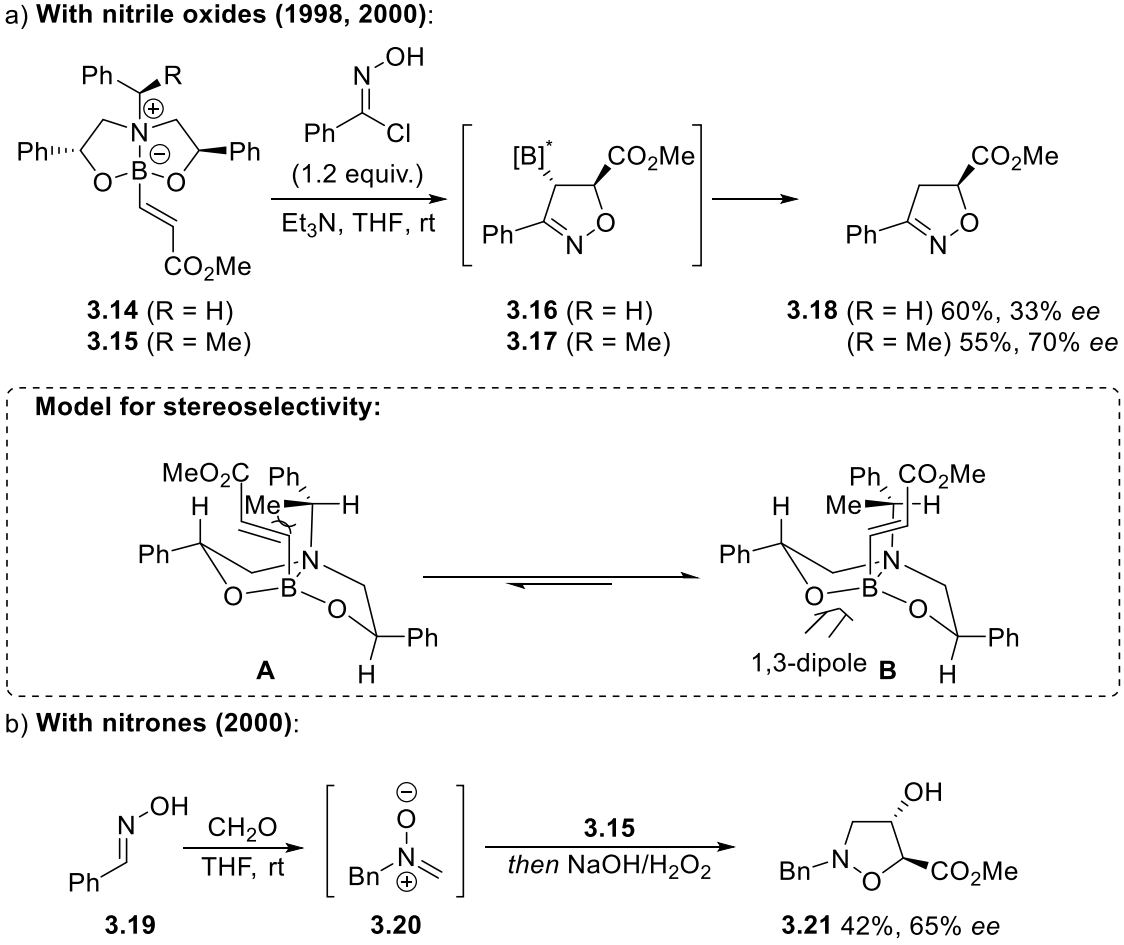
3.12
2:1 *dr*



3.13
2.8:1 *dr*

Ar = 3,5-di-MePh

Scheme 3.5. Marsden's Chiral Diethanolamine Auxiliary in [3+2] Cycloaddtion Reactions



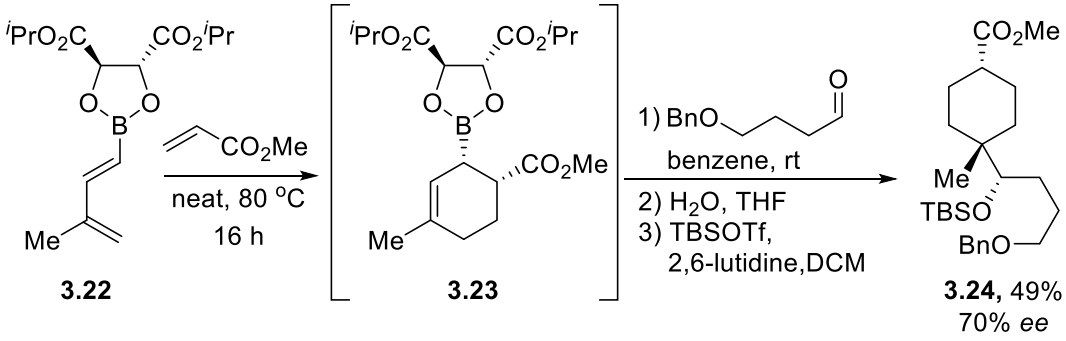
3.2.1.3. [4+2] Cycloaddition

Diene Containing Boron. In 1996, Lallemand reported a diastereoselective Diels-Alder reaction using chiral 1,3-dienylboronates (Scheme 3.6a). Dienylboronate **3.22** bearing a tartaric acid derivative as chiral auxiliary on boron underwent [4+2] cycloaddition with methyl acrylate to form cycloadduct **3.23**. After allylboration and protection, **3.24** formed with 70% *ee*.

Diastereoselective hetero-Diel-Alder reaction was also reported. Jiang achieved the diastereoselective cycloaddition of dienylboronate **3.25** with diazo-derived dienophile **3.26**, forming cycloadduct **3.27** in good yield and excellent diastereoselectivity.

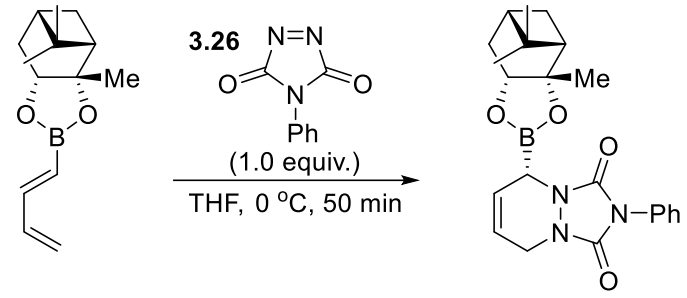
Scheme 3.6. Examples of Diastereoselective Diel-Alder Reactions Involving Boron on the Diene

a) **Lallemand (1996)**:



3.22 **3.23** **3.24,** 49%
70% *ee*

b) **Jiang (2001)**:



3.25 **3.27** 84%,
>20:1 *dr*

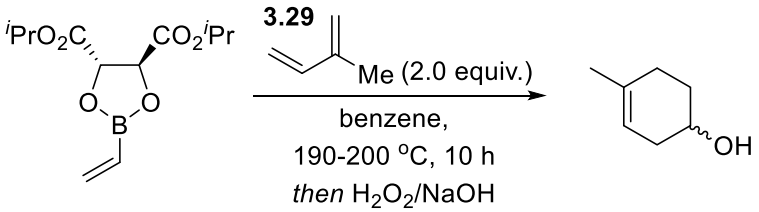
Boron-Containing Dienophile. Alkenyl boron compounds have also been employed as dienophiles in Diels-Alder reactions. In 1999, Avery examined vinyl boronate **3.28** attached to a tartaric acid-derived auxiliary in the cycloaddition reaction with diene **3.29** (Scheme 3.7a).[12] After oxidation of the boronate, the product was obtained in moderate stereoselectivity (33% *ee*). Using both computational and experimental methods,

(12) Bonk, J. D.; Avery, M. A. *Tetrahedron Asymmetry* **1997**, *8*, 1149–1152.

Pellegrinet evaluated an extensive library of alkylhalovinylboranes connected to alkyl groups from the chiral pool.[13] These compounds proved to be highly reactive, allowing Diels-Alder reactions to take place at 0 °C. However, most of the chiral dienophiles examined provided low stereoselectivity in [4+2] cycloaddition reactions. The highest enantioselectivity (40% *ee*) was obtained by reacting (+)-2-carene-derived chlorovinylborane **3.31** with cyclopentadiene (**3.32**) (Scheme 3.7b).

Scheme 3.7. Examples of Diastereoselective Diel-Alder Reactions Involving Boron on the Dienophile

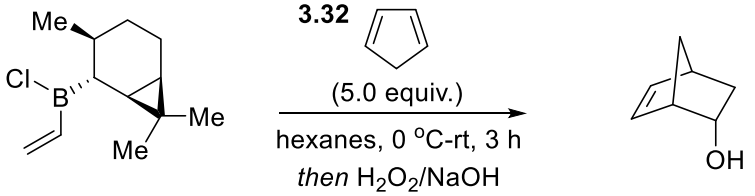
a) **Avery (1999)**:



3.28

3.30 61%, 33% *ee*

b) **Pellegrinet (2018)**:



3.31

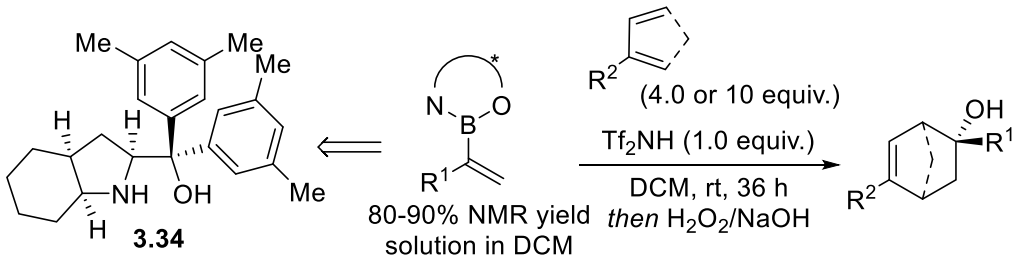
3.33 34%, 40% *ee*

In 2020, Brown provided a solution to the problem related to low stereoselectivity in the Diels Alder reaction by employing chiral proline-derived auxiliary **3.34** (Scheme 3.8).[14] The auxiliary was installed on alkenyl boroxines by heating in toluene at reflux in a Dean-Stark apparatus. The resulting boronates were used without separation in cycloaddition reactions. A range of dienes and

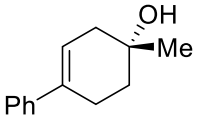
(13) Pisano, P. L.; Pellegrinet, S. C. *RSC Adv.* **2018**, *8*, 33864–33871.
(14) Ni, D.; Witherspoon, B. P.; Zhang, H.; Zhou, C.; Houk, K. N.; Brown, M. K. *Angew. Chem. Int. Ed.* **2020**, *59*, 11432–11439.

dienophiles were tested, giving generally good regio- and stereoselectivity. In the stereoselectivity model proposed by the authors, the diene was forced to approach from the face not blocked by the bulky six-membered ring.

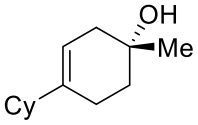
Scheme 3.8. Brown's Diastereoselective Diel-Alder Reaction with Chiral Alkenylboronates



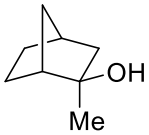
Selected Examples:



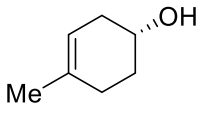
3.35, 69%
>20:1 *rr*,
93:7 *er*



3.36, 70%
>20:1 *rr*,
90:10 *er*

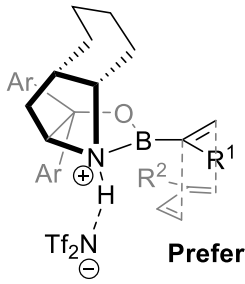


3.37, 62%
>20:1 *rr*,
93:7 *er*



3.38, 78%
>20:1 *rr*,
97:3 *er*

Model of Stereoselectivity:

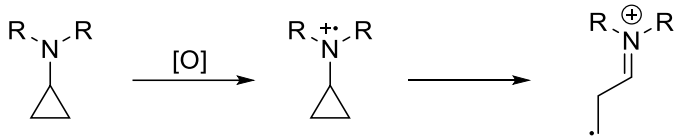


Prefered face of approach

3.2.2. Photocatalyzed Radical Ring-Opening/ Closing Cycloaddition of Cyclopropylamine Derivatives

Over the past few decades, the field of photocatalysis in organic chemistry has seen significant growth.[15] Upon excitement with visible light, ruthenium or iridium polypyridyl complexes, as well as organic photocatalysts[16], can either transfer an electron to or receive an electron from a second catalyst or substrate. Amines can undergo single electron oxidation with excited photocatalysts into aminyl radical cations, and are historically used as sacrificial reductants to regenerate photocatalysts.[17]

Scheme 3.9. Ring-Opening of Cyclopropylaminyl Radical Cation



3.39 **3.40** **3.41**

Cyclopropylamine (**3.39**, Scheme 3.9), upon oxidation to an aminyl radical cation (**3.40**), is known to undergo irreversible ring-opening to form an iminium cation and a carbon-centered radical (**3.41**). This reactivity has been utilized in intramolecular reactions, including radical cyclization[18] and cycloaddition[19] induced by chemical oxidants like oxygen and CAN.

(15) Reviews: (a) Shaw, M. H.; Twilton, J.; MacMillan, D. W. C. *J. Org. Chem.* **2016**, *81*, 6898–6926. (b) Romero, N. A.; Nicewicz, D. A. *Chem. Rev.* **2016**, *116*, 10075–10166. (c) Liu, Q.; Wu, L. Z. *Natl. Sci. Rev.* **2017**, *4*, 359–380.

(16) Review: Bobo, M. V.; Kuchta, J. J.; Vannucci, A. K. *Org. Biomol. Chem.* **2021**, *19*, 4816–4834.

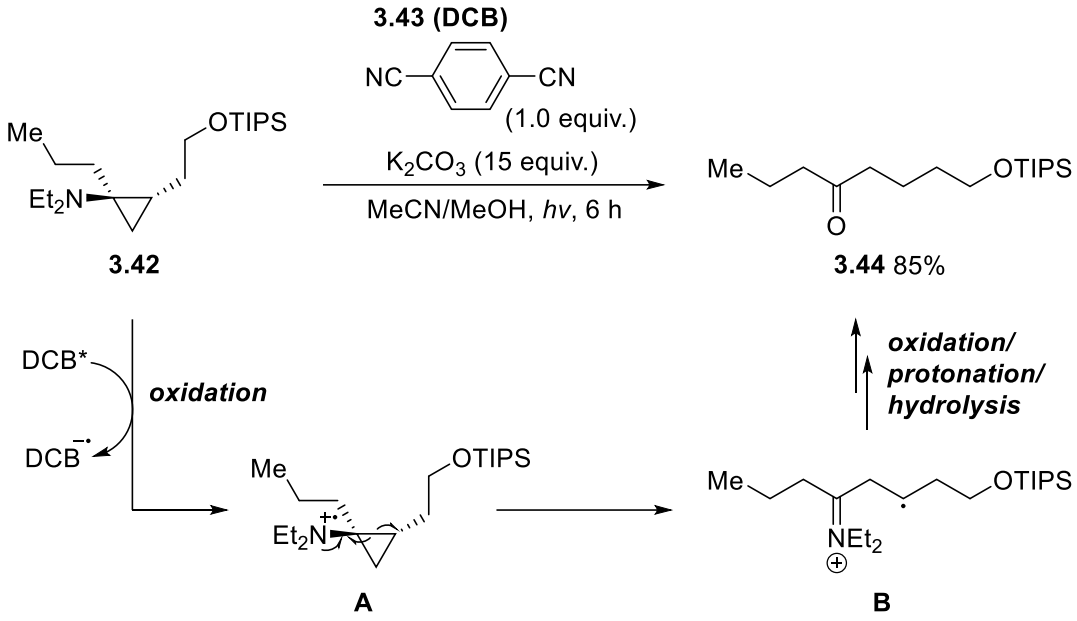
(17) (a) DeLaive, P. J.; Foreman, T. K.; Whitten, D. G.; Giannotti, C. *J. Am. Chem. Soc.* **1980**, *102*, 5627–5631. (b) DeLaive, P. J.; Sullivan, B. P.; Meyer, T. J.; Whitten, D. G. *J. Am. Chem. Soc.* **1979**, *101*, 4007–4008.

(18) Lee, H. B.; Sung, M. J.; Blackstock, S. C.; Cha, J. K. *J. Am. Chem. Soc.* **2001**, *123*, 11322–11324.

(19) Takemoto, Y.; Yamagata, S.; Furuse, S. I.; Hayase, H.; Echigo, T.; Iwata, C. *Chem. Commun.* **1998**, *6*, 651–652.

In a report in 1997, Cha demonstrated the oxidation of cyclopropylamine by a photooxidant 1,4-dicyanobenzene (DCB, **3.43**) (Scheme 3.10).[20] Tertiary cyclopropylamine **3.42** was oxidized by photosensitized DCB into aminyl radical cation **A**, and radical ring-opening of the strained cyclopropyl ring produced carbon-centered radical intermediate **B**. After oxidation/protonation of the radical followed by hydrolysis of the iminium ion, ketone **3.44** was isolated in 85% yield.

Scheme 3.10. Cha's Ring Opening of Cyclopropylamines by Photooxidation

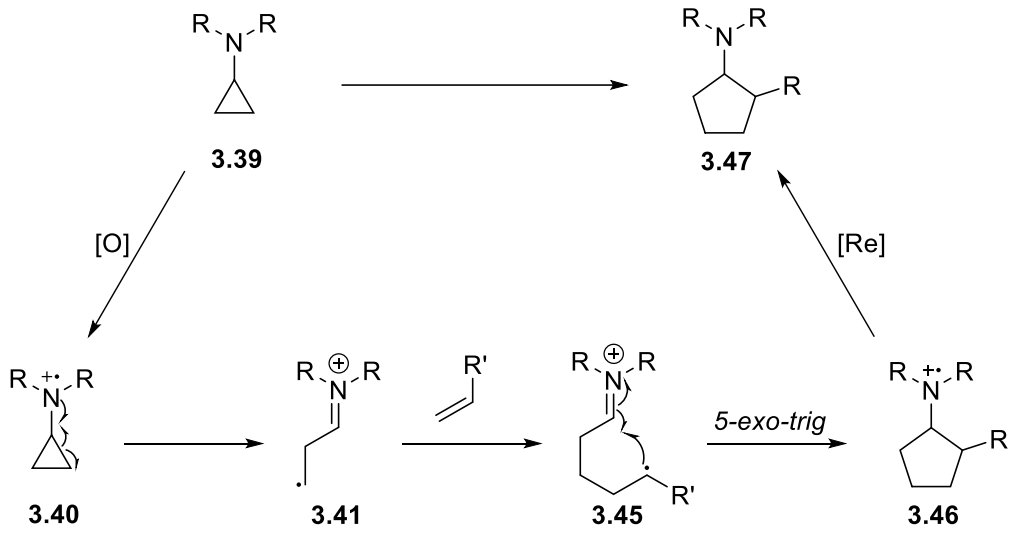


Because the ring-opening of cyclopropylaminyl radical cations is thermodynamically favored, the resulting carbon-centered radical will not undergo radical addition to the iminium cation and reconstruct the strained cyclopropyl ring. However, if the carbon-centered radical is trapped by an alkene, the newly formed radical (**3.45**, Scheme 3.11) may undergo 5-exo-trig intramolecular radical addition to the iminium cation to form 5-membered ring **3.46**. Through the sequence of elementary reactions, cyclopropylamine **3.39** effectively undergoes a [3+2] cycloaddition to form cyclopentylamine **3.47**. The overall reaction is redox neutral, requiring a SET oxidation (**3.39** to

(20) Lee, J.; U, J. S.; Blackstock, S. C.; Cha, J. K. *J. Am. Chem. Soc.* **1997**, *119*, 10241–10242.

3.40) and a SET reduction (**3.46** to **3.47**). This mode of reaction has the potential to be realized by a photocatalyst.

Scheme 3.11. Radical Ring-Opening/Closing [3+2] Cycloaddition of Cyclopropylamines

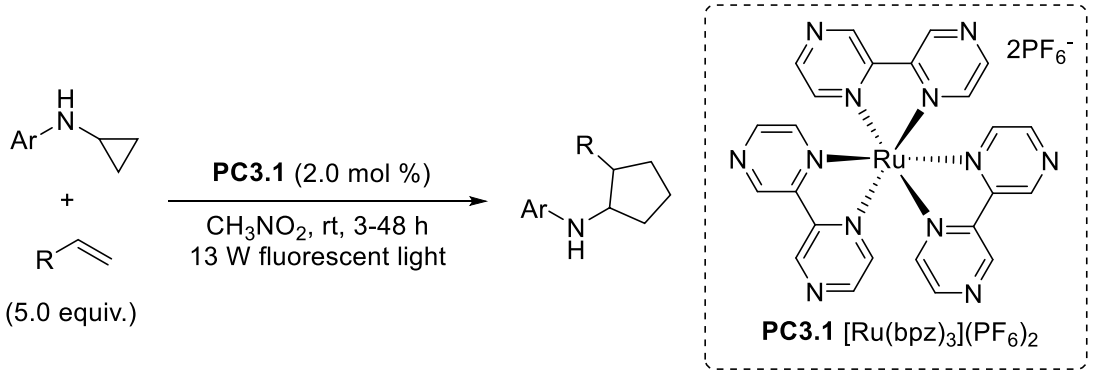


In 2012, Zheng developed the first intermolecular [3+2] cycloaddition of cyclopropylamines with olefins using visible-light photocatalysis (Scheme 3.12).[21] Cyclopropylanilines bearing different aryl groups on the nitrogen were engaged in reactions with styrenes (as in **3.49, 3.50**), acrylonitrile (**3.51**) and dienes (**3.52**), forming cyclopentylanilines in moderate to good yield. The optimal photocatalyst was $[Ru(bpz)_3](PF_6)_2$ (**PC3.1**). In the catalytic cycle proposed by the author, cyclopropylaniline **A** was oxidized by photoexcited catalyst (Ru^{II*}) into aminyl radical cation **B**. After ring-opening/radical addition/5-exo-trig addition, aminyl radical cation **F** was reduced by Ru^{I} forming cycloaddition product **G** and regenerating the photocatalyst (Ru^{II}). The aryl group on the amine was essential for the stabilization of the intermediate radical cation, and substitution on alkene **D** was required to provide stabilization of the α-radical in intermediate **E**. In a later report

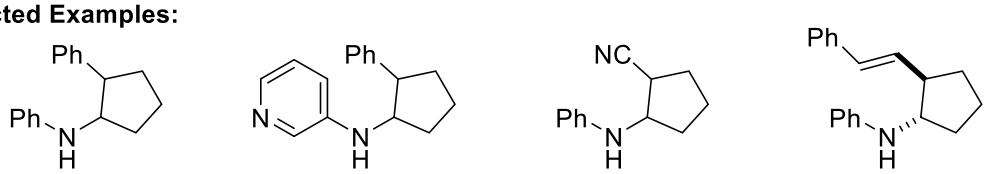
(21) Maity, S.; Zhu, M.; Shinabery, R. S.; Zheng, N. *Angew. Chem. Int. Ed.* **2012**, *51*, 222–226.

in 2017, observation of fleeting aminyl radical cation **B** and **F** by mass spectrometric techniques lent credibility to the proposed catalytic cycle.[22]

Scheme 3.12. Zheng's Ruthenium-Catalyzed [3+2] Cycloaddition of Cyclopropylamine with Olefins



Selected Examples:



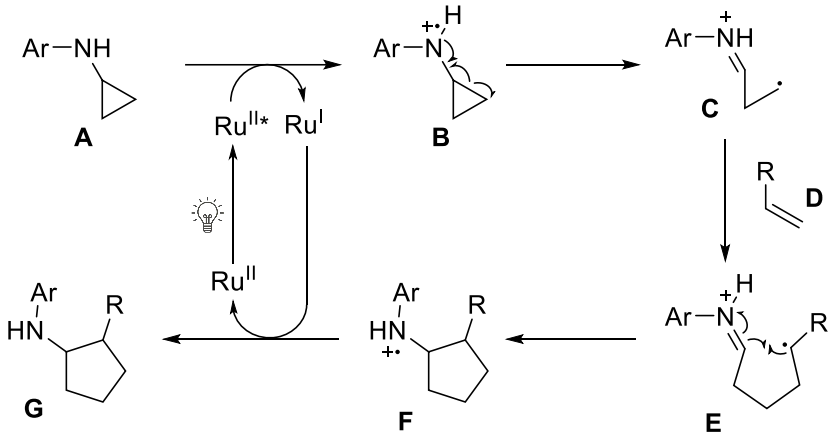
3.49 87%
1:1 *dr*

3.50 46%
1:1 *dr*

3.51 52%
1:1 *dr*

3.52 40%
2:1 *dr*

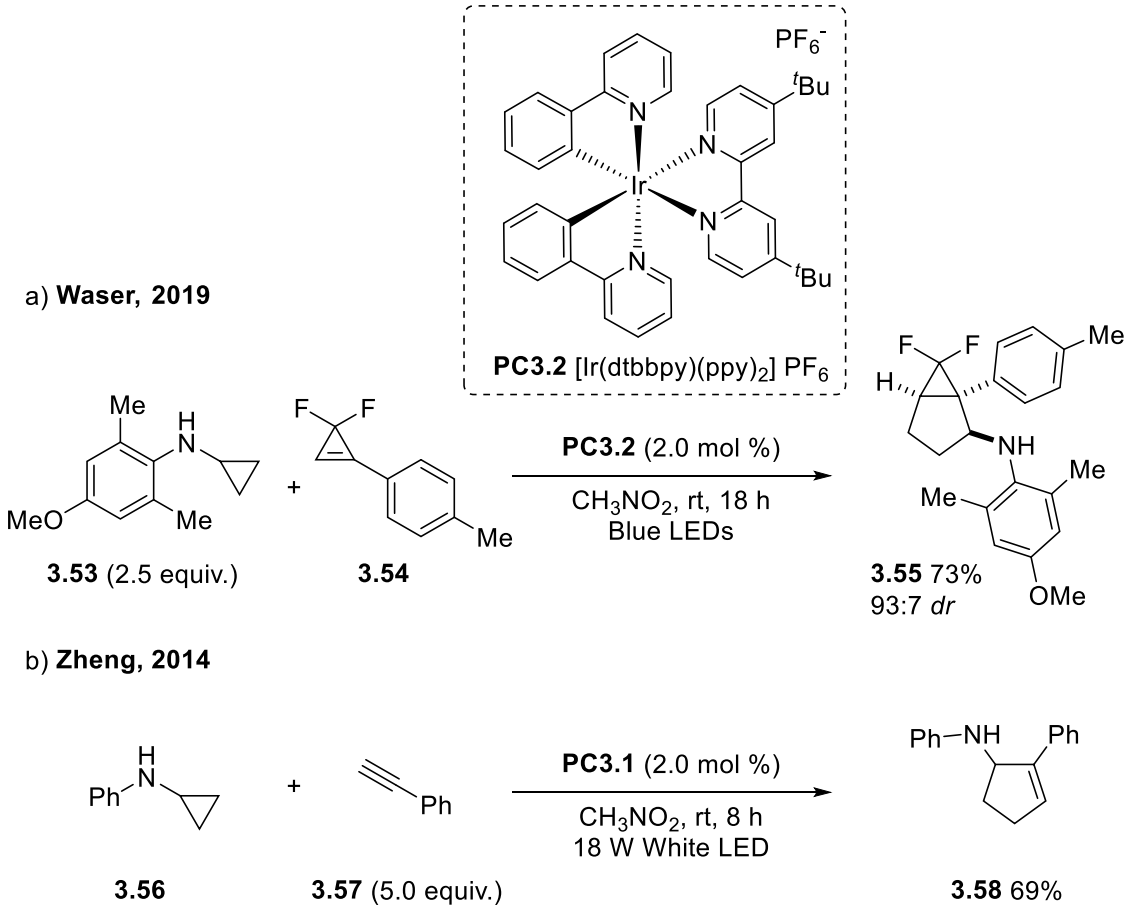
Proposed Catalytic Cycle:



(22) Cai, Y.; Wang, J.; Zhang, Y.; Li, Z.; Hu, D.; Zheng, N.; Chen, H. *J. Am. Chem. Soc.* **2017**, *139*, 12259–12266.

Waser utilized this reactivity in the synthesis of bicyclo[3.1.0]hexanes (Scheme 3.13a).[23] Using $[Ir(dtbbpy)(ppy)_2]PF_6$ (**PC3.2**) as photocatalyst under blue LED, cyclopropylaniline (**3.53**) and difluorocyclopropene (**3.54**) underwent cycloaddition to form bicycle **3.55** in good yield and diastereoselectivity. Zheng expanded the scope of the [3+2] cycloaddition by employing arylacetylenes as radical acceptors, producing aminylcyclopentenes in high efficiency (Scheme 3.13b).[24] Of note, [4+2] cycloadditions of cyclobutylanilines with alkenes[25] and alkynes[26] were accomplished by Zheng using similar conditions.

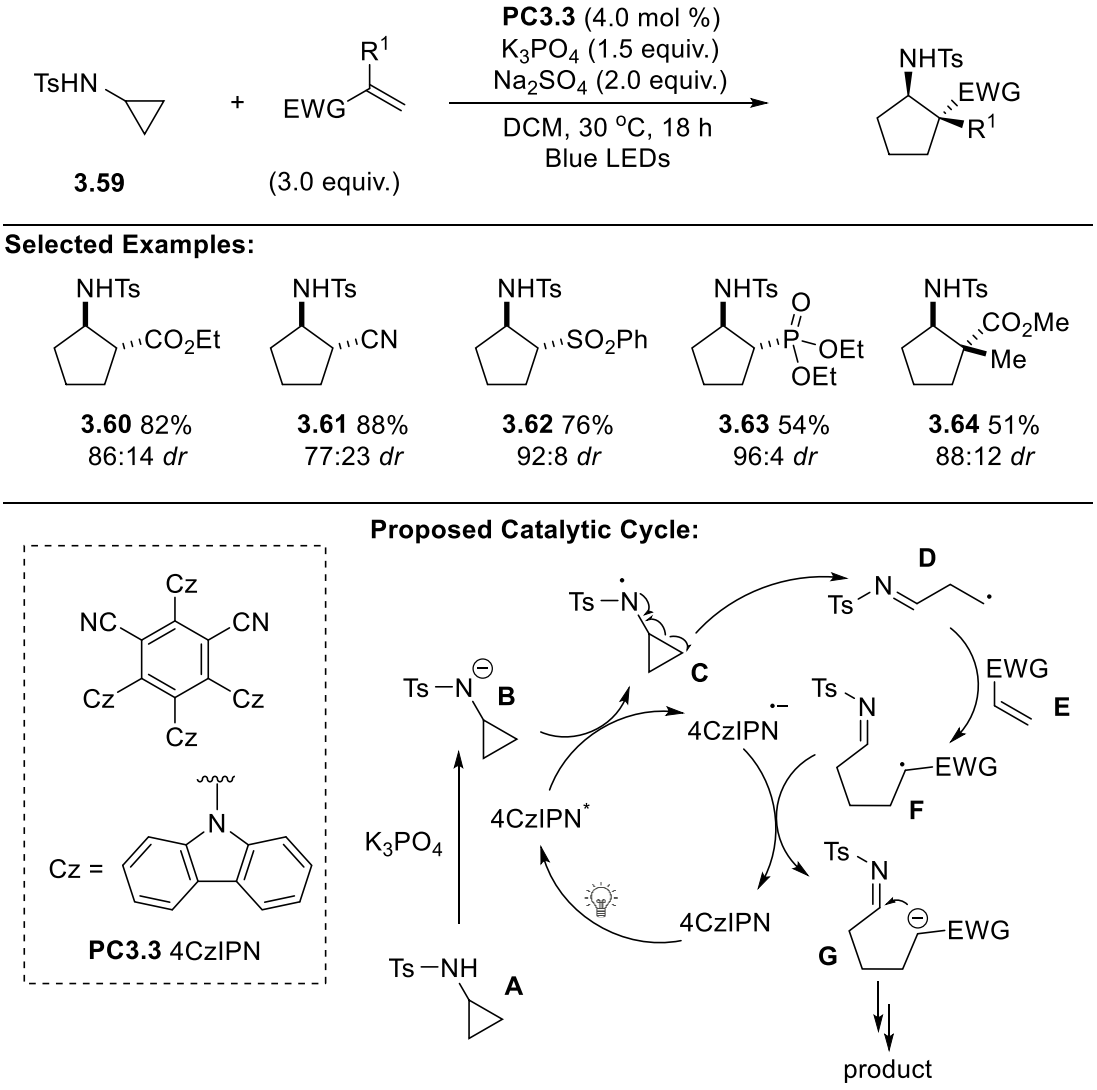
Scheme 3.13. Examples of [3+2] Cycloaddition of Cyclopropylamines



(23) Muriel, B.; Gagnebin, A.; Waser, J. *Chem. Sci.* **2019**, *10*, 10716–10722.
(24) Nguyen, T. H.; Morris, S. A.; Zheng, N. *Adv. Synth. Catal.* **2014**, *356*, 2831–2837.
(25) Wang, J.; Nguyen, T. H.; Zheng, N. *Sci. China Chem.* **2016**, *59*, 180–183.
(26) (a) Wang, J.; Zheng, N. *Angew. Chem. Int. Ed.* **2015**, *54*, 11424–11427. (b) Wang, Q.; Zheng, N. *ACS Catal.* **2017**, *7*, 4197–4201.

In 2020, Aggarwal reported a [3+2] cycloaddition of N-sulfonyl cyclopropylamines with eletron-poor olefins (Scheme 3.14).[27] Alkenes bearing a range of different electron-withdrawing groups participated in the reaction, yielding cyclopentylamines in good diastereoselectivity. An organophotocatalyst 4CzIPN (**PC3.3**) was employed. Mechanistic studies showed that the reaction

Scheme 3.14. Aggarwal's Diastereoselective [3 + 2] Cycloadditions of N-Sulfonyl Cyclopropylamines



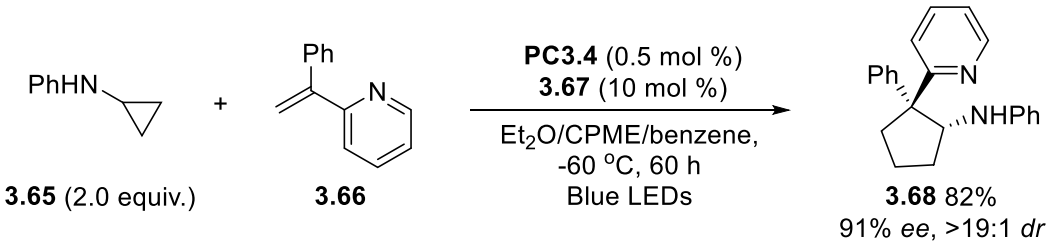
went through a different pathway from the radical [3+2] reactions mentioned above. Radical

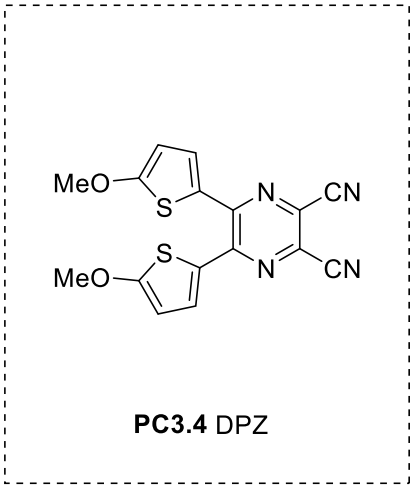
(27) White, D. H.; Noble, A.; Booker-Milburn, K. I.; Aggarwal, V. K. *Org. Lett.* **2021**, *23*, 3038–3042.

intermediate **F**, forming after radical addition to olefin **E**, was proposed to be reduced to stabilized carboanion **G** before a 5-exo-trig cyclization took place

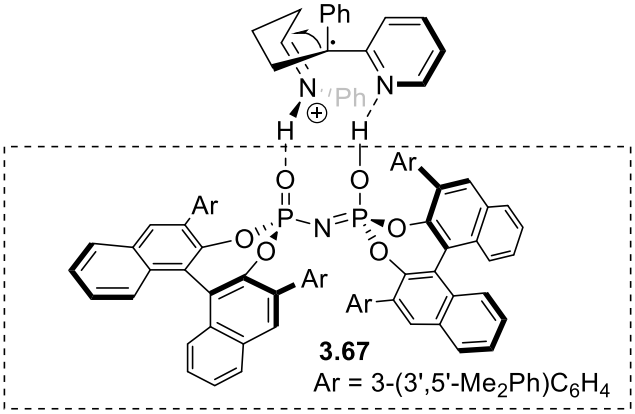
Enantioselective Cycloadditions. Even though no catalyst was directly involved in the stereochemistry-determining step (presumably the 5-exo-trig cyclization step) in the forementioned cases, enantioselective [3+2] cycloadditions were accomplished using directing group strategies. In 2020, Huang and Jiang utilized a chiral Brønsted acid catalyst (**3.67**, Scheme 3.15) to induce enantioselectivity in the cycloaddition of cyclopropyl aniline (**3.65**) with 2-(1-phenylvinyl)pyridine (**3.66**). The iminium cation and the pyridine was proposed to coordinate with the chiral Brønsted acid *via* hydrogen-bonds, forcing the 5-exo-trig radical addition to take place from the *si* face of the iminium cation. In 2021, Ooi achieved enantioselective cycloaddition of cyclopropylurea (**3.69**,

Scheme 3.15. Huang and Jiang's Enantioselective [3 + 2] Cycloadditions of Cyclopropylamines



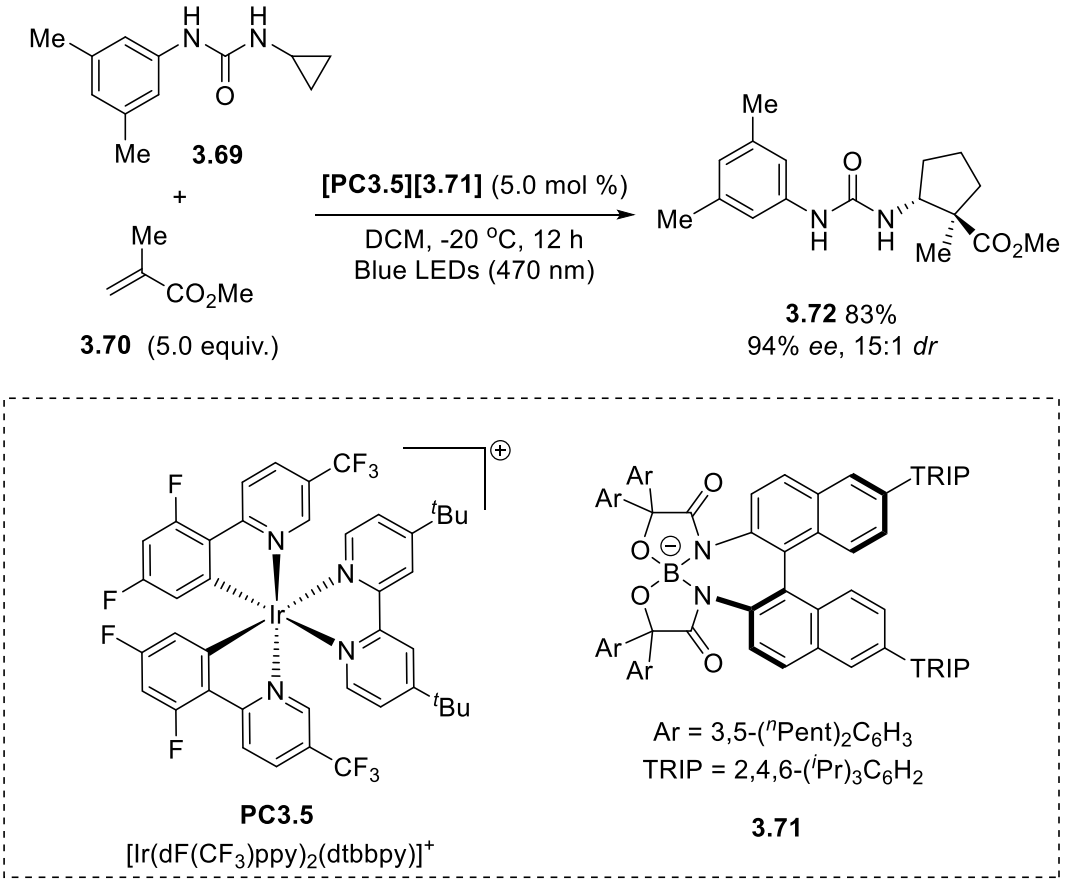


Model of Stereoselectivity:



Scheme 3.16) and alkene **3.70** through the hydrogen-bond interaction between urea directing group and catalytic chiral borate anion **3.71**. [28]

Scheme 3.16. Ooi's Enantioselective [3+2] Cycloadditions Directed by Urea Group

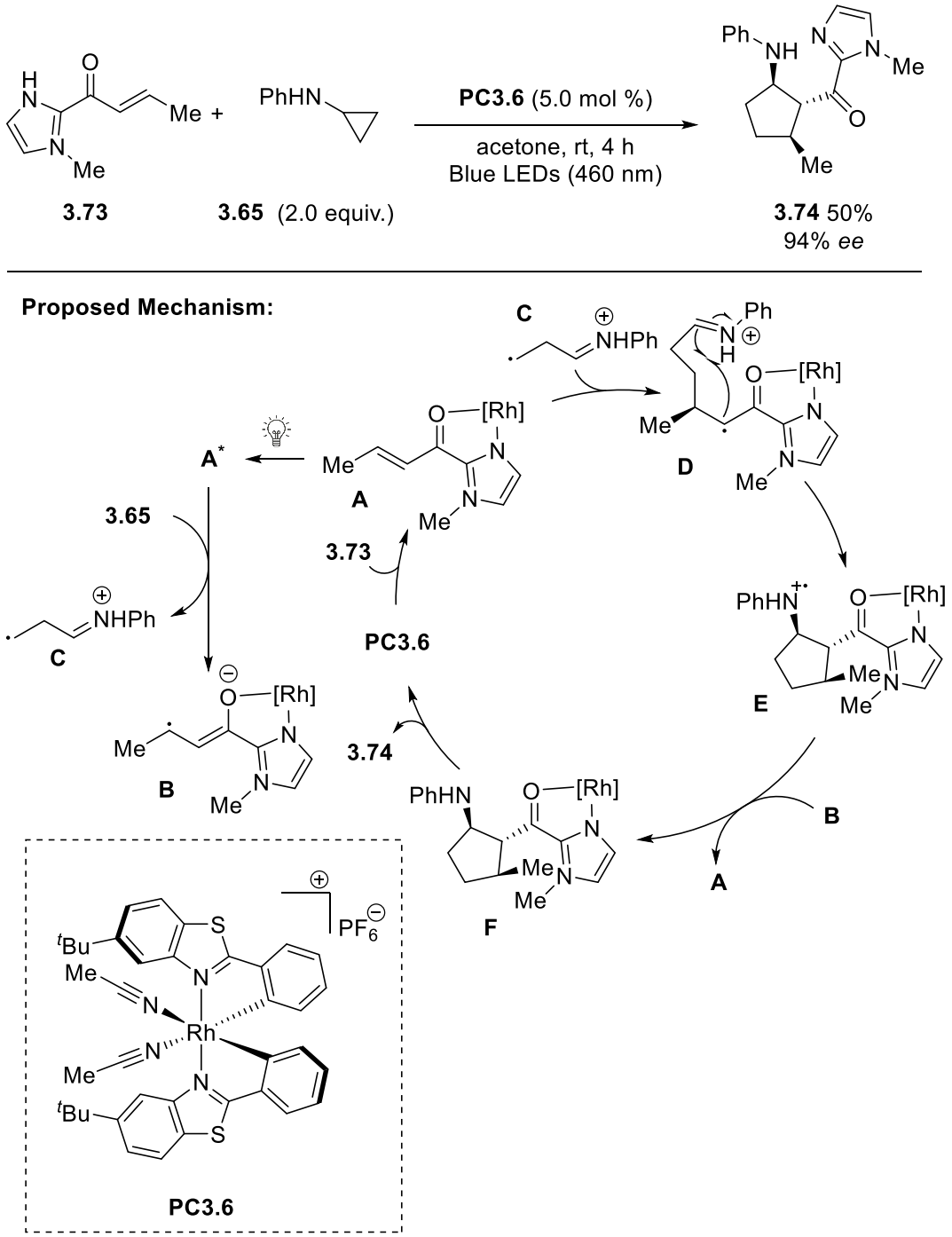


The enantioselectivity could also be controlled by chiral photocatalysts that coordinated directly to the substrates. In 2022, Fraile and Aleman reported an enantioselective cycloaddition between α,β-unsaturated acyl imidazole **3.73** and cyclopropylaniline (**3.65**) using a chiral rhodium photocatalyst (**PC3.6**) (Scheme 3.17).[29] In the proposed catalytic cycle, **PC3.6** would coordinate with **3.73** to form photosensitized complex **A**, which would oxidize **3.65** to form radical **C** after ring-opening. Intermediate **C** would undergo radical addition to another molecule of **A** to produce

(28) Kimura, Y.; Uraguchi, D.; Ooi, T. *Org. Biomol. Chem.* **2021**, *19*, 1744–1747.
(29) Mollari, L.; Valle-Amores, M. A.; Martínez-Gualda, A. M.; Marzo, L.; Fraile, A.; Aleman, J. *Chem. Commun.* **2022**, *58*, 1334–1337.

radical **D**, which would cyclize to form aminyl radical cation **E**. Reduction by **B** followed by dissociation from rhodium photocatalyst would yield the final product **3.74**.

Scheme 3.17. Fraile and Aleman's Enantioselective [3+2] Cycloadditions with Chical Rhodium Photocatalyst



3.3. Development of a Novel Boron-Based Chiral Auxiliary and its Use in Enantioselecitive Radical [3+2] Cycloaddition of Cyclopropylaniline and Alkenyl Diazaborolidines[30]

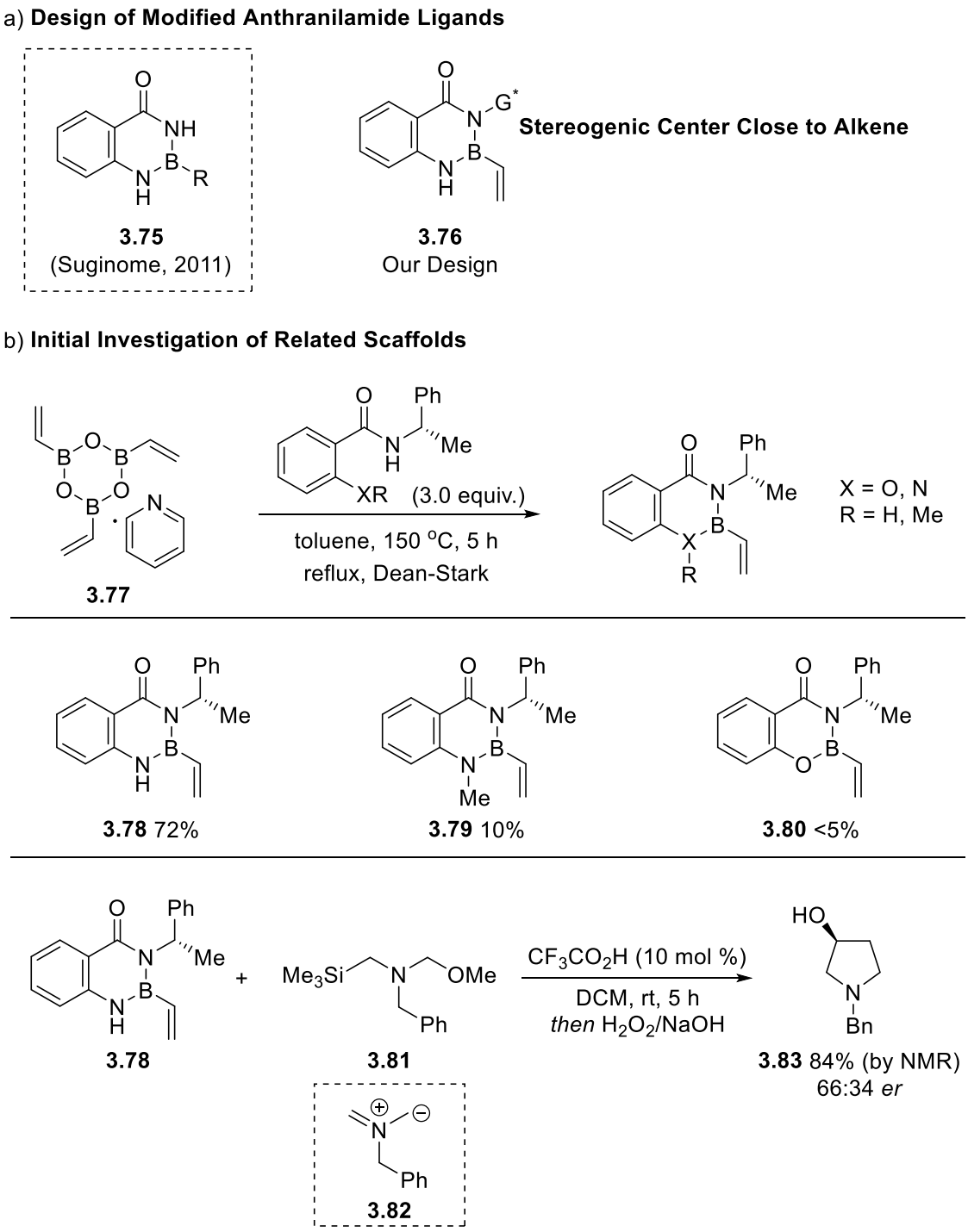
3.3.1. Development of a Novel Chiral Auxiliary on Boron

As shown in section **3.2.1**, it proved to be challenging for chiral auxiliaries on boron to effectively control the stereoselectivity of cycloaddition reactions. The stereogenic centers in many auxiliary scaffolds, such as diol ligands derived from tartaric acid and TADDOL, were positioned on the backbone of the ligand and far away from the reacting double bond. We reasoned that the use of nitrogen-based ligands would allow the installation of stereogenicity closer to the reaction center leading to enhanced steric bias between the two faces of the reacting alkene. In addition, bidentate ligands were preferred because they preserved the valence deficiency of three-coordinate boron centers that could assist cycloaddition reactions by lowering the LUMO energy of the connected alkenes.

Besides being effective in stereoselective reactions, the auxiliary was required to be easily synthesized from inexpensive starting materials and to provide stable boron-based derivatives. Searching in literature for suitable scaffolds, we set our eyes on anthranilamide, a bisamino ligand that was found by Suginome to form stable diazaborolidines (**3.75**, Scheme 3.18a) with boronic acids.[31] Installation of a chiral substituent G* on the amide nitrogen would position a stereogenic center close to the alkene.

(30) Zhang, M.; Xu, P.; Vendola, A. J.; Allais, C.; Dechert Schmitt, A.-M.; Singer, R.; Morken, J. P. *Angew. Chem. Int. Ed.* **2022**, e202205454.
(31) Ihara, H.; Koyanagi, M.; Suginome, M. *Org. Lett.* **2011**, *13*, 2662–2665.

Scheme 3.18. Initial Investigation of Bisamino Ligands



My coworker Mingkai Zhang synthesized a series of related ligands bearing a (*R*)-1-methylbenzyl substituent on the amide nitrogen and attempted condensation with vinyl

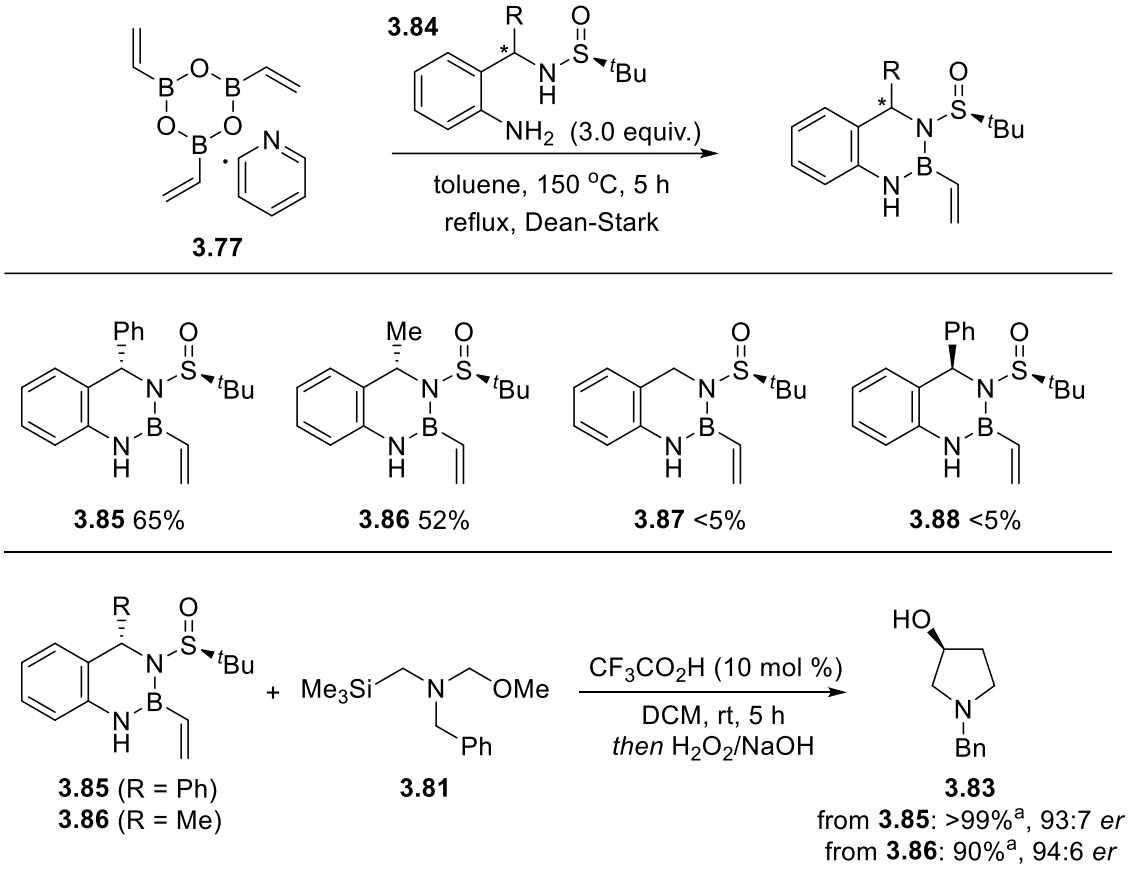
boroxine pyridine complex (**3.77**, Scheme 3.18b). Vinyl diazaborolidine **3.78** was synthesized in 72% yield. However, when the aniline was substituted with a methyl group (**3.79**) or replaced by a phenol group (**3.80**), the condensation reactions turned out to be ineffective. Compound **3.78** was tested in the [3+2] cycloaddition with azomethine ylide **3.82** derived from acid-promoted elimination of TMSOMe from precursor **3.81**. After oxidation, the cycloadduct **3.83** formed in 84% yield (determined by NMR analysis with an internal standard) and moderate stereoselectivity of 66:34 *er*. We reasoned that the alkyl substituent on the amide nitrogen could rotate freely around the C-N bond axis, and this might impair the stereocontrol.

Looking for potential auxiliary scaffolds that could lead to more rigid molecule, we considered a family of bisamino ligands (**3.84**, Scheme 3.19) containing chiral sulfinamides derived from Ellman's auxiliary. Of note, these compounds were prepared by Suna [32], Sun [33] and Maruoka [34] for completely different purposes. We attempted the condensation of these compounds with **3.77**, and found that vinyl diazaborolidine **3.85** and **3.86** were successfully isolated in moderate to good yield. Compound **3.87**, with no substitution on the benzylic carbon, was found to be unstable for purification on silica gel column chromatography. Attempts to synthesize compound **3.88** failed, possibly due to the penalizing interaction between the phenyl group and the sulfinamide group that developed during formation of the diazaborolidine. Testing **3.85** and **3.86** in cycloaddition with **3.81**, we were pleased to find that hydroxyl pyrrolidine **3.83** formed in excellent yield and good stereoselectivity. The results from **3.85** and **3.86** were comparable, and because **3.85** was

(32) Martjuga, M.; Belyakov, S.; Liepinsh, E.; Suna, E. *J. Org. Chem.* **2011**, *76*, 2635–2647.
(33) Huang, L.; Cao, Y.; Zhao, M.; Tang, Z.; Sun, Z. *Org. Biomol. Chem.* **2014**, *12*, 6554–6556.
(34) Lee, H. J.; Arumugam, N.; Almansour, A. I.; Kumar, R. S.; Maruoka, K. *Synlett*, **2019**, *30*, 401–404.

more easily synthesized and more soluble, we decided to proceed with the auxiliary (**3.87**, Scheme 3.20) with phenyl substitution at the benzylic position, and it was referred to as '**sam**' (**s**ulfon**a**mide-a**m**ine).

Scheme 3.19. Initial Investigation of Sulfinylamide Ligands

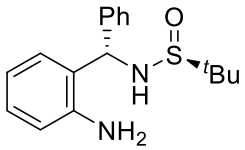


a) Yield determined by 1H NMR analysis with externally added internal standard.

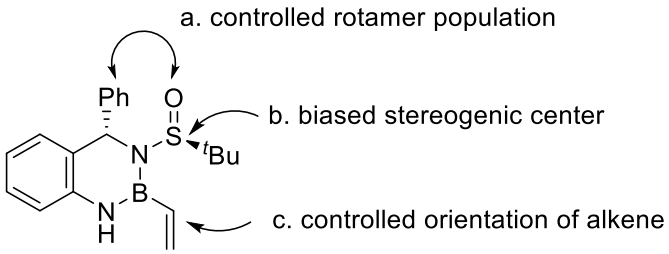
The excellent ability of 'sam' auxiliary to control stereoselectivity of cycloaddition reactions came from several structural advantages when installed on an alkenylboron (Scheme 3.20). As demonstrated in the x-ray crystallography of **3.85**, the benzylic phenyl substituent controlled the configuration of the chiral sulfinyl group, forcing the bulky *tert*-butyl group to take the opposite direction in space. Moreover, as the alkene π-system was in conjugation with the empty boron p_z orbital, the vinyl group was coplanar with the N-

B-N π face, while being pushed to the direction pointing away from the bulky sulfonamide group. In the model for stereoselectivity (Scheme 3.21), the *Si* face was blocked by the tert-butyl group (transition state **A**), so the dipole would approach from the *Re* face.

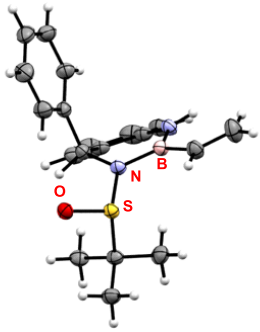
Scheme 3.20. Sam Auxiliary and its Structural Advantage



3.87 'sam'
(**s**ulfin**a**mide-a**m**ine)

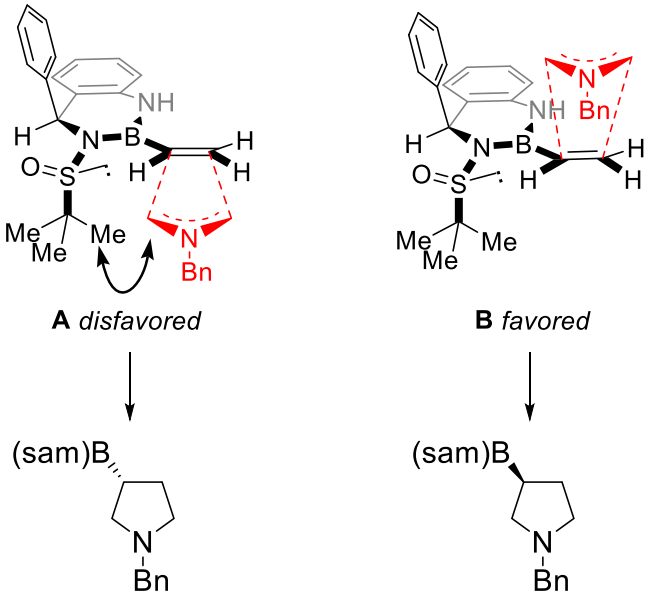


3.85 vinylB(sam)



X-ray crystallography of **3.85**

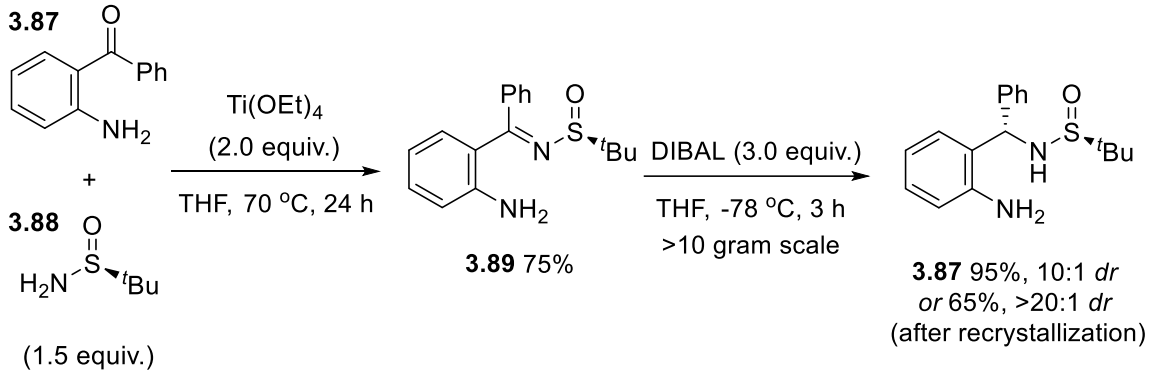
Scheme 3.21. Model for Stereoselectivity



3.3.2. Synthesis of 'Sam' Auxiliary

The 'sam' auxiliary could be synthesized from inexpensive aminobenzophenone (**3.87**) and Ellman's auxiliary (**3.88**), and the latter was available in both enantiomeric forms. Condensation in the presence of $Ti(OEt)_4$ yielded the imine **3.89** in 75% yield as a yellow powder. The crude powder could be used directly in the next step, or it could be further purified by recrystallization from diethyl ether. Imine **3.89** was reduced with DIBAL in quantitative yield and with a *dr* of 10:1. Recrystallization could give 65% of the purified diastereomer. The synthesis has been carried out at over 10-gram scale.

Scheme 3.22. Synthesis of Sam Auxiliary

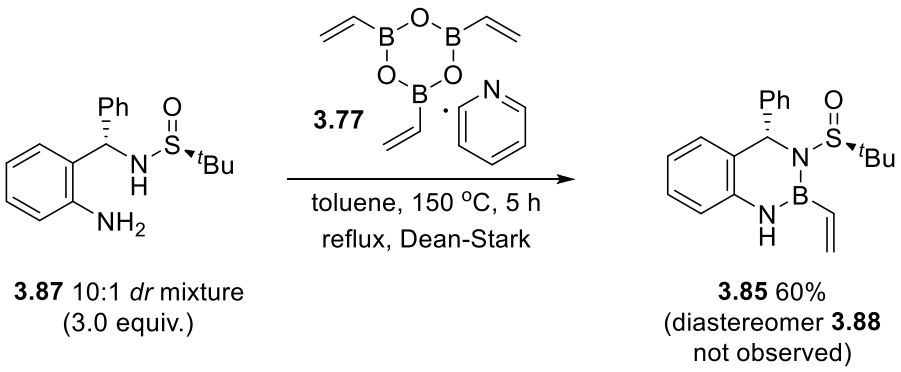


3.3.3. Installation of Sam Auxiliary on Alkenylboron

As was discussed in section **3.3.1**, the 'sam' auxiliary could be installed on alkenylboroxines or boronic acids by refluxing the mixture in toluene using Dean-Stark apparatus under inert atmosphere. The condensation was carried out at a low concentration (< 0.25 M) to fully dissolve the starting materials and the forming product, the latter of which, if precipitated, would be exposed to high temperature and decompose on the inner wall of the apparatus.

The sam auxiliary resulting from DIBAL reduction could be used without purification as a diastereomeric mixture of 10:1 *dr*. Diazaborolidine **3.88** stemming from the minor diastereomer was not observed in the crude ^{1}H NMR spectrum.

Scheme 3.23. Use of Diastereomeric Mixture of 'Sam' Auxiliary in Condensation

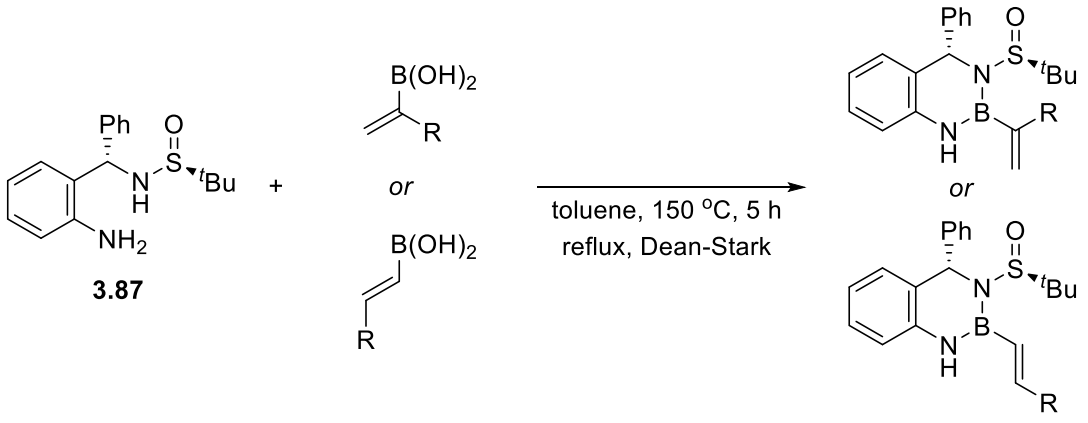


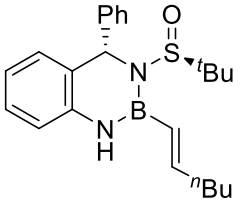
3.87 10:1 *dr* mixture
(3.0 equiv.)

3.85 60%
(diastereomer **3.88**
not observed)

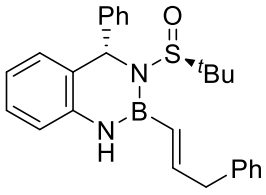
A series of alkenyl B(sam)-containing diazaborolidines bearing α- or β-substituents were synthesized from boronic acids (Scheme 3.24), including ones bearing silyl ethers (**3.92**, **3.97**), protected amines (**3.93**, **3.98**), a chlorine atom (**3.94**) or an ester (**3.95**). β-alkylB(sam) derivatives (**3.90**-**3.95**) were synthesized in generally moderate to good yield, while reactions using α-alkyl boronic acids were less efficient (**3.96**-**3.98**).

Scheme 3.24. Installation of 'Sam' Auxiliary on Alkenyl Boronic Acids

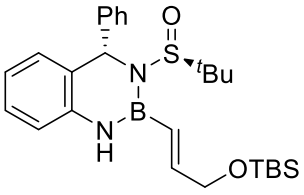




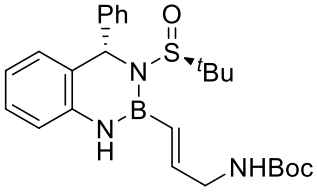
3.90 77%



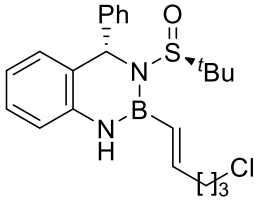
3.91 76%



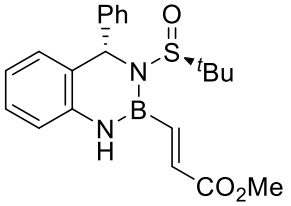
3.92 46%



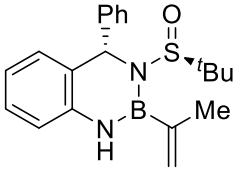
3.93 58%



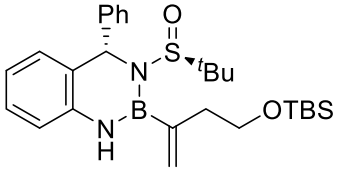
3.94 73%



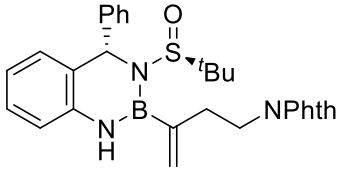
3.95 43%



3.96 60%



3.97 19%

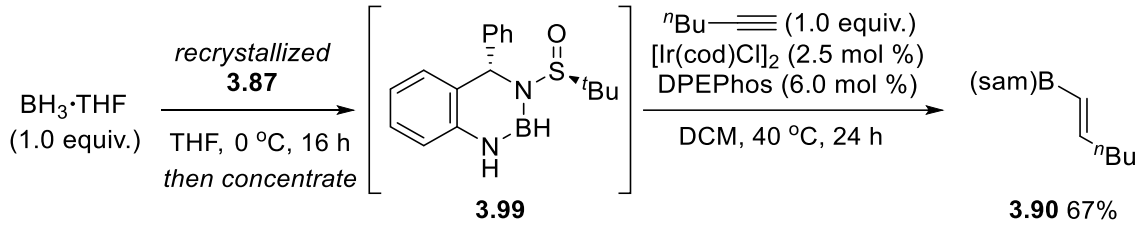


3.98 26%

We also developed iridium-catalyzed hydroboration of terminal alkynes using 'sam' borane (**3.99**, Scheme 3.25) generated *in situ* from borane-THF complex and recrystallized

3.87. *β*-AlkylB(sam) diazaborolidines such as **3.90** could be synthesized using this alternative method.

Scheme 3.25. Iridium-catalyzed Hydroboration with HB(sam)



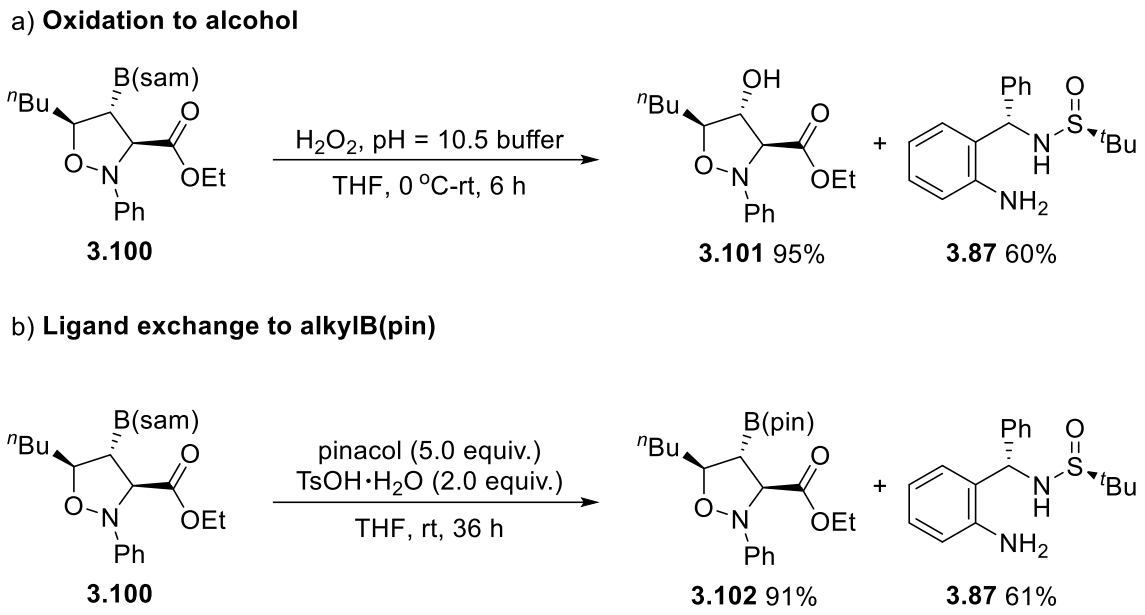
3.3.4. Transformations of AlkylB(sam)

We investigated the transformations of B(sam) into other useful functional groups. As depicted in Scheme 3.26, alkylB(sam) **3.100** (whose synthesis will be discussed in section **3.3.10.**) underwent oxidation to secondary alcohol **3.101** in quantitative yield after being treated with hydrogen peroxide under mildly basic conditions (Scheme 3.26a). After oxidation, 60% of sam auxiliary (**3.87**) was recovered by column chromatography. The oxidation of alkylB(sam) occured with similar reactivity as that of boronic esters and was much more facile than diaminonaphthalene-derived diazoborolidines (**B(dan)**) that required prior transformation to boronic esters to be oxidized.[35] This observation suggested that the electron-withdrawing sulfinyl group attached to the nitrogen atom rendered the boron more electrophilic and thus more reactive towards nucleophilic oxidants like hydrogen peroxide.

We also discovered that alkylB(sam) **3.100** could be converted to pinacolboronic ester **3.102** in high yield when treated with pinacol and 4-methylbenzenesulfonic acid hydrate (Scheme 3.26b), with 61% of the 'sam' auxiliary recovered.

(35) López-Pérez, A.; Segler, M.; Adrio, J.; Carretero, J. C. *J. Org. Chem.* **2011**, *76*, 1945–1948.

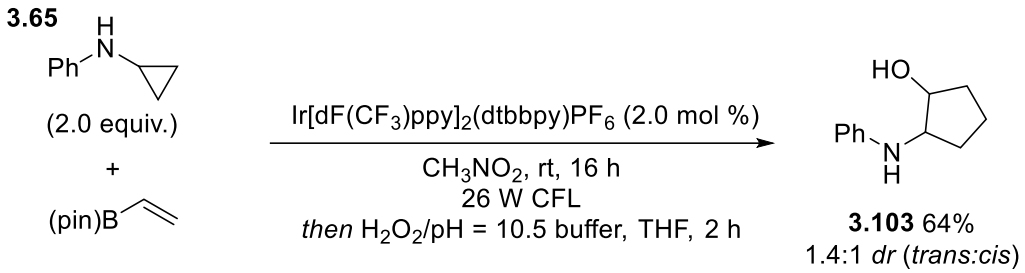
Scheme 3.26. Transformations of AlkylB(sam)



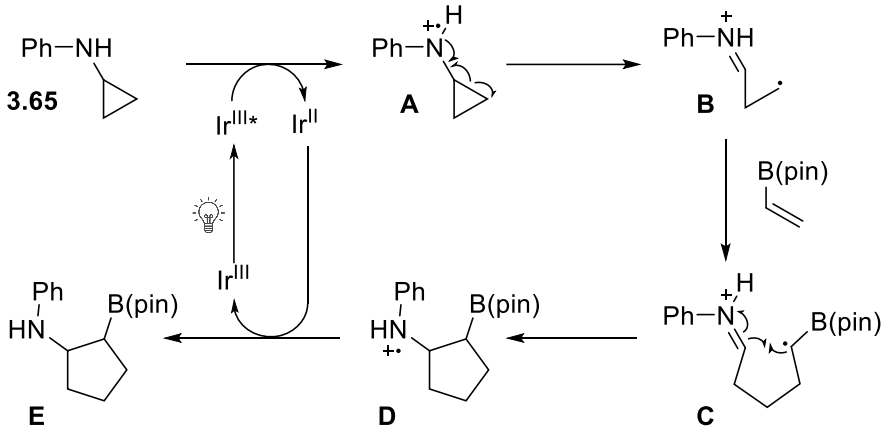
3.3.5. Initial Investigation of Radical [3+2] Cycloaddition of Cyclopropylanilines with Alkenylboronates

The ability of the B(sam) group to modulate the stereoselectivity in concerted cycloaddition reactions was demonstrated in the reaction with azomethine ylide **3.82** (as depicted in Scheme 3.19). We would like to study whether the B(sam) group could control the stereoselectivity of radical-based reactions. We considered that Zheng's radical [3+2] cycloaddition of cyclopropylanilines was an excellent model reaction.[21] Before attempting the cycloaddtion with alkenylB(sam), we examined whether cyclopropylaniline (**3.65**, Scheme 3.27) could react with achiral alkenylboronates to form cyclic 1,2-aminoboronates. A test reaction was conducted with vinylB(pin) and using $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ as the catalyst under irradiation from a household compact fluorescent yellow light (CFL). After 16 h of irradiation followed by oxidation of the crude mixture, the cycloaddition product **3.103** formed as a 1.4:1 diastereomeric mixture in 64% overall yield.

Scheme 3.27. Initial Attempt of Radical [3+2] Cycloaddition of Cyclopropylanilines with Alkenylboronates



Scheme 3.28. Catalytic Cycle of Radical [3+2] Cycloaddition of Cyclopropyl Aniline and VinylB(pin)

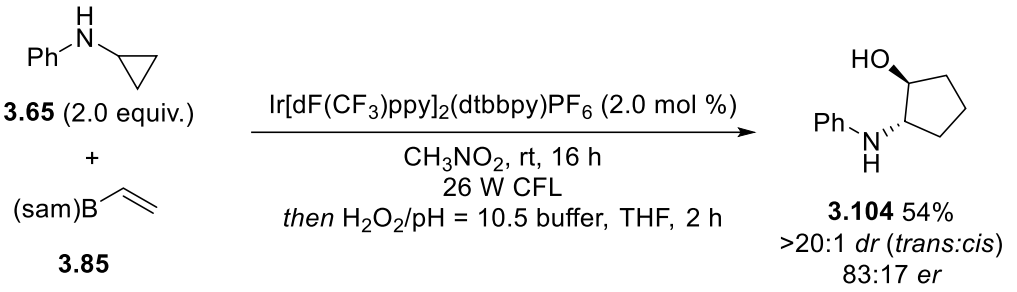


This results of the cycloaddition showed that primary radical **B**, resulting from the ring opening of cyclopropylaminyl radical cation **A,** could undergo radical addition to an alkenyl boronate to give the stabilized α-boryl radical **C** (Scheme 3.28). The α-boryl radical **C** could add to the iminium cation in a 5-exo-trig cyclization to close the 5-membered ring. With this promising result, we set out to investigate whether this reaction could be rendered stereoselective using the newly developed 'sam' auxiliary.

3.3.6. Radical [3+2] Cycloaddition of Cyclopropylanilines with AlkenylB(sam)

We examined the cycloaddition of vinylB(sam) (**3.85**, Scheme 3.29) and cyclopropylaniline as the reaction partner. After oxidation of the reaction mixture, only the *trans*-amino alcohol (**3.104**) was observed, and further purification delivered the product in 54% yield. Chiral SFC analysis determined the enantiomeric ratio to be 83:17. This result demonstrated the potential for 'sam' auxiliary to moderate the face selectivity of radical cyclization by an α-boryl radical. The complex spatial configuration also provided the opportunity to control the diastereoseletivity.

Scheme 3.29. Initial Result of Radical [3+2] Cycloaddition of Cyclopropylaniline with VinylB(sam)



3.3.7. Modification of the Auxiliary

To improve the stereoselectivity of the radical cycloaddition reaction, we examined a steric model of the cycloaddition step, which we assume to be the stereodetermining step. In the transition state model **A** shown in Scheme 3.30, the iminium cation would be forced to approach the α-boryl radical from the top face so as to avoid interaction with the bulky ^{t}Bu group on the sulfinamide. We postulated that the phenyl group on the auxiliary could hinder the top face of the α-boryl radical, thus cancelling the difference of transition state energy between the approach from the two faces and thereby erode stereoselectivity. This

problem could potentially be remedied by replacing the phenyl group (A value = 3.0 kcal/mol) with a less bulky methyl group (A value = 1.7 kcal/mol).[36]

Scheme 3.30. Postulated Reason for Lower Stereoselectivity and Potential Modification

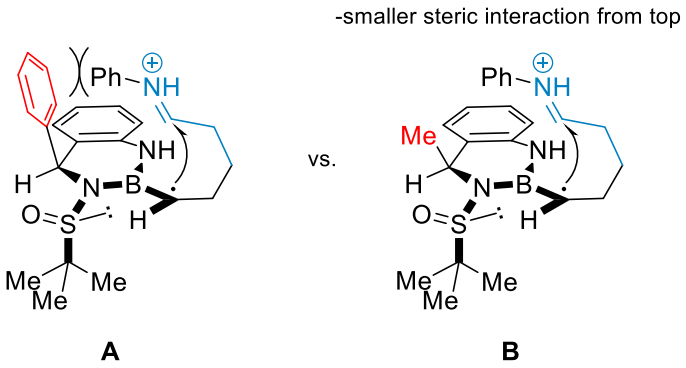
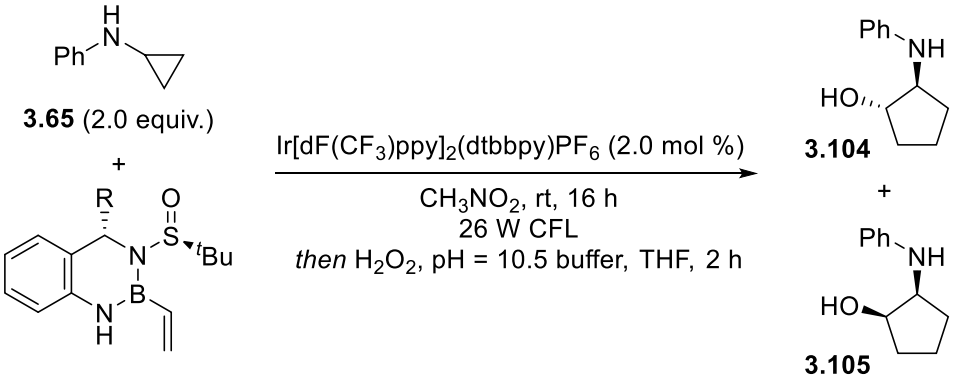


Table 3.1. Modification of Auxiliary



Entry	VinylB(sam)	Yield of **3.104** (%)	*er* of **3.104**	*dr* (**3.104**:**3.105**)
1	**3.85** (R = Ph)	54	83:17	>20:1
2	**3.86** (R = Me)	5	93:7	1.0:1
3	**3.106** (R = ^{n}Bu)	35	88:12	1.4:1

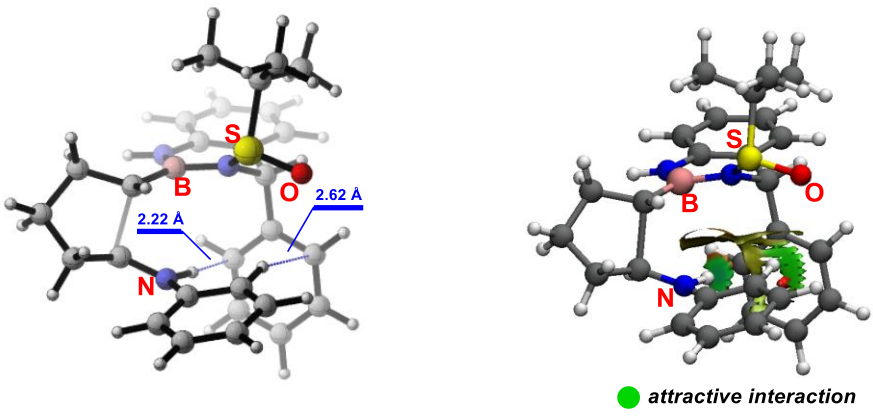
We tested the methyl-substituted vinylB(sam) **3.86** in the reaction (Table 3.1, entry 2) and, consistent with our hypothesis, the *er* of *trans* cycloaddition product **3.104** was indeed improved (93:7). Unfortunately, the diastereoselectivity decreased dramatically, and the

(36) A values: Romers, C.; Altona, C.; Buys, H.R.; Havinga, E. *Topics in Stereochemistry*, 4th ed.; John Wiley & Sons, Inc.: New York, 1969; pp 40.

low solubility of **3.86** in nitromethane resulted in low conversion. To improve the solubility, we synthesized another variant (**3.106**) with R = ^{n}Bu, which increased the lipophilicity such that the substrate fully dissolved in nitromethane at the reaction concentration (0.15 M). With this modification, the conversion increased (entry 3), but the enantioselectivity was lower (88:12 *er*) compared to the reaction employing methyl variant **3.86** and the diastereoseletivity was still unsatisfactory compared to the case of phenyl 'sam' auxiliary.

The high diastereoselectivity provided by the phenyl group-containing auxiliary was intriguing. Preliminary computational studies of the transition state (Scheme 3.31) showed that during the radical cyclization step, the protons on the nitrogen atom and the phenyl ring of the iminium cation were in close distance (2.22 Å and 2.62 Å, respectively) with the phenyl group of B(sam). This result indicated that the π-bond on the phenyl group of B(sam) may have non-covalent attractive interactions[37] with protons on the iminium cation.

Scheme 3.31. Computation of Non-Covalent Interactions. DFT: B3LYP(D3)/6-31g*/IEFPCM($MeNO_2$).



(37) Computational repesentation of non-covalent interactions: Johnson, E. R.; Keinan, S.; Morisa, P.; Contreras-garcı, J.; Cohen, A. J.; Yang, W. *J. Am. Soc. Chem.* **2010**, *132*, 6498–6506.

These edge-to-face H-π interactions[38] might have assisted in moderating the diastereo-selectivity of the 5-exo-trig cyclization step.

3.3.8. Optimization of the Solvent

We conducted a solvent survey to further improve the reaction (Table 3.2). To our surprise, reactions conducted in other polar solvents (ACN, DMF, DMA) widely used in photocatalyzed reactions did not provide product (Table 3.2, entry 2-4). Use of nitromethane appeared to be crucial for the reactivity. A few other solvent combinations with nitromethane were examined and to our delight, the reaction conducted in a 1:1 mixture of nitromethane/DMA occurred with increased enantioselectivity (91:9, entry 7). The yield was further improved to 73% by employing 5.0 equiv. of **3.65** (entry 8).

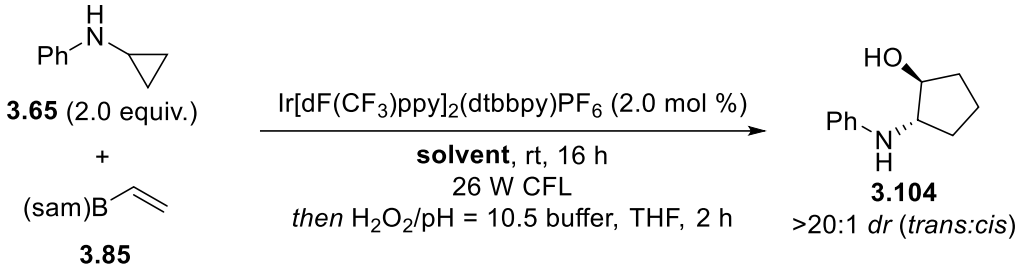
We also discovered that the reaction can be conducted in DMA with as low as 5 equiv. nitromethane as an additive without large drop in yield and *er* (entry 9). This outcome suggests the close involvement of nitromethane in the reaction. It was reported that nitromethane could stabilize carbocations via hydrogen bond coordination[39] and we suspected it could also stabilize iminium cations through a similar effect (Scheme 3.32). There are also reports of nitromethane serving as an oxidant to regenerate iridium photocatalyst, and this may also be relevant.[40]

(38) Edge-to-face H-π aromatic interactions: (a) González-Rosende, M. E.; Castillo, E.; Jennings, W. B.; Malone, J. F. *Org. Biomol. Chem.* **2017**, *15*, 1484–1494. (b) Wheeler, S. E.; Houk, K. N. *Mol. Phys.* **2009**, *107*, 749–760.

(39) Cristóbal, J. A.; Rusca, J. B., *J. Chem. Soc., Perkin Trans. 2*, **1985**, 1237–1240.

(40) Condie, A. G.; González-Gómez, J. C.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2010**, *132*, 1464–1465.

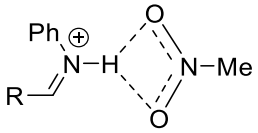
Table 3.2. Optimization of the Solvent



Entry	**Solvent**	Yield (%)	*er*
1	CH_3NO_2	54	83:17
2	ACN	<5	N.D.
3	DMF	<5	N.D.
4	DMA	<5	N.D.
5	CH_3NO_2:ACN (1:1)	53	85:15
6	CH_3NO_2:DMF (1:1)	46	90:10
7	CH_3NO_2:DMA (1:1)	56	91:9
8[a]	CH_3NO_2:DMA (1:1)	73	91:9
9	DMA + 5 equiv. CH_3NO_2	49	92:8

a) 5.0 equiv. of **3.65** instead of 2.0 equiv.

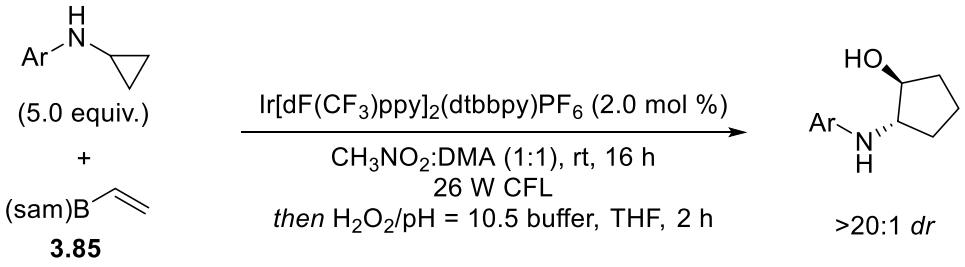
Scheme 3.32. Postulated Stabilizing Effect of Nitromethane on Iminium Ion

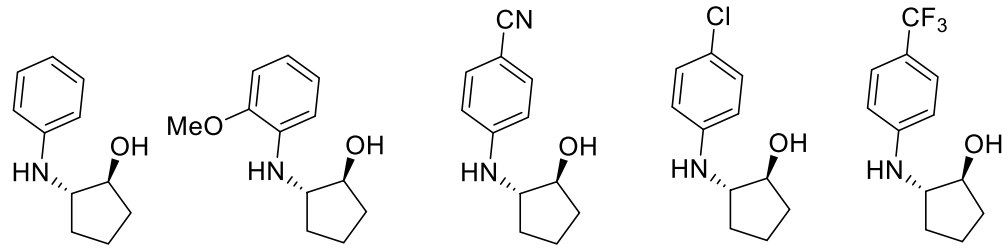


3.3.9. Substrate Scope

3.3.9.1. Scope of Aryl Groups on Cyclopropylaniline

Scheme 3.33. Scope of Aryl Groups on Cyclopropylaniline





3.104 74%
91:9 *er*

3.107 65%
91:9 *er*

3.108 67%
94:6 *er*

3.109 66%
92:8 *er*

3.110 71%
92:8 *er*

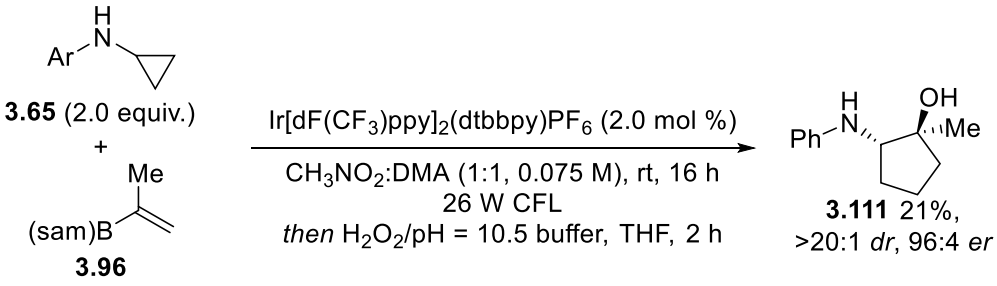
With the optimized conditions in hand, we tested the substrate scope of the reaction (Scheme 3.33). Cyclopropylamines bearing aryl groups with different electron donating groups, such as *ortho*-methoxy (**3.107**), or electron withdrawing functional groups like *para*-cyano (**3.108**), chloro (**3.109**), or trifluoromethyl (**3.110**) could be employed in the reaction, giving *trans*-amino alcohols in good yield and enantioselectivity.

3.3.9.2. Scope of α-Alkyl AlkenylB(sam)

Cycloaddition with *α*-alkyl alkenylB(sam) derivatives could enable the construction of tertiary alcohols. When we subjected *α*-methyl vinylB(sam) (**3.96**, Table 3.7) to the reaction, we were pleased to find that it yielded the trans amino alcohol after oxidation with very good stereoselectivity, although the conversion was unsatisfactory.

We then screened different conditions to improve the yield (Table 3.3). The $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ photocatalyst that performed well in the case of vinylB(sam) had a lower oxidative potential ($E_{1/2}$ vs SCE = 1.21 eV)[41] compared to cyclopropylaniline ($E_{1/2}$ vs SCE = 1.30 eV)[42], which might result in a low population of amino radical cation, leading to a slow reaction. However, switching to a $[Ru(bpz)_3](PF_6)_2$ photocatalyst with higher oxidative potential ($E_{1/2}$ vs SCE = 1.45 eV)[43] resulted in lower yield (entry 1). This was contrary to the trend observed by Zheng[21] in the radical [3+2] cycloaddition of cyclopropylaniline with styrene. We suspected that the aniline NH on 'sam' auxiliary could be oxidized by a stronger oxidant, resulting in a worse reaction.

Table 3.3. Optimization of Cycloaddition with α-Substituted Alkenyl B(sam)



Entry	Variations	Yield (%)[a]
1	$[Ru(bpz)_3](PF_6)_2$ (2.0 mol%)	15
2	$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (5.0 mol%)	34
3	CH_3NO_2:DMA (1:1, 0.15 M)	27
4	CH_3NO_2 (0.15 M)	37
5	CH_3NO_2 (0.15 M), 5.0 equiv. **3.65**	51
6	CH_3NO_2 (0.15 M), 5.0 equiv. **3.65,** 36 h	60 (95:5 *er*)

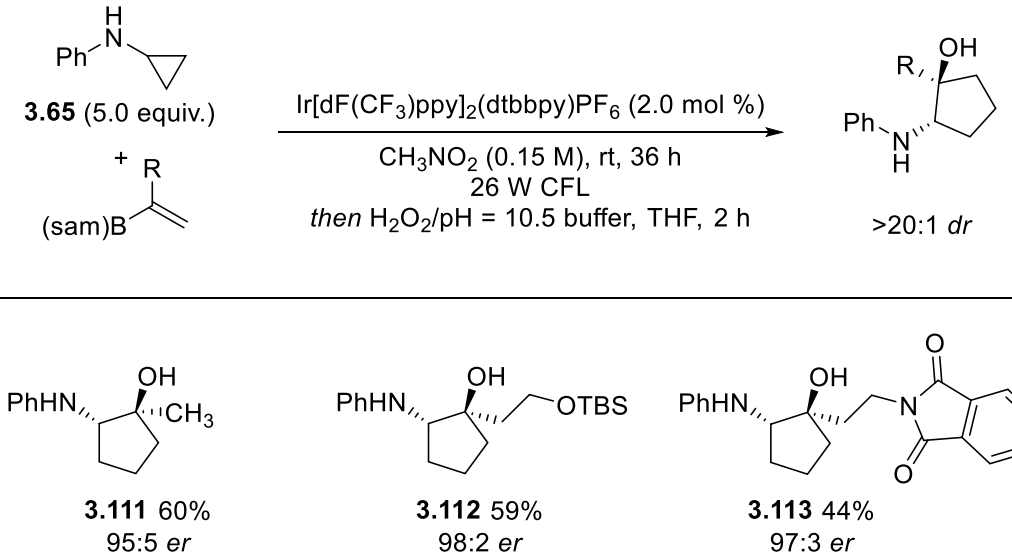
[a] Yields determined by NMR using PhTMS as internal stardard

(41) Shang, T. Y.; Lu, L. H.; Cao, Z.; Liu, Y.; He, W. M.; Yu, B. *Chem. Commun.* **2019**, *55*, 5408–5419.
(42) Yin, Y.; Li, Y.; Gonçalves, T. P.; Zhan, Q.; Wang, G.; Zhao, X.; Qiao, B.; Huang, K. W.; Jiang, Z. *J. Am. Chem. Soc.* **2020**, *142*, 19451–19456.
(43) Schultz, D. M.; Sawicki, J. W.; Yoon, T. P. *Beilstein J. Org. Chem.* **2015**, *11*, 61–65.

Using higher loading of $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ resulted in a slight improvement on the yield (entry 2). Doubling the reaction concentration led to an increase in conversion (entry 3), and running the reaction in pure nitromethane gave better results (entry 4). We were pleased to find that increasing the equivalents of **3.65** to 5.0 equiv. led to a sizable boost in yield (entry 5), and elongating the reaction time to 36 hours gave 60% yield and 95:5 *er* (entry 6).

We examined other substrates using the optimized conditions (Scheme 3.34). *α*-Alkyl alkenylB(sam) bearing a TBS protected alcohol (**3.112**) or a phthalimide group (**3.113**) were tolerated in the reaction, giving moderate yield and excellent enantioselectivity.

Scheme 3.34. Scope of α-Alkyl Alkenyl B(sam)

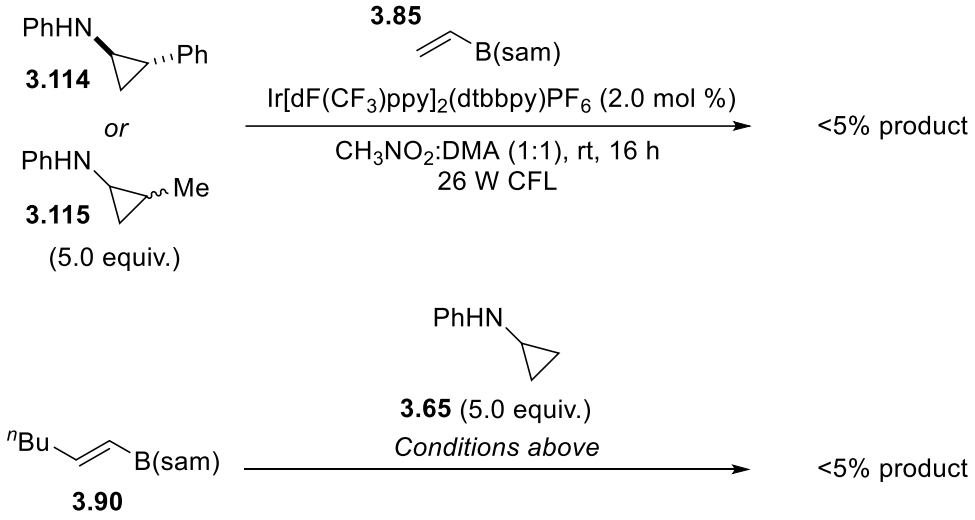


3.3.9.3. Unreactive Substrates

Apart from the substrates listed above, a few other substrates were tested (Scheme 3.35). 2-Phenyl (**3.114**) and 2-methyl cyclopropylanilines (**3.115**) were each subjected to the reaction conditions, and we observed full consumption of the cyclopropylaniline but no sign of the desired product. These substrates, once oxidized by activated photocatalyst,

should be able to ring open to form stabilized benzylic or secondary radical, as was described by Zheng in the radical [3+2] annulation of cyclopropylanilines with alkynes under similar conditions.[24] However, the radical addition to alkenylB(sam) might be hampered by the added substitution. *β*-Alkyl alkenylB(sam) **3.90** was also unreactive. These results suggested that the first radical addition step to alkenylB(sam) was sensitive to steric factors.

Scheme 3.35. Unreactive Substrates



3.3.10. Other Stereoselective Cycloaddition Reactions Enabled by 'Sam' Auxiliary

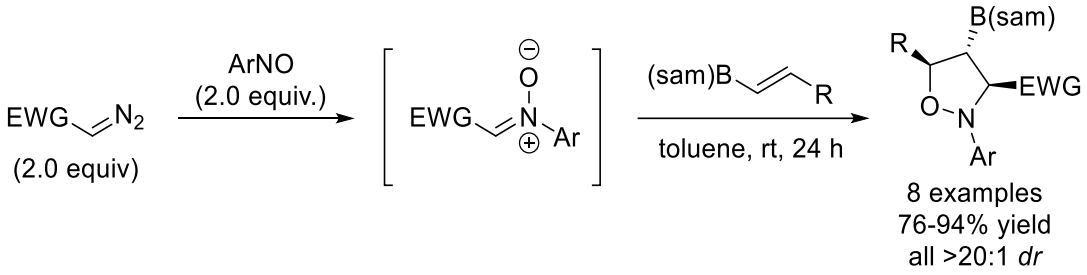
Apart from the radical ring opening/closing [3+2] cycloaddition described above, two other diastereoselective cycloaddition reactions of 1,3-dipoles with 'sam'-derived alkenylboron compounds were developed by my coworkers Mingkai Zhang and Alex Vendola, and are summarized here.

Nitrone dipole generated by mixing diazo and nitrosoarene could undergo cycloaddition with alkenylB(pin) to generate racemic isoxazoles.[44] As depicted in Scheme 3.36, when

(44) Carboni, B.; Ollivault, M.; Bouguenec, F. Le; Carrié, R.; Jazouli, M. *Tetrahedron Lett.* **1997**, *38*, 6665–6668.

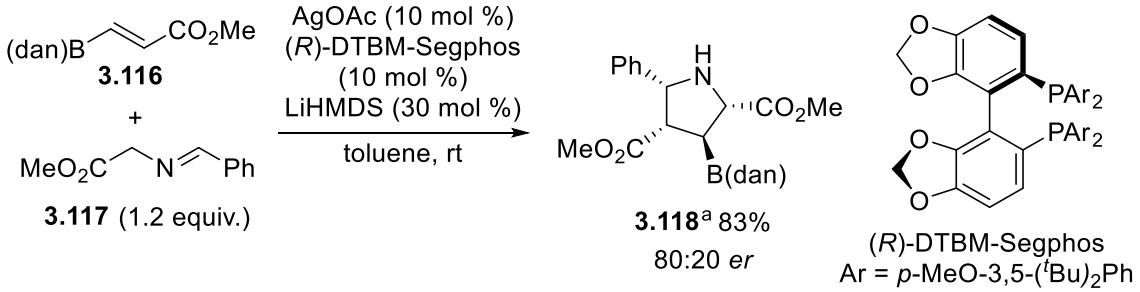
alkenylB(sam) diazaborolidines were subjected to nitrone dipole, diastereoselective cycloaddition took place with >20:1 *dr* in all cases, leading to densely functionalized boron-containing isoxazoles in high yield.

Scheme 3.36. Cycloaddition between Nitrone Dipole and AlkenylB(sam)



Silver-catalyzed 1,3-dipolar cycloaddition of azomethine ylides with *β*-boryl acrylates was reported by Adrio and Carretero.[45] The process had been conducted with expensive DTBMSegPhos as a ligand, but only moderate enantioselectivity of 60% *ee* was achieved so far (Scheme 3.37).

Scheme 3.37. Enantioselective 1,3-Dipolar Cycloaddition of Azomethine Ylides with β-Boryl Acrylates Enabled by Chiral Catalyst

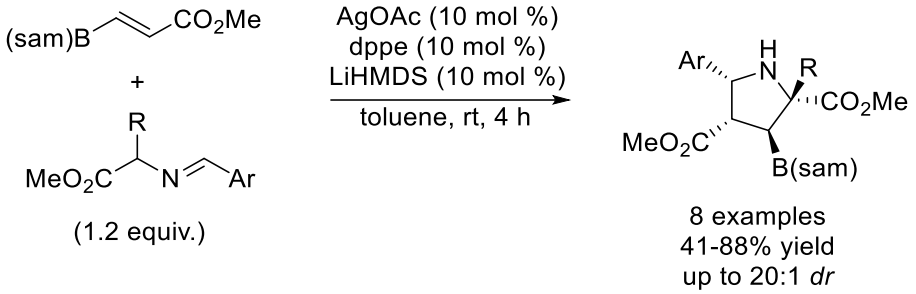


a) Absolute configurarion not determined.

We demonstrated the outstanding ability of 'sam' auxiliary to control stereoselectivity in this reaction. As shown in Scheme 3.38, cycloadditions between substituted glycine imines and alkenylB(sam) occured with high levels of diastereoselectivity.

(45) López-Pérez, A.; Segler, M.; Adrio, J.; Carretero, J. C. *J. Org. Chem.* **2011**, *76*, 1945–1948.

Scheme 3.38. Cycloaddition between Substituted Glycine Imine and Alkenyl B(sam)



3.3.11. Conclusion

In this chapter, we described the development of a novel chiral auxiliary 'sam' that could be synthesized with ease from inexpensive starting materials. Stable alkenylB(sam) diazaborolidines could be produced from boroxines or boronic acids by condensation, or from terminal alkynes by iridium-catalyzed hydroboration. The ability of 'sam' auxiliary to control the stereoselecitivity of organic reactions was preliminarily demonstrated in the [3+2] cycloaddition of alkenylB(sam) diazaborolidines with azamethine ylides. In addition, the development of a stereoselective radical [3+2] cycloaddition of alkenylB(sam) with cyclopropylanilines was described in detail. This method allowed the synthesis of cyclic *trans*-amino alcohols in high diastereo- and enantioselectivity. An interesting effect of nitromethane as a non-innocent solvent was observed. Lastly, the stereoselective synthesis of a range of highly substituted heterocycles were achieved using two newly developed [3+2] cycloaddition reactions of alkenylB(sam) with nitrone or azamethine ylides, respectively.

3.4. Experimental

3.4.1. General Information

^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz) or Varian Gemini-600 (600 MHz) spectrometer. Chemical shifts were reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data were reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz) or Varian Gemini-600 (150 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) spectrometer; chemical shifts were reported in ppm using $BF_3{\cdot}Et_2O$ as the external standard ($BF_3{\cdot}Et_2O$: 0.0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies were reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). High-resolution mass spectrometry (DART+) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Thin layer chromatography (TLC) was performed on aluminum backed 200 μm silica gel plates from Silicycle with F254nm indicator. Visualization was performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM), or potassium permanganate ($KMnO_4$).

Selected single crystals suitable for X-ray crystallographic analysis were used for structural determination. The X-ray intensity data were measured at 173(2) K (Oxford Cryostream 700) on a Bruker Kappa APEX Duo diffractometer system equipped with a sealed Mo-target X-ray tube (λ = 0.71073 Å) and a high brightness IμS copper source (λ = 1.54178

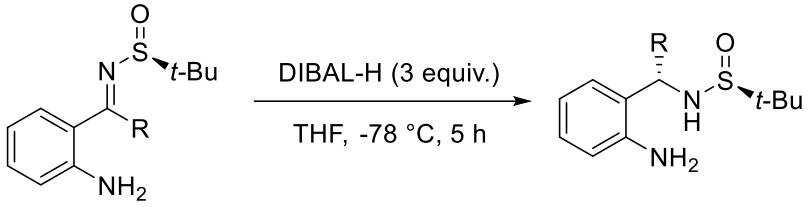
Å), coupled with a PHOTON II detector. The crystals were mounted on a goniometer head with paratone oil. The detector was placed at a distance of 5.000 from the crystal. For each experiment, data collection strategy was determined by APEX software package and all frames were collected with a scan width of 0.75° in ω and φ with an exposure time of 5 or 10 s/frame.

The frames were integrated with the Bruker SAINT Software package using a narrow-frame integration algorithm to a maximum 2θ angle of 56.54° (0.75 Å resolution) for Mo data and of 134° (0.84 Å resolution) for Cu data. The final cell constants are based upon the refinement of the XYZ-centroids of several thousand reflections above 20 σ(I). Analysis of the data showed negligible decay during data collection. Data were corrected for absorption effects using the empirical method (SADABS). The structures were solved and refined by full-matrix least squares procedures on $|F^2|$ using the Bruker SHELXTL (version 6.12) software package. All hydrogen atoms were included in idealized positions for structure factor calculations except for those forming hydrogen bonds or on a chiral center. Anisotropic displacement parameters were assigned to all non-hydrogen atoms, except those disordered. Relevant crystallographic data are summarized in Table 1.

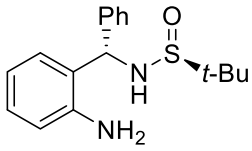
All reactions were conducted in oven- or flame-dried glassware. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (CH_2Cl_2) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon.

3.4.2. Procedures for Preparation of Sulfinamide-Amine Ligands

General Procedure A: DIBAL-H Reduction of Corresponding Imine



To a solution of the corresponding imine (1.0 equiv.) in THF was added DIBAL-H (neat, 3.0 equiv.) at -78 ºC dropwise slowly. The mixture was stirred at -78 ºC for 5 hours and quenched with brine. The mixture was allowed to warm to room temperature slowly and stir for further 16 hours. The mixture was then filtered through Celite. The filtrate was extracted for 3 times with ethyl acetate. The combined organic extracts were dried with sodium sulfate, filtered, and concentrated. The residue was purified by silica gel column chromatography. The residue can also be purified by recrystallization with ethyl acetate and hexane.



(*S*)-*N*-((*S*)-(2-aminophenyl)(phenyl)methyl)-2-methylpropane-2-sulfinamide (3.87): This reaction was performed according to the *general procedure A* with (*S*,*E*)-*N*-((2-aminophenyl)(phenyl)methylene)-2-methylpropane-2-sulfinamide[46] (23.8 g, 79.2 mmol, 1.0 equiv.), DIBAL-H (42.4 mL, 238 mmol, 3.0 equiv.) and THF (300 mL). The crude

(46) The compound was prepared according to the procedure reported in Sun, *Org. Biomol. Chem.* **2014**, *12*, 6554–6556. All spectral data was in accordance with previously published results.

(20.1 g, 10:1 *dr*, 66.5 mmol, 84% yield) can be used directly in next step. The single diastereomer was obtained with silica gel chromatography (50% ethyl acetate in hexane to 90% ethyl acetate in hexane) as white solid (15.7 g, 51.9 mmol, 65% yield).

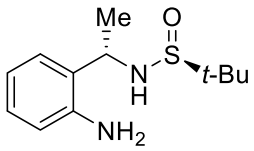
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.41 (m, 2H), 7.41 – 7.36 (m, 2H), 7.34 – 7.30 (m, 1H), 7.15 – 7.07 (m, 1H), 6.74 – 6.64 (m, 2H), 6.64 – 6.59 (m, 1H), 5.67 (d, *J* = 2.5 Hz, 1H), 4.35 (s, 2H), 3.71 (d, *J* = 2.5 Hz, 1H), 1.27 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.5, 140.7, 129.2, 129.1, 128.6, 128.4, 127.7, 126.2, 118.1, 116.8, 57.6, 55.9, 22.8.

IR (neat) ν_{max} 3352 (br), 3238 (br), 2960 (w), 1637 (m), 1602 (w), 1493 (s), 1456 (s), 1364 (w), 1311 (w), 1047 (s), 897 (w), 797 (w), 751 (s), 700 (m) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{17}H_{23}N_2OS$ 303.1526; Found 303.1533.

Optical Rotation $[\alpha]_D^{20}$: 106.6 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm)



(*S*)-*N*-((*S*)-1-(2-aminophenyl)ethyl)-2-methylpropane-2-sulfinamide (SI-1): This reaction was performed according to the *general procedure A* with (*S*,*E*)-*N*-(1-(2-aminophenyl)ethylidene)-2-methylpropane-2-sulfinamide (600 mg, 2.52 mmol, 1.0 equiv.), DIBAL-H (1.53 mL, 7.55 mmol, 3.0 equiv.) and THF (20 mL). The crude was purified with silica gel chromatography (50% ethyl acetate in hexane to 100% ethyl acetate) as white solid (315 mg, 1.31 mmol, 52% yield).

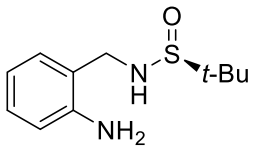
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 7.7 Hz, 1H), 7.14 (td, *J* = 7.6, 1.5 Hz, 1H), 6.78 (t, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 7.9 Hz, 1H), 4.57 (q, *J* = 6.7 Hz, 1H), 3.51 (s, 1H), 1.60 (d, *J* = 6.6 Hz, 3H), 1.22 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.75, 129.03, 126.93, 125.83, 118.11, 116.76, 55.34, 49.92, 22.65, 19.95.

IR (neat) ν_{max} 3423 (br), 3349 (br), 3243 (br), 3974 (m), 3926 (m), 2868 (w), 1692 (w), 1496 (m), 1457 (m), 1364 (w), 1309 (w), 1049 (s), 909 (w), 749 (s) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{12}H_{21}N_2OS$ 241.1369; Found 241.1371.

Optical Rotation $[\alpha]_D^{20}$: 139.8 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).



(*S*)-*N*-((*S*)-1-(2-aminophenyl)ethyl)-2-methylpropane-2-sulfinamide (SI-2): This reaction was performed according to the *general procedure A* with (*S*,*E*)-*N*-(2-aminobenzylidene)-2-methylpropane-2-sulfinamide (449 mg, 2.00 mmol, 1.0 equiv.), DIBAL-H (1.22 mL, 6.00 mmol, 3.0 equiv.) and THF (10 mL). The crude was purified with silica gel chromatography (50% ethyl acetate in hexane to 100% ethyl acetate) as white solid (207 mg, 0.915 mmol, 46% yield).

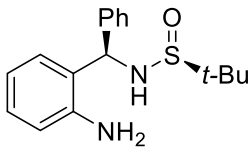
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 – 7.12 (m, 2H), 6.81 – 6.74 (m, 2H), 4.32 – 4.18 (m, 2H), 3.52 (s, 1H), 1.24 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.7, 130.7, 129.6, 122.0, 118.5, 116.4, 56.0, 46.7, 22.8.

IR (neat) ν_{max} 3454 (w), 3362 (w), 3172 (m), 2957 (w), 2924 (w), 2865 (w), 1619 (m), 1583 (w), 1497 (m), 1459 (m), 1365 (w), 1302 (w), 1038 (s), 1023 (m), 752 (m), 663 (w) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{11}H_{19}N_2OS$ 227.1213; Found 227.1224.

Optical Rotation $[\alpha]_D^{20}$: 110.5 (c = 1.0 g/100 mL, MeOH, *l*=50 mm).



(*S*)-*N*-((*R*)-(2-aminophenyl)(phenyl)methyl)-2-methylpropane-2-sulfinamide (SI-3): To a solution (*S*,*E*)-*N*-((2-aminophenyl)(phenyl)methylene)-2-methylpropane-2-sulfinamide (449 mg, 2.00 mmol, 1.0 equiv.) in THF was added phenylmagnesium bromide (1 M solution in THF, 6 mL, 3.0 equiv.) at -78 ºC dropwise slowly. The mixture was stirred at -78 ºC for 5 hours and quenched with saturated aqueous ammonium chloride solution. The mixture was allowed to warm to room temperature slowly and stir for further 16 hours. The mixture was then filtered through Celite. The filtrate was extracted for 3 times with ethyl acetate. The combined organic extracts were dried with sodium sulfate, filtered. The residue was purified by silica gel column chromatography (50% ethyl acetate in hexane to 100% ethyl acetate).

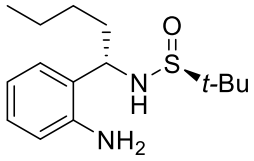
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.38 (m, 2H), 7.38 – 7.31 (m, 2H), 7.31 – 7.27 (m, 1H), 7.19 – 7.16 (m, 1H), 7.13 (td, *J* = 7.6, 1.6 Hz, 1H), 6.84 – 6.75 (m, 2H), 5.75 (d, *J* = 4.5 Hz, 1H), 3.99 (s, 1H), 1.23 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.5, 141.2, 129.4, 128.9, 128.85, 127.90, 127.7, 125.8, 118.9, 117.3, 58.0, 56.2, 22.9.

IR (neat) ν_{max} 3342 (br), 3225 (br), 2959 (w), 1623 (w), 1602 (w), 1493 (m), 1456 (m), 1363 (w), 1297 (w), 1050 (s), 1009 (m), 897 (w), 751 (s), 700 (m), 666 (w) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{17}H_{23}N_2OS$ 303.1526; Found 303.1531.

Optical Rotation $[\alpha]_D^{20}$: 54.7 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).



(S)-N-((R)-1-(2-aminophenyl)pentyl)-2-methylpropane-2-sulfinamide (SI-4): This reaction was performed according to the *general procedure A* (S,E)-N-(1-(2-aminophenyl)pentylidene)-2-methylpropane-2-sulfinamide (2.20 g, 7.85 mmol, 1.0 equiv.), DIBAL-H (4.20 mL, 23.5 mmol, 3.0 equiv.) and THF (50 mL). The crude was purified with silica gel chromatography (50% ethyl acetate in hexane to 100% ethyl acetate) as white solid (2.0 g, 7.08 mmol, 90% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.09 (td, *J* = 7.7, 7.7, 1.6 Hz, 1H), 6.72 (td, *J* = 7.5, 7.5, 1.2 Hz, 1H), 6.67 (dd, *J* = 7.9, 1.3 Hz, 0H), 4.32 (td, *J* = 7.3, 7.3, 2.8 Hz, 1H), 4.15 (s, 2H), 3.35 (d, *J* = 2.9 Hz, 1H), 1.98 (q, *J* = 7.5, 7.4, 7.4 Hz, 2H), 1.37 – 1.28 (m, 3H), 1.20 (s, 9H), 0.87 (t, *J* = 7.1, 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.2, 128.8, 127.5, 124.9, 118.0, 117.0, 55.4, 54.7, 33.8, 28.5, 22.6, 14.0.

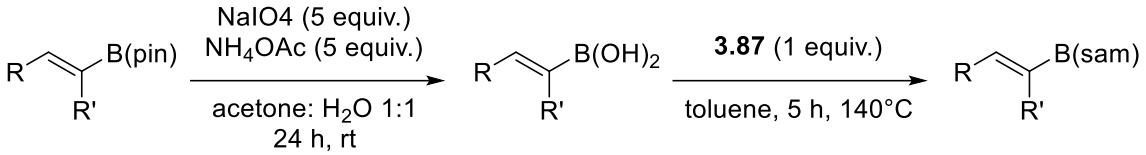
IR (neat) ν_{max} 3319 (m), 2953 (m), 2866 (w), 1609 (w), 1480 (s), 1384 (m), 1289 (m), 1183 (w), 1069 (s), 1007 (m), 958 (m), 755 (m), 751 (s) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{15}H_{27}N_2OS$ 283.1839; Found 283.1843.

Optical Rotation $[\alpha]_D^{20}$: 54.7 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).

3.4.3. Procedures for Preparation of Alkenyldiazaborolidine Substrates

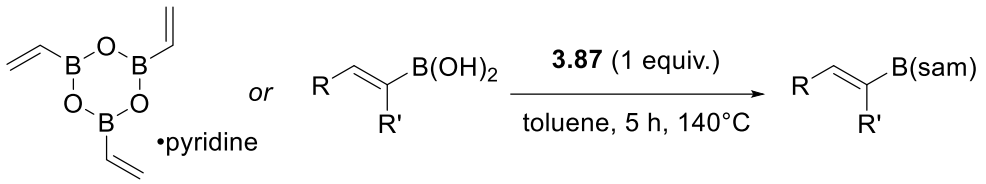
General Procedure B: from Alkenyl Pinacol Boronic Ester



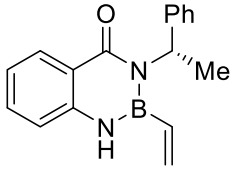
In a round bottom flask, a solution of alkenyl pinacol boronic ester (1.0 equiv.) in acetone was added dropwise to a solution of sodium periodate (5.0 equiv.), ammonium acetate (5.0 equiv.) in water (25 mL) at room temperature and allowed to stir for 24 hours. Acetone was removed under vacuum and the reaction was extracted for 3 times with ethyl acetate. The combined organic extracts were dried with sodium sulfate, filtered, and concentrated to afford the crude corresponding boronic acid. The crude boronic acid was dried with high vacuum for 6 hours to remove all the acetic acid and used in next step without further purification.

In a round bottom flask, the crude alkenyl boronic acid (1.0 equiv.) and (*S*)-*N*-((*S*)-(2-aminophenyl)(phenyl)methyl)-2-methylpropane-2-sulfinamide (1.0 equiv.) was added. A Dean-Stark Apparatus was installed to the round bottom flask with Na_2SO_4 in the collection arm. The whole system was purged with nitrogen and toluene was added. After the reaction was heated to reflux for 5 hours and cooled down to room temperature, toluene was removed under vacuum. The pure products were isolated by chromatography.

General Procedure C: from Alkenyl Boronic Acid or Boroxine



In a round bottom flask, 2,4,6-Trivinylcyclotriboroxane pyridine complex (0.33 equiv.) or alkenyl boronic acid (1.0 equiv.) and (*S*)-*N*-((*S*)-(2-aminophenyl)(phenyl)methyl)-2-methylpropane-2-sulfinamide (1.0 equiv.) was added. A Dean-Stark Apparatus was installed to the round bottom flask with Na_2SO_4 in the collection arm. The whole system was purged with nitrogen and toluene was added. After the reaction was heated to reflux for 5 hours and cooled down to room temperature, toluene was removed under vacuum. The crude reaction material was purified with the use of flash column chromatography with silica or alumina gel.



(S)-3-(1-phenylethyl)-2-vinyl-2,3-dihydrobenzo[d][1,3,2]diazaborinin-4(1H)-one (3.78): This reaction was performed according to the *general procedure C* with 2,4,6-trivinylcyclotriboroxane pyridine complex (240 mg, 1.0 mmol, 0.33 equiv.), (*S*)-2-amino-N-(1-phenylethyl)benzamide[47] (0.72 g, 3 mmol, 1.0 equiv.), toluene (20 mL) and heated to reflux with a Dean-Stark Apparatus for 5 hours. The compound was purified with silica gel chromatography (20% ethyl acetate in hexane) as a yellow solid (0.6 g, 72% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.50 (td, *J* = 7.6, 7.5, 1.6

(47) The compound was prepared according to the procedure reported in Priego, J.; Flores, P.; Ortiz-Nava, C.; Escalante, J. *Tetrahedron Asymmetry* **2004**, *15*, 3545–3549. All spectral data was in accordance with previously published results.

Hz, 1H), 7.36 – 7.28 (m, 4H), 7.22 (t, *J* = 7.0, 7.0 Hz, 1H), 7.14 (t, *J* = 7.6, 7.6 Hz, 1H), 7.00 (d, *J* = 8.3 Hz, 1H), 6.52 (s, 1H), 6.12 (q, *J* = 7.1, 7.1, 6.9 Hz, 1H), 6.02 (dd, *J* = 19.8, 13.9 Hz, 1H), 5.81 (dd, *J* = 19.9, 3.0 Hz, 1H), 5.73 (dd, *J* = 13.9, 3.1 Hz, 1H).

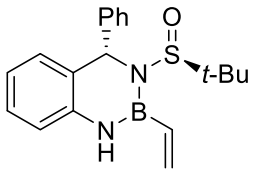
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 143.2, 143.2, 133.4, 130.6, 129.8, 128.3, 126.6, 126.5, 121.7, 119.2, 117.0, 18.9.

^{11}B NMR (160 MHz, $CDCl_3$) δ 30.5.

IR (neat) ν_{max} 3316 (br), 1616 (s), 1515 (s), 1488 (s), 1438 (w), 1386 (w), 1265 (w), 1153 (w), 761 (m).

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{17}H_{18}BN_2O$ 277.1507; Found 277.1506.

Optical Rotation $[\alpha]_D^{20}$: -96.582 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).



(*S*)-3-((*S*)-*tert*-butylsulfinyl)-4-phenyl-2-vinyl-1,2,3,4-tetrahydrobenzo[*d*][1,3,2]diazaborinine (3.85): This reaction was performed according to the *general procedure C* with 2,4,6-trivinylcyclotriboroxane pyridine complex (802 mg, 3.3 mmol, 0.33 equiv.), **3.87** (3.02 g, 10 mmol, 1.0 equiv.), toluene (100 mL) and heated to reflux with a Dean-Stark Apparatus for 5 hours. The compound was purified with silica gel chromatography (20% ethyl acetate in hexane) as a white solid (2.04 g, 60% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 2H), 7.24 – 7.17 (m, 4H), 7.15 – 7.11 (m, 1H), 6.99 (t, *J* = 7.0 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 6.40 (dd, *J* = 19.7, 13.8 Hz, 1H), 6.00 (s, 1H), 5.97 – 5.93 (m, 1H), 5.93 – 5.90 (m, 1H), 5.79 (s, 1H), 1.11 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.7, 139.5, 132.2, 128.5, 128.1, 128.0, 126.92, 126.89,

125.7, 121.7, 116.8, 60.5, 53.4, 23.1.

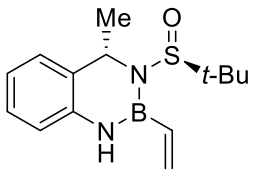
^{11}B NMR (160 MHz, $CDCl_3$) δ 29.1.

IR (neat) ν_{max} 3317 (br), 3058 (w), 2962 (w), 1610 (w), 1480 (s), 1435 (m), 1368 (m), 1287 (m), 1256 (w), 1179 (w), 1070 (m), 1013 (m), 960 (m), 755 (m), 708 (w), 694 (w) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{19}H_{24}BN_2OS$ 339.1697; Found 339.1697.

Optical Rotation $[\alpha]_D^{20}$: 239.9 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).

The absolute configuration and conformation of alkene was determined by X-ray crystallography. **4** was recrystallized from hexane and ethyl acetate. (See **X-Ray 1**)



(*S*)-3-((*S*)-*tert*-butylsulfinyl)-4-methyl-2-vinyl-1,2,3,4-tetrahydrobenzo[*d*][1,3,2]diazaborinine (3.86): This reaction was performed according to the *general procedure C* with 2,4,6-Trivinylcyclotriboroxane pyridine complex (80.2 mg, 0.33 mmol, 0.33 equiv.), **SI-1** (240 mg, 1.00 mmol, 1.0 equiv.), toluene (10 mL) and heated to reflux with a Dean-Stark Apparatus for 5 hours. The compound was purified with silica gel chromatography (20% ethyl acetate in hexane) as a white solid (52.3 mg, 57% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (td, *J* = 7.6, 1.6 Hz, 1H), 7.00 (d, *J* = 6.0 Hz, 1H), 6.91 (td, *J* = 7.4, 1.1 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 6.38 (dd, *J* = 19.9, 13.8 Hz, 1H), 5.96 – 5.86 (m, 2H), 5.76 (s, 1H), 5.00 (q, *J* = 6.6 Hz, 1H), 1.30 (d, *J* = 6.6 Hz, 3H), 1.07 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 139.1, 131.4, 128.1, 128.0, 126.3, 121.7, 116.3, 60.0, 47.8, 27.1, 23.2.

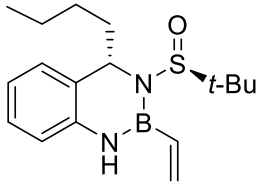
^{11}B NMR (160 MHz, $CDCl_3$) δ 28.8.

IR (neat) ν_{max} 3337 (w), 2907 (w), 1611 (w), 1485 (s), 1433 (w), 1378 (m), 1288 (m), 1183

(w), 1061 (s), 957 (m), 758 (m) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{14}H_{22}BN_2OS$ 277.1540; Found 277.1546.

Optical Rotation $[\alpha]_D^{20}$: 217.0 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).



(S)-4-butyl-3-((S)-tert-butylsulfinyl)-2-vinyl-1,2,3,4-tetrahydrobenzo[d][1,3,2]diazaborinine (3.106): This reaction was performed according to the *general procedure C* with 2,4,6-Trivinylcyclotriboroxane pyridine complex (284 mg, 1.18 mmol, 0.33 equiv.), **SI-4** (1.00 g, 3.54 mmol, 1.0 equiv.), toluene (20 mL) and heated to reflux with a Dean-Stark Apparatus for 5 hours. The compound was purified with silica gel chromatography (20% ethyl acetate in hexane) as a white solid (0.58 g, 51% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (td, *J* = 7.5, 7.4, 1.6 Hz, 1H), 7.00 – 6.88 (m, 2H), 6.80 – 6.76 (m, 1H), 6.38 (dd, *J* = 19.7, 13.9 Hz, 1H), 5.97 – 5.86 (m, 2H), 5.72 (s, 1H), 4.76 (dd, *J* = 8.7, 5.2 Hz, 1H), 1.69 – 1.53 (m, 3H), 1.31 – 1.12 (m, 3H), 1.05 (s, 10H), 0.81 (t, *J* = 7.2, 7.2 Hz, 3H).

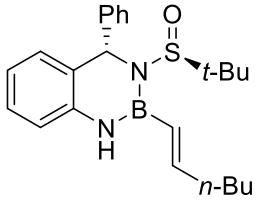
^{13}C NMR (126 MHz, $CDCl_3$) δ 139.4, 131.5, 128.0, 127.6, 126.2, 121.1, 116.3, 60.1, 51.8, 39.4, 28.1, 23.2, 22.7, 14.2.

^{11}B NMR (160 MHz, $CDCl_3$) δ 29.2.

IR (neat) ν_{max} 3347 (w), 3235 (w), 2978 (s), 2871 (s), 1628 (w), 1459 (w), 1379 (w), 1138 (s), 1046 (s), 934 (w), 749 (m) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{17}H_{28}BN_2OS$ 319.2010; Found 319.2011.

Optical Rotation $[\alpha]_D^{20}$: 224.76 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).



(*S*)-3-((*S*)-*tert*-butylsulfinyl)-2-((*E*)-hex-1-en-1-yl)-4-phenyl-1,2,3,4-tetrahydrobenzo[*d*][1,3,2]diazaborinine (3.90): This reaction was performed according to the *general procedure C* with (*E*)-hex-1-en-1-ylboronic acid (640 mg, 5.0 mmol, 1.0 equiv.), **3.87** (1.51 g, 5.0 mmol, 1.0 equiv.), toluene (50 mL) and heated to reflux with a Dean-Stark Apparatus for 5 hours. The compound was purified with silica gel chromatography (20% ethyl acetate in hexane) as a white solid (1.52 g, 77% yield).

The same product can be synthesized from hydroboration of HB(sam) and 1-hexyne[48]: Into the glovebox was brought an oven dried 20 mL vial equipped with a stirbar. To this vial was added **3.87** (151 mg, 0.5 mmol, 1.0 equiv.) and THF (5 mL). The vial is then sealed with a rubber septum and removed from the glovebox and allowed to stir at 0 ºC. Borane tetrahydrofuran complex solution (1 M in THF, 0.5 mL, 1.0 equiv.) was added dropwise with a needle to the vial and the solution was allowed to stir at the same temperature for further 12 hours to form HB(sam) solution, before being brought into the glove box. In the glove box, a two dram vial was charged with bis(1,5-cyclooctadiene)diiridium(I) dichloride (8.4 mg, 0.0125mmol, 2.5 mol%), DPEPhos (16.2 mg, 0.030 mmol, 6 mol%) and THF (1 mL) and the solution was allowed to stir for 30 minutes. Into the 20 mL vial containing HB(sam) was added 1-hexyne (68.6 µL, 0.6 mmol, 1.2 equiv.) followed by the Ir-ligand complex solution. The rubber septum on the 20 mL vial was replaced with a PTFE cap. And the vial was sealed and brought out from the glove box. The reaction was allowed to stir at 40 ºC for 24 hours before filtered through a plug of silica gel using

(48) Yoshida, H.; Kimura, M.; Tanaka, H.; Murashige, Y.; Kageyuki, I.; Osaka, I. *Chem. Commun.* **2019**, *55*, 5420–5422.

dichloromethane and concentrated under reduced pressure. The compound was purified with silica gel chromatography (20% ethyl acetate in hexane) as a white solid (132 mg, 67% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 2H), 7.22 – 7.16 (m, 4H), 7.15 – 7.10 (m, 1H), 6.97 (td, *J* = 7.5, 1.2 Hz, 1H), 6.79 (d, *J* = 7.9 Hz, 1H), 6.39 (dt, *J* = 18.0, 6.5 Hz, 1H), 5.98 (s, 1H), 5.94 (dt, *J* = 18.0, 1.5 Hz, 1H), 5.71 (s, 1H), 2.24 – 2.13 (m, 2H), 1.45 – 1.38 (m, 2H), 1.34 (dq, *J* = 13.8, 7.1 Hz, 2H), 1.10 (s, 9H), 0.91 (t, *J* = 7.2 Hz, 3H).

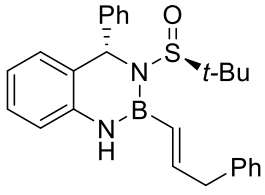
^{13}C NMR (126 MHz, $CDCl_3$) δ 149.6, 143.8, 139.8, 128.4, 128.1, 128.0, 126.9, 126.8, 125.8, 123.9, 121.4, 116.6, 60.4, 53.2, 35.7, 30.8, 23.2, 22.3, 14.0.

^{11}B NMR (160 MHz, $CDCl_3$) δ 29.1.

IR (neat) ν_{max} 3322 (br), 2955 (w), 2925 (w), 2869 (w), 1629 (m), 1607 (w), 1478 (s), 1428 (m), 1368 (m), 1284 (m), 1177 (w), 1067 (s), 1034 (m), 993 (s), 962 (s), 752 (s), 694 (s), 608 (m) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{23}H_{32}BN_2OS$ 395.2323; Found 395.2322.

Optical Rotation $[\alpha]_D^{20}$: 194.3 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).



(*S*)-3-((*S*)-*tert*-butylsulfinyl)-4-phenyl-2-((*E*)-3-phenylprop-1-en-1-yl)-1,2,3,4-tetrahydrobenzo[*d*][1,3,2]diazaborinine (3.91): This reaction was performed according to the *general procedure C* with (*E*)-(3-phenylprop-1-en-1-yl)boronic acid (486 mg, 3.00 mmol, 1.0 equiv.), **3.87** (907 mg, 3.00 mmol, 1.0 equiv.), toluene (30 mL) and heated to reflux with a Dean-Stark Apparatus for 5 hours. The compound was purified with SiO_2 chromatography (20% ethyl acetate in hexane) as a white solid (980 mg, 76% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 4H), 7.25 – 7.10 (m, 8H), 6.97 (td, *J* = 7.4, 1.1 Hz, 1H), 6.76 (d, *J* = 7.9 Hz, 1H), 6.48 (dt, *J* = 17.9, 6.5 Hz, 1H), 6.03 (dt, *J* = 17.8, 1.6 Hz, 1H), 5.98 (s, 1H), 5.71 (s, 1H), 3.53 (d, *J* = 6.1 Hz, 2H), 1.10 (s, 9H).

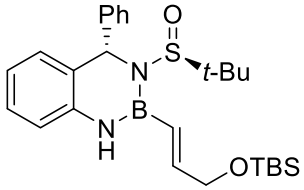
^{13}C NMR (126 MHz, $CDCl_3$) δ 147.3, 143.7, 139.7, 139.5, 128.9, 128.7, 128.4, 128.1, 128.0, 126.97, 126.96, 126.9, 126.5, 125.8, 121.6, 116.6, 60.5, 53.3, 42.6, 23.2.

^{11}B NMR (160 MHz, $CDCl_3$) δ 28.9.

IR (neat) ν_{max} 3314 (br), 3025 (w), 2962 (w), 1628 (w), 1601 (w), 1476 (s), 1421 (m), 1368 (m), 1286 (m), 1264 (w), 1179 (w), 1068 (s), 1032 (m), 962 (s), 752 (s), 735 (s), 695 (s), 607 (w) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{26}H_{30}BN_2OS$ 429.2166; Found 429.2148.

Optical Rotation $[\alpha]_D^{20}$: 216.0 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).



(*S*)-2-((*E*)-3-((*tert*-butyldimethylsilyl)oxy)prop-1-en-1-yl)-3-((*S*)-*tert*-butylsulfinyl)-4-phenyl-1,2,3,4-tetrahydrobenzo[*d*][1,3,2]diazaborinine (3.92): This reaction was performed according to the *general procedure C* with (*E*)-(3-((*tert*-butyldimethylsilyl)oxy)prop-1-en-1-yl)boronic acid (648 mg, 3.00 mmol, 1.0 equiv.), **3.87** (907 mg, 3.00 mmol, 1.0 equiv.), toluene (30 mL) and heated to reflux with a Dean-Stark Apparatus for 5 hours. The compound was purified with SiO_2 chromatography (20% ethyl acetate in hexane) as a white solid (660 mg, 46% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 2H), 7.24 – 7.15 (m, 4H), 7.14 – 7.10 (m, 1H), 6.98 (td, *J* = 7.5, 1.1 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 6.44 (dt, *J* = 18.1, 3.8 Hz, 1H), 6.24 (dt, *J* = 18.1, 1.9 Hz, 1H), 5.99 (s, 1H), 5.75 (s, 1H), 4.30 (dd, *J* = 3.9, 2.0 Hz, 2H),

1.10 (s, 9H), 0.94 (s, 9H), 0.10 (s, 3H), 0.10 (s, 3H).

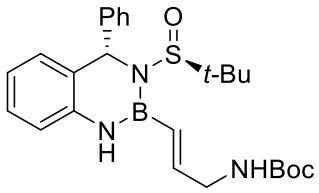
^{13}C NMR (126 MHz, $CDCl_3$) δ 147.1, 143.7, 139.7, 128.5, 128.1, 128.0, 126.92, 126.88, 125.8, 121.6, 116.7, 65.1, 60.4, 53.4, 26.1, 23.2, 18.6, -5.1.

^{11}B NMR (160 MHz, $CDCl_3$) δ 28.8.

IR (neat) ν_{max} 3320 (br), 2954 (w), 2927 (w), 2855 (w), 1636 (w), 1479 (s), 1429 (w), 1368 (m), 1252 (m), 1177 (w), 1125 (m), 1069 (s), 1007 (m), 966 (m), 937 (m), 834 (s), 775 (s), 753 (s), 694 (s), 609 (m) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{26}H_{40}BN_2O_2SSi$ 483.2667; Found 483.2678.

Optical Rotation $[\alpha]_D^{20}$: 172.8 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).



***tert*-butyl ((*E*)-3-((*S*)-3-((*S*)-*tert*-butylsulfinyl)-4-phenyl-3,4-dihydrobenzo[*d*][1,3,2]diazaborinin-2(1*H*)-yl)allyl)carbamate (3.93):** This reaction was performed according to the *general procedure C* with (*E*)-(3-((*tert*-butoxycarbonyl)amino)prop-1-en-1-yl)boronic acid (603 mg, 3.00 mmol, 1.0 equiv.), **3.87** (907 mg, 3.00 mmol, 1.0 equiv.), toluene (30 mL) and heated to reflux with a Dean-Stark Apparatus for 5 hours. The compound was purified with SiO_2 chromatography (20% ethyl acetate in hexane) as a white solid (811 mg, 58% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 2H), 7.23 – 7.16 (m, 4H), 7.12 (t, *J* = 7.3 Hz, 1H), 6.99 (t, *J* = 7.5 Hz, 0H), 6.80 (d, *J* = 7.4 Hz, 1H), 6.35 (dt, *J* = 18.2, 4.8 Hz, 1H), 6.07 (dt, *J* = 18.1, 1.8 Hz, 1H), 5.99 (s, 1H), 5.76 (s, 1H), 4.71 (s, 1H), 3.93 – 3.80 (m, 2H), 1.47 (s, 9H), 1.10 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9, 144.5, 143.7, 139.6, 128.5, 128.2, 128.1, 126.99,

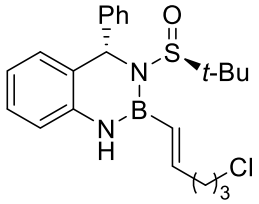
126.96, 125.8, 121.8, 116.7, 79.8, 60.6, 53.4, 44.4, 28.6, 23.2.

^{11}B NMR (160 MHz, $CDCl_3$) δ 29.4.

IR (neat) ν_{max} 3326 (br), 2976 (w), 1693 (m), 1635 (w), 1478 (s), 1422 (m), 1365 (m), 1281 (m), 1248 (m), 1166 (s), 1068 (m), 965 (m), 754 (s), 734 (s), 695 (s) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{25}H_{35}BN_3O_3S$ 468.2487; Found 468.2491.

Optical Rotation $[\alpha]_D^{20}$: 186.6 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).



(*S*)-3-((*S*)-*tert*-butylsulfinyl)-2-((*E*)-5-chloropent-1-en-1-yl)-4-phenyl-1,2,3,4-tetrahydrobenzo[*d*][1,3,2]diazaborinine (3.94): This reaction was performed according to the *general procedure C* with (*E*)-(5-chloropent-1-en-1-yl)boronic acid (445 mg, 3.00 mmol, 1.0 equiv.), **3.87** (907 mg, 3.00 mmol, 1.0 equiv.), toluene (30 mL) and heated to reflux with a Dean-Stark Apparatus for 5 hours. The compound was purified with SiO_2 chromatography (20% ethyl acetate in hexane) as a white solid (907 mg, 73% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.24 (m, 2H), 7.24 – 7.16 (m, 4H), 7.15 – 7.09 (m, 1H), 6.99 (td, *J* = 7.5, 1.1 Hz, 1H), 6.80 (dd, *J* = 7.9, 1.1 Hz, 1H), 6.36 (dt, *J* = 18.1, 6.4 Hz, 1H), 6.04 – 5.96 (m, 2H), 5.73 (s, 1H), 3.55 (t, *J* = 6.6 Hz, 2H), 2.41 – 2.31 (m, 2H), 1.99 – 1.88 (m, 2H), 1.10 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 147.1, 143.7, 139.7, 128.5, 128.1, 128.0, 126.93, 126.91, 125.8, 121.6, 116.7, 60.5, 53.3, 44.4, 33.0, 31.4, 23.2.

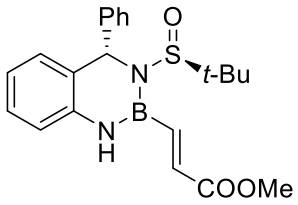
^{11}B NMR (160 MHz, $CDCl_3$) δ 29.4.

IR (neat) ν_{max} 3320 (br), 2957 (w), 1631 (w), 1607 (w), 1477 (s), 1427 (m), 1269 (m), 1285 (m), 1178 (w), 1067 (s), 992 (m), 962 (m), 896 (w), 811 (w), 754 (s), 736 (m), 695 (m) cm^{-}

[1].

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{22}H_{29}BClN_2OS$ 415.1777; Found 415.1780.

Optical Rotation $[\alpha]_D^{20}$: 204.1 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).



(*E*)-3-((*S*)-3-((*S*)-*tert*-butylsulfinyl)-4-phenyl-3,4-dihydrobenzo[*d*][1,3,2]diazaborinin-2(1*H*)-yl)acrylate (3.95): This reaction was performed with adaption according to the *general procedure C* with [(*E*)-3-methoxy-3-oxo-prop-1-enyl]boronic acid (1.2 g, 9.24 mmol), **3.87** (2.79 g, 9.24 mmol, 1.0 equiv.) and toluene (40 mL), and heated to reflux with a Dean-Stark Apparatus for four hours. After cooling the reaction to room temperature, the reaction was concentrated under reduced pressure until all toluene was removed. To the crude orange solid was then added diethyl ether, and the crude reaction underwent sonication. The reaction was then filtered, and the collected solid was washed with diethyl ether. The solid was then dissolved in dichloromethane and loaded onto a fritted funnel of silica. Ethyl acetate (150 mL) is then passed through the fritted funnel, and the resulting mixture was concentrated under, resulting in spectroscopically pure product as a white solid (1.57 g, 43% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 18.3 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 3H), 7.20 (t, *J* = 6.4 Hz, 3H), 7.14 (t, *J* = 7.4 Hz, 1H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 6.47 (d, *J* = 18.3 Hz, 1H), 6.03 (s, 1H), 5.86 (s, 1H), 3.80 (s, 3H), 1.11 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 143.4, 139.0, 134.2, 129.4, 128.7, 128.3, 128.2, 127.2, 126.9, 125.6, 122.5, 117.0, 60.7, 53.5, 52.1, 23.1.

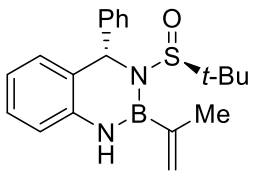
^{11}B NMR (160 MHz, $CDCl_3$) δ 28.8.

IR (neat) ν_{max} 3315 (br), 2980 (s), 2889 (m), 1721 (m), 1610 (m), 1482 (s), 1461 (w), 1433 (m), 1381 (s), 1314 (w), 1279 (m), 1250 (m), 1168 (s), 1072 (s), 1034 (w), 999 (w), 964 (m), 813 (w), 756 (m), 697 (w), 625 (w), 583 (w), 549 (w) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calcd for $C_{21}H_{26}BN_2O_3S$ 397.1752; Found 397.1747.

Optical Rotation $[\alpha]_D^{20}$: 211.2 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).

The absolute configuration and conformation of alkene was determined by X-ray crystallography. **3.95** was recrystallized from hexanes and ethyl acetate. (See **X-Ray 2**)



(*S*)-3-((*S*)-*tert*-butylsulfinyl)-4-phenyl-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydro-benzo[*d*][1,3,2]diazaborinine (3.96): This reaction was performed according to the *general procedure C* with prop-1-en-2-ylboronic acid (0.34 g, 4.00 mmol, 1.0 equiv.), **3.87** (1.21 g, 4.00 mmol, 1.0 equiv.) and toluene (30 mL), and heated to reflux with a Dean-Stark Apparatus for 5 hours. The compound was purified with SiO_2 chromatography (20% ethyl acetate in hexane) as a fluffy white solid (1.07 g, 60% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 – 7.16 (m, 6H), 7.16 – 7.12 (m, 1H), 7.02 (td, *J* = 7.5, 7.5, 1.2 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 5.99 (s, 1H), 5.75 (s, 1H), 5.58 – 5.53 (m, 1H), 5.51 – 5.46 (m, 1H), 1.94 (s, 3H), 1.09 (s, 9H).

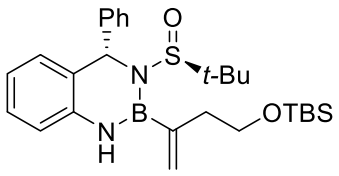
^{13}C NMR (151 MHz, $CDCl_3$) δ 143.7, 139.6, 128.5, 128.3, 128.1, 127.4, 127.0, 127.0, 125.6, 121.9, 116.9, 60.1, 52.5, 23.2, 22.3.

^{11}B NMR (160 MHz, $CDCl_3$) δ 30.4.

IR (neat) ν_{max} 3310 (w), 3057 (w), 2956 (w), 1770 (w), 1610 (m), 1481 (s), 1430 (m), 1366 (m), 1315 (w), 1252 (m), 1068 (m), 999 (m), 967 (m), 755 (s), 698 (w) cm^{-1}.

HRMS (DART+) for $C_{20}H_{25}BN_2OS$ $[M+H]^+$: Calc'd: 353.1853, found: 353.1855.

Optical Rotation $[\alpha]_D^{20}$: 149.9 (c = 1.0, $CHCl_3$, l = 50 mm)



(*S*)-2-(4-((*tert*-butyldimethylsilyl)oxy)but-1-en-2-yl)-3-((*S*)-*tert*-butylsulfinyl)-4-phenyl-1,2,3,4-tetrahydrobenzo[*d*][1,3,2]diazaborinine (3.97): This reaction was performed according to the *general procedure B* with *tert*-butyldimethyl((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)oxy)silane (1.25 g, 4.00 mmol, 1.0 equiv.), sodium periodate (4.28 g, 20.0 mmol, 5.0 equiv.), ammonium acetate (1.54 g, 20.0 mmol, 5.0 equiv.), acetone (25 mL), water (25 mL), stir at room temperature for 16 hours, then with **3.87** and toluene (30 mL), and heated to reflux with a Dean-Stark Apparatus for 5 hours. The compound was purified with SiO_2 chromatography (20% ethyl acetate in hexane) as a fluffy white solid (0.36 g, 19% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 – 7.20 (m, 3H), 7.20 – 7.15 (m, 2H), 7.16 – 7.10 (m, 2H), 7.03 – 6.97 (m, 1H), 6.83 (d, J = 7.9 Hz, 1H), 6.21 (s, 1H), 6.00 (s, 1H), 5.63 – 5.59 (m, 2H), 3.68 – 3.60 (m, 1H), 3.44 – 3.38 (m, 1H), 2.52 – 2.45 (m, 1H), 2.40 – 2.32 (m, 1H), 1.07 (s, 9H), 0.84 (s, 9H), -0.03 (s, 3H), -0.06 (s, 3H).

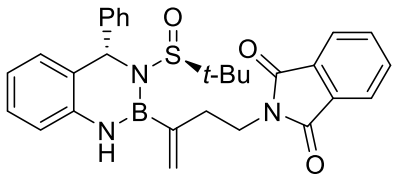
^{13}C NMR (126 MHz, $CDCl_3$) δ 143.6, 139.8, 129.0, 128.5, 128.3, 128.2, 127.4, 127.0, 125.5, 121.9, 116.8, 64.1, 60.2, 52.5, 39.5, 26.1, 23.2, 18.5, -5.2, -5.2.

^{11}B NMR (160 MHz, $CDCl_3$) δ 31.8.

IR (neat) ν_{max} 3320 (w), 2955 (m), 2928 (w), 2857 (w), 2360 (w), 1770 (m), 1759 (m), 1609 (w), 1480 (s), 1367 (m), 1248 (s), 1088 (m), 997 (w), 836 (m), 755 (m) cm^{-1}.

HRMS (DART+) for $C_{27}H_{42}BN_2O_2SiS$ $[M+H]^+$: Calc'd: 497.2823, found: 497.2807.

Optical Rotation $[\alpha]_D^{20}$: 124.2 (c = 1.0, $CHCl_3$, l = 50 mm)



2-(3-((*S*)-3-((*S*)-tert-butylsulfinyl)-4-phenyl-3,4-dihydro-benzo[d][1,3,2]diazaborinin-2(1*H*)-yl)but-3-en-1-yl)isoindoline-1,3-dione (3.98): This reaction was performed according to the *general procedure B* with 2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)isoindoline-1,3-dione (1.30 g, 4.00 mmol, 1.0 equiv.), sodium periodate (4.28 g, 20.0 mmol, 5.0 equiv.), ammonium acetate (1.54 g, 20.0 mmol, 5.0 equiv.), acetone (25 mL), water (25 mL), stir at room temperature for 16 hours, then with **3.87** (1.21 g, 4.00 mmol, 1.0 equiv.) and toluene (30 mL), and heated to reflux with a Dean-Stark Apparatus for 5 hours. The compound was purified with SiO_2 chromatography (20% ethyl acetate in hexane) as a fluffy white solid (0.6 g, 26% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 – 7.79 (m, 2H), 7.74 – 7.68 (m, 2H), 7.32 – 7.28 (m, 2H), 7.24 – 7.19 (m, 2H), 7.19 – 7.16 (m, 1H), 7.15 – 7.10 (m, 1H), 7.06 – 6.99 (m, 2H), 6.40 (s, 1H), 6.02 (s, 1H), 5.53 (s, 2H), 3.71 – 3.61 (m, 1H), 3.53 – 3.45 (m, 1H), 2.73 – 2.63 (m, 1H), 2.53 – 2.44 (m, 1H), 1.10 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 143.6, 139.8, 134.1, 132.2, 129.1, 128.6, 128.2, 128.2, 127.3, 127.0, 125.7, 123.4, 122.1, 117.4, 60.4, 52.7, 37.9, 35.6, 23.3.

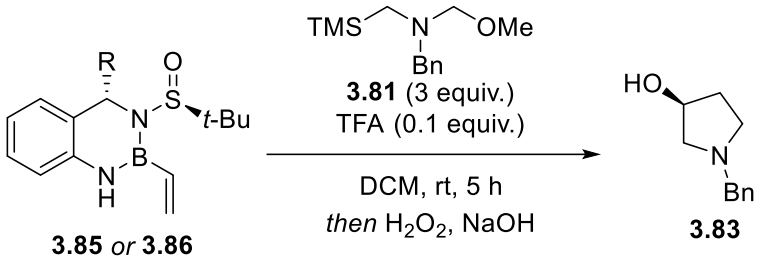
^{11}B NMR (160 MHz, $CDCl_3$) δ 31.6.

IR (neat) ν_{max} 2995 (w), 2360 (w), 1342 (w), 1770 (s), 1759 (m), 1711 (m), 1481 (w), 1370 (w), 1246 (s), 1061 (w), 758 (w) cm^{-1}.

HRMS (DART+) for $C_{29}H_{31}BN_3O_3S$ $[M+H]^+$: Calc'd: 512.2173, found: 512.2164.

Optical Rotation $[\alpha]_D^{20}$: 119.4 (c = 1.0, $CHCl_3$, l = 50 mm)

3.4.4. Procedures for Cycloaddition of Azomethine Ylide and Analysis of Stereochemistry

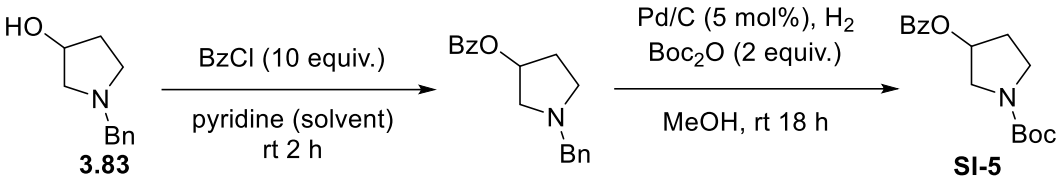


Into the glovebox was brought an oven dried two-dram vial equipped with a stirbar. To this vial was added **3.85** or **3.86** (0.2 mmol, 1 equiv.), **7** (142 mg, 0.6 mmol, 3 equiv.) followed by DCM (2 mL), and the solution was removed from the glovebox. Trifluoroacetic acid (1.54 μL, 0.02 mmol, 0.1 equiv.) was added and the reaction was stirred at room temperature for further 5 hours. The solution was then concentrated under reduced pressure. THF (1 mL) and NaOH solution (3 M, 1mL) was added followed by H_2O_2 (0.5 mL, 35 wt% in water) at 0 °C. The reaction was allowed to warm to room temperature and stir for 1 hour. The mixture was then brought to 0 ºC and quenched with saturated sodium thiosulfate solution (2 mL) carefully. The reaction was extracted for 3 times with ethyl acetate. After the crude was concentrated under vacuum, NMR yield was determined using 1,1,2,2-tetrachloroethane (20~30 mg) as internal standard.

From **3.85**, >99% NMR yield, 93:7 er

From **3.86**, 90% NMR yield, 94:6 er

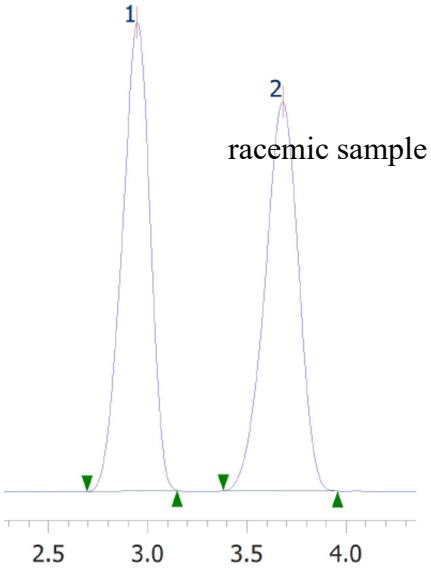
Analysis of Stereochemistry:



The crude was treated with benzoyl chloride (10 equiv.), pyridine as solvent. After purified with silica gel, the resulting benzoate was treated with palladium on carbon (10 wt%), di-*tert*-butyl dicarbonate (Boc_2O) and H_2 (1 atm). The crude was purified with silica gel. The resulting amide **SI-5** was compared by chiral SFC with the racemic and optical pure compounds prepared using the same method from (racemic)-**3.83** and (*S*)-**3.83**. ^{1}H and ^{13}C NMR spectra was in accordance with previously published results.[3]

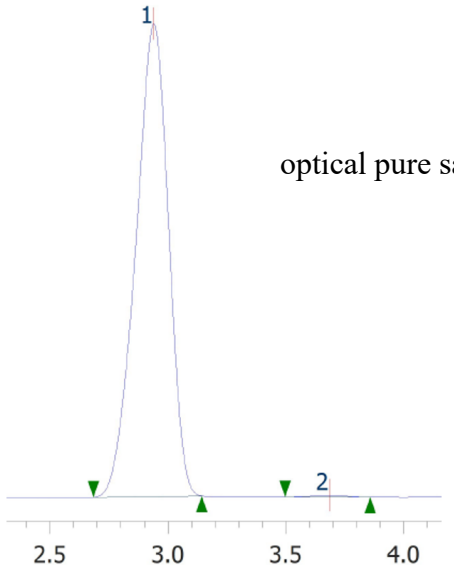
Chiral SFC (Chiracel OJ-H, 5% isopropanol, 3.0 mL/min, 40 °C, 220 nm), analysis of tert-butyl 3-(benzoyloxy)pyrrolidine-1-carboxylate.

racemic sample

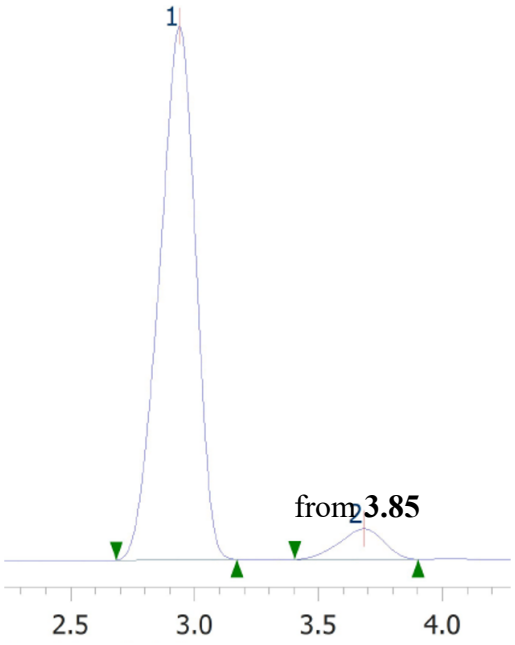


#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%
1	Unknown	9	2.947	3766327	382746	49.965
2	Unknown	9	3.680	3771622	317857	50.035

optical pure sample

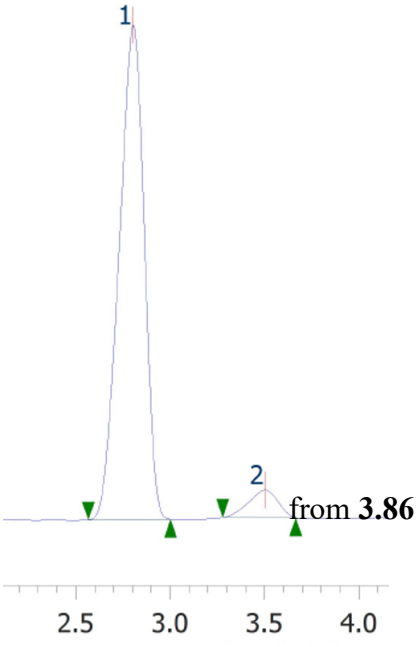


#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%
1	Unknown	9	2.940	3172390	328104	99.651
2	Unknown	9	3.683	11100	1188	0.349



from **3.85**

#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%
1	Unknown	9	2.940	3399454	334967	93.478
2	Unknown	9	3.680	237196	19084	6.522

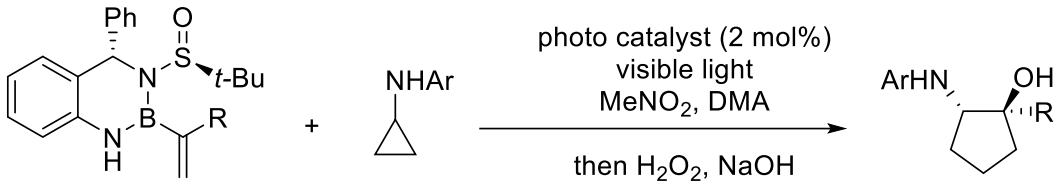


from **3.86**

#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%
1	Unknown	9	2.803	2822993	305900	93.896
2	Unknown	9	3.500	183521	16995	6.104

3.4.5. Procedures for Radical Cycloaddition of Aminocyclopropanes, Characterization of the Cycloadducts and Analysis of Stereochemistry

General procedure G:

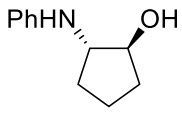


In the glovebox, an oven-dried 2-dram vial was loaded with Ir[dF(CF_3)ppy]$_2$(dtbbpy)PF_6 (2.0 mol%), alkenyl B(sam) (1.0 equiv.), and *N*-cyclopropylaniline (5.0 equiv.), followed by the addition of solvent. The vial was sealed, brought out of the glovebox, and then irradiate with one CFL (26 watts) positioned 8 cm from the vial for 16 h at around 30 ºC. After the reaction is complete, the crude solution was diluted with diethyl ether and filtered through silica gel plug. After removal of volatile solvent under vacuum, the crude material was dissolved in THF (1.0 mL) followed by the addition of 30% H_2O_2 (0.6 mL) and 3M NaOH (1.0 mL). After 90 minutes, the crude solution was extracted with ethyl acetate (3×5 mL), and the combined organic phase was dried by passing through a plug of anhydrous sodium sulfate. After removal of solvent, the product was purified using SiO_2 chromatography.

For compound **3.104**, **3.107**, **3.108**, **3.109** and **3.110** this section, the absolute configuration was determined via analogy by X-ray crystallography of **SI-5** and indicated *anti*-amino alcohol derivatives. (See **X-ray 3**)

For compound **3.111**, **3.112** and **3.113** this section, the relevant configuration was determined (via analogy) by X-ray crystallography of **SI-6** and indicated *anti*-amino alcohol derivatives. (See **X-ray 4**)

Cyclopropylanilines were synthesized using the methods described in Nguyen, T. H.; Maity, S.; Zheng, N. *Beilstein J. Org. Chem.* **2014**, *10*, 975–980. and Ref. 84. All spectra were in accordance with the record.



(1*S*,2*S*)-2-(phenylamino)cyclopentan-1-ol (3.104): This reaction was performed according to the *general procedure G* with **3.85** (50.7 mg, 0.150 mmol, 1.0 equiv.), *N*-cyclopropylaniline (100 mg, 0.750 mmol, 5.0 equiv.), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (3.7 mg, 0.0030 mmol, 2.0 mol%), $MeNO_2$ (1.0 mL) and DMA (1.0 mL). The reaction was stirred under irradiation for 16 h. The compound was purified with SiO_2 chromatography (0-50% ethyl acetate in hexane) as a colorless oil (19.6 mg, 74% yield, 91:9 *er*).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 – 7.16 (m, 2H), 6.75 – 6.70 (m, 1H), 6.70 – 6.65 (m, 2H), 4.12 – 4.04 (m, 1H), 3.67 – 3.59 (m, 1H), 2.34 – 2.25 (m, 1H), 2.05 – 1.95 (m, 1H), 1.90 – 1.71 (m, 2H), 1.70 – 1.62 (m, 1H), 1.48 – 1.36 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 147.8, 129.4, 117.7, 113.5, 78.4, 62.3, 33.0, 31.3, 21.2.

IR (neat) ν_{max} 3366 (m), 2958 (w), 1602 (s), 1504 (m), 1317 (w), 1180 (w), 1106 (w), 749 (m) cm^{-1}.

HRMS (DART+) for $C_{11}H_{16}NO$ $[M+H]^+$: Calc'd: 178.1226, found: 178.1228.

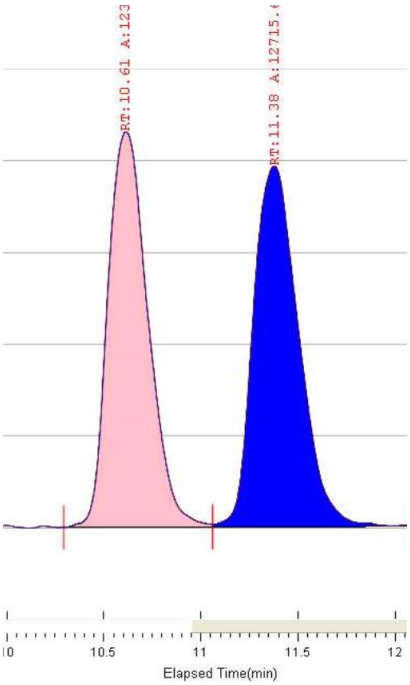
Optical Rotation $[\alpha]_D^{20}$: +20.3 (*c* = 1.0, $CHCl_3$, *l* = 50 mm)

Analysis of Stereochemistry:

Enantiomeric ratio was determined in comparison to the racemic compound synthesized from 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane.

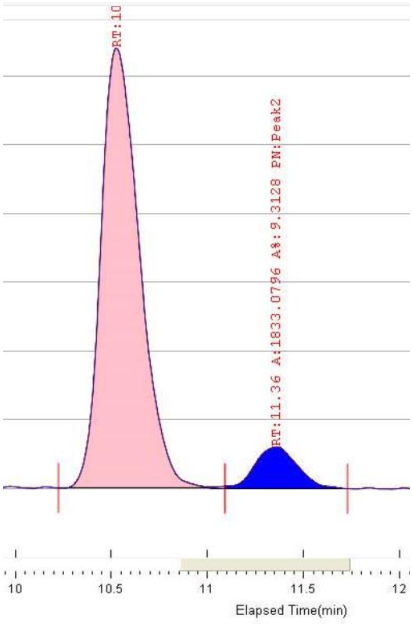
Chiral SFC (Chiracel OD-H, 10% isopropanol, 3.0 mL/min, 35 °C, 210-290 nm), analysis of (1S,2S)-2-(phenylamino)cyclopentan-1-ol

Racemic Material

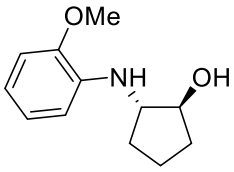


Peak No	% Area	RT (min)
1	49.2278	10.61
2	50.7722	11.38

Enantioenriched Material



Peak No	% Area	RT (min)
1	90.6872	10.53
2	9.3128	11.36



(1*S*,2*S*)-2-((2-methoxyphenyl)amino)cyclopentan-1-ol (3.107): This reaction was performed according to *general procedure G* with **3.85** (50.7 mg, 0.150 mmol, 1.0 equiv.), *N*-cyclopropyl-2-methoxyaniline (123 mg, 0.750 mmol, 5.0 equiv.), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (3.7 mg, 0.0030 mmol, 2.0 mol%), $MeNO_2$ (1.0 mL) and DMA (1.0 mL). The reaction was stirred under irradiation for 16 h. The compound was purified with SiO_2 chromatography (0-50% ethyl acetate in hexane) as a colorless oil (20.1 mg, 65% yield, 91:9 *er*).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 – 6.85 (m, 1H), 6.79 – 6.72 (m, 2H), 6.71 – 6.65 (m, 1H), 4.14 – 4.08 (m, 1H), 3.84 (s, 3H), 3.65 – 3.58 (m, 1H), 2.35 – 2.24 (m, 1H), 2.06 – 1.96 (m, 1H), 1.89 – 1.73 (m, 2H), 1.69 – 1.61 (m, 1H), 1.51 – 1.41 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 146.9, 137.8, 121.5, 116.7, 110.8, 109.6, 78.5, 62.0, 55.5, 33.1, 31.4, 21.3.

IR (neat) ν_{max} 3416 (w), 2955 (w), 1770 (m), 1759 (m), 1602 (m), 1512 (s), 1455 (m), 1428 (w), 1246 (w), 1122 (w), 1028 (w), 738 (w) cm^{-1}.

HRMS (DART+) for $C_{12}H_{18}NO_2$ $[M+H]^+$: Calc'd: 178.1226, found: 178.1228.

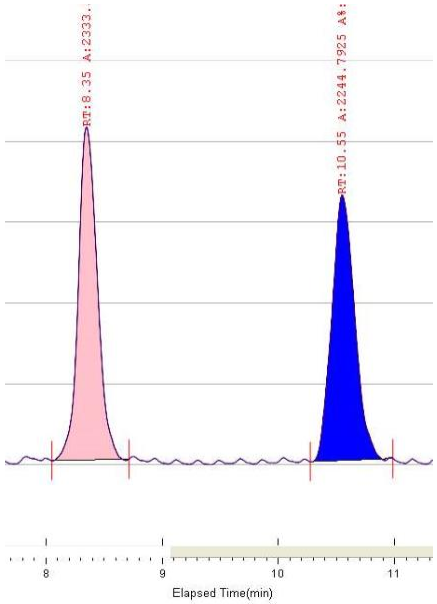
Optical Rotation $[\alpha]_D^{20}$: +15.4 (c = 1.0, $CHCl_3$, l = 50 mm)

Analysis of Stereochemistry:

Enantiomeric ratio was determined in comparison to the racemic compound synthesized from 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane.

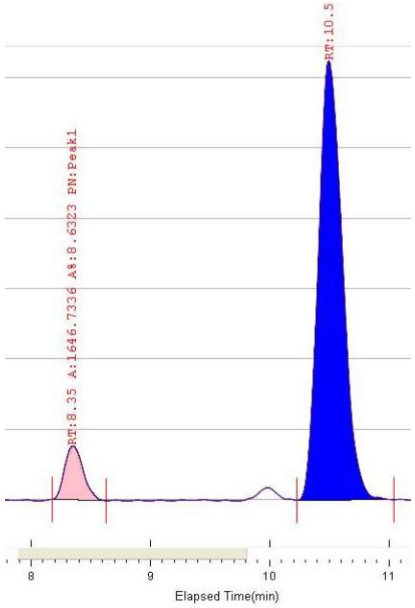
Chiral SFC (Chiracel OD-H, 10% isopropanol, 3.0 mL/min, 35 °C, 210-290 nm), analysis of (1S,2S)-2-((2-methoxyphenyl)amino)cyclopentan-1-ol

Racemic Material

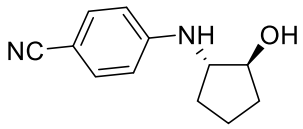


Peak No	Area %	RT (min)
1	50.9695	8.35
2	49.0305	10.55

Enantioenriched Material



Peak No	% Area	RT (min)
1	8.6323	8.35
2	91.3677	10.5



4-(((1*S*,2*S*)-2-hydroxycyclopentyl)amino)benzonitrile (3.108): This reaction was performed according to *general procedure G* **3.85** (50.7 mg, 0.150 mmol, 1.0 equiv.), 4-(cyclopropylamino)benzonitrile (119 mg, 0.750 mmol, 5.0 equiv.), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (3.7 mg, 0.0030 mmol, 2.0 mol%), $MeNO_2$ (1.0 mL) and DMA (1.0 mL). The reaction was stirred under irradiation for 16 h. The compound was purified with SiO_2 chromatography (0-50% ethyl acetate in hexane) as a colorless oil (20.4 mg, 67% yield, 94:6 *er*).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, J = 8.8 Hz, 2H), 6.64 (d, J = 8.8 Hz, 2H), 4.12 – 4.05 (m, 1H), 3.72 – 3.62 (m, 1H), 2.36 – 2.27 (m, 1H), 2.05 – 1.96 (m, 1H), 1.92 – 1.82 (m, 1H), 1.82 – 1.73 (m, 1H), 1.72 – 1.64 (m, 1H), 1.49 – 1.39 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.0, 133.9, 133.9, 120.5, 112.9, 99.1, 78.3, 61.7, 33.5, 31.4, 21.3.

IR (neat) ν_{max} 3361 (w), 2995 (w), 2360 (w), 2212 (w), 1770 (m), 1759 (m), 1606 (s), 1524 (w), 1246 (w), 1172 (w), 1057 (w), 825 (w) cm^{-1}.

HRMS (DART+) for $C_{12}H_{15}N_2O$ $[M+H]^+$: Calc'd: 203.1179, found: 203.1177.

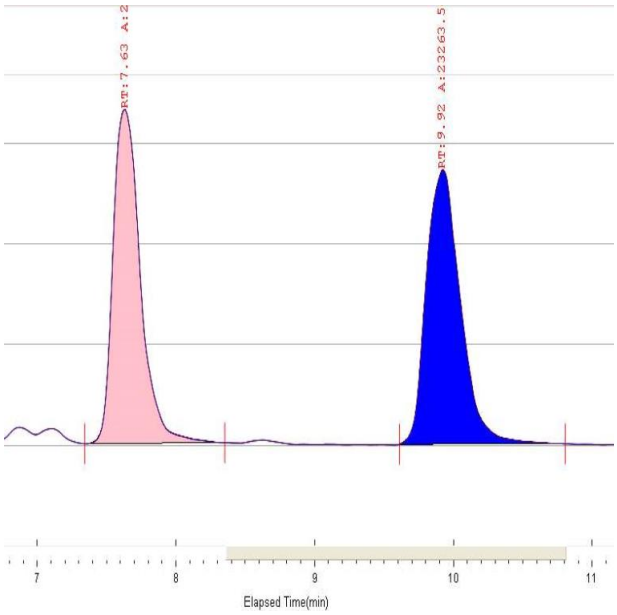
Optical Rotation $[\alpha]_D^{20}$: +4.5 (c = 1.0, $CHCl_3$, l = 50 mm)

Analysis of Stereochemistry:

Enantiomeric ratio was determined in comparison to the racemic compound synthesized from 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane.

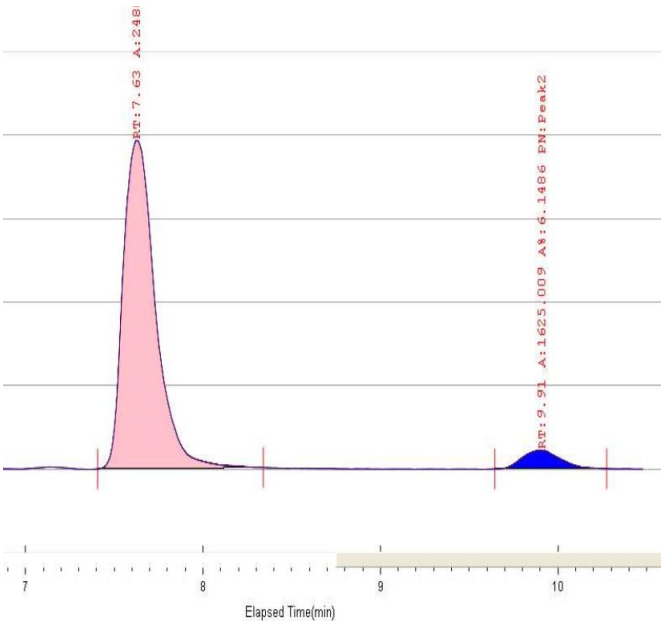
Chiral SFC (Chiracel OD-H, 10% isopropanol, 3.0 mL/min, 35 °C, 210-290 nm), analysis of 4-(((1S,2S)-2-hydroxycyclopentyl)amino)benzonitrile

Racemic Material

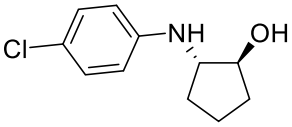


Peak No	% Area	RT (min)
1	49.3477	7.63
2	50.6523	9.92

Enantioenriched Material



Peak No	% Area	RT (min)
1	93.8514	7.63
2	6.1486	9.91



(1*S*,2*S*)-2-((4-chlorophenyl)amino)cyclopentan-1-ol (3.109): This reaction was performed according to *general procedure G* with **3.85** (50.7 mg, 0.150 mmol, 1.0 equiv.), 4-chloro-*N*-cyclopropylaniline (126 mg, 0.750 mmol, 5.0 equiv.), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (3.7 mg, 0.0030 mmol, 2.0 mol%), $MeNO_2$ (1.0 mL) and DMA (1.0 mL). The reaction was stirred under irradiation for 16 h. The compound was purified with SiO_2 chromatography (0-50% ethyl acetate in hexane) as a colorless oil (21.0 mg, 66% yield, 92:8 *er*).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, J = 8.8 Hz, 2H), 6.59 (d, J = 8.8 Hz, 2H), 4.07 – 4.03 (m, 1H), 3.59 – 3.54 (m, 1H), 2.32 – 2.22 (m, 1H), 2.04 – 1.94 (m, 1H), 1.90 – 1.70 (m, 2H), 1.69 – 1.61 (m, 1H), 1.45 – 1.36 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 146.4, 129.2, 122.3, 114.5, 78.4, 62.4, 33.3, 31.4, 21.2.

IR (neat) ν_{max} 3363 (w), 2961 (w), 1770 (m), 1759 (m), 1600 (s), 1498 (s), 1374 (w), 1317 (w), 1246 (s), 1091 (w), 1051 (w), 816 (m) cm^{-1}.

HRMS (DART+) for $C_{11}H_{15}NOCl$ $[M+H]^+$: Calc'd: 212.0837, found: 212.0836.

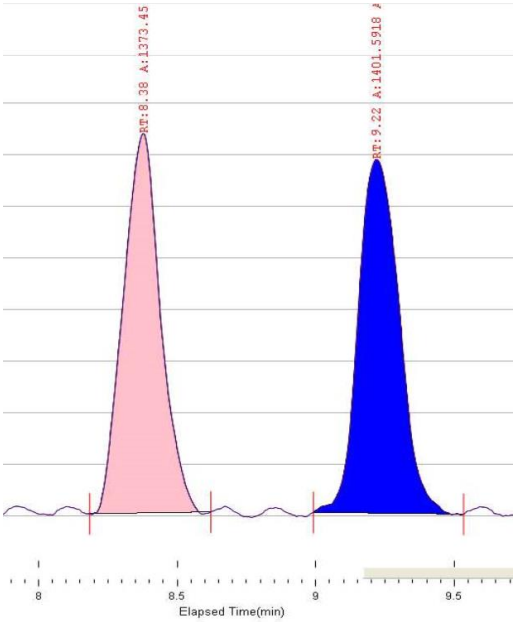
Optical Rotation $[\alpha]_D^{20}$: +10.2 (*c* = 1.0, $CHCl_3$, *l* = 50 mm)

Analysis of Stereochemistry:

Enantiomeric ratio was determined in comparison to the racemic compound synthesized from 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane.

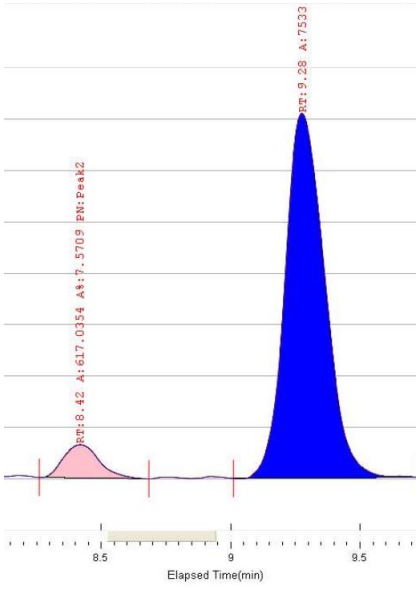
Chiral SFC (Chiracel OJ-H, 10% isopropanol, 3.0 mL/min, 35 °C, 210-290 nm), analysis of (1S,2S)-2-((4-chlorophenyl)amino)cyclopentan-1-ol

Racemic Material

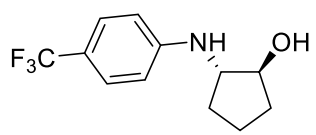


Peak No	% Area	RT (min)
1	49.4931	8.38
2	50.5069	9.22

Enantioenriched Material



Peak No	% Area	RT (min)
1	7.5709	8.42
2	92.4291	9.28



(1*S*,2*S*)-2-((4-(trifluoromethyl)phenyl)amino)cyclopentan-1-ol (3.110): This reaction was performed according *general procedure G* with **4** (50.7 mg, 0.150 mmol, 1.0 equiv.), *N*-cyclopropyl-4-(trifluoromethyl)aniline (150 mg, 0.750 mmol, 5.0 equiv.), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (3.7 mg, 0.0030 mmol, 2.0 mol%), $MeNO_2$ (1.0 mL) and DMA (1.0 mL). The reaction was stirred under irradiation for 16 h. The compound was purified with SiO_2 chromatography (0-50% ethyl acetate in hexane) as a colorless oil (26.0 mg, 71% yield, 92:8 *er*).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.6 Hz, 2H), 6.67 (d, *J* = 8.5 Hz, 2H), 4.12 – 4.04 (m, 1H), 3.92 (brs, 1H), 3.71 – 3.62 (m, 1H), 2.38 – 2.23 (m, 1H), 2.05 – 1.95 (m, 1H), 1.92 – 1.82 (m, 1H), 1.81 – 1.72 (m, 1H), 1.71 – 1.63 (m, 1H), 1.61 (brs, 1H), 1.48 – 1.38 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.4, 126.7 (q, *J* =3.8 Hz, 1C), 125.1 (q, *J* = 270.3 Hz, 1C), 119.0 (q, *J* = 32.8 Hz, 1C), 112.5, 78.3, 61.8, 33.3, 31.3, 21.2.

IR (neat) ν_{max} 3349 (w), 2964 (w), 2359 (w), 1770 (m), 1759 (m), 1617 (m), 1532 (w), 1324 (s), 1246 (m), 1108 (m), 1065 (m), 826 (w) cm^{-1}.

HRMS (DART+) for $C_{12}H_{15}NOF_3$ $[M+H]^+$: Calc'd: 246.1100, found: 246.1112.

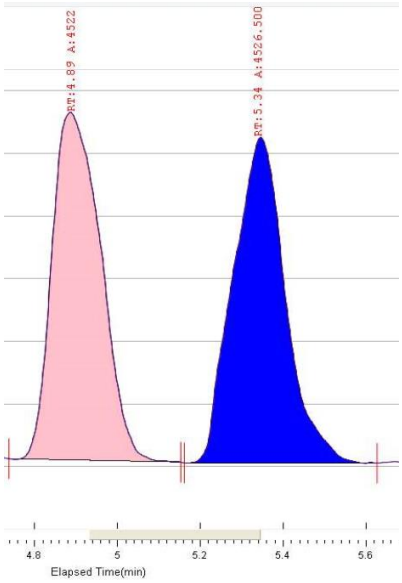
Optical Rotation $[\alpha]_D^{20}$: +9.8 (*c* = 1.0, $CHCl_3$, *l* = 50 mm)

Analysis of Stereochemistry:

Enantiomeric ratio was determined in comparison to the racemic compound synthesized from 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane.

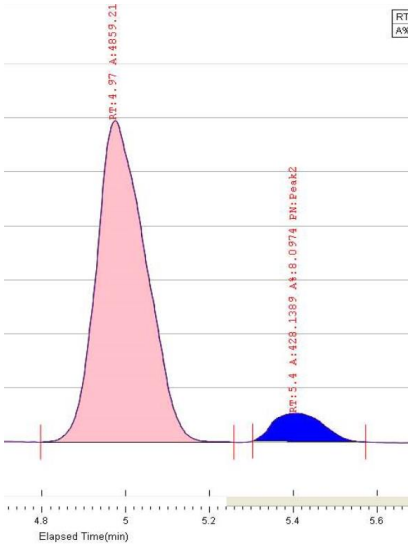
Chiral SFC (Chiracel OD-H, 10% isopropanol, 3.0 mL/min, 35 °C, 210-290 nm), analysis of (1S,2S)-2-((4-(trifluoromethyl)phenyl)amino)cyclopentan-1-ol

Racemic Material

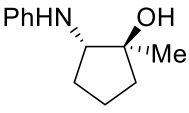


Peak No	% Area	RT (min)
1	49.9756	4.89
2	50.0244	5.34

Enantioenriched Material



Peak No	% Area	RT (min)
1	91.9026	4.97
2	8.0974	5.4



(1*S*,2*S*)-1-methyl-2-(phenylamino)cyclopentan-1-ol (3.111): This reaction was performed according to the *general procedure G* with **3.96** (52.8 mg, 0.150 mmol, 1.0 equiv.), *N*-cyclopropylaniline (100 mg, 0.750 mmol, 5.0 equiv.), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (3.7 mg, 0.0030 mmol, 2.0 mol%) and $MeNO_2$ (1.0 mL). The reaction was stirred under irradiation for 36 h. The compound was purified with SiO_2 chromatography (0-50% ethyl acetate in hexane) as a colorless oil (17.3 mg, 60% yield, 95:5 *er*).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 – 7.13 (m, 2H), 6.74 – 6.66 (m, 3H), 3.73 (t, *J* = 8.0, 8.0 Hz, 1H), 2.34 – 2.23 (m, 1H), 1.87 – 1.72 (m, 3H), 1.71 – 1.61 (m, 1H), 1.43 – 1.32 (m, 1H), 1.28 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 148.2, 129.4, 117.5, 113.4, 81.0, 63.7, 39.3, 31.6, 23.2, 19.6.

IR (neat) ν_{max} 3404 (w), 2962 (m), 1601 (s), 1505 (s), 1313 (m), 1257 (w), 1112 (w), 922 (w), 748 (m), 693 (m) cm^{-1}.

HRMS (DART+) for $C_{12}H_{18}NO$ $[M+H]^+$: Calc'd: 192.1383, found: 192.1379.

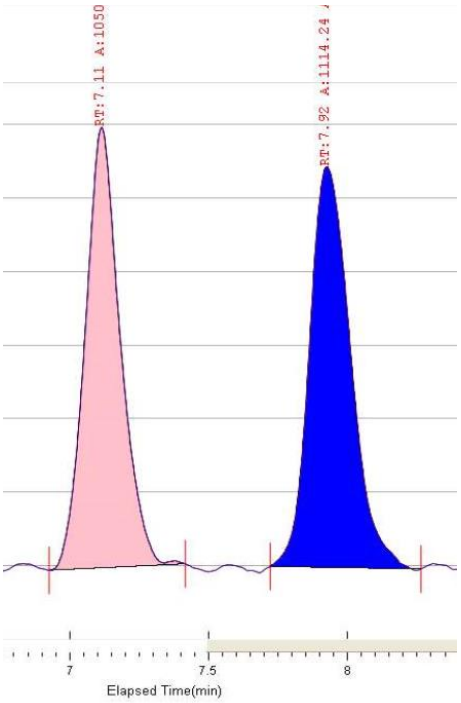
Optical Rotation $[\alpha]_D^{20}$: +52.0 (*c* = 1.0, $CHCl_3$, *l* = 50 mm)

Analysis of Stereochemistry:

Enantiomeric ratio was determined in comparison to the racemic compound synthesized from 4,4,5,5-tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane.

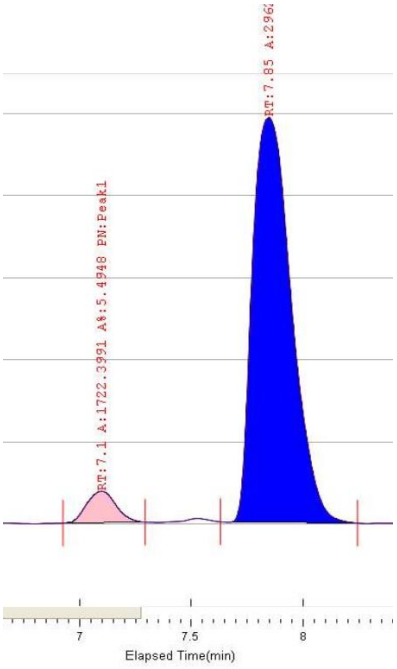
Chiral SFC (Chiracel OD-H, 10% isopropanol, 3.0 mL/min, 35 °C, 210-290 nm), analysis of (1S,2S)-1-methyl-2-(phenylamino)cyclopentan-1-ol

Racemic Material

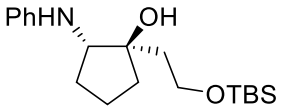


Peak No	Area %	RT (min)
1	48.5203	7.11
2	51.4797	7.92

Enantioenriched Material



Peak No	% Area	RT (min)
1	5.4948	7.1
2	94.5052	7.85



(1*R*,2*S*)-1-(2-((*tert*-butyldimethylsilyl)oxy)ethyl)-2-(phenylamino)cyclopentan-1-ol (3.112): This reaction was performed according to the *general procedure G* with **3.97** (74.4 mg, 0.150 mmol, 1.0 equiv.), *N*-cyclopropylaniline (100 mg, 0.750 mmol, 5.0 equiv.), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (3.7 mg, 0.0030 mmol, 2.0 mol%) and $MeNO_2$ (1.0 mL). The reaction was stirred under irradiation for 36 h. The compound was purified with SiO_2 chromatography (0-50% ethyl acetate in hexane) as a colorless oil (29.8 mg, 59% yield, 98:2 *er*).

^{1}H NMR (500 MHz, CDCl3) δ 7.17 (t, J = 7.9 Hz, 2H), 6.74 – 6.65 (m, 3H), 4.23 (brs, 1H), 3.96 – 3.87 (m, 2H), 3.70 (t, J = 6.2 Hz, 1H), 3.43 (brs, 1H), 2.36 – 2.26 (m, 1H), 2.03

– 1.95 (m, 1H), 1.93 – 1.83 (m, 2H), 1.78 – 1.65 (m, 3H), 1.48 – 1.39 (m, 1H), 0.91 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 148.1, 129.3, 117.2, 113.4, 84.0, 63.7, 62.0, 37.3, 36.1, 32.1, 26.0, 20.7, 18.2, -5.5, -5.5.

IR (neat) ν_{max} 3497 (w), 2954 (w), 2857 (w), 2359 (w), 1770 (m), 1759 (m), 1602 (w), 1506 (w), 1384 (w), 1247 (s), 1081 (w), 896 (w), 837 (w), 778 (w), 747 (w) cm^{-1}.

HRMS (DART+) for $C_{19}H_{34}NO_2Si$ $[M+H]^+$: Calc'd: 336.2353, found: 336.2349.

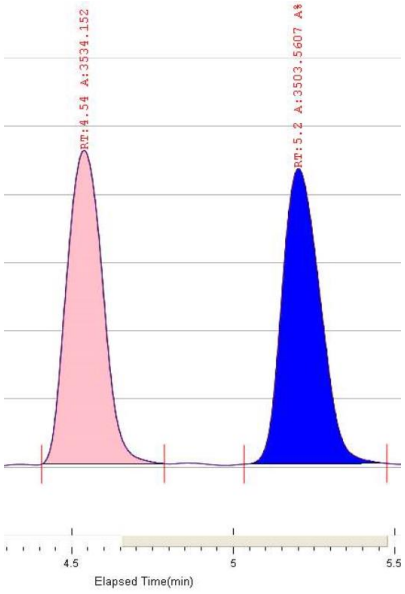
Optical Rotation $[\alpha]_D^{20}$: +12.3 (*c* = 1.0, $CHCl_3$, *l* = 50 mm)

Analysis of Stereochemistry:

Enantiomeric ratio was determined in comparison to the racemic compound synthesized from tert-butyldimethyl((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)oxy)silane.

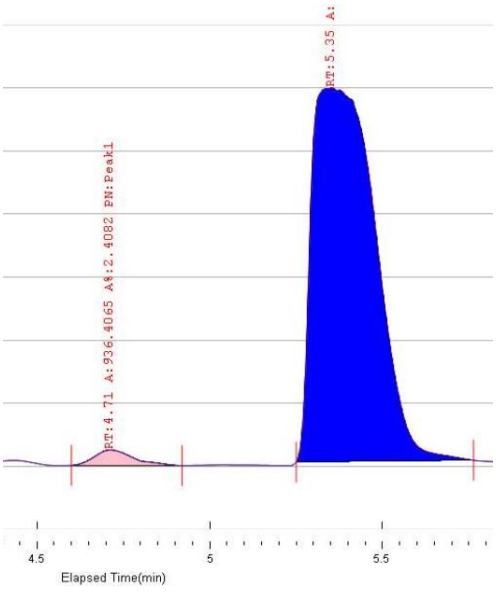
Chiral SFC (Chiracel OJ-H, 5% isopropanol, 3.0 mL/min, 35 °C, 210-290 nm), analysis of (1R,2S)-1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-(phenylamino)cyclopentan-1-ol

Racemic Material

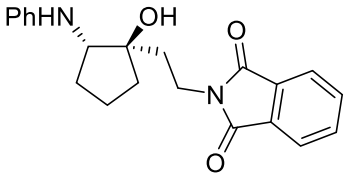


Peak No	% Area	RT (min)
1	50.2173	4.54
2	49.7827	5.2

Enantioenriched Material



Peak No	% Area	RT (min)
1	2.4082	4.71
2	97.5918	5.35



2-(2-((1*R*,2*S*)-1-hydroxy-2-(phenylamino)cyclopentyl)ethyl)isoindoline-1,3-dione (3.113): This reaction was performed according to the *general procedure G* with **3.98** (76.7 mg, 0.150 mmol, 1.0 equiv.), *N*-cyclopropylaniline (100 mg, 0.750 mmol, 5.0 equiv.), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (3.7 mg, 0.0030 mmol, 2.0 mol%) and $MeNO_2$ (1.0 mL). The reaction was stirred under irradiation for 36 h. The compound was purified with SiO_2 chromatography (0-50% ethyl acetate in hexane) as a colorless oil (23.2 mg, 44% yield, 97:3 *er*).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 – 7.71 (m, 2H), 7.67 – 7.61 (m, 2H), 7.05 (t, *J* = 7.4, 7.4 Hz, 2H), 6.60 (t, *J* = 7.9 Hz, 1H), 6.55 (d, *J* = 8.2 Hz, 2H), 4.00 – 3.89 (m, 1H), 3.89 – 3.78 (m, 1H), 3.64 (t, *J* = 6.1 Hz, 1H), 3.41 (s, 1H), 2.29 – 2.19 (m, 2H), 2.14 – 2.06 (m, 1H), 1.97 – 1.91 (m, 1H), 1.85 – 1.77 (m, 3H), 1.72 – 1.65 (m, 1H), 1.50 – 1.43 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.9, 147.4, 134.0, 132.2, 129.3, 123.3, 117.5, 113.3, 82.3, 63.8, 37.6, 34.3, 34.0, 31.7, 20.4.

IR (neat) ν_{max} 2954 (w), 2362 (m), 2340 (w), 1770 (m), 1705 (s), 1602 (m), 1507 (w), 1466 (w), 1400 (w), 1371 (w), 1316 (w), 1247 (s), 1058 (w), 750 (w), 717 (w) cm^{-1}.

HRMS (DART+) for $C_{21}H_{23}N_2O_3[M+H]^+$: Calc'd: 351.1703, found: 351.1698.

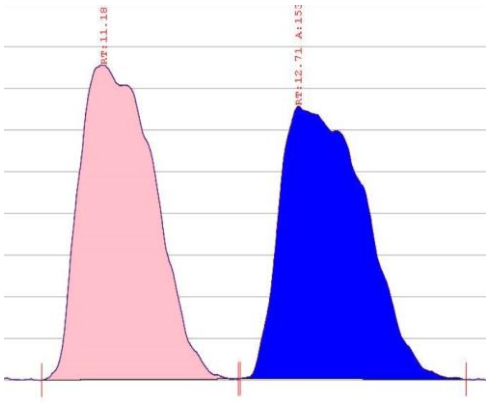
Optical Rotation $[\alpha]_D^{20}$: -2.6 (*c* = 1.0, $CHCl_3$, *l* = 50 mm)

Analysis of Stereochemistry:

Enantiomeric ratio was determined in comparison to the racemic compound synthesized from 2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)isoindoline-1,3-dione.

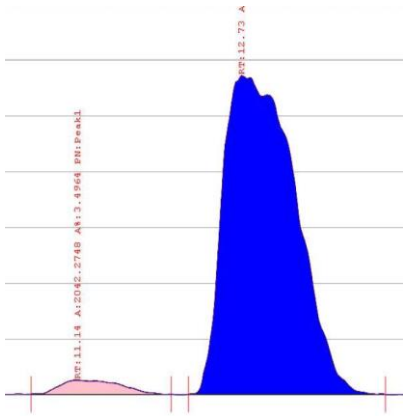
Chiral SFC (Chiracel OJ-H, 10% isopropanol, 3.0 mL/min, 35 °C, 210-290 nm), analysis of 2-(2-((1R,2S)-1-hydroxy-2-(phenylamino)cyclopentyl)ethyl)isoindoline-1,3-dione

Racemic Material

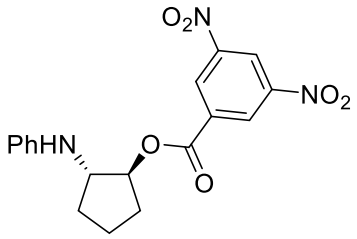


Peak No	% Area	RT (min)
1	50.3241	11.18
2	49.6759	12.71

Enantioenriched Material



Peak No	% Area	RT (min)
1	3.4964	11.14
2	96.5036	12.73



(1*S*,2*S*)-2-(phenylamino)cyclopentyl 3,5-dinitrobenzoate (SI-5): (1*S*,2*S*)-2-(phenylamino)cyclopentan-1-ol (16.0 mg, 0.09 mmol, 1.0 equiv.), 3,5-dinitrobenoyl chloride (51.9 mg, 0.23 mmol, 2.5 equiv.), 4-dimethylaminopyridine (16.5 mg, 0.14 mmol, 1.5 equiv.) and trimethylamine (91.0 mg, 0.90 mmol, 10 equiv.) were stirred in DCM (1 mL) over 16 hours. After removal of solvent, the compound was purified with SiO_2 chromatography (0-30% ethyl acetate in hexane) as a red crystalline solid (23.4 mg, 76% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.22 (t, *J* = 2.2, 2.2 Hz, 1H), 9.13 (d, *J* = 2.2 Hz, 2H), 7.22 – 7.13 (m, 2H), 6.77 – 6.64 (m, 3H), 5.45 – 5.34 (m, 1H), 4.10 – 3.97 (m, 1H), 2.44 – 2.34 (m, 1H), 2.32 – 2.24 (m, 1H), 2.02 – 1.89 (m, 3H), 1.69 – 1.59 (m, 1H).

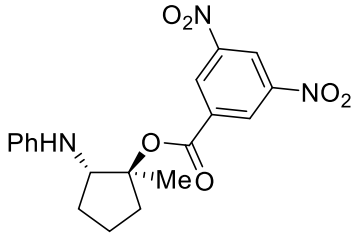
^{13}C NMR (126 MHz, $CDCl_3$) δ 162.5, 148.8, 147.1, 134.1, 129.6, 129.5, 122.5, 118.1, 113.4, 83.2, 59.6, 31.5, 30.2, 21.4.

IR (neat) ν_{max} 3408 (w), 3101 (w), 2963 (w), 2366 (w), 1726 (m), 1628 (m), 1602 (w), 1543 (s), 1507 (w), 1344 (s), 1277 (m), 1167 (m), 1075 (w), 921 (w), 720 (w) cm^{-1}.

HRMS (DART+) for $C_{18}H_{18}N_3O_6[M+H]^+$: Calc'd: 372.1190, found: 372.1179.

Optical Rotation $[\alpha]_D^{20}$: +75.5 (*c* = 1.0, $CHCl_3$, *l* = 50 mm)

The absolute configuration was determined by X-ray crystallography. **SI-5** was recrystallized from hexane and ethyl acetate and indicated an *anti*-amino alcohol derivative. (See **X-Ray 3**)



(1*S*,2*S*)-1-methyl-2-(phenylamino)cyclopentyl 3,5-dinitrobenzoate (SI-6): (1*S*,2*S*)-1-methyl-2-(phenylamino)cyclopentan-1-ol (19.1 mg, 0.10 mmol, 1.0 equiv.), 3,5-dinitrobenoyl chloride (56.4 mg, 0.25 mmol, 2.5 equiv.), 4-dimethylaminopyridine (18.3 mg, 0.15 mmol, 1.5 equiv.) and trimethylamine (101 mg, 1.0 mmol, 10 equiv.) were stirred in DCM (1 mL) over 16 hours. After removal of solvent, the compound was purified with SiO_2 chromatography (0-30% ethyl acetate in hexane) as a red crystalline solid (27.0 mg, 70% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.22 (t, *J* = 2.1 Hz, 1H), 9.12 (d, *J* = 2.1 Hz, 2H), 7.31 – 7.26 (m, 2H), 6.85 (d, *J* = 7.9 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 4.38 (t, *J* = 8.3 Hz, 1H), 2.42 – 2.27 (m, 3H), 1.97 – 1.79 (m, 2H), 1.69 (s, 3H), 1.62 – 1.46 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 162.1, 148.8, 147.6, 135.2, 129.7, 129.5, 122.3, 118.0, 113.3, 94.2, 61.7, 36.5, 30.7, 19.6, 19.2.

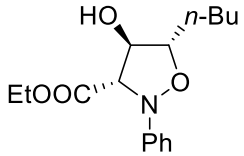
IR (neat) ν_{max} 2995 (w), 2363 (w), 1770 (m), 1541 (w), 1376 (w), 1344 (w), 1246 (s), 1058 (w) cm^{-1}.

HRMS (DART+) for $C_{19}H_{20}N_3O_6[M+H]^+$: Calc'd: 386.1347, found: 386.1361.

Optical Rotation $[\alpha]_D^{20}$: +104.4 (*c* = 1.0, $CHCl_3$, *l* = 50 mm)

The relevant configuration was determined by X-ray crystallography. **SI-6** was recrystallized from hexane and ethyl acetate and indicated a trans amino alcohol derivative. (See **X-Ray 4**)

3.4.6. Procedures for Transformation of B(sam) Containing Cycloadducts, Characterization of the Products and Analysis of Stereochemistry



ethyl (3*S*,4*R*,5*S*)-5-butyl-4-hydroxy-2-phenylisoxazolidine-3-carboxylate (3.101): Into a 20 mL glass scintillation vial equipped with a stirbar was added **3.100** (118 mg, 0.20 mmol, 1.0 equiv.), pH = 10.5 buffer (1mL, 0.1 M Na_2CO_3/$NaHCO_3$) and THF (2 mL). After the vial was cooled down to 0 ºC, H_2O_2 (1 mL, 35 wt% in water) was added dropwise. The reaction was allowed to warm to room temperature and stir for 6 hours. The mixture was then brought to 0 ºC and quenched with saturated sodium thiosulfate solution (4 mL) carefully. The reaction was extracted for 3 times with ethyl acetate. The combined organic extracts were dried with sodium sulfate, filtered, and concentrated. The residue was purified by silica gel column chromatography (30% ethyl acetate in hexane to 100% ethyl acetate). Title compound can be obtained as yellow oil (55.7 mg, 95% yield) as well as **3.87** (36.2 mg, 60% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 2H), 7.08 – 7.02 (m, 2H), 7.01 – 6.93 (m, 1H), 4.62 (dd, *J* = 6.7, 3.8 Hz, 1H), 4.32 – 4.25 (m, 2H), 4.24 – 4.23 (m, 1H), 3.94 – 3.86 (m, 1H), 2.42 (s, 1H), 1.83 – 1.67 (m, 2H), 1.64 – 1.51 (m, 1H), 1.50 – 1.36 (m, 3H), 1.31 – 1.31 (m, 3H), 0.94 (t, *J* = 7.3 Hz, 3H).

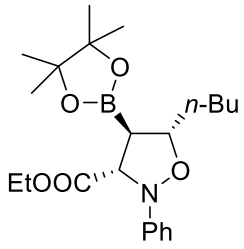
^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 151.1, 129.2, 122.0, 114.1, 83.9, 83.4, 75.9, 62.0, 30.4, 28.3, 22.8, 14.2, 14.0.

IR (neat) ν_{max} 2956 (w), 2933 (w), 1734 (s), 1597 (m), 1488 (s), 1453 (w), 1372 (w), 1254 (s), 1185 (s), 1065 (m), 1028 (m), 753 (m), 693 (s) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{16}H_{24}NO_4$ 294.1700; Found 294.1687.

Optical Rotation $[\alpha]_D^{20}$: -160.0 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).

The racemic product can be obtained by using (*racemic*)-**3.102** as starting material.



ethyl (3*S*,4*R*,5*S*)-5-butyl-2-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoxazolidine-3-carboxylate (3.102): Into a 20 mL glass scintillation vial equipped with a stirbar was added **3.100** (118mg, 0.20 mmol, 1.0 equiv.), 4-methylbenzenesulfonic acid hydrate (76.1 mg, 0.40 mmol, 2 equiv.), pinacol (118 mg, 1.0 mmol, 5 equiv.) and THF (2 mL). The reaction was allowed to stir at room temperature for 36 hours. The mixture was then filtered through a plug of silica gel and concentrated under vacuum. The residue was purified by silica gel column chromatography (20% ethyl acetate in hexane to 100% ethyl acetate). Title compound can be obtained as white solid (73.5 mg, 91% yield) as well as **3.87** (38.4 mg, 61% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.23 (m, 2H), 7.08 – 7.02 (m, 2H), 6.98 – 6.90 (m, 1H), 4.39 (d, *J* = 8.1 Hz, 1H), 4.35 – 4.20 (m, 2H), 4.05 – 3.97 (m, 1H), 2.20 (dd, *J* = 10.2, 8.0 Hz, 1H), 1.81 – 1.65 (m, 2H), 1.60 – 1.49 (m, 1H), 1.48 – 1.35 (m, 3H), 1.34 – 1.29 (m, 3H), 1.15 (s, 12H), 0.93 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.9, 152.1, 129.0, 121.5, 114.3, 84.2, 81.3, 71.7, 61.7, 32.4, 28.8, 24.8, 246, 22.8, 14.4, 14.1.

^{11}B NMR (160 MHz, $CDCl_3$) δ 33.0.

IR (neat) ν_{max} 2978 (m), 2933 (m), 1746 (m), 1597 (w), 1488 (m), 1381 (s), 1371 (s), 1333 (s), 1212 (m), 1143 (s), 967 (w), 849 (w), 753 (w), 695 (w) cm^{-1}.

HRMS (DART+) m/z: $[M+H]^+$ Calc'd for $C_{22}H_{35}BNO_5$ 404.2603; Found 404.2623.

Optical Rotation $[\alpha]_D^{20}$: -121.3 (c = 1.0 g/100 mL, $CHCl_3$, *l*=50 mm).

The racemic product can be obtained by using (*E*)-2-(hex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane as starting material.

3.4.7. X-Ray Data

X-Ray 1: compound **3.85**, CCDC Deposition Number 2164906

Table 1. Crystal data and structure refinement for C19H23BN2OS.

Identification code	C19H23BN2OS	
Empirical formula	C19 H23 B N2 O S	
Formula weight	338.26	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 9.6562(6) Å	α= 90°.
	b = 13.3422(8) Å	β= 90°.
	c = 14.4220(10) Å	γ = 90°.
Volume	1858.1(2) $Å^3$	
Z	4	
Density (calculated)	1.209 Mg/m^3	
Absorption coefficient	0.182 mm^{-1}	
F(000)	720	
Crystal size	0.280 x 0.220 x 0.140 mm^3	
Theta range for data collection	2.079 to 28.291°.	
Index ranges	-11<=h<=12, -17<=k<=17, -19<=l<=19	
Reflections collected	44767	
Independent reflections	4605 [R(int) = 0.0493]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7457 and 0.7031	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4605 / 1 / 220	
Goodness-of-fit on F^2	1.042	
Final R indices [I>2sigma(I)]	R1 = 0.0310, wR2 = 0.0723	
R indices (all data)	R1 = 0.0387, wR2 = 0.0779	
Absolute structure parameter	0.01(2)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.180 and -0.213 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for C19H23BN2OS. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	5017(1)	7033(1)	6705(1)	23(1)
O(2)	6348(2)	7473(1)	6361(1)	27(1)
N(1)	5262(2)	5805(1)	6868(1)	24(1)
N(2)	4204(2)	4257(1)	7359(1)	27(1)
B(1)	4452(2)	5282(2)	7561(2)	26(1)
C(1)	3208(3)	5322(2)	9109(2)	45(1)
C(2)	3888(2)	5793(2)	8452(2)	33(1)
C(3)	4416(2)	3847(2)	6477(2)	27(1)
C(4)	3711(2)	2986(2)	6184(2)	37(1)
C(5)	3950(3)	2604(2)	5306(2)	43(1)
C(6)	4864(3)	3070(2)	4711(2)	43(1)
C(7)	5548(3)	3932(2)	4990(2)	33(1)
C(8)	5342(2)	4319(1)	5876(2)	26(1)
C(9)	6150(2)	5206(2)	6229(1)	24(1)
C(10)	7499(2)	4911(2)	6720(2)	25(1)
C(11)	7874(2)	3917(2)	6869(2)	31(1)
C(12)	9132(2)	3687(2)	7296(2)	38(1)
C(13)	10023(3)	4440(2)	7567(2)	39(1)
C(14)	9658(2)	5430(2)	7426(2)	41(1)
C(15)	8406(2)	5666(2)	7009(2)	35(1)
C(16)	3807(2)	7113(2)	5716(2)	27(1)
C(17)	3551(3)	8239(2)	5624(2)	35(1)
C(18)	4394(2)	6692(2)	4815(2)	31(1)
C(19)	2493(2)	6563(2)	6011(2)	37(1)

Table 3. Bond lengths [Å] and angles [°] for C19H23BN2OS.

S(1)-O(2)	1.4971(15)
S(1)-N(1)	1.6726(16)
S(1)-C(16)	1.846(2)
N(1)-B(1)	1.449(3)
N(1)-C(9)	1.490(3)
N(2)-C(3)	1.400(3)
N(2)-B(1)	1.418(3)
N(2)-H(2N)	0.860(19)
B(1)-C(2)	1.553(3)
C(1)-C(2)	1.313(3)
C(1)-H(1A)	0.9500
C(1)-H(1B)	0.9500
C(2)-H(2)	0.9500
C(3)-C(8)	1.395(3)
C(3)-C(4)	1.401(3)
C(4)-C(5)	1.383(4)
C(4)-H(4)	0.9500
C(5)-C(6)	1.380(4)
C(5)-H(5)	0.9500
C(6)-C(7)	1.386(3)
C(6)-H(6)	0.9500
C(7)-C(8)	1.394(3)
C(7)-H(7)	0.9500
C(8)-C(9)	1.506(3)
C(9)-C(10)	1.534(3)
C(9)-H(9)	1.0000
C(10)-C(11)	1.392(3)
C(10)-C(15)	1.398(3)
C(11)-C(12)	1.396(3)
C(11)-H(11A)	0.9500
C(12)-C(13)	1.379(4)
C(12)-H(12)	0.9500
C(13)-C(14)	1.382(3)
C(13)-H(13)	0.9500

C(14)-C(15)	1.386(3)
C(14)-H(14)	0.9500
C(15)-H(15)	0.9500
C(16)-C(18)	1.526(3)
C(16)-C(19)	1.526(3)
C(16)-C(17)	1.528(3)
C(17)-H(17A)	0.9800
C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800

O(2)-S(1)-N(1)	108.01(9)
O(2)-S(1)-C(16)	105.38(9)
N(1)-S(1)-C(16)	104.78(9)
B(1)-N(1)-C(9)	118.65(16)
B(1)-N(1)-S(1)	119.52(14)
C(9)-N(1)-S(1)	121.27(13)
C(3)-N(2)-B(1)	122.64(18)
C(3)-N(2)-H(2N)	117.0(17)
B(1)-N(2)-H(2N)	119.7(17)
N(2)-B(1)-N(1)	114.44(19)
N(2)-B(1)-C(2)	122.3(2)
N(1)-B(1)-C(2)	123.26(19)
C(2)-C(1)-H(1A)	120.0
C(2)-C(1)-H(1B)	120.0
H(1A)-C(1)-H(1B)	120.0
C(1)-C(2)-B(1)	124.2(2)
C(1)-C(2)-H(2)	117.9
B(1)-C(2)-H(2)	117.9
C(8)-C(3)-N(2)	118.73(18)
C(8)-C(3)-C(4)	119.6(2)

N(2)-C(3)-C(4)	121.6(2)
C(5)-C(4)-C(3)	119.8(2)
C(5)-C(4)-H(4)	120.1
C(3)-C(4)-H(4)	120.1
C(6)-C(5)-C(4)	120.7(2)
C(6)-C(5)-H(5)	119.6
C(4)-C(5)-H(5)	119.6
C(5)-C(6)-C(7)	119.8(2)
C(5)-C(6)-H(6)	120.1
C(7)-C(6)-H(6)	120.1
C(6)-C(7)-C(8)	120.4(2)
C(6)-C(7)-H(7)	119.8
C(8)-C(7)-H(7)	119.8
C(7)-C(8)-C(3)	119.56(19)
C(7)-C(8)-C(9)	121.8(2)
C(3)-C(8)-C(9)	118.53(18)
N(1)-C(9)-C(8)	109.38(16)
N(1)-C(9)-C(10)	109.89(17)
C(8)-C(9)-C(10)	113.20(16)
N(1)-C(9)-H(9)	108.1
C(8)-C(9)-H(9)	108.1
C(10)-C(9)-H(9)	108.1
C(11)-C(10)-C(15)	118.5(2)
C(11)-C(10)-C(9)	122.45(18)
C(15)-C(10)-C(9)	119.01(18)
C(10)-C(11)-C(12)	120.2(2)
C(10)-C(11)-H(11A)	119.9
C(12)-C(11)-H(11A)	119.9
C(13)-C(12)-C(11)	120.6(2)
C(13)-C(12)-H(12)	119.7
C(11)-C(12)-H(12)	119.7
C(12)-C(13)-C(14)	119.7(2)
C(12)-C(13)-H(13)	120.2
C(14)-C(13)-H(13)	120.2
C(13)-C(14)-C(15)	120.2(2)
C(13)-C(14)-H(14)	119.9

C(15)-C(14)-H(14)	119.9
C(14)-C(15)-C(10)	120.8(2)
C(14)-C(15)-H(15)	119.6
C(10)-C(15)-H(15)	119.6
C(18)-C(16)-C(19)	111.65(18)
C(18)-C(16)-C(17)	110.33(18)
C(19)-C(16)-C(17)	111.28(18)
C(18)-C(16)-S(1)	113.66(14)
C(19)-C(16)-S(1)	106.47(15)
C(17)-C(16)-S(1)	103.11(14)
C(16)-C(17)-H(17A)	109.5
C(16)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(16)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(16)-C(18)-H(18A)	109.5
C(16)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(16)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(16)-C(19)-H(19A)	109.5
C(16)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(16)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for C19H23BN2OS. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	26(1)	18(1)	24(1)	0(1)	2(1)	-1(1)
O(2)	27(1)	22(1)	33(1)	1(1)	2(1)	-4(1)
N(1)	27(1)	18(1)	26(1)	0(1)	2(1)	1(1)
N(2)	31(1)	22(1)	28(1)	4(1)	2(1)	-2(1)
B(1)	25(1)	25(1)	28(1)	2(1)	-1(1)	1(1)
C(1)	55(2)	42(1)	38(1)	-3(1)	17(1)	-5(1)
C(2)	39(1)	27(1)	33(1)	1(1)	6(1)	0(1)
C(3)	29(1)	20(1)	32(1)	2(1)	-6(1)	1(1)
C(4)	39(1)	26(1)	45(1)	3(1)	-9(1)	-4(1)
C(5)	53(2)	26(1)	48(2)	-6(1)	-19(1)	-4(1)
C(6)	59(2)	36(1)	34(1)	-11(1)	-13(1)	4(1)
C(7)	39(1)	33(1)	28(1)	-2(1)	-4(1)	2(1)
C(8)	29(1)	21(1)	28(1)	-1(1)	-5(1)	4(1)
C(9)	28(1)	22(1)	22(1)	0(1)	2(1)	0(1)
C(10)	24(1)	29(1)	22(1)	0(1)	3(1)	0(1)
C(11)	32(1)	28(1)	34(1)	-1(1)	-1(1)	3(1)
C(12)	37(1)	38(1)	39(1)	2(1)	0(1)	12(1)
C(13)	28(1)	57(1)	33(1)	5(1)	-2(1)	5(1)
C(14)	35(1)	46(1)	43(1)	3(1)	-7(1)	-7(1)
C(15)	34(1)	30(1)	40(1)	2(1)	-4(1)	-3(1)
C(16)	26(1)	26(1)	28(1)	1(1)	-3(1)	0(1)
C(17)	38(1)	27(1)	40(1)	5(1)	-3(1)	5(1)
C(18)	34(1)	33(1)	26(1)	0(1)	-5(1)	1(1)
C(19)	27(1)	36(1)	47(1)	4(1)	-2(1)	-3(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{-3}) for C19H23BN2OS.

	x	y	z	U(eq)
H(2N)	3800(20)	3884(17)	7762(16)	33
H(1A)	3034	4623	9055	54
H(1B)	2891	5679	9637	54
H(2)	4045	6491	8526	40
H(4)	3071	2665	6586	44
H(5)	3479	2016	5112	51
H(6)	5024	2801	4110	51
H(7)	6162	4260	4574	40
H(9)	6392	5638	5686	29
H(11A)	7271	3392	6679	38
H(12)	9376	3007	7401	46
H(13)	10884	4279	7849	47
H(14)	10266	5951	7616	50
H(15)	8162	6349	6918	42
H(17A)	3174	8499	6207	52
H(17B)	4426	8579	5483	52
H(17C)	2888	8361	5122	52
H(18A)	5234	7062	4647	47
H(18B)	4619	5982	4899	47
H(18C)	3705	6762	4320	47
H(19A)	2145	6852	6591	55
H(19B)	1788	6632	5526	55
H(19C)	2702	5851	6105	55

Table 6. Torsion angles [°] for C19H23BN2OS.

O(2)-S(1)-N(1)-B(1)	151.69(16)
C(16)-S(1)-N(1)-B(1)	-96.34(17)
O(2)-S(1)-N(1)-C(9)	-37.04(18)
C(16)-S(1)-N(1)-C(9)	74.93(17)
C(3)-N(2)-B(1)-N(1)	-15.0(3)
C(3)-N(2)-B(1)-C(2)	164.7(2)
C(9)-N(1)-B(1)-N(2)	-21.2(3)
S(1)-N(1)-B(1)-N(2)	150.27(15)
C(9)-N(1)-B(1)-C(2)	159.10(19)
S(1)-N(1)-B(1)-C(2)	-29.4(3)
N(2)-B(1)-C(2)-C(1)	3.7(4)
N(1)-B(1)-C(2)-C(1)	-176.7(2)
B(1)-N(2)-C(3)-C(8)	23.8(3)
B(1)-N(2)-C(3)-C(4)	-155.4(2)
C(8)-C(3)-C(4)-C(5)	0.8(3)
N(2)-C(3)-C(4)-C(5)	180.0(2)
C(3)-C(4)-C(5)-C(6)	-0.8(4)
C(4)-C(5)-C(6)-C(7)	-0.3(4)
C(5)-C(6)-C(7)-C(8)	1.4(4)
C(6)-C(7)-C(8)-C(3)	-1.4(3)
C(6)-C(7)-C(8)-C(9)	175.2(2)
N(2)-C(3)-C(8)-C(7)	-178.91(19)
C(4)-C(3)-C(8)-C(7)	0.3(3)
N(2)-C(3)-C(8)-C(9)	4.4(3)
C(4)-C(3)-C(8)-C(9)	-176.36(19)
B(1)-N(1)-C(9)-C(8)	45.1(2)
S(1)-N(1)-C(9)-C(8)	-126.27(15)
B(1)-N(1)-C(9)-C(10)	-79.8(2)
S(1)-N(1)-C(9)-C(10)	108.88(17)
C(7)-C(8)-C(9)-N(1)	147.2(2)
C(3)-C(8)-C(9)-N(1)	-36.2(2)
C(7)-C(8)-C(9)-C(10)	-89.9(2)
C(3)-C(8)-C(9)-C(10)	86.7(2)
N(1)-C(9)-C(10)-C(11)	118.8(2)

C(8)-C(9)-C(10)-C(11)	-3.9(3)
N(1)-C(9)-C(10)-C(15)	-62.9(2)
C(8)-C(9)-C(10)-C(15)	174.49(19)
C(15)-C(10)-C(11)-C(12)	-0.2(3)
C(9)-C(10)-C(11)-C(12)	178.2(2)
C(10)-C(11)-C(12)-C(13)	-0.6(4)
C(11)-C(12)-C(13)-C(14)	1.0(4)
C(12)-C(13)-C(14)-C(15)	-0.5(4)
C(13)-C(14)-C(15)-C(10)	-0.3(4)
C(11)-C(10)-C(15)-C(14)	0.6(3)
C(9)-C(10)-C(15)-C(14)	-177.8(2)
O(2)-S(1)-C(16)-C(18)	50.37(17)
N(1)-S(1)-C(16)-C(18)	-63.46(17)
O(2)-S(1)-C(16)-C(19)	173.71(14)
N(1)-S(1)-C(16)-C(19)	59.87(16)
O(2)-S(1)-C(16)-C(17)	-69.07(15)
N(1)-S(1)-C(16)-C(17)	177.09(14)

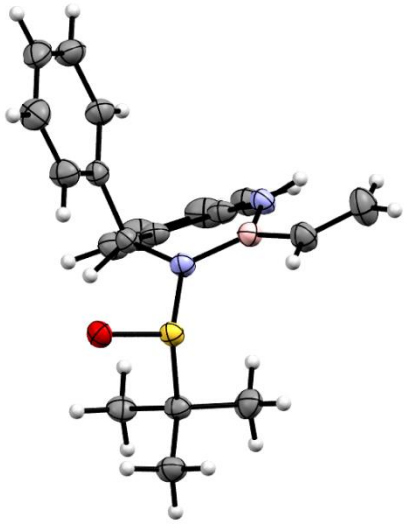
Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for C19H23BN2OS [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2N)...S(1)#1	0.860(19)	2.83(2)	3.3461(18)	120.4(19)
N(2)-H(2N)...O(2)#1	0.860(19)	2.27(2)	3.060(2)	152(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y-1/2,-z+3/2



3-D Ortep figure of Compound 3.85 ($C_{19}H_{23}BN_2OS$) (50% ellipsoid contour probability level)

X-Ray 2: compound **3.95**, CCDC Deposition Number 2164908

Table 1. Crystal data and structure refinement for C21H25BN2O3S.

Identification code	C21H25BN2O3S	
Empirical formula	C21 H25 B N2 O3 S	
Formula weight	396.30	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.0724(3) Å	α= 90°.
	b = 15.3924(8) Å	β= 90°
	c = 17.0505(8) Å	γ = 90°.
Volume	2118.59(17) $Å^3$	
Z	4	
Density (calculated)	1.242 Mg/m^3	
Absorption coefficient	0.176 mm^{-1}	
F(000)	840	
Crystal size	0.420 x 0.360 x 0.200 mm^3	
Theta range for data collection	1.782 to 28.295°.	
Index ranges	-10<=h<=10, -20<=k<=20, -22<=l<=22	
Reflections collected	54741	
Independent reflections	5268 [R(int) = 0.0430]	
Completeness to theta = 25.242°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7457 and 0.6998	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5268 / 1 / 261	
Goodness-of-fit on F^2	1.053	
Final R indices [I>2sigma(I)]	R1 = 0.0292, wR2 = 0.0739	
R indices (all data)	R1 = 0.0334, wR2 = 0.0773	
Absolute structure parameter	-0.005(17)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.217 and -0.226 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for C21H25BN2O3S. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	5405(1)	4741(1)	2030(1)	22(1)
N(1)	4751(2)	5560(1)	2594(1)	20(1)
N(2)	3849(2)	7058(1)	2616(1)	24(1)
O(1)	9337(2)	7193(1)	964(1)	50(1)
O(2)	8458(2)	8561(1)	949(1)	56(1)
O(3)	5610(2)	3966(1)	2547(1)	29(1)
B(1)	5028(2)	6447(1)	2353(1)	22(1)
C(1)	10865(4)	7481(2)	606(2)	74(1)
C(2)	8249(3)	7816(1)	1120(1)	31(1)
C(3)	6753(2)	7495(1)	1528(1)	29(1)
C(4)	6559(2)	6715(1)	1843(1)	25(1)
C(5)	2333(2)	6807(1)	2953(1)	23(1)
C(6)	970(2)	7366(1)	2970(1)	30(1)
C(7)	-516(3)	7088(1)	3290(1)	34(1)
C(8)	-676(2)	6254(1)	3591(1)	33(1)
C(9)	680(2)	5698(1)	3576(1)	27(1)
C(10)	2180(2)	5969(1)	3266(1)	21(1)
C(11)	3687(2)	5389(1)	3296(1)	20(1)
C(12)	4693(2)	5518(1)	4046(1)	23(1)
C(13)	4764(2)	6313(1)	4428(1)	29(1)
C(14)	5672(3)	6410(2)	5117(1)	38(1)
C(15)	6491(3)	5709(2)	5432(1)	45(1)
C(16)	6447(3)	4917(2)	5058(2)	47(1)
C(17)	5561(3)	4818(1)	4361(1)	37(1)
C(18)	3589(2)	4501(1)	1396(1)	29(1)
C(19)	3373(4)	5284(2)	862(2)	54(1)
C(20)	2041(3)	4312(2)	1876(1)	38(1)
C(21)	4097(3)	3695(2)	926(1)	40(1)

Table 3. Bond lengths [Å] and angles [°] for C21H25BN2O3S.

S(1)-O(3)	1.4915(13)
S(1)-N(1)	1.6720(14)
S(1)-C(18)	1.8583(19)
N(1)-B(1)	1.444(2)
N(1)-C(11)	1.496(2)
N(2)-C(5)	1.406(2)
N(2)-B(1)	1.411(2)
N(2)-H(2N)	0.864(18)
O(1)-C(2)	1.327(2)
O(1)-C(1)	1.446(3)
O(2)-C(2)	1.195(3)
B(1)-C(4)	1.566(3)
C(1)-H(1A)	0.9800
C(1)-H(1B)	0.9800
C(1)-H(1C)	0.9800
C(2)-C(3)	1.478(3)
C(3)-C(4)	1.325(3)
C(3)-H(3)	0.9500
C(4)-H(4)	0.9500
C(5)-C(6)	1.398(2)
C(5)-C(10)	1.401(2)
C(6)-C(7)	1.385(3)
C(6)-H(6)	0.9500
C(7)-C(8)	1.388(3)
C(7)-H(7)	0.9500
C(8)-C(9)	1.389(3)
C(8)-H(8)	0.9500
C(9)-C(10)	1.385(2)
C(9)-H(9)	0.9500
C(10)-C(11)	1.510(2)
C(11)-C(12)	1.527(2)
C(11)-H(11)	1.0000
C(12)-C(13)	1.389(3)
C(12)-C(17)	1.393(3)

C(13)-C(14)	1.392(3)
C(13)-H(13)	0.9500
C(14)-C(15)	1.374(4)
C(14)-H(14)	0.9500
C(15)-C(16)	1.377(4)
C(15)-H(15)	0.9500
C(16)-C(17)	1.394(3)
C(16)-H(16)	0.9500
C(17)-H(17)	0.9500
C(18)-C(19)	1.521(3)
C(18)-C(20)	1.522(3)
C(18)-C(21)	1.533(3)
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800
C(21)-H(21C)	0.9800

O(3)-S(1)-N(1)	107.35(7)
O(3)-S(1)-C(18)	105.82(8)
N(1)-S(1)-C(18)	103.60(8)
B(1)-N(1)-C(11)	118.97(13)
B(1)-N(1)-S(1)	120.04(12)
C(11)-N(1)-S(1)	120.52(11)
C(5)-N(2)-B(1)	122.25(15)
C(5)-N(2)-H(2N)	116.6(15)
B(1)-N(2)-H(2N)	120.6(15)
C(2)-O(1)-C(1)	115.30(19)
N(2)-B(1)-N(1)	115.77(15)
N(2)-B(1)-C(4)	122.27(16)
N(1)-B(1)-C(4)	121.95(16)
O(1)-C(1)-H(1A)	109.5

O(1)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5
O(1)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5
H(1B)-C(1)-H(1C)	109.5
O(2)-C(2)-O(1)	123.46(19)
O(2)-C(2)-C(3)	123.34(19)
O(1)-C(2)-C(3)	113.20(17)
C(4)-C(3)-C(2)	126.12(18)
C(4)-C(3)-H(3)	116.9
C(2)-C(3)-H(3)	116.9
C(3)-C(4)-B(1)	123.79(17)
C(3)-C(4)-H(4)	118.1
B(1)-C(4)-H(4)	118.1
C(6)-C(5)-C(10)	119.31(16)
C(6)-C(5)-N(2)	121.62(16)
C(10)-C(5)-N(2)	119.06(15)
C(7)-C(6)-C(5)	119.96(18)
C(7)-C(6)-H(6)	120.0
C(5)-C(6)-H(6)	120.0
C(6)-C(7)-C(8)	120.77(17)
C(6)-C(7)-H(7)	119.6
C(8)-C(7)-H(7)	119.6
C(7)-C(8)-C(9)	119.32(18)
C(7)-C(8)-H(8)	120.3
C(9)-C(8)-H(8)	120.3
C(10)-C(9)-C(8)	120.66(18)
C(10)-C(9)-H(9)	119.7
C(8)-C(9)-H(9)	119.7
C(9)-C(10)-C(5)	119.97(16)
C(9)-C(10)-C(11)	120.85(15)
C(5)-C(10)-C(11)	119.10(15)
N(1)-C(11)-C(10)	109.31(13)
N(1)-C(11)-C(12)	109.94(13)
C(10)-C(11)-C(12)	112.31(14)
N(1)-C(11)-H(11)	108.4

C(10)-C(11)-H(11)	108.4
C(12)-C(11)-H(11)	108.4
C(13)-C(12)-C(17)	118.65(17)
C(13)-C(12)-C(11)	121.99(15)
C(17)-C(12)-C(11)	119.36(17)
C(12)-C(13)-C(14)	120.8(2)
C(12)-C(13)-H(13)	119.6
C(14)-C(13)-H(13)	119.6
C(15)-C(14)-C(13)	119.9(2)
C(15)-C(14)-H(14)	120.0
C(13)-C(14)-H(14)	120.0
C(14)-C(15)-C(16)	120.1(2)
C(14)-C(15)-H(15)	120.0
C(16)-C(15)-H(15)	120.0
C(15)-C(16)-C(17)	120.3(2)
C(15)-C(16)-H(16)	119.8
C(17)-C(16)-H(16)	119.8
C(12)-C(17)-C(16)	120.2(2)
C(12)-C(17)-H(17)	119.9
C(16)-C(17)-H(17)	119.9
C(19)-C(18)-C(20)	112.3(2)
C(19)-C(18)-C(21)	111.0(2)
C(20)-C(18)-C(21)	110.27(17)
C(19)-C(18)-S(1)	106.37(14)
C(20)-C(18)-S(1)	111.89(13)
C(21)-C(18)-S(1)	104.71(14)
C(18)-C(19)-H(19A)	109.5
C(18)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(18)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
C(18)-C(20)-H(20A)	109.5
C(18)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(18)-C(20)-H(20C)	109.5

H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
C(18)-C(21)-H(21A)	109.5
C(18)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(18)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for C21H25BN2O3S. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	25(1)	16(1)	26(1)	-3(1)	3(1)	0(1)
N(1)	24(1)	14(1)	22(1)	0(1)	3(1)	0(1)
N(2)	31(1)	13(1)	28(1)	1(1)	2(1)	-1(1)
O(1)	54(1)	34(1)	62(1)	14(1)	31(1)	10(1)
O(2)	59(1)	28(1)	80(1)	9(1)	31(1)	-6(1)
O(3)	35(1)	16(1)	37(1)	0(1)	-2(1)	4(1)
B(1)	28(1)	16(1)	21(1)	-1(1)	0(1)	-3(1)
C(1)	59(2)	73(2)	89(2)	30(2)	46(2)	19(2)
C(2)	39(1)	25(1)	28(1)	0(1)	7(1)	-2(1)
C(3)	32(1)	23(1)	31(1)	1(1)	3(1)	-1(1)
C(4)	31(1)	20(1)	24(1)	-1(1)	4(1)	-1(1)
C(5)	27(1)	21(1)	22(1)	-4(1)	-2(1)	2(1)
C(6)	36(1)	24(1)	30(1)	-3(1)	-4(1)	8(1)
C(7)	28(1)	34(1)	39(1)	-8(1)	-4(1)	13(1)
C(8)	22(1)	38(1)	40(1)	-6(1)	2(1)	1(1)
C(9)	25(1)	26(1)	29(1)	-2(1)	2(1)	-1(1)
C(10)	22(1)	19(1)	22(1)	-2(1)	0(1)	1(1)
C(11)	21(1)	18(1)	23(1)	3(1)	3(1)	0(1)
C(12)	20(1)	28(1)	22(1)	4(1)	3(1)	0(1)
C(13)	28(1)	34(1)	24(1)	-1(1)	0(1)	0(1)
C(14)	32(1)	57(1)	25(1)	-7(1)	-1(1)	-4(1)
C(15)	31(1)	78(2)	27(1)	5(1)	-5(1)	-1(1)
C(16)	38(1)	58(2)	46(1)	20(1)	-9(1)	9(1)
C(17)	37(1)	33(1)	40(1)	8(1)	-5(1)	5(1)
C(18)	34(1)	22(1)	31(1)	-5(1)	-6(1)	-2(1)
C(19)	78(2)	36(1)	49(1)	10(1)	-30(1)	-10(1)
C(20)	29(1)	43(1)	44(1)	-16(1)	-4(1)	-4(1)
C(21)	40(1)	38(1)	40(1)	-19(1)	1(1)	-6(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for C21H25BN2O3S.

	x	y	z	U(eq)
H(2N)	3970(30)	7605(12)	2517(13)	29(6)
H(1A)	10612	7834	143	111
H(1B)	11522	6975	448	111
H(1C)	11495	7829	983	111
H(3)	5846	7886	1569	35
H(4)	7398	6293	1755	30
H(6)	1062	7937	2763	36
H(7)	-1437	7472	3303	41
H(8)	-1701	6065	3804	40
H(9)	578	5127	3781	32
H(11)	3308	4770	3275	24
H(13)	4185	6797	4218	34
H(14)	5725	6960	5369	46
H(15)	7089	5772	5909	54
H(16)	7023	4435	5275	57
H(17)	5550	4272	4101	44
H(19A)	4435	5425	614	81
H(19B)	2992	5782	1171	81
H(19C)	2553	5150	456	81
H(20A)	1169	4089	1531	58
H(20B)	1659	4849	2128	58
H(20C)	2297	3878	2279	58
H(21A)	3210	3543	559	59
H(21B)	4291	3209	1286	59
H(21C)	5115	3819	633	59

Table 6. Torsion angles [°] for C21H25BN2O3S.

O(3)-S(1)-N(1)-B(1)	156.53(13)
C(18)-S(1)-N(1)-B(1)	-91.79(15)
O(3)-S(1)-N(1)-C(11)	-31.45(15)
C(18)-S(1)-N(1)-C(11)	80.23(14)
C(5)-N(2)-B(1)-N(1)	-12.4(2)
C(5)-N(2)-B(1)-C(4)	168.63(16)
C(11)-N(1)-B(1)-N(2)	-21.2(2)
S(1)-N(1)-B(1)-N(2)	150.91(13)
C(11)-N(1)-B(1)-C(4)	157.71(15)
S(1)-N(1)-B(1)-C(4)	-30.1(2)
C(1)-O(1)-C(2)-O(2)	3.3(4)
C(1)-O(1)-C(2)-C(3)	-176.5(2)
O(2)-C(2)-C(3)-C(4)	-168.5(2)
O(1)-C(2)-C(3)-C(4)	11.3(3)
C(2)-C(3)-C(4)-B(1)	172.65(18)
N(2)-B(1)-C(4)-C(3)	-9.8(3)
N(1)-B(1)-C(4)-C(3)	171.32(17)
B(1)-N(2)-C(5)-C(6)	-158.15(18)
B(1)-N(2)-C(5)-C(10)	20.6(3)
C(10)-C(5)-C(6)-C(7)	-0.4(3)
N(2)-C(5)-C(6)-C(7)	178.36(17)
C(5)-C(6)-C(7)-C(8)	-0.4(3)
C(6)-C(7)-C(8)-C(9)	0.6(3)
C(7)-C(8)-C(9)-C(10)	0.0(3)
C(8)-C(9)-C(10)-C(5)	-0.9(3)
C(8)-C(9)-C(10)-C(11)	176.02(17)
C(6)-C(5)-C(10)-C(9)	1.1(3)
N(2)-C(5)-C(10)-C(9)	-177.77(16)
C(6)-C(5)-C(10)-C(11)	-175.88(17)
N(2)-C(5)-C(10)-C(11)	5.3(2)
B(1)-N(1)-C(11)-C(10)	42.9(2)
S(1)-N(1)-C(11)-C(10)	-129.17(13)
B(1)-N(1)-C(11)-C(12)	-80.78(18)
S(1)-N(1)-C(11)-C(12)	107.11(14)

C(9)-C(10)-C(11)-N(1)	148.46(16)
C(5)-C(10)-C(11)-N(1)	-34.6(2)
C(9)-C(10)-C(11)-C(12)	-89.23(19)
C(5)-C(10)-C(11)-C(12)	87.67(18)
N(1)-C(11)-C(12)-C(13)	91.10(19)
C(10)-C(11)-C(12)-C(13)	-30.8(2)
N(1)-C(11)-C(12)-C(17)	-89.24(19)
C(10)-C(11)-C(12)-C(17)	148.81(17)
C(17)-C(12)-C(13)-C(14)	-0.5(3)
C(11)-C(12)-C(13)-C(14)	179.11(17)
C(12)-C(13)-C(14)-C(15)	-1.0(3)
C(13)-C(14)-C(15)-C(16)	1.5(3)
C(14)-C(15)-C(16)-C(17)	-0.5(4)
C(13)-C(12)-C(17)-C(16)	1.5(3)
C(11)-C(12)-C(17)-C(16)	-178.14(19)
C(15)-C(16)-C(17)-C(12)	-1.0(4)
O(3)-S(1)-C(18)-C(19)	-179.64(16)
N(1)-S(1)-C(18)-C(19)	67.56(17)
O(3)-S(1)-C(18)-C(20)	57.41(16)
N(1)-S(1)-C(18)-C(20)	-55.39(16)
O(3)-S(1)-C(18)-C(21)	-62.04(15)
N(1)-S(1)-C(18)-C(21)	-174.83(13)

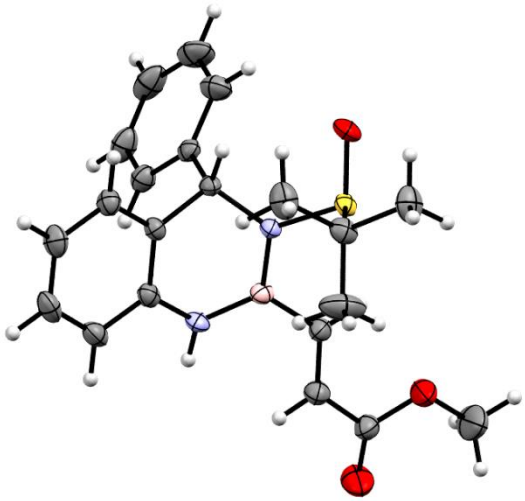
Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for C21H25BN2O3S [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2N)...O(3)#1	0.864(18)	2.125(19)	2.9824(19)	171(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y+1/2,-z+1/2



3-D Ortep figure of Compound 3.95 ($C_{21}H_{25}BN_2O_3S$) (50% ellipsoid contour probability level)

X-Ray 3: Compound **SI-5**, CCDC Deposition Number 2164907

Table 1. Crystal data and structure refinement for C18H17N3O6.

Identification code	C18H17N3O6	
Empirical formula	C18 H17 N3 O6	
Formula weight	371.34	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 7.4170(5) Å	α= 90°.
	b = 16.5260(11) Å	β= 93.543(2)°.
	c = 14.1991(9) Å	γ = 90°.
Volume	1737.1(2) $Å^3$	
Z	4	
Density (calculated)	1.420 Mg/m^3	
Absorption coefficient	0.915 mm^{-1}	
F(000)	776	
Crystal size	0.480 x 0.320 x 0.220 mm^3	
Theta range for data collection	3.118 to 66.578°.	
Index ranges	-8<=h<=8, -19<=k<=19, -16<=l<=16	
Reflections collected	35039	
Independent reflections	6037 [R(int) = 0.0240]	
Completeness to theta = 66.578°	99.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7528 and 0.6466	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6037 / 19 / 515	
Goodness-of-fit on F^2	1.049	
Final R indices [I>2sigma(I)]	R1 = 0.0314, wR2 = 0.0892	
R indices (all data)	R1 = 0.0317, wR2 = 0.0896	
Absolute structure parameter	0.01(5)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.162 and -0.185 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for C18H17N3O6. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(2)	-865(2)	9278(1)	3530(1)	44(1)
O(3)	3034(3)	5982(1)	4296(2)	56(1)
O(4)	1099(3)	5095(1)	3734(2)	62(1)
O(5)	-4791(3)	5990(1)	2495(2)	63(1)
O(6)	-5468(3)	7254(2)	2557(2)	67(1)
N(2)	1579(3)	5794(1)	3907(2)	43(1)
N(3)	-4413(3)	6690(1)	2663(2)	43(1)
C(1)	165(3)	11282(2)	3835(2)	39(1)
C(2)	-1105(3)	11895(2)	3710(2)	38(1)
C(3)	-623(4)	12694(2)	3842(2)	42(1)
C(4)	1140(4)	12881(2)	4127(2)	41(1)
C(5)	2426(4)	12286(2)	4257(2)	40(1)
C(6)	1976(3)	11478(2)	4086(2)	41(1)
N(1)	3350(3)	10901(1)	4125(2)	45(1)
C(7)	3104(3)	10068(2)	3824(2)	32(1)
C(8)	4955(4)	9658(3)	3728(3)	40(1)
C(9)	5420(7)	9208(3)	4666(4)	38(1)
C(10)	3894(9)	9411(4)	5288(4)	41(1)
C(11)	2292(4)	9568(2)	4602(2)	34(1)
O(1)	1747(2)	8778(1)	4226(1)	32(1)
N(1X)	2860(20)	10822(8)	4683(14)	45(1)
C(7X)	2440(20)	9945(10)	4672(12)	32(1)
C(8X)	3920(50)	9470(30)	5280(20)	40(1)
C(9X)	5430(40)	9350(30)	4550(30)	38(1)
C(10X)	4600(30)	9610(30)	3610(20)	41(1)
C(11X)	2630(20)	9639(10)	3695(11)	34(1)
O(1X)	1912(13)	8815(7)	3621(9)	32(1)
C(12)	126(3)	8718(2)	3737(2)	37(1)
C(13)	-355(3)	7854(1)	3546(2)	30(1)
C(14)	851(3)	7234(1)	3788(2)	32(1)
C(15)	299(3)	6447(1)	3639(2)	33(1)

C(16)	-1414(3)	6242(2)	3265(2)	35(1)
C(17)	-2565(3)	6878(2)	3047(2)	33(1)
C(18)	-2078(3)	7679(1)	3169(2)	31(1)
O(7)	8096(2)	1192(1)	1406(1)	33(1)
O(8)	10966(2)	749(1)	1622(1)	37(1)
O(9)	6839(2)	3952(1)	690(1)	49(1)
O(10)	8679(3)	4892(1)	1212(2)	56(1)
O(11)	14690(3)	4144(1)	2422(2)	53(1)
O(12)	15448(2)	2883(1)	2496(2)	56(1)
N(4)	7079(3)	-808(1)	326(2)	39(1)
N(5)	8280(3)	4181(1)	1072(2)	39(1)
N(6)	14354(3)	3427(1)	2317(1)	38(1)
C(19)	9987(3)	-1274(2)	1018(2)	37(1)
C(20)	11119(3)	-1915(2)	1279(2)	40(1)
C(21)	10527(4)	-2707(2)	1195(2)	44(1)
C(22)	8763(4)	-2859(2)	852(2)	42(1)
C(23)	7619(3)	-2224(2)	588(2)	37(1)
C(24)	8225(3)	-1421(1)	652(2)	33(1)
C(25)	7531(3)	45(1)	365(2)	31(1)
C(26)	6107(3)	539(2)	-214(2)	34(1)
C(27)	4653(3)	771(2)	470(2)	38(1)
C(28)	5353(3)	462(2)	1442(2)	35(1)
C(29)	7378(3)	371(1)	1367(2)	30(1)
C(30)	9886(3)	1289(1)	1532(1)	30(1)
C(31)	10366(3)	2167(1)	1562(1)	28(1)
C(32)	9104(3)	2759(1)	1294(2)	30(1)
C(33)	9613(3)	3558(1)	1368(2)	31(1)
C(34)	11307(3)	3805(1)	1711(2)	31(1)
C(35)	12530(3)	3192(1)	1955(1)	29(1)
C(36)	12109(3)	2382(1)	1882(1)	29(1)

Table 3. Bond lengths [Å] and angles [°] for C18H17N3O6.

O(2)-C(12)	1.206(3)
O(3)-N(2)	1.222(3)
O(4)-N(2)	1.228(3)
O(5)-N(3)	1.212(3)
O(6)-N(3)	1.221(3)
N(2)-C(15)	1.472(3)
N(3)-C(17)	1.476(3)
C(1)-C(2)	1.386(3)
C(1)-C(6)	1.406(4)
C(1)-H(1)	0.9500
C(2)-C(3)	1.378(4)
C(2)-H(2)	0.9500
C(3)-C(4)	1.380(4)
C(3)-H(3)	0.9500
C(4)-C(5)	1.374(4)
C(4)-H(4)	0.9500
C(5)-C(6)	1.393(4)
C(5)-H(5)	0.9500
C(6)-N(1)	1.394(3)
N(1)-C(7)	1.450(4)
N(1)-H(1N)	0.95(4)
C(7)-C(11)	1.532(4)
C(7)-C(8)	1.545(4)
C(7)-H(7)	1.0000
C(8)-C(9)	1.545(5)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(10)	1.515(6)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(10)-C(11)	1.512(6)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(11)-O(1)	1.458(4)

C(11)-H(11)	1.0000
O(1)-C(12)	1.355(3)
C(12)-C(13)	1.493(3)
C(13)-C(18)	1.385(3)
C(13)-C(14)	1.389(3)
C(14)-C(15)	1.376(3)
C(14)-H(14)	0.9500
C(15)-C(16)	1.389(3)
C(16)-C(17)	1.377(3)
C(16)-H(16)	0.9500
C(17)-C(18)	1.379(3)
C(18)-H(18)	0.9500
O(7)-C(30)	1.338(3)
O(7)-C(29)	1.458(3)
O(8)-C(30)	1.201(3)
O(9)-N(5)	1.229(3)
O(10)-N(5)	1.224(3)
O(11)-N(6)	1.218(3)
O(12)-N(6)	1.228(3)
N(4)-C(24)	1.384(3)
N(4)-C(25)	1.449(3)
N(4)-H(4N)	0.90(3)
N(5)-C(33)	1.471(3)
N(6)-C(35)	1.469(3)
C(19)-C(20)	1.388(4)
C(19)-C(24)	1.397(3)
C(19)-H(19)	0.9500
C(20)-C(21)	1.384(4)
C(20)-H(20)	0.9500
C(21)-C(22)	1.390(4)
C(21)-H(21)	0.9500
C(22)-C(23)	1.387(4)
C(22)-H(22)	0.9500
C(23)-C(24)	1.402(3)
C(23)-H(23)	0.9500
C(25)-C(29)	1.531(3)

C(25)-C(26)	1.533(3)
C(25)-H(25)	1.0000
C(26)-C(27)	1.544(3)
C(26)-H(26A)	0.9900
C(26)-H(26B)	0.9900
C(27)-C(28)	1.533(3)
C(27)-H(27A)	0.9900
C(27)-H(27B)	0.9900
C(28)-C(29)	1.520(3)
C(28)-H(28A)	0.9900
C(28)-H(28B)	0.9900
C(29)-H(29)	1.0000
C(30)-C(31)	1.494(3)
C(31)-C(36)	1.389(3)
C(31)-C(32)	1.391(3)
C(32)-C(33)	1.375(3)
C(32)-H(32)	0.9500
C(33)-C(34)	1.382(3)
C(34)-C(35)	1.390(3)
C(34)-H(34)	0.9500
C(35)-C(36)	1.377(3)
C(36)-H(36)	0.9500

O(3)-N(2)-O(4)	124.6(2)
O(3)-N(2)-C(15)	117.8(2)
O(4)-N(2)-C(15)	117.6(2)
O(5)-N(3)-O(6)	124.5(2)
O(5)-N(3)-C(17)	118.2(2)
O(6)-N(3)-C(17)	117.3(2)
C(2)-C(1)-C(6)	119.7(2)
C(2)-C(1)-H(1)	120.2
C(6)-C(1)-H(1)	120.2
C(3)-C(2)-C(1)	120.9(2)
C(3)-C(2)-H(2)	119.6
C(1)-C(2)-H(2)	119.6
C(2)-C(3)-C(4)	119.2(2)

C(2)-C(3)-H(3)	120.4
C(4)-C(3)-H(3)	120.4
C(5)-C(4)-C(3)	121.1(2)
C(5)-C(4)-H(4)	119.5
C(3)-C(4)-H(4)	119.5
C(4)-C(5)-C(6)	120.4(2)
C(4)-C(5)-H(5)	119.8
C(6)-C(5)-H(5)	119.8
C(5)-C(6)-N(1)	118.8(2)
C(5)-C(6)-C(1)	118.6(2)
N(1)-C(6)-C(1)	122.5(2)
C(6)-N(1)-C(7)	124.0(2)
C(6)-N(1)-H(1N)	118(2)
C(7)-N(1)-H(1N)	118(2)
N(1)-C(7)-C(11)	110.4(2)
N(1)-C(7)-C(8)	110.2(3)
C(11)-C(7)-C(8)	102.6(2)
N(1)-C(7)-H(7)	111.1
C(11)-C(7)-H(7)	111.1
C(8)-C(7)-H(7)	111.1
C(7)-C(8)-C(9)	106.7(3)
C(7)-C(8)-H(8A)	110.4
C(9)-C(8)-H(8A)	110.4
C(7)-C(8)-H(8B)	110.4
C(9)-C(8)-H(8B)	110.4
H(8A)-C(8)-H(8B)	108.6
C(10)-C(9)-C(8)	105.1(3)
C(10)-C(9)-H(9A)	110.7
C(8)-C(9)-H(9A)	110.7
C(10)-C(9)-H(9B)	110.7
C(8)-C(9)-H(9B)	110.7
H(9A)-C(9)-H(9B)	108.8
C(11)-C(10)-C(9)	104.4(4)
C(11)-C(10)-H(10A)	110.9
C(9)-C(10)-H(10A)	110.9
C(11)-C(10)-H(10B)	110.9

C(9)-C(10)-H(10B)	110.9
H(10A)-C(10)-H(10B)	108.9
O(1)-C(11)-C(10)	105.7(3)
O(1)-C(11)-C(7)	109.4(2)
C(10)-C(11)-C(7)	103.2(3)
O(1)-C(11)-H(11)	112.6
C(10)-C(11)-H(11)	112.6
C(7)-C(11)-H(11)	112.6
C(12)-O(1)-C(11)	118.04(19)
O(2)-C(12)-O(1X)	117.7(5)
O(2)-C(12)-O(1)	125.2(2)
O(2)-C(12)-C(13)	123.7(2)
O(1)-C(12)-C(13)	110.95(19)
C(18)-C(13)-C(14)	120.4(2)
C(18)-C(13)-C(12)	118.3(2)
C(14)-C(13)-C(12)	121.2(2)
C(15)-C(14)-C(13)	118.6(2)
C(15)-C(14)-H(14)	120.7
C(13)-C(14)-H(14)	120.7
C(14)-C(15)-C(16)	123.0(2)
C(14)-C(15)-N(2)	118.2(2)
C(16)-C(15)-N(2)	118.7(2)
C(17)-C(16)-C(15)	116.1(2)
C(17)-C(16)-H(16)	121.9
C(15)-C(16)-H(16)	121.9
C(16)-C(17)-C(18)	123.3(2)
C(16)-C(17)-N(3)	118.1(2)
C(18)-C(17)-N(3)	118.5(2)
C(17)-C(18)-C(13)	118.5(2)
C(17)-C(18)-H(18)	120.8
C(13)-C(18)-H(18)	120.8
C(30)-O(7)-C(29)	118.24(17)
C(24)-N(4)-C(25)	124.28(19)
C(24)-N(4)-H(4N)	119(2)
C(25)-N(4)-H(4N)	117(2)
O(10)-N(5)-O(9)	124.3(2)

O(10)-N(5)-C(33)	118.3(2)
O(9)-N(5)-C(33)	117.4(2)
O(11)-N(6)-O(12)	124.0(2)
O(11)-N(6)-C(35)	118.6(2)
O(12)-N(6)-C(35)	117.4(2)
C(20)-C(19)-C(24)	120.2(2)
C(20)-C(19)-H(19)	119.9
C(24)-C(19)-H(19)	119.9
C(21)-C(20)-C(19)	121.0(2)
C(21)-C(20)-H(20)	119.5
C(19)-C(20)-H(20)	119.5
C(20)-C(21)-C(22)	119.2(2)
C(20)-C(21)-H(21)	120.4
C(22)-C(21)-H(21)	120.4
C(23)-C(22)-C(21)	120.3(2)
C(23)-C(22)-H(22)	119.8
C(21)-C(22)-H(22)	119.8
C(22)-C(23)-C(24)	120.7(2)
C(22)-C(23)-H(23)	119.6
C(24)-C(23)-H(23)	119.6
N(4)-C(24)-C(19)	122.6(2)
N(4)-C(24)-C(23)	118.9(2)
C(19)-C(24)-C(23)	118.5(2)
N(4)-C(25)-C(29)	110.30(18)
N(4)-C(25)-C(26)	110.25(18)
C(29)-C(25)-C(26)	102.92(17)
N(4)-C(25)-H(25)	111.0
C(29)-C(25)-H(25)	111.0
C(26)-C(25)-H(25)	111.0
C(25)-C(26)-C(27)	106.23(17)
C(25)-C(26)-H(26A)	110.5
C(27)-C(26)-H(26A)	110.5
C(25)-C(26)-H(26B)	110.5
C(27)-C(26)-H(26B)	110.5
H(26A)-C(26)-H(26B)	108.7
C(28)-C(27)-C(26)	105.83(17)

C(28)-C(27)-H(27A)	110.6
C(26)-C(27)-H(27A)	110.6
C(28)-C(27)-H(27B)	110.6
C(26)-C(27)-H(27B)	110.6
H(27A)-C(27)-H(27B)	108.7
C(29)-C(28)-C(27)	104.51(18)
C(29)-C(28)-H(28A)	110.8
C(27)-C(28)-H(28A)	110.8
C(29)-C(28)-H(28B)	110.8
C(27)-C(28)-H(28B)	110.8
H(28A)-C(28)-H(28B)	108.9
O(7)-C(29)-C(28)	105.42(17)
O(7)-C(29)-C(25)	108.35(17)
C(28)-C(29)-C(25)	103.33(17)
O(7)-C(29)-H(29)	113.0
C(28)-C(29)-H(29)	113.0
C(25)-C(29)-H(29)	113.0
O(8)-C(30)-O(7)	125.1(2)
O(8)-C(30)-C(31)	124.2(2)
O(7)-C(30)-C(31)	110.64(18)
C(36)-C(31)-C(32)	120.5(2)
C(36)-C(31)-C(30)	118.21(19)
C(32)-C(31)-C(30)	121.33(19)
C(33)-C(32)-C(31)	118.5(2)
C(33)-C(32)-H(32)	120.7
C(31)-C(32)-H(32)	120.7
C(32)-C(33)-C(34)	123.4(2)
C(32)-C(33)-N(5)	118.3(2)
C(34)-C(33)-N(5)	118.3(2)
C(33)-C(34)-C(35)	115.9(2)
C(33)-C(34)-H(34)	122.0
C(35)-C(34)-H(34)	122.0
C(36)-C(35)-C(34)	123.3(2)
C(36)-C(35)-N(6)	118.9(2)
C(34)-C(35)-N(6)	117.8(2)
C(35)-C(36)-C(31)	118.4(2)

C(35)-C(36)-H(36)	120.8
C(31)-C(36)-H(36)	120.8

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for C18H17N3O6. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(2)	29(1)	32(1)	72(1)	-3(1)	-1(1)	6(1)
O(3)	38(1)	52(1)	76(1)	6(1)	-11(1)	13(1)
O(4)	64(1)	33(1)	88(2)	4(1)	-6(1)	11(1)
O(5)	52(1)	56(1)	79(2)	-22(1)	-18(1)	-11(1)
O(6)	36(1)	62(1)	100(2)	6(1)	-24(1)	2(1)
N(2)	42(1)	37(1)	49(1)	6(1)	0(1)	9(1)
N(3)	35(1)	48(1)	44(1)	-4(1)	-7(1)	-2(1)
C(1)	36(1)	35(1)	46(1)	0(1)	-7(1)	5(1)
C(2)	34(1)	48(1)	31(1)	-3(1)	-1(1)	12(1)
C(3)	51(1)	42(1)	32(1)	-4(1)	-1(1)	20(1)
C(4)	57(2)	33(1)	31(1)	-6(1)	-1(1)	5(1)
C(5)	43(1)	38(1)	38(1)	-2(1)	-5(1)	-1(1)
C(6)	36(1)	33(1)	52(1)	0(1)	-9(1)	3(1)
N(1)	27(1)	30(1)	76(2)	6(1)	-10(1)	-1(1)
C(7)	26(1)	30(1)	42(1)	6(1)	-1(1)	4(1)
C(8)	27(2)	46(2)	48(2)	14(2)	6(2)	16(2)
C(9)	37(1)	31(3)	45(2)	9(1)	-10(1)	5(1)
C(10)	45(2)	43(2)	33(1)	8(1)	-9(1)	-16(1)
C(11)	31(1)	32(1)	39(1)	-1(1)	2(1)	-3(1)
O(1)	28(1)	30(1)	39(1)	4(1)	-5(1)	-1(1)
N(1X)	27(1)	30(1)	76(2)	6(1)	-10(1)	-1(1)
C(7X)	26(1)	30(1)	42(1)	6(1)	-1(1)	4(1)
C(8X)	27(2)	46(2)	48(2)	14(2)	6(2)	16(2)
C(9X)	37(1)	31(3)	45(2)	9(1)	-10(1)	5(1)
C(10X)	45(2)	43(2)	33(1)	8(1)	-9(1)	-16(1)
C(11X)	31(1)	32(1)	39(1)	-1(1)	2(1)	-3(1)
O(1X)	28(1)	30(1)	39(1)	4(1)	-5(1)	-1(1)
C(12)	25(1)	35(1)	51(1)	-1(1)	1(1)	1(1)
C(13)	26(1)	33(1)	30(1)	-2(1)	2(1)	2(1)
C(14)	26(1)	38(1)	32(1)	0(1)	0(1)	4(1)
C(15)	34(1)	33(1)	33(1)	3(1)	2(1)	7(1)

C(16)	40(1)	33(1)	32(1)	-2(1)	1(1)	0(1)
C(17)	28(1)	40(1)	29(1)	-1(1)	-3(1)	-1(1)
C(18)	29(1)	35(1)	30(1)	1(1)	0(1)	6(1)
O(7)	26(1)	30(1)	42(1)	-4(1)	-4(1)	4(1)
O(8)	29(1)	33(1)	49(1)	-4(1)	-1(1)	8(1)
O(9)	33(1)	49(1)	64(1)	9(1)	-9(1)	10(1)
O(10)	54(1)	30(1)	83(2)	6(1)	-6(1)	8(1)
O(11)	49(1)	47(1)	62(1)	-8(1)	-11(1)	-13(1)
O(12)	30(1)	55(1)	80(1)	7(1)	-13(1)	2(1)
N(4)	29(1)	32(1)	53(1)	-7(1)	-10(1)	2(1)
N(5)	35(1)	39(1)	44(1)	8(1)	2(1)	9(1)
N(6)	32(1)	46(1)	34(1)	0(1)	-4(1)	-4(1)
C(19)	33(1)	37(1)	40(1)	-6(1)	-2(1)	4(1)
C(20)	37(1)	49(1)	34(1)	-4(1)	-1(1)	10(1)
C(21)	56(2)	44(1)	30(1)	-2(1)	1(1)	21(1)
C(22)	62(2)	32(1)	31(1)	-3(1)	2(1)	6(1)
C(23)	41(1)	36(1)	33(1)	-5(1)	-2(1)	1(1)
C(24)	32(1)	34(1)	32(1)	-6(1)	-1(1)	6(1)
C(25)	25(1)	36(1)	33(1)	-3(1)	-1(1)	2(1)
C(26)	34(1)	37(1)	32(1)	4(1)	-4(1)	-1(1)
C(27)	30(1)	41(1)	42(1)	1(1)	-4(1)	8(1)
C(28)	30(1)	38(1)	38(1)	3(1)	5(1)	4(1)
C(29)	28(1)	30(1)	33(1)	1(1)	-1(1)	4(1)
C(30)	27(1)	34(1)	30(1)	-4(1)	0(1)	4(1)
C(31)	27(1)	31(1)	25(1)	-2(1)	2(1)	5(1)
C(32)	24(1)	35(1)	30(1)	0(1)	0(1)	3(1)
C(33)	29(1)	34(1)	29(1)	2(1)	1(1)	7(1)
C(34)	33(1)	31(1)	29(1)	0(1)	3(1)	0(1)
C(35)	26(1)	37(1)	25(1)	-1(1)	1(1)	0(1)
C(36)	25(1)	34(1)	27(1)	-2(1)	0(1)	5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for C18H17N3O6.

	x	y	z	U(eq)
H(1)	-186	10733	3751	47
H(2)	-2324	11762	3530	45
H(3)	-1494	13111	3739	51
H(4)	1471	13430	4234	49
H(5)	3628	12426	4464	48
H(1N)	4520(50)	11070(20)	4360(20)	54
H(7)	2338	10034	3220	39
H(8A)	5889	10069	3615	48
H(8B)	4890	9272	3194	48
H(9A)	5488	8617	4560	45
H(9B)	6592	9397	4958	45
H(10A)	3650	8953	5711	49
H(10B)	4188	9897	5675	49
H(11)	1288	9856	4901	41
H(1X)	3741	10976	5088	54
H(7X)	1202	9839	4889	39
H(8X1)	3463	8943	5495	48
H(8X2)	4378	9789	5836	48
H(9X1)	6494	9694	4732	45
H(9X2)	5818	8782	4538	45
H(10C)	5067	10142	3430	49
H(10D)	4901	9208	3119	49
H(11X)	2025	10005	3212	41
H(14)	2031	7351	4050	39
H(16)	-1772	5695	3165	42
H(18)	-2905	8100	2998	38
H(4N)	5950(40)	-935(19)	120(20)	47
H(19)	10412	-734	1087	44
H(20)	12319	-1808	1520	48
H(21)	11316	-3142	1370	52

H(22)	8339	-3401	798	50
H(23)	6412	-2334	362	44
H(25)	8766	143	143	38
H(26A)	5569	212	-745	41
H(26B)	6657	1030	-474	41
H(27A)	4485	1365	482	46
H(27B)	3483	514	274	46
H(28A)	5088	854	1942	42
H(28B)	4794	-65	1586	42
H(29)	7954	9	1863	37
H(32)	7917	2614	1065	36
H(34)	11618	4361	1775	37
H(36)	12988	1979	2046	35

Table 6. Torsion angles [°] for C18H17N3O6.

C(6)-C(1)-C(2)-C(3)	-1.0(4)
C(1)-C(2)-C(3)-C(4)	-1.7(3)
C(2)-C(3)-C(4)-C(5)	1.6(4)
C(3)-C(4)-C(5)-C(6)	1.2(4)
C(4)-C(5)-C(6)-N(1)	173.0(3)
C(4)-C(5)-C(6)-C(1)	-3.8(4)
C(2)-C(1)-C(6)-C(5)	3.7(4)
C(2)-C(1)-C(6)-N(1)	-173.0(3)
C(5)-C(6)-N(1)-C(7)	-170.3(3)
C(1)-C(6)-N(1)-C(7)	6.3(5)
C(6)-N(1)-C(7)-C(11)	-81.3(3)
C(6)-N(1)-C(7)-C(8)	166.0(3)
N(1)-C(7)-C(8)-C(9)	95.5(4)
C(11)-C(7)-C(8)-C(9)	-22.0(4)
C(7)-C(8)-C(9)-C(10)	-3.2(6)
C(8)-C(9)-C(10)-C(11)	27.8(6)
C(9)-C(10)-C(11)-O(1)	72.6(4)
C(9)-C(10)-C(11)-C(7)	-42.2(5)
N(1)-C(7)-C(11)-O(1)	169.6(2)
C(8)-C(7)-C(11)-O(1)	-73.0(3)
N(1)-C(7)-C(11)-C(10)	-78.2(4)
C(8)-C(7)-C(11)-C(10)	39.2(4)
C(10)-C(11)-O(1)-C(12)	167.1(3)
C(7)-C(11)-O(1)-C(12)	-82.4(3)
C(11)-O(1)-C(12)-O(2)	5.1(4)
C(11)-O(1)-C(12)-C(13)	-170.42(19)
O(2)-C(12)-C(13)-C(18)	-4.5(3)
O(1)-C(12)-C(13)-C(18)	171.13(19)
O(2)-C(12)-C(13)-C(14)	179.1(2)
O(1)-C(12)-C(13)-C(14)	-5.3(3)
C(18)-C(13)-C(14)-C(15)	0.4(3)
C(12)-C(13)-C(14)-C(15)	176.8(2)
C(13)-C(14)-C(15)-C(16)	-0.6(3)
C(13)-C(14)-C(15)-N(2)	-179.33(18)

O(3)-N(2)-C(15)-C(14)	4.0(3)
O(4)-N(2)-C(15)-C(14)	-177.0(2)
O(3)-N(2)-C(15)-C(16)	-174.9(2)
O(4)-N(2)-C(15)-C(16)	4.2(3)
C(14)-C(15)-C(16)-C(17)	-0.1(3)
N(2)-C(15)-C(16)-C(17)	178.64(19)
C(15)-C(16)-C(17)-C(18)	1.0(3)
C(15)-C(16)-C(17)-N(3)	-178.9(2)
O(5)-N(3)-C(17)-C(16)	-5.2(3)
O(6)-N(3)-C(17)-C(16)	173.2(2)
O(5)-N(3)-C(17)-C(18)	174.8(2)
O(6)-N(3)-C(17)-C(18)	-6.7(3)
C(16)-C(17)-C(18)-C(13)	-1.2(3)
N(3)-C(17)-C(18)-C(13)	178.72(18)
C(14)-C(13)-C(18)-C(17)	0.5(3)
C(12)-C(13)-C(18)-C(17)	-176.0(2)
C(24)-C(19)-C(20)-C(21)	-0.8(3)
C(19)-C(20)-C(21)-C(22)	-0.7(3)
C(20)-C(21)-C(22)-C(23)	0.7(3)
C(21)-C(22)-C(23)-C(24)	0.8(3)
C(25)-N(4)-C(24)-C(19)	-3.0(4)
C(25)-N(4)-C(24)-C(23)	179.0(2)
C(20)-C(19)-C(24)-N(4)	-175.9(2)
C(20)-C(19)-C(24)-C(23)	2.1(3)
C(22)-C(23)-C(24)-N(4)	176.0(2)
C(22)-C(23)-C(24)-C(19)	-2.1(3)
C(24)-N(4)-C(25)-C(29)	-77.4(3)
C(24)-N(4)-C(25)-C(26)	169.6(2)
N(4)-C(25)-C(26)-C(27)	90.0(2)
C(29)-C(25)-C(26)-C(27)	-27.6(2)
C(25)-C(26)-C(27)-C(28)	4.3(3)
C(26)-C(27)-C(28)-C(29)	21.1(2)
C(30)-O(7)-C(29)-C(28)	167.67(17)
C(30)-O(7)-C(29)-C(25)	-82.2(2)
C(27)-C(28)-C(29)-O(7)	75.1(2)
C(27)-C(28)-C(29)-C(25)	-38.5(2)

N(4)-C(25)-C(29)-O(7)	171.75(16)
C(26)-C(25)-C(29)-O(7)	-70.6(2)
N(4)-C(25)-C(29)-C(28)	-76.8(2)
C(26)-C(25)-C(29)-C(28)	40.9(2)
C(29)-O(7)-C(30)-O(8)	-0.4(3)
C(29)-O(7)-C(30)-C(31)	-179.54(17)
O(8)-C(30)-C(31)-C(36)	-12.3(3)
O(7)-C(30)-C(31)-C(36)	166.79(17)
O(8)-C(30)-C(31)-C(32)	168.8(2)
O(7)-C(30)-C(31)-C(32)	-12.1(3)
C(36)-C(31)-C(32)-C(33)	-1.1(3)
C(30)-C(31)-C(32)-C(33)	177.79(19)
C(31)-C(32)-C(33)-C(34)	-1.1(3)
C(31)-C(32)-C(33)-N(5)	179.23(18)
O(10)-N(5)-C(33)-C(32)	173.9(2)
O(9)-N(5)-C(33)-C(32)	-6.8(3)
O(10)-N(5)-C(33)-C(34)	-5.8(3)
O(9)-N(5)-C(33)-C(34)	173.5(2)
C(32)-C(33)-C(34)-C(35)	2.1(3)
N(5)-C(33)-C(34)-C(35)	-178.27(18)
C(33)-C(34)-C(35)-C(36)	-0.9(3)
C(33)-C(34)-C(35)-N(6)	179.57(18)
O(11)-N(6)-C(35)-C(36)	-176.6(2)
O(12)-N(6)-C(35)-C(36)	3.3(3)
O(11)-N(6)-C(35)-C(34)	2.9(3)
O(12)-N(6)-C(35)-C(34)	-177.2(2)
C(34)-C(35)-C(36)-C(31)	-1.1(3)
N(6)-C(35)-C(36)-C(31)	178.38(17)
C(32)-C(31)-C(36)-C(35)	2.1(3)
C(30)-C(31)-C(36)-C(35)	-176.77(18)

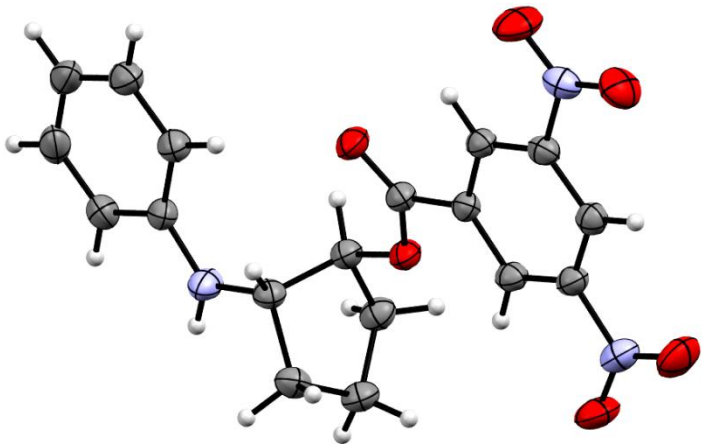
Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for C18H17N3O6 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1^a)-H(1N^a)...O(3)#1	0.95(4)	2.55(4)	3.390(3)	147(3)
N(4)-H(4N)...O(9)#2	0.90(3)	2.31(3)	3.188(2)	166(3)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y+1/2,-z+1 #2 -x+1,y-1/2,-z



3-D Ortep figure of Compound SI-5 ($C_{18}H_{17}N_3O_6$) (50% ellipsoid contour probability level)

X-ray 4: Compound **SI-6**, CCDC Deposition Number 2164935

Table 1. Crystal data and structure refinement for C19H19N3O6.

Identification code	C19H19N3O6	
Empirical formula	C19 H19 N3 O6	
Formula weight	385.37	
Temperature	173(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$Pna2_1$	
Unit cell dimensions	a = 10.5762(7) Å	α= 90°.
	b = 20.5110(15) Å	β= 90°.
	c = 8.2915(6) Å	γ = 90°.
Volume	1798.7(2) $Å^3$	
Z	4	
Density (calculated)	1.423 Mg/m^3	
Absorption coefficient	0.904 mm^{-1}	
F(000)	808	
Crystal size	0.220 x 0.080 x 0.060 mm^3	
Theta range for data collection	4.311 to 66.635°.	
Index ranges	-12<=h<=12, -24<=k<=24, -9<=l<=9	
Reflections collected	17472	
Independent reflections	3123 [R(int) = 0.0890]	
Completeness to theta = 66.635°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7528 and 0.6010	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3123 / 1 / 257	
Goodness-of-fit on F^2	1.069	
Final R indices [I>2sigma(I)]	R1 = 0.0476, wR2 = 0.1064	
R indices (all data)	R1 = 0.0600, wR2 = 0.1153	
Absolute structure parameter	-0.3(2)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.251 and -0.167 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for C19H19N3O6. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	8647(4)	7335(2)	1450(5)	67(1)
O(2)	10269(4)	6738(2)	2027(5)	67(1)
O(3)	9817(3)	4963(2)	5751(5)	61(1)
O(4)	8129(4)	4873(2)	7182(5)	70(1)
O(5)	4874(3)	7250(2)	4825(4)	51(1)
O(6)	4517(2)	6306(1)	6150(4)	38(1)
N(1)	9167(4)	6902(2)	2216(5)	49(1)
N(2)	8752(3)	5143(2)	6148(5)	48(1)
N(3)	2412(4)	5330(2)	7172(6)	51(1)
C(1)	7221(4)	6788(2)	3801(6)	39(1)
C(2)	8420(4)	6561(2)	3450(5)	41(1)
C(3)	8951(4)	6028(2)	4187(6)	42(1)
C(4)	8216(4)	5716(2)	5329(5)	38(1)
C(5)	7005(4)	5915(2)	5720(5)	38(1)
C(6)	6508(4)	6459(2)	4954(5)	38(1)
C(7)	5215(4)	6721(2)	5287(5)	38(1)
C(8)	3203(4)	6482(2)	6548(6)	39(1)
C(9)	3085(5)	7112(2)	7496(6)	47(1)
C(10)	1844(5)	7034(2)	8440(7)	55(1)
C(11)	1614(5)	6297(3)	8568(8)	61(1)
C(12)	2748(4)	5966(2)	7764(6)	44(1)
C(13)	3276(4)	4847(2)	6722(6)	46(1)
C(14)	2877(5)	4377(2)	5627(7)	56(1)
C(15)	3621(7)	3856(3)	5231(8)	69(2)
C(16)	4807(7)	3783(3)	5914(9)	78(2)
C(17)	5224(5)	4250(3)	6965(8)	70(2)
C(18)	4467(5)	4789(2)	7392(7)	53(1)
C(19)	2423(4)	6471(2)	5004(6)	48(1)

Table 3. Bond lengths [Å] and angles [°] for C19H19N3O6.

O(1)-N(1)	1.221(5)
O(2)-N(1)	1.224(5)
O(3)-N(2)	1.230(5)
O(4)-N(2)	1.216(5)
O(5)-C(7)	1.205(5)
O(6)-C(7)	1.334(5)
O(6)-C(8)	1.473(5)
N(1)-C(2)	1.470(6)
N(2)-C(4)	1.472(6)
N(3)-C(13)	1.398(6)
N(3)-C(12)	1.438(6)
N(3)-H(3N)	0.98(5)
C(1)-C(2)	1.382(6)
C(1)-C(6)	1.392(6)
C(1)-H(1)	0.9500
C(2)-C(3)	1.373(6)
C(3)-C(4)	1.382(6)
C(3)-H(3)	0.9500
C(4)-C(5)	1.382(6)
C(5)-C(6)	1.388(6)
C(5)-H(5)	0.9500
C(6)-C(7)	1.495(6)
C(8)-C(9)	1.518(6)
C(8)-C(19)	1.523(6)
C(8)-C(12)	1.539(6)
C(9)-C(10)	1.537(7)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(10)-C(11)	1.534(7)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(11)-C(12)	1.531(7)
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900

C(12)-H(12)	1.0000
C(13)-C(18)	1.381(7)
C(13)-C(14)	1.390(7)
C(14)-C(15)	1.367(8)
C(14)-H(14)	0.9500
C(15)-C(16)	1.385(10)
C(15)-H(15)	0.9500
C(16)-C(17)	1.367(10)
C(16)-H(16)	0.9500
C(17)-C(18)	1.412(8)
C(17)-H(17)	0.9500
C(18)-H(18)	0.9500
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800

C(7)-O(6)-C(8)	119.1(3)
O(1)-N(1)-O(2)	124.3(4)
O(1)-N(1)-C(2)	117.8(4)
O(2)-N(1)-C(2)	118.0(4)
O(4)-N(2)-O(3)	123.3(4)
O(4)-N(2)-C(4)	118.7(4)
O(3)-N(2)-C(4)	118.0(4)
C(13)-N(3)-C(12)	124.9(4)
C(13)-N(3)-H(3N)	117(3)
C(12)-N(3)-H(3N)	113(3)
C(2)-C(1)-C(6)	118.6(4)
C(2)-C(1)-H(1)	120.7
C(6)-C(1)-H(1)	120.7
C(3)-C(2)-C(1)	123.3(4)
C(3)-C(2)-N(1)	118.0(4)
C(1)-C(2)-N(1)	118.7(4)
C(2)-C(3)-C(4)	116.3(4)
C(2)-C(3)-H(3)	121.8
C(4)-C(3)-H(3)	121.8
C(3)-C(4)-C(5)	123.1(4)

C(3)-C(4)-N(2)	117.9(4)
C(5)-C(4)-N(2)	119.0(4)
C(4)-C(5)-C(6)	118.7(4)
C(4)-C(5)-H(5)	120.6
C(6)-C(5)-H(5)	120.6
C(5)-C(6)-C(1)	119.9(4)
C(5)-C(6)-C(7)	123.5(4)
C(1)-C(6)-C(7)	116.6(4)
O(5)-C(7)-O(6)	125.4(4)
O(5)-C(7)-C(6)	122.6(4)
O(6)-C(7)-C(6)	112.1(4)
O(6)-C(8)-C(9)	113.7(4)
O(6)-C(8)-C(19)	108.6(4)
C(9)-C(8)-C(19)	113.8(4)
O(6)-C(8)-C(12)	105.9(3)
C(9)-C(8)-C(12)	102.8(4)
C(19)-C(8)-C(12)	111.8(4)
C(8)-C(9)-C(10)	104.2(4)
C(8)-C(9)-H(9A)	110.9
C(10)-C(9)-H(9A)	110.9
C(8)-C(9)-H(9B)	110.9
C(10)-C(9)-H(9B)	110.9
H(9A)-C(9)-H(9B)	108.9
C(11)-C(10)-C(9)	105.8(4)
C(11)-C(10)-H(10A)	110.6
C(9)-C(10)-H(10A)	110.6
C(11)-C(10)-H(10B)	110.6
C(9)-C(10)-H(10B)	110.6
H(10A)-C(10)-H(10B)	108.7
C(12)-C(11)-C(10)	106.5(4)
C(12)-C(11)-H(11A)	110.4
C(10)-C(11)-H(11A)	110.4
C(12)-C(11)-H(11B)	110.4
C(10)-C(11)-H(11B)	110.4
H(11A)-C(11)-H(11B)	108.6
N(3)-C(12)-C(11)	111.0(4)

N(3)-C(12)-C(8)	118.5(4)
C(11)-C(12)-C(8)	103.0(4)
N(3)-C(12)-H(12)	108.0
C(11)-C(12)-H(12)	108.0
C(8)-C(12)-H(12)	108.0
C(18)-C(13)-C(14)	118.7(4)
C(18)-C(13)-N(3)	123.3(5)
C(14)-C(13)-N(3)	117.8(4)
C(15)-C(14)-C(13)	121.6(6)
C(15)-C(14)-H(14)	119.2
C(13)-C(14)-H(14)	119.2
C(14)-C(15)-C(16)	120.5(6)
C(14)-C(15)-H(15)	119.8
C(16)-C(15)-H(15)	119.8
C(17)-C(16)-C(15)	118.6(5)
C(17)-C(16)-H(16)	120.7
C(15)-C(16)-H(16)	120.7
C(16)-C(17)-C(18)	121.7(6)
C(16)-C(17)-H(17)	119.2
C(18)-C(17)-H(17)	119.2
C(13)-C(18)-C(17)	118.9(6)
C(13)-C(18)-H(18)	120.5
C(17)-C(18)-H(18)	120.5
C(8)-C(19)-H(19A)	109.5
C(8)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(8)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for C19H19N3O6. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	60(2)	80(3)	60(2)	23(2)	1(2)	-20(2)
O(2)	58(2)	72(2)	70(2)	-3(2)	29(2)	-9(2)
O(3)	29(2)	59(2)	96(3)	3(2)	-3(2)	4(2)
O(4)	53(2)	70(2)	85(3)	31(2)	12(2)	15(2)
O(5)	44(2)	43(2)	67(2)	15(2)	0(2)	5(2)
O(6)	26(1)	40(2)	48(2)	4(1)	4(1)	1(1)
N(1)	48(3)	59(3)	41(2)	-3(2)	6(2)	-16(2)
N(2)	30(2)	49(2)	65(3)	1(2)	-6(2)	1(2)
N(3)	33(2)	41(2)	78(3)	-6(2)	3(2)	-2(2)
C(1)	38(2)	38(2)	41(2)	0(2)	-5(2)	-9(2)
C(2)	39(2)	45(3)	38(2)	-5(2)	1(2)	-15(2)
C(3)	26(2)	52(3)	47(3)	-11(2)	1(2)	-9(2)
C(4)	27(2)	41(2)	44(3)	-3(2)	-5(2)	-4(2)
C(5)	31(2)	41(2)	42(2)	3(2)	-2(2)	-5(2)
C(6)	32(2)	41(2)	40(2)	0(2)	-3(2)	-7(2)
C(7)	31(2)	42(2)	42(2)	1(2)	1(2)	-4(2)
C(8)	28(2)	41(2)	48(3)	-1(2)	1(2)	4(2)
C(9)	47(3)	43(2)	51(3)	0(2)	-2(2)	0(2)
C(10)	51(3)	52(3)	63(3)	-5(3)	11(3)	3(2)
C(11)	56(3)	54(3)	74(4)	2(3)	25(3)	4(3)
C(12)	38(2)	38(2)	55(3)	0(2)	8(2)	-2(2)
C(13)	37(2)	41(2)	58(3)	8(2)	15(2)	1(2)
C(14)	56(3)	51(3)	62(3)	12(3)	10(3)	-1(2)
C(15)	96(5)	44(3)	68(4)	3(3)	28(4)	4(3)
C(16)	92(5)	52(3)	90(5)	24(4)	49(4)	28(4)
C(17)	47(3)	78(4)	86(4)	40(4)	24(3)	19(3)
C(18)	44(3)	52(3)	64(3)	12(3)	8(3)	-2(2)
C(19)	38(2)	57(3)	49(3)	-3(2)	-3(2)	3(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{-3}) for C19H19N3O6.

	x	y	z	U(eq)
H(3N)	1580(50)	5320(20)	6650(60)	50(13)
H(1)	6890	7160	3267	47
H(3)	9777	5881	3926	50
H(5)	6523	5683	6498	46
H(9A)	3044	7492	6763	56
H(9B)	3810	7168	8238	56
H(10A)	1921	7231	9526	66
H(10B)	1138	7248	7862	66
H(11A)	1549	6164	9712	74
H(11B)	820	6176	8010	74
H(12)	3422	5910	8598	52
H(14)	2067	4419	5142	68
H(15)	3322	3542	4481	83
H(16)	5320	3418	5657	94
H(17)	6045	4209	7420	84
H(18)	4771	5108	8128	64
H(19A)	1545	6587	5252	72
H(19B)	2772	6786	4235	72
H(19C)	2450	6033	4533	72

Table 6. Torsion angles [°] for C19H19N3O6.

C(6)-C(1)-C(2)-C(3)	-0.3(6)
C(6)-C(1)-C(2)-N(1)	179.1(4)
O(1)-N(1)-C(2)-C(3)	172.8(4)
O(2)-N(1)-C(2)-C(3)	-7.6(6)
O(1)-N(1)-C(2)-C(1)	-6.7(6)
O(2)-N(1)-C(2)-C(1)	173.0(4)
C(1)-C(2)-C(3)-C(4)	0.0(6)
N(1)-C(2)-C(3)-C(4)	-179.4(4)
C(2)-C(3)-C(4)-C(5)	0.7(6)
C(2)-C(3)-C(4)-N(2)	-179.9(4)
O(4)-N(2)-C(4)-C(3)	178.3(4)
O(3)-N(2)-C(4)-C(3)	-1.4(6)
O(4)-N(2)-C(4)-C(5)	-2.3(6)
O(3)-N(2)-C(4)-C(5)	178.0(4)
C(3)-C(4)-C(5)-C(6)	-1.2(6)
N(2)-C(4)-C(5)-C(6)	179.5(4)
C(4)-C(5)-C(6)-C(1)	0.9(6)
C(4)-C(5)-C(6)-C(7)	-179.6(4)
C(2)-C(1)-C(6)-C(5)	-0.2(6)
C(2)-C(1)-C(6)-C(7)	-179.8(4)
C(8)-O(6)-C(7)-O(5)	2.2(6)
C(8)-O(6)-C(7)-C(6)	-178.4(3)
C(5)-C(6)-C(7)-O(5)	167.3(4)
C(1)-C(6)-C(7)-O(5)	-13.1(6)
C(5)-C(6)-C(7)-O(6)	-12.2(6)
C(1)-C(6)-C(7)-O(6)	167.4(4)
C(7)-O(6)-C(8)-C(9)	-58.8(5)
C(7)-O(6)-C(8)-C(19)	69.0(5)
C(7)-O(6)-C(8)-C(12)	-170.8(4)
O(6)-C(8)-C(9)-C(10)	-153.7(4)
C(19)-C(8)-C(9)-C(10)	81.3(5)
C(12)-C(8)-C(9)-C(10)	-39.8(5)
C(8)-C(9)-C(10)-C(11)	23.2(6)
C(9)-C(10)-C(11)-C(12)	2.4(6)

C(13)-N(3)-C(12)-C(11)	-164.4(5)
C(13)-N(3)-C(12)-C(8)	76.7(6)
C(10)-C(11)-C(12)-N(3)	-154.4(5)
C(10)-C(11)-C(12)-C(8)	-26.5(6)
O(6)-C(8)-C(12)-N(3)	-76.6(5)
C(9)-C(8)-C(12)-N(3)	163.9(4)
C(19)-C(8)-C(12)-N(3)	41.5(5)
O(6)-C(8)-C(12)-C(11)	160.4(4)
C(9)-C(8)-C(12)-C(11)	40.9(5)
C(19)-C(8)-C(12)-C(11)	-81.4(5)
C(12)-N(3)-C(13)-C(18)	29.1(8)
C(12)-N(3)-C(13)-C(14)	-155.4(5)
C(18)-C(13)-C(14)-C(15)	1.5(7)
N(3)-C(13)-C(14)-C(15)	-174.2(5)
C(13)-C(14)-C(15)-C(16)	-0.2(8)
C(14)-C(15)-C(16)-C(17)	-1.2(9)
C(15)-C(16)-C(17)-C(18)	1.5(9)
C(14)-C(13)-C(18)-C(17)	-1.2(7)
N(3)-C(13)-C(18)-C(17)	174.2(5)
C(16)-C(17)-C(18)-C(13)	-0.2(8)

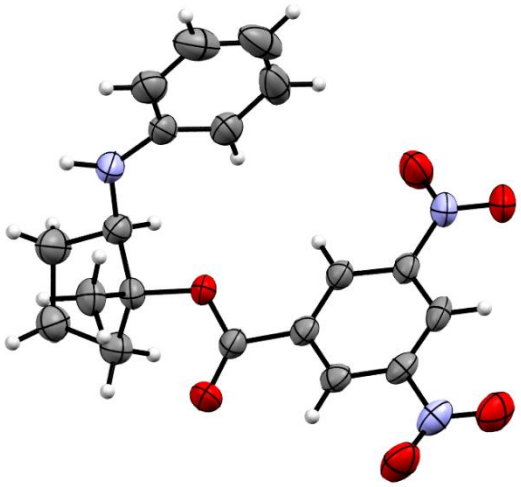
Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for C19H19N3O6 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(3)-H(3N)...O(3)#1	0.98(5)	2.14(5)	3.080(5)	160(4)

Symmetry transformations used to generate equivalent atoms:

#1 x-1,y,z

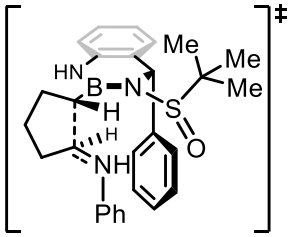


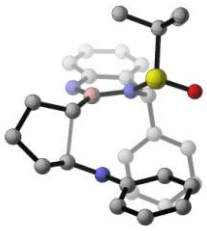
3-D Ortep figure of Compound SI-6 ($C_{19}H_{19}N_3O_6$) (50% ellipsoid contour probability level)

3.4.8. Computational Result for Scheme 3.31

All calculations were conducted using density functional theory (DFT) implemented in Gaussian 16 suite of program. All molecular structures were optimized by B3LYP-D3 functional with 6-31G* basis sets. Frequency calculations were performed at the same level of theory to characterize the stationary points (no imaginary frequencies for local minima), and transition states (single imaginary frequency).

Cartesian coordinates of computed structures





IEFPCM ($MeNO_2$)

0 3

S	0.10566800	-1.74365700	-1.13804900
O	-0.13114400	-1.19607200	-2.53773900
N	0.78164600	-0.50557500	-0.20005200
N	1.75144100	0.10535000	1.95280400
H	1.75670200	0.16112100	2.96388600
B	0.64358200	-0.50784400	1.26092400
C	2.86938300	0.63514500	1.32339700
C	4.02714300	0.99411500	2.04711700
H	4.03215300	0.87511200	3.12883300
C	5.15084900	1.48000100	1.38943900

H	6.03292200	1.74679000	1.96634900
C	5.15628200	1.61578400	-0.00812600
H	6.03880000	1.98080700	-0.52515200
C	4.00332200	1.28218100	-0.72510000
H	3.98065400	1.40974300	-1.80605100
C	2.85670800	0.80988300	-0.08665800
C	1.57803900	0.57060800	-0.86643800
H	1.83176500	0.23264400	-1.87226600
C	0.71114200	1.80378400	-1.01485500
C	0.32889100	2.57718300	0.10999300
H	0.77599900	2.37916200	1.07898300
C	-0.55032500	3.66027500	-0.04415100
H	-0.82151800	4.25359200	0.82623200
C	-1.08241900	3.97399700	-1.29348900
H	-1.77139900	4.80696000	-1.40306700
C	-0.72102800	3.19851400	-2.41136900
H	-1.13193500	3.42893500	-3.39086200
C	0.16702800	2.13300800	-2.26516900
H	0.42036800	1.51747300	-3.12445200
C	1.54202300	-2.97379000	-1.33924900
C	0.92459700	-4.13446200	-2.13200100
H	0.06814000	-4.57309200	-1.60560600
H	0.59258400	-3.80247600	-3.12067100

H	1.67444200	-4.92282100	-2.26729200
C	2.69498900	-2.33510300	-2.11078800
H	2.33320000	-1.88177200	-3.03926200
H	3.20407400	-1.57248000	-1.51401900
H	3.43093200	-3.10628500	-2.36973700
C	1.96529000	-3.41955500	0.06150900
H	1.11821500	-3.81235900	0.63664600
H	2.71127300	-4.21934100	-0.02524100
H	2.41143200	-2.59478700	0.62456200
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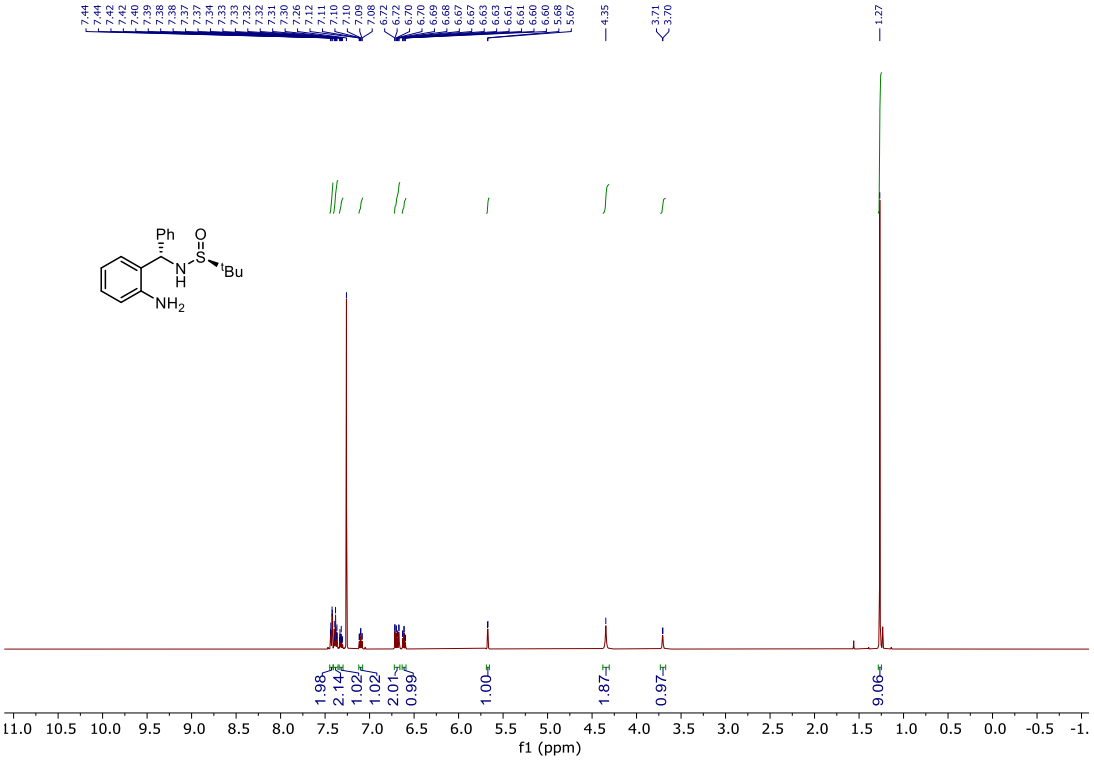
C	-0.59081300	-1.55175200	3.42894700
H	-1.28410700	-1.60849200	1.36220600
C	-1.86288500	-1.09029600	4.20598700
H	0.30991900	-1.22468500	3.95949200
H	-0.54270000	-2.64777100	3.38585000
C	-2.81795200	-0.42936900	3.19306200
H	-2.35323700	-1.91681000	4.72847400
H	-1.58170700	-0.35321400	4.96714900
H	-3.33321100	-1.19616400	2.60431400
H	-3.58509000	0.17705700	3.69153200
C	-1.90963400	0.37542400	2.30328700
C	-3.20213000	0.42397100	0.14630400
C	-2.86215400	0.39512100	-1.23946300

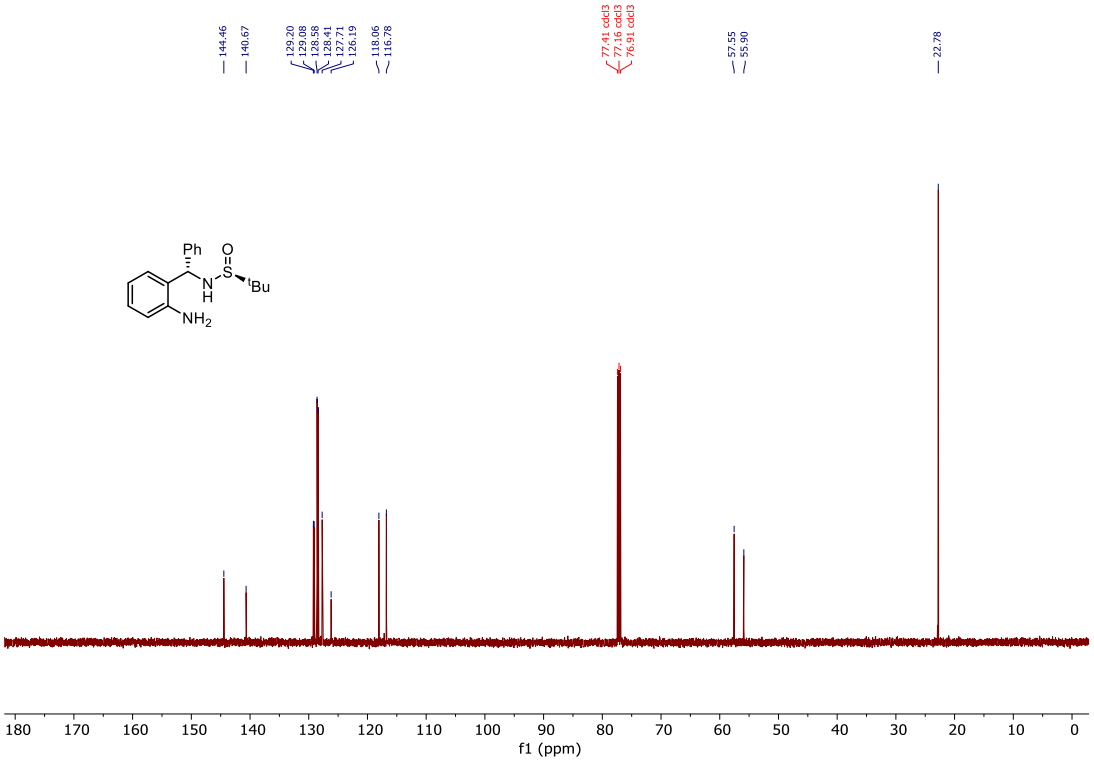
C	-4.53215200	0.11013200	0.54854100
C	-3.81206600	0.02113100	-2.17198700
H	-1.84567700	0.61540200	-1.54557300
C	-5.46819100	-0.24426900	-0.40678300
H	-4.81808400	0.19181400	1.58965000
C	-5.12167300	-0.30482800	-1.77211900
H	-3.53585300	-0.02583300	-3.22148300
H	-6.48446700	-0.47013100	-0.09705000
H	-5.86323100	-0.59450300	-2.50985100
H	-1.44178700	1.34098100	0.60788700
N	-2.22740300	0.82266100	1.03305400
H	-1.29294400	1.11330100	2.81931800

3.4.9. NMR Spectral Data

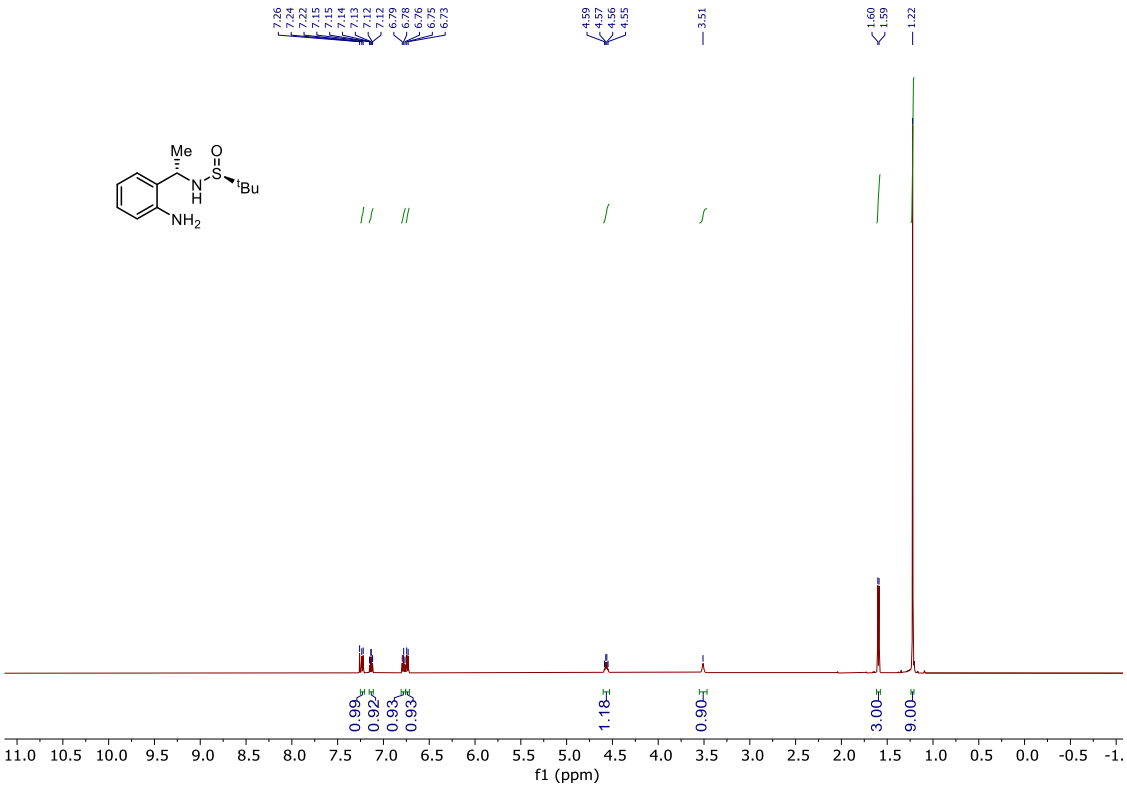
^{1}H NMR (500 MHz, $CDCl_3$) (**3.87**)



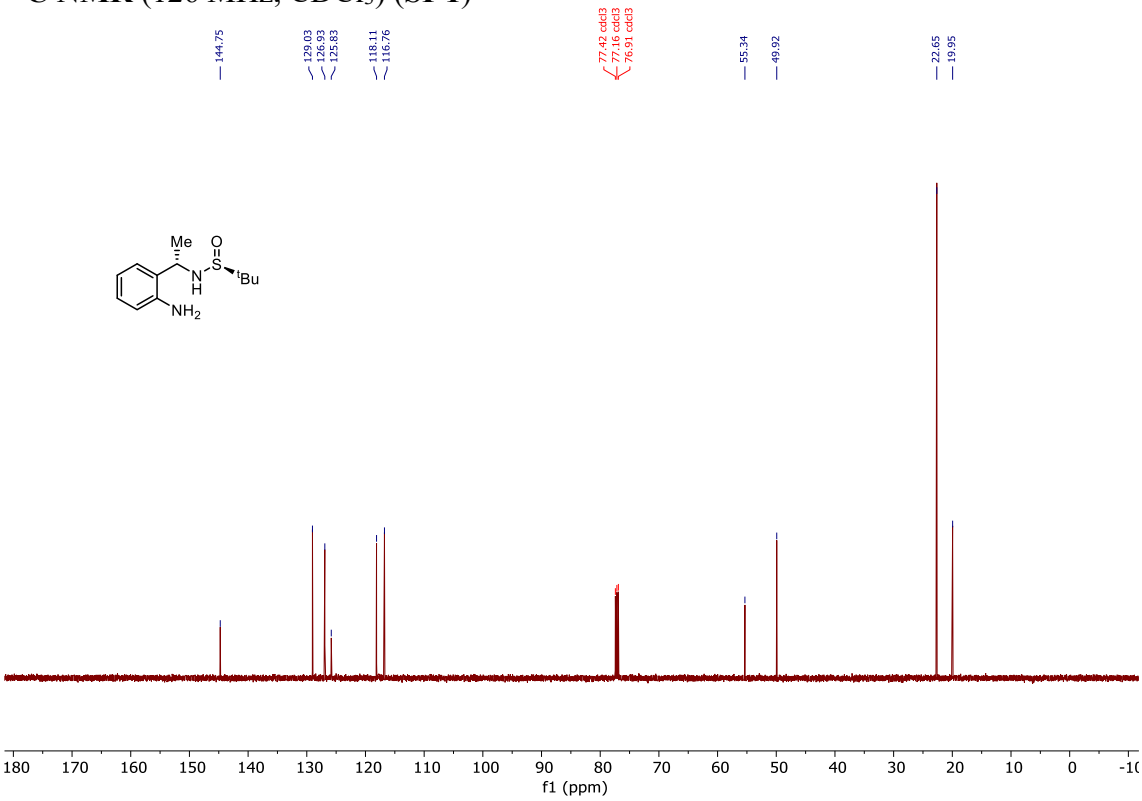
^{13}C NMR (126 MHz, $CDCl_3$) (**3.87**)



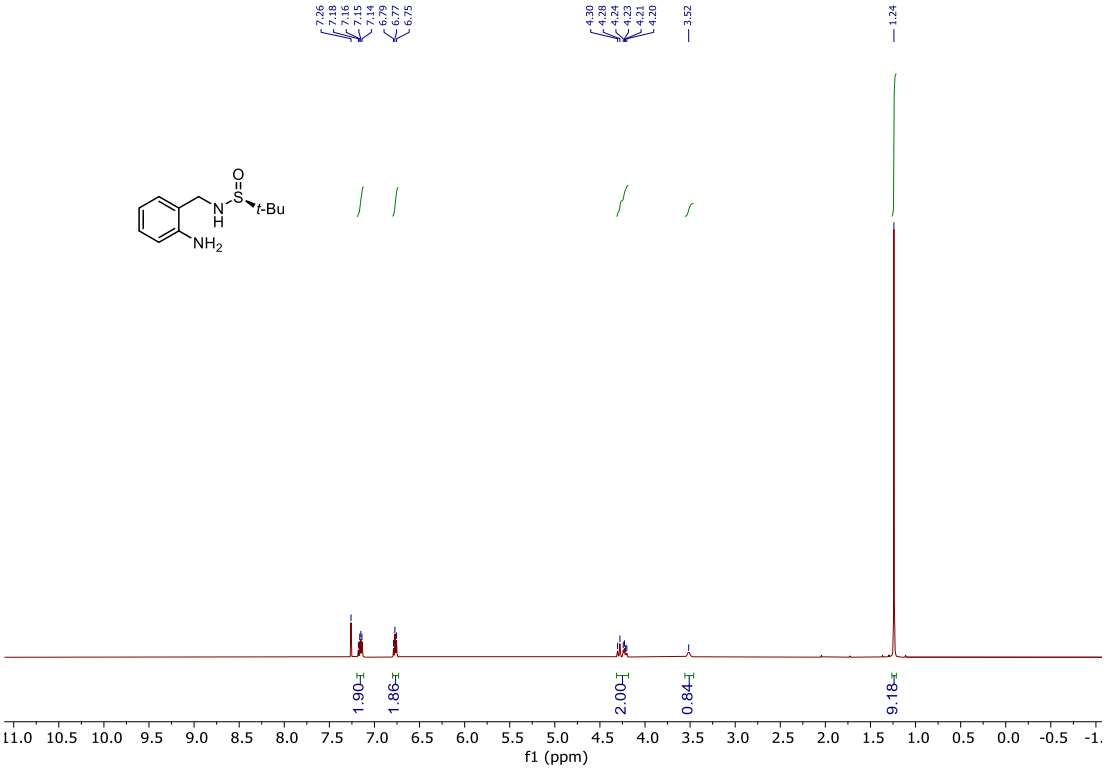
^{1}H NMR (500 MHz, $CDCl_3$) (**SI-1**)



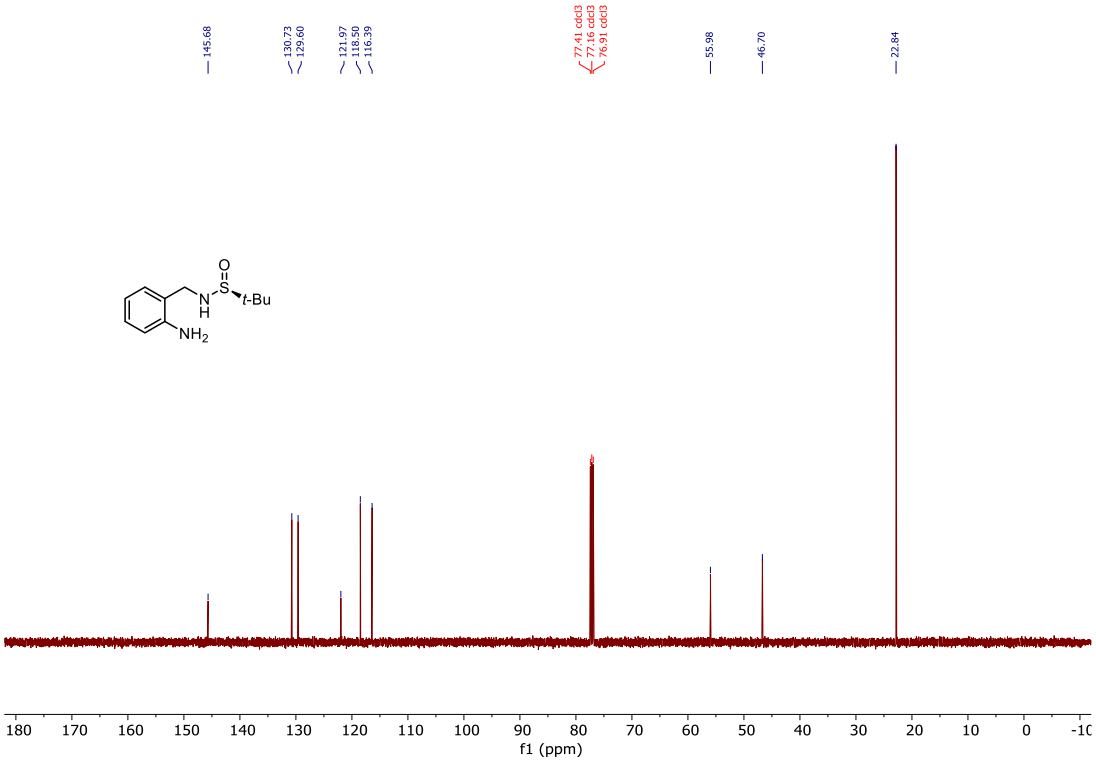
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-1**)



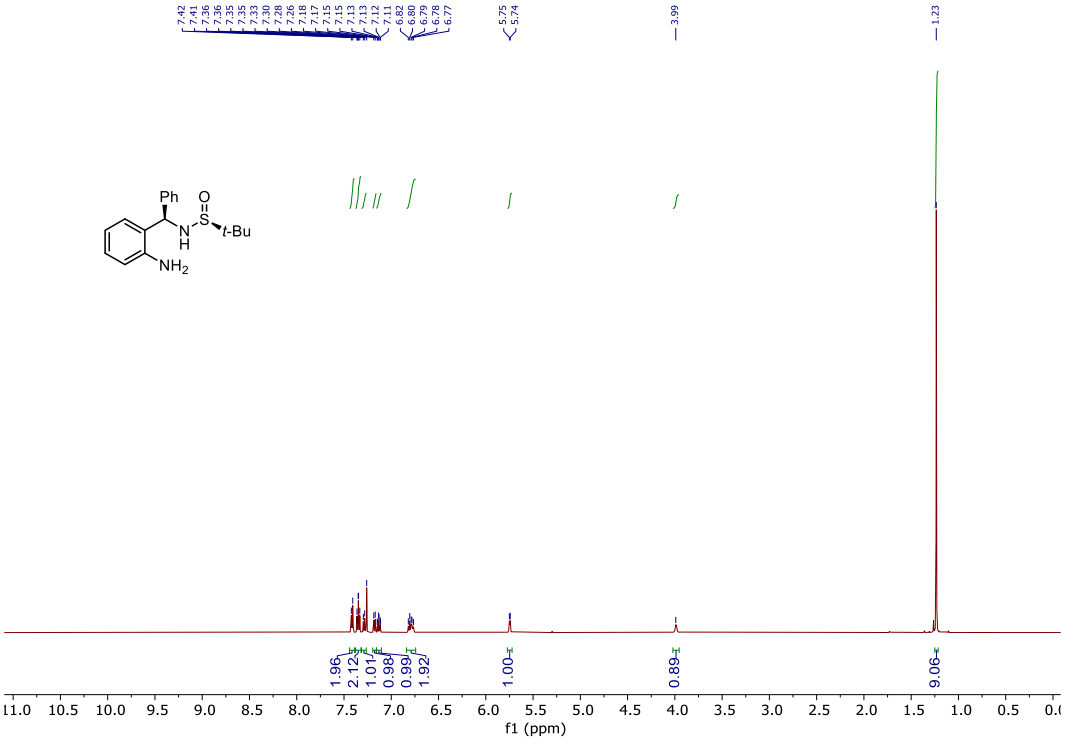
^{1}H NMR (500 MHz, $CDCl_3$) (**SI-2**)



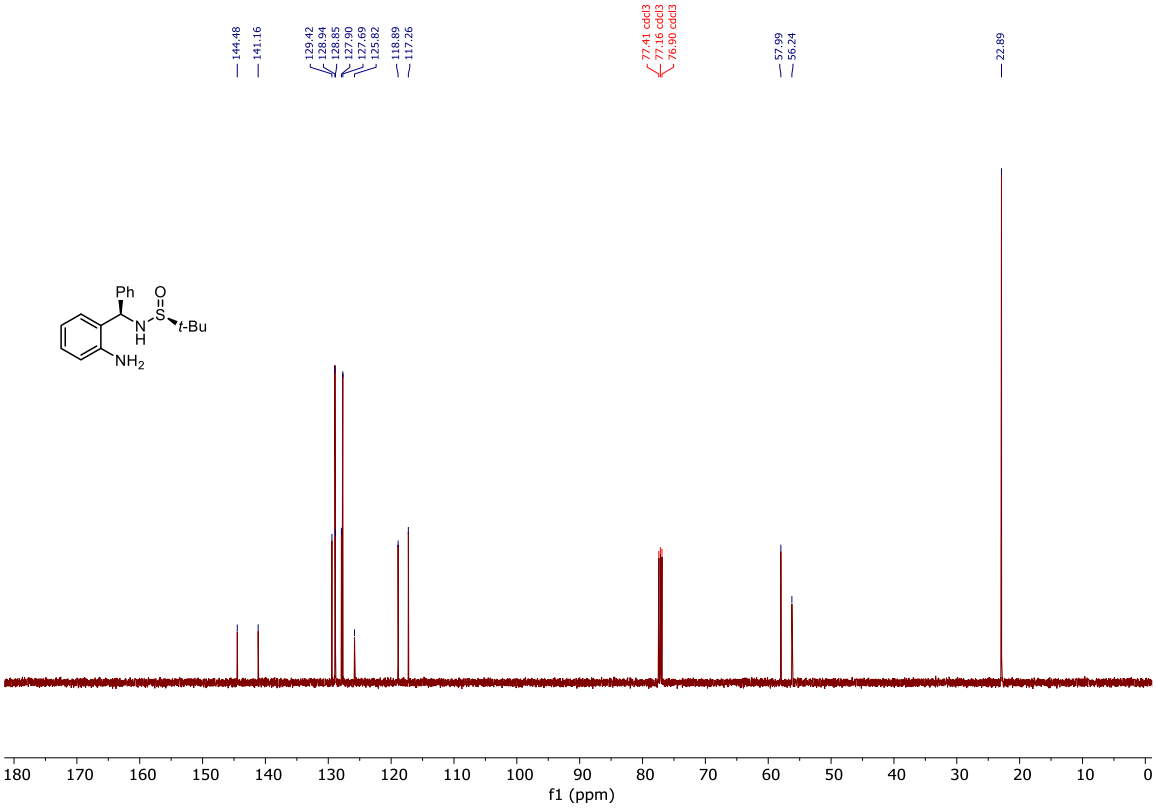
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-2**)



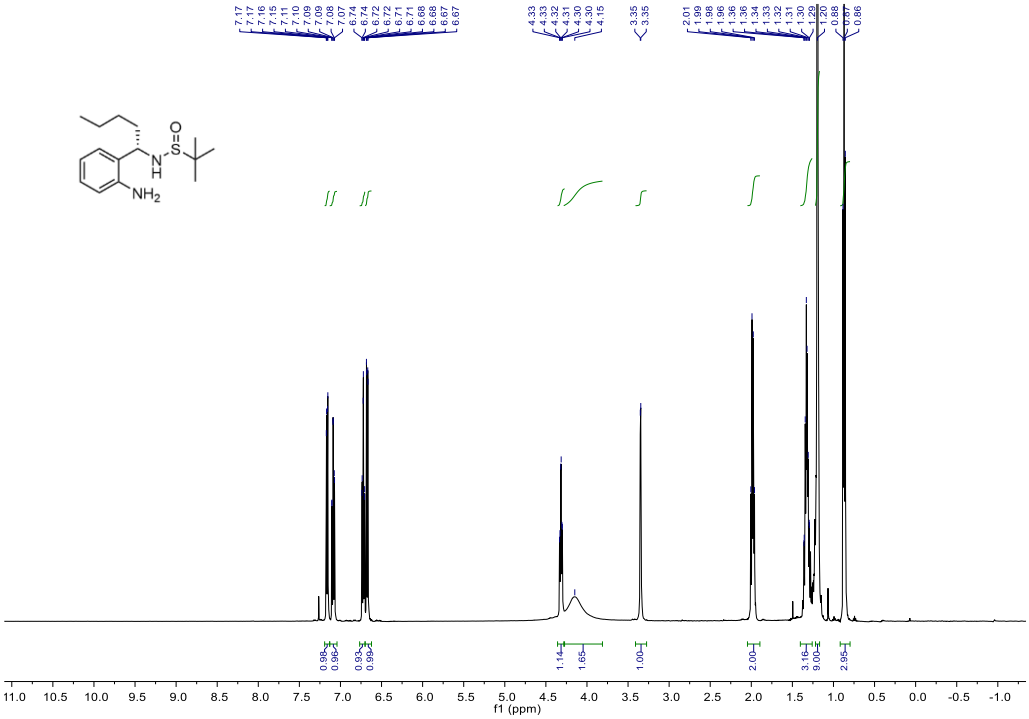
^{1}H NMR (500 MHz, $CDCl_3$) (**SI-3**)



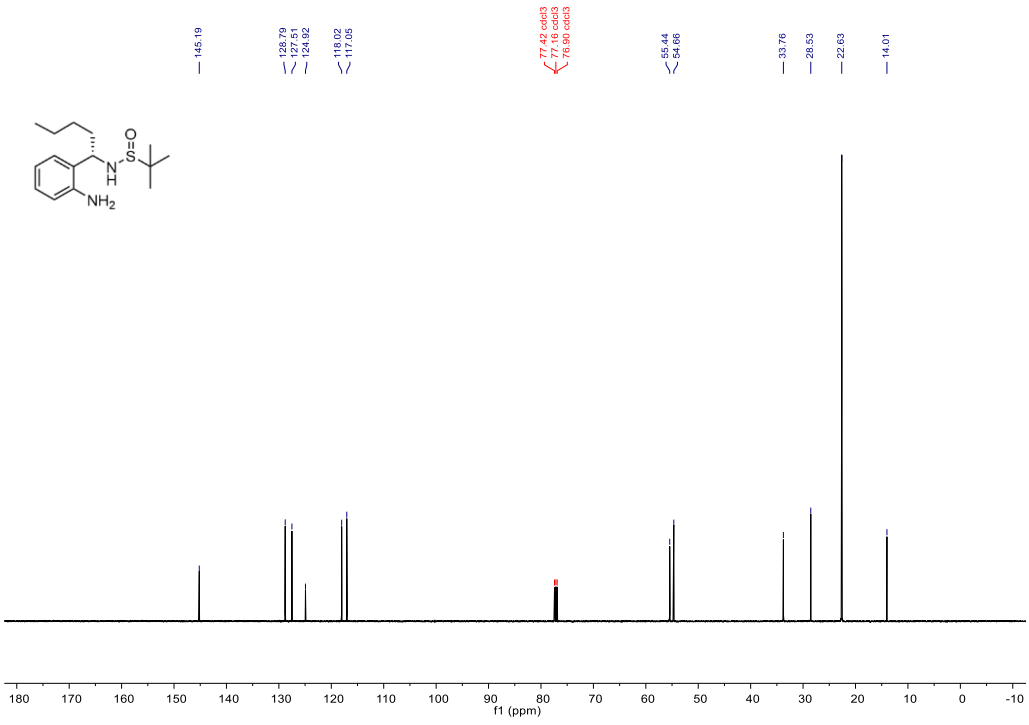
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-3**)



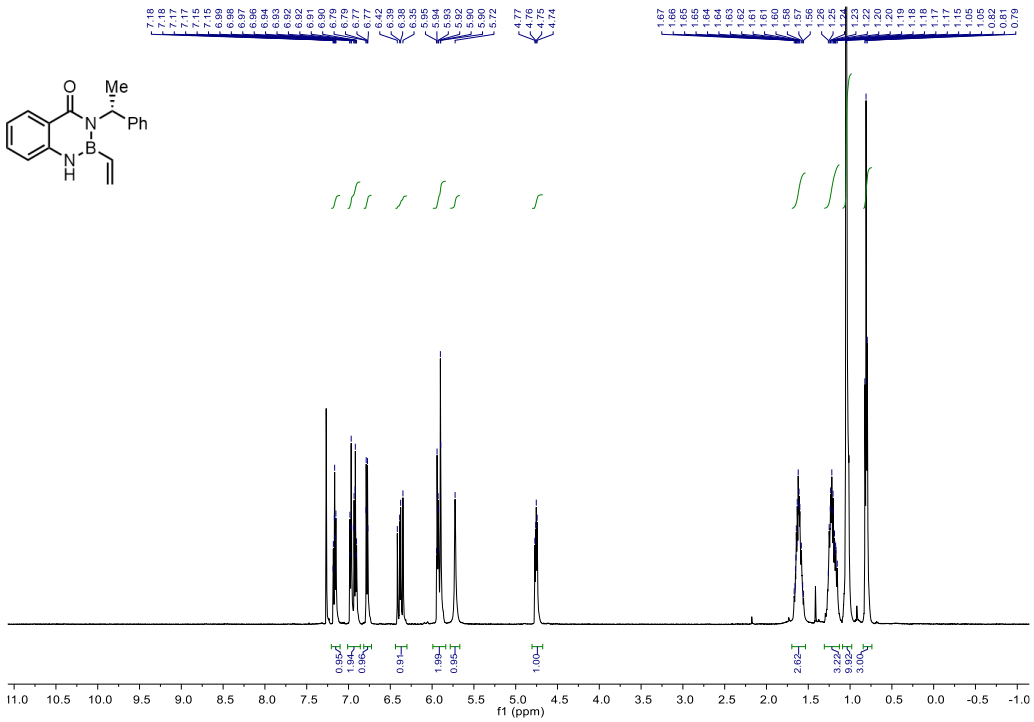
^{1}H NMR (500 MHz, $CDCl_3$) (**SI-4**)



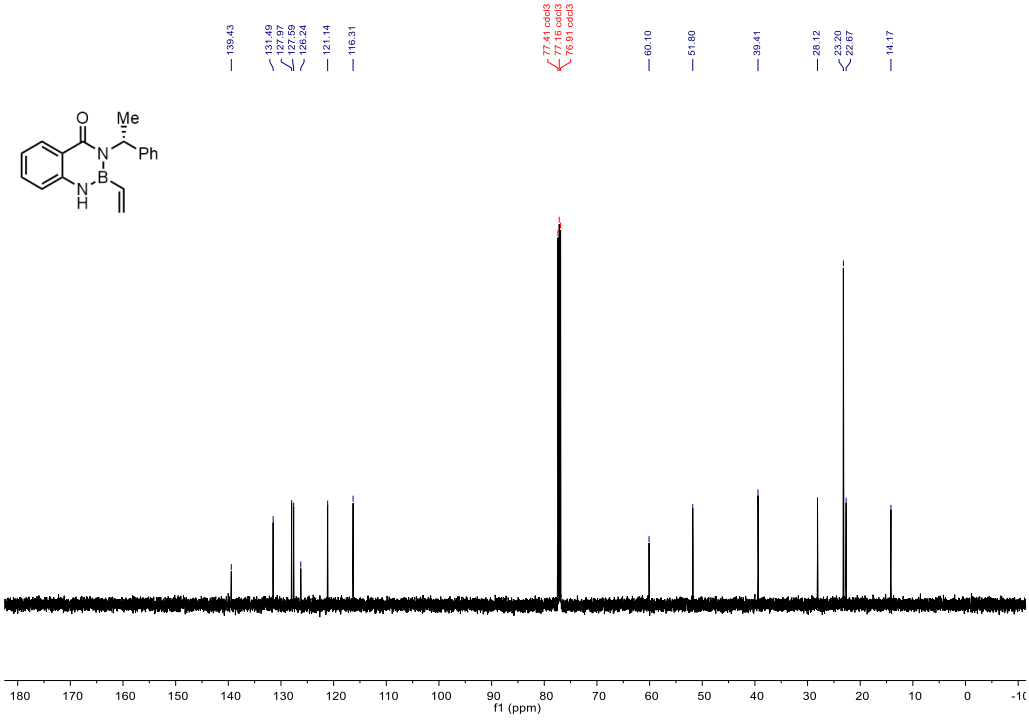
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-4**)



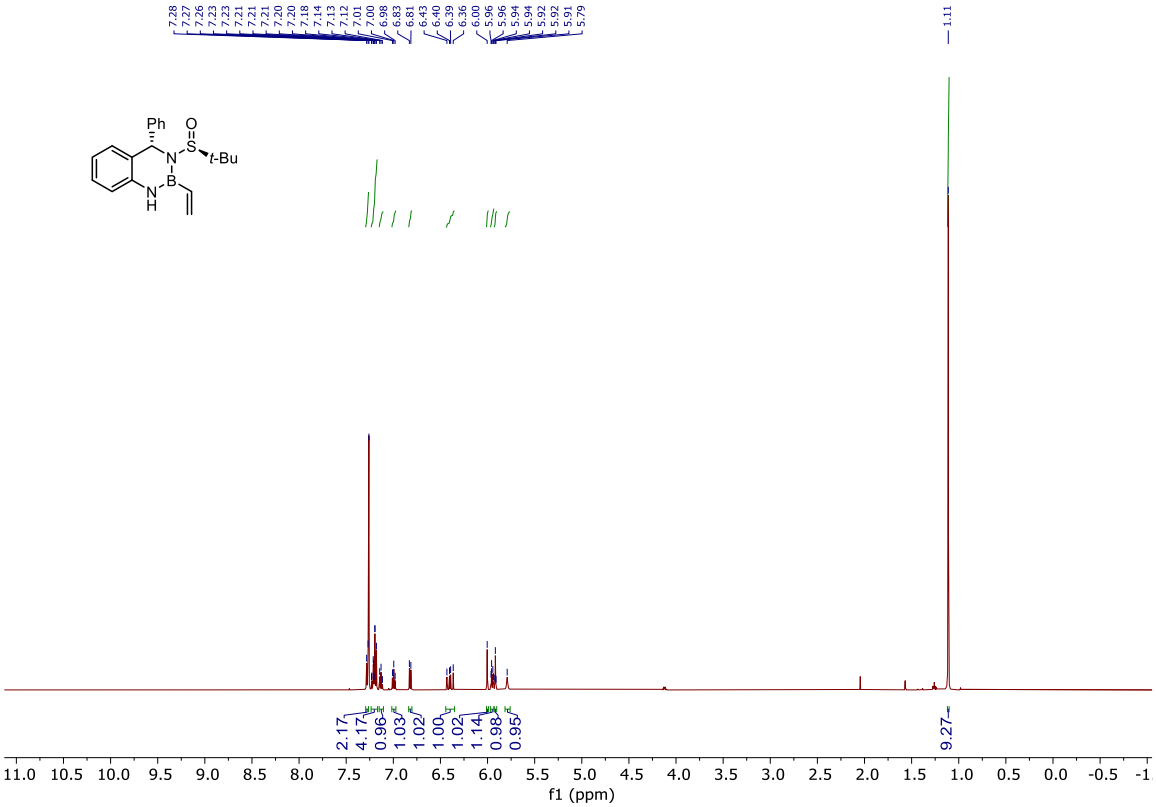
^{1}H NMR (500 MHz, $CDCl_3$) (**3.78**)



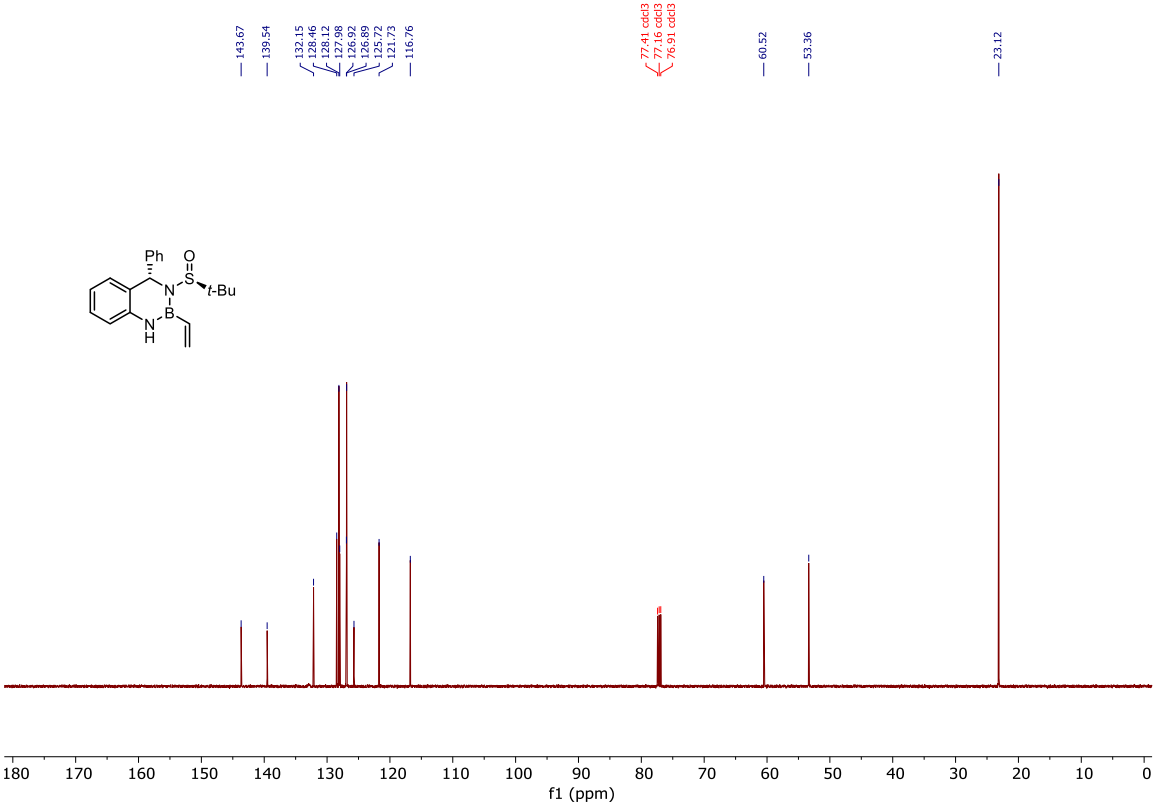
^{13}C NMR (126 MHz, $CDCl_3$) (**3.78**)



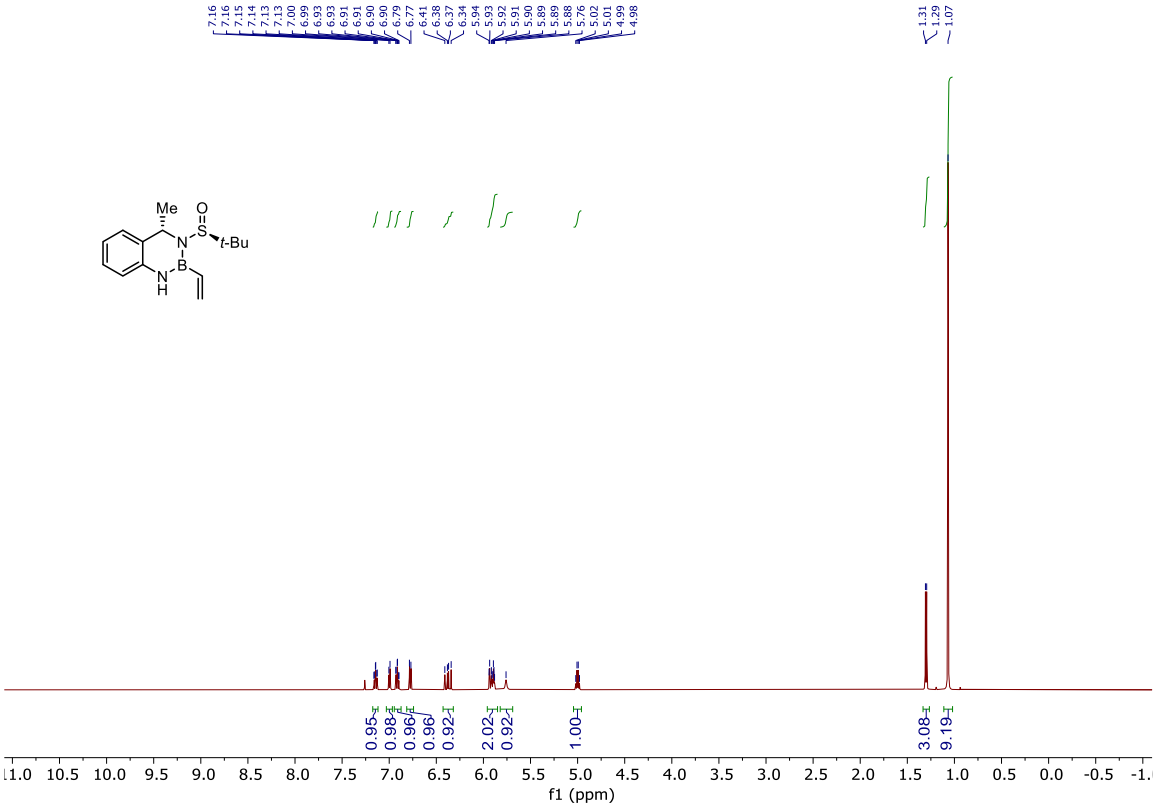
^{1}H NMR (500 MHz, $CDCl_3$) (**3.85**)



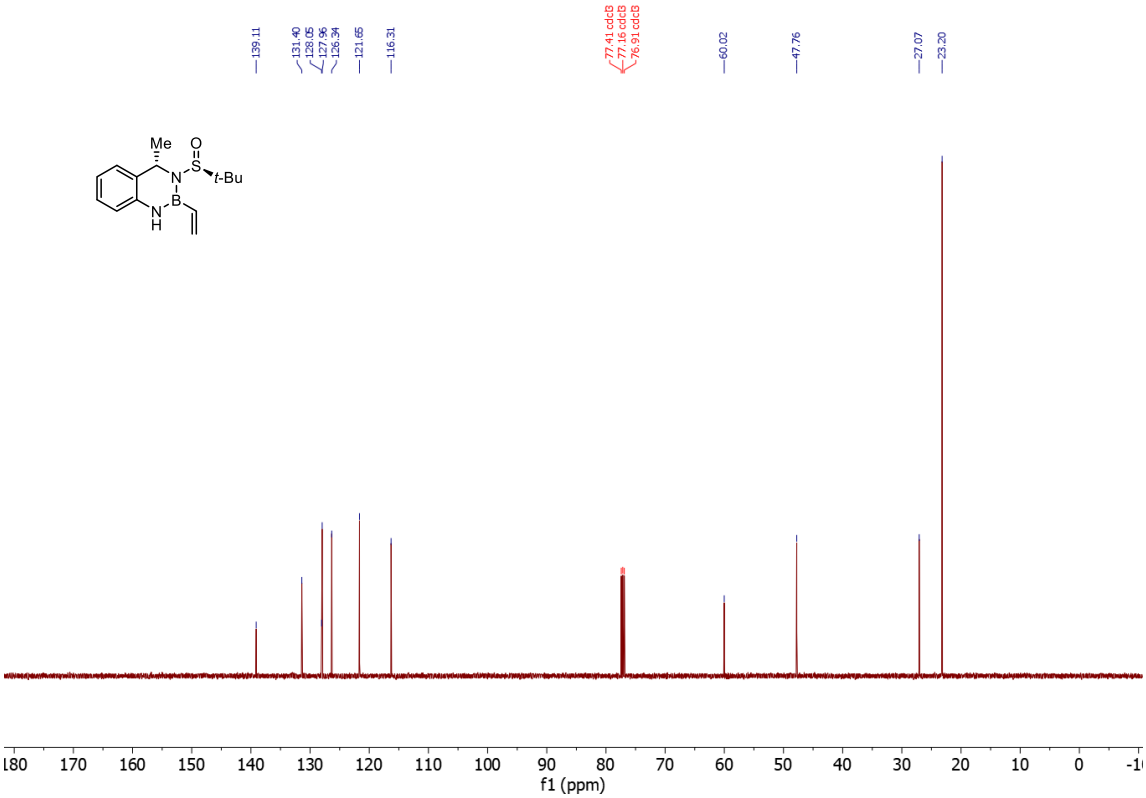
^{13}C NMR (126 MHz, $CDCl_3$) (**3.85**)



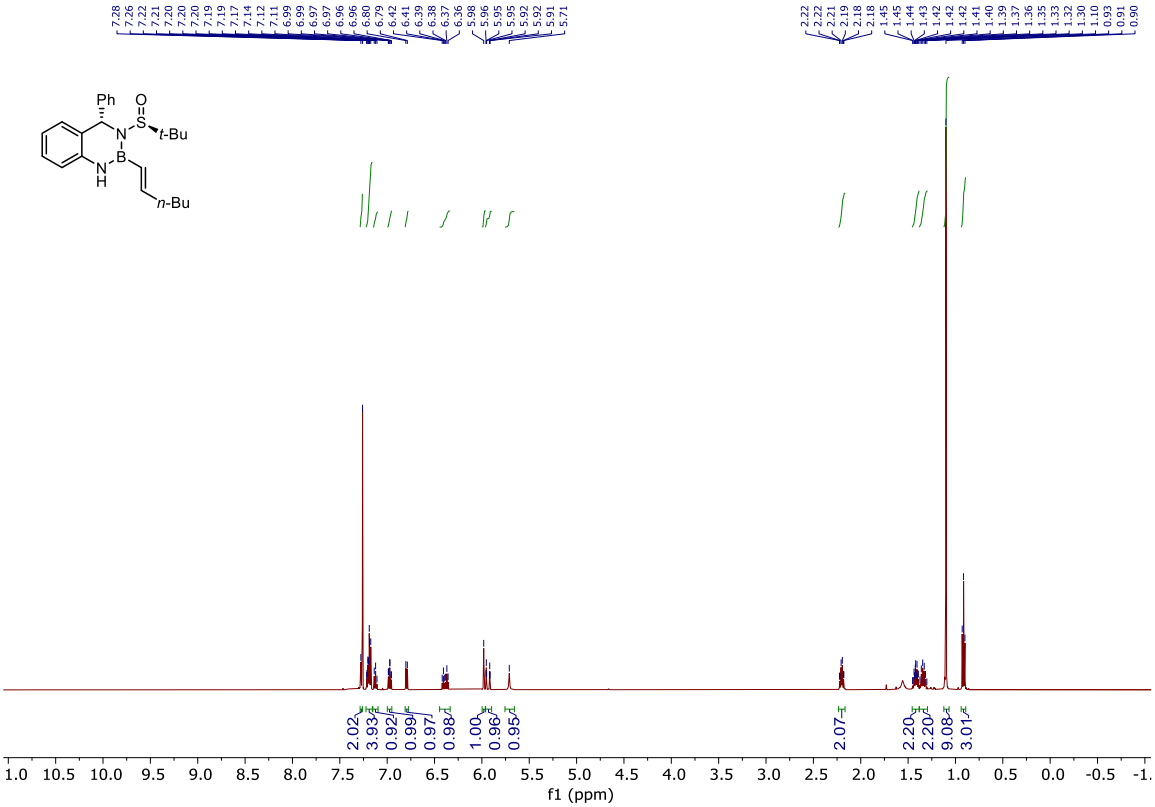
^{1}H NMR (500 MHz, $CDCl_3$) (**3.86**)



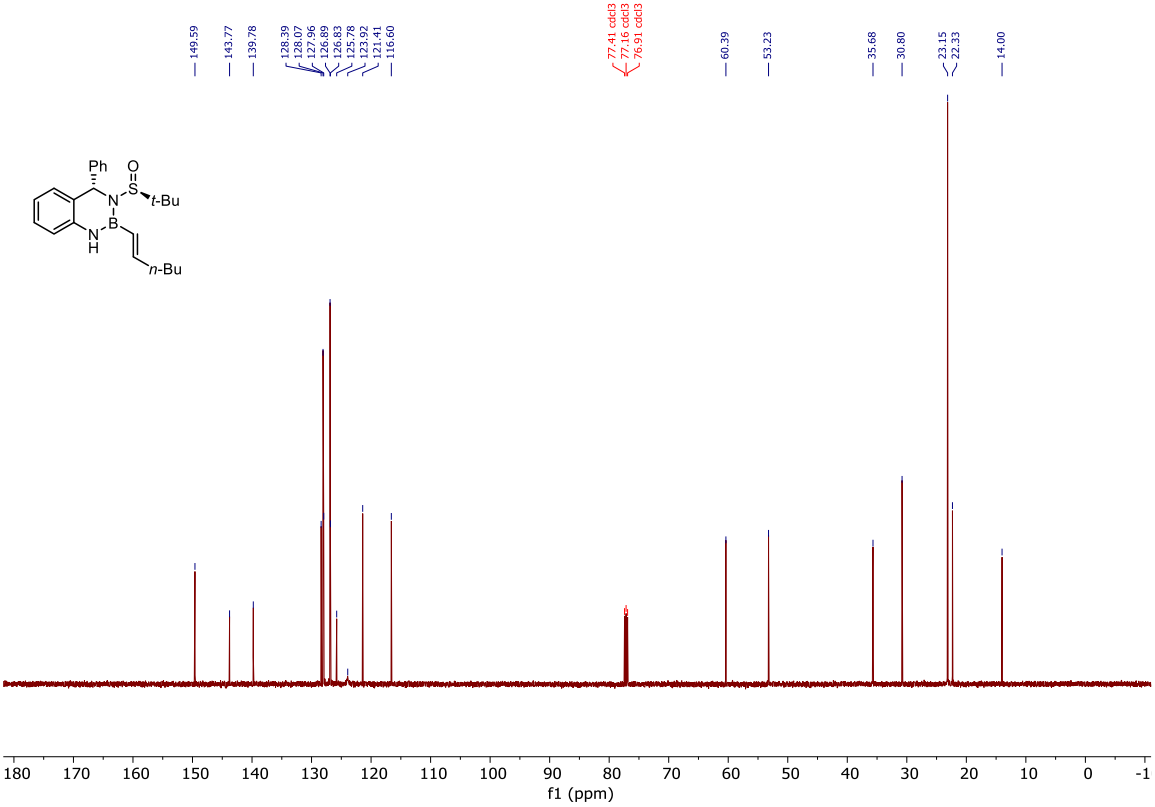
^{13}C NMR (126 MHz, $CDCl_3$) (**3.86**)



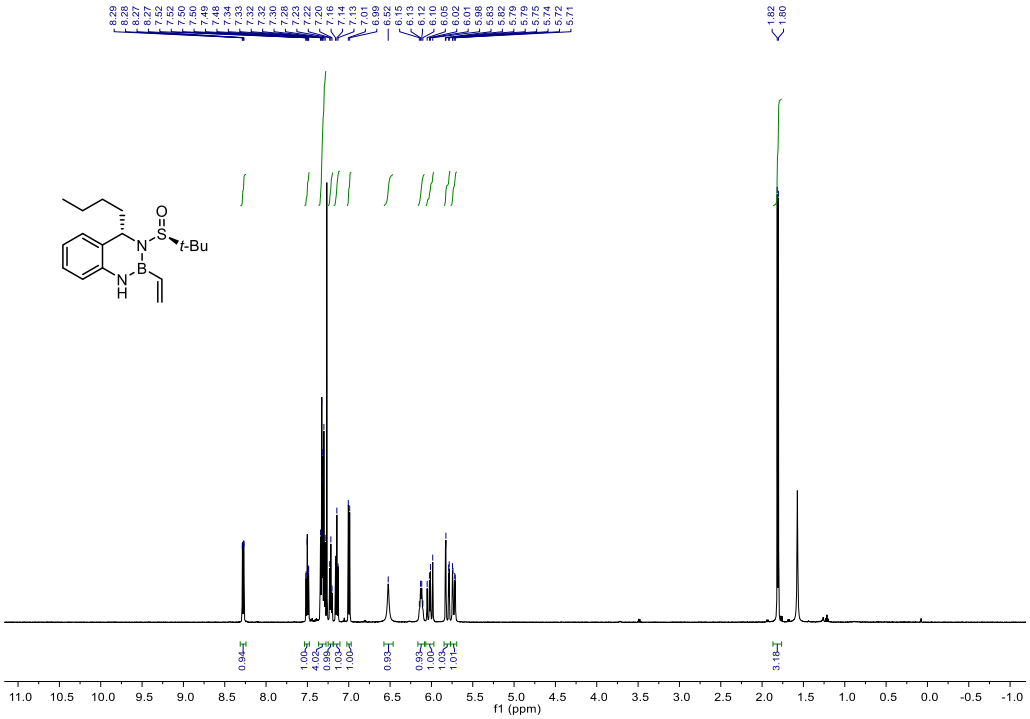
^{1}H NMR (500 MHz, $CDCl_3$) (**3.90**)



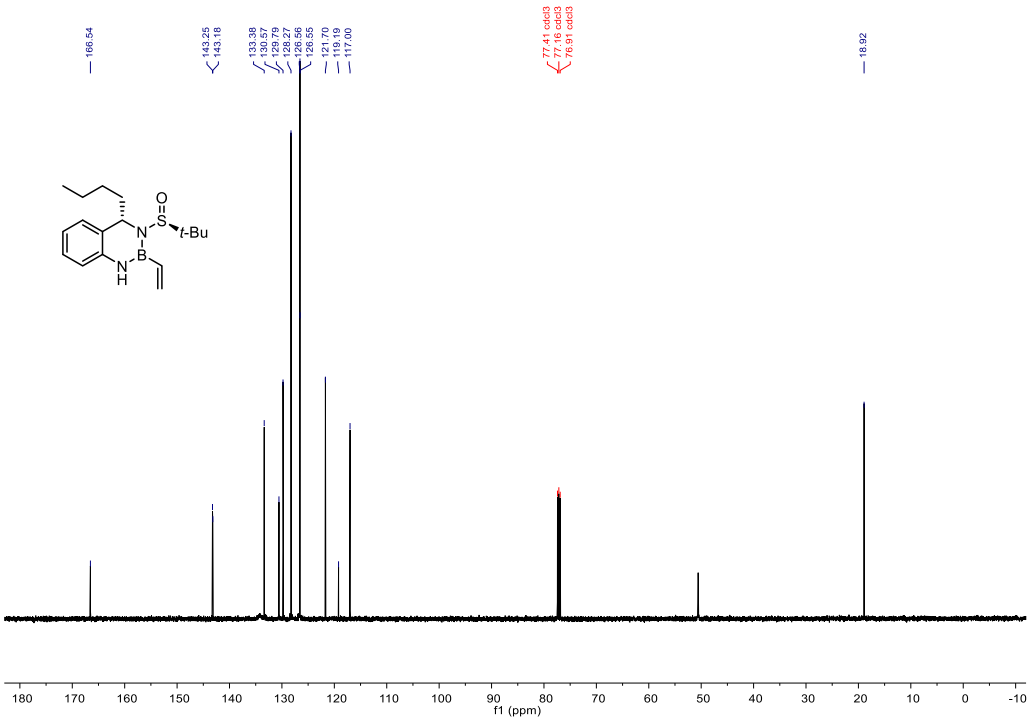
^{13}C NMR (126 MHz, $CDCl_3$) (**3.90**)



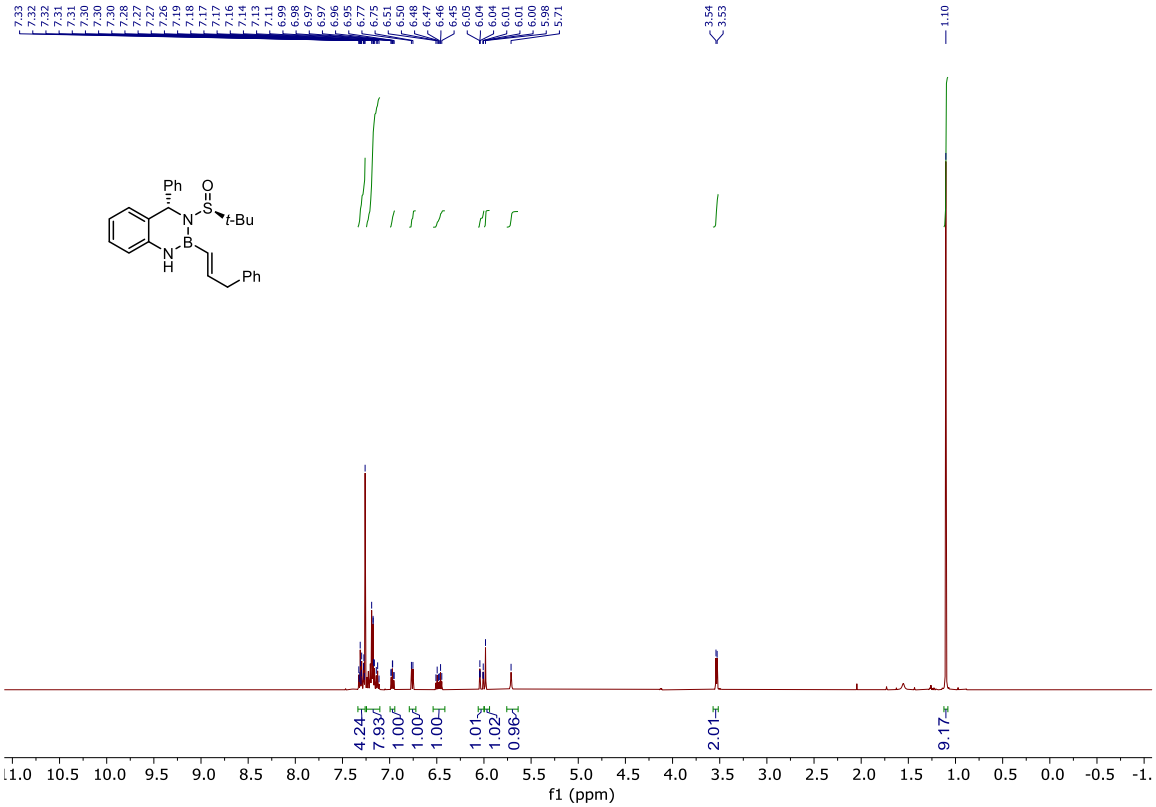
^{1}H NMR (500 MHz, $CDCl_3$) (**3.106**)



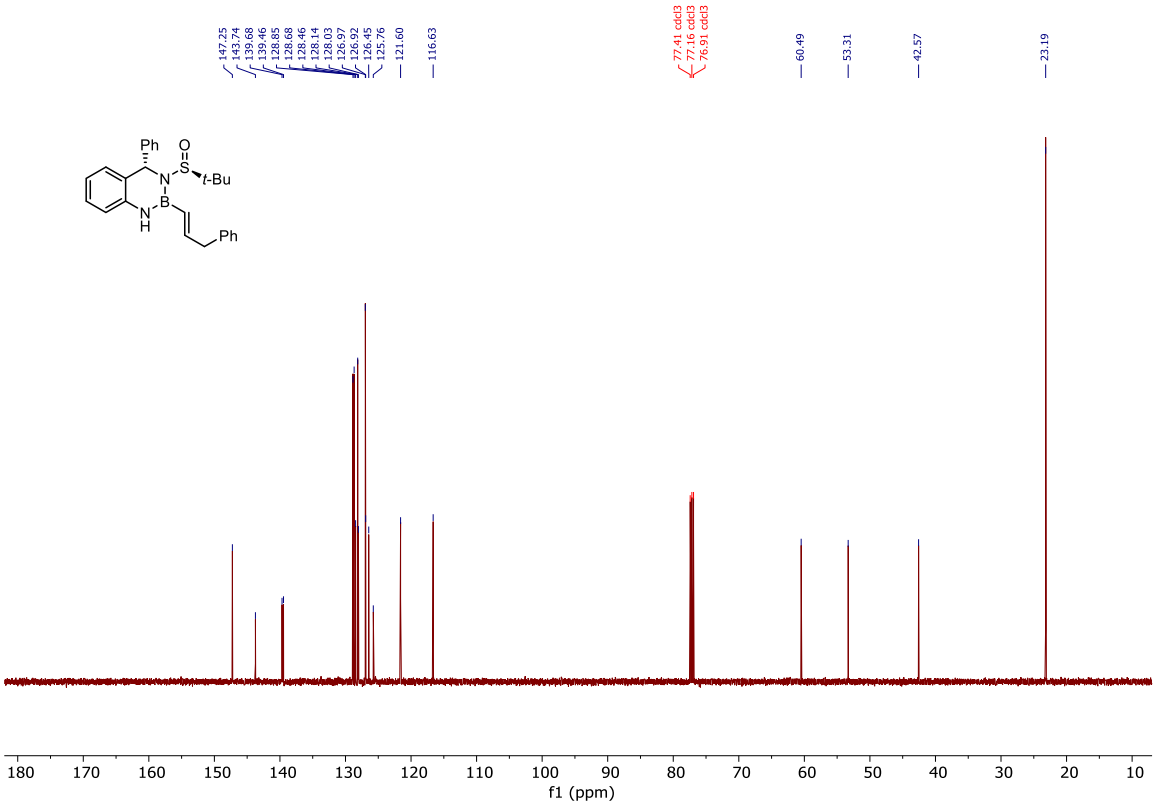
^{13}C NMR (126 MHz, $CDCl_3$) (**3.106**)



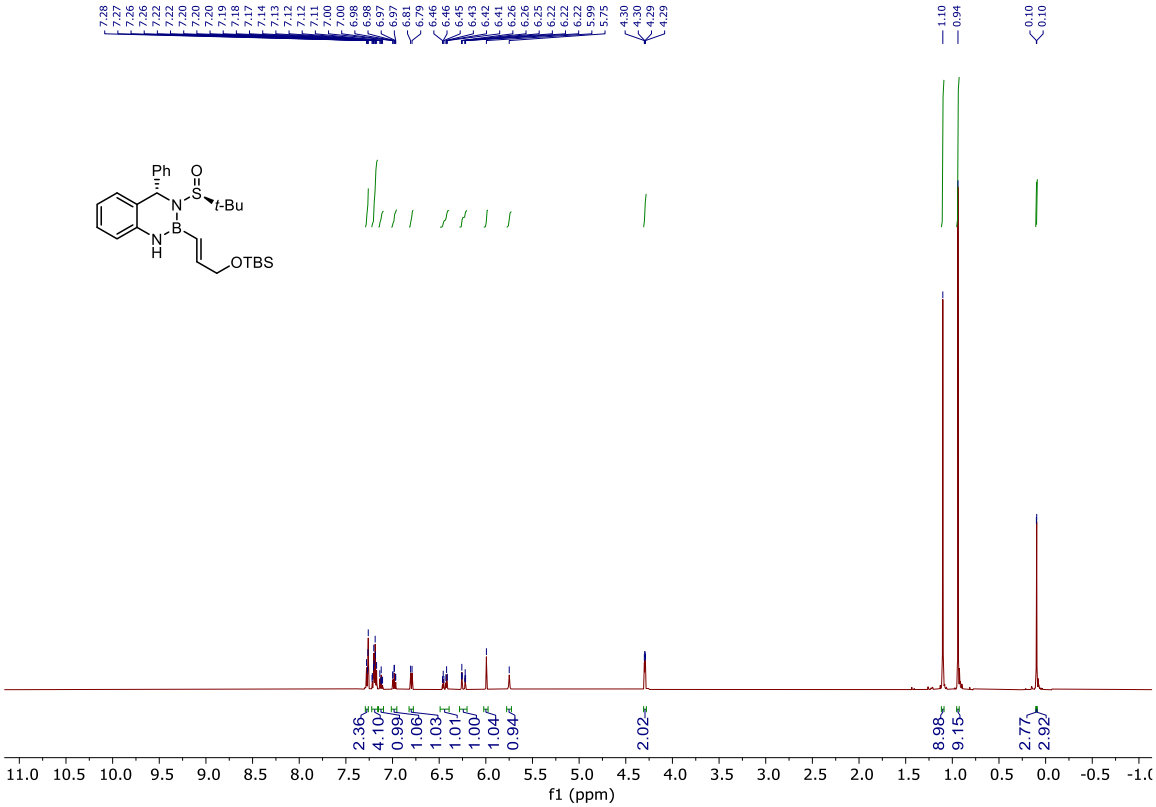
^{1}H NMR (500 MHz, $CDCl_3$) (**3.91**)



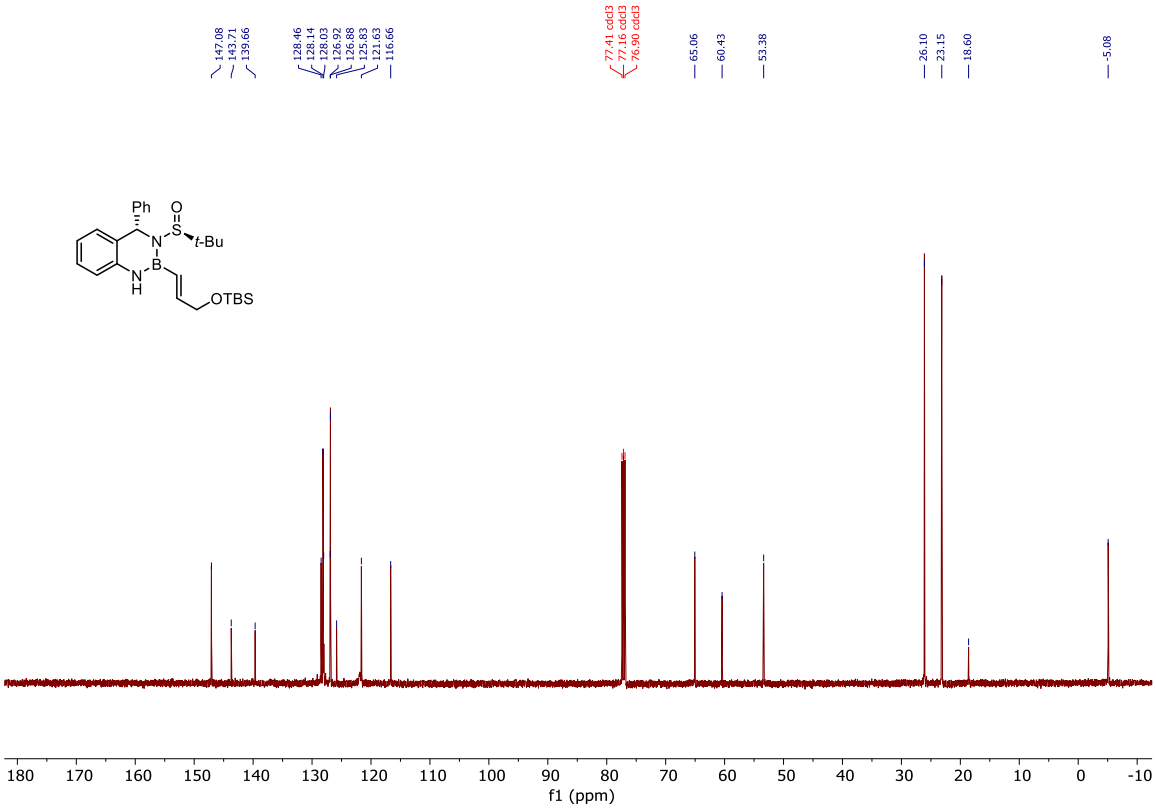
^{13}C NMR (126 MHz, $CDCl_3$) (**3.91**)



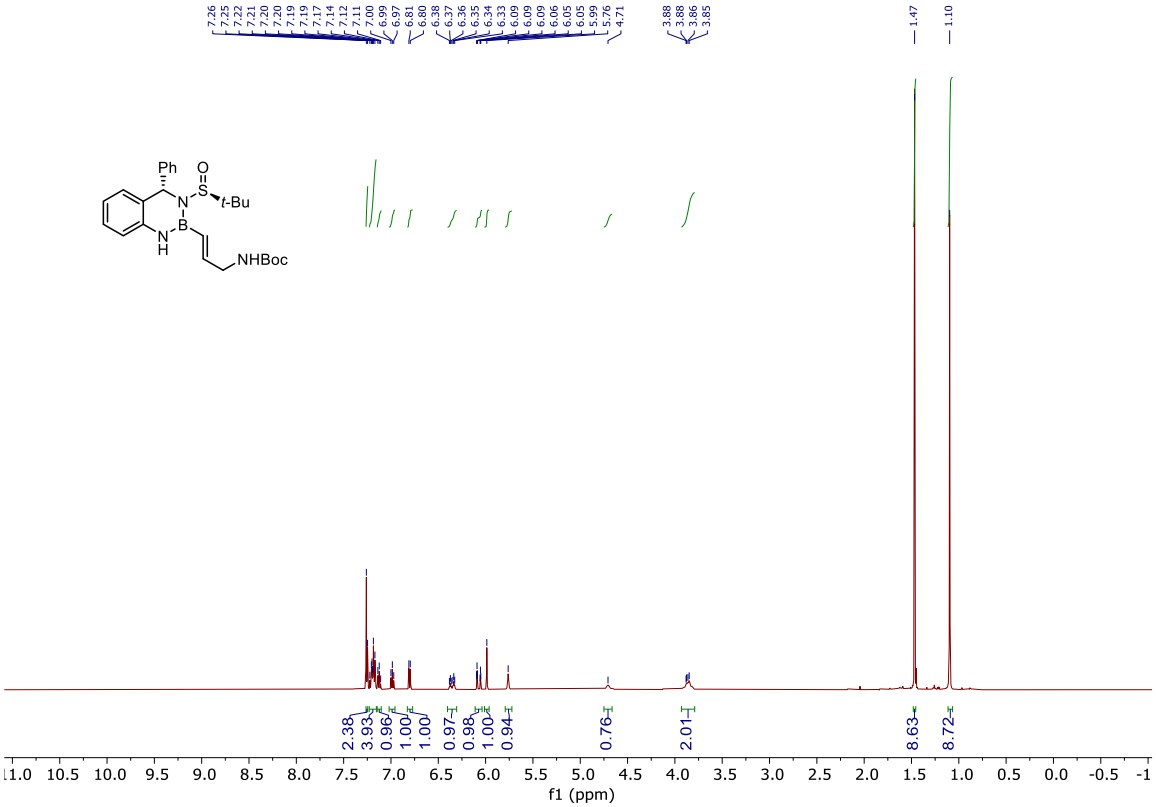
^{1}H NMR (500 MHz, $CDCl_3$) (**3.92**)



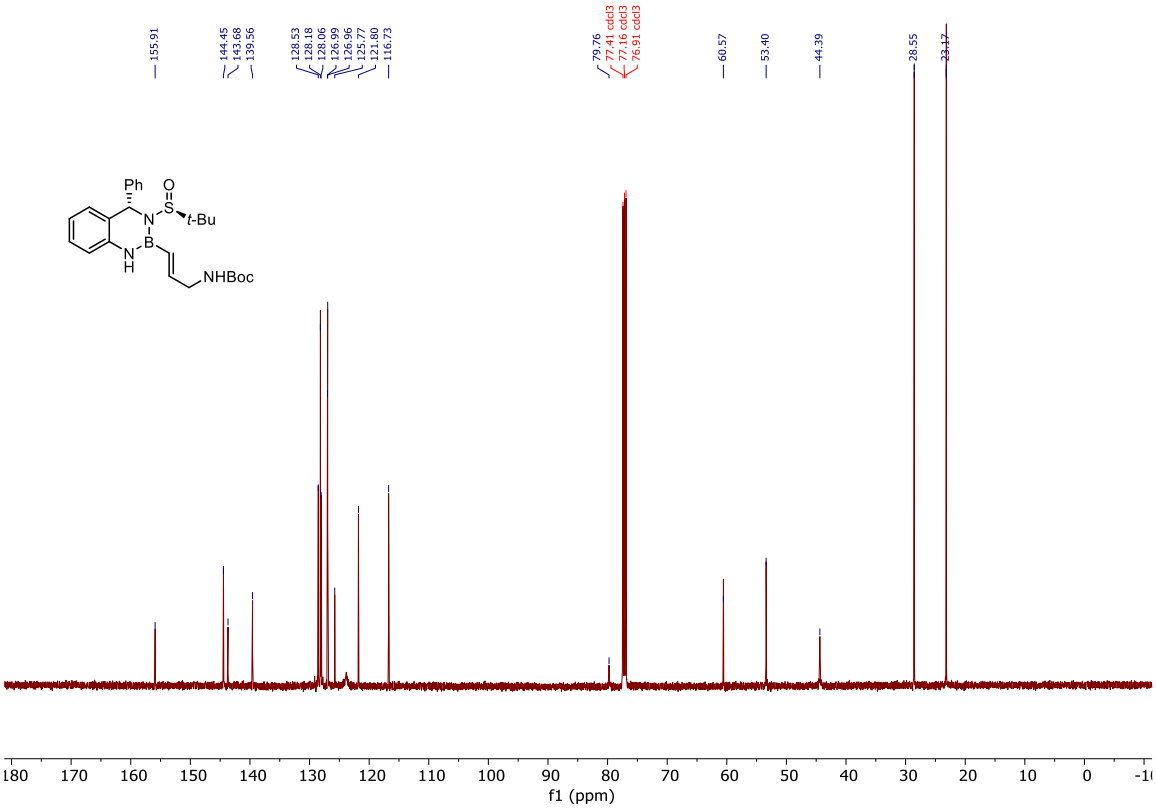
^{13}C NMR (126 MHz, $CDCl_3$) (**3.92**)



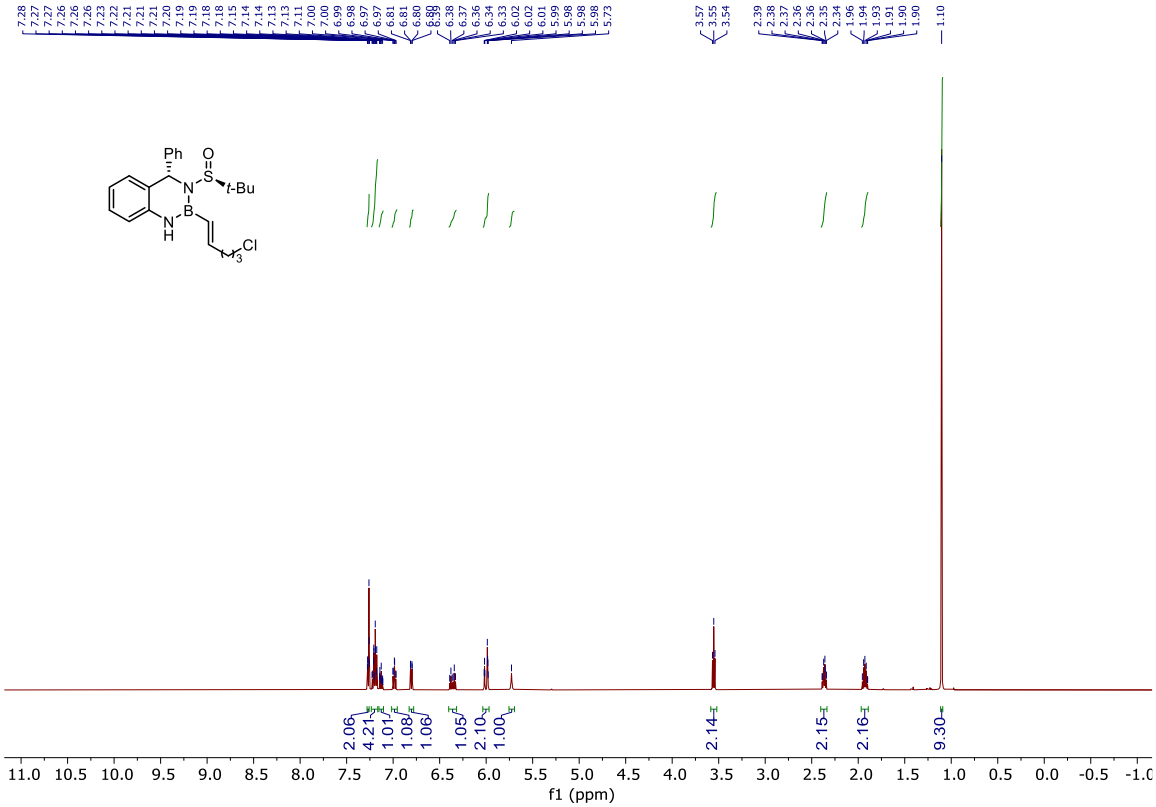
^{1}H NMR (500 MHz, $CDCl_3$) (**3.93**)



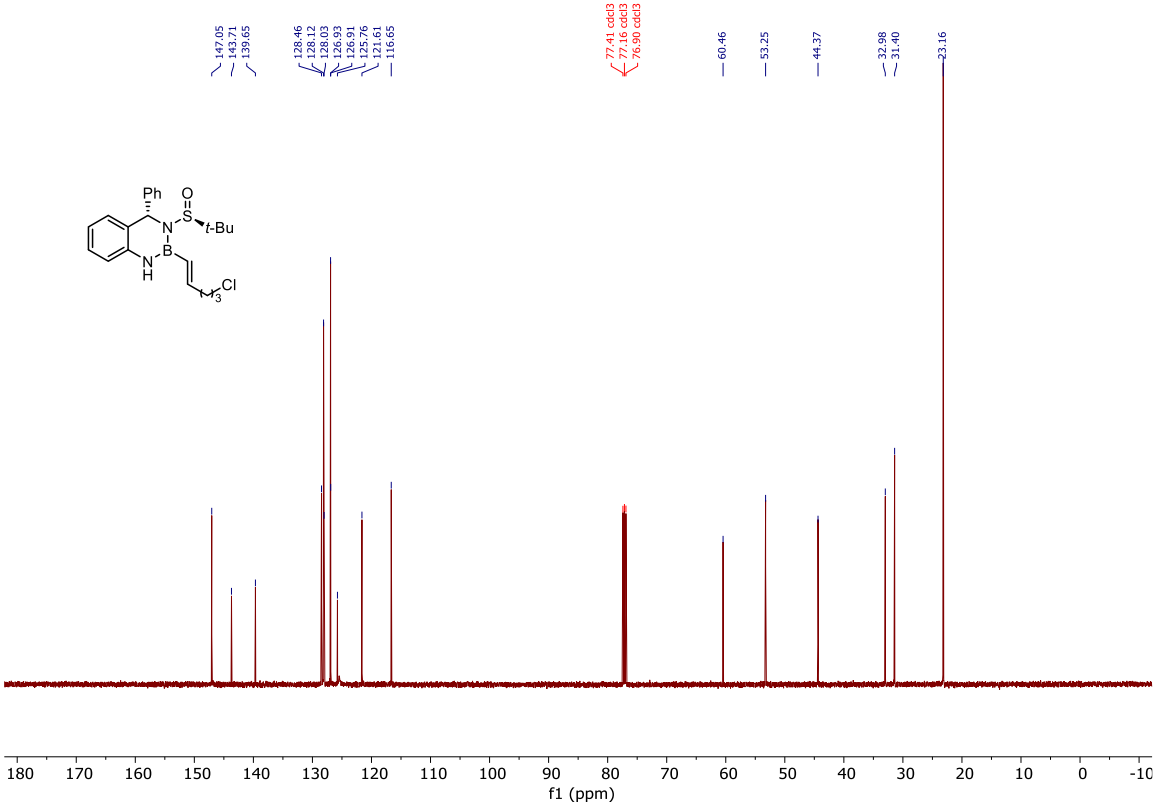
^{13}C NMR (126 MHz, $CDCl_3$) (**3.93**)



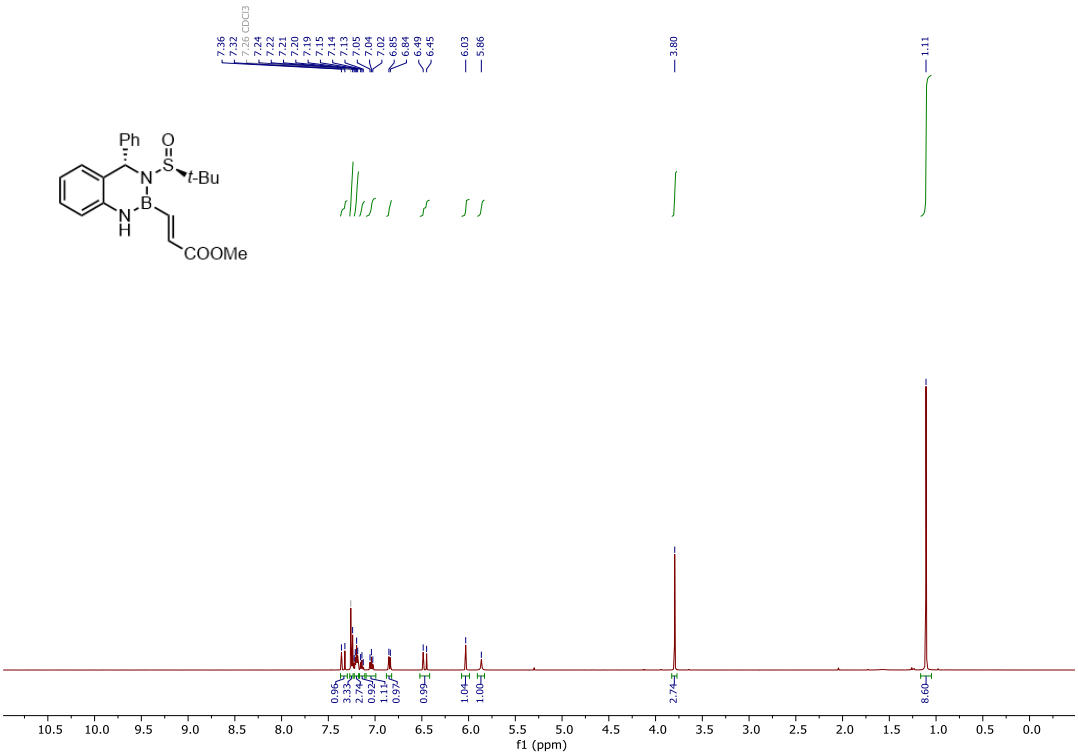
^{1}H NMR (500 MHz, $CDCl_3$) (**3.94**)



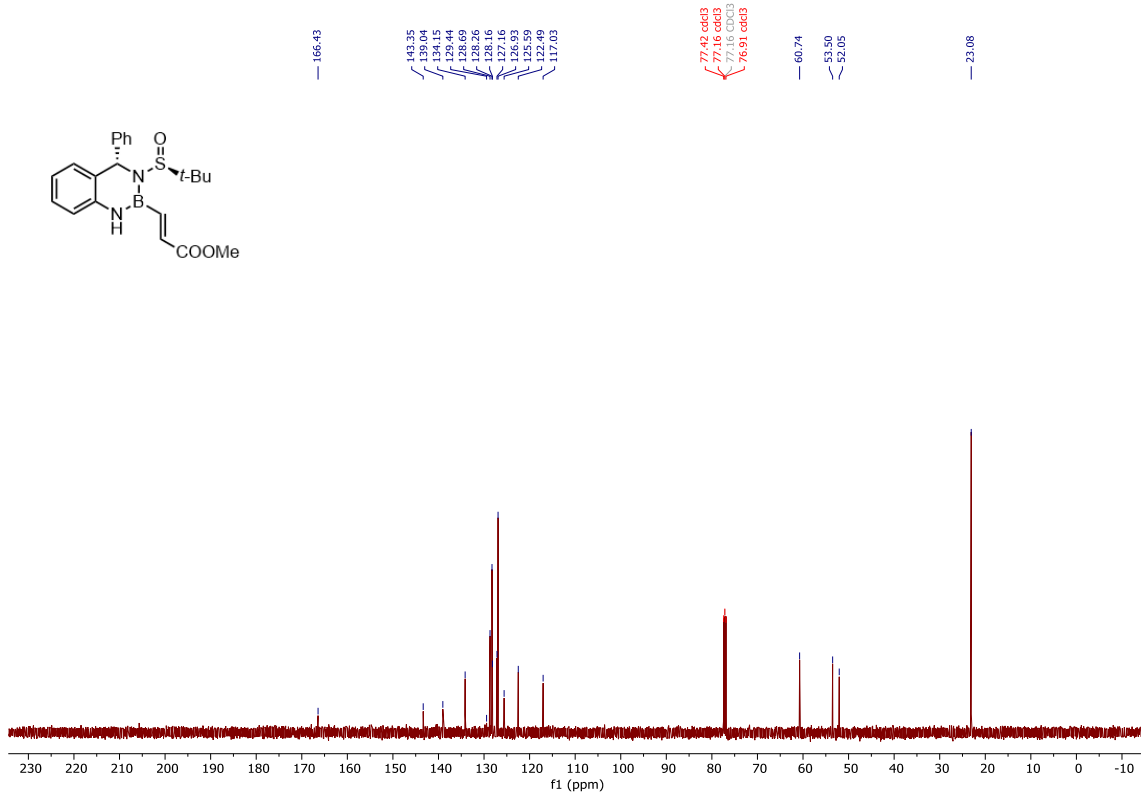
^{13}C NMR (126 MHz, $CDCl_3$) (**3.94**)



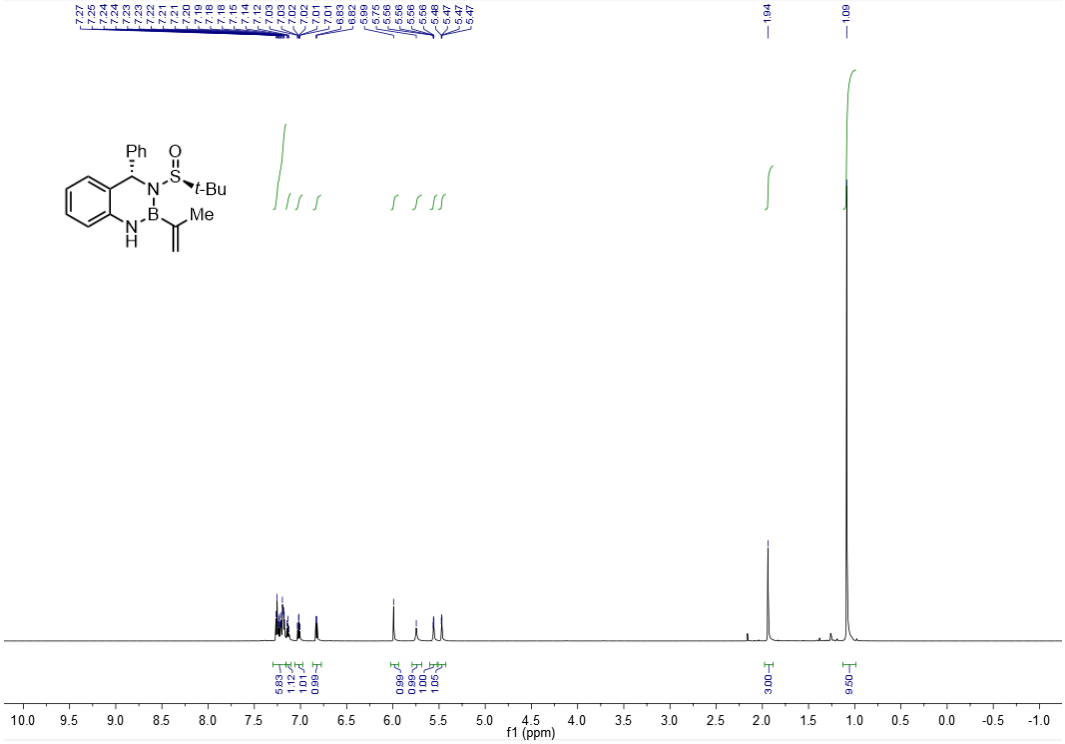
^{1}H NMR (500 MHz, $CDCl_3$) (**3.95**)



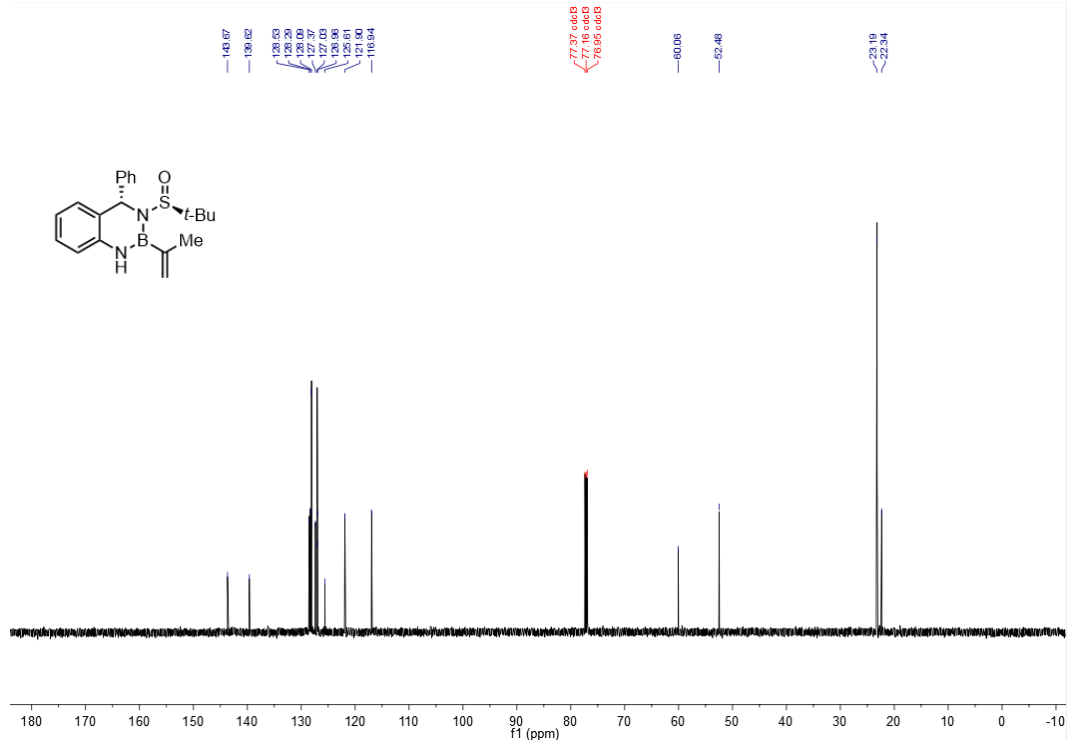
^{13}C NMR (126 MHz, $CDCl_3$) (**3.95**)



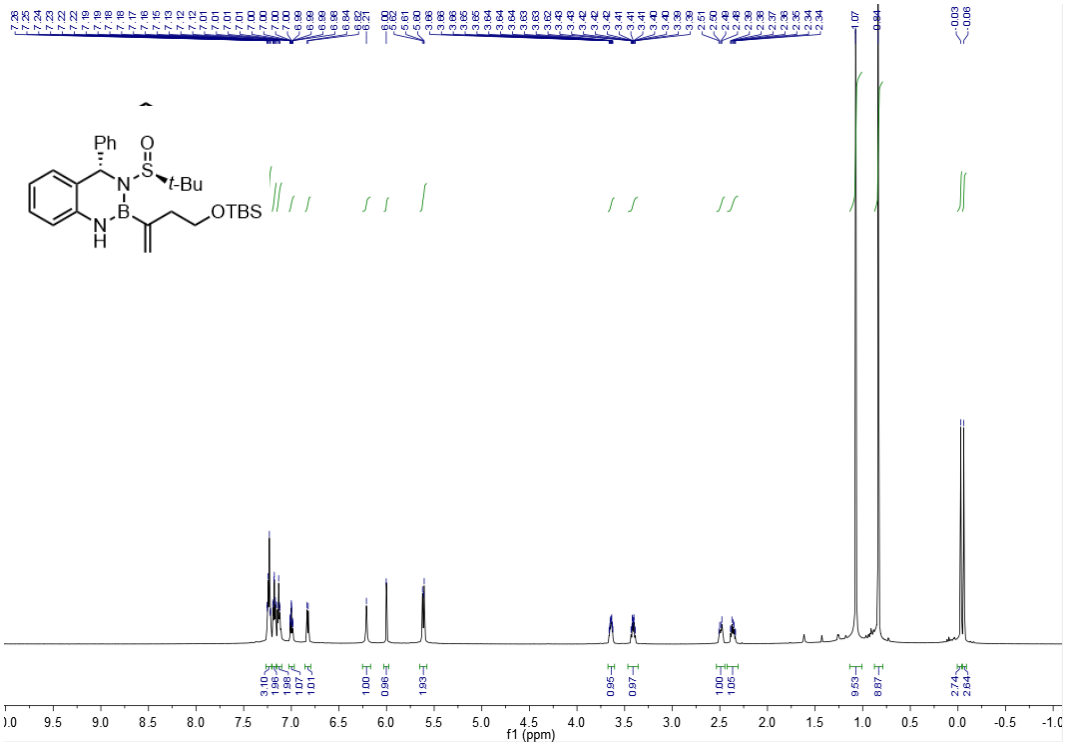
^{1}H NMR (600 MHz, $CDCl_3$) (**3.96**)



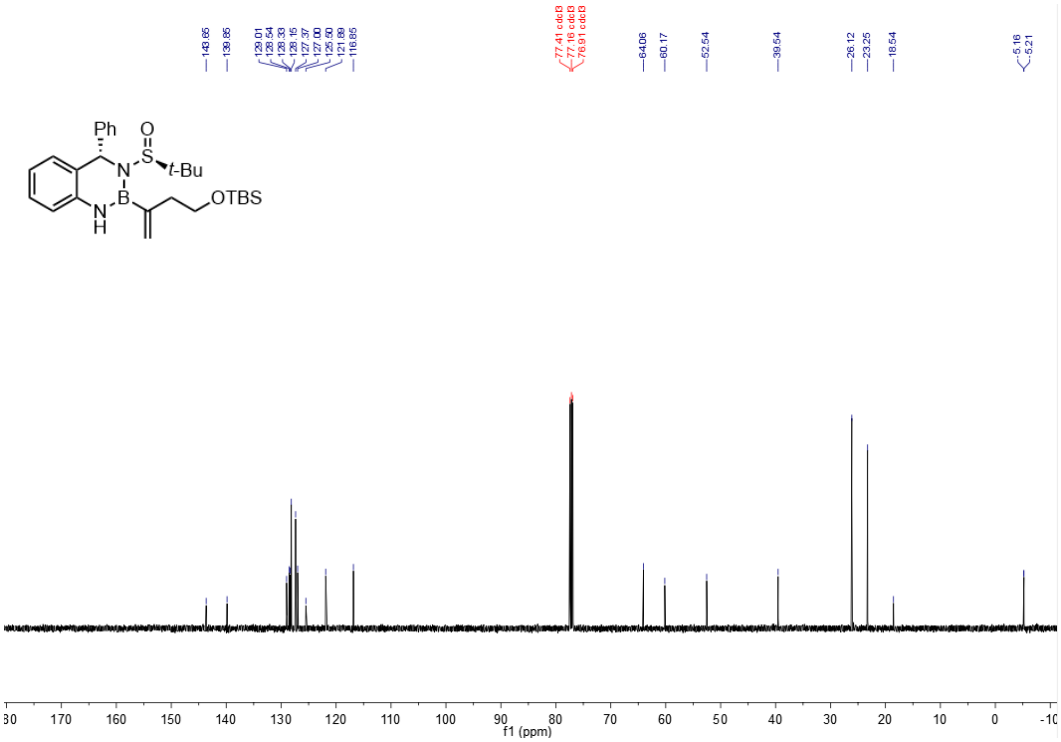
^{13}C NMR (151 MHz, $CDCl_3$) (**3.96**)



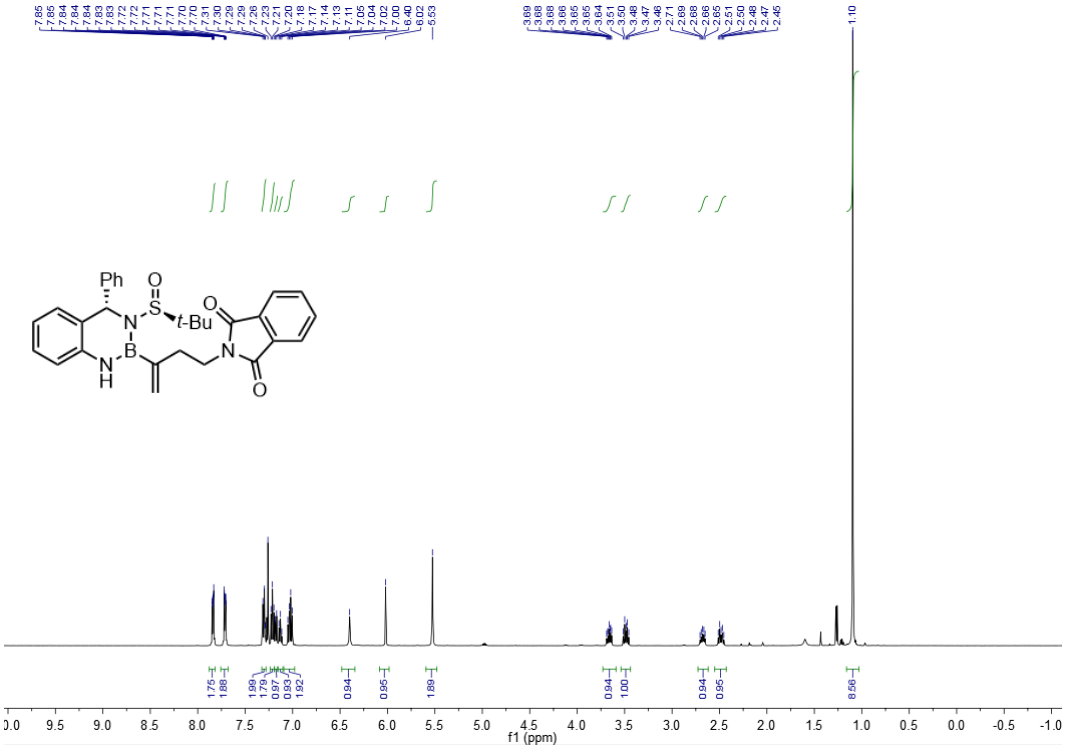
^{1}H NMR (600 MHz, $CDCl_3$) (**3.97**)



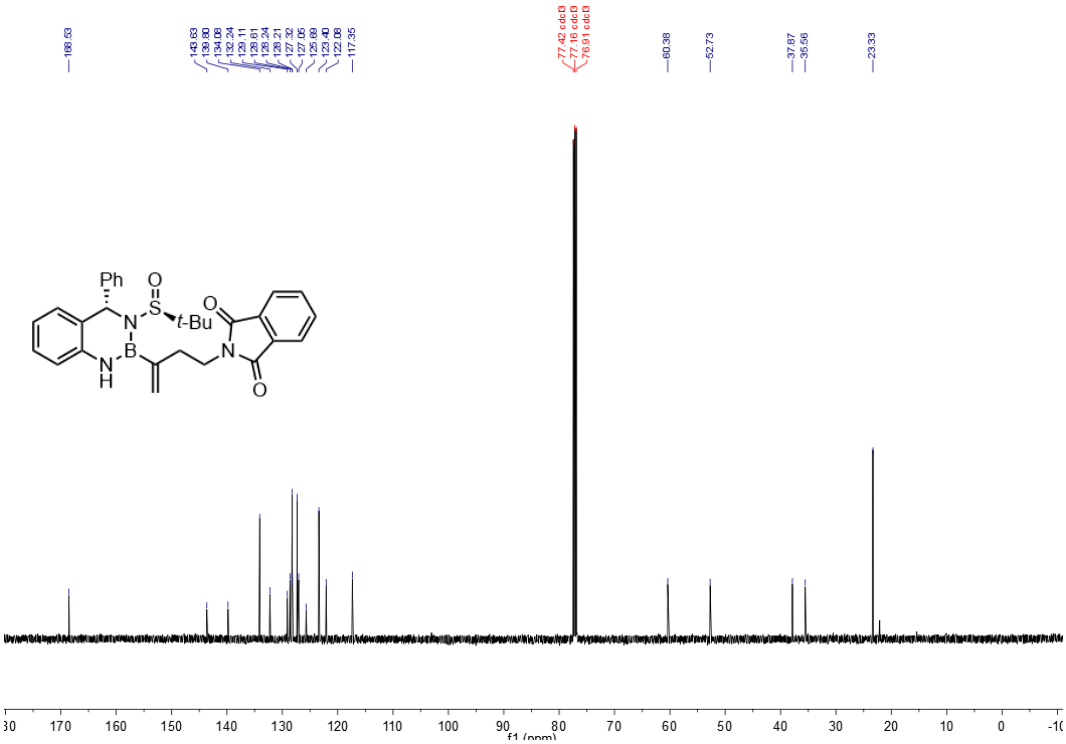
^{13}C NMR (126 MHz, $CDCl_3$) (**3.97**)



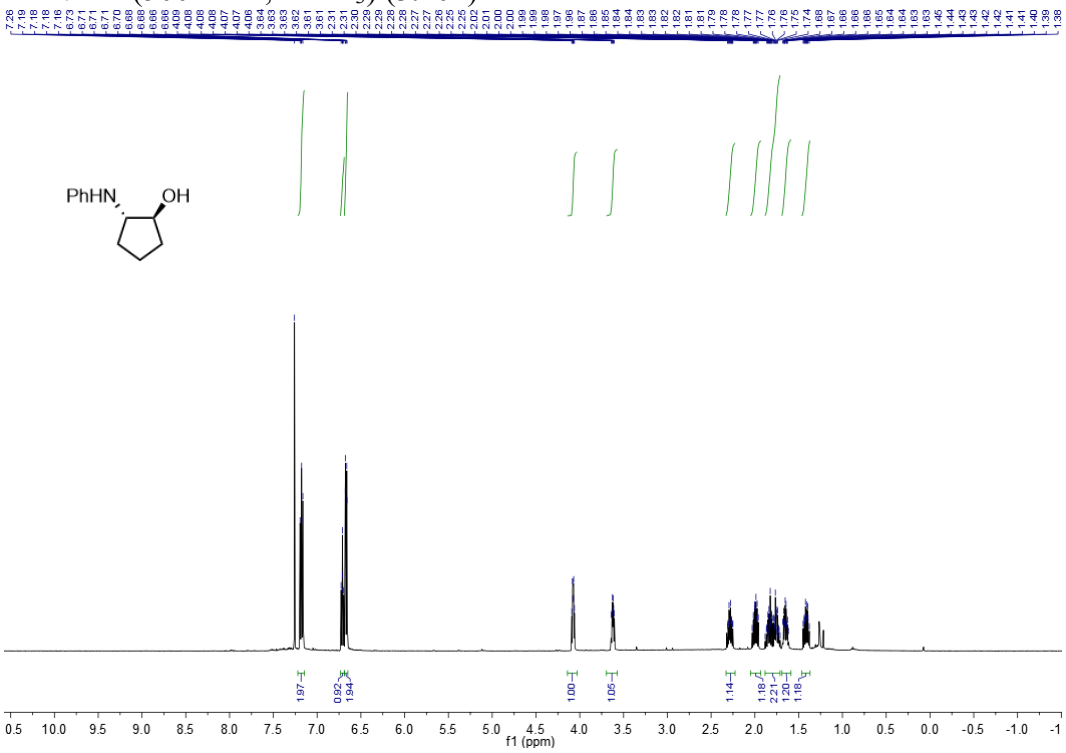
^{1}H NMR (500 MHz, $CDCl_3$) (**3.98**)



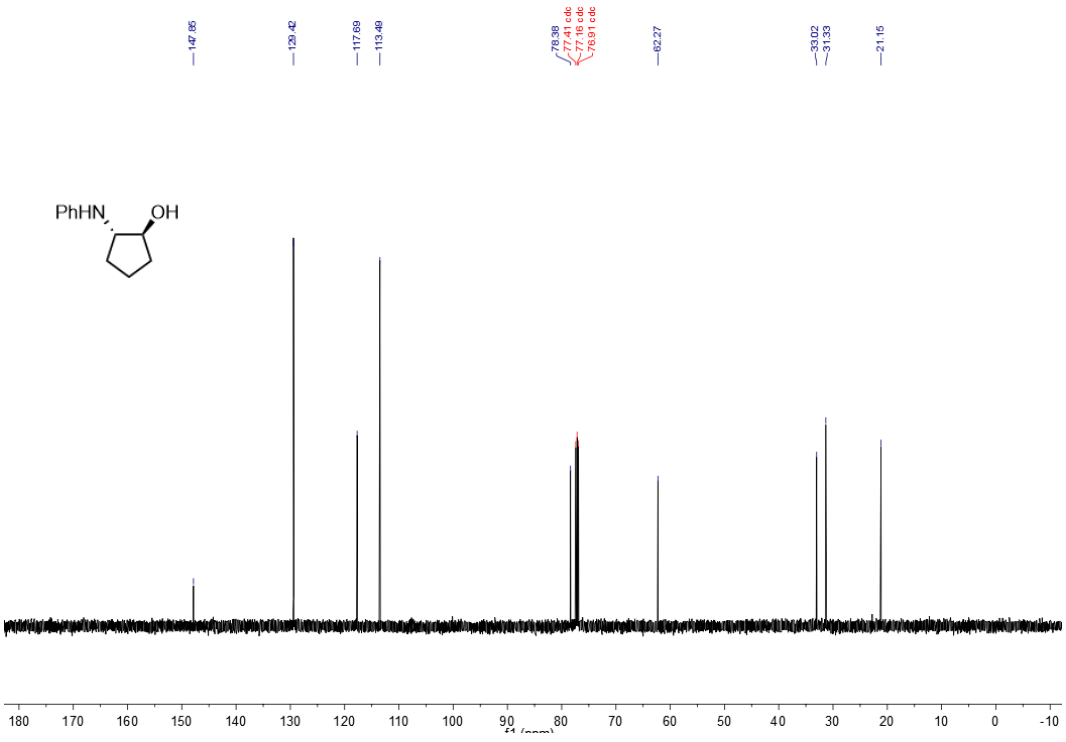
^{13}C NMR (126 MHz, $CDCl_3$) (**3.98**)



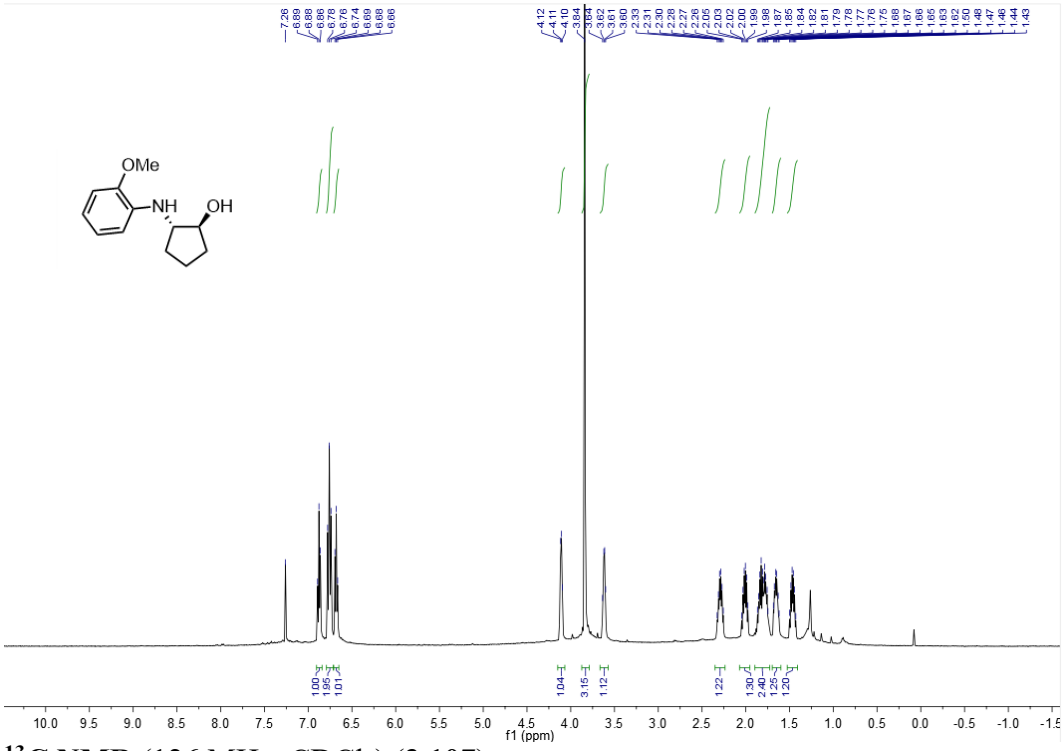
^{1}H NMR (500 MHz, $CDCl_3$) (**3.104**)



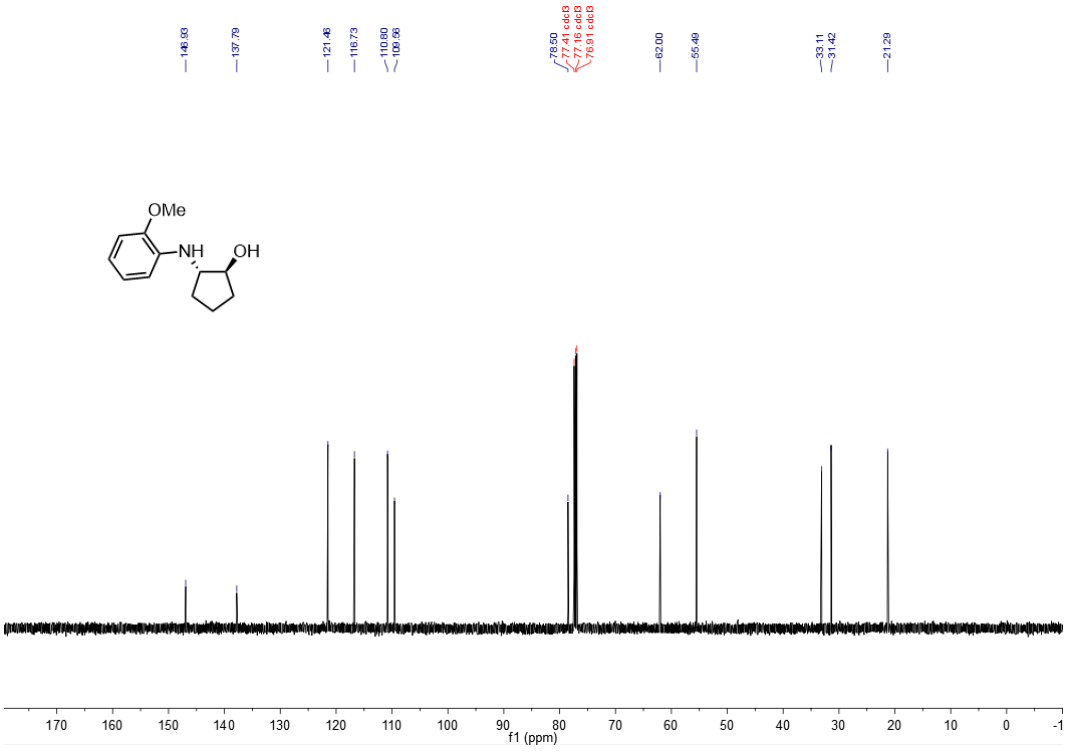
^{13}C NMR (126 MHz, $CDCl_3$) (**3.104**)



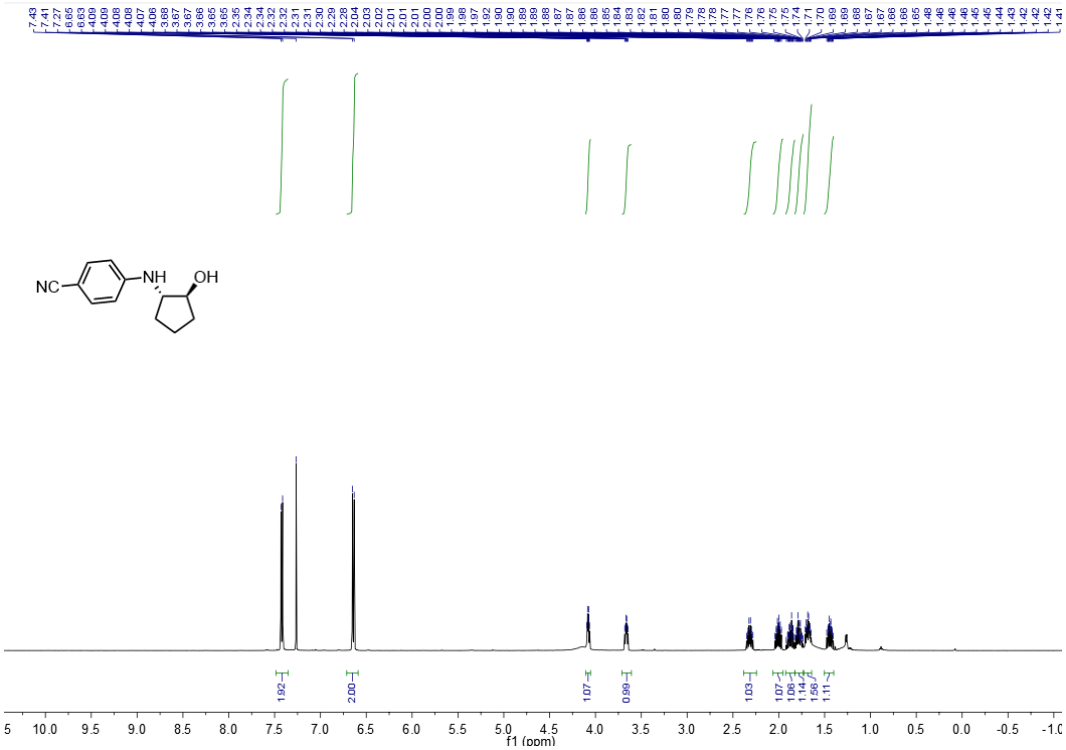
^{1}H NMR (500 MHz, $CDCl_3$) (**3.107**)



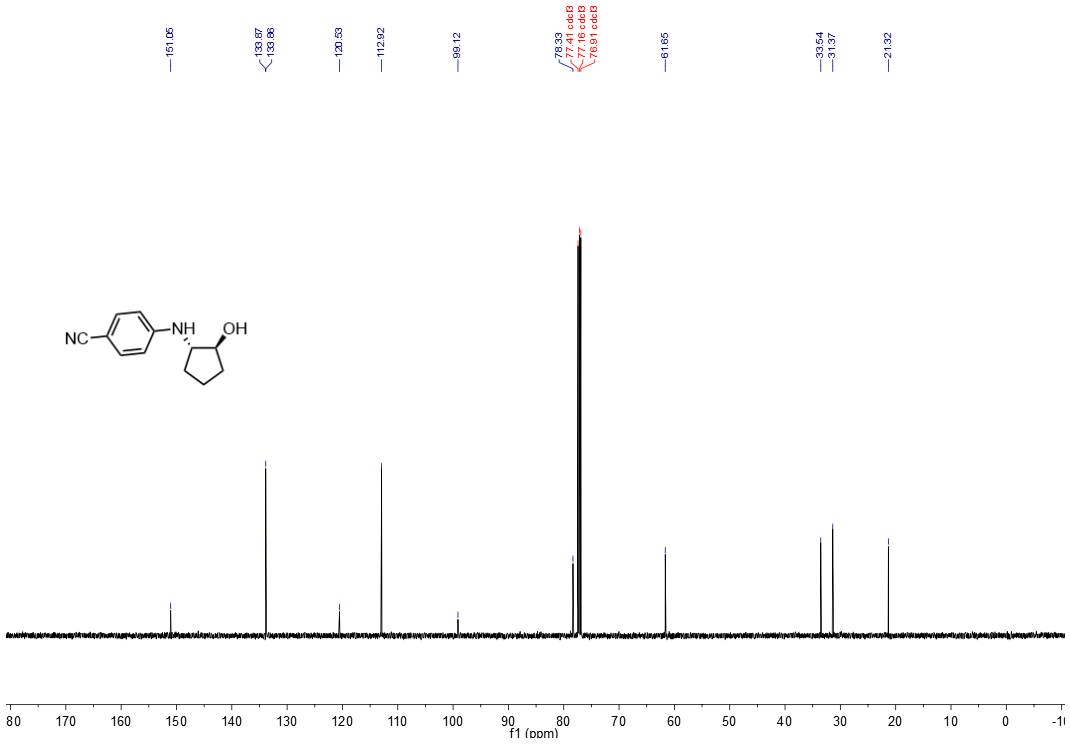
^{13}C NMR (126 MHz, $CDCl_3$) (**3.107**)



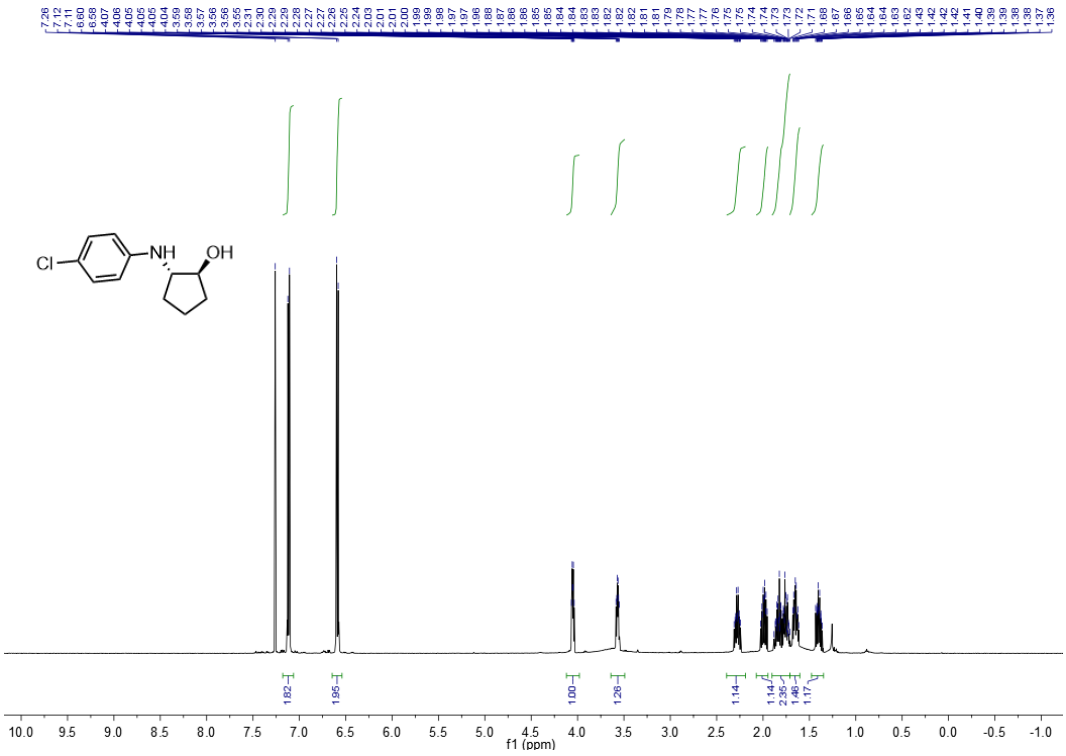
^{1}H NMR (500 MHz, $CDCl_3$) (**3.108**)



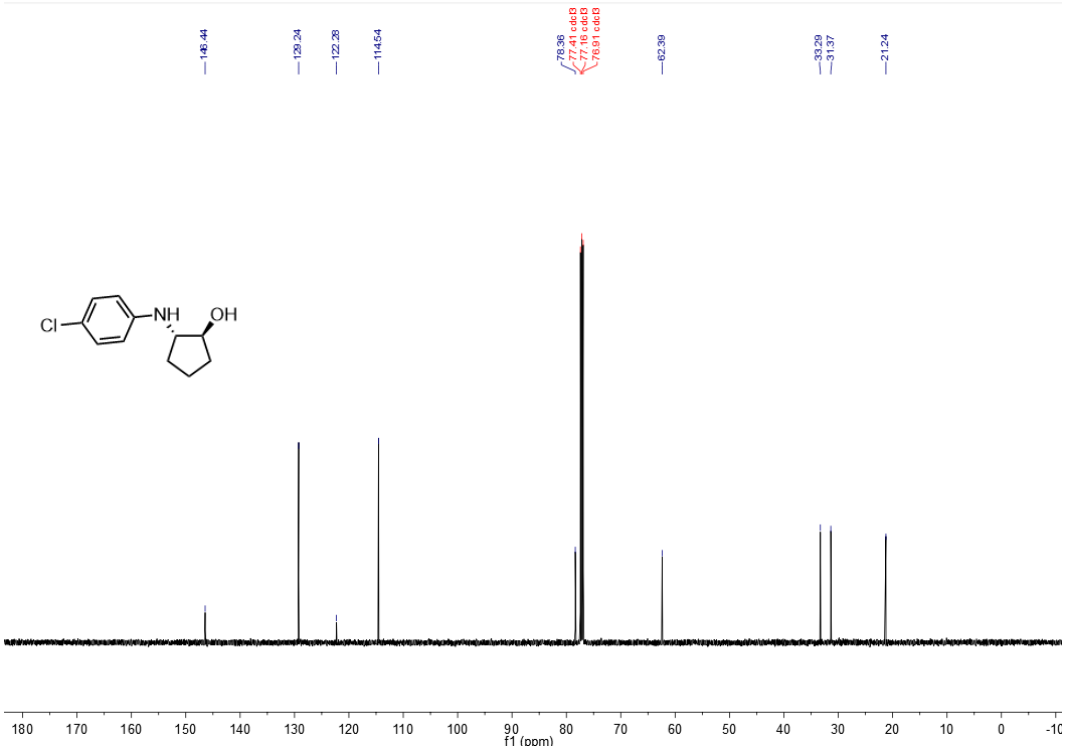
^{13}C NMR (126 MHz, $CDCl_3$) (**3.108**)



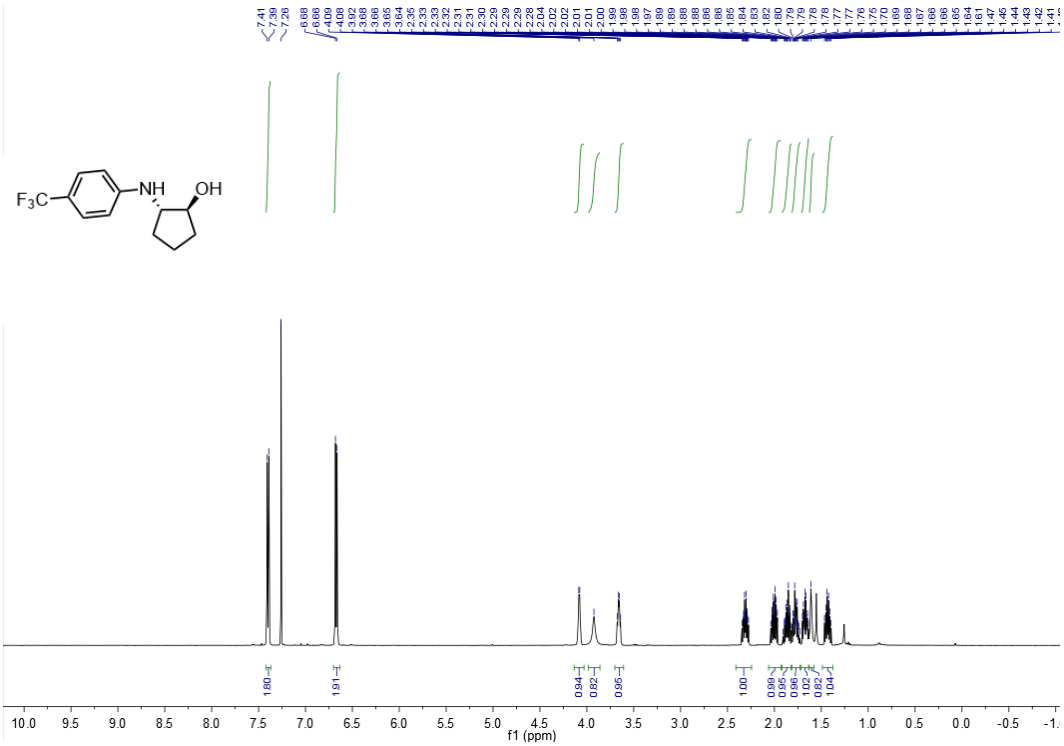
^{1}H NMR (500 MHz, $CDCl_3$) (**3.109**)



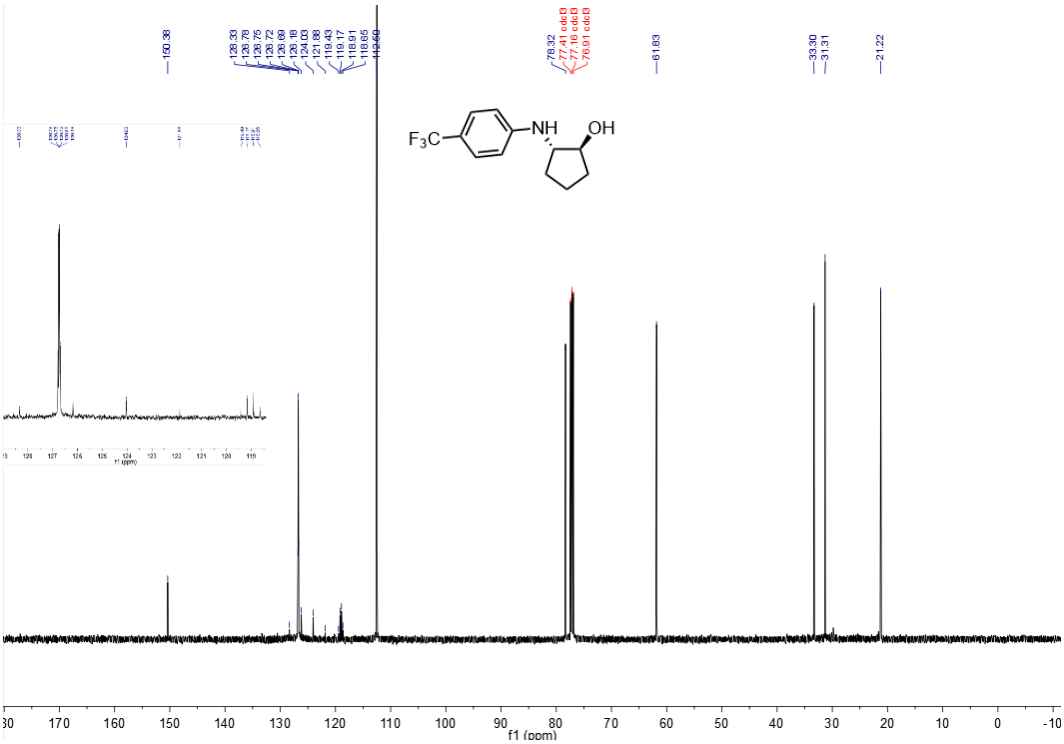
^{13}C NMR (126 MHz, $CDCl_3$) (**3.109**)



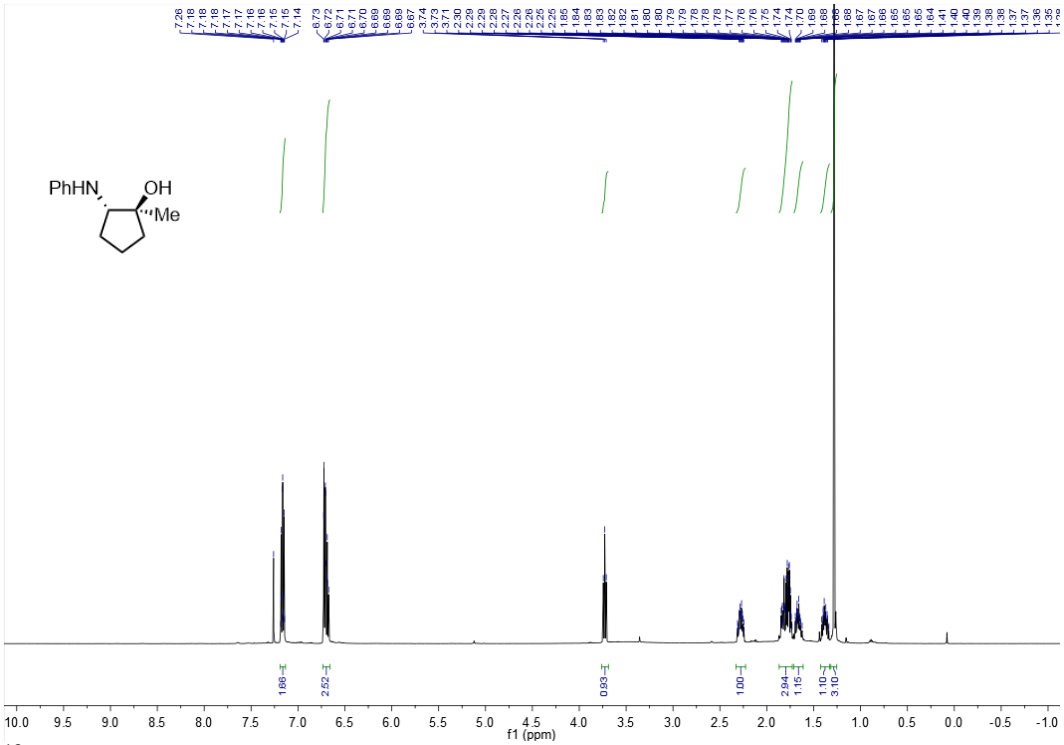
^{1}H NMR (500 MHz, $CDCl_3$) (**3.110**)



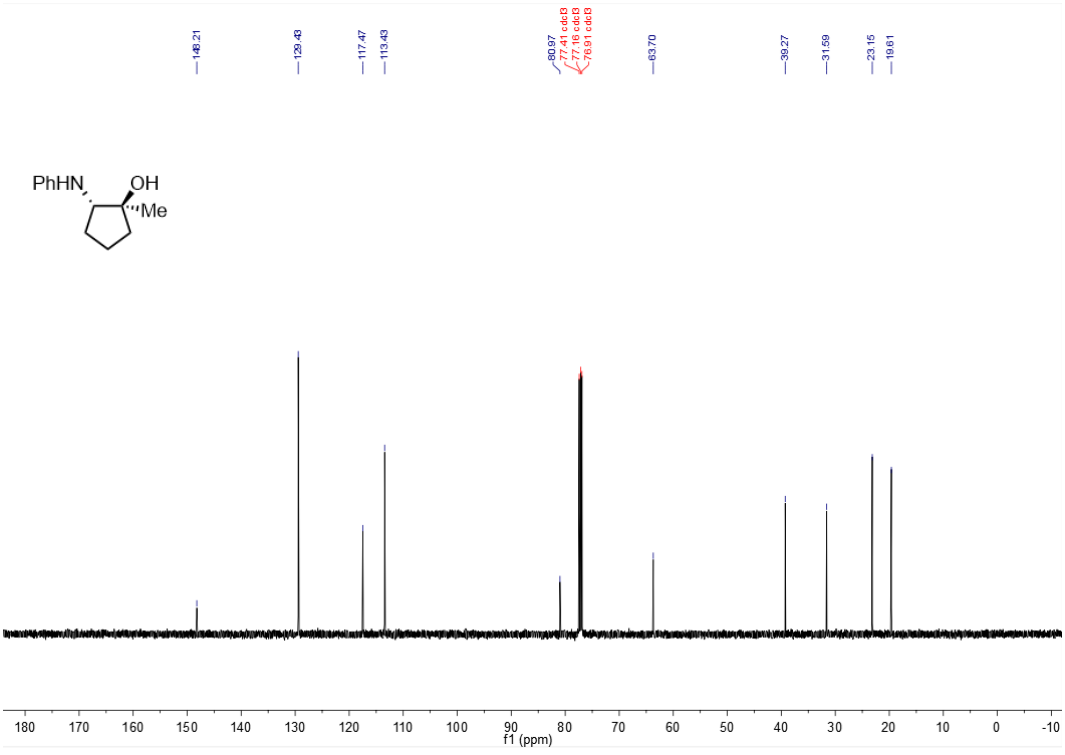
^{13}C NMR (126 MHz, $CDCl_3$) (**3.110**)



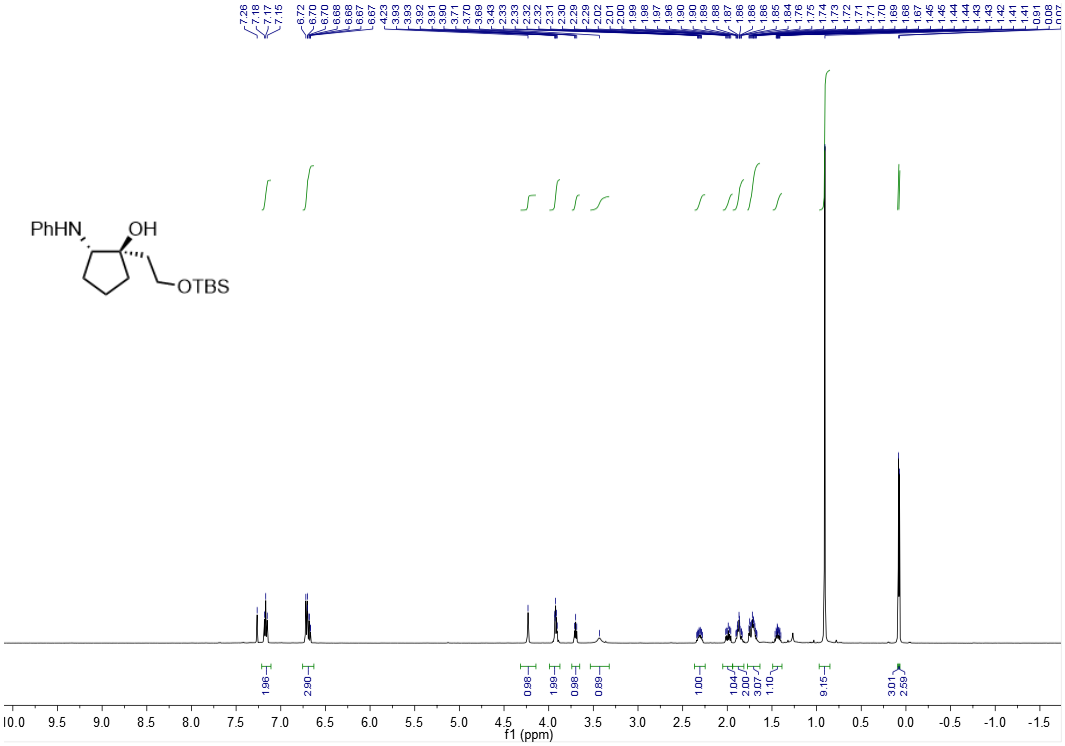
^{1}H NMR (500 MHz, $CDCl_3$) (**3.111**)



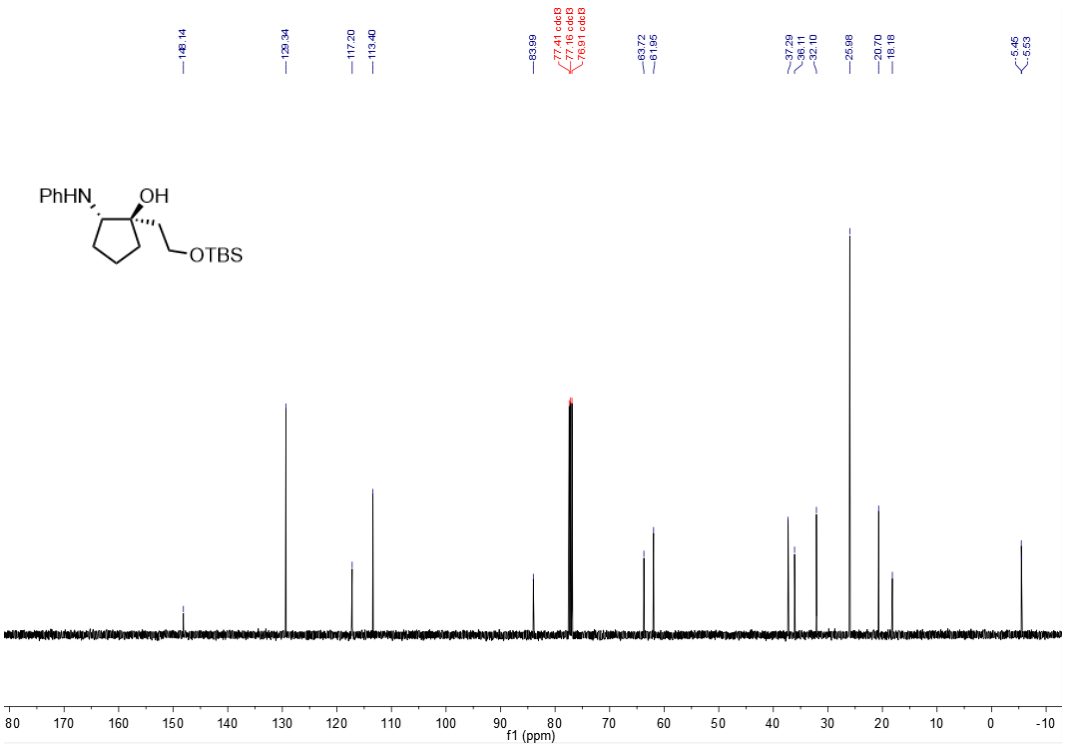
^{13}C NMR (126 MHz, $CDCl_3$) (**3.111**)



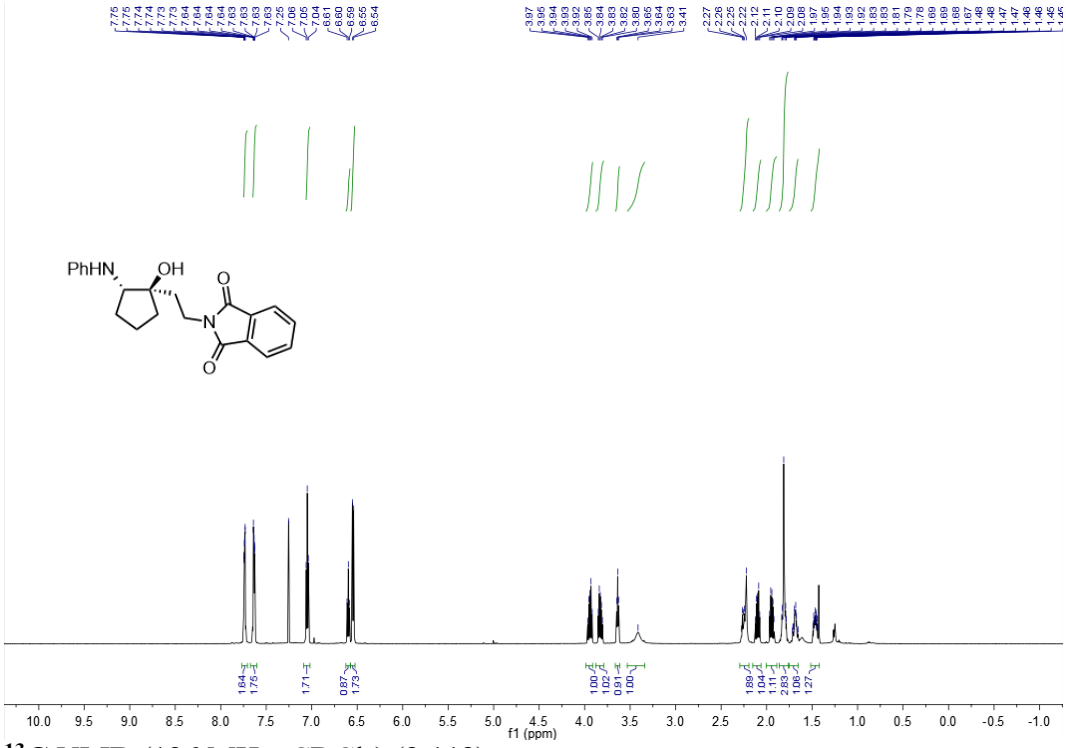
^{1}H NMR (500 MHz, $CDCl_3$) (**3.112**)



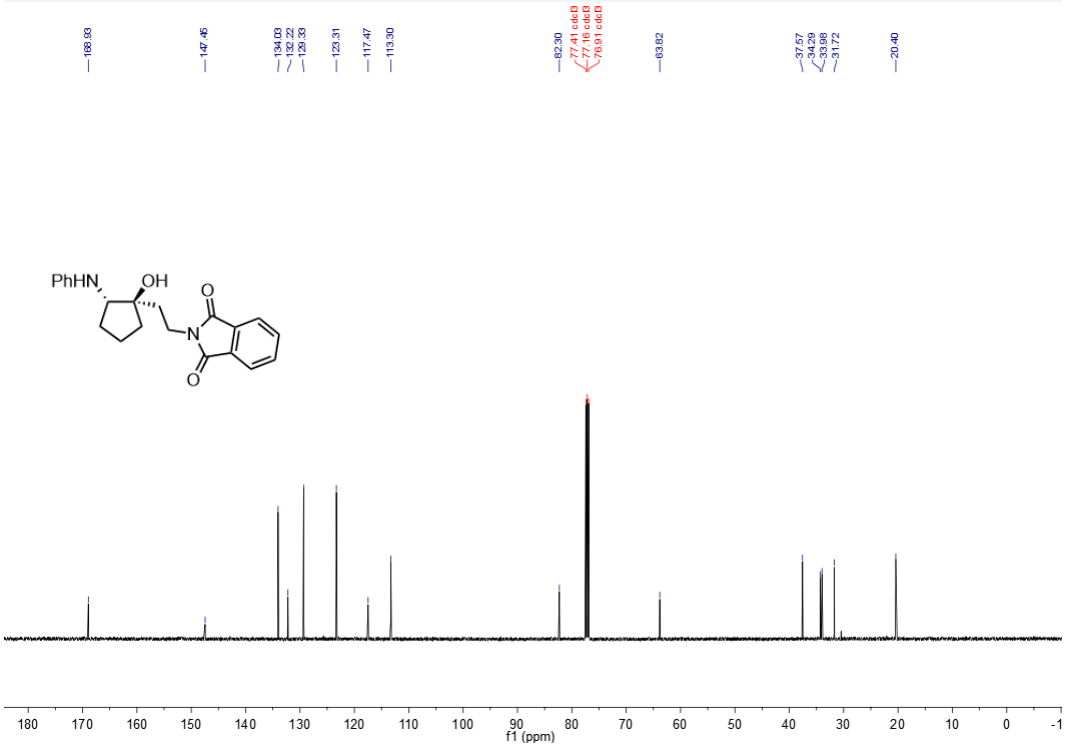
^{13}C NMR (126 MHz, $CDCl_3$) (**3.112**)



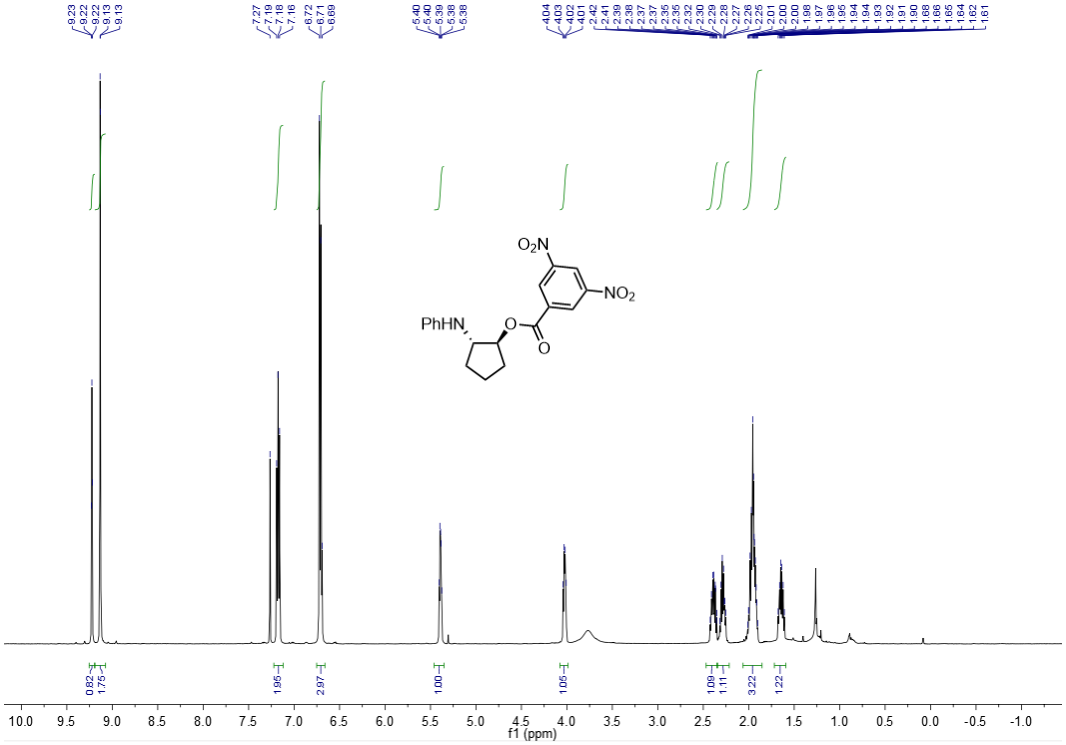
^{1}H NMR (500 MHz, $CDCl_3$) (**3.113**)



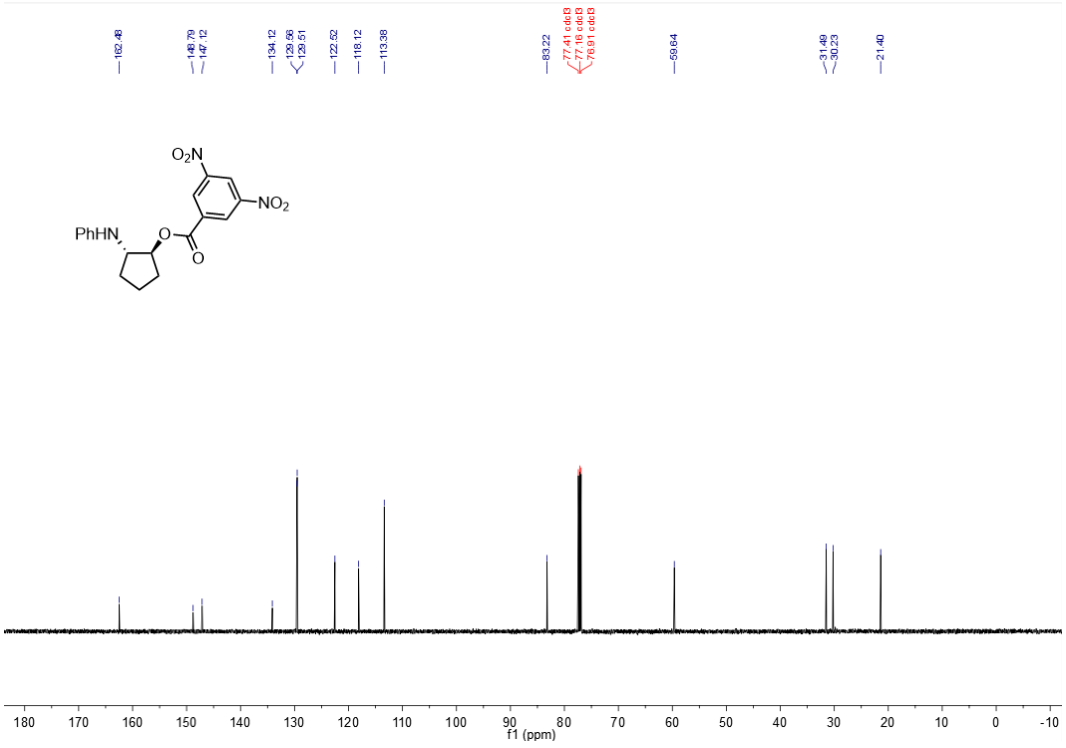
^{13}C NMR (126 MHz, $CDCl_3$) (**3.113**)



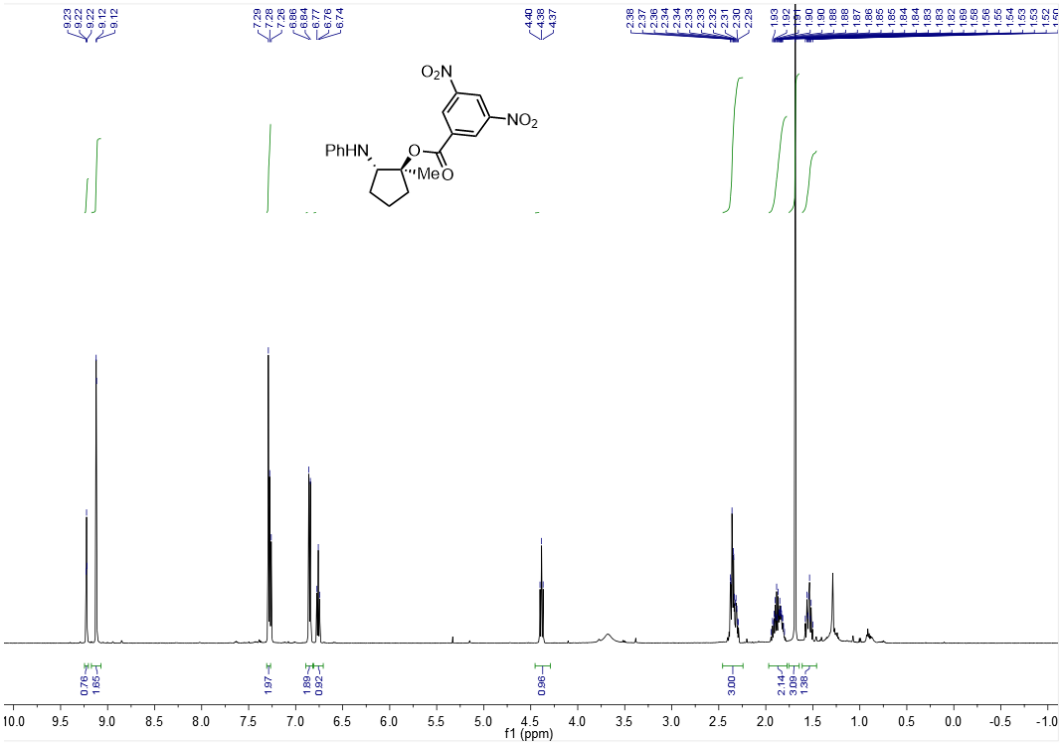
^{1}H NMR (500 MHz, $CDCl_3$) (**SI-5**)



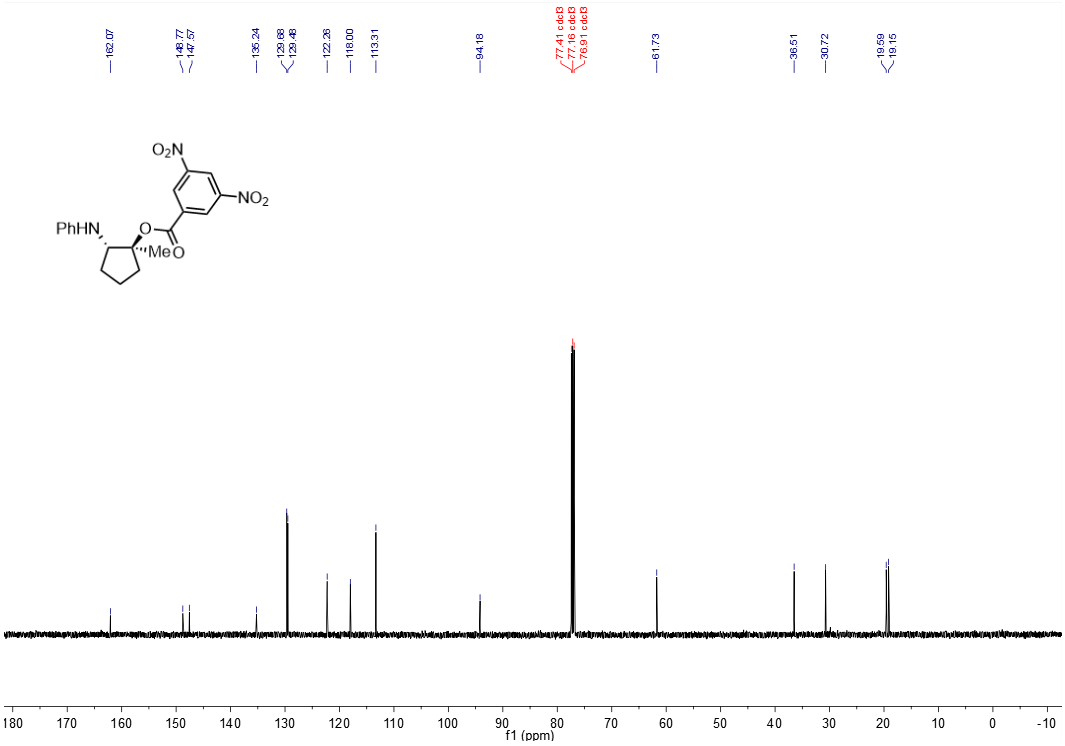
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-5**)



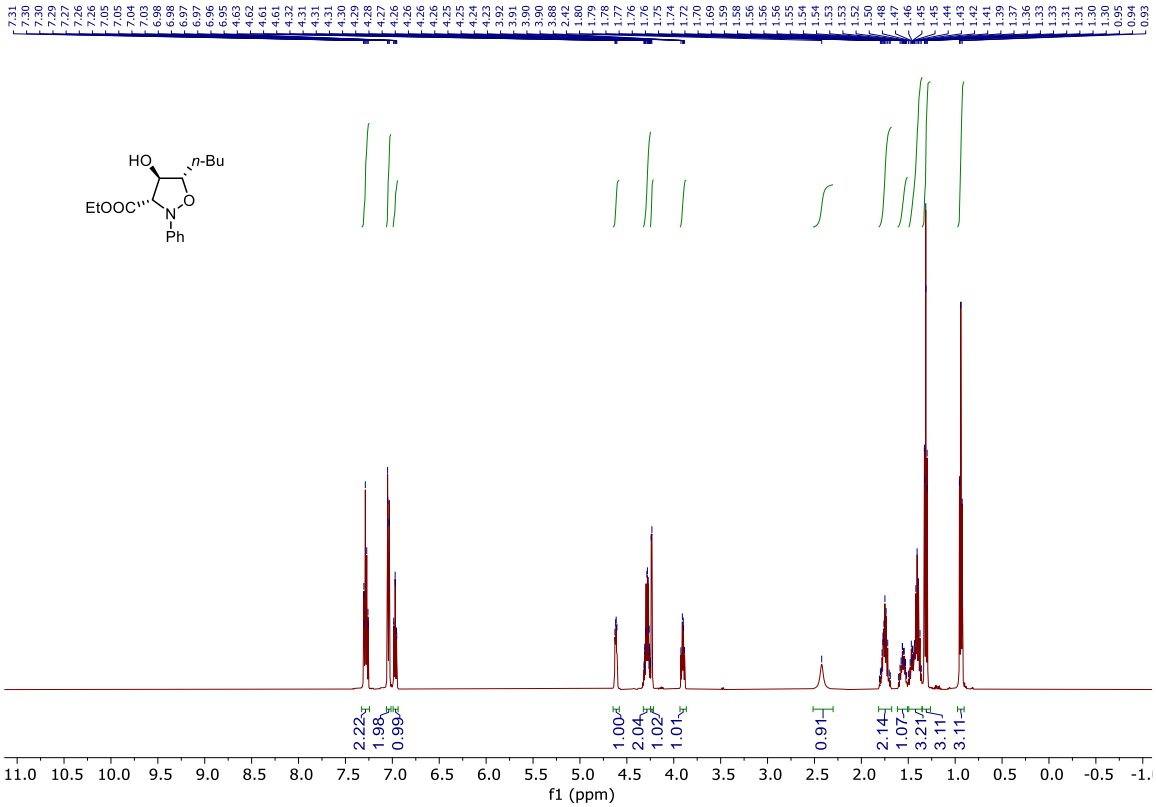
^{1}H NMR (500 MHz, $CDCl_3$) (**SI-6**)



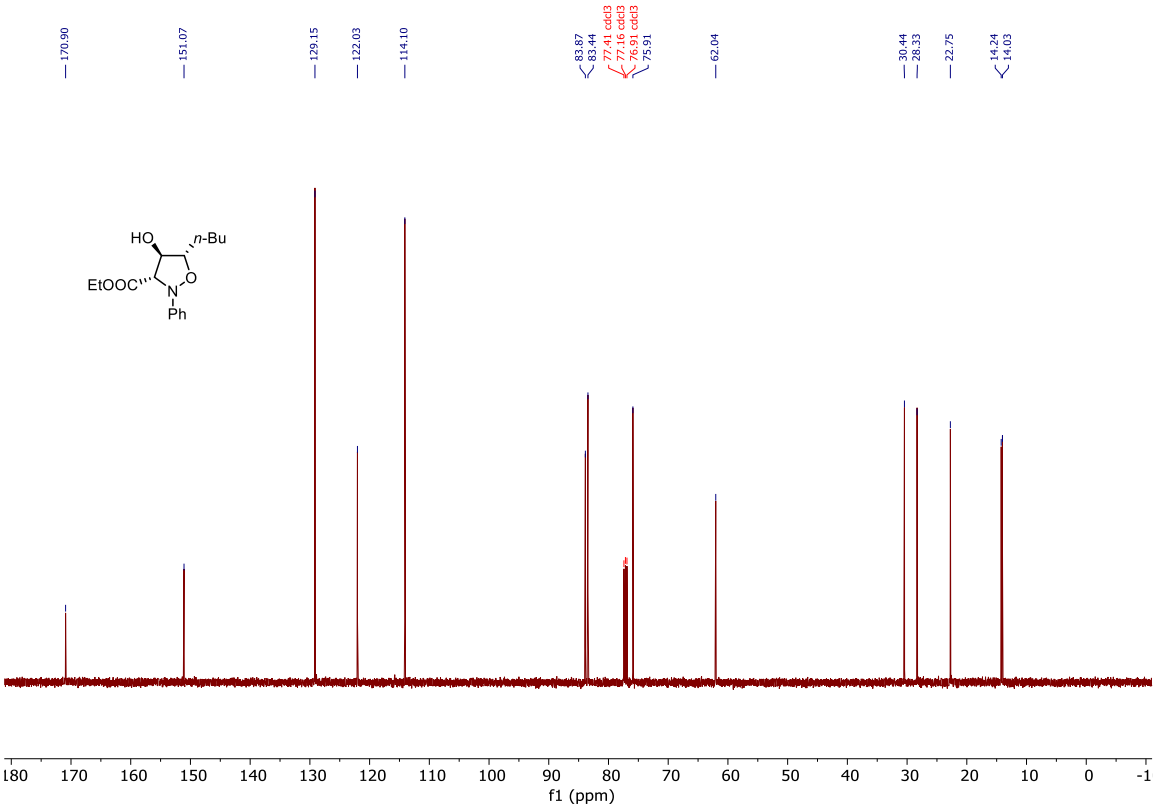
^{13}C NMR (126 MHz, $CDCl_3$) (**SI-6**)



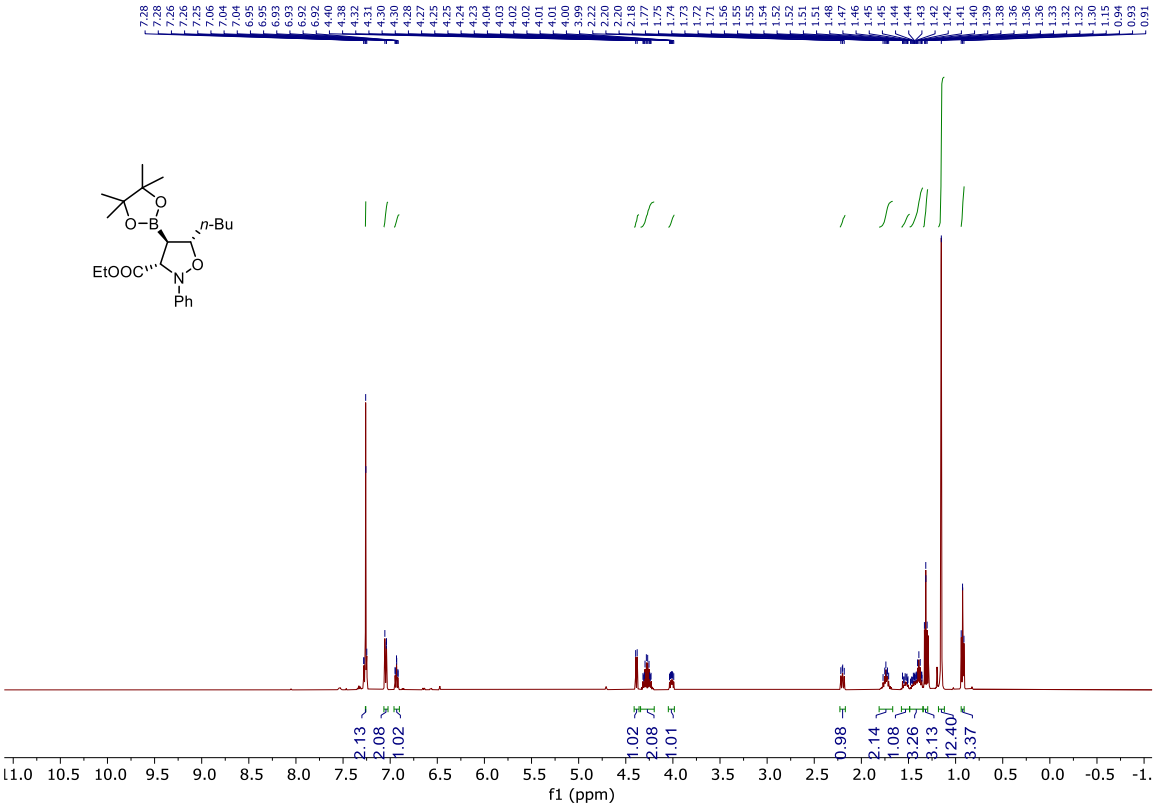
^{1}H NMR (500 MHz, $CDCl_3$) (**3.101**)



^{13}C NMR (126 MHz, $CDCl_3$) (**3.101**)



^{1}H NMR (500 MHz, $CDCl_3$) (**3.102**)



^{13}C NMR (126 MHz, $CDCl_3$) (**3.102**)