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Amphiphilic π-Allyliridium Catalyzed Nucleophilic and Electrophilic Allylation

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Abstract

Amphiphilic π-Allyliridium Catalyzed Nucleophilic and Electrophilic Allylation

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The University of Texas at Austin, 2020

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Transition metal-catalyzed allylic substitution has emerged as a powerful method for stereoselective C-N bond formation. Chiral iridium-phosphoramidite complexes have proven especially effective as catalysts for regio- and enantioselective allylic amination, but are limited to aryl-substituted π-allyl electrophiles. With commercially available π-allyliridium *C,O*-benzoates, which are stable to air, water and SiO_2 chromatography, and are well known to catalyze allylic acetate mediated carbonyl allylation, highly regio- and enantioselective electrophilic allylation of aliphatic amines, primary and secondary aromatic or heteroaromatic amines were demonstrated. Furthermore, indoles and related azoles can also undergo the amination and generate enantiomerically enriched *N*-allyl indoles with completely *N*-selective and exclusive branched regioselectivity, which are an unmet challenge in this field. Moreover, indoles and related azoles are prevalent structural motifs in clinical candidates and FDA approved drugs, so these results also show the utility and importance of asymmetric allylic alkylation.

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1.1 Introduction

Since the pioneering work of Tsuji and Trost on allylic substitution reactions catalyzed by late transition metals, diverse synthetic methodologies for enantioselective allylic substitution have emerged over the last decades.[1] With the use of suitable chiral ligands around the catalyst metal center, enantioselective allylic substitution allows for the construction of covalent bonds between carbon and various other elements in a stereocontrolled fashion. A wide range of carbon-carbon and carbon-heteroatom bonds have been constructed *via* enantioselective allylic substitutions catalyzed by late transition metals. In particular, enantioselective allylic aminations have been highlighted

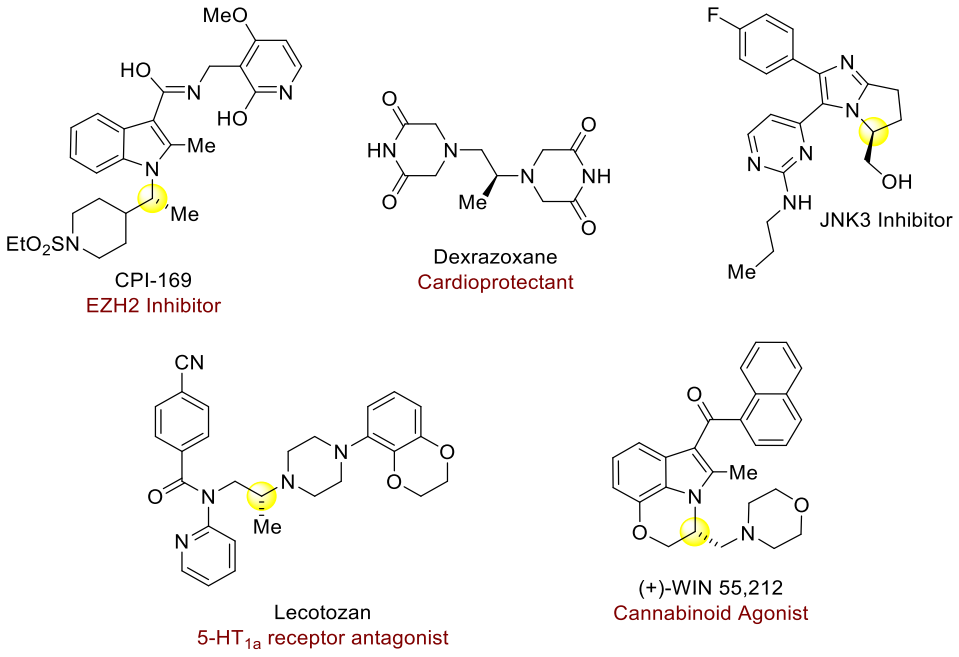


Figure 1.1 Examples of Bioactive Molecules Bearing α-Chiral Amines.

as one of the most powerful methods to provide enantiomerically enriched allylic amine products. The efficient enantioselective construction of this synthetically useful motif can streamline the approaches for natural products, semisynthetic and synthetic pharmaceutical and agrochemical ingredients.

In this review, we summarize intermolecular enantioselective allylic aminations employing racemic allylic derivatives, dienes, allenes, and alkynes fragments as allyl donors catalyzed by late transition metals. Literature is organized by transition metal catalyst. Asymmetric hydrogenations, enantio- and diastereospecific allylic aminations are not discussed. Cyclic allylic proelectrophiles and symmetric allylic derivatives are not explicitly depicted.

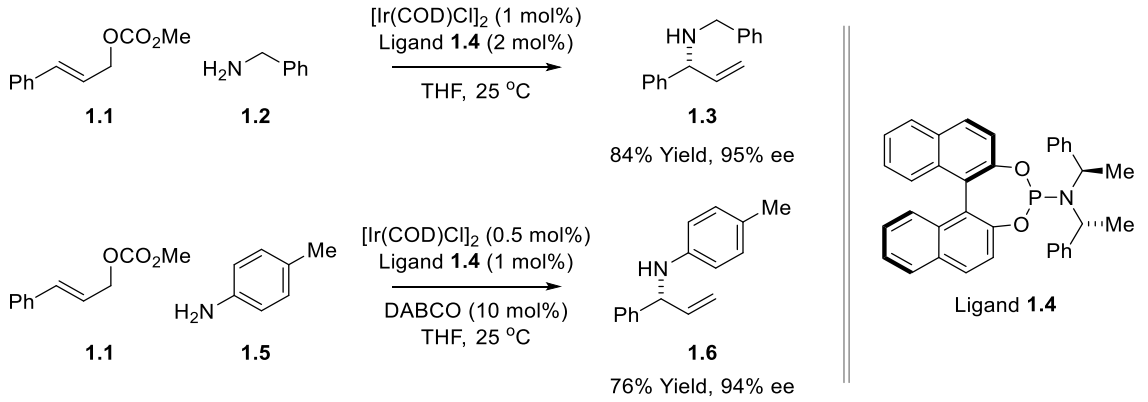
1.2 Intermolecular Iridium Catalyzed Enantioselective Allylic Amination

The formation of branched chiral allylic amines has been greatly enabled by late transition metal catalyzed enantioselective allylic amination. Since the seminal work of Tsuji and Trost, iridium catalysts feature prominently in these transformations. In 1997, the first iridium catalyzed allylic amination was reported by Takeuchi.[2] Using $[Ir(COD)Cl]_2$ and triphenyl phosphite, high levels of regioselectivity for branched products were observed, which is distinct from that of palladium catalyzed reactions, which give linear products from nucleophilic attack of the amine on the less substituted terminus of the allylic group. Utilizing this complementary regioselectivity, the first iridium catalyzed enantioselective allylic alkylation was reported by Helmchen in 1997,[3] opening a new avenue for the construction of synthetically useful chiral products utilizing catalysts modified by chiral ligands. A series of studies by Helmchen and Takeuchi aimed at better understanding iridium catalyzed allylic substitutions have initiated the

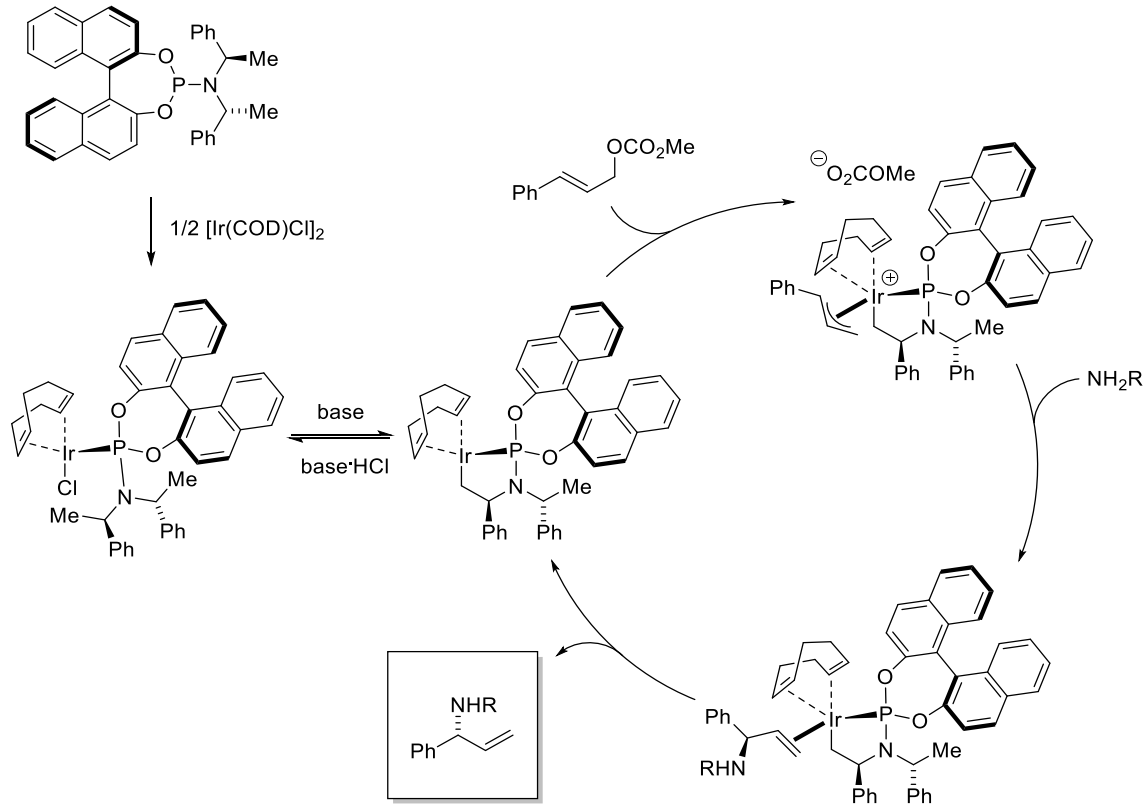
large expansion of this enantioselective allylic amination chemistry over the past decade to form chiral branched allylic amines.

1.2.1 Allylic Carbonate

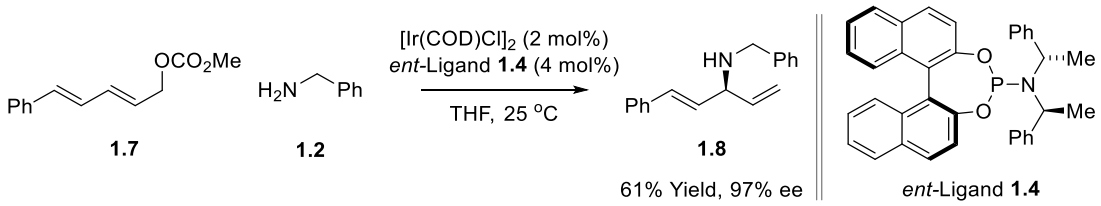
In 2001, Takeuchi reported the very first iridium catalyzed allylic amination, generating racemic branched allylic amine products.[4] Subsequent to this effort, in 2002, Hartwig reported the first iridium catalyzed enantioselective allylic amination (Scheme 1.1).[5] Using the Feringa ligand **1.4**, which was used for enantioselective conjugate additions and known for its π-accepting properties,[6] primary and secondary aliphatic amines reacted with allylic carbonates to form enantiomerically enriched allylic amines with high yields, and excellent regio- and enantioselectivities. Further mechanistic investigations revealed that the active species was the cyclometalated iridacycle formed from base mediated C–H activation of the initial iridium complex coordinated by the phosphoramidite ligand (Scheme 1.2).[7,8] For this reason, weak nucleophiles, such as aniline, were not strong enough to enable this cyclometallation process to occur and therefore did not furnish the product of chiral allylic amines. To address this issue, Hartwig demonstrated that adding a catalytic amount of additional base such as DABCO plays a key role in this activation process and enforces the formation of branched allylic aryl amines with high regio- and enantioselectivity.[9] Another approach to generate this cyclometalated complex is the *in situ* preparation where heating of $[Ir(COD)Cl]_2$, phosphoramidite ligand, and *N*-propylamine in THF at 50 ^{o}C, followed by vacuum evaporation, yields the active catalyst. Many of the following works have exploited these *in situ* conditions for the generation of catalytically competent catalyst.



Scheme 1.1 First Enantioselective Iridium Catalyzed Allylic Amination.



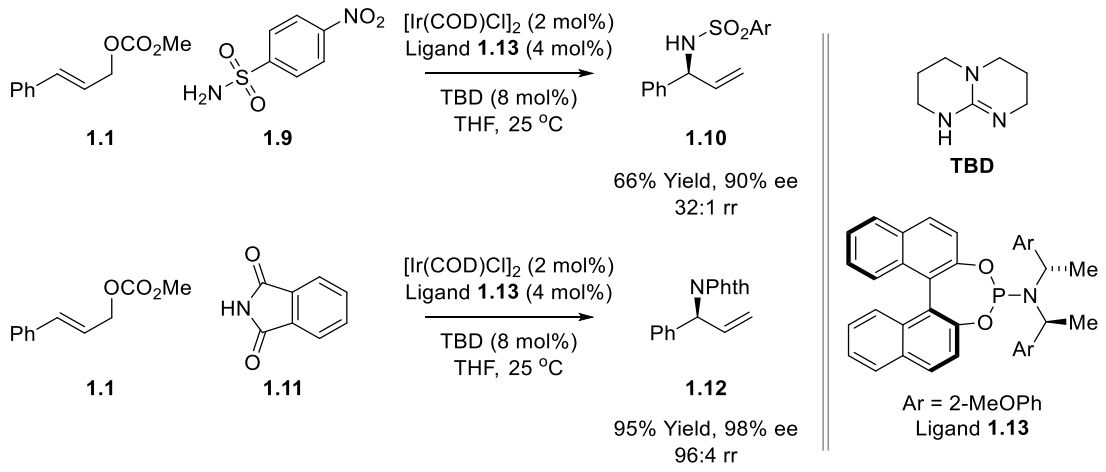
Scheme 1.2 Proposed Catalytic Cycle for Iridium Catalyzed Allylic Amination.



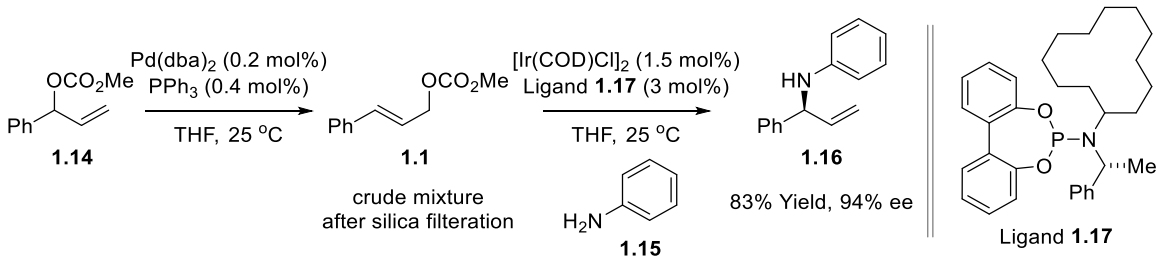
Scheme 1.3 Iridium Catalyzed Enantioselective Allylic Amination to Form Highly Functionalized Chiral Branched Amines.

In 2004, Helmchen reported the iridium catalyzed regio- and enantioselective allylic amination of linear dienyl carbonates (Scheme 1.3).[10] Using iridium catalysts modified by a chiral phosphoramidite ligand, excellent levels of regio- and enantioselectivity of highly functionalized branched amines were observed. One year later, it was shown that the loading of the iridium catalyst could be decreased with the use of catalytic amounts of Pb(II) salts and tetrahydrothiophene (THT). These additives were effective in helping to vacate coordination sites at the iridium complex, allowing for oxidative addition of allylic proelectrophiles and significantly enhancing reaction rate.[11]

In 2005, using an iridium pre-catalyst and the chiral phosphoramidite ligand **1.13** developed by Alexakis,[12] Helmchen reported an enantioselective allylic amination of sulfonamides in good yields with high regio- and enantioselectivity, although reactions with alkyl-substituted allylic proelectrophiles yielded incomplete regioselectivities (Scheme 1.4).[13] Use of base to generate anionic *N*-nucleophiles resulted in slightly higher yields and enantioselectivities. A year later, the scope of these conditions was extended with the use of phthalimide and *ortho*-nosylamine as nucleophiles.[14] The allylic amine products can be readily transformed into enantiomerically enriched primary amine hydrochloride salts. This method was later extended to other carboxamide for the asymmetric synthesis of amino alcohols (not shown).[15]



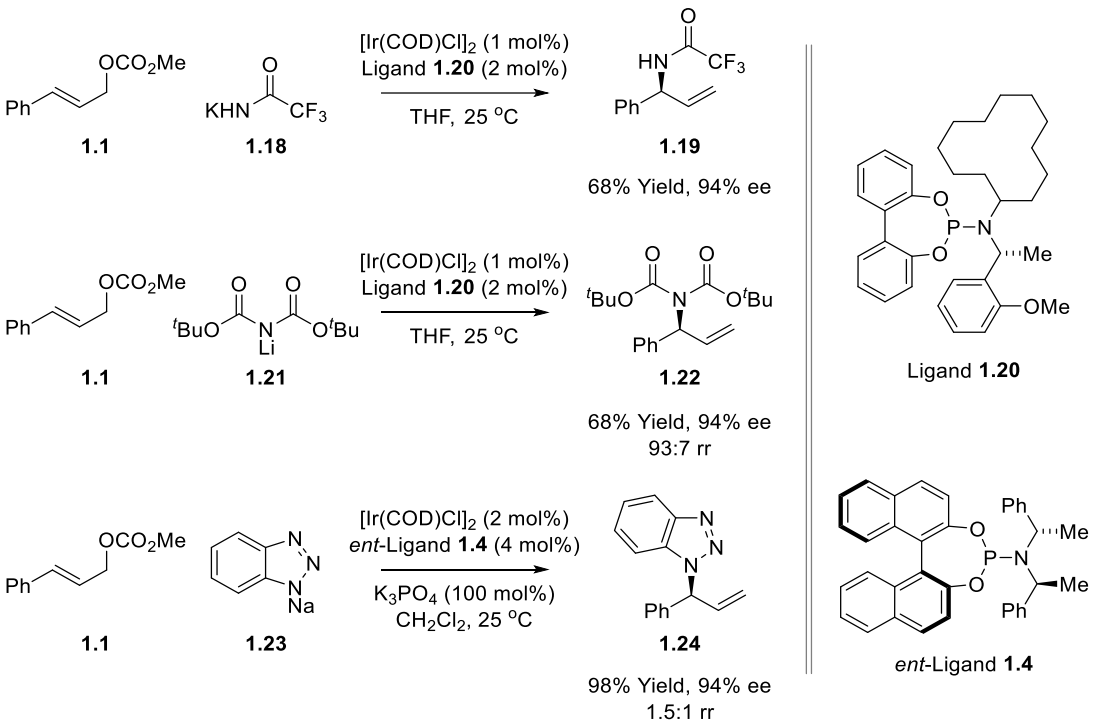
Scheme 1.4 Iridium Catalyzed Enantioselective Allylic Amination with Sulfonamide and Carboxamide.



Scheme 1.5 Sequential Catalytic Isomerization and Enantioselective Allylic Amination.

In 2006, Hartwig reported a sequential, two catalytic process using a palladium catalyst and then an iridium catalyst modified by the phosphoramidite ligand **1.17**[16] which was developed to enforce both yield and selectivity (Scheme 1.5).[17] Iridium catalyzed allylic amination with racemic branched allylic proelectrophiles represents a challenge due to low levels of enantioselectivity typically observed.[18] To broaden the scope of electrophiles for this transformation, a sequence of palladium catalyzed isomerization followed by iridium catalyzed allylic amination was developed, allowing

the formation of branched allylic amines in good yields with high regio- and enantioselectivity, using aliphatic and aromatic amines.

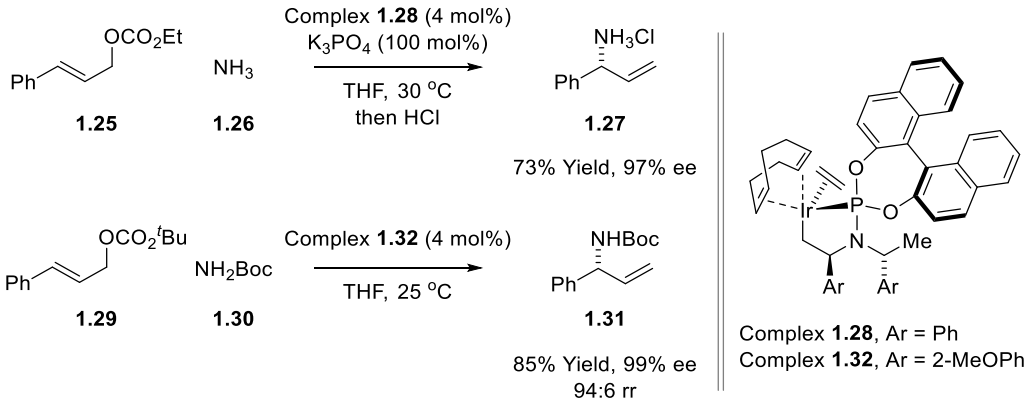


Scheme 1.6 Iridium Catalyzed Enantioselective Allylic Aminations with Premetalated Nucleophiles.

In 2007, Hartwig developed an enantioselective allylic amination using di-tert-butyliminodicarboxylate and trifluoroacetamide as ammonia surrogates to form allylic amines in high yields with good regio- and enantioselectivity (Scheme 1.6).[19] Although the generation of stoichiometric premetalated nucleophiles and metallic byproducts, from treatment of amide with stoichiometric potassium and lithium salts was inevitable, the resulting products could be easily transformed to the enantiomerically enriched allylic carbamates or primary amines. In an analogous manner, the enantioselective allylic amination of sodium benzotriazolide was reported by Zhao in 2012.[20] Using an iridium

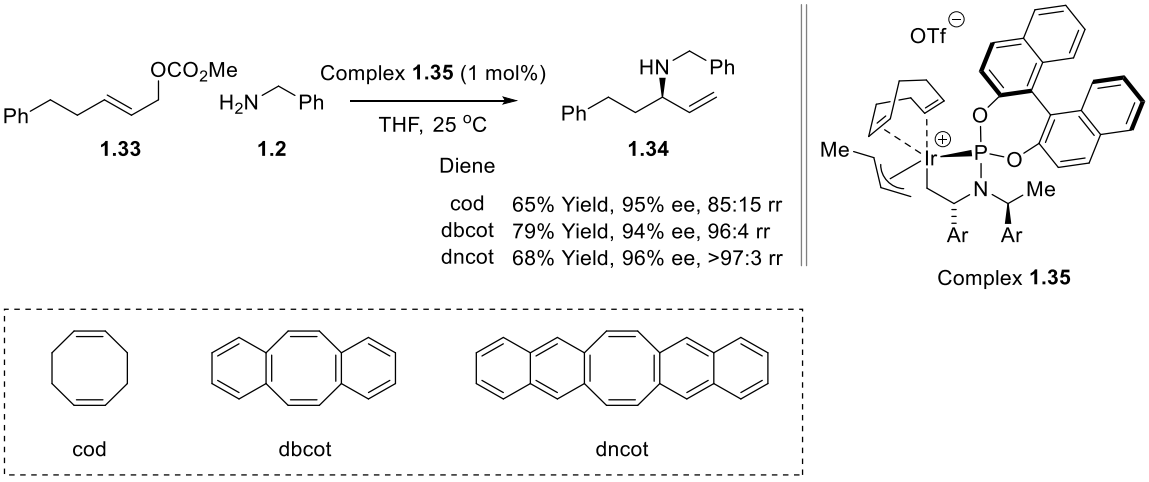
catalyst modified by a Feringa ligand, excellent yields and enantioselectivity were observed, although the branched N1 and N2 regioselectivities were modest.

A few years later, to streamline such stepwise processes, the direct allylation of ammonia and primary carbamates were disclosed (scheme 1.7).[21] Enantioselective monoallylation of ammonia generally poses an intrinsic limitation for two reasons. First, an ammonia molecule bounded to a metal complex is no longer catalytically competent. These ammonia molecules can displace chiral ligands around the metal, resulting in the formation of an achiral complex. Second, the monoallylated product is more nucleophilic than ammonia, which promotes further allylation. Using ethylene ligated cyclometalated iridium catalysts modified by a chiral phosphoramidite ligand, which are stable to excess ammonia, both aryl and alkyl-substituted allylic carbonates react with ammonia to form monoallylation products in good yields with excellent levels of enantioselectivity. In an analogous manner, primary carbamates also participate in enantioselective iridium catalyzed allylic aminations.[22]



Scheme 1.7 Iridium Catalyzed Enantioselective Monoallylation of Ammonia and Primary Carbamate.

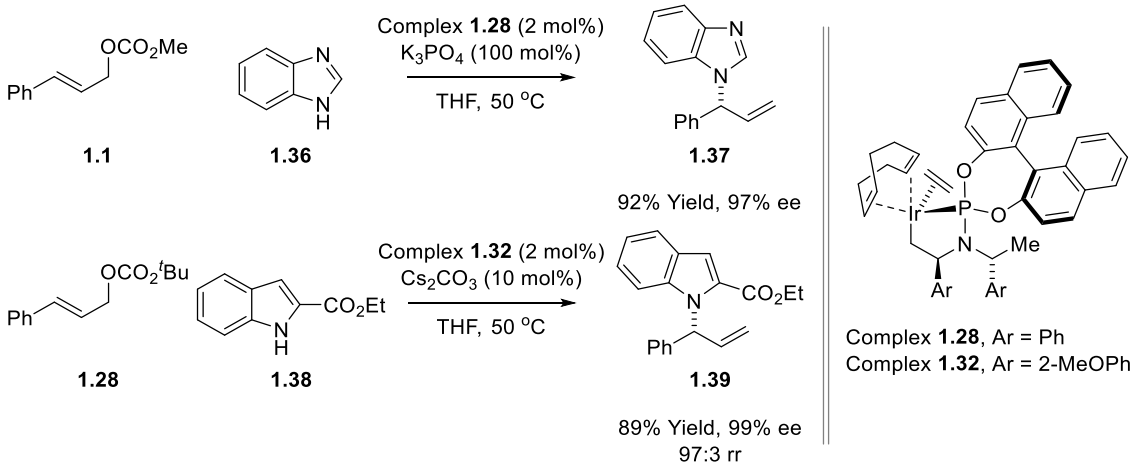
Throughout extensive studies towards enantioselective allylic aminations, it has been found that the most active iridium catalyst species are those generated from $[Ir(COD)Cl]_2$ and chiral phosphoramidite ligands with the use of bases (DABCO, TBD or $^{n}PrNH_2$). However, formation of the cyclometalated iridacycle is very sensitive to the presence of either oxygen or water. To address these issues, air stable iridium catalysts derived from a chiral phosphoramidite ligand and dibenzo[a,e]cyclooctatetraene (dbcot), which displays strong binding affinity to iridium, were reported by Helmchen in 2008.[23] Taking advantage of this air stable catalyst, which avoids the need for Schlenk techniques and requirement for an inert atmosphere, Nelson and Marsdena reported iridium catalyzed allylic amination reactions of highly functionalized amines. The resulting products have the physicochemical properties, which can be useful drug-like space (Not shown).[24] In 2013, You reported an air stable iridium complex derived from dinaphthocyclooctatetraene (dncot) and a phosphoramidite ligand (Scheme 1.8).[25] Remarkably, using the more stable iridium catalysts derived from dbcot and dncot,



Scheme 1.8 Air Stable Iridium Catalysts Derived from Other Diene Ligands.

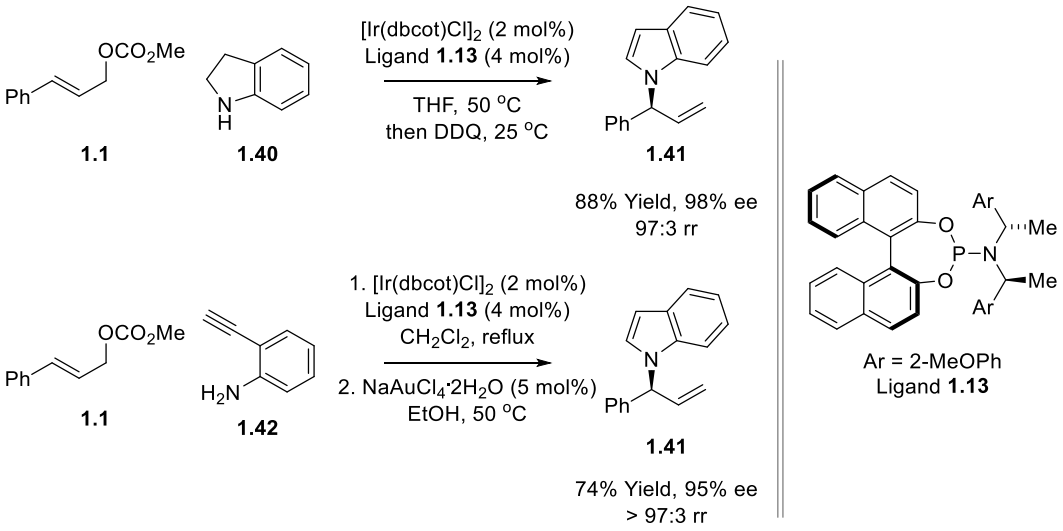
regioselectivity was considerably improved for substrates which showed incomplete regioselectivity from the cod complex.

In 2009, Hartwig reported an iridium catalyzed enantioselective *N*-allylation of imidazole, benzimidazole, and purine heterocycles (Scheme 1.9).[26] Using an ethylene ligated cyclometalated iridium complex that was proven effective for such transformations,[8] high yields and good to excellent levels of regio- and enantioselectivities were observed. Notably, the process was deployed for the formal synthesis of a JNK3 inhibitor, which represents the utility of enantioselective allylic amination in synthesis applications. This method was later extended to the use of indoles.[27] In general, the C3 position of indole is the most reactive site for electrophilic aromatic substitution, which poses intrinsic challenges to undertake *N*-substitution due to largely weak acidity of N-H. In this process, installing electron withdrawing groups on the indole core increases the acidity of N-H, enabling enantioselective *N*-allylation of indoles with high regio- and enantioselectivity, although incomplete regioselectivity of alkyl-substituted allylic carbonates was observed.

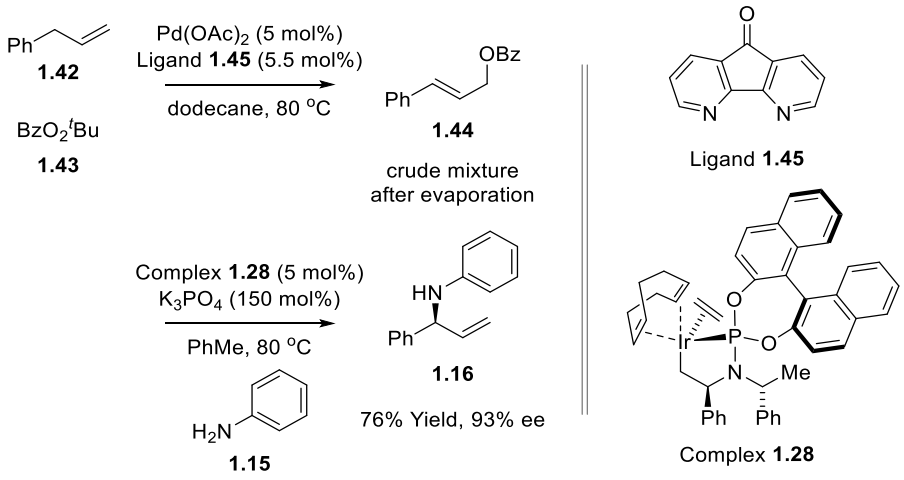


Scheme 1.9 Iridium Catalyzed Enantioselective Allylic Amination with Indoles and Azoles.

In 2012, You developed the synthesis of *N*-allylindoles through a one-pot reaction involving an iridium catalyzed enantioselective allylic amination of indoline, followed by DDQ mediated oxidation (Scheme 1.10).[28] Using iridium catalysts, which were proven effective as more stable iridium species,[23] indoline reacts with allylic carbonates and the subsequent oxidation forms α-chiral indole derivatives with excellent levels of regio- and enantioselectivity, although incomplete regioselectivity upon use of alkyl-substituted allylic proelectrophiles was observed. Two years later, to broaden scope of indole derivatives, You disclosed another approach to the synthesis of enantiomerically enriched *N*-allylindoles.[29] *N*-allylation of 2-(phenylethynyl)aniline in the presence of an iridium catalyst modified by a chiral phosphoramidite ligand, followed by a gold catalyzed cyclization reaction, led to the enantiopure indole derivatives in good yields with high regio- and enantioselectivities.

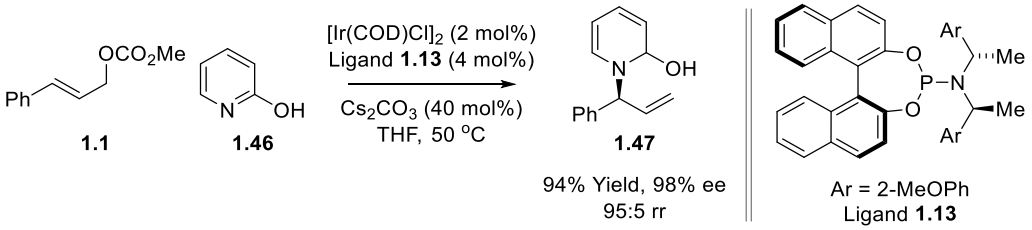


Scheme 1.10 Iridium Catalyzed Enantioselective Allylic Aminations to Form α-Chiral Indole Derivatives.



Scheme 1.11 Sequential Allylic C-H Functionalization and Enantioselective Allylic Amination.

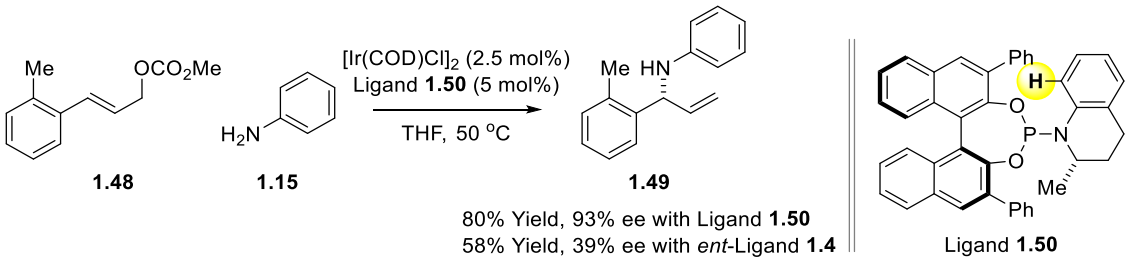
In 2013, Hartwig reported a sequence of two catalytic processes: allylic C–H functionalization and allylic amination (Scheme 1.11).[30] Using 4,5-diazafluorenone as a ligand, which reportedly promotes allylic C-H acetoxylation,[31] and using *tert*-butyl perbenzoate as the oxidant and source of the benzoate group, the linear allylic ester was formed with a high linear-to-branched ratio. Subsequent allylic amination provides *α*-branched chiral allylic amines using both aliphatic and aromatic amines, and azoles.



Scheme 1.12 Regio- and Enantioselective Synthesis of *N*-Substituted 2-Pyridones.

In 2015, You reported an enantioselective allylic amination of 2-pyridones (Scheme 1.12).[32] Despite competition between *O*- and *N*-alkylation when using iridium catalysts modified by an Alexakis ligand, high levels of regio- and enantioselectivity were achieved for *N*-allylated 2-pyridones.

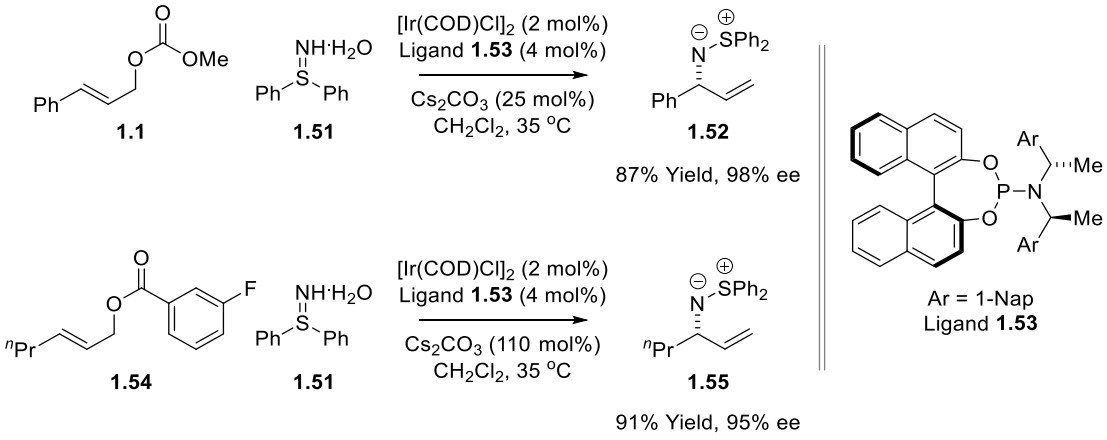
In 2016, You developed iridium catalyzed enantioselective allylic aminations with a *N*-aryl phosphoramidite ligand (Scheme 1.13).[33] In general, iridium catalysts modified by a Feringa type ligand provide excellent regio- and enantioselectivity for a variety of substrates, although *ortho*-substituted phenyl allylic proelectrophiles were found to lead to a decrease in either yield or regio- and enantioselectivity in many cases. To address this issue, a series of *N*-aryl phosphoramidite ligands were identified that provided superior results to previously reported asymmetric allylic aminations of *ortho*-substituted cinnamyl carbonates. Presumably, the cyclometalated iridium complex formed through C-H (indicated in Scheme 1.13) activation of the ligand **1.50** is less sterically hindered in comparison with those derived from a Feringa type ligand, leading to high regio- and enantioselective control of diverse substrates containing sterically congested nucleophiles.



Scheme 1.13 Enantioselective Allylic Amination with *N*-Aryl Phosphoramidite Ligands.

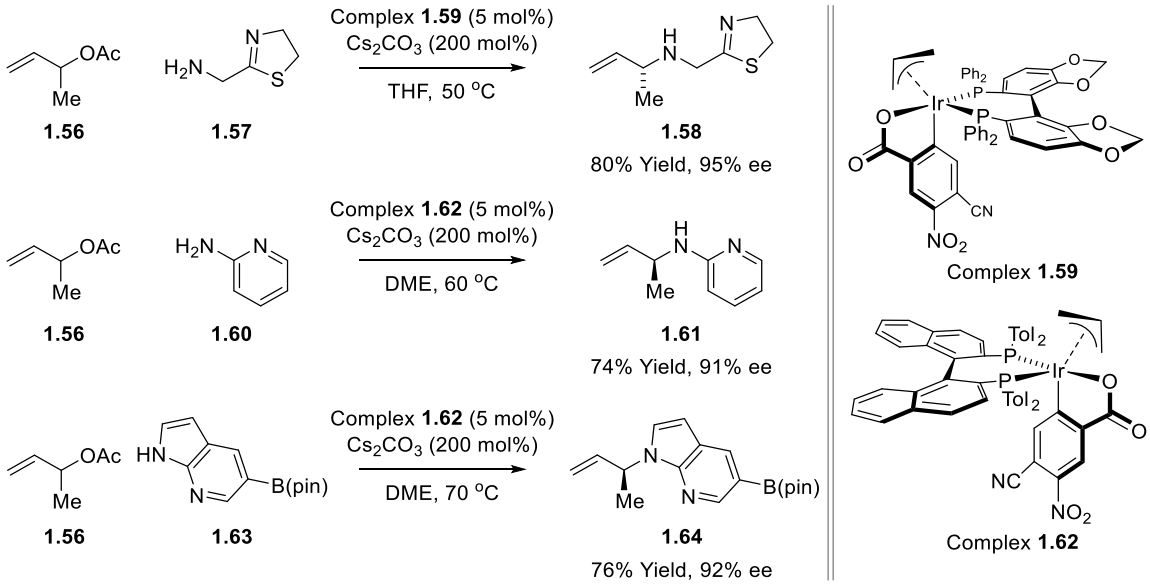
1.2.2 Allylic Ester

In 2015, Evans reported a highly regio- and enantioselective allylic amination of the sulfur stabilized aza-ylide, diphenylsulfilimine (Scheme 1.14).[34] An iridium complex modified by ligand **1.53** catalyzed the formation of chiral allylic sulfilimines, which readily undergo cleavage with acid to afford enantiomerically enriched primary amine hydrochloride salts. Whereas carbonate leaving groups are generally used with aryl-substituted allylic proelectrophiles for high regio- and enantioselectivity, allylic benzoate electrophiles enforce both improved reactivity and selectivity for alkyl substituents.



Scheme 1.14 Enantioselective Iridium Catalyzed Allylic Aminations of Diphenylsulfilimine.

In 2018, the Krische group found that neutral π-allyliridium *C,O*-benzoates modified by SEGPHOS, which are well-known to catalyze nucleophilic carbonyl allylations,[35] promote highly regio- and enantioselective allylic aminations of branched allylic acetates bearing linear alkyl groups using primary aliphatic amines (Scheme 1.15).[36] Whereas the iridium phosphoramidite catalyzed allylic substitutions occur by way of cationic π-allylmetal intermediates, these π-allyliridium-*C,O*-benzoates react by



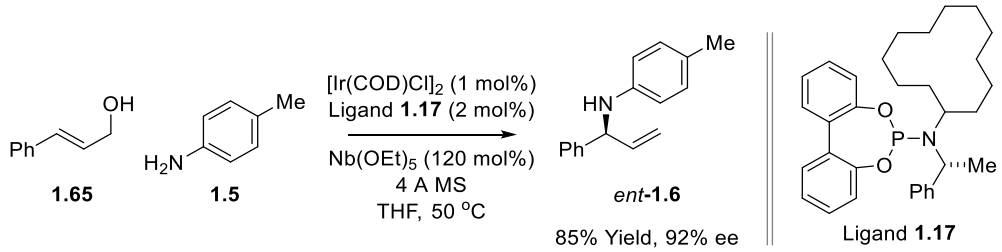
Scheme 1.15 Enantioselective Iridium Catalyzed Electrophilic Allylations of Alkyl-Substituted Allylic Acetates.

way of neutral π-allylmetal intermediates, which may account for their amphiphilic character. Notably, these aminations enable complete branched regioselectivity, overcoming a significant limitation associated with previously reported iridium-phosphoramidite catalysts, which display incomplete regioselectivity for alkyl-substituted allylic proelectrophiles. A year later, Krische showed that the corresponding tol-BINAP-modified iridium catalyst provides a significant expansion in scope, enabling highly enantioselective aminations of branched alkyl-substituted allylic acetates with electronically diverse primary and secondary aryl amines, including site-selective reactions of bis(amine) nucleophiles.[37] Mechanistic studies involving amination of the enantiomerically enriched, deuterium labeled acetate corroborates C-N bond formation *via* outer-sphere addition. Remarkably, the tol-BINAP-modified iridium *C,O*-benzoates catalyze highly enantioselective *N*-allylations of indoles and related azoles.[38] This

reaction complements previously reported metal catalyzed indole allylations, enabling complete levels of *N*- *versus* C3-, and branched *versus* linear regioselectivity.

1.2.3 Allylic Alcohol

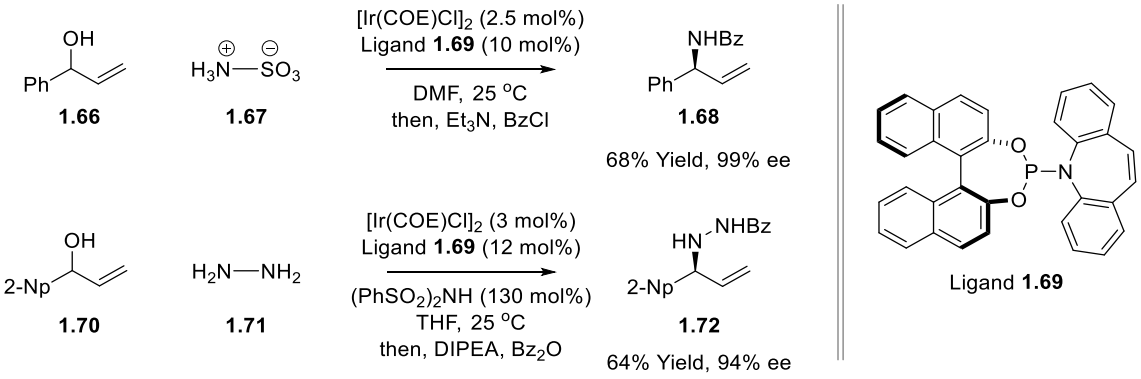
Whereas significant progress has been made in the formation of chiral allylic amines *via* iridium catalyzed allylic amination of allylic carbonate and ester, the use of allylic alcohols remains a challenge. Generally, these allylic proelectrophiles are made from the corresponding allylic alcohol; hence, direct use of allylic alcohols could streamline synthetic sequences. In 2007, Hartwig reported an enantioselective allylic amination with allylic alcohols (Scheme 1.16).[39] Using niobium ethoxide or triphenyl borane as an activator of the allylic alcohol, iridium catalysts modified by the ligand **1.17** formed branched allylic amines with high regio- and enantioselectivity, using primary and secondary aliphatic amines, and aryl amines.



Scheme 1.16 Enantioselective Allylic Aminations of Allylic Alcohols Activated by Lewis Acids.

A new approach to allylic amination was discovered in 2007 by the Carreira group.[40] Branched allylic alcohols have excellent reactivity under acidic conditions. With the use of iridium complex modified by phosphine-olefin ligands, branched allylic amines were formed regioselectively. Compared to iridium-phosphoramidite systems derived

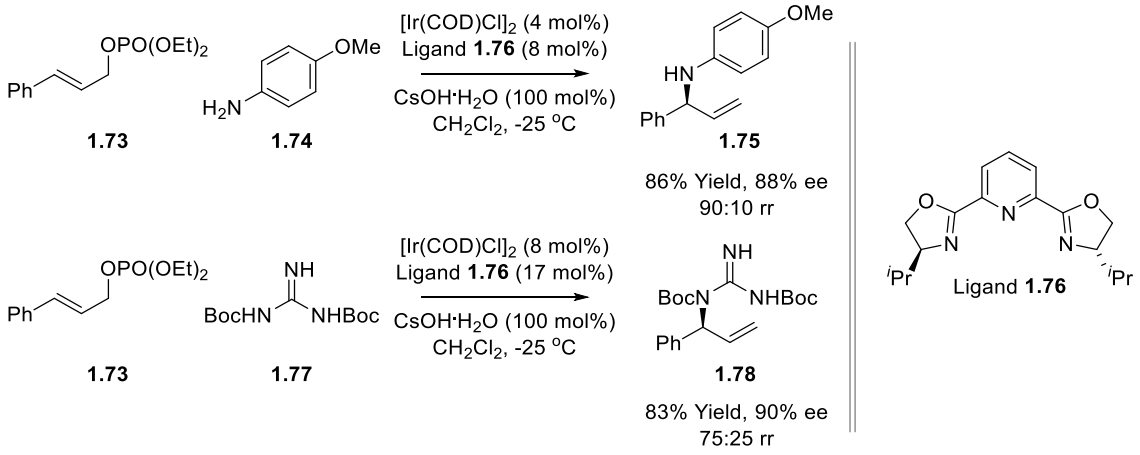
from a Feringa type ligand, the η^3-allyliridium complex derived from two phosphine-olefin ligands is more electrophilic in character, which enables highly facile electrophilic allylic substitution. Subsequent to these efforts, an enantioselective allylic amination of racemic secondary allylic alcohols was achieved in 2012 by Carreira (Scheme 1.17).[41] Chirally modified phosphine-olefin ligands were used, which allow the reaction to occur in a non-stereospecific fashion, probably due to displacement of the π-bond of (σ+π)-allyl (enyl) iridium intermediates by the tethered olefin of the phosphoramidite ligand. A diverse range of protected chiral allylic amines, all with high regio- and enantioselectivity, was observed. In 2019, Carreira demonstrated highly reactive or unstable nucleophiles such as hydrazines or *N*-hydroxylamines also participated in the enantioselective allylic amination reactions.[42] While numerous transition metal catalyzed reactions require anhydrous systems to maintain their efficiency, utilizing commercially available aqueous solutions of these unstable molecules as nucleophiles is a significant advance.



Scheme 1.17 Enantioselective Allylic Aminations by Iridium Complex Modified by Chiral Phosphine-Olefin Ligands.

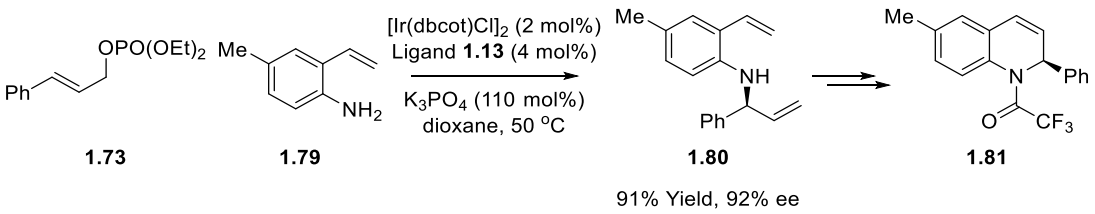
1.2.4 Allylic Phosphate

Whereas the pioneering reactions of enantioselective allylic substitution to form chiral branched allylic amines was catalyzed by an iridium-phosphoramidite complex, Takemoto applied a chiral Pybox ligand to the enantioselective allylic aminations of allylic phosphates in 2004 (Scheme 1.18).[43] Using an iridium catalyst modified by a chiral Pybox ligand, the chiral branched product was isolated with good yield and enantioselectivity. Notably, 1-naphthyl-substituted allylic proelectrophile could improve regioselectivity up to >95:5 branched to linear ratio. This method was later extended to the use of guanidines.[44] With electron withdrawing groups on the guanidines, products of monoallylation were observed in good yield with high enantioselectivity, albeit with lower levels of regiocontrol.



Scheme 1.18 Enantioselective Allylic Aminations of Allylic Phosphate Proelectrophiles with Iridium Pybox Complexes.

In 2011, You and Helmchen reported enantioselective allylic aminations of allylic phosphates with *ortho*-amino styrenes (Scheme 1.19).[45] Due to the highly electrophilic π-allyl iridium complex, sequential allylic vinylation and amination reactions were inevitable. To suppress the undesired pathway, the allylic phosphate was exploited, which led to exclusive *N*-allylation of amino styrenes with excellent levels of chemo-, regio-, and enantioselectivity. Notably, the amination product was transformed into 1,2-dihydroquinolines, which are a structural motif found in numerous bioactive molecules.



1.73 **1.79** **1.80** **1.81**

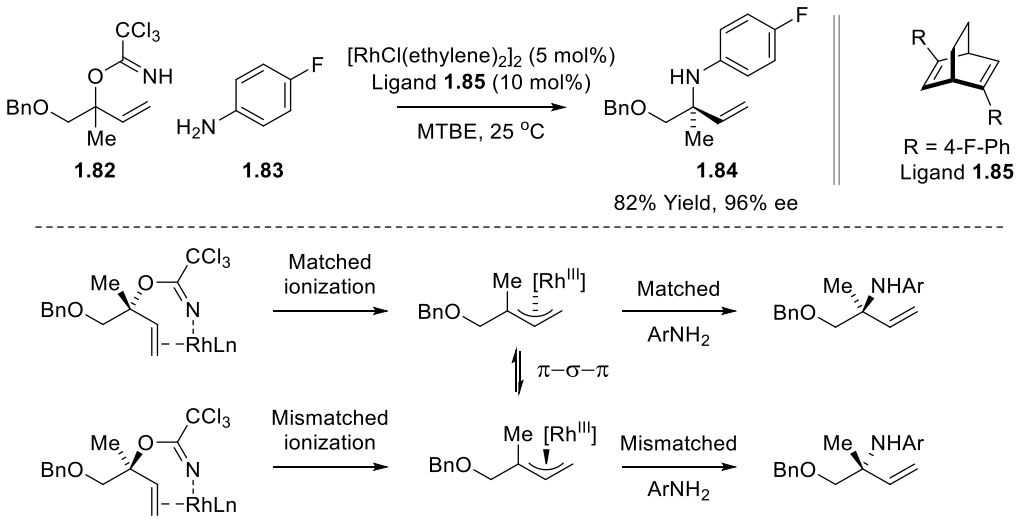
91% Yield, 92% ee

Scheme 1.19 Iridium Catalyzed Enantioselective Allylic Aminations with Allylic Phosphates.

1.3 Intermolecular Rhodium Catalyzed Enantioselective Allylic Amination

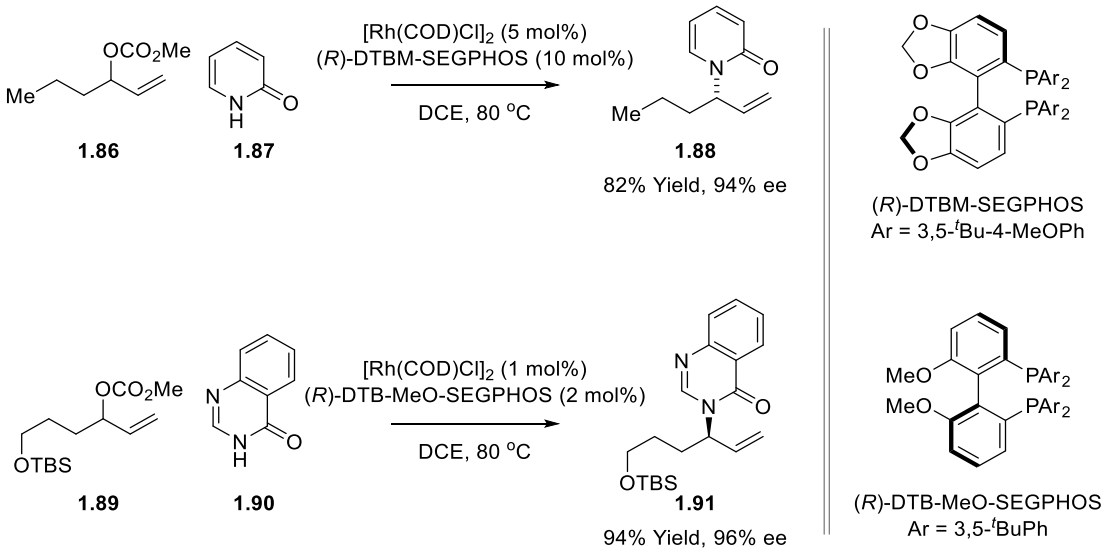
1.3.1 Allylic Derivatives

In 2012, Nguyen reported rhodium catalyzed regio- and enantioselective aminations of racemic tertiary allylic trichloroacetimidates with aryl amines *via* dynamic kinetic asymmetric transformation (DYKAT) (Scheme 1.20).[46] Whereas rhodium catalyzed allylic substitutions of allylic derivatives to form chiral allylic amines have largely focused on stereospecific processes[47] or kinetic resolution[48], a rhodium catalyst modified by a chiral diene ligand allows the formation of branched chiral allylic amines using racemic secondary allylic carbonates and a wide range of aniline nucleophiles.[49-52] DYKAT of tertiary allylic trichloroacetimidates promotes ionization of the allylic proelectrophile to form diasteromeric π-allylrhodium species. The matched π-allylrhodium intermediates enable facile substitution by anilines to form the preferred enantiomer of the product whereas a chirally modified rhodium complex could decrease the rate of nucleophilic attack by anilines, allowing rapid π-σ-π interconversion.



Scheme 1.20 Rhodium Catalyzed Formation of Enantiomerically Enriched Allylic Amines Bearing *α*-Tetrasubstituted Tertiary Carbons.

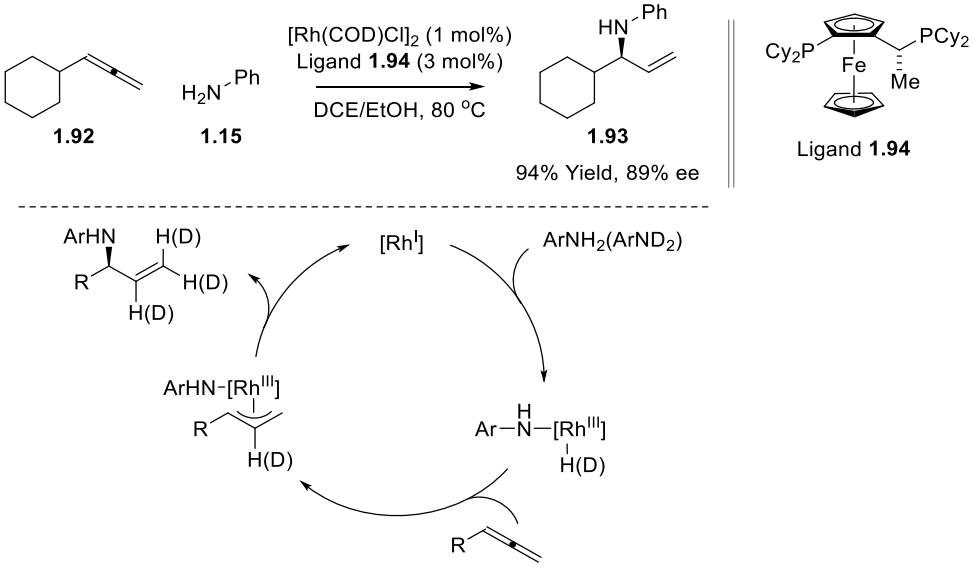
In 2016, Breit reported rhodium catalyzed dynamic kinetic asymmetric allylations of 2-hydroxypyridines with alkyl-substituted allylic carbonates (Scheme 1.21).[53] The combination of a rhodium catalyst with chiral DTBM-SEGPHOS ligand led to excellent levels of asymmetric induction for the *N*-allylation of 2-hydroxypyridines. The collective data corroborate a mechanism involving rhodium(I)-mediated allylic carbonate oxidative addition, which operates through a formal S_N2' mechanism to form a σ-allylrhodium complex. Releasing methanol and CO_2, the phenolate bound π-allylrhodium complex undergoes reductive elimination to form the *N*-selective allylation product. A year later, this was extended to the use of quinazolinones.[54] Using a rhodium catalyst modified by DTB-MeO-BIPHEP, quinazolinones reacted with both alkyl- and aryl-substituted allylic carbonates to form enantiomerically enriched allylic amines in good yields with high regio- and enantioselectivity, which was applied in the enantioselective formal synthesis of (-)-chaetominine.



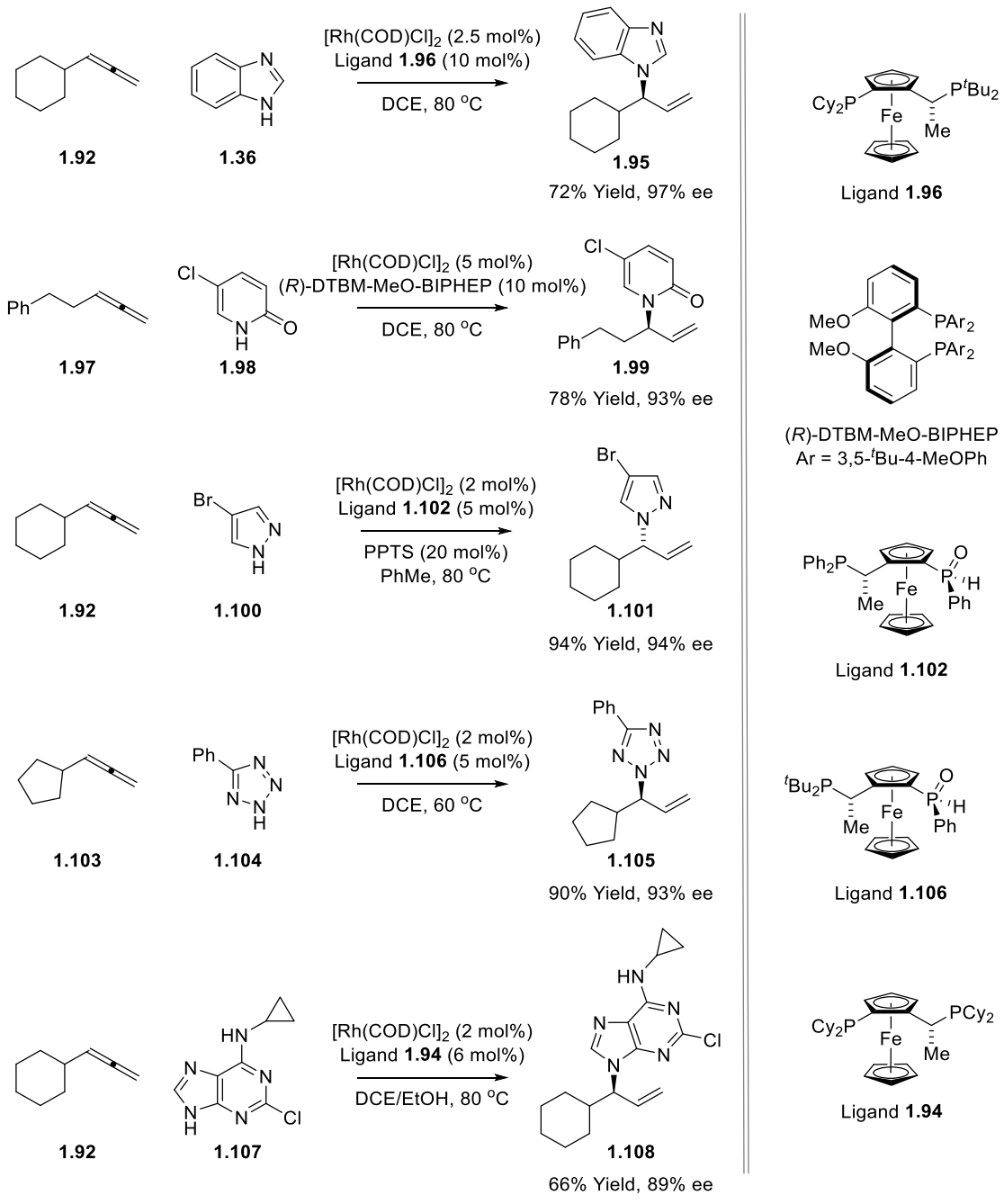
Scheme 1.21 Enantioselective Synthesis of Branched Allylic Amines *via* Rhodium Catalyzed Allylic Substitution.

1.3.2 C-H Functionalization

Formation of *α*-chiral allylic amines *via* enantioselective hydroamination is a highly attractive and atom economical approach. In 2012, Breit reported an enantioselective rhodium catalyzed synthesis of chiral allylic amines (Scheme 1.22).[55] Using a rhodium catalyst modified the Josiphos ligand **1.94**, cyclohexylallene reacts with a variety of anilines to form chiral allylic amines. The proposed mechanism involves a rhodium(I)-mediated aniline oxidative addition followed by reversible hydrometallation of the terminal allene double bond to form a π-allylrhodium complex, which upon reductive elimination releases the branched allylic amine. This method was later extended to the use of imidazoles,[56] 2-pyridones,[57] 4-pyridones,[58] pyrazoles,[59] purines,[60] tetrazoles,[61] 2-aminothiazoles,[62] and pyridazineones,[63] leading to regio-, chemo- and enantioselective *N*-allylation of these heterocycles, which are all useful building blocks for natural products and pharmaceuticals (Scheme 1.23).

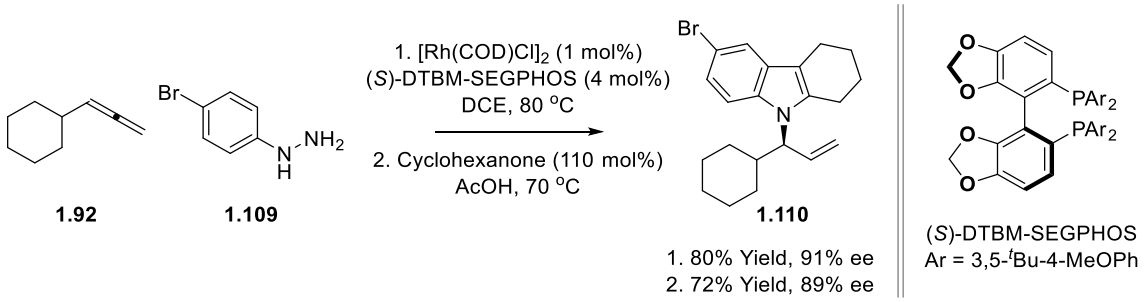


Scheme 1.22 Enantioselective Synthesis of Branched Allylic Amines *via* Rhodium Catalyzed Hydroamination.



Scheme 1.23 Rhodium Catalyzed Enantioselective Synthesis of Branched Allylic Amines Using a Variety of Nucleophiles.

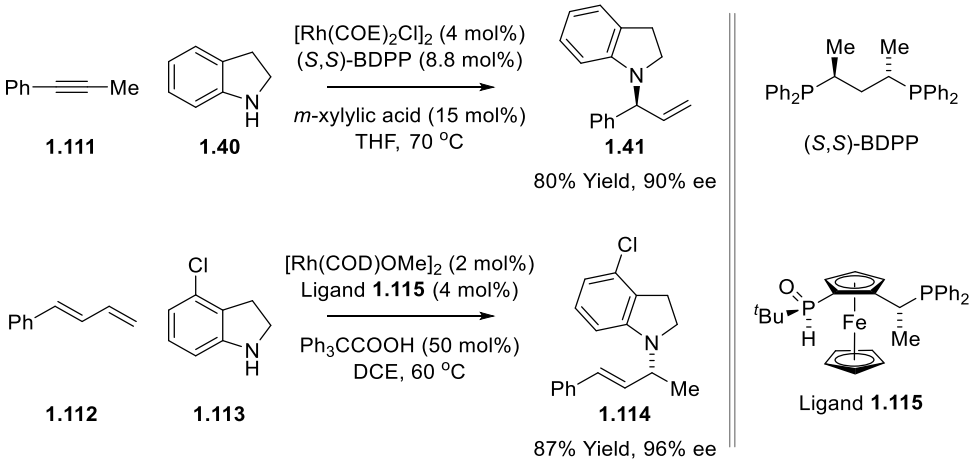
In 2016, Breit developed a one-pot procedure for an enantioselective synthesis of indole derivatives (Scheme 1.24).[64] Using a rhodium catalyst modified by DTBM-SEGPHOS, various aryl hydrazines were coupled with terminal allenes, generating selective *N*-allylated hydrazines. The more acidic N-H bond at N1 compared to N2 promotes facile oxidative addition to the rhodium complex, which could differentiate nitrogen selectivity. Products through regio- and enantioselective allylation of aryl hydrazines were subjected to Fischer indolization, allowing the construction of α-chiral indole derivatives with high yields and enantioselectivity.



Scheme 1.24 Sequential Allylic C-H Functionalization and Fischer Indole Synthesis.

On the basis of Breit's prior observation that alkyne could serve as precursors to form π-allylrhodium species,[65] a rhodium catalyzed enantioselective coupling of indolines with internal alkyne using a rhodium catalyst modified by JoSPOphos was reported by Dong in 2015 (Scheme 1.25).[66] An allene intermediate was formed *via* rhodium hydride mediated alkyne isomerization, which upon hydroamination releases allylic amines instead of the enamine or imine product which are competing side products of alkyne mediated hydroamination. It was found that acidic additives play a key role to afford high regioselectivity of branched allylic amines in good yields with high enantioselectivity. Two years later, Dong disclosed a method for the hydrofunctionalization of 1,3-dienes

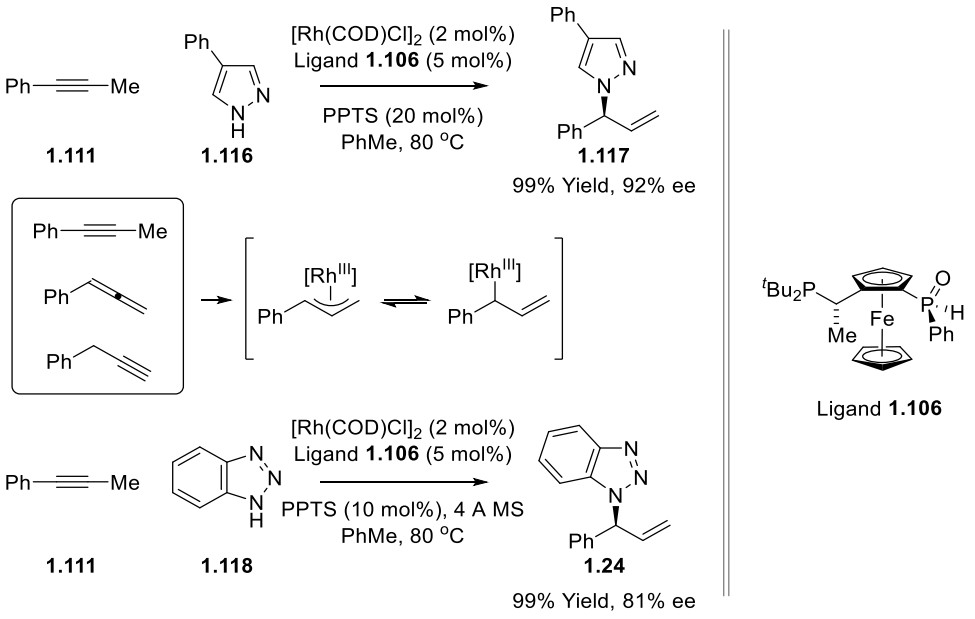
with indolines.[67] It was found that conjugated dienes could generate analogous π-allylrhodium complexes which are typically generated by hydrometallation of an allene or alkyne. Using a rhodium catalyst modified by JoSPOphos, the enantioselective coupling of indolines with 1,3-dienes afforded *N*-allylated indolines with good yields along with high regio- and enantioselectivity was reported.



Scheme 1.25 Rhodium Catalyzed Hydrofunctionalization to Form Chiral Allylic Amines.

In 2016, Breit developed a regio- and enantioselective allylic amination of pyrazoles with internal alkynes in an atom-economic manner using a rhodium catalyst modified by JosPOphos (Scheme 1.26).[68] The reaction displays a broad substrate range of substituted pyrazoles and alkynes to provide chiral pyrazole derivatives in good yields along with good regio- and enantioselectivities. To note, both allenes and terminal alkynes also participate in the enantioselective synthesis of branched allylic amines which represents a highly flexible approach *via* an interconverting π-allyl and σ-allyl haptomers from allenes, internal and terminal alkynes. In a similar manner, Breit

expanded the scope of internal alkyne with triazoles while the synthesis of *N*-allylated trizoles in combination with the desired *N*-selectivity, high branched regio- and enantioselectivity remains uncommon. Using a modified rhodium catalyst with JoSPOphos ligand, good yields, and modest to good level of regio- and enantioselectivity were observed.[69]



Scheme 1.26 Rhodium Catalyzed Hydrofunctionalization to Form Chiral Allylic Amines *via* Alkyne Isomerization.

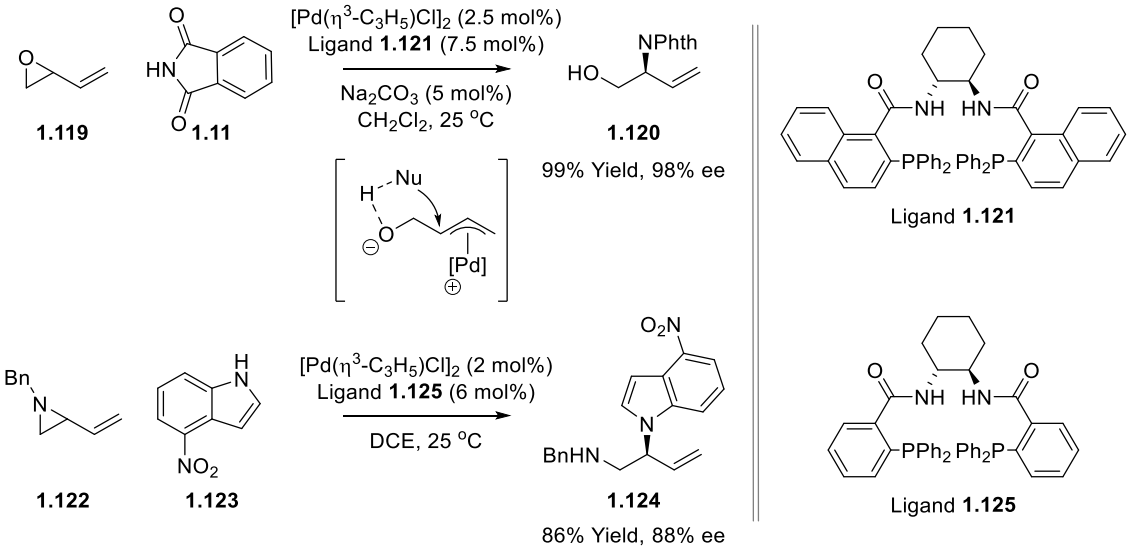
1.4 Intermolecular Palladium Catalyzed Enantioselective Allylic Amination

While numerous iridium and rhodium catalyzed allylic aminations of allylic proelectrophiles with one terminal substituent to form branched products with excellent regio- and enantioselectivity have been documented, palladium catalyzed allylic amination forming chiral branched products remains less developed. Here, we mainly

summarized examples of palladium catalyzed allylic amination forming branched products *via* unsymmetrical π-allyl palladium species.

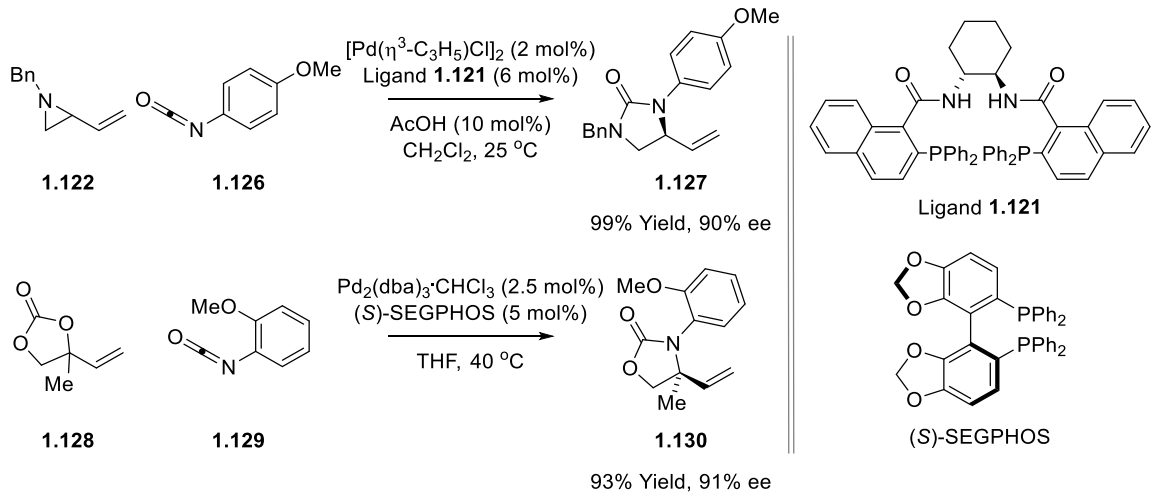
1.4.1 Allylic Epoxide, Aziridine, Cyclic Carbonate and Carbamate

In 2001, Trost performed a dynamic kinetic asymmetric transformation (DYKAT) with commercially available butadiene monoxide (Scheme 1.27).[70] Using a palladium catalyst modified by a Trost type ligand, vinylglycinol products were formed in high yields with excellent regio- and enantioselectivity. Coordination of the pronucleophile to the oxygen leaving group *via* intramolecular hydrogen bond would help to deliver the nucleophile to the adjacent carbon. This allows high levels of the regioselective branched product despite the regio-control problem since nucleophilic attack in such systems are normally favored at the less substituted carbon.[71] This method was later extended to use of a variety of nucleophiles including hydrazines, hydroxylamines, isatin derivatives, and purines (not shown).[72-74] Taking advantage of ring strain to facilitate ring opening, the analogous vinyl aziridines were employed for hetereocycles bearing chiral 1,2-diamines using biologically active pyrroles and indoles.[75] In these processes, the amide anion leaving group in the π-allylpalladium intermediate was sufficiently basic enough to deprotonate the N-H from the nucleophiles and facilitate the transformation. *N*-allylated pyrroles and indoles were observed in good yields with high regio- and enantioselectivity, although a strong electron withdrawing group was necessary to give high levels of both reactivity and enantioselectivity.



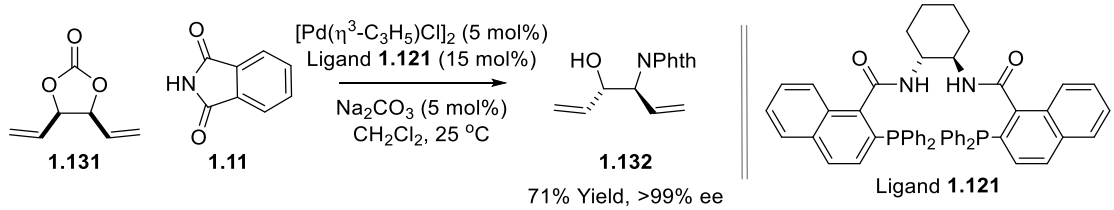
Scheme 1.27 Palladium Catalyzed Dynamic Kinetic Asymmetric Transformation of Butadiene Monoxide and Vinyl Aziridine.

In 2003, Trost disclosed the asymmetric cycloaddition of isocyanates to vinyl aziridines (Scheme 1.28).[76] High yields and enantioselectivities were obtained for a broad array of imidazolidin-2-ones upon use of a palladium catalyst modified by a Trost ligand. To note, acidic additives are required to achieve high enantioselectivity since protonating the nitrogen upon opening of the aziridine which slows the cyclization rate. This allows π-σ-π interconversion of the diastereomeric π-allyl palladium intermediates, which can ultimately compete with product formation. In a similar manner, Zhang recently developed an efficient method for the enantioselective construction of vinylglycinol derivatives bearing *α*-tetrasubstituted tertiary carbons through decarboxylative cycloaddition of vinylethylene carbonates with isocyanates.[77] Using a palladium catalyst modified by SEGPHOS, good yields with good to excellent levels of enantioselectivity were observed.



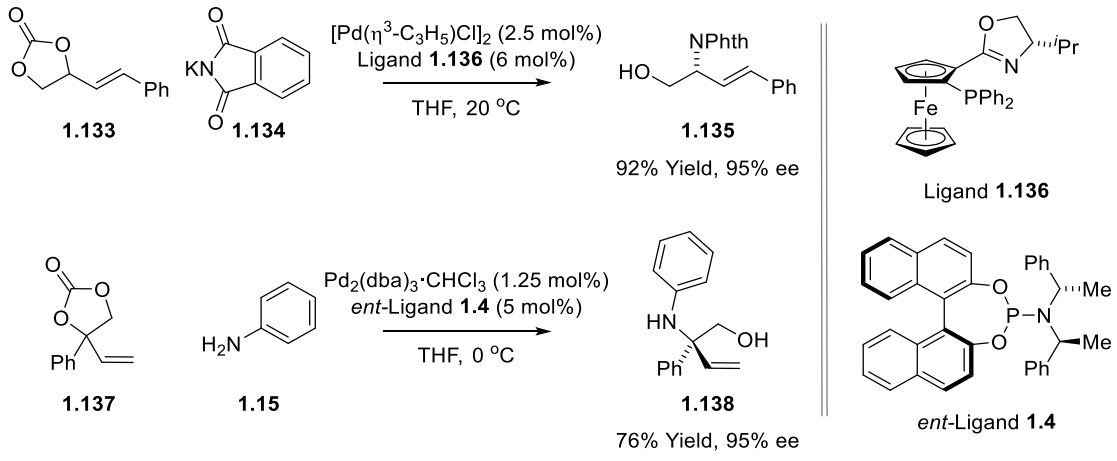
Scheme 1.28 Palladium Catalyzed Dynamic Kinetic Asymmetric Cycloadditions of Isocyanates.

In 2006, Trost reported a palladium catalyzed asymmetric allylic alkylation of *meso*- and *dl*-divinylethylene carbonates (Scheme 1.29).[78] Using a palladium catalyst modified by a Trost ligand, only the *syn*-diastereomer was formed in good yields and high enantioselectivity, which was unexpected based on the well-established double inversion mechanism.[79] Due to the Curtin-Hammett type effects where the rapid and reversible matched ionization is unproductive, mismatched ionization followed by rapid π-σ-π interconversion to relieve steric repulsion between the substrate and asymmetric palladium complex effectively forms the unexpected diastereomer.



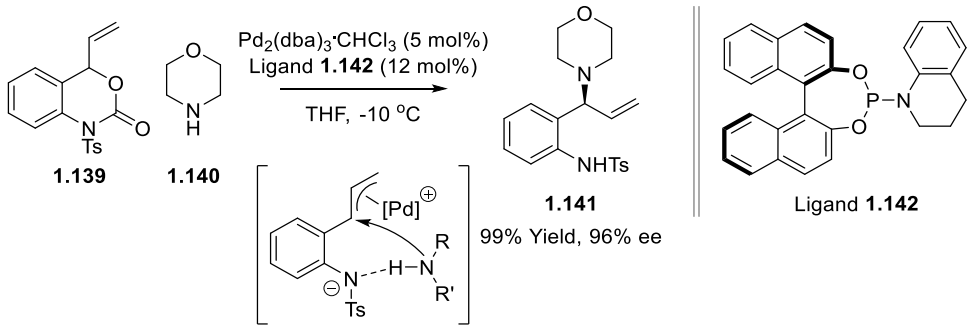
Scheme 1.29 Palladium Catalyzed Enantioselective Allylic Aminations of Divinylethylene Carbonate.

In 2013, Liu and Zhang found an efficient palladium catalyzed allylic amination of vinyl cyclic carbonates followed by the cleavage of phthalimide group, forming a series of chiral *β*-aryl-*α,β*-unsaturated amino alcohols (Scheme 1.30).[80] Using a palladium catalyst modified by a planar chiral ferrocene-based phosphinooxazoline (PHOX) ligand, products with good yields and high regio- and enantioselectivity were shown. In 2016, Kleij reported a palladium catalyzed regio- and enantioselective synthesis of allylic aryl amines bearing *α*-tetrasubstituted tertiary carbons using vinyl cyclic carbonates.[81] The combination of a palladium catalyst and a Feringa chiral phosphoramidite ligand enabled DYKATs where the π-σ-π interconversion occurs faster than the subsequent nucleophilic attack. While it is generally known that palladium catalyzed allylic substitution undergoes through an outer sphere process which leads to formation of linear products, it is demonstrated density functional theory (DFT) calculations and mechanistic studies corroborate chelation assisted amine nucleophilic attack *via* inner sphere process which accounts for experimentally observed branched high regio- and enantioselectivity.[82]



Scheme 1.30 Palladium Catalyzed Enantioselective Allylic Aminations of Vinylic Cyclic Carbonate.

In 2017, Lu reported a palladium catalyzed enantioselective allylic amination of vinyl benzoxazinones (Scheme 1.31).[83] While the branched products in such substrates were usually generated with limited enantiocontrol, presumably due to the steric repulsion between the ortho substituent and the metal complex,[5,14,23,26,33] this protocol using the directing effect of the hydrogen bond presented chiral allylic amines with a variety of aliphatic amines in good yields with excellent regio- and enantioselectivty.

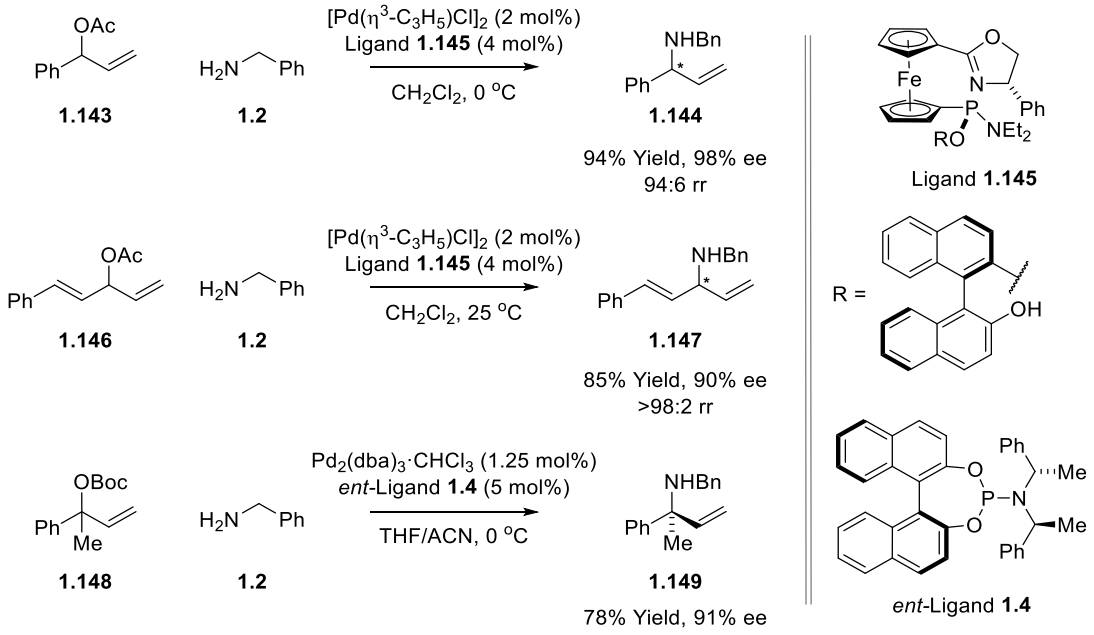


Scheme 1.31 Palladium Catalyzed Enantioselective Allylic Amination of Vinyl Benzoxazinones.

1.4.2 Allylic Ester and Carbonate

In 2001, Hou and Dai reported a palladium catalyzed allylic amination of mono-substituted allylic acetates (Scheme 1.32).[84] Employing a palladium catalyst modified by the ferrocene *P*,*N*-ligand **1.145**, good yields with high regio- and enantioselectivity were observed. In the amination reaction, a hydrogen bond between the amine and the free OH in the ligand might direct intramolecular nucleophilic attack, leading to high levels of regioselective ratio of branched to linear products. It was later found that the ferrocene modified palladium complex was highly efficient for enantioselective allylic aminations of both alkyl- and aryl-substituted dienyl esters.[85] In a similar manner, using a ferrocene

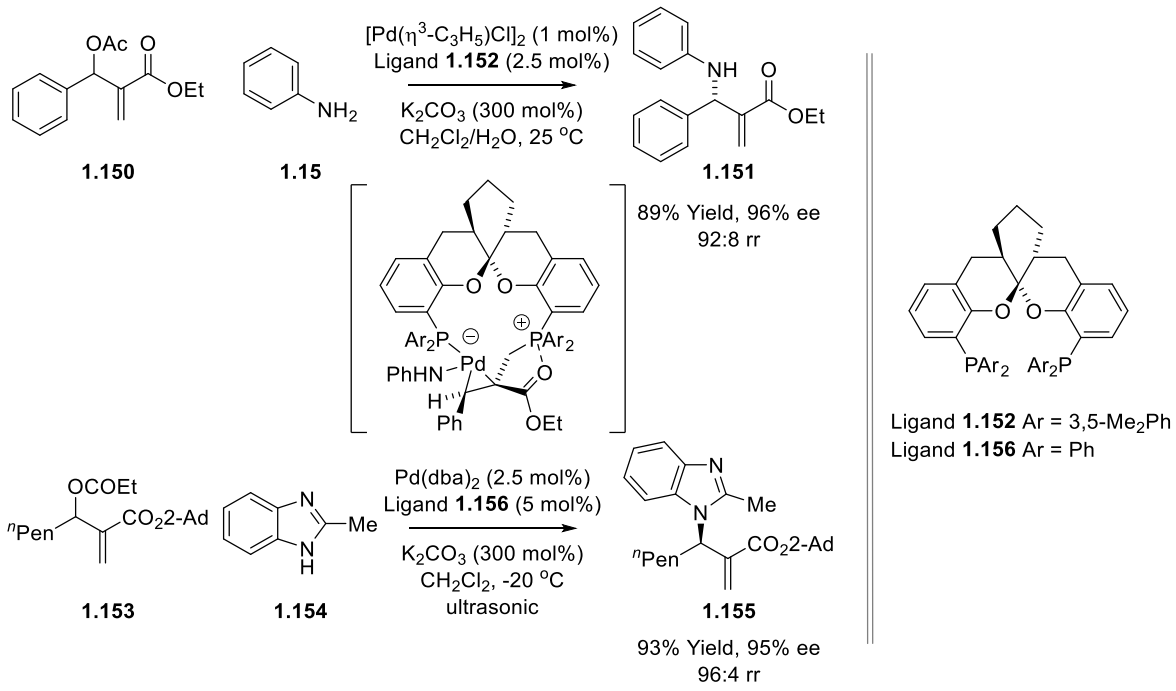
based ligands SIOCPhos, Hou recently reported regio- and enantioselective allylic aminations of mono-substituted allylic proelectrophiles with *N*-Boc-*O*-methylhydroxylamine (not shown).[86] In 2017, Kleij developed a palladium catalyzed allylic amination of allylic proelectrophiles and aliphatic amines, providing allylic amines bearing α-tetrasubstituted tertiary carbons with good regio- and enantioselectivity.[87]



Scheme 1.32 Palladium Catalyzed Enantioselective Allylic Aminations of Allylic Proelectrophiles.

While the formation of branched products at the sterically more hindered position of allylic substrates is challenging in palladium catalyzed transformations, a palladium catalyzed enantioselective allylic amination of acyclic Morita-Baylis-Hillman (MBH) adducts using a variety of anilines as nucleophiles was reported in 2012 by Liu, Wang and Ding (Scheme 1.33).[88] Using a palladium catalyst modified by a spiroketal-based bisphosphine ligand, optically active β-arylamino acid esters were formed in good yields

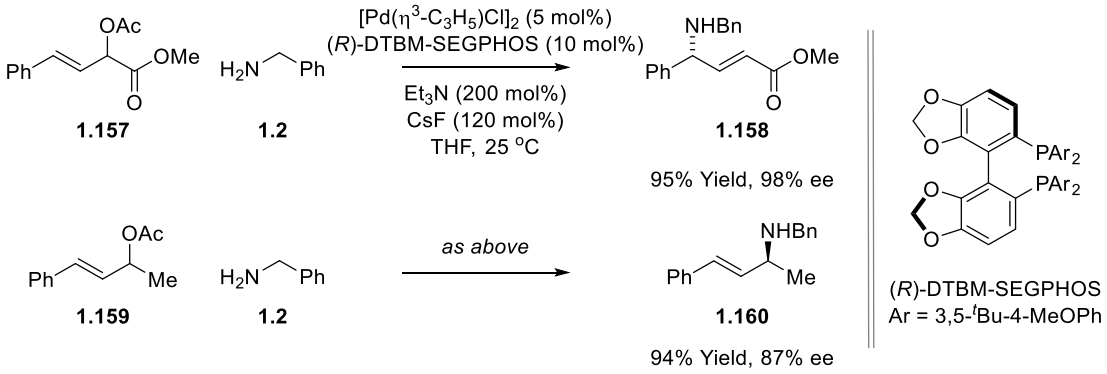
with high regio- and enantioselectivities. Further mechanistic investigation revealed that the ligand plays a bifunctional role in the process: one P atom forms a carbon-phosphine σ-bond with the terminal carbon atom of the allyl moiety, and the other P atom coordinates to palladium, leading to an uncommon regioselective formation of the branched product.[89] This method was later extended to other *N*-heterocyclic nucleophiles, including imidazoles, triazoles and purines, with alkyl-substituted MBH propionate species.[90]



Scheme 1.33 Palladium Catalyzed Enantioselective Allylic Aminations of Racemic Morita-Baylis-Hillman Adducts.

In 2017, Liu and Zhang reported a synthesis of chiral *α,β*-unsaturated *γ*-amino esters *via* enantioselective allylic amination reactions (Scheme 1.34).[91] Using a palladium catalyst modified by DTBM-SEGPHOS, high yields with excellent regio- and

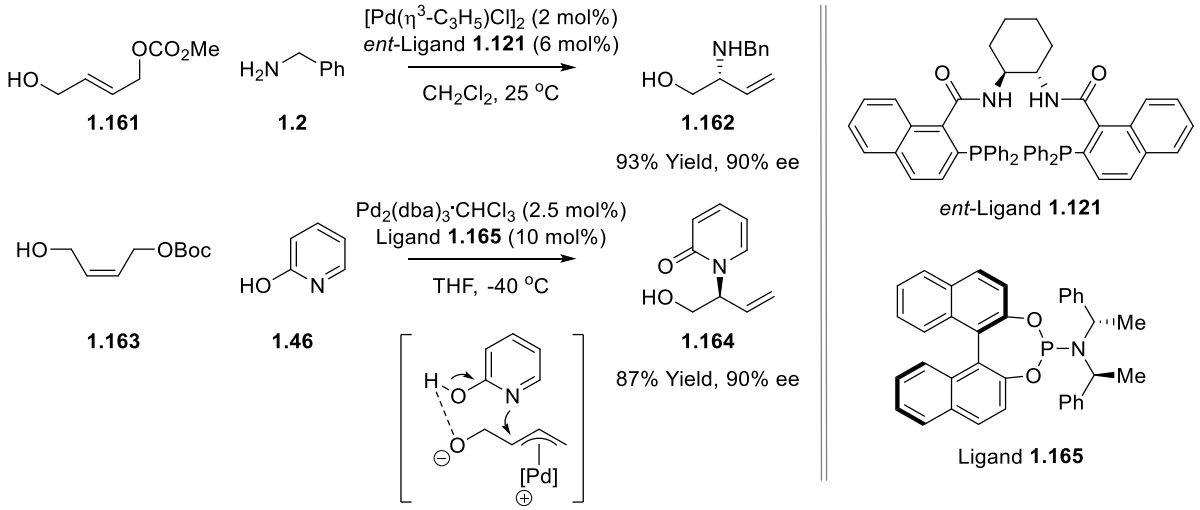
enantioselectivities were observed. Notably, control experiments found that the regioselectivity of aminated products might depend on steric hindrance on the right side of the allyl substrates.



Scheme 1.34 A Palladium Catalyzed Synthesis of Chiral α,*β*-Unsaturated *γ*-Amino Esters.

In 2016, Diaz and Castillon reported a palladium catalyzed asymmetric allylic amination of linear allylic carbonates (Scheme 1.35).[92] Using a palladium catalyst modified by a Trost ligand, optically active vinylglycines were observed in good yields with high regio- and enantioselectivities. In this process, the excellent control of regioselectivity was shown to be due to hydrogen bonding interactions between the hydroxyl group in the substrate and the DACH-naphthyl ligand in the palladium complex, as absence of the hydroxyl group led to the opposite regioselectivity. In 2019, Zhang reported a method for the synthesis of *N*-substituted 2-pyridones *via* a palladium catalyzed regio- and enantioselective allylic amination of hydroxyl-containing allylic carbonates.[93] Complete levels of chemo-, regio- and enantioselectivities were observed upon use of a palladium complex modified by a chiral phosphoramidite ligand. Control experiments determined that the hydrogen bond interaction between a π-allylpalladium

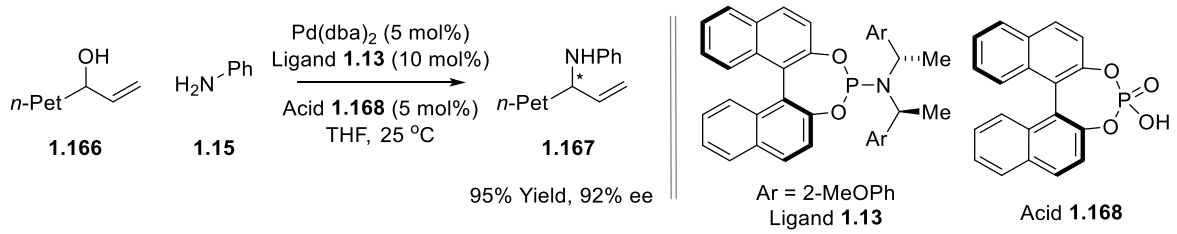
intermediate and 2-hydroxypyridine played a crucial role in resultant high levels of branched regioselectivity accompanied by high yields.



Scheme 1.35 Palladium Catalyzed Regio- and Enantioselective Allylic Aminations of 2-Pyridones.

1.4.3 Allylic Alcohol

In 2014, Beller disclosed an enantioselective allylic amination of racemic allylic alcohols (Scheme 1.36).[94] A palladium catalyst modified by a phosphoramidite ligand in combination with a chiral phosphoric acid promoted formation of a variety of functionalized amines in high yields with complete levels of regio- and enantioselectivities, using racemic cyclic and acyclic alkyl-substituted allylic alcohols. Mechanistic studies involving amination of the deuterium labeled allylic alcohol found that the rate of σ-π-σ interconversion of allylic palladium intermediates is slower than the rate of a nucleophilic attack, which enables the highly regioselective formation of branched allylic amines.

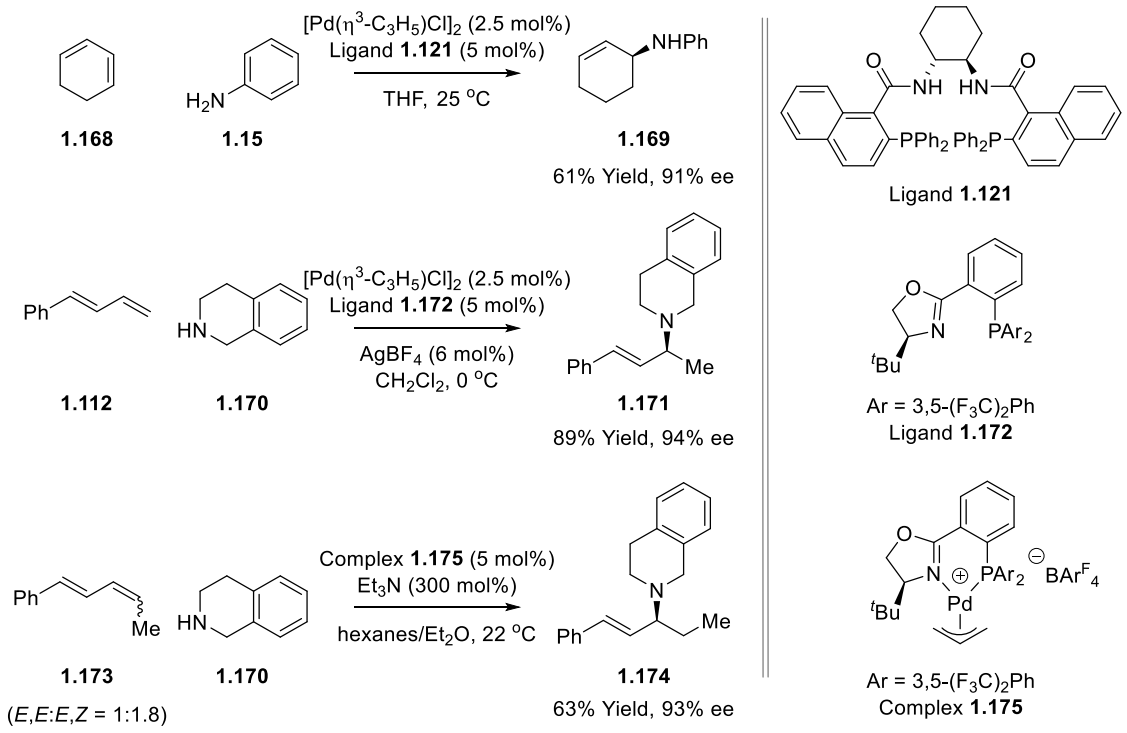


Scheme 1.36 Cooperative Catalysis by Palladium and a Chiral Phosphoric Acid Promoted Regio- and Enantioselective Allylic Aminations.

1.4.4 C-H Functionalization

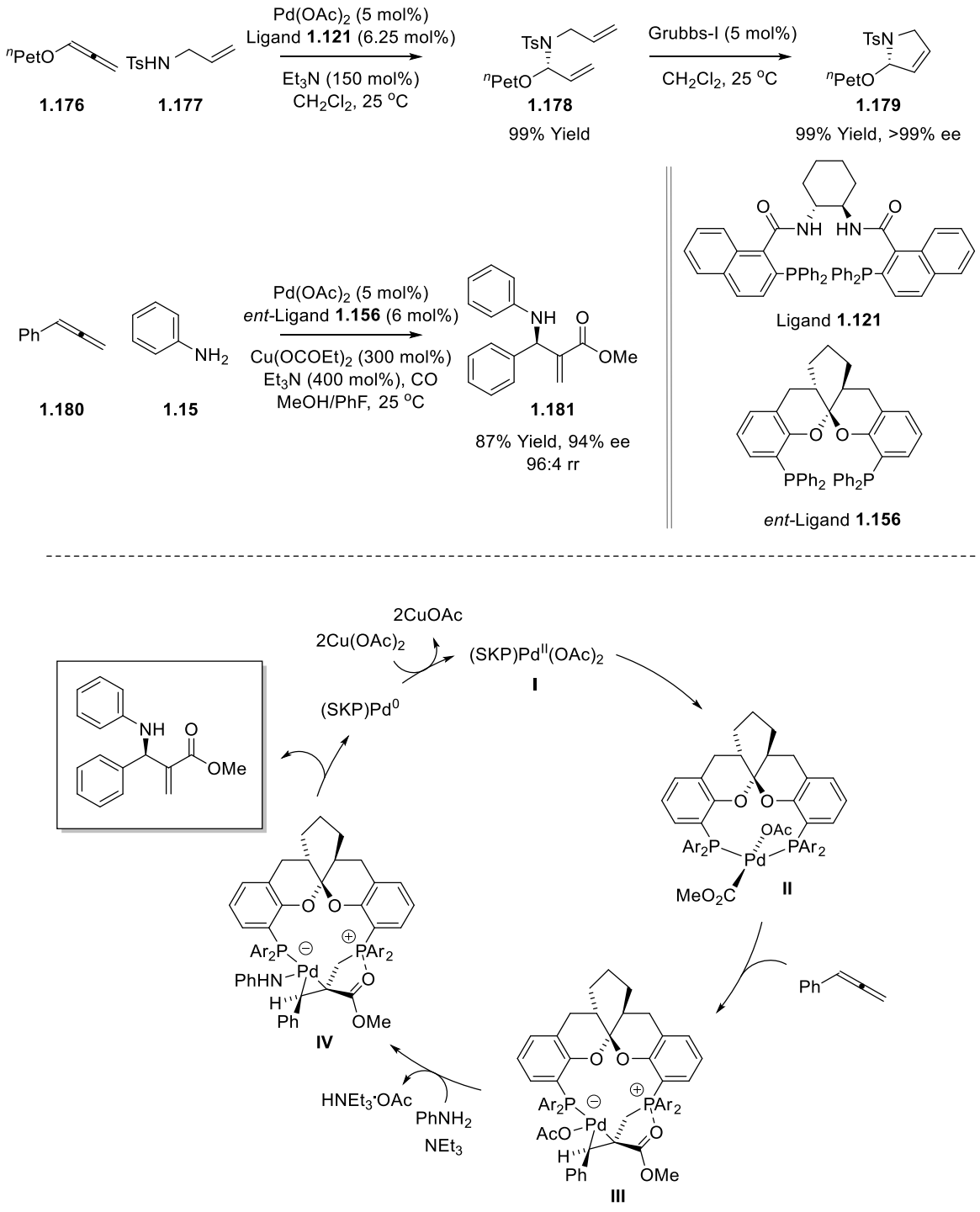
In 2001, Hartwig reported a palladium catalyzed hydroamination of cyclohexadiene with arylamines using a palladium catalyst modified by a Trost ligand (Scheme 1.37).[95] Good yields with high enantioselectivities were achieved although amine nucleophile scopes were limited to aryl amines. Mechanistic studies later showed that hydropalladation of the cyclohexadiene generates a π-allylpalladium complex followed by outer sphere amine addition to form the resulting ammonium salts which oxidatively protonate palladium to regenerate palladium hydride species.[96] In 2017, Malcolmson applied a PHOX ligand in palladium catalyzed allylic aminations of acyclic 1,3-dienes.[97] Using aliphatic amines, good yields of chiral allylic amines with excellent levels of regio- and enantioselectivity were reported. Interestingly, the electron deficient PHOX ligand was required for high regiomeric ratios of chiral branched to achiral linear products. Subsequent to these efforts, Malcolmson recently disclosed the development of palladium catalyzed hydroaminations of 1,4-disubstituted acyclic dienes with both aliphatic and aromatic amines.[98] Whereas enantioselective intermolecular hydrofunctionalizations of dienes are largely limited to terminal 1,3-dienes, this protocol using palladium complexes with a noncoordinating BAr^F_4 counteranion promoted the

hydroamination of internal 1,3-dienes to form chiral allylic amines in good yields along with high levels of regio- and enantioselectivity.



Scheme 1.37 Palladium Catalyzed Enantioselective Hydroamination of 1,3-Dienes.

In 2012, Rhee reported a palladium catalyzed intermolecular hydroamination of alkoxyallenes (Scheme 1.38).[99] In an extension of their reported work,[100] using a palladium catalyst modified by a Trost ligand, hydroamination products were observed in excellent yield and enantioselectivity, which upon a subsequent ring-closing metathesis reaction formed allylic *N*,*O*-acetals.



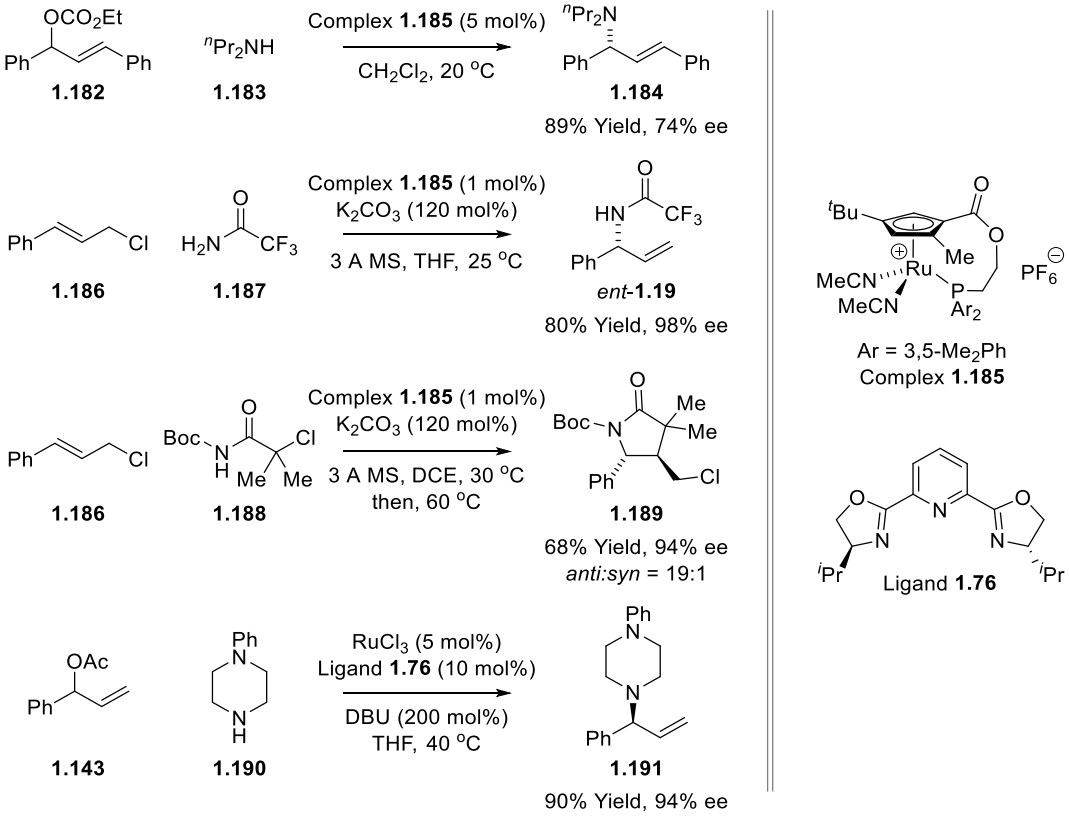
Scheme 1.38 Palladium Catalyzed Regio- and Enantioselective Hydroaminations of Terminal Allenes.

Recently, Wang and Ding found an enantioselective alkoxycarbonylative amination of terminal allenes to form *β*-arylamino acid esters in good yields with high regio- and enantioselectivities.[101] On the basis of their prior work (Scheme 1.33),[88] using a palladium catalyst modified by an aromatic spiroketal based diphosphine ligand, the corresponding phosphonium palladium intermediate **IV** was generated, presumably *via* methoxy carbonylpalladation of the allene and subsequent intramolecular rearrangement. The rest of the catalytic cycles proceeded in the presence of a copper salt as an oxidant. This protocol would effectively promote straightforward access to chiral *α*-methylene-*β*-arylamino acid esters, avoiding the tedious synthesis of MBH adducts.

1.5 Intermolecular Ruthenium Catalyzed Enantioselective Allylic Amination

Whereas transition metal catalyzed enantioselective allylic aminations have been developed largely by effective palladium and iridium catalysts, such transformations catalyzed by ruthenium catalysts remain uncommon. In 2001, Takahashi reported the first example of enantioselective allylic aminations catalyzed by the planar-chiral cyclopentadienyl ruthenium complex **1.185**, allowing the formation of branched products with high regioselectivity and up to 74% enantioselectivity (Scheme 1.39).[102] Of note, it is the pioneering work toward asymmetric induction by planar-chiral complexes of late transition metals. Subsequent to this work, the same planar-chiral ruthenium complex was used for asymmetric auto tandem catalysis.[103] Regio- and enantioselective allylic substitution reactions of mono-substituted allylic halides with carboxamides produced enantiomerically enriched branched allylic amines in good yields with excellent levels of regio- and enantioselectivity. Further investigation found that the allylic substitution reaction followed by atom transfer radical cyclization formed optically active *γ*-lactams in a one pot process. In 2014, Kawatsura and Itoh reported regio- and enantioselective

allylic aminations of racemic mono-substituted allylic esters with cyclic secondary amines.[104] Using a ruthenium catalyst modified by (*S*,*S*)-*ip*-Pybox, enantiomerically enriched allylic amines with excellent regio- and enantioselectivities were formed.



Scheme 1.39 Ruthenium Catalyzed Enantioselective Allylic Aminations.

1.6 Conclusion

Enantioselective late transition metal catalyzed allylic aminations have become a widely applicable reaction for the synthesis of enantiomerically enriched allylic amines, which are versatile building blocks for natural products, semisynthetic and synthetic pharmaceutical and agrochemical ingredients. The improvement of ligand design in the catalyst has allowed a wide range of amine nucleophiles with mono- and di-substituted allylic electrophiles. As illustrated in this review, late transition metal catalyst has been proven efficient for the formation of highly regio- and enantioselective allylic amines with good functional group tolerance, which have been applied in asymmetric total synthesis of a variety of complex chiral molecules. Like any other synthetic methodology though, there are still some limitations to the use of late transition metal catalyzed allylic amination. For example, the use of tri-substituted allylic electrophiles and alkyl-substituted allylic derivatives remains challenging. Thus, to address these issues, future developments will be expected to provide more unforeseen aspects for late transition metal catalyzed enantioselective allylic aminations.

Chapter 2: Asymmetric Allylation of Glycidols Mediated by Allyl Acetate *via* Iridium Catalyzed Hydrogen Transfer*

2.1 Introduction

Epoxides are important building blocks in chemical synthesis, including the construction of polyketide natural products where they also appear as native structural motifs.[1] Accordingly, several methods have been reported for the asymmetric allylation[2] of glycidic aldehydes using reagents based on boron,[3,4] tin,[5,6] silicon,[7,8] indium,[9] and magnesium.[10] These methods have proven effective in certain contexts;[3−10] however, due to pronounced match−mismatch effects, only one diastereomer of the secondary homoallylic glycidol is generally accessible in highly diastereomerically enriched form.[11] Additionally, indirect formation of secondary homoallylic glycidols *via* enantioselective allylation of *α,β*-unsaturated aldehydes followed by Sharpless asymmetric epoxidation is problematic, as modest diastereoselectivities are evident in reactions of secondary (*Z*)-allylic alcohols.[12] By harnessing the native reducing ability of alcohols, we have discovered a new, redox-economic class of C−C bond formations that merge the characteristics of carbonyl addition and transfer hydrogenation.[13] These hydrogen auto transfer processes utilize alcohol oxidation to drive reductive generation of transient organometallic nucleophiles. The resulting carbonyl−organometal pair combines to furnish products of addition, directly converting lower alcohols to higher alcohols. Based on this pattern of reactivity, diverse enantioselective alcohol C−H functionalizations have been developed including the C−H allylation[14] and crotylation[15,16] of primary alcohols to

*This chapter is based on the published work:
Kim, S. W.; Lee, W.; Krische, M. J. *Org. Lett.* **2017**, *19*, 1252.

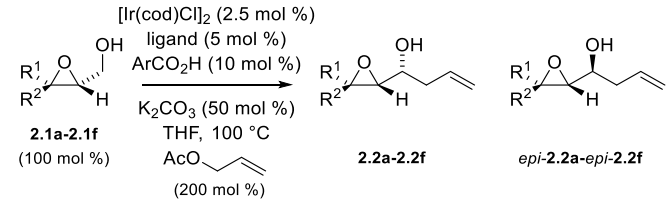
form secondary homoallylic alcohols. In the present account, this allylation method is applied to the conversion of primary glycidols to secondary homoallylic glycidols.

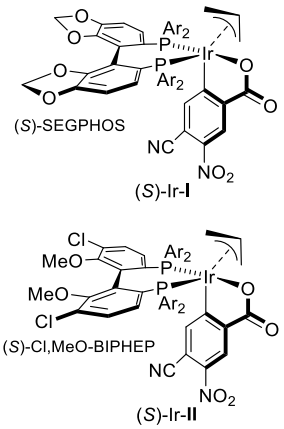
2.2 Reaction Development and Scope

Initial studies were focused on the allylation of glycidol **2.1a**, which is prepared through Sharpless asymmetric epoxidation of geraniol.[17] For the sake of convenience, the cyclometalated π-allyliridium *C,O*-benzoate catalysts were generated *in situ* from commercial components. Thus, glycidol **2.1a** was exposed to allyl acetate in the presence of $[Ir(cod)Cl]_2$, a series of 4-substituted 3-nitro-benzoic acids, assorted axially chiral chelating phosphine ligands, and various inorganic bases. A small set of optimization experiments quickly led to the identification of effective conditions. Thus, using the iridium catalysts (*R*)- or (*S*)-Ir-I modified by SEGPHOS, the diastereomeric secondary homoallylic glycidols **2.2a** and *epi*-**2.2a** were obtained in excellent yields and diastereoselectivities, respectively (Table 2.1). Notably, unlike the corresponding allylborations,[11] the enantiomeric catalysts delivered **2.2a** and *epi*-**2.2a** with roughly equivalent levels of catalyst directed diastereoselectivity (**2.2a**/*epi*-**2.2a** = 11:1 vs 1:12), suggesting the present iridium catalysts are insensitive to match−mismatch effects. Indeed, using an achiral iridium catalyst modified by dppf, a 1:1 mixture of diastereomeric secondary homoallylic glycidols **2.2b** and *epi*-**2.2b** was obtained. The identification of favorable conditions for the asymmetric C−H allylation of glycidol **2.1a** prompted a more detailed investigation into the scope of this process (Table 2.1). *cis*-Glycidols **2.1b−2.1e** were specifically selected for study as the corresponding secondary homoallylic glycidols **2.2b−2.2e** and *epi*-**2.2b**−*epi*-**2.2e** are inaccessible using conventional allylation methods[2−10] due to the modest diastereoselectivities reported in Sharpless asymmetric epoxidations of secondary (*Z*)-allylic alcohols[12] along with the

stereochemically labile nature of (*Z*)-*α,β*-unsaturated aldehydes. In the event, *cis*-glycidols **2.1b**−**2.1e** were converted to the secondary homoallylic glycidols **2.2b**−**2.2e** and *epi*-**2.2b**−*epi*-**2.2e**, respectively, in good yields and good levels of catalyst-directed diastereoselectivity. In certain cases, the iridium catalysts (*R*)- or (*S*)-Ir-II modified by Cl,MeO-BIPHEP were found to enforce higher yields and diastereoselectivities than the iridium catalysts (*R*)- or (*S*)-Ir-I modified by SEGPHOS. To complete this study, the allylation of *trans*-glycidol **2.1f** was explored. Whereas secondary homoallylic glycidol **2.2f** was formed with excellent levels of catalyst-directed diastereoselectivity, the isomeric glycidol *epi*-**2.2f** was formed in low yield with less pronounced levels of stereocontrol. These data suggest match−mismatch effects may be more important in reactions of *trans*-glycidols. Finally, it is worth noting that due to the Horeau principle, all major reaction products derived from **2.1a, 2.1b**, and **2.1f**, are obtained in >99% enantiomeric excess.[18]

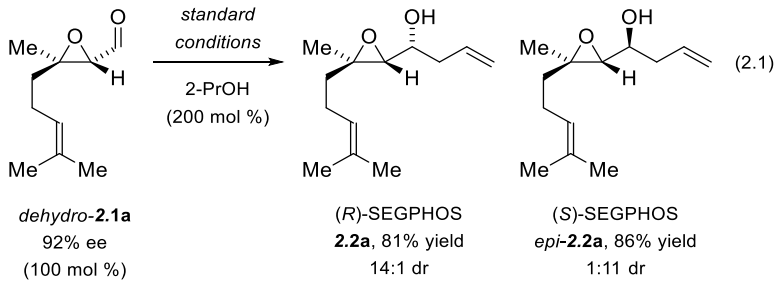
Table 2.1 Iridium catalyzed C-H allylation of glycidols **2.1a-2.2f** to form adducts **2.2a-2.2f** and *epi*-**2.2a-2.2f**.[a]





1a-1e	2a-2f	*epi*-2a-*epi*-2f
2.1a, 92% ee	(*R*)-SEGPHOS **2.2a**, 85% yield[b] 11:1 dr	(*S*)-SEGPHOS *epi*-**2.2a**, 86% yield 1:12 dr
2.1b, 87% ee	(*R*)-Cl,MeO-BIPHEP **2.2b**, 76% yield 9:1 dr	(*S*)-Cl,MeO-BIPHEP *epi*-**2.2b**, 79% yield 1:8 dr
2.1c	(*R*)-Cl,MeO-BIPHEP **2.2c**, 84% yield 10:1 dr	(*S*)-Cl,MeO-BIPHEP *epi*-**2.2c**, 83% yield 1:6 dr
2.1d	(*R*)-SEGPHOS **2.2d**, 76% yield 10:1 dr	(*S*)-SEGPHOS *epi*-**2.2d**, 72% yield 1:9 dr
2.1e	(*R*)-SEGPHOS **2.2e**, 79% yield 10:1 dr	(*S*)-SEGPHOS *epi*-**2.2e**, 79% yield 1:6 dr
2.1f, 93% ee	(*R*)-Cl,MeO-BIPHEP **2.2f**, 65% yield 17:1 dr	(*S*)-Cl,MeO-BIPHEP *epi*-**2.2f**, 32% yield 1:7 dr

[a]Cited yields are of material isolated by silica gel chromatography. $ArCO_2H$ refers to 4-cyano-3-nitrobenzoic acid. Diastereomeric ratios were determined by ^1H NMR of crude reaction mixtures. See Supporting Information for further experimental details. [b]1 mmol scale.of material isolated by silica gel chromatography. All reactions were conducted using enantiomerically enriched starting materials. See Supporting Information for further experimental details.

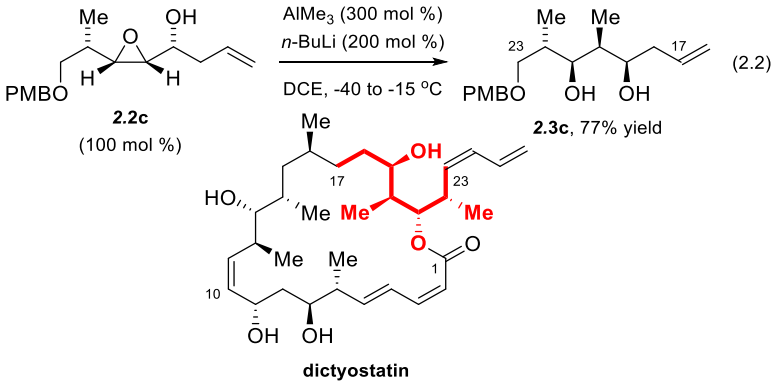


(2.1)

2.3 Discussion

The direct C−H allylation of primary glycidols **2.1a**−**2.1e** is both step-economic and redox-economic as it avoids discrete formation and isolation of less tractable glycidic aldehydes. Nevertheless, under certain circumstances it may be desirable to conduct the allylation from the aldehyde oxidation level. To assess the feasibility of utilizing glycidic aldehydes as reactants, the reductive coupling of allyl acetate with *dehydro*-**2.1a** was performed using 2-propanol as the terminal reductant under otherwise standard conditions (eq 2.1). The respective secondary homoallylic glycidols **2.2a** and *epi*-**2.2a** were formed in good yields with excellent levels of catalyst-directed diastereoselectivity. The efficiencies observed in the reactions of glycidic aldehyde *dehydro*-**2.1a** were roughly equivalent to those observed using the corresponding glycidol **2.1a** (Table 2.1). To illustrate how the present method may be applied to polyketide construction, secondary homoallylic glycidol **2.2c** was subjected to conditions for regioselective epoxide ring opening using $AlMe_3$-*n*-BuLi (eq 2.2).[19] The desired adduct **2.3c**, which was obtained in 77% yield, embodies a propionate-based stereotetrad spanning C17−C23 of

dictyostatin, a marine macrolide that displays antimitotic activity against multidrug-resistant cancer cell lines at nanomolar levels.[20,21]



2.4 Conclusion

In summary, we report that glycidols prepared through Sharpless asymmetric epoxidation participate in direct carbinol C−H allylation with excellent levels of catalyst-directed diastereoselectivity. This method is redox- and step-economic, as it avoids discrete formation of less tractable glycidic aldehydes. Further, this method overcomes limitations evident in corresponding allylations of glycidic aldehydes using allylboron reagents.[3a,b,11] Finally, as Sharpless asymmetric epoxidations of secondary (*Z*)-allylic alcohols display low levels of diastereoselectivity,[12] indirect formation of the present secondary homoallylic glycidols through an asymmetric enal allylation−epoxidation sequence is not feasible. Future studies will focus on the use of α-olefins[22] as pronucleophiles in alcohol-mediated carbonyl addition.

2.5 Experimental Details

General Information

All reactions were run under an atmosphere of argon. Sealed tubes (13x100 mm) were purchased from Fischer Scientific (catalog number 14-959-35C) and were flame dried followed by cooling in a desiccator. Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. Dichloromethane was distilled from calcium hydride under a nitrogen atmosphere prior to use. Anhydrous solvents were transferred by oven-dried syringes. Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Dynanmic Absorbents F254). Visualization was accomplished with UV light followed by dipping in potassium permanganate or *p*-anisaldehyde stain solution and then heating. Purification of reactions was carried out by flash chromatography using Silacycle silica gel (40-63 μm, unless indicated specifically). Potassium carbonate was purchased through Fisher Chemical, flame dried prior to use, and stored in a desiccator.

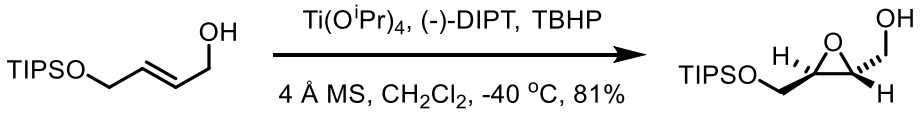
Spectroscopy, Spectrometry and Data Collection

Infrared spectra were recorded on a Perkin-Elmer 1600 spectrometer. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/z (relative intensity). Specific optical rotations were recorded on an Atago AP-300 automatic polarimeter at the sodium line (589 nm) in $CHCl_3$. Solution concentrations are given in the units of 10^{-2} g mL^{-1}. Accurate masses are reported for the molecular ion (M-H, M, M+H, M+Na, or M+K), or a suitable fragment. ^{1}H nuclear magnetic resonance spectra were recorded on an Agilent MR (400 MHz). Chemical shifts are reported as parts per million (ppm) relative to residual $CHCl_3$ δ_H (7.26 ppm). ^{13}C nuclear magnetic

resonance spectra were recorded on an Agilent MR (100 MHz) for $CDCl_3$ solutions, and chemical shifts are reported as parts per million (ppm) relative to residual $CDCl_3$ δ_C (77.0 ppm).

Experimental Details and Spectral Data

Glycidols **2.1a**,[1,2] *dehydro*-**2.1a**,[3] **2.1b**,[1,4] **2.1c**,[5] **2.1d**[4,6] and **2.1e**[6] were prepared according to the published procedures and were identical in all respects to the reported materials.



To a flame dried round-bottomed flask charged with dry 4 Å molecular sieves (1 g) under an argon atmosphere was added CH_2Cl_2 (33 mL, 0.1 M with respect to allylic alcohol). The reaction vessel was placed in -40 ºC bath and Ti(O^{i}Pr)$_4$ (1.93 mL, 6.54 mmol, 200 mol%) was added followed by D-(–)-diisopropyl tartrate (1.70 mL, 8.1 mmol, 250 mol%). The mixture was stirred vigorously for 30 minutes, at which point *tert*-butyl hydrogen peroxide (1.2 mL, 5.0-6.0 M in decane, 6.54 mmol, 200 mol%). After 30 minutes a solution of allylic alcohol[7] (0.8 g, 3.27 mmol) in dry CH_2Cl_2 (17 mL, 0.2 M) was added slowly and the mixture was stirred for 40 h. The reaction vessel was transferred to an ice batch. Water (30 mL) and NaOH (30 mL, 10% aqueous solution) were added to the reaction mixture. The mixture was allowed to stir for 2 hours. The reaction mixture was filtered (celite) with the aid of CH_2Cl_2 (50 mL) and the filtrate was transferred to a separatory funnel. The organic layer was extracted with CH_2Cl_2 (50 mL ×

2) and the combined organic layers were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–7:1) to furnish the title compound as a colorless oil (690 mg, 2.65 mmol) in 81% yield. The spectral data were identical to those reported for the corresponding racemate.[7]

TLC (SiO_2) R_f = 0.29 (hexanes/ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.94 (m, 2H), 3.77 (dd, *J* = 11.9, 4.1 Hz, 1H), 3.62 (dq, *J* = 12.2, 3.8 Hz, 1H), 3.13 (m, 2H), 1.05 (m, 21H).

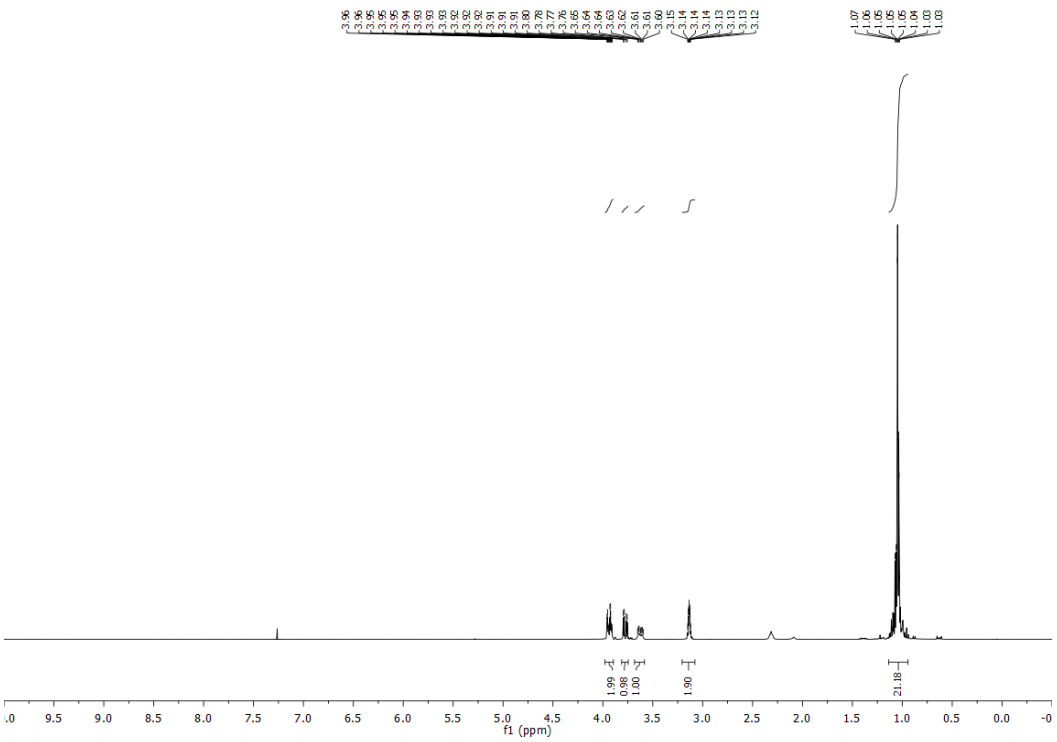
^{13}C NMR (100 MHz, $CDCl_3$): δ = 62.8, 61.3, 56.0, 55.7, 17.8, 11.9.

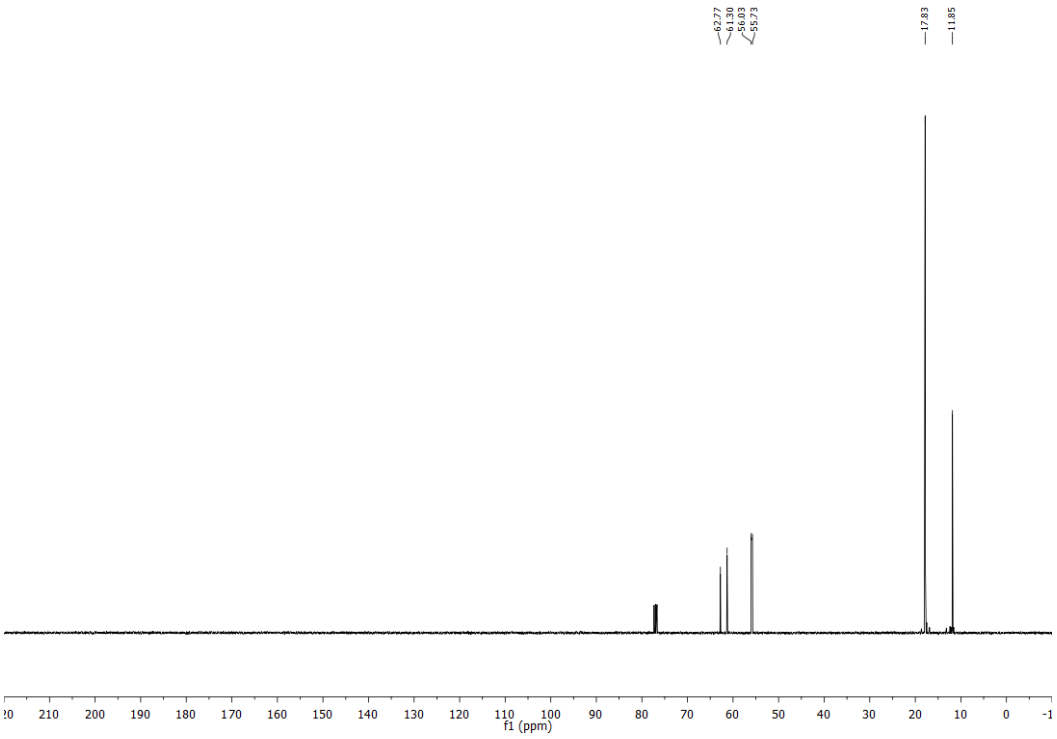
HRMS (ESI) Calculated for $C_{13}H_{28}O_3Si$ [M+Na^+] = 283.1700, Found 283.1701.

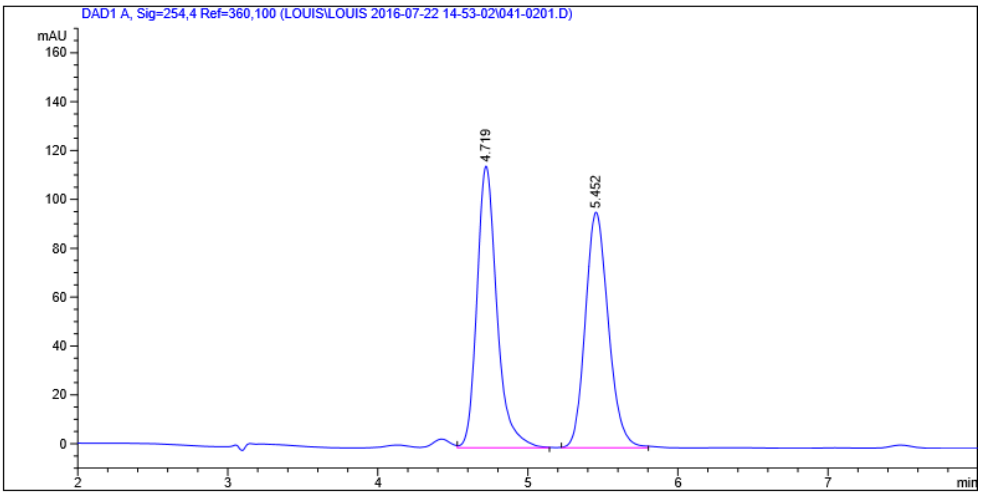
FTIR (neat) 3432, 2942, 2865, 1463, 1112, 1065, 995, 881, 779, 681 cm^{-1}.

$[\alpha]_D^{28}$: +16.33 (*c* 1.0, $CHCl_3$).

HPLC: Enantiomeric excess was determined by HPLC analysis of the benzoate derivative of the product (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 254 nm), t_{major} = 4.7 min, t_{minor} = 5.5 min; *ee* = 93%.

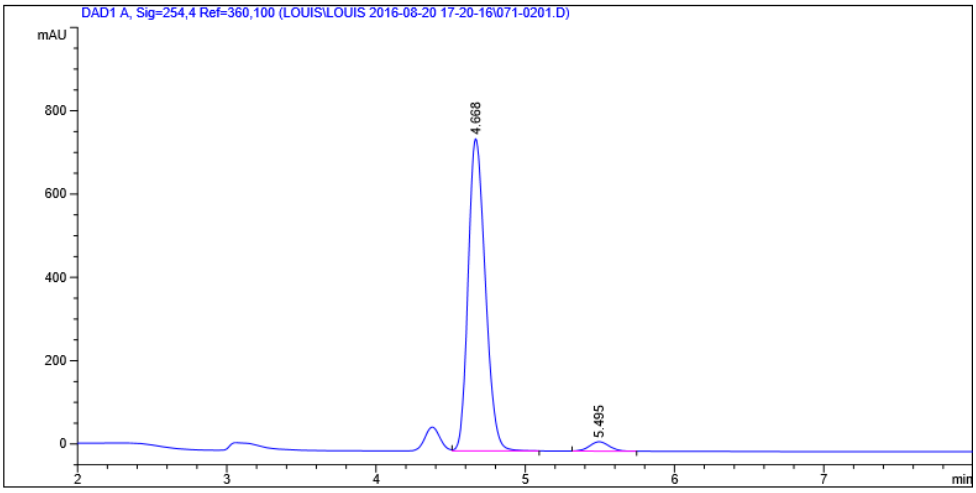

f1 (ppm)


f1 (ppm)



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.719	VB	0.1416	1063.94421	115.38085	50.9285
2	5.452	BB	0.1640	1025.14819	96.45261	49.0715
Totals :				2089.09241	211.83346	

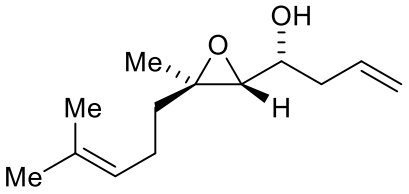


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.668	VB	0.1250	5977.96289	750.03583	96.6786
2	5.495	BB	0.1420	205.37094	22.60398	3.3214
Totals :				6183.33383	772.63981	

Procedures and Spectral Data for the Synthesis of Secondary Homoallylic Glycidols 2.2a-2.2f, *epi*-2.2a-2.2f

***(R)*-1-((2*R*,3*R*)-3-methyl-3-(4-methylpent-3-en-1-yl)oxiran-2-yl)but-3-en-1-ol (2.2a)**



Detailed Procedures

From alcohol oxidation level: An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(R)*-SEGPHOS (6.1 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), alcohol **1a** (34 mg, 0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.1 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (0.5 mL, 0.4 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–10:1) to furnish the title compound as a colorless oil (35.7 mg, 0.17 mmol, anti:syn = 11:1) in 85% yield.

From alcohol oxidation level: An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (17 mg, 0.025 mmol, 2.5 mol%), *(R)*-SEGPHOS (30.5 mg, 0.05 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (19.0 mg, 0.1 mmol, 10 mol%), alcohol **1a** (170 mg, 1.0 mmol, 100 mol%) and K_2CO_3 (69.0 mg, 0.5 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (2.5 mL, 0.4 M) and allyl acetate (0.22 mL, 2.0 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–10:1) to furnish the title compound as a colorless oil (171 mg, 0.17 mmol, anti:syn = 10:1) in 81% yield.

From aldehyde oxidation level: An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(R)*-SEGPHOS (6.1 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), aldehyde *dehydro*-**1a** (0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.01 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (0.5 mL, 0.4 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–10:1) to furnish the title compound as a colorless oil (34.1 mg, 0.16 mmol, anti:syn = 14:1) in 81% yield.

Spectral data is reported for the major isomer.

TLC (SiO_2) R_f = 0.62 (hexanes/ethyl acetate = 2:1).

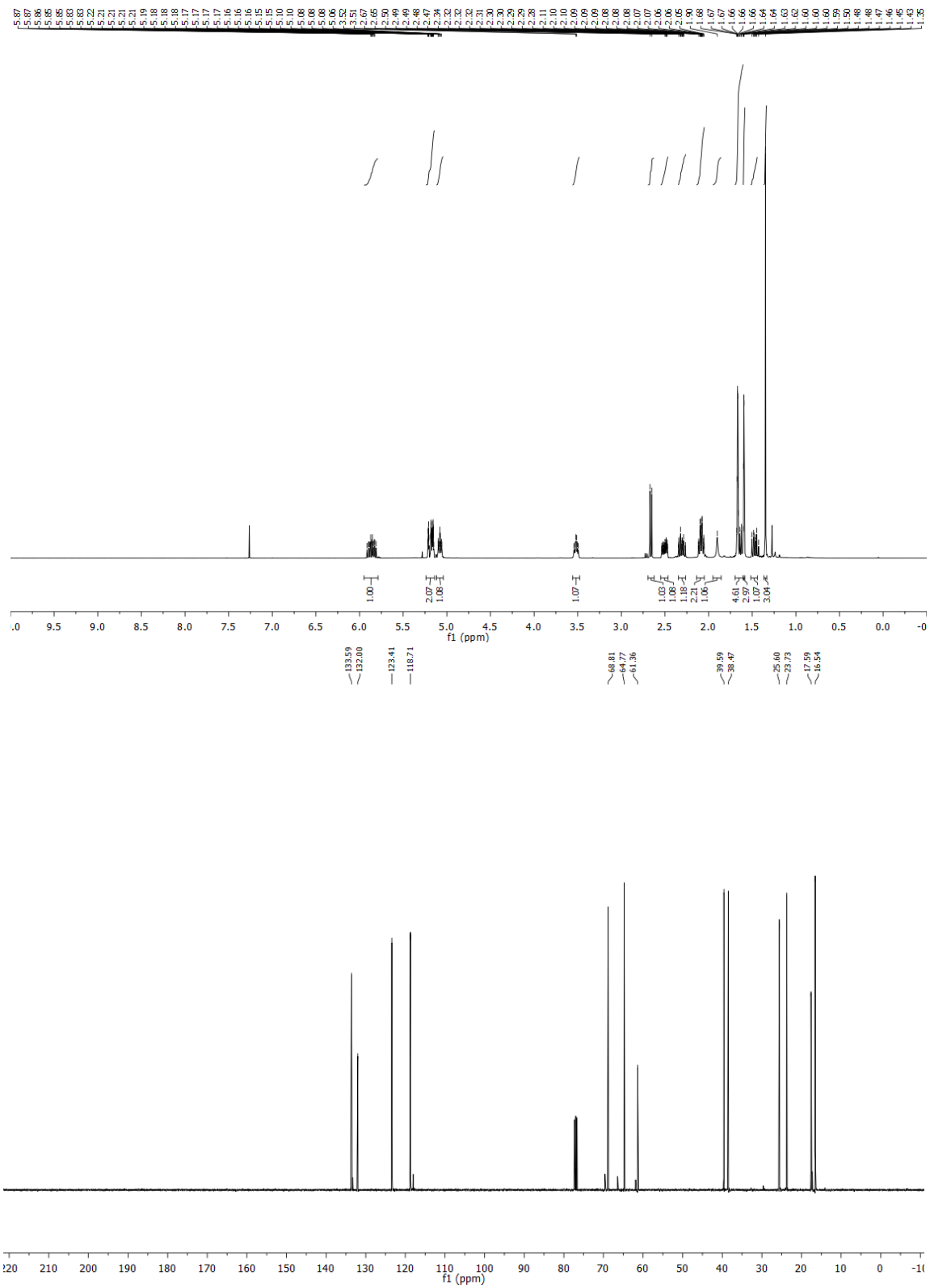
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.86 (m, 1H), 5.19 (m, 2H), 5.08 (m, 1H), 3.52 (td, *J* = 8.1, 3.9 Hz, 1H), 2.66 (d, *J* = 8.1 Hz, 1H), 2.5 (m, 1H), 2.30 (m, 1H), 2.08 (m, 2H), 1.90 (brs, 1H), 1.66 (m, 4H), 1.59 (m, 3H), 1.47 (m, 1H), 1.35 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.6, 132.0, 123.4, 118.7, 68.8, 64.8, 61.4, 39.6, 38.5, 25.6, 23.7, 17.6, 16.5.

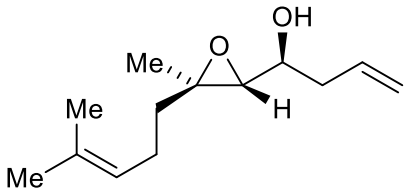
HRMS (ESI) Calculated for $C_{13}H_{22}O_2$ $[M+Na^+]$ = 233.1512, Found 233.1506.

FTIR (neat) 3435, 2927, 2358, 1436, 1384, 1072, 986, 914, 819 cm^{-1}.

$[\alpha]_D^{25}$: +21.17 (*c* 1.0, $CHCl_3$)


f1 (ppm)
f1 (ppm)

***(S)*-1-((2*R*,3*R*)-3-methyl-3-(4-methylpent-3-en-1-yl)oxiran-2-yl)but-3-en-1-ol (*epi*-2.2a)**



Detailed Procedures

From alcohol oxidation level: An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(S)*-SEGPHOS (6.1 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), alcohol **1a** (34 mg, 0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.1 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (0.5 mL, 0.4 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–10:1) to furnish the title compound as a colorless oil (36.1 mg, 0.17 mmol, anti:syn = 1:12) in 86% yield.

From aldehyde oxidation level: An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(S)*-SEGPHOS (6.1 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%),

aldehyde *dehydro*-**1a** (0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.01 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (0.5 mL, 0.4 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–10:1) to furnish the title compound as a colorless oil (34.9 mg, 0.17 mmol, anti:syn = 1:11) in 83% yield.

Spectral data is reported for the major isomer.

TLC (SiO_2) R_f = 0.50 (hexanes/ethyl acetate = 2:1).

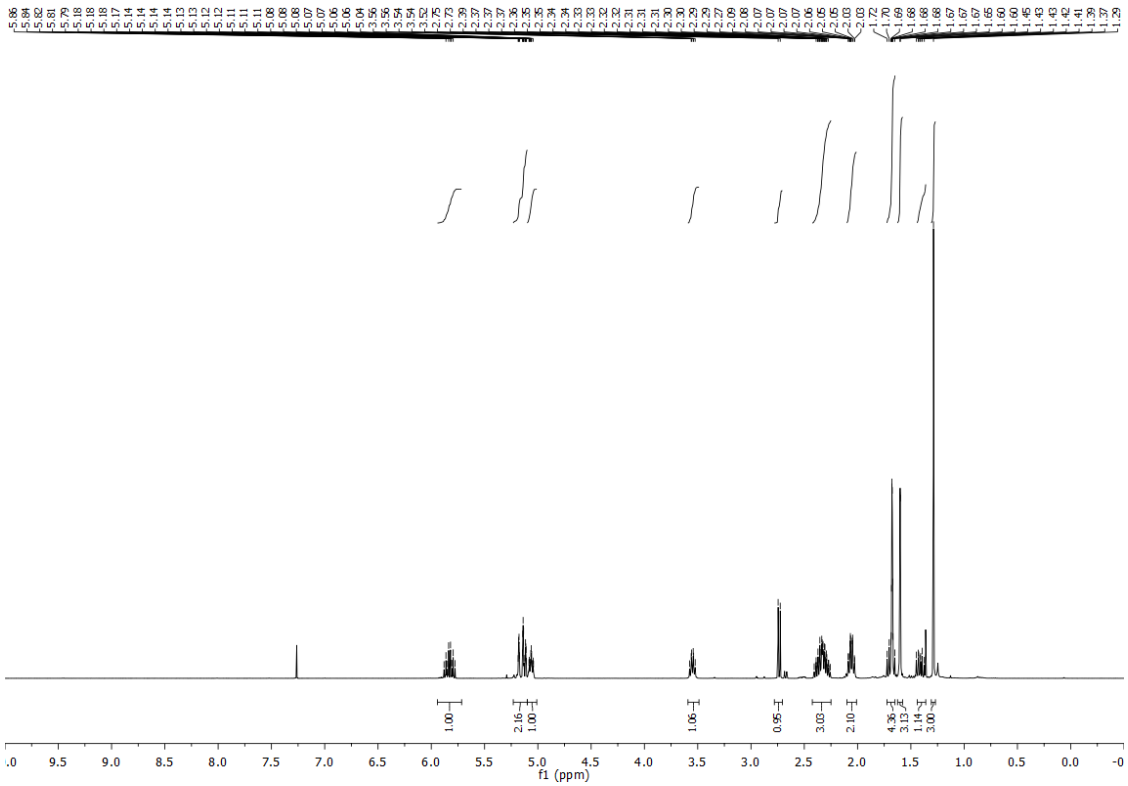
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.82 (m, 1H), 5.23–5.10 (m, 2H), 5.06 (m, 1H), 3.55 (td, *J* = 7.5, 5.9 Hz, 1H), 2.74 (d, *J* = 7.9 Hz, 1H), 2.42–2.25 (m, 3H), 2.08 (m, 2H), 1.69 (m, 4H), 1.60 (m, 3H), 1.41 (m, 1H), 1.29 (s, 3H).

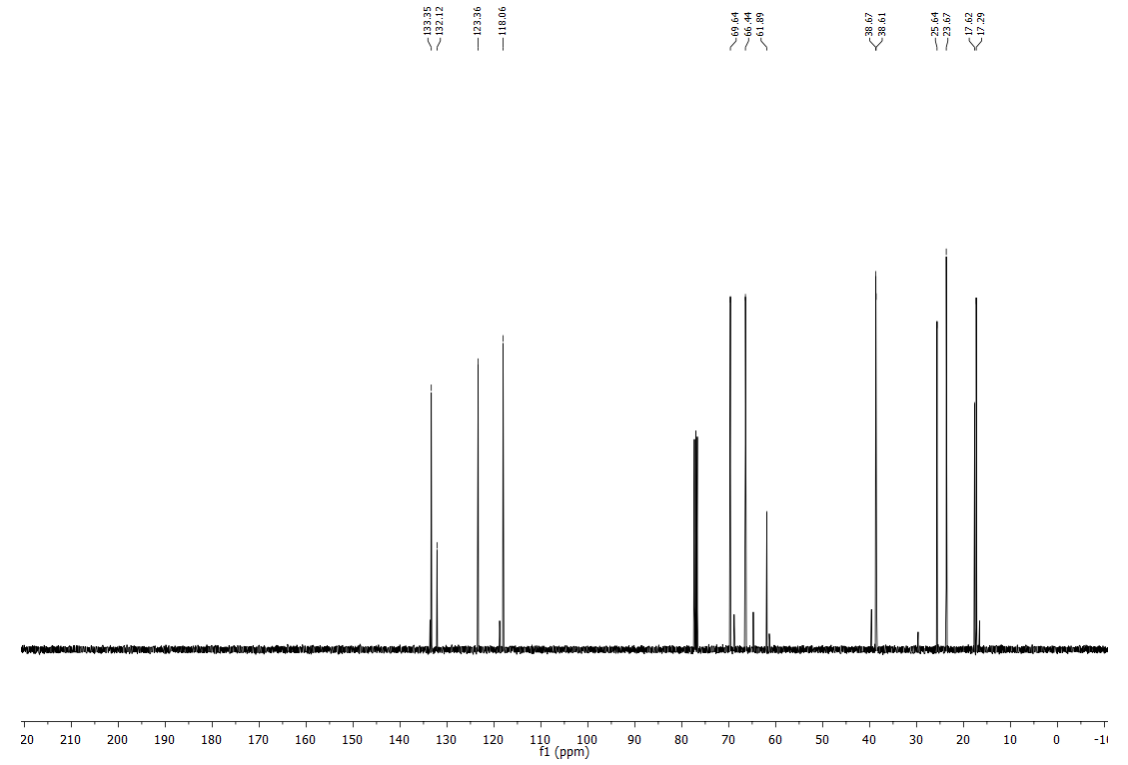
^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.4, 132.1, 123.4, 118.1, 69.6, 66.4, 61.9, 38.7, 38.6, 25.6, 23.7, 17.6, 17.3.

HRMS (ESI) Calculated for $C_{13}H_{22}O_2$ [M+Na^+] = 233.1512, Found 233.1514.

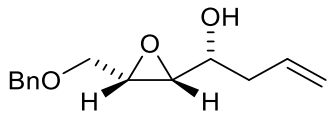
FTIR (neat) 3435, 2924, 2362, 1435, 1383, 1043, 997, 914, 822 cm^{-1}.

$[\alpha]_D^{25}$: −0.33 (*c* 1.0, $CHCl_3$).


f1 (ppm)


f1 (ppm)

***(R)*-1-((2*R*,3*S*)-3-((benzyloxy)methyl)oxiran-2-yl)but-3-en-1-ol (2.2b)**



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(R)*-Cl-MeO-BIPHEP (6.5 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), alcohol **1b** (39 mg, 0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.1 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (1.0 mL, 0.2 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1–3:1) to furnish the title compound as a colorless oil (35.6 mg, 0.15 mmol, anti:syn = 9:1) in 76% yield.

Spectral data is reported for the major isomer.

TLC (SiO_2) R_f = 0.42 (hexanes/ethyl acetate = 2:1).

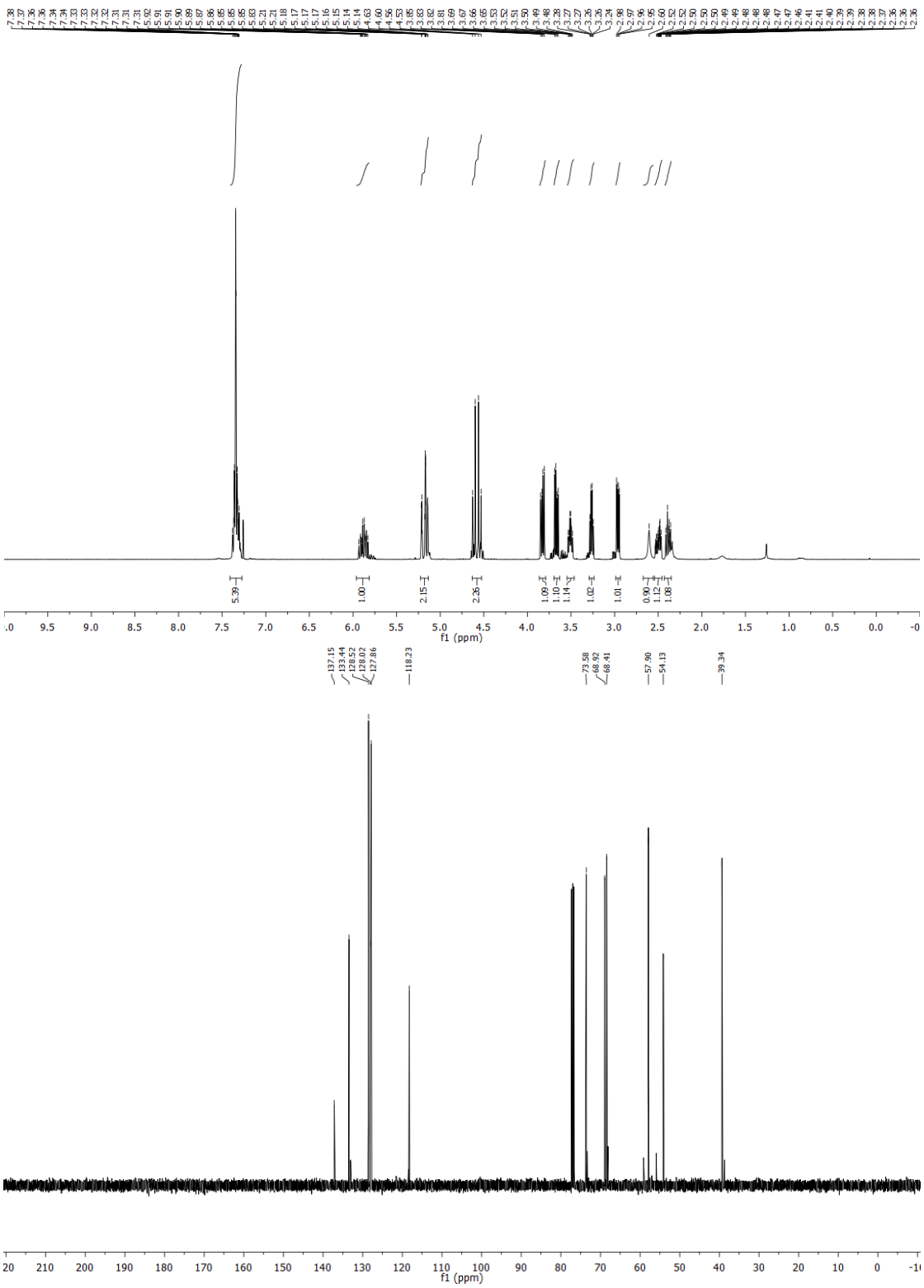
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (m, 5H), 5.88 (m, 1H), 5.17 (m, 2H), 4.58 (m, 2H), 3.83 (dd, *J* = 10.9, 6.0 Hz, 1H), 3.67 (dd, *J* = 10.8, 5.7 Hz, 1H), 3.50 (td, *J* = 7.8, 4.8 Hz, 1H), 3.26 (td, *J* = 5.9, 4.3 Hz, 1H), 2.96 (dd, *J* = 8.0, 4.3 Hz, 1H), 2.60 (brs, 1H), 2.49 (m, 1H), 2.38 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.2, 133.4, 128.5, 128.0, 127.9, 118.2, 73.6, 68.9, 68.4, 57.9, 54.1, 39.3.

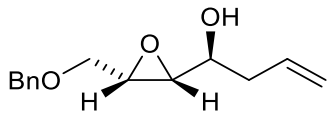
HRMS (ESI) Calculated for $C_{14}H_{18}O_3$ [M+Na^+] =257.1148, Found 257.1151.

FTIR (neat) 3454, 2921, 1718, 1453, 1271, 1075, 1028, 918, 698 cm^{-1}.

$[\alpha]_D^{25}$: −55.34 (*c* 1.0, $CHCl_3$).



***(S)*-1-((2*R*,3*S*)-3-((benzyloxy)methyl)oxiran-2-yl)but-3-en-1-ol (*epi*-2.2b)**



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(S)*-Cl-MeO-BIPHEP (6.5 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), alcohol **2.1b** (39 mg, 0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.1 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (1.0 mL, 0.2 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1–3:1) to furnish the title compound as a colorless oil (37.0 mg, 0.16 mmol, anti:syn = 1:8) in 79% yield.

Spectral data is reported for the major isomer.

TLC (SiO_2) R_f = 0.35 (hexanes/ethyl acetate = 2:1).

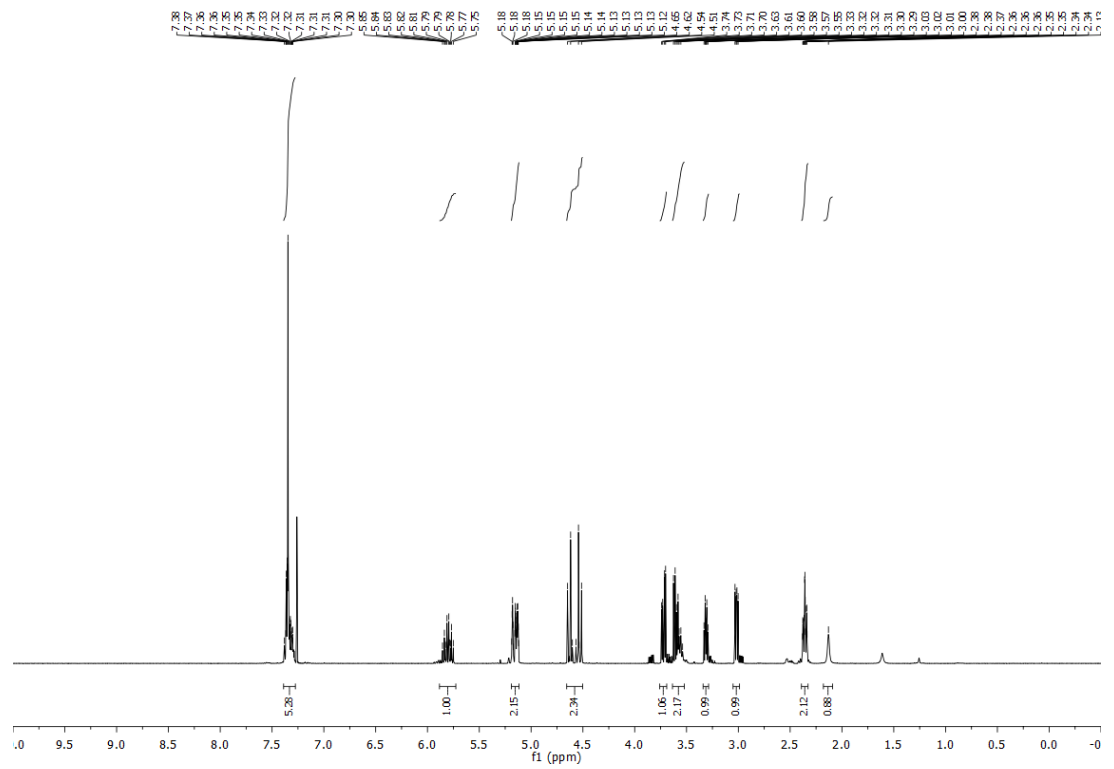
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (m, 5H), 5.80 (m, 1H), 5.15 (m, 2H), 4.58 (m, 2H), 3.72 (dd, *J* = 11.2, 4.1 Hz, 1H), 3.63–3.53 (m, 2H), 3.31 (dt, *J* = 6.5, 4.3 Hz, 1H), 3.02 (dd, *J* = 7.4, 4.5 Hz, 1H), 2.36 (m, 2H), 2.13 (brs, 1H).

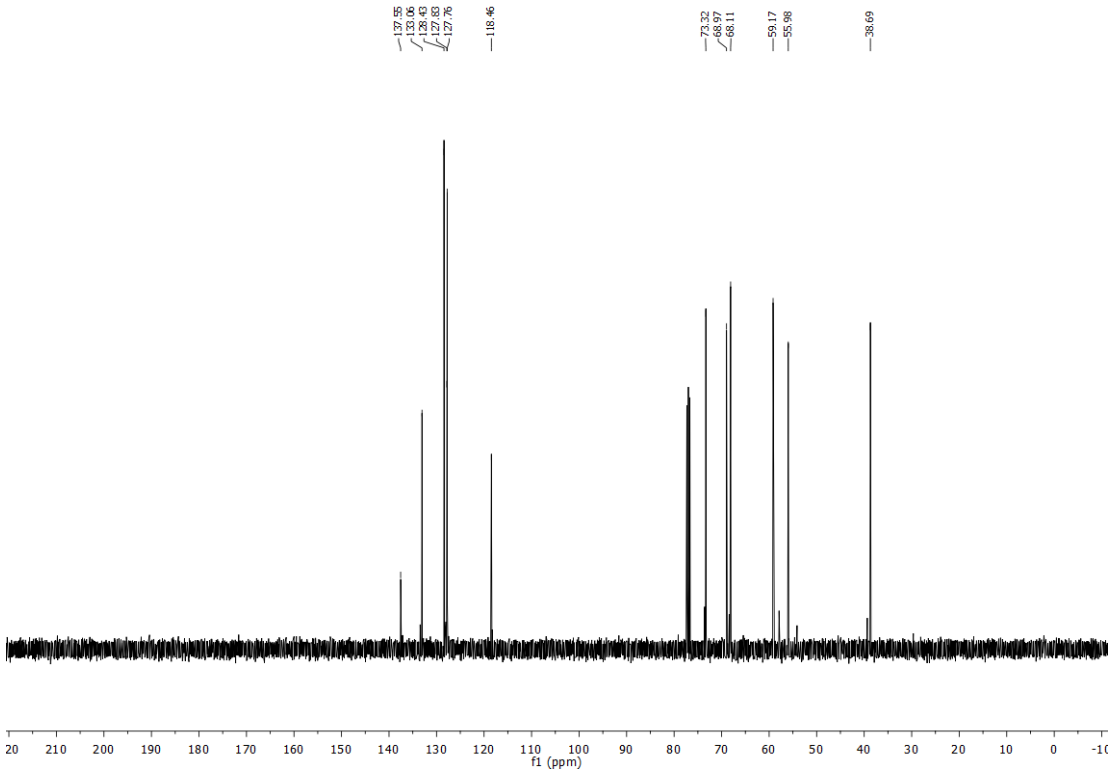
^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.6, 133.1, 128.4, 127.8, 127.8, 118.5, 73.3, 69.0, 68.1, 59.2, 56.0, 38.7.

HRMS (ESI) Calculated for $C_{14}H_{18}O_3$ [M+Na^+] =257.1148, Found 257.1155.

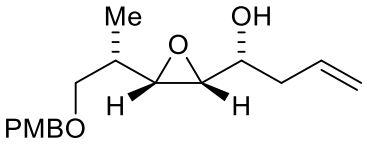
FTIR (neat) 3421, 2926, 1737, 1365, 1229, 1094, 1027, 918, 700 cm^{-1}.

$[\alpha]_D^{25}$: −86.67 (*c* 1.0, $CHCl_3$).


f1 (ppm)


f1 (ppm)

***(R)*-1-((2*R*,3*S*)-3-(*(S)*-1-((4-methoxybenzyl)oxy)propan-2-yl)oxiran-2-yl)but-3-en-1-ol (2.2c)**



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(R)*-Cl-MeO-BIPHEP (6.5 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), alcohol **2.1c** (51 mg, 0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.1 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (1.0 mL, 0.2 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1–3:1) to furnish the title compound as a colorless oil (49.1 mg, 0.17 mmol, anti:syn = 10:1) in 84% yield.

Spectral data is reported for the major isomer.

TLC (SiO_2) R_f = 0.36 (hexanes/ethyl acetate = 2:1).

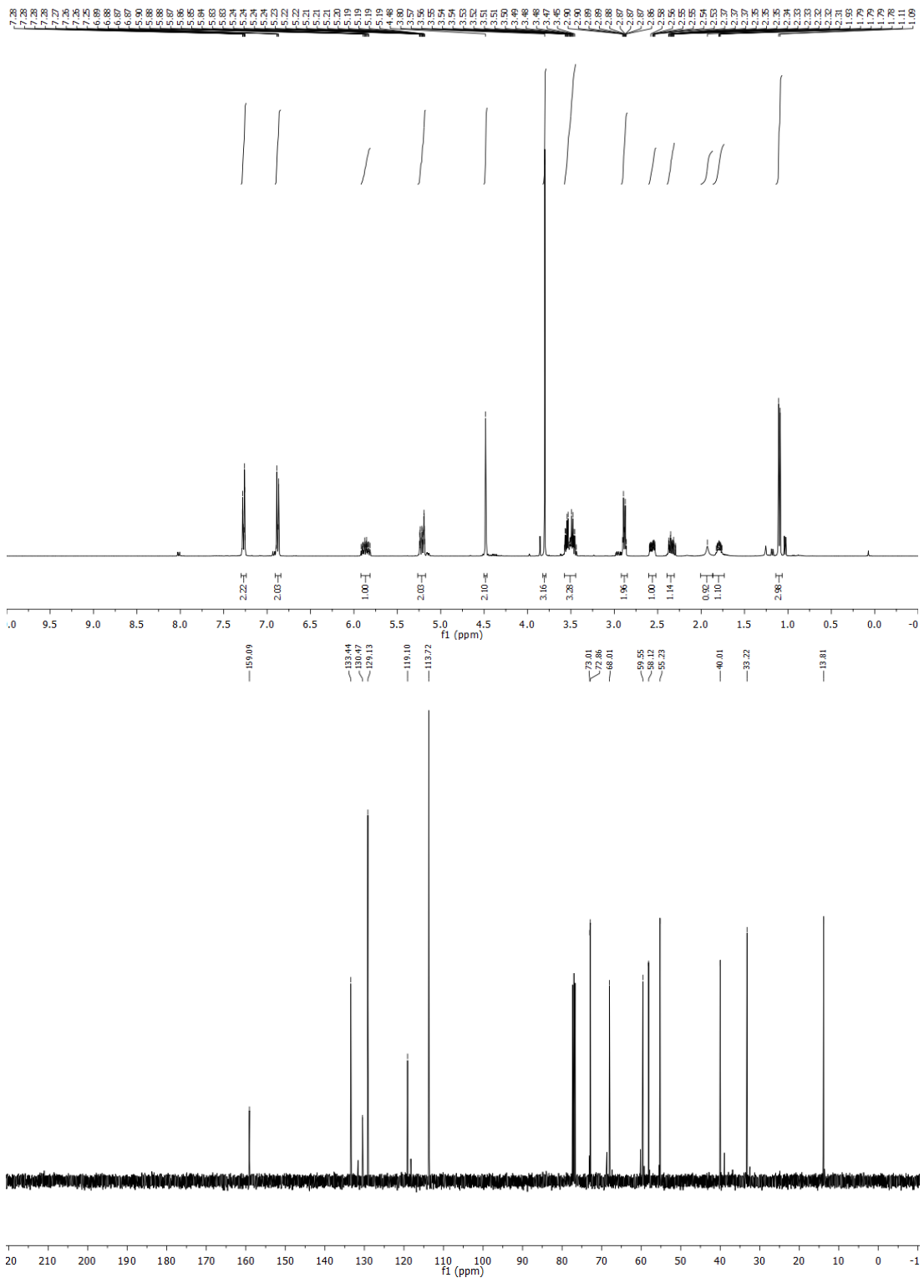
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27 (m, 2H), 6.88 (m, 2H), 5.86 (m, 1H), 5.21 (m, 2H), 4.48 (s, 2H), 3.80 (s, 3H), 3.52 (m, 3H), 2.88 (m, 2H), 2.56 (m, 1H), 2.34 (m, 1H), 1.93 (brs, 1H), 1.79 (m, 1H), 1.10 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 133.4, 130.5, 129.1, 119.1, 113.7, 73.0, 72.9, 68.0, 59.6, 58.1, 55.2, 40.0, 33.2, 13.8.

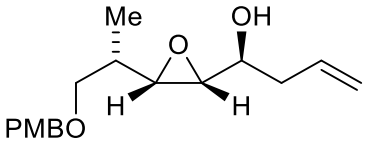
HRMS (ESI) Calculated for $C_{17}H_{24}O_4$ [M+Na^+] = 315.1567, Found 315.1561.

FTIR (neat) 3438, 2962, 2362, 1612, 1513, 1247, 1088, 1034, 820 cm^{-1}.

$[\alpha]_D^{25}$: +23.00 (*c* 1.0, $CHCl_3$).



***(S)*-1-((2*R*,3*S*)-3-(*(S)*-1-((4-methoxybenzyl)oxy)propan-2-yl)oxiran-2-yl)but-3-en-1-ol (*epi*-2.2c)**



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(S)*-Cl-MeO-BIPHEP (6.5 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), alcohol **2.1c** (51 mg, 0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.1 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (1.0 mL, 0.2 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1–3:1) to furnish the title compound as a colorless oil (48.5 mg, 0.17 mmol, anti:syn = 1:6) in 83% yield.

Spectral data is reported for the major isomer.

TLC (SiO_2) R_f = 0.29 (hexanes/ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27 (m, 2H), 6.87 (m, 2H), 5.86 (m, 1H), 5.16 (m, 2H), 4.47 (s, 2H), 3.80 (s, 3H), 3.56 (m, 2H), 3.45 (dd, *J* = 9.0, 6.5 Hz, 1H), 2.97 (dd, *J* =

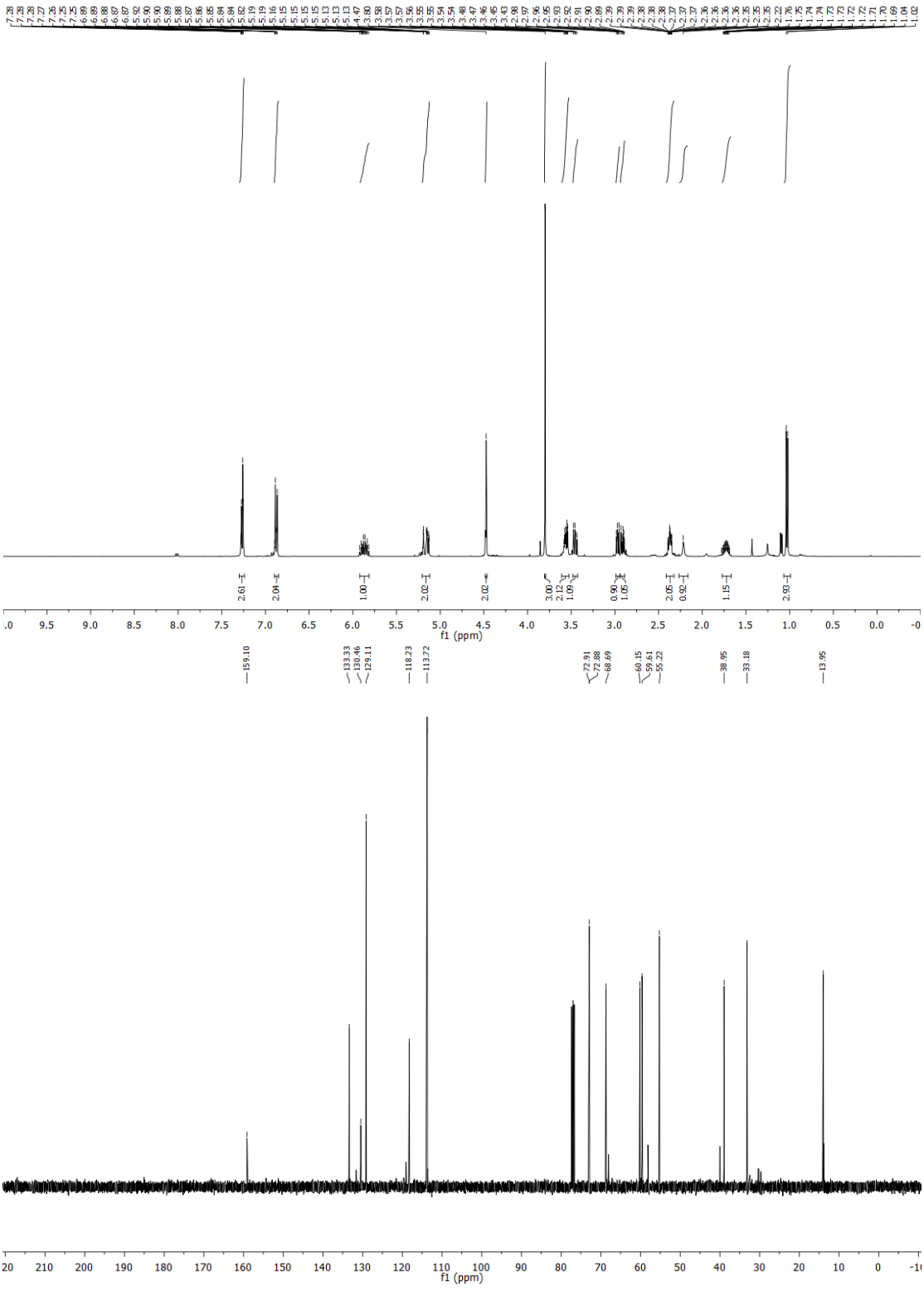
7.6, 4.3 Hz, 1H), 2.91 (dd, *J* = 9.5, 4.3 Hz, 1H), 2.37 (m, 2H), 2.21 (brs, 1H), 1.73 (m, 1H), 1.03 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 133.3, 130.5, 129.1, 118.2, 113.7, 72.9, 72.9, 68.7, 60.2, 59.6, 55.2, 39.0, 33.2, 14.0.

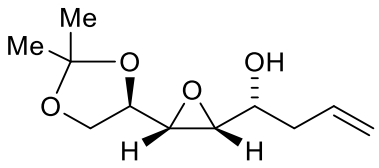
HRMS (ESI) Calculated for $C_{17}H_{24}O_4$ [M+Na^+] = 315.1567, Found 315.1556.

FTIR (neat) 3423, 2963, 2361, 1612, 1512, 1247, 1088, 1034, 820 cm^{-1}.

$[\alpha]_D^{25}$: +25.00 (*c* 1.0, $CHCl_3$).


f1 (ppm)
f1 (ppm)

***(R)*-1-((2*R*,3*S*)-3-(*(R)*-2,2-dimethyl-1,3-dioxolan-4-yl)oxiran-2-yl)but-3-en-1-ol (2.2d)**



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(R)*-SEGPHOS (6.1 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), alcohol **2.1d** (35 mg, 0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.1 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (1.0 mL, 0.2 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1–3:1) to furnish the title compound as a colorless oil (32.6 mg, 0.15 mmol, anti:syn = 10:1) in 76% yield.

Spectral data is reported for the major isomer.

TLC (SiO_2) R_f = 0.42 (hexanes/ethyl acetate = 2:1).

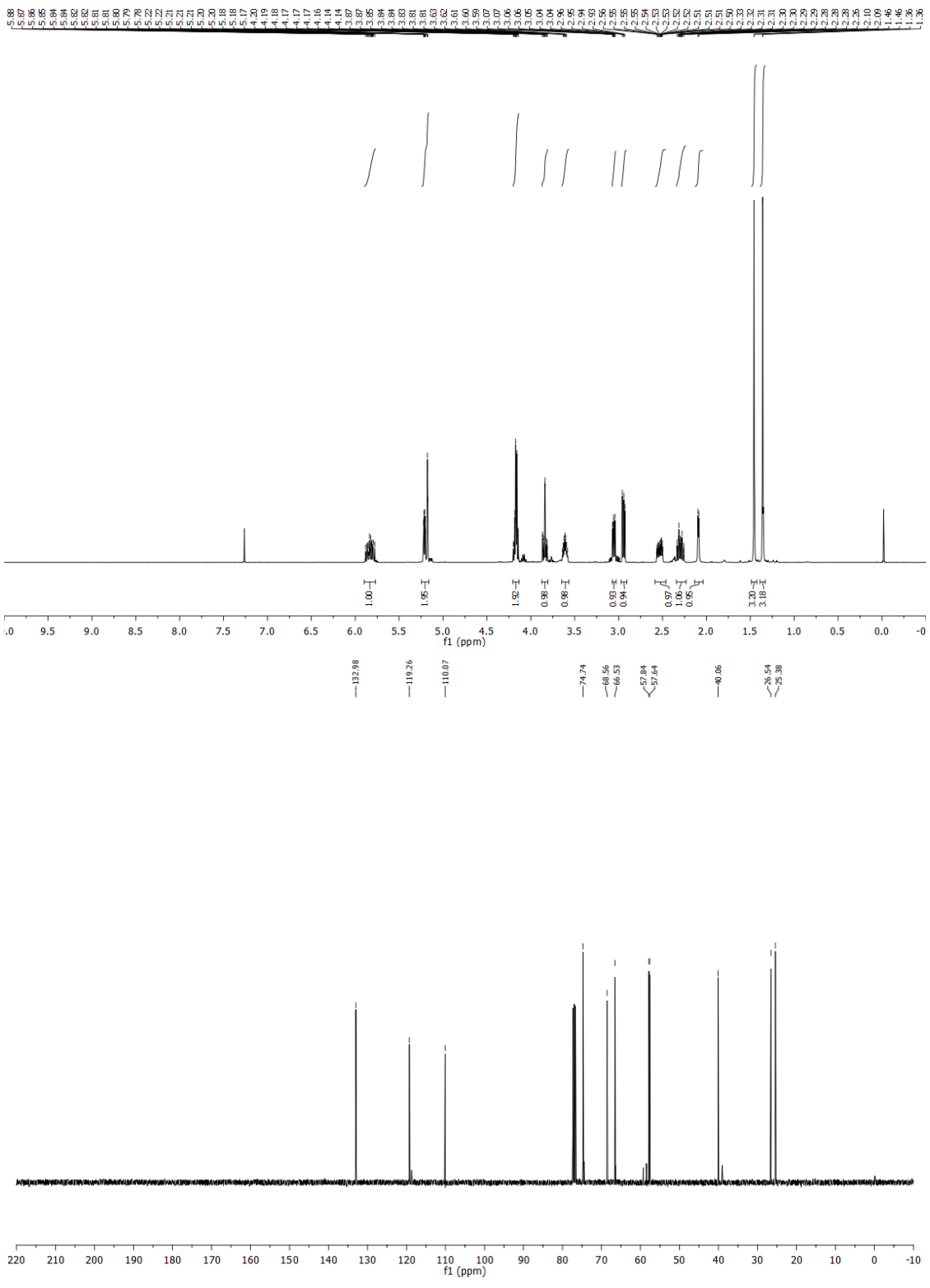
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.84 (m, 1H), 5.22 (m, 2H), 4.18 (m, 2H), 3.85 (m, 1H), 3.63 (dt, *J* = 7.7, 3.9 Hz, 1H), 3.07 (m, 1H), 2.96 (dd, *J* = 7.3, 4.3 Hz, 1H), 2.55 (m, 1H), 2.31(m, 1H), 2.11 (d, *J* = 3.7 Hz, 1H), 1.48 (s, 3H), 1.38 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.0, 119.3, 110.1, 74.7, 68.6, 66.5, 57.8, 57.6, 40.1, 26.5, 25.4.

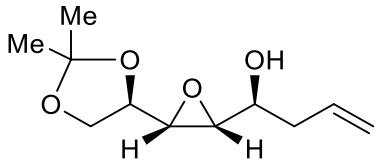
HRMS (ESI) Calculated for $C_{11}H_{18}O_4$ [M+Na^+] = 237.1097, Found 237.1095.

FTIR (neat) 3444, 2986, 1372, 1254, 1211,1154, 1058, 916, 840 cm^{-1}.

$[\alpha]_D^{30}$: +89.00 (*c* 1.0, $CHCl_3$).



***(S)*-1-((2*R*,3*S*)-3-(*(R)*-2,2-dimethyl-1,3-dioxolan-4-yl)oxiran-2-yl)but-3-en-1-ol (*epi*-2.2d)**



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(S)*-SEGPHOS (6.1 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), alcohol **2.1d** (35 mg, 0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.1 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (1.0 mL, 0.2 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1–3:1) to furnish the title compound as a colorless oil (30.9 mg, 0.14 mmol, anti:syn = 9:1) in 72% yield.

Spectral data is reported for the major isomer.

TLC (SiO_2) R_f = 0.38 (hexanes/ethyl acetate = 2:1).

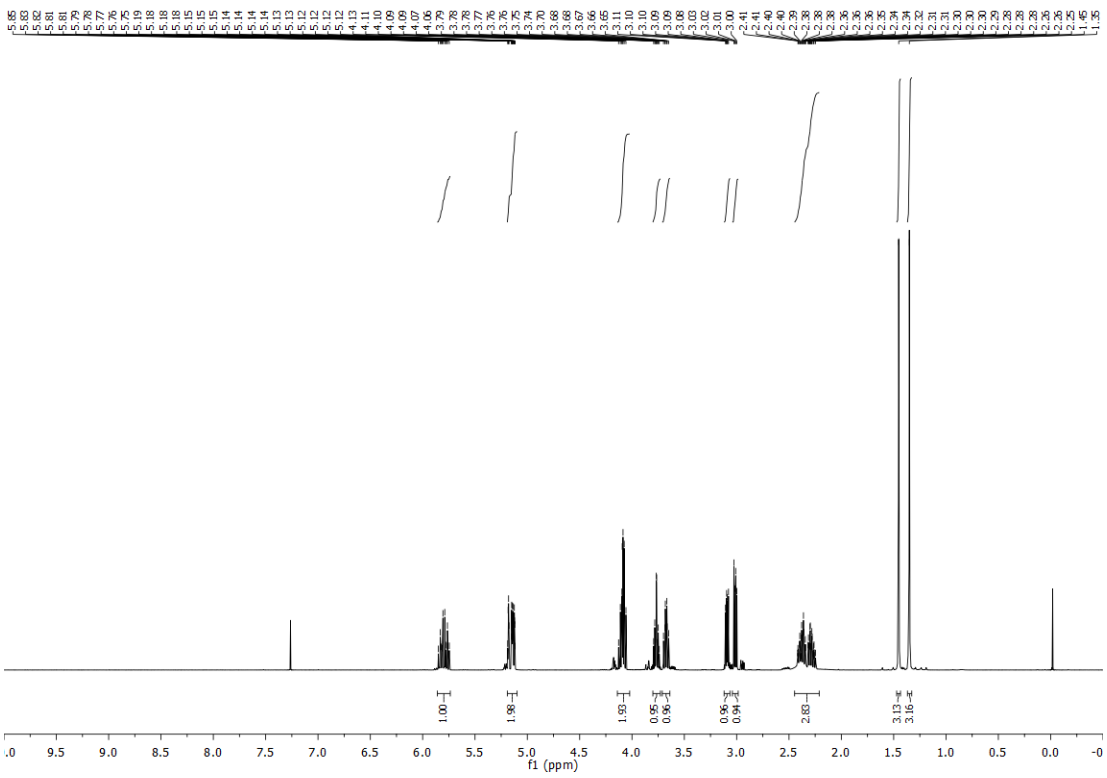
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.82 (m, 1H), 5.17 (m, 2H), 4.11 (dt, *J* = 11.2, 6.3 Hz, 2H), 3.79 (dq, *J* = 7.1, 4.1 Hz, 1H), 3.69 (td, *J* = 7.0, 5.9 Hz, 1H), 3.11 (dd, *J* = 7.1, 4.4 Hz, 1H), 3.03 (dd, *J* = 6.9, 4.4 Hz, 1H), 2.35 (m, 3H), 1.47 (s, 3H), 1.37 (s, 3H).

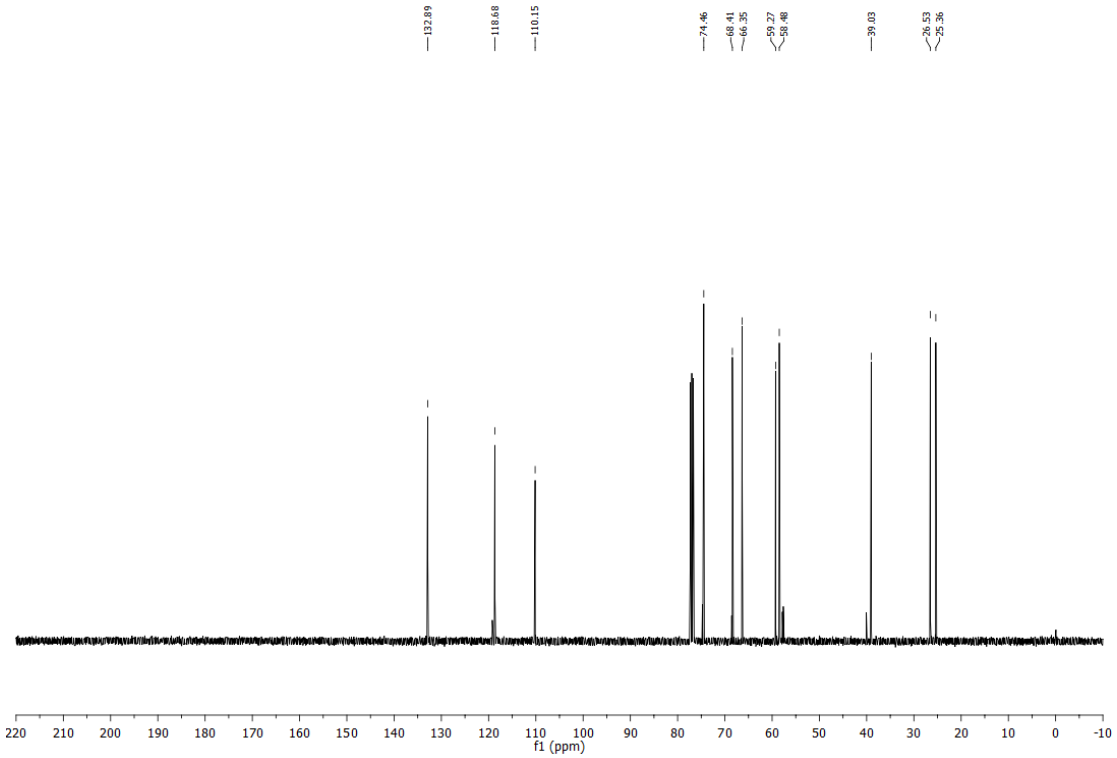
^{13}C NMR (100 MHz, $CDCl_3$): δ = 132.9, 118.7, 110.1, 74.5, 68.4, 66.4, 59.3, 58.5, 39.0, 26.5, 25.4.

HRMS (ESI) Calculated for $C_{11}H_{18}O_4$ [M+Na^+] = 237.1097, Found 237.1094.

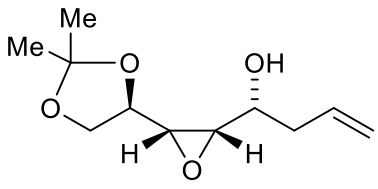
FTIR (neat) 3452, 2985, 1372, 1255, 1211,1154, 1057, 915, 843 cm^{-1}.

$[\alpha]_D^{30}$: +127.33 (*c* 1.0, $CHCl_3$).


f1 (ppm)


f1 (ppm)

***(R)*-1-((2*S*,3*R*)-3-(*(R)*-2,2-dimethyl-1,3-dioxolan-4-yl)oxiran-2-yl)but-3-en-1-ol (2.2e)**



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(R)*-SEGPHOS (6.1 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), alcohol **2.1e** (35 mg, 0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.1 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (1.0 mL, 0.2 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1–3:1) to furnish the title compound as a colorless oil (33.9 mg, 0.16 mmol, anti:syn = 1:10) in 79% yield.

Spectral data is reported for the major isomer.

TLC (SiO_2) R_f = 0.52 (hexanes/ethyl acetate = 2:1).

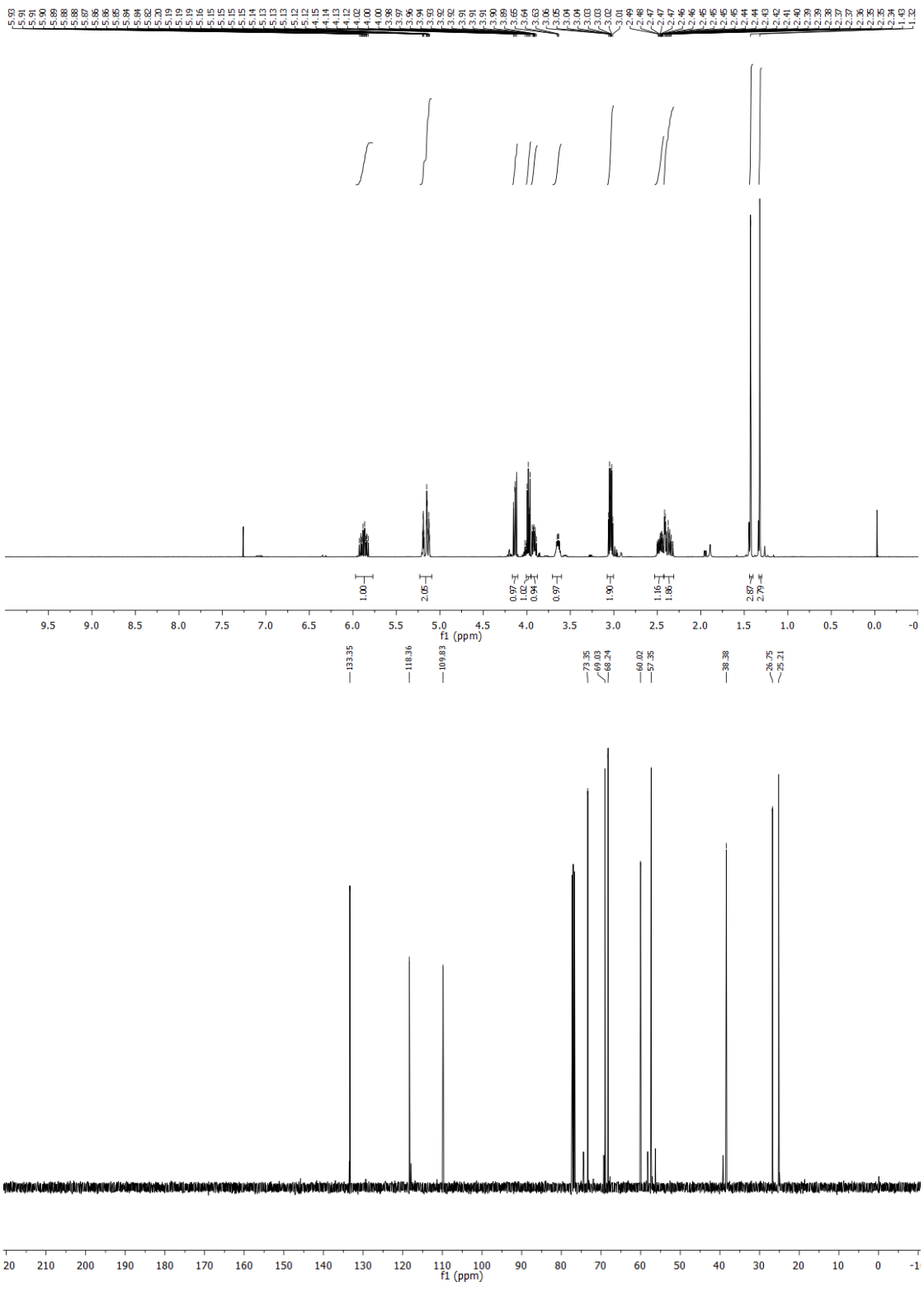
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.88 (m, 1H), 5.16 (m, 2H), 4.14 (dd, *J* = 8.5, 6.1 Hz, 1H), 4.14 (dd, *J* = 8.5, 5.1 Hz, 1H), 3.92 (m, 1H), 3.65 (m, 1H), 3.04 (m, 2H), 2.47 (m, 1H), 2.37 (m, 2H), 1.45 (s, 3H), 1.35 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.4, 118.4, 109.8, 73.4, 69.0, 68.2, 60.0, 57.4, 38.4, 26.8, 25.2.

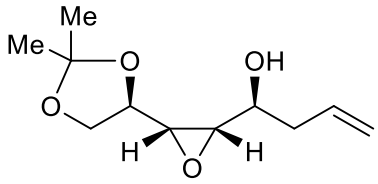
HRMS (ESI) Calculated for $C_{11}H_{18}O_4$ [M+Na^+] = 237.1097, Found 237.1094.

FTIR (neat) 3447, 2985, 2936, 1642, 1436, 1372, 1253, 1222, 1152, 1065, 918, 845 cm^{-1}.

$[\alpha]_D^{27}$: −108.33 (*c* 1.0, $CHCl_3$).


f1 (ppm)
f1 (ppm)

***(S)*-1-((2*S*,3*R*)-3-(*(R)*-2,2-dimethyl-1,3-dioxolan-4-yl)oxiran-2-yl)but-3-en-1-ol (*epi*-2.2e)**



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(S)*-SEGPHOS (6.1 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), alcohol **2.1e** (35 mg, 0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.1 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (1.0 mL, 0.2 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1–3:1) to furnish the title compound as a colorless oil (31.7 mg, 0.15 mmol, anti:syn = 6:1) in 74% yield.

Spectral data is reported for the major isomer.

TLC (SiO_2) R_f = 0.48 (hexanes/ethyl acetate = 2:1).

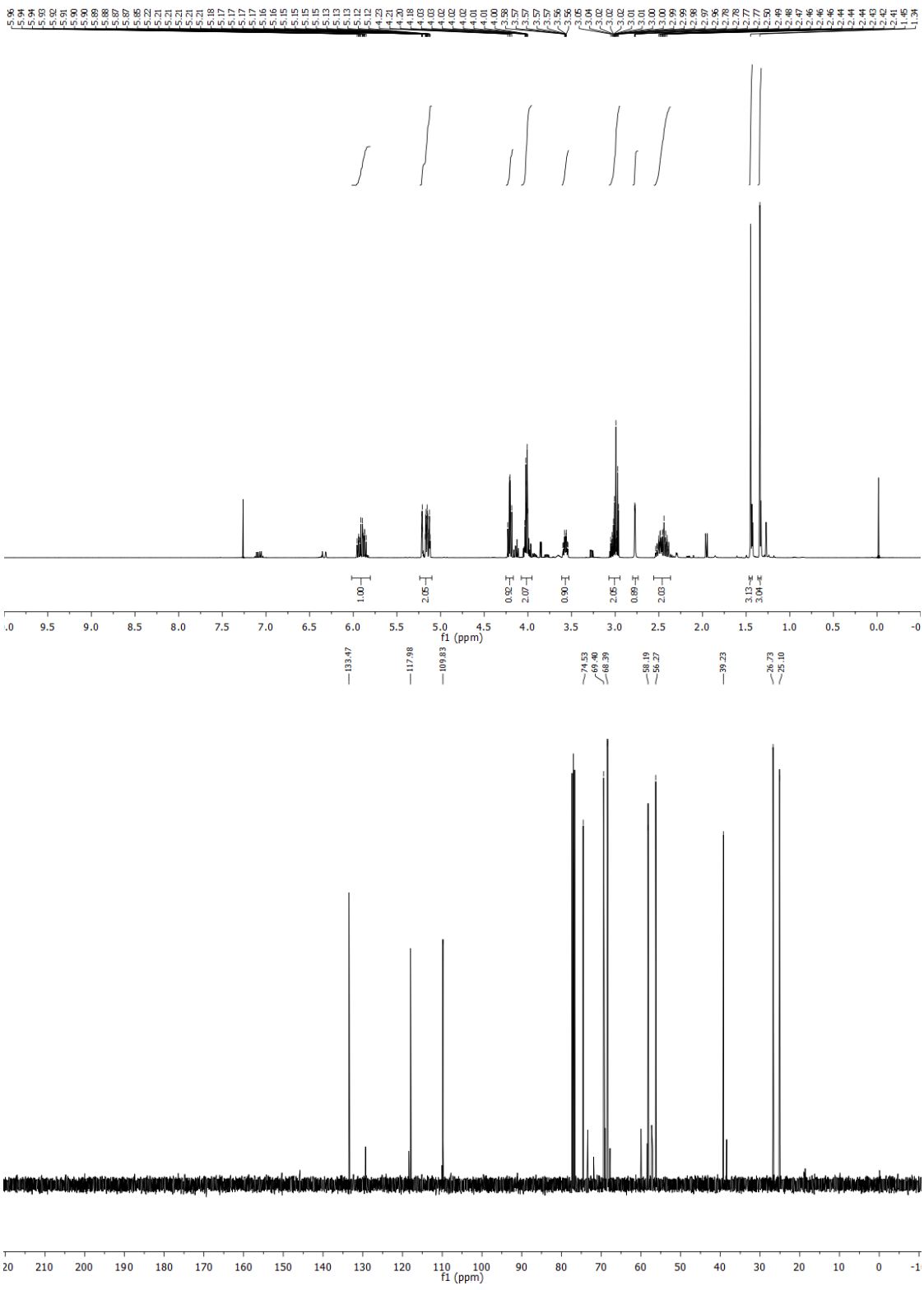
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.90 (m, 1H), 5.17 (m, 2H), 4.20 (m, 1H), 4.02 (m, 1H), 3.57 (m, 1H), 3.00 (m, 2H), 2.77 (dd, *J* = 2.4, 0.8 Hz, 1H), 2.44 (m, 2H), 1.45 (s, 3H), 1.34 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.5, 118.0, 109.8, 74.5, 69.4, 68.4, 58.2, 56.3, 39.2, 26.7, 25.1.

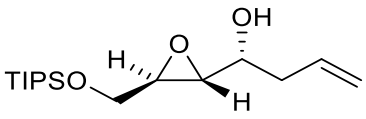
HRMS (ESI) Calculated for $C_{11}H_{18}O_4$ [M+Na^+] = 237.1097, Found 237.1095.

FTIR (neat) 3447, 2985, 2936, 1642, 1436, 1372, 1253, 1222, 1152, 1065, 918, 845 cm^{-1}.

$[\alpha]_D^{26}$: −126.33 (*c* 1.0, $CHCl_3$).



***(R)*-1-((2*R*,3*R*)-3-(((triisopropylsilyl)oxy)methyl)oxiran-2-yl)but-3-en-1-ol (2.2f)**



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(R)*-Cl-MeO-BIPHEP (6.5 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), alcohol **2.1f** (52 mg, 0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.1 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (1.0 mL, 0.2 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–12:1) to furnish the title compound as a colorless oil (39.1 mg, 0.13 mmol, anti:syn = 17:1) in 65% yield.

Spectral data is reported for the major isomer.

TLC (SiO_2) R_f = 0.58 (hexanes/ethyl acetate = 4:1).

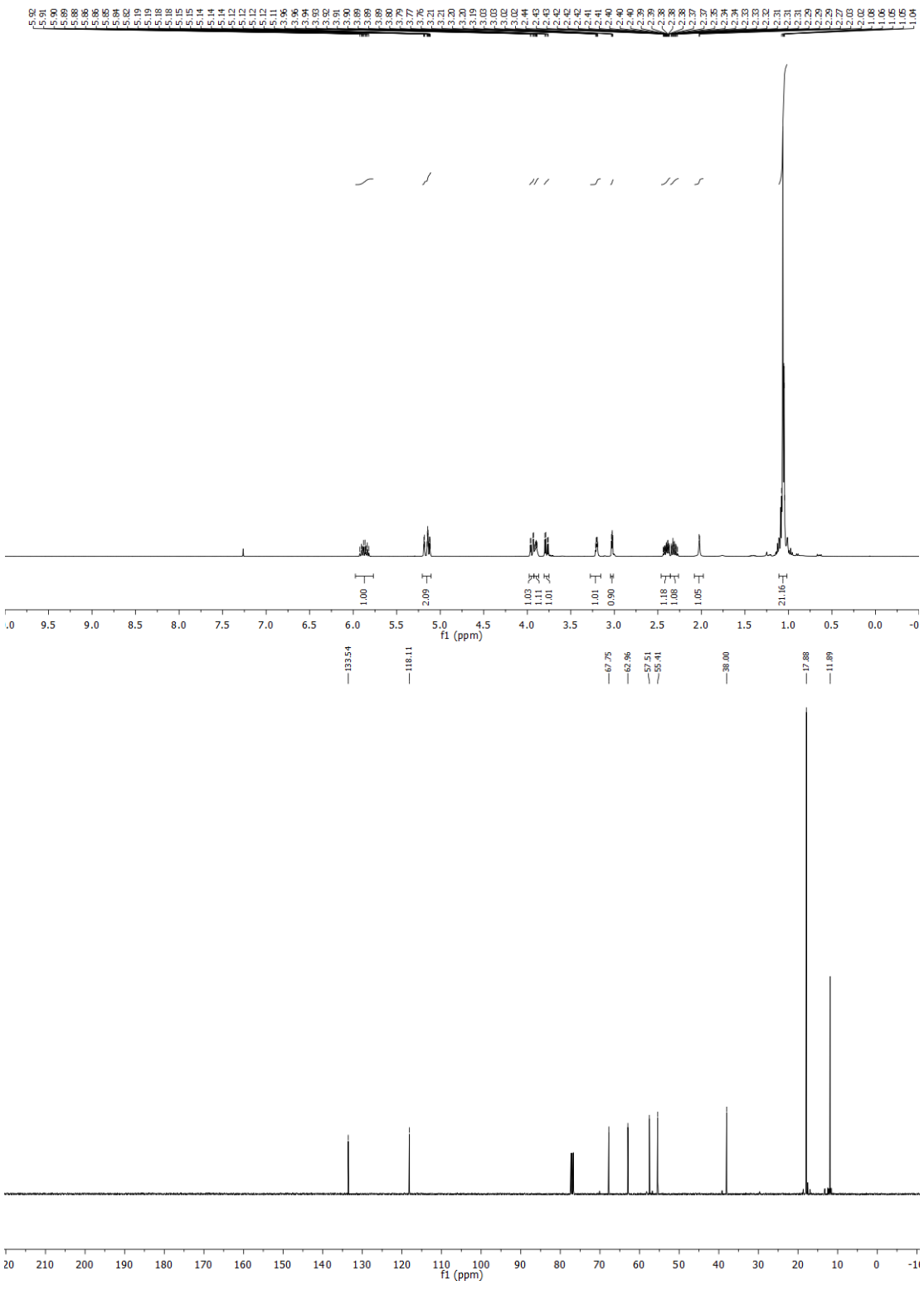
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.87 (m, 1H), 5.14 (m, 2H), 3.94 (dd, *J* = 11.8, 3.0 Hz, 1H), 3.89 (m, 1H), 3.77 (dd, *J* = 11.8, 4.5 Hz, 1H), 3.20 (m, 1H), 3.02 (dd, *J* = 3.3, 2.3 Hz, 1H), 2.40 (m, 1H), 2.31 (m ,1H), 2.02 (brs, 1H), 1.05 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.5, 118.1, 67.8, 63.0, 57.5, 55.4, 38.0, 17.9, 11.9.

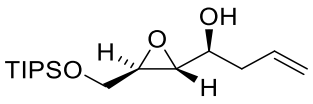
HRMS (ESI) Calculated for $C_{16}H_{32}O_3Si$ [M+Na^+] =323.2013, Found 323.2013.

FTIR (neat) 3438, 2942, 1463, 1114, 1067, 996, 882, 777, 682 cm^{-1}.

$\mathbf{[\alpha]_D^{30}}$**:** +106.00 (*c* 1.0, $CHCl_3$).



***(S)*-1-((2*R*,3*R*)-3-(((triisopropylsilyl)oxy)methyl)oxiran-2-yl)but-3-en-1-ol (*epi*-2.2f)**



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with $[Ir(cod)Cl]_2$ (3.4 mg, 0.005 mmol, 2.5 mol%), *(S)*-Cl-MeO-BIPHEP (6.5 mg, 0.01 mmol, 5 mol%), 4-CN,3-NO-benzoic acid (3.8 mg, 0.02 mmol, 10 mol%), alcohol **2.1f** (52 mg, 0.2 mmol, 100 mol%) and K_2CO_3 (13.8 mg, 0.1 mmol, 50 mol%). The vessel was purged with argon for 5 minutes. Anhydrous THF (1.0 mL, 0.2 M) and allyl acetate (43 µL, 0.4 mmol, 200 mol%) were sequentially added via syringe. The reaction vessel was sealed and the reaction mixture was allowed to stir at 100 ˚C for 48 h. After reaching ambient temperature, the reaction mixture was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–12:1) to furnish the title compound as a colorless oil (19.2 mg, 0.06 mmol, anti:syn = 1:7) in 32% yield.

Spectral data is reported for the major isomer.

TLC (SiO_2) R_f = 0.54 (hexanes/ethyl acetate = 4:1).

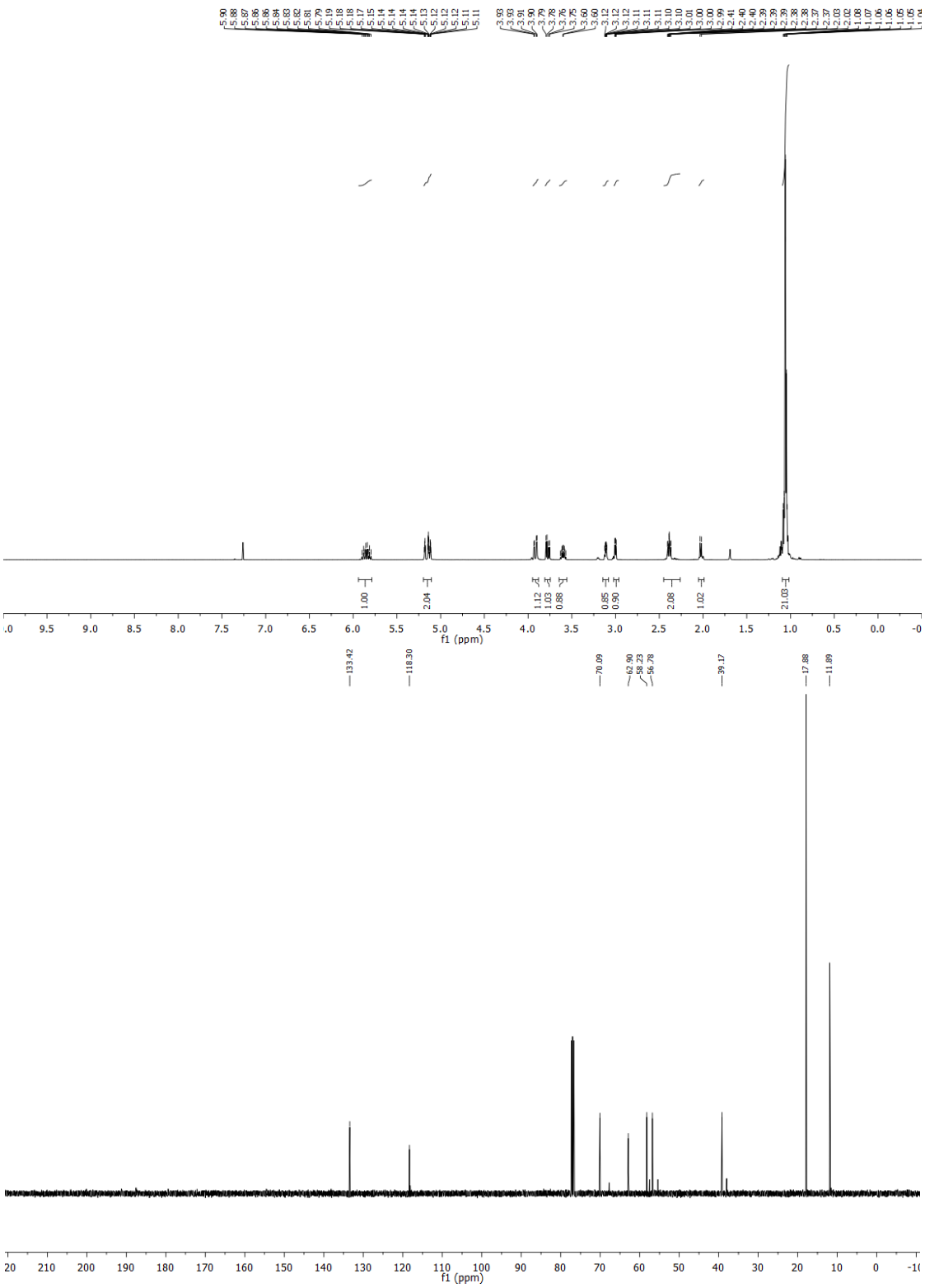
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.85 (m, 1H), 5.14 (m, 2H), 3.92 (dd, *J* = 11.7, 2.9 Hz, 1H), 3.77 (dd, *J* = 11.8, 4.5 Hz, 1H), 3.60 (m, 1H), 3.11 (ddd, *J* = 4.6, 3.1, 2.3 Hz, 1H), 3.00 (dd, *J* = 4.7, 2.3 Hz, 1H), 2.39 (m, 2H), 2.03 (m, 1H), 1.06 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.4, 118.3, 70.1, 62.9, 58.2, 56.8, 39.2, 17.9, 11.9.

HRMS (ESI) Calculated for $C_{16}H_{32}O_3Si$ [M+Na^+] =323.2013, Found 323.2014.

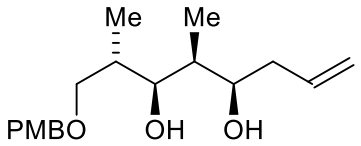
FTIR (neat) 3426, 2942, 1463, 1112, 1067, 996, 882, 781, 682 cm^{-1}.

$[\alpha]_D^{30}$: +107.33 (*c* 1.0, $CHCl_3$).


f1 (ppm)
f1 (ppm)

Procedures and Spectral Data for the Synthesis of 2.3c

(2*S*,3*S*,4*S*,5*R*)-1-((4-methoxybenzyl)oxy)-2,4-dimethyloct-7-ene-3,5-diol (2.3c)



Detailed Procedures

To a round-bottomed flask with **2.2c** (30.0 mg, 0.10 mmol) under an argon atmosphere was added 1,2-dichloroethane (3.0 mL, 0.03 M). The reaction vessel was placed in -40 ºC bath and *n*-BuLi (80 µL, 2.5 M in hexanes, 0.25 mmol, 200 mol%) was added. The mixture was stirred for 30 minutes, at which point trimethylaluminum (0.16 mL, 2.0 M in toluene, 0.31 mmol, 300 mol%) was added dropwise. The mixture was allowed to warm to -15 ºC over 4 h. Water (3 mL) was added to the mixture and the mixture was transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (10 mL × 3). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 7:1–4:1) to furnish the title compound as a colorless oil (23.7 mg, 0.08 mmol) in 77% yield.

TLC (SiO_2) R_f = 0.40 (hexanes/ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (m, 2H), 6.89 (m, 2H), 5.82 (m, 1H), 5.09 (m, 2H), 4.46 (s, 2H), 4.36 (brs, 1H), 3.90 (ddd, *J* = 7.8, 6.3, 1.8 Hz, 1H), 3.81 (s, 3H), 3.75

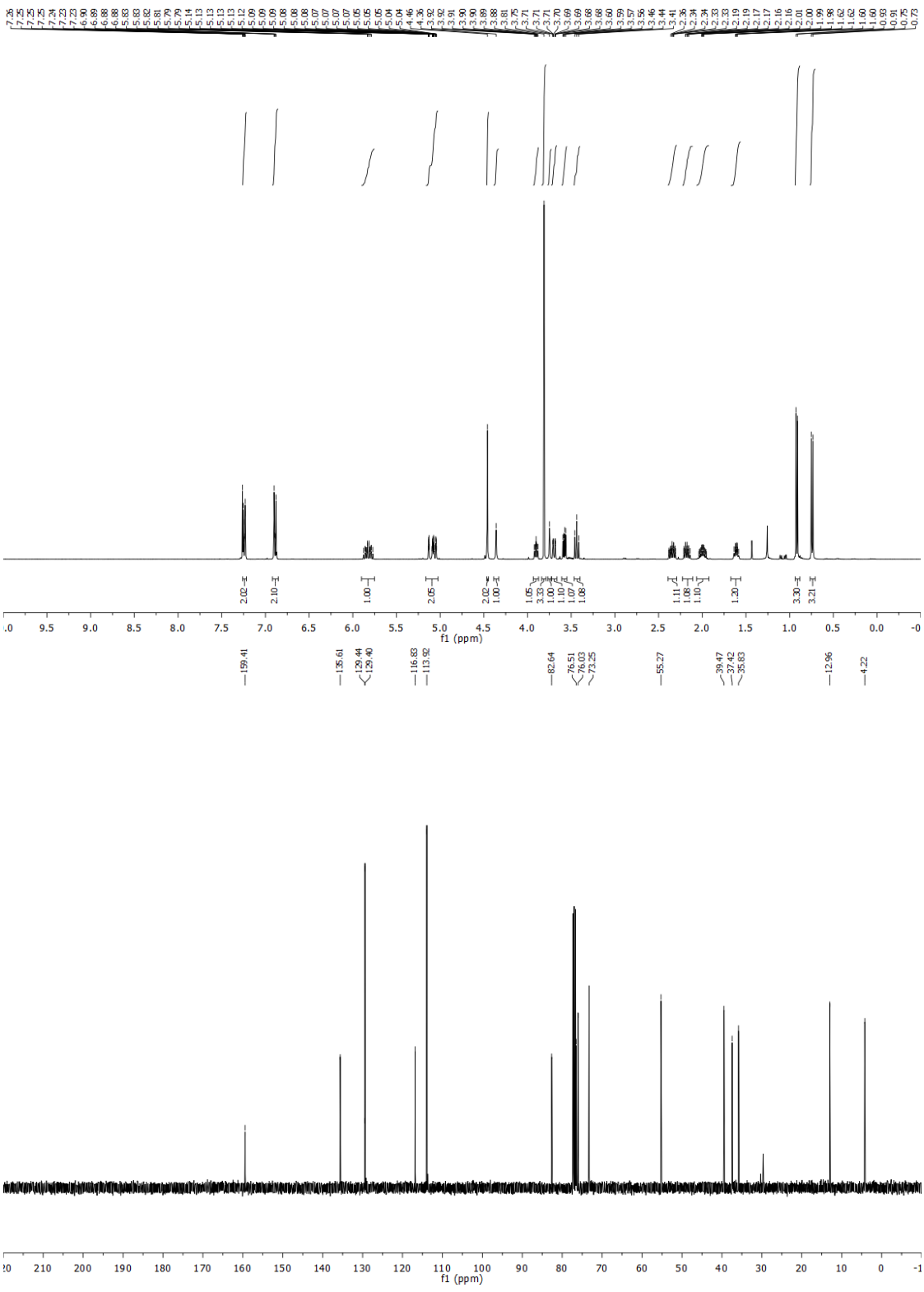
(brs, 1H), 3.70 (m, 1H), 3.58 (dd, *J* = 9.1, 4.0 Hz, 1H), 3.44 (t, *J* = 9.2 Hz, 1H), 2.34 (m, 1H), 2.17 (m, 1H), 2.00 (m, 1H), 1.61 (m, 1H), 0.92 (d, *J* = 7.0 Hz, 3H), 0.74 (d, *J* = 6.9 Hz, 3H).

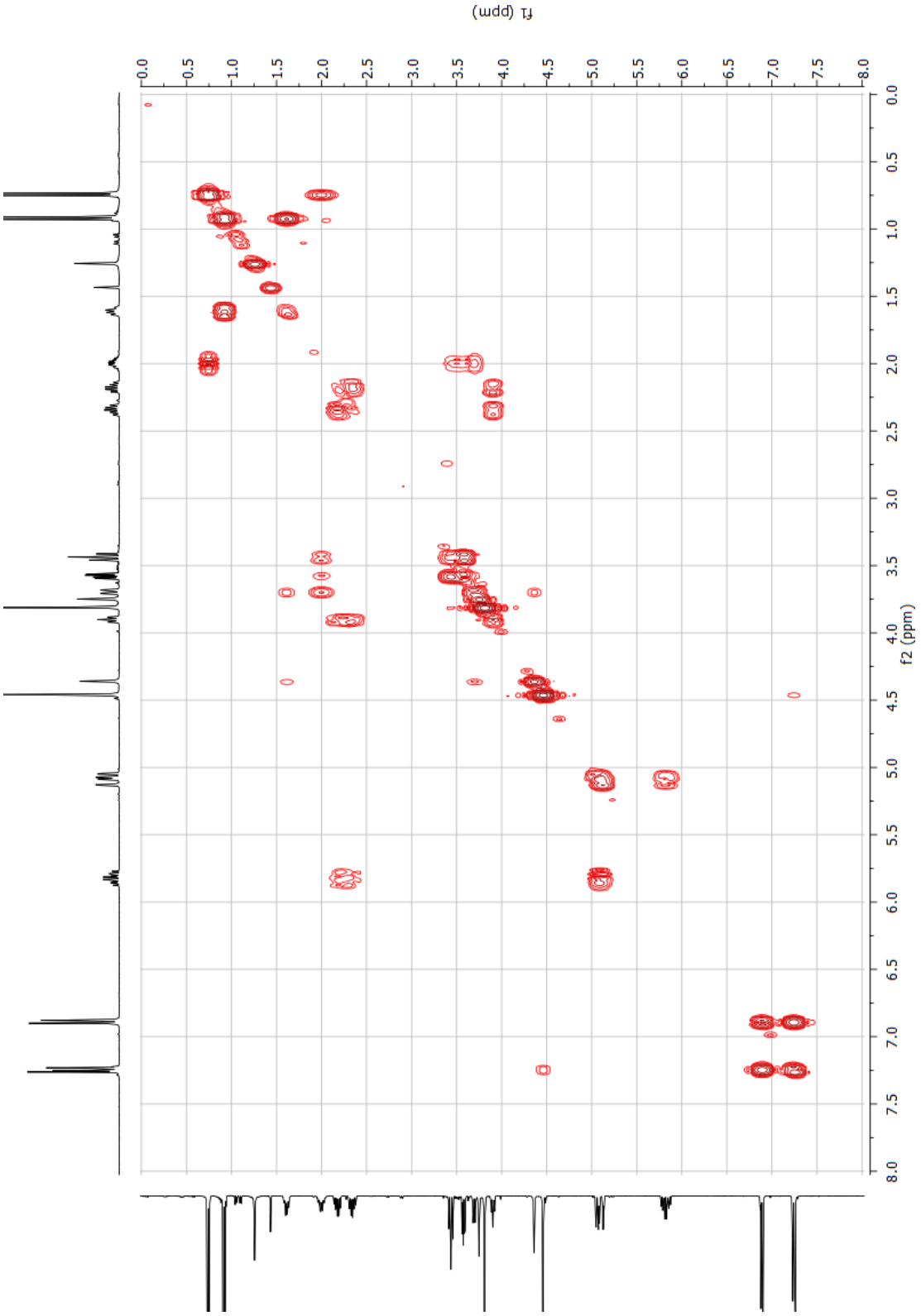
^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 135.6, 129.4, 129.4, 116.8, 113.9, 82.6, 76.5, 76.0, 73.3, 55.3, 39.5, 37.4, 35.8, 13.0, 4.2.

HRMS (ESI) Calculated for $C_{18}H_{28}O_4$ [M+K^+] = 347.1619, Found 347.1611.

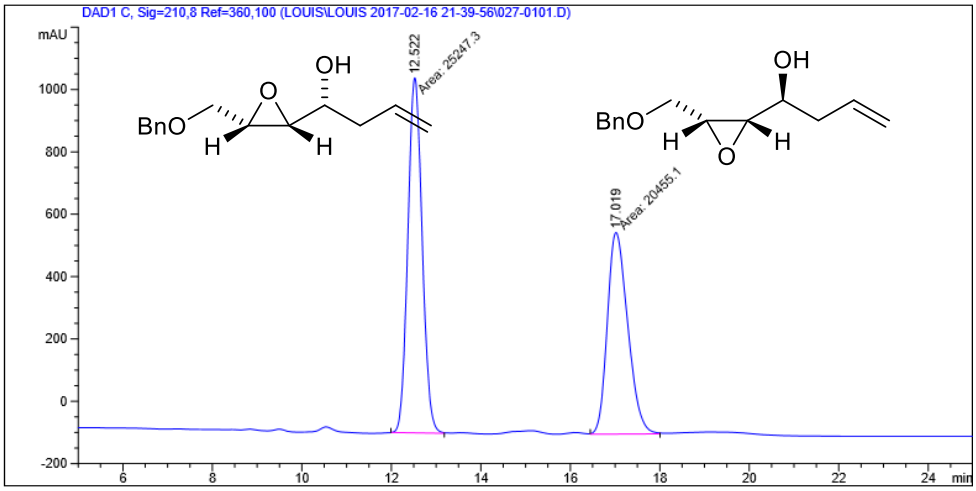
FTIR (neat) 3431, 2915, 1612, 1513, 1247, 1079, 1035, 970, 753 cm^{-1}.

$[\alpha]_D^{30}$: +42.83 (*c* 1.0, $CHCl_3$).



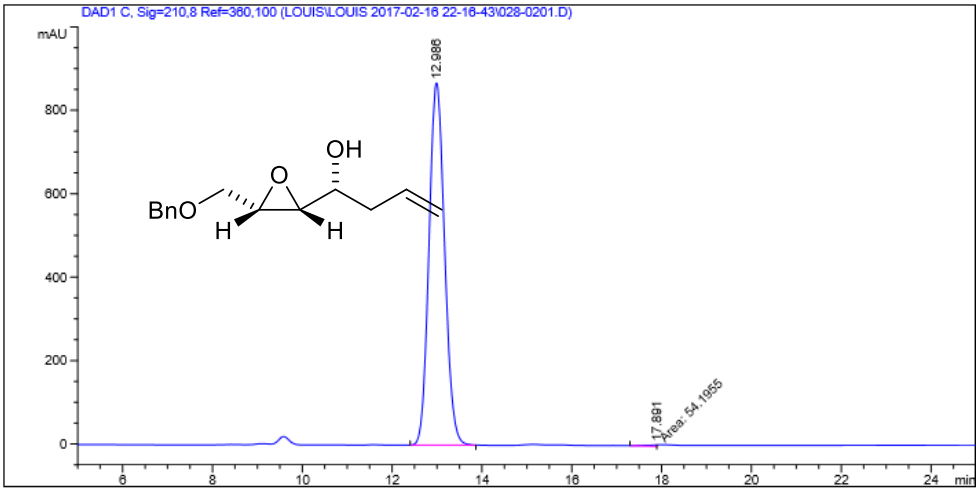

f1 (ppm)
f2 (ppm)

HPLC Data Establishing the Horeau Effect in the Allylation of Glycidols 2.2a



Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.522	MM	0.3696	2.52473e4	1138.46338	55.2428
2	17.019	MM	0.5271	2.04551e4	646.80481	44.7572
Totals :				4.57024e4	1785.26819	



Signal 1: DAD1 C, Sig=210,8 Ref=360,100

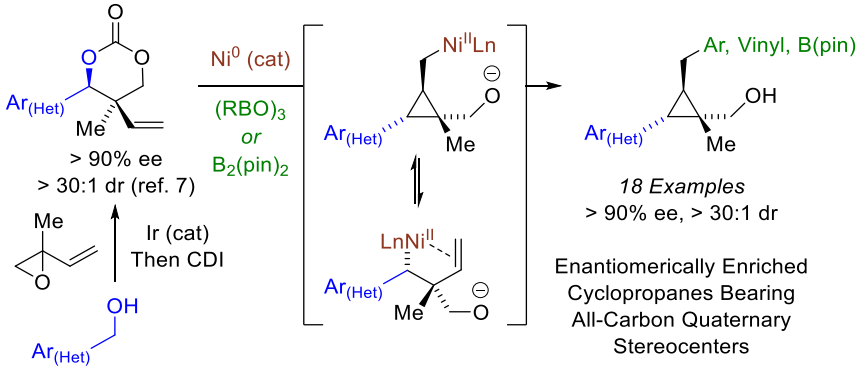
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.986	BB	0.3752	2.09295e4	868.34589	99.7417
2	17.891	MM	0.2433	54.19551	3.71199	0.2583
Totals :				2.09837e4	872.05788	

HPLC: Enantiomeric excess was determined by HPLC analysis of the benzoate derivative of the product (Chiralcel OD-H column, hexanes:*i*-PrOH = 90:10, 1.00 mL/min, 210 nm), *ee* = 99.5%.

Chapter 3: Nickel-Catalyzed Cross-Coupling of Vinyl Dioxanones to Form Enantiomerically Enriched Cyclopropanes*

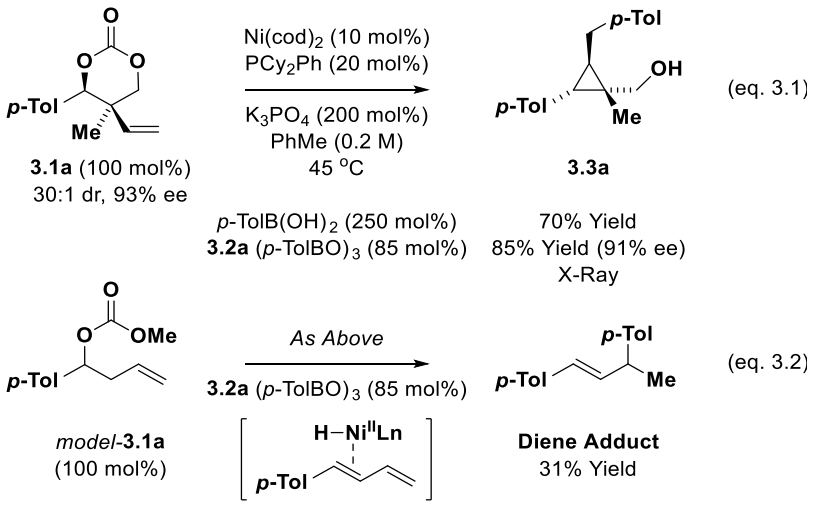
3.1 Introduction

Cyclopropanes appear as substructures across diverse secondary metabolites[1] and are frequently found in commercial medicines, agrochemicals and fragrances.[2] Hence, the development of methods for cyclopropane formation represents a persistent challenge in chemical research.[3] Among the most effective methods for the preparation of enantiomerically enriched cyclopropanes is the reaction of olefins with metal carbenoids.[3] Here, we report a strategy for the asymmetric synthesis of cyclopropanes under the conditions of metal catalyzed cross-coupling. Specifically, nickel(0) catalysts[4,5] react with enantiomerically enriched 4-aryl-5-vinyl-1,3-dioxanones to form (cyclopropyl-carbinyl)nickel(II) species, which, in the presence of organoboron reagents or $B_2(pin)_2$ deliver cyclopropanes in a stereospecific manner. Thus, the enantioselective synthesis of tetra-substituted cyclopropanes bearing all-carbon quaternary stereocenters is achieved (Scheme 3.1).



Scheme 3.1 Synthesis of enantiomerically enriched cyclopropanes from vinyl-dioxanones by way of transient (cyclopropyl-carbinyl)nickel species.

*This chapter is based on the published work:
Guo, Y.-A.; Liang, T.; Kim, S. W.; Xiao, H.; Krische, M. J. *J. Am. Chem. Soc.* **2017**, *139*, 6847.



In connection with ongoing investigations into the formation of C-C bonds *via* hydrogenation and transfer hydrogenation,[6] we recently reported an iridium catalyzed coupling of primary alcohols with isoprene oxide to form products of tert-(hydroxy)-prenylation – a byproduct-free transformation that occurs with exceptional control of *anti*-diastereo- and enantioselectivity.[7] It was posited that cyclic carbonates derived from these reaction products should be predisposed toward cyclopropane formation under cross-coupling conditions, as geminal substitution of the neopentyl glycol precludes competing *β*-hydride elimination of the σ-benzylmetal intermediate and should conformationally bias the system toward olefin insertion[8] *via* Thorpe-Ingold effect.[9] However, the facility of conventional benzylic cross-coupling rendered the feasibility of the proposed cyclopropane formation uncertain.[10]

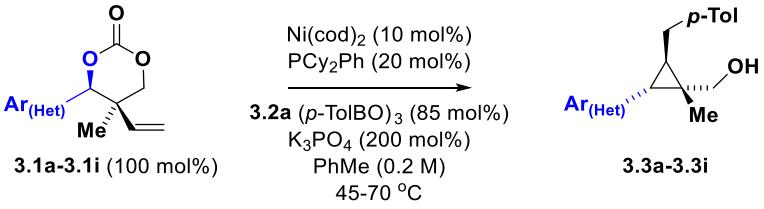
3.2 Reaction Development and Scope

In an initial experiment, vinyl-dioxanone **3.1a** was exposed to the catalyst derived from $Ni(cod)_2$ (10 mol%) and PCy_3 (20 mol%) in the presence of tri(*p*-tolyl)boroxine **3.2a** and K_3PO_4 (200 mol%) in toluene (0.1 M) at 60 ^oC. To our delight, cyclopropane **3.3a** was formed in 36% yield as a single diastereomer. Conversion was found to be sensitive to concentration and temperature. At 45 ^oC under otherwise identical conditions, a 53% yield of cyclopropane **3.3a** was obtained. Using the nickel catalyst modified by PCy_2Ph (20 mol%), cyclopropane **3.3a** was obtained in 77% yield. Finally, at slightly higher concentration (toluene, 0.2 M), an 85% yield of cyclopropane **3.3a** was achieved (eq. 3.1). Stereospecificity was corroborated by chiral stationary phase HPLC analysis of cyclopropane **3.3a**. Relative stereochemistry of cyclopropane **3.3a** was confirmed by single crystal X-ray diffraction analysis. *p*-Tolylboronic acid also delivers cyclopropane **3.3a** (eq. 3.1), but in slightly lower yield. Application of these optimal conditions to unsubstituted methyl carbonate *model*-**3.1a** did not result in cyclopropane formation; rather, the indicated product obtained through β-hydride elimination of the σ-benzyl intermediate was formed (eq. 3.2). Cyclic carbonate **3.1a** reacted more efficiently than related acyclic carbonates, suggesting the internal alkoxide generated upon ionization-decarboxylation facilitates group transfer from boron to nickel through an internal boron ate-complex.

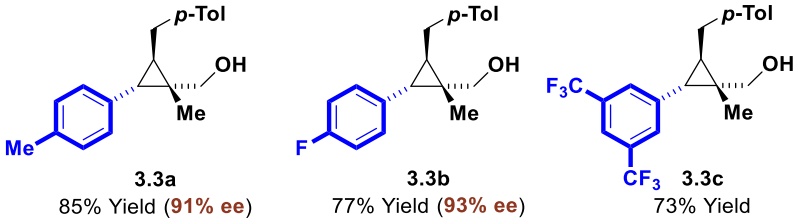
Optimal conditions utilizing tri(*p*-tolyl)boroxine **3.2a** were applied to a structurally diverse set of enantiomerically enriched vinyl-dioxanones **3.1a**-**3.1i** (Table 3.1). Vinyl dioxanones bearing a variety of substituted aromatic (**3.1a**-**3.1d**) and heteroaromatic (**3.1e**-**3.1i**) rings were converted to cyclopropanes **3.3a**-**3.3i** in good yield with complete levels of diastereoselectivity. Relative stereochemistry was assigned in analogy to that determined for **3.3a**. Although the preexisting non-epimerizable

quaternary stereocenter serves as an "internal standard," stereospecificity was spot-checked for compounds **3.3a, 3.3b, 3.3d** and **3.3h**. Notably, unlike prior work involving nickel catalyzed benzylic substitution, extended aromatic systems are not required.[11] Standard conditions also were applied to the coupling of vinyl-dioxanones **3.1a** and 1h with boroxines **3.2b-3.2d**, which incorporate *p*-CF_3-phenyl, *p*-methoxyphenyl and (*E*)-styryl moieties, respectively (Table 3.2).

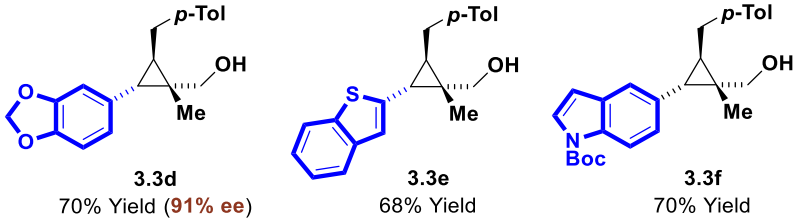
Table 3.1 Stereospecific nickel-catalyzed cross coupling of vinyl-dioxanones **3.1a-3.1i** with tri(*p*-tolyl)boroxine **3.2a** to form cyclopropanes **3.3a-3.3i**.[a]



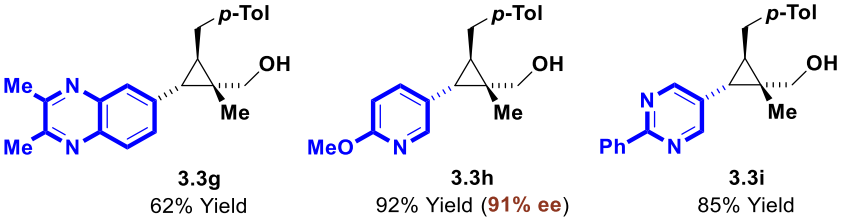
3.1a, Ar = *p*-Tol (30:1 dr, **93% ee**)
3.1b, Ar = *p*-F-Ph (30:1 dr, **94% ee**)
3.1c, Ar = 3,5-$(CF_3)_2$-Ph (70:1 dr, **94% ee**)
3.1d, Ar = Benzodioxolyl (60:1 dr, **91% ee**)
3.1e, Ar = 2-Benzothienyl (20:1 dr, **97% ee**)
3.1f, Ar = 5-(*N*-Boc-Indolyl) (85:1 dr, **88% ee**)
3.1g, Ar = 6-(2,3-Me_2-Quinoxalyl) (30:1 dr, **90% ee**)
3.1h, Ar = 5-(2-MeOPyridyl) (99:1 dr, **90% ee**)
3.1i, Ar = 5-(2-Ph-Pyrimidyl) (99:1 dr, **96% ee**)



3.3a 85% Yield (**91% ee**) X-Ray
3.3b 77% Yield (**93% ee**)
3.3c 73% Yield



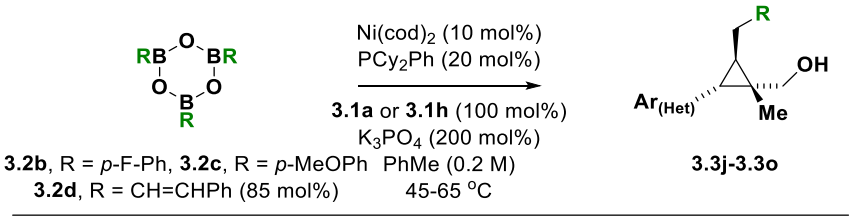
3.3d 70% Yield (**91% ee**)
3.3e 68% Yield
3.3f 70% Yield

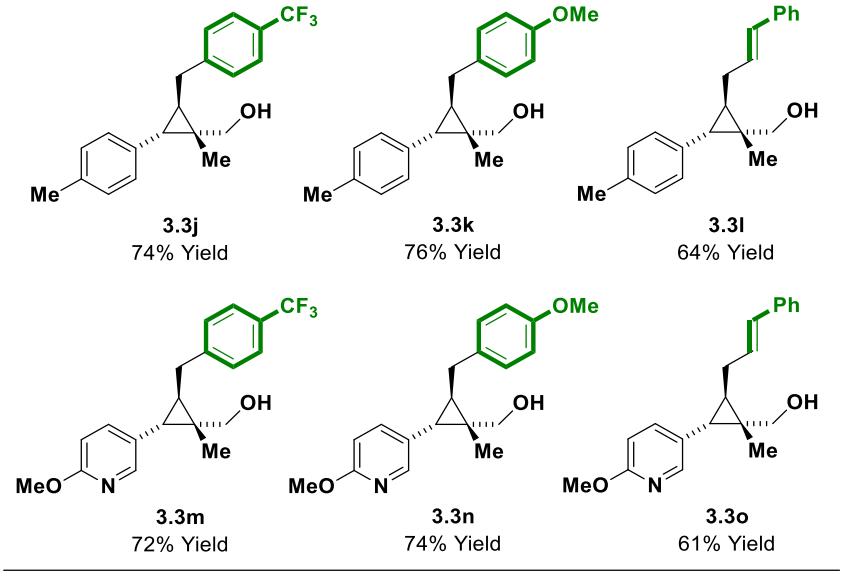


3.3g 62% Yield
3.3h 92% Yield (**91% ee**)
3.3i 85% Yield

[a]Yields of material isolated by silica gel chromatography. All reactions were conducted using enantiomerically enriched starting materials. See Supporting Information for further experimental details.

Table 3.2 Stereospecific nickel-catalyzed cross coupling of vinyl-dioxanones **3.1a** or **3.1h** with boroxines **3.2b-3.2d** to form cyclopropanes **3.3j-3.3o**.[a]

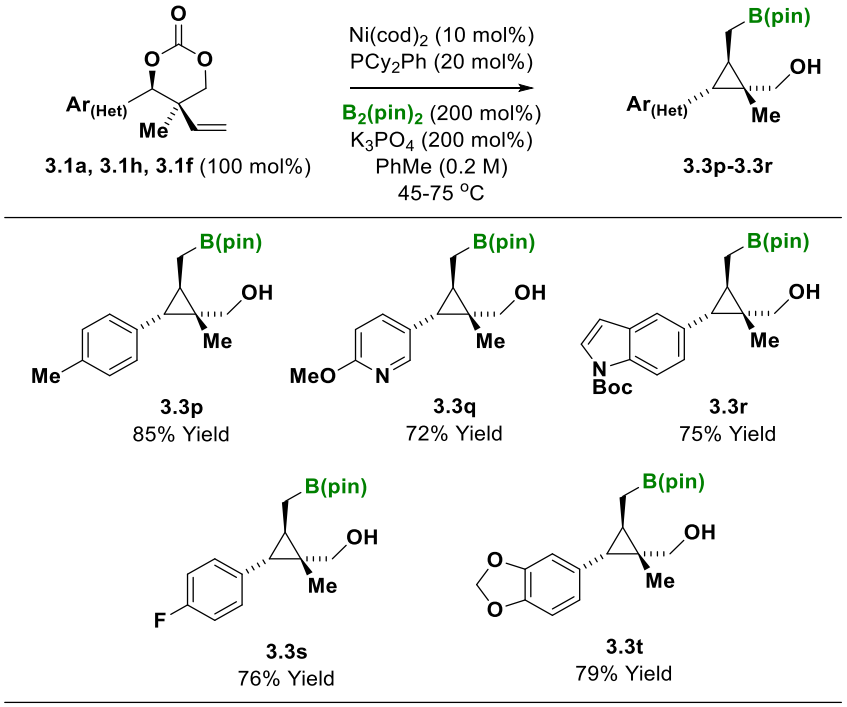




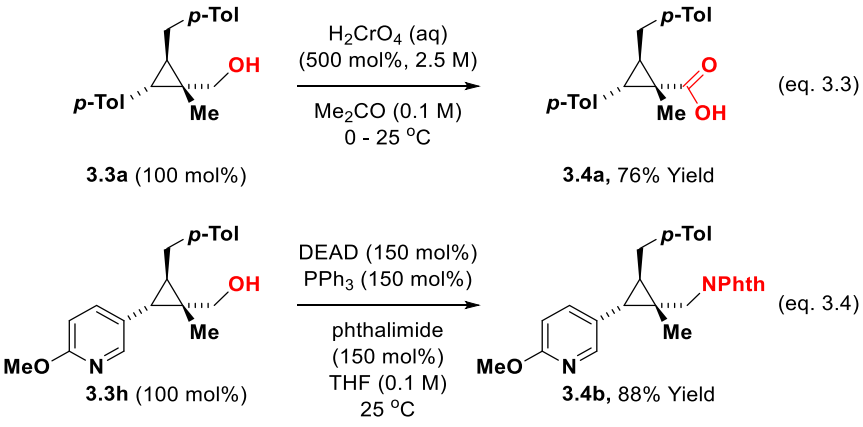
[a]Yields of material isolated by silica gel chromatography. All reactions were conducted using enantiomerically enriched starting materials. See Supporting Information for further experimental details.

The resulting cyclopropanes **3.3j-3.3o** were formed in good yield in a completely stereoselective fashion. The coupling of vinyl-dioxanones **3.1a, 3.1b, 3.1d, 3.1h** and **3.1f** with $B_2(pin)_2$ under standard conditions delivers the cyclopropylcarbinyl boronates **3.3p-3.3t** in good yield with complete stereocontrol (Table 3.3).[12] To briefly illustrate the utility of coupling products, the neopentyl alcohol **3.3a** was subjected to Jones oxidation to provide the cyclopropyl carboxylic acid **3.4a** in good yield (eq. 3.3). Additionally, the cyclopropylcarbinyl alcohol **3.3h** was exposed to Mitsunobu conditions in the presence of phthalimide to furnish **3.4b** in excellent yield (eq. 3.4).

Table 3.3 Stereospecific nickel-catalyzed cross coupling of vinyl-dioxanones **3.1a, 3.1b, 3.1d, 3.1h** and **3.1f** with $B_2(pin)_2$ to form cyclopropanes **3.3p-3.3t**.[a]



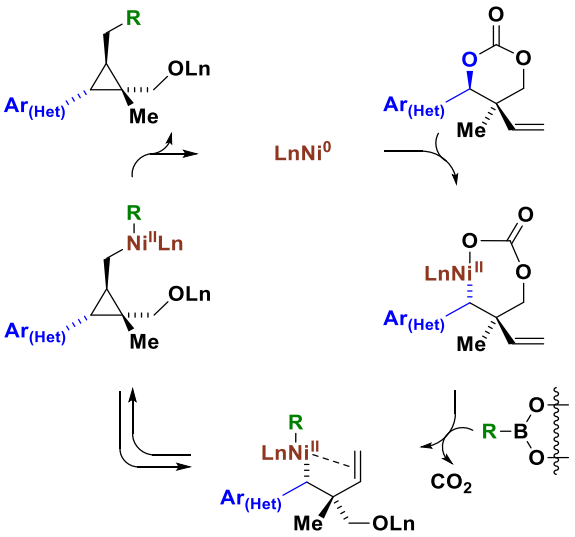
[a]Yields of material isolated by silica gel chromatography. All reactions were conducted using enantiomerically enriched starting materials. See Supporting Information for further experimental details.



3.3 Discussion

A general mechanism for stereospecific cyclopropane formation under the conditions of nickel catalyzed cross-coupling has been proposed (Scheme 3.2). Stereospecific oxidative addition of a nickel(0) species to the benzylic C-O bond occurs with inversion to furnish the indicated σ-benzylnickel(II) complex.[10] Decarboxylation and transmetalation delivers the indicated alkene complex, which upon reversible migratory insertion[8] provides a (cyclopropylcarbinyl)nickel(II) complex. Regardless of the kinetic diastereoselectivity of olefin insertion, reductive elimination occurs exclusively from a single stereoisomer of the (cyclopropylcarbinyl)nickel(II) species to release the cyclopropane and regenerate the zero-valent nickel catalyst.

Scheme 3.2 General catalytic mechanism. Haptomeric equilibria are excluded for clarity.



3.4 Conclusion

In summary, we report a new method for the preparation of enantiomerically enriched cyclopropanes *via* stereospecific nickel catalyzed cross-coupling of vinyl-dioxanones with boroxines or $B_2(pin)_2$. The collective data are consistent with a catalytic mechanism involving nickel(0)-mediated benzylic oxidative addition with inversion of stereochemistry followed by reversible olefin insertion to form a (cyclopropylcarbinyl) nickel complex, which upon reductive elimination delivers the cyclopropane. The novel reactivity embodied by this process should serve as the basis for the syntheses of diverse enantiomerically enriched cyclopropanes.

3.5 Experimental Details

General Information

All reactions were run under an atmosphere of argon. Sealed tubes (13x100 mm) were purchased from Fischer Scientific (catalog number 14-959-35C) and were oven-dried followed by cooling in a desiccator. Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. Ethyl Acetate was dried over potassium carbonate and distilled immediately prior to use. Anhydrous solvents were transferred by oven-dried syringes. Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Dynanmic Absorbents F254). Visualization was accomplished with UV light followed by dipping in *p*-anisaldehyde stain solution then heating. Purification of reactions was carried out by flash chromatography using Silacycle silica gel (40-63 μm, unless indicated specifically). Potassium phosphate was purchased through Acros Organics, flame dried prior to use and stored in a desiccator. $Ni(cod)_2$ was purchased from Strem Chemicals. (*S*)-Ir-Tol-BINAP was synthesized

according to literature procedures[1]. *p*-Tolyl-boroxine (**3.2a**)[2], 4-(trifluoromethyl)phenyl-boroxine (**3.2b**)[3], 4-methoxyphenyl-boroxine (**3.2c**)[3] and (*E*)-styryl-boroxine (**3.2d**)[3] were synthesized according to literature procedures.

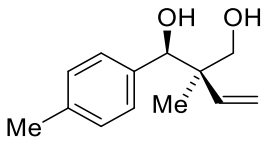
Spectroscopy, Spectrometry and Data Collection

Infrared spectra were recorded on a Perkin-Elmer 1600 spectrometer. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion (M, M+H, or M-H), or a suitable fragment ion. ^{1}H Nuclear magnetic resonance spectra were recorded using a 400 MHz or a 500 MHz spectrometer. Coupling constants are reported in Hertz (Hz) for $CDCl_3$ solutions, and chemical shifts are reported as parts per million (ppm) relative to residual $CHCl_3$ δ_H (7.26 ppm). ^{13}C Nuclear magnetic resonance spectra were recorded using a 100 MHz or a 125 MHz spectrometer for $CDCl_3$ solutions, and chemical shifts are reported as parts per million (ppm) relative to residual $CDCl_3$ δ_C (77.0 ppm). Fluorine-19 nuclear magnetic resonance (^{19}F NMR) spectra were recorded with a Varian Gemini 400 (100 MHz) or a Bruker 500 (125 MHz) spectrometer. Melting points were taken on a Stuart SMP3 melting point apparatus.

Experimental Details and Spectral Data

Procedures and Spectral Data for the Synthesis of Vinyl-Dioxanones 3.1a-3.1i:

(1*R*,2*R*)-2-methyl-1-(*p*-tolyl)-2-vinylpropane-1,3-diol (SI-**3.1a**)



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with K_3PO_4 (42.4 mg, 0.2 mmol, 5 mol%), (*S*)-Ir-Tol-BINAP (220 mg, 0.2 mmol, 5 mol%) and *p*-tolylmethanol (488 mg, 4.0 mmol, 100 mol%). Under an atmosphere of argon, anhydrous THF (8 mL, 0.5 M) and isoprene monoxide (1.18 mL, 12 mmol, 300 mol%) were sequentially added via syringe. After sealing the tube with cap, the reaction mixture was stirred at 45 ˚C for 24 h. The reaction was cooled to ambient temperature and concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, methylene chloride: acetone = 30:1) to furnish the title compound as a yellow oil (626 mg, 3.0 mmol, *anti*:*syn* > 20:1) in 76% yield.

TLC (SiO_2) R_f = 0.30 (methylene chloride: acetone = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 – 7.07 (m, 4H), 6.03 (dd, *J* = 17.7, 11.0 Hz, 1H), 5.20 (dd, *J* = 11.0, 1.1 Hz, 1H), 5.01 (dd, *J* = 17.8, 1.2 Hz, 1H), 4.62 (s, 1H), 3.60 (d, *J* = 10.7 Hz, 1H), 3.51 (d, *J* = 10.7 Hz, 1H), 3.18 (brs, 1H), 2.90 (brs, 1H), 2.33 (s, 3H), 0.90 (s, 3H).

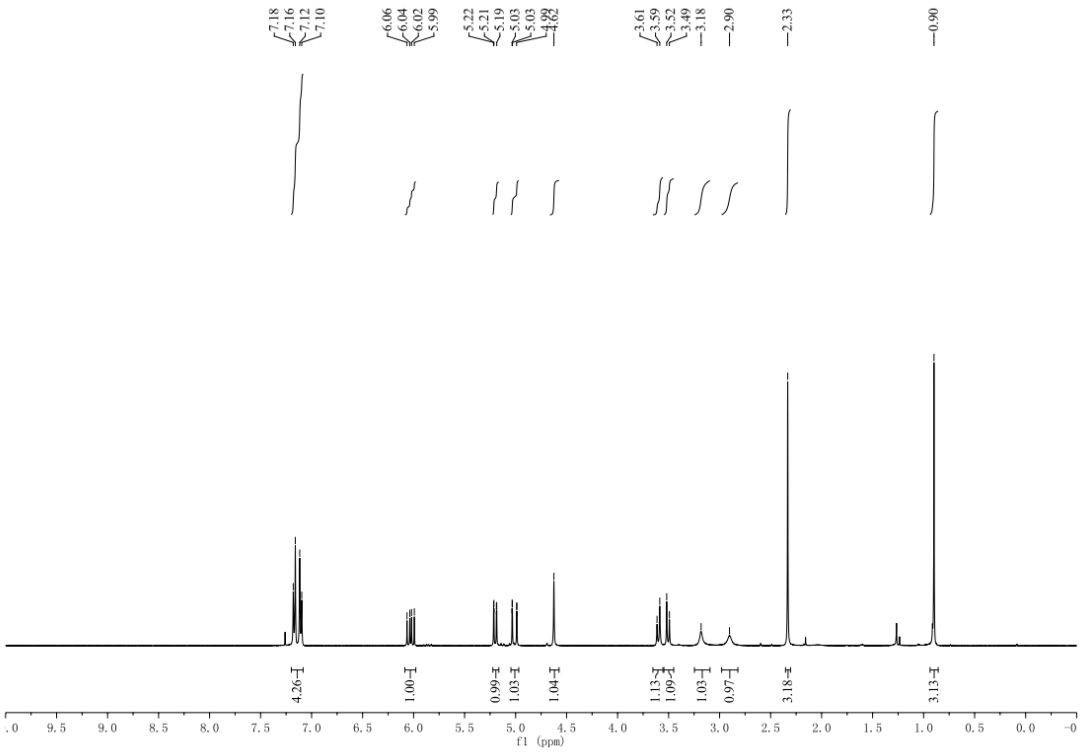
^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6, 137.8, 137.2, 128.3, 127.6, 115.9, 79.9, 69.7, 46.2, 21.0, 17.8.

HRMS (ESI) Calcd. for $C_{13}H_{18}NaO_2^+$ $[M+Na]^+$: 229.1199, Found: 229.1201.

FTIR (neat): 3377, 2966, 2919, 2977, 1637, 1515, 1460, 1415, 1378, 1201, 1039, 1018, 919, 821, 678 cm^{-1}.

$[\alpha]_D^{33}$: -34.7 (*c* = 1.0, $CHCl_3$).

HPLC (two connected chiralcel OJ-H columns, hexanes:*i*-PrOH = 98:2, 0.80 mL/min, 230 nm), *anti*:*syn* = 35:1, ee = 93%.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5.03
4.99
4.62
3.61
3.59
3.52
3.49
3.18
2.90
2.33
0.90
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1.04
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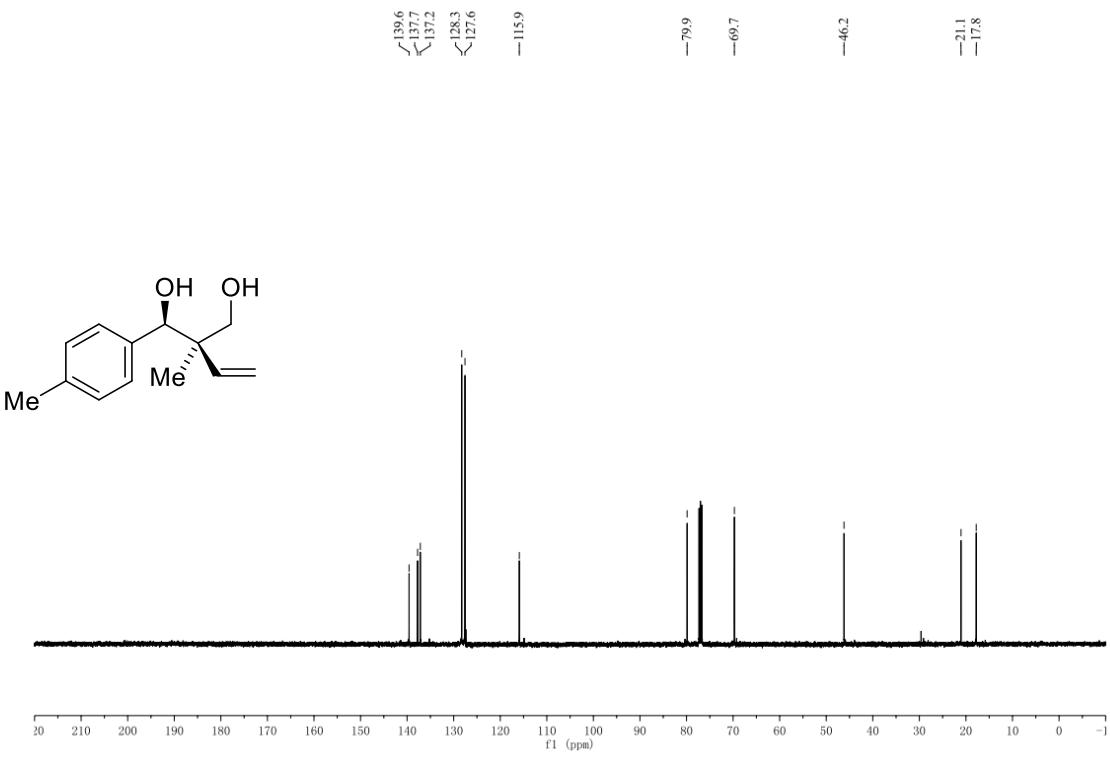
0.97
3.18
3.13
f1 (ppm)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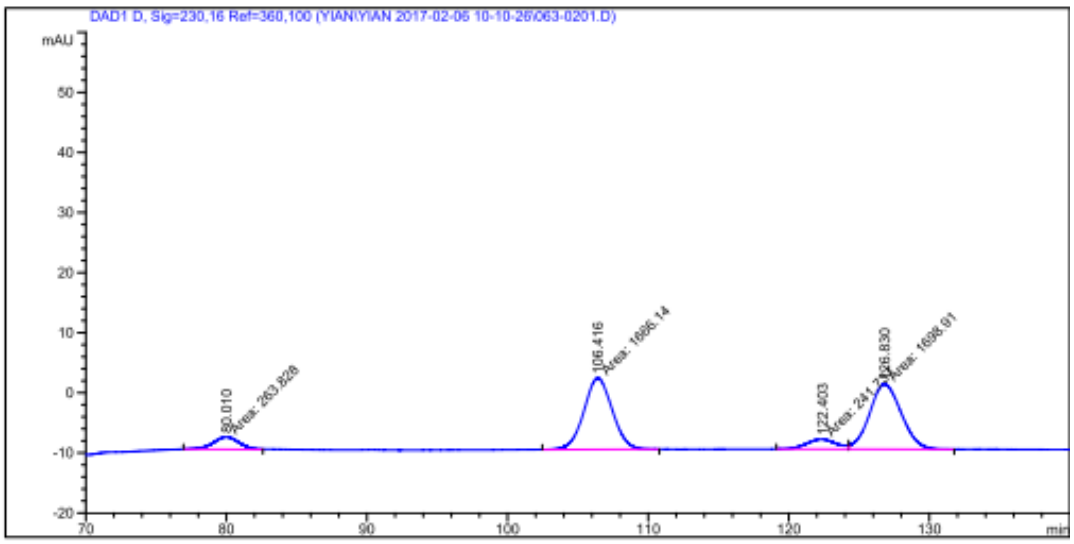
Me
f1 (ppm)



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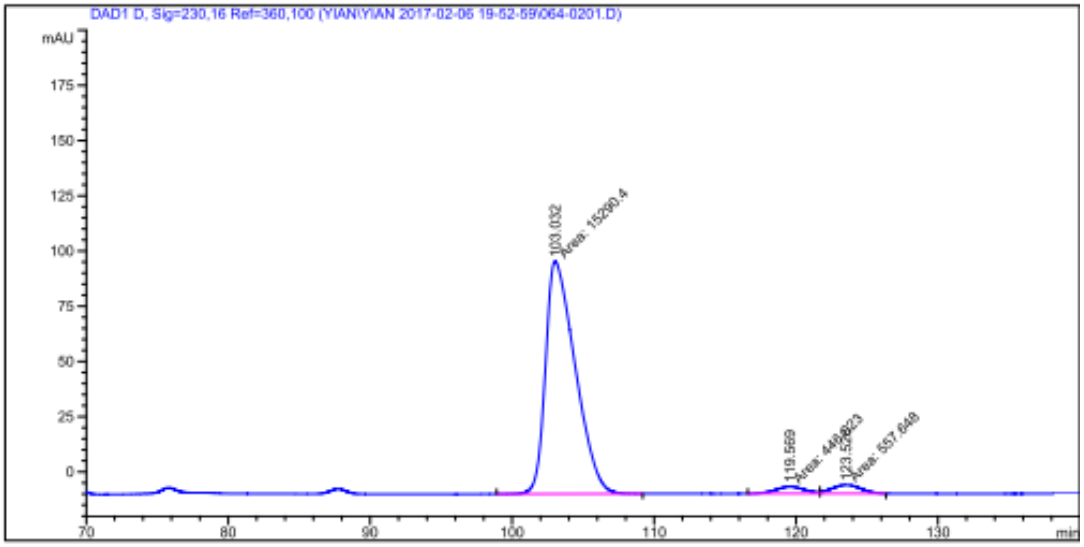
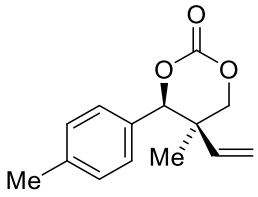
2	106.416	MM	2.3370	1666.13733	11.88241	43.0458
3	122.403	MF	2.4703	241.73686	1.63098	6.2454
4	126.830	FM	2.6114	1698.91028	10.84294	43.8925



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	103.032	MM	2.4195	1.52904e4	105.32902	93.8403
2	119.569	MF	2.3737	446.02286	3.13167	2.7373
3	123.526	FM	2.3616	557.64777	3.93557	3.4224

(4*R*,5*R*)-5-methyl-4-(*p*-tolyl)-5-vinyl-1,3-dioxan-2-one (3.1a)



Detailed Procedures

An oven-dried vial equipped with a magnetic stir bar was charged with diol **SI-1a** (50 mg, 0.24 mmol, 100 mol%). Under argon atmosphere, acetonitrile (2.4 mL, 0.1 M) was added via syringe. CDI (77.8 mg, 0.48 mmol, 200 mol%) was added in one portion at ambient temperature. The reaction mixture was stirred at 25 ˚C for 16 h. The reaction was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 3:1) to furnish the title compound as a white solid (46.3 mg, 0.20 mmol) in 82 % yield.

TLC (SiO_2) R_f = 0.25 (hexanes/ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 – 7.12 (m, 4H), 5.65 (ddd, *J* = 17.6, 11.1, 0.8 Hz, 1H), 5.30 (d, *J* = 11.1 Hz, 1H), 5.25 (s, 1H), 5.23 (d, *J* = 17.6 Hz, 1H), 4.42 (d, *J* = 11.0 Hz, 1H), 4.30 (dd, *J* = 11.0, 0.9 Hz, 1H), 2.36 (s, 3H), 1.04 (s, 3H).

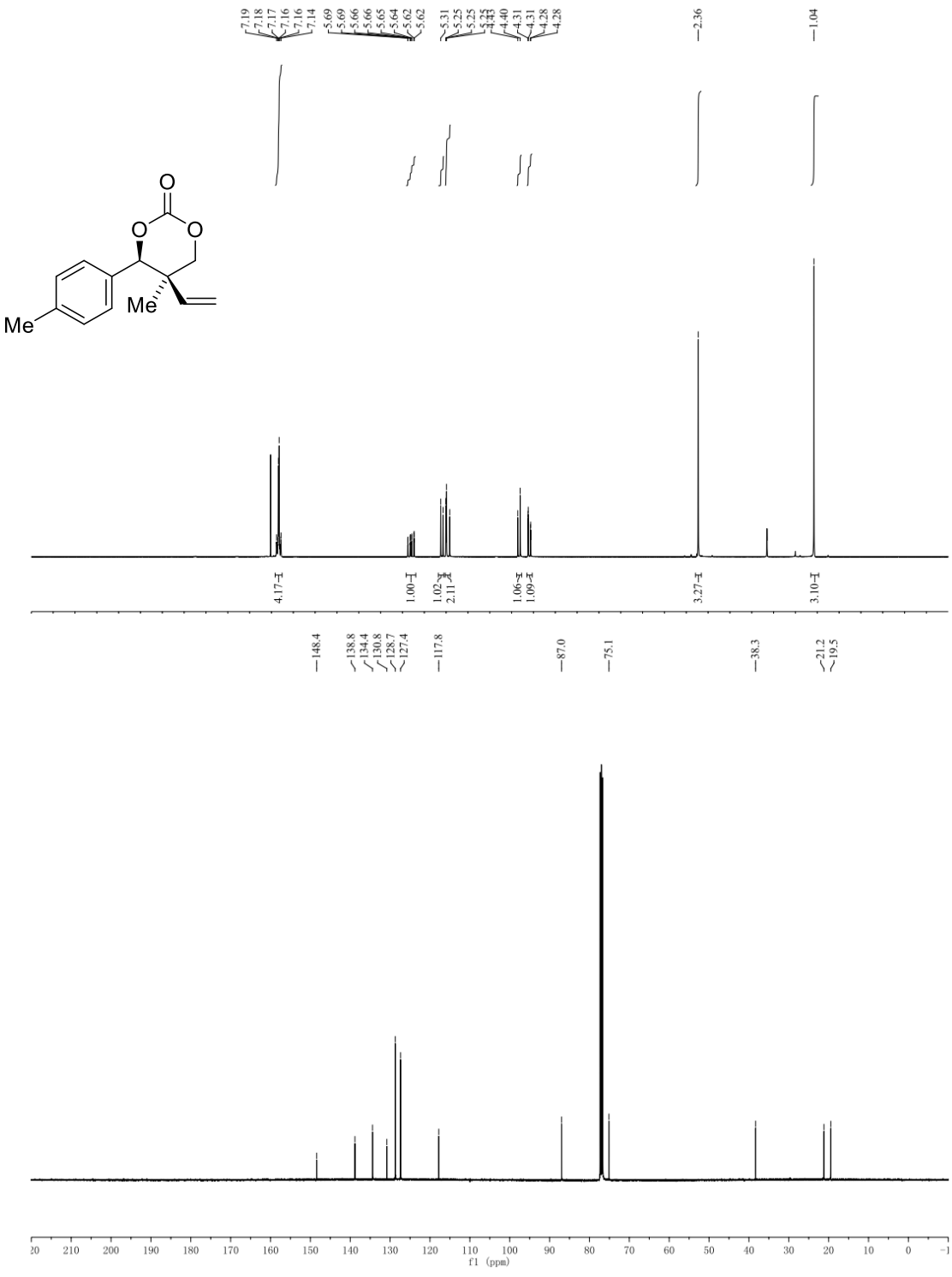
^{13}C NMR (100 MHz, $CDCl_3$) δ 148.4, 138.8, 134.4, 130.8, 128.7, 127.4, 117.8, 87.0, 75.1, 38.3, 21.2, 19.5.

HRMS (ESI) Calcd. for $C_{14}H_{16}NaO_3^+$ $[M+Na]^+$: 255.0992, Found: 255.0994.

$[\alpha]_D^{33}$: -73.7 (*c* = 1.0, $CHCl_3$).

m.p. : 85-86 ˚C

FTIR (neat): 2977, 1747, 1517, 1478, 1456, 1399, 1378, 1341, 1241, 1200, 1712, 1135, 1102, 1007, 931, 819, 764, 688 cm^{-1}.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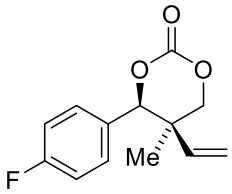
5.25
5.23
4.40
4.31
4.31
4.28
4.28
2.36
1.04
O
O
O
Me
Me
4.17
1.00
1.02
2.11
1.06
1.09
3.27
3.10
148.4
138.8
134.4
130.8
128.7
127.4
117.8
87.0
75.1
38.3
21.2
19.5
f1 (ppm)

(4*R*,5*R*)-4-(4-fluorophenyl)-5-methyl-5-vinyl-1,3-dioxan-2-one (3.1b)



Detailed Procedures

An oven-dried vial equipped with a magnetic stir bar was charged with (1*R*,2*R*)-1-(4-fluorophenyl)-2-methyl-2-vinylpropane-1,3-diol[4] (100 mg, 0.48 mmol, 100 mol%). Under argon atmosphere, acetonitrile (4.8 mL, 0.1 M) was added via syringe. CDI (154 mg, 0.95 mmol, 200 mol%) was added in one portion at ambient temperature. The reaction mixture was stirred at 25 ˚C for 16 h. The reaction was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 3:1) to furnish the title compound as a white solid (90.7 mg, 0.38 mmol) in 81 % yield.

TLC (SiO_2) R_f = 0.23 (hexanes/ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 2H), 7.10 – 7.03 (m, 2H), 5.64 (ddd, *J* = 17.6, 11.0, 0.7 Hz, 1H), 5.32 (d, *J* = 11.1 Hz, 1H), 5.28 (s, 1H), 5.22 (d, *J* = 17.6 Hz, 1H), 4.40 (d, *J* = 11.0 Hz, 1H), 4.33 (dd, *J* = 11.0, 0.8 Hz, 1H), 1.02 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9 (d, *J* = 248.3 Hz), 148.1, 133.9, 129.6 (d, *J* = 3.2 Hz), 129.3 (d, *J* = 8.3 Hz), 118.2, 115.1 (d, *J* = 21.7 Hz), 86.3, 75.2, 38.3, 19.2.

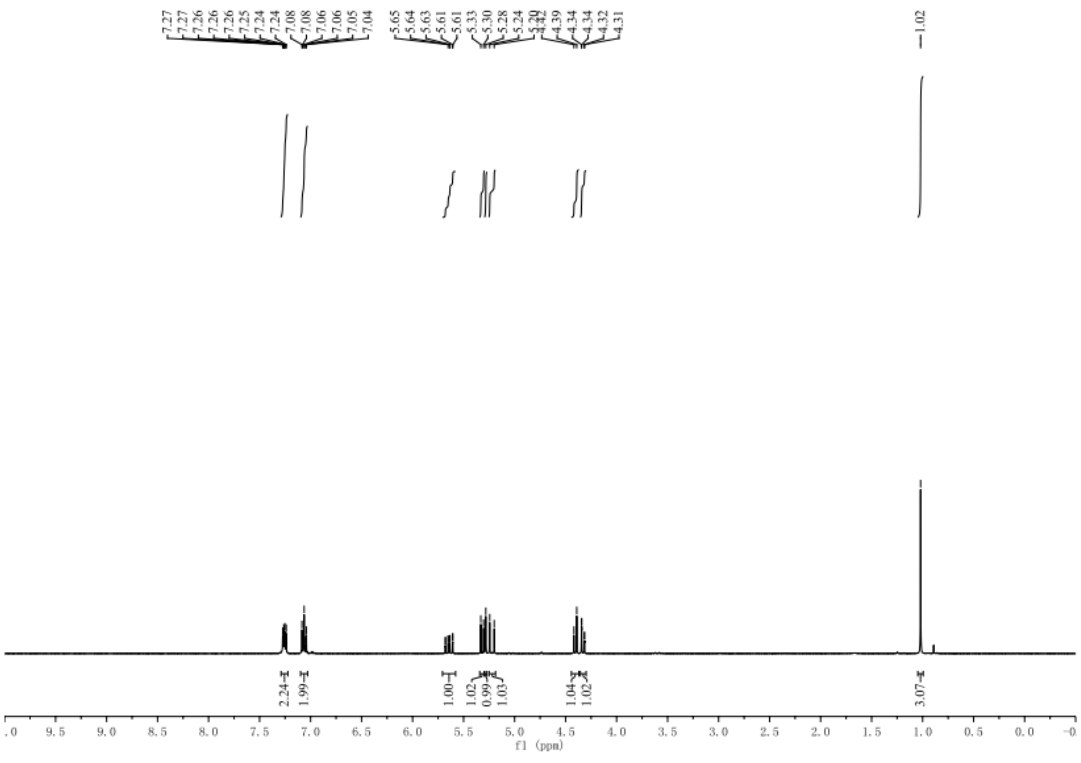
^{19}F NMR (376 MHz, $CDCl_3$) δ -112.4 (tt, *J* = 8.6, 5.2 Hz).

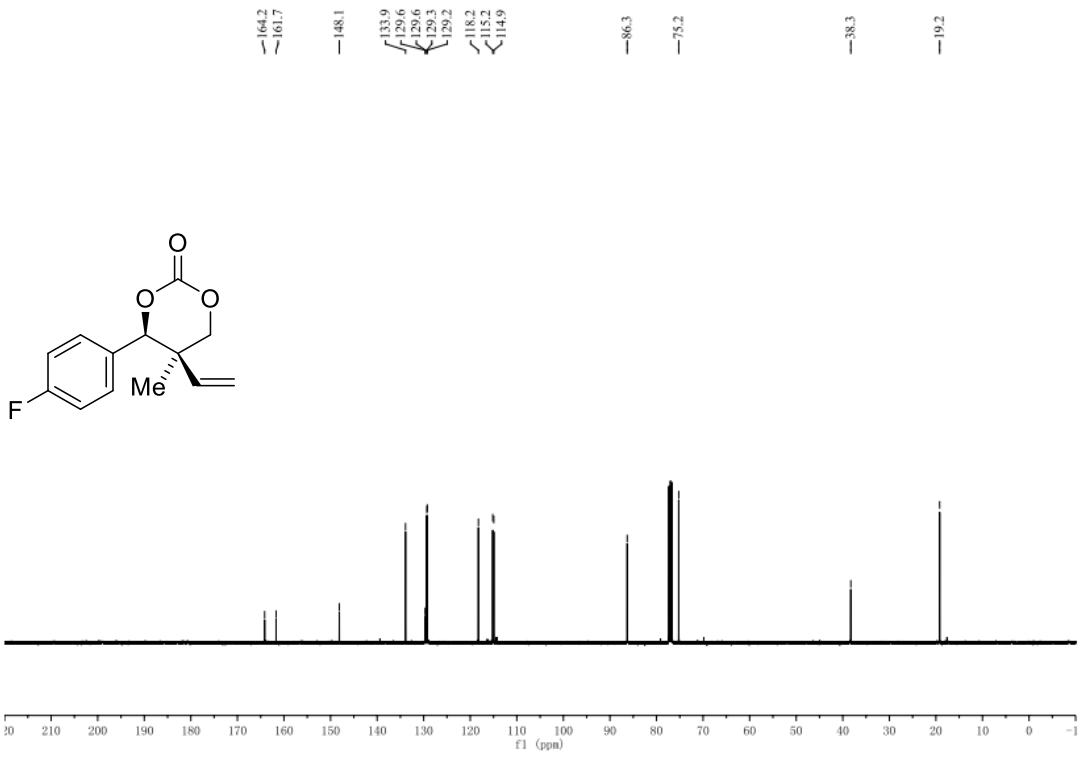
HRMS (ESI) Calcd. for $C_{13}H_{13}FNaO_3^+$ $[M+Na]^+$: 259.0741, Found: 259.0744.

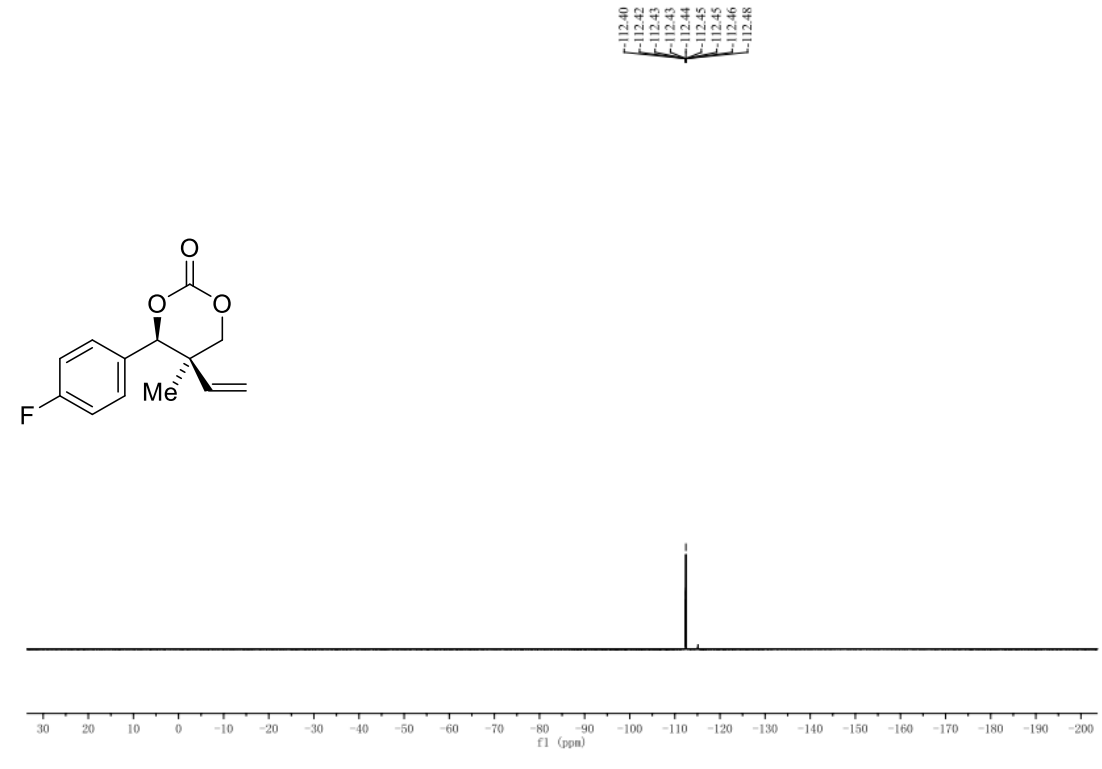
$[\alpha]_D^{33}$: -46.0 (*c* = 1.0, $CHCl_3$).

m.p. : 108-109 ˚C

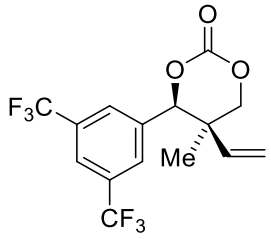
FTIR (neat): 2977, 1748, 1608, 1512, 1480, 1456, 1378, 1228, 1203, 1174, 1134, 1098, 929, 832, 769 cm^{-1}.




164.2
161.7
148.1
133.9
129.6
129.6
129.3
129.2
118.2
115.2
114.9
86.3
75.2
38.3
19.2
O
O
O
Me
F
f1 (ppm)


112.40
112.42
112.43
112.43
112.44
112.45
112.45
112.46
112.48
O
O
O
Me
F
f1 (ppm)

(4*R*,5*R*)-4-(3,5-bis(trifluoromethyl)phenyl)-5-methyl-5-vinyl-1,3-dioxan-2-one (3.1c)



Detailed Procedures

An oven-dried vial equipped with a magnetic stir bar was charged with (1*R*,2*R*)-1-(3,5-bis(trifluoromethyl)phenyl)-2-methyl-2-vinylpropane-1,3-diol[4] (164 mg, 0.5 mmol, 100 mol%). Under argon atmosphere, acetonitrile (5 mL, 0.1 M) was added via syringe. CDI (81 mg, 0.5 mmol, 100 mol%) was added in one portion at ambient temperature. The reaction mixture was stirred at 25 ˚C for 16 h. The reaction was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 3:1) to furnish the title compound as a white solid (115 mg, 0.32 mmol) in 65% yield.

TLC (SiO_2) R_f = 0.23 (hexanes/ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.74 (d, *J* = 1.5 Hz, 2H), 5.65 (dd, *J* = 17.5, 11.0 Hz, 1H), 5.52 – 5.34 (m, 2H), 5.22 (d, *J* = 17.5 Hz, 1H), 4.55 – 4.18 (m, 2H), 1.07 (s, 3H).

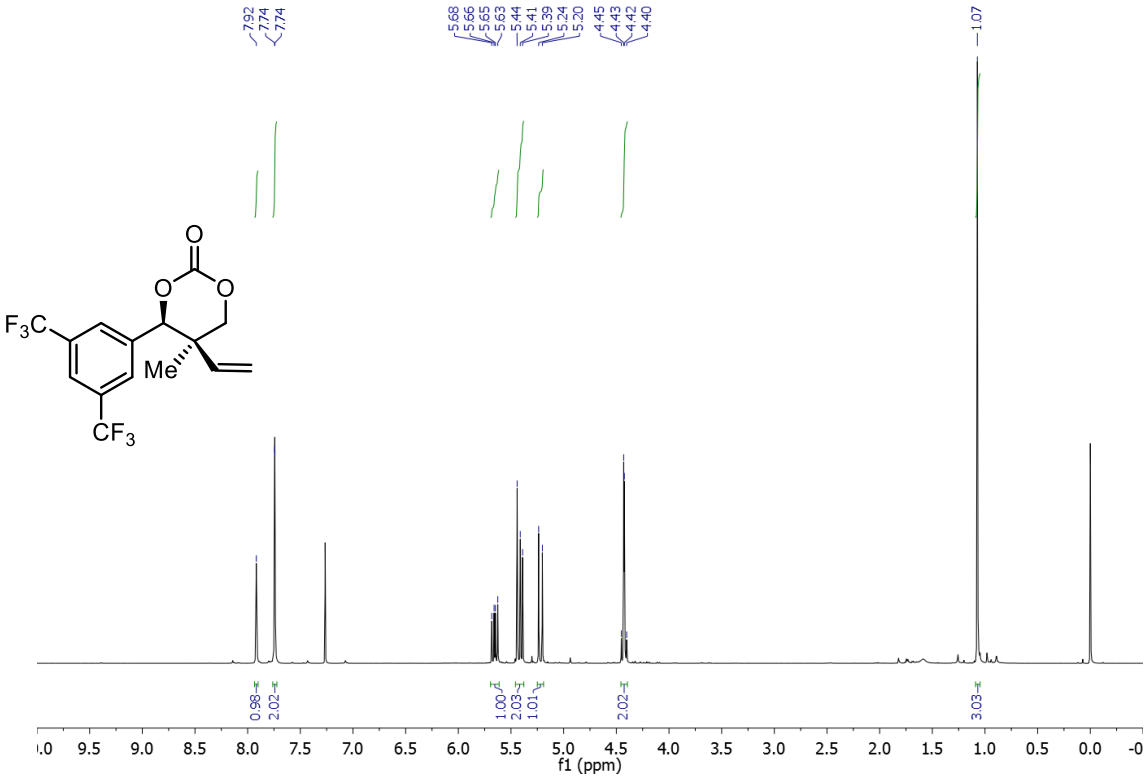
^{13}C NMR (125 MHz, $CDCl_3$) δ 147.3, 136.4, 132.6, 131.6 (q, *J* = 33.8 Hz), 127.6 (d, *J* = 4.1 Hz), 124.0, 123.3 – 122.7 (m), 121.8, 119.6, 85.4.

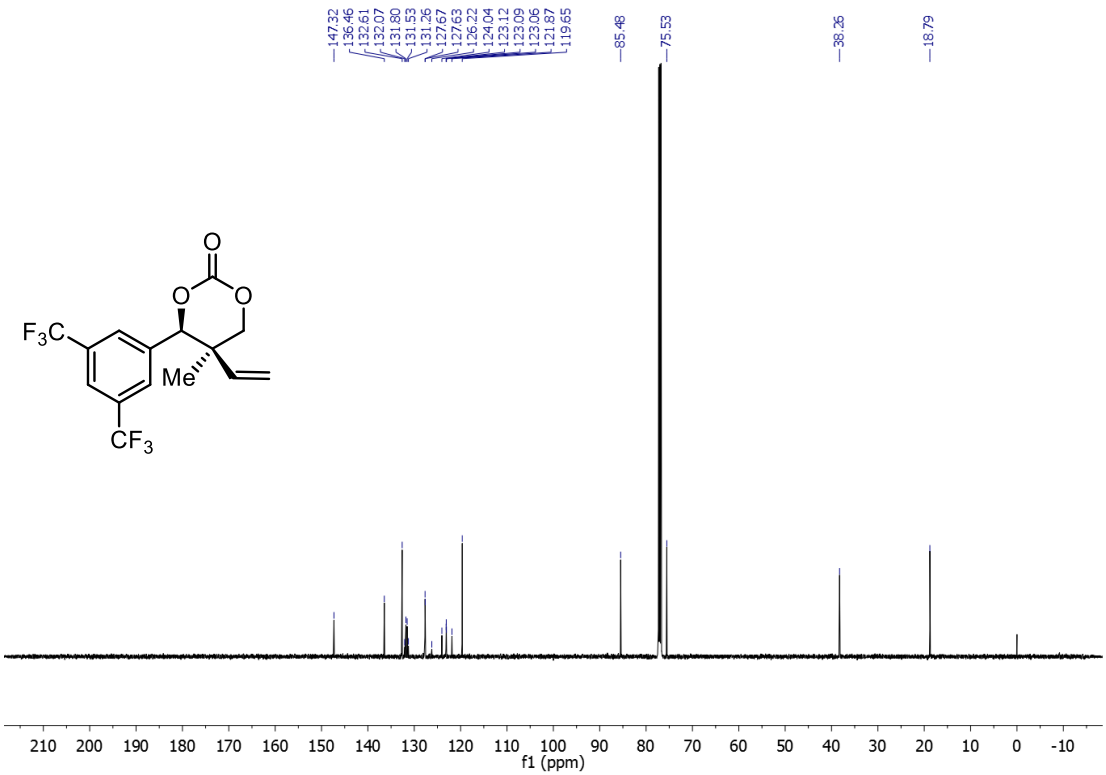
HRMS (ESI) Calcd. for $C_{15}H_{12}F_6NaO_3^+$ $[M+Na]^+$: 377.0583, Found: 377.0590.

$[\alpha]_D^{31}$: -44.0 (*c* = 1.0, $CHCl_3$).

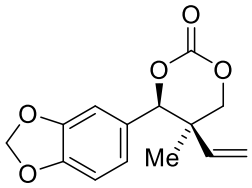
m.p. : 61-62˚C

FTIR (neat): 2977, 1744, 1467, 1402, 1276, 1225, 1167, 1126, 1104, 1000, 904, 759, 681 cm^{-1}.


7.92
7.74
7.74
5.68
5.66
5.65
5.63
5.44
5.41
5.39
5.24
5.20
4.45
4.43
4.42
4.40
1.07
O
O
O
F3C
Me
CF3
0.98
2.02
1.00
2.03
1.01
2.02
3.03
f1 (ppm)


147.32
136.46
132.61
132.07
131.80
131.53
131.26
127.67
127.63
126.22
124.04
123.12
123.09
123.06
121.87
119.65
85.48
75.53
38.26
18.79
O
O
O
F3C
Me
CF3
f1 (ppm)

(4*R*,5*R*)-4-(benzo[*d*][1,3]dioxol-5-yl)-5-methyl-5-vinyl-1,3-dioxan-2-one (3.1d)



Detailed Procedures

An oven-dried vial equipped with a magnetic stir bar was charged with (1*R*,2*R*)-1-(benzo[*d*][1,3]dioxol-5-yl)-2-methyl-2-vinylpropane-1,3-diol[1] (90 mg, 0.38 mmol, 100 mol%). Under argon atmosphere, acetonitrile (3.8 mL, 0.1 M) was added via syringe. CDI (124 mg, 0.76 mmol, 200 mol%) was added in one portion at ambient temperature. The reaction mixture was stirred at 25 ˚C for 16 h. The reaction was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 2:1) to furnish the title compound as a white solid (99.6 mg, 0.32 mmol) in 84 % yield.

TLC (SiO_2) R_f = 0.20 (hexanes/ethyl acetate = 2:1).

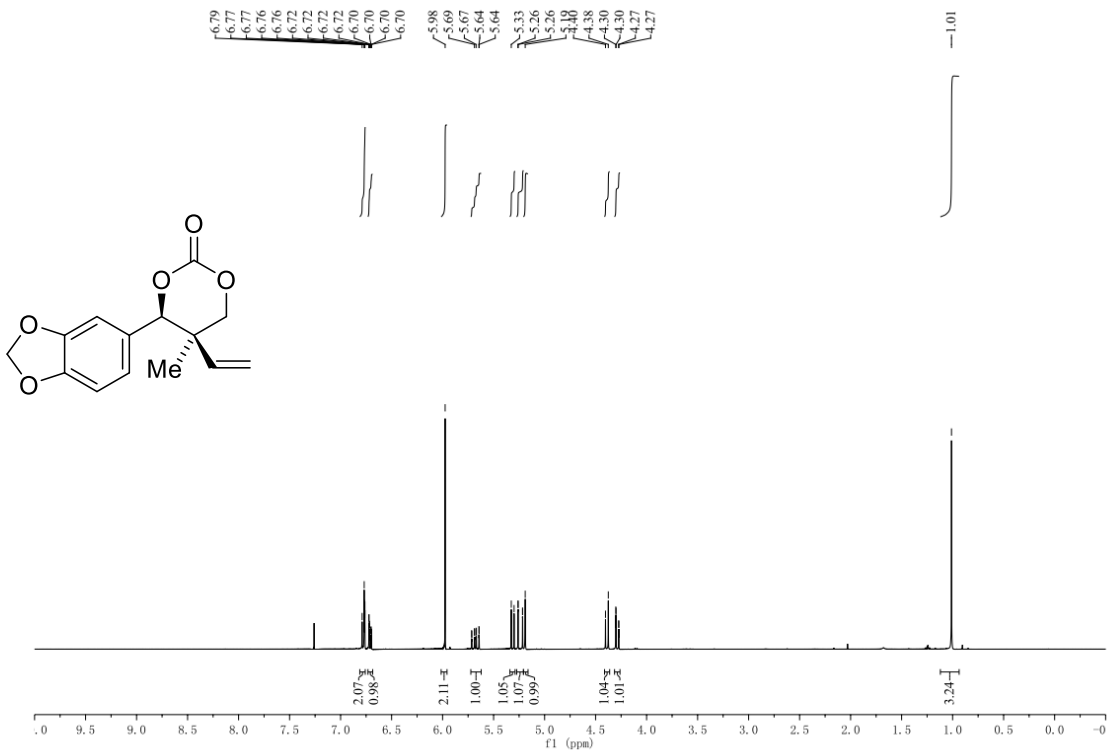
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 – 6.75 (m, 2H), 6.71 (ddd, *J* = 8.0, 1.8, 0.5 Hz, 1H), 5.98 (s, 2H), 5.68 (ddd, *J* = 17.6, 11.1, 0.9 Hz, 1H), 5.31 (d, *J* = 11.0 Hz, 1H), 5.24 (d, *J* = 17.6 Hz, 1H), 5.19 (s, 1H), 4.39 (d, *J* = 11.0 Hz, 1H), 4.29 (dd, *J* = 11.0, 0.9 Hz, 1H), 1.01 (s, 3H).

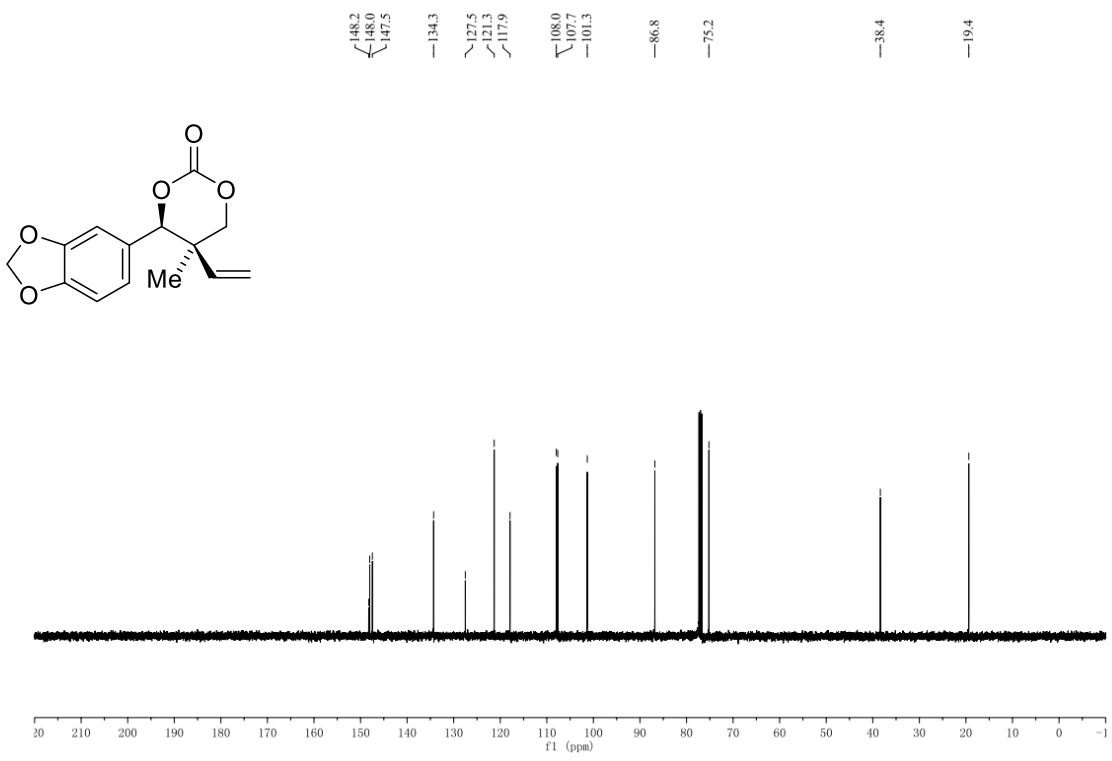
^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 148.0, 147.5, 134.3, 127.5, 121.3, 117.9, 108.0, 107.6, 101.3, 86.8, 75.2, 38.4, 19.4.

HRMS (ESI) Calcd. for $C_{14}H_{14}NaO_5^+$ $[M+Na]^+$: 285.0733, Found: 285.0741.

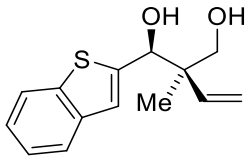
$[\alpha]_D^{33}$: -62.3 (*c* = 1.0, $CHCl_3$).

FTIR (neat): 2970, 2360, 2341, 1748, 1505, 1491, 1447, 1399, 1377, 1253, 1205, 1102, 1038, 933, 815, 768, 669 cm^{-1}


6.79
6.77
6.77
6.76
6.76
6.72
6.72
6.72
6.72
6.70
6.70
6.70
6.70
5.98
5.69
5.67
5.64
5.64
5.33
5.26
5.26
5.19
4.40
4.38
4.30
4.30
4.27
4.27
1.01
O
O
O
O
O
Me
2.07
0.98
2.11
1.00
1.05
1.07
0.99
1.04
1.01
3.24
f1 (ppm)


148.2
148.0
147.5
134.3
127.5
121.3
117.9
108.0
107.7
101.3
86.8
75.2
38.4
19.4
O
O
O
O
O
Me
f1 (ppm)

(1S,2R)-1-(benzo[b]thiophen-2-yl)-2-methyl-2-vinylpropane-1,3-diol (SI-3.1e)



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with K_3PO_4 (10.6 mg, 0.05 mmol, 5 mol%), (*S*)-Ir-Tol-BINAP (55.0 mg, 0.05 mmol, 5 mol%) and benzo[*b*]thiophen-2-ylmethanol (82.1 mg, 0.5 mmol, 100 mol%). Under an atmosphere of argon, anhydrous THF (1.0 mL, 0.5 M) and isoprene monoxide (147 µL, 15 mmol, 300 mol%) were sequentially added via syringe. After sealing the tube with cap, the reaction mixture was stirred at 45 ˚C for 24 h. The reaction was cooled to ambient temperature and concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, methylene chloride: acetone = 30:1) to furnish the title compound as a yellow oil (102 mg, 0.41 mmol, *anti*:*syn* > 20:1) in 82% yield.

TLC (SiO_2) R_f = 0.32 (dichloromethane/acetone = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 – 7.07 (m, 4H), 6.03 (dd, *J* = 17.7, 11.0 Hz, 1H), 5.20 (dd, *J* = 11.0, 1.1 Hz, 1H), 5.01 (dd, *J* = 17.8, 1.2 Hz, 1H), 4.62 (s, 1H), 3.60 (d, *J* = 10.7 Hz, 1H), 3.51 (d, *J* = 10.7 Hz, 1H), 3.18 (brs, 1H), 2.90 (brs, 1H), 2.33 (s, 3H), 0.90 (s, 3H).

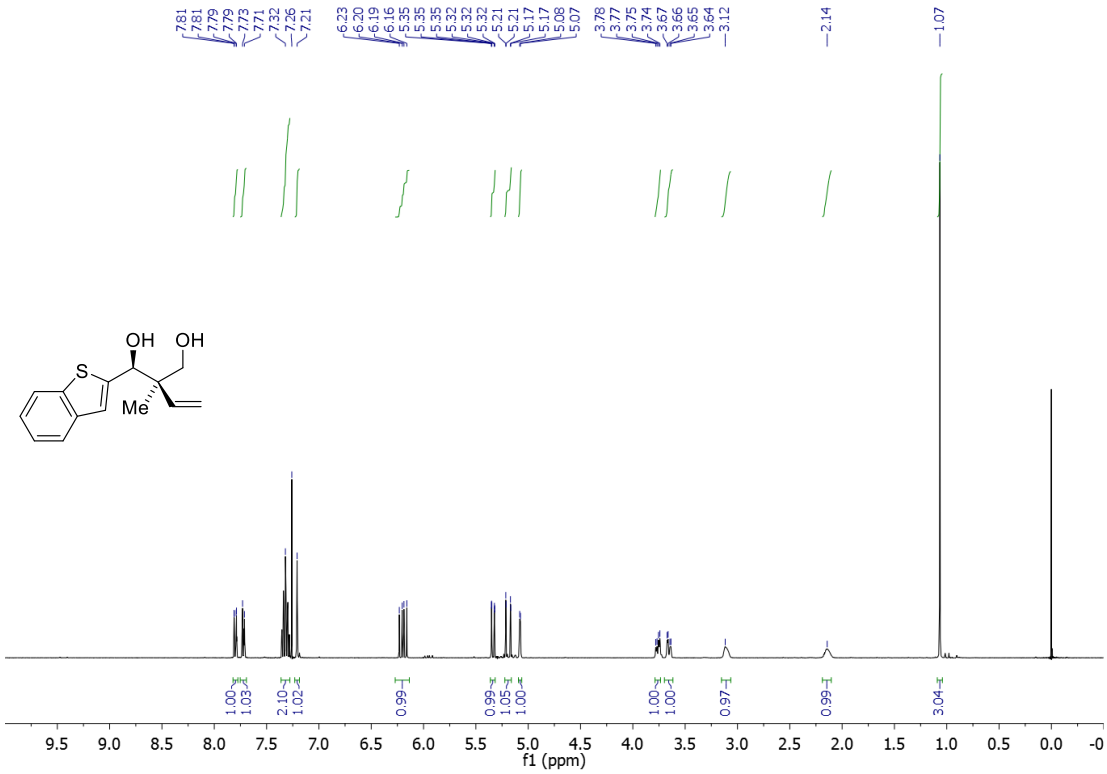
^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 139.5, 139.1, 139.0, 124.1, 124.1, 123.3, 122.2, 122.1, 117.0, 69.7, 46.4, 18.0.

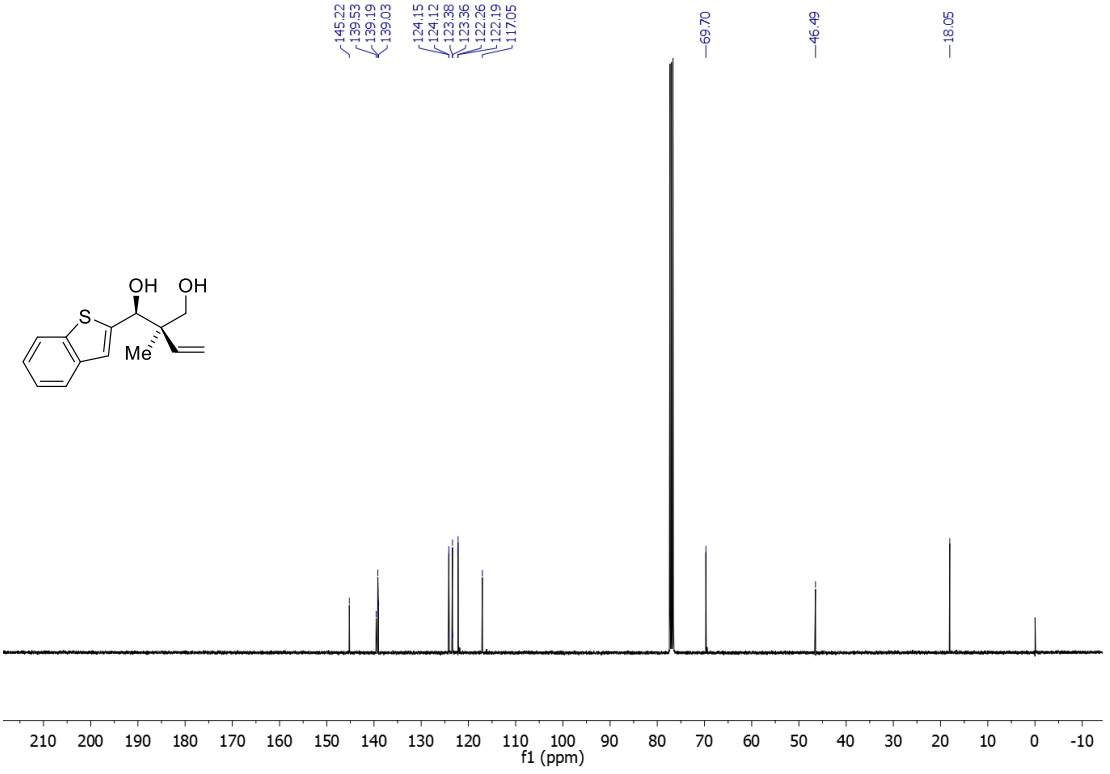
HRMS (ESI) Calcd. for $C_{14}H_{16}NaO_2S^+$ $[M+Na]^+$: 271.0763, Found: 271.0772.

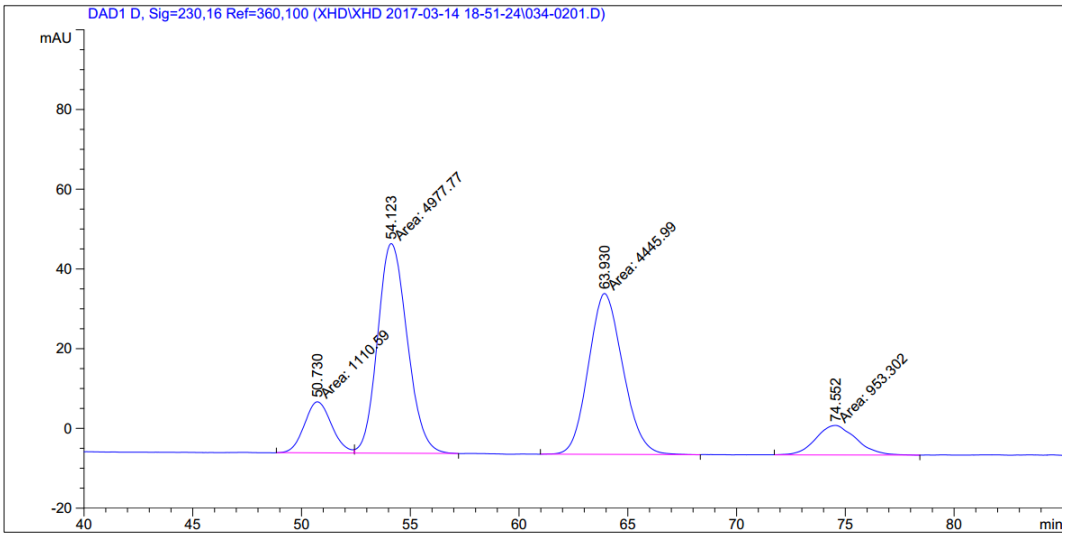
FTIR (neat): 3345, 2964, 1636, 1457, 1415, 1124, 1014, 921. 832, 745, 725, 709 cm^{-1}.

$[\alpha]_D^{33}$: -26.2 (*c* = 1.0, $CHCl_3$).

HPLC (one chiralcel OD-H columns, hexanes:*i*-PrOH = 97:3, 1.0 mL/min, 30 nm), *anti*:*syn* = 20:1, ee = 93%.


7.81
7.81
7.79
7.79
7.73
7.71
7.32
7.26
7.21
6.23
6.20
6.19
6.16
5.35
5.35
5.32
5.32
5.32
5.21
5.21
5.17
5.17
5.08
5.07
3.78
3.77
3.75
3.74
3.67
3.66
3.65
3.64
3.12
2.14
1.07
OH
OH
S
Me
1.00
1.03
2.10
1.02
0.99
0.99
1.05
1.00
1.00
1.00
0.97
0.99
3.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)


145.22
139.53
139.19
139.03
124.15
124.12
123.38
123.36
122.26
122.19
117.05
69.70
46.49
18.05
OH
OH
S
Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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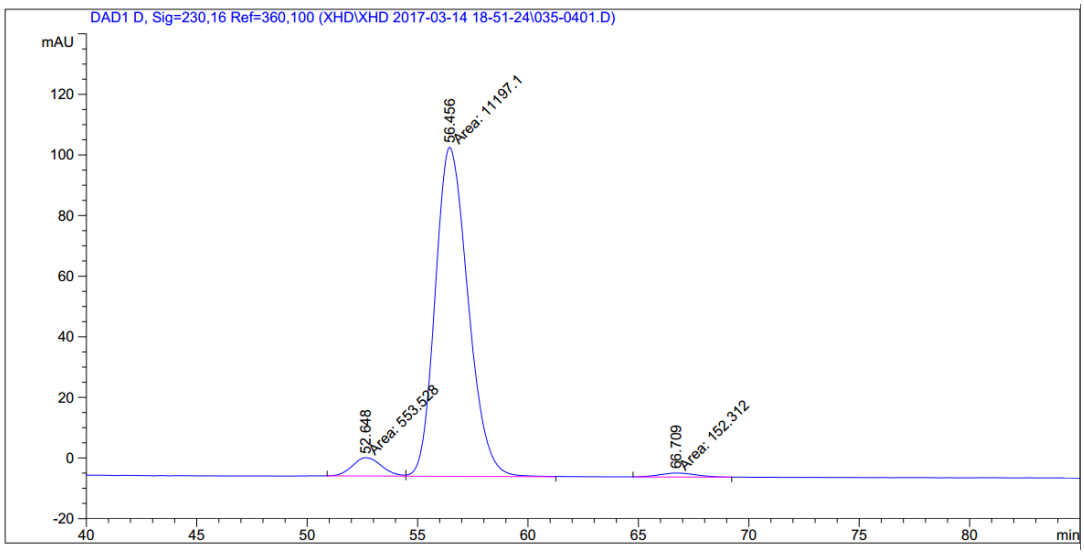
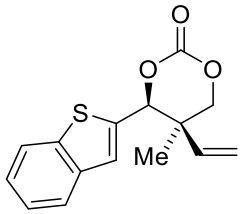
2	54.123	FM	1.5781	4977.77246	52.56989	43.3315
3	63.930	MM	1.8361	4445.99365	40.35715	38.7024
4	74.552	MM	2.1445	953.30170	7.40889	8.2985
Totals :				1.14877e4	113.14198	



Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	52.648	MF	1.5267	553.52832	6.04287	4.6504
2	56.456	FM	1.7190	1.11971e4	108.56383	94.0700
3	66.709	MM	1.9341	152.31200	1.31253	1.2796
Totals :				1.19029e4	115.91923	

(4*S*,5*R*)-4-(benzo[b]thiophen-2-yl)-5-methyl-5-vinyl-1,3-dioxan-2-one (3.1e)



Detailed Procedures

An oven-dried vial equipped with a magnetic stir bar was charged with diol **SI-3.1e** (99.3 mg, 0.4 mmol, 100 mol%). Under argon atmosphere, acetonitrile (4 mL, 0.1 M) was added via syringe. CDI (65 mg, 0.4 mmol, 100 mol%) was added in one portion at ambient temperature. The reaction mixture was stirred at 25 ˚C for 16 h. The reaction was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 3:1) to furnish the title compound as a white solid (83.3 mg, 0.30 mmol) in 75% yield.

TLC (SiO_2) R_f = 0.32 (dichloromethane/acetone = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.80 (m, 1H), 7.79 – 7.76 (m, 1H), 7.40 – 7.35 (m, 2H), 7.32 (t, *J* = 0.7 Hz, 1H), 5.92 (ddd, *J* = 17.6, 11.1, 0.7 Hz, 1H), 5.59 (s, 1H), 5.38 (d, *J* = 11.1 Hz, 1H), 5.34 (d, *J* = 17.6 Hz, 1H), 4.46 (d, *J* = 11.1 Hz, 1H), 4.33 (dd, *J* = 11.0, 0.8 Hz, 1H), 1.21 (s, 3H).

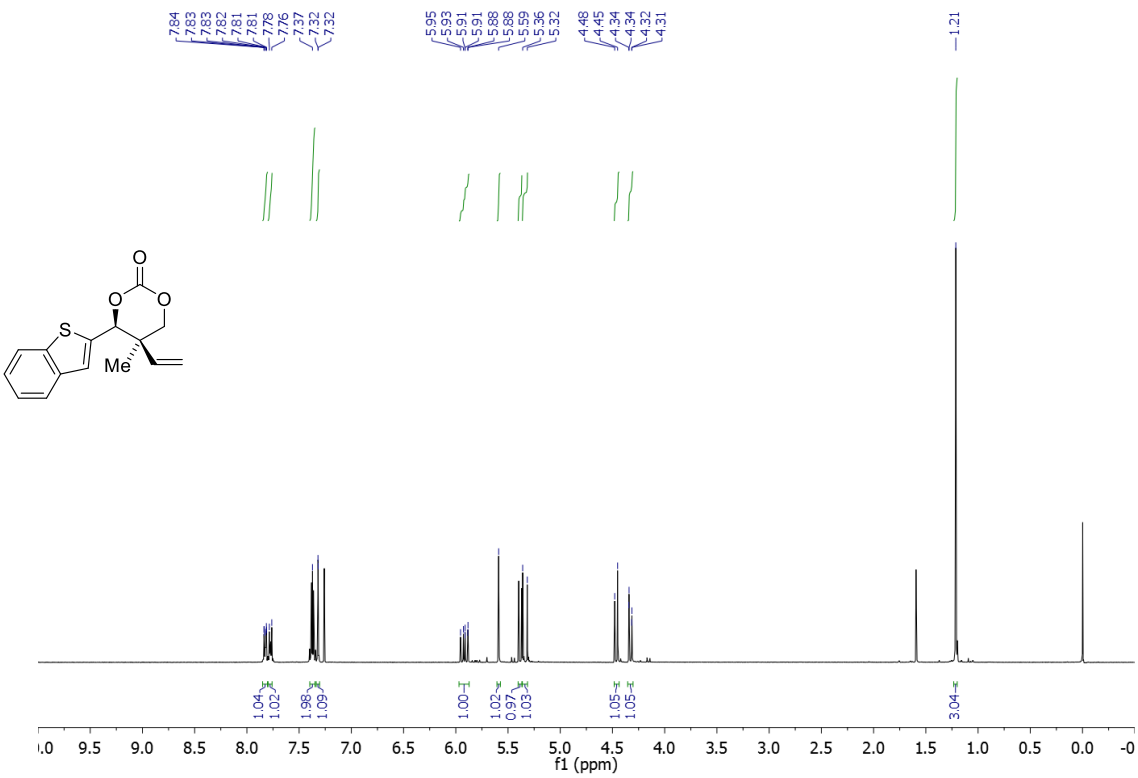
^{13}C NMR (125 MHz, $CDCl_3$) δ 147.4, 139.7, 138.5, 136.7, 134.2, 125.0, 124.6, 124.2, 123.9, 122.2, 118.6, 84.1, 75.3, 38.5, 19.4.

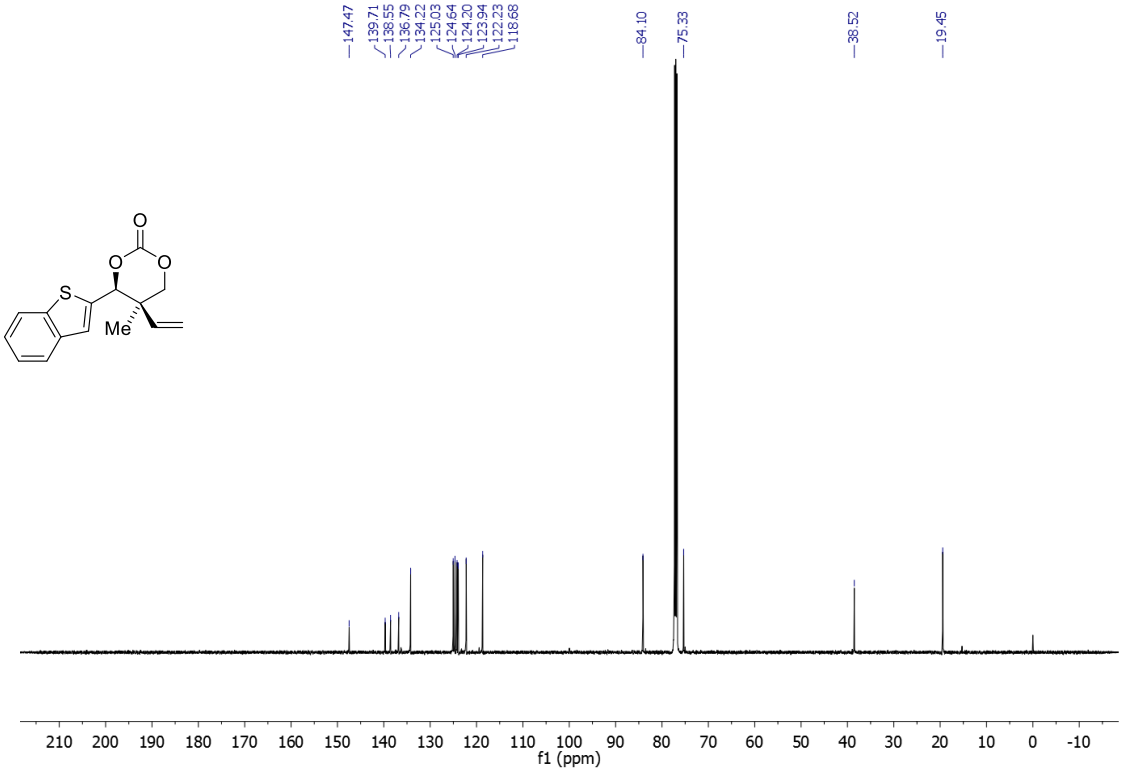
HRMS (ESI) Calcd. for $C_{15}H_{14}NaO_3S^+$ $[M+Na]^+$: 297.0556, Found: 2970561.

$[\alpha]_D^{32}$: -37.1 (*c* = 1.0, $CHCl_3$).

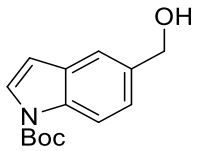
m.p. : 146-147 ˚C

FTIR (neat): 2979, 17332, 1488, 1404, 1332, 1222, 1180, 1127, 1091, 1046, 944, 840, 758, 728, 661 cm^{-1}.


7.84
7.83
7.83
7.82
7.81
7.81
7.78
7.76
7.37
7.32
7.32
5.95
5.93
5.91
5.91
5.88
5.88
5.59
5.36
5.32
4.48
4.45
4.34
4.34
4.32
4.31
1.21
O
O
O
S
Me
1.04
1.02
1.98
1.09
1.00
1.02
0.97
1.03
1.05
1.05
3.04
f1 (ppm)


147.47
139.71
138.55
136.79
134.22
125.03
124.64
124.20
123.94
122.23
118.88
84.10
75.33
38.52
19.45
O
O
O
S
Me
f1 (ppm)

***tert*-butyl 5-(hydroxymethyl)-1*H*-indole-1-carboxylate (SI-3.4)**



Detailed Procedures

To a round-bottomed flask charged with *tert*-butyl 5-formyl-1*H*-indole-1-carboxylate[5] (1.70 g, 6.88 mmol, 100 mol%) under an argon atmosphere was added EtOH (26.0 mL, 0.3 M). The reaction vessel was placed in an ice bath. After 10 minutes, sodium borohydride (390 mg, 10.32 mmol, 150 mol%) was added and the mixture was stirred for 1 h. Water (20 mL) was added to the reaction mixture and the mixture was extracted with CH_2Cl_2 (30 mL × 3). The combined organic layers were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–5:1) to furnish the title compound as a colorless oil (1.60 g, 6.5 mmol) in 94% yield.

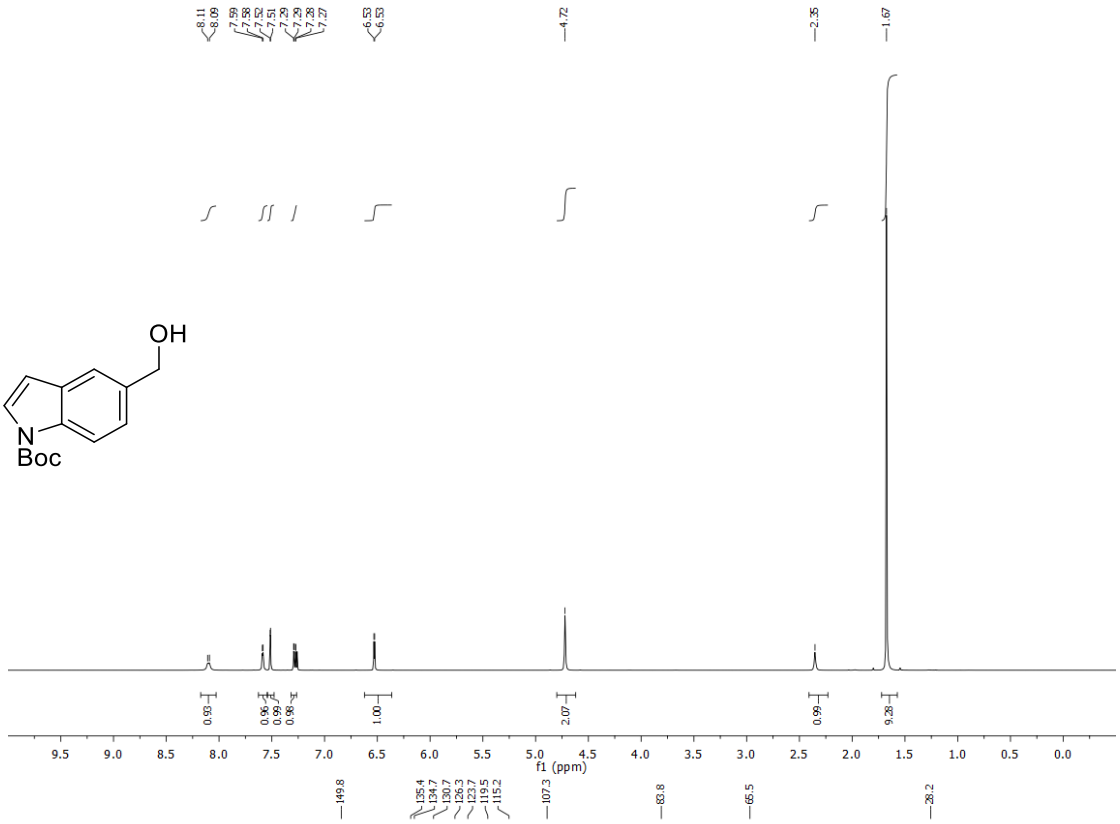
TLC (SiO_2) R_f = 0.39 (hexanes/ethyl acetate = 2:1).

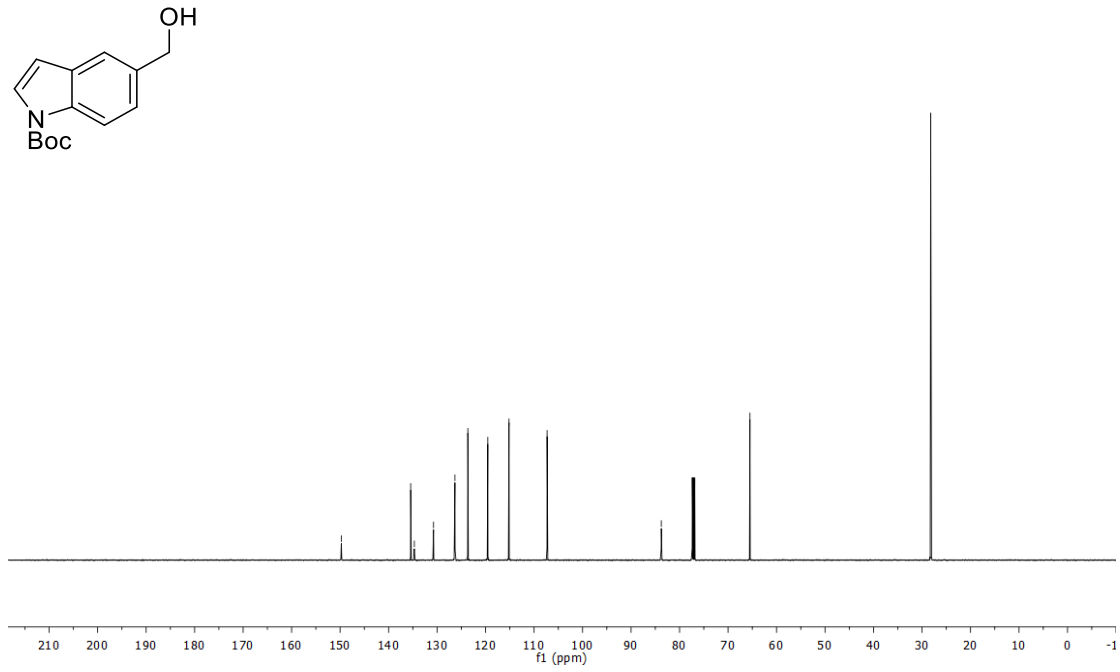
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.6 Hz, 1H), 7.59 (d, *J* = 3.7 Hz, 1H), 7.51 (d, *J* = 1.6 Hz, 1H), 7.28 (dd, *J* = 8.5, 1.7 Hz, 1H), 6.53 (d, *J* = 3.7 Hz, 1H), 4.72 (s, 2H), 2.35 (s, 1H), 1.67 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 149.8, 135.4, 134.7, 130.7, 126.3, 123.7, 119.5, 115.2, 107.3, 83.8, 65.5, 28.2.

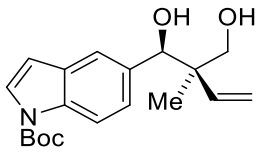
HRMS (ESI) Calcd. for $C_{14}H_{17}NO_3$ $[M+Na]^+$: 270.1101, Found: 270.1101.

FTIR (neat): 3357, 2978, 1729, 1472, 1369, 1218, 1158, 1081, 1021, 759, 723 cm^{-1}.


8.11
8.09
7.59
7.58
7.52
7.51
7.29
7.29
7.28
7.27
6.53
6.53
4.72
2.35
1.67
OH
N
Boc
0.93
0.96
0.99
0.98
1.00
2.07
0.99
9.28
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


149.8
135.4
134.7
130.7
125.3
123.7
119.5
115.2
107.3
83.8
65.5
28.2
OH
N
Boc
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

***tert*-butyl 5-((1R,2R)-1-hydroxy-2-(hydroxymethyl)-2-methylbut-3-en-1-yl)-1H-indole-1-carboxylate (SI-3.1f)**



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with K_3PO_4 (4.2 mg, 0.02 mmol, 5 mol%), (*S*)-Ir-Tol-BINAP (22 mg, 0.02 mmol, 5 mol%) and alcohol **SI-3.4** (100 mg, 0.40 mmol, 100 mol%). Under an atmosphere of argon, anhydrous THF (0.8 mL, 0.5 M) and isoprene monoxide (0.12 mL, 1.2 mmol, 300 mol%) were sequentially added via syringe. After sealing the tube with cap, the reaction mixture was stirred at 45 ˚C for 48 h. The reaction was cooled to ambient temperature and concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1–4:1) to furnish the title compound as a yellow oil (98 mg, 0.30 mmol, *anti*:*syn* > 20:1) in 74% yield.

TLC (SiO_2) R_f = 0.28 (hexanes/ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.5 Hz, 1H), 7.61 (d, *J* = 3.7 Hz, 1H), 7.54 (d, *J* = 1.5 Hz, 1H), 7.31 – 7.27 (m, 1H), 6.57 (d, *J* = 3.7 Hz, 1H), 6.12 (dd, *J* = 17.8, 11.0 Hz, 1H), 5.27 (dd, *J* = 11.0, 1.2 Hz, 1H), 5.08 (dd, *J* = 17.8, 1.3 Hz, 1H), 4.85 (d, *J* = 2.5 Hz, 1H), 3.68 (dd, *J* = 10.7, 6.1 Hz, 1H), 3.62 (dd, *J* = 10.7, 5.1 Hz, 1H), 2.73 (d, *J* = 2.8 Hz, 1H), 2.34 (t, *J* = 5.8 Hz, 1H), 1.69 (s, 9H), 0.98 (s, 3H).

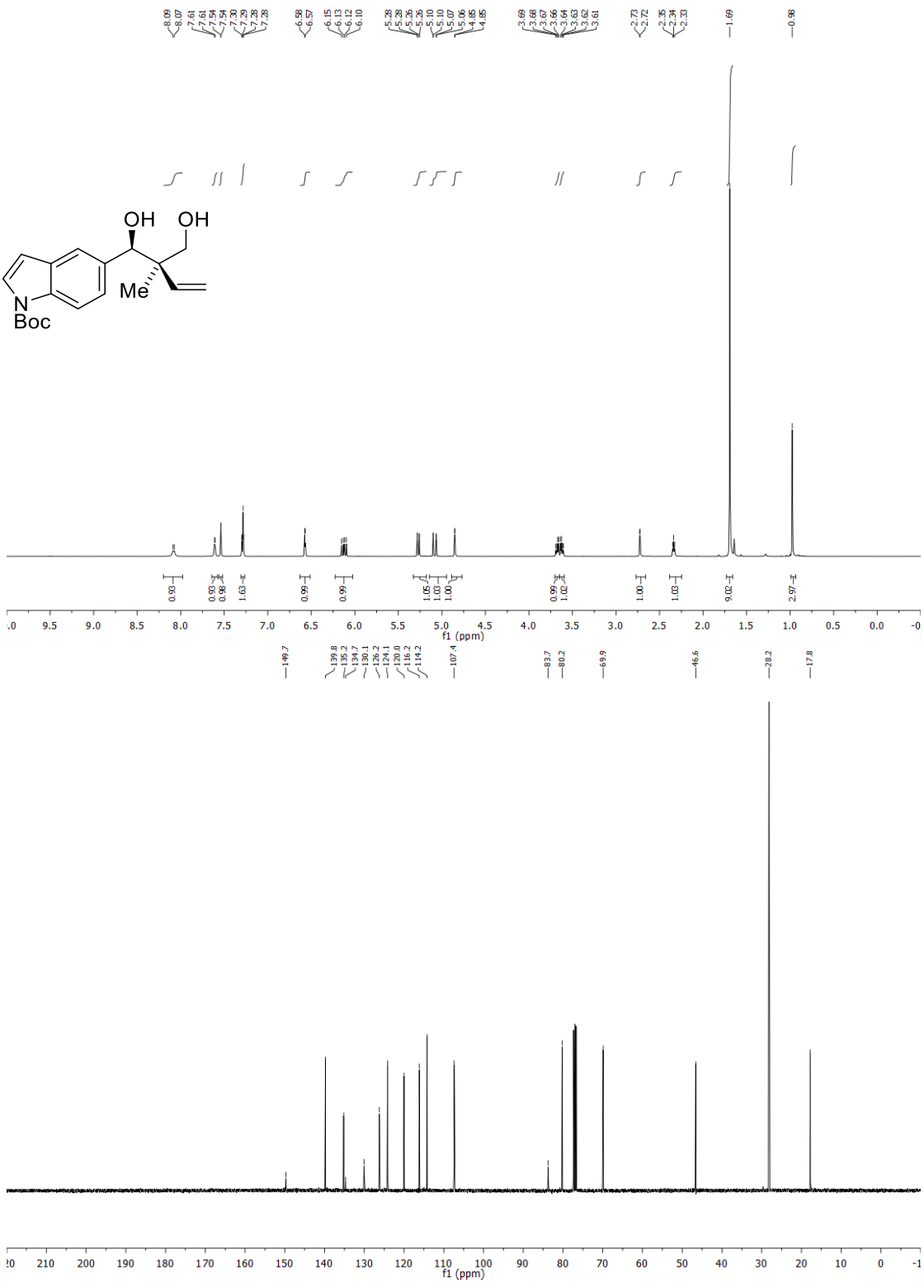
^{13}C NMR (125 MHz, $CDCl_3$) δ 149.7, 139.8, 135.2, 134.7, 130.1, 126.2, 124.1, 120.0, 116.2, 114.2, 107.4, 83.7, 80.1, 69.9, 46.7, 28.2, 17.7.

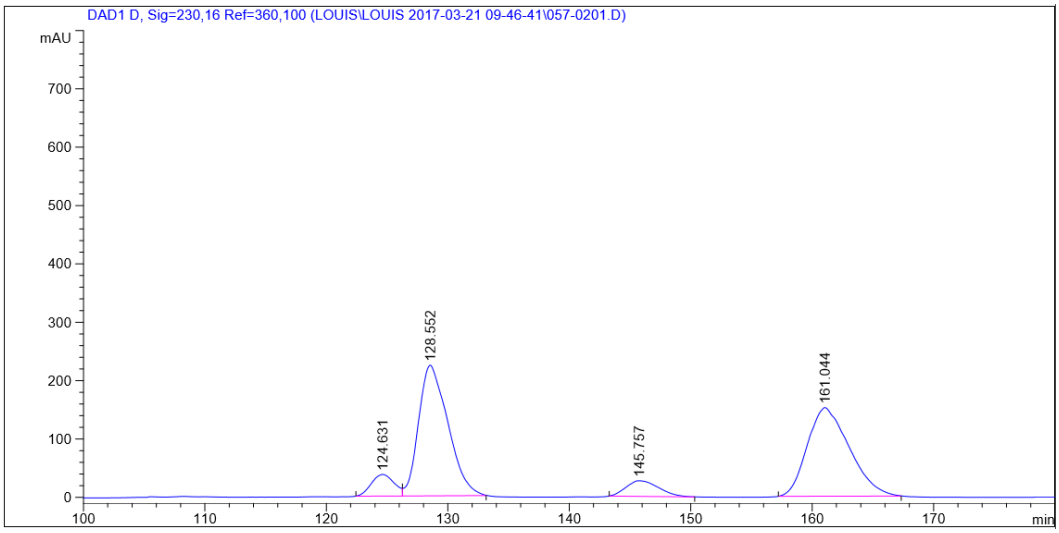
HRMS (ESI) Calcd. for $C_{19}H_{25}NO_4$ $[M+Na]^+$: 354.1676, Found: 354.1680.

FTIR (neat): 3384, 2978, 1732, 1469, 1352, 1255, 1160, 1022, 754 cm^{-1}.

$[\alpha]_D^{29}$: –24.0 (*c* = 1.0, $CHCl_3$).

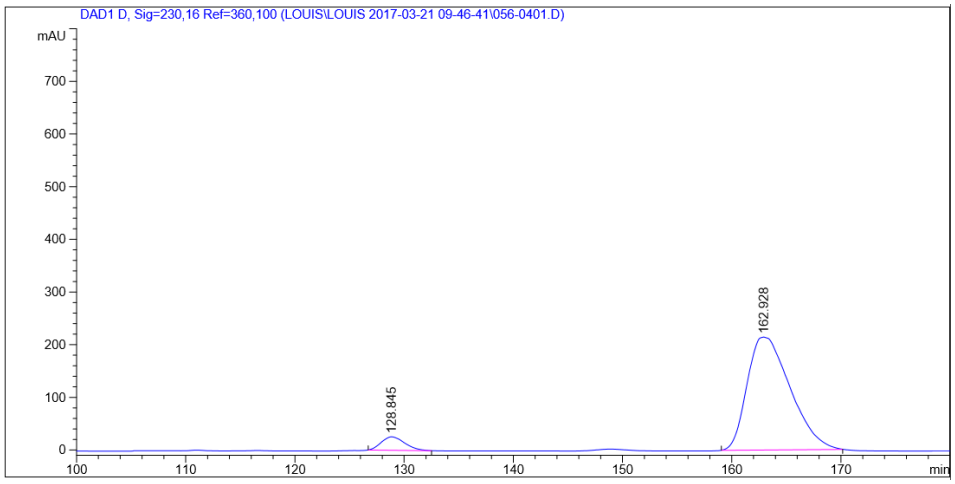
HPLC (Chiralcel AS-H columns, hexanes:*i*-PrOH = 99:1 (100 minutes) – 98:2 (100 minutes), 1.00 mL/min, 230 nm), *anti*:*syn* = 85:1, ee = 88%.


OH
OH
Me
N
Boc
f1 (ppm)
f1 (ppm)



Signal 1: DAD1 D, Sig=230,16 Ref=360,100

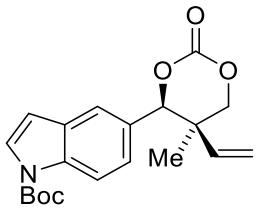
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	124.631	BV	1.7583	4827.00732	36.99244	5.7545
2	128.552	VB	2.3487	3.76106e4	223.79434	44.8377
3	145.757	BB	2.1991	4984.88232	26.66442	5.9427
4	161.044	BB	2.9672	3.64593e4	151.84721	43.4650



Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	128.845	BB	1.8847	3805.69751	25.50686	6.0828
2	162.928	BB	3.2629	5.87588e4	214.43245	93.9172

***tert*-butyl 5-((4*R*,5*R*)-5-methyl-2-oxo-5-vinyl-1,3-dioxan-4-yl)-1H-indole-1-carboxylate (3.1f)**



Detailed Procedures

An oven-dried vial equipped with a magnetic stir bar was charged with diol **SI-3.1f** (160 mg, 0.48 mmol, 100 mol%). Under argon atmosphere, acetonitrile (4.8 mL, 0.1 M) was added via syringe. CDI (156 mg, 0.97 mmol, 200 mol%) was added in one portion at ambient temperature. The reaction mixture was stirred at 25 ˚C for 16 h. The reaction was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 2:1) to furnish the title compound as a white solid (147 mg, 0.41 mmol) in 85% yield.

TLC (SiO_2) R_f = 0.45 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 3.7 Hz, 1H), 7.49 (d, *J* = 1.7 Hz, 1H), 7.19 (dd, *J* = 8.6, 1.8 Hz, 1H), 6.57 (d, *J* = 3.8 Hz, 1H), 5.68 (dd, *J* = 17.6, 11.1 Hz, 1H), 5.38 (s, 1H), 5.30 (d, *J* = 11.1 Hz, 1H), 5.23 (d, *J* = 17.7 Hz, 1H), 4.44 (d, *J* = 11.0 Hz, 1H), 4.33 (d, *J* = 10.9 Hz, 1H), 1.67 (s, 9H), 1.05 (s, 3H).

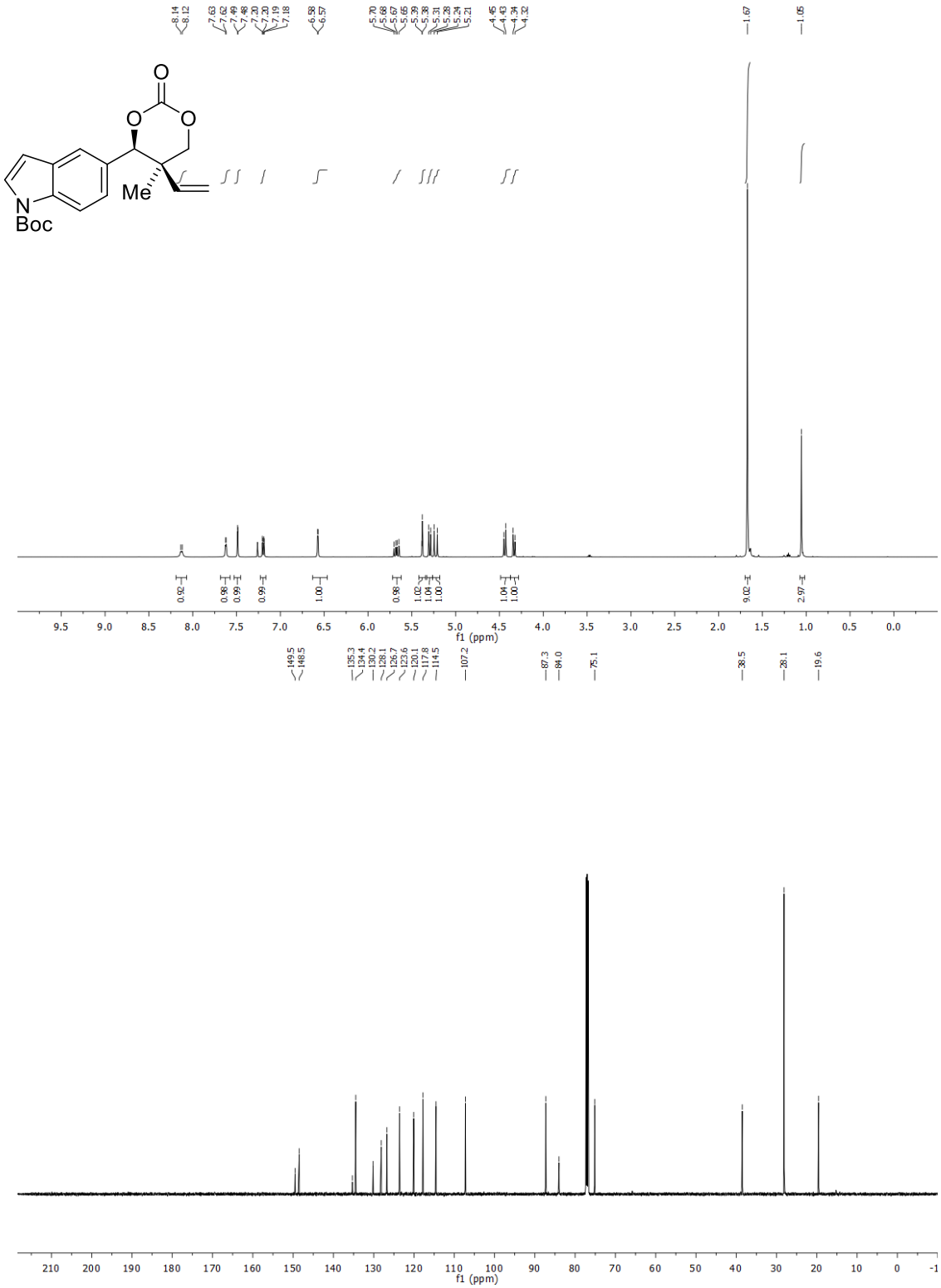
^{13}C NMR (125 MHz, $CDCl_3$) δ 149.5, 148.5, 135.3, 134.5, 130.2, 128.1, 126.7, 123.6, 120.1, 117.8, 114.5, 107.2, 87.3, 84.0, 75.1, 38.5, 28.1, 19.6.

HRMS (ESI) Calcd. for $C_{20}H_{23}NO_5$ $[M+Na]^+$: 380.1468, Found: 380.1468.

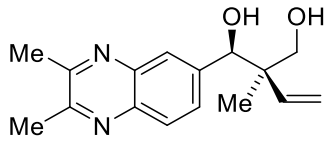
$[\alpha]_D^{29}$: –43.3 (*c* = 1.0, $CHCl_3$).

m.p. : 158–162 ˚C

FTIR (neat): 2978, 1734, 1473, 1358, 1222, 1161, 1102, 1024, 760 cm^{-1}.


O
O
O
Me
N
Boc
f1 (ppm)
f1 (ppm)

(1*R*,2*R*)-1-(2,3-dimethylquinoxalin-6-yl)-2-methyl-2-vinylpropane-1,3-diol (SI-3.1g)



Detailed Procedures

An oven-dried pressure tube equipped with a magnetic stir bar was charged with K_3PO_4 (4.2 mg, 0.02 mmol, 5 mol%), (*S*)-Ir-Tol-BINAP (22.0 mg, 0.02 mmol, 5 mol%) and (2,3-dimethylquinoxalin-6-yl)methanol[6] (75.2 mg, 0.4 mmol, 100 mol%). Under an atmosphere of argon, anhydrous THF (0.8 mL, 0.5 M) and isoprene monoxide (0.16 mL, 1.6 mmol, 400 mol%) were sequentially added via syringe. After sealing the tube with cap, the reaction mixture was stirred at 60 ˚C for 24 h. The reaction was cooled to ambient temperature and concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 1:10) to furnish the title compound as a yellow oil (92.0 mg, 0.34 mmol, *anti*:*syn* > 20:1) in 85% yield.

TLC (SiO_2) R_f = 0.31 (hexanes/ethyl acetate = 1:20).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 1.3 Hz, 1H), 7.84 (d, *J* = 8.6 Hz, 1H), 7.64 (dd, *J* = 8.6, 1.7 Hz, 1H), 6.12 (dd, J = 17.7, 11.0 Hz, 1H), 5.20 (dd, *J* = 11.0, 0.8 Hz, 1H), 4.98 (dd, *J* = 17.8, 0.9 Hz, 1H), 4.93 (s, 1H), 4.04 (brs, 1H), 3.71 (d, *J* = 10.6 Hz, 1H), 3.61 (d, *J* = 10.6 Hz, 1H), 3.24 (brs, 1H), 2.68 (s, 3H), 2.67 (s, 3H), 0.95 (s, 3H).

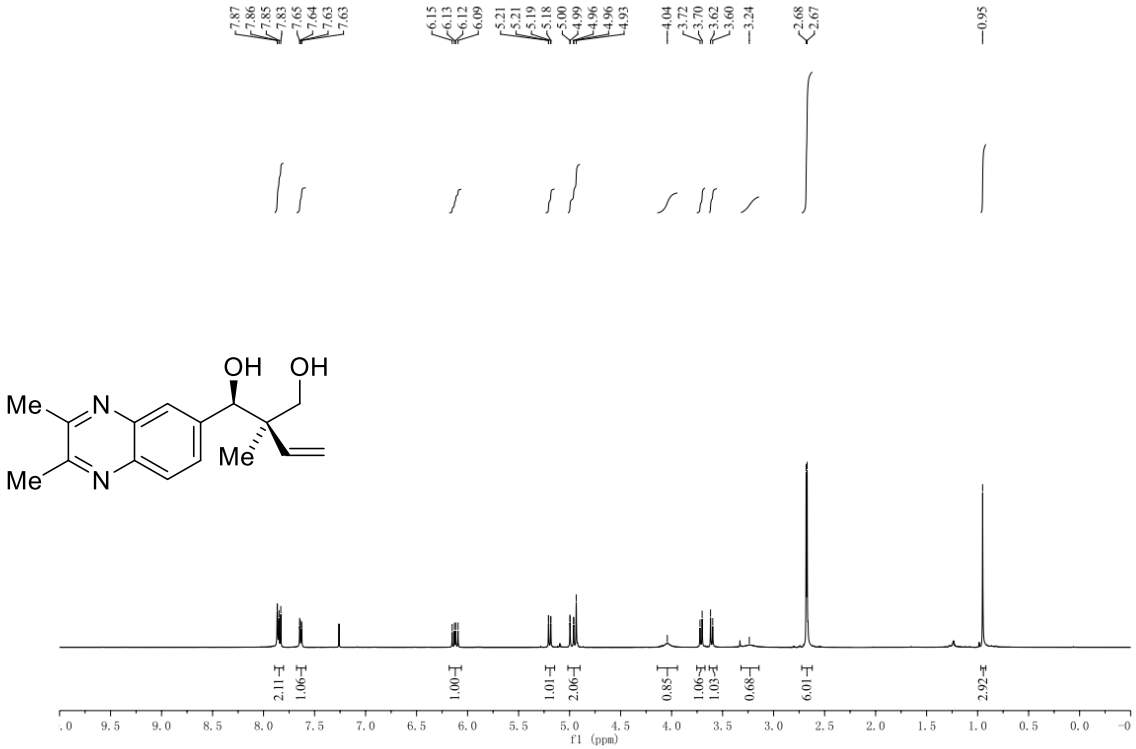
^{13}C NMR (125 MHz, $CDCl_3$) δ 153.5, 153.4, 142.3, 140.4, 140.1, 139.3, 129.0, 127.1, 126.8, 116.3, 79.5, 69.7, 46.4, 23.0, 18.0.

HRMS (ESI) Calcd. for $C_{16}H_{21}N_2O_2^+$ $[M+H]^+$: 273.1598, Found: 273.1597.

FTIR (neat): 3325, 2965, 2877, 1637, 1496, 1450, 1405, 1380, 1334, 1254, 1164, 1148, 1043, 021, 838, 809, 757, 666 cm^{-1}.

$[\alpha]_D^{33}$: -23.8 (*c* = 1.0, $CHCl_3$).

HPLC (two connected chiralcel AD-H columns, hexanes:*i*-PrOH = 95:5, 0.80 mL/min, 230 nm), *anti*:*syn* = 30:1, ee = 90%.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7.85
7.83
7.65
7.64
7.63
7.63
6.15
6.13
6.12
6.09
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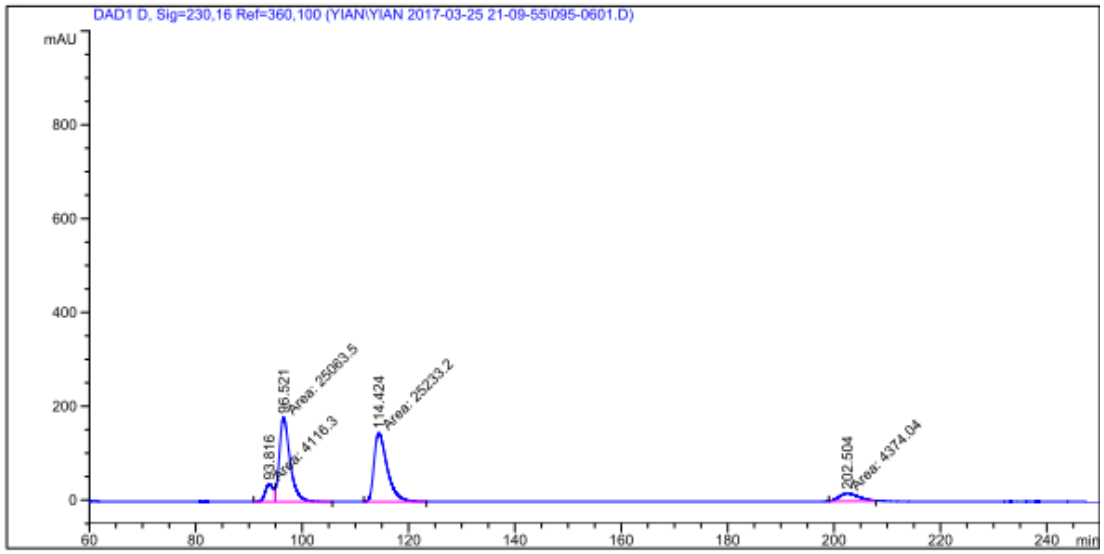
5.21
5.19
5.18
5.00
4.99
4.96
4.96
4.93
4.04
3.72
3.70
3.62
3.60
3.24
2.68
2.67
0.95
OH
OH
Me
N
Me
N
Me
2.11
1.06
1.00
1.01
2.06
0.85
1.06
1.03
0.68
6.01
2.92
f1 (ppm)


153.5
153.4
142.3
140.4
140.1
139.3
129.0
127.1
126.8
116.3
79.5
69.7
46.4
23.0
18.0
OH
OH
Me
N
Me
N
Me
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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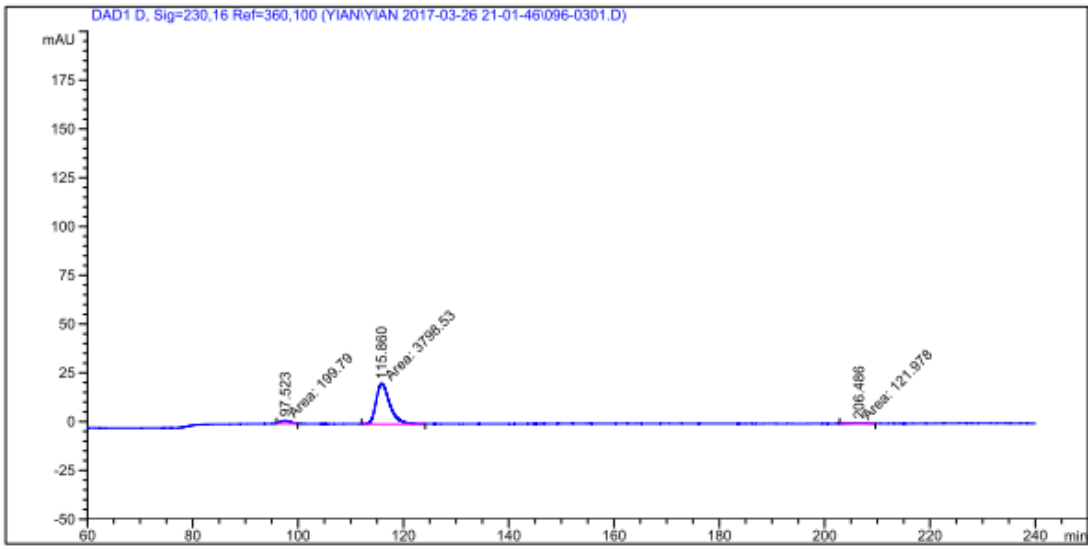
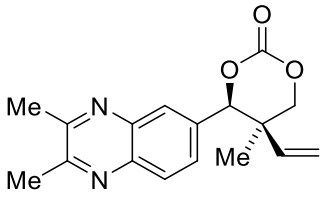
2	96.521	FM	2.3351	2.50635e4	178.88995	42.6344
3	114.424	MM	2.8763	2.52332e4	146.21553	42.9231
4	202.504	MM	4.3698	4374.04248	16.68301	7.4405



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	97.523	MM	2.2133	199.78983	1.50443	4.8489
2	115.860	MM	3.0432	3798.53394	20.80317	92.1907
3	206.486	MM	4.6694	121.97781	4.35381e-1	2.9604

(4*R*,5*R*)-4-(2,3-dimethylquinoxalin-6-yl)-5-methyl-5-vinyl-1,3-dioxan-2-one (3.1g)



Detailed Procedures

An oven-dried vial equipped with a magnetic stir bar was charged with diol **SI-3.1g** (65.0 mg, 0.24 mmol, 100 mol%). Under argon atmosphere, acetonitrile (2.4 mL, 0.1 M) was added via syringe. CDI (77.4 mg, 0.48 mmol, 200 mol%) was added in one portion at ambient temperature. The reaction mixture was stirred at 25 ˚C for 16 h. The reaction was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 1:10) to furnish the title compound as a yellow solid (51.0 mg, 0.17 mmol) in 72 % yield.

TLC (SiO_2) R_f = 0.37 (hexanes/ethyl acetate = 1:10).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.7 Hz, 1H), 7.88 (d, *J* = 1.4 Hz, 1H), 7.60 (dd, *J* = 8.7, 1.8 Hz, 1H), 5.69 (dd, *J* = 17.6, 11.1 Hz, 1H), 5.50 (s, 1H), 5.32 (d, *J* = 11.1 Hz, 1H), 5.22 (d, *J* = 17.6 Hz, 1H), 4.45 (d, *J* = 11.0 Hz, 1H), 4.39 (d, *J* = 11.1 Hz, 1H), 2.74 (s, 3H), 2.74 (s, 3H), 1.10 (s, 3H).

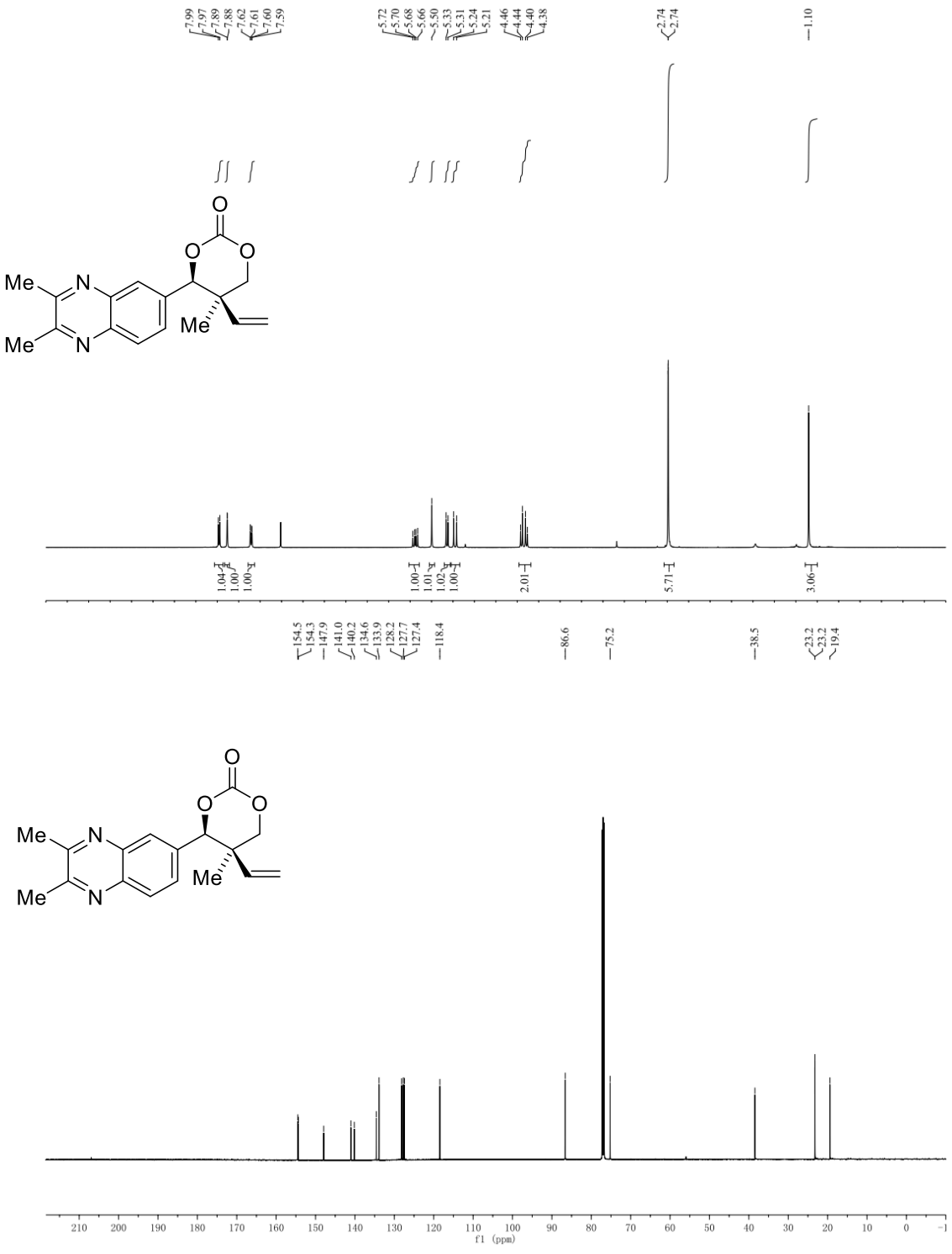
^{13}C NMR (125 MHz, $CDCl_3$) δ 154.5, 154.4, 147.9, 141.0, 140.2, 134.6, 133.9, 128.2, 127.7, 127.4, 118.4, 86.6, 75.2, 38.5, 23.2, 23.2, 19.4.

HRMS (ESI) Calcd. for $C_{17}H_{19}N_2O_3^+$ $[M+Na]^+$: 299.1390, Found: 299.1392.

$[\alpha]_D^{33}$: -70.8 (*c* = 1.0, $CHCl_3$).

m.p. : 218-220 ˚C (decomposed)

FTIR (neat): 2970, 1747, 1456, 1401, 1335, 1240, 1210, 1166, 1134, 1103, 999, 974, 841, 767, 670 cm^{-1}.


7.99
7.97
7.89
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7.60
7.59
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5.70
5.68
5.66
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5.33
5.31
5.24
5.21
4.46
4.44
4.40
4.38
2.74
2.74
1.10
Me
N
Me
N
O
O
O
Me
1.04
1.00
1.00
1.00
1.01
1.02
1.00
2.01
5.71
3.06
154.5
154.3
147.9
141.0
140.2
134.6
133.9
128.2
127.7
127.4
118.4
86.6
75.2
38.5
23.2
23.2
19.4
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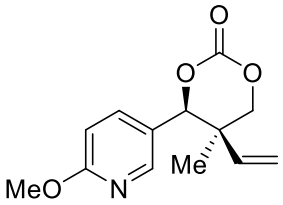
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

(*4R,5R*)-4-(6-methoxypyridin-3-yl)-5-methyl-5-vinyl-1,3-dioxan-2-one (3.1h)



Detailed Procedures

An oven-dried vial equipped with a magnetic stir bar was charged with (1*R*,2*R*)-1-(6-methoxypyridin-3-yl)-2-methyl-2-vinylpropane-1,3-diol[4] (558 mg, 2.5 mmol, 100 mol%). Under argon atmosphere, acetonitrile (25 mL, 0.1 M) was added via syringe. CDI (810 mg, 5.0 mmol, 200 mol%) was added in one portion at ambient temperature. The mixture was stirred at 25 ˚C for 16 h. The reaction was concentrated in *vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 1:1) to furnish the title compounds as a white solid (418 mg, 1.68 mmol) in 82% yield.

TLC (SiO_2) R_f = 0.31 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 2.6 Hz, 1H), 7.56 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.78 (d, *J* = 8.7 Hz, 1H), 5.74 (dd, *J* = 17.6, 11.1 Hz, 1H), 5.38 (d, *J* = 11.1 Hz, 1H), 5.28 (s, 1H), 5.25 (d, *J* = 15.0 Hz, 1H), 4.42 (d, *J* = 11.0 Hz, 1H), 4.36 (d, *J* = 11.0 Hz, 1H), 3.97 (s, 3H), 1.04 (s, 3H).

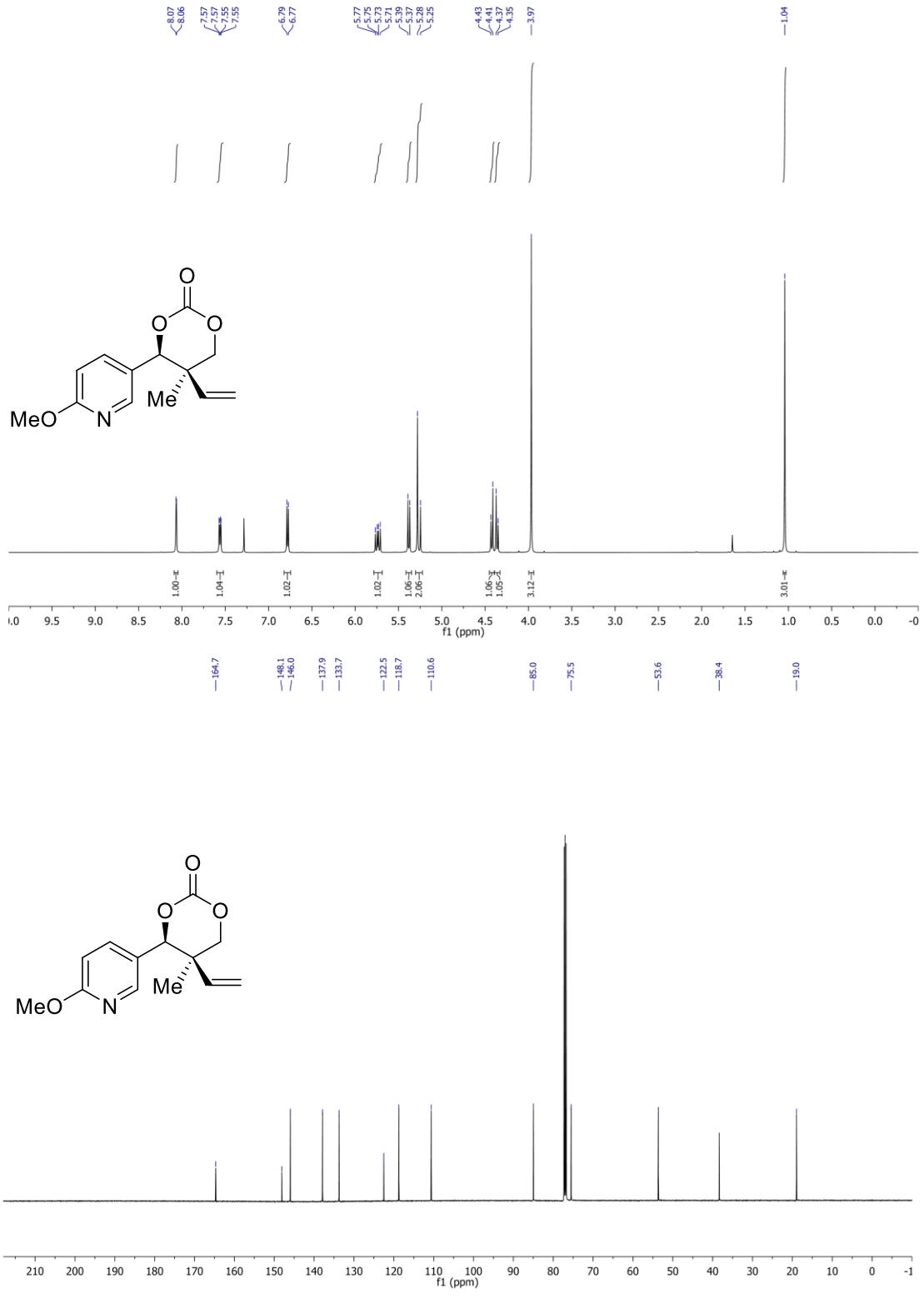
^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 148.1, 146.0, 137.9, 133.7, 122.5, 118.7, 110.6, 85.0, 75.5, 53.6, 38.4, 19.0.

HRMS (ESI) Calcd. for $C_{13}H_{15}NNaO_4^+$ $[M+Na]^+$: 272.0894, Found: 272.0892

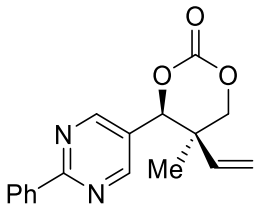
$[\alpha]_D^{30}$: +110.9 (c = 0.61, $CHCl_3$)

m.p.: 102 – 104 ˚C

FTIR (neat): 1733, 1608, 1495, 1400, 1286, 1242, 1207, 1130, 1100, 1025, 940, 832, 768 cm^{-1}.


8.07
8.06
7.57
7.57
7.55
7.55
6.79
6.77
5.77
5.75
5.73
5.71
5.39
5.37
5.28
5.25
4.43
4.41
4.37
4.35
3.97
1.04
O
O
O
Me
MeO
N
1.00
1.04
1.02
1.02
1.06
2.06
1.06
1.05
3.12
3.01
f1 (ppm)
164.7
148.1
146.0
137.9
133.7
122.5
118.7
110.6
85.0
75.5
53.6
38.4
19.0
f1 (ppm)

(*4R,5R*)-5-methyl-4-(2-phenylpyrimidin-5-yl)-5-vinyl-1,3-dioxan-2-one (3.1i)



Detailed Procedures

An oven-dried vial equipped with a magnetic stir bar was charged with (1*R*,2*R*)-2-methyl-1-(2-phenylpyrimidin-5-yl)-2-vinylpropane-1,3-diol[4] (162 mg, 0.6 mmol, 100 mol%). Under argon atmosphere, acetonitrile (6 mL, 0.1 M) was added via syringe. CDI (194 mg, 1.2 mmol, 200 mol%) was added in one portion at ambient temperature. The mixture was stirred at 25 ˚C for 16 h. The reaction was concentrated in *vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 1:1) to furnish the title compounds as a white solid (128 mg, 0.43 mmol) in 72% yield.

TLC (SiO_2) R_f = 0.25 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (s, 2H), 8.52 – 8.40 (m, 2H), 7.57 – 7.48 (m, 3H), 5.82 (dd, *J* = 17.5, 11.0 Hz, 1H), 5.47 (d, *J* = 11.0 Hz, 1H), 5.39 (s, 1H), 5.29 (d, *J* = 17.5 Hz, 1H), 4.46 (d, *J* = 11.0 Hz, 1H), 4.43 (d, *J* = 11.1 Hz, 1H), 1.11 (s, 3H).

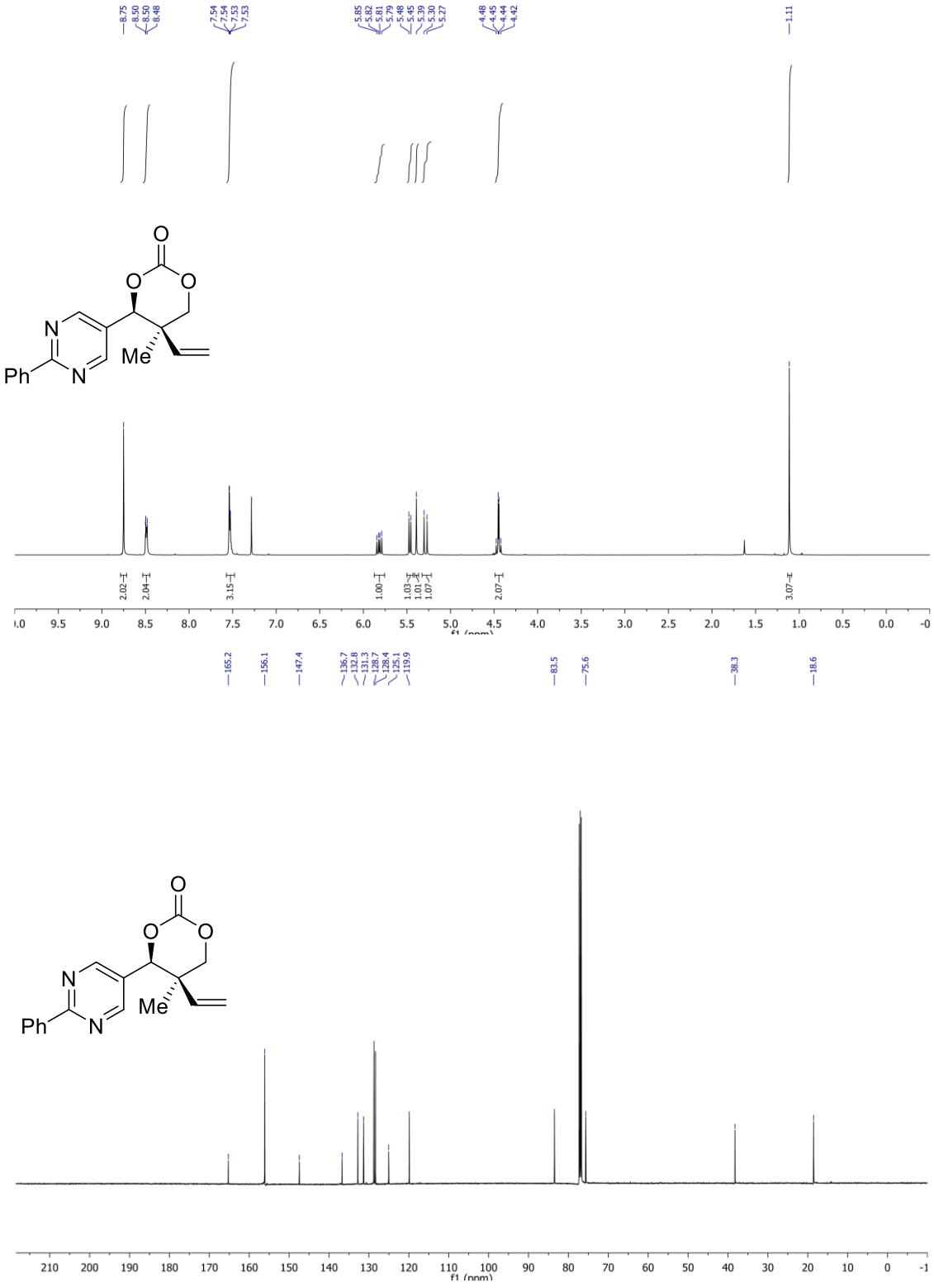
^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 156.1, 147.4, 136.7, 132.8, 131.3, 128.7, 128.4, 125.1, 119.9, 83.50, 75.7, 38.3, 18.6.

HRMS (ESI) Calcd. for $C_{17}H_{16}N_2NaO_3^+$ $[M+Na]^+$: 319.1054, Found: 319.1059

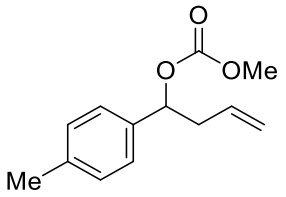
$[\alpha]_D^{30}$: +139.9 (c = 0.56, $CHCl_3$)

m.p.: 153 – 154 ˚C

FTIR (neat): 1736, 1722, 1588, 1544, 1434, 1398, 1242, 1211, 1133, 1102, 753, 730, 693 cm^{-1}.


8.75
8.50
8.50
8.48
7.54
7.54
7.53
7.53
5.85
5.82
5.81
5.79
5.48
5.45
5.39
5.30
5.27
4.48
4.45
4.44
4.42
1.11
O
O
O
N
N
Ph
Me
2.02
2.04
3.15
1.00
1.03
1.01
1.07
2.07
3.07
f1 (ppm)
165.2
156.1
147.4
136.7
132.8
131.3
128.7
128.4
125.1
119.9
83.5
75.6
38.3
18.6
f1 (ppm)

Procedures and Spectral Data for the Model study of Cyclopropane Formation: methyl (1-(*p*-tolyl)but-3-en-1-yl) carbonate (*model*-3.1a)



Detailed Procedures

An oven-dried vial equipped with a magnetic stir bar was charged with 1-(*p*-tolyl)but-3-en-1-ol (324 mg, 2.0 mmol, 100 mol%) and 4-dimethylaminopyridine (439 mg, 3.6 mmol, 180 mol%). Under argon atmosphere, DCM (5 mL, 0.4 M) was added via syringe. Then, methyl chloroformate (0.23 mL, 3.0 mmol, 150 mol%) was added dropwise at 0 ˚C. The reaction mixture was stirred at ambient temperature for 16 h. Saturated aqueous ammonium chloride (15 mL) was added. The aqueous layer was extracted with ethyl acetate (30 mL x 2). The combined organic layers were washed with brine (20 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 30:1) to furnish the title compound as a colorless oil (356 mg, 1.7 mmol) in 86% yield.

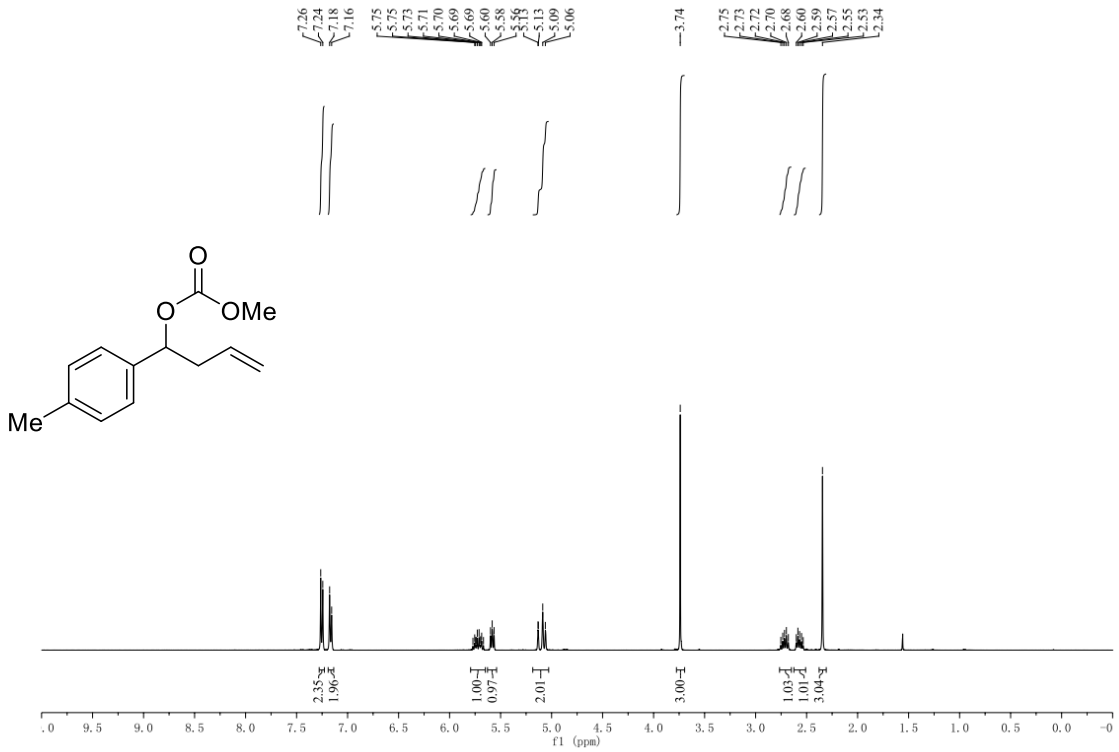
TLC (SiO_2) R_f = 0.35 (hexanes/ethyl acetate = 10:1).

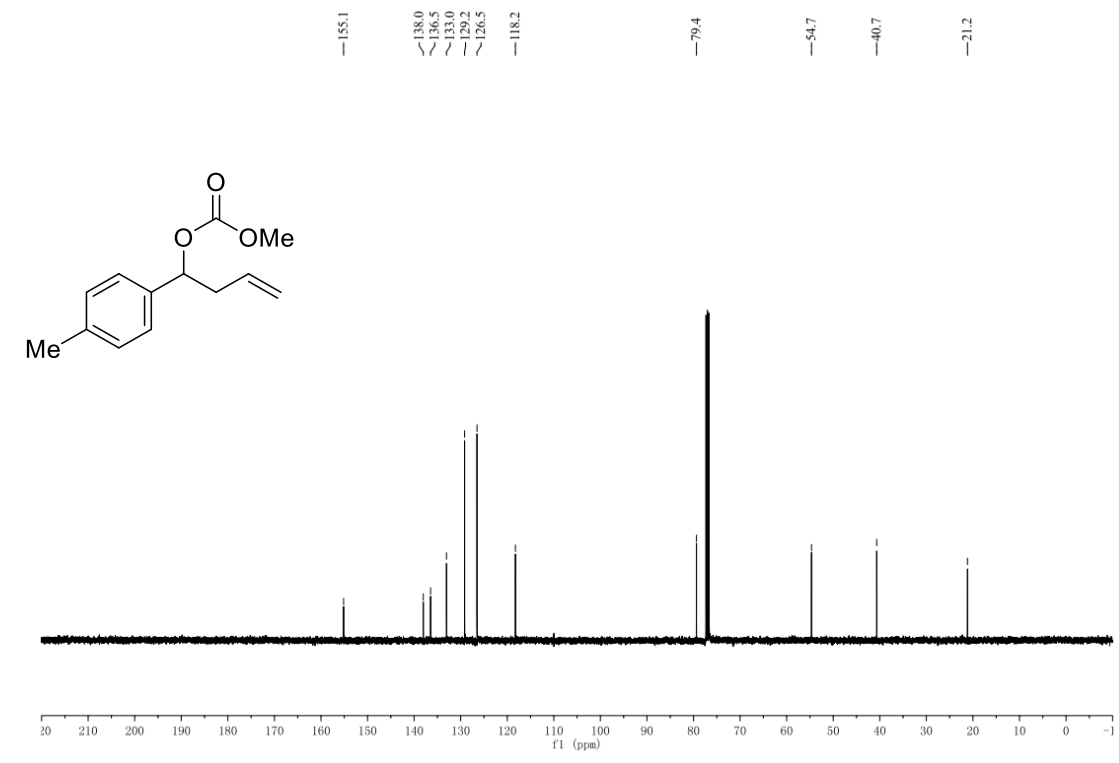
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 5.72 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.61 – 5.55 (m, 1H), 5.15 – 5.04 (m, 2H), 3.74 (s, 3H), 2.77 – 2.65 (m, 1H), 2.62 – 2.51 (m, 1H), 2.34 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 138.0, 136.5, 133.0, 129.2, 126.5, 118.2, 79.4, 54.7, 40.6, 21.2.

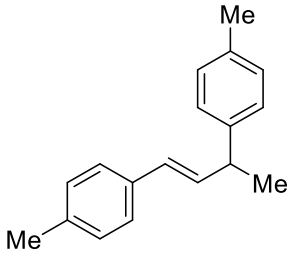
HRMS (ESI) Calcd. for $C_{11}H_{13}^+$ $[M\text{-}OCO_2Me]^+$: 145.1012, Found: 145.1011.

FTIR (neat): 2955, 1745, 1516, 1441, 1261, 1110, 1041, 939, 866, 791, 720 cm^{-1}.


7.26
7.24
7.18
7.16
5.75
5.75
5.73
5.71
5.70
5.69
5.69
5.60
5.58
5.56
5.13
5.09
5.06
3.74
2.75
2.73
2.72
2.70
2.68
2.60
2.59
2.57
2.55
2.53
2.34
O
O
OMe
Me
2.35
1.96
1.00
0.97
2.01
3.00
1.03
1.01
3.04
f1 (ppm)


155.1
138.0
136.5
133.0
129.2
126.5
118.2
79.4
54.7
40.7
21.2
O
O
OMe
Me
f1 (ppm)

(*E*)-4,4'-(but-1-ene-1,3-diyl)bis(methylbenzene) (SI-3.5)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with carbonate *model*-**3.1a** (22.0 mg, 0.1 mmol, 100 mol%), tri(*p*-tolyl)boroxine (30.1 mg, 0.085 mmol, 85 mol%) **3.2a**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 45 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes) to furnish the known title compound[7] as a colorless oil (7.3 mg, 0.03 mmol) in 31% yield.

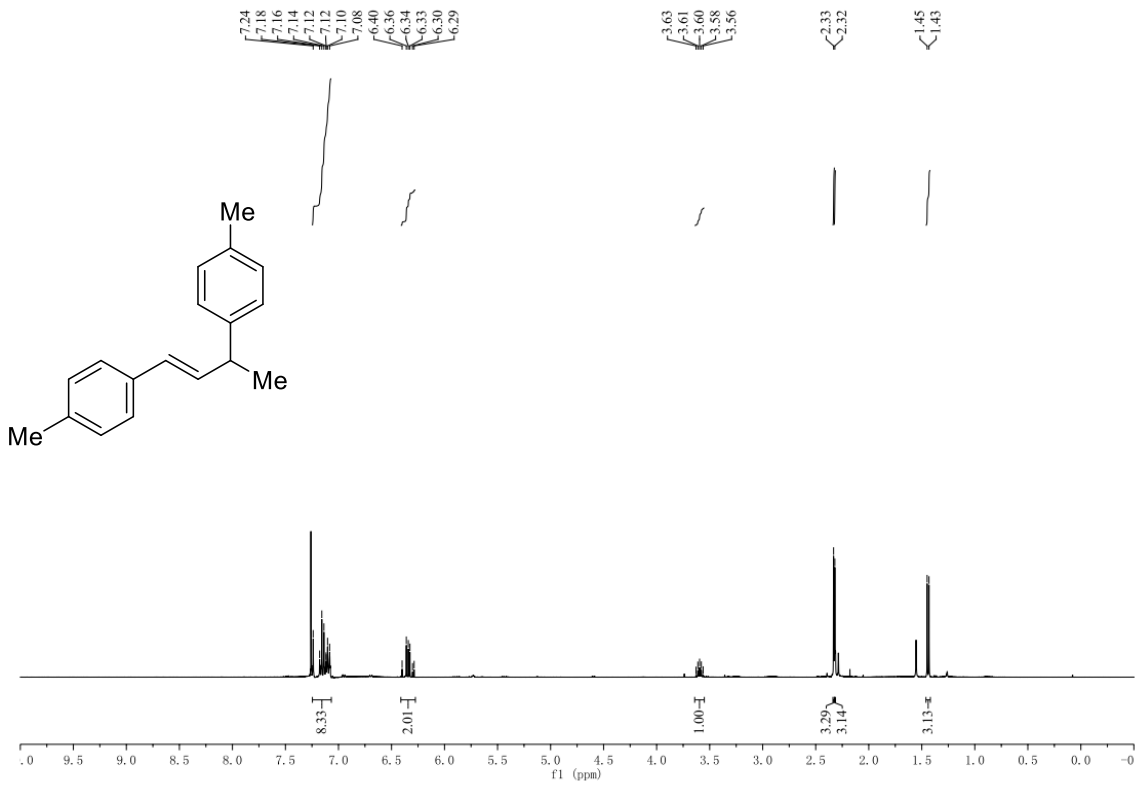
TLC (SiO_2) R_f = 0.28 (hexanes).

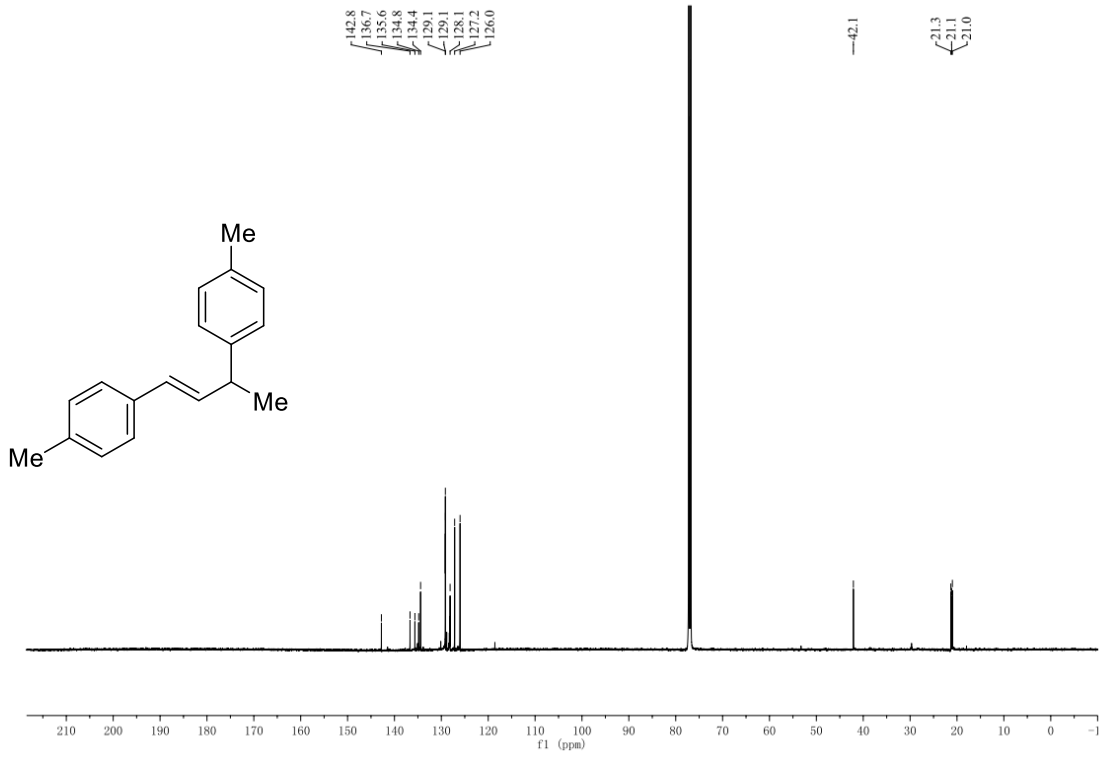
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.07 (m, 8H), 6.38 (d, *J* = 16.0 Hz, 1H), 6.31 (dd, *J* = 15.9, 6.2 Hz, 1H), 3.64 – 3.56 (m, 1H), 2.33 (s, 3H), 2.32 (s, 3H), 1.44 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8, 136.7, 135.6, 134.8, 134.4, 129.1, 129.1, 128.1, 127.2, 126.0, 42.1, 21.3, 21.1, 21.0.

HRMS (CI) Calcd. for $C_{18}H_{20}^{+}$ $[M]^{+}$: 236.1560, Found: 236.1570.

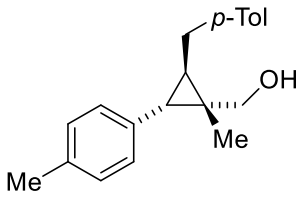
FTIR (neat): 3020, 2962, 2922, 2865, 1513, 1451, 1371, 1111, 1015, 967, 816, 798, 723 cm^{-1}


7.24
7.18
7.16
7.14
7.12
7.12
7.10
7.08
6.40
6.36
6.34
6.33
6.30
6.29
3.63
3.61
3.60
3.58
3.56
2.33
2.32
1.45
1.43
Me
Me
Me
8.33
2.01
1.00
3.29
3.14
3.13
f1 (ppm)


142.8
136.7
135.6
134.8
134.4
129.1
129.1
128.1
127.2
126.0
42.1
21.3
21.1
21.0
Me
Me
Me
f1 (ppm)

Procedures and Spectral Data for the Synthesis of Enantiomerically Enriched Cyclopropanes 3.3a-3.3r:

((1*S*,2*R*,3*S*)-1-methyl-2-(4-methylbenzyl)-3-(*p*-tolyl)cyclopropyl)methanol (3.3a)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1a** (23.2 mg, 0.1 mmol, 100 mol%), tri(*p*-tolyl)boroxine (30.1 mg, 0.085 mmol, 85 mol%) **3.2a**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 45 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1) to furnish the title compound as a white solid (23.8 mg, 0.08 mmol) in 85% yield.

TLC (SiO_2) R_f = 0.45 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 – 7.05 (m, 8H), 3.39 (dd, *J* = 11.6, 7.6 Hz, 1H), 3.24 (dd, *J* = 11.6, 4.4 Hz, 1H), 2.89 – 2.74 (m, 2H), 2.33 (s, 3H), 2.31 (s, 3H), 1.89 (d, *J* = 5.9 Hz, 1H), 1.52 (dd, *J* = 13.0, 7.1 Hz, 1H), 1.41 (s, 3H), 0.93 – 0.87 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 135.7, 135.7, 135.3, 129.1, 129.1, 128.3, 128.0, 68.2, 35.1, 34.2, 29.6, 27.4, 21.0, 21.0, 17.2.

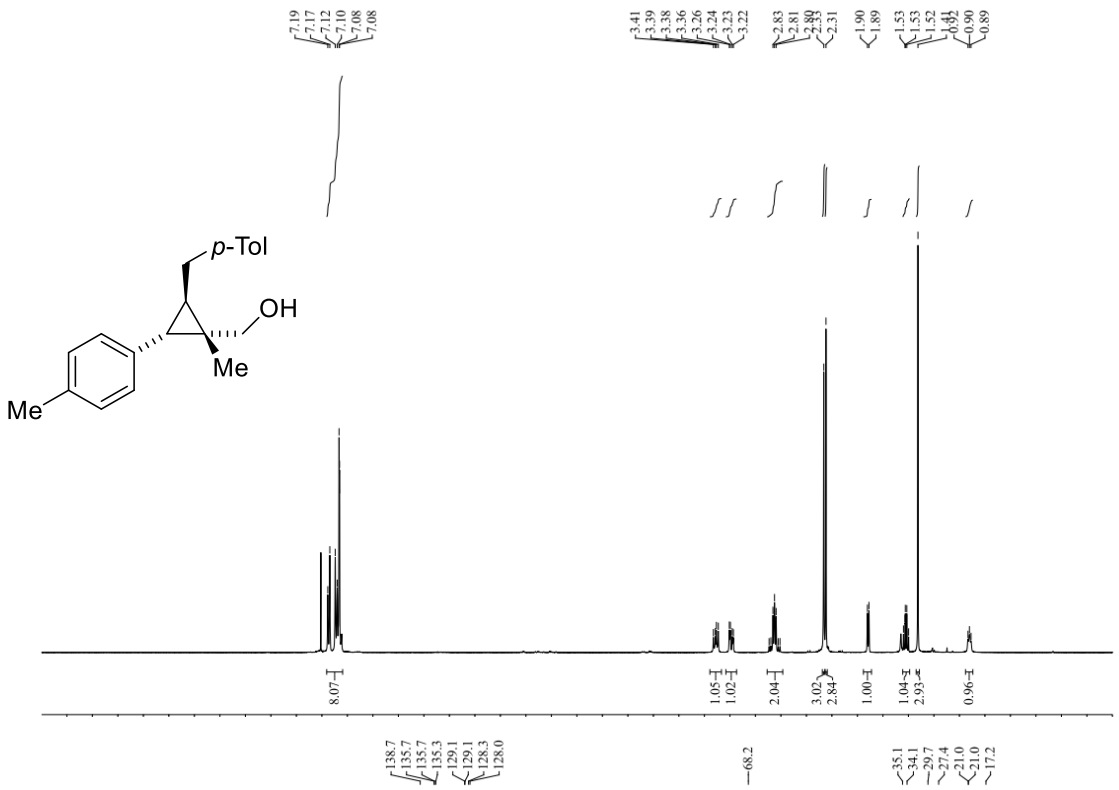
HRMS (ESI) Calcd. for $C_{20}H_{24}NaO^+$ $[M+Na]^+$: 303.1719, Found: 303.1720.

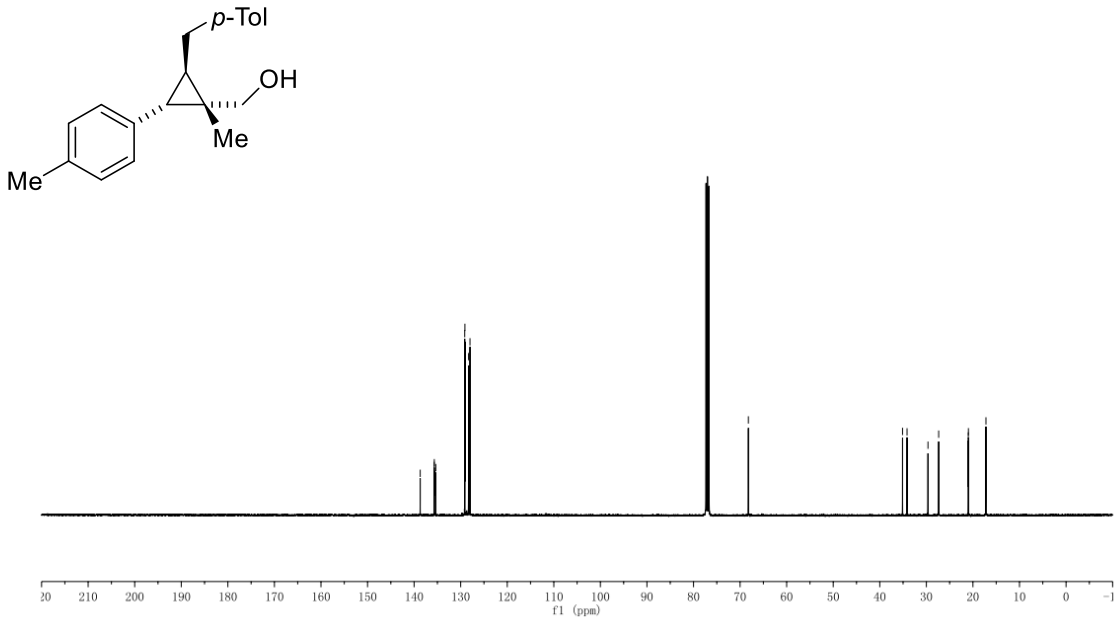
$[\alpha]_D^{33}$: +24.0 (*c* = 1.0, $CHCl_3$).

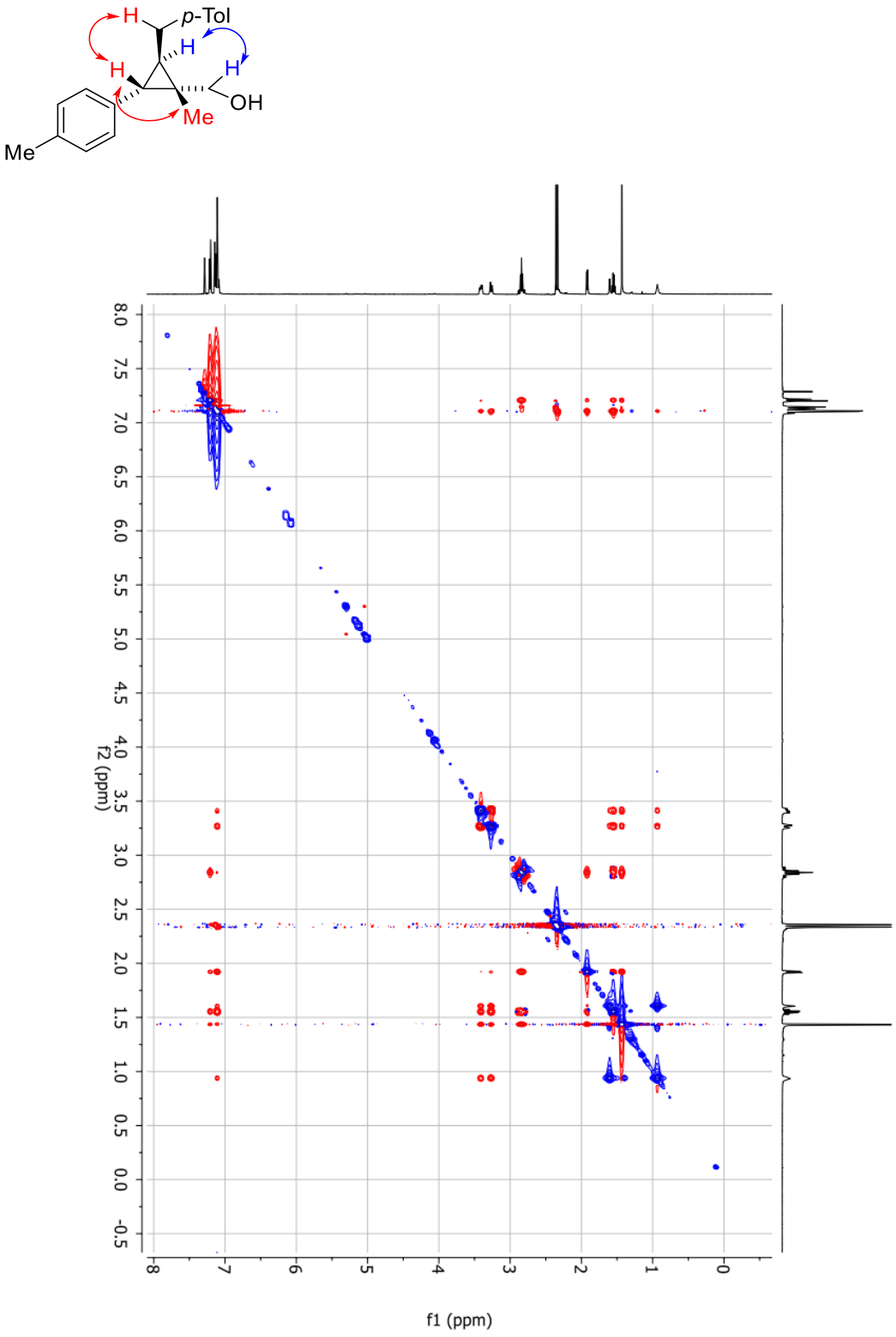
m.p. : 59-60 ˚C

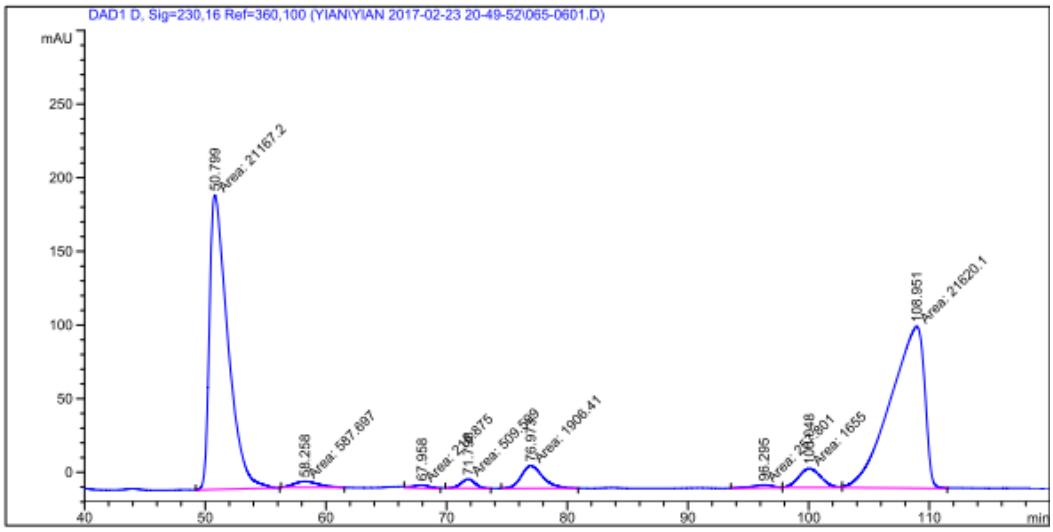
FTIR (neat): 3394, 2920, 2361, 2342, 1514, 1460, 1113, 1020, 825, 807, 759, 669 cm^{-1}

HPLC (two connected chiralcel OJ-H columns, hexanes:*i*-PrOH = 98:2, 1.0 mL/min, 230 nm), ee = 91%.

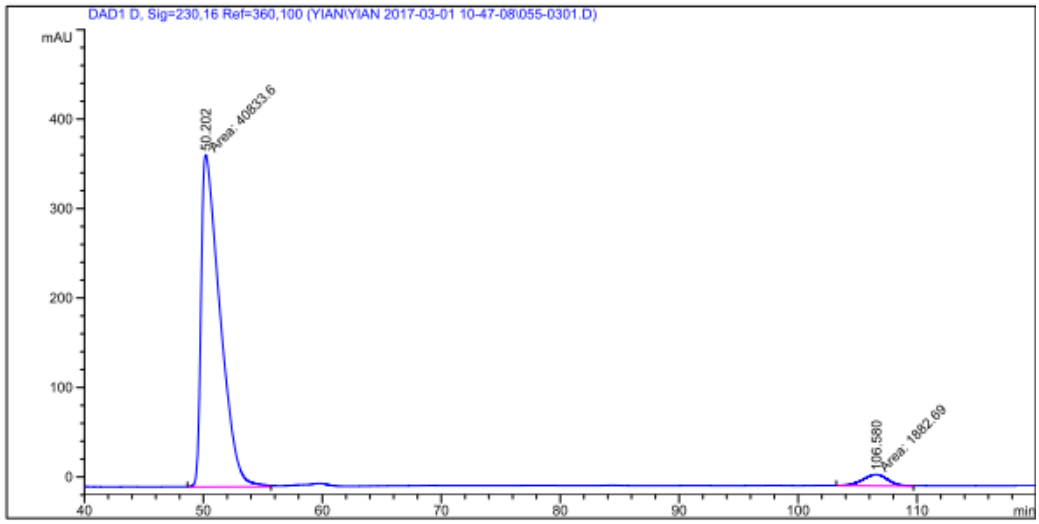

7.19
7.17
7.12
7.10
7.08
7.08
3.41
3.39
3.38
3.36
3.26
3.24
3.23
3.22
2.83
2.81
2.80
2.33
2.31
1.90
1.89
1.53
1.53
1.52
0.92
0.90
0.89
p-Tol
OH
Me
Me
8.07
1.05
1.02
2.04
3.02
2.84
1.00
1.04
2.93
0.96


138.7
135.7
135.7
135.3
129.1
129.1
128.3
128.0
68.2
35.1
34.1
29.7
27.4
21.0
21.0
17.2
p-Tol
OH
Me
Me
f1 (ppm)


H
p-Tol
H
H
H
OH
Me
Me
f2 (ppm)
f1 (ppm)

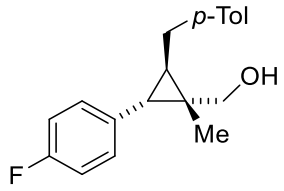


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	50.799	MM	1.7645	2.11672e4	199.93961	44.1714
2	58.258	MM	2.3894	587.69690	4.09932	1.2264
3	67.958	MM	1.7158	216.87540	2.10667	0.4526
4	71.798	MM	1.3703	509.59866	6.19798	1.0634
5	76.973	MM	2.0695	1906.41321	15.35360	3.9783
6	96.295	MM	2.1431	257.80118	2.00491	0.5380
7	100.048	MM	2.1311	1654.99817	12.94301	3.4536
8	108.951	MM	3.2794	2.16201e4	109.87929	45.1164



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	50.202	MM	1.8339	4.08336e4	371.09204	95.5926
2	106.580	MM	2.4865	1882.69165	12.61956	4.4074

((1*S*,2*S*,3*R*)-2-(4-fluorophenyl)-1-methyl-3-(4-methylbenzyl)cyclopropyl)methanol (3.3b)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1a** (23.6 mg, 0.1 mmol, 100 mol%), tri(*p*-tolyl)boroxine (30.1 mg, 0.085 mmol, 85 mol%) **3.2a**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 45 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1) to furnish the title compound as a white solid (21.9 mg, 0.08 mmol) in 77% yield.

TLC (SiO_2) R_f = 0.31 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 – 7.10 (m, 6H), 6.98 – 6.91 (m, 2H), 3.35 (d, *J* = 11.5 Hz, 1H), 3.22 (d, *J* = 11.5 Hz, 1H), 2.88 – 2.73 (m, 2H), 2.34 (s, 3H), 1.89 (d, J = 5.9 Hz, 1H), 1.50 – 1.44 (m, 1H), 1.41 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (d, *J* = 244.5 Hz), 138.5, 135.4, 134.5 (d, *J* = 3.1 Hz), 130.0 (d, *J* = 7.8 Hz), 129.2, 128.0, 115.1 (d, J = 21.2 Hz), 68.1, 34.7, 34.1, 29.5, 27.9, 21.0, 17.1.

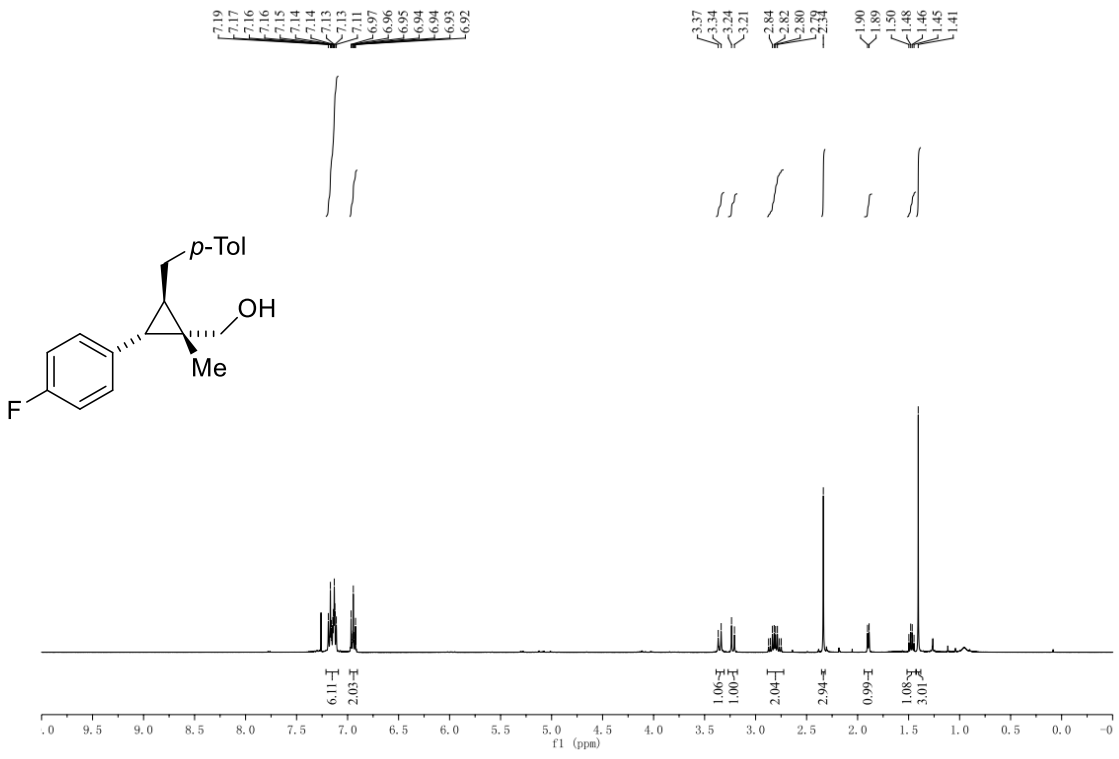
^{19}F NMR (376 MHz, $CDCl_3$) δ -116.8 – -116.9 (m).

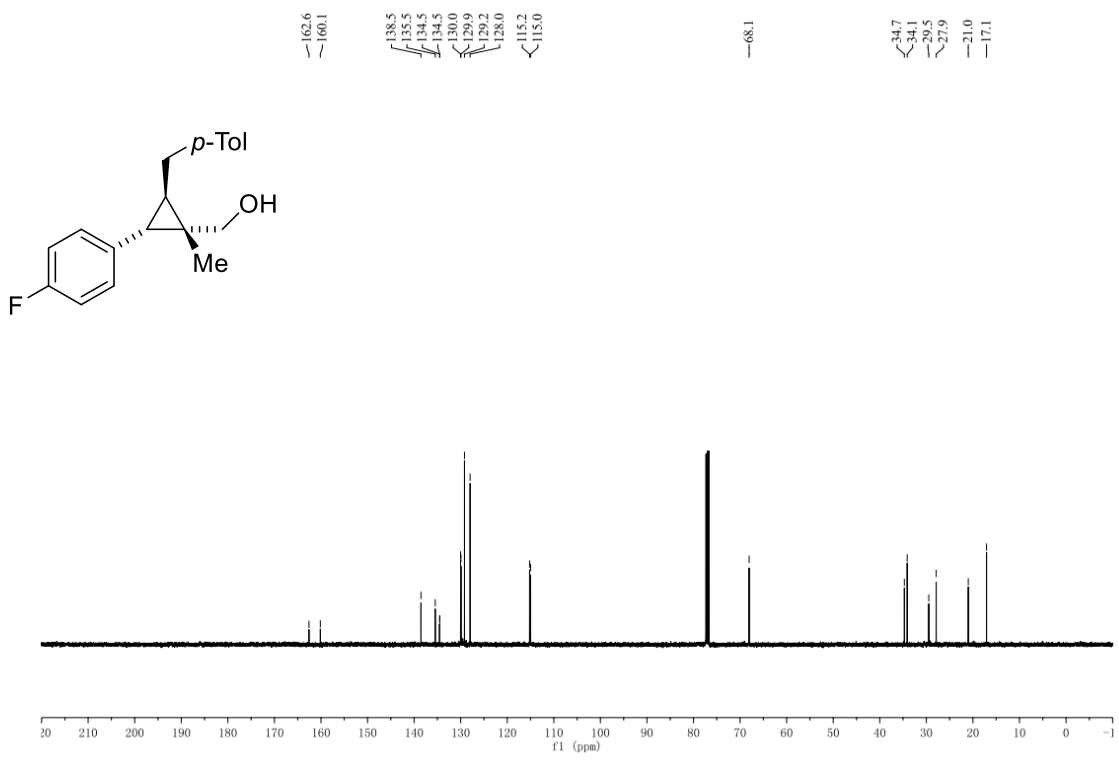
HRMS (CI) Calcd. for $C_{19}H_{20}FO^+$ $[M-H]^+$: 283.1493, Found: 283.1492.

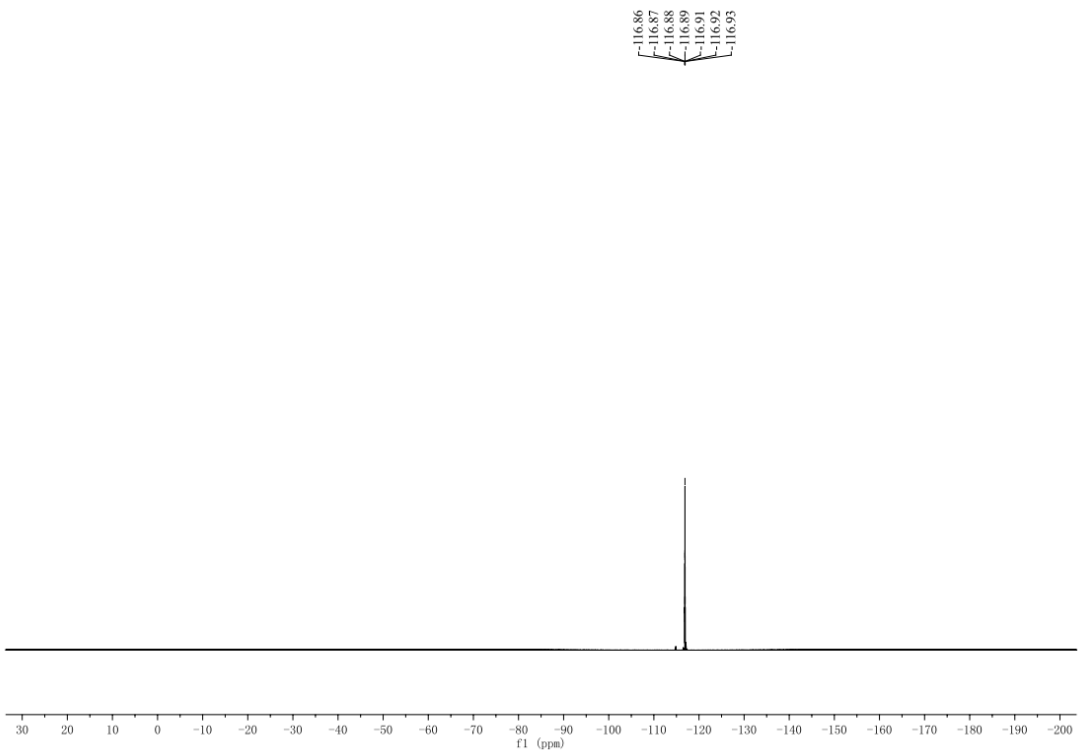
$[\alpha]_D^{33}$: +26.7 (*c* = 1.0, $CHCl_3$).

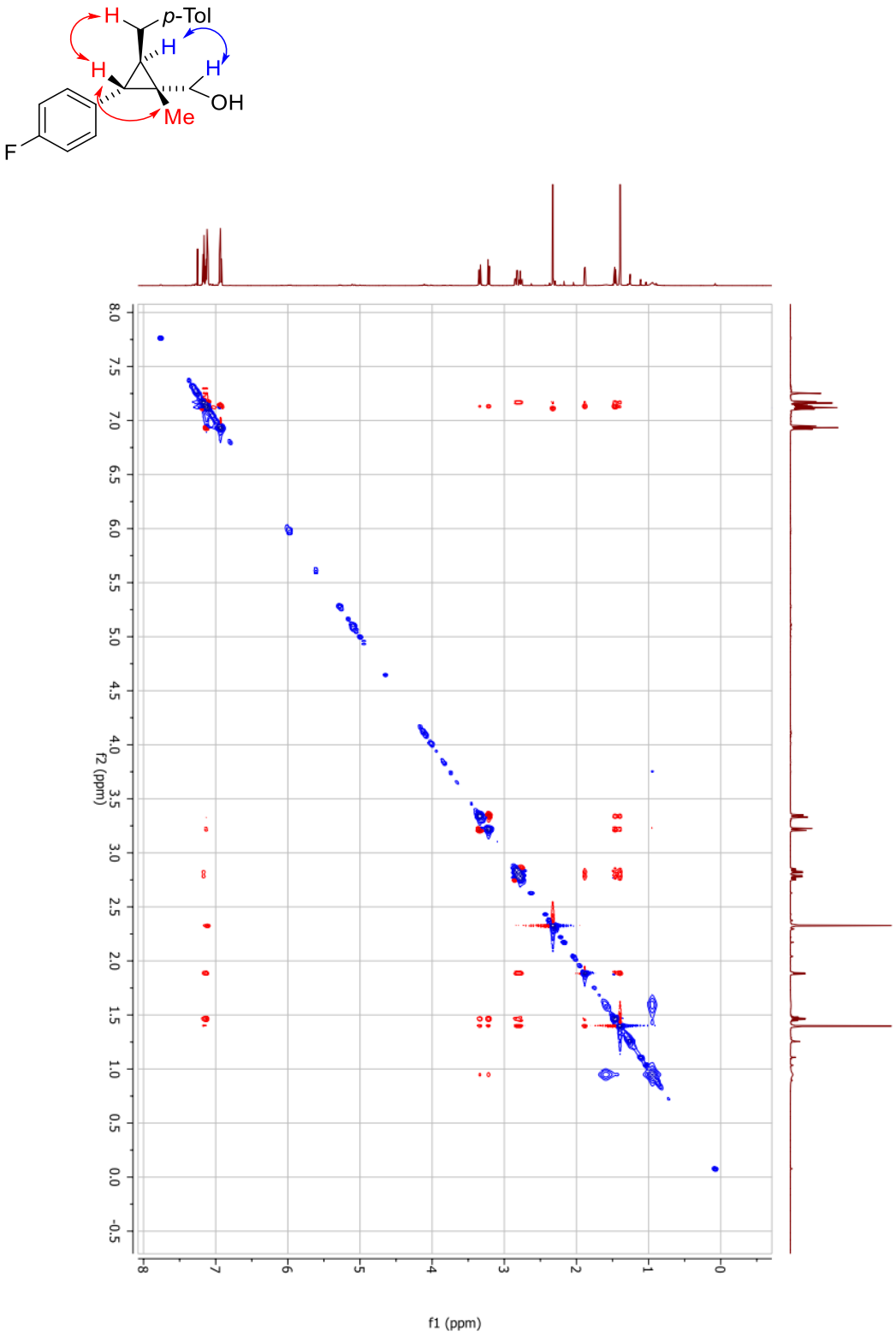
FTIR (neat): 3360, 2921, 1604, 1510, 1456, 1222, 1157, 1103, 1069, 1015, 838, 769 cm^{-1}

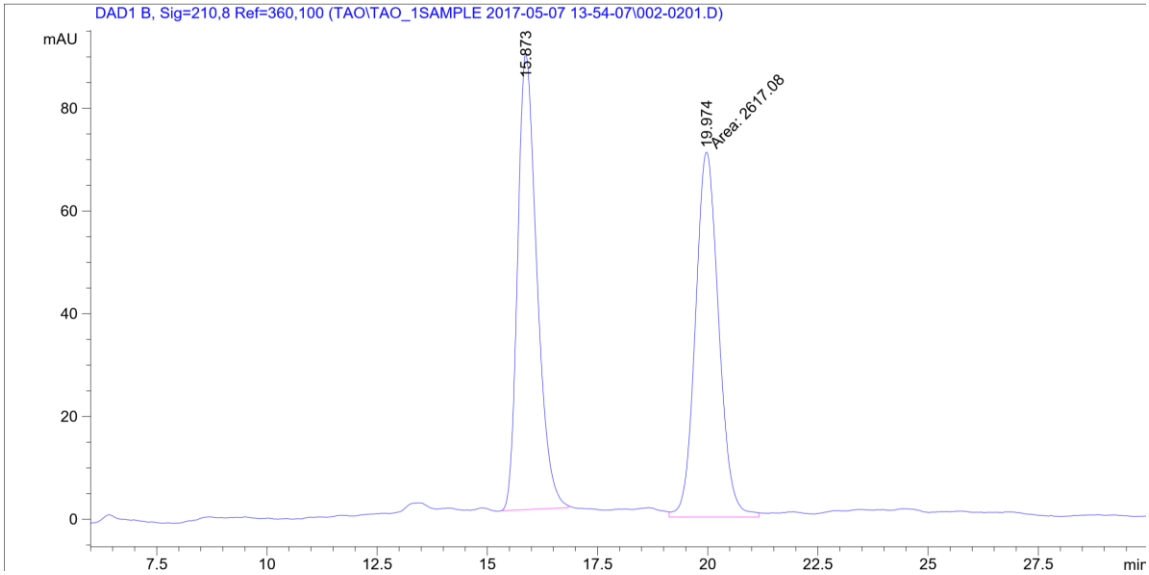
HPLC (chiralcel OJ-H columns, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm), ee = 93%


7.19
7.17
7.16
7.16
7.15
7.14
7.14
7.13
7.13
7.11
6.97
6.96
6.95
6.94
6.94
6.93
6.92
3.37
3.34
3.24
3.21
2.84
2.82
2.80
2.34
1.90
1.89
1.50
1.48
1.46
1.45
1.41
p-Tol
OH
Me
F
6.11
2.03
1.06
1.00
2.04
2.94
0.99
1.08
3.01
f1 (ppm)

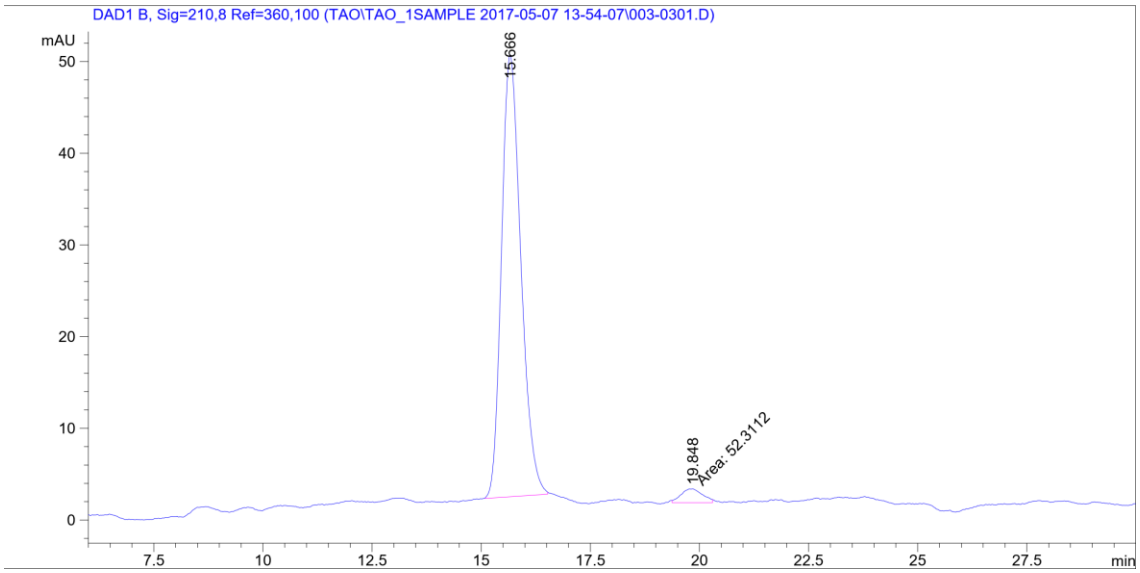

162.6
160.1
138.5
135.5
134.5
134.5
130.0
129.9
129.2
128.0
115.2
115.0
68.1
34.7
34.1
29.5
27.9
21.0
17.1
p-Tol
OH
Me
F
f1 (ppm)


−116.86
−116.87
−116.88
−116.89
−116.91
−116.92
−116.93
30 20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200
f1 (ppm)


H
p-Tol
H
H
H
OH
Me
F
f2 (ppm)
f1 (ppm)

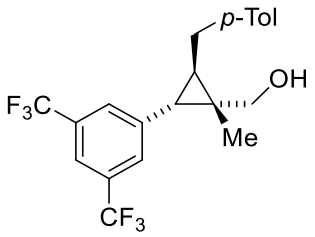


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.873	BB	0.4597	2689.99170	88.72736	50.6870
2	19.974	MM	0.6138	2617.07690	71.06053	49.3130



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.666	BB	0.4719	1486.19409	48.18341	96.5999
2	19.848	MM	0.5743	52.31120	1.51814	3.4001

((1*S*,2*R*,3*S*)-1-methyl-2-(4-methylbenzyl)-3-(*p*-tolyl)cyclopropyl)methanol (3.3c)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1a** (35.4 mg, 0.1 mmol, 100 mol%), tri(p-tolyl)boroxine (30.1 mg, 0.085 mmol, 85 mol%) **3.2a**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 55 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1) to furnish the title compound as a colorless oil (22.7 mg, 0.07 mmol) in 73% yield.

TLC (SiO_2) R_f = 0.41 (hexanes/ethyl acetate = 5:1).

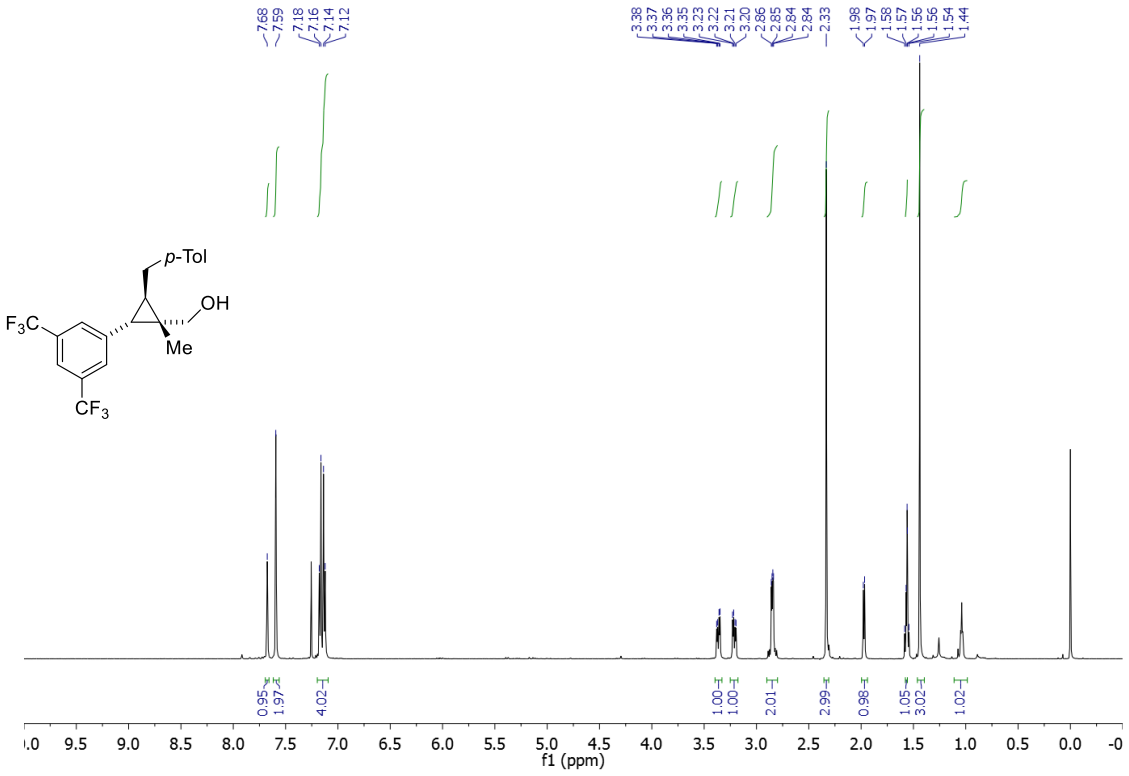
^{1}H NMR (500 MHz, CDCl3) δ 7.68 (s, 1H), 7.59 (s, 2H), 7.23 – 7.04 (m, 4H), 3.36 (dd, *J* = 11.3, 4.9 Hz, 1H), 3.21 (dd, *J* = 11.3, 5.0 Hz, 1H), 2.84-2.86 (m, *J* = 7.2, 3.5 Hz, 2H), 2.33 (s, 3H), 1.97 (d, *J* = 6.0 Hz, 1H), 1.64 – 1.48 (m, 1H), 1.44 (s, 3H), 1.04 (t, *J* = 5.4 Hz, 1H).

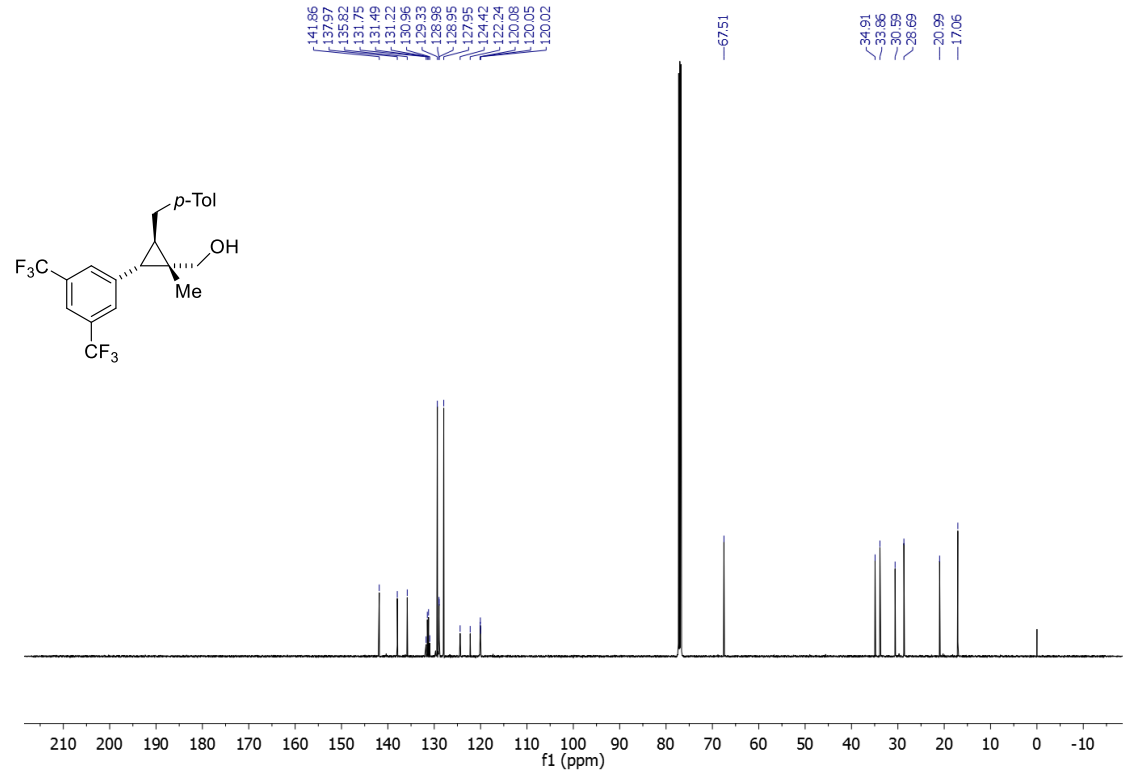
^{13}C NMR (125 MHz, CDCl3) δ 141.8, 137.9, 135.8, 131.3 (q, *J* = 33.1 Hz), 129.3, 128.9 (d, *J* = 3.7 Hz), 127.9, 124.4, 122.2, 120.8 – 119.6 (m), 67.5, 34.9, 33.8, 30.5, 28.69, 20.9, 17.0.

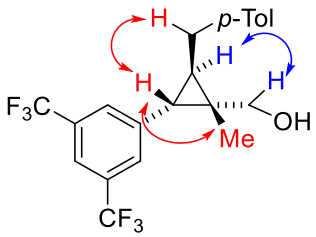
HRMS (ESI) Calcd. for $C_{21}H_{20}F_6NaO^+$ $[M+Na]^+$: 425.1311, Found: 425.1315.

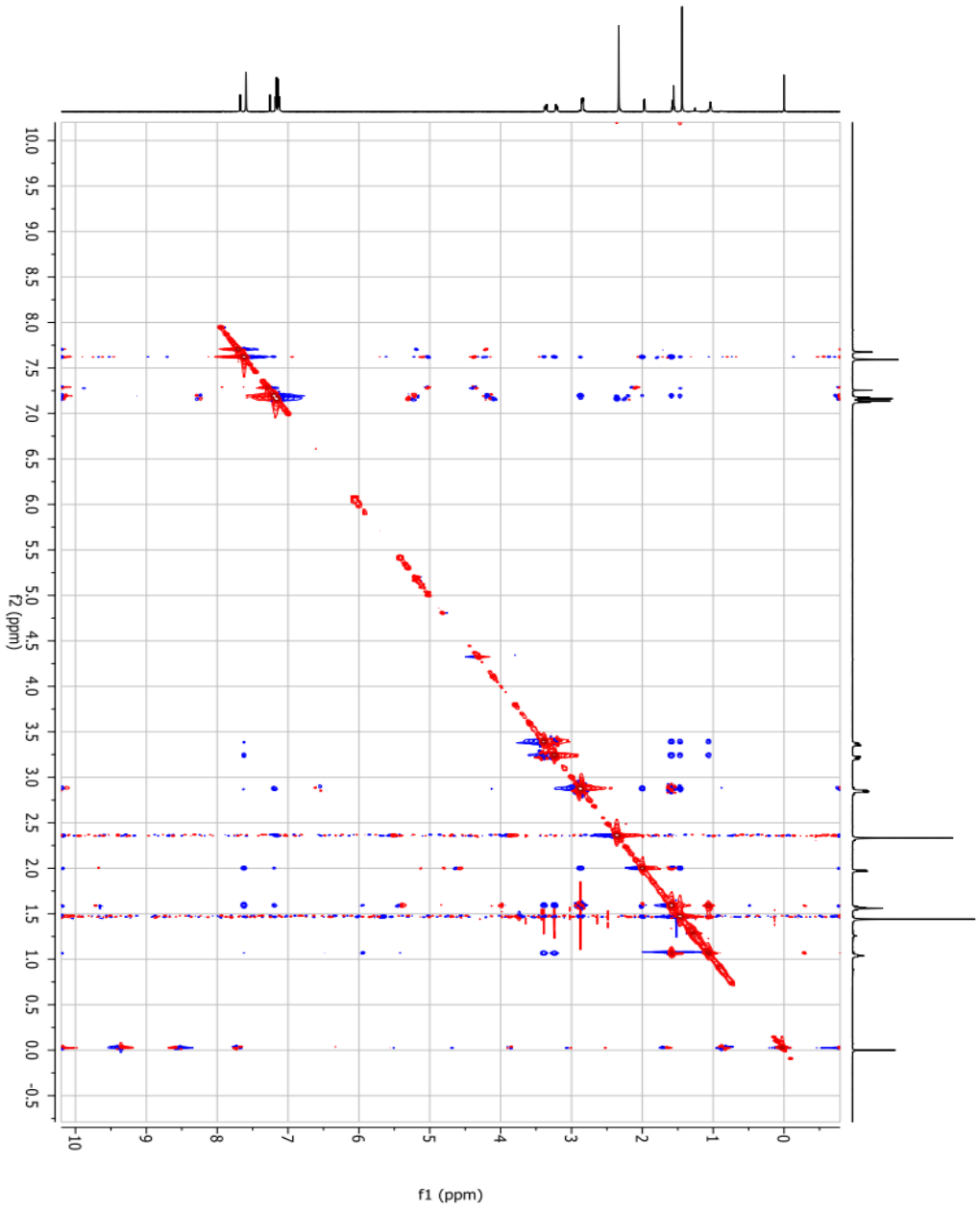
$[\alpha]_D^{32}$: +23.0 (*c* = 1.0, $CHCl_3$).

FTIR (neat): 3360, 2923, 1515, 1374, 1275, 1169, 1127, 1021, 894, 682 cm^{-1}.

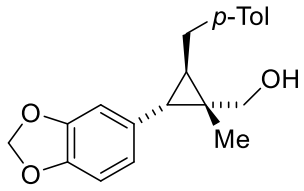

7.68
7.59
7.18
7.16
7.14
7.12
3.38
3.37
3.36
3.35
3.23
3.22
3.21
3.20
2.86
2.85
2.84
2.84
2.33
1.98
1.97
1.58
1.57
1.56
1.56
1.54
1.44
p-Tol
OH
Me
F3C
CF3
0.95
1.97
4.02
1.00
1.00
2.01
2.99
0.98
1.05
3.02
1.02
f1 (ppm)


141.86
137.97
135.82
131.75
131.49
131.22
130.96
129.33
128.98
128.95
127.95
124.42
122.24
120.08
120.05
120.02
67.51
34.91
33.86
30.59
28.69
20.99
17.06
p-Tol
OH
Me
F3C
CF3
f1 (ppm)


H
p-Tol
H
H
H
F3C
OH
Me
CF3


f2 (ppm)
f1 (ppm)

((1*S*,2*S*,3*R*)-2-(benzo[*d*][1,3]dioxol-5-yl)-1-methyl-3-(4-methylbenzyl)cyclopropyl)methanol (3.3d)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1a** (26.2 mg, 0.1 mmol, 100 mol%), tri(*p*-tolyl)boroxine (30.1 mg, 0.085 mmol, 85 mol%) **3.2a**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 55 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1) to furnish the title compound as a white solid (21.6 mg, 0.07 mmol) in 70% yield.

TLC (SiO_2) R_f = 0.25 (hexanes/ethyl acetate = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.07 (m, 4H), 6.74 – 6.62 (m, 3H), 5.92 (s, 2H), 3.38 (dd, *J* = 11.5, 4.4 Hz, 1H), 3.25 (d, *J* = 11.5 Hz, 1H), 2.88 – 2.70 (m, 2H), 2.33 (s, 3H), 1.86 (d, *J* = 5.9 Hz, 1H), 1.46 – 1.40 (m, 1H), 1.39 (s, 3H), 0.98 (brs, 1H).

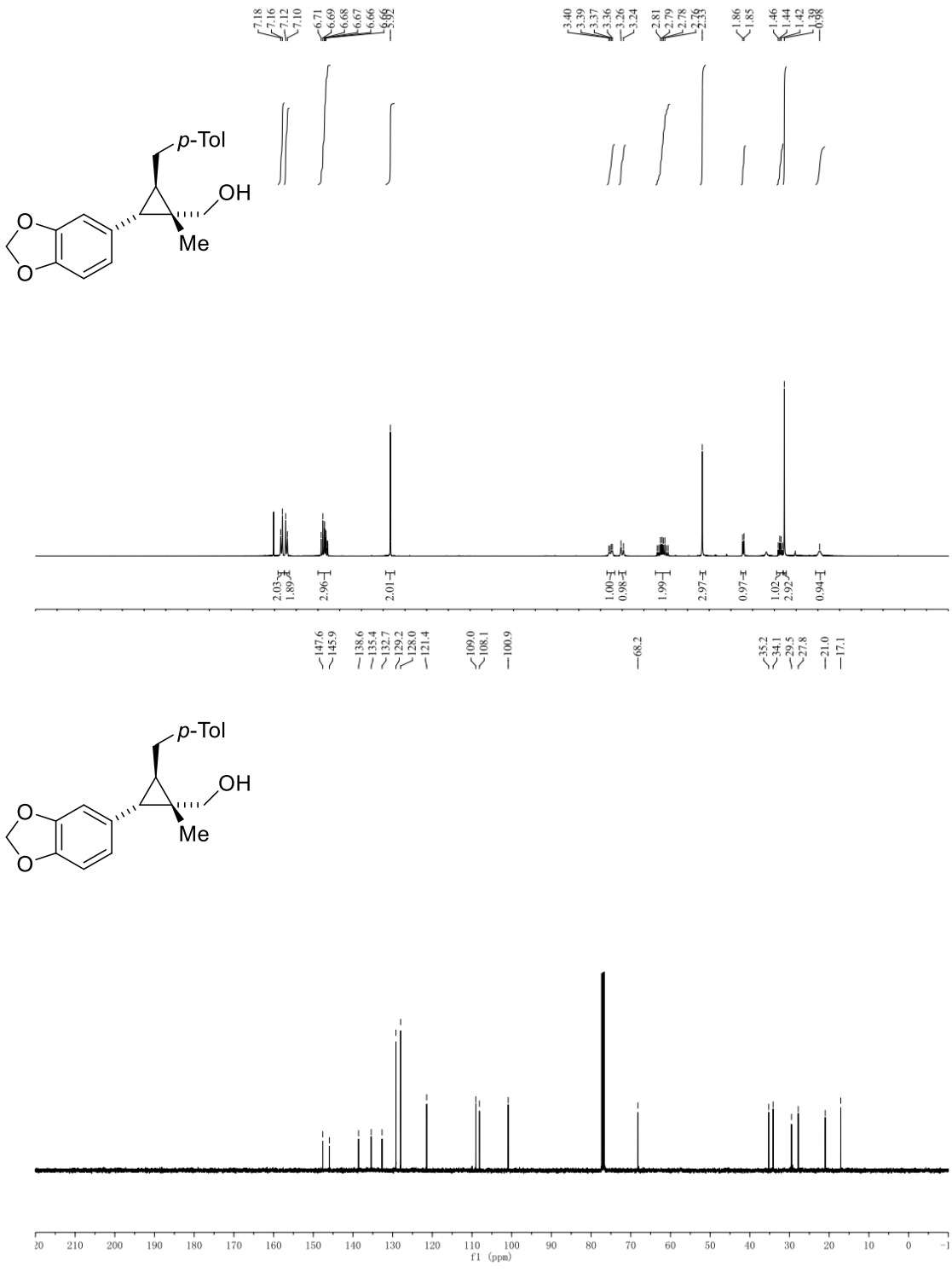
^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 145.9, 138.6, 135.4, 132.7, 129.2, 128.0, 121.4, 109.0, 108.1, 100.9, 68.2, 35.2, 34.1, 29.5, 27.8, 21.0, 17.1.

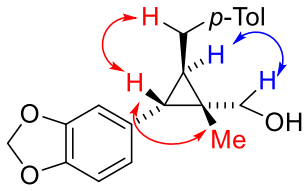
HRMS (CI) Calcd. for $C_{20}H_{22}O_3^+$ $[M]^+$: 310.1563, Found: 310.1567.

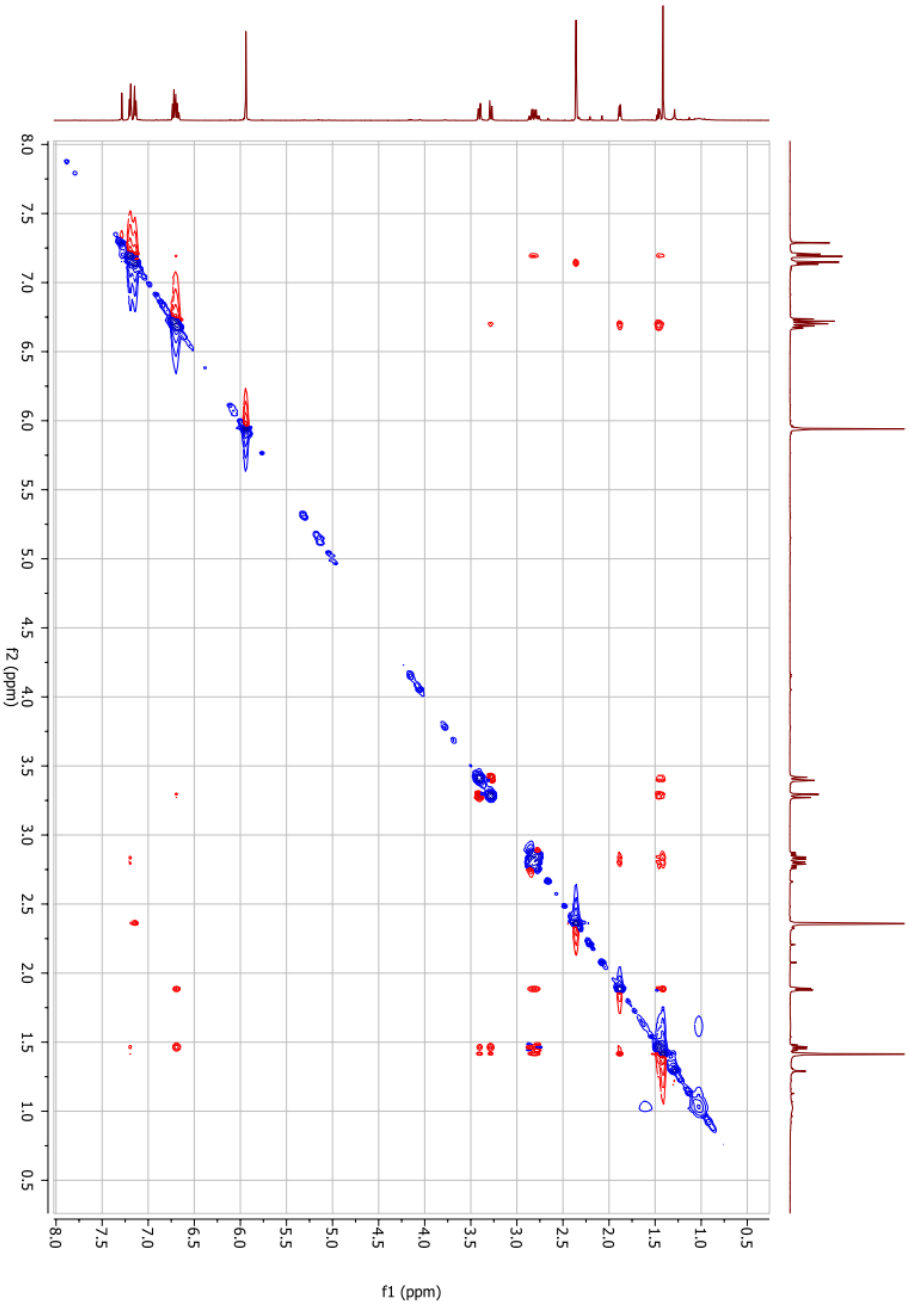
$[\alpha]_D^{33}$: +25.7 (*c* = 1.0, $CHCl_3$).

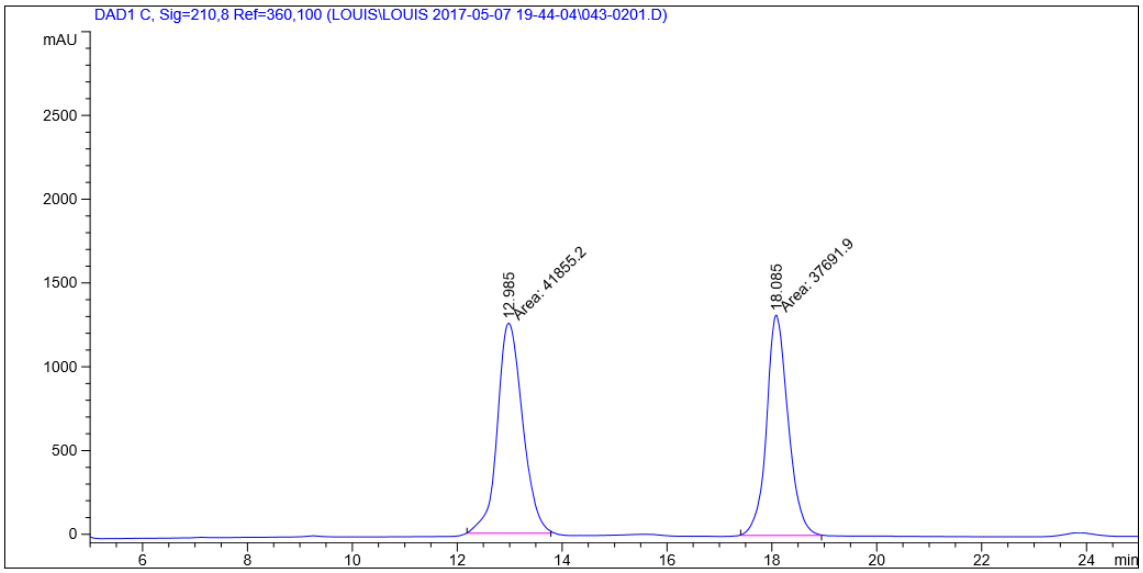
FTIR (neat): 3430, 2919, 1608 1503, 1490, 1441, 1234, 1189, 1039, 935, 808 cm^{-1}

HPLC (chiralcel AS-H columns, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 210 nm), ee = 91%

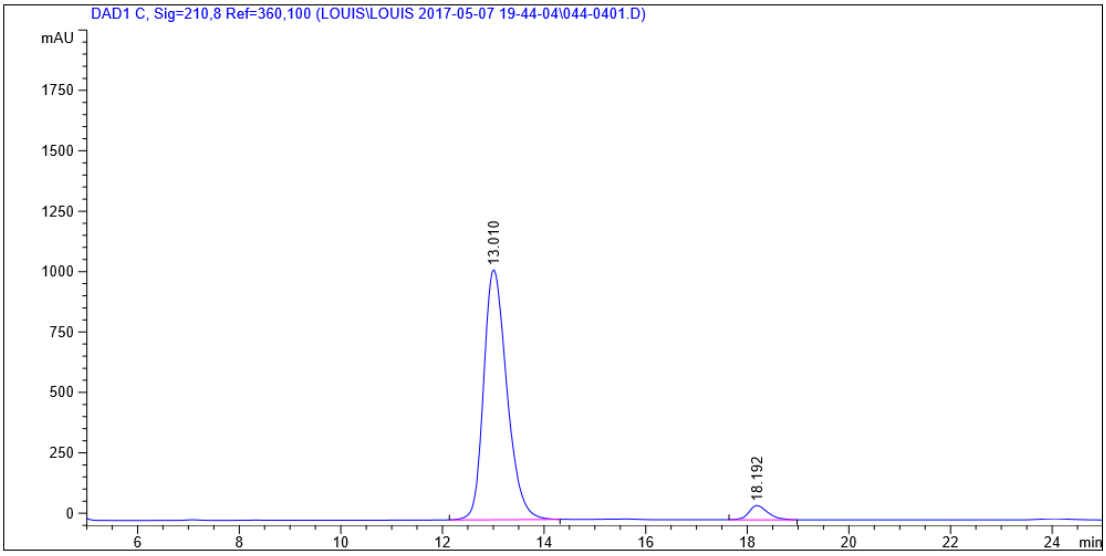

p-Tol
OH
Me
O
O
7.18
7.16
7.12
7.10
6.71
6.69
6.68
6.67
6.66
3.40
3.39
3.37
3.36
3.26
3.24
2.81
2.79
2.78
1.86
1.85
1.46
1.44
1.42
2.03
1.89
2.96
2.01
1.00
0.98
1.99
2.97
0.97
1.02
2.92
0.94
147.6
145.9
138.6
135.4
132.7
129.2
128.0
121.4
109.0
108.1
100.9
68.2
35.2
34.1
29.5
27.8
21.0
17.1
f1 (ppm)


H
p-Tol
H
H
H
OH
Me
O
O


f2 (ppm)
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

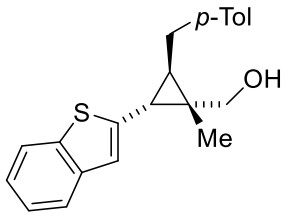


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.985	MM	0.5564	4.18552e4	1253.68042	52.6169
2	18.085	MM	0.4777	3.76919e4	1314.98645	47.3831



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.010	BB	0.4885	3.28360e4	1033.99109	95.5466
2	18.192	BB	0.3950	1530.47754	59.32614	4.4534

((1*S*,2*R*,3*S*)-1-methyl-2-(4-methylbenzyl)-3-(*p*-tolyl)cyclopropyl)methanol (3.3e)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1a** (27.4 mg, 0.1 mmol, 100 mol%), tri(p-tolyl)boroxine (30.1 mg, 0.085 mmol, 85 mol%) **3.2a**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 45 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1) to furnish the title compound as a colorless oil (15.7 mg, 0.068 mmol) in 68% yield.

TLC (SiO_2) R_f = 0.26 (hexanes/ethyl acetate = 5:1).

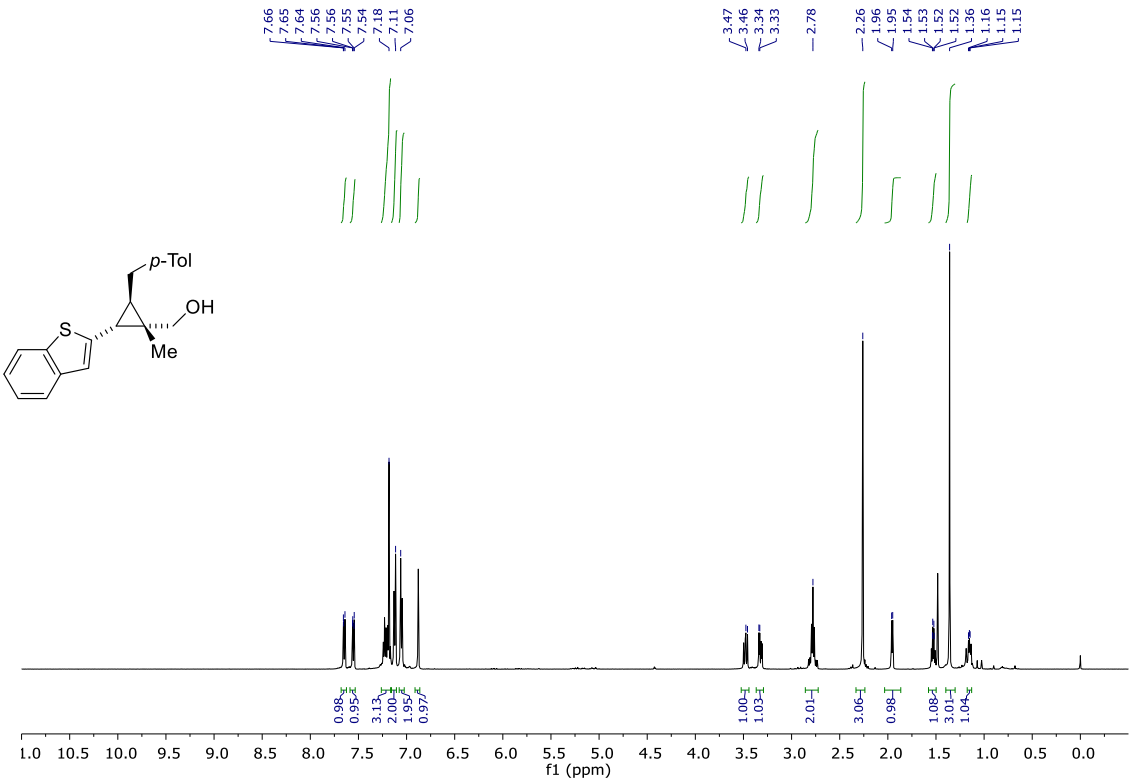
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.69 (m, 1H), 7.66 – 7.60 (m, 1H), 7.36 – 7.27 (m, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.96 (t, *J* = 1.0 Hz, 1H), 3.56 (d, *J* = 11.8 Hz, 1H), 3.40 (d, *J* = 11.8 Hz, 1H), 2.91 – 2.80 (m, 2H), 2.34 (s, 3H), 2.03 (d, *J* = 5.7 Hz, 1H), 1.61 (td, *J* = 7.1, 5.7 Hz, 1H), 1.44 (s, 3H).

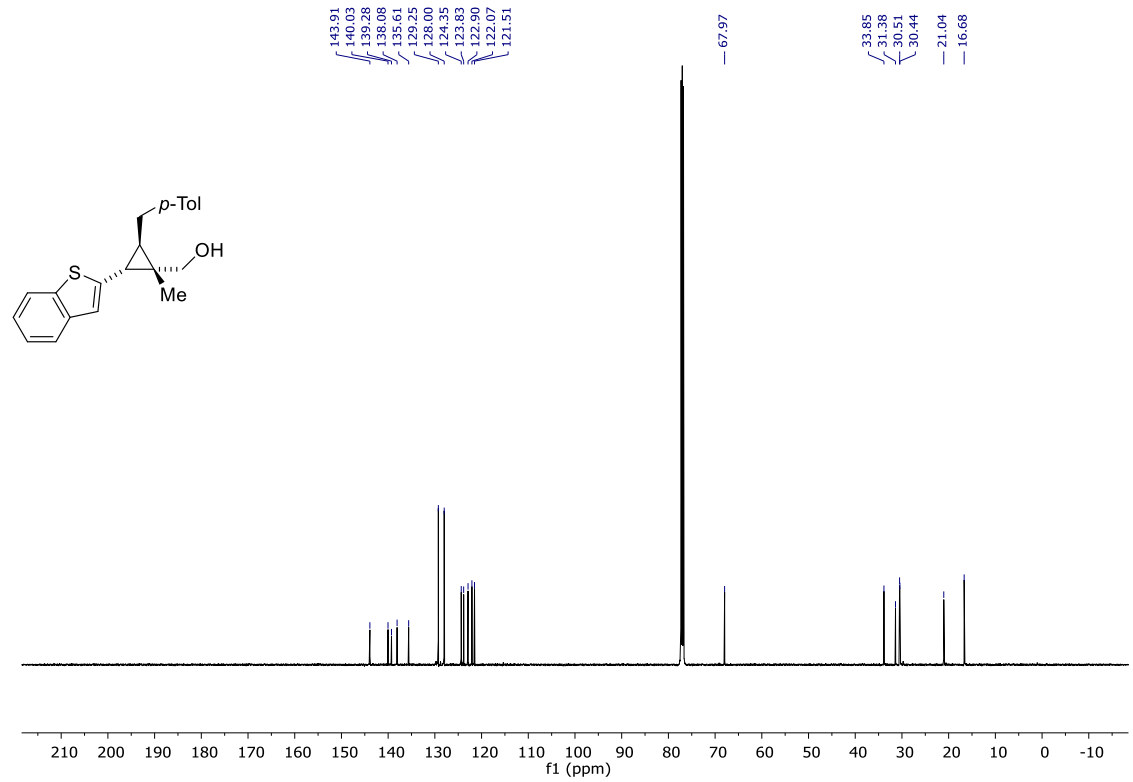
^{13}C NMR (125 MHz, $CDCl_3$) δ 143.9, 140.0, 139.2, 138.0, 135.6, 129.2, 128.0, 124.3, 123.8, 122.9, 122.0, 121.5, 67.9, 33.8, 31.3, 30.4 (d, *J* = 7.9 Hz), 21.0, 16.6.

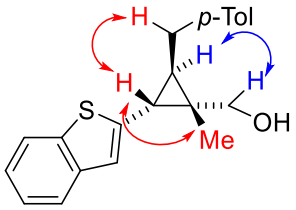
HRMS (ESI) Calcd. for $C_{21}H_{22}NaOS^+$ $[M+Na]^+$: 345.1284, Found: 345.1295.

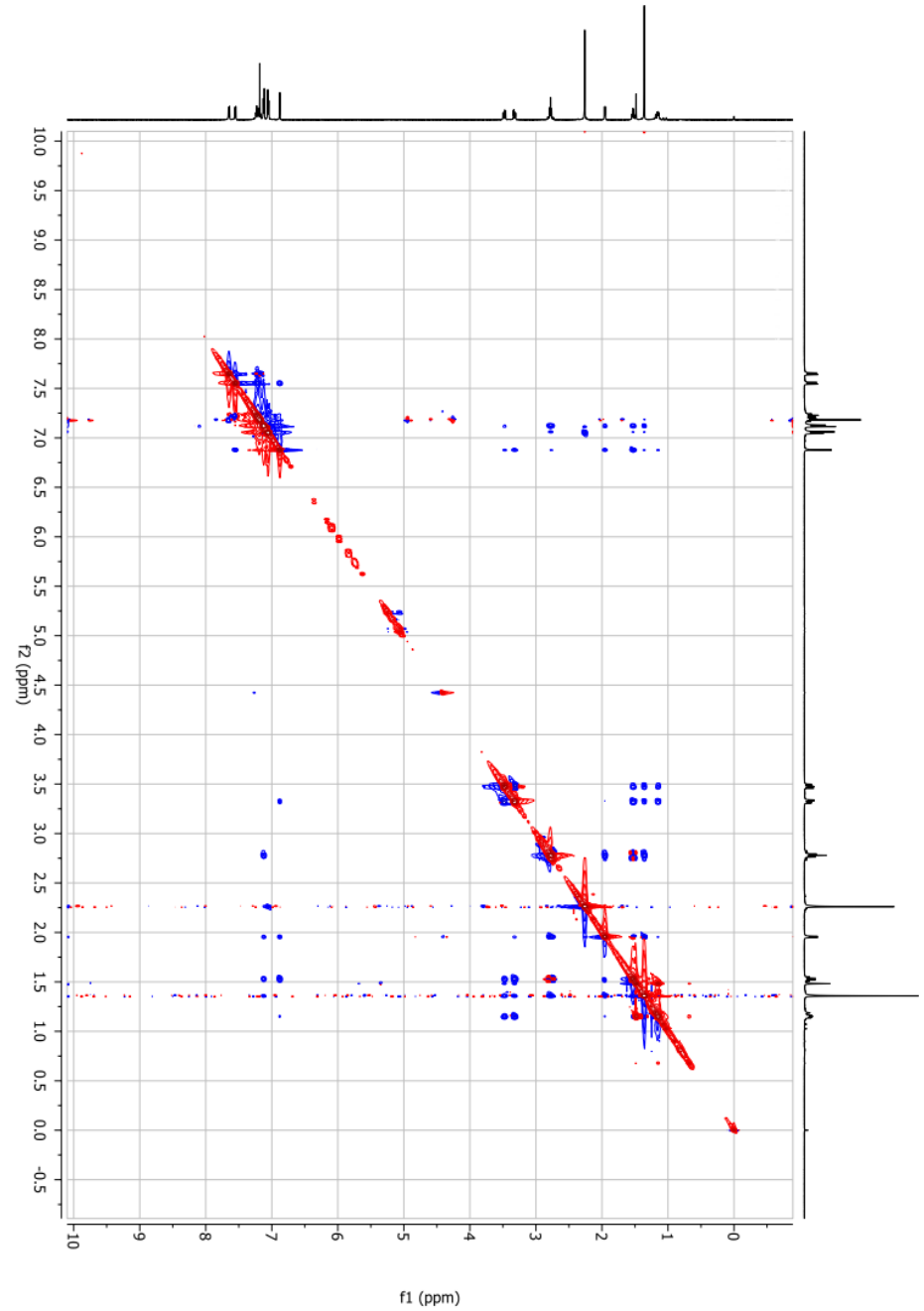
$[\alpha]_D^{33}$: +17.0 (*c* = 1.0, $CHCl_3$).

FTIR (neat): 2285, 2922, 2359, 2340, 1514, 1457, 1436, 1068, 1020, 805, 746, 668 cm^{-1}

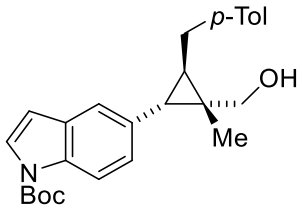

7.66
7.65
7.64
7.56
7.56
7.55
7.54
7.18
7.11
7.06
3.47
3.46
3.34
3.33
2.78
2.26
1.96
1.95
1.54
1.53
1.52
1.52
1.36
1.16
1.15
1.15
p-Tol
OH
S
Me
0.98
0.95
3.13
2.00
1.95
0.97
1.00
1.03
2.01
3.06
0.98
1.08
3.01
1.04
f1 (ppm)


143.91
140.03
139.28
138.08
135.61
129.25
128.00
124.35
123.83
122.90
122.07
121.51
67.97
33.85
31.38
30.51
30.44
21.04
16.68
p-Tol
OH
S
Me
f1 (ppm)


H
p-Tol
H
H
H
S
OH
Me


f2 (ppm)
f1 (ppm)

***tert*-butyl 5-((1*S*,2*S*,3*R*)-2-(hydroxymethyl)-2-methyl-3-(4-methylbenzyl)cyclopropyl)-1H-indole-1-carboxylate (3.3f)**



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1e** (35.7 mg, 0.1 mmol, 100 mol%), tri(p-tolyl)boroxizne (30.1 mg, 0.085 mmol, 85 mol%) **3.2a**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 70 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 12:1) to furnish the title compound as a colorless oil (28.4 mg, 0.07 mmol) in 70% yield.

TLC (SiO_2) R_f = 0.43 (hexanes/ethyl acetate = 4:1).

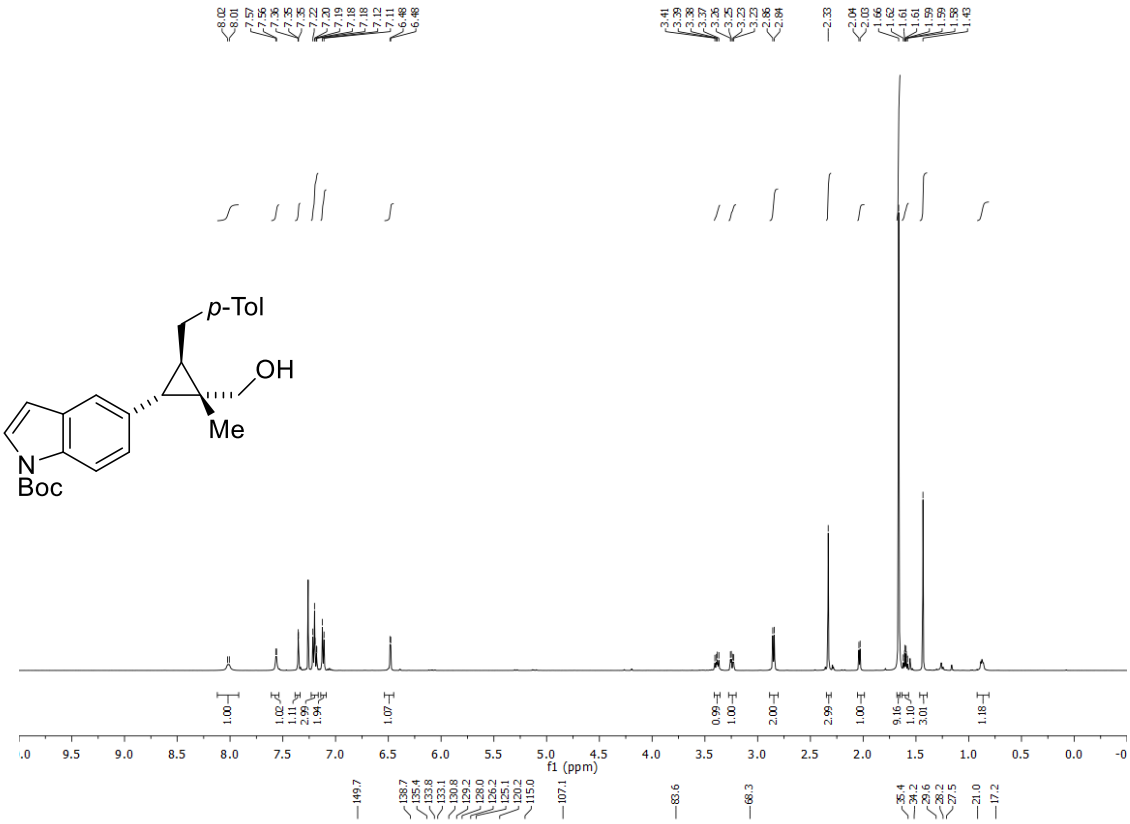
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.5 Hz, 1H), 7.56 (d, *J* = 3.7 Hz, 1H), 7.38 – 7.34 (m, 1H), 7.23 – 7.16 (m, 3H), 7.12 (d, *J* = 7.7 Hz, 2H), 6.48 (d, *J* = 3.7 Hz, 1H), 3.39 (dd, *J* = 11.6, 7.5 Hz, 1H), 3.24 (dd, *J* = 11.6, 4.2 Hz, 1H), 2.85 (d, *J* = 7.0 Hz, 2H), 2.33 (s, 3H), 2.03 (d, *J* = 5.8 Hz, 1H),tbs 1.66 (s, 9H), 1.60 (td, *J* = 7.1, 5.8 Hz, 1H), 1.43 (s, 3H), 0.87 (dd, *J* = 7.8, 5.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 149.7, 138.8, 135.4, 133.8, 133.1, 130.8, 129.2, 128.0, 126.2, 125.1, 120.2, 115.0, 107.1, 83.6, 68.3, 35.5, 34.2, 29.6, 28.2, 27.5, 21.0, 17.2.

HRMS (ESI) Calcd. for $C_{26}H_{31}NO_3^+$ $[M+Na]^+$: 428.2196, Found: 428.2200.

$[\alpha]_D^{25}$: +33.2 (*c* = 1.0, $CHCl_3$).

FTIR (neat): 3394, 2976, 1731, 1473, 1369, 1251, 1163, 1132, 1022, 746 cm^{-1}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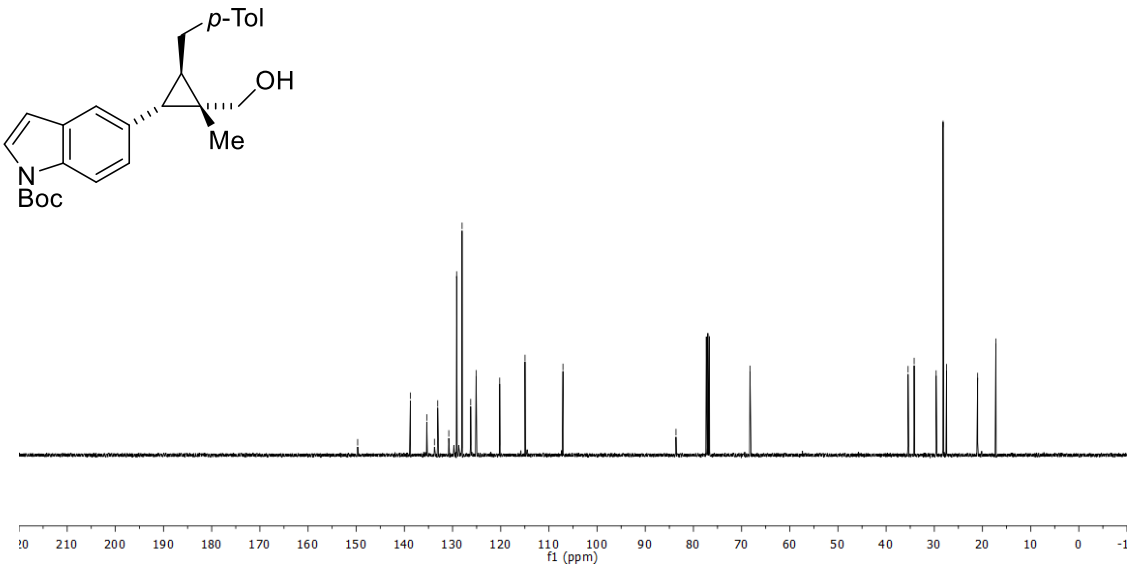
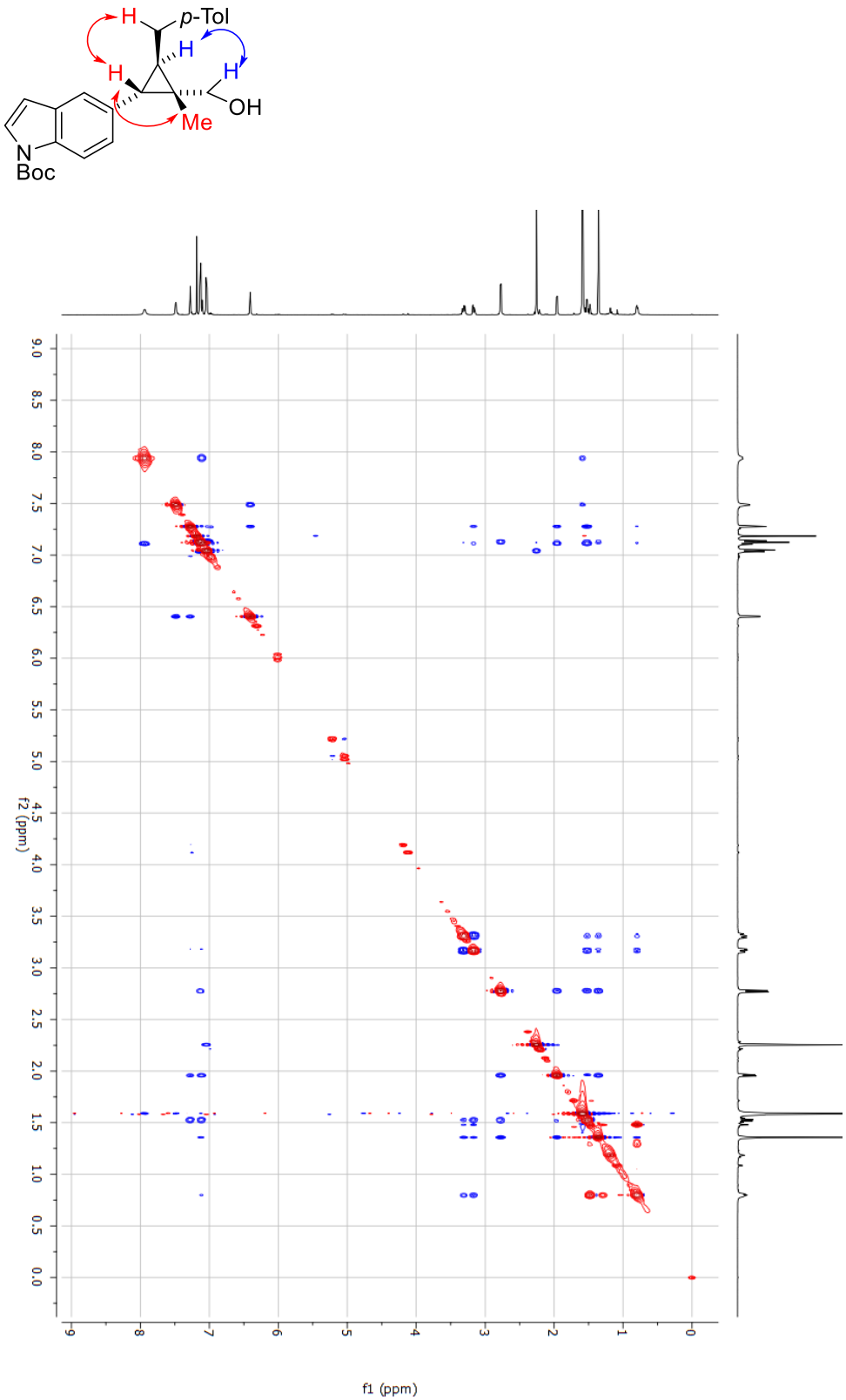
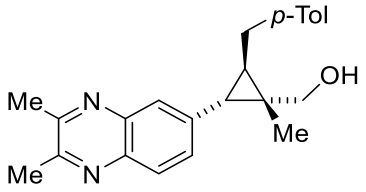
OH
Me
N
Boc
f1 (ppm)


p-Tol
OH
Me
N
Boc
f1 (ppm)


H
p-Tol
H
H
H
OH
Me
N
Boc
f2 (ppm)
f1 (ppm)

((1*S*,2*S*,3*R*)-2-(2,3-dimethylquinoxalin-6-yl)-1-methyl-3-(4-methylbenzyl)cyclopropyl)methanol (3.3g)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1g** (29.8 mg, 0.1 mmol, 100 mol%), tri(*p*-tolyl)boroxine (30.1 mg, 0.085 mmol, 85 mol%) **3.2a**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 55 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 1:1) to furnish the title compound as a yellow solid (21.4 mg, 0.06 mmol) in 62% yield.

TLC (SiO_2) R_f = 0.29 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.6 Hz, 1H), 7.69 (s, 1H), 7.56 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.20 – 7.07 (m, 4H), 3.40 (d, *J* = 11.3 Hz, 1H), 3.29 (d, *J* = 11.5 Hz, 1H),

2.92 – 2.81 (m, 2H), 2.69 (s, 3H), 2.69 (s, 3H), 2.32 (s, 3H), 2.09 (d, *J* = 5.9 Hz, 1H), 1.75 – 1.71 (m, 1H), 1.47 (s, 3H), 1.13 (brs, 1H).

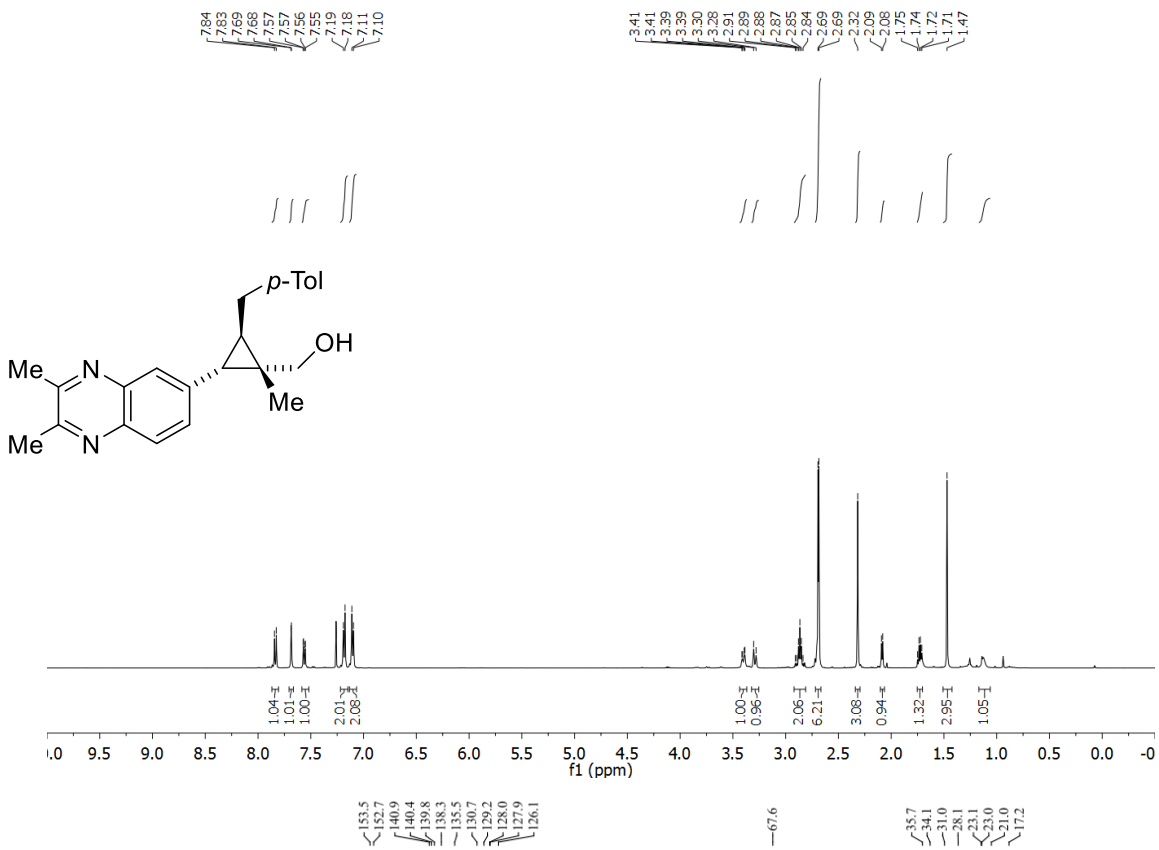
^{13}C NMR (125 MHz, $CDCl_3$) δ 153.5, 152.8, 140.9, 140.4, 139.8, 138.3, 135.5, 130.7, 129.2, 128.0, 127.9, 126.1, 67.6, 35.7, 34.1, 31.0, 28.1, 23.1, 23.0, 21.0, 17.2.

HRMS (ESI) Calcd. for $C_{23}H_{27}N_2O^+$ $[M+H]^+$: 347.2118, Found: 347.2120.

$[\alpha]_D^{33}$: +25.0 (*c* = 1.0, $CHCl_3$).

m.p. : 152-153 ˚C

FTIR (neat): 3350, 2920, 2866, 2360, 2343, 1619, 1556, 1514, 1498, 1449, 1379, 1334, 1185, 1157, 1041, 1022, 837, 806, 669 cm^{-1}


7.84
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7.69
7.68
7.57
7.57
7.56
7.55
7.19
7.18
7.11
7.10
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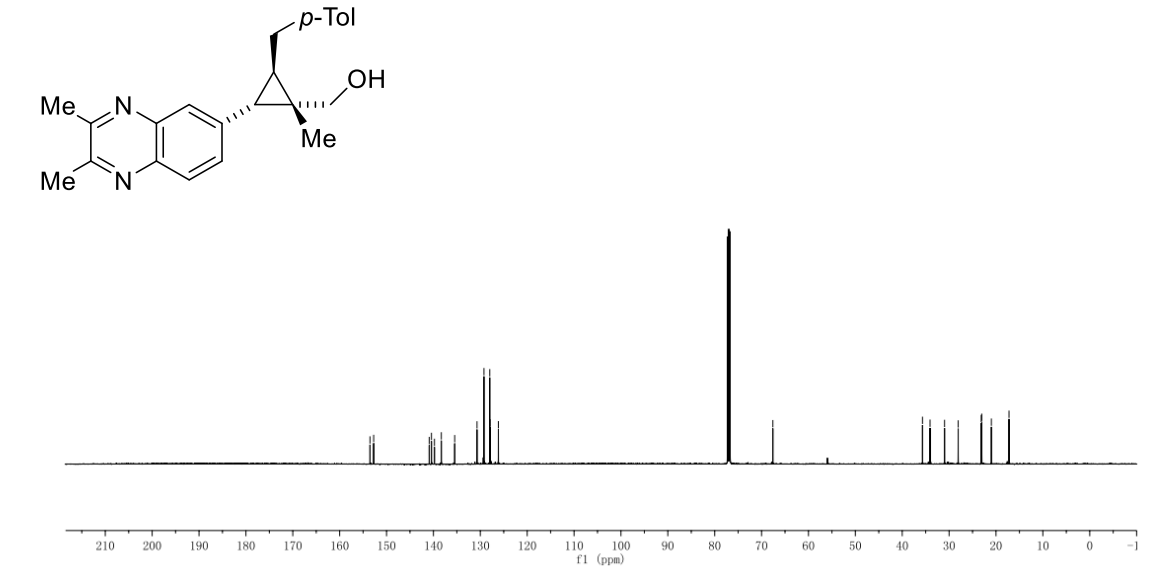
3.41
3.39
3.39
3.30
3.28
2.91
2.89
2.88
2.87
2.85
2.84
2.69
2.69
2.32
2.09
2.08
1.75
1.74
1.72
1.71
1.47
p-Tol
OH
Me
N
Me
N
Me
1.04
1.01
1.00
2.01
2.08
1.00
0.96
2.06
6.21
3.08
0.94
1.32
2.95
1.05
f1 (ppm)


153.5
152.7
140.9
140.4
139.8
138.3
135.5
130.7
129.2
128.0
127.9
126.1
67.6
35.7
34.1
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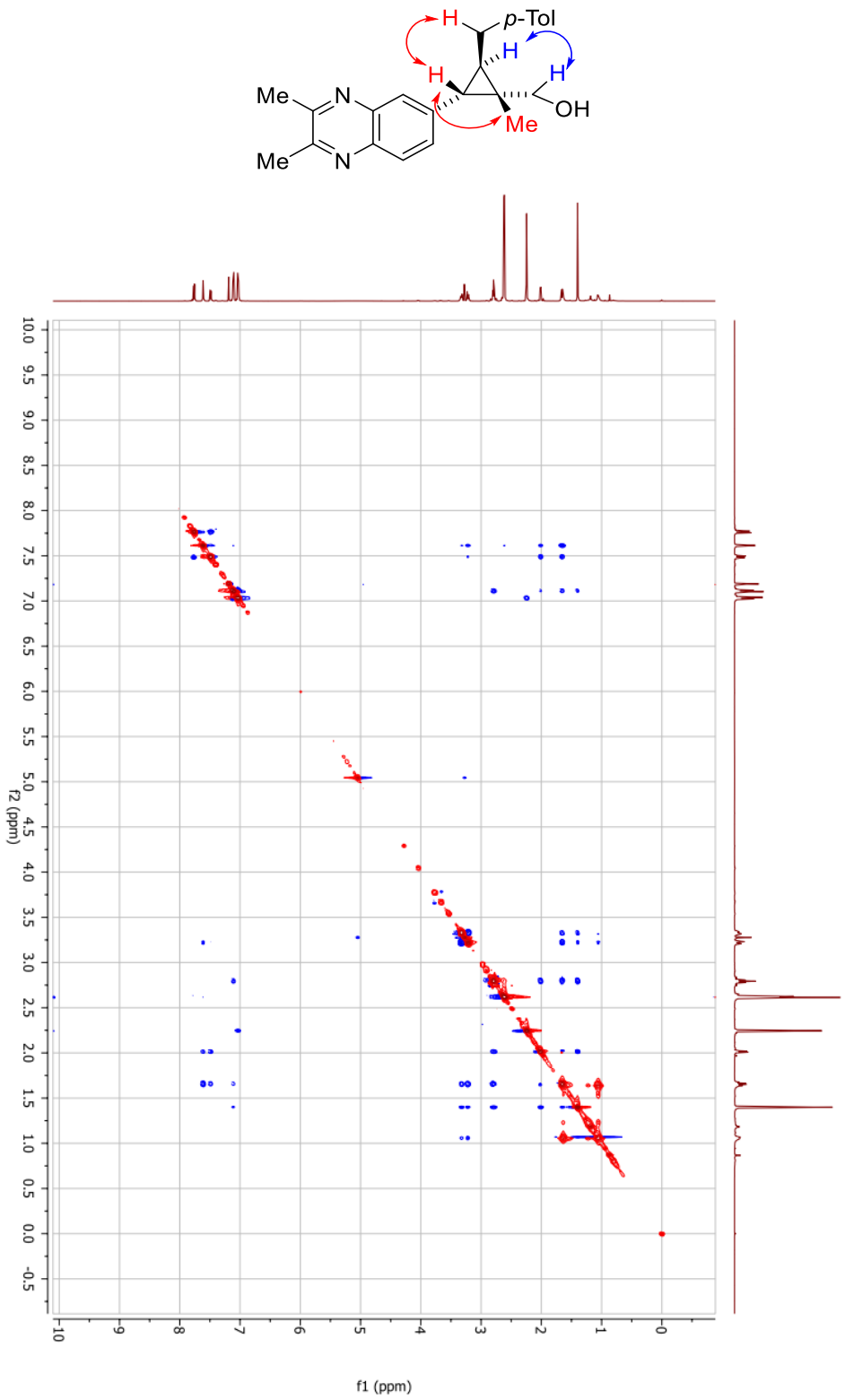
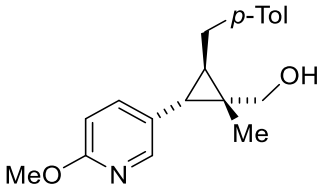
OH
Me
N
Me
N
Me
f1 (ppm)


H
p-Tol
H
H
H
Me
N
Me
N
Me
OH
f2 (ppm)
f1 (ppm)

((*1S,2S,3R*)-2-(6-methoxypyridin-3-yl)-1-methyl-3-(4-methylbenzyl)cyclopropyl)methanol (3.3h)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1h** (24.9 mg, 0.1 mmol, 100 mol%), tri(p-tolyl)boroxine (30.1 mg, 0.085 mmol, 85 mol%) **3.2a**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 45 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated in *vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 4:1) to furnish the title compound as oil (27.2 mg, 0.92 mmol) in 92% yield.

TLC (SiO_2) R_f = 0.10 (hexanes/ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 2.5 Hz, 1H), 7.38 (ddd, *J* = 8.5, 2.5, 0.7 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.63 (dd, *J* = 8.5, 0.7 Hz, 1H), 3.89 (s, 3H), 3.35 (dd, *J* = 11.6, 4.7 Hz, 1H), 3.22 (dd, *J* = 11.5, 3.8 Hz, 1H), 2.87 (dd, *J* = 15.0, 6.6 Hz, 1H), 2.73 (dd, *J* = 15.0, 7.6 Hz, 1H), 2.33 (s, 3H), 1.79 (d, *J* = 5.9 Hz, 1H), 1.46 – 1.41 (m, 1H), 1.40 (s, 3H), 1.13 (t, *J* = 5.4 Hz, 1H).

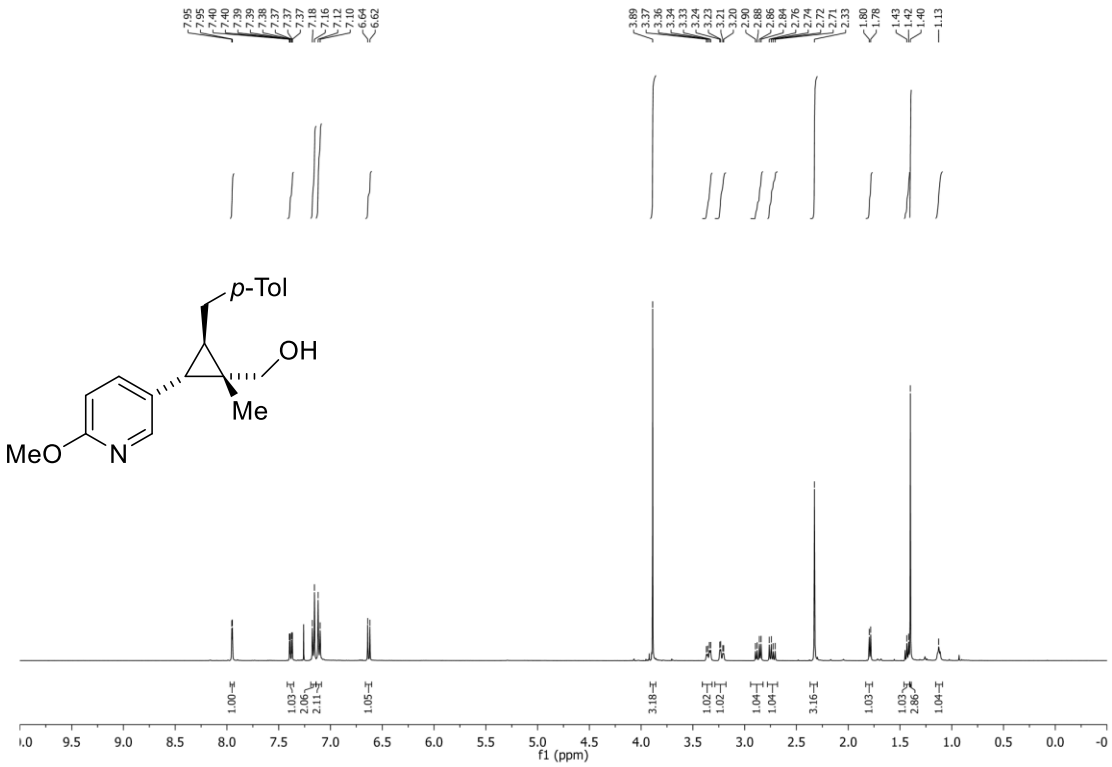
^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 146.6, 139.4, 138.4, 135.5, 129.2, 128.0, 127.1, 110.2, 68.0, 53.3, 34.2, 32.0, 29.0, 27.8, 21.0, 17.0.

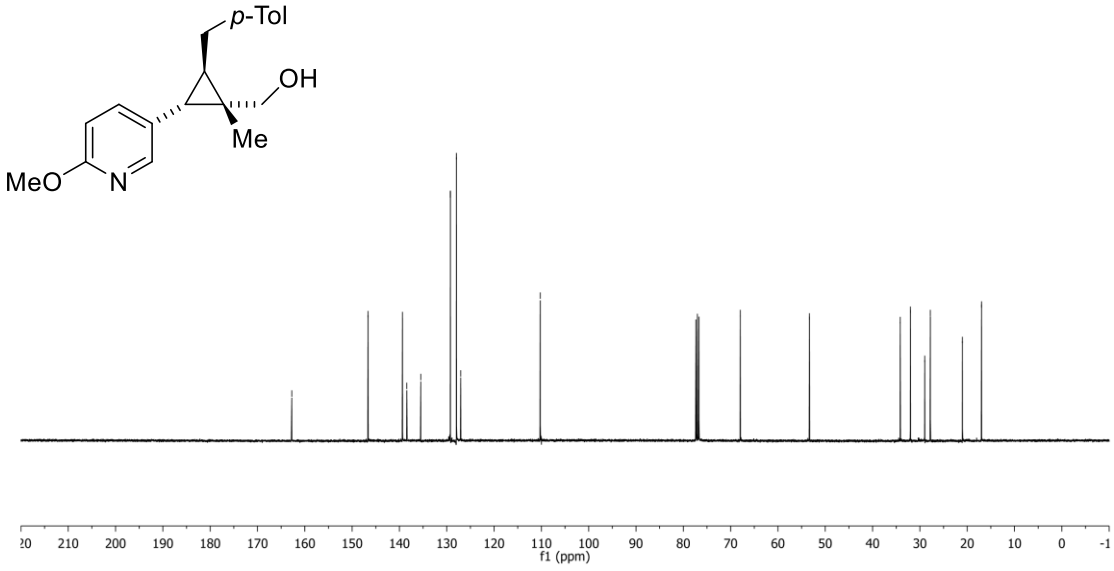
HRMS (ESI) Calcd. for $C_{19}H_{23}NNaO_2^+$ $[M+Na]^+$: 320.1621, Found: 320.1625

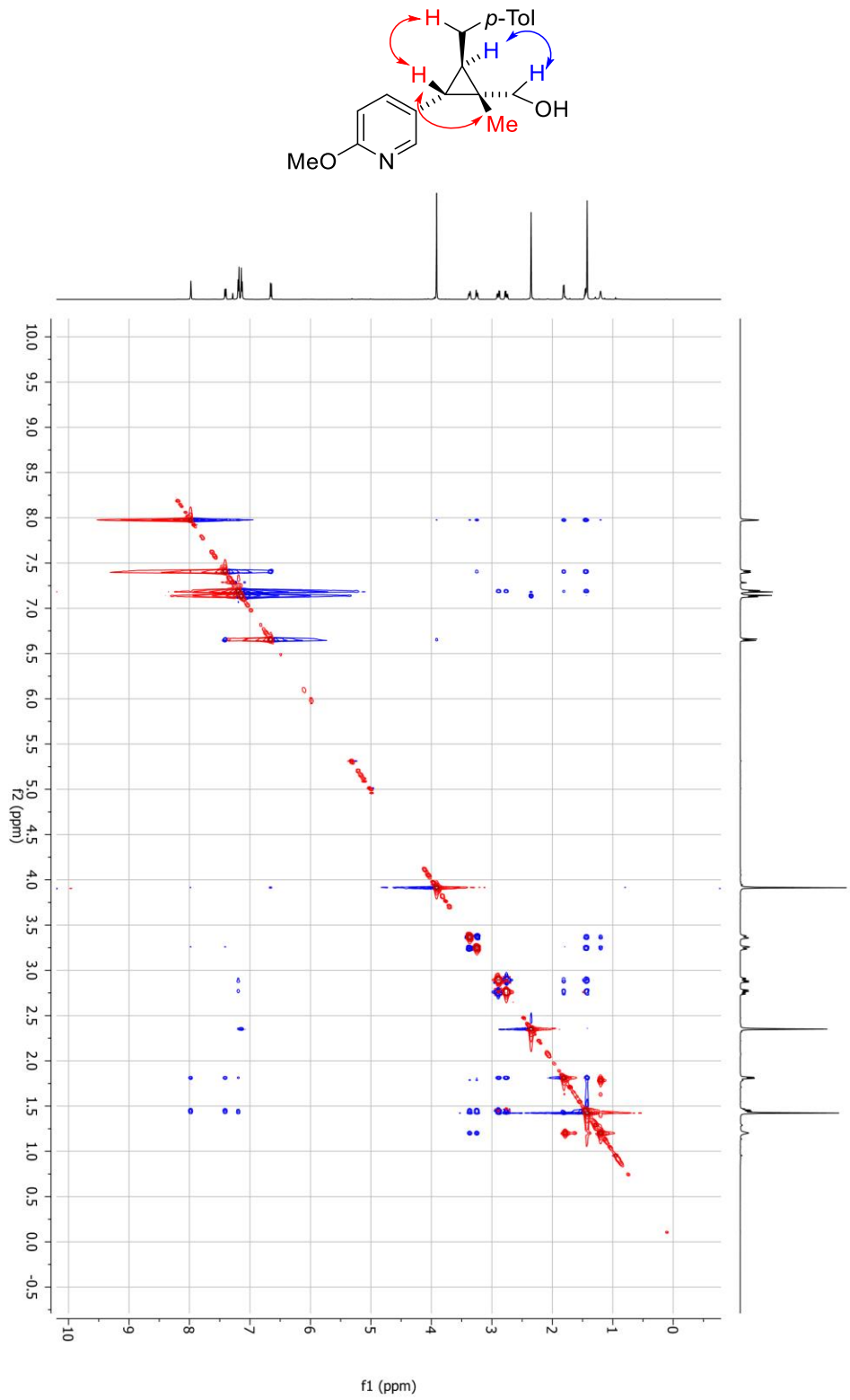
$[\alpha]_D^{31}$: +100.6 (c = 1.3, $CHCl_3$)

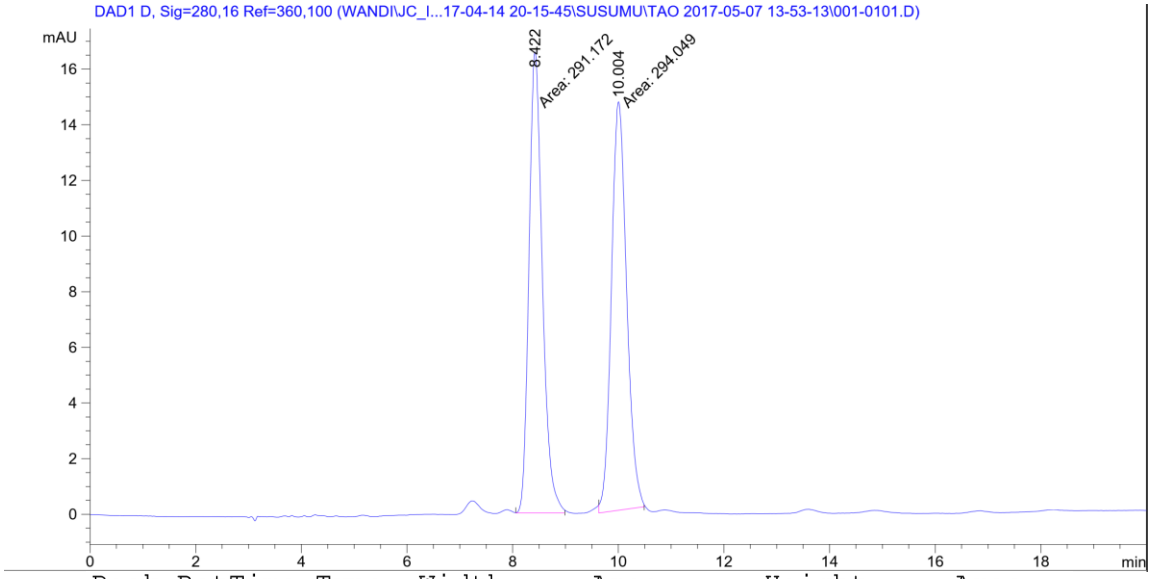
FTIR (neat): 1607, 1494, 1408, 1373, 1316, 1283, 1258, 1109, 1022, 814, 726 cm^{-1}.

HPLC (chiralcel AS-H columns, hexanes:*i*-PrOH = 95:5, 1.0 mL/min, 280 nm), ee = 91%

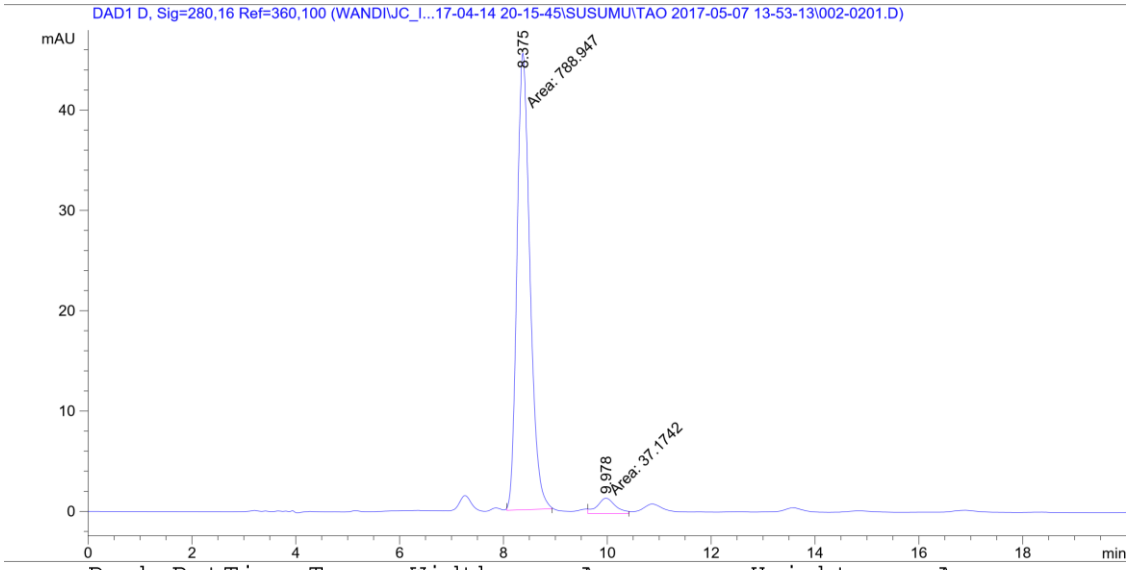

p-Tol
OH
Me
MeO
N
f1 (ppm)


p-Tol
OH
Me
MeO
N
f1 (ppm)


H
p-Tol
H
H
H
OH
Me
MeO
N
f2 (ppm)
f1 (ppm)

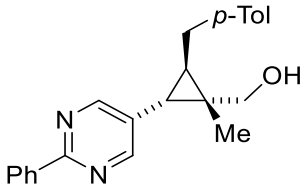


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.422	MM	0.2928	291.17212	16.57316	49.7542
2	10.004	MM	0.3338	294.04904	14.68404	50.2458



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.375	MM	0.2889	788.94690	45.51741	95.5002
2	9.978	MM	0.4068	37.17419	1.52319	4.4998

((*1S,2R,3S*)-1-methyl-2-(4-methylbenzyl)-3-(2-phenylpyrimidin-5-yl)cyclopropyl)methanol (3.3i)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1i** (29.6 mg, 0.1 mmol, 100 mol%), tri(p-tolyl)boroxine (30.1 mg, 0.085 mmol, 85 mol%) **3.2a**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 45 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated in *vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 4:1) to furnish the title compound (29.2 mg, 0.85 mmol) in 85% yield.

TLC (SiO_2) R_f = 0.10 (hexanes/ethyl acetate = 4:1).

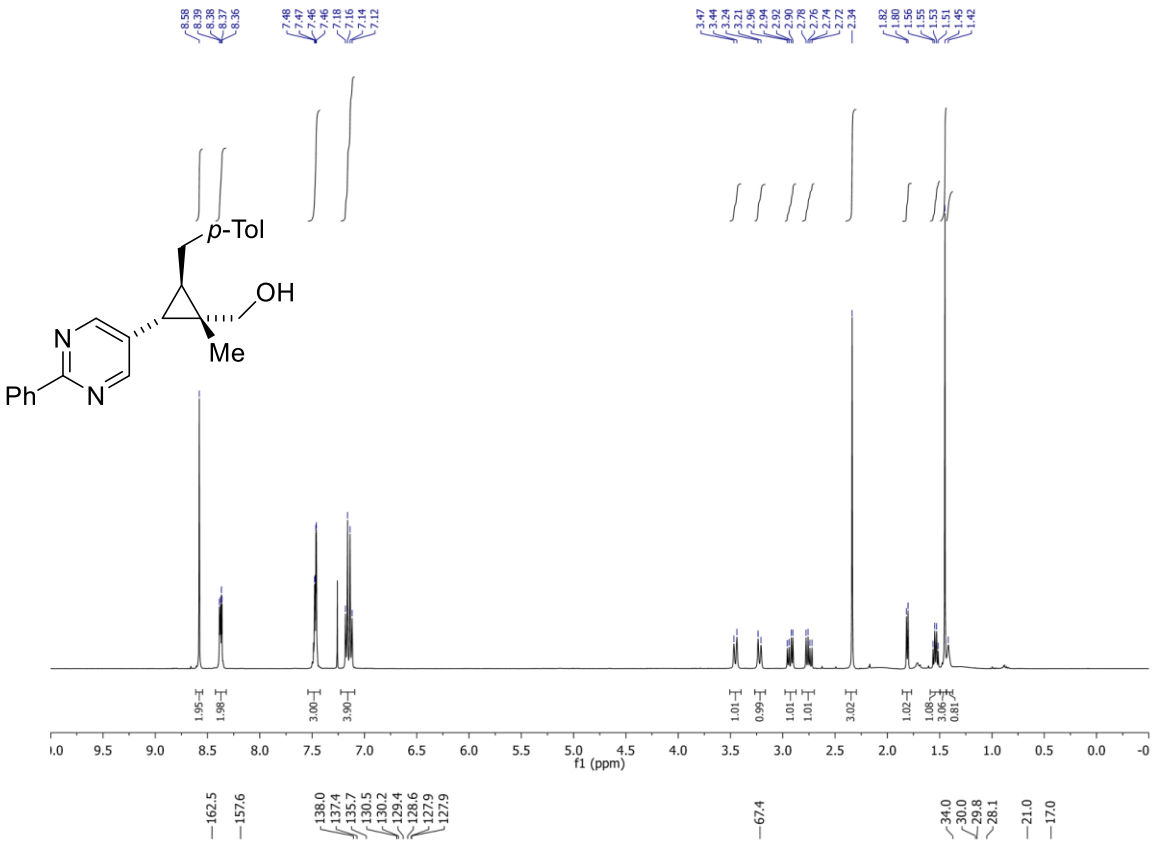
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 2H), 8.41 – 8.33 (m, 2H), 7.47 (s, 3H), 7.15 (s, 4H), 3.45 (d, *J* = 11.3 Hz, 1H), 3.22 (d, *J* = 11.3 Hz, 1H), 2.93 (dd, *J* = 14.9, 6.5 Hz, 1H), 2.75 (dd, *J* = 14.9, 7.8 Hz, 1H), 2.34 (s, 3H), 1.81 (d, *J* = 5.9 Hz, 1H), 1.54 (dt, *J* = 7.9, 6.3 Hz, 1H), 1.45 (s, 3H), 1.42 (s, 1H).

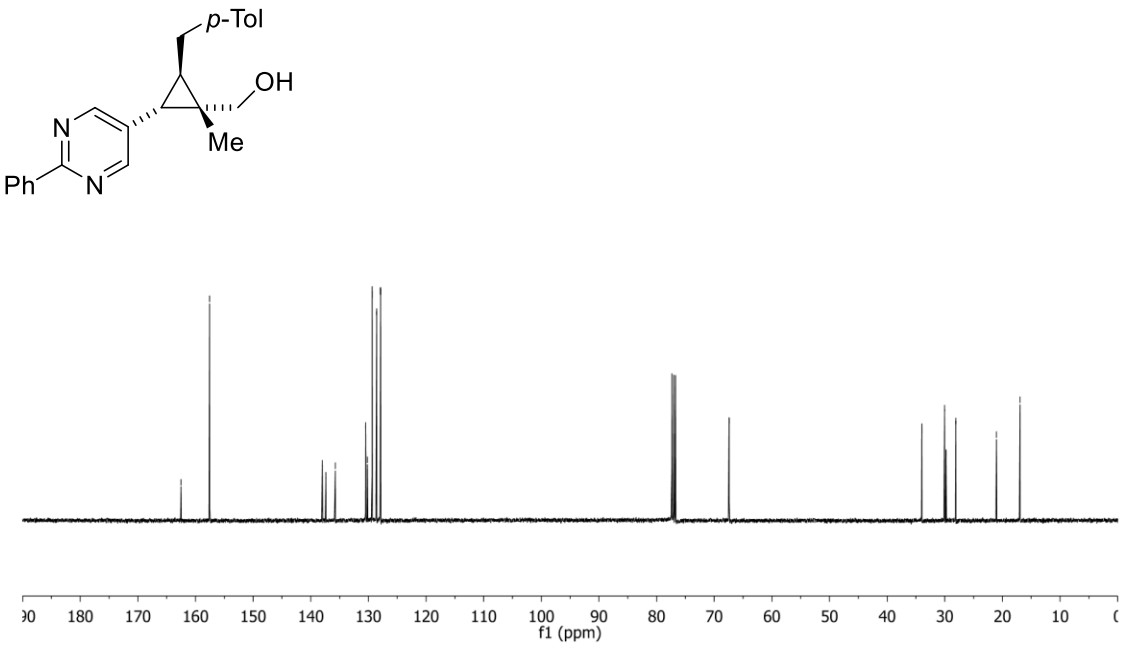
^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 157.6, 138.0, 137.4, 135.7, 130.5, 130.2, 129.4, 128.6, 127.9, 127.9, 67.4, 34.0, 30.0, 29.8, 28.1, 21.0, 17.0.

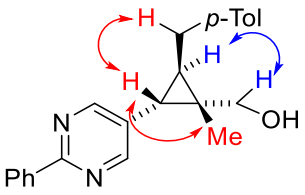
HRMS (ESI) Calcd. for $C_{23}H_{24}N_2NaO^+$ $[M+Na]^+$: 367.1781, Found: 367.1784

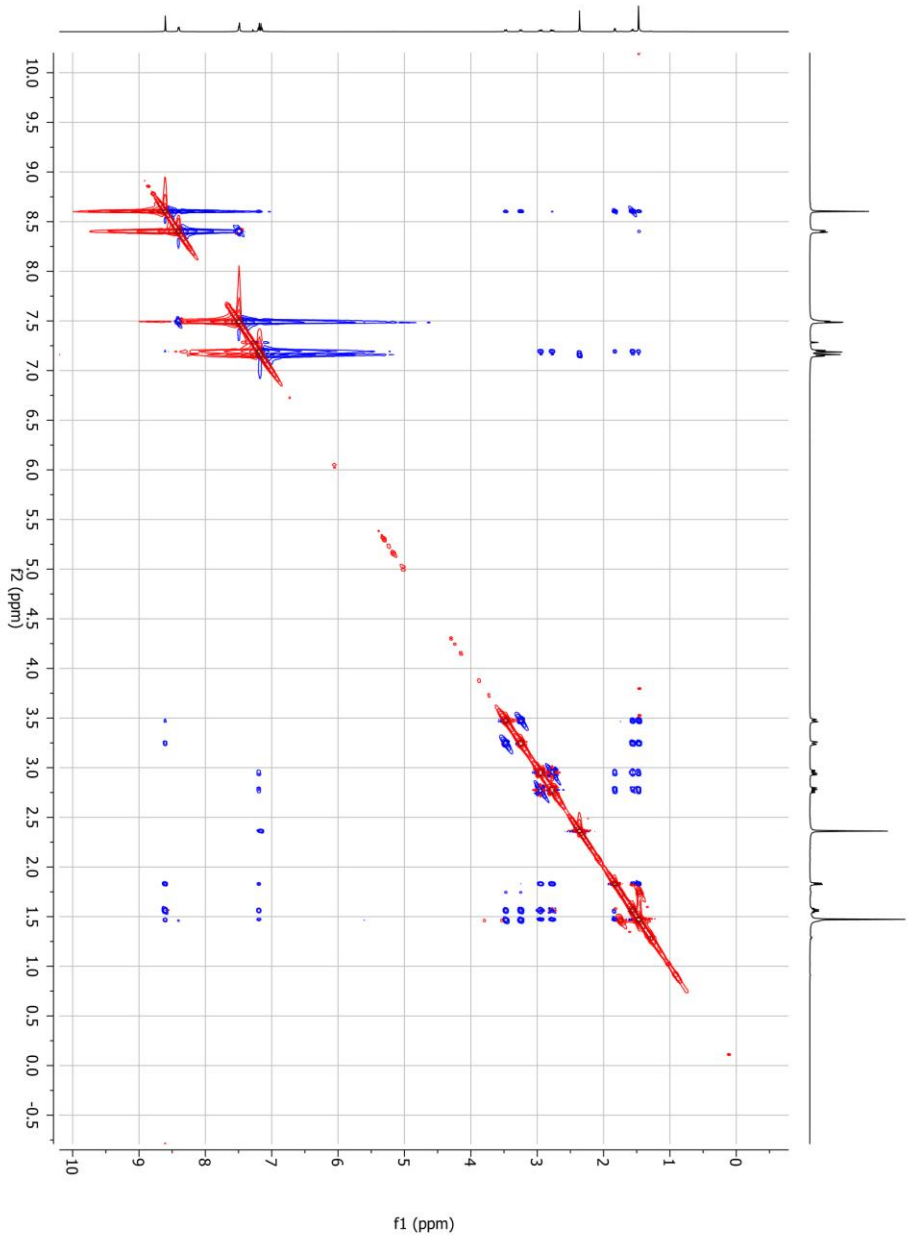
$[\alpha]_D^{31}$: +120.3 (c = 1.1, $CHCl_3$)

FTIR (neat): 2361, 2343, 2331, 1515, 1438, 1421, 1024, 748, 693, 669 cm^{-1}.

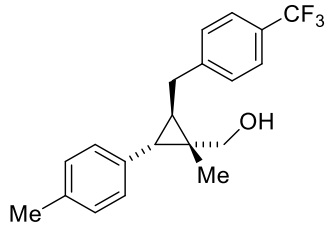

p-Tol
OH
Me
N
Ph
N
f1 (ppm)


p-Tol
OH
Me
N
Ph
N
f1 (ppm)


H
p-Tol
H
H
H
N
OH
Me
Ph
N


f2 (ppm)
f1 (ppm)

((*1S,2S,3R*)-1-methyl-2-(p-tolyl)-3-(4-(trifluoromethyl)benzyl)cyclopropyl)methanol (3.3j)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1a** (23.3 mg, 0.1 mmol, 100 mol%), tri(p-tolyl)boroxine (43.9 mg, 0.085 mmol, 85 mol%) **3.2b**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 45 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated in *vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 4:1) to furnish the title compound as oil (24.7 mg, 0.74 mmol) in 74% yield.

TLC (SiO_2) R_f = 0.30 (hexanes/ethyl acetate = 4:1).

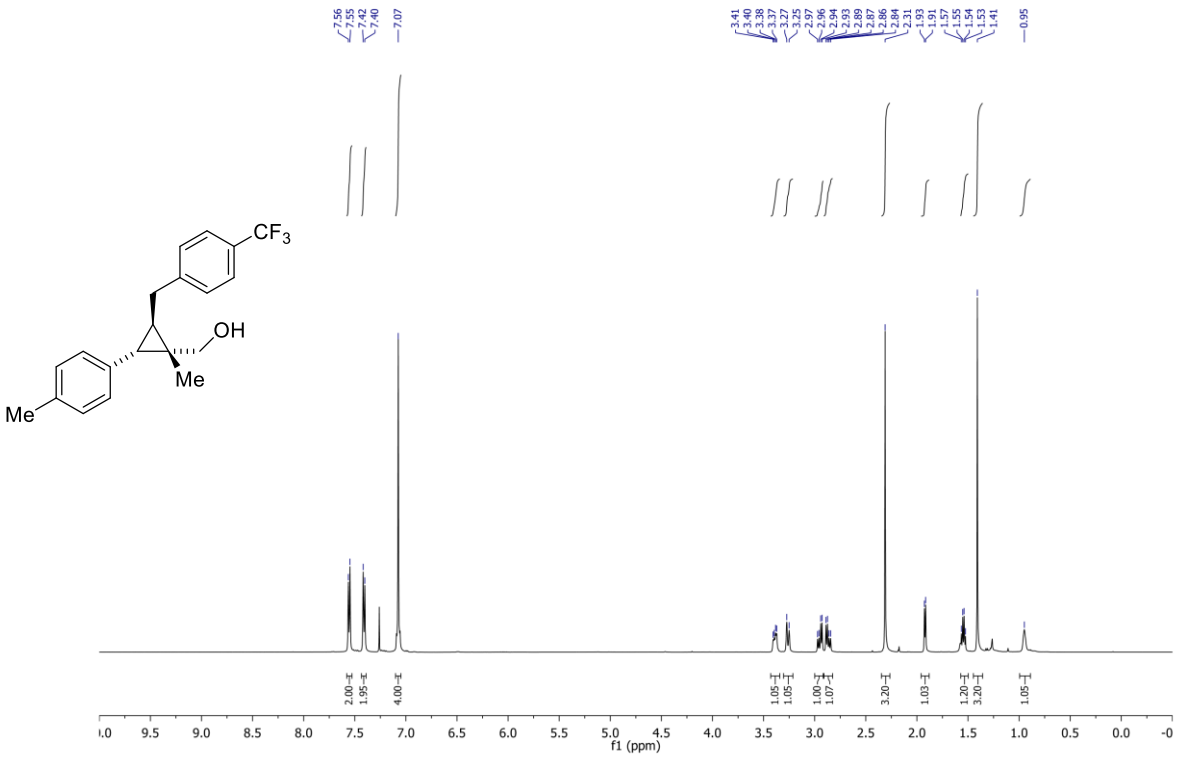
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.9 Hz, 2H), 7.41 (d, *J* = 7.9 Hz, 2H), 7.11 – 7.03 (m, 4H), 3.39 (dd, *J* = 11.9, 5.6 Hz, 1H), 3.26 (d, *J* = 11.4 Hz, 1H), 2.95 (dd, *J* = 15.4, 6.8 Hz, 1H), 2.87 (dd, *J* = 15.4, 7.5 Hz, 1H), 2.31 (s, 3H), 1.92 (d, *J* = 5.8 Hz, 1H), 1.55 (q, *J* = 6.8 Hz, 1H), 1.41 (s, 3H), 0.95 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 145.9, 136.0, 135.2, 129.2, 128.5, 128.5, 128.2, 125.5, 125.4, 125.4, 125.4, 123.3, 68.0, 35.1, 34.5, 29.6, 26.7, 21.0, 17.2.

HRMS (ESI) Calcd. for $C_{20}H_{21}F_3NaO^+$ $[M+Na]^+$: 357.1437, Found: 357.1442

$[\alpha]_D^{29}$: +19.7 (c = 0.76, $CHCl_3$)

FTIR (neat): 1515, 1324, 1275, 1161, 1121, 1067, 1018, 913, 819, 749 cm^{-1}.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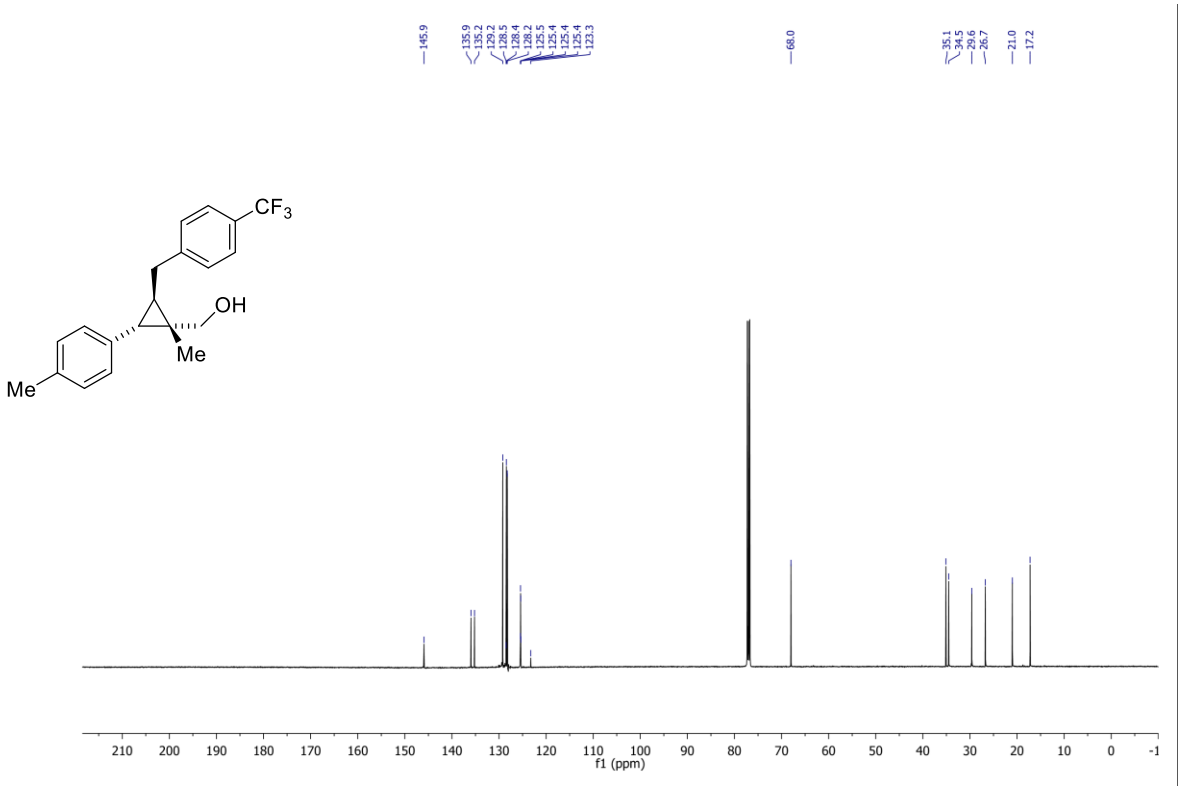
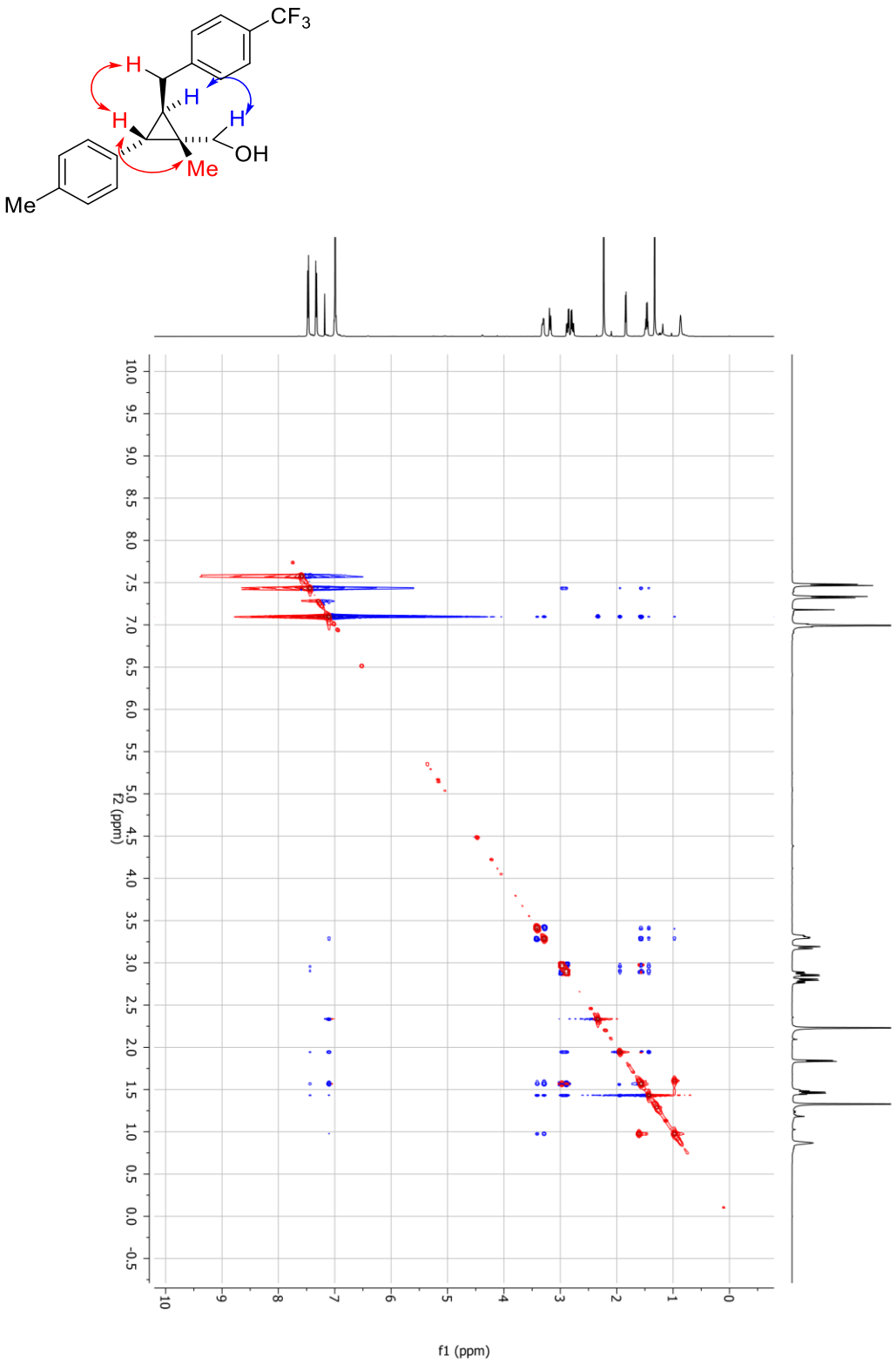
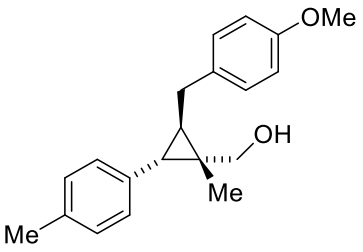
OH
Me
Me
f1 (ppm)


CF3
OH
Me
Me
f1 (ppm)


CF3
H
H
H
H
OH
Me
Me
f2 (ppm)
f1 (ppm)

((1*S*,2*R*,3*S*)-2-(4-methoxybenzyl)-1-methyl-3-(*p*-tolyl)cyclopropyl)methanol (3.3k)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1a** (29.8 mg, 0.1 mmol, 100 mol%), tri(*p*-methoxyphenyl)boroxine (34.2 mg, 0.085 mmol, 85 mol%) **3.2c**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 55 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 8:1) to furnish the title compound as a yellow solid (22.5 mg, 0.08 mmol) in 76% yield.

TLC (SiO_2) R_f = 0.30 (hexanes/ethyl acetate = 4:1).

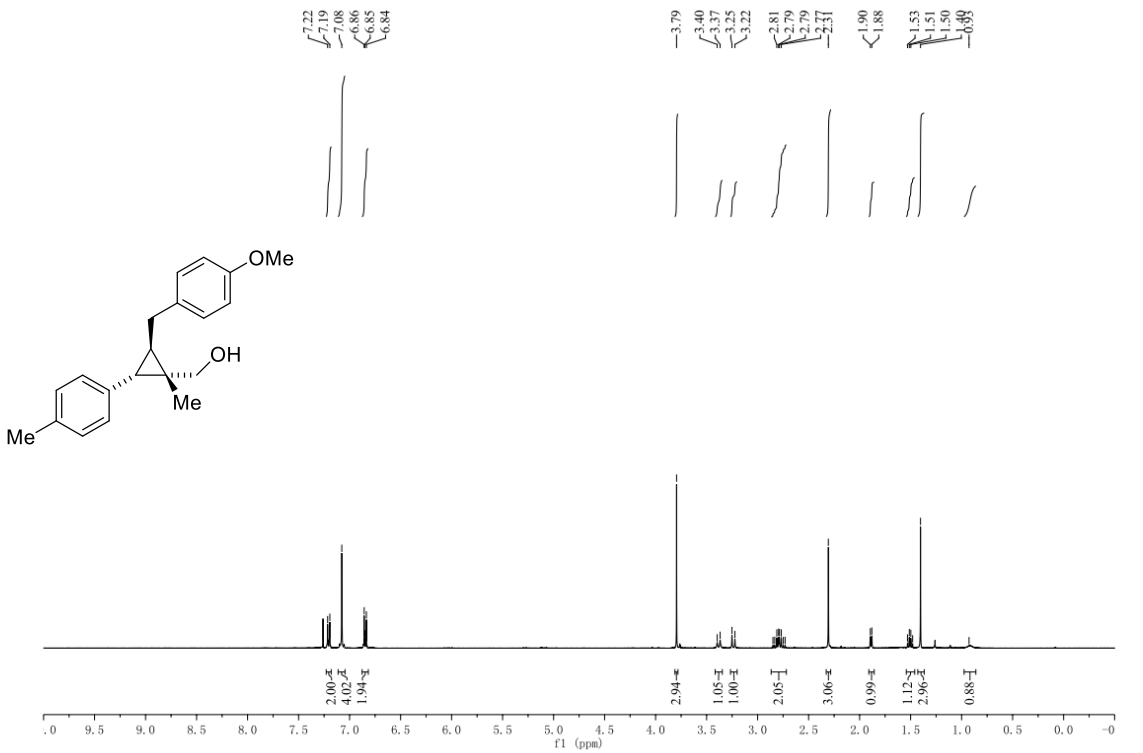
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.18 (m, 2H), 7.10 – 7.04 (m, 4H), 6.87 – 6.82 (m, 2H), 3.79 (s, 3H), 3.38 (d, *J* = 11.6 Hz, 1H), 3.24 (d, *J* = 11.6 Hz, 1H), 2.82 (dd, *J* = 15.1, 6.9 Hz, 1H), 2.76 (dd, *J* = 15.1, 7.3 Hz, 1H), 2.31 (s, 3H), 1.89 (d, *J* = 5.9 Hz, 1H), 1.51 (dd, *J* = 13.1, 7.1 Hz, 1H), 1.40 (s, 3H), 0.93 (brs, 1H).

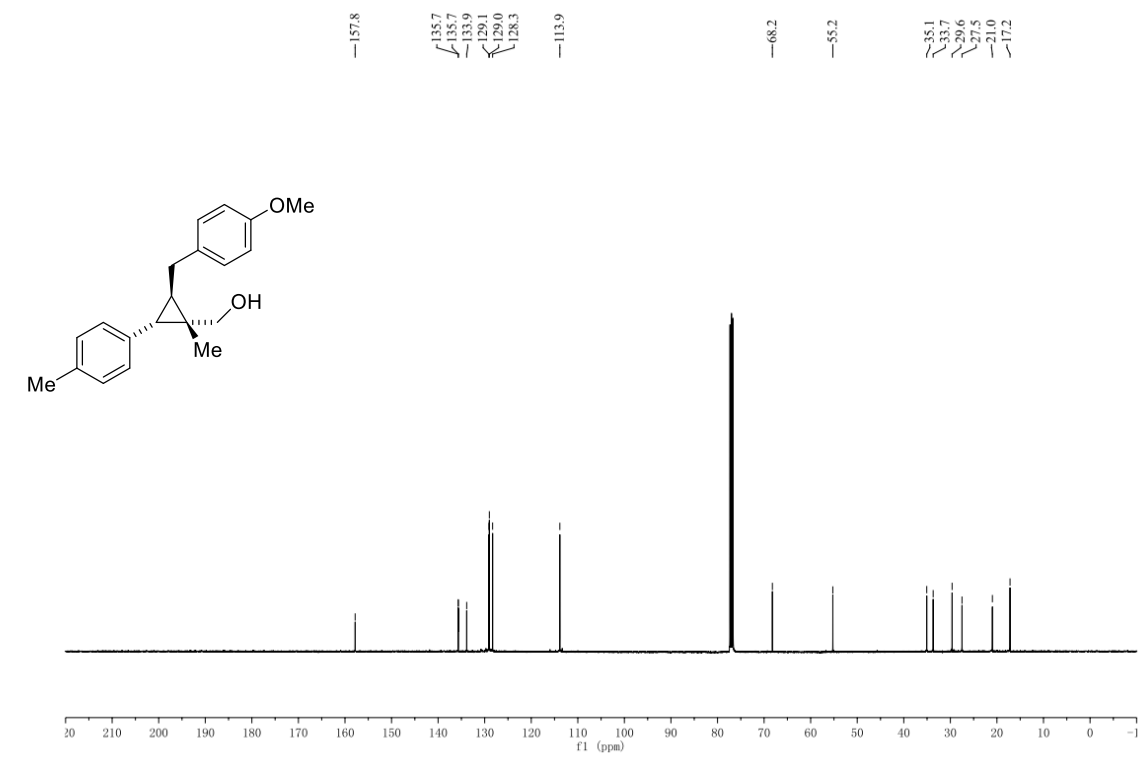
^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 135.7, 135.7, 133.9, 129.1, 129.0, 128.3, 113.9, 68.2, 55.2, 35.1, 33.7, 29.6, 27.5, 21.0, 17.2.

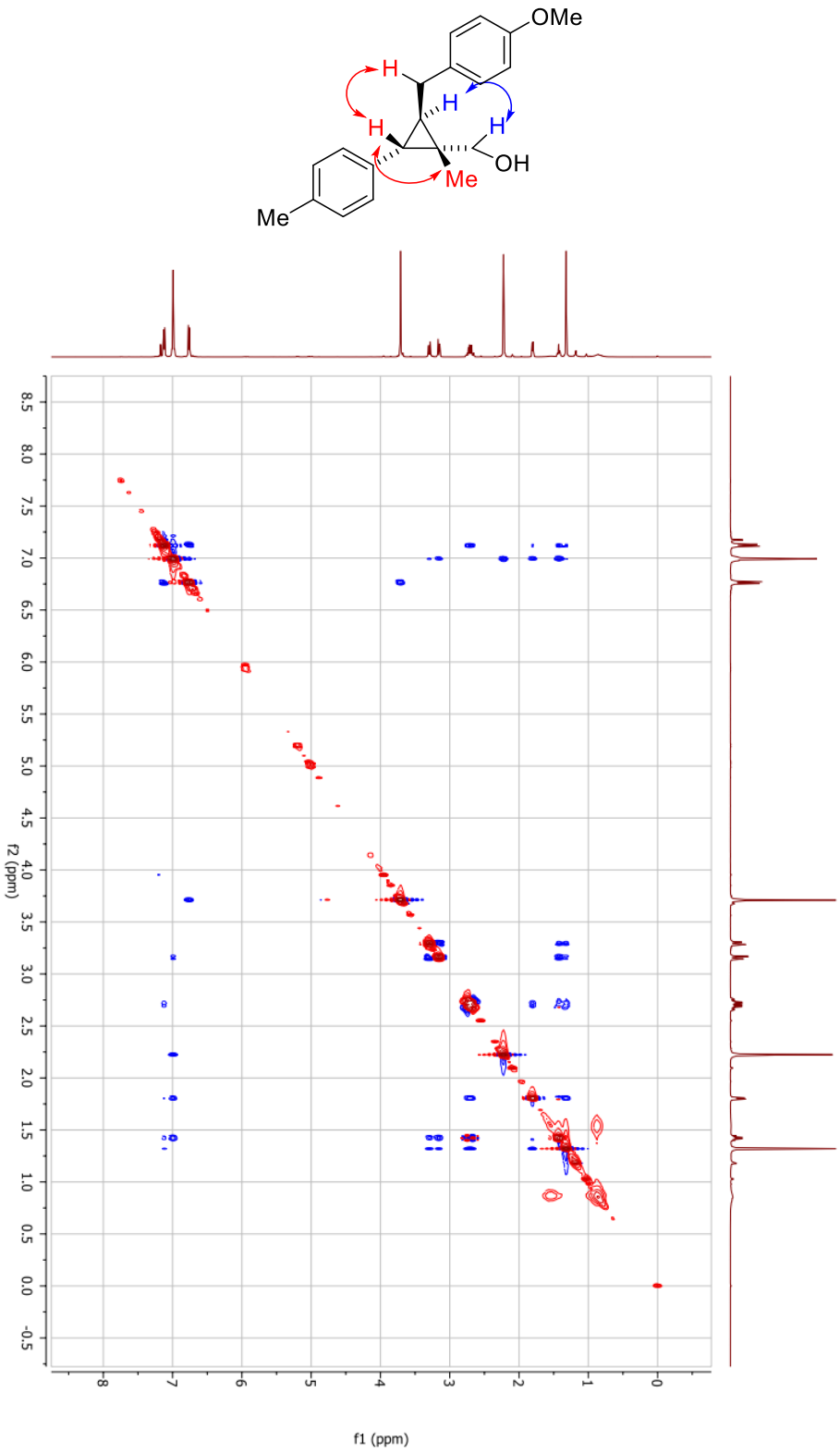
HRMS (CI) Calcd. for $C_{20}H_{24}O_2^+$ $[M]^+$: 296.1771, Found: 296.1771.

$[\alpha]_D^{33}$: +29.0 (*c* = 1.0, $CHCl_3$).

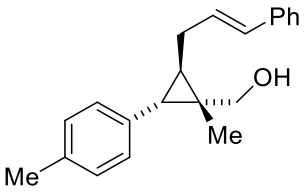
FTIR (neat): 3414, 2921, 1611, 1511, 1463, 1301, 1244, 1177, 1035, 824, 744 cm^{-1}


7.22
7.19
7.08
6.86
6.85
6.84
3.79
3.40
3.37
3.25
3.22
2.81
2.79
2.79
2.77
2.31
1.90
1.88
1.53
1.51
1.50
1.40
0.93
OMe
OH
Me
Me
2.00
4.02
1.94
2.94
1.05
1.00
2.05
3.06
0.99
1.12
2.96
0.88
f1 (ppm)


157.8
135.7
135.7
133.9
129.1
129.0
128.3
113.9
68.2
55.2
35.1
33.7
29.6
27.5
21.0
17.2
OMe
OH
Me
Me
f1 (ppm)


OMe
H
H
H
H
OH
Me
Me
f2 (ppm)
f1 (ppm)

((1S,2R,3S)-2-cinnamyl-1-methyl-3-(p-tolyl)cyclopropyl)methanol (3.3l)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1a** (23.2 mg, 0.1 mmol, 100 mol%), tri(phenylvinyl)boroxine **3.2d** (33.2 mg, 0.085 mmol, 85 mol%), dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 65 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1) to furnish the title compound as a colorless oil (18.7 mg, 0.064 mmol) in 64% yield.

TLC (SiO_2) R_f = 0.35 (hexanes/ethyl acetate = 4:1).

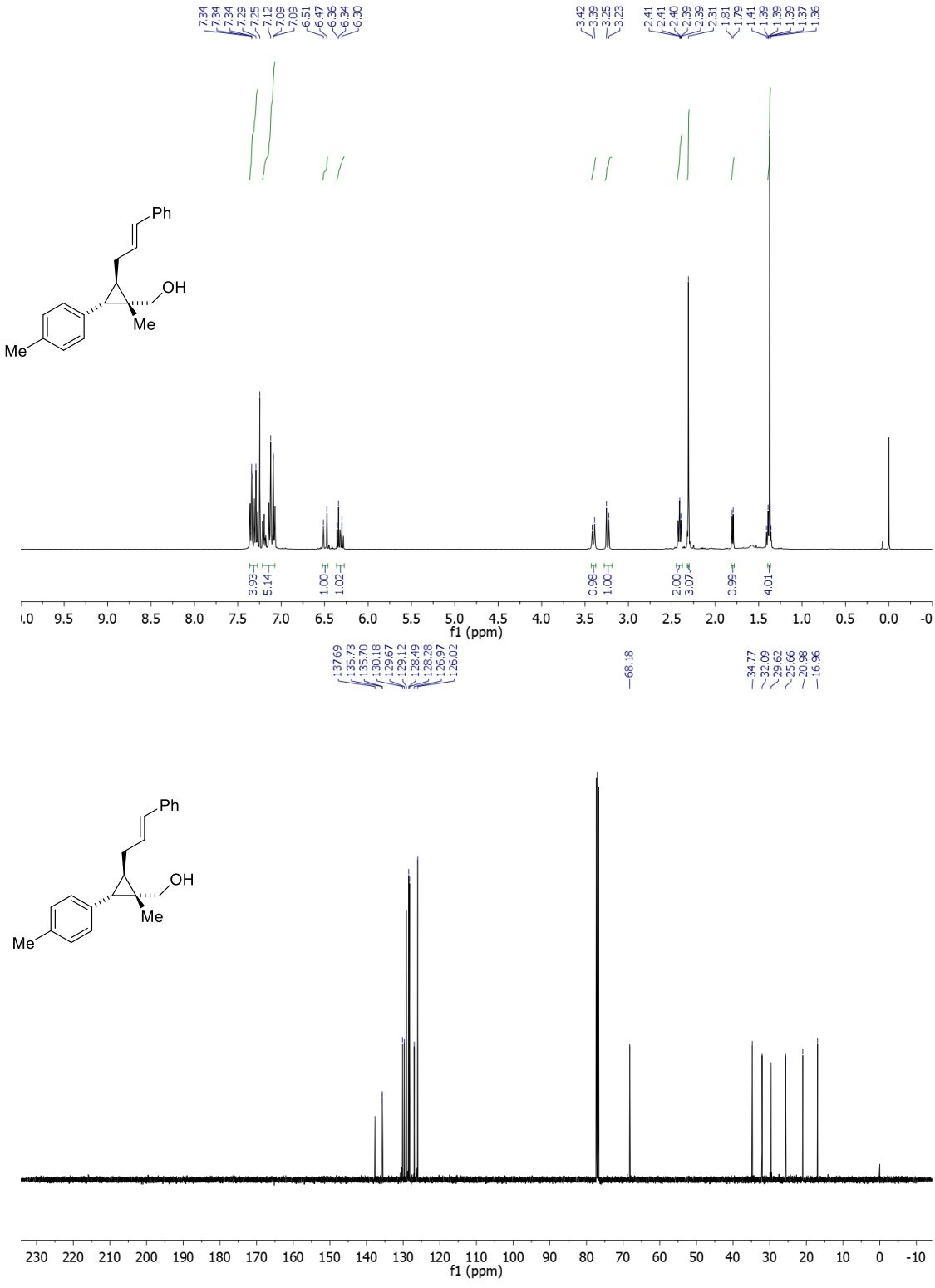
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 4H), 7.22 – 7.05 (m, 5H), 6.54 – 6.43 (m, 1H), 6.32 (dt, *J* = 15.8, 6.5 Hz, 1H), 3.40 (d, *J* = 11.6 Hz, 1H), 3.24 (d, *J* = 11.6 Hz, 1H), 2.41-2.39 (m, 2H), 2.31 (s, 3H), 1.80 (d, *J* = 5.9 Hz, 1H), 1.41-1.36(m, 1H), 1.37 (s, 3H)

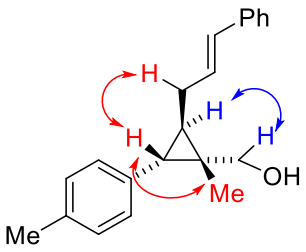
^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 135.7 (d, *J* = 2.3 Hz), 130.1, 129.6, 129.1, 128.4, 128.2, 126.9, 126.0, 68.1, 34.7, 32.0, 29.6, 25.6, 20.9, 16.9.

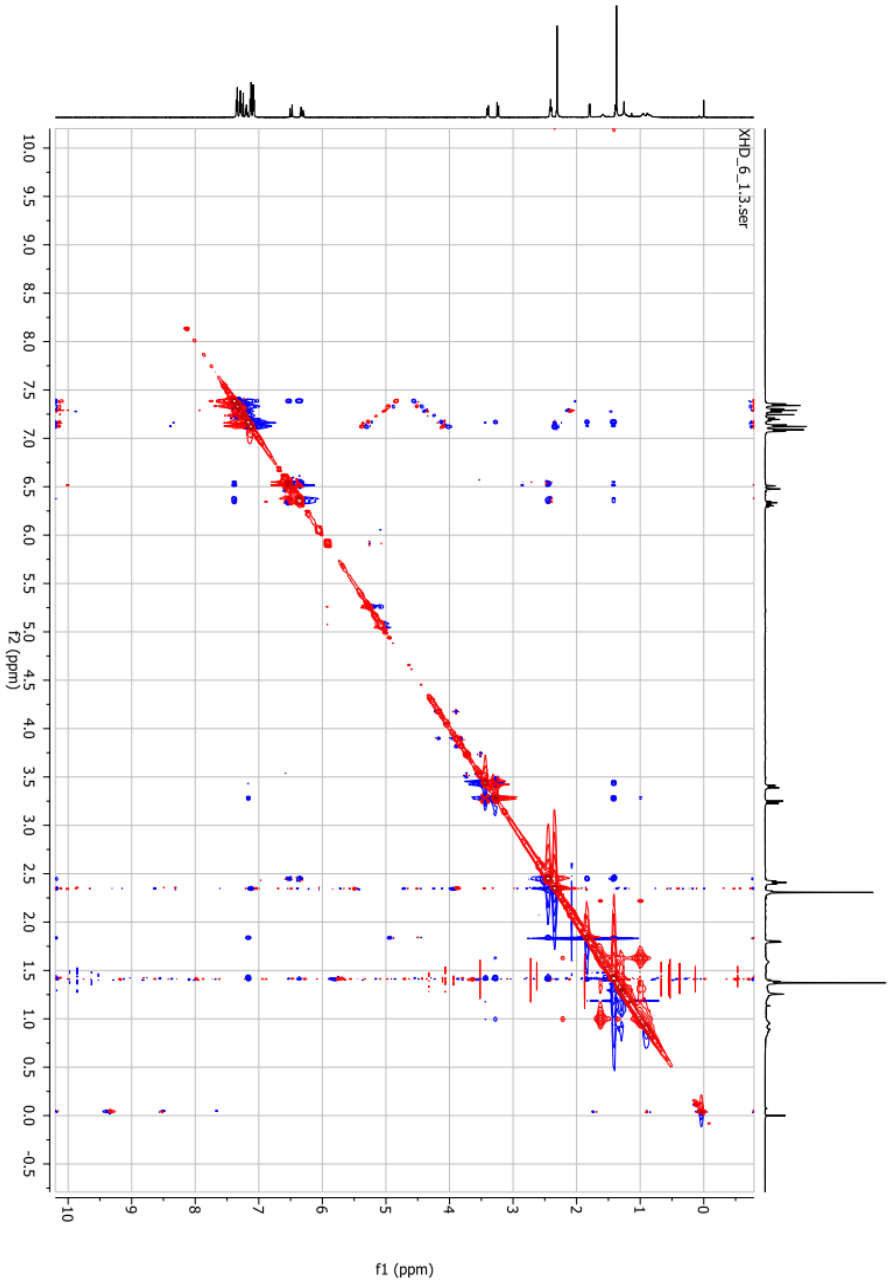
HRMS (ESI) Calcd. for $C_{21}H_{24}NaO^+$ $[M+Na]^+$: 315.1719, Found: 315.1729.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{33}}$: +9.7 (*c* = 1.0, $CHCl_3$).

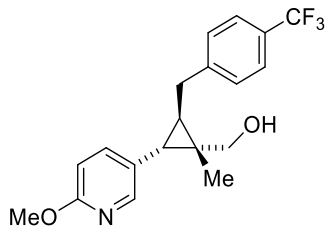
FTIR (neat): 3406, 2922, 1514, 1448, 1378, 1019, 963, 825, 803, 741, 692 cm^{-1}.


Ph
OH
Me
Me
f1 (ppm)
f1 (ppm)


Ph
H
H
H
H
OH
Me
Me


XHD_6_1.3.ser
f2 (ppm)
f1 (ppm)

((*1S,2S,3R*)-2-(6-methoxypyridin-3-yl)-1-methyl-3-(4-(trifluoromethyl)benzyl)cyclopropyl)methanol (3.3m)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1h** (24.9 mg, 0.1 mmol, 100 mol%), tri(p-tolyl)boroxine (43.9 mg, 0.085 mmol, 85 mol%) **3.2b**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 55 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated in *vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 3:1,) to furnish the title compound as oil (25.2 mg, 0.72 mmol) in 72% yield.

TLC (SiO_2) R_f = 0.10 (hexanes/ethyl acetate = 3:1).

^{1}H NMR 1H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 2.4 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 7.38 (dd, *J* = 6.4, 2.3 Hz, 1H), 6.64 (d, *J* = 8.4 Hz, 1H),

3.89 (s, 3H), 3.36 (d, J = 11.4 Hz, 1H), 3.25 (d, J = 11.4 Hz, 1H), 2.97 (dd, J = 15.2, 6.6 Hz, 1H), 2.84 (dd, J = 15.2, 7.7 Hz, 1H), 1.82 (d, J = 5.8 Hz, 1H), 1.46 (q, J = 6.5 Hz, 1H), 1.40 (s, 3H), 1.10 (s, 1H).

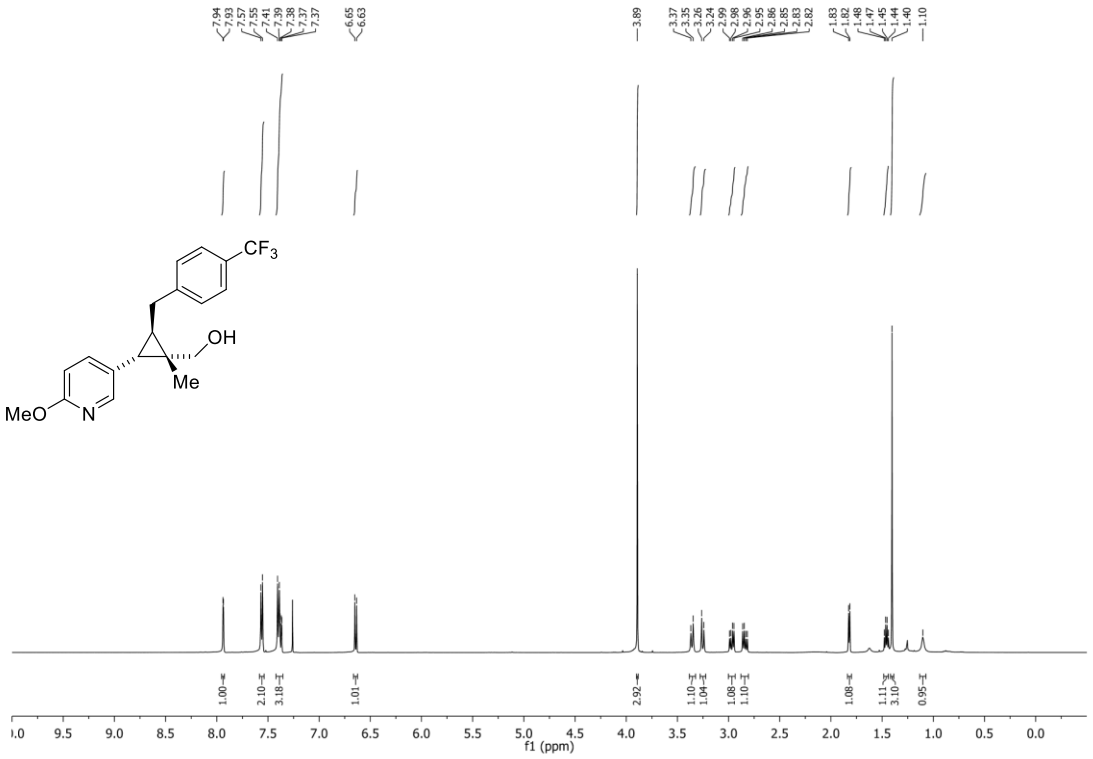
^{13}C NMR (125 MHz, $CDCl_3$) δ 163.1, 146.7, 145.8, 139.4, 128.6 (q, J^3_{CF} = 32.5 Hz), 128.6, 126.7, 125.6 (q, J^1_{CF} = 3.8 Hz), 124.4 (q, J^2_{CF} = 271 Hz, 110.5, 67.9, 53.5, 34.7, 32.2, 29.1, 27.2, 17.1.

^{19}F NMR (470 MHz, $CDCl_3$) δ -62.3.

HRMS (ESI) Calcd. for $C_{19}H_{20}F_3NNaO_2^+$ $[M+Na]^+$: 374.1339, Found: 374.1343

$[\alpha]_D^{29}$: +5.7 (c = 0.82, $CHCl_3$)

FTIR (neat): 1607, 1495, 1375, 1324, 1286, 1259, 1161, 1120, 1067, 1018, 832, 732 cm^{-1}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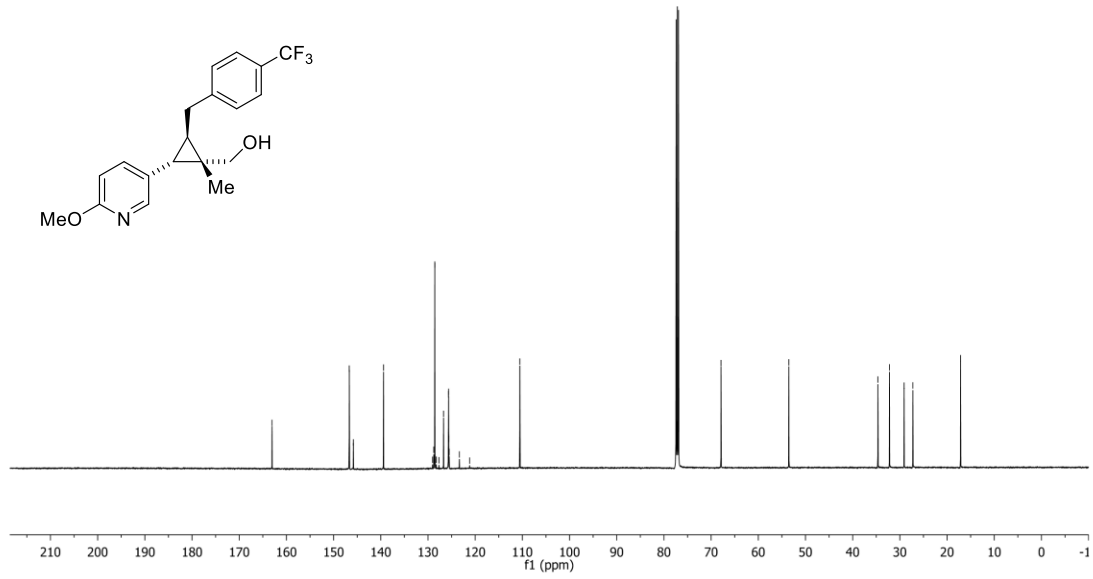
Me
MeO
N
f1 (ppm)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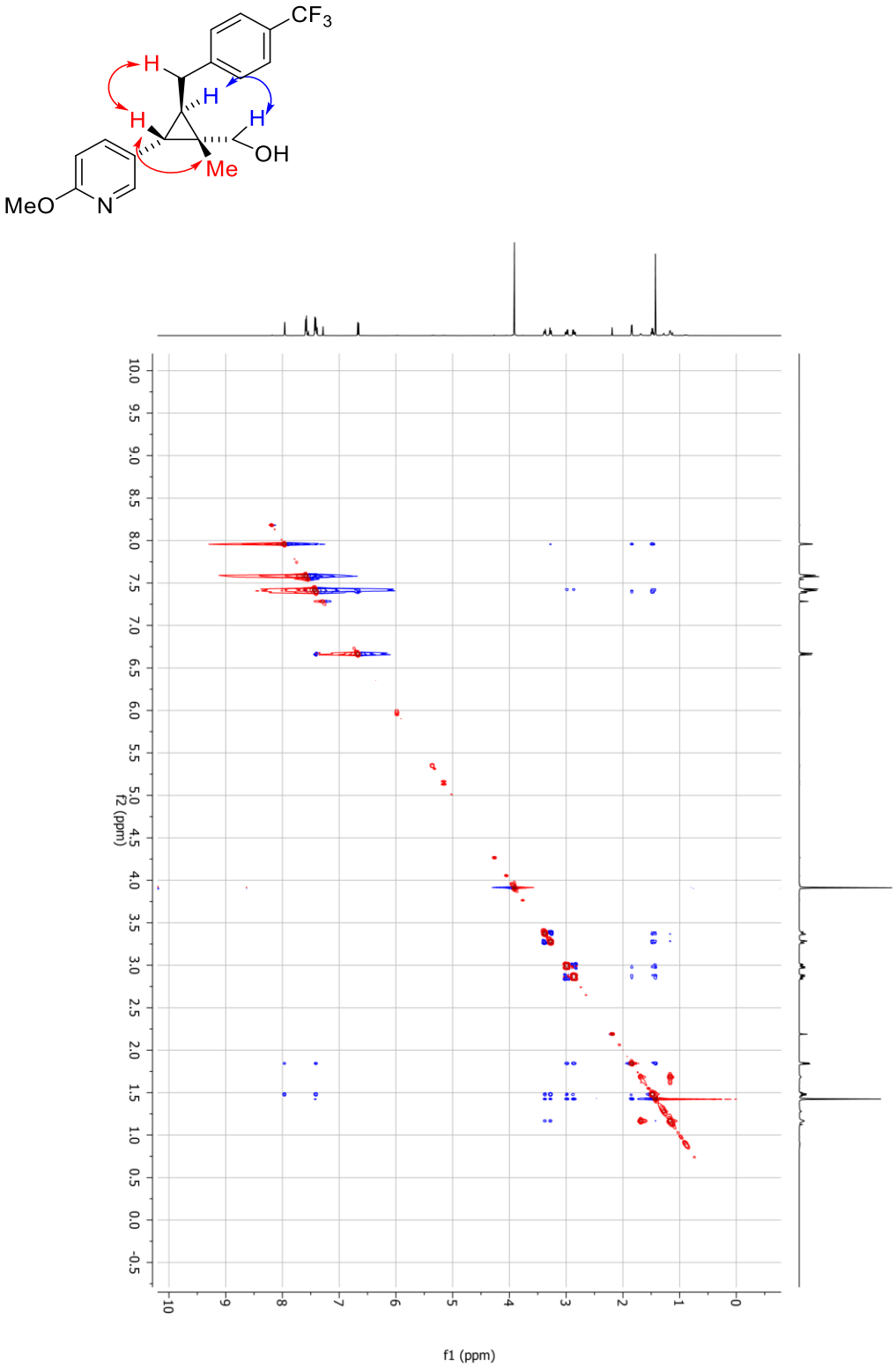
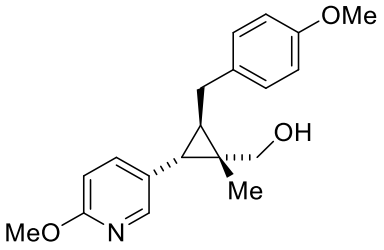
Me
MeO
N
f1 (ppm)


CF3
H
H
H
H
OH
Me
MeO
N
f2 (ppm)
f1 (ppm)

((1*S*,2*R*,3*S*)-2-(4-methoxybenzyl)-3-(6-methoxypyridin-3-yl)-1-methylcyclopropyl)methanol (3.3n)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1h** (29.8 mg, 0.1 mmol, 100 mol%), tri(*p*-tolyl)boroxine **3.2d** (34.2 mg, 0.085 mmol, 85 mol%), dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 55 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 3:1) to furnish the title compound as a yellow solid (23.2 mg, 0.07 mmol) in 74% yield.

TLC (SiO_2) R_f = 0.24 (hexanes/ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 2.5 Hz, 1H), 7.38 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.22 – 7.15 (m, 2H), 6.90 – 6.80 (m, 2H), 6.63 (d, *J* = 8.5 Hz, 1H), 3.89 (s, 3H), 3.79 (s, 3H), 3.34 (d, *J* = 11.4 Hz, 1H), 3.22 (d, *J* = 11.4 Hz, 1H), 2.85 (dd, *J* = 14.9, 6.6 Hz, 1H),

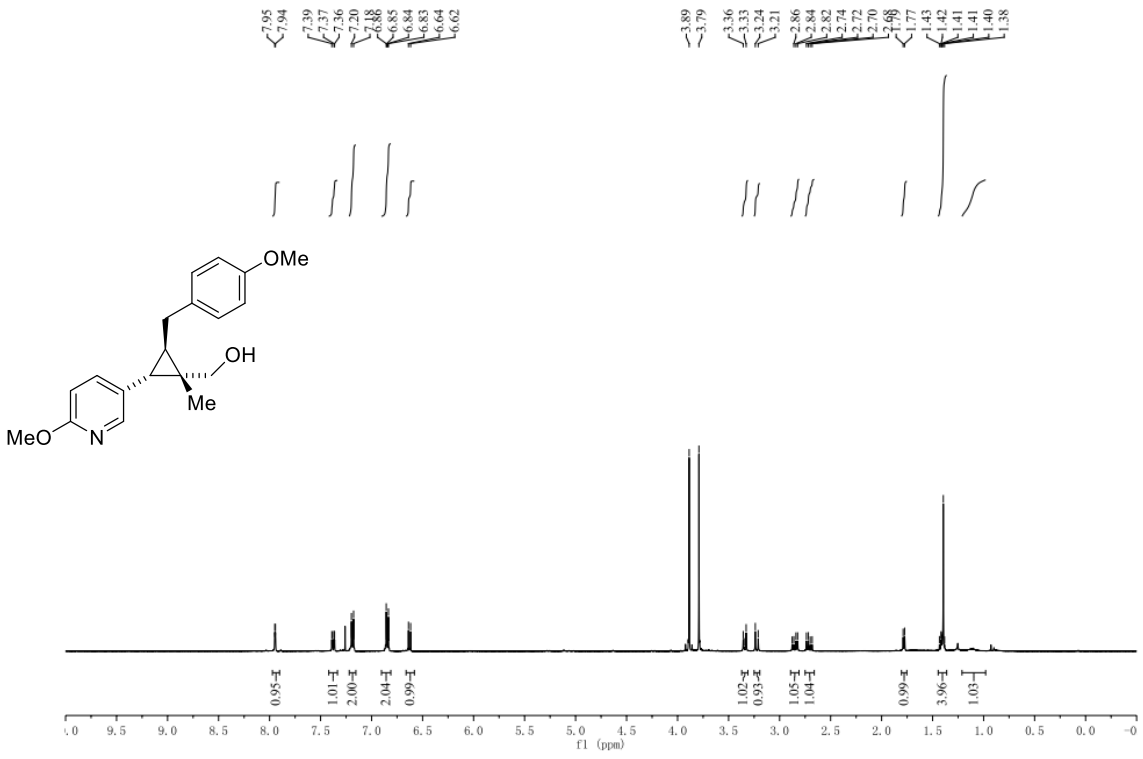
2.71 (dd, *J* = 15.0, 7.7 Hz, 1H), 1.78 (d, *J* = 5.8 Hz, 1H), 1.44 – 1.37 (m, 1H), 1.40 (s, 3H), 1.10 (brs, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 162.8, 157.9, 146.6, 139.4, 133.6, 129.0, 127.0, 114.0, 110.2, 68.0, 55.2, 53.3, 33.7, 32.0, 29.0, 28.0, 16.9.

HRMS (ESI) Calcd. for $C_{19}H_{24}NO_3^+$ $[M+H]^+$: 314.1751, Found: 314.1754.

$[\alpha]_D^{33}$: +9.0 (*c* = 1.0, $CHCl_3$).

FTIR (neat): 3351, 2949, 1606, 1511, 1495, 1374, 1284, 1245, 1177, 1031, 830 cm^{-1}


7.95
7.94
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7.37
7.36
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7.18
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6.84
6.83
6.64
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3.89
3.79
3.36
3.33
3.24
3.21
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2.70
2.68
1.77
1.43
1.42
1.41
1.41
1.40
1.38
OMe
OH
Me
MeO
N
0.95
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2.00
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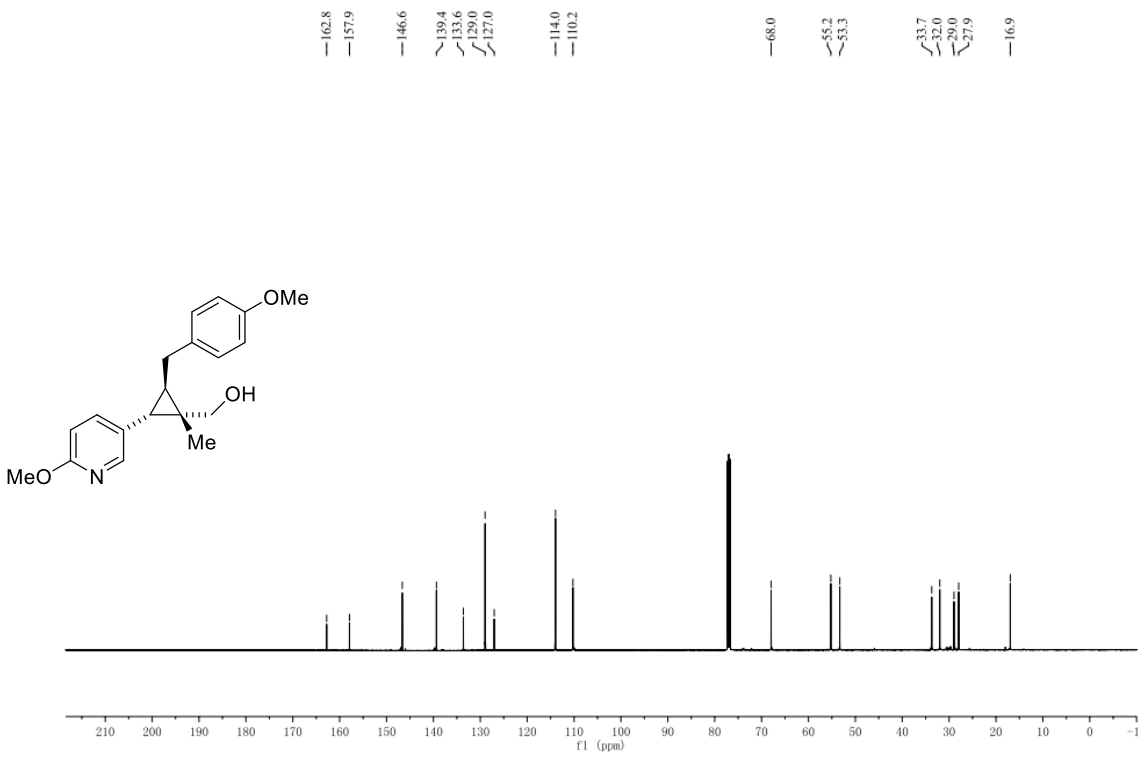
0.99
1.02
0.93
1.05
1.04
0.99
3.96
1.03
f1 (ppm)


162.8
157.9
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133.6
129.0
127.0
114.0
110.2
68.0
55.2
53.3
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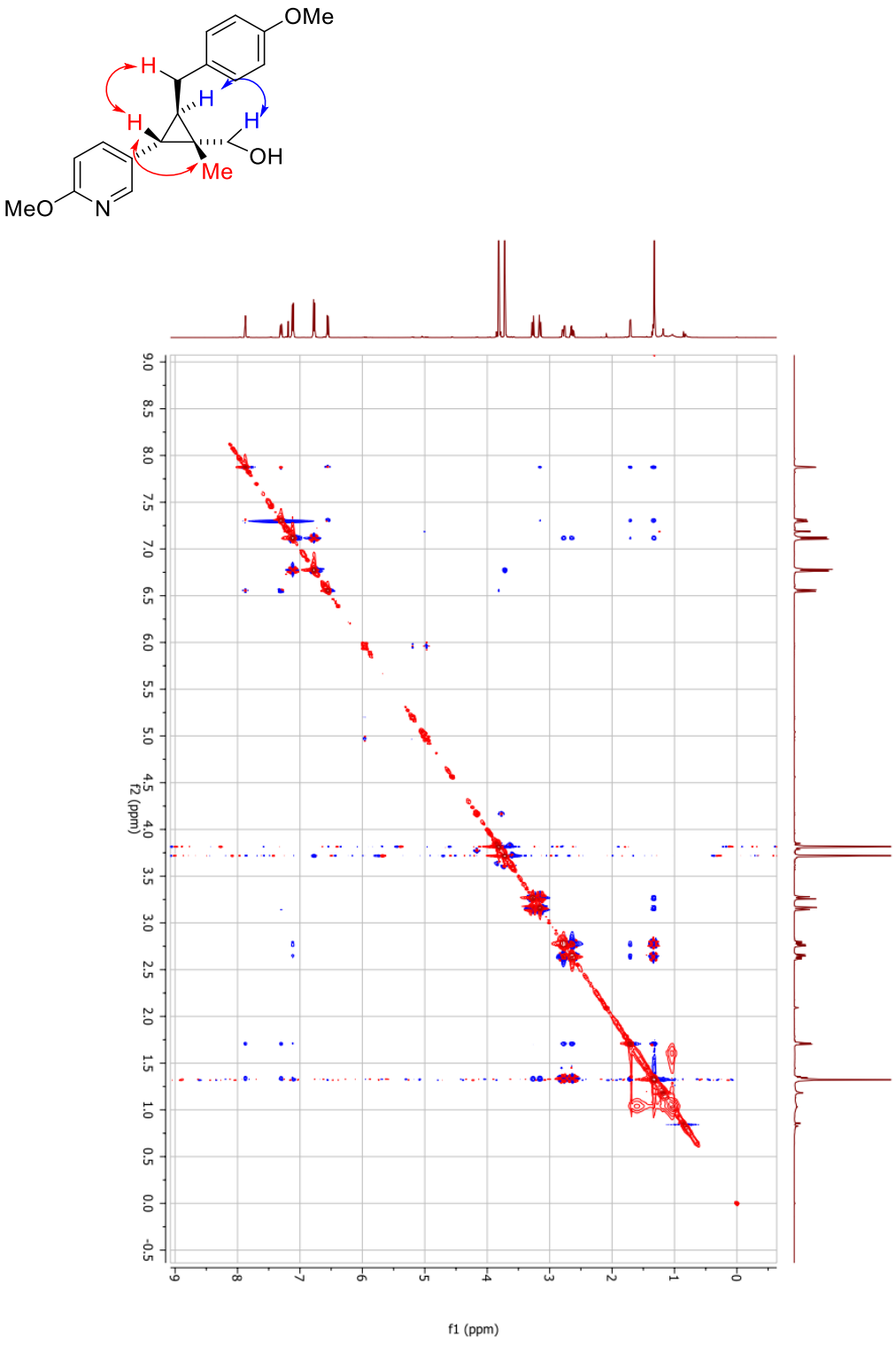
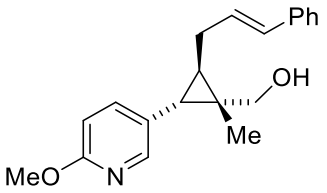
16.9
OMe
OH
Me
MeO
N
f1 (ppm)


OMe
H
H
H
H
OH
Me
MeO
N
f2 (ppm)
f1 (ppm)

((1*S*,2*R*,3*S*)-2-cinnamyl-1-methyl-3-(*p*-tolyl)cyclopropyl)methanol (3.3o)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1h** (23.2 mg, 0.1 mmol, 100 mol%), tri(phenylvinyl)boroxine **3.2d** (33.2 mg, 0.085 mmol, 85 mol%), dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 60 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1) to furnish the title compound as a colorless oil (18.9 mg, 0.061 mmol) in 61% yield.

TLC (SiO_2) R_f = 0.40 (hexanes/ethyl acetate = 3:1).

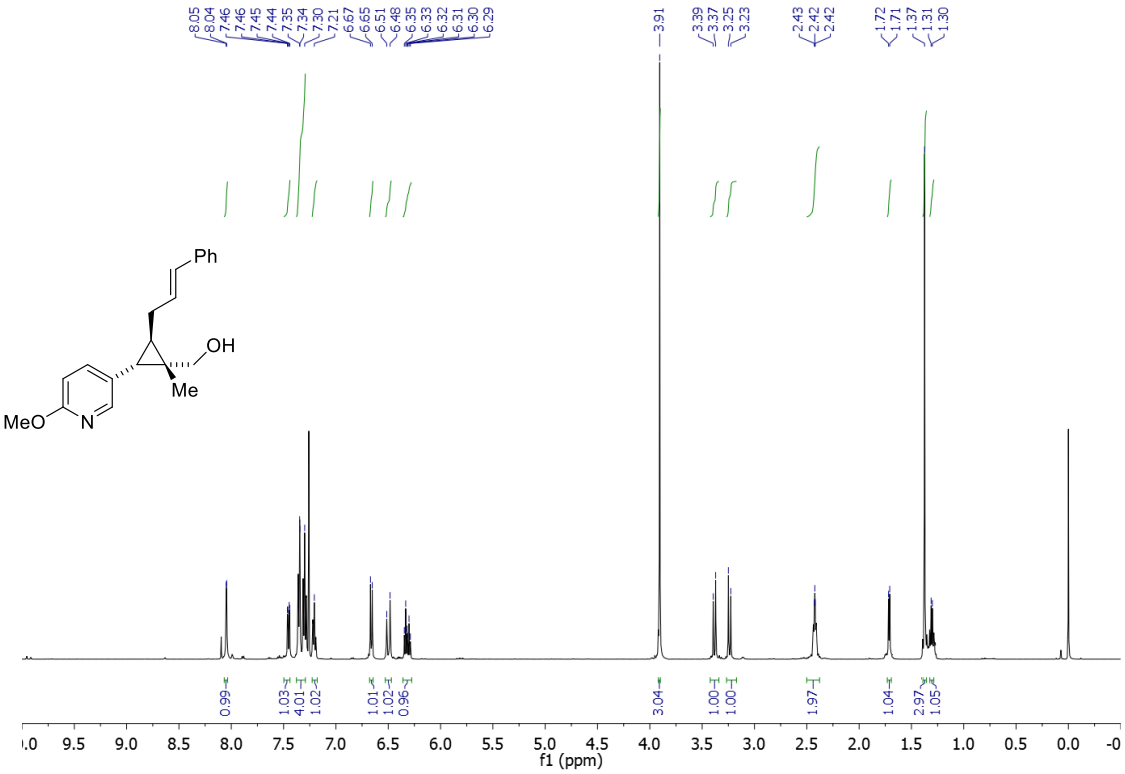
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 2.4 Hz, 1H), 7.45 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.39 – 7.27 (m, 4H), 7.24 – 7.19 (m, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 6.52 – 6.46 (m, 1H), 6.32 (dt, *J* = 15.8, 6.5 Hz, 1H), 3.38 (d, *J* = 11.4 Hz, 3H), 3.24 (d, *J* = 11.5 Hz, 1H), 2.43-2.42 (m, 2H), 1.71 (d, *J* = 5.8 Hz, 1H), 1.37 (s, 3H), 1.31 (td, *J* = 7.2, 5.9 Hz, 1H).

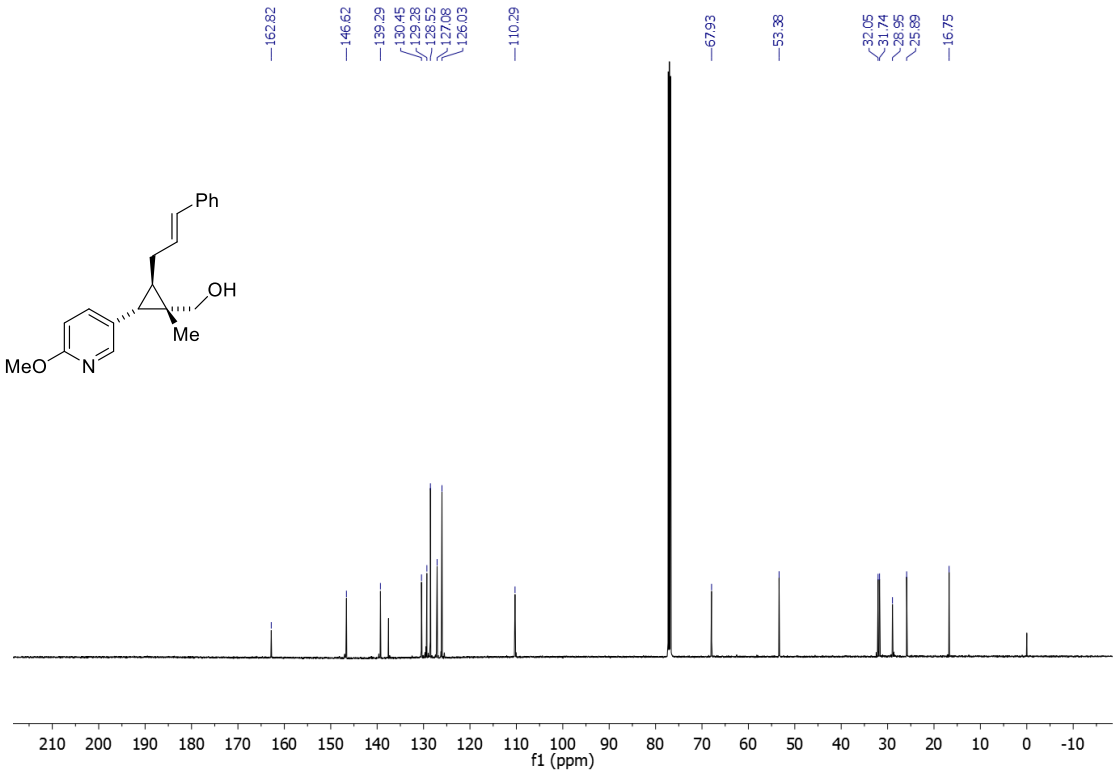
^{13}C NMR (125 MHz, $CDCl_3$) δ 162.8, 146.6, 139.2, 137.5, 130.4, 129.2, 128.5, 127.0, 126.0, 110.2, 67.9, 53.3, 32.0, 31.7, 28.9, 25.8, 16.7.

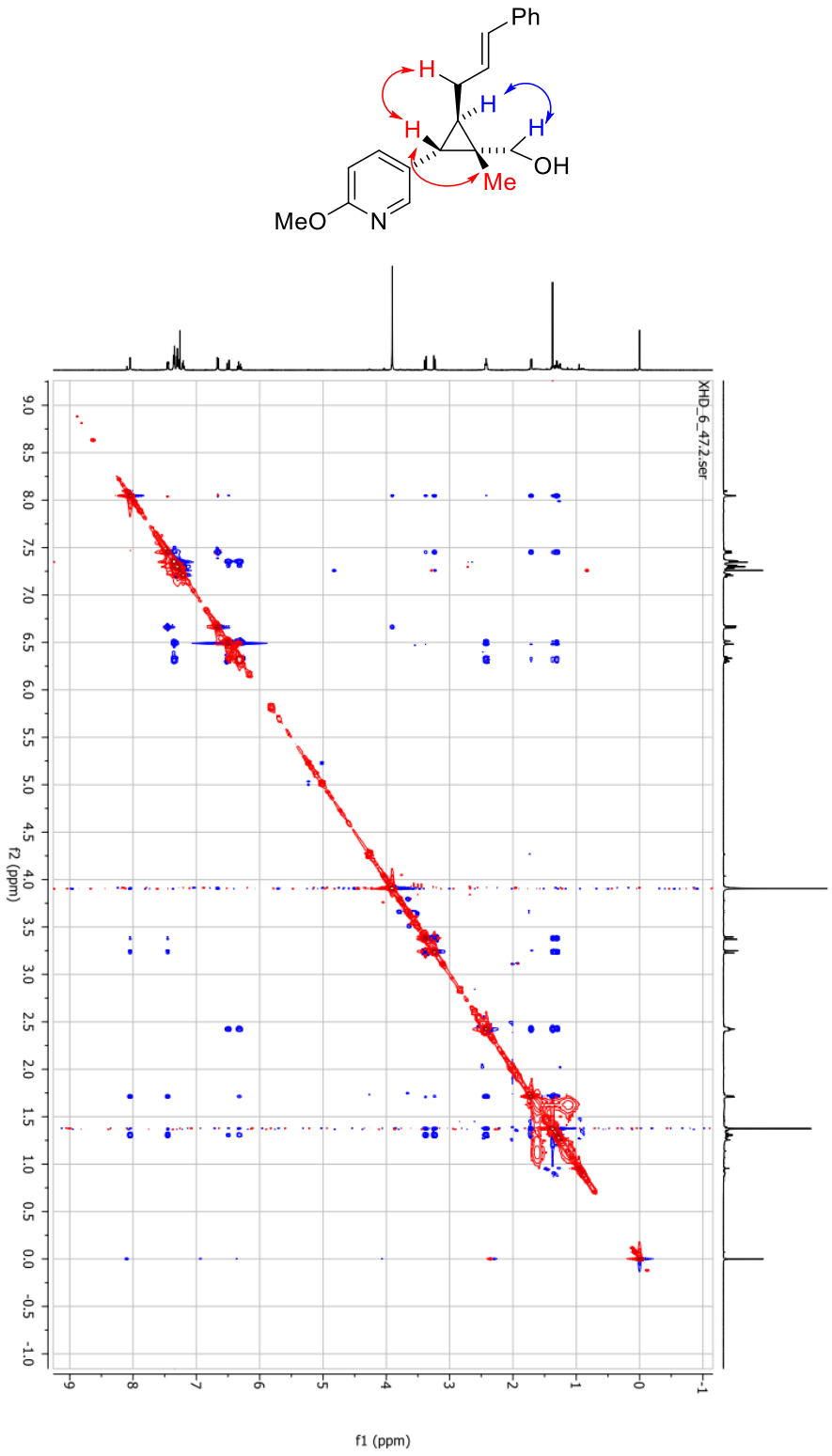
HRMS (ESI) Calcd. for $C_{20}H_{23}NaNO_2^+$ $[M+Na]^+$: 310.1802, Found: 310.1800.

$[\alpha]_D^{33}$: +5.5 (*c* = 1.0, $CHCl_3$).

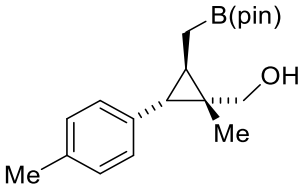
FTIR (neat): 3415, 2951, 1605, 1494, 1374, 1284, 1027, 964, 831, 742, 693 cm^{-1}.


8.05
8.04
7.46
7.46
7.45
7.44
7.35
7.34
7.30
7.21
6.67
6.65
6.51
6.48
6.35
6.33
6.32
6.31
6.30
6.29
3.91
3.39
3.37
3.25
3.23
2.43
2.42
2.42
1.72
1.71
1.37
1.31
1.30
Ph
OH
Me
MeO
N
0.99
1.03
4.01
1.02
1.01
1.02
0.96
3.04
1.00
1.00
1.97
1.04
2.97
1.05
f1 (ppm)


162.82
146.62
139.29
130.45
129.28
128.52
127.08
126.03
110.29
67.93
53.38
32.05
31.74
28.95
25.89
16.75
Ph
OH
Me
MeO
N
f1 (ppm)


Ph
H
H
H
H
OH
Me
MeO
N
XHD_6_47.2.ser
f2 (ppm)
f1 (ppm)

((1*S*,2*R*,3*S*)-1-methyl-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-3- (*p*-tolyl)cyclopropyl)methanol (3.3p)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1a** (29.8 mg, 0.1 mmol, 100 mol%), B_2pin_2 (50.8 mg, 0.2 mmol, 200 mol%) **3.2a**, dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 55 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 4:1) to furnish the title compound as a yellow solid (26.8 mg, 0.08 mmol) in 85% yield.

TLC (SiO_2) R_f = 0.30 (hexanes/ethyl acetate = 4:1).

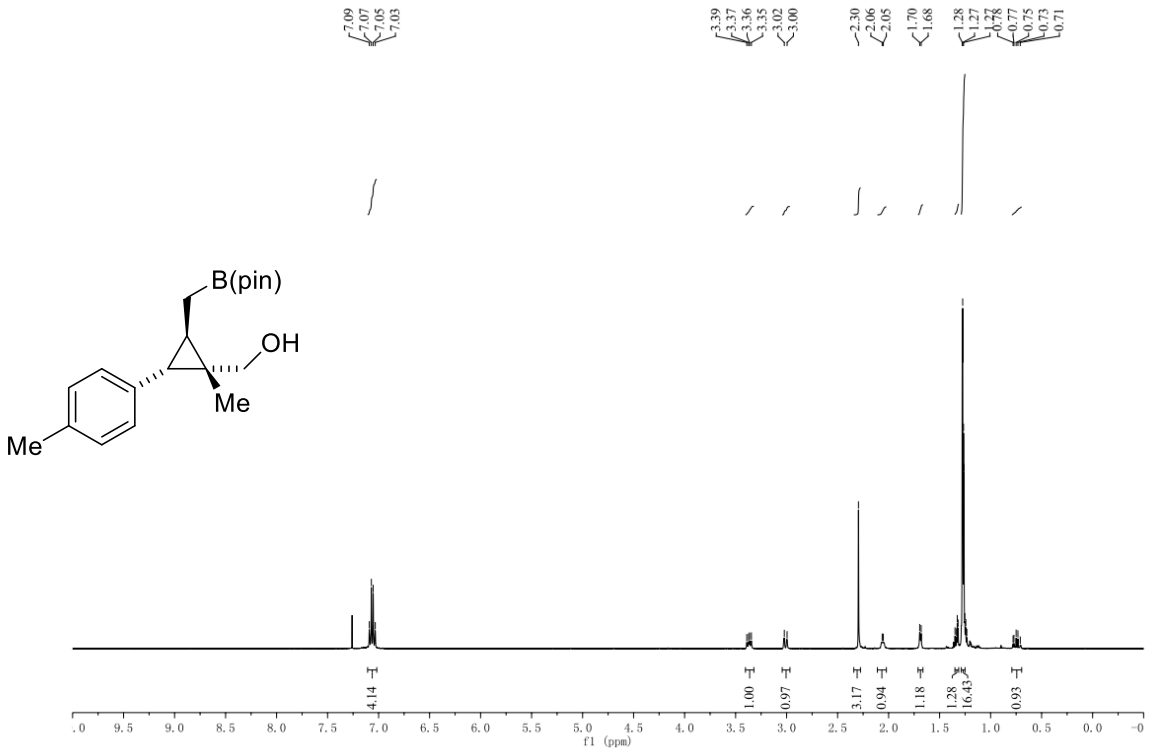
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 – 7.02 (m, 4H), 3.37 (dd, J = 10.9, 7.2 Hz, 1H), 3.01 (d, J = 10.9 Hz, 1H), 2.30 (s, 3H), 2.06 (brs, 1H), 1.35 – 1.31 (m, 1H), 1.29 – 1.25 (m, 16H), 0.78 – 0.71 (m, 1H).

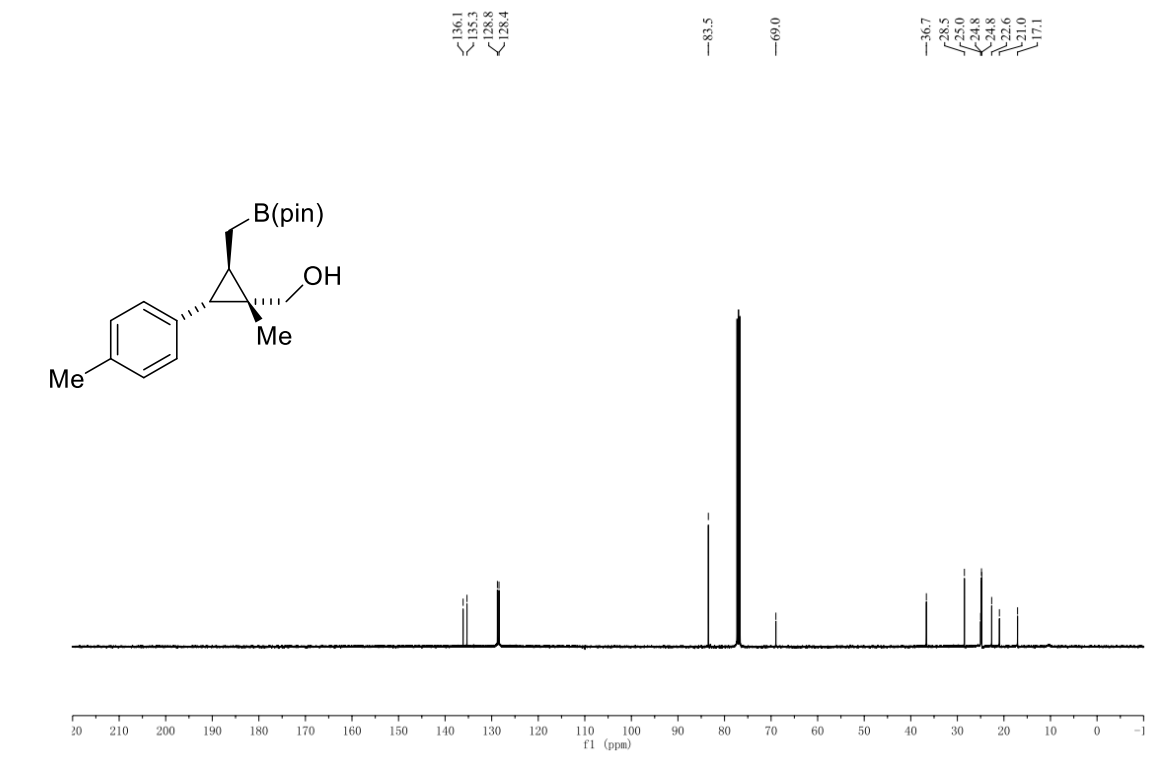
^{13}C NMR (100 MHz, $CDCl_3$) δ 136.1, 135.3, 128.8, 128.4, 83.5, 69.0, 36.6, 28.5, 25.0, 24.8, 24.8, 22.6, 21.0, 17.1.

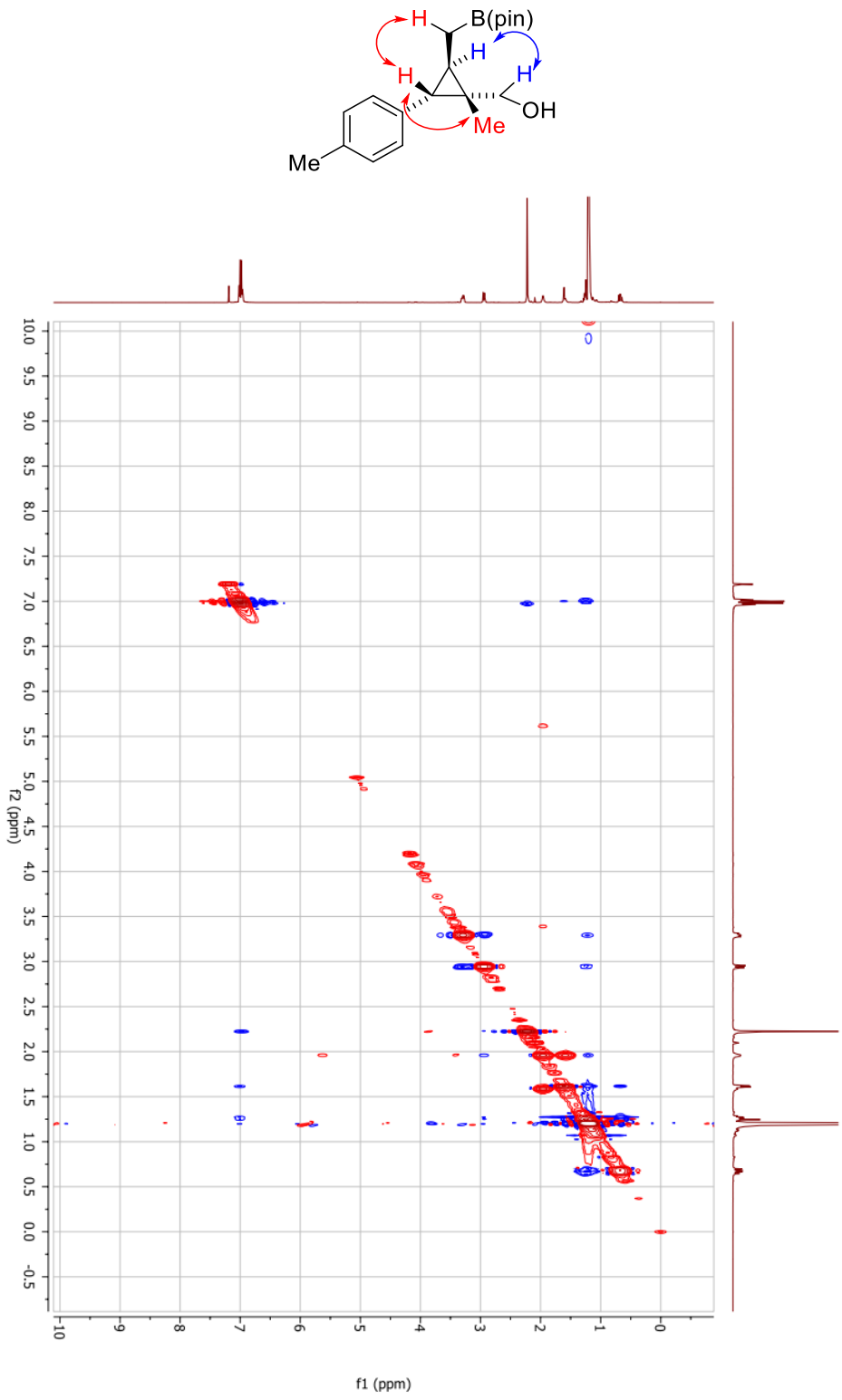
HRMS (CI) Calcd. for $C_{19}H_{29}BO_3^+$ $[M]^+$: 316.2204, Found: 316.2204.

$[\alpha]_D^{33}$: +38.7 (*c* = 1.0, $CHCl_3$).

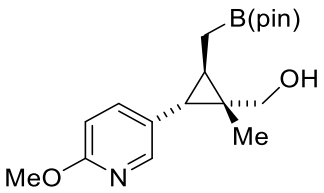
FTIR (neat): 3497, 2977, 2925, 1515, 1364, 1319, 1143, 1018, 967, 883, 848, 820, 748, 675 cm^{-1}


B(pin)
OH
Me
Me
7.09
7.07
7.05
7.03
3.39
3.37
3.36
3.35
3.02
3.00
2.30
2.06
2.05
1.70
1.68
1.28
1.27
0.78
0.77
0.75
0.73
0.71
4.14
1.00
0.97
3.17
0.94
1.18
1.28
16.43
0.93
f1 (ppm)


B(pin)
OH
Me
Me
136.1
135.3
128.8
128.4
83.5
69.0
36.7
28.5
25.0
24.8
24.8
22.6
21.0
17.1
f1 (ppm)


H
B(pin)
H
H
H
OH
Me
Me
f2 (ppm)
f1 (ppm)

((1*S*,2*S*,3*R*)-2-(6-methoxypyridin-3-yl)-1-methyl-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopropyl)methanol (3.3q)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1h** (24.9 mg, 0.1 mmol, 100 mol%), bis(pinacolato)diboron (50.8 mg, 0.2 mmol, 200 mol%), dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 45 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, CH_2Cl_2: acetone = 20:1–10:1) to furnish the title compound as a colorless oil (24.0 mg, 0.07 mmol) in 72% yield.

TLC (SiO_2) R_f = 0.41 (hexanes/ethyl acetate = 1:1).

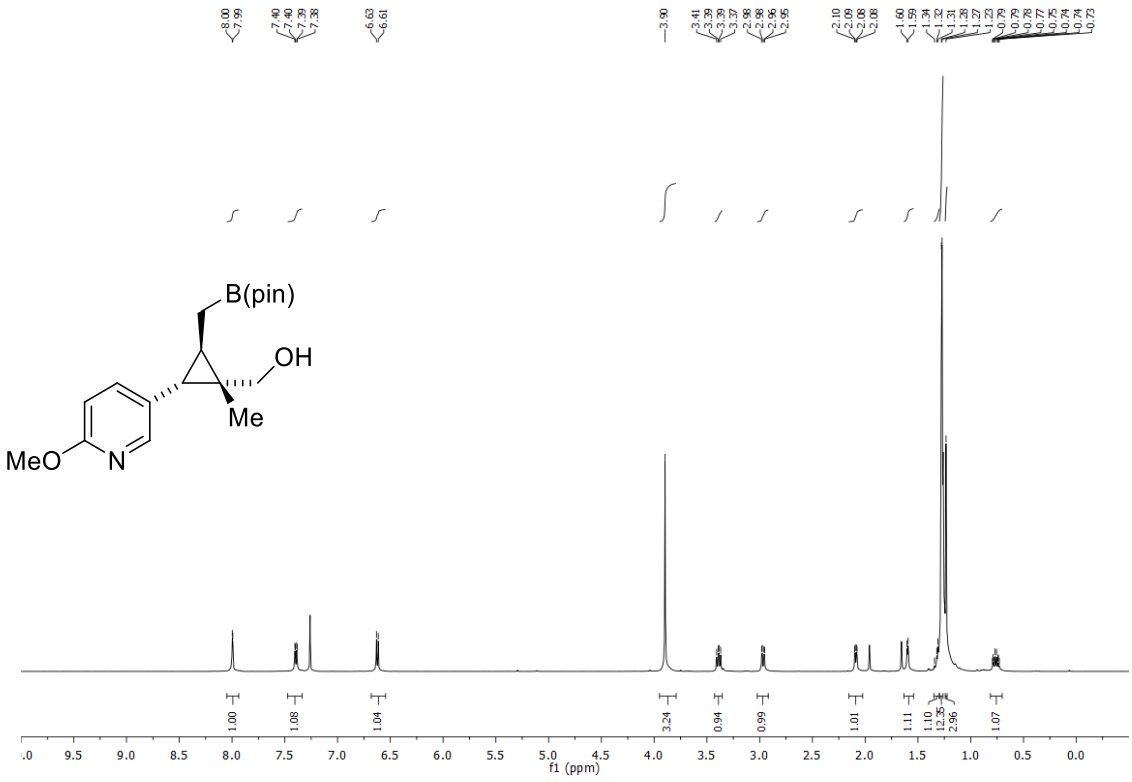
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 2.4 Hz, 1H), 7.39 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.62 (d, *J* = 8.5 Hz, 1H), 3.90 (s, 3H), 3.39 (dd, *J* = 10.9, 8.0 Hz, 1H), 2.97 (dd, *J* = 10.9, 2.9 Hz, 1H), 2.09 (dd, *J* = 8.2, 3.1 Hz, 1H), 1.60 (d, *J* = 5.4 Hz, 1H), 1.34 – 1.29 (m, *J* = 5.9 Hz, 1H), 1.27 (d, *J* = 3.2 Hz, 12H), 1.23 (s, 3H), 0.81 – 0.70 (m, 1H).

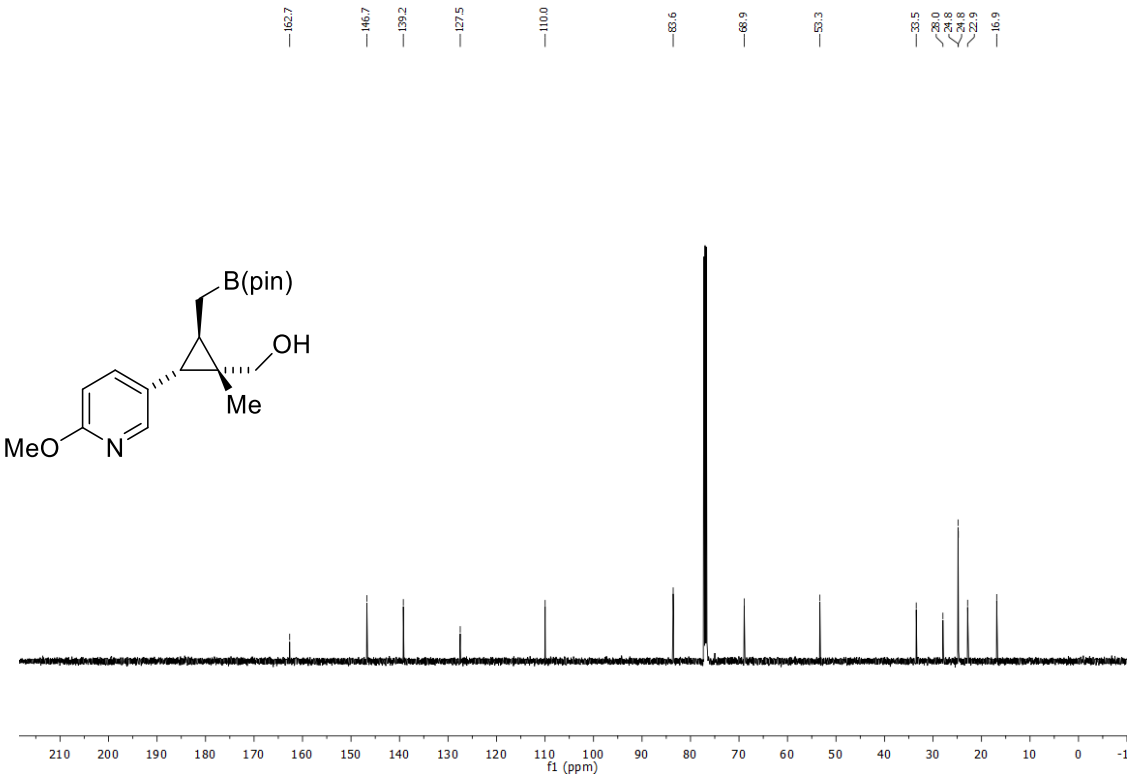
^{13}C NMR (125 MHz, $CDCl_3$) δ 162.7, 146.7, 139.2, 127.5, 110.0, 83.6, 68.9, 53.3, 33.5, 28.0, 24.8, 24.8, 22.9, 16.9.

HRMS (ESI) Calcd. for $C_{18}H_{28}BNO_4$ $[M+H]^+$: 334.2187, Found: 334.2192.

$[\alpha]_D^{25}$: +33.7 (*c* = 1.0, $CHCl_3$).

FTIR (neat): 3433, 2978, 1606, 1495, 1371, 1284, 1143, 1030, 967, 846, 755 cm^{-1}




162.7
146.7
139.2
127.5
110.0
83.6
68.9
53.3
33.5
28.0
24.8
24.8
22.9
16.9
B(pin)
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MeO
N
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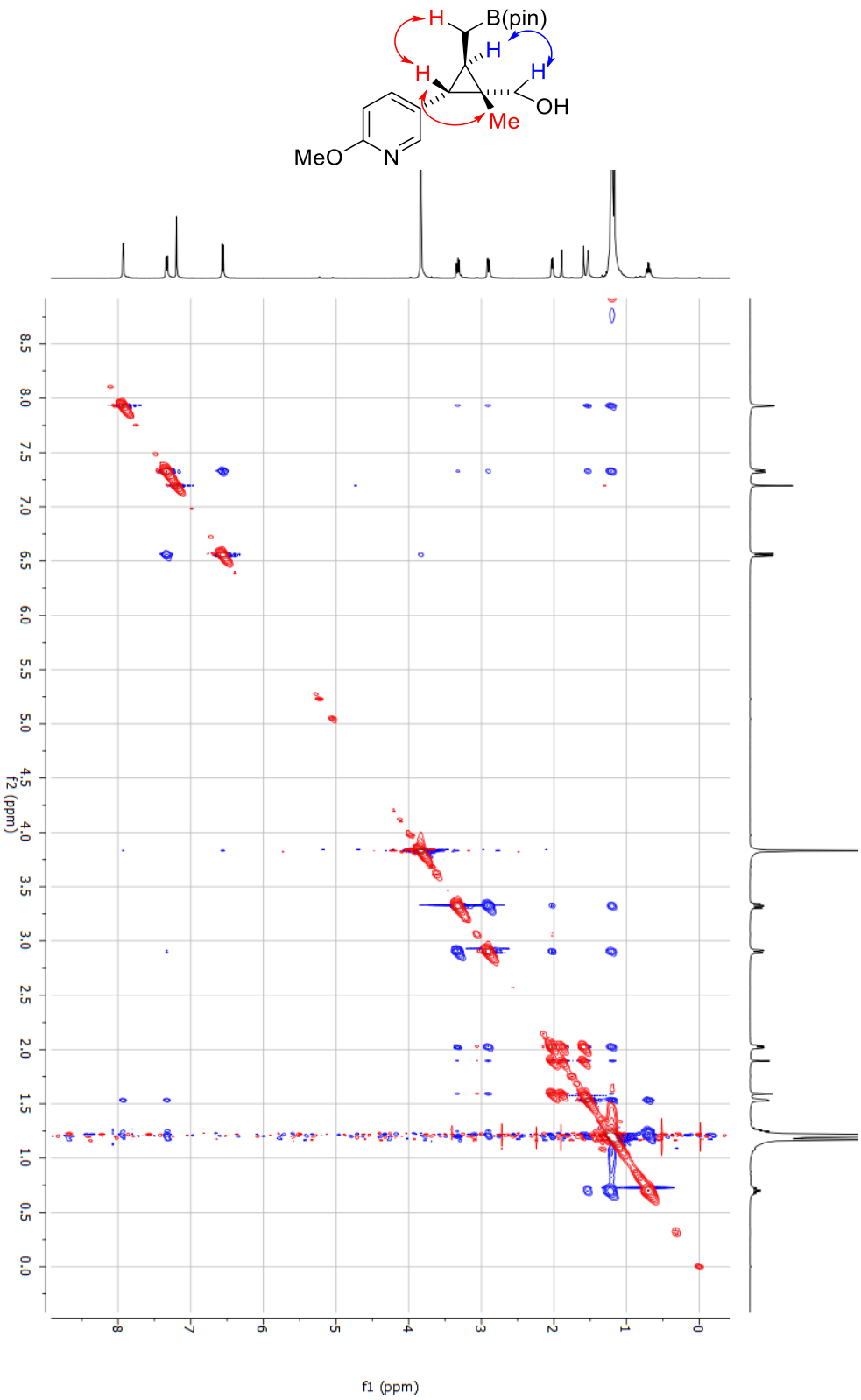
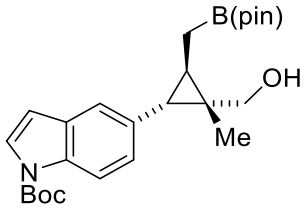
f1 (ppm)


H
B(pin)
H
H
H
OH
Me
MeO
N
f2 (ppm)
f1 (ppm)

***tert*-butyl 5-((1*S*,2*S*,3*R*)-2-(hydroxymethyl)-2-methyl-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopropyl)-1H-indole-1-carboxylate (3.3r)**



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1e** (35.7 mg, 0.1 mmol, 100 mol%), bis(pinacolato)diboron (50.8 mg, 0.2 mmol, 200 mol%), dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 75 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–10:1) to furnish the title compound as a colorless oil (33.1 mg, 0.08 mmol) in 75% yield.

TLC (SiO_2) R_f = 0.43 (hexanes/ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.5 Hz, 1H), 7.55 (d, *J* = 3.7 Hz, 1H), 7.38 (s, 1H), 7.17 (dd, *J* = 8.5, 1.6 Hz, 1H), 6.48 (d, *J* = 3.7 Hz, 1H), 3.43 – 3.32 (m, 1H), 3.00 (d,

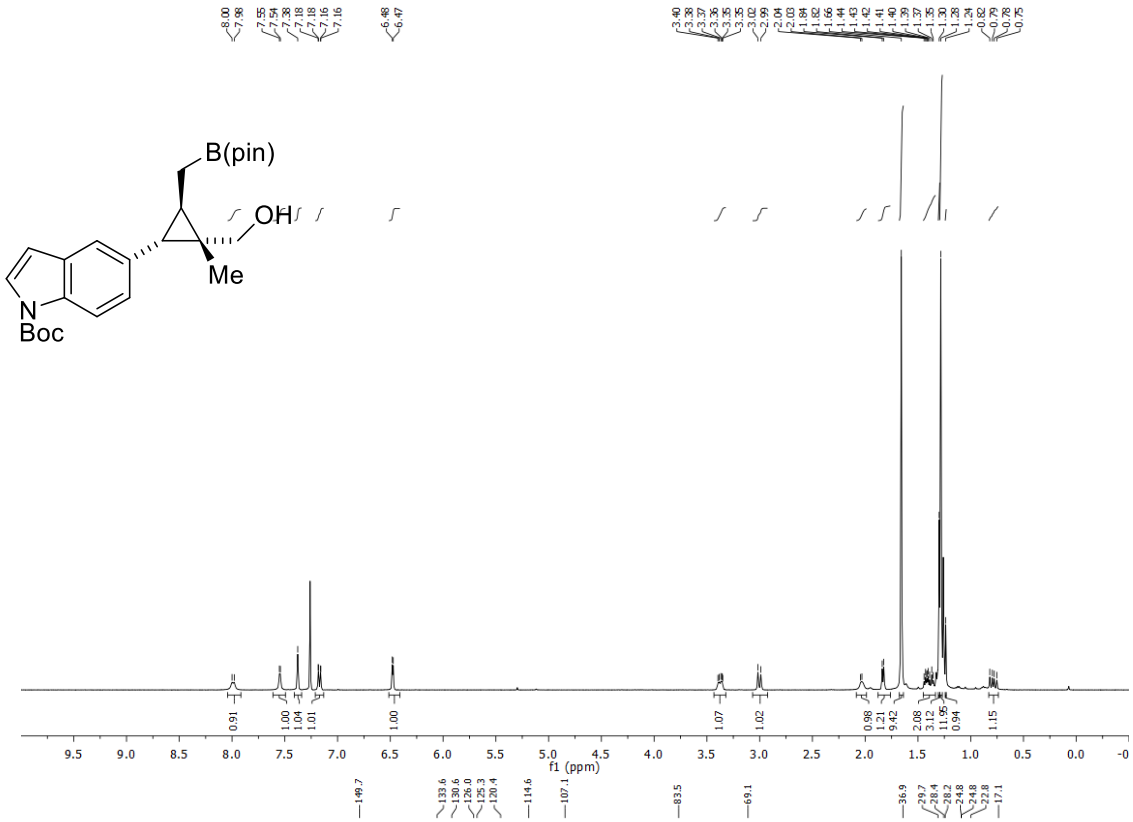
J = 11.0 Hz, 1H), 2.04 (d, *J* = 5.3 Hz, 1H), 1.83 (d, *J* = 6.0 Hz, 1H), 1.66 (s, 9H), 1.45 – 1.33 (m, 2H), 1.30 (s, 3H), 1.28 (s, 12H), 1.24 (s, 1H), 0.79 (dd, *J* = 16.9, 9.8 Hz, 1H).

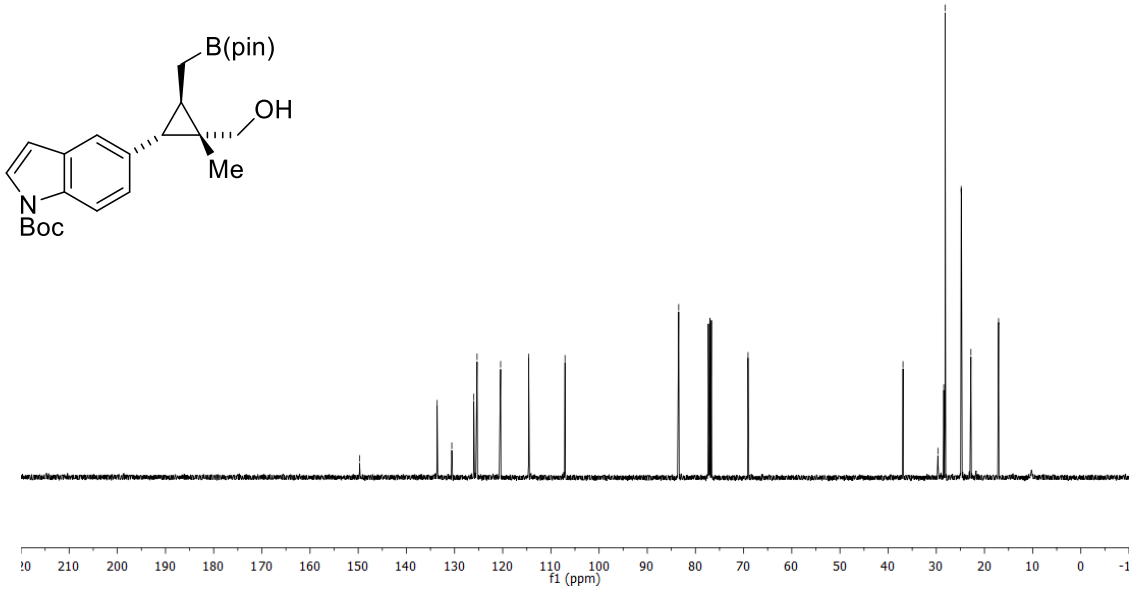
^{13}C NMR (125 MHz, $CDCl_3$) δ 149.7, 133.6, 130.6, 126.0, 125.3, 120.4, 114.6, 107.1, 83.5, 69.1, 36.9, 29.7, 28.5, 28.2, 24.8, 24.8, 22.8, 17.1.

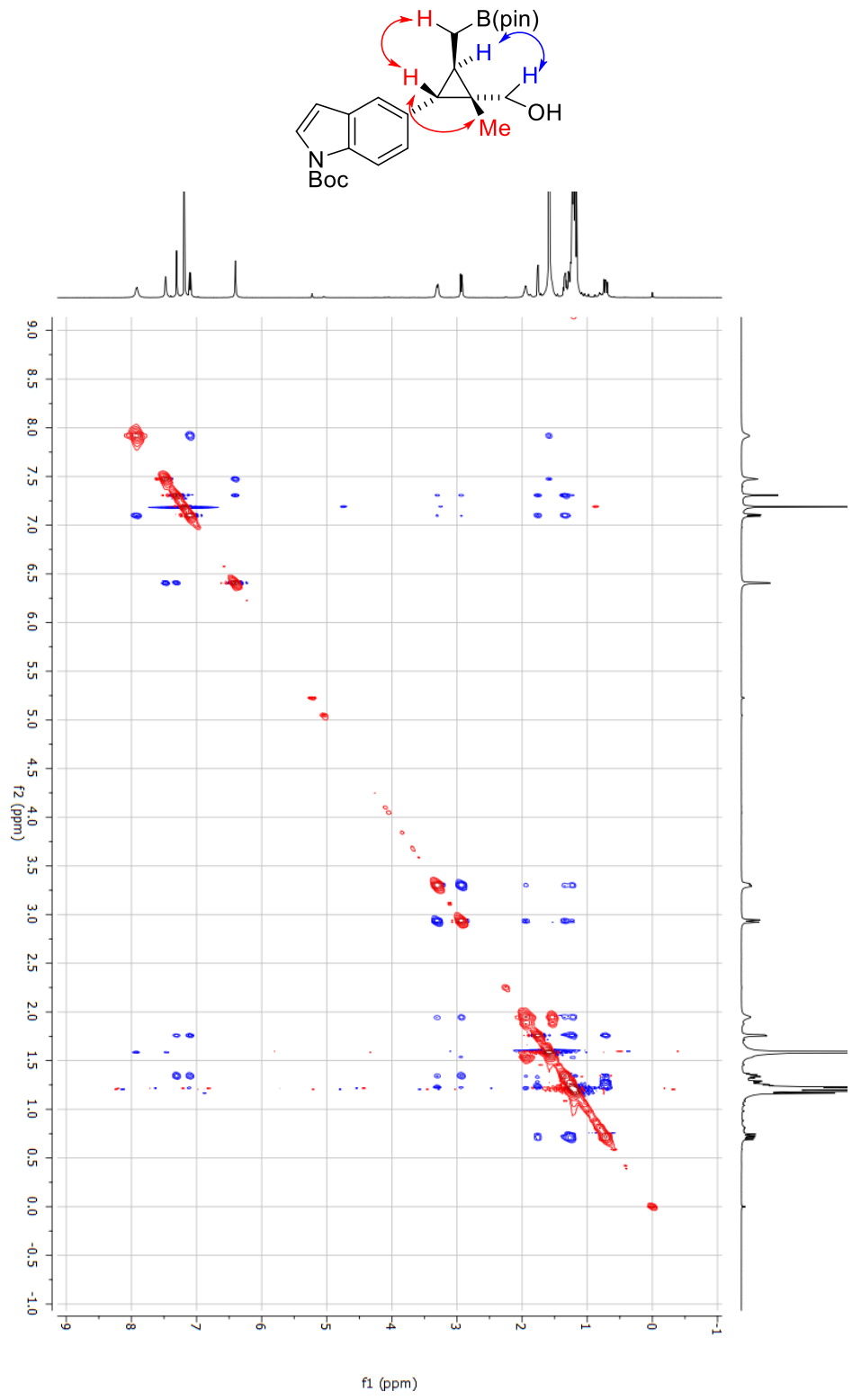
HRMS (ESI) Calcd. for $C_{25}H_{36}BNO_5$ $[M+K]^+$: 480.2323, Found: 480.2339.

$[\alpha]_D^{24}$: +31.7 (*c* = 1.0, $CHCl_3$).

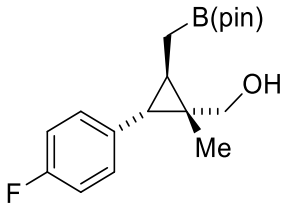
FTIR (neat): 3486, 2978, 1732, 1474, 1369, 1264, 1216, 1133, 1023, 797 cm^{-1}


B(pin)
OH
Me
N
Boc
f1 (ppm)


B(pin)
OH
Me
N
Boc
f1 (ppm)


H
B(pin)
H
H
H
OH
Me
N
Boc
f2 (ppm)
f1 (ppm)

((1*S*,2*S*,3*R*)-2-(4-fluorophenyl)-1-methyl-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopropyl)methanol (3.3s)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1b** (23.6 mg, 0.1 mmol, 100 mol%), bis(pinacolato)diboron (50.8 mg, 0.2 mmol, 200 mol%), dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 55 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1) to furnish the title compound as a colorless oil (24.3 mg, 0.076 mmol) in 76% yield.

TLC (SiO_2) R_f = 0.7 (hexanes/ethyl acetate = 1:1).

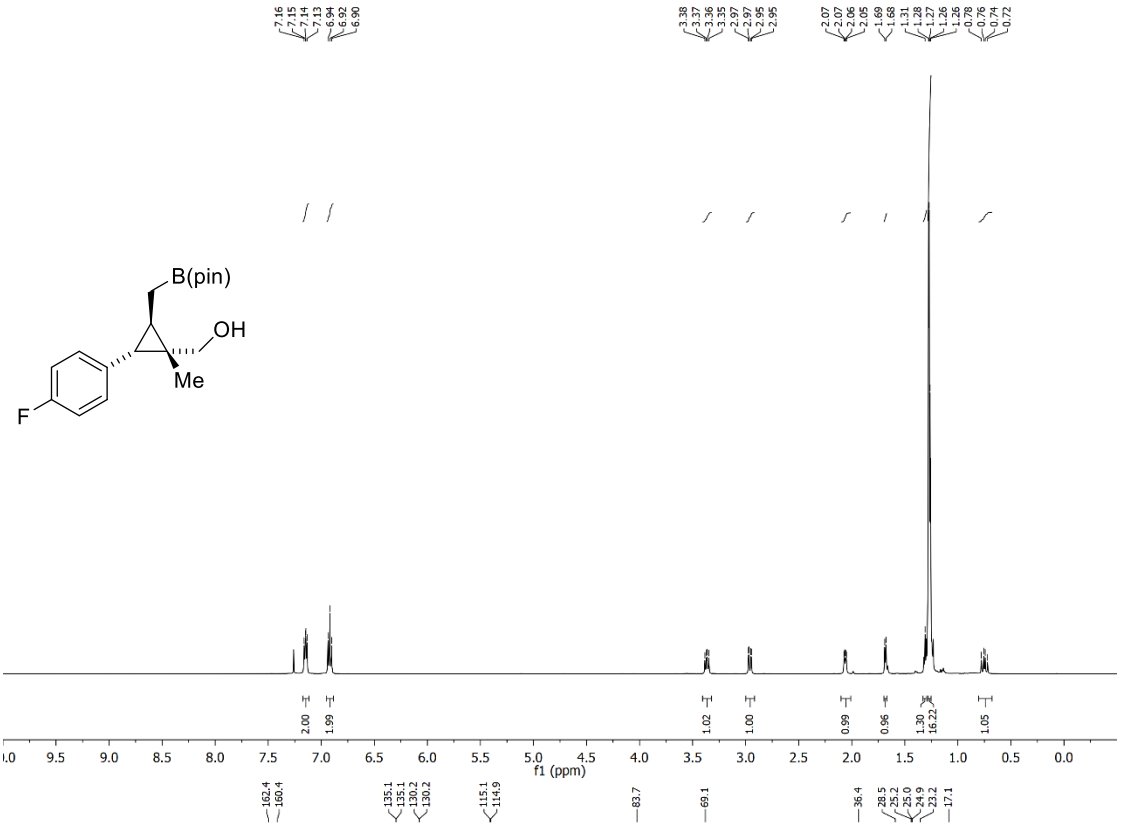
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (dd, *J* = 8.4, 5.5 Hz, 2H), 6.92 (t, *J* = 8.7 Hz, 2H), 3.37 (dd, *J* = 11.0, 7.7 Hz, 1H), 2.96 (dd, *J* = 11.0, 2.7 Hz, 1H), 2.06 (dd, *J* = 8.0, 3.2 Hz, 1H), 1.68 (d, *J* = 5.8 Hz, 1H), 1.32 – 1.29 (m, 1H), 1.28 – 1.25 (m, 16H), 0.75 (dd, *J* = 18.2, 11.2 Hz, 1H).

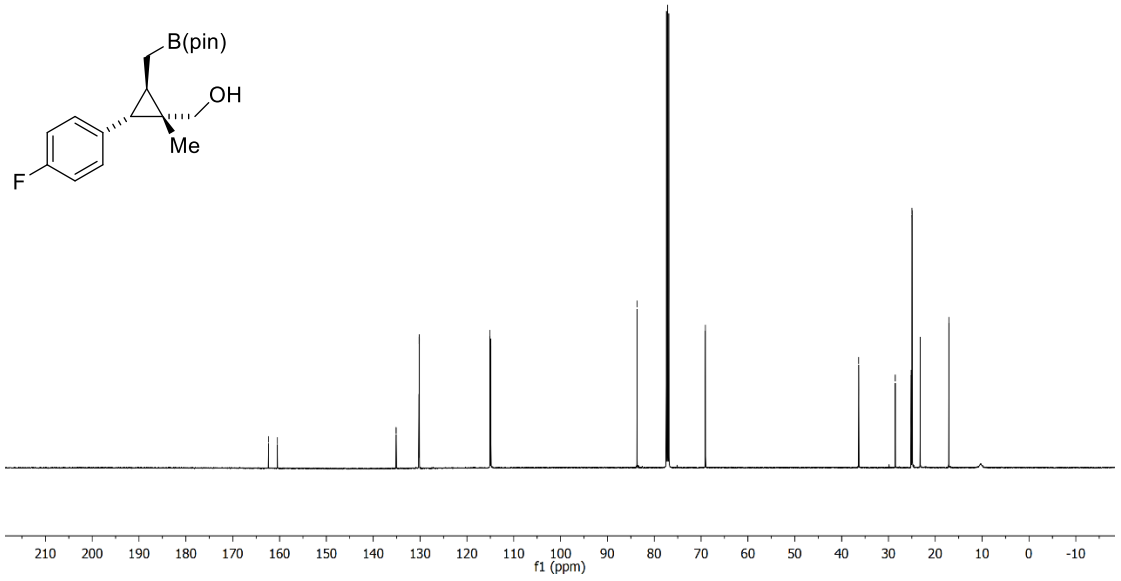
^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4 (d, J^1_{CF} = 243.9 Hz), 135.1 (d, J^4_{CF} = 3.1 Hz), 130.2 (d, J^3_{CF} = 7.8 Hz), 115.0 (d, J^2_{CF} = 21.1 Hz), 83.7, 69.1, 36.4, 28.5, 25.2, 25.0, 24.9, 23.2, 17.1.

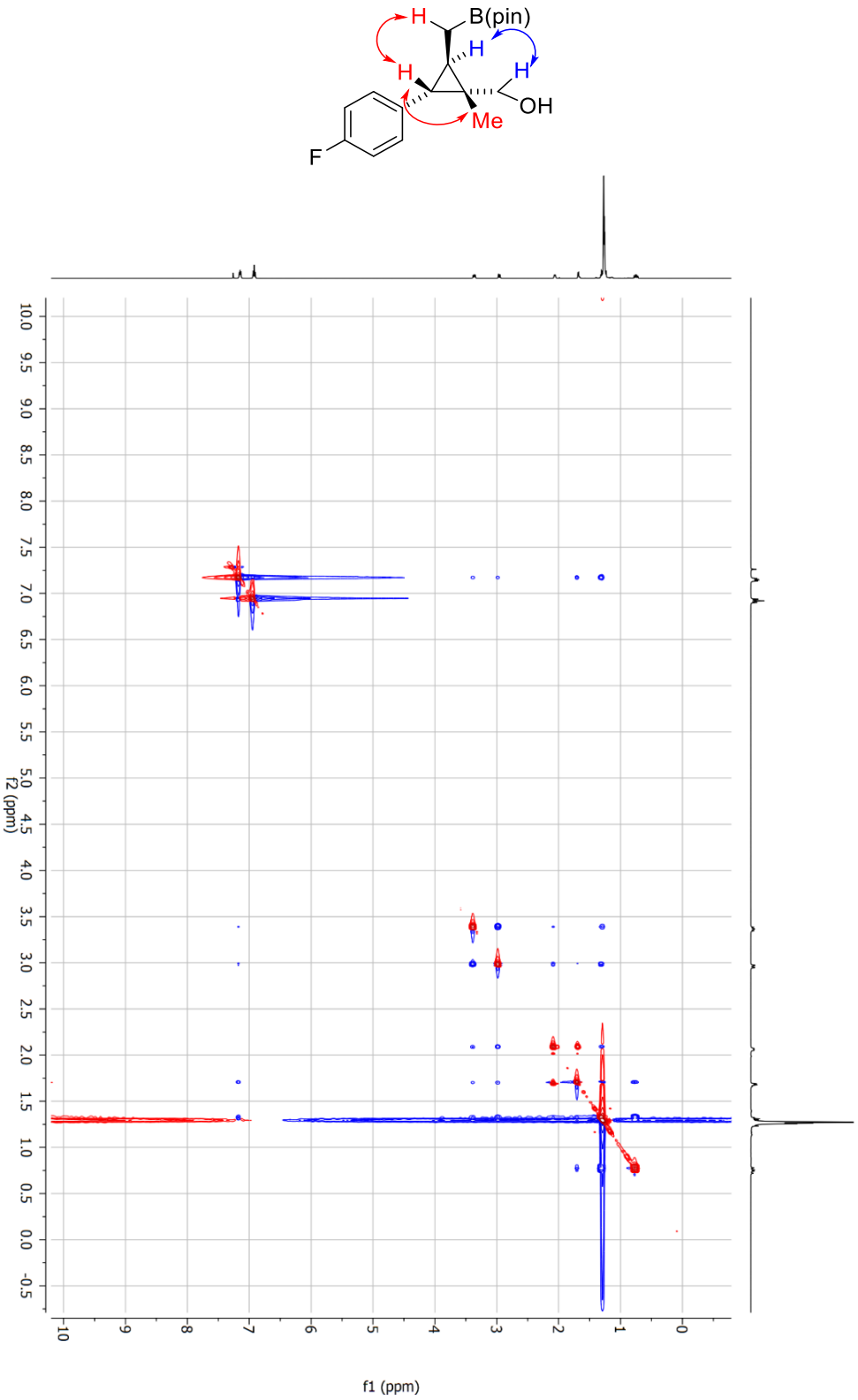
HRMS (ESI) Calcd. for $C_{18}H_{26}BFNaO_3$ $[M+Na]^+$: 343.1851, Found: 343.1857.

$[\alpha]_D^{24}$: +25.6 (*c* = 1.2, $CHCl_3$).

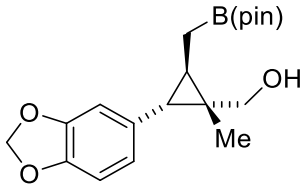
FTIR (neat): 1510, 1363, 1319, 1215, 1142, 1125, 1017, 967, 848, 756 cm^{-1}


B(pin)
OH
Me
F
f1 (ppm)


B(pin)
OH
Me
F
f1 (ppm)


H
B(pin)
H
H
H
OH
Me
F
f2 (ppm)
f1 (ppm)

((1*S*,2*S*,3*R*)-2-(benzo[d][1,3]dioxol-5-yl)-1-methyl-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)cyclopropyl)methanol (3.3t)



Detailed Procedures

An oven-dried sealed tube equipped with a magnetic stir bar was charged with vinyl-dioxanone **3.1d** (26.2 mg, 0.1 mmol, 100 mol%), bis(pinacolato)diboron (50.8 mg, 0.2 mmol, 200 mol%), dicyclohexylphenylphosphine (5.8 mg, 0.02 mmol, 20 mol%, 95%wt) and potassium phosphate (42.4 mg, 0.2 mmol, 200 mol%). This tube was transferred into an argon-atmosphere glovebox. $Ni(cod)_2$ (2.8 mg, 0.01 mmol, 10 mol%) and toluene (0.5 mL, 0.2 M) were added. After sealing the tube with cap, the tube was removed from the glovebox and the reaction mixture was stirred at 55 ˚C for 48 h. The reaction was cooled to ambient temperature, diluted with Et_2O (1 mL) and filtered through a plug of silica gel, which was rinsed with Et_2O (2 mL). The combined organic solution was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1) to furnish the title compound as a colorless oil (27.3 mg, 0.079 mmol) in 79% yield.

TLC (SiO_2) R_f = 0.25 (hexanes/ethyl acetate = 4:1).

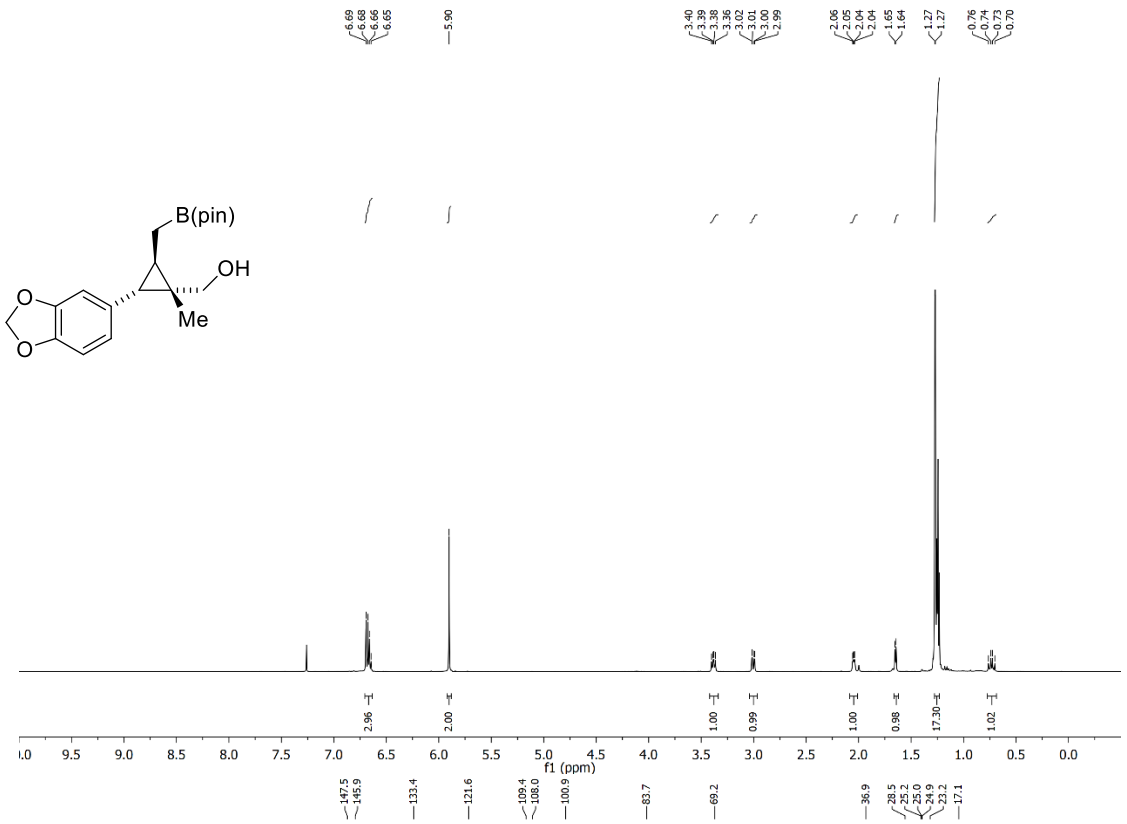
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.70 – 6.63 (m, 3H), 5.90 (s, 2H), 3.38 (dd, *J* = 10.9, 7.5 Hz, 1H), 3.00 (dd, *J* = 11.1, 2.8 Hz, 1H), 2.05 (t, *J* = 7.5, 3.0 Hz, 1H), 1.65 (d, *J* = 5.5 Hz, 1H), 1.28 – 1.23 (m, 17H), 0.73 (dd, *J* = 18.5, 11.2 Hz, 1H).

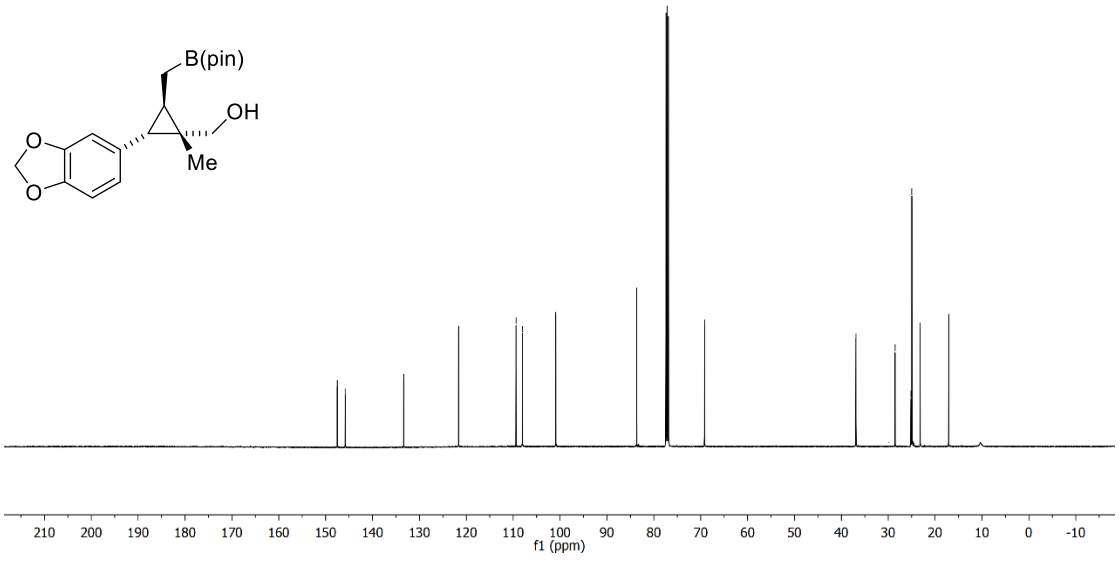
^{13}C NMR (125 MHz, $CDCl_3$) δ 147.5, 145.9, 133.4, 121.6, 109.4, 108.0, 100.9, 83.7, 69.2, 36.9, 28.5, 25.2, 25.0, 24.9, 23.2, 17.1.

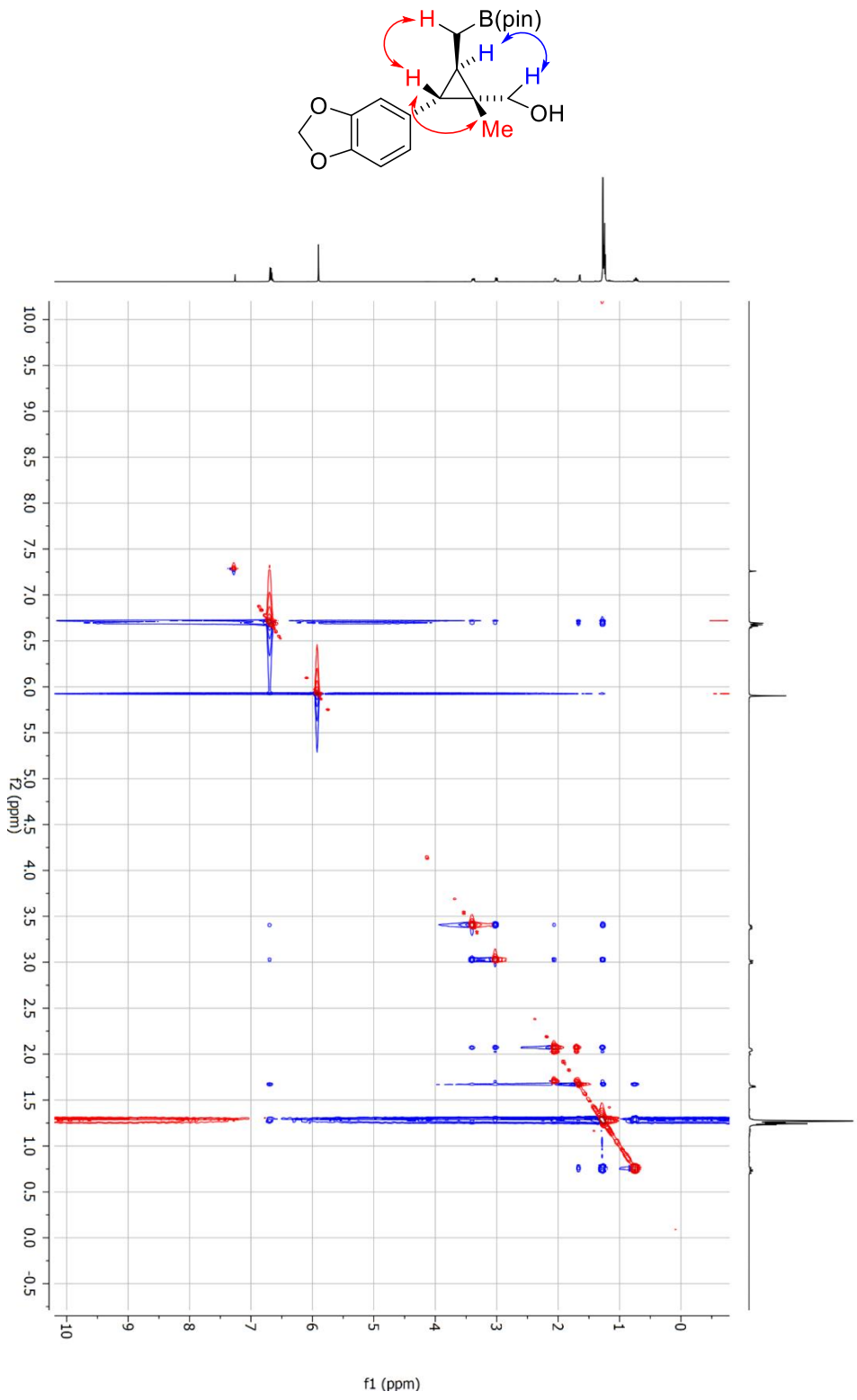
HRMS (ESI) Calcd. for $C_{19}H_{27}BNaO_5$ $[M+Na]^+$: 369.1844, Found: 369.1838.

$[\alpha]_D^{24}$: +57.3 (*c* = 1.1, $CHCl_3$).

FTIR (neat): 1504, 1491, 1441, 1365, 1316, 1232, 1193, 1142, 1038, 936, 879, 810, 759, 733 cm^{-1}

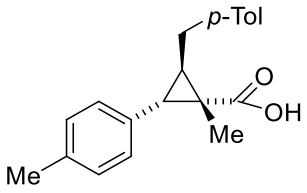

B(pin)
OH
Me
O
O
6.69
6.68
6.66
6.65
5.90
3.40
3.39
3.38
3.36
3.02
3.01
3.00
2.99
2.06
2.05
2.04
2.04
1.65
1.64
1.27
1.27
0.76
0.74
0.73
0.70
2.96
2.00
1.00
0.99
1.00
0.98
17.30
1.02
f1 (ppm)
147.5
145.9
133.4
121.6
109.4
108.0
100.9
83.7
69.2
36.9
28.5
25.2
25.0
24.9
23.2
17.1


B(pin)
OH
Me
O
O
f1 (ppm)


H
B(pin)
H
H
H
O
O
OH
Me
f2 (ppm)
f1 (ppm)

Procedures and Spectral Data for the Synthesis of 3.4a-3.4b:

(1*S*,2*R*,3*S*)-1-methyl-2-(4-methylbenzyl)-3-(*p*-tolyl)cyclopropane-1-carboxylic acid (3.4a)



Detailed Procedures

A vial equipped with a magnetic stir bar was charged with **3.3a** (22.4 mg, 0.08 mmol, 100 mol%). Under argon atmosphere, acetone (0.8 mL, 0.1 M) was added via syringe. The mixture was cooled to 0 °C and freshly prepared H_2CrO_4 (0.16 mL, 2.5 M, 500 mol%) was added dropwise. The reaction mixture was stirred at ambient temperature for 4 h. 2-propanol (0.5 mL) was slowly added. The mixture was filtered through a plug of sodium sulfate, which was rinsed with ethyl acetate (2 mL). The filtrate was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 3:1) to furnish the title compound as a colorless oil (17.8 mg, 0.06 mmol) in 76% yield.

TLC (SiO_2) R_f = 0.23 (hexanes/ethyl acetate = 3:1).

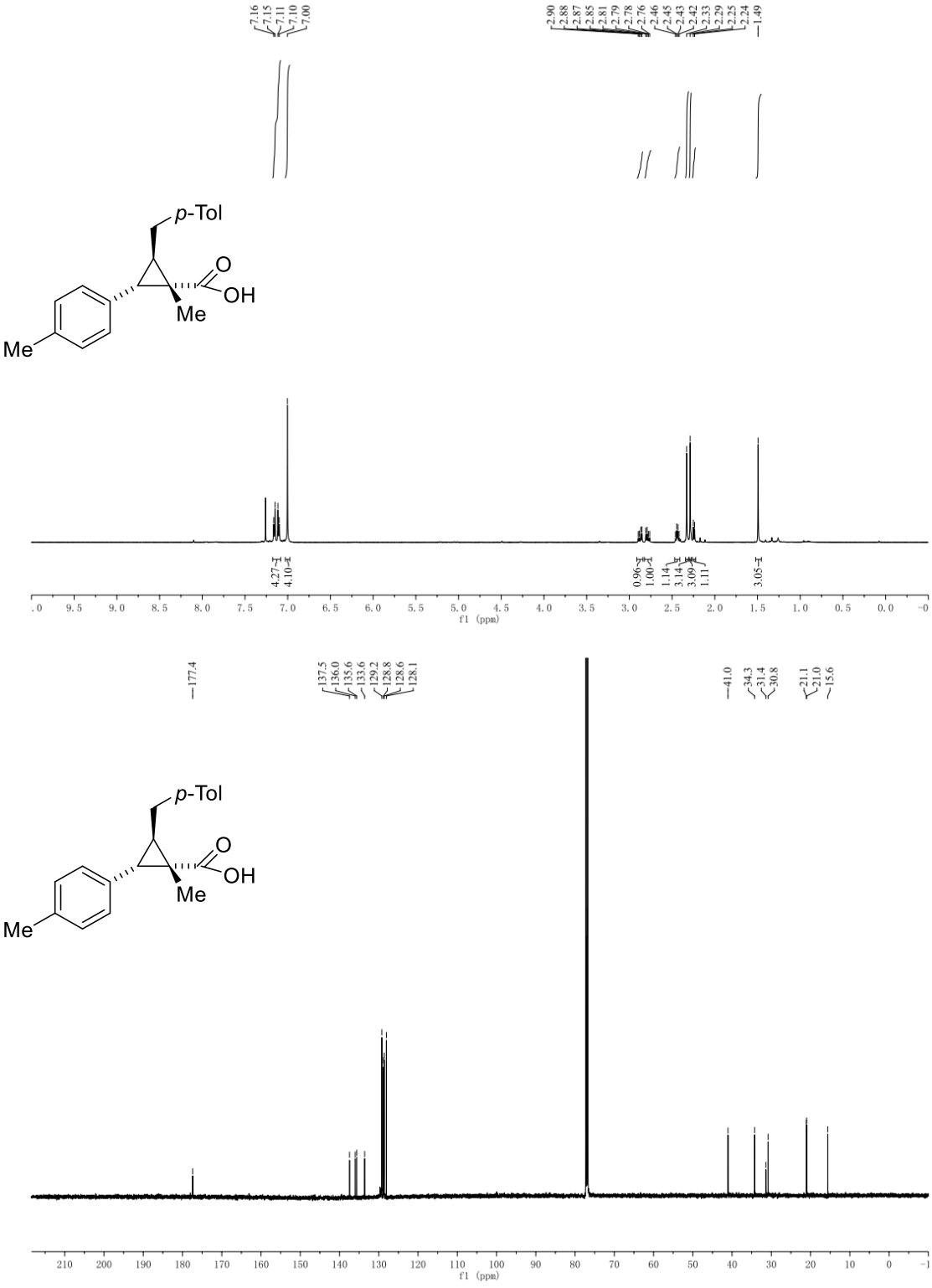
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 – 7.08 (m, 4H), 7.00 (s, 4H), 2.87 (dd, *J* = 15.1, 6.8 Hz, 1H), 2.79 (dd, *J* = 15.1, 7.7 Hz, 1H), 2.47 – 2.40 (m, 1H), 2.33 (s, 3H), 2.29 (s, 3H), 2.24 (d, *J* = 7.5 Hz, 1H), 1.49 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 177.4, 137.4, 136.0, 135.6, 133.6, 129.2, 128.8, 128.6, 128.1, 41.0, 34.2, 31.4, 30.8, 21.1, 21.0, 15.6.

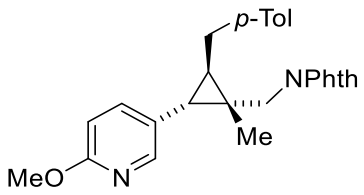
HRMS (ESI) Calcd. for $C_{20}H_{22}NaO_2^+$ $[M+Na]^+$: 317.1512, Found: 317.1512.

$[\boldsymbol{\alpha}]_{\mathbf{D}}^{\mathbf{34}}$: -10.0 (*c* = 0.88, $CHCl_3$).

FTIR (neat): 2921, 2361, 1686, 1515, 1461, 1419, 1306, 1218, 1119, 1021, 915, 807 cm^{-1}


7.16
7.15
7.11
7.10
7.00
2.90
2.88
2.87
2.85
2.81
2.79
2.78
2.76
2.46
2.45
2.43
2.42
2.33
2.29
2.25
2.24
1.49
p-Tol
O
OH
Me
Me
4.27
4.10
0.96
1.00
1.14
3.14
3.09
1.11
3.05
f1 (ppm)
177.4
137.5
136.0
135.6
133.6
129.2
128.8
128.6
128.1
41.0
34.3
31.4
30.8
21.1
21.0
15.6
p-Tol
O
OH
Me
Me
f1 (ppm)

2-(((1S,2R,3R)-2-(6-methoxypyridin-3-yl)-1-methyl-3-(4-methylbenzyl)cyclopropyl)methyl) isoindoline-1,3-dione (3.4b)



Detailed Procedures

An oven-dried vial equipped with a magnetic stir bar was charged with **3.3h** (29.7 mg, 0.1 mmol, 100 mol%), triphenylphosphine (39.3 mg, 0.15 mmol, 150 mol%), phthalimide (22.1 mg, 0.15 mmol, 150 mol%). Under argon atmosphere, THF (1 mL, 0.1 M) was added via syringe. DEAD (65.3 mg, 0.15 mmol, 150 mol%, 40% w/w in toluene) was added slowly at ambient temperature. The mixture was stirred at 25 ˚C for 2 h. Saturated $NaHCO_3$ was added and the mixture was extracted by EA (20 mL x 2), dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 4:1) to furnish the title compounds as oil (37.4 mg, 0.88 mmol) in 88% yield.

TLC (SiO_2) R_f = 0.20 (hexanes/ethyl acetate = 4:1).

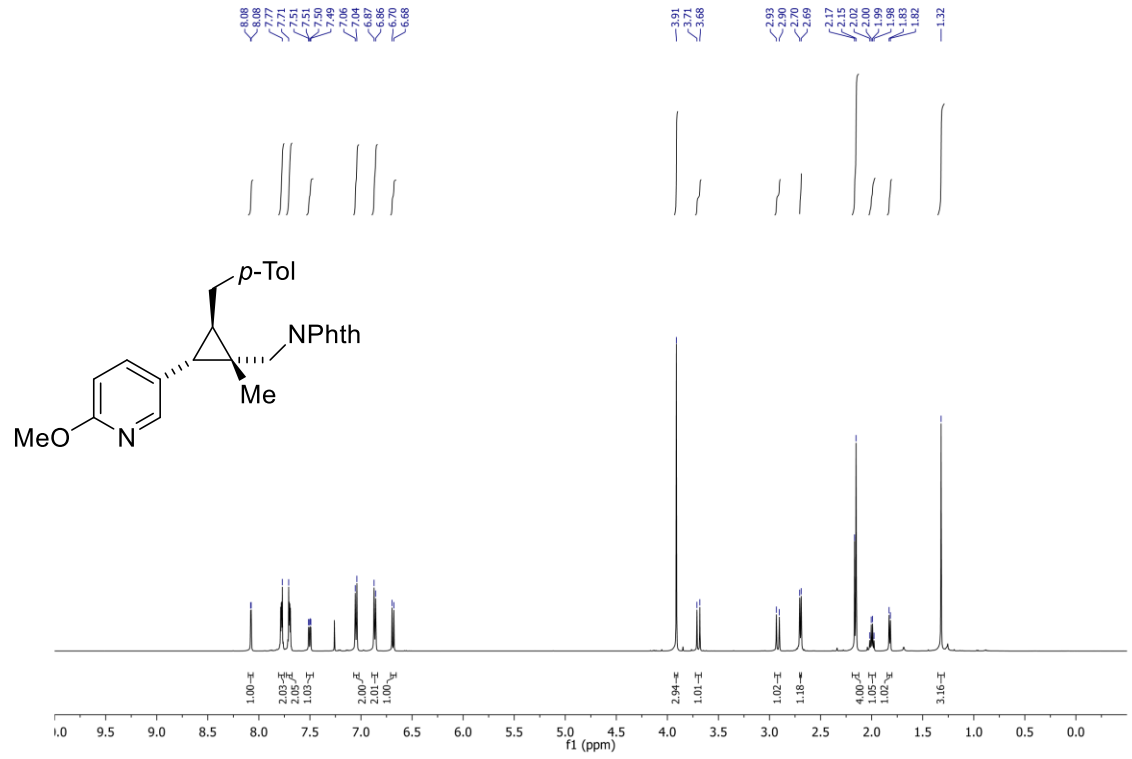
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 2.5 Hz, 1H), 7.77 (s, 2H), 7.71 (s, 2H), 7.50 (dd, *J* = 8.5, 2.4 Hz, 1H), 7.05 (d, *J* = 7.7 Hz, 2H), 6.86 (d, *J* = 7.7 Hz, 2H), 6.69 (d, *J* = 8.5 Hz, 1H), 3.91 (s, 3H), 3.70 (d, *J* = 14.2 Hz, 1H), 2.92 (d, *J* = 14.2 Hz, 1H), 2.70 (d, *J* = 7.3 Hz, 1H), 2.17 – 2.14 (m, 4H), 2.00 (q, *J* = 7.1 Hz, 1H), 1.82 (d, *J* = 6.3 Hz, 1H), 1.32 (s, 3H).

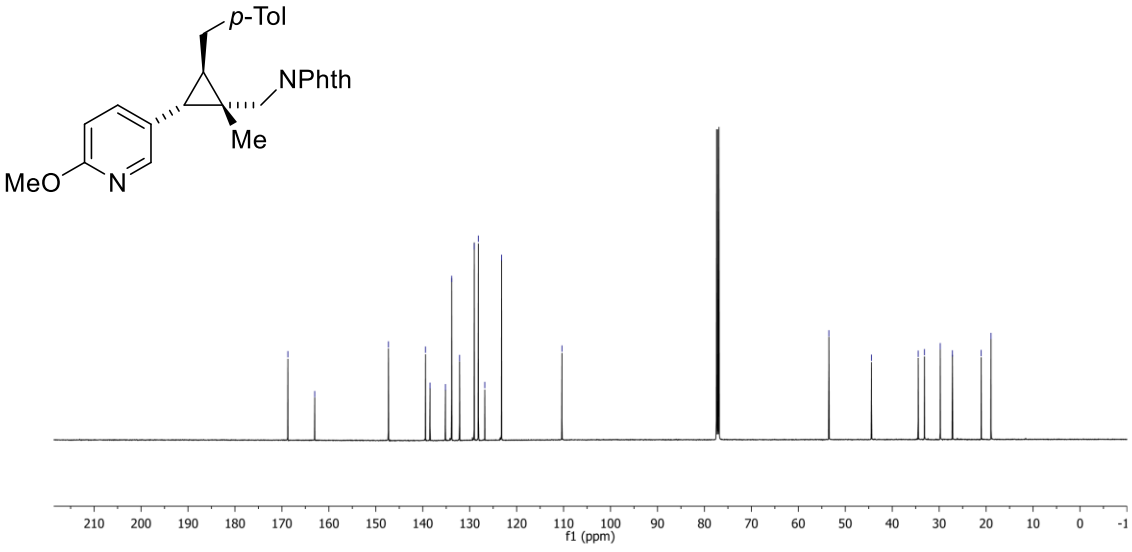
^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 163.0, 147.3, 139.4, 138.5, 135.2, 133.8, 132.2, 129.0, 128.2, 126.8, 123.2, 110.4, 53.5, 44.4, 34.5, 33.1, 29.8, 27.2, 21.1, 19.0.

HRMS (ESI) Calcd. for $C_{27}H_{26}N_2NaO_3^+$ $[M+Na]^+$: 449.1836, Found: 449.1840

$[\alpha]_D^{30}$: +97.0 (c = 1.0, $CHCl_3$)

FTIR (neat): 1709, 1493, 1396, 1383, 1349, 1285, 1259, 1060, 1024, 927, 833, 732, 711 cm^{-1}


p-Tol
NPhth
Me
MeO
N
f1 (ppm)

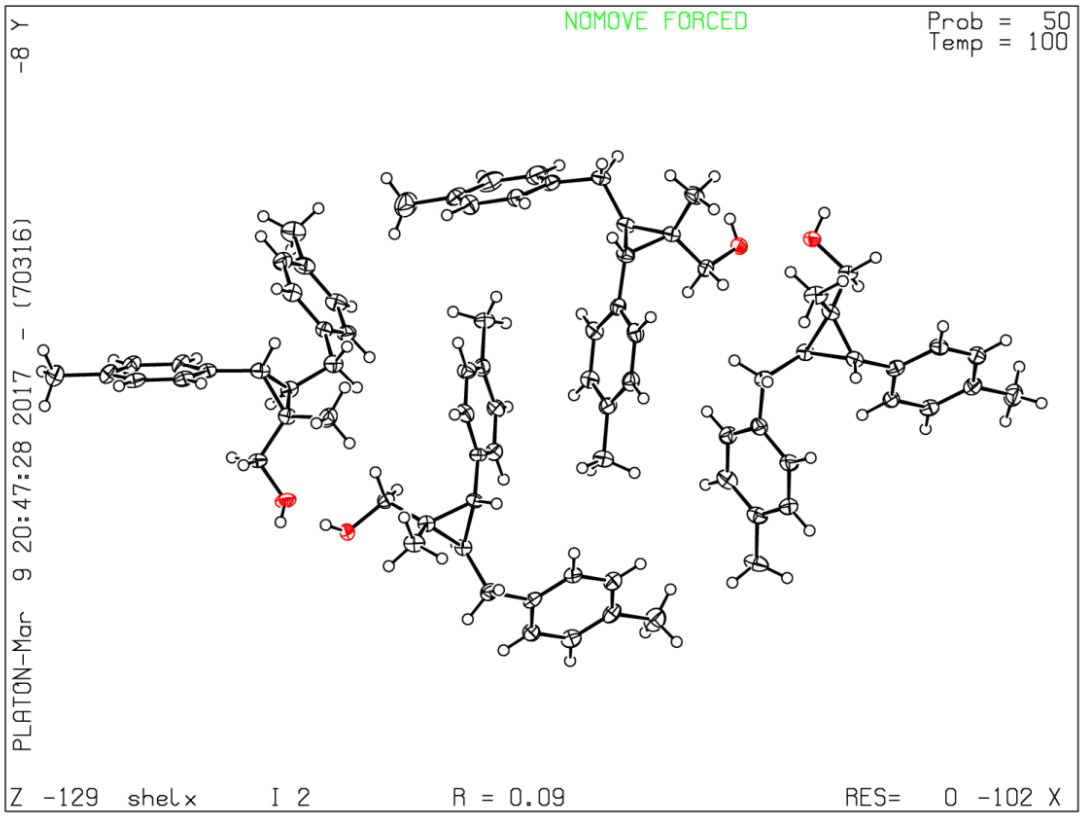

p-Tol
NPhth
Me
MeO
N
f1 (ppm)

Crystallographic Material for 3.3a:

Table 1. Crystal data and structure refinement for 1.

Empirical formula	C20 H24 O	
Formula weight	280.39	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	I 2	
Unit cell dimensions	a = 34.187(2) Å	□= 90°.
	b = 5.8361(4) Å	□= 91.395(7)°.
	c = 33.294(3) Å	□ = 90°.
Volume	6640.8(8) $Å^3$	
Z	16	
Density (calculated)	1.122 Mg/m^3	
Absorption coefficient	0.510 mm^{-1}	
F(000)	2432	
Crystal size	0.350 x 0.038 x 0.032 mm^3	
Theta range for data collection	2.586 to 75.298°.	
Index ranges	-42<=h<=41, -3<=k<=7, -41<=l<=41	
Reflections collected	11258	
Independent reflections	8398 [R(int) = 0.0792]	
Completeness to theta = 67.684°	98.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00 and 0.408	

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8398 / 505 / 773
Goodness-of-fit on F^2	1.122
Final R indices [I>2sigma(I)]	R1 = 0.0897, wR2 = 0.2422
R indices (all data)	R1 = 0.1131, wR2 = 0.2616
Absolute structure parameter	-0.3(6)
Extinction coefficient	n/a
Largest diff. peak and hole	0.403 and -0.404 e.Å^{-3}



Chapter 4: Amphiphilic π-Allyliridium *C,O*-Benzoates Enable Regio- and Enantioselective Amination of Branched Allylic Acetates Bearing Linear Alkyl Groups*

4.1 Introduction

Since the discovery of the Tsuji-Trost reaction,[1] diverse catalytic systems for metal catalyzed allylic substitution have emerged.[2] Among the many useful transformations based on this pattern of reactivity, enantioselective iridium catalyzed aminations figure prominently.[3-11] Largely due to the pioneering work of Takeuchi,[3,4] Helmchen,[5,6] Hartwig,[7,8] Carreira[9] and You,[10,11] a broad range of amine nucleophiles can now be accommodated in highly regio- and enantioselective reactions of linear or branched allylic acetates (and in certain cases allylic alcohols).[3-11] Two classes of iridium catalysts may be distinguished on the basis of their ability to promote regio- and enantioselective reactions of either linear or branched allylic acetates (Figure 1). For type I catalysts, linear allyl proelectrophiles are used under basic conditions. For type II catalysts, branched allyl proelectrophiles are used under acidic conditions. While type I catalysts are modified by one phosphoramidite and one external diene ligand, type II catalysts incorporate an internal mono-olefin ligand and two phosphoramidites, which may account for their exceptional electrophilicity. The internal olefin of type II catalysts may enhance enantioselectivity in reactions of branched allyl proelectrophiles by displacing the π-bond of (σ+π)-allyl (enyl) iridium intermediates,[12] thus enabling rapid π-facial interconversion in otherwise stereospecific substitutions.[13]

*This chapter is based on the published work:
Meza, A. T.; Wurm, T.; Smith, L.; Kim, S. W.; Zbieg, J. R.; Stivala, C. E.; Krische, M. J. *J. Am. Chem. Soc.* **2018**, *140*, 1275.

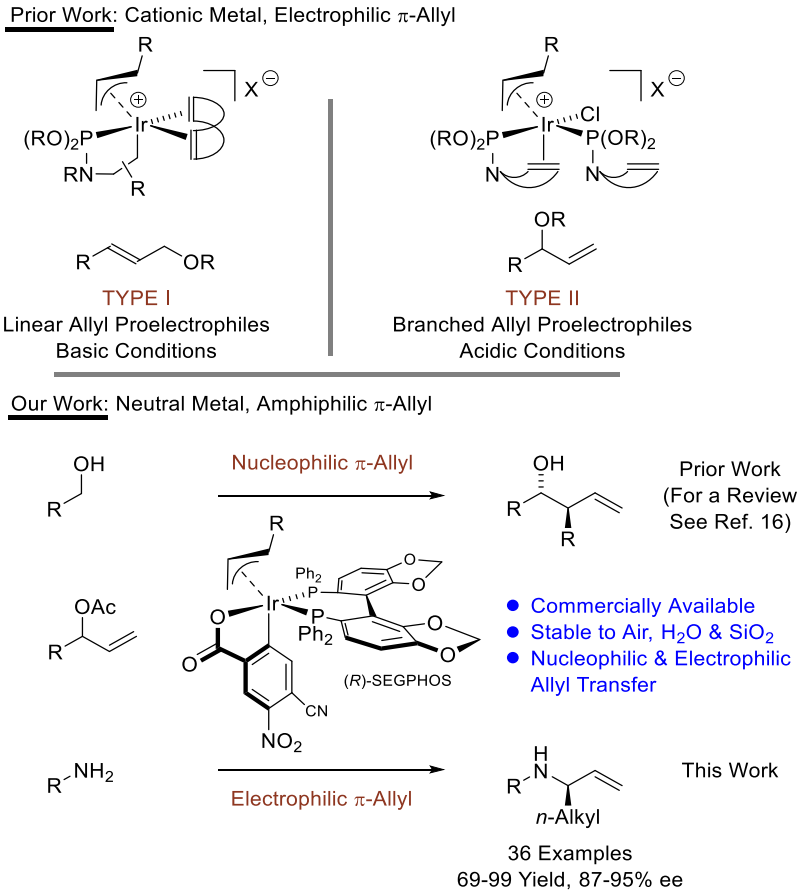


Figure 4.1 Phosphoramidite modified iridium complexes and amphiphilic π-allyliridium *C,O*-benzoates for regio- and enantioselective allylic amination.

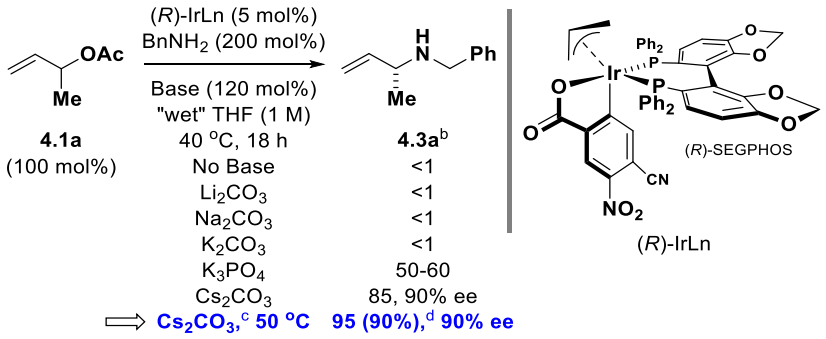
Both type I and II catalysts bear π-acidic ligands and a formal positive charge at the metal center. These features enforce electrophilic properties of the allyliridium intermediate. In contrast, we have developed π-allyliridium *C,O*-benzoates, which are neutral and incorporate relatively strong σ-donor ligands (Figure 4.1).[14,15] As demonstrated by their ability to promote diverse allylative carbonyl additions, the supporting ligands of this catalyst confer nucleophilic character onto the allyl moiety.[16] However, as observed in our initial studies,[14b] carbonyl allylation is often accompanied

by small quantities of *O*-allylation, suggesting amphiphilic character of these π-allyl complexes. Pursuant to an accumulation of similar observations by coauthors at Genentech, a systematic attempt to evoke electrophilic behavior was undertaken in the context of allylic amination. Here, we show that the commercially available π-allyliridium *C,O*-benzoate modified by SEGPHOS catalyzes asymmetric allylic amination. This catalyst overcomes a significant limitation in scope across all known catalytic systems – the ability to engage branched allylic acetates bearing linear alkyl groups with uniformly high levels of regio- and enantioselectivity.[3-11,17,18]

4.2 Reaction Development and Scope

In an initial set of experiments, α-methyl allyl acetate **4.1a** (100 mol%) was exposed to benzyl amine **4.2a** (200 mol%) in the presence of the SEGPHOS modified π-allyliridium *C,O*-benzoate (5 mol%) in THF (1 M) at 40 ^{o}C (Table 4.1). In the absence of base, products of amination were not observed. However, after screening various heterogeneous bases, it was found that reactions conducted in the presence of Cs_2CO_3 (120 mol%) provided the desired product of allylic amination **4.3a** exclusively as the branched regioisomer with high levels of enantiomeric enrichment. After further optimization, the allylic amine **4.3a** could be obtained in 90% isolated yield as a single regioisomer in 90% enantiomeric excess. Wet THF solvent is required, perhaps to partially solubilize Cs_2CO_3. Using distilled THF under otherwise optimal conditions, **4.3a** was obtained in only 61% yield. Optimal yields were re-stored using distilled THF in combination with water (250 mol%). The absolute stereochemistry of **4.3a** was determined by comparison of its optical rotation to that of an authentic sample reported in the literature (and x-ray analysis of **4.3j′**).[19]

Table 4.1 Influence of Base in the Amination of α-Methyl Allyl Acetate **4.1a** to Form Allylic Amine **4.3a**.[a]

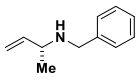
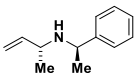
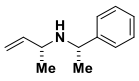
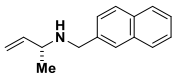
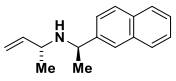
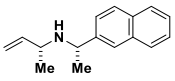
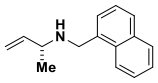
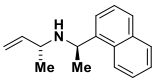
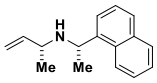
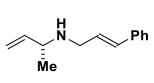
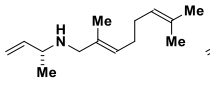
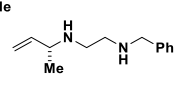
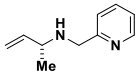
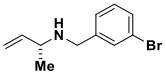
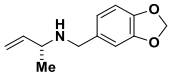
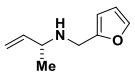
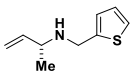
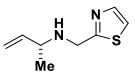
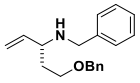
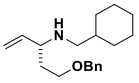
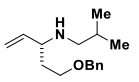
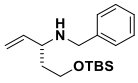
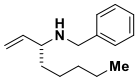
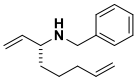
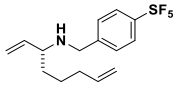
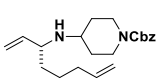
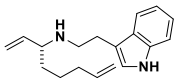
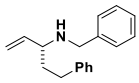
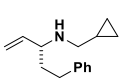
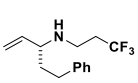
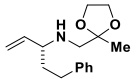
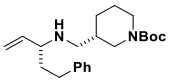
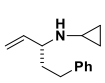
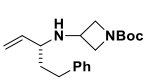
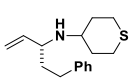
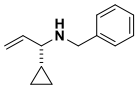


[a]All reactions were performed on a 0.44 mmol scale. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details. [b]Conversion was determined by ^{1}H NMR. [c]Cs_2CO_3 (200 mol%). [d]Yield of material isolated by silica gel chromatography.

Under these optimized conditions, primary benzylic, allylic and aliphatic amines serve as nucleophilic partners in aminations of diverse branched allylic acetates (Table 4.2). Complete branched-regioselectivity was accompanied by high levels of enantioselectively (^{1}H NMR & HPLC). Additionally, the levels of chemoselectivity in favor of primary amine allylation were sufficiently high that *N*-benzyl ethylene diamine and tryptamine could be converted to the respective amination products **4.3l** and **4.3a′** without competing allylation of the secondary amine. As demonstrated by the formation of **4.3z**, **4.3g′**, **4.3h′**, **4.3i′**, primary amines that are branched at the α-position are effective nucleophilic partners. Further, as illustrated by the formation of **4.3b** vs **4.3c**, **4.3e** vs **4.3f** and **4.3h** vs **4.3i**, excellent levels of catalyst-directed stereoinduction are observed. Perhaps the notable feature of this catalytic system, however, resides in the ability to engage branched allylic acetates bearing linear alkyl groups in highly regio- and

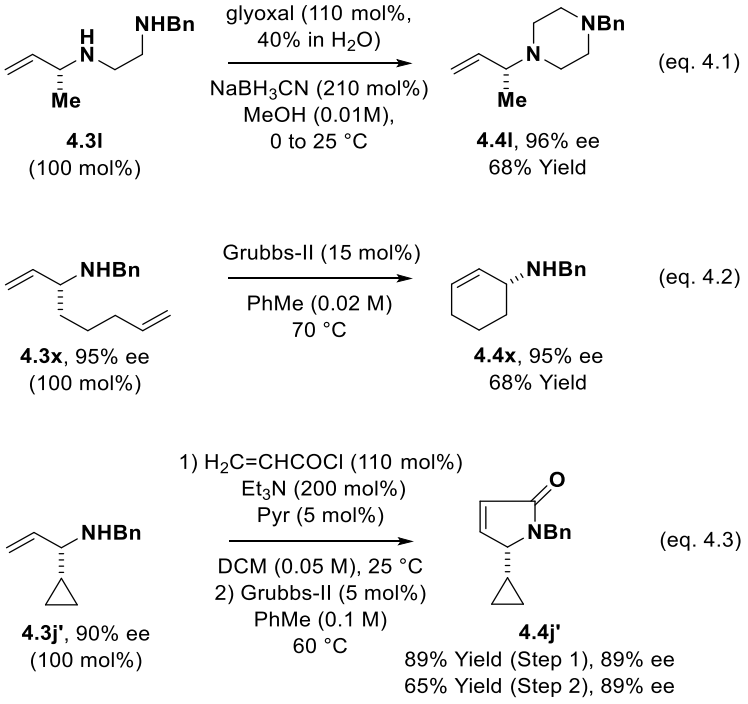
enantioselective aminations – a capability that complements the scope of previously reported iridium catalysts for allylic amination.[3-11,17,18]

Table 4.2 Regio- and Enantioselective Iridium-catalyzed Amination of Branched Allylic Carboxylates.[a]

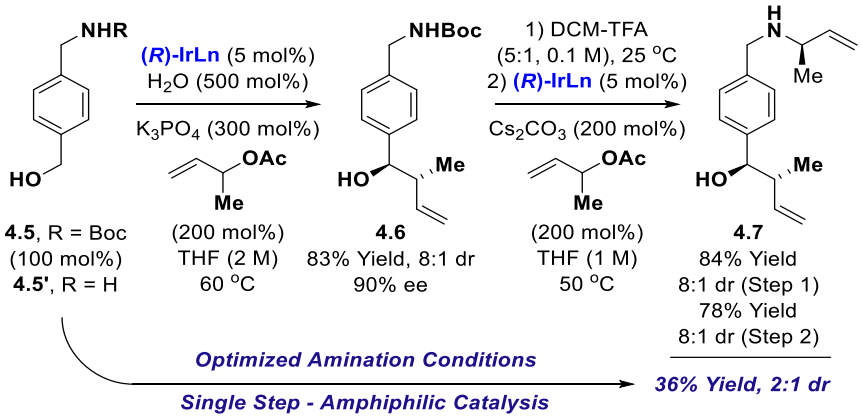
 **4.3a**, 90% Yield 90% ee	 **4.3b**, 93% Yield 20:1 dr	 **4.3c**, 92% Yield 14:1 dr	 **4.3d**, 99% Yield 90% ee	 **4.3e**, 95% Yield >20:1 dr	 **4.3f**, 97% Yield 16:1 dr
 **4.3g**, 88% Yield 87% ee	 **4.3h**, 91% Yield 17:1 dr	 **4.3i**, 95% Yield >20:1 dr	 **4.3j**, 85% Yield 93% ee	 **4.3k**, 90% Yield 94% ee	 **4.3l**, 71% Yield[b] 96% ee
 **4.3m**, 90% Yield 94% ee	 **4.3n**, 86% Yield 91% ee	 **4.3o**, 92% Yield 99% ee	 **4.3p**, 74% Yield 92% ee	 **4.3q**, 98% Yield 89% ee	 **4.3r**, 80% Yield 96% ee
 **4.3s**, 84% Yield 94% ee	 **4.3t**, 85% Yield 91% ee	 **4.3u**, 78% Yield 93% ee	 **4.3v**, 80% Yield 95% ee	 **4.3w**, 82% Yield 93% ee	 **4.3x**, 85% Yield 95% ee
 **4.3y**, 73% Yield 92% ee	 **4.3z**, 70% Yield 91% ee	 **4.3a'**, 69% Yield[c] 91% ee	 **4.3b'**, 78% Yield 94% ee	 **4.3c'**, 75% Yield 93% ee	 **4.3d'**, 80% Yield 87% ee
 **4.3e'**, 83% Yield 93% ee	 **4.3f'**, 83% Yield 17:1 dr	 **4.3g'**, 79% Yield 94% ee	 **4.3h'**, 74% Yield 91% ee	 **4.3i'**, 79% Yield 95% ee	 **4.3j'**, 76% Yield 90% ee

[a]Yields of material isolated by silica gel chromatography. Standard conditions: (*R*)-IrLn (5 mol%), amine (200 mol%), Cs_2CO_3 (200 mol%), "wet" THF (1 M), 50 °C. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details. [b]$H_2NCH_2CH_2NHBn$ (400 mol%), ee% determined at the stage of **4.4l** (eq. 4.1). [c]The cyclometallated iridium catalyst modified by the Roche ligand was used.[18]

To illustrate the utility of the reaction products a series of transformations were performed. The *N*-benzyl ethylene diamine adduct **4.3l** was subjected to reductive amination with glyoxal to form the piperazine **4.4l** (eq. 4.1).[20] Adducts **4.3x** and **4.3j′** were converted to 1-(*N*-benzyl-amino)-2-cyclohexene **4.4x** (eq. 4.2)[21] and the cyclopropyl substituted lactam **4.4j′** through ring-closing metathesis (eq. 4.3).[5g]



Scheme 4.1 Identical π-allyliridium *C,O*-benzoate complexes promote both nucleophilic and electrophilic allylation.[a]



[a]See Supporting Information for further experimental details.

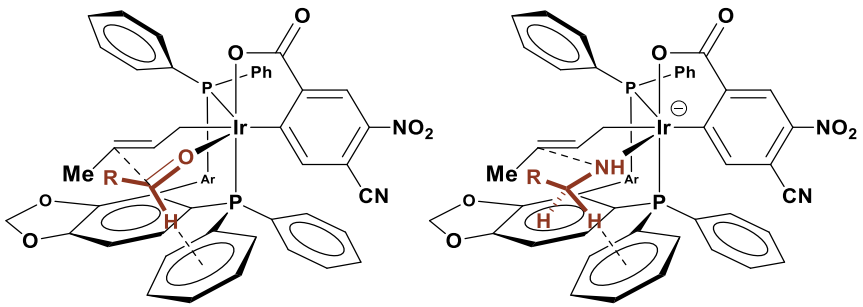
While numerous reports of "umpoled allylations" exist,[22] the amphiphilic properties displayed by π-allyliridium *C,O*-benzoates appear quite unique.[23] The same catalyst, (*R*)-IrLn (5 mol%), will promote both nucleophilic and electrophilic allylation under very similar conditions. For example, under standard amination conditions, 4-aminomethyl-benzyl alcohol and α-methyl allyl acetate are directly converted to compound **4.7** in 36% yield. Alternatively, compound **4.5** can be converted to compound **4.7** in a step-wise manner with higher levels of stereoselectivity using the same iridium catalyst (Scheme 4.1).

4.3 Discussion

The nature of the C-N bond forming event merits discussion. For related enantioselective iridium catalyzed allylic aminations, an outer-sphere mechanism is postulated.[3-11] While it is likely such pathways are also operative in aminations catalyzed by π-allyliridium *C,O*-benzoates, an inner-sphere mechanism cannot be excluded. The

more stringent steric constraints of an inner-sphere mechanism may account for the fact that primary amines engage in allylation while secondary amines do not. Furthermore, enantiofacial selectivity for amination through an inner sphere mechanism matches that observed in nucleophilic allylations of α-substituted allylic acetates (Figure 4.2). Computational studies are underway to evaluate outer vs inner sphere pathways.

Figure 4.2 Stereochemical models accounting for equivalent π-facial selectivity in crotylation and amination.



4.4 Conclusion

In summary, highly tractable and commercially available π-allyliridium *C,O*-benzoates, which are well known to catalyze nucleophilic carbonyl allylation, are now shown to catalyze chemo-, regio- and enantioselective electrophilic aminations of branched allylic acetates bearing linear alkyl groups. These processes broaden access to chiral *N*-containing building blocks[24] and establish unique amphiphilic properties of π-allyliridium *C,O*-benzoates, which should inform the design of new catalytic process. More broadly, this work demonstrates how academic-industrial collaboration accelerates the discovery of robust, innovative methods for chemical synthesis.

4.5 Experimental Details

General Information

All reactions were carried out under inert gas atmosphere (nitrogen or argon) unless otherwise indicated. Resealable pressure tubes (13x100 mm) were purchased from Fischer Scientific (catalog number 14-959-35C) and were flame dried followed by cooling in a desiccator or under a stream of inter gas prior to use. All commercial reagents and anhydrous solvents were used as received from vendors (Fischer Scientific, Sigma Aldrich and Combi Blocks) without further purification. The used Iridium catalyst [(R)-(+)-5,5'-bis(diphenylphosphino)-4,4'-bi-1,3-benzodioxole][4-cyano-3-nitrobenzenecarboxylato][1,2,3-eta-2-propenyl Ir(III)] and its enantiomer were either obtained from Strem Chemicals (catalog numbers: 77-5074 (R-catalyst) 77-5075 (S-catalyst)) or prepared according to literature known procedures.[1] The compounds (4-(pentafluoro-λ6-sulfaneyl)phenyl)methanamine,[2] (E)-3-phenylprop-2-en-1-amine,[3] geranylamine,[4] 5-phenylpenten-3-yl acetate,[5] α-cyclopropyl allyl acetate,[6] and 1,7-octadien-3-yl acetate[7] were also prepared according to literature procedures. Preparative column chromatography employing Silicycle silica gel (40-63 μm) was performed according to the method of Still[8] or on a Teledyne Isco Combiflash R_f utilizing Silicycle HP columns using a mobile phase composed of either heptane/isopropyl acetate, hexane/ethyl acetate or dichloromethane/methanol. Reactions were monitored by a Shimadzu LCMS/UV system with LC-30AD solvent pump, 2020 MS, Sil-30AC autosampler, SPD-M30A UV detector, CTO-20A column oven, using a 2-98% acetonitrile/0.1% formic acid (or 0.001% ammonia) gradient over 2.5 minutes. Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Dynamic Absorbents F). Visualization was accomplished with UV light followed

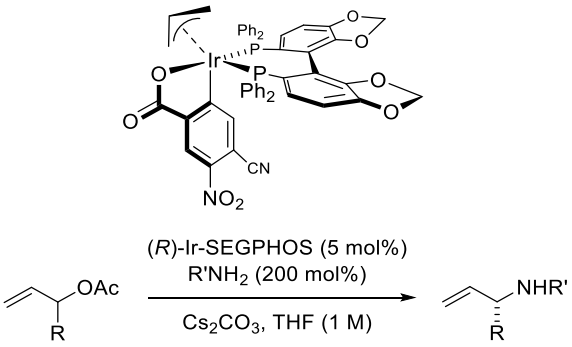
by dipping in CAM, *p*-Anisaldehyde (PAA), or $KMnO_4$ stain solution followed by heating. Specific optical rotations were recorded on an Atago AP-300 automatic polarimeter at the sodium line (589.3 nm) in CHCl3 Solution concentrations are given in the units of 10-2 g ml^{-1}.

Spectroscopy, Spectrometry and Data Collection

Infrared spectra were recorded on a Perkin-Elmer 1600 spectrometer. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion (M+H, M+Na), or a suitable fragment ion. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with a Bruker BioSpin GmbG, Varian Gemini (400 MHz) or Varian INOVA (500 MHz) spectrometer equipped with a Bruker cryoprobe. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from tetramethylsilane or ppm relative to the center of the singlet at 7.26 ppm for deuteriochloroform. Data reported as multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Integration and coupling constants were reported in Hertz (Hz). Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a Bruker BioSpin GmbG, Varian Gemini (100 MHz) or Varian INOVA (125 MHz) spectrometer and were routinely run with broadband decoupling. Chemical shifts are reported in delta (δ) units, ppm relative to the center of the triplet at 77.16 ppm for deuteriochloroform. Fluorine-19 nuclear magnetic resonance (^{19}F NMR) spectra were recorded with a Varian Gemini (376 MHz) spectrometer.

Experimental Details and Spectral Data

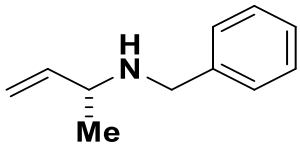
Enantioselective iridium catalyzed allylic alkylation with primary amine nucleophiles-



General procedure

An oven-dried pressure tube equipped with a magnetic stir bar was charged with cesium carbonate (200 mol%), (*R*)-Ir-SEGPHOS (5 mol%). The tube was purged with argon for 5 minutes. THF (1.0 M) was added followed by the allylic acetate (100 mol%) and the amine (200 mol%). The tube was sealed with a PTFE lined cap and was placed in an oil bath at the indicated temperature and stirred for the indicated period of time. After reaching ambient temperature, the crude reaction mixture was directly subjected to flash column chromatography.

(*R*)-N-benzylbut-3-en-2-amine (4.3a)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (94.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (50 °C, 18 hr). The title compound was obtained in 90% yield (63.2 mg, 0.39 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.20 (hexanes:ethyl acetate 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 - 7.26 (m, 4H), 7.26 – 7.17 (m, 1H), 5.72 (ddd, *J* = 17.6, 10.2, 7.7 Hz, 1H), 5.18 – 5.09 (m, 1H), 5.09 - 5.05 (m, 1H), 3.81 (d, *J* = 13.2 Hz, 1H), 3.69 (d, *J* = 13.3 Hz, 1H), 3.28 – 3.16 (m, 1H), 1.18 (d, *J* = 6.5 Hz, 3H).

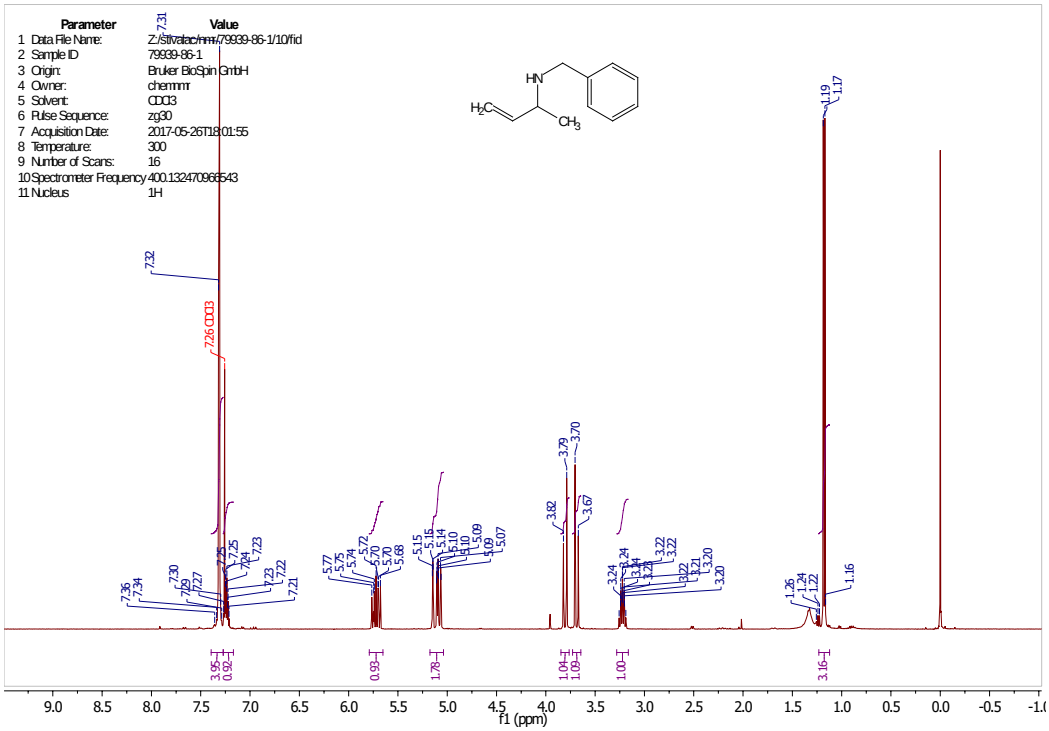
^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.6, 140.7, 128.4, 128.1, 126.8, 114.7, 56.0, 51.4, 21.8.

HRMS (ESI): Calculated for $C_{11}H_{16}N$ [M+H$^+$] = 162.1283, found 162.1274.

FTIR (neat): 3063, 3027, 2971, 1640, 1495, 1452, 1415, 1369, 1312, 1166, 1114, 1073, 1028, 993, 916, 731, 696 cm^{-1}.

$[\alpha]_D^{24}$ = –5.6 (*c* 0.35, $CHCl_3$).

HPLC (Chiralcel OD-H column, heptane:*i*-PrOH = 97.5:2.5, 1.00 mL/min, 220 nm), *ee* = 90%.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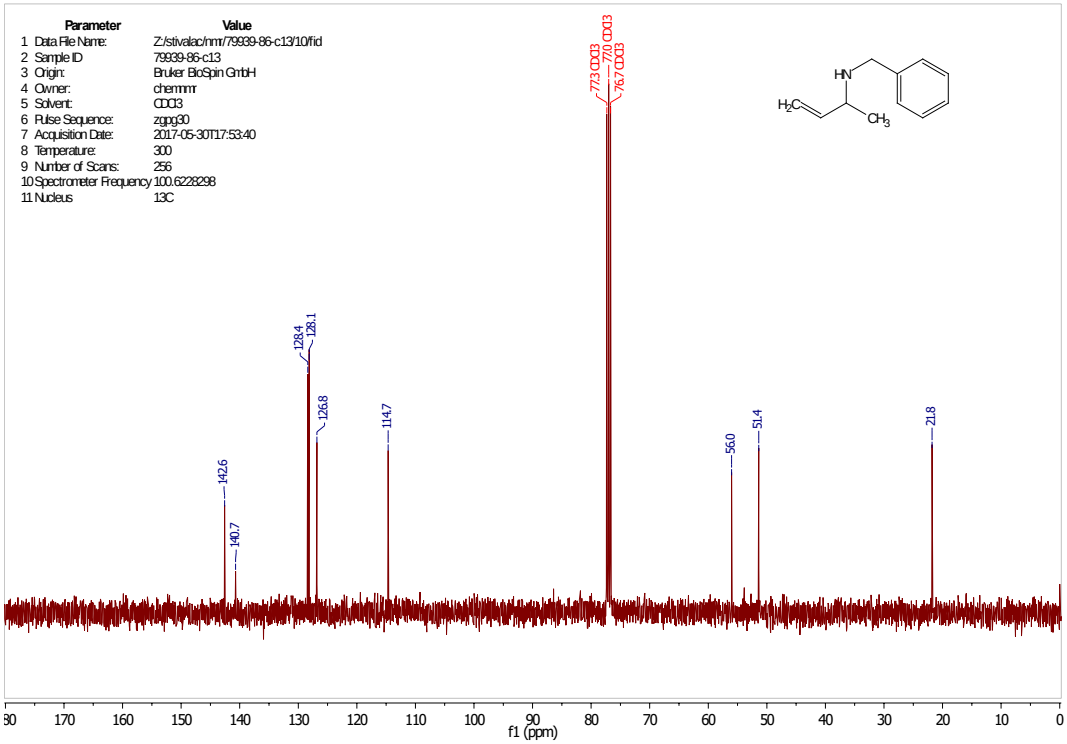
CH3
f1 (ppm)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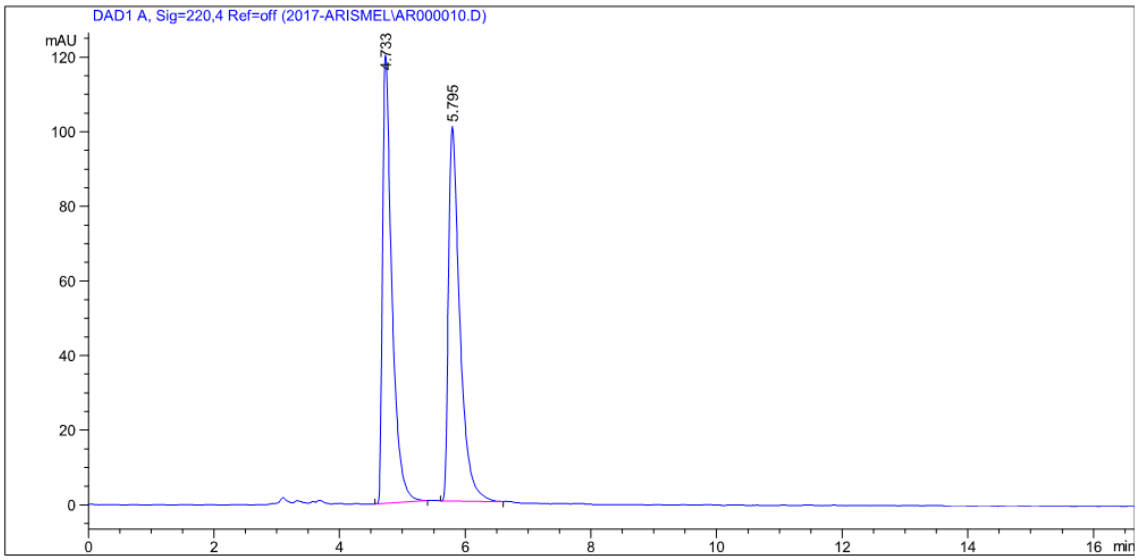
5 Solvent: CDCl3
6 Pulse Sequence: zgpg30
7 Acquisition Date: 2017-05-30T17:53:40
8 Temperature: 300
9 Number of Scans: 256
10 Spectrometer Frequency 100.6228298
11 Nucleus 13C
HN
H2C
CH3
f1 (ppm)



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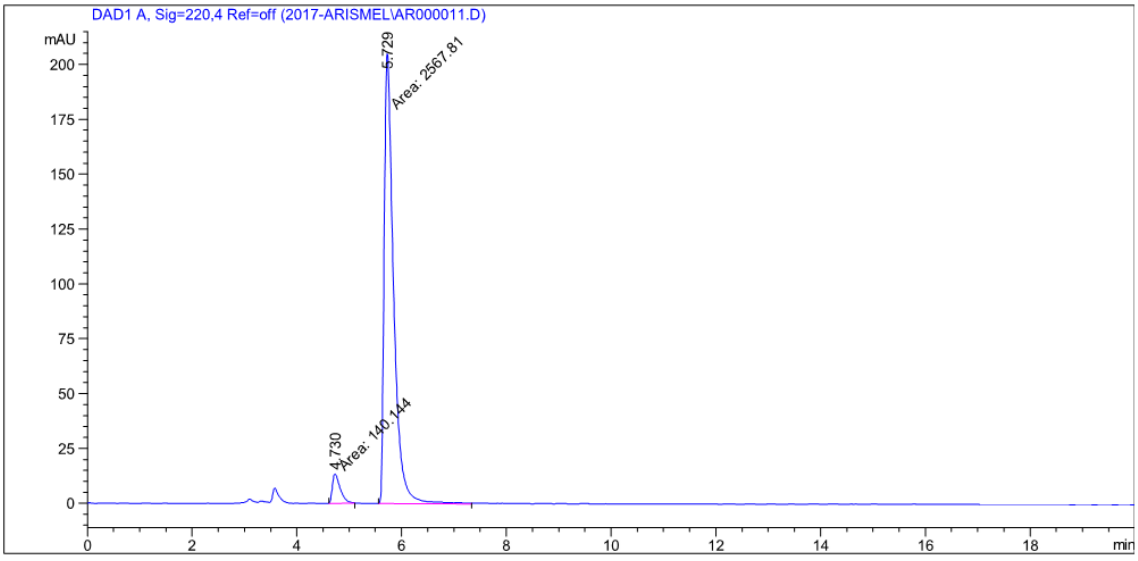

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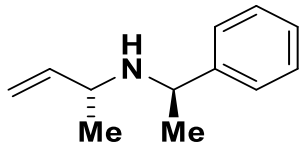
2	5.729	MM	0.2087	2567.80518	205.06187	94.8247

(*R*)-N-((*R*)-1-phenylethyl)but-3-en-2-amine (4.3b)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (107 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (50 °C, 18 hr). The title compound was obtained in 93% yield, >20:1 dr (71.4 mg, 0.41 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.32 (hexanes:ethyl acetate 1:1).

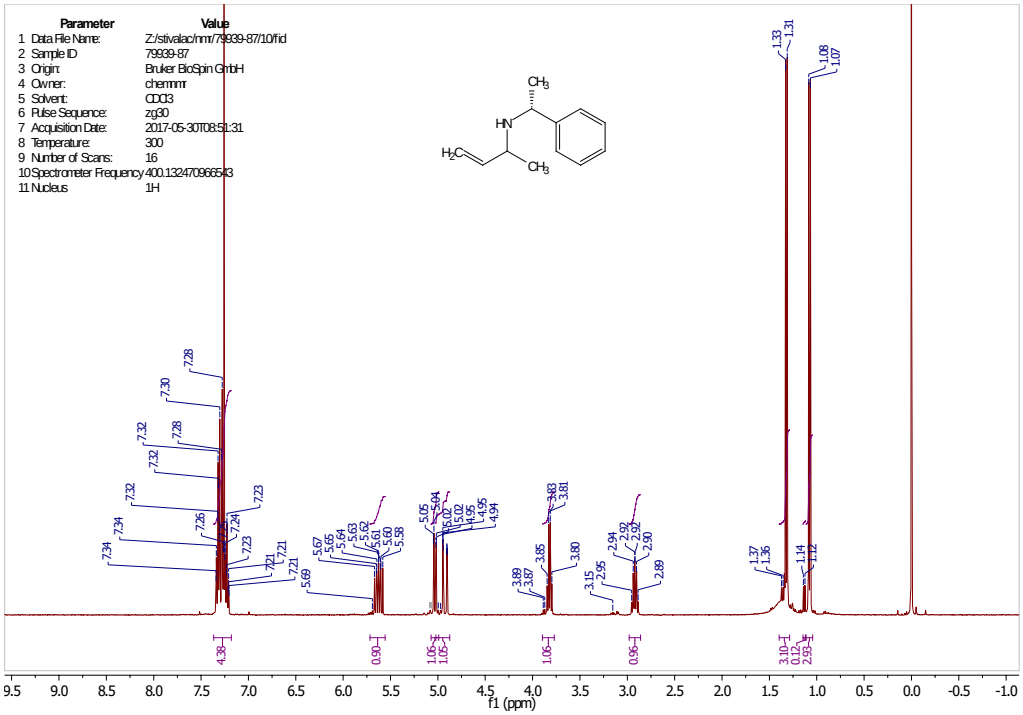
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 – 7.18 (m, 5H), 5.63 (ddd, *J* = 17.1, 10.1, 8.0 Hz, 1H), 5.03 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.92 (ddd, *J* = 17.1, 2.0, 0.9 Hz, 1H), 3.82 (q, *J* = 6.7 Hz, 1H), 2.98 – 2.86 (m, 1H), 1.32 (d, *J* = 6.7 Hz, 3H), 1.08 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.9, 142.5, 128.4, 126.7, 126.6, 114.5, 54.9, 53.7, 25.0, 22.5.

HRMS (ESI): Calculated for $C_{12}H_{18}N$ [M+H$^+$] = 176.1439, found 176.1430

FTIR (neat): 2959, 2924, 1672, 1602, 1492, 1450, 1415, 1368, 1306, 1120, 1081, 1027, 993, 956, 916, 845, 761, 699 cm^{-1}.

$[\alpha]_D^{24}$= +12.3 (*c* 0.97, $CHCl_3$).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4 Owner: chemmr
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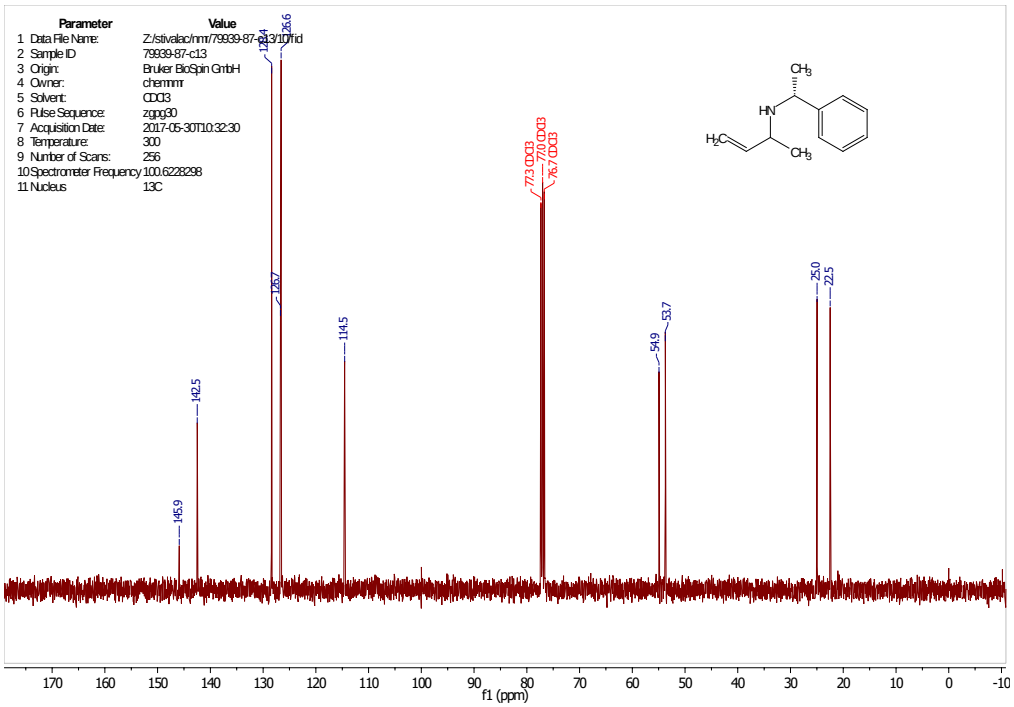
11 Nucleus 1H
f1 (ppm)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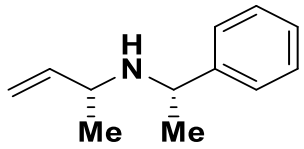
6 Pulse Sequence: zgpg30
7 Acquisition Date: 2017-05-30T10:32:30
8 Temperature: 300
9 Number of Scans: 256
10 Spectrometer Frequency 100.6228298
11 Nucleus 13C
f1 (ppm)

(*R*)-N-((*S*)-1-phenylethyl)but-3-en-2-amine (4.3c)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (107 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (50 °C, 18 hr). The title compound was obtained in 92% yield, 14:1 dr (70.6 mg, 0.40 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.32 (hexanes:ethyl acetate 1:1).

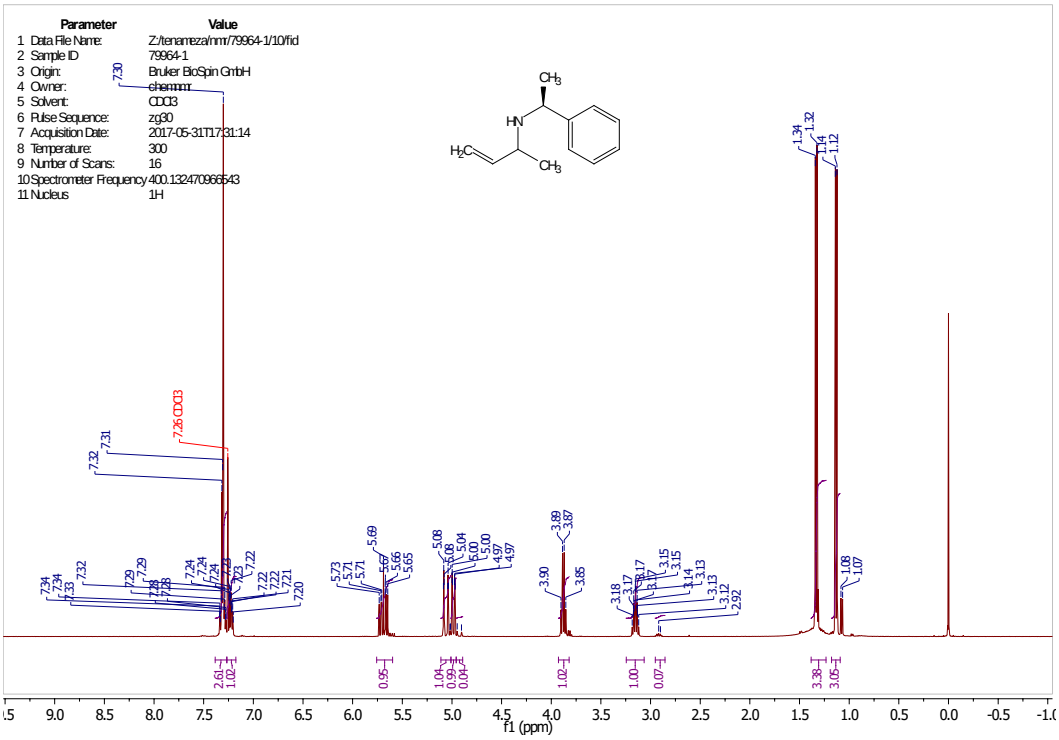
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 - 7.70 (m, 5H), 5.69 (ddd, *J* = 17.3, 10.2, 7.2 Hz, 1H), 5.09 - 5.02 (m, 1H), 5.01 - 4.96 (m, 1H), 3.88 (q, *J* = 6.6 Hz, 1H), 3.21 – 3.09 (m, 1H), 1.33 (d, *J* = 6.6 Hz, 3H), 1.13 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.0, 143.0, 128.4, 126.8, 126.5, 113.7, 54.7, 53.3, 23.8, 20.9.

HRMS (ESI): Calculated for $C_{12}H_{18}N$ $[M+H^+]$ = 176.1439, found 176.1430

FTIR (neat): 2966, 2926, 1638, 1492, 1451, 1416, 1368, 1326, 1209, 1127, 993, 915, 844, 760, 698 cm^{-1}.

$[\alpha]_D^{24}$ = –78.8 (*c* 0.31, $CHCl_3$).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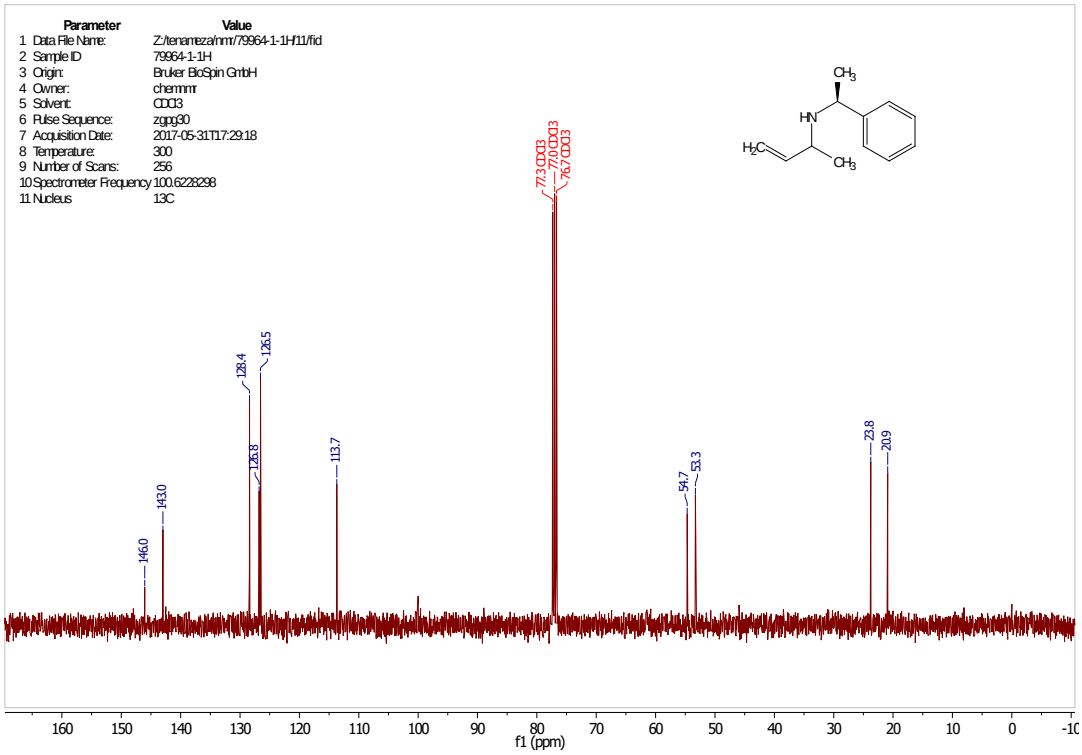
f1 (ppm)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6 Pulse Sequence: zgpg30
7 Acquisition Date: 2017-05-31T17:29:18
8 Temperature: 300
9 Number of Scans: 256
10 Spectrometer Frequency 100.6228298
11 Nucleus 13C
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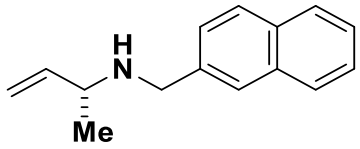
(*R*)-N-(naphthalen-2-ylmethyl)but-3-en-2-amine (4.3d)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (138 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (50 °C, 18 hr). The title compound was obtained in 99% yield (92.0 mg, 0.44 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.20 (hexanes:ethyl acetate 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 – 7.72 (m, 4H), 7.51 – 7.39 (m, 3H), 5.76 (ddd, *J* = 17.5, 10.2, 7.6 Hz, 1H), 5.19 – 5.06 (m, 2H), 3.98 (d, *J* = 13.2 Hz, 1H), 3.86 (d, *J* = 13.3 Hz, 1H), 3.34 – 3.21 (m, 1H), 1.21 (d, *J* = 6.4 Hz, 3H).

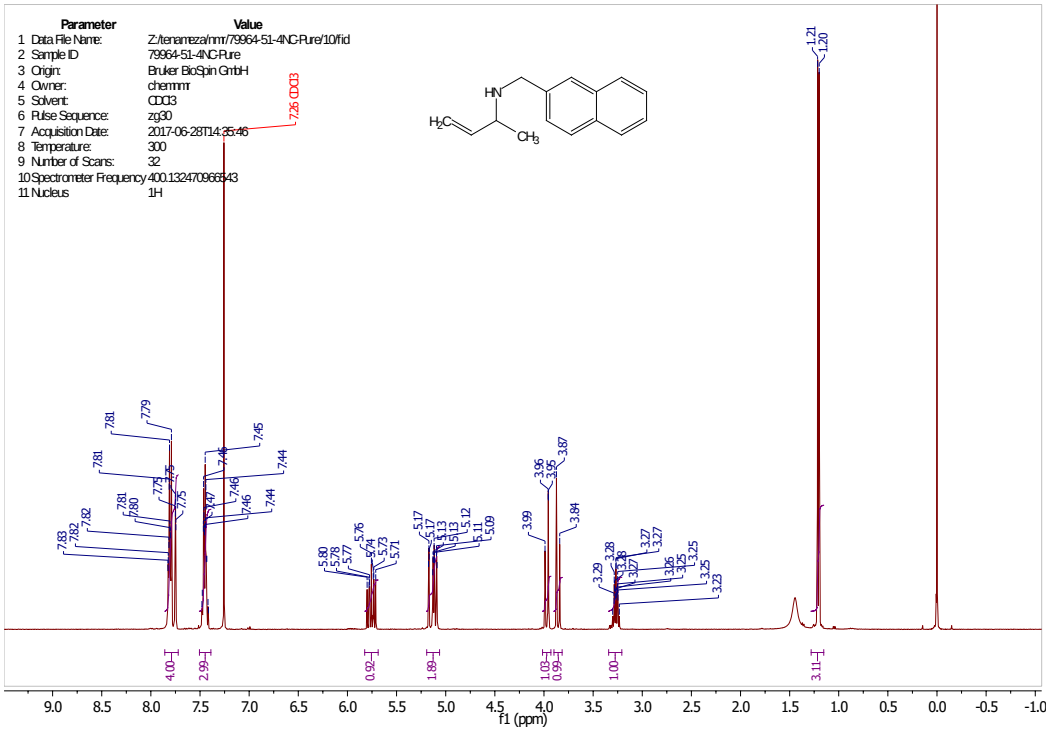
^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.6, 138.2, 133.5, 132.6, 128.0, 127.7, 127.6, 126.7, 126.4, 126.0, 125.5, 114.8, 56.0, 51.5, 21.8.

HRMS (ESI): Calculated for $C_{15}H_{18}N$ [M+H$^+$] = 212.1439, found 212.1429.

FTIR (neat): 3053, 2968, 2817, 2362, 1636, 1600, 1508, 1438, 1414, 1367, 1311, 1270, 1170, 1124, 993, 916, 854, 814, 746, 682 cm^{-1}.

$[\alpha]_D^{24}$ = –8.1 (*c* 0.41, $CHCl_3$).

HPLC (Chiralcel OD-H column, heptane:*i*-PrOH = 99.0:1.0, 2.00 mL/min, 254 nm), *ee* = 90%.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8 Temperature: 300
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7.79
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7.47
7.82
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5.78
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3.87
3.84
3.29
3.28
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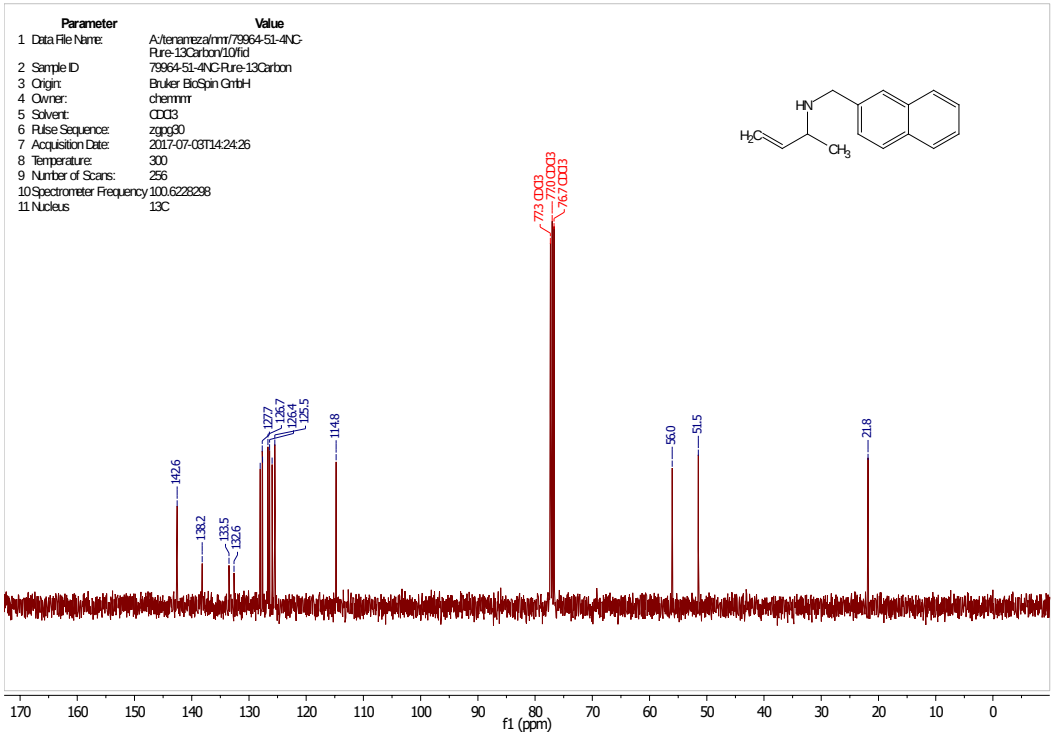
3.11
f1 (ppm)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8 Temperature: 300
9 Number of Scans: 256
10 Spectrometer Frequency 100.6228298
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77.0 CDCl3
76.7 CDCl3
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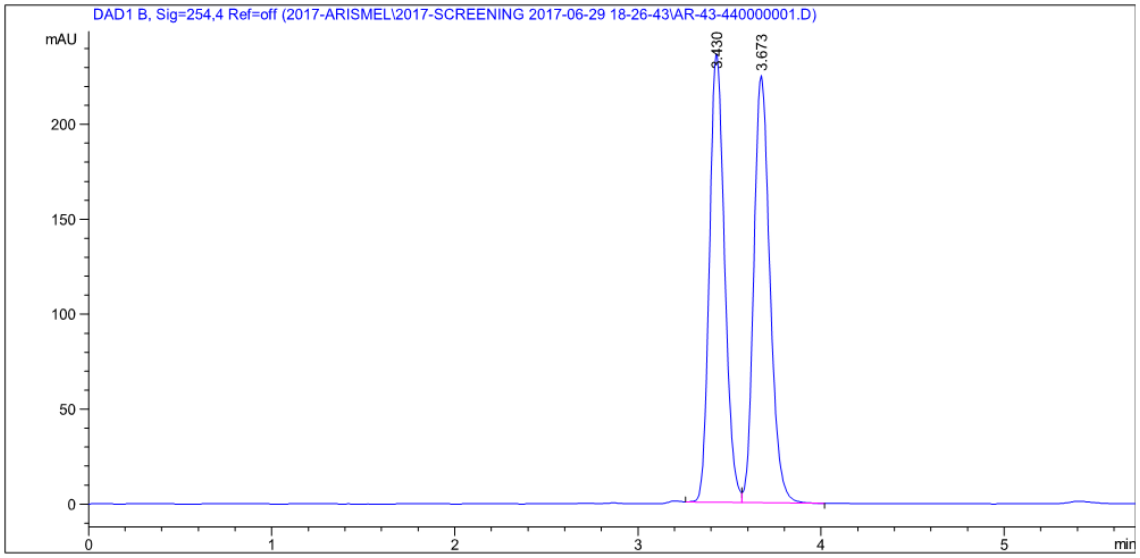
21.8
f1 (ppm)



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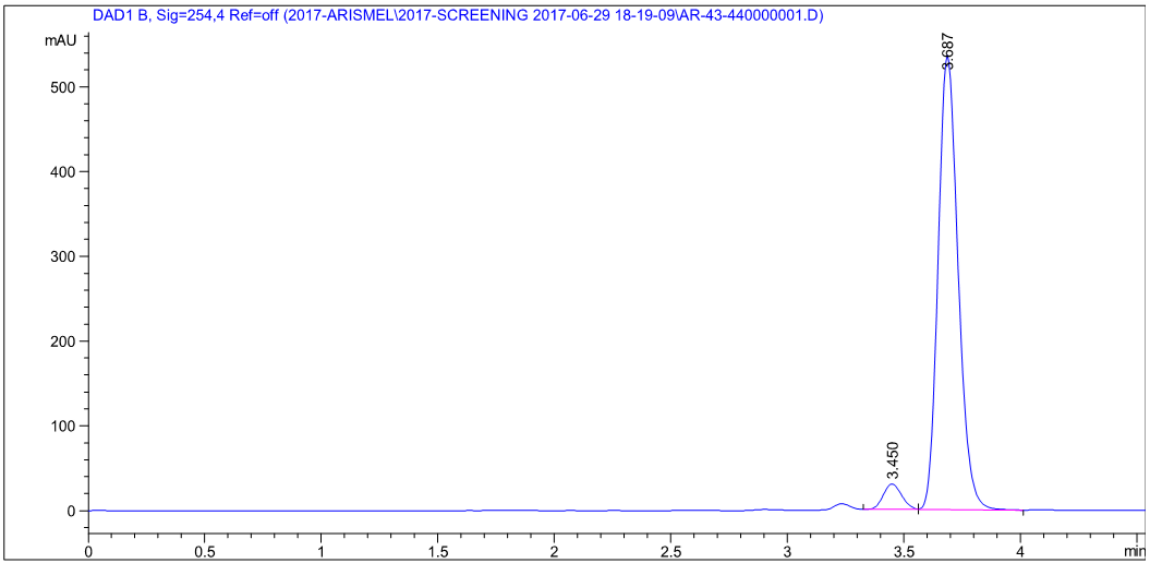

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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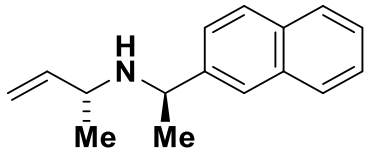
2	3.687	VB	0.0914	3194.00635	536.56372	95.0975

(*R*)-N-((*R*)-1-(naphthalen-2-yl)ethyl)but-3-en-2-amine (4.3e)



Procedures

The allylic acetate (22.8 mg, 0.20 mmol, 100 mol%) and the primary amine (68.5 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 95% yield, >20:1 dr (43.0 mg, 0.19 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–3:1).

TLC (SiO_2) R_f = 0.34 (hexanes/ethyl acetate = 1:1).

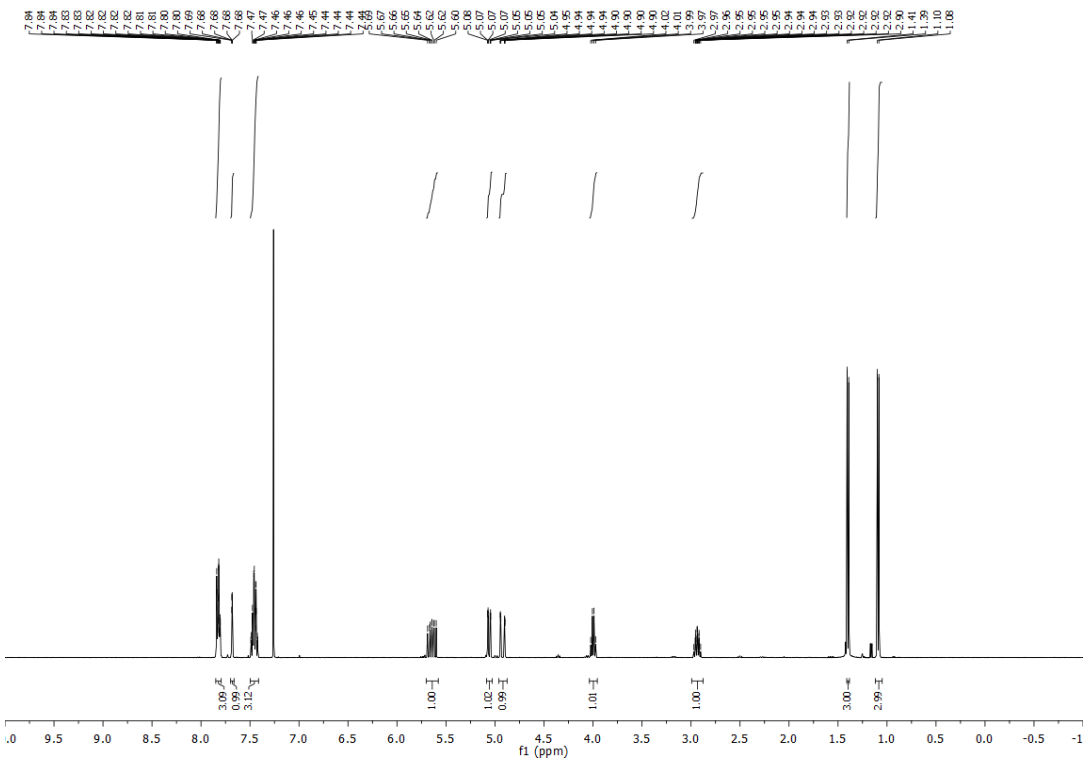
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (ddt, *J* = 7.1, 5.4, 0.7 Hz, 3H), 7.68 (dd, *J* = 1.5, 0.9 Hz, 1H), 7.50 – 7.41 (m, 3H), 5.64 (ddd, *J* = 17.1, 10.2, 8.1 Hz, 1H), 5.06 (ddd, *J* = 10.1, 1.8, 0.6 Hz, 1H), 4.92 (ddd, *J* = 17.1, 1.8, 0.8 Hz, 1H), 4.00 (q, *J* = 6.7 Hz, 1H), 2.94 (ddt, *J* = 8.0, 7.2, 6.1 Hz, 1H), 1.40 (d, *J* = 6.7 Hz, 3H), 1.09 (d, *J* = 6.6 Hz, 3H).

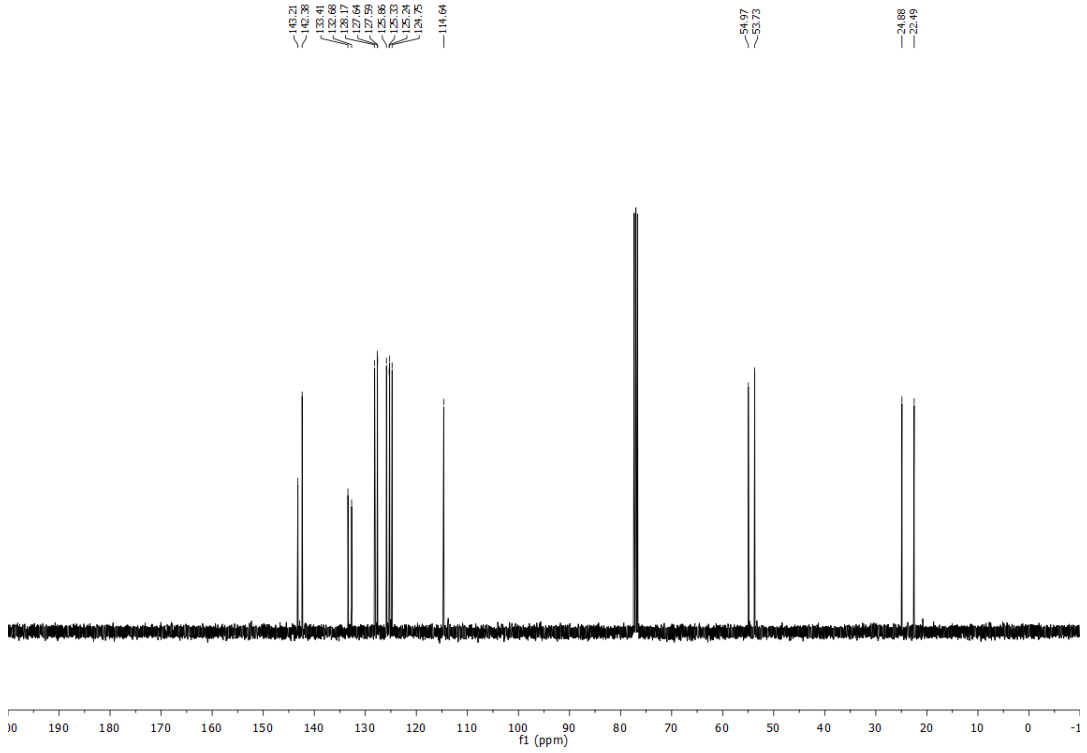
^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.2, 142.4, 133.4, 132.7, 128.2, 127.6, 127.6, 125.9, 125.3, 125.2, 124.8, 114.6, 55.0, 53.7, 24.9, 22.5.

HRMS (ESI): Calculated for $C_{16}H_{19}N$ [M+H$^+$] = 226.1590, Found 226.1584.

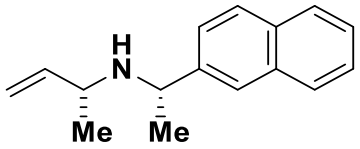
FTIR (neat): 2960, 1449, 1368, 1126, 917, 856, 819, 746 cm^{-1}.

$[\alpha]_D^{29}$ = +55.0 (*c* 1.0, $CHCl_3$).


f1 (ppm)


f1 (ppm)

(*R*)-N-((*S*)-1-(naphthalen-2-yl)ethyl)but-3-en-2-amine (4.3f)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (151 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (50 °C, 18 hr). The title compound was obtained in 97% yield, 16:1 dr (96.0 mg, 0.43 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.30 (hexanes:ethyl acetate 1:1).

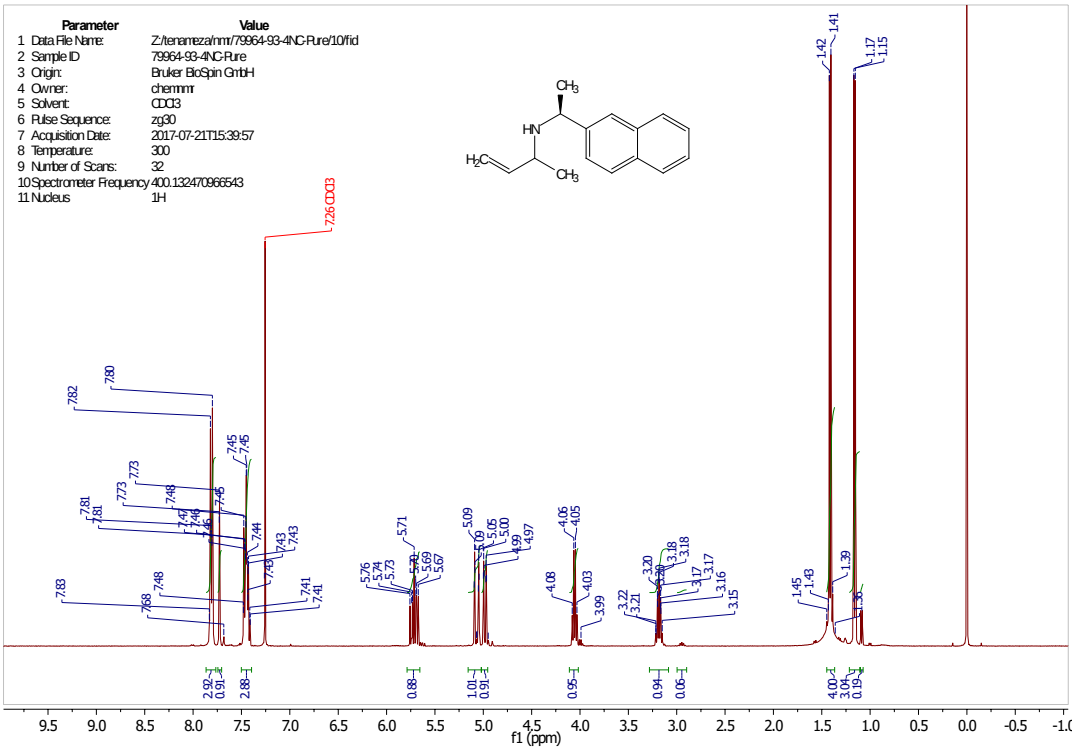
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 – 7.76 (m, 3H), 7.74 - 7.71 (m, 1H), 7.50 - 7.40 (m, 3H), 5.71 (ddd, *J* = 17.3, 10.2, 7.1 Hz, 1H), 5.07 (dt, *J* = 17.3, 1.4 Hz, 1H), 4.98 (dt, *J* = 10.2, 1.3 Hz, 1H), 4.06 (q, *J* = 6.5 Hz, 1H), 3.28 – 3.08 (m, 1H), 1.41 (d, *J* = 6.5 Hz, 4H), 1.16 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.5, 143.0, 133.5, 132.7, 128.2, 127.7, 127.6, 125.9, 125.4, 125.1, 125.0, 113.8, 54.8, 53.4, 23.8, 20.9.

HRMS (ESI): Calculated for $C_{16}H_{20}N$ $[M+H^+]$ = 226.1596, found 226.1586

FTIR (neat): 3055, 2965, 2923, 1637, 1600, 1506, 1451, 1415, 1367, 1315, 1269, 1128, 1019, 993, 947, 915, 891, 855, 817, 744, 659 cm^{-1}.

$[\alpha]_D^{24}$ = –66.2 (*c* 0.58, $CHCl_3$).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5 Solvent: CDCl3
6 Pulse Sequence: zg30
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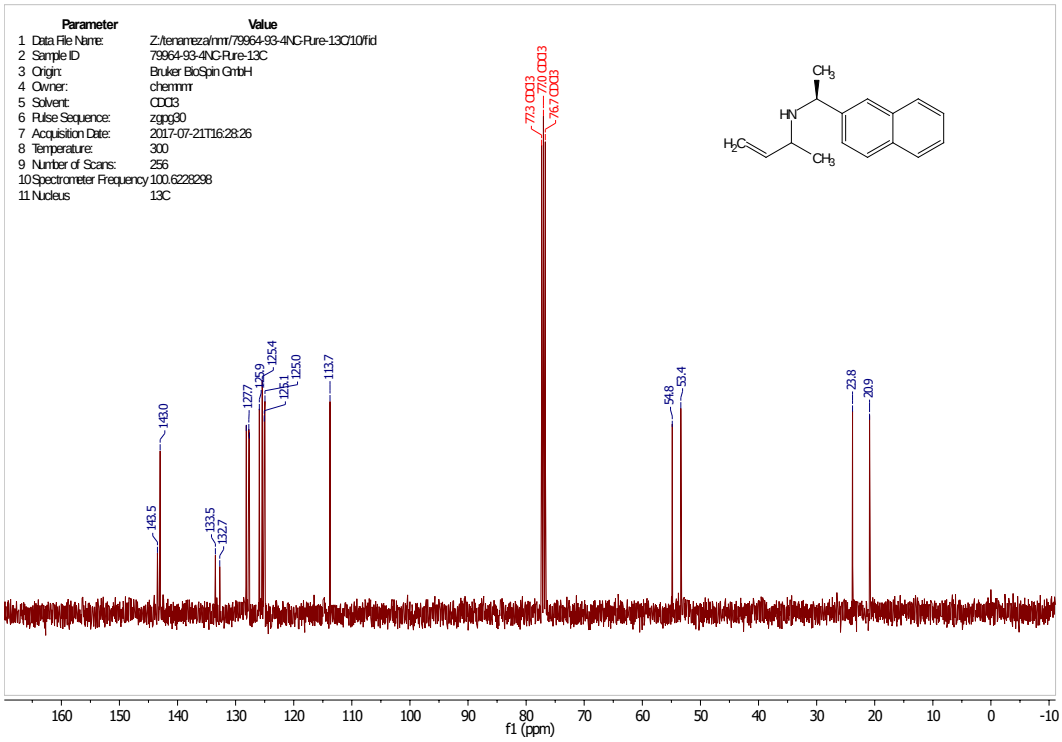
8 Temperature: 300
9 Number of Scans: 32
10 Spectrometer Frequency 400.132470966543
11 Nucleus 1H
f1 (ppm)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7 Acquisition Date: 2017-07-21T16:28:26
8 Temperature: 300
9 Number of Scans: 256
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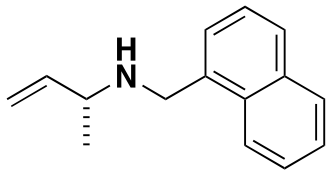
11 Nucleus 13C
f1 (ppm)

(*R*)-*N*-(naphthalen-1-ylmethyl)but-3-en-2-amine (4.3g)



Procedures

The allylic acetate (22.8 mg, 0.20 mmol, 100 mol%) and the primary amine (62.9 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 88% yield (37.2 mg, 0.18 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 1:1).

TLC (SiO_2) R_f = 0.52 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 8.6 Hz, 1H), 7.84 (d, *J* = 8.6 Hz, 1H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.54-7.44 (m, 3H), 7.43-7.38 (m, 1H), 5.79 (ddd, *J* = 17.2, 10.2, 7.8 Hz, 1H), 5.2 (d, *J* = 17.2 Hz, 1H), 5.13 (d, *J* = 10.2 Hz, 1H), 4.26 (d, *J* = 13.0 Hz, 1H), 4.26 (d, *J* = 13.0 Hz, 1H), 4.08 (d, *J* = 13.0 Hz, 1H), 3.36-3.28 (m, 1H), 1.62 (bs, 1H), 1.21 (d, *J* = 6.5 Hz, 3H).

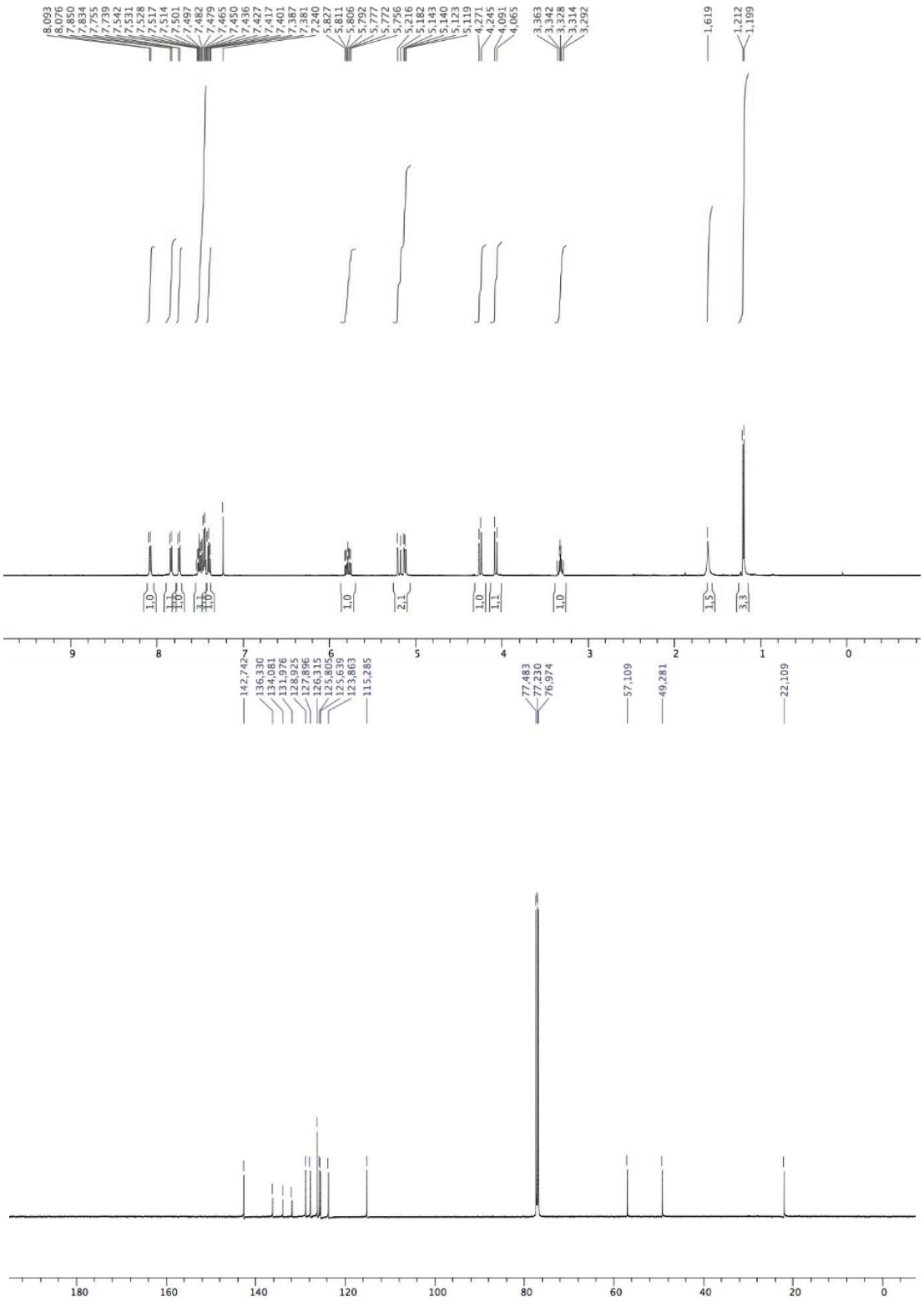
^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.7, 136.3, 134.1, 132.0, 128.9, 127.9, 126.3(x2), 125.8, 125.6, 123.9, 115.3, 57.1, 49.3, 22.1.

HRMS (ESI): Calculated for $C_{15}H_{17}N$ [M+H$^+$] = 212.1434, Found 212.1429.

FTIR (neat): 3063, 3027, 2970, 2923, 1640, 1495, 1452, 1415, 1369, 1312, 1113, 1073, 1028, 993, 916, 713, 696 cm^{-1}.

$[\alpha]_D^{24}$= –42.5 (*c* 2.1, $CHCl_3$).

HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 230 nm), *ee* = 88%.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8.076
7.850
7.834
7.755
7.739
7.542
7.531
7.528
7.517
7.514
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7.497
7.482
7.479
7.465
7.450
7.436
7.427
7.417
7.401
7.387
7.381
7.240
5.827
5.811
5.806
5.792
5.777
5.772
5.756
5.216
5.182
5.143
5.140
5.123
5.119
4.271
4.245
4.091
4.065
3.363
3.342
3.328
3.314
3.292
1.619
1.212
1.199
1.0
1.0
1.0
3.1
1.6
1.0
2.1
1.0
1.1
1.0
1.5
3.3
9
8
7
6
5
4
3
2
1
0
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136.330
134.081
131.976
128.925
127.896
126.315
125.805
125.639
123.863
115.285
77.483
77.230
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57.109
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140
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80
60
40
20
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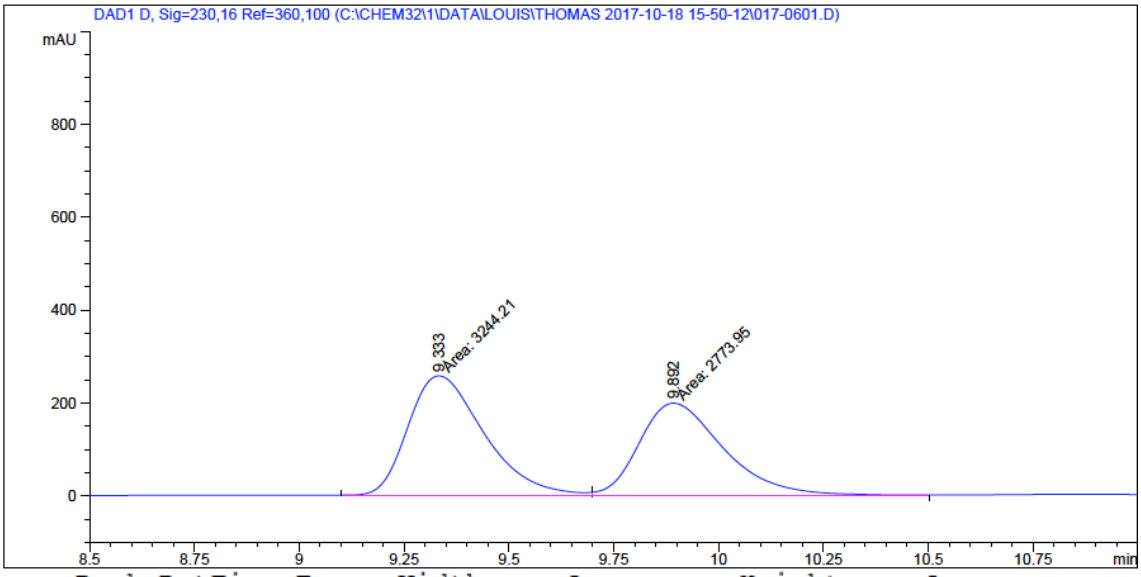

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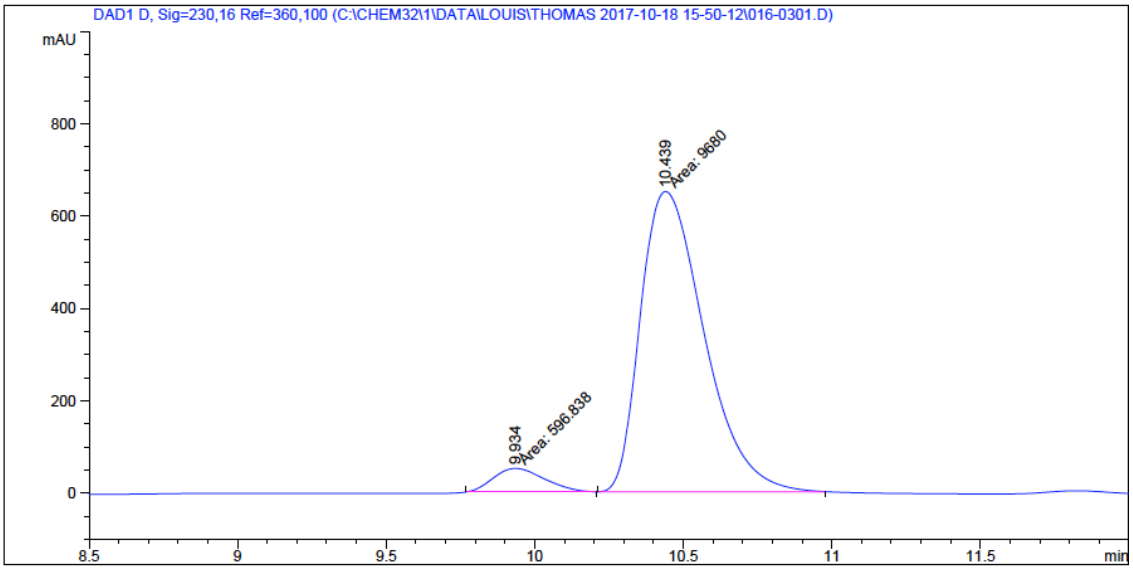

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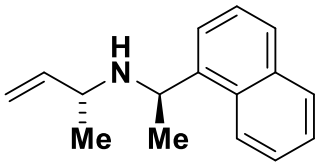
2	10.439	MM	0.2480	9680.00000	650.64429	94.1924

(*R*)-N-((*R*)-1-(naphthalen-1-yl)ethyl)but-3-en-2-amine (4.3h)



Procedures

The allylic acetate (60.5 mg, 0.53 mmol, 100 mol%) and the primary amine (182 mg, 1.06 mmol, 200 mol%) were subject to standard reaction conditions (50 ^{o}C, 18 hr). The title compound was obtained in 91% yield, 17:1 dr (108 mg, 0.48 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.43 (hexanes:ethyl acetate 1:1).

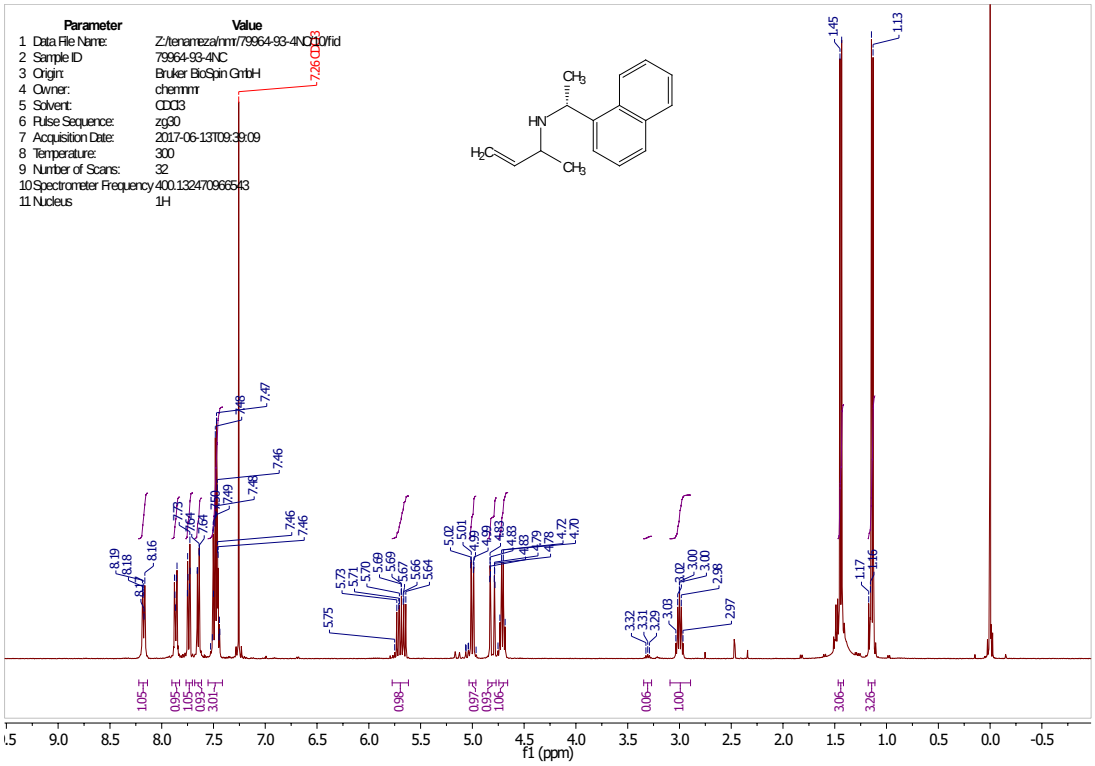
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 – 8.14 (m, 1H), 7.90 – 7.84 (m, 1H), 7.76 - 7.71 (m, 1H), 7.67 - 7.62 (m, 1H), 7.55 – 7.41 (m, 3H), 5.69 (ddd, *J* = 17.1, 10.1, 7.9 Hz, 1H), 5.04 – 4.84 (m, 1H), 4.81 (ddd, *J* = 17.2, 1.9, 0.9 Hz, 1H), 4.71 (q, *J* = 6.7 Hz, 1H), 3.06 – 2.94 (m, 1H), 1.44 (d, *J* = 6.7 Hz, 3H), 1.14 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.7, 141.7, 134.0, 131.4, 128.9, 127.0, 125.7, 125.6, 125.2, 123.0, 122.6, 114.6, 54.0, 50.4, 24.6, 22.4.

HRMS (ESI): Calculated for $C_{16}H_{20}N$ [M+H$^+$] = 226.1596, found 226.1585.

FTIR (neat): 3064, 2969, 2923, 1595, 1509, 1448, 1417, 1393, 1367, 1323, 1230, 1171, 1125, 1087, 992, 918, 859, 798, 777, 735, 681 cm^{-1}.

$[\alpha]_D^{24}$ = –26.3 (*c* 0.37, $CHCl_3$).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4 Owner: chemmr
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6 Pulse Sequence: zg30
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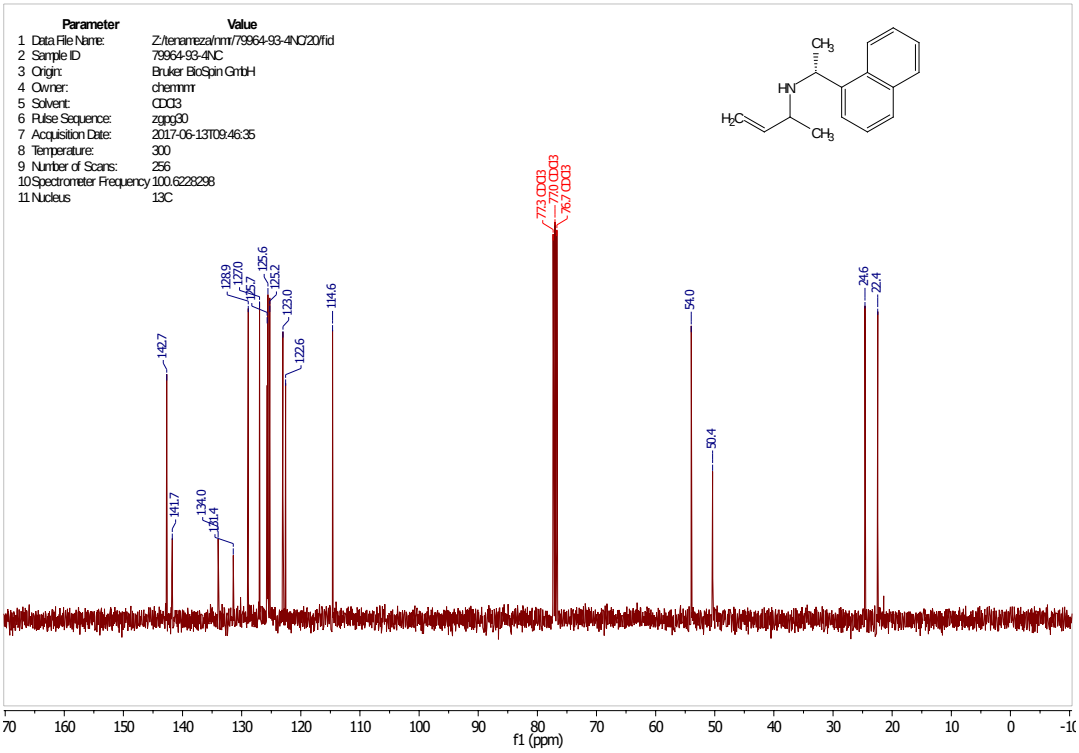
8 Temperature: 300
9 Number of Scans: 32
10 Spectrometer Frequency 400.132470966543
11 Nucleus 1H
f1 (ppm)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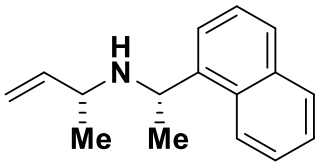
7 Acquisition Date: 2017-06-13T09:46:35
8 Temperature: 300
9 Number of Scans: 256
10 Spectrometer Frequency 100.6228298
11 Nucleus 13C
f1 (ppm)

(*R*)-N-((*S*)-1-(naphthalen-1-yl)ethyl)but-3-en-2-amine (4.3i)



Procedures

The allylic acetate (60.5 mg, 0.53 mmol, 100 mol%) and the primary amine (182 mg, 1.06 mmol, 200 mol%) were subject to standard reaction conditions (50 ^{o}C, 18 hr). The title compound was obtained in 95% yield, > 20:1 dr (113 mg, 0.50 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.43 (hexanes:ethyl acetate 1:1).

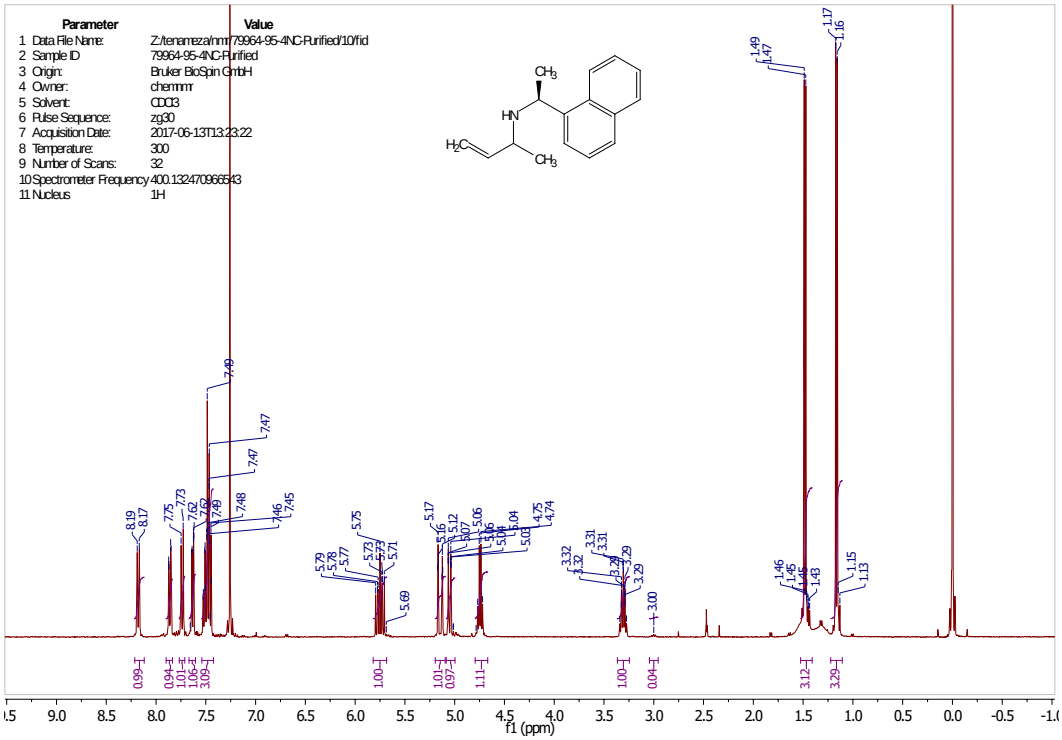
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20-8.16 (m, 1H), 7.88-7.84 (m, 1H), 7.77 - 7.72 (m, 1H), 7.66 - 7.60 (m, 1H), 7.55 – 7.38 (m, 3H), 5.75 (ddd, *J* = 17.4, 10.2, 7.4 Hz, 1H), 5.20 - 5.10 (m, 1H), 5.08 - 5.02 (m, 1H), 4.74 (q, *J* = 6.5 Hz, 1H), 3.37 – 3.25 (m, 1H), 1.48 (d, *J* = 6.5 Hz, 3H), 1.16 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.9, 141.8, 134.0, 131.1, 128.9, 127.1, 125.8, 125.7, 125.3, 123.0, 122.9, 114.0, 53.6, 49.7, 22.9, 21.4.

HRMS (ESI): Calculated for $C_{16}H_{20}N$ [M+H$^+$] = 226.1596, found 226.1586.

FTIR (neat): 3049, 2967, 1638, 1595, 1509, 1450, 1416, 1394, 1367, 1317, 1230, 1169, 1128, 995, 916, 859, 798, 776, 754, 684 cm^{-1}.

$[\alpha]_D^{24}$ = –56.7 (*c* 0.38, $CHCl_3$).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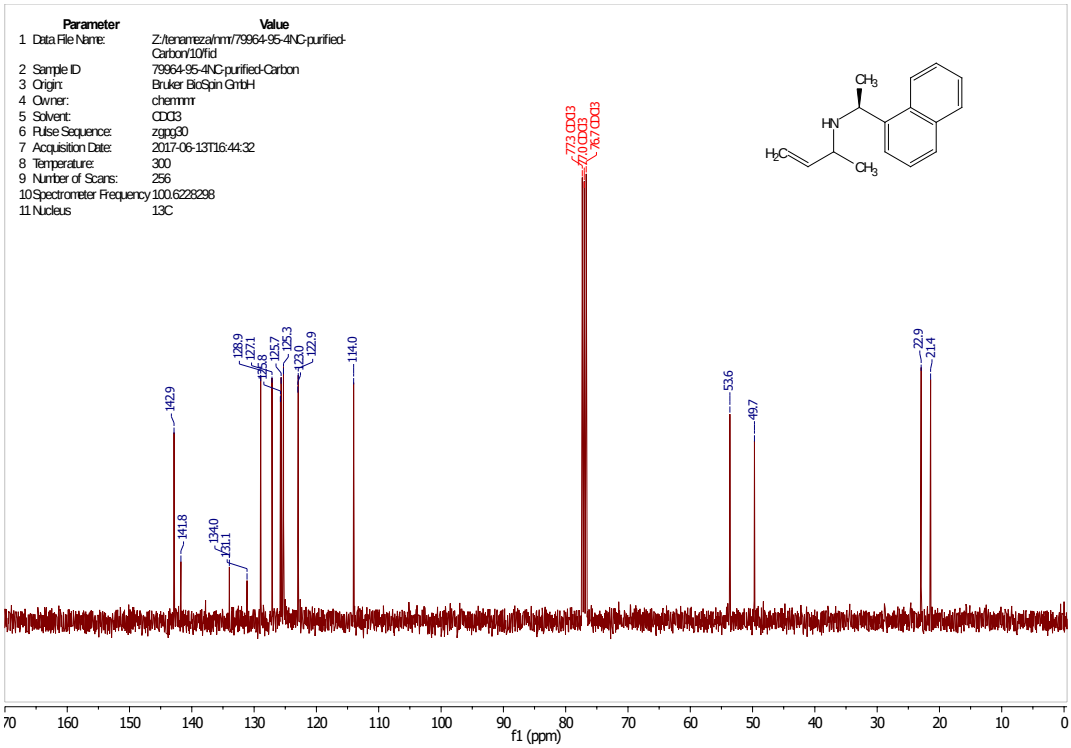
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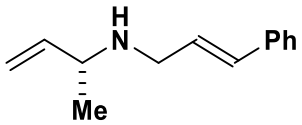
11 Nucleus 13C
f1 (ppm)

(*R*)-N-cinnamylbut-3-en-2-amine (4.3j)



Procedures

The allylic acetate (22.8 mg, 0.20 mmol, 100 mol%) and the primary amine (53.3 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (50 °C, 18 hr). The title compound was obtained in 85% yield (32.0 mg, 0.17 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–1:1).

TLC (SiO_2) R_f = 0.20 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 – 7.34 (m, 2H), 7.33 – 7.27 (m, 2H), 7.24 – 7.19 (m, 1H), 6.51 (dt, *J* = 15.9, 1.5 Hz, 1H), 6.30 (ddd, *J* = 15.9, 6.6, 6.1 Hz, 1H), 5.70 (ddd, *J* = 17.2, 10.2, 7.7 Hz, 1H), 5.18 – 5.04 (m, 2H), 3.43 (ddd, *J* = 13.9, 6.1, 1.5 Hz, 1H), 3.33 (ddd, *J* = 13.9, 6.6, 1.3 Hz, 1H), 3.29 – 3.22 (m, 1H), 1.47 (br, 1H), 1.19 (d, *J* = 6.5 Hz, 3H).

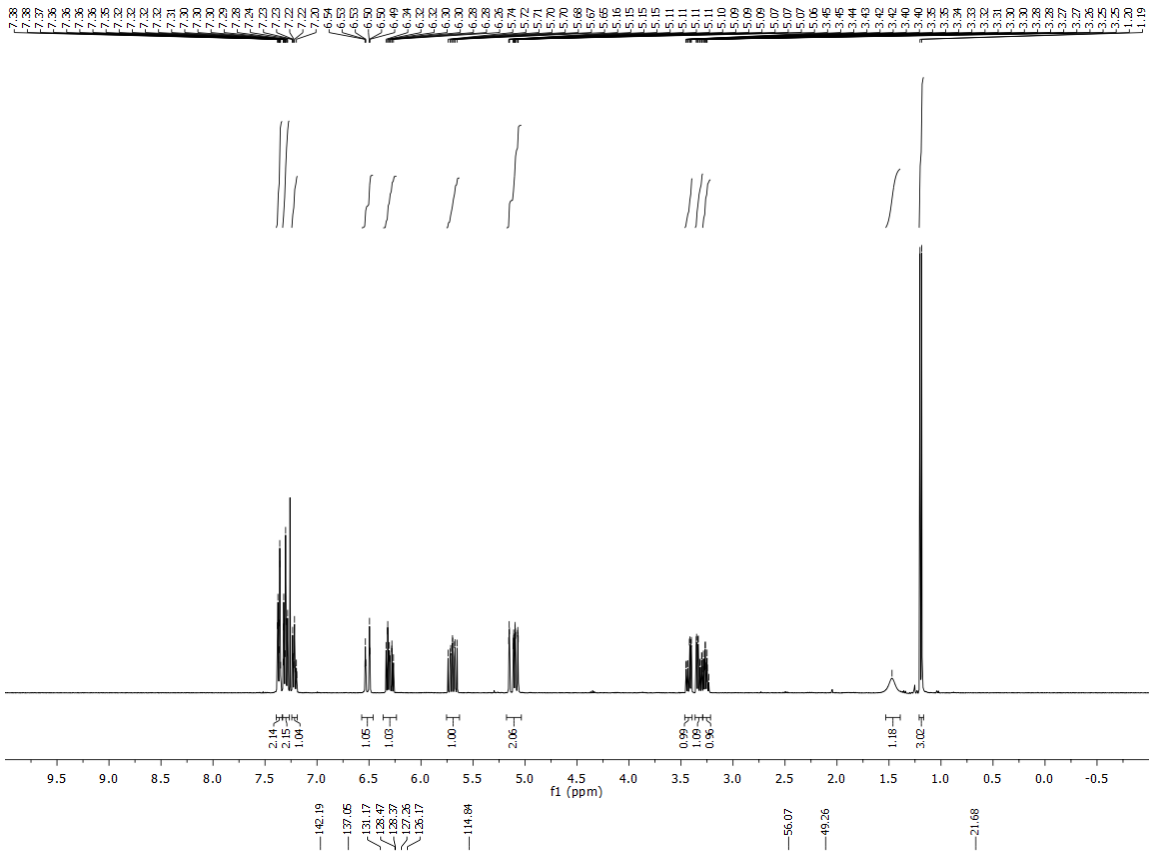
^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.2, 137.1, 131.2, 128.5, 128.4, 127.3, 126.2, 114.8, 56.1, 49.3, 21.7.

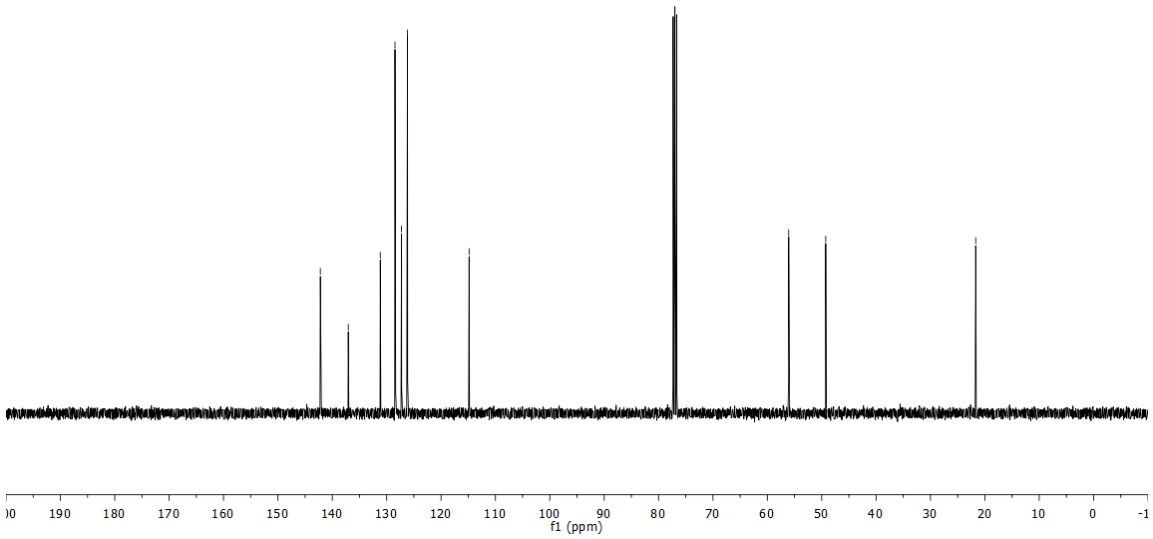
HRMS (ESI): Calculated for $C_{13}H_{17}N$ [M+H$^+$] = 188.1434, Found 188.1427.

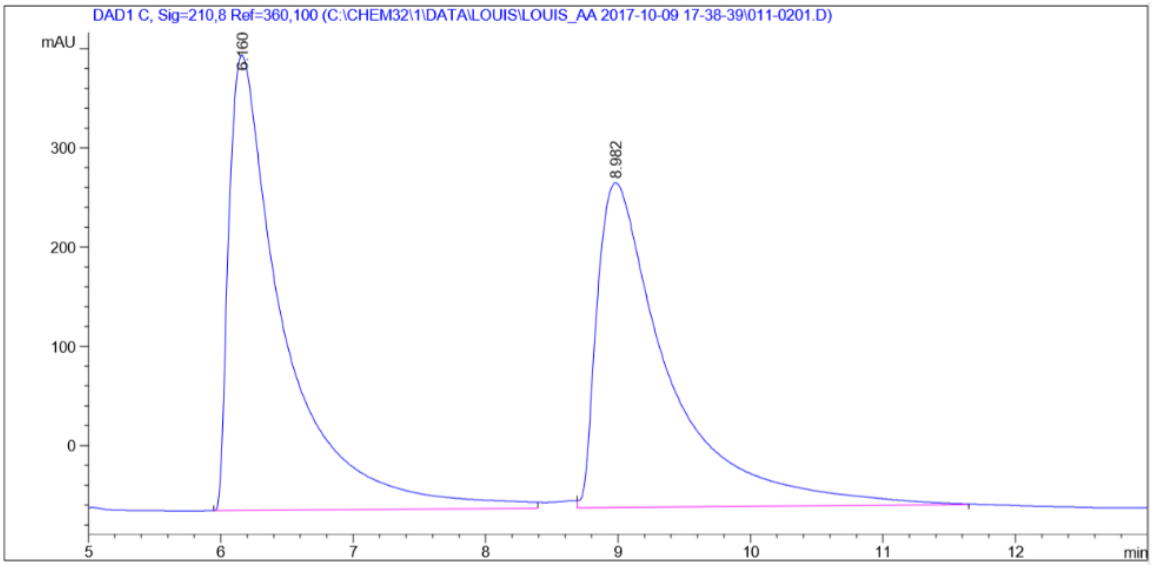
FTIR (neat): 2970, 1738, 1448, 1368, 1216, 1116, 966, 918, 747, 691 cm^{-1}.

$[\alpha]_D^{30}$ = –8.00 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AS-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm), *ee* = 96%.







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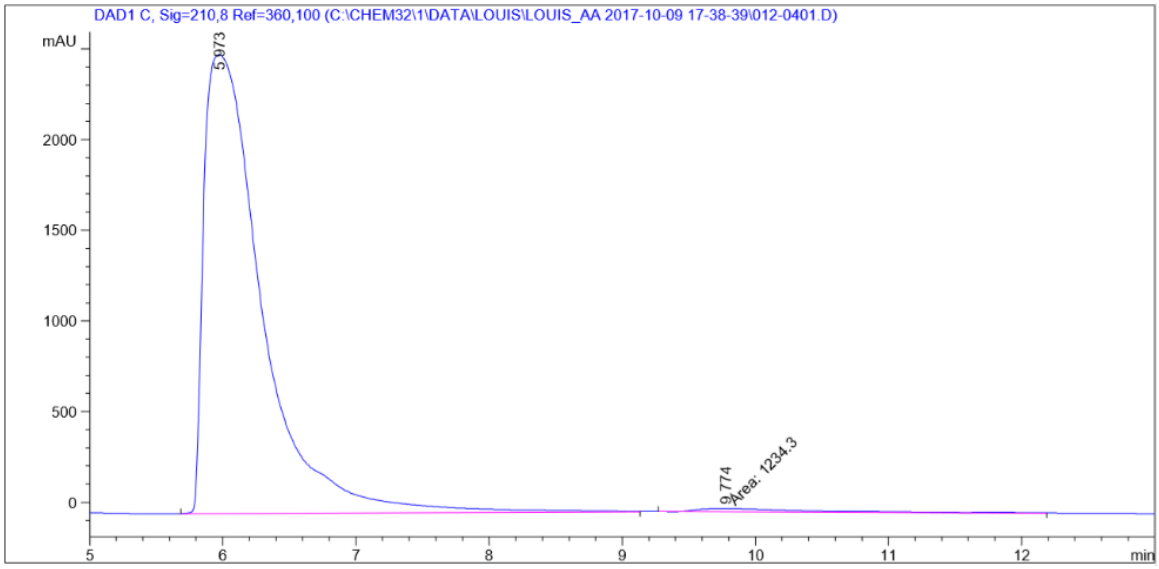

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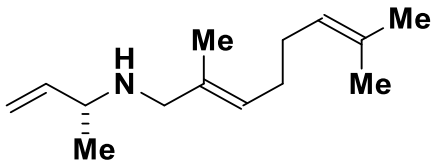
2	9.774	MM	1.0909	1234.29871	18.85817	1.5838

(*R*,*E*)-N-(but-3-en-2-yl)-2,7-dimethylocta-2,6-dien-1-amine (4.3k)



Procedures

The allylic acetate (22.8 mg, 0.20 mmol, 100 mol%) and the primary amine (61.3 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (50 °C, 18 hr). The title compound was obtained in 90% yield (37.3 mg, 0.18 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–1:1).

TLC (SiO_2) R_f = 0.16 (methanol/ethyl acetate = 1:9).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.69 (ddd, *J* = 17.1, 10.2, 7.9 Hz, 1H), 5.28 – 5.20 (m, 1H), 5.13 – 5.02 (m, 3H), 3.19 (dtd, *J* = 25.9, 12.8, 6.8 Hz, 3H), 3.03 (br, 1H), 2.09 – 1.95 (m, 4H), 1.66 (d, *J* = 1.3 Hz, 3H), 1.60 (s, 3H), 1.58 (s, 3H), 1.17 (d, *J* = 6.5 Hz, 3H).

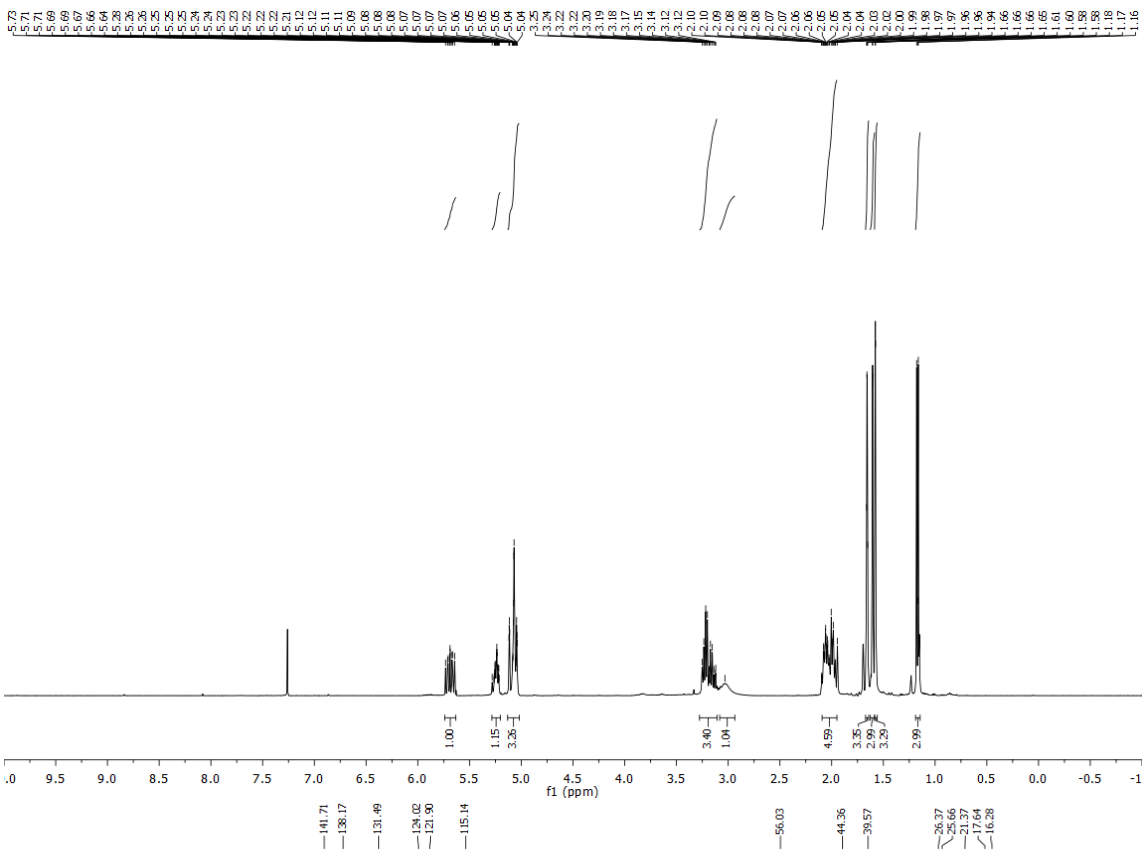
^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.7, 138.2, 131.5, 124.0, 121.9, 115.1, 56.0, 44.4, 39.6, 26.4, 25.7, 21.4, 17.6, 16.3.

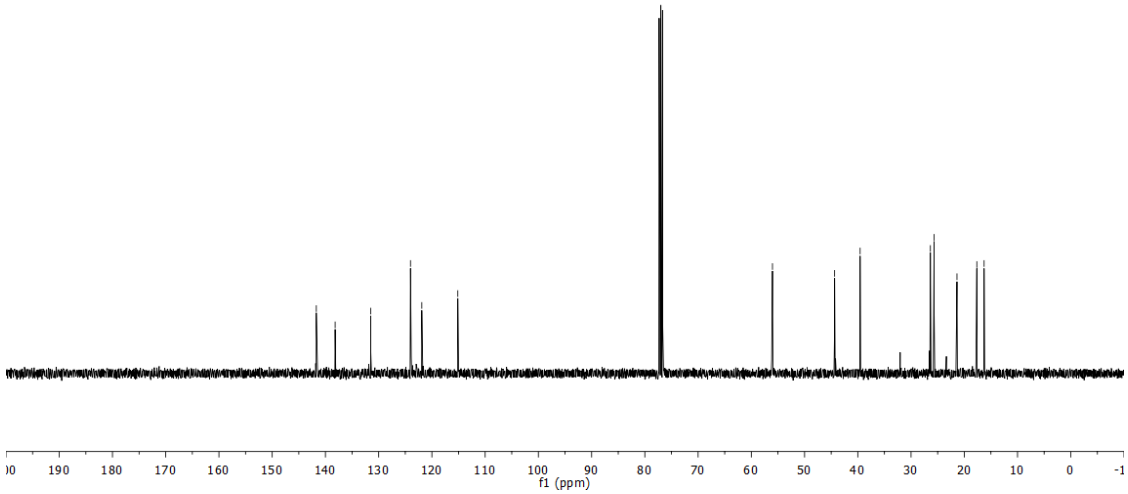
HRMS (ESI): Calculated for $C_{14}H_{25}N$ [M+H$^+$] = 208.2060, Found 208.2054.

FTIR (neat): 2924, 2359, 1629,1439, 1376, 1108, 993, 916, 753 cm^{-1}.

$[\alpha]_D^{28}$= –6.38 (*c* 1.0, $CHCl_3$).

HPLC Enantiomeric excess was determined by HPLC analysis of the *p*-tosyl derivative of the product (Chiralcel OJ-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm), *ee* = 94%.


f1 (ppm)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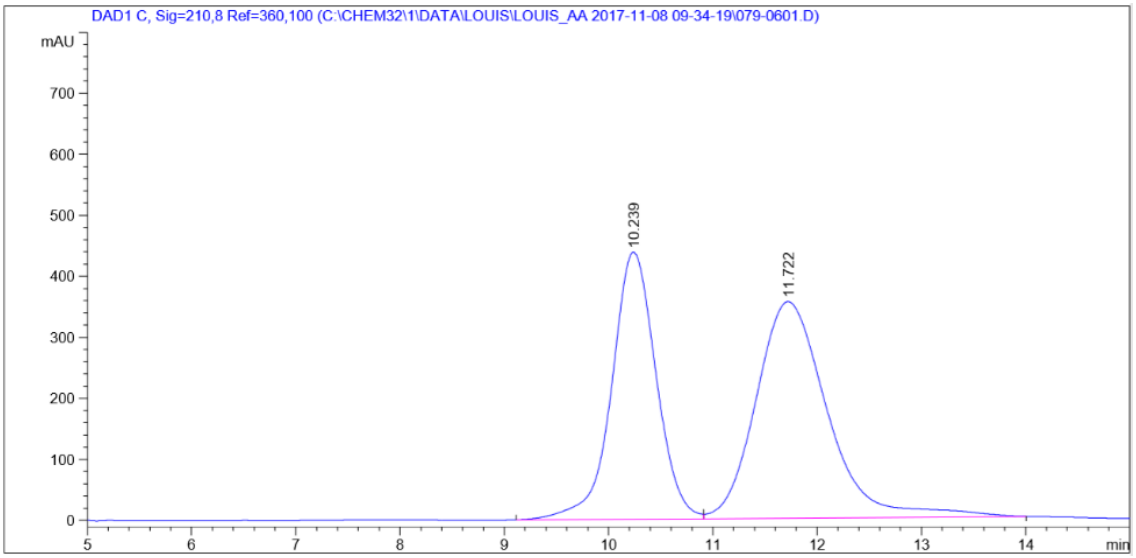
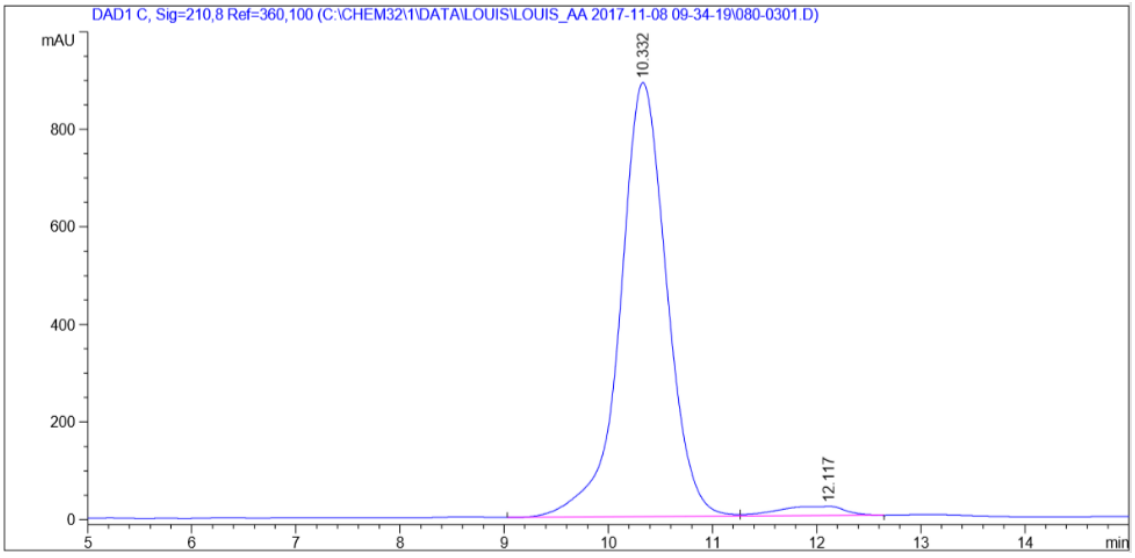
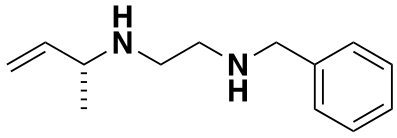


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.239	BV	0.4560	1.29841e4	437.85291	43.4180
2	11.722	VB	0.7340	1.69207e4	355.07404	56.5820



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.332	VB	0.4721	2.76141e4	889.66278	96.9946
2	12.117	BV	0.5806	855.63910	18.95768	3.0054

(*R*)-N^1-benzyl-N^2-(but-3-en-2-yl)ethane-1,2-diamine (4.3l)



Procedures

The allylic acetate (22.8 mg, 0.20 mmol, 100 mol%) and the amine (120 mg, 0.80 mmol, 400 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 710% yield (28.9 mg, 0.14 mmol) as a pale red oil after purification by flash column chromatography (SiO_2, ethyl acetate : MeOH = 10:1–3:1).

TLC (SiO_2) R_f = 0.10 (ethyl acetate).

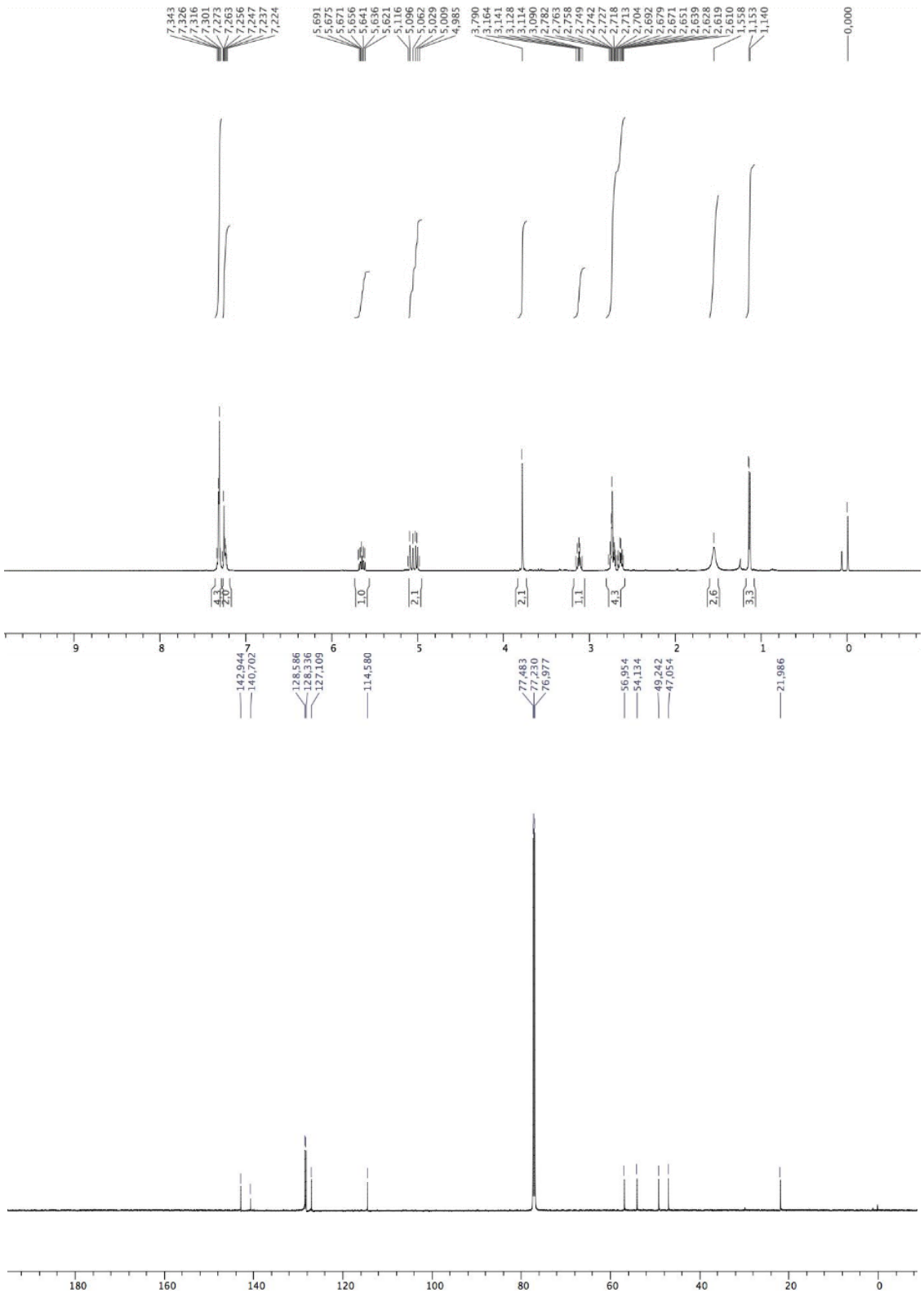
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34-7.30 (m, 4H), 7.27-7.22 (m, 1H), 5.66 (ddd, *J* = 17.0, 10.2, 7.6 Hz, 1H), 5.08 (d, *J* = 17.0 Hz, 1H), 5.02 (d, *J* = 10.2 Hz, 1H), 3.79 (s, 2H), 3.16-3.09 (m, 1H), 2.78-2.69 (m, 3H), 2.68-2.61 (m, 1H), 1.56 (bs, 1H), 1.15 (d, *J* = 6.5 Hz, 3H)

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.9, 140.7, 128.6 (2C), 128.3 (2C), 127.1, 114.6, 57.0, 54.1, 49.2, 47.1, 22.0.

HRMS (ESI): Calculated for $C_{13}H_{20}N_2$ [M+H$^+$] = 205.1699, Found 205.1693.

FTIR (neat): 3315, 3063, 3027, 2971, 2925, 2819, 2187, 1639, 1602, 1494, 1452, 1415, 1369, 1312, 1114 1073, 1027, 993, 911, 729, 697 cm^{-1}.

$[\alpha]_D^{24}$ = –5.4 (*c* 1.1, $CHCl_3$).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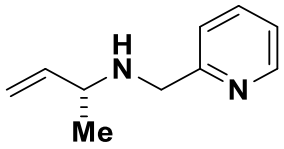
(*R*)-N-(pyridin-2-ylmethyl)but-3-en-2-amineamine (4.3m)



Procedures

The allylic acetate (22.8 mg, 0.20 mmol, 100 mol%) and the primary amine (43.2 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (50 ^{o}C, 18 hr). The title compound was obtained in 90% yield (29.0 mg, 0.18 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 2:1–1:2).

TLC (SiO_2) R_f = 0.13 (ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.55 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.62 (td, *J* = 7.7, 1.8 Hz, 1H), 7.28 (m, 1H), 7.15 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 5.73 (ddd, *J* = 17.2, 10.2, 7.8 Hz, 1H), 5.16 – 5.05 (m, 2H), 3.91 (d, *J* = 14.0 Hz, 1H), 3.81 (d, *J* = 14.0 Hz, 1H), 3.27 – 3.18 (m, 1H), 1.87 (br, 1H), 1.21 (d, *J* = 6.5 Hz, 3H).

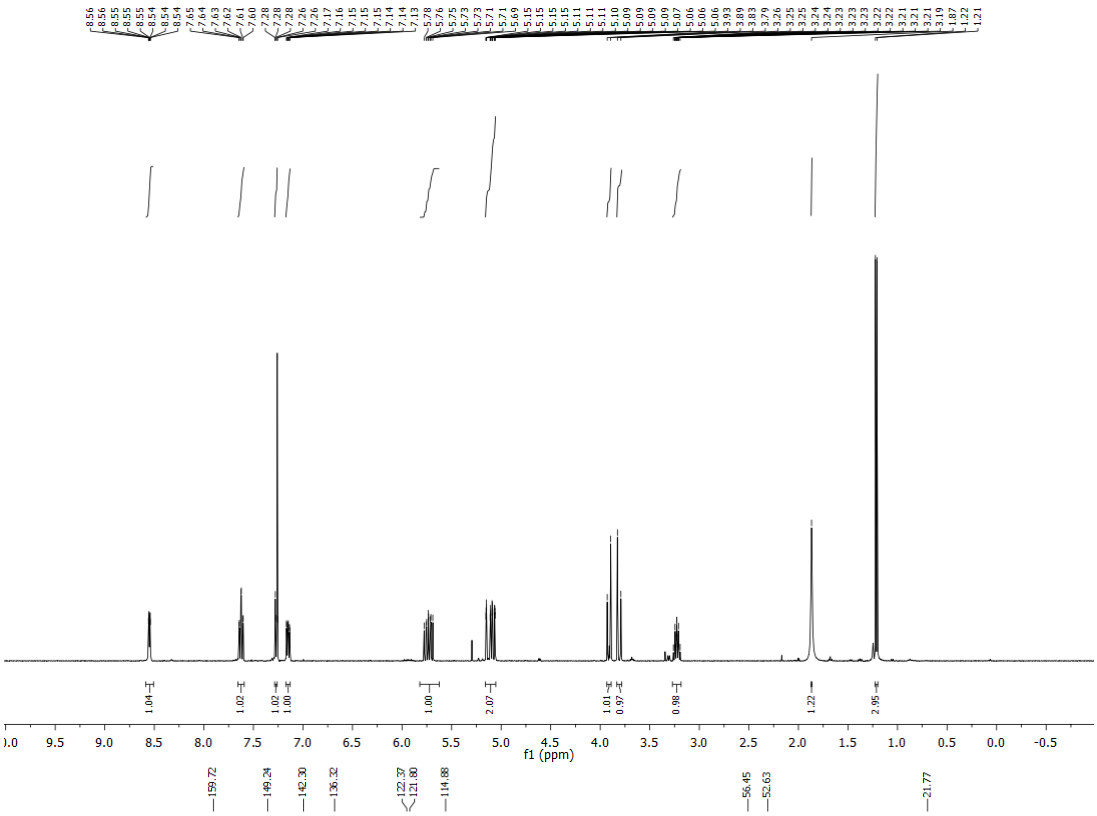
^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.7, 149.2, 142.3, 136.3, 122.4, 121.8, 114.9, 56. 5, 52.6, 21.8.

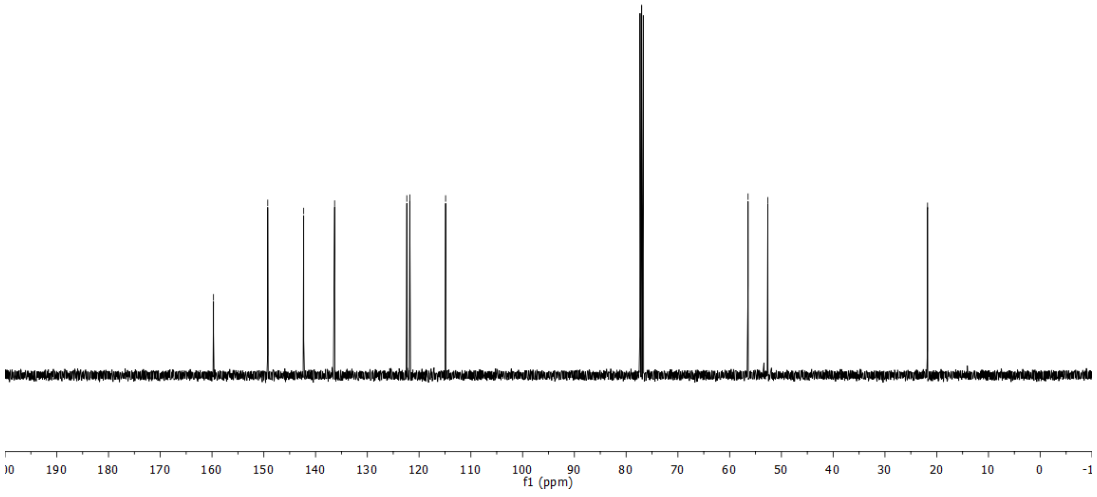
HRMS (ESI): Calculated for $C_{10}H_{14}N_2$ [M+H$^+$] = 163.1230, Found 163.1226.

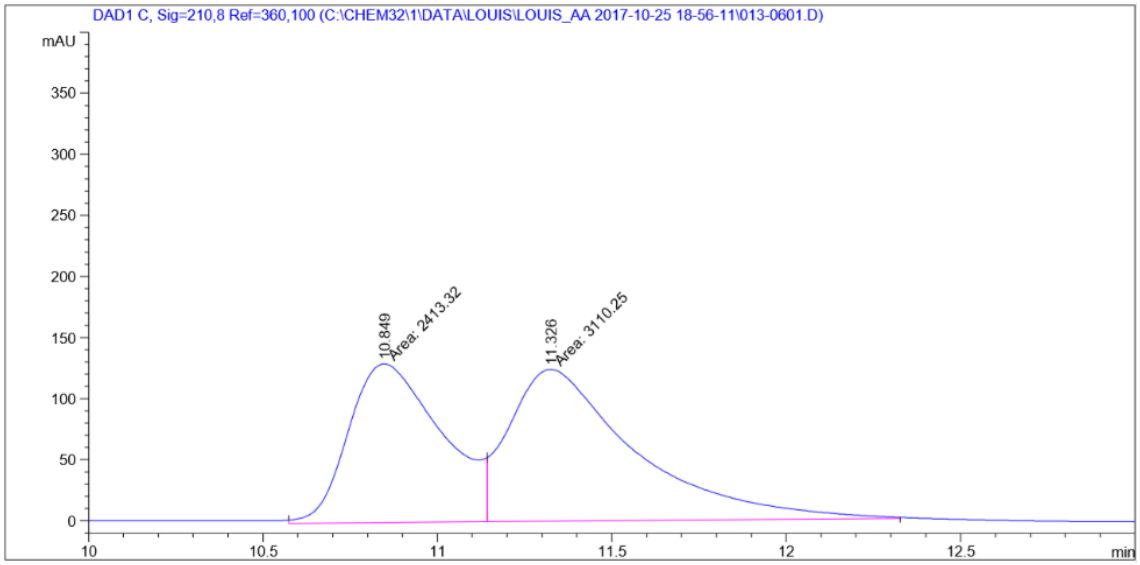
FTIR (neat): 2962, 1592, 1434, 1216, 1118, 995, 921, 751 cm^{-1}.

$[\alpha]_D^{30}$= –19.50 (*c* 1.0, $CHCl_3$).

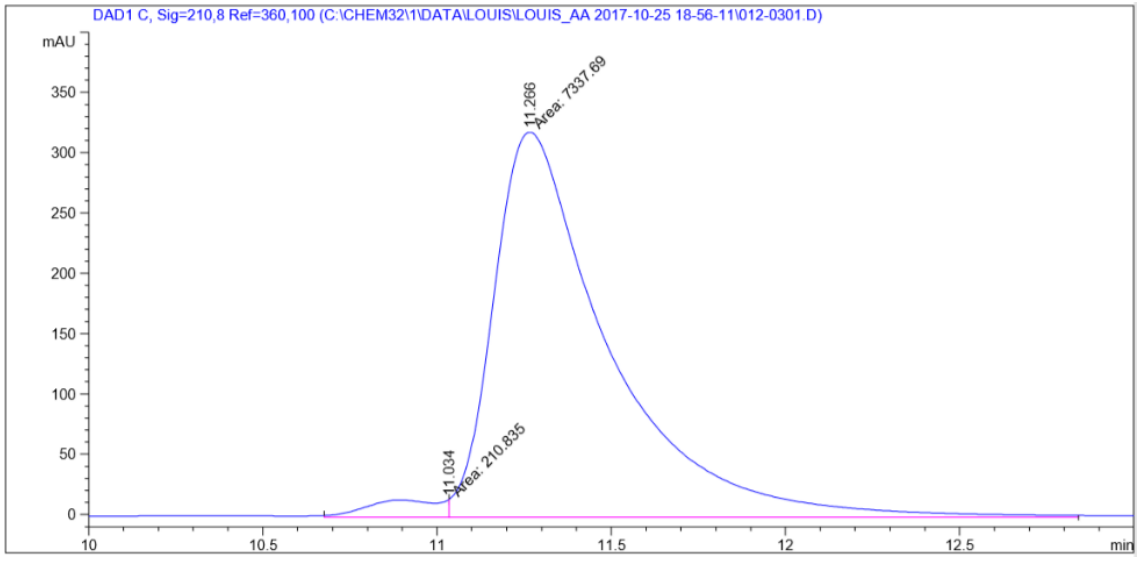
HPLC Enantiomeric excess was determined by HPLC analysis of the product with (*S*)-Ir-SEGPHOS (Chiralcel AD column, hexanes:*i*-PrOH = 98:2, 0.80 mL/min, 210 nm), *ee* = 94%.


f1 (ppm)


f1 (ppm)

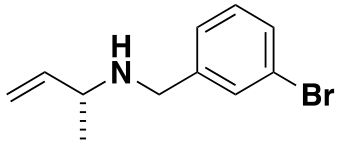


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.849	MF	0.3098	2413.31958	129.82436	43.6913
2	11.326	FM	0.4170	3110.24976	124.30628	56.3087



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.034	MF	0.2420	210.83543	14.52171	2.7931
2	11.266	FM	0.3831	7337.68896	319.22510	97.2069

(*R*)-*N*-(3-bromobenzyl)but-3-en-2-amine (4.3n)



Procedures

The allylic acetate (22.8 mg, 0.20 mmol, 100 mol%) and the primary amine (74.4 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 86% yield (41.3 mg, 0.17 mmol) as a pale yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 1:1).

TLC (SiO_2) R_f = 0.64 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49 (s, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.18 (t, *J* = 7.8 Hz, 1H), 5.69 (ddd, *J* = 17.2, 10.2, 7.7 Hz, 1H), 5.16-5.06 (m, 2H), 3.77 (d, *J* = 13.4 Hz, 1H), 3.65 (d, *J* = 13.4 Hz, 1H), 3.23-3.16 (m, 1H), 1.36 (bs, 1H), 1.18 (d, *J* = 6.5 Hz, 3H).

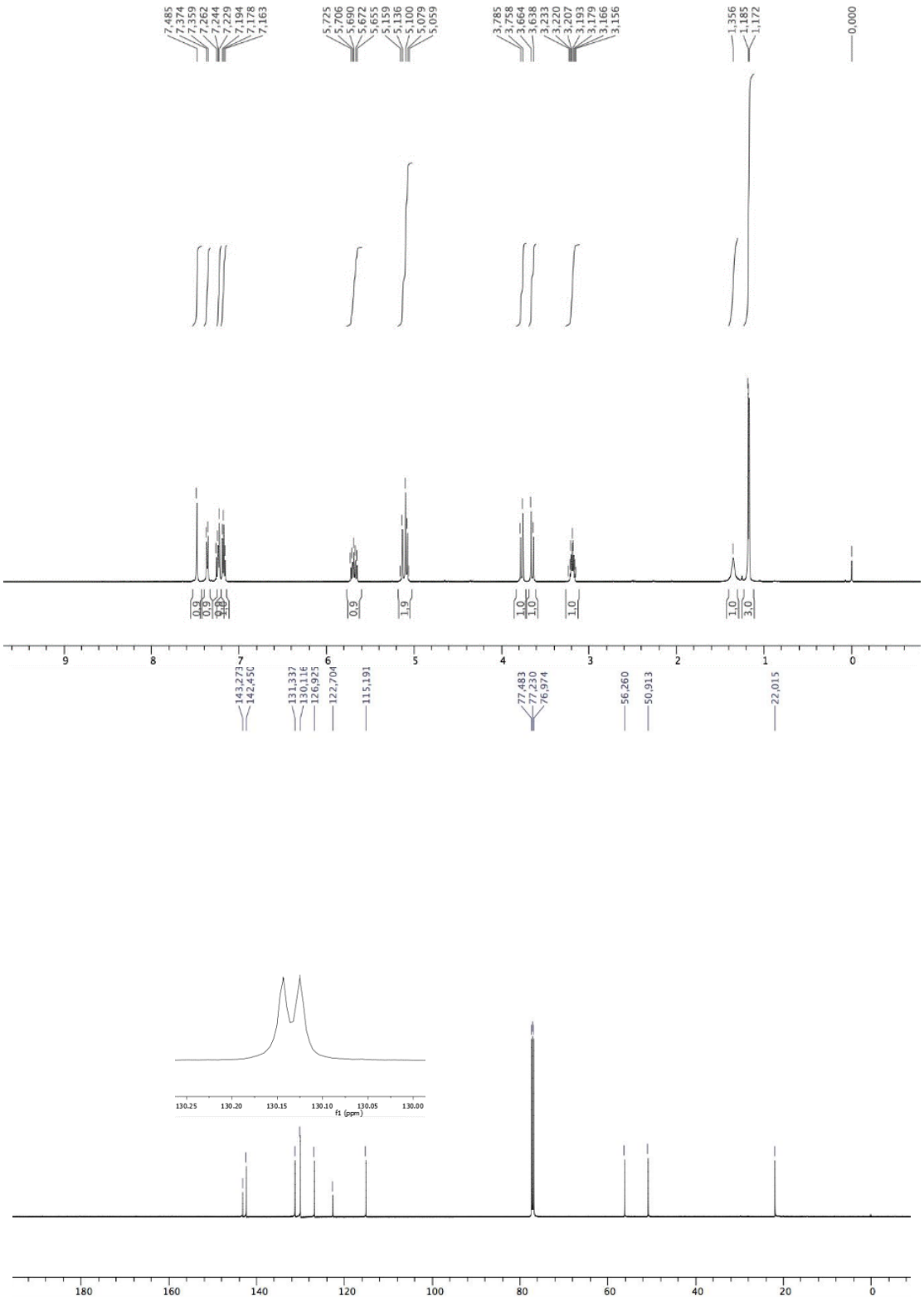
^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.3, 142.5, 131.3, 130.1(x2), 126.9, 122.7, 115.2, 56.3, 50.9, 22.0.

HRMS (ESI): Calculated for $C_{11}H_{14}BrN$ [M+H$^+$] = 240.0382, Found 240.0375.

FTIR (neat): 3311, 3073, 2971, 2923, 2818, 1775, 1640, 1594, 1568, 1470, 145, 1370, 1312, 1195, 1165, 1114, 1068, 1038, 994, 918, 883, 859, 829, 775, 683, 667 cm^{-1}.

$[\alpha]_D^{24}$ = –8.3 (*c* 3.1, $CHCl_3$).

HPLC (3x Chiralcel AD-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 230 nm), *ee* = 92 %.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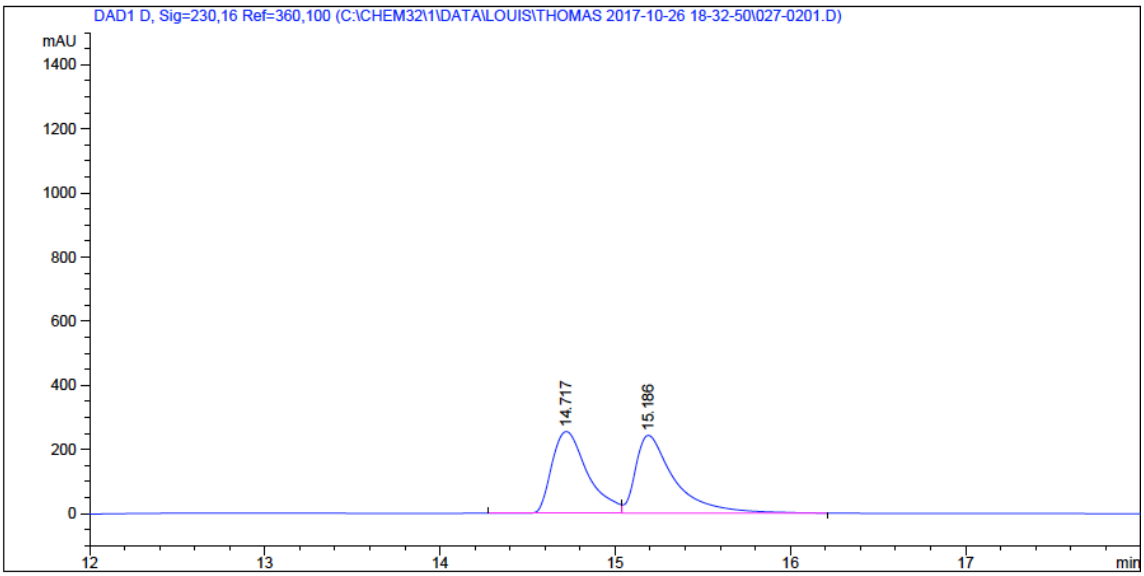
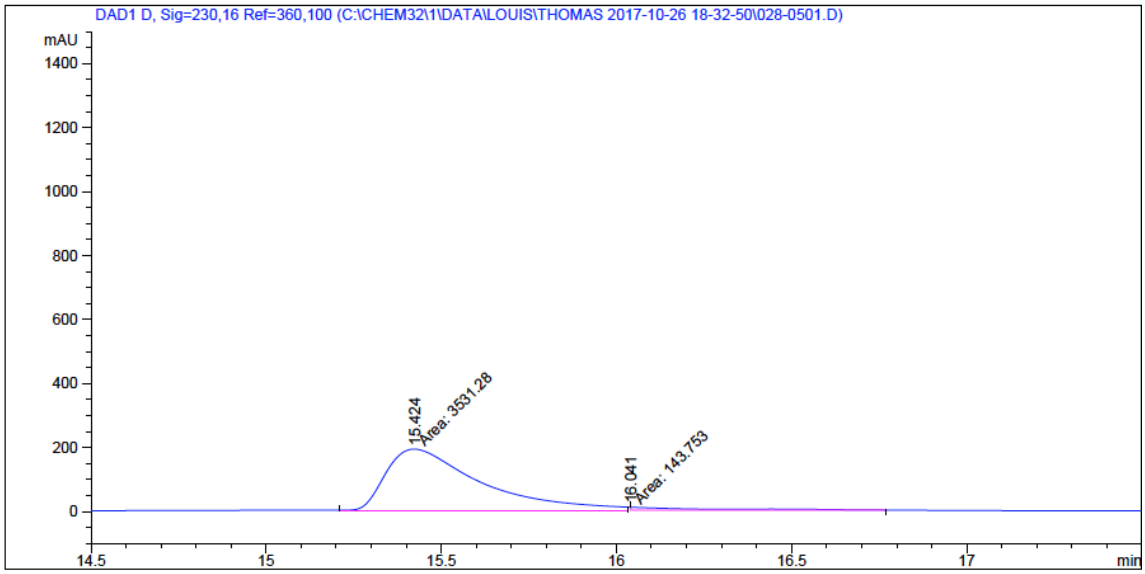
f1 (ppm)

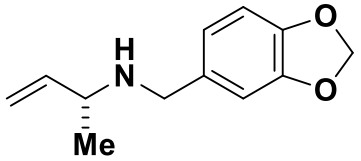


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.717	BV	0.2193	3613.74463	255.02808	49.0108
2	15.186	VB	0.2265	3759.61377	243.01231	50.9892



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.424	MF	0.3084	3531.27563	190.84509	96.0884
2	16.041	MM	0.2438	143.75337	9.21139	3.9116

(*R*)-N-(benzo[d][1,3]dioxol-5-ylmethyl)but-3-en-2-amine (4.3o)



Procedures

The allylic acetate (22.8 mg, 0.20 mmol, 100 mol%) and the primary amine (60.5 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (50 °C, 18 hr). The title compound was obtained in 92% yield (37.7 mg, 0.18 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–1:1).

TLC (SiO_2) R_f = 0.22 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.83 (s, 1H), 6.75 (d, *J* = 1.1 Hz, 2H), 5.93 (s, 2H), 5.69 (ddd, *J* = 17.2, 10.2, 7.7 Hz, 1H), 5.16 – 5.03 (m, 2H), 3.70 (d, *J* = 13.1 Hz, 1H), 3.58 (d, *J* = 13.0 Hz, 1H), 3.24 – 3.15 (m, 1H), 1.16 (d, *J* = 6.5 Hz, 3H).

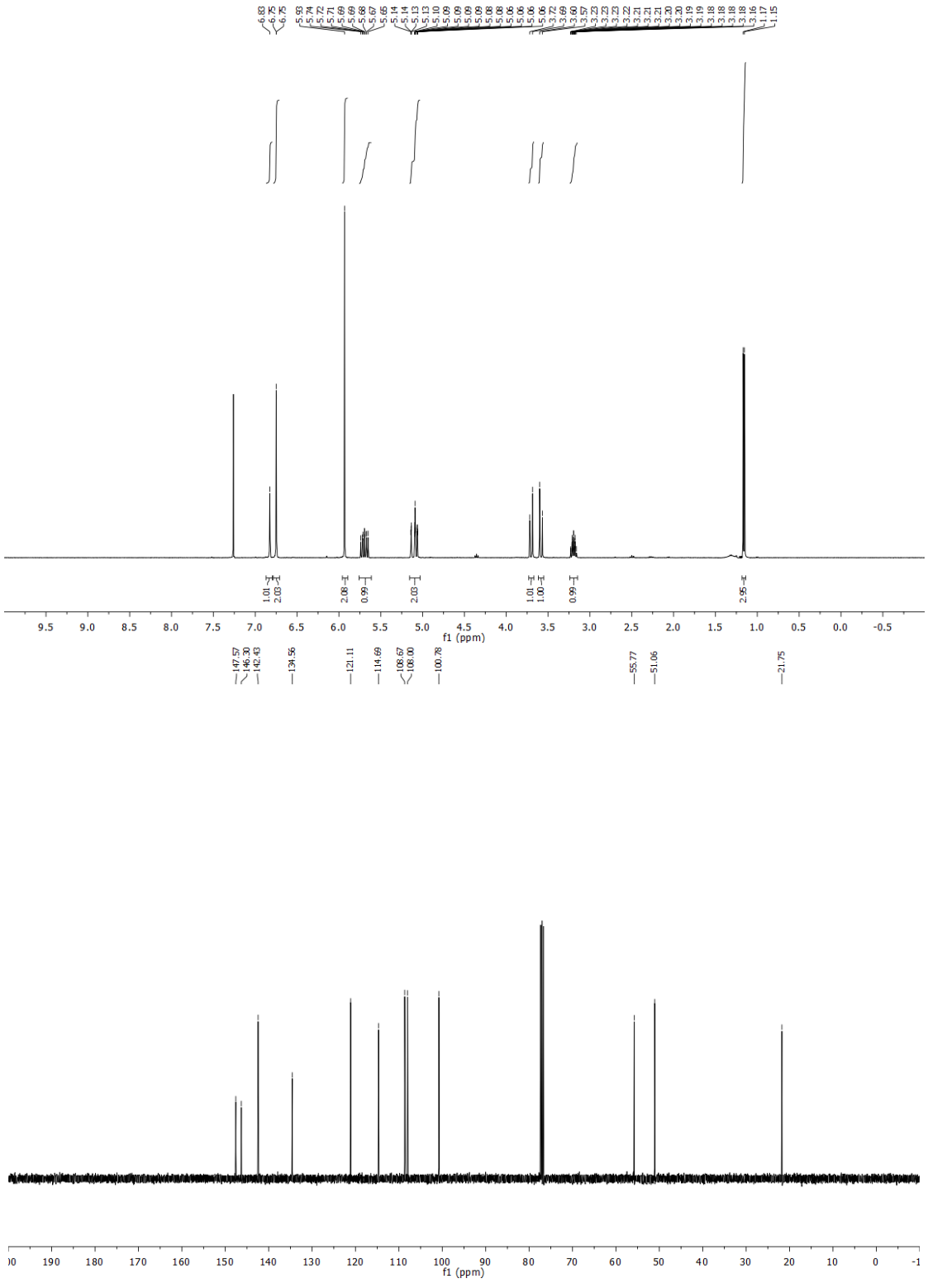
^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.6, 146.3, 142.4, 134.6, 121.1, 114.7, 108.7, 108.0, 100.8, 55.8, 51.1, 21.8.

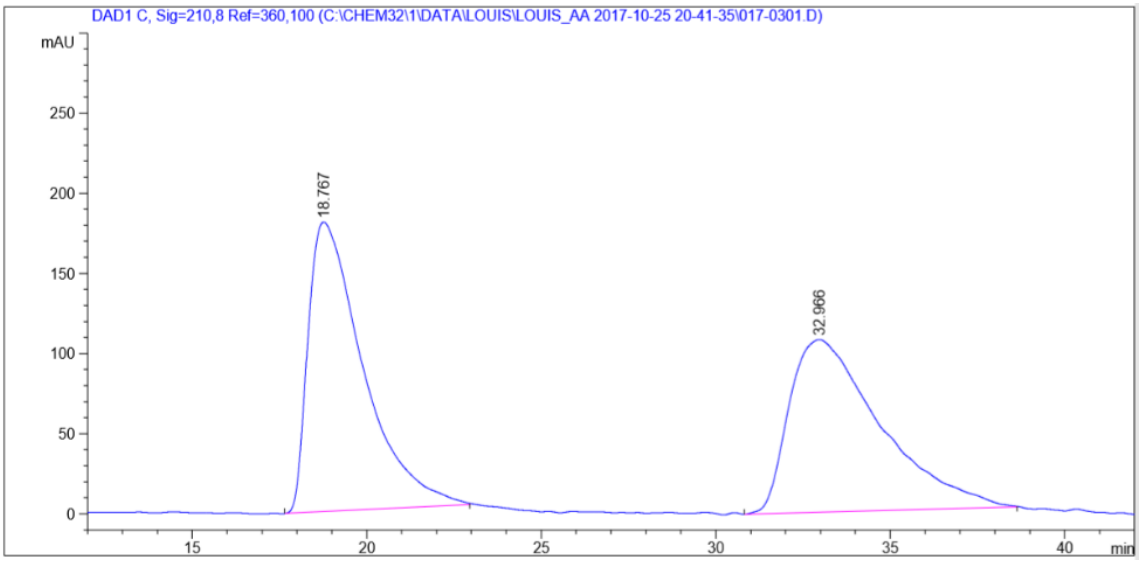
HRMS (ESI): Calculated for $C_{12}H_{15}NO_2$ $[M+H^+]$ = 206.1176, Found 206.1169.

FTIR (neat): 2971, 1488, 1441, 1249, 1040, 923, 808, 754 cm^{-1}.

$[\alpha]_D^{28}$ = –6.25 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AS-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm), *ee* = 99%.


f1 (ppm)
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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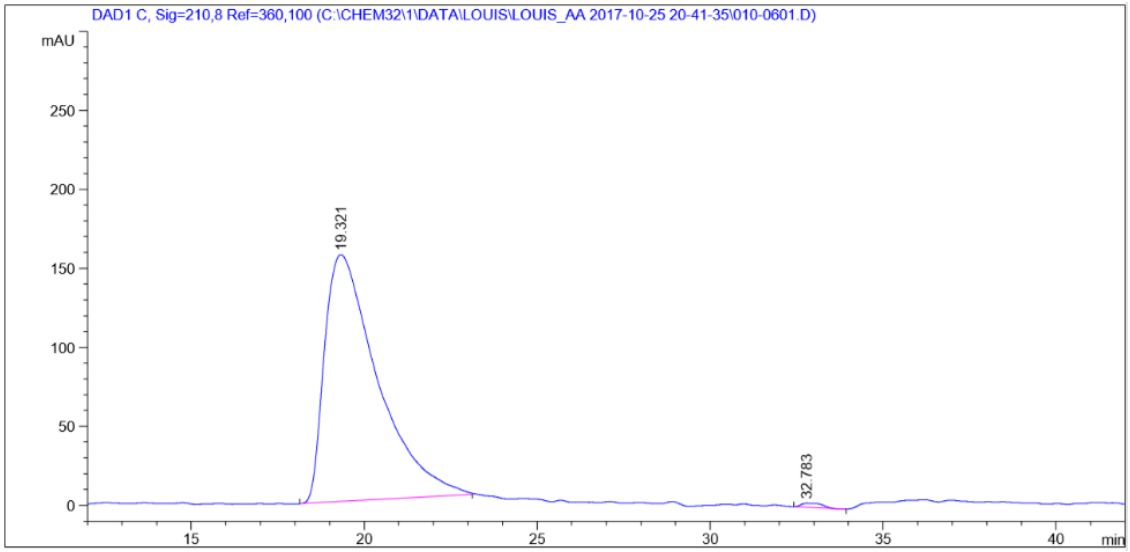
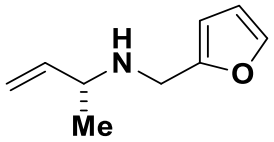
2	32.966	VB	2.2070	1.95257e4	107.80961	49.7215



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.321	BB	1.5339	1.66242e4	156.16505	99.3684
2	32.783	BB	0.5224	105.67055	2.53473	0.6316

(*R*)-N-(furan-2-ylmethyl)but-3-en-2-amine (4.3p)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (85.5 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (50 ^{o}C, 18 hr). The title compound was obtained in 74% yield (48.9 mg, 0.32 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.23 (hexanes:ethyl acetate 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37-7.34 (m, 1H), 6.32-6.28 (m, 1H), 6.17-6.12 (m, 1H), 5.68 (ddd, *J* = 17.5, 10.2, 7.8 Hz, 1H), 5.17 – 5.04 (m, 2H), 3.79 (d, *J* = 14.3 Hz, 1H), 3.69 (d, *J* = 14.4 Hz, 1H), 3.24 - 3.15 (m, 1H), 1..17 (d, *J* = 6.5 Hz, 3H).

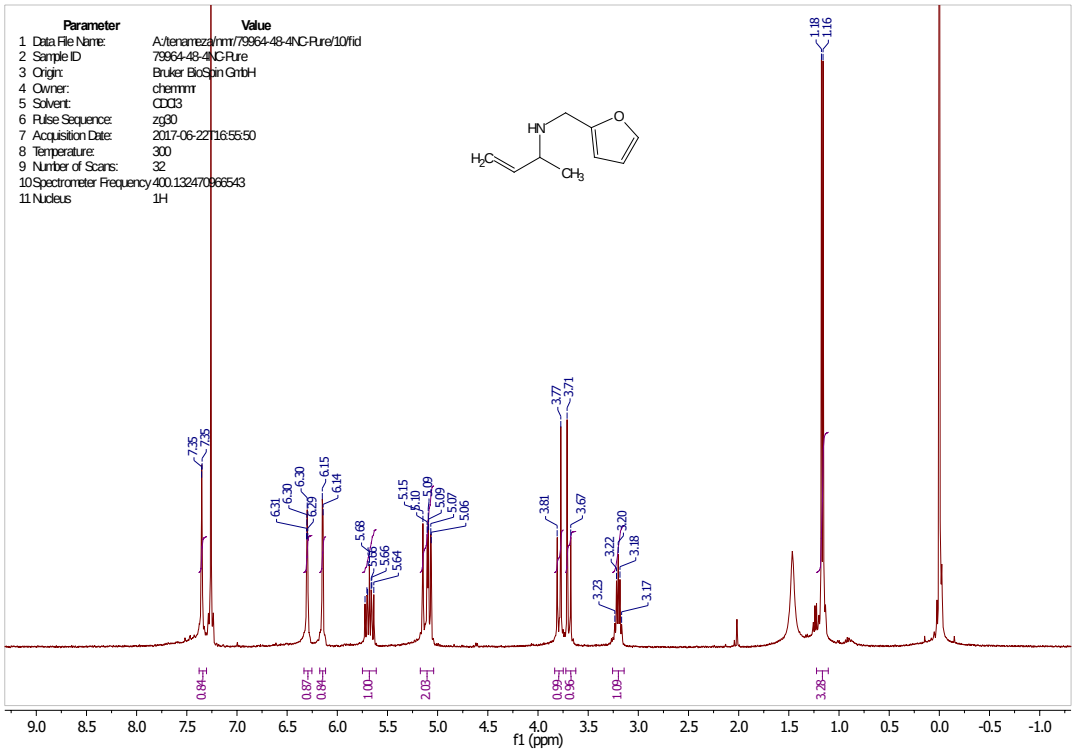
^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.1, 142.1, 141.7, 115.1, 110.0, 106.7, 55.7, 43.7, 21.7.

HRMS (ESI): Calculated for $C_9H_{14}NO$ $[M+H^+]$ = 152.1075, found 152.1067.

FTIR (neat): 2973, 1672, 1600, 1505, 1439, 1416, 1370, 1315, 1251, 1147, 1110, 1074, 1011, 995, 918, 884, 804, 730 cm^{-1}.

$[\alpha]_D^{24}$= +18.5 (*c* 0.63, $CHCl_3$).

HPLC (Chiralcel OD-H column, heptane:*i*-PrOH = 99.0:1.0, 1.00 mL/min, 220 nm), *ee* = 92%.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5 Solvent: CDCl3
6 Pulse Sequence: zg30
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8 Temperature: 300
9 Number of Scans: 32
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6.30
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6.14
5.68
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5.66
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5.09
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3.23
3.22
3.20
3.18
3.17
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2.08
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0.96
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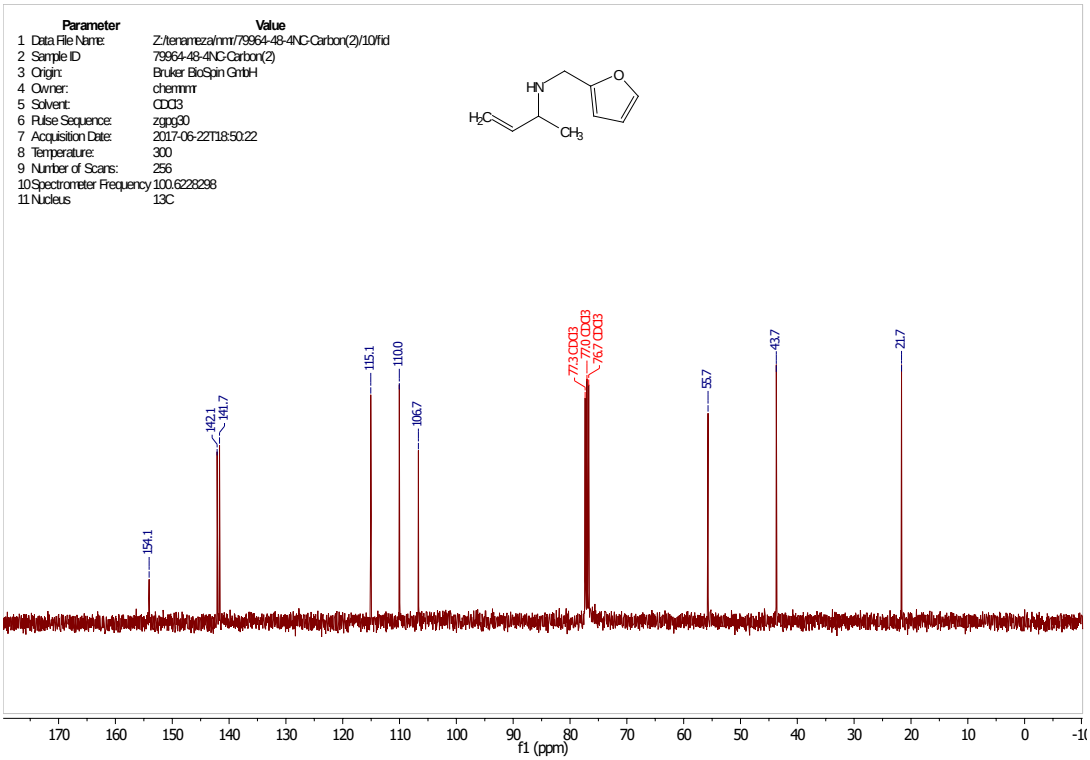
3.28
f1 (ppm)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8 Temperature: 300
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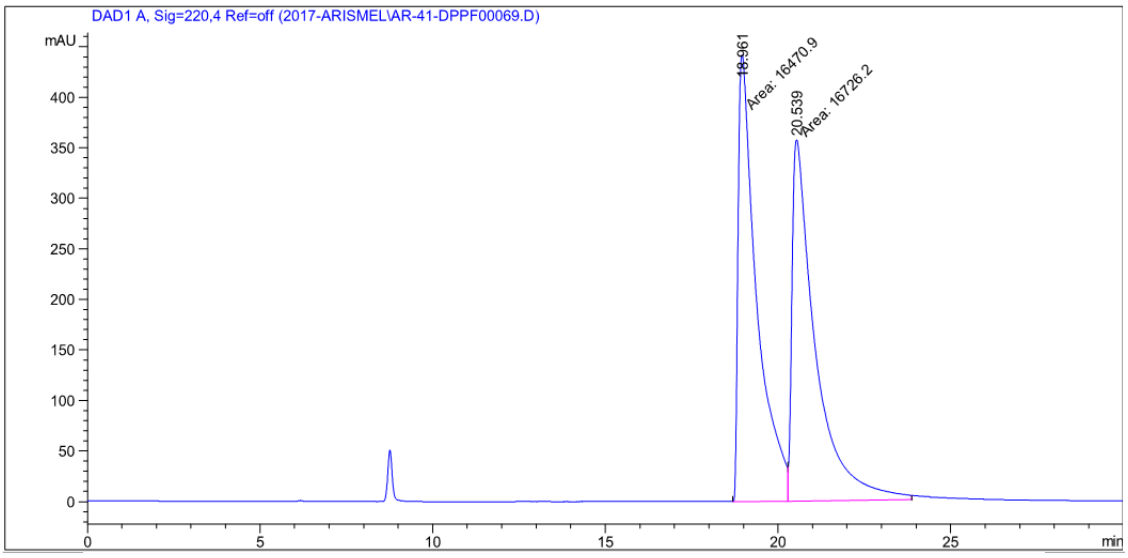
21.7
f1 (ppm)



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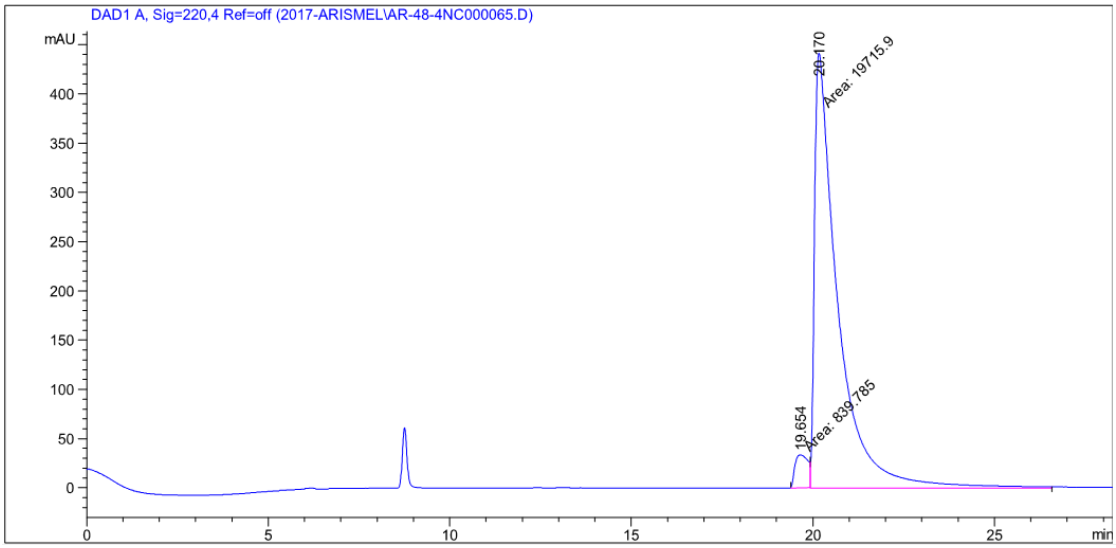
2	20.539	FM	0.7797	1.67262e4	357.55142	50.3845



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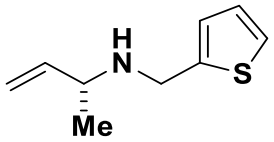
1	19.654	MM	0.4181	839.78534	33.47266	4.0854
2	20.170	MM	0.7445	1.97159e4	441.38776	95.9146

(*R*)-N-(thiophen-2-ylmethyl)but-3-en-2-amine (4.3q)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (99.6 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (50 ^{o}C, 18 hr). The title compound was obtained in 98% yield (71.5 mg, 0.43 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.40 (hexanes:ethyl acetate 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22 - 7.17 (m, 1H), 6.96 – 6.92 (m, 1H), 6.92 - 6.89 (m, 1H), 5.69 (ddd, *J* = 17.6, 10.2, 7.7 Hz, 1H), 5.18 – 5.05 (m, 2H), 3.99 (dd, *J* = 14.1, 0.9 Hz, 1H), 3.90 (dd, *J* = 14.1, 0.8 Hz, 1H), 3.31 - 3.21 (m, 1H), 1.17 (d, *J* = 6.5 Hz, 3H).

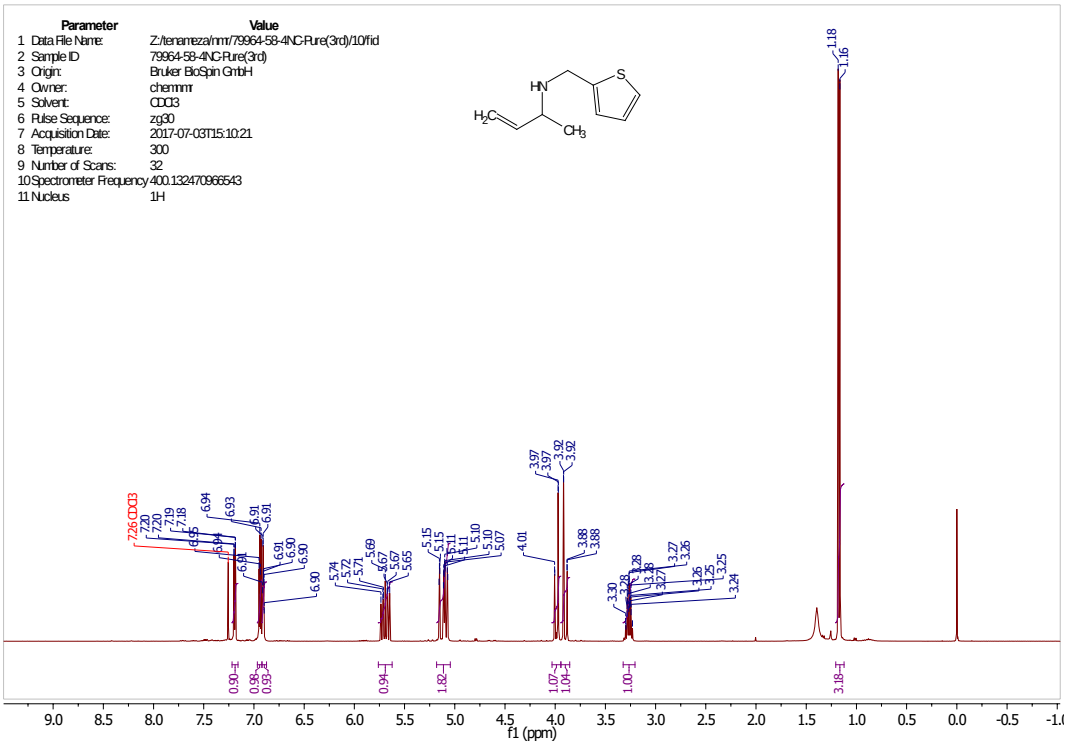
^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.4, 142.2, 126.6, 124.7, 124.2, 115.0, 55.6, 45.7, 21.7.

HRMS (ESI): Calculated for $C_9H_{14}NS$ [M+H$^+$] = 168.0847, found 168.0838.

FTIR (neat): 3072, 2971, 1636, 1439, 1416, 1369, 1311, 1218, 1171, 1111, 1038, 993, 918, 852, 824, 693 cm^{-1}.

$[\alpha]_D^{24}$= +18.5 (*c* 0.63, $CHCl_3$).

HPLC (Chiralcel OD-H column, heptane:*i*-PrOH = 99.0:1.0, 0.50 mL/min, 220 nm), *ee* = 89%.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2 Sample ID 79964-58-4NC-Pure(3rd)
3 Origin: Bruker BioSpin GmbH
4 Owner: chemmr
5 Solvent: CDCl3
6 Pulse Sequence: zg30
7 Acquisition Date: 2017-07-03T15:10:21
8 Temperature: 300
9 Number of Scans: 32
10 Spectrometer Frequency 400.132470966543
11 Nucleus 1H
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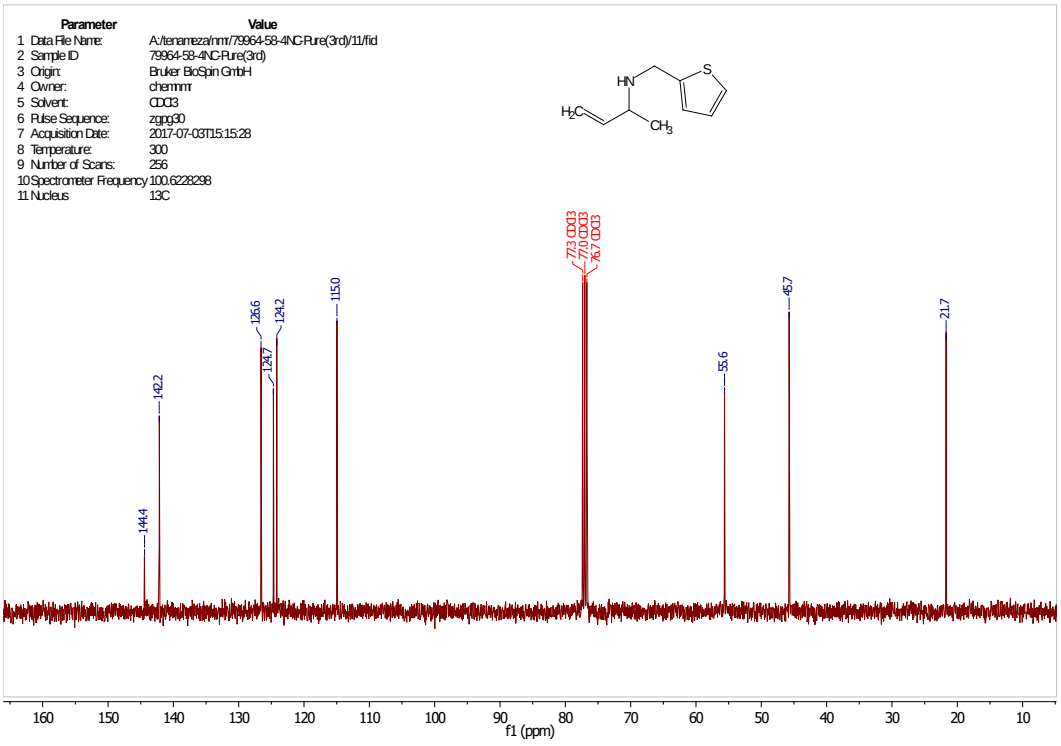
H2C
CH3
f1 (ppm)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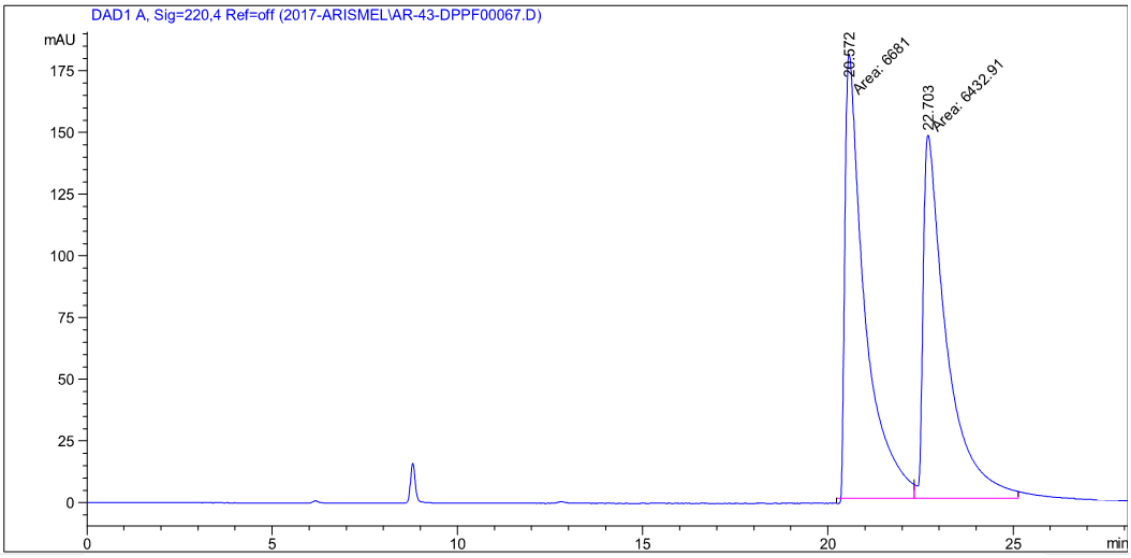
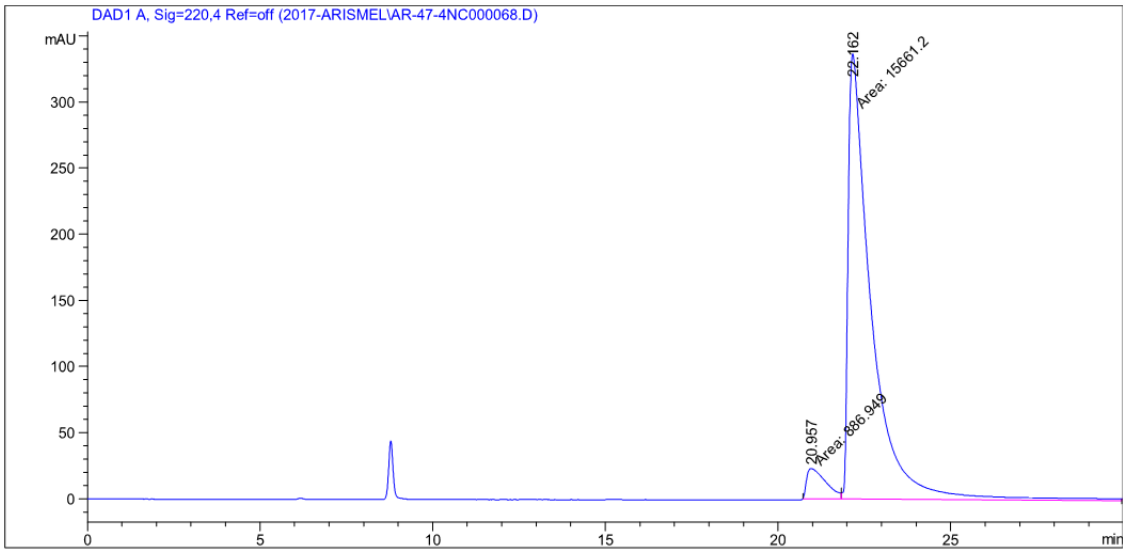
3 Origin: Bruker BioSpin GmbH
4 Owner: chemmr
5 Solvent: CDCl3
6 Pulse Sequence: zgpg30
7 Acquisition Date: 2017-07-03T15:15:28
8 Temperature: 300
9 Number of Scans: 256
10 Spectrometer Frequency 100.6228298
11 Nucleus 13C
HN
S
H2C
CH3
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.572	MM	0.6187	6681.00391	179.98734	50.9459
2	22.703	MM	0.7280	6432.90674	147.27884	49.0541



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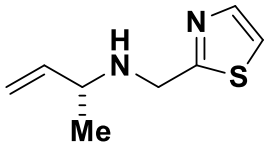
1	20.957	MF	0.6449	886.94867	22.92145	5.3598
2	22.162	FM	0.7751	1.56612e4	336.73889	94.6402

(*R*)-N-(thiazol-2-ylmethyl)but-3-en-2-amine (4.3r)



Procedures

The allylic acetate (22.8 mg, 0.20 mmol, 100 mol%) and the primary amine (45.6 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (50 ^{o}C, 18 hr). The title compound was obtained in 80% yield (26.8 mg, 0.16 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–1:1).

TLC (SiO_2) R_f = 0.21 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 3.3 Hz, 1H), 7.25 (d, *J* = 3.3 Hz, 1H), 5.69 (ddd, *J* = 17.2, 10.2, 7.6 Hz, 1H), 5.17 – 5.07 (m, 2H), 4.12 (d, *J* = 15.4 Hz, 1H), 4.06 (d, *J* = 15.4 Hz, 1H), 3.28 (ddt, *J* = 7.4, 6.5, 0.9 Hz, 1H), 1.94 (br, 1H), 1.21 (d, *J* = 6.5 Hz, 3H).

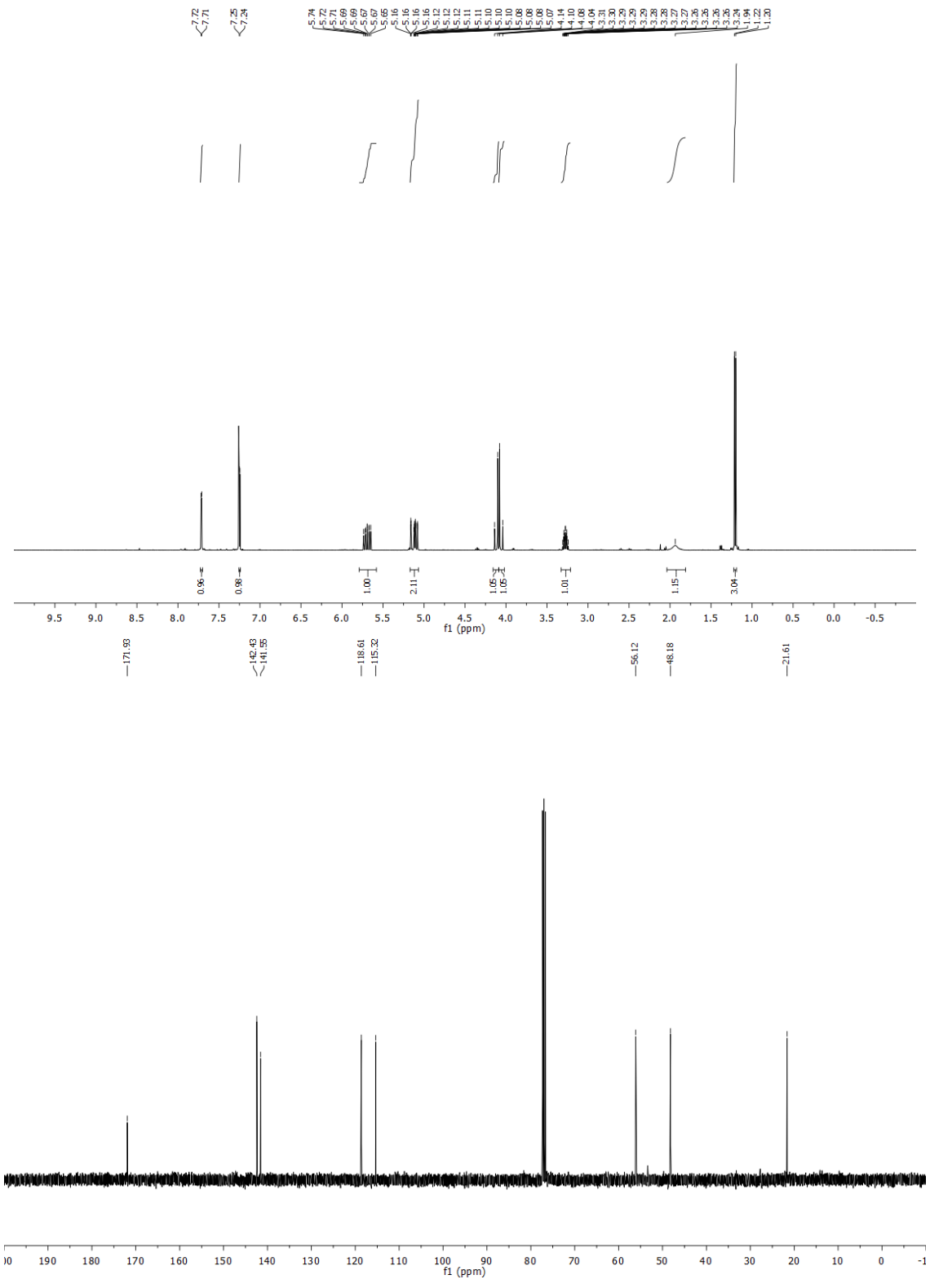
^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.0, 142.4, 141.6, 118.6, 115.3, 56.1, 48.2, 21.6.

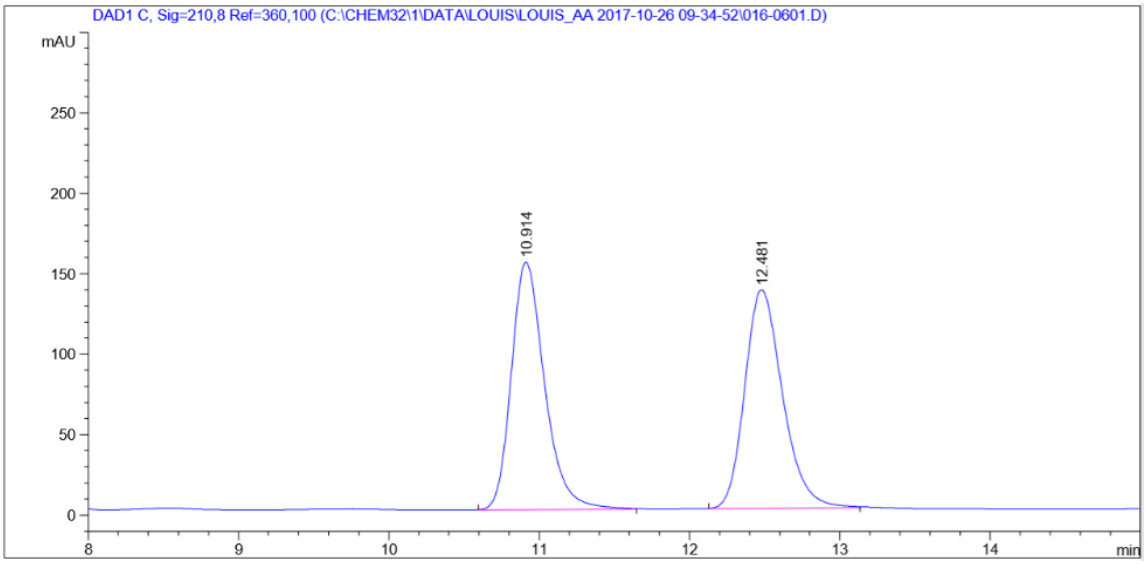
HRMS (ESI): Calculated for $C_8H_{12}N_2S$ [M+H$^+$] = 169.0794, Found 169.0789.

FTIR (neat): 2972, 1505, 1214, 1185, 1137, 993, 922, 750 cm^{-1}.

$[\alpha]_D^{28}$= –8.25 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm), *ee* = 96%.





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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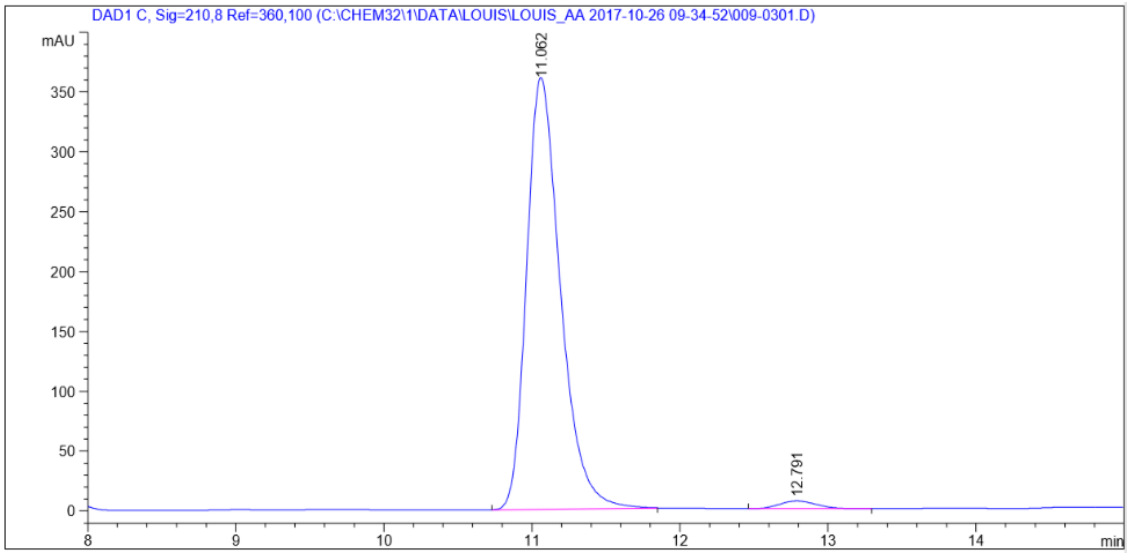
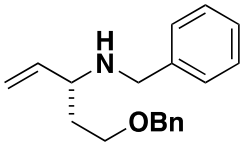
2	12.481	BB	0.2701	2377.31030	135.91629	50.0532



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.062	BB	0.2417	5741.66064	360.64893	98.0529
2	12.791	BB	0.2723	114.01456	6.51035	1.9471

(*R*)-*N*-benzyl-5-(benzyloxy)pent-1-en-3-amine (4.3s)



Procedures

The allylic acetate (103 mg, 0.44 mmol, 100 mol%) and the primary amine (94.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ^{o}C, 60 hr). The title compound was obtained in 84% yield (103 mg, 0.37 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.26 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 – 7.19 (m, 10H), 5.65 (ddd, *J* = 16.8, 10.5, 8.1 Hz, 1H), 5.18 – 5.07 (m, 2H), 4.48 (d, *J* = 11.8 Hz, 1H), 4.45 (d, *J* = 11.8 Hz, 1H) 3.82 (d, *J* = 13.3 Hz, 1H), 3.63 (d, *J* = 13.1 Hz, 1H), 3.62 – 3.46 (m, 2H), 3.27 – 3.19 (m, 1H), 1.90 - 1.80 (m, 1H), 1.78 - 1.67 (m, 1H).

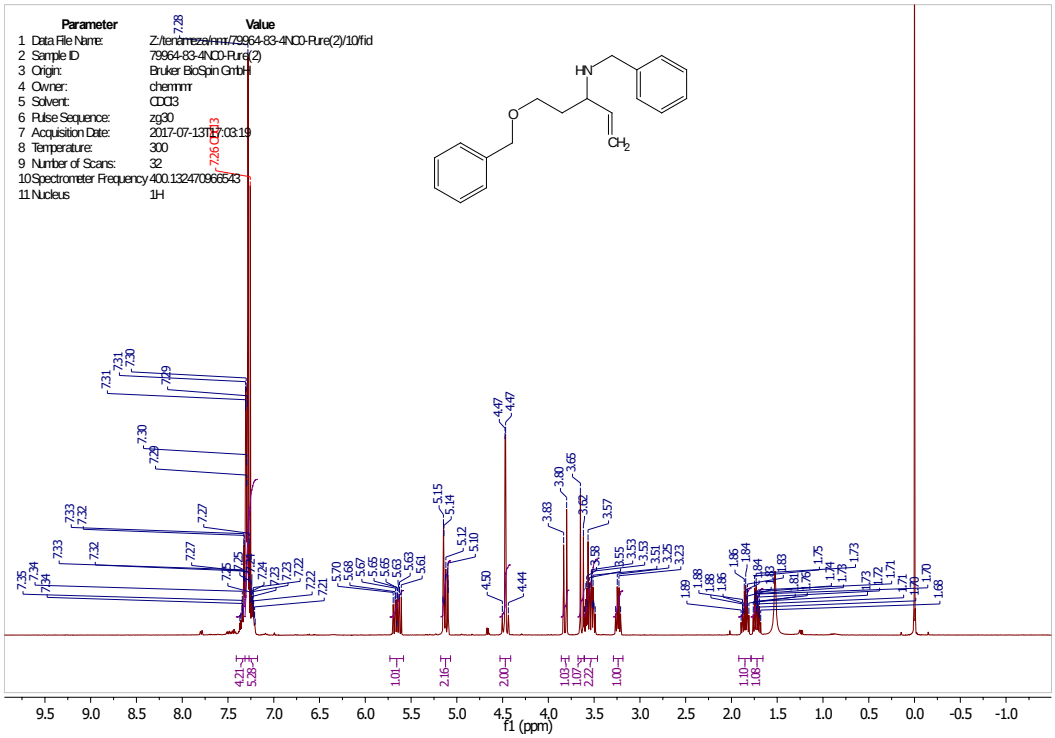
^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.5, 140.7, 138.5, 128.3, 128.2, 127.7, 127.5, 126.8, 116.1, 100.0, 73.0, 67.8, 59.0, 51.3, 35.7.

HRMS (ESI): calcd for $C_{19}H_{24}NO$ $[M+H]^+$: 282.1858, found: 282.1846

FTIR (neat): 3028, 2856, 1639, 1494, 1453, 1362, 1203, 1098, 1027, 994, 918, 733, 695 cm^{-1}.

$[\alpha]_D^{24}$ = –3.4 (*c* 0.84, $CHCl_3$).

HPLC (Chiralpak OD-H; heptane/isopropanol 90.0:10.0, 0.9 mL/min, 220 nm) ee = 94%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4 Owner: chemmr
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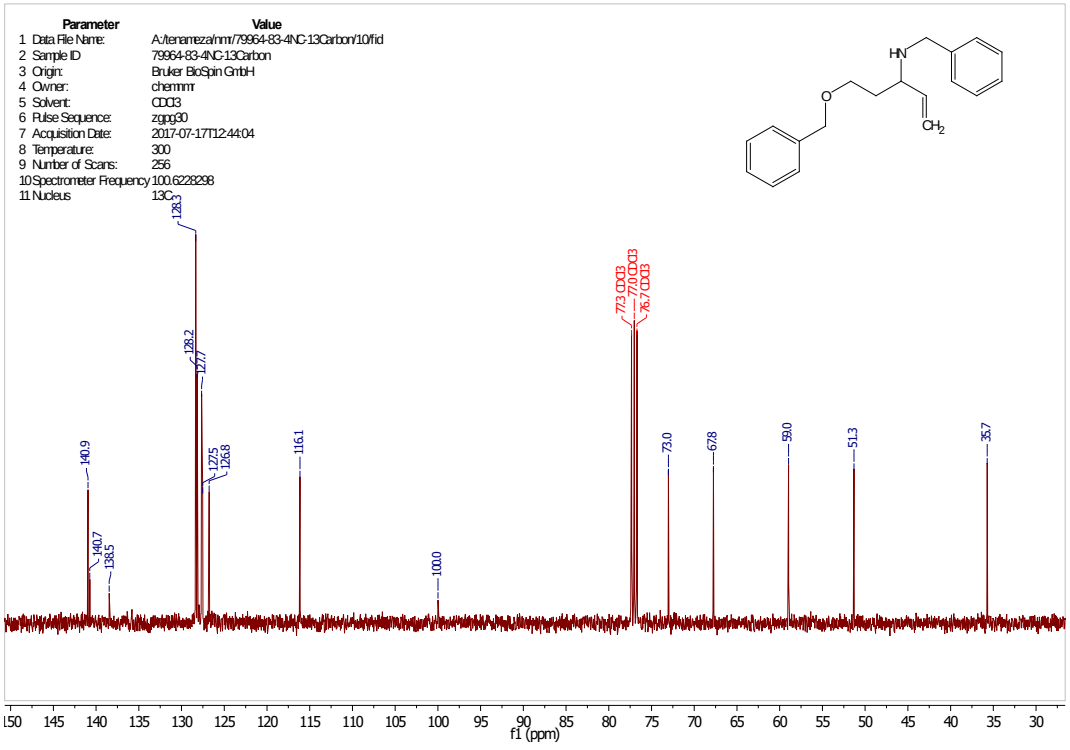
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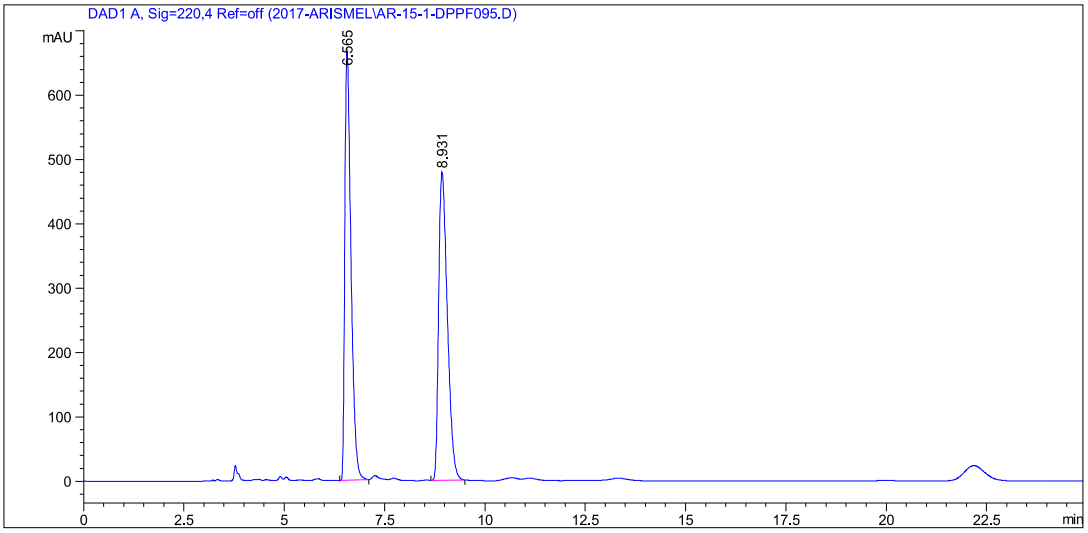
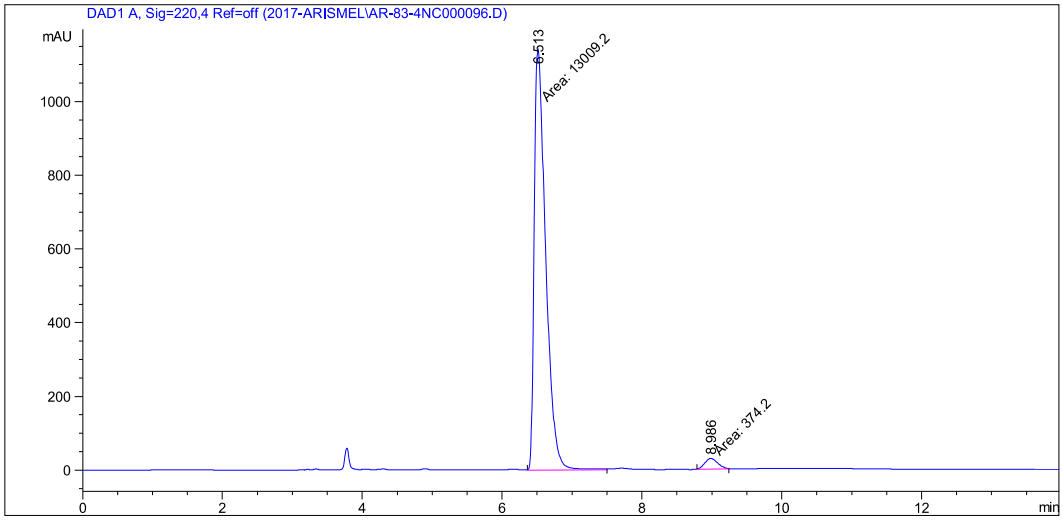
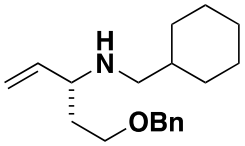


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.565	BB	0.1626	7125.07422	667.20642	49.7021
2	8.931	BBA	0.2338	7210.49121	478.39182	50.2979



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.513	MM	0.1902	1.30092e4	1140.16272	97.2040
2	8.986	MM	0.2166	374.20016	28.78831	2.7960

(*R*)-5-(benzyloxy)-*N*-(cyclohexylmethyl)pent-1-en-3-amine (4.3t)



Procedures

The allylic acetate (103 mg, 0.44 mmol, 100 mol%) and the primary amine (99.6 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ^{o}C, 60 hr). The title compound was obtained in 85% yield (107 mg, 0.37 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.17 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 - 7.22 (m, 5H), 5.59 (ddd, *J* = 17.0, 10.3, 8.1 Hz, 1H), 5.13 – 5.02 (m, 2H), 4.51 (d, *J* = 11.9 Hz, 1H) ,4.47 (d, *J* = 12.0 Hz, 1H), 3.62 – 3.46 (m, 2H), 3.18 - 3.09 (m, 1H), 2.43 (dd, *J* = 11.5, 6.8 Hz, 1H), 2.29 (dd, *J* = 11.6, 6.6 Hz, 1H), 1.88 - 1.77 (m, 1H), 1.76 – 1.60 (m, 6H), 1.45 - 1.32 (m, 1H), 1.29 – 1.07 (m, 3H), 0.95 - 0.80 (m, 2H).

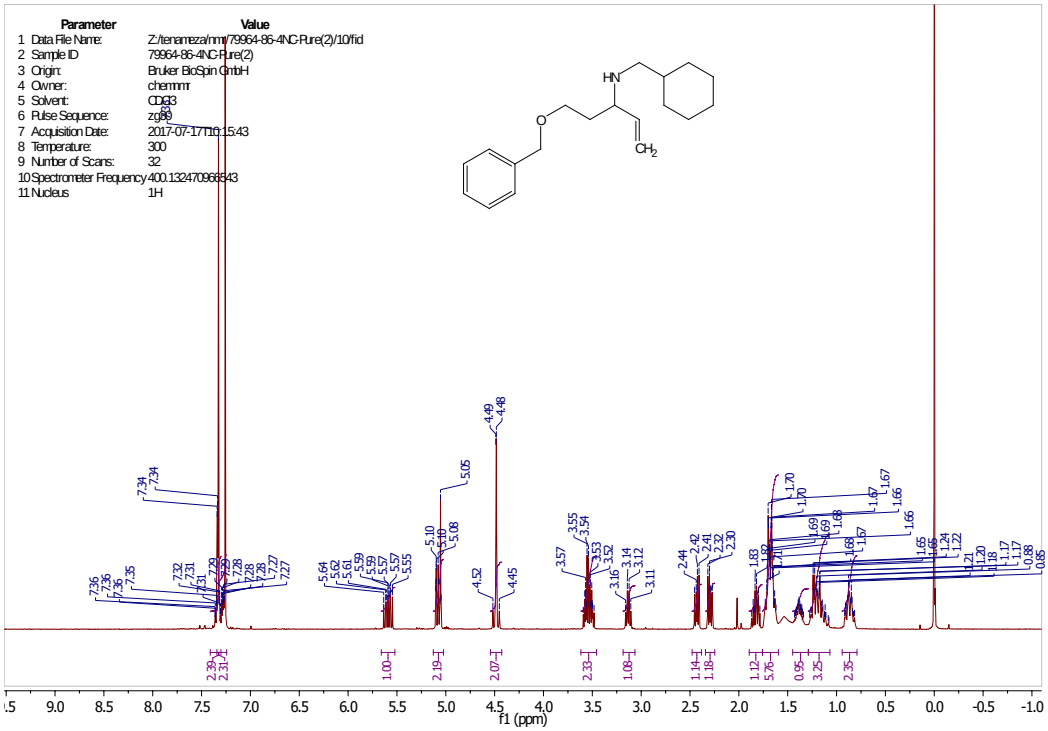
^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.4, 128.3, 127.7, 127.5, 115.6, 100.0, 73.0, 67.8, 59.7, 54.2, 38.1, 35.7, 31.6, 31.5, 26.7, 26.1(x2).

HRMS (ESI): calcd for $C_{19}H_{30}NO$ $[M+H]^+$: 288.2327, found: 288.2316

FTIR (neat): 2920, 2850, 1639, 1495, 1450, 1415, 1363, 1261, 1206, 1100, 1027, 993, 916, 733, 696 cm^{-1}.

$[\alpha]_D^{24}$ = –10.7 (*c* 0.30, $CHCl_3$).

HPLC (Chiralpak OD-H, heptane/isopropanol 100:0, 0.9 mL/min, 220 nm) ee = 91%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9 Number of Scans: 32
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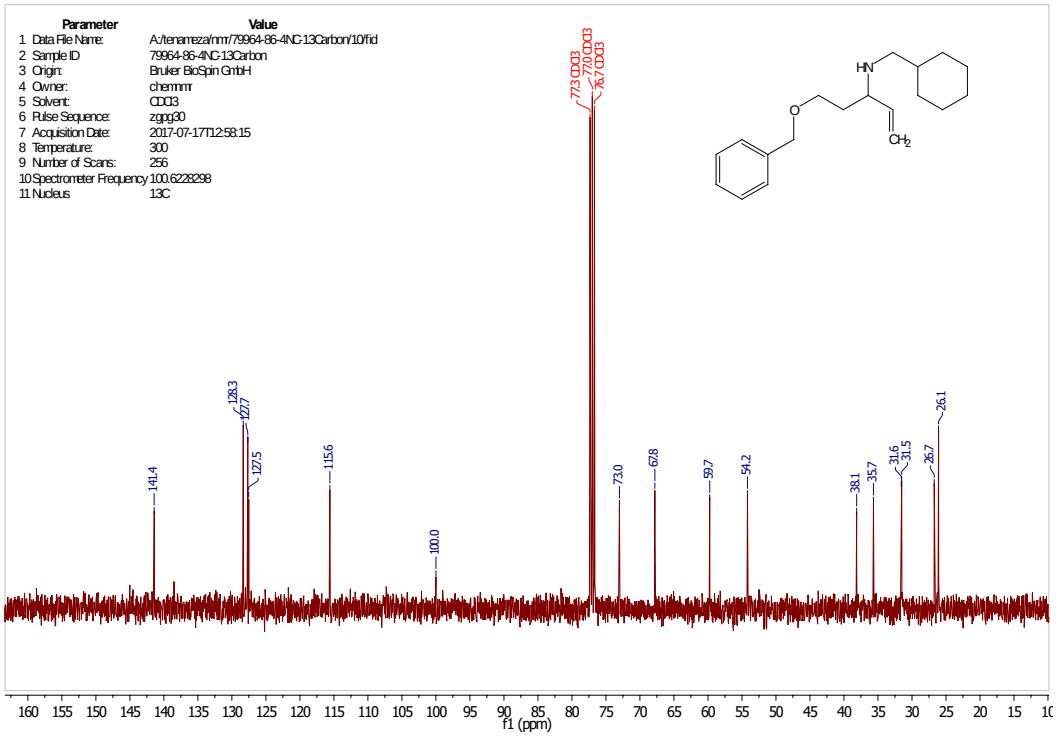
CH2
f1 (ppm)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5 Solvent: CDCl3
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77.0 CDCl3
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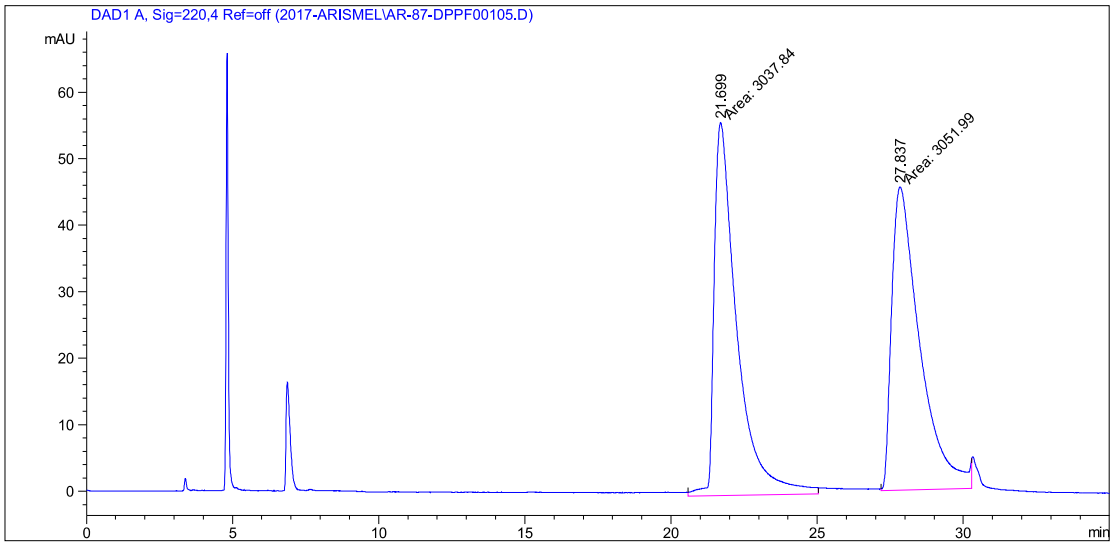
O
CH2
f1 (ppm)



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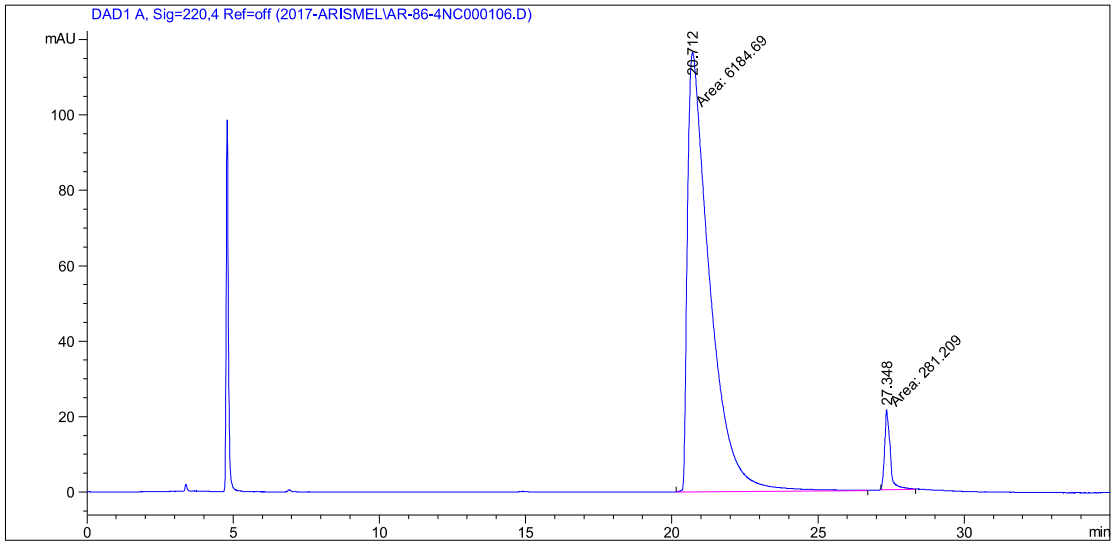
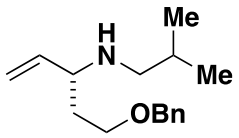
2	27.837	MM	1.1153	3051.99438	45.60812	50.1162



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.712	MM	0.8846	6184.69434	116.52329	95.6509
2	27.348	MM	0.2210	281.20883	21.21123	4.3491

(*R*)-5-(benzyloxy)-*N*-isobutylpent-1-en-3-amine (4.3u)



Procedures

The allylic acetate (103 mg, 0.44 mmol, 100 mol%) and the primary amine (64.4 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ^{o}C, 60 hr). The title compound was obtained in 78% yield (84.4 mg, 0.34 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.19 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 – 7.22 (m, 5H), 5.60 (ddd, *J* = 17.0, 10.3, 8.1 Hz, 1H), 5.13 – 5.03 (m, 2H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.47 (d, *J* = 11.9 Hz, 1H), 3.62 – 3.46 (m, 2H), 3.19 - 3.10 (m, 1H), 2.41 (dd, *J* = 11.5, 6.9 Hz, 1H), 2.28 (dd, *J* = 11.5, 6.6 Hz, 1H), 1.88 - 1.77 (m, 1H), 1.75 – 1.60 (m, 2H), 0.88 (d, *J* = 6.7, 3H), 0.87 (d, *J* = 6.7, 3H).

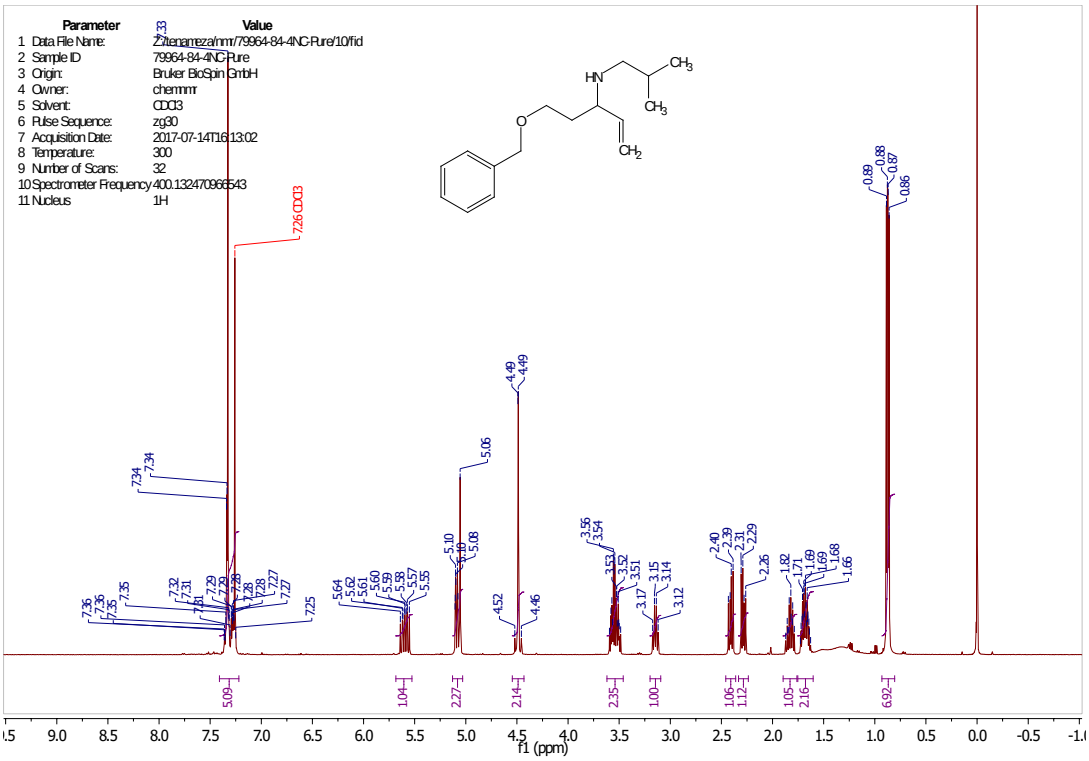
^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.4, 138.5, 128.3, 127.7, 127.5, 115.6, 73.0, 67.8, 59.6, 55.5, 35.7, 28.4, 20.8, 20.7.

HRMS (ESI): calcd for $C_{16}H_{26}NO$ $[M+H]^+$: 248.2014, found: 248.2004

FTIR (neat): 3031, 2952, 2867, 1639, 1495, 1453, 1415, 1385, 1363, 1246, 1203, 1101, 1027, 994, 916, 733, 696 cm^{-1}.

$[\alpha]_D^{24}$ = –13.8 (*c* 0.72, $CHCl_3$).

HPLC (Chiralpak OD-H; heptane/isopropanol 100:0, 0.9 mL/min, 220 nm). ee = 93%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CH2
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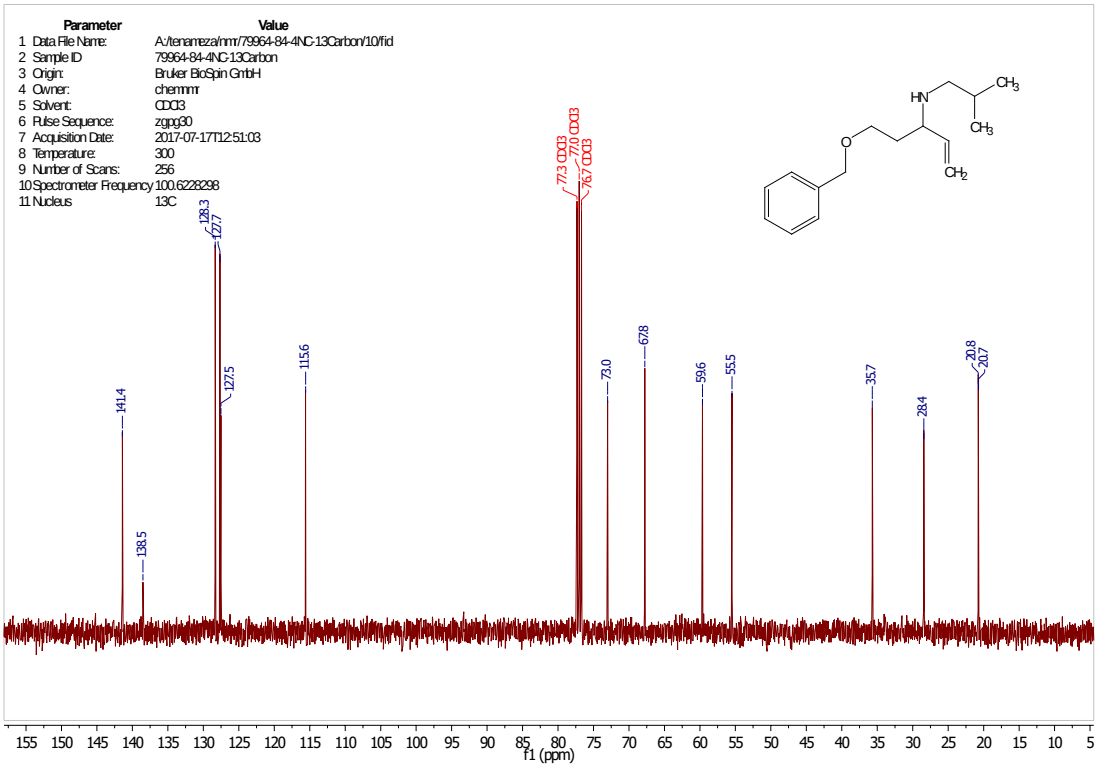
f1 (ppm)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5 Solvent: CDCl3
6 Pulse Sequence: zgpg30
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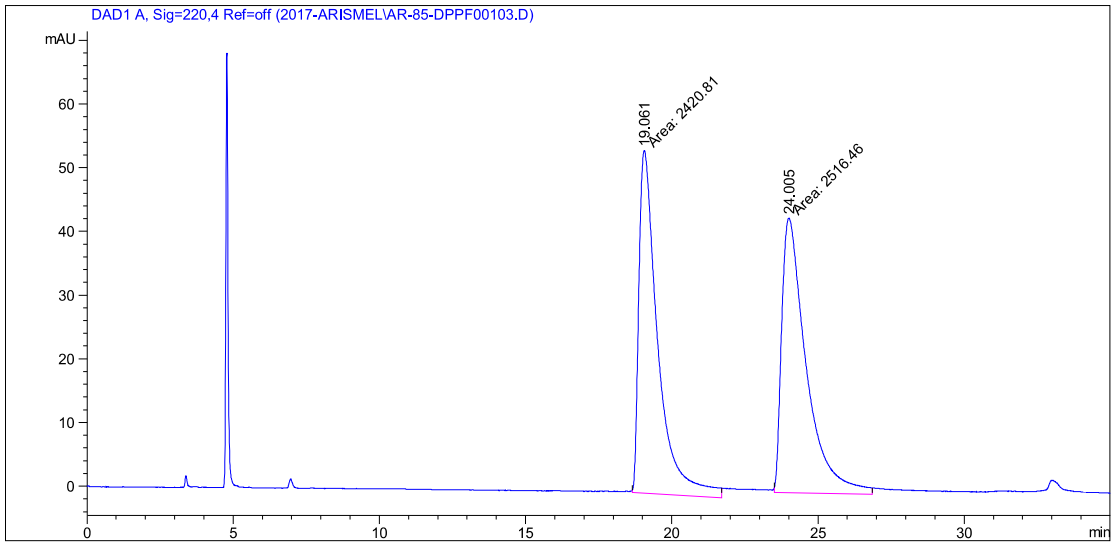
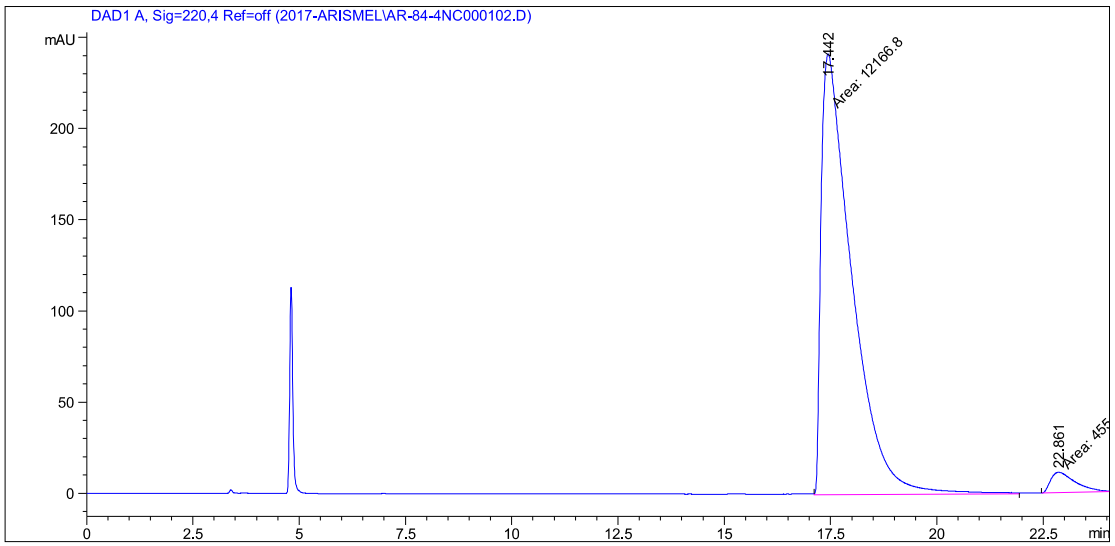
8 Temperature: 300
9 Number of Scans: 256
10 Spectrometer Frequency 100.6228298
11 Nucleus 13C
HN
CH3
CH3
O
CH2
77.3 CDCl3
77.0 CDCl3
76.7 CDCl3
f1 (ppm)

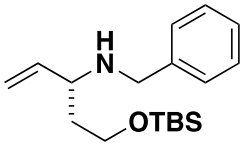


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.061	MM	0.7498	2420.80908	53.80821	49.0313
2	24.005	MM	0.9731	2516.46460	43.10054	50.9687



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.442	MM	0.8391	1.21668e4	241.65115	96.3900
2	22.861	MM	0.6815	455.67279	11.14368	3.6100

(*R*)-*N*-benzyl-5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-3-amine (4.3v)



Procedures

The allylic acetate (114 mg, 0.44 mmol, 100 mol%) and the primary amine (94.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ^{o}C, 60 hr). The title compound was obtained in 80% yield (107 mg, 0.35 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.51 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 – 7.18 (m, 5H), 5.66 (ddd, *J* = 16.4, 11.0, 8.2 Hz, 1H), 5.17 – 5.08 (m, 2H), 3.83 (d, *J* = 13.2 Hz, 1H), 3.75 - 3.61 (m, 2H), 3.63 (d, *J* = 13.2 Hz, 1H), 3.22 (q, *J* = 6.7 Hz, 1H), 1.82 – 1.68 (m, 1H), 1.68 - 1.58 (m, 1H), 0.86 (s, 9H), 0.03 (s, 6H).

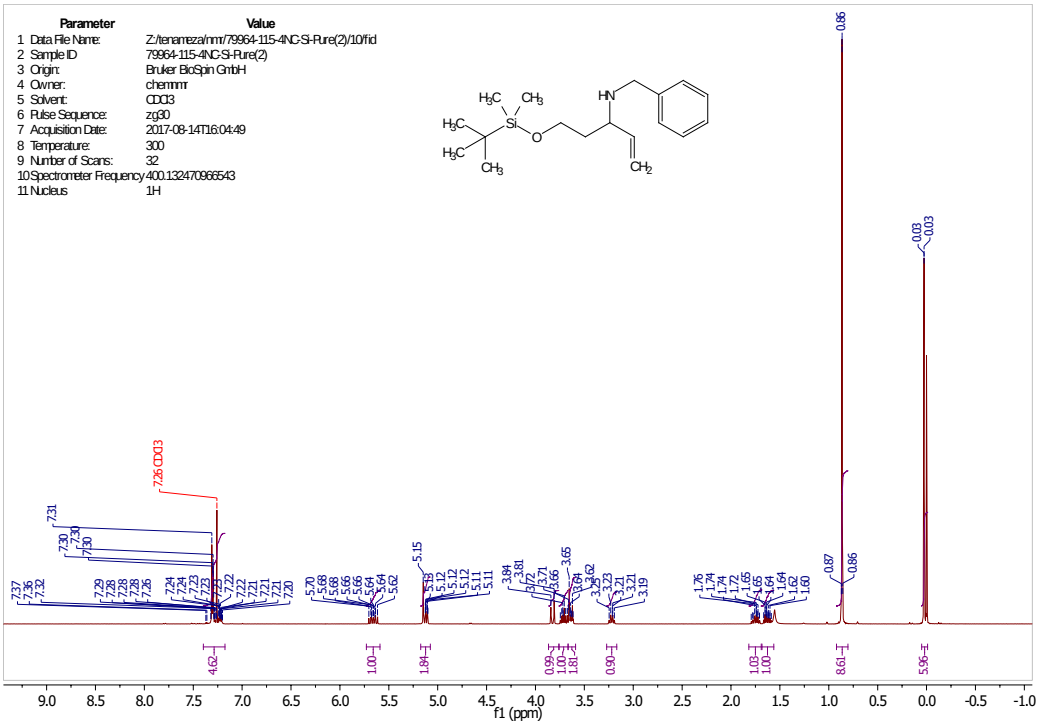
^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.1, 140.8, 128.3, 128.2, 126.7, 115.9, 60.7, 58.9, 51.3, 38.6, 25.9, 18.2, -5.4.

HRMS (ESI): calcd for $C_{18}H_{32}NOSi$ $[M+H]^+$: 306.2253 found: 306.2244

FTIR (neat): 2952, 2927, 2856, 1494, 1471, 1462, 1415, 1387, 1360, 1254, 1091, 1028, 1004, 918, 833, 773, 730, 696, 662 cm^{-1}.

$[\alpha]_D^{24}$ = –3.5 (*c* 0.51, $CHCl_3$,).

HPLC (Chiralpak AD-H, heptane/isopropanol 60:40, 1.0 mL/min, 254 nm) ee = 95% (NOTE: ee determined on *N*-benzyl-*N*-(5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-3-yl)-4-nitrobenzamide)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4 Owner: chemmr
5 Solvent: CDCl3
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8 Temperature: 300
9 Number of Scans: 32
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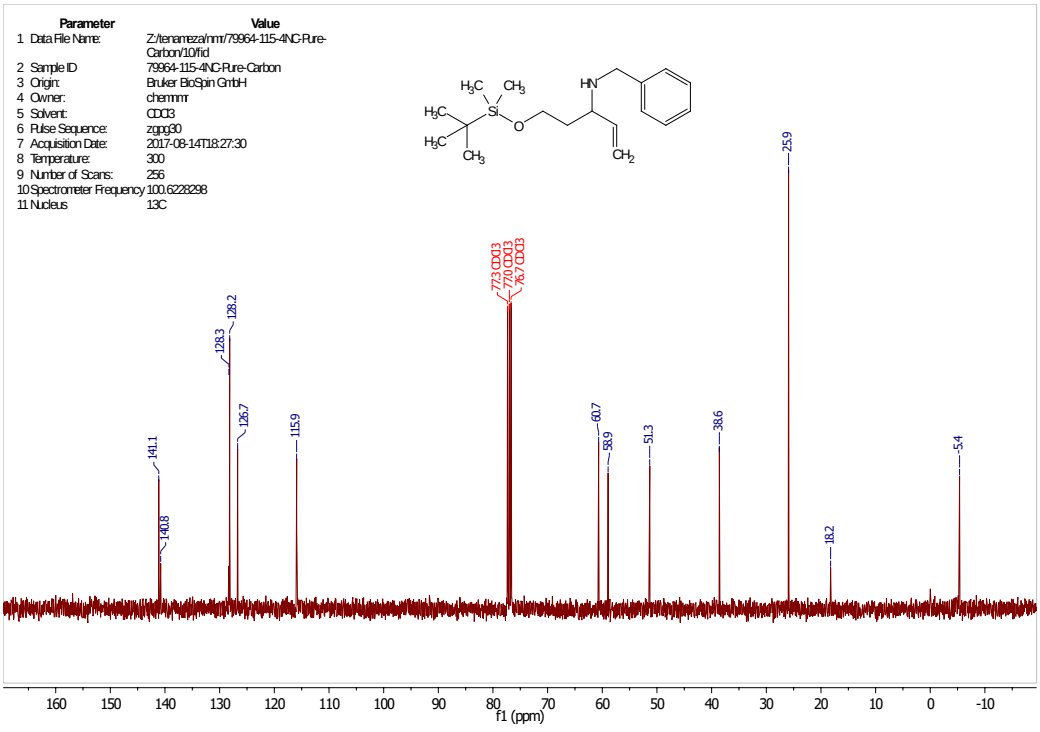
f1 (ppm)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8 Temperature: 300
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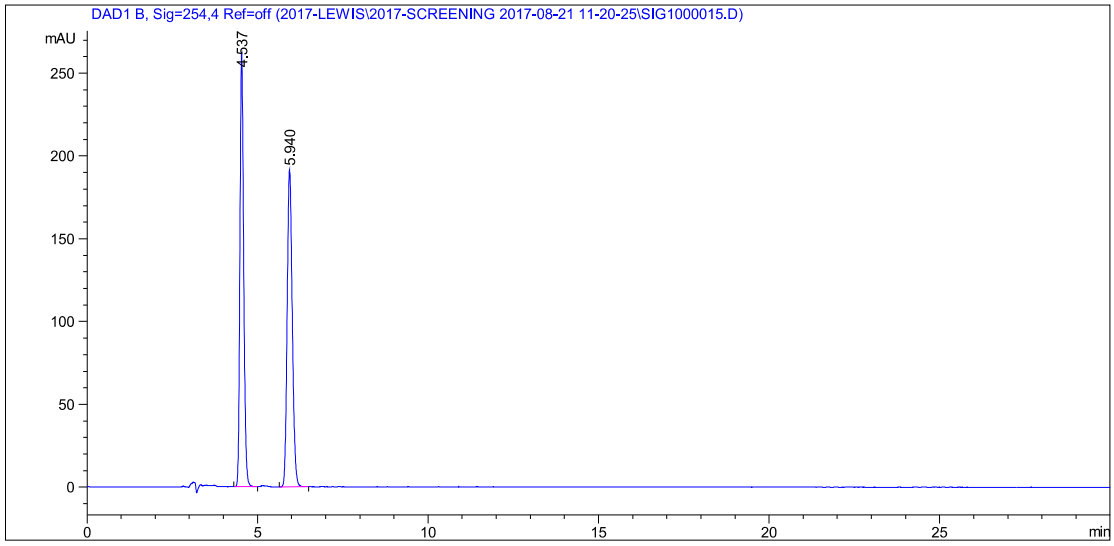
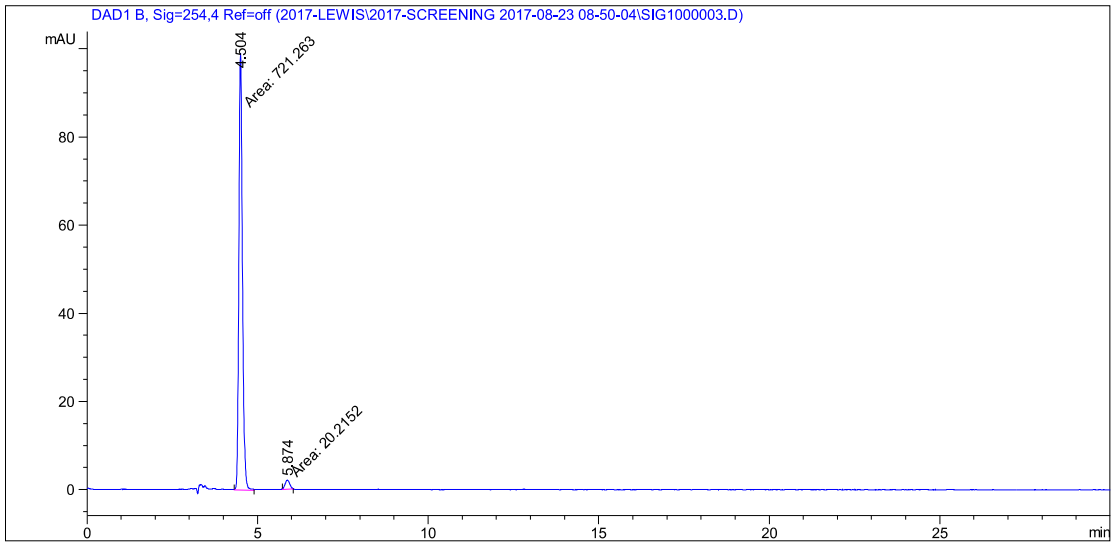
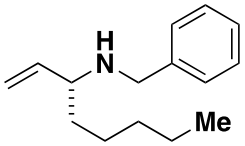


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.537	BB	0.1173	2010.84546	262.58258	50.0417
2	5.940	BB	0.1623	2007.49463	191.48045	49.9583



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.504	MM	0.1210	721.26343	99.31726	97.2737
2	5.874	MM	0.1626	20.21516	2.07224	2.7263

(*R*)-*N*-benzyloct-1-en-3-amine (4.3w)



Procedures

The allylic acetate (74.9 mg, 0.44 mmol, 100 mol%) and the primary amine (94.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ^{o}C, 60 hr). The title compound was obtained in 82% yield (79.0 mg, 0.36 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.54 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 - 7.28 (m, 4H), 7.28 – 7.18 (m, 1H), 5.62 (ddd, *J* = 17.1, 10.3, 8.2 Hz, 1H), 5.18 – 5.05 (m, 2H), 3.83 (d, *J* = 13.1 Hz, 1H), 3.64 (d, *J* = 13.2 Hz, 1H), 3.05 - 2.97 (m, 1H), 1.70 – 1.15 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H).

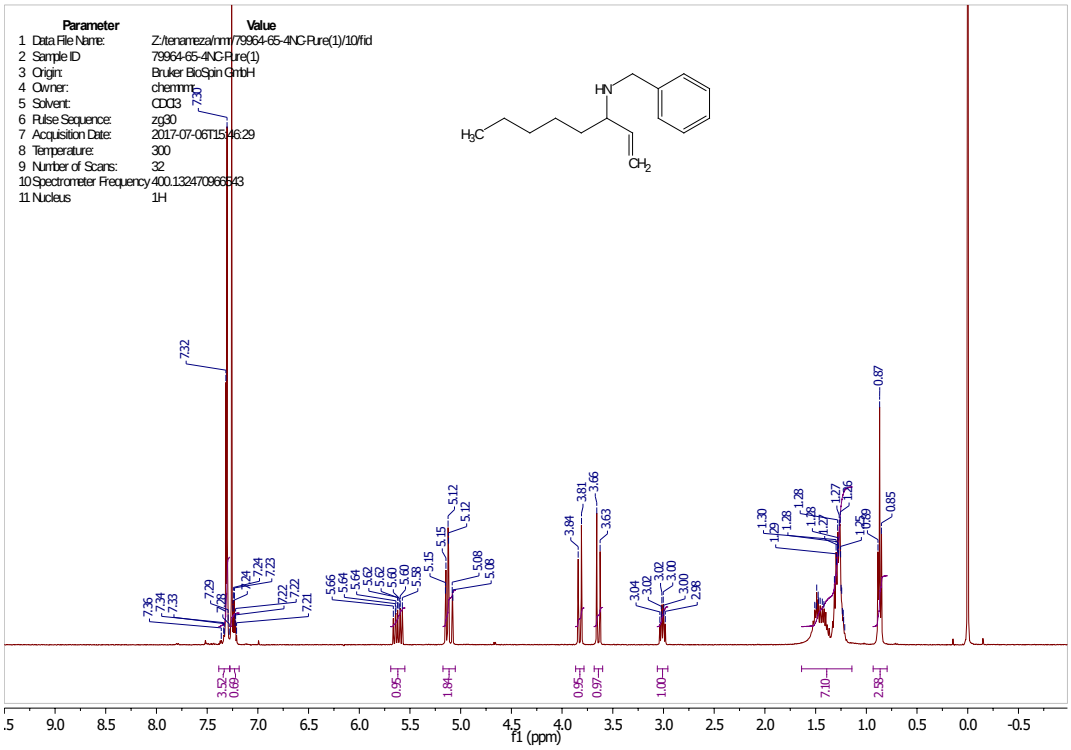
^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.5, 140.8, 128.3, 128.2, 126.8, 115.9, 61.3, 51.3, 35.8, 31.9, 25.6, 22.6, 14.0.

HRMS (ESI): calcd for $C_{15}H_{24}N$ $[M+H]^+$: 218.1909, found: 218.1899

FTIR (neat): 3063, 3027, 2955, 2927, 2856, 1639, 1494, 1453, 1414, 1377, 1200, 1111, 1028, 993, 916, 729, 697 cm^{-1}.

$[\alpha]_D^{24}$= +1.6 (*c* 0.77, $CHCl_3$).

HPLC (Chiralpak OD-H, heptane/isopropanol 99.0:1.0, 0.5 mL/min, 220 nm) ee = 93%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6 Pulse Sequence: zg30
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8 Temperature: 300
9 Number of Scans: 32
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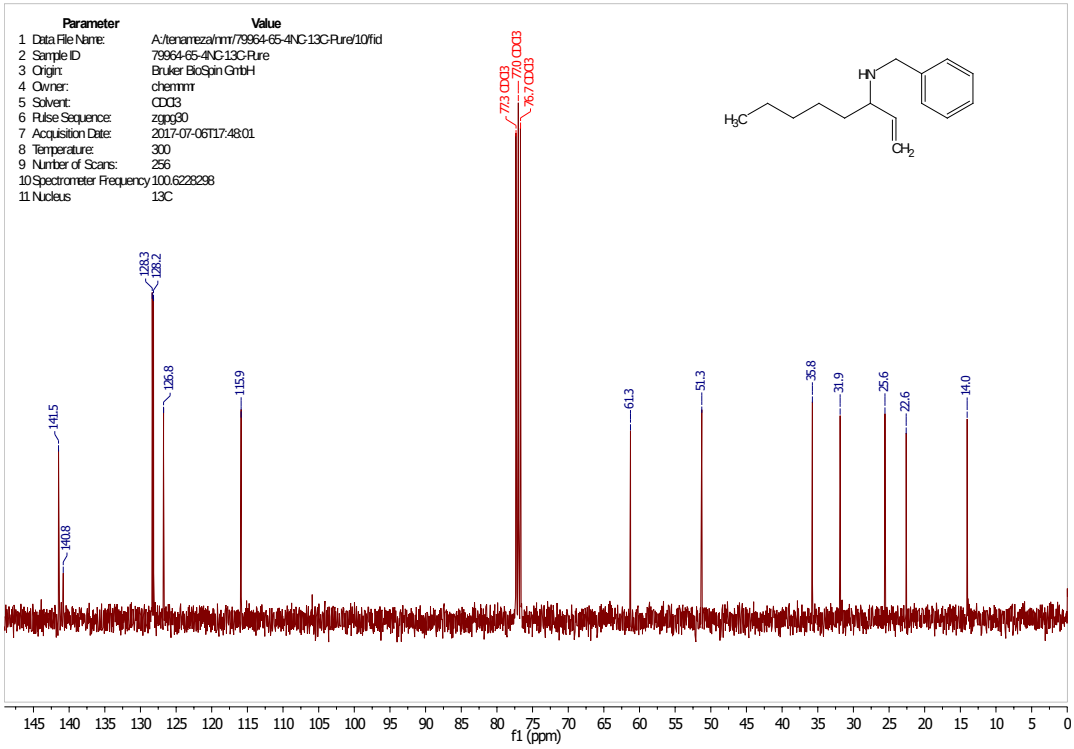
11 Nucleus 1H
HN
H3C
CH2
f1 (ppm)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5 Solvent: CDCl3
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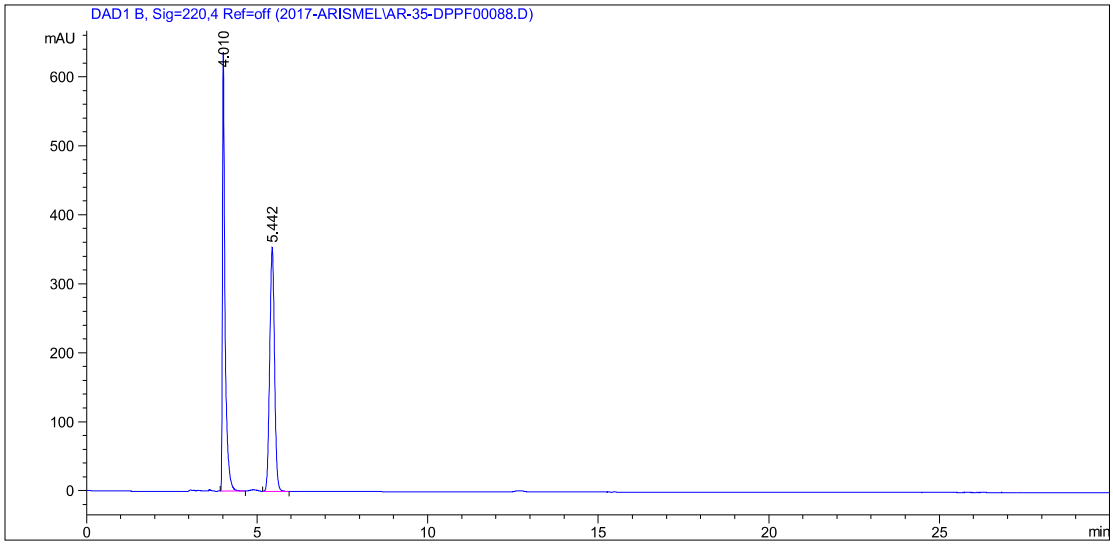
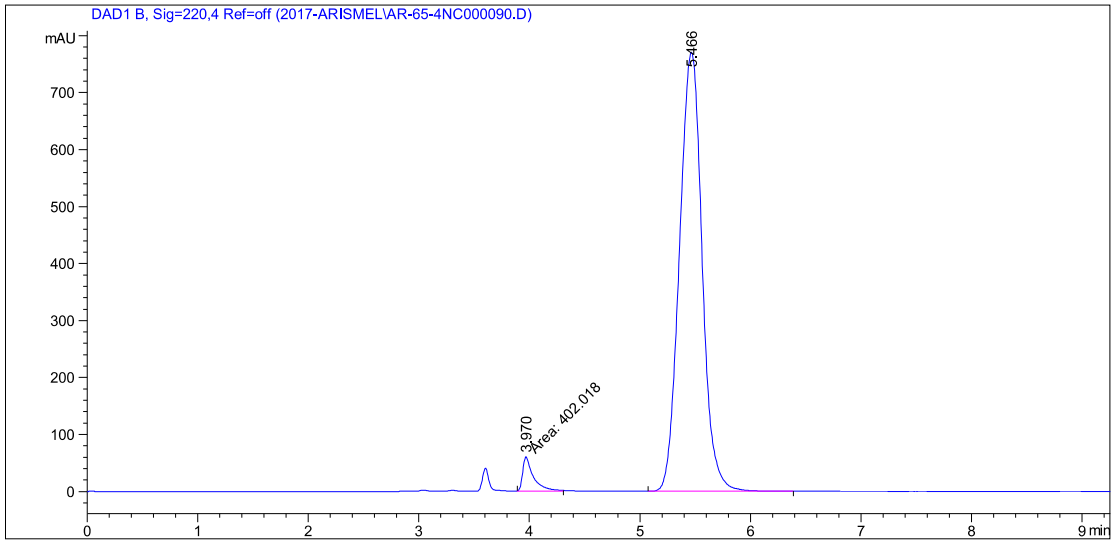
CH2
f1 (ppm)

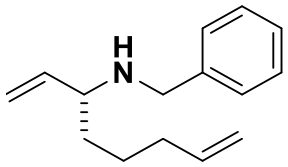


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.010	BB	0.0758	3388.96338	640.17517	49.8766
2	5.442	BB	0.1502	3405.73291	354.28845	50.1234



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.970	MM	0.1107	402.01782	60.50248	3.5479
2	5.466	BB	0.2236	1.09291e4	770.10669	96.4521

(*R*)-N-benzylocta-1,7-dien-3-amine (4.3x)



Procedures

The allylic acetate (33.6 mg, 0.20 mmol, 100 mol%) and the primary amine (42.9 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 85% yield (36.5 mg, 0.17 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–2:1).

TLC (SiO_2) R_f = 0.55 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 – 7.17 (m, 5H), 5.78 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.62 (ddd, *J* = 17.1, 10.3, 8.3 Hz, 1H), 5.28 – 5.06 (m, 2H), 5.03 – 4.85 (m, 2H), 3.83 (d, *J* = 13.2 Hz, 1H), 3.64 (d, *J* = 13.2 Hz, 1H), 3.02 (td, *J* = 7.7, 5.4 Hz, 1H), 2.03 (tdt, *J* = 7.1, 5.4, 1.4 Hz, 2H), 1.61 – 1.36 (m, 4H), 1.31 (br, 1H).

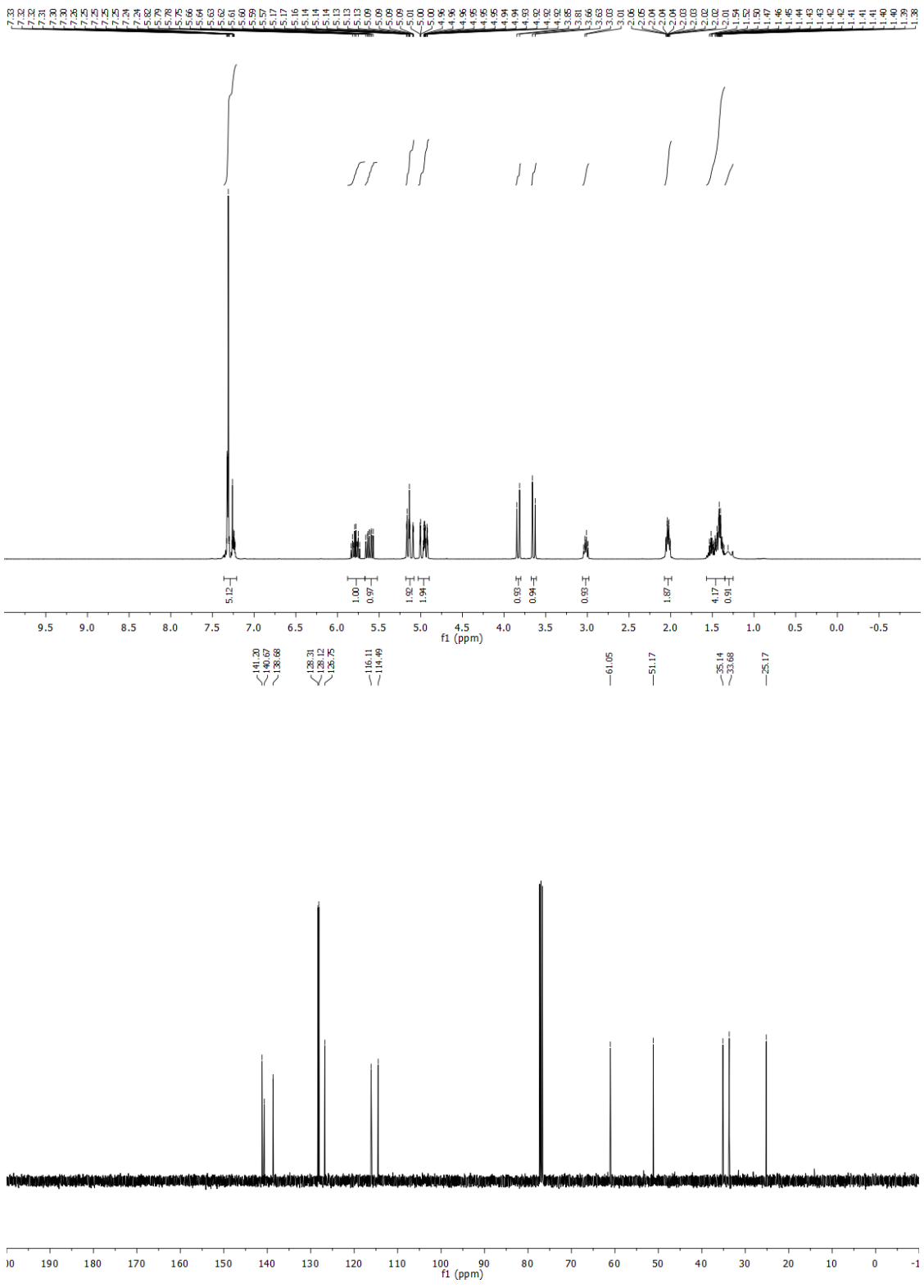
^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.2, 140.7, 138.7, 128.3, 128.1, 126.8, 116.1, 114.5, 61.1, 51.2, 35.1, 33.7, 25.2.

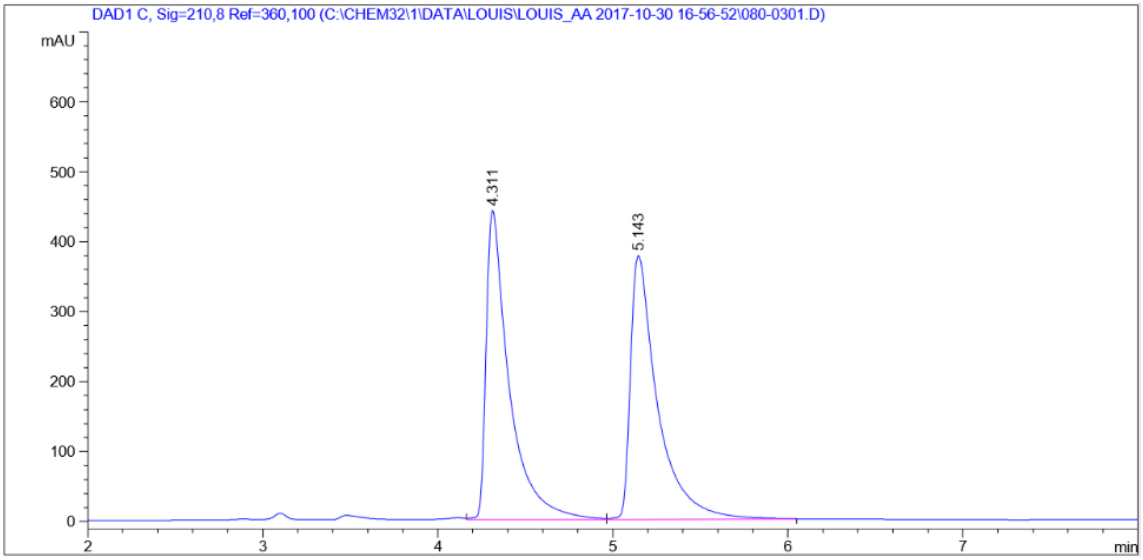
HRMS (ESI): Calculated for $C_{15}H_{21}N$ [M+H$^+$] = 216.1747, Found 216.1743.

FTIR (neat): 2928, 1640, 1454, 1216, 993, 913, 752, 698 cm^{-1}.

$[\alpha]_D^{31}$ = –51.0 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm), *ee* = 95%.





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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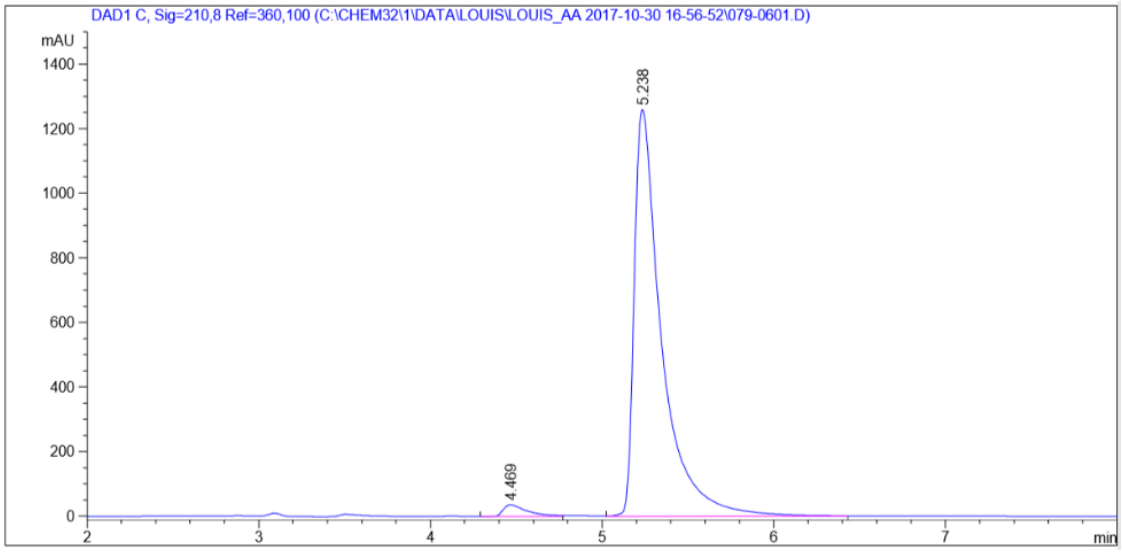
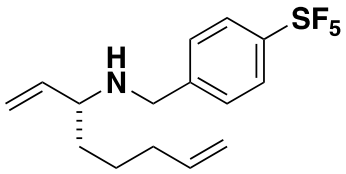
2	5.143	VB	0.1550	4044.31030	377.34579	50.0362



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.469	VV	0.1408	357.93893	36.36859	2.4950
2	5.238	VB	0.1616	1.39881e4	1259.30676	97.5050

(*R*)-*N*-(4-(pentafluoro-λ^6-sulfaneyl)benzyl)octa-1,7-dien-3-amine (4.3y)



Procedures

The allylic acetate (33.6 mg, 0.20 mmol, 100 mol%) and the primary amine (93.3 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 73% yield (49.8 mg, 0.15 mmol) as a pale yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1).

TLC (SiO_2) R_f = 0.72 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.6 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 5.81-5.70 (m, 1H), 5.60-5.51 (m, 1H), 5.17-5.04 (m, 2H), 4.99-4.89 (m, 2H), 3.84 (d, *J* = 14.1 Hz, 1H), 3.68 (d, *J* = 14.1 Hz, 1H), 3.00-2.92 (m, 1H), 2.05-1.98 (m, 2H), 1.5z9-1.35 (m, 5H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.7 (m, J_{CF} = 15.7 Hz), 145.1, 141.0, 138.8, 128.4, 126.2 (2C), (m, J_{CF} = 4.6 Hz, 2C), 116.7, 114.8, 61.3, 50.4, 35.4, 33.9, 25.4.

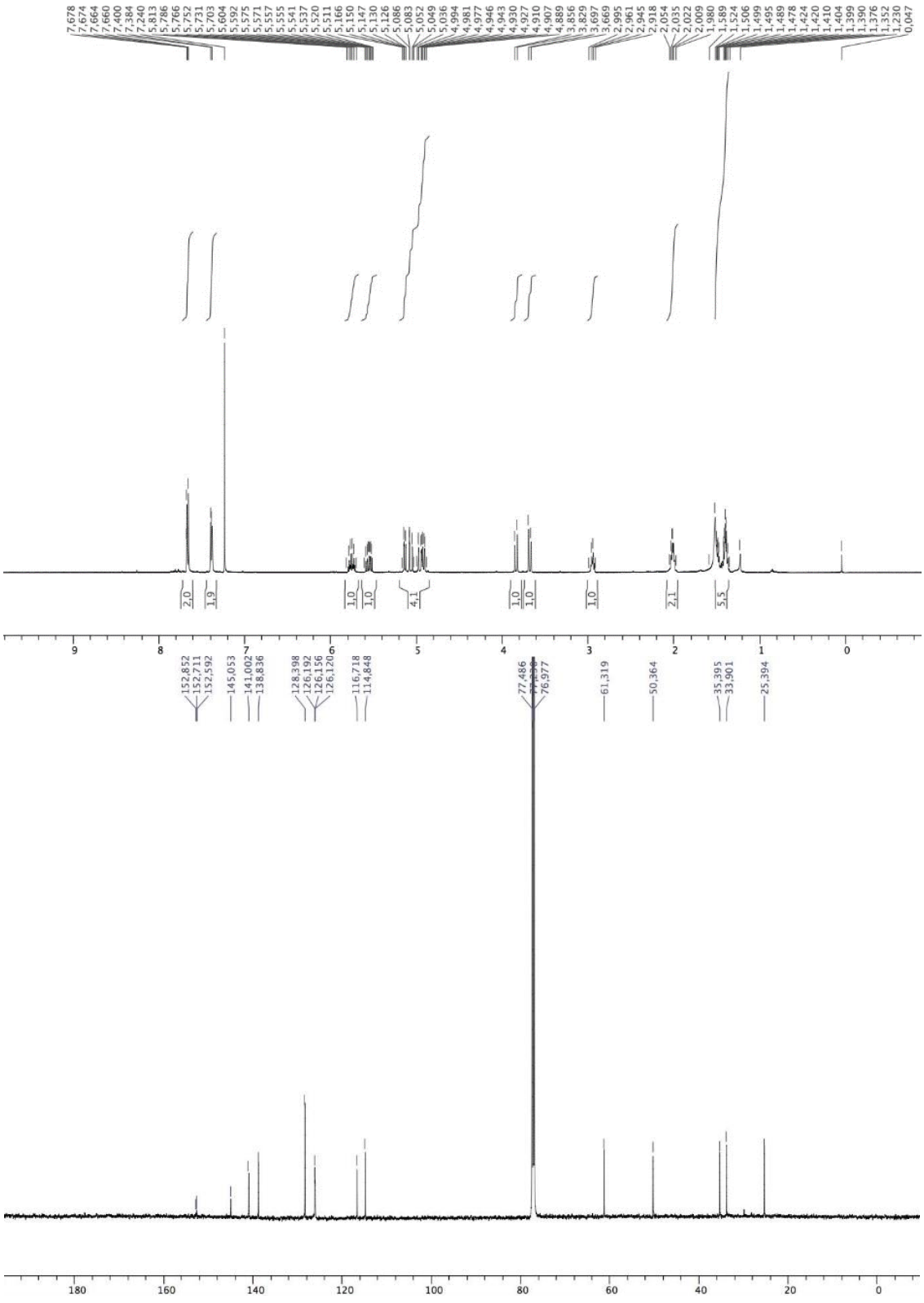
^{19}F NMR (376 MHz, $CDCl_3$): δ = 87.2 – 83.4 (m, 1F), 63.0 (d, *J* = 149.8 Hz, 4F).

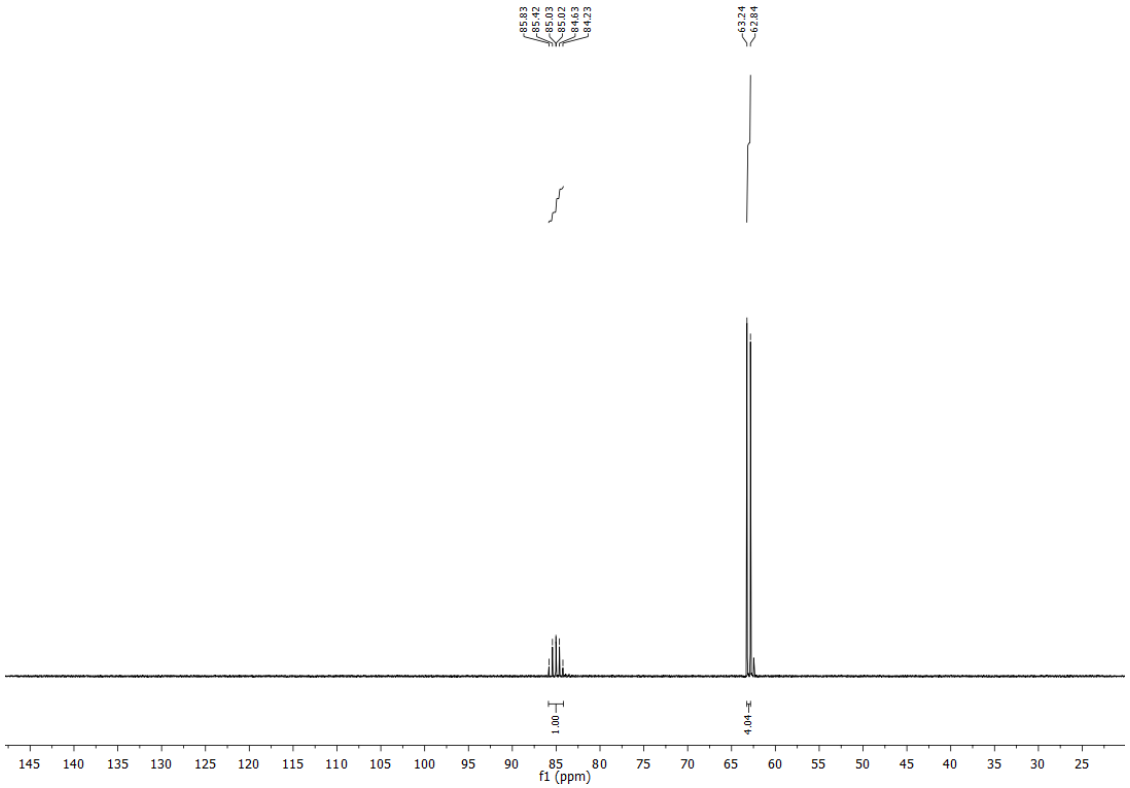
HRMS (ESI): Calculated for $C_{15}H_{20}F_5NS$ [M+H$^+$] = 342.1309, Found 342.1302.

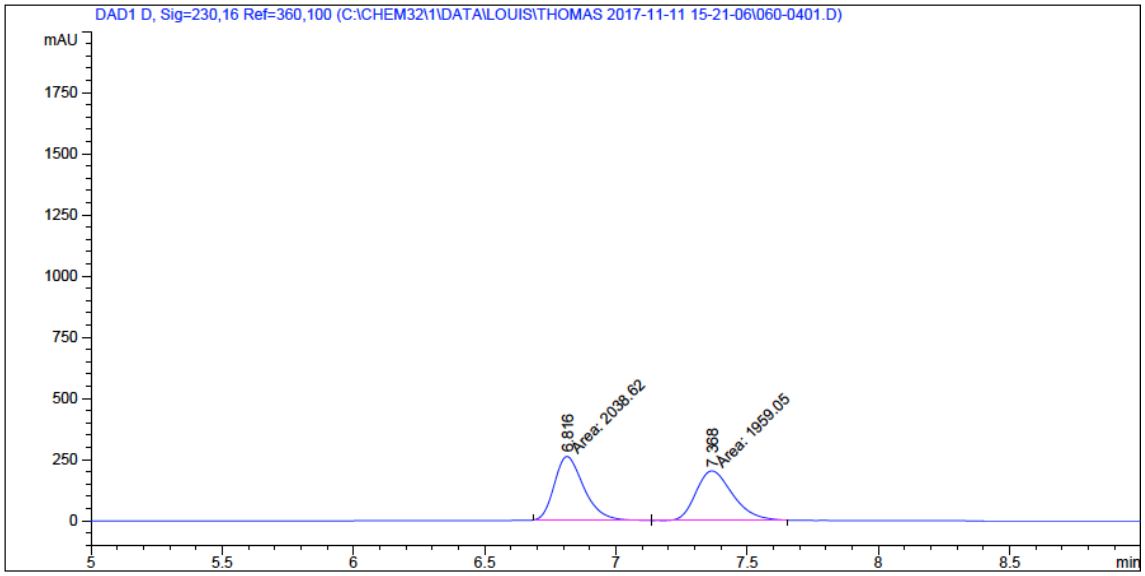
FTIR (neat): 2926, 1641, 1459, 1414, 1095, 993, 915, 830, 669 cm^{-1}.

$[\alpha]_D^{23}$ = –37.2 (*c* 1.3, $CHCl_3$).

HPLC (2x Chiralcel AS-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm), *ee* = 92%.




85.83
85.42
85.03
85.02
84.63
84.23
63.24
62.84
1.00
4.04
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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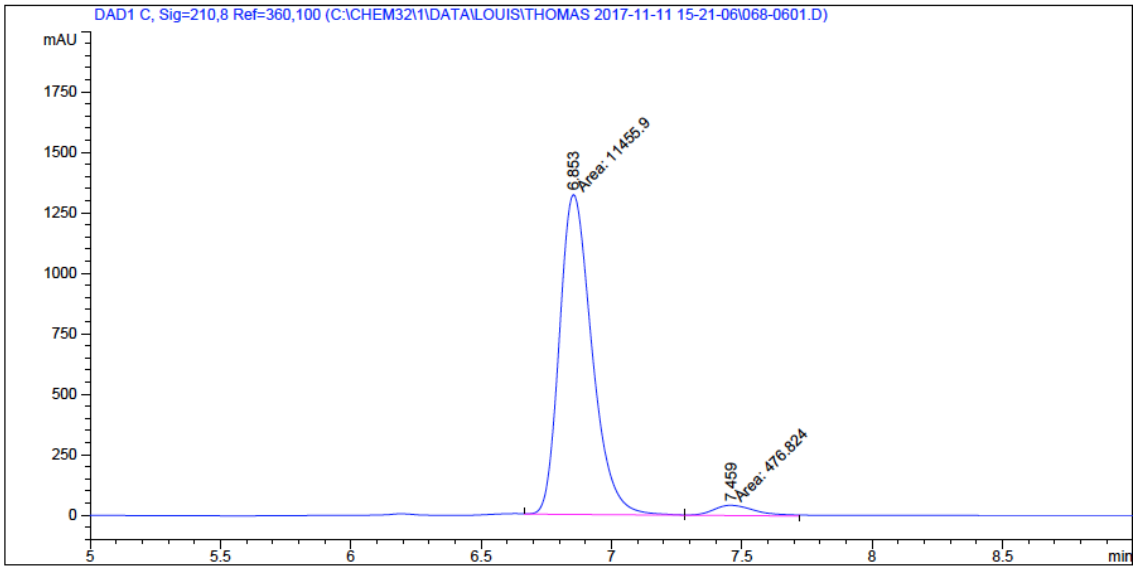
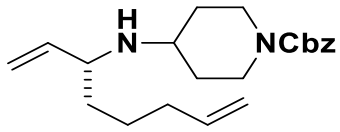
2	7.368	FM	0.1616	1959.05334	202.02185	49.0049



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.853	MF	0.1443	1.14559e4	1323.44482	96.0041
2	7.459	FM	0.1861	476.82385	42.71313	3.9959

benzyl (*R*)-4-(octa-1,7-dien-3-ylamino)piperidine-1-carboxylate (4.3z)



Procedures

The allylic acetate (33.6 mg, 0.20 mmol, 100 mol%) and the primary amine (93.7 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 70% yield (48.0 mg, 0.14 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–2:1).

TLC (SiO_2) R_f = 0.28 (ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 – 7.25 (m, 5H), 5.76 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.51 (ddd, *J* = 17.0, 10.3, 8.3 Hz, 1H), 5.09 (s, 2H), 5.08 – 4.89 (m, 4H), 4.08 (br, 2H), 3.16 – 3.05 (m, 1H), 2.95 – 2.75 (m, 2H), 2.66 (tt, *J* = 10.2, 3.9 Hz, 1H), 2.09 – 1.96 (m, 2H), 1.87 (br, 1H), 1.79 – 1.66 (m, 1H), 1.47 – 1.01 (m, 8H).

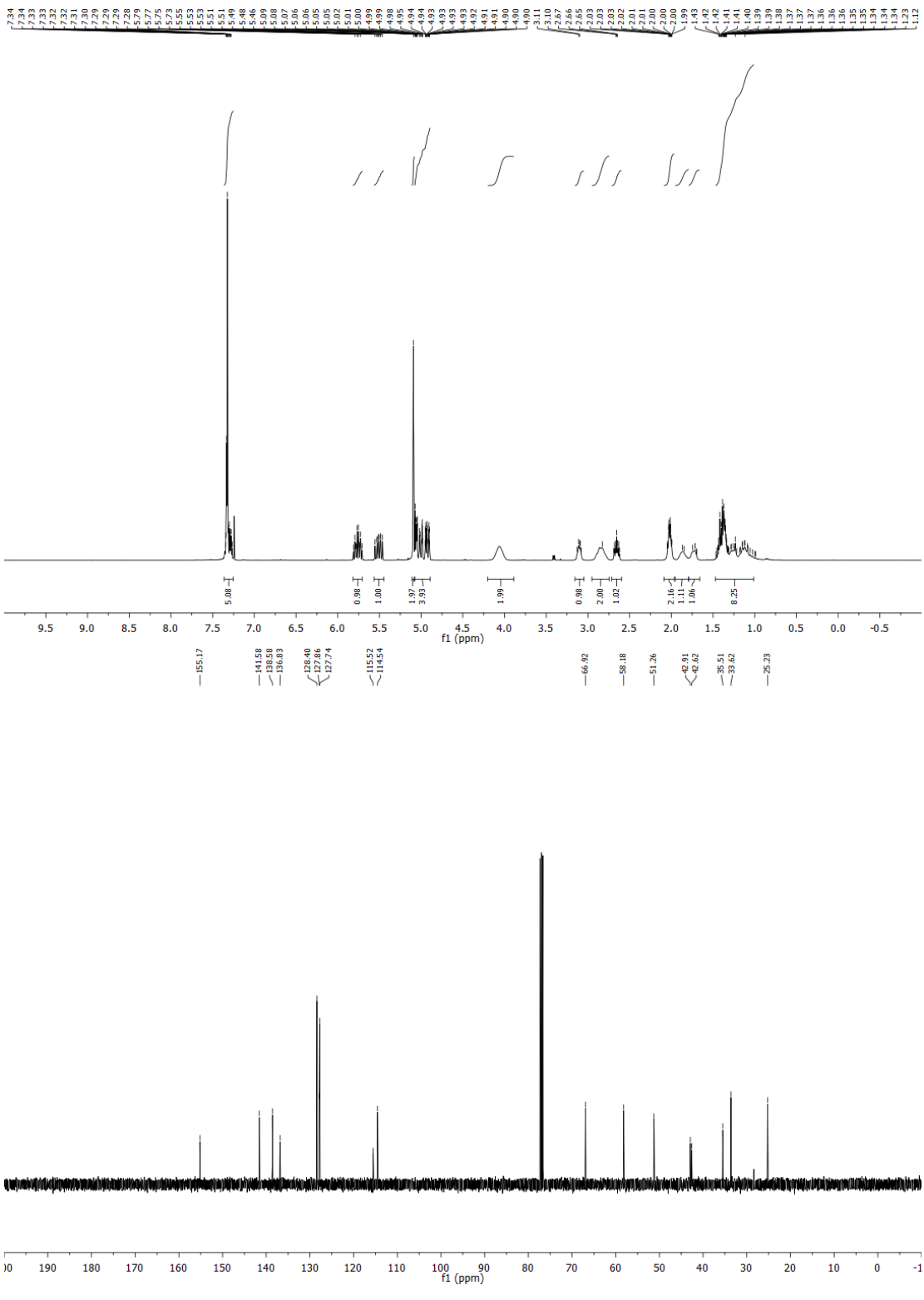
^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.2, 141.6, 138.6, 136.8, 128.4, 127.9, 127.7, 115.5, 114.5, 66.9, 58.2, 51.3, 42.9, 42.6, 35.5, 33.6, 25.2.

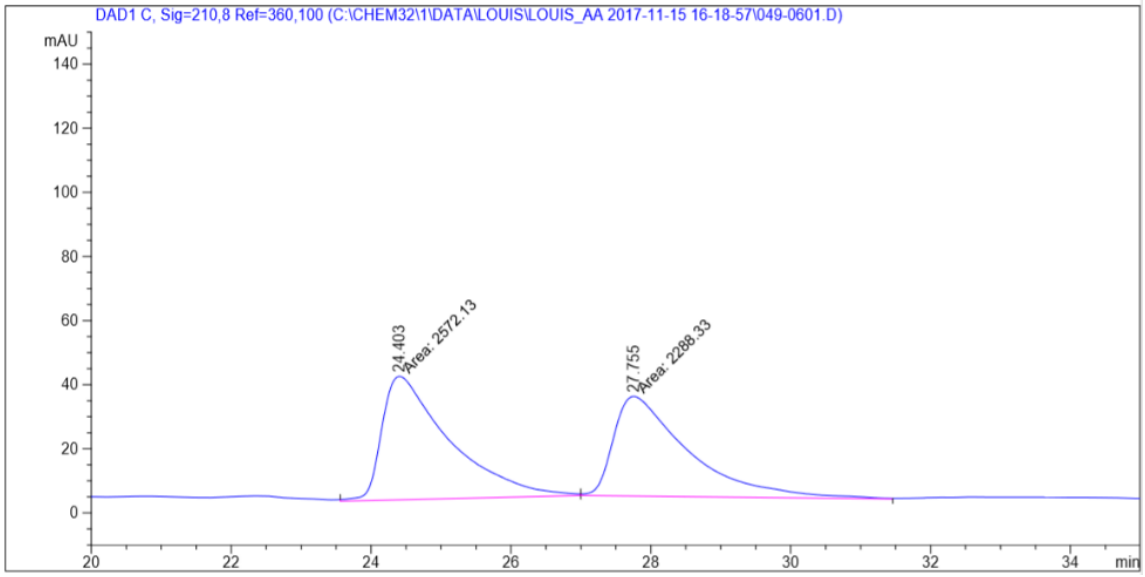
HRMS (ESI): Calculated for $C_{21}H_{30}N_2O_2$ [M+H$^+$] = 343.2380, Found 343.2376.

FTIR (neat): 2930, 1691, 1433, 1364, 1228, 996, 914, 752, 697cm^{-1}.

$[\alpha]_D^{25}$ = +51.0 (*c* 1.0, $CHCl_3$).

HPLC (two connected chiralcel OD-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm), *ee* = 91%.





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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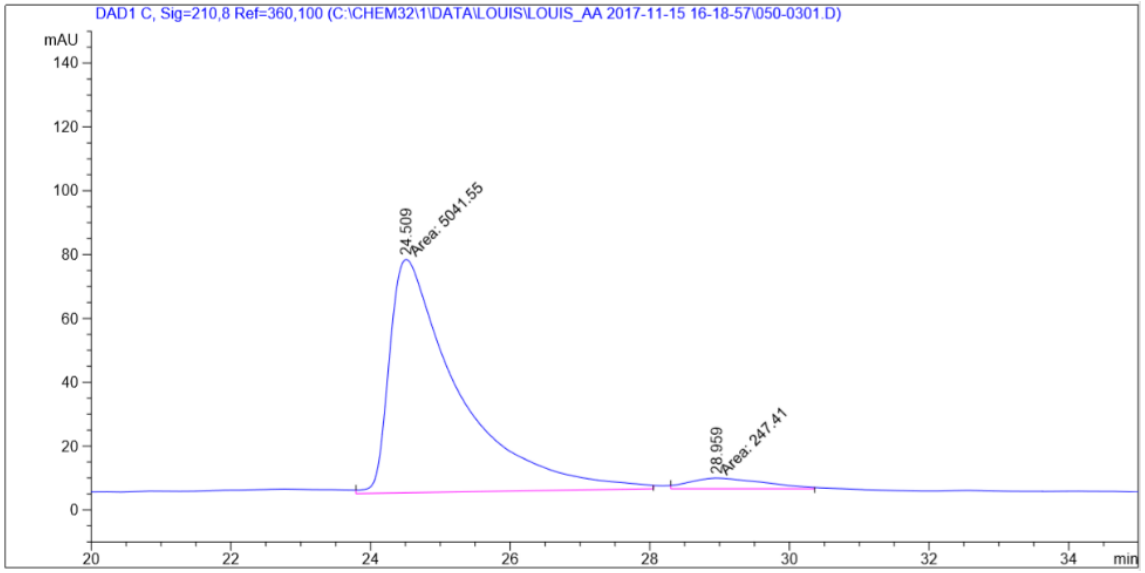
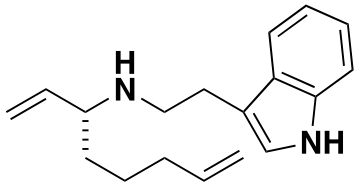
2	27.755	MM	1.2275	2288.32983	31.06971	47.0805



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.509	MM	1.1493	5041.54980	73.10957	95.3221
2	28.959	MM	1.2373	247.41043	3.33259	4.6779

(*R*)-*N*-(2-(1*H*-indol-3-yl)ethyl)octa-1,7-dien-3-amine (4.3a')



Procedures

The allylic acetate (33.6 mg, 0.20 mmol, 100 mol%) and the primary amine (64.1 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 69% yield (37.0 mg, 0.14 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, ethyl acetate).

TLC (SiO_2) R_f = 0.15 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.10 (s, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 7.9 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.03 (s, 1H), 5.80 - 5.70 (m, 1H), 5.55 (ddd, *J* = 16.7, 10.8, 8.4 Hz, 1H), 5.13-5.04 (m, 2H), 5.00-4.98 (m, 2H), 3.03-2.92 (m, 4H), 2.87-2.81 (m, 1H), 2.07-1.95 (m, 2H), 1.59-1.22 (m, 5H).

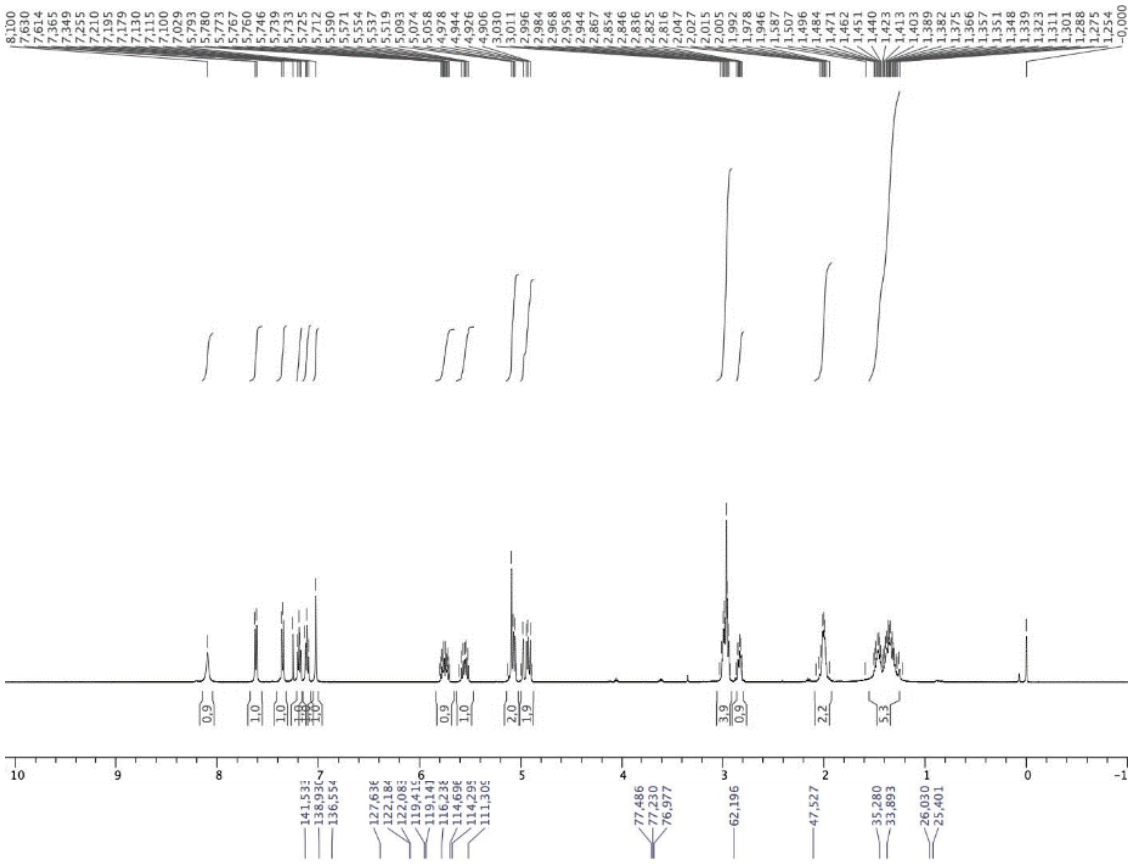
^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.5, 138.9, 136.6, 127.6, 122.2, 122.1, 119.4, 119.1, 116.2, 114.7, 114.3, 111.3, 62.2, 47.5, 35.3, 33.9, 26.0, 25.4.

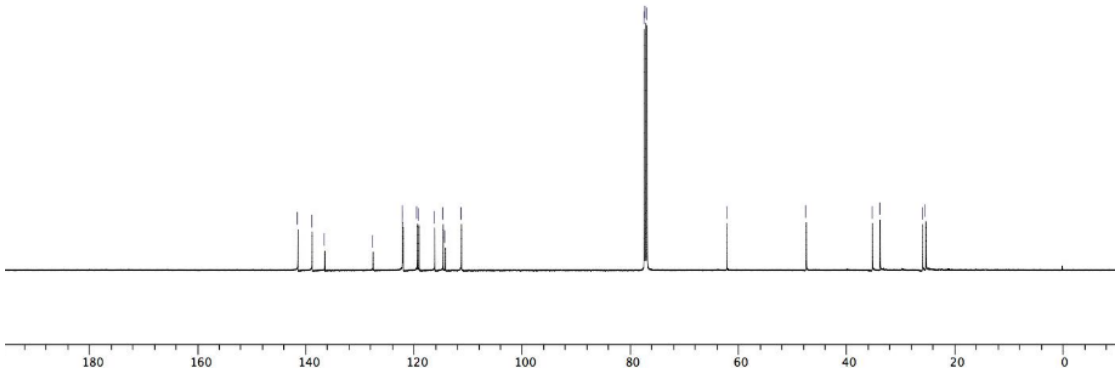
HRMS (ESI): Calculated for $C_{18}H_{24}N_2$ [M+H$^+$] = 269.2012, Found 269.2017.

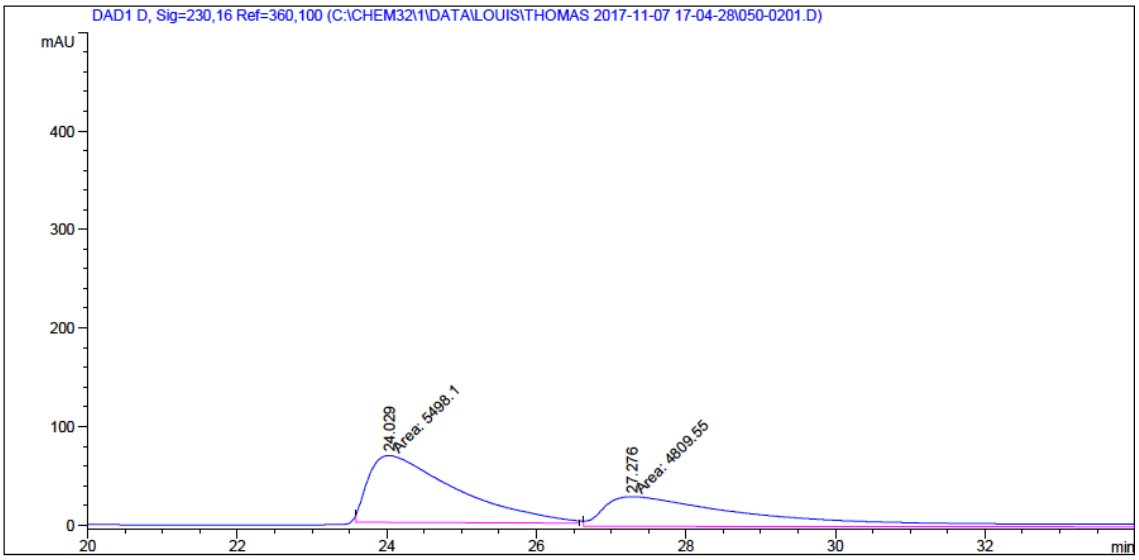
FTIR (neat): 3296, 2969, 2928, 1457, 1414, 1378, 1339, 1306, 1231, 1160, 1127, 1104, 994, 951, 916, 816, 739 cm^{-1}.

$[\alpha]_D^{24}$= +48.5 (*c* 1.5, $CHCl_3$).

HPLC (2x Chiralcel OD-H column , hexanes:*i*-PrOH = 90:10, 1.00 mL/min, 230 nm), *ee* = 91%.







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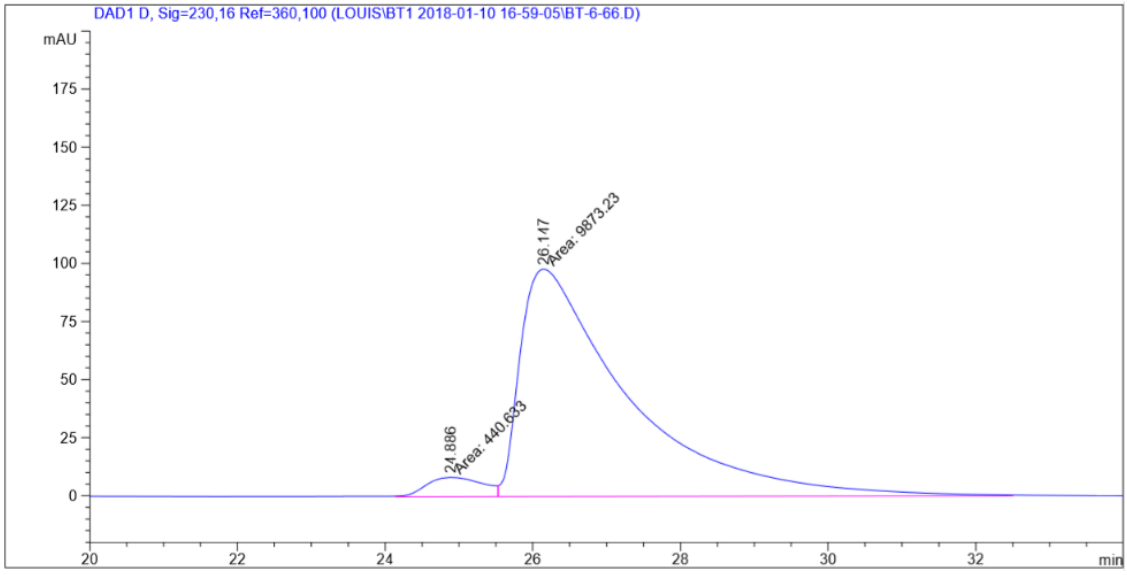
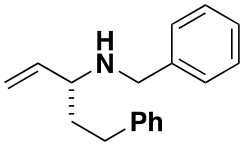


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.886	MF	0.8855	440.63269	8.29353	4.2722
2	26.147	FM	1.6819	9873.23047	97.83595	95.7278

(*R*)-*N*-benzyl-5-phenylpent-1-en-3-amine (4.3b')



Procedures

The allylic acetate (89.9 mg, 0.44 mmol, 100 mol%) and the primary amine (94.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ^{o}C, 60 hr). The title compound was obtained in 78% yield (85.3 mg, 0.34 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.45 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 – 7.12 (m, 10H), 5.68 (ddd, *J* = 17.3, 10.3, 8.2 Hz, 1H), 5.24 – 5.10 (m, 2H), 3.83 (d, *J* = 13.1 Hz, 1H), 3.64 (d, *J* = 13.1 Hz, 1H), 3.12 - 3.03 (m, 1H), 2.74 – 2.56 (m, 2H), 1.91 – 1.68 (m, 2H).

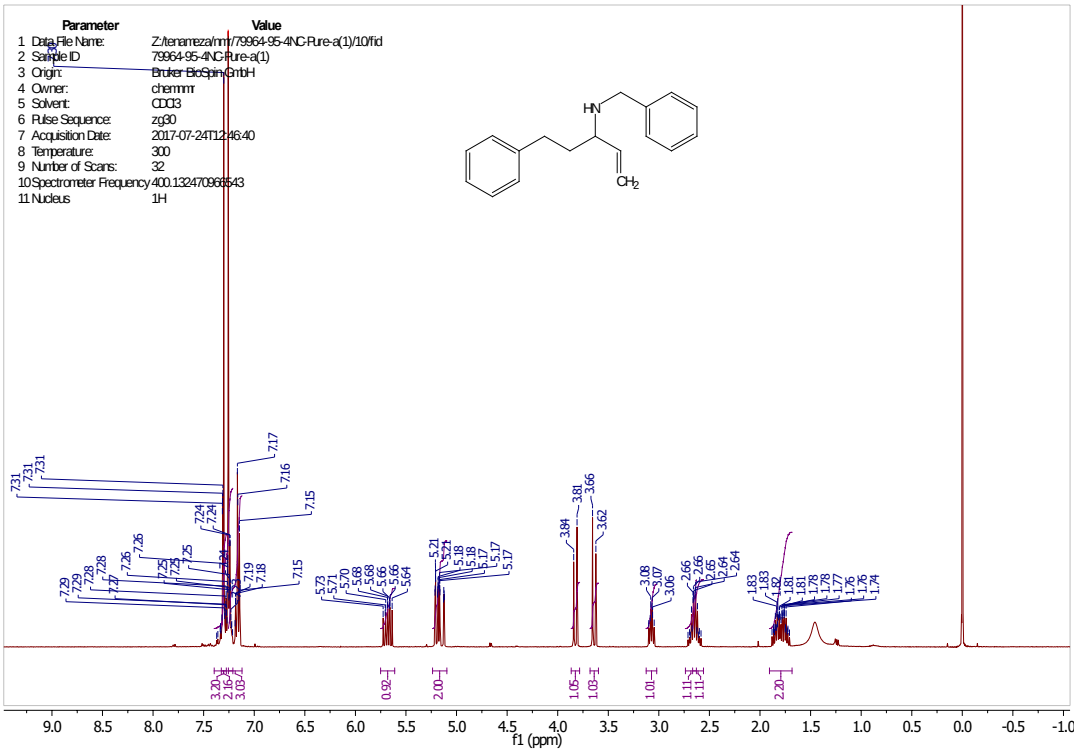
^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.2, 141.0, 140.7, 128.4, 128.4, 128.3, 128.2, 126.8, 125.7, 116.4, 60.8, 51.2, 37.4, 32.2.

HRMS (ESI): calcd for $C_{18}H_{22}N$ $[M+H]^+$: 252.1752, found: 252.1743

FTIR (neat): 3061, 3025, 2920, 1639, 1602, 1495, 1452, 1108, 1072, 1028, 993, 918, 742, 696 cm^{-1}.

$[\alpha]_D^{24}$ = +7.4 (*c* 0.48, $CHCl_3$).

HPLC (Chiralpak OD-H; heptane/isopropanol 99:1.0, 1.0 mL/min, 220 nm) ee = 94%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4 Owner: chemmm
5 Solvent: CDCl3
6 Pulse Sequence: zg30
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8 Temperature: 300
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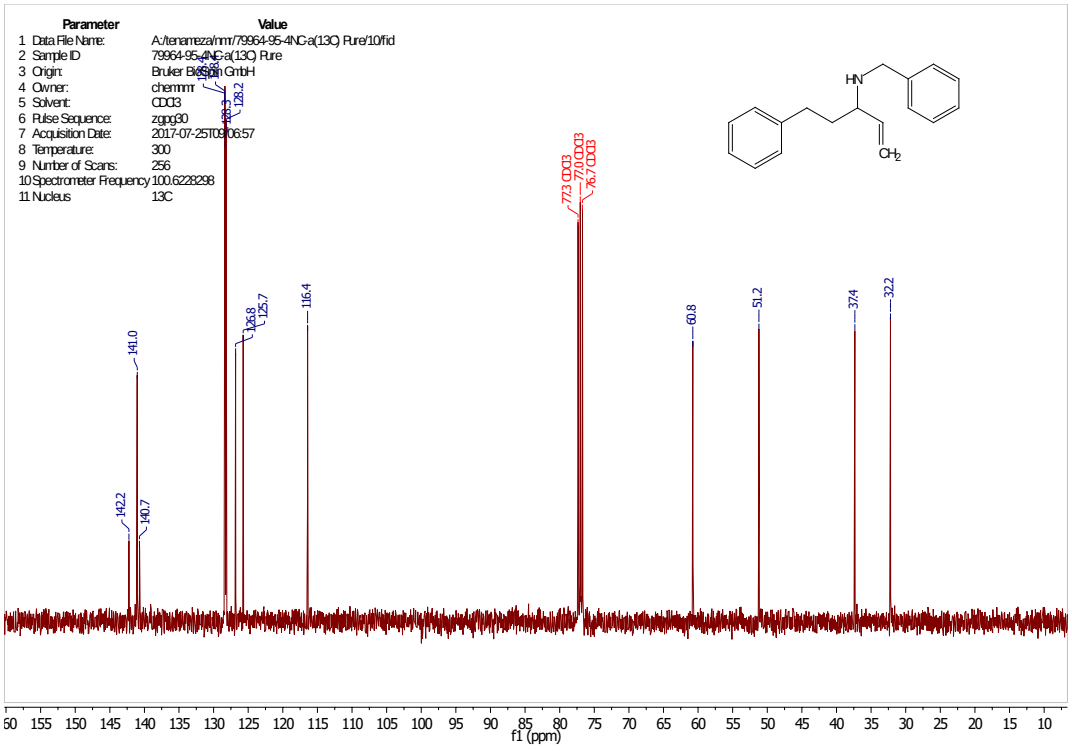
10 Spectrometer Frequency 400.13247096543
11 Nucleus 1H
HN
CH2
f1 (ppm)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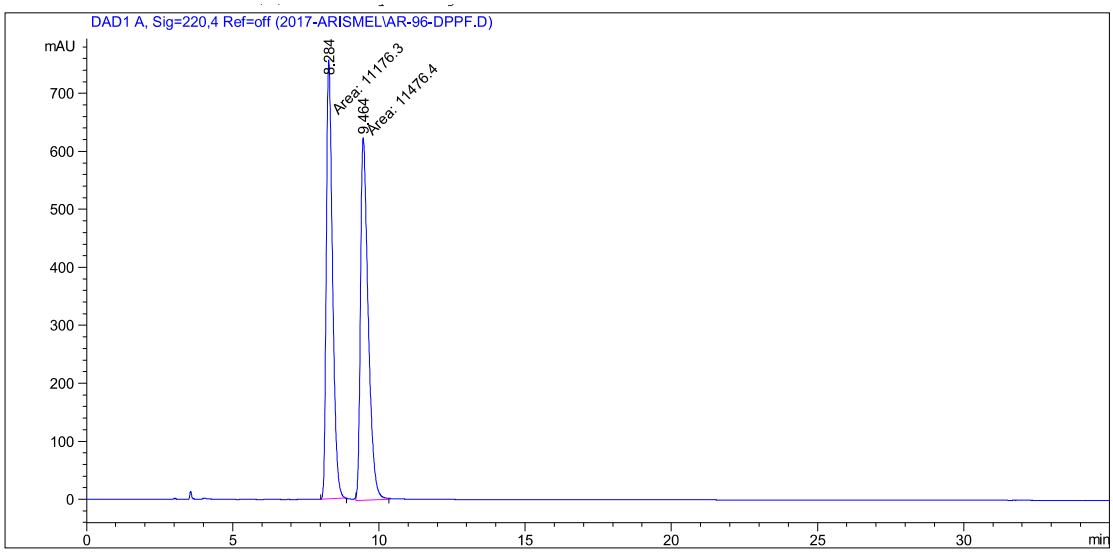
CH2
f1 (ppm)



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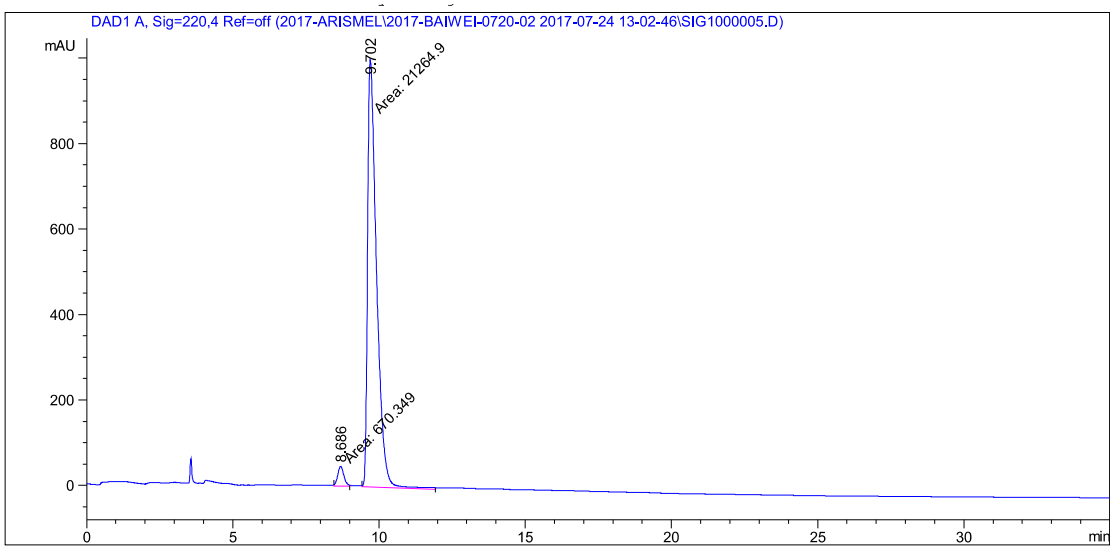

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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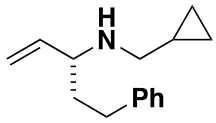
2	9.702	MM	0.3546	2.12649e4	999.55920	96.9440

(*R*)-*N*-(cyclopropylmethyl)-5-phenylpent-1-en-3-amine (4.3c')



Procedures

The allylic acetate (89.9 mg, 0.44 mmol, 100 mol%) and the primary amine (62.6 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 75% yield (70.3 mg, 0.33 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, dichloromethane : methanol = 1:0 – 20:1).

TLC (SiO_2) R_f = 0.45 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 - 7.12 (m, 5H), 5.63 (ddd, *J* = 17.0, 10.3, 8.3 Hz, 1H), 5.19 – 5.06 (m, 2H), 3.09 - 2.99 (m, 1H), 2.74 - 2.54 (m, 2H), 2.46 (dd, *J* = 12.0, 7.0 Hz, 1H), 2.35 (dd, *J* = 12.0, 6.8 Hz, 1H), 1.92 - 1.80 (m, 1H), 1.80 - 1.67 (m, 1H), 1.00 – 0.85 (m, 1H), 0.52 – 0.39 (m, 2H), 0.16 – 0.03 (m, 2H).

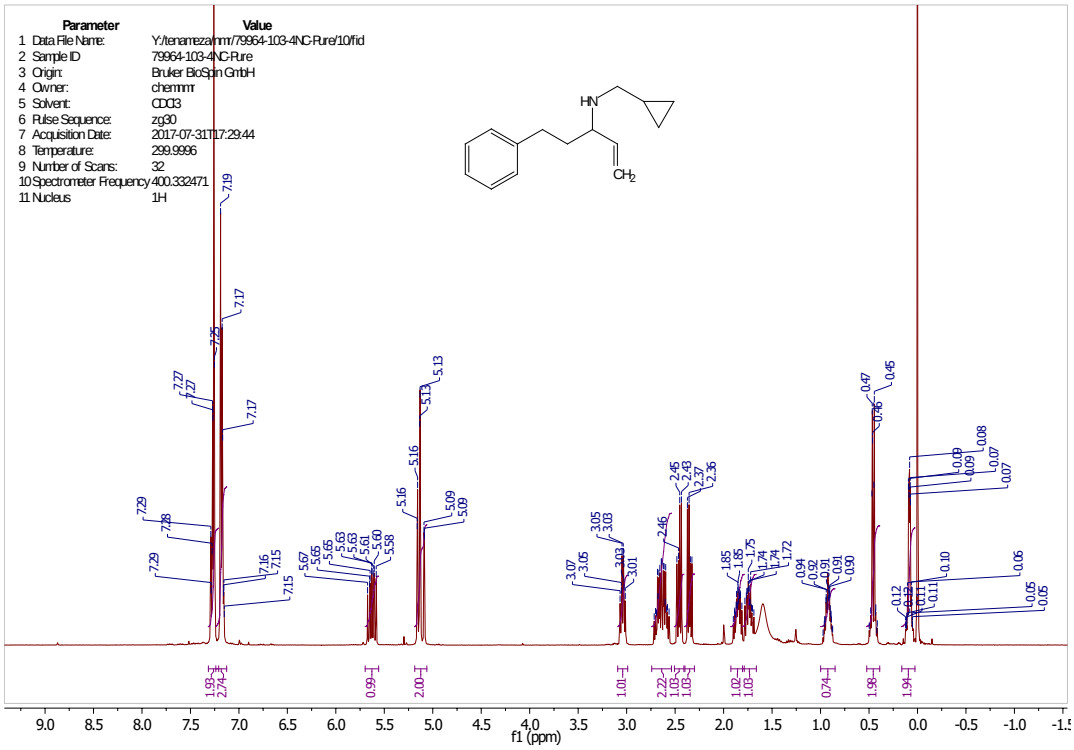
^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.1, 141.0, 128.4, 128.3, 125.7, 116.4, 61.4, 52.4, 37.1, 32.2, 11.3, 3.5, 3.3.

HRMS (ESI): calcd for $C_{15}H_{22}N$ $[M+H]^+$: 216.1752, found: 216.1742

FTIR (neat): 3077, 3002, 2921, 1603, 1496, 1453, 1318, 1113, 1045, 1016, 994, 917, 825, 748, 697 cm^{-1}.

$[\alpha]_D^{24}$ = +4.2 (*c* 0.42, $CHCl_3$).

HPLC (Chiralpak OD-H, heptane/isopropanol 99.0:1.0, 1.0 mL/min, 220 nm) ee = 93%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4 Owner: chemmnr
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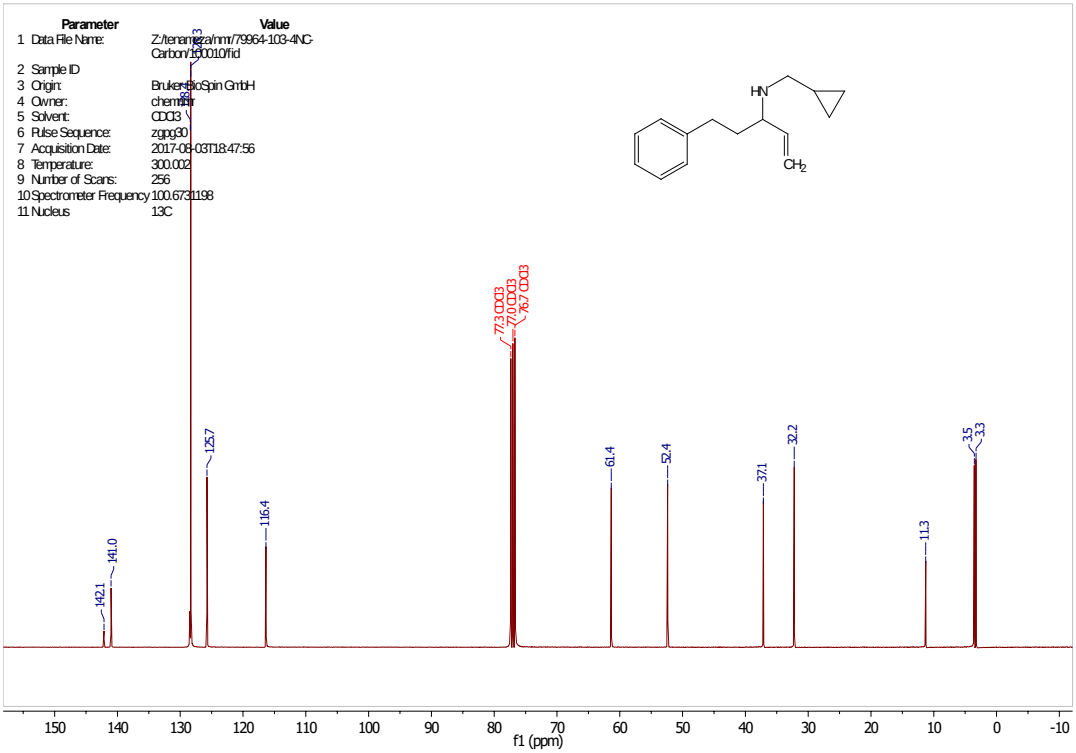
f1 (ppm)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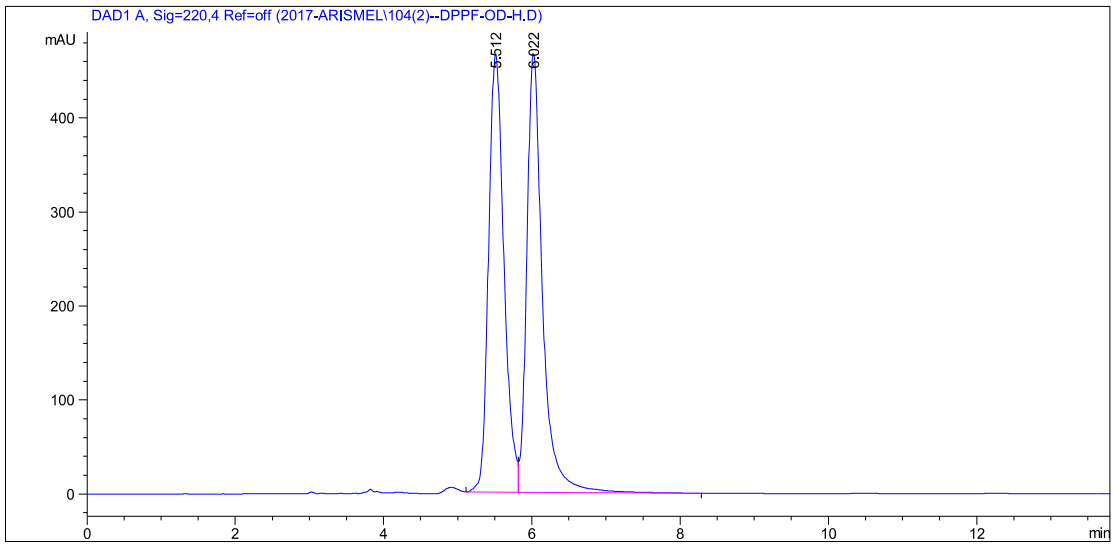
8 Temperature: 300.002
9 Number of Scans: 256
10 Spectrometer Frequency 100.6731198
11 Nucleus 13C
HN
CH2
f1 (ppm)



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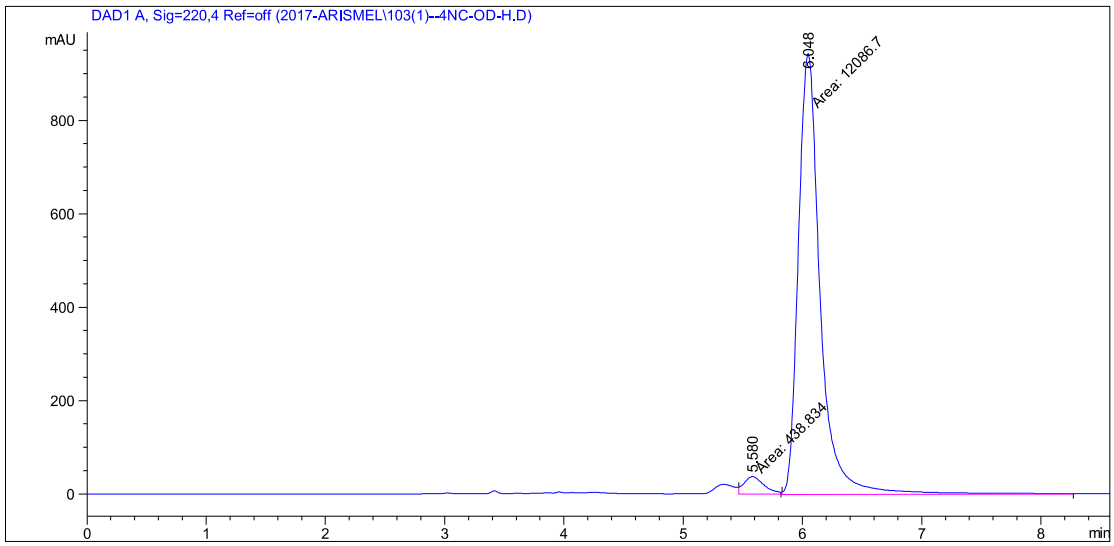
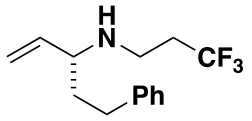
2	6.022	VB	0.2192	6846.67529	466.44180	50.4616



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.580	MM	0.1946	438.83371	37.58027	3.5035
2	6.048	MM	0.2135	1.20867e4	943.63098	96.4965

(*R*)-5-phenyl-*N*-(3,3,3-trifluoropropyl)pent-1-en-3-amine (4.3d')



Procedures

The allylic acetate (89.9 mg, 0.44 mmol, 100 mol%) and the primary amine (99.5 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ^{o}C, 60 hr). The title compound was obtained in 80% yield (89.9 mg, 0.35 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.61 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 – 7.14 (m, 5H), 5.59 (ddd, *J* = 17.1, 10.2, 8.2 Hz, 1H), 5.22 – 5.09 (m, 2H), 3.04 - 2.96 (m, 1H), 2.88 (dt, *J* = 12.3, 7.3 Hz, 1H), 2.78 – 2.55 (m, 3H), 2.33 - 2.16 (m, 2H), 1.87 – 1.65 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.9, 140.5, 128.4(x2), 125.8, 116.8, 61.3, 40.0 (q, *J* = 3.7 Hz), 37.2, 34.5 (d, J = 27.4 Hz), 32.1.

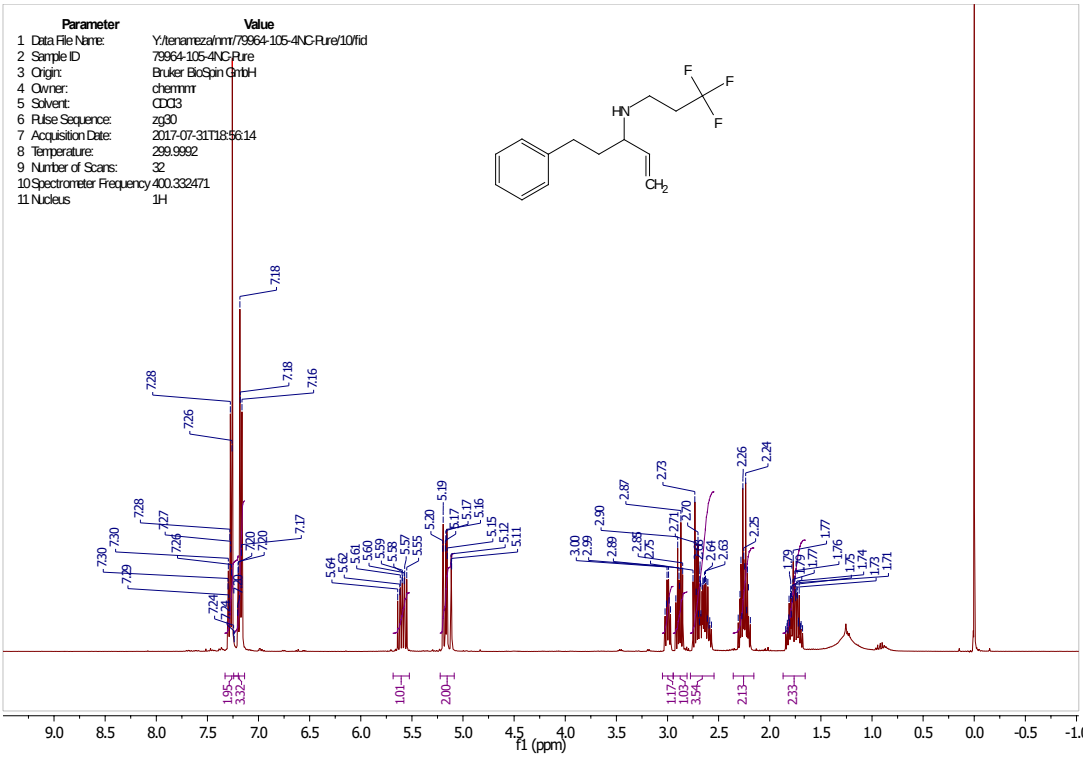
^{19}F NMR (376 MHz, $CDCl_3$): δ = –65.1 (t, *J* = 10.9 Hz, 3F).

HRMS (ESI): calcd for $C_{14}H_{19}F_3N$ $[M+H]^+$: 258.1470, found: 258.1460

FTIR (neat): 3028, 2926, 2859, 1641, 1603, 1496, 1454, 1440, 1384, 1339, 1252, 1139, 1030, 996, 921, 845, 748, 698, 654 cm^{-1}.

$[\alpha]_D^{24}$= +5.9 (*c* 0.47, $CHCl_3$).

HPLC (Chiralpak OD-H, heptane/isopropanol 99.0:1.0, 1.0 mL/min, 220 nm) ee = 87%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4 Owner: chemmm
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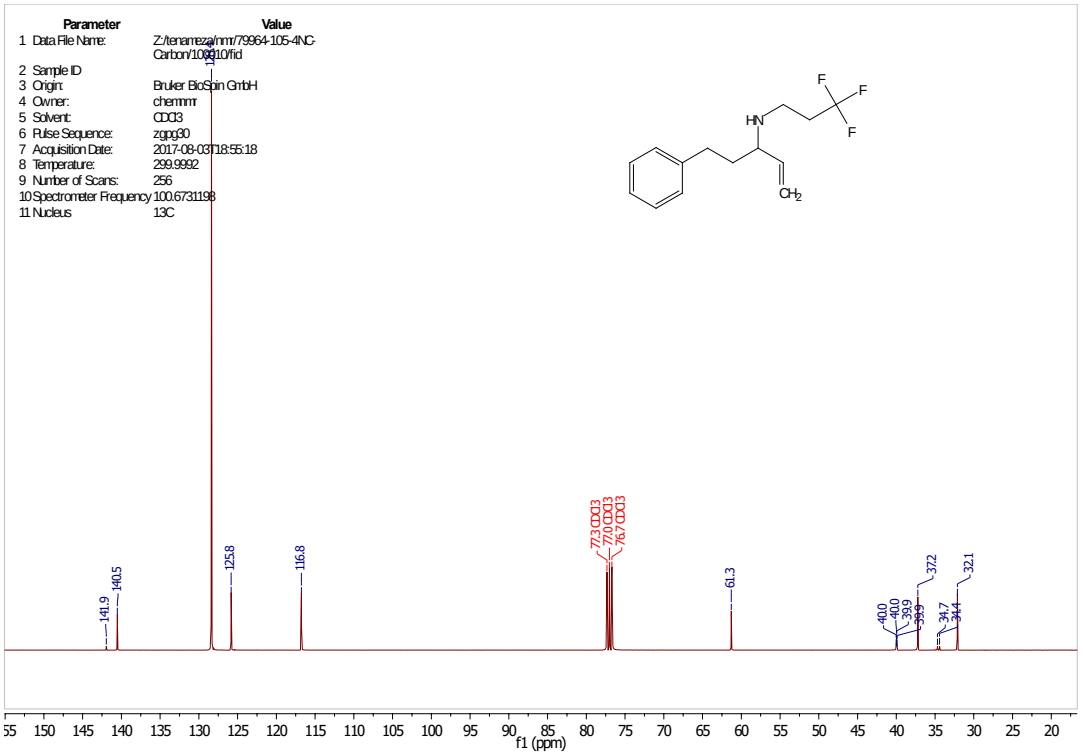
CH2
f1 (ppm)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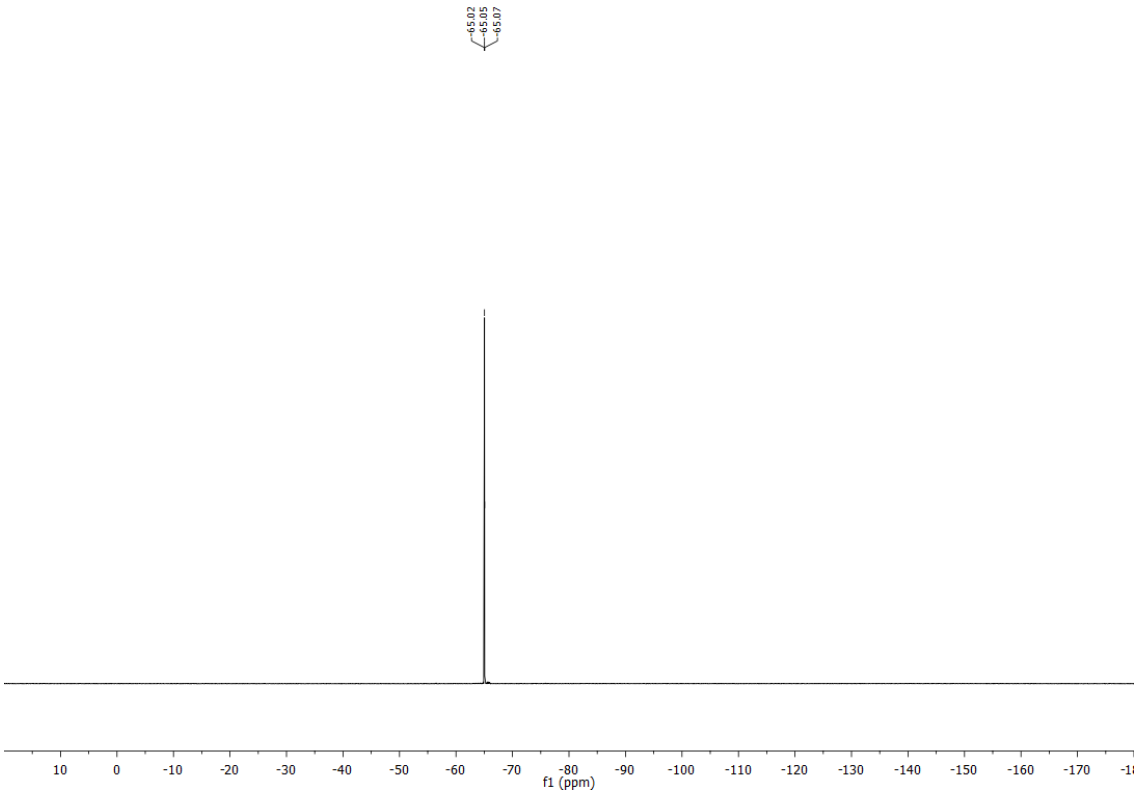
HN
CH2
f1 (ppm)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10
0
-10
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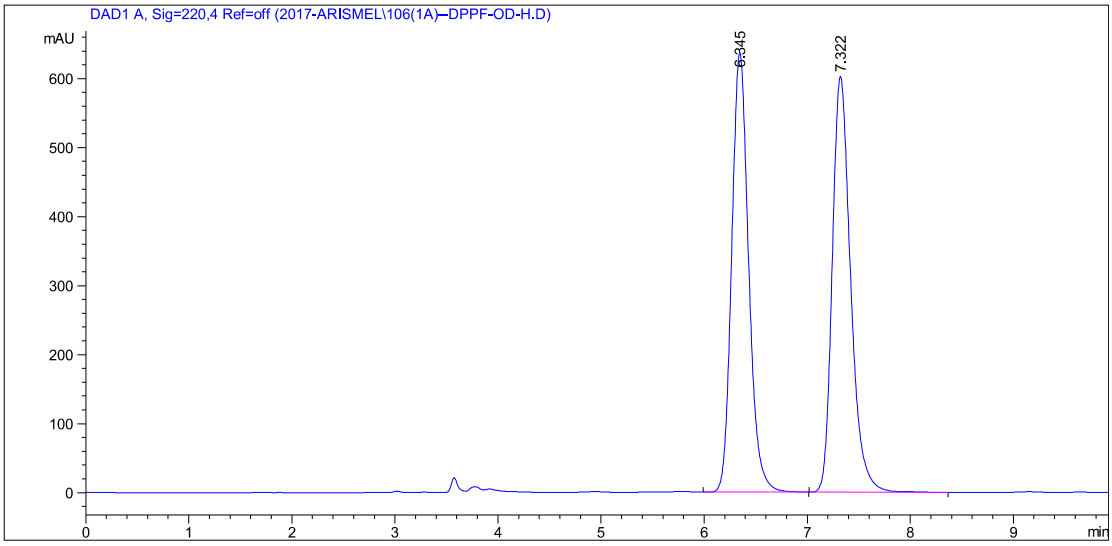
-140
-150
-160
-170
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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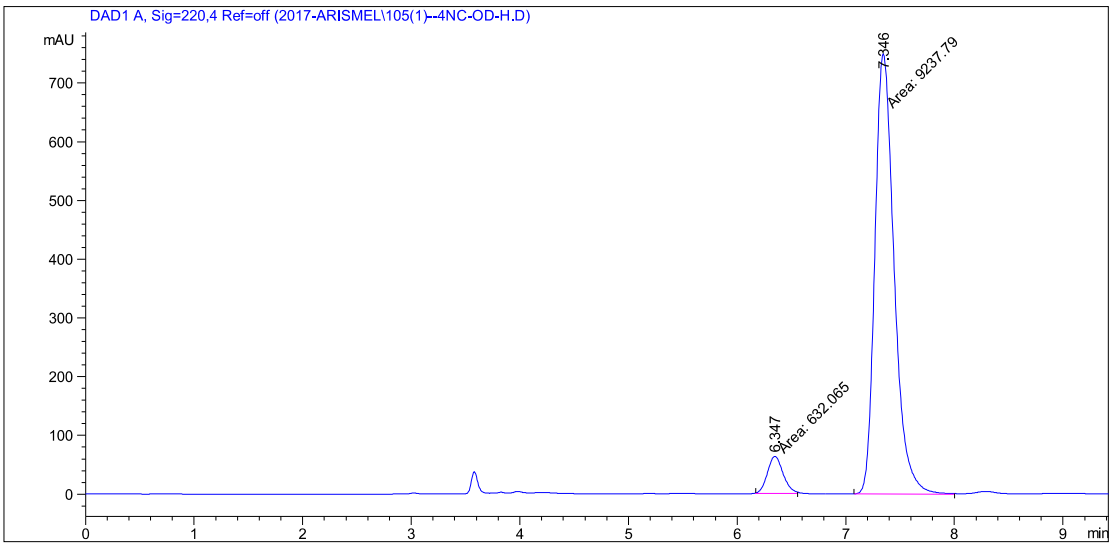
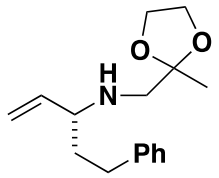
2	7.322	BB	0.1903	7455.92529	602.83063	50.6451



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.347	MM	0.1670	632.06519	63.07525	6.4040
2	7.346	MM	0.2054	9237.78613	749.45416	93.5960

(*R*)-*N*-((2-methyl-1,3-dioxolan-2-yl)methyl)-5-phenylpent-1-en-3-amine (4.3e')



Procedures

The allylic acetate (89.9 mg, 0.44 mmol, 100 mol%) and the primary amine (103 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ^{o}C, 60 hr). The title compound was obtained in 83% yield (94.7 mg, 0.36 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.39 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 – 7.22 (m, 2H), 7.21 – 7.12 (m, 3H), 5.62 (ddd, *J* = 17.1, 10.3, 8.1 Hz, 1H), 5.18 – 5.06 (m, 2H), 4.01 – 3.87 (m, 4H), 3.06 - 2.97 (m, 1H), 2.76 (d, *J* = 12.3 Hz, 1H), 2.73 – 2.59 (m, 2H), 2.56 (d, *J* = 12.2 Hz, 1H), 1.89 – 1.65 (m, 2H), 1.37 (s, 3H).

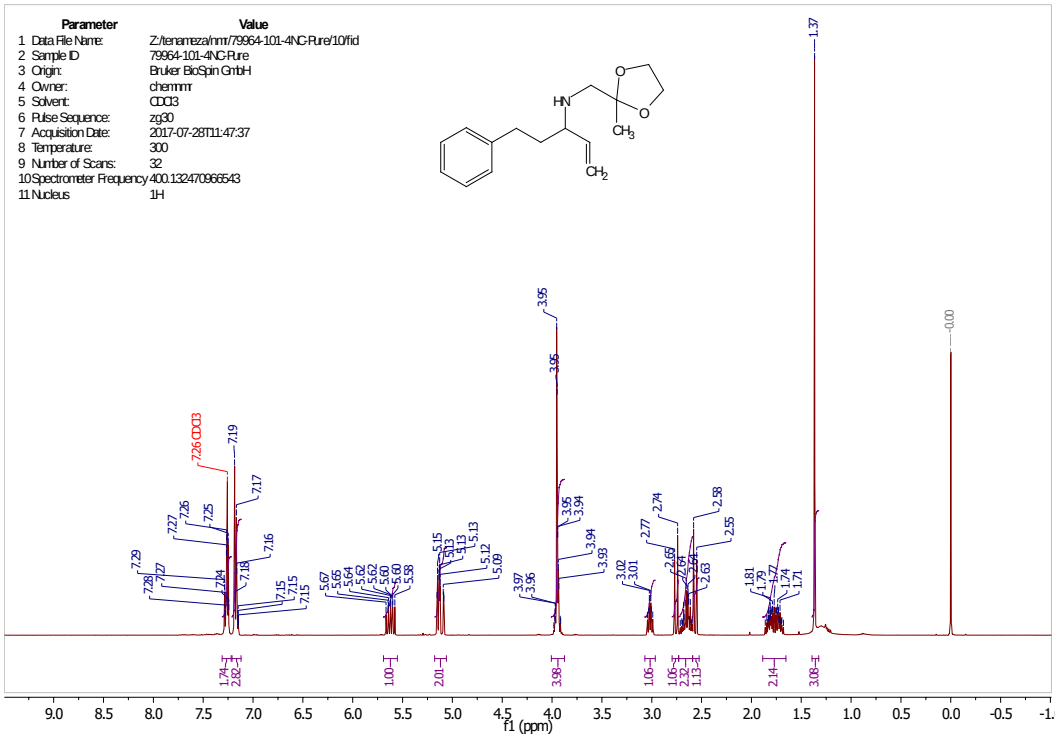
^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.3, 141.2, 128.4, 128.3, 125.7, 116.1, 109.5, 64.9, 64.9, 61.5, 53.6, 37.3, 32.2, 22.9.

HRMS (ESI): calcd for $C_{16}H_{24}NO_2$ $[M+H]^+$: 262.1807, found: 262.1795

FTIR (neat): 2980, 2879, 1603, 1496, 1454, 1376, 122, 1162, 1118, 1051, 994, 945, 918, 859, 749, 698 cm^{-1}.

$[\alpha]_D^{24} = +1.7$ (*c* 0.47, $CHCl_3$,).

HPLC (Chiralpak OD-H (2x), heptane/isopropanol 99.6:0.4; 1.0 mL/min, 220 nm), ee = 93%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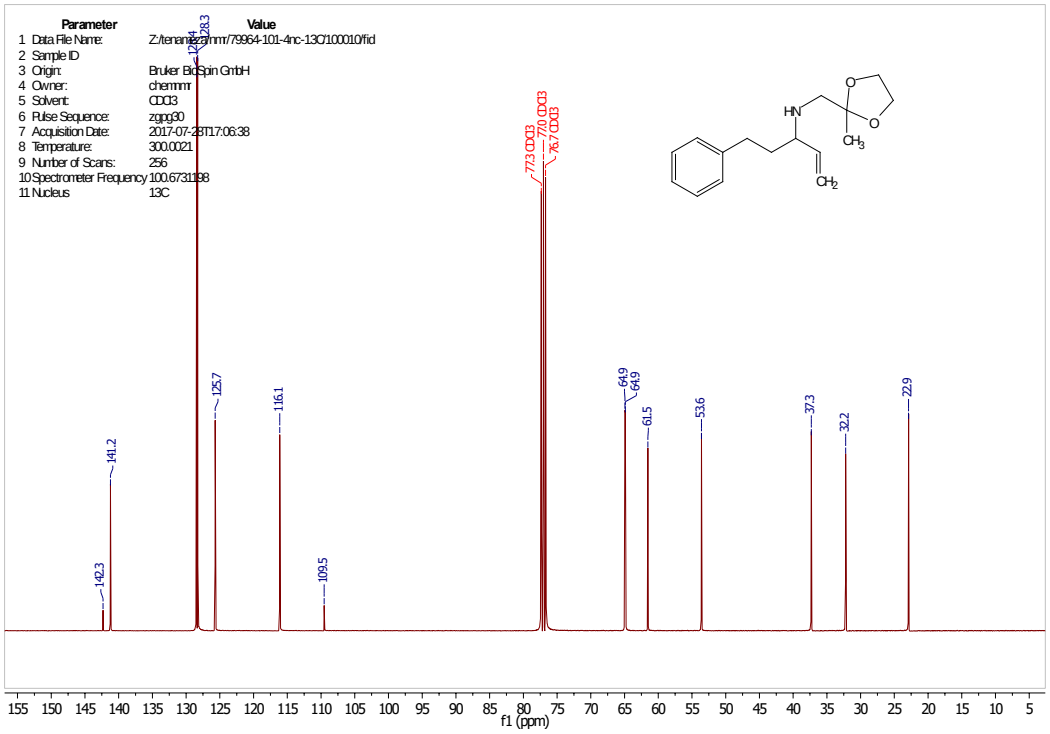
CH2
f1 (ppm)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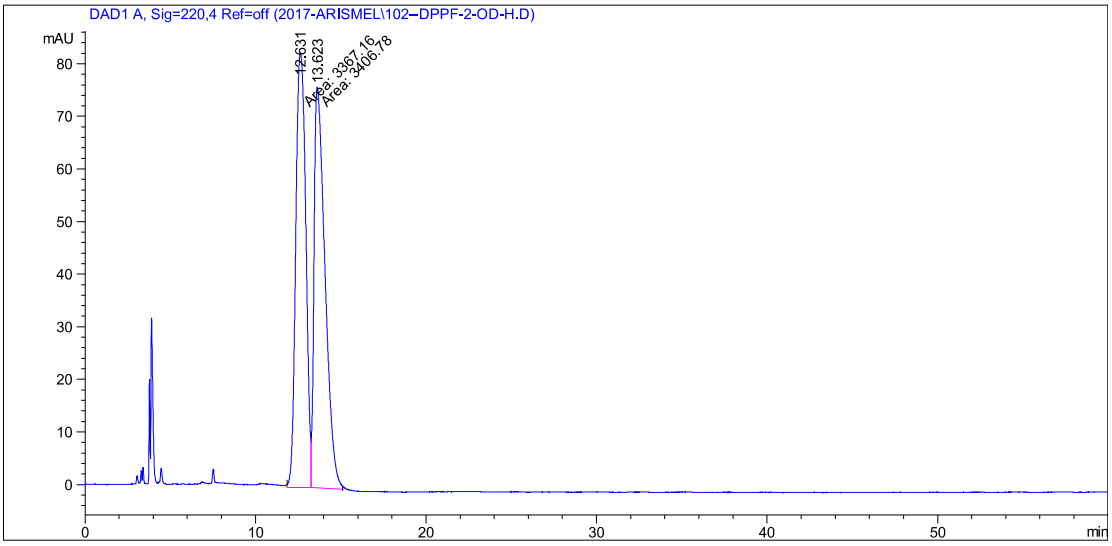
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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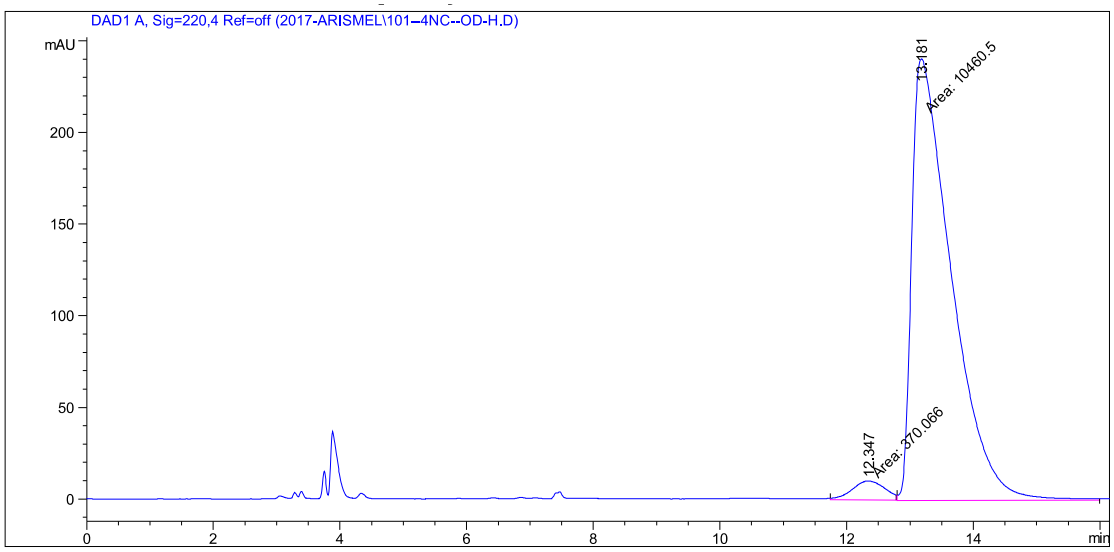
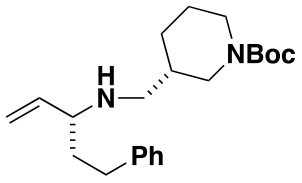
2	13.623	MM	0.7457	3406.77734	76.14778	50.2924



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.347	MM	0.5959	370.06595	10.35074	3.4169
2	13.181	MM	0.7237	1.04605e4	240.90688	96.5831

tert-butyl-(*S*)-3-((((*R*)-5-phenylpent-1-en-3-yl)amino)methyl)piperidine-1-carboxylate (4.3f')



Procedures

The allylic acetate (89.9 mg, 0.44 mmol, 100 mol%) and the primary amine (189 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ^{o}C, 60 hr). The title compound was obtained in 83% yield, 17:1 dr (130 mg, 0.36 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, dichloromethane: methanol = 1:0–20:1).

TLC (SiO_2) R_f = 0.39 (hexanes/ethyl acetate = 1:1).

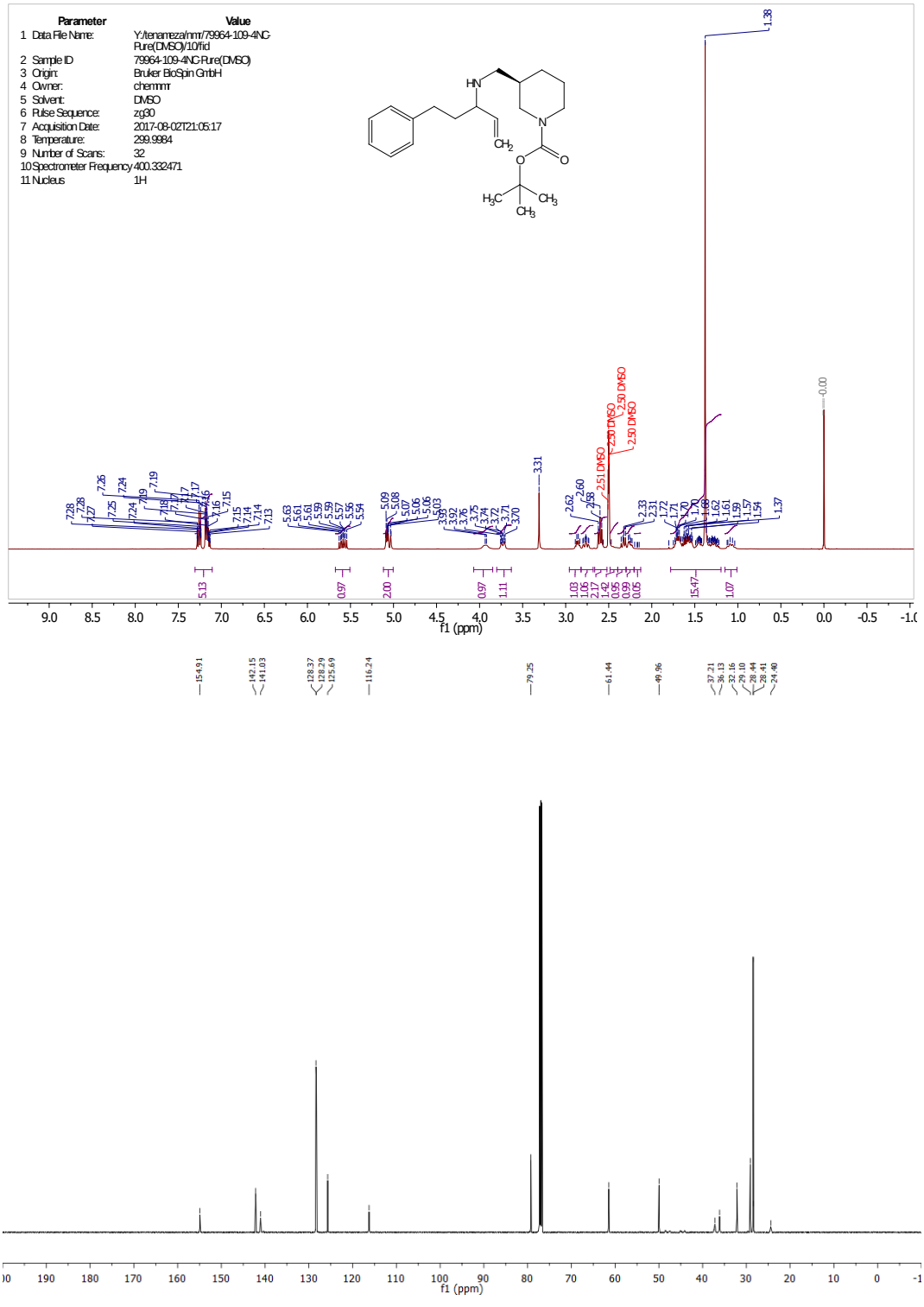
^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.31 – 7.11 (m, 5H), 5.59 (ddd, *J* = 17.0, 10.4, 7.9 Hz, 1H), 5.12 – 5.00 (m, 2H), 4.07 – 3.85 (m, 1H), 3.80 - 3.67 (m, 1H), 2.86 (q, *J* = 7.0 Hz, 1H), 2.77 (ddd, *J* = 13.6, 11.0, 3.1 Hz, 1H), 2.60 (t, *J* = 8.0 Hz, 2H), 2.56 – 2.43 (m, 1H), 2.33 (dd, *J* = 11.8, 8.1 Hz, 1H), 2.25 (dd, *J* = 11.9, 5.5 Hz, 1H), 1.78 – 1.20 (m, 15H), 1.14 - 1.00 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.9, 142.2, 141.1, 128.4, 128.3, 125.7, 116.2, 79.3, 61.4, 50.0, 37.2, 36.1(x2), 32.2, 29.1, 28.4(x2), 24.4.

HRMS (ESI): calcd for $C_{22}H_{35}N_2O_2$ $[M+H]^+$: 359.2699, found: 359.2686

FTIR (neat): 2975, 2928, 2853, 1685, 1496, 1420, 1390, 1364, 1265, 1240, 1174, 1147, 1030, 994, 967, 917, 881, 750, 698, 665 cm^{-1}.

$[\alpha]_D^{24}$ = –14.3 (*c* 0.41, $CHCl_3$).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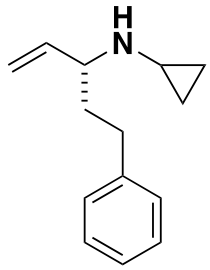
HN
N
O
O
CH2
H3C
CH3
CH3
f1 (ppm)
f1 (ppm)

(*R*)-*N*-(5-phenylpent-1-en-3-yl)cyclopropanamine (4.3g')



Procedures

The allylic acetate (40.9 mg, 0.20 mmol, 100 mol%) and the primary amine (22.8 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 79% yield (31.8 mg, 0.16 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 1:1).

TLC (SiO_2) R_f = 0.54 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24-7.17 (m, 2H), 7.14-7.07 (m, 3H), 5.67-5.56 (m, 1H), 5.11-5.08 (m, 1H), 5.07-5.04 (m, 1H), 3.10-3.02 (m, 1H), 2.63-2.47 (m, 2H), 2.07-2.00 (m, 1H), 1.83-1.72 (m, 1H), 1.68-1.56 (m, 1H), 0.42-0.26 (m, 3H), 0.24-0.16 (m, 1H).

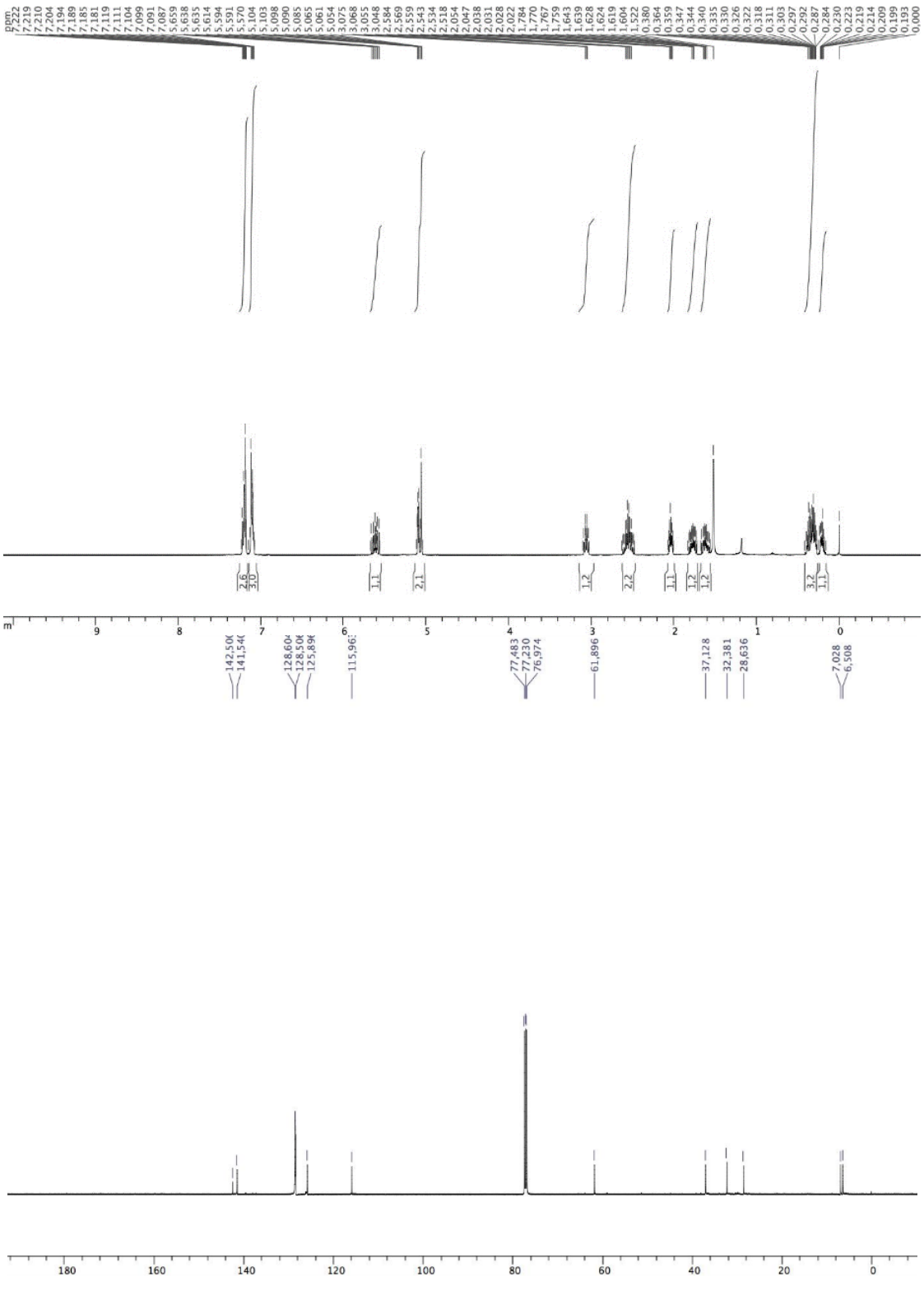
^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.5, 141.5, 128.6 (2C), 128.5 (2C), 125.9, 116.0, 61.9, 37.1, 32.4, 28.6, 7.0, 6.5.

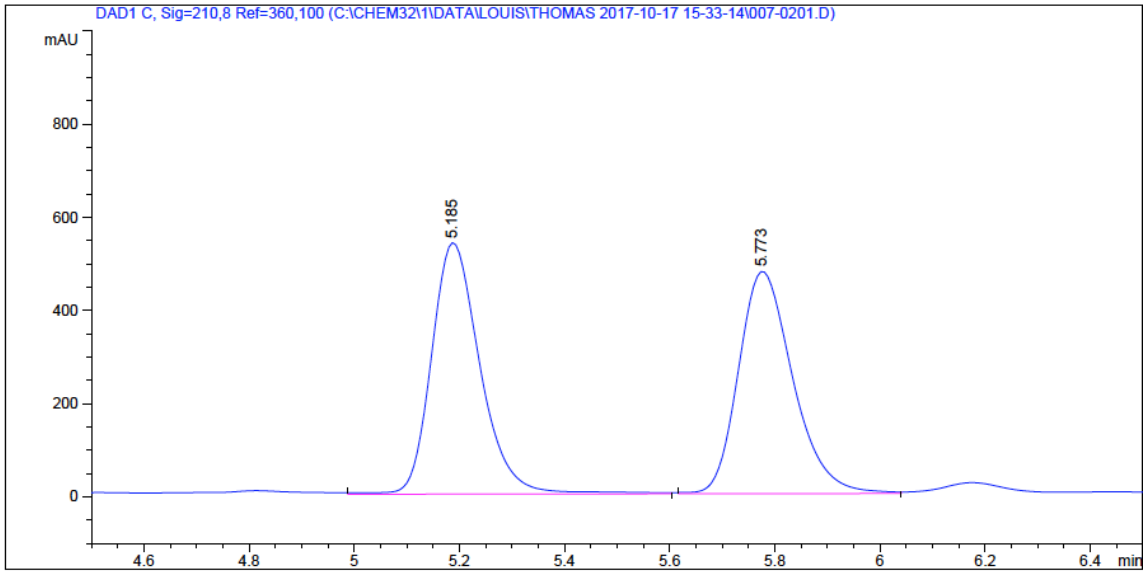
HRMS (ESI): Calculated for $C_{14}H_{19}N$ [M+H$^+$] = 202.1590, Found 202.1586.

FTIR (neat): 3084, 3026, 2924, 1738, 1639, 1603, 1496, 1453, 1369, 1237, 1014, 993, 916, 827, 746, 697 cm^{-1}.

$[\alpha]_D^{24}$ = –11.3 (*c* 1.1, $CHCl_3$,).

HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 210 nm), *ee* = 94%.





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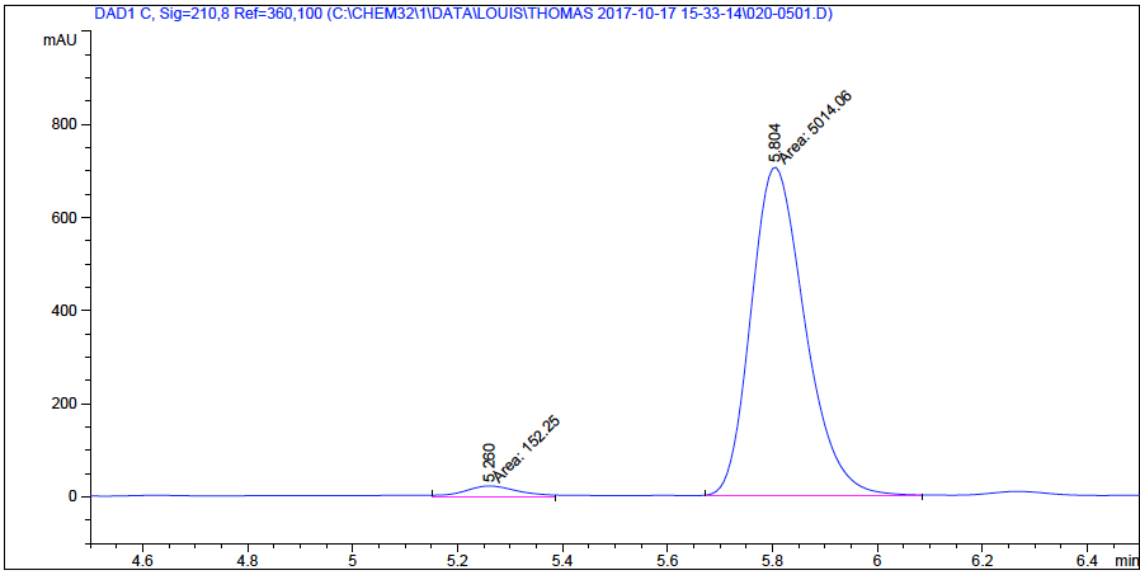
2	5.773	BV	0.1118	3433.14063	477.73456	49.6677



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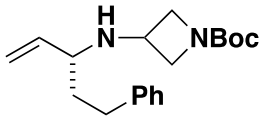
1	5.260	MM	0.1147	152.24989	22.12654	2.9470
2	5.804	MM	0.1184	5014.06445	705.73468	97.0530

***tert*-Butyl (*R*)-3-((5-phenylpent-1-en-3-yl)amino)azetidine-1-carboxylate (4.3h')**



Procedures

The allylic acetate (89.9 mg, 0.44 mmol, 100 mol%) and the primary amine (152 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ^{o}C, 60 hr). The title compound was obtained in 74% yield (102 mg, 0.32 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptane: isopropyl acetate = 1:0–0:1).

TLC (SiO_2) R_f = 0.32 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 – 7.22 (m, 2H), 7.23 – 7.13 (m, 3H), 5.60 (ddd, *J* = 17.0, 10.2, 8.5 Hz, 1H), 5.18 – 5.06 (m, 2H), 4.09 – 3.97 (m, 2H), 3.64 – 3.52 (m, 3H), 3.04 - 2.94 (m, 1H), 2.73 – 2.53 (m, 2H), 1.87 – 1.65 (m, 2H), 1.43 (s, 9H).

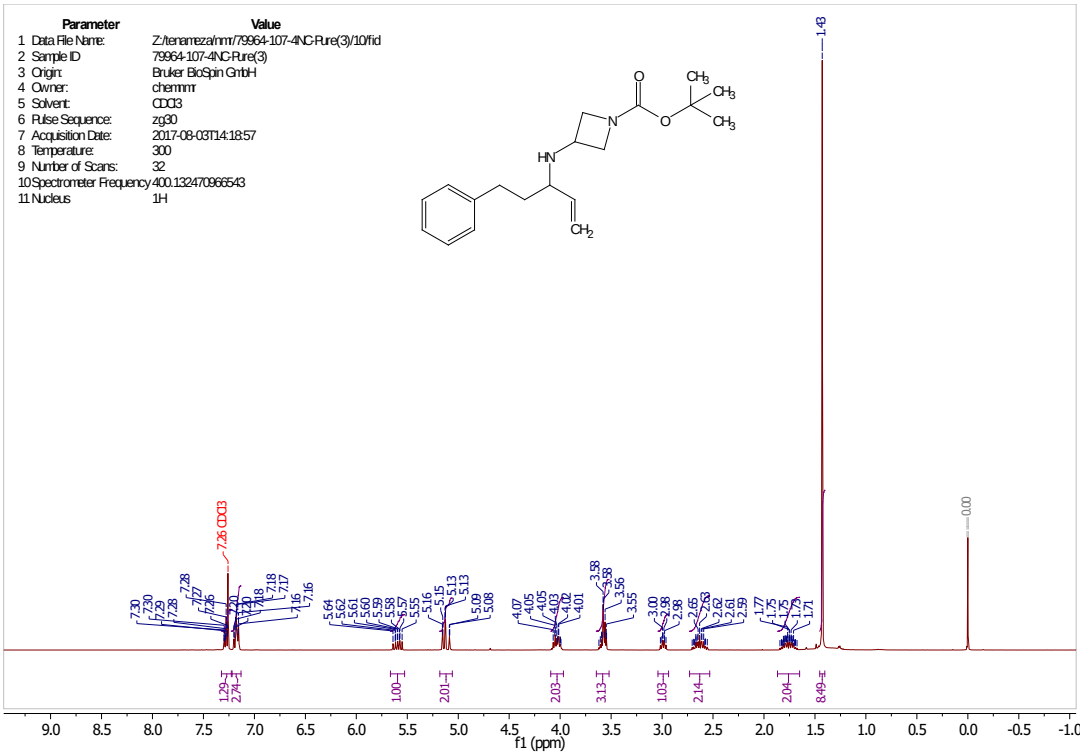
^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1, 141.7, 140.6, 128.4, 128.3, 125.9, 116.9, 79.0, 60.1, 45.9, 37.2, 32.1, 28.4, 25.4.

HRMS (ESI): calcd for $C_{19}H_{29}N_2O_2$ $[M+H]^+$: 317.2229, found: 317.2215

FTIR (neat): 2973, 2876, 1692, 1603, 1496, 1476, 1454, 1401, 1365, 1290, 1251, 1158, 1118, 1030, 995, 919, 861, 750, 698 cm^{-1}.

$[\alpha]_D^{24} = +4.5$ (*c* 0.40, $CHCl_3$).

HPLC (Chiralpak OD-H, heptane/isopropanol 70.0:30.0, 1.0 mL/min, 220 nm) ee = 91%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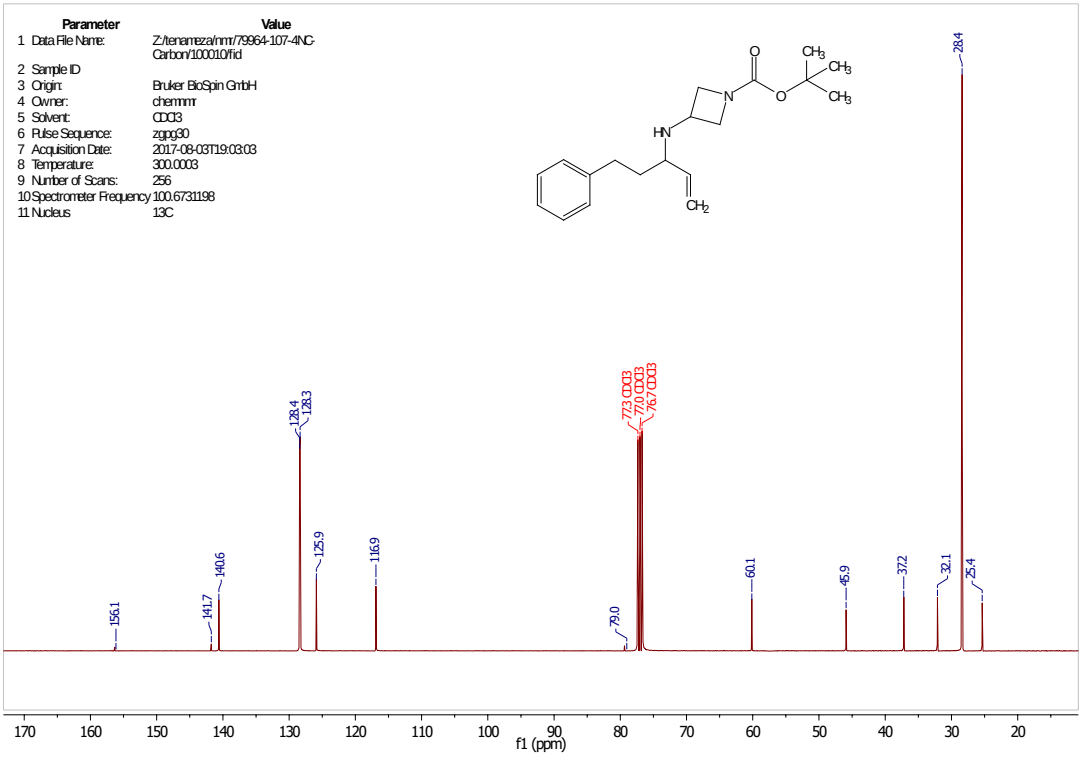
4 Owner: chemmm
5 Solvent: CDCl3
6 Pulse Sequence: zg30
7 Acquisition Date: 2017-08-03T14:18:57
8 Temperature: 300
9 Number of Scans: 32
10 Spectrometer Frequency 400.13247096643
11 Nucleus 1H
f1 (ppm)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4 Owner: chemmm
5 Solvent: CDCl3
6 Pulse Sequence: zgpg30
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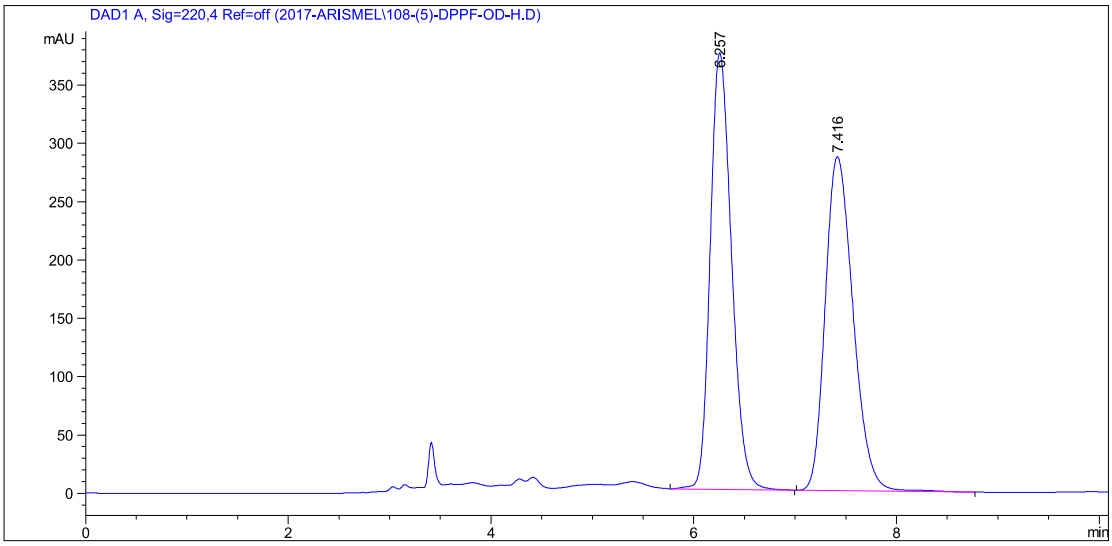
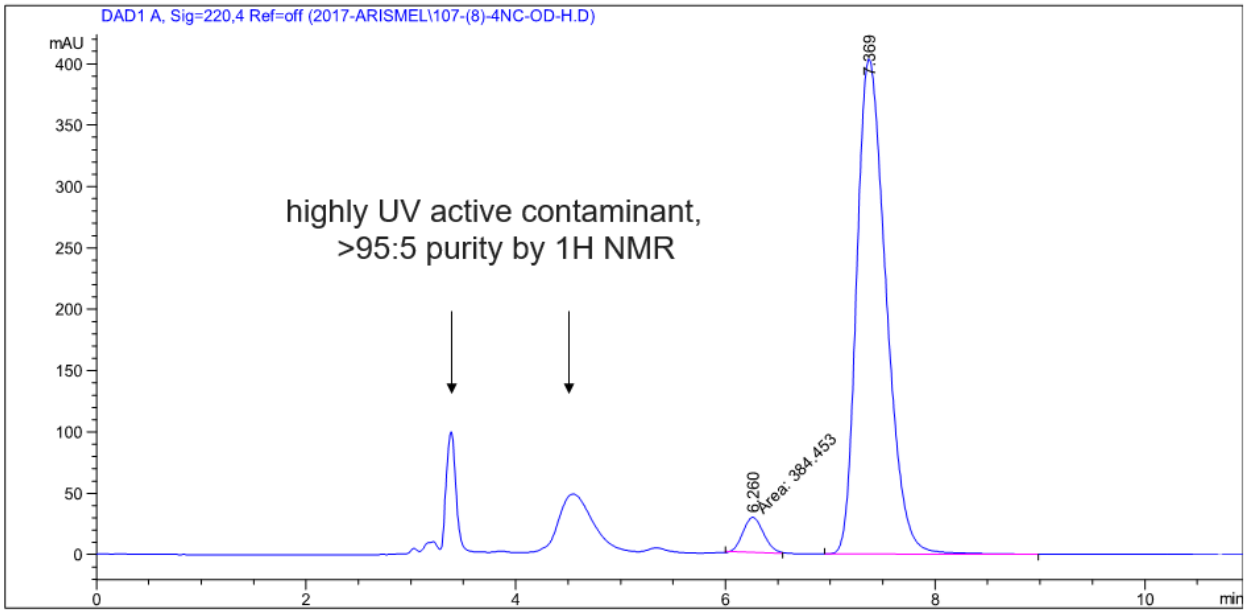
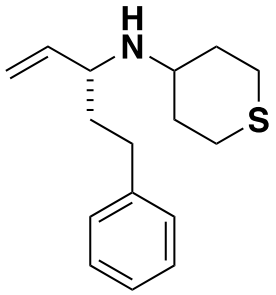


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.257	BB	0.2280	5452.42285	374.15463	49.8600
2	7.416	BB	0.2994	5483.03271	286.37350	50.1400



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.260	MM	0.2257	384.45261	28.38801	4.6706
2	7.369	BB	0.3029	7846.83154	403.46817	95.3294

(*R*)-*N*-(5-phenylpent-1-en-3-yl)tetrahydro-2*H*-thiopyran-4-amine (4.3i')



Procedures

The allylic acetate (40.9 mg, 0.20 mmol, 100 mol%) and the primary amine (46.9 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 79% yield (41.8 mg, 0.16 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 1:1).

TLC (SiO_2) R_f = 0.50 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30 – 7.25 (m, 2H), 7.20 - 7.15 (m, 3H), 5.58 (ddd, *J* = 17.2, 10.2, 8.3 Hz, 1H), 5.13 (d, *J* = 10.2 Hz, 1H), 5.08 (d, *J* = 17.2 Hz, 1H), 3.2-3.12 (m, 1H), 2.72-2.46 (m, 7H), 2.17-2.11 (m, 1H), 2.07-2.01 (m,1H), 1.83-1.65 (m, 2H), 1.57-1.48 (m, 1H), 1.44-1.34 (m, 1H), 1.09 (bs, 1H).

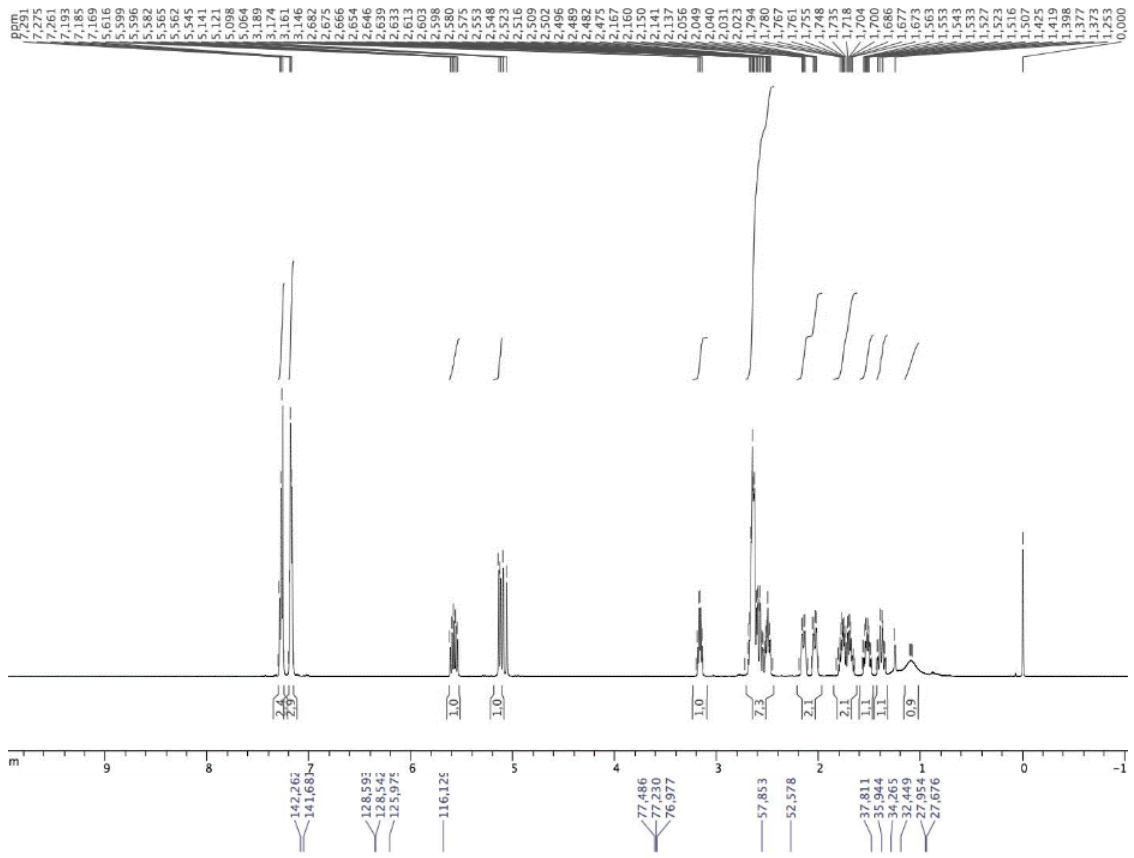
^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.3, 141.7, 128.6 (2C), 128.5 (2C), 126.0, 116.1, 57.9, 52.6, 37.8, 35.9, 34.3, 32.4, 28.0, 27.7.

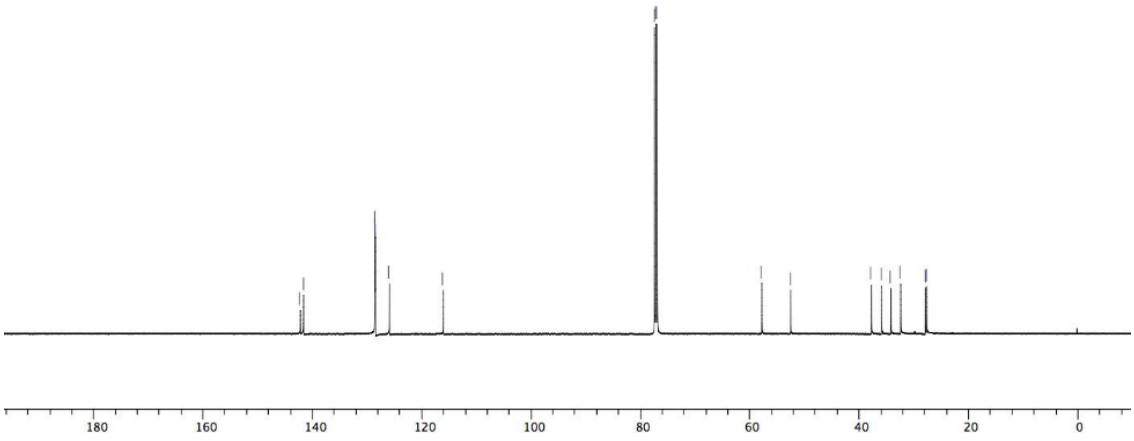
HRMS (ESI): Calculated for $C_{16}H_{23}NS$ [M+H$^+$] = 262.1624, Found 262.1620.

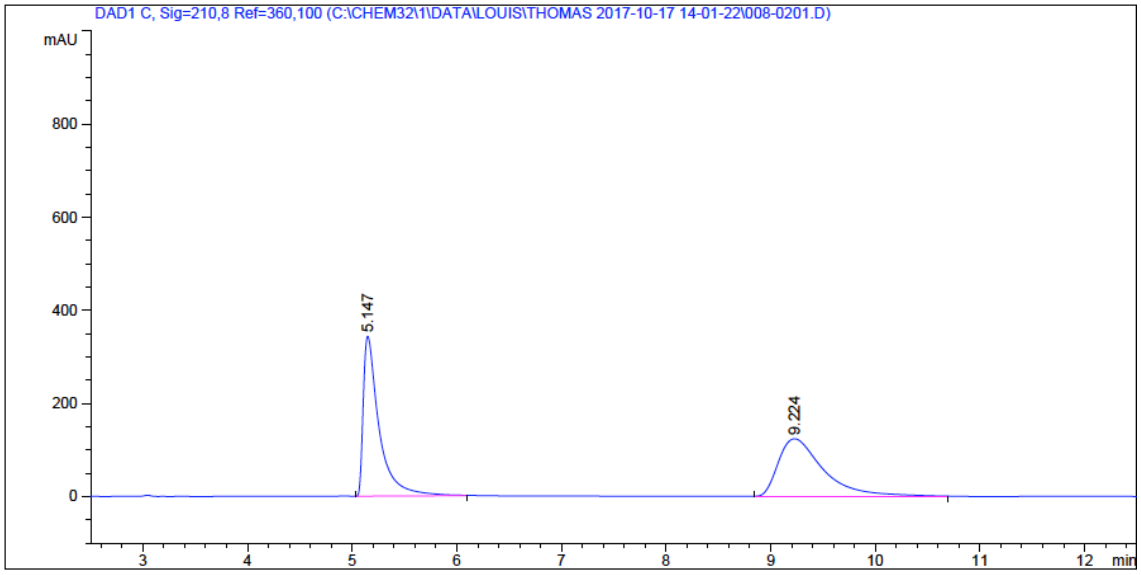
FTIR (neat): 3024, 2922, 2841, 1775, 1697, 1638, 1602, 1495, 1453, 1427, 1365, 1268, 1235, 1118, 1030, 994, 916, 747, 698, 659 cm^{-1}.

$[\alpha]_D^{24}$ = –15.6 (*c* 1.4, $CHCl_3$,).

HPLC (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 210 nm), *ee* = 95%.







Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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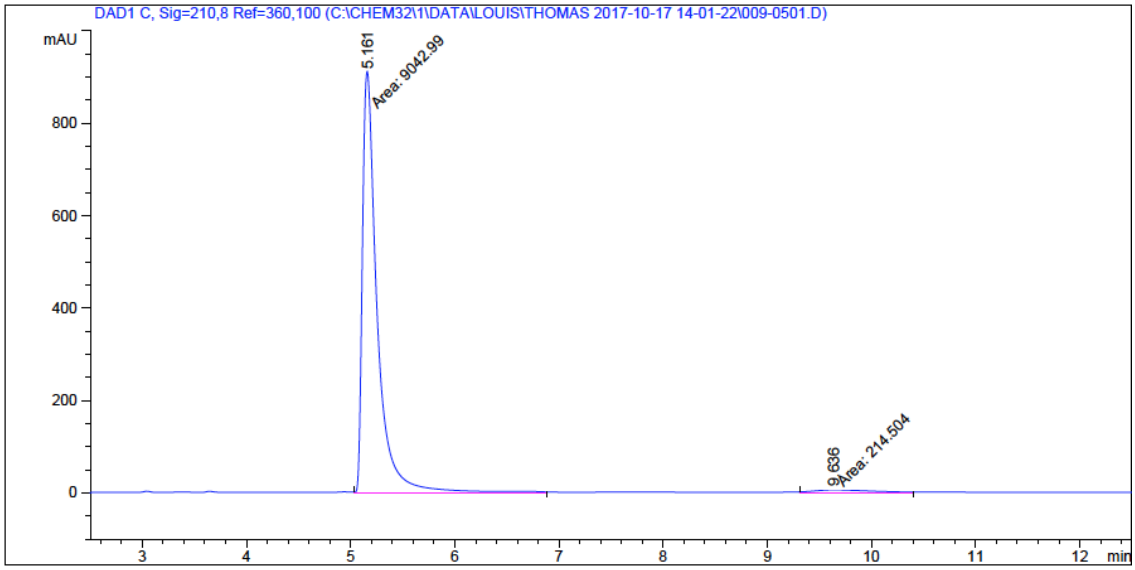
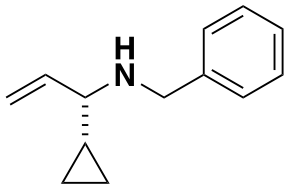
2	9.224	BB	0.4528	3700.40771	123.76275	50.5053



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.161	MM	0.1650	9042.98828	913.42432	97.6829
2	9.636	MM	0.6269	214.50421	5.70313	2.3171

(*S*)-*N*-benzyl-1-cyclopropylprop-2-en-1-amine (4.3j')



Procedures

The allylic acetate (28.0 mg, 0.20 mmol, 100 mol%) and the primary amine (42.9 mg, 0.40 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 76% yield (28.5 mg, 0.15 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 1:1).

TLC (SiO_2) R_f = 0.4 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29-7.21 (m, 4H), 7.21-7.15 (m, 1H), 5.74 (m, 1H), 5.09-5.02 (m, 2H), 3.78, (d, *J* = 13.3 Hz, 1H), 3.62, (d, *J* = 13.3 Hz, 1H), 2.24 (dd, *J* = 8.6, 7.8 Hz, 1H), 1.58 (s, 1H), 0.89 – 0.80 (m, 1H), 0.5-0.35 (m, 2H), 0.15-0.05.

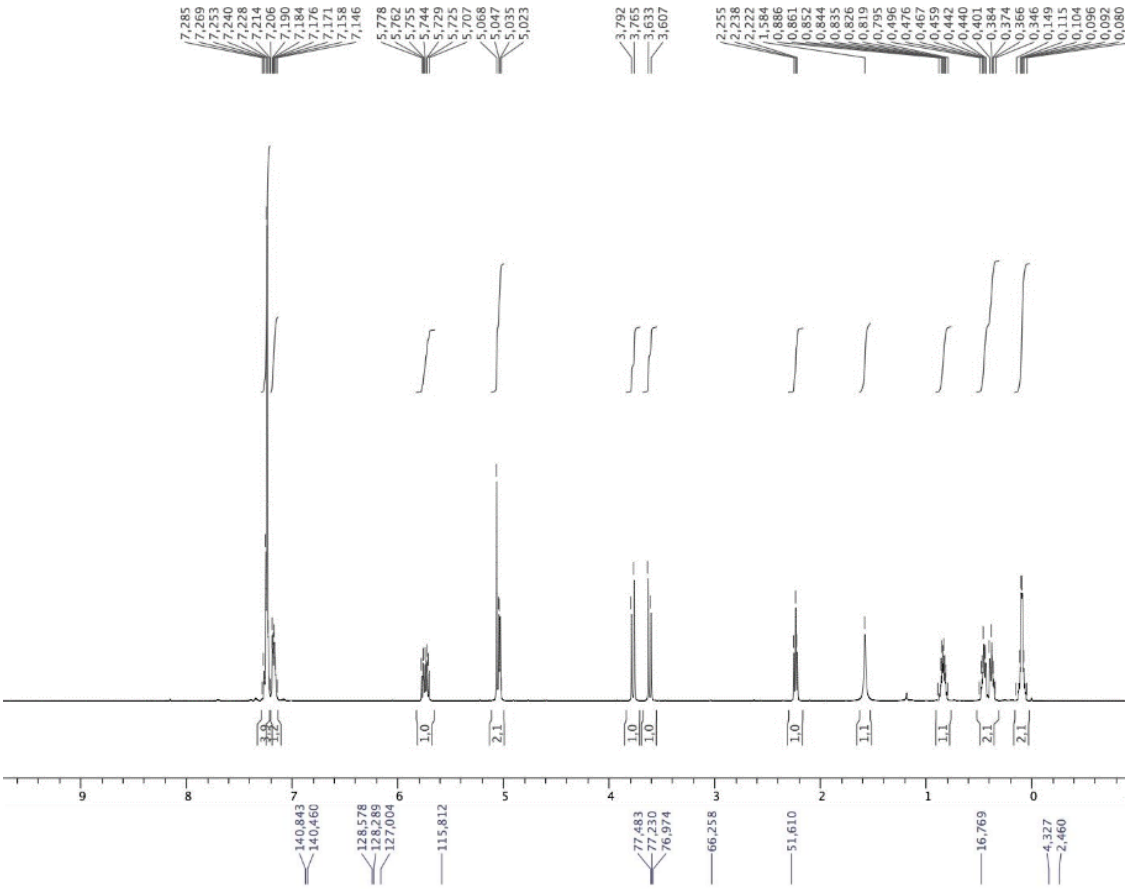
^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.8, 140.5, 128.6 (2C), 128.3 (2C), 127.0, 115.8, 66.3, 51.6, 16.8, 4.3, 2.5.

HRMS (ESI): Calculated for $C_{13}H_{17}N$ [M+H$^+$] = 188.1434, Found 188.1433.

FTIR (neat): 3339, 3076, 3025, 3002, 2815, 1640, 1603, 1494, 1453, 1428, 1413, 1358, 1302, 1172, 1101, 1074, 1046, 1018, 993, 917, 859, 822, 733, 697, 672 cm^{-1}.

$[\alpha]_D^{24}$ = –14.6 (*c* 1.4, $CHCl_3$,).

HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 97.5:2.5, 1.00 mL/min, 230 nm), *ee* = 90%.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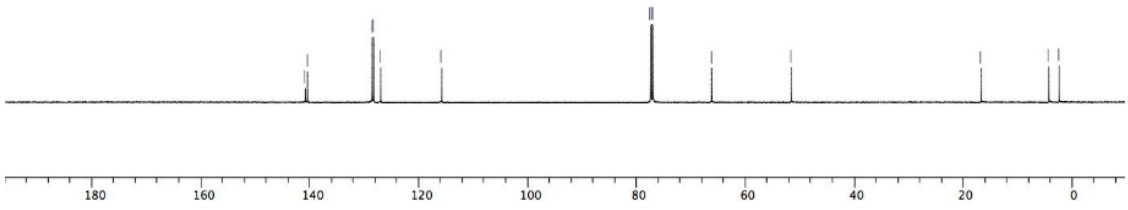
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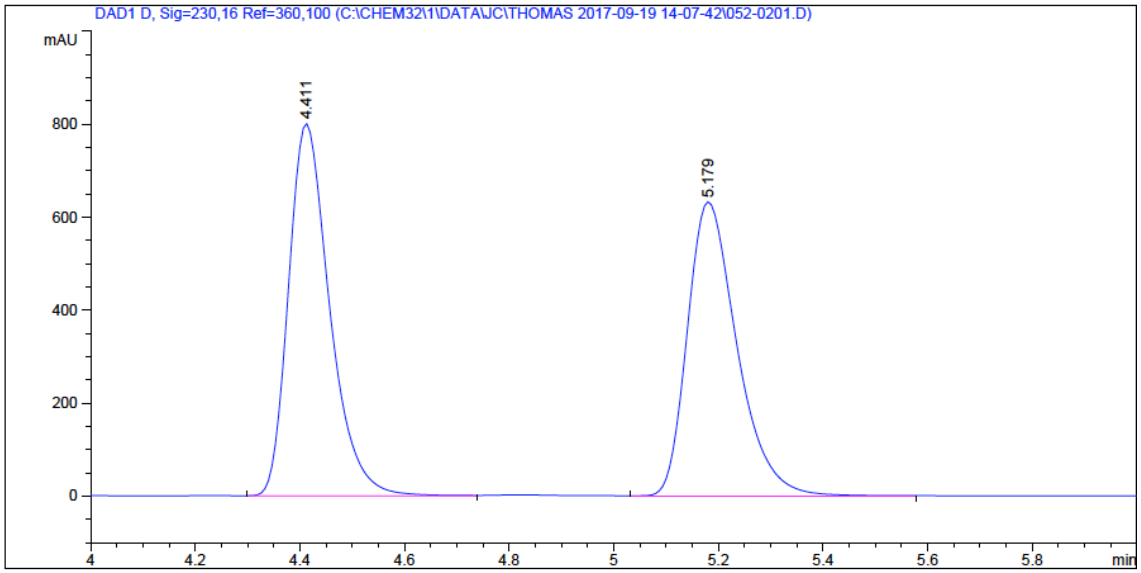
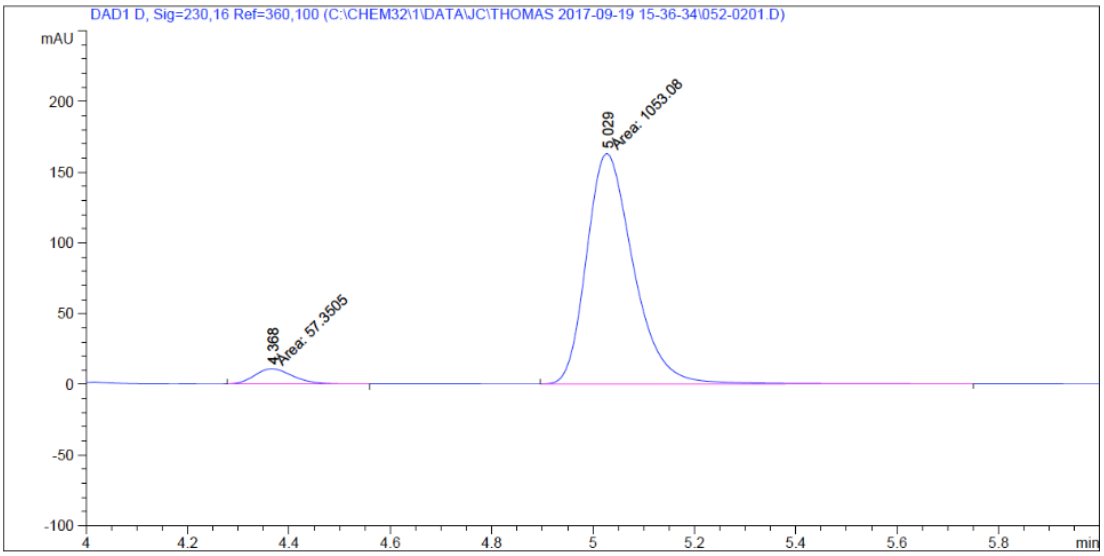
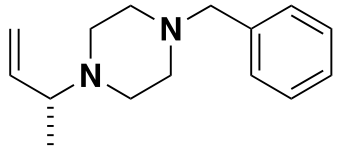


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.411	BV	0.0837	4377.27539	801.40802	51.2957
2	5.179	VB	0.1006	4156.14307	632.82068	48.7043



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.368	MM	0.0879	57.35049	10.86856	5.1647
2	5.029	MM	0.1074	1053.08301	163.44626	94.8353

(*R*)-1-benzyl-4-(but-3-en-2-yl)piperazine (4.4l)



Procedures

To a round bottomed flask equipped with a magnetic stir bar charged with **4.3l** (60 mg, 0.3 mmol, 100 mol%) dissolved in methanol (30 ml, 0.01M) was added glyoxal (4.5 µl, 0.33 mmol, 110 mol%, of a 40 wt% aqueous solution). This mixture was cooled to 0 °C with an icewater bath, before sodium cyanoborohydride (37.0 mg, 0.63 mmol, 210 mol%) was added. The resulting reaction mixture was stirred for 17 hours. During this time the cooling bath was allowed to warm to room temperature. The reaction was quenched with $NaHCO_3$ (20 ml of a saturated aqueous solution) and further diluted with water (20 ml). The obtained aqueous solution was extracted with CH_2Cl_2 (3 x 30 ml). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The resulting residue was subjected to flash column chromatography (SiO_2, hexanes, ethyl acetate 1:1) to furnish the title compound as a pale yellow oil in 69 % yield (47.5 mg, 0.21 mmol).

TLC (SiO_2) R_f = 0.20 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30-7.26 (m, 4H), 7.25-7.20 (m, 1H), 5.76 (ddd, *J* = 17.1, 10.4, 7.9 Hz, 1H), 5.10-5.02 (m, 2H), 3.49 (s, 2H), 2.91-2.83 (m, 1H), 2.49 (bs, 8H), 1.14 (d, *J* = 6.6 Hz, 3H).

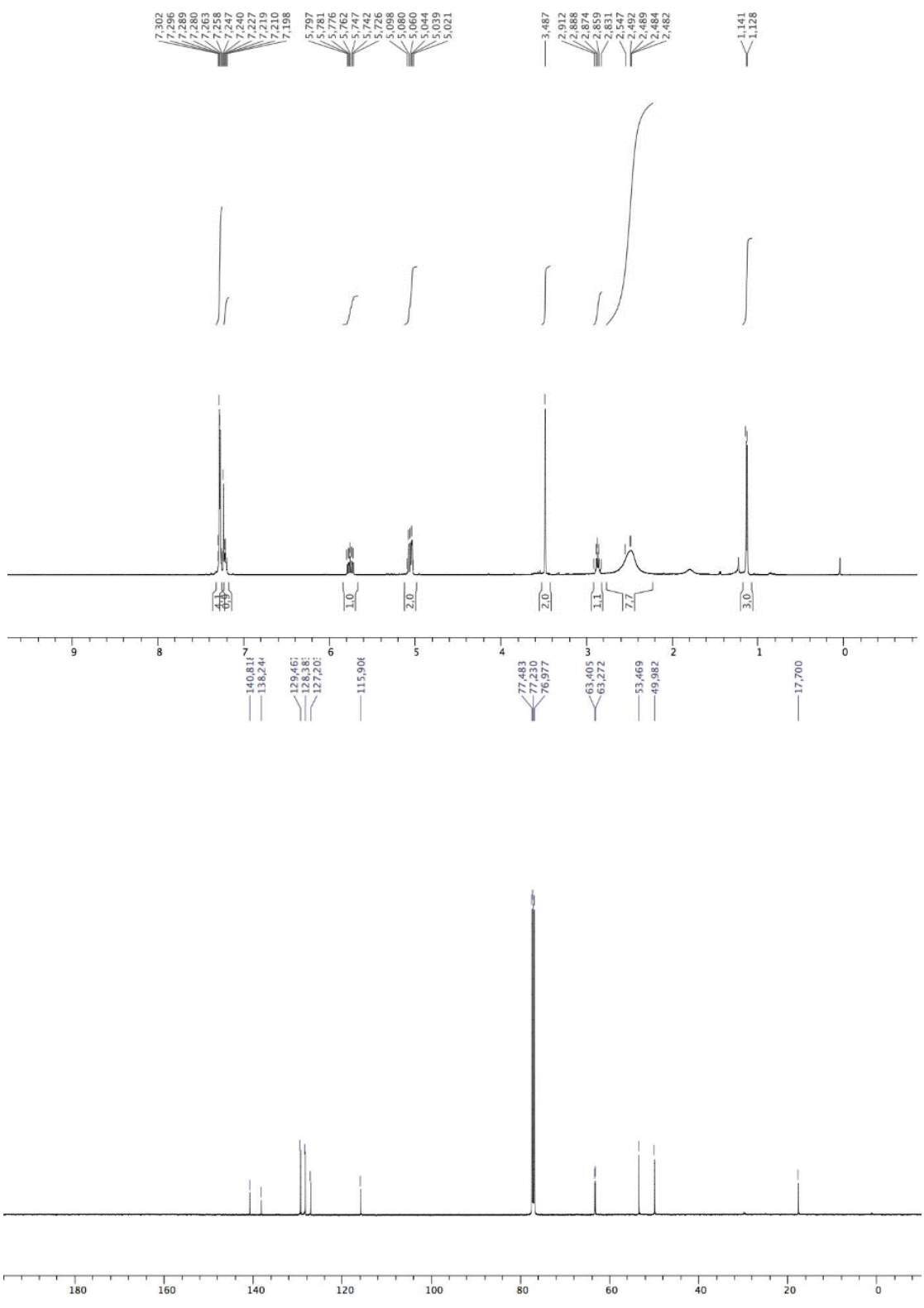
^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.8, 138.2, 129.5 (2C), 128.4 (2C), 127.2, 115.9, 63.4, 63.3, 53.5 (2C), 50.0 (2C), 17.7.

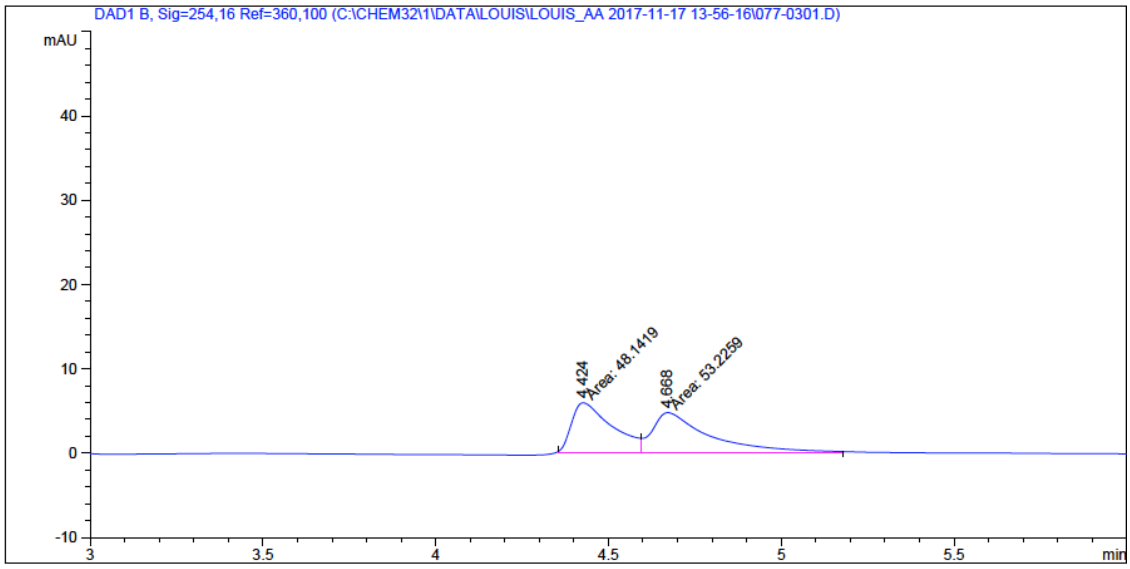
HRMS (ESI): Calculated for $C_{15}H_{22}N_2$ [M+H$^+$] =231.1856, Found 231.1851.

FTIR (neat): 2932, 2807, 2764, 1494, 1453, 1372, 1318, 1265, 1139, 1073, 1048, 1028, 1011, 953, 916, 815, 736, 697 cm^{-1}.

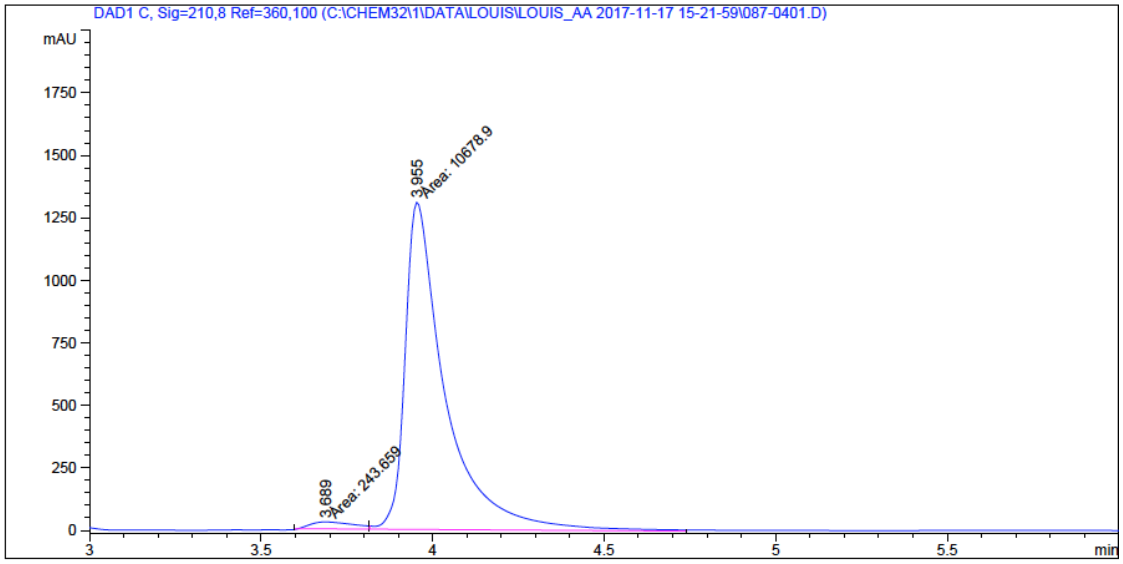
$[\alpha]_D^{24}$= –18.3 (*c* 1.5, $CHCl_3$,).

HPLC (Chiralcel AD-H column (2x), hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 210 nm), *ee* = 96%.



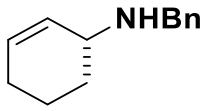


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.424	MF	0.1362	48.14185	5.89295	47.4923
2	4.668	FM	0.1874	53.22592	4.73412	52.5077



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.689	MF	0.1470	243.65883	27.63461	2.2308
2	3.955	FM	0.1357	1.06789e4	1312.00842	97.7692

(*R*)-N-benzylcyclohex-2-en-1-amine (4.4x)



Detailed Procedures

To a round-bottomed flask with a magnetic stir bar was charged with **4.3x** (32.3 mg, 0.15 mmol, 100 mol%). Under argon atmosphere, toluene (6.5 mL, 0.02 M) was added via syringe, followed by the addition of a solution of Grubbs Catalyst II (19.1 mg, 0.023 mmol, 15 mol%) in toluene (1.0 mL). The reaction mixture was heated to 70 °C. After this mixture was cooled to ambient temperature, it was concentrated *in vacuo*. The residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1–2:1) to give 19.1 mg, 0.10 mmol (68%) as a light dark oil.

TLC (SiO_2) R_f = 0.21 (hexanes/ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 – 7.22 (m, 5H), 5.87 – 5.64 (m, 2H), 3.88 (d, *J* = 13.0 Hz, 1H), 3.83 (d, *J* = 13.0 Hz, 1H), 3.22 (dp, *J* = 7.0, 2.3 Hz, 1H), 2.04 – 1.86 (m, 3H), 1.81 – 1.71 (m, 1H), 1.62 – 1.42 (m, 2H), 1.31 (br, 1H).

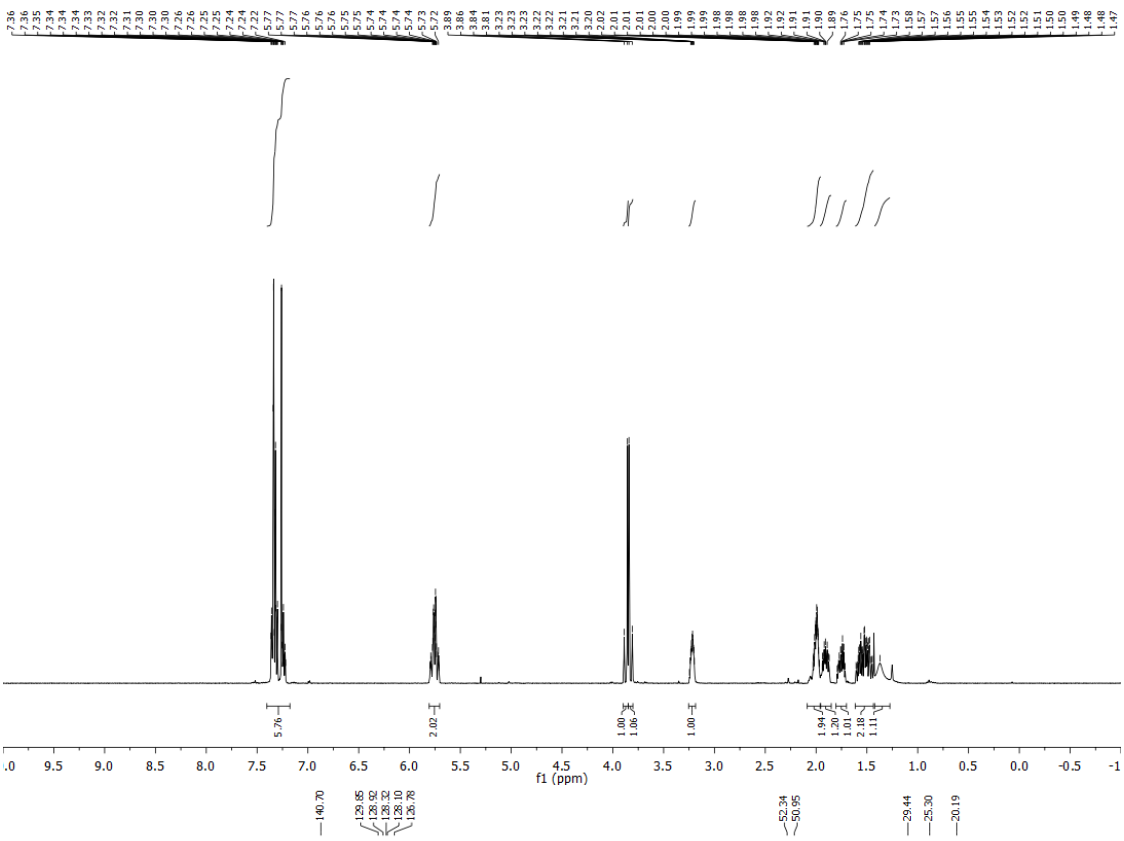
^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.7, 129.9, 128.9, 128.3, 128.1, 126.8, 52.3, 51.0, 29.4, 25.3, 20.2.

HRMS (ESI): Calculated for $C_{13}H_{17}N$ [M+H$^+$] = 188.1434, Found 188.1430.

FTIR (neat): 2929, 1452, 1215, 1103, 748, 689, 667 cm^{-1}.

$[\alpha]_D^{26}$= +67.5 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AS-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm), *ee* = 95%.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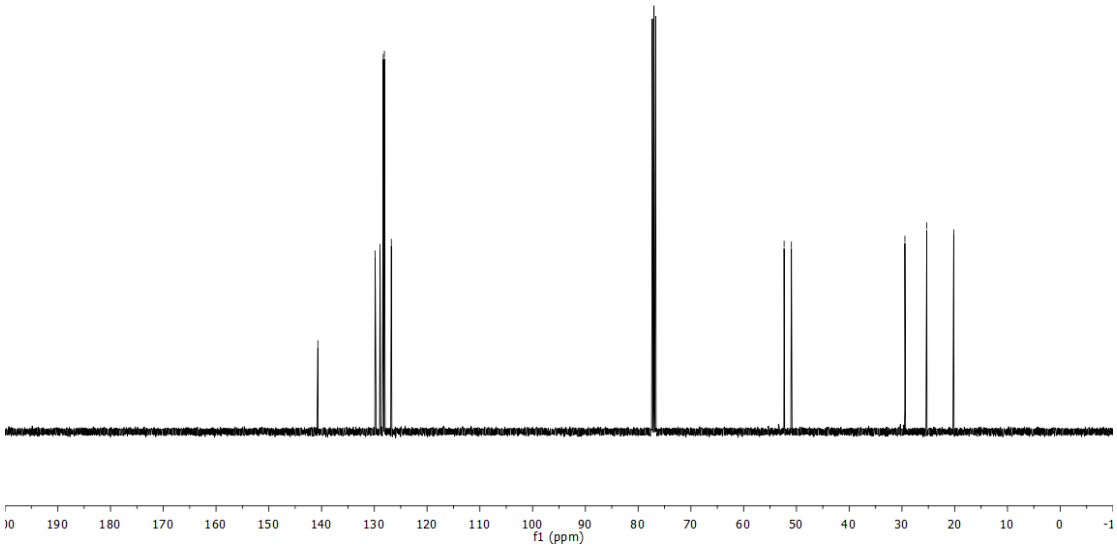
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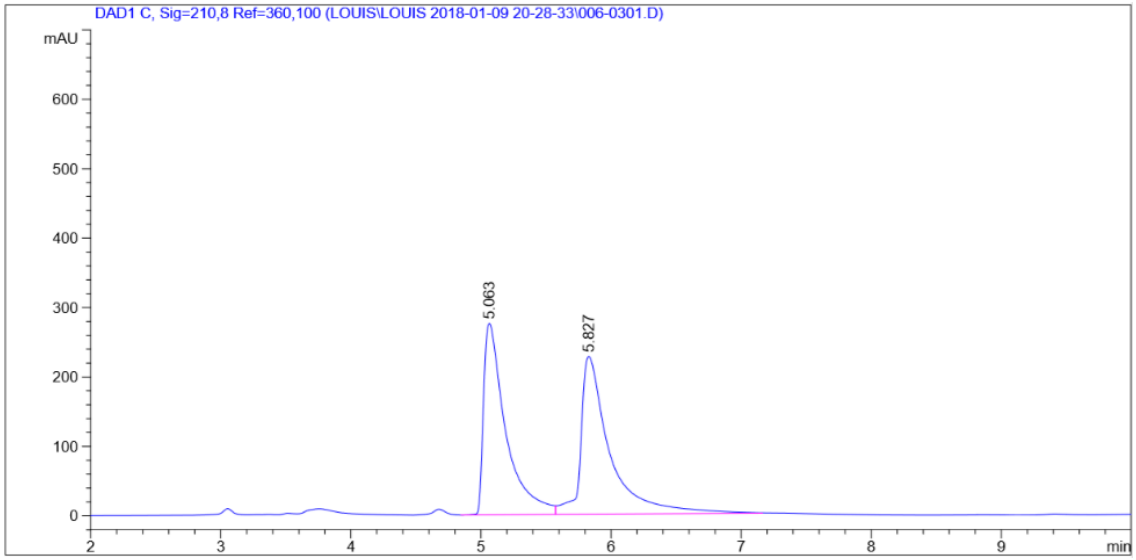

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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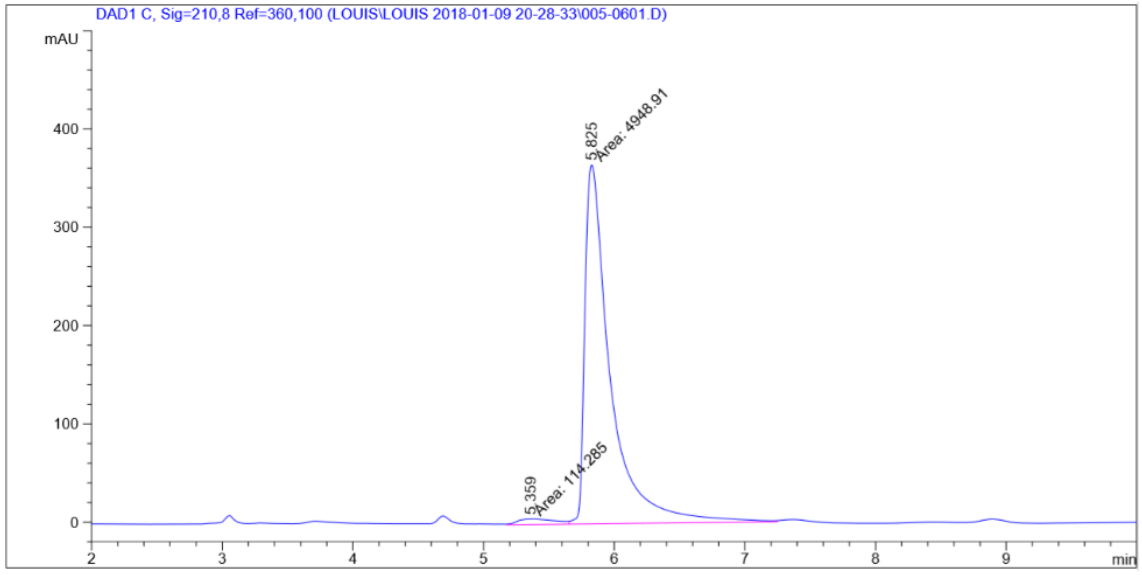
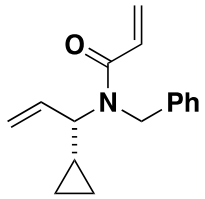
2	5.827	VB	0.2203	3512.28540	227.26389	51.8072



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.359	MF	0.3344	114.28487	5.69653	2.2572
2	5.825	FM	0.2257	4948.90576	365.39276	97.7428

(*S*)-*N*-benzyl-*N*-(1-cyclopropylallyl)acrylamide (4.4j*)



Procedures

To a round bottomed flask equipped with a magnetic stir bar charged with **3j'** (90 mg, 0.48 mmol, 100 mol%) dissolved in absolute dichloromethane (10 ml, 0.05M) under an athmosphere of argon, acryloyl chloride (47.8 mg, 0.53 mmol, 110 mol%), triethylamine (97.3 mg, 0.96 mmol, 200 mol%) and Pyridine (2.0 mg, 0.024 mmol, 5 mol%) were added in this order. The resulting reaction mixture was stirred for 17 hours at room temperature. After this time the solvent was removed *in vacuo* and the resulting residue was directly subjected to flash column chromatography (SiO_2, hexanes, ethyl acetate 10:1 -> 5:1) to furnish the title compound as a colorless viscous oil in 89 % yield (104 mg, 0.48 mmol). According to the recorded NMR data the compound exists in solution as a 4:1 mixture of rotamers.

TLC (SiO_2) R_f = 0.43 (hexanes/ethyl acetate = 5:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37-7.14 (m, 7.4H, major, minor), 6.60-6.49 (m, 0.4H, minor), 6.64-6.31 (m, 2.4H, major,minor), 5.87-5.75 (m, 1.4H, major, minor), 5.70-5.57 (m, 1.4 H, major, minor), 5.35-5.15 (m, 2.8H, major, minor), 4.92 (d, *J*=15.4 Hz, 0.4H, minor), 4.67 (d, *J*=18.4 Hz, 1.0H, major), 4.59-4.49 (m, 2.0H, major), 4.49 (d, *J* =15.4 Hz, 0.4H, minor), 3.66-3.56 (m, 0.3H, minor), 0.98-0.88 (m, 0.4 H, minor), 0.88-0.76 (m,

1.0H, major), 0.66-0.54 (m, 1.4H, major, minor), 0.47-0.38 (m, 1.0H, major), 0.33-0.17 (m, 2.8H, major, minor), 0.15-0.7 (m, 0.4H, minor).

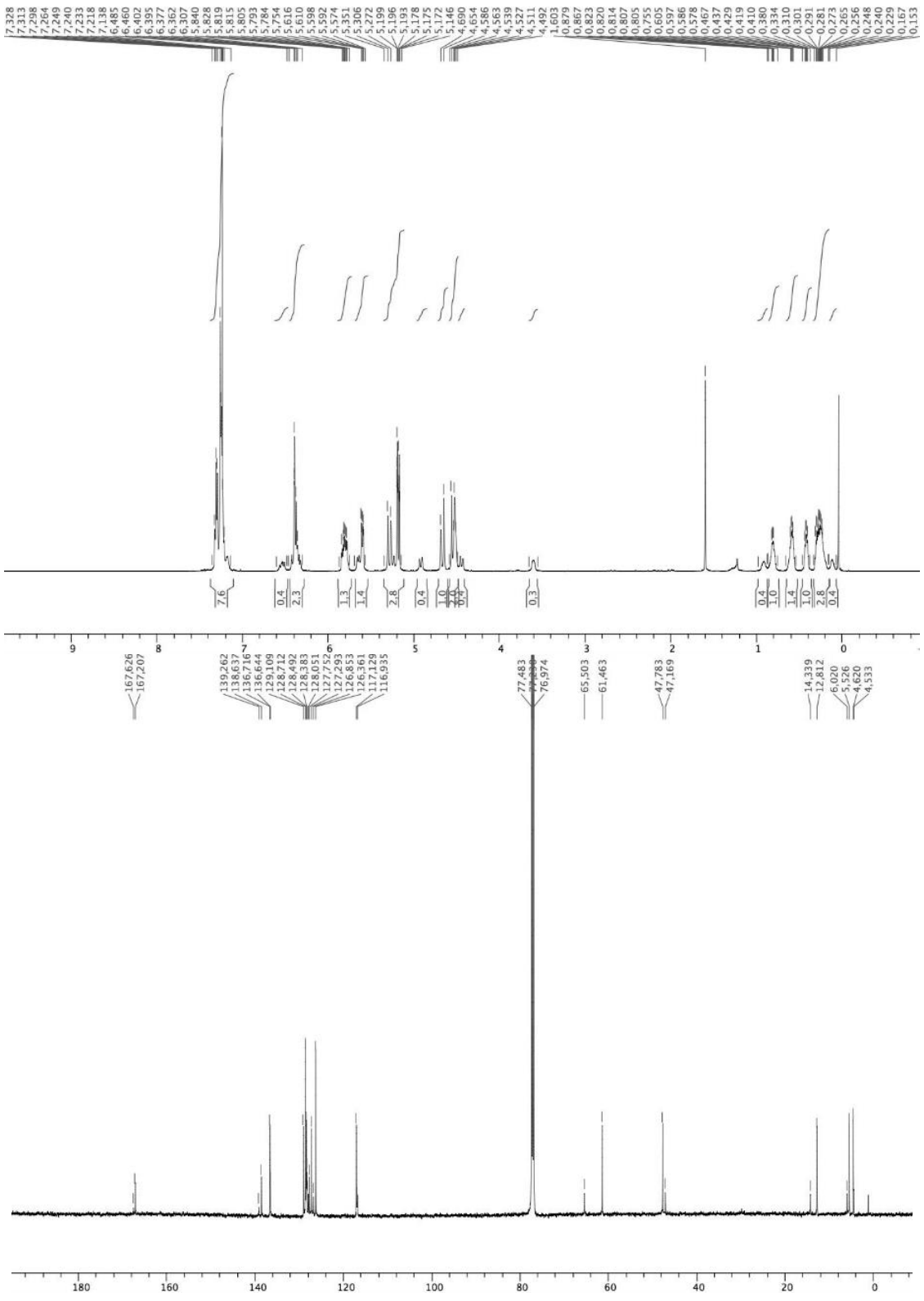
^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.6 (minor), 167.2 (major), 139.2 (minor), 138.6 (major), 136.7 (major), 136.6 (minor), 129.1 (major, minor), 128.7 (major), 128.5 (major), 128.4 (minor), 128.1 (minor), 127.7 (minor), 127.3 (major), 126.9 (minor), 126.4 (major), 117.1 (major), 116.9 (minor), 65.5 (minor), 61.5 (major), 47.8 (major), 47.1 (minor), 14.3 (minor), 12.8 (major), 6.0 (minor), 5.5 (major), 4.6 (major), 4.5 (minor).

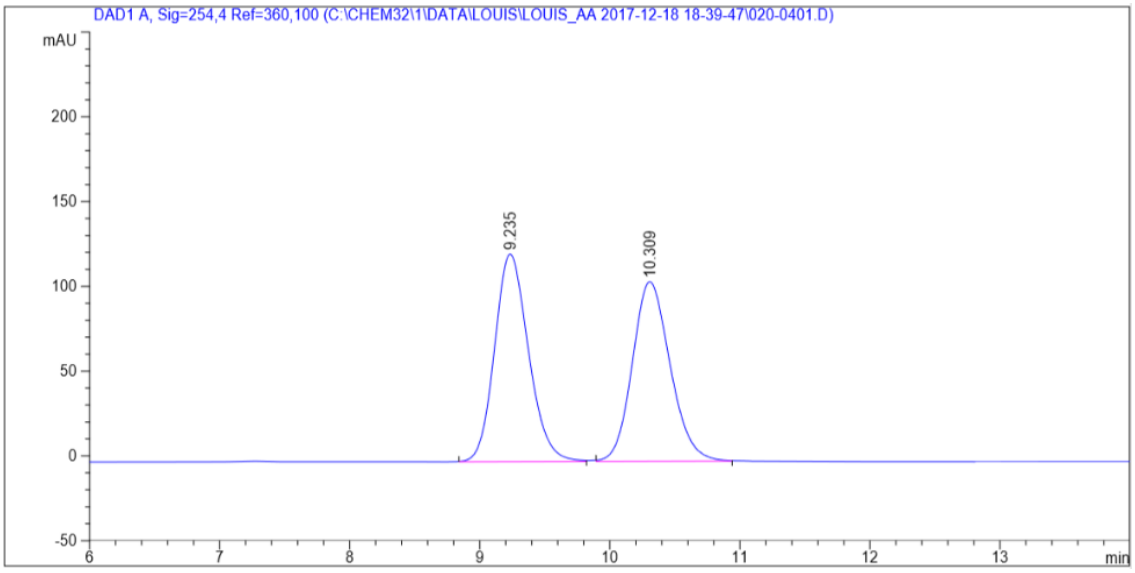
HRMS (ESI): Calculated for $C_{16}H_{19}N$ [M+Na^+] = 264.1359, Found 264.1355.

FTIR (neat): 3083, 3004, 1647, 1609, 1495, 1452, 1419, 1358, 1322, 1289, 1234, 1199, 1161, 1078, 1058, 1021, 978, 956, 923, 832, 794, 732, 697 cm^{-1}.

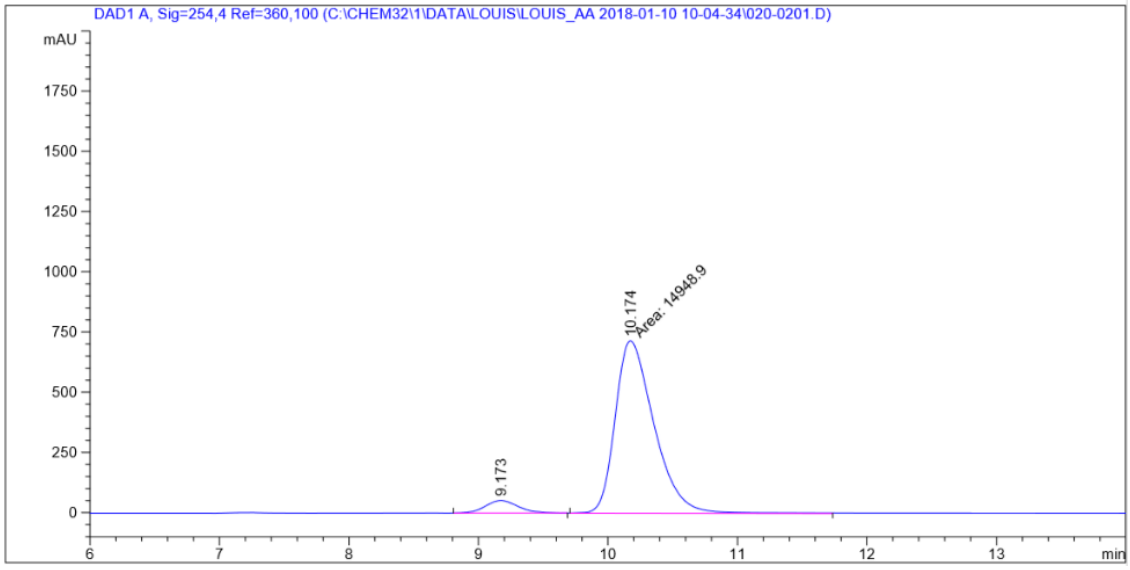
$[\alpha]_D^{24}$ = +3.9 (*c* 1.4, $CHCl_3$,).

HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm), *ee* = 89%.



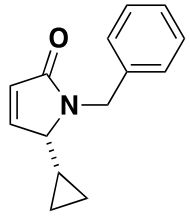


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.235	BB	0.2792	2215.52246	122.37241	50.9210
2	10.309	BB	0.3113	2135.37793	105.87894	49.0790



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.173	BB	0.2687	905.62146	52.13631	5.7121
2	10.174	MM	0.3479	1.49489e4	716.24500	94.2879

(*R*)-1-benzyl-5-cyclopropyl-1,5-dihydro-2*H*-pyrrol-2-one (4.4j')



Procedures

To a round bottomed flask equipped with a magnetic stir bar and charged with Grubbs II (4.1 mg, 0.005 mmol, 5 mol%) 1.0 ml of a 0.1 M solution of **4j*** in toluene is added under an atmosphere of argon. (Caution: The substrate solution was degassed by bubbling argon through the solution for 3 minutes before usage.) The resulting reaction mixture is heated to 60 °C for 17 h. After this time the reaction mixture is directly subjected to flash column chromatography (SiO_2, hexanes, ethyl acetate 5:1–2:1) to furnish the compound as a pale violet oil in 65 % yield (15.6 mg, 0.065 mmol).

TLC (SiO_2) R_f = 0.15 (hexanes/ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34-7.16 (m, 5H), 6.99 (dd, *J* = 1.8, 5.9 Hz, 1H), 6.19 (dd, *J* = 1.8, 5.9 Hz, 1H), 5.15 (d, *J* = 15.4 Hz, 1H), 4.31 (d, *J* = 15.4 Hz, 1H), 3.14 (td, *J* = 1.8, 9.1 Hz), 0.71-0.44 (m, 3H), 0.31-0.23 (m, 1H),0.17-0.10 (m, 1H).

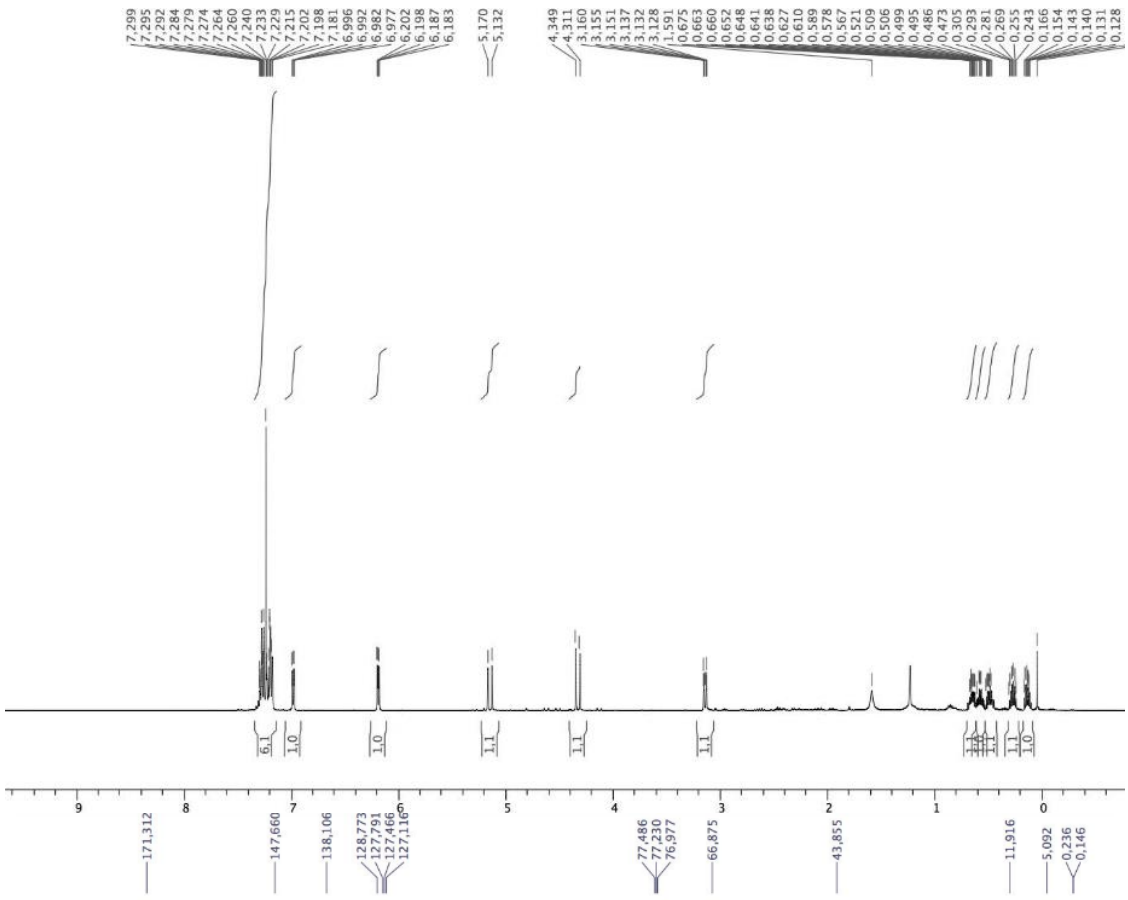
^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.3, 147.7, 138.1, 128.8, 127.8, 127.5, 127.1, 66.9, 43.9, 11.9, 5.1, 0.2, 0.1.

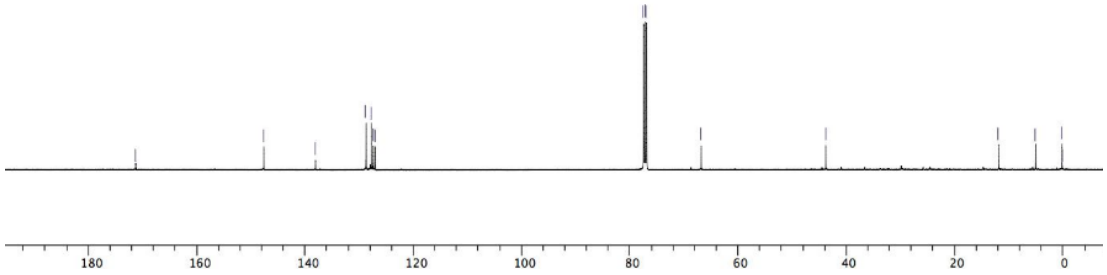
HRMS (ESI): Calculated for $C_{14}H_{15}N$ $[M+H^+]$ =214.1226, Found 214.1222.

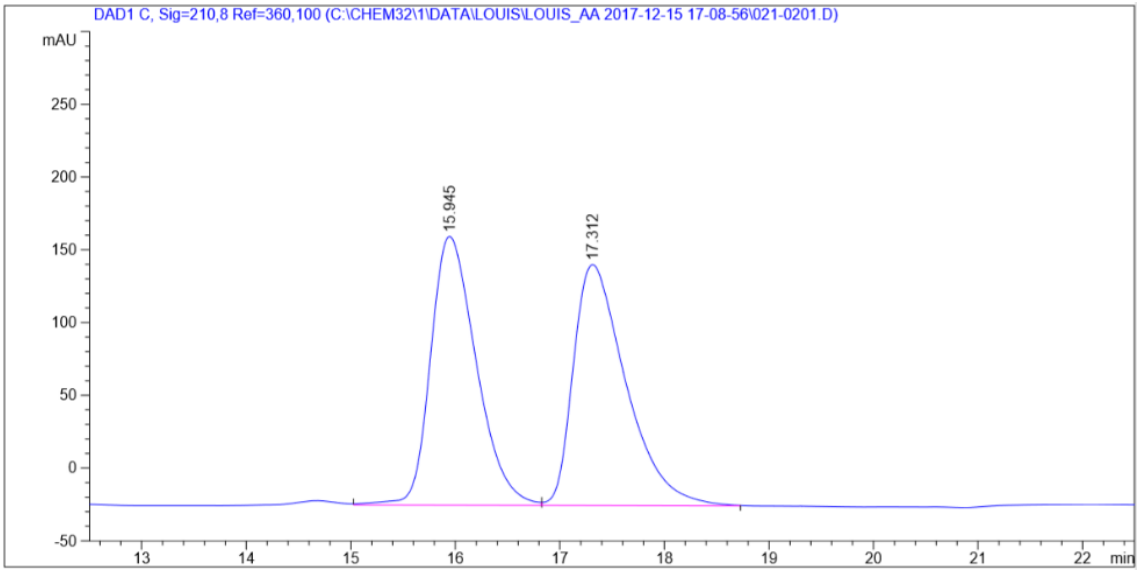
FTIR (neat): 3004, 2922, 1683, 1495, 1433, 1403, 1358, 1338, 1270, 1223, 1078, 1026, 969, 867, 852, 807, 703 cm^{-1}.

$[\alpha]_D^{24}$ = +4.5 (*c* 1.7, $CHCl_3$).

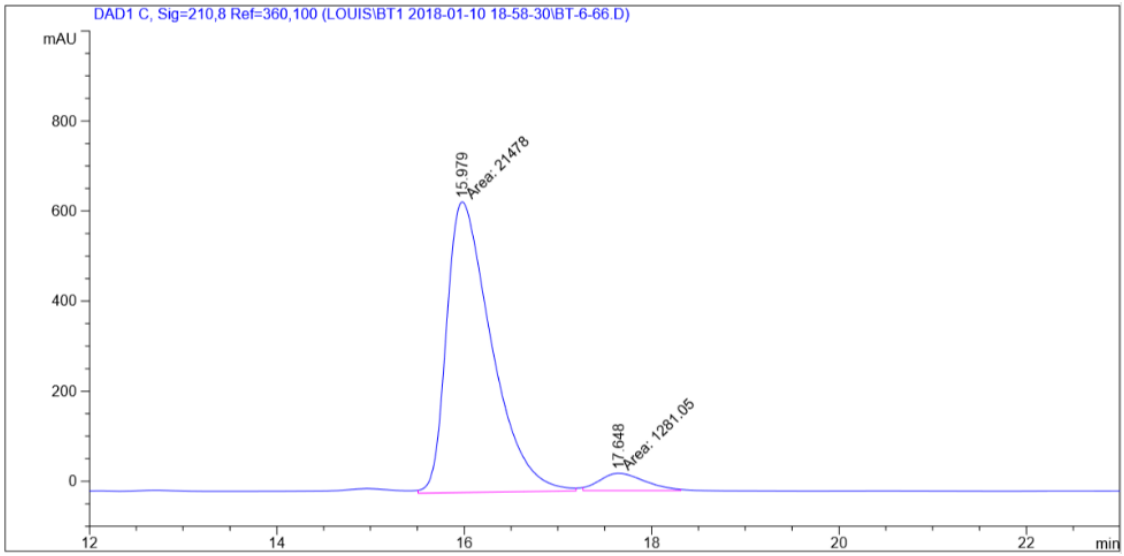
HPLC (Chiralcel OD-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 210 nm), *ee* = 89%.





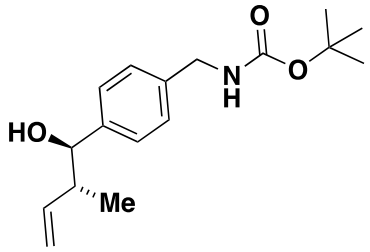


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.945	VV	0.4706	5614.51221	184.72955	49.2245
2	17.312	VB	0.5262	5791.41504	165.52718	50.7755



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.979	MM	0.5546	2.14780e4	645.41998	94.3713
2	17.648	MM	0.5569	1281.04956	38.34068	5.6287

***tert*-butyl (4-((1*R*,2*R*)-1-hydroxy-2-methylbut-3-en-1-yl)benzyl)carbamate (4.6)**



Procedures

An oven-dried sealed tube under an atmosphere of N_2 was charged with *tert*-butyl (4-(hydroxymethyl)benzyl)carbamate **(5)** (150 mg, 0.63 mmol, 100 mol%), (*R*)-IrLn (32.5 mg, 0.03 mmol, 5 mol%), K_3PO_4 (67 mg, 0.32 mmol 50 mol%), THF (0.31 ml, 2.0 M) and H_2O (57 µl, 3.2 mmol, 500 mol%). But-3-en-2-yl acetate (144mg, 1.26 mmol, 200 mol%) was added and the reaction mixture was allowed to stir at ambient temperature for 0.5 h. The reaction vessel was placed in an oil bath preheated to 60 °C. The reaction was stirred at this temperature for 48 h. After this time the reaction muxture was concentrated *in vacuo*. Purification of the remaining residue by column chromatography (SiO_2; hexanes: ethyl acetate 4:1) provided **6** as a colorless viscous oil in 83 % yield (152 mg, 0.52 mmol, 8:1 dr).

TLC (SiO_2) R_f = 0.30 (hexanes:ethyl acetate 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32-7.21 (m, 4H), 5.77 (ddd, J= 17.2, 10.3, 8.3 Hz, 1H), 5.24-5.14 (m, 2H), 4.36-4.25 (m, 3H), 2.51-2.39 (m, 1H), 1.44 (s, 9H), 0.84 (d, J = 6.9 Hz, 3H).

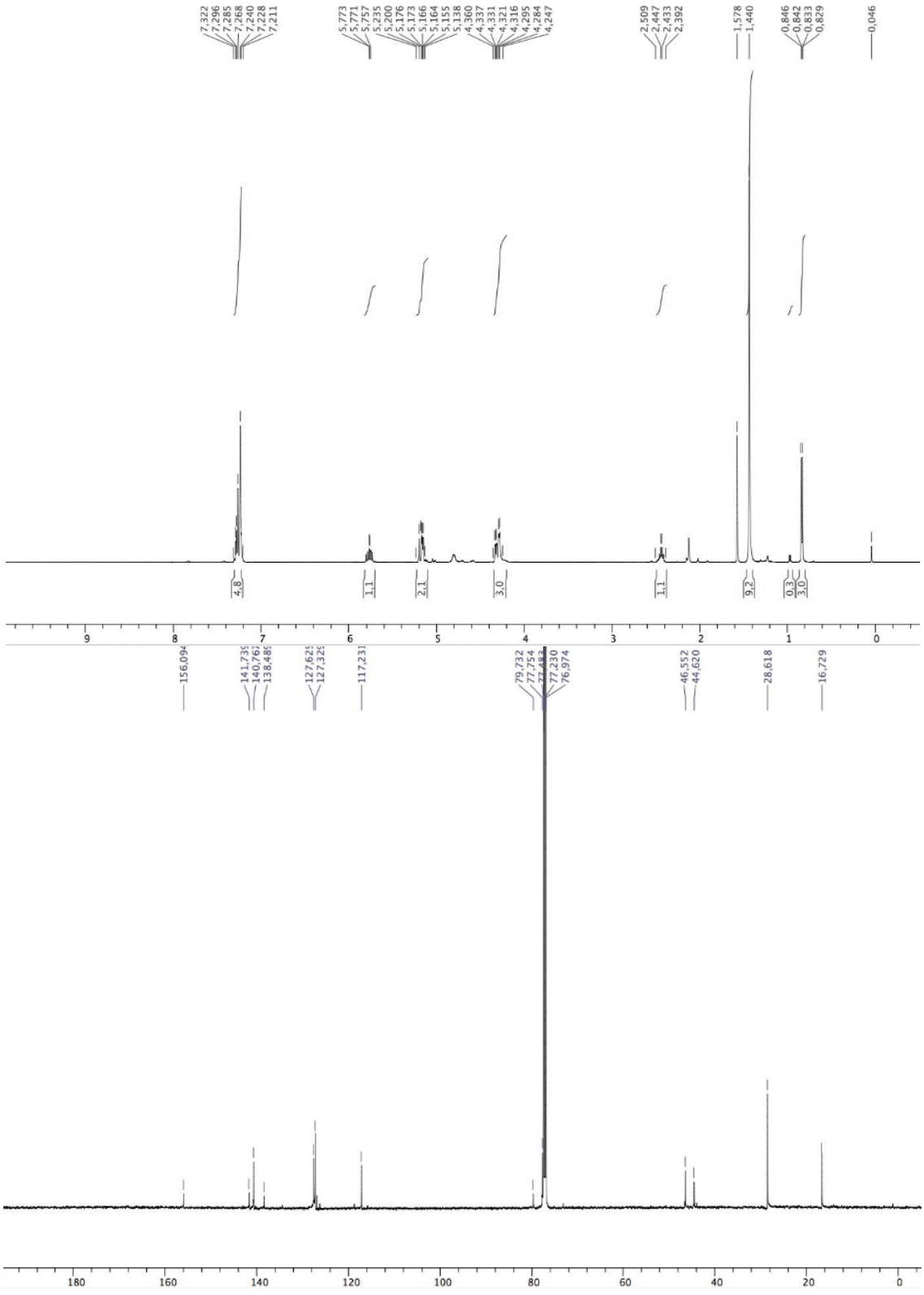
^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.1, 141.7, 140.7, 138.5, 127.6 (2C), 127.3 (2C), 117.2, 79.7, 77.5, 46.6, 44.6, 28.6 (3C), 16.73.

HRMS (ESI): Calculated for $C_{17}H_{25}NO_3$ [M+Na^+] = 314.1727, Found 314.1720.

FTIR (neat) 3359, 2976, 2929, 1687, 1513, 1455, 1421, 1391, 1365, 1271, 1249, 1211, 1164, 1046, 1017, 915, 864, 82:5, 783, 676 cm^{-1}.

$[\alpha]_D^{24}$ = –34.3 (*c* 1.1, $CHCl_3$,).

HPLC (Chiralcel AS-H column (2x), hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 210 nm), *ee* = 90%.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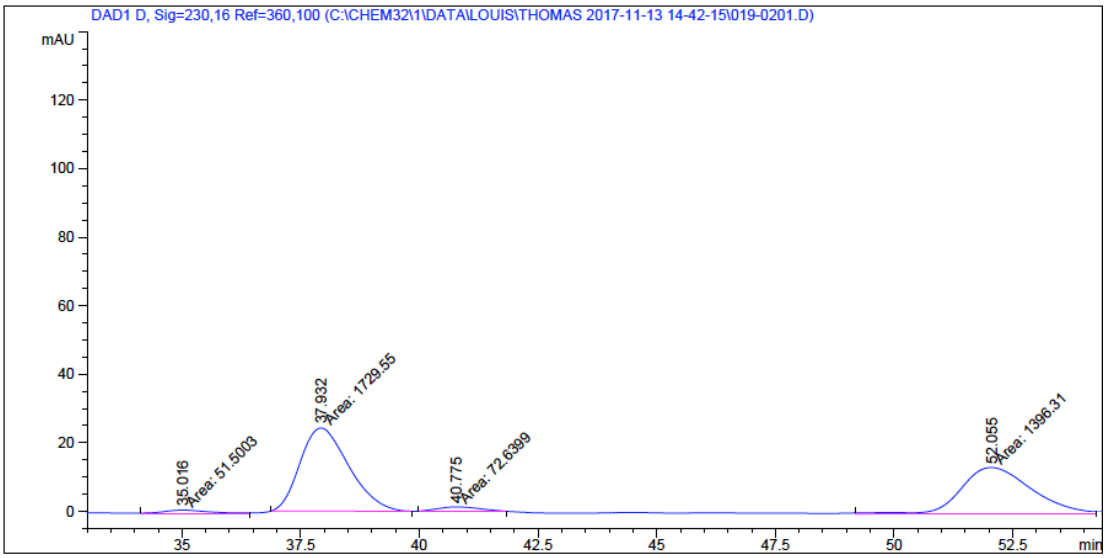
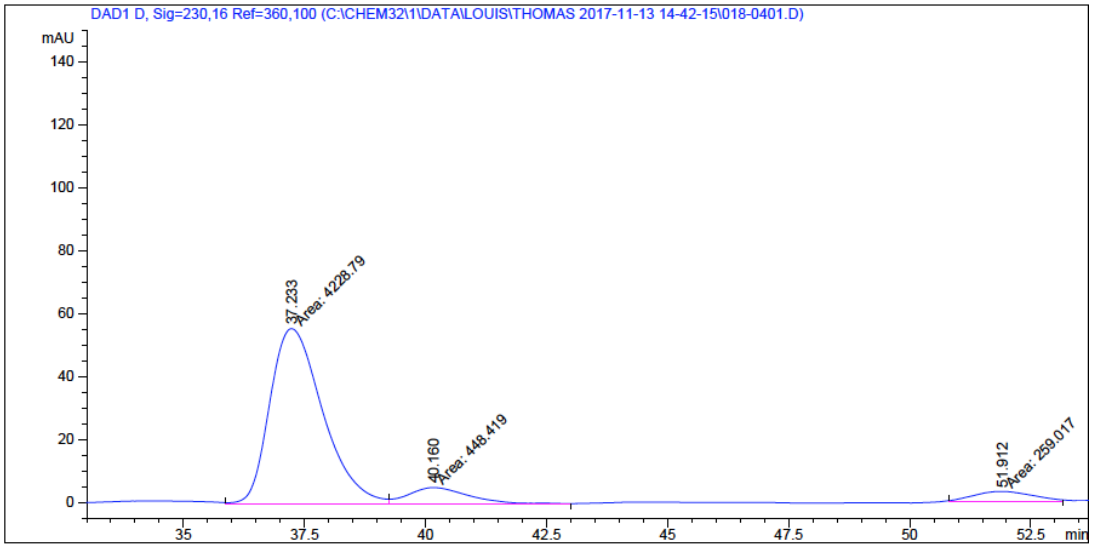
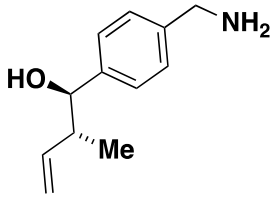


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.016	MM	0.9544	51.50033	8.99366e-1	1.5846
2	37.932	MM	1.1876	1729.55017	24.27228	53.2170
3	40.775	MM	0.9908	72.63990	1.22196	2.2351
4	52.055	MM	1.7222	1396.30652	13.51264	42.9633



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.233	MF	1.2672	4228.79395	55.61788	85.6685
2	40.160	FM	1.4403	448.41876	5.18905	9.0842
3	51.912	MM	1.3927	259.01746	3.09968	5.2473

(1*R*,2*R*)-1-(4-(aminomethyl)phenyl)-2-methylbut-3-en-1-ol (4.6')



Procedures

To a round bottomed flask equipped with a magnetic stir bar charged with **6** (140 mg, 0.48 mmol, 100 mol%) was added DCM (0.4 ml) and afterwards TFA (80 μl). The resulting reaction mixture (0.1 M) was stirred for two hours at room temperature. After this time water (5 ml) and NaOH (20 ml of an 0.1 M aqueous solution) were added. The phases were separated and the aqueous phase was extracted with DCM (3x 20 ml). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The resulting residue was subjected to flash column chromatography (SiO_2, hexanes, ethyl acetate 1:1) to furnish the title compound as a colorless oil in 84 % yield (77.0 mg, 0.40 mmol, 8:1 dr).

TLC (SiO_2) R_f = 0.12 (hexanes: ethyl acetate 1:1).

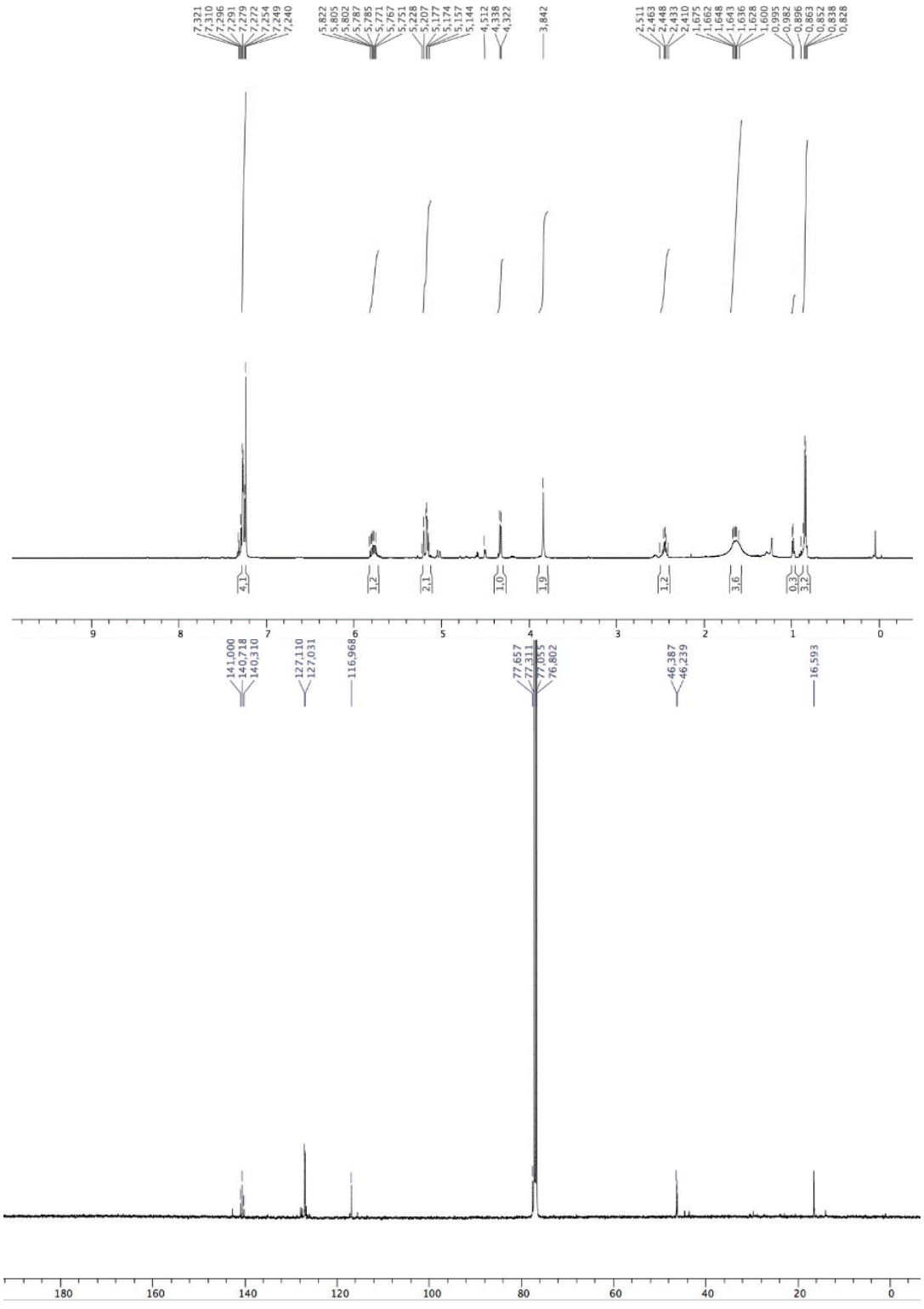
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31-7.25 (m, 4H), 5.77 (ddd, J= 17.1, 10.4, 8.3 Hz, 1H), 5.23-5.14 (m, 2H), 4.33 (d, J= 7.8 Hz, 1H), 3.84 (s, 2H), 2.51-2.41 (m, 1H),1.64 (bs, 3H), 0.85 (d, J = 6.8 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.00, 140.7, 140.3, 127.1 (2C), 127.0 (2C), 117.0, 77.7, 46.4, 46.2, 16.6.

HRMS (ESI): Calculated for $C_{12}H_{17}NO$ [M+H$^+$] =192.1383, Found 192.1385.

FTIR (neat): 3293, 3076, 2971, 2928, 2868, 1737, 1638, 1511, 1455, 1438, 1415, 1371, 1262, 1228, 1175, 1097, 1034, 1017, 995, 914, 821, 735, 300 cm^{-1}.

$[\alpha]_D^{24}$ = –19.8 (*c* 1.2, $CHCl_3$,).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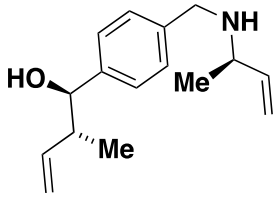
(1*R*,2*R*)-1-(4-((((*R*)-but-3-en-2-yl)amino)methyl)phenyl)-2-methylbut-3-en-1-ol (4.7)



Procedures

Synthesis starting from compound 4.6'

Using General Procedure 1: the title compound was afforded after purification by flash column chromatography (ethyl acetate) to give 57.3 mg, 0.23 mmol (78%) as a pale orange oil. According to recorded NMR data the compound consisted of a 8:1 mixture of diastereomers.

Synthesis starting from (4-(aminomethyl)phenyl)methanol (4.5')

[(R)-(+)-5,5'-bis(diphenylphosphino)-4,4'-bi-1,3-benzodioxole][4-cyano-3-nitrobenzenecarboxylato] [1,2,3-eta-2-propenyl Ir(III)] (20.7 mg, 0.02 mmol, 10 mol%), cesium carbonate (197 mg, 0.6 mmol, 300 mol%), and **5'** (27.4 mg, 0.2 mmol, 100 mol%) were added to an oven-dried resealable pressure tube equipped with a magnetic stir bar. The tube was purged with argon for 5 minutes. Afterwards THF 0.2 ml, (1.0 M) was added followed by the addition of but-3-en-2-yl acetate (91.3 mg, 0.8 mmol, 400 mol%). The tube was sealed with a PTFE lined cap and heated at 80°C for 48 h. After reaching ambient temperature, the crude reaction mixture was directly subjected to flash column chromatography (SiO_2, ethyl acetate) to give 18 mg, 0.073 mmol (36 %) of the

title compound as a pale orange oil. According to recorded NMR data the compound consisted of a 2:1 mixture of diastereomers.

TLC (SiO_2) R_f = 0.18 (ethyl acetate).

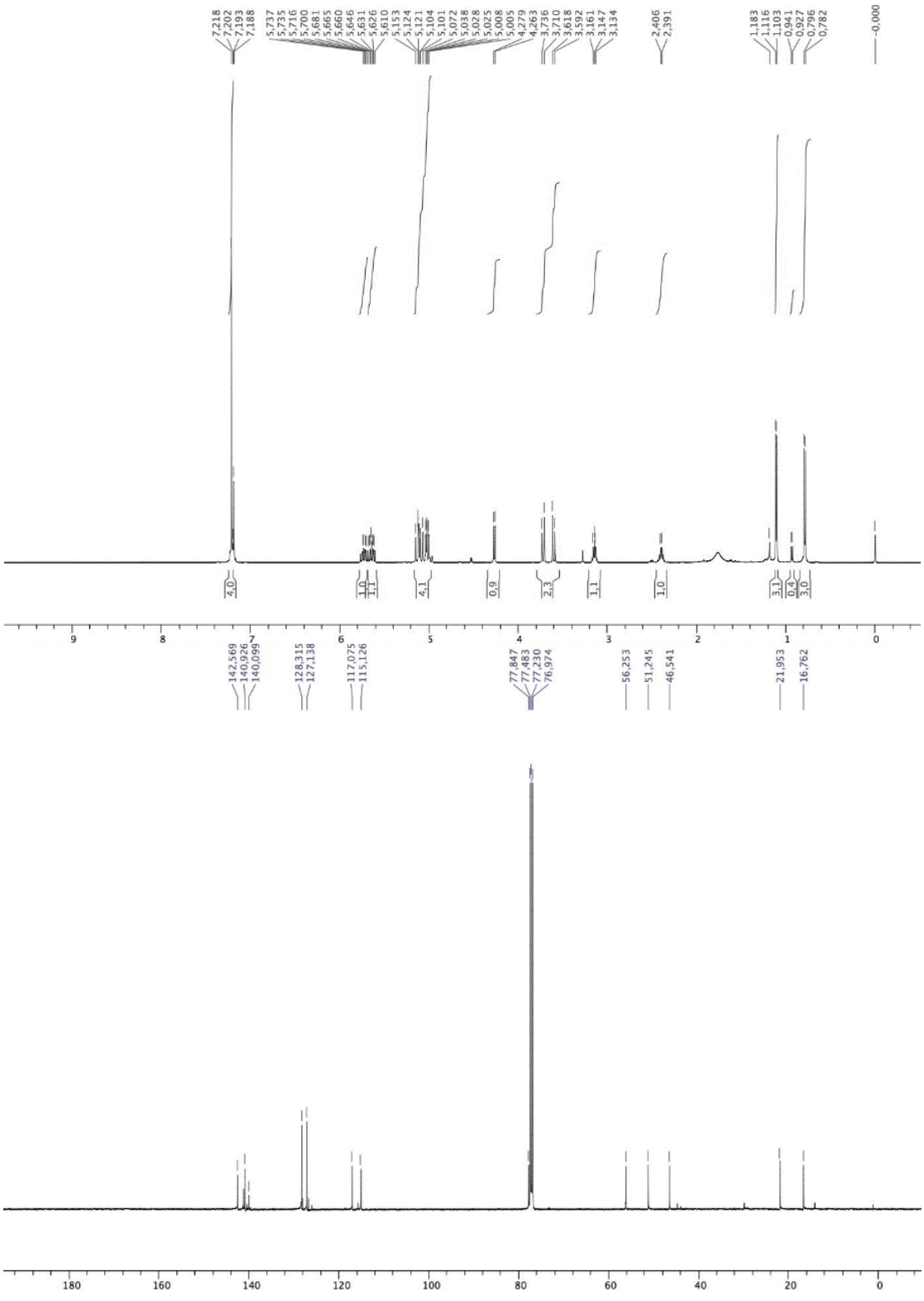
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.25-7.19 (m, 4H), 5.79-5.59 (m, 2H), 5.17-4.99 (m, 4H), 4.27 (d, *J* = 7.9 Hz, 1H), 3.72 (d, *J* = 12.8 Hz, 1H), 3.60 (d, *J* = 12.8 Hz, 1H), 3.18-3.11 (m, 1H), 2.45-2.35 (m, 1H), 1.77 (bs, 2H), 1.11 (d, *J* = 6.5 Hz, 3H), 0.79 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.6, 141.3, 140.9, 140.1, 128.3, 127.1, 117.1, 115.1, 77.8, 56.3, 51.2, 46.5, 22.0, 16.8.

HRMS (ESI): Calculated for $C_{16}H_{23}NO$ $[M+H^+]$ = 246.1852, Found 246.1842.

FTIR (neat): 3339, 3076, 3025, 3002, 2815, 1640, 1603, 1494, 1453, 1428, 1413, 1358, 1302, 1172, 1101, 1074, 1046, 1018, 993, 917, 859, 822, 733, 697, 672 cm^{-1}.

$[\alpha]_D^{24}$ = –38.9 (*c* 1.1, $CHCl_3$,).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Single Crystal Diffraction Data for 4.3j'

Empirical formula	C13 H18 Cl N	
Formula weight	223.73	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	P 21	
Unit cell dimensions	a = 10.993(2) Å	α= 90°.
	b = 9.035(3) Å	β = 109.866(7)°.
	c = 13.737(4) Å	γ = 90°.
Volume	1283.2(6) $Å^3$	
Z	4	
Density (calculated)	1.158 Mg/m^3	
Absorption coefficient	0.268 mm^{-1}	
F(000)	480	
Crystal size	0.510 x 0.130 x 0.030 mm^3	
Theta range for data collection	3.056 to 27.480°.	
Index ranges	-14<=h<=14, -11<=k<=11, -17<=l<=17	
Reflections collected	21792	
Independent reflections	5883 [R(int) = 0.0393]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	

Max. and min. transmission	1.00 and 0.783
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5883 / 1 / 288
Goodness-of-fit on F^2	1.038
Final R indices [I>2sigma(I)]	R1 = 0.0451, wR2 = 0.1108
R indices (all data)	R1 = 0.0533, wR2 = 0.1160
Absolute structure parameter	0.00(10)
Extinction coefficient	n/a
Largest diff. peak and hole	0.529 and -0.213 e.$Å^{-3}$

Figure S1. View of the cation 1 of **4.3j'** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.

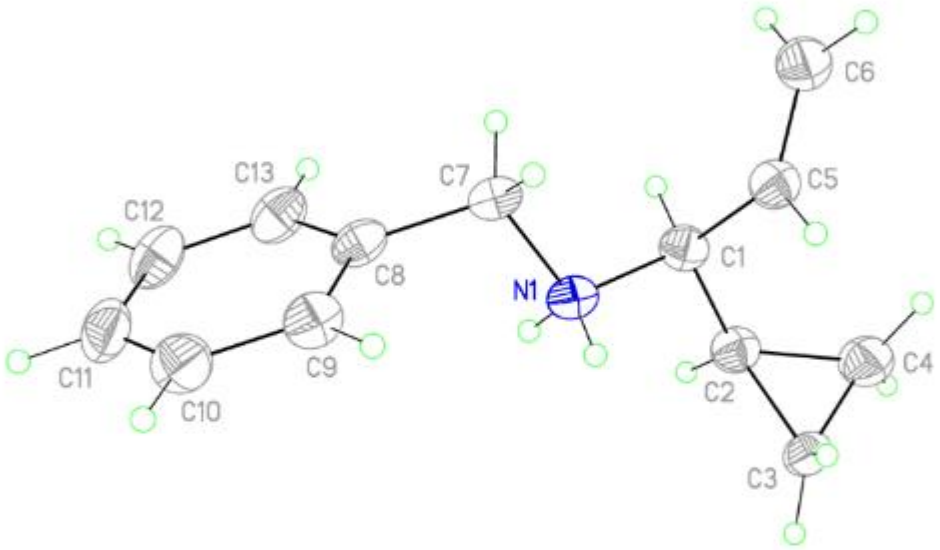
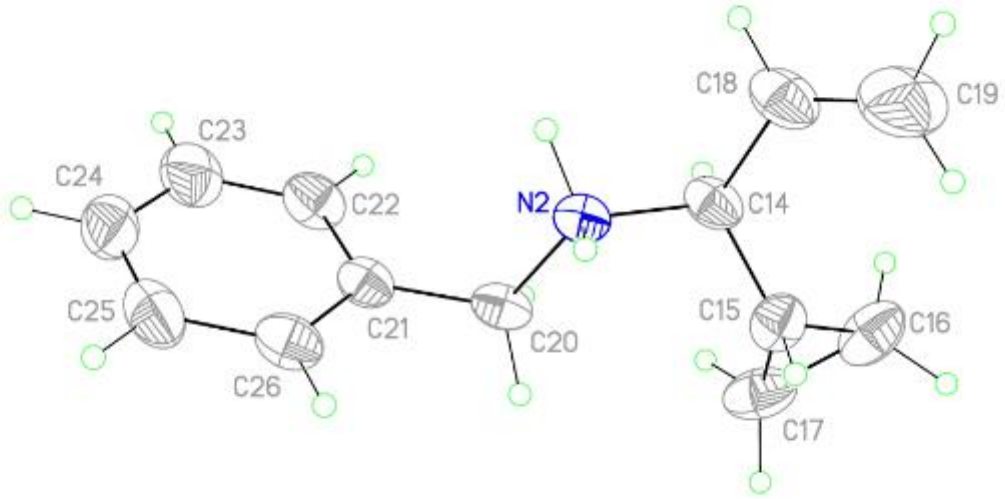


Figure S2. View of the cation 2 of **4.3j'** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



Chapter 5: Regio- and Enantioselective Iridium-Catalyzed Amination of Branched Alkyl-Substituted Allylic Acetates with Primary and Secondary Aromatic and Heteroaromatic Amines*

5.1 Introduction

Cyclometallated π-allyliridium *C,O*-benzoate complexes have been shown to catalyze diverse alcohol-mediated carbonyl allylations using allyl carboxylates as pronucleophiles.[1] In these umpoled allylations,[2] the *C,O*-benzoate moiety assists in maintaining neutrality and, hence, nucleophilicity of the π-allyliridium intermediate. Neutral iridium complexes that are not cyclometallated also display nucleophilic properties.[3] In contrast, as illustrated by enantioselective Tsuji-Trost-type allylic aminations developed by Takeuchi,[4,5] Helmchen,[6,7] Hartwig,[8,9] Carreira[10] and You,[11,12] cationic π-allyliridium species invariably serve as electrophiles. In this latter context, two distinct classes of iridium catalysts have emerged. Type I catalysts are used under basic conditions in combination with linear allyl proelectrophiles (as branched allyl proelectrophiles react stereospecifically).[13] Type II catalysts are used under acidic conditions in combination with branched allyl proelectrophiles, which react in a non-stereospecific fashion, perhaps due to displacement of the π-bond of (σ+π)-allyl (enyl) iridium intermediates by the tethered olefin of the phosphoramidite ligand (Figure 5.1).[14]

The present authors recently found that neutral π-allyliridium *C,O*-benzoate complexes, which typically act as nucleophiles, can also display electrophilic behavior, representing the first examples of amphiphilic reactivity in the context of transition metal catalysis.

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*This chapter is based on the published work:
Kim, S. W.; Schwartz, L. A.; Zbieg, J. R.; Stivala, C. E.; Krische, M. J. *J. Am. Chem. Soc.* **2019**, *141*, 671.

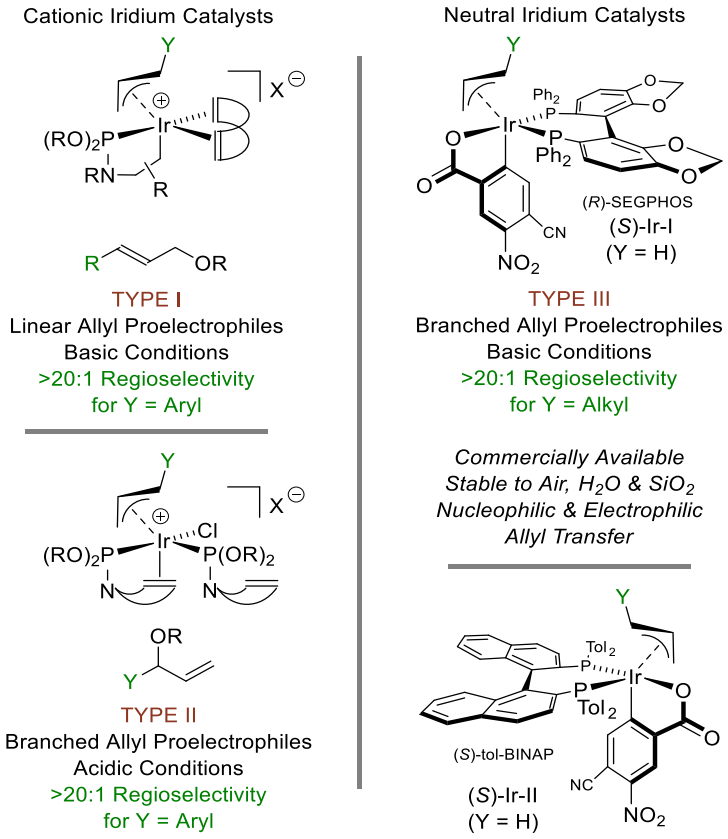


Figure 5.1 Cationic vs neutral chiral iridium complexes for regio- and enantioselective allylic amination.

In the initial communication of these findings, enantioselective allylic aminations of branched allylic acetates bearing linear alkyl groups with primary aliphatic amines were disclosed.[15] These aminations proceed with complete branched regioselectivity, overcoming a significant limitation associated with Type I and II catalysts, which display incomplete regioselectivity for π-allyl precursors bearing linear alkyl groups.[16,17] With regard to the amine nucleophile, the Type III SEGPHOS-modified π-allyliridium complexes used in our initial study enforced high enantioselectivities in reactions of primary aliphatic amines (Figure 5.1). Here, we show that the corresponding tol-BINAP-

modified iridium catalyst avail a significant expansion in scope, enabling highly enantioselective aminations of branched alkyl substituted allylic acetates with electronically diverse primary and secondary aryl amines, including site-selective reactions of bis(amine) nucleophiles. Additionally, we report deuterium labelling studies that corroborate C-N bond formation through an outer-sphere mechanism.

5.2 Reaction Development and Scope

To develop highly regio- and enantioselective allylic aminations mediated by aryl amines, a series of π-allyliridium *C,O*-benzoate complexes were evaluated in reactions of α-methyl allyl acetate (100 mol%) and aniline (200 mol%) under conditions previously optimized for primary aliphatic amines.[15] The iridium catalyst modified by tol-BINAP, *(S)*-Ir-II, delivered the product of allylic amination **5.4a** with significantly higher levels of enantioselectivity than the corresponding SEGPHOS-modified catalyst, *(S)*-Ir-I, but a lower isolated yield of **5.4a** was observed (eq. 5.1). Changing the solvent from THF to DME improved the isolated yield of **5.4a**, and by decreasing the reaction temperature from 80 °C to 70 °C **5.4a** could be formed in 82% yield and 89% enantiomeric excess (eq. 5.1).

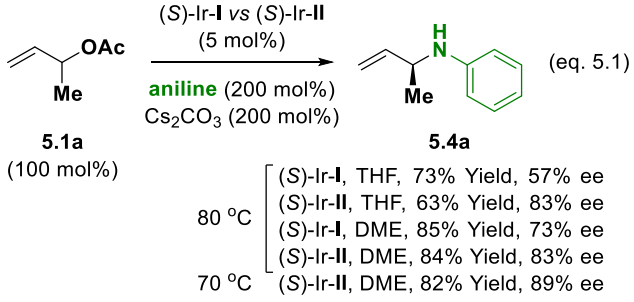
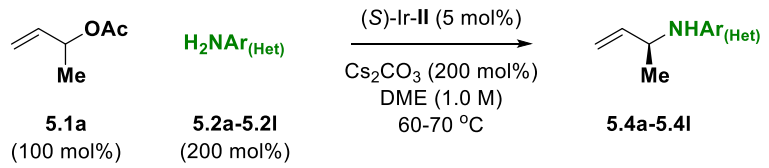
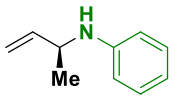


Table 5.1 Iridium-catalyzed amination of α-methyl allyl acetate **5.1a** with primary aromatic and heteroaromatic amines **5.2a-5.2l** to form enantiomerically enriched allylic amines **5.4a-5.4l**.[a]

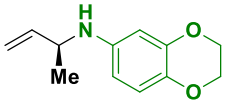


5.1a (100 mol%) **5.2a-5.2l** (200 mol%) **5.4a-5.4l**

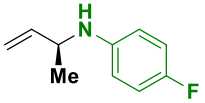
5.2a, Ar = Ph; **5.2b**, Ar = 6-(benzodioxane); **5.2c**, Ar = 4-F-Ph
5.2d, Ar = 3-Me-4-B(pin)-Ph; **5.2e**, Ar = 2-F-4-OMe-Ph; **5.2f**, Ar = 4-NMe_2-Ph
5.2g, Ar = 6-(*N*-Me-Indazole); **5.2h**, Ar = 5-(2-morph-pym); **5.2i**, Ar = 7-(benzothiazole)
5.2j, Ar = 3-SO_2Me-Ph; **5.2k**, Ar = 2-(pyridine); **5.2l**, R = 3-(pyridine)



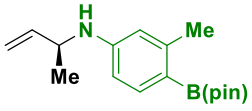
5.4a, 82% Yield, >99:1 rr
89% ee, $[\alpha]_D$ = -3.9
(c = 0.2, $CHCl_3$)



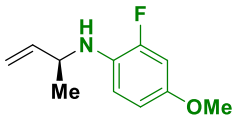
5.4b, 85% Yield, >99:1 rr
90% ee



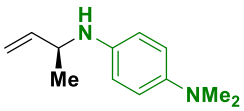
5.4c, 83% Yield, >99:1 rr
90% ee



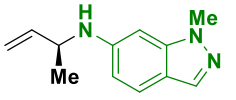
5.4d, 78% Yield, >99:1 rr
89% ee



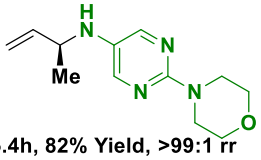
5.4e, 79% Yield, >99:1 rr
88% ee



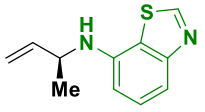
5.4f, 89% Yield, >99:1 rr
90% ee



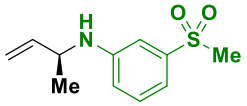
5.4g, 81% Yield, >99:1 rr
87% ee



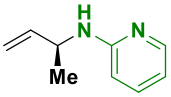
5.4h, 82% Yield, >99:1 rr
89% ee



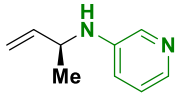
5.4i, 61% Yield, >99:1 rr
90% ee



5.4j, 76% Yield, >99:1 rr
91% ee



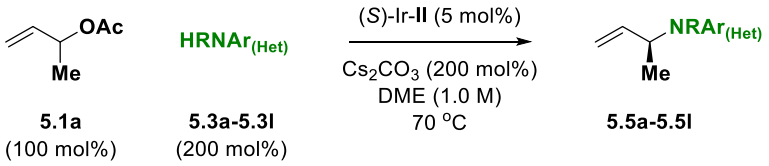
5.4k, 74% Yield, >99:1 rr
91% ee



5.4l, 87% Yield, >99:1 rr
91% ee

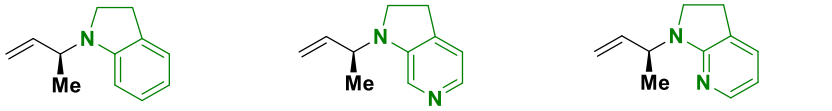
[a]Yields of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details.

Table 5.2 Iridium-catalyzed amination of α-methyl allyl acetate **5.1a** with secondary aromatic and heteroaromatic amines **5.3a-5.3l** to form enantiomerically enriched allylic amines **5.5a-5.5l**.[a]



5.1a (100 mol%) **5.3a-5.3l** (200 mol%) **5.5a-5.5l**

5.3a, indoline **5.3b**, 6-*aza*-indoline **5.3c**, 7-*aza*-indoline
5.3d, 3,3-spiro-indoline **5.3e**, (*S*)-2-Me-indoline **5.3f**, (*R*)-2-Me-indoline
5.3g, *N*-Me-aniline **5.3h**, 4-CN-*N*-Me-aniline **5.3i**, 4-MeO-*N*-Me-aniline
5.3j, 3-Br-*N*-Me-aniline **5.3k**, 3,4-Cl_2-*N*-Me-aniline **5.3l**, 2-(NHMe)-*N*-Me-benzimidazole

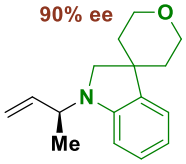


5.5a, 92% Yield, >99:1 rr

5.5b, 78% Yield, >99:1 rr

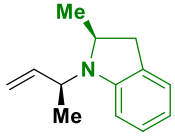
5.5c, 74% Yield, >99:1 rr

90% ee



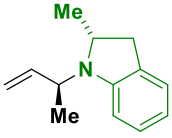
5.5d, 85% Yield, >99:1 rr
88% ee

93% ee

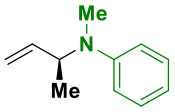


5.5e, 80% Yield, >99:1 rr
>20:1 dr

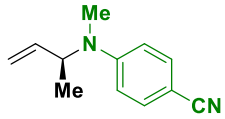
92% ee



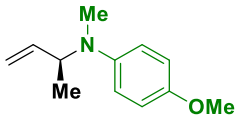
5.5f, 48% Yield, >99:1 rr
5:1 dr



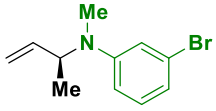
5.5g, 71% Yield, >99:1 rr
91% ee



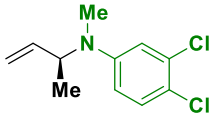
5.5h, 79% Yield, >99:1 rr
89% ee



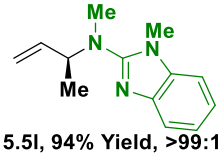
5.5i, 89% Yield, >99:1 rr
93% ee



5.5j, 64% Yield, >99:1 rr
90% ee



5.5k, 76% Yield, >99:1 rr
91% ee



5.5l, 94% Yield, >99:1 rr
87% ee

[a]Yields of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details.

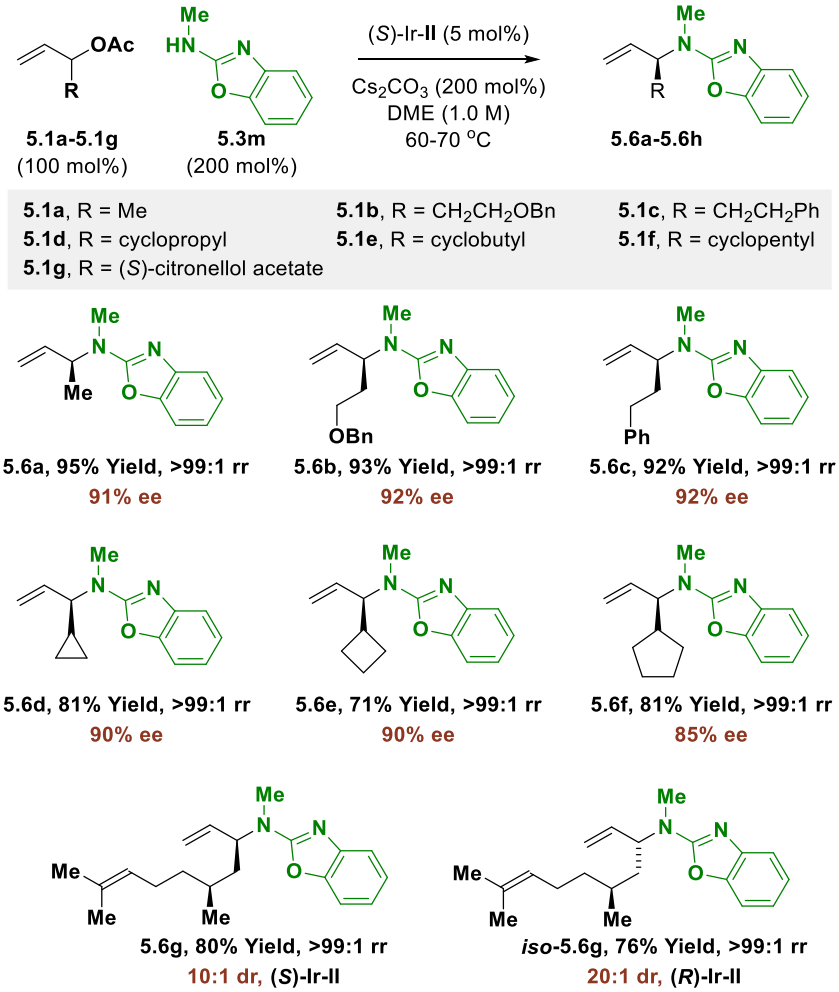
Deviation from these reaction parameters did not avail further improvement, and given the low cost of tol-BINAP these conditions were adopted to explore the scope of primary aromatic and heteroaromatic amine nucleophiles **5.2a-5.2l** in aminations of α-methyl allyl acetate (Table 5.1). Amine nucleophiles containing a diverse array of functional groups were examined to mirror challenges faced in medicinal chemistry. In each case, the targeted products of allylic amination **5.4a-5.4l** were formed with complete branched regioselectivity and uniformly high levels of enantioselectivity. As illustrated in the formation of **5.4d**, which incorporates a pinacol boronate moiety, the reaction conditions tolerate rather sensitive functional groups. The tolerance of ortho-substituted anilines, as demonstrated by the formation of **5.4e**, is also noteworthy. Perhaps the most striking feature, however, is the compatibility of the catalyst with electronically diverse aryl amine partners and the tolerance of Lewis basic *N*-heterocycles, as illustrated by the formation **5.4k** and **5.4l**. The absolute stereochemical assignment of adducts **5.4b-5.4l** is made in analogy to that determined for compound **5.4a**, which has been prepared in enantiomerically enriched form in two separate reports.[8d,18]

In a further exploration of scope, optimized conditions were applied to the amination of α-methyl allyl acetate using secondary aromatic and heteroaromatic amine nucleophiles **5.3a-5.3l** (Table 5.2). Indoline **5.3a**, 6- and 7-aza-indolines **5.3b** and **5.3c** and the 3,3-spirocyclic indoline **5.3d** each underwent asymmetric allylation with complete branched regioselectivity and high levels of enantioselectivity. Pronounced match-mismatched effects were observed in the conversion of chiral nonracemic *(S)*- and (*R*)-2-methyl indolines **5.3e** and **5.3f** to adducts **5.5e** and **5.5f**, respectively, suggesting the potential for kinetic resolution. The amination of **5.1a** using *N*-methyl aniline **5.3g** and related compounds **5.3h** and **5.3i** bearing electron withdrawing and donating groups at the para-position proceeded smoothly to form adducts **5.5g-5.5i**, respectively. Among these

three *N*-methyl aniline derivatives (**5.3g-5.3i**), amination using the more electron rich *N*-methyl-para-anisidine **5.3i** occurred with notably higher levels of enantioselectivity. As illustrated by the formation of **5.5j** and **5.5k**, *N*-methyl anilines containing bromide (**5.3j**) and chloride (**5.3k**) functional groups are tolerated. Finally, amination of **5.1a** using *N*-Methyl-2-(methylamino)benzimidazole **5.3l** is remarkably efficient, providing adduct **5.5l** in 94% yield with complete selectivity for allylation of the extranuclear 2-(methylamino) moiety.

To assess how structural variation of the π-allyliridium intermediate impacts reactivity, regio- and stereoselectivity, a set of branched allylic acetates **5.1a-5.1g** were explored in aminations mediated by 2-(methylamino)benzoxazole 5.**3m** (Table 5.3). In addition to α-methyl allyl acetate **5.1a**, linear alkyl substituted allylic acetates **5.1b** and **5.1c** smoothly underwent amination to form adducts **5.6a-5.6c** as single regioisomers with high levels of enantiomeric enrichment. Allylic acetates **5.1d-5.1f**, which incorporate cycloalkyl-substituents, delivered adducts **5.6d-5.6f** as single regioisomers, although an erosion in enantioselectivity is observed using the larger cyclopentyl-substituted allyl acetate **5.1f**. Finally, using the enantiomeric iridium catalysts *(S)*-Ir-II and (*R*)-Ir-II, the *(S)*-citronellol-derived allylic acetate **5.1g** reacts with **5.3m** to form **5.6g** and iso-**5.6g**, respectively, with good levels of catalyst-directed diastereoselectivity.

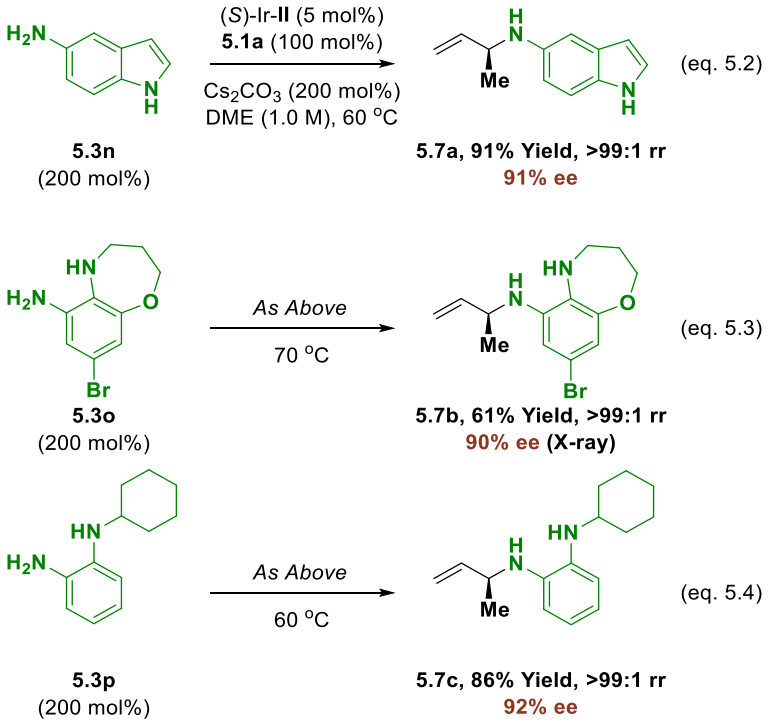
Table 5.3 Iridium-catalyzed amination of α-substituted allyl acetates **5.1a-5.1g** with secondary heteroaromatic amine **5.3m** to form enantiomerically enriched allylic amines **5.6a-5.6g**.[a]



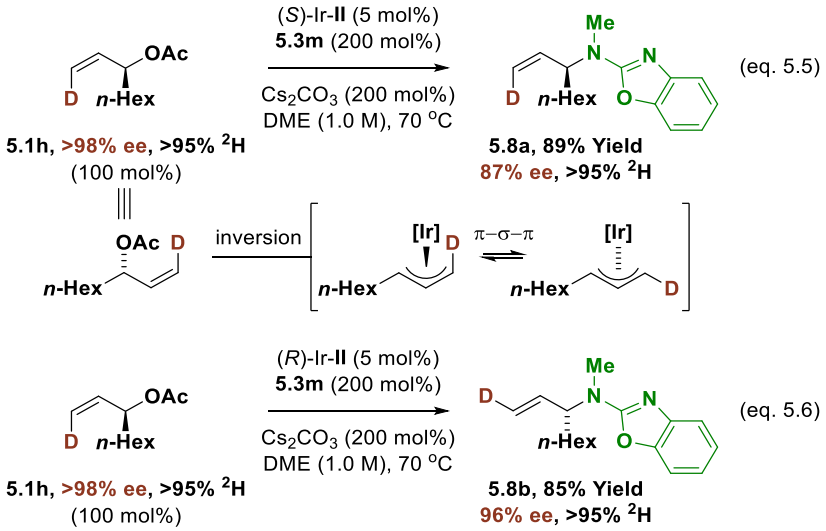
[a]Yields of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details.

Having established the ability to functionalize both primary and secondary aromatic amines, the site-selective modification of reactants **5.3n-5.3p**, which incorporate both primary and secondary aromatic amines, was attempted using the branched allylic acetate **5.1a** (eq. 5.2-5.4). Upon exposure to standard conditions, 5-aminoindole **5.3n** undergoes completely chemoselective functionalization at the primary amine to form

adduct **5.7a** as a single constitutional isomer with excellent levels of enantioselectivity (eq. 5.2). Similarly, in the conversion of **5.3o** to adduct **5.7b**, complete control of regio- and site-selectivity is accompanied by high levels of enantioselectivity (eq. 5.3). The structure of adduct **5.7b** was verified by single crystal X-ray diffraction analysis, further corroborating the absolute stereochemical assignment of adducts **5.4a-5.4l**, **5.5a-5.5l** and **5.6a-5.6g**. Finally, *N*-cyclohexyl-1,2-diaminobenzene **5.3p** reacts with **5.1a** to deliver adduct **5.7c**, which is modified exclusively at the primary amine (eq. 5.4). The ability to engage diamines in site-selective regio- and enantioselective amination enhances step economy by avoiding manipulations devoted to *N*-protection-deprotection.



Scheme 5.1 Iridium-catalyzed amination of enantiomerically enriched deuterated allylic acetate **5.1h** with the enantiomeric catalysts (*S*)-Ir-II and (*R*)-Ir-II.[a]



[a]Yields of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details.

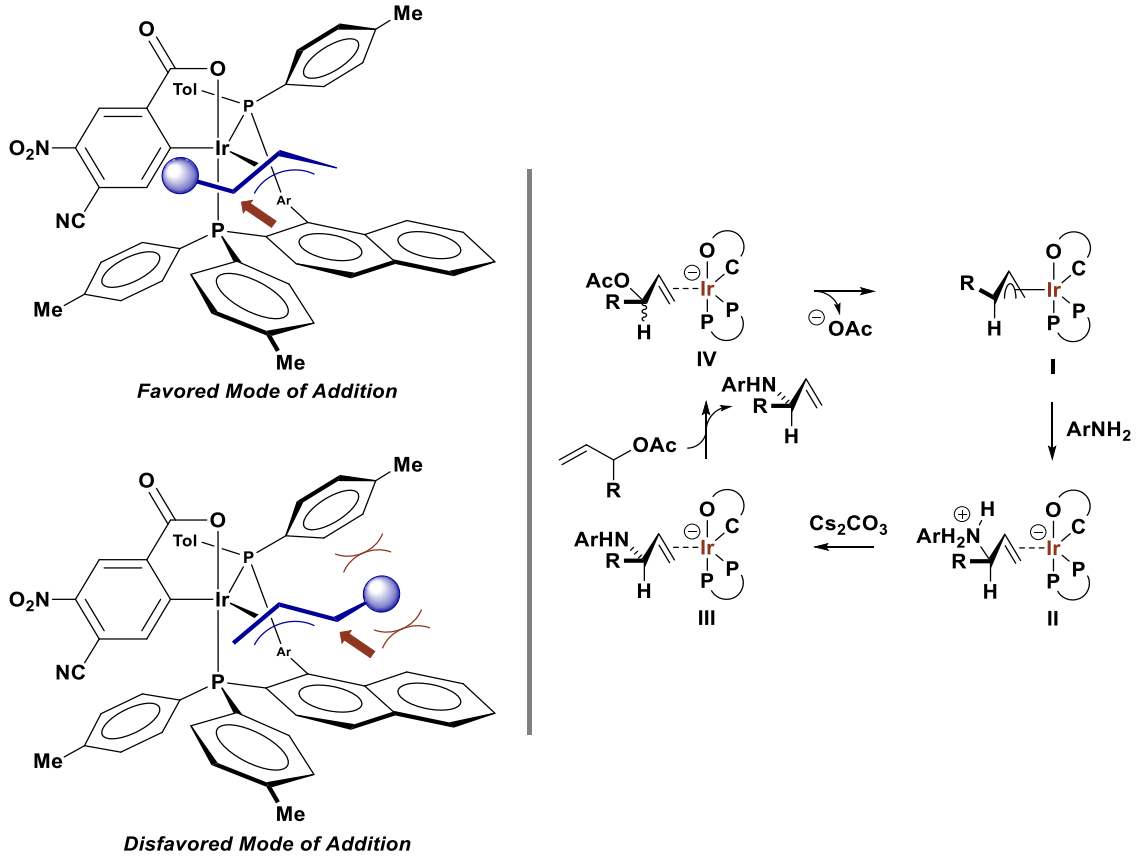
5.3 Discussion

To better understand the nature of the C-N bond forming event, asymmetric amination of the enantiomerically enriched (*Z*)-deuterated allylic acetate **5.1h** was conducted under standard conditions using *(S)*-Ir-II (Scheme 5.1, eq. 5.5).[19] Compound **5.8a** is formed with complete alkene (*Z*)-stereoselectivity, as determined by ^{1}H NMR. Assuming formation of the π-allyliridium occurs with inversion of stereochemistry, as established in analogous iridium phosphoramidite catalyzed processes,[4-12] the stereochemistry of the amination product **5.8a** is consistent with outer-sphere addition of the nitrogen nucleophile. To corroborate the veracity of this experiment, the amination of allylic acetate **5.1h** was conducted using the enantiomeric iridium catalyst, (*R*)-Ir-II (Scheme 1, eq. 5.6). The amination product **5.8b** is formed with complete alkene (*E*)-

stereoselectivity, as de-termined by ^{1}H NMR. The stereochemistry of **5.8a** is again consistent with outer-sphere C-N bond formation.

Based on the collective data, a general catalytic mechanism and stereochemical model were proposed (Scheme 5.2). The π-allyliridium(I) complex **I** is subject to outer-sphere amine addition amine to form the C-N bond and the zwitterionic iridium(I) olefin complex **II**. Deprotonation of ammonium moiety of complex **II** mediated by cesium carbonate generates the anionic iridium(I) species **III**. Alkene exchange with the allylic acetate releases the product of allylic amination and forms the olefin complex **IV**. Loss of acetate ion regenerates the π-allyliridium(I) complex **I** to close the catalytic cycle. The indicated stereochemical model accounts for the observed sense of absolute stereoinduction for outer sphere addition of a nucleophile to the neutral iridium π-allyl complex **I**. This model is based upon the coordination mode revealed in closely related crystal structures.[20] Orientation of the π-allyl is controlled through alleviation of steric clashes between the naphthyl and tolyl substituents of the phosphine ligand with the R-group of the resulting π-allyl, as illustrated in the disfavored mode of addition (Scheme 5.2).

Scheme 5.2 General catalytic mechanism and stereochemical model for enantioselective iridium-catalyzed allylic amination.



5.4 Conclusion

Previously reported enantioselective allylic aminations are largely restricted to chiral iridium-phosphoramidite catalysts.[4-12] We have shown that air and water stable π-allyliridium *C,O*-benzoates, which are well-known for their ability to catalyze nucleophilic carbonyl allylation,[1,2] also promote highly regio- and enantioselective electrophilic allylation of aliphatic amines[15] and, as demonstrated here, primary and secondary aromatic or heteroaromatic amines. These π-allyliridium *C,O*-benzoate catalyzed processes overcome a longstanding limitation associated with all known

catalytic systems for asymmetric allylic amination - the ability to promote highly enantioselective aminations of branched allylic acetates bearing n-alkyl groups with complete levels of regioselectivitity.[4-12,16] Another notable feature of these catalysts involves the ability to promote site-selective *N*-allylations of reactants that incorporate both primary and secondary aromatic amines. Mechanistic studies establish an outer-sphere mechanism for C-N bond formation. This work, along with our initially communicated studies,[15] significantly expands the scope of catalytic asymmetric allylic amination methodology, broadening access to chiral α-stereogenic amines.

5.5 Experimental Details

General Information

All reactions were carried out under inert gas atmosphere (nitrogen or argon) unless otherwise indicated. Resealable pressure tubes (13x100 mm) were purchased from Fischer Scientific (catalog number 14-959-35C) and were flame dried followed by cooling in a desiccator or under a stream of inter gas prior to use. All commercial reagents and anhydrous solvents were used as received from vendors (Fischer Scientific, Sigma Aldrich and Combi Blocks) without further purification. The used Iridium catalyst (*S*)-Ir-II and (*R*)-Ir-II was prepared according to literature known procedures.[1] Cesium carbonate was used as received from Rockwell Lithium. Preparative column chromatography employing Silicycle silica gel (40-63 μm) was performed according to the method of Still[2] or on a Teledyne Isco Combiflash Rf utilizing Silicycle HP columns using a mobile phase composed of either heptane/isopropyl acetate, heptanes/ethyl acetate or dichloromethane/methanol. Reactions were monitored by a Shimadzu LCMS/UV system with LC-30AD solvent pump, 2020 MS, Sil-30AC autosampler, SPD-

M30A UV detector, CTO-20A column oven, using a 2-98% acetonitrile/0.1% formic acid (or 0.001% ammonia) gradient over 2.5 minutes. Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Dynamic Absorbents F). Visualization was accomplished with UV light followed by dipping in CAM, *p*-Anisaldehyde (PAA), or $KMnO_4$ stain solution followed by heating.

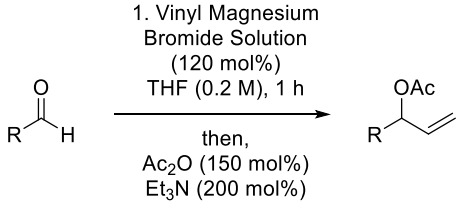
Spectroscopy, Spectrometry and Data Collection

Infrared spectra were recorded on a Perkin-Elmer 1600 spectrometer using a diamond ATR unit. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion (M+H, M+Na), or a suitable fragment ion. Nuclear magnetic resonance (^1H, ^{13}C, ^{19}F NMR) spectra were recorded with a Bruker BioSpin GmbG, Varian Gemini (400 MHz) or Varian INOVA (500 MHz) spectrometer equipped with a Bruker cryoprobe. The chemical shifts are given as parts per million (ppm) and were referenced to the residual solvent signal ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm). Specific optical rotations were recorded on an Atago AP-300 automatic polarimeter at the sodium line (589 nm) in CHCl3. Solution concentrations are given in the units of 10–2 g mL^{-1}.

Experimental Details and Spectral Data

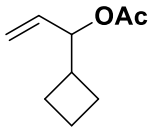
Synthesis of Allylic Acetates 5.1e-5.1g

General procedure for the synthesis of allylic acetates. The allylic acetates **5.1e, 5.1f,** and **5.1g** were prepared by the Grignard reaction and acetylation of the as shown below. The allylic acetates **5.1b**,[3] **5.1c**,[4] and **5.1d**[5] were identical in all respects to the reported materials.



To a round-bottomed flask charged with the corresponding aldehyde under an argon atmosphere was added THF (0.2 M). The reaction flask was placed an ice batch. After 10 minutes, vinyl magnesium bromide solution (120 mol%, 1.0 M in THF) was added slowly and the mixture was stirred at room temperature for 1 hour, at which point acetic anhydride (150 mol%) and triethylamine (200 mol%) were added and the reaction was stirred vigorously overnight. After water was added, the mixture was transferred to a separatory funnel. The organic layer was extracted with diethyl ether and the combined organic layers were washed with 1 N HCl, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash column chromatography give the corresponding allylic acetate over 2 steps.

1-cyclobutylallyl acetate (5.1e)



The title compound was prepared by the general procedure.

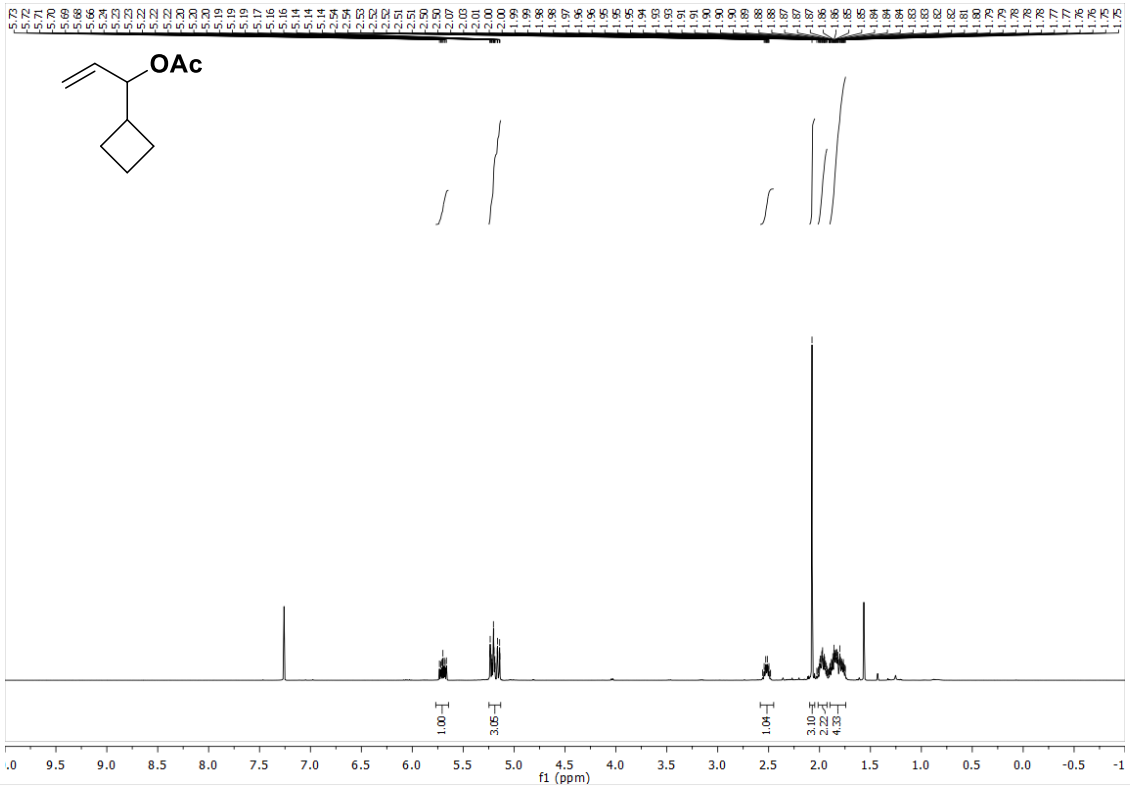
TLC (SiO_2) R_f = 0.61 (heptanes: isopropyl acetate = 4:1).

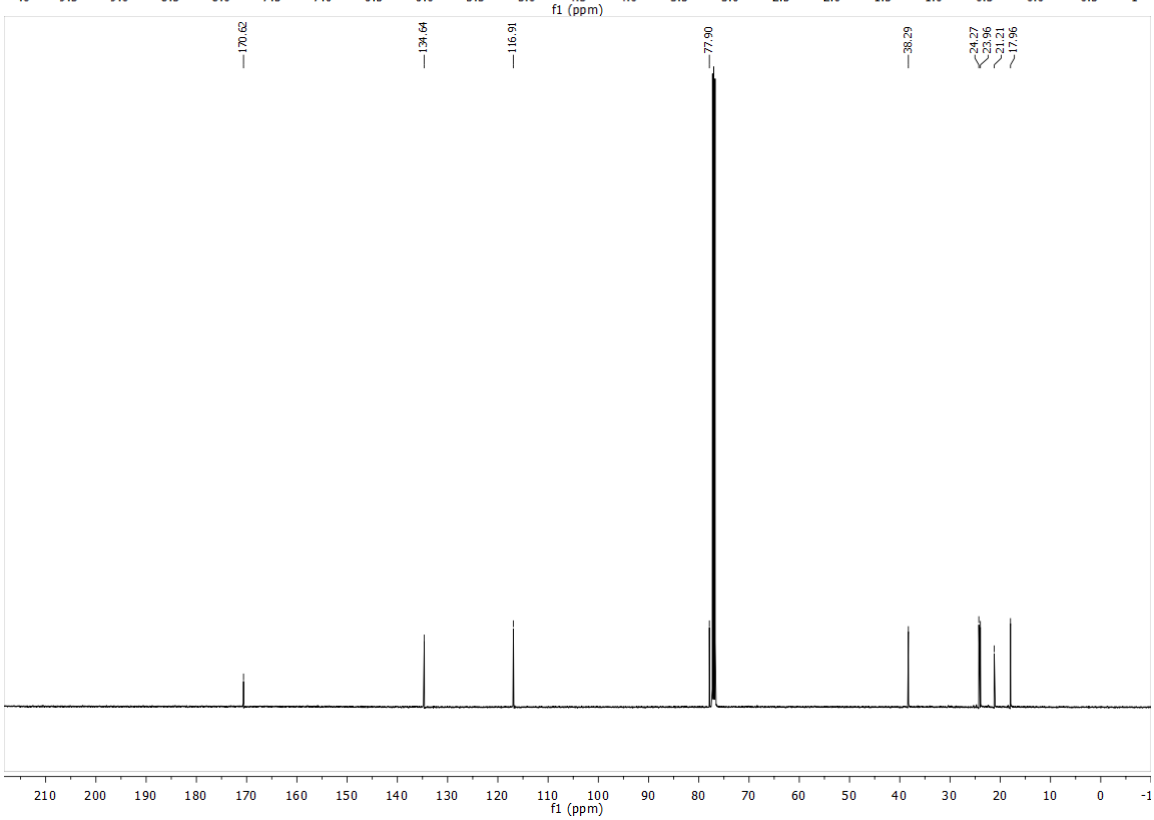
^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.70 (ddd, J = 17.2, 10.5, 6.3 Hz, 1H), 5.25 – 5.13 (m, 3H), 2.58 – 2.45 (m, 1H), 2.07 (s, 3H), 1.97 (dddd, J = 18.3, 9.9, 8.0, 4.7 Hz, 2H), 1.90 – 1.74 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 134.6, 116.9, 77.9, 38.3, 24.3, 24.0, 21.2, 18.0.

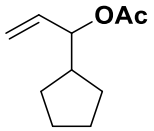
LRMS (CI): Calculated for C_7H_{11} $[M–OAc]^+$ = 95, Found 95.

FTIR (neat): 2941, 1737, 1370, 1232, 1102, 1018, 972, 925 cm^{-1}.


OAc
1.00
3.05
1.04
3.10
2.22
4.33
f1 (ppm)


170.62
134.64
116.91
77.90
38.29
24.27
23.96
21.21
17.96
f1 (ppm)

1-cyclopentylallyl acetate (5.1f)



The title compound was prepared by the general procedure.

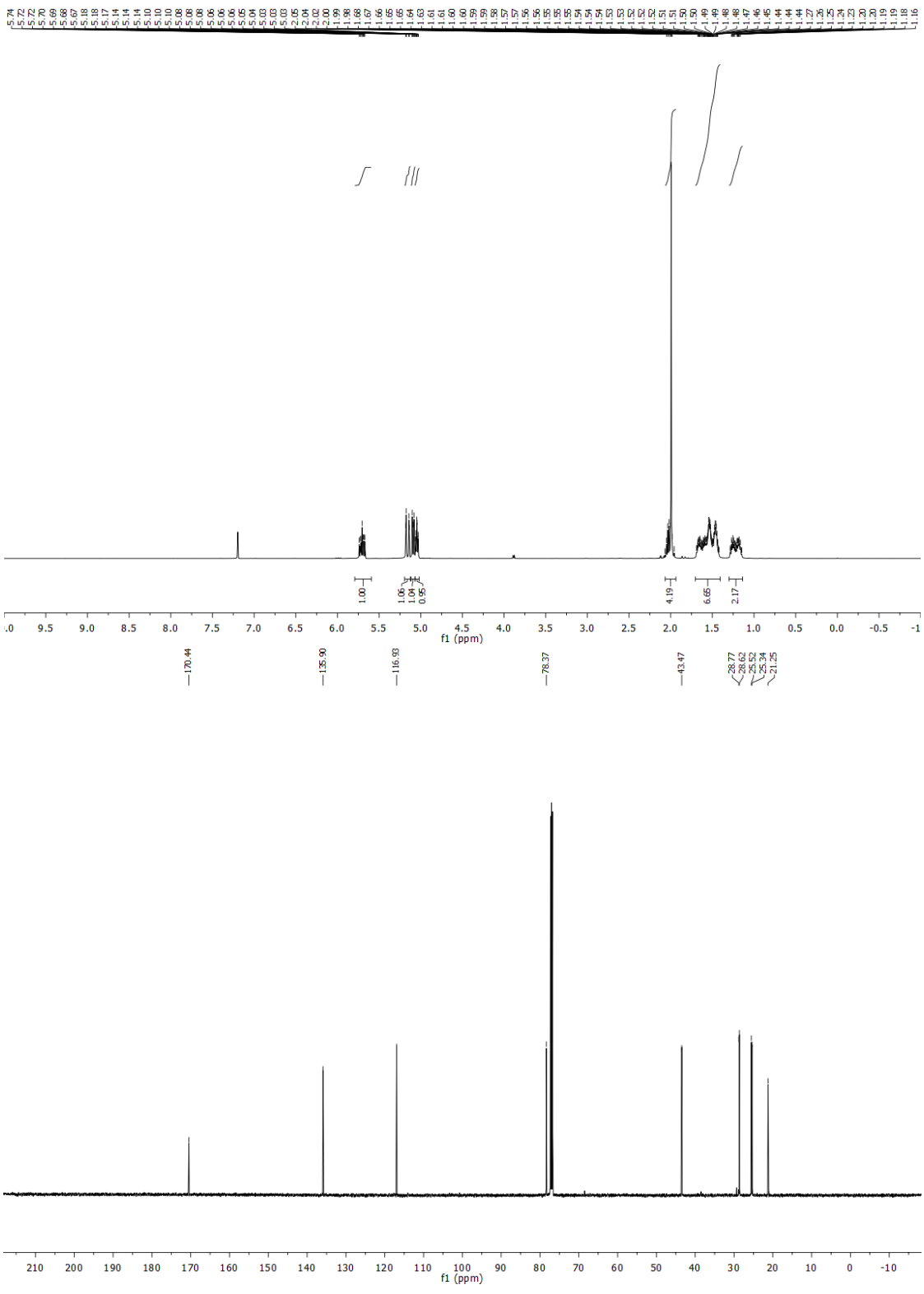
TLC (SiO_2) R_f = 0.61 (heptanes: isopropyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.70 (ddd, J = 17.2, 10.5, 6.7 Hz, 1H), 5.16 (dt, J = 17.2, 1.4 Hz, 1H), 5.09 (dt, J = 10.6, 1.3 Hz, 1H), 5.07 – 5.02 (m, 1H), 2.07 – 1.94 (m, 4H), 1.70 – 1.41 (m, 6H), 1.30 – 1.14 (m, 2H).

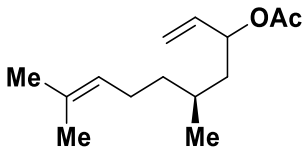
^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 135.9, 116.9, 78.4, 43.5, 28.8, 28.6, 25.5, 25.3, 21.3.

LRMS (CI): Calculated for C_8H_{13} $[M–OAc]^+$ = 109, Found 109.

FTIR (neat): 2954, 2869, 1738, 1370, 1232, 1018, 929, 893 cm^{-1}.


f1 (ppm)
f1 (ppm)

(5*S*)-5,9-dimethyldeca-1,8-dien-3-yl acetate (5.1g)



The title compound was prepared by the general procedure.

TLC (SiO_2) R_f = 0.46 (heptane: isopropyl acetate = 9:1).

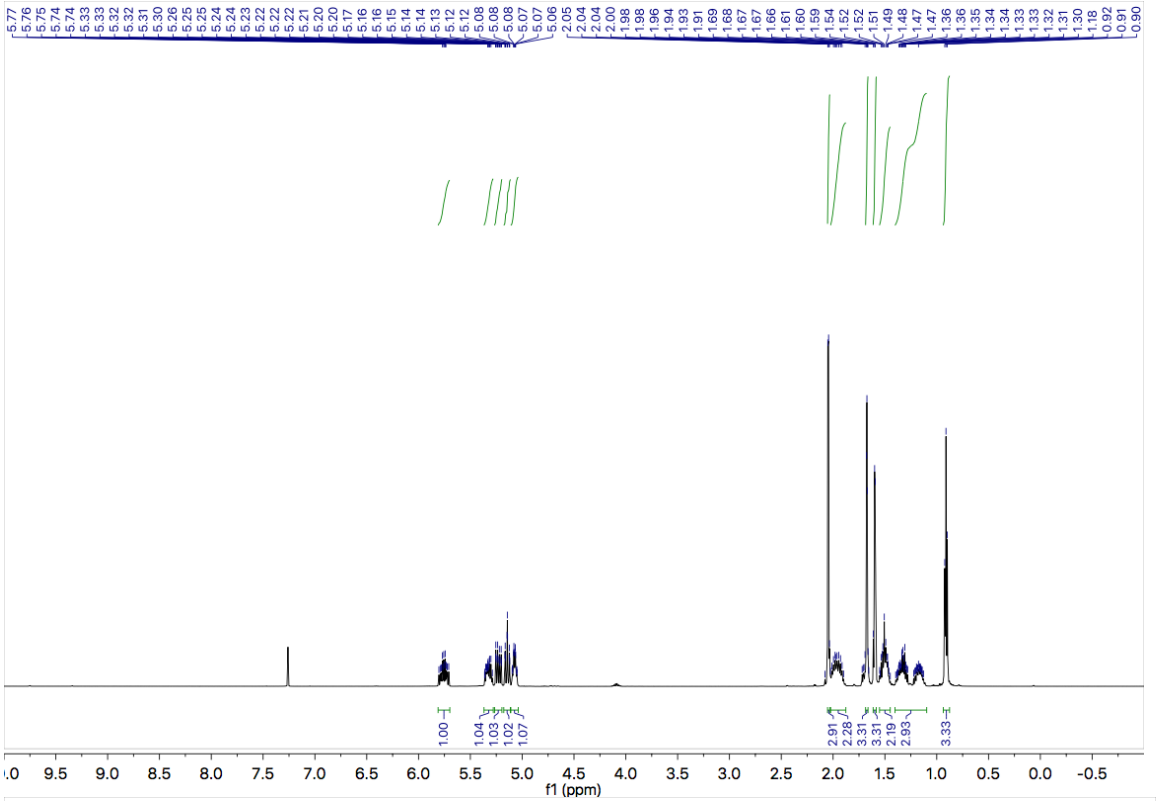
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.76 (dddd, *J* = 17.2, 13.3, 10.5, 6.5 Hz, 1H), 5.38 – 5.27 (m, 1H), 5.23 (ddt, *J* = 17.2, 8.7, 1.3 Hz, 1H), 5.14 (tt, *J* = 10.5, 1.2 Hz, 1H), 5.08 (tdd, *J* = 8.4, 4.9, 3.5 Hz, 1H), 2.05 (d, *J* = 3.9 Hz, 3H), 2.02-1.87 (m, 2H), 1.67 (s, 3H), 1.60 (d, *J* = 3.1 Hz, 3H), 1.55-1.45 (m, 2H), 1.40-1.10(m, 3H), 0.91 (t, *J* = 6.4 Hz, 3H).

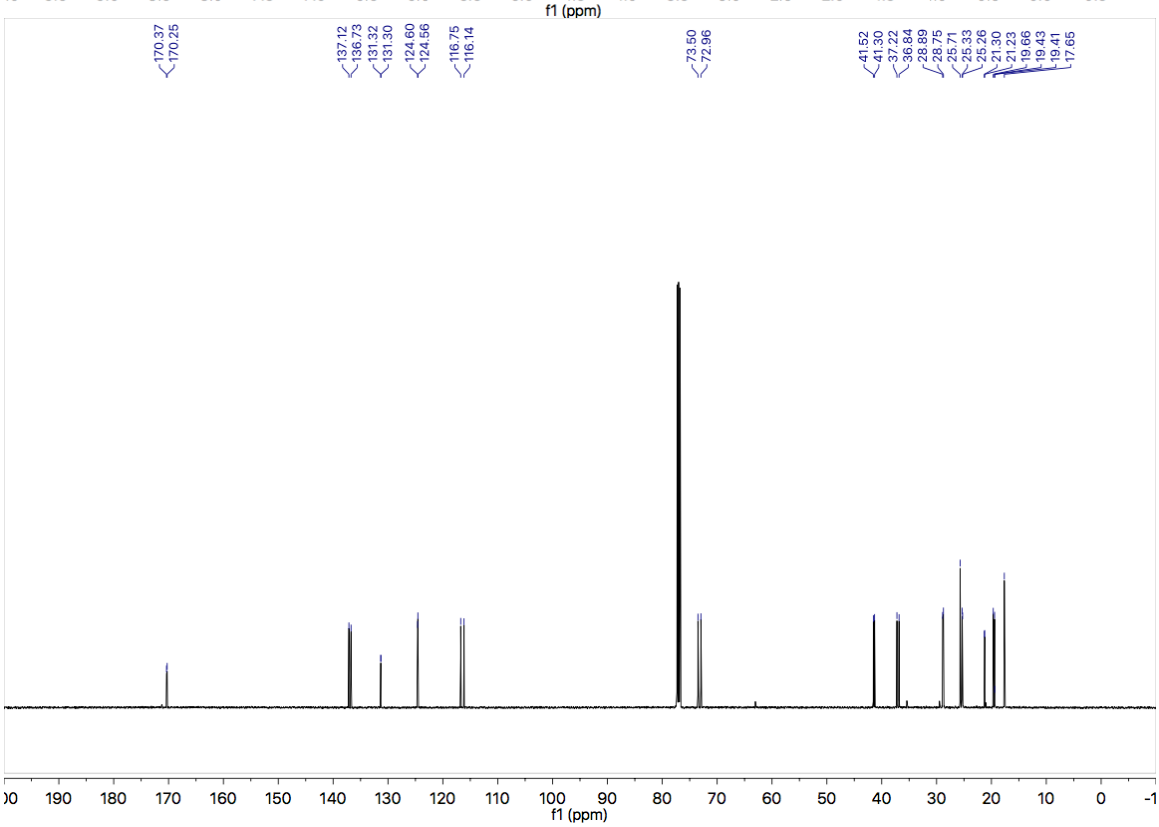
^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.3 (d, *J* = 14.9 Hz), 136.9 (d, *J* = 48.9 Hz), 131.3 (d, *J* = 2.2 Hz), 124.6 (d, *J* = 5.1 Hz), 116.4 (d, *J* = 76.0 Hz), 73.2 (d, *J* = 68.0 Hz), 41.4 (d, *J* = 28.2 Hz), 37.0 (d, *J* = 48.7 Hz), 28.8 (d, *J* = 18.5 Hz), 25.7, 25.3 (d, *J* = 8.3 Hz), 21.3 (d, *J* = 8.2 Hz), 19.6 (d, *J* = 29.8 Hz), 17.7.

HRMS (CI): Calculated for $C_{14}H_{24}O_2$ $[M–OAc]^+$ = 165.1643, Found 165.1635.

FTIR (neat): 2965, 2917, 2367, 1741, 1338, 1372, 1237, 1020, 988, 929, 668 cm^{-1}.

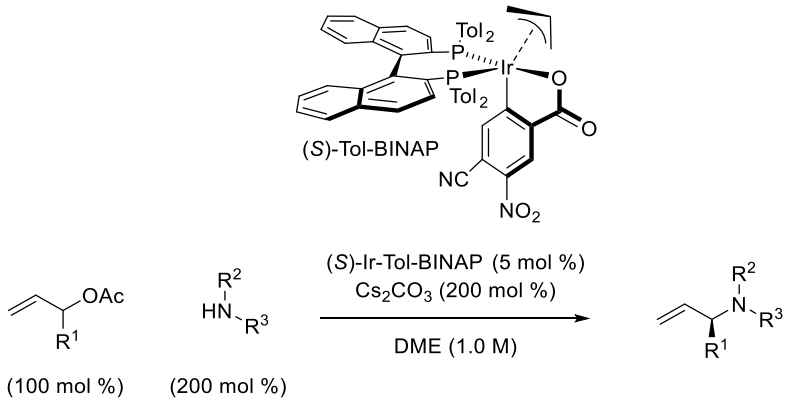
$[\alpha]_D^{28}$= –3.56 (*c* 0.2, $CHCl_3$).


f1 (ppm)


f1 (ppm)

Procedures and Spectral Data for Synthesis of Allylic Amines 5.4a-5.4l, 5.5a-5.5l, 5.6a-5.6g, 5.7a-5.7c

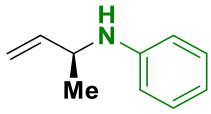
Enantioselective iridium catalyzed allylic alkylation with amine nucleophiles-



General procedure

An pressure tube equipped with a magnetic stir bar was charged with cesium carbonate (200 mol%), (*S*)-Ir-II (5 mol%). The tube was purged with argon for 5 minutes. DME (1.0 M) was added followed by the allylic acetate (100 mol%) and the amine (200 mol%). The tube was sealed with a PTFE lined cap and was placed in an oil bath at the indicated temperature and stirred for the indicated period of time. After reaching ambient temperature, the crude reaction mixture was directly subjected to flash column chromatography.

(*S*)-N-(but-3-en-2-yl)aniline (5.4a)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (81.6 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 82% yield (53.1 mg, 0.36 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 20 min).

TLC (SiO_2) R_f = 0.40 (heptanes: isopropyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20 – 7.09 (m, 2H), 6.68 (tt, *J* = 7.4, 1.1 Hz, 1H), 6.63 – 6.57 (m, 2H), 5.83 (ddd, *J* = 17.2, 10.3, 5.6 Hz, 1H), 5.21 (dt, *J* = 17.2, 1.4 Hz, 1H), 5.08 (dt, *J* = 10.4, 1.4 Hz, 1H), 3.98 (dddd, *J* = 9.5, 6.6, 4.8, 3.3 Hz, 1H), 3.59 (s, 1H), 1.31 (d, *J* = 6.6 Hz, 3H).

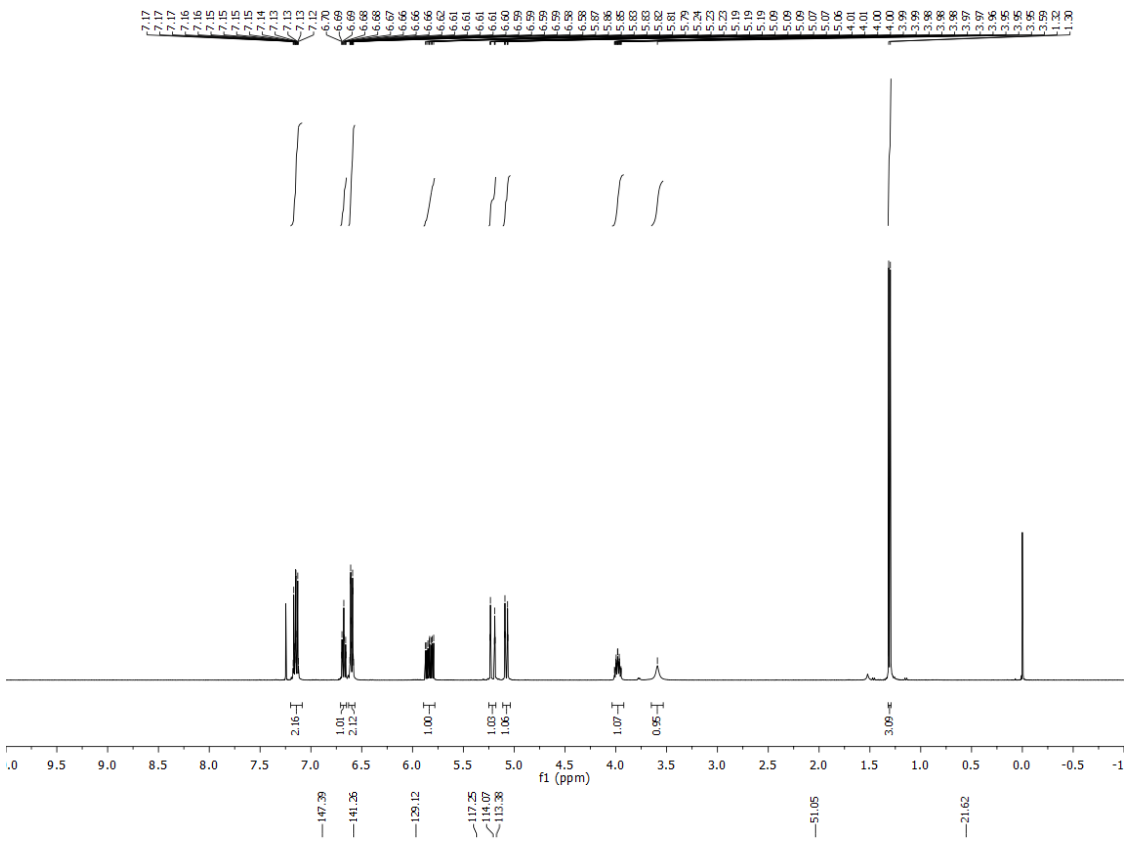
^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.4, 141.3, 129.1, 117.3, 114.1, 113.4, 51.1, 21.6.

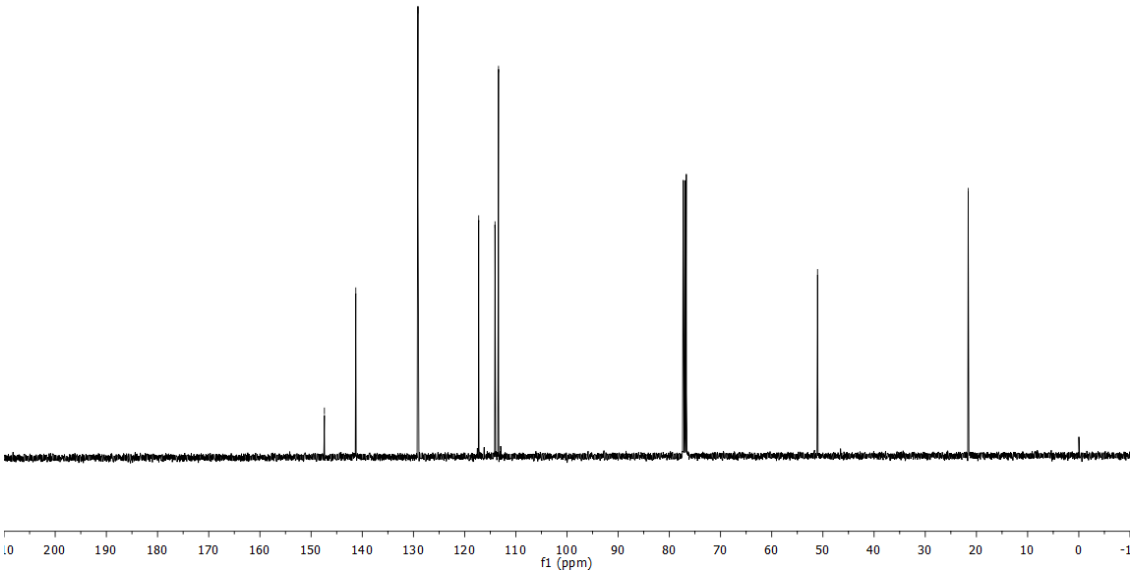
HRMS (ESI): Calculated for $C_{10}H_{13}N$ [M+H$^+$] = 148.1126, Found 148.1122.

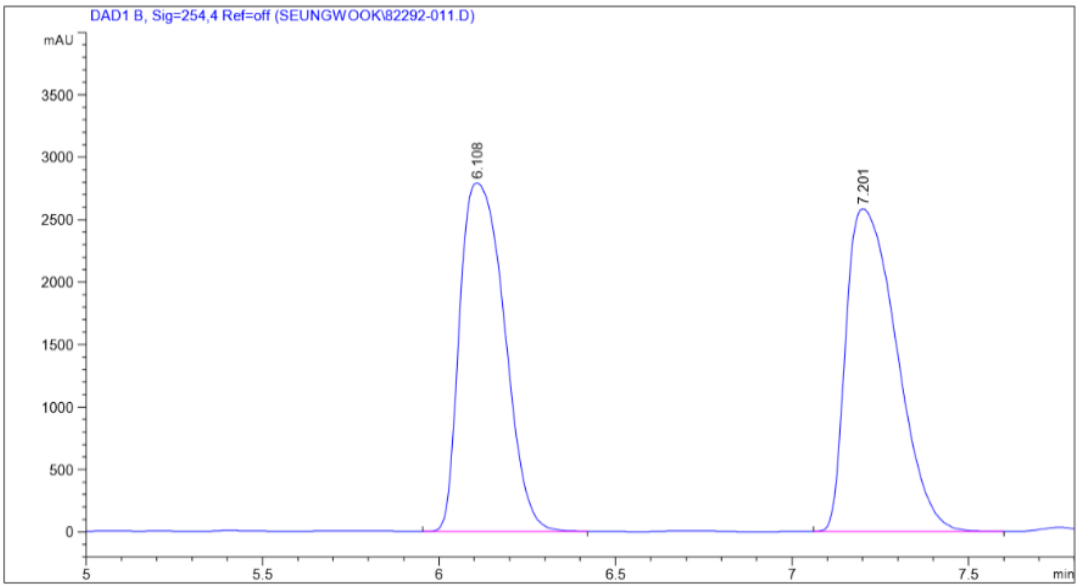
FTIR (neat): 3404, 2975, 1601, 1504, 1317, 1254, 992, 919, 748, 692 cm^{-1}.

$[\alpha]_D^{28}$= –3.9 (*c* 0.2, $CHCl_3$).

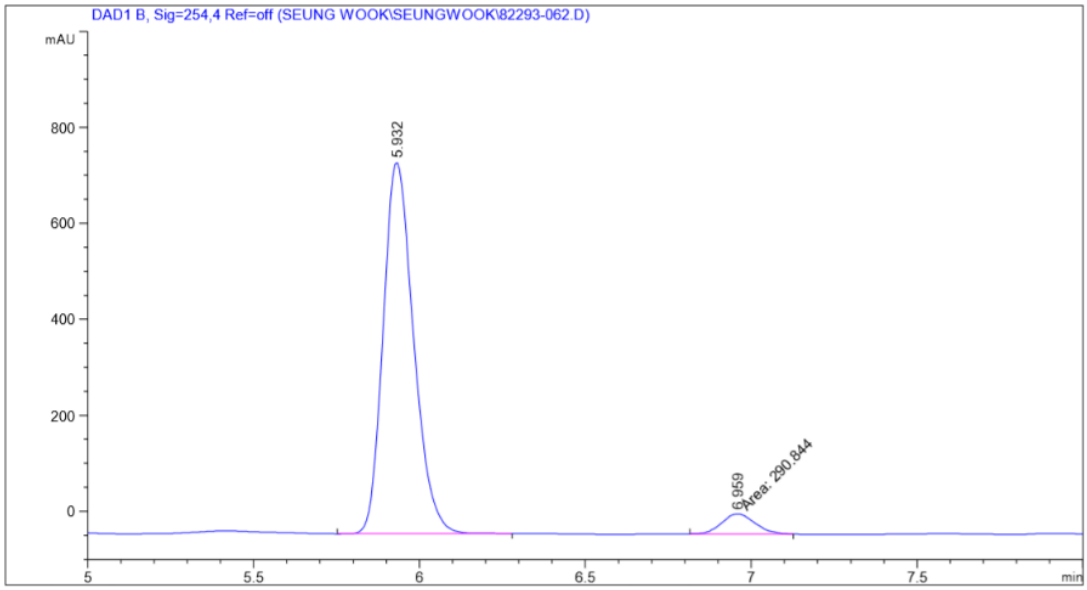
HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 97.5:2.5, 1.00 mL/min, 254 nm), *ee* = 89%.





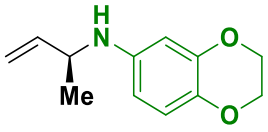


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.108	BB	0.1443	2.44570e4	2790.51685	48.7471
2	7.201	BB	0.1601	2.57142e4	2583.42285	51.2529



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.932	BB	0.0982	4926.29297	774.15454	94.4252
2	6.959	MM	0.1153	290.84390	42.03476	5.5748

(*S*)-N-(but-3-en-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-amine (5.4b)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (133.0 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 24 hr). The title compound was obtained in 85% yield (76.5 mg, 0.37 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 20 min).

TLC (SiO_2) R_f = 0.23 (heptanes: isopropyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.68 (dd, *J* = 8.5, 0.4 Hz, 1H), 6.17 (d, *J* = 2.7 Hz, 1H), 6.14 (dd, *J* = 8.5, 2.7 Hz, 1H), 5.81 (ddd, *J* = 17.2, 10.3, 5.7 Hz, 1H), 5.20 (dt, *J* = 17.3, 1.4 Hz, 1H), 5.07 (dt, *J* = 10.3, 1.4 Hz, 1H), 4.34 – 4.18 (m, 2H), 4.21 – 4.13 (m, 2H), 4.00 – 3.77 (m, 1H), 3.33 (br, 1H), 1.28 (d, *J* = 6.6 Hz, 3H).

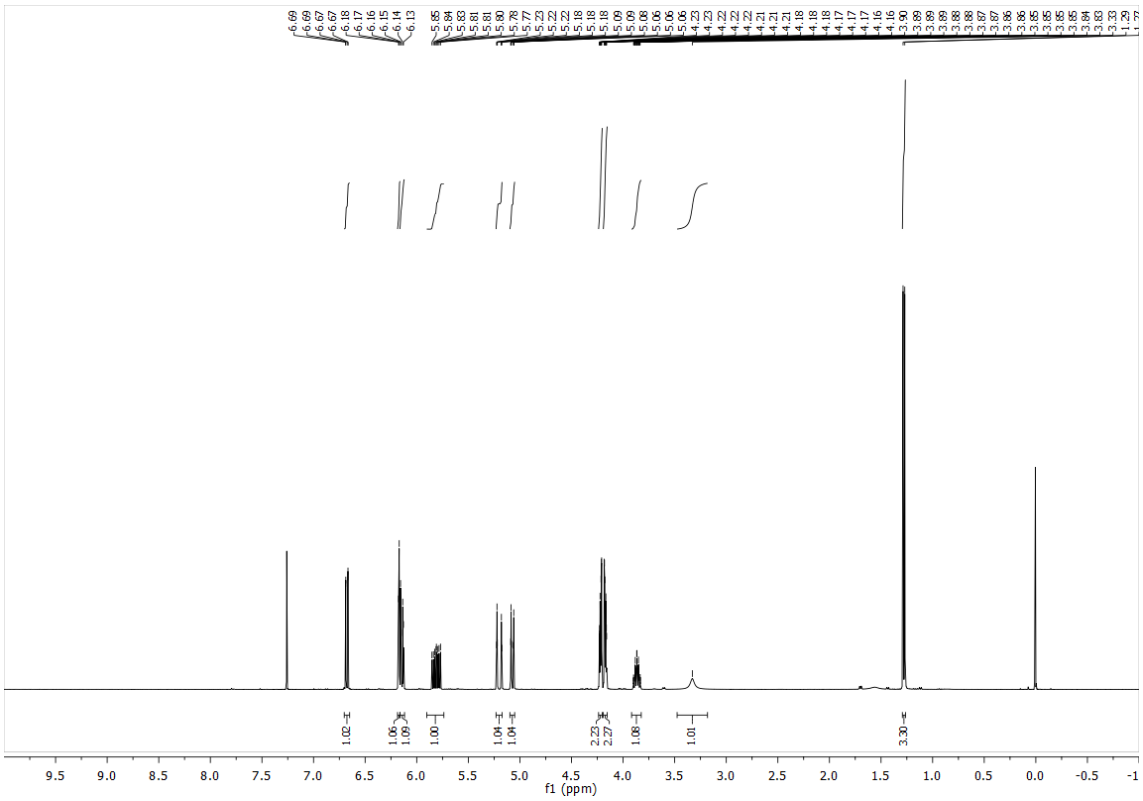
^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.9, 142.4, 141.5, 135.5, 117.5, 114.1, 107.4, 102.3, 64.8, 64.2, 51.9, 21.7.

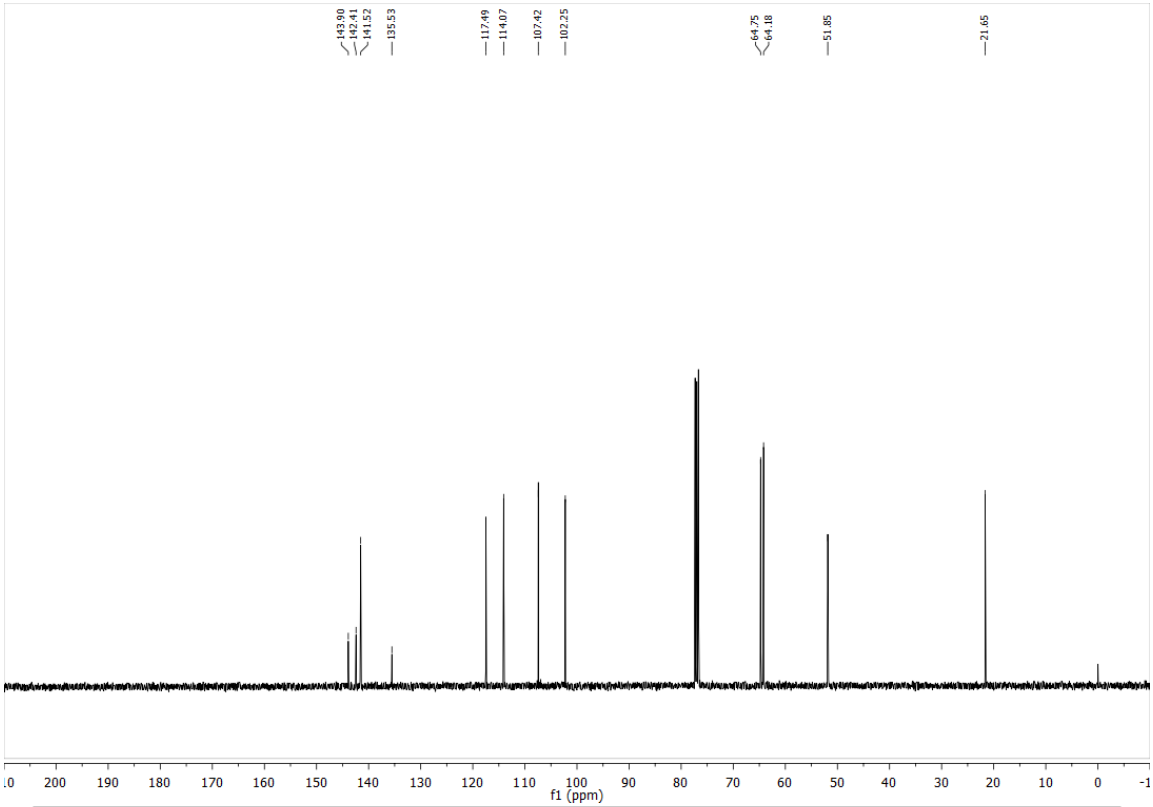
HRMS (ESI): Calculated for $C_{12}H_{15}NO_2$ [M+H$^+$] = 206.1176, Found 206.1183.

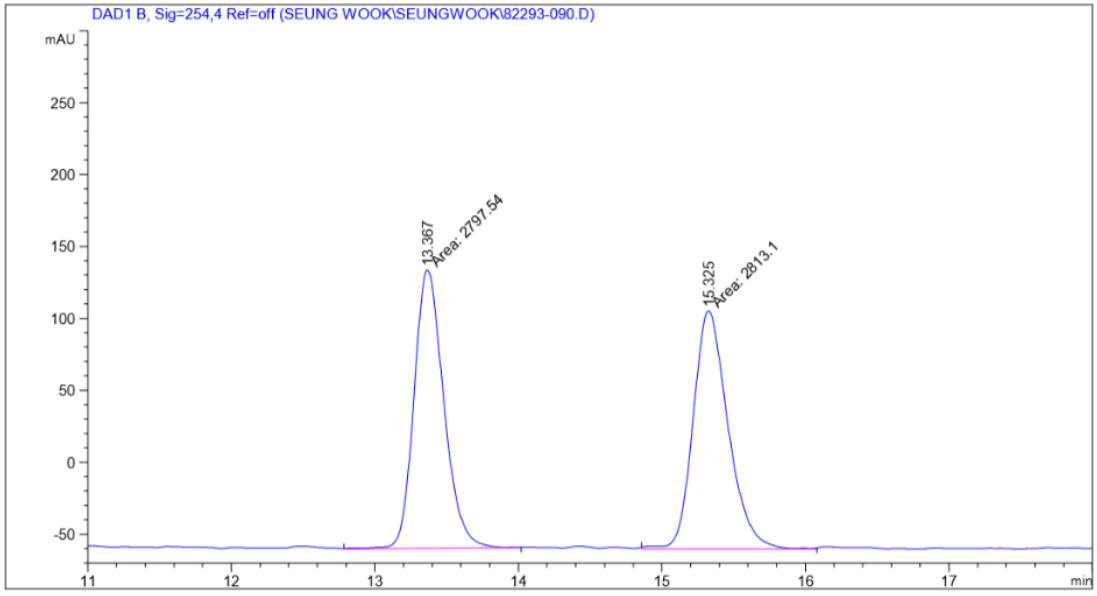
FTIR (neat): 3394, 2973, 1507, 1207, 1068, 915, 884, 794, 740 cm^{-1}.

$[\alpha]_D^{28}$ = –0.87 (*c* 0.2, $CHCl_3$).

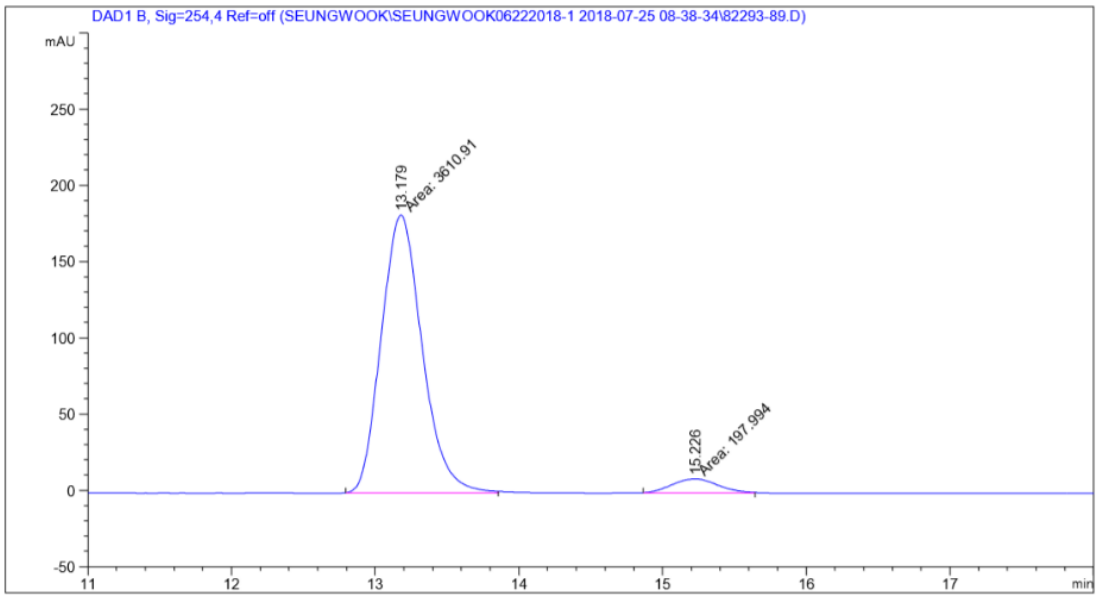
HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 97.5:2.5, 1.00 mL/min, 254 nm), *ee* = 90%.


f1 (ppm)



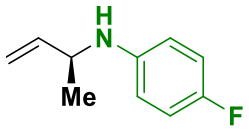


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.367	MM	0.2409	2797.53516	193.58287	49.8613
2	15.325	MM	0.2831	2813.09619	165.62939	50.1387



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.179	MM	0.3303	3610.91309	182.21223	94.8018
2	15.226	MM	0.3657	197.99403	9.02356	5.1982

(*S*)-N-(but-3-en-2-yl)-4-fluoroaniline (5.4c)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (97.8 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ^{o}C, 24 hr). The title compound was obtained in 83% yield (60.3 mg, 0.37 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 20 min).

TLC (SiO_2) R_f = 0.36 (heptanes: isopropyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1H NMR (400 MHz, Chloroform-d) δ 6.91 – 6.81 (m, 2H), 6.58 – 6.49 (m, 2H), 5.81 (ddd, *J* = 17.2, 10.3, 5.7 Hz, 1H), 5.20 (dt, *J* = 17.2, 1.4 Hz, 1H), 5.09 (dt, *J* = 10.4, 1.3 Hz, 1H), 4.01 – 3.83 (m, 1H), 3.48 (br, 1H), 1.31 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9, 154.5, 143.7, 141.2, 115.6, 115.4, 114.3, 114.2, 51.8, 21.7.

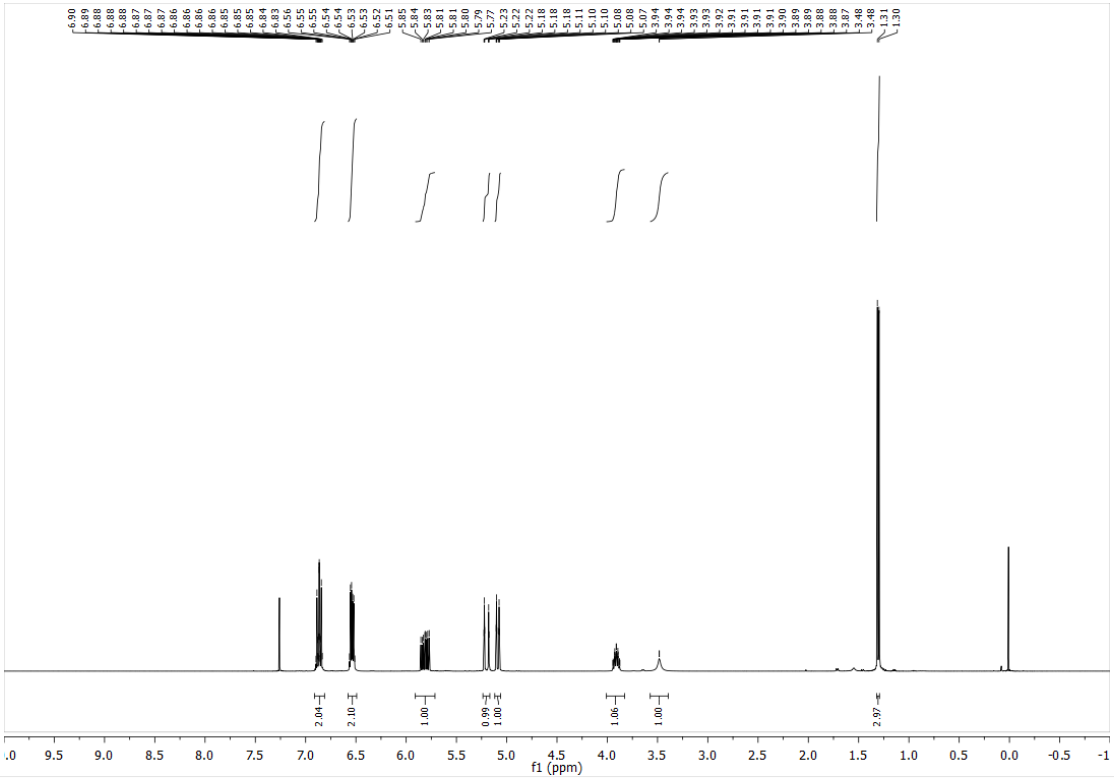
^{19}F NMR (376 MHz, $CDCl_3$): δ = –128.3.

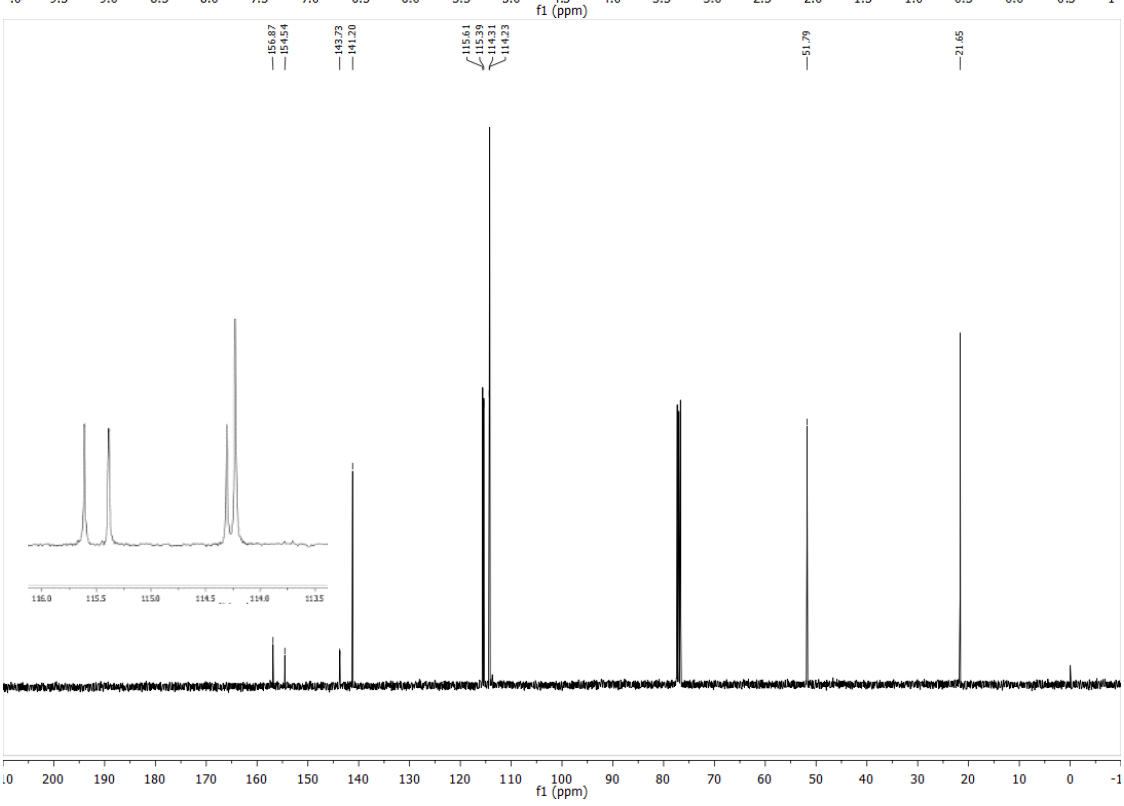
HRMS (ESI): Calculated for $C_{10}H_{12}NF$ $[M+H^+]$ = 166.1027, Found 166.1028.

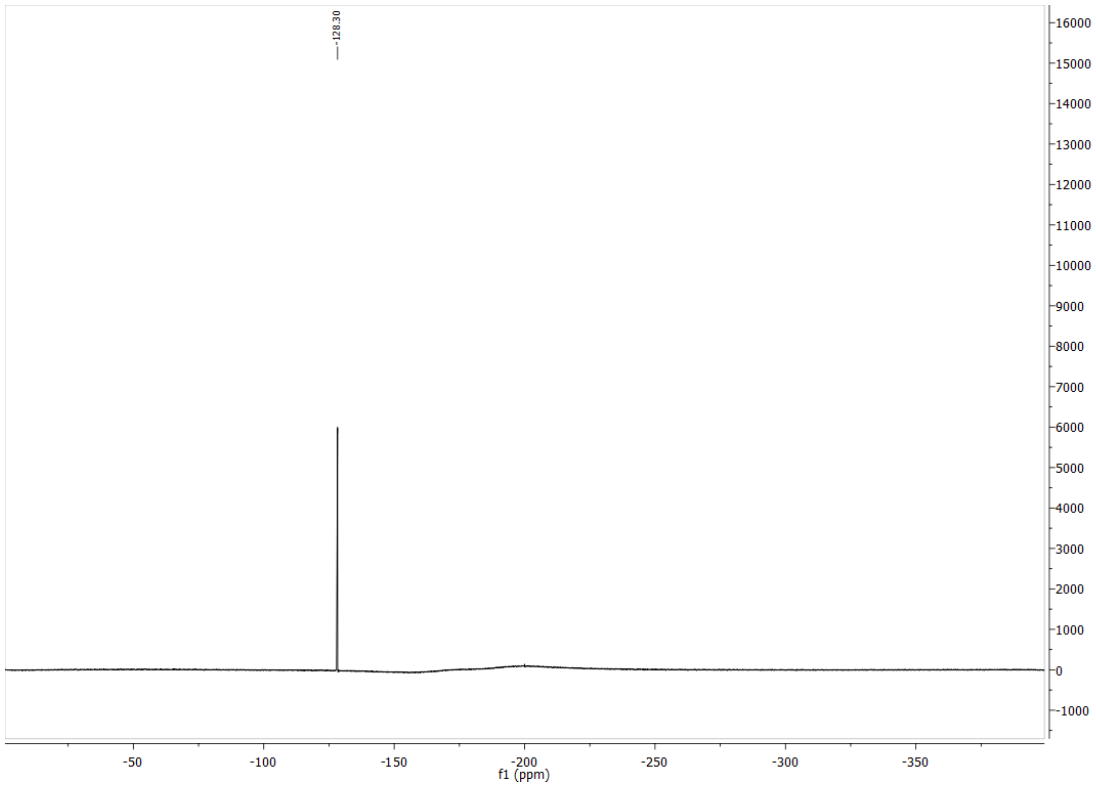
FTIR (neat): 2975, 1505, 1309, 1213, 1155, 991, 918, 815, 770, 506 cm^{-1}.

$[\alpha]_D^{28}$= +1.78 (*c* 0.2, $CHCl_3$).

HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 90%.


f1 (ppm)


f1 (ppm)


-128.30
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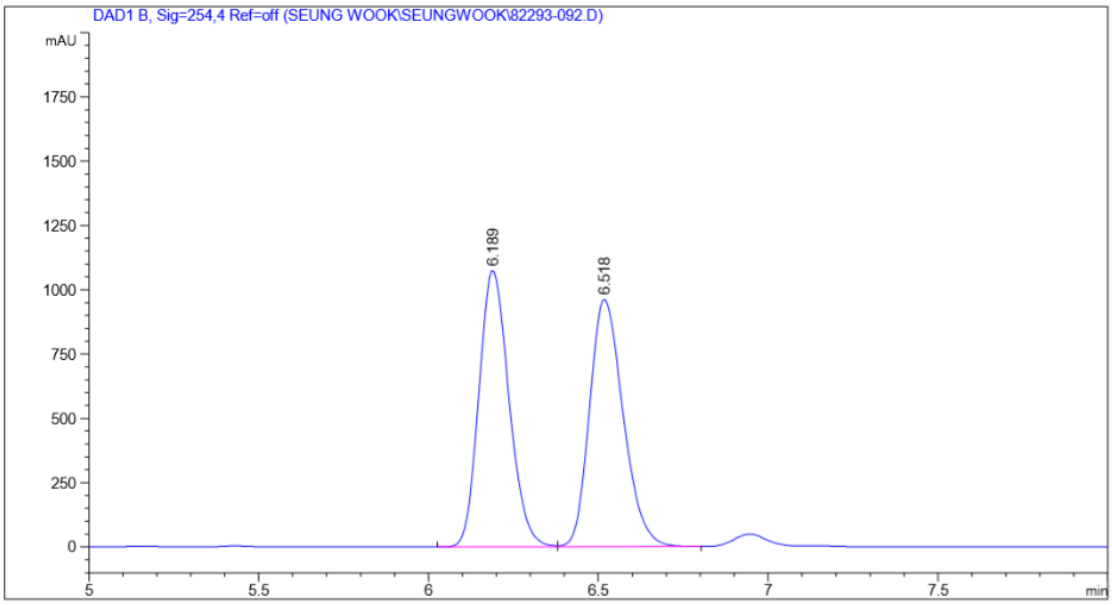
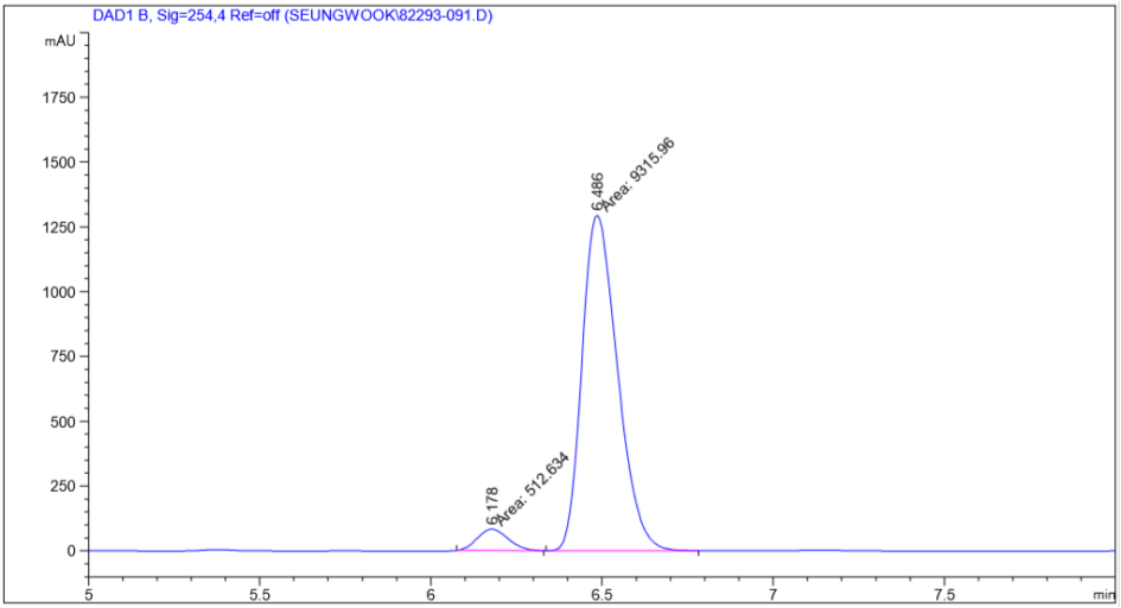
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-50
-100
-150
-200
-250
-300
-350
f1 (ppm)

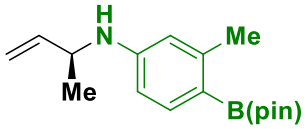


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.189	BV	0.0958	6617.14795	1075.90527	50.0313
2	6.518	VB	0.1061	6608.87158	962.52228	49.9687



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.178	MM	0.1040	512.63373	82.19147	5.2157
2	6.486	MM	0.1198	9315.95605	1295.97278	94.7843

(*S*)-*N*-(but-3-en-2-yl)-3-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (5.4d)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (205.1 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 40 hr). The title compound was obtained in 85% yield (98.6 mg, 0.34 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.58 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.7 Hz, 1H), 6.40 (d, *J* = 7.0 Hz, 2H), 5.83 (ddd, *J* = 17.2, 10.4, 5.3 Hz, 1H), 5.20 (dt, *J* = 17.2, 1.4 Hz, 1H), 5.08 (dt, *J* = 10.4, 1.3 Hz, 1H), 4.04 (p, *J* = 6.5 Hz, 1H), 3.74 (br, 1H), 2.47 (s, 3H), 1.33 – 1.29 (m, 15H).

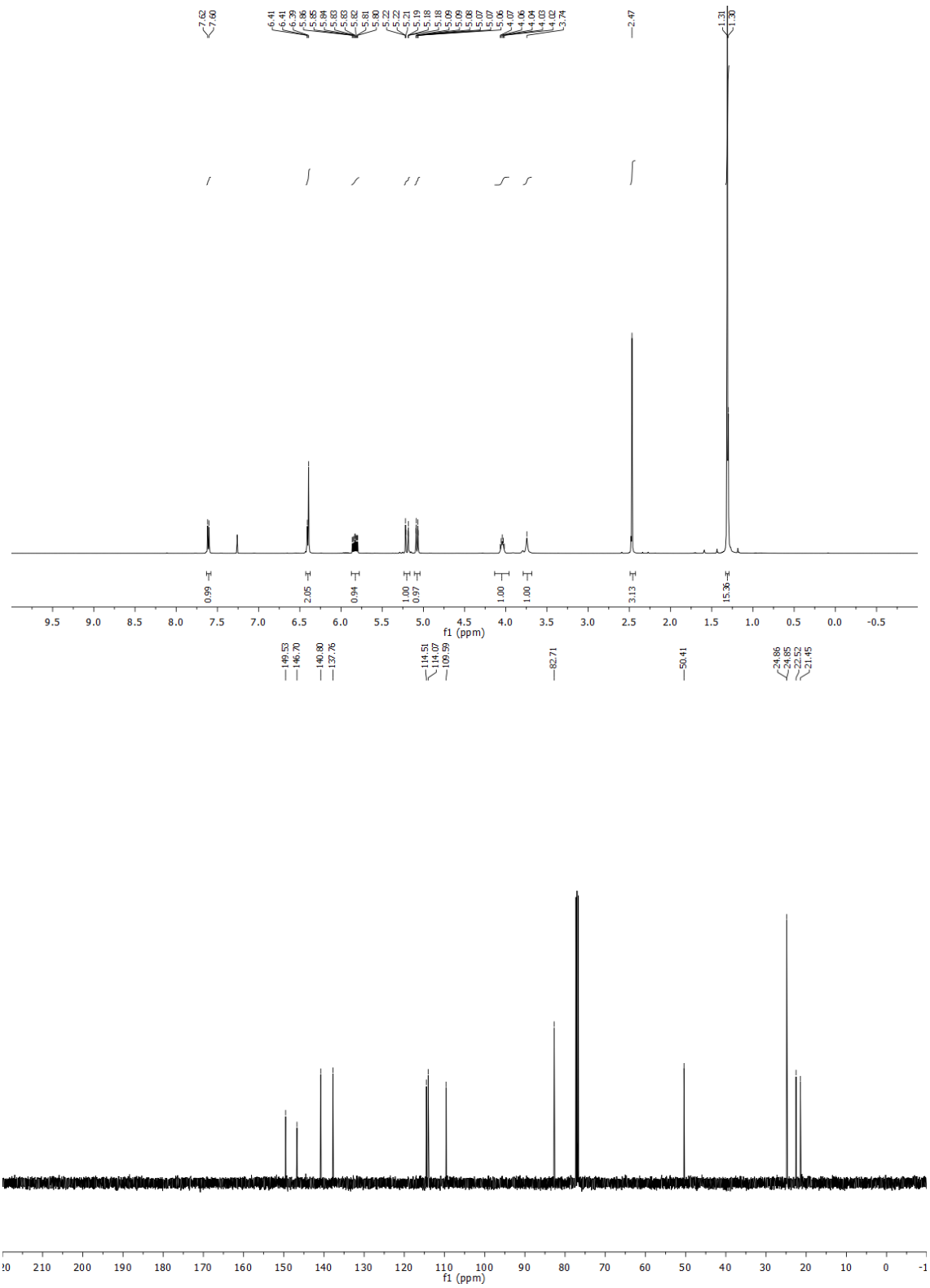
^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.5, 146.7, 140.8, 137.8, 114.5, 114.1, 109.6, 82.7, 50.4, 24.9, 24.9, 22.5, 21.5.

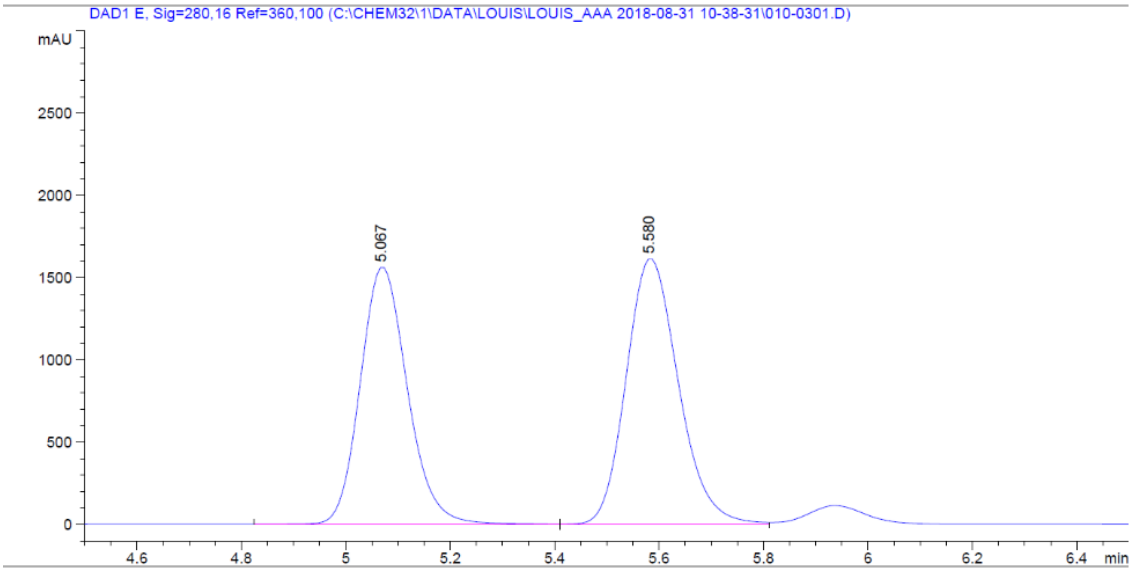
HRMS (ESI): Calculated for $C_{17}H_{26}NO_2$ [M+H$^+$] = 288.2132, Found 288.2138.

FTIR (neat): 2978, 2362, 1602, 1349, 1215, 1146, 754 cm^{-1}.

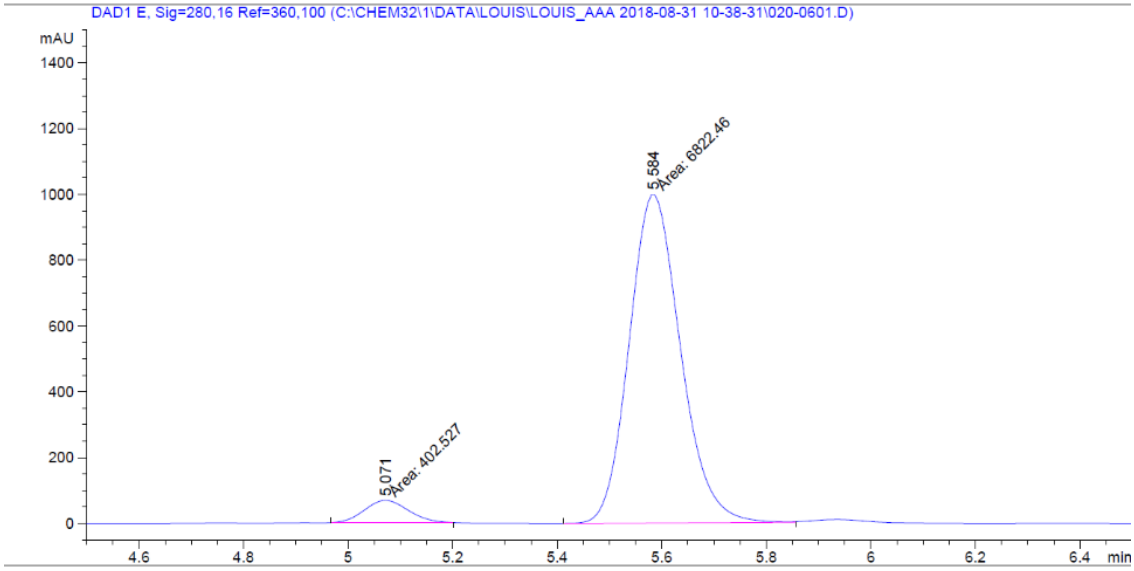
$[\alpha]_D^{28}$= –1.0 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 280 nm), *ee* = 89%.



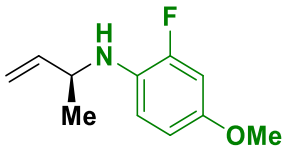


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.067	VV	0.0972	9832.24707	1566.88391	46.6365
2	5.580	VV	0.1091	1.12505e4	1618.21069	53.3635



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.071	MM	0.0981	402.52716	68.38924	5.5713
2	5.584	MM	0.1136	6822.46045	1000.98846	94.4287

(*S*)-N-(but-3-en-2-yl)-2-fluoro-4-methoxyaniline (5.4e)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (124.2 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 78% yield (67.1 mg, 0.34 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.58 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.69 – 6.60 (m, 2H), 6.56 (dd, *J* = 8.9, 2.7 Hz, 1H), 5.82 (ddd, *J* = 16.7, 10.3, 5.8 Hz, 1H), 5.20 (dd, *J* = 17.3, 1.4 Hz, 1H), 5.08 (dd, *J* = 10.4, 1.4 Hz, 1H), 3.91 (p, *J* = 6.5 Hz, 1H), 3.73 (s, 3H), 3.52 (br, 1H), 1.33 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.08, 151.5 (d, *J* = 9.9 Hz), 150.71, 141.28, 129.7 (d, *J* = 12.1 Hz), 114.4 (d, *J* = 4.6 Hz), 114.19, 109.1 (d, *J* = 3.3 Hz), 102.38 (d, *J* = 22.7 Hz), 55.8, 51.9, 21.7.

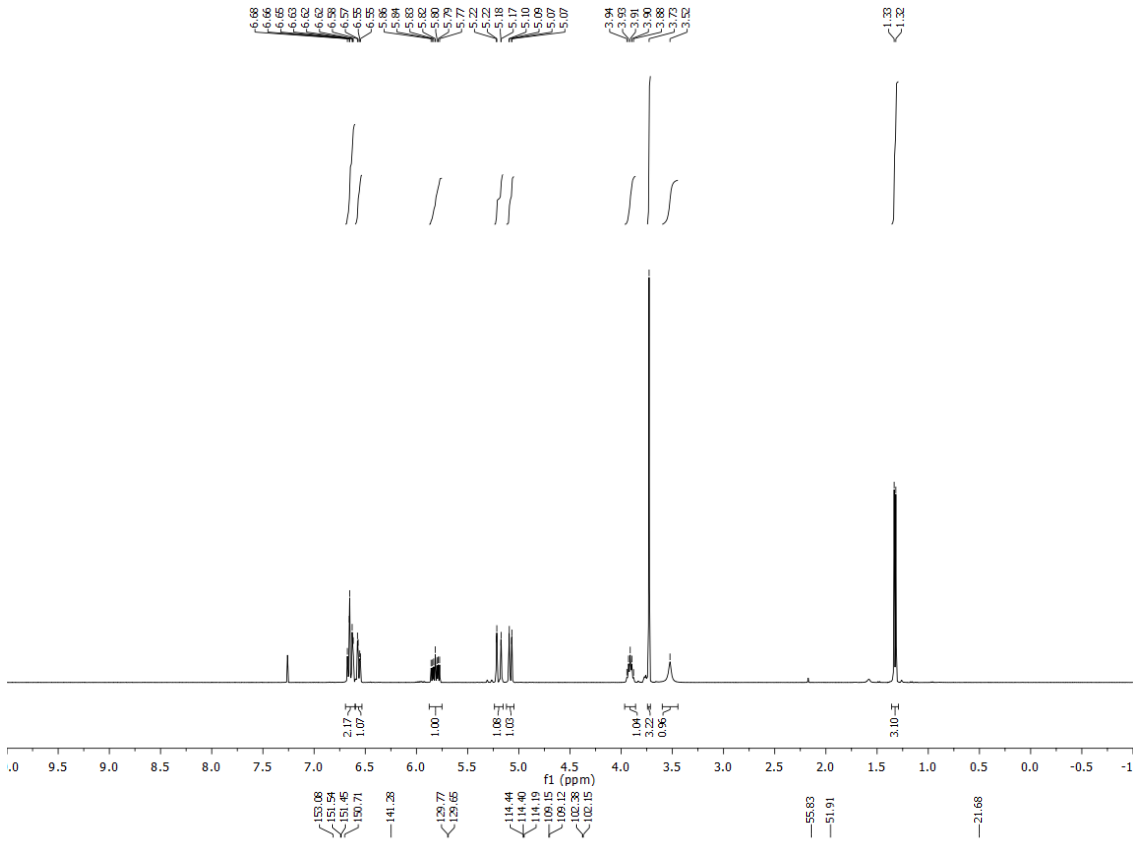
^{19}F NMR (471 MHz, $CDCl_3$): δ = –133.0 (dd, *J* = 12.9, 9.8 Hz, 1F).

HRMS (ESI): Calculated for $C_{11}H_{14}FNO$ [M+H$^+$] = 196.1132, Found 196.1129.

FTIR (neat): 2964, 1515, 1279, 1214, 1152, 1035, 923, 755 cm^{-1}.

$[\alpha]_D^{28}$= +6.3 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AS-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 88%.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3.88
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2.17
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1.00
1.08
1.03
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0.96
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f1 (ppm)
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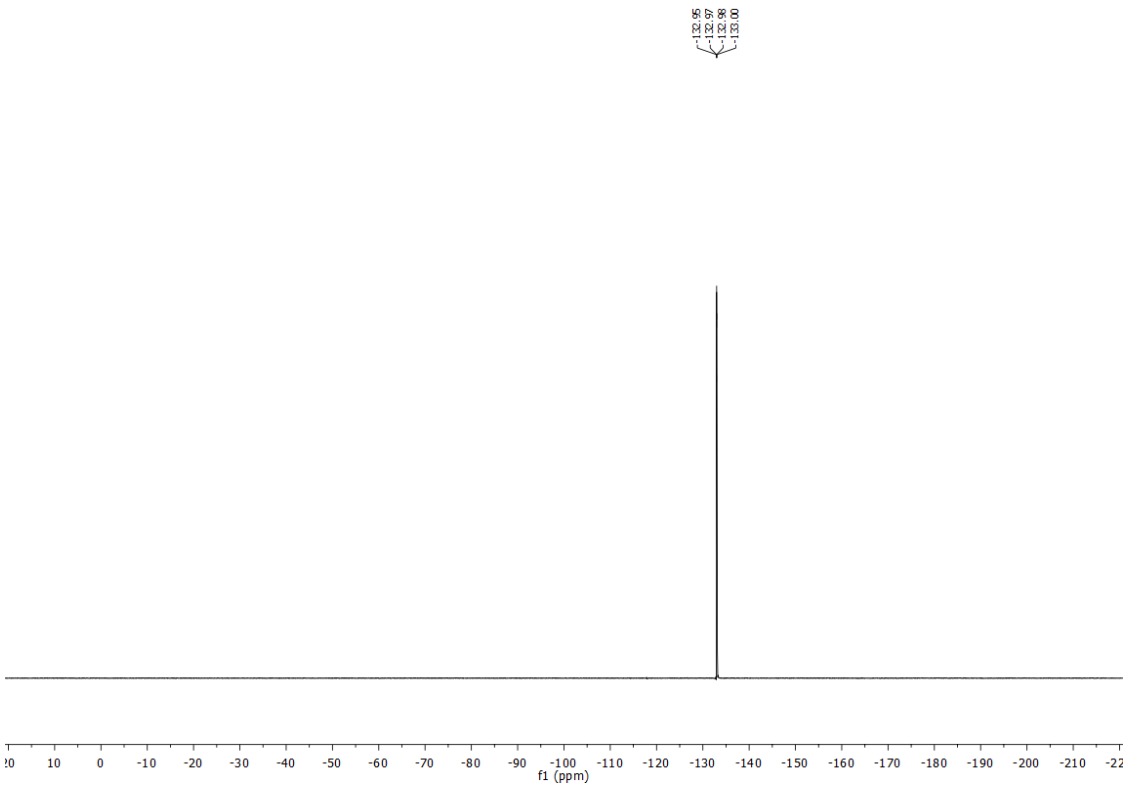
21.68
f1 (ppm)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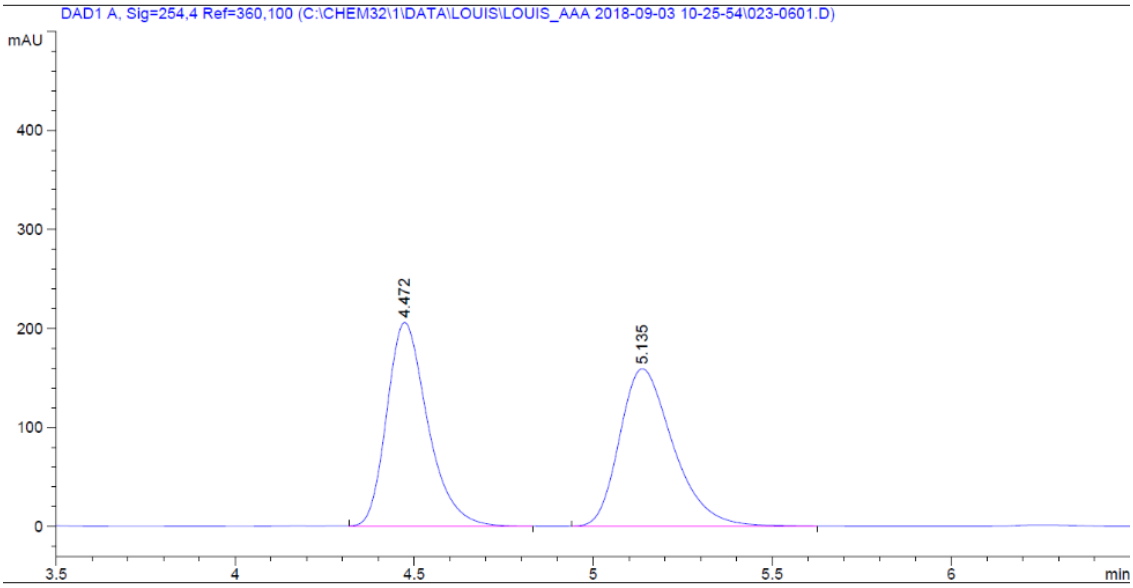
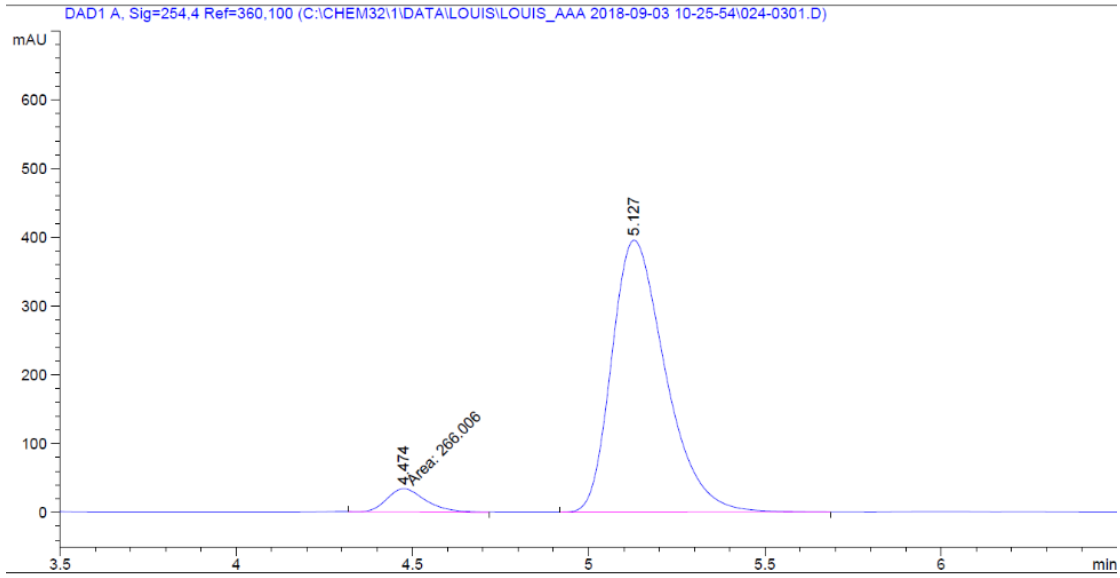
f1 (ppm)

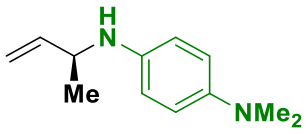


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.472	BB	0.1229	1642.40771	206.31035	49.6953
2	5.135	BB	0.1598	1662.54736	159.29028	50.3047



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.474	MM	0.1299	266.00577	34.12355	5.9477
2	5.127	BB	0.1639	4206.39307	396.07928	94.0523

(*S*)-N1-(but-3-en-2-yl)-N4,N4-dimethylbenzene-1,4-diamine (5.4f)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (120.0 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 89% yield (74.5 mg, 0.39 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–4:1).

TLC (SiO_2) R_f = 0.34 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.74 – 6.68 (m, 2H), 6.64 – 6.57 (m, 2H), 5.84 (ddd, *J* = 17.2, 10.3, 5.7 Hz, 1H), 5.20 (dt, *J* = 17.2, 1.4 Hz, 1H), 5.06 (dt, *J* = 10.4, 1.4 Hz, 1H), 3.90 (ttd, *J* = 6.6, 5.3, 1.3 Hz, 1H), 3.25 (br, 1H), 2.81 (s, 6H), 1.28 (d, *J* = 6.6 Hz, 3H).

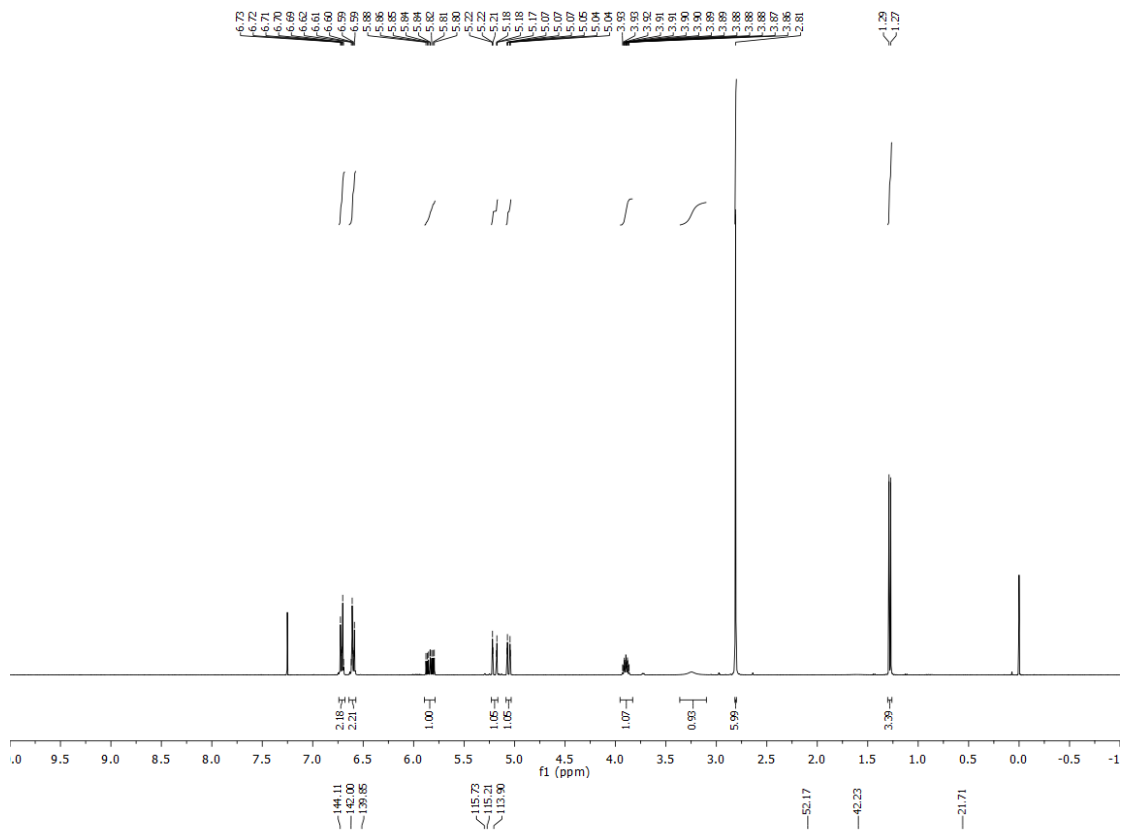
^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.1, 142.0, 139.9, 115.7, 115.2, 113.9, 52.2, 42.2, 21.7.

HRMS (ESI): Calculated for $C_{12}H_{18}N_2$ [M+H$^+$] = 191.1543, Found 191.1535.

FTIR (neat): 2979, 2361, 1515, 1216, 814, 753 cm^{-1}.

$[\alpha]_D^{28}$= –26.3 (*c* 0.2, $CHCl_3$).

HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 254 nm), *ee* = 90%.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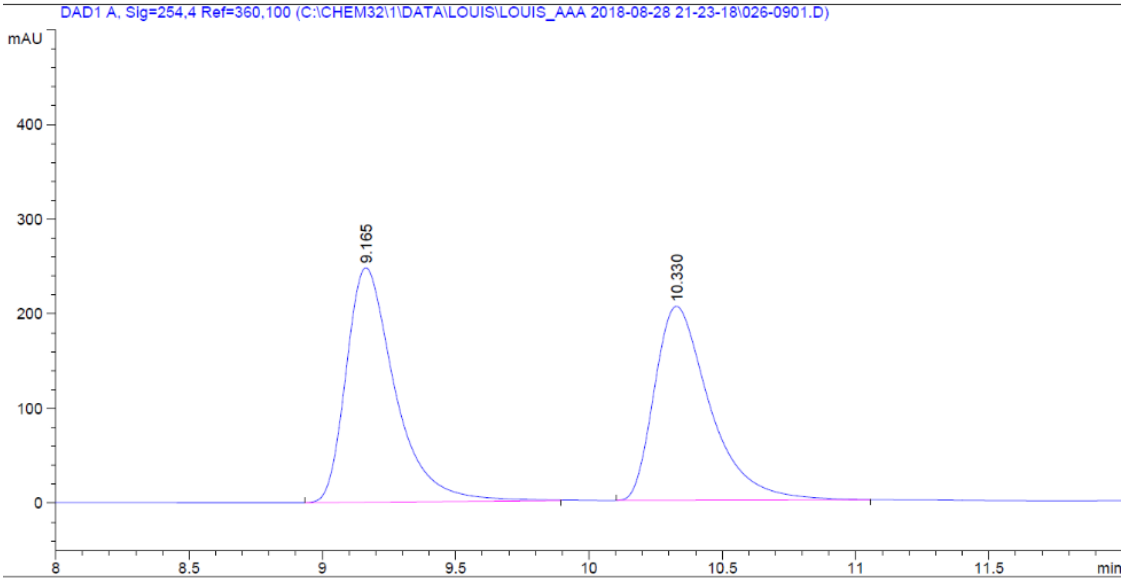
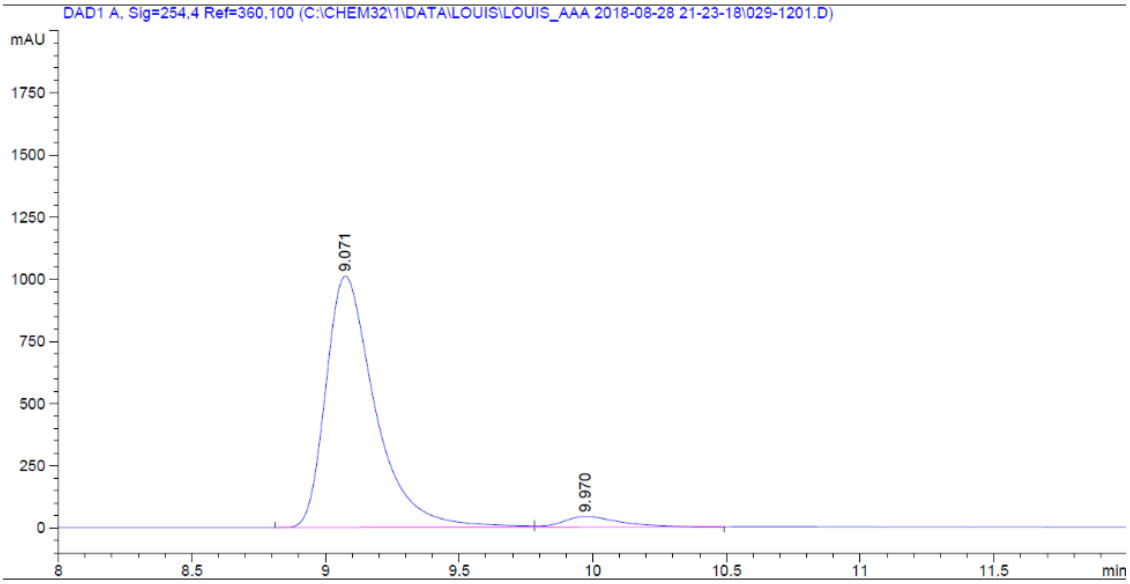
3.88
3.87
3.86
2.81
1.29
1.27
2.18
2.21
1.00
1.05
1.05
1.07
0.93
5.99
3.39
f1 (ppm)
144.11
142.00
139.85
115.73
115.21
113.90
52.17
42.23
21.71
f1 (ppm)

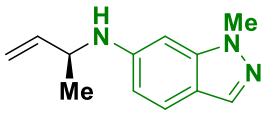


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.165	BB	0.1925	3157.57959	248.03835	51.5715
2	10.330	BB	0.2187	2965.14429	205.01358	48.4285



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.071	BV	0.1917	1.29836e4	1011.83209	95.0162
2	9.970	VB	0.2304	681.02032	43.55310	4.9838

(*S*)-N-(but-3-en-2-yl)-1-methyl-1H-indazol-6-amine (5.4g)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (129.5 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 30 hr). The title compound was obtained in 81% yield (71.7 mg, 0.36 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 30% over 20 min).

TLC (SiO_2) R_f = 0.38 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 1.0 Hz, 1H), 7.43 (dd, *J* = 8.6, 0.6 Hz, 1H), 6.49 (dd, *J* = 8.7, 1.9 Hz, 1H), 6.33 (dt, *J* = 1.7, 0.8 Hz, 1H), 5.88 (ddd, *J* = 17.2, 10.3, 5.5 Hz, 1H), 5.27 (dt, *J* = 17.2, 1.4 Hz, 1H), 5.13 (dt, *J* = 10.4, 1.3 Hz, 1H), 4.07 (dtd, *J* = 8.1, 6.7, 5.2 Hz, 1H), 3.93 (s, 3H), 3.91 – 3.82 (m, 1H), 1.37 (d, *J* = 6.6 Hz, 3H).

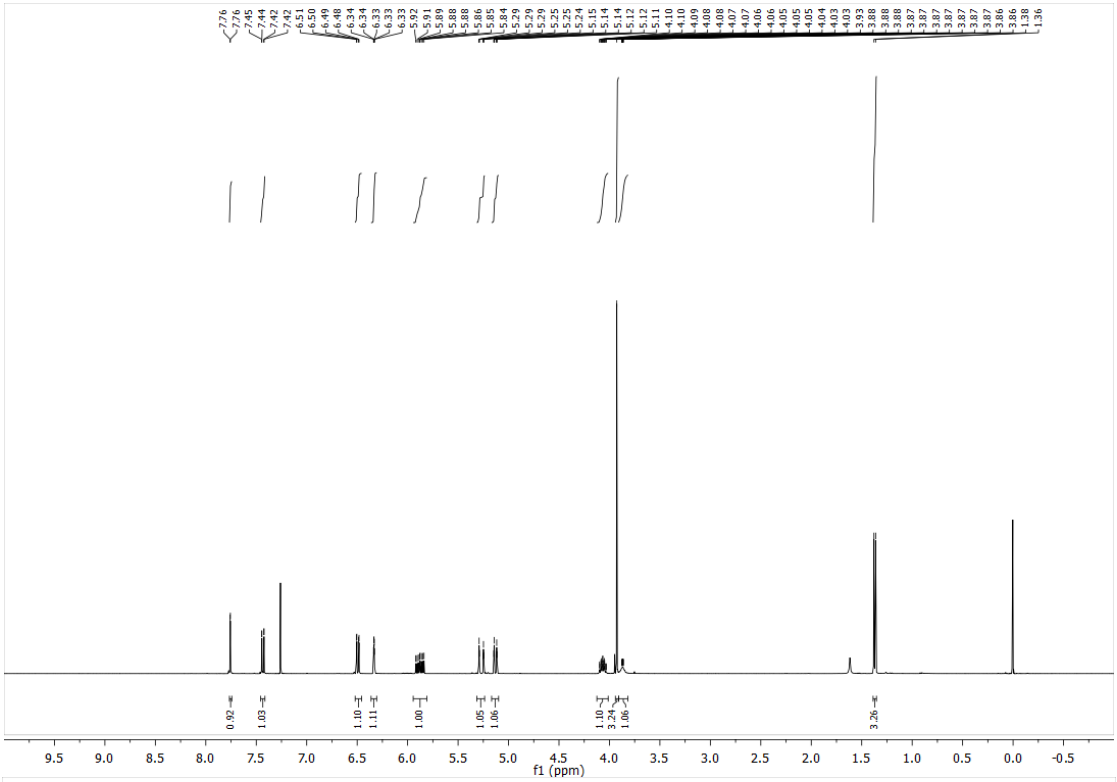
^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.6, 141.8, 140.8, 132.6, 121.5, 117.0, 114.3, 112.4, 88.6, 51.3, 35.2, 21.6.

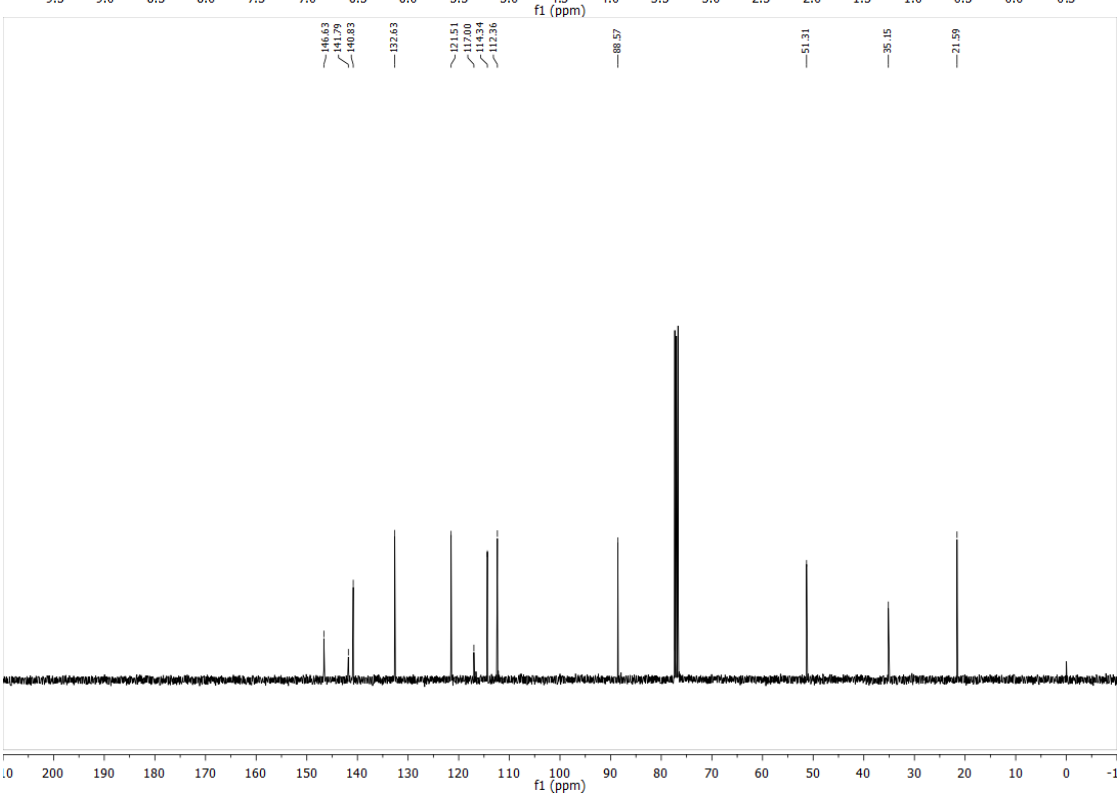
HRMS (ESI): Calculated for $C_{12}H_{15}N_3$ [M+H$^+$] = 202.1339, Found 202.1339.

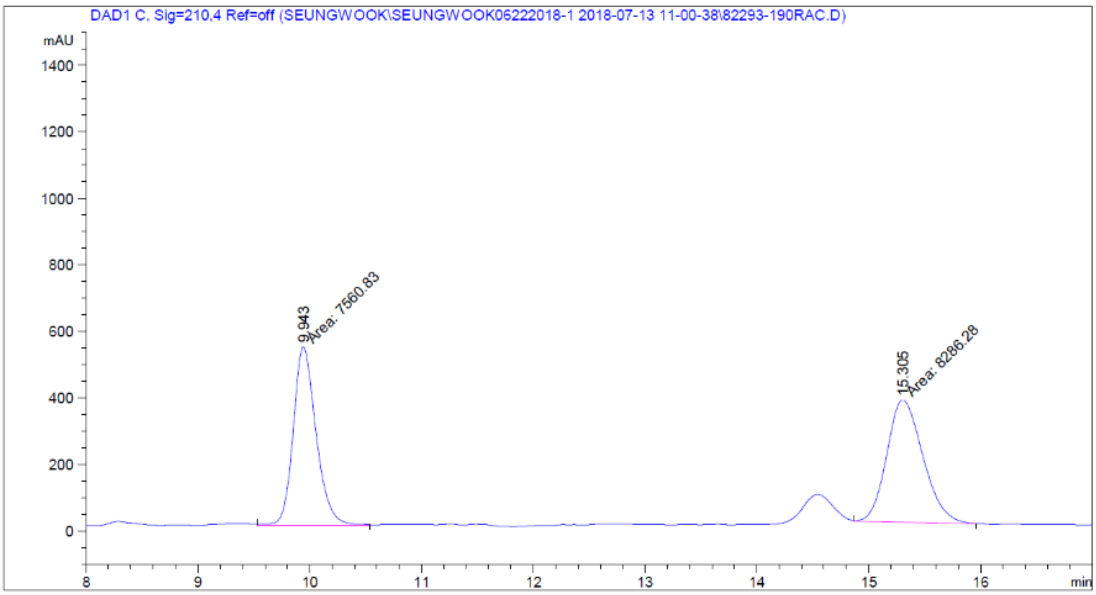
FTIR (neat): 3312, 2973, 1624, 1492, 1254, 1098, 982, 919, 732, 620 cm^{-1}.

$[\alpha]_D^{28}$= –60.3 (*c* 0.2, $CHCl_3$).

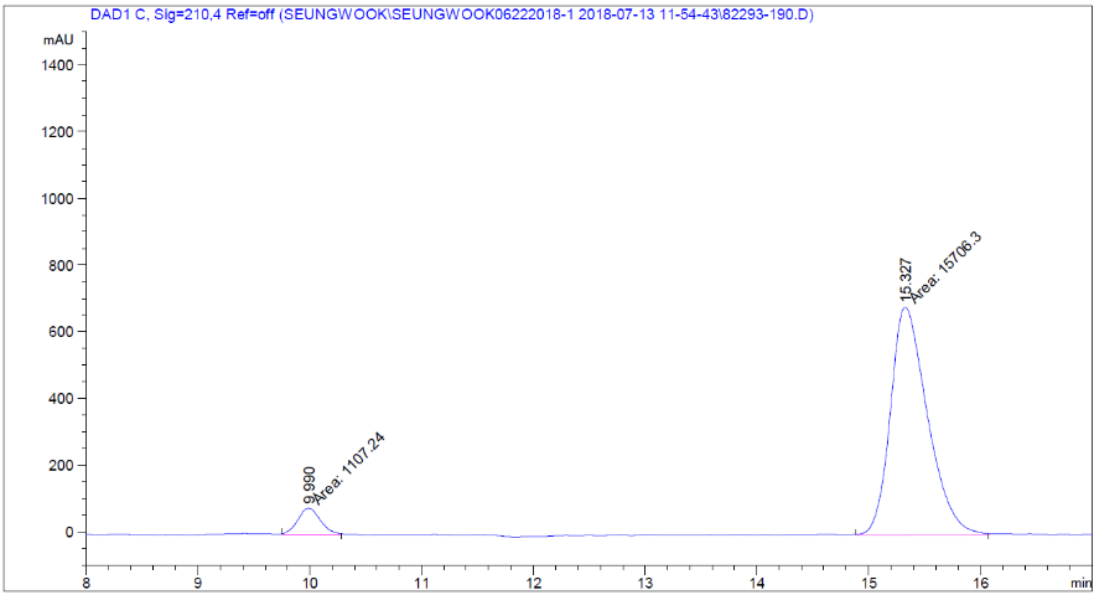
HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 90:10, 1.00 mL/min, 210 nm), *ee* = 87%.


f1 (ppm)


f1 (ppm)

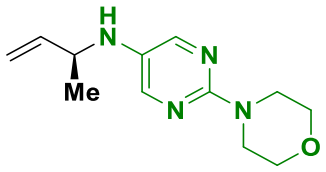


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.943	MM	0.2355	7560.83301	535.11896	47.7111
2	15.305	MM	0.3755	8286.28027	367.83386	52.2889



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.990	MM	0.2335	1107.24475	79.04131	6.5854
2	15.327	MM	0.3831	1.57063e4	683.38605	93.4146

(*S*)-*N*-(but-3-en-2-yl)-2-morpholinopyrimidin-5-amine (5.4h)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (158.6 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 82% yield (84.5 mg, 0.36 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 80% over 20 min).

TLC (SiO_2) R_f = 0.37 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (s, 2H), 5.76 (ddd, *J* = 17.2, 10.3, 6.2 Hz, 1H), 5.18 (dt, *J* = 17.2, 1.3 Hz, 1H), 5.11 (dt, *J* = 10.3, 1.2 Hz, 1H), 3.87 – 3.80 (m, 1H), 3.79 – 3.76 (m, 4H), 3.63 (dd, *J* = 5.7, 4.0 Hz, 4H), 1.31 (d, *J* = 6.6 Hz, 3H).

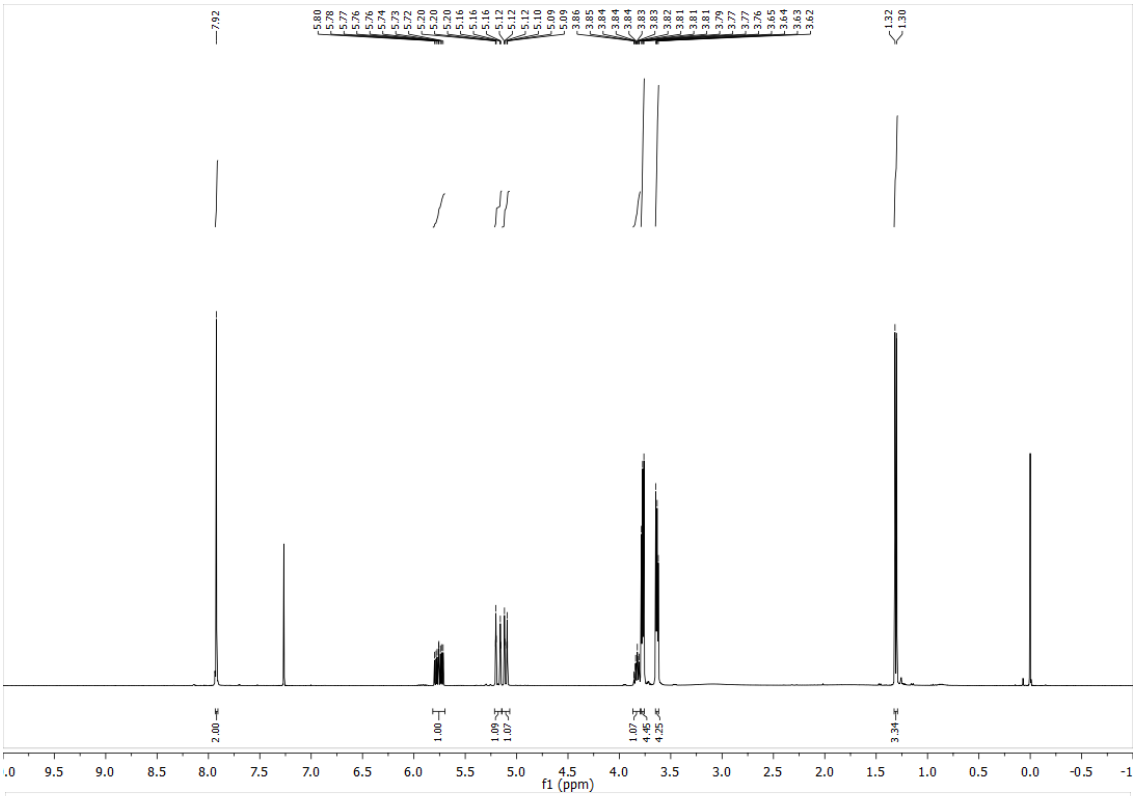
^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2, 145.2, 140.6, 133.4, 115.1, 66.9, 52.8, 45.2, 21.7.

HRMS (ESI): Calculated for $C_{12}H_{18}N_4O$ [M+H$^+$] = 235.1553, Found 235.1555.

FTIR (neat): 2968, 1480, 1444, 1264, 1116, 954, 731 cm^{-1}.

$[\alpha]_D^{28}$ = +9.92 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 85:15, 1.00 mL/min, 230 nm), *ee* = 89%.


7.92
5.80
5.78
5.77
5.76
5.76
5.74
5.73
5.72
5.20
5.20
5.20
5.16
5.16
5.16
5.12
5.12
5.12
5.10
5.09
5.08
3.86
3.85
3.84
3.84
3.84
3.83
3.83
3.82
3.81
3.81
3.81
3.79
3.77
3.77
3.76
3.65
3.64
3.63
3.62
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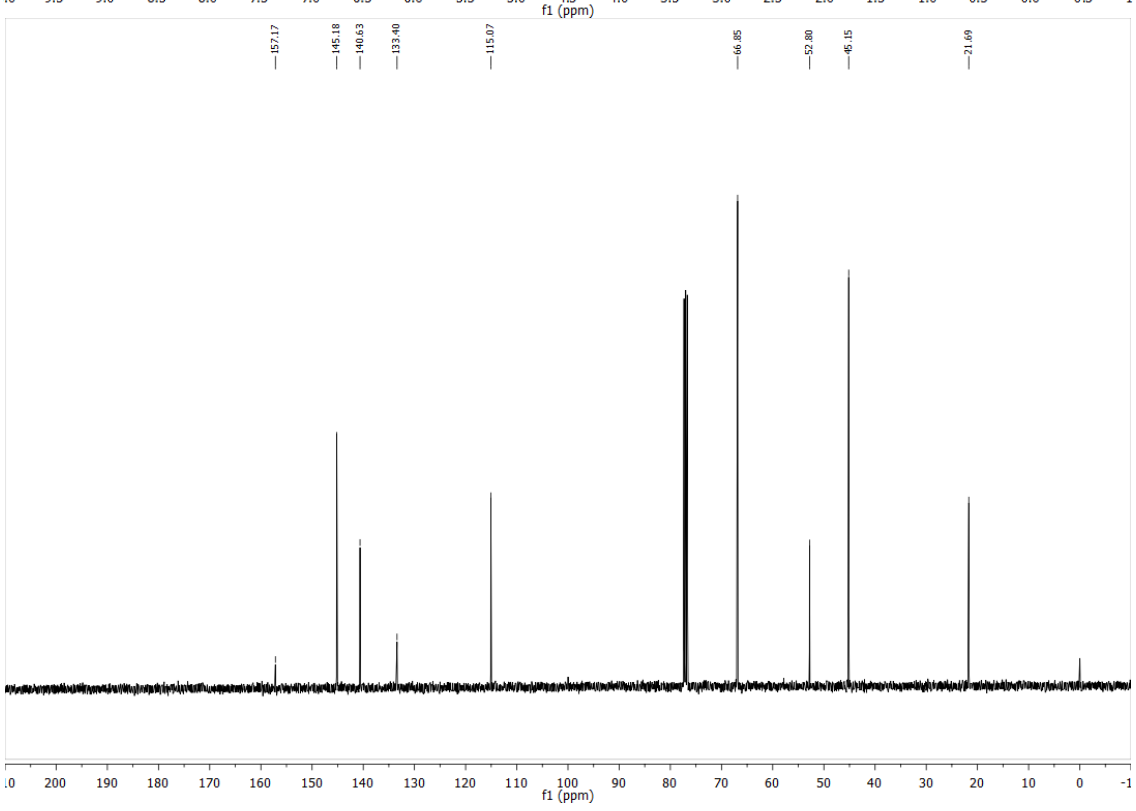
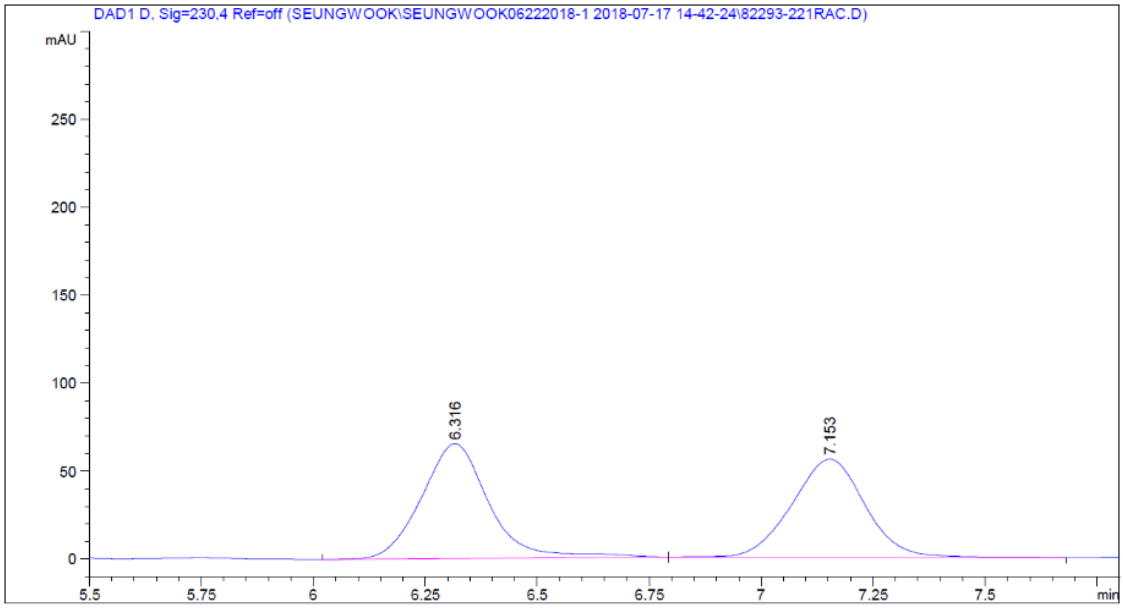
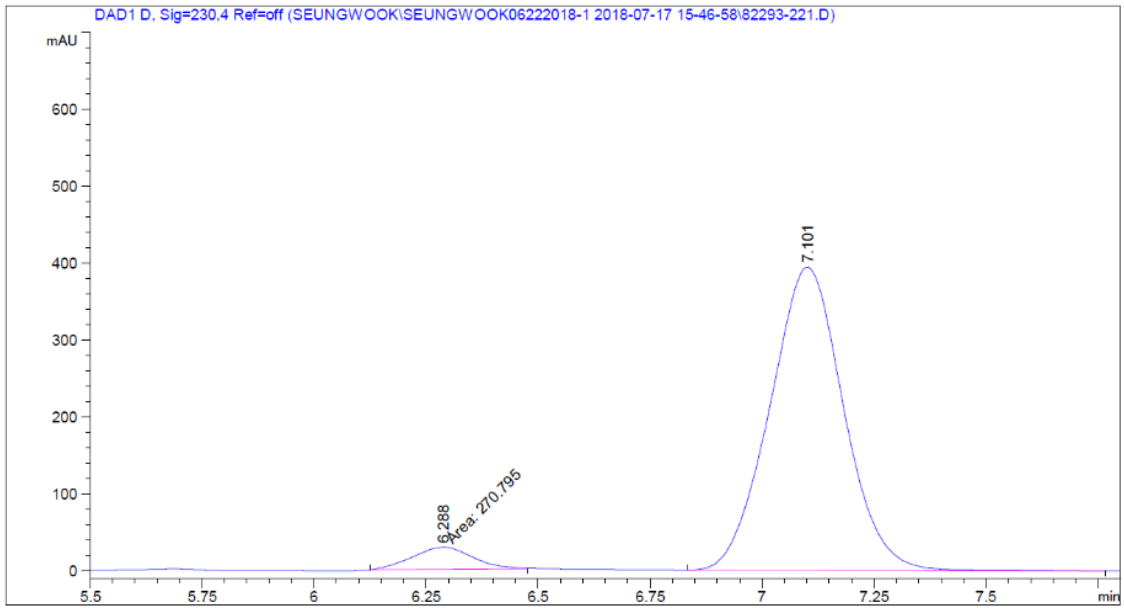
1.00
1.09
1.07
1.07
4.45
4.25
3.34
f1 (ppm)


157.17
145.18
140.63
133.40
115.07
66.85
52.80
45.15
21.69
f1 (ppm)

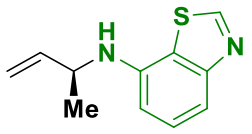


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.316	BB	0.1542	685.04590	65.40804	51.8899
2	7.153	BB	0.1726	635.14404	55.87535	48.1101



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.288	MM	0.1566	270.79501	28.82882	5.6630
2	7.101	BB	0.1734	4511.04883	394.44131	94.3370

(*S*)-*N*-(but-3-en-2-yl)benzo[d]thiazol-7-amine (5.4i)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (132.2 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 30 hr). The title compound was obtained in 81% yield (72.8 mg, 0.36 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 30% over 20 min).

TLC (SiO_2) R_f = 0.52 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.92 (s, 1H), 7.57 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 6.67 (d, *J* = 7.9 Hz, 1H), 5.90 (ddd, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.26 (dt, *J* = 17.3, 1.4 Hz, 1H), 5.13 (dt, *J* = 10.3, 1.3 Hz, 1H), 4.20 (dtd, *J* = 8.2, 6.7, 1.5 Hz, 1H), 3.60 (d, *J* = 6.7 Hz, 1H), 1.42 (d, *J* = 6.6 Hz, 3H).

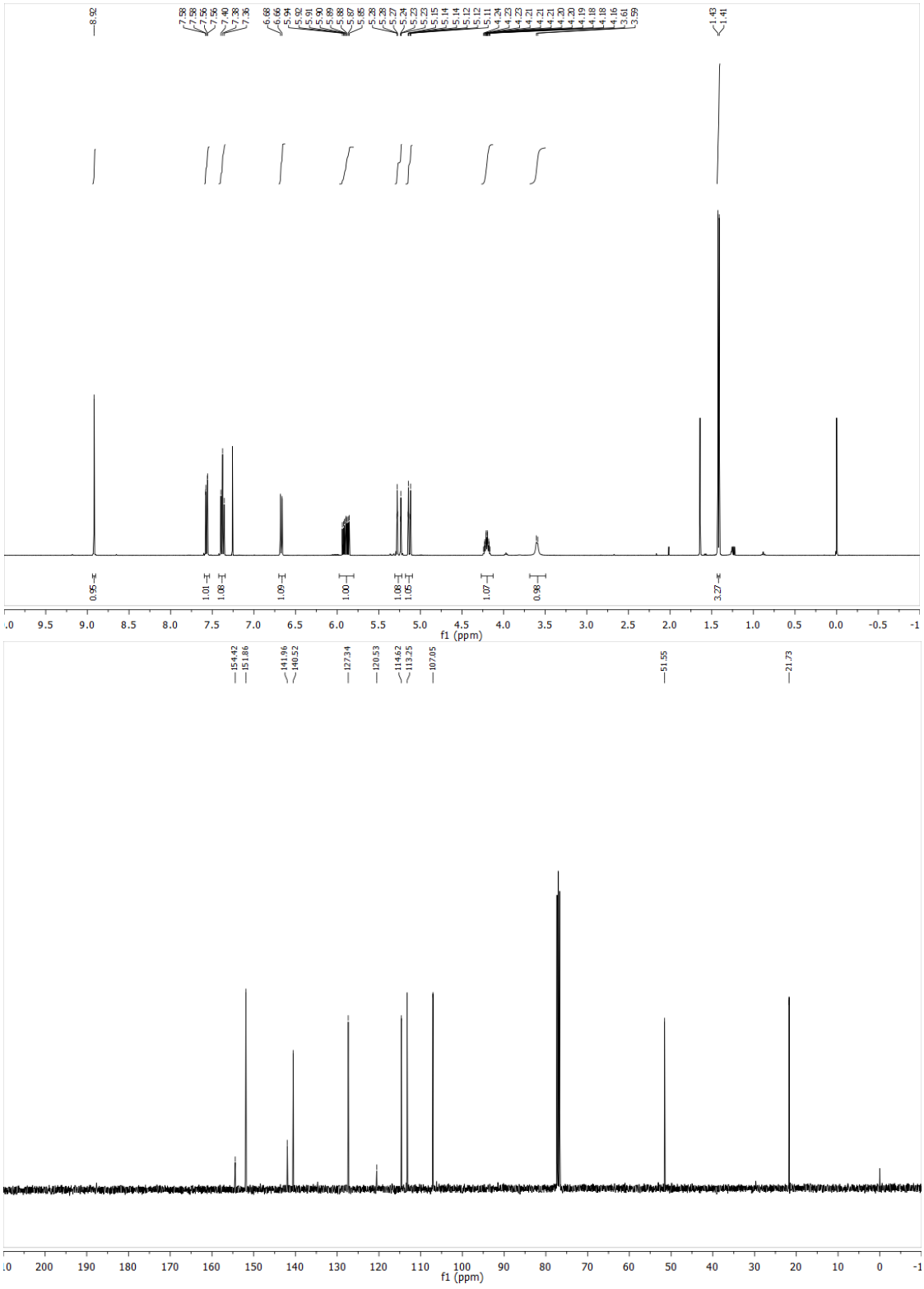
^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.4, 151.9, 142.0, 140.5, 127.3, 120.5, 114.6, 113.3, 107.1, 51.6, 21.7.

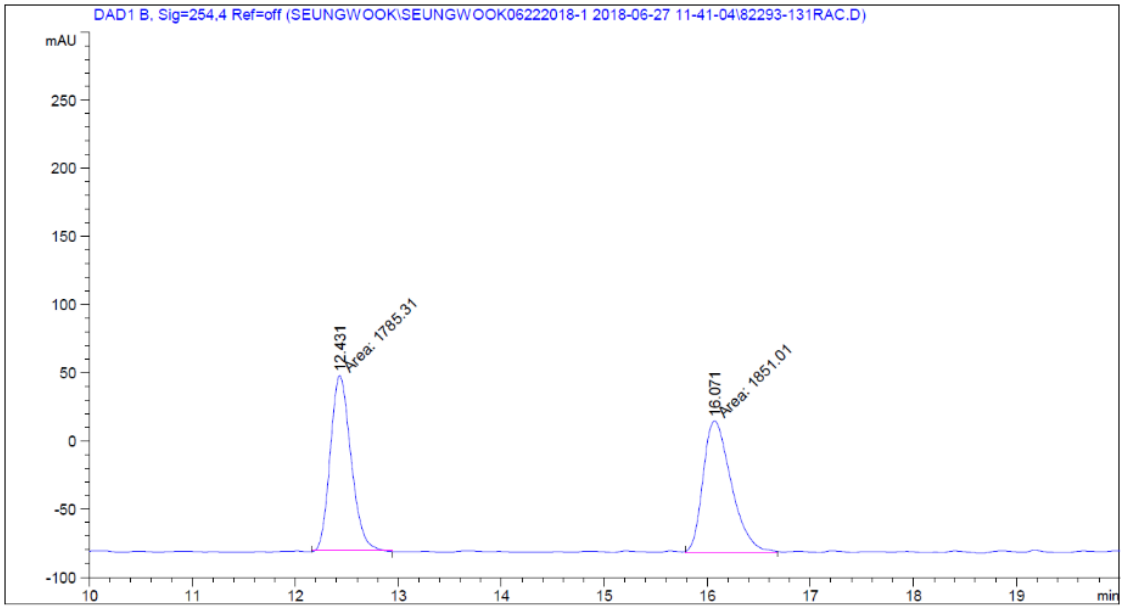
HRMS (ESI): Calculated for $C_{11}H_{12}N_2S$ [M+H$^+$] = 205.0794, Found 205.0802.

FTIR (neat): 3292, 2974, 1575, 1472, 1287, 1145, 1049, 920, 774, 717 cm^{-1}.

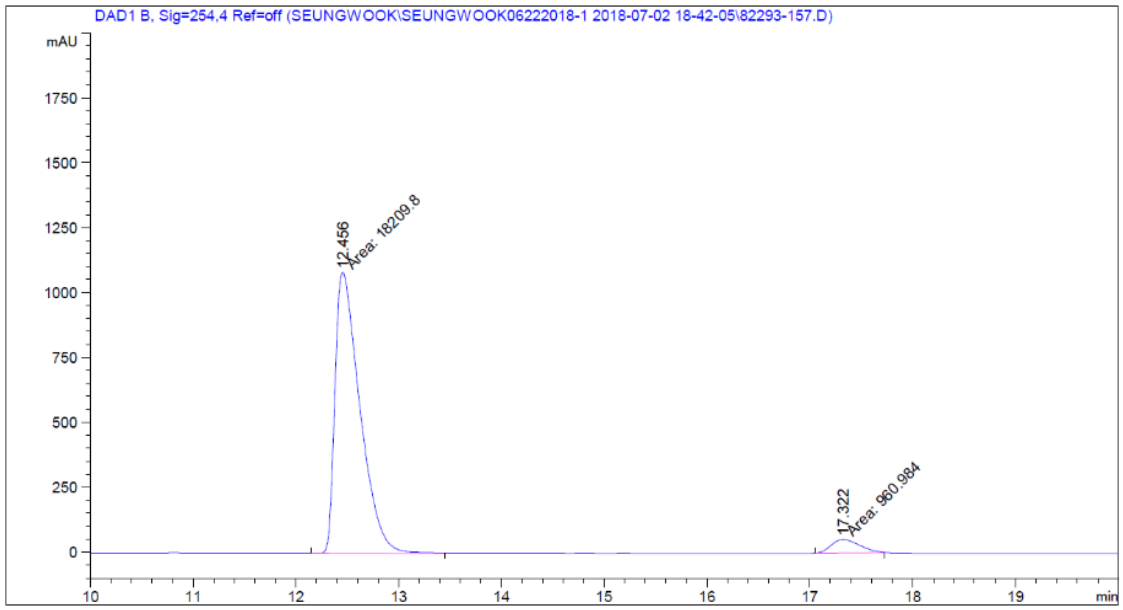
$[\alpha]_D^{28}$= +31.68 (*c* 0.2, $CHCl_3$).

HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 97.5:2.5, 1.00 mL/min, 254 nm), *ee* = 90%.


8.92
7.58
7.58
7.56
7.56
7.40
7.38
7.36
6.68
6.66
5.94
5.92
5.91
5.90
5.89
5.88
5.87
5.85
5.28
5.28
5.27
5.24
5.23
5.23
5.15
5.14
5.14
5.12
5.12
5.11
4.24
4.23
4.23
4.21
4.21
4.21
4.20
4.20
4.19
4.18
4.18
4.16
3.61
3.59
1.43
1.41
0.95
1.01
1.08
1.09
1.00
1.08
1.05
1.07
0.98
3.27
f1 (ppm)
154.42
151.86
141.96
140.52
127.34
120.53
114.62
113.25
107.05
51.55
21.73
f1 (ppm)

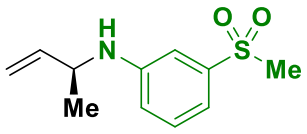


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.431	MM	0.2323	1785.31116	128.06386	49.0967
2	16.071	MM	0.3197	1851.00720	96.50237	50.9033



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.456	MM	0.2805	1.82098e4	1082.00134	94.9872
2	17.322	MM	0.3134	960.98425	51.09868	5.0128

(*S*)-N-(but-3-en-2-yl)-3-(methylsulfonyl)aniline (5.4j)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (150.7 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 40 hr). The title compound was obtained in 76% yield (75.3 mg, 0.33 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–4:1).

TLC (SiO_2) R_f = 0.41 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30 (t, *J* = 7.9 Hz, 1H), 7.18 (ddd, *J* = 7.7, 1.7, 0.9 Hz, 1H), 7.10 (t, *J* = 2.1 Hz, 1H), 6.84 – 6.74 (m, 1H), 5.79 (ddd, *J* = 17.0, 10.3, 5.4 Hz, 1H), 5.22 (dd, *J* = 17.3, 1.3 Hz, 1H), 5.12 (dt, *J* = 10.3, 1.2 Hz, 1H), 4.13 – 3.90 (m, 2H), 3.01 (s, 3H), 1.34 (d, *J* = 6.3 Hz, 3H).

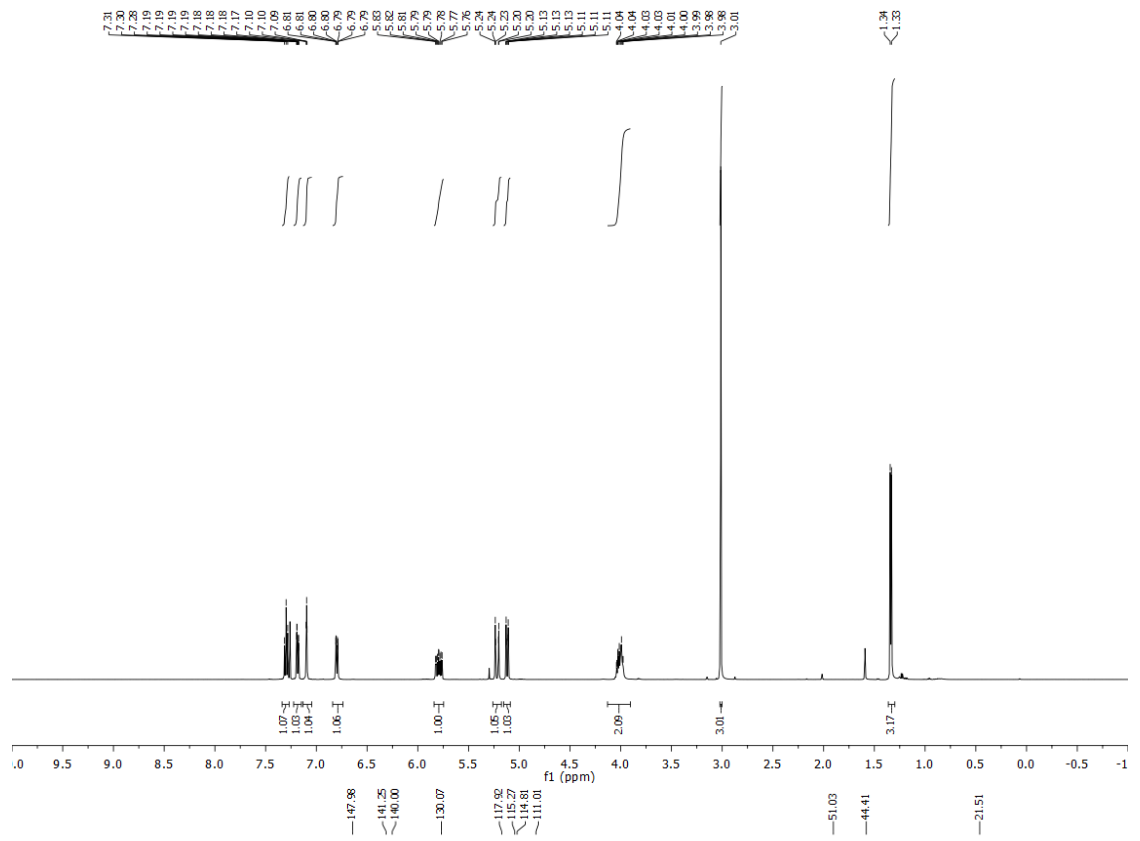
^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.0, 141.3, 140.0, 130.1, 118.0, 115.3, 114.8, 111.0, 51.0, 44.4, 21.5.

HRMS (ESI): Calculated for $C_{11}H_{15}NO_2S$ [M+H$^+$] = 226.0896, Found 226.0900.

FTIR (neat): 3379, 1599, 1487, 1296, 1141, 961, 757, 683 cm^{-1}.

$[\alpha]_D^{28}$ = –33.3 (*c* 1.0, $CHCl_3$).

HPLC (Two connected chiralcel AD-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 254 nm), *ee* = 91%.


7.31
7.30
7.28
7.19
7.19
7.19
7.19
7.18
7.18
7.18
7.17
7.10
7.10
7.09
6.81
6.81
6.80
6.80
6.79
6.79
6.79
5.83
5.82
5.81
5.79
5.79
5.78
5.77
5.76
5.24
5.24
5.23
5.20
5.20
5.13
5.13
5.13
5.11
5.11
5.11
4.04
4.04
4.03
4.03
4.01
4.00
3.99
3.98
3.98
3.01
1.34
1.33
1.07
1.03
1.04
1.06
1.00
1.05
1.03
2.09
3.01
3.17
f1 (ppm)
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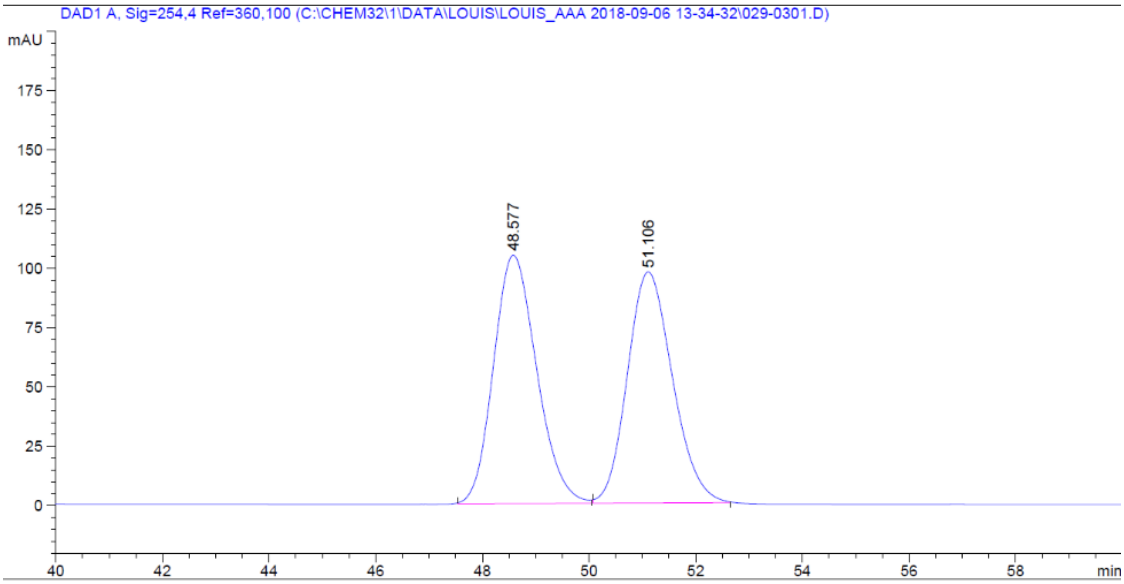
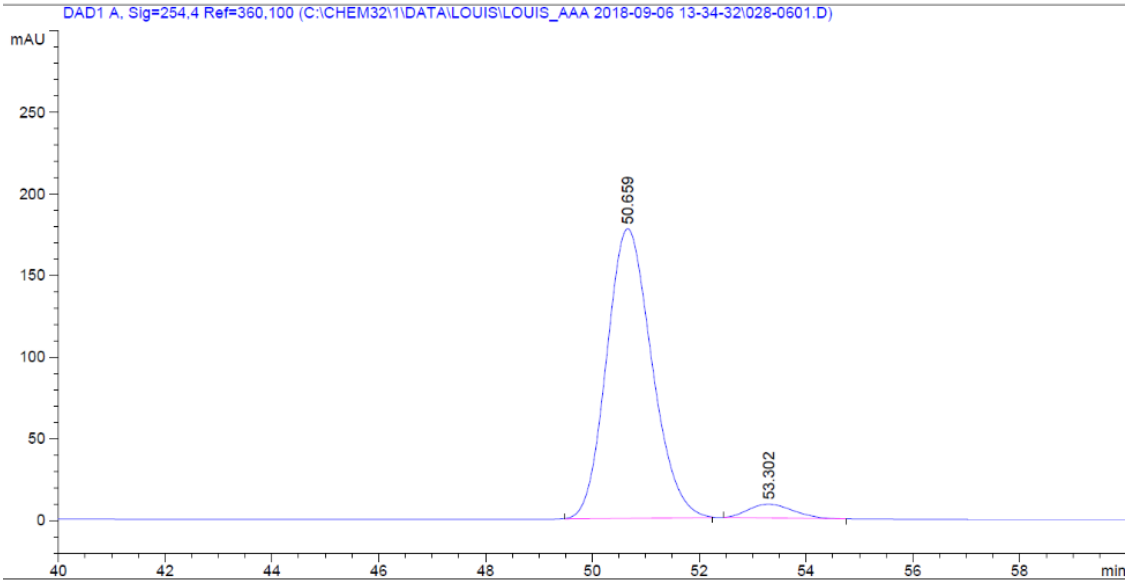
115.27
114.81
111.01
51.03
44.41
21.51
f1 (ppm)

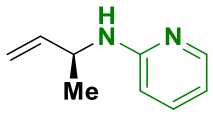


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	48.577	BB	0.8665	5887.28076	104.62562	50.7171
2	51.106	BB	0.8990	5720.79297	97.43137	49.2829



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	50.659	BB	0.9036	1.04261e4	177.42329	95.5102
2	53.302	BB	0.7200	490.10962	8.48417	4.4898

(*S*)-N-(but-3-en-2-yl)pyridin-2-amine (5.4k)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (82.8 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 74% yield (48.3 mg, 0.33 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–4:1).

TLC (SiO_2) R_f = 0.45 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07 (ddd, *J* = 5.0, 2.0, 0.9 Hz, 1H), 7.40 (ddd, *J* = 8.8, 7.1, 1.9 Hz, 1H), 6.56 (ddd, *J* = 7.1, 5.0, 1.0 Hz, 1H), 6.36 (dt, *J* = 8.4, 1.0 Hz, 1H), 5.87 (ddd, *J* = 17.2, 10.4, 5.3 Hz, 1H), 5.21 (dt, *J* = 17.2, 1.4 Hz, 1H), 5.08 (dt, *J* = 10.4, 1.4 Hz, 1H), 4.48 (br, 1H), 4.32 – 4.20 (m, 1H), 1.33 (d, *J* = 6.7 Hz, 3H).

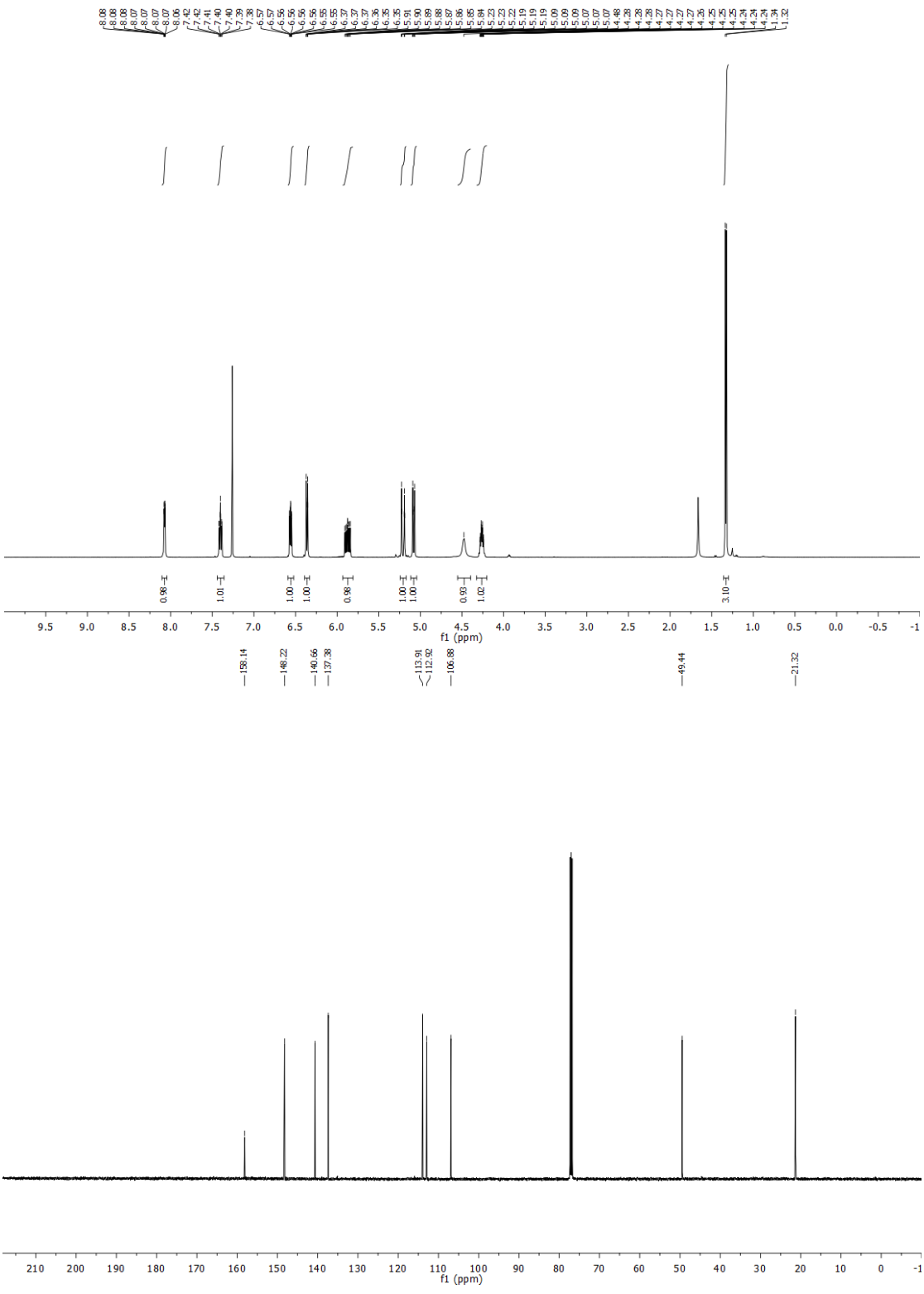
^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.1, 148.2, 140.7, 137.4, 113.9, 112.9, 106.9, 49.4, 21.3.

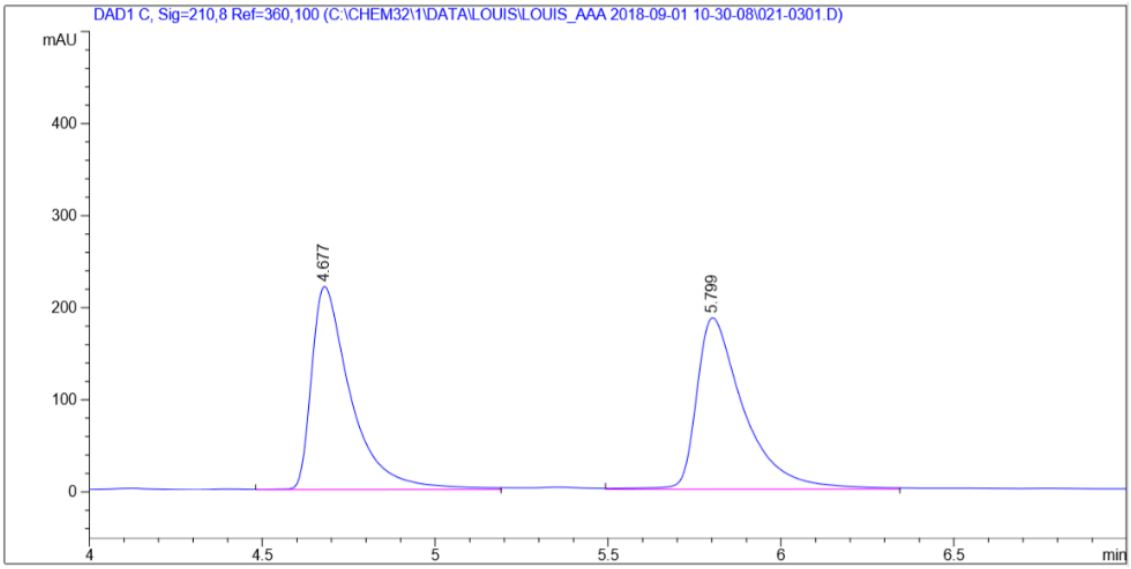
HRMS (ESI): Calculated for $C_9H_{12}N_2$ [M+H$^+$] = 149.1073, Found 149.1073.

FTIR (neat): 3528, 2974, 1599, 1445, 1330, 1154, 987, 920, 751 cm^{-1}.

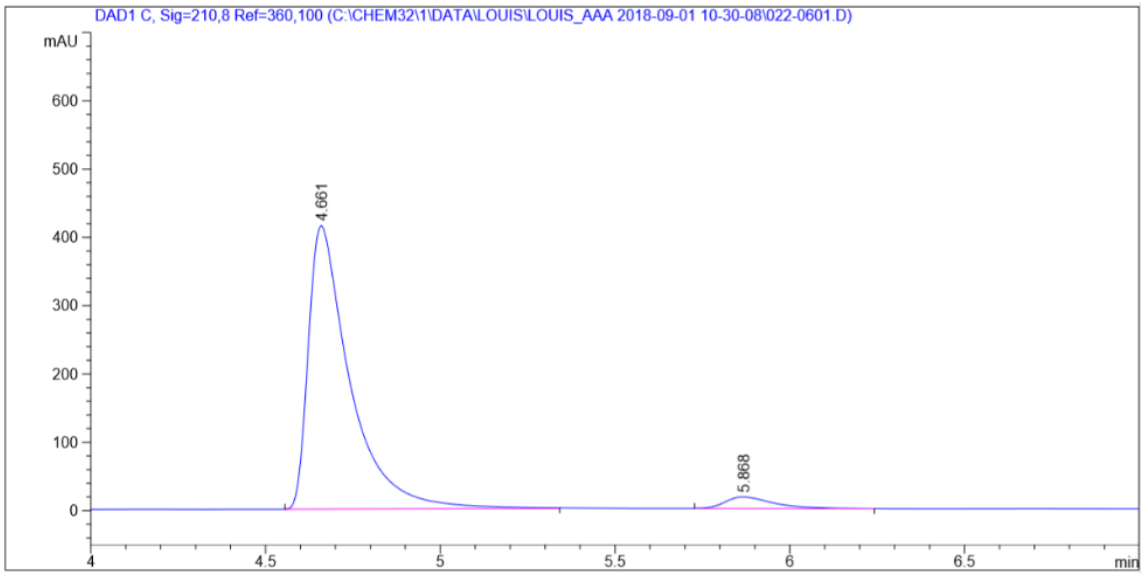
$[\alpha]_D^{28}$ = +6.3 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 90:10, 1.00 mL/min, 210 nm), *ee* = 91%.



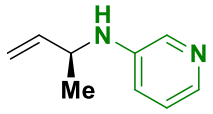


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.677	VB	0.1161	1744.52979	221.07109	49.5692
2	5.799	VB	0.1390	1774.85303	186.55690	50.4308



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.661	BB	0.1185	3436.27466	415.40756	95.3755
2	5.868	BB	0.1433	166.61571	17.15253	4.6245

(*S*)-N-(but-3-en-2-yl)pyridin-3-amine (5.4l)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (82.8 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 30 hr). The title compound was obtained in 87% yield (56.7 mg, 0.38 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 50% over 20 min).

TLC (SiO_2) R_f = 0.22 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (dd, *J* = 2.9, 0.7 Hz, 1H), 7.93 (dd, *J* = 4.7, 1.4 Hz, 1H), 7.05 (ddd, *J* = 8.3, 4.7, 0.7 Hz, 1H), 6.86 (ddd, *J* = 8.3, 2.9, 1.4 Hz, 1H), 5.80 (ddd, *J* = 17.2, 10.3, 5.6 Hz, 1H), 5.21 (dt, *J* = 17.2, 1.3 Hz, 1H), 5.11 (dt, *J* = 10.4, 1.3 Hz, 1H), 3.97 (s, 1H), 3.69 (br, 1H), 1.34 (d, *J* = 6.7 Hz, 3H).

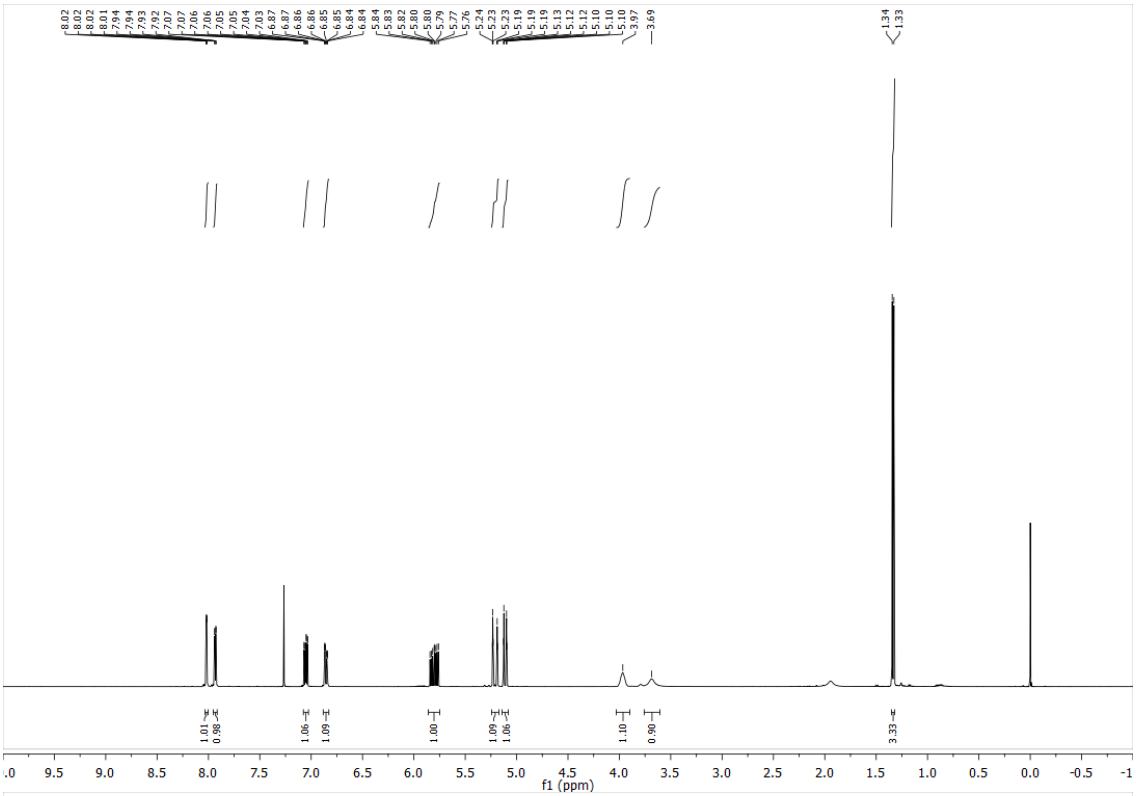
^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.3, 140.3, 138.7, 136.6, 123.6, 119.1, 114.7, 51.0, 21.6.

HRMS (ESI): Calculated for $C_9H_{12}N_2$ [M+H$^+$] = 149.1073, Found 149.1075.

FTIR (neat): 3253, 2973, 1578, 1481, 1414, 1241, 991, 917, 791, 706 cm^{-1}.

$[\alpha]_D^{28}$= –12.7 (*c* 0.2, $CHCl_3$).

HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 90:10, 1.00 mL/min, 210 nm), *ee* = 91%.


8.02
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8.02
8.01
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7.93
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3.97
3.69
1.34
1.33
1.01
0.98
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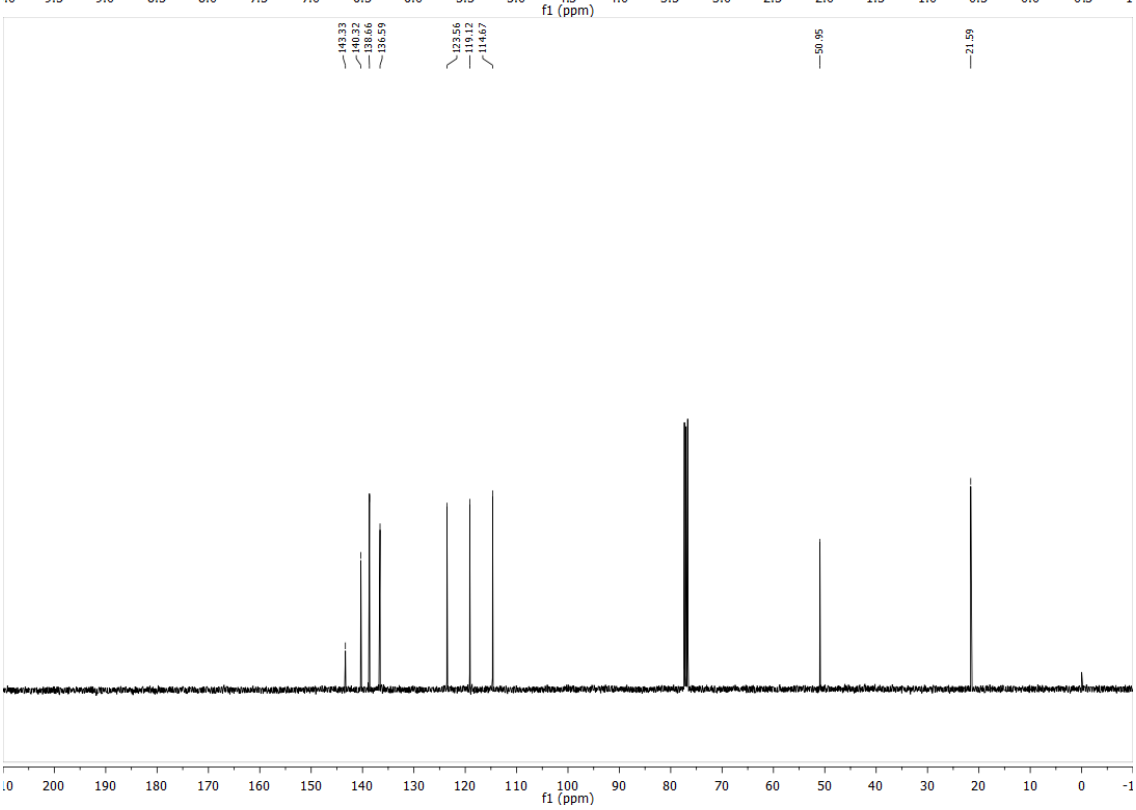
1.09
1.00
1.09
1.06
1.10
0.90
3.33
f1 (ppm)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136.59
123.56
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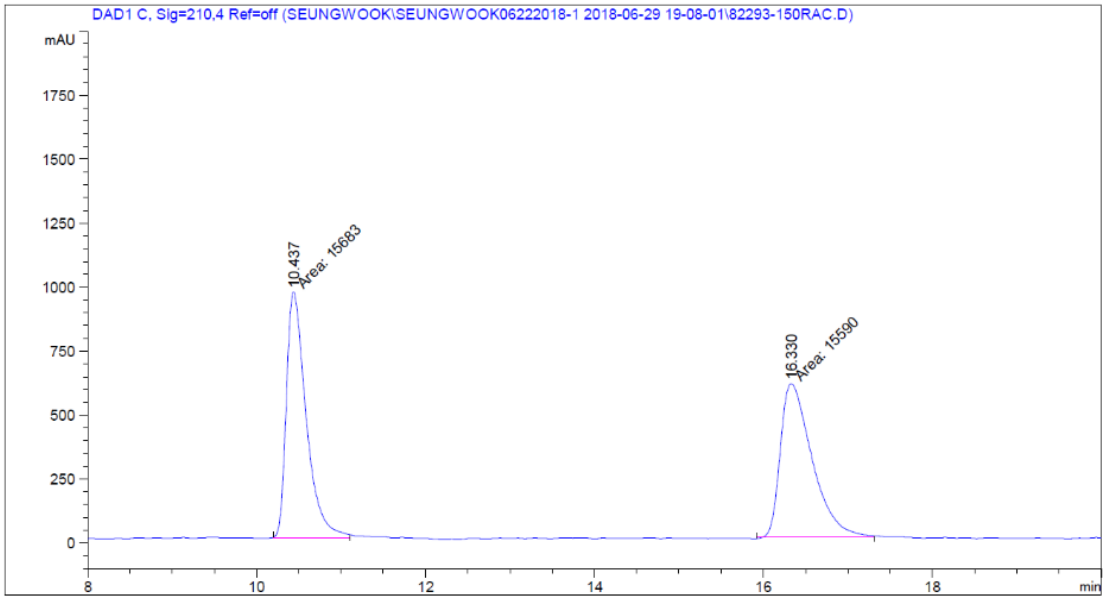
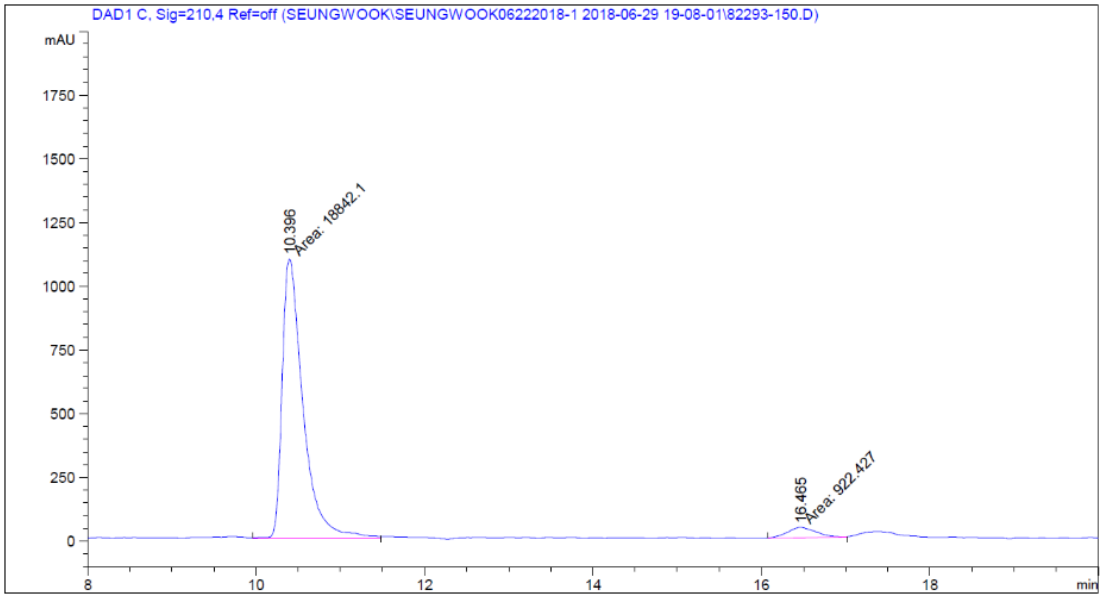
114.67
50.95
21.59
f1 (ppm)

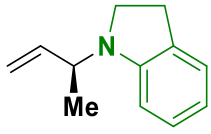


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.437	MM	0.2717	1.56830e4	962.08154	50.1488
2	16.330	MM	0.4339	1.55900e4	598.80670	49.8512



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.396	MM	0.2865	1.88421e4	1096.21130	95.3329
2	16.465	MM	0.3773	922.42676	40.75188	4.6671

(*S*)-1-(but-3-en-2-yl)indoline (5.5a)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (104.9 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 92% yield (70.1 mg, 0.40 mmol) as a light purple oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 10 min).

TLC (SiO_2) R_f = 0.49 (heptane: isopropyl acetate = 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10-7.02 (m, 2H), 6.63 (t, *J* = 7.3 Hz, 1H), 6.49 (d, *J* = 7.8 Hz, 1H), 5.94 (ddd, *J* = 17.5, 10.5, 5.3 Hz, 1H), 5.26-5.15 (m, 2H), 4.22 (qd, *J* = 6.9, 5.1 Hz, 1H), 3.44-3.30 (m, 2H), 2.96 (t, *J* =18.5 Hz, 2H), 1.32 (d, *J* = 6.8 Hz, 3H).

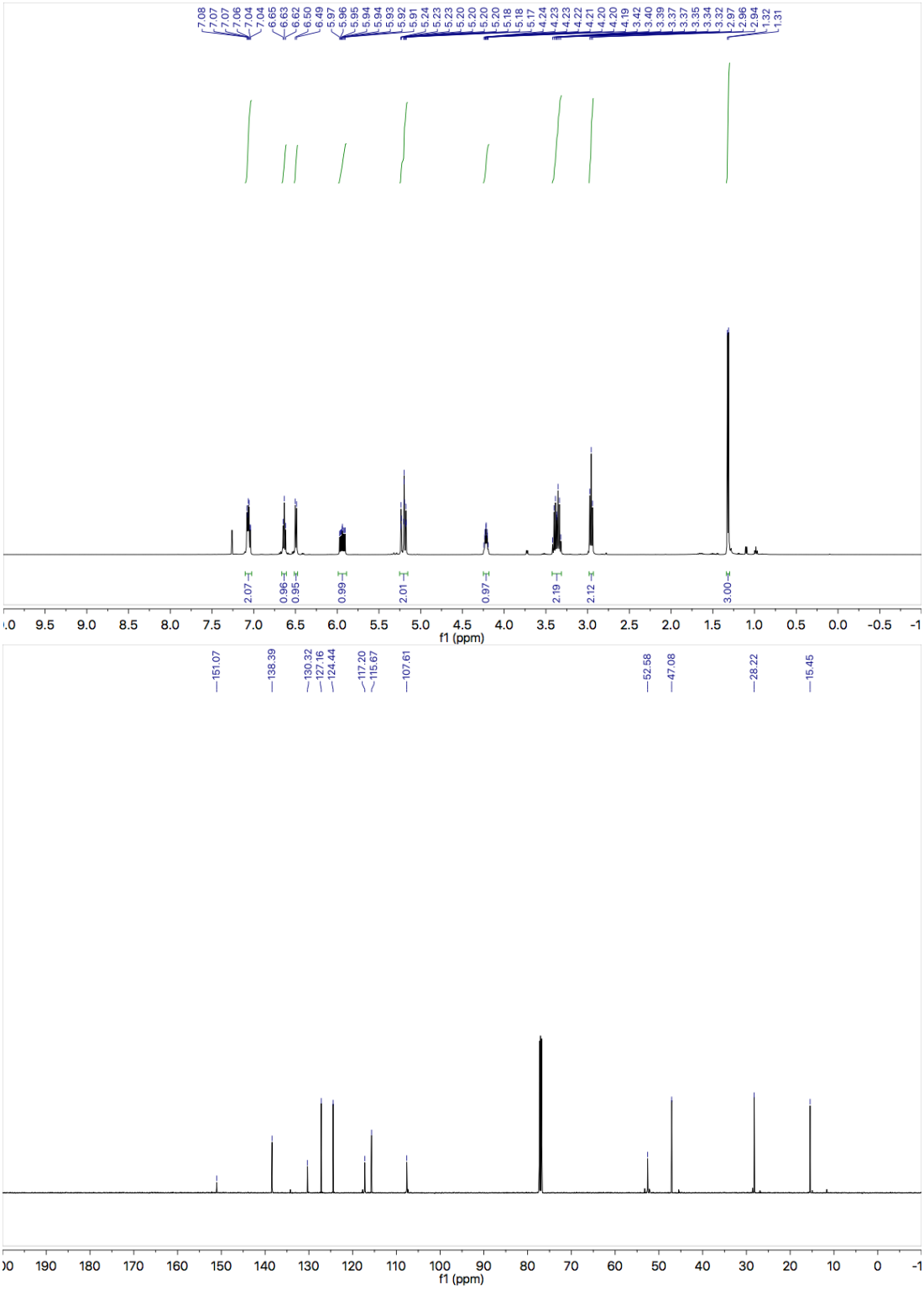
^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1, 138.4, 130.3, 127.2, 124.4, 117.2, 115.7, 107.6, 52.6, 47.1, 28.2, 15.5.

HRMS (ESI): Calculated for $C_{12}H_{15}N$ $[M+H^+]$ = 174.1277, Found 174.1227.

FTIR (neat): 3047, 3024, 2973, 2933, 2845, 1606, 1487, 1473, 1458, 1257, 1185, 1023, 919, 743 cm^{-1}.

$[\alpha]_D^{28}$ = -551.36 (*c* 0.2, $CHCl_3$).

HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 95:5, 1.00 mL/min, 254 nm), *ee* = 92%.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3.32
2.97
2.96
2.94
1.32
1.31
2.07
0.96
0.95
0.99
2.01
0.97
2.19
2.12
3.00
f1 (ppm)
151.07
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130.32
127.16
124.44
117.20
115.67
107.61
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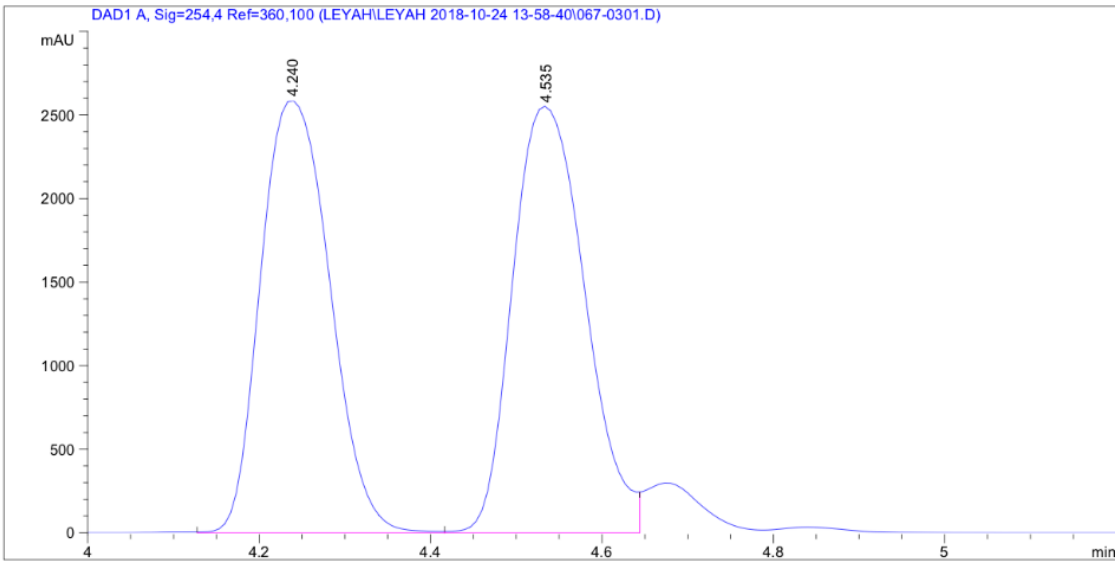
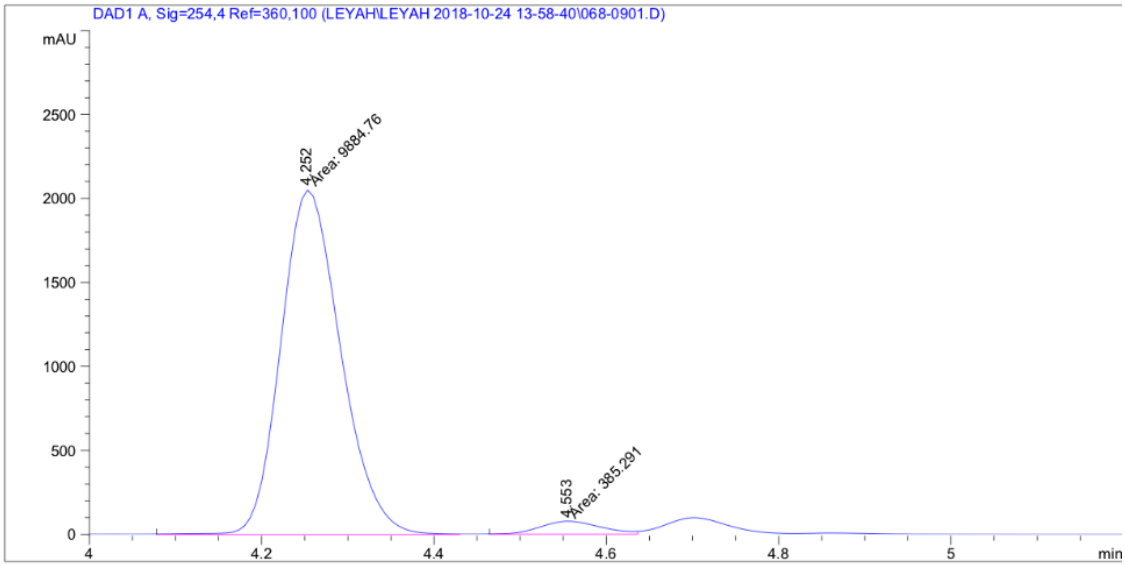
47.08
28.22
15.45
f1 (ppm)

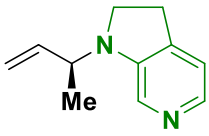


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.240	VV	0.0915	1.45323e4	2589.30933	49.2911
2	4.535	VV	0.0943	1.49503e4	2553.09814	50.7089



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.252	MM	0.0801	9884.76270	2055.56738	96.2484
2	4.553	MM	0.0827	385.29080	77.64413	3.7516

(*S*)-1-(but-3-en-2-yl)-2,3-dihydro-1*H*-pyrrolo[2,3-*c*]pyridine (5.5b)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (105.7 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 78% yield (59.8 mg, 0.34 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 20% over 20min).

TLC (SiO_2) R_f = 0.25 (heptane: isopropyl acetate =1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 4.6 Hz, 1H), 7.80 (d, *J* = 0.9 Hz, 1H), 6.97 (dq, *J* = 4.6, 1.0 Hz, 1H), 5.88 (ddd, *J* = 17.4, 10.5, 5.5 Hz, 1H), 5.21 (dt, *J* = 12.2, 1.4 Hz, 1H), 5.18 (dt, *J* = 5.3, 1.4 Hz, 1H), 4.18 (qdt, *J* = 7.0, 5.5, 1.6 Hz, 1H), 3.45-3.32 (m, 2H), 2.98-2.91 (m, 2H), 1.31 (d, *J* = 6.9 Hz, 3H).

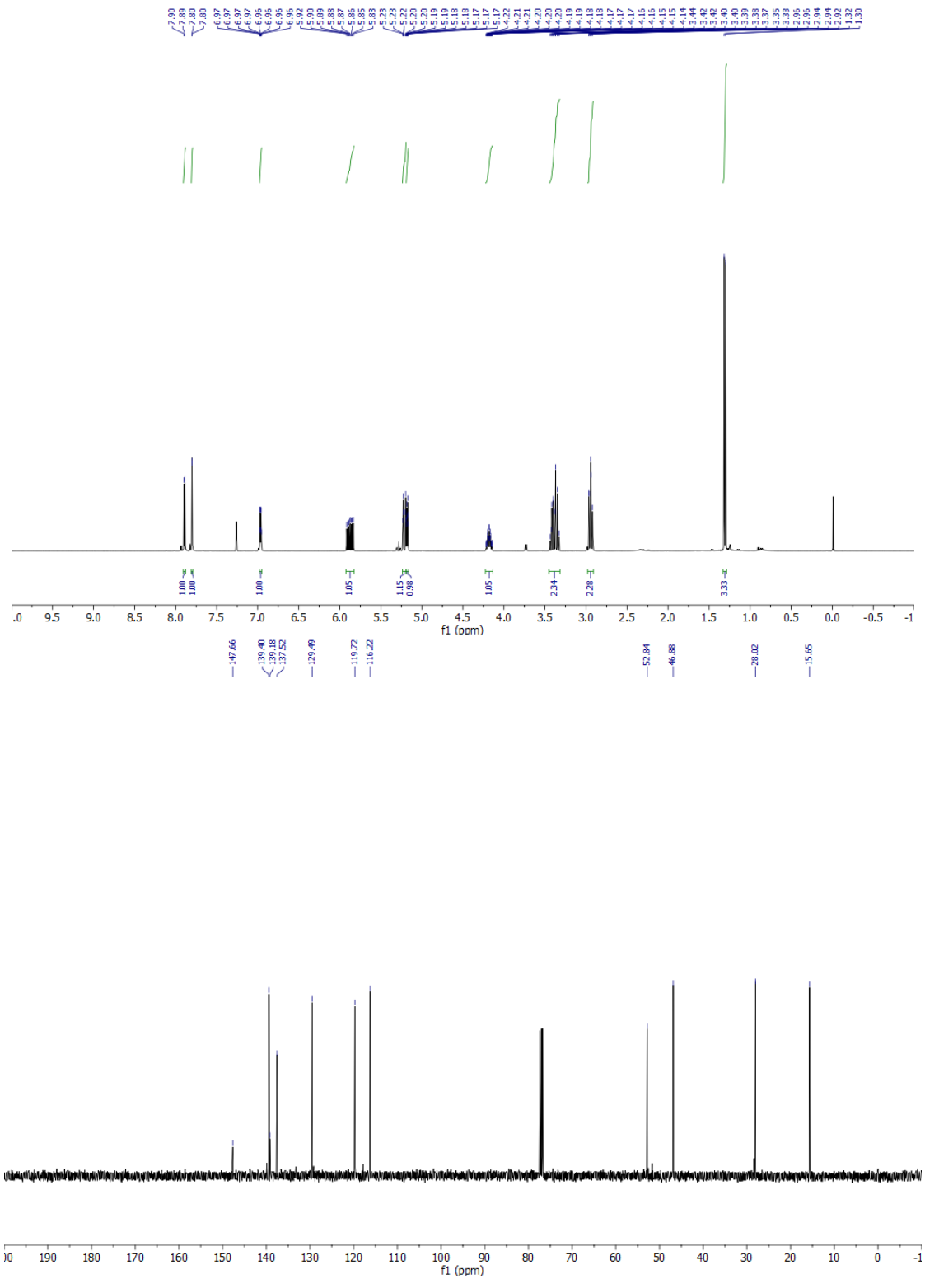
^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.7, 139.4, 139.2, 137.5, 129.5, 119.7, 116.2, 52.8, 46.9, 28.0, 15.7.

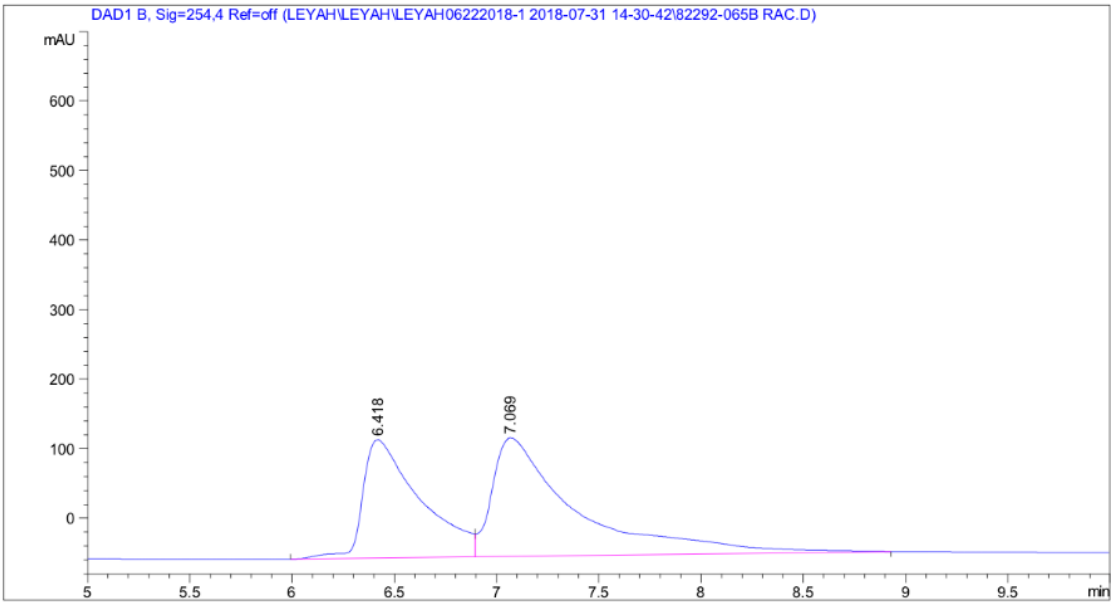
HRMS (ESI): Calculated for $C_{11}H_{14}N_2$ $[M+H^+]$ =175.1230, Found 175.1226.

FTIR (neat): 3037, 2974, 2360, 2341, 1597, 1493, 1426, 129.4, 1183, 923, 819, 772, 669, 567 cm^{-1}.

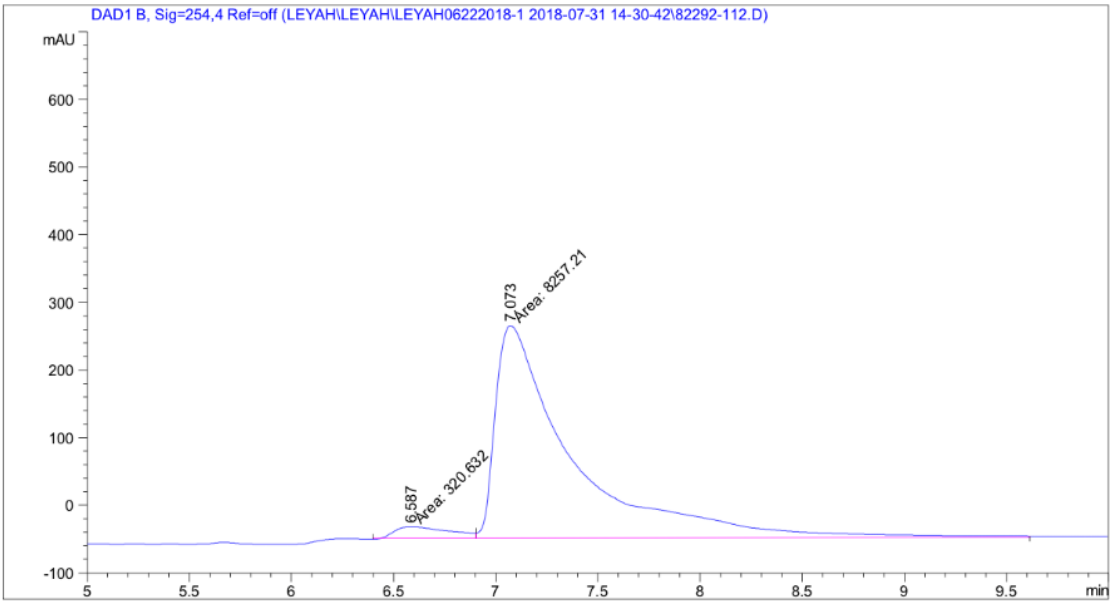
$[\alpha]_D^{28}$= –44.4 (*c* 0.2, $CHCl_3$).

HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 85:15, 1.00 mL/min, 254 nm), *ee* = 93%.



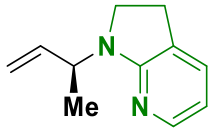


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.418	BV	0.2722	3296.05127	170.00136	40.7217
2	7.069	VB	0.3849	4798.03174	170.18459	59.2783



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.587	MF	0.3146	320.63168	16.98651	3.7379
2	7.073	FM	0.4379	8257.20508	314.27136	96.2621

(*S*)-1-(but-3-en-2-yl)-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyridine (5.5c)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (105.7 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 74% yield (56.8 mg, 0.33 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 10 min).

TLC (SiO_2) R_f = 0.25 (heptane: isopropyl acetate =9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85-7.83 (m, 1H), 7.13 (dq, *J* = 6.9, 1.4 Hz, 1H), 6.37 (dd, *J* = 7.0, 5.3 Hz, 1H), 5.91 (ddd, *J* = 17.4, 10.5, 4.9 Hz, 1H), 5.20-5.14 (m, 2H), 4.86 (qdt, *J* = 6.8, 4.9, 1.8 Hz, 1H), 3.46-3.41 (m, 2H), 2.95-2.91 (m, 2H), 1.28 (d, *J* = 6.9Hz, 3H).

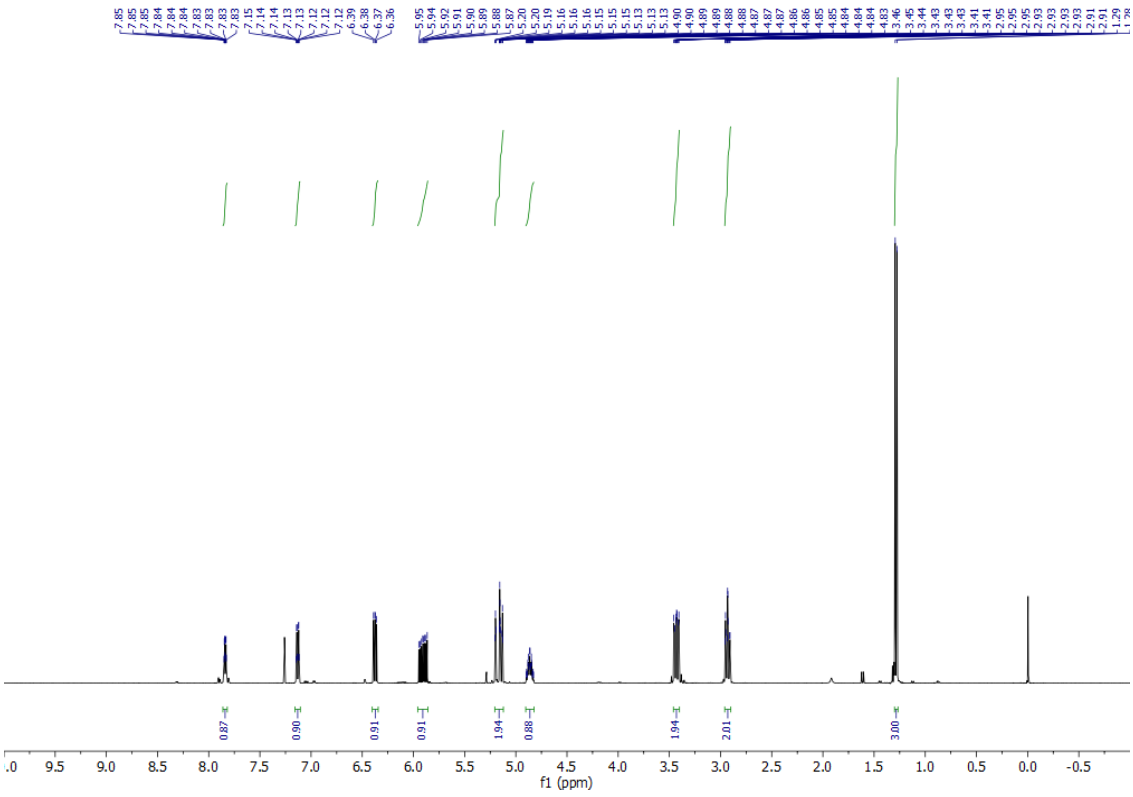
^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.5, 145.8, 138.4, 138.4, 130.7, 123.2, 115.4, 111.9, 49.5, 43.6, 25.7, 15.5.

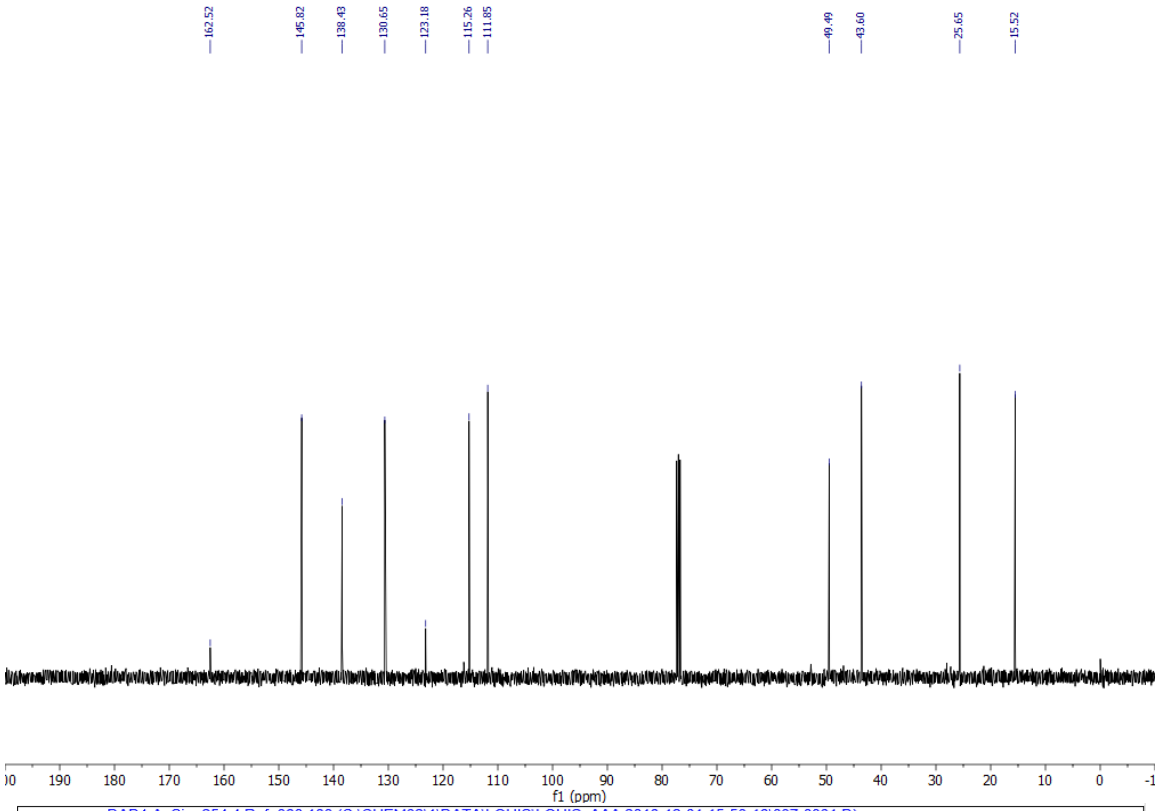
HRMS (ESI): Calculated for $C_{11}H_{14}N_2$ [M+H$^+$] = 175.1230, Found 175.1225.

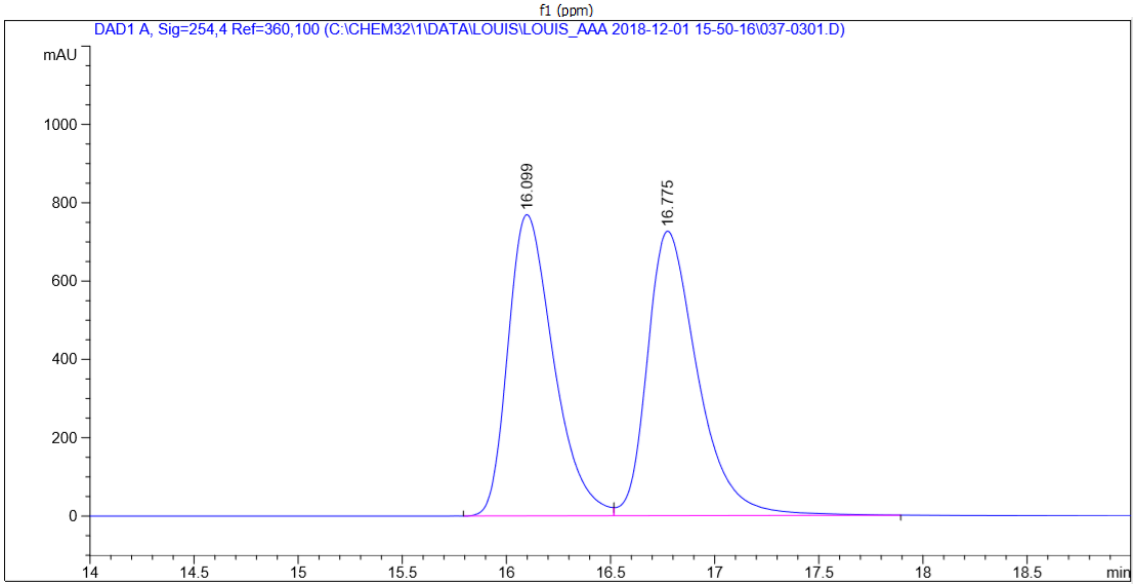
FTIR (neat): 3709, 2972, 2360, 2341, 1610, 1577, 1491, 1463, 1443, 1391, 771, 669cm^{-1}.

$[\alpha]_D^{28}$ = –31.7 (*c* 0.2, $CHCl_3$).

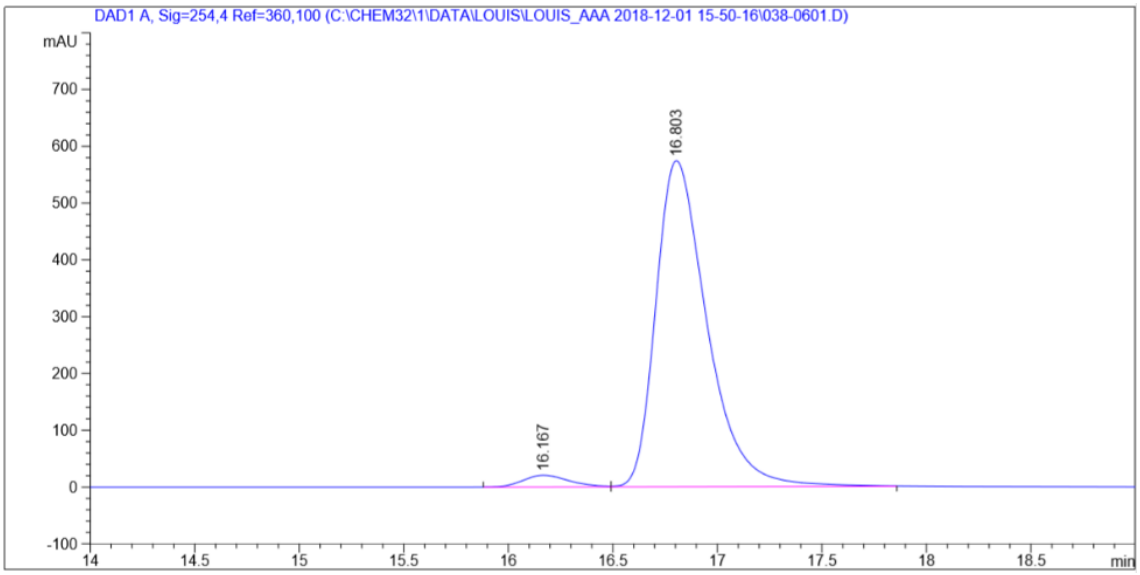
HPLC (Two connected chiralcel OD-3 & OD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 94%.





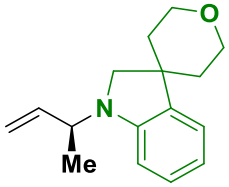


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.099	BV	0.2350	1.16750e4	769.46112	48.9281
2	16.775	VB	0.2557	1.21865e4	726.54614	51.0719



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.167	BV	0.2339	311.74313	20.67129	3.0986
2	16.803	VB	0.2601	9749.09570	574.03931	96.9014

(*S*)-1-(but-3-en-2-yl)-2',3',5',6'-tetrahydrospiro[indoline-3,4'-pyran] (5.5d)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (166.5 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 85% yield (88.9 mg, 0.37 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 10%).

TLC (SiO_2) R_f = 0.33 (heptane: isopropyl acetate =9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.11-7.03 (m, 2H), 6.67 (td, *J* = 7.4, 1.0 Hz, 1H), 6.49 (dd, *J* = 7.8, 0.9 Hz, 1H), 5.92 (ddd, *J* = 17.4, 10.5, 5.1 Hz, 1H), 5.22 (dt, *J* = 10.4, 1.5 Hz, 1H), 5.18 (dt, *J* = 3.3, 1.5 Hz, 1H), 4.23 (qdt, *J* = 6.8, 5.1, 1.7 Hz, 1H), 3.97 (ddd, *J* = 11.8, 4.5, 2.2 Hz, 2H), 3.57 (tdd, *J* = 12.0, 7.7, 2.3 Hz, 2H), 3.39-3.29 (m, 2H), 1.97 (dtd, *J* = 13.9, 12.2, 4.7 Hz, 2H), 1.69-1.59 (m, 2H), 1.32 (d, *J* = 6.9 Hz, 3H).

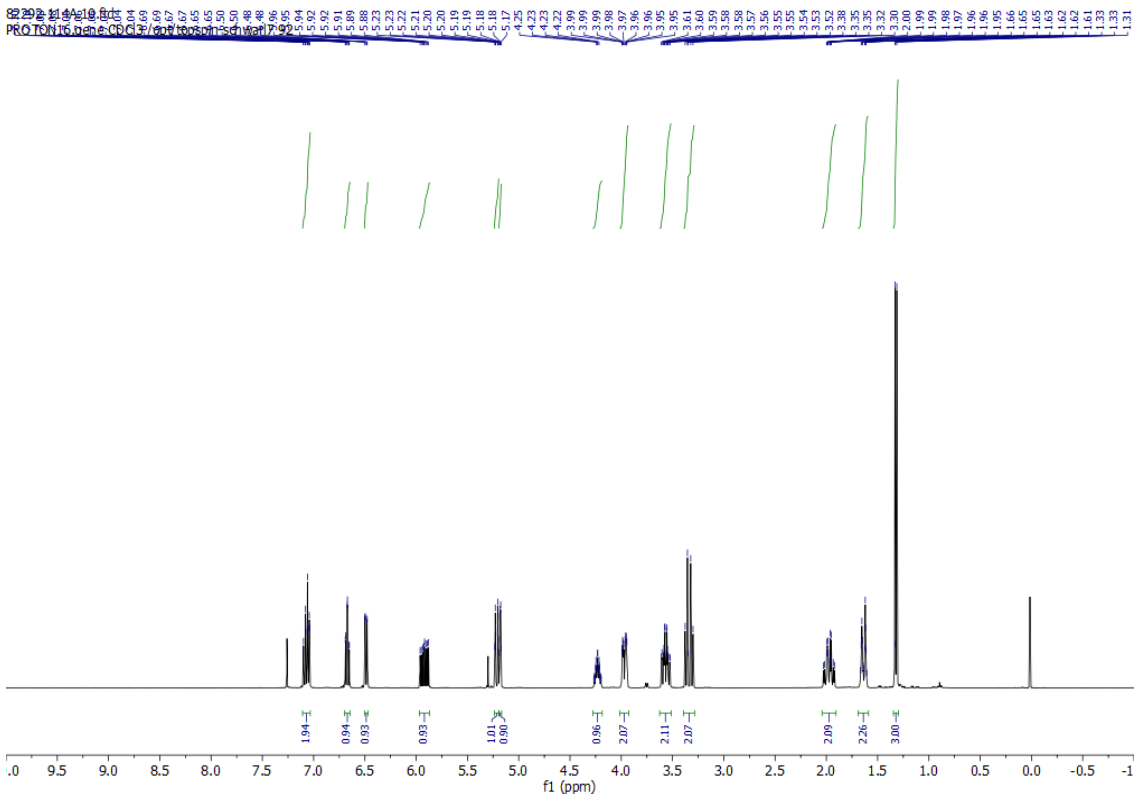
^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.0, 138.3, 137.3, 127.9, 122.4, 117.3, 115.7, 107.5, 65.2, 56.4, 52.1, 41.7, 36.7, 36.6, 36.5, 15.5.

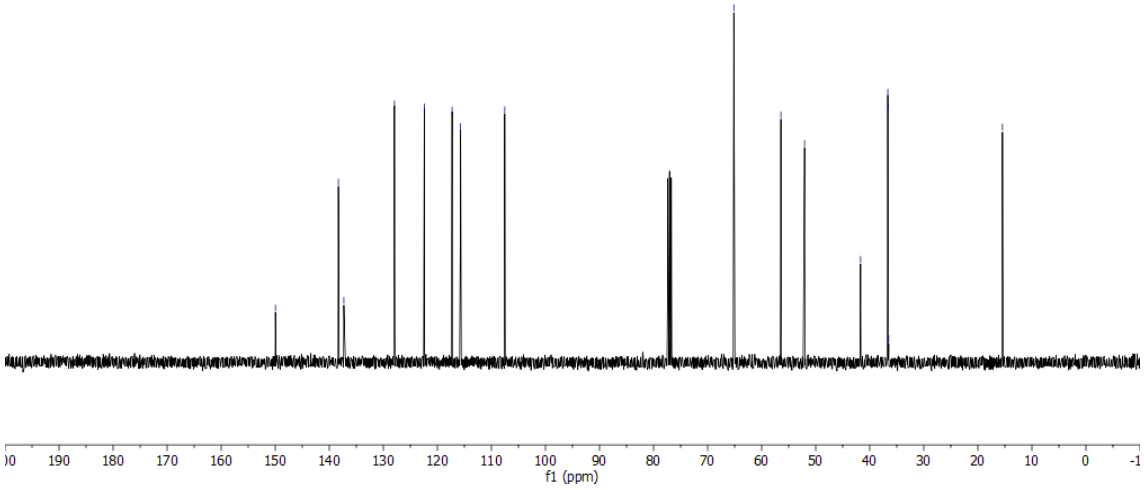
HRMS (ESI): Calculated for $C_{16}H_{22}NO$ $[M+H^+]$ = 244.1696, Found 244.1699.

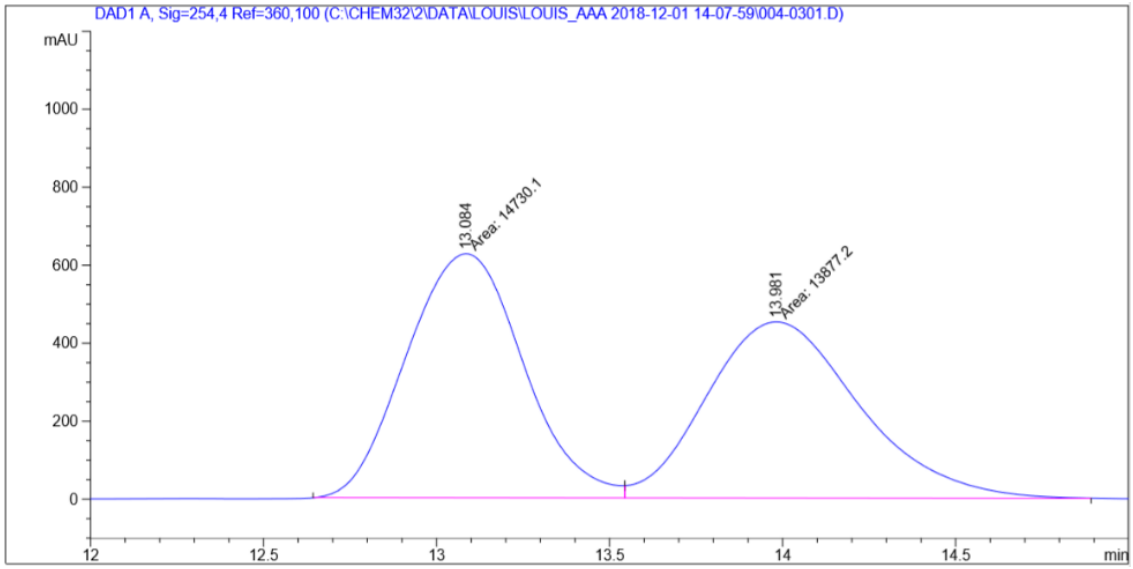
FTIR (neat): 2936, 2848, 2360, 2341, 1660, 1482, 1462, 1251, 1104, 1027, 837, 750, 668, 547, 464 cm^{-1}.

$[\alpha]_D^{28}$= –44.7 (*c* 0.2, $CHCl_3$).

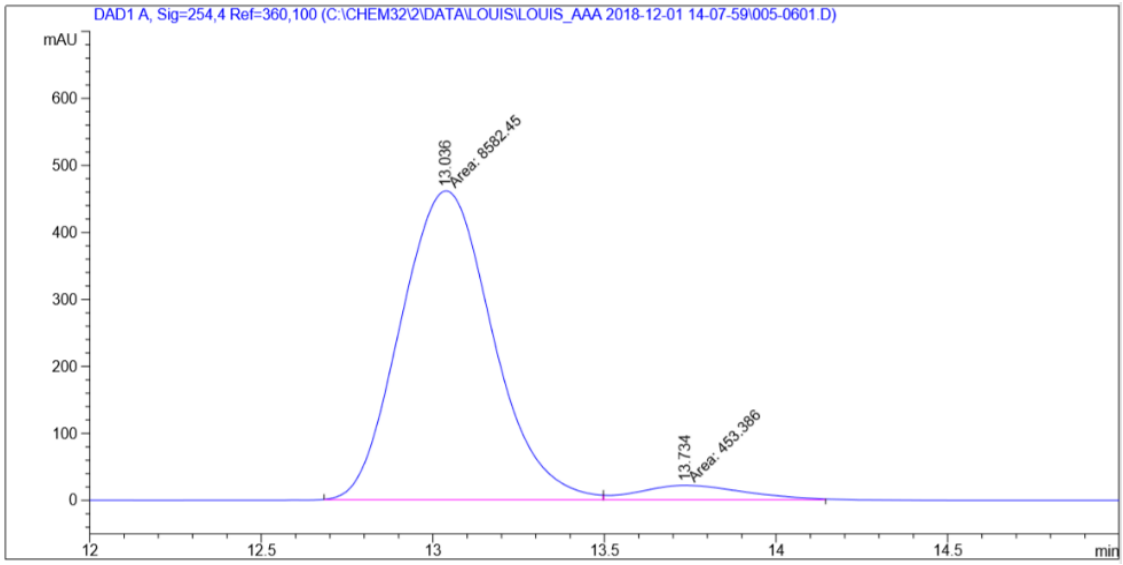
HPLC (Two connected chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 90%.


f1 (ppm)


f1 (ppm)

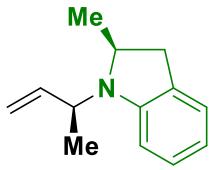


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.084	MF	0.3922	1.47301e4	625.96423	51.4907
2	13.981	FM	0.5117	1.38772e4	451.98029	48.5093



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.036	MF	0.3102	8582.44727	461.11133	94.9824
2	13.734	FM	0.3500	453.38596	21.59124	5.0176

(*S*)-1-((*S*)-but-3-en-2-yl)-2-methylindoline (5.5e)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (117.2 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 80% yield, >20:1 dr (69.2 mg, 0.37 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Heptane).

TLC (SiO_2) R_f = 0.50 (heptane: isopropyl acetate = 9:1).

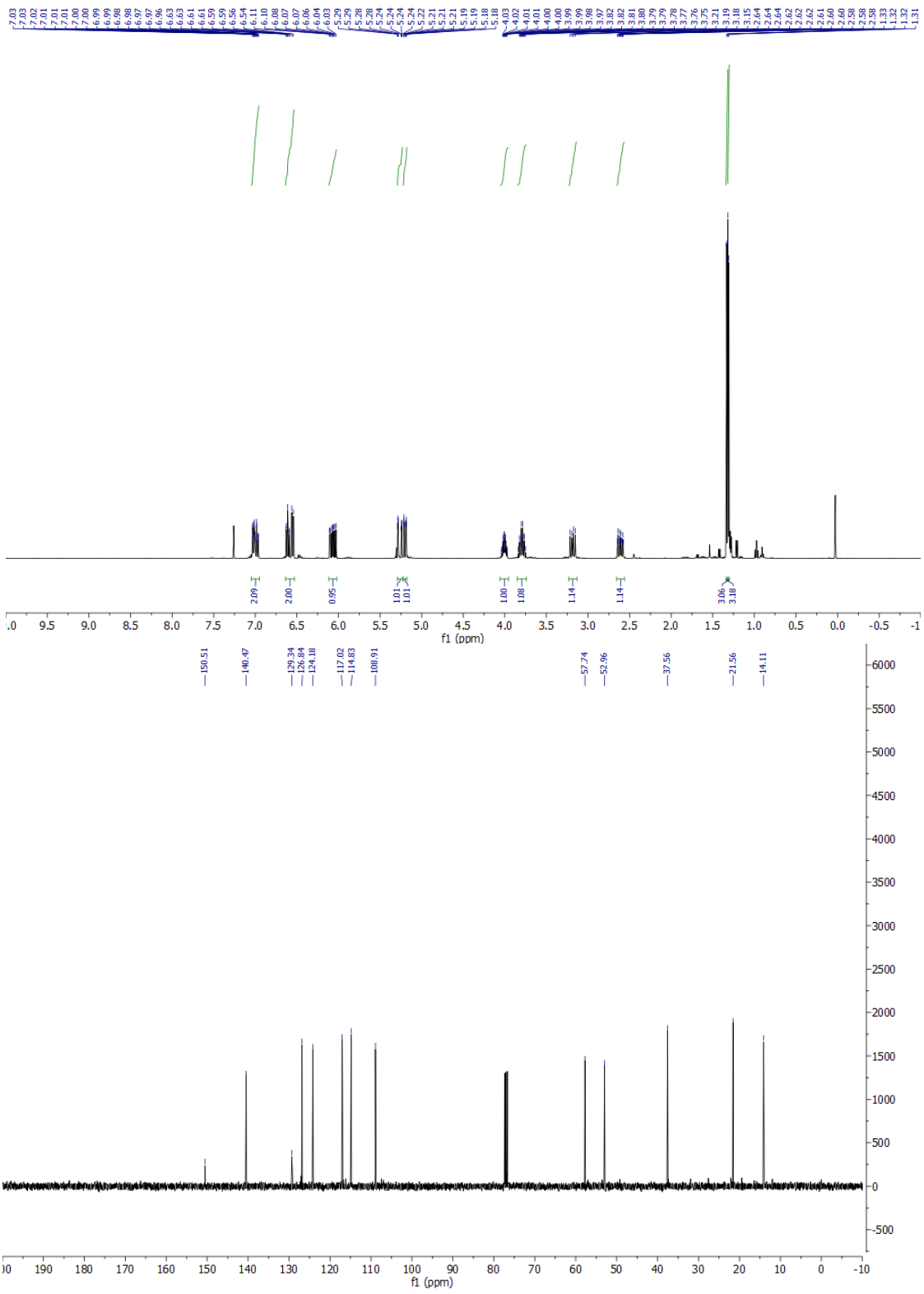
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.03-6.96 (m, 2H), 6.63-6.54 (m, 2H), 6.07 (ddd, *J* = 17.5, 10.6, 4.2 Hz, 1H), 5.26 (ddd, *J* = 17.5, 2.1, 1.5 Hz, 1H), 5.20, (ddd, *J* = 10.6, 2.2, 1.5 Hz, 1H), 4.01 (qdt, *J* = 6.8, 4.3, 2.2 Hz, 1H), 3.79 (tq, *J* = 8.9, 6.1 Hz, 1H), 3.18 (dd, *J* = 15.6, 9.1 Hz, 1H), 2.61 (ddt, *J* = 15.7, 8.8, 1.2 Hz, 1H), 1.33 (d, *J* = 5.3 Hz, 3H), 1.31 (d, *J* = 4.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.5, 140.5, 129.3, 126.8, 124.2, 117.0, 114.8, 108.9, 57.7, 53.0, 37.6, 21.6, 14.1.

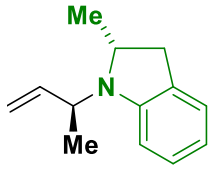
HRMS (ESI): Calculated for $C_{13}H_{17}N$ $[M+H^+]$ =188.1434, Found 188.1427.

FTIR (neat): 3726, 2966, 2360, 2341, 1605, 1481, 1459, 1257, 772, 747, 720, 669, 656, 419 cm^{-1}.

$[\alpha]_D^{28}$= +57.9 (*c* 0.2, $CHCl_3$).


f1 (ppm)
f1 (ppm)

(*R*)-1-((*S*)-but-3-en-2-yl)-2-methylindoline (5.5f)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (117.2mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 48% yield, 5:1 dr (39.8 mg, 0.21 mmol) as a light orange oil after purification by flash column chromatography (4g SiO_2, Heptane).

TLC (SiO_2) R_f = 0.50 (heptane: isopropyl acetate = 9:1).

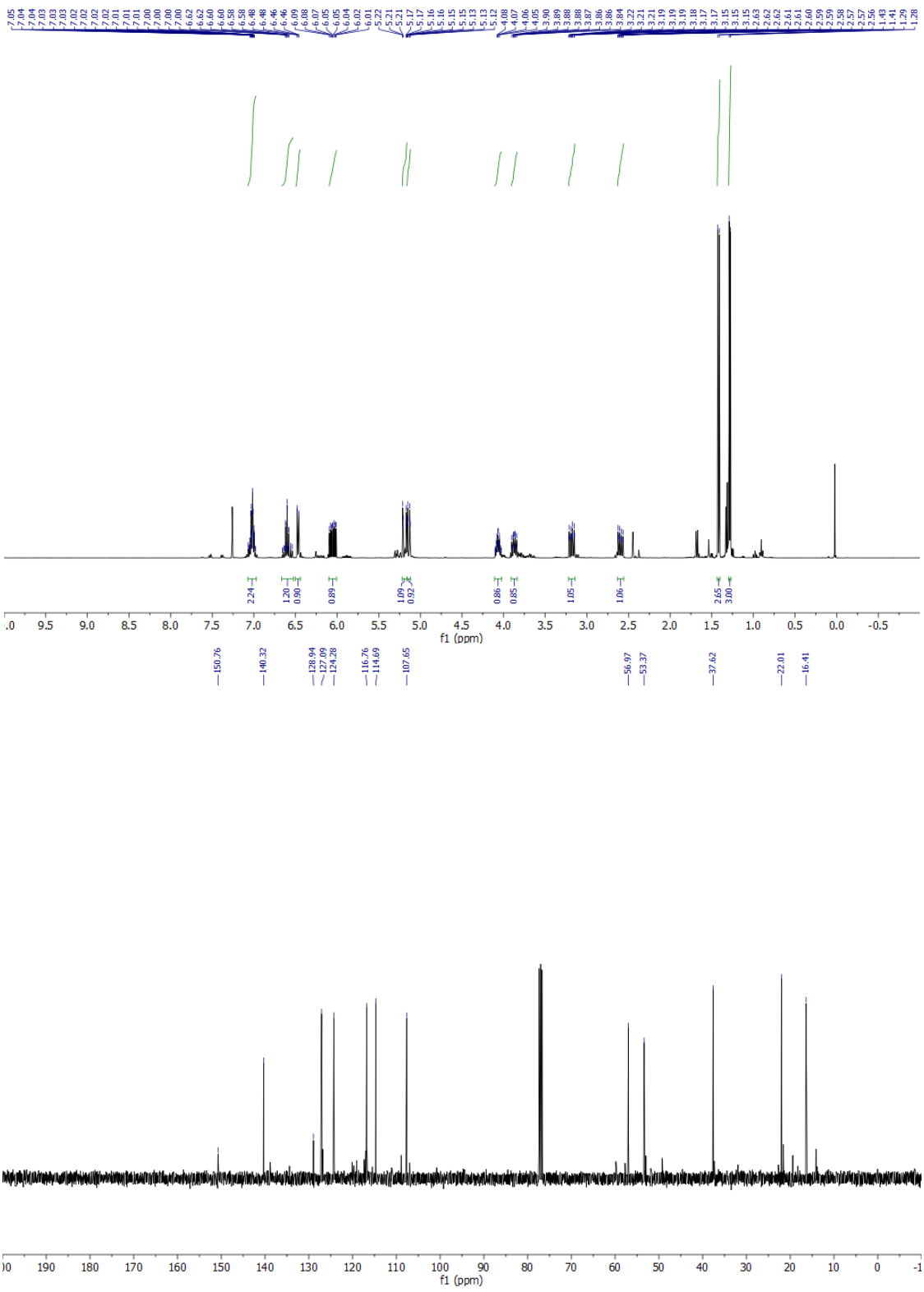
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.07-6.98 (m, 2H), 6.66-6.54 (m, 1H), 6.48-6.46 (m, 1H), 6.05 (ddd, *J* = 17.3, 10.5, 5.3 Hz, 1H), 5.19 (dt, *J* = 17.4, 1.7 Hz, 1H), 5.14 (dt, *J* = 10.5, 1.6 Hz, 1H), 4.10-4.03 (m, 1H), 3.91-3.84 (m, 1H), 3.18 (ddt, *J* = 15.6, 9.2, 0.9 Hz, 1H), 2.60 (ddt, *J* = 15.6, 7.9, 1.1 Hz, 1H), 1.42 (d, *J* = 7.0 Hz, 3H), 1.28 (d, *J* = 6.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.8, 140.3, 128.9, 127.1, 124.3, 116.8, 114.7, 107.7, 57.0, 53.4, 37.6, 22.0, 16.4.

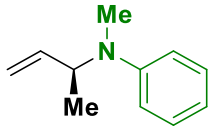
HRMS (ESI): Calculated for $C_{13}H_{17}N$ $[M+H^+]$ =188.1434, Found 188.1428.

FTIR (neat): 3706, 3627, 2971, 2360, 2341, 1606, 1483, 1459, 1258, 746, 720, 669, 409 cm^{-1}.

$[\alpha]_D^{28}$= –24.6 (*c* 0.2, $CHCl_3$).


f1 (ppm)
f1 (ppm)

(*S*)-*N*-(but-3-en-2-yl)-*N*-methylaniline (5.5g)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (94.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 71% yield (50.3 mg, 0.31 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Heptane).

TLC (SiO_2) R_f = 0.47 (heptane: isopropyl acetate = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25-7.19 (m, 2H), 6.82-6.77 (m, 2H), 6.70 (tt, *J* = 7.3, 1.0 Hz, 1H), 5.91 (ddd, *J* = 17.2, 10.8, 4.2 Hz, 1H), 5.17 (p, *J* = 1.4 Hz, 1H), 5.13 (ddd, *J* = 9.3, 2.0, 1.4 Hz, 1H), 4.48 (qdt, *J* = 6.6, 4.1, 2.0 Hz, 1H), 2.73 (s, 3H), 1.25 (d, *J* = 6.8 Hz, 3H).

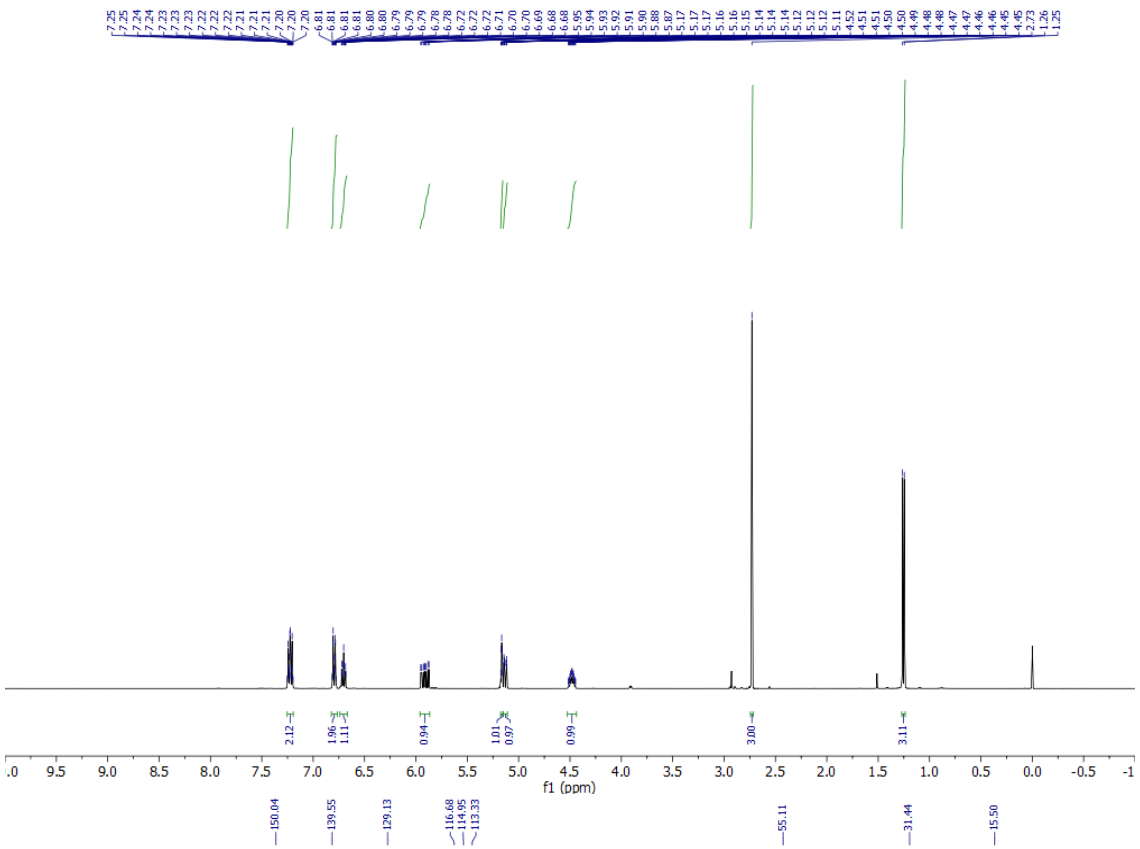
^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.0, 139.6, 129.1, 116.7, 115.0, 133.3, 55.1, 31.4, 15.5.

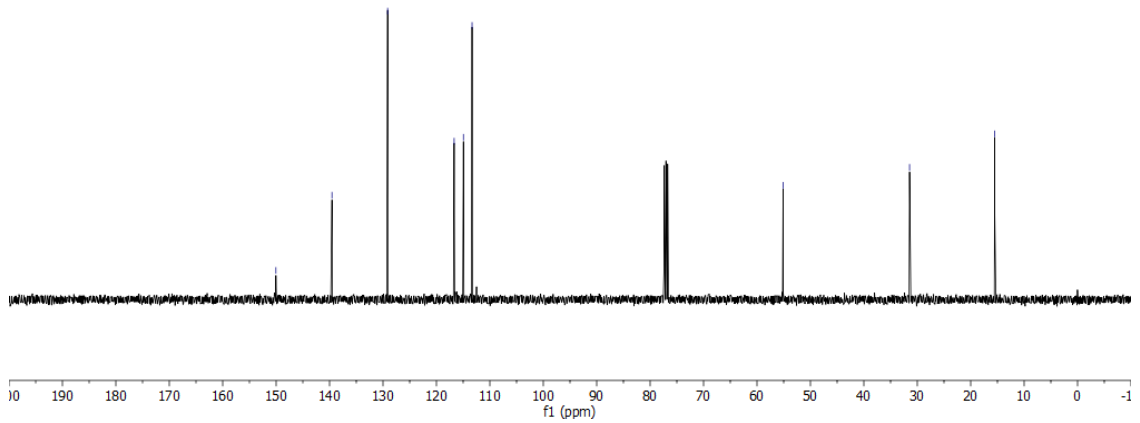
HRMS (ESI): Calculated for $C_{11}H_{15}N$ [M+H^{+}] = 162.1277, Found 162.1278.

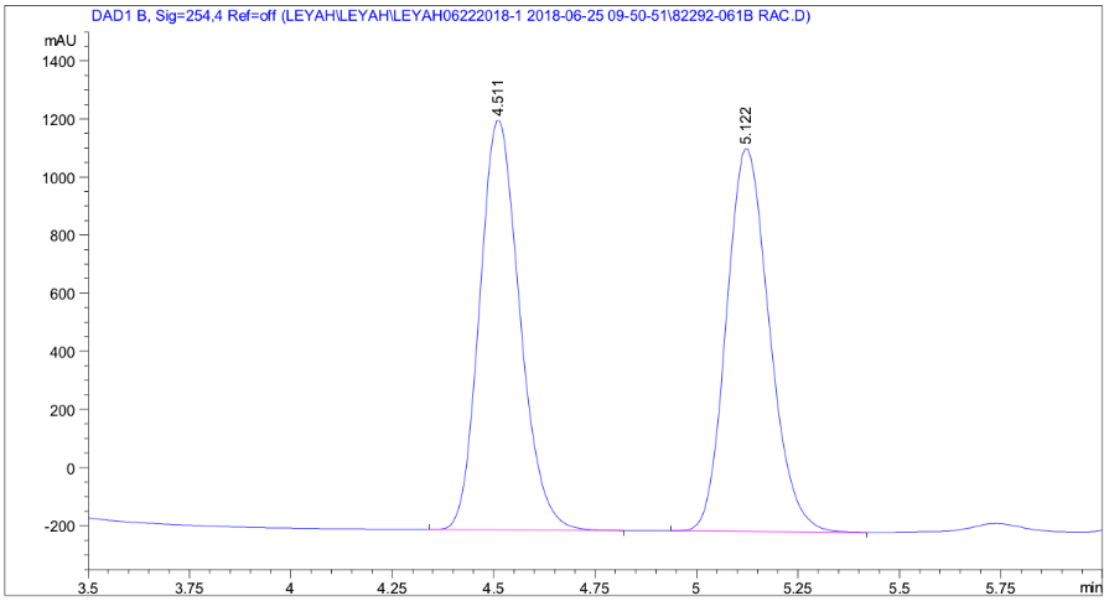
FTIR (neat): 3061, 2973, 2812, 2360, 2341, 1597, 1501, 1308, 1137, 1035, 990, 917, 746, 690, 518cm^{-1}.

$[\alpha]_D^{28}$ = –185.6 (*c* 0.2, $CHCl_3$).

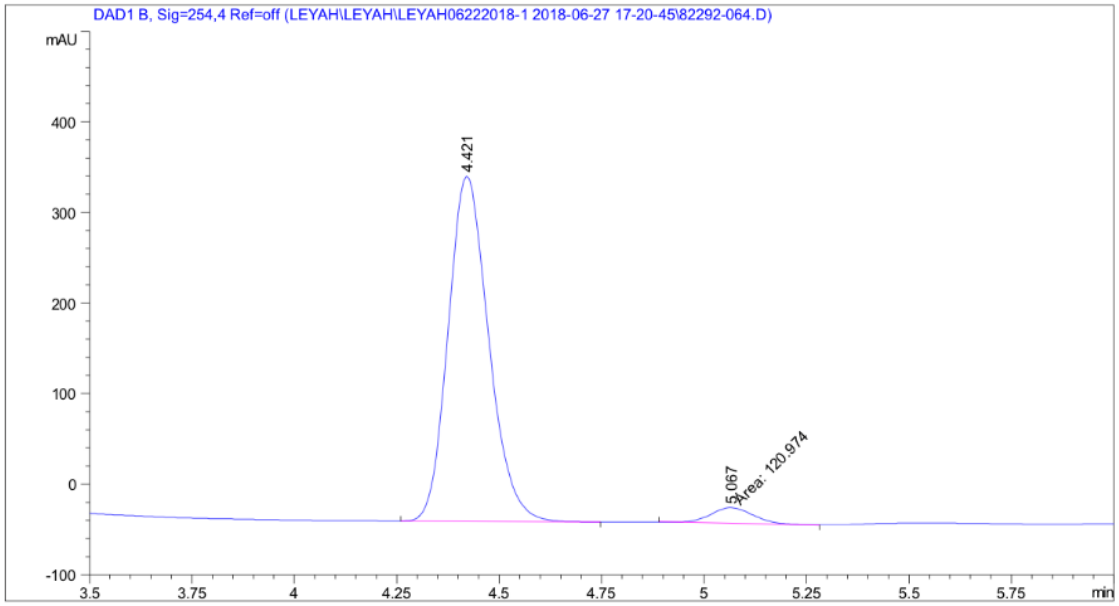
HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 91%.


f1 (ppm)


f1 (ppm)

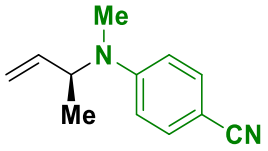


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.511	BB	0.1061	9688.04102	1411.46924	50.0019
2	5.122	BB	0.1137	9687.29688	1318.63684	49.9981



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.421	BB	0.1062	2622.18921	381.43484	95.5900
2	5.067	MM	0.1176	120.97383	17.14165	4.4100

(*S*)-4-(but-3-en-2-yl(methyl)amino)benzonitrile (5.5h)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (116.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 79% yield (64.7 mg, 0.35 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 10 min).

TLC (SiO_2) R_f = 0.25 (heptane: isopropyl acetate = 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48-7.43 (m, 2H), 6.74-6.69 (m, 2H), 5.86 (ddd, *J* = 17.3, 10.6, 4.0 Hz, 1H), 5.21 (ddd, *J* = 10.6, 2.0, 1.1 Hz, 1H), 5.14 (ddd, *J* = 17.4, 2.0, 1.1, 1H), 4.53 (qdt, *J* = 6.7, 4.1, 2.0 Hz, 1H), 2.81 (s, 3H), 1.32 (d, *J* = 6.8 Hz, 3H).

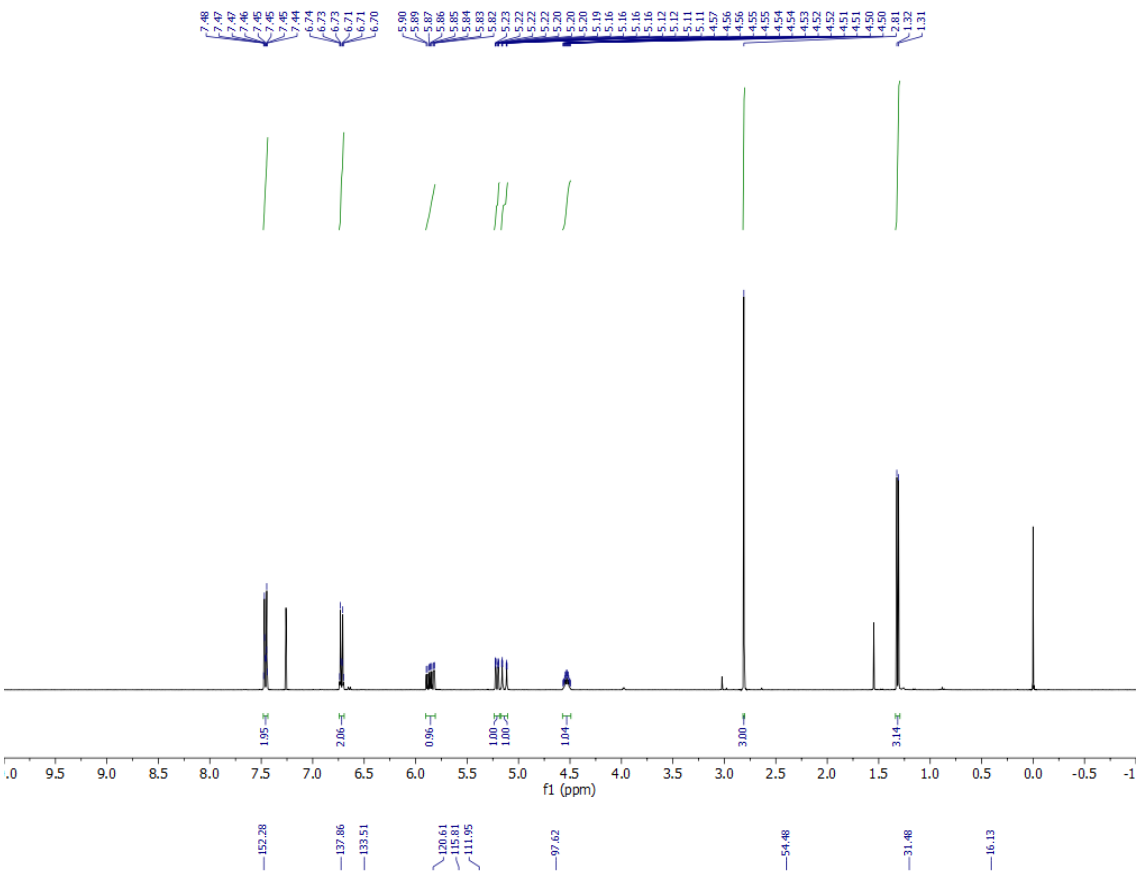
^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.3, 137.9, 133.5, 120.6, 115.8, 112.0, 97.6, 54.5, 31.5, 16.1.

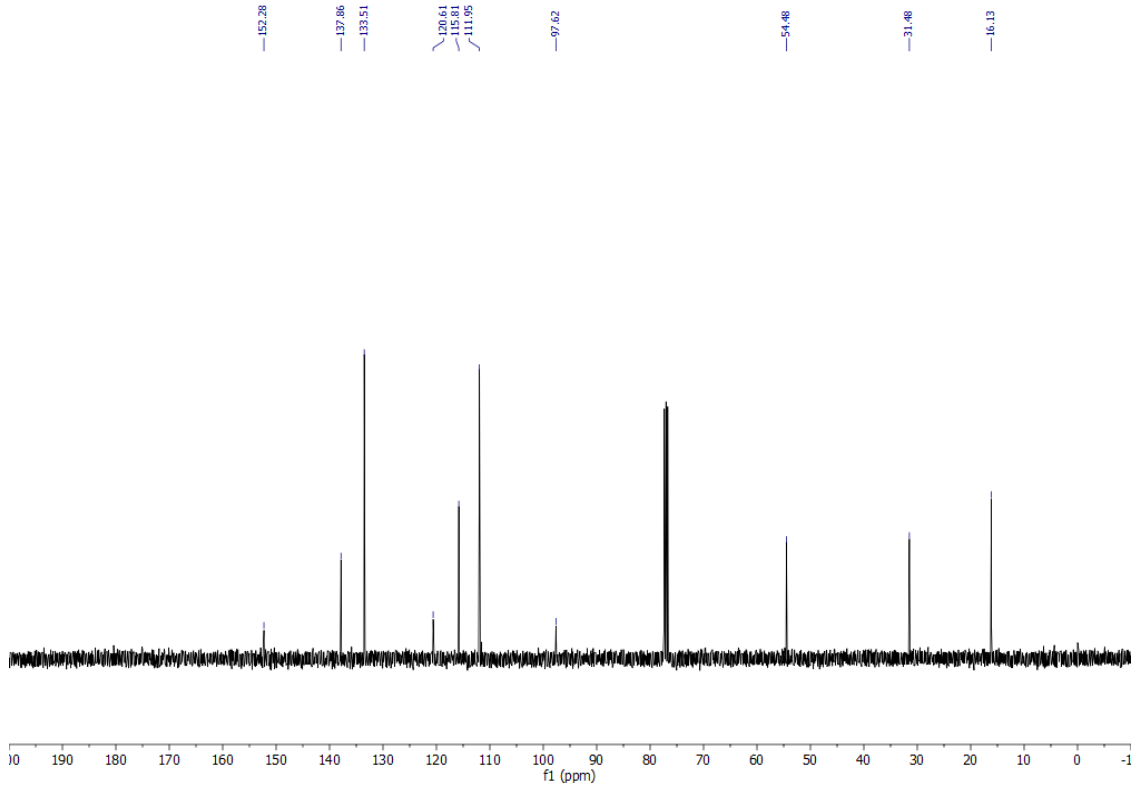
HRMS (ESI): Calculated for $C_{12}H_{14}N_2$ [M+H$^+$] = 187.1230, Found 187.1231.

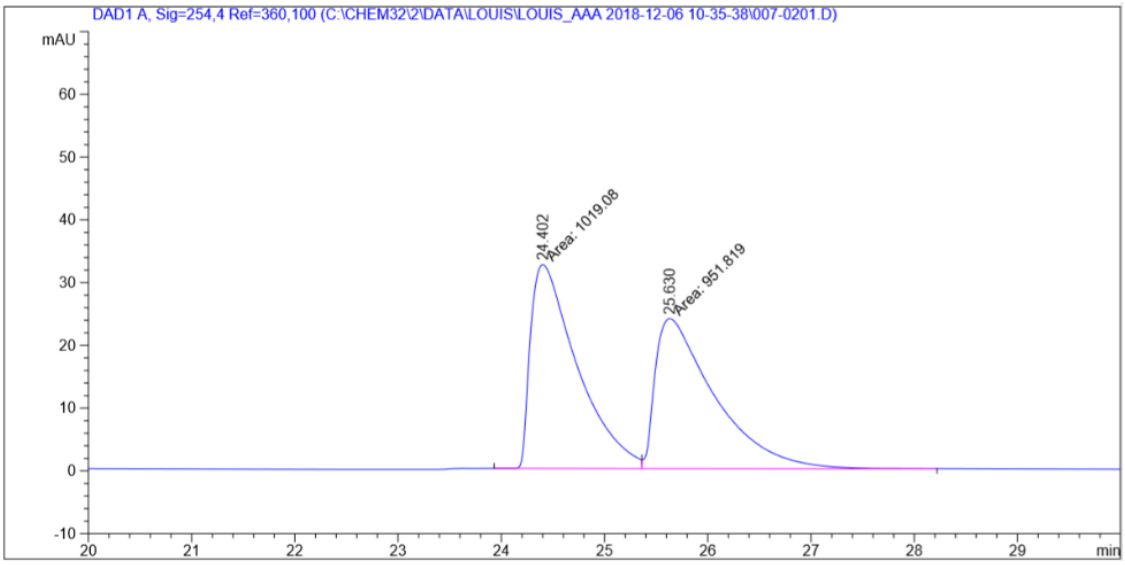
FTIR (neat): 3726, 3627, 2360, 2341, 2111, 1602, 1517, 1383, 1179, 1111, 922, 816, 669, 543 cm^{-1}.

$[\alpha]_D^{28}$= –207.8 (*c* 0.2, $CHCl_3$).

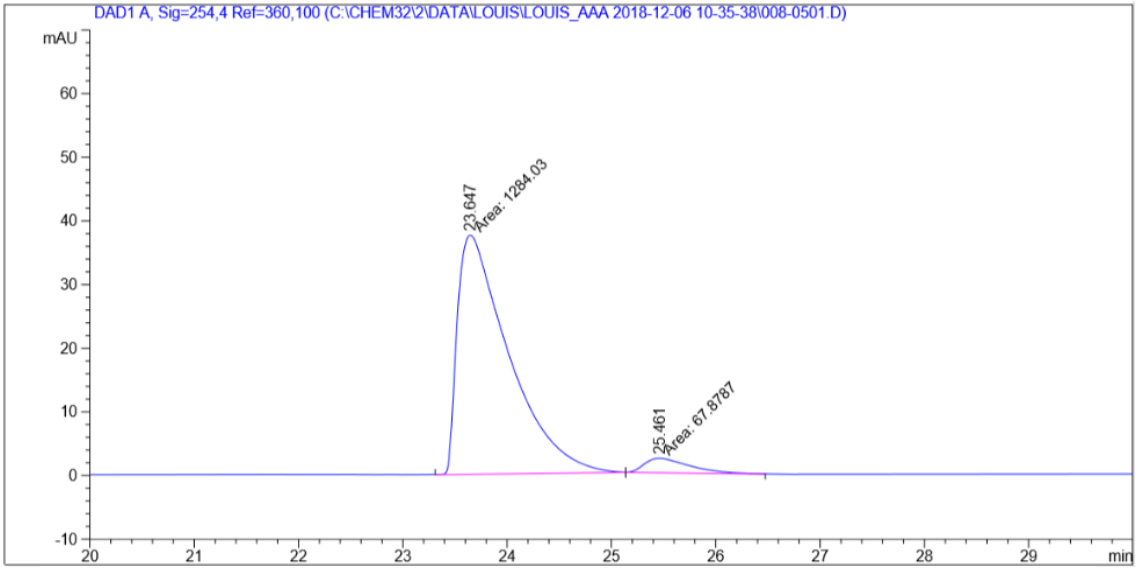
HPLC (Two connected chiralcel OD-3 & OD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 90%.


7.48 7.47 7.47 7.46 7.46 7.45 7.45 7.44 6.74 6.73 6.73 6.71 6.71 6.70
5.90 5.89 5.87 5.86 5.85 5.84 5.83 5.82 5.23 5.22 5.22 5.20 5.20 5.20 5.19 5.16 5.16 5.16 5.12 5.12 5.11 5.11 4.57 4.56 4.56 4.55 4.55 4.54 4.54 4.53 4.52 4.51 4.51 4.50 4.50 2.81 1.32 1.31
1.95 2.06 0.96 1.00 1.00 1.04 3.00 3.14
f1 (ppm)


152.28 137.86 133.51 120.61 115.81 111.95 97.62 54.48 31.48 16.13
f1 (ppm)

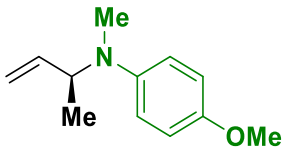


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.402	MF	0.5228	1019.07697	32.49002	51.7063
2	25.630	FM	0.6645	951.81891	23.87190	48.2937



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.647	MM	0.5696	1284.03052	37.56815	94.9790
2	25.461	MM	0.5000	67.87875	2.26275	5.0210

(*S*)-N-(but-3-en-2-yl)-4-methoxy-N-methylaniline (5.5i)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the secondary amine (120.7 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 89% yield (74.9 mg, 0.39 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–10:1).

TLC (SiO_2) R_f = 0.38 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.86 – 6.77 (m, 4H), 5.92 (ddd, *J* = 17.2, 10.7, 4.6 Hz, 1H), 5.18 – 5.09 (m, 2H), 4.28 (dtdd, *J* = 8.5, 6.6, 3.9, 1.8 Hz, 1H), 3.77 (s, 3H), 2.67 (s, 3H), 1.21 (d, *J* = 6.7 Hz, 3H).

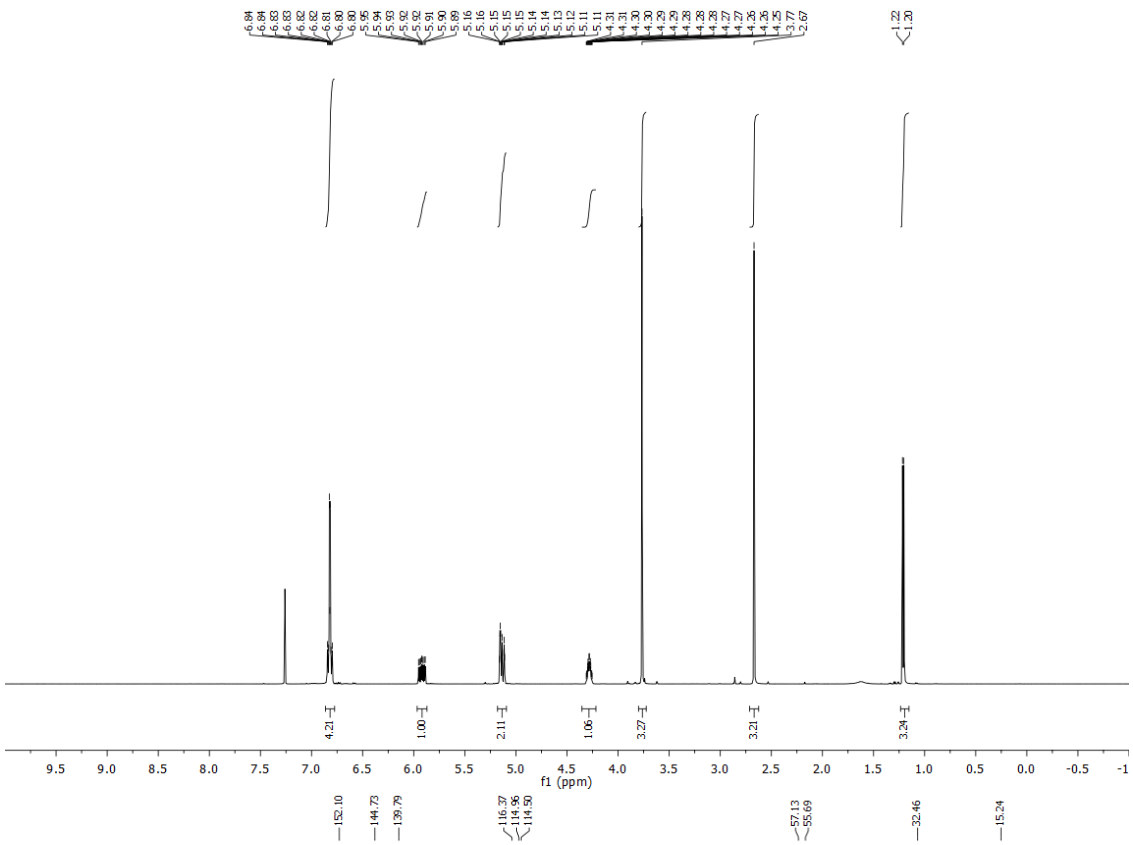
^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.1, 144.7, 139.8, 116.4, 115.0, 114.5, 57.1, 55.7, 32.5, 15.2.

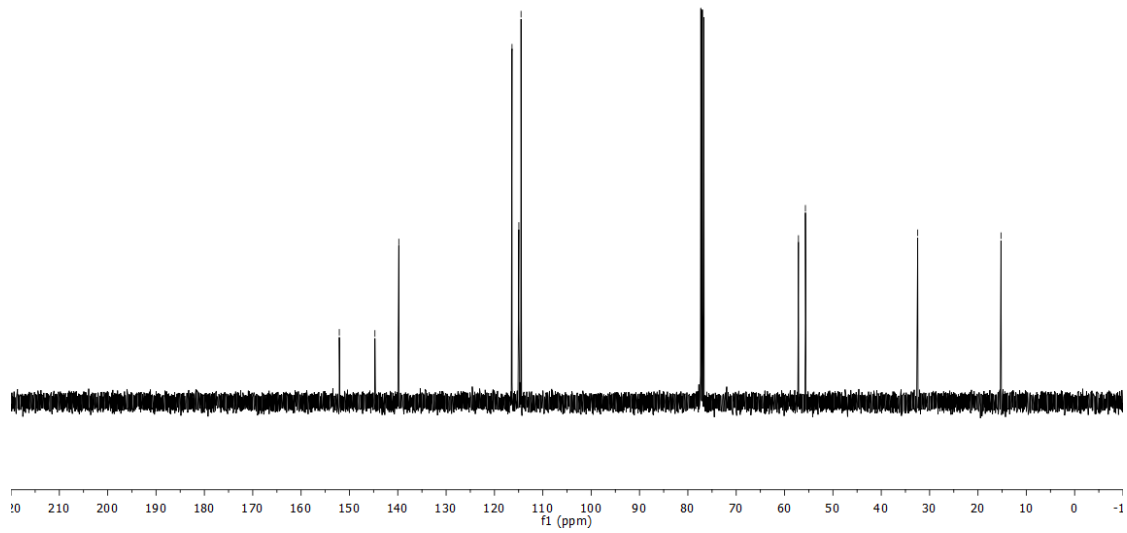
HRMS (ESI): Calculated for $C_{12}H_{17}NO$ [M+H$^+$] = 192.1383, Found 192.1381.

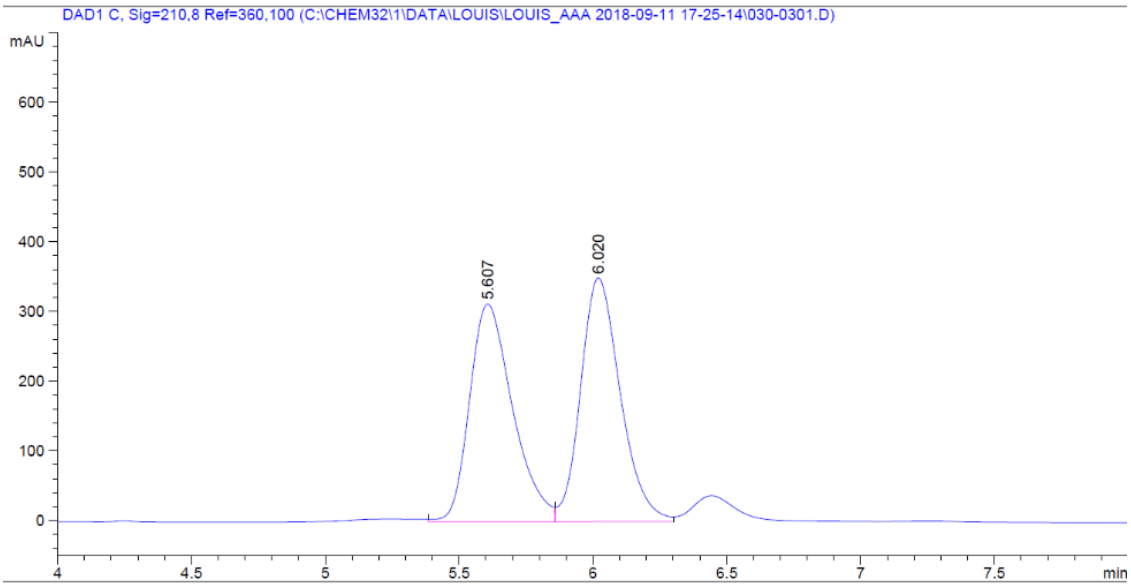
FTIR (neat): 2975, 1509, 1464, 1242, 1110, 1039, 919, 815, 754 cm^{-1}.

$[\alpha]_D^{28}$= –112.0 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 210 nm), *ee* = 93%.







Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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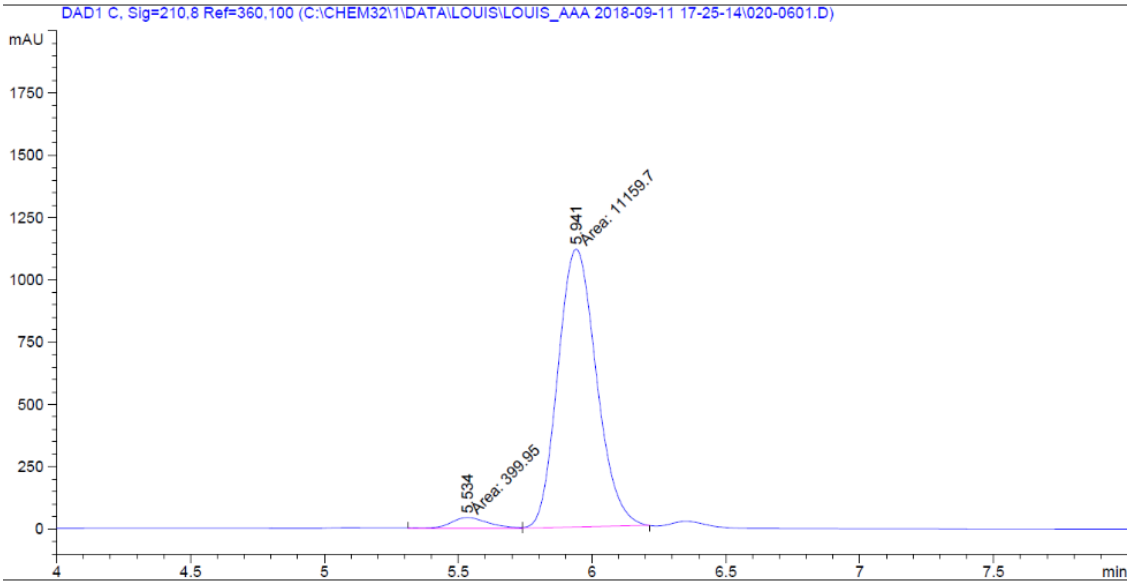
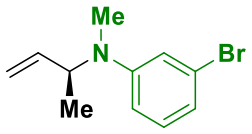
2	6.020	VV	0.1584	3610.33838	349.97104	50.7636



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.534	MM	0.1567	399.95032	42.53660	3.4599
2	5.941	MM	0.1665	1.11597e4	1116.88684	96.5401

(*S*)-3-bromo-N-(but-3-en-2-yl)-N-methylaniline (5.5j)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the secondary amine (163.7 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 60 hr). The title compound was obtained in 64% yield (67.6 mg, 0.28 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 40:1–20:1).

TLC (SiO_2) R_f = 0.59 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.06 (t, *J* = 8.1 Hz, 1H), 6.89 (t, *J* = 2.2 Hz, 1H), 6.81 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.69 (dd, *J* = 8.5, 2.5 Hz, 1H), 5.88 (ddd, *J* = 17.4, 10.6, 4.1 Hz, 1H), 5.20 – 5.11 (m, 2H), 4.44 (qdt, *J* = 6.5, 4.0, 2.0 Hz, 1H), 2.72 (s, 3H), 1.27 (d, *J* = 6.8 Hz, 3H).

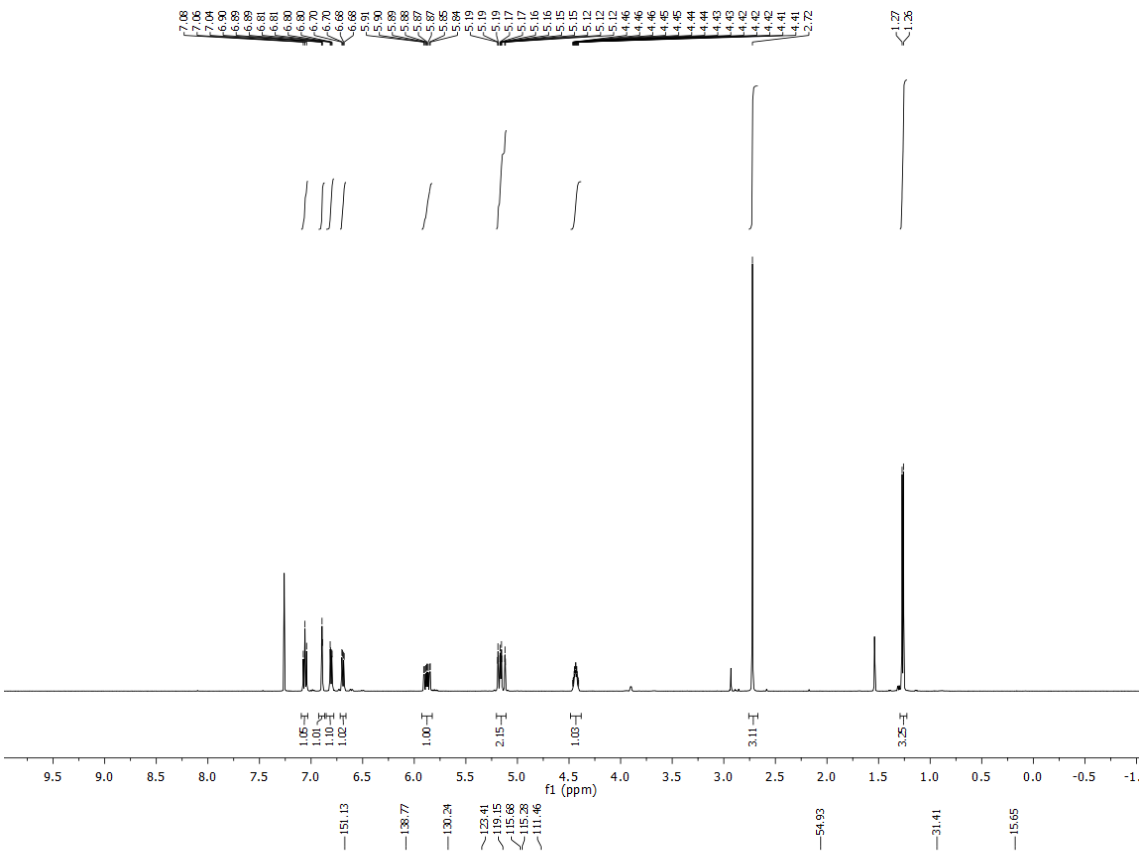
^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1, 138.8, 130.2, 123.4, 119.2, 115.7, 115.3, 111.5, 54.9, 31.4, 15.7.

HRMS (ESI): Calculated for $C_{11}H_{14}BrN$ [M+H$^+$] = 240.0382, Found 240.0382.

FTIR (neat): 1590, 1554, 1487, 1215, 1114, 981, 925, 752, 681 cm^{-1}.

$[\alpha]_D^{28}$ = –95.8 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 90%.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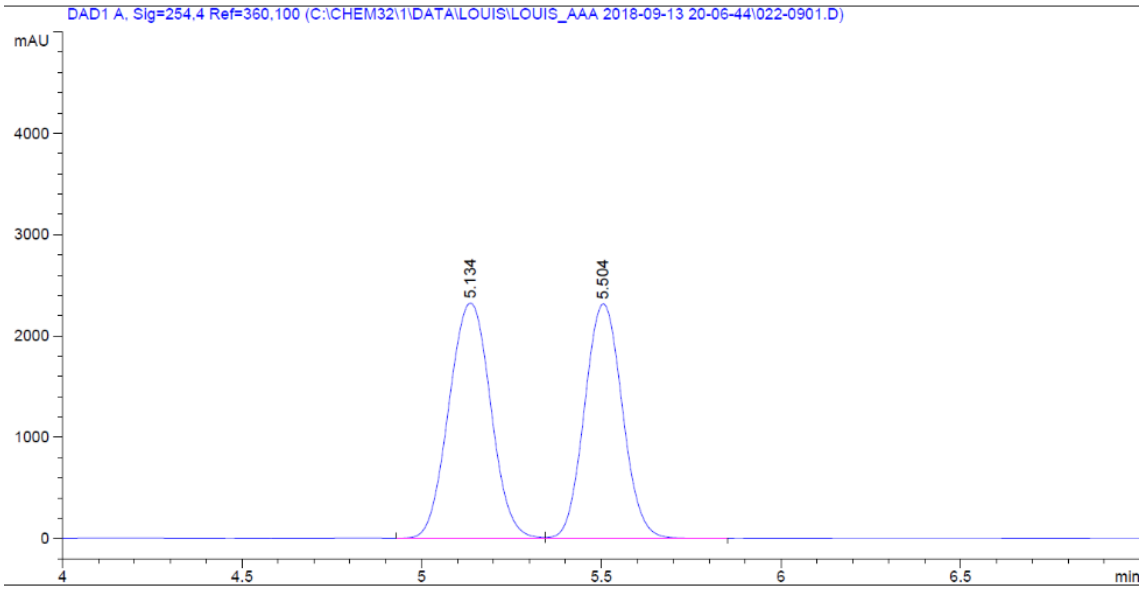
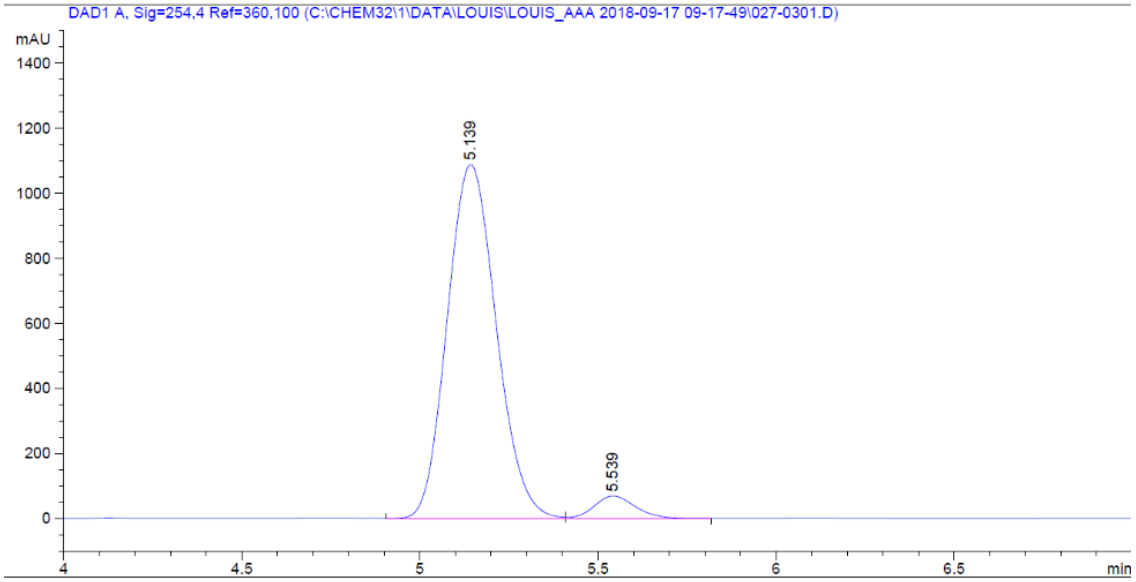
15.65
f1 (ppm)

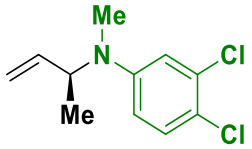


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.134	VV	0.1282	1.87770e4	2325.36768	52.6472
2	5.504	VB	0.1150	1.68887e4	2317.19702	47.3528



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.139	VV	0.1494	1.03940e4	1088.91272	94.9763
2	5.539	VB	0.1230	549.78442	68.94199	5.0237

(*S*)-N-(but-3-en-2-yl)-3,4-dichloro-N-methylaniline (5.5k)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the secondary amine (154.9 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 60 hr). The title compound was obtained in 76% yield (76.9 mg, 0.33 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 40:1–20:1).

TLC (SiO_2) R_f = 0.59 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.22 (d, *J* = 9.0 Hz, 1H), 6.81 (d, *J* = 2.9 Hz, 1H), 6.60 (dd, *J* = 9.0, 3.0 Hz, 1H), 5.86 (ddd, *J* = 17.4, 10.6, 4.1 Hz, 1H), 5.18 (ddd, *J* = 10.6, 2.0, 1.2 Hz, 1H), 5.13 (ddd, *J* = 17.4, 2.0, 1.2 Hz, 1H), 4.39 (qdt, *J* = 6.5, 4.1, 2.1 Hz, 1H), 2.71 (s, 3H), 1.26 (d, *J* = 6.8 Hz, 3H).

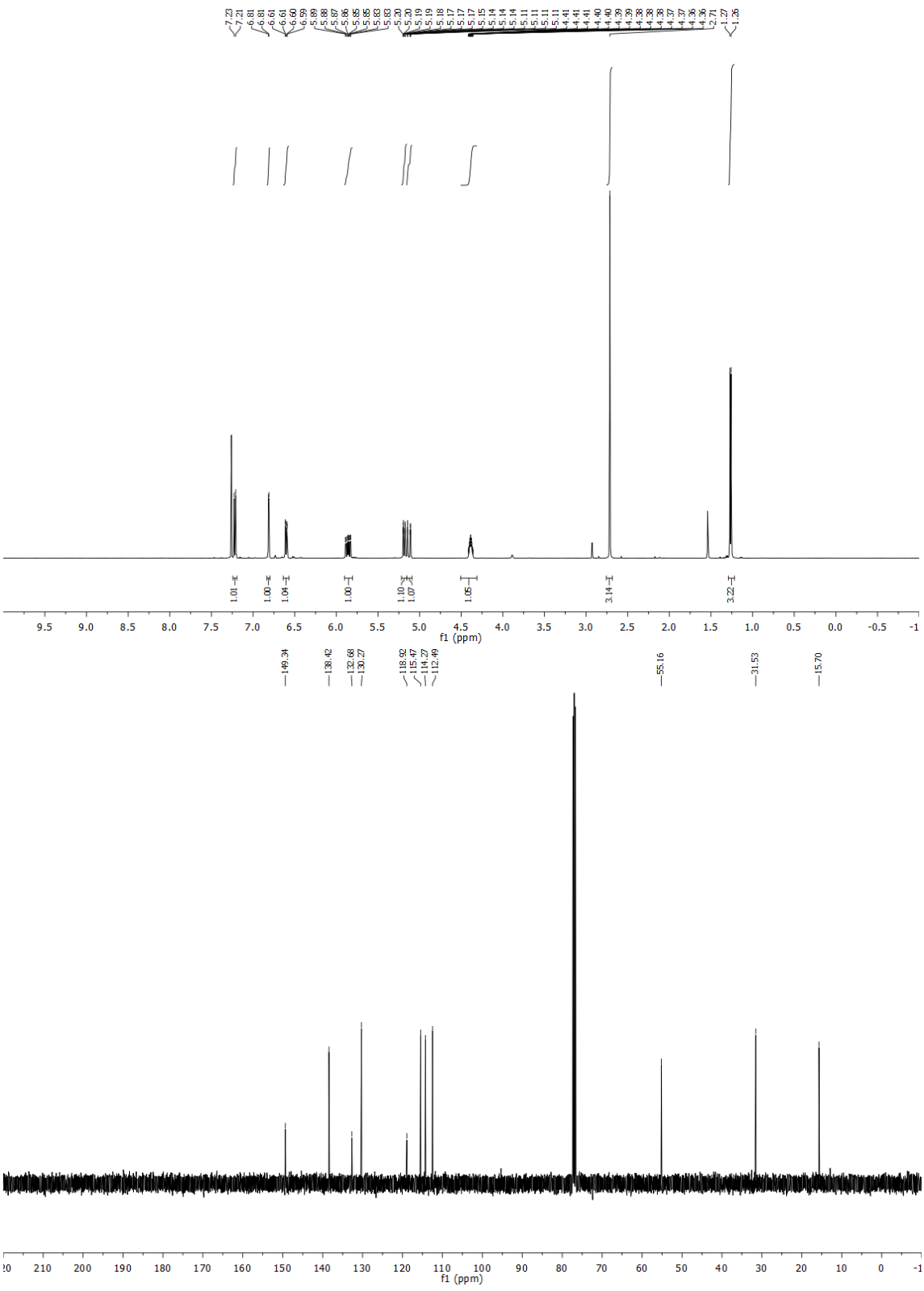
^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.3, 138.4, 132.7, 130.3, 118.9, 115.5, 114.3, 112.5, 55.2, 31.5, 15.7.

HRMS (ESI): Calculated for $C_{11}H_{13}Cl_2N$ [M+H$^+$] = 230.0498, Found 230.0496.

FTIR (neat): 2976, 1593, 1487, 1371, 1214, 1112, 997, 924 cm^{-1}.

$[\alpha]_D^{28}$= –100.0 (*c* 1.0, $CHCl_3$).

HPLC (Two connected chiralcel OD-3 & OD-H column, hexanes:*i*-PrOH = 99.5:0.5, 1.00 mL/min, 254 nm), *ee* = 91%.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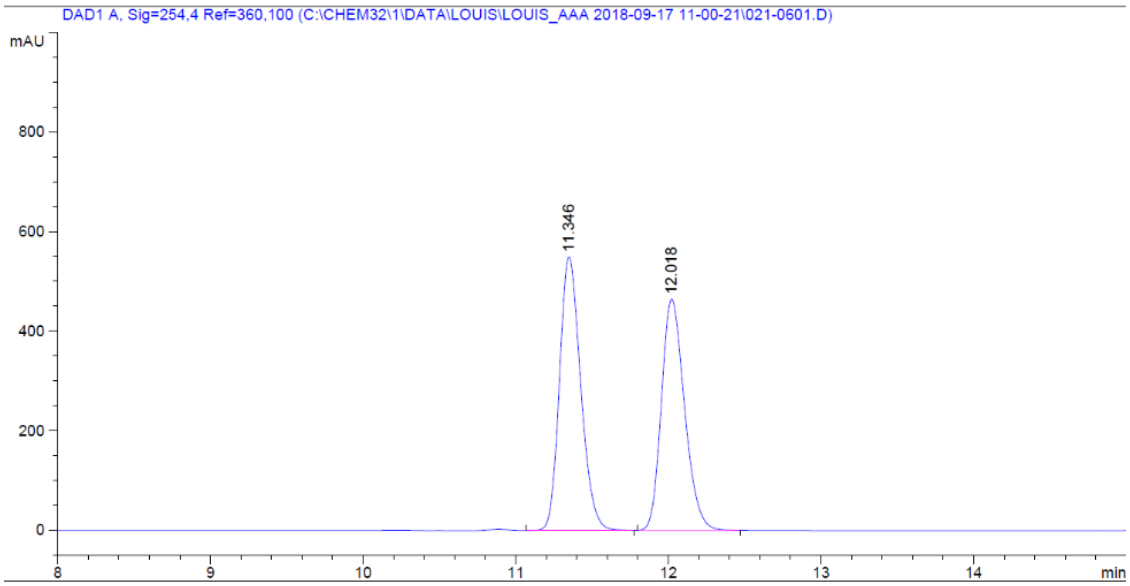
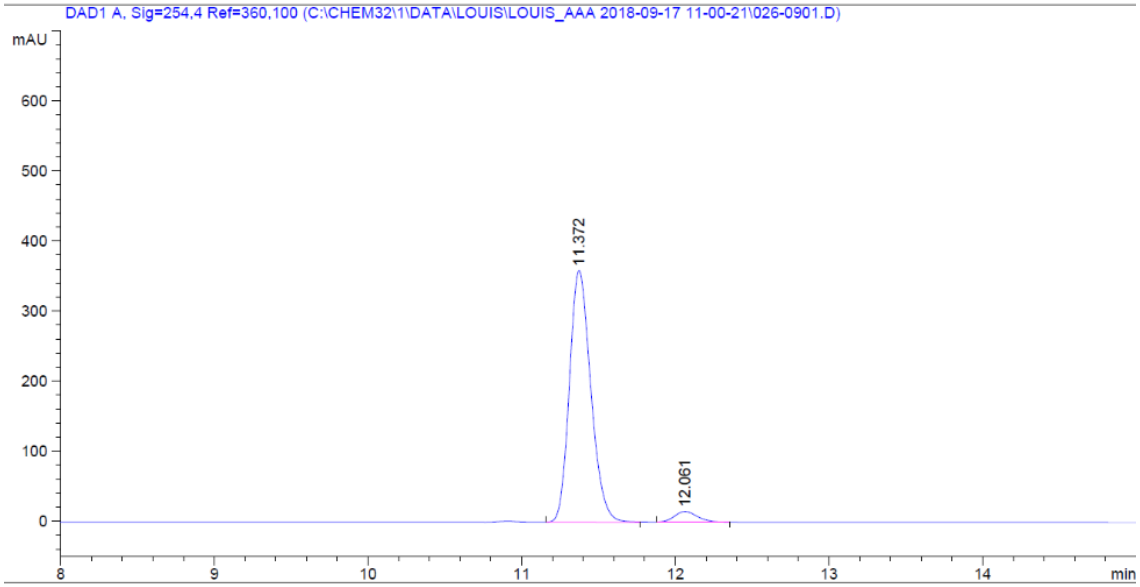
112.49
55.16
31.53
15.70
f1 (ppm)

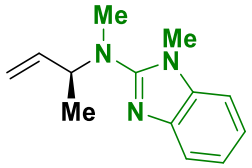


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.346	VB	0.1486	5312.18115	550.45233	52.0154
2	12.018	BB	0.1629	4900.53076	465.21292	47.9846



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.372	BB	0.1507	3472.61035	359.44650	95.5948
2	12.061	BB	0.1602	160.02368	15.27661	4.4052

(*S*)-*N*-(but-3-en-2-yl)-*N*,1-dimethyl-1*H*-benzo[*d*]imidazole-2-amine (5.5l)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the primary amine (141.9 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 94% yield (89.1 mg, 0.41 mmol) as a light orange oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 20%).

TLC (SiO_2) R_f = 0.25 (heptane: isopropyl acetate = 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61-7.58 (m, 1H), 7.20-7.14 (m, 4H), 6.02 (ddd, *J* = 17.4, 10.5, 4.9 Hz, 1H), 5.29-5.25 (m, 1H), 5.25-5.23 (m, 1H), 4.16 (qdt, *J* = 6.8, 4.9, 1.8 Hz, 1H), 3.61 (d, 3H), 2.84 (s, 3H), 1.32 (d, *J* = 6.8 Hz, 3H).

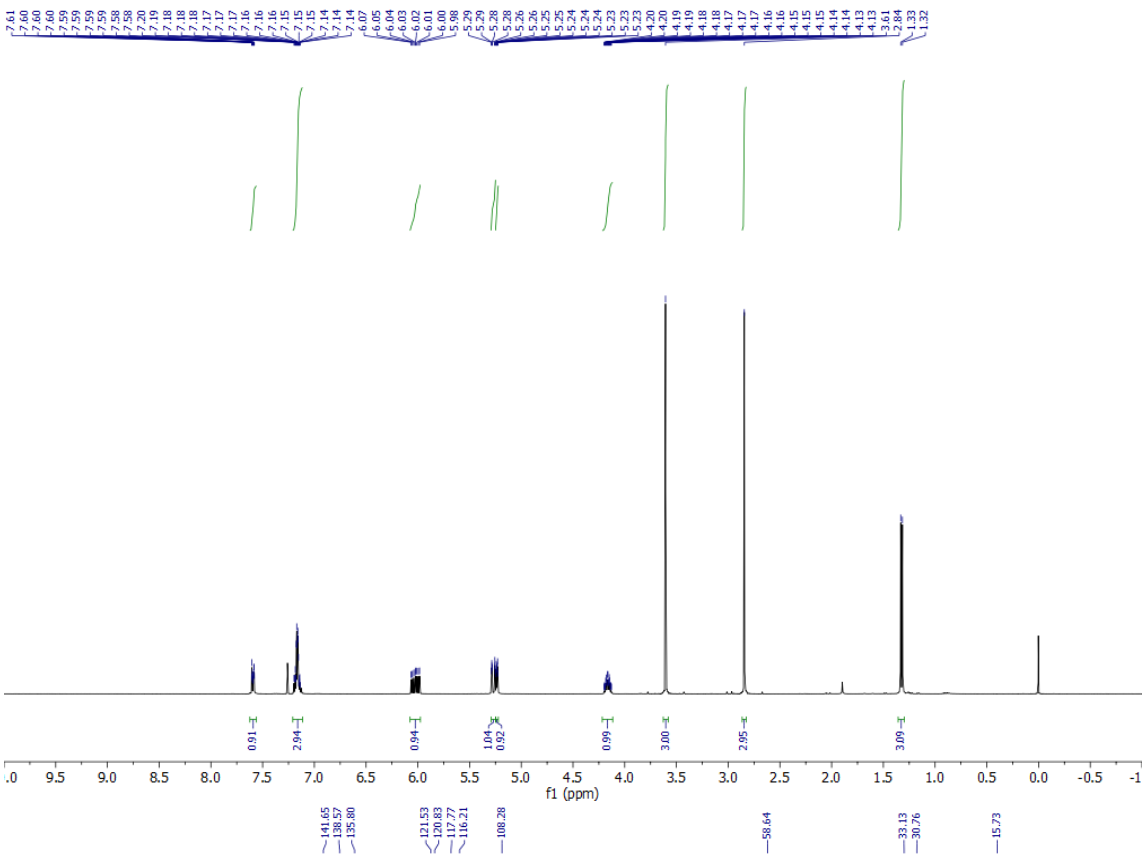
^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.7, 138.6, 135.8, 121.5, 120.8, 117.8, 116.2, 108.3, 58.6, 33.1, 30.8, 15.7.

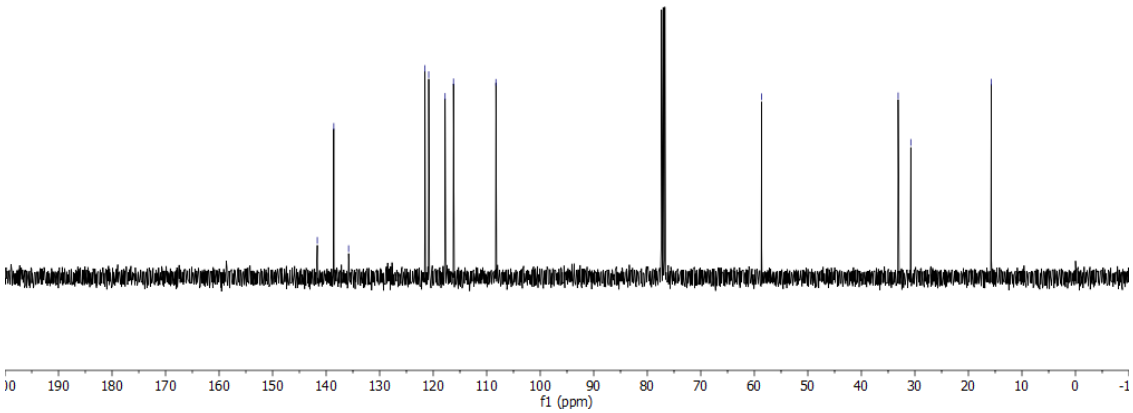
HRMS (ESI): Calculated for $C_{13}H_{17}N_3$ [M+H$^+$] = 216.1495, Found 216.1498.

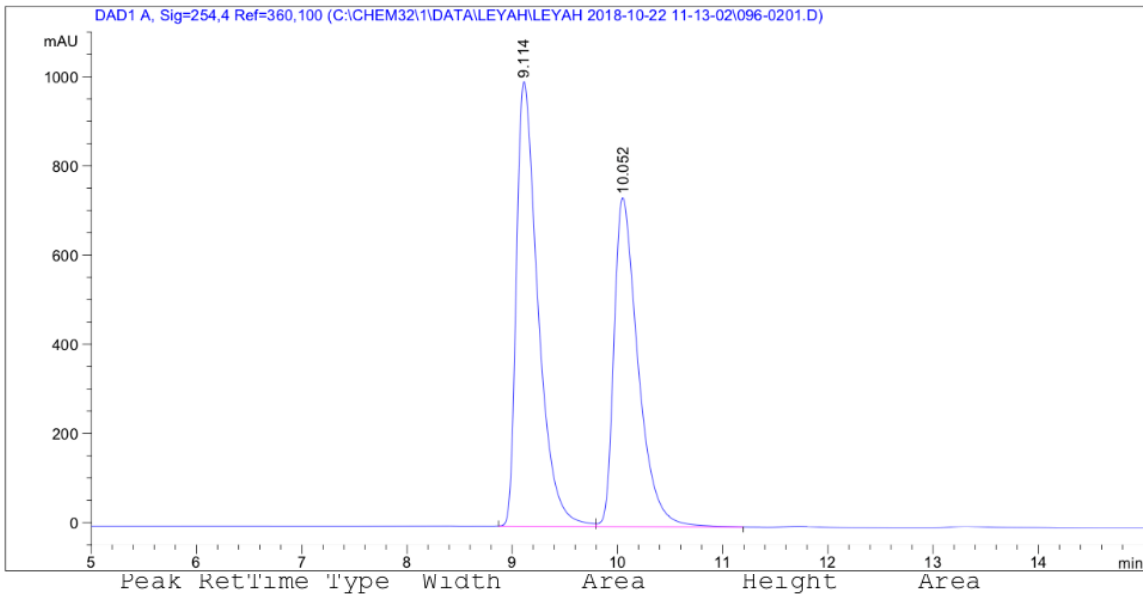
FTIR (neat): 2972, 2360, 2341, 1615, 1594, 1524, 1463, 1390, 1285, 1116, 922, 800, 741, 669 cm^{-1}.

$[\alpha]_D^{28}$ = –129.9 (*c* 0.2, $CHCl_3$).

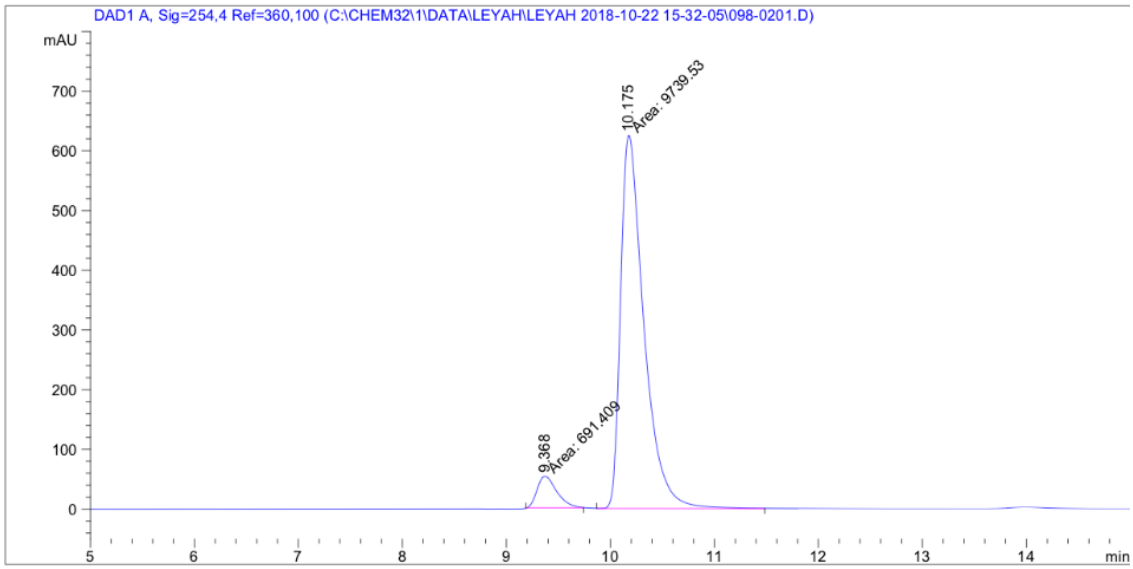
HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 95:5, 1.00 mL/min, 254 nm), *ee* = 87%.


f1 (ppm)


f1 (ppm)

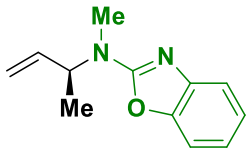


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.114	BV	0.2144	1.42238e4	997.30060	54.8302
2	10.052	VB	0.2394	1.17178e4	737.44312	45.1698



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.368	MM	0.2172	691.40906	53.04517	6.6284
2	10.175	MM	0.2597	9739.53223	625.12000	93.3716

(*S*)-N-(but-3-en-2-yl)-N-methylbenzo[d]oxazol-2-amine (5.6a)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the secondary amine (130.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 94% yield (83.7 mg, 0.41 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, heptanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.63 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 7.7 Hz, 1H), 7.15 (t, *J* = 7.7 Hz, 1H), 7.03 – 6.96 (m, 1H), 5.91 (ddd, *J* = 17.3, 10.7, 4.5 Hz, 1H), 5.28 – 5.20 (m, 2H), 5.04 (dqd, *J* = 8.8, 6.4, 5.6, 2.0 Hz, 1H), 3.02 (s, 3H), 1.38 (d, *J* = 6.9 Hz, 3H).

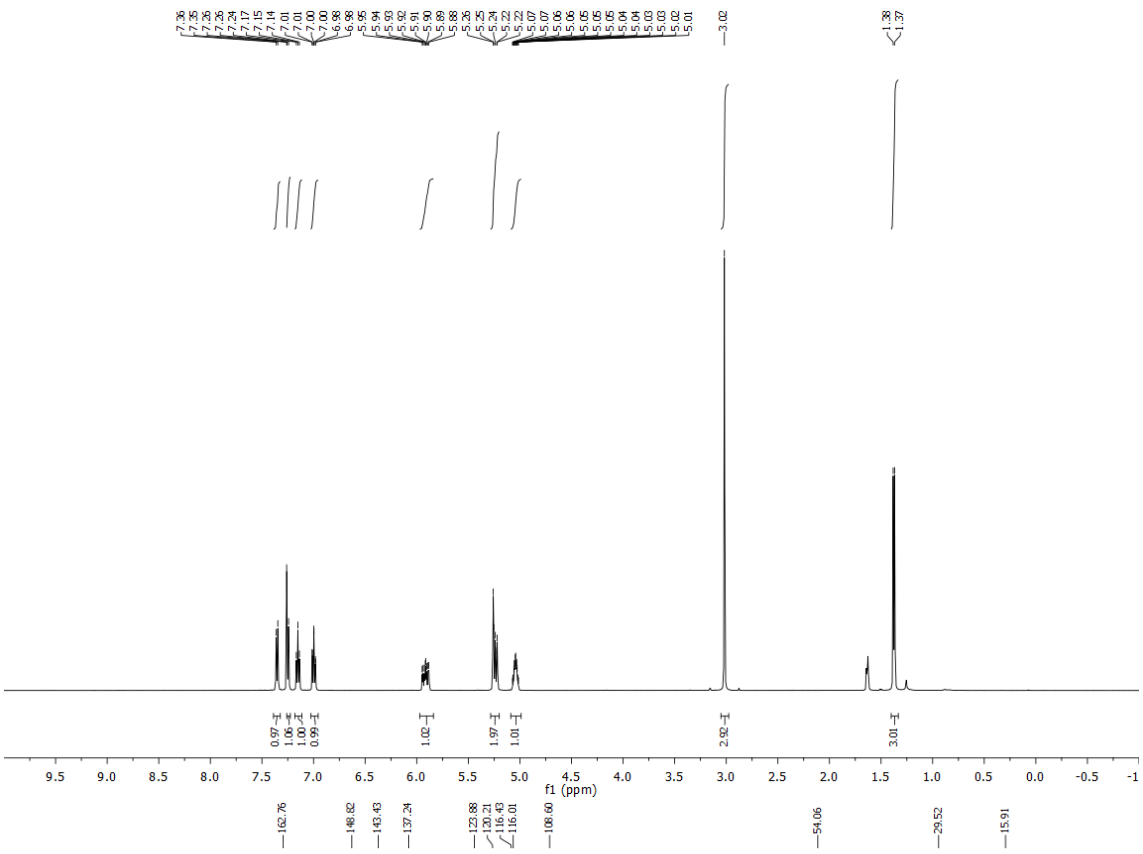
^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.8, 148.8, 143.4, 137.2, 123.9, 120.2, 116.4, 116.0, 108.6, 54.1, 29.5, 15.9.

HRMS (ESI): Calculated for $C_{12}H_{14}N_2O$ [M+H$^+$] = 203.1179, Found 203.1180.

FTIR (neat): 2975, 1632, 1575, 1459, 1424, 1246, 1127, 1001, 925, 793, 740 cm^{-1}.

$[\alpha]_D^{28}$ = –94.5 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 254 nm), *ee* = 91%.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3.02
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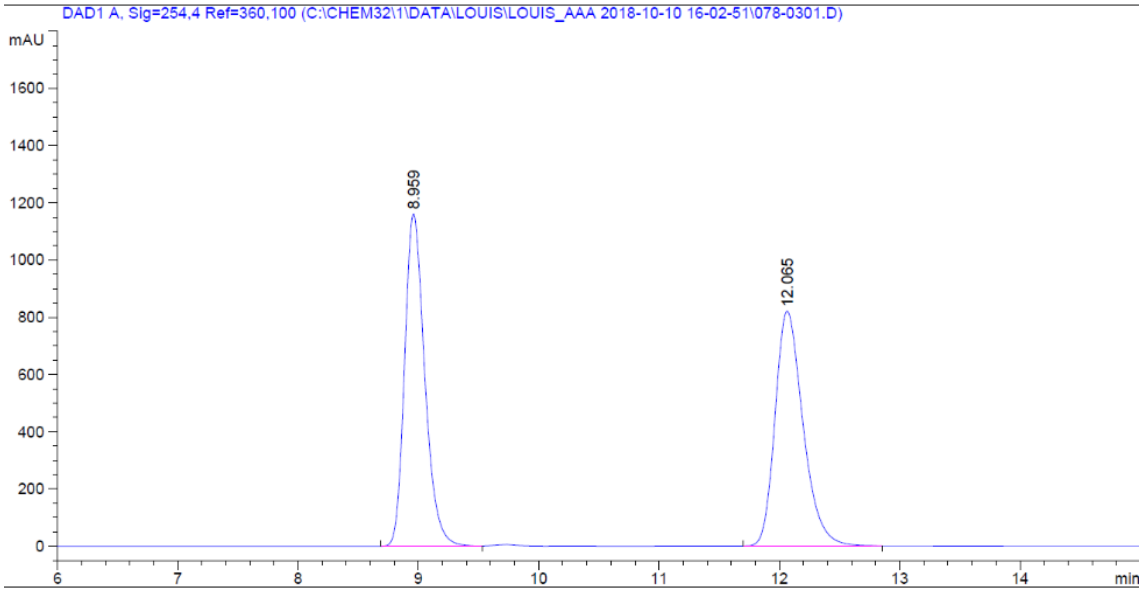
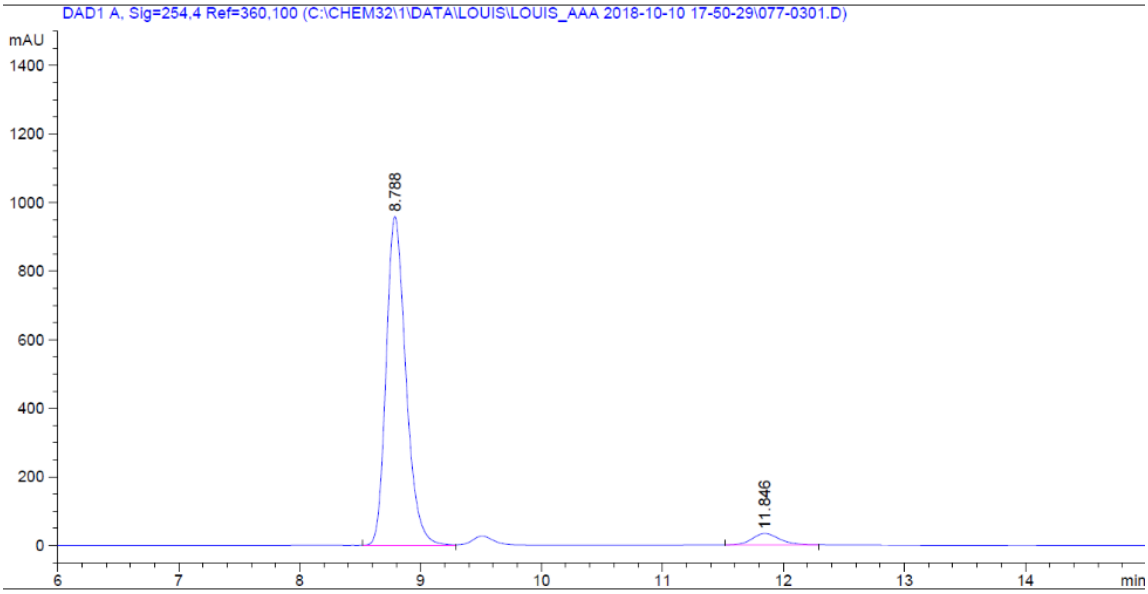
15.91
f1 (ppm)

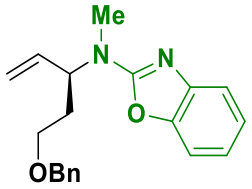


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.959	BV	0.1776	1.35025e4	1161.68359	50.4440
2	12.065	BB	0.2465	1.32648e4	820.81213	49.5560



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.788	BV	0.1742	1.08714e4	959.04358	95.3952
2	11.846	BB	0.2421	524.76575	33.25109	4.6048

(*S*)-N-(5-(benzyloxy)pent-1-en-3-yl)-N-methylbenzo[d]oxazol-2-amine (5.6b)



Procedures

The allylic acetate (103.1 mg, 0.44 mmol, 100 mol%) and the secondary amine (130.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 93% yield (131.9 mg, 0.41 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.44 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.43 – 7.37 (m, 1H), 7.30 – 7.23 (m, 6H), 7.19 (td, *J* = 7.7, 1.1 Hz, 1H), 7.03 (td, *J* = 7.7, 1.2 Hz, 1H), 5.92 (ddd, *J* = 17.6, 10.4, 5.2 Hz, 1H), 5.30 – 5.27 (m, 1H), 5.25 (dt, *J* = 3.5, 1.3 Hz, 1H), 5.07 (ddd, *J* = 13.2, 7.0, 3.6 Hz, 1H), 4.44 (d, *J* = 2.8 Hz, 2H), 3.58 (dt, *J* = 9.5, 5.8 Hz, 1H), 3.52 (dt, *J* = 9.4, 6.7 Hz, 1H), 3.06 (s, 3H), 2.15 – 2.00 (m, 2H).

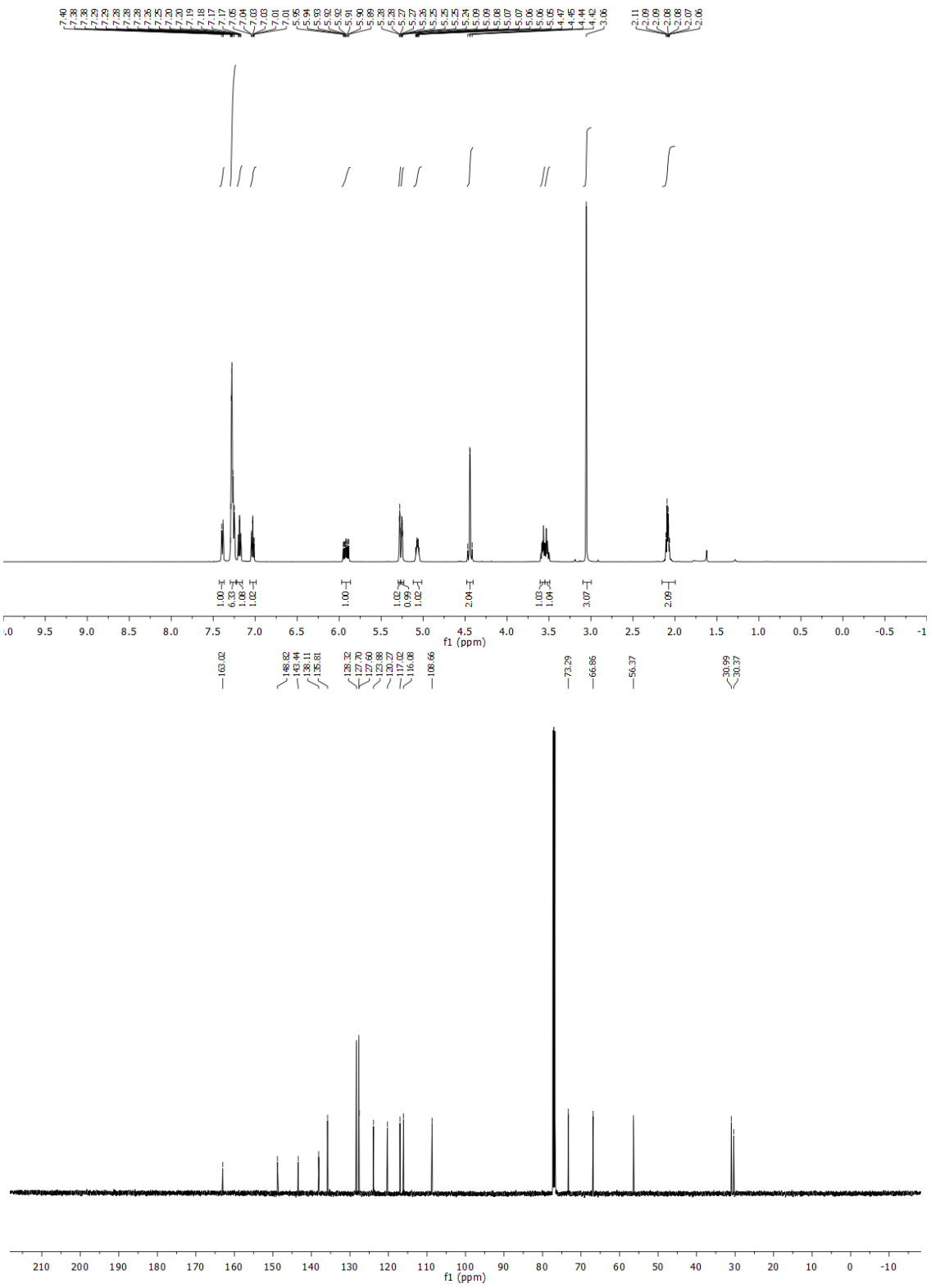
^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.0, 148.8, 143.4, 138.1, 135.8, 128.3, 127.7, 127.6, 123.9, 120.3, 117.0, 116.1, 108.7, 73.3, 66.9, 56.4, 31.0, 30.4.

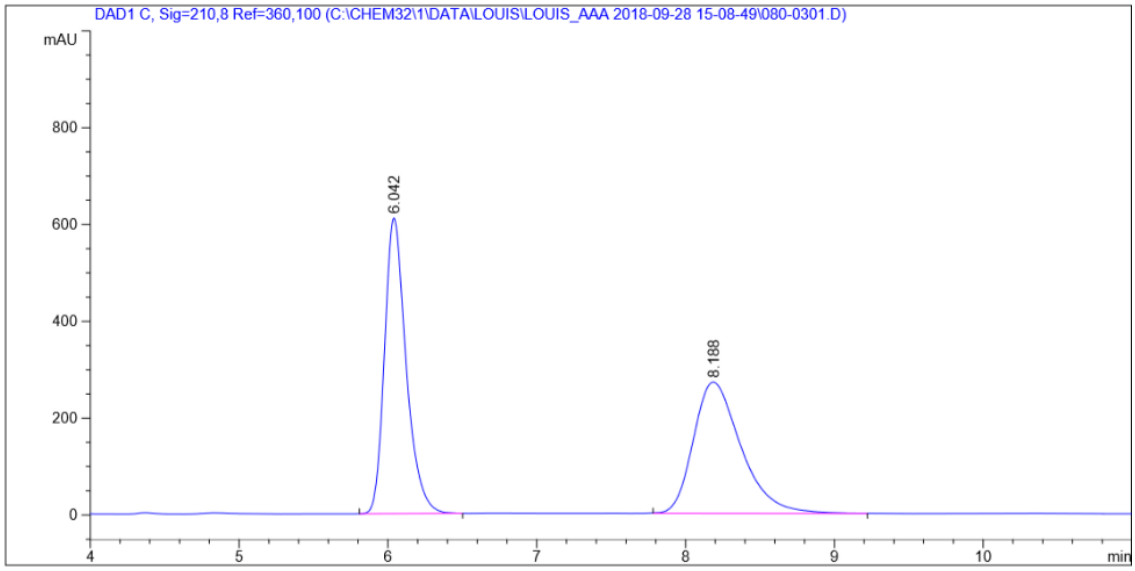
HRMS (ESI): Calculated for $C_{20}H_{22}N_2O_2$ [M+H$^+$] = 323.1754, Found 323.1757.

FTIR (neat): 2857, 1631, 1575, 1459, 1414, 1284, 1246, 1098, 1002, 907, 736, 697 cm^{-1}.

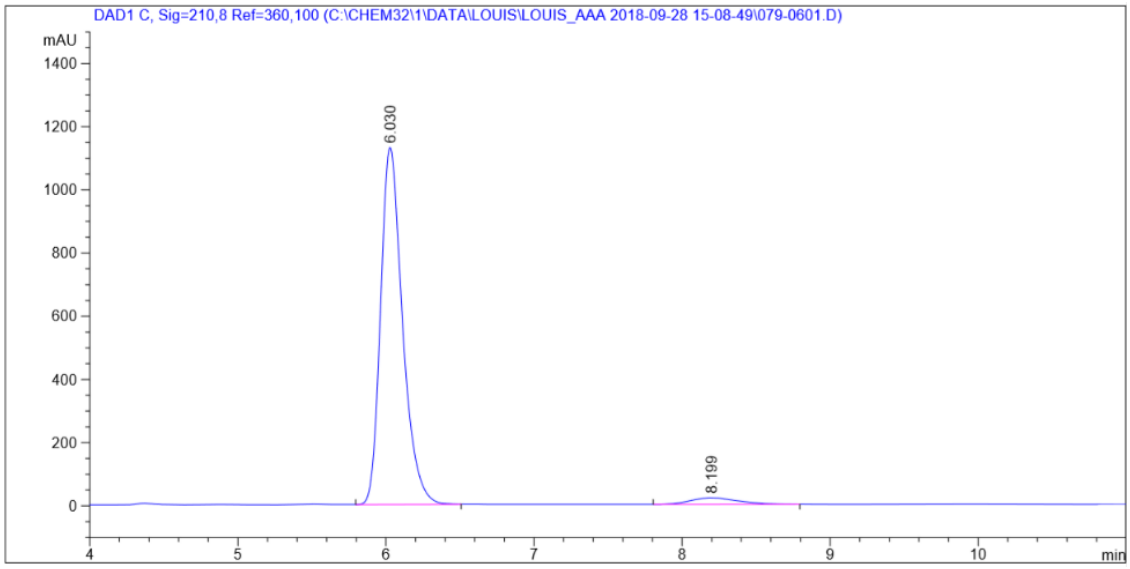
$[\alpha]_D^{28}$= –78.3 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AS-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm), *ee* = 92%.


f1 (ppm)
f1 (ppm)

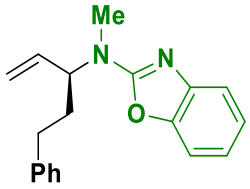


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.042	BB	0.1517	6161.05078	610.68341	50.5683
2	8.188	BB	0.3392	6022.58301	271.04453	49.4317



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.030	BB	0.1580	1.16281e4	1130.74524	96.1479
2	8.199	BB	0.3410	465.86823	20.98823	3.8521

(*S*)-N-methyl-N-(5-phenylpent-1-en-3-yl)benzo[d]oxazol-2-amine (5.6c)



Procedures

The allylic acetate (89.8 mg, 0.44 mmol, 100 mol%) and the secondary amine (130.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 92% yield (118.3 mg, 0.40 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.44 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.30 – 7.25 (m, 3H), 7.24 – 7.14 (m, 4H), 7.04 (td, *J* = 7.8, 1.2 Hz, 1H), 5.91 (ddd, *J* = 17.6, 10.3, 5.2 Hz, 1H), 5.29 (t, *J* = 1.4 Hz, 1H), 5.26 (dt, *J* = 5.2, 1.3 Hz, 1H), 4.94 – 4.85 (m, 1H), 3.08 (s, 3H), 2.70 (t, *J* = 8.0 Hz, 2H), 2.15 – 2.00 (m, 2H).

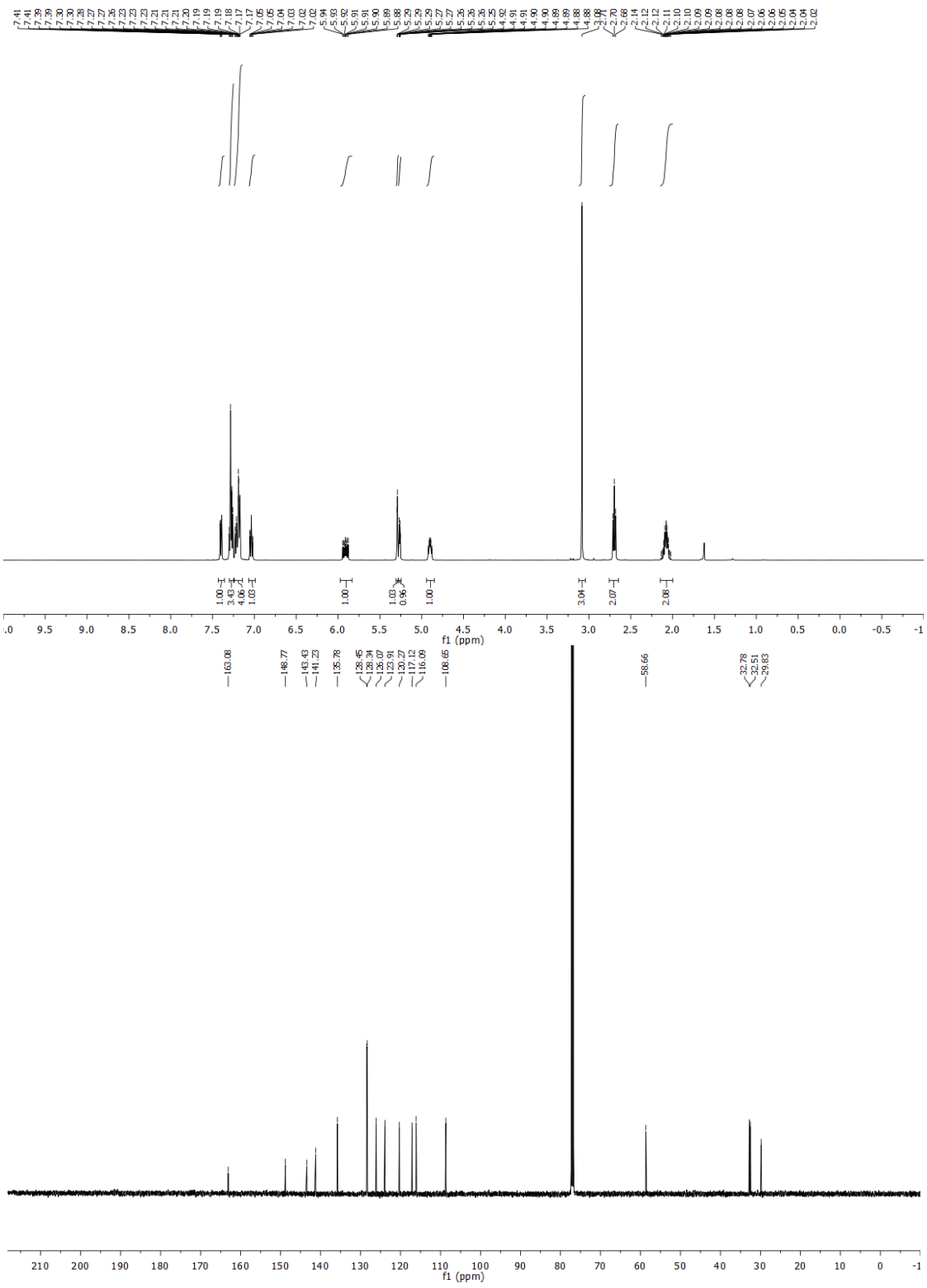
^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.1, 148.8, 143.4, 141.2, 135.8, 128.5, 128.3, 126.1, 123.9, 120.3, 117.1, 116.1, 108.7, 58.7, 32.8, 32.5, 29.8.

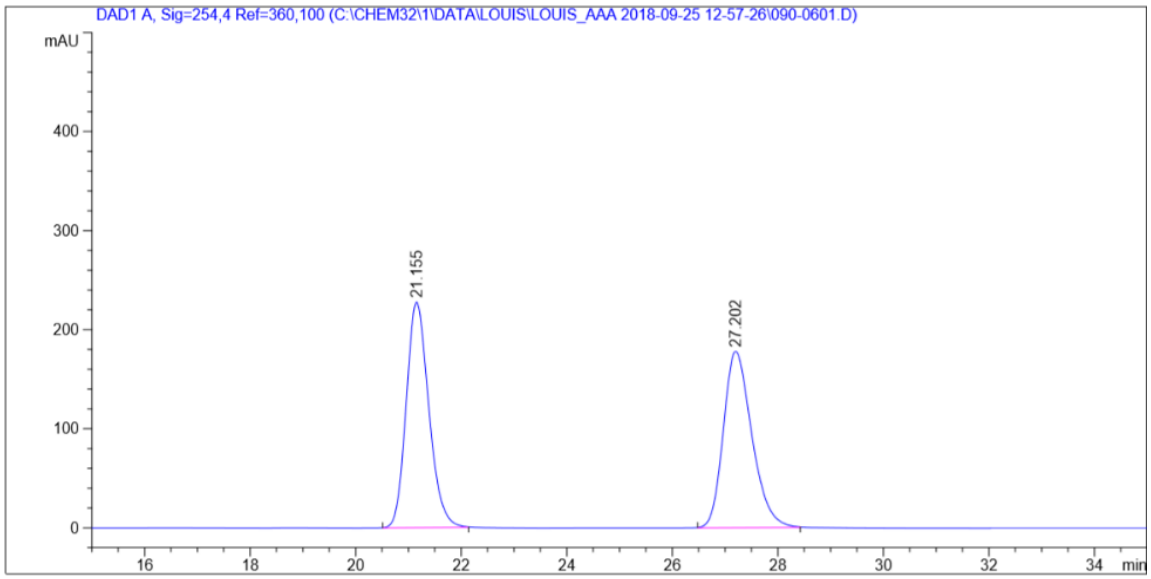
HRMS (ESI): Calculated for $C_{19}H_{20}N_2O$ [M+H$^+$] = 293.1648, Found 293.1656.

FTIR (neat): 2941, 1630, 1574, 1496, 1458, 1245, 1125, 1000, 926, 738, 698 cm^{-1}.

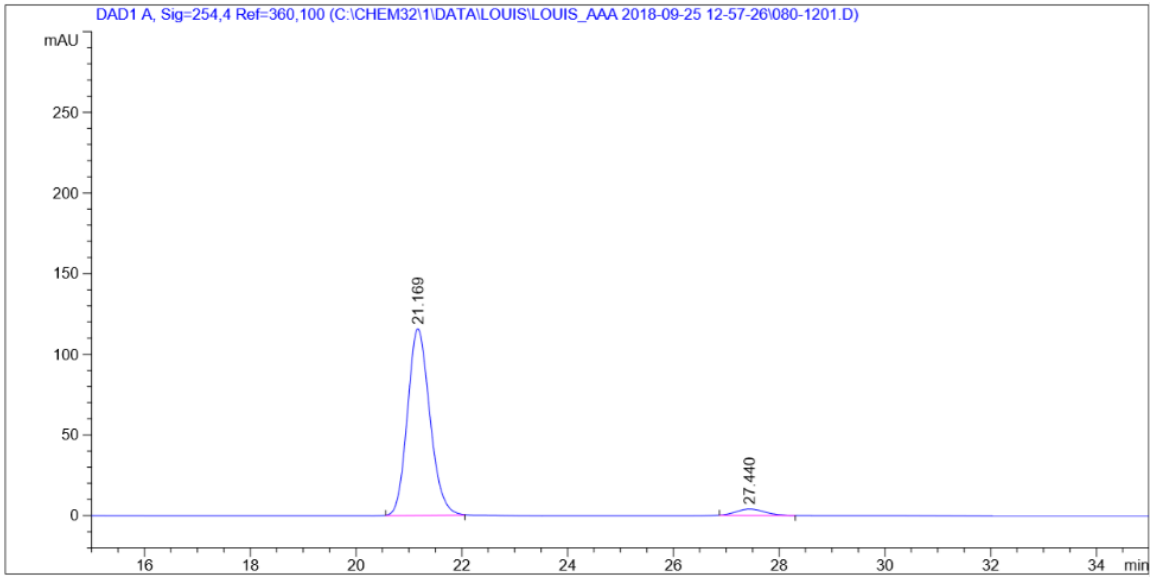
$[\alpha]_D^{28}$ = –29.5 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 92%.


f1 (ppm)
f1 (ppm)

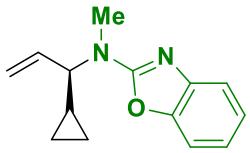


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.155	BB	0.4589	6768.60742	227.63060	50.3637
2	27.202	BB	0.5754	6670.84033	177.91081	49.6363



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.169	BB	0.4553	3404.30225	115.69923	95.9147
2	27.440	BB	0.4669	144.99965	3.98118	4.0853

(*R*)-N-(1-cyclopropylallyl)-N-methylbenzo[d]oxazol-2-amine (5.6d)



Procedures

The allylic acetate (61.7 mg, 0.44 mmol, 100 mol%) and the secondary amine (130.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 48 hr). The title compound was obtained in 81% yield (81.3 mg, 0.36 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 30:1–15:1).

TLC (SiO_2) R_f = 0.56 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.23 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.14 (td, *J* = 7.6, 1.2 Hz, 1H), 6.99 (td, *J* = 7.8, 1.3 Hz, 1H), 5.93 (ddd, *J* = 17.4, 10.5, 4.4 Hz, 1H), 5.36 (dt, *J* = 17.3, 1.6 Hz, 1H), 5.26 (dt, *J* = 10.5, 1.6 Hz, 1H), 4.16 – 4.04 (m, 1H), 3.16 (s, 3H), 1.14 (dtt, *J* = 9.6, 8.0, 4.9 Hz, 1H), 0.74 (dddd, *J* = 8.0, 6.7, 4.7, 3.3 Hz, 1H), 0.54 (tdd, *J* = 10.2, 4.3, 3.2 Hz, 1H), 0.48 – 0.35 (m, 2H).

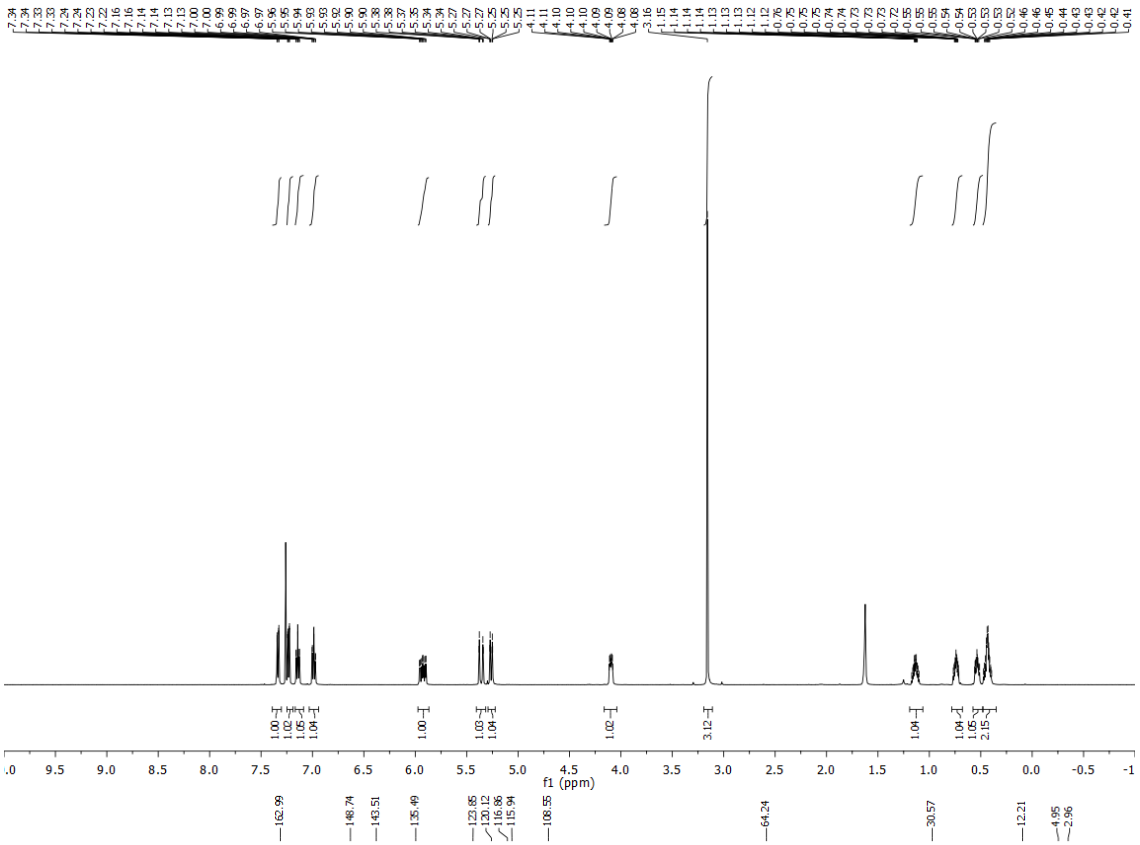
^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.0, 148.7, 143.5, 135.5, 123.9, 120.1, 116.9, 115.9, 108.6, 64.2, 30.6, 12.2, 5.0, 3.0.

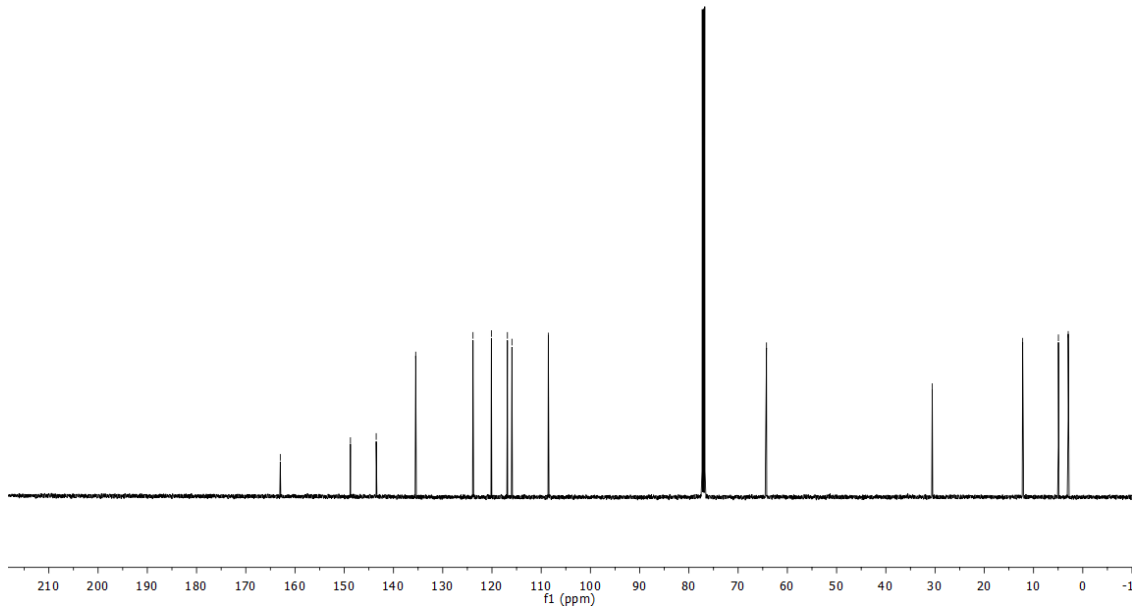
HRMS (ESI): Calculated for $C_{14}H_{16}N_2O$ [M+H$^+$] = 229.1335, Found 229.1337.

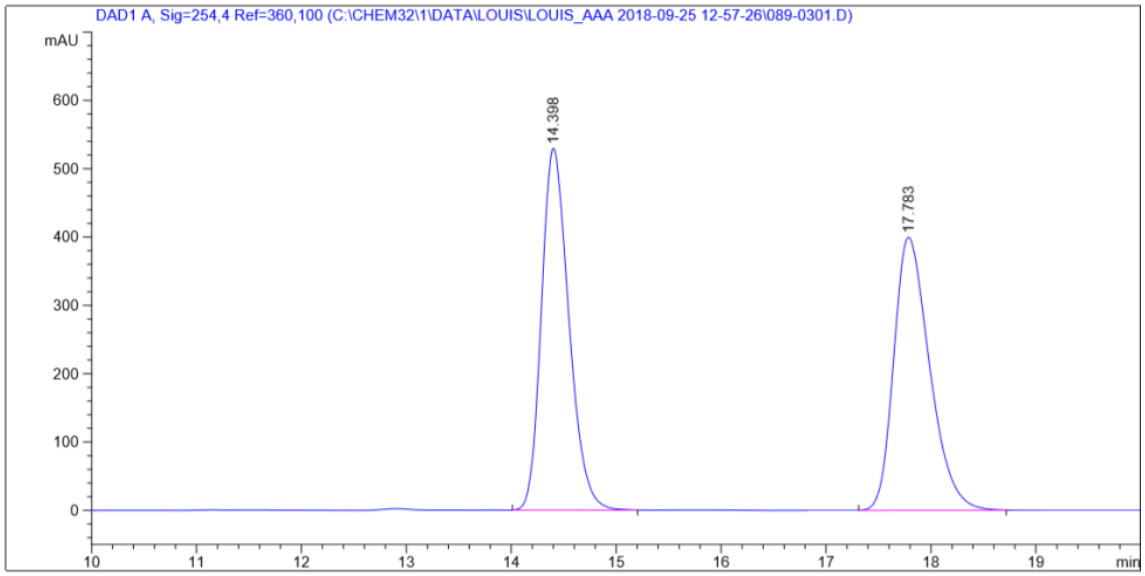
FTIR (neat): 3007, 1629, 1573, 1458, 1423, 1245, 1124, 992, 908, 815, 738 cm^{-1}.

$[\alpha]_D^{28}$= –35.3 (*c* 1.0, $CHCl_3$).

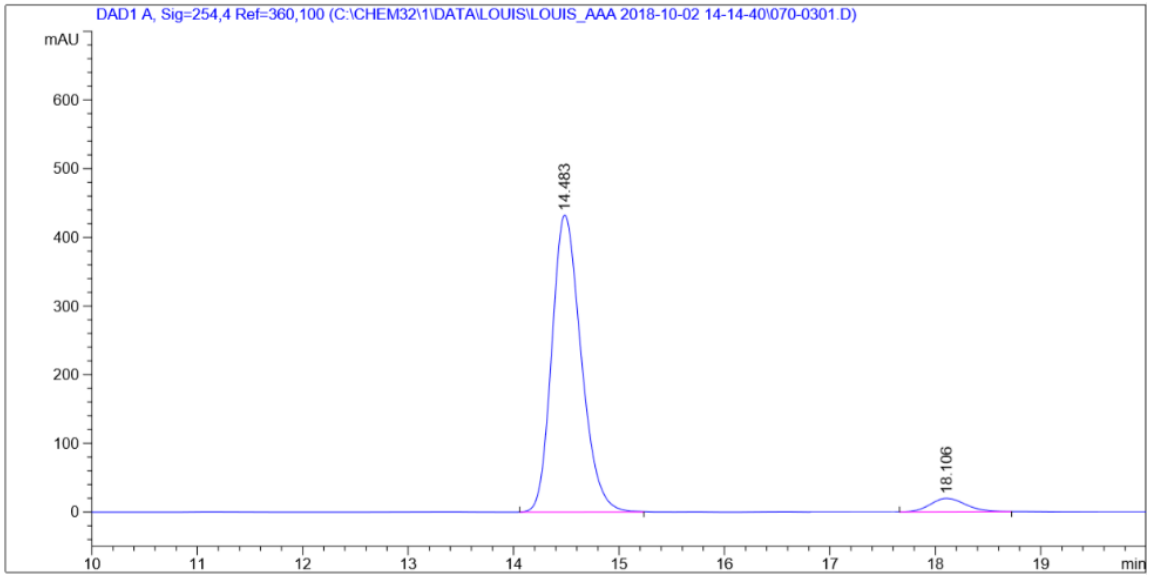
HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 90%.





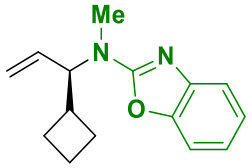


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.398	BB	0.2802	9628.84277	529.48486	50.3624
2	17.783	BB	0.3651	9490.25781	399.62079	49.6376



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.483	BB	0.2968	8335.59668	432.53293	94.8171
2	18.106	BB	0.3575	455.64526	19.72274	5.1829

(*R*)-N-(1-cyclobutylallyl)-N-methylbenzo[d]oxazol-2-amine (5.6e)



Procedures

The allylic acetate (67.9 mg, 0.44 mmol, 100 mol%) and the secondary amine (130.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 48 hr). The title compound was obtained in 71% yield (75.7 mg, 0.31 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.44 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39 – 7.32 (m, 1H), 7.25 (d, *J* = 5.9 Hz, 1H), 7.15 (td, *J* = 7.7, 1.2 Hz, 1H), 7.00 (td, *J* = 7.7, 1.3 Hz, 1H), 5.79 (ddd, *J* = 17.4, 10.7, 5.2 Hz, 1H), 5.26 – 5.14 (m, 2H), 4.82 – 4.69 (m, 1H), 2.99 (s, 3H), 2.71 (dq, *J* = 11.0, 7.7 Hz, 1H), 2.15 (dt, *J* = 12.6, 7.7 Hz, 1H), 2.05 – 1.77 (m, 5H).

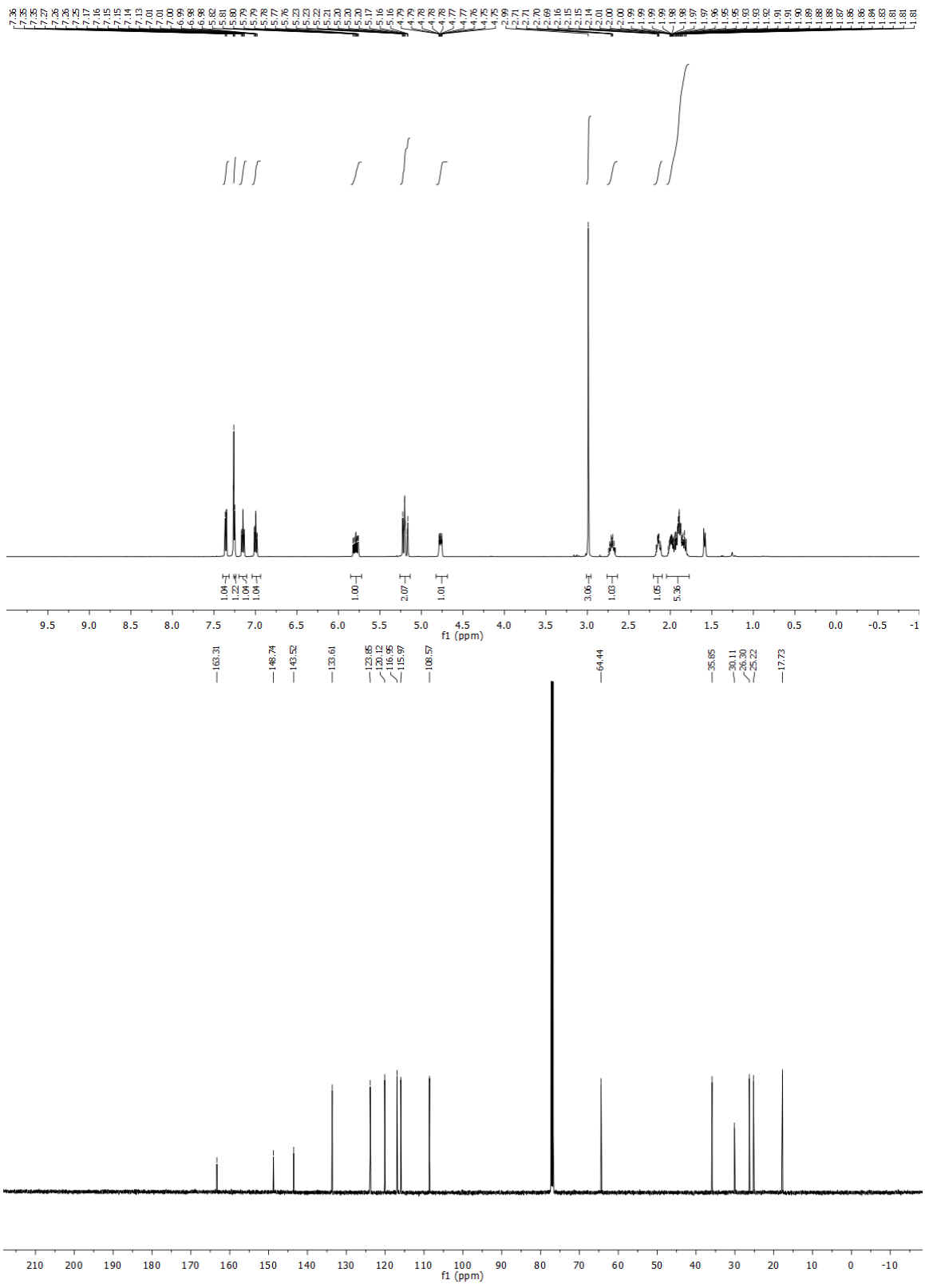
^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.3, 148.7, 143.5, 133.6, 123.9, 120.1, 117.0, 116.0, 108.6, 64.4, 35.9, 30.1, 26.3, 25.2, 17.7.

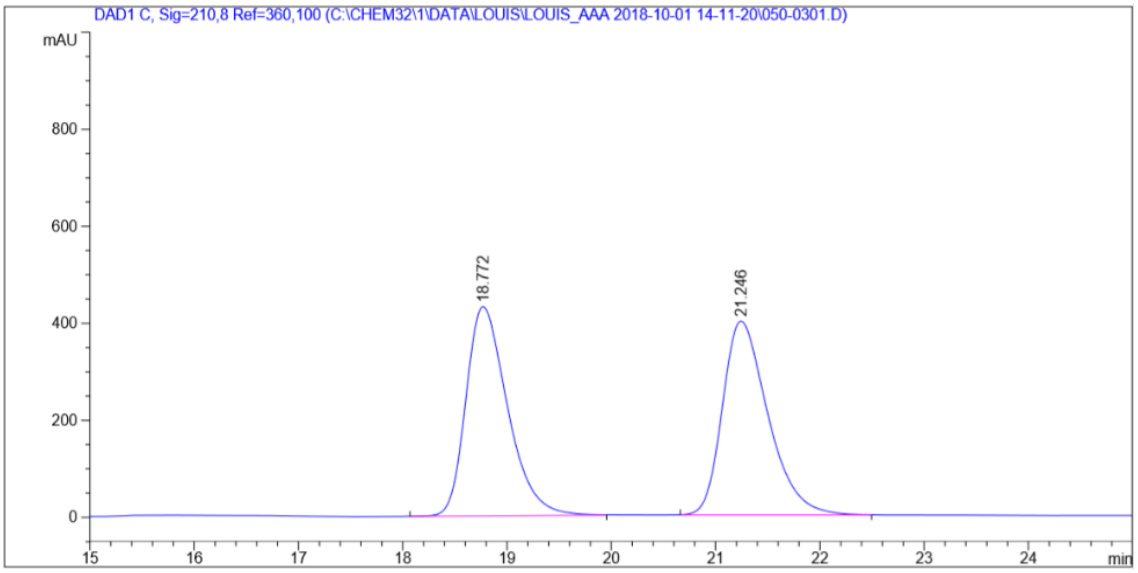
HRMS (ESI): Calculated for $C_{15}H_{18}N_2O$ [M+H$^+$] = 243.1492, Found 243.1495.

FTIR (neat): 2938, 1629, 1573, 1458, 1416, 1245, 1122, 990, 917, 821, 738 cm^{-1}.

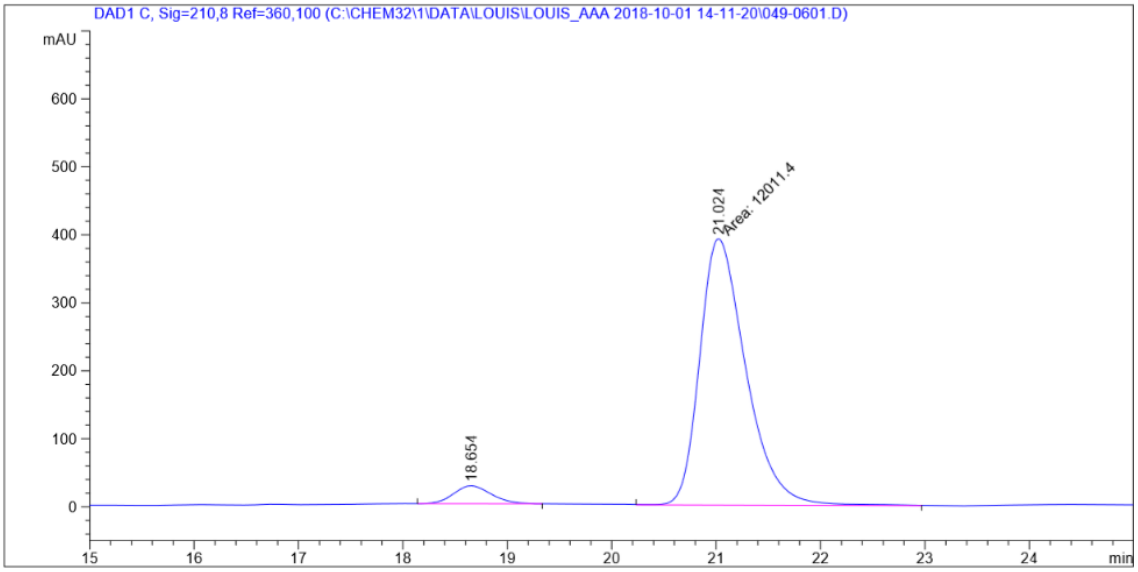
$[\alpha]_D^{28}$ = –98.8 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm), *ee* = 90%.


f1 (ppm)
f1 (ppm)

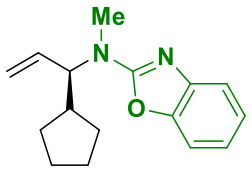


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.772	BB	0.4275	1.19520e4	431.09497	49.6819
2	21.246	BB	0.4634	1.21050e4	399.59698	50.3181



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.654	BB	0.3952	664.82928	26.45481	5.2447
2	21.024	MM	0.5111	1.20114e4	391.67349	94.7553

(*R*)-N-(1-cyclopentylallyl)-N-methylbenzo[d]oxazol-2-amine (5.6f)



Procedures

The allylic acetate (74.0 mg, 0.44 mmol, 100 mol%) and the secondary amine (130.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 60 hr). The title compound was obtained in 81% yield (91.3 mg, 0.36 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.44 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.25 (d, *J* = 7.7 Hz, 1H), 7.14 (td, *J* = 7.7, 1.2 Hz, 1H), 6.99 (td, *J* = 7.7, 1.2 Hz, 1H), 5.89 (ddd, *J* = 17.0, 10.5, 6.0 Hz, 1H), 5.30 – 5.18 (m, 2H), 4.56 – 4.45 (m, 1H), 3.06 (s, 3H), 2.25 (dp, *J* = 10.9, 8.0 Hz, 1H), 1.82 (dp, *J* = 12.5, 4.5, 3.8 Hz, 1H), 1.74 – 1.50 (m, 5H), 1.33 (dddd, *J* = 16.2, 10.9, 7.9, 2.4 Hz, 2H).

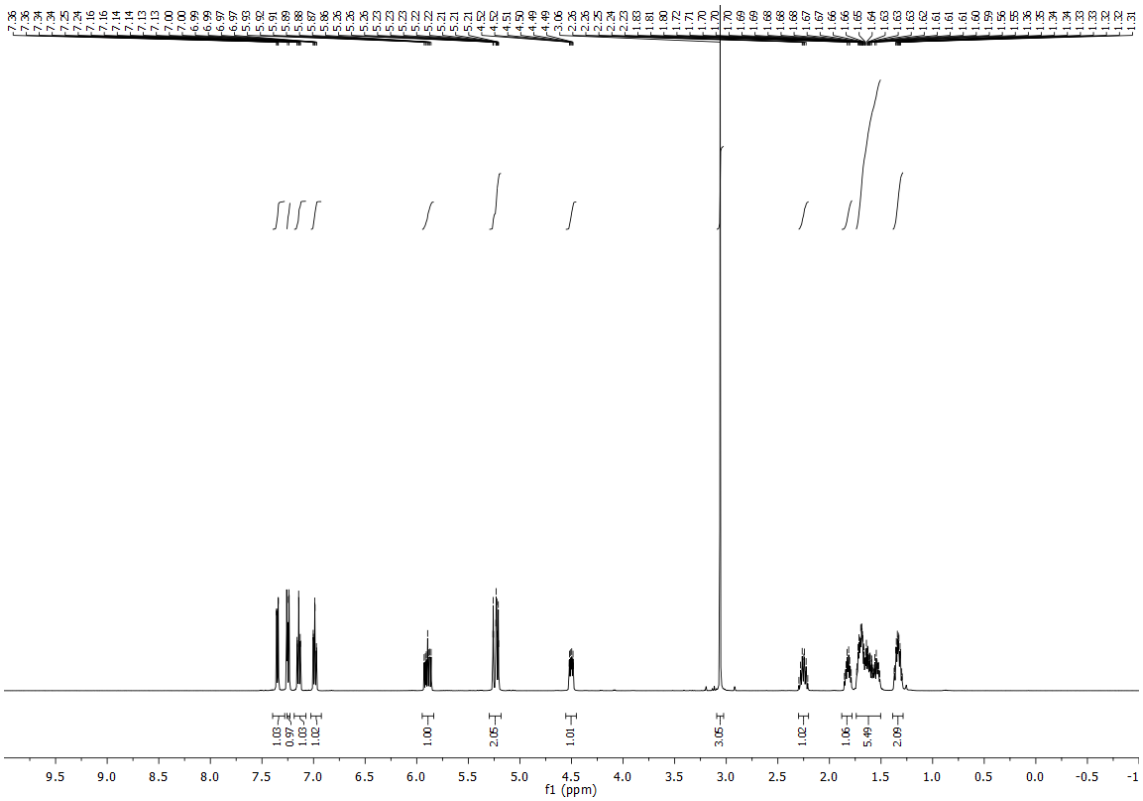
^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.2, 148.7, 143.6, 135.1, 123.8, 120.1, 117.3, 116.0, 108.6, 64.6, 41.0, 30.5, 30.3, 30.0, 25.6, 25.3.

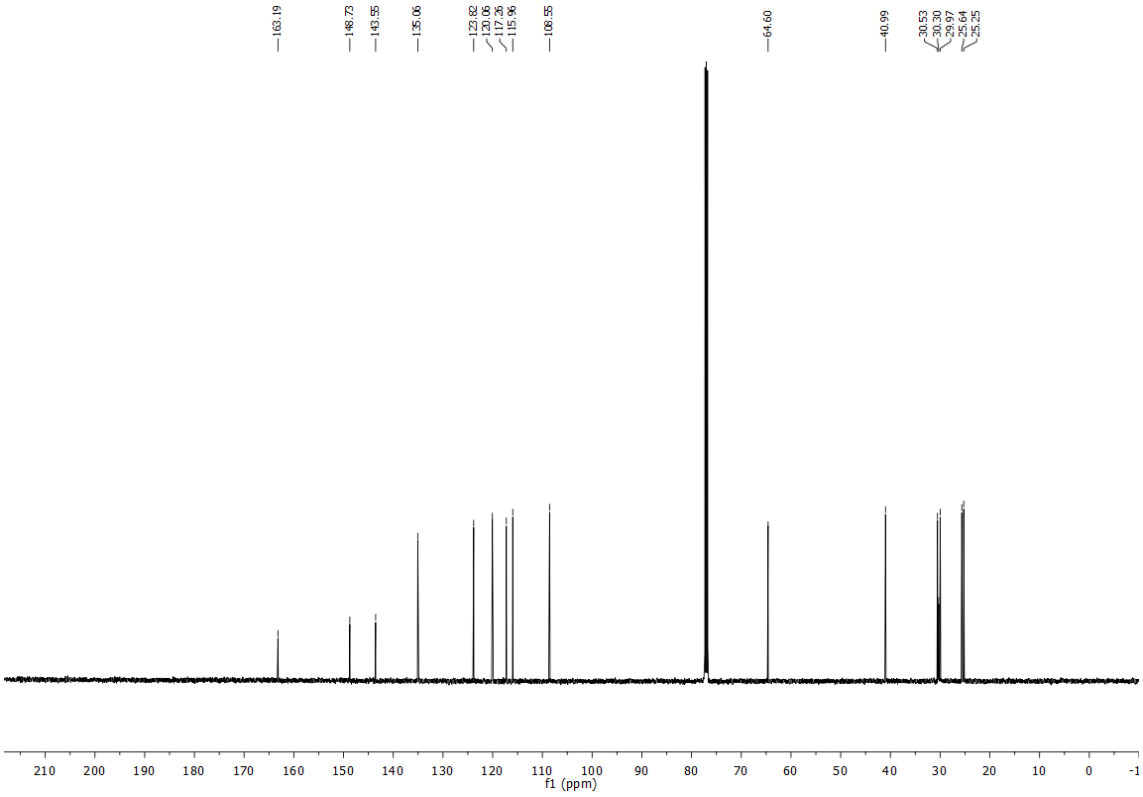
HRMS (ESI): Calculated for $C_{16}H_{20}N_2O$ [M+H$^+$] = 257.1648, Found 257.1650.

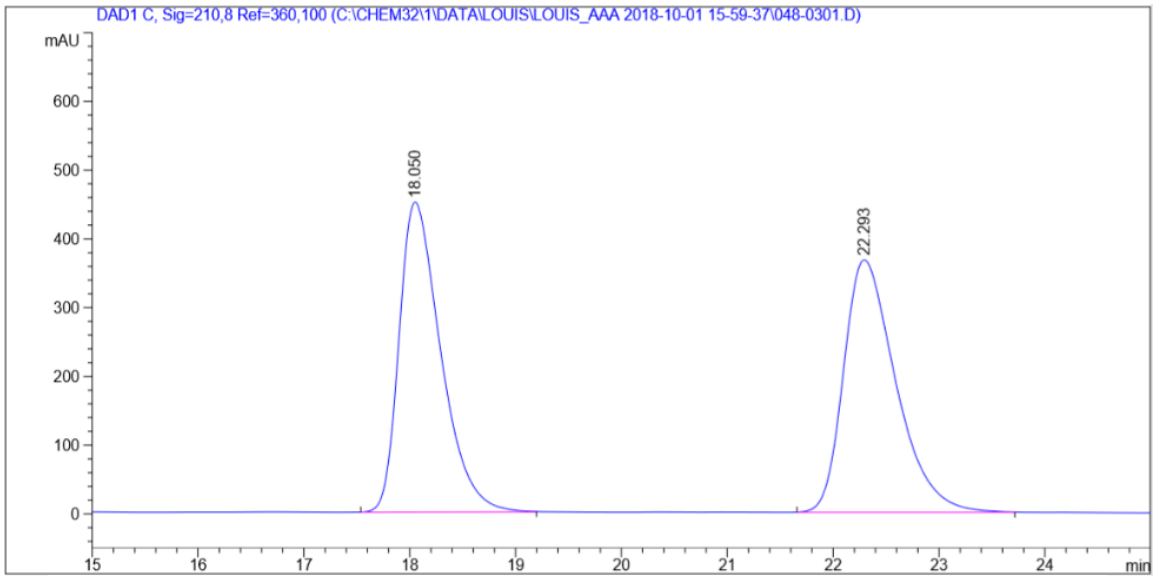
FTIR (neat): 2951, 1629, 1573, 1458, 1245, 1123, 990, 921, 819, 738 cm^{-1}.

$[\alpha]_D^{28}$ = –92.0 (*c* 1.0, $CHCl_3$).

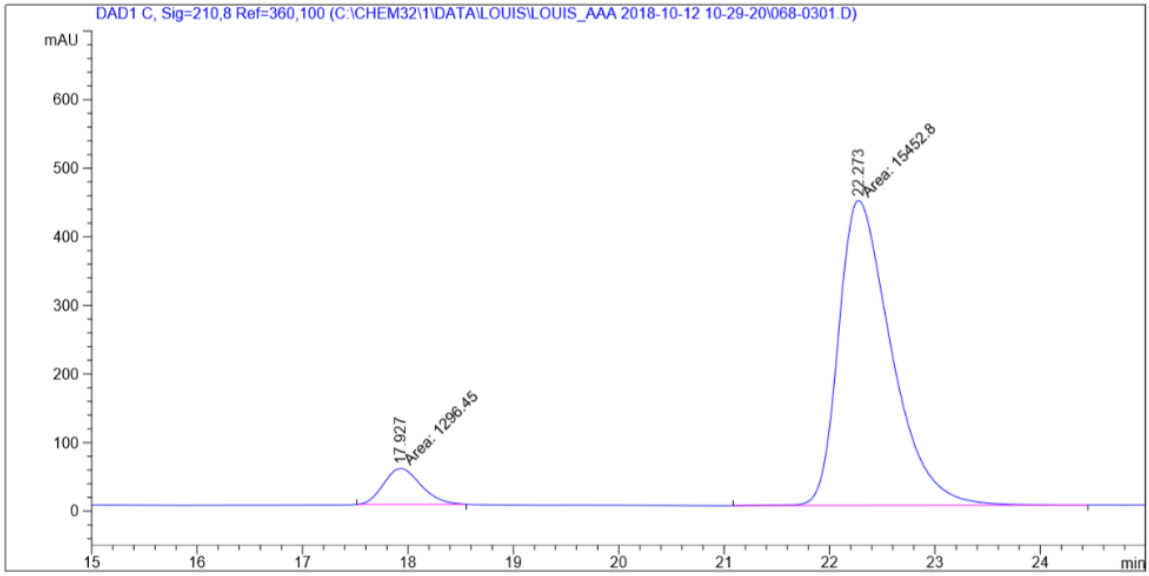
HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm), *ee* = 85%.


f1 (ppm)


f1 (ppm)

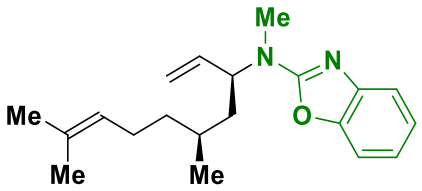


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.050	BB	0.4168	1.23153e4	450.69016	49.4850
2	22.293	BB	0.5236	1.25717e4	367.08105	50.5150



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.927	MM	0.4104	1296.45154	52.64453	7.7403
2	22.273	MM	0.5792	1.54528e4	444.68332	92.2597

***N*-((3*S*,5*S*)-5,9-dimethyldeca-1,8-dien-3-yl)-*N*-methylbenzo[*d*]oxazol-2-amine (5.6g)**



Procedures

The allylic acetate (98.7 mg, 0.44 mmol, 100 mol%) and the primary amine (130.4 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 60 hr). The title compound was obtained in 80% yield, 10:1 dr (110.2 mg, 0.35 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 10 min).

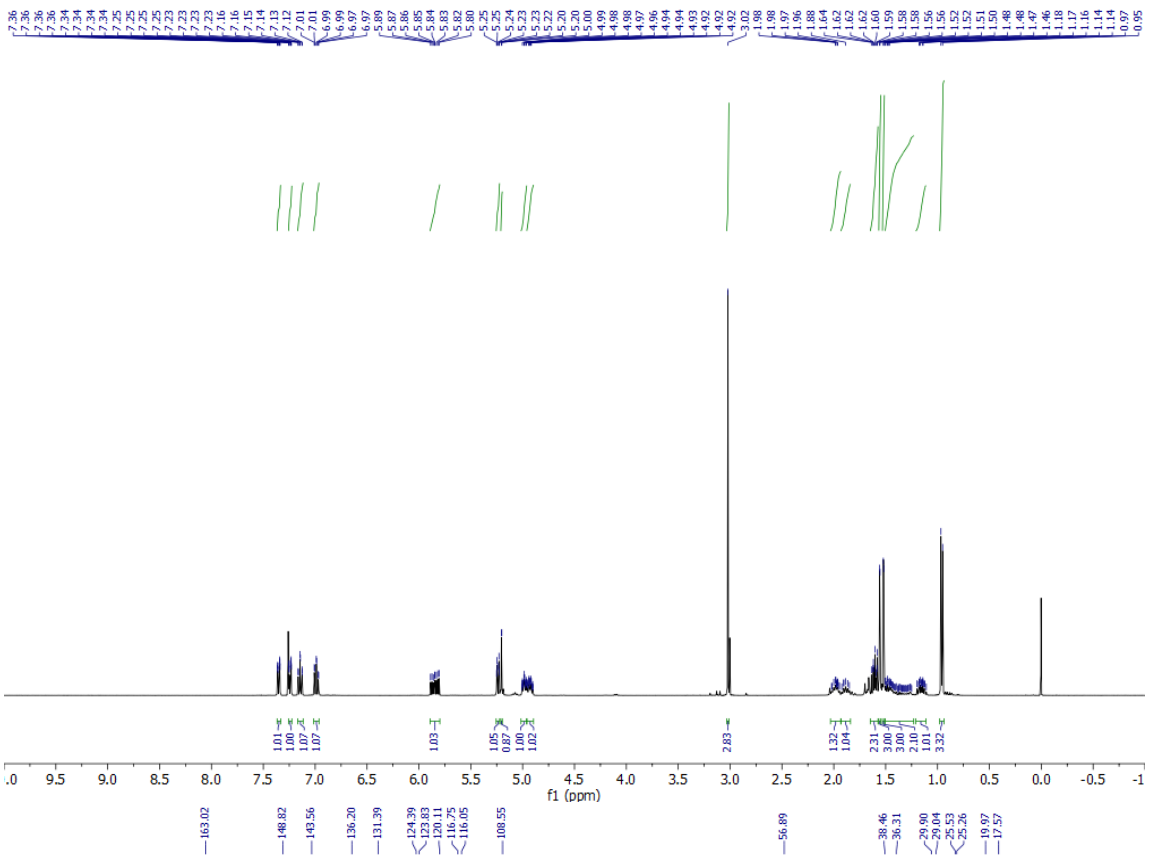
TLC (SiO_2) R_f = 0.33 (heptane: isopropyl acetate = 9:1).

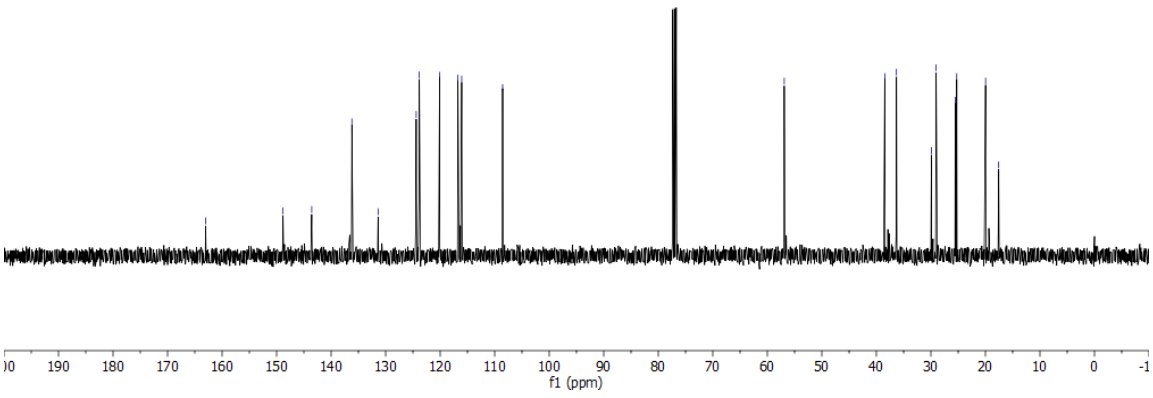
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (ddd, *J* = 7.8, 1.3, 0.6 Hz, 1H), 7.24 (ddd, *J* = 7.9, 1.2, 0.6 Hz, 1H), 7.14 (td, *J* = 7.7, 1.1 Hz, 1H), 6.99 (td, *J* = 7.7, 1.2 Hz, 1H), 5.85 (ddd, *J* = 172., 10.6, 5.4 Hz, 1H), 5.24 (dt, *J* = 7.5, 1.3 Hz, 1H), 5.20 (d, *J* = 1.5 Hz, 1H), 4.99 (ddq, *J* = 8.5, 5.6, 1.4 Hz, 1H), 4.93 (dddt, *J* = 8.4, 6.9, 5.4, 1.6 Hz, 1H), 3.02 (s, 3H), 2.03-1.93 (m, 1H), 1.89 (dt, *J* = 14.7, 7.1 Hz, 1H), 1.65-1.57 (m, 2H), 1.56 (d, *J* = 1.4 Hz, 3H), 1.52 (d, *J* = 1.3 Hz, 3H), 1.50-1.23 (m, 2H), 1.21-1.11 (m, 1H), 0.96 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0, 148.8, 143.6, 136.2, 131.4, 124.4, 123.8, 120.1, 116.8, 116.1, 108.6, 56.9, 38.5, 36.3, 29.9, 29.0, 25.5, 25.3, 20.0, 17.6.

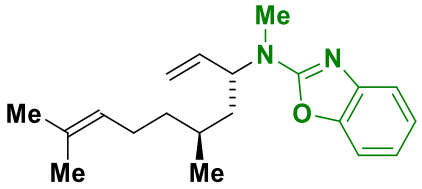
HRMS (ESI): Calculated for $C_{20}H_{28}N_2O$ [M+H$^+$] = 313.2274, Found 313.2276.

FTIR (neat): 3726, 2961, 2914, 2360, 2341, 1632, 1575, 1459, 1246, 1125, 922, 754, 739, 669, 429 cm^{-1}.


f1 (ppm)


f1 (ppm)

***N*-((3*R*,5*S*)-5,9-dimethyldeca-1,8-dien-3-yl)-*N*-methylbenzo[*d*]oxazol-2-amine (iso-5.6g)**



Procedures

The allylic acetate (98.7 mg, 0.44 mmol, 100 mol%) and the primary amine (130.4 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 60 hr) with (*R*)-Ir-II. The title compound was obtained in 76% yield, 20:1 dr (104.4 mg, 0.33 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 10 min).

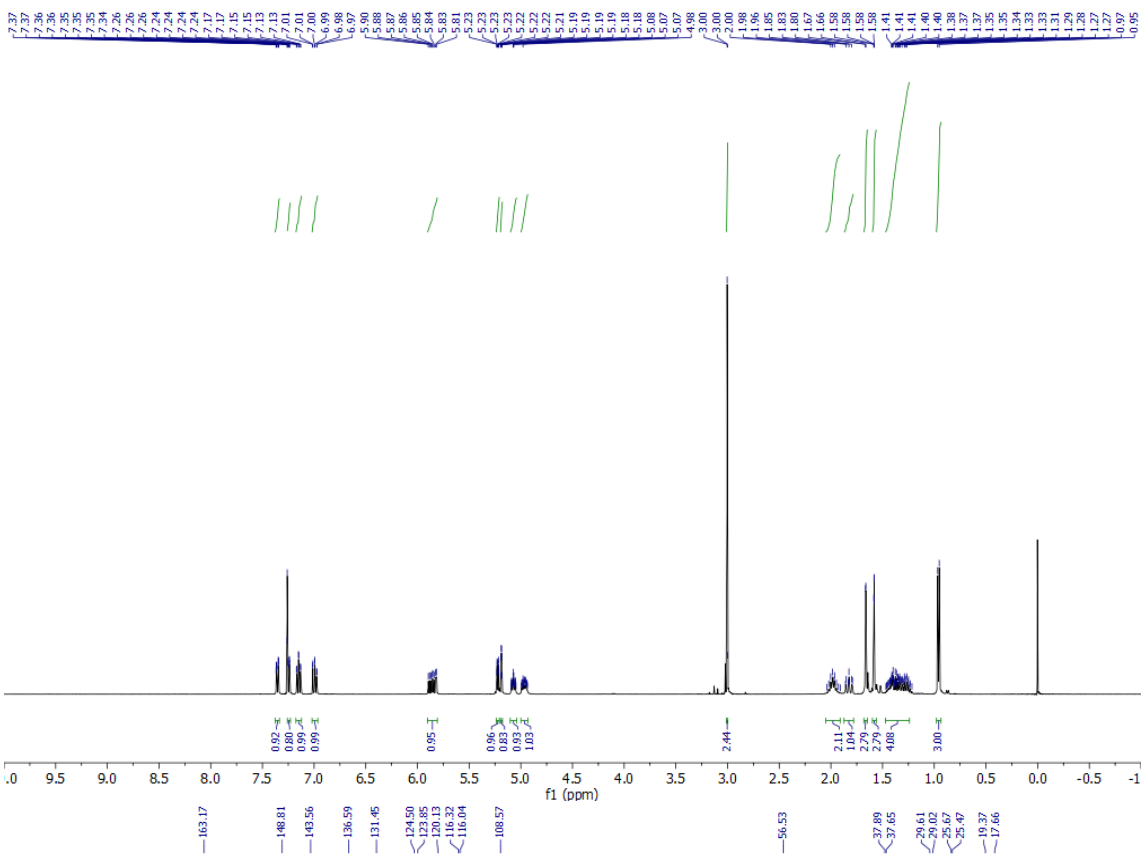
TLC (SiO_2) R_f = 0.33 (heptane: isopropyl acetate = 9:1).

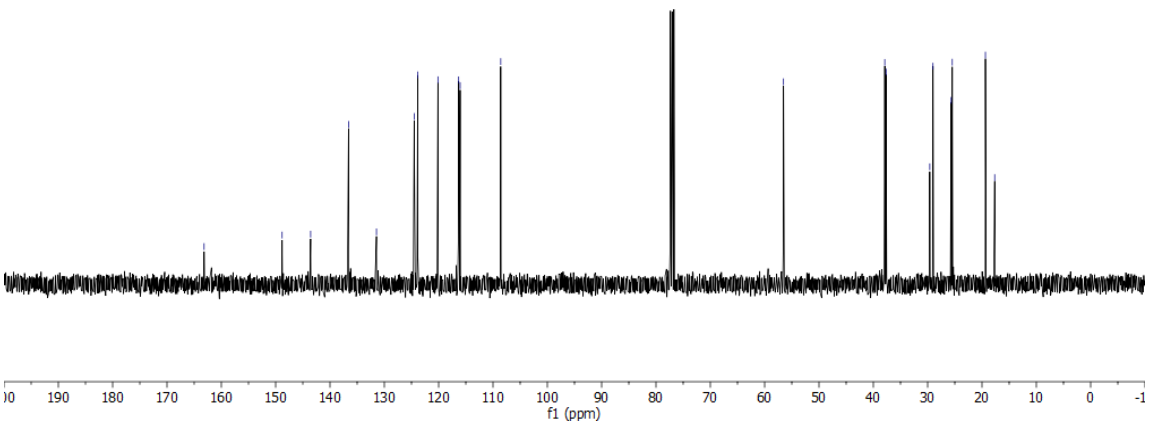
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (ddd, *J* = 7.8, 1.3, 0.6 Hz, 1H), 7.26-7.23 (m, 1H), 7.15 (td, *J* =7.7, 1.2 Hz, 1H), 7.02-6.96 (m, 1H), 5.85 (ddd, *J* = 17.5, 10.4, 5.0 Hz, 1H), 5.22 (ddd, *J* = 5.3, 1.7, 1.2 Hz, 1H), 5.19 (td, *J* = 1.8, 1.2 Hz, 1H), 5.07 (ddq, *J* = 8.5, 5.7, 1.3 Hz, 1H), 4.97 (dtt, *J* = 11.1, 4.5, 1.7 Hz, 1H), 3.00 (s, 2H), 1.98 (p, *J* =7.3 Hz, 2H), 1.83 (ddd, *J* = 13.6, 10.9, 2.9 Hz, 1H), 1.66 (d, *J* = 1.3 Hz, 3H), 1.60-1.56 (m, 3H), 1.47-1.24(m, 4H), 0.96 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.2, 148.8, 143.6, 136.6, 131.5, 134.5, 123.9, 120.1, 116.3, 116.0, 108.6, 56.5, 37.9, 37.7, 29.6, 29.0, 25.7, 25.5, 19.4, 17.7.

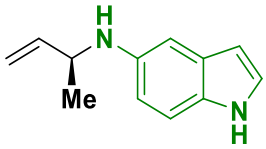
HRMS (ESI): Calculated for $C_{20}H_{28}N_2O$ [M+H$^+$] = 313.2274, Found 313.2278.

FTIR (neat): 2915, 2360, 2341, 1634, 1577, 1460, 1577, 1460, 1247, 924, 754, 740, 669, 650 cm^{-1}.


f1 (ppm)


f1 (ppm)

(*S*)-*N*-(but-3-en-2-yl)-1H-indol-5-amine (5.7a)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the amine (116.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 24 hr). The title compound was obtained in 91% yield (74.5 mg, 0.40 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 40% over 20 min).

TLC (SiO_2) R_f = 0.32 (heptanes: ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (br, 1H), 7.19 (dt, *J* = 8.6, 0.8 Hz, 1H), 7.12 – 7.08 (m, 1H), 6.86 (d, *J* = 2.3 Hz, 1H), 6.63 (ddd, *J* = 8.7, 2.3, 0.4 Hz, 1H), 6.39 (ddd, *J* = 3.1, 2.0, 0.9 Hz, 1H), 5.90 (ddd, *J* = 17.3, 10.4, 5.7 Hz, 1H), 5.25 (dt, *J* = 17.2, 1.4 Hz, 1H), 5.08 (dt, *J* = 10.3, 1.4 Hz, 1H), 4.07 – 3.97 (m, 1H), 1.34 (d, *J* = 6.6 Hz, 3H).

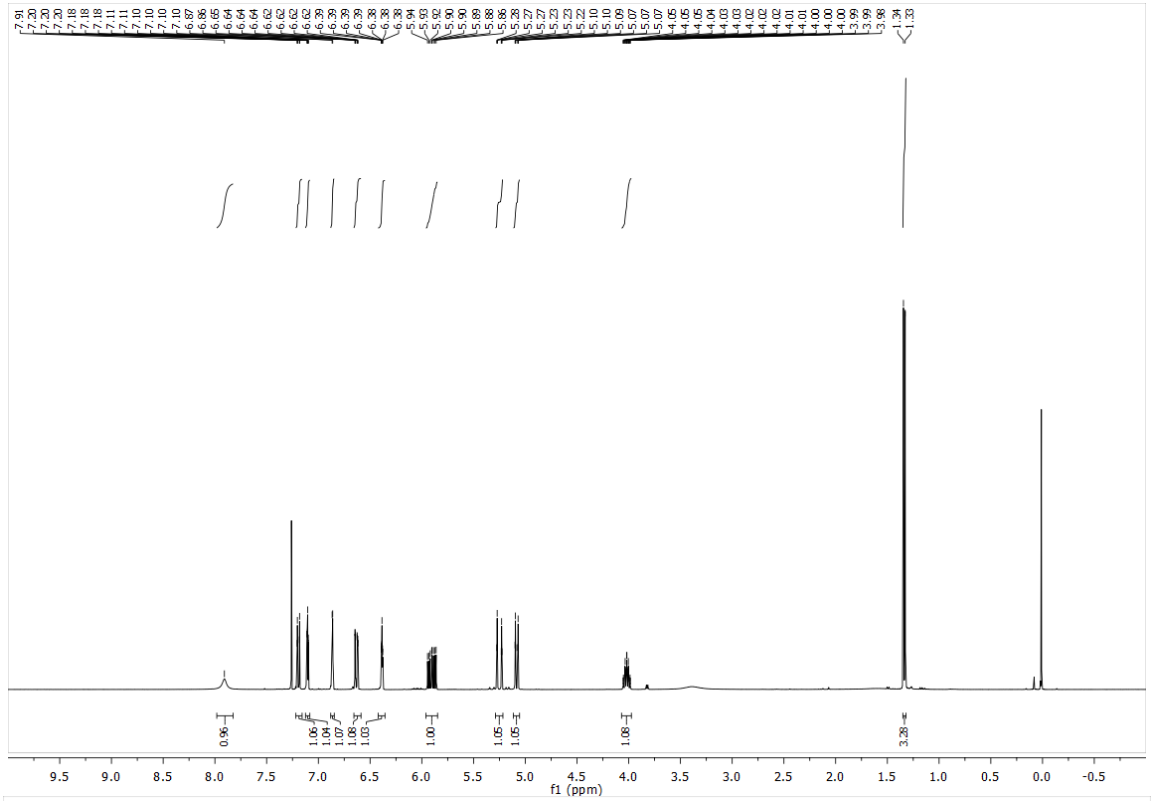
^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.1, 141.4, 130.1, 128.8, 124.4, 113.9, 112.8, 111.5, 103.7, 101.8, 52.5, 21.7.

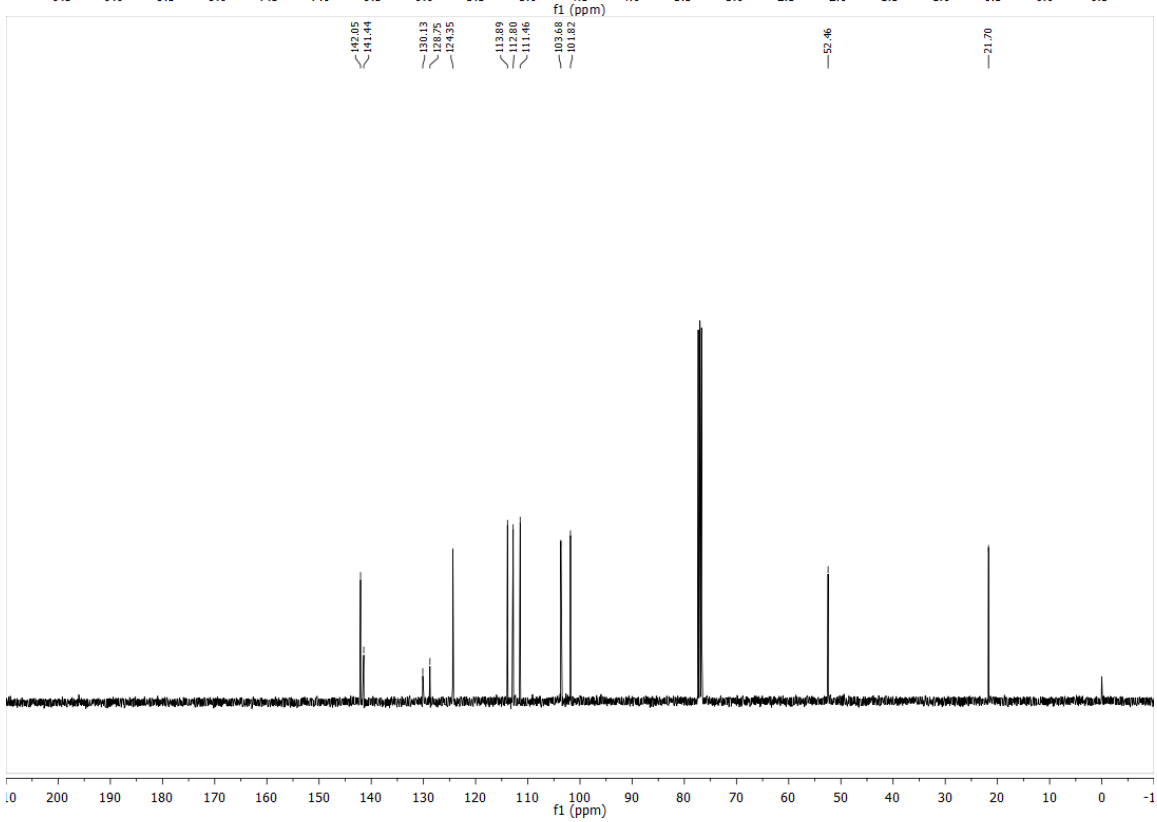
HRMS (ESI): Calculated for $C_{12}H_{15}N_2$ $[M+H^+]$ = 187.1230, Found 187.1230.

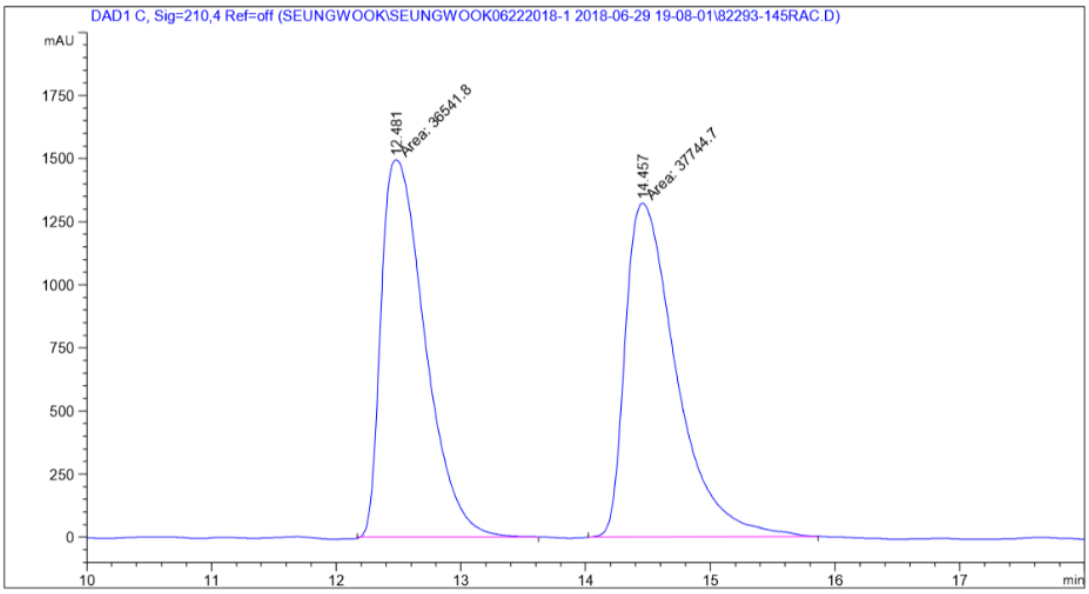
FTIR (neat): 3404, 2975, 1626, 1581, 1469, 1231, 1167, 919, 797, 724, 602 cm^{-1}.

$[\alpha]_D^{28}$ = –5.0 (*c* 0.2, $CHCl_3$).

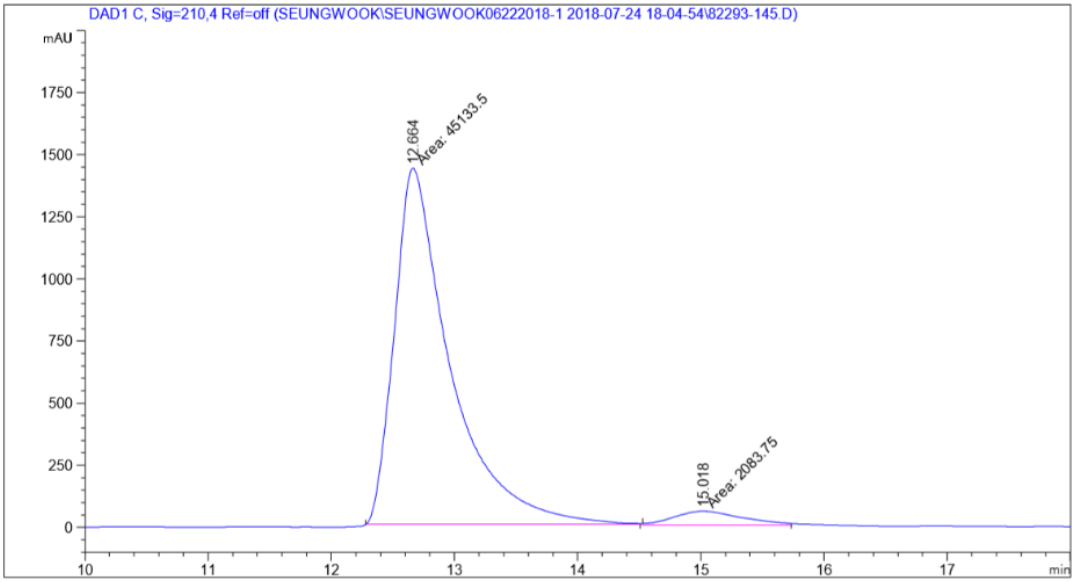
HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 80:20, 1.00 mL/min, 210 nm), *ee* = 91%.


f1 (ppm)


142.05
141.44
130.13
128.75
124.35
113.89
112.80
111.46
103.68
101.82
52.46
21.70
f1 (ppm)

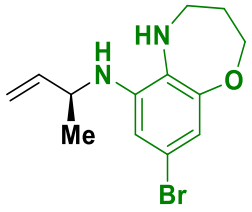


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.481	MM	0.4075	3.65418e4	1494.69006	49.1904
2	14.457	MM	0.4756	3.77447e4	1322.68848	50.8096



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.664	MM	0.5249	4.51335e4	1433.09302	95.5869
2	15.018	MM	0.6329	2083.75391	54.86946	4.4131

(*S*)-8-bromo-*N*-(but-3-en-2-yl)-2,3,4,5-tetrahydrobenzo[b][1,4]oxazepin-6-amine (5.7b)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the amine (213.9 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 61% yield (79.8 mg, 0.27 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–5:1).

TLC (SiO_2) R_f = 0.24 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.53 (d, *J* = 2.2 Hz, 1H), 6.46 (d, *J* = 2.2 Hz, 1H), 5.81 (ddd, *J* = 17.2, 10.3, 5.6 Hz, 1H), 5.17 (dt, *J* = 17.2, 1.3 Hz, 1H), 5.09 (dt, *J* = 10.3, 1.3 Hz, 1H), 4.50 (d, *J* = 6.3 Hz, 1H), 4.13 (t, *J* = 5.5 Hz, 2H), 3.85 (q, *J* = 6.3 Hz, 1H), 3.25 – 3.08 (m, 2H), 2.60 (br, 1H), 2.01 (ddd, *J* = 10.0, 6.5, 4.8 Hz, 2H), 1.31 (d, *J* = 6.6 Hz, 3H).

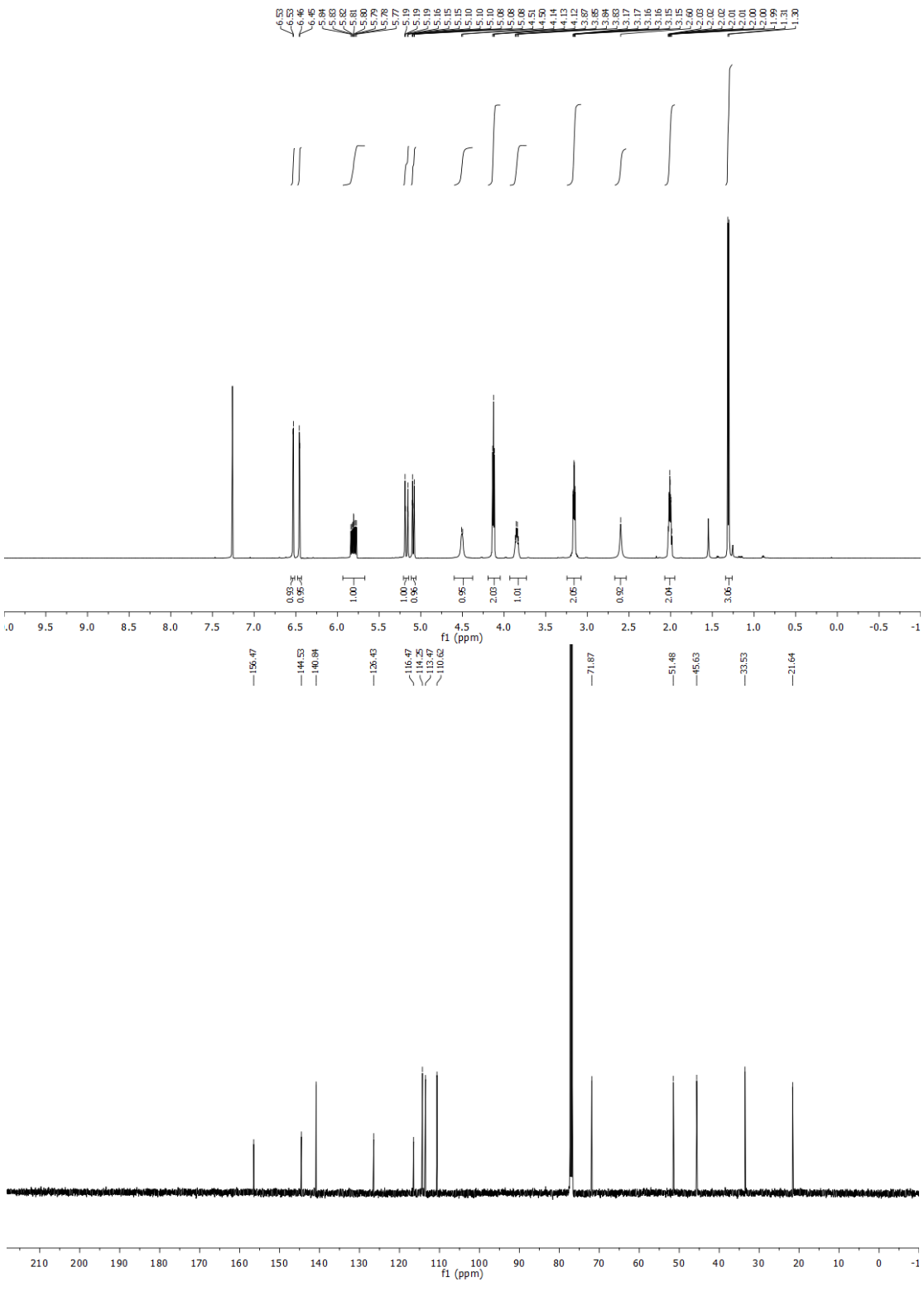
^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.5, 144.5, 140.8, 126.4, 116.5, 114.3, 113.5, 110.6, 71.9, 51.5, 45.6, 33.5, 21.6.

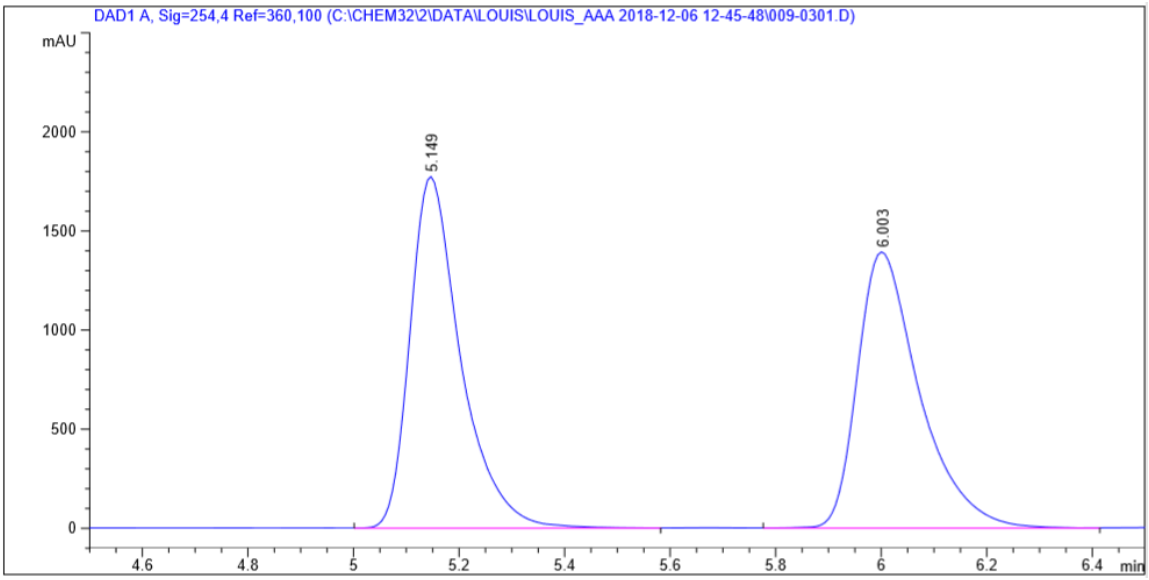
HRMS (ESI): Calculated for $C_{13}H_{17}BrN_2O$ [M+H$^+$] = 297.0597, Found 297.0581.

FTIR (neat): 3314, 2918, 1576, 1498, 1422, 1377, 1256, 1214, 1081, 955, 918, 814, 684 cm^{-1}.

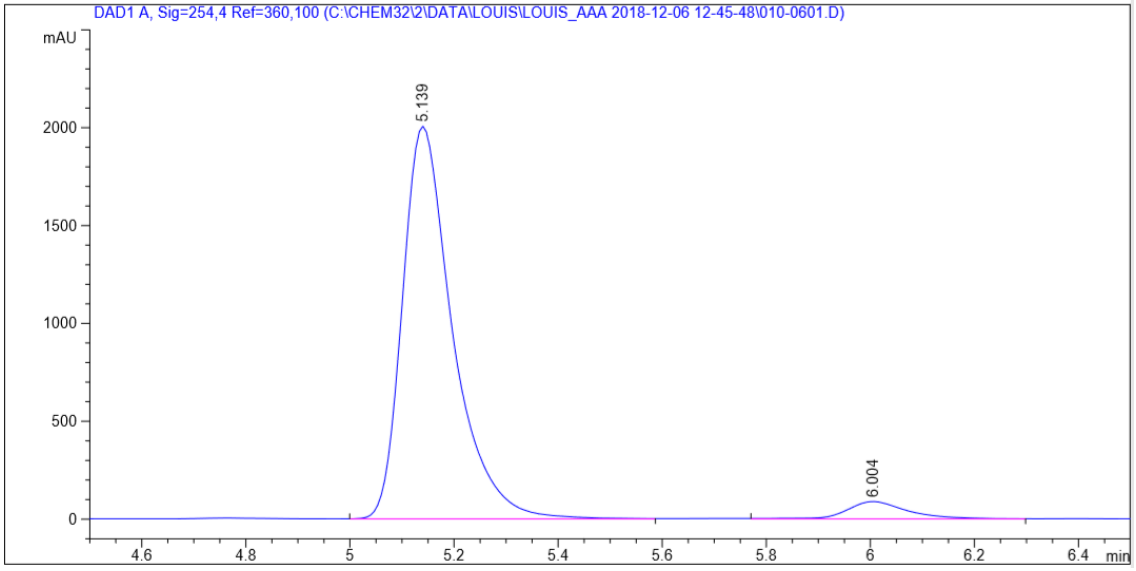
$[\alpha]_D^{28}$ = –1.8 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 90:10, 1.00 mL/min, 254 nm), *ee* = 90%.


f1 (ppm)
f1 (ppm)

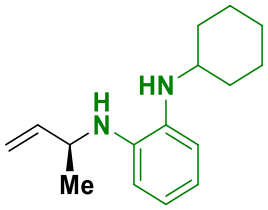


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.149	VV	0.0999	1.18412e4	1774.31335	51.0129
2	6.003	VV	0.1211	1.13710e4	1394.24512	48.9871



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.139	BV	0.1000	1.34241e4	2006.97974	94.8630
2	6.004	VV	0.1213	726.94116	89.03390	5.1370

(*S*)-*N*1-(but-3-en-2-yl)-*N*2-cyclohexylbenzene-1,2-diamine (5.7c)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the amine (167.4 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 °C, 24 hr). The title compound was obtained in 86% yield (92.5 mg, 0.38 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 5% over 20 min).

TLC (SiO_2) R_f = 0.46 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.80 – 6.65 (m, 4H), 6.01 – 5.76 (m, 1H), 5.21 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.08 (dd, *J* = 10.4, 1.6 Hz, 1H), 3.93 (p, *J* = 6.5 Hz, 1H), 3.38 – 3.11 (m, 3H), 2.12 – 1.99 (m, 2H), 1.84 – 1.72 (m, 2H), 1.66 (dt, *J* = 13.1, 3.9 Hz, 1H), 1.39 (dd, *J* = 14.7, 11.5 Hz, 2H), 1.34 (d, *J* = 6.6 Hz, 3H), 1.31 – 1.14 (m, 3H).

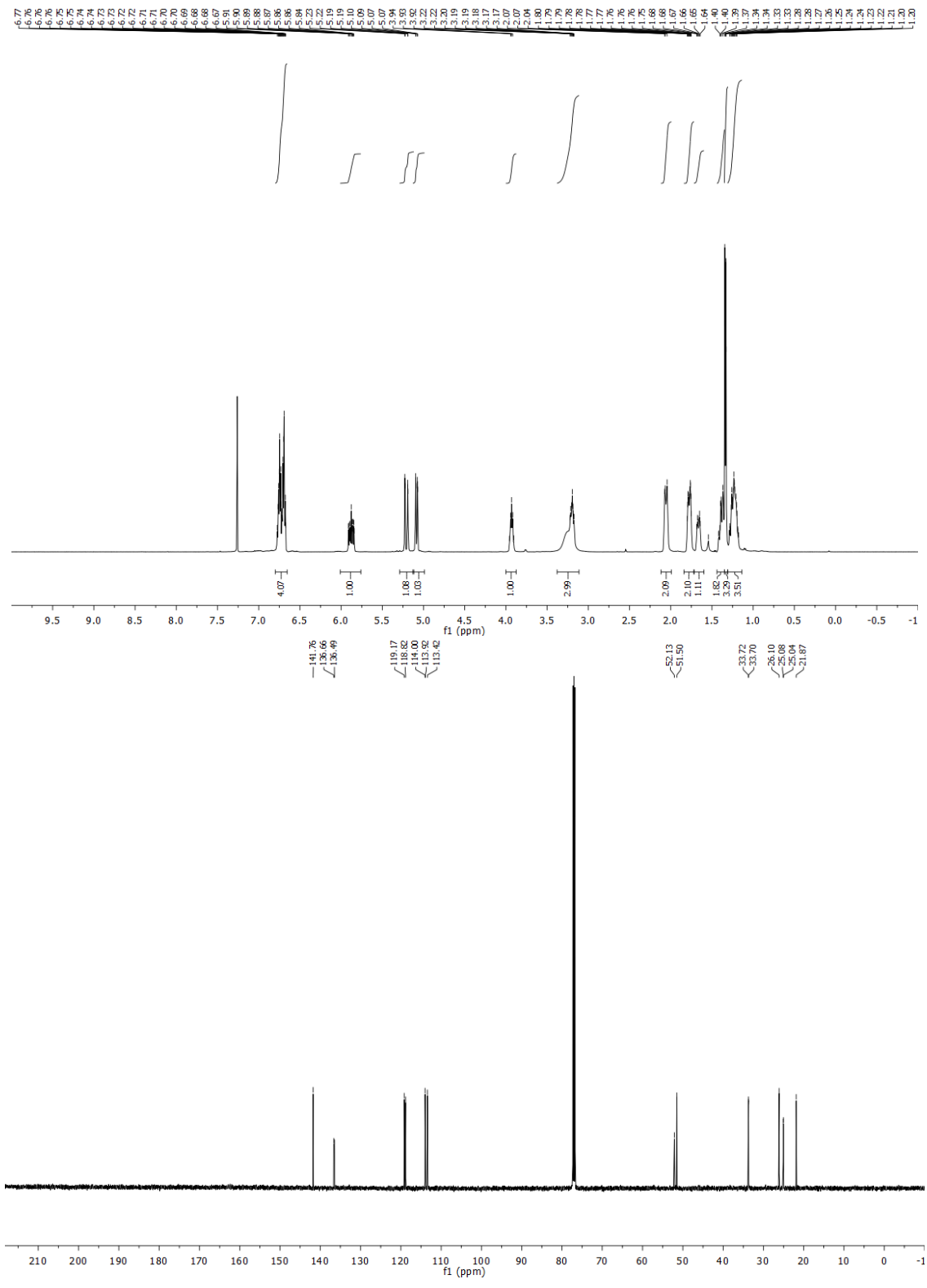
^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.8, 136.7, 136.5, 119.2, 118.8, 114.0, 113.9, 113.4, 52.1, 51.5, 33.7 (d), 26.10, 25.0 (d), 21.87.

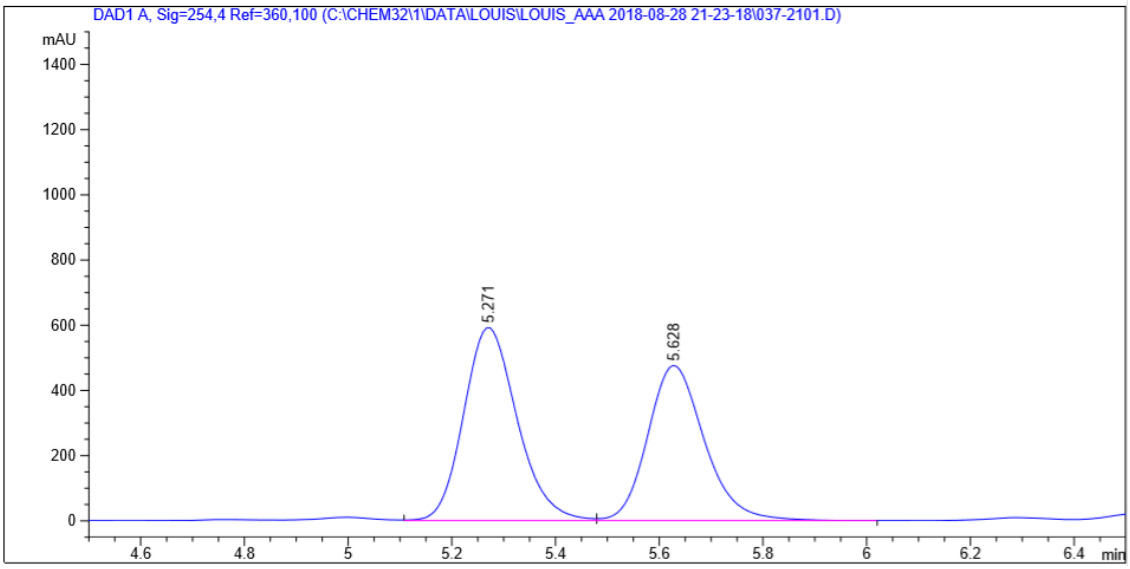
HRMS (ESI): Calculated for $C_{16}H_{24}N_2$ [M+H$^+$] = 245.2012, Found 245.2016.

FTIR (neat): 3330, 2926, 1598, 1508, 1448, 1304, 1252, 1148, 916, 733 cm^{-1}.

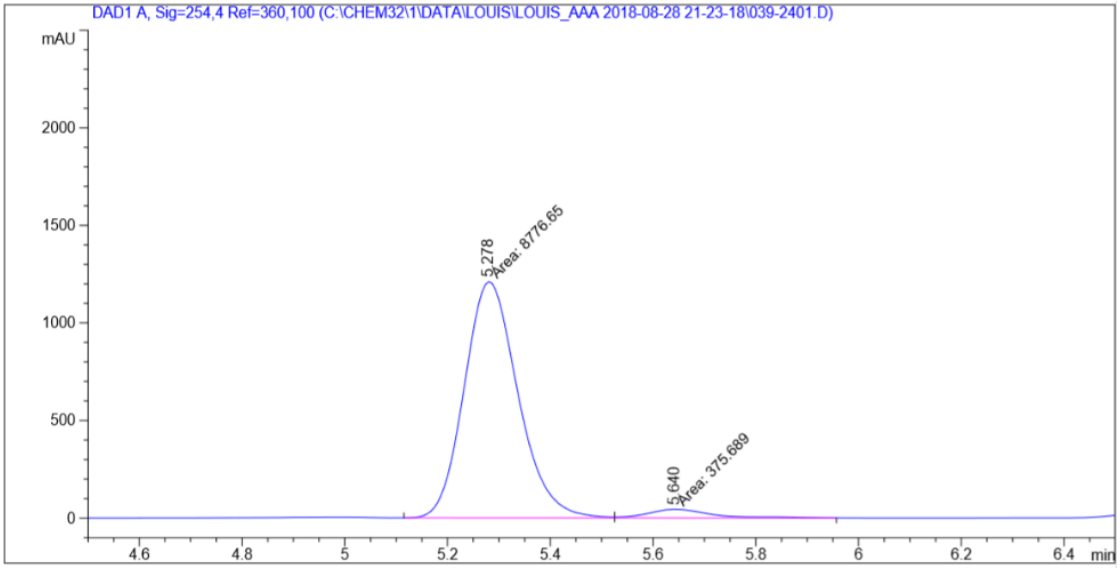
$[\alpha]_D^{28}$= +30.0 (*c* 0.1, $CHCl_3$).

HPLC (Chiralcel AD-H column, heptanes:*i*-PrOH = 98:2, 1.00 mL/min, 254 nm), *ee* = 92%.





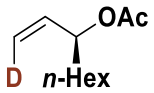
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.271	VV	0.1116	4247.09521	593.03601	54.0182
2	5.628	VB	0.1165	3615.25073	476.42450	45.9818



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.278	MF	0.1207	8776.64844	1211.57275	95.8952
2	5.640	FM	0.1409	375.68869	44.43553	4.1048

Procedures and Spectral Data for the deuterium labelling experiments

Preparation of (S,Z)-oct-1-en-3-yl-1-d acetate (5.1h). **5.1h** synthesized from commercially available (*S*)-(-)-1-Octyn-3-ol, >98% ee.



Procedures

To a round-bottomed flask charged with potassium carbonate (380.1 mg, 2.8 mmol, 110 mol%) was added deuterium oxide (6.8 mL, 0.37 M, 99.9 atom % D), followed by (*S*)-(-)-1-Octyn-3-ol (315 mg, 2.5 mmol, 100 mol%). The mixture was stirred at room temperature overnight. After anhydrous CH_2Cl_2 (10 mL) were added to the reaction mixture, the mixture was transferred to a separatory funnel. The organic layer was extracted with CH_2Cl_2 (5 mL × 2) and the combined organic layers were washed with H_2O (20 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to the next step without further purification.

To a round-bottomed flask charged with the crude substrate under an argon atmosphere was added anhydrous CH_2Cl_2 (10 mL, 0.25 M with respect to propargylic alcohol). The reaction vessel was placed in an ice batch. After 5 minutes DIBAL (3 mL, 3.0 mmol, 1 M in hexanes) was added slowly and the solution was stirred at room temperature for 30 minutes. After the reaction vessel was placed in an ice batch, Schwartz's reagent (773.6 mg, 3.0 mmol, 120 mol%) was added to the reaction mixture. The mixture was stirred at room temperature for 2 hours, at which point saturated aqueous sodium bicarbonate (5 mL) were added and the reaction was stirred vigorously. After 2 hours, the reaction mixture was filtered (celite) with the aid of CH_2Cl_2 (10 mL) and the filtrate was

transferred to a separatory funnel. The organic layer was extracted with CH_2Cl_2 (10 mL × 2) and the combined organic layers were washed with H_2O (20 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to the next step without further purification.

To a round-bottomed flask charged with the crude substrate and 4-dimethylaminopyridine (15.2 mg, 0.13 mmol, 5 mol%) under an argon atmosphere was added CH_2Cl_2 (12.5 mL, 0.25 M with respect to propargylic alcohol), followed by acetic anhydride (0.28 mL, 3.0 mmol, 120 mol%) and triethylamine (0.41 mL, 3.0 mmol, 120 mol%). After 1 hour, saturated aqueous sodium bicarbonate (10 mL) was added and the mixture was transferred to a separatory funnel. The organic layer was extracted with CH_2Cl_2 (10 mL × 2) and the combined organic layers were washed with 1 N HCl (10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 30:1) to furnish the title compound as a light yellow oil (240 mg, 1.40 mmol) in 56% yield over 3 steps.

TLC (SiO_2) R_f = 0.72 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.76 (ddt, J = 10.4, 6.3, 2.6 Hz, 1H), 5.25 – 5.19 (m, 1H), 5.14 (dd, J = 10.5, 1.1 Hz, 1H), 2.06 (s, 3H), 1.66 – 1.52 (m, 2H), 1.34 – 1.25 (m, 6H), 0.91 – 0.84 (m, 3H).

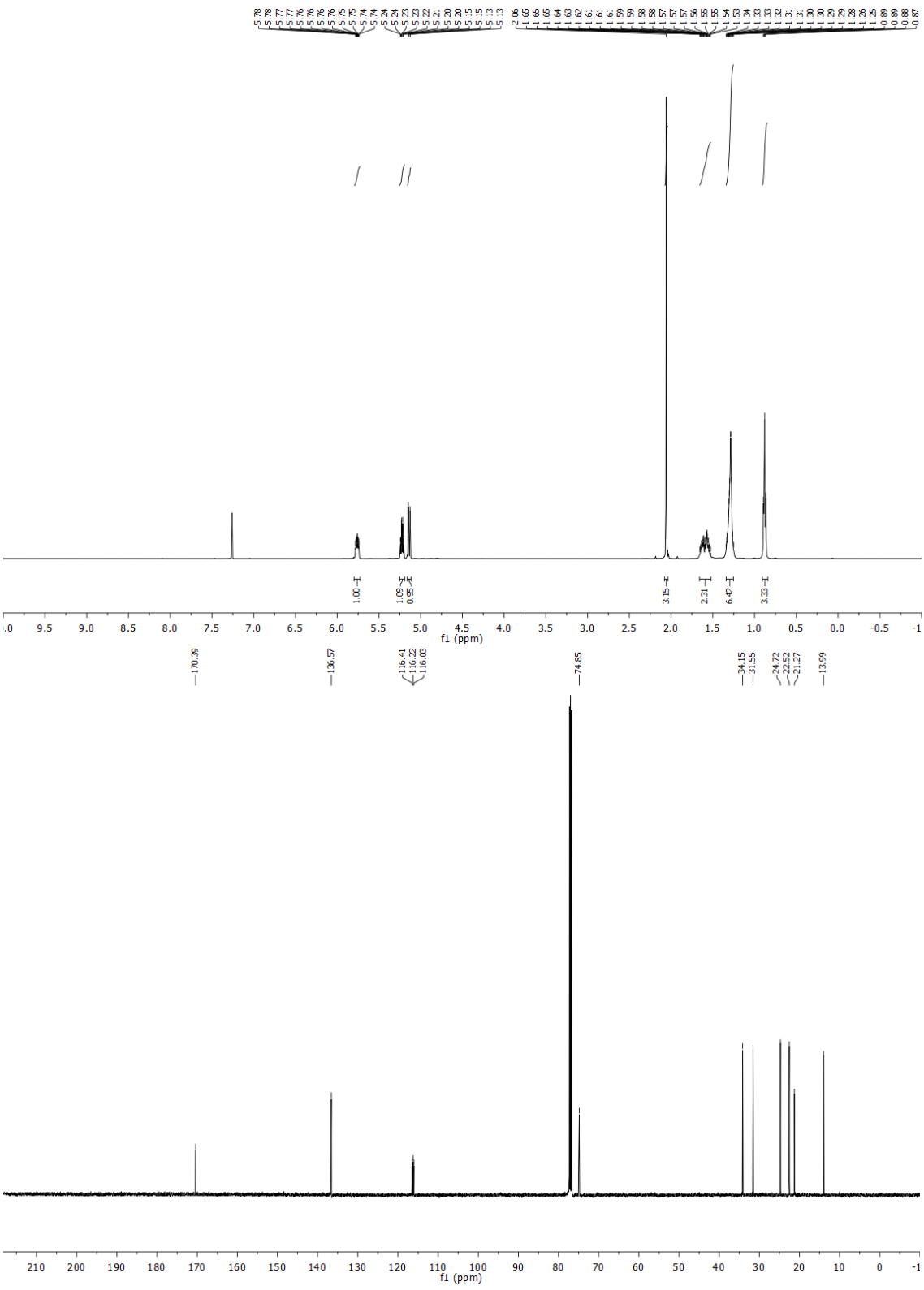
^{2}H NMR (92 MHz, $CHCl_3$): δ = 5.28 (s, 1D).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 136.6, 116.2 (t), 74.9, 34.2, 31.6, 24.7, 22.5, 21.3, 14.0.

LRMS (CI): Calculated for $C_8H_{14}D$ $[M–OAc]^+$ = 112, Found 112.

FTIR (neat): 2932, 1731, 1372, 1247, 1021, 756, 667 cm^{-1}.

$\mathbf{[\alpha]_D^{28}}$**=** – 74.5(*c* 1.0, $CHCl_3$).


5.78
5.78
5.77
5.77
5.76
5.76
5.76
5.76
5.75
5.75
5.74
5.74
5.24
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5.23
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5.22
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5.20
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5.15
5.13
5.13
2.06
1.65
1.65
1.64
1.64
1.63
1.62
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1.61
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1.31
1.30
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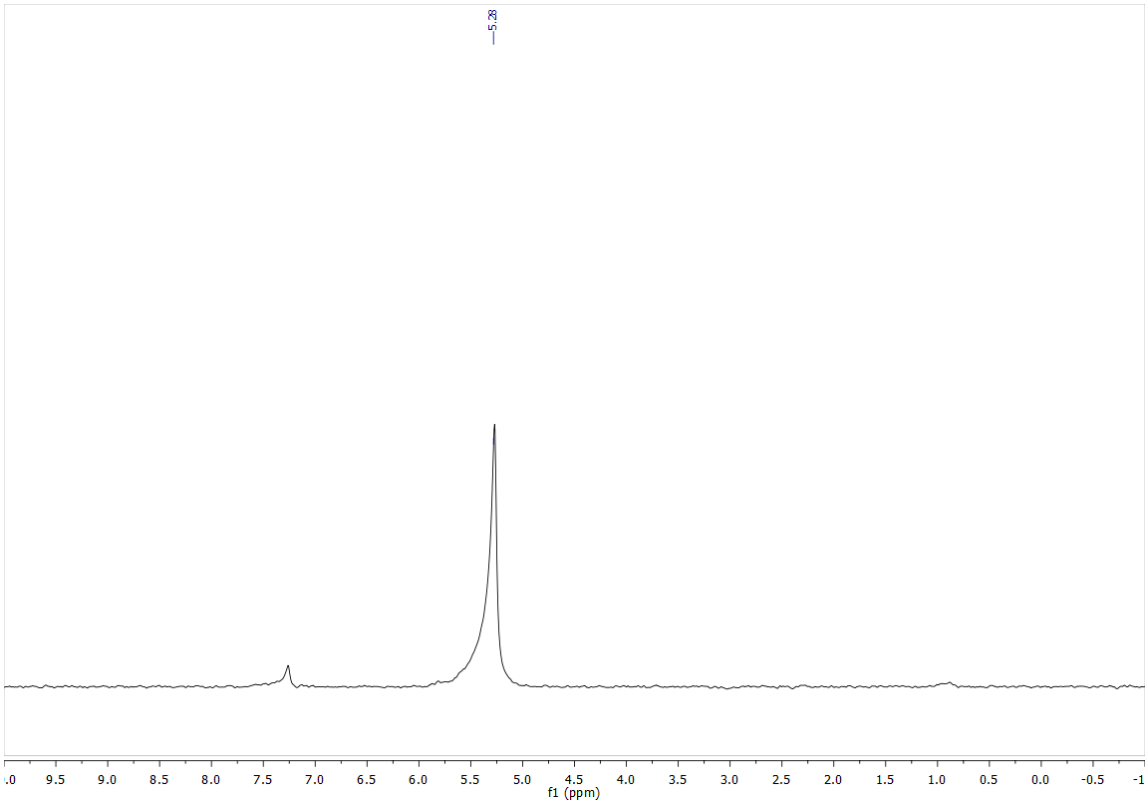
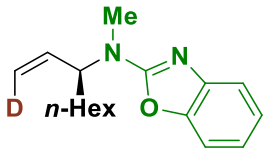
1.28
1.26
1.25
0.89
0.89
0.88
0.87
1.00
1.09
0.95
3.15
2.31
6.42
3.33
f1 (ppm)
170.39
136.57
116.41
116.22
116.03
74.85
34.15
31.55
24.72
22.52
21.27
13.99
f1 (ppm)


5.28
.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

(*S*,*Z*)-N-methyl-N-(oct-1-en-3-yl-1-d)benzo[d]oxazol-2-amine (5.8a)



Procedures

An pressure tube equipped with a magnetic stir bar was charged with the amine **5.3m** (59.3 mg, 0.4 mmol, 200 mol%), cesium carbonate (130.3 mg, 0.4 mmol, 200 mol%) and (*S*)-Ir-II (11.1 mg, 0.01 mmol, 5 mol%). The tube was purged with argon for 5 minutes. DME (0.2 mL, 1.0 M) was added followed by the deuterated allylic acetate **5.1h** (34.3 mg, 0.2 mmol, 100 mol%). The tube was sealed with a PTFE lined cap and was placed in an oil bath at 70 ^{o}C for 24 hours. After reaching ambient temperature, the crude reaction mixture was directly subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–15:1). The title compound was obtained in 89% yield (46.2 mg, 0.18 mmol) as a colorless oil.

TLC (SiO_2) R_f = 0.55 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (dd, J = 7.8, 1.1 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.15 (td, J = 7.7, 1.1 Hz, 1H), 6.99 (td, J = 7.7, 1.2 Hz, 1H), 5.85 (ddd, J = 10.5, 5.1, 2.4 Hz, 1H), 5.20 (dd, J = 10.6, 1.6 Hz, 1H), 4.86 – 4.77 (m, 1H), 3.02 (s, 3H), 1.74 – 1.66 (m, 2H), 1.36 – 1.27 (m, 6H), 0.86 (t, J = 6.9 Hz, 3H).

^{2}H NMR (92 MHz, $CHCl_3$): δ = 5.28 (s, 1D).

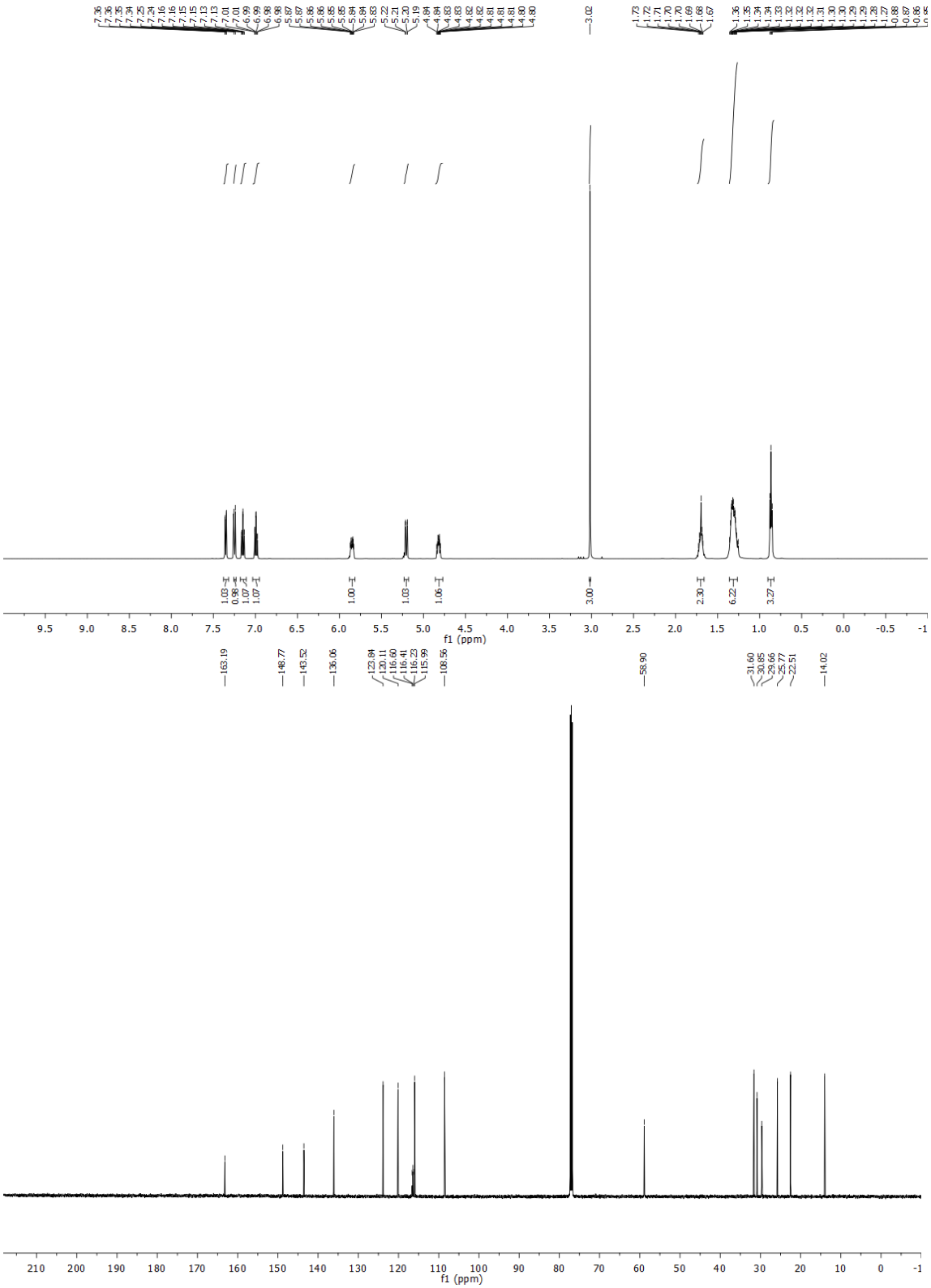
^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.2, 148.8, 143.5, 136.1, 123.8, 120.1, 116.4 (t), 116.0, 108.6, 58.9, 31.6, 30.9, 29.7, 25.8, 22.5, 14.0.

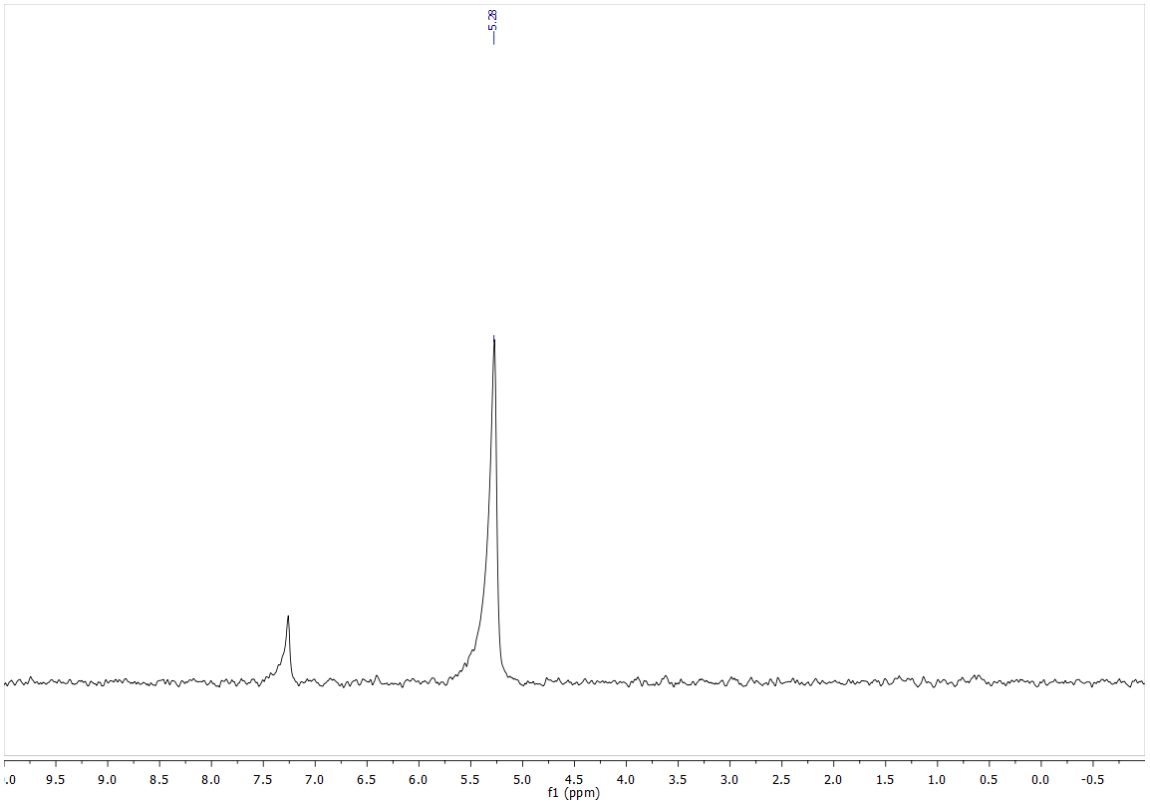
HRMS (ESI): Calculated for $C_{16}H_{21}DN_2O$ [M+H$^+$] = 260.1868, Found 260.1870.

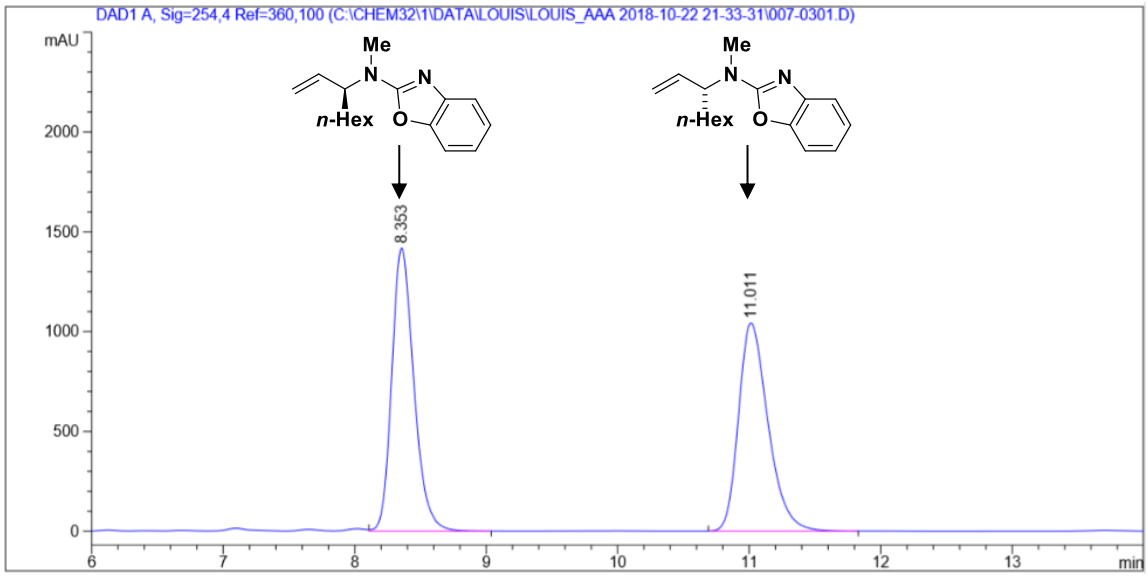
FTIR (neat): 2930, 1636, 1577, 1460, 1246, 1216, 748 cm^{-1}.

$[\alpha]_D^{28}$ = –71.3 (*c* 1.0, $CHCl_3$).

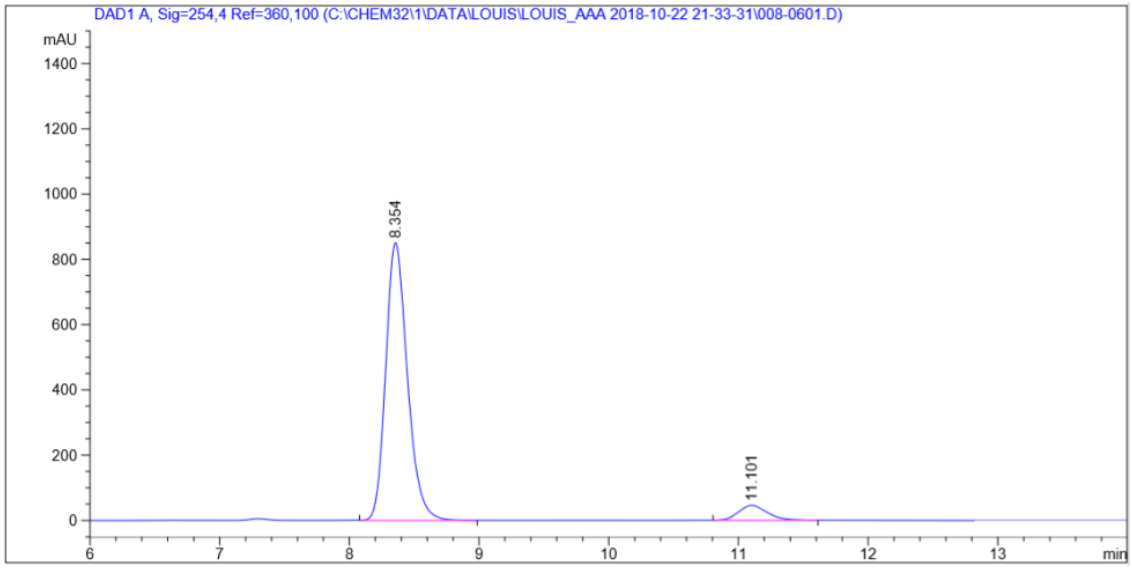
HPLC (Chiralcel AD-H column, heptanes:*i*-PrOH = 98:2, 1.00 mL/min, 254 nm), *ee* = 87%**.**




5.28
.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

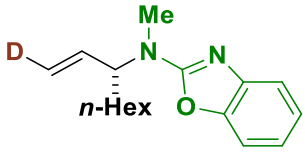


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.353	VB	0.1803	1.65706e4	1418.74658	50.4411
2	11.011	BB	0.2382	1.62808e4	1042.75146	49.5589



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.354	VB	0.1794	9878.64551	851.14398	93.3375
2	11.101	BB	0.2386	705.14496	45.54940	6.6625

(*R*,*E*)-*N*-methyl-*N*-(oct-1-en-3-yl-1-d)benzo[d]oxazol-2-amine (5.8b)



Procedures

An pressure tube equipped with a magnetic stir bar was charged with the amine **5.3m** (59.3 mg, 0.4 mmol, 200 mol%), cesium carbonate (130.3 mg, 0.4 mmol, 200 mol%) and (***R***)-Ir-II (11.1 mg, 0.01 mmol, 5 mol%). The tube was purged with argon for 5 minutes. DME (0.2 mL, 1.0 M) was added followed by the deuterated allylic acetate **5.1h** (34.3 mg, 0.2 mmol, 100 mol%). The tube was sealed with a PTFE lined cap and was placed in an oil bath at 70 ^{o}C for 24 hours. After reaching ambient temperature, the crude reaction mixture was directly subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–15:1). The title compound was obtained in 85% yield (44.1 mg, 0.17 mmol) as a colorless oil.

TLC (SiO_2) R_f = 0.55 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (dd, J = 7.8, 1.1 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.15 (td, J = 7.7, 1.1 Hz, 1H), 6.99 (td, J = 7.8, 1.2 Hz, 1H), 5.86 (dd, J = 17.3, 5.3 Hz, 1H), 5.21 (dd, J = 17.4, 1.7 Hz, 1H), 4.82 (dddd, J = 8.6, 6.8, 5.3, 1.7 Hz, 1H), 3.02 (s, 3H), 1.76 – 1.63 (m, 2H), 1.41 – 1.21 (m, 6H), 0.87 (t, J = 7.0 Hz, 3H).

^{2}H NMR (92 MHz, $CHCl_3$): δ = 5.28 (s, 1D).

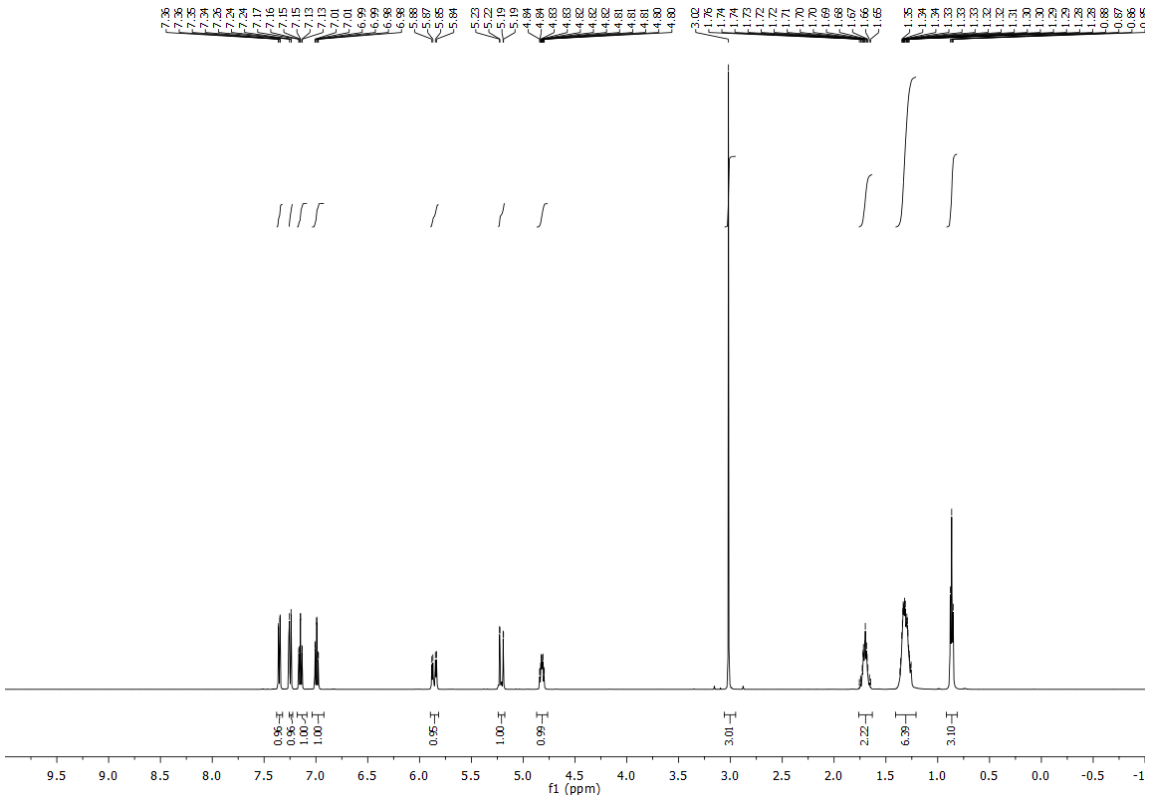
^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.2, 148.8, 143.5, 136.2, 136.0, 123.8, 120.1, 116.6, 116.4, 116.2, 116.0, 108.6, 58.9, 31.6, 30.9, 29.7, 25.8, 22.5, 14.0.

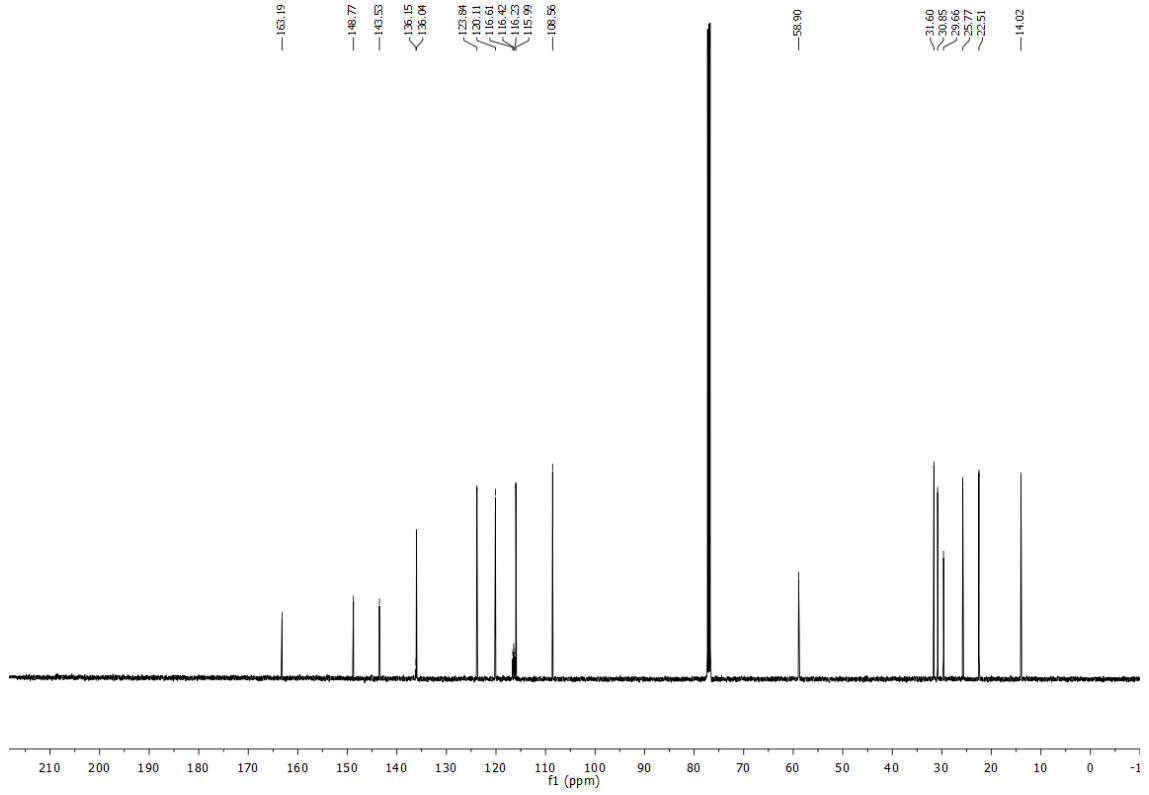
HRMS (ESI): Calculated for $C_{16}H_{21}DN_2O$ [M+H$^+$] = 260.1868, Found 260.1872.

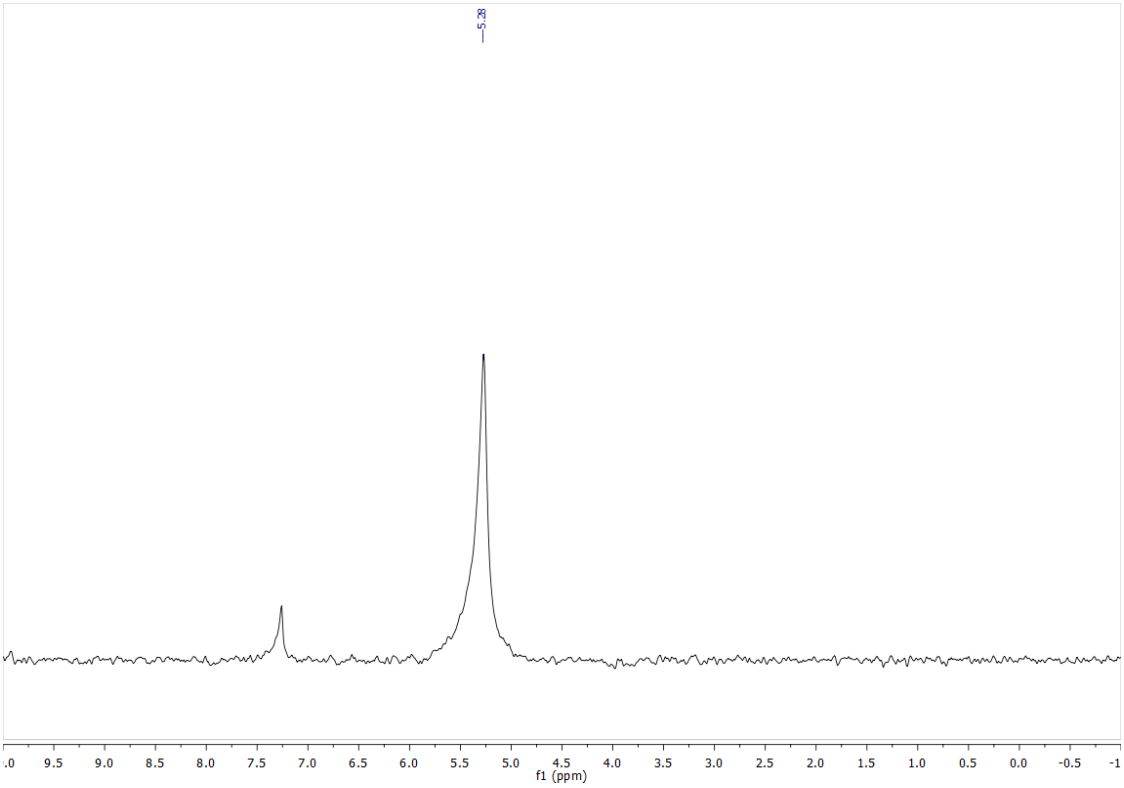
FTIR (neat): 2930, 1636, 1577, 1460, 1246, 1216, 753 cm^{-1}.

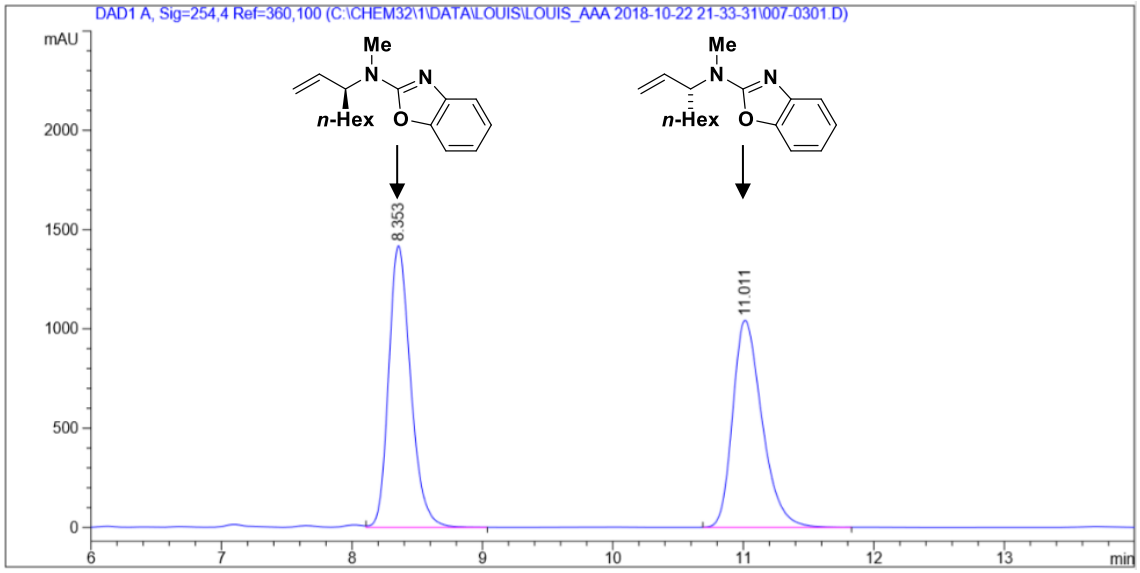
$[\alpha]_D^{28}$= +70.8 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AD-H column, heptanes:*i*-PrOH = 98:2, 1.00 mL/min, 254 nm), *ee* = 96%.

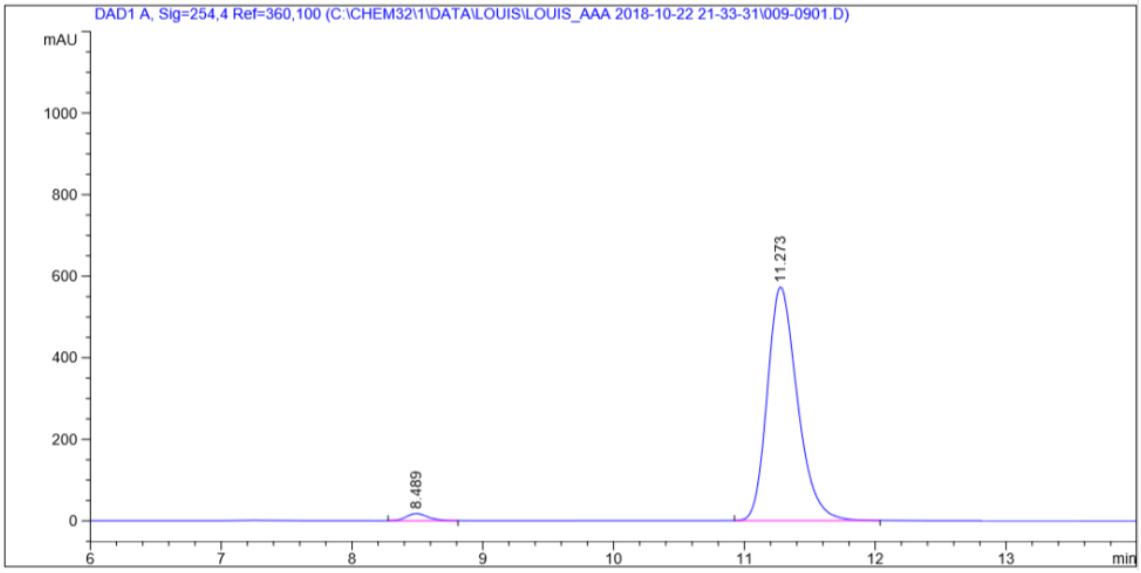

f1 (ppm)


f1 (ppm)


5.28
.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.353	VB	0.1803	1.65706e4	1418.74658	50.4411
2	11.011	BB	0.2382	1.62808e4	1042.75146	49.5589



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.489	BB	0.1769	204.68243	17.69532	2.1833
2	11.273	BB	0.2468	9170.32715	572.78448	97.8167

Single Crystal Diffraction Data for 5.7b

Empirical formula	C13 H18 Br Cl N2 O	
Formula weight	333.65	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	P 21	
Unit cell dimensions	a = 7.1967(3) Å	α= 90°.
	b = 19.2597(4) Å	β= 105.491(5)°.
	c = 10.4450(4) Å	γ = 90°.
Volume	1395.15(9) $Å^3$	
Z	4	
Density (calculated)	1.588 Mg/m^3	
Absorption coefficient	5.697 mm^{-1}	
F(000)	680	
Crystal size	0.160 x 0.070 x 0.030 mm^3	
Theta range for data collection	4.393 to 75.594°.	
Index ranges	-8<=h<=8, -23<=k<=23, -12<=l<=12	
Reflections collected	21291	
Independent reflections	5628 [R(int) = 0.0497]	
Completeness to theta = 67.684°	100.0 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5628 / 2 / 351	
Goodness-of-fit on F^2	1.063	

Final R indices [I>2sigma(I)]	R1 = 0.0362, wR2 = 0.0947
R indices (all data)	R1 = 0.0369, wR2 = 0.0955
Absolute structure parameter	-0.009(15)
Extinction coefficient	n/a
Largest diff. peak and hole	0.701 and -0.579 e.Å^{-3}

Figure 1. View of cation 1 in **5.7b** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.

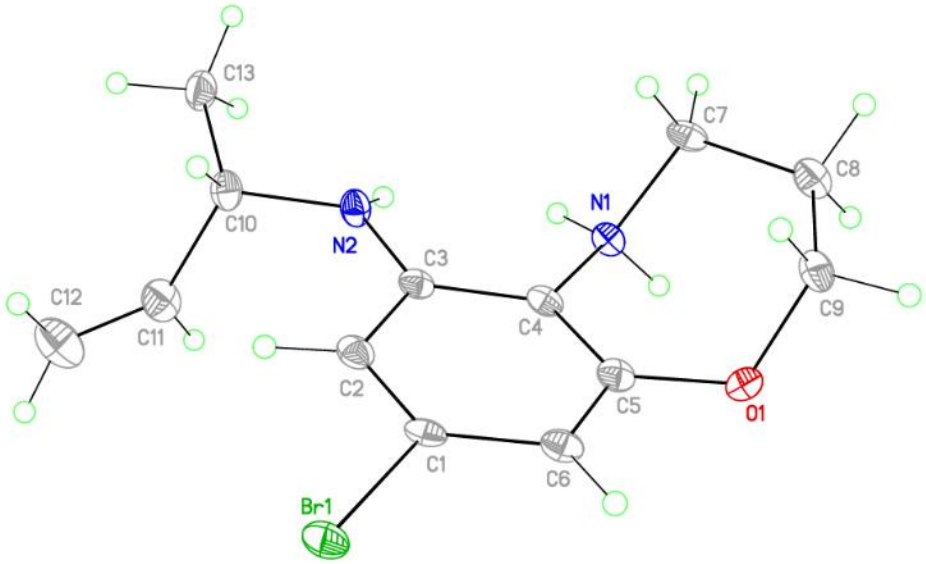
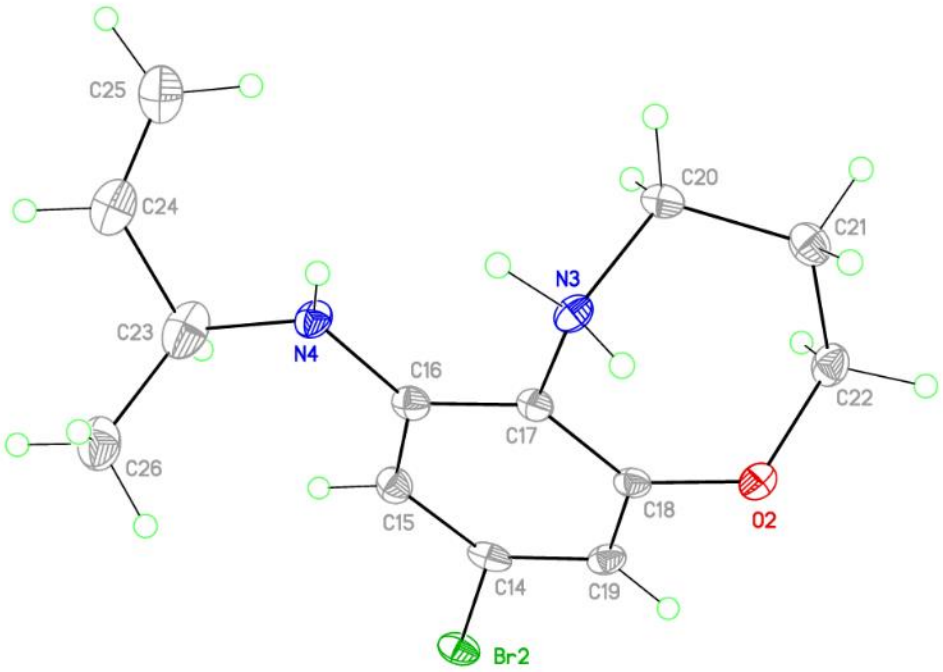


Figure 2. View of cation 2 in **5.7b** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



Chapter 6: Regio- and Enantioselective Iridium-Catalyzed *N*-Allylation of Indoles and Related Azoles with Racemic Branched Alkyl-Substituted Allylic Acetates*

6.1 Introduction

Iridium-catalyzed allylic amination has emerged as an important method for enantioselective C-N bond formation.[1-9] Pursuant to the pioneering work of Takeuchi,[1,2] studies from the laboratories of Helmchen,[3,4] Hartwig,[5,6] Carreira[7] and You[8,9] have shown that chiral phosphoramidite-modified iridium complexes are especially effective in this regard (Figure 6.1). Like the parent palladium-catalyzed Tsuji-Trost reactions,[10] the iridium-phosphoramidite-catalyzed allylic alkylations occur by way of cationic π-allylmetal intermediates. Recently, we found that π-allyliridium-*C,O*-benzoates, which are well-known to promote nucleophilic allylation of carbonyl compounds,[11,12] are also effective catalysts for highly regio- and enantioselective electrophilic allylation of amines.[13] These π-allyliridium-*C,O*-benzoates react by way of neutral π-allylmetal intermediates, which may account for their amphiphilic character. One advantage of the π-allyliridium-*C,O*-benzoate catalysts relates to their facile preparation and remarkable stability toward air, water and SiO_2.[14] Using SEGPHOS-modified π-allyliridium-*C,O*-benzoate catalysts, allylic aminations mediated by aliphatic amine nucleophiles occur with high levels of regio- and enantioselectivity.[13a] It was later found that the tol-BINAP-modified π-allyliridium-*C,O*-benzoate *(S)*-Ir-I is a superior catalyst, enabling highly regio- and enantioselective allylation of electronically diverse primary and secondary (hetero)aryl amines.[13b]

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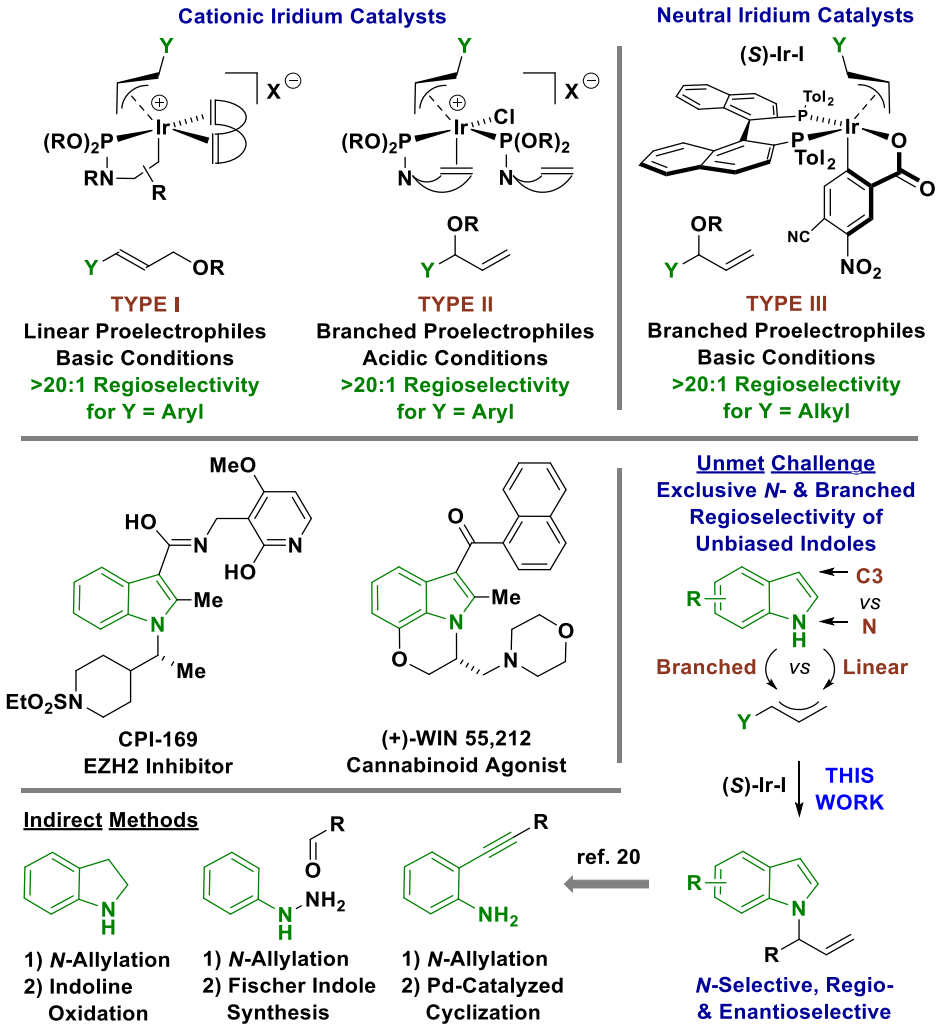
*This chapter is based on the published work:
Kim, S. W.; Schempp, T. T.; Zbieg, J. R.; Stivala, C. E.; Krische, M. J. *Angew. Chem. Int. Ed.* **2019**, *58*, 7762.

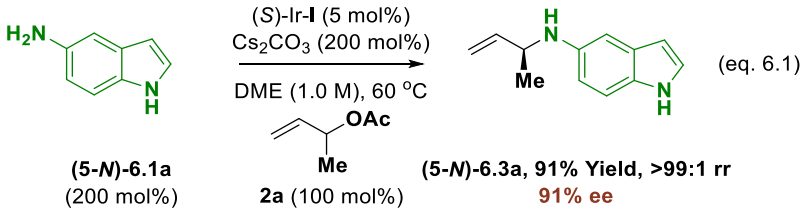
Figure 6.1 Iridium catalysts for asymmetric allylic amination and chiral indole-containing clinical candidates.



6.2 Reaction Development and Scope

In the latter study, it was shown that 5-amino-indole (5-*N*)-**6.1a** undergoes allylic alkylation at the 5-amino moiety to furnish (5-*N*)-**6.3a** with complete site-selectivity (eq. 6.1), suggesting indoles may not be subject to π-allyliridium-*C*,*O*-benzoate-catalyzed *N*-allylation. To challenge this assumption, the parent indole **6.1a** was exposed to

essentially identical conditions for allylic alkylation (eq. 6.2). To our delight, the product **6.3a** was obtained in excellent yield as a single regioisomer in 93% enantiomeric excess. These results were deemed significant, as indoles and related azoles are prevalent structural motifs in clinical candidates and FDA approved drugs (Figure 6.1),[15,16] and allylation at C3 is the major product observed in the intermolecular allylation of structurally and electronically unbiased indoles using palladium,[17] ruthenium[18] or iridium[19] catalysts. For example, to enforce *N*-allylation, use of electron deficient indoles[17j,19c] or heteroatom substituted π-allylmetal species (from alkoxyallenes) is required.[17o] These limitations have necessitated the development of indirect methods for the synthesis of enantiomerically enriched *N*-allyl indoles (Figure 6.1).[20] As the development of enantioselective methods for intermolecular indole allylation that are completely *N*-selective and display exclusive branched regioselectivity remains an unmet challenge,[17-20] an effort to assess the scope the π-allyliridium-*C*,*O*-benzoate-catalyzed indole allylation was undertaken. Here, we show that the tol-BINAP-modified iridium complex *(S)*-Ir-I catalyzes highly enantioselective allylation of diverse indoles and azoles with complete *N*-regioselectivity and complete branched regioselectivity.



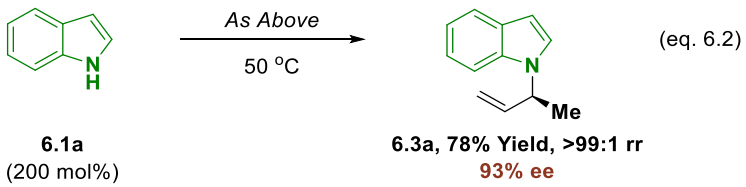
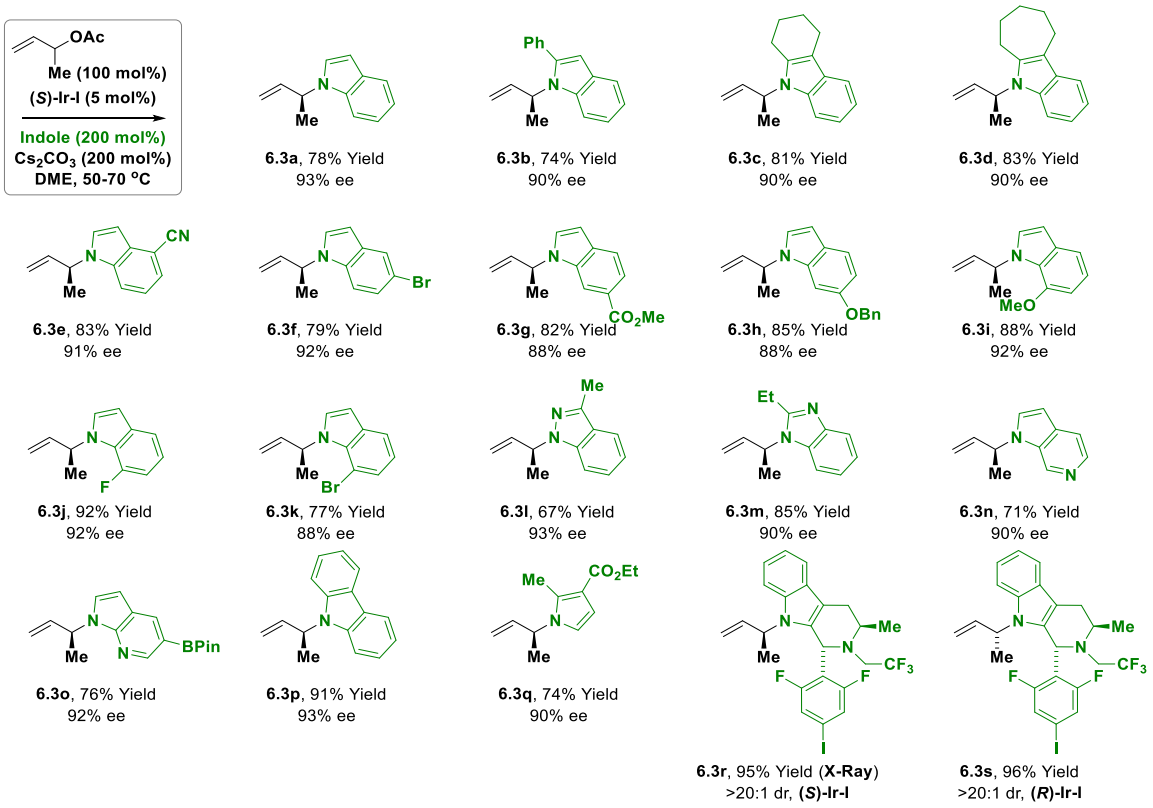


Table 6.1 Regio- and enantioselective iridium-catalyzed allylic alkylation of indoles and related azoles **6.1a-6.1s** using α-methyl allyl acetate **6.2a**.[a]



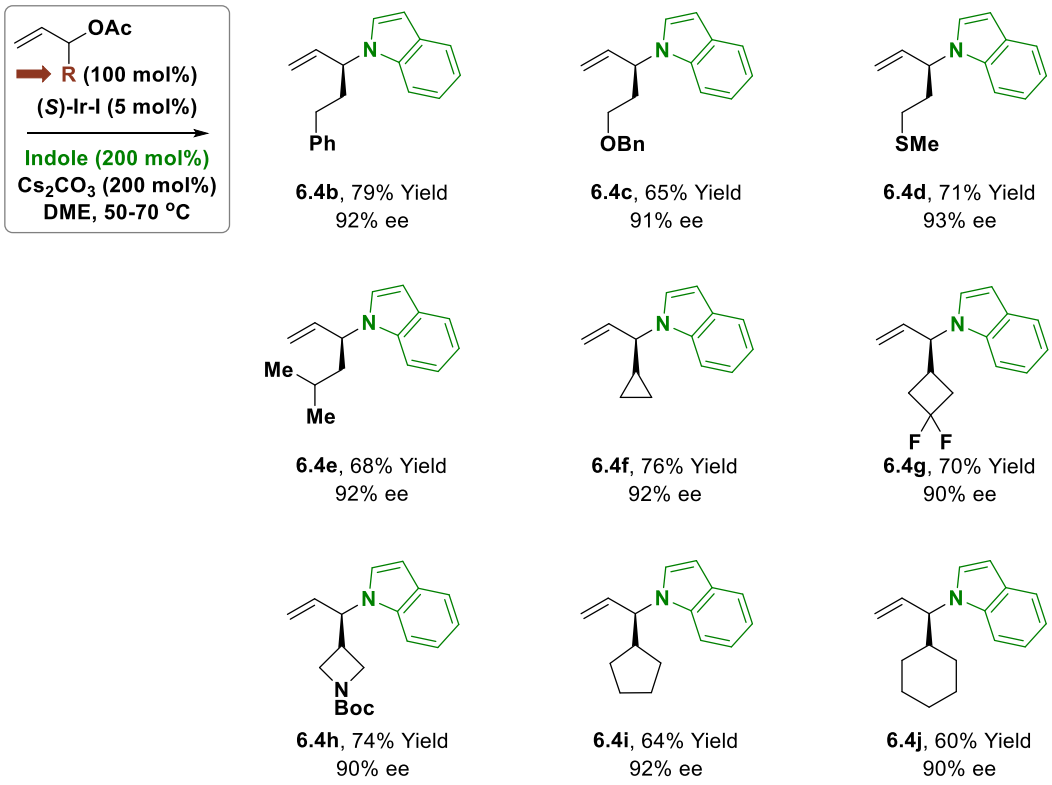
[a]Yields of material isolated by silica gel chromatography. Regio- and diastereoselectivities were determined by ^{1}H NMR analysis of crude reaction mixtures. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details.

To assess the generality of indole allylation catalyzed by *(S)*-Ir-**I**, the reaction conditions utilized in equation 6.2 were applied to structural diverse indoles and azoles **6.1a-6.1p** (Table 6.1). Beyond the parent indole **6.1a**, electronically diverse indoles substituted at the 2-position (**6.1b**), 4-position (**6.1e**), 5-position (**6.1f**), 6-position (**6.1g, 6.1h**) and 7-position (**6.1i-6.1k**) each underwent efficient allylation to deliver the respective adducts (**6.3b, 6.3e-6.3k**) with complete *N*-regioselectivity, complete branched

regioselectivity and uniformly high levels of enantioselectivity. The structurally related azoles tetrahydro-carbazole **6.1c**, the "homo-tetrahydro-carbazole" **6.1d**, 3-methyl-indazole **6.1l**, 2-ethyl- benzimidazole **6.1m**, 6-azaindole **6.1n**, 7-azaindole **6.1o**, carbazole **6.1p** and 2-methyl-3-carboxypyrrole ethyl ester **6.1q** also underwent efficient *N*-allylation to form adducts **6.3c**, **6.3d** and **6.3l-6.3q**, respectively, as single constitutional isomers with high levels of enantiomeric enrichment. Of relevance to medicinal chemistry applications, the formation of adduct **6.3o** demonstrates tolerance of a pinacol boronate moiety under the conditions of asymmetric *N*-allylation. Additionally, to further test the limits of our method, catalyst-directed diastereoselectivity was explored in the allylation of the structurally complex chiral azole **6.1r**, which is related to AZD-9496, a clinical stage non-steroidal oral estrogen receptor inhibitor.[21] Remarkably, the enantiomeric iridium catalysts *(S)*-Ir-I and (*R*)-Ir-I deliver the diastereomeric adducts **6.3r** and **6.3s** in >95% yield with complete levels of catalyst-directed stereoinduction.

Using diverse α-substituted allyl acetates **6.2b-6.2j**, the scope of the electrophilic partner was subsequently evaluated in *N*-allylations of the parent indole **6.1a** (Table 6.2). Branched allylic acetates bearing linear alkyl groups **6.2b-6.2d**, which incorporate phenyl, benzyl ether and methyl sulfide moieties, respectively, were efficiently converted to adducts **6.4b-6.4d**. As illustrated by the formation adduct **6.4e**, branched alkyl groups are tolerated. Finally, the preparation of adducts **6.4f-6.4j** highlight the tolerance of cycloalkyl substituents. All adducts **6.4b-6.4j** were formed as single constitutional isomers and with high levels of enantiomeric enrichment. The absolute stereochemistry of adducts **6.3a-6.3s** and **6.4b-6.4j** was assigned in analogy to adduct **6.3a**, which was determined through comparison of its optical rotation to a sample reported in the literature.[8b]

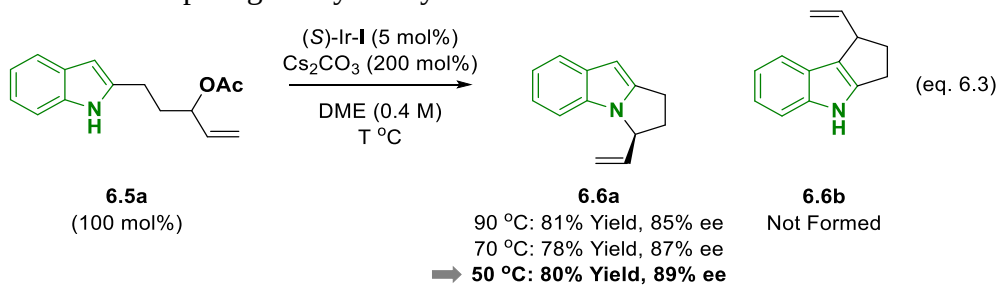
Table 6.2 Regio- and enantioselective iridium-catalyzed allylic alkylation of indole **6.1a** using diverse α-substituted allyl acetates **6.2b-6.2j**.[a]



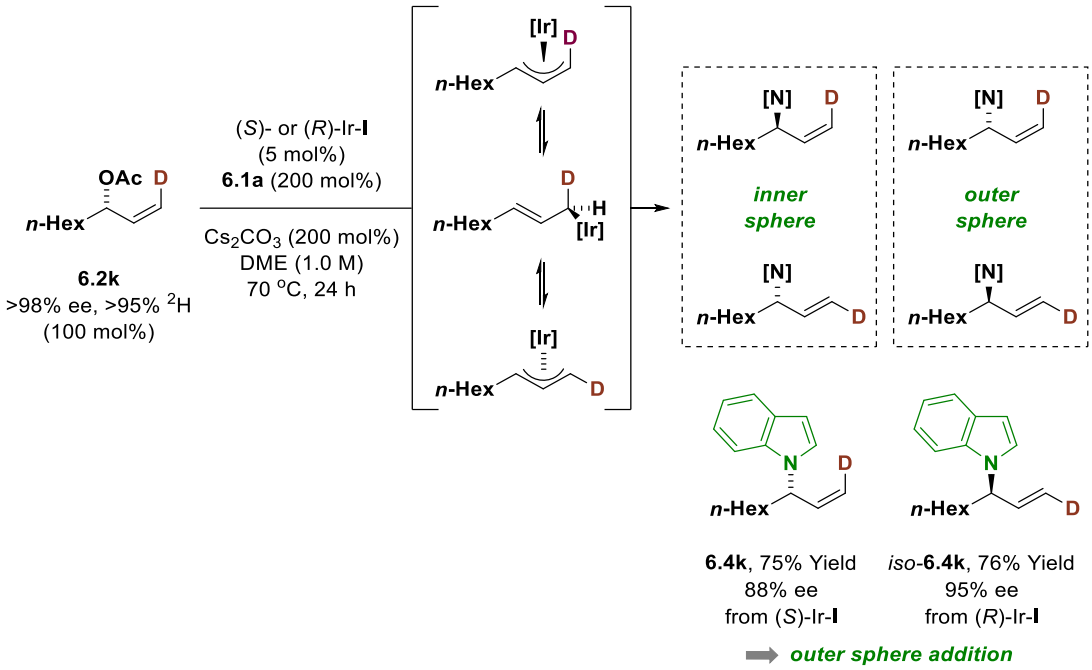
[a]Yields of material isolated by silica gel chromatography. Regio- and diastereoselectivities were determined by ^{1}H NMR analysis of crude reaction mixtures. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details.

To further assess the breadth of the present protocol for catalytic enantioselective *N*-allylation, the cyclization of racemic allylic acetate **6.5a** was explored (eq. 6.3). The cyclization of 5a provides an opportunity to test the limits of stereoinduction, as the rate of enantiotopic π-facial interconversion must exceed the rate of 5-membered ring formation.[22] The cyclization of **6.5a** also provides another context to evaluate the fidelity of *N*- vs C3-regioselectivity. In the event, exposure of **6.5a** to *(S)*-Ir-I under standard

conditions at 50 °C provided the product of *N*-cycloallylation **6.6a** as single constitutional isomer without competing C3-cycloallylation.



Scheme 6.1 Iridium-catalyzed amination of enantiomerically enriched deuterated allylic acetate **6.2k** with the enantiomeric catalysts *(S)*-Ir-I and (*R*)-Ir-I.[a]



[a]Yields of material isolated by silica gel chromatography. Regio- and diastereoselectivities were determined by ^{1}H NMR analysis of crude reaction mixtures. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details.

6.3 Discussion

The basicity of the reaction conditions and the acidity of indoles suggest the active nucleophiles in the present protocol for iridium-catalyzed *N*-allylation are *N*-centered anions. In previously reported allylic aminations catalyzed by π-allyliridium-*C,O*-benzoates, significantly less acidic aliphatic and aromatic amines were utilized, which likely serve as neutral *N*-nucleophiles.[13] Hence, although a mechanism involving outer-sphere addition was established in the previously reported allylic aminations of the less acidic aliphatic and aromatic amines, it was unclear whether inner- or outer-sphere addition pathways were operative in the present indole-mediated asymmetric aminations. To address this question, the enantiomerically enriched (*Z*)-deuterated allylic acetate **6.2k** was subjected to standard conditions for allylic amination using indole **6.1a** (Scheme 1).[23] Using the enantiomeric catalysts *(S)*-Ir-I and (*R*)-Ir-I the stereoisomeric products **6.4k** and iso-**6.4k** are generated, which corroborates C-N bond formation through outer-sphere addition.

6.4 Conclusion

In summary, using π-allyliridium-*C,O*-benzoate catalysts in combination with racemic branched alkyl-substituted allylic acetate proelectrophiles, we report the first highly enantioselective intermolecular Tsuji-Trost-type indole *N*-allylations wherein complete *N*-regioselectivity is accompanied by complete branched-regioselectivity. Future work will explore related electrophilic *N*- and C-allylations catalyzed by cyclometallated π-allyliridium *C,O*-benzoates. These efforts illustrate the effectiveness of

academic-industrial collaboration vis-á-vis development of asymmetric methods for unmet challenges in synthetic chemistry of relevance to the drug discovery enterprise.

6.5 Experimental Details

General Information

All reactions were carried out under inert gas atmosphere (nitrogen or argon) unless otherwise indicated. Resealable pressure tubes (13x100 mm) were purchased from Fischer Scientific (catalog number 14-959-35C) and were flame dried followed by cooling in a desiccator or under a stream of inter gas prior to use. All commercial reagents and anhydrous solvents were used as received from vendors (Fischer Scientific, Sigma Aldrich and Combi Blocks) without further purification. The used Iridium catalyst *(S)*-Ir-I and (*R*)-Ir-I was prepared according to literature known procedures.[1] Cesium carbonate was used as received from Rockwell Lithium. Preparative column chromatography employing Silicycle silica gel (40-63 μm) was performed according to the method of Still[2] or on a Teledyne Isco Combiflash R_f utilizing Silicycle HP columns using a mobile phase composed of either heptane/isopropyl acetate, heptanes/ethyl acetate or dichloromethane/methanol. Reactions were monitored by a Shimadzu LCMS/UV system with LC-30AD solvent pump, 2020 MS, Sil-30AC autosampler, SPD-M30A UV detector, CTO-20A column oven, using a 2-98% acetonitrile/0.1% formic acid (or 0.001% ammonia) gradient over 2.5 minutes. Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Dynamic Absorbents F). Visualization was accomplished with UV light followed by dipping in CAM, *p*-Anisaldehyde (PAA), or KMnO4 stain solution followed by heating.

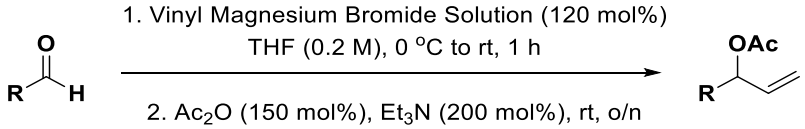
Spectroscopy, Spectrometry and Data Collection

Infrared spectra were recorded on a Perki*N*-Elmer 1600 spectrometer using a diamond ATR unit. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion (M+H, M+Na), or a suitable fragment ion. Nuclear magnetic resonance (^{1}H, ^{13}C, ^{19}F NMR) spectra were recorded with a Bruker BioSpin GmbG, Varian Gemini (400 MHz) or Varian INOVA (500 MHz) spectrometer equipped with a Bruker cryoprobe. The chemical shifts are given as parts per million (ppm) and were referenced to the residual solvent signal ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm). Specific optical rotations were recorded on an Atago AP-300 automatic polarimeter at the sodium line (589 nm) in CHCl3. Solution concentrations are given in the units of 10–2 g mL^{-1}.

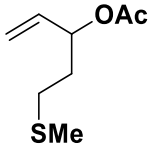
Experimental Details and Spectral Data

Synthesis of Allylic Acetates 6.2d, 6.2g, and 6.2h

The allylic acetates **6.2d, 6.2g,** and **6.2h** were prepared by the Grignard reaction and acetylation of the as shown below. The allylic acetates **6.2b**,[3] **6.2c**,[4] **6.2e**,[5] **6.2f**,[6] **6.2i**,[7] **6.2j**,[5] and **6.2k**[7] were identical in all respects to the reported materials.



***(S)*-5-(methylthio)pent-1-en-3-yl acetate (6.2d)**



Procedures

To a round-bottomed flask charged with the corresponding aldehyde (1.04 g, 10.0 mmol, 100 mol%) under an argon atmosphere was added THF (50.0 mL, 0.2 M). The reaction flask was placed an ice batch. After 10 minutes, vinyl magnesium bromide solution (12.0 mL, 12.0 mmol, 120 mol%, 1.0 M in THF) was added slowly and the mixture was stirred at room temperature for 1 hour, at which point acetic anhydride (1.42 mL, 15.0 mmol, 150 mol%) and triethylamine (2.79 mL, 20.0 mmol, 200 mol%) were added and the reaction was stirred vigorously overnight. After water (50 mL) was added, the mixture was transferred to a separatory funnel. The organic layer was extracted with diethyl ether (50 mL × 2) and the combined organic layers were washed with 1 N HCl (50 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash column chromatography (SiO_2, pentanes: diethyl ether = 40:1–20:1) to furnish the title compound as a colorless oil (1.31 g, 4.58 mmol) in 75% yield over 2 steps.

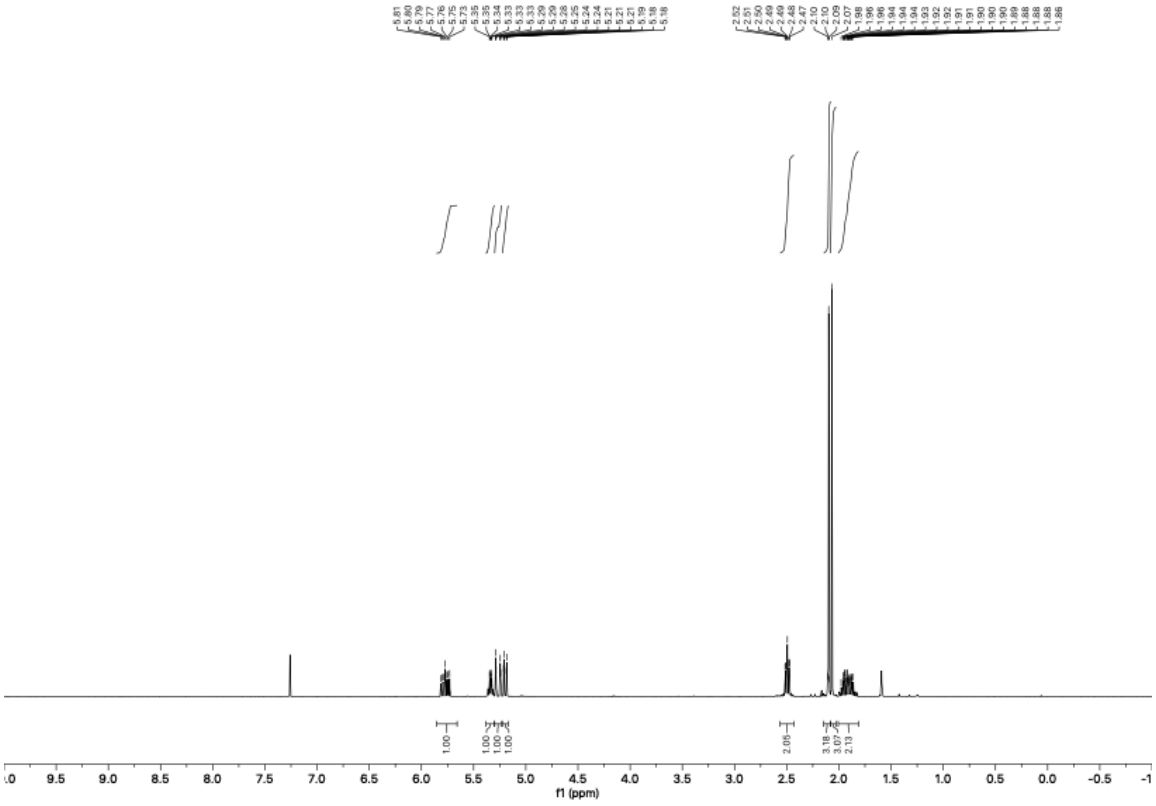
TLC (SiO_2) R_f = 0.40 (hexanes: ethyl acetate = 5:1).

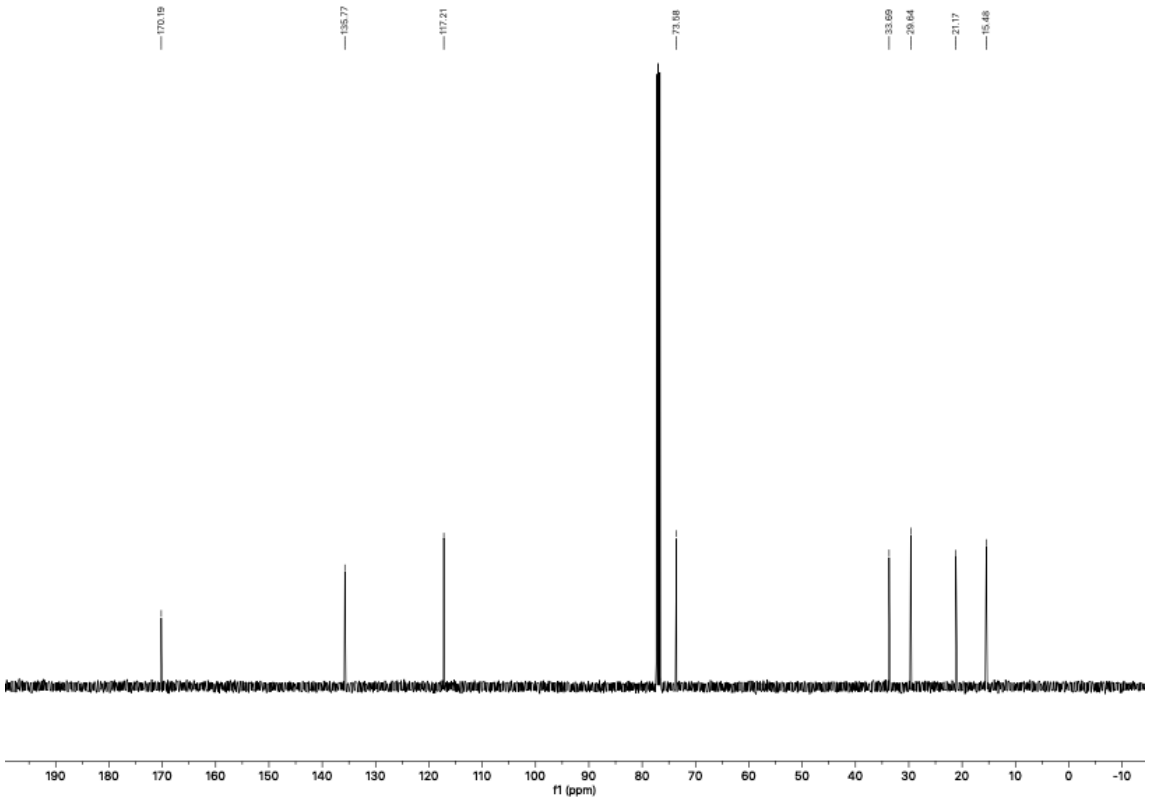
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.77 (ddd, *J* = 17.0, 10.5, 6.4 Hz, 1H), 5.34 (dt, *J* = 7.3, 1.0 Hz, 1H), 5.27 (dt, *J* = 17.2, 1.3 Hz, 1H), 5.20 (dt, *J* = 10.5, 1.2 Hz, 1H), 2.49 (ddd, *J* = 8.4, 6.7, 1.9 Hz, 2H), 2.10 (s, 3H), 2.07 (s, 3H), 2.01 – 1.81 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 170.2, 135.8, 117.2, 73.6, 33.7, 29.6, 21.2, 15.5.

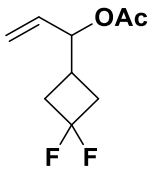
HRMS (ESI): Calculated for $C_8H_{14}O_2S$ [M+Na^+] = 197.0607, Found 197.0607.

FTIR (neat): 3024, 2918, 1736, 1428, 1237, 1022, 753 cm^{-1}.





1-(3,3-difluorocyclobutyl)allyl acetate (6.2g)



Procedures

To a round-bottomed flask charged with the corresponding aldehyde (0.90 g, 7.50 mmol, 100 mol%) under an argon atmosphere was added THF (37.5 mL, 0.2 M). The reaction flask was placed an ice batch. After 10 minutes, vinyl magnesium bromide solution (9.0 mL, 9.0 mmol, 120 mol%, 1.0 M in THF) was added slowly and the mixture was stirred at room temperature for 1 hour, at which point acetic anhydride (1.06 mL, 11.3 mmol, 150 mol%) and triethylamine (2.09 mL, 15.0 mmol, 200 mol%) were added and the

reaction was stirred vigorously overnight. After water (50 mL) was added, the mixture was transferred to a separatory funnel. The organic layer was extracted with diethyl ether (50 mL × 2) and the combined organic layers were washed with 1 N HCl (50 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash column chromatography (SiO_2, pentanes: diethyl ether = 40:1–20:1) to furnish the title compound as a colorless oil (0.87 g, 4.58 mmol) in 61% yield over 2 steps.

TLC (SiO_2) R_f = 0.39 (hexanes: ethyl acetate = 10:1).

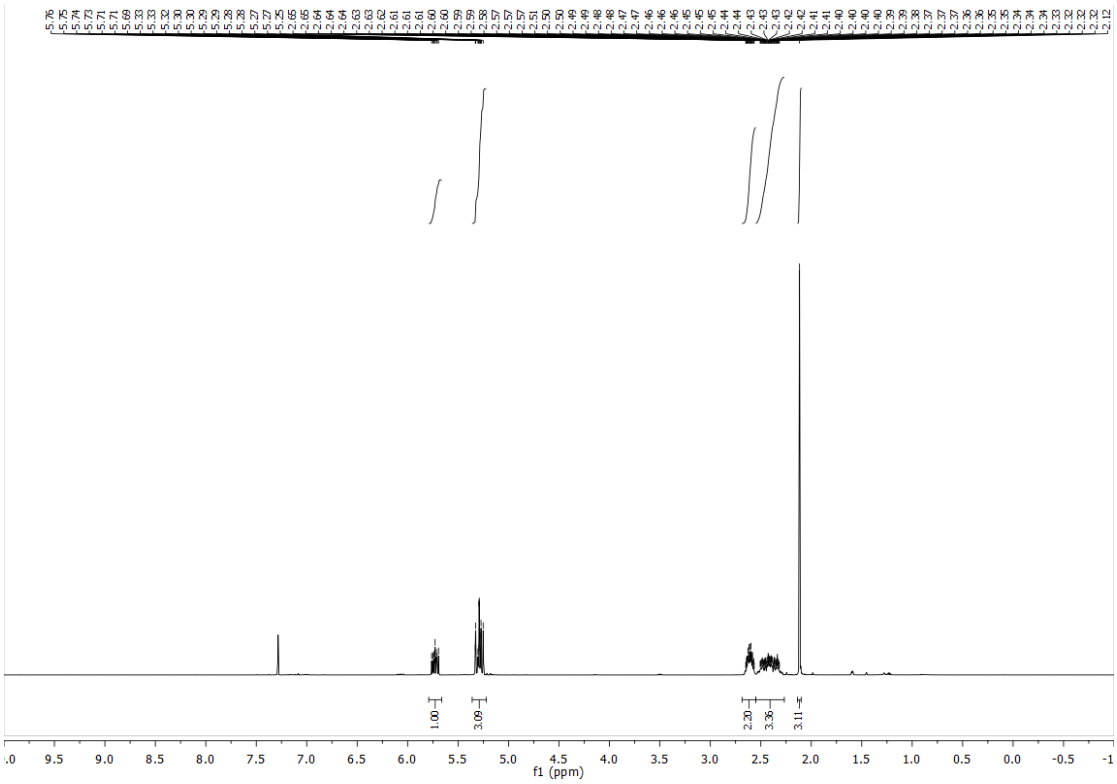
^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.73 (ddd, *J* = 17.1, 10.5, 6.6 Hz, 1H), 5.36 – 5.22 (m, 3H), 2.61 (dtdd, *J* = 16.0, 10.7, 5.1, 3.0 Hz, 2H), 2.55 – 2.27 (m, 3H), 2.12 (s, 3H).

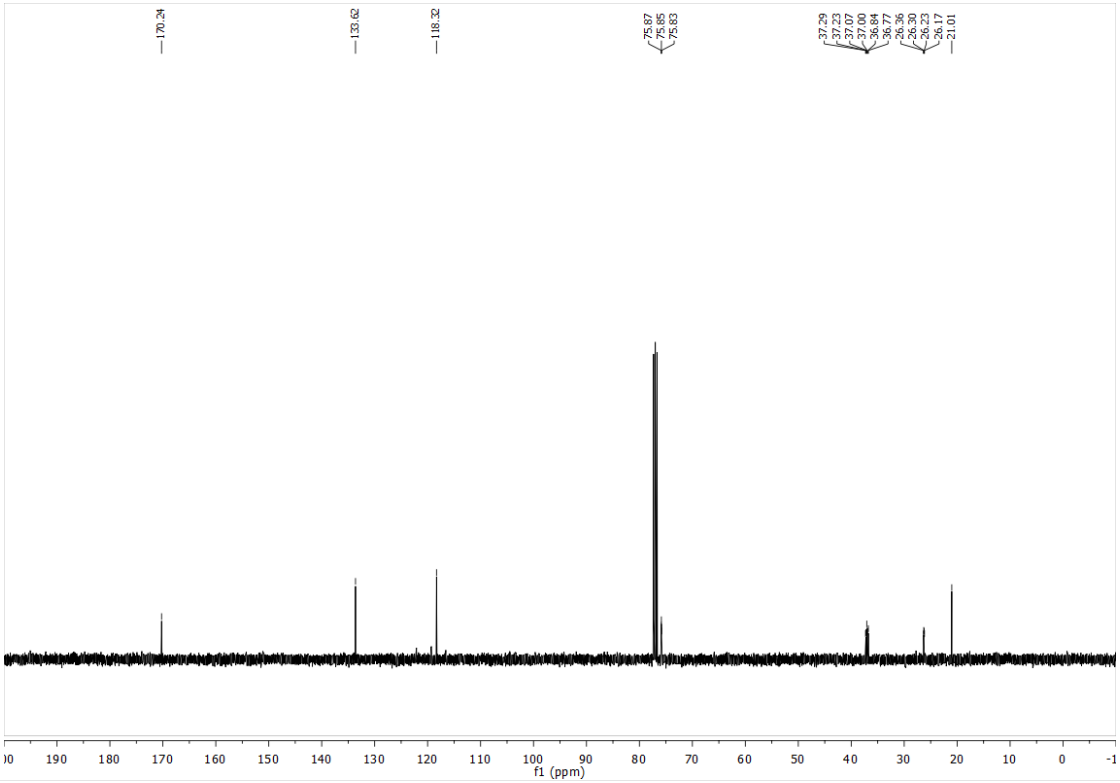
^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.2, 133.6, 118.3, 75.89 – 75.81 (m), 37.34 – 36.70 (m, 2C), 26.27 (dd, *J* = 13.7, 5.9 Hz), 21.01.

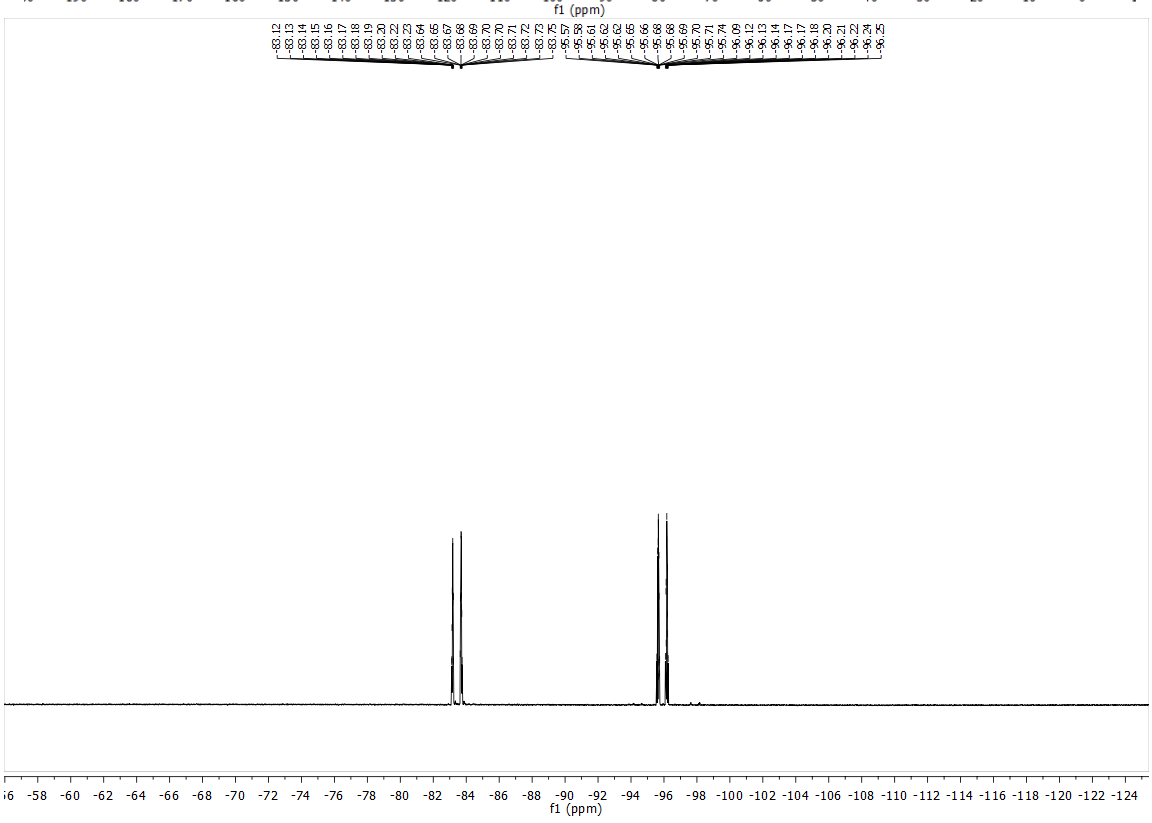
^{19}F NMR (376 MHz, $CDCl_3$): δ = -83.1 – -83.8 (m, 1F), -95.6 – -96.3 (m, 1F).

LRMS (CI): Calculated for $C_7H_9F_2$ $[M–OAc]^+$ = 131, Found 131.

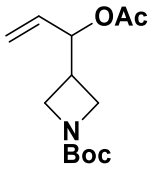
FTIR (neat): 2958, 1738, 1413, 1372, 1297, 1229, 1170, 1020, 908 cm^{-1}.


1.00
3.09
2.20
3.36
3.11
f1 (ppm)


170.24
133.62
118.32
75.87
75.85
75.83
37.29
37.23
37.07
37.00
36.84
36.77
26.36
26.30
26.23
26.17
21.01
f1 (ppm)


-83.12
-83.13
-83.14
-83.15
-83.16
-83.17
-83.18
-83.19
-83.20
-83.22
-83.23
-83.64
-83.65
-83.67
-83.68
-83.69
-83.70
-83.70
-83.71
-83.72
-83.73
-83.75
-95.57
-95.58
-95.61
-95.62
-95.62
-95.65
-95.66
-95.68
-95.68
-95.69
-95.70
-95.71
-95.74
-96.09
-96.12
-96.13
-96.14
-96.17
-96.17
-96.18
-96.20
-96.21
-96.22
-96.24
-96.25
f1 (ppm)

tert-butyl 3-(1-acetoxyallyl)azetidine-1-carboxylate (6.2h)



Procedures

To a round-bottomed flask charged with the corresponding aldehyde (0.90 g, 7.50 mmol, 100 mol%) under an argon atmosphere was added THF (37.5 mL, 0.2 M). The reaction flask was placed an ice batch. After 10 minutes, vinyl magnesium bromide solution (9.0 mL, 9.0 mmol, 120 mol%, 1.0 M in THF) was added slowly and the mixture was stirred at room temperature for 1 hour, at which point acetic anhydride (1.06 mL, 11.3 mmol, 150 mol%) and triethylamine (2.09 mL, 15.0 mmol, 200 mol%) were added and the

reaction was stirred vigorously overnight. After water (50 mL) was added, the mixture was transferred to a separatory funnel. The organic layer was extracted with diethyl ether (50 mL × 2) and the combined organic layers were washed with 1 N HCl (50 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash column chromatography (SiO_2, pentanes: diethyl ether = 40:1–20:1) to furnish the title compound as a colorless oil (1.09 g, 4.28 mmol) in 57% yield over 2 steps.

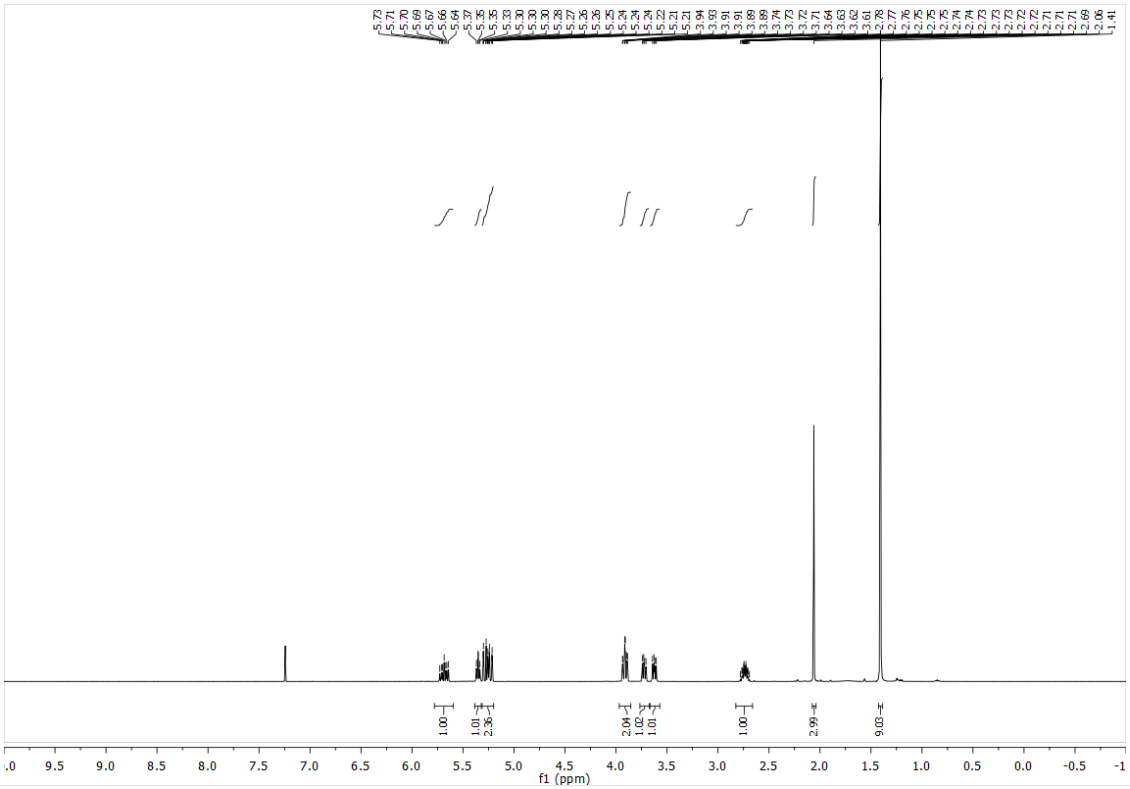
TLC (SiO_2) R_f = 0.24 (hexanes: ethyl acetate = 4:1).

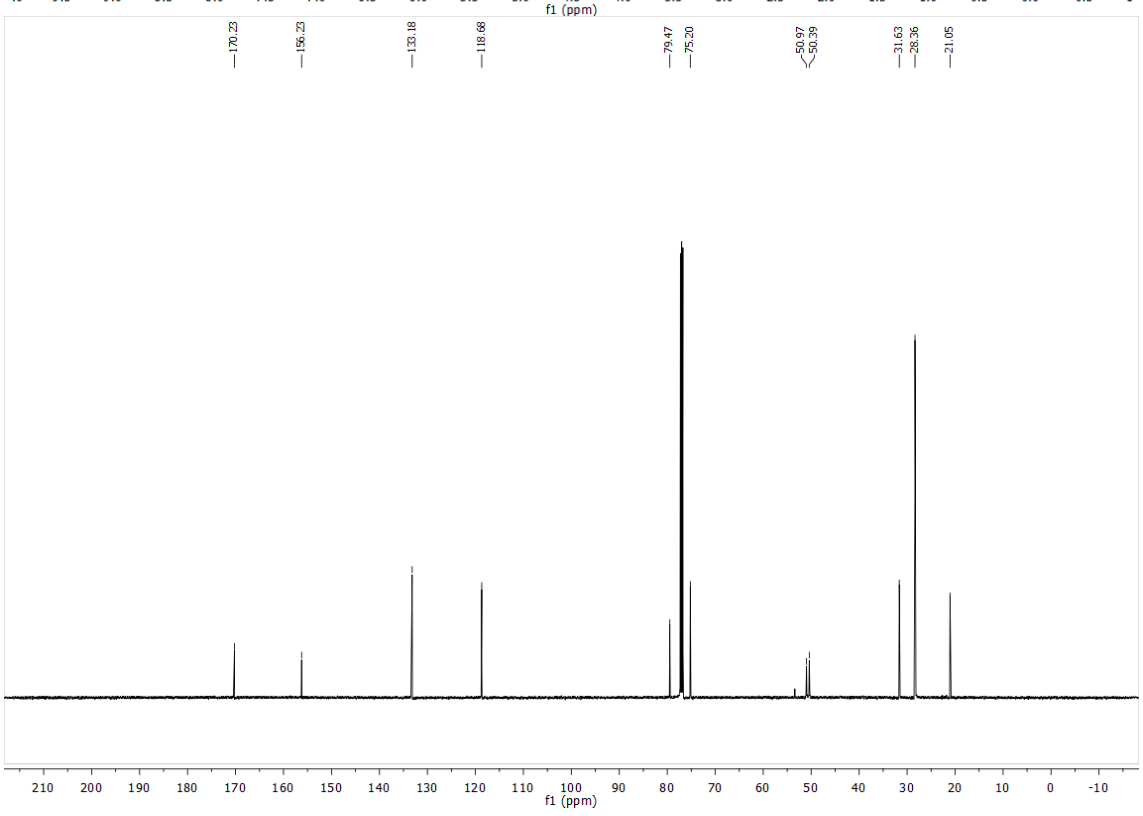
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.69 (ddd, *J* = 17.1, 10.5, 6.4 Hz, 1H), 5.38 – 5.32 (m, 1H), 5.31 – 5.20 (m, 2H), 3.91 (td, *J* = 8.6, 2.5 Hz, 2H), 3.72 (dd, *J* = 8.8, 5.5 Hz, 1H), 3.62 (dd, *J* = 8.9, 5.6 Hz, 1H), 2.82 – 2.66 (m, 1H), 2.06 (s, 3H), 1.41 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2, 156.2, 133.2, 118.7, 79.5, 75.2, 50.7 (d, *J* = 72.7 Hz), 31.6, 28.4, 21.1.

HRMS (ESI): Calculated for $C_{13}H_{21}NO_4$ [M+Na^+] = 278.1363, Found 278.1371.

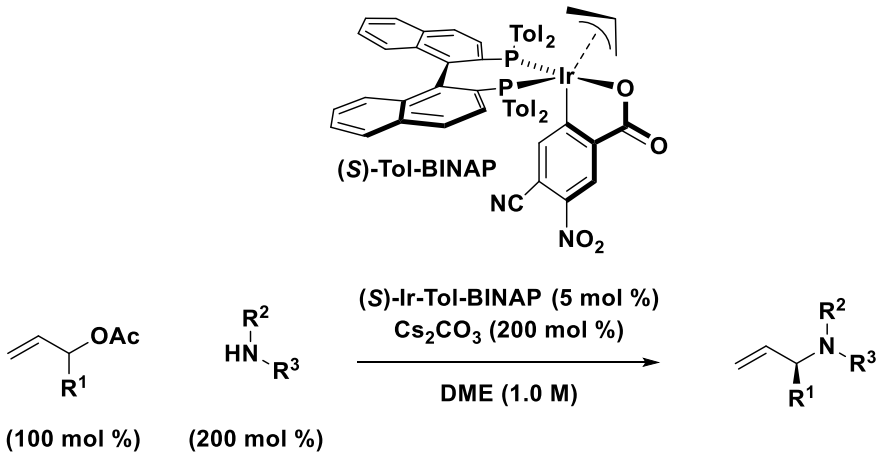
FTIR (neat): 2973, 1697, 1392, 1365, 1227, 1134, 1020, 942, 772, 735 cm^{-1}.


f1 (ppm)


170.23
156.23
133.18
118.68
79.47
75.20
50.97
50.39
31.63
28.36
21.05
f1 (ppm)

Procedures and Spectral Data for Synthesis of Allylic Amines 6.3a-6.3q, 6.4b-6.4j

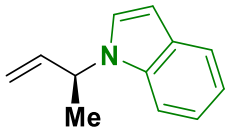
Enantioselective Ir-catalyzed allylic alkylation with amine nucleophiles



General procedure

A pressure tube equipped with a magnetic stir bar was charged with cesium carbonate (200 mol%), ***(S)*-Ir-I** (5 mol%). The tube was purged with argon for 5 minutes. DME (1.0 M) was added followed by the allylic acetate (100 mol%) and the amine (200 mol%). The tube was sealed with a PTFE lined cap and was placed in an oil bath at the indicated temperature and stirred for the indicated period of time. After reaching ambient temperature, the crude reaction mixture was directly subjected to flash column chromatography.

***(S)*-1-(but-3-en-2-yl)-1H-indole (6.3a)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (103.1 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (50 °C, 24 hr). The title compound was obtained in 78% yield (58.8 mg, 0.34 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.44 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.36 (dd, *J* = 8.3, 0.9 Hz, 1H), 7.22 – 7.16 (m, 2H), 7.10 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 6.52 (dd, *J* = 3.2, 0.8 Hz, 1H), 6.05 (ddd, *J* = 17.5, 10.4, 4.7 Hz, 1H), 5.18 (ddd, *J* = 10.4, 1.6, 0.9 Hz, 1H), 5.12 – 5.04 (m, 2H), 1.65 (d, *J* = 6.9 Hz, 3H).

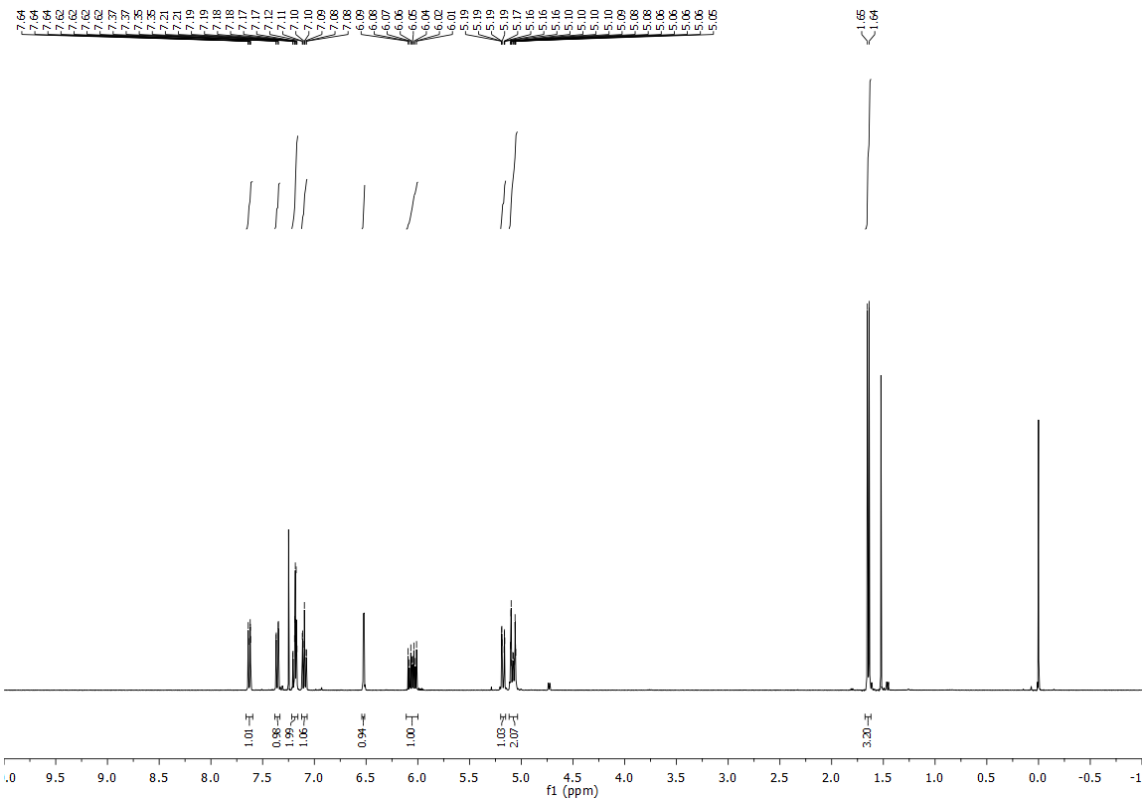
^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.8, 135.7, 128.7, 124.7, 121.3, 121.0, 119.4, 115.5, 109.8, 101.4, 53.1, 19.7.

HRMS (ESI): Calculated for $C_{12}H_{13}N$ [M+H$^+$] = 172.1126, Found 172.1122.

FTIR (neat): 2980, 1509, 1459, 1310, 1264, 1213, 926, 735 cm^{-1}.

$[\alpha]_D^{28}$= –20.6 (*c* 0.2, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 93%.


7.64
7.64
7.64
7.62
7.62
7.62
7.62
7.37
7.35
7.21
7.21
7.19
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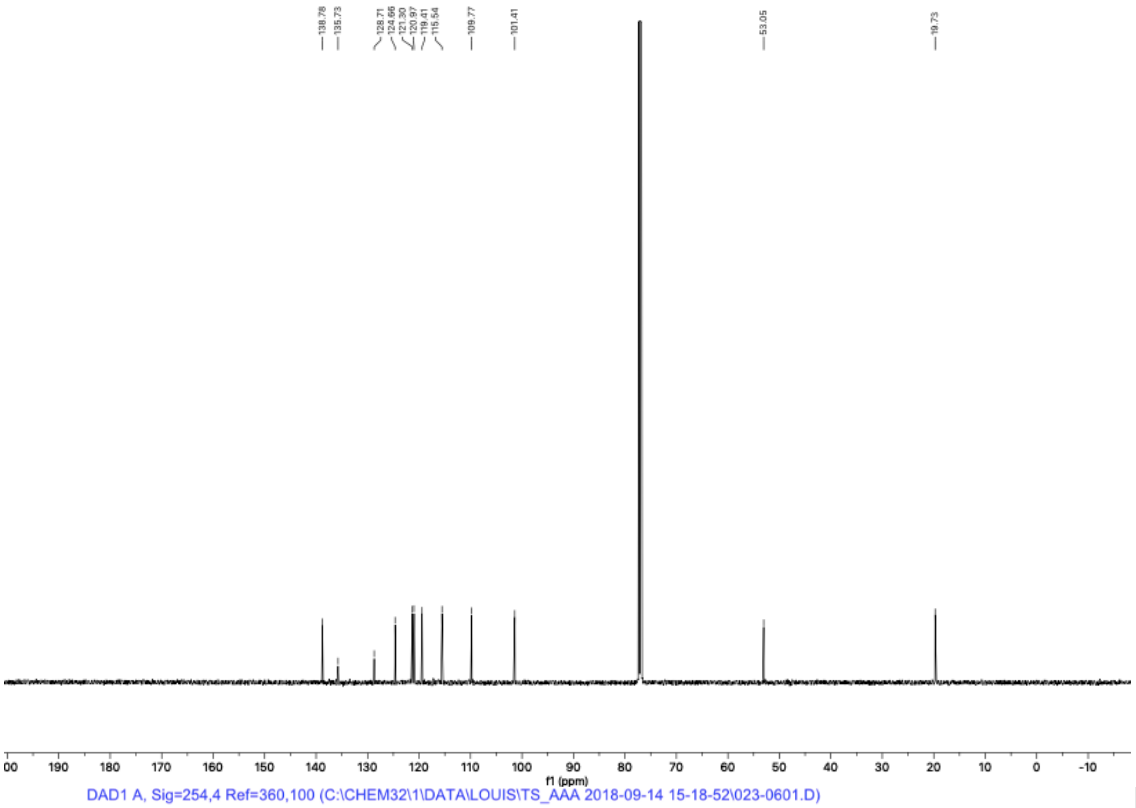
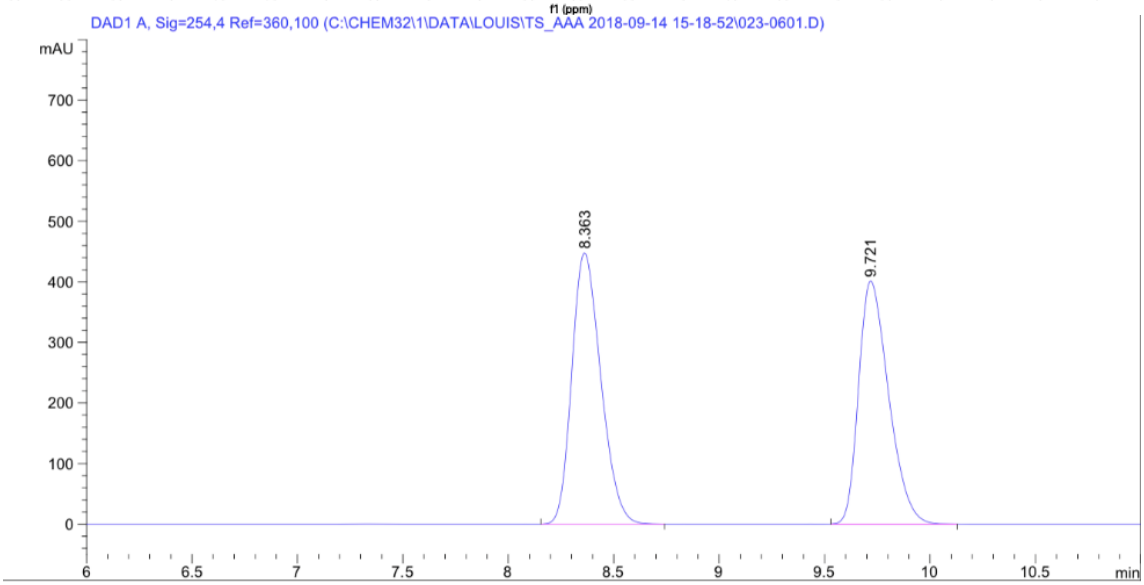
7.18
7.17
7.17
7.12
7.11
7.10
7.10
7.09
7.08
7.08
6.09
6.08
6.07
6.06
6.05
6.04
6.02
6.01
5.19
5.19
5.19
5.17
5.16
5.16
5.16
5.10
5.10
5.10
5.09
5.08
5.08
5.06
5.06
5.06
5.06
5.05
1.65
1.64
1.01
0.98
1.99
1.06
0.94
1.00
1.03
2.07
3.20
f1 (ppm)





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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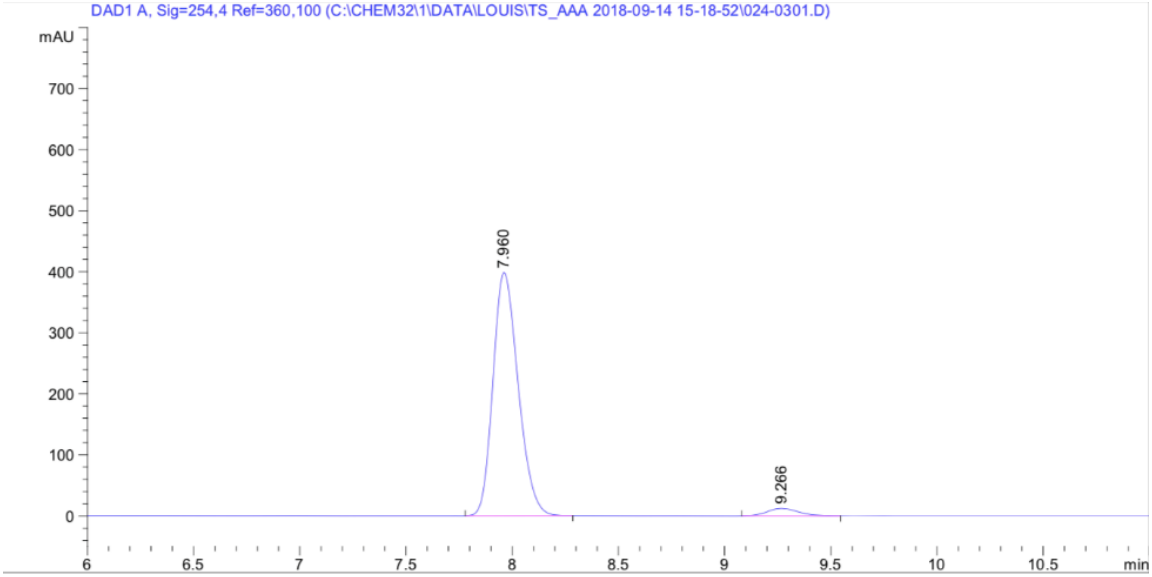
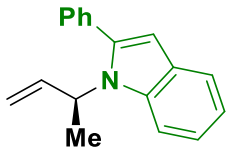
2	9.721	BB	0.1515	3974.83081	401.62894	48.1168



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.960	BB	0.1281	3286.46777	398.86353	96.3105
2	9.266	BB	0.1569	125.89999	12.35635	3.6895

***(S)*-1-(but-3-en-2-yl)-2-phenyl-1H-indole (6.3b)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (170.1 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 74% yield (80.5 mg, 0.33 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 20 min).

TLC (SiO_2) R_f = 0.43 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 – 7.62 (m, 1H), 7.52 – 7.39 (m, 6H), 7.14 (qdd, J = 8.1, 6.7, 1.2 Hz, 2H), 6.52 (d, J = 0.8 Hz, 1H), 6.22 (dddd, J = 17.3, 10.6, 3.7, 0.7 Hz, 1H), 5.29 (ddd, J = 10.6, 2.3, 1.0 Hz, 1H), 5.20 (ddt, J = 17.3, 2.0, 0.9 Hz, 1H), 5.17 – 5.10 (m, 1H), 1.62 (d, J = 7.1 Hz, 3H).

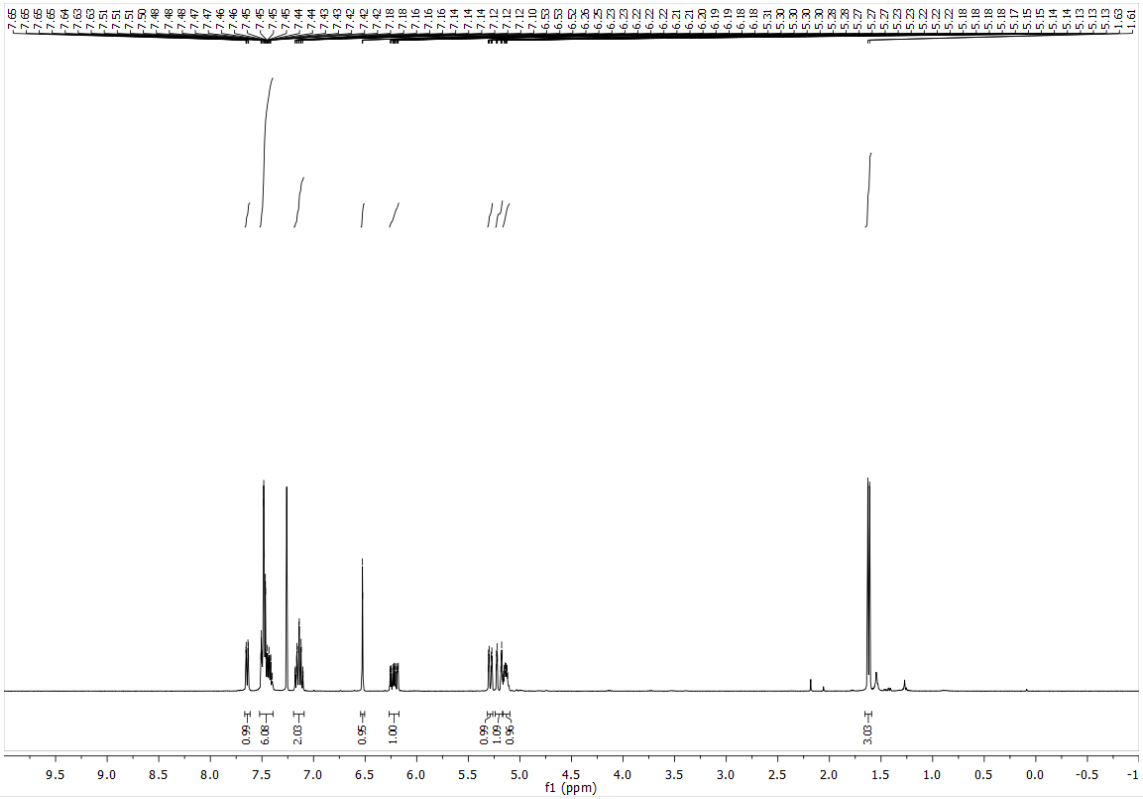
^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.5, 138.8, 135.9, 133.3, 129.4, 129.0, 128.5, 128.0, 121.0, 120.7, 119.7, 115.6, 113.0, 102.4, 52.9, 18.2.

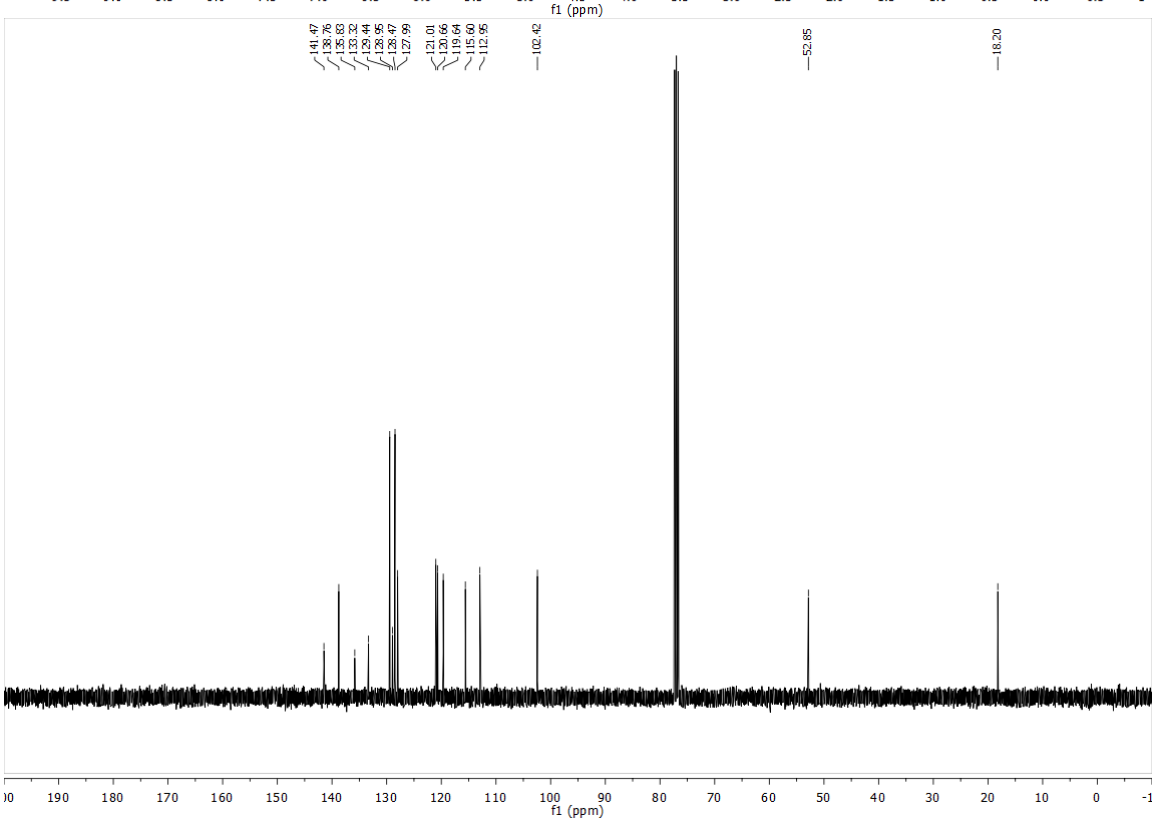
HRMS (ESI): Calculated for $C_{18}H_{17}N$ $[M+H^+]$ = 248.1434, Found 248.1435.

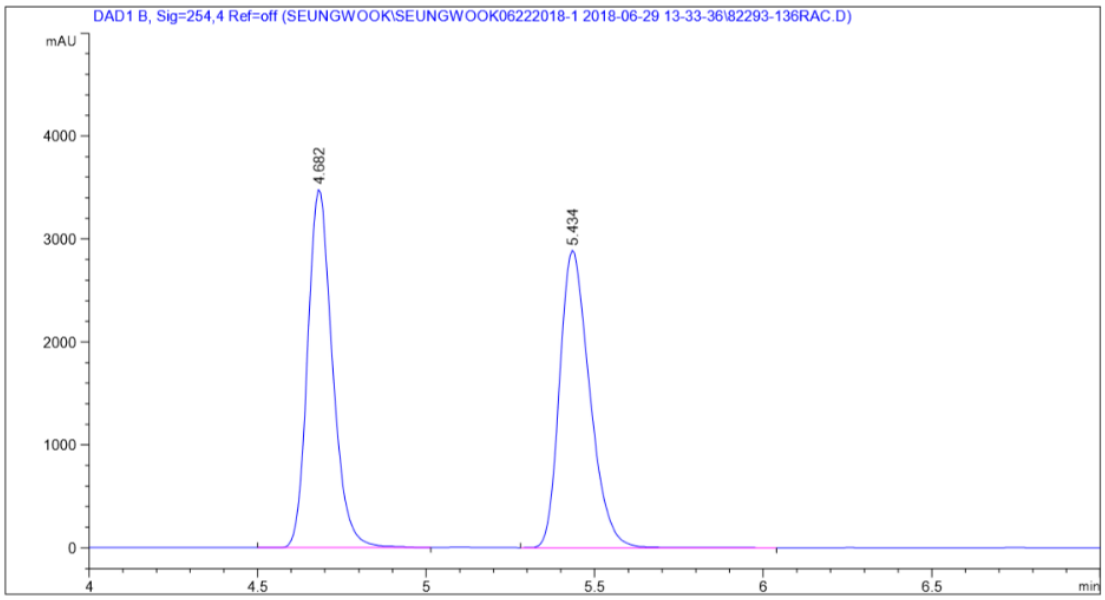
FTIR (neat): 2980, 1604, 1455, 1347, 1313, 1163, 921, 763, 700 cm^{-1}.

$[\alpha]_D^{28}$= –40.8 (*c* 0.2, $CHCl_3$).

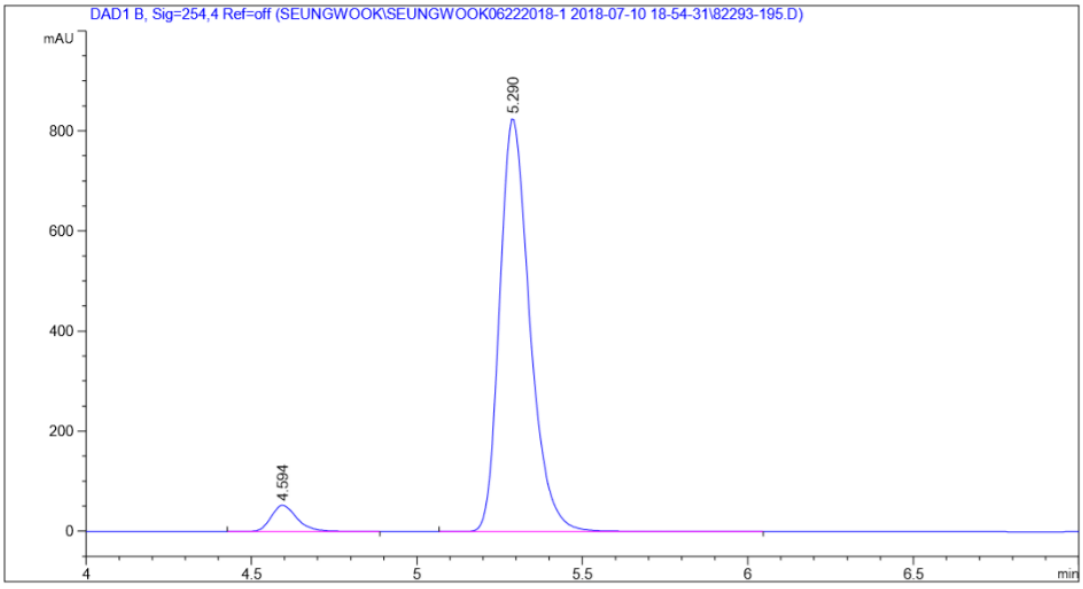
HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 97.5:2.5, 1.00 mL/min, 254 nm), *ee* = 90%.


0.99
6.08
2.03
0.95
1.00
0.99
1.09
0.96
3.03
f1 (ppm)


141.47
138.76
135.83
133.32
129.44
128.95
128.47
127.99
121.01
120.66
119.64
115.60
112.95
102.42
52.85
18.20
f1 (ppm)

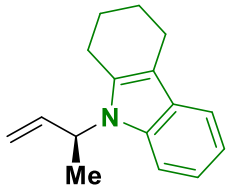


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.682	BB	0.0776	1.78126e4	3486.30713	49.9202
2	5.434	BB	0.0941	1.78695e4	2891.06543	50.0798



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.594	BB	0.0813	286.77493	52.82874	5.2001
2	5.290	BB	0.0978	5228.01807	826.88037	94.7999

***(S)*-9-(but-3-en-2-yl)-2,3,4,9-tetrahydro-1H-carbazole (6.3c)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (150.7 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 81% yield (80.3 mg, 0.36 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 20 min).

TLC (SiO_2) R_f = 0.46 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 – 7.45 (m, 1H), 7.39 – 7.34 (m, 1H), 7.14 – 7.03 (m, 2H), 6.19 (ddd, *J* = 17.3, 10.6, 4.0 Hz, 1H), 5.23 (ddd, *J* = 10.6, 2.3, 1.0 Hz, 1H), 5.15 (ddd, *J* = 17.4, 2.2, 1.0 Hz, 1H), 5.04 (dddd, *J* = 11.1, 7.1, 4.8, 2.0 Hz, 1H), 2.77 – 2.71 (m, 4H), 1.98 – 1.91 (m, 2H), 1.90 – 1.83 (m, 2H), 1.65 (d, *J* = 7.1 Hz, 3H).

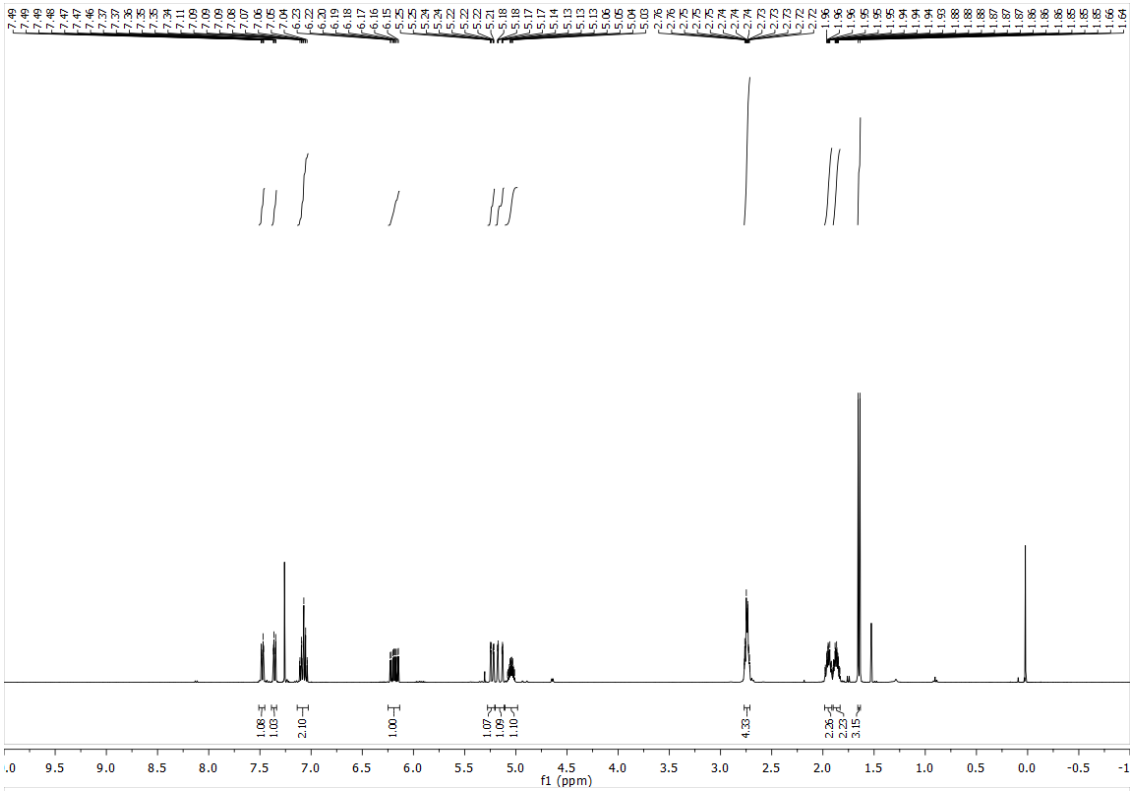
^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.1, 135.2, 135.1, 127.9, 120.2, 118.4, 117.7, 115.2, 110.7, 109.8, 51.5, 23.5, 23.2, 23.1, 21.1, 18.4.

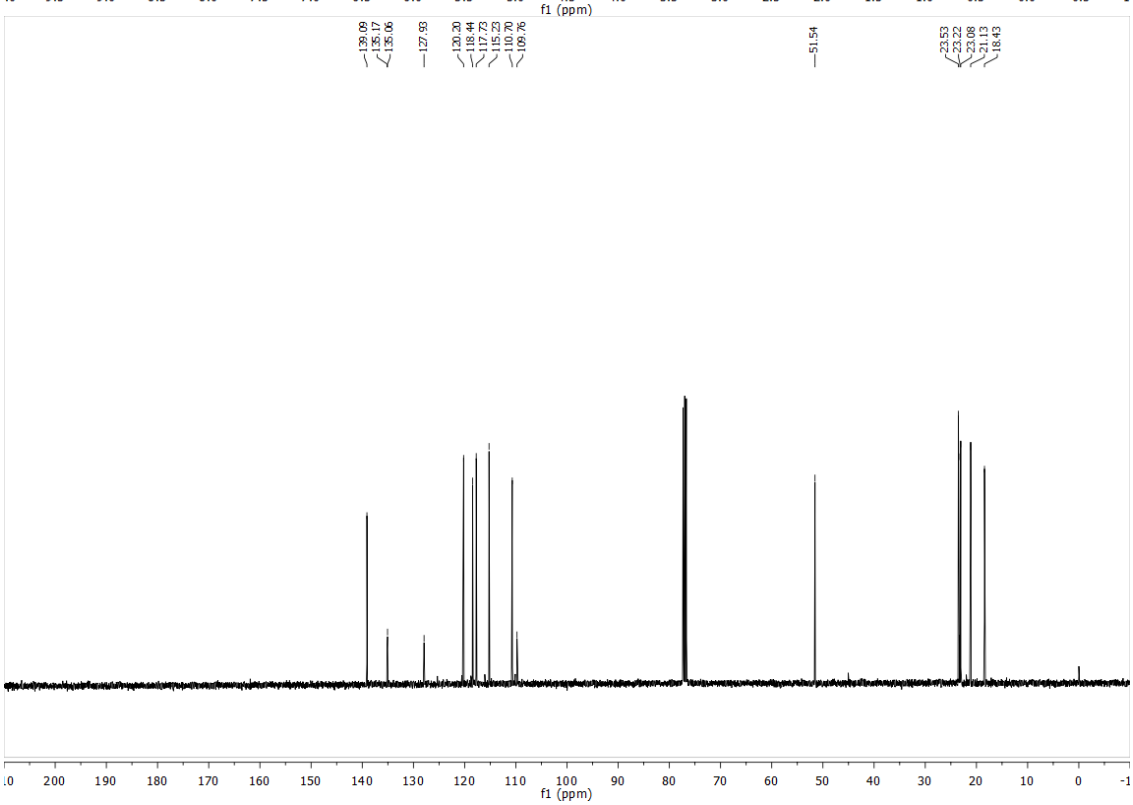
HRMS (ESI): Calculated for $C_{16}H_{19}N$ [M+H$^+$] = 226.1596, Found 226.1605.

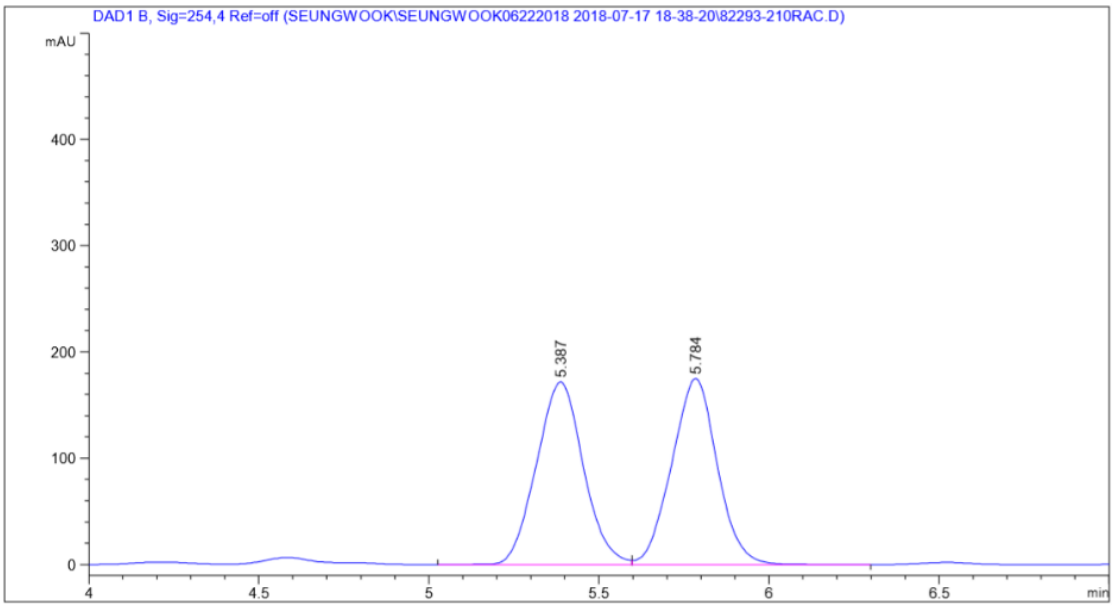
FTIR (neat): 2933, 1462, 1368, 1264, 1175, 922, 732, 703 cm^{-1}.

$[\alpha]_D^{28}$ = –7.7 (*c* 0.2, $CHCl_3$).

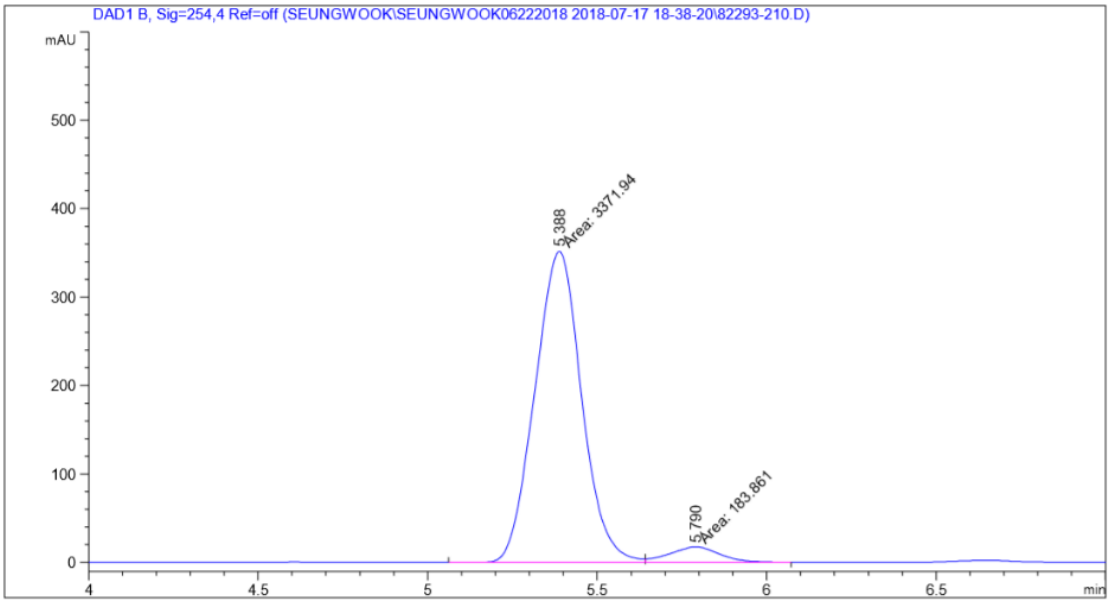
HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 90%.


f1 (ppm)


f1 (ppm)

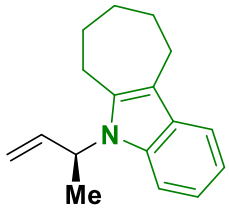


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.387	BV	0.1477	1646.09485	171.90953	50.3050
2	5.784	VB	0.1403	1626.13586	175.14908	49.6950



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.388	MF	0.1594	3371.94116	352.46402	94.8293
2	5.790	FM	0.1743	183.86134	17.58341	5.1707

***(S)*-5-(but-3-en-2-yl)-5,6,7,8,9,10-hexahydrocyclohepta[b]indole (6.3d)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (163.0 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 83% yield (87.4 mg, 0.37 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 20 min).

TLC (SiO_2) R_f = 0.46 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 – 7.46 (m, 1H), 7.37 – 7.31 (m, 1H), 7.11 – 7.04 (m, 2H), 6.20 (ddd, *J* = 17.4, 10.5, 3.8 Hz, 1H), 5.24 (ddd, *J* = 10.7, 2.4, 0.9 Hz, 1H), 5.22 – 5.13 (m, 2H), 2.92 – 2.82 (m, 4H), 1.94 – 1.87 (m, 2H), 1.80 – 1.74 (m, 4H), 1.63 (d, *J* = 7.0 Hz, 3H).

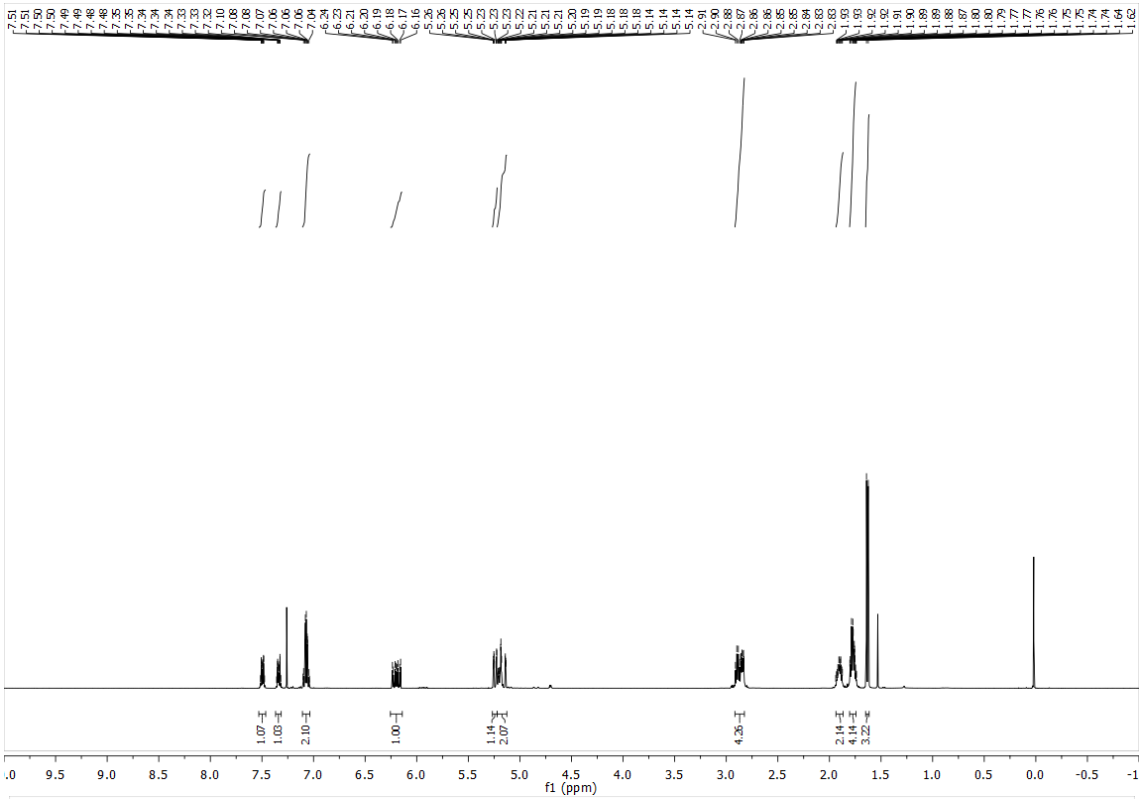
^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.7, 138.9, 134.5, 128.2, 119.9, 118.5, 117.5, 115.0, 114.5, 110.3, 51.2, 31.7, 28.1, 27.3, 26.9, 24.1, 18.9.

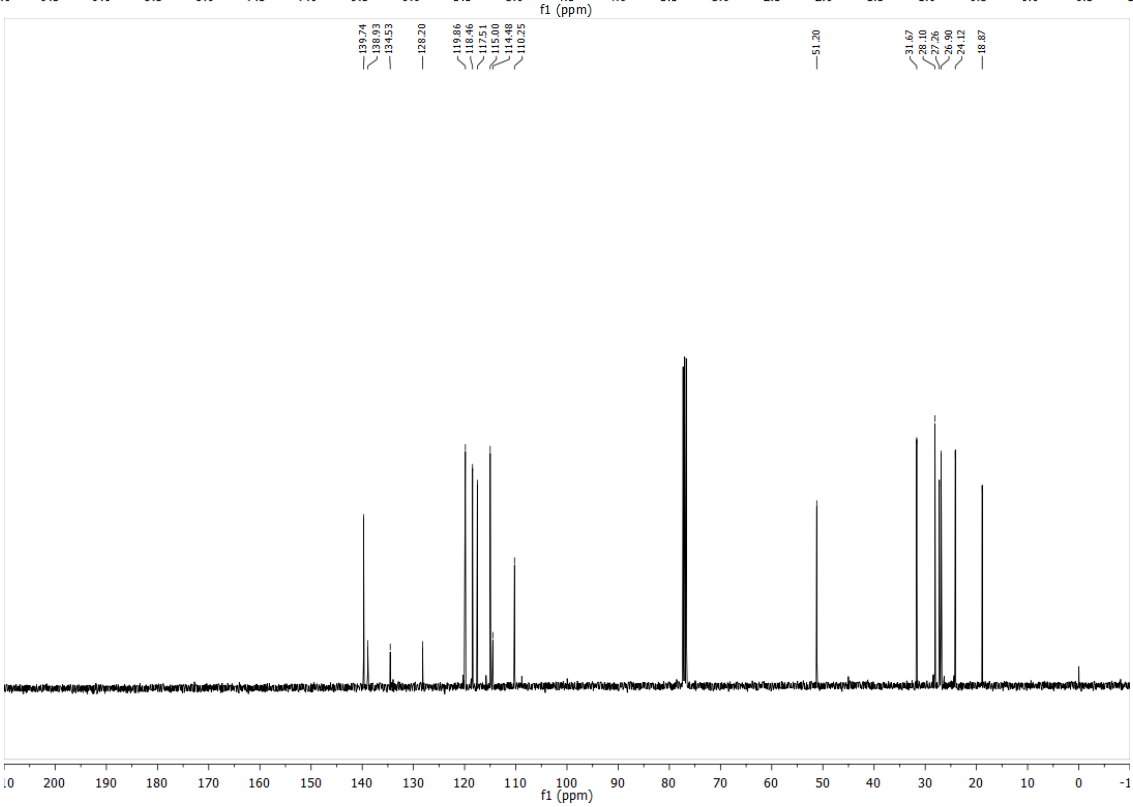
HRMS (ESI): Calculated for $C_{17}H_{21}N$ [M+H$^+$] = 240.1747, Found 240.1747.

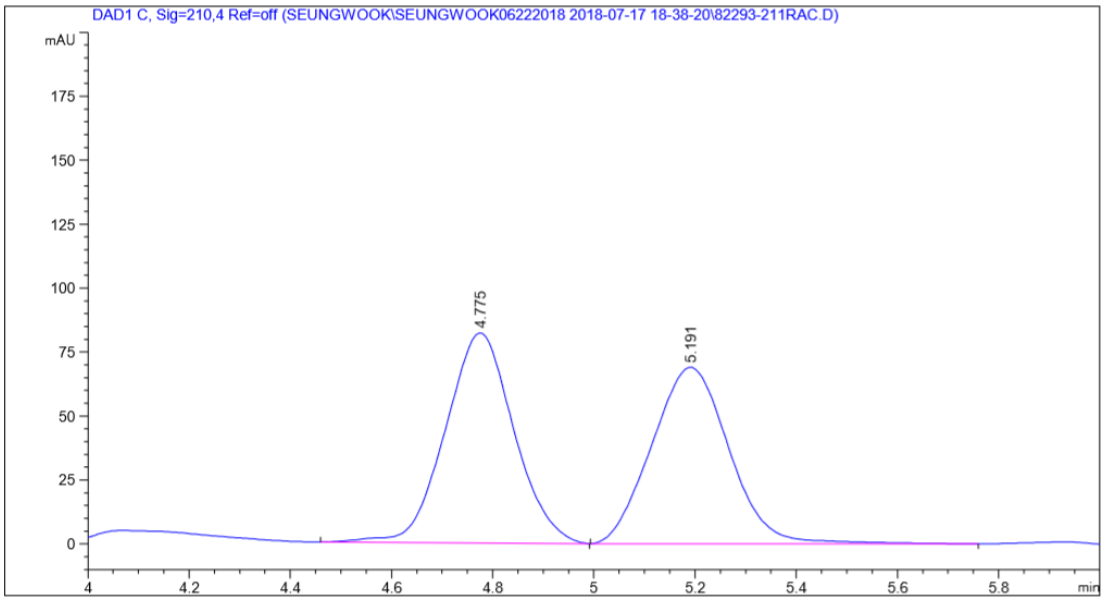
FTIR (neat): 2917, 2845, 1463, 1346, 1204, 1086, 919, 735 cm^{-1}.

$[\alpha]_D^{28}$ = –8.8 (*c* 0.2, $CHCl_3$).

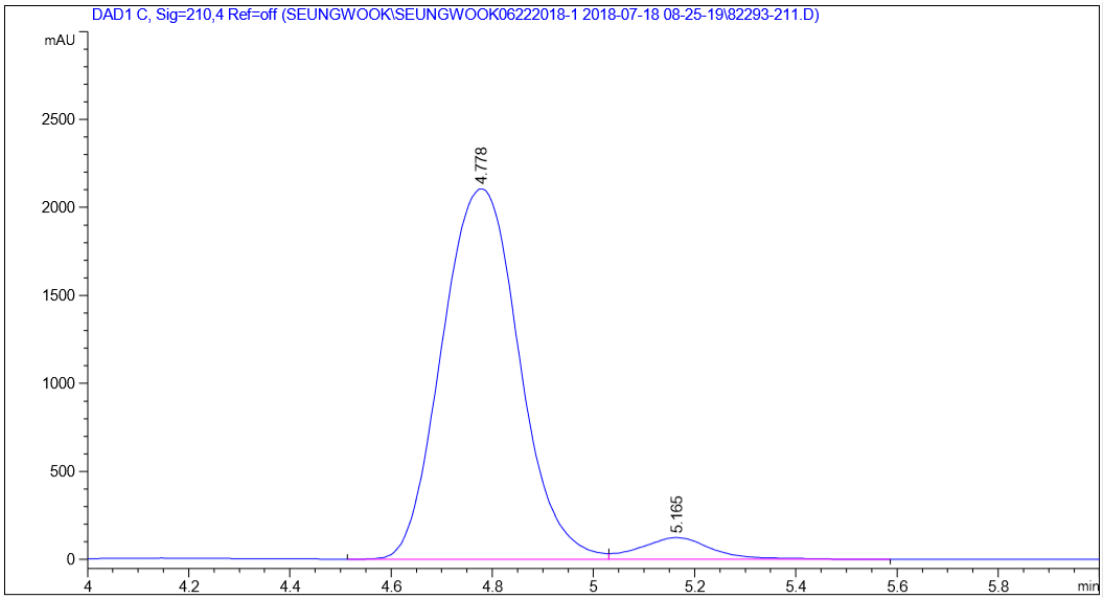
HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 99:1, 1.00 mL/min, 210 nm), *ee* = 90%.


f1 (ppm)


f1 (ppm)

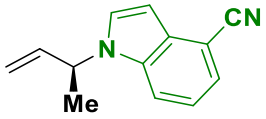


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.775	BB	0.1436	772.08258	82.21450	51.3615
2	5.191	BB	0.1656	731.14893	68.98771	48.6385



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.778	BV	0.1675	2.22654e4	2104.01807	94.8784
2	5.165	VB	0.1438	1201.90173	123.21155	5.1216

***(S)*-1-(but-3-en-2-yl)-1*H*-indole-4-carbonitrile (6.3e)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (125.1 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (50 ºC, 24 hr). The title compound was obtained in 83% yield (72.0 mg, 0.37 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1).

TLC (SiO_2) R_f = 0.26 (hexanes: ethyl acetate = 5:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58 (d, *J* = 8.3 Hz, 1H), 7.47 (dd, *J* = 7.3, 0.8 Hz, 1H), 7.36 (d, *J* = 3.3 Hz, 1H), 7.22 (dd, *J* = 8.3, 7.4 Hz, 1H), 6.77 – 6.70 (m, 1H), 6.03 (ddd, *J* = 17.1, 10.4, 5.1 Hz, 1H), 5.22 (dd, *J* = 10.5, 1.6 Hz, 1H), 5.14 – 5.03 (m, 2H), 1.68 (d, *J* = 6.9 Hz, 3H).

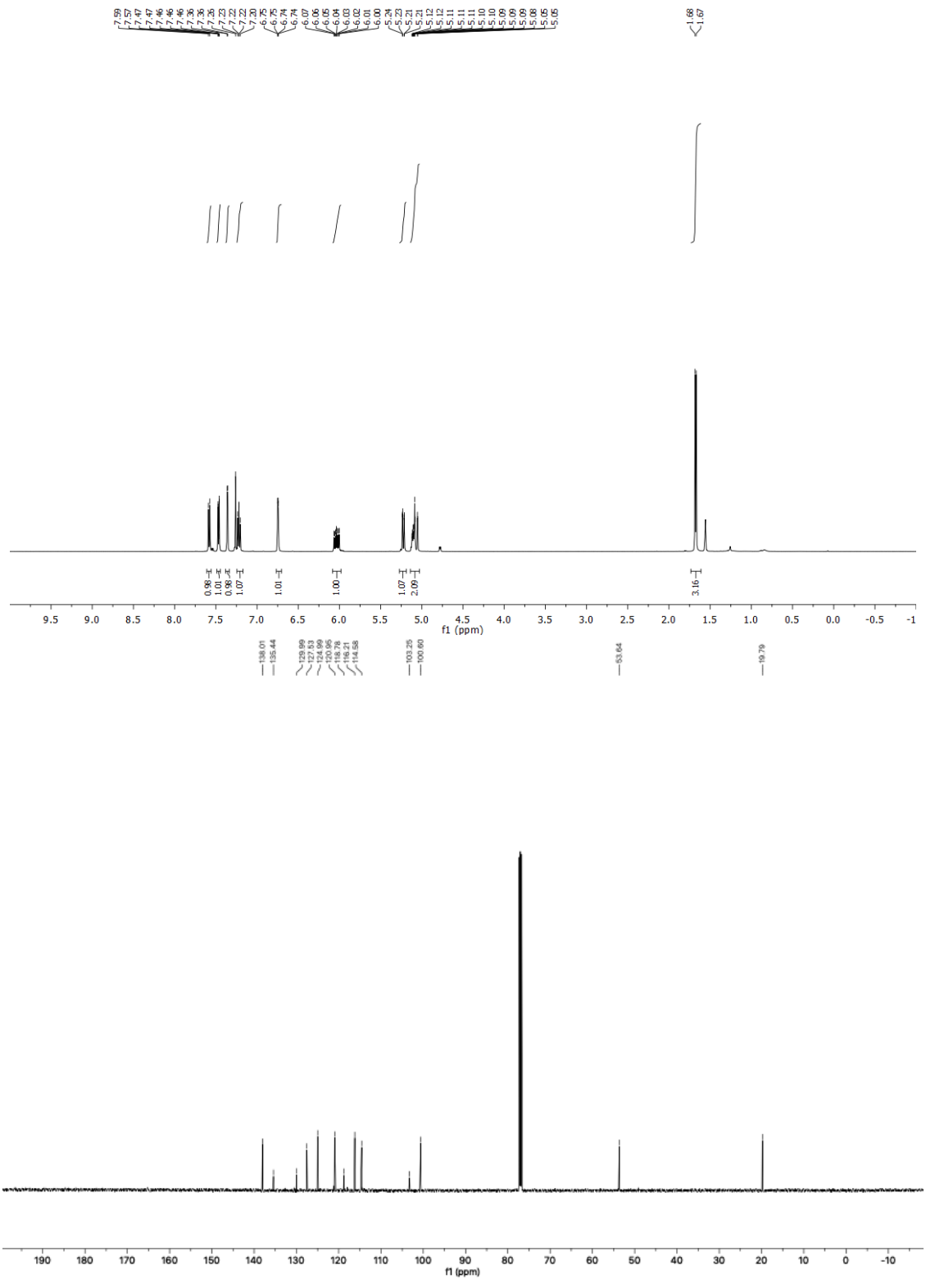
^{13}C NMR (125 MHz, $CDCl_3$): δ 138.0, 135.4, 130.0, 127.5, 125.0, 121.0, 118.8, 116.2, 114.6, 103.3, 100.6, 53.6, 19.8.

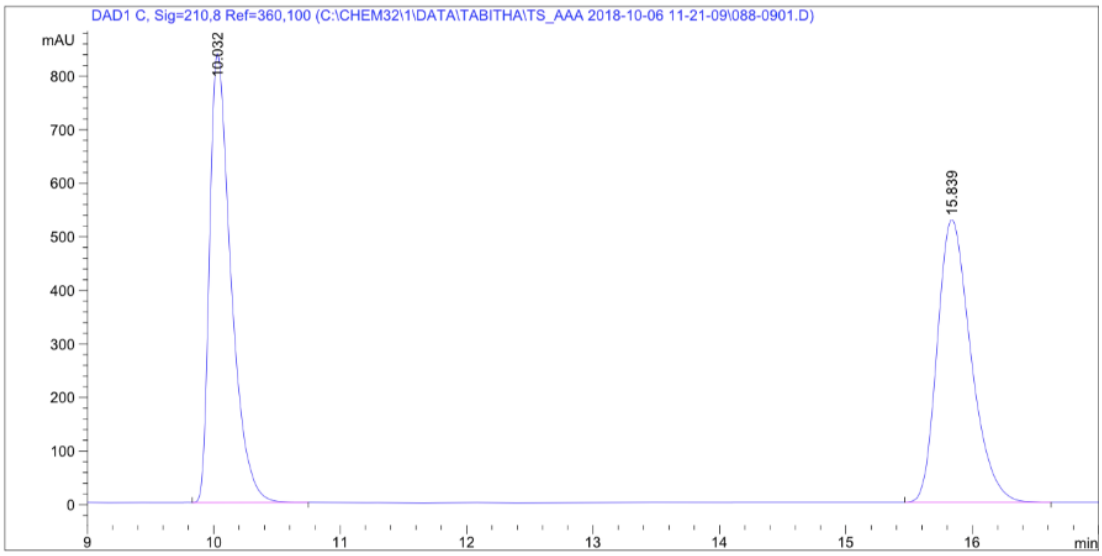
HRMS (ESI): Calculated for $C_{13}H_{12}N_2$ [M+H$^+$] = 219.0893, Found 219.0900.

FTIR (neat): 2983, 2360, 2342, 2222, 1435, 1274, 1260, 750 cm^{-1}.

$[\alpha]_D^{28}$= –9.0 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 210 nm), *ee* = 91%.

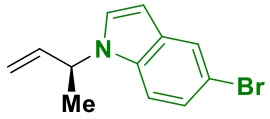

f1 (ppm)
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.032	BB	0.1771	9854.00098	838.59320	50.2308
2	15.839	BB	0.2837	9763.45801	528.09882	49.7692

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.026	MM	0.1981	1.06365e4	894.94000	95.4132
2	15.960	MM	0.2969	511.33237	28.70204	4.5868

***(S)*-5-bromo-1-(but-3-en-2-yl)-1*H*-indole (6.3f)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (172.5 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (50 ºC, 24 hr). The title compound was obtained in 79% yield (87.0 mg, 0.35 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1).

TLC (SiO_2) R_f = 0.35 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.27 (d, *J* = 9.0 Hz, 1H), 7.25 – 7.14 (m, 2H), 6.47 (dd, *J* = 3.3, 0.8 Hz, 1H), 6.02 (ddd, *J* = 17.3, 10.4, 4.9 Hz, 1H), 5.19 (ddd, *J* = 10.3, 1.6, 0.8 Hz, 1H), 5.09 – 4.98 (m, 2H), 1.64 (d, *J* = 6.9 Hz, 3H).

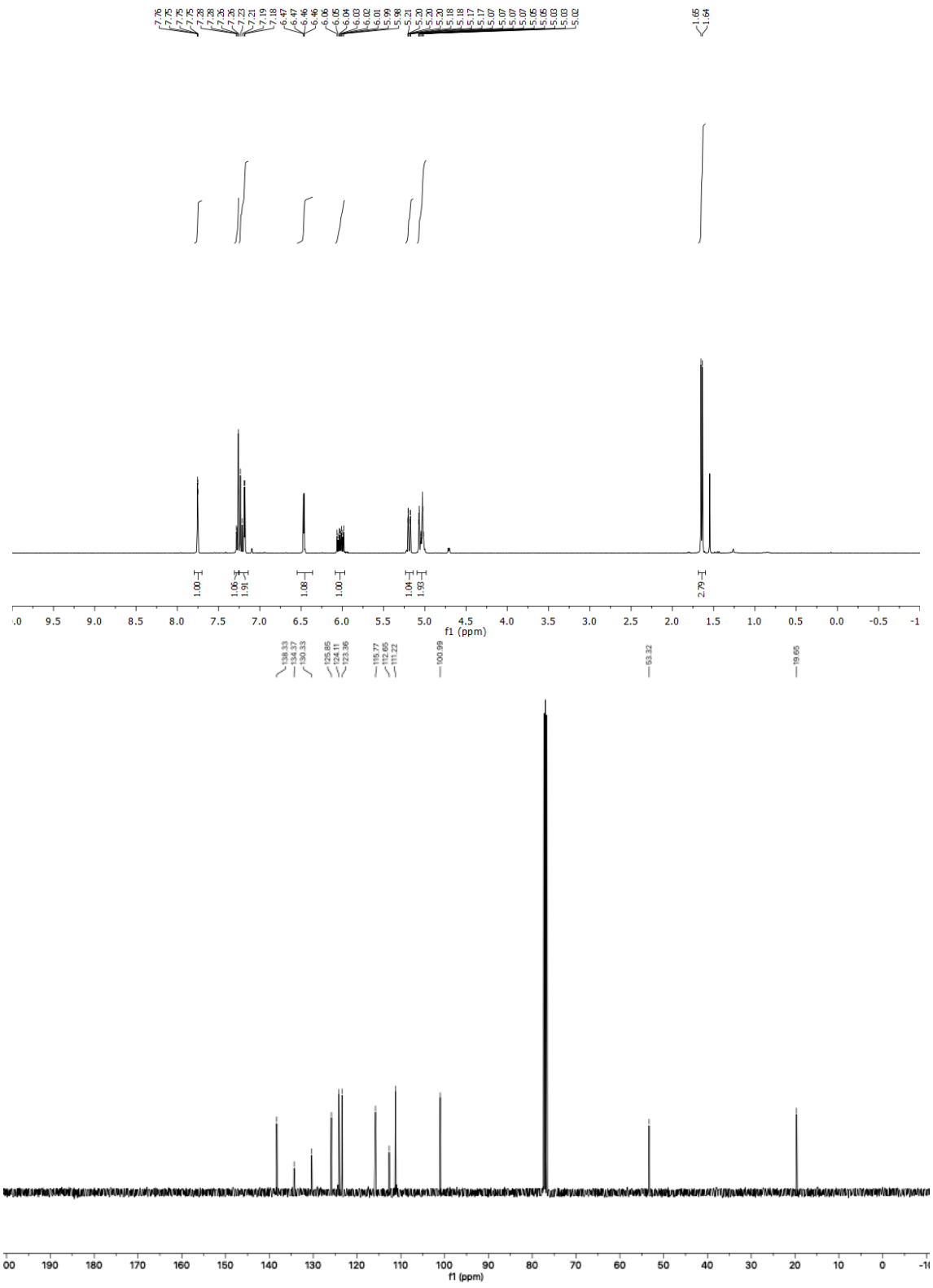
^{13}C NMR (125 MHz, $CDCl_3$): δ 138.3, 134.4, 130.3, 125.9, 124.1, 123.4, 115.8, 112.7, 111.2, 101.0, 53.3, 19.7.

HRMS (ESI): Calculated for $C_{12}H_{12}BrN$ [M+H$^+$] = 250.0226, Found 250.0228.

FTIR (neat): 2982, 2370, 2342, 1462, 1275, 1262, 1208, 751 cm^{-1}.

$[\alpha]_D^{28}$= –18.5 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 92%.


7.76
7.75
7.75
7.75
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6.46
6.06
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6.04
6.03
6.02
6.01
5.99
5.98
5.21
5.20
5.20
5.20
5.18
5.18
5.17
5.17
5.07
5.07
5.07
5.05
5.05
5.03
5.02
1.65
1.64
1.00
1.06
1.91
1.00
1.00
1.04
1.93
2.79
f1 (ppm)
158.33
154.37
150.33
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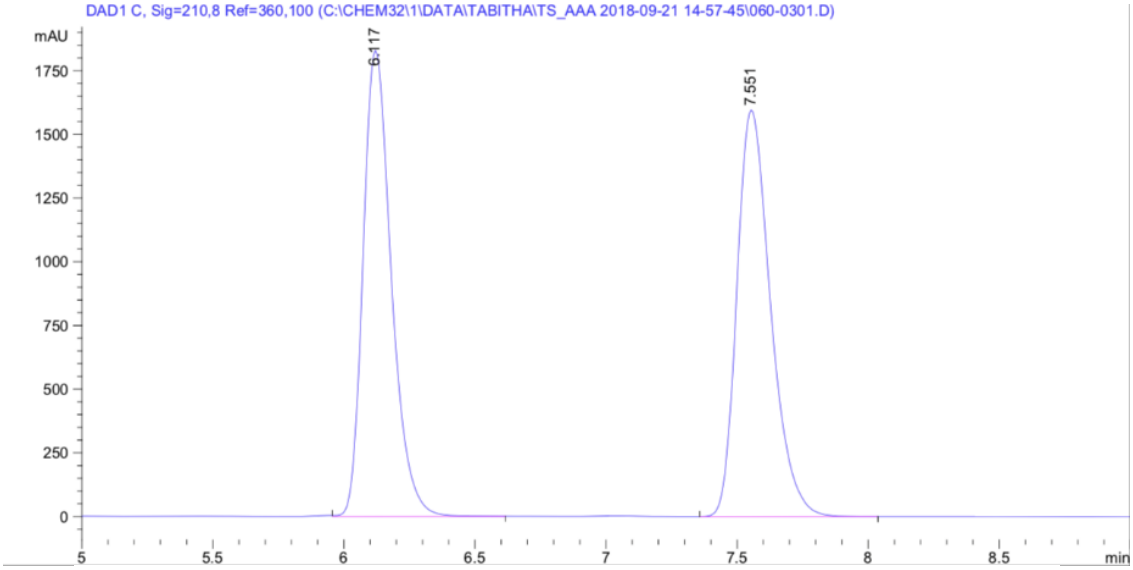
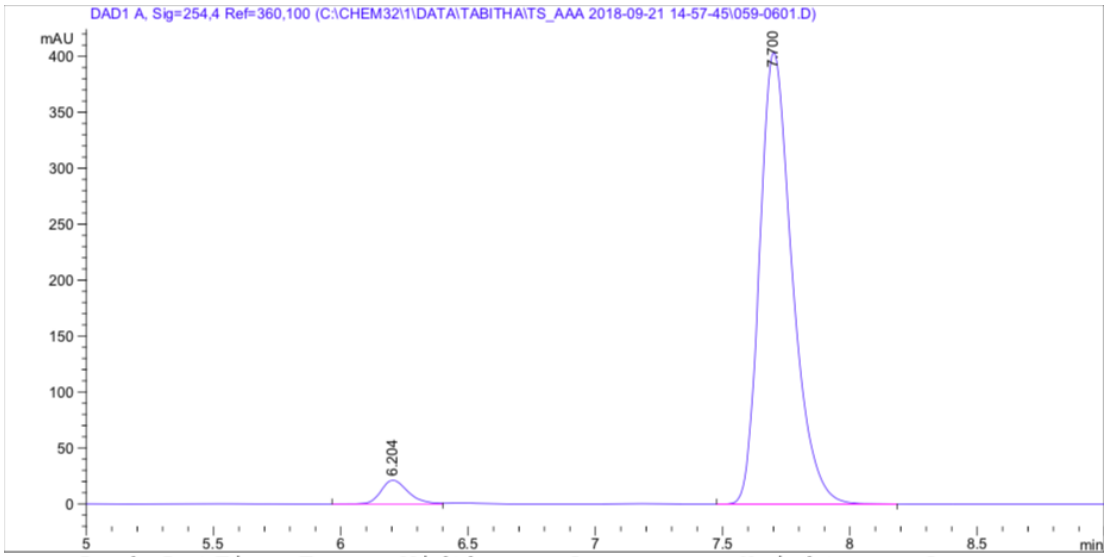
115.77
112.65
111.22
100.99
53.32
19.65
f1 (ppm)

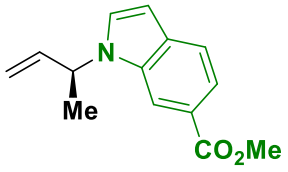


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.117	VB	0.1174	1.36998e4	1829.67810	49.0333
2	7.551	BB	0.1381	1.42400e4	1596.41650	50.9667



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.204	BV	0.1147	159.21573	21.41434	4.2491
2	7.700	VB	0.1376	3587.79883	404.17206	95.7509

Methyl *(S)*-1-(but-3-en-2-yl)-1*H*-indole-6-carboxylate (6.3g)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (154.2 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ºC, 24 hr). The title compound was obtained in 82% yield (82.0 mg, 0.36 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1).

TLC (SiO_2) R_f = 0.38 (hexanes: ethyl acetate = 5:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (s, 1H), 7.80 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.34 (d, *J* = 3.2 Hz, 1H), 6.59 – 6.53 (m, 1H), 6.07 (ddd, *J* = 17.2, 10.4, 5.0 Hz, 1H), 5.19 (ddt, *J* = 13.9, 6.9, 1.6 Hz, 2H), 5.14 – 5.05 (m, 1H), 3.94 (s, 3H), 1.67 (d, *J* = 6.9 Hz, 3H).

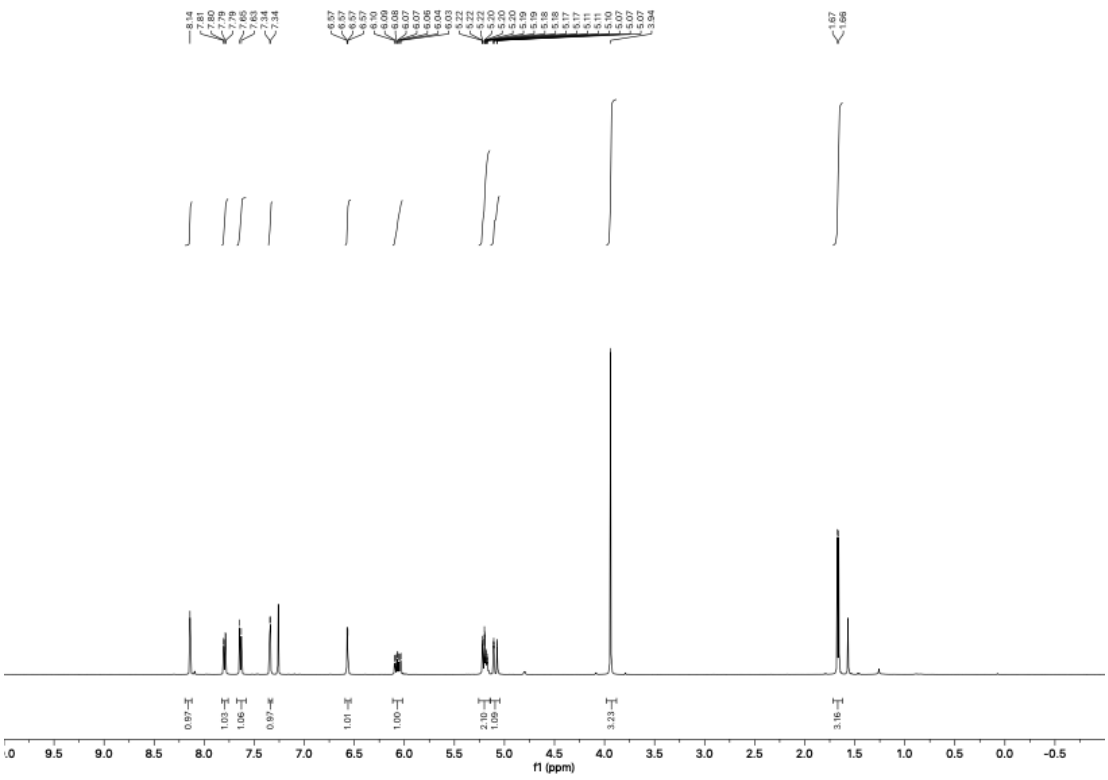
^{13}C NMR (125 MHz, $CDCl_3$): δ 168.3, 138.3, 135.1, 132.3, 128.0, 123.0, 120.5, 120.4, 115.9, 112.1, 101.9, 53.1, 51.9, 19.9.

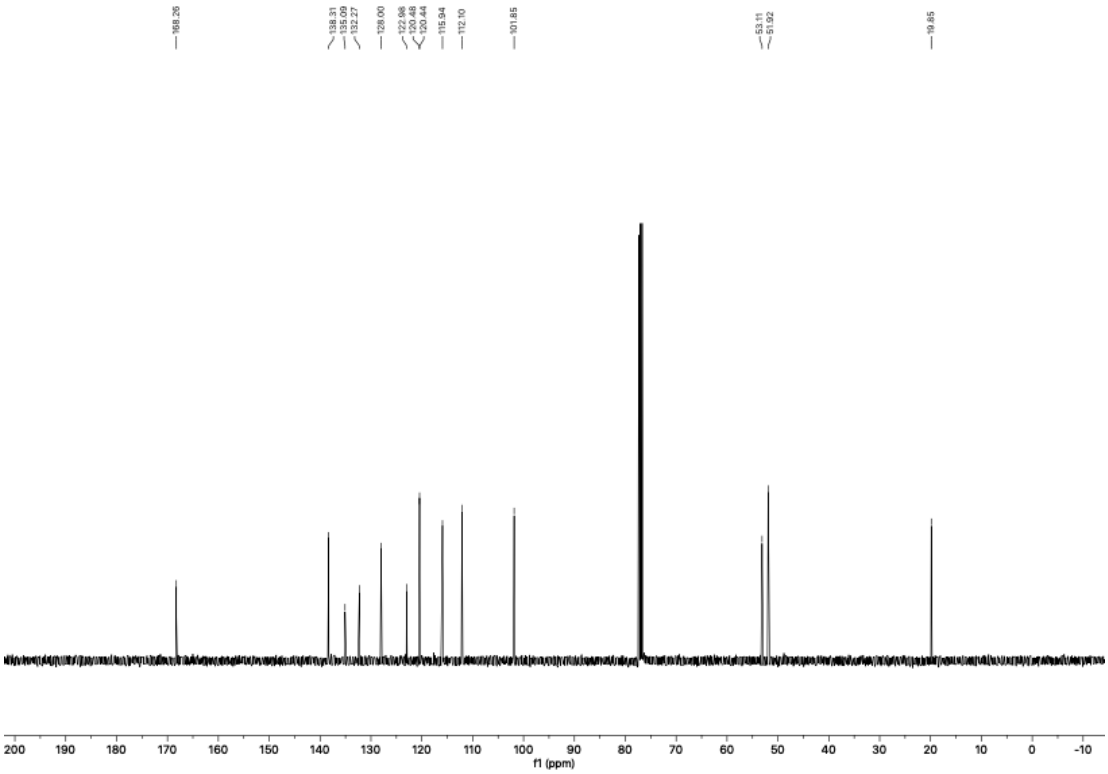
HRMS (ESI): Calculated for $C_{14}H_{15}NO_2$ [M+H$^+$] = 252.0995, Found 252.1003.

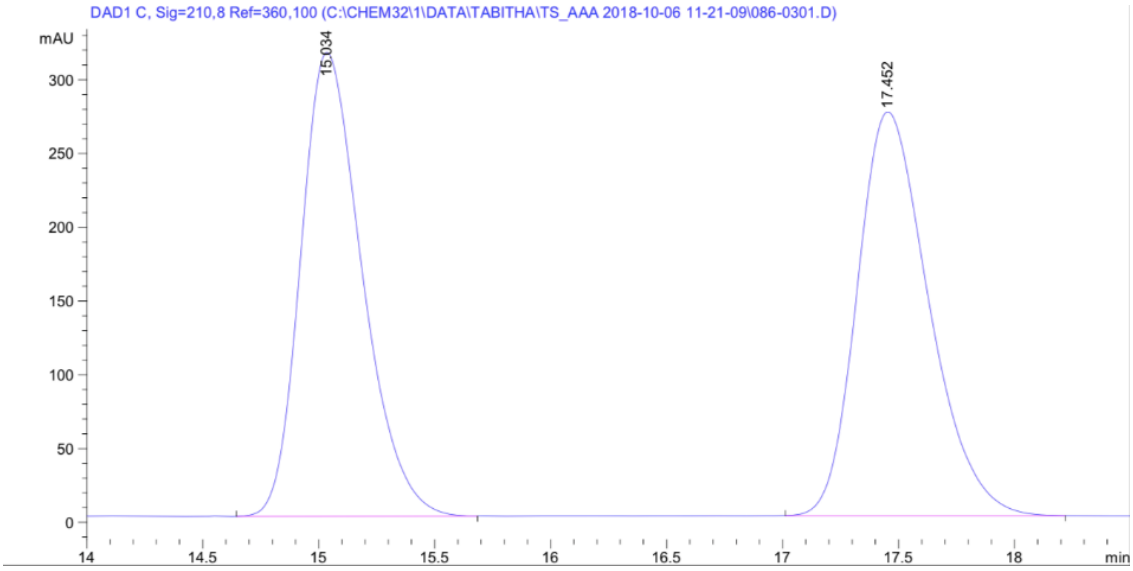
FTIR (neat): 2983, 2950, 2359, 2342, 1708, 1242, 750, cm^{-1}.

$[\alpha]_D^{28}$ = –46.3 (*c* 1.0, $CHCl_3$).

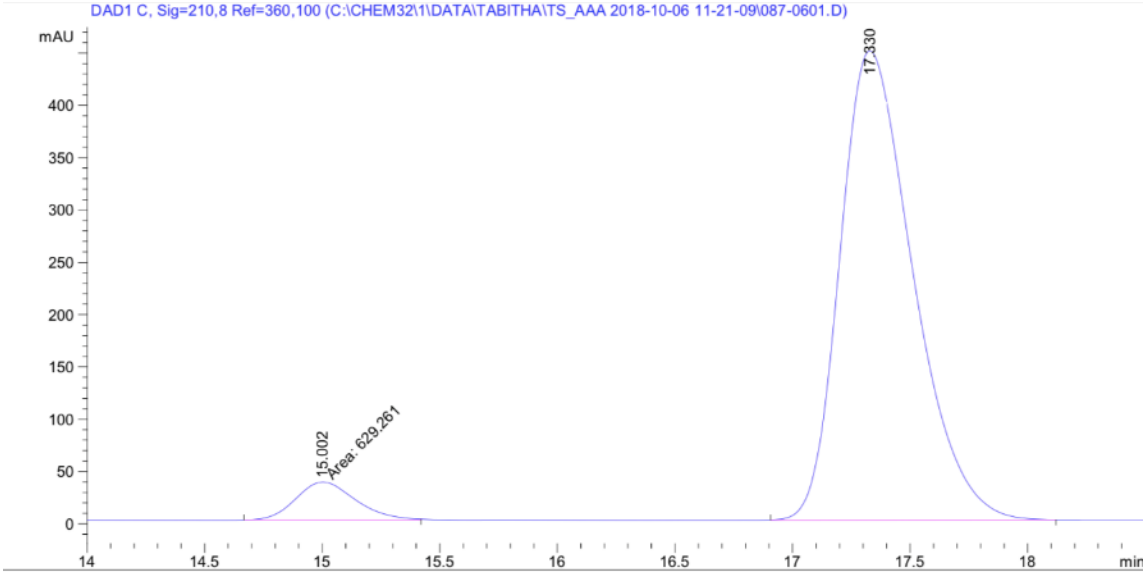
HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 210 nm), *ee* = 88%.


8.14
7.81
7.80
7.79
7.79
7.65
7.63
7.34
7.34
6.57
6.57
6.57
6.57
6.10
6.09
6.08
6.07
6.07
6.06
6.04
6.03
5.22
5.22
5.21
5.20
5.20
5.19
5.19
5.18
5.18
5.17
5.17
5.11
5.11
5.10
5.07
5.07
3.94
1.67
1.66
0.97
1.03
1.06
0.97
1.01
1.00
2.10
1.09
3.23
3.16
f1 (ppm)


168.26
138.31
135.09
132.27
126.00
122.98
120.48
120.44
115.94
112.10
101.85
53.11
51.92
19.85
f1 (ppm)

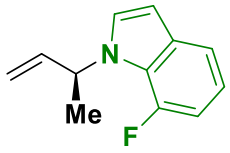


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.034	BB	0.2826	5786.02490	314.52017	49.5490
2	17.452	BB	0.3309	5891.36279	273.91739	50.4510



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.002	MM	0.2909	629.26111	36.04988	6.1074
2	17.330	BB	0.3296	9674.00879	448.64526	93.8926

***(S)*-1-(but-3-en-2-yl)-7-fluoro-1*H*-indole (6.3h)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (118.9 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ºC, 24 hr). The title compound was obtained in 92% yield (77.0 mg, 0.41 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1).

TLC (SiO_2) R_f = 0.53 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 (d, *J* = 7.9 Hz, 1H), 7.19 (d, *J* = 3.2 Hz, 1H), 6.99 (td, *J* = 7.8, 4.4 Hz, 1H), 6.91 – 6.84 (m, 1H), 6.57 – 6.49 (m, 1H), 6.16 – 6.07 (m, 1H), 5.48 (tt, *J* = 5.3, 1.6 Hz, 1H), 5.18 (d, *J* = 10.4 Hz, 1H), 5.08 (d, *J* = 18.6 Hz, 1H), 1.64 (d, *J* = 7.9 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 151.1, 149.2, 139.2, 132.5, 125.7, 123.8, 119.6, 116.7, 115.4, 107.4, 102.4, 54.9, 54.9, 20.4.

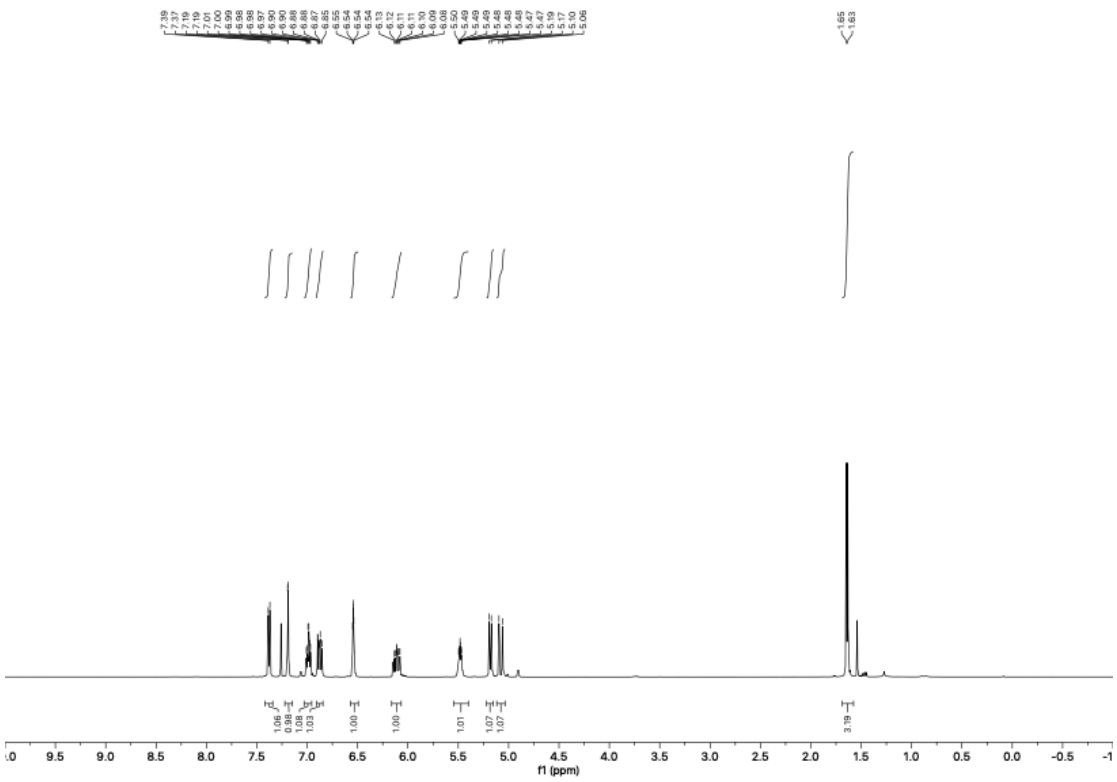
^{19}F NMR (376 MHz, $CDCl_3$): δ = -134.1.

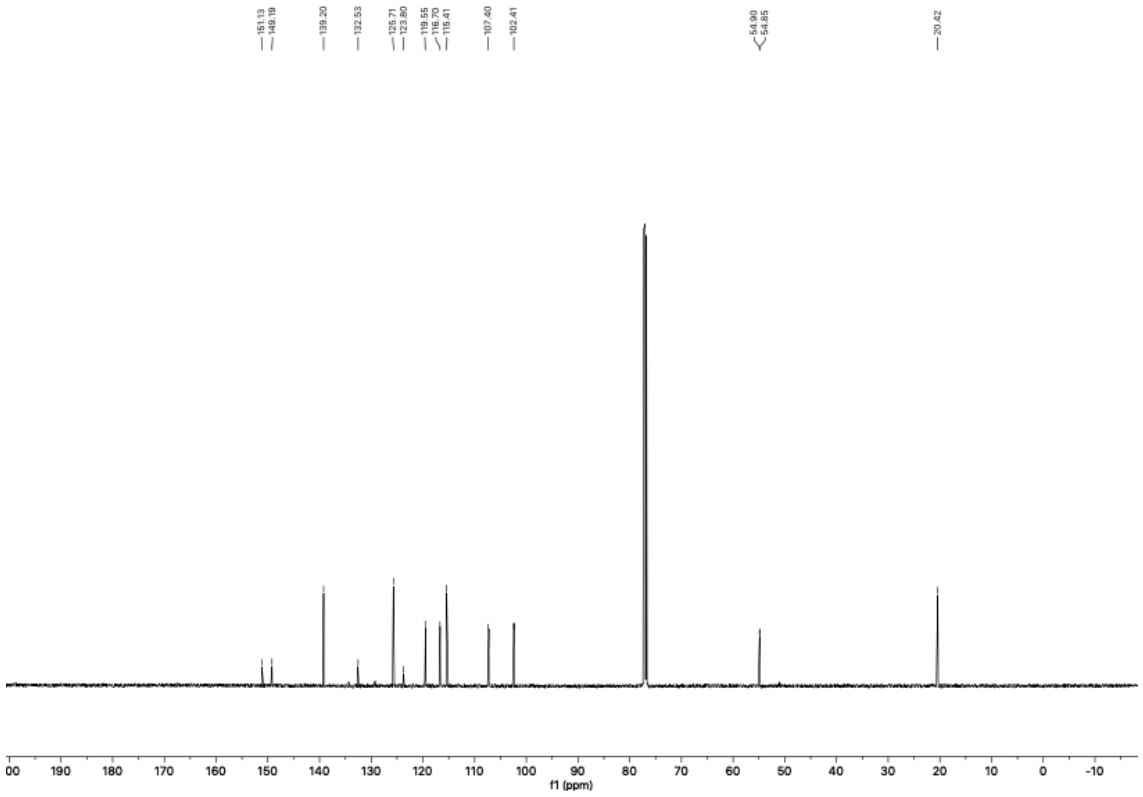
HRMS (ESI): Calculated for $C_{12}H_{12}FN$ $[M+H^+]$ = 190.1027, Found 190.1026.

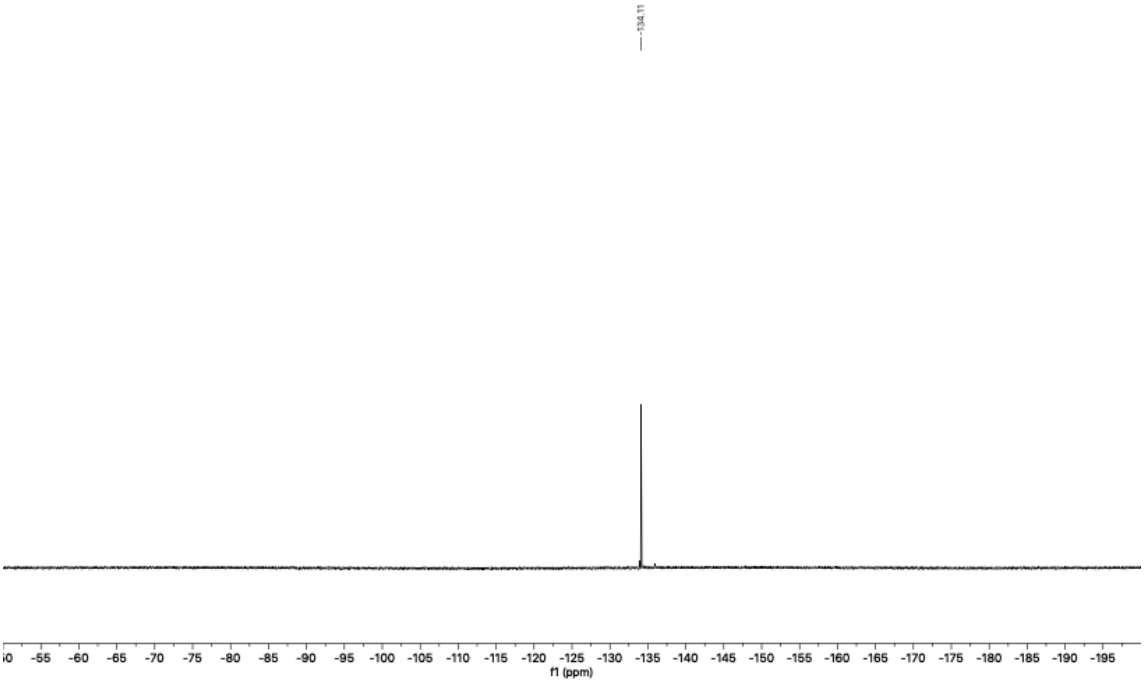
FTIR (neat): 2984, 2360, 2342, 1275, 1261, 1236, 750 cm^{-1}.

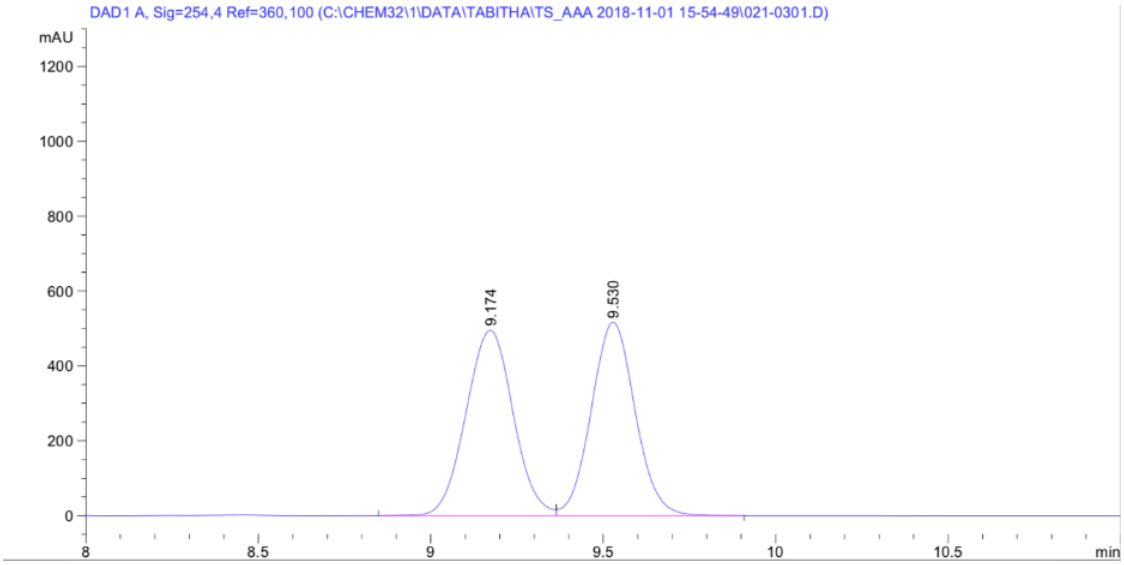
$[\alpha]_D^{28}$= –37.8 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 92%.

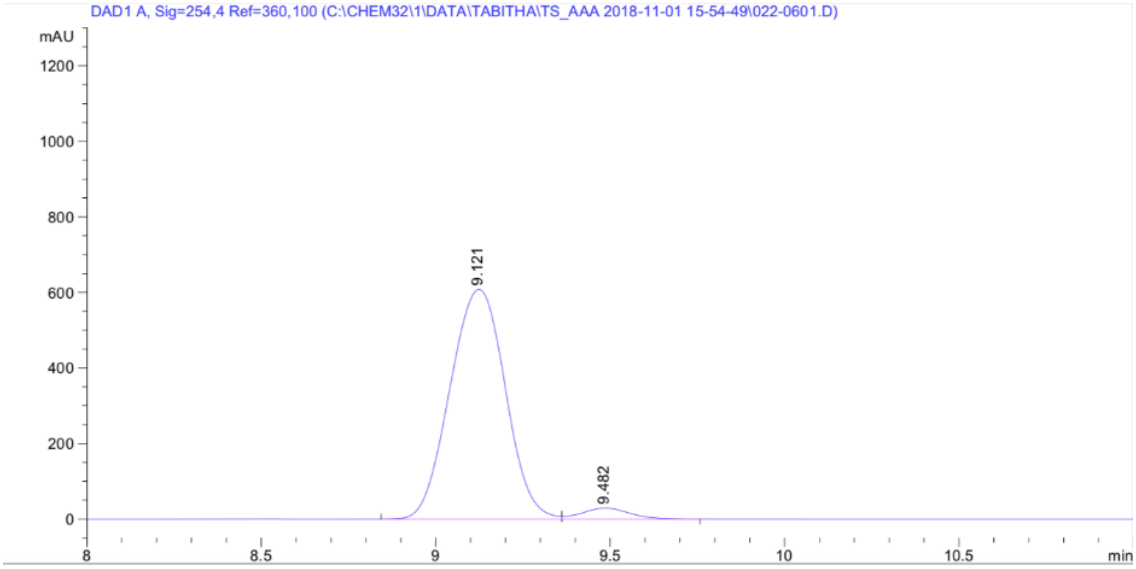

7.39
7.37
7.19
7.01
7.00
6.99
6.98
6.97
6.90
6.88
6.88
6.87
6.85
6.55
6.54
6.54
6.54
6.13
6.12
6.11
6.11
6.10
6.09
6.08
5.50
5.49
5.49
5.48
5.48
5.48
5.47
5.47
5.19
5.17
5.10
5.06
1.65
1.63
1.06
0.98
1.08
1.03
1.00
1.00
1.01
1.07
1.07
3.19
f1 (ppm)


151.13
149.19
139.20
132.53
125.71
123.80
119.55
116.70
116.41
107.40
102.41
54.90
54.85
20.42
f1 (ppm)


-134.11
f1 (ppm)

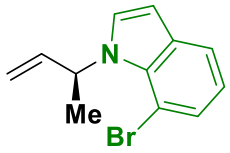


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.174	BV	0.1489	4715.25830	495.92075	50.7873
2	9.530	VB	0.1371	4569.06006	516.92603	49.2127



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.121	BV	0.1764	6696.99414	608.50061	96.0720
2	9.482	VB	0.1432	273.80969	29.25745	3.9280

***(S)*-7-bromo-1-(but-3-en-2-yl)-1*H*-indole (6.3i)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (177.5 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 77% yield (84.7 mg, 0.34 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 40:1).

TLC (SiO_2) R_f = 0.60 (hexanes: ethyl acetate = 5:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.36 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.23 (d, *J* = 3.4 Hz, 1H), 6.93 (t, *J* = 7.7 Hz, 1H), 6.53 (d, *J* = 3.3 Hz, 1H), 6.36 (ddt, *J* = 6.6, 4.2, 2.0 Hz, 1H), 6.14 (ddd, *J* = 17.3, 10.5, 4.4 Hz, 1H), 5.22 (ddd, *J* = 10.5, 1.8, 0.9 Hz, 1H), 5.06 (ddd, *J* = 17.3, 2.0, 1.0 Hz, 1H), 1.61 (d, *J* = 6.8 Hz, 3H).

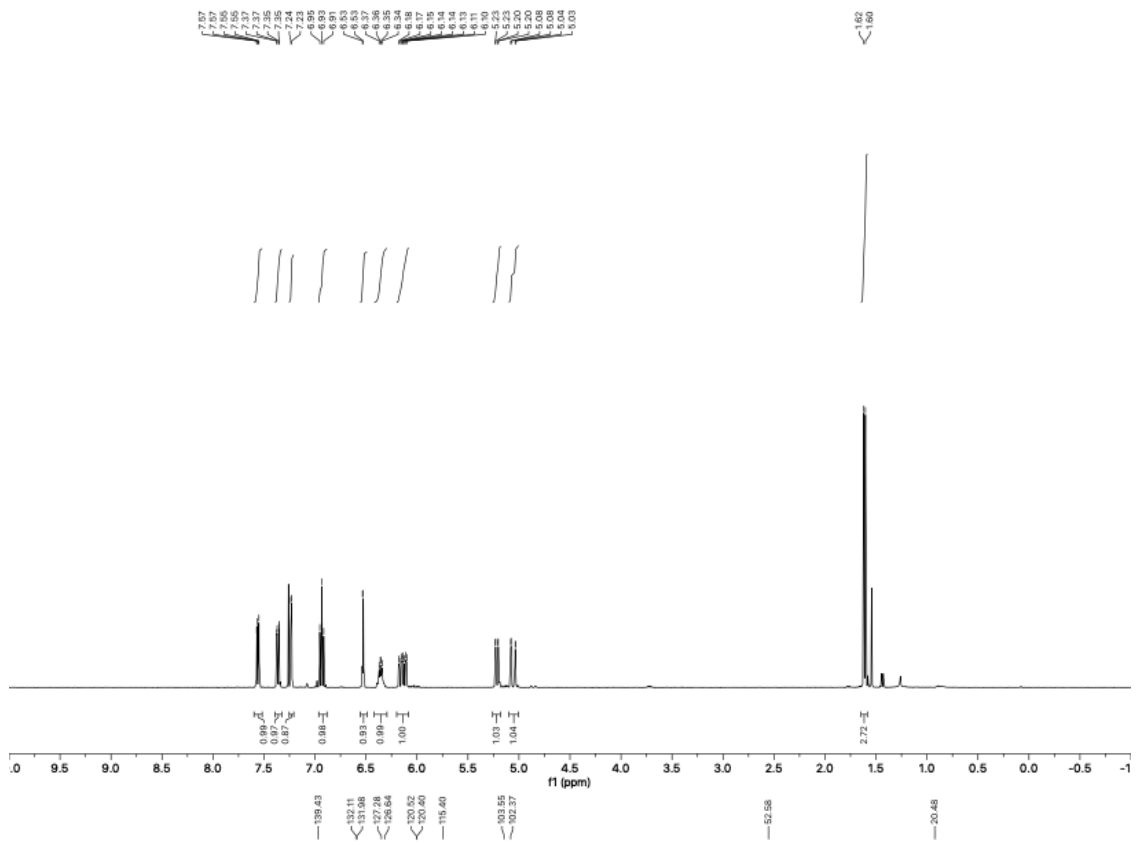
^{13}C NMR (125 MHz, $CDCl_3$): δ 139.4, 132.1, 132.0, 127.3, 126.6, 120.5, 120.4, 115.4, 103.6, 102.4, 52.6, 20.5.

HRMS (ESI): Calculated for $C_{12}H_{12}BrN$ [M+H$^+$] = 250.0226, Found 250.0223.

FTIR (neat): 2980, 2360, 2342, 1333, 1301, 751, 718 cm^{-1}.

$[\alpha]_D^{28}$ = –7.3 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 88%.


7.57
7.57
7.55
7.55
7.37
7.37
7.35
7.35
7.24
7.23
6.95
6.93
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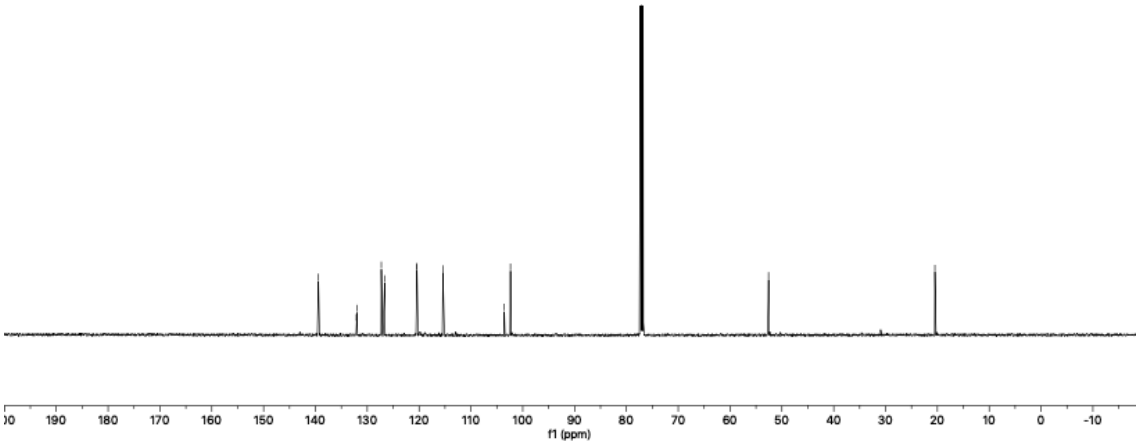
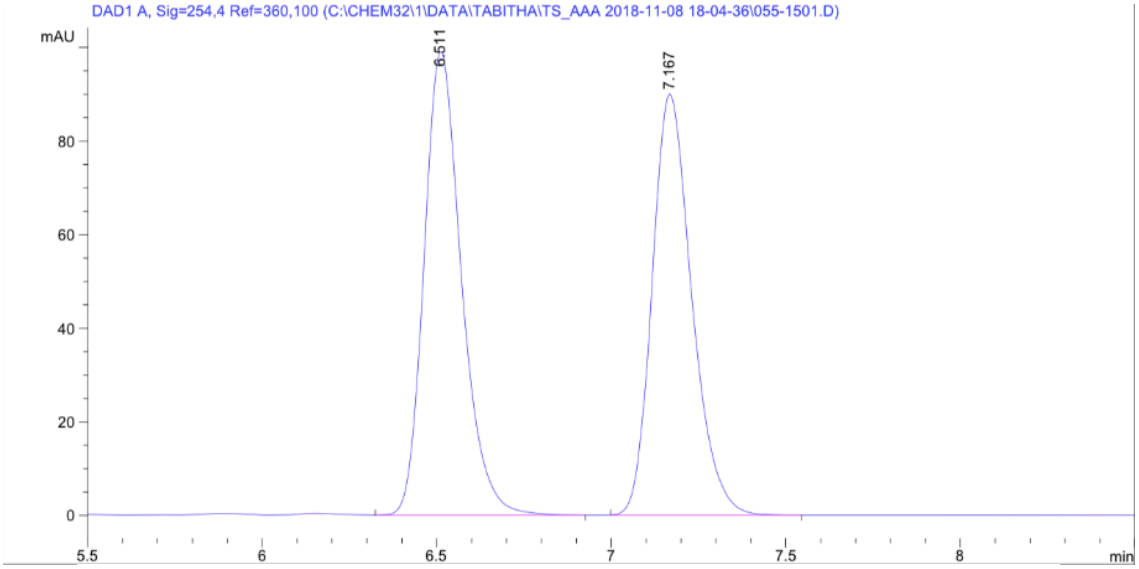
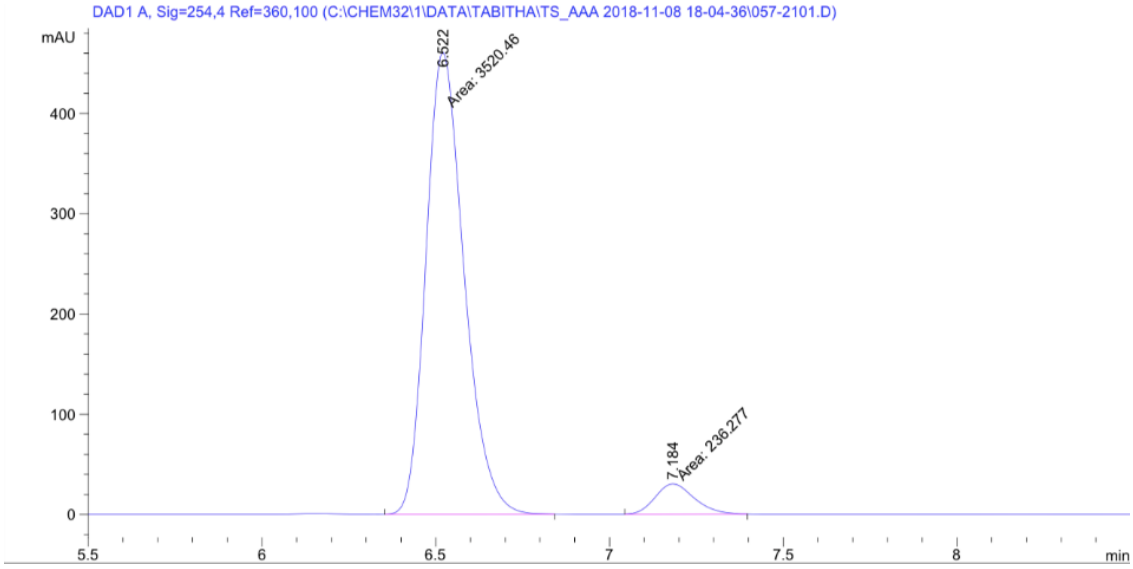
6.53
6.53
6.37
6.36
6.35
6.34
6.18
6.17
6.15
6.14
6.14
6.13
6.11
6.10
5.23
5.23
5.20
5.20
5.08
5.08
5.04
5.03
1.62
1.60
0.99
0.97
0.87
0.98
0.93
0.99
1.00
1.03
1.04
2.72
f1 (ppm)
139.43
132.11
131.98
127.28
126.64
120.52
120.40
115.40
103.55
102.37
52.58
20.48


f1 (ppm)

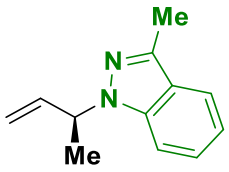


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.511	VB	0.1149	739.47772	99.22390	51.0136
2	7.167	BB	0.1220	710.09106	90.08806	48.9864



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.522	MM	0.1271	3520.45825	461.63266	93.7106
2	7.184	MM	0.1300	236.27725	30.28531	6.2894

***(S)*-1-(but-3-en-2-yl)-3-methyl-1*H*-indazole (6.3j)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (116.3 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ºC, 24 hr). The title compound was obtained in 67% yield (55.9 mg, 0.30 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 40:1).

TLC (SiO_2) R_f = 0.19 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.38 (dt, *J* = 8.5, 1.0 Hz, 1H), 7.33 (ddd, *J* = 8.4, 6.7, 1.1 Hz, 1H), 7.11 (ddd, *J* = 7.9, 6.7, 1.0 Hz, 1H), 6.20 – 6.06 (m, 1H), 5.25 – 5.14 (m, 2H), 5.13 (dt, *J* = 17.2, 1.3 Hz, 1H), 2.59 (s, 3H), 1.72 (d, *J* = 6.9 Hz, 3H).

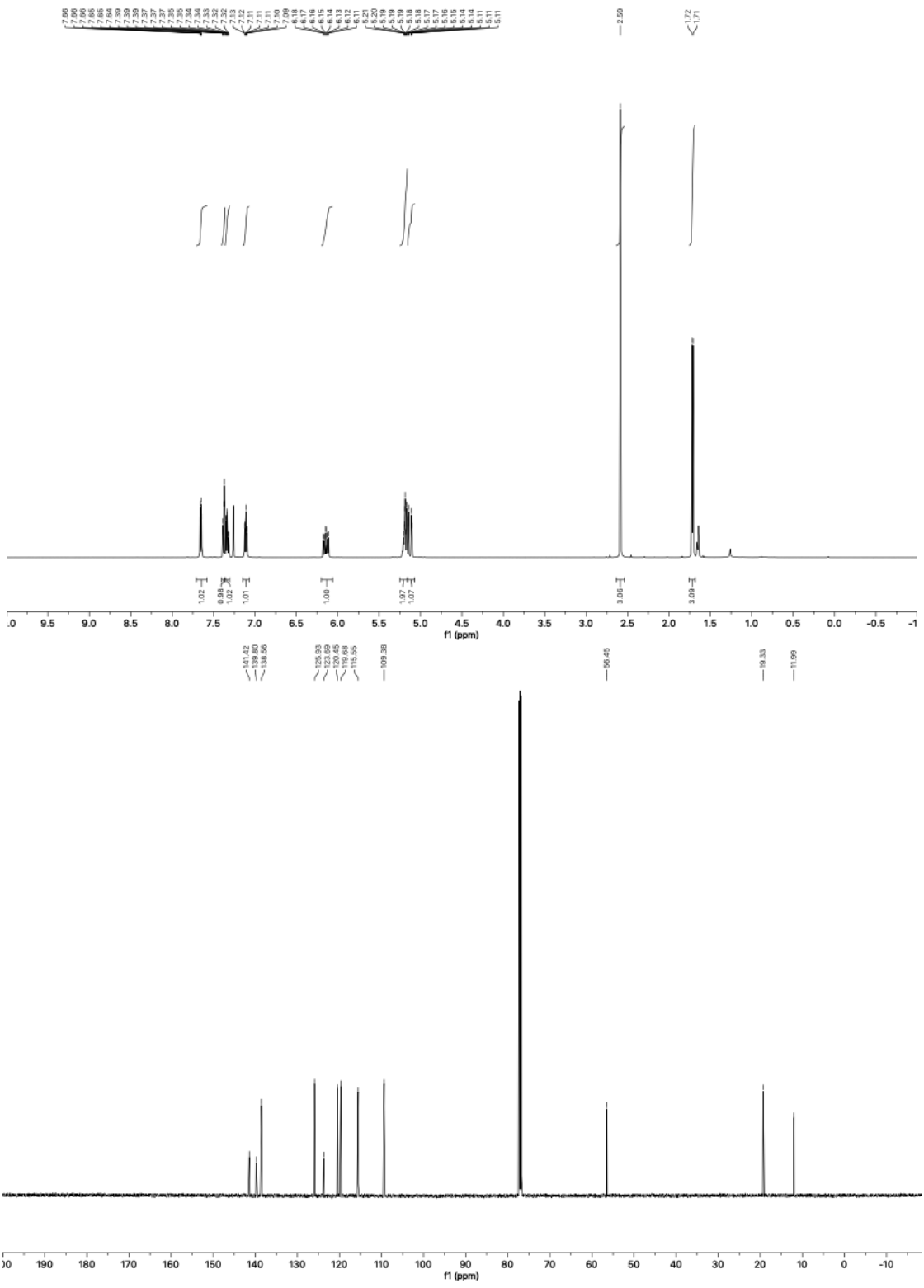
^{13}C NMR (125 MHz, $CDCl_3$): δ 141.4, 139.8, 138.6, 125.9, 123.7, 120.5, 119.7, 115.6, 109.4, 56.5, 19.3, 12.0.

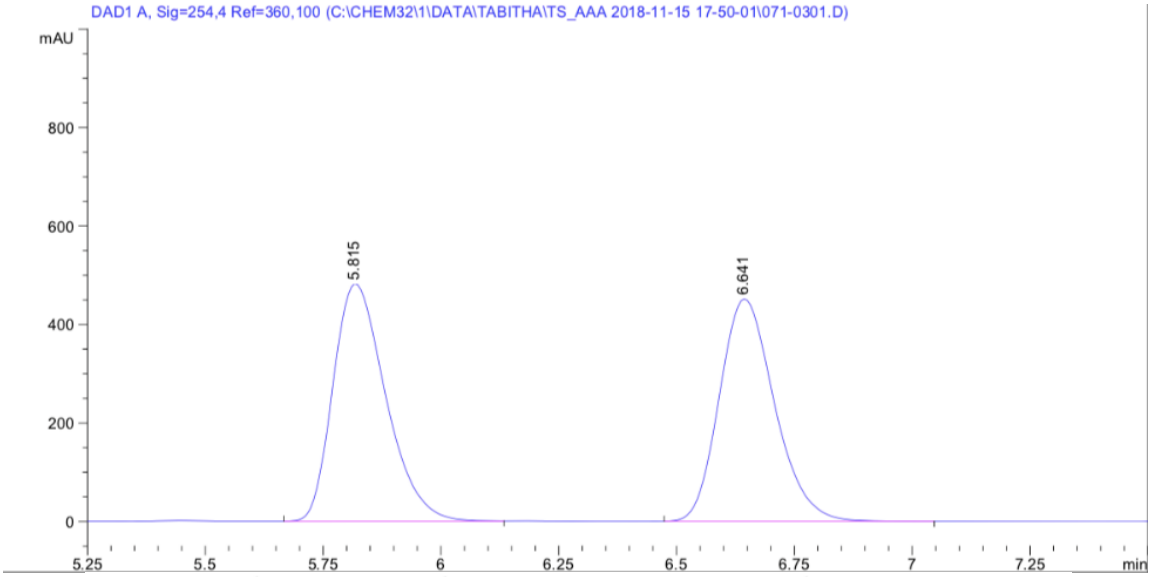
HRMS (ESI): Calculated for $C_{12}H_{14}N_2$ [M+H$^+$] = 187.1230, Found 187.1233.

FTIR (neat): 2360, 2342, 1276, 1261, 764, 750 cm^{-1}.

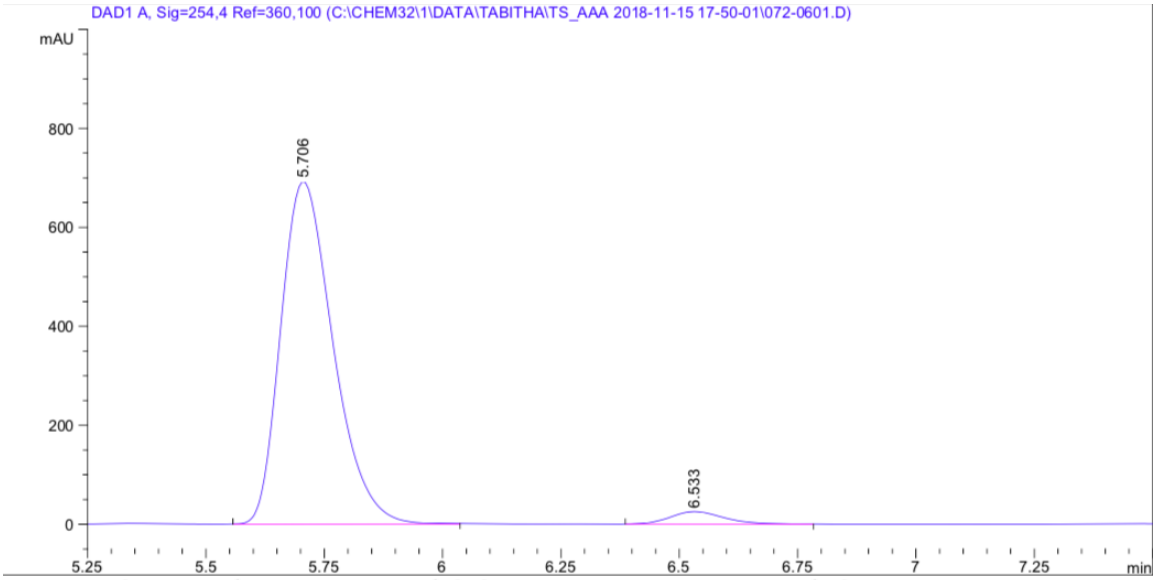
$[\alpha]_D^{28}$= –10.2 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 93%.


f1 (ppm)
f1 (ppm)

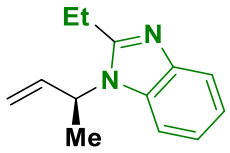


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.816	VV	0.1211	3773.56641	483.24493	50.5964
2	6.641	VB	0.1251	3684.60156	452.22260	49.4036



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.706	VV	0.1197	5332.67236	693.30334	96.3522
2	6.533	VB	0.1231	201.89259	25.29173	3.6478

***(S)*-1-(but-3-en-2-yl)-2-ethyl-1H-benzo[d]imidazole (6.3k)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the benzimidazole (128.6 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (60 ^{o}C, 24 hr). The title compound was obtained in 85% yield (74.9 mg, 0.37 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 2:1).

TLC (SiO_2) R_f = 0.26 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.73 (dt, *J* = 8.0, 0.9 Hz, 1H), 7.37 (dt, *J* = 7.9, 0.9 Hz, 1H), 7.18 (dddd, *J* = 22.6, 8.4, 7.2, 1.2 Hz, 2H), 6.14 (ddd, *J* = 17.3, 10.6, 4.0 Hz, 1H), 5.30 (ddd, *J* = 10.5, 2.2, 0.7 Hz, 1H), 5.18 (ddd, *J* = 17.3, 2.2, 0.7 Hz, 1H), 5.11 (ttd, *J* = 7.1, 4.7, 2.0 Hz, 1H), 2.92 (qd, *J* = 7.5, 1.3 Hz, 2H), 1.70 (d, *J* = 7.1 Hz, 3H), 1.45 (t, *J* = 7.5 Hz, 3H).

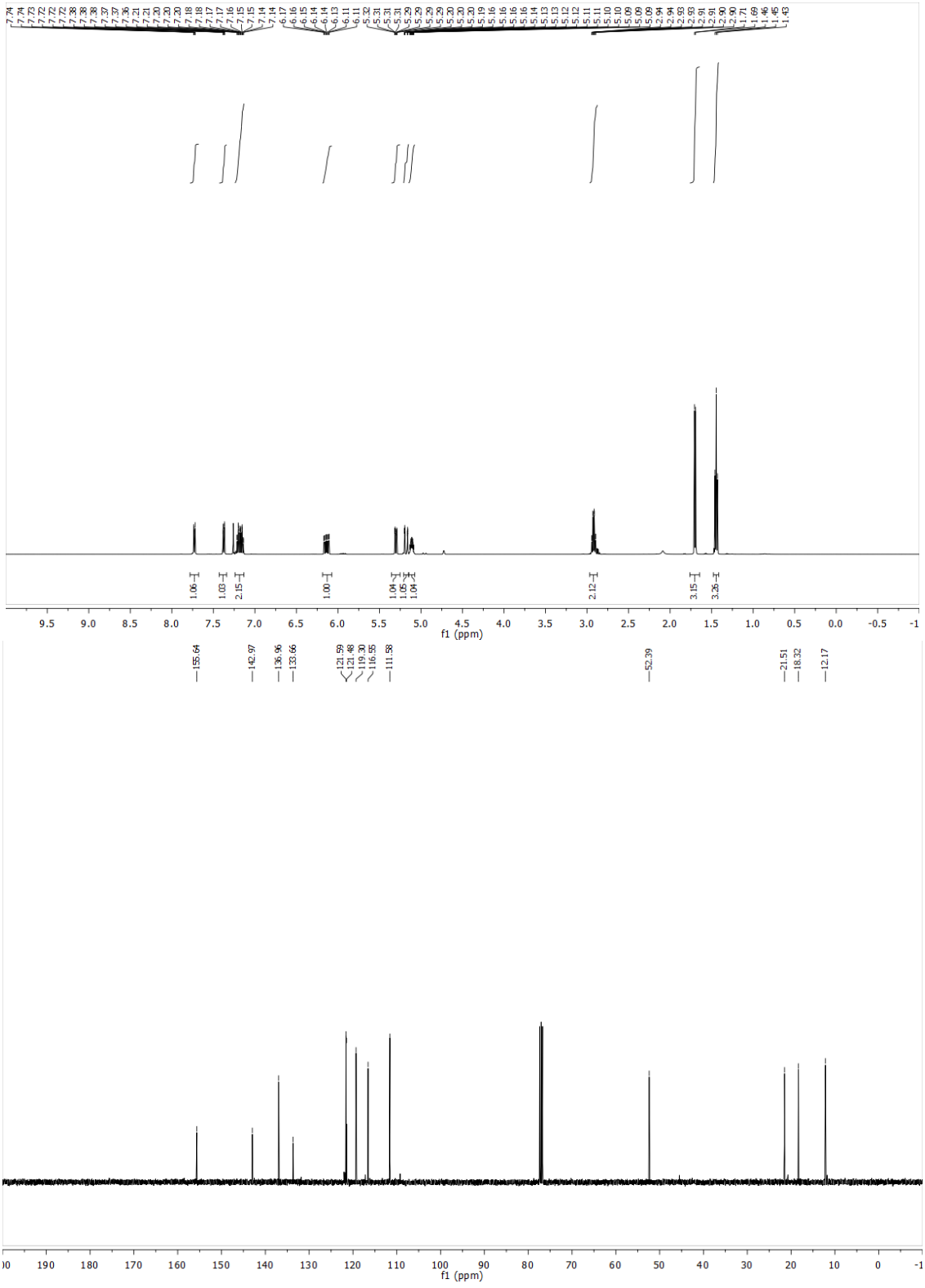
^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 143.0, 137.0, 133.7, 121.6, 121.5, 119.3, 116.6, 111.6, 52.4, 21.5, 18.3, 12.2.

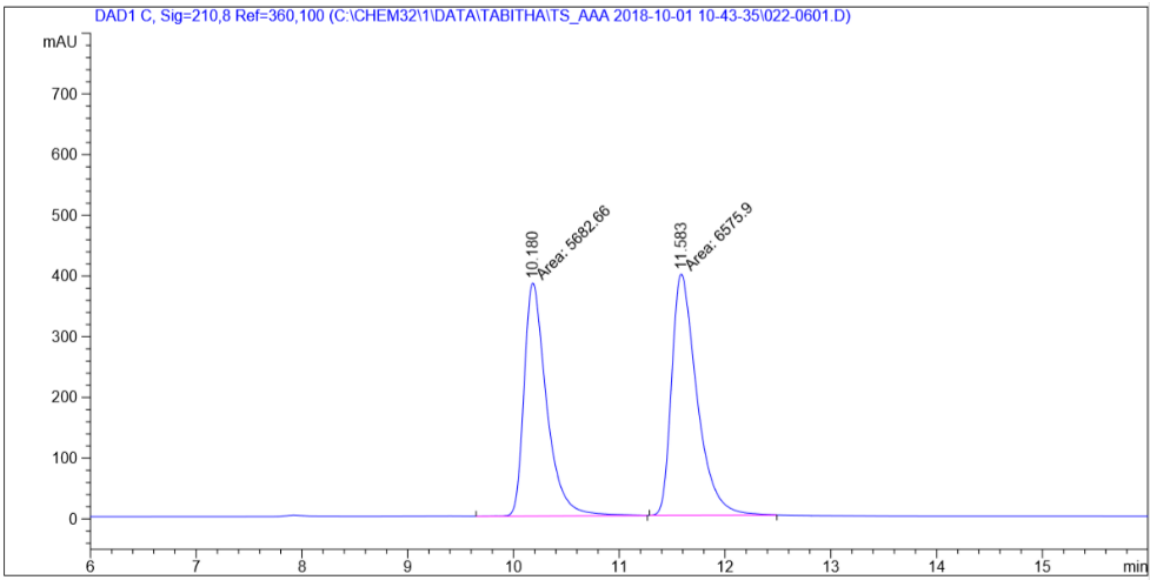
HRMS (ESI): Calculated for $C_{13}H_{16}N_2$ [M+H$^+$] = 201.1386, Found 201.1390.

FTIR (neat): 2978, 1517, 1457, 1402, 1277, 927, 745 cm^{-1}.

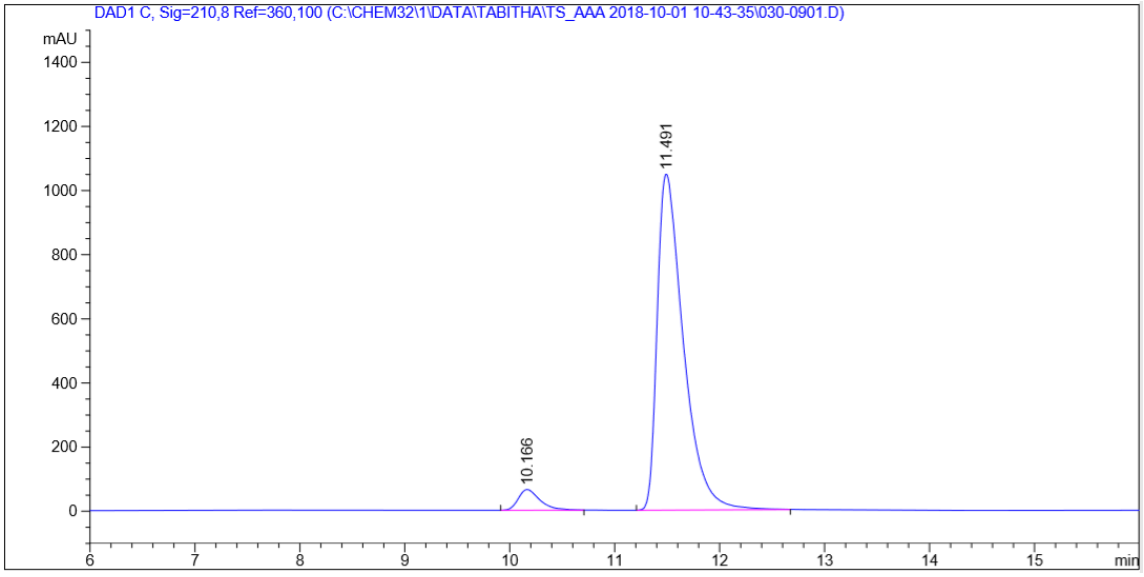
$[\alpha]_D^{28}$= +13.3 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm), *ee* = 90%.



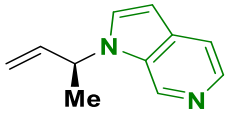


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.180	MM	0.2466	5682.65625	384.06061	46.3566
2	11.583	MM	0.2758	6575.90430	397.36398	53.6434



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.166	BB	0.2157	933.27924	64.91156	4.8935
2	11.491	BB	0.2619	1.81385e4	1048.09033	95.1065

***(S)*-1-(but-3-en-2-yl)-1*H*-pyrrolo[2,3-*c*]pyridine (6.3l)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (104.0 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ºC, 24 hr). The title compound was obtained in 71% yield (53.0 mg, 0.31 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.31 (hexanes: ethyl acetate = 1:4).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.80 (s, 1H), 8.23 (d, *J* = 5.5 Hz, 1H), 7.51 (dd, *J* = 5.5, 1.1 Hz, 1H), 7.32 (d, *J* = 3.2 Hz, 1H), 6.52 (d, *J* = 3.1 Hz, 1H), 6.12 – 6.01 (m, 1H), 5.26 – 5.20 (m, 1H), 5.17 (dd, *J* = 7.0, 5.2 Hz, 1H), 5.11 (dt, *J* = 17.2, 1.2 Hz, 1H), 1.69 (d, *J* = 7.0 Hz, 3H).

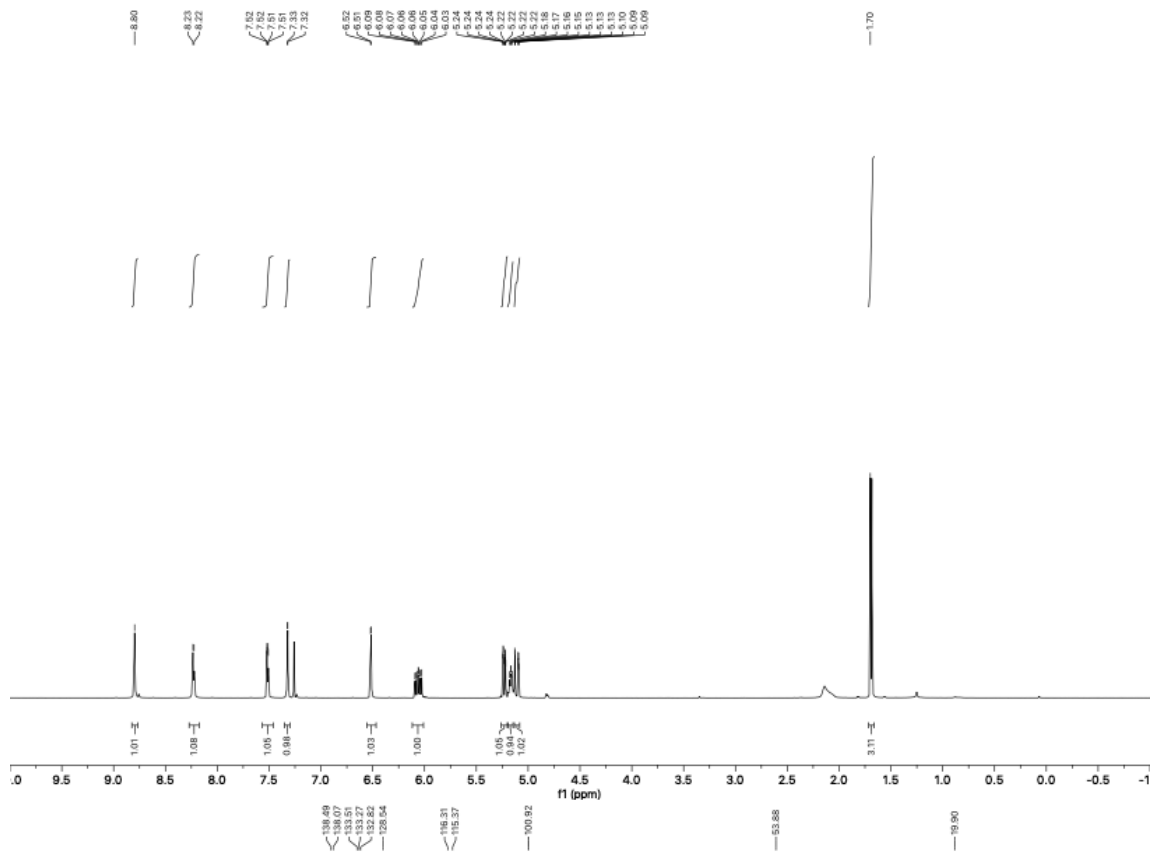
^{13}C NMR (125 MHz, $CDCl_3$): δ 138.5, 138.1, 133.5, 133.3, 132.8, 128.5, 116.3, 115.4, 100.9, 53.9, 19.9.

HRMS (ESI): Calculated for $C_{11}H_{12}N_2$ [M+H$^+$] = 173.1073, Found 173.1073.

FTIR (neat): 3084, 3035, 3016, 2980, 2343, 1642, 1598, 1558, 1496, 817, 776, 734 cm^{-1}.

$[\alpha]_D^{28}$ = –18.5 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 210 nm), *ee* = 90%.


8.80
8.23
8.22
7.52
7.52
7.51
7.51
7.33
7.32
6.52
6.51
6.09
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6.07
6.06
6.06
6.05
6.04
6.03
5.24
5.24
5.24
5.24
5.22
5.22
5.22
5.22
5.18
5.17
5.16
5.15
5.15
5.13
5.13
5.10
5.09
5.09
1.70
1.01
1.08
1.05
0.98
1.03
1.00
1.05
0.94
1.02
3.11
f1 (ppm)
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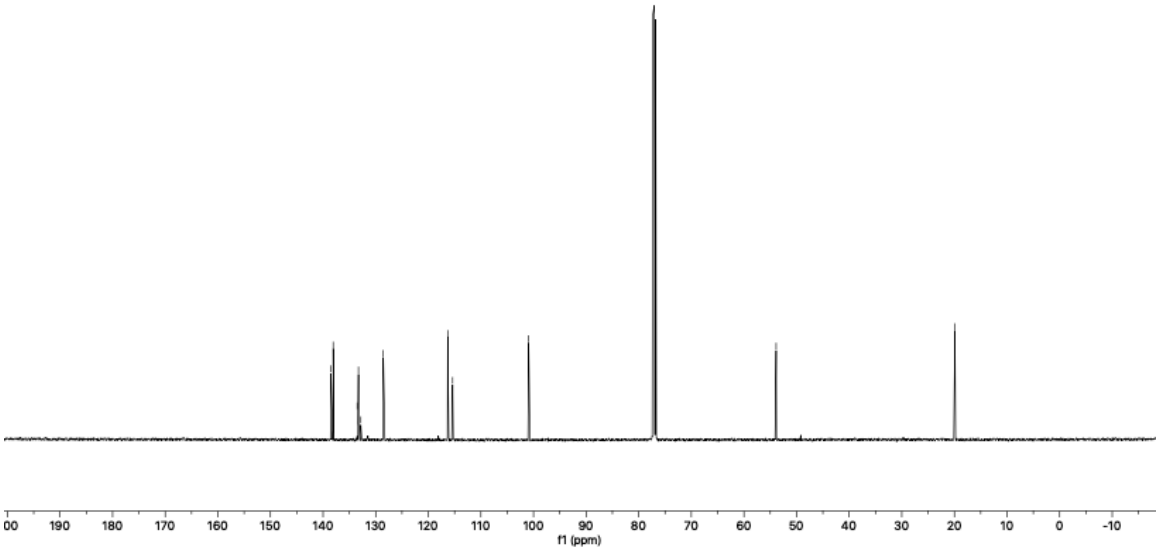
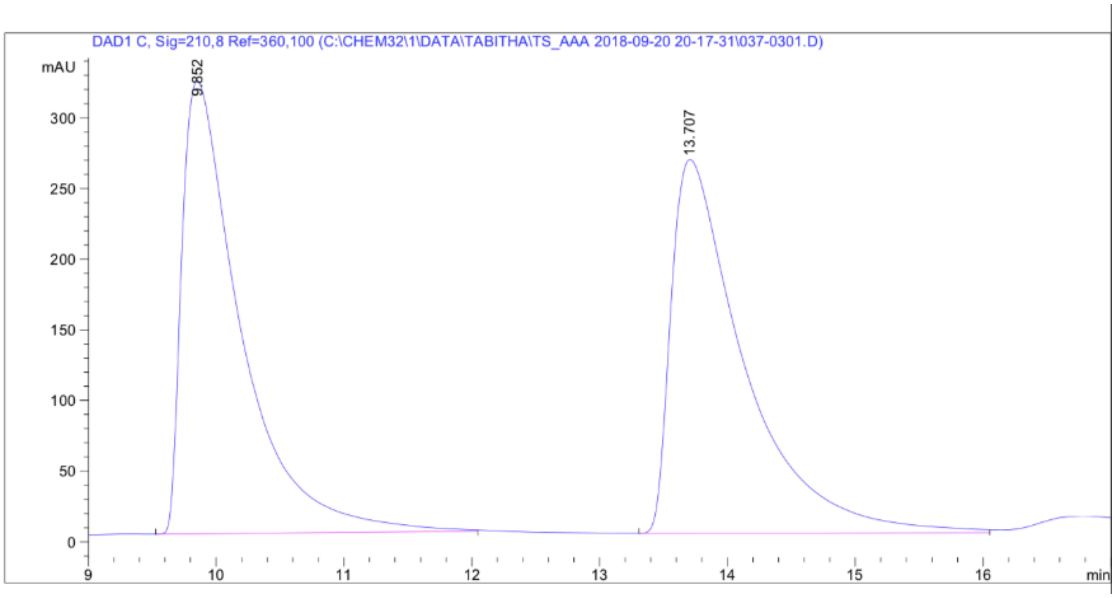
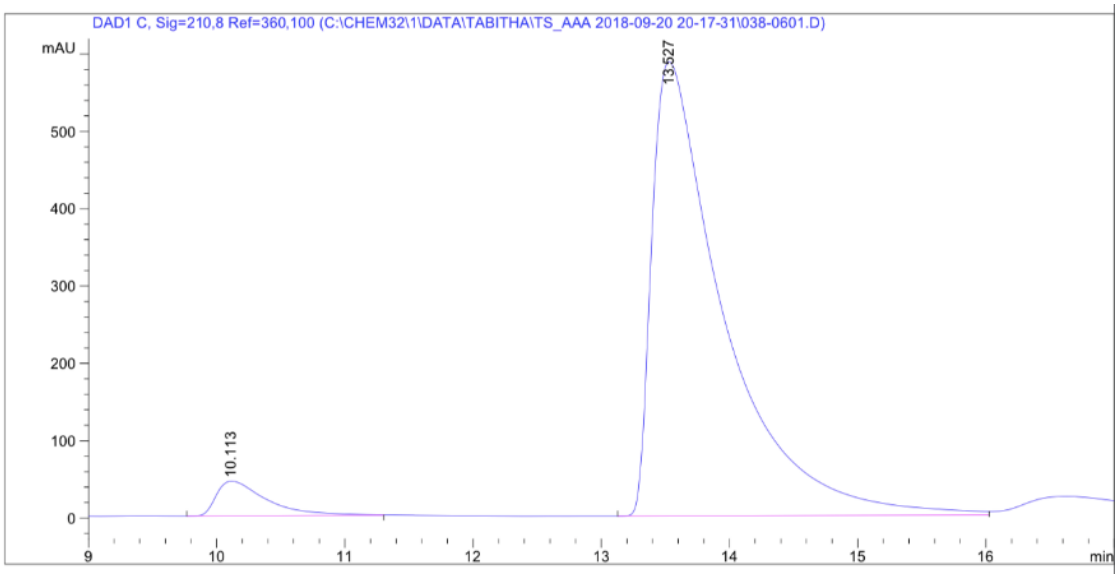
138.07
133.51
133.27
132.82
128.54
116.31
115.37
100.92
53.88
19.90


f1 (ppm)

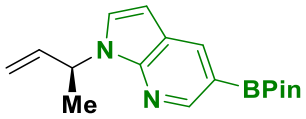


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.852	BB	0.4665	1.02844e4	320.42792	49.3618
2	13.707	BB	0.5734	1.05503e4	264.46320	50.6382



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.113	BB	0.3894	1216.41345	44.99434	5.0519
2	13.527	BB	0.5540	2.28618e4	587.43329	94.9481

***(S)*-1-(but-3-en-2-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridine (6.3m)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (213.9 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 76% yield (100 mg, 0.34 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1).

TLC (SiO_2) R_f = 0.39 (hexanes: ethyl acetate = 5:1).

^{1}H NMR (500 MHz, $CDCl_3$): (d, *J* = 1.6 Hz, 1H), 8.35 (d, *J* = 1.7 Hz, 1H), 7.24 (d, *J* = 3.6 Hz, 1H), 6.48 (d, *J* = 3.6 Hz, 1H), 6.10 (d, *J* = 2.0 Hz, 1H), 5.72 (d, *J* = 2.0 Hz, 1H), 5.17 (dt, *J* = 10.5, 1.4 Hz, 1H), 5.11 – 4.98 (m, 1H), 1.60 (d, *J* = 7.0 Hz, 3H), 1.36 (s, 12H).

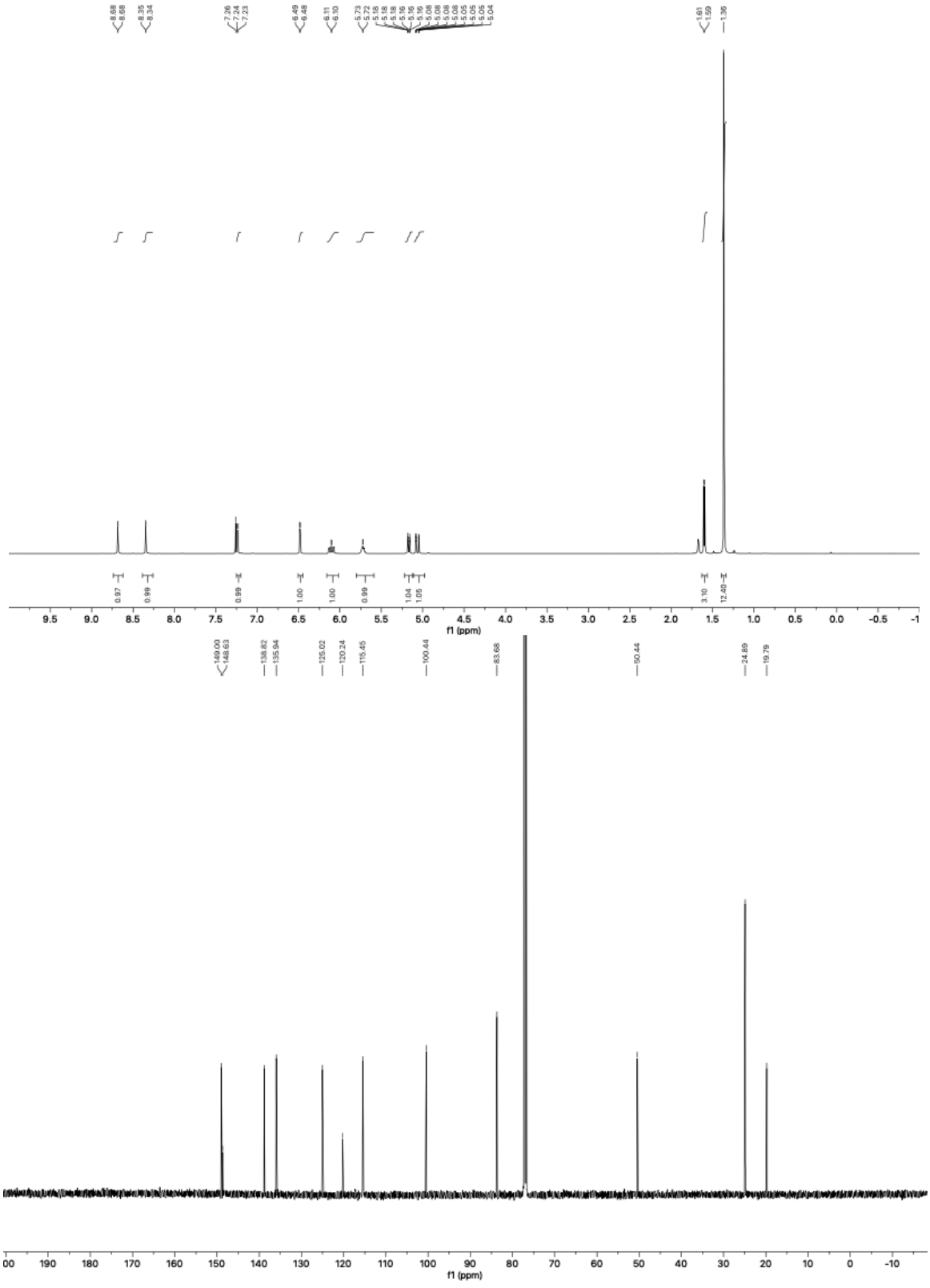
^{13}C NMR (125 MHz, $CDCl_3$): δ 149.0, 148.6, 138.8, 135.9, 125.0, 120.2, 115.5, 100.4, 83.7, 50.4, 24.9, 19.8.

HRMS (ESI): Calculated for $C_{17}H_{23}BN_2O_2$ [M+H$^+$] = 299.1928, Found 299.1937.

FTIR (neat): 2978, 2360, 2342, 1363, 1348, 1275, 1261, 764, 750, cm^{-1}.

$[\alpha]_D^{28}$= –24.3 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 210 nm), *ee* = 92%.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8.68
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7.23
6.49
6.48
6.11
6.10
5.73
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5.16
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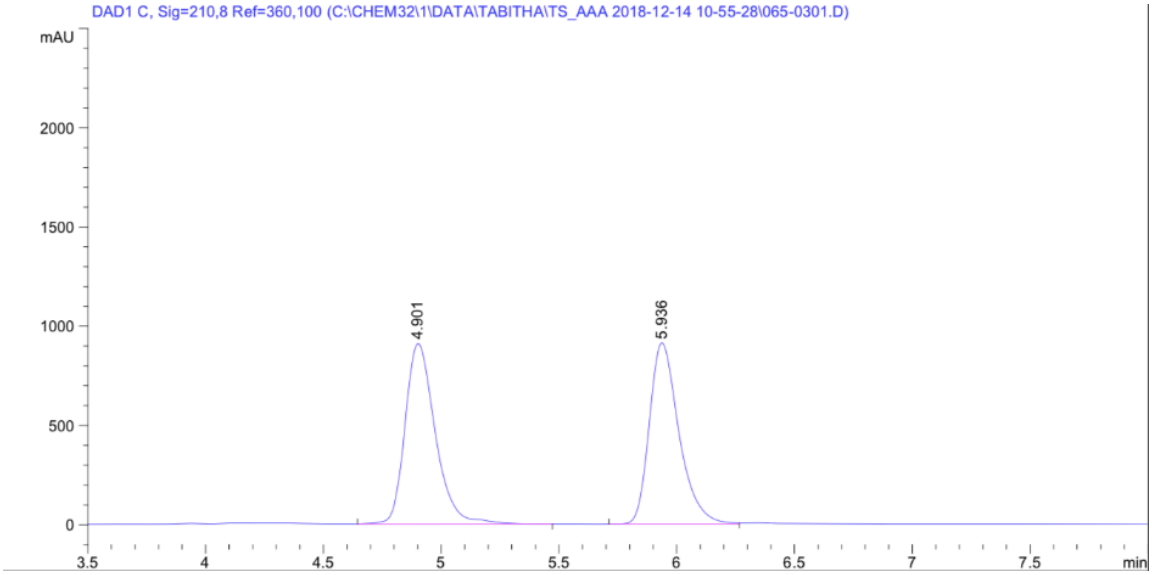
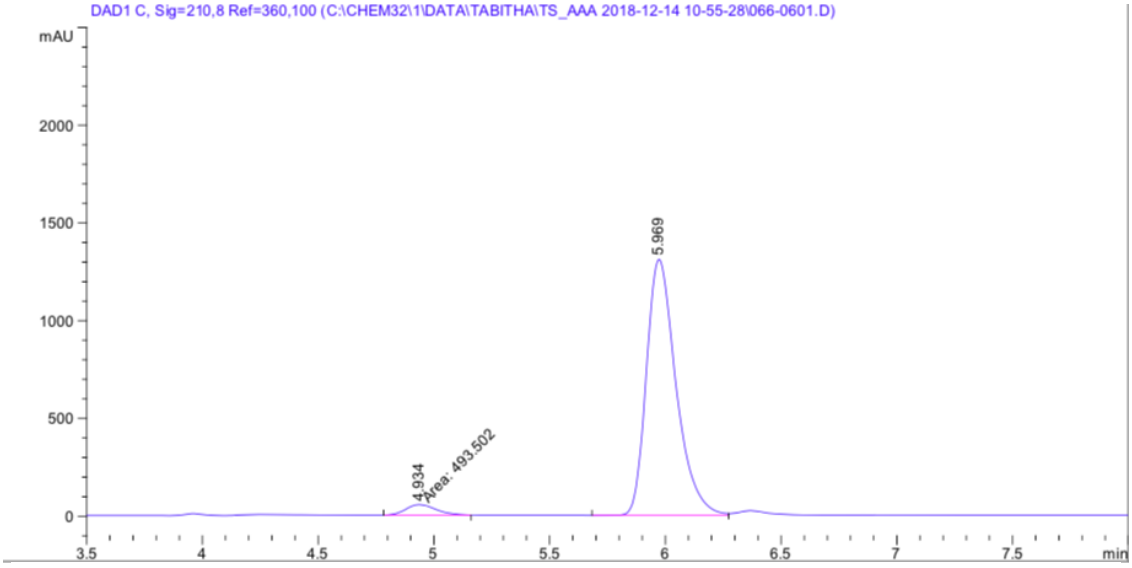
5.08
5.08
5.05
5.05
5.05
5.05
5.04
1.61
1.59
1.36
0.97
0.99
0.99
1.00
1.00
0.99
1.04
1.05
3.10
12.40
f1 (ppm)
149.00
148.63
138.82
135.94
125.02
120.24
115.45
100.44
83.68
50.44
24.89
19.79
f1 (ppm)

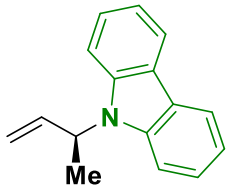


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.901	BB	0.1364	8141.02783	910.04974	50.5092
2	5.936	BV	0.1339	7976.89355	912.89844	49.4908



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.934	MM	0.1515	493.50156	54.27274	4.0569
2	5.969	VV	0.1359	1.16710e4	1310.49268	95.9431

***(S)*-9-(but-3-en-2-yl)-9H-carbazole (6.3n)**



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the carbazole (147.0 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 91% yield (88.6 mg, 0.40 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1).

TLC (SiO_2) R_f = 0.43 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.15 (dt, *J* = 7.8, 1.0 Hz, 2H), 7.52 (dt, *J* = 8.3, 0.9 Hz, 2H), 7.46 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 2H), 7.30 – 7.24 (m, 2H), 6.31 (ddd, *J* = 17.4, 10.6, 3.7 Hz, 1H), 5.46 (ttd, *J* = 7.0, 4.5, 1.7 Hz, 1H), 5.39 – 5.31 (m, 2H), 1.77 (d, *J* = 7.1 Hz, 3H).

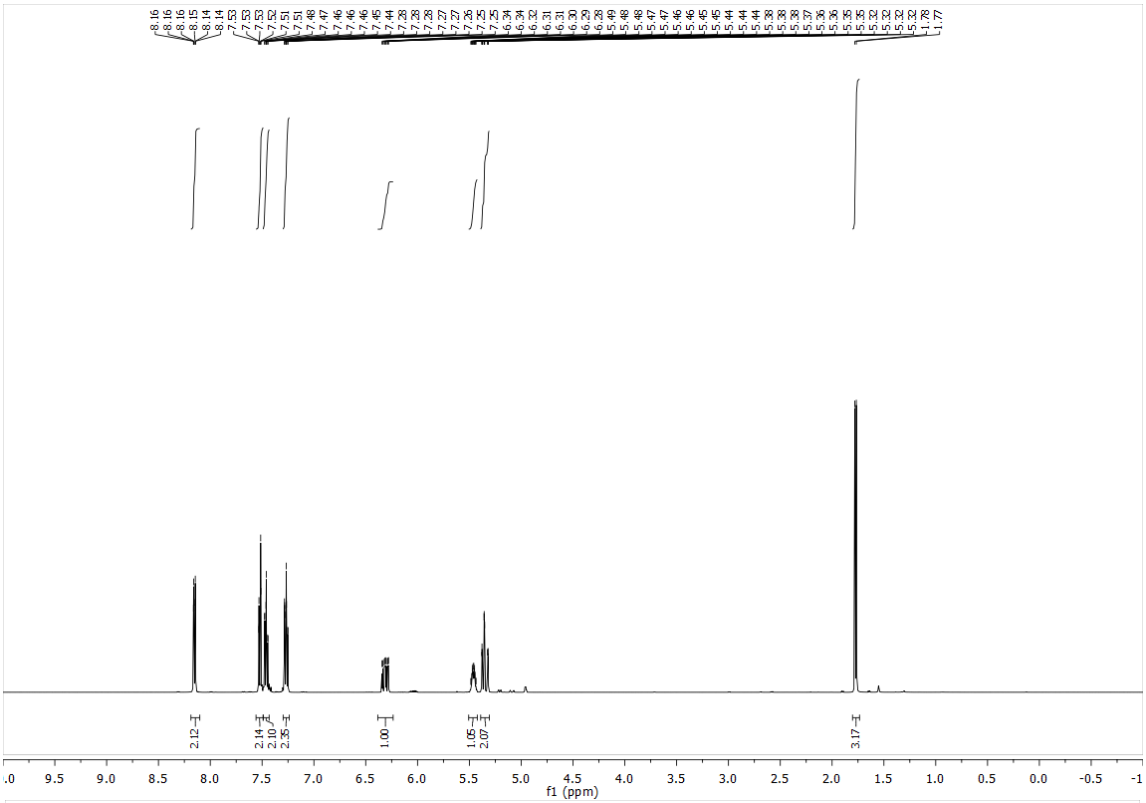
^{13}C NMR (125 MHz, $CDCl_3$): δ = δ 139.6, 138.3, 125.4, 123.4, 120.3, 118.8, 116.0, 110.1, 51.5, 17.1.

HRMS (ESI): Calculated for $C_{16}H_{15}N$ [M+H$^+$] = 222.1277, Found 222.1279.

FTIR (neat): 2982, 1595, 1481, 1452, 1328, 1223, 1155, 924, 747, 722 cm^{-1}.

$[\alpha]_D^{28}$= +2.0 (*c* 1.0, $CHCl_3$).

HPLC (Two connected chiralcel OJ-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 93%.


8.16
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8.14
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7.46
7.45
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5.44
5.44
5.44
5.38
5.38
5.37
5.36
5.36
5.35
5.35
5.32
5.32
5.32
5.32
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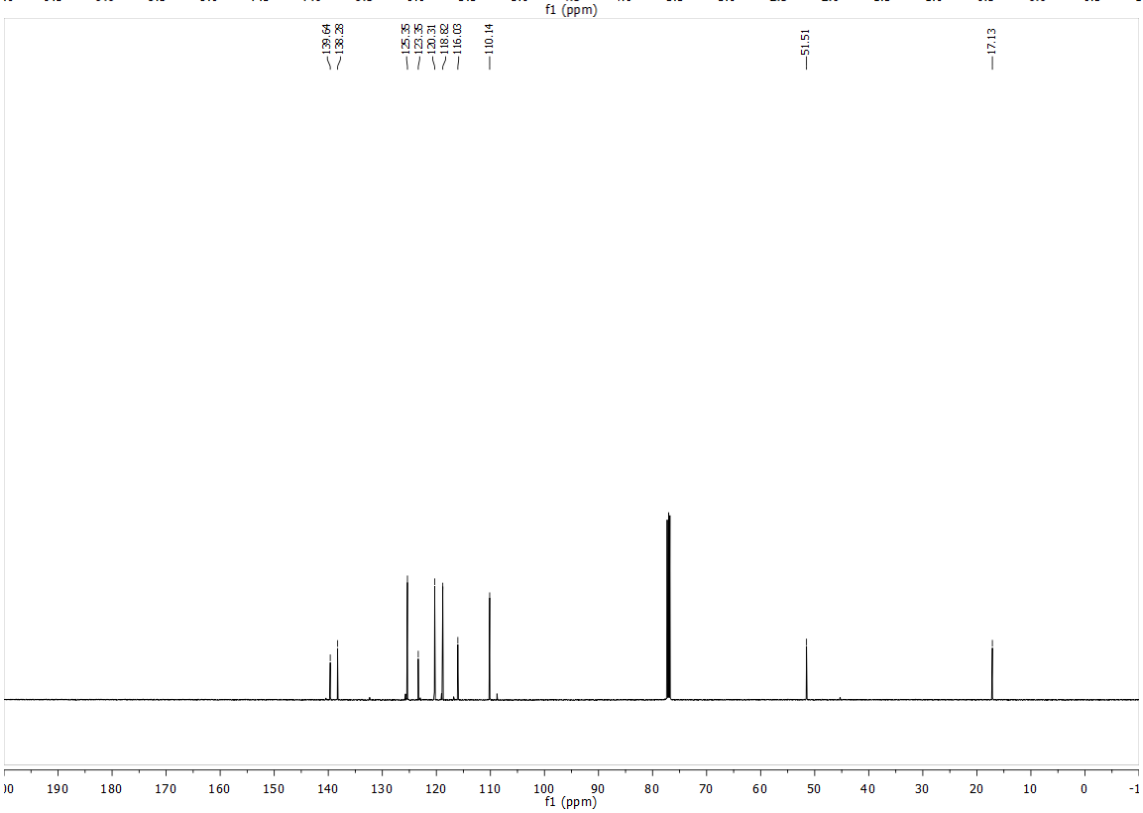
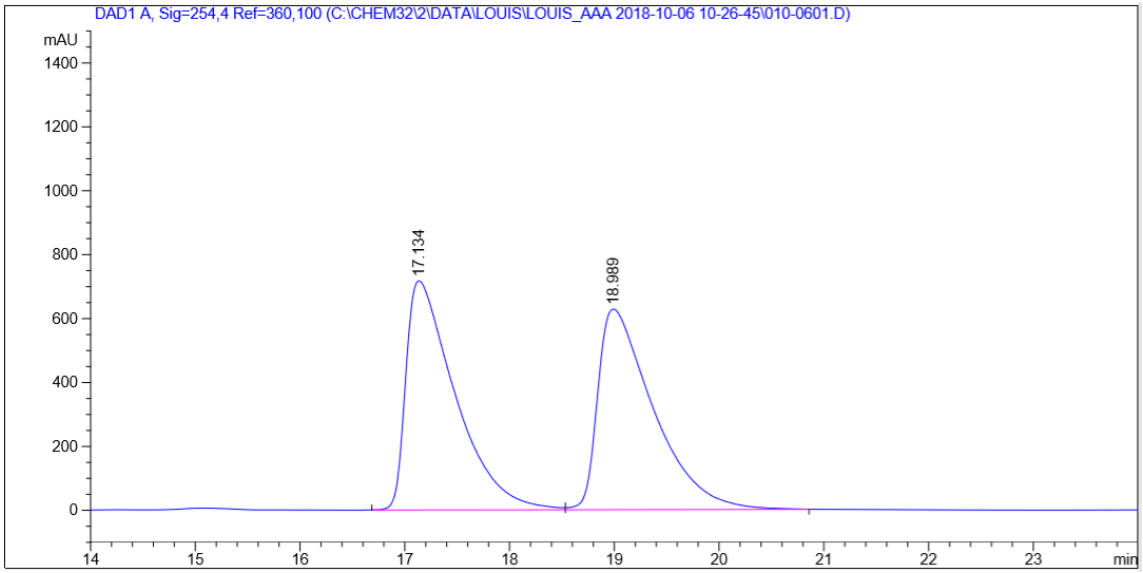
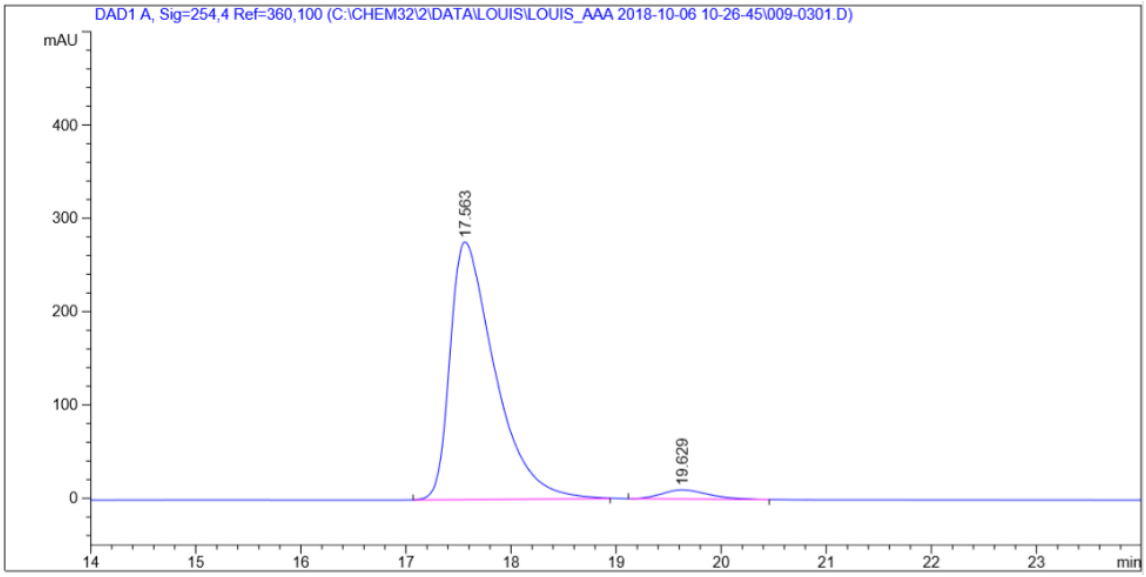
2.14
2.10
2.35
1.00
1.05
2.07
3.17
f1 (ppm)


139.64
138.28
125.35
123.35
120.31
118.82
116.03
110.14
51.51
17.13
f1 (ppm)

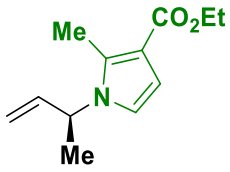


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.134	BV	0.4834	2.34451e4	717.15167	50.3593
2	18.989	VB	0.5433	2.31105e4	628.02814	49.6407



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.563	BB	0.4435	8175.97510	276.11520	96.4959
2	19.629	BB	0.4708	296.89554	9.76250	3.5041

Ethyl *(S)*-1-(but-3-en-2-yl)-2-methyl-1*H*-pyrrole-3-carboxylate (6.3o)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (110.1 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ºC, 24 hr). The title compound was obtained in 74% yield (68 mg, 0.33 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1).

TLC (SiO_2) R_f = 0.39 (hexanes: ethyl acetate = 5:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.56 (s, 2H), 5.93 (ddd, *J* = 17.2, 10.5, 4.8 Hz, 1H), 5.15 (ddd, *J* = 10.5, 1.8, 0.9 Hz, 1H), 4.90 (ddd, *J* = 17.1, 1.9, 0.9 Hz, 1H), 4.73 (dd, *J* = 6.9, 4.9 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.52 (s, 3H), 1.53 (d, *J* = 6.9 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).

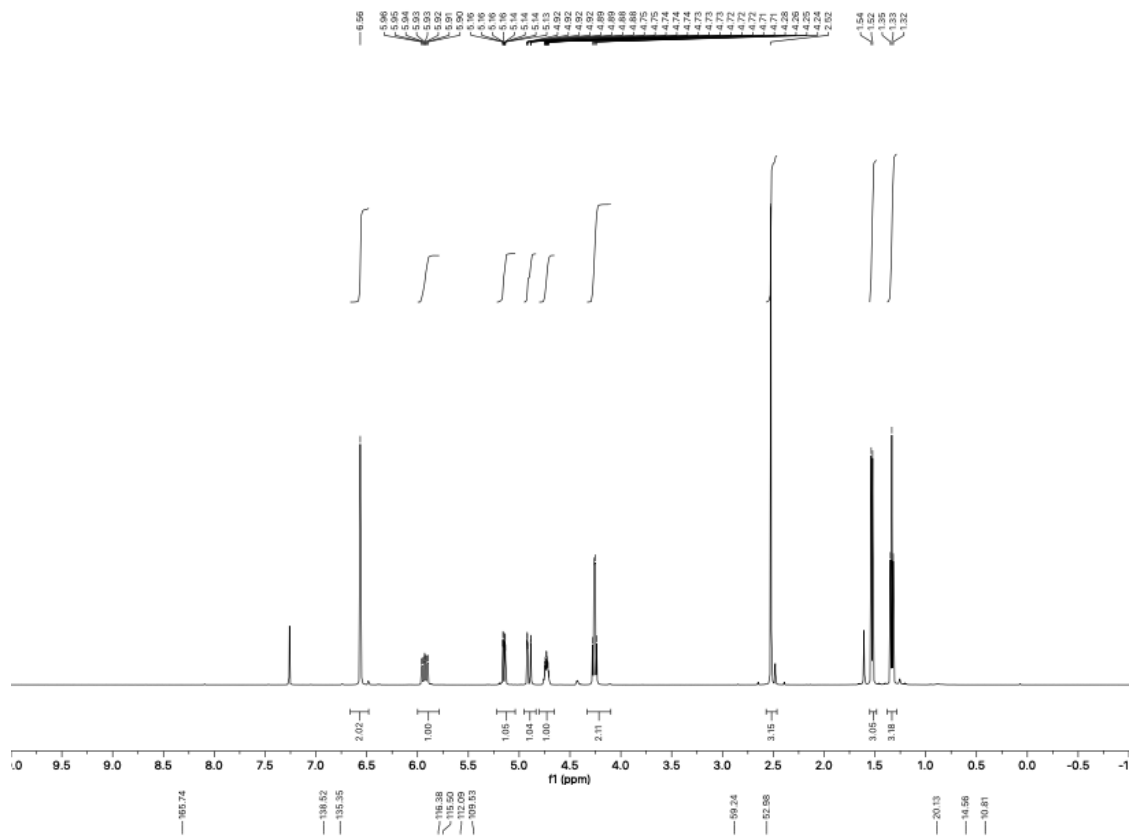
^{13}C NMR (125 MHz, $CDCl_3$): δ 165.7, 138.5, 135.4, 116.4 115.5, 112.1, 109.5, 59.2, 53.0, 20.1, 14.6, 10.8.

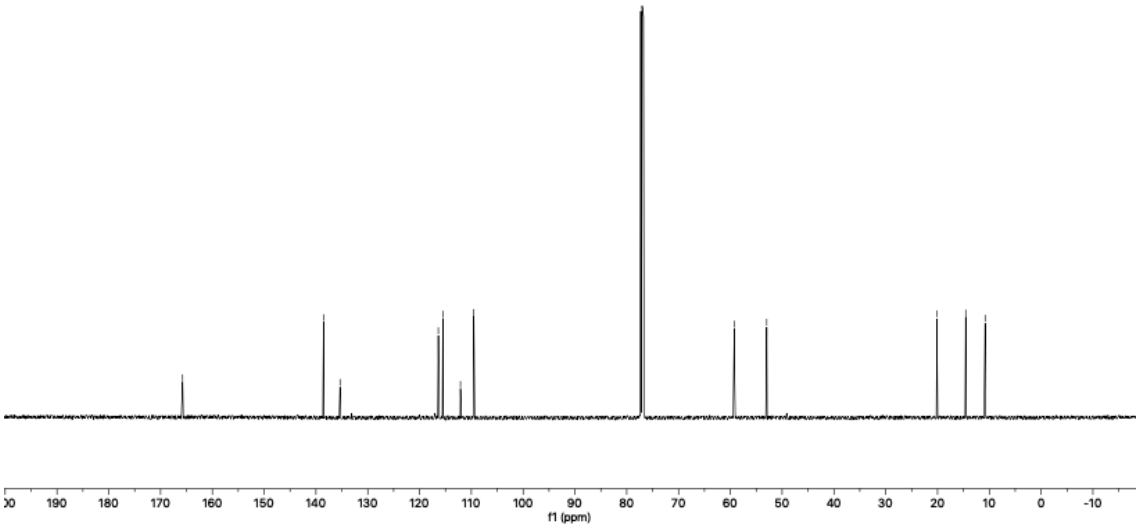
HRMS (ESI): Calculated for $C_{12}H_{17}NO_2$ [M+H$^+$] = 208.1332, Found 208.1331.

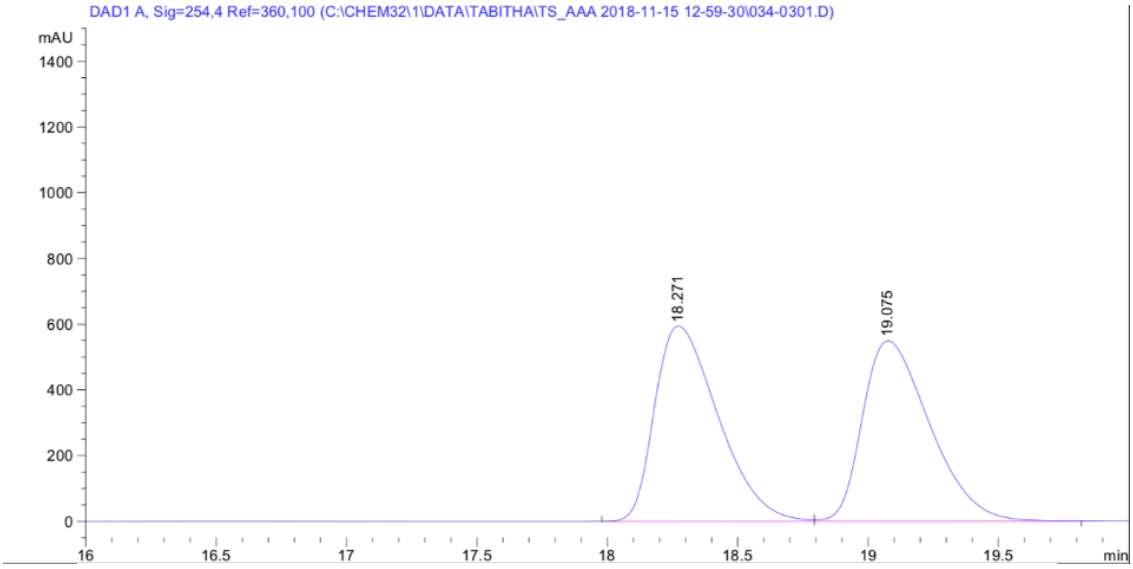
FTIR (neat): 2982, 2360, 2342, 1696, 1223, 929, 764, 750 cm^{-1}.

$[\alpha]_D^{28}$ = –9.2 (*c* 1.0, $CHCl_3$).

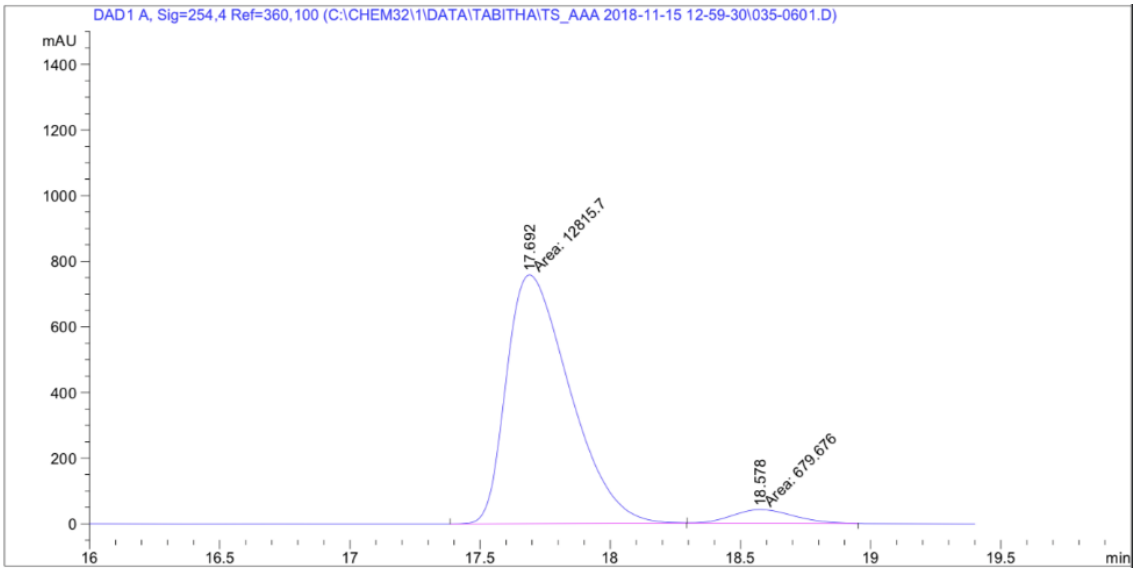
HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 90%.


f1 (ppm)


f1 (ppm)

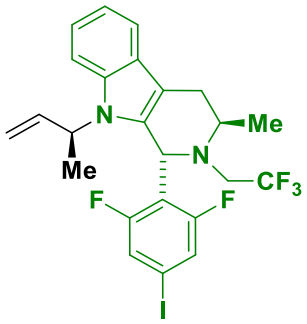


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.271	BV	0.2614	1.00539e4	594.10718	50.5675
2	19.075	VB	0.2789	9828.20996	548.91382	49.4325



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.692	MM	0.2818	1.28157e4	758.07782	94.9636
2	18.578	MM	0.2710	679.67615	41.80506	5.0364

(1*R*,3*R*)-9-((*S*)-but-3-en-2-yl)-1-(2,6-difluoro-4-iodophenyl)-3-methyl-2-(2,2,2-trifluoroethyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (6.3p)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (445.5 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ºC, 24 hr). The title compound was obtained in 95% yield, >20:1 dr (234.2 mg, 0.42 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 30:1).

TLC (SiO_2) R_f = 0.43 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 – 7.51 (m, 1H), 7.36 – 7.32 (m, 1H), 7.25 – 7.16 (m, 2H), 7.16 – 7.07 (m, 2H), 5.87 (ddd, *J* = 17.4, 10.6, 4.0 Hz, 1H), 5.31 (s, 1H), 5.07 (ddd, *J* = 10.6, 2.3, 0.9 Hz, 1H), 4.86 (ddd, *J* = 17.4, 2.3, 0.9 Hz, 1H), 4.64 – 4.54 (m, 1H), 3.38 (dq, *J* = 12.3, 6.5 Hz, 1H), 3.25 (dq, *J* = 15.7, 9.9 Hz, 1H), 3.00 – 2.82 (m, 2H), 2.61 (ddd, *J* = 16.2, 9.7, 1.3 Hz, 1H), 1.49 (d, *J* = 7.1 Hz, 3H), 1.20 (d, *J* = 6.7 Hz, 3H).

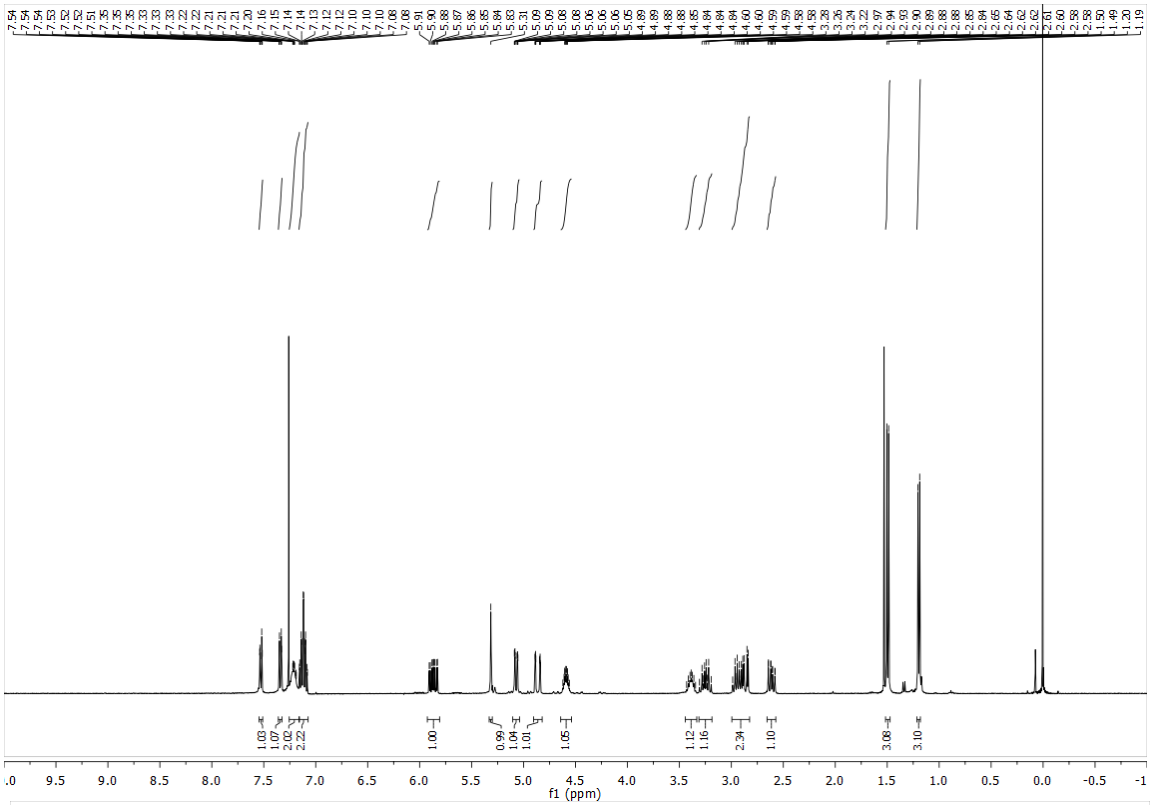
^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.3, 135.6, 130.7, 127.5, 127.0, 124.3, 121.7 (d, *J* = 25.9 Hz), 121.3, 119.05, 118.4, 116.8 (t, *J* = 14.5 Hz), 115.9, 111.9, 109.6, 91.9 (t, *J* = 10.9 Hz), 54.1, 52.4, 49.5, 48.7 (q, *J* = 32.3 Hz), 25.5, 18.5, 18.4.

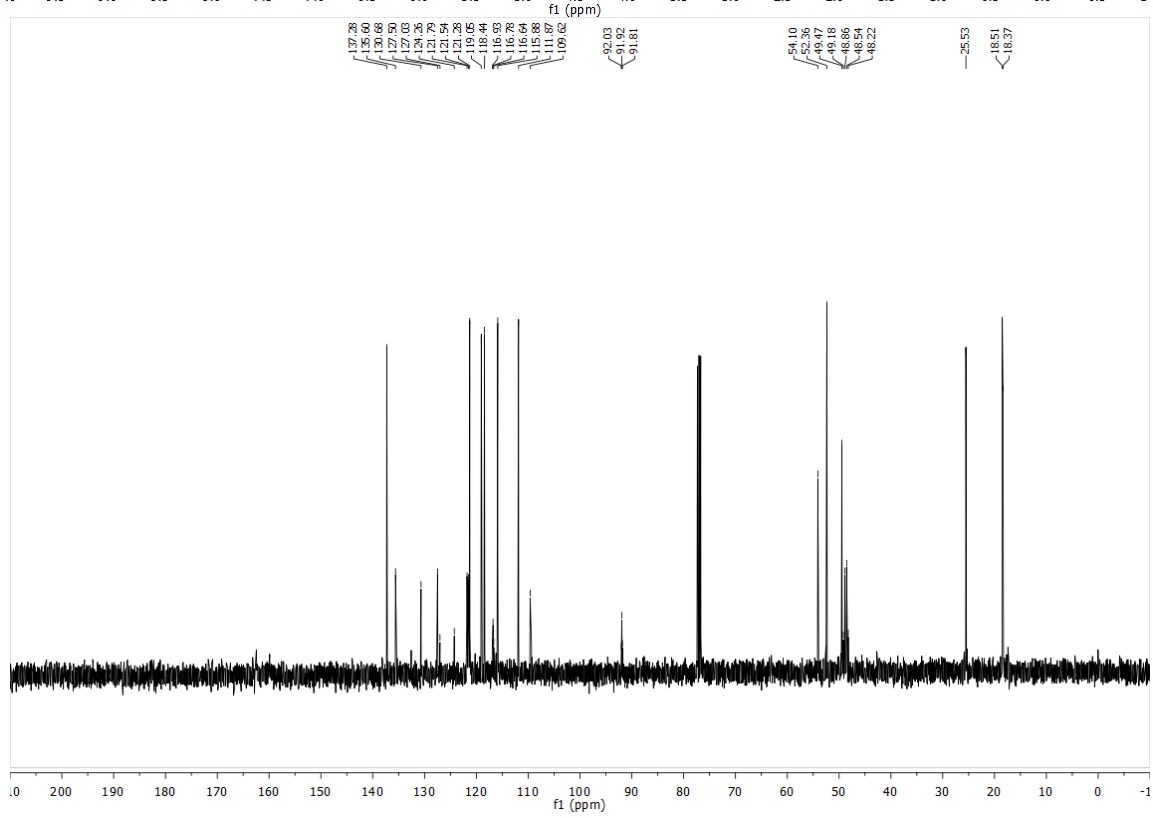
^{19}F NMR (376 MHz, $CDCl_3$): δ = -70.77, -110.47.

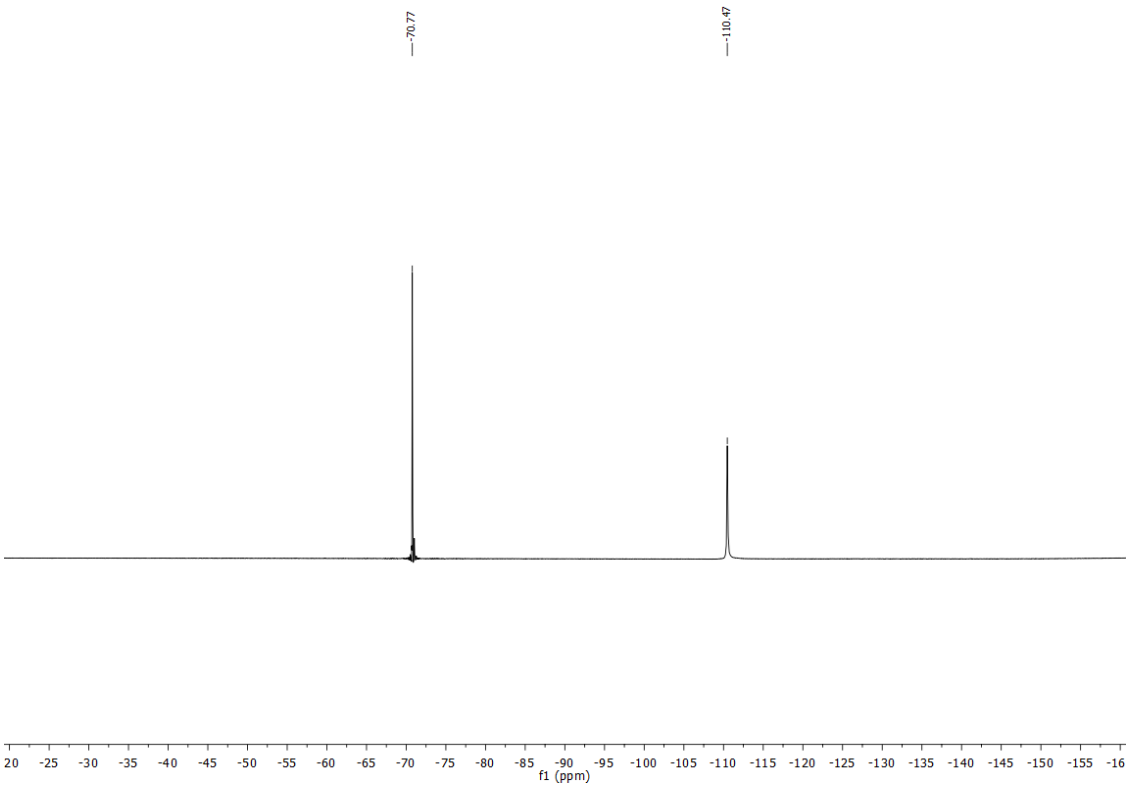
HRMS (ESI): Calculated for $C_{24}H_{22}N_2F_5I$ $[M+H^+]$ = 561.0821, Found 561.0821.

FTIR (neat): 2982, 1606, 1569, 1409, 1195, 1140, 1051, 1022, 843, 739 cm^{-1}.

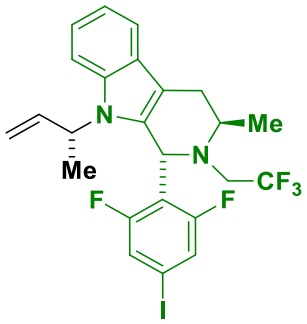
$[\alpha]_D^{28}$= –88.6 (*c* 0.2, $CHCl_3$).


f1 (ppm)


f1 (ppm)


-70.77
-110.47
20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -16
f1 (ppm)

(1*R*,3*R*)-9-((*R*)-but-3-en-2-yl)-1-(2,6-difluoro-4-iodophenyl)-3-methyl-2-(2,2,2-trifluoroethyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole (6.3q)



Procedures

The allylic acetate (50.2 mg, 0.44 mmol, 100 mol%) and the indole (445.5 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions with **(*R*)-Ir-I** (70 ^{o}C, 24 hr). The title compound was obtained in 96% yield, >20:1 dr (236.7 mg, 0.42 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 30:1).

TLC (SiO_2) R_f = 0.43 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 – 7.51 (m, 1H), 7.37 – 7.31 (m, 1H), 7.26 – 7.18 (m, 2H), 7.12 (pd, *J* = 7.0, 1.4 Hz, 2H), 6.01 (ddd, *J* = 17.3, 10.6, 4.1 Hz, 1H), 5.27 (s, 1H), 5.13 (ddd, *J* = 10.5, 2.2, 0.8 Hz, 1H), 5.05 (ddd, *J* = 17.3, 2.2, 0.9 Hz, 1H), 4.53 (ttd, *J* = 7.0, 4.7, 2.0 Hz, 1H), 3.39 (dq, *J* = 12.2, 6.0 Hz, 1H), 3.24 (dq, *J* = 15.7, 9.8 Hz, 1H), 2.97 – 2.83 (m, 2H), 2.61 (ddd, *J* = 16.1, 9.5, 1.3 Hz, 1H), 1.34 (d, *J* = 7.1 Hz, 3H), 1.19 (d, *J* = 6.6 Hz, 3H).

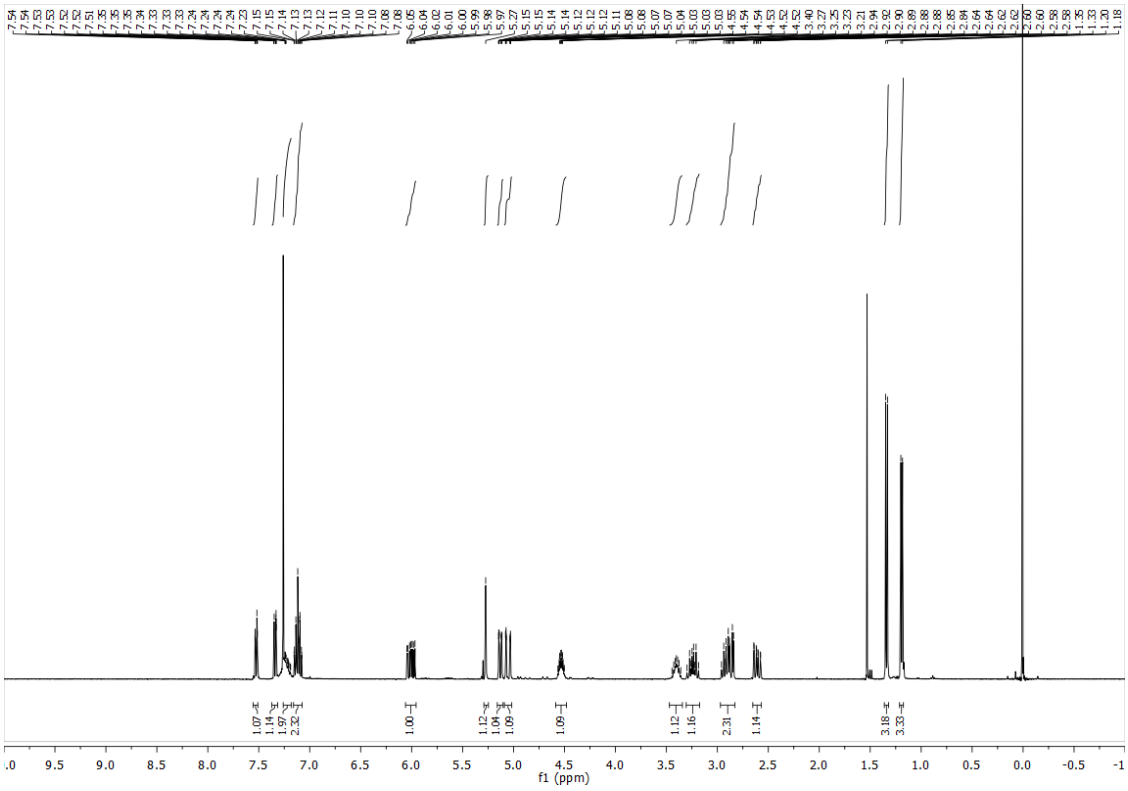
^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.2, 135.4, 130.7, 127.6, 127.0, 124.2, 121.7 (d, *J* = 26.5 Hz), 121.2, 119.0, 118.4, 116.8 (t, *J* = 14.5 Hz), 115.7, 112.0, 109.4, 92.0 (t, *J* = 11.1 Hz), 54.1, 52.5, 50.0, 48.7 (q, *J* = 32.1 Hz), 25.5, 18.3, 17.7.

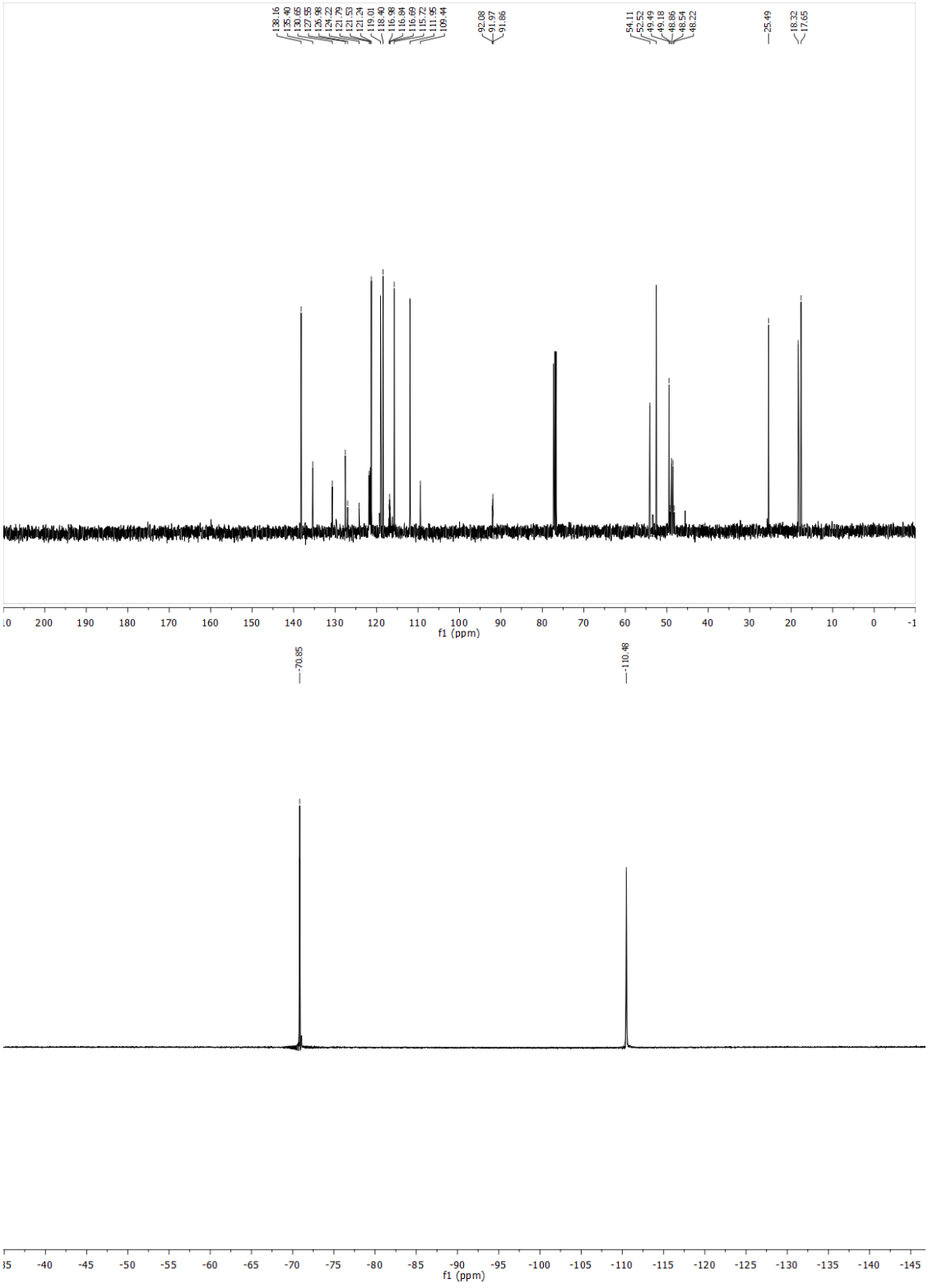
^{19}F NMR (376 MHz, $CDCl_3$): δ = -70.9, -110.5.

HRMS (ESI): Calculated for $C_{24}H_{22}N_2F_5I$ $[M+H^+]$ = 561.0821, Found 561.0828.

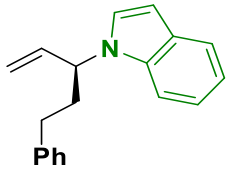
FTIR (neat): 2981, 1606, 1569, 1408, 1264, 1139, 1049, 1021, 843, 735 cm^{-1}.

$[\alpha]_D^{28}$= –75.2 (*c* 0.2, $CHCl_3$).




138.16
135.40
130.65
127.55
126.98
124.22
121.79
121.53
121.24
119.01
118.40
116.98
116.84
116.69
115.72
111.95
109.44
92.08
91.97
91.86
54.11
52.52
49.49
49.18
48.86
48.54
48.22
25.49
18.32
17.65
f1 (ppm)
-70.85
-110.48
f1 (ppm)

***(S)*-1-(5-phenylpent-1-en-3-yl)-1*H*-indole (6.4b)**



Procedures

The allylic acetate (89.8 mg, 0.44 mmol, 100 mol%) and the indole (103.0 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 79% yield (91.0 mg, 0.35 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1).

TLC (SiO_2) R_f = 0.36 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (dq, *J* = 7.8, 1.0 Hz, 1H), 7.28 (dd, *J* = 6.9, 1.1 Hz, 3H), 7.24 – 7.15 (m, 3H), 7.15 – 7.01 (m, 3H), 6.58 (dt, *J* = 3.2, 0.9 Hz, 1H), 6.02 (dddd, *J* = 16.8, 10.5, 5.6, 0.7 Hz, 1H), 5.16 (ddt, *J* = 10.5, 1.7, 0.8 Hz, 1H), 5.02 (ddt, *J* = 17.1, 1.8, 0.9 Hz, 1H), 4.86 (d, *J* = 8.0 Hz, 1H), 2.56 (t, *J* = 7.7 Hz, 2H), 2.45 – 2.24 (m, 2H).

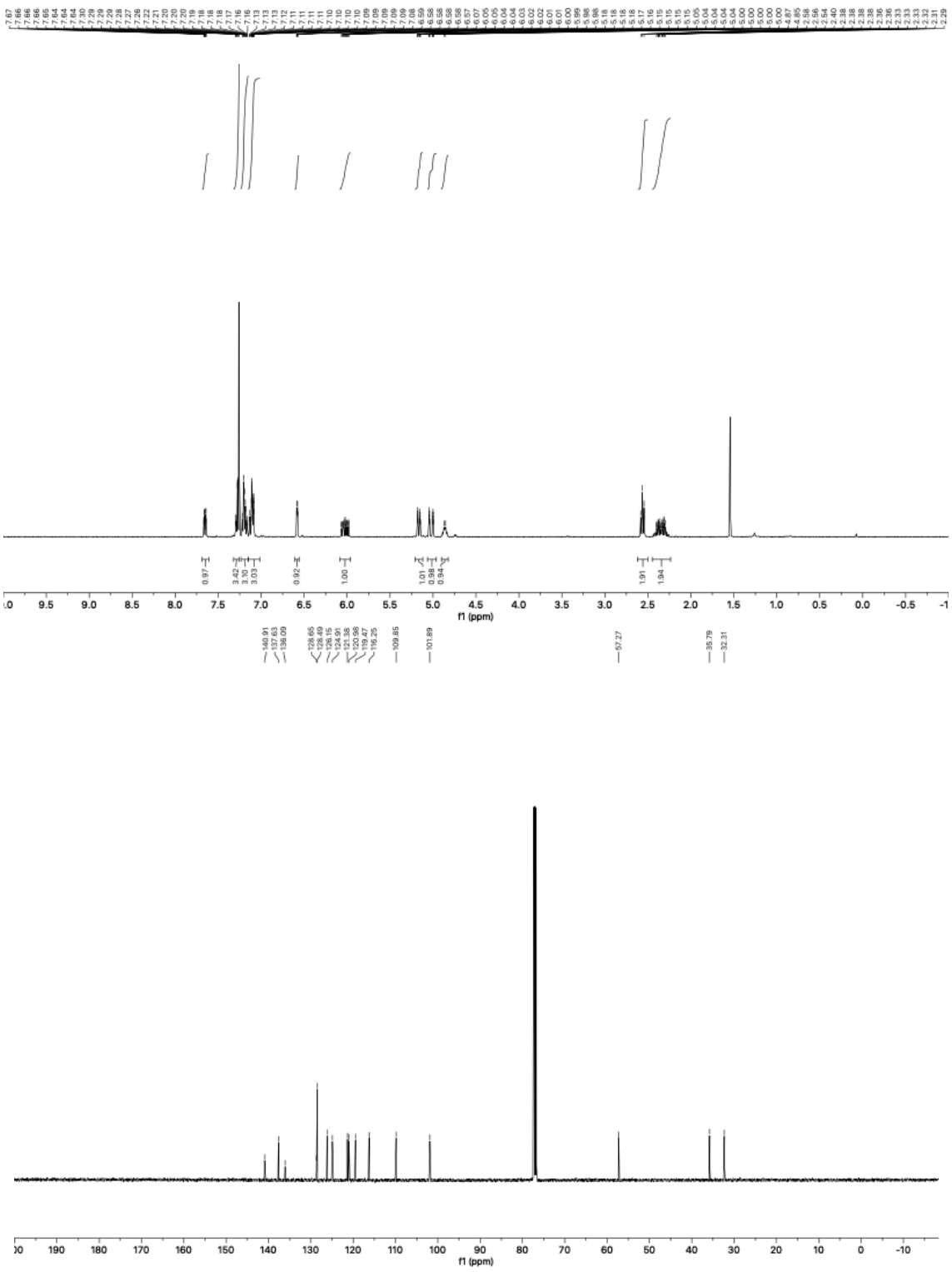
^{13}C NMR (125 MHz, $CDCl_3$): δ 140.9, 137.6, 136.1, 128.7, 128.5, 126.2, 124.9, 121.4, 121.0, 119.5, 116.3, 109.9, 101.9, 57.3, 35.8, 32.3.

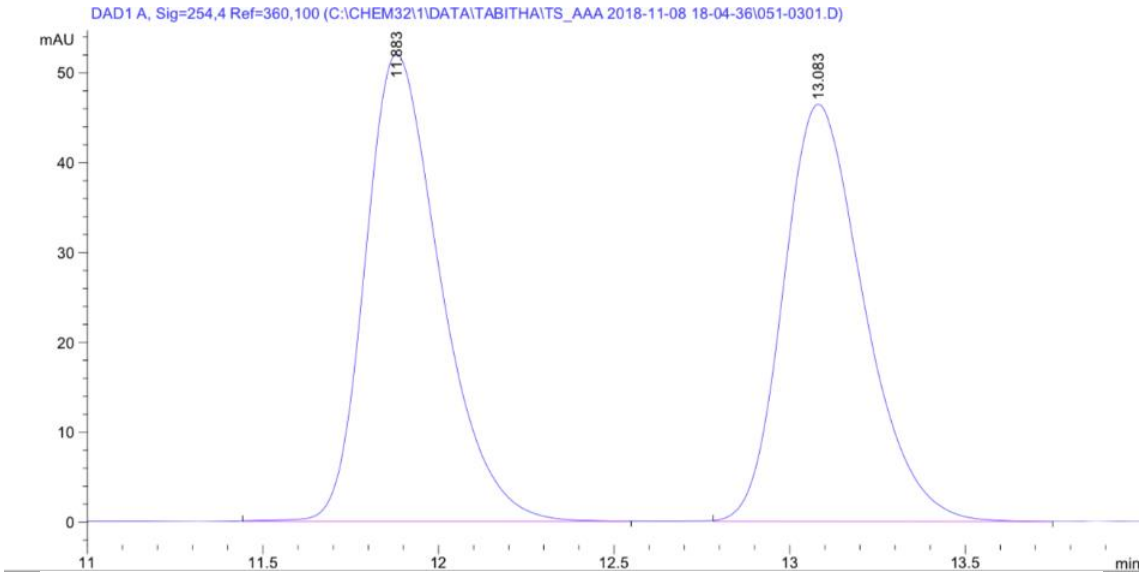
HRMS (ESI): Calculated for $C_{19}H_{19}N$ [M+H$^+$] = 262.1590, Found 262.1598.

FTIR (neat): 3026, 2928, 2360, 2342, 1610, 1476, 1459, 740 cm^{-1}.

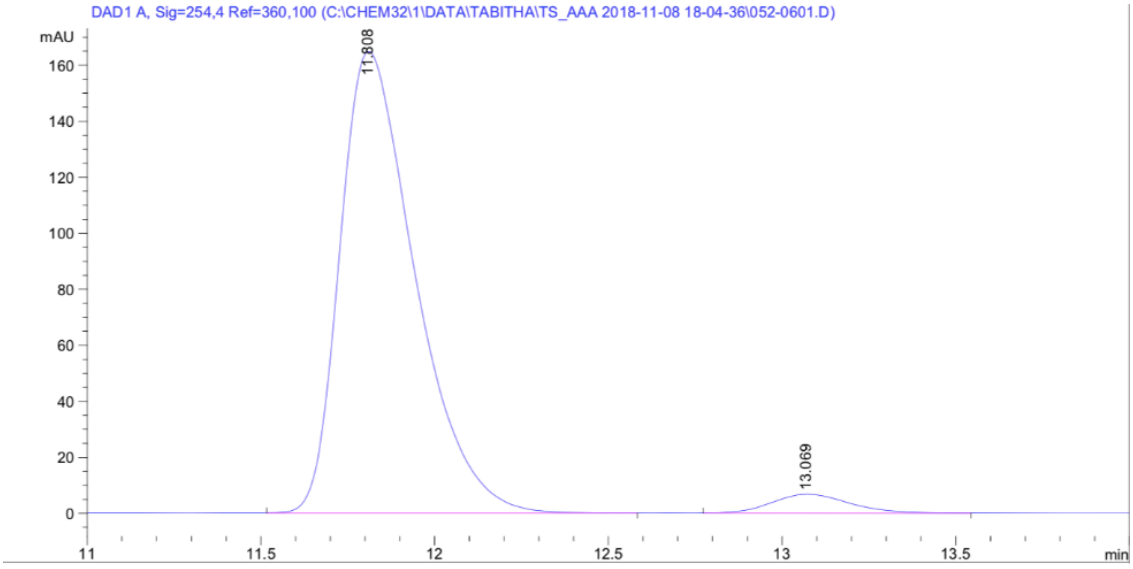
$[\alpha]_D^{28}$= +32.1 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 92%.



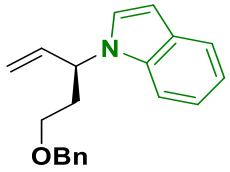


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.883	BB	0.2299	775.45197	52.03645	51.1519
2	13.083	BB	0.2460	740.52808	46.45793	48.8481



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.808	BB	0.2294	2479.68091	164.90477	95.8581
2	13.069	BB	0.2436	107.14393	6.80830	4.1419

***(S)*-1-(5-(benzyloxy)pent-1-en-3-yl)-1H-indole (6.4c)**



Procedures

The allylic acetate (103.1 mg, 0.44 mmol, 100 mol%) and the indole (103.1 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ºC, 24 hr). The title compound was obtained in 65% yield (67.0 mg, 0.29 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 20 min).

TLC (SiO_2) R_f = 0.53 (heptanes: isopropyl acetate = 5:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.41 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.36 – 7.26 (m, 5H), 7.19 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.15 – 7.09 (m, 2H), 6.55 (dd, *J* = 3.2, 0.8 Hz, 1H), 6.07 (ddd, *J* = 17.2, 10.4, 5.3 Hz, 1H), 5.26 – 5.15 (m, 2H), 5.09 (ddd, *J* = 17.3, 1.7, 1.0 Hz, 1H), 4.36 (s, 2H), 3.47 (dt, *J* = 9.8, 5.1 Hz, 1H), 3.16 (ddd, *J* = 9.5, 8.5, 4.8 Hz, 1H), 2.38 – 2.22 (m, 2H).

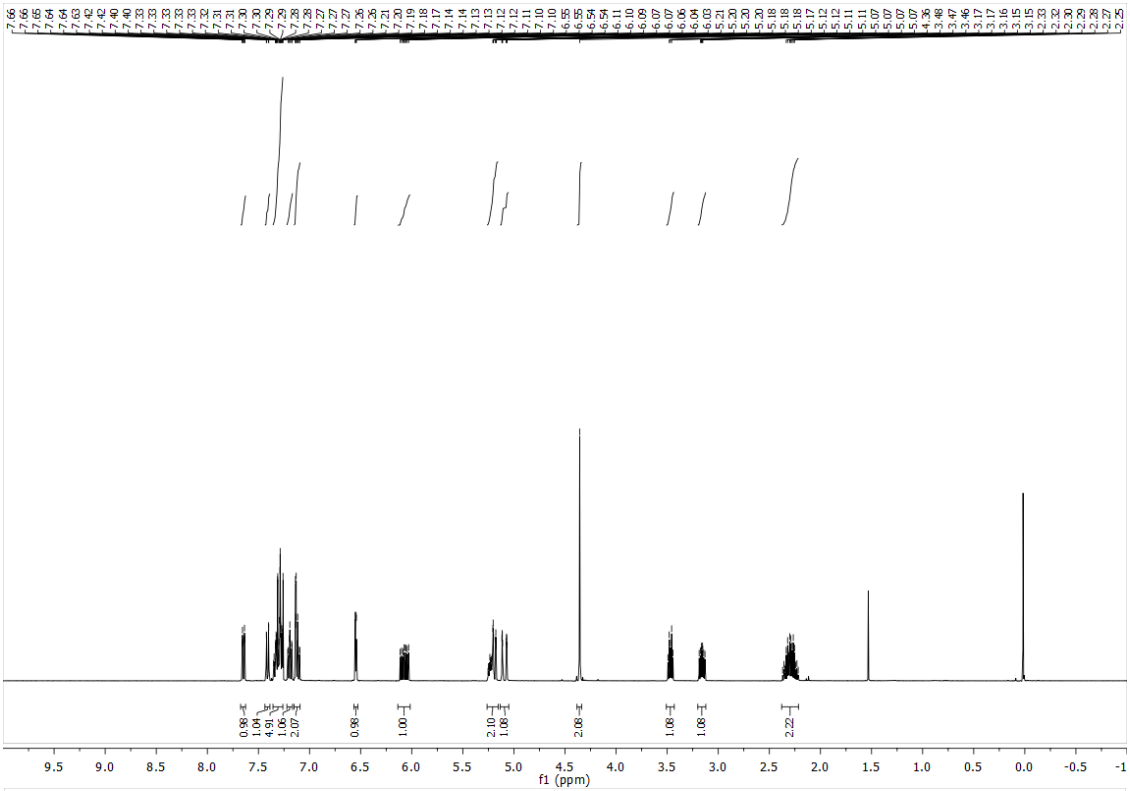
^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.2, 137.6, 136.1, 128.6, 128.4, 127.7, 127.6, 125.3, 121.3, 120.9, 119.4, 116.2, 110.1, 101.8, 73.1, 66.3, 54.7, 34.3.

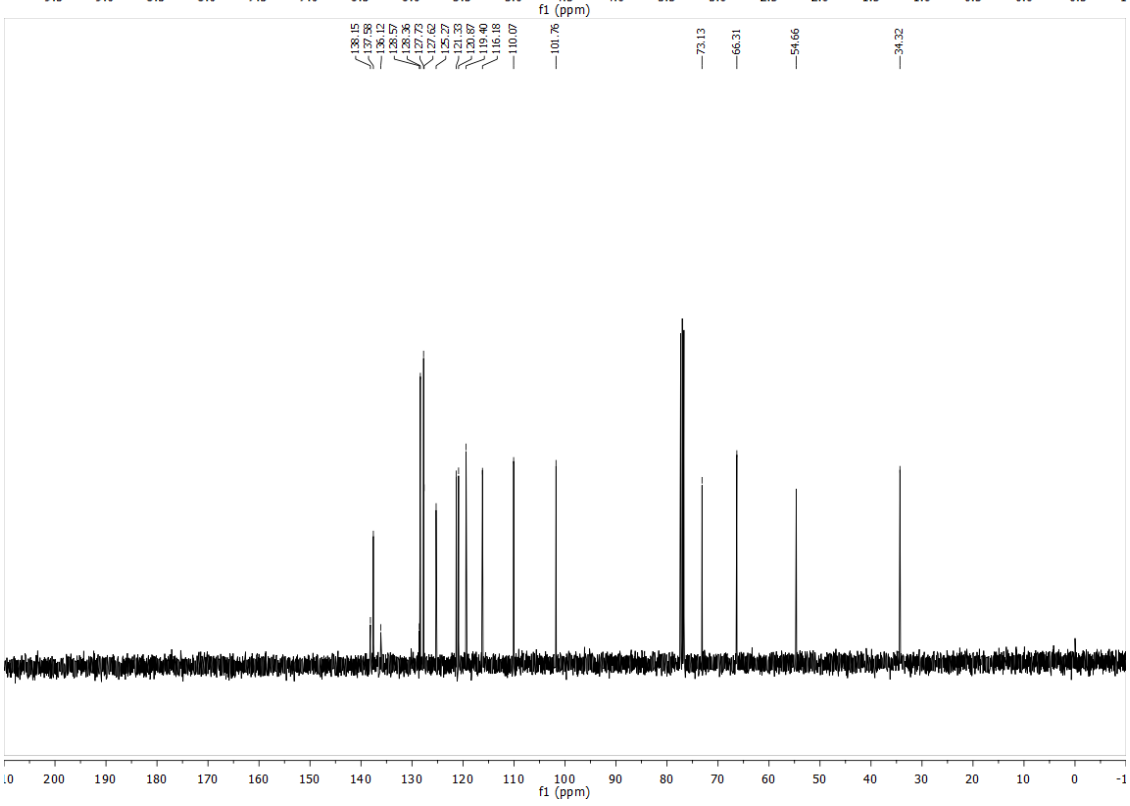
HRMS (ESI): Calculated for $C_{20}H_{21}NO$ [M+H$^+$] = 292.1696, Found 292.1698.

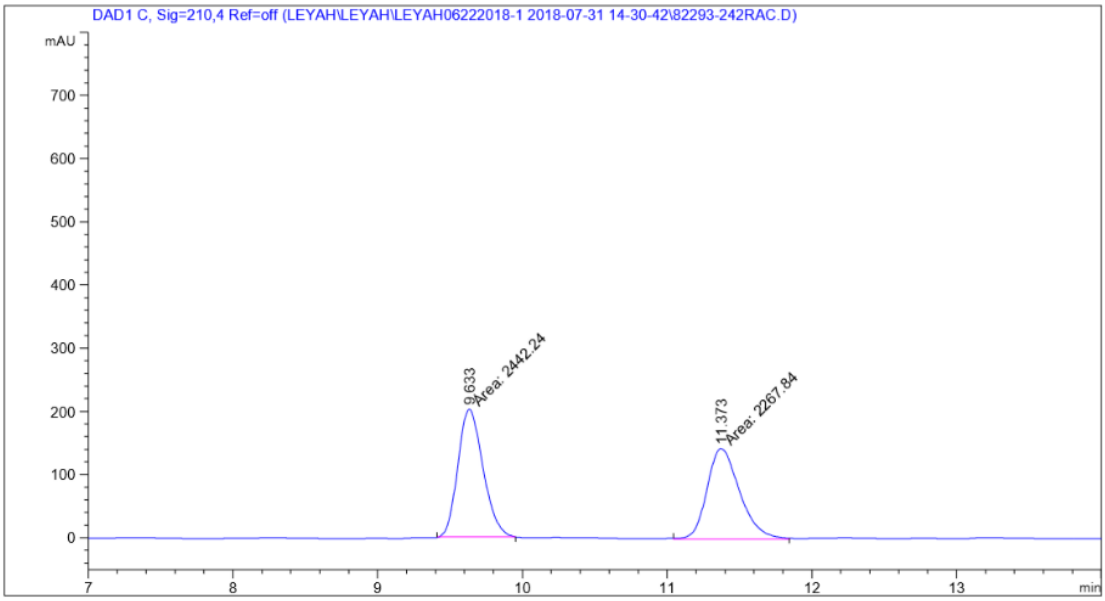
FTIR (neat): 2862, 1458, 1308, 1264, 1195, 1105, 734, 700 cm^{-1}.

$[\alpha]_D^{28}$ = –20.7 (*c* 0.2, $CHCl_3$).

HPLC (Chiralcel OD-3 column, heptanes:*i*-PrOH = 99:1, 1.00 mL/min, 210 nm), *ee* = 91%.







Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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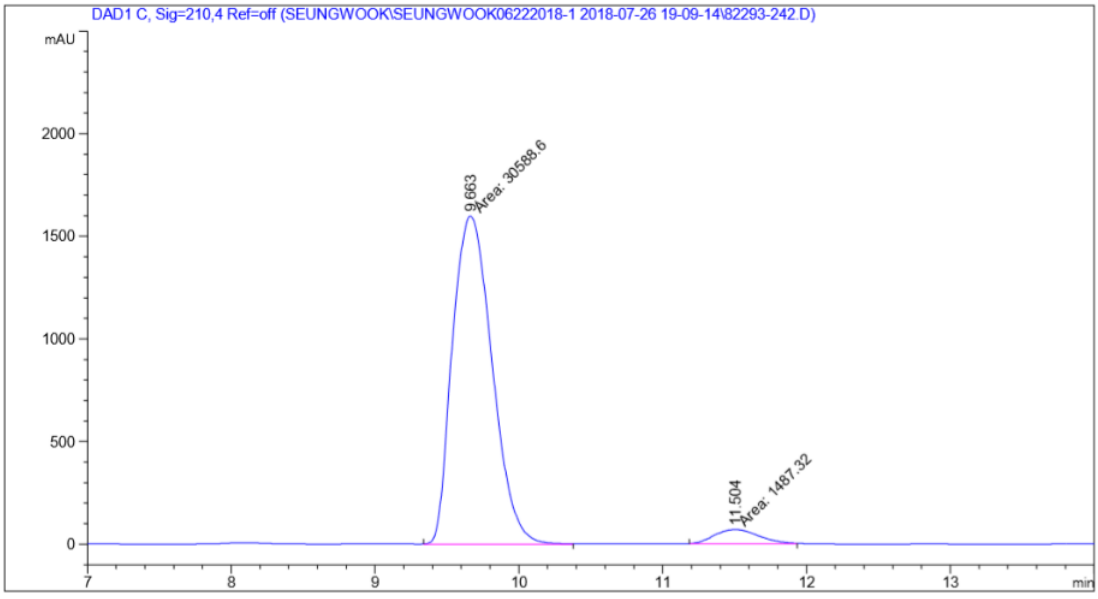
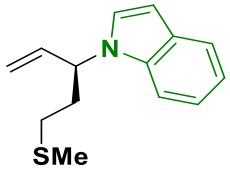
2	11.373	MM	0.2632	2267.83960	143.61632	48.1487



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.663	MM	0.3191	3.05886e4	1597.86682	95.3631
2	11.504	MM	0.3580	1487.31580	69.24165	4.6369

***(S)*-1-(5-(methylthio)pent-1-en-3-yl)-1*H*-indole (6.4d)**



Procedures

The allylic acetate (34.9 mg, 0.2 mmol, 100 mol%) and the indole (46.9 mg, 0.84 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 71% yield (33.0 mg, 0.14 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1).

TLC (SiO_2) R_f = 0.32 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.23 – 7.17 (m, 1H), 7.16 (d, *J* = 3.3 Hz, 1H), 7.11 (td, *J* = 7.4, 7.0, 1.0 Hz, 1H), 6.56 (d, *J* = 3.2 Hz, 1H), 6.05 (ddd, *J* = 17.2, 10.5, 5.6 Hz, 1H), 5.21 (dt, *J* = 10.5, 1.3 Hz, 1H), 5.18 – 5.06 (m, 2H), 2.48 – 2.16 (m, 4H), 2.05 (s, 3H).

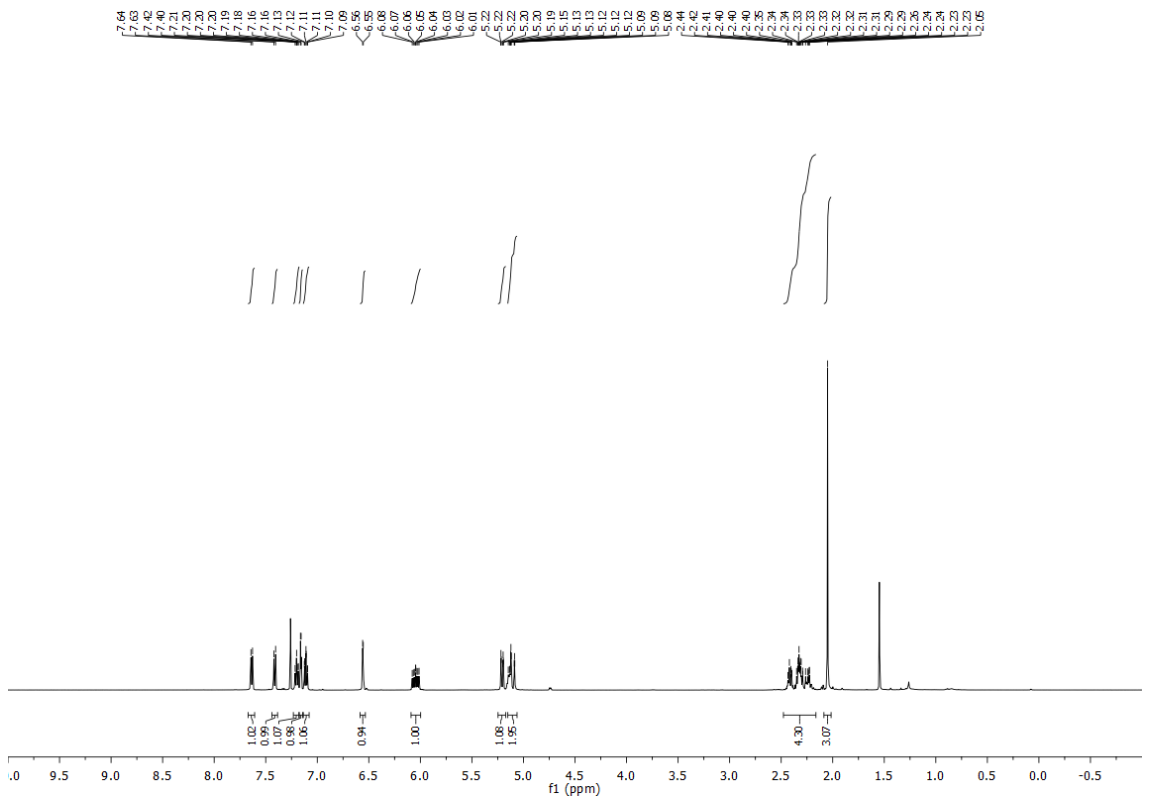
^{13}C NMR (125 MHz, $CDCl_3$): δ 137.2, 136.1, 128.6, 125.0, 121.5, 121.0, 119.6, 116.6, 109.9, 102.0, 56.6, 33.3, 30.7, 15.6.

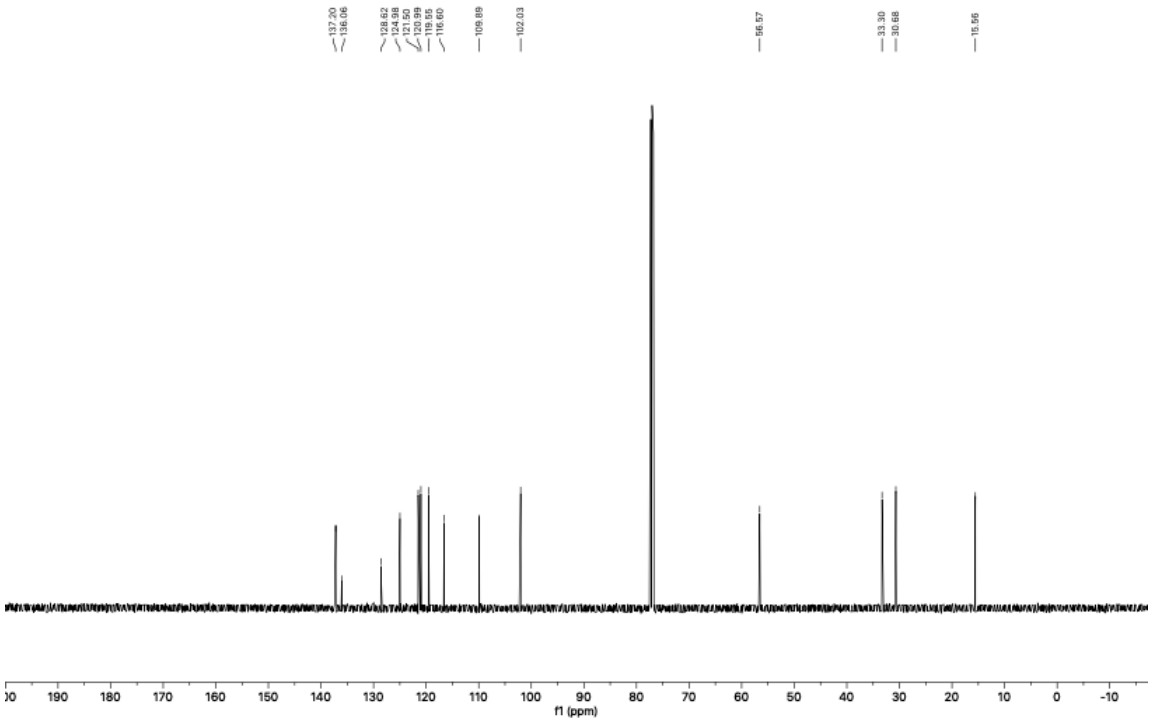
HRMS (ESI): Calculated for $C_{14}H_{17}NS$ $[M+H^+]$ = 232.1154, Found 232.1156.

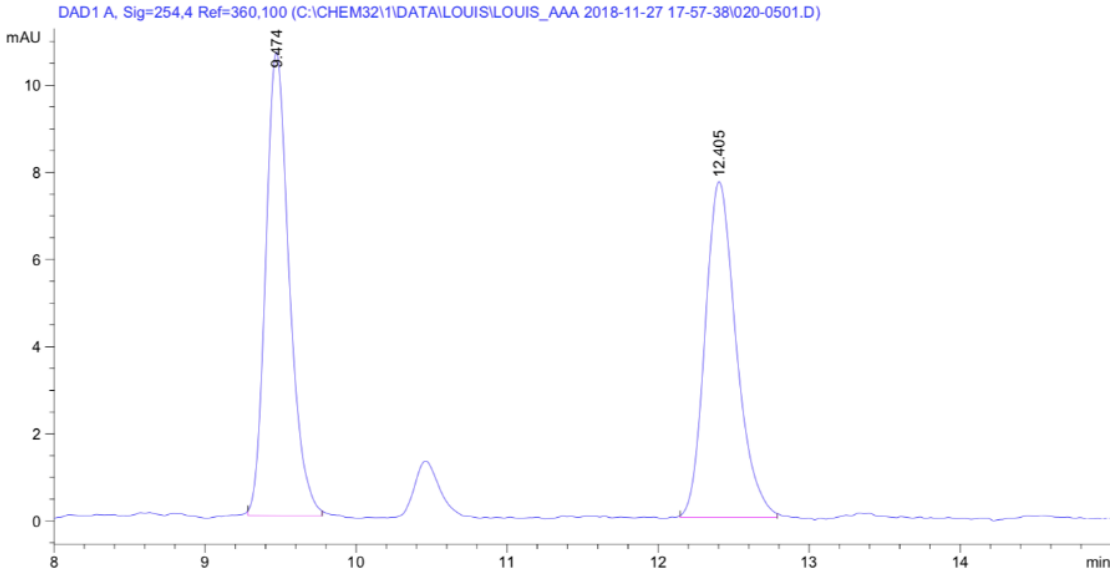
FTIR (neat): 2916, 1611, 1511, 1476, 1459, 1424, 1309, 1216, 1014, 989, 927, 740, 667 cm^{-1}.

$[\alpha]_D^{28}$ = – 37.5 (*c* 1.0, $CHCl_3$).

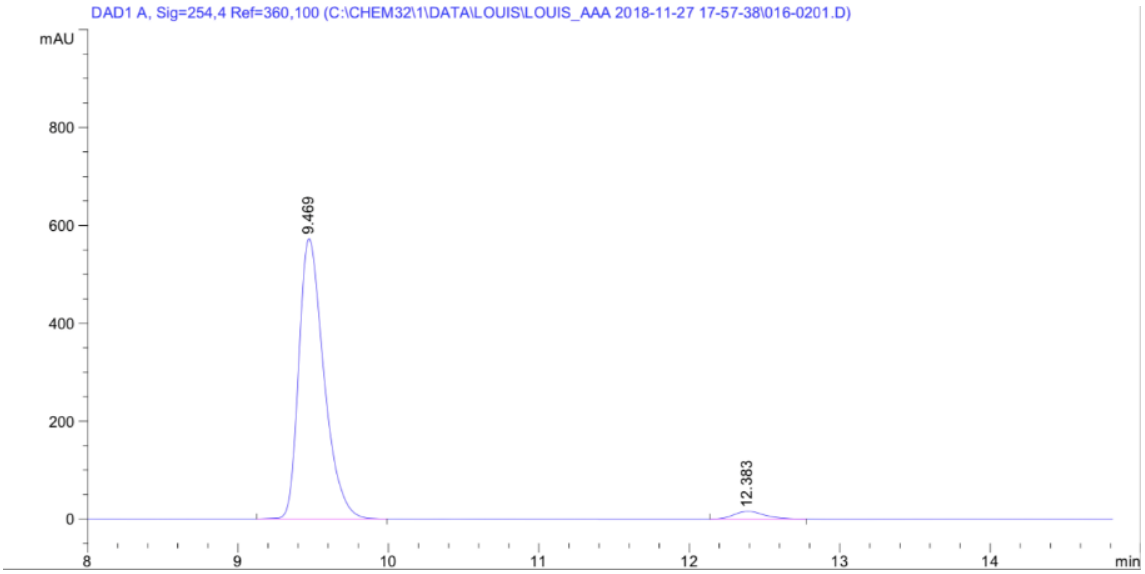
HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 93%.


f1 (ppm)


f1 (ppm)

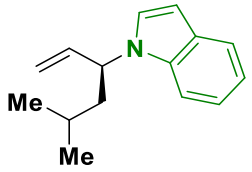


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.474	BB	0.1644	115.26079	10.63568	51.0550
2	12.405	BB	0.2193	110.49744	7.70669	48.9450



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.469	BB	0.1771	6635.59619	573.15259	96.6352
2	12.383	BB	0.2169	231.04927	16.14637	3.3648

***(S)*-1-(5-methylhex-1-en-3-yl)-1H-indole (6.4e)**



Procedures

The allylic acetate (31.2 mg, 0.2 mmol, 100 mol%) and the indole (46.9 mg, 0.4 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 48 hr). The title compound was obtained in 68% yield (29.0 mg, 0.14 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 40:1).

TLC (SiO_2) R_f = 0.63 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.64 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.23 – 7.15 (m, 2H), 7.10 (td, *J* = 7.4, 1.0 Hz, 1H), 6.55 (d, *J* = 3.1 Hz, 1H), 6.00 (ddd, *J* = 17.3, 10.4, 5.4 Hz, 1H), 5.16 – 5.09 (m, 1H), 5.02 – 4.95 (m, 2H), 2.00 (ddd, *J* = 13.8, 9.4, 5.7 Hz, 1H), 1.79 (ddd, *J* = 14.0, 8.2, 5.9 Hz, 1H), 1.53 – 1.42 (m, 1H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.7 Hz, 3H).

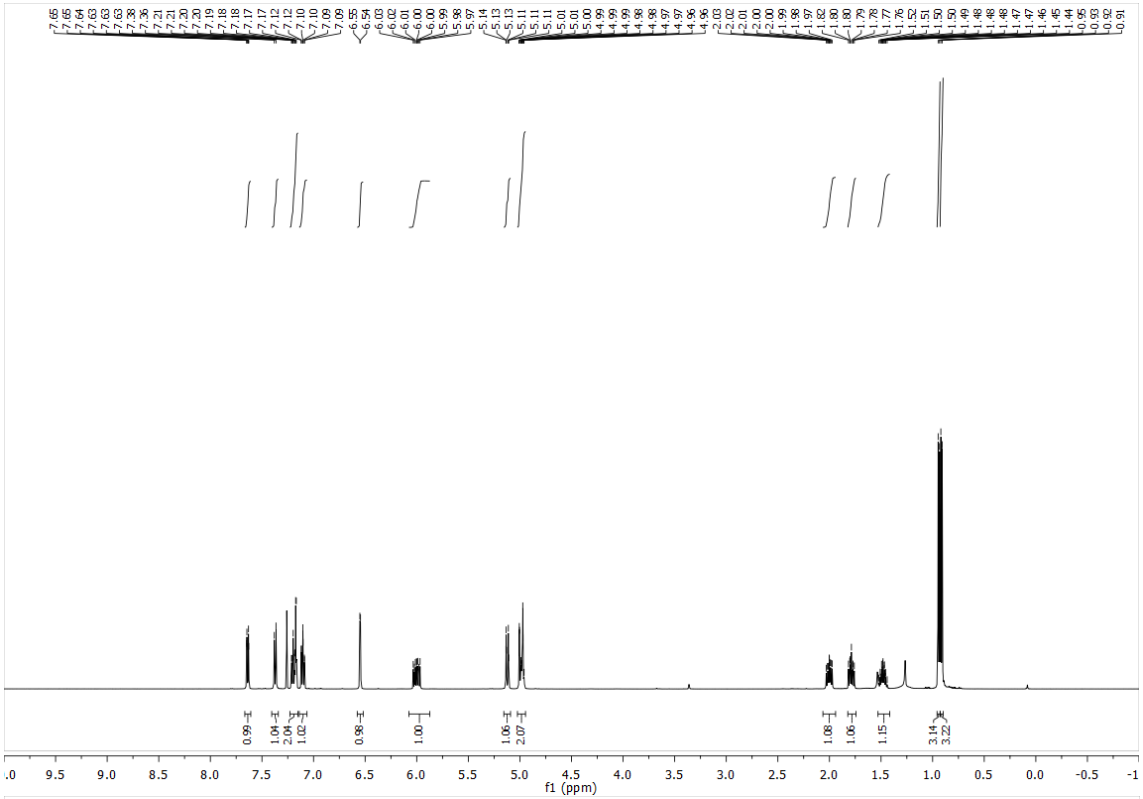
^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.2, 136.0, 128.5, 124.9, 121.3, 120.9, 119.3, 115.6, 109.6, 101.6, 56.0, 43.2, 24.6, 22.9, 22.2.

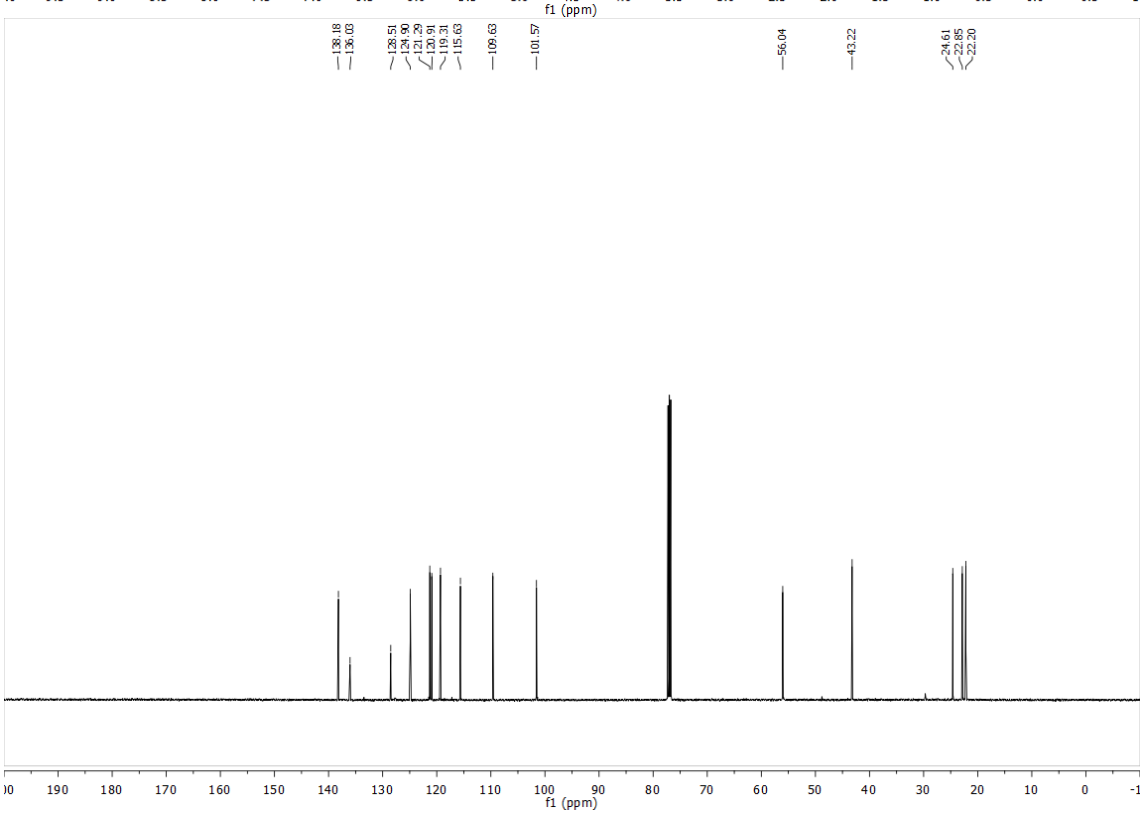
HRMS (ESI): Calculated for $C_{15}H_{19}N$ [M+H$^+$] = 214.1590, Found 214.1592.

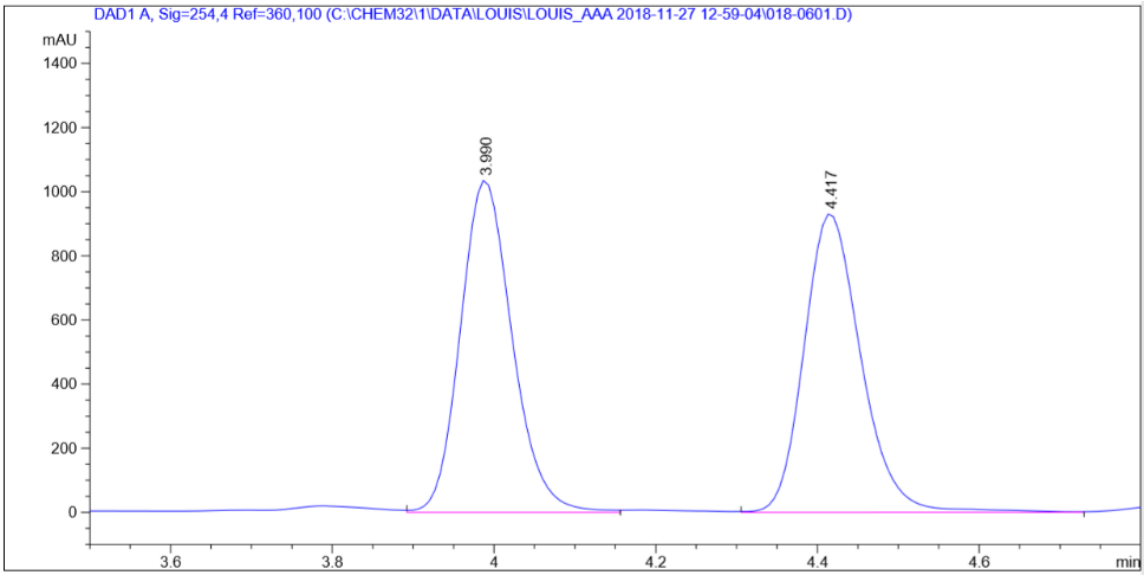
FTIR (neat): 2957, 1459, 1309, 1215, 923, 755, 739, 667 cm^{-1}.

$[\alpha]_D^{28}$ = +10.3 (*c* 1.0, $CHCl_3$).

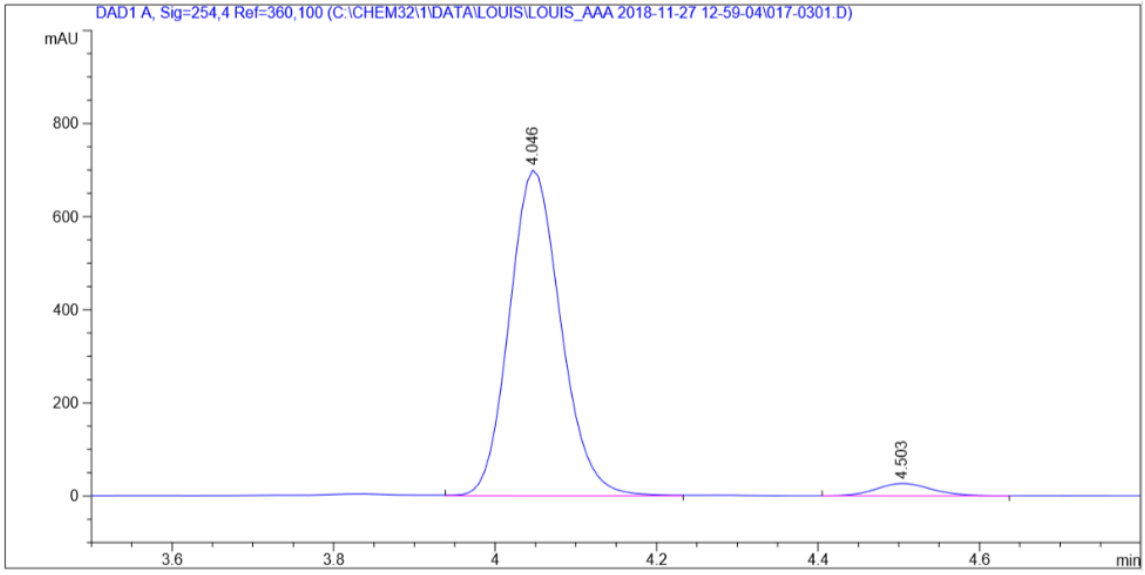
HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 92%.


f1 (ppm)


f1 (ppm)

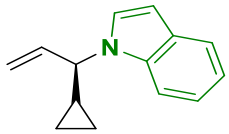


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.990	VV	0.0700	4615.55762	1036.52917	50.3166
2	4.417	VV	0.0750	4557.47168	932.08258	49.6834



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.046	VV	0.0696	3093.94727	700.01801	96.0607
2	4.503	BV	0.0737	126.87827	26.57938	3.9393

(*R*)-1-(1-cyclopropylallyl)-1H-indole (6.4f)



Procedures

The allylic acetate (61.7 mg, 0.44 mmol, 100 mol%) and the indole (103.1 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 74% yield (64.2 mg, 0.33 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 20 min).

TLC (SiO_2) R_f = 0.66 (heptanes: isopropyl acetate = 5:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (ddd, *J* = 7.8, 1.3, 0.7 Hz, 1H), 7.36 (d, *J* = 3.2 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.18 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.11 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 6.55 (dd, *J* = 3.2, 0.8 Hz, 1H), 6.03 (ddd, *J* = 17.2, 10.4, 5.3 Hz, 1H), 5.20 (ddd, *J* = 10.4, 1.2 Hz, 1H), 5.12 (ddd, *J* = 17.2, 1.7, 1.2 Hz, 1H), 4.29 (ddt, *J* = 8.5, 5.3, 1.7 Hz, 1H), 1.45 (qt, *J* = 8.2, 4.9 Hz, 1H), 0.86 – 0.75 (m, 1H), 0.62 (dddd, *J* = 9.1, 8.0, 5.7, 4.7 Hz, 1H), 0.49 (ddt, *J* = 9.4, 5.8, 4.8 Hz, 1H), 0.38 (ddt, *J* = 9.4, 5.8, 4.9 Hz, 1H).

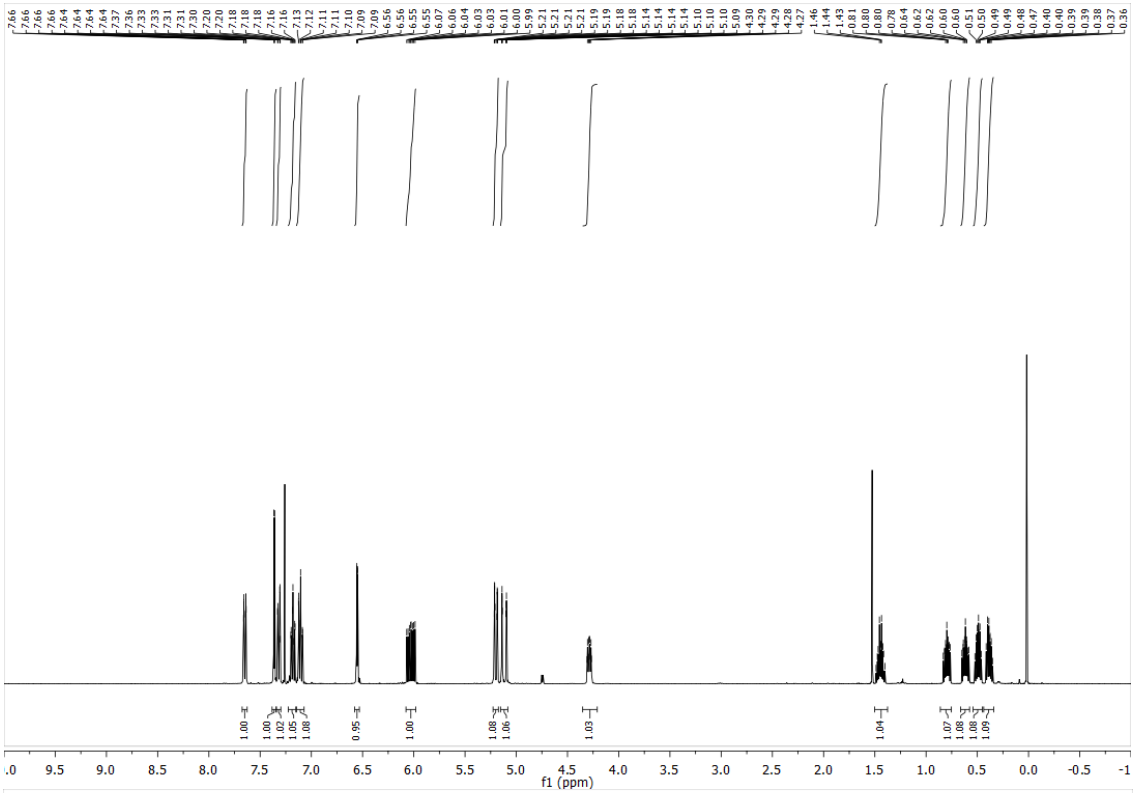
^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.7, 136.0, 128.7, 125.6, 121.2, 120.9, 119.3, 116.4, 109.9, 101.2, 62.6, 14.9, 4.4, 3.6.

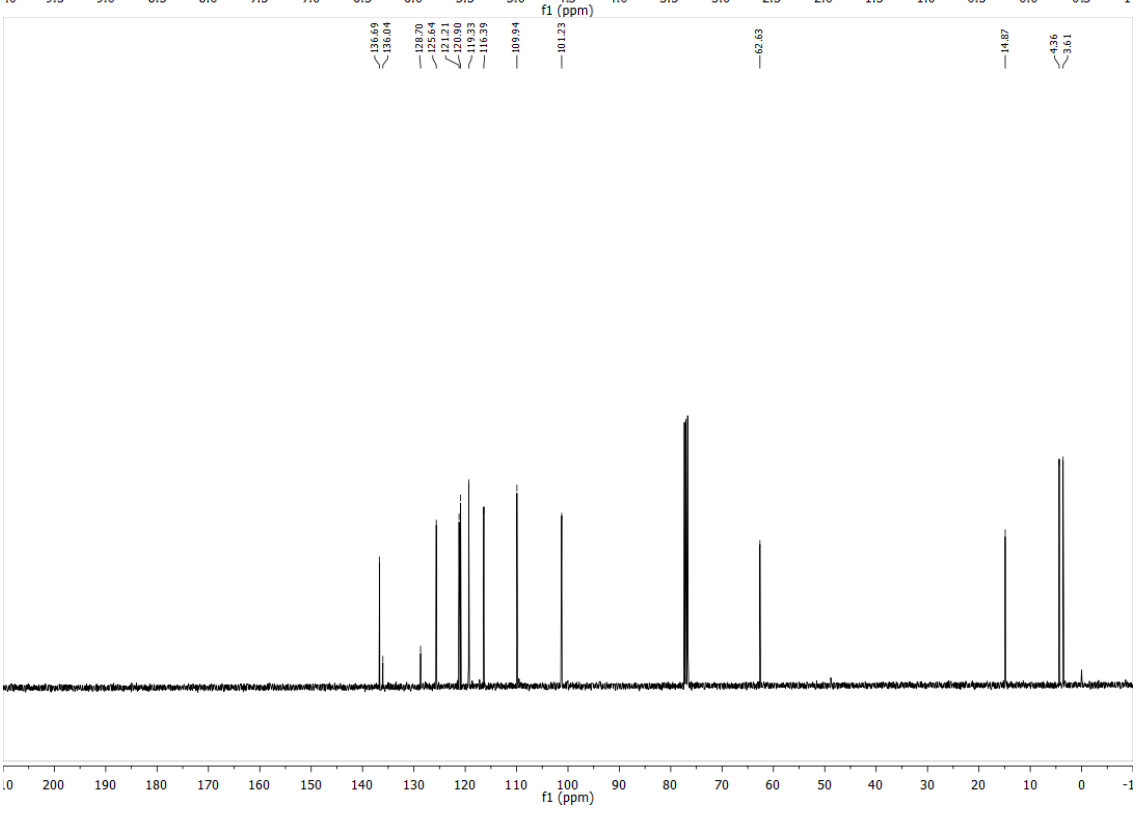
HRMS (ESI): Calculated for $C_{14}H_{15}N$ [M+H$^+$] = 198.1283, Found 198.1279.

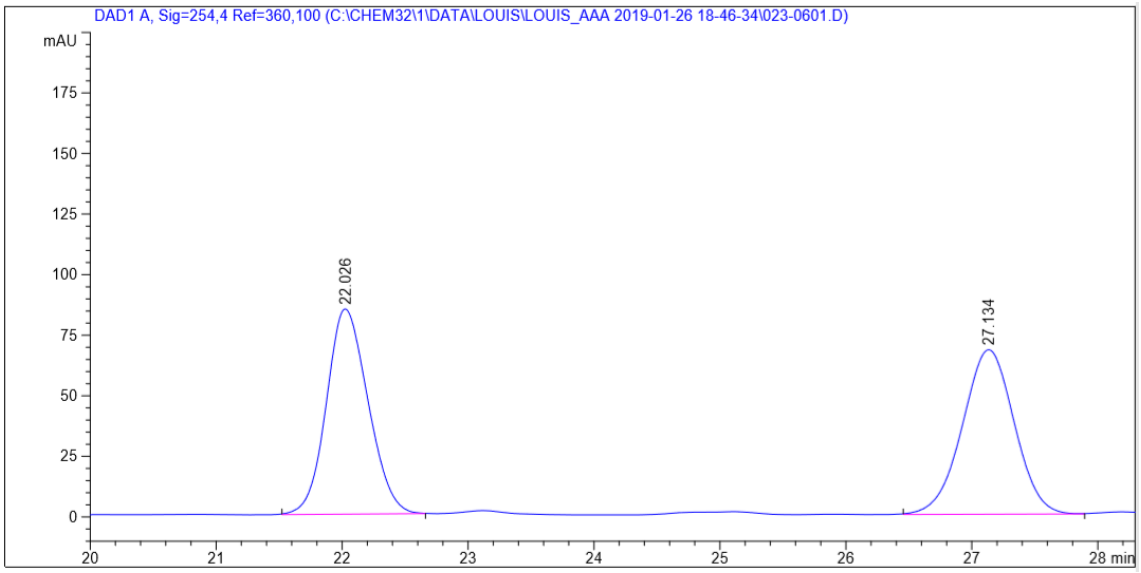
FTIR (neat): 3007, 1458, 1308, 1264, 1218, 927, 737 cm^{-1}.

$[\alpha]_D^{28}$= +25.5 (*c* 1.0, $CHCl_3$).

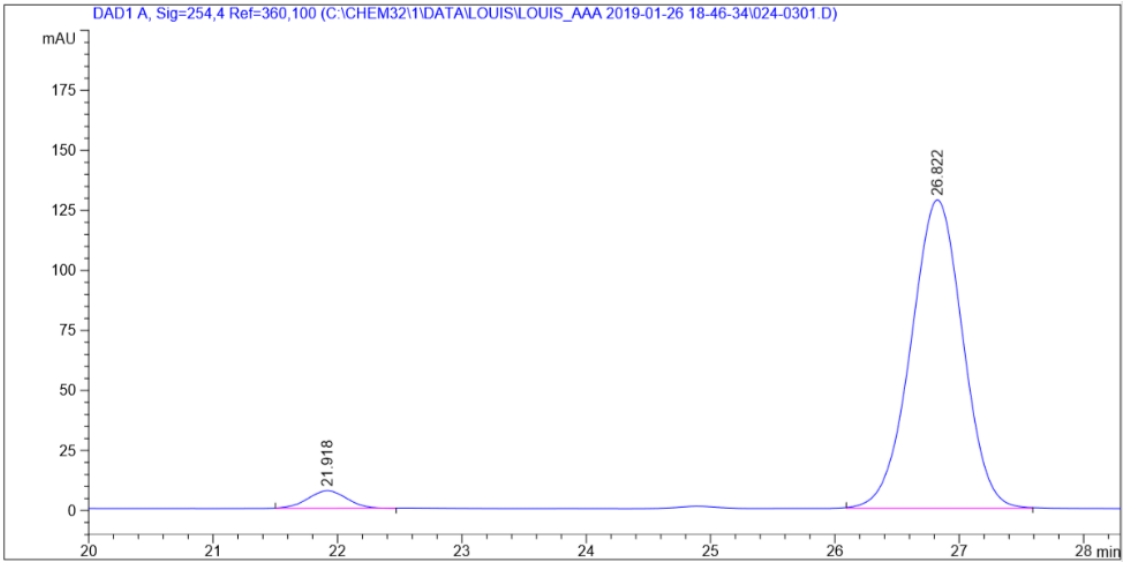
HPLC (Two connected chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 254 nm), *ee* = 92%.


f1 (ppm)


f1 (ppm)

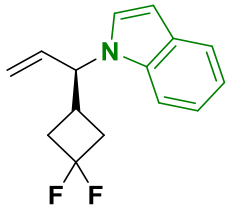


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.026	BB	0.3558	1944.38708	84.72250	50.0336
2	27.134	BB	0.4455	1941.77197	67.91904	49.9664



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.918	BB	0.3218	156.23650	7.29569	4.0415
2	26.822	BB	0.4490	3709.60669	128.43961	95.9585

(*R*)-1-(1-(3,3-difluorocyclobutyl)allyl)-1H-indole (6.4g)



Procedures

The allylic acetate (83.7 mg, 0.44 mmol, 100 mol%) and the indole (103.1 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 24 hr). The title compound was obtained in 70% yield (76.2 mg, 0.31 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 20 min).

TLC (SiO_2) R_f = 0.60 (heptanes: isopropyl acetate = 5:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.37 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.21 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.15 – 7.10 (m, 1H), 7.09 (d, *J* = 3.3 Hz, 1H), 6.55 (dd, *J* = 3.3, 0.8 Hz, 1H), 5.95 (ddd, *J* = 17.2, 10.4, 6.0 Hz, 1H), 5.24 (dt, *J* = 10.4, 1.1 Hz, 1H), 5.12 (ddd, *J* = 17.2, 1.5, 0.9 Hz, 1H), 4.84 – 4.73 (m, 1H), 2.89 – 2.79 (m, 2H), 2.59 – 2.42 (m, 2H), 2.29 – 2.15 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.2, 134.6, 128.6, 124.6, 121.8, 121.1, 119.7, 119.4(m), 117.8, 109.6, 102.4, 62.7 (d, *J* = 4.1 Hz), 38.9 (dt, *J* = 49.0, 23.0 Hz), 26.8 (dd, *J* = 11.2, 7.9 Hz).

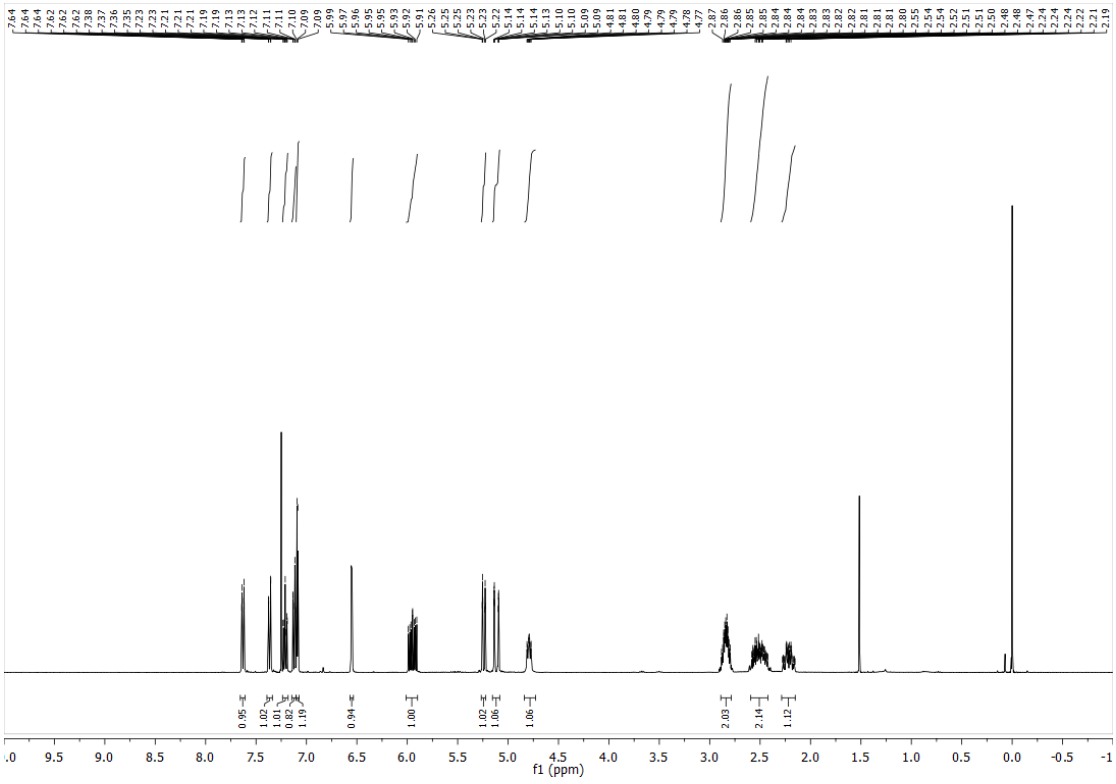
^{19}F NMR (376 MHz, $CDCl_3$): δ = -83.08 – -84.39 (m, 1F), -92.95 – -94.40 (m, 1F).

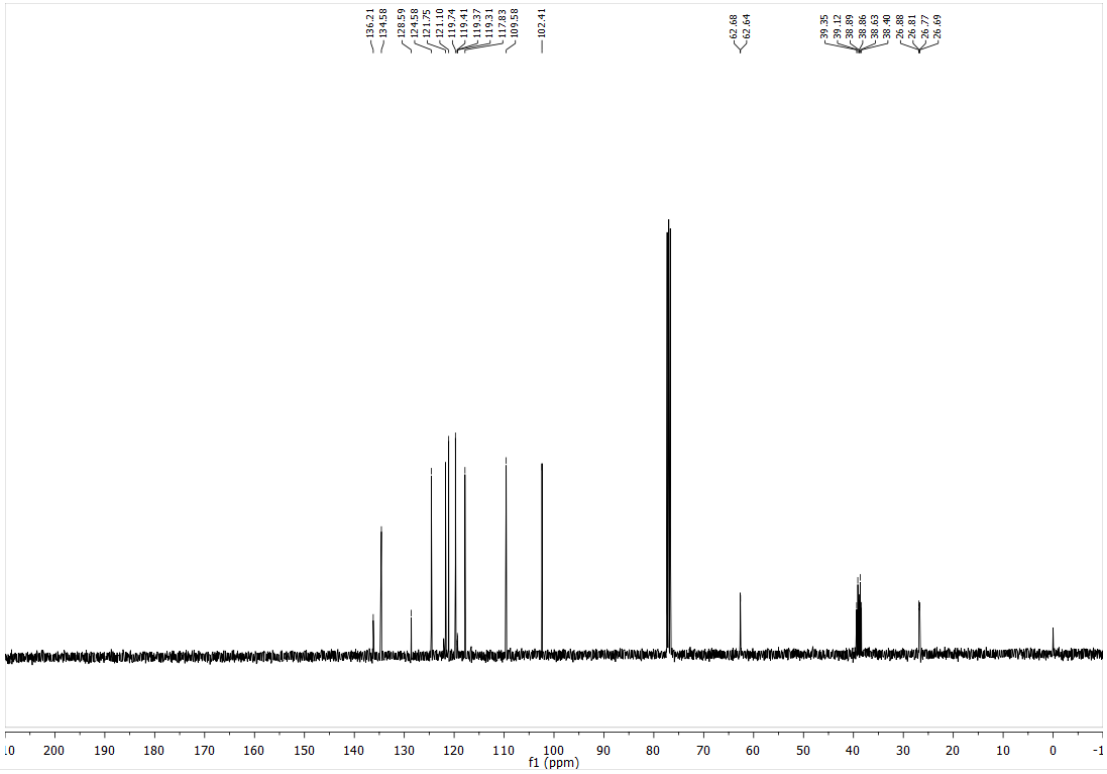
HRMS (ESI): Calculated for $C_{15}H_{15}NF_2$ [M+H$^+$] = 248.1245, Found 248.1247.

FTIR (neat): 3052, 1458, 1298, 1265, 1171, 901, 737 cm^{-1}.

$[\alpha]_D^{28}$= +14.0 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AD-3 column, heptanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 90%.




136.21
134.58
128.59
124.58
121.75
121.10
119.74
119.41
119.37
119.31
117.83
109.58
102.41
62.68
62.64
39.35
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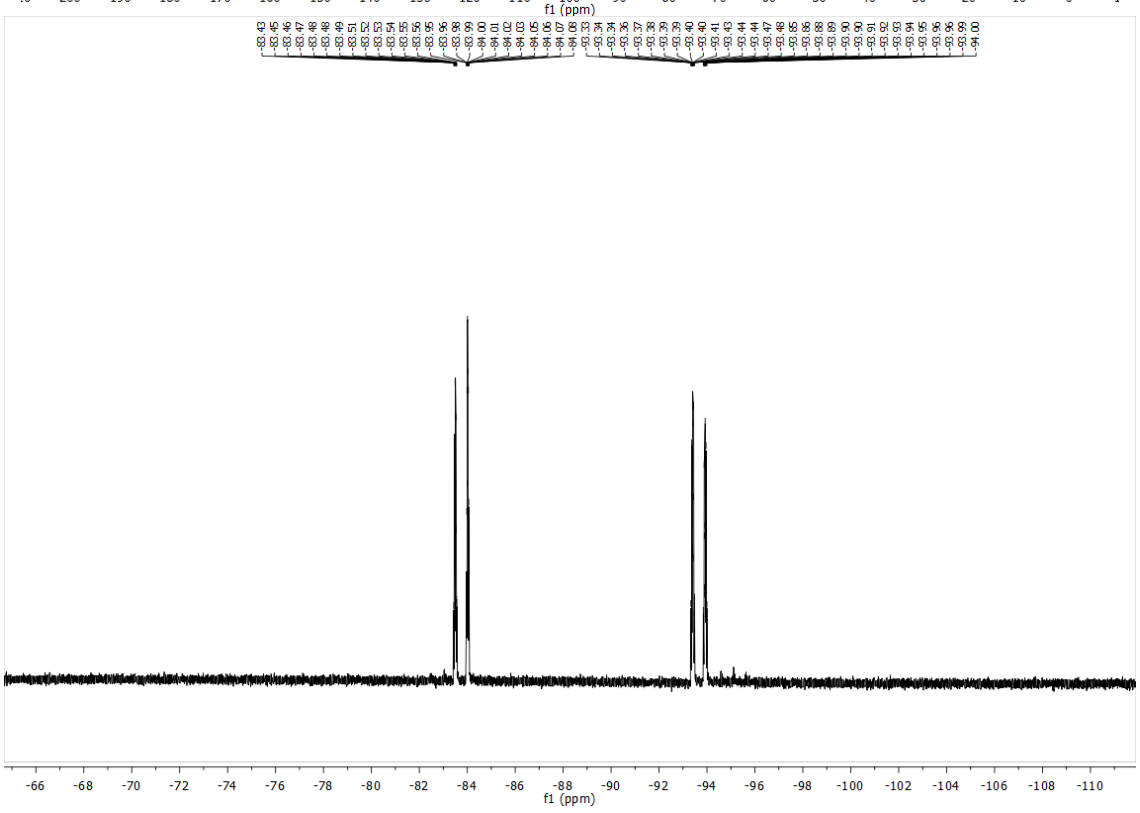
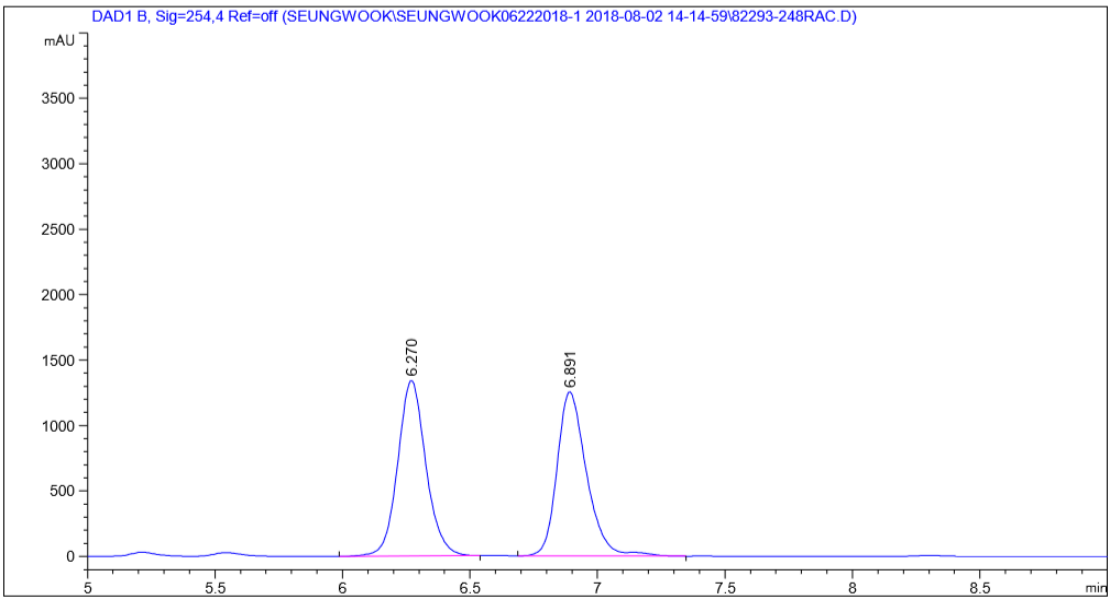
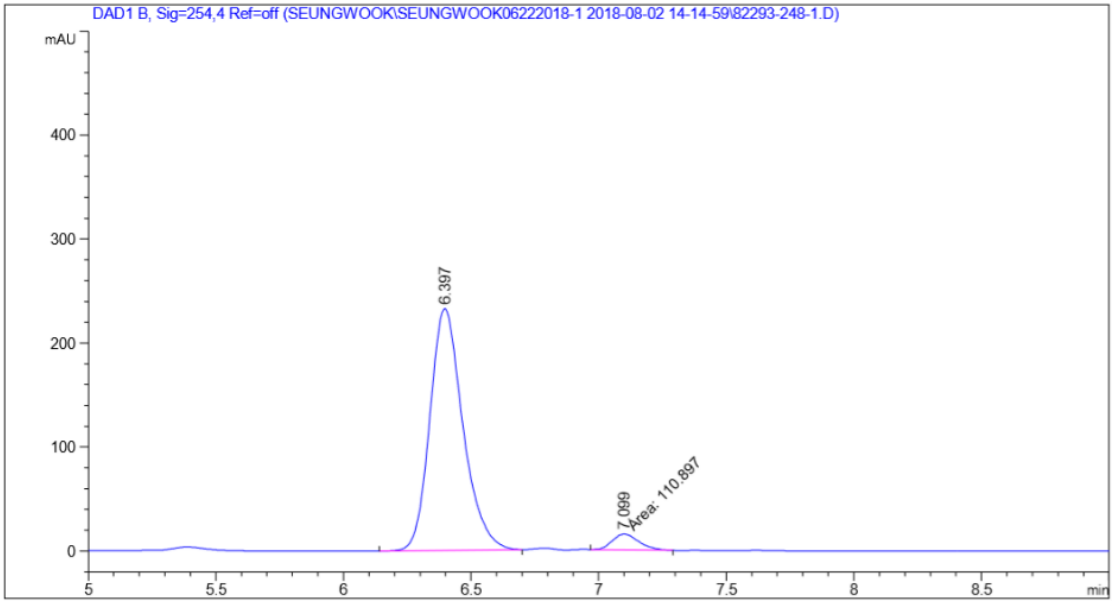
38.89
38.86
38.63
38.40
26.88
26.81
26.77
26.69
f1 (ppm)


f1 (ppm)

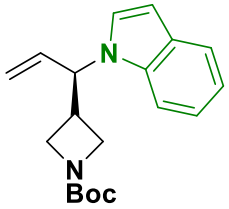


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.270	BB	0.1153	1.02753e4	1341.92273	50.4968
2	6.891	BB	0.1218	1.00731e4	1253.07727	49.5032



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.397	BB	0.1371	2095.27197	232.68350	94.9733
2	7.099	MM	0.1208	110.89703	15.30575	5.0267

tert-butyl (*R*)-3-(1-(1H-indol-1-yl)allyl)azetidine-1-carboxylate (6.4h)



Procedures

The allylic acetate (51.1 mg, 0.2 mmol, 100 mol%) and the indole (46.9 mg, 0.4 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 24 hr). The title compound was obtained in 74% yield (46.2 mg, 0.15 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 6:1).

TLC (SiO_2) R_f = 0.39 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 1H), 7.22 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.16 – 7.08 (m, 1H), 7.05 (d, *J* = 3.3 Hz, 1H), 6.55 (d, *J* = 3.1 Hz, 1H), 5.93 (ddd, *J* = 16.8, 10.4, 6.0 Hz, 1H), 5.25 (dt, *J* = 10.5, 1.1 Hz, 1H), 5.12 (dt, *J* = 17.1, 1.1 Hz, 1H), 5.06 – 4.98 (m, 1H), 4.16 (t, *J* = 8.6 Hz, 1H), 3.90 (t, *J* = 8.6 Hz, 1H), 3.83 (dd, *J* = 8.9, 5.2 Hz, 1H), 3.55 (dd, *J* = 9.1, 5.3 Hz, 1H), 3.22 (dtt, *J* = 10.6, 8.1, 5.3 Hz, 1H), 1.43 (s, 9H).

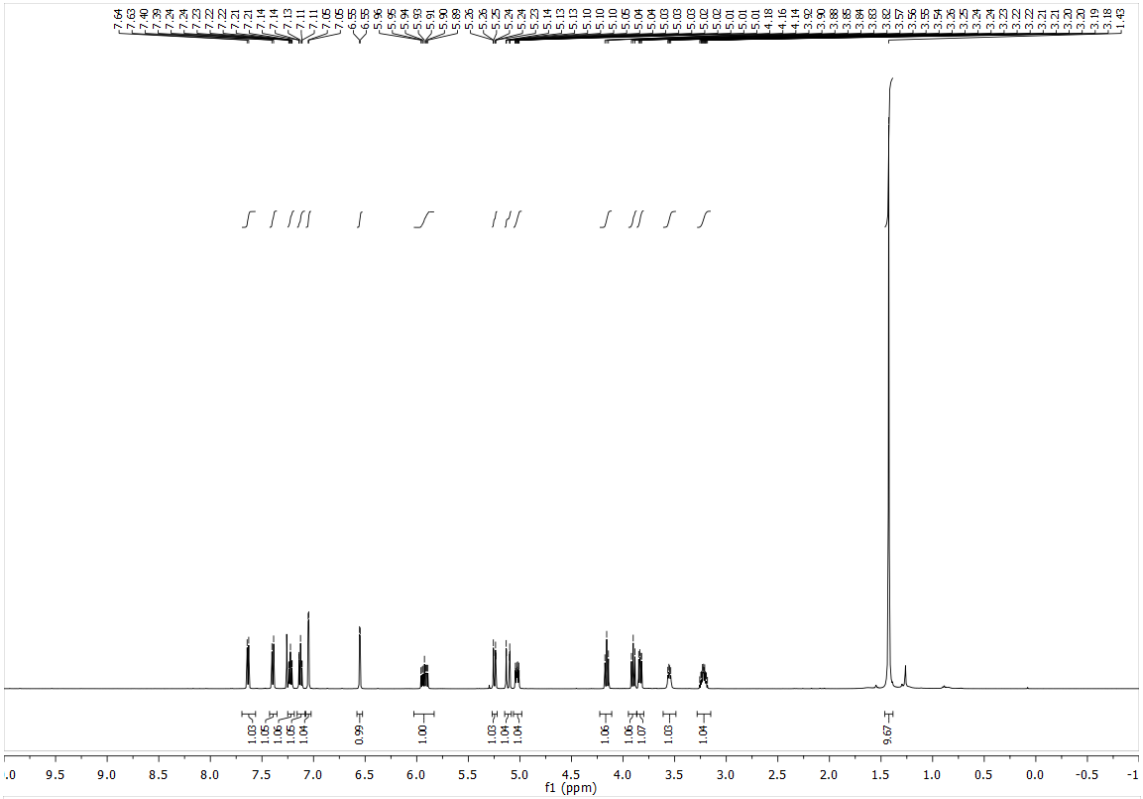
^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.2, 136.1, 134.3, 128.6, 124.4, 121.7, 121.1, 119.7, 117.9, 109.7, 102.4, 79.7, 61.6, 32.0, 28.3.

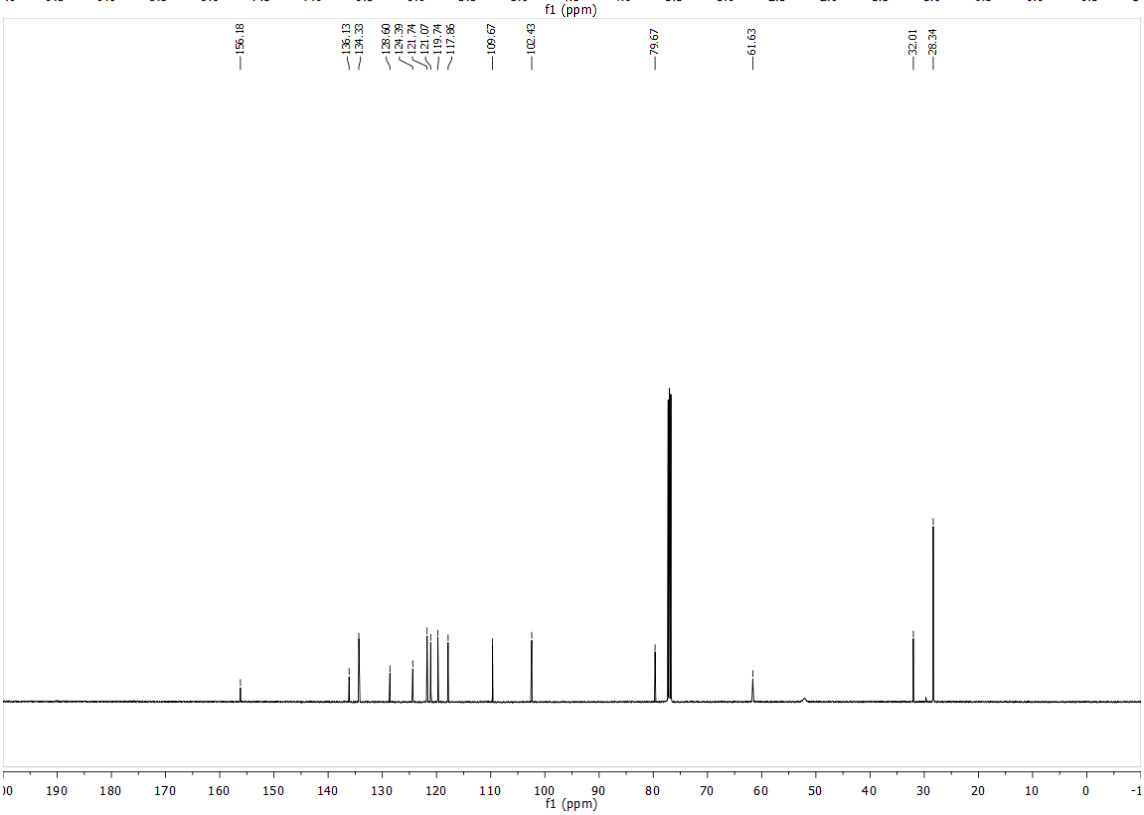
HRMS (ESI): Calculated for $C_{19}H_{24}N_2O_2$ [M+Na^+] = 335.1730, Found 335.1738.

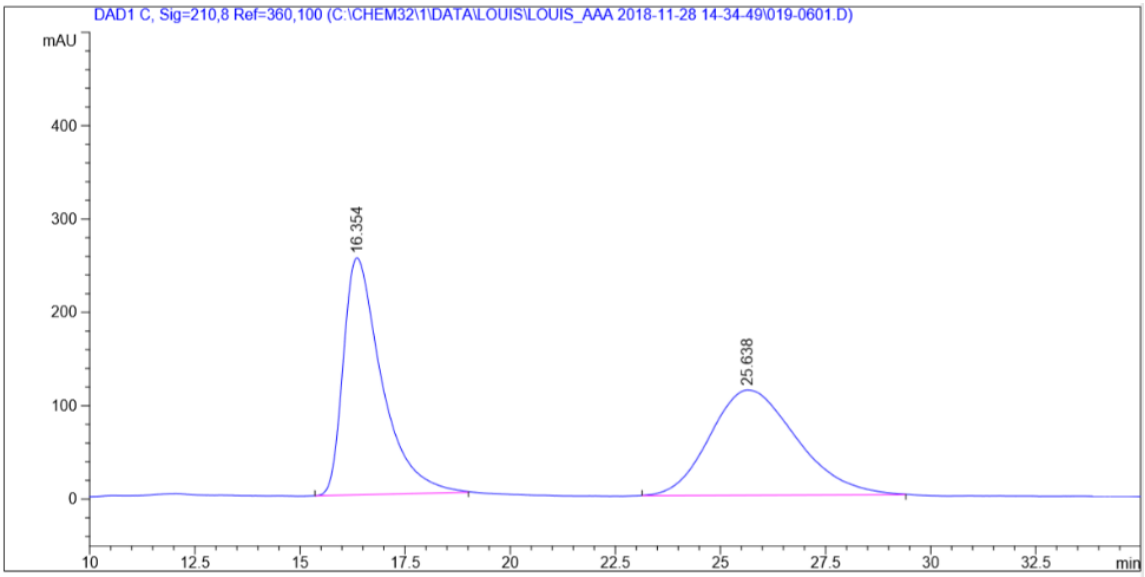
FTIR (neat): 2973, 1693, 1405, 1366, 1216, 1143, 931, 741 cm^{-1}.

$[\alpha]_D^{28}$= +25.5 (*c* 1.0, $CHCl_3$).

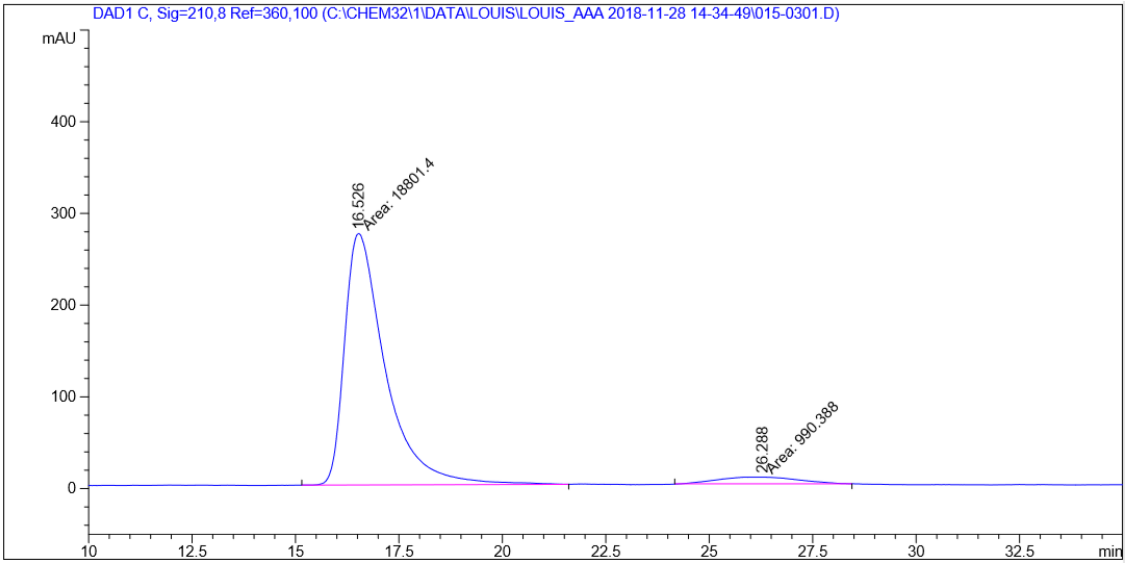
HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm), *ee* = 90%.


f1 (ppm)


f1 (ppm)

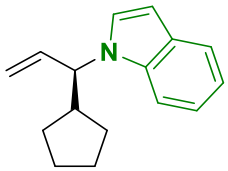


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.354	BB	0.9288	1.61213e4	253.89438	49.8715
2	25.638	BB	1.6917	1.62044e4	112.81745	50.1285



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.526	MM	1.1433	1.88014e4	274.07758	94.9960
2	26.288	MM	2.2510	990.38843	7.33282	5.0040

(*R*)-1-(1-cyclopentylallyl)-1H-indole (6.4i)



Procedures

The allylic acetate (33.6 mg, 0.2 mmol, 100 mol%) and the indole (46.9 mg, 0.4 mmol, 200 mol%) were subject to standard reaction conditions (70 ^{o}C, 60 hr). The title compound was obtained in 64% yield (28.8 mg, 0.13 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 40:1).

TLC (SiO_2) R_f = 0.63 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.63 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.22 – 7.16 (m, 2H), 7.09 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.54 (d, *J* = 3.5 Hz, 1H), 6.06 (ddd, *J* = 16.9, 10.4, 6.3 Hz, 1H), 5.12 (dt, *J* = 10.4, 1.3 Hz, 1H), 5.00 (dt, *J* = 17.1, 1.3 Hz, 1H), 4.62 – 4.52 (m, 1H), 2.64 – 2.48 (m, 1H), 1.94 (dtd, *J* = 12.5, 7.6, 4.5 Hz, 1H), 1.71 (dddd, *J* = 16.2, 10.2, 7.5, 3.0 Hz, 1H), 1.67 – 1.55 (m, 2H), 1.55 – 1.49 (m, 2H), 1.43 (dq, *J* = 12.8, 8.4 Hz, 1H), 1.18 – 1.08 (m, 1H).

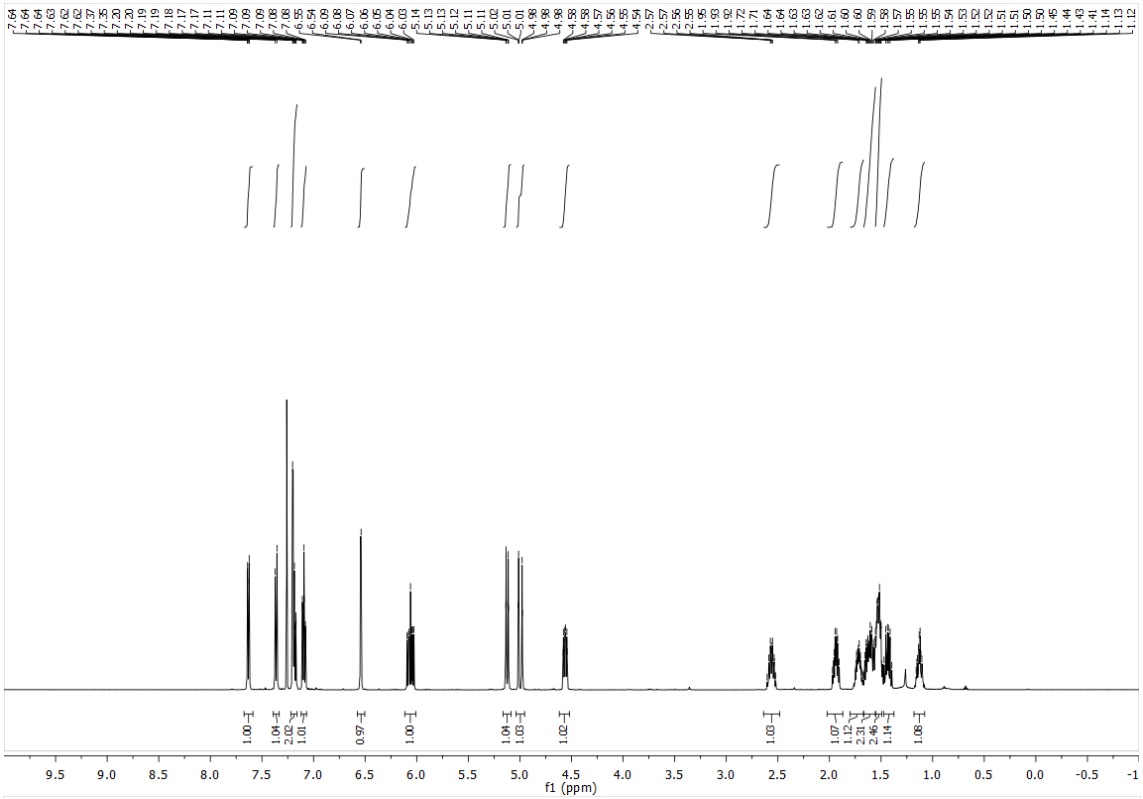
^{13}C NMR (125 MHz, $CDCl_3$): δ = 137.1, 136.3, 128.4, 125.4, 121.2, 120.9, 119.3, 116.4, 109.8, 101.5, 63.8, 44.2, 30.8, 30.3, 25.6, 25.1.

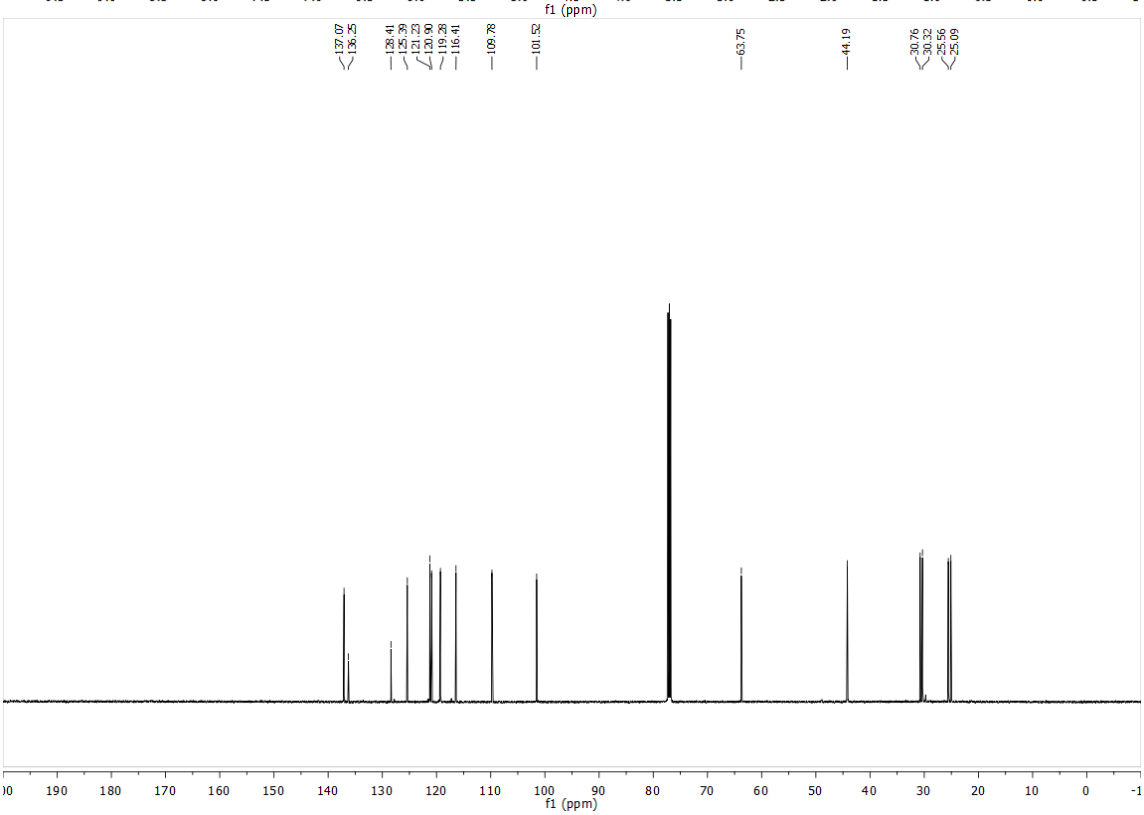
HRMS (ESI): Calculated for $C_{16}H_{19}N$ [M+H$^+$] = 226.1590, Found 226.1588.

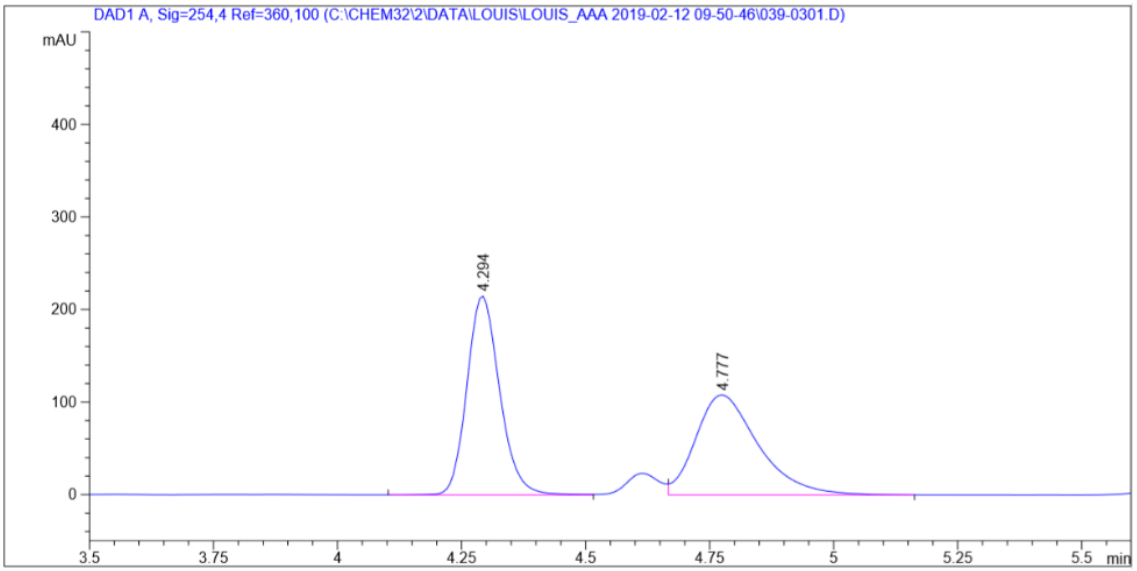
FTIR (neat): 2955, 1458, 1215, 987, 924, 754, 738, 667 cm^{-1}.

$[\alpha]_D^{28}$ = +23.0 (*c* 1.0, $CHCl_3$).

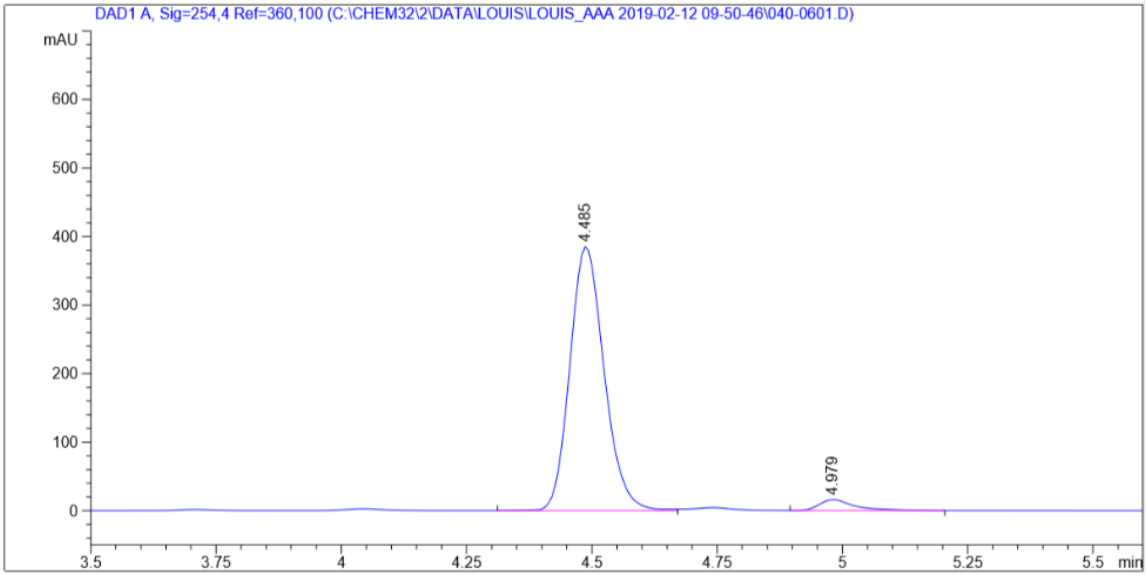
HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 92%.





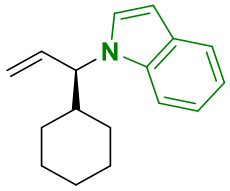


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.294	VB	0.0696	988.51697	215.21788	50.9640
2	4.777	VB	0.1326	951.11951	108.19317	49.0360



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.485	BB	0.0735	1833.39441	385.62463	95.8892
2	4.979	VB	0.0706	78.59872	16.18746	4.1108

(*R*)-1-(1-cyclohexylallyl)-1H-indole (6.4j)



Procedures

The allylic acetate (80.2 mg, 0.44 mmol, 100 mol%) and the indole (103.1 mg, 0.88 mmol, 200 mol%) were subject to standard reaction conditions (70 °C, 60 hr). The title compound was obtained in 60% yield (63.2 mg, 0.26 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 10% over 20 min).

TLC (SiO_2) R_f = 0.60 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (ddd, *J* = 7.8, 1.3, 0.8 Hz, 1H), 7.37 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.19 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.16 (d, *J* = 3.2 Hz, 1H), 7.09 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 6.54 (dd, *J* = 3.2, 0.9 Hz, 1H), 6.11 (ddd, *J* = 17.0, 10.3, 7.5 Hz, 1H), 5.23 – 5.08 (m, 2H), 4.56 – 4.47 (m, 1H), 1.99 – 1.89 (m, 2H), 1.80 (ddq, *J* = 13.2, 3.4, 1.8 Hz, 1H), 1.70 – 1.57 (m, 2H), 1.36 – 1.00 (m, 5H), 0.93 – 0.82 (m, 1H).

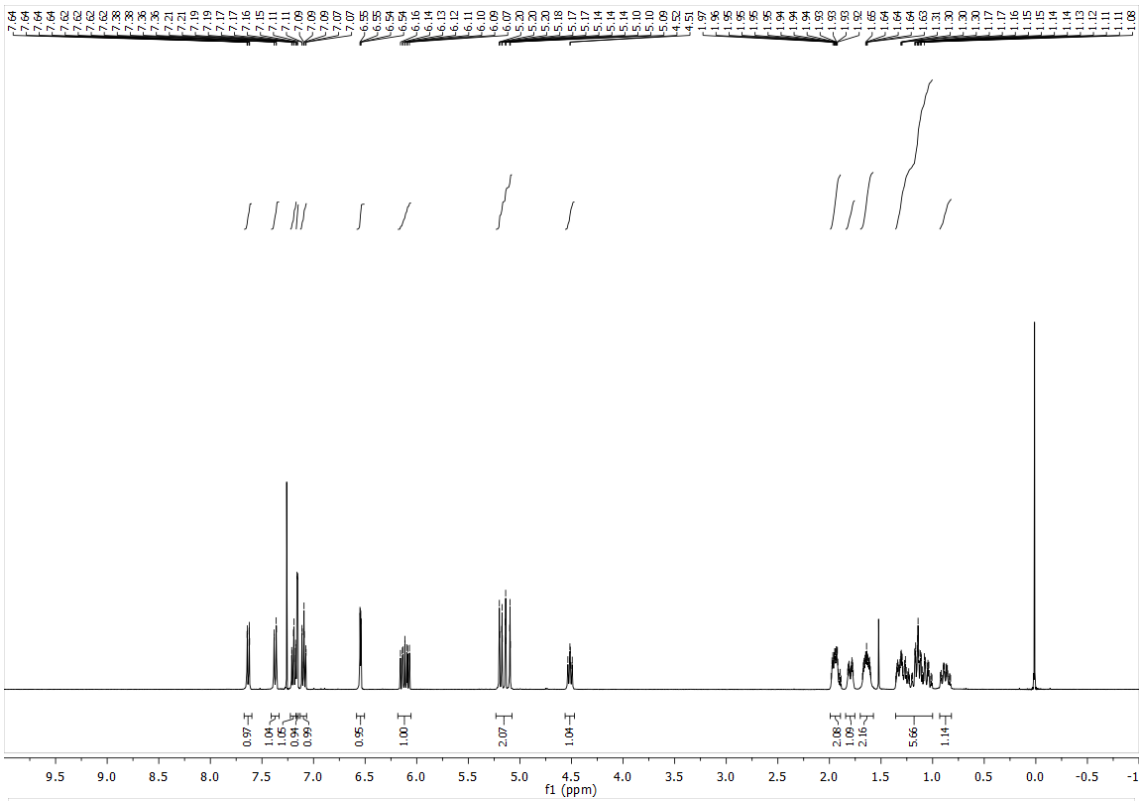
^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.2, 136.0, 128.3, 125.3, 121.2, 120.9, 119.2, 117.6, 109.8, 101.5, 64.4, 41.9, 30.6, 29.8, 26.3, 26.0, 25.8.

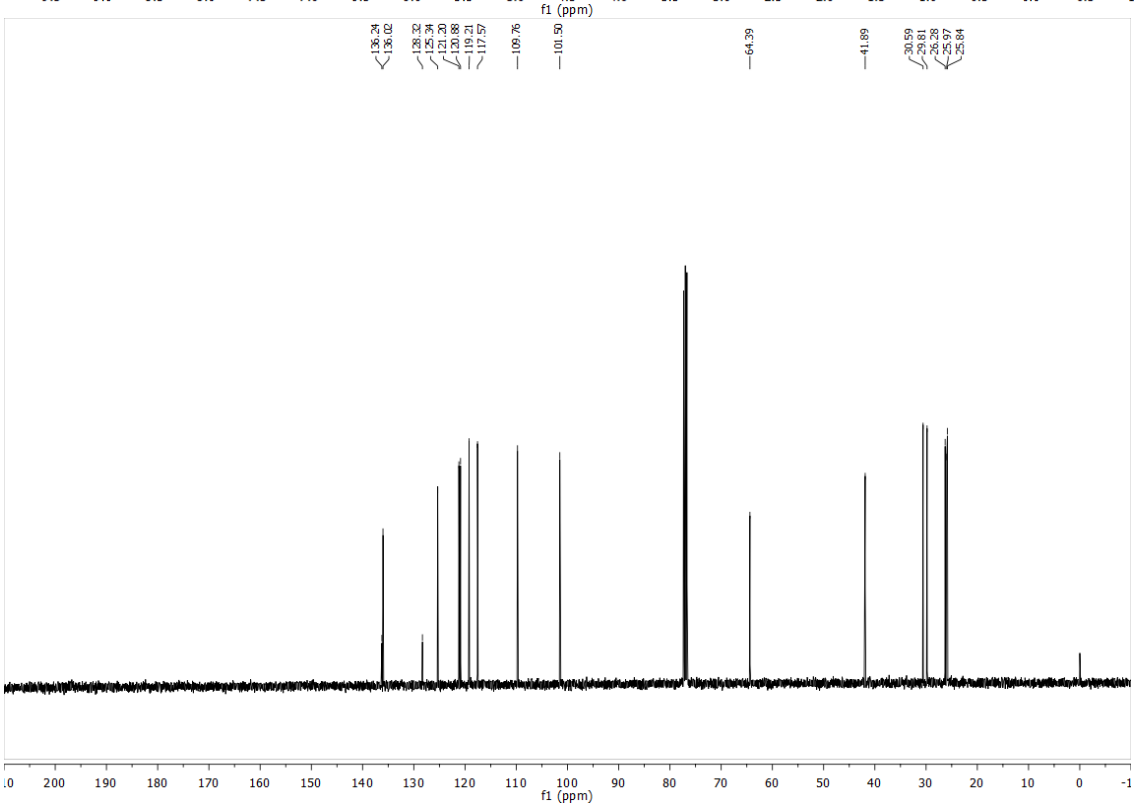
HRMS (ESI): Calculated for $C_{17}H_{21}N$ [M+H$^+$] = 240.1747, Found 240.1752.

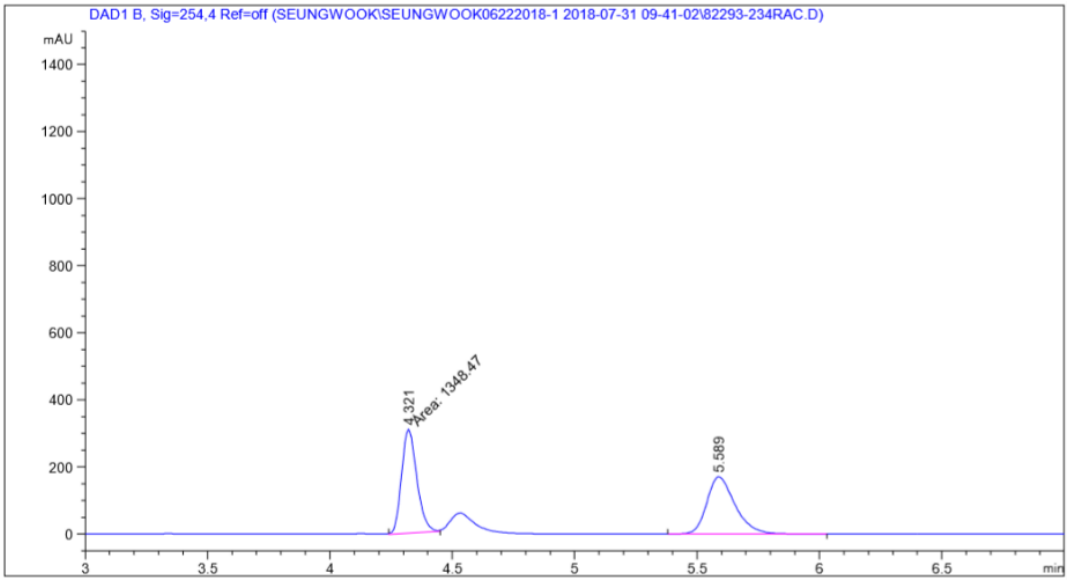
FTIR (neat): 2922, 2850, 1509, 1457, 1304, 1263, 1203, 986, 924, 734 cm^{-1}.

$[\alpha]_D^{28}$ = +40.9 (*c* 0.2, $CHCl_3$).

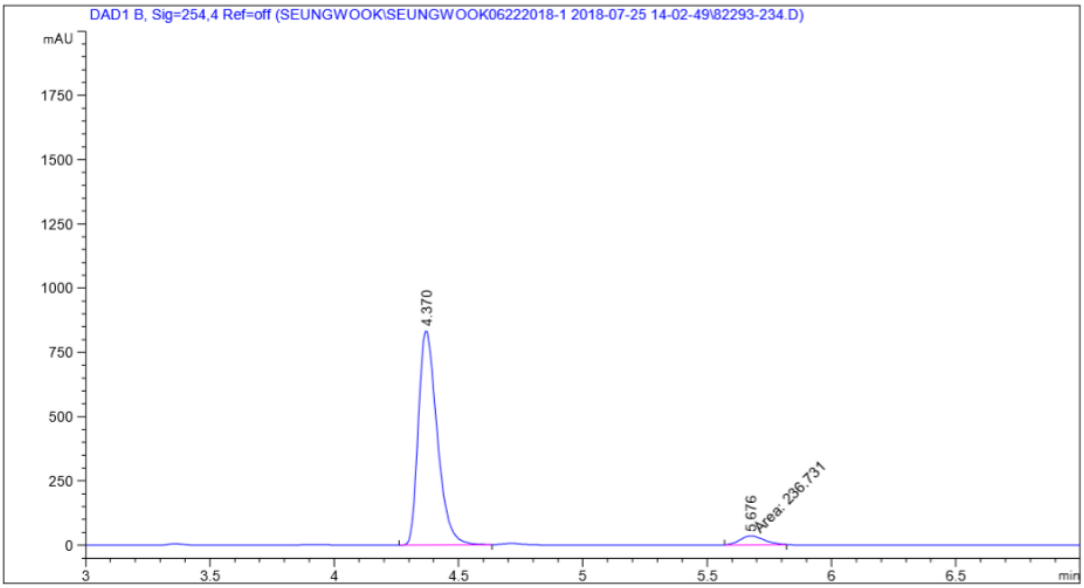
HPLC (Chiralcel AD-3 column, heptanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 90%.


f1 (ppm)


f1 (ppm)



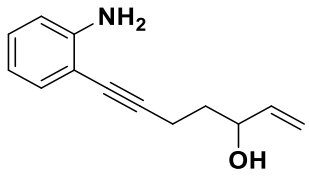
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.321	MM	0.0725	1348.46997	310.06155	49.7787
2	5.589	BB	0.1212	1360.46155	170.27304	50.2213



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.370	BB	0.0812	4375.51221	834.19043	94.8673
2	5.676	MM	0.1140	236.73058	34.61901	5.1327

Procedures and Spectral Data for Synthesis of 6.5a, 6.6a

7-(2-aminophenyl)hept-1-en-6-yn-3-ol (6.5a')



Procedures

To a round-bottomed flask charged with 2-Iodoaniline (527.8 mg, 2.41 mmol, 100 mol%), hept-1-en-6-yn-3-ol[8] (318.6 mg, 2.89 mmol, 120 mol%), copper iodide (50.1 mg, 0.26 mmol, 10 mol%) and Tetrakis(triphenylphosphine)palladium (60.8 mg, 0.053 mmol, 2 mol%) under an argon atmosphere was added triethylamine (4.8 mL, 0.5 M). The reaction was placed in an oil bath at 40 °C for 24 hours, at which point saturated aqueous ammonium chloride (5 mL) were added and the mixture was transferred to a separatory funnel. The organic layer was extracted with ethyl acetate (10 mL × 3) and the combined organic layers were washed with H_2O (10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–3:1) to furnish the title compound as a light yellow oil (408.6 mg, 2.03 mmol) in 84% yield.

TLC (SiO_2) R_f = 0.33 (dichloromethane: diethyl ether = 4:1).

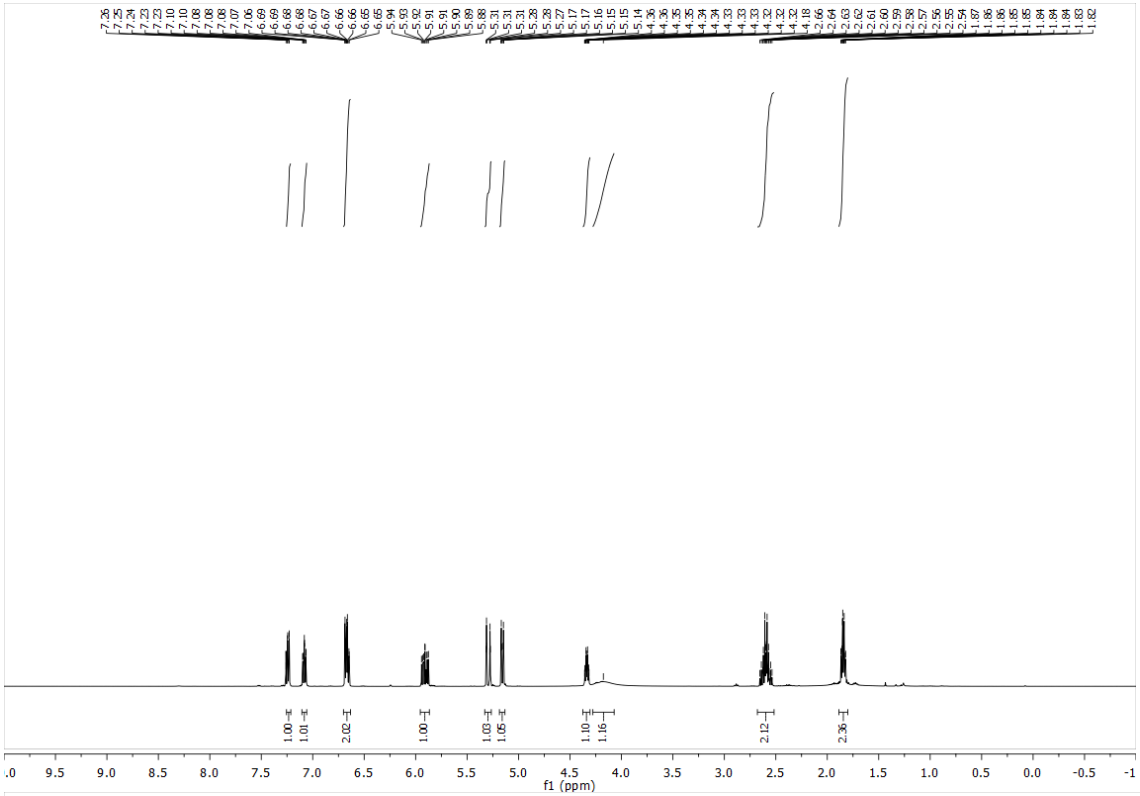
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.24 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.08 (ddd, *J* = 8.7, 7.4, 1.6 Hz, 1H), 6.70 – 6.63 (m, 2H), 5.91 (ddd, *J* = 17.1, 10.4, 6.0 Hz, 1H), 5.29 (dt, *J* =

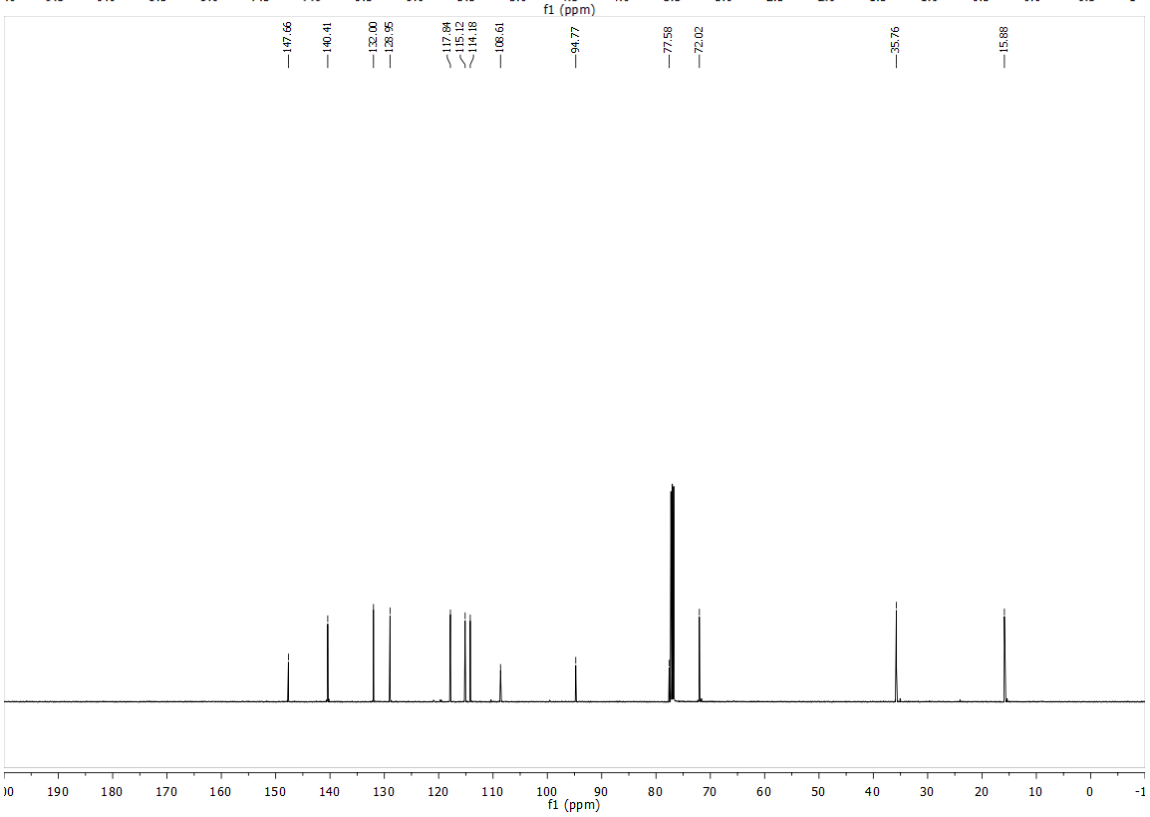
17.2, 1.4 Hz, 1H), 5.16 (dt, *J* = 10.5, 1.3 Hz, 1H), 4.37 – 4.31 (m, 1H), 4.18 (br, 1H), 2.68 – 2.52 (m, 2H), 1.84 (qd, *J* = 7.1, 1.9 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.7, 140.4, 132.0, 129.0, 117.8, 115.1, 114.2, 108.6, 94.8, 77.6, 72.0, 35.8, 15.9.

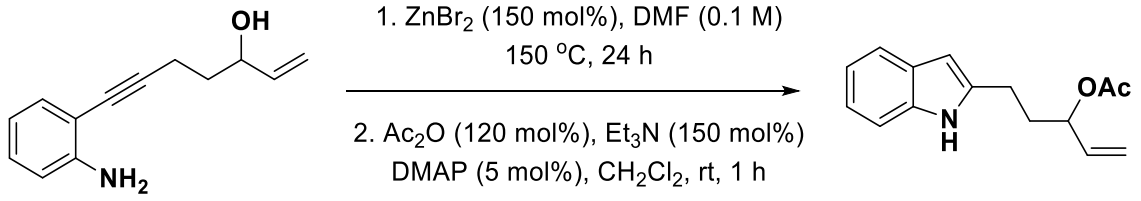
HRMS (ESI): Calculated for $C_{13}H_{15}NO$ $[M+H^+]$ = 202.1226, Found 202.1233.

FTIR (neat): 3530, 2923, 1613, 1492, 1455, 1307, 1120, 1051, 991, 923, 748 cm^{-1}.


f1 (ppm)


f1 (ppm)

5-(1H-indol-2-yl)pent-1-en-3-yl acetate (6.5a)



Procedures

To a round-bottomed flask charged with **6.5a'** (408.6 mg, 2.03 mmol, 100 mol%) and zinc bromide (685.7 mg, 3.04 mmol, 150 mol%) under an argon atmosphere was added dimethylformamide (20.3 mL, 0.1 M). The reaction was placed in an oil bath at 150 °C for 24 hours. After reaching ambient temperature, the mixture was concentrated under reduced pressure, at which point ethyl acetate (10 mL) and H_2O (10 mL) were added and the mixture was transferred to a separatory funnel. The organic layer was extracted with ethyl acetate (10 mL × 3) and the combined organic layers were washed with H_2O (15 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to the next step without further purification.

To a round-bottomed flask charged with the crude substrate and 4-dimethylaminopyridine (12.4 mg, 0.10 mmol, 5 mol%) under an argon atmosphere was added CH_2Cl_2 (10.1 mL, 0.2 M with respect to **5a'**), followed by acetic anhydride (0.23 mL, 2.4 mmol, 120 mol%) and triethylamine (0.42 mL, 3.0 mmol, 150 mol%). After 1 hour, saturated aqueous sodium bicarbonate (10 mL) was added and the mixture was transferred to a separatory funnel. The organic layer was extracted with CH_2Cl_2 (10 mL × 2) and the combined organic layers were washed with 1 N HCl (10 mL), dried ($MgSO_4$),

filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 8:1–4:1) to furnish the title compound as a light yellow oil (350.4 mg, 1.44 mmol) in 71% yield over 2 steps.

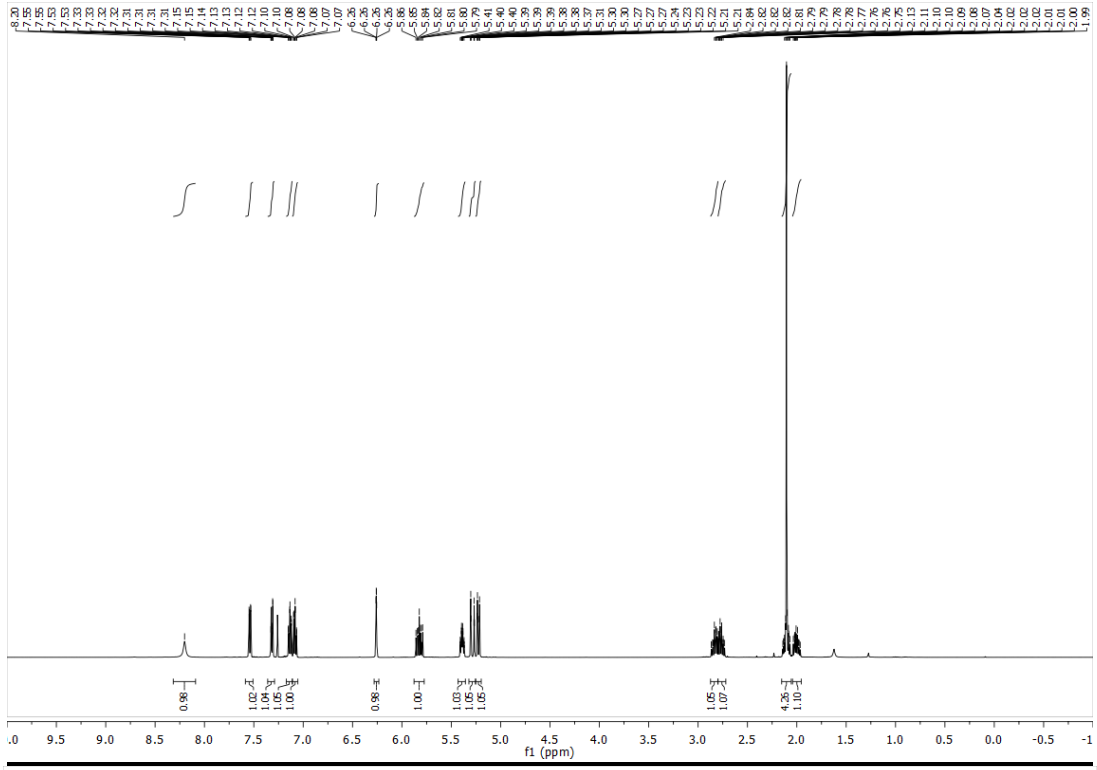
TLC (SiO_2) R_f = 0.47 (hexanes: ethyl acetate = 2:1).

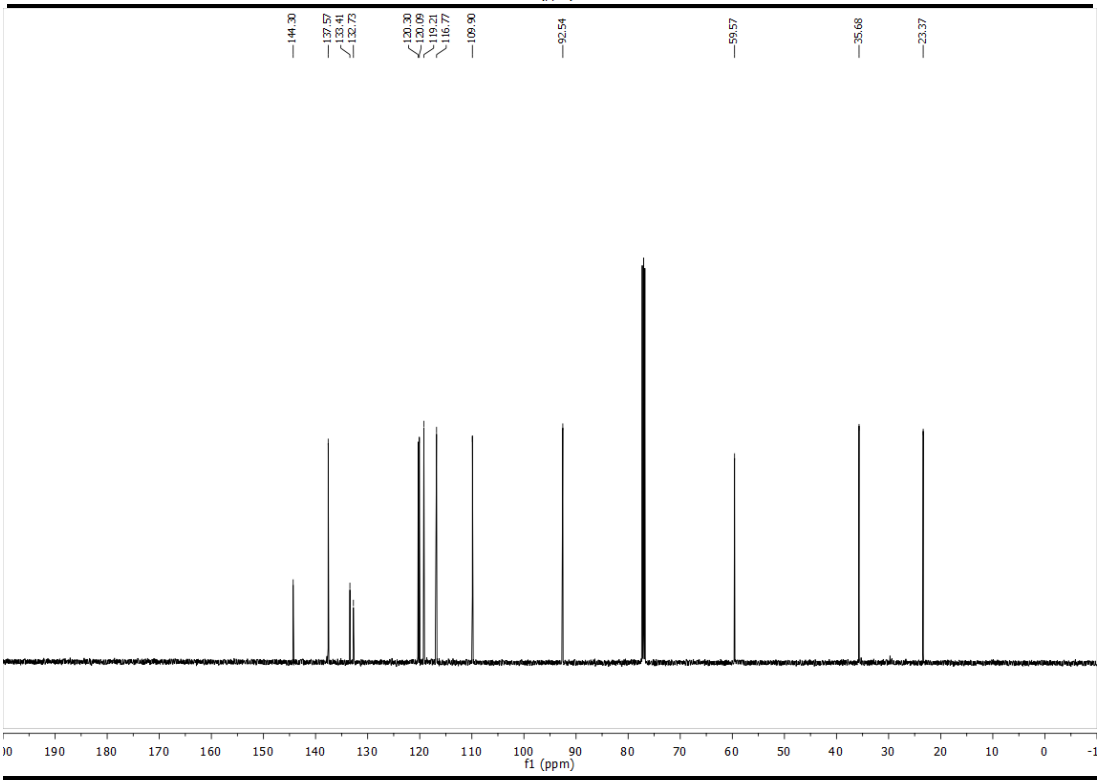
^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.20 (s, 1H), 7.54 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.32 (dq, *J* = 8.1, 1.0 Hz, 1H), 7.13 (ddd, *J* = 8.1, 7.1, 1.3 Hz, 1H), 7.08 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 6.26 (dd, *J* = 2.1, 1.0 Hz, 1H), 5.82 (ddd, *J* = 17.0, 10.5, 6.3 Hz, 1H), 5.43 – 5.36 (m, 1H), 5.29 (dt, *J* = 17.2, 1.3 Hz, 1H), 5.22 (dt, *J* = 10.5, 1.2 Hz, 1H), 2.87 – 2.80 (m, 1H), 2.80 – 2.72 (m, 1H), 2.15 – 2.06 (m, 4H), 2.00 (dddd, *J* = 13.9, 8.6, 7.0, 5.3 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.8, 138.5, 136.0 (2C), 128.8, 121.2, 119.8, 119.7, 117.2, 110.5, 100.0, 74.2, 33.9, 23.9, 21.3.

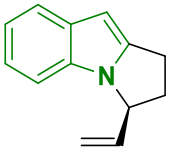
HRMS (ESI): Calculated for $C_{15}H_{17}NO_2$ [M+Na^+] = 266.1151, Found 266.1160.

FTIR (neat): 3395, 1721, 1457, 1372, 1244, 1024, 962, 782, 749 cm^{-1}.


f1 (ppm)


144.30
137.57
133.44
132.73
120.30
120.09
119.21
116.77
109.90
92.54
59.57
35.68
23.37
f1 (ppm)

***(S)*-3-vinyl-2,3-dihydro-1H-pyrrolo[1,2-a]indole (6.6a)**



Procedures

A pressure tube equipped with a magnetic stir bar was charged with cesium carbonate (130.3 mg, 0.4 mmol, 200 mol%) and ***(S)*-Ir-I** (11.1 mg, 0.01 mmol, 5 mol%). The tube was purged with argon for 5 minutes. DME (0.5 mL, 0.4 M) was added followed by the allylic acetate **5a** (48.7 mg, 0.2 mmol, 100 mol%). The tube was sealed with a PTFE lined cap and was placed in an oil bath at 70 ^{o}C for 24 hours. After reaching ambient temperature, the crude reaction mixture was directly subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–15:1). The title compound was obtained in 80% yield (29.3 mg, 0.16 mmol) as a colorless oil.

TLC (SiO_2) R_f = 0.34 (hexanes: ethyl acetate = 20:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.58 – 7.49 (m, 1H), 7.32 – 7.27 (m, 1H), 7.12 – 7.02 (m, 2H), 6.16 (s, 1H), 6.02 – 5.90 (m, 1H), 5.26 (s, 1H), 5.23 (dd, *J* = 6.1, 1.1 Hz, 1H), 4.92 – 4.85 (m, 1H), 3.07 (dddd, *J* = 14.9, 8.6, 6.1, 1.1 Hz, 1H), 2.97 (dddd, *J* = 15.8, 8.5, 5.9, 1.1 Hz, 1H), 2.85 – 2.75 (m, 1H), 2.36 (ddt, *J* = 12.5, 8.7, 5.6 Hz, 1H).

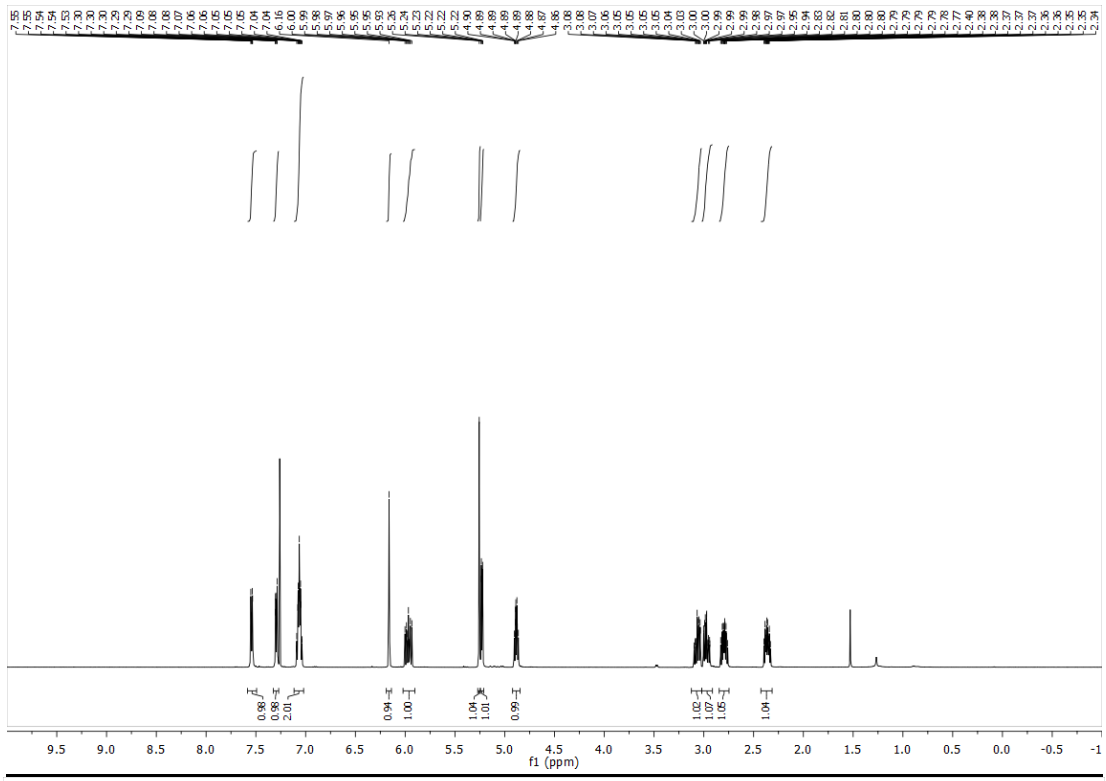
^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.3, 137.6, 133.4, 132.7, 120.3, 120.1, 119.2, 116.8, 109.9, 92.5, 59.6, 35.7, 23.4.

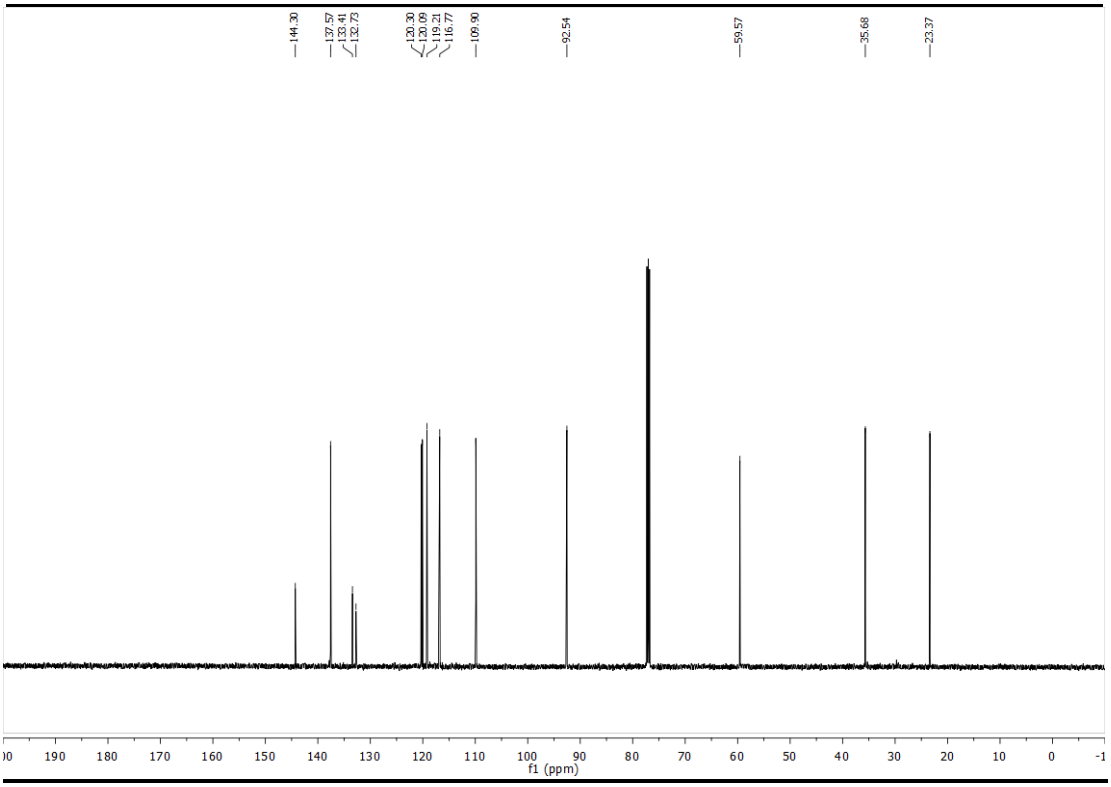
HRMS (ESI): Calculated for $C_{13}H_{13}N$ [M+H$^+$] = 184.1121, Found 184.1127.

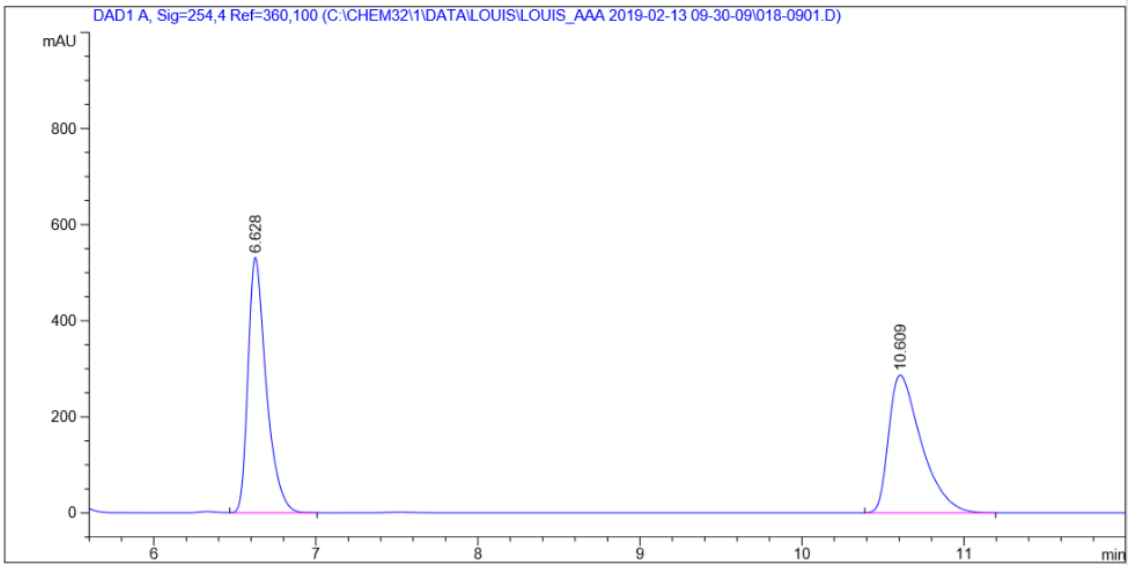
FTIR (neat): 2952, 1454, 1264, 1217, 989, 924, 740, 702 cm^{-1}.

$[\alpha]_D^{28}$= –53.8 (*c* 1.0, $CHCl_3$).

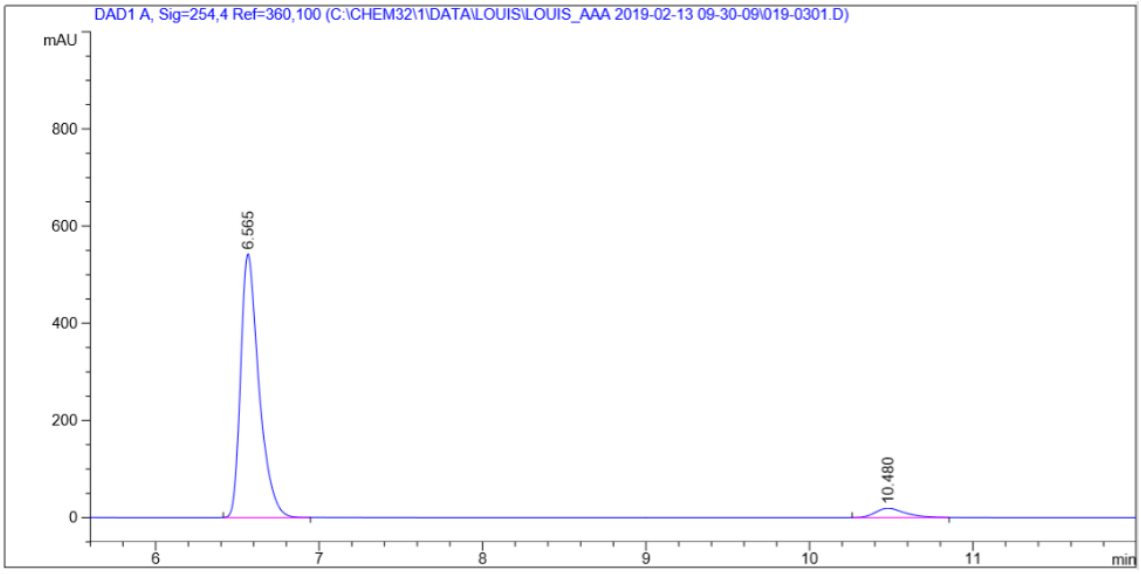
HPLC (Chiralcel OD-3 column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 254 nm), *ee* = 89%.


f1 (ppm)


144.30
137.57
133.41
132.73
120.30
120.09
119.21
116.77
109.90
92.54
59.57
35.68
23.37
f1 (ppm)



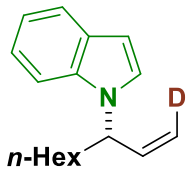
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.628	VB	0.1170	4149.02490	531.82904	50.8154
2	10.609	BB	0.2114	4015.87451	286.79831	49.1846



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.565	BB	0.1144	4211.96924	543.37781	94.5752
2	10.480	BB	0.1897	241.59578	19.34306	5.4248

Procedures and Spectral Data for Deuterium Labelling Experiments

(*S*,*Z*)-1-(oct-1-en-3-yl-1-d)-1H-indole (6.4k)



Procedures

A pressure tube equipped with a magnetic stir bar was charged with the indole (46.9 mg, 0.4 mmol, 200 mol%), cesium carbonate (130.3 mg, 0.4 mmol, 200 mol%) and ***(S)*-Ir-I** (11.1 mg, 0.01 mmol, 5 mol%). The tube was purged with argon for 5 minutes. DME (0.2 mL, 1.0 M) was added followed by the deuterated allylic acetate **2k**[7] (34.3 mg, 0.2 mmol, 100 mol%). The tube was sealed with a PTFE lined cap and was placed in an oil bath at 70 ^{o}C for 24 hours. After reaching ambient temperature, the crude reaction mixture was directly subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–15:1). The title compound was obtained in 75% yield (34.2 mg, 0.15 mmol) as a colorless oil.

TLC (SiO_2) R_f = 0.63 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.63 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.22 – 7.14 (m, 2H), 7.10 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.54 (d, *J* = 3.2 Hz, 1H), 6.01 (ddd, *J* = 10.4, 5.5, 2.6 Hz, 1H), 5.13 (dd, *J* = 10.5, 1.5 Hz, 1H), 4.91 – 4.82 (m, 1H), 2.08 – 1.92 (m, 2H), 1.32 – 1.21 (m, 6H), 0.84 (t, *J* = 6.9 Hz, 3H).

^{2}H NMR (92 MHz, $CHCl_3$): δ = 5.07 (s, 1D).

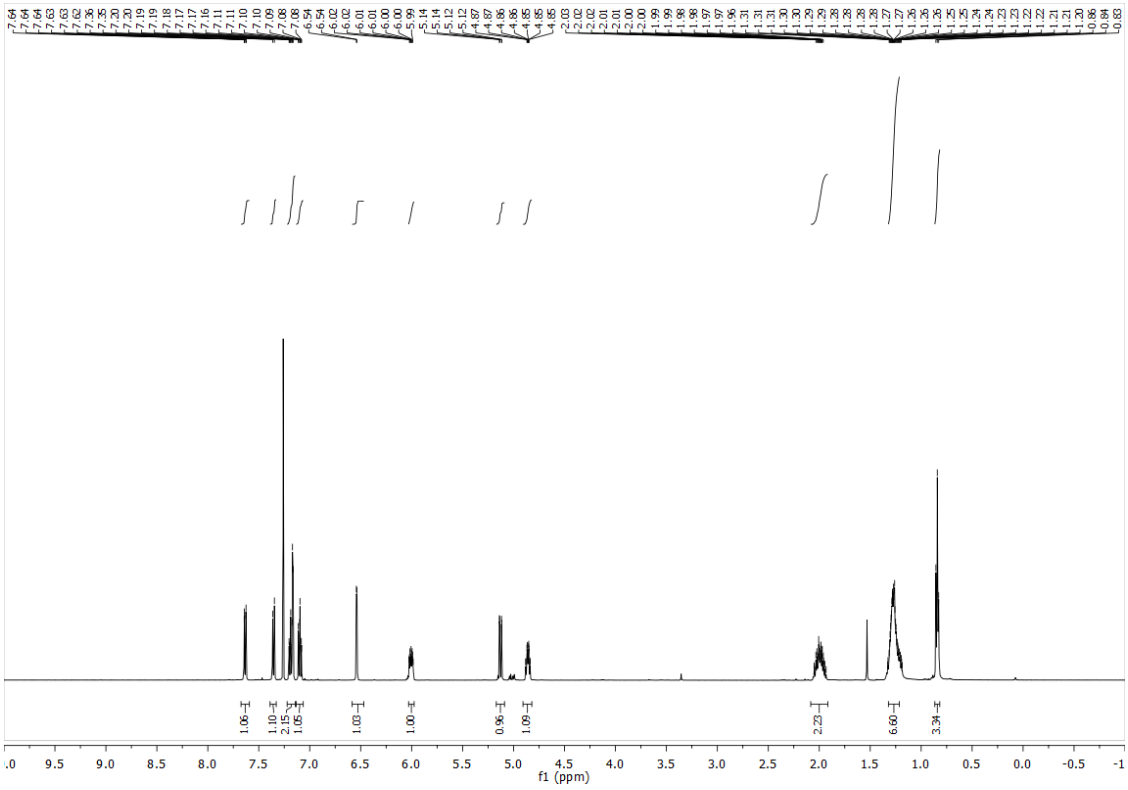
^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.9, 136.1, 128.6, 124.9, 121.2, 120.9, 119.3, 115.9 – 115.3 (m), 109.8, 101.5, 58.2, 34.2, 31.5, 25.9, 22.5, 14.0.

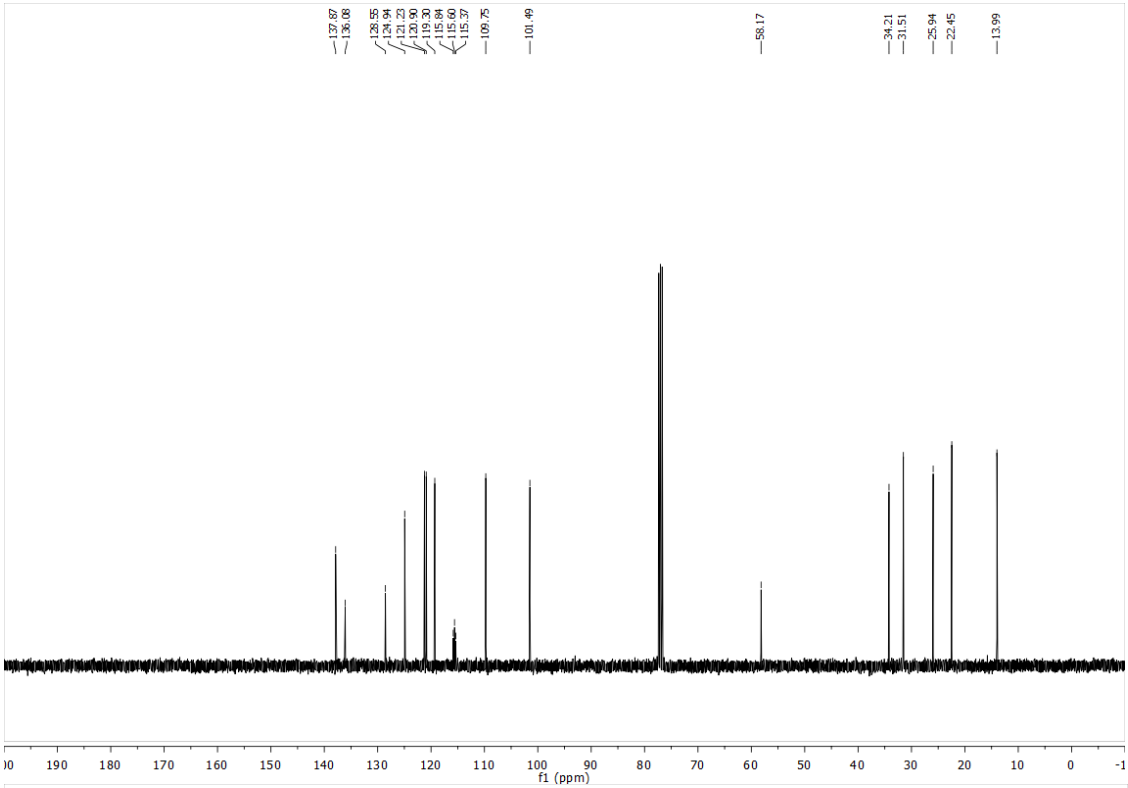
HRMS (ESI): Calculated for $C_{16}H_{20}DN$ [M+H$^+$] = 229.1810, Found 229.1813.

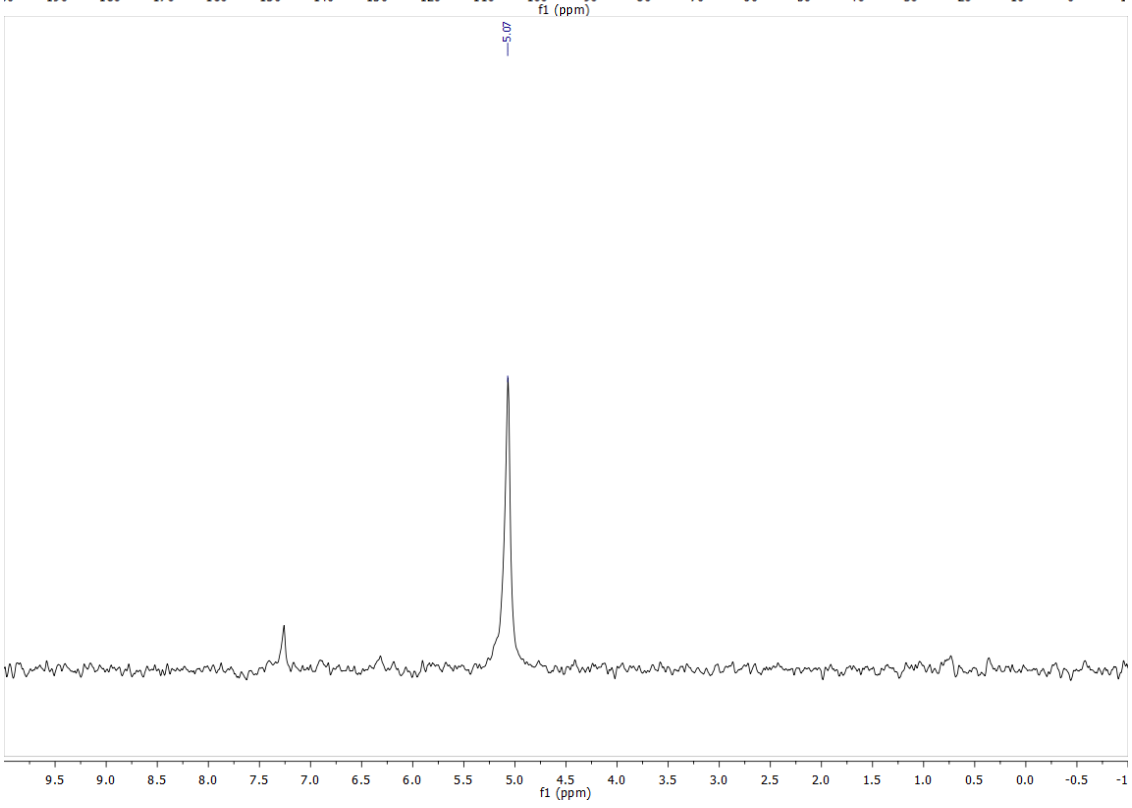
FTIR (neat): 2931, 1459, 1309, 1214, 750, 668 cm^{-1}.

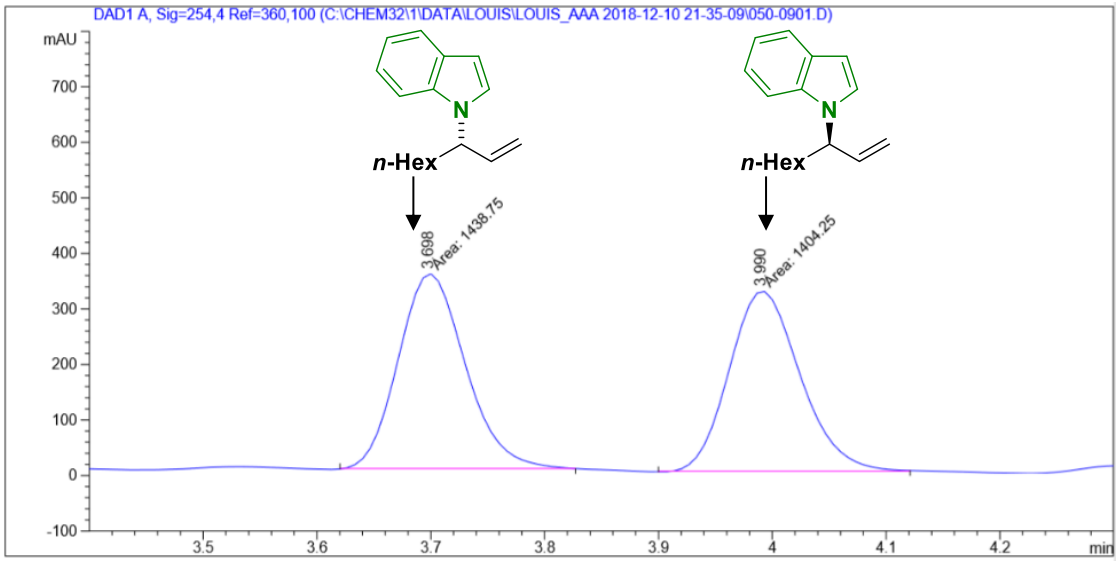
$[\alpha]_D^{28}$= +19.8 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 88%.

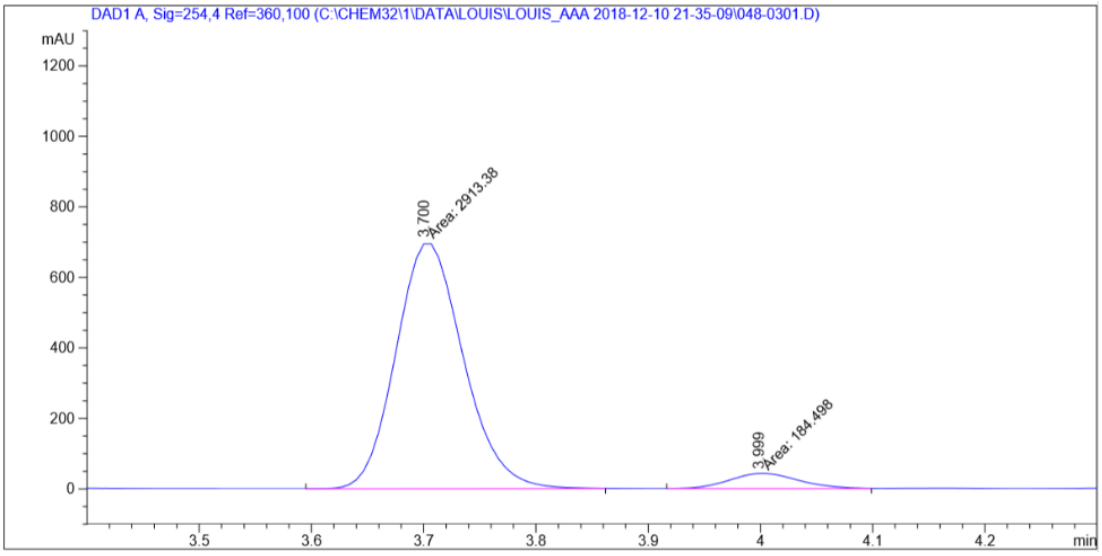



137.87
136.08
128.55
124.94
121.23
120.90
119.30
115.84
115.60
115.37
109.75
101.49
58.17
34.21
31.51
25.94
22.45
13.99
f1 (ppm)


5.07
f1 (ppm)

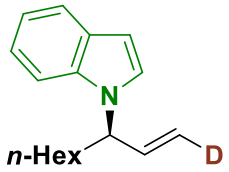


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.698	MM	0.0681	1438.75464	352.09875	50.6069
2	3.990	MM	0.0719	1404.24683	325.40305	49.3931



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.700	MM	0.0692	2913.38037	701.34546	94.0444
2	3.999	MM	0.0711	184.49831	43.23700	5.9556

(*R*,*E*)-1-(oct-1-en-3-yl-1-d)-1H-indole (*iso*-6.4k)



Procedures

A pressure tube equipped with a magnetic stir bar was charged with the indole (46.9 mg, 0.4 mmol, 200 mol%), cesium carbonate (130.3 mg, 0.4 mmol, 200 mol%) and **(*R*)-Ir-I** (11.1 mg, 0.01 mmol, 5 mol%). The tube was purged with argon for 5 minutes. DME (0.2 mL, 1.0 M) was added followed by the deuterated allylic acetate **2k** (34.3 mg, 0.2 mmol, 100 mol%). The tube was sealed with a PTFE lined cap and was placed in an oil bath at 70 ^{o}C for 24 hours. After reaching ambient temperature, the crude reaction mixture was directly subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–15:1). The title compound was obtained in 76% yield (34.7 mg, 0.15 mmol) as a colorless oil.

TLC (SiO_2) R_f = 0.63 (hexanes: ethyl acetate = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.63 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.22 – 7.15 (m, 2H), 7.10 (ddd, *J* = 7.9, 6.9, 1.0 Hz, 1H), 6.54 (dd, *J* = 3.2, 0.8 Hz, 1H), 6.01 (dd, *J* = 17.1, 5.8 Hz, 1H), 5.01 (dd, *J* = 17.2, 1.6 Hz, 1H), 4.86 (dtd, *J* = 8.0, 6.1, 1.5 Hz, 1H), 2.10 – 1.91 (m, 2H), 1.32 – 1.23 (m, 6H), 0.84 (t, *J* = 6.9 Hz, 3H).

^{2}H NMR (92 MHz, $CHCl_3$): δ = 5.19 (s, 1D).

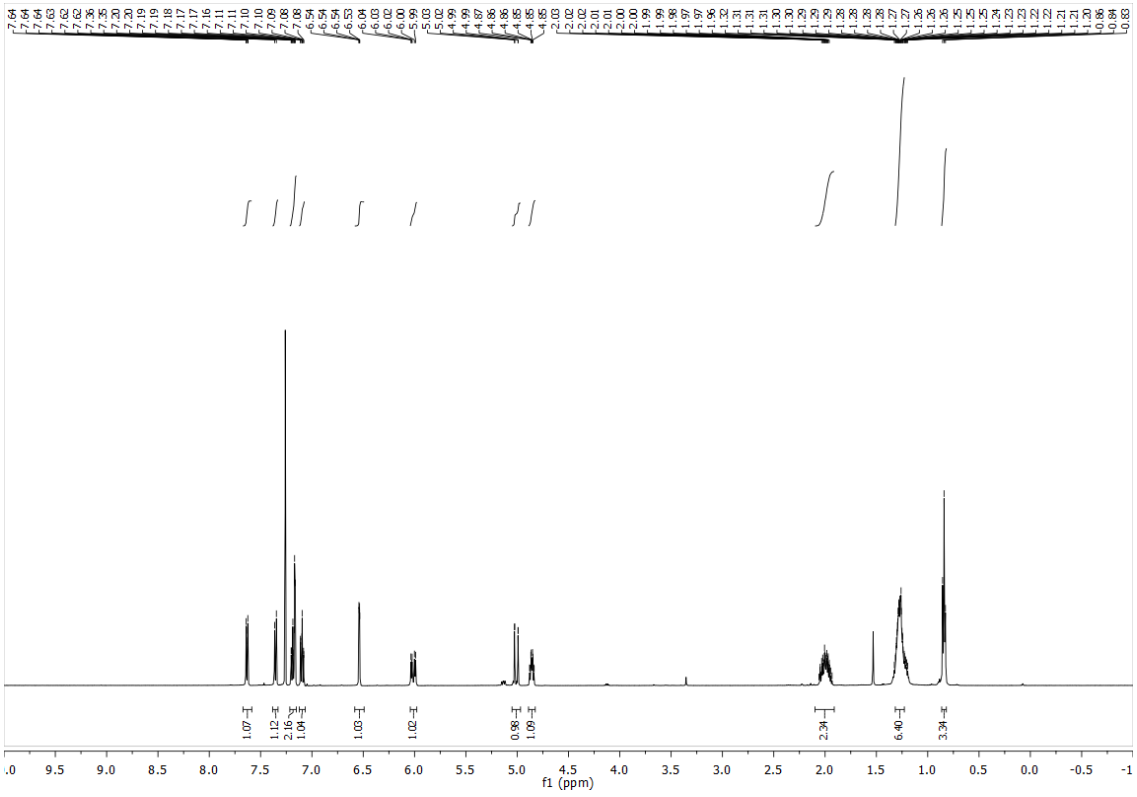
^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.9, 136.1, 128.5, 124.9, 121.2, 120.9, 119.3, 115.9 – 115.3 (m), 109.8, 101.5, 58.2, 34.2, 31.5, 25.9, 22.5, 14.0.

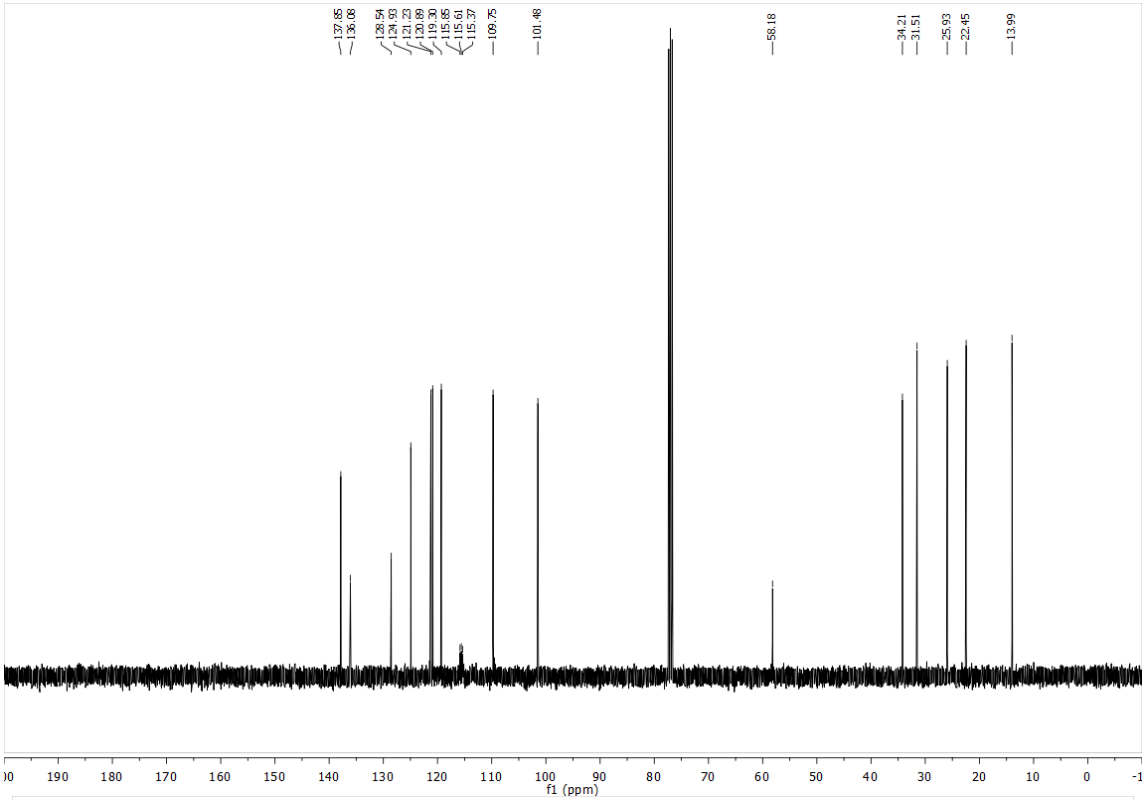
HRMS (ESI): Calculated for $C_{16}H_{20}DN$ [M+H$^+$] = 229.1810, Found 229.1814.

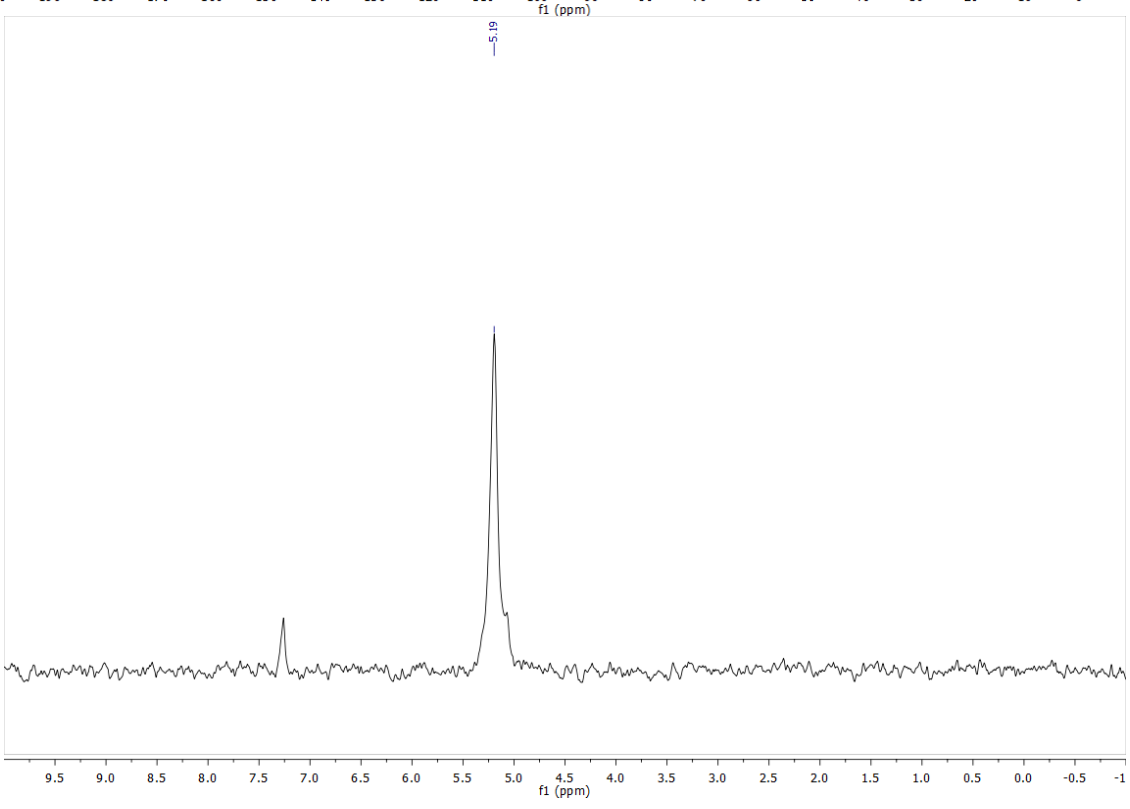
FTIR (neat): 2932, 1459, 1309, 1215, 754, 668 cm^{-1}.

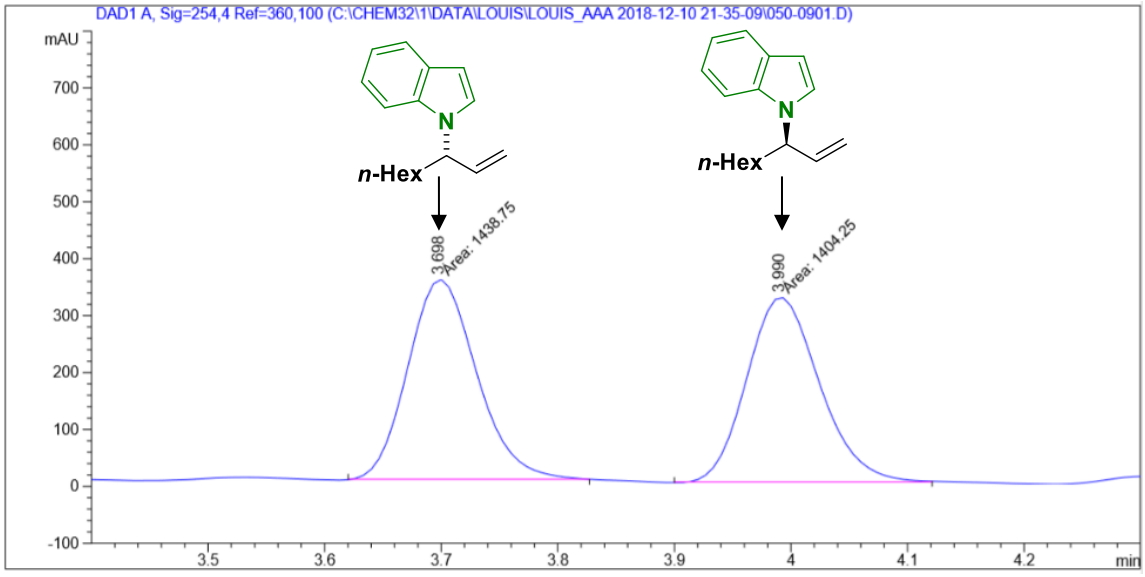
$[\alpha]_D^{28}$= –22.8 (*c* 1.0, $CHCl_3$).

HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 99:1, 1.00 mL/min, 254 nm), *ee* = 95%.

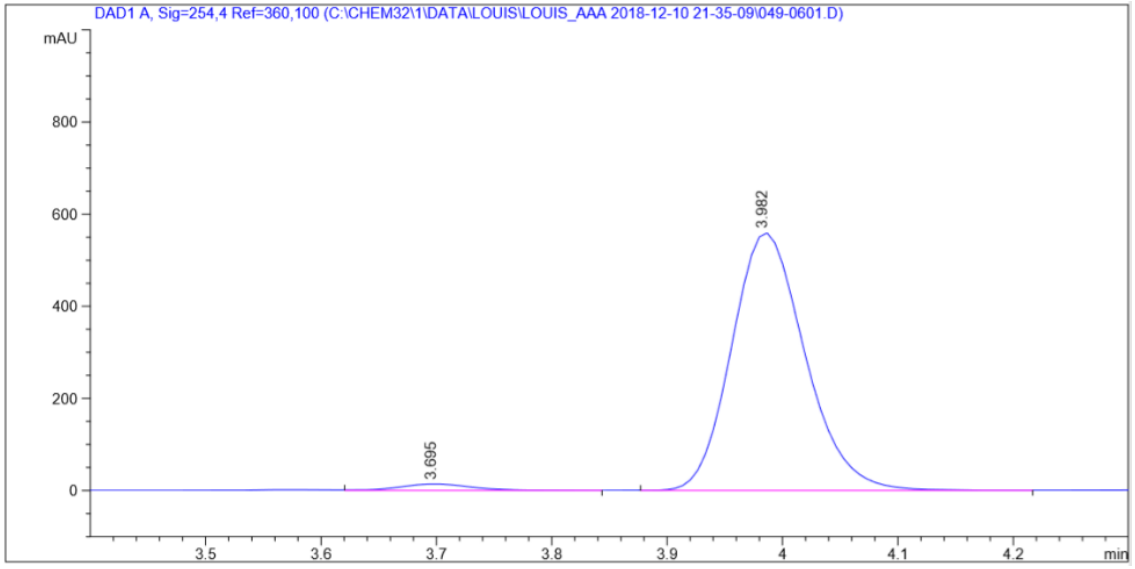



137.85
136.08
128.54
124.93
121.23
120.89
119.30
115.65
115.61
115.37
109.75
101.48
58.18
34.21
31.51
25.93
22.45
13.99
f1 (ppm)


5.19
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.698	MM	0.0681	1438.75464	352.09875	50.6069
2	3.990	MM	0.0719	1404.24683	325.40305	49.3931



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.695	VB	0.0651	60.04575	14.26813	2.3658
2	3.982	BB	0.0677	2478.05151	559.63654	97.6342

Single Crystal Diffraction Data for 6.3p

Empirical formula	C24 H24 Cl2 F5 I N2	
Formula weight	633.25	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 11.5320(11) Å	α= 90°.
	b = 11.5452(11) Å	β= 90°.
	c = 18.4648(19) Å	γ = 90°.
Volume	2458.4(4) $Å^3$	
Z	4	
Density (calculated)	1.711 Mg/m^3	
Absorption coefficient	1.574 mm^{-1}	
F(000)	1256	
Crystal size	0.342 x 0.146 x 0.107 mm^3	
Theta range for data collection	2.082 to 30.656°.	
Index ranges	-16<=h<=16, -16<=k<=16, -26<=l<=26	
Reflections collected	45429	
Independent reflections	7552 [R(int) = 0.0574]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Numerical	
Max. and min. transmission	0.9878 and 0.6732	
Refinement method	Full-matrix least-squares on F^2	

Data / restraints / parameters	7552 / 0 / 318
Goodness-of-fit on F^2	1.025
Final R indices [I>2sigma(I)]	R1 = 0.0336, wR2 = 0.0772
R indices (all data)	R1 = 0.0428, wR2 = 0.0796
Absolute structure parameter	-0.003(17)
Extinction coefficient	n/a
Largest diff. peak and hole	1.229 and -0.621 e.$Å^{-3}$

Figure 1. View of the cation in **1** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.

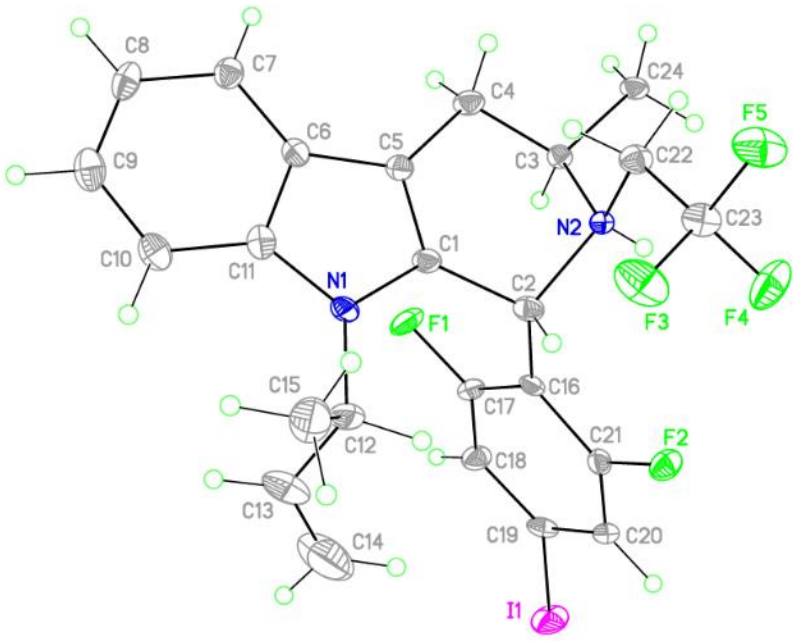
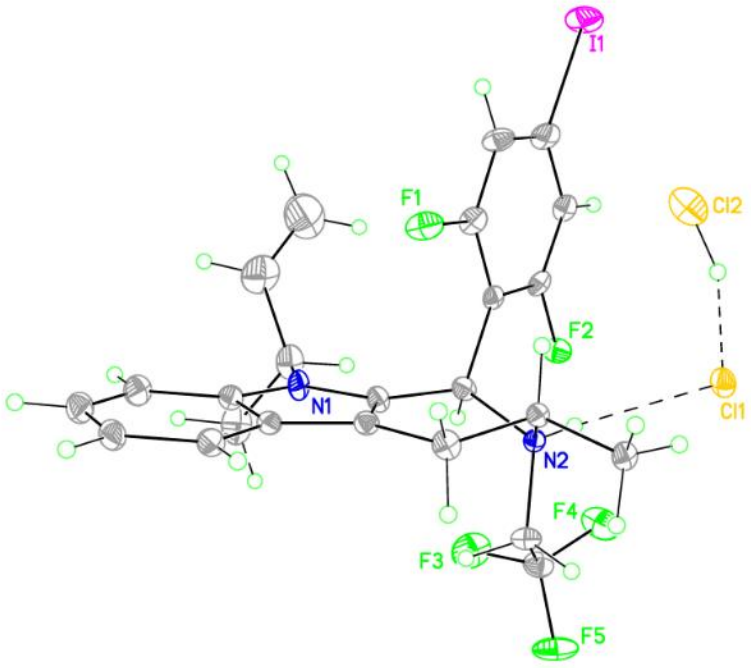


Figure 2. View of **1** showing the heteroatom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. The Cl-H...Cl anion is shown.



Chapter 7: Hydroamination *versus* Allylic Amination in Iridium Catalyzed Reactions of Allylic Acetates with Amines: 1,3-Aminoalcohols *via* Ester-Directed Regioselectivity*

7.1 Introduction

The importance of nitrogen-containing compounds in pharmaceutical and agrochemical research continues to inspire efforts toward the development of metal catalysts for alkene hydroamination.[1,2] Among late transition metal catalysts,[1g] those based on rhodium[3,4] and iridium[5,6] have shown great promise, however, despite decades of research, significant challenges remain. Many hydroaminations are limited to intramolecular processes.[4,6] Intermolecular variants often require highly activated alkenes,[3b,5a-d] are accompanied by oxidative amination side-products[3c-i,5f] or exploit specialized directing groups to control regioselectivity.[3j,k] Further, the mechanisms of these processes are obfuscated by the fact that simple brønsted acids – even ammonium salts[7b,f] – catalyze hydroamination with levels of efficiency equal to or greater than the corresponding metal catalyzed reactions.[7,8] Here, we report the first hydroaminations of allylic acetates. Specifically, using a neutral dppf-modified iridium catalyst in the presence of Cs_2CO_3, linear allylic acetates react with primary amines to form products of hydroamination with complete 1,3-regioselectivity. These results are remarkable, as iridium complexes are well-known to catalyze the substitution of allylic acetates with amines to form products of allylic amination (Figure 7.1).[9]

*This chapter is based on the published work:
Kim, S. W.; Wurm, T.; Brito, G. A.; Jung, W.-O.; Zbieg, J. R.; Stivala, C. E.; Krische, M. J. *J. Am. Chem. Soc.* **2018**, *140*, 9087.

Recently, in a collaborative endeavor, we reported that commercially available π-allyliridium *C,O*-benzoates catalyze highly enantioselective substitutions of branched allylic acetates with primary amines.[10] In the course of developing this process, significant quantities (30-40% yield) of hydroamination product were formed as single regioisomers in attempted substitutions of linear allylic acetates. Both iridium *C,O*-benzoates and non-cyclometallated phosphine-modified iridium complexes derived *in situ* from $[Ir(cod)Cl]_2$ displayed roughly equivalent efficiencies. In both cases, chiral ligands did not induce asymmetry, so the simpler non-cyclometallated complexes were chosen for further optimization. From a survey of achiral phosphine ligands, the phosphine ligand dppf, 1,1'-bis(diphenylphosphino)ferrocene, was found to be most effective. Hydroamination products were not observed in the absence of metal, phosphine ligand or upon use of monophosphine ligands.

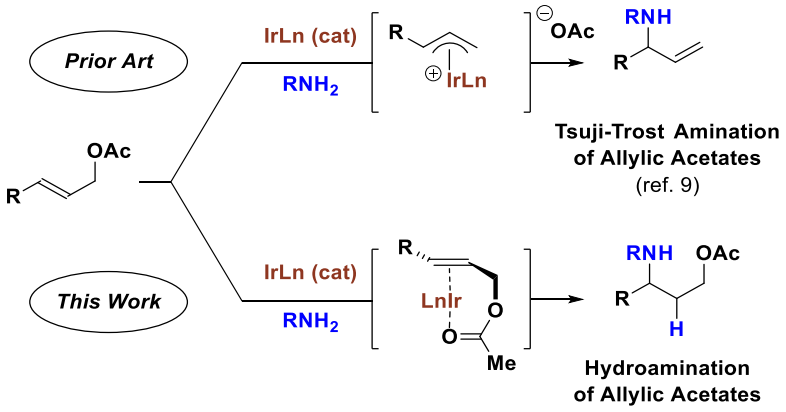


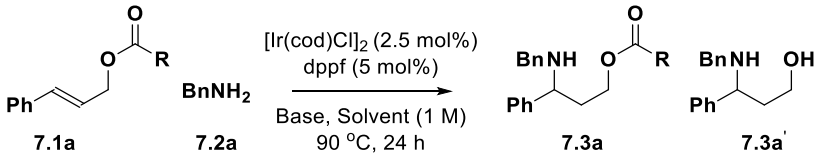
Figure 7.1 Cationic *vs* neutral iridium catalysts promote Tsuji-Trost allylic amination and hydroamination, respectively.

7.2 Reaction Development and Scope

The effect of base was systematically investigated (Table 7.1, entries 1-5). In the presence of $[Ir(cod)Cl]_2$ (2.5 mol%), dppf (5 mol%) and Cs_2CO_3 (200 mol%) at 90 °C in THF (1 M), cinnamyl acetate **7.1a** (100 mol%) and benzyl amine **7.2a** (200 mol%) were converted the hydroamination products **7.3a** and the deactylated compound **7.3a′** in a 2:1 ratio and a combined 66% yield along with trace amounts of cinnamyl alcohol. In an attempt to minimize formation of **7.3a**, lower loadings of Cs_2CO_3 were explored (Table 7.1, entries 1-3), however, although the reaction is heterogeneous, the combined yield hydroamination products **7.3a** and **7.3a'** declined.[11] Other bases were explored (Table 7.1, entries 4,5), but Cs_2CO_3 provided superior results. The use of cinnamic esters less prone to saponification were explored (Table 7.1, entries 6-10), but this also led to a decrease in the combined yield of hydroamination products **7.3a** and **7.3a'**. In all experiments, products of acyl transfer to benzyl amine were not observed.

Acute sensitivity to the steric features of the cinnamic ester (cf. Table 7.1, entries 1 and 7) along with the regioselectivity of hydroamination suggested chelation of iridium by the acetate carbonyl and olefin moieties might play an integral role in the mechanism. To perhaps favor chelation of iridium and minimize formation of **7.3a′** the stoichiometry of cinnamyl acetate **7.1a** and benzyl amine **7.2a** was altered (Table 7.1, entries 11-13). Using cinnamyl acetate **7.1a** (300 mol%) and benzyl amine **7.2a** (100 mol%), the hydroamination product **7.3a** was obtained in 76% yield accompanied by only trace quantities of the **7.3a′** (Table 7.1, entry 13). To mitigate solvent evaporation, a number of higher boiling solvents were evaluated and it was found that 1,2-dimethoxyethane (DME), provided **7.3a** with equivalent efficiencies (Table 7.1, entry 14). Finally, although this effect was not pronounced in reactions of cinnamyl acetate **7.1a**, it was also found that in certain cases milled Cs_2CO_3 led to higher and more reproducible yields.[11]

Table 7.1 Selected optimization experiments in the reaction of cinnamyl acetate **7.1a** with benzyl amine **7.2a** to form hydroamination product **7.3a**.[a]



7.1a **7.2a** **7.3a** **7.3a'**

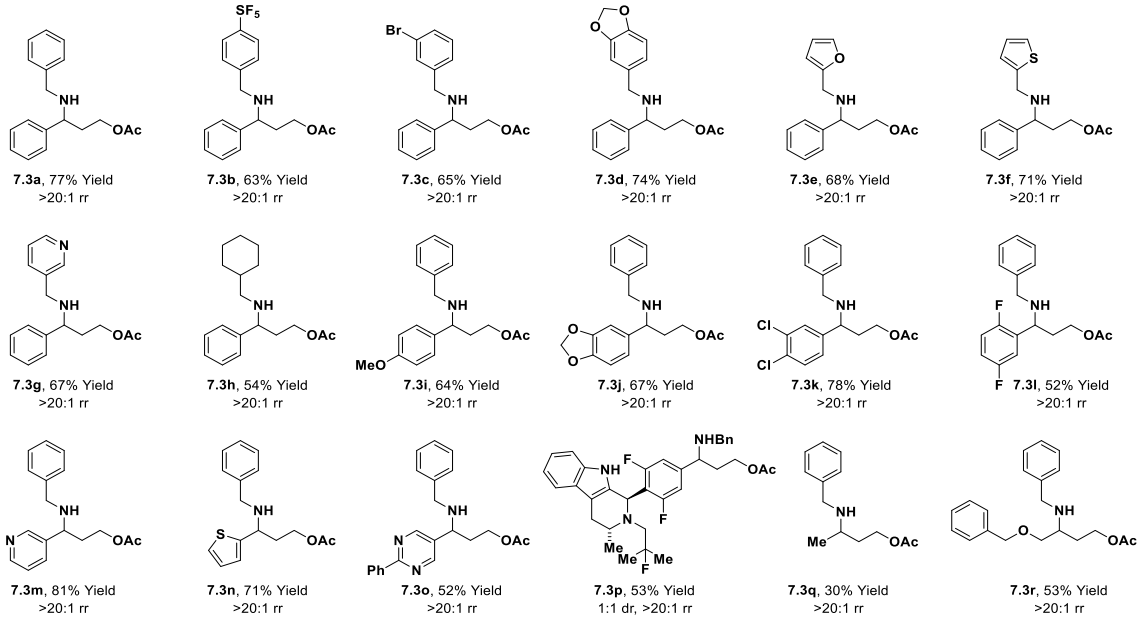
Entry	**7.1a / 7.2a** (mol%)	R	Base (mol%)	Solvent	**7.3a /7.3a'** Yield (%)
1	100 / 200	Me	**Cs_2CO_3 (200 mol%)**	THF	45 / 21
2	100 / 200	Me	**Cs_2CO_3 (50 mol%)**	THF	15 / 6
3	100 / 200	Me	**Cs_2CO_3 (20 mol%)**	THF	trace
4	100 / 200	Me	**K_2CO_3 (200 mol%)**	THF	trace
5	100 / 200	Me	**K_3PO_4 (200 mol%)**	THF	22 / 8
6	100 / 200	**Et**	Cs_2CO_3 (200 mol%)	THF	28 / 9
7	100 / 200	**^{i}Pr**	Cs_2CO_3 (200 mol%)	THF	12 / trace
8	100 / 200	**^{t}Bu**	Cs_2CO_3 (200 mol%)	THF	NR
9	100 / 200	**OMe**	Cs_2CO_3 (200 mol%)	THF	NR
10	100 / 200	**NMe_2**	Cs_2CO_3 (200 mol%)	THF	NR
11	**100 / 100**	Me	Cs_2CO_3 (200 mol%)	THF	36 / trace
12	**200 / 100**	Me	Cs_2CO_3 (200 mol%)	THF	65 / trace
13	**300 / 100**	Me	Cs_2CO_3 (200 mol%)	THF	76 / trace
14	300 / 100	Me	Cs_2CO_3 (200 mol%)	**DME**	77 / trace

[a]All reactions were performed on 0.2 mmol scale. All yields are of material isolated by silica gel chromatography. See Supporting In-formation for further experimental details.

To illustrate scope, optimal conditions for hydroamination were applied across a diverse set of reactants (Table 7.2). As demonstrated by the formation of hydroamination products **7.3a-7.3g**, primary benzylic amines are effective partners for hydroamination. Saturated primary amines provide moderate yields of hydroamination product (**7.3h**). A range of aryl-substituted linear allylic acetates also were evaluated (**7.3i-7.3p**). These experiments, which were all conducted using benzyl amine, reveal that both electron rich and electron deficient aryl groups, as well as heteroaryl groups, are tolerated. The formation of adduct **7.3p**, derived from AZD-9496 (a non-steroidal oral estrogen receptor inhibitor),[12] which incorporates an unprotected indole moiety, highlights the functional group tolerance of the present hydroamination method. As illustrated by formation of **7.3q** and **7.3r**, alkyl-substituted allylic acetates provide modest yields of hydroamination

product as single regioisomers. The regioselective formation **7.3r** is noteworthy, as it provides strong evidence of the directing influence of the acetate moiety. Indeed, as cinnamyl methyl ether, *trans*-*β*-methyl styrene and 1-octene do engage in hydroamination under these conditions, it would appear that the acetate moiety not only directs regioselectivity, but is required for hydroamination to proceed.

Table 7.2 Regioselective iridium-catalyzed hydroamination of linear allylic acetates.[a]

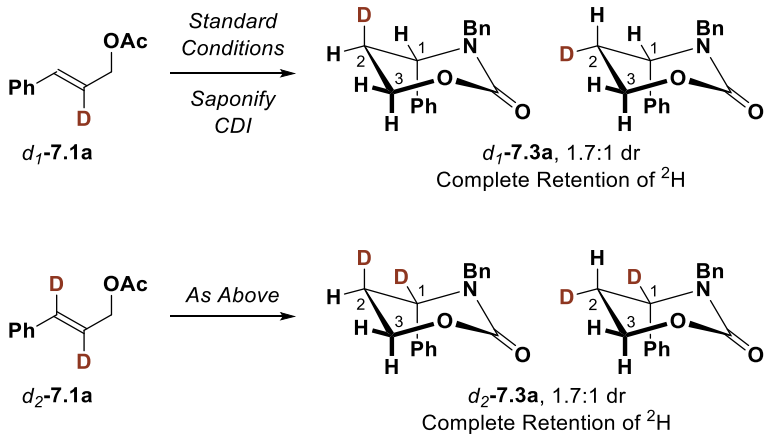


[a]Yields of material isolated by silica gel chromatography. Standard conditions: $[Ir(cod)Cl]_2$ (2.5 mol%), dppf (5 mol%), Cs_2CO_3 (200 mol%), amine (100 mol%), DME (1 M), 90 °C. All yields are of material isolated by silica gel chromatography. See Supporting Information for further experimental details.

7.3 Discussion

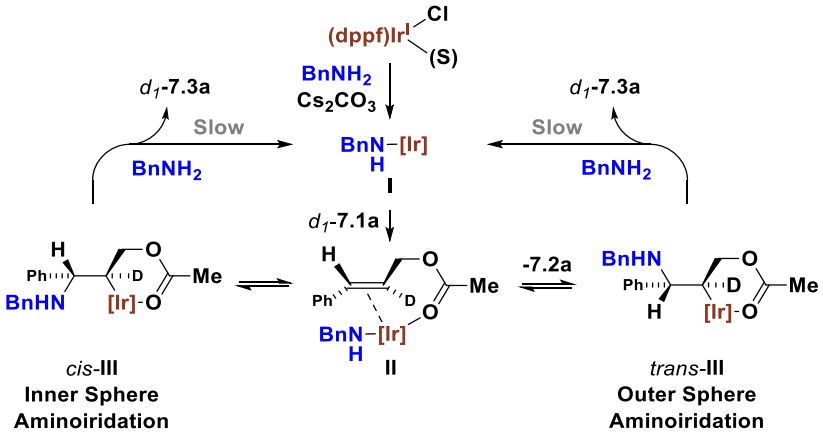
To gain insight into the reaction mechanism, *mono*- and *di*-deuterated cinnamyl acetates d_1-**7.1a** and d_2-**7.1a** were exposed to standard hydroamination conditions (Scheme 7.1). To facilitate assignment of relative stereochemistry, the reaction products were converted to the cyclic carbamates d_1-**7.3a** and d_2-**7.3a**. Axial disposition of the phenyl moiety was corroborated by nOe experiments and is presumably due to nonbonded interactions with the *N*-benzyl moiety. As determined by ^{1}H NMR, ^{2}H NMR and HRMS, both compounds d_1-**7.3a** and d_2-**7.3a**, completely retain deuterium and were each generated as 1.7:1 mixtures of diastereomers. Guided by the results of deuterium labeling, a general catalytic mechanism for iridium catalyzed hydroamination of linear allylic acetates was proposed (Scheme 7.2). Base-induced formation of amidoiridium species **I** enables entry into the catalytic cycle.[11] Association of d_1-**7.1a** provides the chelated olefin complex **II**, which undergoes rapid and reversible inner- or outer-sphere alkene aminoiridation to form the σ-alkyliridium species *cis*-**III** and *trans*-**III**, respectively. Equilibration between *cis*-**III** and *trans*-**III** occurs in advance of turn-over limiting proto-demetalation mediated by benzyl amine to release the product d_1-**7.3a** and regenerate amidoiridium species **I** to close the catalytic cycle. Consistent with this mechanistic interpretation, chiral iridium complexes do not deliver enantiomerically enriched hydroamination product. Additionally, using *cis*-cinnamyl acetate, low conversion to hydroamination product is observed (15% yield) and recovered cinnamyl acetate is partially isomerized to the *trans*-isomer (8:1, *cis:trans*). These data suggest the small quantity of hydroamination product observed in reactions of *cis*-cinnamyl acetate are likely formed by way of the *trans*-isomer and, for *cis*-cinnamyl acetate, allylic strain may prevent acetate-mediated chelation of the olefin by iridium. On the basis of these data, mechanisms involving alkene isomerization appear less plausible.

Scheme 7.1 Deuterium labelling experiments.[a]



[a]Reactants and products characterized by ^{1}H NMR, ^{2}H NMR and HRMS. See Supporting Information for further experimental details.

Scheme 7.2 General catalytic mechanism for iridium catalyzed hydroamination of linear allylic acetates, as corroborated by deuterium labeling.



7.4 Conclusion

To summarize, allylic acetates are well-known to undergo Tsuji-Trost amination upon exposure to amines in the presence of iridium catalysts with cationic character. Here, using neutral iridium catalysts under basic conditions, we report the first examples of allylic acetates hydroamination. The collective data, including deuterium labeling studies, corroborate a catalytic mechanism involving rapid, reversible acetate-directed aminoiridation with inner sphere/outer-sphere crossover in advance of turn-over limiting amine-mediated proto-demetalation. The present studies establish a new mechanistic pathway for alkene hydroamination under basic conditions, broadening access to 1,3-aminoalcohols and related *N*-containing compounds.[13] More broadly, this study and prior collaborative work from the present authors[10] demonstrate the effectiveness of academic-industrial cooperation for the discovery of useful and robust methods for chemical synthesis.

7.5 Experimental Details

General Information

All reactions were carried out under inert gas atmosphere (nitrogen or argon) unless otherwise indicated. Resealable pressure tubes (13x100 mm) were purchased from Fischer Scientific (catalog number 14-959-35C) and were flame dried followed by cooling in a desiccator or under a stream of inter gas prior to use. All commercial reagents and anhydrous solvents were used as received from vendors (Fischer Scientific, Sigma Aldrich and Combi Blocks) without further purification. $[Ir(cod)Cl]_2$ and dppf were used as received from Strem Chemicals Inc. Cs_2CO_3 was used as received from Rockwell Lithium. The compounds (4-(pentafluoro-λ^6-sulfaneyl)phenyl)methanamine[1]

was prepared according to literature procedures. Preparative column chromatography employing Silicycle silica gel (40-63 μm) was performed according to the method of Still[2] or on a Teledyne Isco Combiflash R_f utilizing Silicycle HP columns using a mobile phase composed of either heptane/isopropyl acetate, hexanes/ethyl acetate or dichloromethane/methanol. Reactions were monitored by a Shimadzu LCMS/UV system with LC-30AD solvent pump, 2020 MS, Sil-30AC autosampler, SPD-M30A UV detector, CTO-20A column oven, using a 2-98% acetonitrile/0.1% formic acid (or 0.001% ammonia) gradient over 2.5 minutes. Analytical thin-layer chromatography (TLC) was carried out using 0.25 mm commercial silica gel plates (Dynamic Absorbents F). Visualization was accomplished with UV light followed by dipping in CAM, *p*-Anisaldehyde (PAA), or $KMnO_4$ stain solution followed by heating. Specific optical rotations were recorded on an Atago AP-300 automatic polarimeter at the sodium line (589.3 nm) in $CHCl_3$ Solution concentrations are given in the units of 10-2 g ml^{-1}.

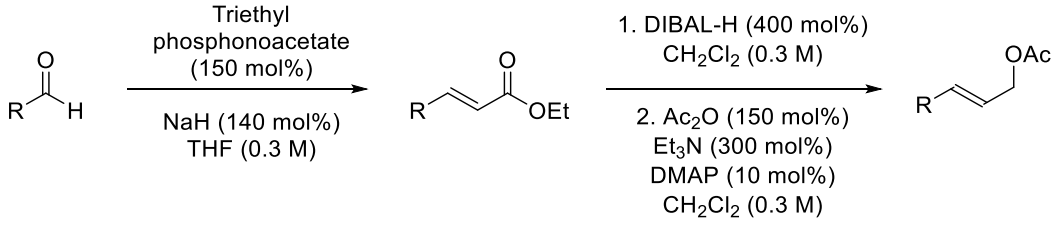
Spectroscopy, Spectrometry and Data Collection

Infrared spectra were recorded on a Perkin-Elmer 1600 spectrometer. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion (M+H, M+Na), or a suitable fragment ion. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with a Bruker BioSpin GmbG, Varian Gemini (400 MHz) or Varian INOVA (500 MHz) spectrometer equipped with a Bruker cryoprobe. Chemical shifts are reported in delta (δ) units, parts per million (ppm) downfield from tetramethylsilane or ppm relative to the center of the singlet at 7.26 ppm for deuteriochloroform. Data reported as multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Integration and coupling constants were reported in Hertz (Hz). Carbon-13 nuclear

magnetic resonance (^{13}C NMR) spectra were recorded with a Bruker BioSpin GmbG, Varian Gemini (100 MHz) or Varian INOVA (125 MHz) spectrometer and were routinely run with broadband decoupling. Chemical shifts are reported in delta (δ) units, ppm relative to the center of the triplet at 77.16 ppm for deuteriochloroform. Fluorine-19 nuclear magnetic resonance (^{19}F NMR) spectra were recorded with a Varian Gemini (376 MHz) spectrometer..

Experimental Details and Spectral Data

General procedure for the synthesis of allylic acetates. The allylic acetate **7.1i, 7.1j, 7.1k, and 7.1o** were prepared by the Horner–Wadsworth–Emmons reaction, DIBAL reduction, and acetylation of the corresponding aldehyde as shown below. The allylic acetate **7.1l** and **7.1r** were prepared by the acetylation of the corresponding allylic alcohol as shown below. The allylic acetates **7.1m**,[3] **7.1n**,[4] and **7.1q**[5] were prepared according to the published procedures and were identical in all respects to the reported materials.



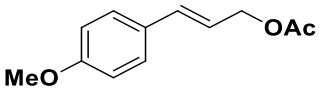
To a round-bottomed flask charged with sodium hydride (140 mol%, 60% in mineral oil) under an argon atmosphere was added THF (0.3 M), followed by triethyl phosphonoacetate (150 mol%). After 10 minutes, the corresponding aldehyde was added and the mixture was stirred at room temperature overnight. After water was added, the

mixture was transferred to a separatory funnel. The organic layer was extracted with ethyl acetate and the combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to the next step without further purification.

To a round-bottomed flask charged with the crude substrate under an argon atmosphere was added CH_2Cl_2 (0.3 M). The reaction flask was placed an ice batch. After 10 minutes, diisobutylaluminum hydride (400 mol%, 1.0 M in hexanes) was added slowly and the mixture was stirred at room temperature for 1 hour, at which point saturated aqueous Rochelle salts were added and the reaction was stirred vigorously overnight. After water was added, the mixture was transferred to a separatory funnel. The organic layer was extracted with ethyl acetate and the combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to the next step without further purification.

To a round-bottomed flask charged with the crude substrate and 4-dimethylaminopyridine (5 mol%) under an argon atmosphere was added CH_2Cl_2 (0.3 M), followed by acetic anhydride (150 mol%) and triethylamine (300 mol%). After 1 hour, saturated aqueous sodium bicarbonate was added and the mixture was transferred to a separatory funnel. The organic layer was extracted with CH_2Cl_2 and the combined organic layers were washed with 1 N HCl, dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash column chromatography give the corresponding allylic acetate over 3 steps.

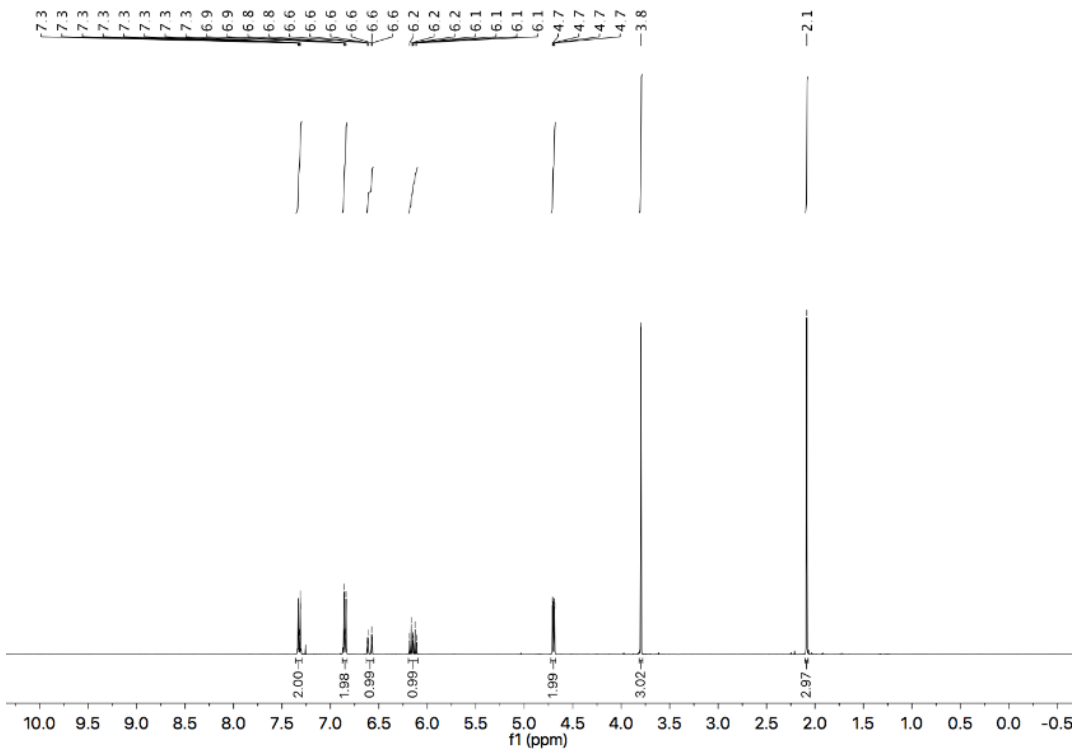
(*E*)-3-(4-methoxyphenyl)allyl acetate (7.1i)

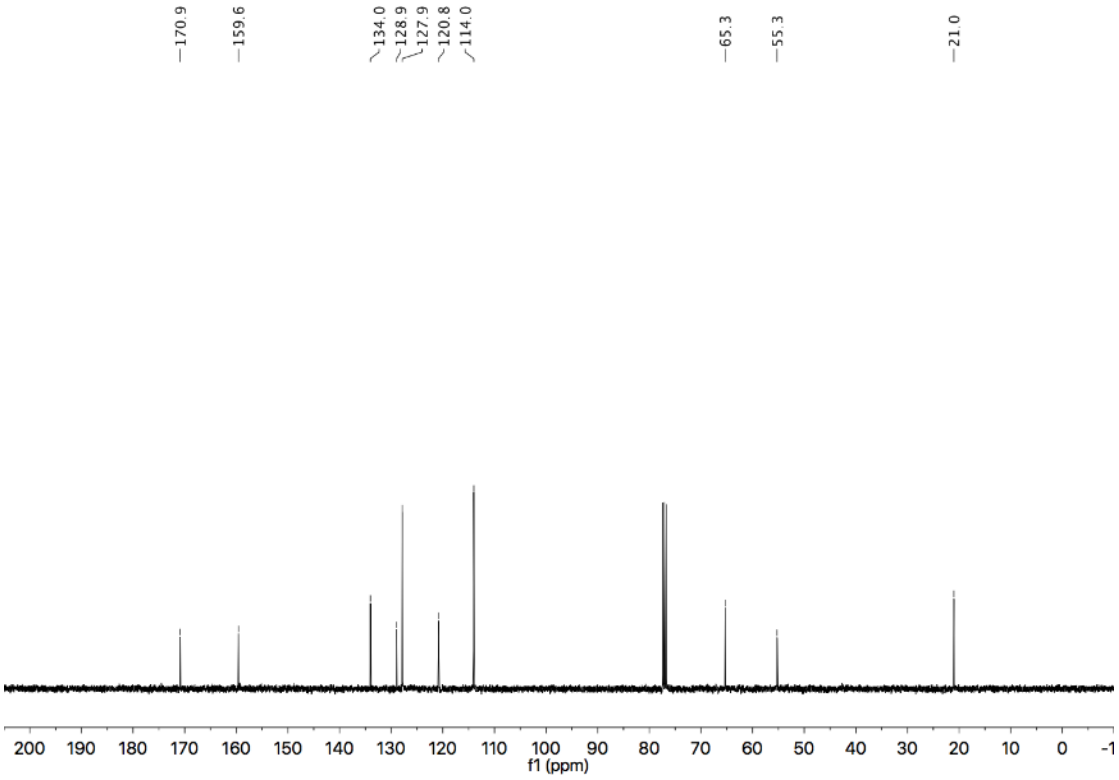


The title compound was prepared by the general procedure (Horner–Wadsworth–Emmons reaction, DIBAL reduction, and acetylation of the corresponding aldehyde). The spectral data were consistent with those reported.[6]

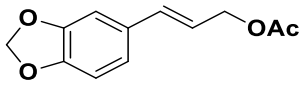
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 – 7.29 (m, 2H), 6.88 – 6.83 (m, 2H), 6.60 (dd, *J* = 16.0, 1.4 Hz, 1H), 6.15 (dt, *J* = 15.8, 6.6 Hz, 1H), 4.70 (dd, *J* = 6.6, 1.3 Hz, 2H), 3.80 (s, 3H), 2.08 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 159.6, 134.0, 128.9, 127.9, 120.8, 114.0, 65.3, 55.3, 21.0.


7.3
7.3
7.3
7.3
7.3
7.3
7.3
7.3
6.9
6.9
6.8
6.8
6.6
6.6
6.6
6.6
6.6
6.6
6.2
6.2
6.2
6.1
6.1
6.1
6.1
4.7
4.7
4.7
4.7
3.8
2.1
2.00
1.98
0.99
0.99
1.99
3.02
2.97
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


170.9
159.6
134.0
128.9
127.9
120.8
114.0
65.3
55.3
21.0
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

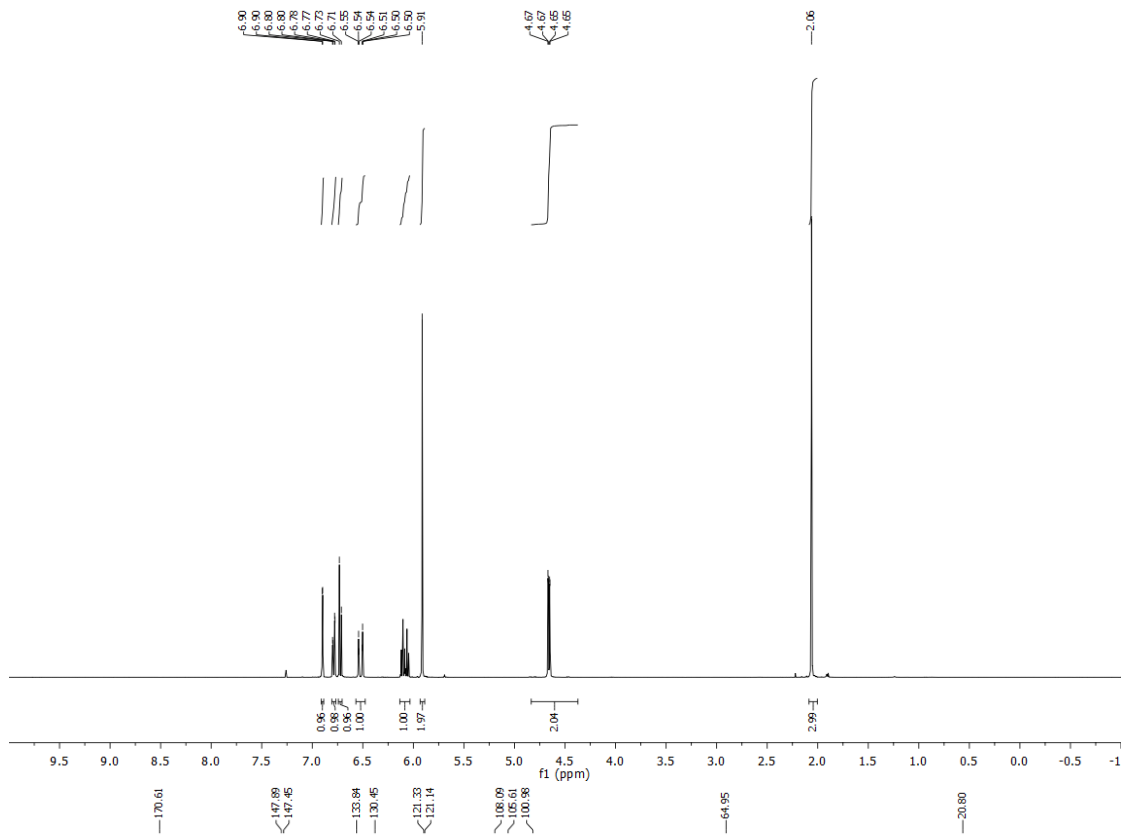
(*E*)-3-(benzo[d][1,3]dioxol-5-yl)allyl acetate (7.1j)



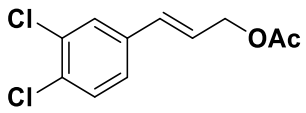
The title compound was prepared by the general procedure (Horner–Wadsworth–Emmons reaction, DIBAL reduction, and acetylation of the corresponding aldehyde). The spectral data were consistent with those reported.[7]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.90 (d, *J* = 1.7 Hz, 1H), 6.79 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 6.52 (dt, *J* = 15.8, 1.4 Hz, 1H), 6.08 (dt, *J* = 15.8, 6.6 Hz, 1H), 5.91 (s, 2H), 4.66 (dd, *J* = 6.6, 1.4 Hz, 2H), 2.06 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 147.9, 147.5, 133.8, 130.5, 121.3, 121.1, 108.1, 105.6, 101.0, 65.0, 20.8.


6.90
6.90
6.88
6.88
6.78
6.77
6.73
6.71
6.55
6.54
6.54
6.51
6.50
6.50
5.91
4.67
4.67
4.65
4.65
2.06
0.96
0.98
0.96
1.00
1.00
1.97
2.04
2.99
f1 (ppm)
170.61
147.89
147.45
133.84
130.45
121.33
121.14
108.09
105.61
100.98
64.95
20.80
f1 (ppm)

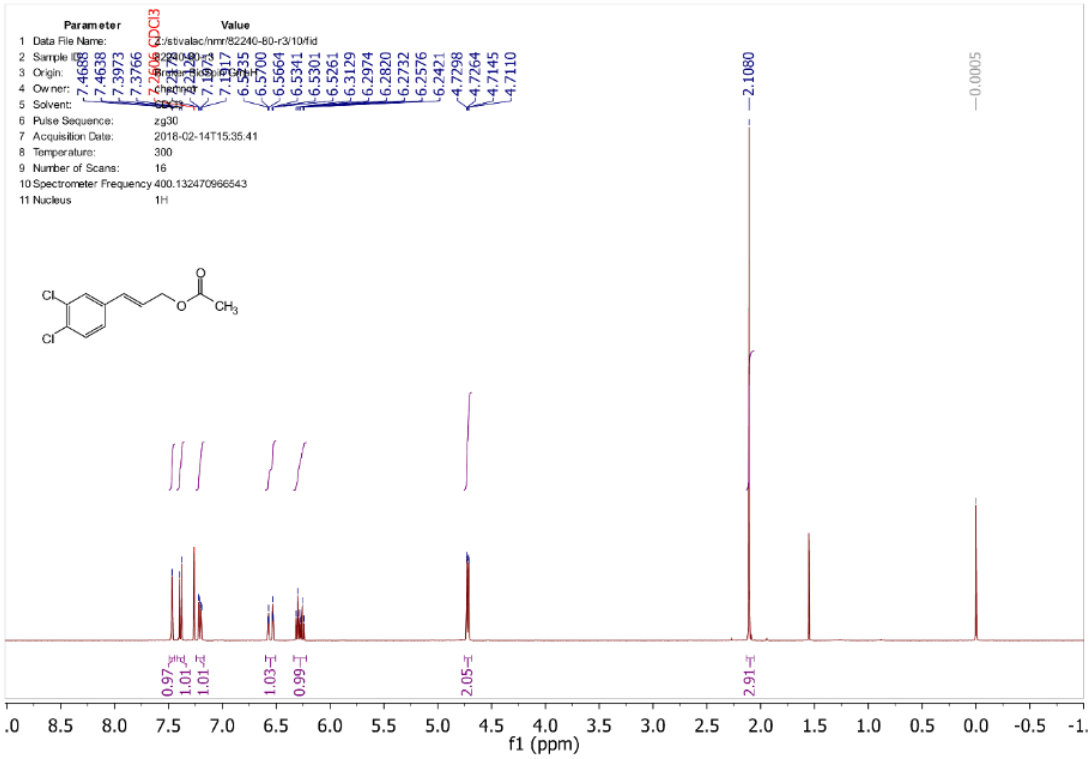
(*E*)-3-(3,4-dichlorophenyl)allyl acetate (7.1k)

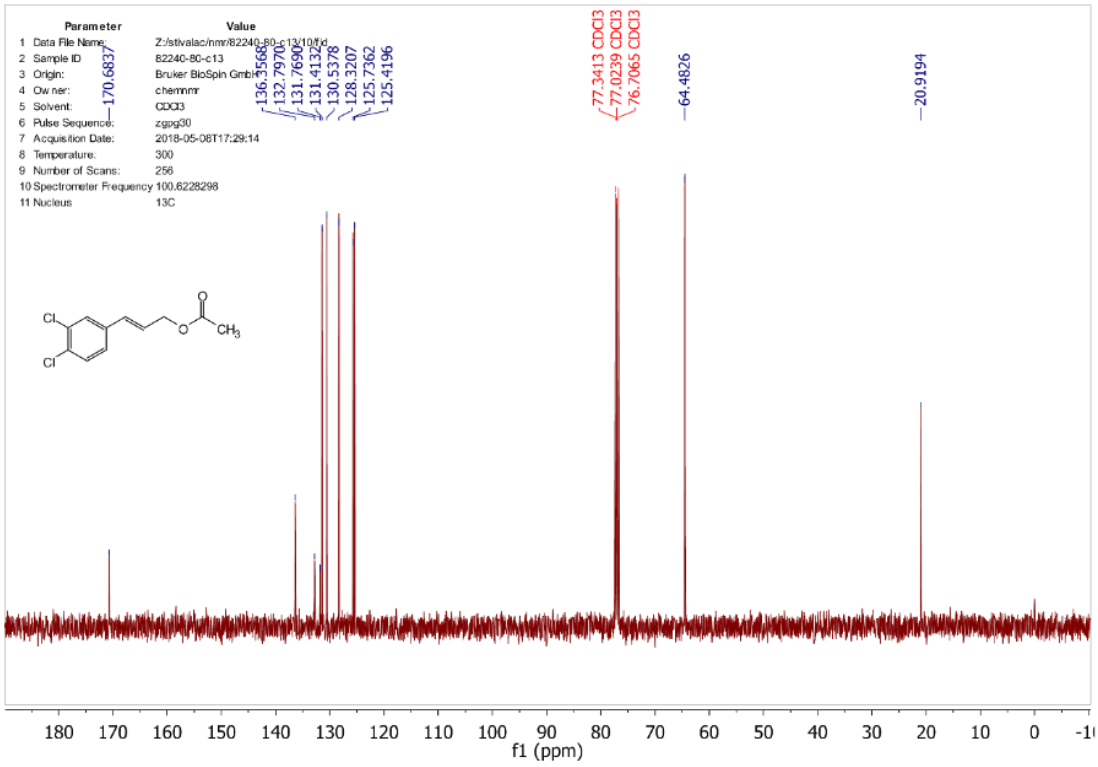


The title compound was prepared by the general procedure (Horner–Wadsworth–Emmons reaction, DIBAL reduction, and acetylation of the corresponding aldehyde). The spectral data were consistent with those reported.[8]

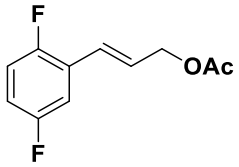
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 2.0 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 7.20 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.55 (dt, *J* = 16.1, 1.5 Hz, 1H), 6.28 (dt, *J* = 16.0, 6.2 Hz, 1H), 4.72 (dd, *J* = 6.2, 1.4 Hz, 2H), 2.11 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.7, 136.4, 132.8, 131.8, 131.4, 130.5, 128.3, 125.7, 125.4, 64.5, 20.9.


Parameter
Value
1 Data File Name: Z:/stivalac/nmr/82240-80-r3/10/fid
2 Sample ID 82240-80-r3
3 Origin: Bruker BioSpin GmbH
4 Owner: chemnmr
5 Solvent: CDCl3
6 Pulse Sequence: zg30
7 Acquisition Date: 2018-02-14T15:35:41
8 Temperature: 300
9 Number of Scans: 16
10 Spectrometer Frequency 400.132470966543
11 Nucleus 1H
7.4688
7.4638
7.3973
7.3766
7.2606 CDCl3
6.5335
6.5700
6.5664
6.5341
6.5301
6.5261
6.3129
6.2974
6.2820
6.2732
6.2576
6.2421
4.7298
4.7264
4.7145
4.7110
2.1080
0.0005
0.97
1.01
1.01
1.03
0.99
2.05
2.91
f1 (ppm)


Parameter
Value
1 Data File Name: Z:/stivalac/nmr/82240-80-c13/10/fid
2 Sample ID 82240-80-c13
3 Origin: Bruker BioSpin GmbH
4 Owner: chemnmr
5 Solvent: CDCl3
6 Pulse Sequence: zgpg30
7 Acquisition Date: 2018-05-08T17:29:14
8 Temperature: 300
9 Number of Scans: 256
10 Spectrometer Frequency 100.6228298
11 Nucleus 13C
170.6837
136.3568
132.7970
131.7690
131.4132
130.5378
128.3207
125.7362
125.4196
77.3413 CDCl3
77.0239 CDCl3
76.7065 CDCl3
64.4826
20.9194
f1 (ppm)

(*E*)-3-(2,5-difluorophenyl)allyl acetate (7.1l)

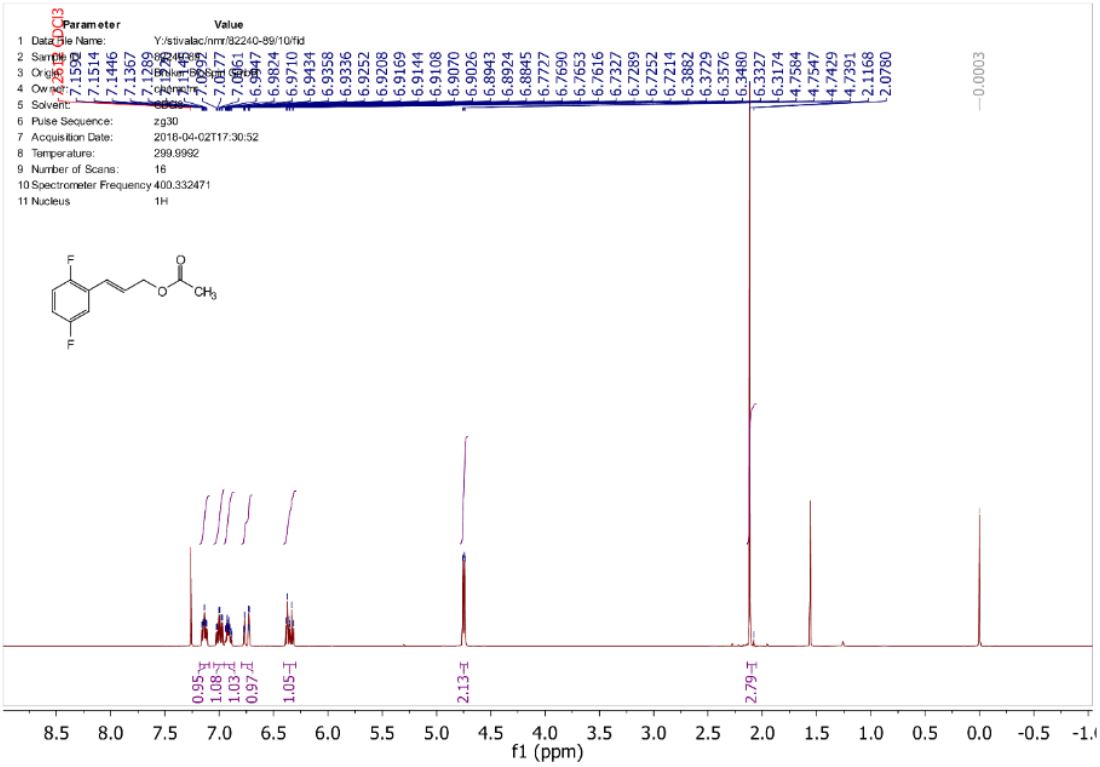


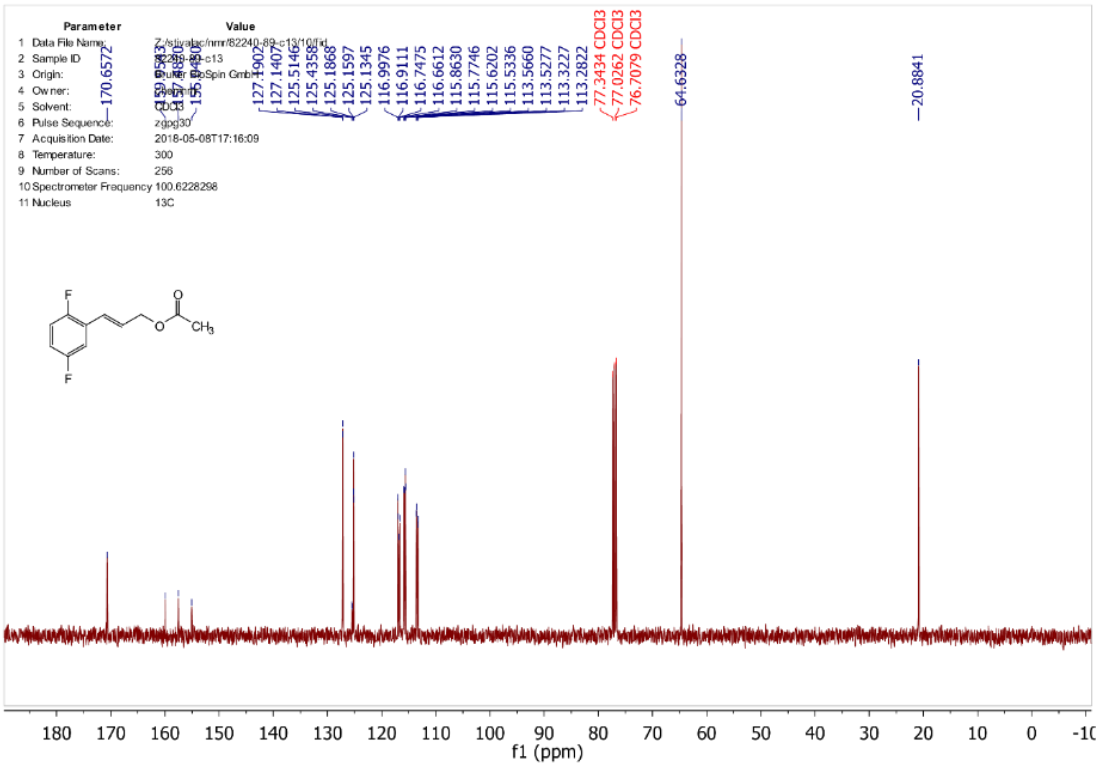
The title compound was prepared by the general procedure (acetylation of the corresponding allylic alcohol). The spectral data were consistent with those reported.[9]

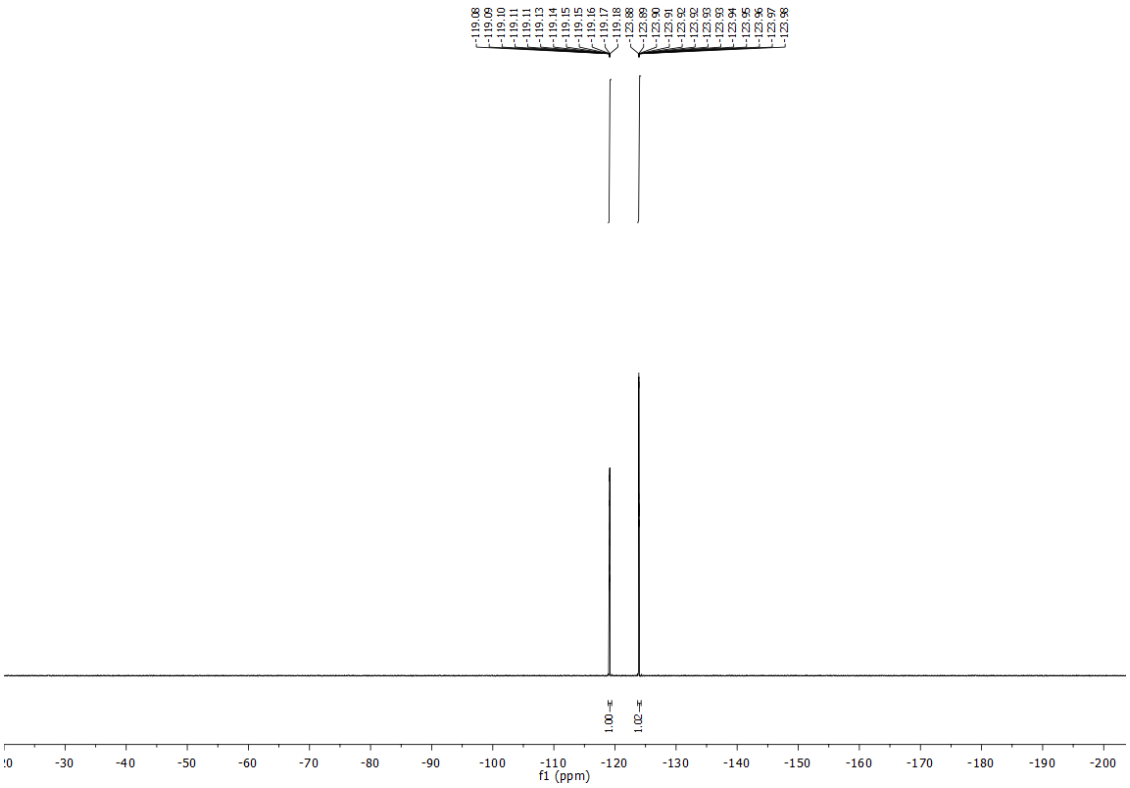
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.14 (ddd, *J* = 8.9, 5.8, 3.1 Hz, 1H), 7.00 (td, *J* = 9.4, 4.6 Hz, 1H), 6.96 – 6.86 (m, 1H), 6.75 (dq, *J* = 16.1, 1.5 Hz, 1H), 6.35 (dt, *J* = 16.1, 6.1 Hz, 1H), 4.75 (dd, *J* = 6.2, 1.5 Hz, 2H), 2.12 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.7, 158.7 (dd, *J* = 242.0, 2.1 Hz), 156.3 (dd, *J* = 245.8, 2.3 Hz), 127.3 – 127.1 (m), 125.4 (dd, *J* = 14.8, 8.0 Hz), 125.2 (t, *J* = 2.6 Hz), 116.8 (dd, *J* = 25.1, 8.7 Hz), 115.7 (dd, *J* = 24.3, 8.8 Hz), 113.4 (dd, *J* = 24.6, 4.0 Hz), 64.6, 20.9.

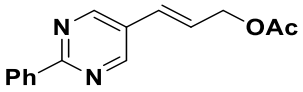
^{19}F NMR (376 MHz, $CDCl_3$): δ = –119.1 (m, 1F), –123.9 (m, 1F).


Parameter Value
1 Data File Name: Y:/stivalac/nmr/82240-89/10/fid
2 Sample ID: 82240-89
3 Origin: Bruker BioSpin GmbH
4 Owner: chemistry
5 Solvent: cdcl3
6 Pulse Sequence: zg30
7 Acquisition Date: 2018-04-02T17:30:52
8 Temperature: 299.9992
9 Number of Scans: 16
10 Spectrometer Frequency 400.332471
11 Nucleus 1H
CDCl3
7.1592
7.1514
7.1446
7.1367
7.1289
7.0977
7.0877
7.0061
6.9947
6.9824
6.9710
6.9434
6.9358
6.9336
6.9252
6.9208
6.9169
6.9144
6.9108
6.9070
6.9026
6.8943
6.8924
6.8845
6.7727
6.7690
6.7653
6.7616
6.7327
6.7289
6.7252
6.7214
6.3882
6.3729
6.3576
6.3480
6.3327
6.3174
4.7584
4.7547
4.7429
4.7391
2.1168
2.0780
0.0003
0.95
1.08
1.03
0.97
1.05
2.13
2.79
f1 (ppm)


Parameter Value
1 Data File Name: Z:/stivalac/nmr/82240-89-c13/10/fid
2 Sample ID: 82240-89-c13
3 Origin: Bruker BioSpin GmbH
4 Owner: chemistry
5 Solvent: CDCl3
6 Pulse Sequence: zgpg30
7 Acquisition Date: 2018-05-08T17:16:09
8 Temperature: 300
9 Number of Scans: 256
10 Spectrometer Frequency 100.6228298
11 Nucleus 13C
170.6572
156.8436
154.4903
127.1902
127.1407
125.5146
125.4358
125.1868
125.1597
125.1345
116.9976
116.9111
116.7475
116.6612
115.8630
115.7746
115.6202
115.5336
113.5660
113.5277
113.3227
113.2822
77.3434 CDCl3
77.0262 CDCl3
76.7079 CDCl3
64.6328
20.8841
f1 (ppm)


-119.08
-119.09
-119.10
-119.11
-119.11
-119.13
-119.14
-119.15
-119.15
-119.16
-119.17
-119.18
-123.88
-123.89
-123.90
-123.91
-123.92
-123.92
-123.93
-123.93
-123.94
-123.95
-123.96
-123.97
-123.98
1.00
1.02
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

(*E*)-3-(2-phenylpyrimidin-5-yl)allyl acetate (7.1o)



The title compound was prepared by the general procedure (Horner–Wadsworth–Emmons reaction, DIBAL reduction, and acetylation of the corresponding aldehyde).

TLC (SiO_2) R_f = 0.56 (hexanes: ethyl acetate = 2:1).

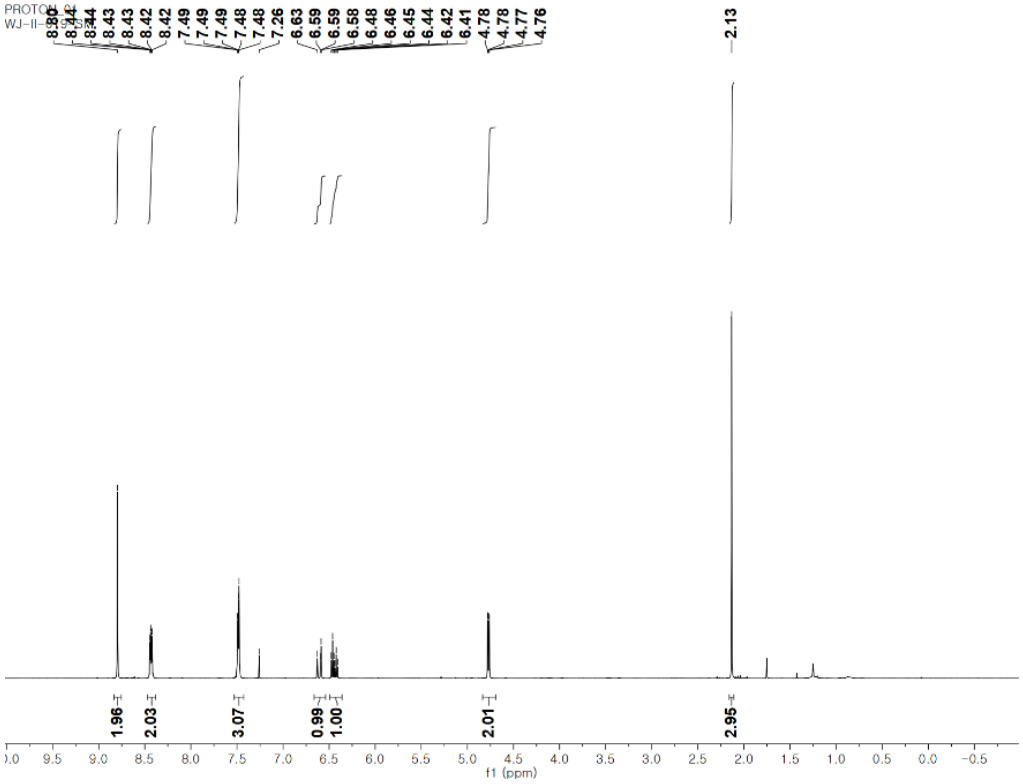
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.80 (s, 2H), 8.47 – 8.38 (m, 2H), 7.53 – 7.43 (m, 3H), 6.66 – 6.54 (m, 1H), 6.44 (dt, *J* = 16.1, 5.9 Hz, 1H), 4.77 (dd, *J* = 5.9, 1.4 Hz, 2H), 2.13 (s, 3H).

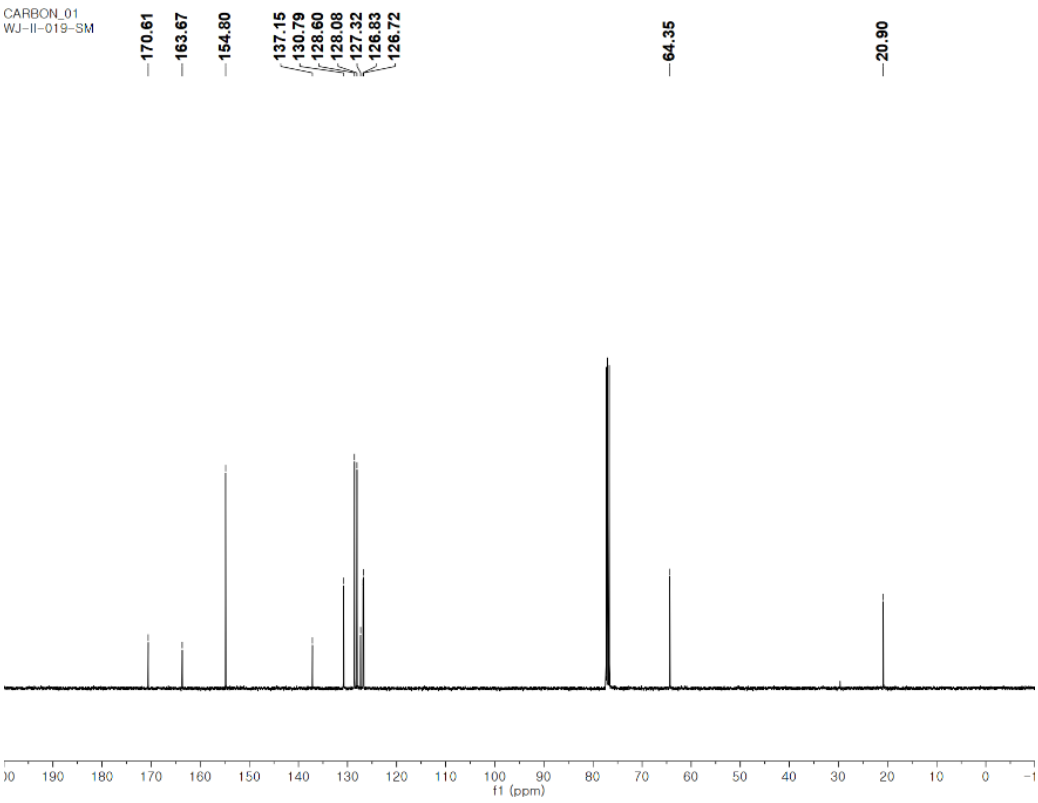
^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 163.7, 154.8, 137.2, 130.8, 128.6, 128.1, 127.3, 126.8, 126.7, 64.4, 20.9.

HRMS (ESI): Calculated for $C_{15}H_{14}N_2O_2$ $[M+H^+]$ = 255.1128, found 255.1128.

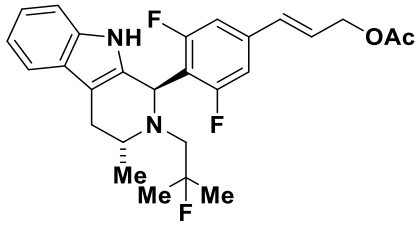
FTIR (neat): 3036, 2939, 1731,1662, 1582, 1540, 1450, 1432, 1385, 1366, 1328, 1316, 1297, 1250, 1228, 1170, 1077, 1065, 1021, 967, 942, 930, 906, 848, 820, 780, 747, 730, 697, 651 cm^{-1}.

Melting Point : 114–118 ˚C


PROTON_01
WJ-II-019-SM
8.44
8.43
8.43
8.42
8.42
7.49
7.49
7.49
7.48
7.48
7.26
6.63
6.59
6.59
6.58
6.48
6.46
6.45
6.44
6.42
6.41
4.78
4.78
4.77
4.76
2.13
1.96
2.03
3.07
0.99
1.00
2.01
2.95
f1 (ppm)


CARBON_01
WJ-II-019-SM
170.61
163.67
154.80
137.15
130.79
128.60
128.08
127.32
126.83
126.72
64.35
20.90
f1 (ppm)

(*E*)-3-(3,5-difluoro-4-((1R,3R)-2-(2-fluoro-2-methylpropyl)-3-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)phenyl)allyl acetate (7.1p)



Step 1: Borane-tetrahydrofuran complex (2.0 M in tetrahydrofuran, 16 mL, 33 mmol) was added to a solution of (E)-3-[3,5-difluoro-4-[(1R,3R)-2-(2-fluoro-2-methyl-propyl)-3-methyl-1,3,4,9-tetrahydropyrido[3,4-b]indol-1-yl]phenyl]prop-2-enoic acid (3.6 g, 8.1 mmol) in THF (16 mL) at rt. After 3 h, methanol was added and the reaction was allowed to stir for 20 minutes. The reaction was concentrated under reduced pressure, and the crude residue was purified by flash column chromatography (silica, 0% to 40% isopropyl acetate - heptane) to give (E)-3-[3,5-difluoro-4-[(1R,3R)-2-(2-fluoro-2-methyl-propyl)-3-methyl-1,3,4,9-tetrahydropyrido[3,4-b]indol-1-yl]phenyl]prop-2-en-1-ol (1.60 g, 3.73 mmol, 46% Yield).

TLC (SiO_2) R_f = 0.48 (hexanes: ethyl acetate = 1:1).

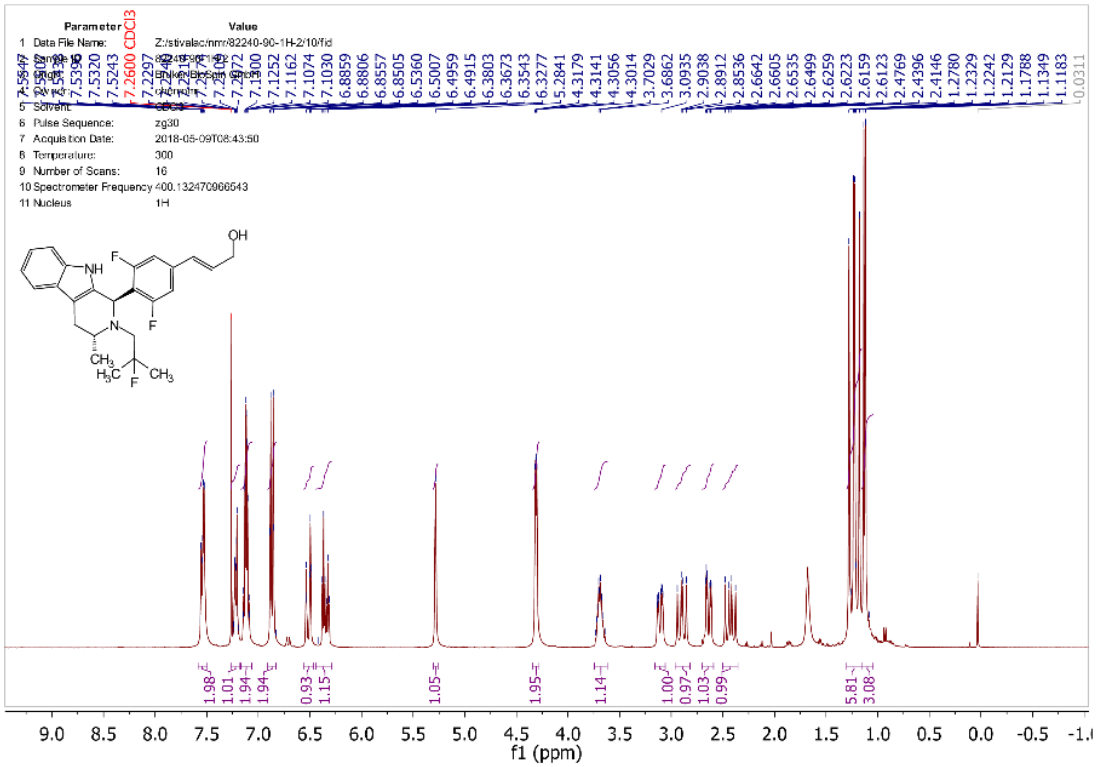
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 – 7.50 (m, 2H), 7.27 – 7.18 (m, 1H), 7.17 – 7.06 (m, 2H), 6.91 – 6.83 (m, 2H), 6.56 – 6.47 (m, 1H), 6.35 (dt, *J* = 15.9, 5.2 Hz, 1H), 5.28 (s, 1H), 4.34 – 4.28 (m, 2H), 3.74 – 3.62 (m, 1H), 3.11 (ddd, *J* = 15.2, 5.2, 2.0 Hz, 1H), 2.90 (dd, *J* = 20.0, 15.0 Hz, 1H), 2.64 (ddd, *J* = 15.1, 4.1, 1.5 Hz, 1H), 2.43 (dd, *J* = 25.0, 14.9 Hz, 1H), 1.23 (dd, *J* = 21.6, 18.1 Hz, 6H), 1.13 (d, *J* = 6.6 Hz, 3H).

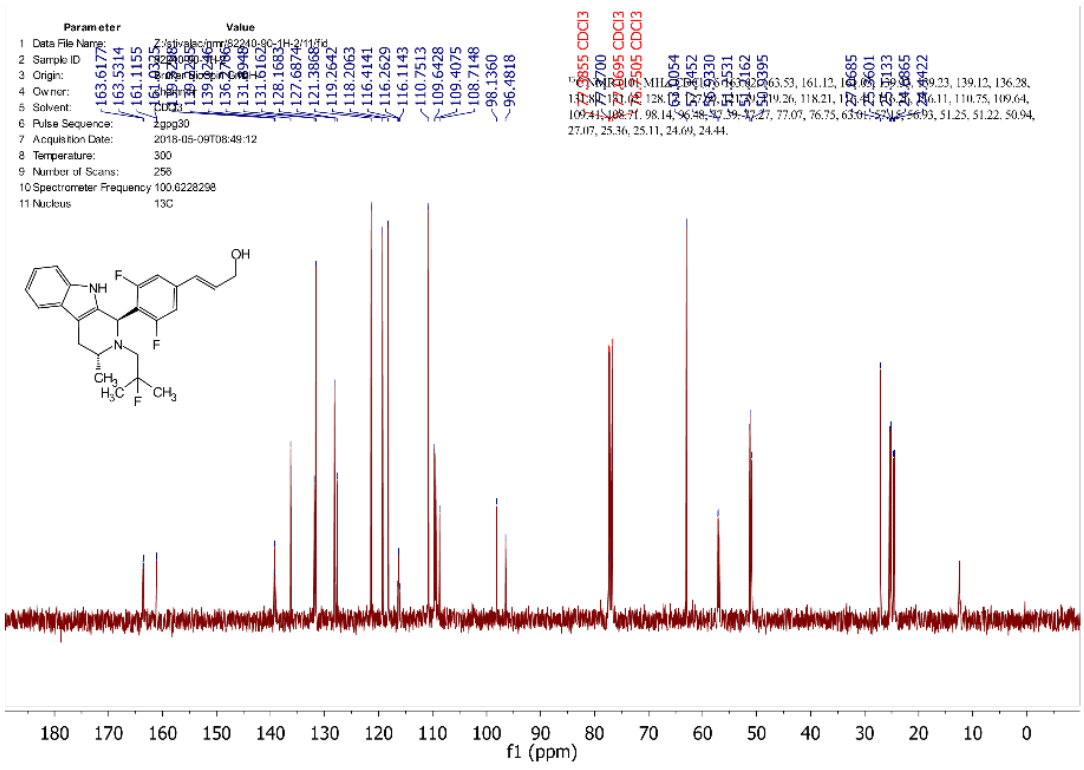
^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.3 (dd, *J* = 251.5, 8.3 Hz), 139.2 (t, *J* = 10.3 Hz), 136.3, 131.9, 131.6, 128.2 (t, *J* = 2.6 Hz), 127.7, 121.4, 119.3, 118.2, 116.3 (t, *J* = 15.0 Hz), 110.8, 109.5 (d, *J* = 22.1 Hz), 108.7, 98.1, 96.5, 63.0, 57.0 (d, *J* = 21.4 Hz), 51.2 (d, *J* = 3.7 Hz), 50.9, 27.1, 25.2 (d, *J* = 24.9 Hz), 24.6 (d, *J* = 24.6 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –139.4 (m).

HRMS (ESI): Calculated for $C_{25}H_{28}ON_2F_3$ $[M+H^+]$ = 429.2148, found 429.2146.

FTIR (neat): 3413, 2979, 1629, 1449, 1372, 1202, 1132,, 1021, 908, 731 cm^{-1}.


Parameter Value
1 Data File Name: Z:/stivalac/nmr/82240-90-1H-2/10/fid
2 Sample ID 82240-90-1H
3 Origin: Bruker BioSpin GmbH
4 Owner: nmrsu
5 Solvent: CDCl3
6 Pulse Sequence: zg30
7 Acquisition Date: 2018-05-09T08:43:50
8 Temperature: 300
9 Number of Scans: 16
10 Spectrometer Frequency 400.132470966543
11 Nucleus 1H
f1 (ppm)


Parameter Value
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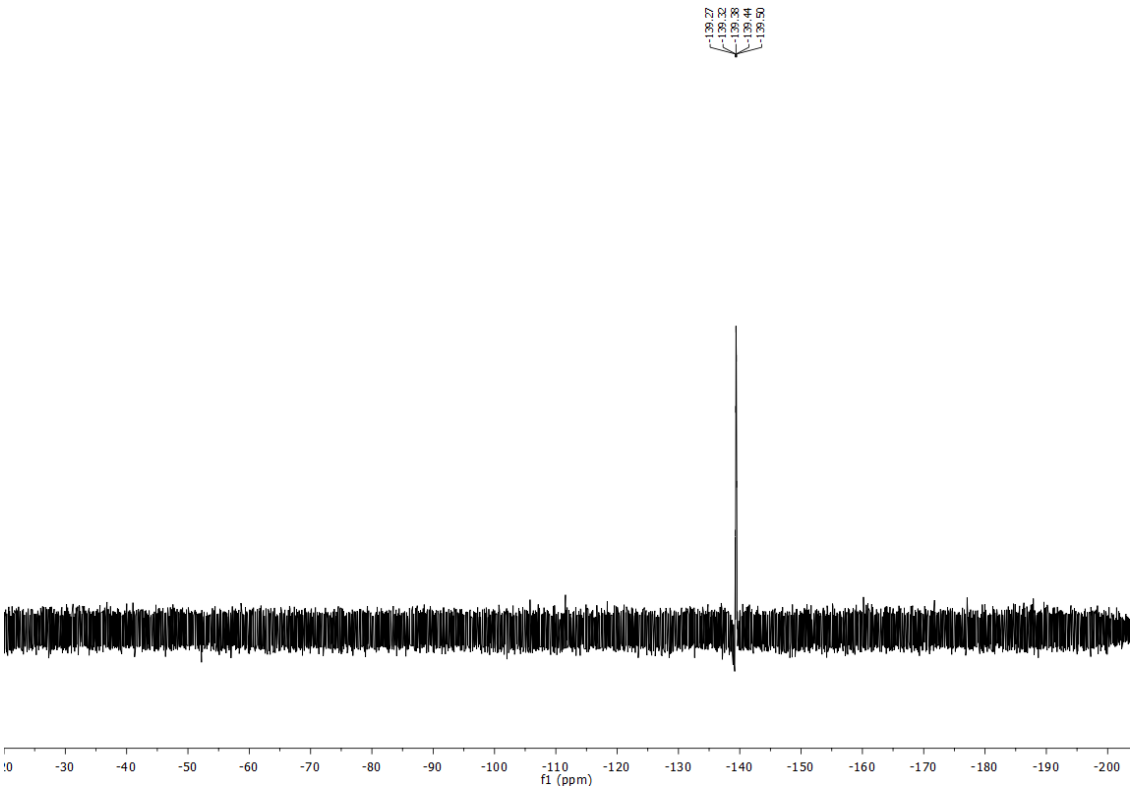
2 Sample ID 82240-90-1H
3 Origin: Bruker BioSpin GmbH
4 Owner: nmrsu
5 Solvent: CDCl3
6 Pulse Sequence: zgpg30
7 Acquisition Date: 2018-05-09T08:49:12
8 Temperature: 300
9 Number of Scans: 256
10 Spectrometer Frequency 100.6228298
11 Nucleus 13C
f1 (ppm)


-139.27
-139.32
-139.38
-139.44
-139.50
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

Step 2: 4-Dimethylaminopyridine (45.6 mg, 0.373 mmol) was added to a solution of (E)-3-[3,5-difluoro-4-[(1R,3R)-2-(2-fluoro-2-methyl-propyl)-3-methyl-1,3,4,9-tetrahydropyrido[3,4-b]indol-1-yl]phenyl]prop-2-en-1-ol (1.60 g, 3.73 mmol) and acetic anhydride (0.420 mL, 4.48 mmol) in dichloromethane (75 mL) at rt. After 30 min, the reaction was concentrated under reduced pressure and the crude residue was purified by flash column chromatography (silica 0% to 30% isopropyl acetate - heptane) to give [(E)-3-[3,5-difluoro-4-[(1R,3R)-2-(2-fluoro-2-methyl-propyl)-3-methyl-1,3,4,9-tetrahydropyrido[3,4-b]indol-1-yl]phenyl]allyl] acetate (1.64 g, 3.49 mmol, 93% Yield).

TLC (SiO_2) R_f = 0.61 (hexanes: ethyl acetate = 2:1).

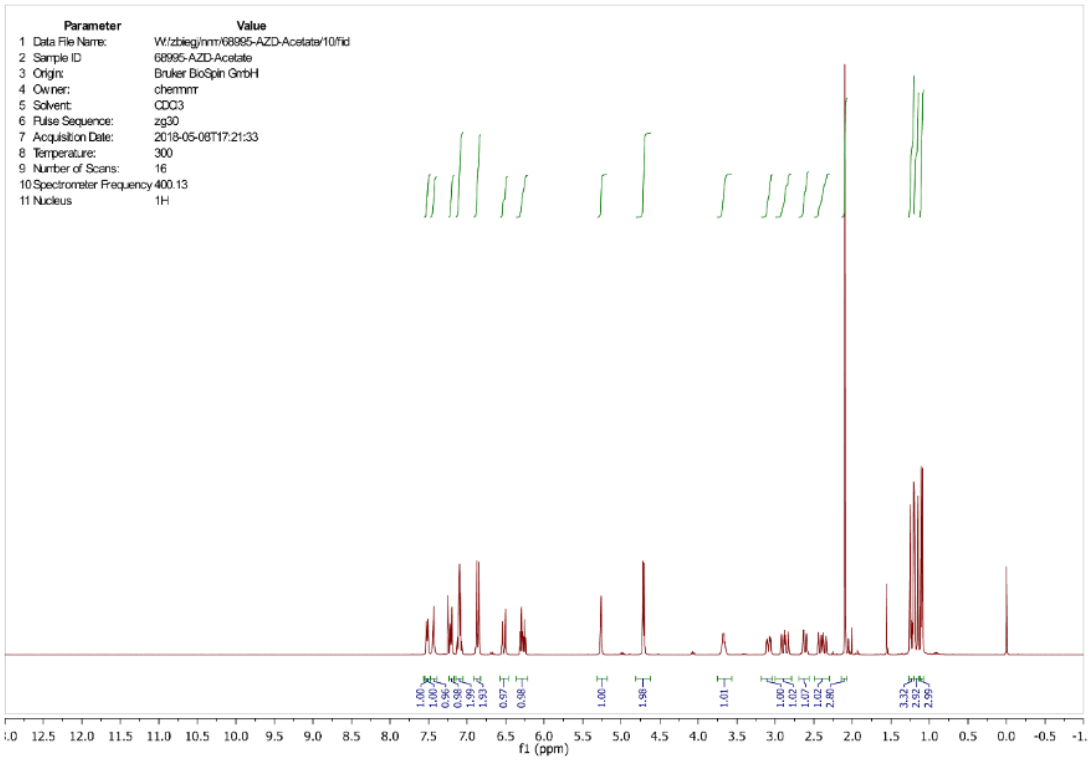
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 – 7.49 (m, 1H), 7.43 (s, 1H), 7.23 – 7.17 (m, 1H), 7.14 – 7.05 (m, 2H), 6.86 (d, *J* = 9.9 Hz, 2H), 6.52 (d, *J* = 16.0 Hz, 1H), 6.28 (dt, *J* = 15.9, 6.1 Hz, 1H), 5.26 (s, 1H), 4.71 (dd, *J* = 6.1, 1.4 Hz, 2H), 3.72 – 3.63 (m, 1H), 3.09 (ddd, *J* = 15.2, 5.0, 1.9 Hz, 1H), 2.88 (dd, *J* = 19.9, 15.0 Hz, 1H), 2.61 (ddd, *J* = 15.1, 4.1, 1.4 Hz, 1H), 2.39 (dd, *J* = 25.1, 15.0 Hz, 1H),1.23 (d, *J* = 18.2 Hz, 3H), 1.17 (d, *J* = 18.4 Hz, 3H), 1.10 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.7 , 162.3 (dd, *J* = 251.8, 8.2 Hz), 138.6 (t, *J* = 10.3 Hz), 136.3, 131.7, 131.2 (d, *J* = 2.7 Hz), 127.7 , 126.4 , 121.4 , 119.3 , 118.2 , 116.7 (t, *J* = 14.9 Hz), 110.7 , 109.7 (dd, *J* = 23.8, 3.3 Hz), 108.8, 98.0, 96.4, 64.3, 57.1 (d, *J* = 21.7 Hz), 51.2 (d, *J* = 3.9 Hz), 50.9, 27.1, 25.2 (d, *J* = 24.9 Hz), 24.5 (d, *J* = 24.8 Hz), 20.9.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –139.3 (m).

HRMS (ESI): Calculated for $C_{27}H_{29}O_2N_2F_3$ [$M+H^+$] = 471.2254, found 471.2247.

FTIR (neat): 3401, 2974, 1732, 1629, 1570, 1428, 1231, 1022, 964, 866, 736, 703 cm^{-1}.


Parameter Value
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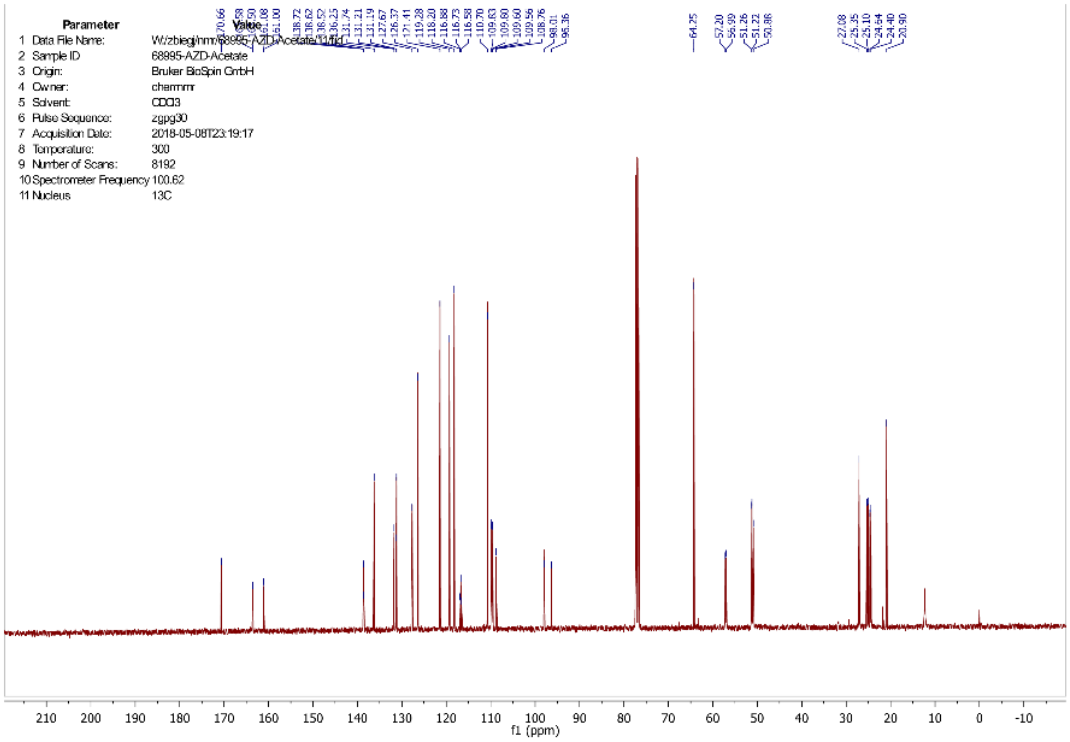
2 Sample ID 68995-AZD-Acetate
3 Origin: Bruker BioSpin GmbH
4 Owner: chemmr
5 Solvent: CDCl3
6 Pulse Sequence: zg30
7 Acquisition Date: 2018-05-08T17:21:33
8 Temperature: 300
9 Number of Scans: 16
10 Spectrometer Frequency 400.13
11 Nucleus 1H
f1 (ppm)


Parameter Value
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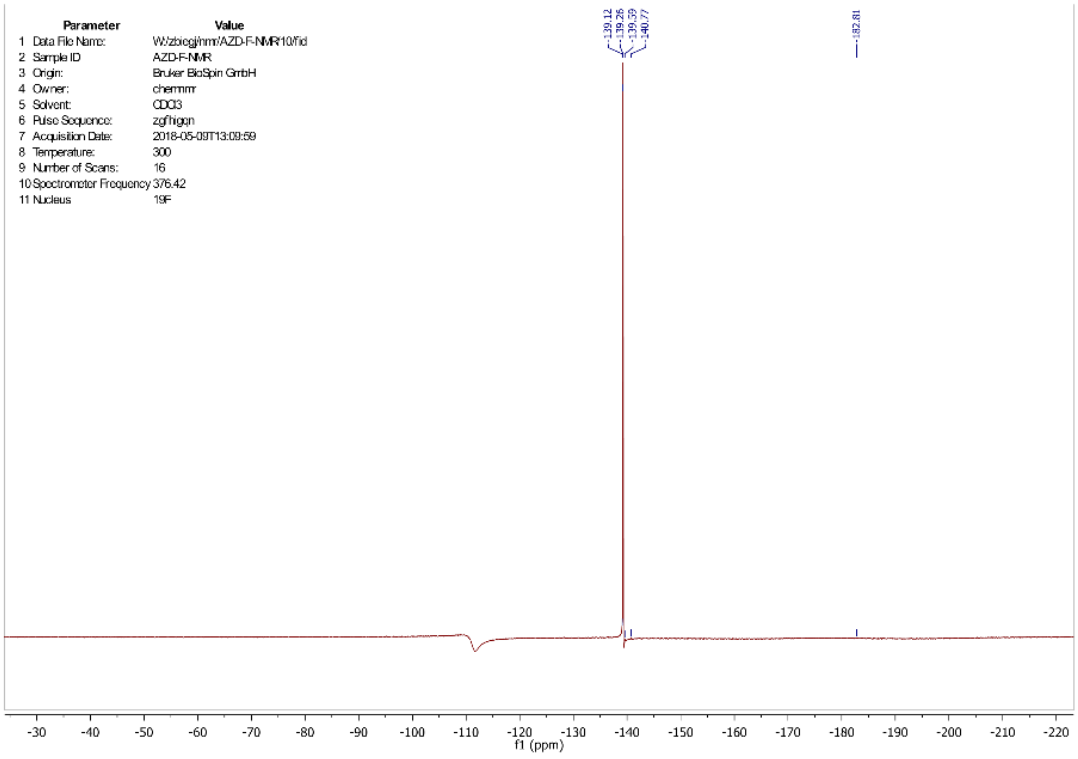
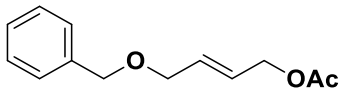
2 Sample ID 68995-AZD-Acetate
3 Origin: Bruker BioSpin GmbH
4 Owner: chemmr
5 Solvent: CDCl3
6 Pulse Sequence: zgpg30
7 Acquisition Date: 2018-05-08T23:19:17
8 Temperature: 300
9 Number of Scans: 8192
10 Spectrometer Frequency 100.62
11 Nucleus 13C
f1 (ppm)


Parameter Value
1 Data File Name: W:\zbicg\hmr\AZD-F-NMR10\fid
2 Sample ID AZD-F-NMR
3 Origin: Bruker BioSpin GmbH
4 Owner: chemmr
5 Solvent: CDCl3
6 Pulse Sequence: zgfhigqn
7 Acquisition Date: 2018-05-09T13:09:59
8 Temperature: 300
9 Number of Scans: 16
10 Spectrometer Frequency 376.42
11 Nucleus 19F
-139.12
-139.26
-139.59
-140.77
-182.81
-30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)

(*E*)-4-(benzyloxy)but-2-en-1-yl acetate (7.1r)



The title compound was prepared by the acetylation of the corresponding allylic alcohol.[10]

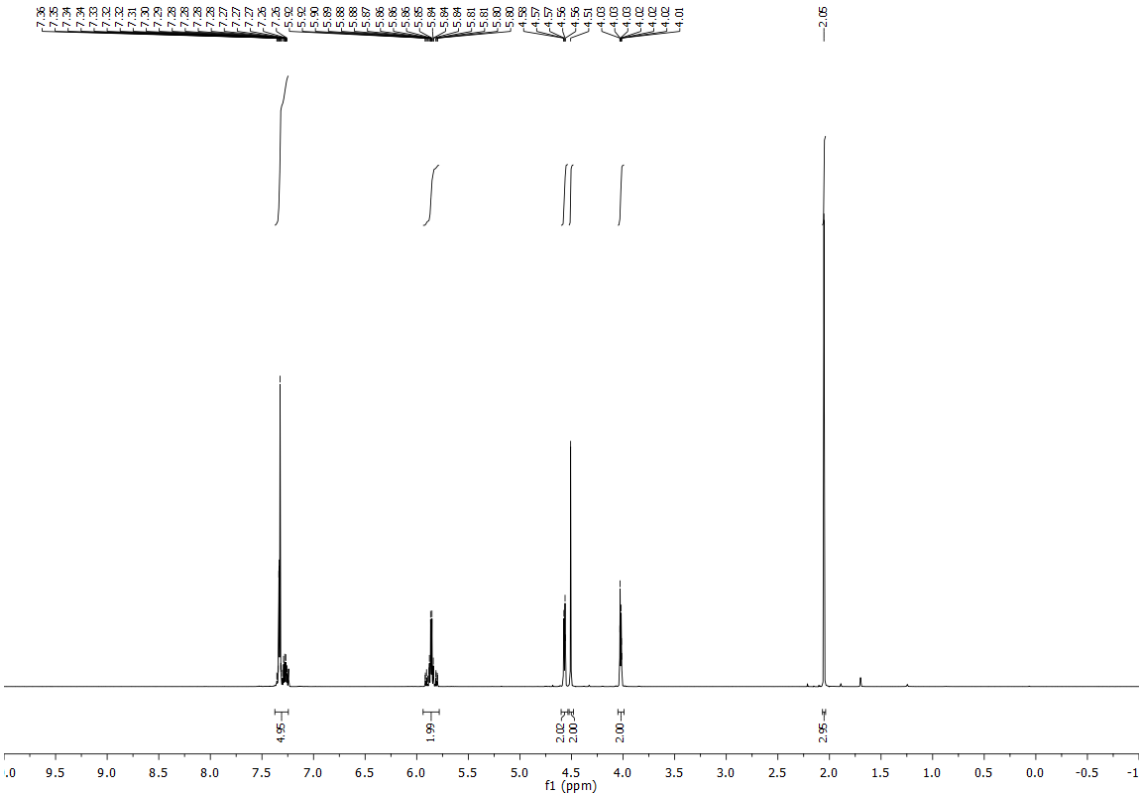
TLC (SiO_2) R_f = 0.45 (hexanes: ethyl acetate = 4:1).

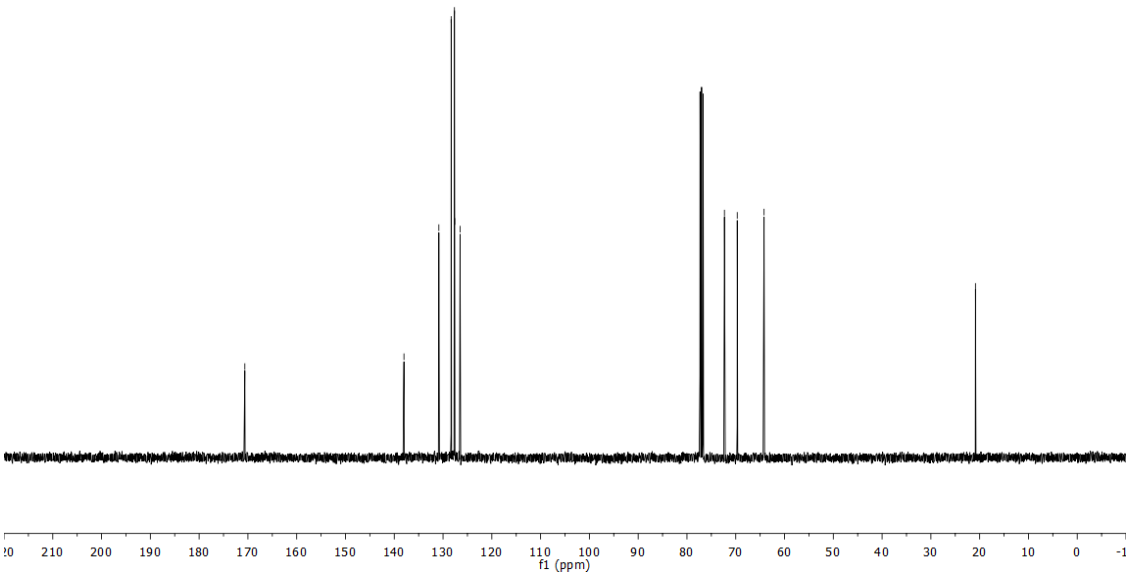
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 – 7.24 (m, 5H), 5.94 – 5.78 (m, 2H), 4.60 – 4.53 (m, 2H), 4.51 (s, 2H), 4.02 (dt, *J* = 3.9, 1.1 Hz, 2H), 2.05 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 138.0, 130.9, 128.3, 127.7, 127.6, 126.5, 72.3, 69.7, 64.2, 20.9.

HRMS (ESI): Calculated for $C_{13}H_{16}O_3$ $[M+NH_4^+]$ = 238.1438, found 238.1442.

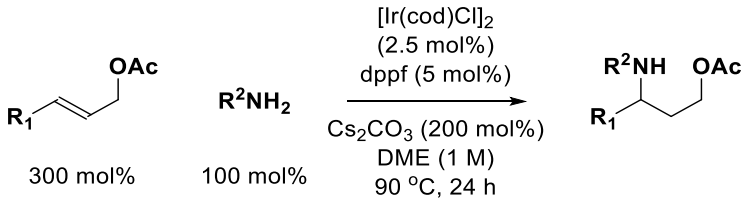
FTIR (neat): 2856, 1736, 1363, 1231, 1026, 908, 729, 669 cm^{-1}.


f1 (ppm)


f1 (ppm)

Procedures and Spectral Data for Synthesis of OAc-Amino Alcohols 7.3a-7.3r:

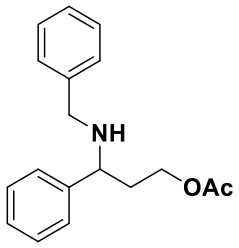
Regioselective Ir-catalyzed hydroamination with primary amine nucleophiles



General Procedure

An oven-dried pressure tube equipped with a magnetic stir bar was charged with cesium carbonate (200 mol%), $[Ir(cod)Cl]_2$ (2.5 mol%), and dppf (5 mol%). The tube was purged with argon for 5 minutes. DME (1.0 M) was added followed by the allylic acetate (300 mol%) and the amine (100 mol%). The tube was sealed with a PTFE lined cap and was placed in an oil bath at 90 ^{o}C and stirred for 24 hours. After reaching ambient temperature, the crude reaction mixture was directly subjected to flash column chromatography under the noted conditions.

3-(benzylamino)-3-phenylpropyl acetate (7.3a)



The allylic acetate (105.7 mg, 0.6 mmol, 300 mol%) and the primary amine (21.4 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions. The title compound was obtained in 77% yield (43.6 mg, 0.15 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, dichloromethane: diethyl ether = 20:1–10:1).

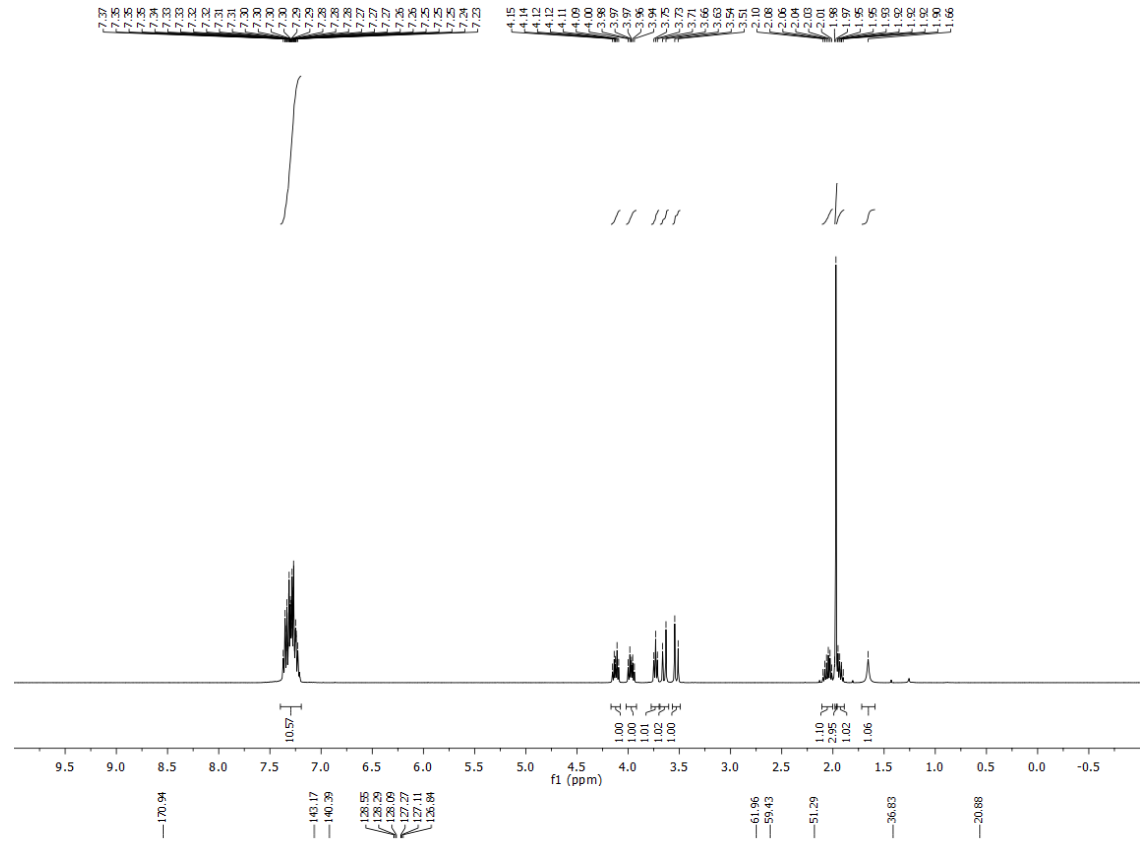
TLC (SiO_2) R_f = 0.22 (dichloromethane: diethyl ether = 5:1).

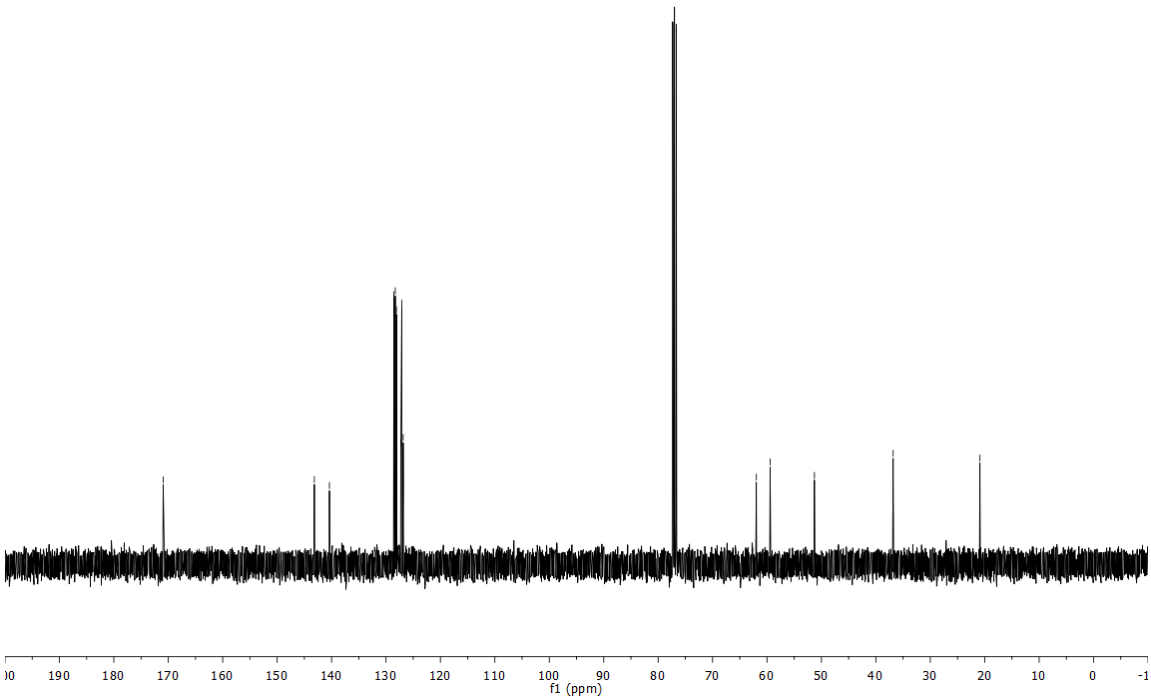
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 – 7.19 (m, 10H), 4.12 (dt, *J* = 11.1, 6.4 Hz, 1H), 3.97 (dt, *J* = 11.1, 6.6 Hz, 1H), 3.73 (t, *J* = 7.0 Hz, 1H), 3.65 (d, *J* = 13.1 Hz, 1H), 3.53 (d, *J* = 13.1 Hz, 1H), 2.05 (dq, *J* = 13.5, 6.7 Hz, 1H), 1.97 (s, 3H), 1.97 – 1.89 (m, 1H), 1.66 (br, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 143.2, 140.4, 128.6, 128.3, 128.1, 127.3, 127.1, 126.8, 62.0, 59.4, 51.3, 36.8, 20.9.

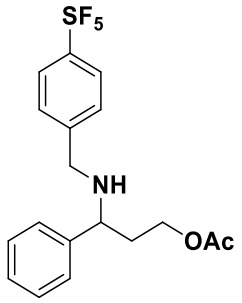
HRMS (ESI): Calculated for $C_{18}H_{21}NO_2$ [M+H$^+$] = 284.1654, found 284.1651.

FTIR (neat): 3029, 1735, 1453, 1364, 1235, 1028, 737, 698 cm^{-1}.





3-((4-(pentafluoro-l6-sulfanyl)benzyl)amino)-3-phenylpropyl acetate (7.3b)



The allylic acetate (105.7 mg, 0.6 mmol, 300 mol%) and the primary amine (46.6 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions. The title compound was obtained in 63% yield (51.6 mg, 0.13 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, dichloromethane: diethyl ether = 1:0–5:1).

TLC (SiO_2) R_f = 0.52 (dichloromethane: diethyl ether = 5:1).

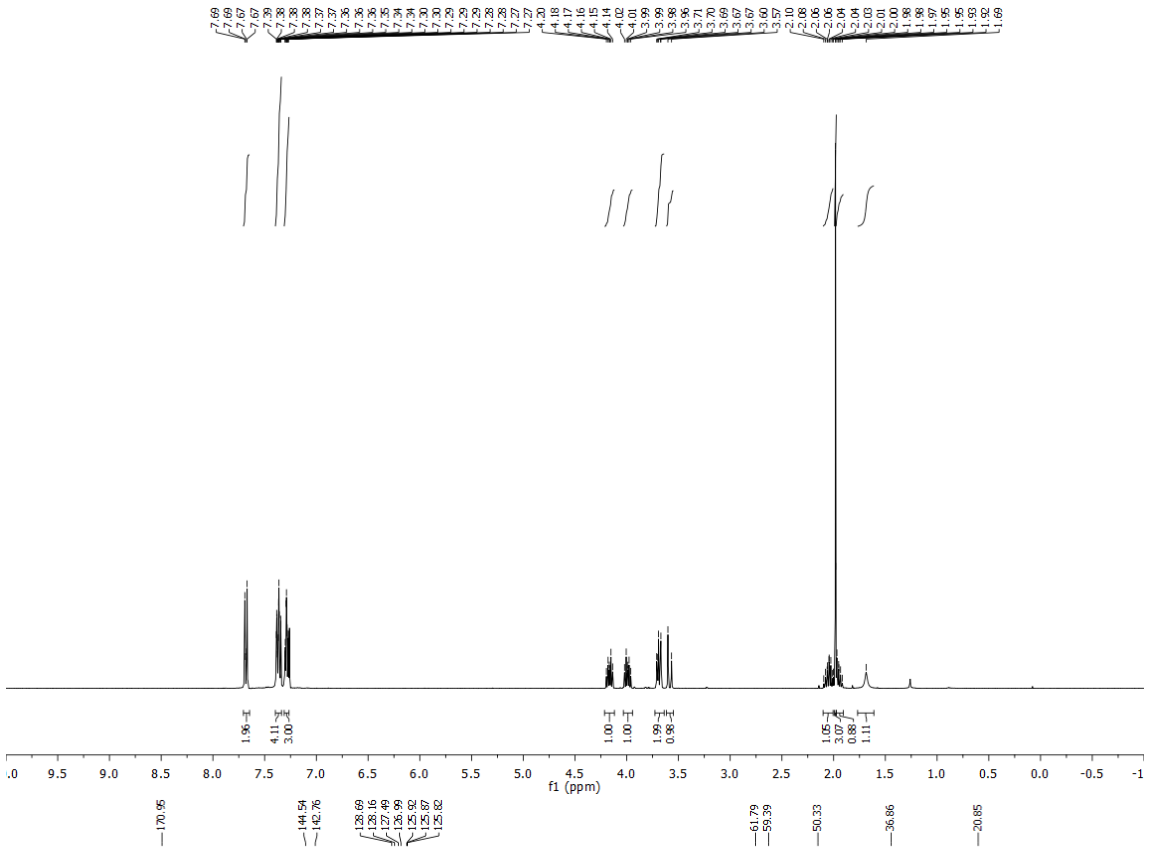
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 – 7.65 (m, 2H), 7.40 – 7.34 (m, 4H), 7.31 – 7.26 (m, 3H), 4.17 (dt, *J* = 11.1, 6.5 Hz, 1H), 3.99 (dt, *J* = 11.1, 6.5 Hz, 1H), 3.73 – 3.64 (m, 2H), 3.58 (d, *J* = 13.9 Hz, 1H), 2.10 – 2.01 (m, 1H), 1.98 (s, 3H), 1.98 – 1.91 (m, 1H), 1.69 (br, 1H).

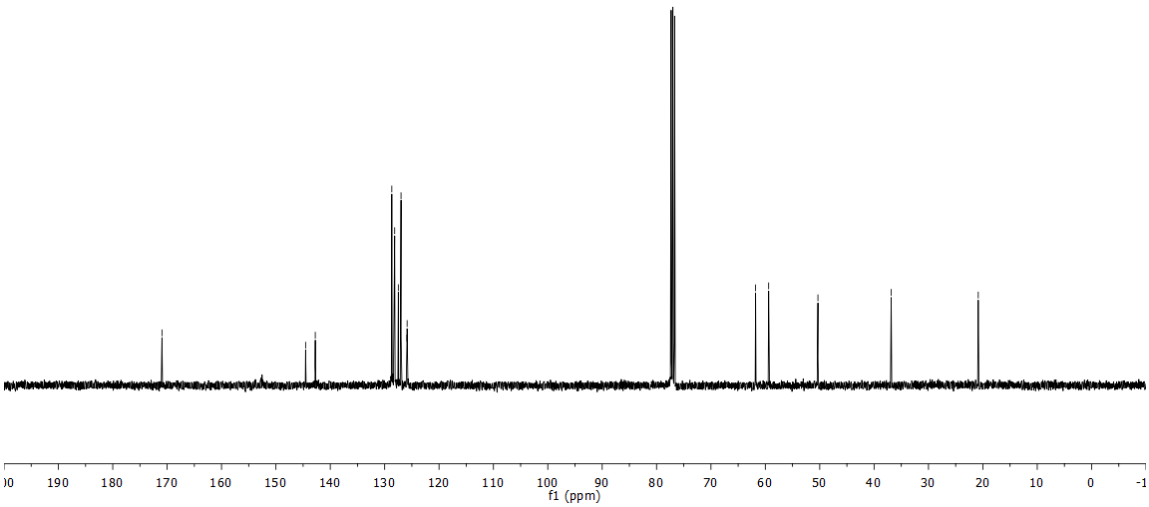
^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 144.5, 142.8, 128.7, 128.2, 127.5, 126.99, 125.87(t), 61.8, 59.4, 50.3, 36.9, 20.9.

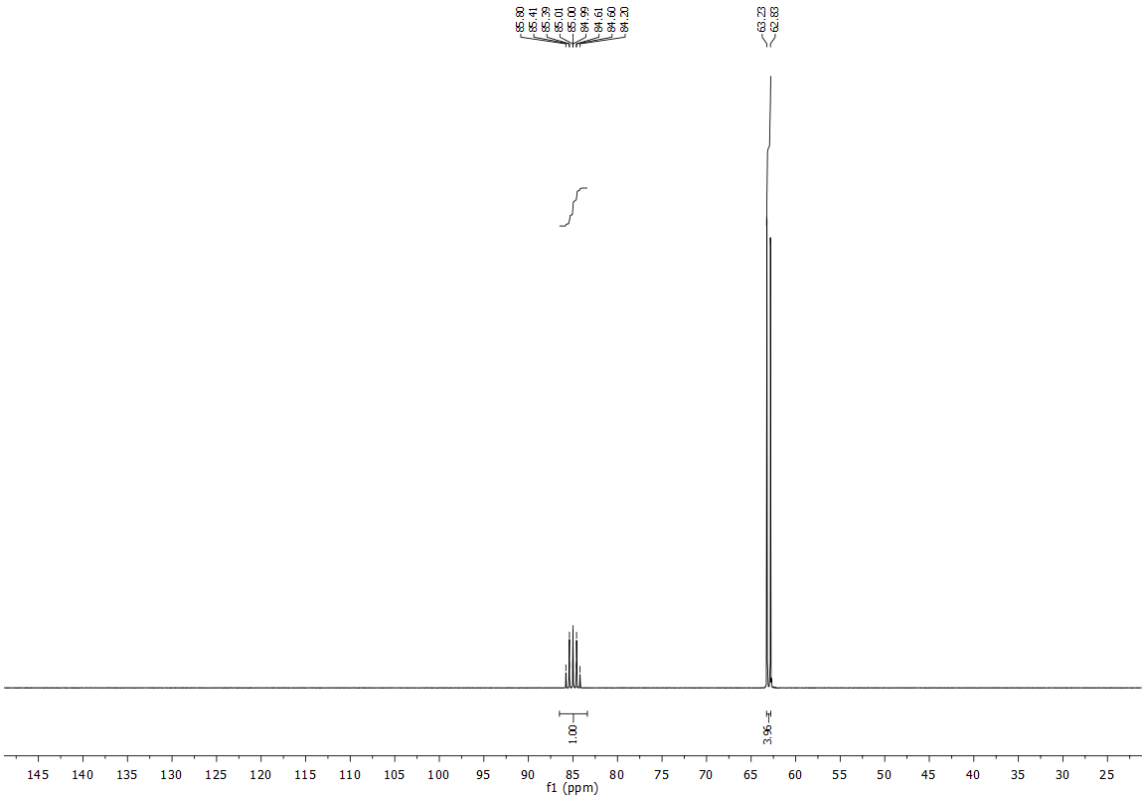
^{19}F NMR (376 MHz, $CDCl_3$): δ = 86.52 – 83.38 (m, 1F), 63.03 (d, *J* = 149.7 Hz, 4F).

HRMS (ESI): Calculated for $C_{18}H_{20}F_5NO_2S$ [M+H$^+$] = 410.1208, found 410.1210.

FTIR (neat): 1736, 1366, 1239, 1039, 833, 701, 670 cm^{-1}.


f1 (ppm)


f1 (ppm)


85.80
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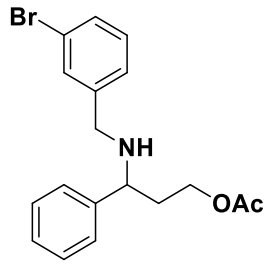
85.39
85.01
85.00
84.99
84.61
84.60
84.20
63.23
62.83
1.00
3.96
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25
f1 (ppm)

3-((3-bromobenzyl)amino)-3-phenylpropyl acetate (7.3c)



The allylic acetate (105.7 mg, 0.6 mmol, 300 mol%) and the primary amine (37.2 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions. The title compound was obtained in 65% yield (51.2 mg, 0.13 mmol) as a yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 4:1).

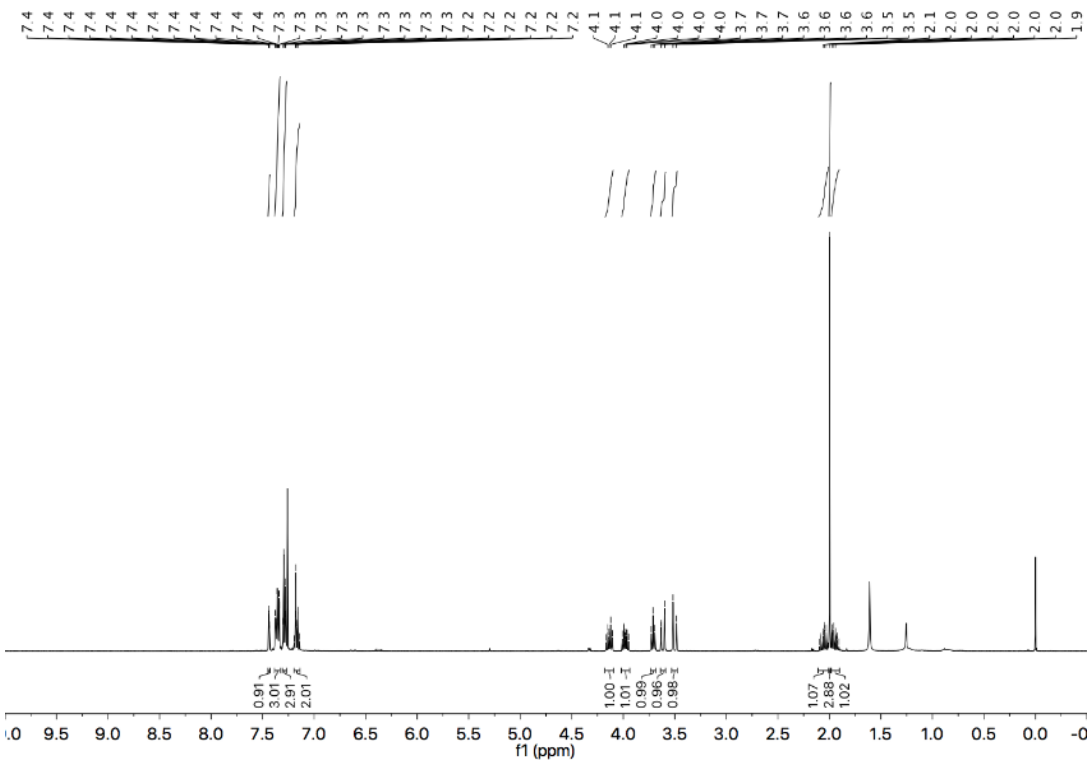
TLC (SiO_2) R_f = 0.20 (hexanes: ethyl acetate = 3:1).

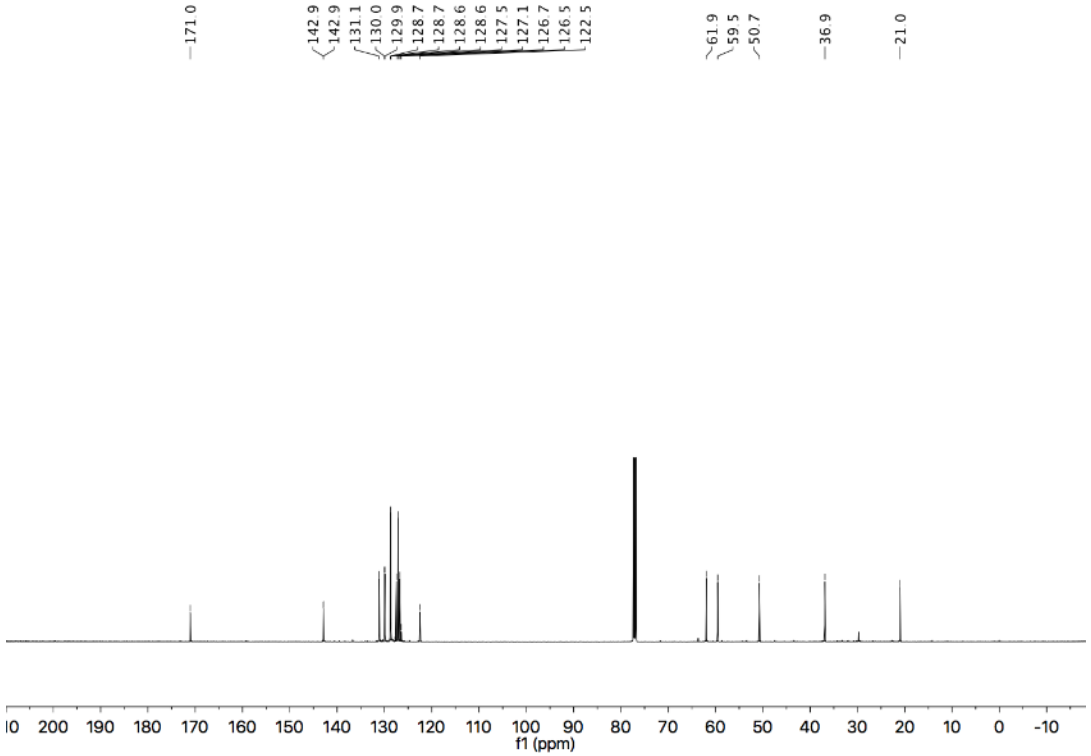
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 – 7.43 (m, 1H), 7.38 – 7.33 (m, 3H), 7.29 (dt, *J* = 7.8, 1.2 Hz, 3H), 7.20 – 7.14 (m, 2H), 4.14 (dt, *J* = 11.1, 6.4 Hz, 1H), 3.98 (ddd, *J* = 11.1, 7.0, 6.2 Hz, 1H), 3.71 (t, *J* = 7.0 Hz, 1H), 3.64 – 3.59 (m, 1H), 3.50 (d, *J* = 13.5 Hz, 1H), 2.06 (ddd, *J* = 14.0, 6.9, 6.2 Hz, 1H), 2.00 (s, 3H), 1.98 – 1.90 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 142.9, 142.9, 131.1, 130.0, 129.9, 128.7, 128.7, 128.7, 128.6, 127.5, 127.1, 126.7, 126.5, 122.5, 61.9, 59.5, 50.7, 36.9, 21.0.

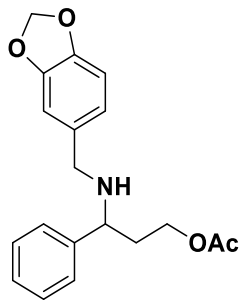
HRMS (ESI): Calculated for $C_{18}H_{20}BrNO_2$ [M+H$^+$] = 362.0750, Found 362.0754.

FTIR (neat): 3025, 2921, 1735, 1568, 1452, 1364, 1236, 1091, 1068, 1030, 996, 968,763, 700, 669 cm^{-1}.


f1 (ppm)


f1 (ppm)

3-((benzo[d][1,3]dioxol-5-ylmethyl)amino)-3-phenylpropyl acetate (7.3d)



The allylic acetate (105.7 mg, 0.6 mmol, 300 mol%) and the primary amine (30.2 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions. The title compound was obtained in 74% yield (48.5 mg, 0.15 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, dichloromethane: diethyl ether = 20:1–5:1).

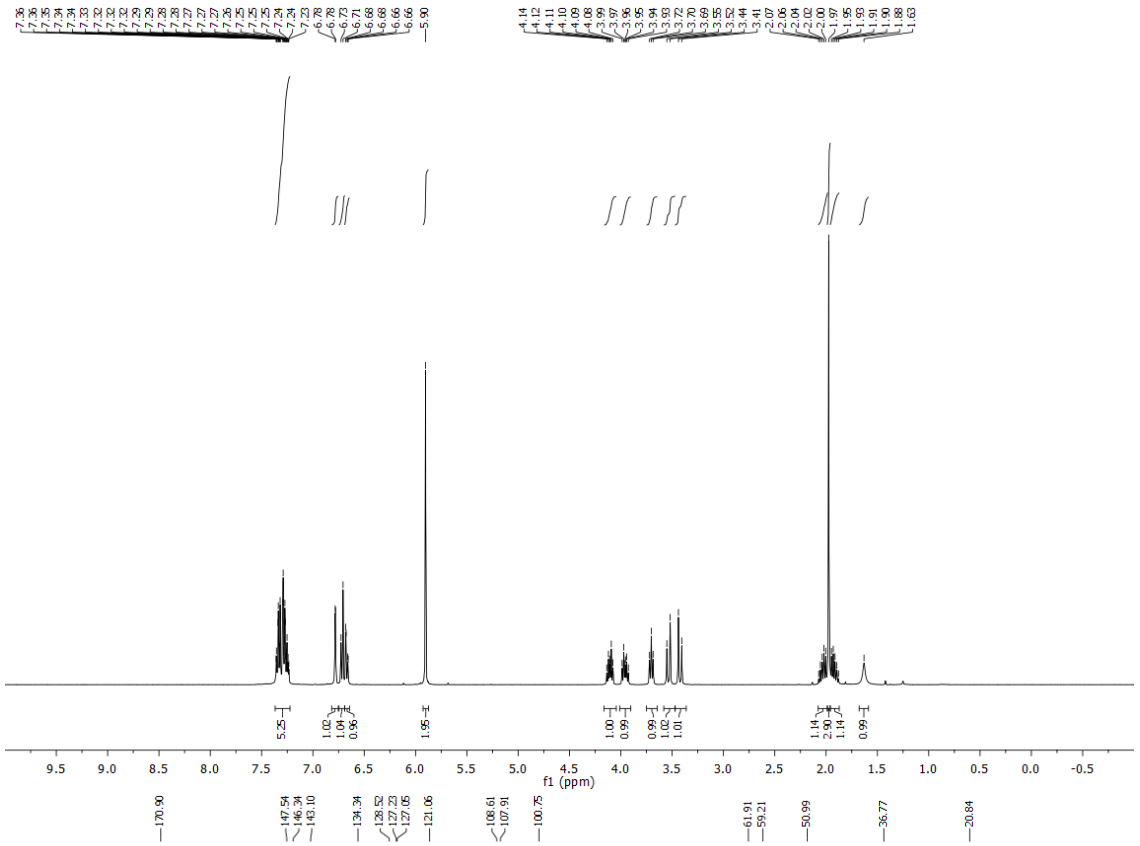
TLC (SiO_2) R_f = 0.19 (dichloromethane: diethyl ether = 5:1).

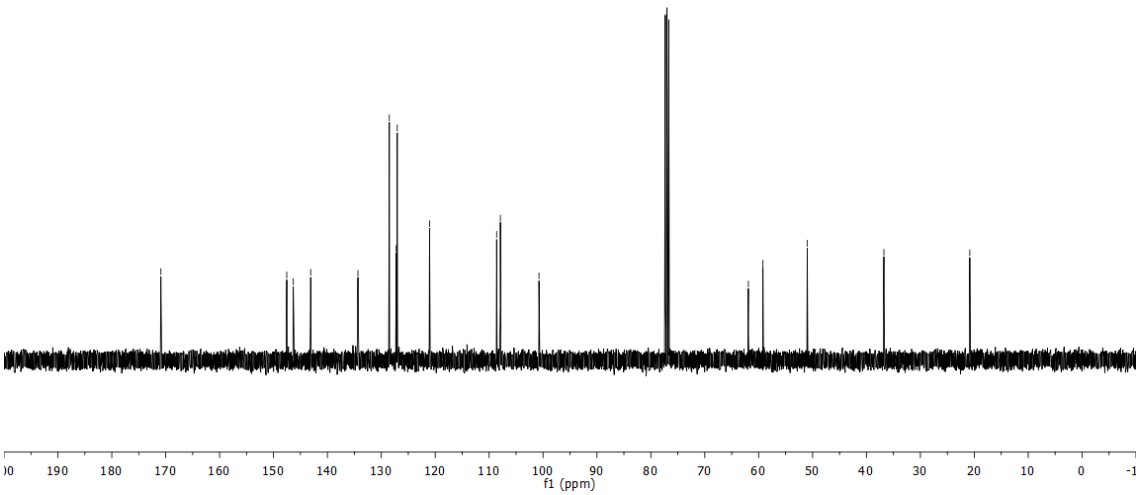
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 – 7.22 (m, 5H), 6.78 (d, *J* = 1.6 Hz, 1H), 6.72 (d, *J* = 7.9 Hz, 1H), 6.67 (d, *J* = 7.9 Hz, 1H), 5.90 (s, 2H), 4.11 (dt, *J* = 11.1, 6.4 Hz, 1H), 3.96 (dt, *J* = 11.1, 6.7 Hz, 1H), 3.70 (t, *J* = 7.0 Hz, 1H), 3.54 (d, *J* = 13.0 Hz, 1H), 3.42 (d, *J* = 13.0 Hz, 1H), 2.04 (dt, *J* = 13.7, 6.8 Hz, 1H), 1.97 (s, 3H), 1.91 (dt, *J* = 13.7, 6.8 Hz, 1H), 1.63 (br, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 147.5, 146.3, 143.1, 134.3, 128.5, 127.2, 127.1, 121.1, 108.6, 107.9, 100.8, 61.9, 59.2, 51.0, 36.8, 20.8.

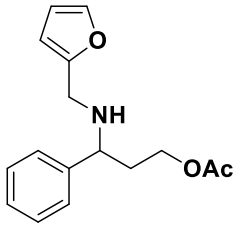
HRMS (ESI): Calculated for $C_{19}H_{21}NO_4$ [M+H$^+$] = 328.1543, found 328.1551.

FTIR (neat): 2984, 1733, 1488, 1440, 1365, 1236, 1036, 929, 808, 734, 701 cm^{-1}.


f1 (ppm)


f1 (ppm)

3-((furan-2-ylmethyl)amino)-3-phenylpropyl acetate (7.3e)



The allylic acetate (105.7 mg, 0.6 mmol, 300 mol%) and the primary amine (19.4 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions. The title compound was obtained in 68% yield (37.1 mg, 0.14 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, dichloromethane: diethyl ether = 30:1–10:1).

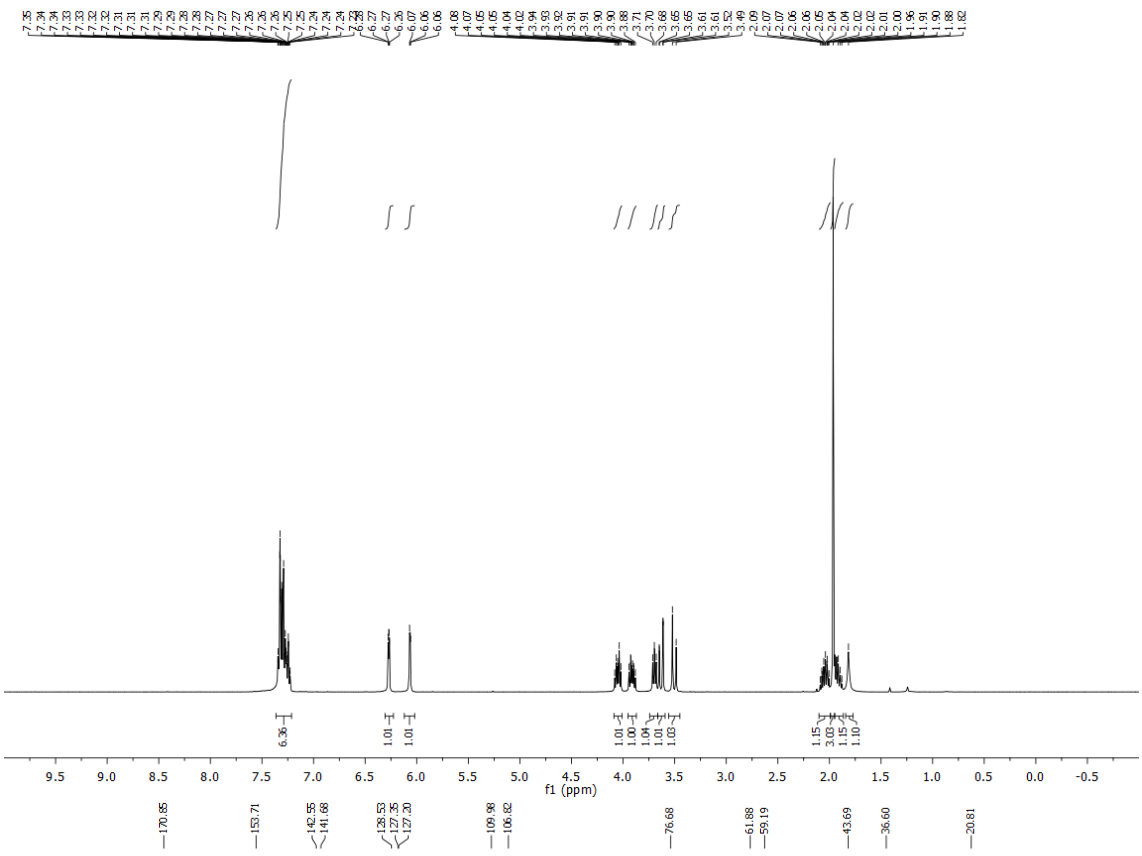
TLC (SiO_2) R_f = 0.33 (dichloromethane: diethyl ether = 5:1).

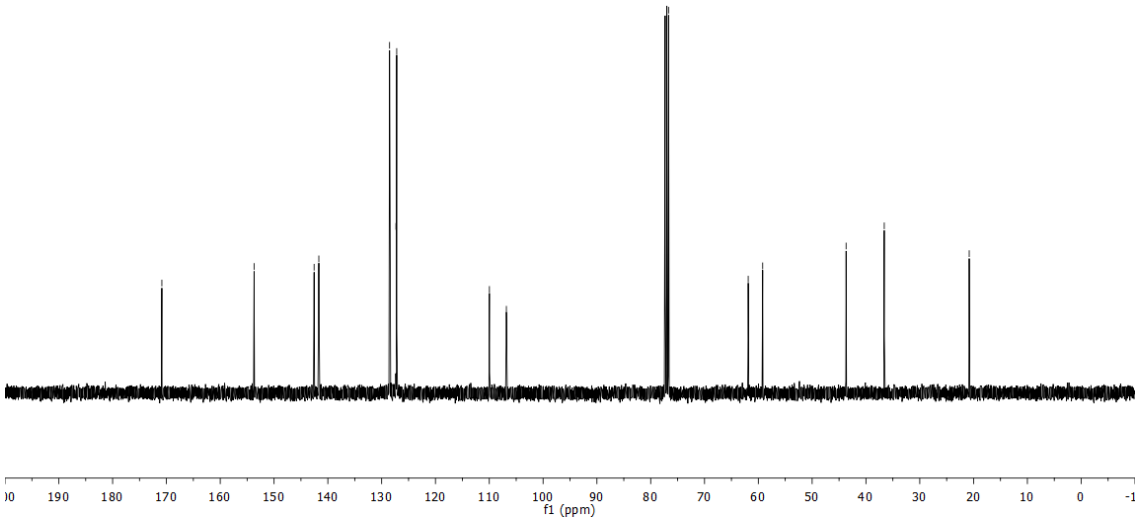
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 – 7.21 (m, 6H), 6.27 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.12 – 6.02 (m, 1H), 4.05 (dt, *J* = 11.1, 6.2 Hz, 1H), 3.91 (dt, *J* = 11.1, 6.2 Hz, 1H), 3.70 (t, *J* = 6.8 Hz, 1H), 3.63 (d, *J* = 14.5 Hz, 1H), 3.50 (d, *J* = 14.5 Hz, 1H), 2.05 (td, *J* = 13.8, 6.3 Hz, 1H), 1.96 (s, 3H), 1.95 – 1.87 (m, 1H), 1.82 (br, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 153.7, 142.6, 141.7, 128.5, 127.4, 127.2, 110.0, 106.8, 76.7, 61.9, 59.2, 43.7, 36.6, 20.8.

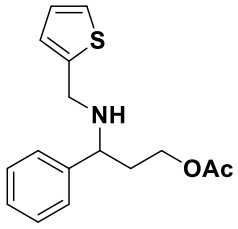
HRMS (ESI): Calculated for $C_{16}H_{19}NO_3$ $[M+H^+]$ = 274.1438, found 274.1445.

FTIR (neat): 2919, 1735, 1365, 1235, 1036, 918, 735, 700 cm^{-1}.


f1 (ppm)


f1 (ppm)

3-phenyl-3-((thiophen-2-ylmethyl)amino)propyl acetate (7.3f)



The allylic acetate (105.7 mg, 0.6 mmol, 300 mol%) and the primary amine (22.6 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions. The title compound was obtained in 71% yield (41.1 mg, 0.14 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, dichloromethane: diethyl ether = 20:1–10:1).

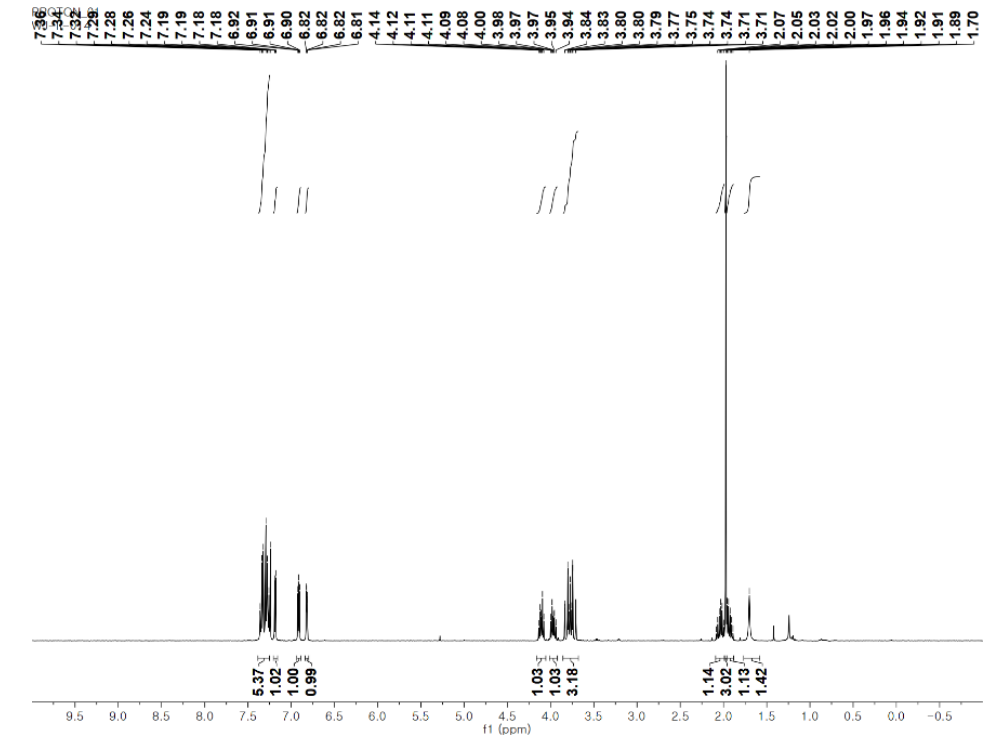
TLC (SiO_2) R_f = 0.52 (dichloromethane: diethyl ether = 5:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 – 7.25 (m, 5H), 7.18 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.91 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.82 (dd, *J* = 3.4, 1.0 Hz, 1H), 4.11 (dt, *J* = 11.1, 6.4 Hz, 1H), 3.97 (dt, *J* = 11.1, 6.6 Hz, 1H), 3.86 – 3.68 (m, 3H), 2.04 (dq, *J* = 13.5, 6.9 Hz, 1H), 1.97 (s, 3H), 1.93 (dd, *J* = 13.9, 7.2 Hz, 1H), 1.70 (br, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 144.3, 142.8, 128.6, 128.6, 127.4, 127.2, 126.5, 124.7, 124.3, 62.0, 59.1, 45.8, 36.8, 20.9.

HRMS (ESI): Calculated for $C_{16}H_{19}NO_2S$ [M+H$^+$] = 290.1209, found 290.1213.

FTIR (neat): 2919, 2849,1735, 1493, 1454, 1387, 1365, 1237, 1110, 1037, 852, 829, 761, 700 cm^{-1}.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7.28
7.26
7.24
7.19
7.19
7.18
7.18
6.92
6.91
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6.90
6.82
6.82
6.81
4.14
4.12
4.11
4.11
4.09
4.08
4.00
3.98
3.97
3.97
3.95
3.94
3.84
3.83
3.80
3.80
3.79
3.77
3.75
3.74
3.74
3.71
3.71
2.07
2.05
2.03
2.02
2.00
1.97
1.96
1.94
1.92
1.91
1.89
1.70
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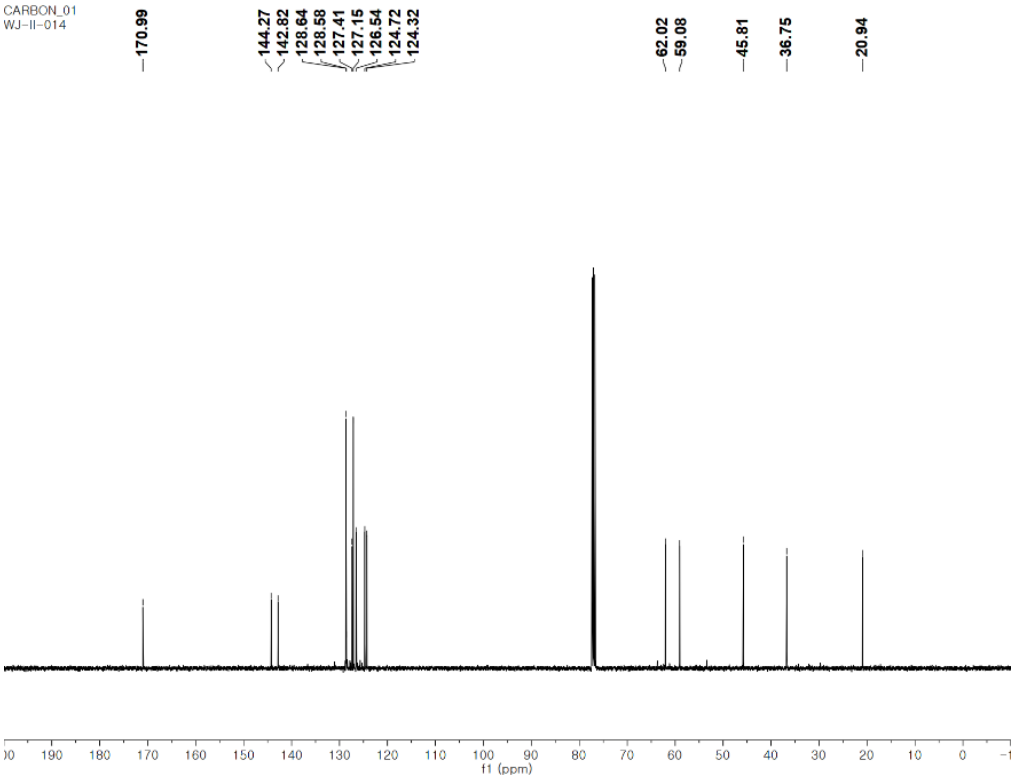
3.02
1.13
1.42
f1 (ppm)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142.82
128.64
128.58
127.41
127.15
126.54
124.72
124.32
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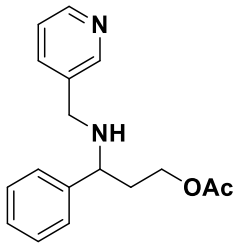
45.81
36.75
20.94
f1 (ppm)

3-phenyl-3-((pyridin-3-ylmethyl)amino)propyl acetate (7.3g)



The allylic acetate (105.7 mg, 0.6 mmol, 300 mol%) and the primary amine (21.6 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions. The title compound was obtained in 67% yield (38 mg, 0.14 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 100% over 30 min).

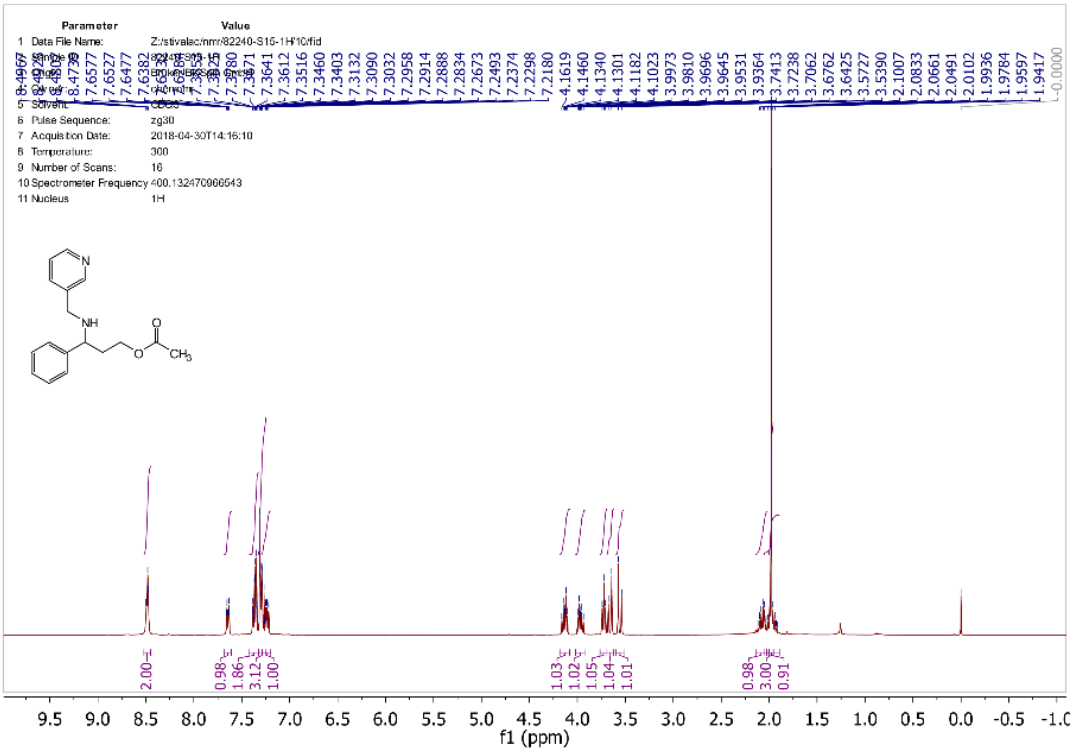
TLC (SiO_2) R_f = 0.30 (ethyl acetate: methanol = 15:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.52 – 8.45 (m, 2H), 7.64 (dt, *J* = 7.7, 2.0 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.33 – 7.24 (m, 3H), 7.23 (dd, *J* = 7.8, 4.7 Hz, 1H), 4.13 (dt, *J* = 11.1, 6.4 Hz, 1H), 3.97 (dt, *J* = 11.2, 6.6 Hz, 1H), 3.72 (t, *J* = 7.0 Hz, 1H), 3.66 (d, *J* = 13.5 Hz, 1H), 3.56 (d, *J* = 13.5 Hz, 1H), 2.08 (dt, *J* = 13.7, 6.7 Hz, 1H), 2.05 – 1.89 (m, 1H), 1.98 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 149.5, 149.2, 134.8, 128.5, 128.3, 127.4, 123.8, 61.4, 57.2, 51.1, 36.3 20.8.

HRMS (ESI): Calculated for $C_{17}H_{21}N_2O_2$ $[M+H^+]$ =285.1598, found 285.1595.

FTIR (neat): 220, 1735, 1424, 13365, 1237, 1028, 762, 702 cm^{-1}.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Value
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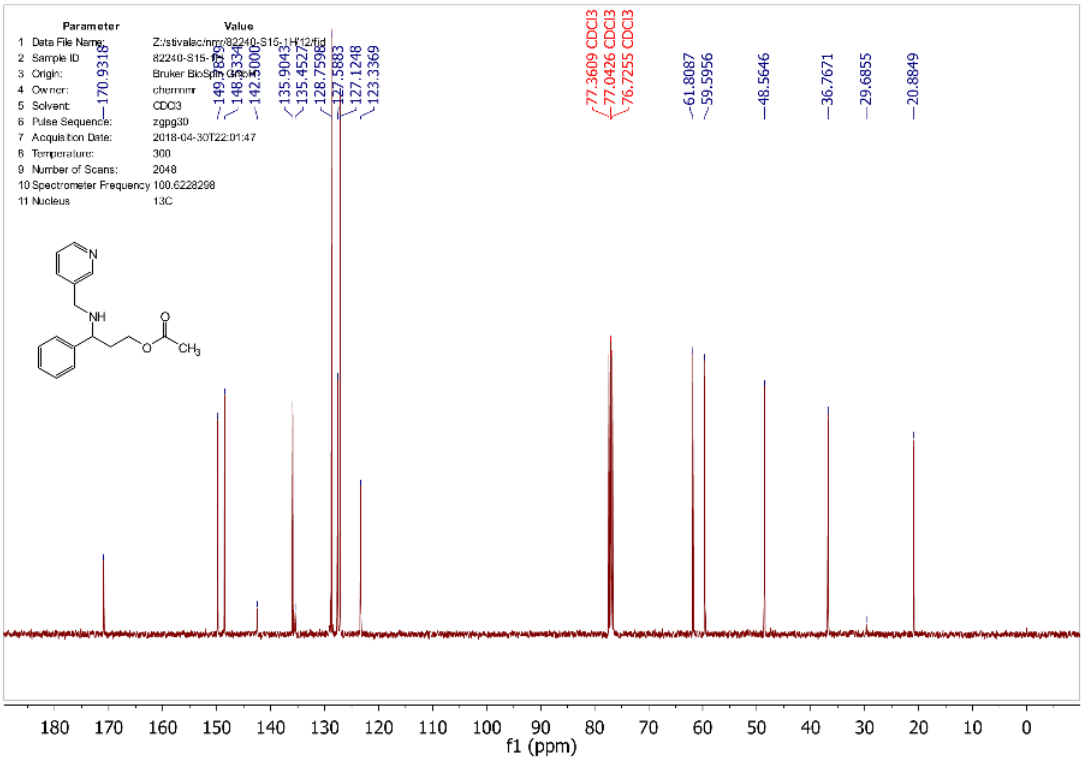
5 Solvent: CDCl3
6 Pulse Sequence: zg30
7 Acquisition Date: 2018-04-30T14:16:10
8 Temperature: 300
9 Number of Scans: 16
10 Spectrometer Frequency 400.132470966543
11 Nucleus 1H
f1 (ppm)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Value
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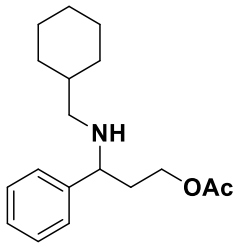
3 Origin: Bruker BioSpin GmbH
4 Owner: chemmr
5 Solvent: CDCl3
6 Pulse Sequence: zgpg30
7 Acquisition Date: 2018-04-30T22:01:47
8 Temperature: 300
9 Number of Scans: 2048
10 Spectrometer Frequency 100.6228298
11 Nucleus 13C
f1 (ppm)

3-((cyclohexylmethyl)amino)-3-phenylpropyl acetate (7.3h)



The cinnamyl acetate (105.7 mg, 0.6 mmol, 300 mol%) and the cyclohexylmethanamine (22.6 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions (90 ^{o}C, 24 hr). The title compound was obtained in 54% yield (31.2 mg, 0.11 mmol) as a yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethylacetate = 3:1).

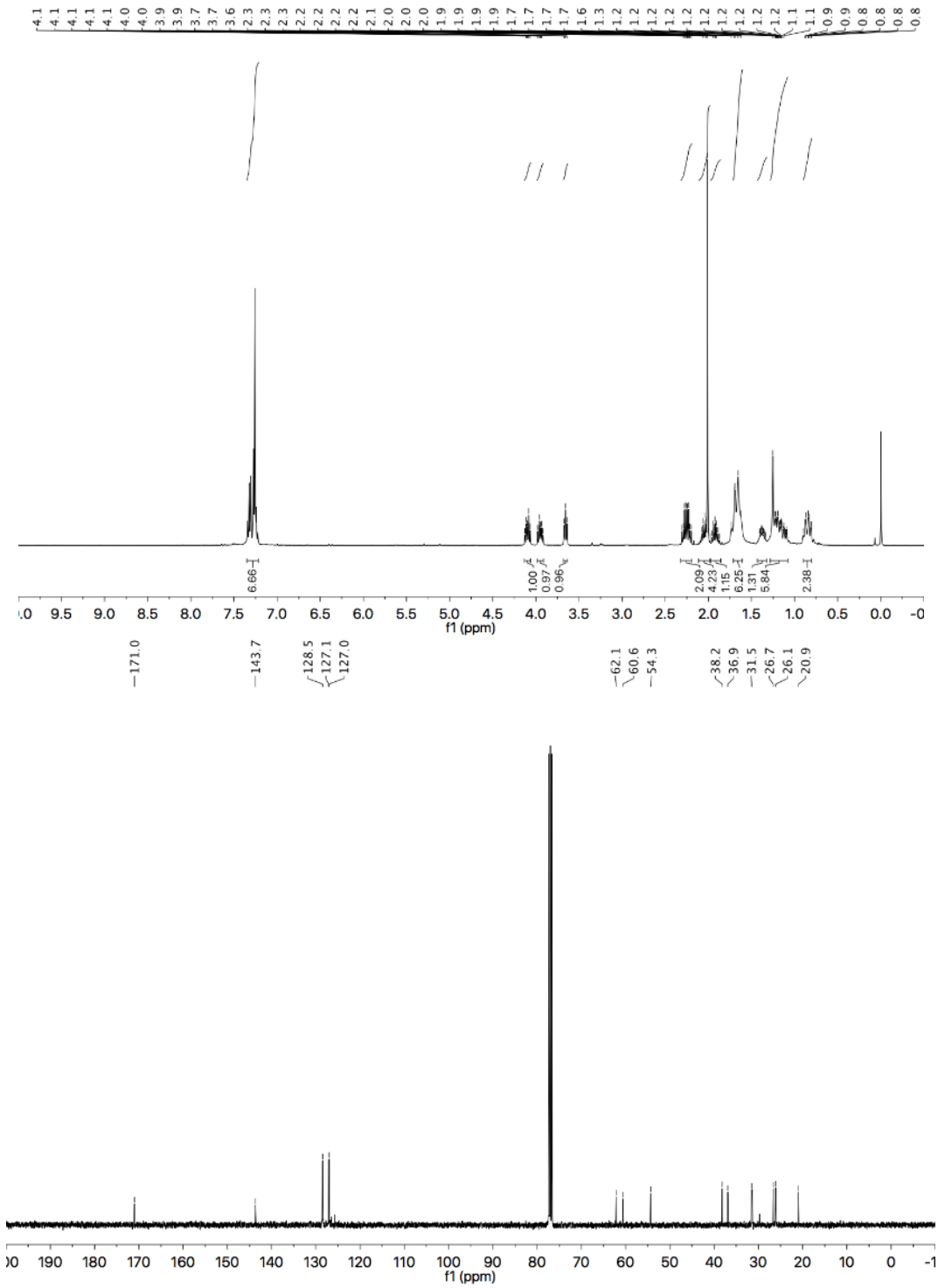
TLC (SiO_2) R_f = 0.19 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 – 7.21 (m, 7H), 4.10 (dt, *J* = 11.1, 6.3 Hz, 1H), 3.95 (dt, *J* = 11.1, 6.8 Hz, 1H), 3.66 (t, *J* = 6.9 Hz, 1H), 2.25 (qd, *J* = 11.5, 6.6 Hz, 2H), 2.01 (s, 4H), 1.97 – 1.86 (m, 1H), 1.71 – 1.61 (m, 6H), 1.38 (ddt, *J* = 11.1, 7.6, 3.4 Hz, 1H), 1.28 – 1.08 (m, 6H), 0.90 – 0.80 (m, 2H).

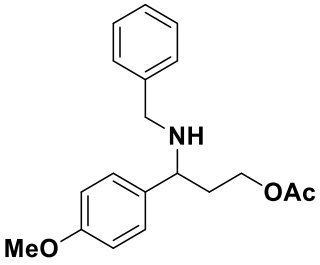
^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 143.7, 128.5, 127.1, 127.0, 62.1, 60.6, 54.3, 38.2, 36.9, 31.5, 26.7, 26.1, 20.9.

HRMS (ESI): Calculated for $C_{18}H_{27}NO_2$ [M+H$^+$] = 290.2115, Found 290.2119.

FTIR (neat): 2920, 2850, 1739, 1450, 1356, 1237, 1037, 761, 700 cm^{-1}.



3-(benzylamino)-3-(4-methoxyphenyl)propyl acetate (7.3i)



The allylic acetate (123.7 mg, 0.6 mmol, 300 mol%) and the benzyl amine (21 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions (90 ^{o}C, 24 hr). The title compound was obtained in 64% yield (40.1 mg, 0.13 mmol) as a yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethylacetate = 2:1).

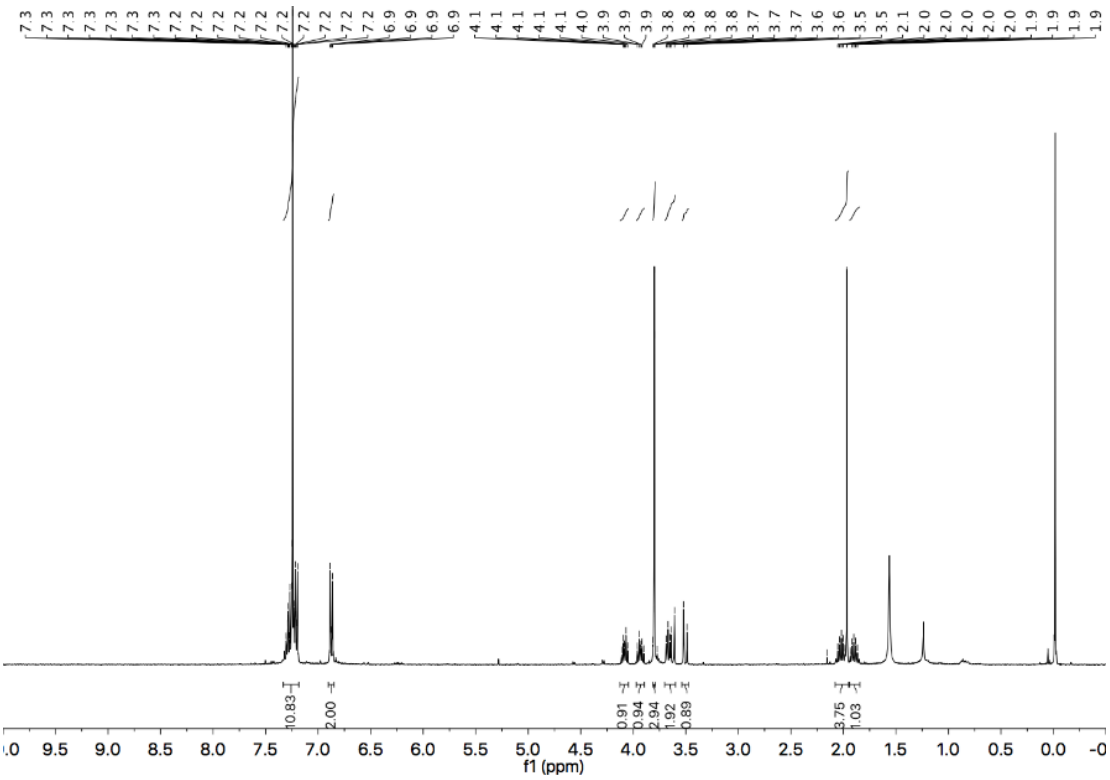
TLC (SiO_2) R_f = 0.17 (hexanes: ethyl acetate = 2:1).

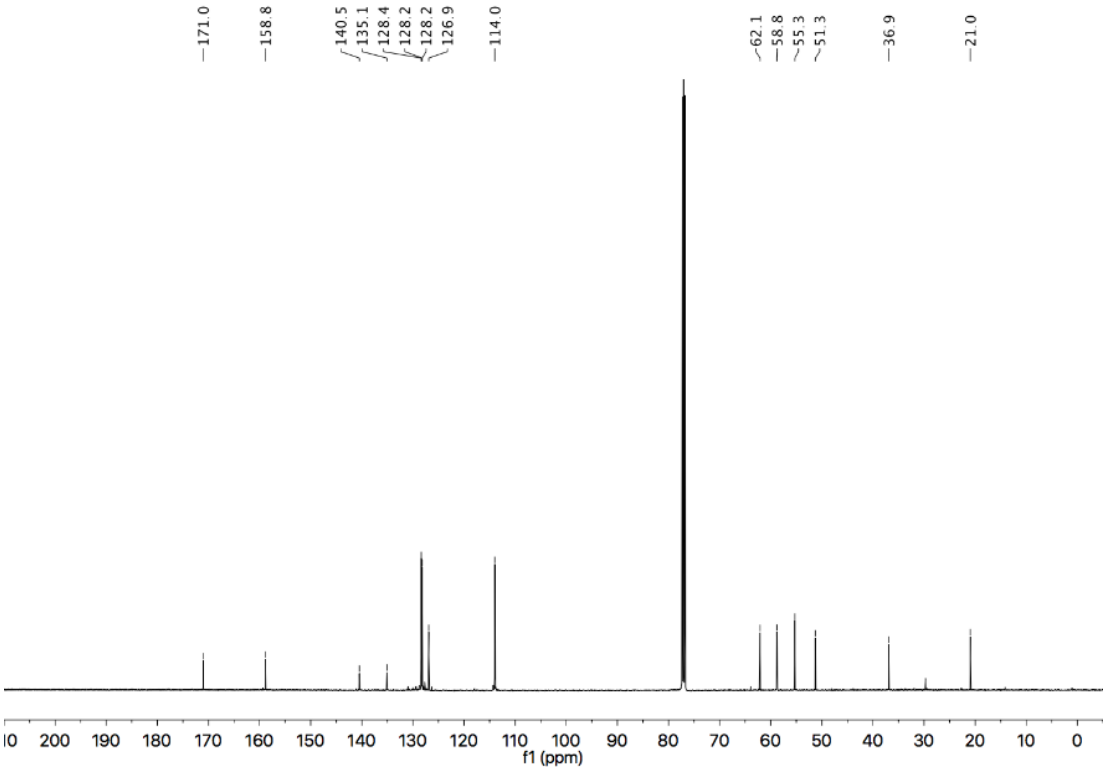
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 – 7.18 (m, 11H), 6.90 – 6.85 (m, 2H), 4.08 (dt, *J* = 11.0, 6.3 Hz, 1H), 3.93 (dt, *J* = 11.1, 6.7 Hz, 1H), 3.80 (d, *J* = 0.5 Hz, 3H), 3.70 – 3.60 (m, 2H), 3.50 (d, *J* = 13.1 Hz, 1H), 2.08 – 1.95 (m, 4H), 1.90 (dt, *J* = 14.0, 6.9 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.0, 158.8, 140.5, 135.1, 128.4, 128. 2, 128.2, 126.9, 114.0, 62.1, 58.8, 55.3, 51.3, 36.9, 21.0.

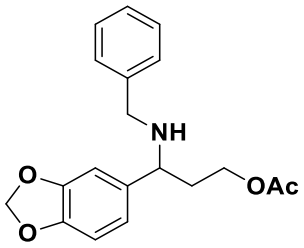
HRMS (ESI): Calculated for $C_{19}H_{23}NO_3$ [M+H^{+}] = 314.1751, Found 313.1751.

FTIR (neat): 2931, 2836, 1735, 1584, 1511, 1454, 1302, 1243, 1176, 1033, 831, 735, 699 cm^{-1}.


f1 (ppm)


f1 (ppm)

3-(benzo[d][1,3]dioxol-5-yl)-3-(benzylamino)propyl acetate (7.3j)



The allylic acetate (132.1 mg, 0.6 mmol, 300 mol%) and the primary amine (21.4 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions for 48 h. The title compound was obtained in 67% yield (43.9 mg, 0.13 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, dichloromethane: diethyl ether = 25:1–5:1).

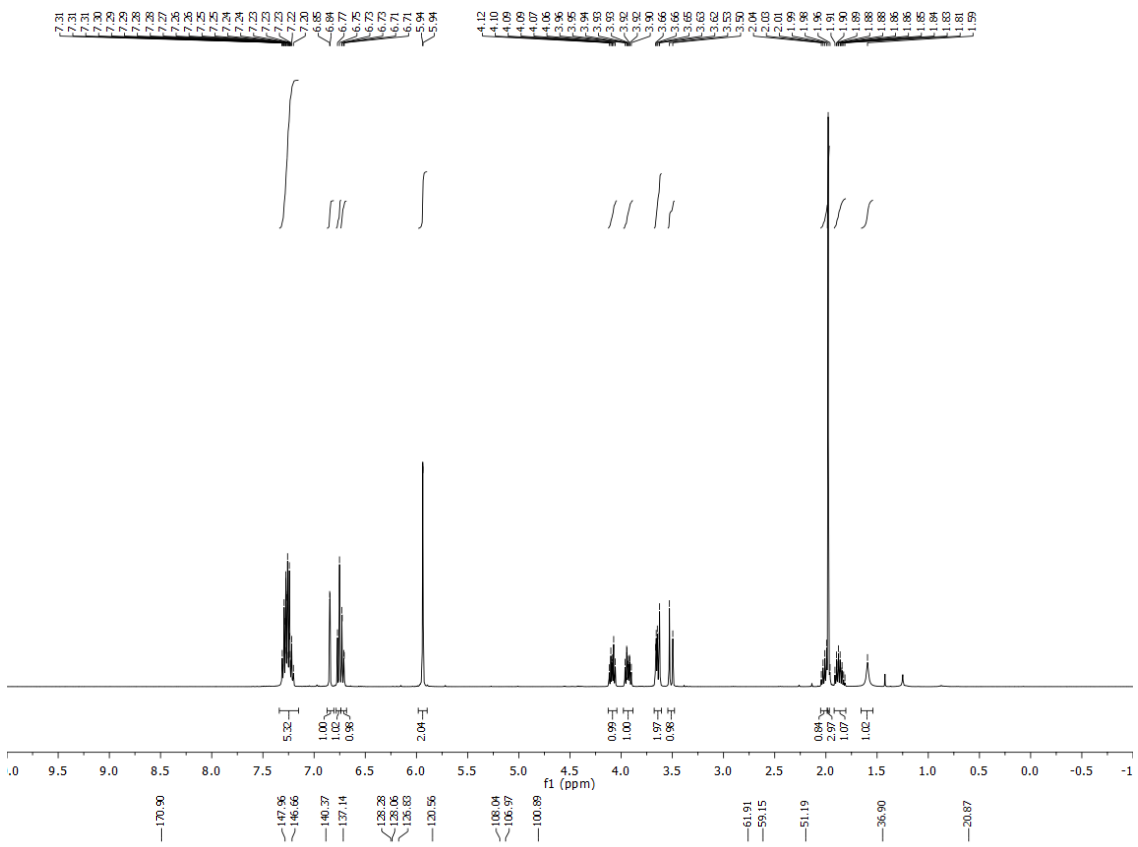
TLC (SiO_2) R_f = 0.30 (dichloromethane: diethyl ether = 3:1).

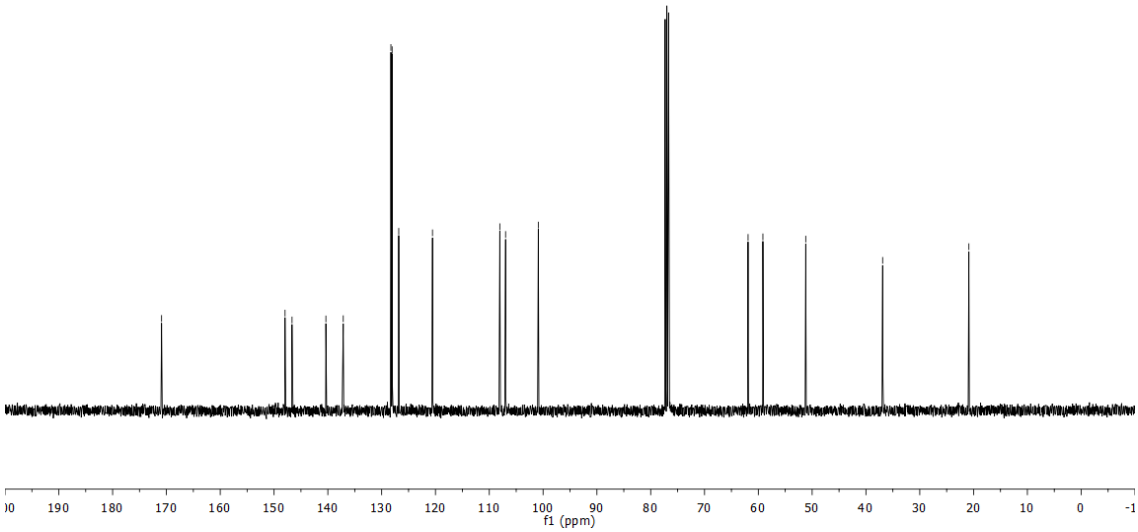
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 – 7.15 (m, 5H), 6.85 (d, *J* = 1.6 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.72 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.94 (d, *J* = 0.8 Hz, 2H), 4.09 (dt, *J* = 11.1, 6.3 Hz, 1H), 3.93 (dt, *J* = 11.1, 6.3 Hz, 1H), 3.68 – 3.61 (m, 2H), 3.51 (d, *J* = 13.2 Hz, 1H), 2.05 – 1.95 (m, 1H), 1.98 (s, 3H), 1.87 (ddt, *J* = 13.8, 7.5, 6.3 Hz, 1H), 1.59 (br, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 148.0, 146.7, 140.4, 137.1, 128.3, 128.1, 126.8, 120.6, 108.0, 107.0, 100.9, 61.9, 59.2, 51.2, 36.9, 20.9.

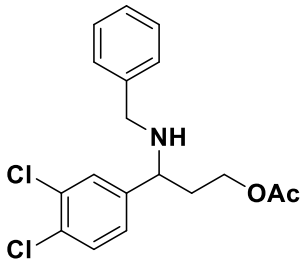
HRMS (ESI): Calculated for $C_{19}H_{21}NO_4$ [M+H$^+$] = 328.1543, found 328.1551.

FTIR (neat): 2917, 1732, 1486, 1365, 1236, 1036, 908, 728, 698 cm^{-1}.


f1 (ppm)


f1 (ppm)

3-(benzylamino)-3-(3,4-dichlorophenyl)propyl acetate (7.3k)



The allylic acetate (147 mg, 0.6 mmol, 300 mol%) and the primary amine (21.6 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions. The title compound was obtained in 78% yield (55 mg, 0.16 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 100% over 30 min).

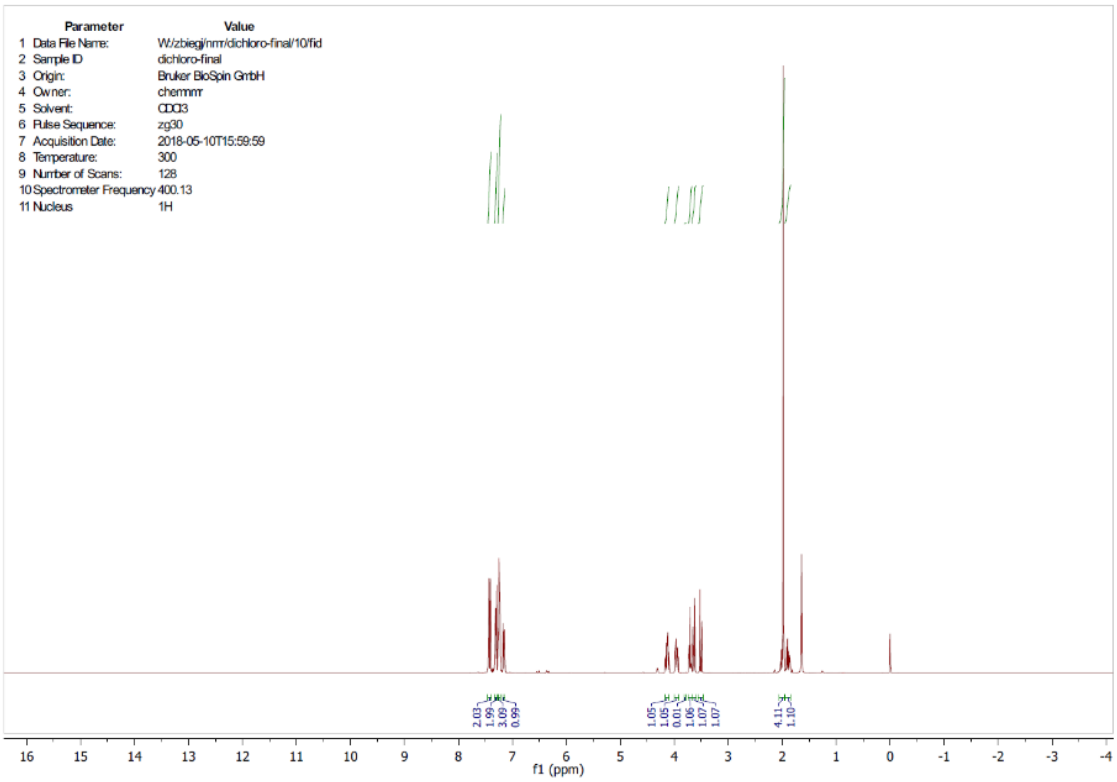
TLC (SiO_2) R_f = 0.42 (hexanes: ethyl acetate = 2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 – 7.39 (m, 2H), 7.34 – 7.28 (m, 2H), 7.24 (td, *J* = 4.8, 2.8 Hz, 3H), 7.16 (dd, *J* = 8.2, 2.0 Hz, 1H), 4.13 (dt, *J* = 11.2, 6.5 Hz, 1H), 3.95 (dt, *J* = 11.2, 6.5 Hz, 1H), 3.71 (t, *J* = 6.9 Hz, 1H), 3.64 (d, *J* = 13.2 Hz, 1H), 3.51 (d, *J* = 13.2 Hz, 1H), 2.05-1.95 (m, 4H), 1.95 – 1.84 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 143.9, 139.9, 132.7, 131.1, 130.6, 129.2, 128.5, 128.1, 127.1, 126.6, 61.5, 58.7, 51.4, 36.8, 20.9.

HRMS (ESI): Calculated for $C_{18}H_{19}Cl_2NO_2$ [M+H$^+$] = 352.0866, found 352.0858.

FTIR (neat): 1735, 1464, 1364, 1236, 1130, 1028, 824, 737, 699 cm^{-1}.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2 Sample ID dichloro-final
3 Origin: Bruker BioSpin GmbH
4 Owner: chemmr
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6 Pulse Sequence: zg30
7 Acquisition Date: 2018-05-10T15:59:59
8 Temperature: 300
9 Number of Scans: 128
10 Spectrometer Frequency 400.13
11 Nucleus 1H
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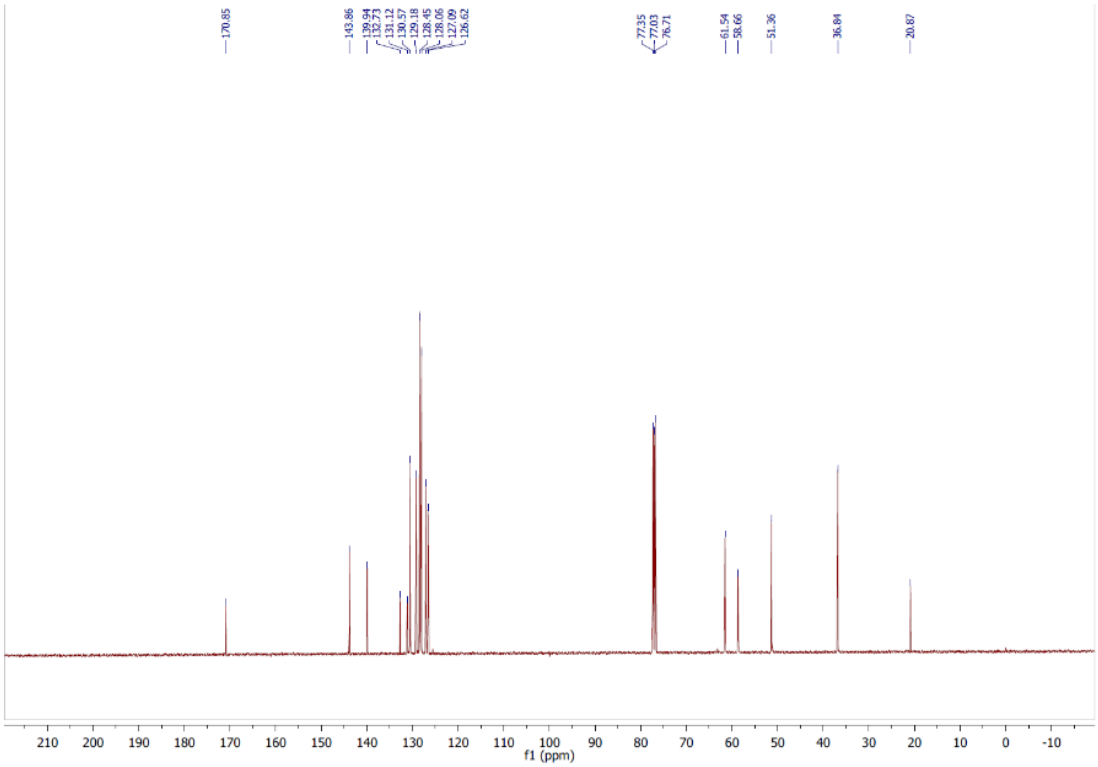
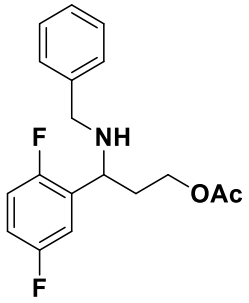
1.99
3.03
0.99
1.05
1.05
0.01
1.06
1.07
1.07
4.11
1.10
f1 (ppm)


170.85
143.86
139.94
137.73
131.12
130.57
129.18
128.45
128.06
127.09
126.62
77.35
77.03
76.71
61.54
58.66
51.36
36.84
20.87
f1 (ppm)

3-(benzylamino)-3-(2,5-difluorophenyl)propyl acetate (7.3l)



The allylic acetate (127 mg, 0.6 mmol, 300 mol%) and the primary amine (21.6 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions. The title compound was obtained in 52% yield (33 mg, 0.10 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Isopropyl Acetate / Heptane = 0% - 100% over 30 min).

TLC (SiO_2) R_f = 0.61 (hexanes: ethyl acetate = 2:1).

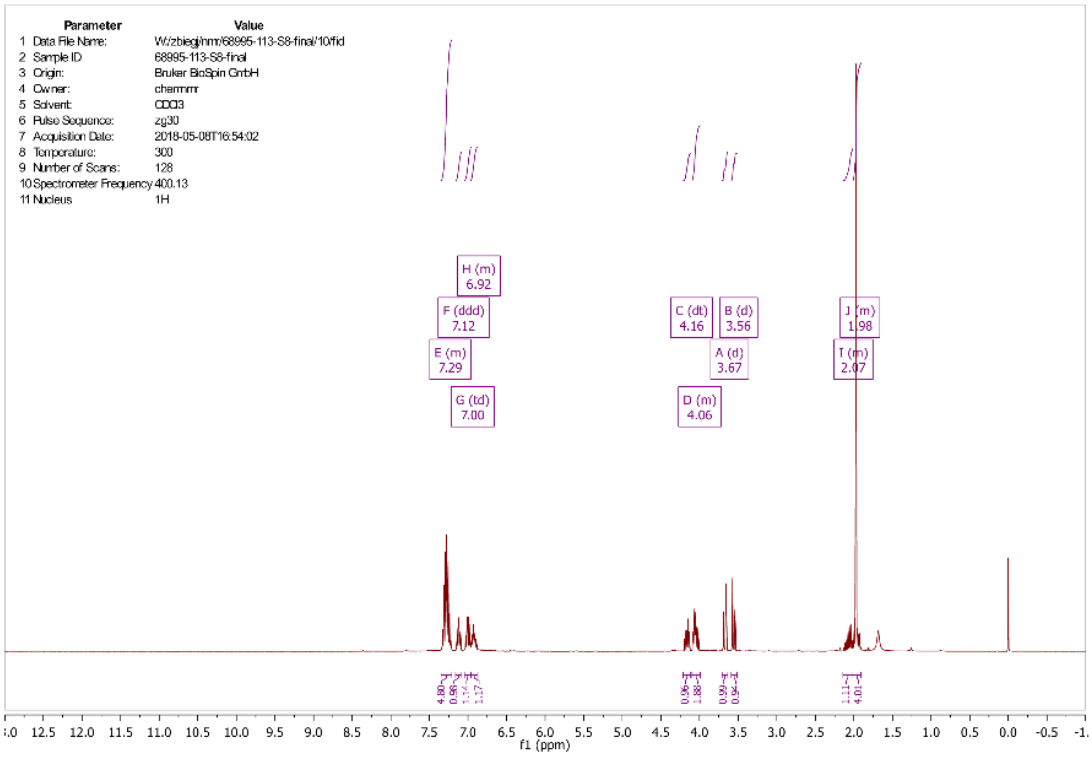
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 – 7.20 (m, 5H), 7.12 (ddd, *J* = 8.8, 5.5, 3.1 Hz, 1H), 7.00 (td, *J* = 9.2, 4.4 Hz, 1H), 6.99 – 6.87 (m, 1H), 4.16 (dt, *J* = 11.1, 6.4 Hz, 1H), 4.11 – 3.99 (m, 2H), 3.67 (d, *J* = 13.0 Hz, 1H), 3.56 (d, *J* = 13.1 Hz, 1H), 2.14 – 2.02 (m, 1H), 1.97 (s, 3H), 2.05 – 1.90 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 159.3 (dd, *J* = 210, 2.3 Hz, 1C), 156.9 (dd, J= 210, 2.3 Hz, 1C) 140.0, 132.2 (dd, *J* = 15.7, 6.5 Hz, 1C), 128.4, 128.1, 127.1, 116.7 (dd, *J* =25.5, 8.4, 1C), 115.1-114.7 (m, 2C), 61.7, 53.3, 51.5, 35.6, 20.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ = -121.9 (dd, *J* = 2644, 18.5 Hz, 1F), -278.1 (dd, J=2244, 18.5 Hz, 1F).

HRMS (ESI): Calculated for $C_{18}H_{19}F_2NO_2$ [M+H$^+$] = 320.1457, found 320.1452.

FTIR (neat): 2960, 1736, 1489, 1366, 1236, 1177, 1040, 874, 814, 737, 699 cm^{-1}.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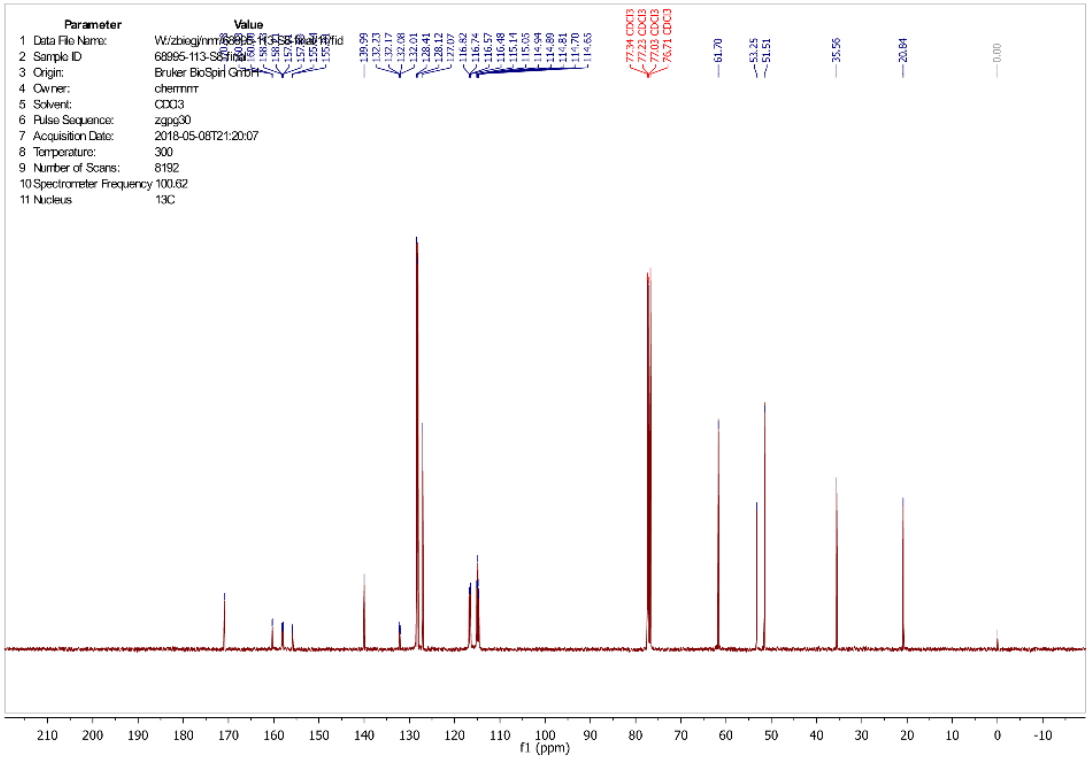
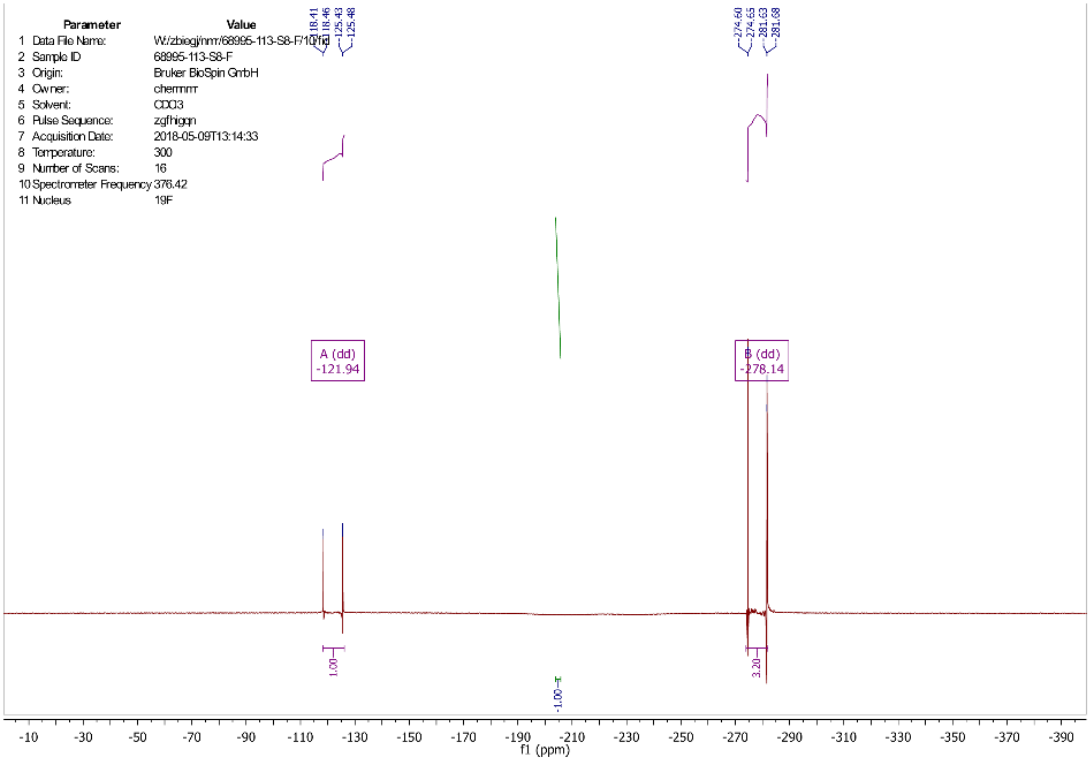
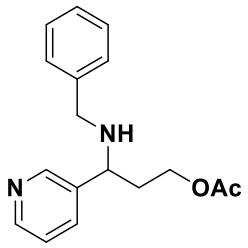
1 Data File Name: W:/zbiegj/nmr/68995-113-S8-final/10/fid
2 Sample ID 68995-113-S8-final
3 Origin: Bruker BioSpin GmbH
4 Owner: chemmr
5 Solvent: CDCl3
6 Pulse Sequence: zg30
7 Acquisition Date: 2018-05-08T16:54:02
8 Temperature: 300
9 Number of Scans: 128
10 Spectrometer Frequency 400.13
11 Nucleus 1H
H (m) 6.92
F (ddd) 7.12
E (m) 7.29
G (td) 7.00
C (dt) 4.16
B (d) 3.56
A (d) 3.67
D (m) 4.06
J (m) 1.98
I (m) 2.07
f1 (ppm)


Parameter Value
1 Data File Name: W:/zbiegj/nmr/68995-113-S8-final/11/fid
2 Sample ID 68995-113-S8-final
3 Origin: Bruker BioSpin GmbH
4 Owner: chemmr
5 Solvent: CDCl3
6 Pulse Sequence: zgpg30
7 Acquisition Date: 2018-05-08T21:20:07
8 Temperature: 300
9 Number of Scans: 8192
10 Spectrometer Frequency 100.62
11 Nucleus 13C
f1 (ppm)


Parameter Value
1 Data File Name: W:/zbiegj/nmr/68995-113-S8-F/10/fid
2 Sample ID 68995-113-S8-F
3 Origin: Bruker BioSpin GmbH
4 Owner: chemmm
5 Solvent: CDCl3
6 Pulse Sequence: zgfhigqn
7 Acquisition Date: 2018-05-09T13:14:33
8 Temperature: 300
9 Number of Scans: 16
10 Spectrometer Frequency 376.42
11 Nucleus 19F
-118.41
-118.46
-125.43
-125.48
-274.60
-274.65
-281.63
-281.68
A (dd)
-121.94
B (dd)
-278.14
1.00
1.00
3.20
-10 -30 -50 -70 -90 -110 -130 -150 -170 -190 -210 -230 -250 -270 -290 -310 -330 -350 -370 -390
f1 (ppm)

3-(benzylamino)-3-(pyridin-3-yl)propyl acetate (7.3m)



The allylic acetate (106 mg, 0.6 mmol, 300 mol%) and the primary amine (21.6 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions. The title compound was obtained in 81% yield (46 mg, 0.16 mmol) as a light yellow oil after purification by flash column chromatography (4g SiO_2, Methanol / DCM = 0% - 10% over 30 min).

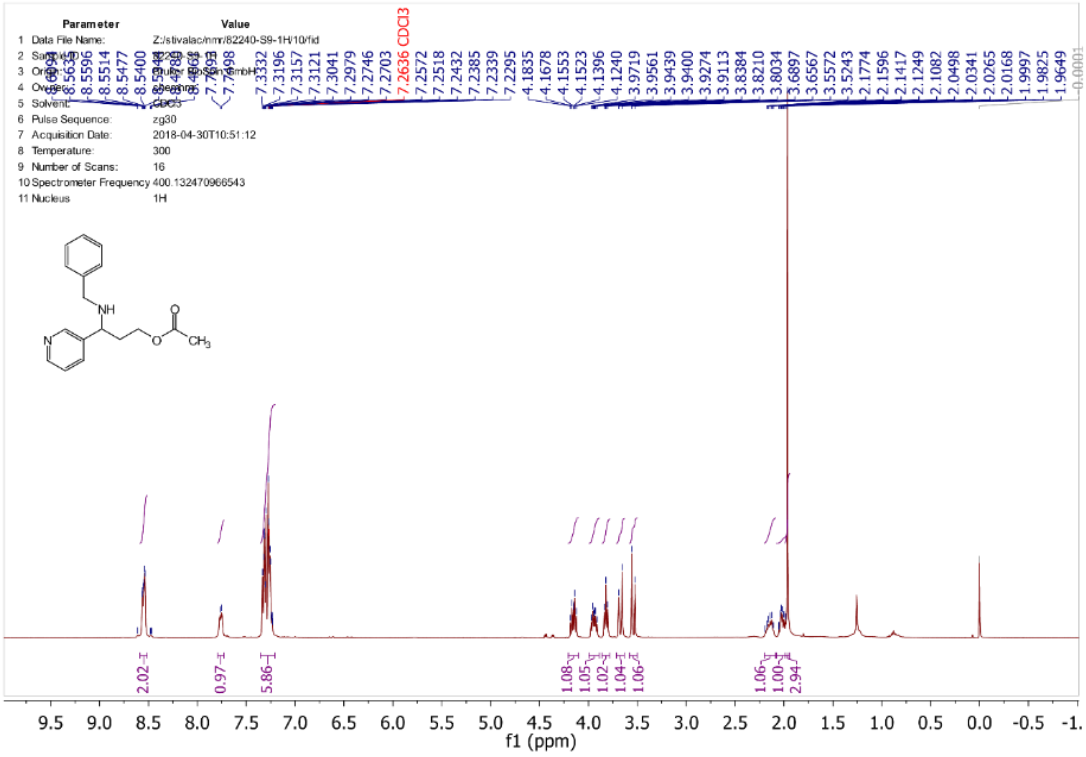
TLC (SiO_2) R_f = 0.45 (ethyl acetate: methanol = 15:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.59 – 8.51 (m, 2H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.36 – 7.21 (m, 6H), 4.15 (dt, *J* = 11.3, 6.3 Hz, 1H), 3.94 (dt, *J* = 11.5, 6.4 Hz, 1H), 3.82 (t, *J* = 7.0 Hz, 1H), 3.67 (d, *J* = 13.2 Hz, 1H), 3.54 (d, *J* = 13.2 Hz, 1H), 2.14 (dt, *J* = 13.4, 6.9 Hz, 1H), 2.08 – 1.96 (m, 1H), 1.96 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 149.5, 149.2, 134.8, 128.5, 128.3, 127.4, 123.8, 61.4, 57.2, 51.1, 36.3 20.8.

HRMS (ESI): Calculated for $C_{17}H_{21}N_2O_2$ $[M+H^+]$ =285.1598, found 285.1598.

FTIR (neat): 2924, 1735, 1426, 1365, 1237, 1026, 810, 737, 717, 700 cm^{-1}.


Parameter
Value
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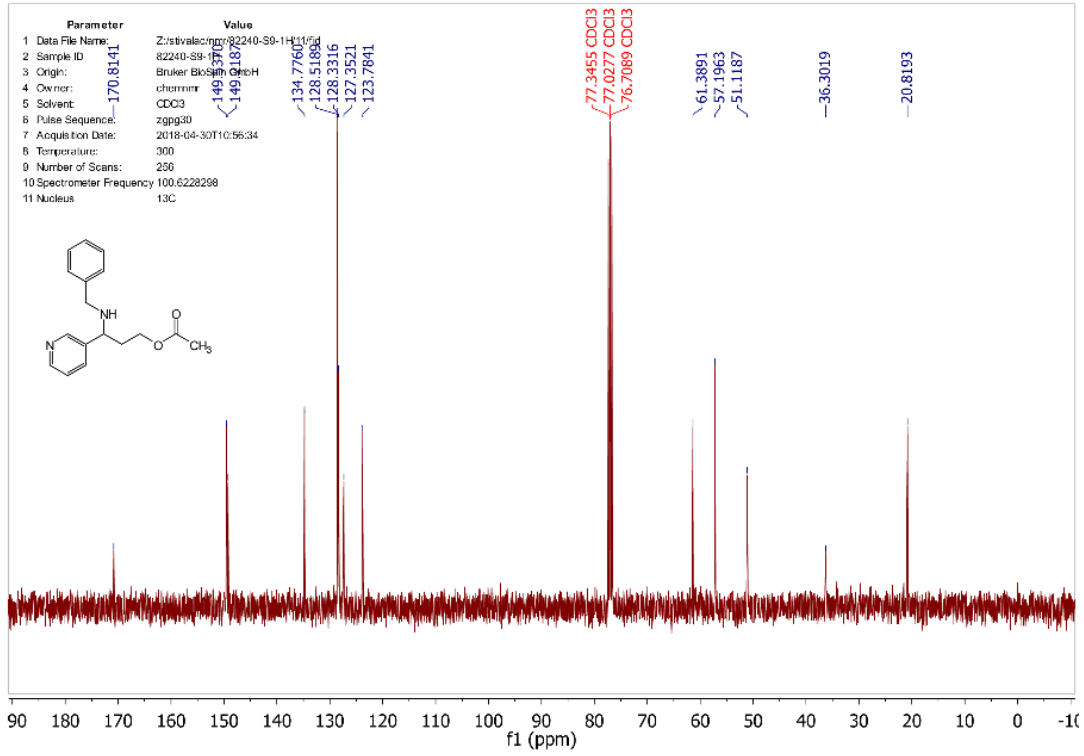
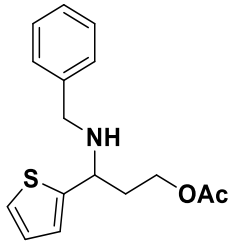
2 Sample ID 82240-S9-1H
3 Origin: Bruker BioSpin GmbH
4 Owner: chemmr
5 Solvent: CDCl3
6 Pulse Sequence: zg30
7 Acquisition Date: 2018-04-30T10:51:12
8 Temperature: 300
9 Number of Scans: 16
10 Spectrometer Frequency 400.132470966543
11 Nucleus 1H
7.2636 CDCl3
2.02
0.97
5.86
1.08
1.05
1.02
1.04
1.06
1.06
1.00
2.94
f1 (ppm)


Parameter
Value
1 Data File Name: Z:\stivalac\nmr\82240-S9-1H\11\fid
2 Sample ID 82240-S9-1H
3 Origin: Bruker BioSpin GmbH
4 Owner: chemmr
5 Solvent: CDCl3
6 Pulse Sequence: zgpg30
7 Acquisition Date: 2018-04-30T10:56:34
8 Temperature: 300
9 Number of Scans: 256
10 Spectrometer Frequency 100.6228298
11 Nucleus 13C
170.8141
149.3970
149.0187
134.7760
128.5185
128.3316
127.3521
123.7841
77.3455 CDCl3
77.0277 CDCl3
76.7089 CDCl3
61.3891
57.1963
51.1187
36.3019
20.8193
f1 (ppm)

3-(benzylamino)-3-(thiophen-2-yl)propyl acetate (7.3n)



The allylic acetate (109.3 mg, 0.6 mmol, 300 mol%) and the primary amine (21.4 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions for 48 h. The title compound was obtained in 71% yield (41.1 mg, 0.14 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 10:1–5:1).

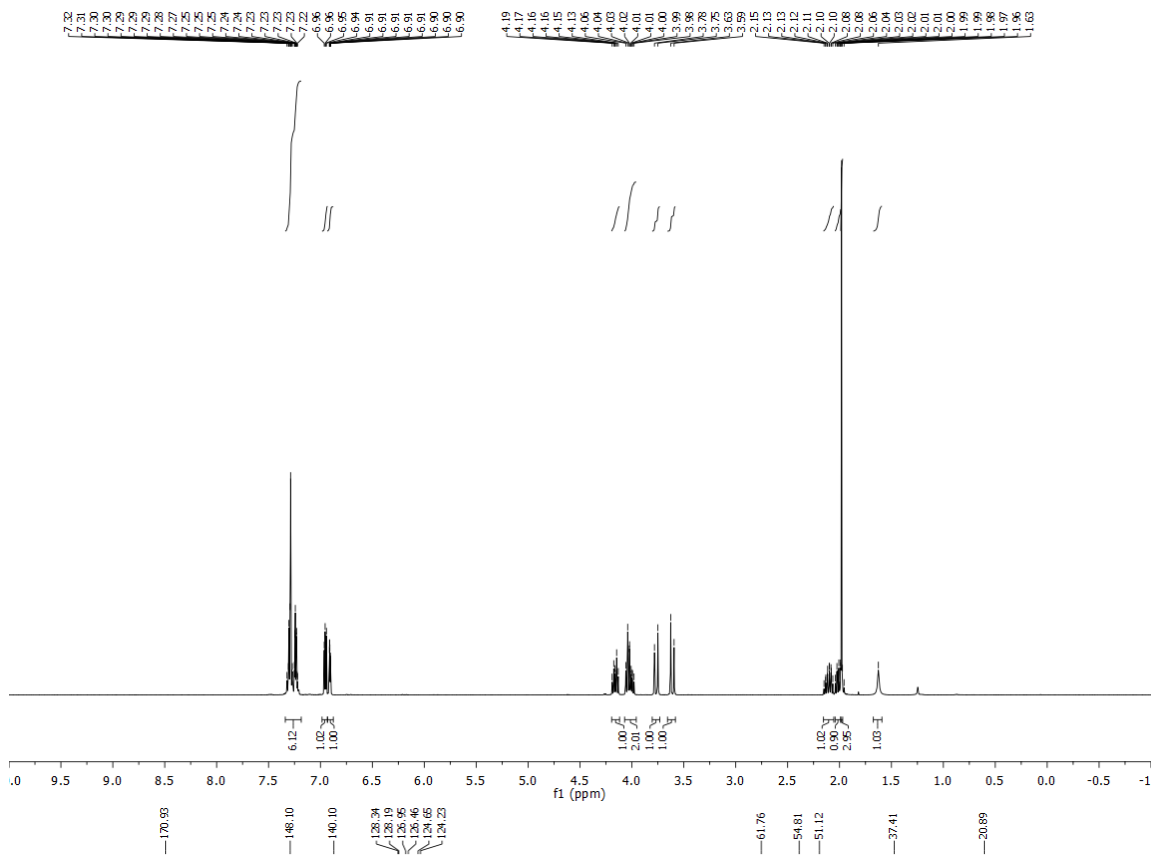
TLC (SiO_2) R_f = 0.40 (hexanes: ethyl acetate = 2:1).

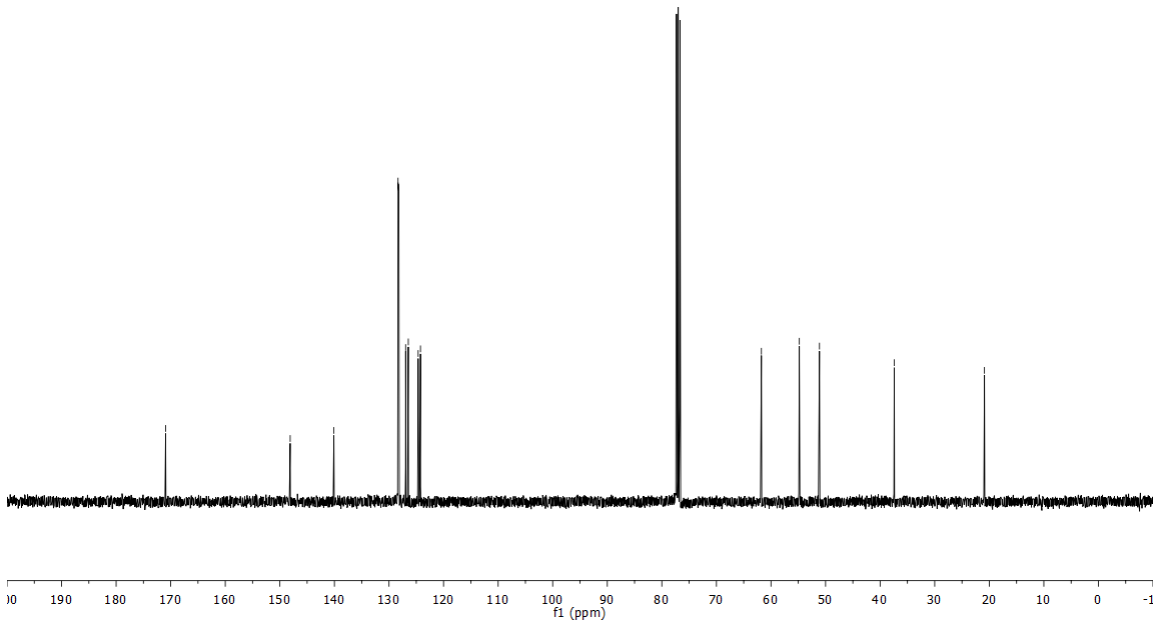
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 – 7.19 (m, 6H), 6.95 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.91 (ddd, *J* = 3.4, 1.3, 0.5 Hz, 1H), 4.16 (dt, *J* = 11.1, 6.2 Hz, 1H), 4.07 – 3.96 (m, 2H), 3.77 (d, *J* = 13.2 Hz, 1H), 3.61 (d, *J* = 13.1 Hz, 1H), 2.11 (dtd, *J* = 14.0, 7.0, 6.1 Hz, 1H), 2.02 (dt, *J* = 7.5, 6.2 Hz, 1H), 1.98 (s, 3H), 1.63 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 148.1, 140.1, 128.3, 128.2, 127.0, 126.5, 124.7, 124.2, 61.8, 54.8, 51.1, 37.4, 20.9.

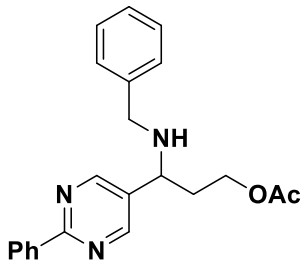
HRMS (ESI): Calculated for $C_{16}H_{19}NO_2S$ [M+H$^+$] = 290.1209, found 290.1211.

FTIR (neat): 2917, 1735, 1365, 1235, 1036, 907, 731, 697 cm^{-1}.


7.32 7.31 7.30 7.30 7.29 7.29 7.29 7.28 7.27 7.25 7.25 7.25 7.24 7.24 7.23 7.23 7.23 7.23 7.22 6.96 6.96 6.95 6.94 6.91 6.91 6.91 6.91 6.90 6.90 6.90
4.19 4.17 4.16 4.16 4.15 4.13 4.06 4.04 4.03 4.02 4.01 4.01 4.00 3.99 3.98 3.78 3.75 3.69 3.69 2.15 2.13 2.13 2.12 2.11 2.10 2.10 2.08 2.08 2.06 2.04 2.03 2.02 2.01 2.01 2.00 1.99 1.99 1.98 1.97 1.96 1.63
6.12 1.02 1.00 1.00 2.01 1.00 1.00 1.02 0.90 2.95 1.03
f1 (ppm)


170.93 148.10 140.10 128.34 128.19 126.95 126.46 124.65 124.23 61.76 54.81 51.12 37.41 20.89
f1 (ppm)

3-(benzylamino)-3-(2-phenylpyrimidin-5-yl)propyl acetate (7.3o)



The allylic acetate (152.1 mg, 0.6 mmol, 300 mol%) and the primary amine (21.4 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions with Cs_2CO_3 (300 mol%). The title compound was obtained in 52% yield (37.6 mg, 0.10 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, toluene: ethyl acetate = 10:1–3:1).

TLC (SiO_2) R_f = 0.55 (toluene: ethyl acetate = 1:1).

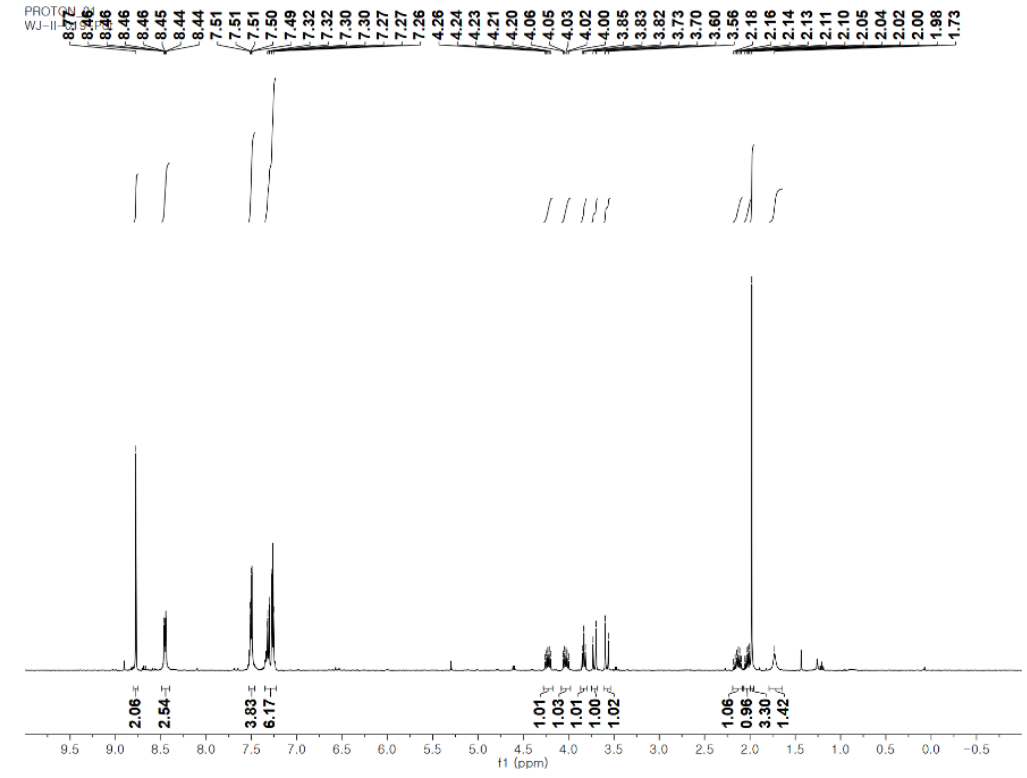
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (s, 2H), 8.49 – 8.40 (m, 3H), 7.50 (dd, *J* = 5.2, 2.1 Hz, 4H), 7.35 – 7.23 (m, 6H), 4.28 – 4.18 (m, 1H), 4.08 – 3.98 (m, 1H), 3.83 (t, *J* = 6.9 Hz, 1H), 3.71 (d, *J* = 13.2 Hz, 1H), 3.58 (d, *J* = 13.2 Hz, 1H), 2.19 – 2.08 (m, 1H), 2.03 (dd, *J* = 12.7, 7.0 Hz, 1H), 1.98 (s, 3H), 1.73 (br, 1H).

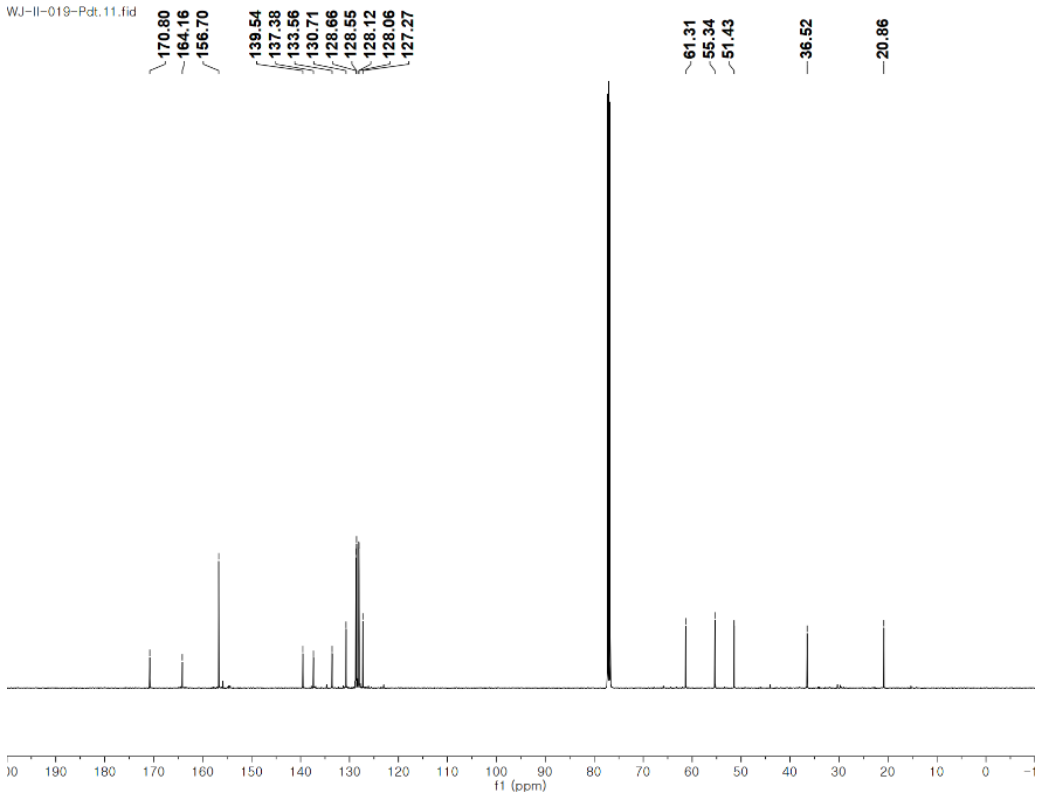
^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 164.2, 156.7, 139.5, 137.4, 133.6, 130.7, 128.7, 128.6, 128.1, 128.1, 127.3, 61.3, 55.3, 51.4, 36.5, 20.9.

HRMS (ESI): Calculated for $C_{22}H_{23}N_3O_2$ $[M+H^+]$ = 362.1863, found 362.1867.

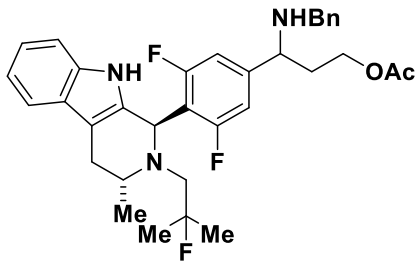
FTIR (neat): 3026, 2926, 1737, 1583, 1543, 1494, 1428, 1322, 1240, 1172, 1025, 927, 749, 694 cm^{-1}.

3-


8.47
8.46
8.45
8.44
7.51
7.50
7.49
7.32
7.30
7.27
7.26
4.26
4.24
4.23
4.21
4.20
4.06
4.05
4.03
4.02
4.00
3.85
3.83
3.82
3.73
3.70
3.60
3.56
2.18
2.16
2.14
2.13
2.11
2.10
2.05
2.04
2.02
2.00
1.98
1.73
2.06
2.54
3.83
6.17
1.01
1.03
1.01
1.00
1.02
1.06
0.96
3.30
1.42
f1 (ppm)


WJ-II-019-Pdt.11.fid
170.80
164.16
156.70
139.54
137.38
133.56
130.71
128.66
128.55
128.12
128.06
127.27
61.31
55.34
51.43
36.52
20.86
f1 (ppm)

(benzylamino)-3-(3,5-difluoro-4-((1R,3R)-2-(2-fluoro-2-methylpropyl)-3-methyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-yl)phenyl)propyl acetate (7.3p)



The allylic acetate (282 mg, 0.6 mmol, 300 mol%) and the primary amine (21.4 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions with Cs_2CO_3 (300 mol%). The title compound was obtained in 53% yield (61 mg, 0.11 mmol) as a light yellow oil after purification by flash column chromatography (12g SiO_2, Isopropyl Acetate / Heptane = 0% - 100% over 30 min).

TLC (SiO_2) R_f = 0.30 (hexanes: ethyl acetate = 2:1).

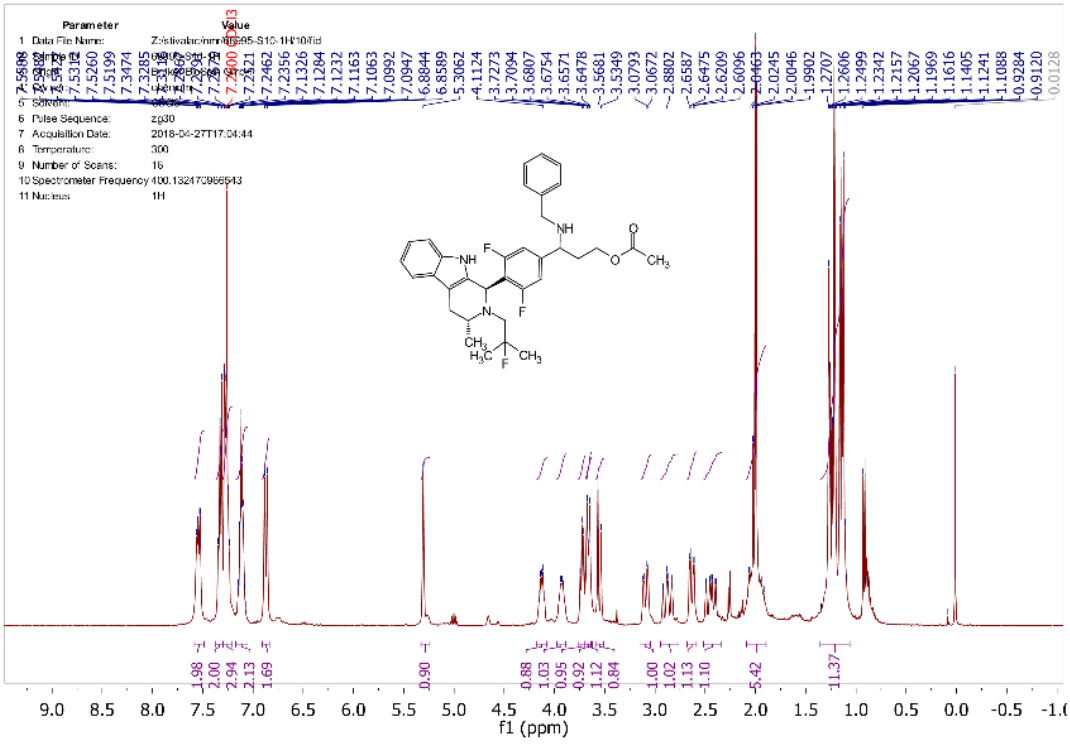
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 – 7.49 (m, 2H), 7.37 – 7.30 (m, 2H), 7.30 – 7.21 (m, 3H), 7.17 – 7.05 (m, 2H), 6.91 – 6.83 (m, 2H), 5.31 (s, 1H), 4.19 – 4.06 (m, 1H), 3.98 – 3.86 (m, 1H), 3.76 – 3.60 (m, 3H), 3.59 – 3.51 (m, 1H), 3.14 – 3.04 (m, 1H), 2.95 – 2.79 (m, 1H), 2.68 – 2.57 (m, 1H), 2.52 – 2.35 (m, 1H), 2.08 - 1.89 (m, 5H), 1.32 – 1.06 (m, 9H).

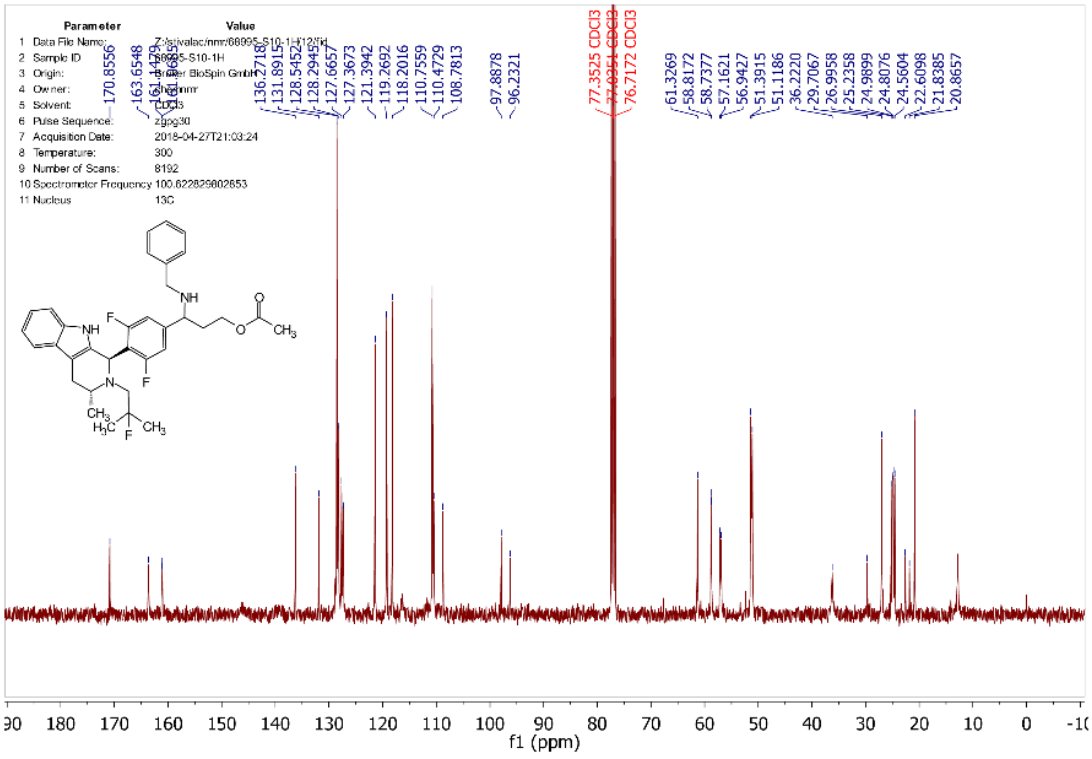
^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 162.4 (dd, *J* = 252.4, 7.8 Hz), 136.3, 131.9, 128.6, 128.3, 127.7, 127.4, 121.4, 119.3, 118.2, 110.8, 110.5, 108.8, 97.9, 96.2, 61.3, 58.8 (d, *J* = 8.0 Hz), 57.1 (d, *J* = 22.1 Hz), 51.6 – 50.8 (m, 2C), 36.2, 29.7, 27.0, 25.1 (d, *J* = 24.7 Hz), 24.7 (d, *J* = 24.9 Hz), 22.6, 21.8, 20.9.

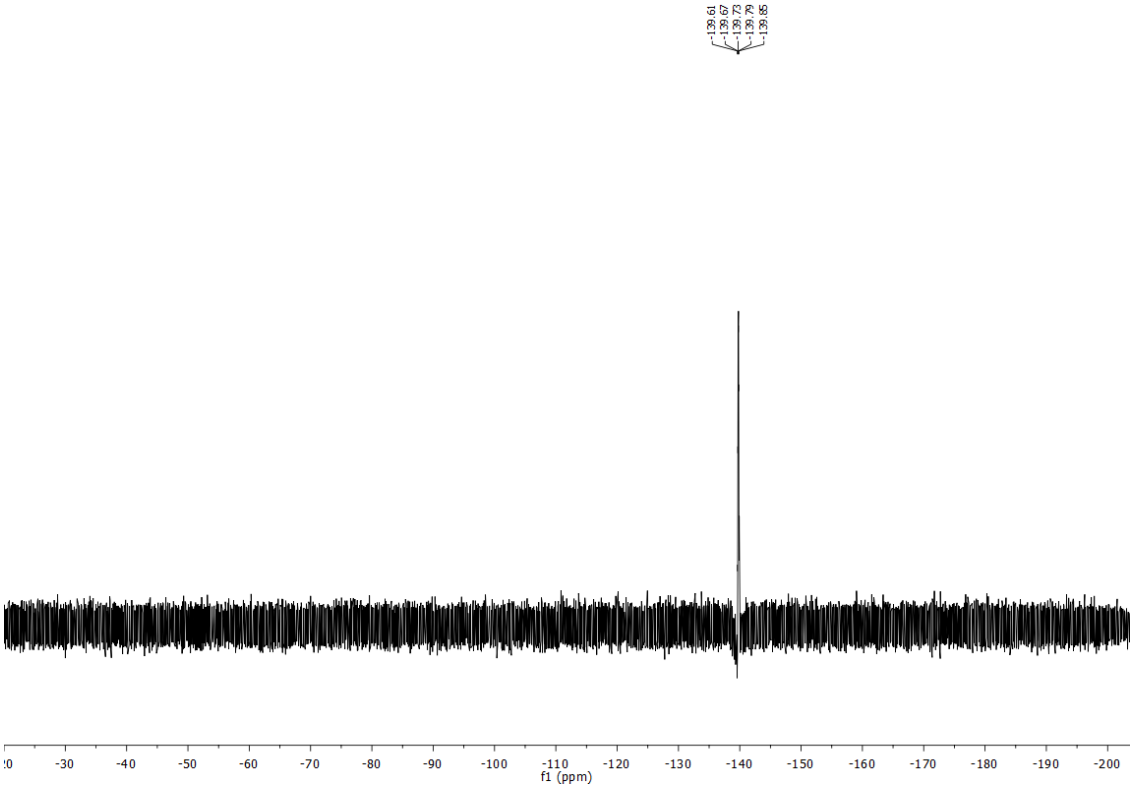
^{19}F NMR (376 MHz, $CDCl_3$): δ = –139.7 (m).

HRMS (ESI): Calculated for $C_{34}H_{39}N_3O_2F_3$ [M+H$^+$] = 578.2989, found 578.2984.

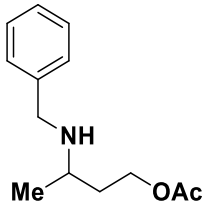
FTIR (neat): 2973, 2926, 1729, 1631, 1578, 1433, 1367, 1239, 1019, 908, 732 cm^{-1}.




Parameter
Value
1 Data File Name:
2 Sample ID
3 Origin:
4 Owner:
5 Solvent:
6 Pulse Sequence:
7 Acquisition Date:
8 Temperature:
9 Number of Scans:
10 Spectrometer Frequency
11 Nucleus
zgpg30
2018-04-27T21:03:24
300
8192
13C
170.8556
163.6548
136.2718
131.8915
128.5452
128.2945
127.6657
127.3673
121.3942
119.2692
118.2016
110.7559
110.4729
108.7813
97.8878
96.2321
77.3525 CDCl3
77.0314 CDCl3
76.7172 CDCl3
61.3269
58.8172
58.7377
57.1621
56.9427
51.3915
51.1186
36.2220
29.7067
26.9958
25.2358
24.9899
24.8076
24.5604
22.6098
21.8385
20.8657
f1 (ppm)


139.61
139.67
139.73
139.79
139.85
f1 (ppm)

3-(benzylamino)butyl acetate (7.3q)



The allylic acetate (68.5 mg, 0.6 mmol, 300 mol%) and the primary amine (21.4 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions. The title compound was obtained in 30% yield (13.3 mg, 0.06 mmol) as a light yellow oil after purification by flash column chrmmatography (SiO_2, hexanes: ethyl acetate = 5:1–1:1).

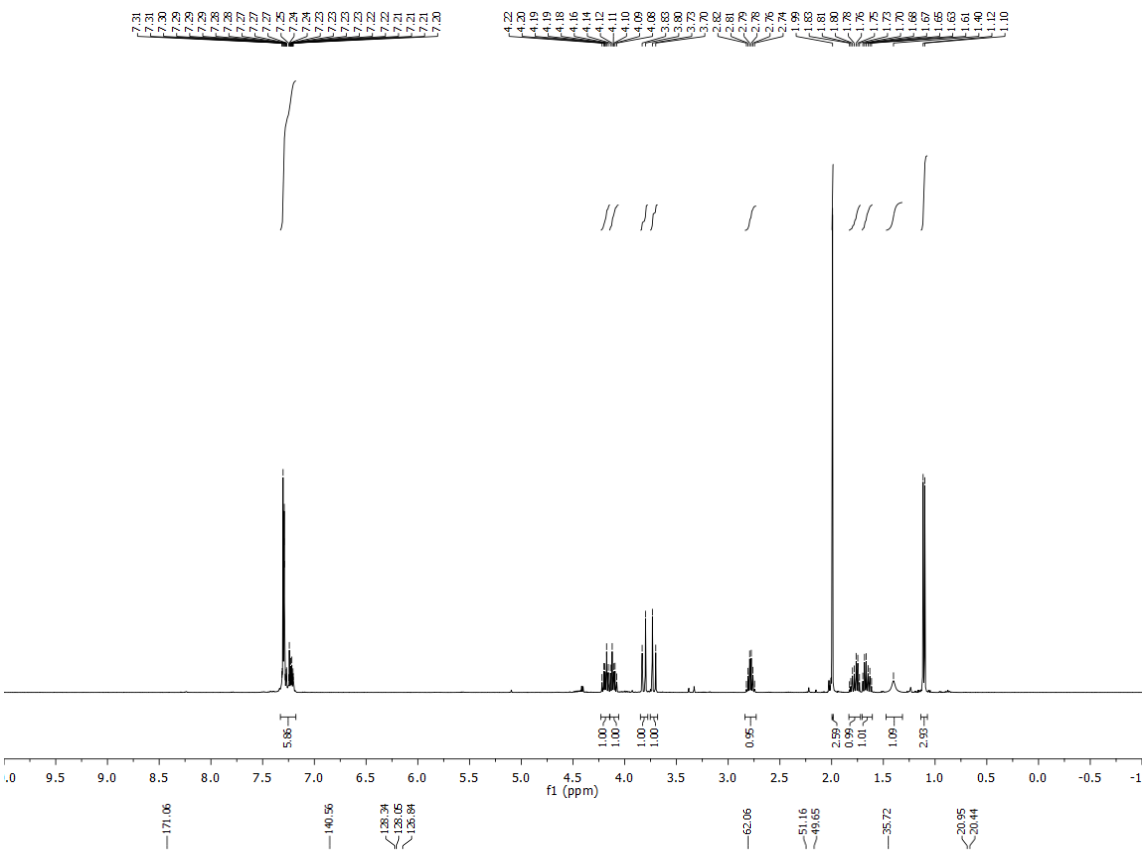
TLC (SiO_2) R_f = 0.24 (ethyl acetate: methanol = 10:1).

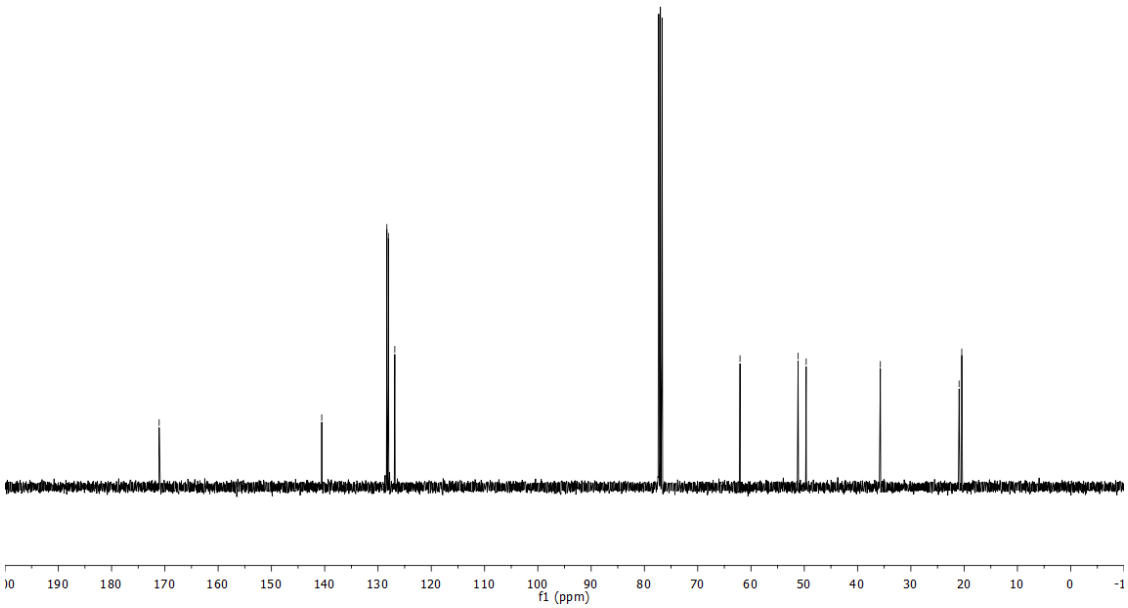
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 – 7.18 (m, 5H), 4.19 (dt, *J* = 11.1, 6.6 Hz, 1H), 4.11 (dt, *J* = 11.1, 6.7 Hz, 1H), 3.82 (d, *J* = 13.0 Hz, 1H), 3.72 (d, *J* = 13.0 Hz, 1H), 2.78 (h, *J* = 6.3 Hz, 1H), 1.99 (s, 3H), 1.83 – 1.72 (m, 1H), 1.71 – 1.61 (m, 1H), 1.40 (br, 1H), 1.11 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 140.6, 128.3, 128.1, 126.8, 62.1, 51.2, 49.7, 35.7, 21.0, 20.4.

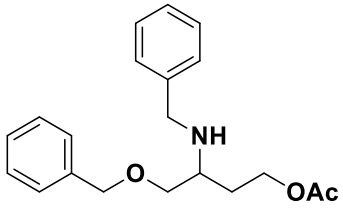
HRMS (ESI): Calculated for $C_{13}H_{19}NO_2$ [M+H$^+$] = 222.1489, found 222.1495.

FTIR (neat): 2962, 1734, 1453, 1365, 1238, 1045, 731, 698 cm^{-1}.





3-(benzylamino)-4-(benzyloxy)butyl acetate (7.3r)



The allylic acetate (132.2 mg, 0.6 mmol, 300 mol%) and the primary amine (21.4 mg, 0.2 mmol, 100 mol%) were subject to standard reaction conditions with Cs_2CO_3 (300 mol%). The title compound was obtained in 53% yield (34.7 mg, 0.11 mmol) as a light yellow oil after purification by flash column chromatography (SiO_2, hexanes: ethyl acetate = 5:1–2:1).

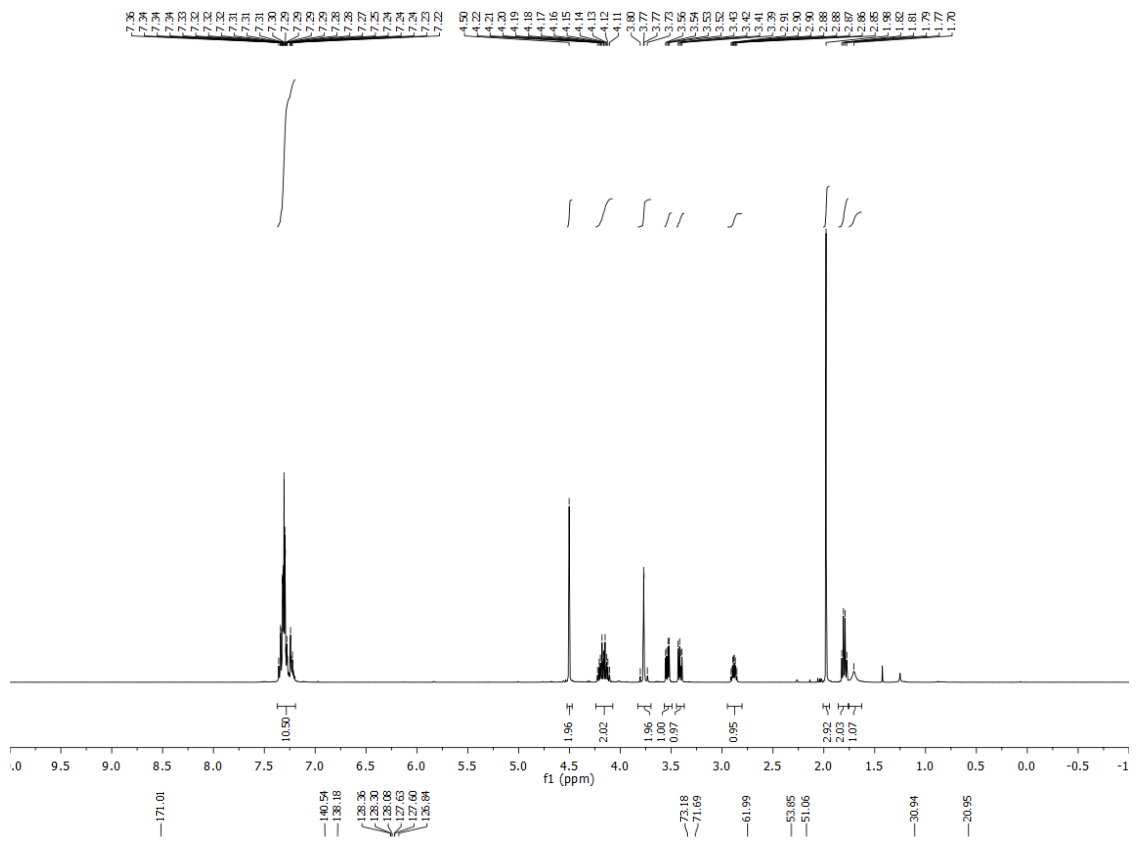
TLC (SiO_2) R_f = 0.30 (hexanes: ethyl acetate = 1:1).

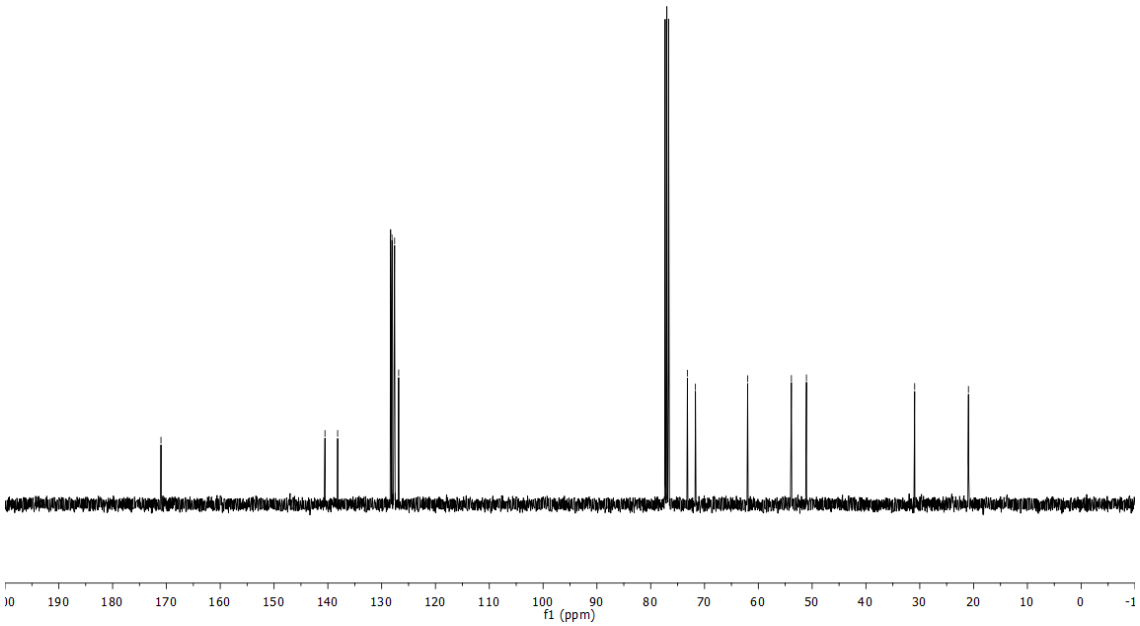
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 – 7.19 (m, 10H), 4.50 (s, 2H), 4.17 (qt, *J* = 11.0, 6.6 Hz, 2H), 3.77 (d, *J* = 1.5 Hz, 2H), 3.54 (dd, *J* = 9.4, 4.3 Hz, 1H), 3.41 (dd, *J* = 9.4, 5.8 Hz, 1H), 2.88 (qd, *J* = 6.2, 4.3 Hz, 1H), 1.98 (s, 3H), 1.80 (q, *J* = 6.6 Hz, 2H), 1.70 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 140.5, 138.2, 128.4, 128.3, 128.1, 127.6, 127.6, 126.8, 73.2, 71.7, 62.0, 53.9, 51.1, 30.9, 21.0.

HRMS (ESI): Calculated for $C_{20}H_{25}NO_3$ [M+H$^+$] = 328.1907, found 328.1907.

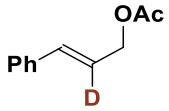
FTIR (neat): 1735, 1453, 1364, 1238, 1093, 1027, 734, 697 cm^{-1}.


f1 (ppm)


f1 (ppm)

Procedures and Spectral Data for Deuterium Labelling Experiments

(*E*)-3-phenylallyl-2-d acetate (*d*$_1$-7.1a)



To a flame dried round-bottomed flask charged with $LiAlD_4$ (210 mg, 5 mmol, 100 mol%) under an argon atmosphere was added THF (15 mL, 0.33 M with respect to propargylic alcohol). The reaction vessel was placed in an ice batch. After 5 minutes a solution of 3-phenyl-2-propyn-1-ol (660 mg, 5 mmol, 100 mol%) in dry THF (5 mL, 1.0 M with respect to propargylic alcohol) was added slowly and the mixture was stirred at room temperature for 3 hours. After the reaction vessel was placed in an ice batch, water (1 mL), NaOH (1 mL, 10% aqueous solution) and water (3 mL) were added to the reaction mixture. After 10 minutes $MgSO_4$ was added, the reaction mixture was filtered (celite) with the aid of CH_2Cl_2 (10 mL) and the filtrate was concentrated under reduced pressure. The resulting oily residue was subjected to the next step without further purification.

To a round-bottomed flask charged with the crude substrate and 4-dimethylaminopyridine (30 mg, 0.25 mmol, 5 mol%) under an argon atmosphere was added CH_2Cl_2 (12.5 mL, 0.4 M), followed by acetic anhydride (0.52 mL, 5.5 mmol, 110 mol%) and triethylamine (1.0 mL, 7.5 mmol, 150 mol%). After 1 hour, saturated aqueous sodium bicarbonate (10 mL) was added and the mixture was transferred to a separatory funnel. The organic layer was extracted with CH_2Cl_2 (10 mL × 2) and the combined organic layers were washed with 1 N HCl (30 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash column chromatography (SiO_2, hexanes: ethyl acetate = 30:1) to furnish the title compound as a colorless oil (790 mg, 4.46 mmol) in 89% yield.

TLC (SiO_2) R_f = 0.38 (hexanes: ethyl acetate = 10:1).

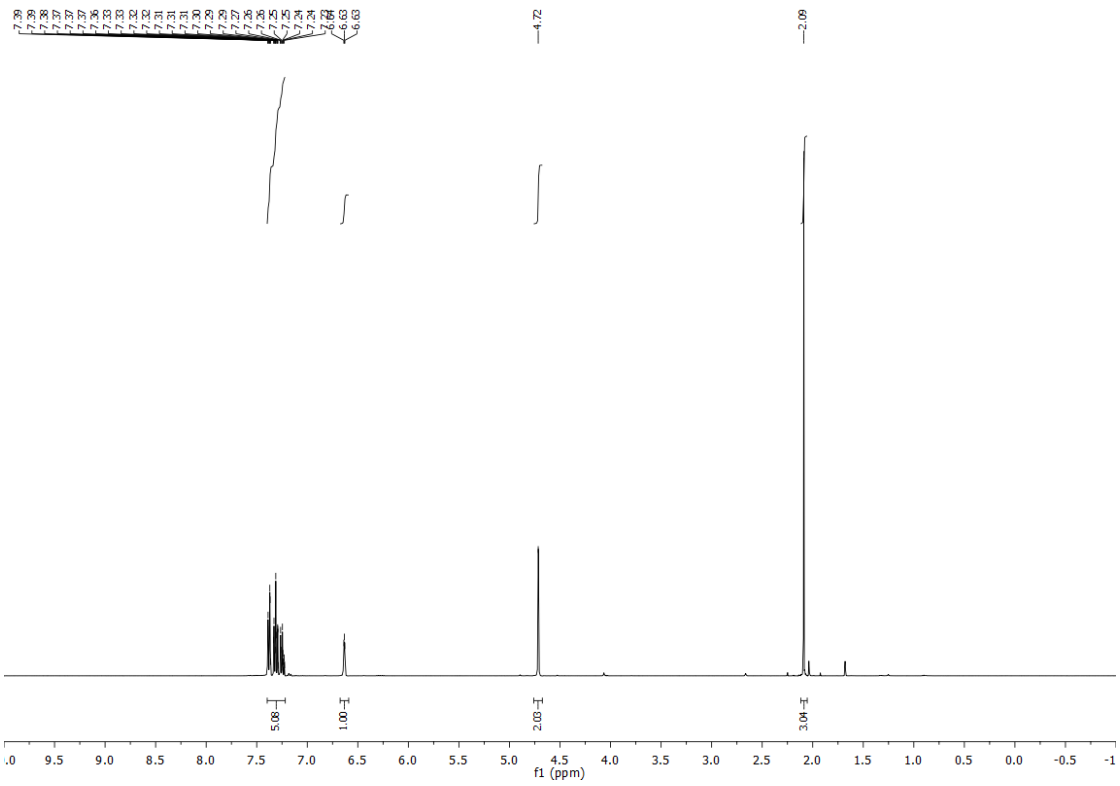
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 – 7.22 (m, 5H), 6.63 (t, *J* = 2.1 Hz, 1H), 4.72 (s, 2H), 2.09 (s, 3H).

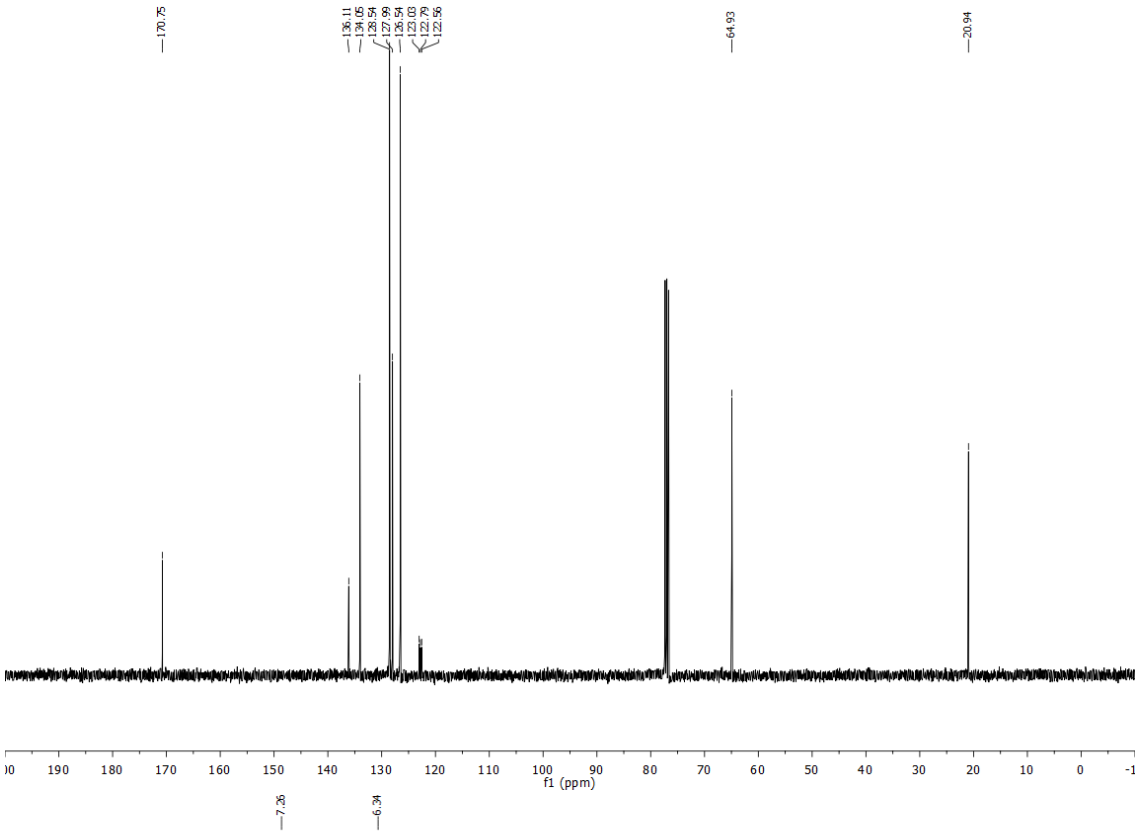
^{2}H NMR (92 MHz, $CDCl_3$) δ = 6.34 (s, 1D)

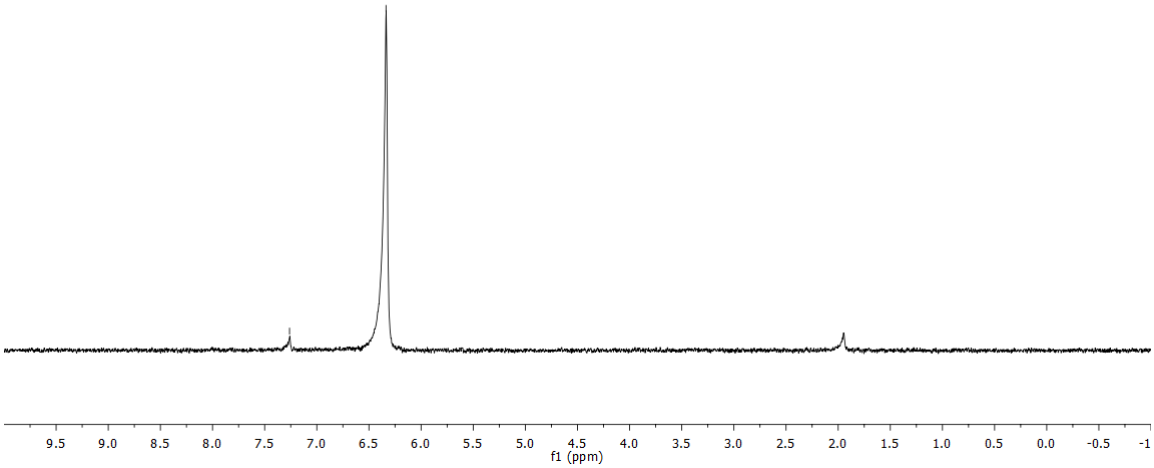
^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 136.1, 134.1, 128.5, 128.0, 126.5, 122.8 (t), 64.9, 20.9.

HRMS (ESI): Calculated for $C_{11}H_{11}DO_2$ [M+Na^+] = 200.0792, found 200.0794.

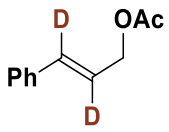
FTIR (neat): 3025, 1733, 1379, 1225, 1021, 922, 764, 699 cm^{-1}.




170.75
136.11
134.05
128.54
127.99
125.54
123.03
122.70
122.56
64.93
20.94
f1 (ppm)


7.26
6.34
f1 (ppm)

(*E*)-3-phenylallyl-2,3-d$_2$ acetate (*d*$_2$-7.1a)



To a flame dried round-bottomed flask charged with $LiAlD_4$ (210 mg, 5 mmol, 100 mol%) under an argon atmosphere was added THF (15 mL, 0.33 M with respect to propargylic alcohol). The reaction vessel was placed in an ice batch. After 5 minutes a solution of 3-phenyl-2-propyn-1-ol (660 mg, 5 mmol, 100 mol%) in dry THF (5 mL, 1.0 M with respect to propargylic alcohol) was added slowly and the mixture was stirred at room temperature for 3 hours. After the reaction vessel was placed in an ice batch, D_2O (1 mL), NaOH (1 mL, 10% aqueous solution) and water (3 mL) were added to the reaction mixture. After 10 minutes $MgSO_4$ was added, the reaction mixture was filtered (celite) with the aid of CH_2Cl_2 (10 mL) and the filtrate was concentrated under reduced pressure. The resulting oily residue was subjected to the next step without further purification.

To a round-bottomed flask charged with the crude substrate and 4-dimethylaminopyridine (30 mg, 0.25 mmol, 5 mol%) under an argon atmosphere was added CH_2Cl_2 (12.5 mL, 0.4 M), followed by acetic anhydride (0.52 mL, 5.5 mmol, 110 mol%) and triethylamine (1.0 mL, 7.5 mmol, 150 mol%). After 1 hour, saturated aqueous sodium bicarbonate (10 mL) was added and the mixture was transferred to a separatory funnel. The organic layer was extracted with CH_2Cl_2 (10 mL × 2) and the combined organic layers were washed with 1 N HCl (30 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily residue was subjected to flash

column chromatography (SiO_2, hexanes: ethyl acetate = 30:1) to furnish the title compound as a colorless oil (802 mg, 4.50 mmol) in 90% yield.

TLC (SiO_2) R_f = 0.38 (hexanes: ethyl acetate = 10:1).

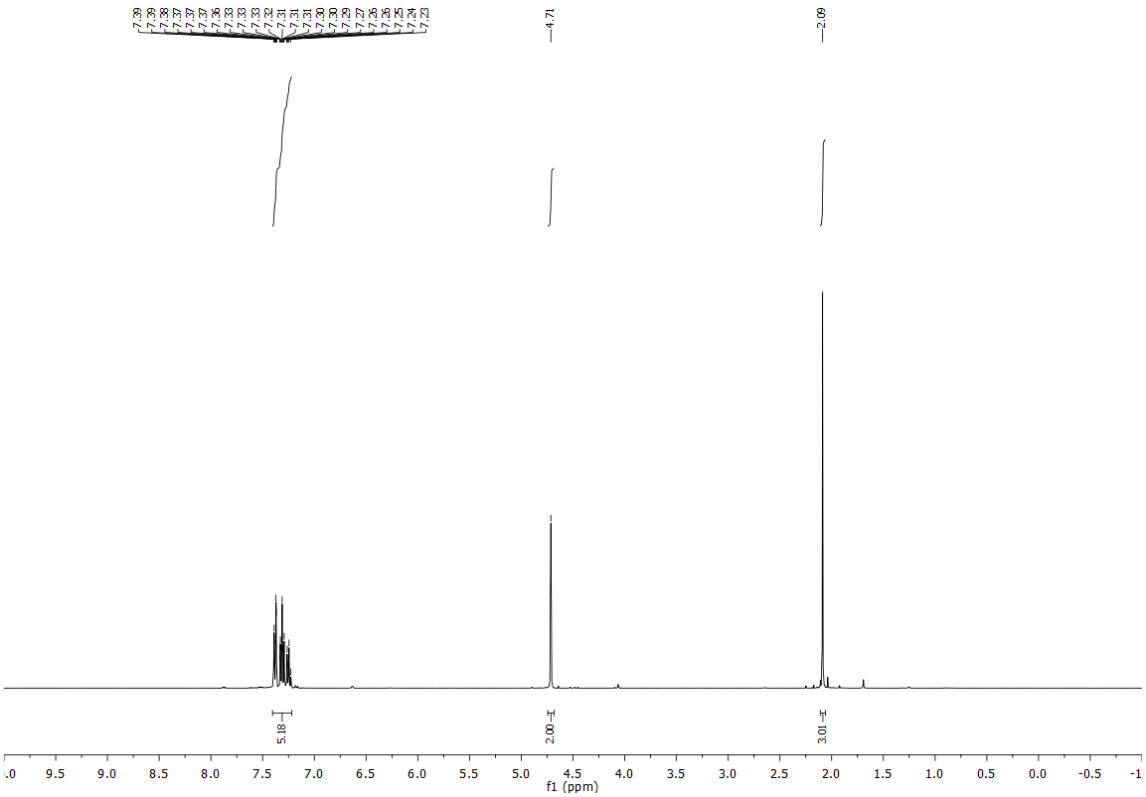
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 – 7.22 (m, 5H), 4.71 (s, 2H), 2.09 (s, 3H).

^{2}H NMR (92 MHz, $CHCl_3$) δ = 6.70 (s, 1D), 6.33 (s, 1D).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 136.0, 133.7 (m), 128.5, 128.0, 126.5, 122.7 (m), 64.9, 20.9.

HRMS (ESI): Calculated for $C_{11}H_{10}D_2O_2$ [M+Na^+] = 201.0855, found 201.0849.

FTIR (neat): 3025, 1733, 1379, 1225, 1021, 922, 751, 700 cm^{-1}.


7.39
7.39
7.38
7.37
7.37
7.37
7.36
7.33
7.33
7.32
7.31
7.31
7.31
7.30
7.30
7.29
7.27
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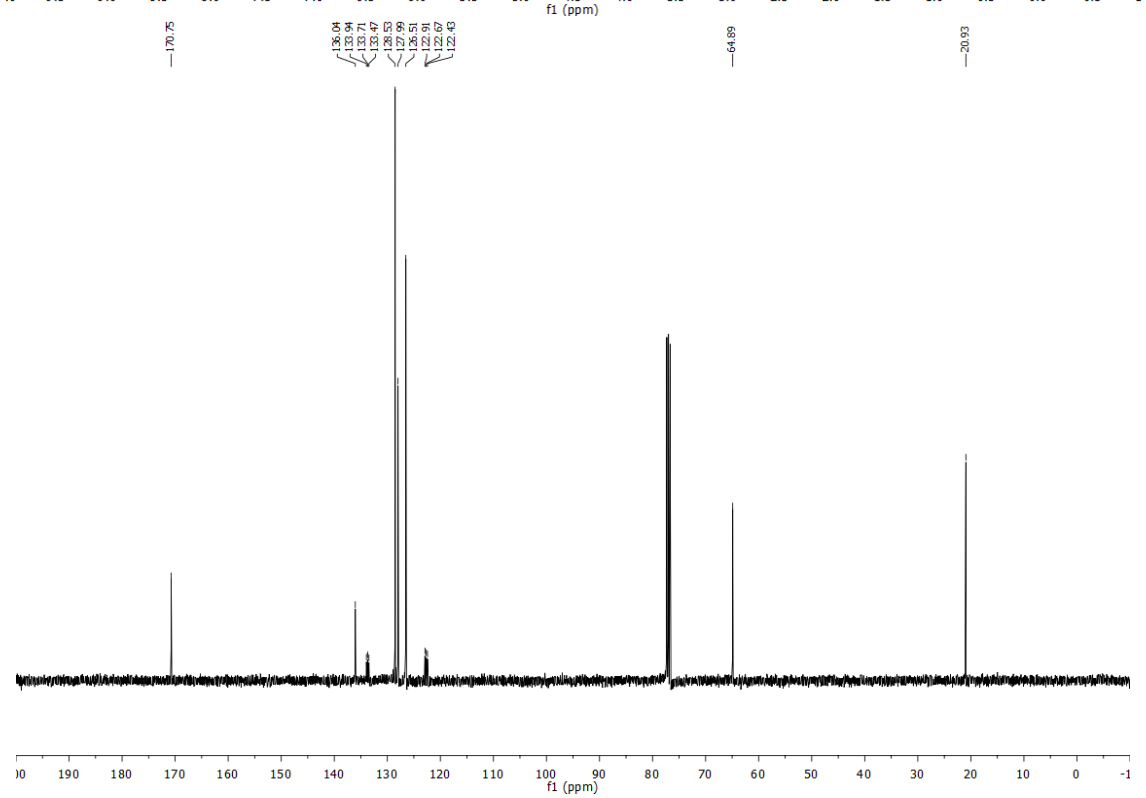
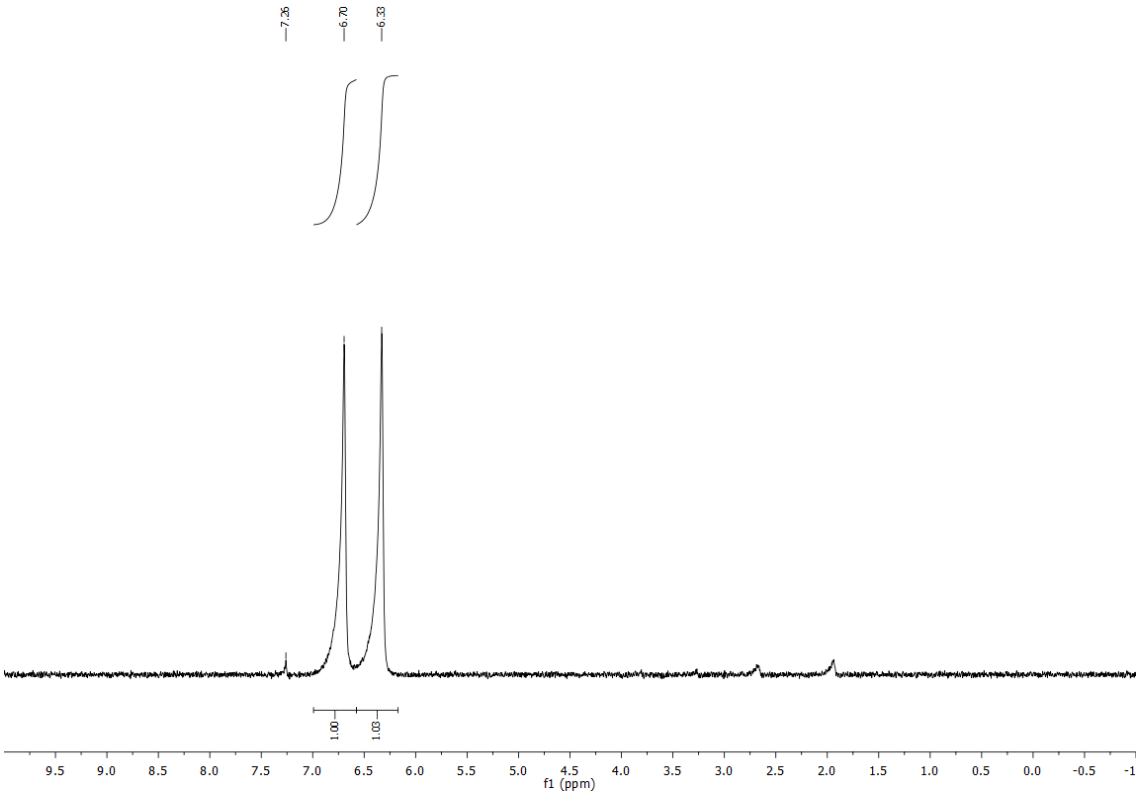
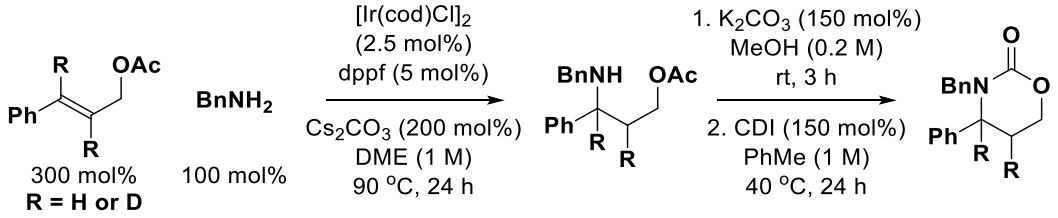
7.25
7.24
7.23
4.71
2.09
5.18
2.00
3.01
f1 (ppm)


170.75
136.04
133.94
133.71
133.47
128.53
127.89
125.51
122.91
122.67
122.43
64.89
20.93
f1 (ppm)


7.26
6.70
6.33
1.00
1.03
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

General procedure for the deuterated cyclic carbamate.

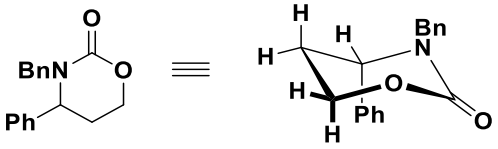


An oven-dried pressure tube equipped with a magnetic stir bar was charged with cesium carbonate (200 mol%), $[Ir(cod)Cl]_2$ (2.5 mol%), and dppf (5 mol%). The tube was purged with argon for 5 minutes. DME (1.0 M) was added followed by the deuterated cinnamyl acetate (300 mol%) and the amine (100 mol%). The tube was sealed with a PTFE lined cap and was placed in an oil bath at 90 ^{o}C and stirred for 24 hours. After reaching ambient temperature, the crude reaction mixture was directly subjected to flash column chromatography.

To a round-bottomed flask charged with the purified substrate under an argon atmosphere was added MeOH (0.2 M), followed by potassium carbonate (150 mol%). After 3 hours, the reaction mixture was filtered (celite) with the aid of CH_2Cl_2 (5 mL) and the filtrate was concentrated under reduced pressure. The crude reaction mixture was subjected to the next step without further purification

To a round-bottomed flask charged with the crude substrate under an argon atmosphere was added toluene (1.0 M), followed by carbonyldiimidazole (150 mol%). The reaction flask was placed an oil bath at 40 ^{o}C and stirred for 24 hours. After reaching ambient temperature, the reaction mixture was concentrated under reduced pressure and the crude reaction mixture was directly subjected to flash column chromatography.

3-benzyl-4-phenyl-1,3-oxazinan-2-one (*d*$_0$-7.3a)



The title compound was prepared by the general procedure.

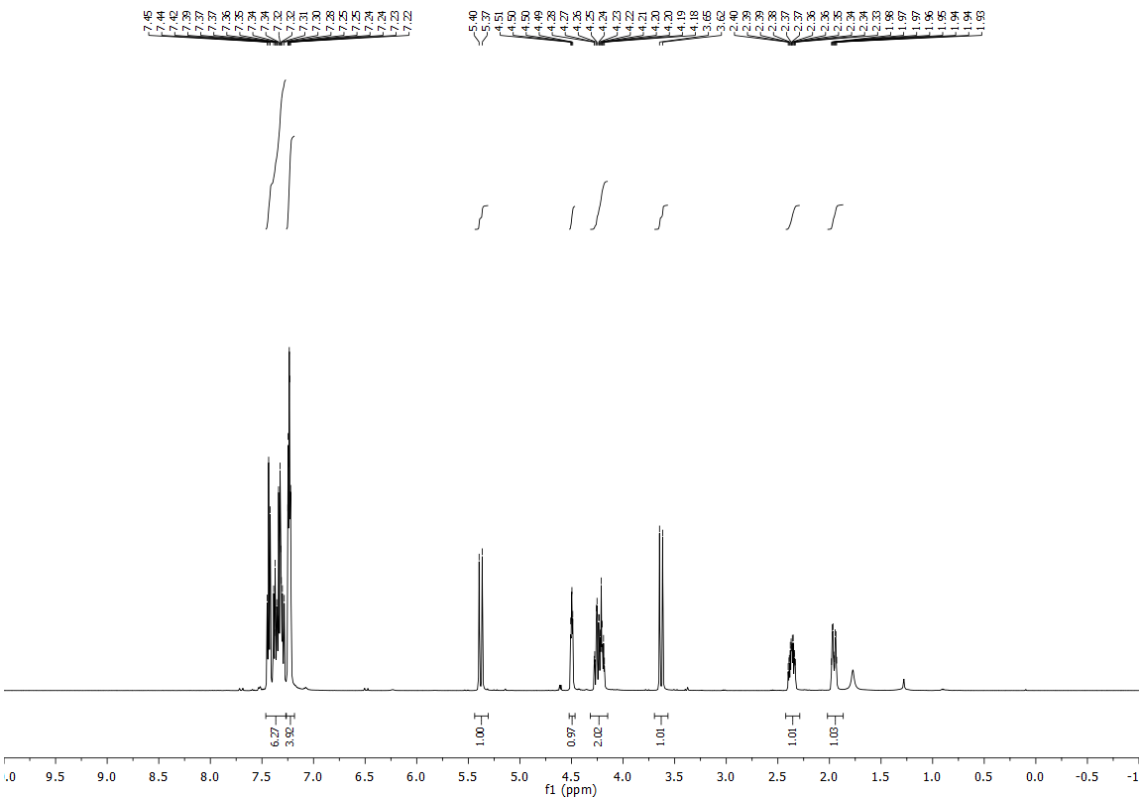
TLC (SiO_2) R_f = 0.24 (hexanes: ethyl acetate = 2:1).

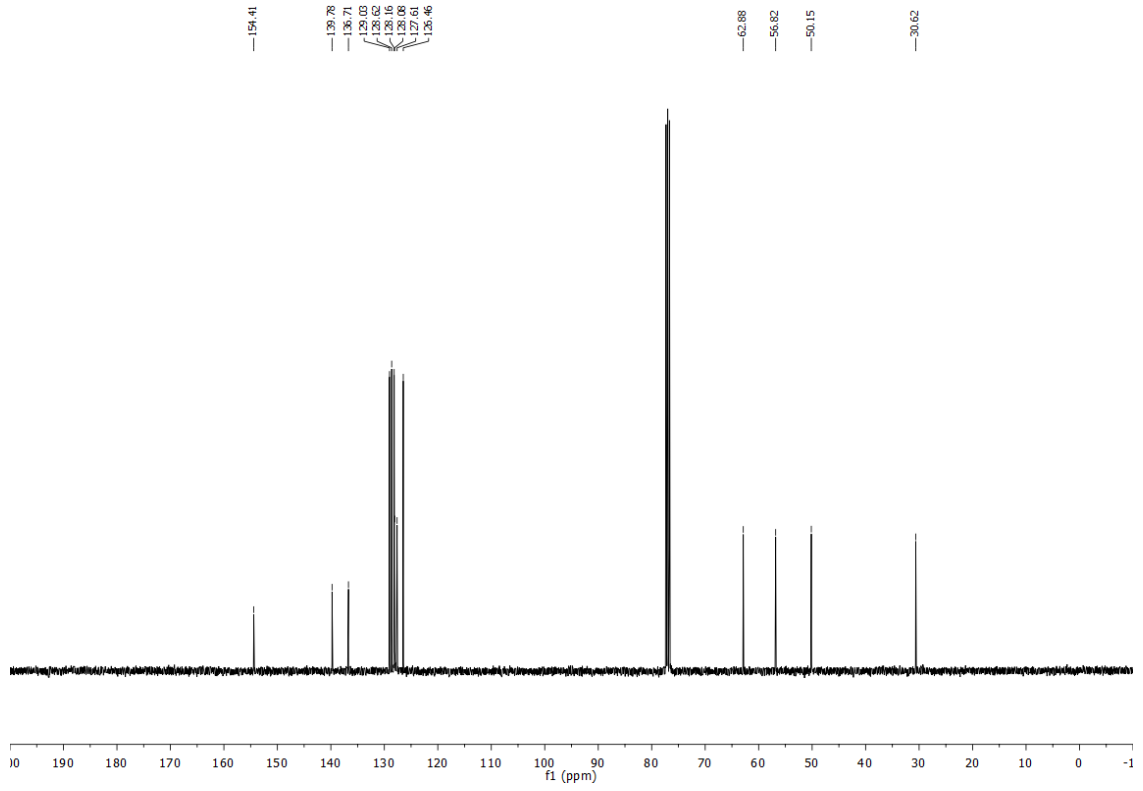
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46 – 7.27 (m, 6H), 7.24 (dt, *J* = 8.8, 3.1 Hz, 4H), 5.38 (d, *J* = 15.0 Hz, 1H), 4.50 (dd, *J* = 5.9, 4.0 Hz, 1H), 4.29 – 4.17 (m, 2H), 3.63 (d, *J* = 15.1 Hz, 1H), 2.37 (dddd, *J* = 14.5, 10.4, 6.0, 4.2 Hz, 1H), 1.96 (dtd, *J* = 14.1, 4.1, 2.9 Hz, 1H).

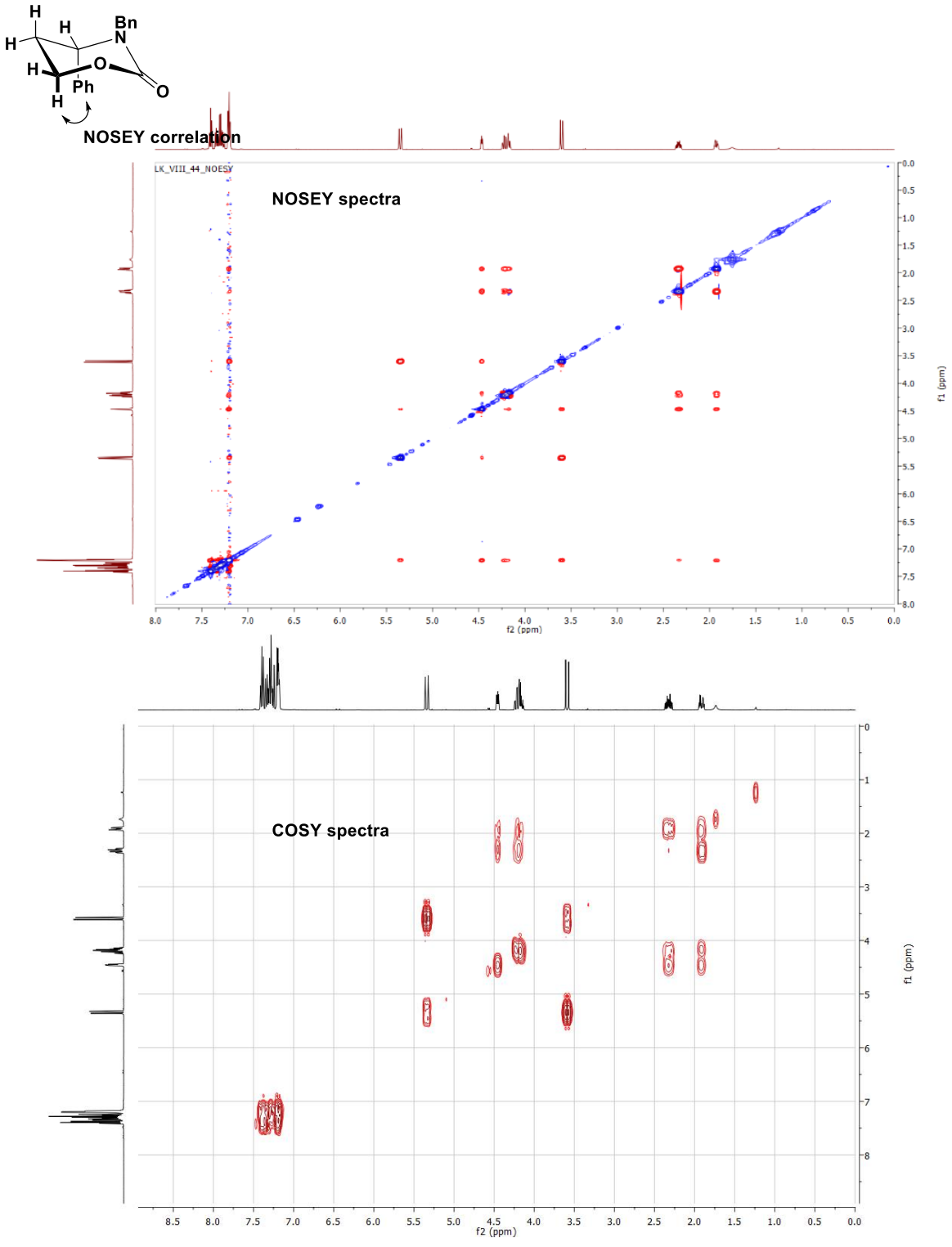
^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4, 139.8, 136.7, 129.0, 128.6, 128.2, 128.1, 127.6, 126.5, 62.9, 56.8, 50.2, 30.6.

HRMS (ESI): Calculated for $C_{17}H_{17}NO_2$ [M+H$^+$] = 268.1332, found 268.1339.

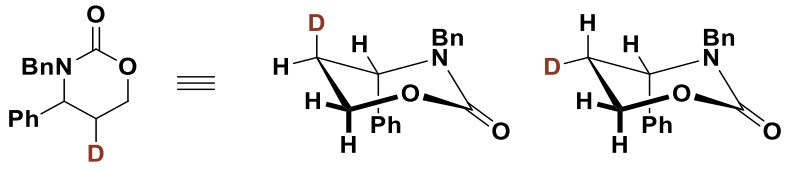
FTIR (neat): 3028, 1683, 1420, 1302, 1215, 1120, 1077, 909, 729, 700 cm^{-1}.


7.45 7.44 7.42 7.39 7.37 7.37 7.36 7.35 7.34 7.34 7.32 7.32 7.31 7.30 7.28 7.25 7.24 7.24 7.23 7.22
5.40 5.37 4.51 4.50 4.49 4.49 4.28 4.27 4.26 4.25 4.24 4.23 4.22 4.21 4.20 4.20 4.19 4.18 3.65 3.62 2.40 2.39 2.39 2.38 2.37 2.37 2.36 2.36 2.35 2.34 2.34 2.33 1.98 1.97 1.97 1.96 1.95 1.94 1.94 1.93
6.27 3.92 1.00 0.97 2.02 1.01 1.01 1.03
f1 (ppm)


154.41 139.78 136.71 129.03 128.62 128.16 128.08 127.61 126.46 62.88 56.82 50.15 30.62
f1 (ppm)


NOSEY correlation
NOSEY spectra
LK_VIII_44_NOESY
f2 (ppm)
f1 (ppm)
COSY spectra
f2 (ppm)
f1 (ppm)

(4*R*,5*S*)-3-benzyl-4-phenyl-1,3-oxazinan-2-one-5-d / (4*R*,5*R*)-3-benzyl-4-phenyl-1,3-oxazinan-2-one-5-d (*d*$_1$-7.3a)



The title compound was prepared by the general procedure.

TLC (SiO_2) R_f = 0.24 (hexanes: ethyl acetate = 2:1).

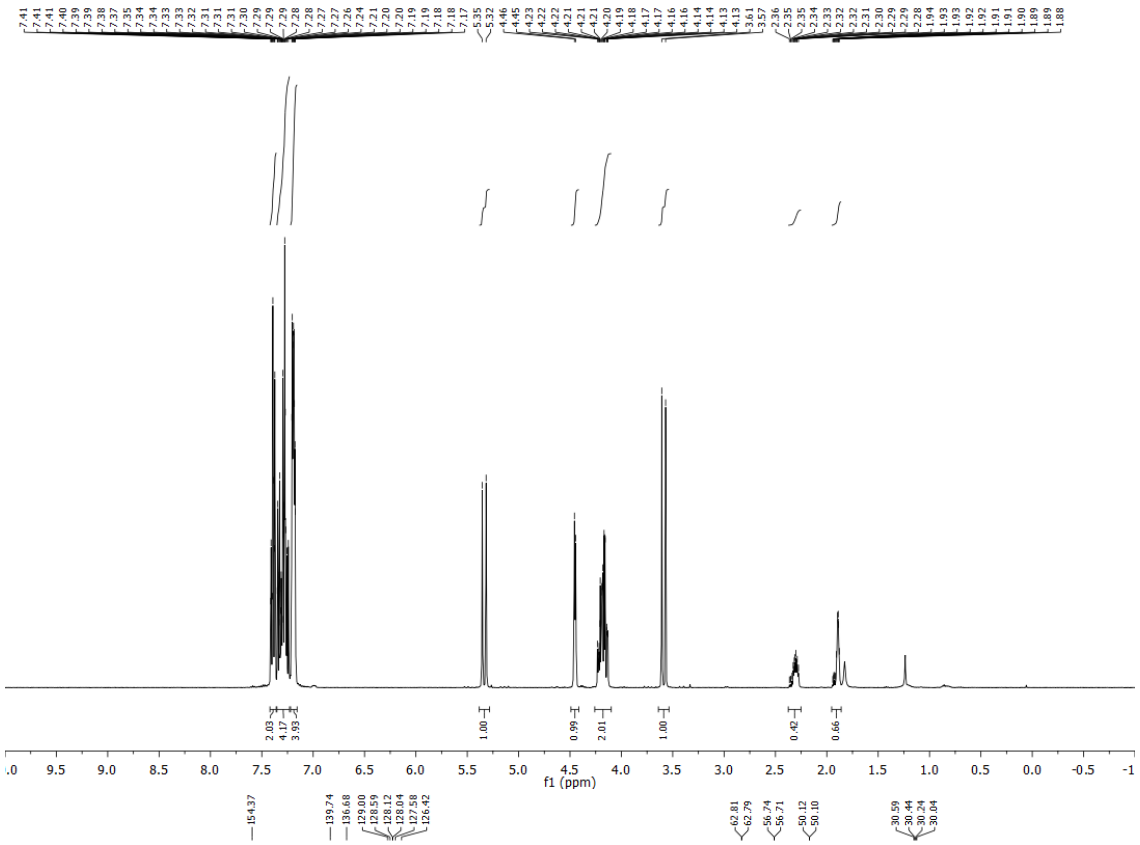
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.36 (m, 2H), 7.35 – 7.23 (m, 4H), 7.19 (ddd, *J* = 7.4, 4.0, 1.6 Hz, 4H), 5.34 (d, *J* = 15.1 Hz, 1H), 4.45 (d, *J* = 4.7 Hz, 1H), 4.26 – 4.10 (m, 2H), 3.59 (d, *J* = 15.1 Hz, 1H), 2.37 – 2.26 (m, 0.42H), 1.95 – 1.86 (m, 0.66H).

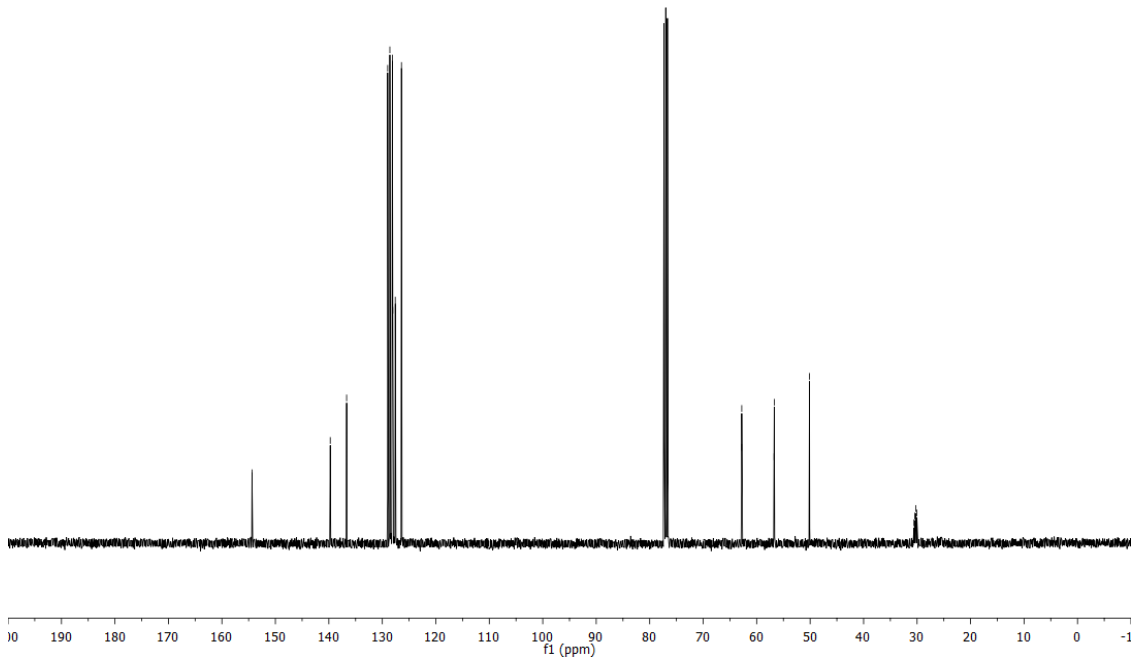
^{2}H NMR (92 MHz, $CHCl_3$) δ = 2.35 (s, 0.63H), 1.94 (s, 0.37H).

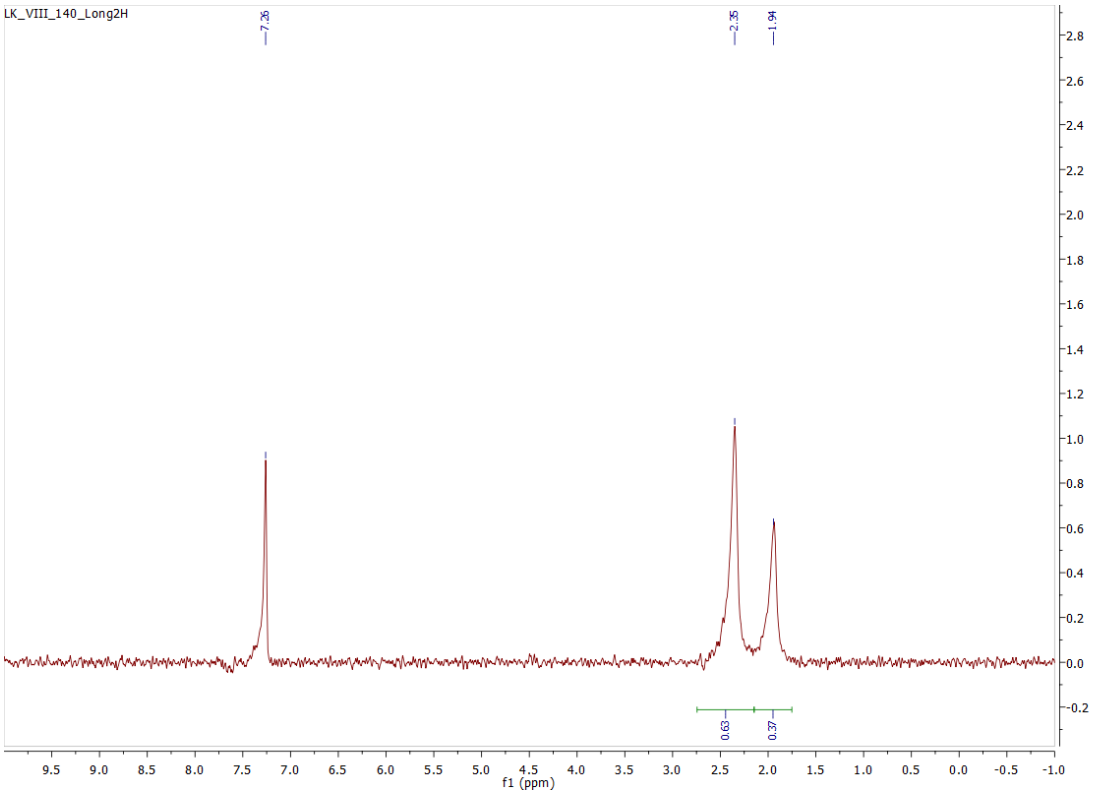
^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.4, 139.7, 136.7, 129.0, 128.6, 128.1, 128.0, 127.6, 126.4, 62.8 (d, *J* = 2.7 Hz), 56.7 (d, *J* = 3.3 Hz), 50.1 (d, *J* = 1.7 Hz), 30.2 (m).

HRMS (ESI): Calculated for $C_{17}H_{16}DNO_2$ [M+H$^+$] = 269.1395, found 269.1396.

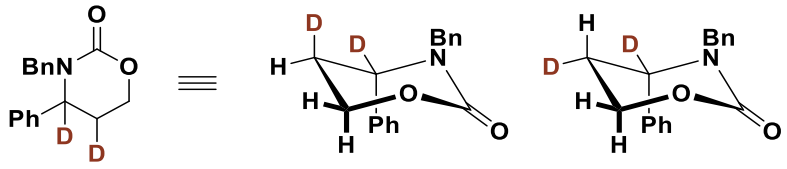
FTIR (neat): 3028, 1684, 1423, 1247, 1215, 1113, 1076, 729, 700 cm^{-1}.






LK_VIII_140_Long2H
7.26
2.35
1.94
0.63
0.37
f1 (ppm)

(4*R*,5*S*)-3-benzyl-4-phenyl-1,3-oxazinan-2-one-4,5-d$_2$ / (4*R*,5*R*)-3-benzyl-4-phenyl-1,3-oxazinan-2-one-4,5-d$_2$ (*d*$_2$-7.3a)



The title compound was prepared by the general procedure.

TLC (SiO$_2$) R_f = 0.24 (hexanes: ethyl acetate = 2:1).

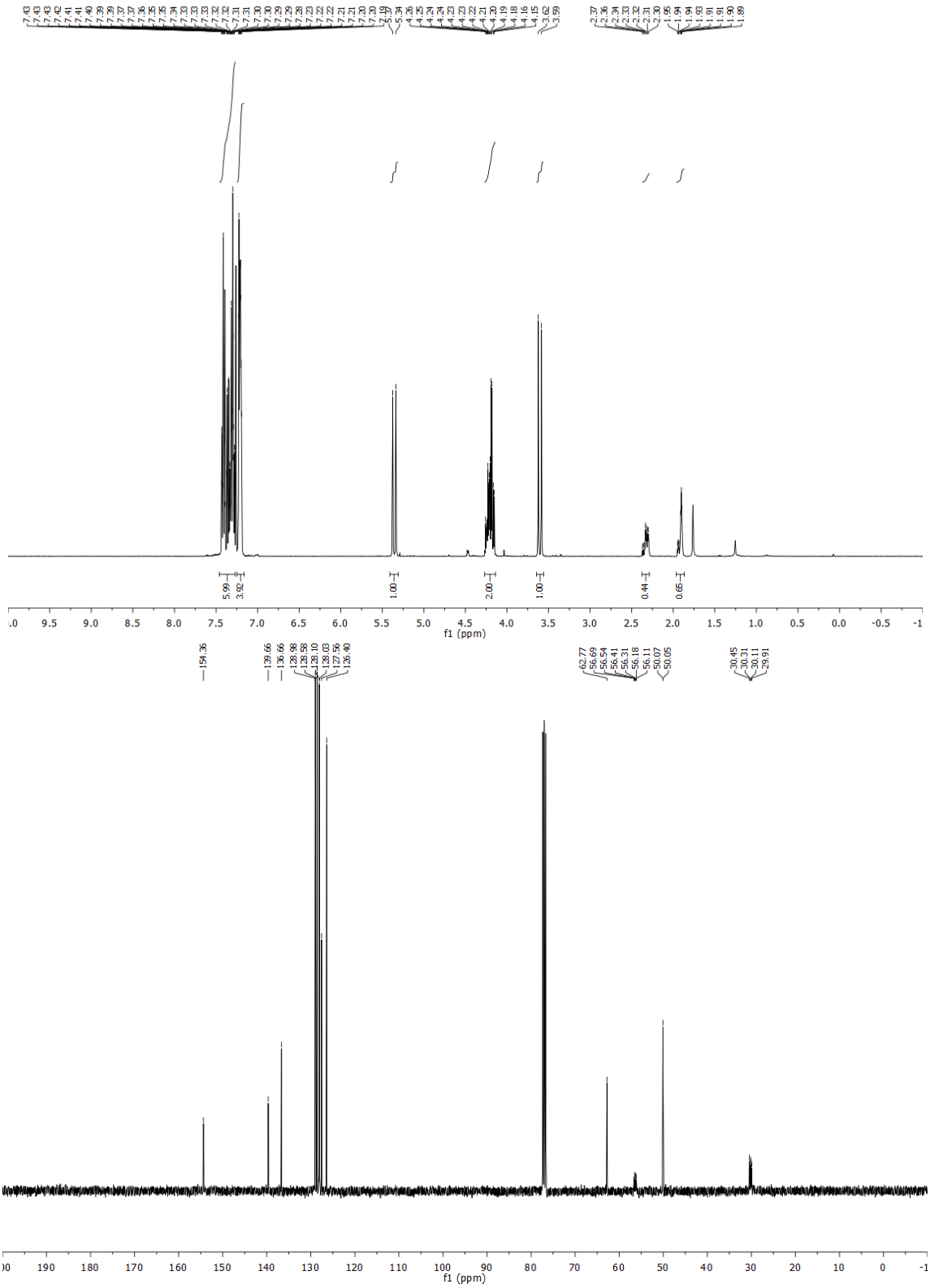
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 – 7.27 (m, 6H), 7.21 (ddd, *J* = 7.2, 4.0, 1.6 Hz, 4H), 5.36 (d, *J* = 15.1 Hz, 1H), 4.27 – 4.14 (m, 2H), 3.60 (d, *J* = 15.1 Hz, 1H), 2.38 – 2.28 (m, 0.43H) 1.92 (ddd, *J* = 14.2, 4.3, 2.8 Hz, 0.66H).

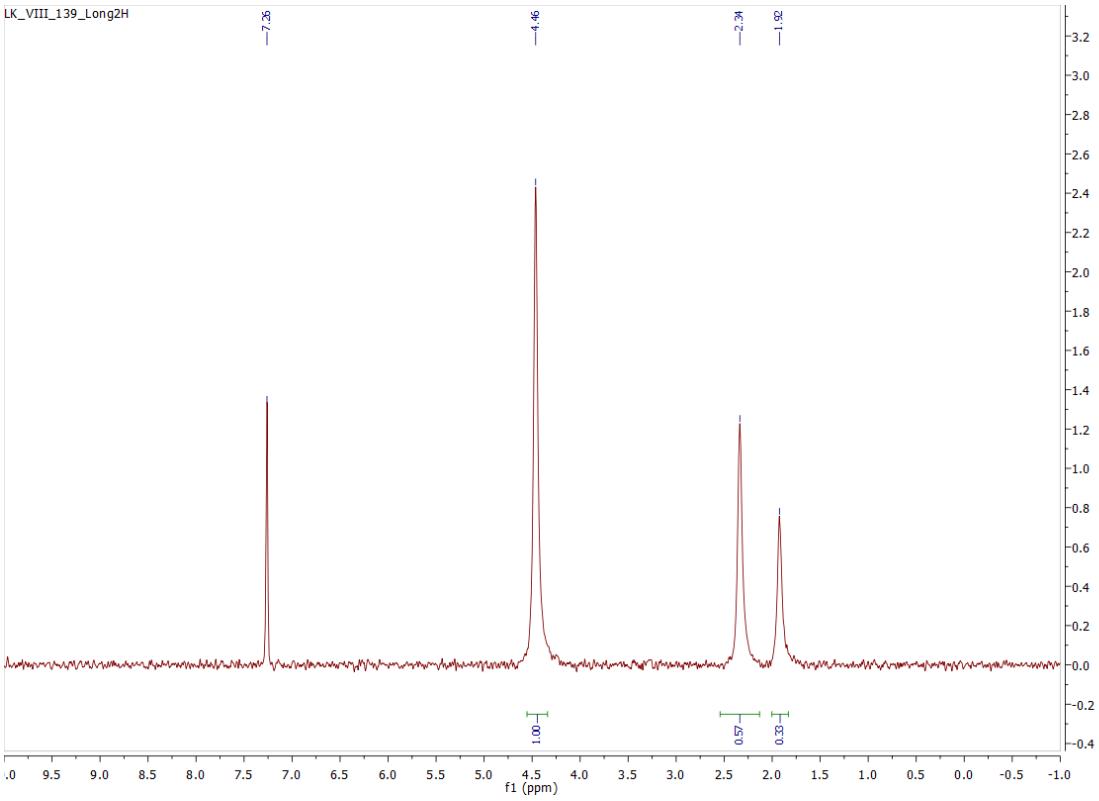
^{2}H NMR (92 MHz, $CHCl_3$) δ = 4.46 (s, 1H), 2.34 (s, 0.57H), 1.92 (s, 0.33H)

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.4, 139.7, 136.7, 129.0, 128.6, 128.1, 128.0, 127.6, 126.4, 62.8, 56.4 (m), 50.1 (d, *J* = 1.7 Hz), 30.2 (dd, *J* = 37.4, 17.2 Hz).

HRMS (ESI): Calculated for $C_{17}H_{15}D_2NO_2$ [M+H$^+$] = 270.1459, found 270.1458.

FTIR (neat): 3028, 1683, 1417, 1302, 1215, 1123, 1077, 909, 727, 700 cm^{-1}.


f1 (ppm)
f1 (ppm)


LK_VIII_139_Long2H
7.26
4.46
2.34
1.92
1.00
0.57
0.33
f1 (ppm)

Chapter 8: Inversion of Enantioselectivity in Allene Gas *versus* Allyl Acetate Reductive Aldehyde Allylation Guided by Metal-Centered Stereogenicity: An Experimental and Computational Study*

8.1 Introduction

In connection with longstanding efforts to use abundant chemical feedstocks as pronucleophiles in metal-catalyzed carbonyl reductive coupling,[1f] a diverse suite of enantioselective C-C couplings was developed in our laboratory.[1,2] A distinguishing feature of these processes resides in the use of inexpensive terminal reductants (e.g. H_2, 2-PrOH) or, more ideally, dual use of alcohols as carbonyl proelectrophiles and reductants in carbonyl addition *via* hydrogen auto-transfer.[1] Given the high occurrence of allenes as constituents in the C3, C4 and C5 petroleum cracking fractions (Figure 8.1), these patterns of reactivity were applied to the first (2007) allene-carbonyl reductive couplings to furnish homoallylic alcohols (Figure 8.2).[3]

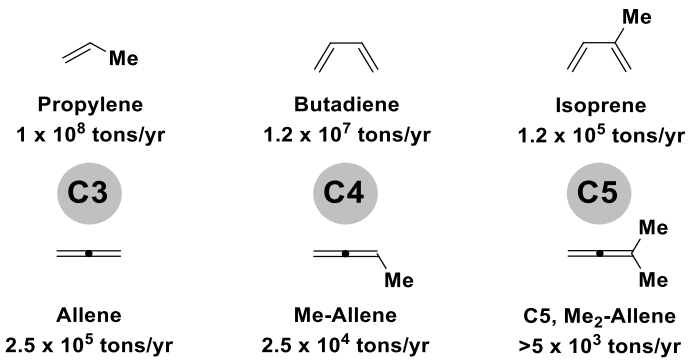


Figure 8.1 Allene feedstocks formed in petroleum cracking.

*This chapter is based on the published work:
Kim, S. W.; Meyer, C. C.; Mai, B. K.; Liu, P.; Krische, M. J. *ACS Catal.* **2019**, *9*, 9158.

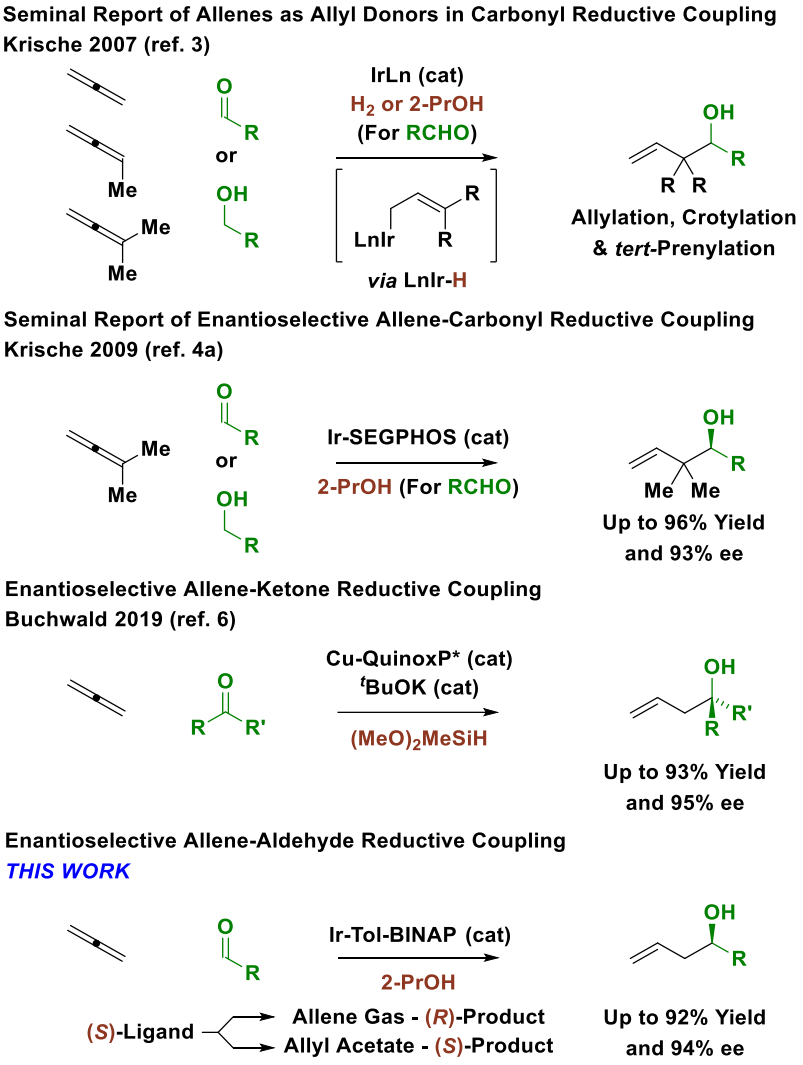


Figure 8.2 Milestones in metal-catalyzed allene-carbonyl reductive coupling and related hydrogen auto-transfer processes.

Using allene, methylallene and dimethylallene as pronucleophiles, products of carbonyl allylation, crotylation and *tert*-prenylation were obtained in reactions conducted from either the alcohol or aldehyde oxidation level.[3] Shortly thereafter (2009), we reported the first enantioselective reactions of this type using dimethyl allene.[4a]

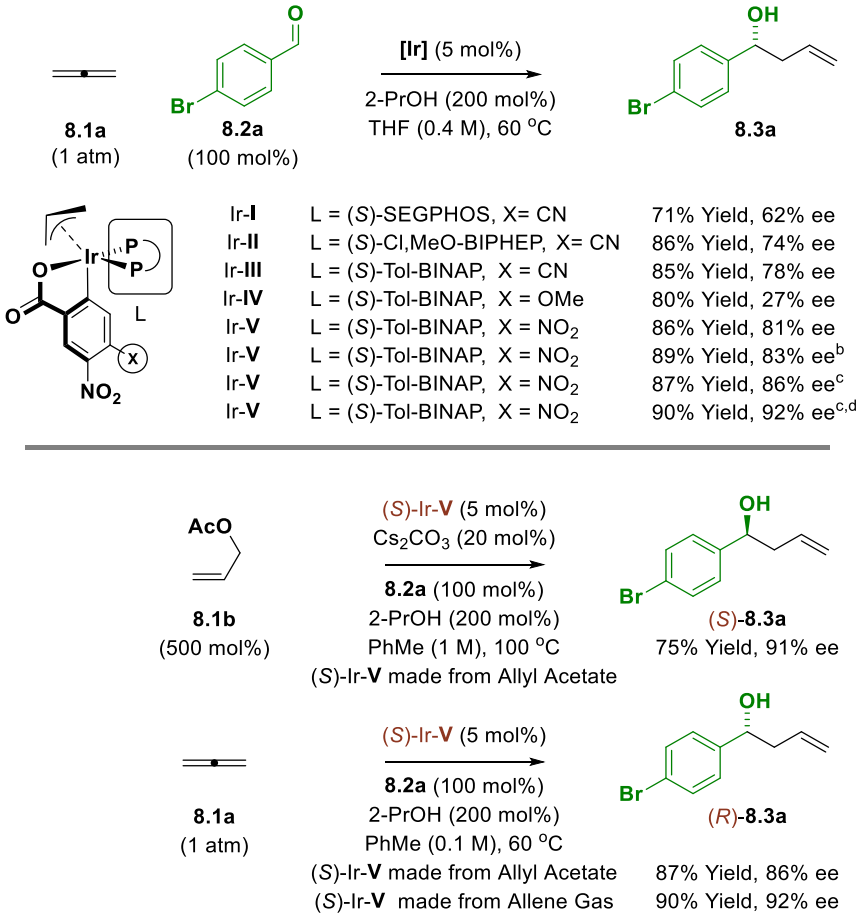
Following this and other catalytic enantioselective allene-carbonyl additions developed in our laboratory,[4,5] Buchwald reported an allene-ketone reductive coupling mediated by $(MeO)_2MeSiH$.[6] In this account, we report the first enantioselective allene-aldehyde reductive couplings.[7] Additionally, we demonstrate that using the same antipode of chiral ligand, (*S*)-tol-BINAP, an inversion of enantioselectivity is observed for carbonyl allylations that employ gaseous allene vs allyl acetate as pronucleophile solely in response to stereogenicity at iridium.[8,9] Experimental and computational studies corroborate intervention of diastereomeric π-allyliridium-*C,O*-benzoate complexes, which arise *via* allene hydrometalation (from a pentacoordinate iridium hydride) vs ionization of allyl acetate (from a square planar iridium species).

8.2 Reaction Development and Scope

An initial series of experiments were conducted in which a sealed reaction vessel back-filled with gaseous allene **8.1a** and charged with aldehyde **8.2a** (100 mol%), 2-propanol (200 mol%), THF (0.4 M) and an iridium catalyst (5 mol%) were heated to 60 ^oC (Table 1) for 24 hours. It was determined that the (*S*)-tol-BINAP-modified iridium catalyst, Ir-**V**, delivered the desired product **8.3a** with the highest levels of enantioselectivity as the (*R*)-enantiomer, which is the opposite enantiomer observed in corresponding carbonyl allylations mediated by allyl acetate **8.1b**.[10] This surprising result compelled us to evaluate the diastereomeric composition of the iridium catalyst Ir-**V**, which is easily accomplished *via* LCMS due to the chromatographic stability of π-allyliridium-*C,O*-benzoates (Figure 8.3). The catalyst prepared from allyl acetate is enriched in diastereomer D, which, as indicated by experiment and computation, is the thermodynamically most stable isomer. In contrast, the catalyst recovered from the reaction mixture using allene or prepared from allene itself is enriched in diastereomer C.

It was posited that use of Ir-**V** derived from allene would improve enantioselectivity in the allene-mediated allylation of aldehyde **8.2a**. Indeed, an increase from 86% to 92% ee in the formation of homoallylic alcohol **8.3a** was observed (Table 8.1). Using catalyst (*S*)-Ir-**V** derived from allene, the scope of the allene-mediated reductive aldehyde allylation mediated by 2-propanol was explored (Table 2). Diverse aryl aldehydes **8.2a-8.2i** and heteroaryl aldehydes **8.2j-8.2p** were converted to the corresponding homoallylic alcohols **8.3a**-**8.3p** in good yield with uniformly high levels of enantioselectivity. As illustrated by the formation of adduct **8.3d**, due to the mild reaction conditions, sensitive functional groups such as pinacol boronates are tolerated. The formation of **8.3l**, which incorporates an unprotected indole nitrogen, also is notable. The α,β-unsaturated aldehyde **8.2q**, as well as linear and branched aliphatic aldehydes **8.2r** and **8.2s** also participate in highly enantioselective allylation. Allene-mediated allylation of **8.2a** mediated by d_8-2-propanol delivers *deuterio*-**8.3a** (eq. 8.1).[11] The pattern of deuterium incorporation corroborates reversible allene hydrometalation with incomplete regiocontrol. The relatively low levels of deuterium incorporation are attributed to reversibility of the hydrometalation event and H/D-exchange with adventitious water.[12]

Table 8.1 Selected optimization experiments in the enantioselective reductive coupling of allene **8.1a** with aldehyde **8.2a** and divergent enantioselectivity observed upon use of allyl acetate vs allene pronucleophiles.[a]



[a]Yields are of material isolated by silica gel chromatography. Enantioselectivities were determined by chiral stationary phase HPLC analysis. [b]PhMe (0.4 M). [c]PhMe (0.1 M). [d](*S*)-Ir-**V** derived from allene. See Supporting Information for experimental details.

Figure 8.3 Diastereomeric composition of the (*S*)-Ir-**V** and calculated thermodynamic stabilities.

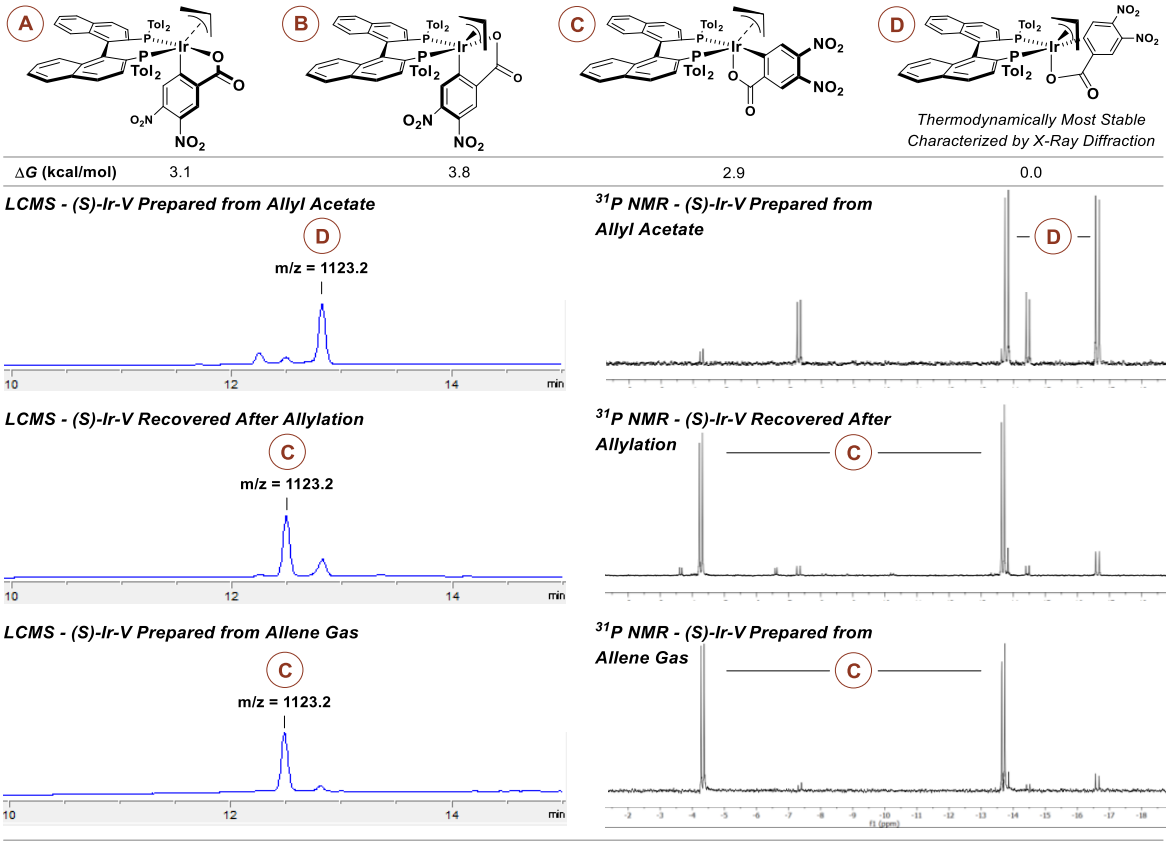
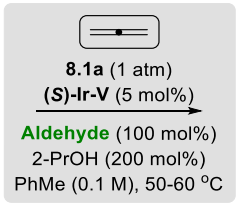
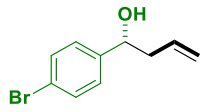
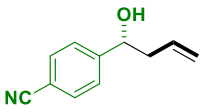


Table 8.2 Enantioselective iridium-catalyzed reductive coupling of gaseous allene **8.1a** with aldehydes **8.2a-8.2s** mediated by 2-propanol.[a]

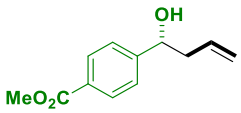




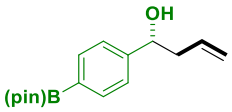
8.3a
90% Yield
92% ee



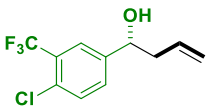
8.3b
88% Yield
88% ee



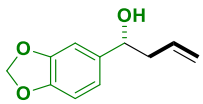
8.3c
88% Yield
92% ee



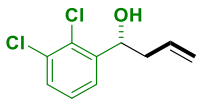
8.3d
85% Yield
92% ee



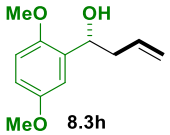
8.3e
74% Yield
90% ee



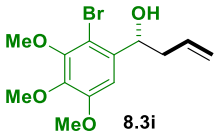
8.3f
84% Yield
94% ee



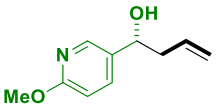
8.3g
82% Yield
91% ee



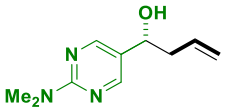
8.3h
84% Yield
92% ee



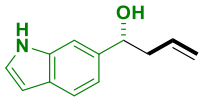
8.3i
92% Yield
91% ee



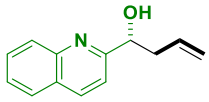
8.3j
91% Yield
92% ee



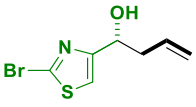
8.3k
76% Yield
93% ee



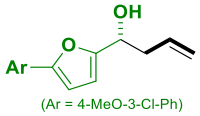
8.3l
79% Yield
87% ee



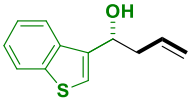
8.3m
88% Yield
87% ee



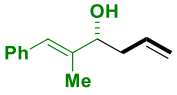
8.3n
71% Yield
89% ee



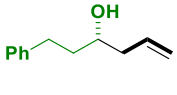
8.3o
79% Yield
88% ee



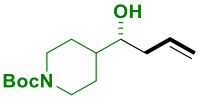
8.3p
81% Yield
93% ee



8.3q
61% Yield
92% ee

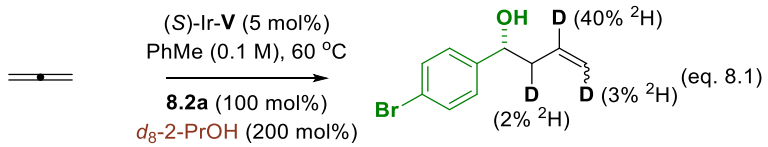


8.3r
65% Yield
90% ee



8.3s
71% Yield
90% ee

[a]Yields of material isolated by silica gel chromatography. The catalyst (*S*)-Ir-**V** prepared from allene was used. Enantioselectivities were determined by chiral stationary phase HPLC analysis. See Supporting Information for further experimental details.



8.1a
(1 atm)

(*S*)-Ir-**V** made from allene

deuterio-**8.3a**
86% Yield, 92% ee

8.3 Discussion

The experimental data suggest that the observed divergence in enantioselectivity in reactions of allene vs allyl acetate is due to intervention of diastereomeric π-allyliridium-*C,O*-benzoate complexes C and D, which arise *via* allene hydrometalation (from an pentacoordinate iridium hydride) vs ionization of allyl acetate (from a square planar iridium species), respectively (Figure 8.4).[13,14]

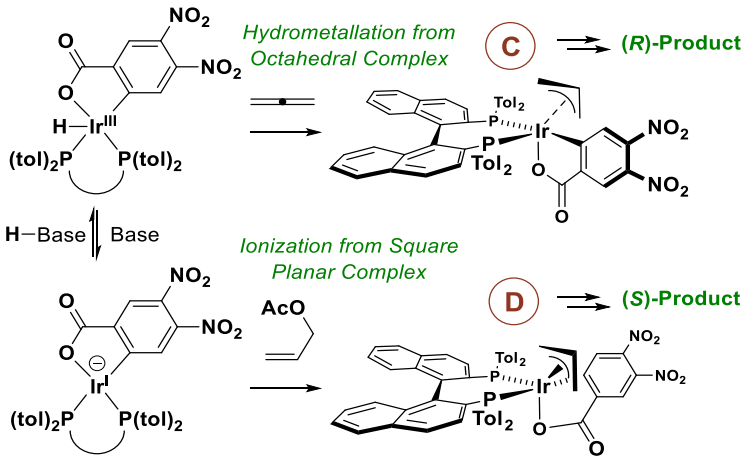


Figure 8.4 Hypothesis for enantiodivergence in aldehyde allylations mediated by gaseous allene vs allyl acetate.

To challenge the veracity of our hypothesis, we then turned our efforts to density functional theory (DFT) calculations.[15] The reaction pathways to form the π-allyliridium complexes under the different experimental conditions were first computed. When allyl acetate pronucleophile is used, the π-allyliridium is formed *via* coordination of allyl acetate to the *C,O*-benzoate complex 4 followed by ionization (TS1, Figure 8.5A). Although the common intermediate 4 can potentially lead to all four diastereomeric π-allyl complexes, formation of D is kinetically and thermodynamically favored (see Figure

S2 for less favorable pathways to A and B). The relatively low barrier of TS1D suggests a reversible ionization process. The thermodynamically more stable complex D is operative in the subsequent aldehyde addition step (*vide infra*). On the other hand, π-allyliridium complexes derived from allene are formed *via* hydrometalation from a square pyramidal iridium hydride (6C or 6D, Figure 8.5B). DFT calculations suggest 6C is thermodynamically more stable than 6D, and subsequent allene coordination to form 7C and hydrometalation *via* TS3C are both very facile. Therefore, π-allyl complex C is formed preferentially from allene hydrometalation. The calculated transition states for allylation of aldehyde **8.2a** by the diastereomeric complexes C and D provide further insight into the origins of enantiodivergence. Complexes C and D are supported by the same antipode of the (*S*)-tol-BINAP ligand, but their stereogenicity at iridium is opposite. Therefore, examination of the transition states for carbonyl addition will reveal whether enantioselectivity is influenced more by the chirality of the metal center[16] or the bisphosphine ligand. The aldehyde addition with C and D occurs by way of Zimmerman-Traxler-type transition states that place the Ar group of the aldehyde in a pseudo-equatorial position (Figure 8.6).[17] In the reaction with D, addition to the (*Si*)-face of the aldehyde (TS2D-S) to form (*S*)-**8.3a** is 2.2 kcal/mol more favorable than the (*Re*)-face addition (TS2D-R) to form (*R*)-**8.3a**. TS2D-R is destabilized by the 1,3-diaxial interactions between the aldehyde hydrogen and the benzene ring of the benzoate, which is co-planar with the aldehyde. In TS2D-S, the axial aldehyde hydrogen and the benzoate are on opposite faces of the chair, which relieves steric repulsion. In the allylation transition states with complex C (Figure 8.6B), because the stereogenicity at iridium is inverted, the (*S*)-selective transition state (TS2C-S) is now destabilized by the 1,3-diaxial interactions be-tween the aldehyde hydrogen and the benzoate. As such, the most

favorable transition state from C is TS2C-R, which eventually leads to the (*R*)-enantiomer of the homoallylic alcohol product **8.3a**.

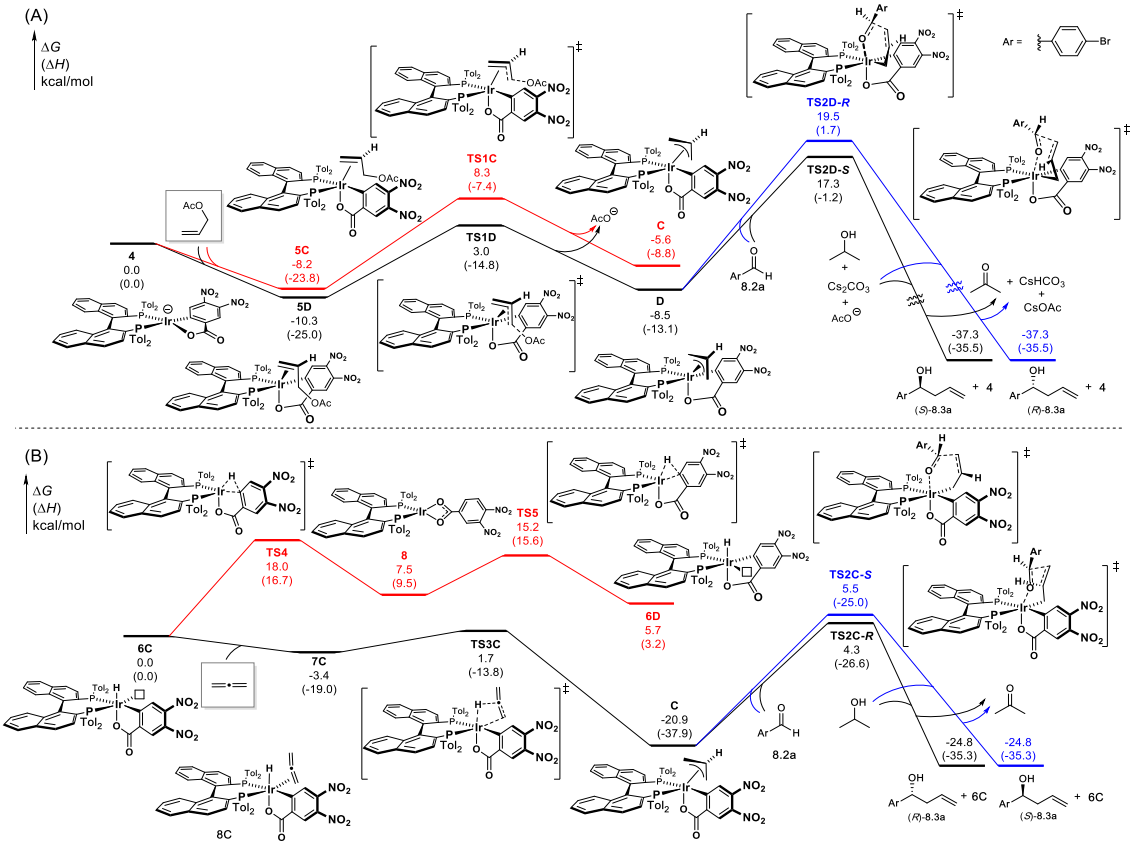


Figure 8.5 Computed energy profiles of the kinetic pathways leading to diastereomers D and C and, therefrom, (*S*)-and (*R*)-product enantiomers, respectively.

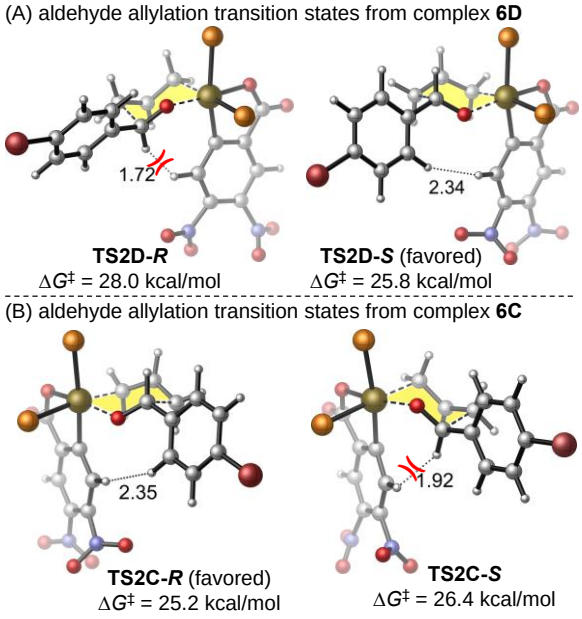


Figure 8.6 Enantioselectivity determining aldehyde allylation transition states with π-allyliridium complexes D and C. Activation free energies are with respect to D and C, respectively.

8.4 Conclusion

In summary, we report the first catalytic enantioselective aldehyde allylations mediated by gaseous allene. These processes exploit a feedstock pronucleophile (allene) in combination with a feedstock reductant (2-propanol) under non-cryogenic conditions with acetone as the sole stoichiometric byproduct. Remarkably, use of allene vs allyl acetate as pronucleophile results in an inversion of enantioselectivity using the same antipode of chiral ligand, (*S*)-tol-BINAP. The collective experimental and computational data corroborate intervention of diastereomeric π-allyliridium-*C,O*-benzoate complexes, which arise *via* allene hydrometalation (from a pentacoordinate iridium hydride) vs allyl acetate ionization (from a square planar iridium species). These data should facilitate the

design of related chiral-at-metal complexes for enantioselective catalysis by providing insight into the structural and interactions features of the catalyst that influence enantioselectivity. More broadly, these studies and other work from our laboratory demonstrate how reactions that traditionally have employed organometallic reagents may now be conducted catalytically in the absence of premetalated reagents using abundant feedstocks.[1f,18]

8.5 Experimental Details

General Information

All reactions were carried out under inert gas atmosphere (nitrogen or argon) unless otherwise indicated. Resealable pressure tubes (13x100 mm) were purchased from Fischer Scientific (catalog number 14-959-35C) and were oven dried followed by cooling in a desiccator or under a stream of inter gas prior to use. All commercial reagents and anhydrous solvents were used as received from vendors (Fischer Scientific, Sigma Aldrich, and Combi Blocks) without further purification. Preparative column chromatography employing Silicycle silica gel (40-63 μm) was performed according to the method of Still[1] or on a Teledyne Isco Combiflash Rf utilizing Silicycle HP column using a mobile phase composed of either hexanes/ethyl acetate, hexanes/acetone, or dichloromethane/methanol. Reactions were monitored by analytical thin-layer chromatography (TLC) using 0.25 mm commercial silica gel plates (Dynamic Absorbents F). Visualization was accomplished with UV light followed by dipping in CAM, *p*-Anisaldehyde (PAA), or $KMnO_4$ stain solution followed by heating.

Spectroscopy, Spectrometry and Data Collection

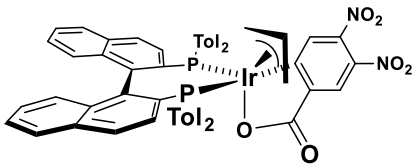
Infrared spectra were recorded on a Perkin-Elmer 1600 spectrometer using a diamond ATR unit. High-resolution mass spectra (HRMS) were obtained on a Karatos MS9 and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion (M+H, M+Na), or a suitable fragment ion. Nuclear magnetic resonance (^1H, ^{13}C, ^{19}F NMR) spectra were recorded with a Bruker BioSpin GmbG, Varian Gemini (400 MHz) or Varian INOVA (500 MHz) spectrometer equipped with a Bruker cryoprobe. The chemical shifts are given as parts per million (ppm) and were referenced

to the residual solvent signal ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm). Specific optical rotations were recorded on an Azzota Corp AP45 (589 nm) in CHCl3. Solution concentrations are given in the units of 10–2 g mL^{-1}.

Experimental Details and Spectral Data

Detailed Procedure for Preparation of Iridium Complexes

*(S)-Ir-V Made from Allyl Acetate (**D**)*



To a sealed tube equipped with a magnetic stir bar was added Cs_2CO_3 (977.5 mg, 3.0 mmol, 200 mol%), 3,4-dinitrobenzoic acid (636.4 mg, 3.0 mmol, 200 mol%), (*S*)-TolBINAP (1.02 g, 1.5 mmol, 100 mol%) and $[Ir(cod)Cl]_2$ (503.8 mg, 0.75 mmol, 50 mol%). The reaction vessel was purged with argon and THF (15.0 mL, 0.1 M) was added followed by allyl acetate (0.40 mL, 3.75 mmol, 250 mol%). The resulting mixture was stirred at room temperature for 30 min, and at 80 ˚C for another 90 min. After cooling to ambient temperature, the mixture was filtered through a celite plug with the aid of DCM (45 mL). The combined filtrate was concentrated *in vacuo* and subjected to flash column chromatography (DCM:THF = 10:1). The resulting gum-like residue was dissolved in THF (2.0 mL). Addition of HPLC grade hexanes (20 mL) led to formation of a precipitate. The product was filtered and washed with HPLC grade hexanes, followed by removal of trace amount of solvent *in vacuo*, to provide a light yellow powder (1.4 g, 1.25 mmol) in 83% yield as a mixture of stereoisomers. The yellow powder was

dissolved in toluene and hexanes was allowed to diffuse into the toluene solution at room temperature *via* slow vapor diffusion, resulting in formation of crystals.

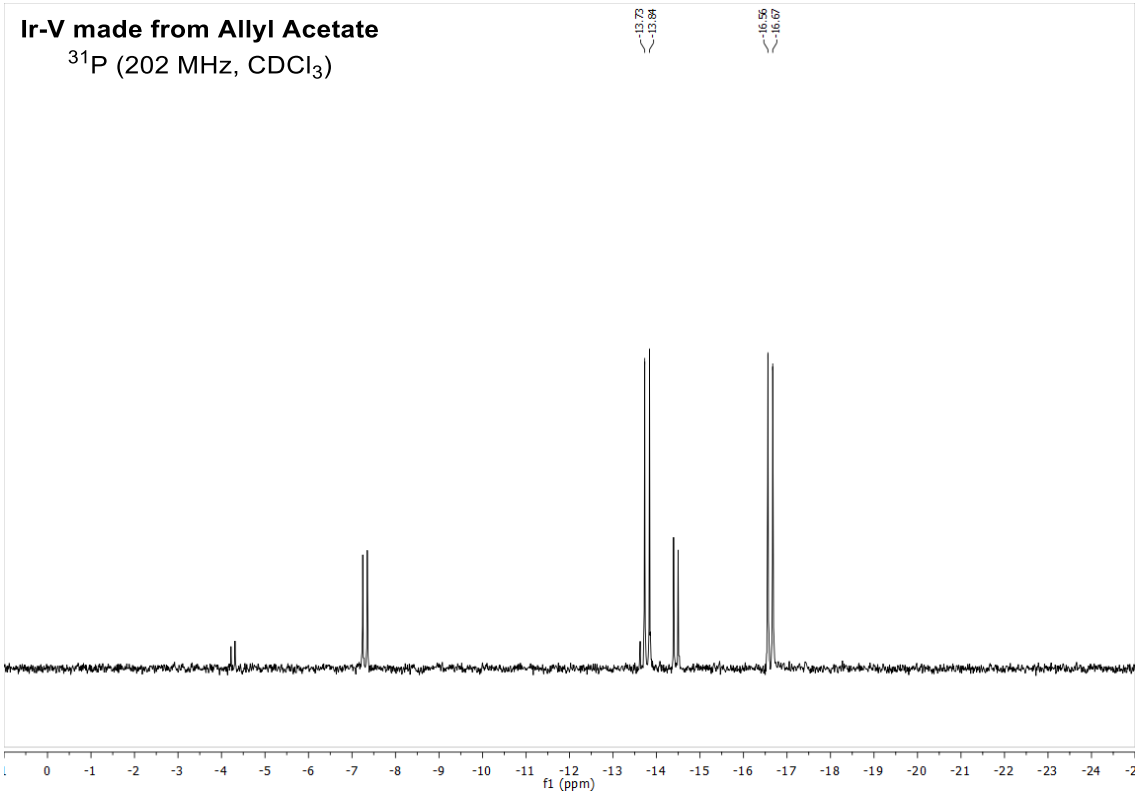
Spectral data is reported for the major isomer.

^{31}P NMR (202 MHz, $CDCl_3$): δ = -13.78 (d, *J* = 22.5 Hz), -16.62 (d, *J* = 22.5 Hz).

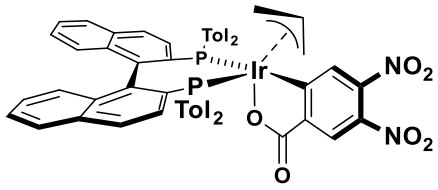
HRMS (ESI): Calculated for $C_{58}H_{47}IrN_2O_6P_2$ [M+H$^+$] = 1123.2616, Found 1123.2624.

$[\alpha]_D^{28}$ = –100.8 (*c* 0.3, $CHCl_3$).

MP: 236-246 °C (decomposes)



*(S)-Ir-V Made from Allene Gas (**C**)*



To a sealed tube equipped with a magnetic stir bar was added K_2CO_3 (110.6 mg, 0.8 mmol, 200 mol%), 3,4-dinitrobenzoic acid (169.7 mg, 0.8 mmol, 200 mol%), (*S*)-TolBINAP (271.5 mg, 0.4 mmol, 100 mol%) and $[Ir(cod)Cl]_2$ (134.3 mg, 0.2 mmol, 50 mol%). The tube was fit with a rubber septum before being evacuated by piercing the septum with a needle connected to a Schlenk line. Immediately after evacuation, an allene balloon fitted with a needle was used to pierce the septum and refill the tube with allene gas. Under the allene balloon, THF (4.0 mL, 0.1 M) was added. The septum was quickly removed and the tube was sealed with a PTFE lined cap. The resulting mixture was stirred at room temperature for 30 min, and at 80 ˚C for another 90 min. After cooling to ambient temperature, the mixture was filtered through a celite plug with the aid of DCM (45 mL). The combined filtrate was concentrated *in vacuo* and subjected to flash column chromatography (DCM:THF = 10:1). The resulting gum-like residue was dissolved in THF (1.0 mL). Addition of HPLC grade hexanes (20 mL) led to formation of a precipitate. The product was filtered and washed with HPLC grade hexanes, followed by removal of trace amount of solvent *in vacuo*, to provide a light yellow powder (358.0 mg, 0.32 mmol) in 80% yield as a mixture of stereoisomers.

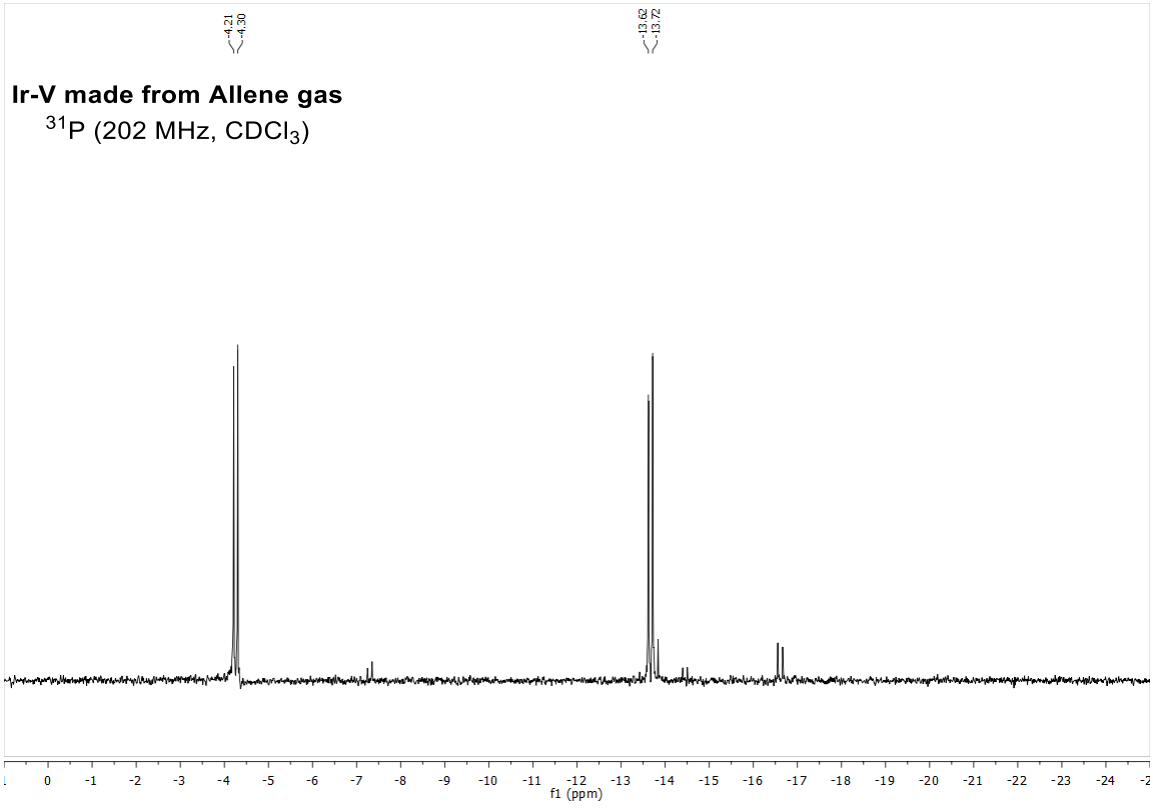
Spectral data is reported for the major isomer.

^{31}P NMR (202 MHz, $CDCl_3$): δ = -4.26 (d, *J* = 18.7 Hz), -13.67 (d, *J* = 19.8 Hz).

HRMS (ESI): Calculated for $C_{58}H_{47}IrN_2O_6P_2$ [M+H$^+$] = 1123.2616, Found 1123.2624.

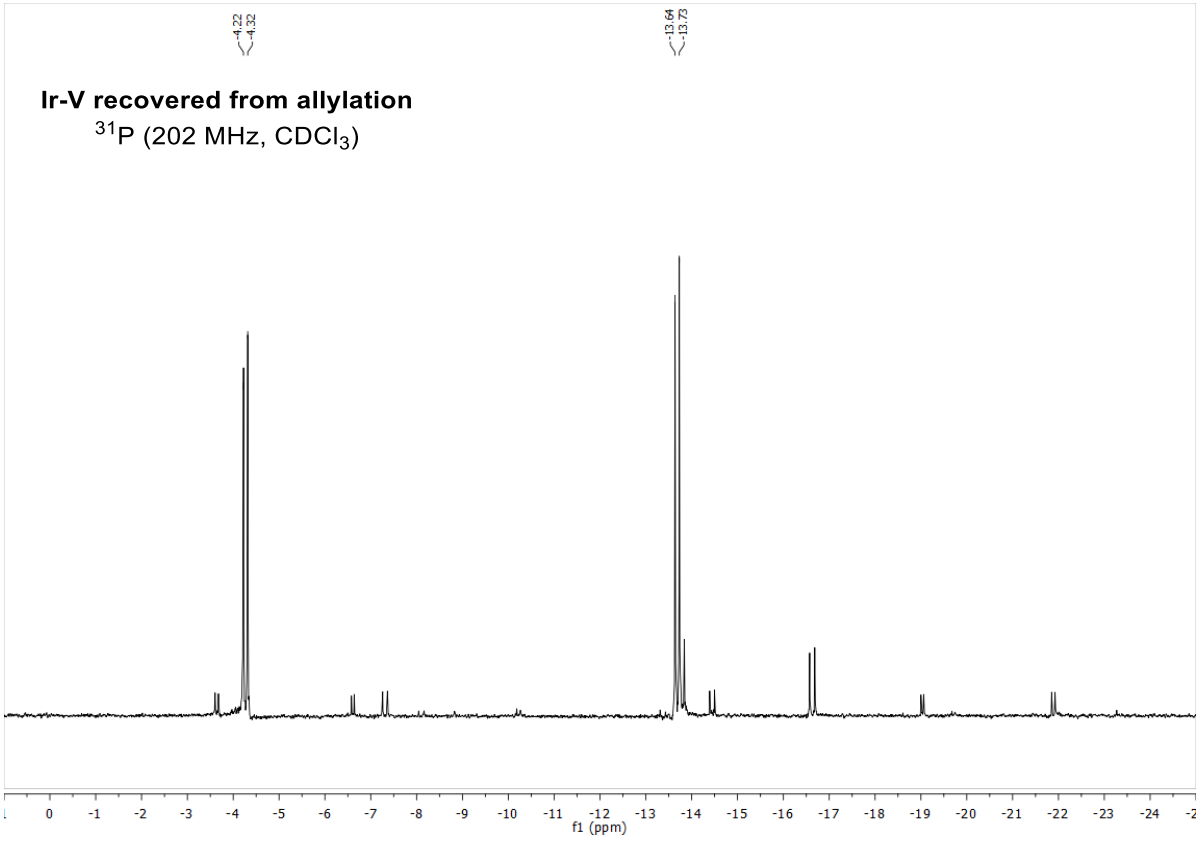
$[\alpha]_D^{28}$ = –282.7 (*c* 0.3, $CHCl_3$).

MP: 226-234 °C (decomposes)



(S)-Ir-V recovered from Allylation - It was prepared according to the following procedures and was identical in all respects to the (S)-Ir-V made from allene gas.

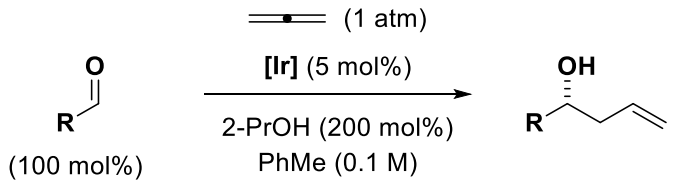
A pressure tube equipped with a magnetic stir bar was charged with aldehyde **2a** (37.0 mg, 0.2 mmol, 100 mol%) and **(*S*)-Ir-V made from allyl acetate** (11.2 mg, 0.01 mmol, 5 mol%). The tube was fit with a rubber septum and was evacuated by piercing the septum with a needle connected to a Schlenk line. Immediately after evacuation, an allene-filled balloon equipped with a needle was used to pierce the septum and refill the tube with allene gas. Under the allene balloon, toluene (2.0 mL, 0.1 M) was added followed by 2-propanol (31 µL, 0.4 mmol, 200 mol%). The septum was removed quickly and the tube was sealed with a PTFE lined cap. The tube was placed at 60 ^{o}C for 24 hours. The solution was allowed to reach ambient temperature before being concentrated *in vacuo*. The residue was directly subjected to flash column chromatography. The title compound was obtained in 54% yield (6.1 mg, 5.4 µmol) as a light yellow solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–10:1 then DCM:THF = 10:1).



Spectral data is reported for the major isomer.

^{31}P NMR (202 MHz, $CDCl_3$): δ = -4.27 (d, J = 19.0 Hz), -13.68 (d, J = 18.7 Hz).

Procedures and Spectral Data for Synthesis of Secondary Alcohols 8.3a-8.3s

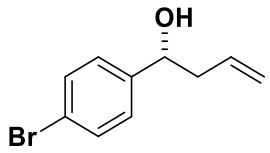


(*S*)-Ir-V made from Allene Gas

General procedure

A pressure tube equipped with a magnetic stir bar was charged with aldehyde (0.2 mmol, 100 mol%) and **(*S*)-Ir-V** (11.2 mg, 0.01 mmol, 5 mol%). The tube was fit with a rubber septum and was evacuated by piercing the septum with a needle connected to a Schlenk line. Immediately after evacuation, an allene-filled balloon equipped with a needle was used to pierce the septum and refill the tube with allene gas. Under the allene balloon, toluene (2.0 mL, 0.1 M) was added followed by 2-propanol (31 µL, 0.4 mmol, 200 mol%). The septum was removed quickly and the tube was sealed with a PTFE lined cap. The tube was placed in an oil bath at the indicated temperature and stirred for the indicated time period. The solution was allowed to reach ambient temperature before being concentrated *in vacuo*. The residue was directly subjected to flash column chromatography.

(*R*)-1-(4-bromophenyl)but-3-en-1-ol (8.3a)



Procedures

The aldehyde (37.0 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 ^{o}C, 24 hr). The title compound was obtained in 90% yield (41.0 mg, 0.18 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–10:1).

TLC (SiO_2) R_f = 0.48 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 5.86 – 5.66 (m, 1H), 5.19 – 5.13 (m, 2H), 4.71 (ddd, *J* = 7.9, 4.8, 2.9 Hz, 1H), 2.54 – 2.41 (m, 2H), 2.06 (t, *J* = 2.8 Hz, 1H).

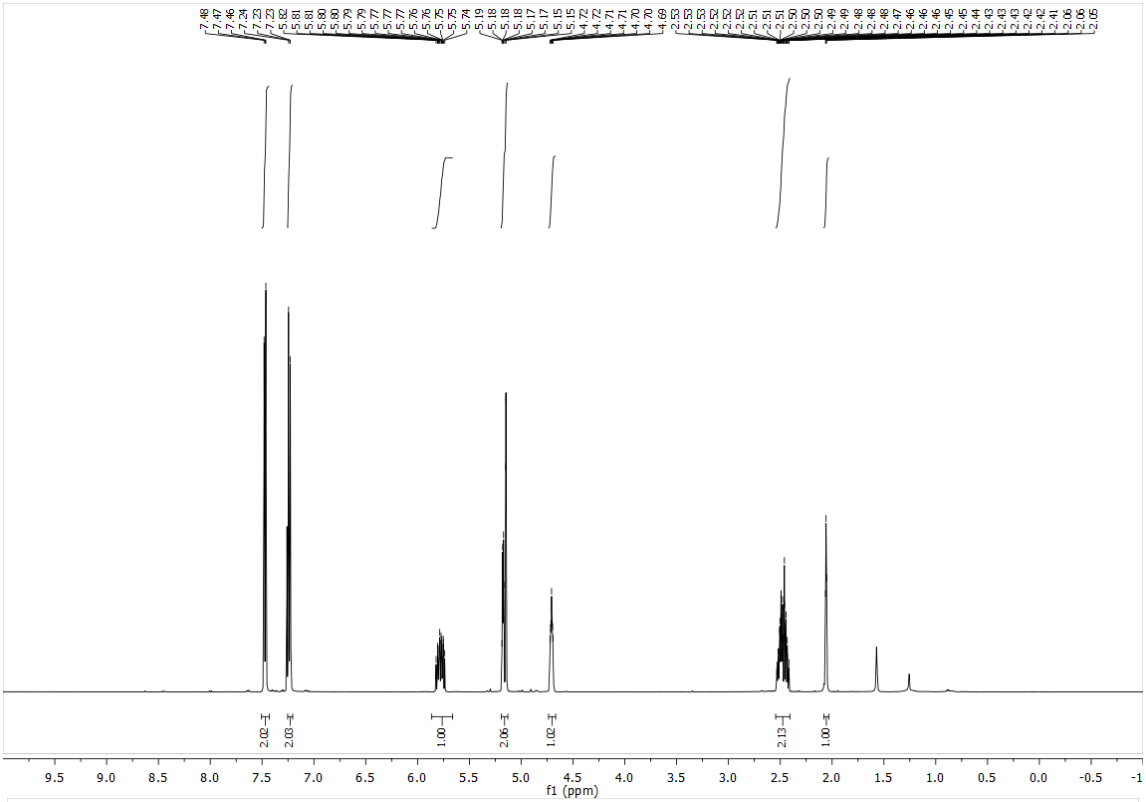
^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.8, 133.9, 131.5, 127.5, 121.2, 118.9, 72.5, 43.8.

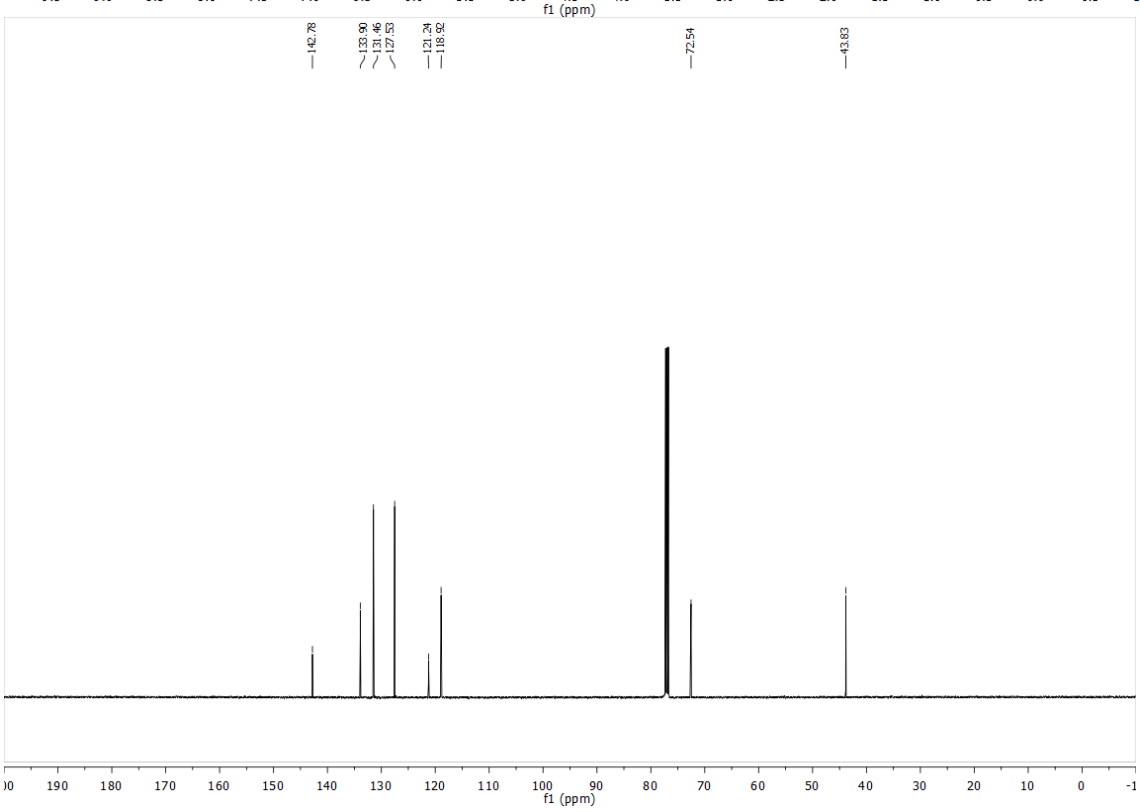
HRMS (EI): Calculated for $C_{10}H_{11}BrO$ [M^+] = 225.9993, Found 225.9990.

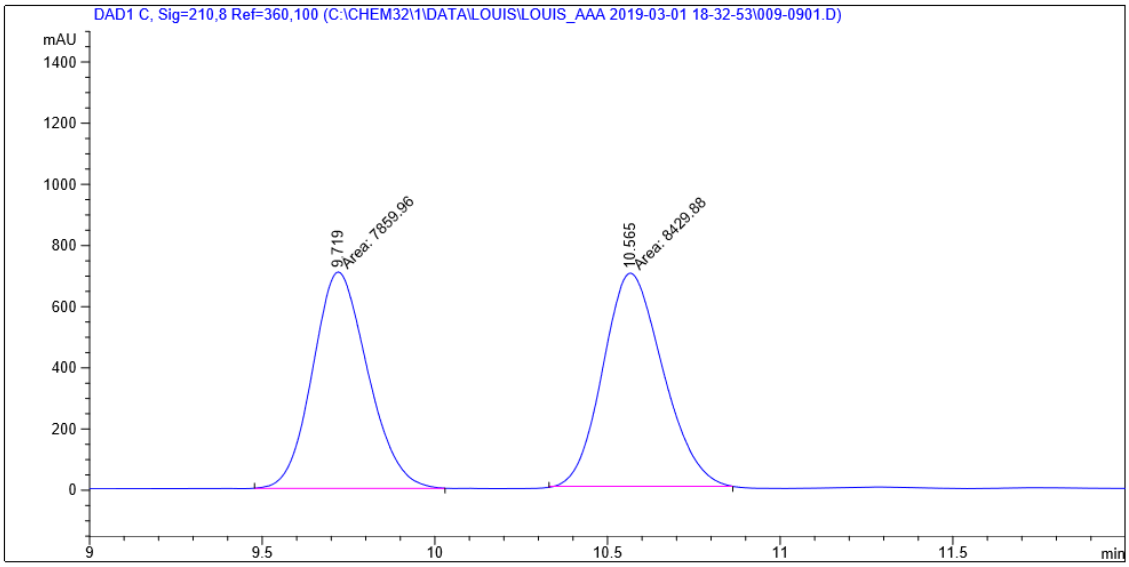
FTIR (neat): 3372, 3079, 2926, 1641, 1592, 1488, 1403, 1069, 1009, 917, 870, 821, 776, 717 cm^{-1}.

$[\alpha]_D^{28}$= +48.0 (*c* 0.25, $CHCl_3$).

HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 210 nm), *ee* = 92%.


f1 (ppm)


142.78
133.90
131.46
127.53
121.24
118.92
72.54
43.83
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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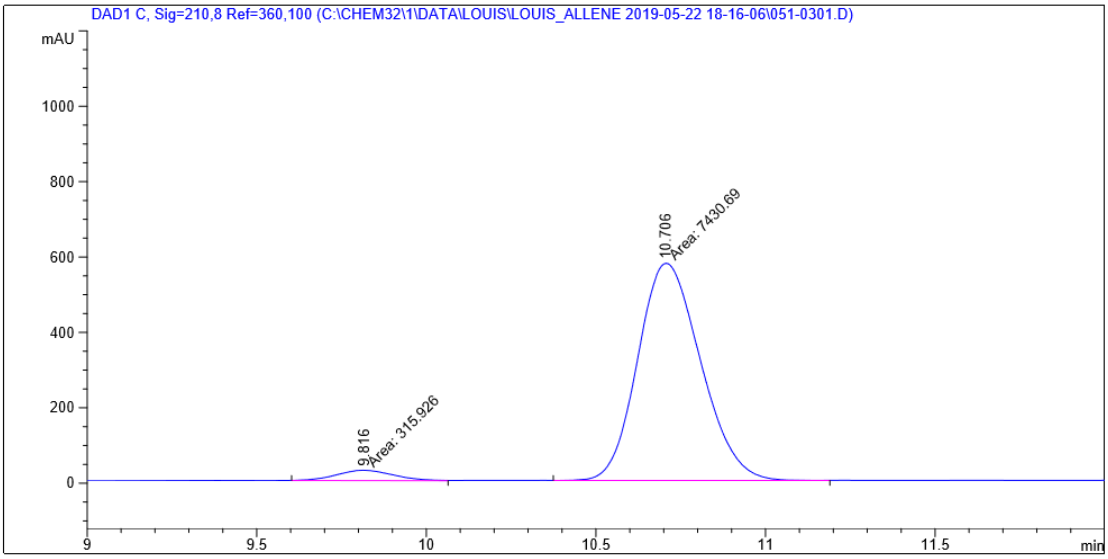
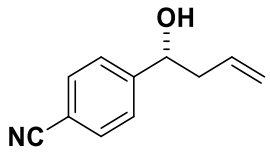
2	10.565	MM	0.2014	8429.87695	697.63104	51.7493



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.816	MM	0.1920	315.92621	27.42419	4.0782
2	10.706	MM	0.2148	7430.69141	576.47485	95.9218

(*R*)-1-(4-cyanophenyl)but-3-en-1-ol (8.3b)



Procedures

The aldehyde (26.2 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 °C, 24 hr). The title compound was obtained in 82% yield (28.4 mg, 0.16 mmol) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.28 (hexanes: ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 8.3 Hz, 2H), 5.87 – 5.65 (m, 1H), 5.29 – 5.05 (m, 2H), 4.80 (dd, *J* = 8.0, 4.7 Hz, 1H), 2.57 – 2.49 (m, 1H), 2.43 (dt, *J* = 14.7, 7.9 Hz, 1H), 2.10 (s, 1H).

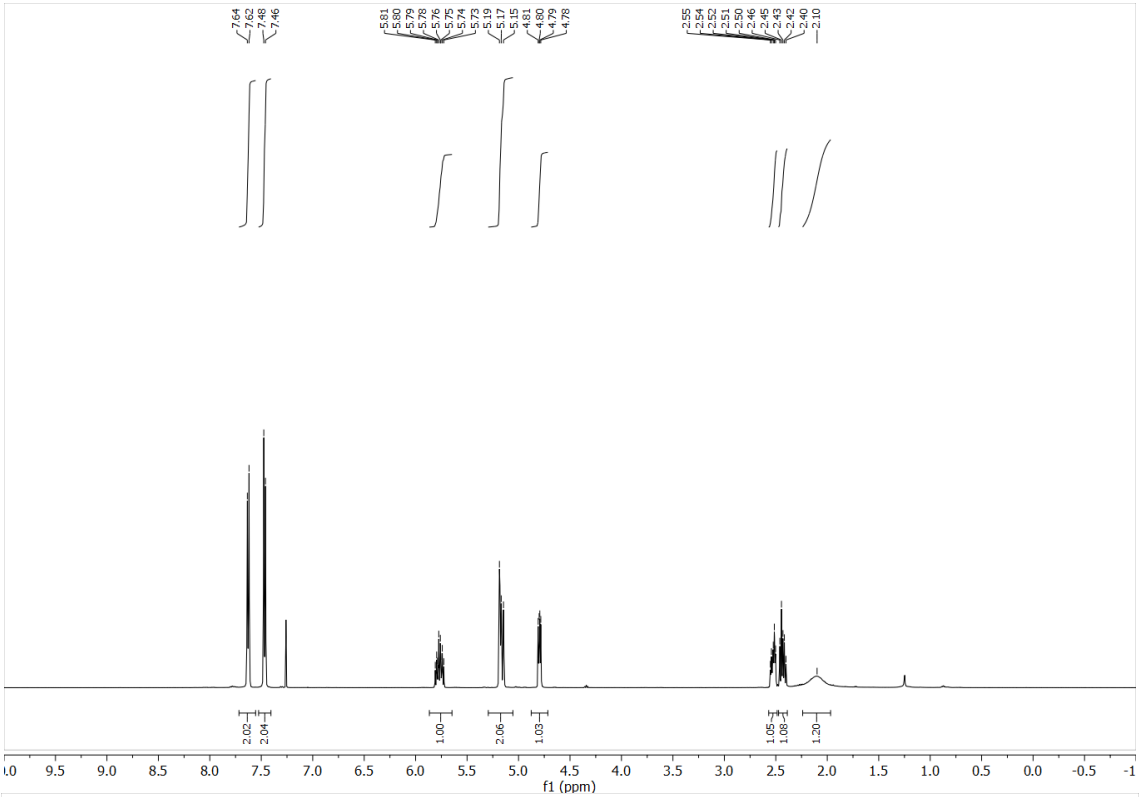
^{13}C NMR (125 MHz, $CDCl_3$): δ = 149.2, 133.4, 132.2, 126.5, 119.5, 118.9, 111.2, 72.4, 43.9.

HRMS (ESI): Calculated for $C_{11}H_{11}NO$ [M+Na^+] = 196.0733, Found 196.0738.

FTIR (neat): 3405, 3077, 2979, 2922, 2228, 1641, 1609, 1604, 1412, 1198, 1055, 990, 919, 838 cm^{-1}.

$[\alpha]_D^{28}$= +46.2 (*c* 0.1, $CHCl_3$).

HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 230 nm), *ee* = 88%.


7.64
7.62
7.48
7.46
5.81
5.80
5.79
5.78
5.76
5.75
5.74
5.73
5.19
5.17
5.15
4.81
4.80
4.79
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2.50
2.46
2.45
2.43
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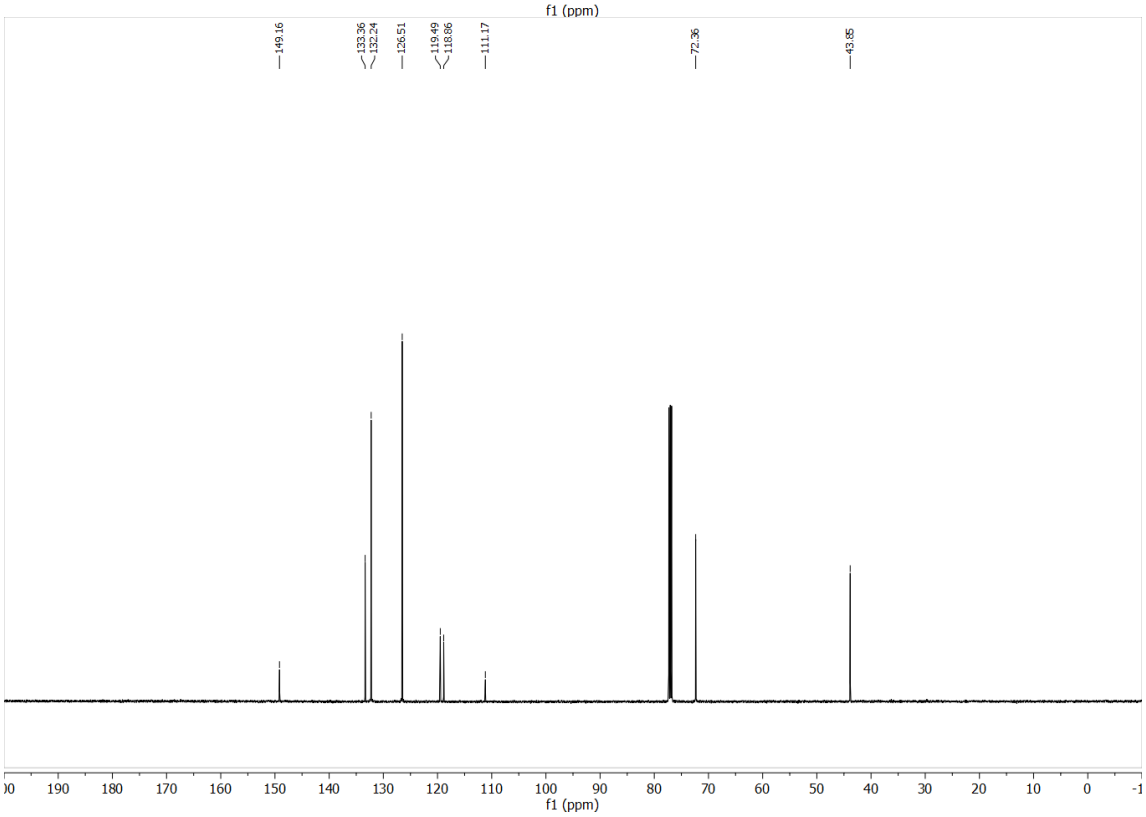
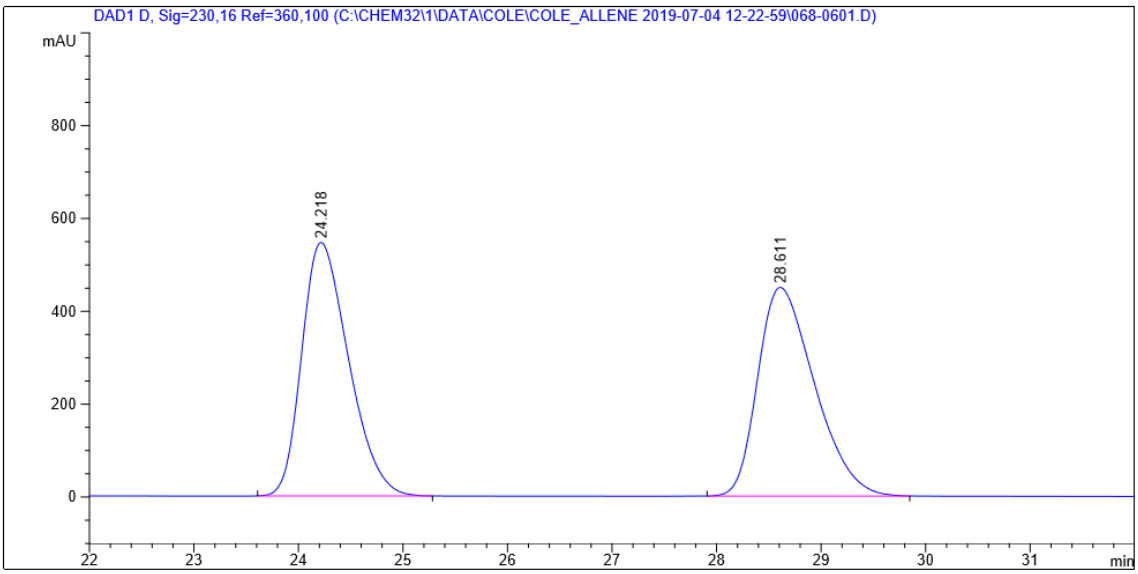
1.03
1.05
1.08
1.20
f1 (ppm)


149.16
133.36
132.24
126.51
119.49
118.86
111.17
72.36
43.85
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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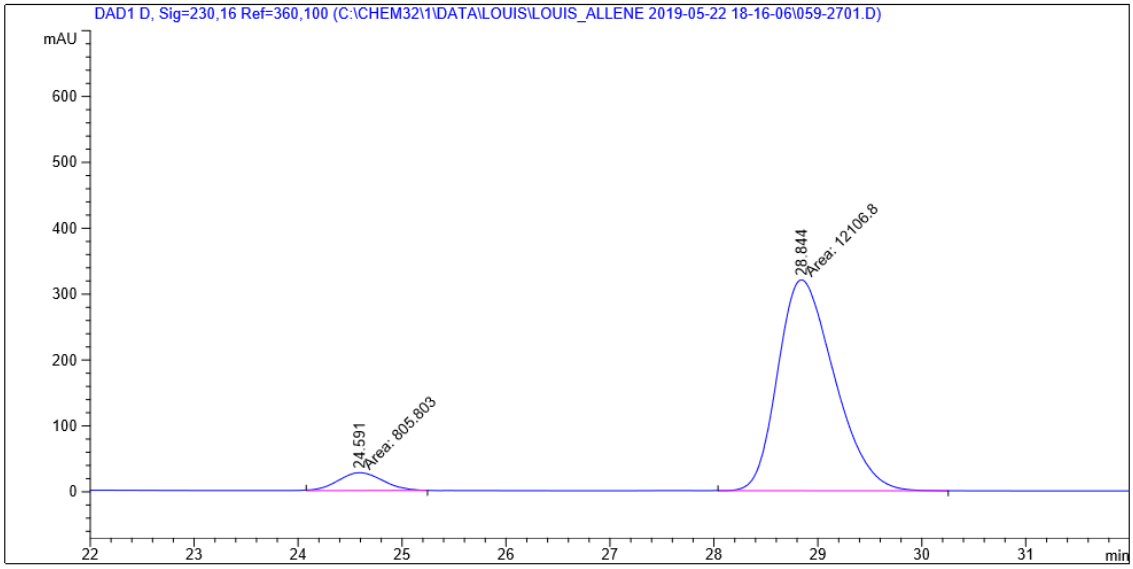
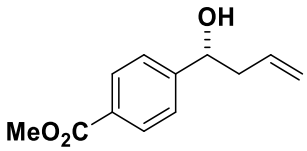
2	28.611	BB	0.5776	1.69470e4	449.78271	49.9266



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.591	MM	0.4932	805.80255	27.22857	6.2404
2	28.844	MM	0.6305	1.21068e4	320.04633	93.7596

methyl (*R*)-4-(1-hydroxybut-3-en-1-yl)benzoate (8.3c)



Procedures

The aldehyde (32.8 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 °C, 24 hr). The title compound was obtained in 88% yield (36.3 mg, 0.18 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–10:1).

TLC (SiO_2) R_f = 0.27 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07 – 7.95 (m, 2H), 7.43 (d, *J* = 8.3 Hz, 2H), 5.79 (dddd, *J* = 17.9, 9.8, 7.7, 6.5 Hz, 1H), 5.24 – 5.10 (m, 2H), 4.81 (dd, *J* = 8.0, 4.8 Hz, 1H), 3.91 (s, 3H), 2.59 – 2.51 (m, 1H), 2.51 – 2.42 (m, 1H), 2.22 – 2.09 (m, 1H).

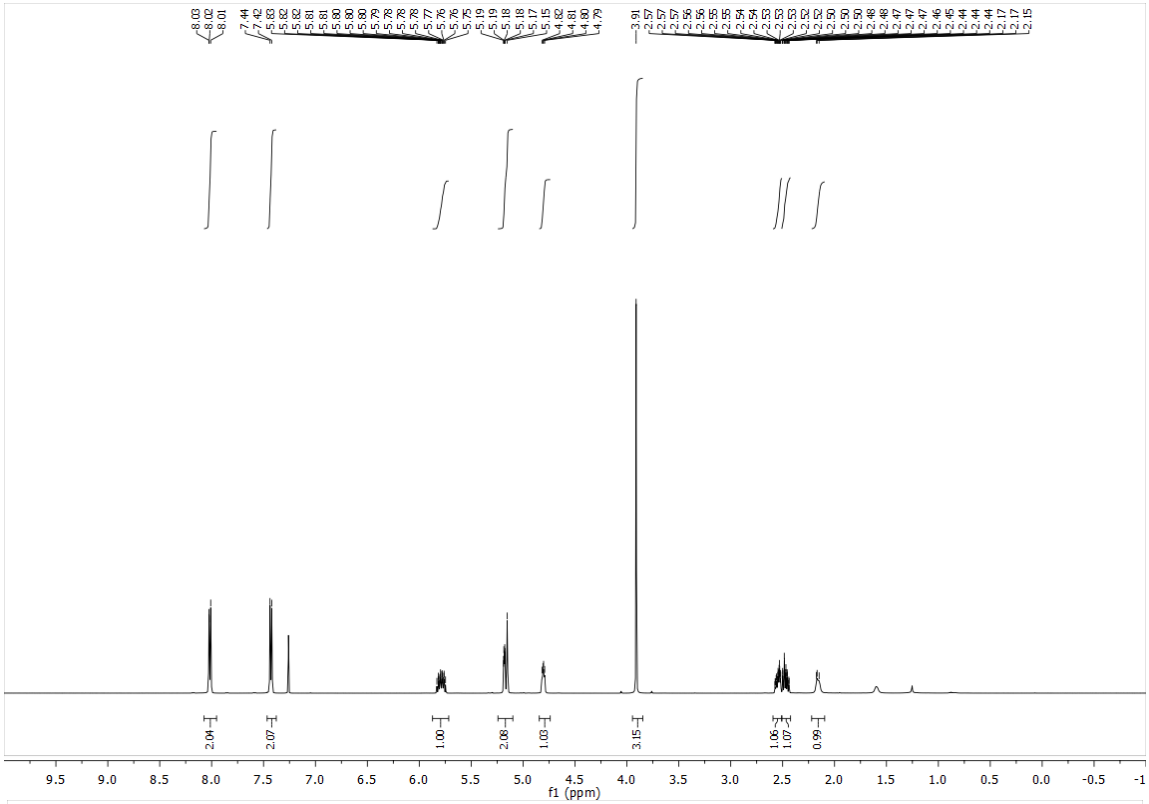
^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.9, 148.9, 133.8, 129.7, 129.3, 125.7, 119.1, 72.7, 52.1, 43.8.

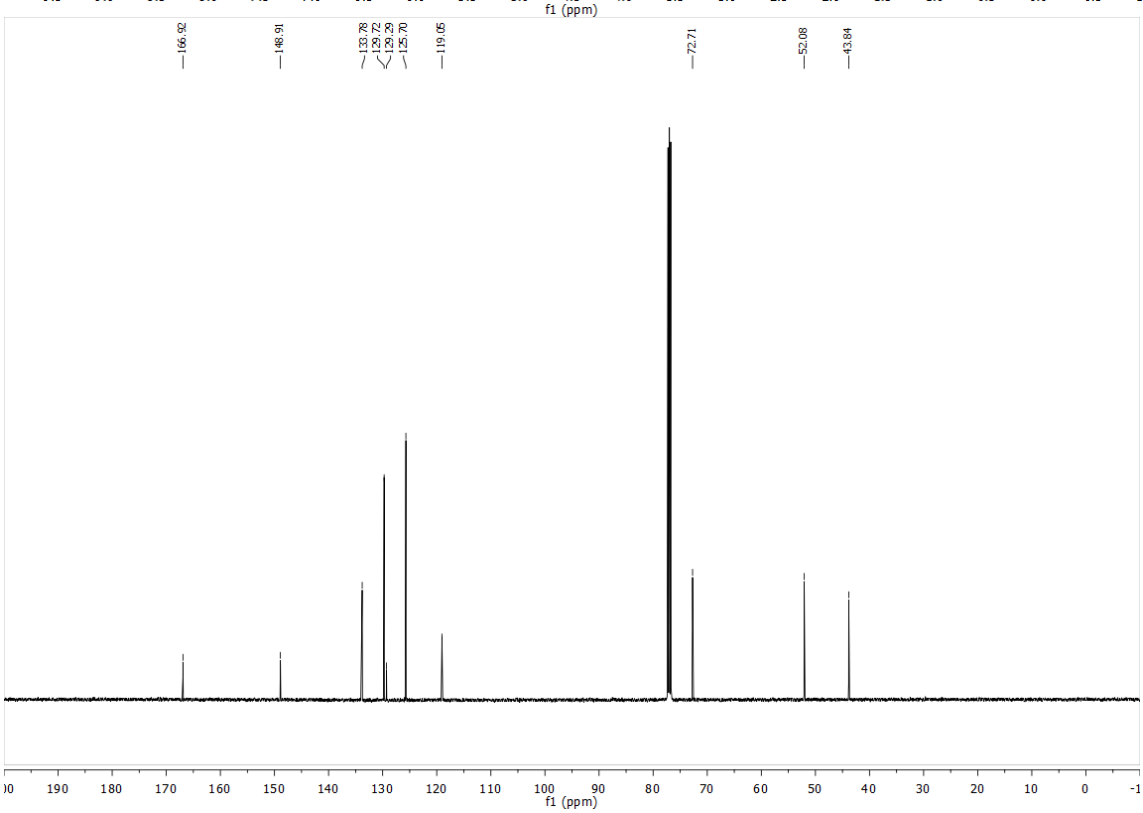
HRMS (ESI): Calculated for $C_{12}H_{14}O_3$ [M+Na^+] = 229.0835, Found 229.0844.

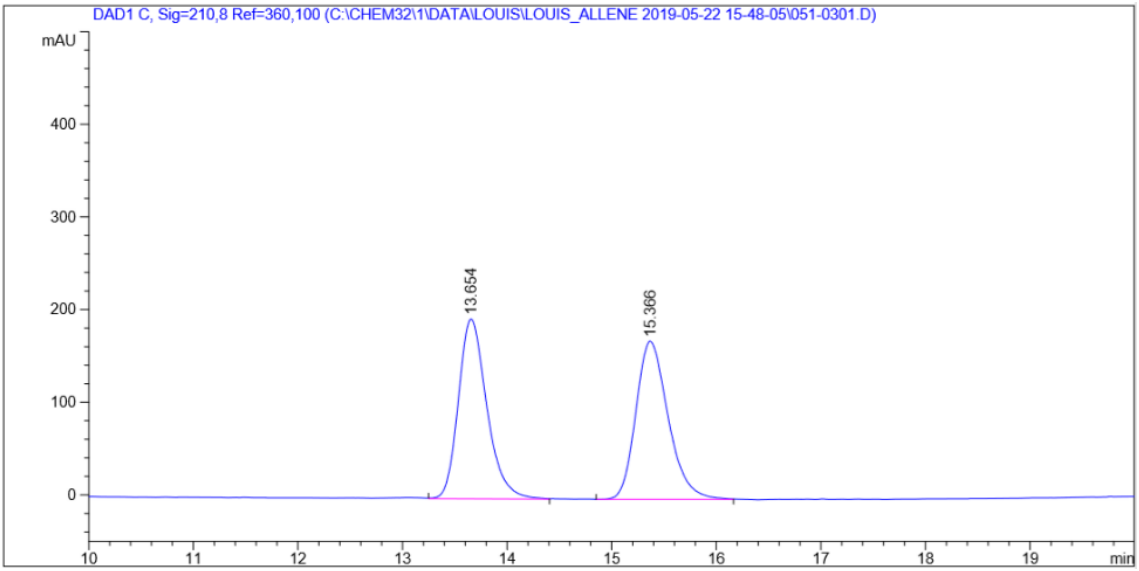
FTIR (neat): 3436, 2952, 1720, 1611, 1436, 1276, 1192, 1111, 1054, 1018, 917, 957, 768, 707 cm^{-1}.

$[\alpha]_D^{28}$ = +45.0 (*c* 0.3, $CHCl_3$).

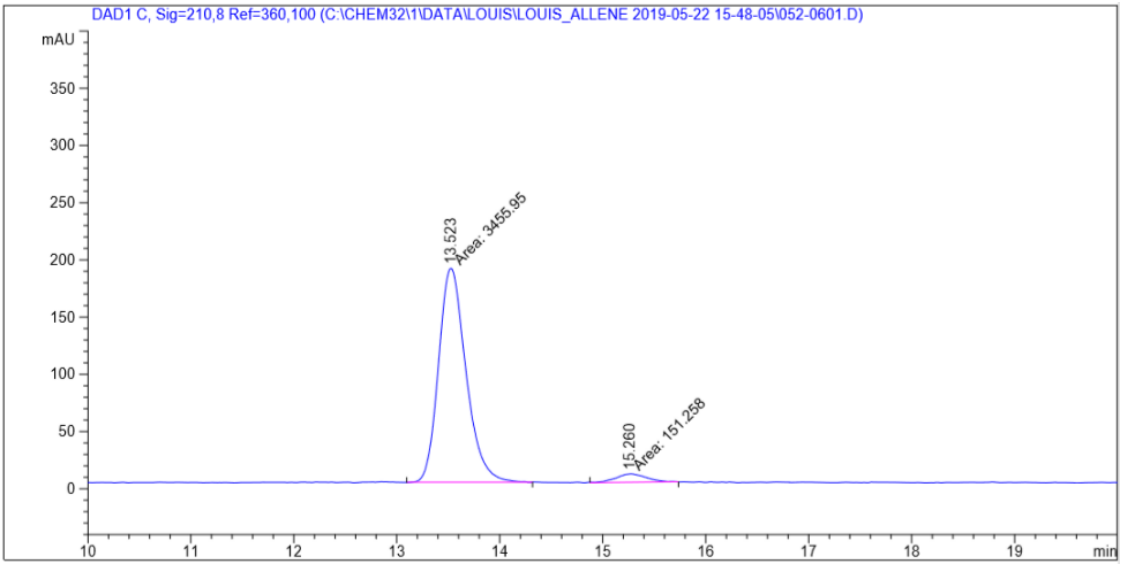
HPLC (Chiralcel AD-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 210 nm), *ee* = 92%.


8.03
8.02
8.01
7.44
7.42
5.83
5.82
5.82
5.81
5.81
5.80
5.80
5.79
5.78
5.78
5.77
5.76
5.76
5.75
5.19
5.19
5.18
5.17
5.15
4.62
4.61
4.60
4.59
3.91
2.57
2.57
2.57
2.56
2.56
2.55
2.55
2.54
2.54
2.53
2.53
2.53
2.52
2.52
2.50
2.50
2.50
2.48
2.47
2.47
2.47
2.46
2.45
2.44
2.44
2.44
2.17
2.17
2.15
2.04
2.07
1.00
2.08
1.03
3.15
1.06
1.07
0.99
f1 (ppm)


166.92
148.91
133.78
129.72
129.29
125.70
119.05
72.71
52.08
43.84
f1 (ppm)

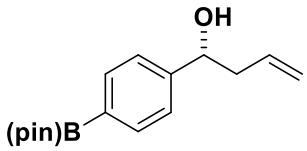


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.654	VV	0.2906	3670.88062	194.11264	50.0716
2	15.366	VB	0.3261	3660.38940	170.78111	49.9284



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.523	MM	0.3078	3455.95239	187.10356	95.8068
2	15.260	MM	0.3346	151.25789	7.53326	4.1932

(*R*)-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)but-3-en-1-ol (8.3d)



Procedures

The aldehyde (46.4 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 ^{o}C, 48 hr). The title compound was obtained in 85% yield (46.6 mg, 0.17 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–5:1).

TLC (SiO_2) R_f = 0.28 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.85 – 7.76 (m, 2H), 7.41 – 7.31 (m, 2H), 5.79 (ddt, *J* = 17.1, 10.0, 7.1 Hz, 1H), 5.21 – 5.09 (m, 2H), 4.76 (ddd, *J* = 8.0, 5.0, 3.2 Hz, 1H), 2.60 – 2.41 (m, 2H), 2.06 (d, *J* = 3.3 Hz, 1H), 1.34 (s, 12H).

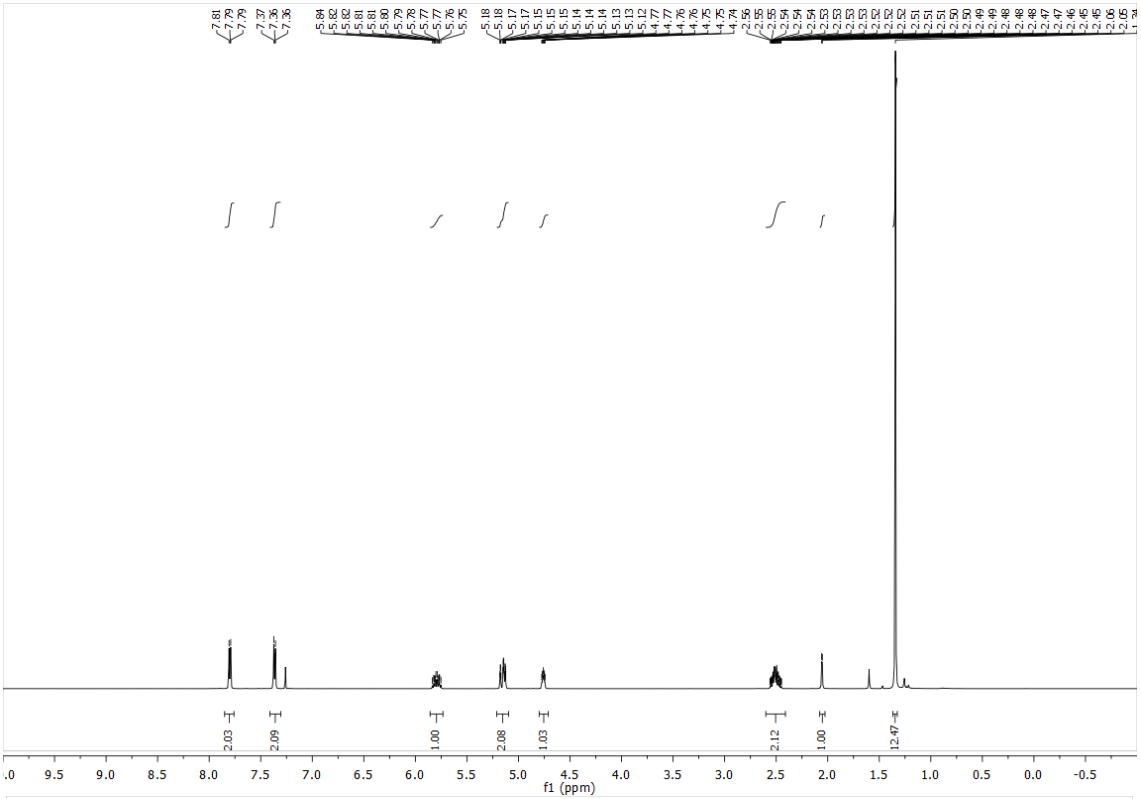
^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.0, 134.9, 134.3, 125.1, 118.5, 83.8, 73.2, 43.8, 24.9.

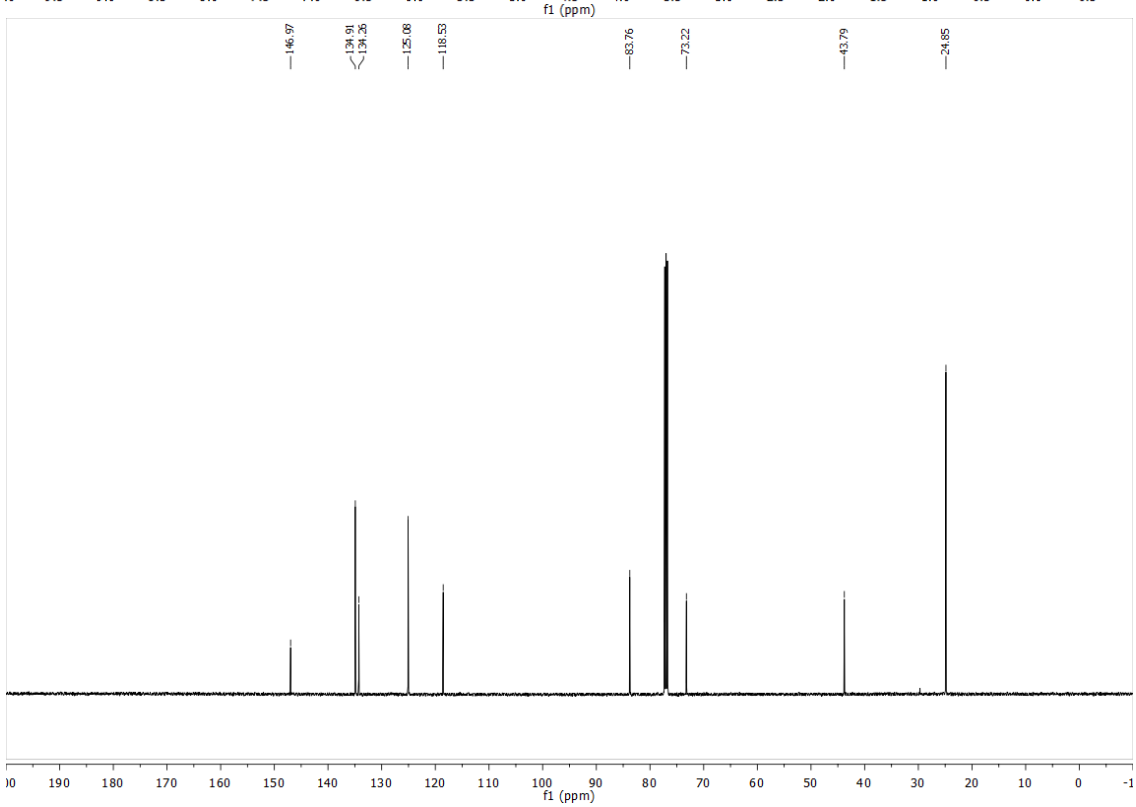
HRMS (ESI): Calculated for $C_{16}H_{23}BO_3$ [M+Na^+] = 297.1625, Found 297.1643.

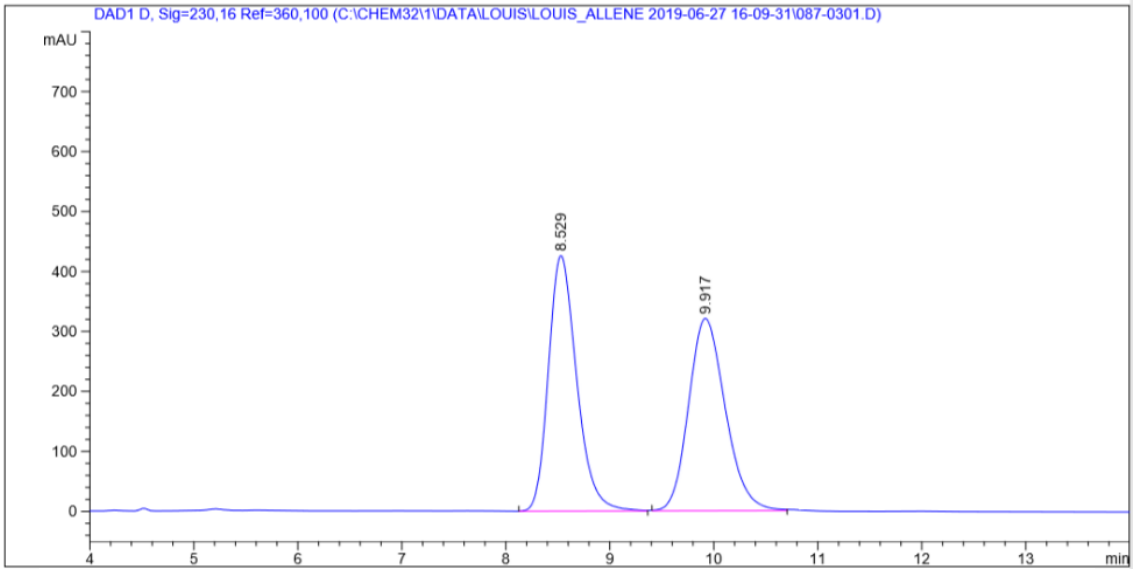
FTIR (neat): 3318, 2980, 2921, 1613, 1359, 1324, 1142, 1090, 1017, 859, 843, 660 cm^{-1}.

$[\alpha]_D^{28}$= +22.5 (*c* 0.4, $CHCl_3$).

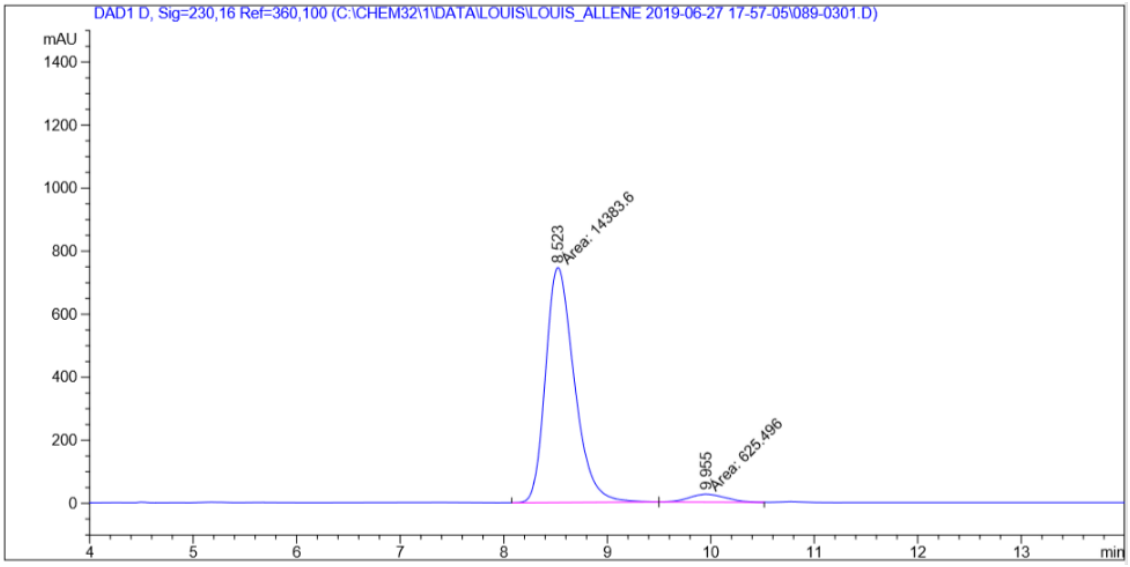
HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 230 nm), *ee* = 92%.


f1 (ppm)


f1 (ppm)

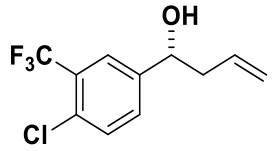


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.529	BB	0.2902	8041.44531	426.08014	50.5841
2	9.917	BB	0.3818	7855.74854	320.64441	49.4159



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.523	MM	0.3214	1.43836e4	745.98456	95.8325
2	9.955	MM	0.4108	625.49646	25.37432	4.1675

(*R*)-1-(4-chloro-3-(trifluoromethyl)phenyl)but-3-en-1-ol (8.3e)



Procedures

The aldehyde (28.8 μL, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 °C, 24 hr). The title compound was obtained in 74% yield (37.1 mg, 0.15 mmol) as a pale yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.38 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.69 (s, 1H), 7.47 (d, *J* = 2.6 Hz, 2H), 5.86 – 5.68 (m, 1H), 5.24 – 5.13 (m, 2H), 4.77 (dd, *J* = 8.2, 4.6 Hz, 1H), 2.59 – 2.35 (m, 2H), 2.10 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.9, 133.3, 131.4, 131.1, 130.2, 125.0 (q, *J* = 4.0 Hz), 124.0, 121.8, 119.6, 71.9, 43.9.

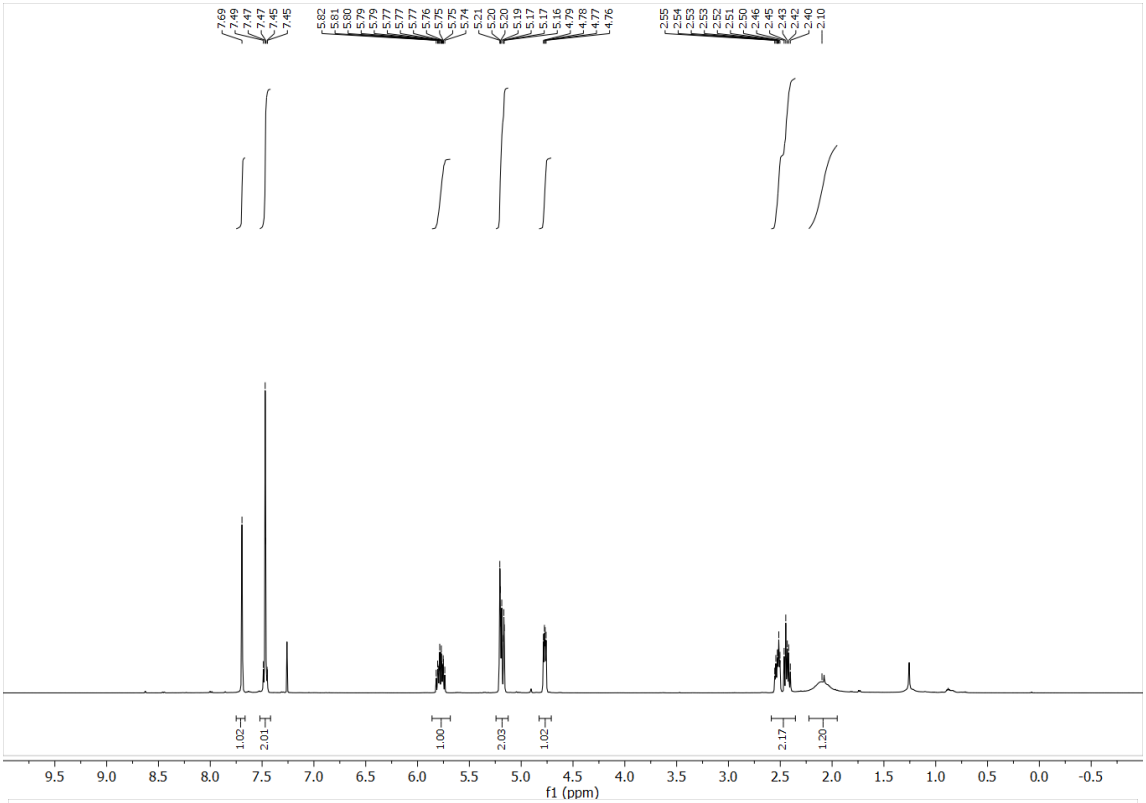
^{19}F NMR (471 MHz, $CDCl_3$): δ = -62.6

HRMS (EI): Calculated for $C_{11}H_{10}ClF_3O$ [M^+] = 250.0372, Found 250.0368.

FTIR (neat): 3392, 2928, 1481, 1422, 1316, 1261, 1171, 1130, 1111, 1034, 921, 832, 664 cm^{-1}.

$[\alpha]_D^{28}$= +46.0 (*c* 0.2, $CHCl_3$).

HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 280 nm), *ee* = 90%.


7.69
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7.47
7.47
7.46
7.45
5.82
5.81
5.80
5.79
5.79
5.77
5.77
5.77
5.76
5.75
5.75
5.74
5.21
5.20
5.20
5.19
5.17
5.17
5.16
4.79
4.78
4.77
4.76
2.55
2.54
2.53
2.53
2.52
2.51
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2.46
2.45
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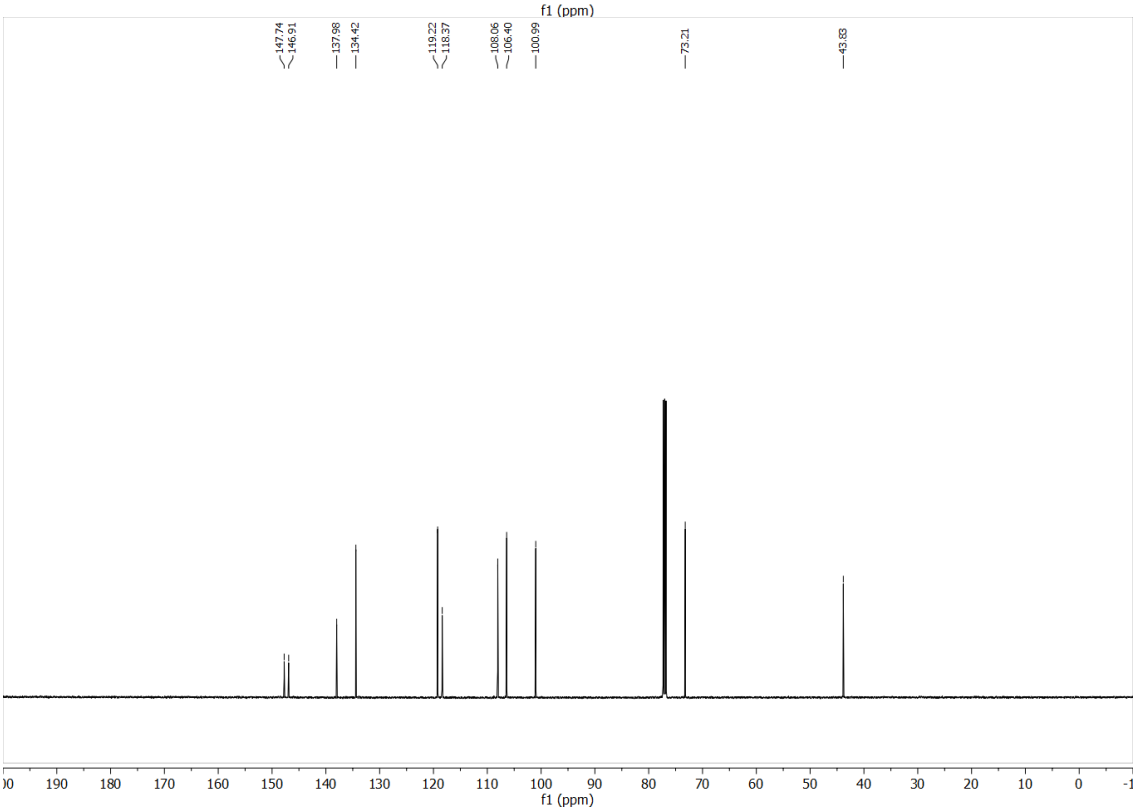
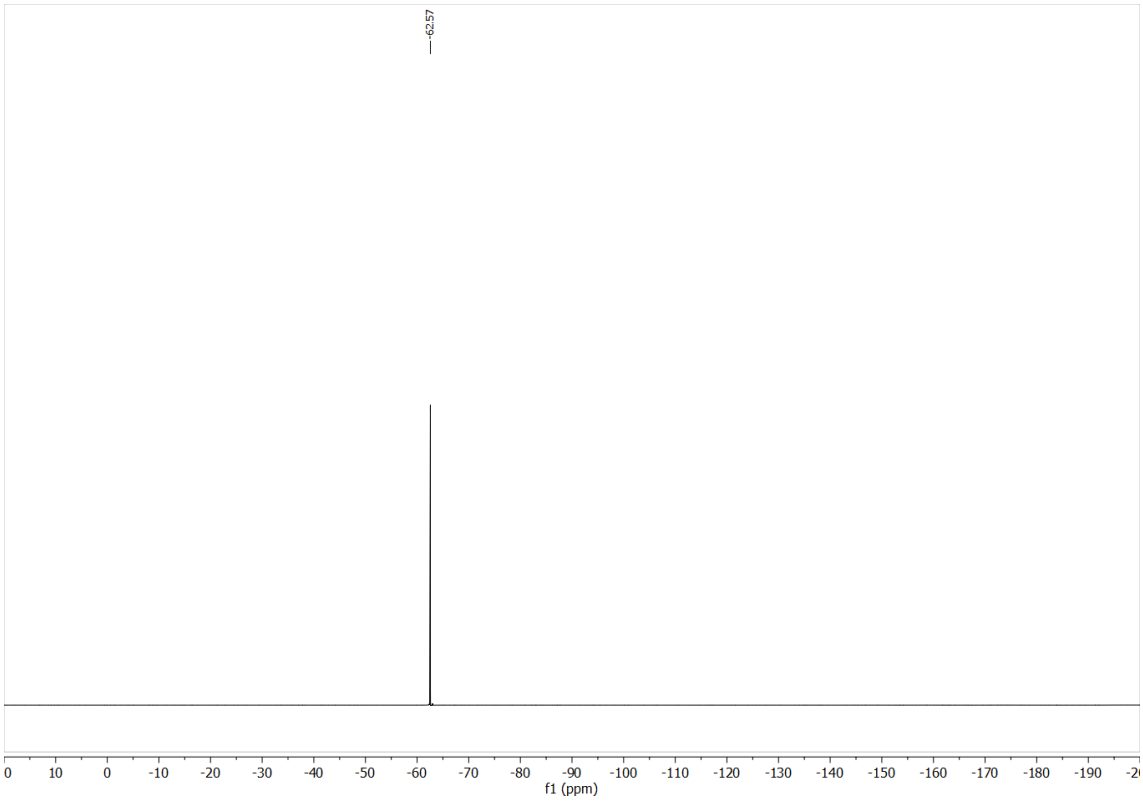
2.03
1.02
2.17
1.20
f1 (ppm)


147.74
146.91
137.98
134.42
119.22
118.37
108.06
106.40
100.99
73.21
43.83
f1 (ppm)


-62.57
0
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
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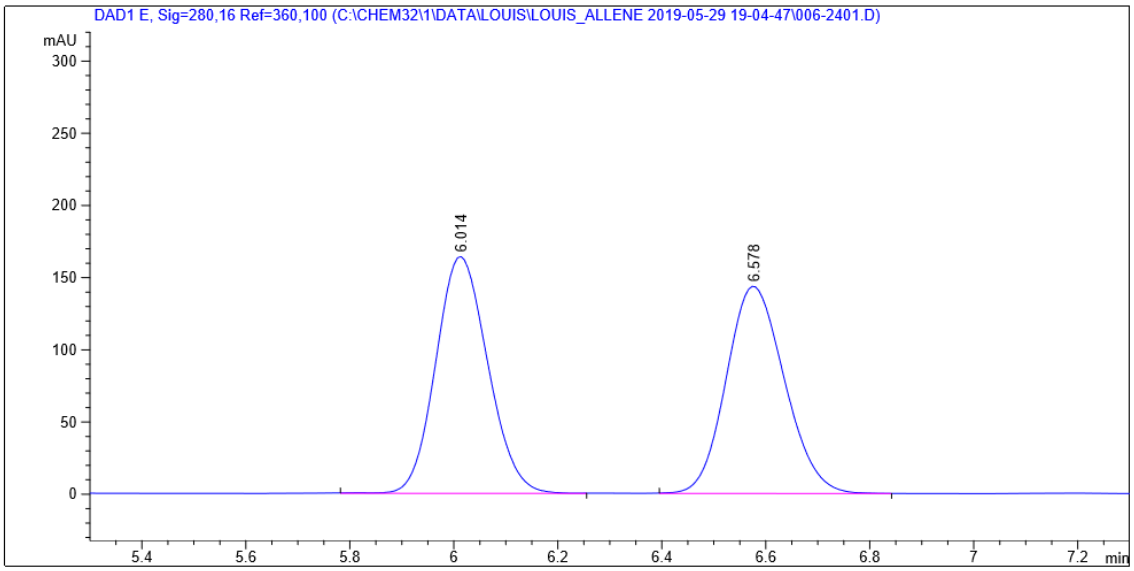
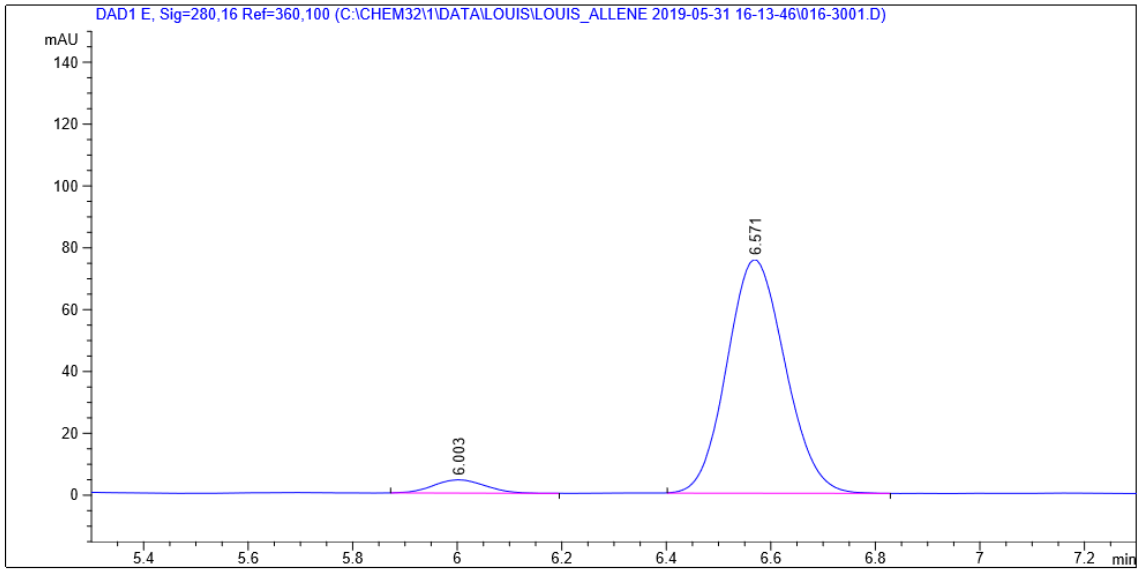
-150
-160
-170
-180
-190
f1 (ppm)

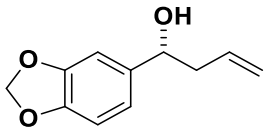


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.014	BB	0.1071	1141.28967	164.21017	50.5467
2	6.578	BB	0.1227	1116.60242	143.62392	49.4533



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.003	BB	0.1078	29.51828	4.31811	4.7997
2	6.571	BB	0.1223	585.48035	75.61100	95.2003

(*R*)-1-(benzo[d][1,3]dioxol-5-yl)but-3-en-1-ol (8.3f)



Procedures

The aldehyde (30.0 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 ^{o}C, 24 hr). The title compound was obtained in 84% yield (32.7 mg, 0.17 mmol) as a brown oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.38 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.87 (s, 1H), 6.78 (q, *J* = 8.0 Hz, 2H), 5.94 (d, *J* = 1.3 Hz, 2H), 5.78 (ddt, *J* = 14.2, 10.1, 7.2 Hz, 1H), 5.24 – 5.02 (m, 2H), 4.64 (t, *J* = 6.4 Hz, 1H), 2.47 (t, *J* = 6.6 Hz, 2H), 2.04 (s, 1H).

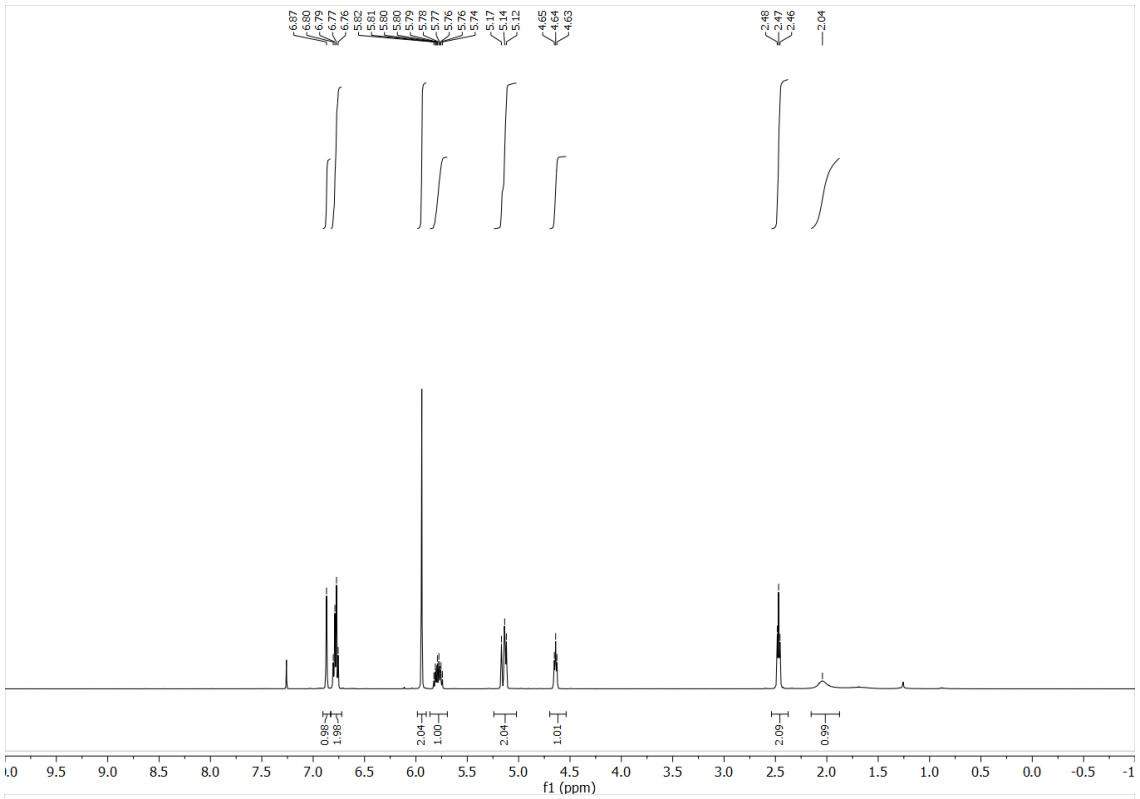
^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.7, 146.9, 138.0, 134.4, 119.2, 118.4, 108.1, 106.4, 101.0, 73.2, 43.8.

HRMS (EI): Calculated for $C_{11}H_{12}O_3$ [M^+] = 192.0786, Found 192.0791.

FTIR (neat): 3391, 2899, 1640, 1503, 1486, 1441, 1239, 1093, 1036, 919, 865, 810 cm^{-1}.

$[\alpha]_D^{28}$= +42.4 (*c* 0.2, $CHCl_3$).

HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 254 nm), *ee* = 94%.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6.79
6.77
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5.82
5.81
5.80
5.80
5.79
5.78
5.77
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5.76
5.74
5.17
5.14
5.12
4.65
4.64
4.63
2.48
2.47
2.46
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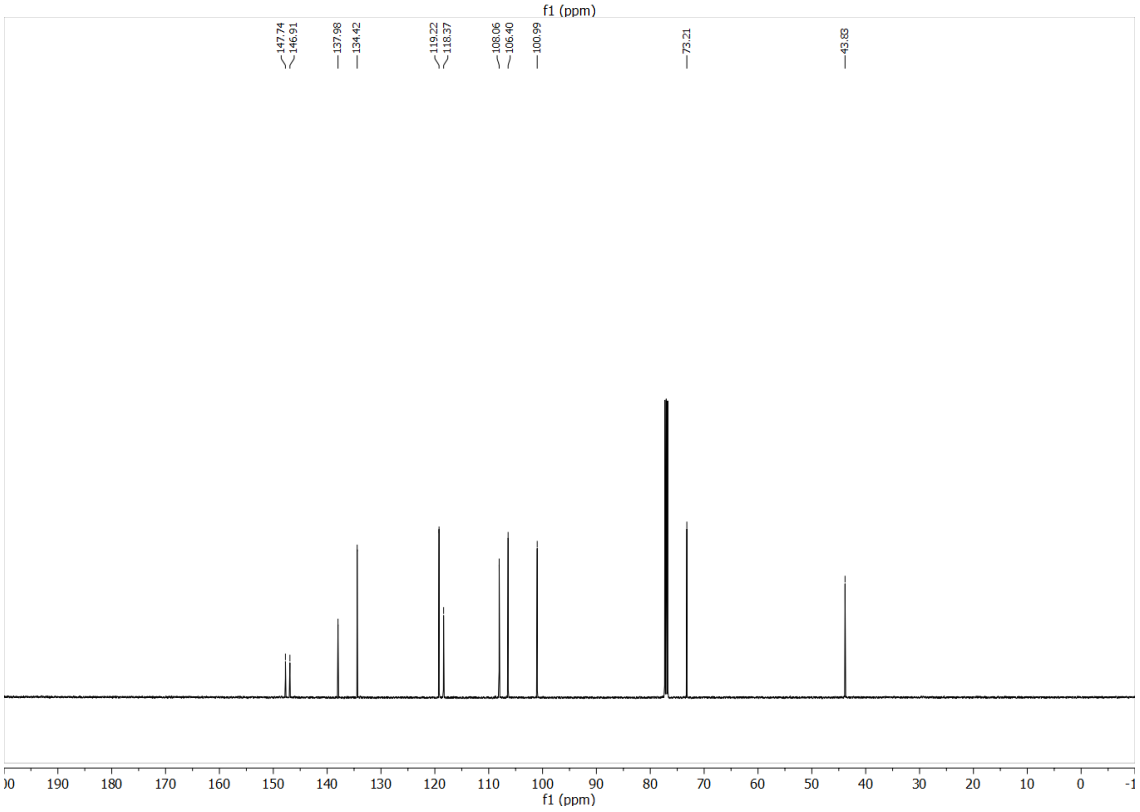
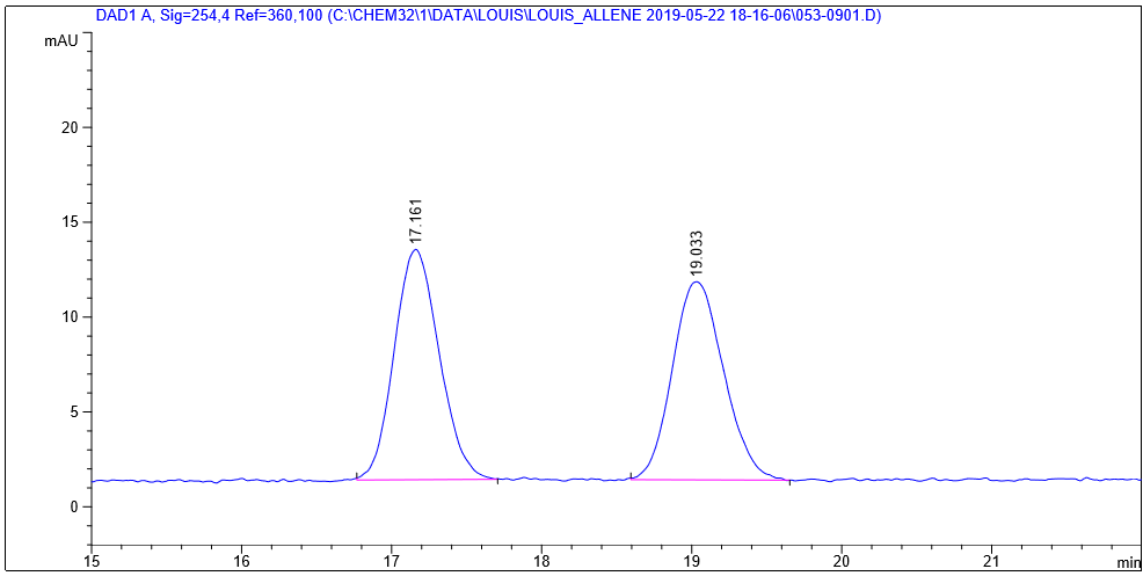
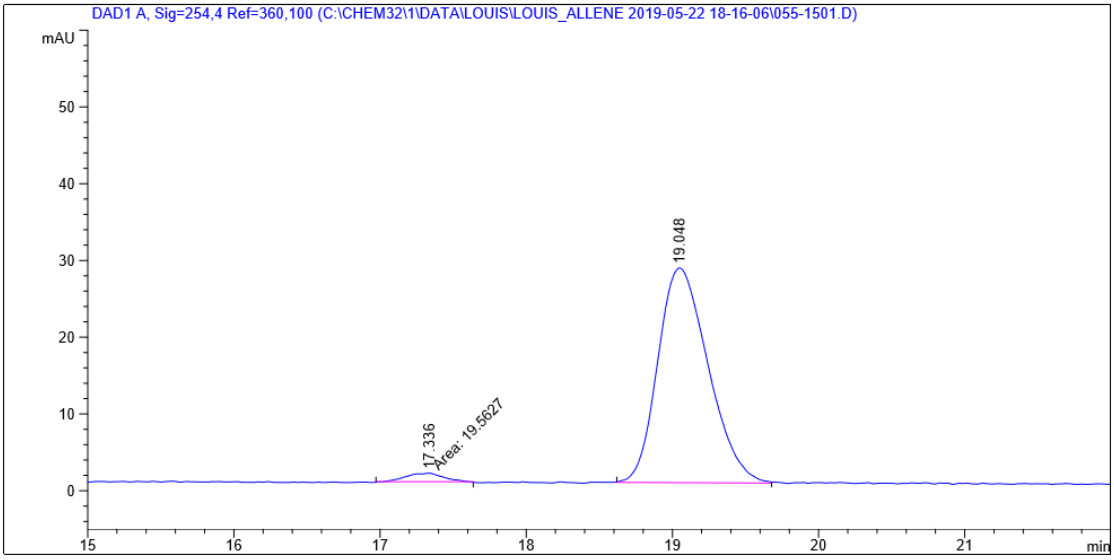
0.98
1.98
2.04
1.00
2.04
1.01
2.09
0.99
f1 (ppm)


147.74
146.91
137.98
134.42
119.22
118.37
108.06
106.40
100.99
73.21
43.83
f1 (ppm)

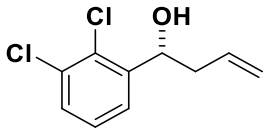


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.161	BB	0.3193	253.09970	12.13810	50.4439
2	19.033	BB	0.3619	248.64478	10.43984	49.5561



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.336	MM	0.2932	19.56268	1.11217	2.8453
2	19.048	BB	0.3666	667.98956	27.97305	97.1547

(*R*)-1-(2,3-dichlorophenyl)but-3-en-1-ol (8.3g)



Procedures

The aldehyde (35.0 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 ^{o}C, 24 hr). The title compound was obtained in 82% yield (35.7 mg, 0.16 mmol) as a pale brown solid after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.45 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.39 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.24 (t, *J* = 7.8 Hz, 1H), 5.86 (dddd, *J* = 17.5, 9.6, 7.8, 6.4 Hz, 1H), 5.23 – 5.20 (m, 1H), 5.20 – 5.15 (m, 2H), 2.71 – 2.55 (m, 1H), 2.42 – 2.26 (m, 1H), 1.95 (s, 1H).

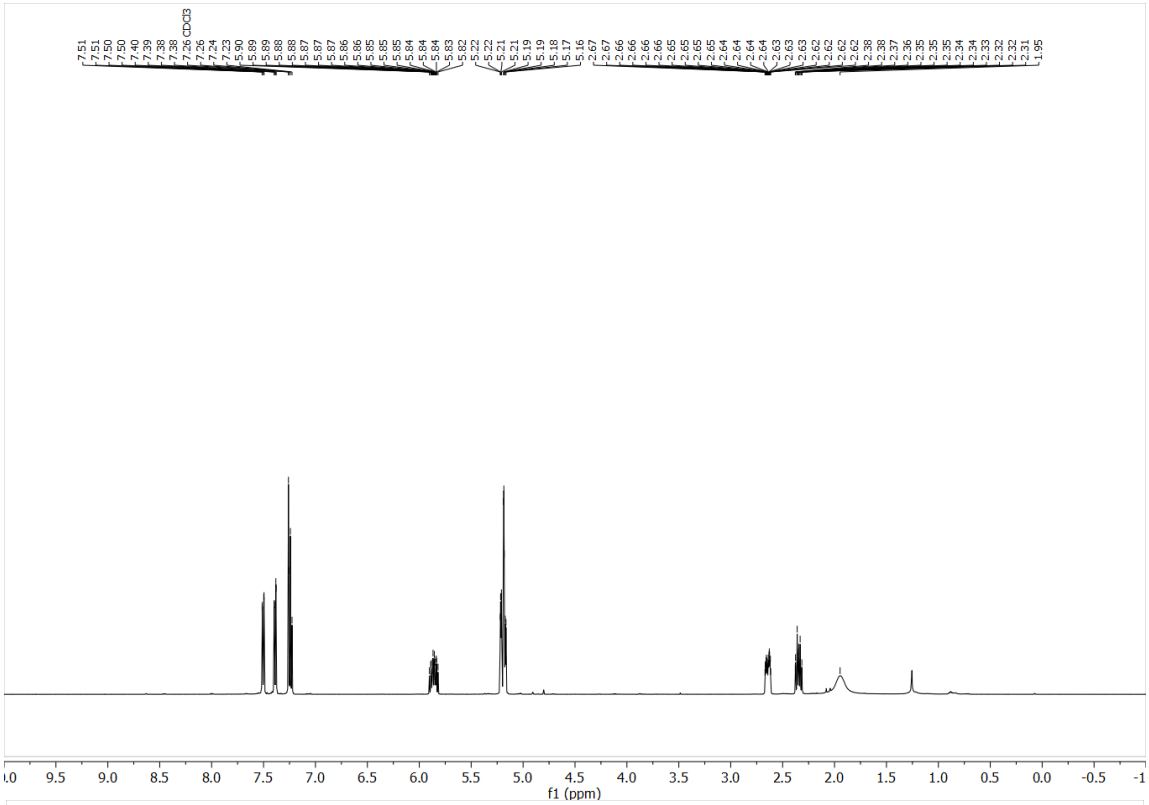
^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.8, 134.0, 133.1, 129.9, 129.3, 127.6, 125.4, 119.3, 70.1, 42.0.

HRMS (EI): Calculated for $C_{10}H_{10}OCl_2$ [M^+] = 216.0109, Found 216.0110.

FTIR (neat): 3288, 3074, 2942, 1640, 1421, 1181, 1103, 918, 779, 718 cm^{-1}.

$[\alpha]_D^{28}$= +92.9 (*c* 0.3, $CHCl_3$).

HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 230 nm), *ee* = 91%.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7.39
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7.38
7.26 CDCl3
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5.86
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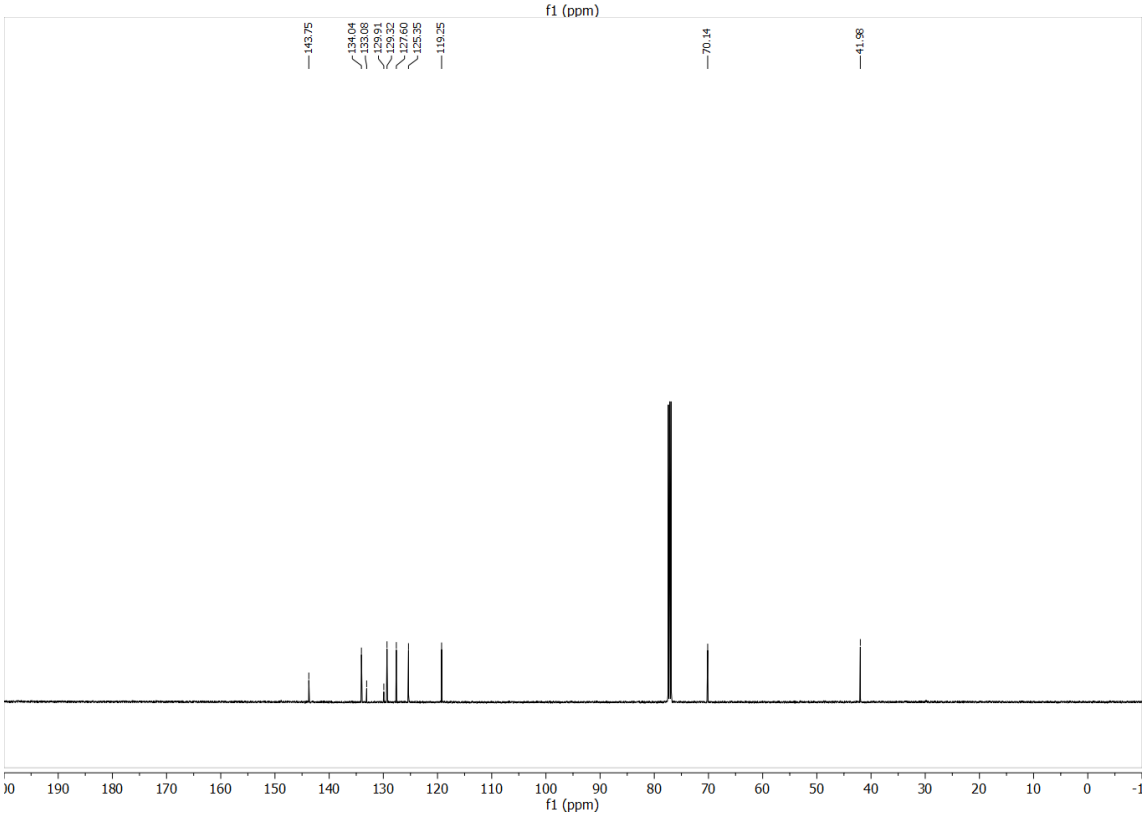
2.32
2.31
1.95
f1 (ppm)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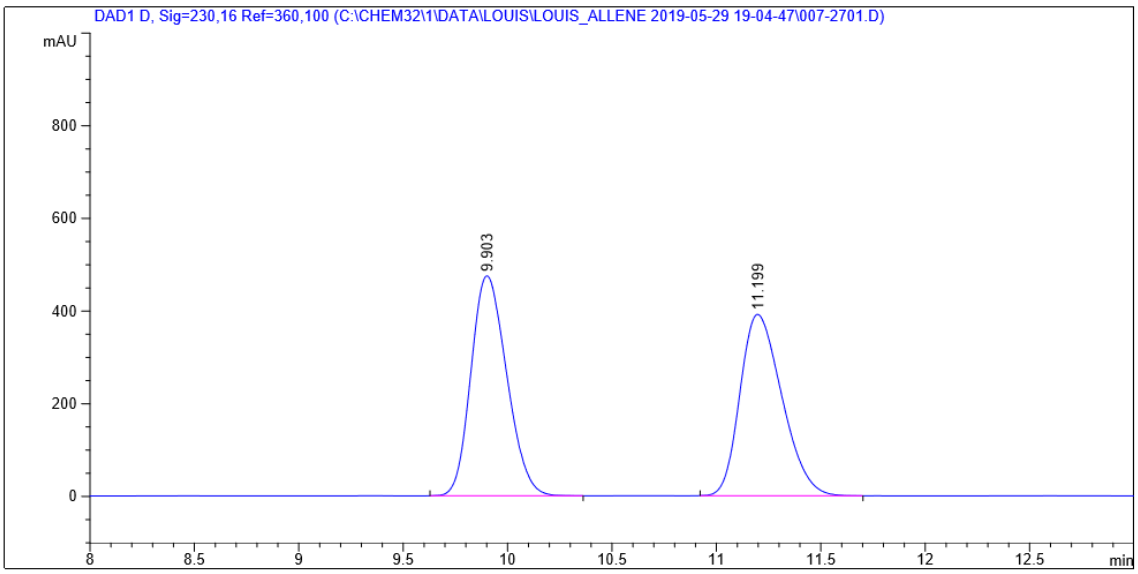
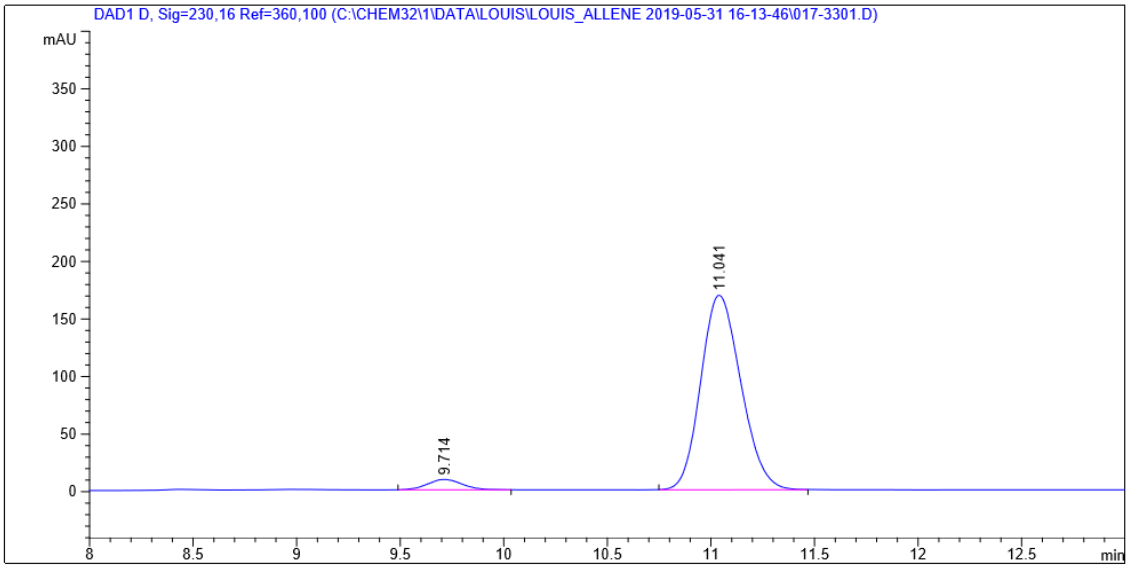
129.32
127.60
125.35
119.25
70.14
41.98
f1 (ppm)

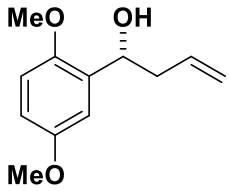


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.903	BB	0.1870	5655.95947	474.80728	50.8670
2	11.199	BB	0.2188	5463.16113	391.51410	49.1330



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.714	BB	0.1777	104.74835	9.00679	4.3921
2	11.041	BB	0.2113	2280.19604	169.12325	95.6079

(*R*)-1-(2,5-dimethoxyphenyl)but-3-en-1-ol (8.3h)



Procedures

The aldehyde (33.2 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 °C, 24 hr). The title compound was obtained in 84% yield (35.0 mg, 0.17 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–4:1).

TLC (SiO_2) R_f = 0.35 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.94 (d, *J* = 3.1 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 1H), 6.76 (dd, *J* = 8.8, 3.0 Hz, 1H), 5.93 – 5.75 (m, 1H), 5.20 – 5.06 (m, 2H), 4.93 (dt, *J* = 8.1, 5.0 Hz, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 2.63 – 2.54 (m, 2H), 2.53 – 2.43 (m, 1H).

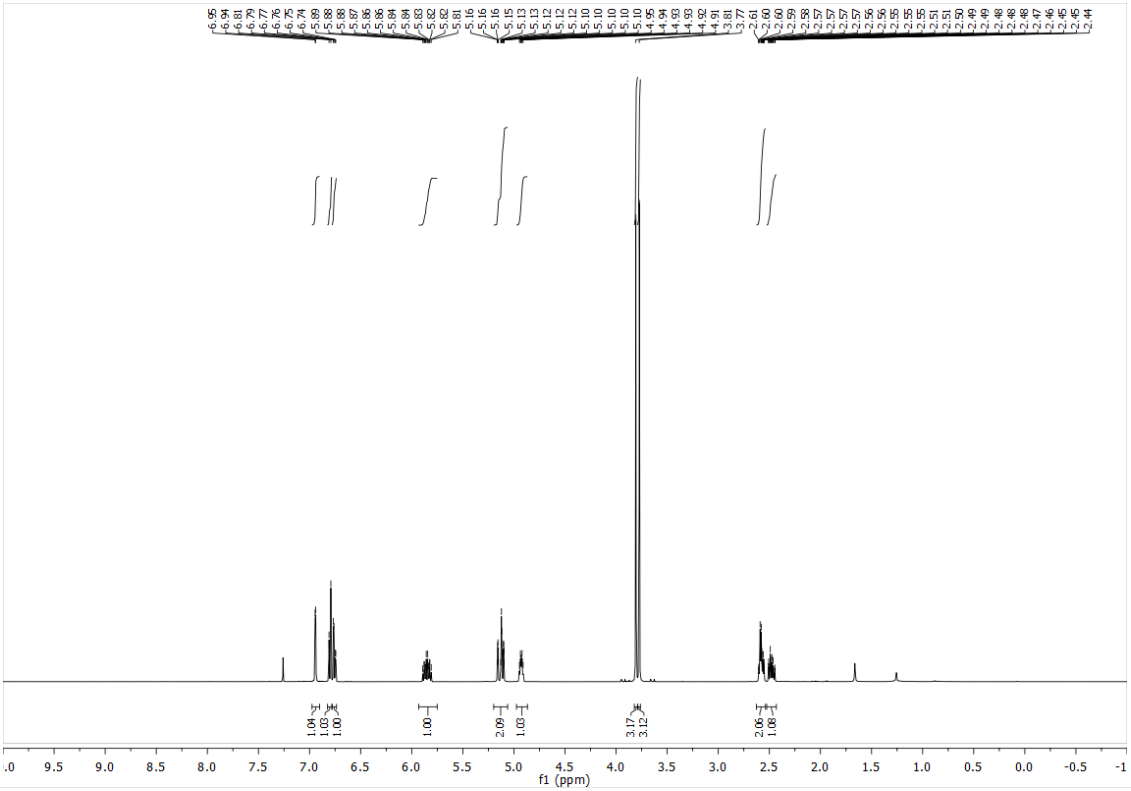
^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.7, 150.5, 135.1, 132.9, 117.7, 112.9, 112.5, 111.4, 69.7, 55.8, 55.7, 41.9.

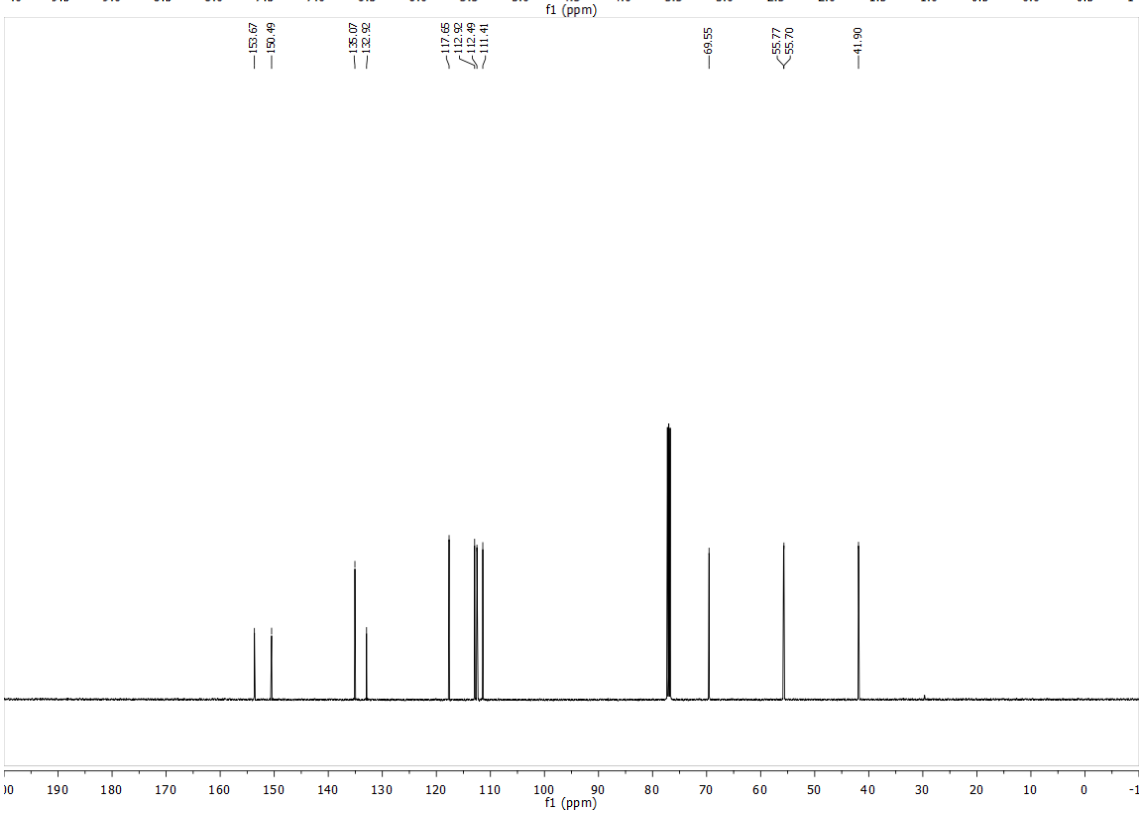
HRMS (ESI): Calculated for $C_{12}H_{13}N$ [M+H$^+$] = 231.0992, Found 231.0991.

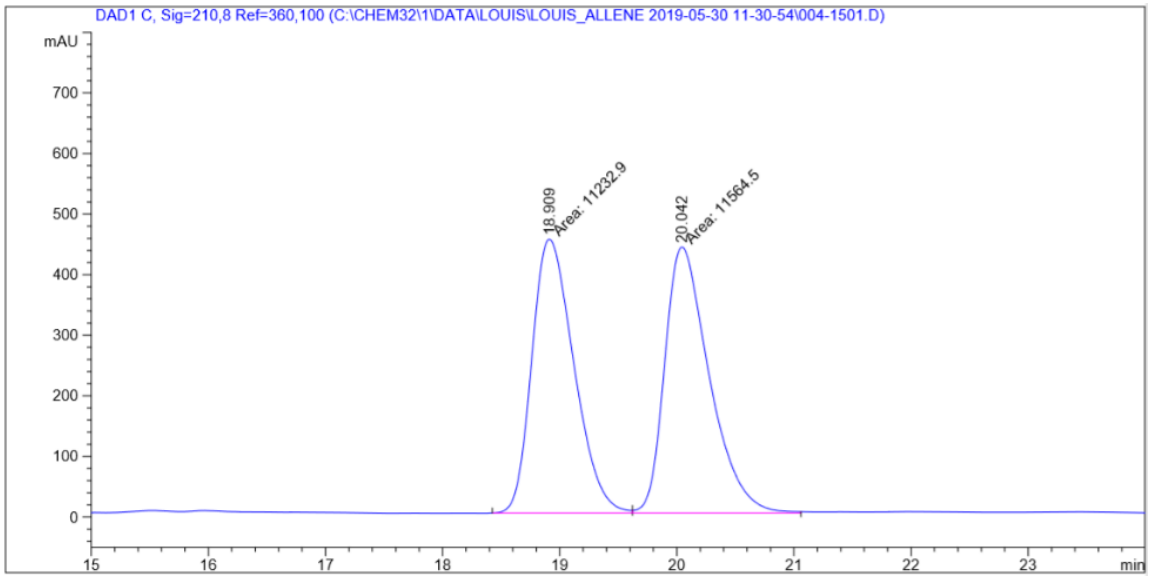
FTIR (neat): 3440, 2941, 2834, 1494, 1464, 1429, 1276, 1213, 1178, 1157, 1043, 914, 803, 708 cm^{-1}.

$[\alpha]_D^{28}$= +36.7 (*c* 0.3, $CHCl_3$).

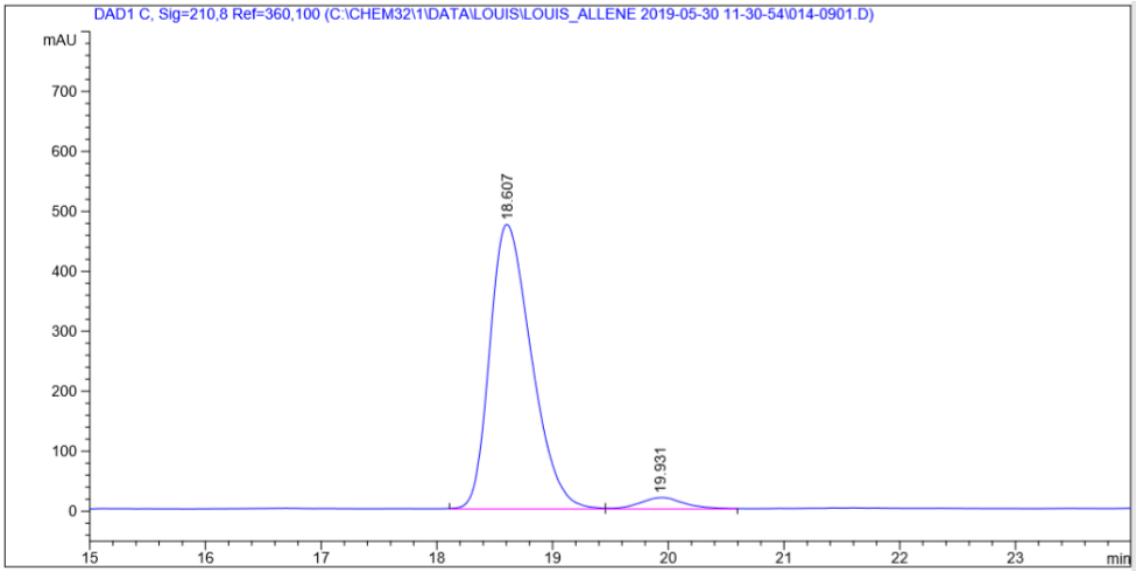
HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm), *ee* = 92%.


f1 (ppm)


f1 (ppm)

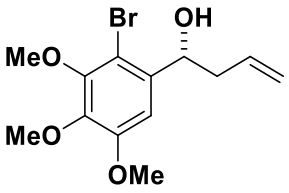


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.909	MF	0.4145	1.12329e4	451.69595	49.2729
2	20.042	FM	0.4393	1.15645e4	438.73416	50.7271



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.607	BV	0.3774	1.18488e4	474.35495	96.0003
2	19.931	VV	0.3166	493.66248	19.03350	3.9997

(*R*)-1-(2-bromo-3,4,5-trimethoxyphenyl)but-3-en-1-ol (8.3i)



Procedures

The aldehyde (55.0 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 °C, 24 hr). The title compound was obtained in 92% yield (58.1 mg, 0.18 mmol) as a pale yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.28 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.97 (s, 1H), 5.99 – 5.82 (m, 1H), 5.28 – 5.14 (m, 2H), 5.09 (dd, *J* = 8.7, 3.4 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.87 (s, 3H), 2.63 (dt, *J* = 13.9, 4.6 Hz, 1H), 2.30 (dt, *J* = 15.2, 8.3 Hz, 1H), 1.99 (s, 1H).

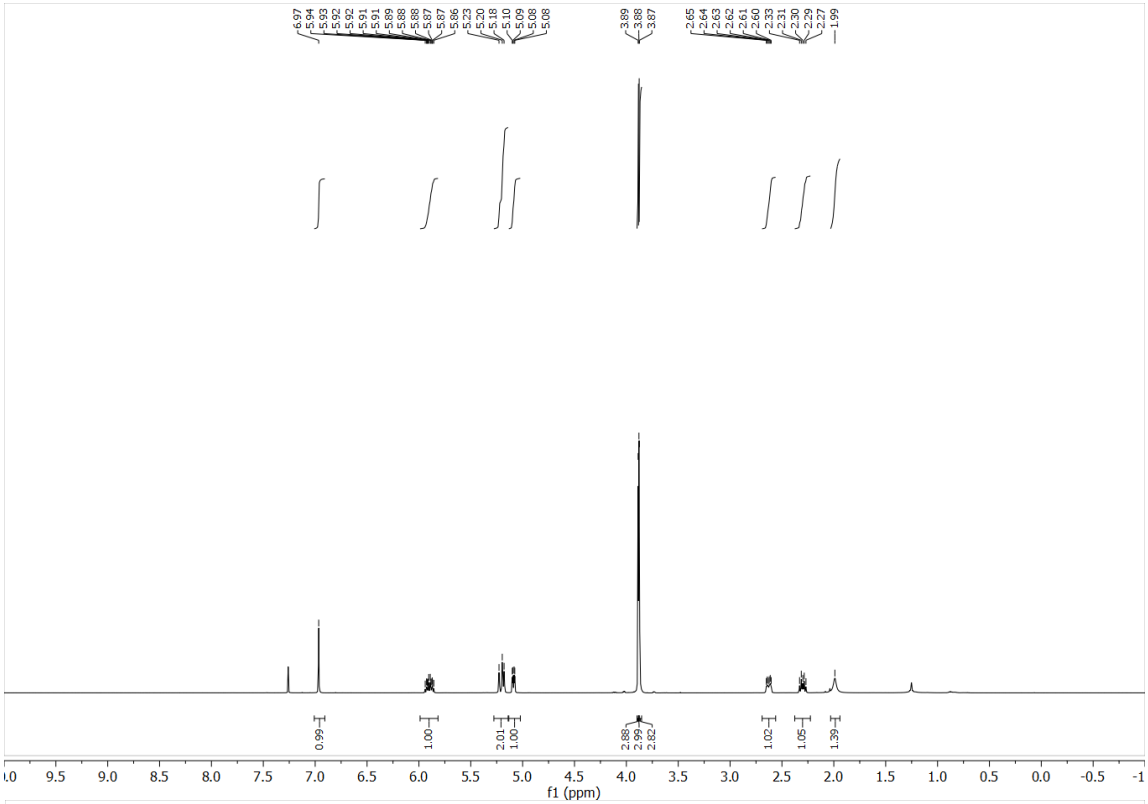
^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.1, 150.6, 142.3, 138.6, 134.6, 118.8, 108.0, 105.9, 72.0, 61.2, 61.2, 56.3, 42.3.

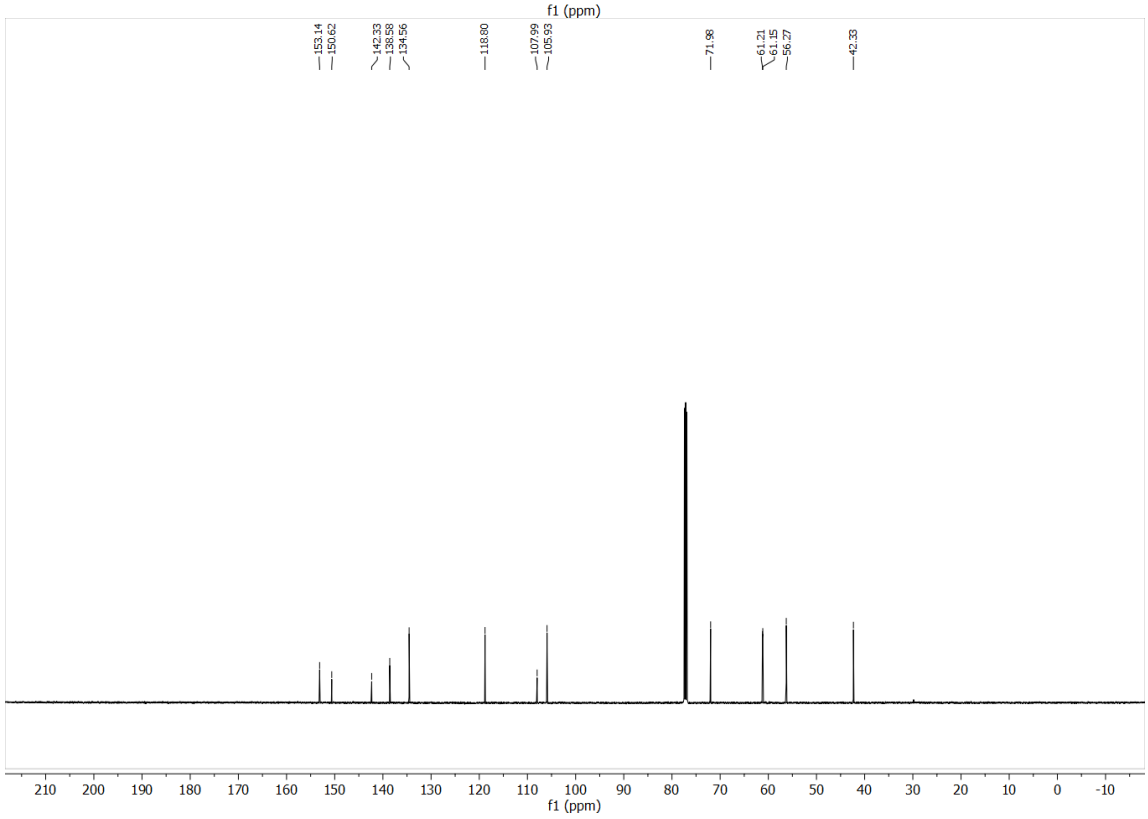
HRMS (ESI): Calculated for $C_{13}H_{17}BrO_4$ [M+Na^+] = 339.0202, Found 339.0206.

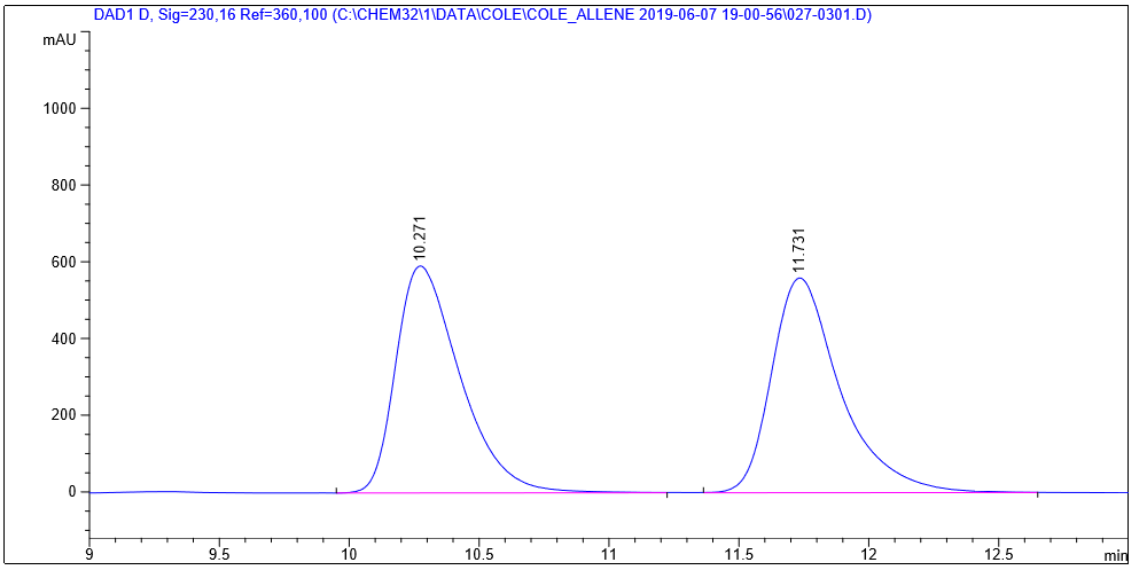
FTIR (neat): 3471, 2937, 1569, 1480, 1393, 1323, 1195, 1161, 1103, 1038, 1006, 919, 851, 816 cm^{-1}.

$[\alpha]_D^{28}$= +56.8 (*c* 0.4, $CHCl_3$).

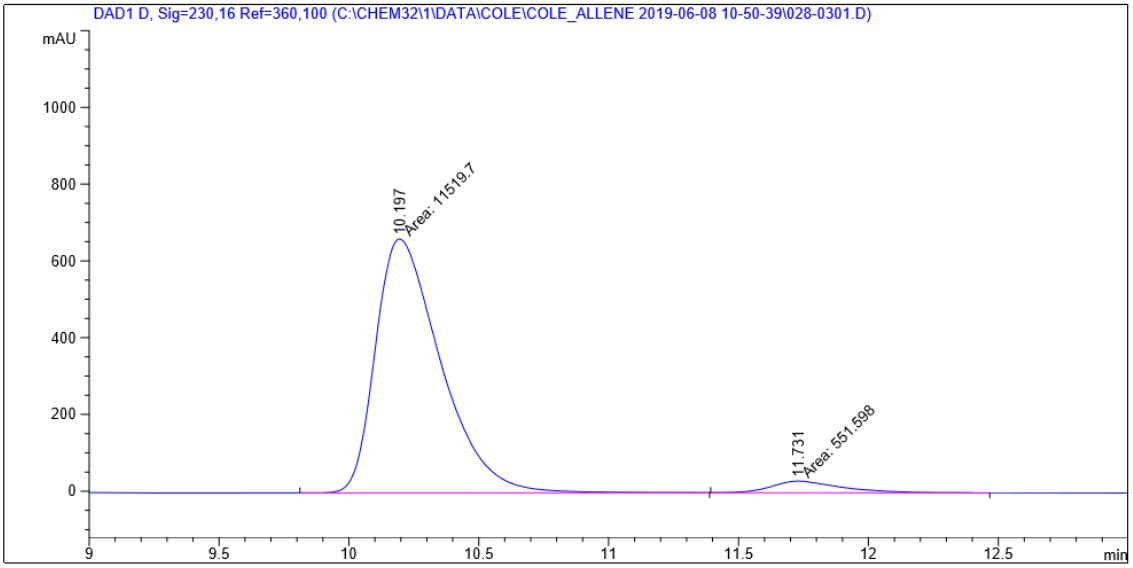
HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 230 nm), *ee* = 91%.


6.97
5.94
5.93
5.92
5.92
5.91
5.91
5.89
5.88
5.87
5.87
5.86
5.23
5.20
5.18
5.10
5.09
5.08
5.08
3.89
3.88
3.87
2.65
2.64
2.63
2.62
2.61
2.60
2.33
2.31
2.30
2.29
2.27
1.99
0.99
1.00
2.01
1.00
2.88
2.99
2.82
1.02
1.05
1.39
f1 (ppm)


153.14
150.62
142.33
138.58
134.56
118.80
107.99
105.93
71.98
61.21
61.15
56.27
42.33
f1 (ppm)

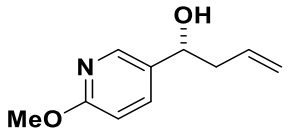


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.271	BB	0.2626	1.01681e4	591.35449	49.6927
2	11.731	BB	0.2766	1.02938e4	559.53711	50.3073



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.197	MM	0.2904	1.15197e4	661.25110	95.4305
2	11.731	MM	0.3037	551.59814	30.27231	4.5695

(*R*)-1-(6-methoxypyridin-3-yl)but-3-en-1-ol (8.3j)



Procedures

The aldehyde (27.4 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 ^{o}C, 24 hr). The title compound was obtained in 91% yield (32.7 mg, 0.18 mmol) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–5:1).

TLC (SiO_2) R_f = 0.23 (hexanes: ethyl acetate = 3:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.19 – 7.99 (m, 1H), 7.60 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.72 (d, *J* = 8.5 Hz, 1H), 5.89 – 5.65 (m, 1H), 5.24 – 5.04 (m, 2H), 4.69 (t, *J* = 6.4 Hz, 1H), 3.91 (d, *J* = 2.1 Hz, 3H), 2.48 (t, *J* = 6.6 Hz, 2H), 2.33 (s, 1H).

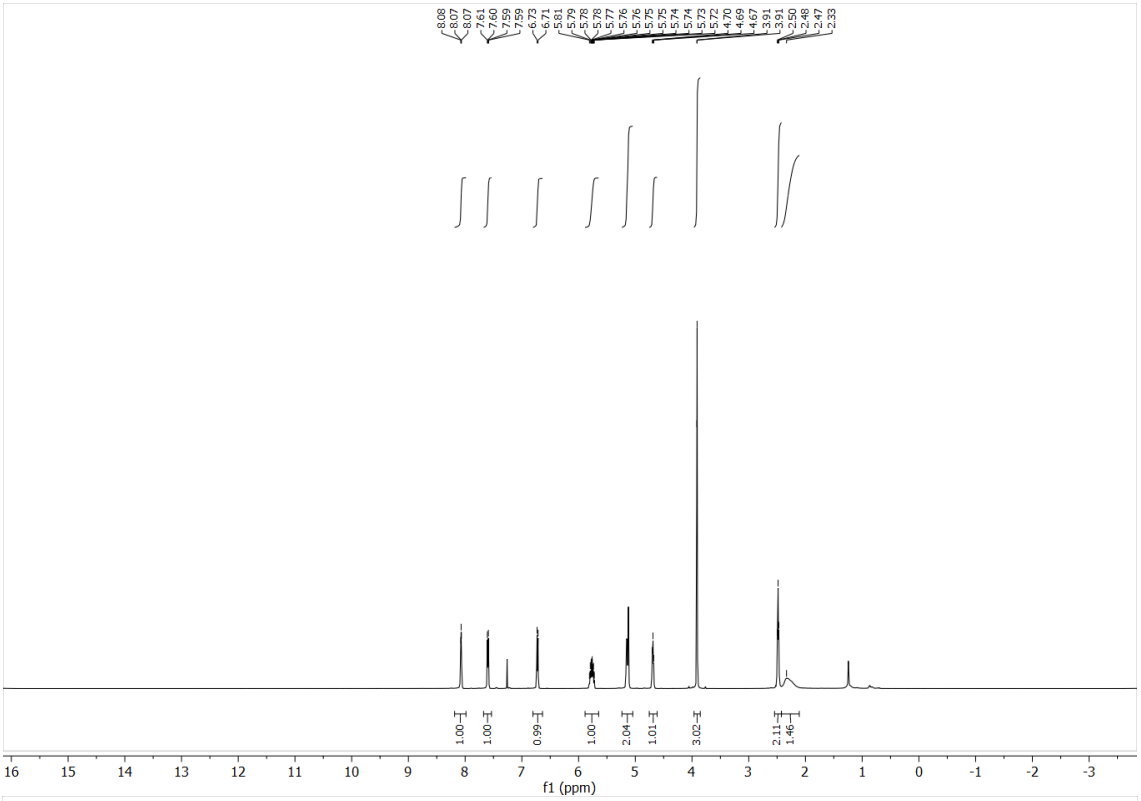
^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.8, 144.5, 136.8, 133.9, 132.0, 118.8, 110.8, 70.8, 53.6, 43.5.

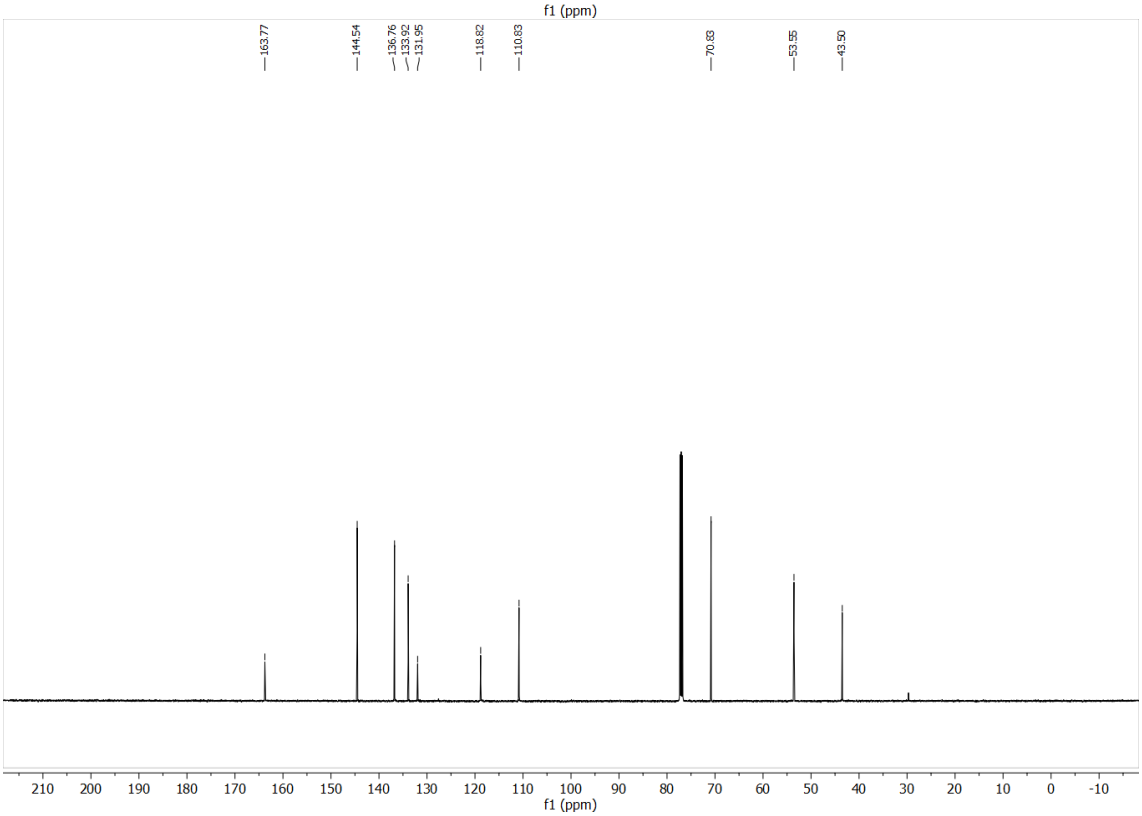
HRMS (ESI): Calculated for $C_{10}H_{13}NO_2$ [M+Na^+] = 202.0838, Found 202.0841.

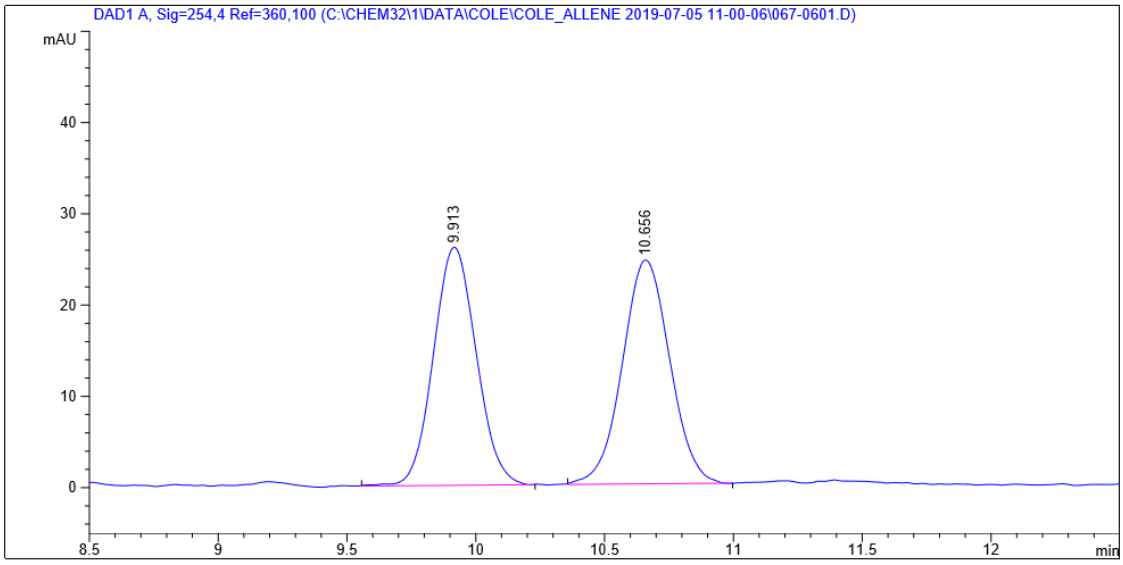
FTIR (neat): 3337, 3077, 2979, 2946, 1608, 1574, 1493, 1395, 1331, 1256, 1125, 1026, 917, 831 cm^{-1}.

$[\alpha]_D^{28}$= +61.3 (*c* 0.4, $CHCl_3$).

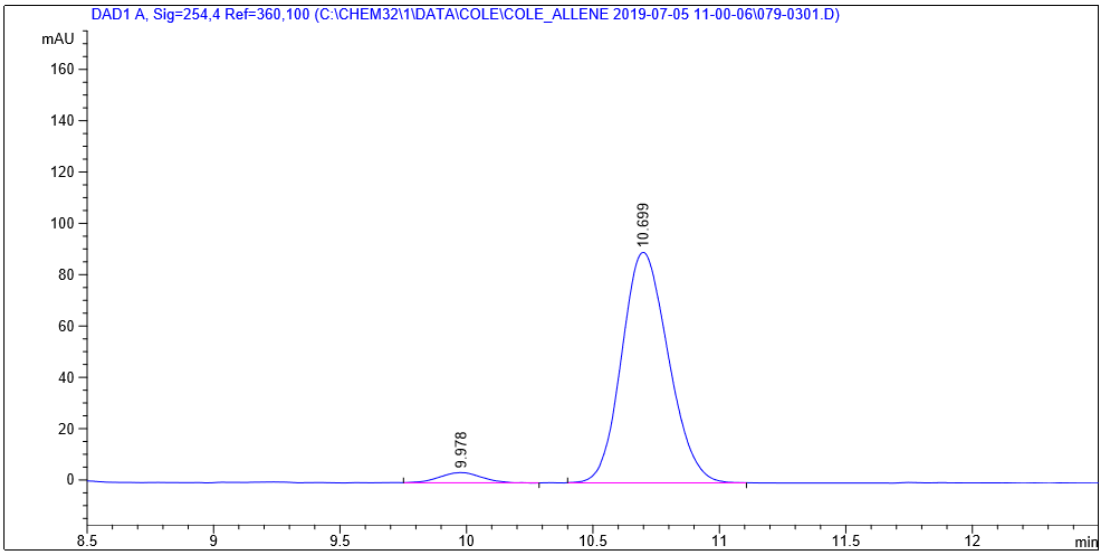
HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 254 nm), *ee* = 92%.


8.08
8.07
8.07
7.61
7.60
7.59
7.59
6.73
6.71
5.81
5.79
5.78
5.78
5.77
5.76
5.76
5.75
5.75
5.74
5.74
5.73
5.72
4.70
4.69
4.67
3.91
3.91
2.50
2.48
2.47
2.33
1.00
1.00
0.99
1.00
2.04
1.01
3.02
2.11
1.46
f1 (ppm)


163.77
144.54
136.76
133.92
131.95
118.82
110.83
70.83
53.85
43.50
f1 (ppm)

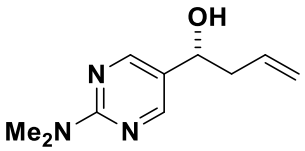


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.913	BB	0.1790	301.85486	26.08936	49.0129
2	10.656	BB	0.1974	314.01324	24.52583	50.9871



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.978	BB	0.1722	45.52981	3.95824	3.8021
2	10.699	BB	0.1996	1151.96326	89.83360	96.1979

(*R*)-1-(2-(dimethylamino)pyrimidin-5-yl)but-3-en-1-ol (8.3k)



Procedures

The aldehyde (30.2 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 °C, 24 hr). The title compound was obtained in 76% yield (29.2 mg, 0.15 mmol) as a yellow oil after isolation by flash column chromatography (SiO_2, hexanes: acetone = 15:1).

TLC (SiO_2) R_f = 0.22 (hexanes: ethyl acetate = 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.29 (s, 2H), 5.86 – 5.69 (m, 1H), 5.20 – 5.06 (m, 2H), 4.60 (t, *J* = 6.6 Hz, 1H), 3.18 (s, 6H), 2.49 (h, *J* = 6.9 Hz, 2H), 2.26 (s, 1H).

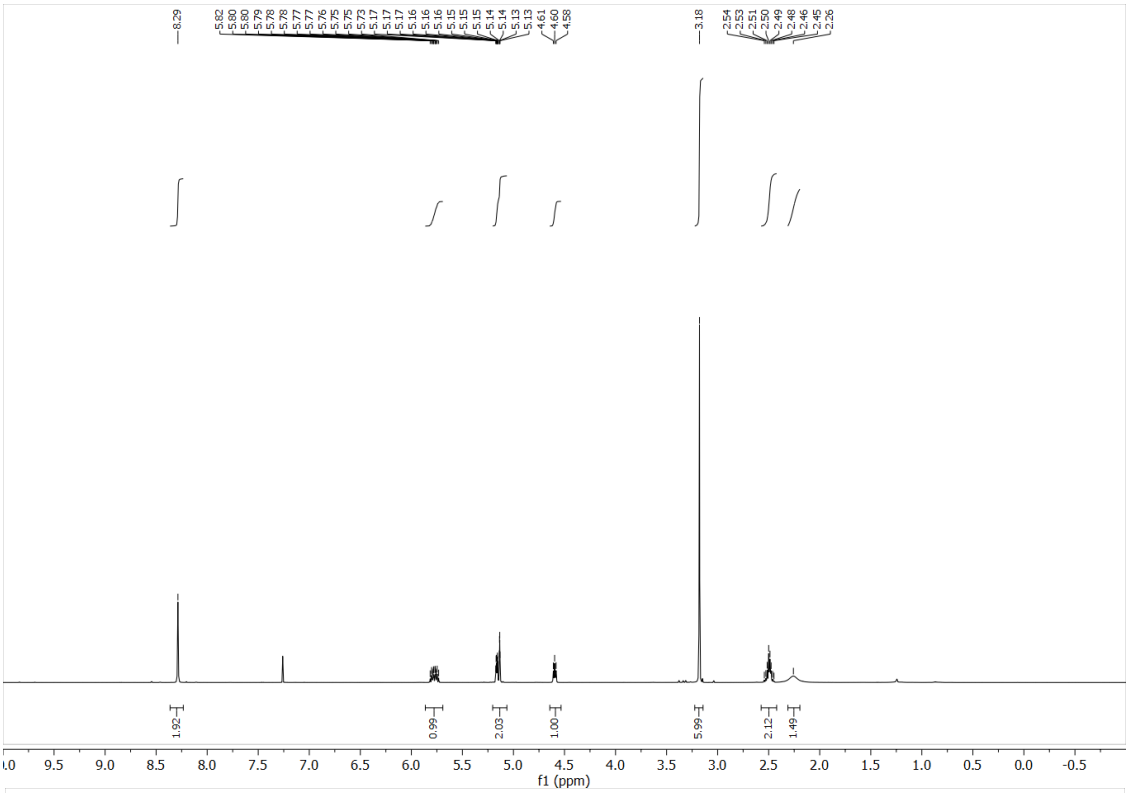
^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.9, 156.2, 133.9, 123.5, 119.1, 69.7, 43.2, 37.4.

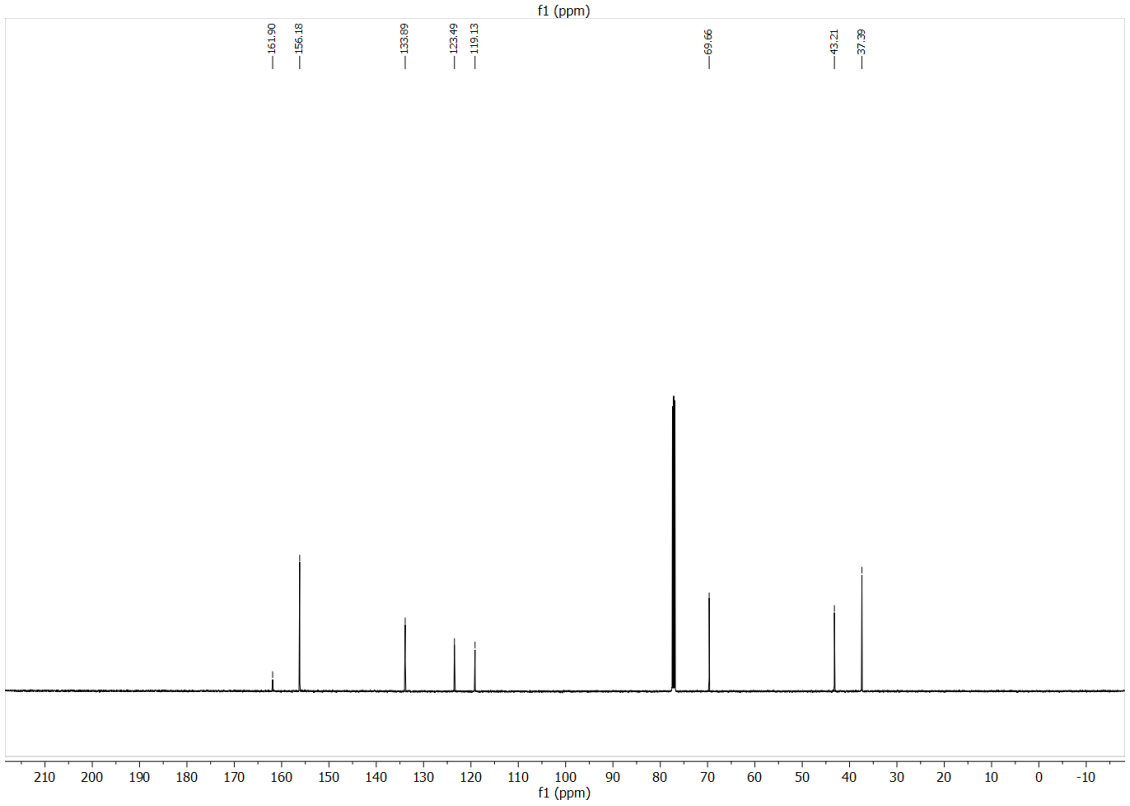
HRMS (ESI): Calculated for $C_{10}H_{15}N_3O$ [M+Na^+] = 194.1288, Found 194.1285.

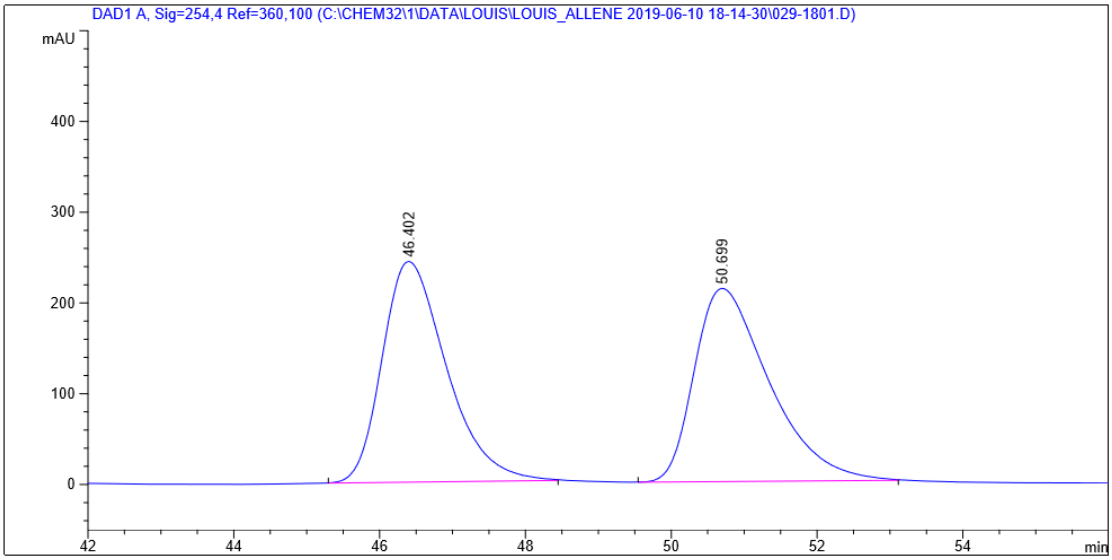
FTIR (neat): 3345, 2929, 1604, 1537, 1405, 1335, 1310, 1192, 1175, 1054, 973, 916, 799, 659 cm^{-1}.

$[\alpha]_D^{28}$= +39.1 (*c* 0.2, $CHCl_3$).

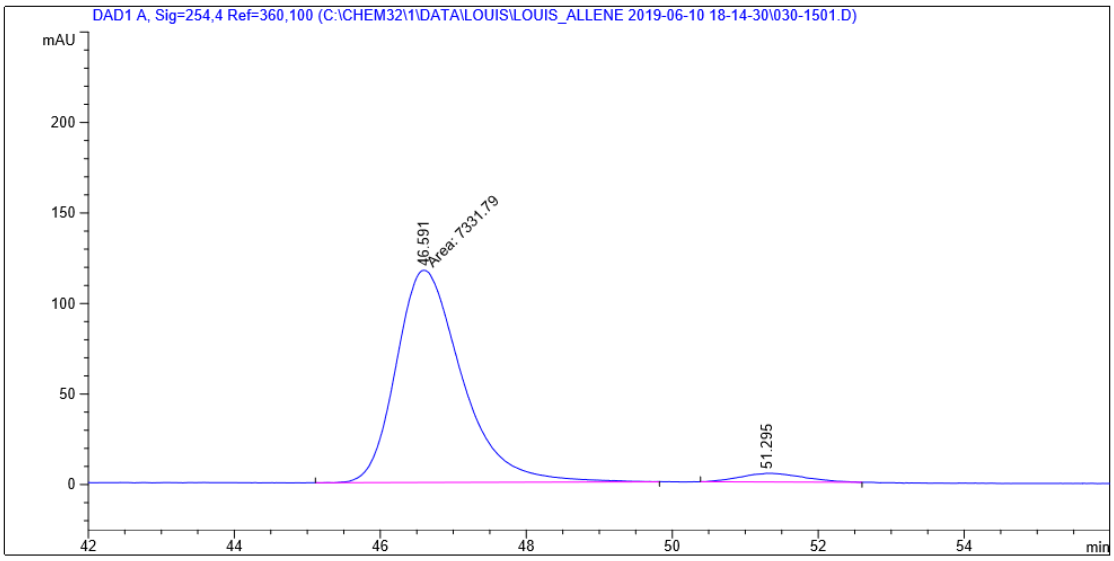
HPLC (two connected Chiralcel OD-H columns, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 254 nm), *ee* = 93%.


8.29
5.82
5.80
5.80
5.79
5.78
5.78
5.77
5.77
5.76
5.75
5.73
5.17
5.17
5.17
5.16
5.16
5.16
5.15
5.15
5.15
5.14
5.14
5.13
4.61
4.60
4.58
3.18
2.54
2.53
2.51
2.50
2.49
2.48
2.46
2.45
2.26
1.92
0.99
2.03
1.00
5.99
2.12
1.49
f1 (ppm)


161.90
156.18
133.89
123.49
119.13
69.66
43.21
37.39
f1 (ppm)

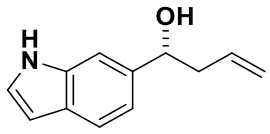


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	46.402	BB	0.9226	1.48952e4	243.19423	49.5089
2	50.699	BB	1.0006	1.51907e4	212.85783	50.4911



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	46.591	MM	1.0419	7331.78516	117.28213	96.2502
2	51.295	BB	0.7067	285.63696	4.81048	3.7498

(*R*)-1-(1H-indol-6-yl)but-3-en-1-ol (8.3l)



Procedures

The aldehyde (29.0 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (50 °C, 48 hr). The title compound was obtained in 79% yield (29.6 mg, 0.16 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, dichloromethane: diethyl ether = 1:0–10:1).

TLC (SiO_2) R_f = 0.28 (dichloromethane: diethyl ether = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = δ 8.24 (s, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.35 (s, 1H), 7.18 (t, *J* = 2.8 Hz, 1H), 7.11 (dd, *J* = 8.1, 1.4 Hz, 1H), 6.54 (t, *J* = 2.5 Hz, 1H), 5.84 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.22 – 5.09 (m, 2H), 4.84 (t, *J* = 6.5 Hz, 1H), 2.59 (t, *J* = 6.6 Hz, 2H), 2.23 (s, 1H).

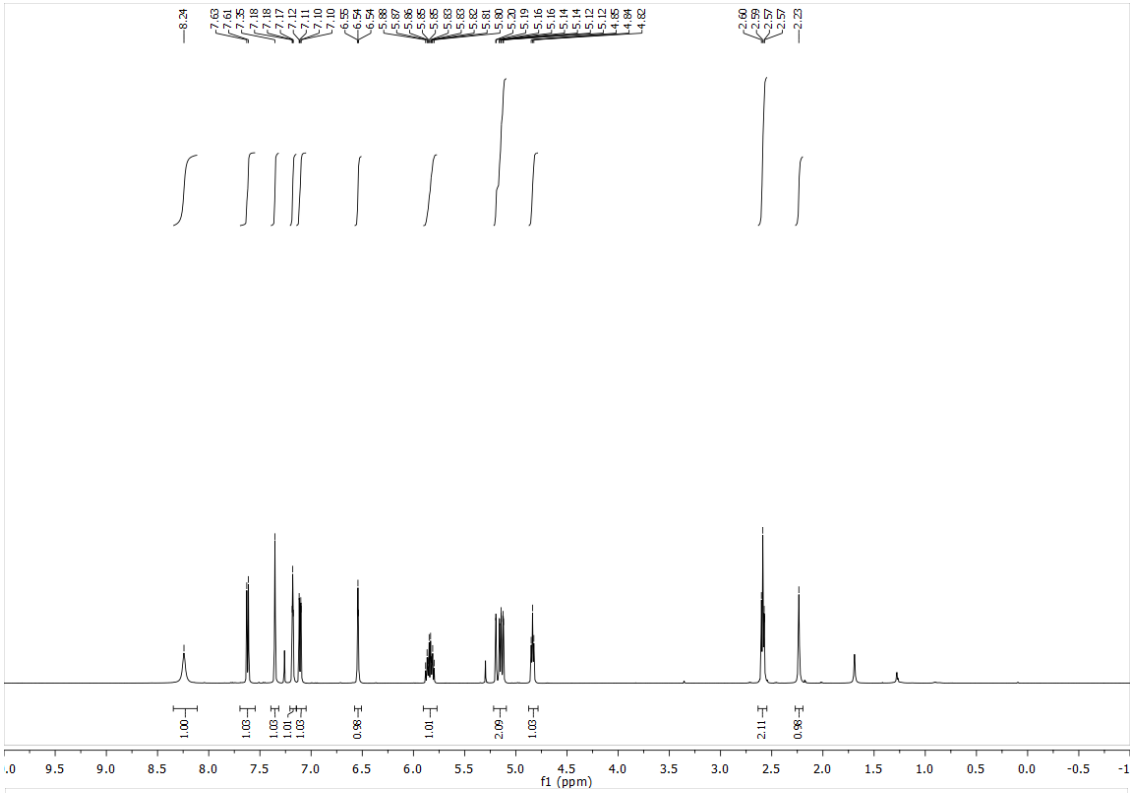
^{13}C NMR (125 MHz, $CDCl_3$): δ = δ 138.0, 135.8, 134.9, 127.3, 124.5, 120.6, 118.1, 118.0, 108.3, 102.3, 74.0, 44.0.

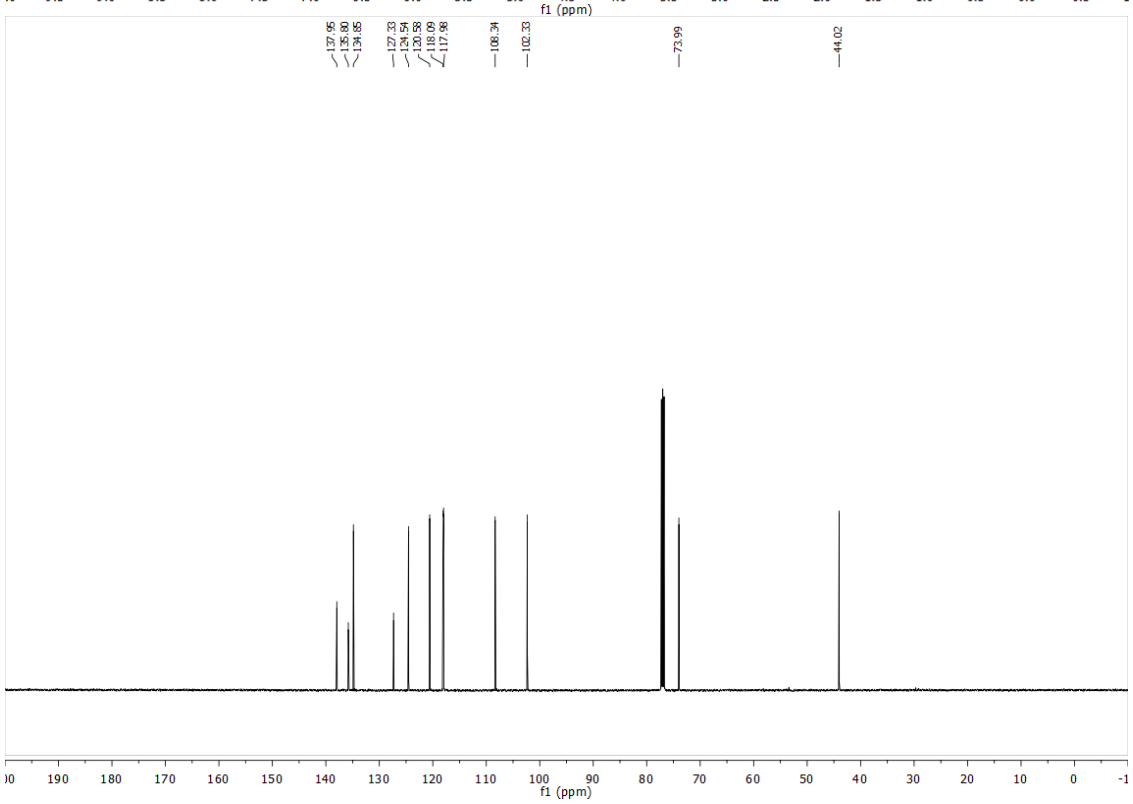
HRMS (ESI): Calculated for $C_{12}H_{13}NO$ [M+Na^+] = 210.0889, Found 210.0884.

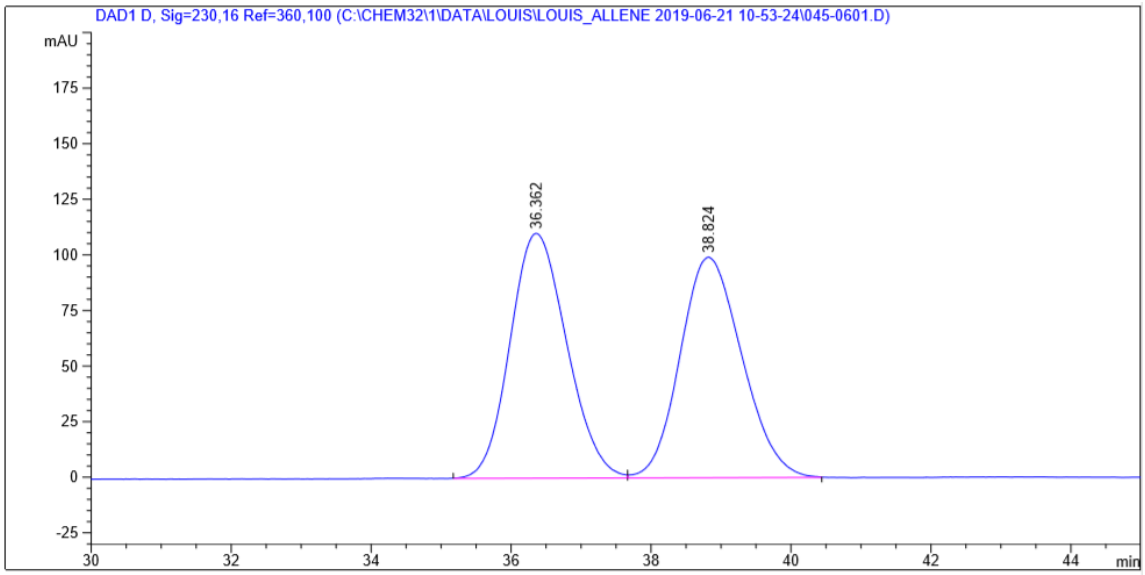
FTIR (neat): 3412, 2918, 1640, 1509, 1453, 1346, 1042, 989, 908, 867, 814, 767, 725 cm^{-1}.

$[\alpha]_D^{28}$= +39.0 (*c* 0.3, $CHCl_3$).

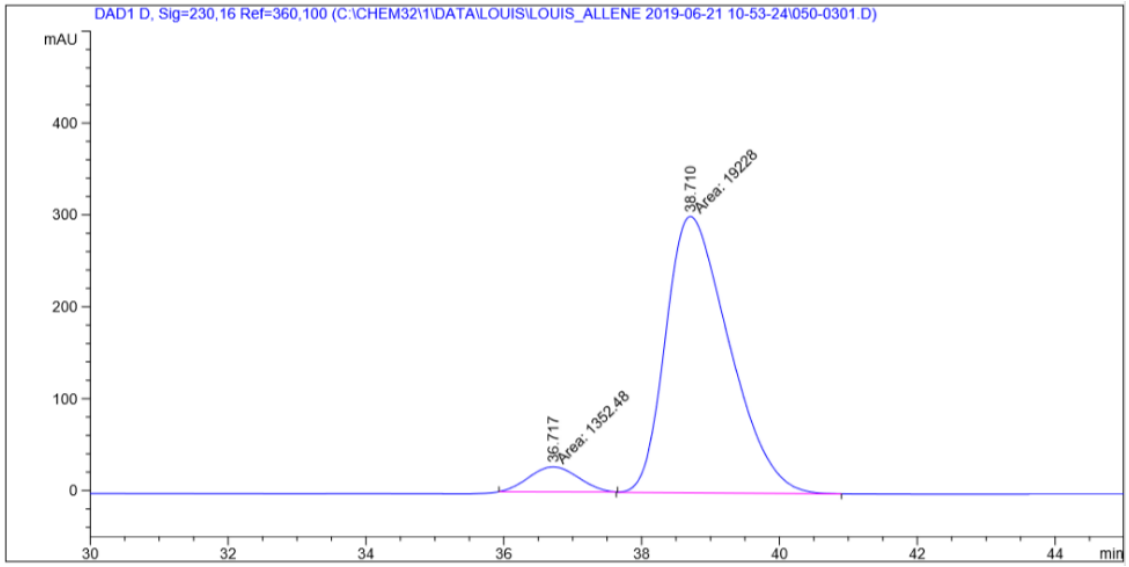
HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 85:15, 1.00 mL/min, 230 nm), *ee* = 87%.


8.24
7.63
7.61
7.35
7.18
7.17
7.12
7.11
7.10
6.55
6.54
6.54
5.88
5.87
5.86
5.85
5.83
5.83
5.82
5.81
5.80
5.20
5.19
5.16
5.16
5.14
5.14
5.12
5.12
4.85
4.84
4.82
2.60
2.59
2.57
2.57
2.23
1.00
1.03
1.03
1.01
1.03
0.98
1.01
2.09
1.03
2.11
0.98
f1 (ppm)


137.95
135.80
134.85
127.33
124.54
120.58
118.09
117.98
108.34
102.33
73.99
44.02
f1 (ppm)

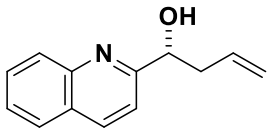


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.362	BV	0.8115	6185.78955	110.09409	50.4231
2	38.824	VB	0.7350	6081.97705	99.24330	49.5769



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.717	MM	0.8255	1352.48303	27.30476	6.5717
2	38.710	MM	1.0655	1.92280e4	300.76227	93.4283

(*R*)-1-(quinolin-2-yl)but-3-en-1-ol (8.3m)



Procedures

The aldehyde (31.4 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 °C, 48 hr). The title compound was obtained in 88% yield (35.1 mg, 0.18 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–5:1).

TLC (SiO_2) R_f = 0.27 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 7.83 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.73 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.54 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 1H), 5.89 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.17 – 5.05 (m, 2H), 4.99 (t, *J* = 6.0 Hz, 1H), 4.89 (s, 1H), 2.75 (dddt, *J* = 14.2, 7.0, 4.6, 1.3 Hz, 1H), 2.56 (dtt, *J* = 14.3, 7.1, 1.3 Hz, 1H).

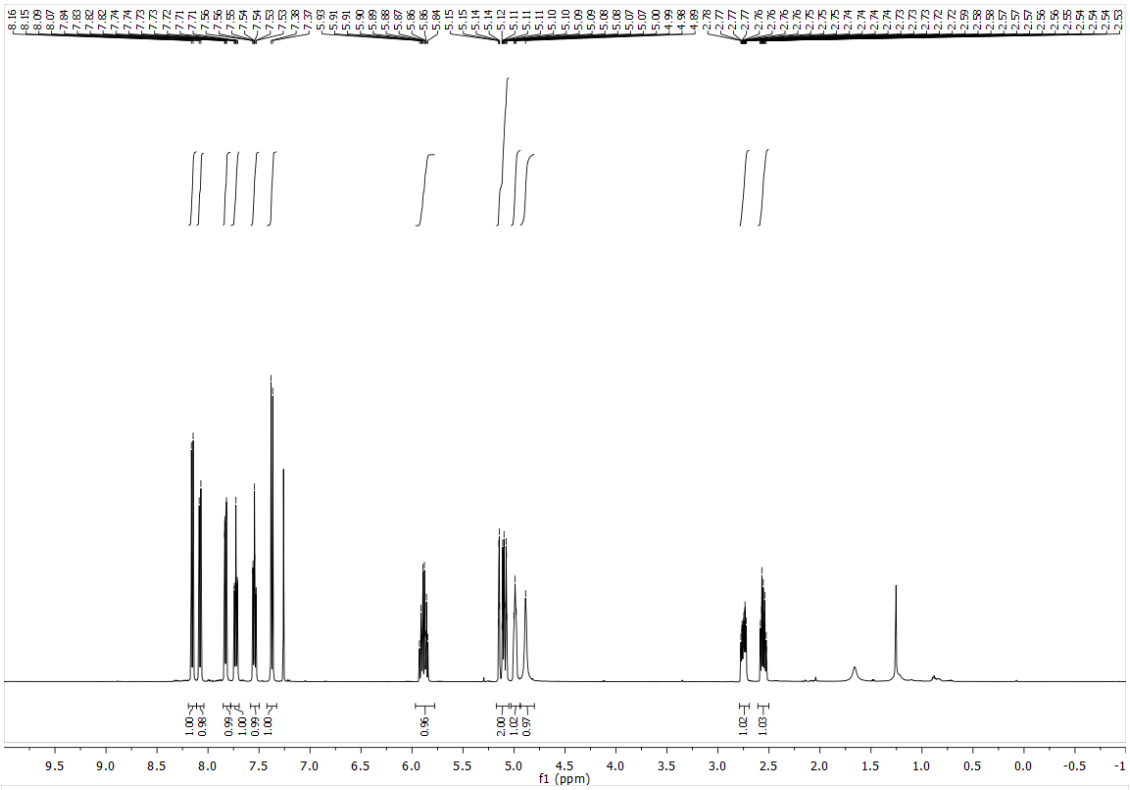
^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.3, 146.5, 136.8, 134.1, 129.8, 128.8, 127.6, 127.5, 126.4, 118.4, 117.9, 72.2, 42.6.

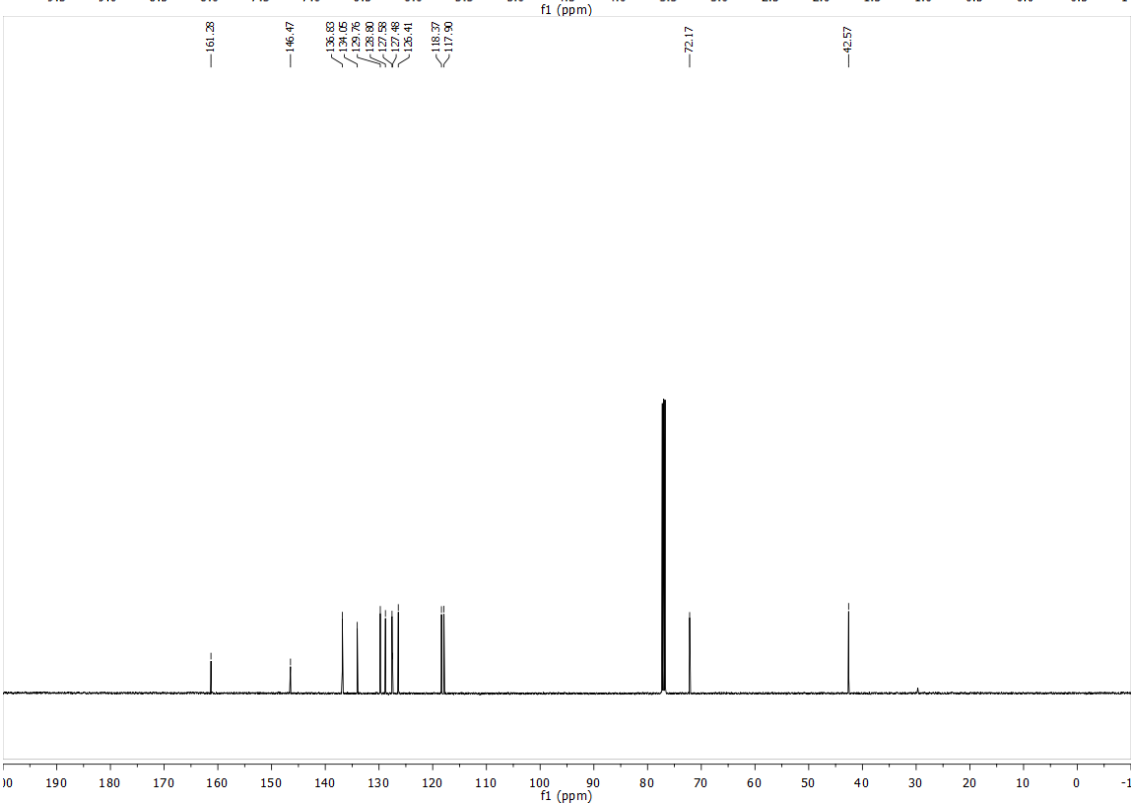
HRMS (ESI): Calculated for $C_{13}H_{13}NO$ [M+Na^+] = 222.0889, Found 222.0896.

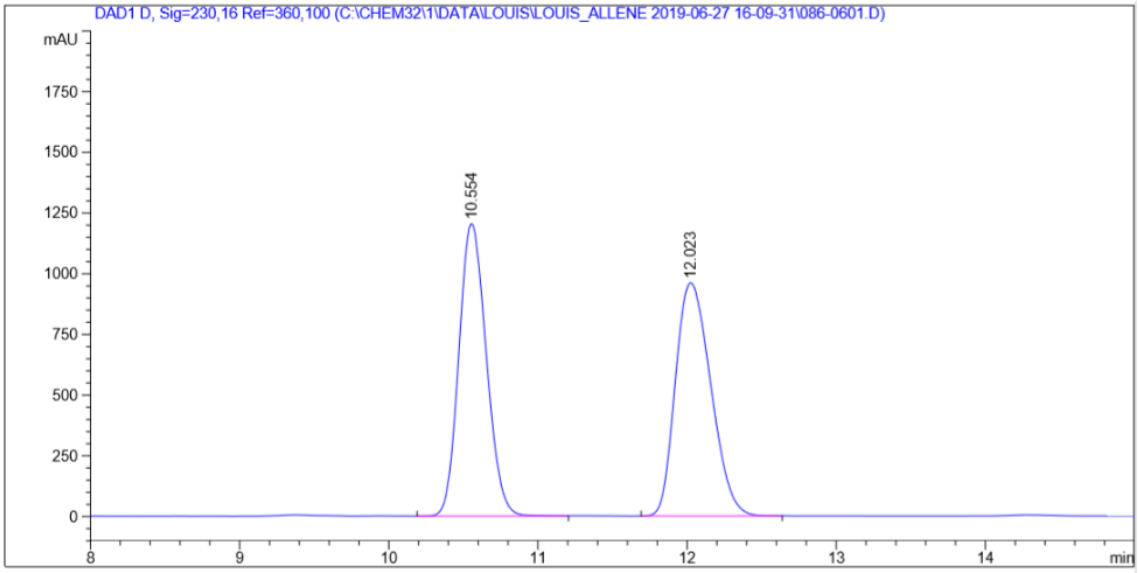
FTIR (neat): 3261, 2921, 2895, 1618, 1599, 1502, 1430, 1304, 1069, 919, 793, 757 cm^{-1}.

$[\alpha]_D^{28}$ = –18.0 (*c* 0.3, $CHCl_3$).

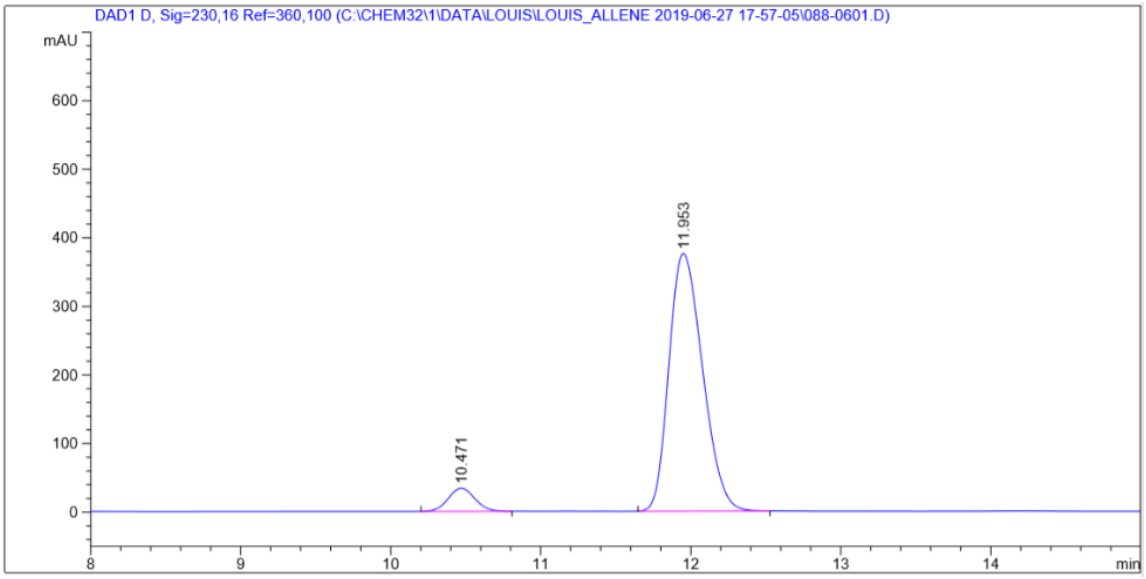
HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 230 nm), *ee* = 87%.


f1 (ppm)


161.28
146.47
136.83
134.05
129.76
128.80
127.58
127.48
126.41
118.37
117.90
72.17
42.57
f1 (ppm)

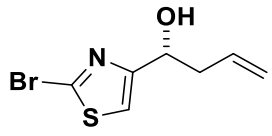


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.554	VB	0.2011	1.53967e4	1204.35229	49.2893
2	12.023	BB	0.2623	1.58407e4	960.83899	50.7107



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.471	BB	0.1895	415.89691	33.82350	6.6330
2	11.953	BB	0.2457	5854.26465	375.94131	93.3670

(*R*)-1-(2-bromothiazol-4-yl)but-3-en-1-ol (8.3n)



Procedures

The aldehyde (38.4 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 ^{o}C, 24 hr). The title compound was obtained in 71% yield (33.1 mg, 0.14 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–4:1).

TLC (SiO_2) R_f = 0.32 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.15 (s, 1H), 5.80 (ddt, *J* = 17.2, 10.2, 7.1 Hz, 1H), 5.21 – 5.14 (m, 2H), 4.85 (dt, *J* = 7.8, 4.9 Hz, 1H), 2.71 (dddt, *J* = 14.1, 6.2, 4.6, 1.3 Hz, 1H), 2.61 – 2.50 (m, 1H), 2.45 (d, *J* = 5.3 Hz, 1H).

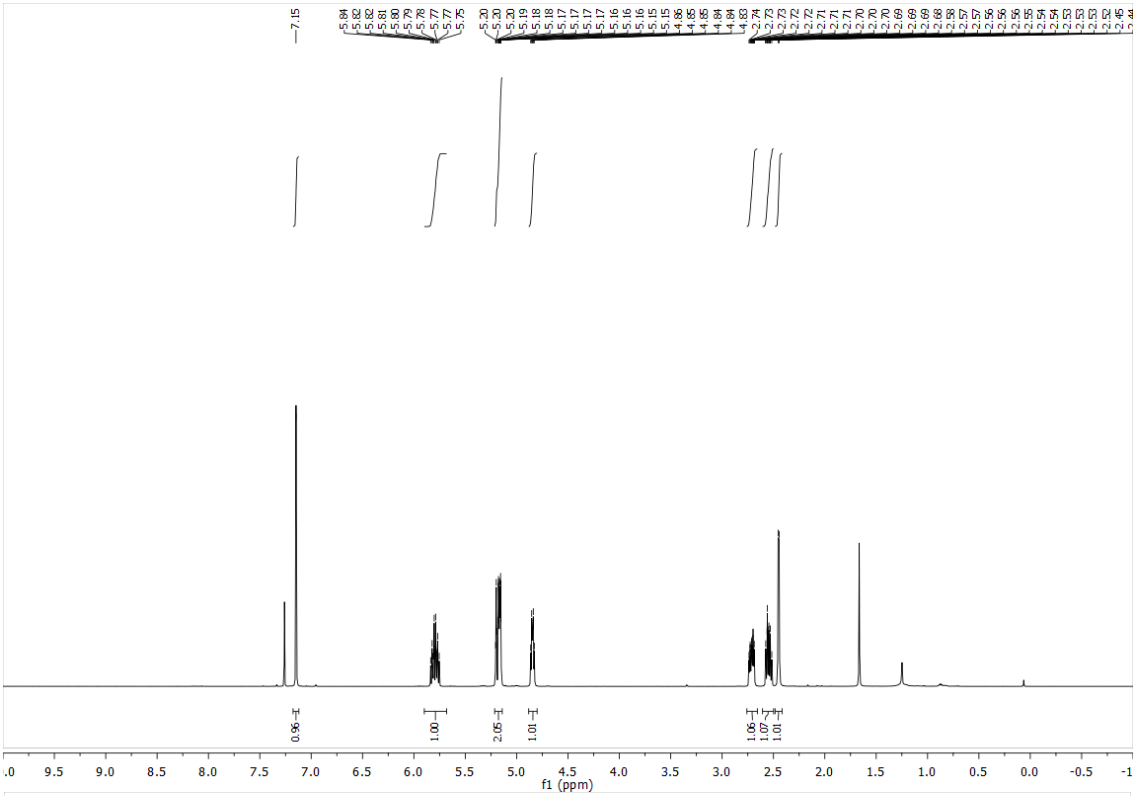
^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.2, 135.9, 133.5, 119.0, 117.6, 69.7, 41.6.

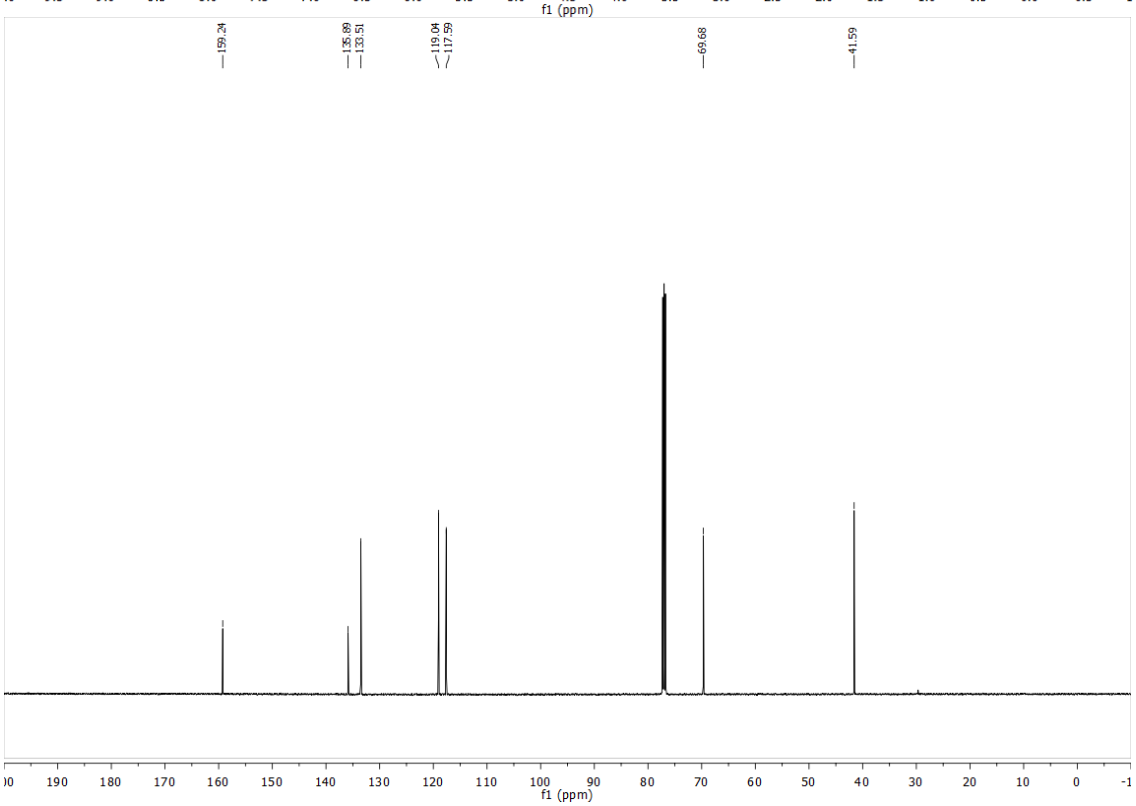
HRMS (ESI): Calculated for C_7H_8BrNOS [M+Na^+] = 257.9381, Found 257.9391.

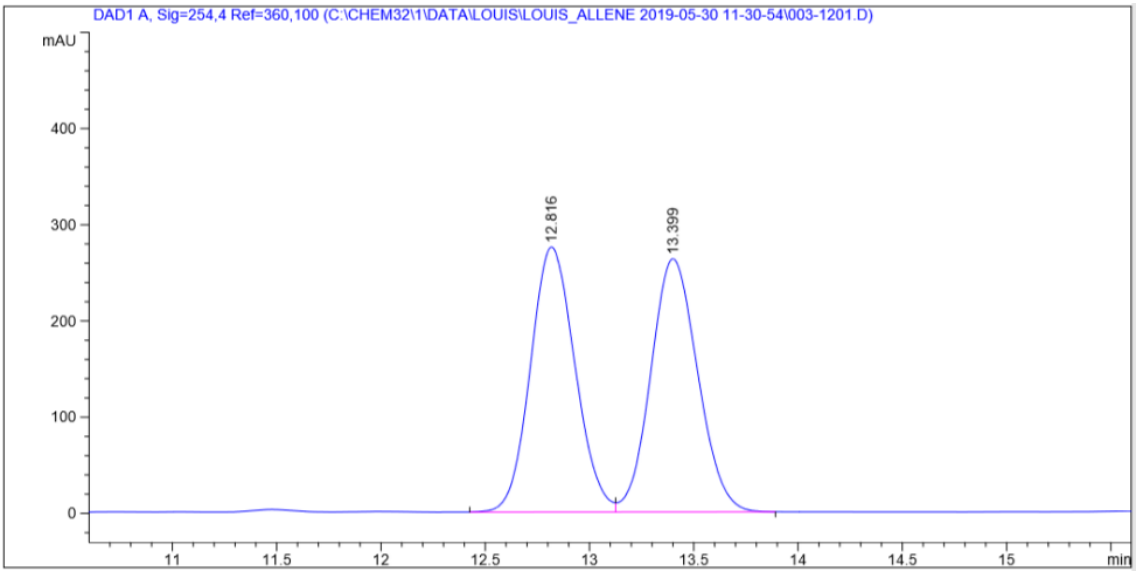
FTIR (neat): 3350, 3076, 2907, 1640, 1519, 1416, 1317, 1243, 1012, 916, 758 cm^{-1}.

$[\alpha]_D^{28}$= +75.0 (*c* 1.0, $CHCl_3$).

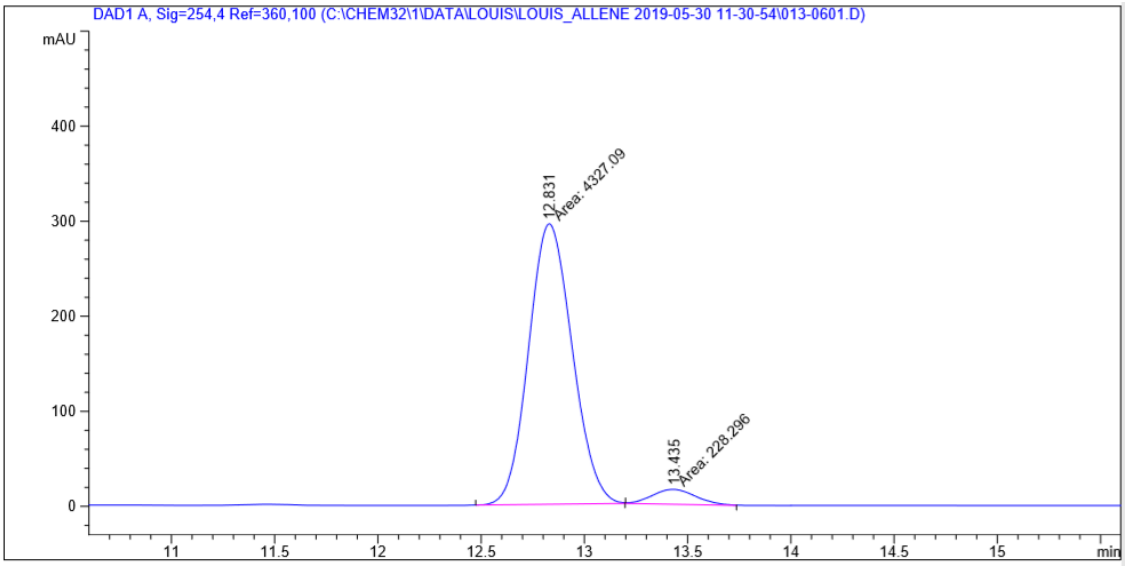
HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 254 nm), *ee* = 90%.


7.15
0.96
1.00
2.05
1.01
1.06
1.07
1.01
f1 (ppm)


159.24
135.89
133.51
119.04
117.59
69.68
41.59
f1 (ppm)

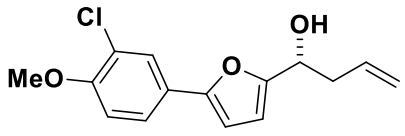


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.816	BV	0.2313	4092.24048	275.44943	49.8869
2	13.399	VB	0.2442	4110.79639	263.15219	50.1131



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.831	MM	0.2445	4327.09326	294.95230	94.9884
2	13.435	MM	0.2420	228.29596	15.72469	5.0116

(*R*)-1-(5-(3-chloro-4-methoxyphenyl)furan-2-yl)but-3-en-1-ol (8.3o)



Procedures

The aldehyde (47.3 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 °C, 48 hr). The title compound was obtained in 79% yield (44.0 mg, 0.16 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, hexanes: dichloromethane = 1:1–0:1).

TLC (SiO_2) R_f = 0.55 (dichloromethane).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 2.2 Hz, 1H), 7.50 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.92 (d, *J* = 8.6 Hz, 1H), 6.47 (d, *J* = 3.3 Hz, 1H), 6.32 (d, *J* = 3.3 Hz, 1H), 5.85 (ddt, *J* = 17.1, 10.2, 7.0 Hz, 1H), 5.25 – 5.10 (m, 2H), 4.79 (dt, *J* = 9.6, 4.9 Hz, 1H), 3.92 (s, 3H), 2.68 (qt, *J* = 7.1, 1.3 Hz, 2H), 2.13 (d, *J* = 4.4 Hz, 1H).

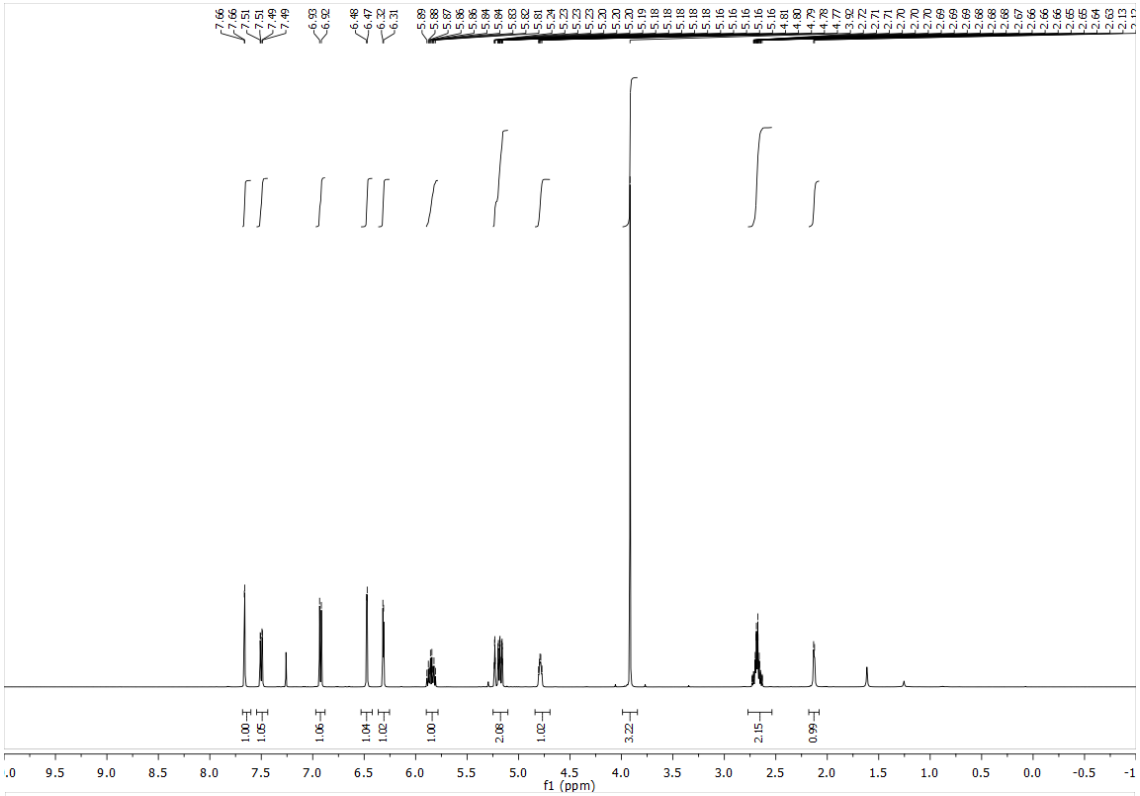
^{13}C NMR (125 MHz, $CDCl_3$): δ = 155.4, 154.2, 152.0, 133.6, 125.7, 124.6, 123.2, 122.8, 118.7, 112.1, 108.3, 104.9, 67.0, 56.2, 40.1.

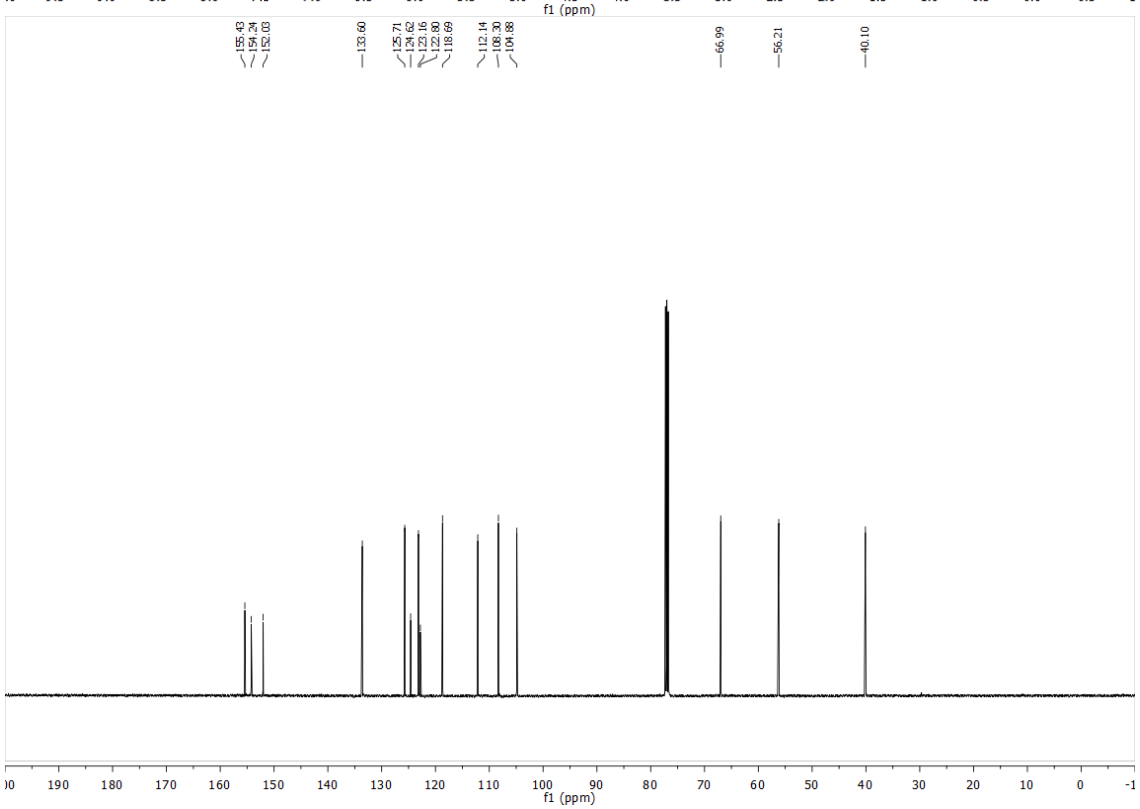
HRMS (ESI): Calculated for $C_{15}H_{15}ClO_3$ [M+Na$^+$] = 301.0602, Found 301.0601.

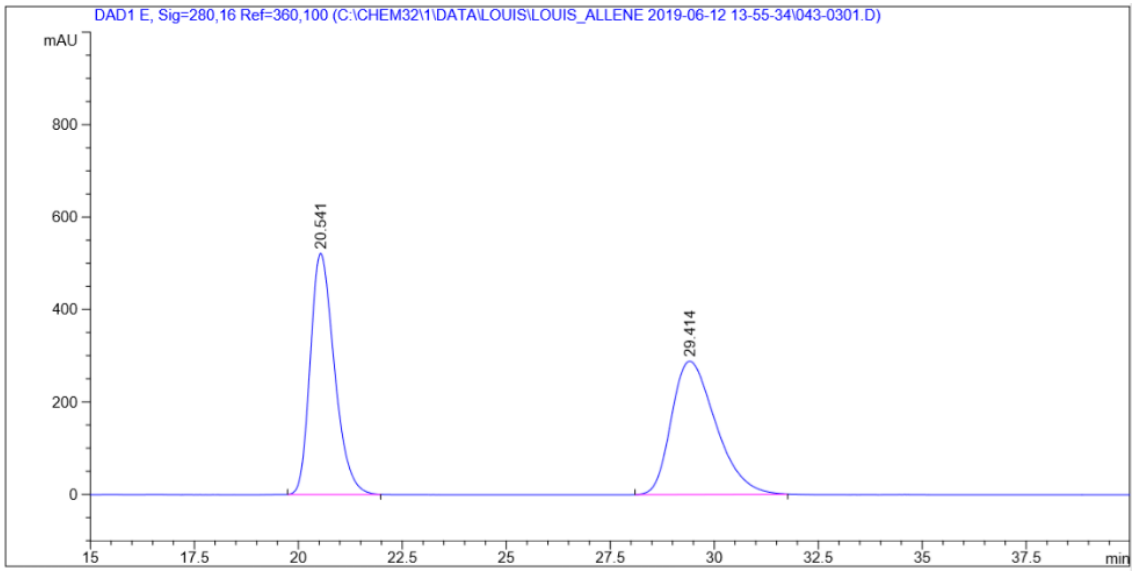
FTIR (neat): 3377, 2939, 1490, 1440, 1289, 1267, 1062, 1019, 909, 787, 730, 708 cm^{-1}.

$[\alpha]_D^{28}$= +30.0 (*c* 0.3, $CHCl_3$).

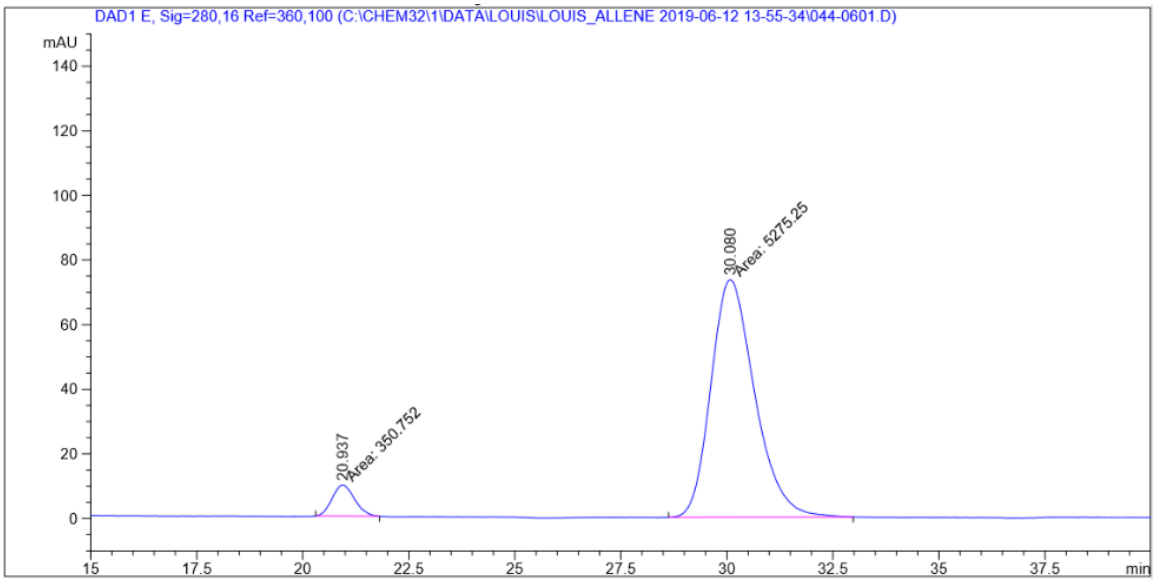
HPLC (Chiralcel AS-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 280 nm), *ee* = 88%.


f1 (ppm)


f1 (ppm)

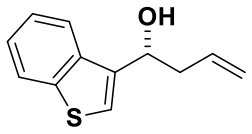


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.541	BB	0.6161	2.10281e4	521.85822	49.5875
2	29.414	BB	1.1191	2.13780e4	288.29727	50.4125



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.937	MM	0.6089	350.75214	9.60105	6.2345
2	30.080	MM	1.1960	5275.25146	73.51225	93.7655

(*R*)-1-(benzo[b]thiophen-3-yl)but-3-en-1-ol (8.3p)



Procedures

The aldehyde (32.4 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 ^{o}C, 24 hr). The title compound was obtained in 81% yield (33.1 mg, 0.16 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–8:1).

TLC (SiO_2) R_f = 0.45 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (ddd, *J* = 7.4, 5.4, 1.4 Hz, 2H), 7.45 – 7.30 (m, 3H), 5.96 – 5.83 (m, 1H), 5.26 – 5.17 (m, 2H), 5.15 (dt, *J* = 8.0, 3.9 Hz, 1H), 2.77 (dddt, *J* = 14.0, 6.2, 4.6, 1.4 Hz, 1H), 2.71 – 2.60 (m, 1H), 2.15 (d, *J* = 3.5 Hz, 1H).

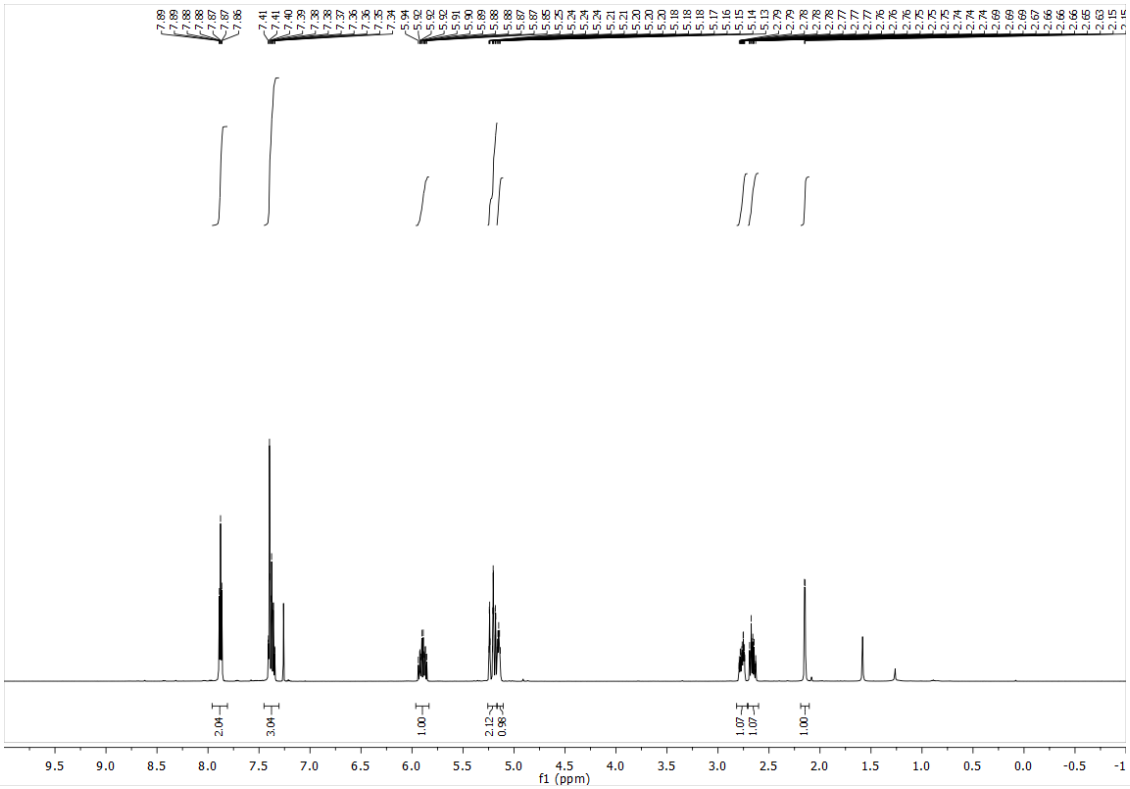
^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.9, 138.8, 137.2, 134.2, 124.4, 124.0, 122.9, 122.2, 122.2, 118.7, 68.9, 41.8.

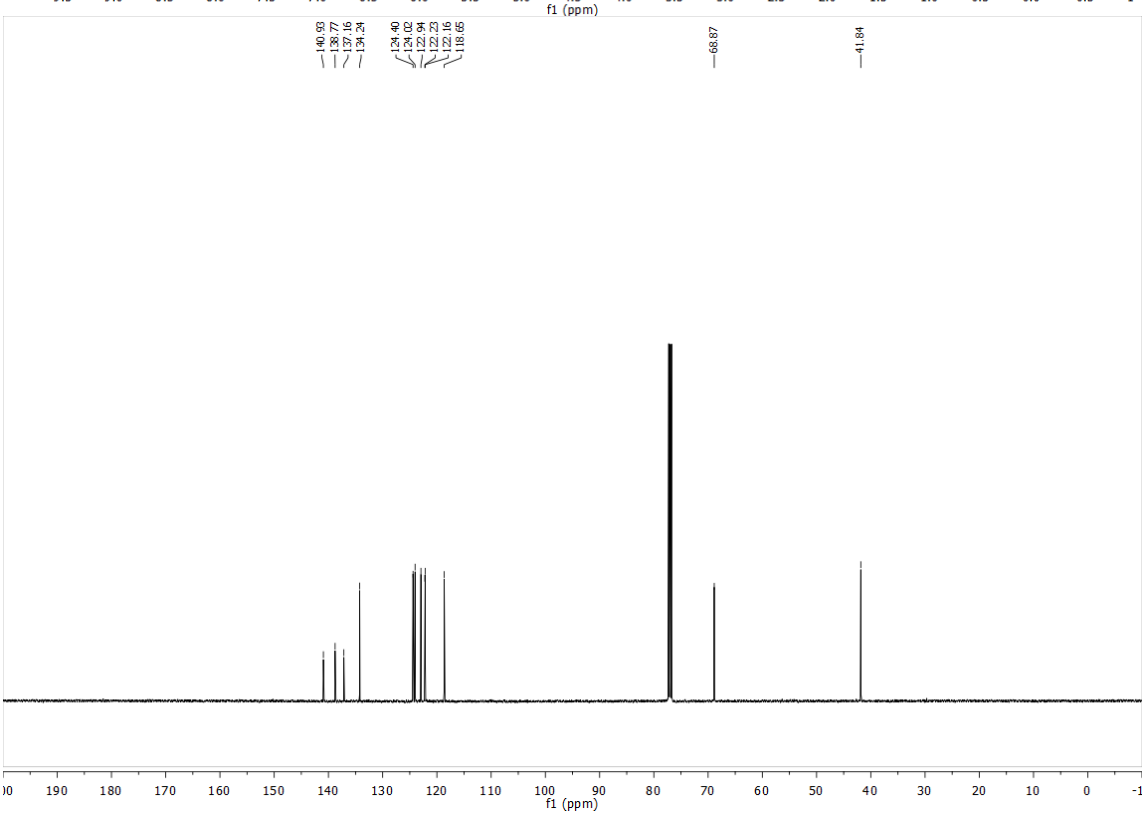
HRMS (ESI): Calculated for $C_{12}H_{12}OS$ [M+Na^+] =227.0501, Found 227.0507.

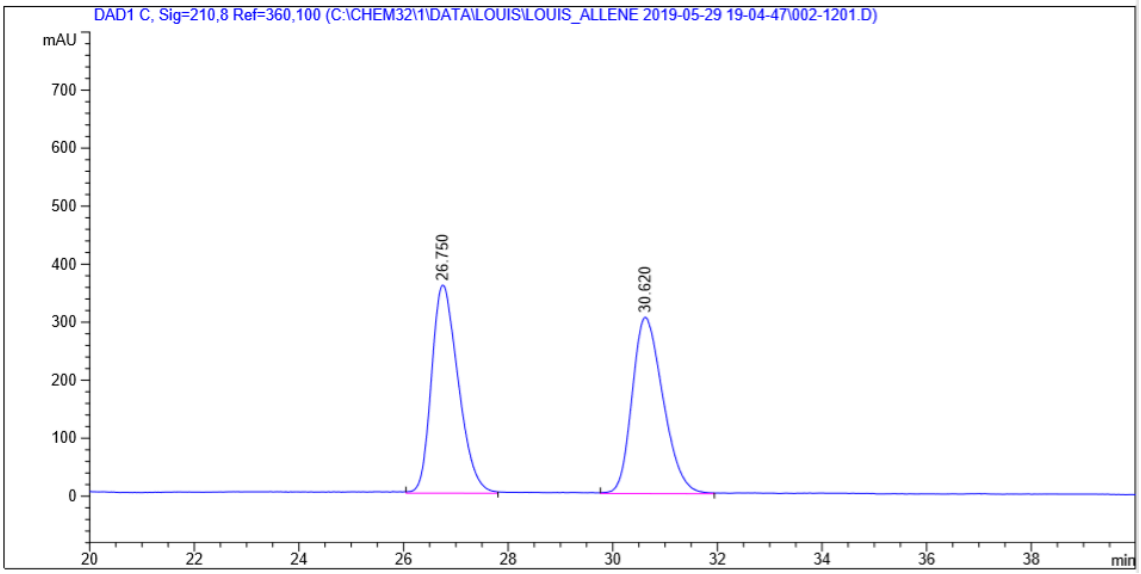
FTIR (neat): 3373, 3075, 2906, 1640, 1459, 1427, 1256, 1140, 1057, 1022, 915, 868, 834, 759, 732 cm^{-1}.

$[\alpha]_D^{28}$= +48.2 (*c* 0.3, $CHCl_3$).

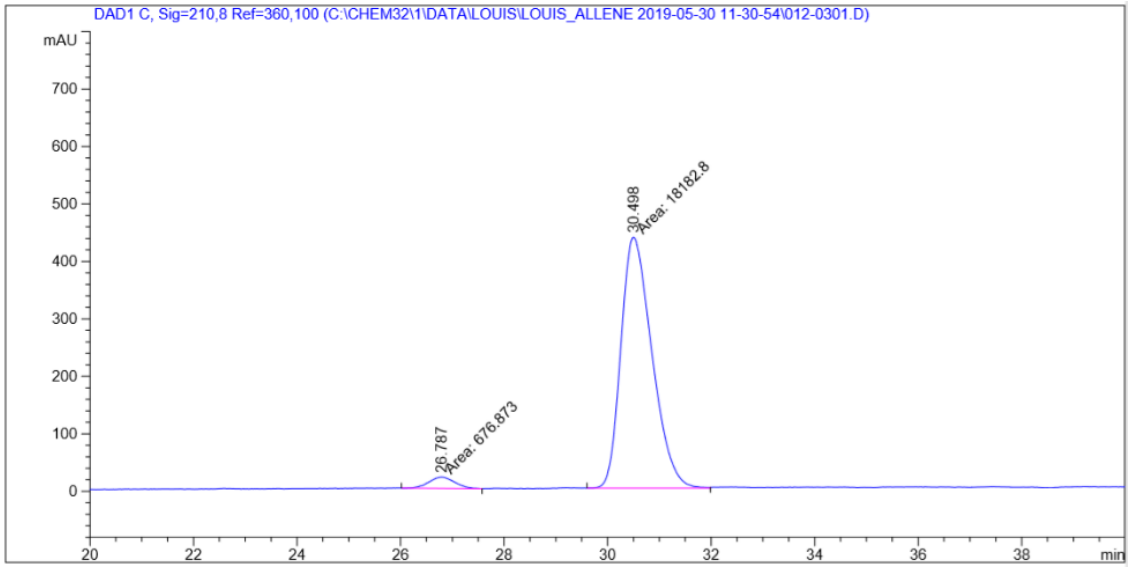
HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 210 nm), *ee* = 93%.


f1 (ppm)


140.93
138.77
137.16
134.24
124.40
124.02
122.94
122.23
122.16
118.65
68.87
41.84
f1 (ppm)

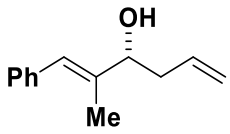


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.750	VV	0.5322	1.27422e4	358.89328	50.5101
2	30.620	VV	0.6214	1.24848e4	303.85849	49.4899



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.787	MM	0.5777	676.87268	19.52680	3.5890
2	30.498	MM	0.6936	1.81828e4	436.90311	96.4110

(*R*,*E*)-2-methyl-1-phenylhexa-1,5-dien-3-ol (8.3q)



Procedures

The aldehyde (29.2 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 °C, 24 hr). The title compound was obtained in 61% yield (23.1 mg, 0.12 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.39 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.33 (t, *J* = 7.6 Hz, 2H), 7.30 – 7.26 (m, 2H), 7.24 – 7.19 (m, 1H), 6.53 (s, 1H), 5.84 (ddt, *J* = 17.2, 10.2, 7.1 Hz, 1H), 5.23 – 5.13 (m, 2H), 4.27 – 4.18 (m, 1H), 2.50 – 2.43 (m, 1H), 2.43 – 2.36 (m, 1H), 1.89 (d, *J* = 1.3 Hz, 3H), 1.80 (d, *J* = 3.0 Hz, 1H).

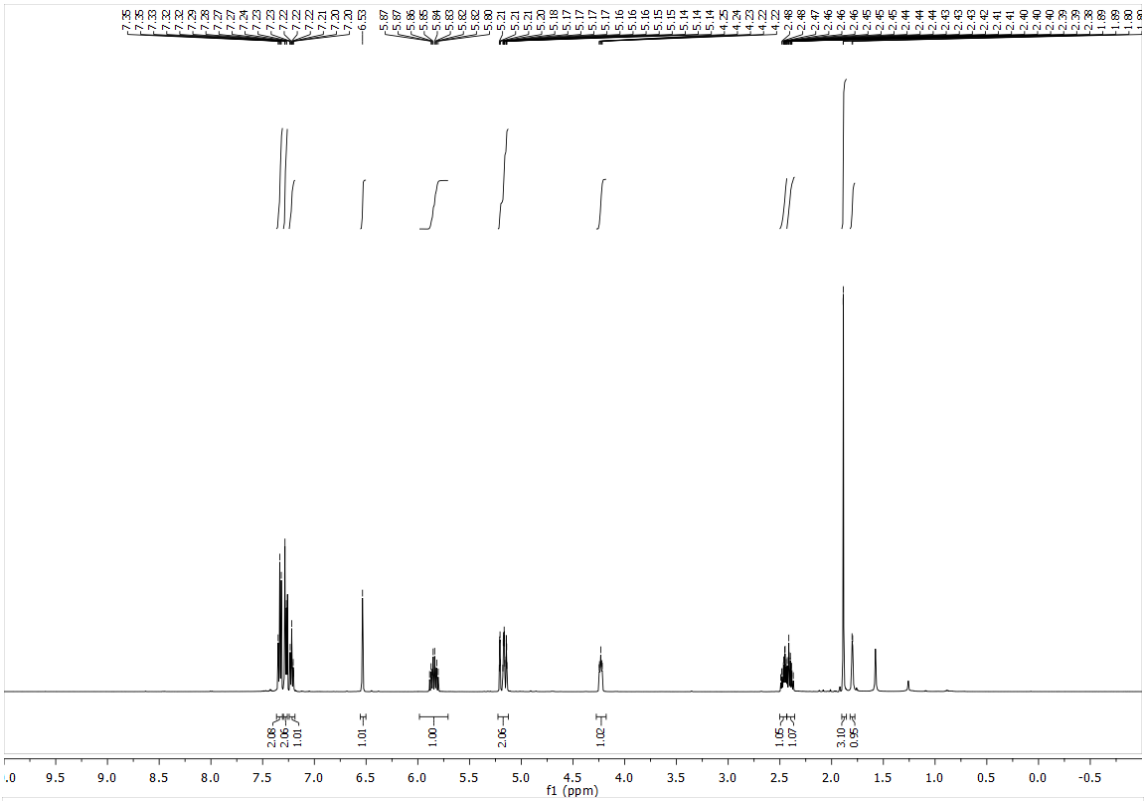
^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.5, 137.5, 134.5, 129.0, 128.1, 126.4, 125.7, 118.1, 76.5, 40.1, 13.7.

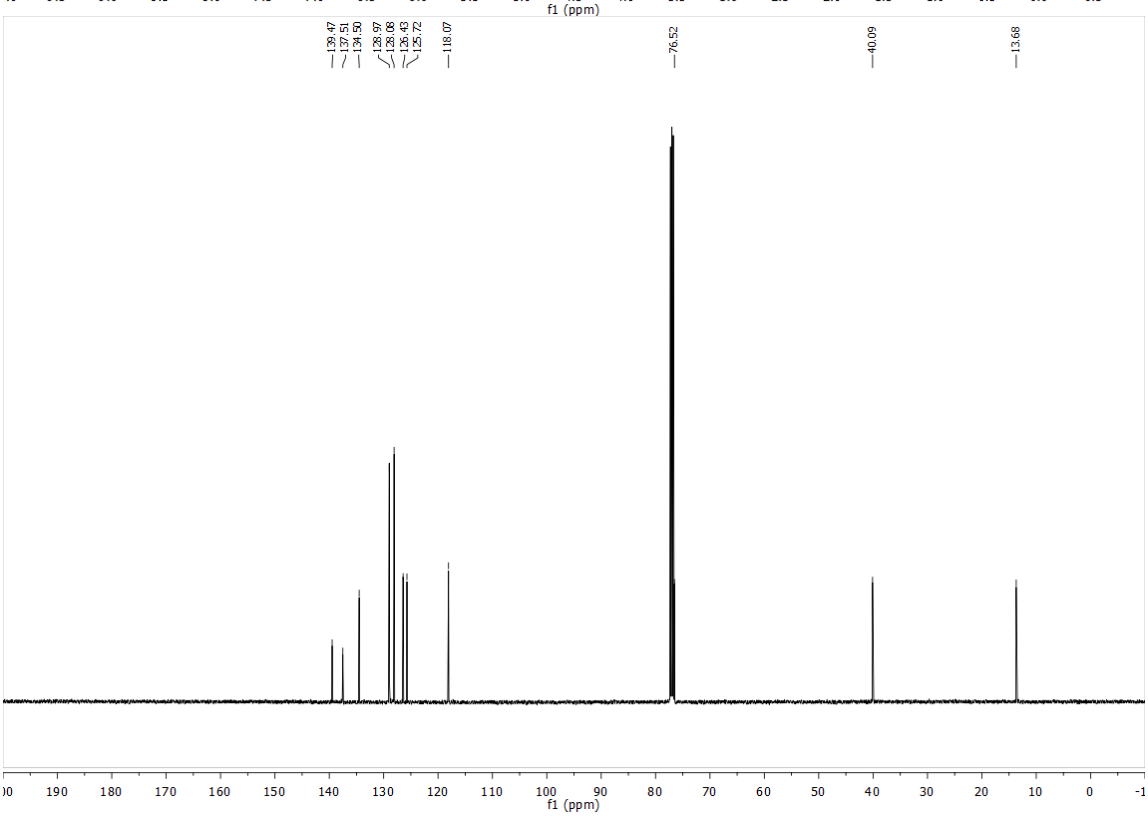
HRMS (EI): Calculated for $C_{13}H_{16}O$ [M^+] = 188.1201, Found 188.1205.

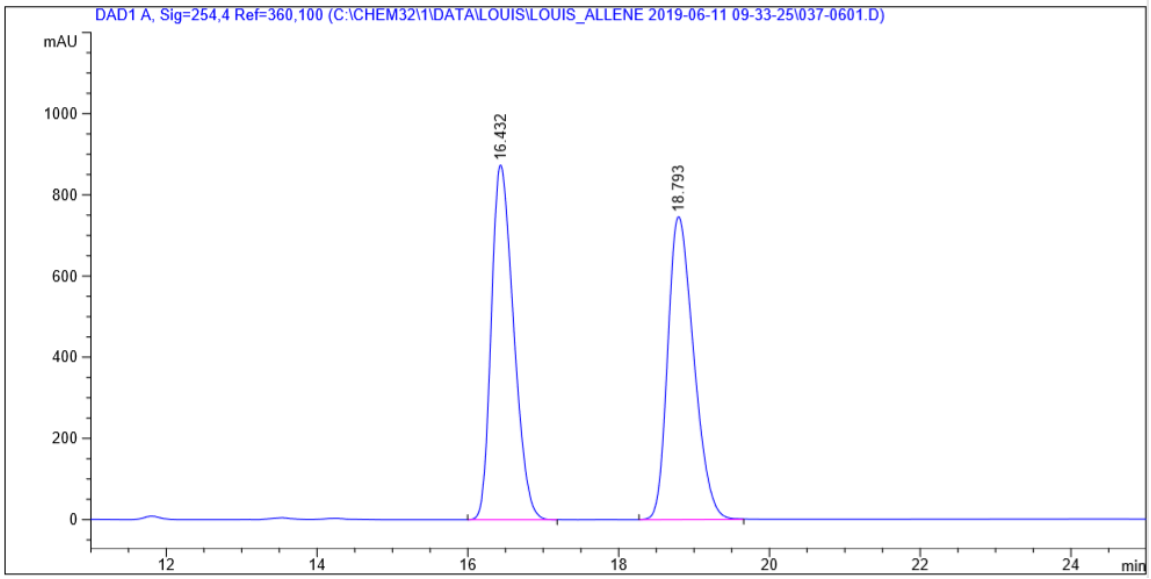
FTIR (neat): 3366, 3079, 2919, 1641, 1442, 992, 915, 867, 747, 697 cm^{-1}.

$[\alpha]_D^{28}$= –4.5 (*c* 0.2, $CHCl_3$).

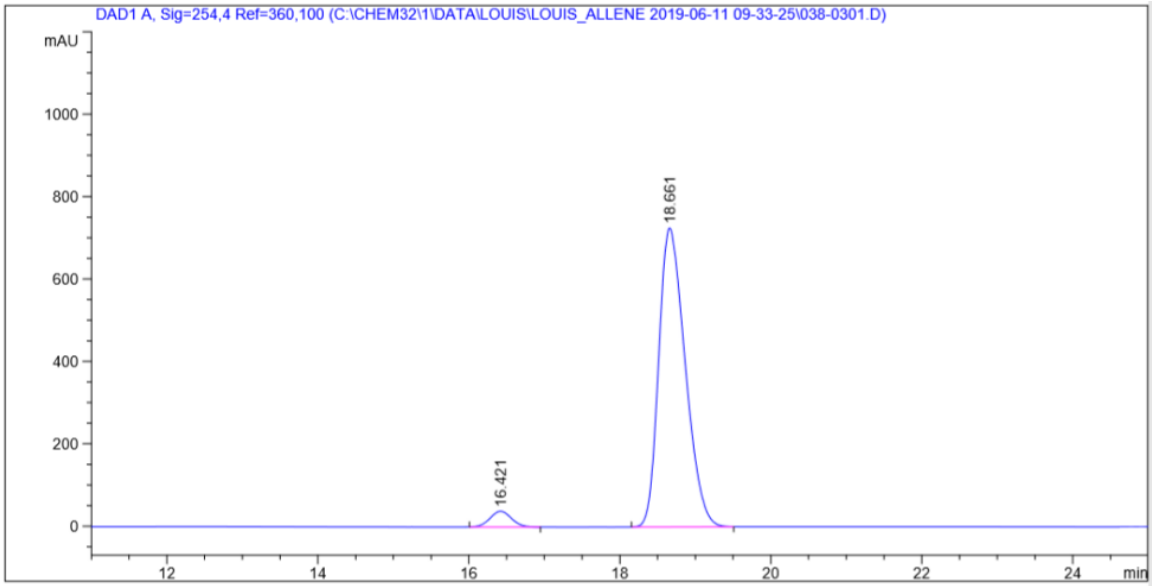
HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 254 nm), *ee* = 92%.


f1 (ppm)


139.47
137.51
134.50
128.97
128.08
126.43
125.72
118.07
76.52
40.09
13.68
f1 (ppm)

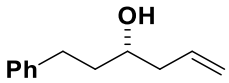


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.432	BB	0.3218	1.79583e4	873.86627	50.1739
2	18.793	BB	0.3707	1.78338e4	746.49213	49.8261



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.421	BB	0.3089	756.51782	38.21876	4.1088
2	18.661	BB	0.3800	1.76558e4	725.21521	95.8912

(*S*)-1-phenylhex-5-en-3-ol (8.3r)



Procedures

The aldehyde (26.8 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 °C, 48 hr). The title compound was obtained in 65% yield (22.9 mg, 0.13 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 20:1–10:1).

TLC (SiO_2) R_f = 0.45 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.29 (t, *J* = 7.6 Hz, 2H), 7.23 – 7.17 (m, 3H), 5.96 – 5.66 (m, 1H), 5.19 – 5.10 (m, 2H), 3.68 (tt, *J* = 7.7, 4.6 Hz, 1H), 2.82 (ddd, *J* = 13.8, 8.9, 6.6 Hz, 1H), 2.70 (dt, *J* = 13.8, 7.8 Hz, 1H), 2.33 (dddt, *J* = 13.7, 5.8, 4.3, 1.3 Hz, 1H), 2.19 (dt, *J* = 13.9, 7.9 Hz, 1H), 1.84 – 1.73 (m, 2H).

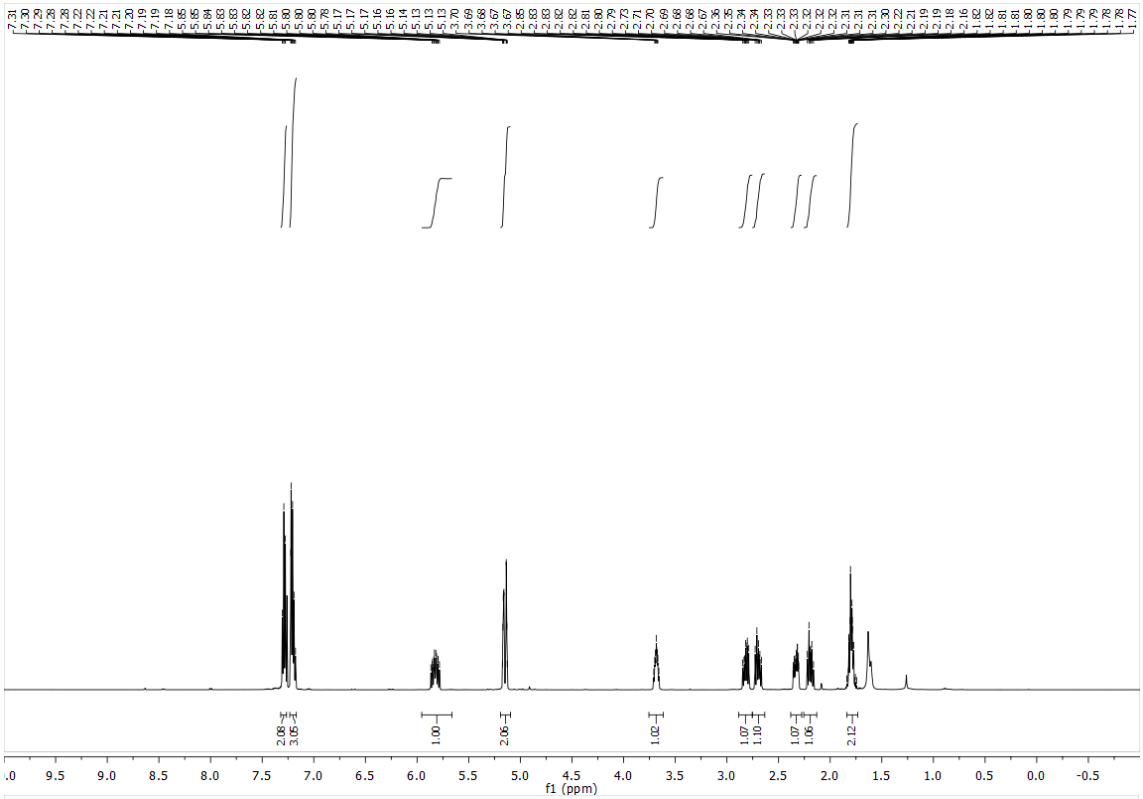
^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.0, 134.6 128.4, 128.4, 125.8, 118.3, 69.9, 42.1, 38.4, 32.0.

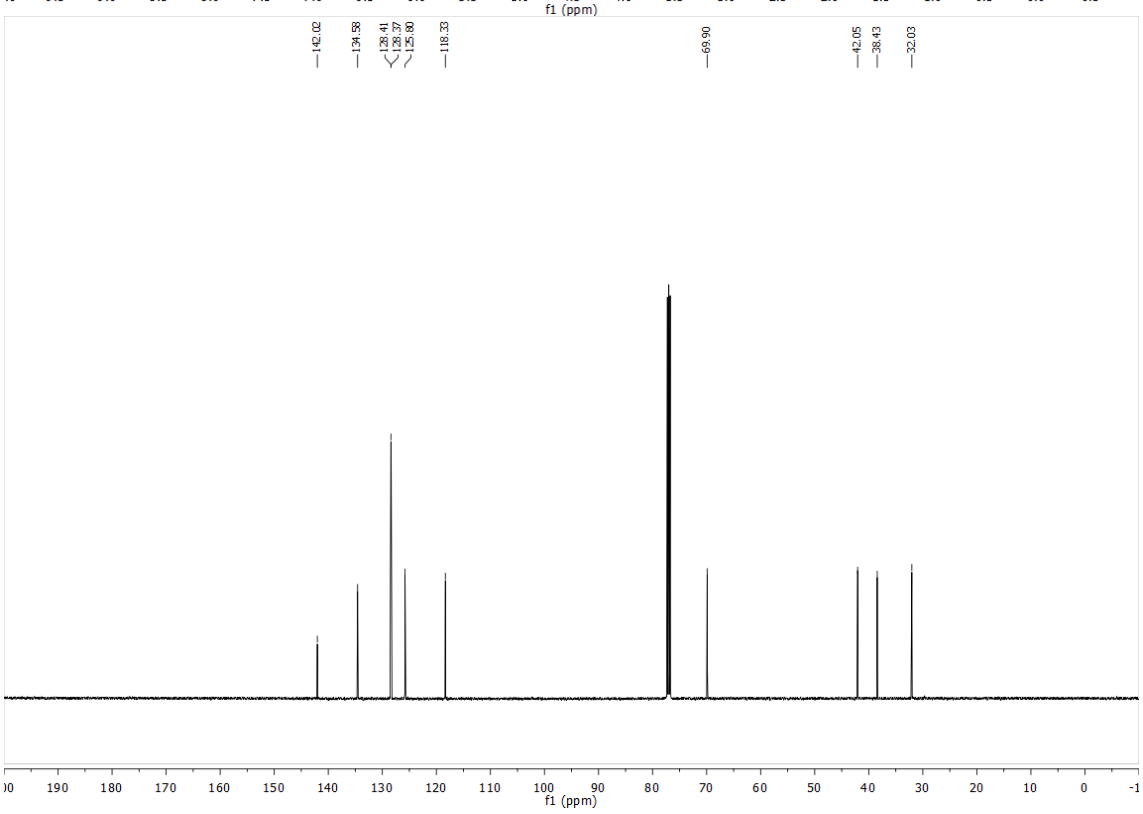
HRMS (ESI): Calculated for $C_{12}H_{16}O$ [M+Na^+] = 199.1093, Found 199.1096.

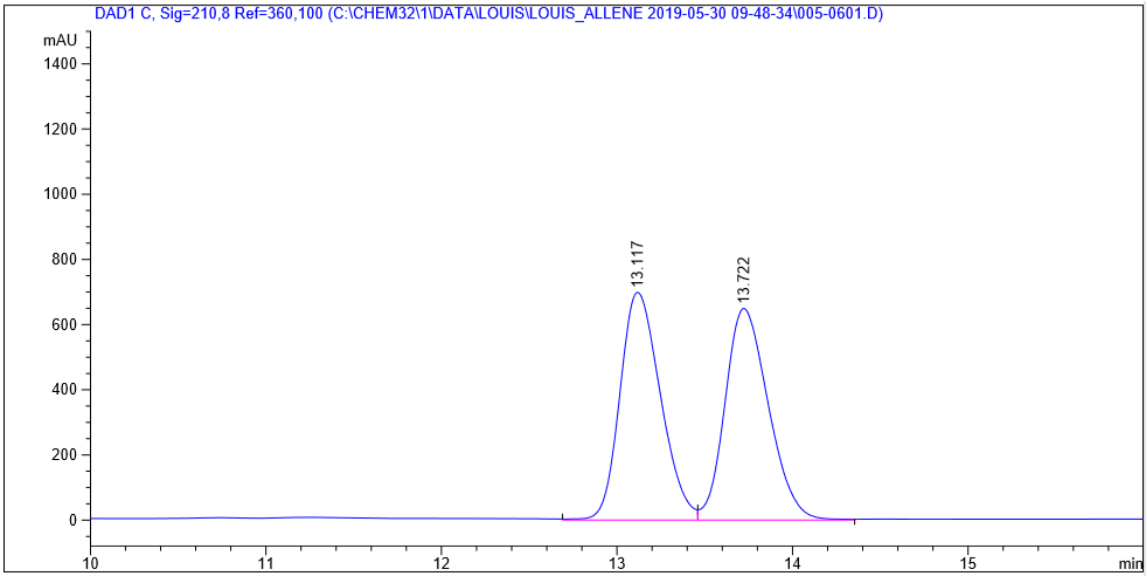
FTIR (neat): 3342, 3026, 2927, 1740, 1640, 1603, 1496, 1454, 1047, 994, 914, 746, 698 cm^{-1}.

$[\alpha]_D^{28}$ = –6.0 (*c* 0.2, $CHCl_3$).

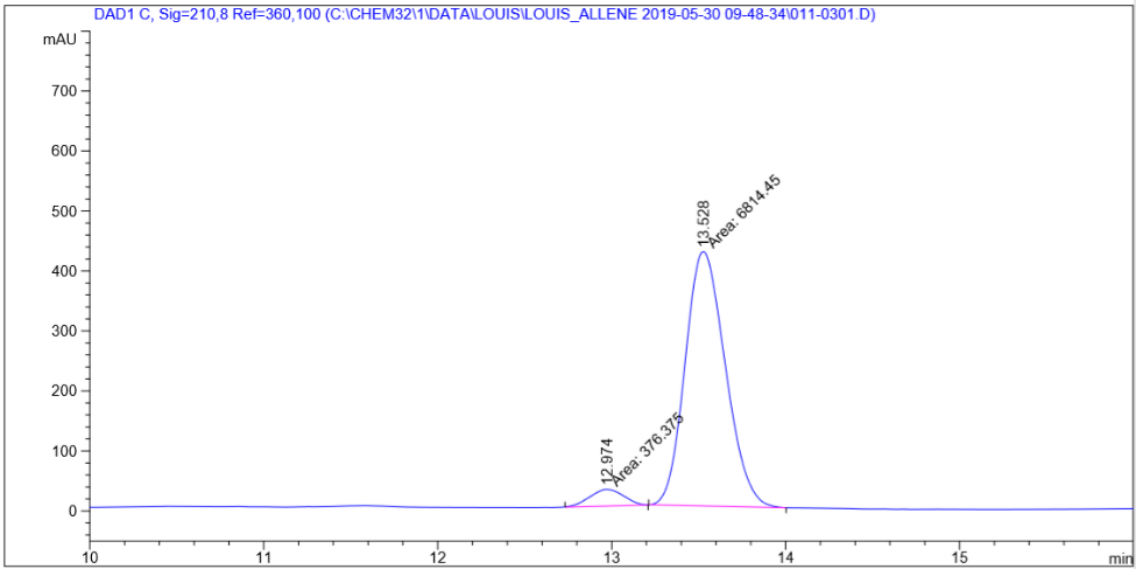
HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 98:2, 1.00 mL/min, 210 nm), *ee* = 90%.


2.08
3.05
1.00
2.06
1.02
1.07
1.10
1.07
1.06
2.12
f1 (ppm)


142.02
134.58
128.41
128.37
125.80
118.33
69.90
42.05
38.43
32.03
f1 (ppm)

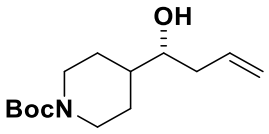


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.117	VV	0.2492	1.12127e4	698.88416	50.1759
2	13.722	VV	0.2660	1.11341e4	649.47003	49.8241



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.974	MM	0.2255	376.37531	27.81357	5.2341
2	13.528	MM	0.2677	6814.45020	424.24902	94.7659

tert-butyl (*R*)-4-(1-hydroxybut-3-en-1-yl)piperidine-1-carboxylate (8.3s)



Procedures

The aldehyde (42.7 mg, 0.20 mmol, 100 mol%) was subjected to standard reaction conditions (60 °C, 48 hr). The title compound was obtained in 71% yield (36.3 mg, 0.14 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 15:1–4:1).

TLC (SiO_2) R_f = 0.29 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.76 (dddd, *J* = 15.5, 11.5, 8.4, 6.1 Hz, 1H), 5.14 – 5.05 (m, 2H), 4.08 (s, 2H), 3.35 (ddd, *J* = 9.2, 6.1, 3.4 Hz, 1H), 2.59 (s, 2H), 2.29 (dddd, *J* = 14.1, 6.3, 3.2, 1.5 Hz, 1H), 2.06 (dt, *J* = 14.0, 8.4 Hz, 1H), 1.75 (dq, *J* = 11.3, 2.8 Hz, 1H), 1.54 (dt, *J* = 13.0, 3.0 Hz, 1H), 1.45 (ddq, *J* = 11.8, 5.7, 3.2 Hz, 1H), 1.39 (s, 9H), 1.26 – 1.14 (m, 2H).

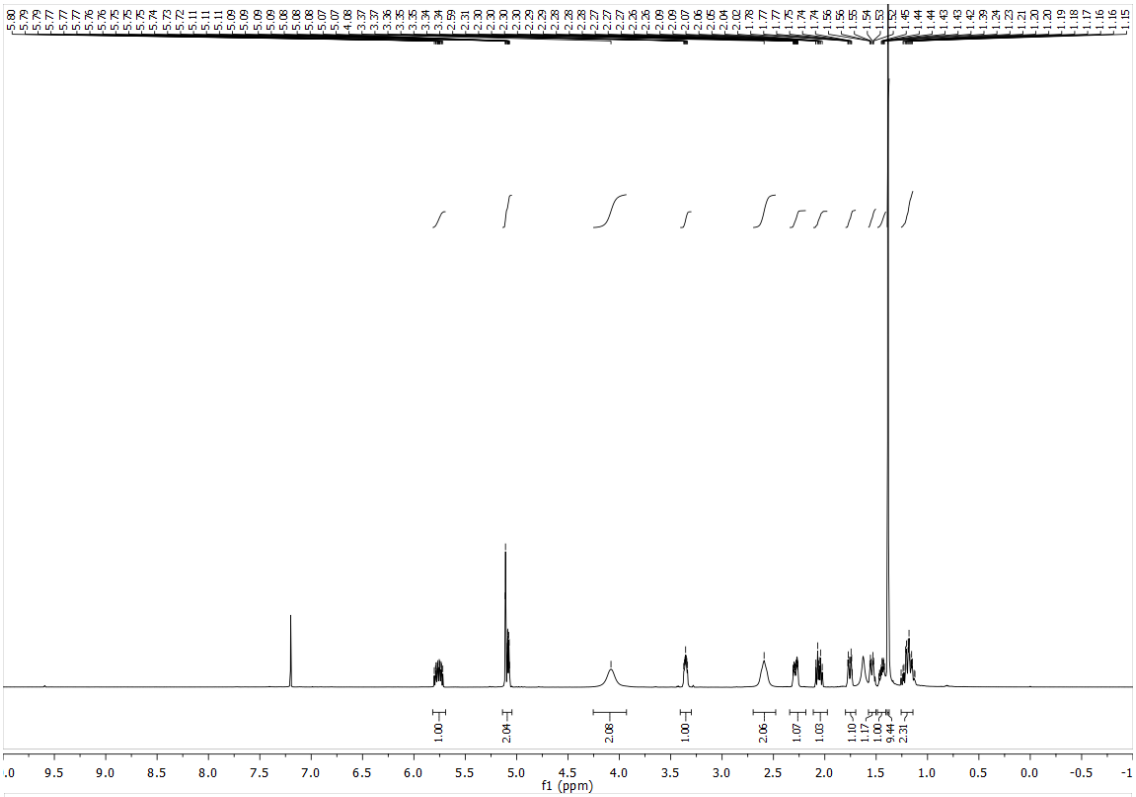
^{13}C NMR (125 MHz, $CDCl_3$): δ = 154.8, 134.8, 118.6, 79.3, 73.7, 43.8, 41.5, 38.8, 28.5, 28.1.

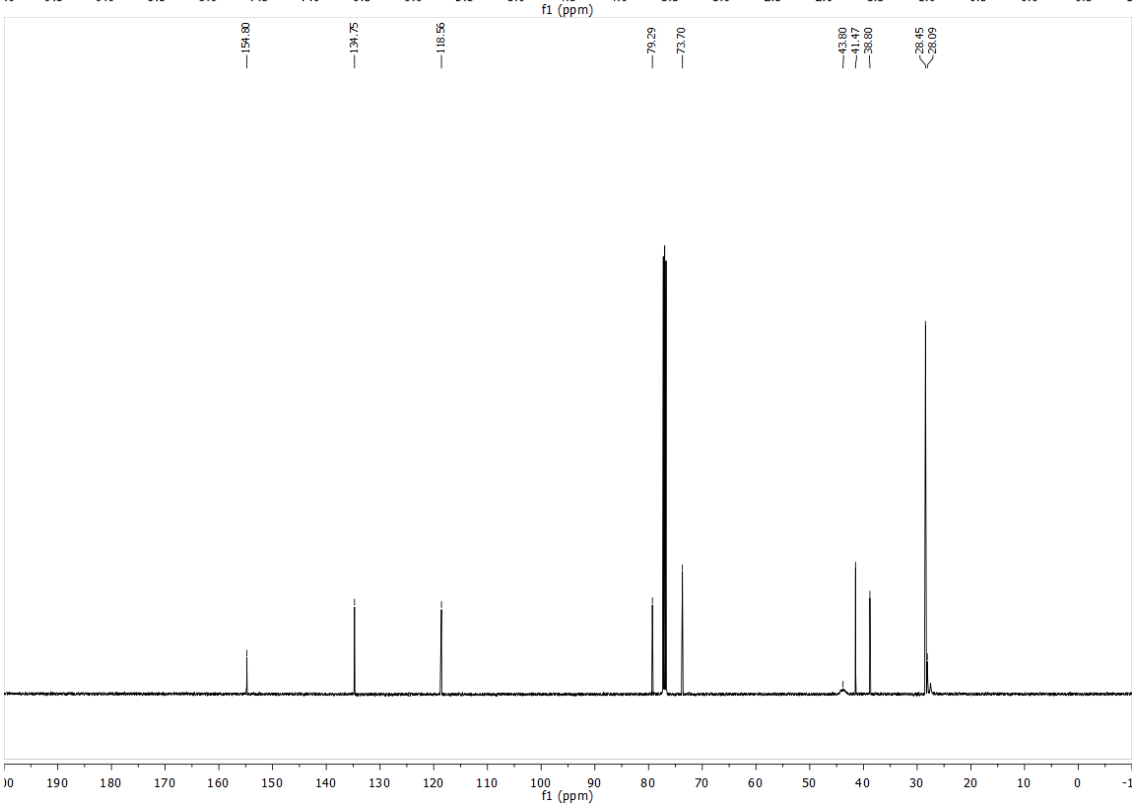
HRMS (ESI): Calculated for $C_{14}H_{25}NO_3$ [M+Na^+] = 278.1727, Found 2788.1726.

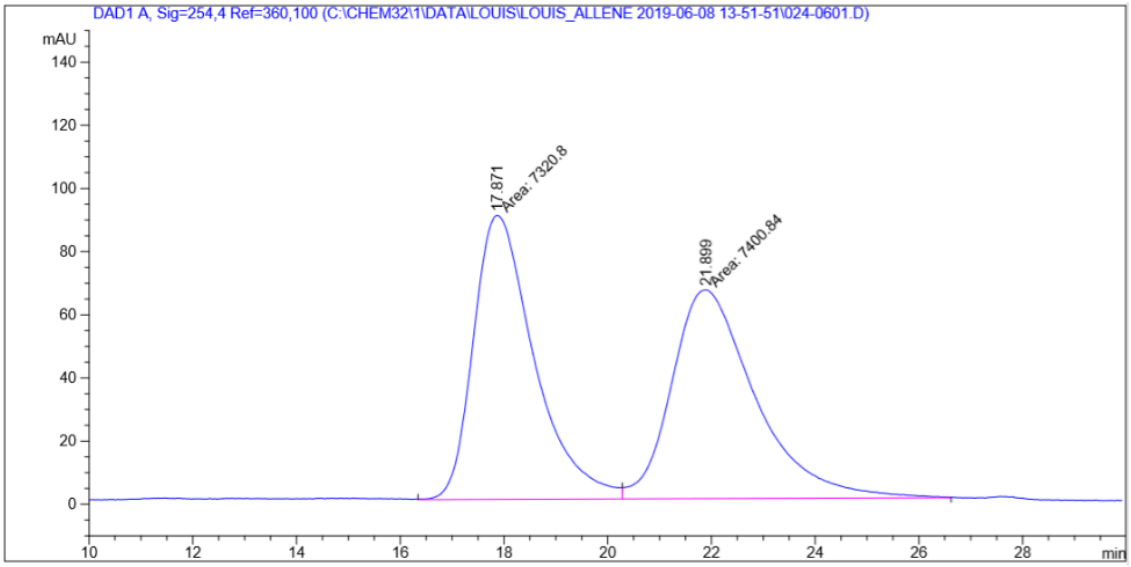
FTIR (neat): 3429, 2976, 2930, 2858, 1668, 1424, 1365, 1277, 1235, 1164, 982, 911, 866, 769 cm^{-1}.

$[\alpha]_D^{28}$= –10.6 (*c* 0.2, $CHCl_3$).

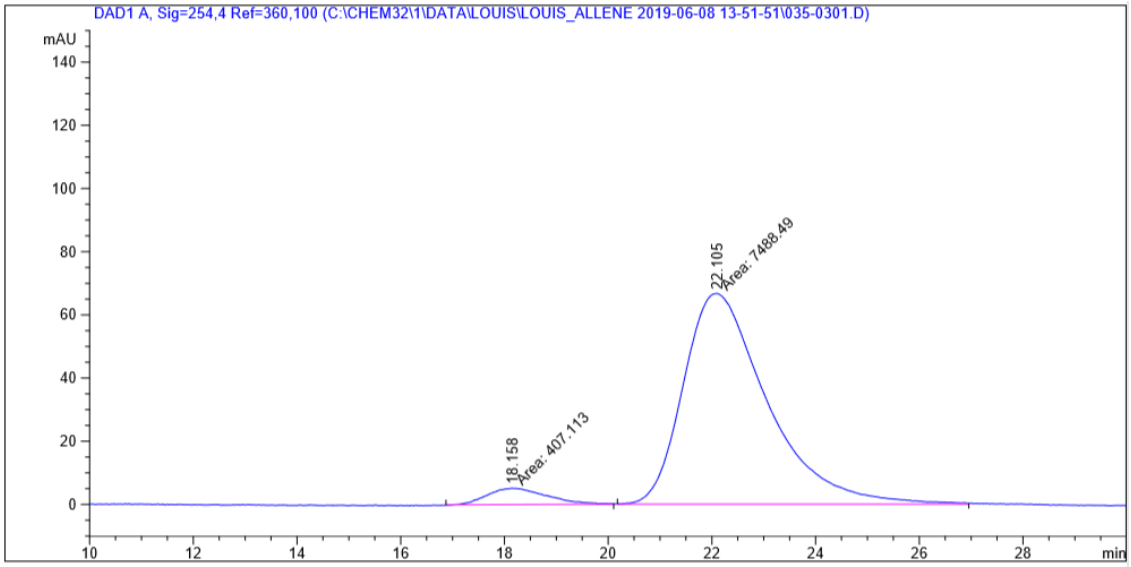
HPLC Enantiomeric excess was determined by HPLC analysis of the *p*-nitrobenzoyl derivative of the product (Chiralcel OJ-H column, hexanes:*i*-PrOH = 97:3, 1.00 mL/min, 254 nm), *ee* = 90%.


f1 (ppm)


154.80
134.75
118.56
79.29
73.70
43.80
41.47
38.80
28.45
28.09
f1 (ppm)



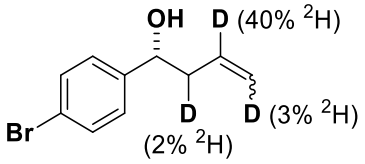
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.871	MF	1.3571	7320.79590	89.90734	49.7282
2	21.899	FM	1.8672	7400.83691	66.05918	50.2718



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.158	MM	1.3195	407.11264	5.14218	5.1562
2	22.105	MM	1.8715	7488.49023	66.68819	94.8438

Procedures and Spectral Data for Synthesis of *deuterio*-8.3a

(*R*)-1-(4-bromophenyl)but-3-en-3-d-1-ol (deuterio-8.3a)



Procedures

A pressure tube equipped with a magnetic stir bar was charged with aldehyde (32.4 mg, 0.20 mmol, 100 mol%) and **(*S*)-Ir-V** (11.2 mg, 0.01 mmol, 5 mol%). The tube was fit with a rubber septum. The tube was evacuated by piercing the septum with a needle connected to a Schlenk line. Immediately after evacuation, an allene balloon fitted with a needle was used to pierce the septum and refill the tube with allene gas. Under the allene balloon, toluene (2.0 mL, 0.1 M) was added followed by d_8-isopropylalcohol (31 µL, 0.4 mmol, 200 mol%). The septum was quickly removed and the tube was sealed with a PTFE lined cap. The tube was placed in an oil bath at 60 °C for 24 hours. The reaction was allowed to reach ambient temperature and concentrated *in vacuo*. The title compound was obtained in 86% yield (39.2 mg, 0.17 mmol) as a light yellow oil after isolation by flash column chromatography (SiO_2, hexanes: ethyl acetate = 25:1–8:1).

TLC (SiO_2) R_f = 0.45 (hexanes: ethyl acetate = 4:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = δ 7.50 – 7.44 (m, 2H), 7.25 – 7.20 (m, 2H), 5.91 – 5.64 (m, 1H), 5.23 – 5.08 (m, 2H), 4.70 (dd, *J* = 7.9, 5.0 Hz, 1H), 2.54 – 2.39 (m, 2H), 2.09 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.8, 133.9, 131.5, 127.5, 121.2, 118.8 (d, *J* = 17.0 Hz), 72.5, 43.8 (d, *J* = 15.1 Hz).

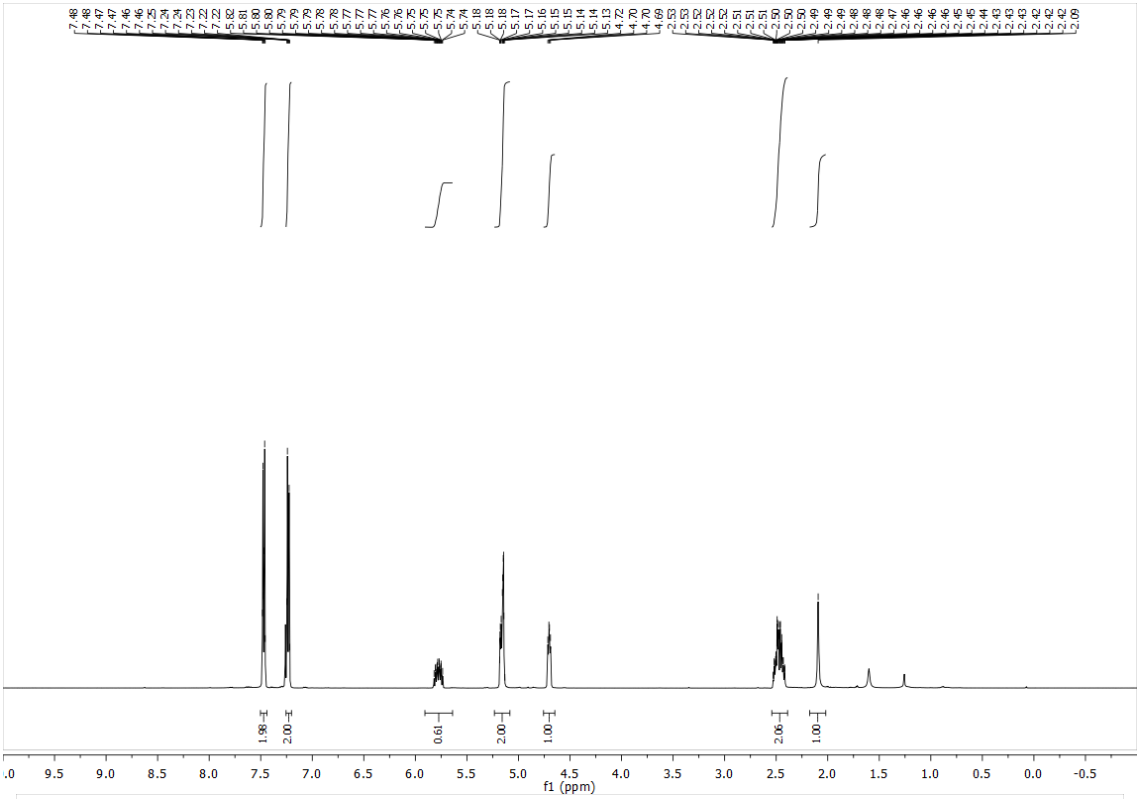
^{2}H NMR (92 MHz, $CHCl_3$): δ = 5.82, 5.20, 2.48 (d, *J* = 3.9 Hz)

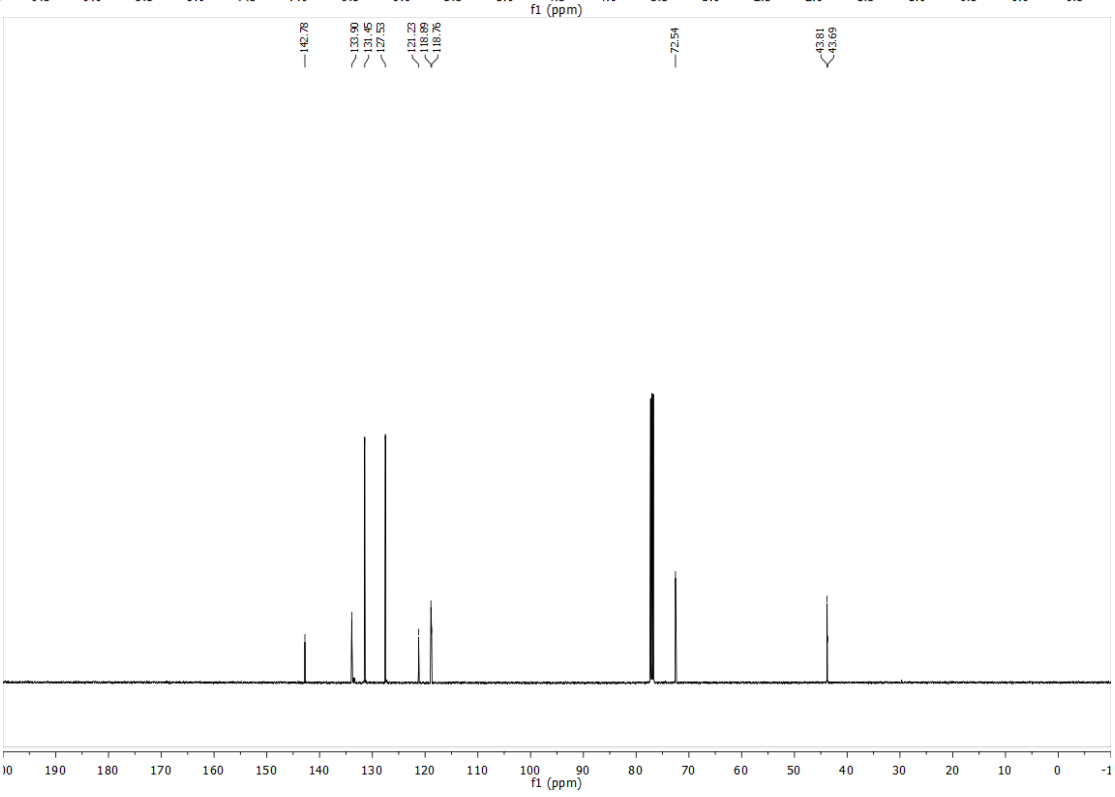
HRMS (EI): Calculated for $C_{10}H_{10}DBrO$ [M^+] = 227.0056, Found 227.0063.

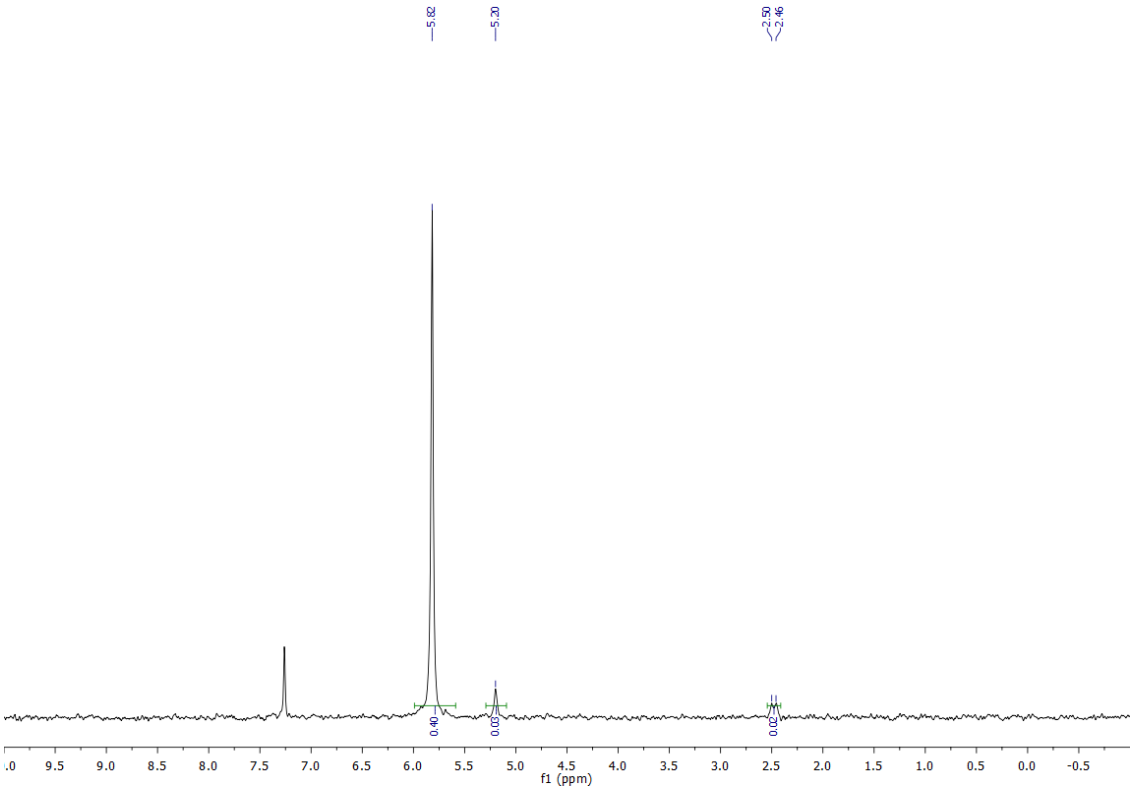
FTIR (neat): 3332, 3075, 2906, 1641, 1593, 1488, 1403, 1069, 1009, 917, 870, 821, 776, 717 cm^{-1}.

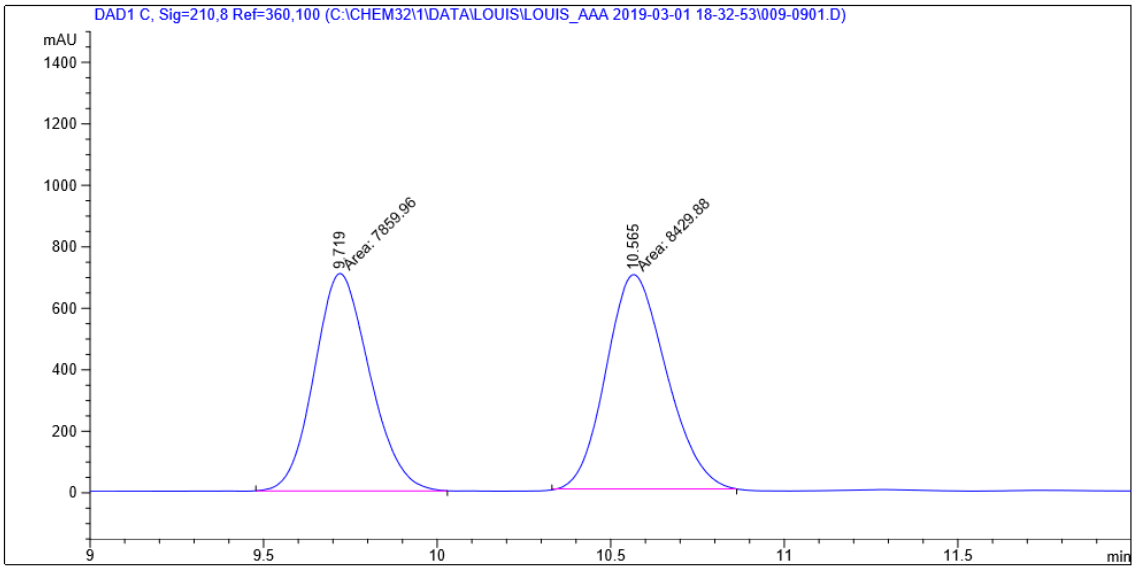
$[\alpha]_D^{28}$= +30.0 (*c* 0.2, $CHCl_3$).

HPLC (Chiralcel OJ-H column, hexanes:*i*-PrOH = 95:5, 1.00 mL/min, 210 nm), *ee* = 92%.

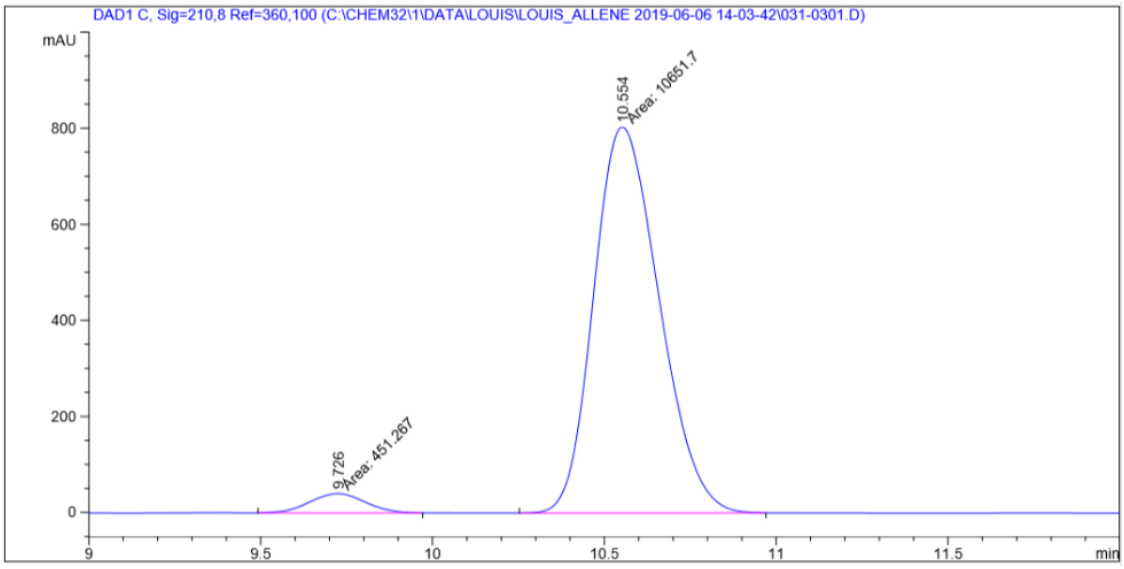

f1 (ppm)


f1 (ppm)


5.82
5.20
2.50
2.46
0.40
0.03
0.02
f1 (ppm)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.719	MM	0.1850	7859.96143	707.96680	48.2507
2	10.565	MM	0.2014	8429.87695	697.63104	51.7493



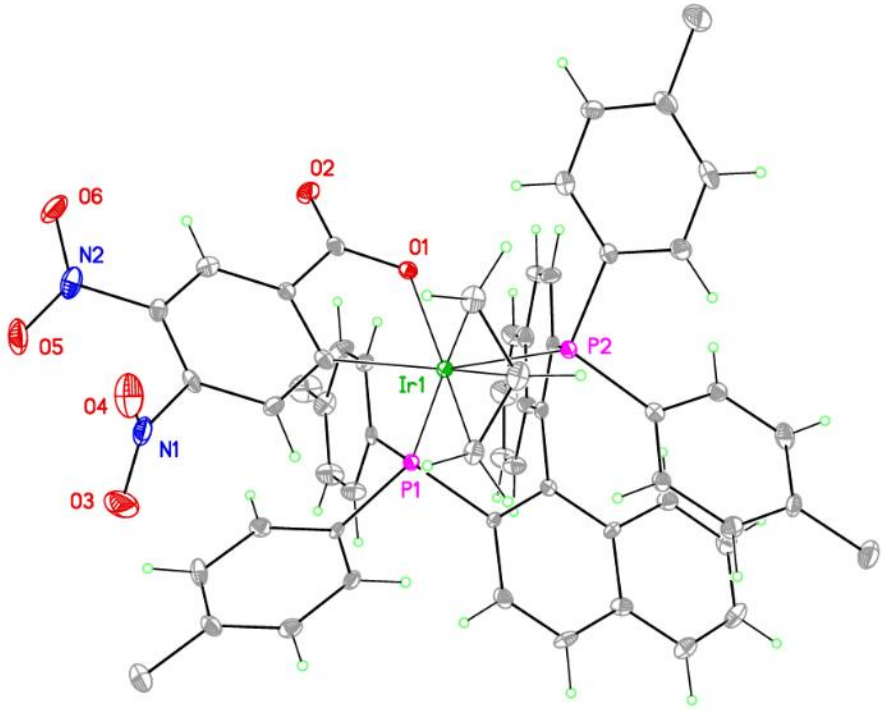
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.726	MM	0.1865	451.26709	40.33411	4.0644
2	10.554	MM	0.2208	1.06517e4	804.05157	95.9356

Single Crystal Diffraction Data for (S)-Ir-V Made from Allyl Acetate

Empirical formula	C72 H63 Ir N2 O6 P2	
Formula weight	1306.38	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 15.155(2) Å	α= 90°.
	b = 17.531(3) Å	β= 90°.
	c = 22.268(3) Å	γ = 90°.
Volume	5916.2(15) $Å^3$	
Z	4	
Density (calculated)	1.467 Mg/m^3	
Absorption coefficient	2.368 mm^{-1}	
F(000)	2656	
Crystal size	0.410 x 0.250 x 0.140 mm^3	
Theta range for data collection	1.776 to 27.877°.	
Index ranges	-19<=h<=19, -23<=k<=22, -29<=l<=29	
Reflections collected	168850	
Independent reflections	14106 [R(int) = 0.0595]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Numerical	
Max. and min. transmission	0.7723 and 0.5359	
Refinement method	Full-matrix least-squares on F^2	

Data / restraints / parameters	14106 / 777 / 819
Goodness-of-fit on F^2	1.045
Final R indices [I>2sigma(I)]	R1 = 0.0215, wR2 = 0.0353
R indices (all data)	R1 = 0.0261, wR2 = 0.0357
Absolute structure parameter	-0.0019(16)
Extinction coefficient	n/a
Largest diff. peak and hole	0.648 and -0.642 e.$Å^{-3}$

Figure S1. View of the Ir complex in **1** showing the heteroatom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level.



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Chapter 1

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Chapter 8 Supporting Information

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