BOSTON COLLEGE

The Graduate School of Arts and Sciences
Department of Chemistry

NOVEL CATALYTIC REACTIONS ENABLED BY METAL-INDUCED BORONATE REARRANGEMENT

a dissertation

by
CHUNYIN MARSHALL LAW

submitted in partial fulfillment of the requirements
for the degree of
Doctor of Philosophy

May 2020

NOVEL CATALYTIC REACTIONS ENABLED BY METAL-INDUCED BORONATE REARRANGEMENT

by
CHUNYIN MARSHALL LAW

Dissertation Advisor:
Professor James P. Morken

ABSTRACT: This dissertation will discuss the development of three methodologies that take advantage of the intrinsic reactivity of organoboron "ate" complex to undergo boronate rearrangement. The first chapter will describe a nickel-catalyzed conjunctive cross-coupling reaction between 9-BBN boranes and aryl halides. This process provides secondary organoboranes enantioselectively from readily available alkenyl starting materials. The second chapter will describe the development of conjunctive cross-coupling between 9-BBN boranes and acyl electrophiles. We will highlight its unique value in the syntheses of β-hydroxyl carbonyls and show that this reaction is complementary to the aldol reaction. In the third and last chapter of this manuscript, we report the conjunctive cross-coupling reaction of simple achiral borylenynes towards the enantio- and diastereoselective synthesis of α-borylallenes, which provides α-allenols upon oxidative workup.

TABLE OF CONTENTS

List of Abbreviations……...**vii**
1.0 Chapter 1: Development of Enantioselective Conjunctive Cross-Coupling of 9-BBN Borates…….....…….…..….....**1**
1.1 Introduction…….……...…….…**2**
1.2 Background…….....……....**3**
1.2.1 Preperation of 9-BBN Reagent…….…….....3
1.2.2 Regioselectivity of Hyroboration…….4
1.2.3 Reactions Governed by 1,2-Metallate Shift of Organoboranes…....6
1.2.4 Migration Selectivity with 9-BBN "Ate" Complexes…….....9
1.2.5 Preparation of Enantioenriched 9-BBN Derivatives……..11
1.2.6 1,2-Metallate Shift onto C(sp^2)-Hybridized Terminus……12
1.2.7 Properties of Organonickel Species……....15
1.2.8 Reactivity of Nickel in Cross-Coupling Reactions…….....17
1.2.9 Olefin-Nickel Complexes in Catalysis……...23
1.3 Nickel-Catalyzed Conjunctive Cross-Coupling of 9-BBN Borate……**25**
1.3.1 Initial Investigations……...25
1.3.2 Substrate Scope……..28
1.3.3 Mechanistic Studies……...33
1.3.4 Transformations of Chiral Secondary 9-BBN Borane……...35
1.3.5 Stereochemical Model of Ni-Catalyzed Conjunctive Coupling Reaction…….....38
1.3.6 Conclusion…….....40
1.4 Experimental Section……..……**41**
1.4.1 General Information……..41
1.4.2 Procedures for Preparation of Alkenyl Substrates……..……..43
1.4.3 Procedures for Preparation of Diamine Ligands……...47
1.4.4 General Procedure for Conjunctive Cross-Coupling……....50
1.4.5 Characterization of Conjunctive Cross-Coupling Products……..53
1.4.6 Procedures and Characterization for Transformations of 9-BBN Borane……..89
1.4.7 Deuterium-Labelling Experiment…….....95
1.4.8 Stoichiometric Experiment……...99
1.4.9 Spectral Data……...102

2.0 Chapter 2: Catalytic Conjunctive Coupling of Carboxylic Acid Derivatives And Derivatives with 9-BBN Ate Complexes…….....**168**
2.1 Introduction…….....**168**
2.2 Background……...……...**169**
2.2.1 Aldol Reactions to Access β-Hydroxyl Carbonyls……..169
2.2.2 Conjugate Borylation Reaction to Access β-Hydroxyl Carbonyls……..……...176
2.2.3 Carboxylic Acid Derivatives in Cross-Coupling Reacions…….180
2.2.4 Utility of Acyl Fluoride in Catalytic Cross-Coupling Reactions……..183
2.2.5 Activation of Ester by Nickel……...185
2.2.6 Activation of Amide by Nickel……187
2.2.7 Acyl Electrophiles in Ni-Catalyzed Reductive Cross-Coupling Reacions……188
2.3 Catalytic Conjunctive Coupling of Carboxylic Acid Derivatives with 9-BBN Ate Complexes……...……..……..**192**
2.3.1 Initial Investigations…….....192
2.3.2 Scope of Ni-Catalyzed Conjunctive Coupling With Acid Derivatives……194
2.3.3 Mechanistic Studies…….....198
2.3.4 Diastereoselective Boron-Enolate Alkylation……..201
2.3.5 Conclusion……..…….....……...204
2.4 Experimental Section……...……..…….**206**
2.4.1 General Information…….206
2.4.2 Procedures for Preparation of Acyl Electrophiles……..…....208
2.4.3 General Procedure for Conjunctive Cross-Coupling……...209
2.4.4 Characterization of Conjunctive Cross-Coupling Products…….211
2.4.5 Procedure and Characterization of Boron-Enolate Alkylation……229
2.4.6 Synthesis and Characterization of 9-BBN Schiff Base……231
2.4.7 Deuterium-Labelling Experiment……234
2.4.8 Stoichiometric Experiments…….239
2.4.9 Experiments with Chiral Bis(oxazoline) Ligands....……241
2.4.10 Spectral Data……246

3.0 Chapter 3: Enantioselective and Diastereoseletive 1,4-Difunctionalization Of Borylenynes by Catalytic Conjunctive Cross-Coupling…….....**303**
3.1 Introduction……..……....**303**
3.2 Background…….. **304**
3.2.1 Catalytic Enantioselective Syntheses of Chiral Allenes……..…304
3.2.2 Enantioselective Syntheses of α-Allenols……310

3.2.3 Halogen-Mediated 1,4-Addition to 1,3-Enynes……...314
3.3 Development of Catalytic Conjunctive Cross-Coupling of Borylenynes…… **317**
3.3.1 Reaction Discovery and Optimization……..317
3.3.2 Substrate Scope with Aryl Migration……320
3.3.3 Origin of Chemoseletivity: 1,4- *vs* 1,2-Acvitation Mode……..323
3.3.4 Optimization Studies and Substrate Scope of Alkyl Migration…325
3.3.5 Synthetic Utility of α-Allenols…….331
3.3.6 Conclusion……....332
3.4 Experimental Section……..……...**333**
3.4.1 General Information……..……...333
3.4.2 Procedure for Preparation of Borylenynes……...335
3.4.3 Representative Procedures for Conjunctive Coupling of Borylenynes…….346
3.4.4 Characterization of Conjunctive Cross-Coupling Products…….352
3.4.5 Procedure and Characterization for Transformation of α-Allenols……398
3.4.6 Spectral Data……405

LIST OF ABBREVIATIONS

Å: angstrom

Ac: acetate

Ar: aryl

acac: acetylacetone

aq: aqueous

B2(cat)2: bis(catecholato)diboron

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

BBD: borabicyclo[3.3.2]decanes

BBN: borabicyclo[3.3.1]nonane

BINOL: binaphthol

Bn: benzyl

Boc: *tert*-butoxycarbonyl

Boc_2O: di-*tert*-butyldicarbonate

Bz: benzoyl

cat: catechol

cod: cyclooctadiene

COSY: correlation spectroscopy

Cy: cyclohexyl

DART: direct analysis in real time

dba: dibenzylidene acetone

DCM: dichloromethane

DFT: density functional theory

DIBAL-H: di-*iso*-butylaluminum hydride

DMAP: 4-dimethylaminopyridine

DMF: dimethylformamide

dppe: 1,2-bis(diphenylphosphino)ethane

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

dppp: 1,3-bis(diphenylphosphino)propane

dr: diastereomeric ratio

ee: enantiomeric excess

eq: equation

equiv: equivalent(s)

er: enantiomeric ratio

ESI: electrospray ionization

Et_2O: diethyl ether

EtOAc: ethyl acetate

GLC: gas liquid chromatography

h: hour(s)

HPLC: high performance liquid chromatography

HRMS: high resolution mass spectrometry

Ipc: *iso*-pinocampheyl

IR: infrared spectroscopy

L: ligand

LG: leaving group

LiHMDS: lithium bis(trimethylsilyl) amide

M: molar or metal

NaHMDS: sodium bis(trimethylsilyl) amide

NHC: *N*-heterocyclic carbene

NMO: 4-methylmorpholine *N*-oxide

NMR: nuclear magnetic resonance

NOESY: nuclear overhauser effect spectroscopy

Nu: nucleophile

Ph: phenyl

pin: pinacol

PMA: phosphomolybdic acid

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

rt: room temperature

SFC: supercritical fluid chromatography

SiO_2: silica gel

TBDPS: *tert*-butyldiphenylsilyl

TBME: *tert*-butyl methyl ether

TBS: *tert*-butyldimethylsilyl

TEMPO: 2,2,6,6-Tetramethyl-1-piperidi-nyloxy

Tf: trifluoromethanesulfonyl

TFA: trifluoroacetyl

THF: tetrahydrofuran

TMEDA: tetramethylethylenediamine

TMSCl: trimethylsilyl chloride

TPAP: tetrapropylammonium perruthenate

TS: transition state

Xantphos: 4,5-Bis(diphenylphosphino)-9,

9-dimethylxanthen

1.0 CHAPTER 1

1.0 CHAPTER 1

DEVELOPMENT OF AN ENANTIOSELECTIVE CONJUNCTIVE CROSS-COUPLING OF 9-BBN BORATES

1.1 Introduction

Organoboron compounds are highly versatile synthetic intermediate, for the reason that the C-B bond has the ability to be transformed into a wide variety of functional groups. Aside from its most well-known use as a nucleophilic reagent in Suzuki-Miyaura cross-coupling reactions, it is also well documented to undergo a wide variety of transition-metal free transformations.[1] The ability to control the stereogenicity of boron-containing carbon would allow access to a variety of enantioenriched compounds containing different functional groups. For this reason, the development of methods that allow for the enantioselective and efficient access to organoboron compounds is an important area of ongoing research. In recent years, significant research has focused on the development of methods to provide enantioenriched secondary organoboronic esters.[2] Organoboronic esters have the advantage of being air-stable and at the same time being able to unveil their latent reactivity upon activation by an activator. With regards to trialkyl organoborane compounds, despite their instability under ambient atmosphere, they possess a more

[1] (a) Leonori, D.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2014**, *54*, 1082. (b) Sandford, C.; Aggarwal, V. K. *Chem. Commun.* **2017**, *53*, 5481. (c) Armstrong, R. J.; Aggarwal, V. K. *Synthesis* **2017**, *49*, 3323.
[2] Collins, B. S. L.; Wilson, C. M.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2017**, *56*, 11700.

electrophilic boron center which allows for unique transformations that cannot be achieved with its organoboronic ester counterparts. In addition, trialkyl boranes can be accessed by direct hydroboration of the corresponding alkenes without necessity of a transition-metal catalyst. Despite their useful characteristics, no available catalytic method for the generation of enantioenriched trialkyl organoborane compounds has been reported. In 2016, the Morken group reported a new class of reactions that are triggered by a Pd-induced 1,2-boronate rearrangement, termed "conjunctive cross-coupling", to generate enantioenriched secondary organoboronic ester compounds.[3] As an effort to expand the scope of this reaction to address existing synthesis challenges, we leveraged conjunctive coupling reaction to access 9-BBN boranes enantioselectively with nickel as the catalyst. This chapter will discuss the work on the development of nickel-catalyzed conjunctive coupling reaction of 9-BBN boranes, as well as precedented reactivities of nickel catalysts that guided us in the development of the reaction.

1.2 Background

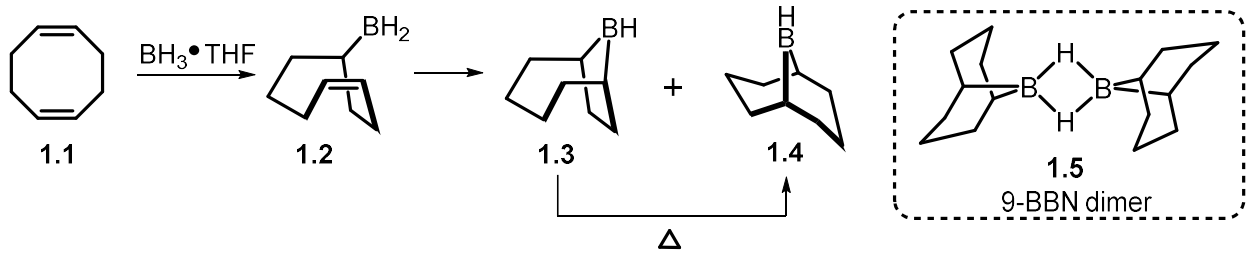
1.2.1 Preparation of 9-BBN Reagent.

There are numerous commercially available trialkylboranes. Among all of them, 9-bora-bicyclo[3.3.1.]nonane (9-BBN) is the one most frequently used in hydroboration[4],

[3] Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. *Science* **2016**, *351*, 70.
[4] Knights, E. F.; Brown, H. C., *J. Am. Chem. Soc.* **1968**, *90*, 5280. (b) Knights, E. F.; Brown, H. C., *J. Am. Chem. Soc.* **1968**, *90*, 5281.

metal-catalyzed cross-coupling reaction[5], as well as transformations based upon 1,2-metallate shift (will be discussed in the next section). 9-BBN is prepared by hydroboration of 1,5-cyclooctadiene **1.1** with BH_3 borane (Scheme 1.1).[3] The initial hydroboration results in a mixture of regioisomers, 9-bora-bicyclo[3.3.1.]nonane **1.4** and the undesired 9-bora-bicyclon[4.2.1.]nonane **1.3**, with the later favored as the kinetic product. However, the [4.2.1] bicyclo ring system isomerizes to the more thermodynamically stable [3.3.1] system upon prolonged heating. Similar to other related borane reagents, 9-BBN itself exists as a dimeric structure **1.5** and engages in three-center two-electron bonding mode. However, the monomeric form can be accessed in the presence of Lewis basic solvent such as THF, which occupies the empty p-orbital of boron.

Scheme 1.1 Preparation of 9-BBN Borane



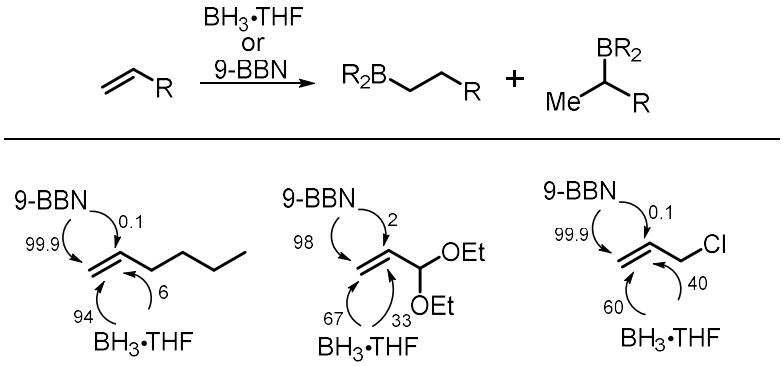
1.2.2 Regioselectivity of Hydroboration.

Due to its steric bulk, 9-BBN borane is capable of hydroborating alkenes with excellent regioselectivity.[6] For comparison (Scheme 1.3), hydroboration with BH_3-THF usually affords lower regioselectivity, with electronic properties of alkenyl substrates being an

[5] Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem. Int. Ed.* **2001**, *40*, 4544.
[6] Thomas, S. E. in *Organic Synthesis The Roles of Boron and Silicon*, Oxford Science Publications, **1991**, pp. 5.

influential factor in the observed regioselectivity. Coupled with the ease of oxidation of C-B moiety, 9-BBN is often a reagent of choice for a net regioselective hydration of alkenes.

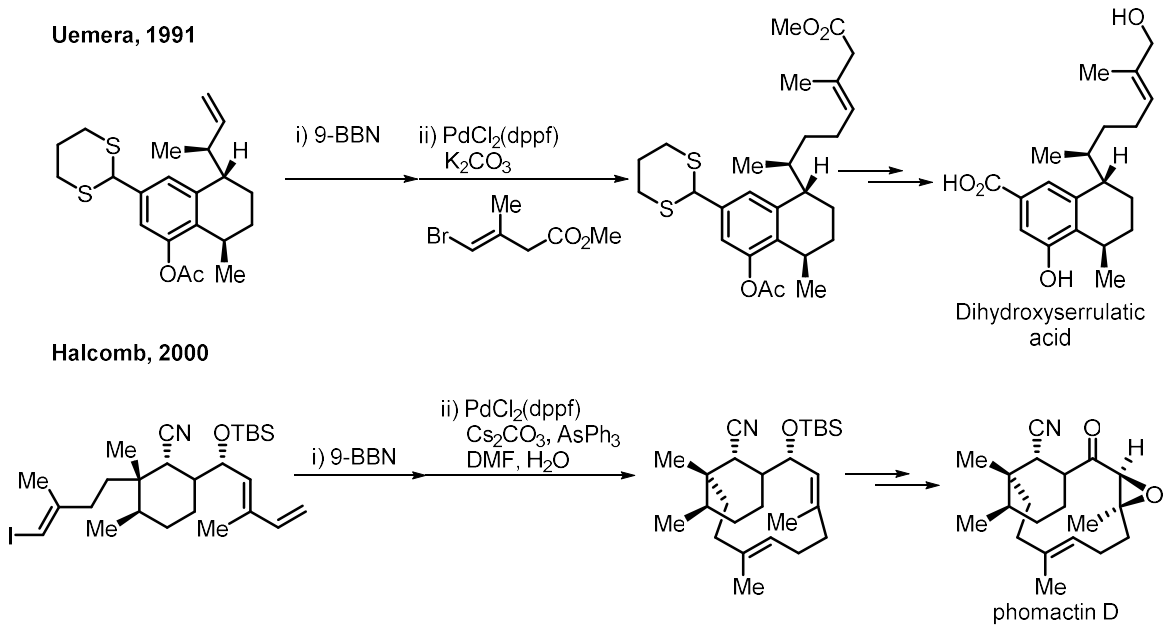
Scheme 1.3 Regioselectivity of Hydroboration with 9-BBN and BH_3



In addition, the ease of preparation of 9-BBN via regioselective hydroboration also facilitates its prevalent use as a nucleophilic reagent in Suzuki-Miyaura coupling reactions.[4] The two-stage hydroboration/cross-coupling sequence has been utilized to connect together sp^2- and sp^3-hybridized carbons in the context of complex molecule synthesis, as exemplified by the syntheses of dihydroxyserrulatic acid[7] and phomactin D.[8]

[7] (a) Uemura, M.; Nishimura, H.; Hayashi, Y. *Tetrahedron Lett.* **1990**, *31*, 2319. (b) Uemura, M.; Nishimura, H.; Minami, T.; Hayashi, Y. *J. Am. Chem. Soc.* **1991**, *113*, 5402.
[8] Kallen, N. C.; Halcomb, R. L. *Org. Lett.* **2000**, *2*, 2687.

Scheme 1.4 Use of 9-BBN in Suzuki-Miyaura Cross-Coupling Reaction

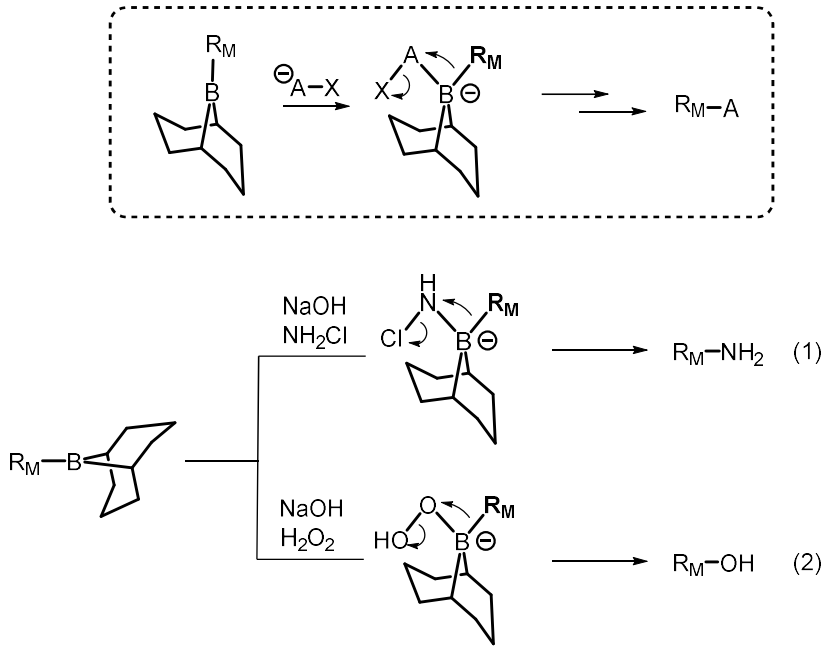


1.2.3 Reactions Governed by 1,2-Metallate Shift of Organoboranes.

Aside from hydroboration reaction, much of the reactivity that organoboranes possess is governed by the ability of boron "ate" complex to undergo 1,2-metallate shift. As shown in Scheme 1.3, the 4-coordinate boron "ate" complex derived from the addition of a nucleophile bearing an appended leaving group would undergo 1,2-metallate shift. During the process, a carbon ligand would undergo migration to form the new "C-A" bond. Some of the most common transformations of organoboranes notably oxidation (eq.1, Scheme 1.3) and amination reactions[9] (eq. 2, Scheme 1.3) are governed by this reactivity.

[9] Brown, H. C.; Kim, K.-W.; Srebnik, M.; Singaram, B. *Tetrahedron* **1987**, *43*, 4071.

Scheme 1.3 General Scheme of 1,2-Metallate Shift

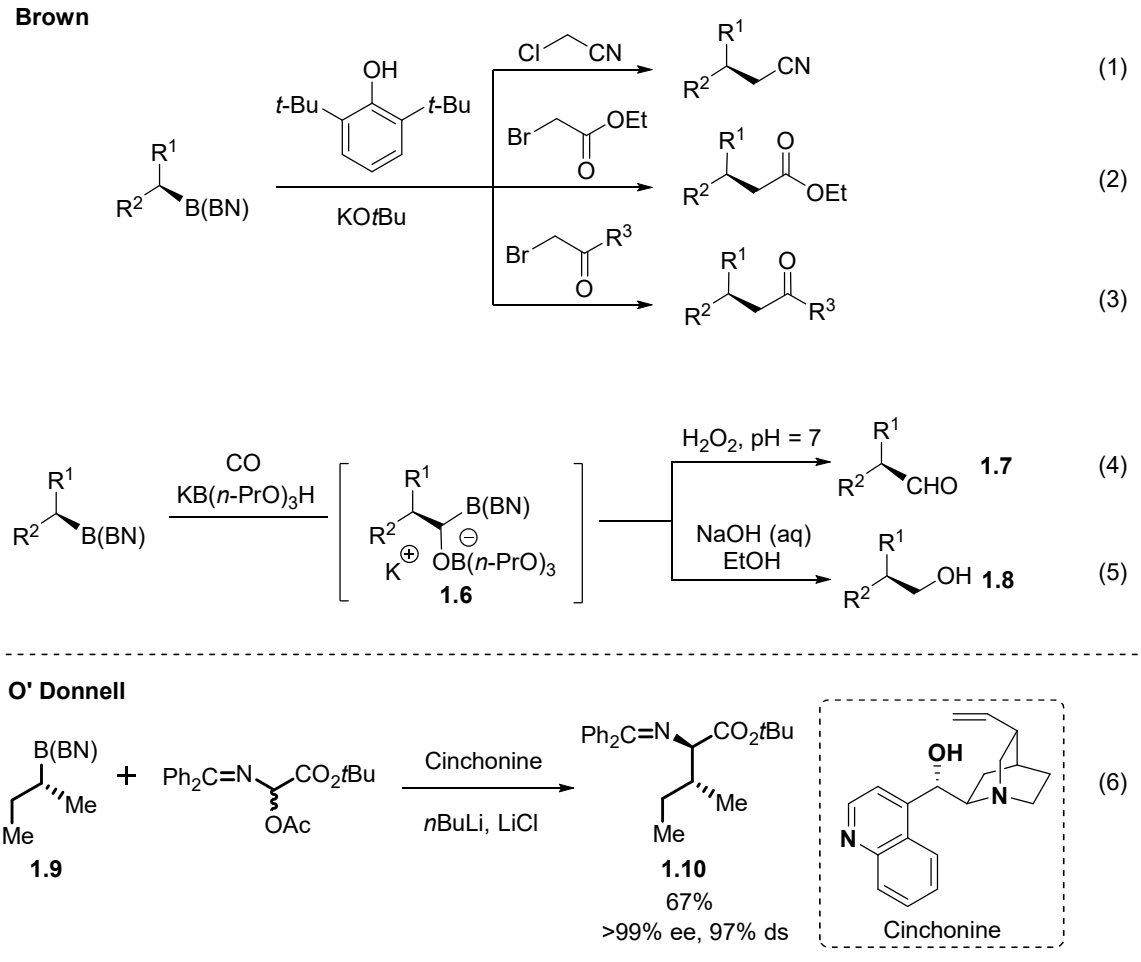


As mentioned earlier, trialkylboranes possess a more electrophilic boron center compared to organoboronic ester counterparts. This feature has allowed for the efficient formation of boron "ate" complex derived from enolate-based nucleophiles (Scheme 1.4, eq. 1-3).[10] Subsequent 1,2-metallate shift then allows for the efficient synthesis of homologated products with stereoretention. H. C. Brown also reported a series of carbon monoxide based homologation reactions.[11] Under the reaction conditions, the boron "ate" complex generated from addition of carbon monoxide, undergoes 1,2-metallate shift and, in the presence of $KBH(OMe)_3$, generates α-hydroxyl boryl intermediate **1.6**. This intermediate could be oxidized to the corresponding aldehyde **1.7** or hydrolyzed to the homologated product **1.8**. A recent report by O'Donnell took advantage of the unique

[10] (a) Brown, H. C.; Hubbard, J. L.; Smith, K. *Synthesis* **1979***,* 701. (b) H. C. Brown, H. C.; Ford, T. M.; Hubbard. J. L. *J. Org. Chem.***1980**, *45*, 4067.
[11] (a) Brown, H. C.; Nambu, H.; Rogic, M. M. *J. Am. Chem. Soc.* **1969***, 91*, 6852. (b) Brown, H. C.; Nambu, H.; Rogic, M. M. *J. Am. Chem. Soc.* **1969***, 91*, 6854. (c) Brown, H. C.; Nambu, H.; Rogic, M. M. *J. Am. Chem. Soc.* **1969***, 91*, 6855. (d) Herbert C. Brown, H. C.; Joshi, N. N.; Pyun, C.; Singaram, B. *J. Am. Chem. Soc.***1989**, *111,* 1754.

reactivity of 9-BBN in the homologation reaction with α-acetoxy/imine derivatives of glycine *tert*-butyl ester. This process affords various amino acid derivatives with excellent stereoselectivity. [12] Protonation by *Cinchona* alkaloid was proposed to be the stereochemistry-determining step and control the configuration of the newly formed stereocenter. It is noteworthy, that in these reactions the bicyclooctyl ligand on boron serves as an inert spectator group on boron, a feature that makes 9-BBN borane an appealing reagent compared to other boranes.

Scheme 1.4 Stereospecific Transformations of Secondary 9-BBN



[12] (a) O'Donnell, M. J.; Drew, M. D.; Cooper, J. T.; Delgado, F.; Zhou, C. *J. Am. Chem. Soc.* **2002**, *124*, 9348. (b) O'Donnell, M. J.; Cooper, J. T.; Mader, M. M. J. Am. Chem. Soc. **2003**, *125*, 2370.

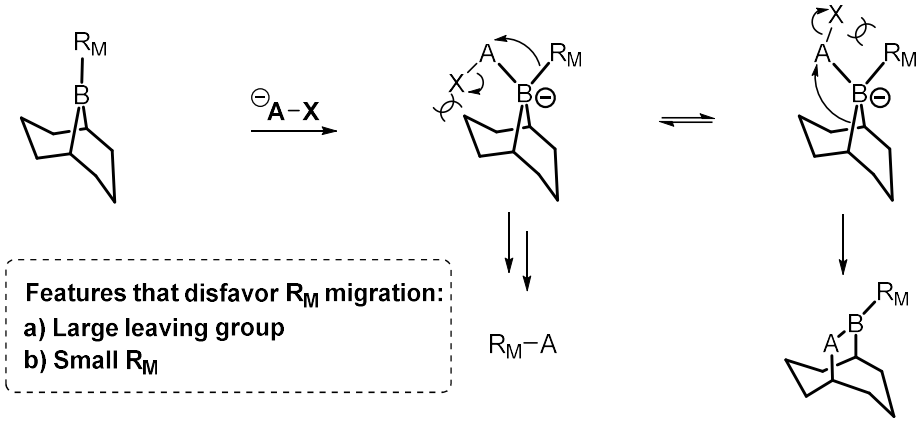
1.2.4 Migration Selectivity with 9-BBN "Ate" Complexes.

To fully reveal the potential of 9-BBN reagents in synthesis, the bicyclooctyl ligand on 9-BBN would be inert to migration. Indeed, there is an inherent steric penalty for the migration of the bicyclooctyl ligand in the reactions mentioned earlier. This selectivity was proposed to be due to additional torsional strain that would result from ring expansion of [3.3.1] fused ring system to a [3.3.2] fused system. However, there are instances when the bicyclooctyl ligand would out-compete the other carbon ligand for migration and this leads to a mixture of constitutional isomers. Several factors influence the relative rates of migrations of different ligands on boron and the final product distribution may not be readily predictable. With regards to electronic effects, the carbon ligand that can most stabilize negative charge would in theory be favored for migration and thus the reactivity would follow the order of $C(sp^2)$ > primary $C(sp^3)$ > secondary $C(sp^3)$ > tertiary $C(sp^3)$.[13] However, as in the case of vinylidenation reaction with iodine, the relative rate of migration of secondary carbon ligand is higher than that of primary carbon ligand, pointing to additional elements that affect product distribution.[14] To explain the relative rates of migration, Slayden invoked the stability of conformers of boron "ate" complex prior to 1,2-metallate shift as an important factor (Scheme 1.4). If the requisite conformer for migration of R_M group suffers substantial steric penalty, the bicyclooctyl ligand would compete for migration. Due to this reason, reactions such as aminations[15], homologations with

[13] Aggarwal, V. K.; Fang, G. Y.; Ginesta, X.; Howells, D. M.; Zaja, M. *Pure Appl. Chem.*, **2006**, *78*, 215.
[14] Slayden, S. W. *J. Org. Chem.* **1981,** *46*, 2311.
[15] (a) Brown, H. C.; Midland, M. M.; Levy, A. B. *Tetrahedron* **1987**, *43*, 4079. (b) Genet, J. P.; Hajicek, J.; Bischoff, L.; Greck, C. *Tetrahedron Lett*. **1992**, *33*, 2677.

iodonium ylide[16] and diazo compounds[17], as well as vinylidenation with α-methoxvinyl lithium[18] give poor yields of the desired products.

Scheme 1.5 Conformational Stability As a Factor of Migration Selectivity

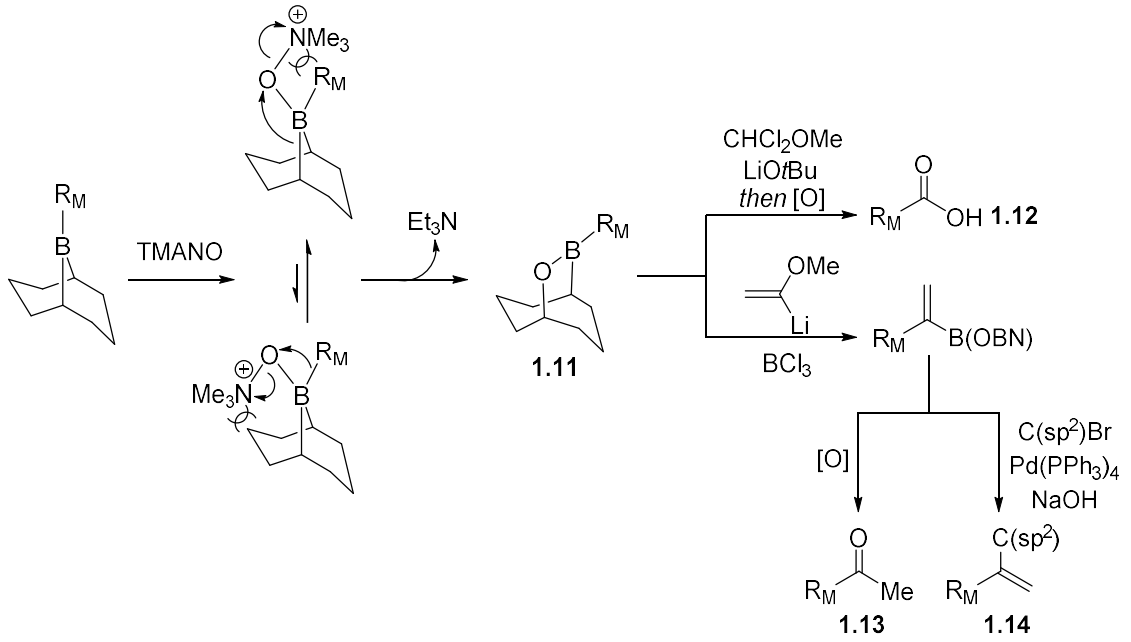


To circumvent the problem of migration selectivity, Soderquist devised a strategy that employs the intermediacy of borinates (Scheme 1.6, **1.11**), which could be conveniently generated by mixing the 9-BBN borane with the bulky oxidizing reagent TMANO.[19] For steric reason, this reaction proceeds with exclusive cyclooctyl ligand migration to generate the borinic ester with a [3.3.2] fused ring system. This borinic ester was then demonstrated to undergo homologation reactions with various reagents with the exclusive migration of R_M group. The product distribution is independent of the electronic and steric properties of the R_M group, as the addition of torsional strain that arises during ring expansion from [3.3.2] bicycle to [3.3.3] bicycle, prevents the bicycle from migration. The borinic ester intermediate has been employed for selective homologation reactions to form the

[16] Ochiai, M.; Tuchimoto, Y.; Higashiura, N. *Org. Lett.* **2004**, *6,* 1505.
[17] Hoos, J.; Gunn, D. M. *Tetrahedron Lett*. **1969**, *40*, 3455.
[18] Soderquist, J. A.; Rivera, I. *Tetrahedron Lett*. **1989**, *30*, 3919
[19] Soderquist, J. A.; Najafi, M. R. *J. Org. Chem*. **1986**, *51*, 1330.

corresponding carboxylic acid **1.12**[20] and 1,1-disubstituted borinate **1.13**[21], which could be further functionalized to the methyl ketone **1.14** or 1,1-disubstituted alkene **1.15** through Suzuki-Miyaura coupling reaction.

Scheme 1.6 Preparation and Utility of Soderquist Borinic Ester



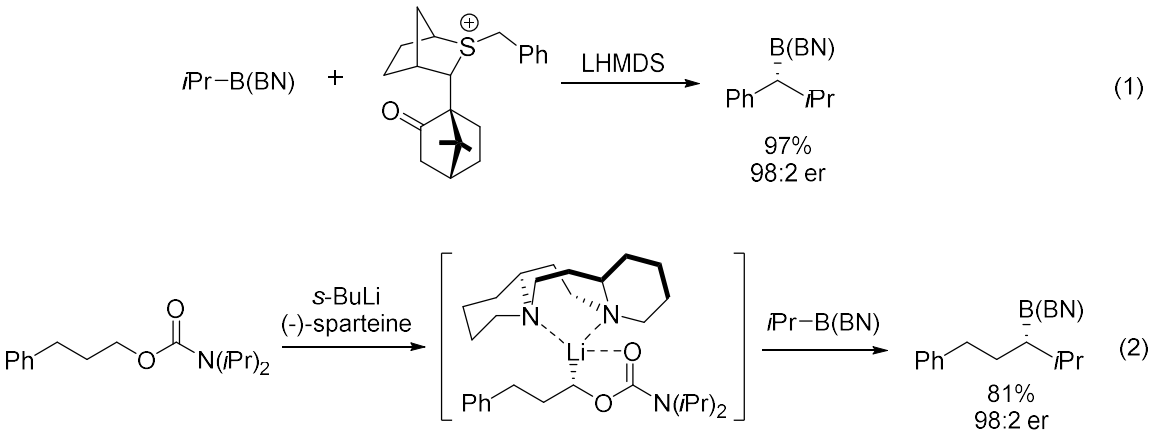
1.2.5 Preparation of Enantioenriched 9-BBN Derivatives.

Surprisingly, given the exciting reactivity of 9-BBN organoboranes, there are only limited examples of its enantioselective synthesis. To the best of our knowledge, the only enantioselective synthesis of 9-BBN relies on the homologation reaction with

[20] Soderquist, J. A.; Martinez, J.; Oyola, Y.; Kock, I. *Tetrahedron Lett.* **2004**, *45*, 5541.
[21] Soderquist, J. A.; Ramos, J.; Matos, K. *Tetrahedron Lett.*, **1997**, *38, 6639.*

stoichiometric chiral reagents such as sulfur ylides[22] (Scheme 1.7, eq. 1) and sparteine[23] (Scheme 1.7, eq. 2), as reported by Aggarwal.

Scheme 1.7 Preparation of Enantioenriched 9-BBN



1.2.6 1,2-Metallate Shift onto C(sp^2)-Hybridized Terminus.

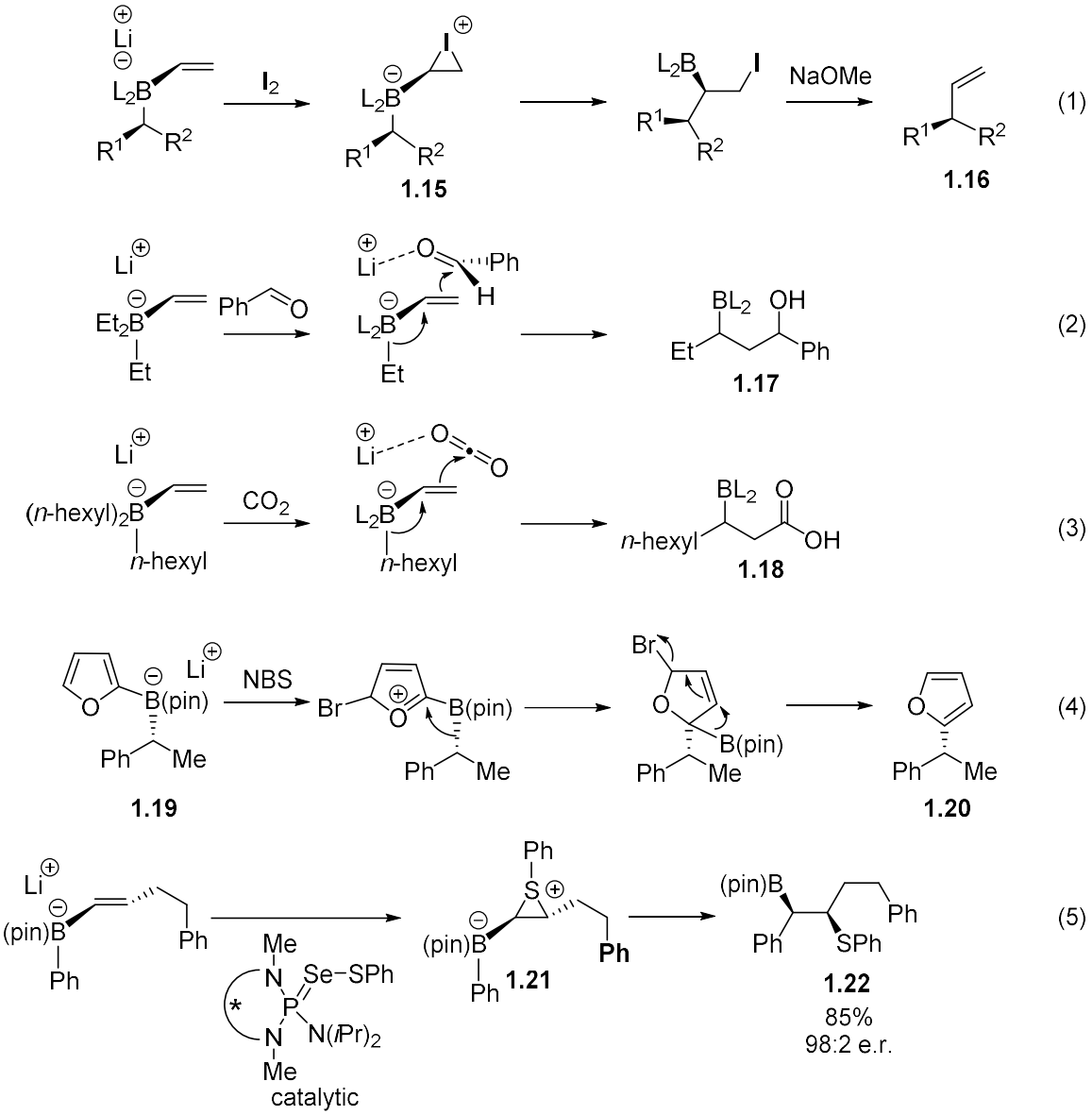
In cases where a boron "ate" complex is derived from an sp^2-hybridized nucleophile, the addition of an electrophile would trigger 1,2-metallate shift to form the new C-C bond and C-E bond. One classic reaction that takes advantage of this mode of reactivity is the Evans-Zweifel-olefination reaction (Scheme 1.8, eq. 1).[24] In this reaction, activation of vinyl organoboron "ate" complex would result in the formation of iodonium intermediate **1.15**. Intermediate **1.15** would then undergo 1,2-metallate rearrangement to form the new C-C bond and C-I bond. Subsequent treatment with base induces elimination to afford the

[22] (a) Fang, G. Y. ; Aggarwal, V. K. Angew. Chem. Int. Ed. **2007**, *46*, 359. (b) Fang, G. Y.; Wallner, O. A.; Blasio, N. D.; Ginesta, X.; Harvey, J. N.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2007**, *129*, 14632.
[23] (a) Stymiest, J. L.; Dutheuil, G.; Mahmood, A.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* 2007, 46, 7491. (b) Stymiest, J. L.; Bagutski, V.; French, R. M.; Aggarwal, V. K. *Nature* **2008**, *456*, 778. (c) Althaus, M.; Mahmood, A.; Suarez, J. R.; Thomas, S. P.; Aggarwal, V. K. *J. Am. Chem. Soc*. **2010**, *132*, 4025.
[24] (a) Jesthi, P. K.; Matteson, D. S. J. Organomet. Chem. **1976**, *110*, 25. (b) Matteson, D. S. *Synthesis* **1975**, 147. (c) Thomas, R. C.; Walker, J. A.; Evans, D. A. *Tetrahedron Lett.* **1976**, *17*, 1427. (d) Crawford, T. C.; Thomas, R. C.; Evans, D. A. *J. Org. Chem.* **1976**, *41*, 3947. (e) Armstrong, R. J.; Aggarwal, V. K. *Synthesis* **2017**, *49*, 3323.

desired olefination product. Alternative electrophilic activators such as aldehydes[25] and carbon dioxide[26] also induce 1,2-metallate shifts of organoboron "ate" complexes to afford β-hydroxyl borane **1.17** and β-boryl carboxylic acid **1.18,** respectively. Later, Aggarwal and co-workers showed that treatment of organoboron "ate" complex **1.19** with N-bromosuccinimide led to coupling product **1.20** through 1,2-metallate shift followed by elimination sequence.[27] Similar reactivity was recently reported by Denmark in a carbosulfenylation reaction of an alkenylboronate (Scheme 1.8, eq. 5). In this reaction, a chiral selenophosphoramide catalyst is combined with the saccharide-derived sulfenylating reagent to form a cationic donor-acceptor complex, which is highly electrophilic at the sulfur atom. The complex then activates the alkene of bonron "ate" complexes to generate the enantioenriched thiaranium ion **1.21** and subsequently induce 1,2-metallate shift to provide the corresponding boronic ester **1.22** containing two vicinal stereocenters.

[25] Uchida, K.; Nozaki, H.; Utimoto, K. *Tetrahedron* **1977**, *33*, 1949.
[26] Lu, D. –A.; Xu, W. –H.; Deng, M. –Z. *J. Chem. Soc., Chem. Commun.* **1985**, *0*, 1478.
[27] Bonet, A.; Odachowski, M.; Leonori, D.; Essafi, S.; Aggarwal, V. K. *Nat. Chem.* **2014**, *6*, 584.

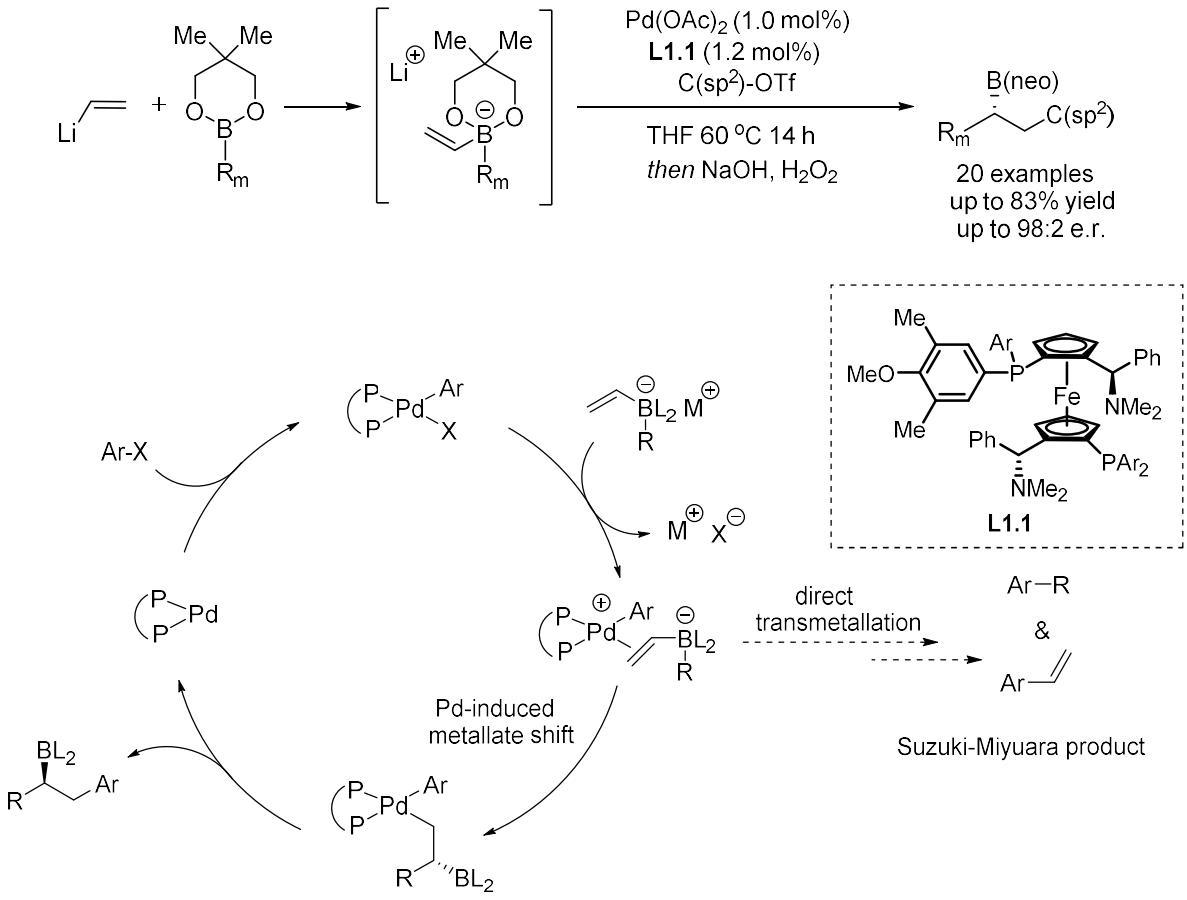
Scheme 1.8 1,2-Metallate Shift with C(sp^2)-Hybridized Migration Terminus



In 2016, inspired by the 1,2-metallate rearrangement chemistry of boron "ate" complex, the Morken group reported a class of reactions, termed "conjunctive cross-coupling", that are triggered by a transition-metal-induced 1,2-metallate rearrangement (Scheme 1.9).[2] These reactions employ a catalytic amount of a transition metal to merge together boron "ate" complex and an electrophile to form a variety of enantioenriched secondary

organoboron products. By merging the 1,2-metallate rearrangement reactivity of boron "ate" complex with the cross-coupling chemistry of transition metal, it enables the development of new C-C bond forming transformations.

Scheme 1.9 Palladium-Catalyzed Conjunctive Cross-Coupling Reaction



1.2.7 Properties of Organonickel Species.

To expand the scope of conjunctive cross-coupling reactions and enabling new modes of reactivity, we set out to explore an alternative metal catalyst. Ideally, the metal of choice

should be sustainable and cost effective. With this in mind, nickel was identified as an ideal candidate for investigations. Despite belonging to the same group 10 family as palladium, organonickel compound shares distinct properties compared to organopalladium species. For examples, nickel has a shorter atomic radius and therefore the Ni-C bond is generally shorter than the Pd-C bond.[28] This feature is beneficial in cases when regio- or stereo-selectivity of a reaction is dependent on steric differentiation between two different substituents on a ligand of nickel, such as in the case of Heck cross-coupling reaction (will be discussed in this chapter). In addition, the rate of β-hydride elimination is slower compared to organopalladium. Calculations have been conducted to suggest that the more difficult β-hydride elimination is due to a higher kinetic barrier for bond rotation which is necessary for agostic interactions with β-hydrogens.[29] This is one of the main reasons nickel is often the more effective catalyst for cross-coupling reactions with $C(sp^3)$-electrophiles. In addition to these features, the higher electropositivity of nickel also contributes to its lower energetic barrier for oxidative addition, allowing nickel to activate C-X bonds that are otherwise inert to Pd catalyst. With regards to the formation of π-complexes, binding of alkenes as well as alkynes is substantially stronger with nickel as compared to palladium.[30] This physical feature, as will be shown in a later section, is instrumental to our development of nickel-catalyzed conjunctive cross-coupling reactions.

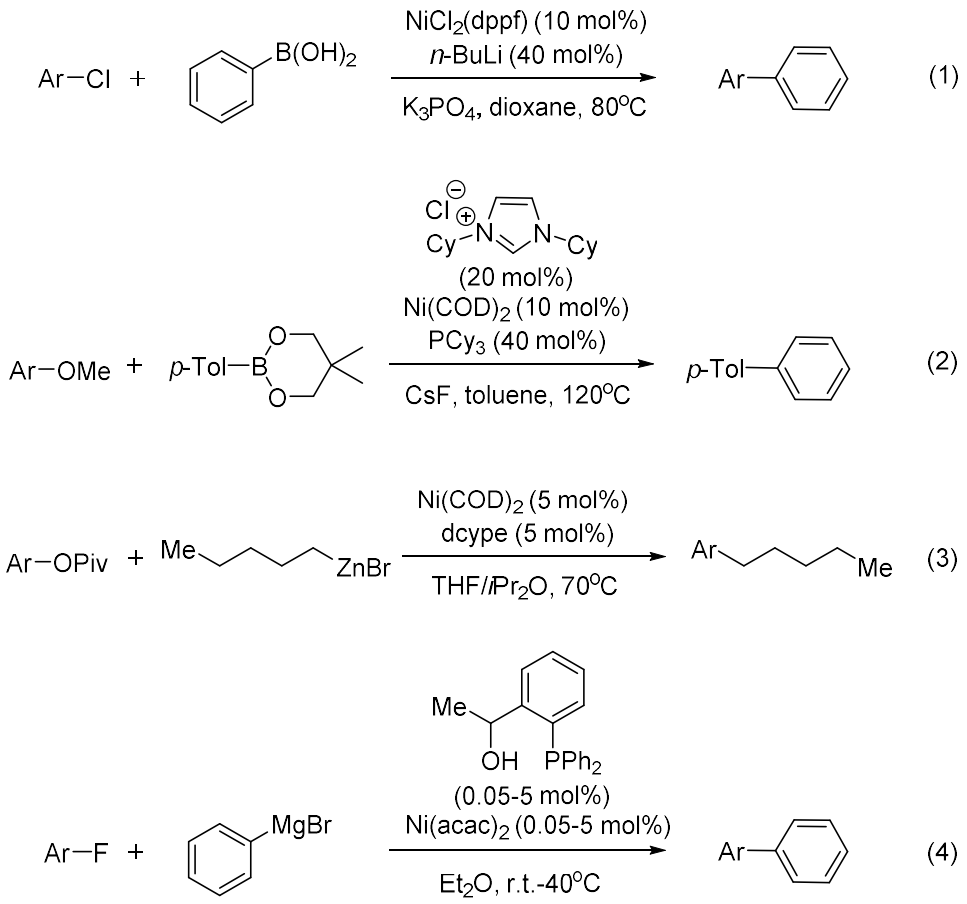
[28] (a) Slater, J. C. *J. Chem. Phys.* **1964**, *41*, 3199. (b) Cordero, B.; Gómez, V.; Platero-Prats, A. E.; Revés, M.; Echeverría, J.; Cremades, E.; Barragána, F.; Alvarez, S. *Dalton Trans*. **2008**, 2832.
[29] Lin, B.-L. *Organometallics* **2004***, 23*, 2114.
[30] (a) Ananikov, V. P.; Musaev, D. G.; Morokuma, K. *J. Am. Chem. Soc.* **2002**, *124*, 2839. (b) Ananikov, V. P.; Musaev, D. G.; Morokuma, K. *Organometallics* **2005**, *24*, 715. (c) Massera, C.; Frenking, G. *Organometallics* **2003**, *22*, 2758.

1.2.8 Reactivity of Nickel in Cross-Coupling Reactions.

Much of the excitement in the area of nickel catalysis comes from the diverse reactivity manifold that it presents. Nickel has readily accessible oxidation states of 0, I, II, III, and IV. For this reason, nickel catalysts can often engage in both polar and non-polar mechanisms. In the context of cross-coupling reaction with $C(sp^2)$ electrophiles, a polar Ni(0)/Ni(II) redox cycle similar to the palladium system is generally proposed to be the operative mechanism. The more facile oxidative addition of nickel catalyst allows for cross-coupling reactions with electrophiles that would otherwise be challenging with palladium catalysts, namely aryl chlorides[31], aryl ethers[32], aryl esters[33], and aryl fluorides[34] (Scheme 1.10).

[31] Saito, S.; Sakai, M.; Miyaura, N. *Tetrahedron Lett*. **1996**, *37*, 2993.
[32] Tobisu, M.; Shimasaki, T.; Chatani, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 4866.
[33] Liu, X.; Jia, J.; Rueping, M. *ACS Catal.* **2017**, *7*, 4491.
[34] Yoshikai, N.; Mashima, H.; Nakamura E. *J. Am. Chem. Soc.* **2005**, *127*, 17978.

Scheme 1.10 Ni-Catalyzed Cross-Coupling Reactions with C(sp^2)-Hybridized Electrophiles via Polar Mechanism

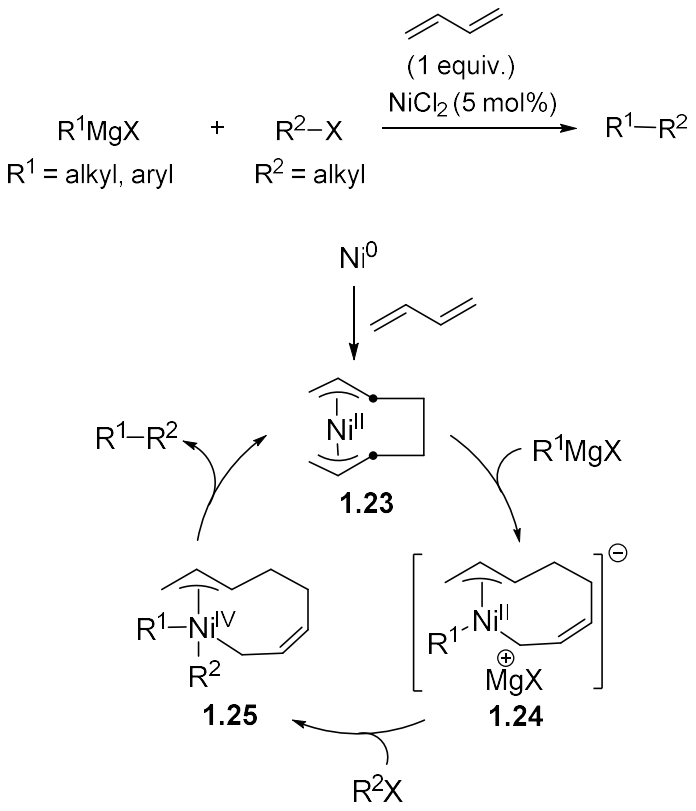


With regards to cross-coupling reaction with the C(sp^3) electrophiles, various reaction systems with different underlying operating redox cycle have been reported. In 2002, Kambe reported the Kumada cross-coupling reaction of Grignard reagents with alkyl halides and tosylates.[35] The reaction was found to proceed only with the addition of 1,3-butadiene as an additive. Under the reaction mechanism, Ni(0) would undergo oxidative cyclization with 2 equivalents of diene to form π-allyl complex **1.23**. It eventually reacts with Grignard reagent to form the nickel "ate" species **1.24**, which is highly nucleophilic

[35] Terao, J.; Watanabe, H.; Ikumi, A.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2002**, *124*, 4222.

and can readily undergo oxidative addition with alkyl electrophile. Overall, this is a polar mechanism and a radical probe experiment was carried out to rule out the involvement of radical intermediate in the catalytic cycle.

Scheme 1.11 Kambe's Kumada Cross-Coupling Reaction

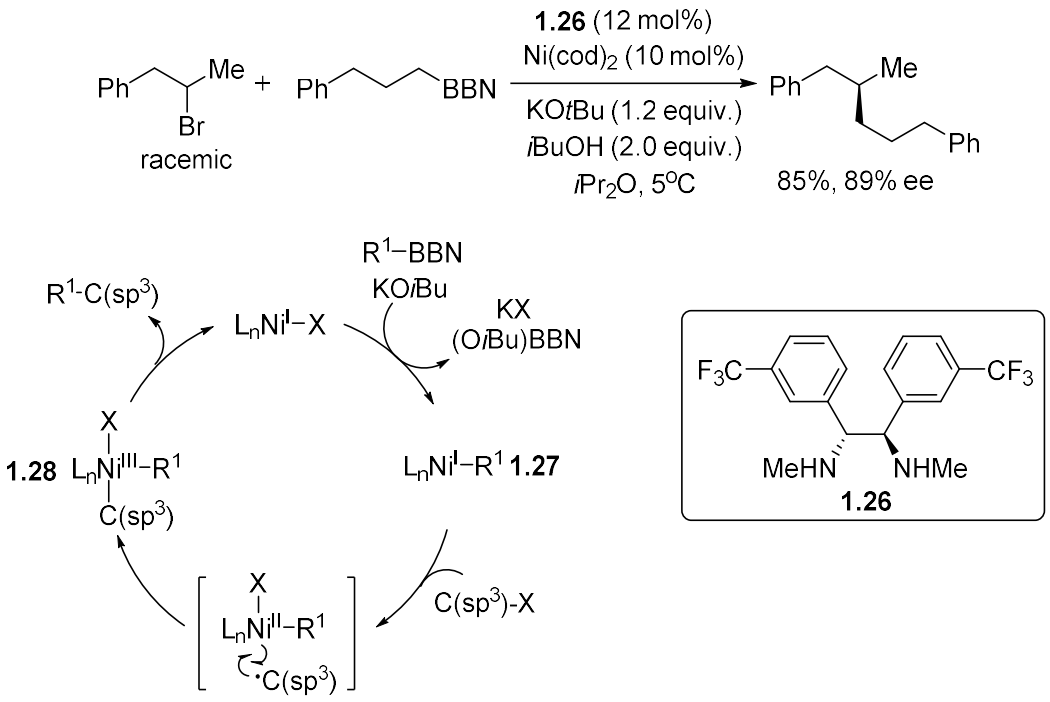


Cross-coupling reactions with alkyl electrophile can also be approached with a non-polar mechanism involving single-electron-transfer to alkyl halide and generation of alkyl radical. In these reactions, Ni(I)/Ni(III) redox cycles are generally invoked. In the case of Suzuki-Miyaura cross-coupling reaction of 9-BBN boranes as reported by Fu[36], it is believed that the process proceeds via a "transmetallation-first" mechanism, in which

[36] (a) Lu, Z.; Wilsily, A.; Fu, G. C. *J. Am. Chem. Soc.* **2011**, *133*, 8154. (b) Wilsily, A.; Tramutola, F.; Owston, N. A.; Fu, G. C. *J. Am. Chem. Soc*. **2012**, *134*, 5794.

Ni(I)-X would undergo transmetallation with 9-BBN reagents followed by single-electron-transfer and subsequent radical recombination to form the Ni(III) interemediate **1.28**. Reductive elimination would then afford the desired cross-coupled product and regenerate the active Ni(I) catalyst. The process is stereoconvergent as the configuration of the starting material becomes irrelevant due to the generation of a carbon-centered radical, the favored absolute configuration of product is determined by the chiral catalyst. Computational work by Molander[37] conducted on a related system suggest that reductive elimination is the stereochemistry-determining step of the catalytic cycle with Ni(III) species such as **1.28** undergoing rapid homolysis/recombination (Curtin-Hammett scenario).

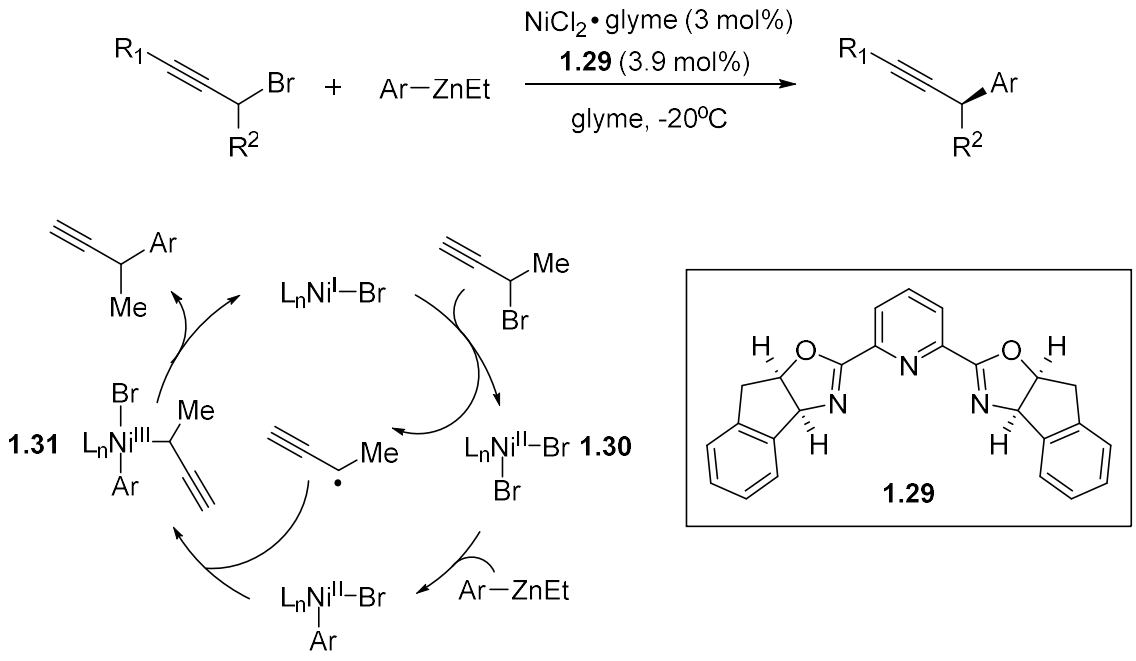
Scheme 1.12 Suzuki-Miyaura Cross-Coupling Reaction with Homobenzylic Bromide



[37] Gutierrez, O.; Tellis, J. C.; Primer, D. N.; Molander, G. A.; Kozlowski, M. C. *J. Am. Chem. Soc.* **2015**, *137*, 4896.

The sequence of elementary steps in the catalytic cycle can be altered as in the case of Negishi cross-coupling reaction with propagylic bromides (Scheme 1.12).[38] Under the proposed mechanism, Ni(I)-Br undergoes single-electron-transfer and generates a propargylic radical. The resultant Ni(II)Br_2 intermediate **1.30** then undergoes transmetallation with an organozinc reagent and then recombines with the propagylic radical. A series of stoichiometric experiments and *in situ* spectroscopy monitoring experiments were conducted to support the proposed mechanism. Similar to the previous example, since a carbon-centered radical is invoked in the mechanism, racemic alkyl halides can be employed as starting material and still afford enantioenriched products.

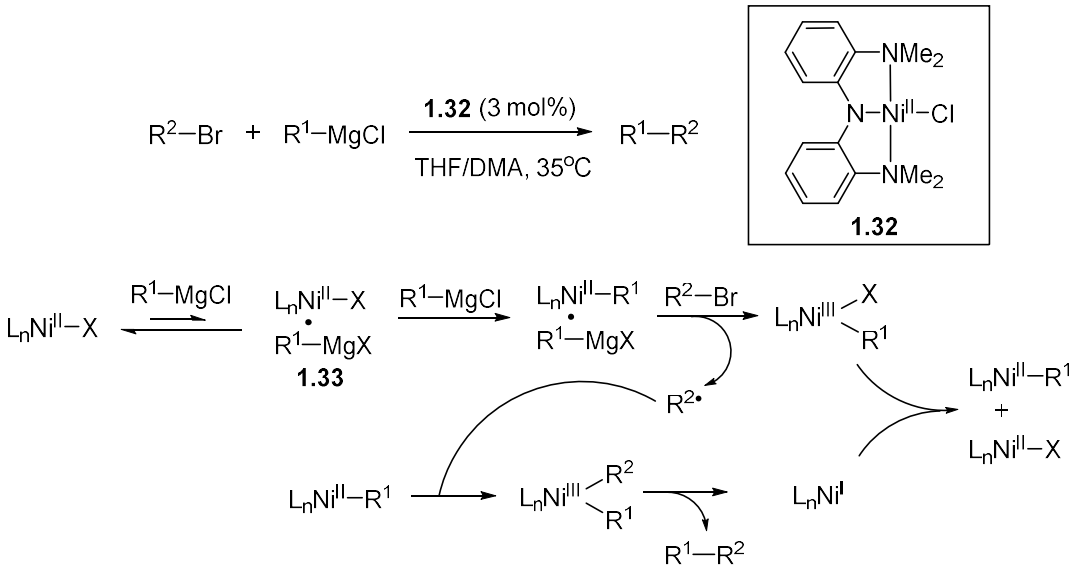
Scheme 1.12 Negishi Cross-Coupling Reaction with Propagylic Bromide



[38] (a) Smith, S. W.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 12645. (b) Schley, N. D.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 16588.

Another breakthrough in the field of cross-coupling reactions with alkyl electrophiles was made by Hu and co-workers when they reported the use of Ni-pincer complex **1.32** as the catalyst in Kumada-Corriu cross-coupling reaction.[39] The reaction was proposed to proceed *via* a bimetallic oxidative addition of alkyl halide involving an alkyl radical which would recombine with another Ni(II)-alkyl complex. The same Ni-pincer complex **1.32** was later demonstrated to be a competent catalyst for Sonogashira cross-coupling reactions.[40]

Scheme 1.13 Hu's Kumada Cross-Coupling Reaction of Unactivated Alkyl Bromide with Nickel-Pincer Complex



[39] Vechorkin, O.; Hu, X. *Angew. Chem. Int. Ed.* **2009**, *48*, 2937.
[40] Vechorkin, O.; Barmaz, D.; Proust, V; Hu, X. *J. Am. Chem. Soc.* **2009**, *131*, 12078.

1.2.9 Olefin-Nickel Complex in Catalysis.

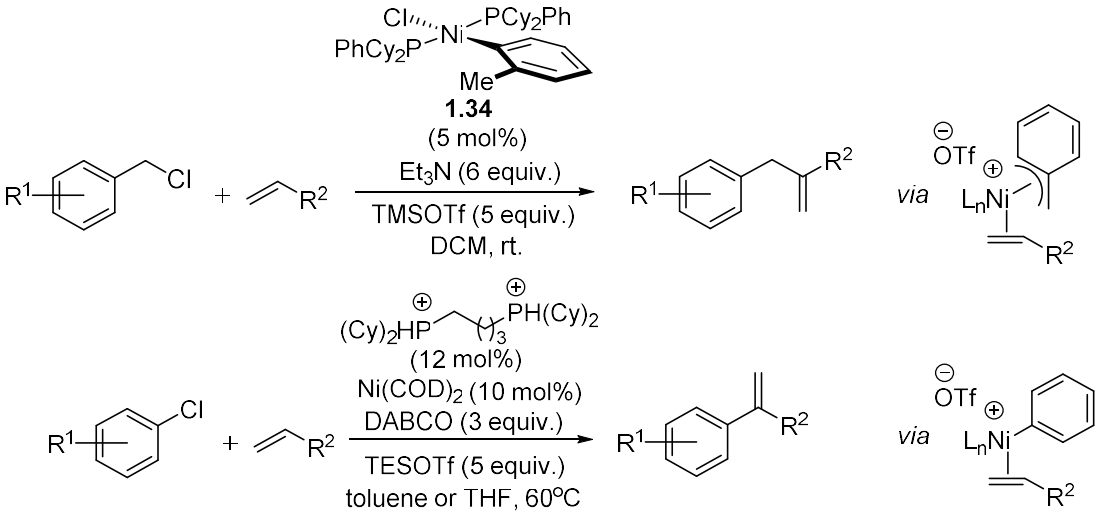
Considering olefin binding to the metal catalyst as a key elementary step in the conjunctive coupling reaction, a discussion of nickel catalysis involving π-complexes warrants discussion. Not only do the unsaturated molecules donate π-electrons to the empty d-orbital of nickel, the alkene π∗ orbital readily accepts electrons from the filled d orbitals of nickel (back-bonding).[29] Computational works by Frenking desmonstrated the strength of back-bonding within a Ni-olefin complex is substantially stronger compared to the palladium counterpart, leading to stronger coordination between Ni and olefins.[41] This delocalization of electron density is reflected by a change in properties of the alkene or alkyne ligand, such as bond angles, partial charges, as well as spectral properties.[42] For the same reason, coordination of nickel to olefins would unveil new reactivity in the unsaturated molecule that would otherwise be inaccessible. In fact, nickel has been heavily relied upon in the arena of reductive coupling and cycloisomerization.[43] These processes often employ π-complexes as key intermediates as part of the catalytic cycle.

Due to the less facile β-hydride elimination, nickel is often not the catalyst of choice for Heck coupling reactions. However, in recent years, there have been a handful of reports by Jamison and coworkers demonstrating that nickel can efficiently catalyze Heck reactions with benzyl and aryl chlorides as electrophiles[44] Often times, these reactions invoke cationic nickel as an intermediate to facilitate β-hydride elimination, and they often exhibit

[41] Massera, C.; Frenking, G. *Organometallics* **2003**, *22*, 2758.
[42] Ananikov, V. P. *ACS Catal.* **2015**, *5*, 1964.
[43] Standley, E. A.; Jamison, T. F. *Acc. Chem. Res*. **2015**, *48*, 1503.
[44] (a) Matsubara, R.; Gutierrez, A. C.; Jamison, T. F. *J. Am. Chem. Soc.* **2011**, *133*, 19020. (b) Standley, E. A.; Jamison, T. F. *J. Am. Chem. Soc.* **2013**, *135*, 1585. (c) Tasker, S. Z.; Gutierrez, A. Z.; Jamison, T. F. *Angew. Chem. Int. Ed.* **2014**, *53*, 1858.

high branch-to-linear regioselectivity. The high regioselectivity was thought to be due to a short Ni-C bond, allowing for better steric differentiation. Other catalytic reactions involving π-complex with nickel include polymerization[45] and oligomerizations.[46] All in all, the prevalence of nickel in the activation of olefins encouraged us to investigate its use in the development of conjunctive coupling reactions.

Scheme 1.14 Jamison's Ni-Catalyzed Heck Coupling Reaction



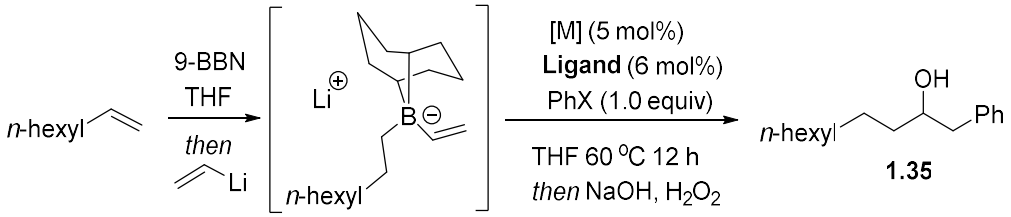
[45] (a) Ittel, S. D.; Johnson, L. K.; Brookhart, M. *Chem.Rev.* **2000**, *100*, 1169. (b) Gibson, V. C.; Spitzmesser, S. K. *Chem.Rev.* **2003**, *103*, 283. (c) Mu, H. L.; Pan, P.; Song, D. P.; Li, Y. S. *Chem. Rev.* **2015**, *115*, 12091. (d) Johnson, L. K.; Killian, C. M.; Brookhart, M. *J. Am.Chem. Soc.***1995**, *117*, 6414.
[46] (a) Killian, C. M.; Johnson, L. K.; Brookhart, M. *Organometallics* **1997**,*16*,2005. (b) Svejda, S. A.; Brookhart, M. *Organometallics* **1999**, *18*, 65. (c) Speiser, F.; Braunstein, P.; Saussine, L. *Acc. Chem. Res.* **2005**, *38*, 784.

1.3 NICKEL-CATALYZED CONJUNCTIVE CROSS-COUPLING OF 9-BBN BORATES

1.3.1 Initial Investigations

During our initial investigations, we attempted to employ 9-BBN-derived organoboronates in conjunctive cross-coupling reactions that use pinacol boronates and palladium catalysis (Scheme 1.15, entry 1). Although significant reactivity was observed, the product obtained was racemic. Considering the distinct steric properties of organonickel compared to organopalladium species, both with respect to C-M bond length as well as strength of binding to alkenes, we set out to use nickel as an alternative catalyst to engender enantioselectivity during conjunctive coupling of 9-BBN derivatives. Initial studies with Ni catalysts employed simple achiral bipyridine ligand and phenyl triflate electrophile. A protocol consisting of hydroboration of the alkene by 9-BBN followed by addition of vinyllithium affords the boron "ate" complex of interest, which was directly treated with the corresponding nickel catalyst and electrophile in an one-pot fashion. We were delighted to observe a 41% isolated yield of product **1.35**. Interestingly, switching the electrophile to iodobenzene boosted the yield of product to 70%, am outcome which was attributed to a more facile oxidative addition.

Scheme 1.15 Initial Optimizations of Conjunctive Coupling with Organoborane.



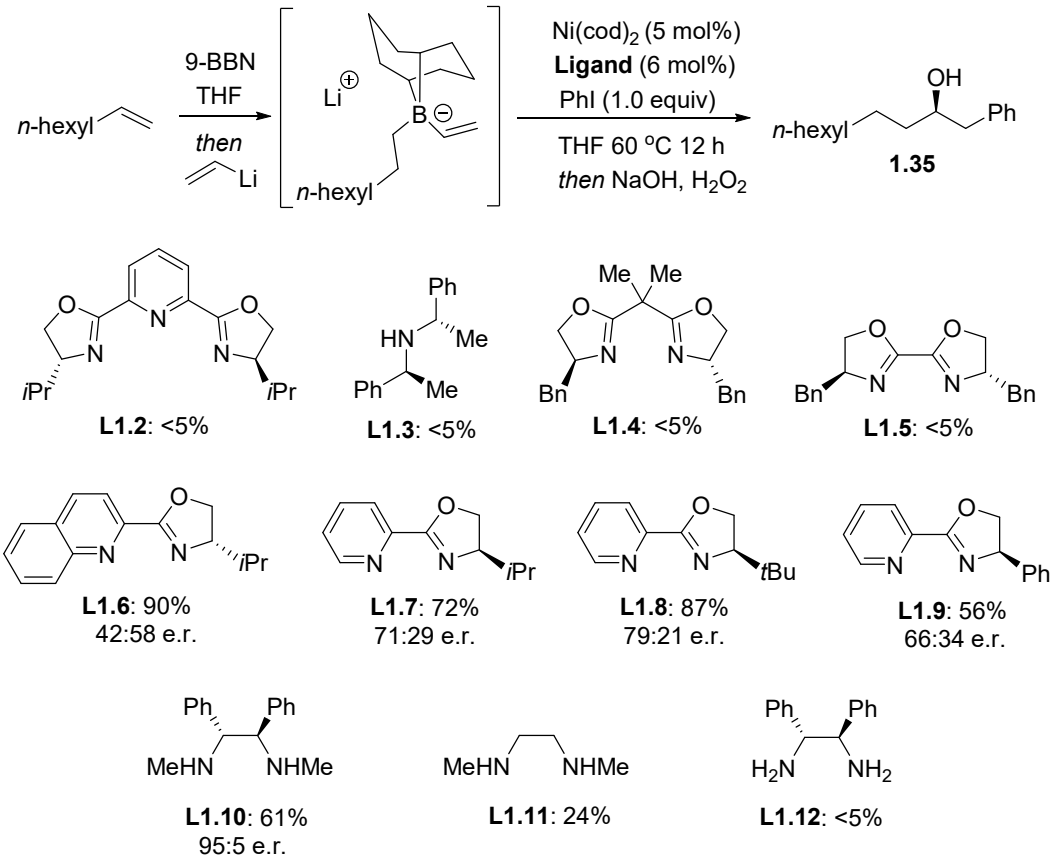
Entry	[M]	Ligand	PhX	Yield (%)
1	$Pd(OAc)_2$	MandyPhos (**L1.1**)	PhOTf	50[a]
2	$Ni(cod)_2$	none	PhOTf	<5
3	$Ni(cod)_2$	bipyridine	PhOTf	41
4	$Ni(cod)_2$	bipyridine	PhI	70

The enantioratio of product was determined by chiral phase SFC to be 50:50.

Having identified a reactive system, we surveyed a variety of chiral non-racemic ligands that might render the reaction enantioselective (Scheme 1.16). Whereas the tridentate PyBox ligand **L1.2** and monodentate ligand **L1.3** did not afford any desired product, the use of bidentate Pyox ligands (**L1.6-L1.9**) afforded the product with high yield though only modest enantioselectivity. Furthermore, bisoxazoline ligand **L1.5** was found to be ineffective for the coupling reaction. To our delight, an aliphatic 1,2-diamine ligand **L1.10** afforded the desired product with both respectable yield and enantioselectivity. Interestingly, with an achiral aliphatic diamine ligand with primary amino group (**L1.12**), poor yield of product was observed with the crude mass consisting of mostly Ullmann coupling biphenyl compounds. This outcome could be attributed to more sterically accessible nickel metal center which would allow an undesired disproportionation pathway. For achiral diamine ligand **L1.11,** without substituents on the backbone, poor

reactivity was observed, which was hypothesized to be due to the lack of a Thorpe-Ingold effect that enhances ligation of diamine to the nickel metal center.

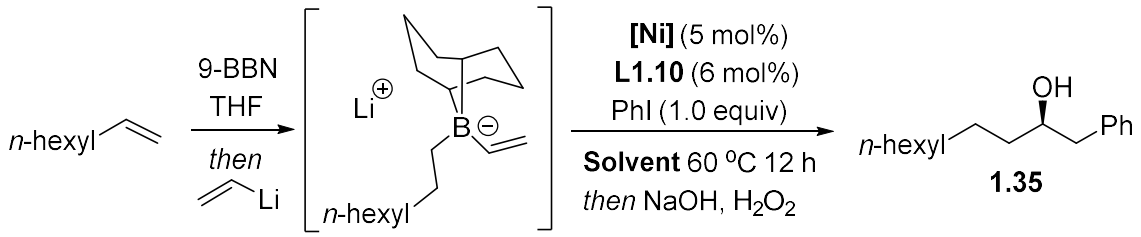
Scheme 1.16 Survey of Chiral Ligands for Ni-Catalyzed Conjunctive Coupling.



Having identified the chiral ligand that provides the highest yield and enantioselectivity, we looked into other parameters to try to further increase the efficiency of the reaction. Reactions in highly coordinating solvents such as DMSO and CH_3CN (Scheme 1.16, entry 1&2) provided diminished yield compared to reactions run in less coordinating solvents such as 1,4-dioxane, toluene and cyclohexane (Scheme 1.16, entry 3-5). This is in line with a mechanistic scenario involving the intermediacy of a cationic nickel species. Gratifyingly, replacing $Ni(COD)_2$ with $Ni(acac)_2$ pre-catalyst (Scheme 1.16, entry 8) proved beneficial to the yield of product. This improvement could be due to more facile

initial ligation of diamine ligand to the metal center, or that the cyclooctadiene ligand that dissociates from $Ni(cod)_2$ could compete with vinyl boronate for the coordination site of nickel center.

Scheme 1.16 Survey of Solvent and Nickel Pre-Catalyst.



Entry	[Ni]	Solvent	Yield	e.r.
1	$Ni(cod)_2$	DMSO	15%	N.D.
2	$Ni(cod)_2$	MeCN	12%	N.D.
3	$Ni(cod)_2$	1,4-dioxane	51%	93:7
4	$Ni(cod)_2$	toluene	42%	83:17
5	$Ni(cod)_2$	cyclohexane	32%	79:21
6	$NiBr_2 \cdot$glyme	THF	60%	94:6
7	NiI_2	THF	<5%	N.D.
8[a]	$Ni(acac)_2$	THF	80%	95:5

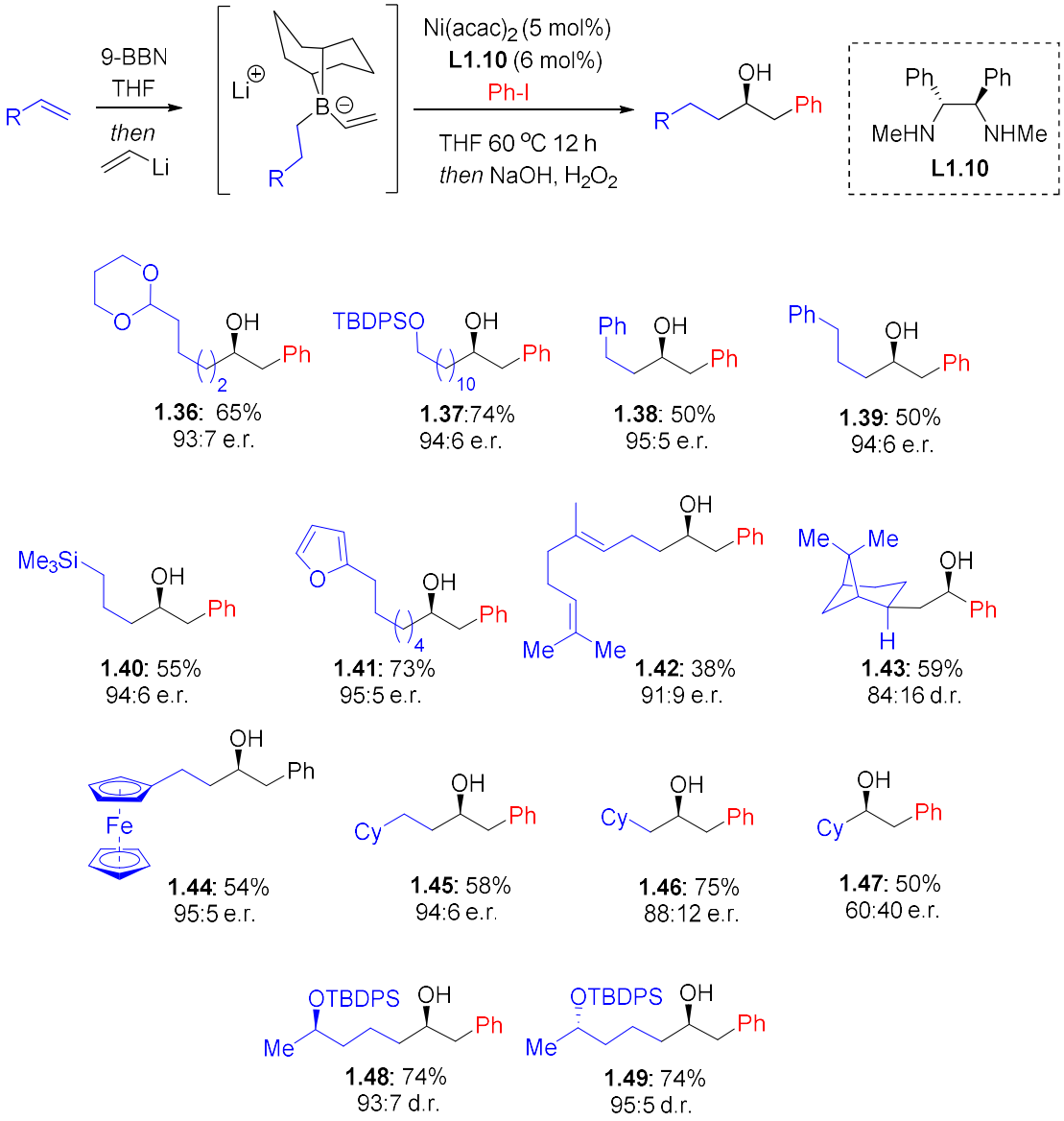
(a) 1.1 equivalents of vinyl boron "ate" was used.

1.3.2 Substrate Scope.

With the optimized conditions in hands, we surveyed the scope of this transformation. Under our reaction system, simple hydroboration of the alkene by 9-BBN reagent would generate the corresponding boranes that could be used *in situ* to form the boron "ate"

complex. The addition of vinyllithium and subjection to conjunctive coupling reaction afforded the corresponding chiral non-racemic secondary alcohols upon oxidative workup. Functional groups such as acetals (**1.36**), silyl ethers (**1.37**), silanes (**1.40**), furans (**1.41**), alkenes (**1.42**), and a ferrocene (**1.44**) were tolerated under the reaction conditions. Migrating groups with α- and β-branching (**1.46** & **1.47**) were found to provide products in moderate yield with diminished enantioselectivity. Surprisingly, the use of more sterically hindered cyclohexyl migrating group (**1.47**) did not afford any detectable amount of product derived from the migration of bicylooctyl group of 9-BBN ligand. Finally, the reaction was shown to operate with predominant catalyst-control of stereoselectivity as demonstrated by the high diastereoselectivies observed in products **1.48** and **1.49** with stereocenters of opposite absolute configurattions in the migrating groups.

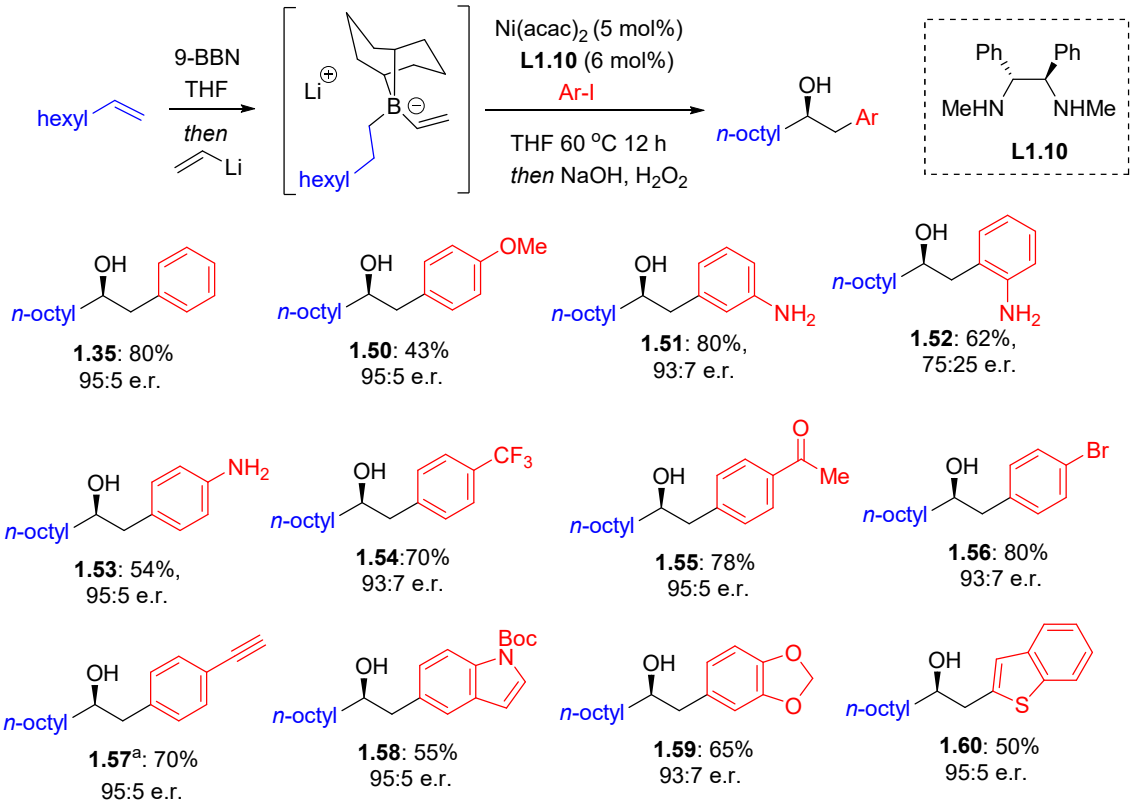
Scheme 1.17 Scope of Migrating Group in Ni-Catalyzed Conjunctive Coupling.



The scope of aryl halides was examined next. Both electron-rich (Scheme 1.18, **1.50**-**1.53**, **1.59**) and electron-poor arenes (**1.54** & **1.55**) can be employed to afford the desired chiral secondary alcohols with high yield and selectivity. Remarkably, for arenes with free amino groups (**1.51**-**1.53**), the reactions can proceed efficiently. However, if the amino group is situated in the ortho-position of the arene as in the case of **1.52**, the

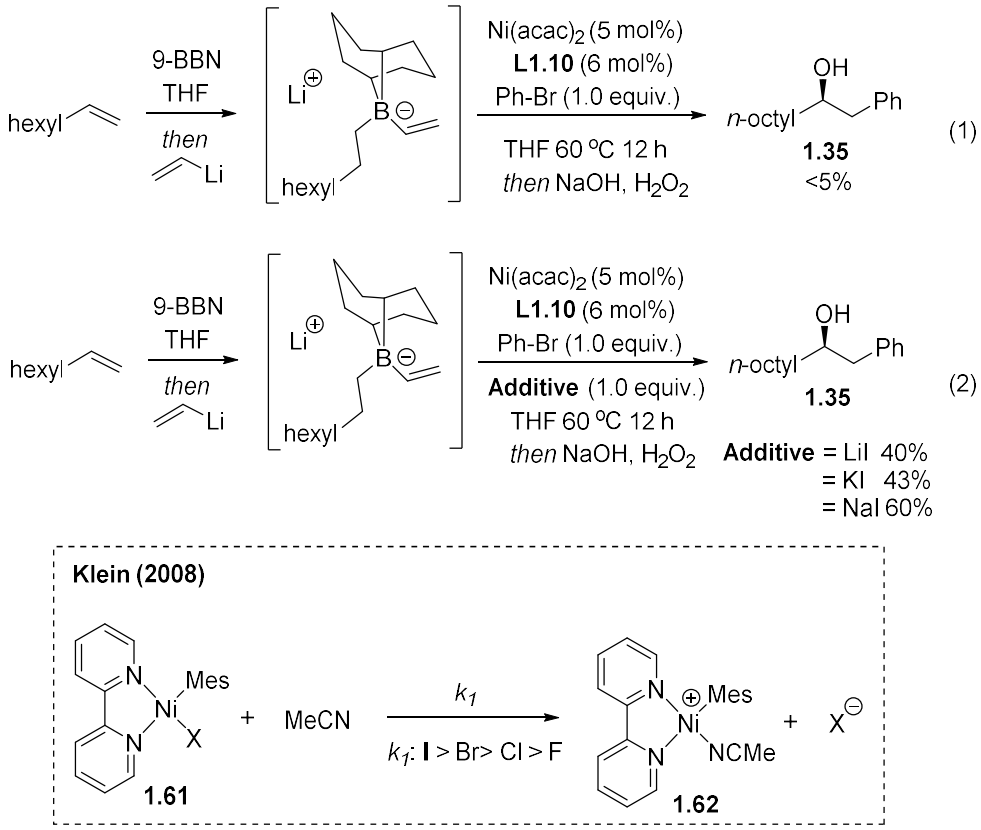
enantioselectivity of the derived secondary alcohol is significantly diminished, presumably due to its ability to chelate to the nickel metal center. Sensitive functional groups such as alkyne (**1.57**), ketone (**1.55**), as well as bromide (**1.56**) can be tolerated in the reaction. Finally, heterocycles such as *N*-Boc protected indole (**1.58**), benzothiophene (**1.60**), and benzodioxole (**1.59**) can be used to afford the desired product with both high yield and enantioselectivity.

Scheme 1.18 Scope of Aryl Iodide in Ni-Catalyzed Conjunctive Coupling.



(a) The arene substrate being employed is (4-iodophenyl)triethylsilyl acetylene, which undergoes desilylation during oxidation.

Scheme 1.19 Bromobenzene as Electrophile in Ni-Catalyzed Conjunctive Coupling.



Under the standard conditions for coupling with iodobenzene, the corresponding bromobenzene did not react in the reaction (Scheme 1.19, eq.1). Based upon the mechanistic studies conducted by Klein and co-workers[47], which showed that the rate of exchange of halide from oxidative addition adduct **1.61** and acetonitrile follows the order of I>Br>Cl>F, we reasoned that the formation of cationic nickel required for binding of vinyl boronate could be challenging with bromobenzene as the electrophile. For this reason, we investigated the use of exogenous iodide additive in our reaction (Scheme 1.19, eq. 2). Presumably, the iodide salt would be able to engage in salt metathesis with Ni(II)-

[47] Klein, A.; Kaiser, A.; Wielandt, W.; Belaj, F.; Wendel, E.; Bertagnolli, H.; Zalis, S. *Inorg. Chem*. **2008**, *47*, 11324.

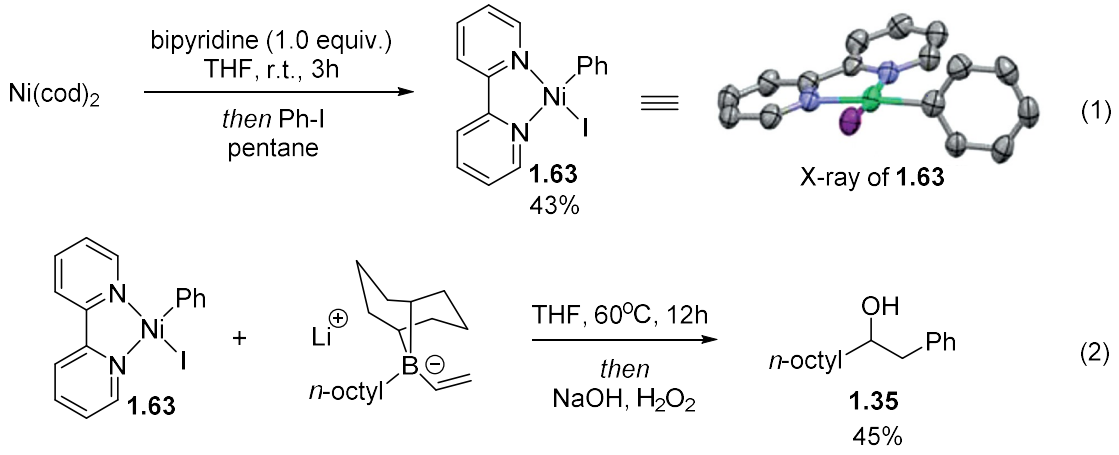
Br oxidative addition adduct to generate the corresponding Ni(II)-I species, which would be more prone towards the formation of cationic Ni intermediate. Indeed, we found that the use of either potassium iodide or sodium iodide was able to recovery reactivity with the later providing even higher yield of desired product.

1.3.3 Mechanistic Studies.

As discussed in the previous section, nickel-catalyzed cross-coupling reactions can often proceed via catalytic cycles that invoke different oxidation states of the metal center as well as sequence of elementary steps. Both sequences of oxidative addition preceding transmetallation and *vice versa* have been shown to be feasible in different catalytic systems. In the case of transmetallation-first mechanism, a Ni(I)/Ni(III) redox cycles is typically believed to be the major operative mechanism. For the conjunctive coupling reaction, we considered both the oxidative addition-first and trasnsmetallation-first mechanisms plausible. To differentiate between the two reaction pathways, we independently synthesized Ni(II) oxidative addition adduct **1.63** by combining $Ni(cod)_2$ with bipyridine and then treating this with iodobenzene in pentane. The reaction resulted in the immediate precipitation of a dark solid which was confirmed by X-ray crystallography to be Ni(II) oxidative addition adduct **1.63**. A stoichiometric reaction between **35** and reactive vinyl boron 'ate' carried out for 1 hour in THF at 60 ºC resulted in product formation (**Scheme 1.20**). This outcome is consistent with the mechanistic scenario in which oxidative addition occurs before 1,2-metallate shift of vinyl boron "ate" complex. However, it is worth pointing out this experiment does not necessarily prove

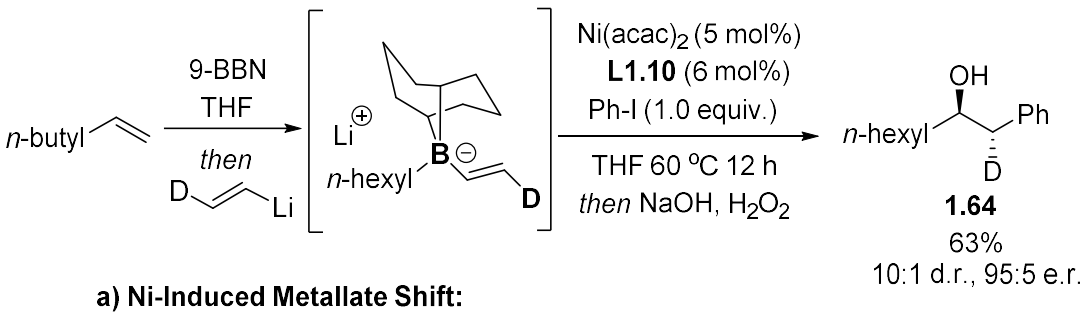
Ni(0)/Ni(II) redox cycle as the operative mechanism, as Ni(II) oxidative addition complexes are well documented to undergo ionization in THF and subsequent disproportionation reactions to generate both Ni(I) and Ni(III) species.

Scheme 1.20 Stoichiometric Experiment.

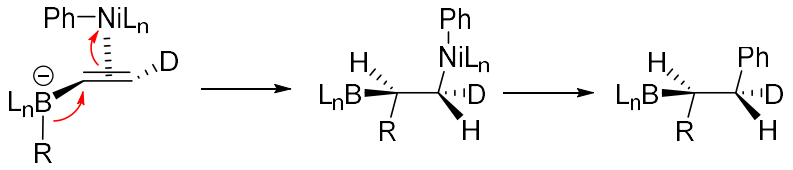


In addition, we also carried out a conjunctive coupling reaction with stereochemically defined, deuterium labeled vinyl lithium. The reaction resulted in the formation of diastereo-enriched product **1.64** with the deuterium and hydroxyl group adopting an *anti*-relative relationship. This stereocenter is consistent with the mechanistic scenario in which nickel induces a stereospecific *anti*-periplanar 1,2-metallate rearrangement of vinyl boron "ate" complex and rules out the possibility of *syn* carbonickelation followed by reductive elimination.

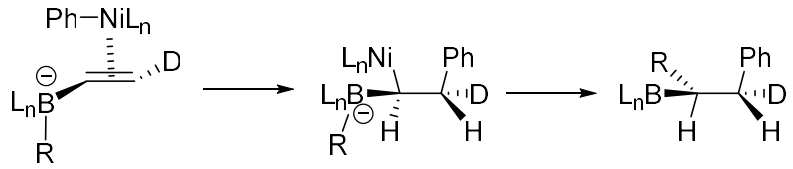
Scheme 1.21 Stoichiometric Experiment.



a) Ni-Induced Metallate Shift:



b) Alternative Carbo-Metallation Pathway:



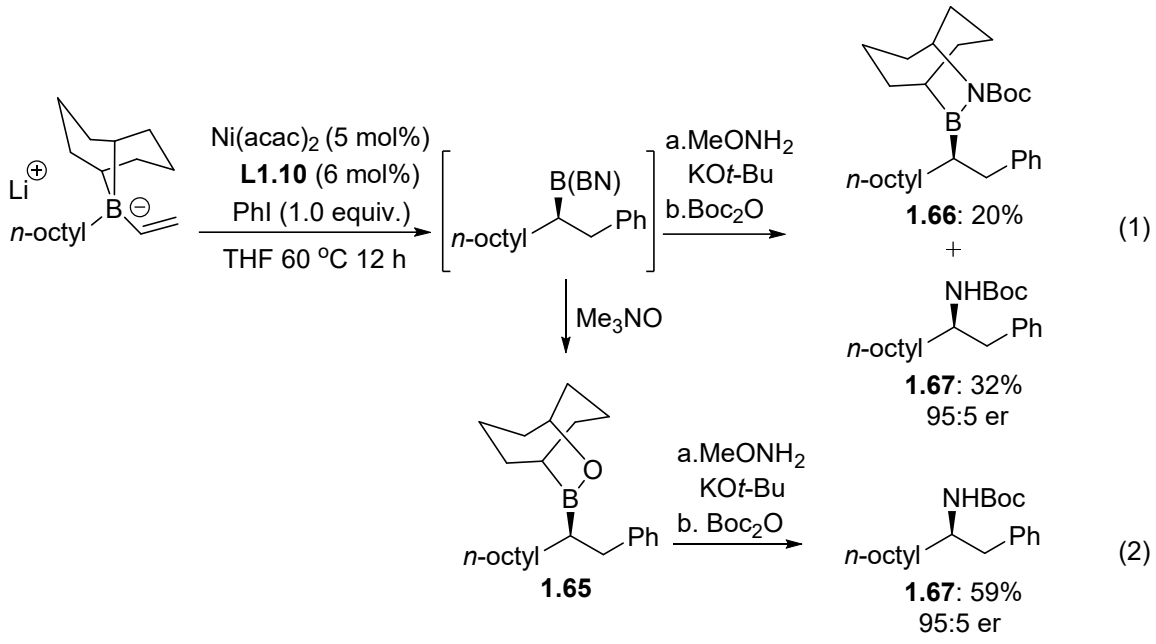
1.3.4 Transformations of Chiral Secondary 9-BBN Borane.

To further demonstrate the synthetic utility of chiral non-racemic secondary borane products, we subjected them to further transformations other than oxidation. Amination of borane was our first target transformation. When this was first attempted using an amination protocol that employs methoxyamine as the aminating reagent[48], the reaction

[48] Edelstein, E. K.; Grote, A. C.; Palkowitz, M. D.; Morken, J. P. *Synlett* **2018**, *29*, 1749.

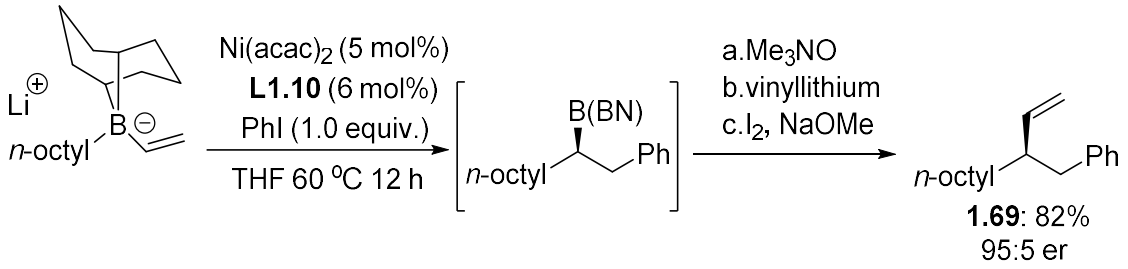
occurred with low chemoselectivity as significant mass balance of the reaction goes towards by-product **1.66** derived from the migration of bicyclooctyl ligand (Scheme 1.22, eq.1). We were inspired by the strategy reported by Soderquist, mentioned earlier in the chapter, in which transformations of boranes proceed *via* the intermediacy of the borinic ester. Indeed, we generated the borinic ester **1.65** by treating the borane product with trimethyl amine N-oxide, which was then directly treated with methoxyamine and KO*t*Bu to afford the desired amination product **1.67** in respectable yield (Scheme 1.22, eq.2).

Scheme 1.22 Intermediacy of Borinic Ester in Amination of BBN Borane.



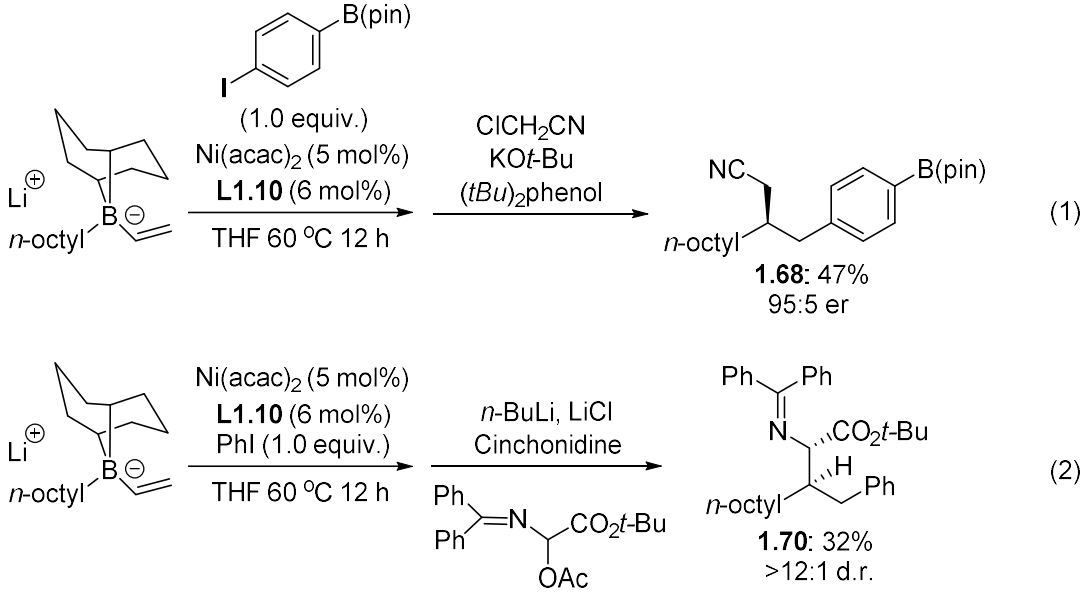
Later, it was later found that the intermediate borinic ester can also be applied to selective Zweifel olefination (Scheme 1.23).

Scheme 1.23 Zweifel Olefination of BBN Borane.



In addition to amination and an olefination, the unique reactivity of the borane, enabled by its high electrophilicity compared to boronic ester, allows useful reactions. To showcase the chemical orthogonality of borane and boronic ester, we carried out cyanomethylation on the bis-borylated compound (not shown) and we were able to obtain a respectable yield of mono-cyanomethylated compound **1.68** with boronic ester moiety intact (Scheme 1.24, eq.1). In addition, the O'Donnell homologation reaction was carried out to afford the corresponding amino-acid derivative **1.70** (Scheme 1.24, eq.2).[49] The diastereoselectivity of this reaction was controlled by the chiral cinchonidine catalyst.

SchemOe 1.24 Cyanomethylation and O' Donnell Homologation of BBN Borane.



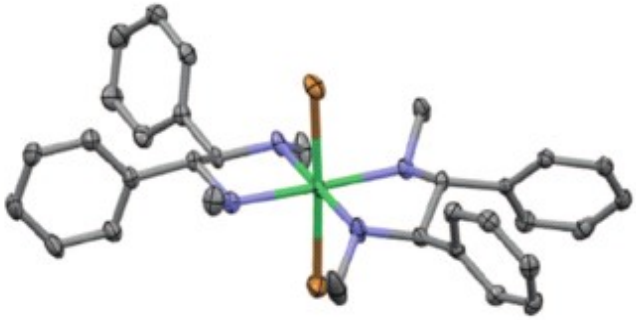
[49] O' Donnell, M. J.; Cooper, J. T.; Mader, M. M. *J. Am Chem. Soc.* **2003**, *125*, 2370.

1.3.5 Stereochemical Model of Ni-Catalyzed Conjunctive Coupling Reaction.

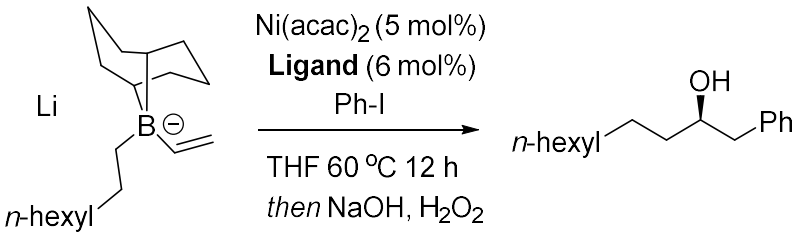
To learn more about the stereochemical outcome of the Ni-catalyzed conjunctive coupling reaction, we prepared a coordination complex from $NiCl_2$•glyme and ligand **L1.10** (Scheme 1.25a). From its X-ray crystal structure, it can be seen that the phenyl groups and *N*-methyl groups adopt pseudo-equatorial positions on the metallacycle. In addition, we also synthesized various analogues of the aliphatic diamine ligand and analyzed the correlation between stereoselectivity and in the structure of the diamine ligand (Scheme 1.25b). Based upon the obtained data, we propose the following stereochemical model in which the vinyl boron "ate" complex would bind in such a way that the bulky bicyclooctyl group would point away from the metallacycle and avoid steric interaction with the *N*-methyl groups. Based upon this proposed model, the high enantioselectivity obtained with **L1.10** would make sense. For **L1.14** in which one nitrogen has two methyl groups and the other has none, its use in conjunctive coupling reaction occurs with little selectivity. This outcome is consistent with the vinyl boron "ate" approaching the metal center either from top or bottom of the cyclic framework. Interestingly, with a diamine ligand with only one stereocenter in the backbone, the enantioselectivity is still high (**L1.15** & **L1.16**). To explain this observed phenomenon, we hypothesized that the phenyl groups would not only have a local gearing effect on the orientation of the adjacent *N*-methyl groups, but also affect the orientation of distal *N*-methyl groups by establishing a ring conformation in which both phenyl groups as well as *N*-methyl groups would occupy pseudo-equatorial positions of the metallacycle.

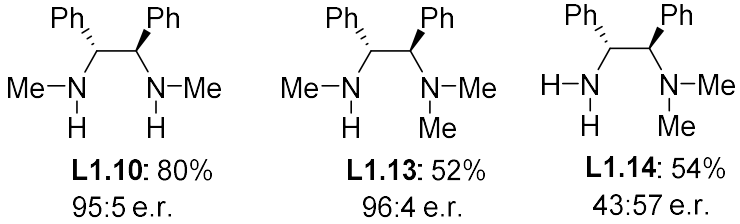
Scheme 1.25 Structure-Activity Relationship of 1,2-Aliphatic Diamine Ligands.

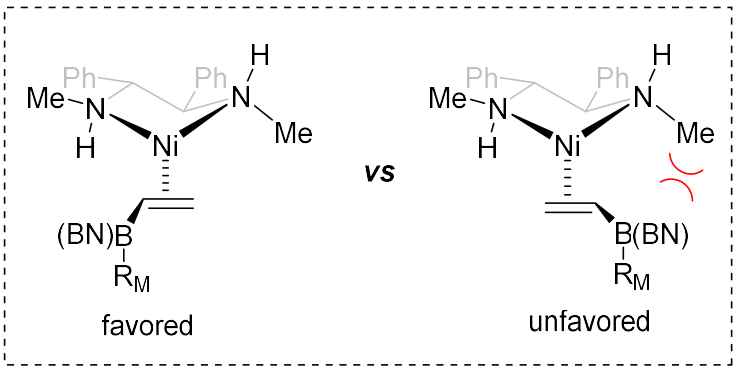
a)



b)







1.3.6 Conclusion.

In conclusion, we have developed the first nickel catalyzed enantioselective conjunctive coupling reaction with 9-BBN borates and aryl halide electrophiles. This transformation offers a facile and practical method to build stereogenicity and complexity from the corresponding alkenes through a sequence of *in situ* hydroboration followed by conjunctive coupling. The reaction proceeds efficiently with a rather broad range of substrates featuring various functionalities as well as steric properties on both electrophile and alkene. We transferred the borane motif into a variety of functional group through stereospecific processes that cannot be achieved with the boronic ester counterpart. For transformations previously shown to be challenging to borane, we demonstrated the adoption of Soderquist borinic ester can overcome the issue of chemoselectivity during migration. Mechanistic studies are in line with a nickel-catalyzed 1,2-metallate shift as opposed to a carbometallation pathway. And finally, we analyzed the relationship between substitution pattern of chiral diamine ligands and level of observed selectivity of the coupling reaction. From doing so, it reveals a function of the backbone stereocenters of the diamine ligands, which may have further implications in ligand design during development of catalytic reactions.

1.4 Experimental Section

1.4.1 General Information

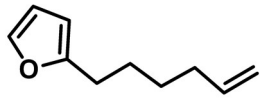
^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.24 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), Varian Gemini-600 (150 MHz) or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). Chemical shifts are reported in ppm using phosphoric acid as the external standard (H_3PO_4: 0.0 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) spectrometer. ^{19}F NMR spectra were recorded on a Varian Gemini-500 (470 MHz) spectrometer. Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART+) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was

performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol or phosphomolybdic acid, and cerium(IV) sulfate in ethanol with sulfuric acid (Seebach).

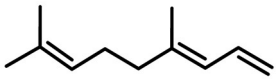
Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol as the modifier.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Nickel(II) acetylacetonate was purchased from Acros Organics, (1*R*,2*R*)-*N*,*N*′-Dimethyl-1,2-diphenylethane-1,2-diamine (***(R,R)*-L1.10**) was purchased from Astatech Inc., and 9-Borabicyclo[3.3.1]nonane 0.5M solution in THF was purchased from Alfa Aesar (of note, cross coupling reactions resulted in slightly diminished yields when a BBN solution from Sigma Aldrich was employed, or when borane reagents were prepared from BBN dimer). All other reagents were purchased from Sigma Aldrich, Alfa Aesar, Oakwood Chemicals, Combi-Blocks, or Acros Organics and used without further purification.

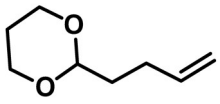
1.4.2 Procedures for Preparation of Alkenyl Substrates



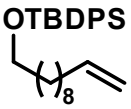
2-(hex-5-enyl)furan (S-1.1). The title compound was prepared according to the procedure reported in the literature.[50] All spectral data was in accordance with previously published results.



***(E)*-4,8-dimethylnona-1,3,7-triene (S-1.2).** The title compound was synthesized in two steps starting with oxidation of geraniol as reported by Stahl *et al.*[51] followed by Wittig olefination. The spectral data was in accordance with the literature.[52]



2-(but-3-en-1-yl)-1,3-dioxane (S-1.3). Prepared from 4-pentenal according to the procedure reported by Karimi *et al*.[53] The spectral data was in accordance with the literature.[54]



***tert*-butyldiphenyl(undec-10-en-1-yloxy)silane (S-1.4).** To a flame-dried round bottom flask equipped with a stir bar was added imidazole (1.02g, 15 mmol). The flask was purged with nitrogen for 5 minutes and dichloromethane (20 mL), undec-10-en-

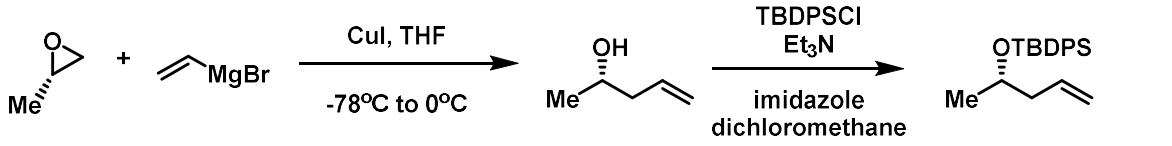
---

[50] S. Hobson, R. Marquez, *Org. Biomol. Chem.* **2006**, *4*, 3808.
[51] J. Hoover, S. Stahl, *J. Am. Chem. Soc.* **2011**, *133*, 16901.
[52] H. Davies, Ø Loe, D. Stafford, *Org. Lett.* **2005**, *7*, 5561.
[53] H. Firouzabadi, N, Iranpoor, B. Karimi, *Synlett*. **1999**, 321.
[54] B. Lin, Y, Zhao, Y. Lai, T. Loh, *Angew. Chem. Int. Ed.* **2012**, *51*, 8041.

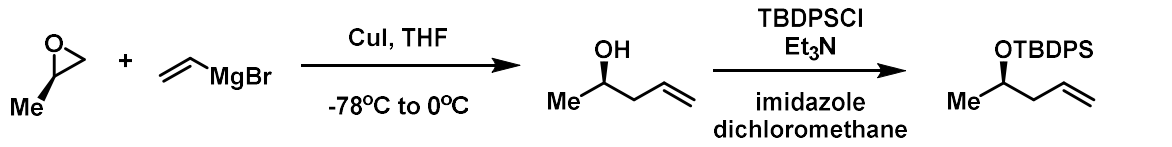
ol (10 mmol), and Et_3N (2.09 mL, 15 mmol) were then added. *tert*-Butyl(chloro)diphenylsilane (2.57 mL, 10 mmol) was added to the reaction mixture drop-wise. The reaction was allowed to stir at room temperature for 16 hours, after which water (20 mL) was added to the reaction. The water layer was extracted 3 times using dichloromethane. The organic layers were combined, dried over sodium sulfate, filtered, and condensed under vacuum. The crude product was purified by silica gel column chromatography (Hexanes, stain in $KMnO_4$) to afford a clear yellow oil (3.92 g, 96% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.66 (m, 4H), 7.44-7.35 (m, 6H), 5.82 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H), 5.00 (dd, J = 17.0, 1.4 Hz, 1H), 4.94 (dd, J = 10.2, 1.4 Hz, 1H), 3.66 (t, J = 6.5 Hz, 1H), 2.08-2.01 (m, 2H), 1.60-1.52 (m, 2H), 1.41-1.23 (m, 14H), 1.05 (s, 9H). **^{13}(150** MHz, $CDCl_3$) δ 139.35, 135.74, 134.36, 129.62, 127.72, 114.28, 64.17, 33.99, 32.75, 29.72, 29.60, 29.52, 29.29, 29.12, 27.05, 25.94, 19.38. **IR** (neat) ν_{max} 2926 (m), 2865 (m), 1427 (m), 1107 (s), 909 (m), 823 (m), 738 (m), 700 (s), 688 (m), 613 (m), 504 (s), 488 (m) cm^{-1}. **HRMS** (DART) for $C_{27}H_{41}OSi$ $[M+H]^+$: Calc'd: 409.2927, found: 409.2926.

Preparation of (*R*)-tert-butyl(pent-4-en-2-yloxy)diphenylsilane and (*S*)-tert-butyl(pent-4-en-2-yloxy)diphenylsilane.



90% yield over two steps

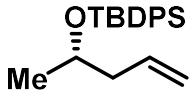


85% yield over two steps

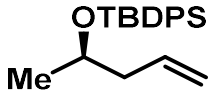
In an argon filled glovebox, a flame-dried round bottom flask equipped with a stir bar was charged with CuI (381mg, 2.0 mmol). The flask was sealed with a rubber septum and taken outside. THF (30 mL) was added under nitrogen. The reaction was cooled down to -78°C with a dry ice/ acetone bath and vinyl magnesium bromide (1M in THF, 20 mL, 20 mmol) was then added dropwise. The reaction was allowed to stir at -78°C for another 15 min, and propylene oxide (0.70 mL, 10 mmol) was added in one portion. The reaction was allowed to stir at -78°C for one hour and at room temperature for another hour. Upon completion the reaction flask was cooled to 0°C and a saturated aqueous ammonium chloride solution was added to the mixture. The organic layer was collected and the aqueous layer was extracted twice with diethyl ether. The organic layers were combined, dried over sodium sulfate, filtered, and concentrated in vacuo. The residue was taken to next step without further purification.

To a flame-dried round bottom flask equipped with a stir bar was added imidazole (1.02g, 15 mmol). The flask was then purged with nitrogen for 10 min. A solution of Crude product and trimethylamine (2.09 mL, 15 mmol) in dichloromethane (15 mL) was added, followed by drop-wise addition of *tert*-butyl(chloro)diphenylsilane (2.60 mL, 10 mmol). The reaction was allowed to stir at room temperature for 16 hours, after which water (20 mL) was added. The organic layer was extracted 3 times using dichloromethane. The

organic layers were combined, dried over sodium sulfate, filtered, and condensed under vacuum to afford the crude product.



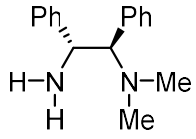
(*R*)-*tert*-butyl(pent-4-en-2-yloxy)diphenylsilane (S-5). The crude material was purified through silica gel column chromatography (hexane, stain in $KMnO_4$) to afford the product as a yellow oil (2.93g, 90% yield over 2 steps). Spectral data were in accordance with previous literature reports.[55]



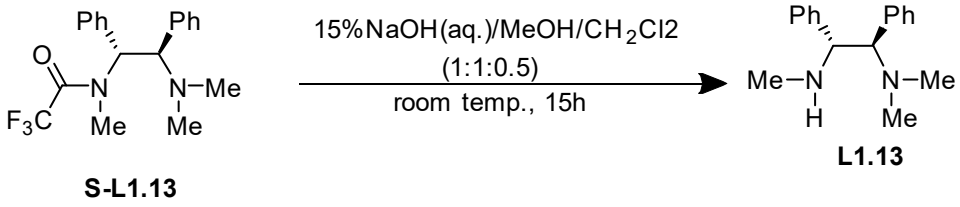
(*S*)-*tert*-butyl(pent-4-en-2-yloxy)diphenylsilane (S-6). The crude material was purified through silica gel column chromatography (hexane, stain in $KMnO_4$) to afford the product as a yellow oil (2.76g, 85% yield over 2 steps). Spectral data were in accordance with previous literature report.[56]

[55] B. Thirupathi, R. Gundapaneni, D. Mohapatra, *Synlett*. **2011**, 2667.
[56] S. Bujaranipalli, S. Das, *Tetrahedron Lett.* **2015**, *56*, 3747.

1.4.3 Procedures for Preparation of Diamine Ligands



(1*R*,2*R*)-N,N-dimethyl-1,2-diphenylethane-1,2-diamine (L1.14). The title compound was prepared according to the procedure reported in the literature.[57] All spectral data was in accordance with the literature.[58]



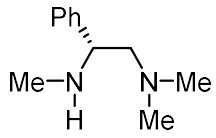
S-L1.13 **L1.13**

(1*R*,2*R*)-N1,N1,N2-trimethyl-1,2-diphenylethane-1,2-diamine (L1.13). The title compound was prepared from hydrolysis of **L1.13**.[9] To a scintillation vial equipped with a magnetic stir bar was added **S-L1.13** (30mg, 0.0856 mmol, 1.0 equiv.) and CH_2Cl_2 (0.5 mL). 15% aq. NaOH (1 mL) and MeOH (1 mL) were added to the vial at room temperature. The reaction mixture was stirred vigorously for 15 hours at room temperature. At the end of 15 hours, H_2O (10 mL) was added. The aqueous phase was extracted with ethyl acetate (10 mLx3) and the combined organic phase was washed with brine (20 mL), dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (10% MeOH and 2% Et_3N in DCM, stained with $KMnO_4$) to afford **L9**[59] as a white solid (11 mg, 50% yield).

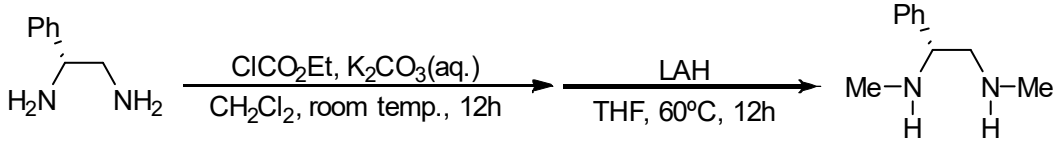
---

[57] M. Shang, X. Wang, S. Koo, J. Youn, J. Chan, W. Yao, B. Hastings, M. Wasa, *J. Am. Chem. Soc.* **2017**, *139*, 95.
[58] H. Yue, H. Huang, G. Bian, H. Zong, F. Li, L. Song., *Tetrahedron: Asymmetry* **2014**, 25, 170.
[59] T. Honjo, S. Sano, M. Shiro, Y. Nagao, *Angew. Chem. Int. Ed.* **2005**, 5838.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-6.98 (m, 10H), 4.00 (d, *J* = 11.0 Hz, 1H), 3.85 (d, *J* = 11.0 Hz, 1H), 2.36 (s, 3H), 2.22 (s, 6H). **HRMS** (ESI) for $C_{17}H_{23}N_2$ $[M+H]^+$: Calc'd: 255.1861, found: 255.1867.



(*R*)-N1,N2,N2-trimethyl-1-phenylethane-1,2-diamine (L1.16). The title compound was prepared according to the procedure reported in the literature.[60] All spectral data was in accordance with the literature.



S-L1.15 **L1.15**

(*R*)-N1,N2-dimethyl-1-phenylethane-1,2-diamine (L1.15). Diamine **L1.15** was prepared by LAH reduction of commercially available D(-)-phenylglycinamide following literature procedures.[61] The yield for the following reactions was not optimized. **S-L1.15** (430 mg, 3.16 mmol) was dissolved in THF (25 mL) in a round bottom flask flushed with argon and cooled to 0 °C. Potassium carbonate (1.09 g, 7.89 mmol, 476.38 uL) in water (3 mL) was added to the flask followed ethylchlorofomate (2.06 g, 18.94 mmol, 1.80 mL). The resulting two-phase mixture was stirred vigorously at ambient temperature for 12 h. Na_2SO_4 was added directly to the reaction mixture which was filtered through a fritted funnel, and solids were further washed with EtOAc. The filtrate was concentrated in vacuo and the crude material was purified by silica gel chromatography (1% Et_3N in DCM,

[60] S. de Sousa, P. O' Brien, C. Pilgram, *Tetrahedron* **2002**, *58*, 4643.
[61] Y. Belokon, L.Pritula, V. Tararov, V. Bakhmutov, Y. Struchkov, *J. Chem. Soc., Dalton Trans.* **1990**, 179.

stained in CAM) to afford ethyl-N-[2-(ethoxycarbonylamino)-1-phenyl-ethyl]carbamate **L1.15** (124.8 mg, 0.45 mmol, 14.10% yield) as a white solid.

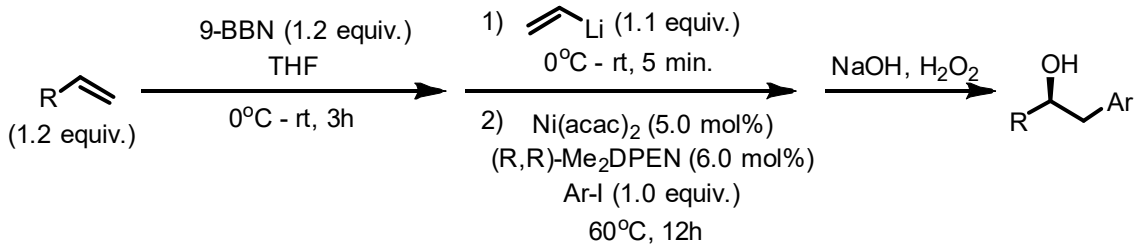
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 5H), 5.58 (s, 1H), 4.91 (s, 1H), 4.81 (s, 1H), 4.16 – 4.07 (m, 4H), 3.51 (s, 3H), 1.24 (t, *J* = 6.5 Hz, 6H).

Step 2: In an argon filled glovebox, lithium aluminum hydride was placed in a two-neck round bottom flask equipped with a stir-bar and waterless reflux condenser. After that, 1 mL of THF was added to the flask which was cooled to 0 ºC. Once cooled, ethyl-N-[2-(ethoxycarbonylamino)-1-phenyl-ethyl]carbamate (124.8 mg, 0.45 mmol, 1.0 equiv.) was added as a solution in 5 mL of THF drop-wise, the mixture was allowed to warm to room temperature over an hour and then heated to reflux for 12 hours. The flask was then cooled to 0 ºC and carefully quenched with 2 mL of H_2O followed by addition of 2 mL of a 3M NaOH solution. The mixture was stirred at room temperature for 1 hour before addition of Na_2SO_4. The suspension was then filtered through celite, the solids washed with EtOAc and the filtrate concentrated in vacuo. The crude material was purified by silica gel chromatography (1-10% MeOH in CH_2Cl_2 with 1% Et_3N, stain in ninhydrin) to afford the product as a pale yellow oil (21 mg, 29% yield). All spectral data was in accordance with the literature. [62]

[62] G. Buono, C. Triantaphylides, G. Peiffer, F. Petit, *ChemInform.* **1983**, 14.

1.4.4 General Procedure for Conjunctive Cross-Coupling

Procedure A



In a glovebox, under argon, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with a solution of 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.). The vial was cooled to 0°C, and the olefin (0.24 mmol, 1.20 equiv.) was added. The reaction mixture was allowed to warm to room temperature and stir for 3 hours before being cooled back to 0°C. Vinyllithium (for synthesis of halide free vinyllithium see ref[63]) in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.) was added to the reaction mixture which was then warmed to room temperature and stirred for 5 minutes. Meanwhile a solution of $Ni(acac)_2$ (0.010 mmol, 0.050 equiv.) and **L1.10** (0.012 mmol, 0.060 equiv.) in THF (0.4 mL) , was allowed to complex for 5 minutes under inert atmosphere. The catalyst solution was added to the boron 'ate' mixture at room temperature followed by addition of aryl iodide (0.20 mmol, 1.00 equiv.) The reaction vial was sealed with a septum cap, taken out of the glovebox and heated at 60 for 12 hours, after which point the reaction mixture was cooled to 0°C and 30% H_2O_2 (0.5 mL) were added along with 3 M NaOH (0.5 mL). The reaction mixture was allowed to

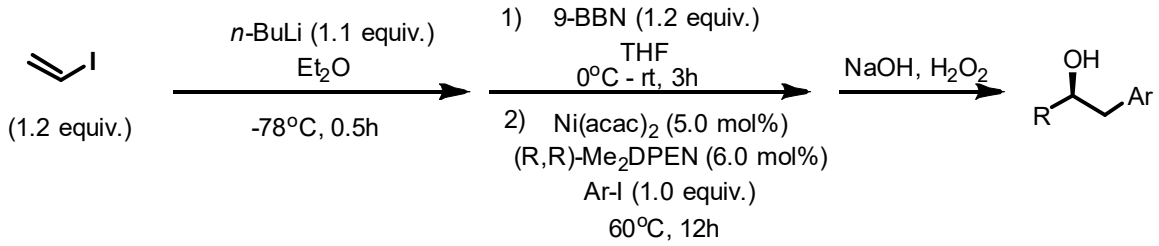
[63]E. Edelstein, S. Namirembe, J. Morken, *J. Am. Chem. Soc.* **2017**, *139*, 5027.

warm up to room temperature and stirred for 3 hours. Aq. saturated $Na_2S_2O_3$ (1 mL) solution was then added to quench the reaction. The aqueous phase was extracted with Et_2O (2 x 2 mL), followed by EtOAc (2 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to provide the desired products.

Note: In all cases, a stock solution of 9-BBN derivatives could be prepared and stored in a freezer for as long as one month, before addition of vinyllithium, without any diminishing yield or stereoselectivity.

Note: The reaction can be carried out using aryl-bromides instead of aryl-iodides by following the same method described in **procedure A** with a slight modification. The reaction requires anhydrous NaI (33.0 mg, 0.22 mmol, 1.1 equiv.) which can be added to the solution of 9-BBN and alkene in THF, prior to addition of vinyllithium. These reactions resulted in slightly lower yields (PhBr: 63% yield and PhI 75% yield) and no erosion in selectivity.

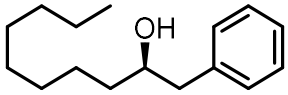
Procedure B



In an argon filled glovebox, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with a solution of 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), cooled to 0°C, and the olefin (0.24 mmol, 1.20 equiv.) was added. The reaction mixture was allowed to warm to room temperature and stir for an additional 3 hours. Meanwhile,

inside the glovebox, a separate oven-dried 2 dram vial was charged with vinyliodide (37.0 mg, 0.24 mmol, 1.2 equiv.) and dissolved in 0.4 mL of Et_2O. The vial was brought outside and cooled to -78ºC. A solution of n-butyllithium (90 µL, 0.22 mmol, 1.10 equiv.) was added drop-wise to the reaction vial and the mixture was stirred at -78ºC for 30 minutes. At this point the alkyl-BBN solution generated previously was added to the vial at -78ºC in a drop-wise fashion. The reaction vessel was warmed to room temperature and the solvent was carefully removed under reduced pressure through a Schlenk line. The vial was brought back inside the glovebox and the contents were dissolved in 0.4 mL of THF. Meanwhile, a solution of $Ni(acac)_2$ (0.010 mmol, 0.050 equiv.) and **L1.10** (0.012 mmol, 0.060 equiv.) in THF (0.4 mL) , was allowed to complex for 5 minutes under inert atmosphere. The catalyst solution was added to the boron 'ate' mixture at room temperature followed by addition of aryl iodide (0.20 mmol, 1.00 equiv.) The reaction vial was sealed with a septum cap and taken out of glovebox and heated at 60 for 12 hours, after which point the reaction mixture was cooled to 0°C, and 30% H_2O_2 (0.5 mL) were added along with 3 M NaOH (0.5 mL). The reaction mixture was allowed to warm up to room temperature and stirred for 3 hours. Aq. saturated $Na_2S_2O_3$ (1 mL) solution was then added to quench the reaction mixture. The aqueous phase was extracted with Et_2O (2 x 2 mL), followed by EtOAc (2 x 2 mL). The combined organic layer was dried over $MgSO_4$, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to provide the desired products.

1.4.5 Characterization of Conjunctive Cross-Coupling Products



***(R)*-1-phenyldecan-2-ol (1.35).** The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (50% DCM in pentane, stain in CAM) to afford the product as a colorless oil (37 mg, 79% yield).

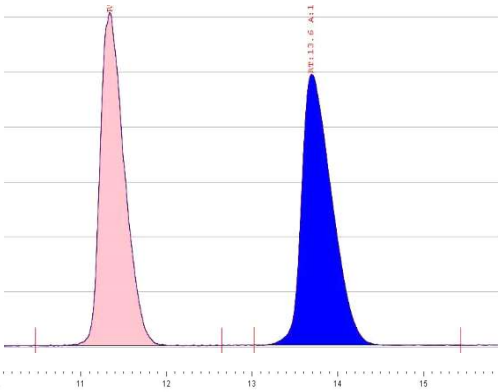
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33-7.30 (m, 2H), 7.25-7.12 (m, 3H), 3.84-3.8 (m, 1H), 2.84 (dd, *J* = 13.6, 4.2 Hz, 1H), 2.65 (dd, *J* = 13.6, 8.4 Hz, 1H), 1.53-1.25 (m, 15 H), 0.89 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 138.81, 129.56, 128.69, 126.56, 72.84, 44.22, 37.02, 32.03, 29.81, 29.73, 29.42, 25.91, 22.82, 14.25. **IR** (neat) ν_{max} 3373.2 (br, s), 3027.7 (w, s), 2923.2 (s), 2853.8 (s), 1495.4 (s), 1454.1 (s), 1377.2 (s), 1126.3 (s), 1031.3 (m), 744.0 (s), 699.7 (s). **HRMS** (DART) for $C_{16}H_{30}NO$ $(M+NH_4)^+$: Calc'd: 252.2337, found: 252.2327. **$[\alpha]_D^{20}$** = -1.02 (*c* =1.4, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure A with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

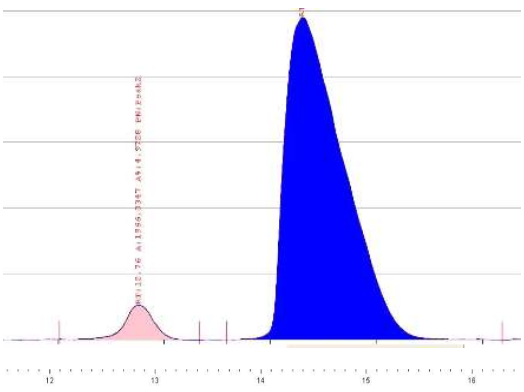
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-phenyldecan-2-ol and (R)-1-phenyldecan-2-ol (from gram scale reaction).

Racemic Material

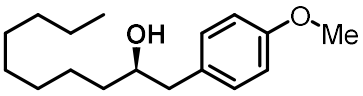


Peak No	% Area	Area	RT (min)
1	49.7027	11395.6892	11.34
2	50.2973	11531.9944	13.6
Total:	100	22927.6836	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	4.9728	1966.0347	12.76
2	95.0272	37570.0141	14.3
Total:	100	39536.0488	



(*R*)-1-(4-methoxyphenyl)decan-2-ol (1.50). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 4-iodoanisole (46.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (80% DCM in hexanes, stained with CAM) to afford a white solid (22.7 mg, 43% yield).

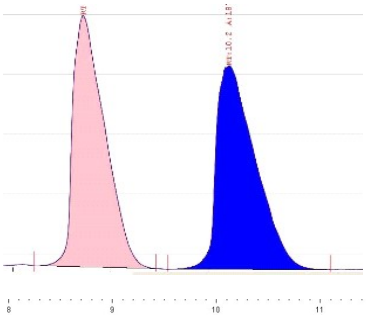
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 3.82-3.73 (m, 4H), 2.78 (dd, J = 13.7, 4.2 Hz, 1H), 2.58 (dd, J = 13.7, 8.4 Hz, 1H), 1.55-1.22 (m, 14H), 0.88 (t, J = 7.0 Hz, 3H).**^{13}C NMR** (150 MHz, $CDCl_3$) δ 158.43, 130.73, 130.51, 114.15, 72.92, 55.41, 43.25, 36.93, 32.02, 29.82, 29.73, 29.42, 25.92, 22.81, 14.25. **IR** (neat) ν_{max} 3382.00 (br, w), 2923.76 (s), 2853.47 (s), 1612.24 (m), 1511.44 (s), 1464.39

(m), 1441.35 (m), 1299.98 (m), 1245.73 (s), 1177.39 (m), 1038.10 (s), 817.67 (m), 570.95 (w), 521.58 (w) cm^{-1}. **HRMS** (DART) for $C_{17}H_{27}O$ $[M+H-H_2O]^+$: Calc'd: 247.2062, found: 247.2072. $[\alpha]_D^{20}$ = -4.8678 (*c* = 10.6, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

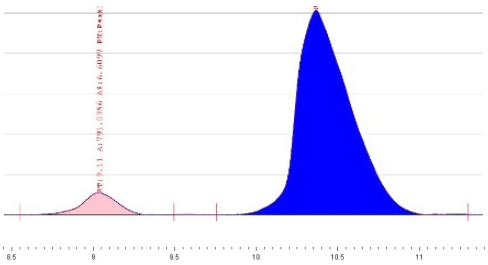
Racemic compound was prepared according to the general **procedure B** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

Racemic Material

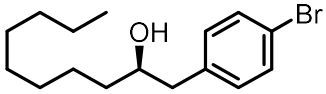


Peak No	% Area	Area	RT (min)
1	50.089	18835.8429	8.72
2	49.911	18768.9061	10.2
Total:	100	37604.749	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	6.6099	791.0956	9.11
2	93.3901	11177.2677	10.4
Total:	100	11968.3633	



***(R)*-1-(4-bromophenyl)decan-2-ol (1.56).** The reaction was performed according to the general **procedure A,** with slight deviation. The reaction was run at room temperature for 12 hours. Heating the reaction resulted in over-coupling. Reagents: 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 1,4-bromoiodobenzene (56.6 mg, 0.20

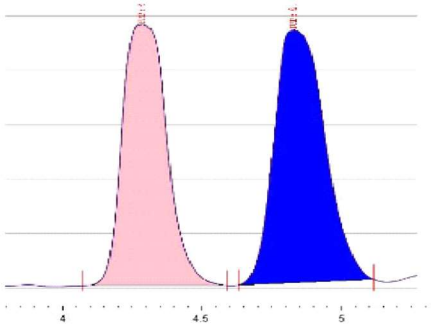
mmol, 1.00 equiv.). The crude mixture was purified by silica gel chromatography (50% DCM in hexanes, stained with CAM) to afford a white solid (50.1 mg, 80% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.7 Hz 2H), 7.10 (d, *J* = 7.7 Hz, 2H), 3.81-3.76 (m, 1H), 2.77 (dd, *J* = 13.7, 4.3 Hz, 1H), 2.61 (dd, *J* = 13.7, 8.2 Hz, 1H), 1.52-1.22 (m, 14H), 0.88 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 137.86, 131.68, 131.30, 120.42, 72.66, 43.51, 37.05, 32.01, 29.76, 29.71, 29.40, 25.86, 22.81, 14.25. **IR** (neat) ν_{max} 3354.91 (br, w), 3291.22 (br, w), 2918.89 (s), 2850.85 (s), 1486.49 (m), 1465.52 (m), 1085.32 (w), 1070.61 (m), 1012.27 (m), 799.33 (m) cm^{-1}. **HRMS** (DART) for $C_{16}H_{26}BrO$ $[M+H]^+$: Calc'd: 330.1433, found: 330.142. **$[\alpha]_D^{20}$** = – 6.073 (*c* = 1.63, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

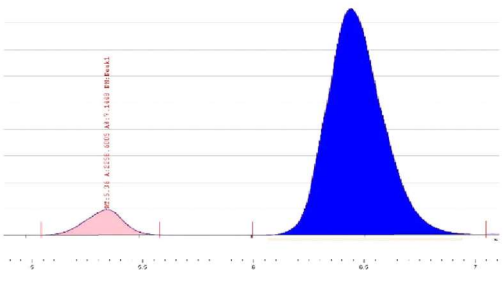
Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

Racemic Material

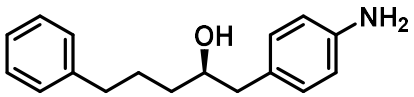


Peak No	% Area	Area	RT (min)
1	47.571	32435.1783	4.17
2	52.429	35747.5313	4.83
Total:	100	68182.7096	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	7.1448	2258.6005	5.36
2	92.8552	29353.0461	6.44
Total:	100	31611.6466	



(*R*)-1-(4-aminophenyl)-5-phenylpentan-2-ol (1.53).

The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), allylbenzene (28.4 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 4-iodoaniline (43.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (60% EtAOc in hexanes, stained with CAM) to afford a yellow solid (27.6 mg, 54% yield).

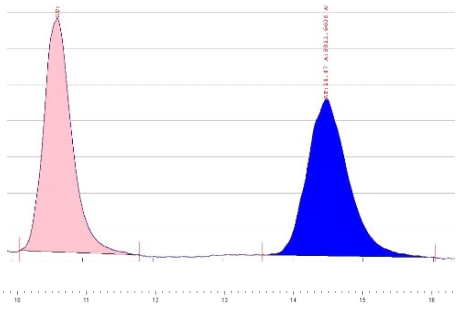
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.15 (m, 5H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.64 (d, *J* = 8.2 Hz, 2H), 3.91-3.29 (m, 3H), 2.72 (dd, *J* = 13.7, 4.1 Hz, 1H), 2.68-2.60 (m, 2H), 2.51 (dd, *J* = 13.7, 8.5 Hz, 1H), 1.90-1.76 (m, 1H), 1.75-1.64 (m, 1H), 1.61-1.48 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 145.04, 142.60, 130.38, 128.56, 128.42, 127.43, 125.84, 115.53, 72.74, 43.31, 36.39, 36.05, 27.79. **IR** (neat) ν_{max} 3343.63 (br, m), 3034.98 (w), 2930.39 (m), 2856.48 (w), 1621.91 (m), 1515.60 (s), 1501.35 (m), 1452.64 (w), 1272.58 (w), 1178.86 (w), 1087.70 (w), 820.26 (m), 749.76 (m), 699.81 (m), 562.06 (w), 509.25 (w) cm^{-1}. **HRMS** (DART) for $C_{17}H_{22}NO$ $[M+H]^+$: Calc'd: 256.1701, found: 256.1702. **$[\alpha]_D^{20}$** = -1.74 (*c* = 1.40, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

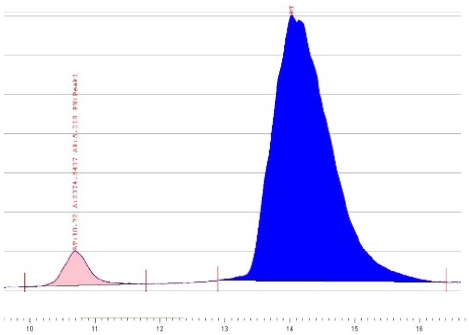
Chiral SFC (Chiracel OJ-H, 20% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(4-aminophenyl)-5-phenylpentan-2-ol.

Racemic Material

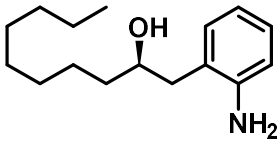


Peak No	% Area	Area	RT (min)
1	50.5473	9006.692	10.64
2	49.4527	8811.6606	14.47
Total:	100	17818.3526	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	5.318	2374.5437	10.72
2	94.682	42276.4197	14.08
Total:	100	44650.9634	



(*R*)-1-(2-aminophenyl)decan-2-ol (1.52). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-octene (32.7 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 2-iodoaniline (43.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (35% EtOAc in hexanes, stained with CAM) to afford a dark oil (30.9 mg, 62% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10-7.01 (m, 2H), 6.81-6.72 (m, 2H), 3.94-3.84 (m, 1H), 3.80-3.44 (br s, 1H). 2.74 (dd, J = 14.3, 3.7 Hz, 1H), 2.66 (dd, J = 14.3, 8.1 Hz, 1H), 1.58-1.19 (m, 14H), 0.88 (t, J = 6.20 Hz, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.73, 131.40, 127.75, 124.92, 119.67, 116.91, 73.22, 39.65, 37.49, 32.01, 29.78, 29.73, 29.41, 25.97, 22.81, 14.24. **IR** (neat) 3347.00 (br, w), 2922.38 (s), 2852.76 (s), 1621.62 (m), 1583.64 (w), 1495.75 (m), 1465.75 (w), 1311.84 (w), 1264.58 (w), 1076.47 (w), 747.99

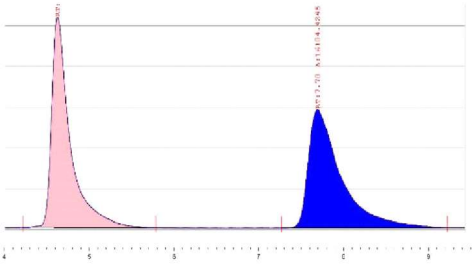
(s), 722.18 (w), 649.21 (w), 616.58 (w), 533.16 (w), 491.23 (w) cm^{-1}. **HRMS** (DART) for $C_{16}H_{28}NO$ $[M+H]^+$: Calc'd: 250.2171, found: 250.2181. $[\alpha]_D^{20}$ = +8.08 (*c* = 4.12, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

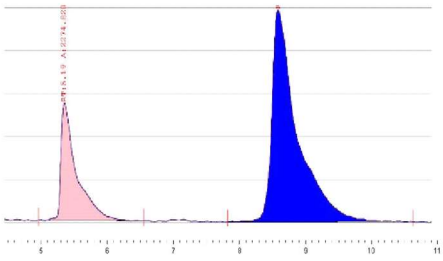
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(2-aminophenyl)decan-2-ol.

Racemic Material

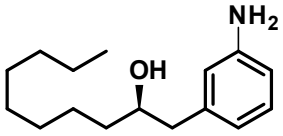


Peak No	% Area	Area	RT (min)
1	50.4002	16364.2842	4.58
2	49.5998	16104.4245	7.78
Total:	100	32468.7087	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	25.2867	2274.8205	5.19
2	74.7133	6721.2976	8.51
Total:	100	8996.1181	



(*R*)-1-(3-aminophenyl)decan-2-ol (1.51). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), (32.7 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 3-iodoaniline (43.8 mg, 0.20 mmol, 1.00

equiv.) The crude mixture was purified by silica gel chromatography (30% EtOAc in hexanes, stained with CAM) to afford a yellow solid (39.9 mg, 80% yield).

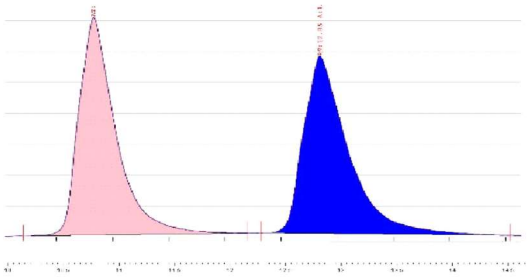
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (t, J = 7.6 Hz, 1H), 6.64-6.51 (m, 3H), 3.89-3.36 (m, 3H), 2.75 (dd, J = 13.5, 4.0 Hz, 1H), 2.53 (dd, J = 13.5, 8.6 Hz, 1H), 1.58-1.18 (m, 14H), 0.89 (t, J = 6.8 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 146.74, 140.00, 129.66, 119.76, 116.23, 113.44, 72.70, 44.25, 37.00, 32.02, 29.82, 29.73, 29.41, 25.92, 22.81, 14.24. **IR** (neat) ν_{max} 3382.23 (br, w), 3316.11 (m), 2953.10 (m), 2922.65 (s), 2853.03 (s), 1601.73 (m), 1463.40 (m), 789.09 (m), 697.50 (m) cm^{-1}. **HRMS** (DART) for $C_{16}H_{28}NO$ $[M+H]^+$: Calc'd: 250.2171, found: 250.2169. **$[\alpha]_D^{20}$** = -11.157 (c = 0.72, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

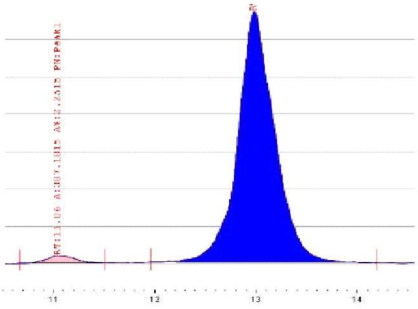
Chiral SFC (Chiracel OJ-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(3-aminophenyl)decan-2-ol.

Racemic Material

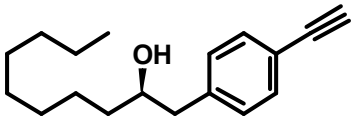


Peak No	% Area	Area	RT (min)
1	50.4733	16097.1974	10.83
2	49.5267	15795.286	12.85
Total:	100	31892.4834	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	2.2515	387.1815	11.06
2	97.7485	16809.2242	12.98
Total:	100	17196.4057	



(*R*)-1-(4-ethynylphenyl)decan-2-ol (1.57). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), (4-iodophenylethynyl)trimethylsilane (60.04 mg, 0.20 mmol, 1.00 equiv.). After oxidation and work-up methanol (1.5 mL) and K_2CO_3 (110.56 mg, 0.80 mmol, 4.00 equiv.) were added to the crude mixture. The reaction mixture was allowed to stir at room temperature for 3 hours. Methanol was then evaporated off under reduced pressure. The resulting residue was diluted with CH_2Cl_2 (4 mL), washed with aq. Saturated $NaHCO_3$ (2mL x 3), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (50% DCM in hexanes, stained with CAM) to afford a white solid (28.5 mg, 55% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 7.9 Hz, 2H), 7.18 (d, J = 7.9 Hz, 2H), 3.89-3.75 (m, 1H), 3.05 (s, 1H), 2.82 (dd, J = 13.6, 4.3 Hz, 1H), 2.66 (dd, J = 13.6, 8.2 Hz, 1H), 1.59-1.18 (m, 14H), 0.88 (t, J = 6.7 Hz, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 139.88, 132.40, 129.58, 120.29, 83.72, 77.08, 72.69, 44.06, 37.06, 32.01, 29.75, 29.70, 29.40, 25.85, 22.81, 14.25. **IR** (neat) ν_{max} 3356.92 (w), 3278.76 (m), 2955.76 (w), 2920.35 (s), 2852.12 (s), 1506.45 (w), 1467.54 (m), 1431.34 (w), 1410.04 (w), 1128.54 (w), 1106.54 (w), 1084.63(m), 1058.94 (w), 1022.94 (m), 907.26 (w), 837.69 (m), 818.04 (s), 722.54 (m), 642.49 (s), 614.39 (s), 578.83 (s), 527.84 (m), 517.54 (m) cm^{-1}. **HRMS** (DART) for

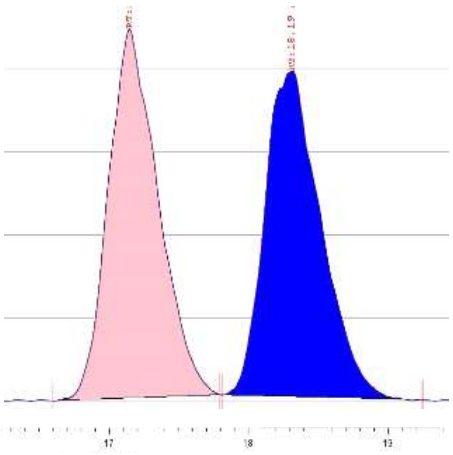
$C_{17}H_{27}O$ $[M+H-H_2O]^+$: Calc'd: 247.2062, found: 247.2072. **$[\alpha]_D^{20}$** = -8.4280(*c* = 0.775, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

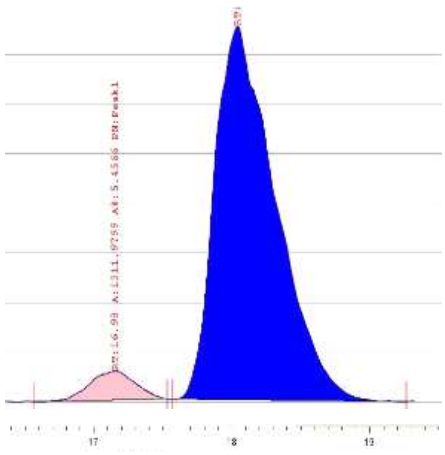
Chiral SFC (Chiracel ODR-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(4-ethynylphenyl)decan-2-ol.

Racemic Material

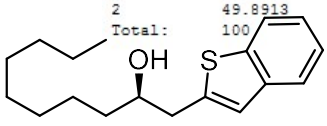


Peak No	% Area	Area	RT (min)
1	50.1087	11087.2775	17.02
2	49.8913	11039.1609	18.19
Total:	100	22126.4384	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	5.4566	1311.9799	16.98
2	94.5434	22731.7993	17.85
Total:	100	24043.7792	



(*R*)-1-(benzo[*b*]thiophen-2-yl)decan-2-ol (1.60). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), (32.7 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg,

0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 2-iodobenzothiophene (52.02 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by silica gel chromatography (5% EtOAc in hexanes, stained with CAM) to afford a yellow oil (29.3 mg, 50% yield).

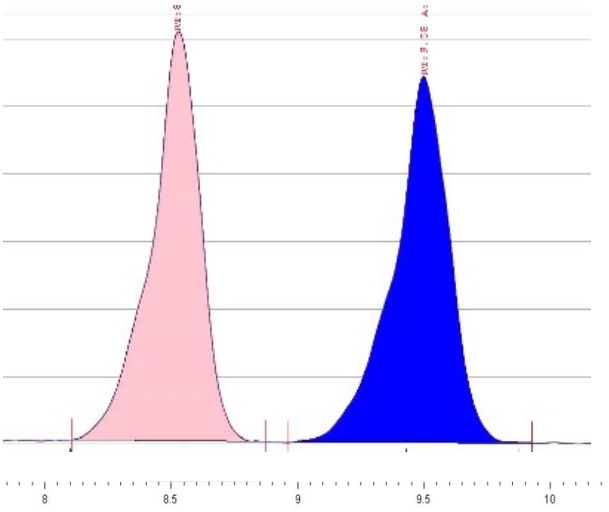
^{1}H NMR (500 MHz, $CDCl_3$) 7.78 (d, *J* = 7.9 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.35 – 7.26 (m, 2H), 7.10 (s, 1H), 3.92 (tq, *J* = 8.5, 4.4 Hz, 1H), 3.10 (dd, *J* = 14.7, 4.0 Hz, 1H), 2.97 (dd, *J* = 14.7, 8.1 Hz, 1H), 1.75 (d, *J* = 4.1 Hz, 1H), 1.60 – 1.47 (m, 3H), 1.44 – 1.19 (m, 12H), 0.89 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.02, 140.17, 139.91, 124.36, 123.88, 123.03, 122.74, 122.27, 72.27, 39.07, 36.85, 32.01, 29.74, 29.70, 29.40, 25.86, 22.81, 14.25. **IR** (neat) ν_{max} 3371.6 (br), 3058.9 (s, w), 2923.4 (s), 2853.2 (s), 1457.8 (s), 1453.8 (s) , 1435.8 (s, w), 1307.1 (s, w), 1253.8 (s, w), 1154.3 (s, w), 1125.3 (s), 1102.9 (s), 1066.2 (s), 854.0 (s), 743.9 (s), 725.9 (s) . **HRMS** (DART) for $C_{18}H_{25}S$ $[M+H-H_2O]^+$: Calc'd: 273.1677, found: 273.1668. **$[\alpha]_D^{20}$** = -7.97 (*c* = 1.00, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

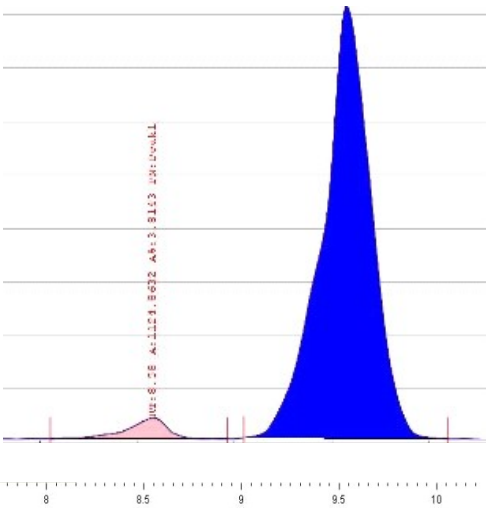
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(benzo[b]thiophen-2-yl)decan-2-ol.

Racemic Material

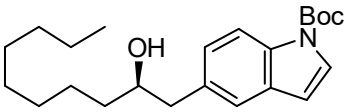


Peak No	% Area	Area	RT (min)
1	49.717	9348.6838	8.48
2	50.283	9455.0956	9.58
Total:	100	18803.7794	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	3.8143	1124.8632	8.58
2	96.1857	28365.5159	9.57
Total:	100	29490.3791	



***tert*-butyl (*R*)-5-(2-hydroxydecyl)-1H-indole-1-carboxylate (1.58).** The reaction was performed according to the general **procedure A,** with slight deviation. The reaction was run at room temperature for 12 hours. Reaction was prepared with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL tert-butyl 5-iodoindole-1-carboxylate (68.63 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by silica gel chromatography (5% EtOAc in hexanes, stained with CAM) to afford a colorless oil (41 mg, 55% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 3.7 Hz, 1H), 7.40 (d, *J* = 1.6 Hz, 1H), 7.17 (dd, *J* = 8.5, 1.7 Hz, 1H), 6.53 (dd, *J* = 3.7, 0.9 Hz, 1H), 3.88 – 3.79 (m, 1H), 2.93 (dd, *J* = 13.6, 4.2 Hz, 1H), 2.72 (dd, *J* = 13.6, 8.4 Hz, 1H), 1.67 (s, 9H), 1.57

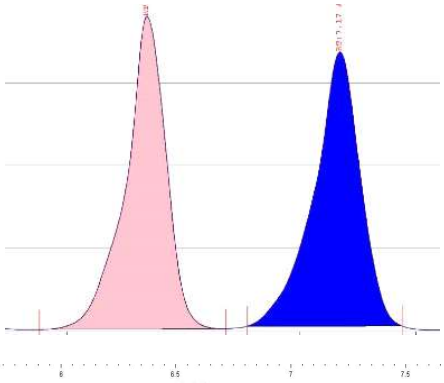
– 1.46 (m, 4H), 1.42 – 1.19 (m, 11H), 0.88 (t, J = 6.8 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 149.89, 134.17, 132.95, 131.07, 126.33, 125.83, 121.62, 115.29, 107.22, 83.76, 73.09, 44.07, 36.93, 32.02, 29.83, 29.74, 29.42, 28.35, 25.95, 22.81, 14.25. **IR** (neat) ν_{max} 3429.9 (br), 2924.5 (s), 2854.1 (s), 1733.1(s), 1580.6 (s, w), 1537.9 (s, w), 1469.1 (s), 1443.1 (s), 1292.9 (s), 1163.5 (s), 1130.7 (s), 1039.8 (s), 1023.2 (s), 886.2 (s), 855.4 (s), 804.7 (s, w), 804.7 (s, w), 765.4 (s), 723.9 (s). **HRMS** (DART) for $C_{23}H_{36}NO_3$ $[M+H]^+$: Calc'd: 374.2913, found: 374.2695. **$[\alpha]_D^{20}$** = -1.43 (c = 1.00, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

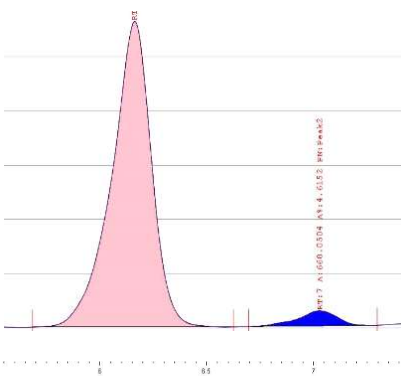
Chiral SFC (Chiracel OJ-H, 6% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of tert-butyl (R)-5-(2-hydroxydecyl)-1H-indole-1-carboxylate.

Racemic Material

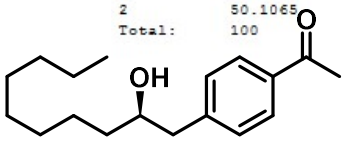


Peak No	% Area	Area	RT (min)
1	49.8935	23002.6909	6.34
2	50.1065	23100.8532	7.17
Total:	100	46103.5441	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	95.3848	13806.9061	6.18
2	4.6152	668.0504	7
Total:	100	14474.9565	



(*R*)-1-(4-(2-hydroxydecyl)phenyl)ethan-1-one (1.55). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48

mL, 0.5 M, 0.24 mmol, 1.20 equiv.), (32.7 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 4'-iodoacetophenone (55.3 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (20% EtOAc in hexanes, stained with CAM) to afford a yellow solid (43.1 mg, 78% yield).

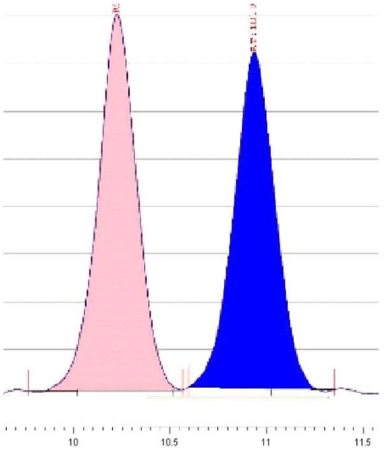
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 3.89-3.82 (m, 1H), 2.88 (dd, *J* = 13.6, 4.3 Hz, 1H), 2.73 (dd, *J* = 13.6, 8.3 Hz, 1H), 2.59 (s, 3H), 1.58-1.20 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 197.95, 144.77, 135.68, 129.79, 128.73, 72.64, 44.12, 37.21, 32.00, 29.74, 29.69, 29.39, 26.72, 25.84, 22.81, 14.25. **IR** (neat) ν_{max} 3425.67 (br, w), 2922.79 (s), 2853.10 (m), 1678.84 (s), 1605.64 (m), 1569.98 (w), 1464.42 (w), 1413.10 (w), 1357.42 (w), 1304.74 (w), 1266.38 (s), 1182.21 (w), 1117.60 (w), 1075.11 (w), 956.57 (w), 837.28 (w), 813.44 (w), 599.71 (m), 585.76 (w) cm^{-1}. **HRMS** (DART) for $C_{18}H_{29}O_2$ $[M+H]^+$: Calc'd: 277.2168, found: 277.2156. **$[\alpha]_D^{20}$** = -8.148 (*c* = 3.46, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

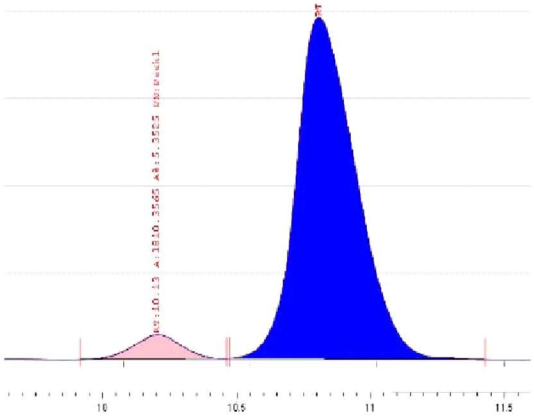
Chiral SFC (Chiracel AD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(4-(2-hydroxydecyl)phenyl)ethan-1-one.

Racemic Material

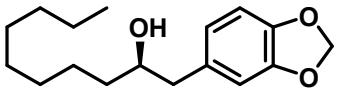


Peak No	% Area	Area	RT (min)
1	51.5576	2225.3493	10.2
2	48.4424	2090.8911	10.91
Total:	100	4316.2404	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	5.3525	1810.3565	10.13
2	94.6475	32012.4898	10.77
Total:	100	33822.8463	



(*R*)-1-(benzo[d][1,3]dioxol-5-yl)decan-2-ol (1.59). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 5-iodo-1,3-benzodioxole (49.6 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (50% DCM in hexanes, stained with CAM) to afford a white solid (36.1 mg, 65% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 (d, *J* = 7.8 Hz, 1H), 6.71 (d, *J* = 1.7 Hz, 1H), 6.66 (dd, *J* = 7.8, 1.7 Hz, 1H), 5.94 (s, 2H), 3.84-3.71 (m, 1H), 2.75 (dd, *J* = 13.7, 4.1 Hz, 1H), 2.55 (dd, *J* = 13.7, 8.5 Hz, 1H), 1.55-1.15 (m, 14H), 0.88 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR** (150

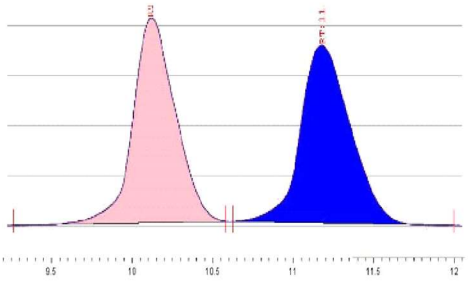
MHz, $CDCl_3$) δ 147.92, 146.32, 132.51, 122.41, 109.85, 108.44, 101.01, 72.87, 43.88, 36.93, 32.02, 29.81, 29.73, 29.41, 25.91, 22.81, 14.24. **IR** (neat) ν_{max} 3406.47 (br, w), 2924.26 (s), 2854.22 (m), 1503.03 (m), 1489.12 (s), 1466.03 (w), 1332.03 (m), 1245.98 (s), 1189.19 (w), 1040.89 (s), 940.18 (m), 928.68 (m), 807.76 (m) cm^{-1}. **HRMS** (DART) for $C_{17}H_{25}O_2$ $[M+H-H_2O]^+$: Calc'd: 261.1855, found: 261.1849. **$[\alpha]_D^{20}$** = – 9.291 (*c* = 1.58, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

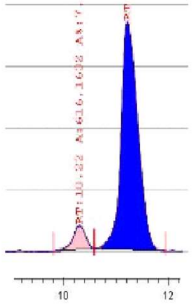
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(benzo[d][1,3]dioxol-5-yl)decan-2-ol.

Racemic Material

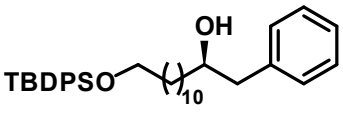


Peak No	% Area	Area	RT (min)
1	49.5546	7242.3644	10.08
2	50.4454	7372.5663	11.11
Total:	100	14614.9307	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	7.2302	616.1632	10.22
2	92.7698	7905.8995	11.1
Total:	100	8522.0627	



(*R*)-13-((*tert*-butyldiphenylsilyl)oxy)-1-phenyltridecan-2-ol (1.37). The reaction was performed according to the general **procedure B** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), (32.7 mg, 0.24 mmol, 1.20 equiv.), halide-

free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), tert-butyldiphenyl(undec-10-en-1-yloxy)silane (**S-1.4**) (98.1 mg, 0.24 mmol, 1.20 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (40% DCM in hexanes, stained with CAM) to afford a colorless oil (78.5 mg, 74% yield).

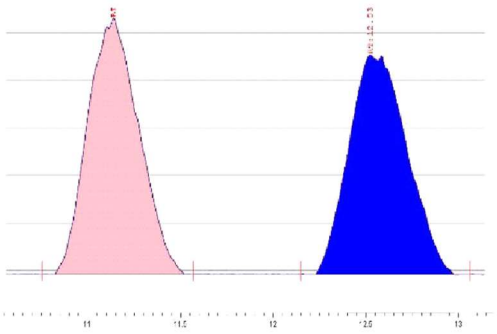
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69-7.65 (m, 4H), 7.44-7.35 (m, 6H), 7.34-7.29 (m, 2H), 7.26-7.20 (m, 3H), 3.86 (m, 1H), 3.65 (t, *J* = 6.5 Hz, 2H), 2.84 (dd, *J* = 13.6, 4.2 Hz, 1H), 2.65 (dd, *J* = 13.6, 8.5 Hz, 1H), 1.59-1.27 (m, 20H), 1.05 (s, 9H). **^{13}C NMR** (150 MHz, CD_3CN) δ 138.94, 134.54, 133.19, 128.85, 128.59, 127.24, 126.87, 125.02, 71.16, 62.94, 42.93, 35.98, 31.40, 29.04, 28.53, 28.49, 28.43, 28.40, 28.13, 25.43, 24.63, 24.59, 17.94. **IR** (neat) ν_{max} 3387.23 (br, w), 2926.31 (s), 2854.13 (m), 1463.04 (w), 1427.68 (w), 1389.36 (w), 1360.85 (w), 1109.82 (s), 1030.21 (w), 1007.61 (w), 823.15 (w), 739.64 (m), 700.25 (s), 613.40 (m), 504.73 (m), 490.04 (w) cm^{-1}. **HRMS** (DART) for $C_{35}H_{51}O_2Si$ $[M+H]^+$: Calc'd: 531.3658, found: 531.3682. **$[\alpha]_D^{20}$** = -0.546 (*c* = 1.83, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

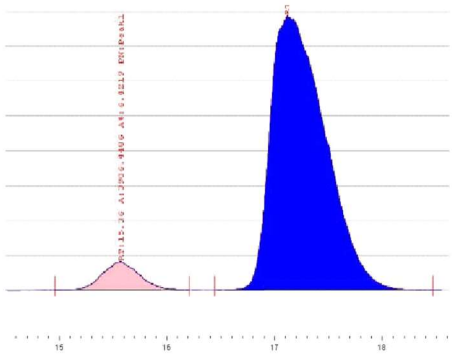
Racemic compound was prepared according to the general **procedure B** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

Chiral SFC (Chiracel ODR-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-13-((tert-butyldiphenylsilyl)oxy)-1-phenyltridecan-2-ol.

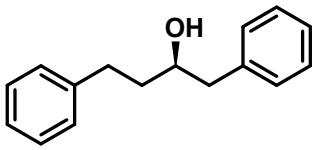
Racemic Material Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	50.5346	10304.1582	11.15
2	49.4654	10086.1642	12.53
Total:	100	20390.3224	



Peak No	% Area	Area	RT (min)
1	6.4219	3906.4486	15.36
2	93.5781	56923.3704	16.94
Total:	100	60829.819	



(*R*)-1,4-diphenylbutan-2-ol (1.38). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), (32.7 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), styrene (25.0 mg, 0.24 mmol, 1.20 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (60% DCM in hexanes, stained with CAM) to afford a colorless oil (22.6 mg, 50% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.14 (m, 10H), 3.92-3.80 (m, 1H), 2.90-2.82 (m, 2H), 2.76-2.66 (m, 2H), 1.94-1.77 (m, 2H), 1.53 (s, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.18, 138.49, 129.58, 128.75, 128.60, 128.56, 126.69, 125.98, 72.10, 44.31, 38.59, 32.27. **IR** (neat) ν_{max} 3405.14 (br,s), 3083.98 (w), 3061.19 (w), 3025.99 (m), 2919.73 (w), 2857.89 (w), 1602.16 (w), 1494.75 (m), 1453.54 (m), 1081.23 (m), 1048.45 (m), 1030.25 (m),

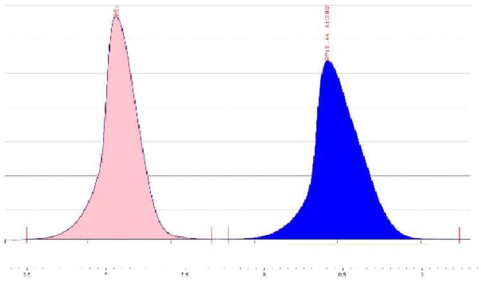
746.25 (s), 698.64 (s), 494.02 (w) cm^{-1}. **HRMS** (DART) for $C_{16}H_{19}O$ $[M+NH_4]^+$: Calc'd: 244.1701, found: 244.1697. $[\alpha]_D^{20}$ = +12.00 (*c* = 0.83, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

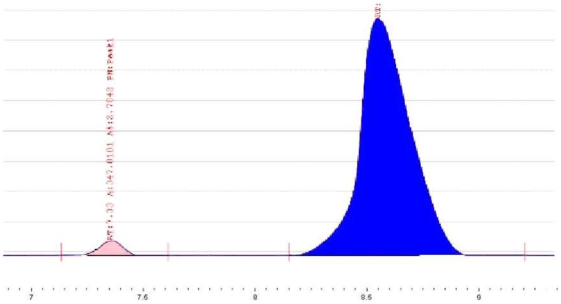
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1,4-diphenylbutan-2-ol.

Racemic Material

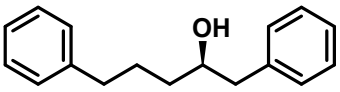


Peak No	% Area	Area	RT (min)
1	49.1242	19332.5243	7.17
2	50.8758	20021.8565	8.44
Total:	100	39354.3808	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	2.7042	347.8181	7.33
2	97.2958	12514.113	8.54
Total:	100	12861.9311	



(*R*)-1,5-diphenylpentan-2-ol (1.39). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), (32.7 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), allylbenzene (28.4 mg, 0.24 mmol, 1.20 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00

equiv.) The crude mixture was purified by silica gel chromatography (65% DCM in hexanes, stained with CAM) to afford a colorless oil (24.0 mg, 50% yield).

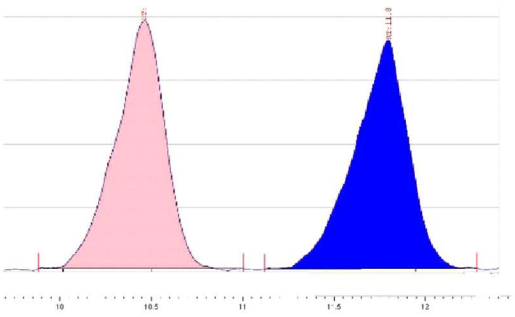
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.14 (m, 10H), 3.90-3.80 (m, 1H), 3.83 (dd, *J* = 13.6, 4.1 Hz, 1H), 2.69-2.60 (m, 3H), 1.91-1.80 (m, 1H), 1.78-1.65 (m, 1H), 1.64-1.51(m, 2H), 1.48 (s, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.52, 138.65, 129.56, 128.74, 128.57, 128.46, 126.64, 125.89, 72.67, 44.24, 36.55, 36.01, 27.75. **IR** (neat) ν_{max} 3405.14 (br,s), 3083.98 (w), 3061.19 (w), 3025.99 (m), 2919.73 (w), 2857.89 (w), 1602.16 (w), 1494.75 (m), 1453.54 (m), 1081.23 (m), 1048.45 (m), 1030.25 (m), 746.25 (s), 698.64 (s), 494.02 (w) cm^{-1}. **HRMS** (DART) for $C_{17}H_{24}NO$ $[M+NH_4]^+$: Calc'd: 258.1858, found: 258.1864. **$[\alpha]_D^{20}$** = -4.35 (*c* = 0.86, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

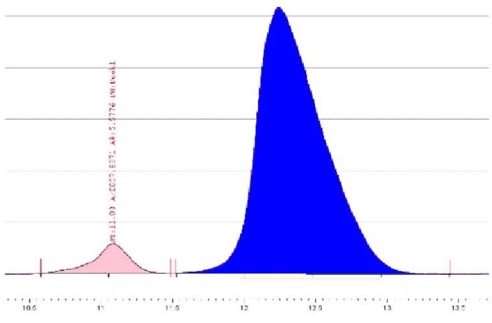
Chiral SFC (Chiracel OJ-H, 9% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1,5-diphenylpentan-2-ol.

Racemic Material

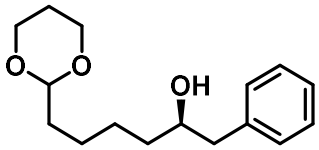


Peak No	% Area	Area	RT (min)
1	49.8175	3788.1127	10.46
2	50.1825	3815.8682	11.85
Total:	100	7603.9809	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	5.5776	2057.8371	11.03
2	94.4224	34836.7459	12.25
Total:	100	36894.583	



(*R*)-6-(1,3-dioxan-2-yl)-1-phenylhexan-2-ol (1.36). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 2-(but-3-en-1-yl)-1,3-dioxane (**S-1.3**) (34.1 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (30% EtOAc in hexanes, stained with CAM) to afford a colorless oil (33.4 mg, 63% yield).

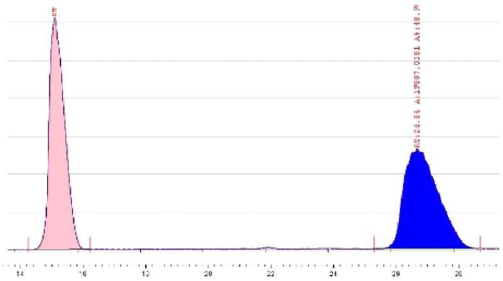
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.12 (m, 5H), 4.51 (t, *J* = 5.1 Hz, 1H), 4.09 (dd, *J* = 12.2, 4.9 Hz, 2H), 3.83-3.72 (m, 1H), 3.75 (td, *J* = 12.2, 2.4 Hz, 2H), 2.81 (dd, *J* = 13.5, 4.2 Hz, 1H), 2.64 (dd, *J* = 13.5, 8.3 Hz, 1H), 2.14-2.01 (m, 1H), 1.73-1.24 (m, 9H).**^{13}(150** MHz, $CDCl_3$) δ 138.71, 129.54, 128.65, 126.54, 102.40, 72.63, 67.01, 44.19, 36.81, 35.27, 25.97, 25.74, 24.07. **IR** (neat) ν_{max} 3451.27 (br, w), 2929.58 (s), 2855.69 (s), 1454.85 (w), 1403.76 (w), 1377.78 (w), 1240.40 (w), 1144.35 (s), 1093.42 (m), 1029.47 (m), 997.56 (m), 747.24 (w), 700.91 (m) cm^{-1}. **HRMS** (DART) for $C_{16}H_{25}O_3$ $[M+H]^+$: Calc'd: 265.1804, found: 265.1796. **$[\alpha]_D^{20}$** = -5.473 (*c* = 1.90, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

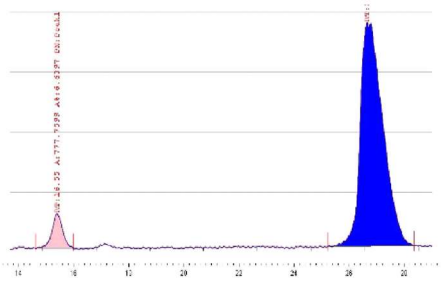
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-6-(1,3-dioxan-2-yl)-1-phenylhexan-2-ol.

Racemic Material

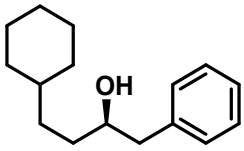


Peak No	% Area	Area	RT (min)
1	51.0169	20712.7843	15.26
2	48.9831	19887.0381	26.84
Total:	100	40599.8224	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	6.6397	777.7899	16.55
2	93.3603	10935.9417	28.09
Total:	100	11713.7016	



(*R*)-4-cyclohexyl-1-phenylbutan-2-ol (1.45). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), vinylcyclohexane (26.4 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (50% DCM in hexanes, stained with CAM) to afford a white solid (27.0 mg, 58% yield).

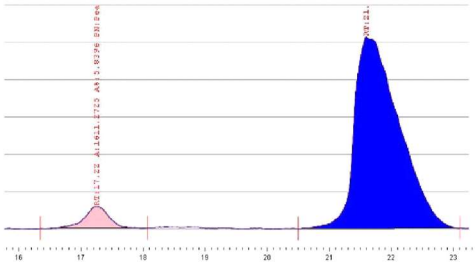
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.20 (m, 5H), 3.82-3.75 (m, 1H), 2.84 (dd, *J* = 13.6, 4.2 Hz, 1H), 2.65 (dd, *J* = 13.6, 8.4 Hz, 1H), 1.75-0.80 (m, 15H).**^{13}C NMR** (150 MHz, $CDCl_3$) δ 138.81, 129.56, 129.55, 128.68, 128.67, 126.56, 73.18, 44.17, 44.15, 37.92, 34.33, 33.64, 33.57, 33.46, 26.84, 26.55, 26.53. **IR** (neat) ν_{max} 3364.05 (br, w), 2920.43 (s), 2849.78 (m), 1495.12 (w), 1450.29 (m), 1079.83 (w), 1030.64 (m), 741.30 (w), 699.12 (m) cm^{-1}. **HRMS** (DART) for $C_{16}H_{28}NO$ $[M+NH_4]^+$: Calc'd: 250.2171, found: 250.2173. **$[\alpha]_D^{20}$** = -8.394 (*c* = 1.42, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

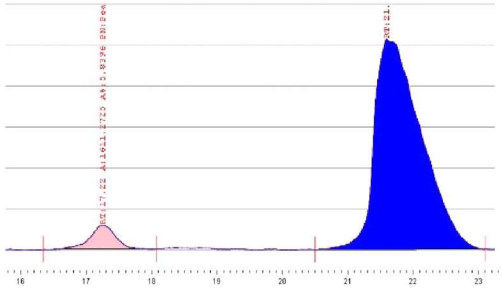
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-4-cyclohexyl-1-phenylbutan-2-ol.

Racemic Material

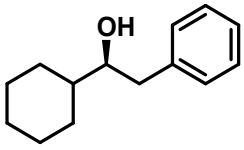


Peak No	% Area	Area	RT (min)
1	5.8396	1611.2725	17.22
2	94.1604	25980.6649	21.61
Total:	100	27591.9374	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	5.8396	1611.2725	17.22
2	94.1604	25980.6649	21.61
Total:	100	27591.9374	



(*R*)-1-cyclohexyl-2-phenylethan-1-ol (1.47). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), cyclohexene (19.7 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (50% DCM in hexanes, stained with CAM) to afford a white solid (20.4 mg, 50% yield). Spectral data matches previously

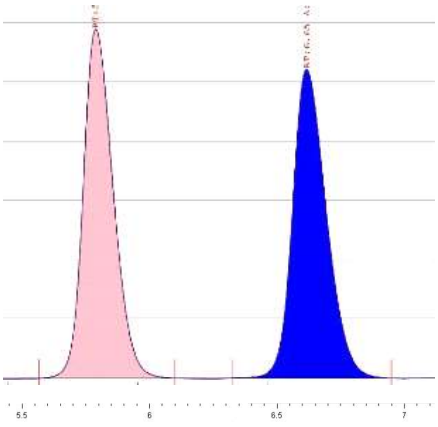
published results.[64] The optical rotation and SFC traces obtained support the assignment of absolute configuration $[\alpha]_D^{20}$ = -3.839 (*c* = 1.00, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

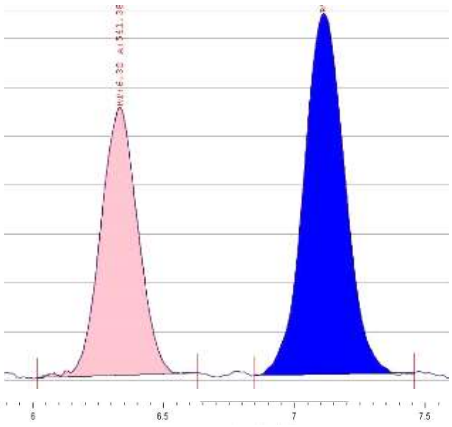
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-cyclohexyl-2-phenylethan-1-ol.

Racemic Material

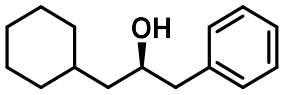


Peak No	% Area	Area	RT (min)
1	50.048	4701.3726	5.84
2	49.952	4692.3455	6.65
Total:	100	9393.7181	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	40.2339	541.3831	6.32
2	59.7661	804.2063	7.1
Total:	100	1345.5894	



(*R*)-1-cyclohexyl-3-phenylpropan-2-ol (1.46). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), methylenecyclohexane (23.1 mg, 0.24 mmol, 1.20

[64] Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. *Science* **2015**, *351* (6268), 70.

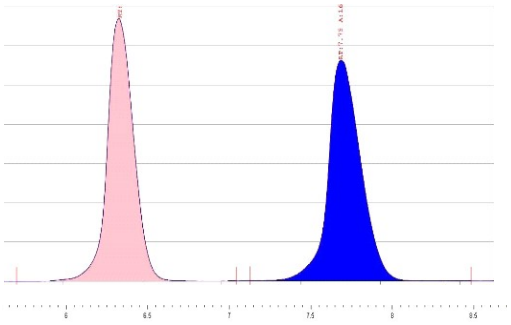
equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (50% DCM in hexanes, stained with CAM) to afford a white solid (27.0 mg, 58% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.38-7.25 (m, 2H), 7.28-7.15 (m, 3H), 4.02-3.90 (m, 1H), 2.81 (dd, *J* = 13.6, 4.1 Hz, 1H), 2.63 (dd, *J* = 13.6, 8.4 Hz, 1H), 1.85-1.74 (m, 1H), 1.75-1.60 (m, 4H), 1.57-1.08 (m, 8H) 1.03-0.79 (2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 138.61, 129.40, 128.52, 126.41, 70.02, 44.69, 44.62, 34.17, 32.87, 26.59, 26.37, 26.19. : **IR** (neat) ν_{max} 3399.8 (br, s), 3027.2 (w, m), 2920.4 (s), 2850 (s), 1601.1 (w), 1495.1 (s), 1134.4 (s), 1077 (s), 745 (s), 699 (s), 523 (w, s). **HRMS** (DART) for $C_{15}H_{21}$ $[M+H-H_2O]^+$: Calc'd:201.1643, found 201.1650: 201.165. **$[\alpha]_D^{20}$** = .9333 (*c* = 1.00, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

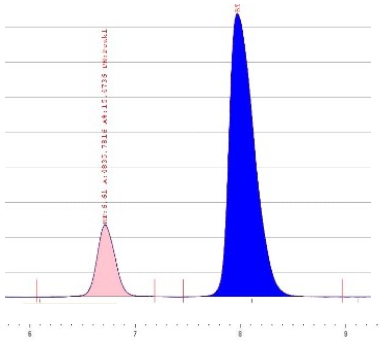
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-4-cyclohexyl-1-phenylbutan-2-ol.

Racemic Material

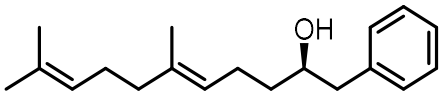


Peak No	% Area	Area	RT (min)
1	49.072	15475.7004	6.36
2	50.928	16061.0519	7.75
Total:	100	31536.7523	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	15.4736	4835.7816	6.61
2	84.5264	26416.0117	7.86
Total:	100	31251.7933	



***(R,E)*-6,10-dimethyl-1-phenylundeca-5,9-dien-2-ol (1.42).** The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), (E)-4,8-dimethylnona-1,3,7-triene (**S-1.2**) (36 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (50% DCM in hexanes, stained with CAM) to afford a colorless oil (21.2 mg, 39% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.20 (m, 5H), 5.18-5.10 (m, 1H), 5.12-5.05 (m, 1H), 3.89-3.79 (m, 1H), 2.83 (dd, *J* = 13.6, 4.3 Hz, 1H), 2.67 (dd, *J* = 13.6, 8.3 Hz, 1H), 2.25-1.97 (m, 6H), 1.68 (s, 3H), 1.64-1.53 (m, 8H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 138.78, 135.91, 131.57, 129.58, 128.67, 126.56, 124.40, 124.04, 72.56, 44.21, 39.87, 36.87, 26.81, 25.84, 24.48, 17.84, 16.18. **IR** (neat) ν_{max} 3398.31 (br, w), 3027.30 (w), 2963.82 (m), 2923.30 (s), 2854.82 (m), 1495.43 (w), 1452.74 (m), 1376.82 (w), 1081.10 (w), 740.88

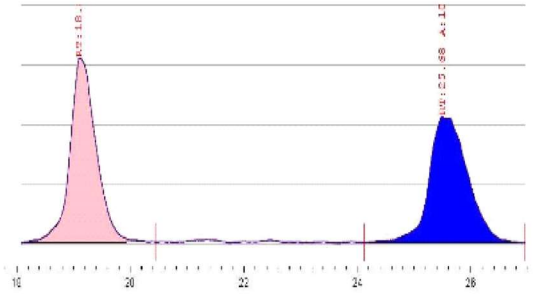
(w), 699.60 (w) cm^{-1}. **HRMS** (DART) for $C_{19}H_{29}O$ $[M+H]^+$: Calc'd: 273.2218, found: 273.2222. $[\alpha]_D^{20}$ = – 2.695 (*c* = 1.63, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

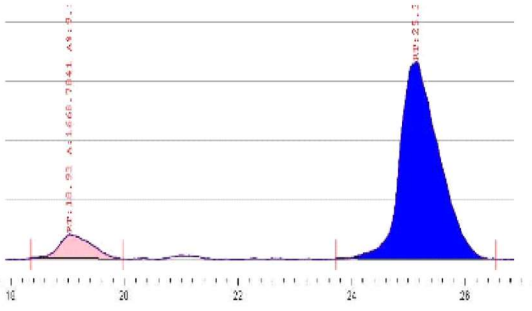
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R,E)-6,10-dimethyl-1-phenylundeca-5,9-dien-2-ol.

Racemic Material

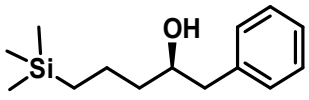


Peak No	% Area	Area	RT (min)
1	50.0529	10620.6165	18.85
2	49.9471	10598.1516	25.68
Total:	100	21218.7681	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	9.1181	1668.7841	18.93
2	90.8819	16633.0882	25.37
Total:	100	18301.8723	



(*R*)-1-phenyl-5-(trimethylsilyl)pentan-2-ol (1.40). The reaction was performed according to the general **procedure B** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), allyltrimethylsilane (27.4 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.)

The crude mixture was purified by silica gel chromatography (60% DCM in hexanes, stained with CAM) to afford a colorless oil (26.1 mg, 55% yield).

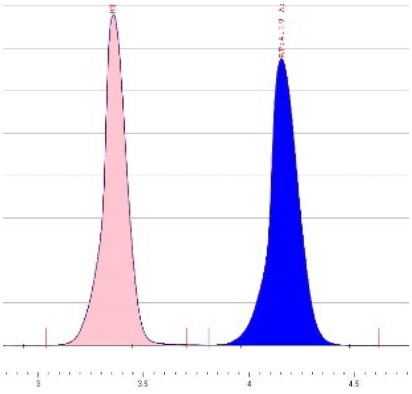
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.7.34-7.30 (m, 2H), 7.25-7.21 (m, 3H), 3.88-3.80 (m, 1H), 2.82 (dd, *J* = 13.6, 4.3 Hz, 1H), 2.66 (dd, *J* = 13.4, 8.4 Hz, 1H), 1.63-1.43 (m, 4H), 1.43-1.34 (m, 1H), 0.66-0.42 (m, 2H), -0.01 (s, 9H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 138.62, 129.40, 128.52, 126.41, 72.40, 44.15, 40.74, 20.17, 16.71, -1.66. **IR** (neat) ν_{max} 3404.2 (br, s) 3028.4 (w, s), 2950.1 (s), 2950 (s), 2858.1 , 1495.0 (w, m), 1409.3 (w, s), 1247.2 (s), 1173.1 (s), 861.9 (m), 740.5 (s), 698.3 (s) cm^{-1}. **HRMS** (DART) for $C_{14}H_{28}OSiN$ $[M+NH_4]^+$: Calc'd: 254.1953, found: 254.1940 **$[\alpha]_D^{20}$** = -1.741 (*c* = 1.00, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure B** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

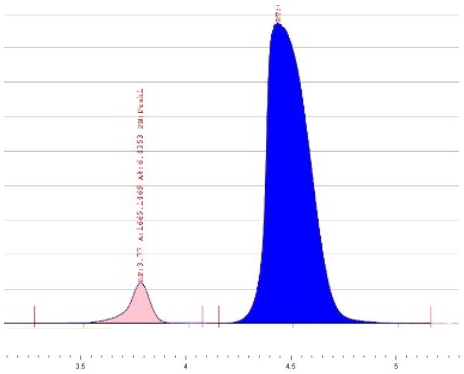
Chiral SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-phenyl-5-(trimethylsilyl)pentan-2-ol.

Racemic Material

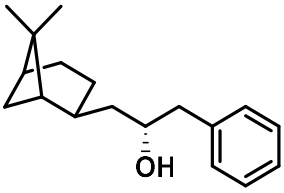


Peak No	% Area	Area	RT (min)
1	48.6805	11888.1196	3.41
2	51.3195	12532.593	4.19
Total:	100	24420.7126	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	6.4353	1665.1469	3.77
2	93.5647	24209.8898	4.43
Total:	100	25875.0367	



(*R*)-1-((1*S*,2*S*,5*S*)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)-3-phenylpropan-2-ol (1.43). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), (1*S*)-(−)-β-pinene (32.7 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (70% DCM in hexanes, stained with CAM) to afford an inseparable mixture of diastereomers as a colorless oil (30.5 mg, 59% yield).

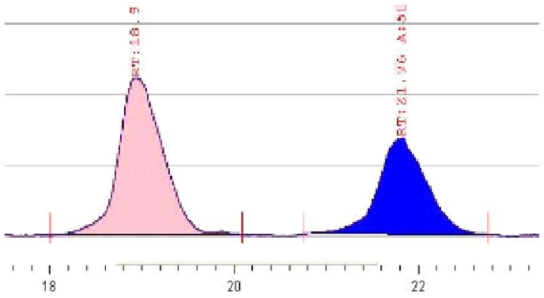
Analysis of Stereochemistry:

The mixture of diastereomers was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Hydroboration has previously been shown to occur from

the face opposite to *gem*-dimethyl group of β-pinene.[65] Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

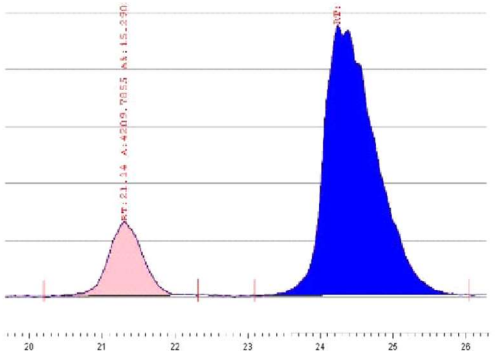
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-((1S,2S,5S)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)-3-phenylpropan-2-ol.

Diastereomic Mixture

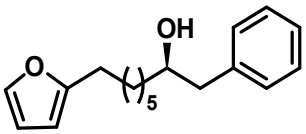


Peak No	% Area	Area	RT (min)
1	60.0783	7660.6494	18.97
2	39.9217	5090.4563	21.96
Total:	100	12751.1057	

Diastereoenriched Material



Peak No	% Area	Area	RT (min)
1	15.2902	4209.7855	21.14
2	84.7098	23322.8155	24.05
Total:	100	27532.601	



(*R*)-8-(furan-2-yl)-1-phenyloctan-2-ol (1.41). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), (32.7 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), 2-(hex-5-enyl)furan (**S-1.1**) (36.1 mg, 0.24 mmol, 1.20 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (10% EtOAc in hexanes, stained with CAM) to afford a yellow oil (36.8 mg, 73% yield).

[65] G. Zweifel, H. Brown, *J. Am. Chem. Soc.* **1964**, *86*, 393.

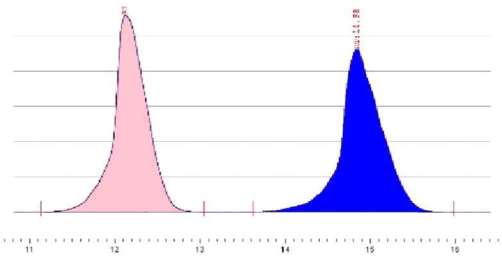
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.06 (m, 6H), 6.28 (dd, *J* = 3.2, 1.9 Hz, 1H), 5.98 (d, *J* = 3.2 Hz, 1H), 3.90-3.77 (m, 1H), 2.83 (dd, *J* = 13.5, 4.2 Hz, 1H), 2.69-2.58 (m, 3H), 1.74-1.25 (m, 10H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 156.63, 140.76, 138.75, 129.55, 128.69, 126.58, 110.16, 104.69, 72.78, 44.22, 36.92, 29.47, 29.24, 28.10, 28.06, 25.77. **IR** (neat) ν_{max} 3388.75 (br, w), 3026.89 (w), 2927.20 (s), 2855.02 (m), 1597.52 (w), 1506.89 (m), 1495.34 (m), 1453.85 (m), 1146.13 (m), 1076.43 (m), 1029.92 (m), 1006.94 (s), 922.05 (w), 884.47 (w), 852.54 (w), 795.29 (m), 726.11 (s), 699.16 (s), 599.28 (m), 543.22 (w), 505.67 (w) cm^{-1}. **HRMS** (DART) for $C_{18}H_{25}O_2$ $[M+H]^+$: Calc'd:273.1855, found: 273.1845. **$[\alpha]_D^{20}$** = -5.92 (*c* = 3.14, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

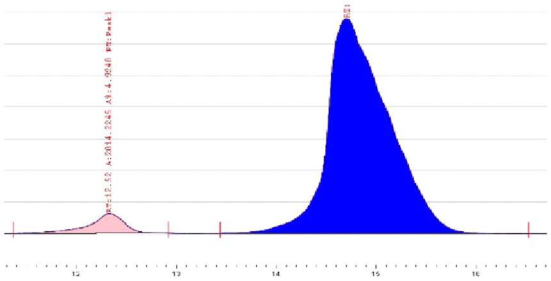
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-8-(furan-2-yl)-1-phenyloctan-2-ol.

Racemic Material

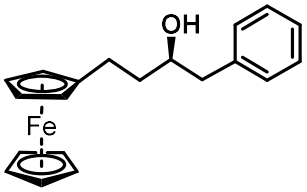


Peak No	% Area	Area	RT (min)
1	49.9478	30493.1904	12.23
2	50.0522	30556.9475	14.98
Total:	100	61050.1379	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	4.9248	2814.2245	12.52
2	95.0752	54329.9001	14.76
Total:	100	57144.1246	



(*R*)-1-phenyl-4-ferrocenylbutan-2-ol (1.44). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), vinylferrocene (50.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (10% EtOAc in pentane, stained with CAM) to afford a red oil (36.1 mg, 53% yield).

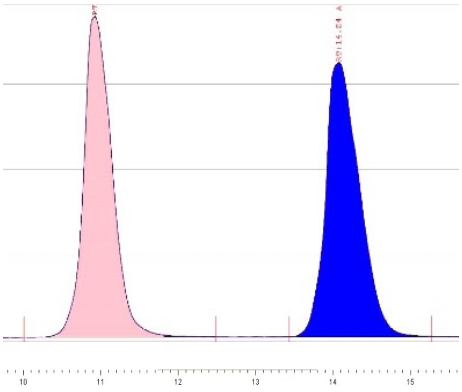
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36-7.30 (m, 2H), 7.25-7.20 (m, 3H), 4.12-4.03 (m, 9H), 3.88-3.81 (m, 1H), 2.85 (dd, *J* = 13.6, 4.3 Hz, 1H), 2.69 (dd, *J* = 13.5, 8.4 Hz, 1H), 2.56 (ddd, *J* = 14.2, 9.8, 5.8 Hz, 1H) 2.42 (ddd, *J* = 14.3, 9.9, 6.4 Hz, 1H), 1.81-1.71 (m, 2H), 1.52 (s, 1H) **^{13}C NMR** (151 MHz, $CDCl_3$) δ 138.52, 129.55, 128.73, 126.66, 88.88, 72.48, 68.66, 68.29, 68.08, 67.32, 44.25, 38.21, 25.92. **IR** (neat) ν_{max} 3559.7 (w, s), 3400.5 (br, s), 3086.6 (m), 3025.9 (s), 2919.9 (s), 2853.5 (s), 1639.07 (br, s), 1601.7 (w, s), 1494.4 (s), 1470.9 (s), 1410.4 (s), 1154.7 (s), 1080.7 (m), 1080.71 (s), 1041.9 (s), 929.8 (s), 816.6 (s), 743.9 (s), 700.0 (s), 599.4 (w, s), 482.7 (s) cm^{-1}. **HRMS** (DART) for $C_{20}H_{23}OFe$ $[M+H]^+$: Calc'd: 335.1098, found: 335.1113. **$[\alpha]_D^{20}$** = -15.472 (*c* = 1.00, $CHCl_3$, *l* = 50 mm). **$[\alpha]_D^{20}$** = -1.741 (*c* = 1.00, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

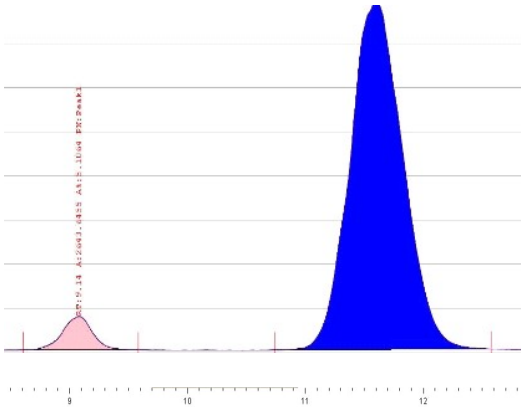
Chiral SFC (Chiracel OJ-H, 13% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-phenyl-4-ferrocenylbutan-2-ol.

Racemic Material

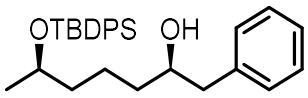


Peak No	% Area	Area	RT (min)
1	49.4303	46023.6816	11.21
2	50.5697	47084.5491	14.24
Total:	100	93108.2307	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	5.1064	2643.6455	9.14
2	94.8936	49127.9267	11.64
Total:	100	51771.5722	



(2*R*,6*R*)-6-((*tert*-butyldiphenylsilyl)oxy)-1-phenylheptan-2-ol (1.48). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), (R)-*tert*-butyl(pent-4-en-2-yloxy)diphenylsilane (77.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica

gel chromatography (50% DCM in hexanes, stained with CAM) to afford a colorless oil (66.0 mg, 74% yield).

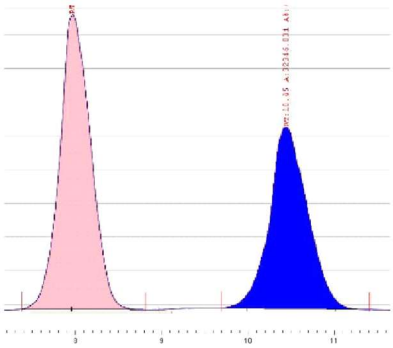
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73-7.67 (m, 4H), 7.45-7.16 (m, 11H), 3.91-3.83 (m, 1H), 3.78-3.69 (m, 1H), 2.77 (dd, *J* = 13.6, 4.2 Hz, 1H), 2.60 (dd, *J* = 13.6, 6.8 Hz, 1H), 1.58-1.29 (m, 8 H), 1.15-1.10 (m, 12H).**^{13}C NMR** (150 MHz, $CDCl_3$) δ 136.04, 136.01, 129.60, 129.54, 128.67, 127.61, 127.54, 126.56, 72.67, 69.57, 44.12, 39.48, 36.90, 27.20, 23.37, 21.55, 19.42. **IR** (neat) ν_{max} 3431.69 (br, w), 2930.37 (s), 2856.98 (m), 1472.08 (w), 1454.48 (w), 1427.39 (m), 1476.44 (w), 1134.39 (m), 1109.43 (s), 1075.12 (m), 1029.38 (m), 997.42 (w), 822.01 (w), 739.73 (s), 700.63 (s), 611.44 (m), 597.58 (s) cm^{-1}. **HRMS** (DART) for $C_{29}H_{39}O_2Si$ $[M+H]^+$: Calc'd: 447.2719, found: 447.2723. **$[\alpha]_D^{20}$** = +10.626 (*c* = 3.67, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

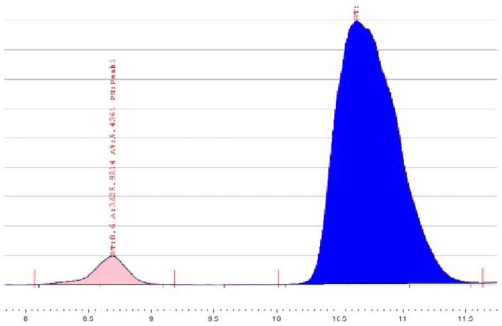
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (2R,6R)-6-((tert-butyldiphenylsilyl)oxy)-1-phenylheptan-2-ol.

Diastereomic Mixture

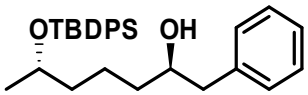


Peak No	% Area	Area	RT (min)
1	57.0781	43014.1003	8.01
2	42.9219	32346.031	10.45
Total:	100	75360.1313	

Diastereoenriched Material



Peak No	% Area	Area	RT (min)
1	5.4341	3625.9214	8.6
2	94.5659	63099.2017	10.57
Total:	100	66725.1231	



(2*R*,6*S*)-6-((*tert*-butyldiphenylsilyl)oxy)-1-phenylheptan-2-ol (1.49). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), (*S*)-*tert*-butyl(pent-4-en-2-yloxy)diphenylsilane (77.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.) The crude mixture was purified by silica gel chromatography (50% DCM in hexanes, stained with CAM) to afford a colorless oil (66.0 mg, 74% yield).

1H NMR (500 MHz, $CDCl_3$) δ 7.75-7.63 (m, 4H), 7.46-7.17 (m, 11H), 3.91-3.84 (m, 1H), 3.79-3.69 (m, 1H), 2.77 (dd, *J* = 13.6, 4.2 Hz, 1H), 2.60 (dd, *J* = 13.6, 8.4 Hz, 1H), 1.57-1.29 (m, 8H), 1.11-1.04 (m, 12H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 136.05, 136.04, 129.60, 129.56, 129.54, 128.67, 127.62, 127.54, 126.56, 72.63, 69.67, 44.07, 39.49, 36.93, 27.20, 23.40, 21.56, 19.41. **IR** (neat) ν_{max} 3421.77 (br, w), 2930.61 (m), 2856.83 (m), 1495.23

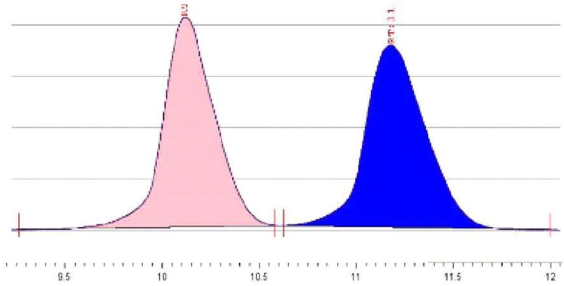
(w), 1472.11 (w) 1427.36 (m), 1376.40 (w), 1361.13 (w), 1134.17 (w), 1109.29 (s), 1078.69 (m), 1049.03 (m), 1028.98 (m), 821.99 (w), 739.64 (m), 700.49 (s), 611.48 (m), 507.32 (m) cm^{-1}. **HRMS** (DART) for $C_{29}H_{39}O_2Si$ $[M+H]^+$: Calc'd: 447.2719, found: 447.2723. $[\alpha]_D^{20}$ = -16.5218 (*c* = 3.06, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

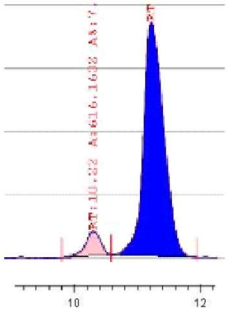
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (2R,6S)-6-((tert-butyldiphenylsilyl)oxy)-1-phenylheptan-2-ol.

Diastereomic Mixture



Peak No	% Area	Area	RT (min)
1	49.5546	7242.3644	10.08
2	50.4454	7372.5663	11.11
Total:	100	14614.9307	

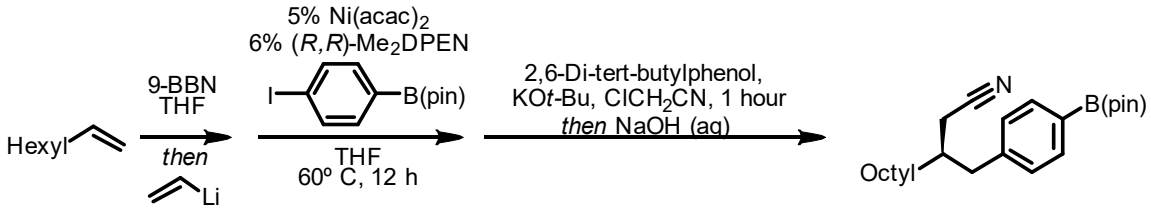
Diastereoenriched Material



Peak No	% Area	Area	RT (min)
1	7.2302	616.1632	10.22
2	92.7698	7905.8995	11.1
Total:	100	8522.0627	

1.4.6 Procedures and Characterization for Transformations of 9-BBN Borane.

Cyanomethylation



(R)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)undecanenitrile **(1.68).** The title compound was prepared from enantiomerically enriched 9-BBN products obtained through the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), and 4-iodophenylboronic acid pinacol ester (66.0 mg, 0.20 mmol, 1.00 equiv.), by replacing the oxidation step with the procedure as in the synthesis of compound **28**. The crude mixture was purified by silica gel chromatography (70% DCM in hexane, stain in PMA) to afford a yellow oil (35.8 mg, 47% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.4 Hz, 2H), 7.18 (d, *J* = 7.4 Hz, 2H), 2.83 (dd, *J* = 13.7, 5.7 Hz, 1H), 2.59 (dd, *J* = 13.7, 8.9 Hz, 1H), 2.26 (dd, *J* = 16.8, 5.3 Hz, 1H), 2.18 (dd, *J* = 16.8, 5.5 Hz, 1H), 2.01 – 1.94 (m, 1H), 1.53 – 1.19 (m, 26H), 0.89 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.54, 135.24, 128.61, 118.64, 83.90, 40.13, 37.34, 33.52, 31.96, 29.67, 29.58, 29.36, 26.89, 24.99, 22.78, 21.14, 14.23. **11B NMR** (160 MHz, CDCl3) 30.6. **IR** (neat) ν_{max} 2977.06 (w), 2924.63 (m), 2854.60 (w), 2245.59 (w), 1611.72 (m), 1518.02 (w), 1465.45 (w), 1398.25 (m), 1358.18 (s), 1321.23 (m), 1271.48 (m), 1214.01 (w), 1143.48 (s), 1089.36

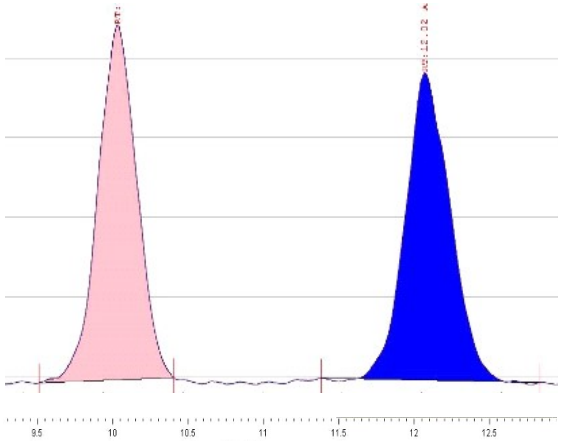
(s), 1021.79 (m), 962.54 (m), 859.14 (m), 829.74 (w), 736.36 (w), 659.62 (s) cm^{-1}. **HRMS** (DART) for $C_{24}H_{42}N_2O_2B$ $[M+NH_4]^+$: Calc'd: 401.3339, found: 401.3335. $[\alpha]_D^{20}$ = -13.998 (*c* =1.54, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared through to same reaction sequence with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

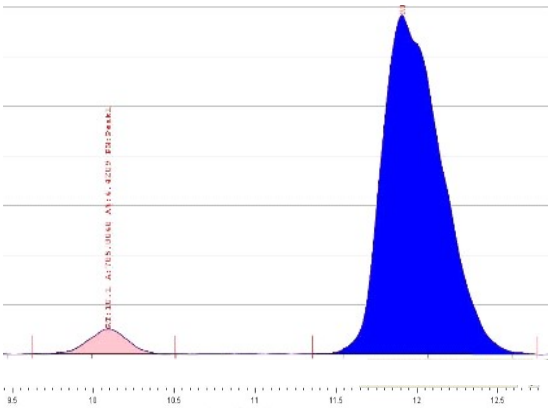
Chiral SFC (Chiracel AD-H, 3 % IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)undecanenitrile.

Racemic material



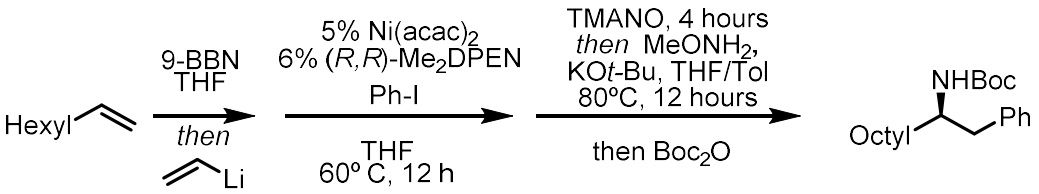
Peak No	% Area	Area	RT (min)
1	49.9809	3793.2285	10.09
2	50.0191	3796.1337	12.02
Total:	100	7589.3622	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	4.4209	785.8048	10.1
2	95.5791	16989.1147	11.85
Total:	100	17774.9195	

Amination



***tert*-butyl (*R*)-(1-phenyldecan-2-yl)carbamate (1.67).** The title compound was prepared from enantiomerically enriched 9-BBN products obtained through the general **procedure A** with modification, using with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), and iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.). After stirring overnight at 60ºC, the mixture was brought back into the glovebox where anhydrous trimethylamine oxide (18.78 mg, 0.25 mmol) was added to the vial. The resulting suspension was sealed and stirred vigorously at room temperature for 4 hours. The solvent was then removed in vacuo using a schlenk line. The crude oil was brought back into glove box and KO*t*Bu (123.43 mg, 1.10 mmol, 5.50 equiv.) was added along with .8 mL of Toluene. The reaction mixture was sealed with a septum cap and a solution of O-methylhydroxylamine (2.53 M, .474 mL, 1.20 mmol, 6.00 equiv.) in THF was added to the vial at room temperature. The reaction was stirred at 80°C overnight. Afterwards the mixture was cooled down to room temperature and a solution of di-tert-butyl-dicarbonate in THF (1M solution, 6.5 equiv. 1.3 mL) was added. After having stirred at rt for 4 hours, 1 mL of H_2O was added and the water layer was extracted 4 times with EtOAc, dried over MgSO4 and concentrated in vacuo. The product

was Isolated by silica gel chromatography (2% EtOAc in pentane, ninhydrin stain) to afford a colorless oil (39.4 mg, 59% i. y.).

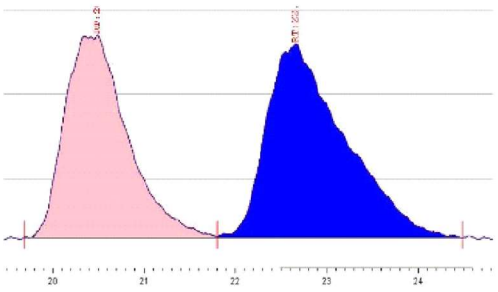
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.14 (m, 5H), 4.28 (br s, 1H), 3.80 (br s, 1H), 2.75 (br s, 2H), 1.50-1.19 (m, 23H), 0.87 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (150 MHz, CD_3CN) δ 155.60, 138.51, 129.65, 128.37, 126.31, 79.04, 77.41, 77.16, 76.91, 51.69, 41.51, 34.35, 31.98, 29.65, 29.59, 29.36, 28.53, 26.12, 22.78, 14.22. **IR** (neat) ν_{max} 3368.23 (br, w), 2956.23 (m), 2949.89 (s), 2854.58 (m), 1810.82 (w), 1699.86 (s), 1520.70 (m), 1496.61 (m), 1454.96 (m), 1390.24 (m), 1365.57 (m), 1248.73 (m), 1170.91 (s), 1118.82 (m), 1069.15 (m), 740.32 (w), 699.79 (m) cm^{-1}. **HRMS** (DART) for $C_{21}H_{36}NO_2$ $[M+H]^+$: Calc'd: 334.2746, found: 334.276. **$[\alpha]_D^{20}$** = +6.50 (*c* = 0.84, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared through to same reaction sequence with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **1.64**, **S-1.64**).

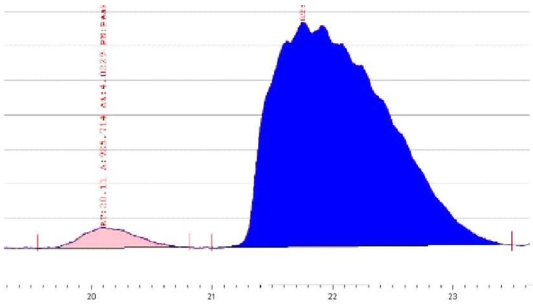
Chiral SFC (Chiracel OD-H, 1 % IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of tert-butyl (R)-(1-phenyldecan-2-yl)carbamate.

Racemic Material



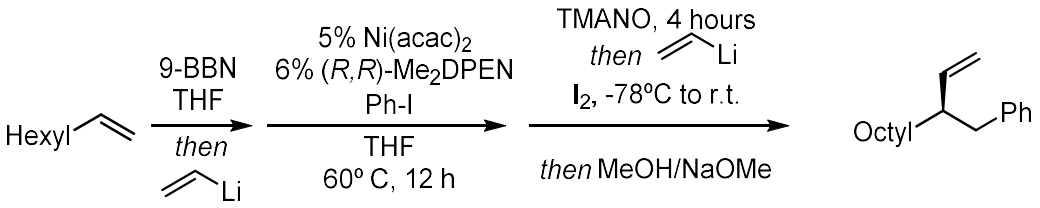
Peak No	% Area	Area	RT (min)
1	45.7469	5763.3965	20.6
2	54.2531	6835.0571	22.78
Total:	100	12598.4536	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	4.0229	925.714	20.11
2	95.9771	22085.2978	21.76
Total:	100	23011.0118	

Olefination



(*R*)-(2-vinyldecyl)benzene (1.69). The title compound was prepared from enantiomerically enriched 9-BBN products obtained through the general **procedure A** with modification, using 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), and iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.). After stirring overnight at 60ºC, the mixture was brought back into the glovebox where anhydrous trimethylamine oxide (18.78 mg, 0.25 mmol) was added to the vial. The resulting suspension was sealed and stirred vigorously at room temperature for 4 hours. The mixture was cooled to -78° C and vinyllithium (1.65 M, 490 uL, 4.00 equiv.), was added to the vial which was allowed to warm up to room temperature and stir for 10 minutes. The mixture was cooled again to -78º C and Iodine (304.57 mg, 1.20 mmol, 6.00 equiv.) was added in 0.5 mL of THF. This mixture was Stirred at -78° C for 1 hour and then allowed to warm to r.t. for 10 min. The reaction was cooled once more to -78º C. Sodium methoxide (129.66 mg, 2.40 mmol, 133.80 uL) was added in 1.5 mL of MeOH. After warming to R.T. the reaction mixture was stirred for 12 hours. Finally, 1 mL of saturated sodium thiosulfate solution was added to the reaction mixture at 0°C. The water layer was extracted 4 times with Pentane, dried over $MgSO_4$ and concentrated under

reduced pressure. The crude product was purified by silica gel chromatography (pentane, stain in CAM) to afford a colorless oil (40.2 mg, 82% yield).

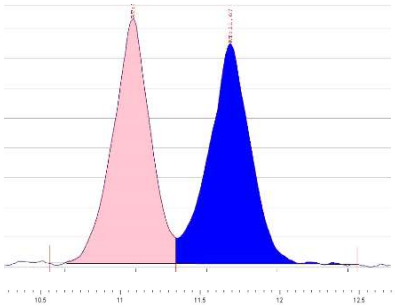
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29-7.07 (m, 5H), 5.64-5.55 (m, 1H), 3.92 (dd, *J* = 10.3, 1.8 Hz, 1H), 4.89 (ddd, *J* = 17.1, 2.0, 0.9 Hz, 1H), 2.65 (dd, *J* = 13.5, 6.6 Hz, 1H), 2.59 (dd, *J* = 13.5, 7.6 Hz, 1H), 2.28 (m, 1H), 1.44 – 1.12 (m, 14H), 0.88 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.69, 140.87, 129.39, 128.12, 125.79, 114.49, 45.76, 41.96, 34.29, 32.01, 29.81, 29.70, 29.43, 27.27, 22.79, 14.23. **IR** (neat) ν_{max} 3065.1 (w, m), 3027 (s), 2955.4 (s), 2924.3 (s), 2854.1 (s), 1639.0 (w, s), 1495.2 (s), 1495.3 (w), 1378.1 (w, s), 1030.3 (w, s), 993.1 (s), 745.2 (w), 698.3 (s). **HRMS** (DART) for $C_{18}H_{29}$ $[M+H]^+$: Calc'd: 245.2269, found: 245.2261. $[\alpha]_D^{20}$ = 4.840 (*c* =1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

In order to obtain separation conditions on the SFC, the title compound was submitted to a hydroboration oxidation sequence and the resulting primary alcohol was compared against the racemic product obtained through the same reaction with 2,2'-bipyridine.

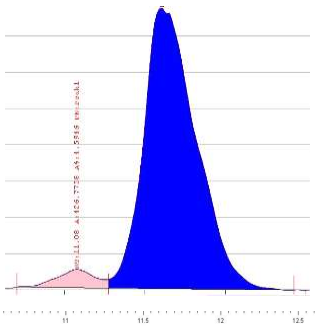
Chiral SFC (Chiracel OJ-H, 2 % IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of tert-butyl (R)-3-benzylundecan-1-ol.

Racemic Material



Peak No	% Area	Area	RT (min)
1	50.0039	3057.1549	10.98
2	49.9961	3056.672	11.67
Total:	100	6113.8269	

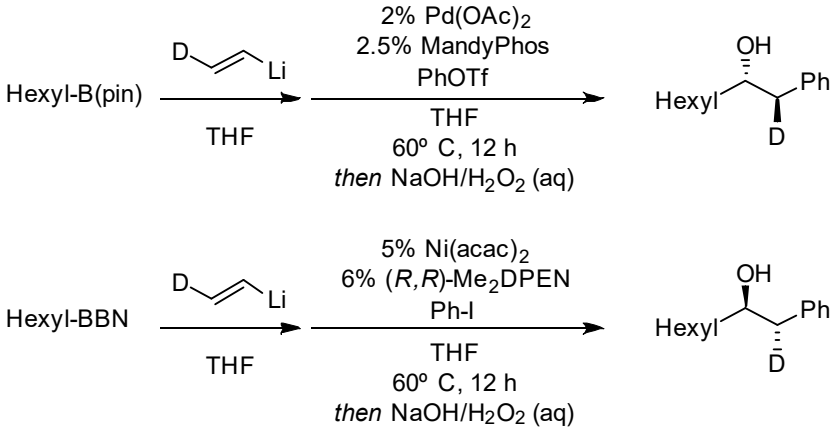
Enantioenriched Material



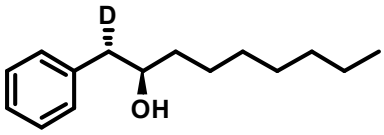
Peak No	% Area	Area	RT (min)
1	4.5946	426.7758	11.08
2	95.4054	8861.79	11.61
Total:	100	9288.5658	

1.4.7 Deuterium-Labeling Experiment

Procedure for the Preparation of *Trans*-deuterium-labeled Vinyl Lithium



The *trans*-deuterium labeled vinyl lithium was prepared as described in previous reports.[66]

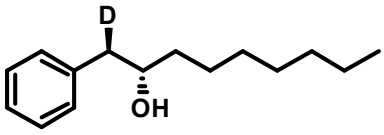


(1*S*,2*R*)-1-phenylnonan-1-d-2-ol (1.64). The cross-couping reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-hexene (20.2 mg, 0.24 mmol, 1.20 equiv.), deuterium labeled vinyllithium in THF (0.14 mL, 1.57 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and **L1.10** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 mmol, 1.00 equiv.). The crude material was purified by column chromatography (40% DCM in pentane, stain in CAM) to afford a white solid (26 mg, 63% yield).

[66] Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. *Science* **2016**, *351*, 70.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.68 – 6.84 (m, 5H), 4.00 – 3.69 (m, 1H), 2.63 (d, J = 8.1 Hz, 1H), 1.61 – 1.18 (m, 11H), 0.89 (t, J = 6.8 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 138.60, 129.39, 128.52, 126.40, 72.64, 43.70, 36.84, 31.82, 29.30, 25.70, 22.59, 14.05. **IR** (neat) ν_{max} cm^{-1} 3363.48 (br s), 3026.64 (s), 2954.49 (s), 2925.27 (s), 2855.42 (s), 1495.09 (s), 1495.09 (s), 1377.75 (s), 1282.19 (m), 1076.80 (m), 737.64 (m), 699.12 (s). **HRMS** (DART) for $C_{14}H_{20}D$ $[M+H-H_2O]^+$: Calc'd: 190.1706, found: 190.1702. **[α]$_D^{20}$** -3.66 (c =3.92, $CHCl_3$, l = 50 mm).

In order to determine the relative stereochemistry of the product, a parallel reaction with known stereochemical outcome was carried out according to our previously published procedure.[64]



(1*R*,2*S*)-1-phenylnonan-1-d-2-ol (S-1.64). To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added alkyl/aryl boronic ester (63.6 mg, 0.30 mmol, 1.0 equiv.) and diethyl ether (0.3 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0°C, and a deuterium labeled vinyllithium solution (.20 mL, 1.57 M, 0.30 mmol, 1.0 equiv.) was added at 0°C. The reaction vial was allowed to warm to room temperature and stirred for 30 minutes. Then, the solvent was carefully removed under reduced pressure, and the reaction vial was brought back into the glovebox. To a separate oven-dried 2-dram vial equipped with a magnetic stir bar in the glovebox was added $Pd(OAc)_2$ (1.4 mg, 0.006 mmol, 0.02 equiv.), (S_P,S'_P)-1,1′-Bis[bis(4-methoxy-3,5-dimethylphenyl)phosphino]-2,2′-bis[(*R*)-α-(dimethylamino)benzyl]ferrocene (**MandyPhos**, 7.6 mg 0.0072 mmol, 0.024

equiv.), and THF (0.6 mL). The $Pd(OAc)_2$ /(S_P, S_P)-**MandyPhos** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$ /(S_P, S_P)- **MandyPhos** solution was transferred into the reaction vial, followed by THF (0.6 mL), and aryl/vinyl triflate (0.33 mmol, 1.10 equiv.) was added. The reaction vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 60°C for 14 hours. The resulting mixture was cooled to room temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure. The reaction mixture was diluted with THF (3 mL), cooled to 0°C, 3M NaOH (2 mL) was added, followed by 30% H_2O_2 (1.0 mL), dropwise. The reaction mixture was allowed to warm to room temperature, and was allowed to stir for 4 hours. The reaction mixture was cooled to 0°C and saturated aq. $Na_2S_2O_3$ (3 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (40% DCM in pentane, stain in CAM) to afford a white solid (24.0 mg, 58% yield). All spectroscopic data matched those obtained from the Ni catalyzed reaction. $[\alpha]_D^{20}$ = 10.56 (*c* =0.76, $CHCl_3$, *l* = 50 mm). Ni catalyzed $[\alpha]_D^{20}$ -3.66 (*c* =3.92, $CHCl_3$, *l* = 50 mm).

In our previous report,[64] a similar deuterium labelled vinyllithium was used in palladium/Mandyphos catalyzed conjunctive cross-coupling, and it was found to generate products with *anti*-stereochemistry between the hydroxyl group and the deuterium atom, consistent with an anti-migration of the organolithium reagent with respect to the metal-bound alkene. Thus, by comparing the products of the two reactions (where the diastereotopic benzylic protons of the product are clearly

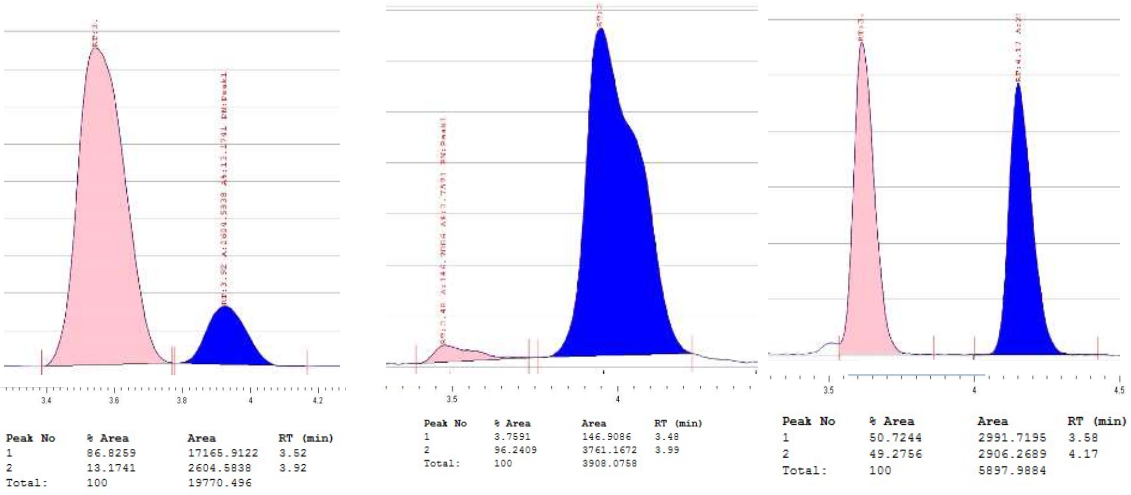
distinguishable by ^{1}H NMR) it was determined that the Ni catalyzed conjunctive cross-coupling yielded the same diastereomer as the products obtained from palladium catalysis.

Analysis of Stereochemistry:

Racemic compound was prepared through the general **procedure A** with 2,2'-bipy (6 mol%) as the ligand, and non-labeled vinyllithium.

Chiral SFC (Chiracel OD-H, 3 % IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of tert-butyl (1R,2S)-1-phenyldecan-1-d-2-ol.

1.64 **S-1.64** Racemic material



Peak No	% Area	Area	RT (min)
1	86.8259	17165.9122	3.52
2	13.1741	2604.5838	3.92
Total:	100	19770.496	

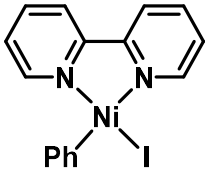
Peak No	% Area	Area	RT (min)
1	3.7591	146.9086	3.48
2	96.2409	3761.1672	3.99
Total:	100	3908.0758	

Peak No	% Area	Area	RT (min)
1	50.7244	2991.7195	3.58
2	49.2756	2906.2689	4.17
Total:	100	5897.9884	

Assignment of Absolute Stereochemistry

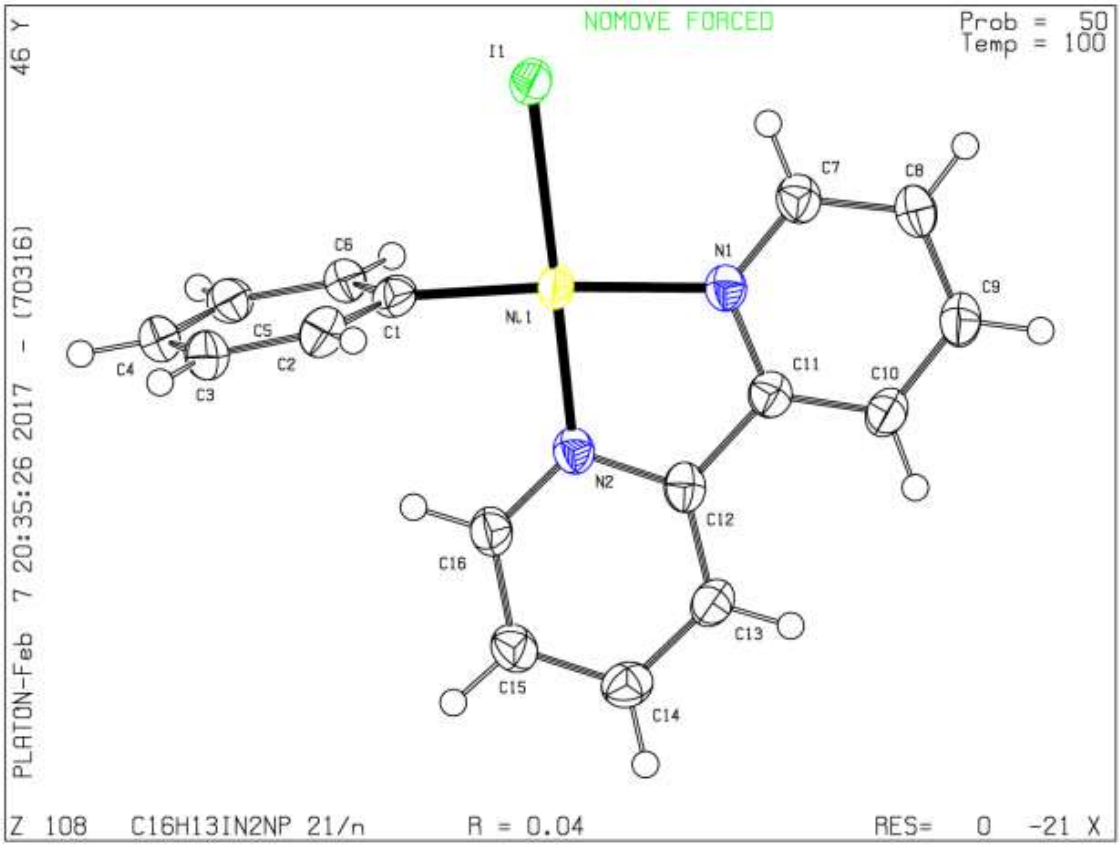
Comparison of the SFC traces and optical rotation of **32** and **S-32** allowed for the assignment of the absolute stereochemistry for the Ni catalyzed conjunctive cross-coupling products. This assignment was also supported by comparison of the SFC trace and optical rotation of the substrate **16** with those previously reported.[64]

1.4.8 Stoichiometric Experiment



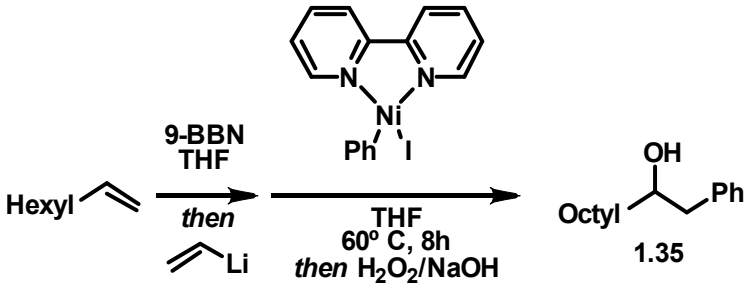
Phenyl(dipyridyl) Nickel Iodide (1.63). In an argon filled glovebox, to an oven dried scintillation vial equipped with a magnetic stirbar was added bis(cyclooctadiene)nickel(0) (82.5 mg, 0.3 mmol, 1.0 equiv.) 2,2'-bipyridine (46.9 mg, 0.3 mmol, 1.0 equiv.) and 2 mL of THF. The vial was sealed with a septum-cap and brought outside. The dark purple solution was allowed to stir for 3 hours at room temperature, after which the solvent was carefully removed through a Schlenk line under reduced pressure. The solid was then mostly redissolved in 8 mL of pentane (the BipyNiCOD complex is slightly soluble in pentane), and iodobenzene (104.1 mg, 0.51 mmol, 1.7 equiv.) was added the vial. The solution turned cloudy and a dark red precipitate began to form. After stirring for 2 hours the suspension was brought back into the glovebox and allowed to settle. The colorless pentane solution was removed via syringe leaving behind a dark red solid which was triturated 4 times with 2 mL portions of Pentane. The vial was sealed and placed under vacuum overnight to remove any residual solvent, leaving behind the product as a red solid (54 mg, 43% yield). The solid could not be characterized by conventional methods as it was not stable enough in solution to provide clean NMR spectra.

The structure was confirmed through x-ray crystallography. Crystals were grown by vapor diffusion with pentane and 2-methyltetrahydrofuran at -18ºC. The metal complex was dissolved in anhydrous 2-methyltetrahydrofuran in a glovebox, filtered through celite.



The structure was confirmed through x-ray crystallography. Crystals were grown by vapor diffusion with pentane and 2-methyltetrahydrofuran at -18ºC. The metal complex was dissolved in anhydrous 2-methyltetrahydrofuran in a glovebox, filtered through celite.

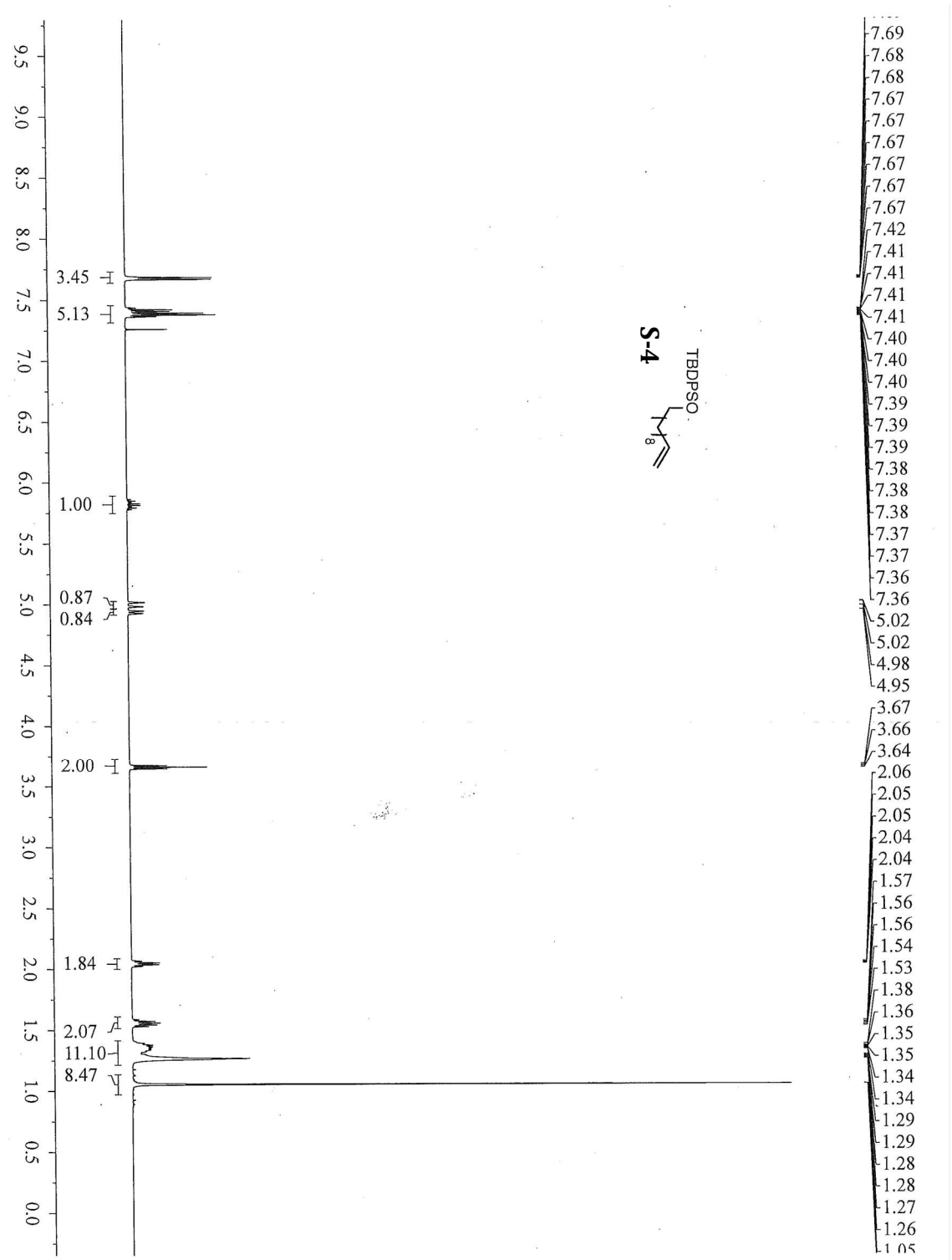
Stoichiometric Conjunctive Cross-Coupling Reaction

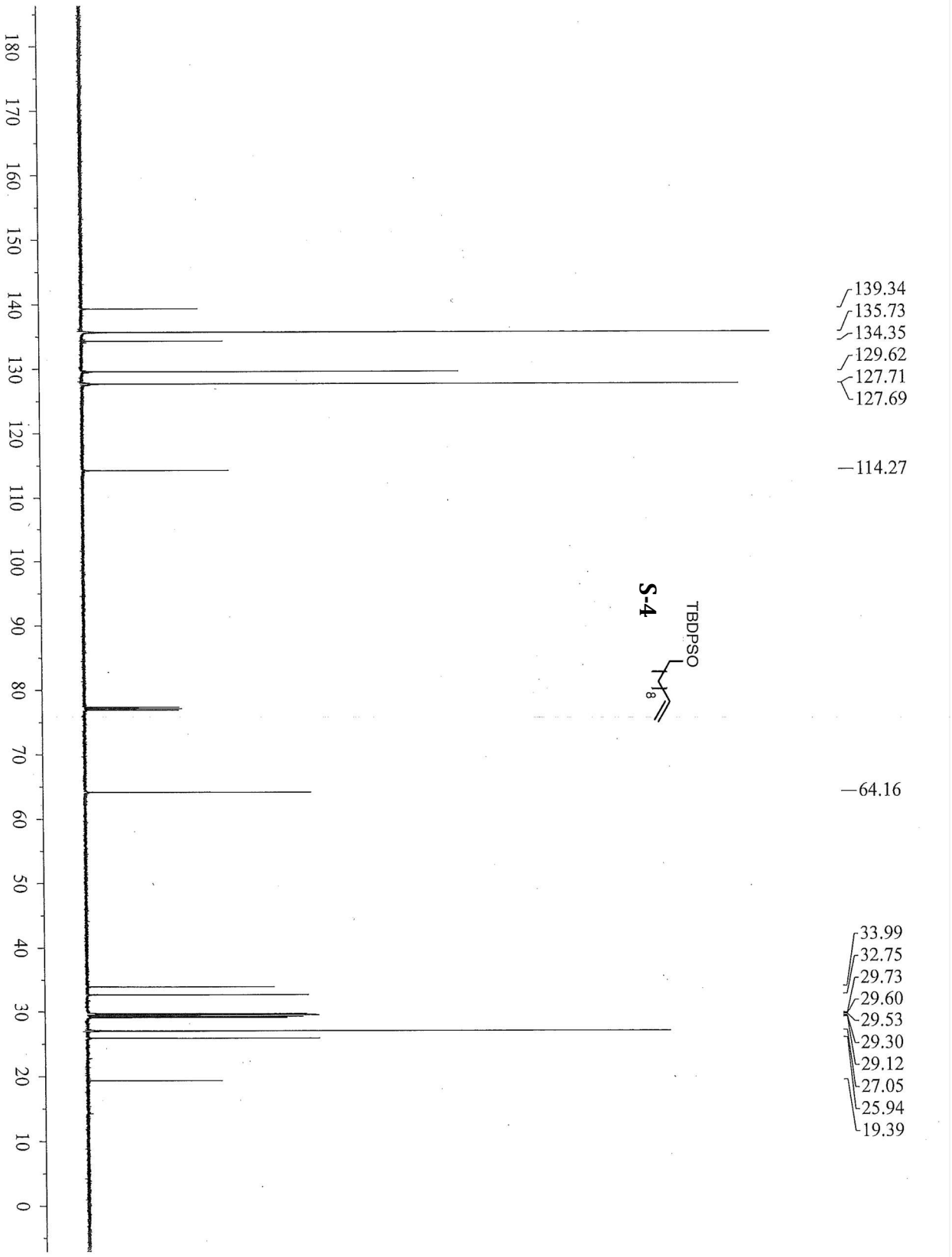


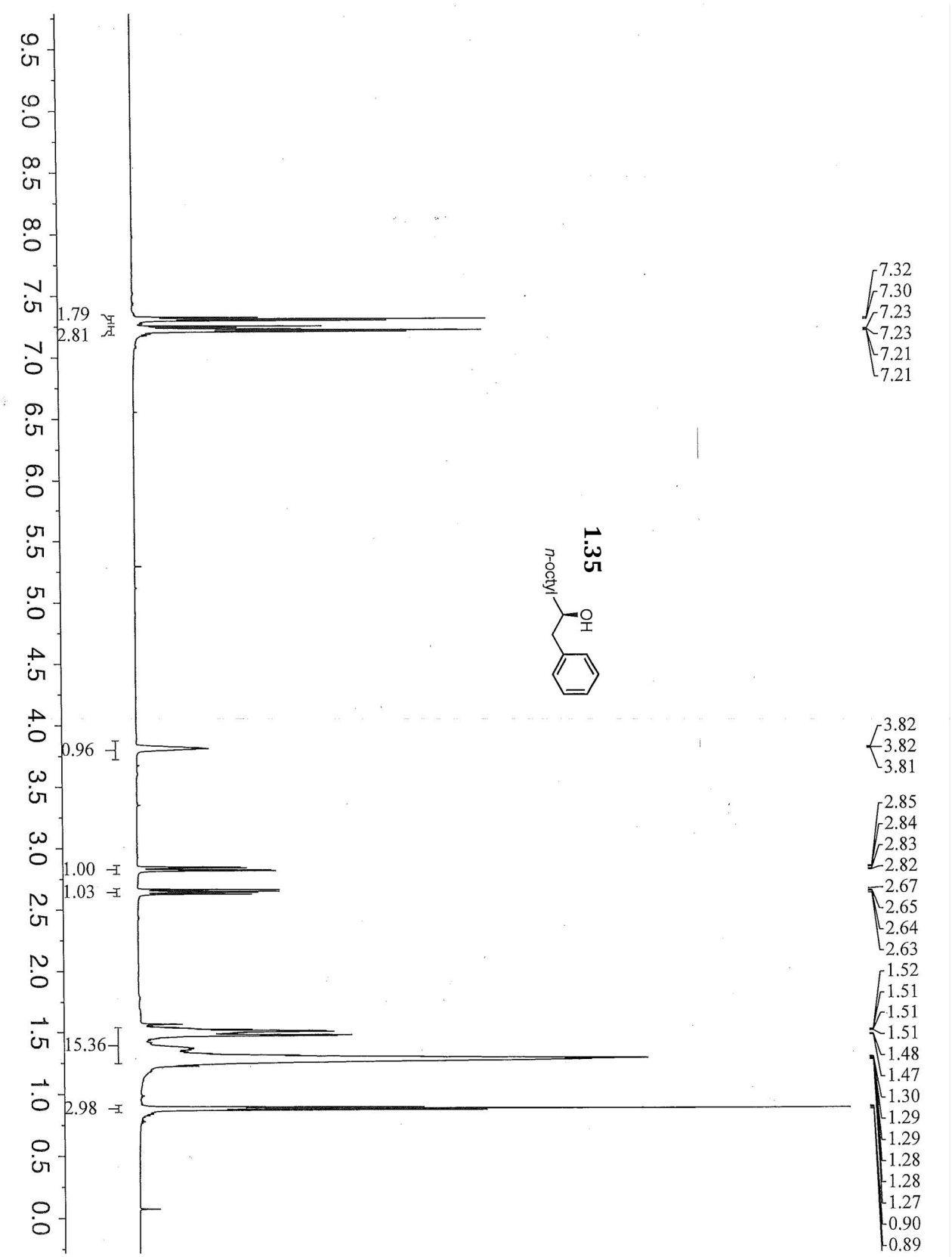
In an argon filled glovebox, in an oven-dried 2-dram vial equipped with a magnetic stirbar, 1-octene (13.5 mg, 0.105 mmol, 1.05 equiv.) was added to a solution of 9-BBN in THF

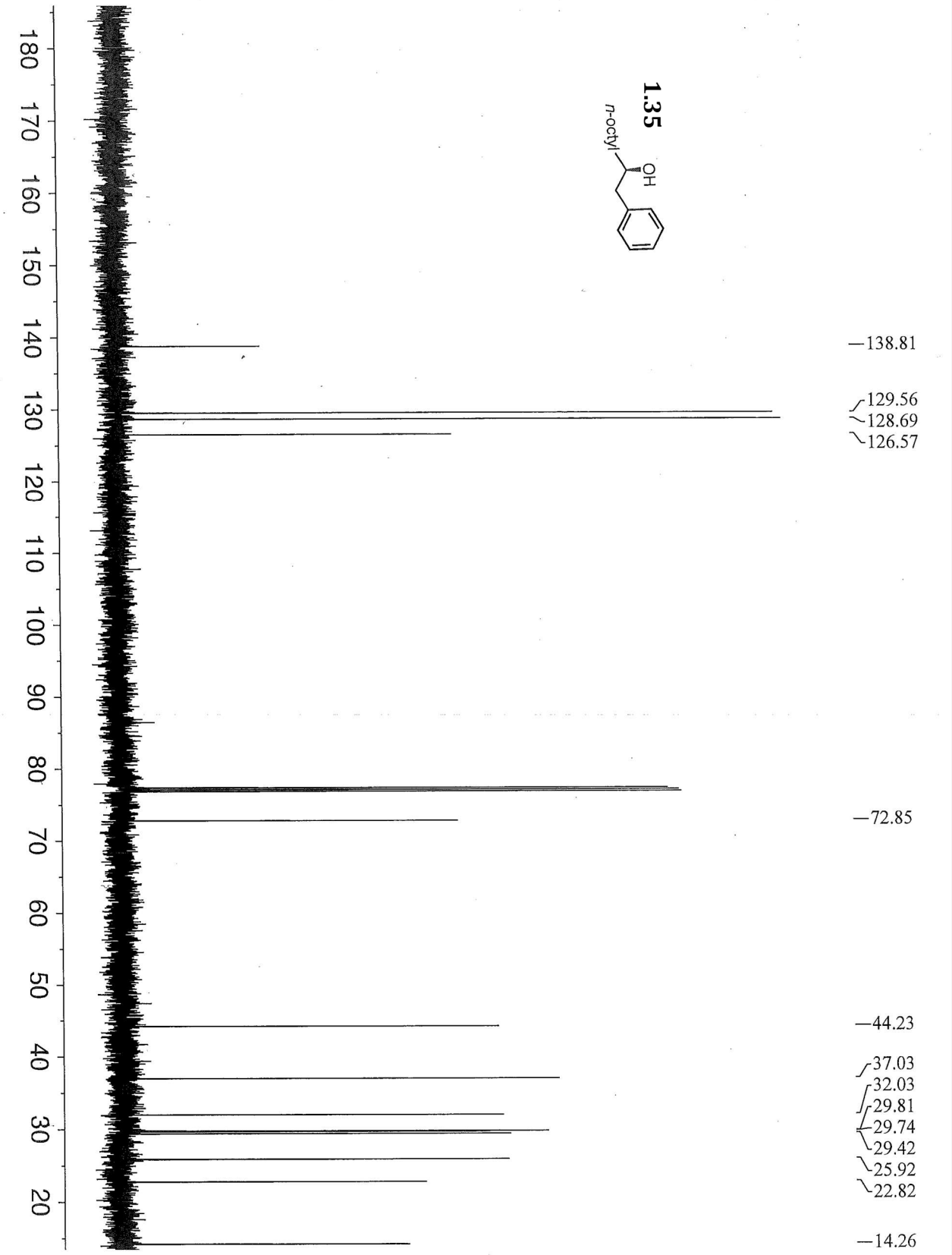
(0.21 mL, 0.5 M, 0.105 mmol, 1.05 equiv.) at 0º C. The reaction mixture was allowed to warm to room temperature and stir for an additional 3 hours before being cooled back to 0°C. Vinyllithium in THF (68 µL, 1.47 M, 0.1 mmol, 1.00 equiv.) was added to the reaction mixture which was then warmed to room temperature and stirred for 5 minutes**.** Phenyl(dipyridyl)nickel iodide (**1.63**) (41.9 mg, 0.1 mmol, 1.0 equiv.) was added to the vial which was then sealed with a septa-cap, brought outside and stirred for 8 hours at 60ºC. The reaction mixture was then cooled to 0°C, and 30% H_2O_2 (0.25 mL) were added along with 3 M NaOH (0.25 mL). The reaction mixture was allowed to warm up to room temperature and stirred for 3 hours, aq. $Na_2S_2O_3$ (0.5 mL) was then added to quench the reaction mixture. The aqueous phase was extracted with Et_2O (2 x 2 mL), followed by EtOAc (2 x 2 mL). The combined organic layer was dried over $MgSO_4$, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to provide **1.35** as a colorless oil (10.5 mg, 45% yield).

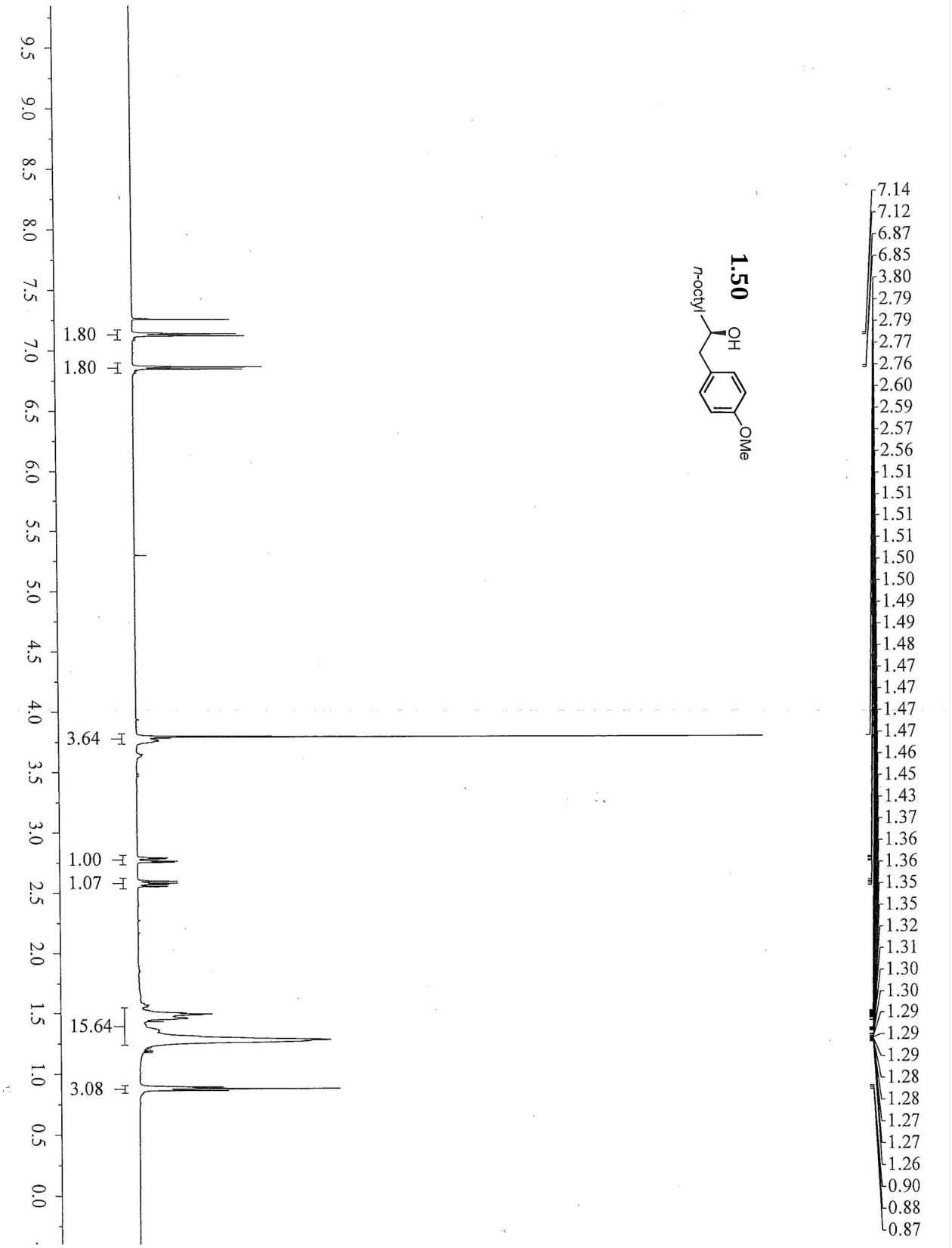
1.4.9 Spectral Data

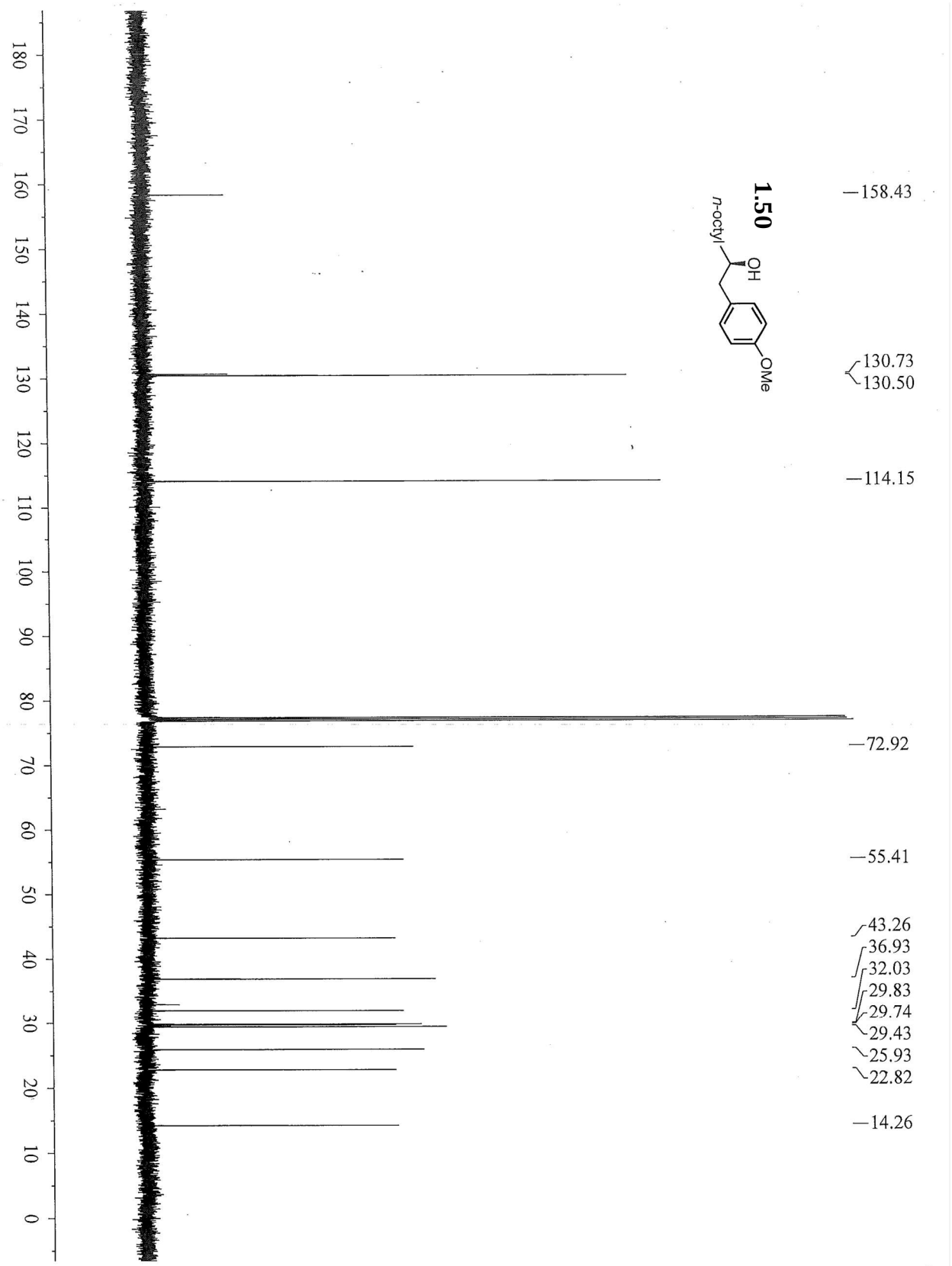


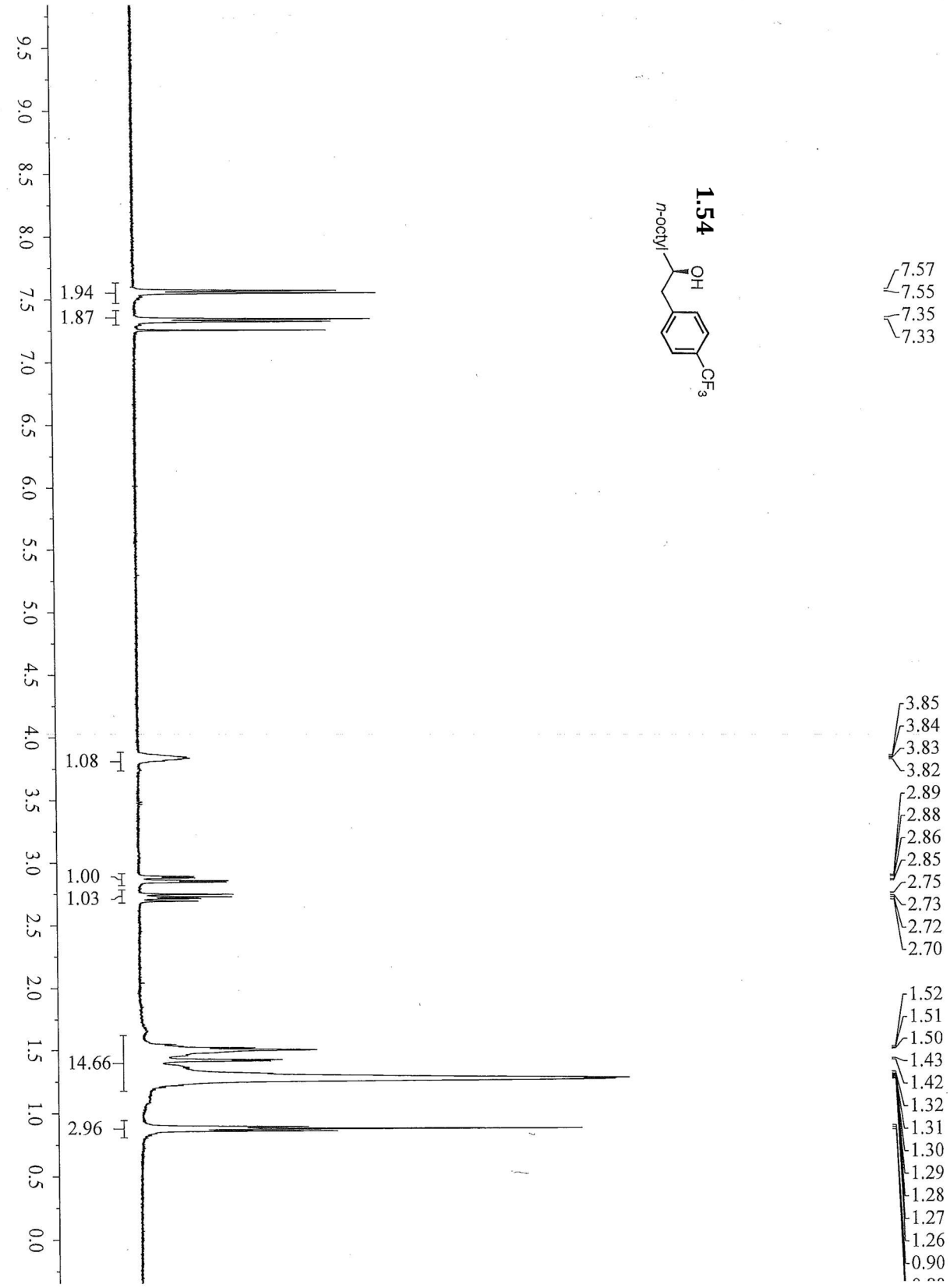

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
139.34
135.73
134.35
129.62
127.71
127.69
114.27
64.16
33.99
32.75
29.73
29.60
29.53
29.30
29.12
27.05
25.94
19.39
S-4
TBDPSO
8

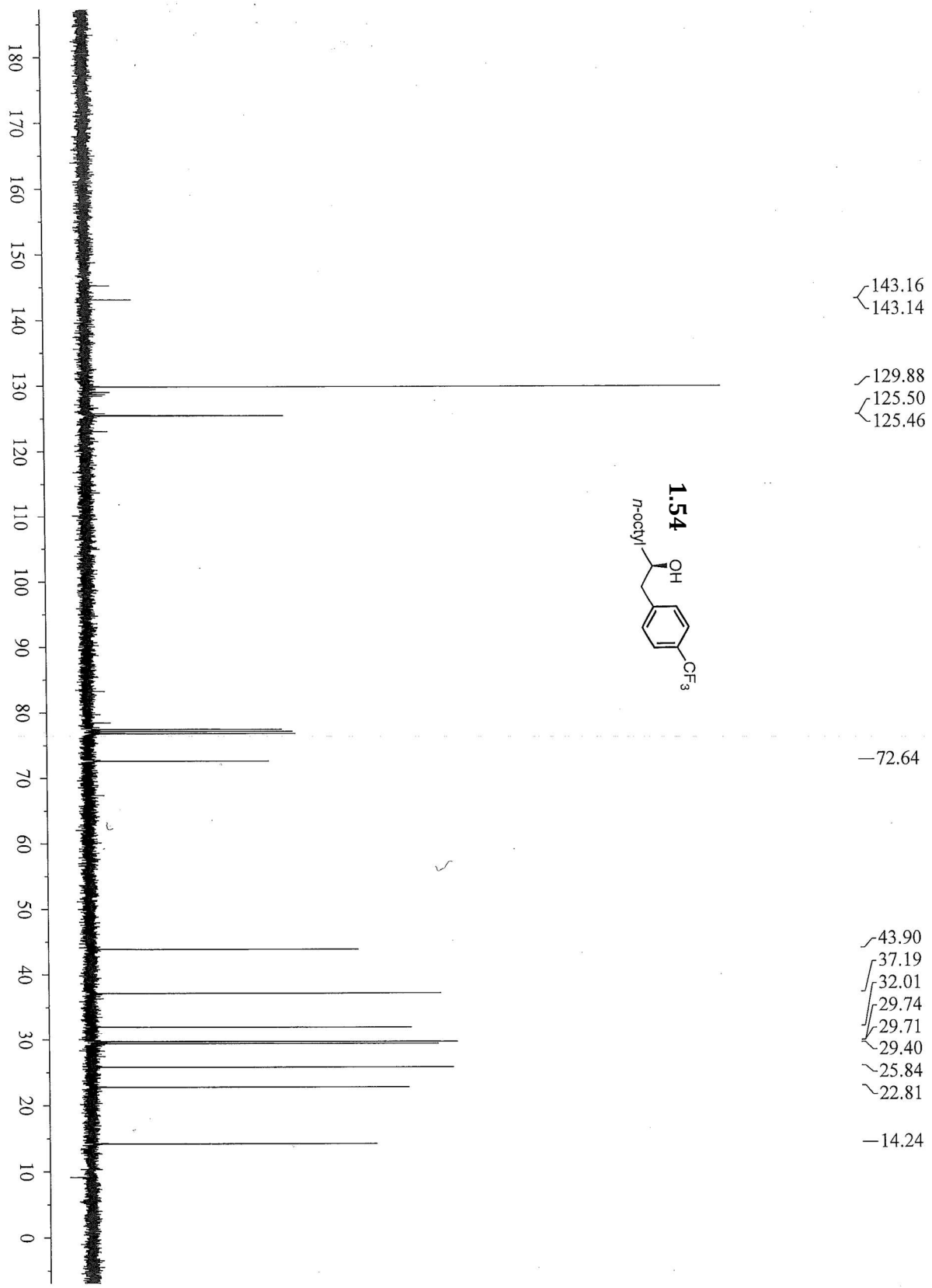

1.35
n-octyl
OH
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
1.79
2.81
0.96
1.00
1.03
15.36
2.98
7.32
7.30
7.23
7.23
7.21
7.21
3.82
3.82
3.81
2.85
2.84
2.83
2.82
2.67
2.65
2.64
2.63
1.52
1.51
1.51
1.51
1.48
1.47
1.30
1.29
1.29
1.28
1.28
1.27
0.90
0.89

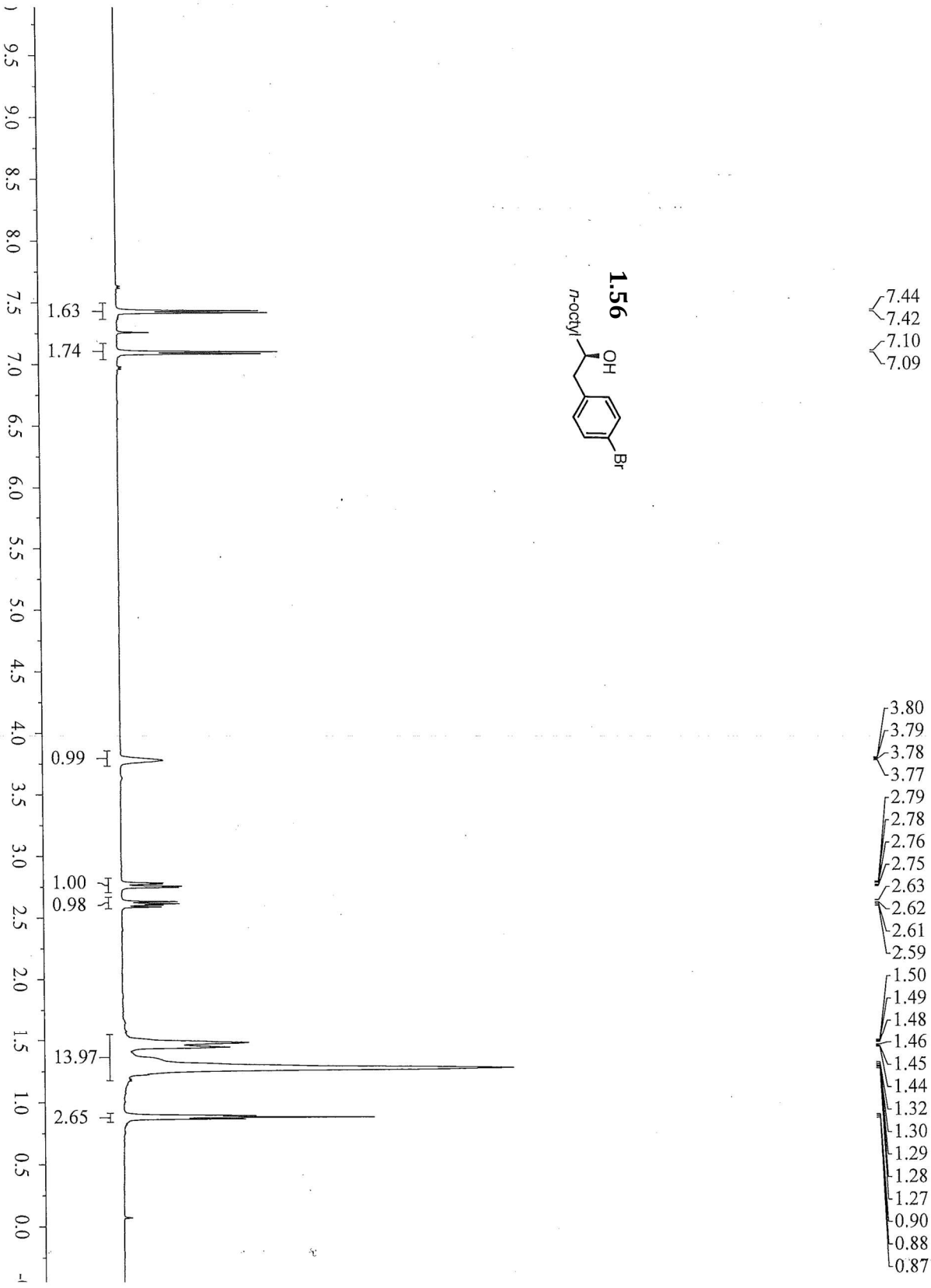

1.35
n-octyl
OH
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
138.81
129.56
128.69
126.57
72.85
44.23
37.03
32.03
29.81
29.74
29.42
25.92
22.82
14.26

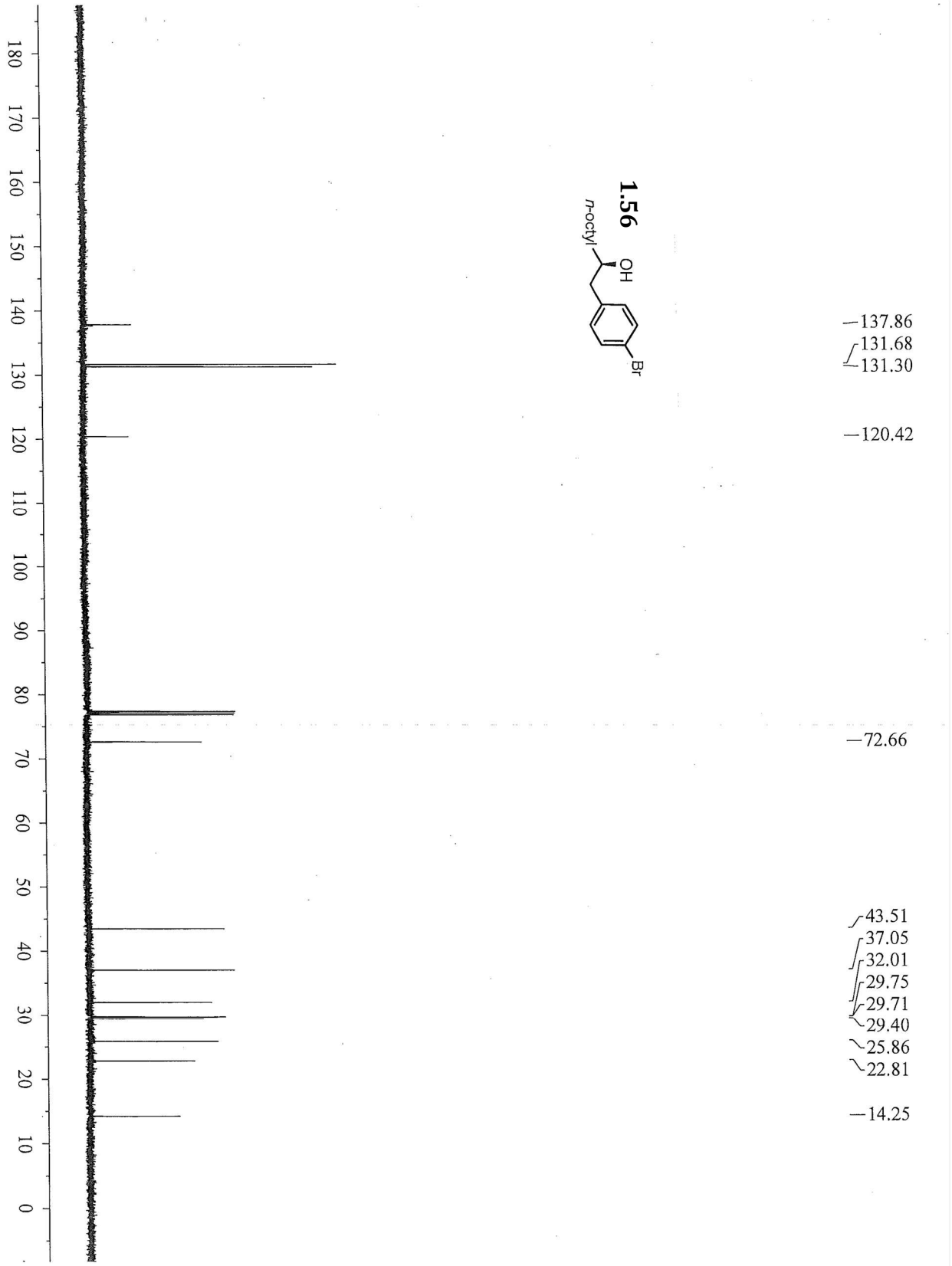

1.50
n-octyl
OH
OMe
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.80
1.80
3.64
1.00
1.07
15.64
3.08
7.14
7.12
6.87
6.85
3.80
2.79
2.79
2.77
2.76
2.60
2.59
2.57
2.56
1.51
1.51
1.51
1.51
1.50
1.50
1.49
1.49
1.48
1.47
1.47
1.47
1.47
1.46
1.45
1.43
1.37
1.36
1.36
1.35
1.35
1.32
1.31
1.30
1.30
1.29
1.29
1.29
1.28
1.28
1.27
1.27
1.26
0.90
0.88
0.87

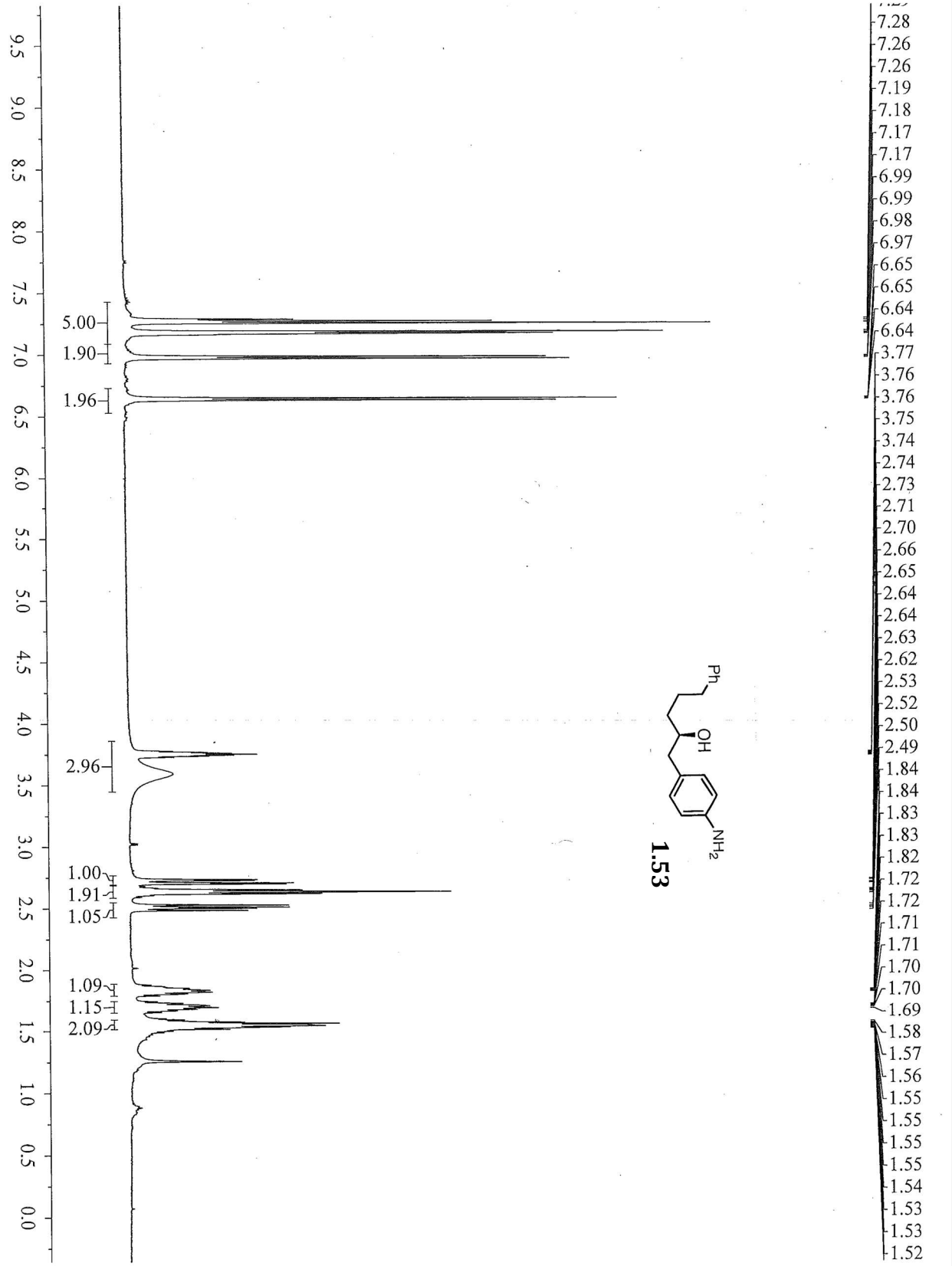

1.50
n-octyl
OH
OMe
158.43
130.73
130.50
114.15
72.92
55.41
43.26
36.93
32.03
29.83
29.74
29.43
25.93
22.82
14.26
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

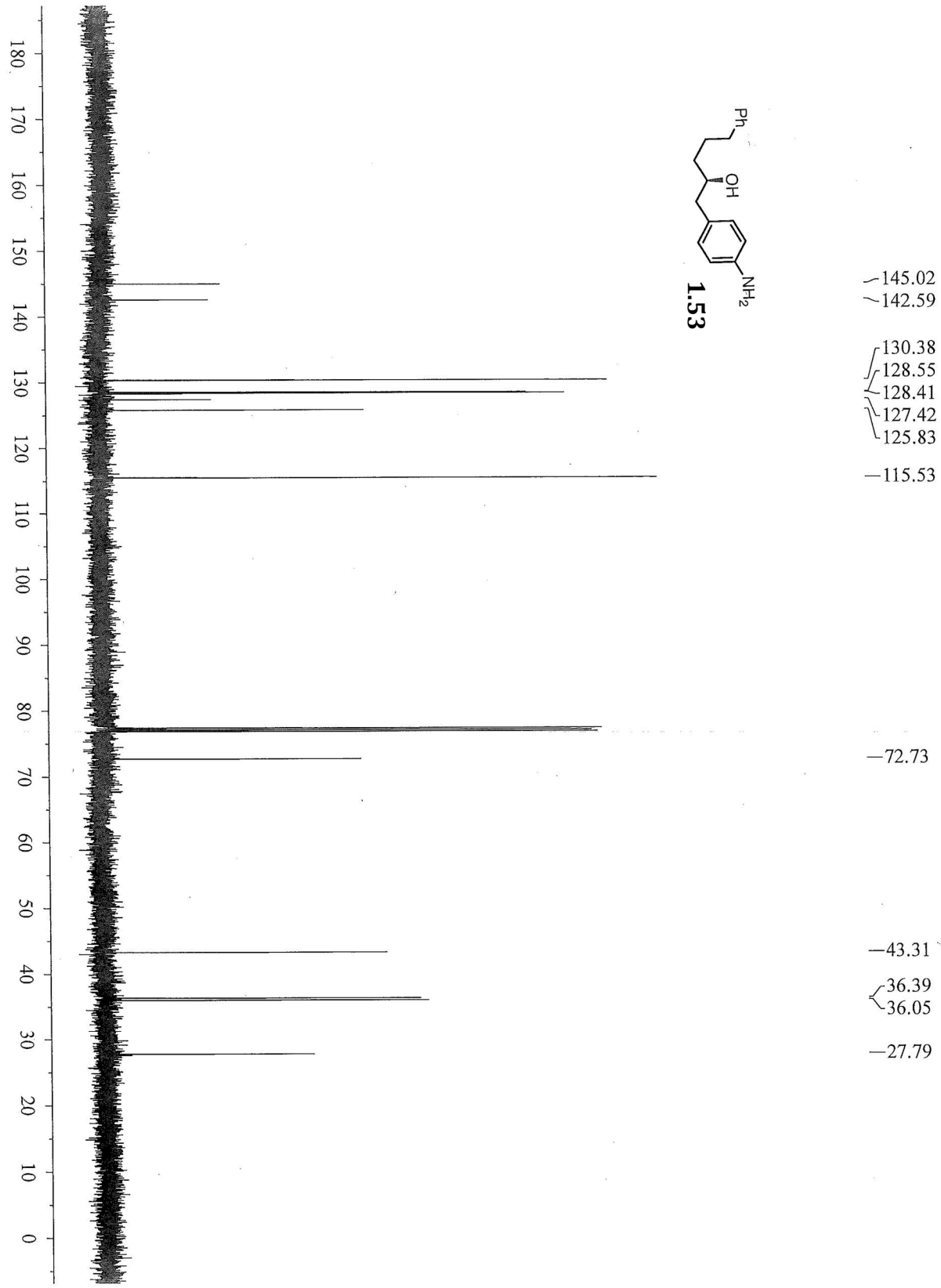

1.54
n-octyl
OH
CF3
7.57
7.55
7.35
7.33
3.85
3.84
3.83
3.82
2.89
2.88
2.86
2.85
2.75
2.73
2.72
2.70
1.52
1.51
1.50
1.43
1.42
1.32
1.31
1.30
1.29
1.28
1.27
1.26
0.90
1.94
1.87
1.08
1.00
1.03
14.66
2.96
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

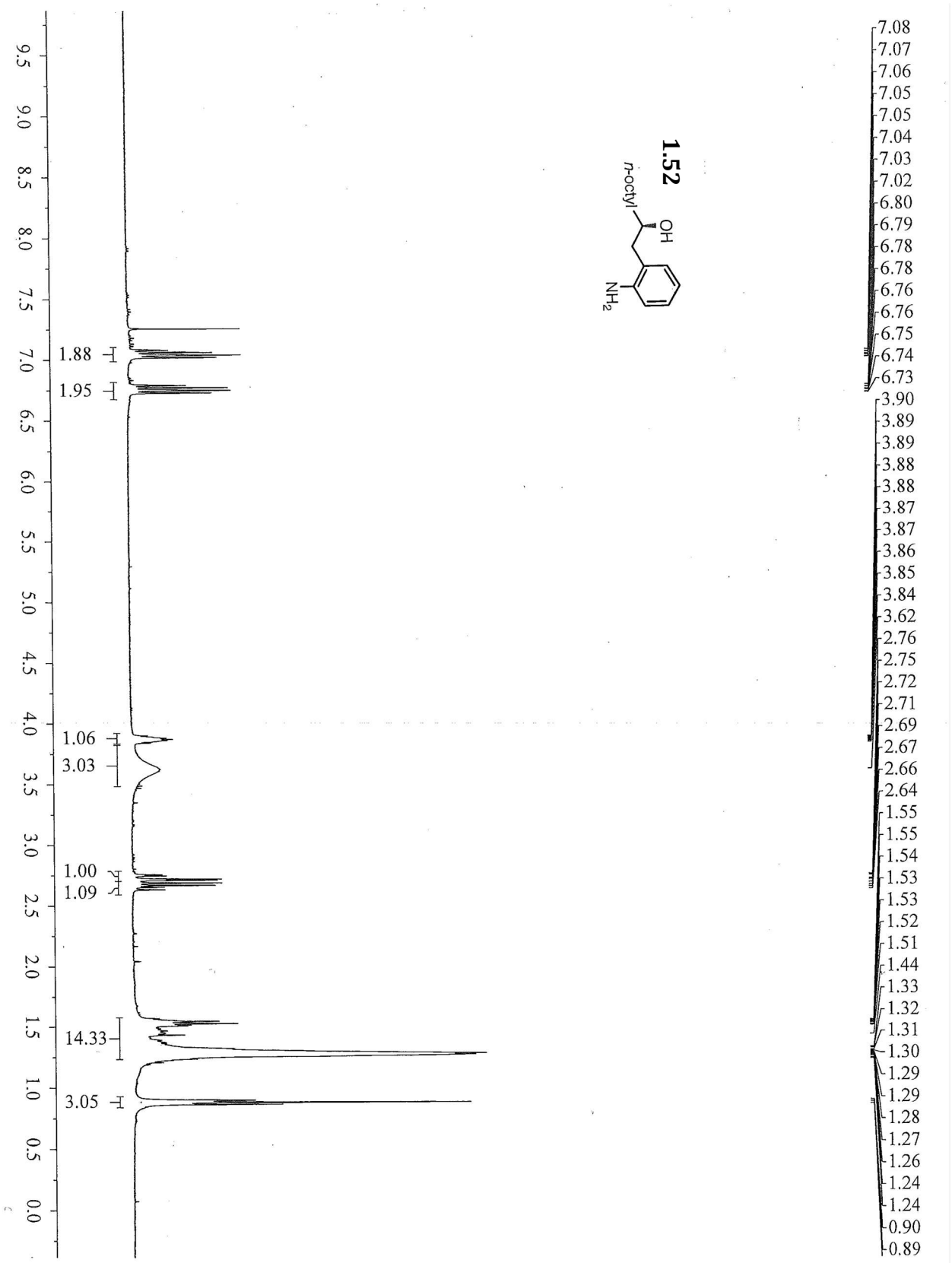

1.54
n-octyl
OH
CF3
143.16
143.14
129.88
125.50
125.46
72.64
43.90
37.19
32.01
29.74
29.71
29.40
25.84
22.81
14.24

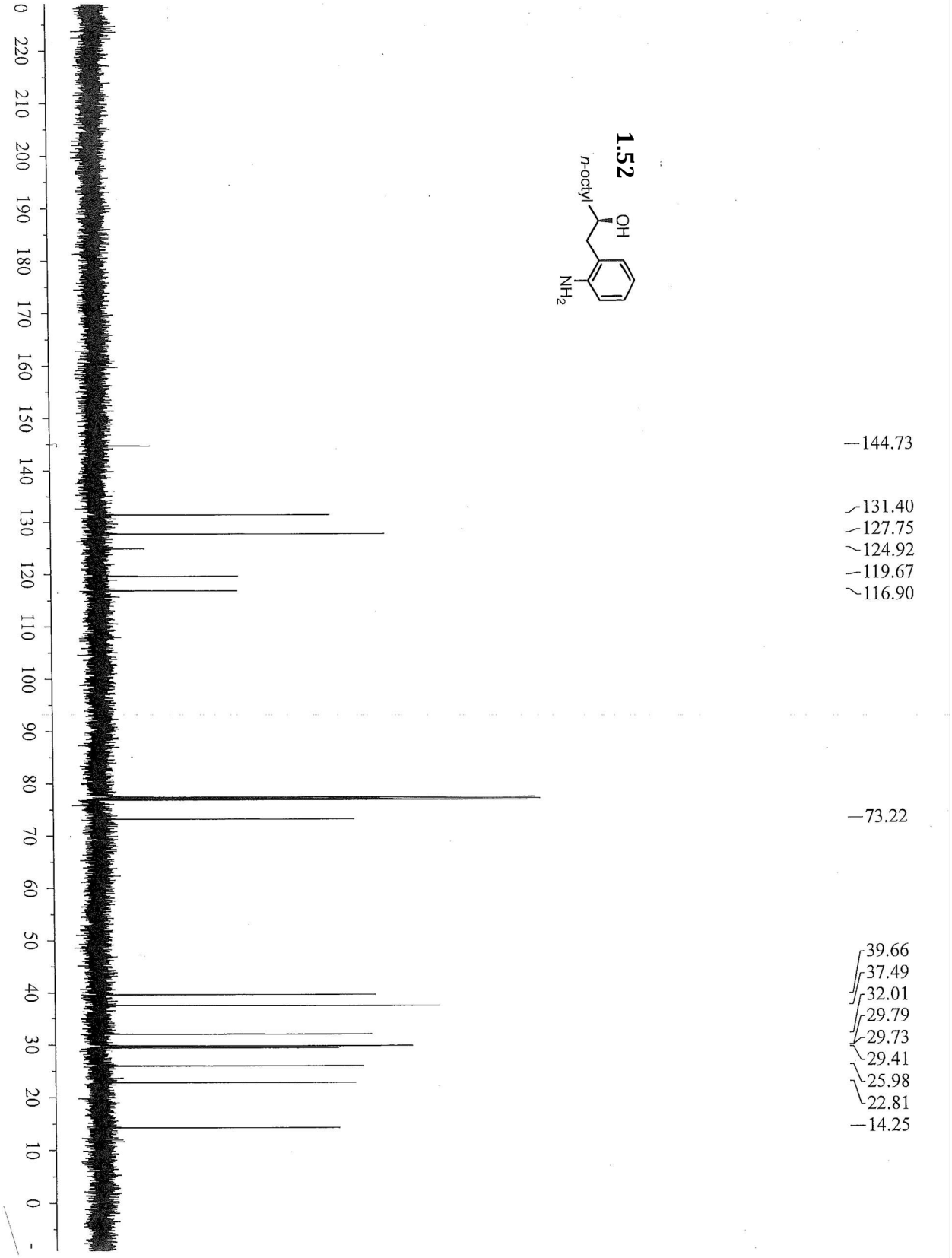

1.56
n-octyl
OH
Br
7.44
7.42
7.10
7.09
3.80
3.79
3.78
3.77
2.79
2.78
2.76
2.75
2.63
2.62
2.61
2.59
1.50
1.49
1.48
1.46
1.45
1.44
1.32
1.30
1.29
1.28
1.27
0.90
0.88
0.87
1.63
1.74
0.99
1.00
0.98
13.97
2.65

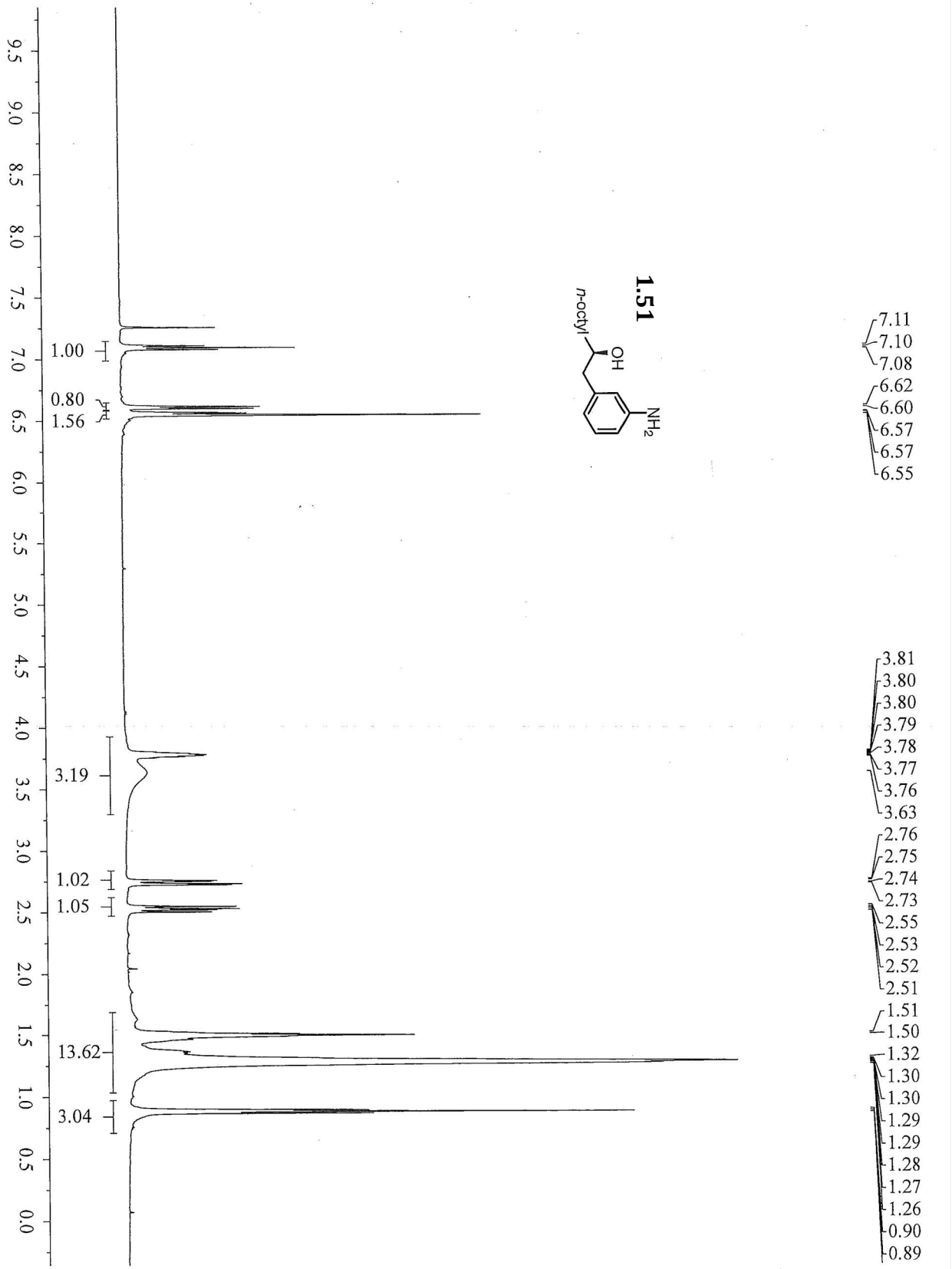

1.56
n-octyl
OH
Br
137.86
131.68
131.30
120.42
72.66
43.51
37.05
32.01
29.75
29.71
29.40
25.86
22.81
14.25
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

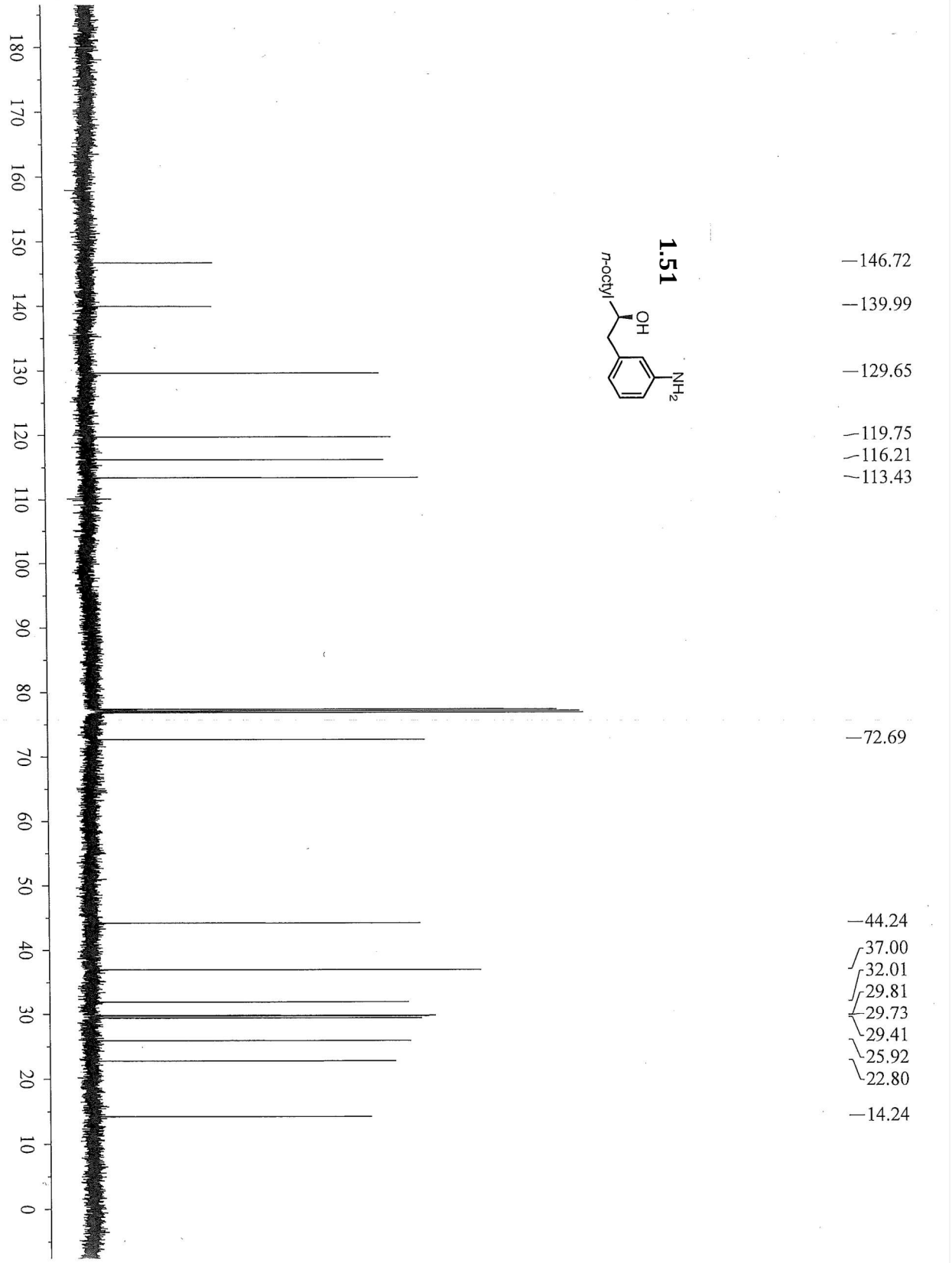

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
5.00
1.90
1.96
2.96
1.00
1.91
1.05
1.09
1.15
2.09
Ph
OH
NH2
1.53
7.28
7.26
7.26
7.19
7.18
7.17
7.17
6.99
6.99
6.98
6.97
6.65
6.65
6.64
6.64
3.77
3.76
3.76
3.75
3.74
2.74
2.73
2.71
2.70
2.66
2.65
2.64
2.64
2.63
2.62
2.53
2.52
2.50
2.49
1.84
1.84
1.83
1.83
1.82
1.72
1.72
1.71
1.71
1.70
1.70
1.69
1.58
1.57
1.56
1.55
1.55
1.55
1.55
1.54
1.53
1.53
1.52

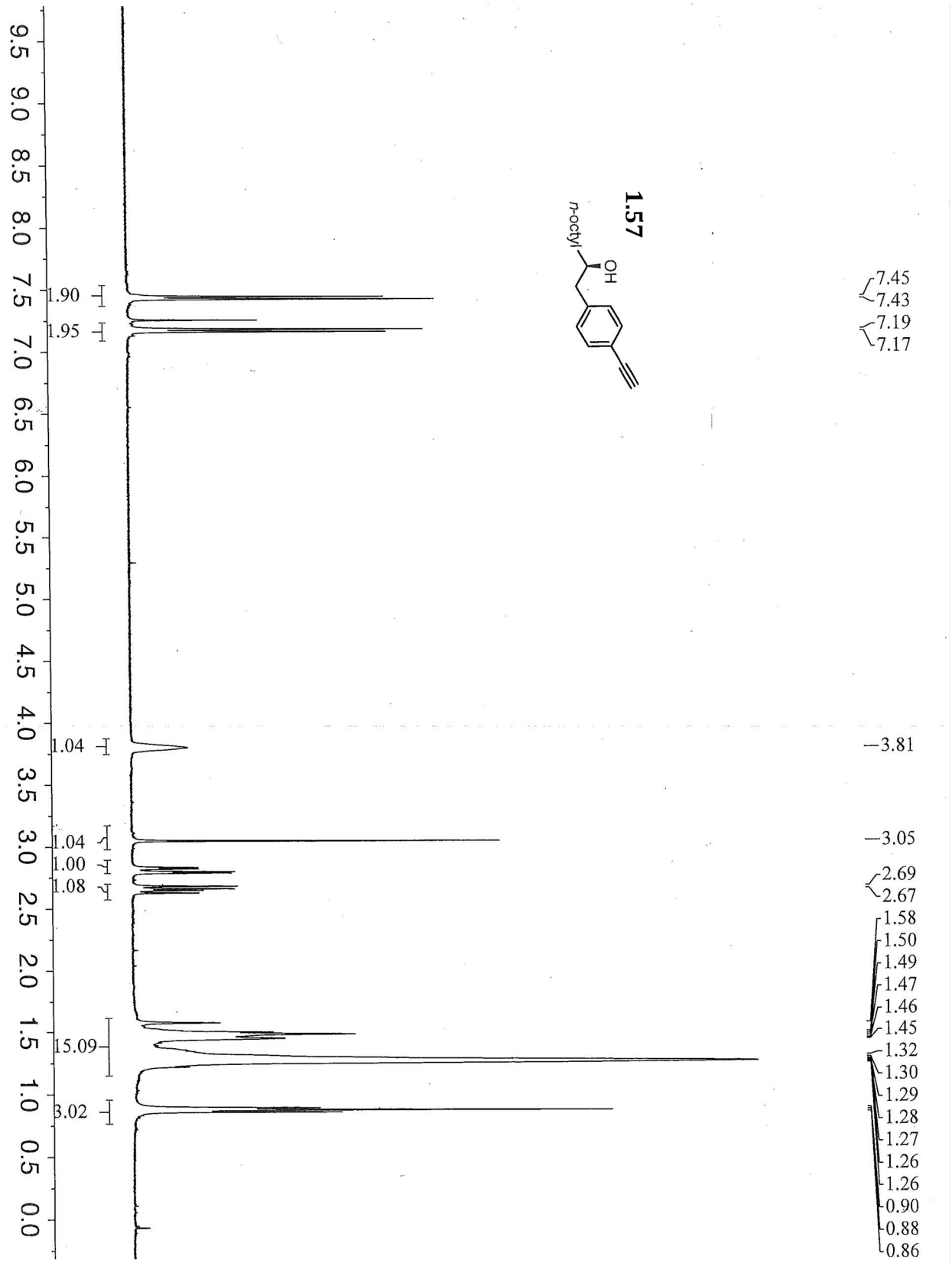

Ph
OH
NH2
1.53
145.02
142.59
130.38
128.55
128.41
127.42
125.83
115.53
72.73
43.31
36.39
36.05
27.79
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

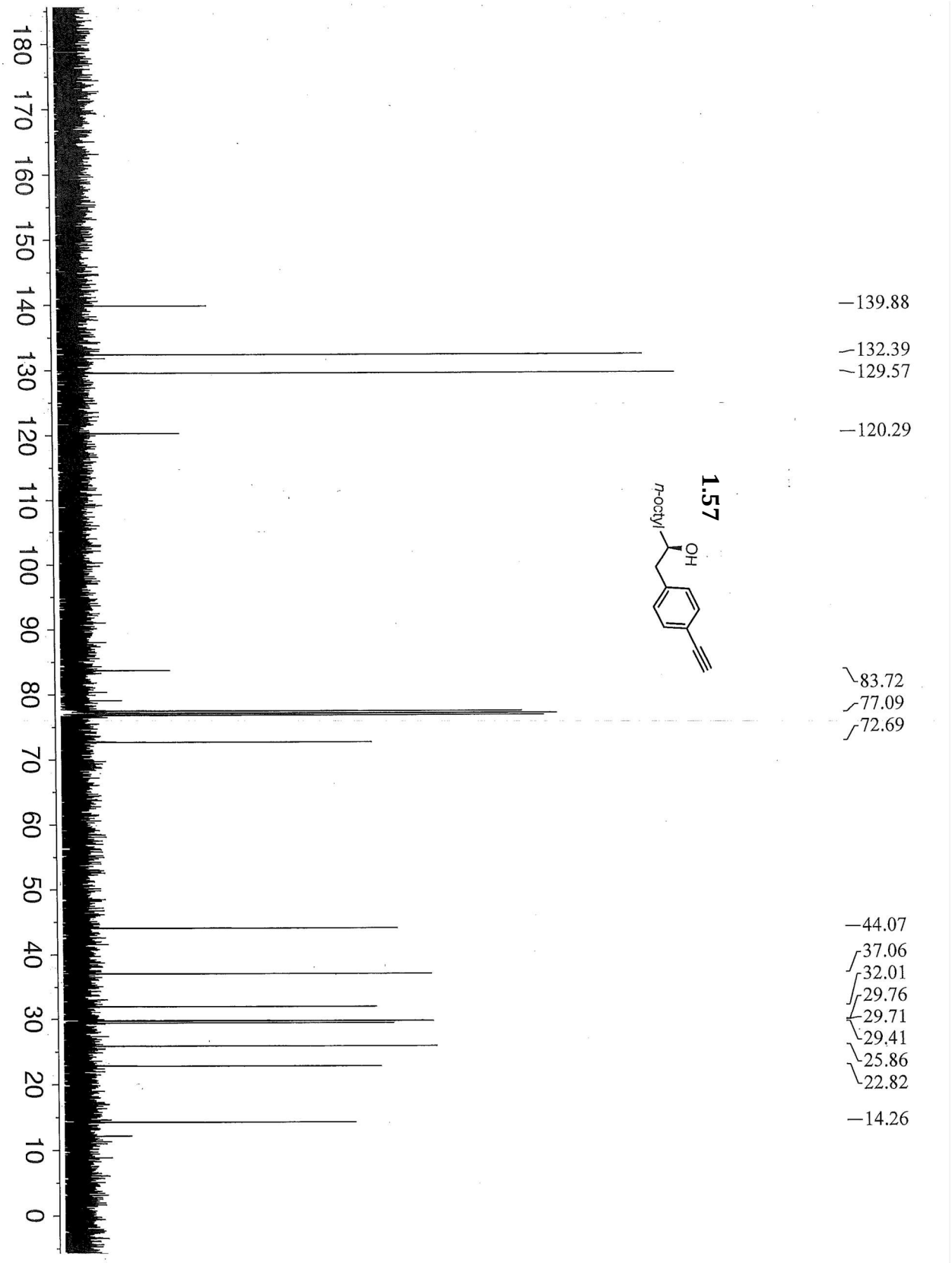

1.52
n-octyl
OH
NH2
1.88
1.95
1.06
3.03
1.00
1.09
14.33
3.05
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
7.08 7.07 7.06 7.05 7.05 7.04 7.03 7.02 6.80 6.79 6.78 6.78 6.76 6.76 6.75 6.74 6.73
3.90 3.89 3.89 3.88 3.88 3.87 3.87 3.86 3.85 3.84 3.62 2.76 2.75 2.72 2.71 2.69 2.67 2.66 2.64
1.55 1.55 1.54 1.53 1.53 1.52 1.51 1.44 1.33 1.32 1.31 1.30 1.29 1.29 1.28 1.27 1.26 1.24 1.24
0.90 0.89

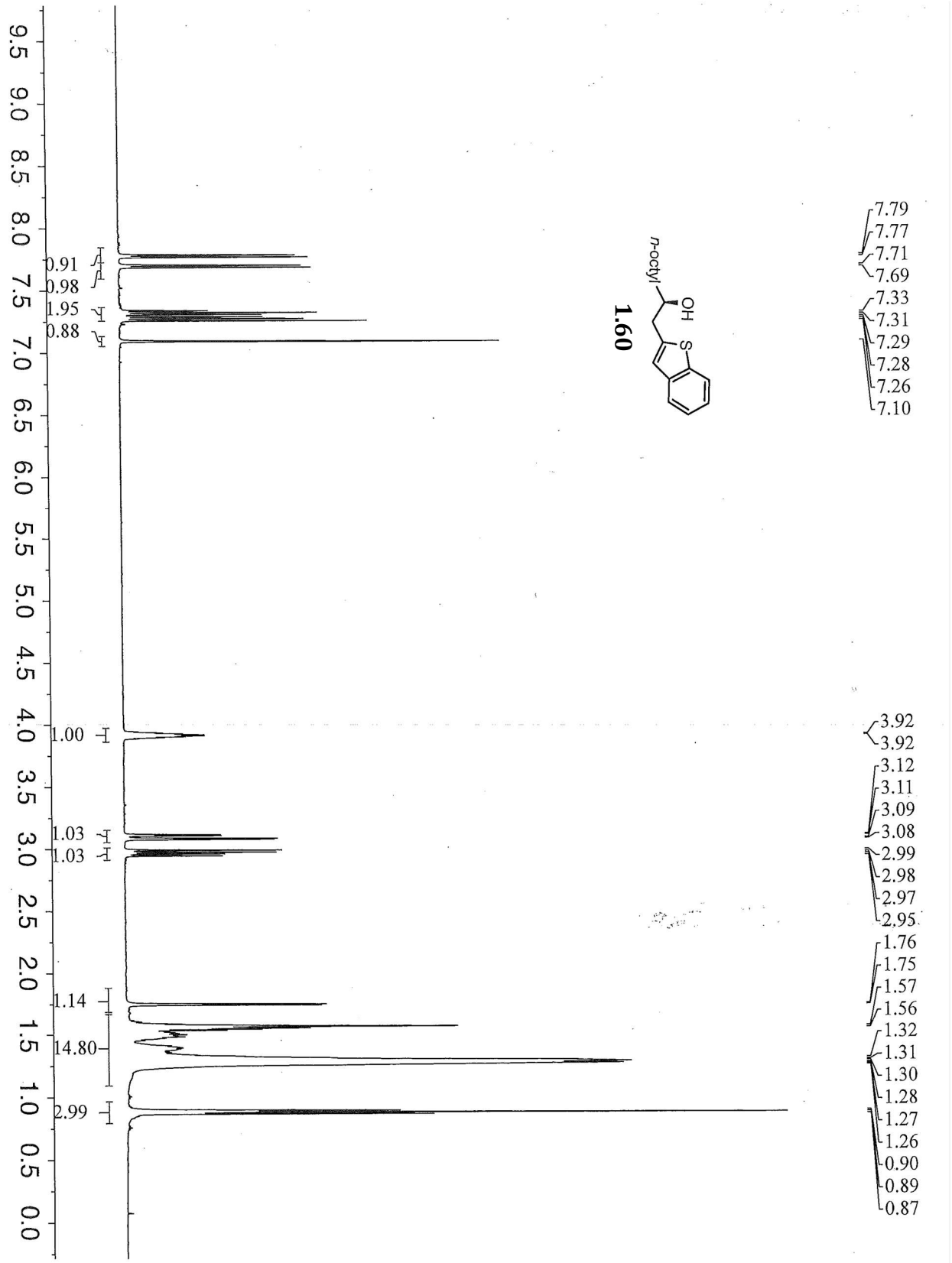

1.52
n-octyl
OH
NH2
144.73
131.40
127.75
124.92
119.67
116.90
73.22
39.66
37.49
32.01
29.79
29.73
29.41
25.98
22.81
14.25

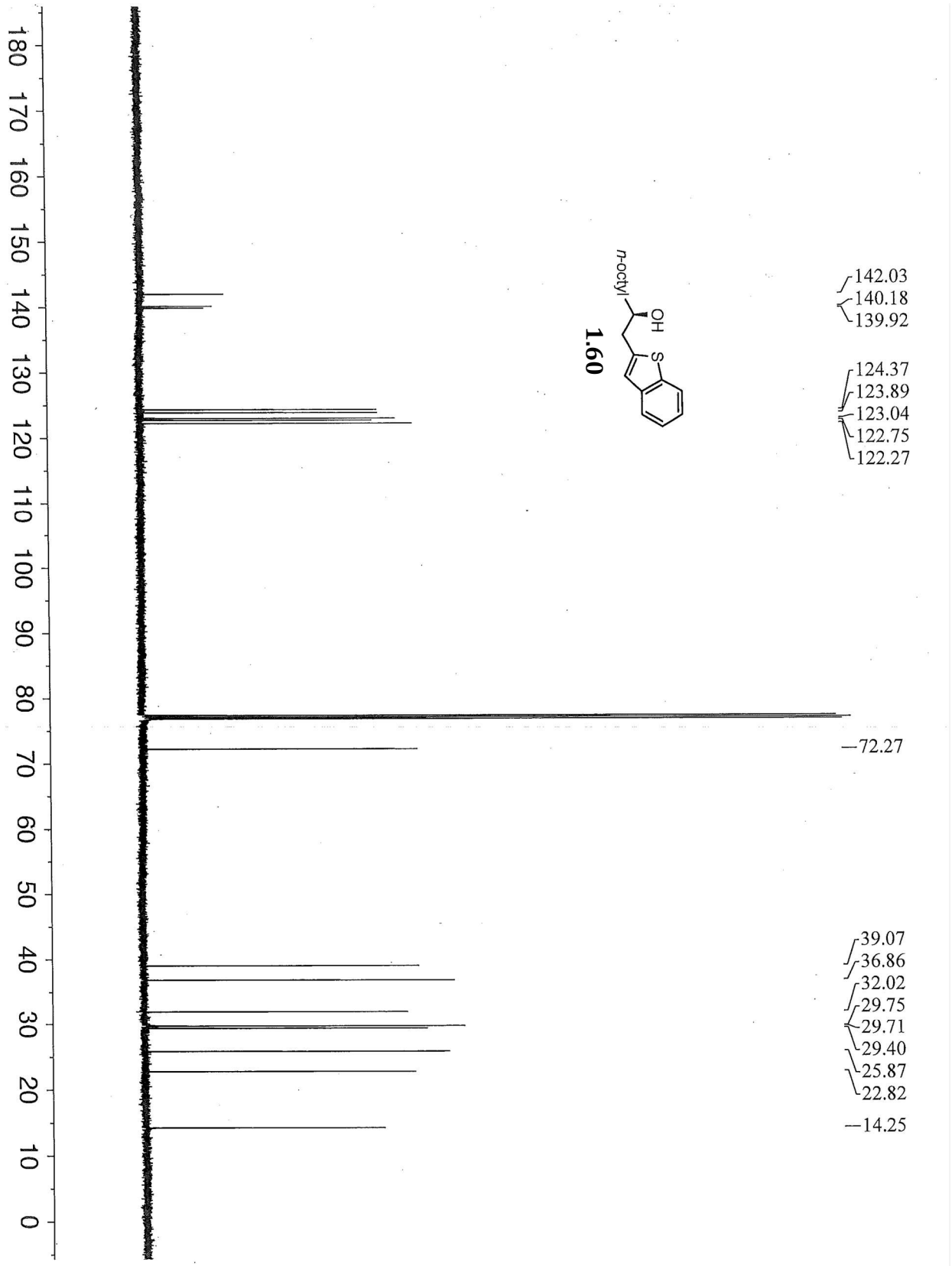

1.51
n-octyl
OH
NH2
1.00
0.80
1.56
3.19
1.02
1.05
13.62
3.04
7.11
7.10
7.08
6.62
6.60
6.57
6.57
6.55
3.81
3.80
3.80
3.79
3.78
3.77
3.76
3.63
2.76
2.75
2.74
2.73
2.55
2.53
2.52
2.51
1.51
1.50
1.32
1.30
1.30
1.29
1.29
1.28
1.27
1.26
0.90
0.89

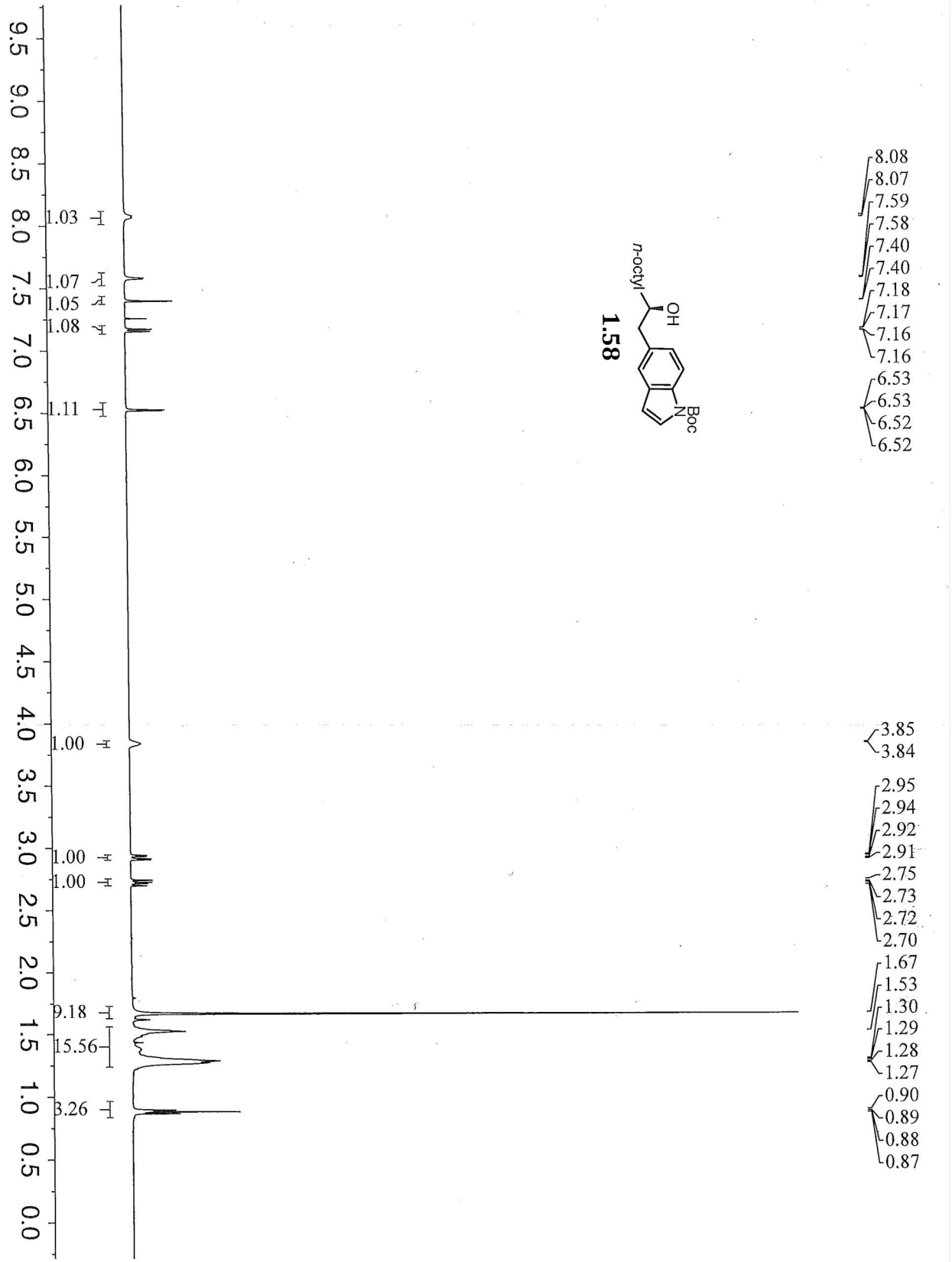

1.51
n-octyl
OH
NH2
146.72
139.99
129.65
119.75
116.21
113.43
72.69
44.24
37.00
32.01
29.81
29.73
29.41
25.92
22.80
14.24
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

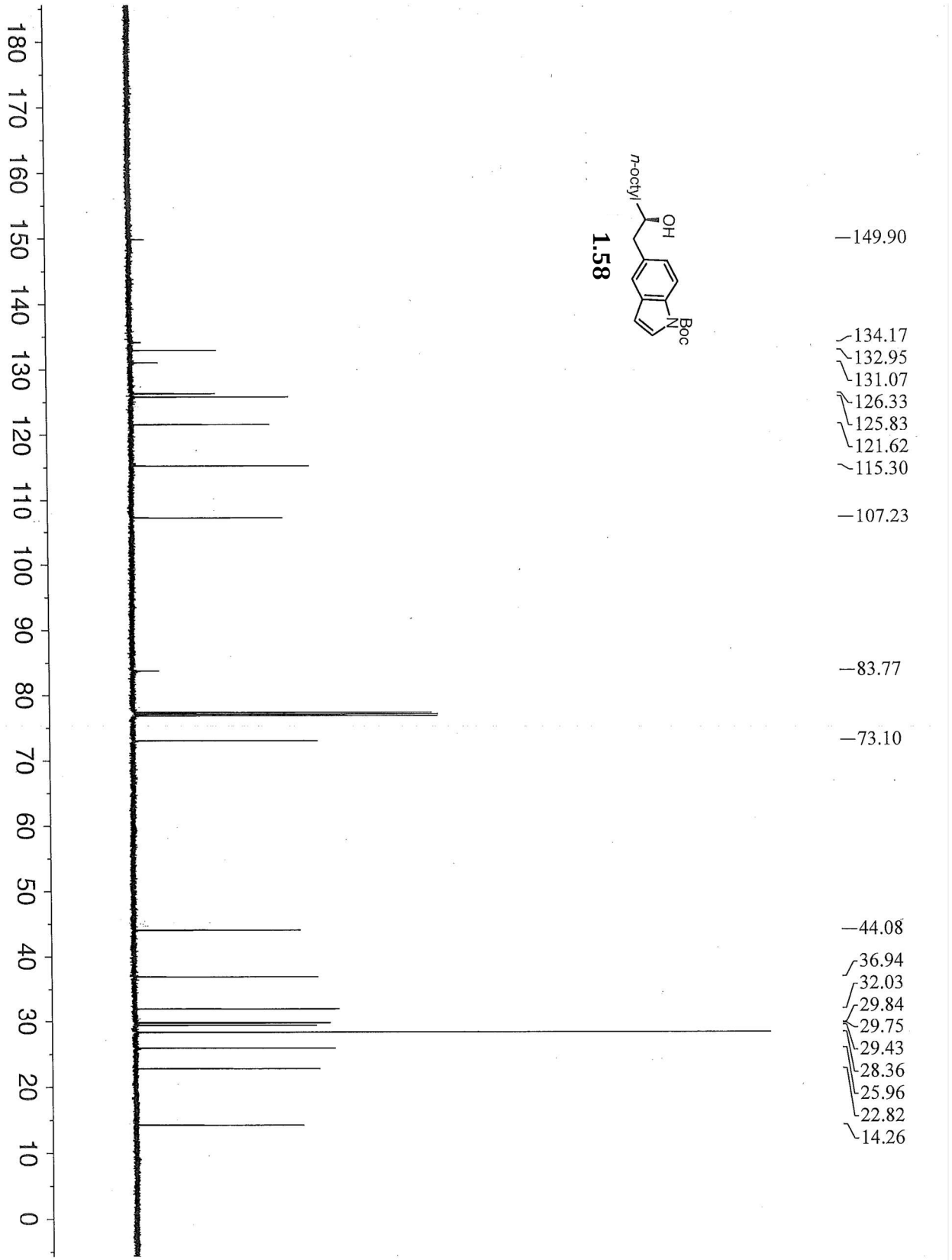

1.57
n-octyl
OH
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
1.90
1.95
1.04
1.04
1.00
1.08
15.09
3.02
7.45
7.43
7.19
7.17
3.81
3.05
2.69
2.67
1.58
1.50
1.49
1.47
1.46
1.45
1.32
1.30
1.29
1.28
1.27
1.26
1.26
0.90
0.88
0.86

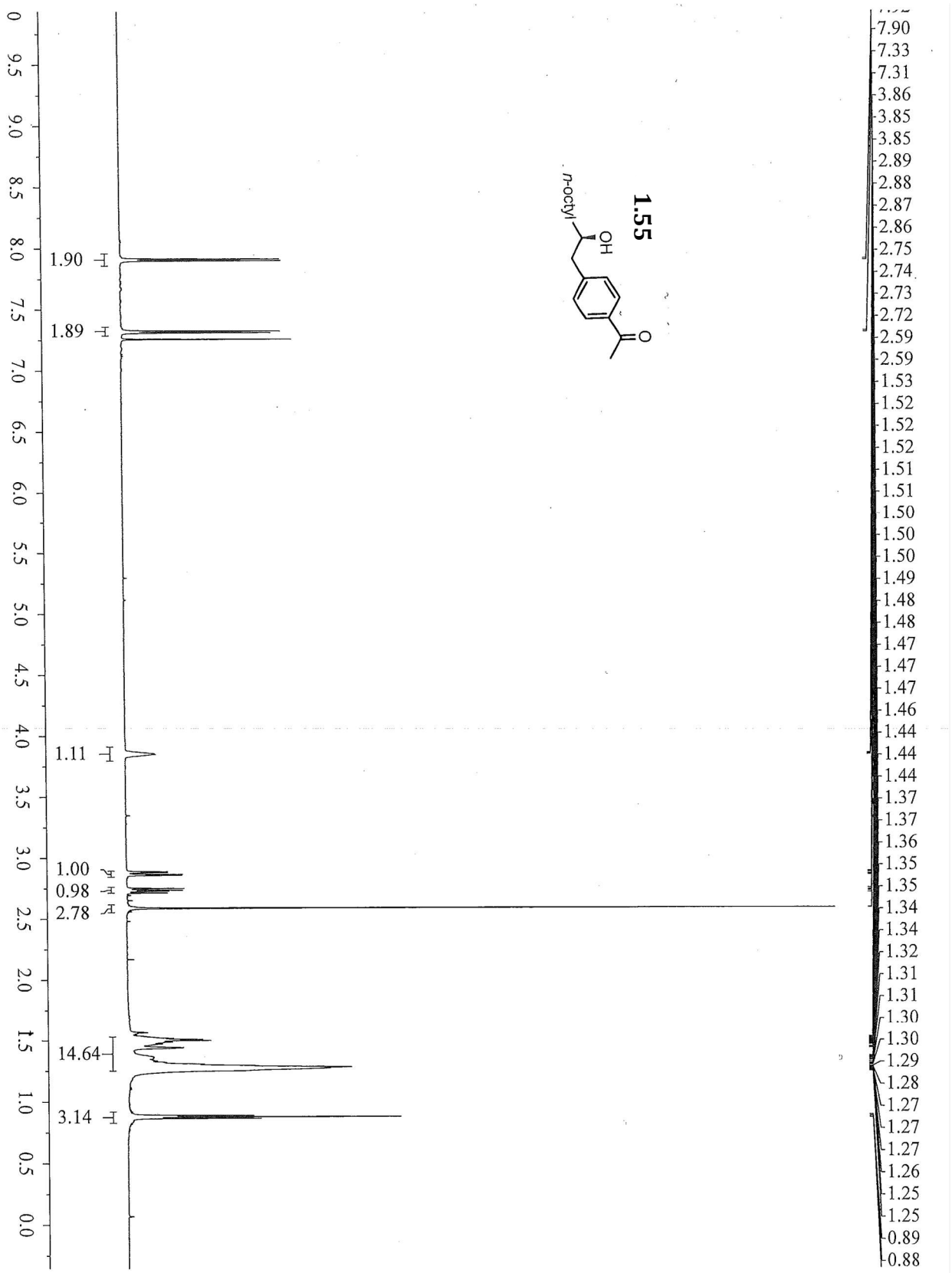

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
139.88
132.39
129.57
120.29
83.72
77.09
72.69
44.07
37.06
32.01
29.76
29.71
29.41
25.86
22.82
14.26
1.57
n-octyl
OH

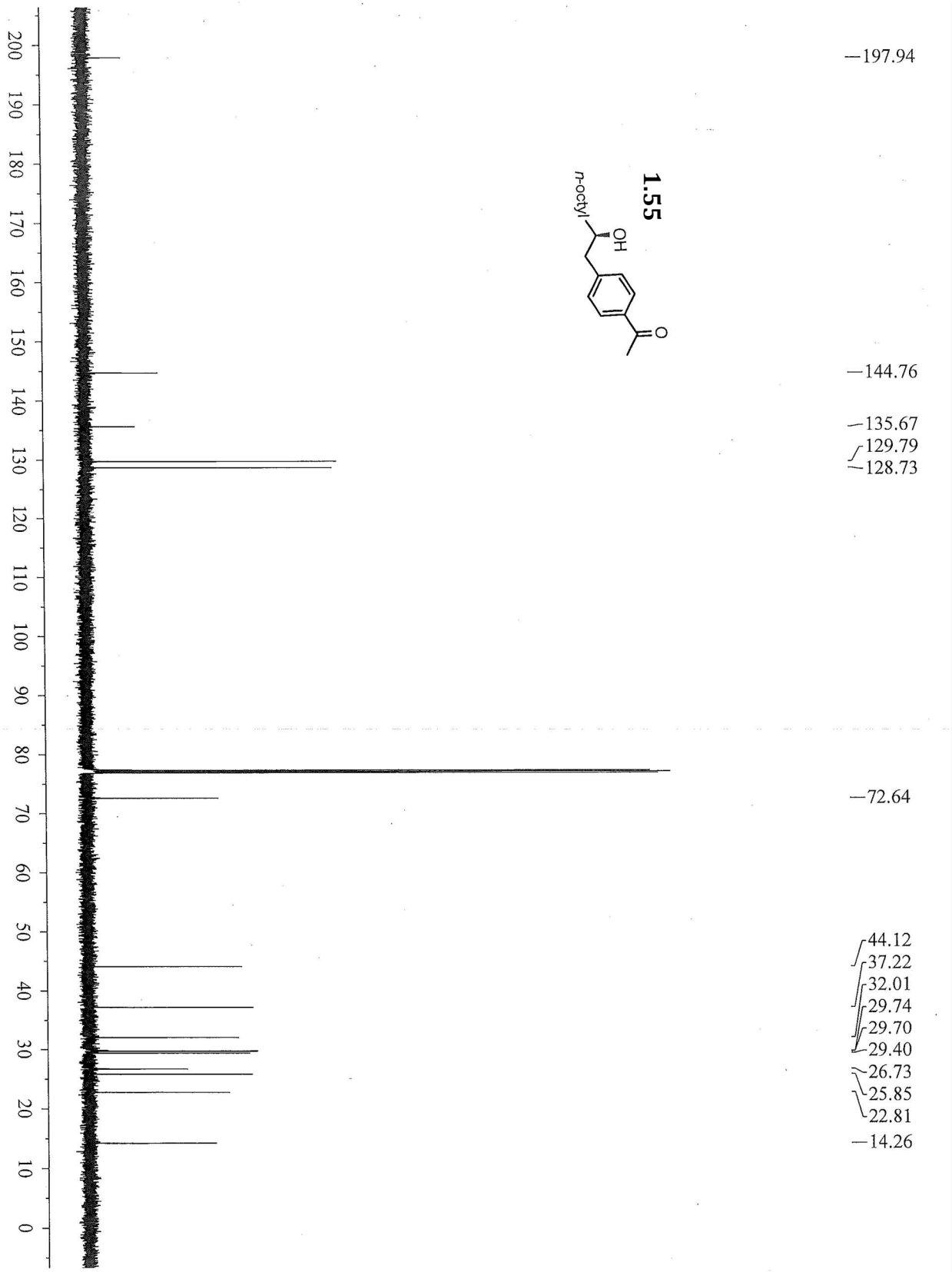

n-octyl
OH
S
1.60
0.91
0.98
1.95
0.88
1.00
1.03
1.03
1.14
14.80
2.99
7.79
7.77
7.71
7.69
7.33
7.31
7.29
7.28
7.26
7.10
3.92
3.92
3.12
3.11
3.09
3.08
2.99
2.98
2.97
2.95
1.76
1.75
1.57
1.56
1.32
1.31
1.30
1.28
1.27
1.26
0.90
0.89
0.87

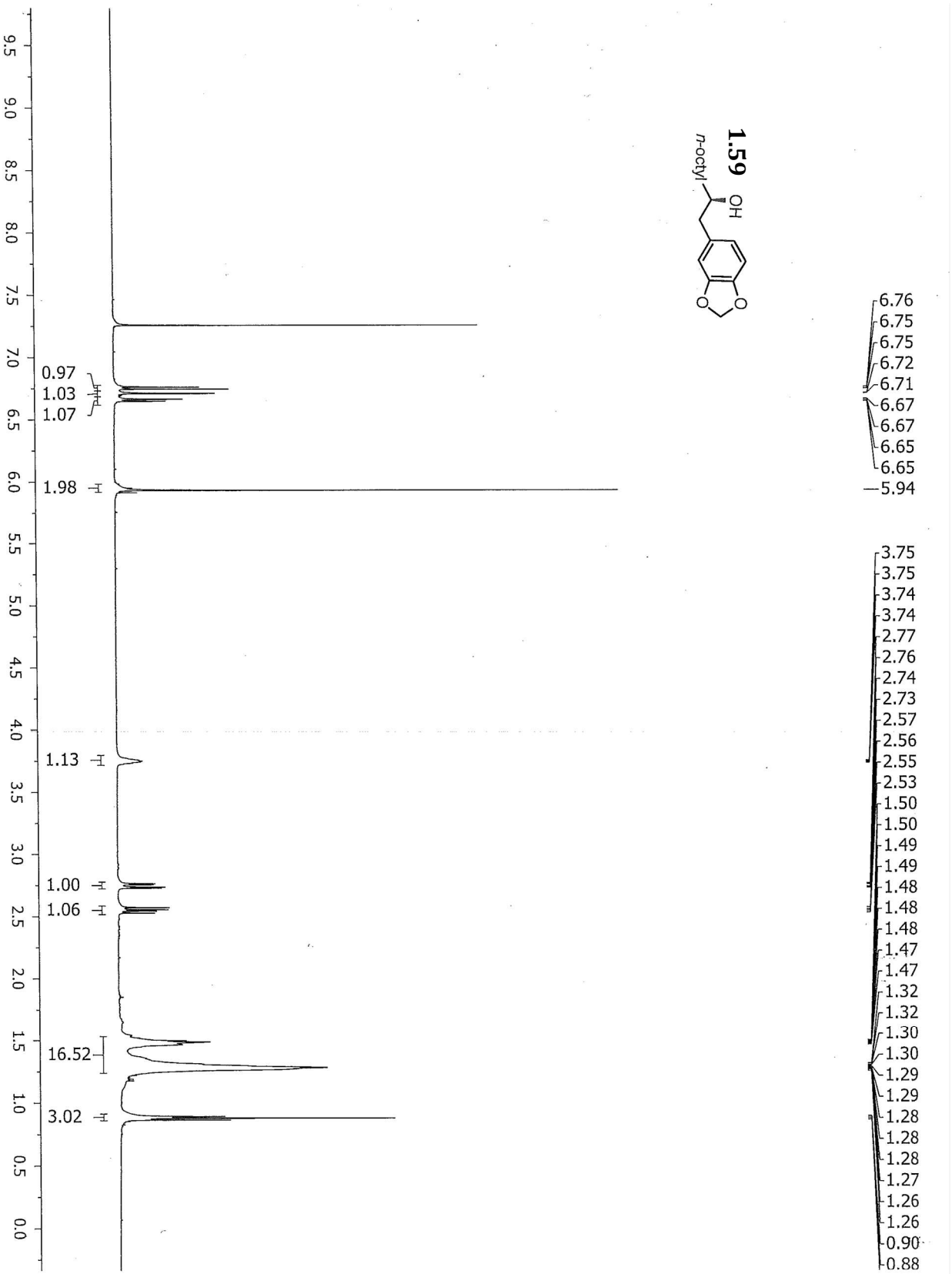

n-octyl
OH
S
1.60
142.03
140.18
139.92
124.37
123.89
123.04
122.75
122.27
72.27
39.07
36.86
32.02
29.75
29.71
29.40
25.87
22.82
14.25
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

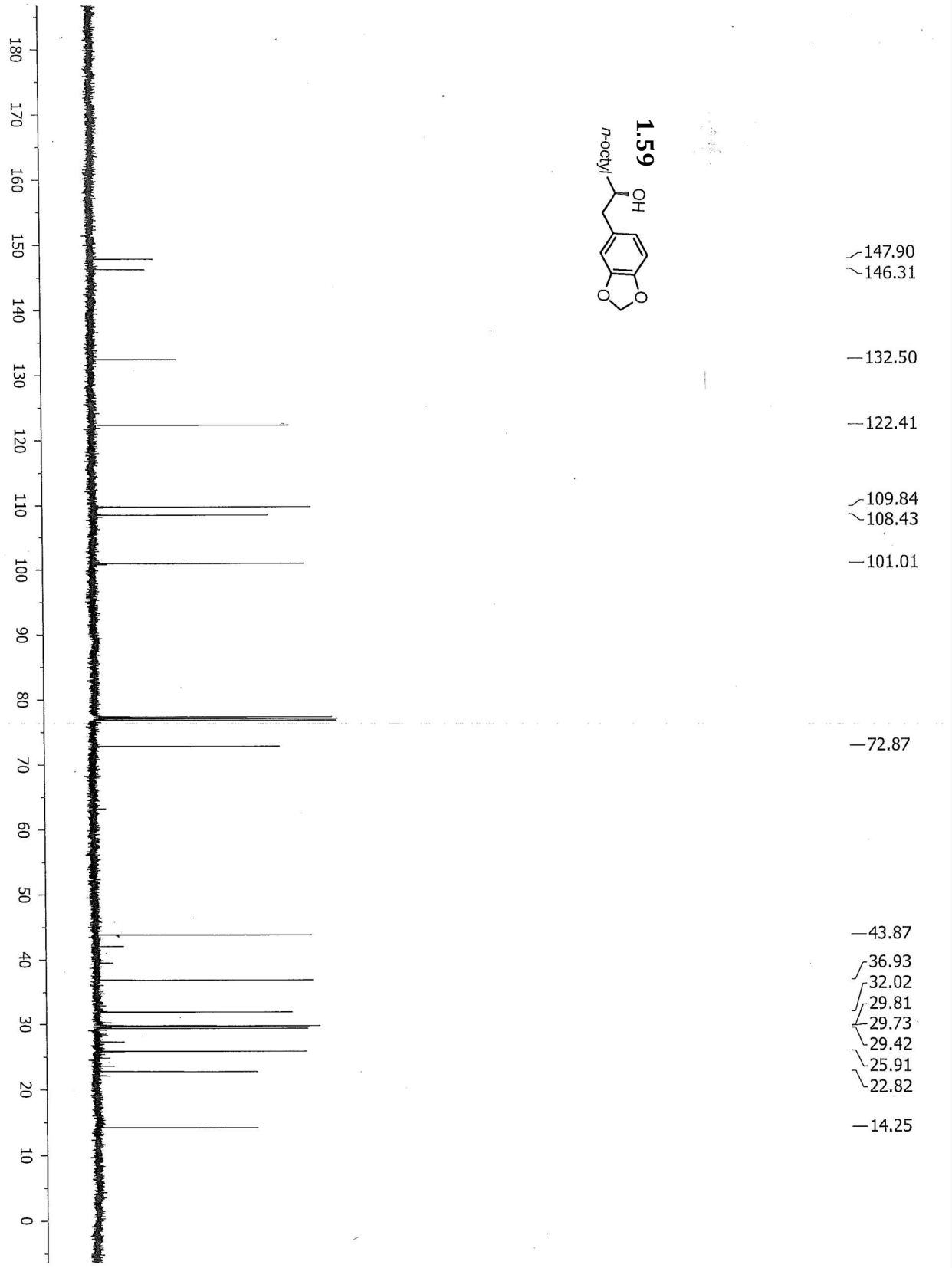

n-octyl
OH
Boc
N
1.58
8.08
8.07
7.59
7.58
7.40
7.40
7.18
7.17
7.16
7.16
6.53
6.53
6.52
6.52
3.85
3.84
2.95
2.94
2.92
2.91
2.75
2.73
2.72
2.70
1.67
1.53
1.30
1.29
1.28
1.27
0.90
0.89
0.88
0.87
1.03
1.07
1.05
1.08
1.11
1.00
1.00
1.00
9.18
15.56
3.26

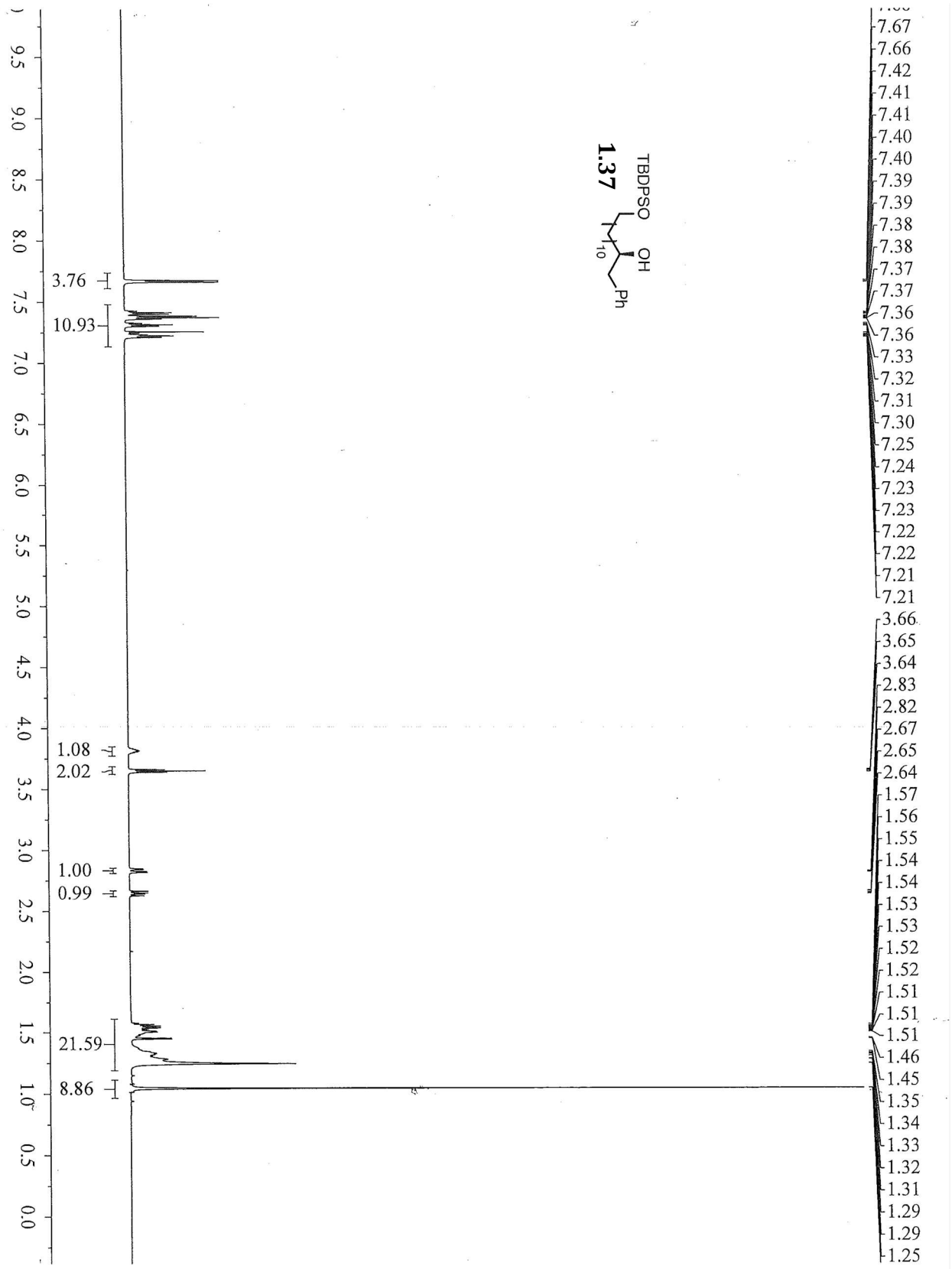

n-octyl
OH
Boc
N
1.58
149.90
134.17
132.95
131.07
126.33
125.83
121.62
115.30
107.23
83.77
73.10
44.08
36.94
32.03
29.84
29.75
29.43
28.36
25.96
22.82
14.26
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

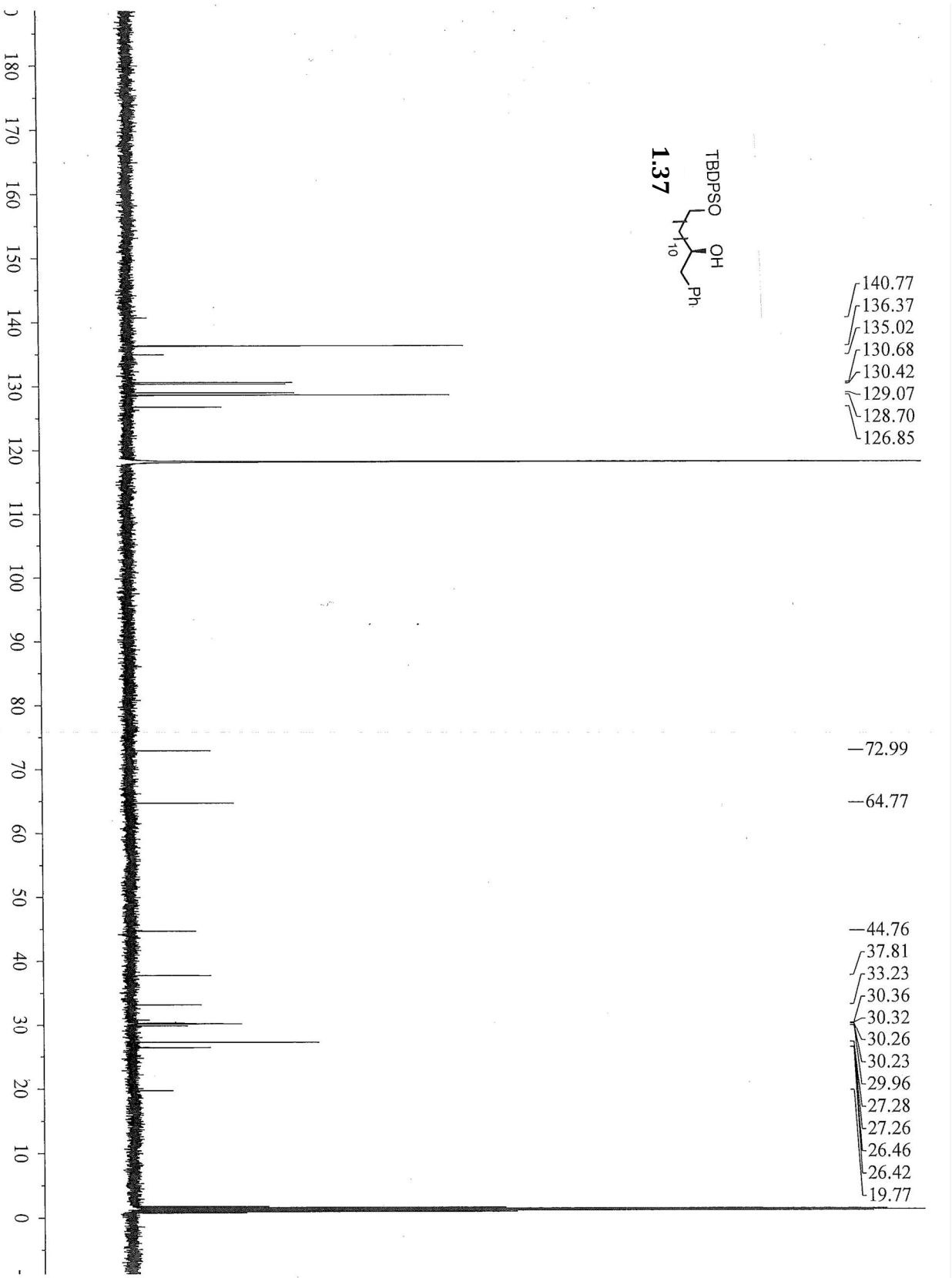

1.55
n-octyl
OH
O
1.90
1.89
1.11
1.00
0.98
2.78
14.64
3.14
0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
7.90
7.33
7.31
3.86
3.85
3.85
2.89
2.88
2.87
2.86
2.75
2.74
2.73
2.72
2.59
2.59
1.53
1.52
1.52
1.52
1.51
1.51
1.50
1.50
1.50
1.49
1.48
1.48
1.47
1.47
1.47
1.46
1.44
1.44
1.44
1.37
1.37
1.36
1.35
1.35
1.34
1.34
1.32
1.31
1.31
1.30
1.30
1.29
1.28
1.27
1.27
1.27
1.26
1.25
1.25
0.89
0.88

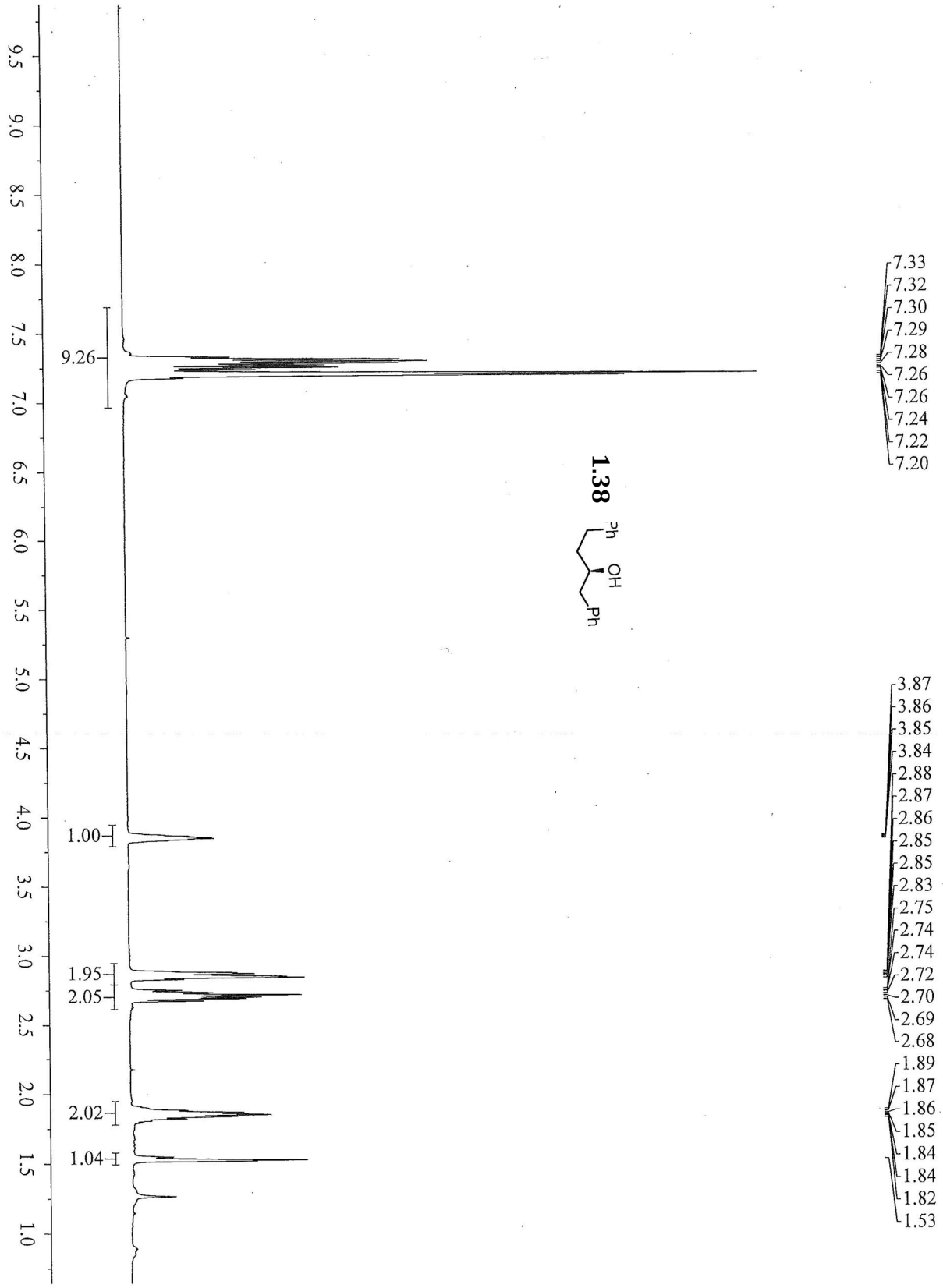

1.55
n-octyl
OH
O
197.94
144.76
135.67
129.79
128.73
72.64
44.12
37.22
32.01
29.74
29.70
29.40
26.73
25.85
22.81
14.26
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

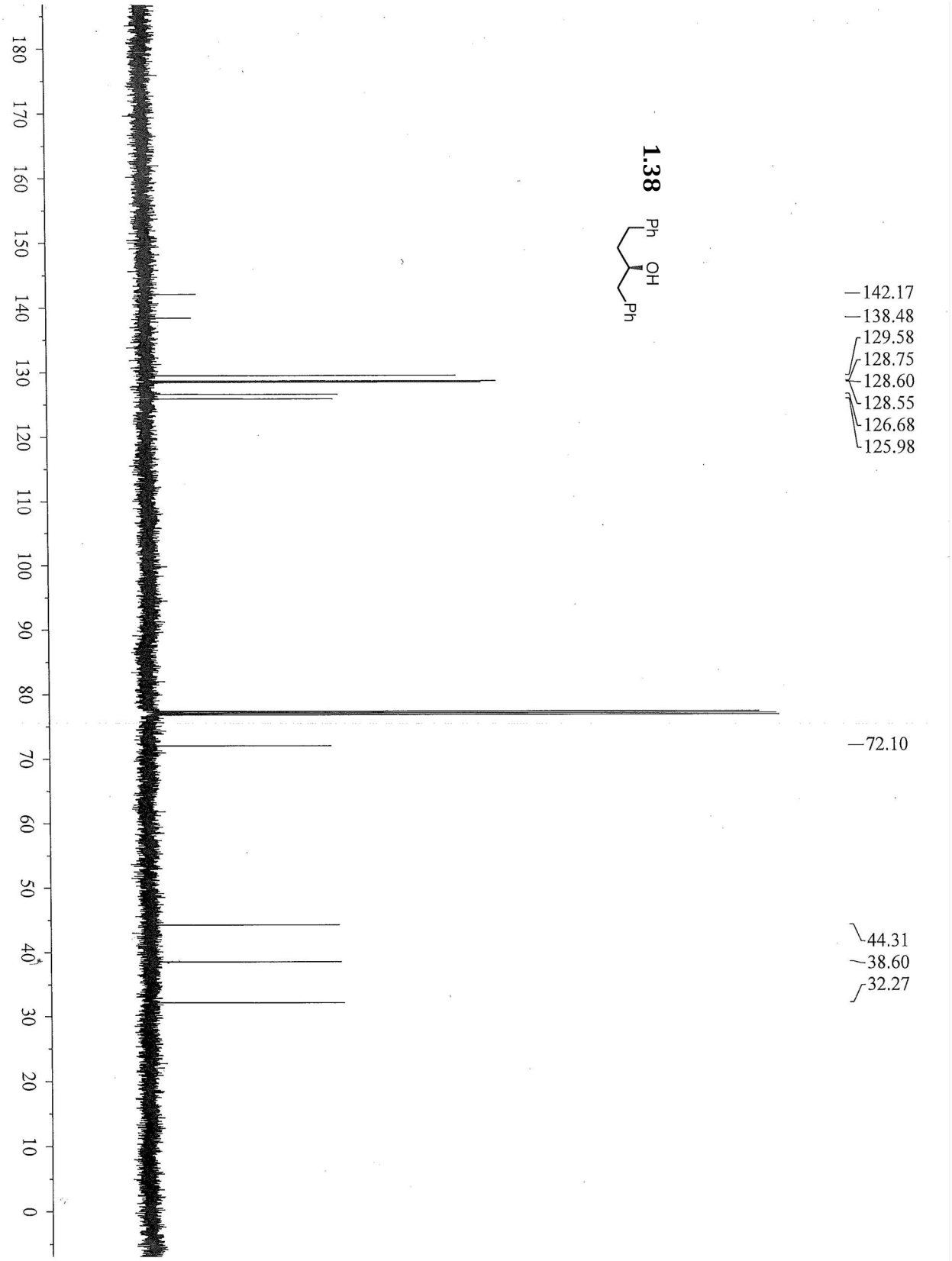

1.59
n-octyl
OH
O
O
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.97
1.03
1.07
1.98
1.13
1.00
1.06
16.52
3.02
6.76
6.75
6.75
6.72
6.71
6.67
6.67
6.65
6.65
5.94
3.75
3.75
3.74
3.74
2.77
2.76
2.74
2.73
2.57
2.56
2.55
2.53
1.50
1.50
1.49
1.49
1.48
1.48
1.48
1.47
1.47
1.32
1.32
1.30
1.30
1.29
1.29
1.28
1.28
1.28
1.27
1.26
1.26
0.90
0.88

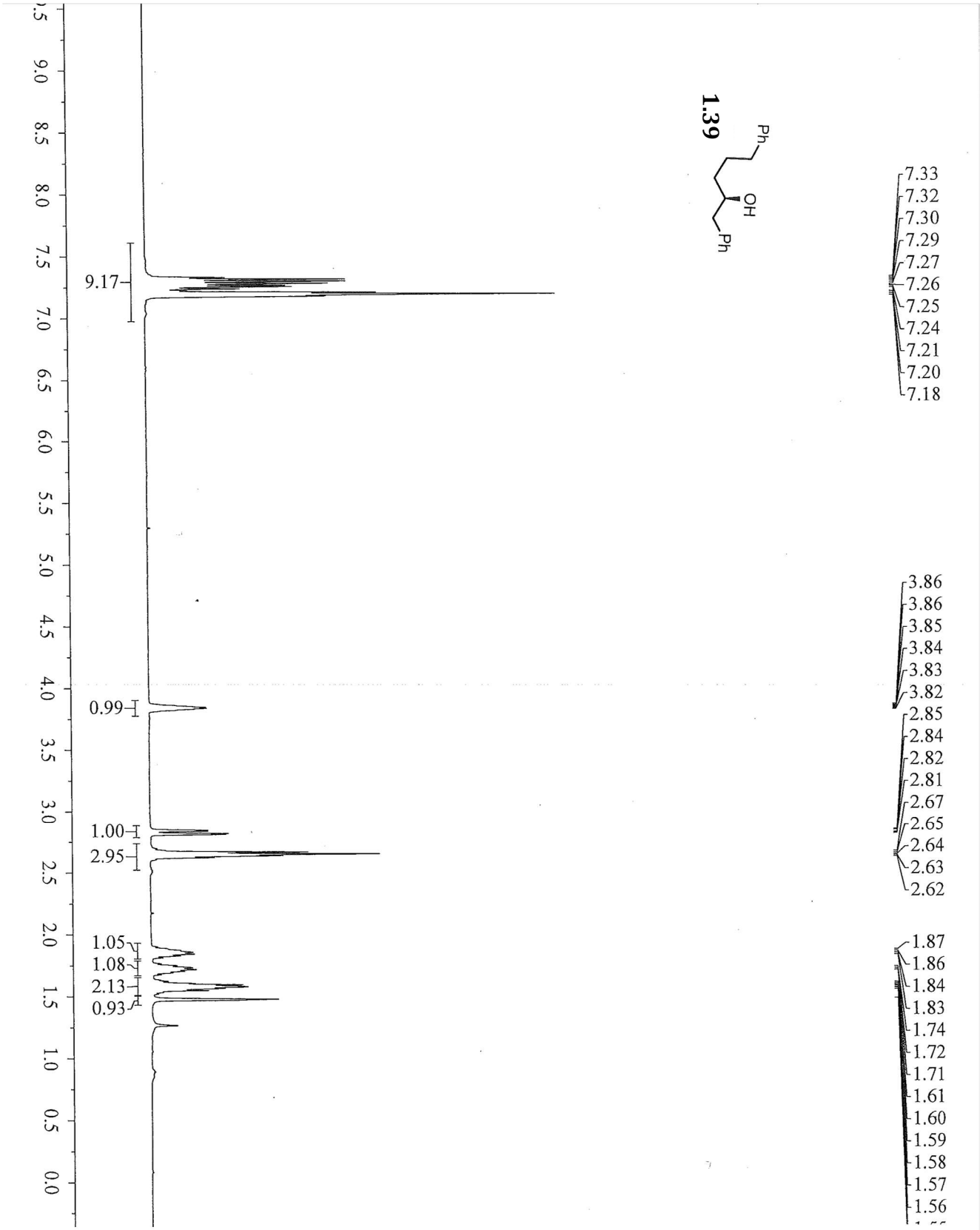

1.59
n-octyl
OH
O
O
147.90
146.31
132.50
122.41
109.84
108.43
101.01
72.87
43.87
36.93
32.02
29.81
29.73
29.42
25.91
22.82
14.25
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

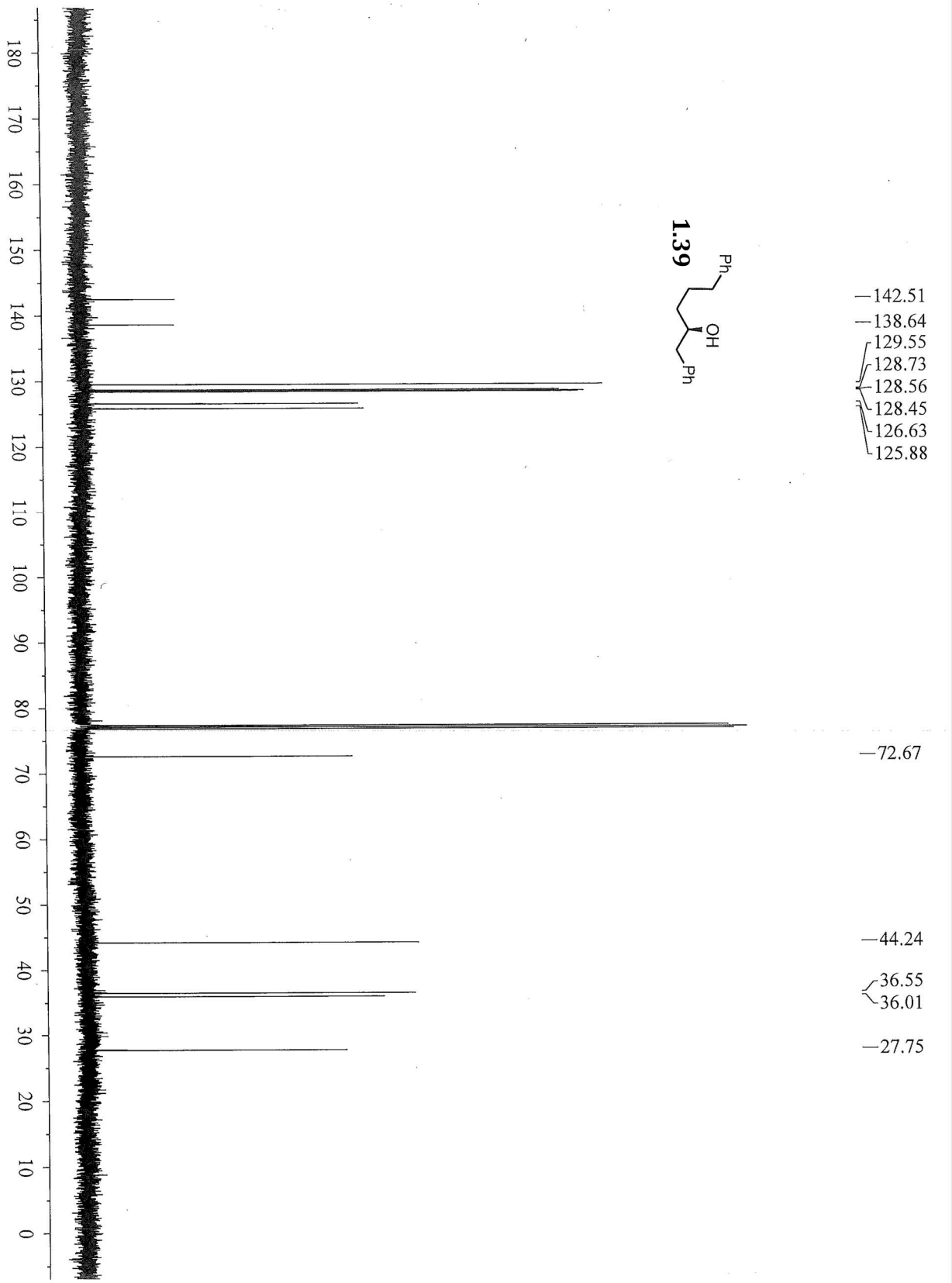

TBDPSO
OH
1.37
10
Ph
3.76
10.93
1.08
2.02
1.00
0.99
21.59
8.86
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
7.67
7.66
7.42
7.41
7.41
7.40
7.40
7.39
7.39
7.38
7.38
7.37
7.37
7.36
7.36
7.33
7.32
7.31
7.30
7.25
7.24
7.23
7.23
7.22
7.22
7.21
7.21
3.66
3.65
3.64
2.83
2.82
2.67
2.65
2.64
1.57
1.56
1.55
1.54
1.54
1.53
1.53
1.52
1.52
1.51
1.51
1.51
1.46
1.45
1.35
1.34
1.33
1.32
1.31
1.29
1.29
1.25

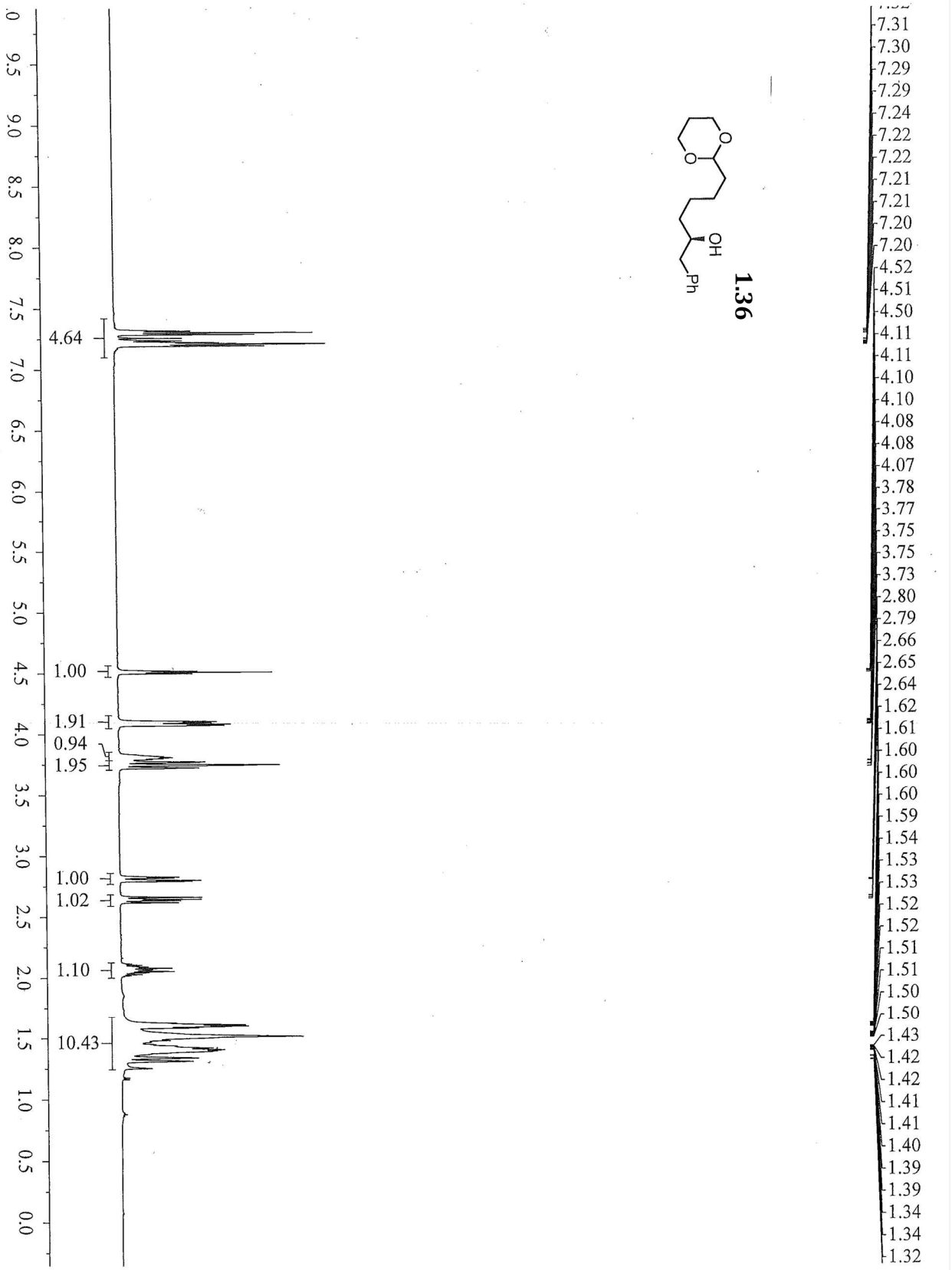

1.37
TBDPSO
OH
10
Ph
140.77
136.37
135.02
130.68
130.42
129.07
128.70
126.85
72.99
64.77
44.76
37.81
33.23
30.36
30.32
30.26
30.23
29.96
27.28
27.26
26.46
26.42
19.77

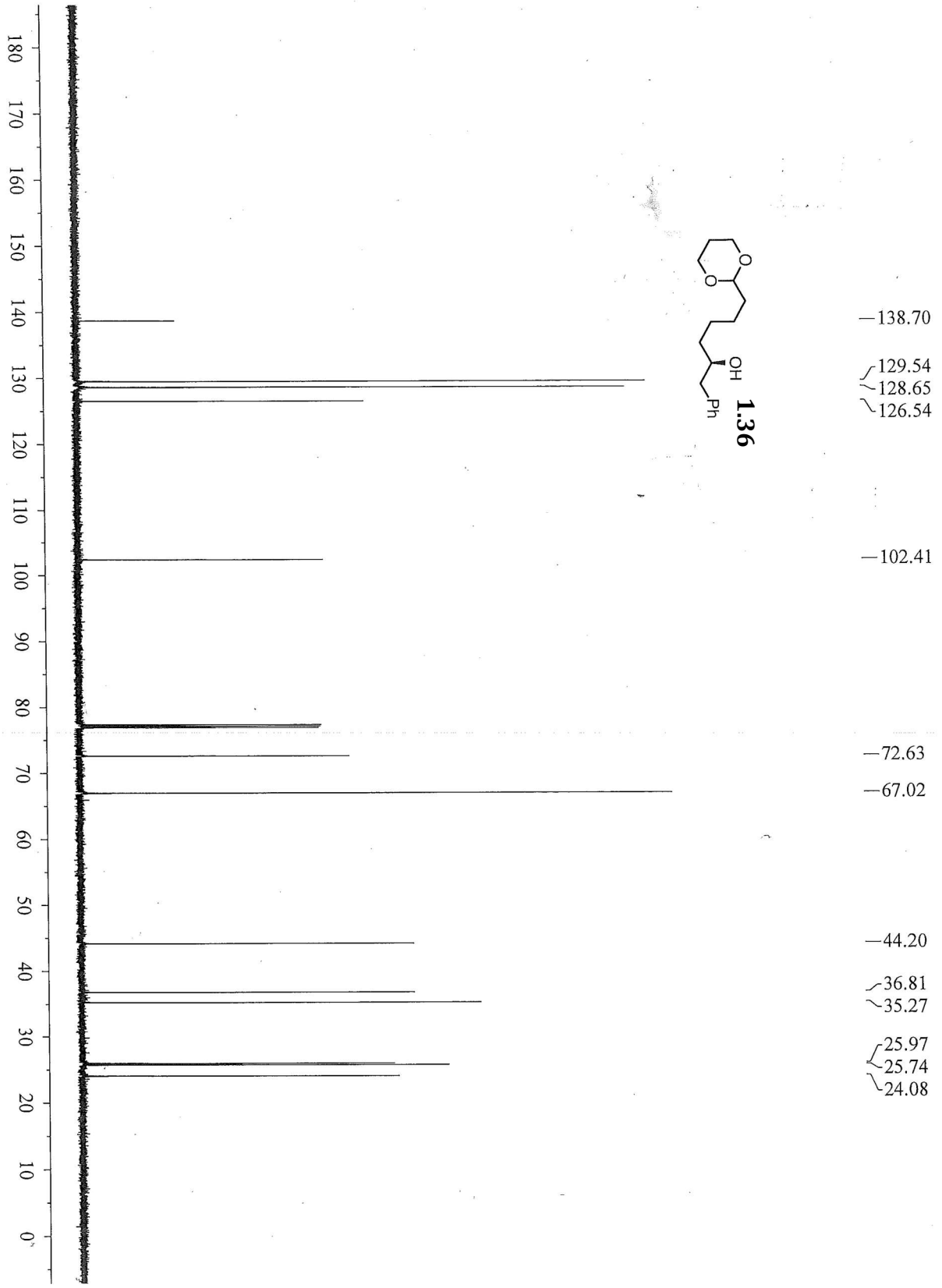

1.38
Ph
OH
Ph
9.26
1.00
1.95
2.05
2.02
1.04
7.33
7.32
7.30
7.29
7.28
7.26
7.26
7.24
7.22
7.20
3.87
3.86
3.85
3.84
2.88
2.87
2.86
2.85
2.85
2.83
2.75
2.74
2.74
2.72
2.70
2.69
2.68
1.89
1.87
1.86
1.85
1.84
1.84
1.82
1.53

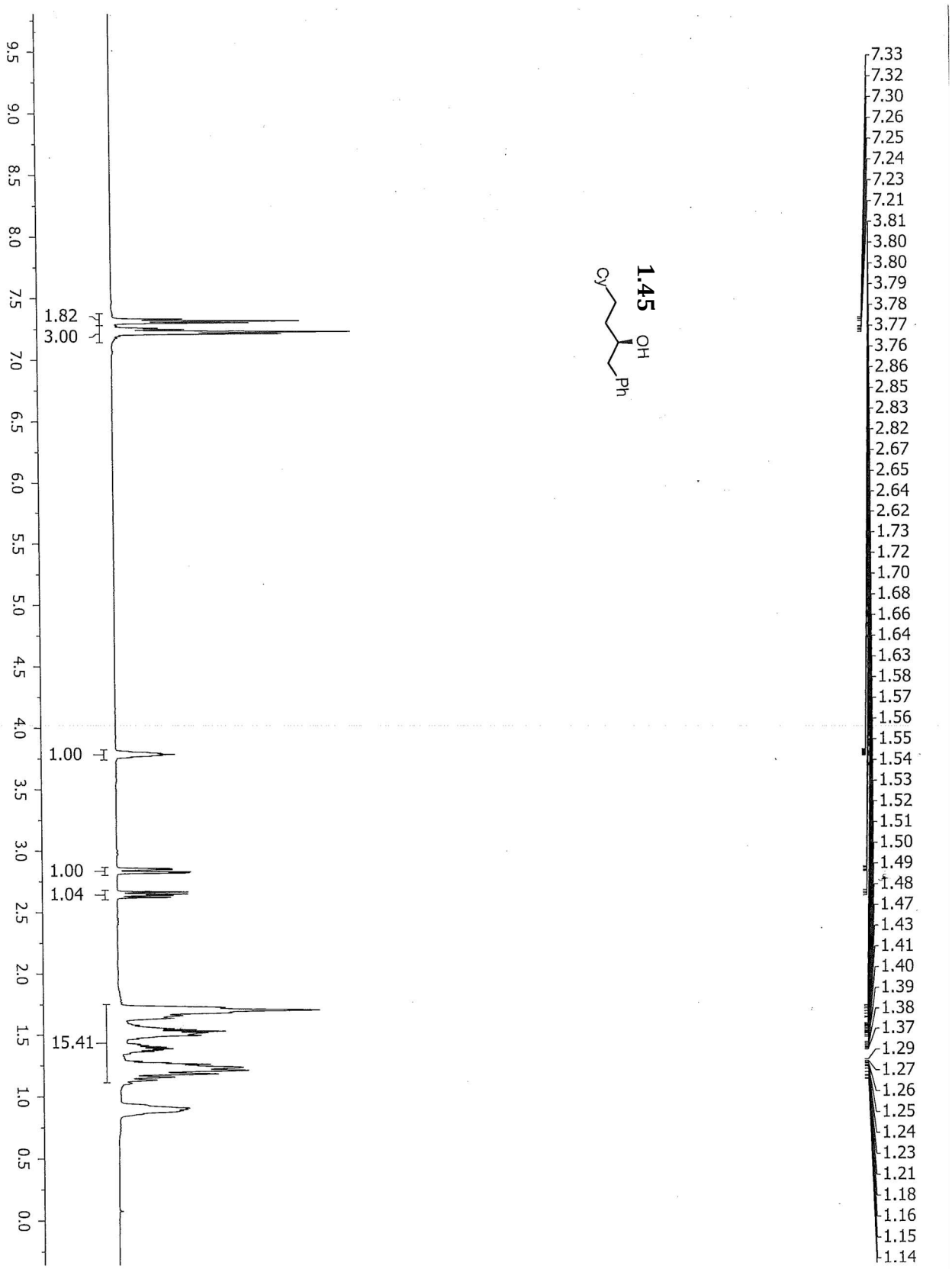

1.38
Ph
OH
Ph
142.17
138.48
129.58
128.75
128.60
128.55
126.68
125.98
72.10
44.31
38.60
32.27
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

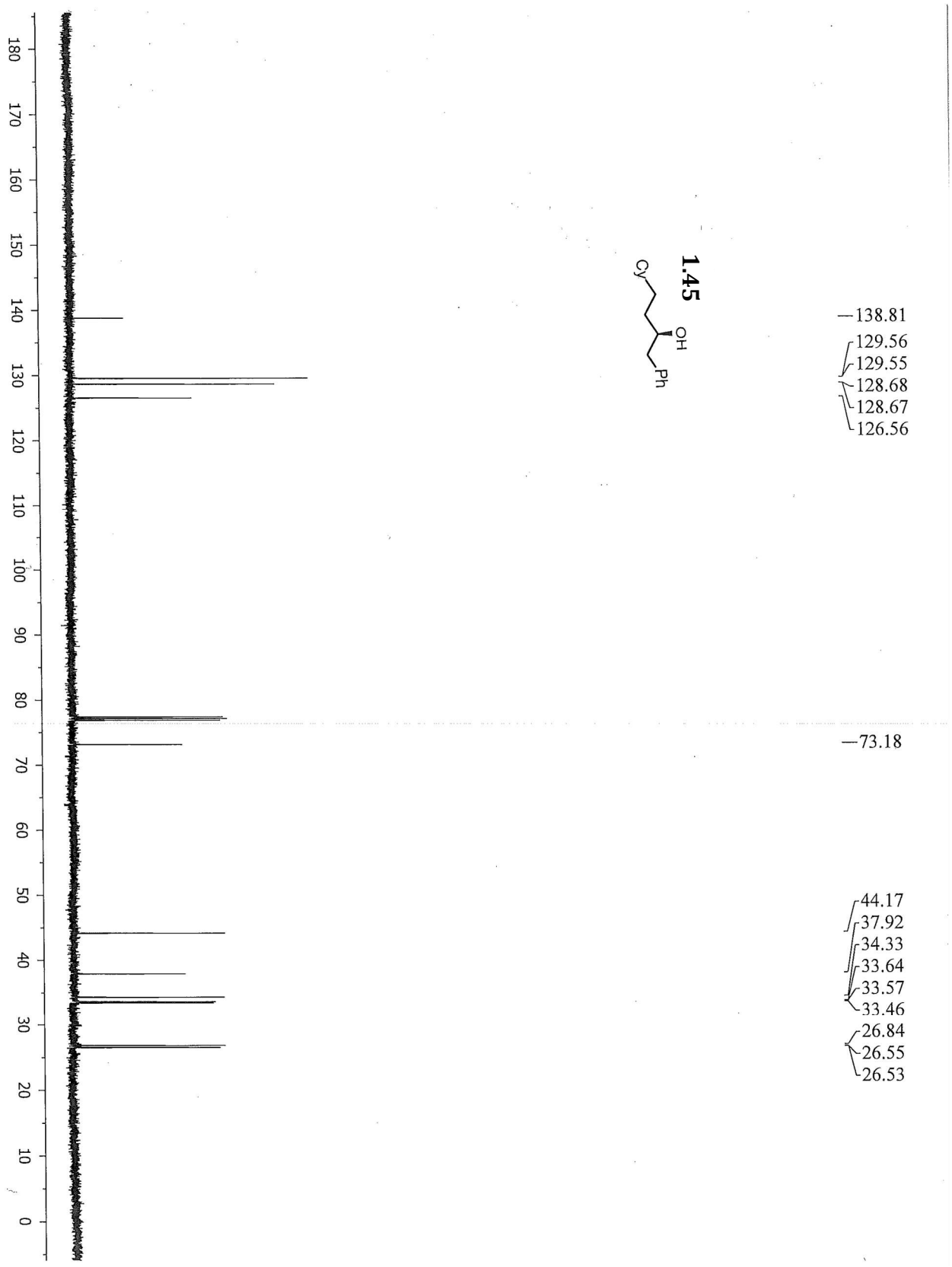

1.39
Ph
OH
Ph
9.17
0.99
1.00
2.95
1.05
1.08
2.13
0.93
7.33
7.32
7.30
7.29
7.27
7.26
7.25
7.24
7.21
7.20
7.18
3.86
3.86
3.85
3.84
3.83
3.82
2.85
2.84
2.82
2.81
2.67
2.65
2.64
2.63
2.62
1.87
1.86
1.84
1.83
1.74
1.72
1.71
1.61
1.60
1.59
1.58
1.57
1.56

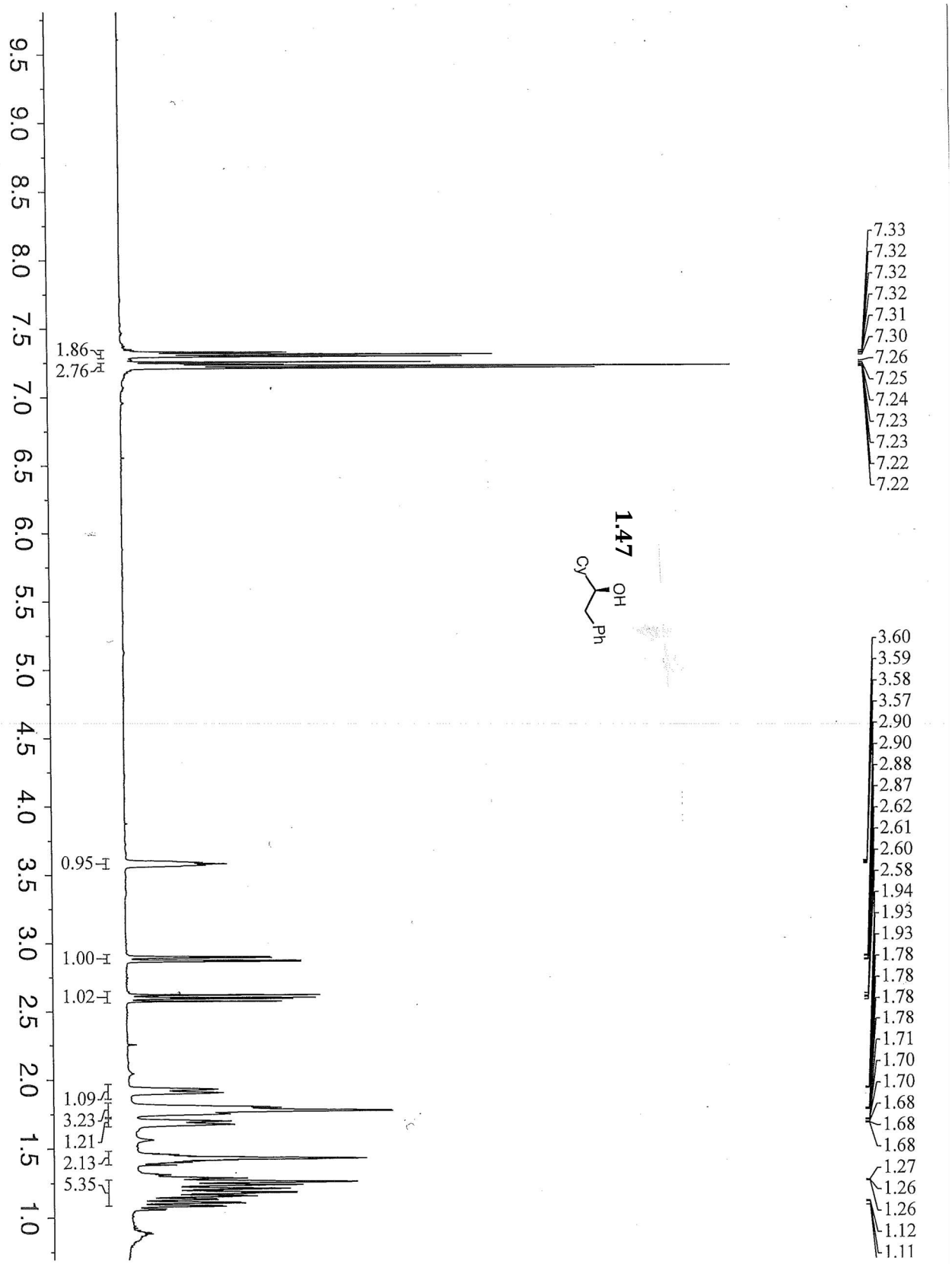

1.39
Ph
OH
Ph
142.51
138.64
129.55
128.73
128.56
128.45
126.63
125.88
72.67
44.24
36.55
36.01
27.75
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

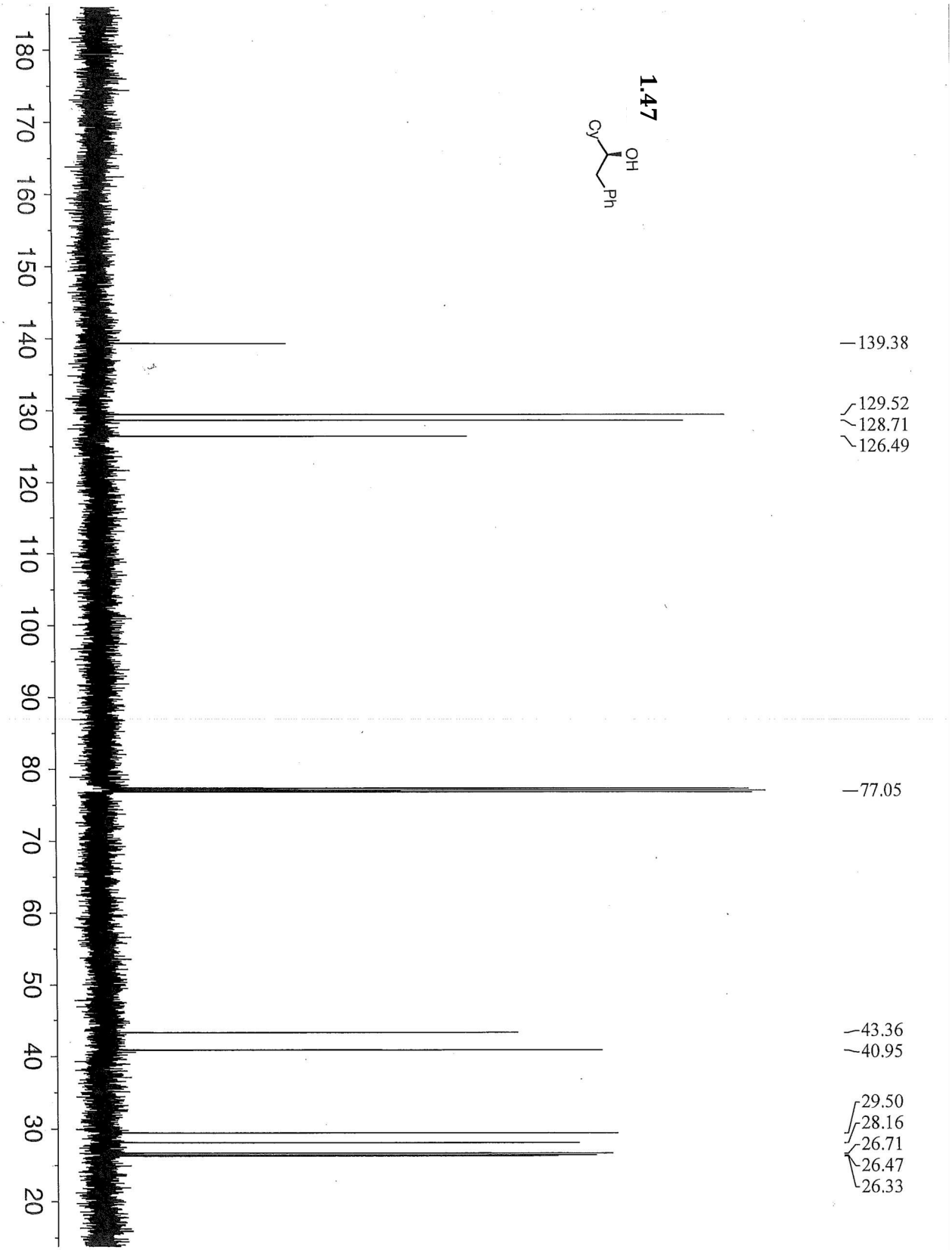

1.36
OH
Ph
4.64
1.00
1.91
0.94
1.95
1.00
1.02
1.10
10.43
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
7.31
7.30
7.29
7.29
7.24
7.22
7.22
7.21
7.21
7.20
7.20
4.52
4.51
4.50
4.11
4.11
4.10
4.10
4.08
4.08
4.07
3.78
3.77
3.75
3.75
3.73
2.80
2.79
2.66
2.65
2.64
1.62
1.61
1.60
1.60
1.60
1.59
1.54
1.53
1.53
1.52
1.52
1.51
1.51
1.50
1.50
1.43
1.42
1.42
1.41
1.41
1.40
1.39
1.39
1.34
1.34
1.32

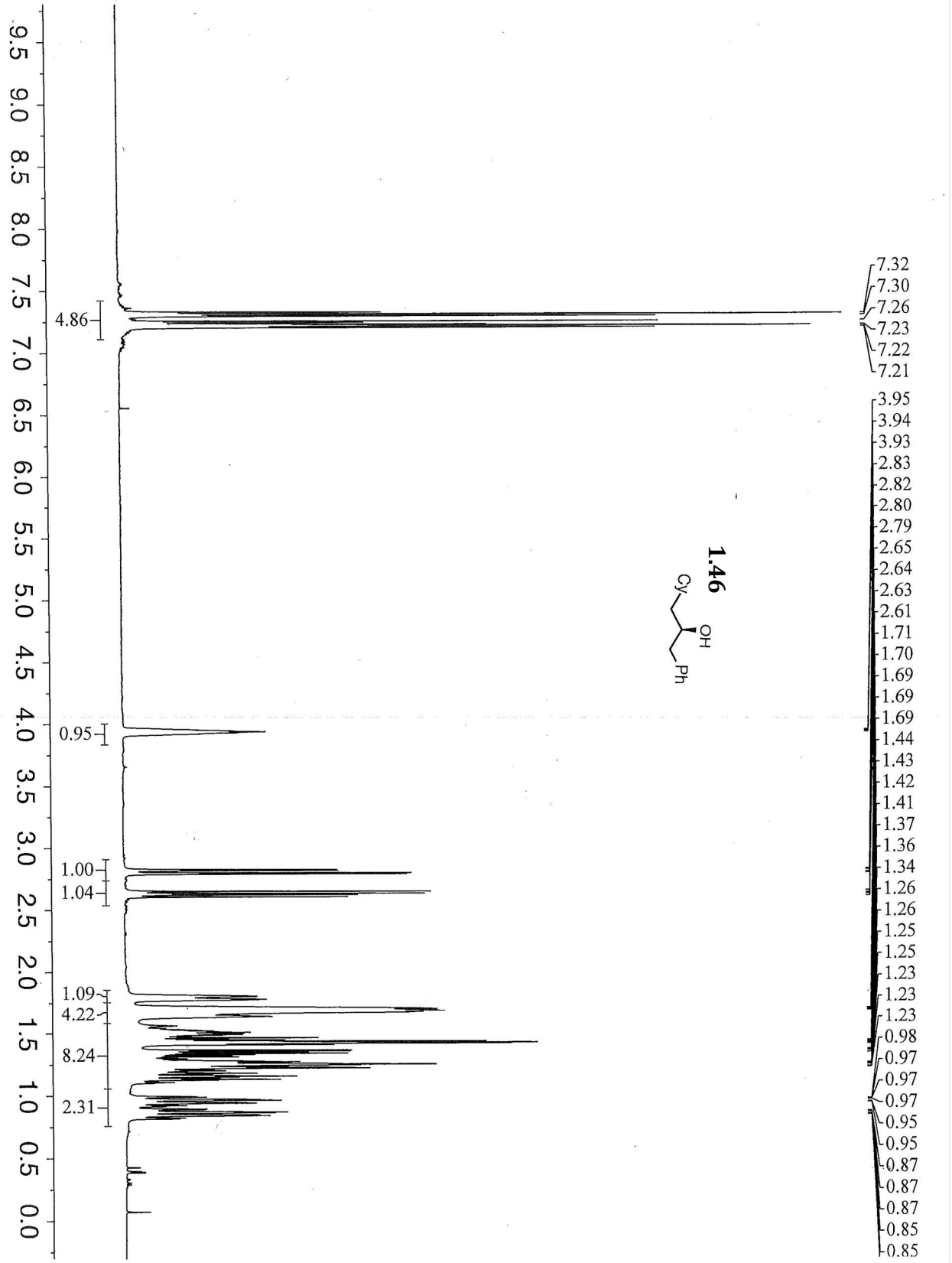

1.36
OH
Ph
O
O
138.70
129.54
128.65
126.54
102.41
72.63
67.02
44.20
36.81
35.27
25.97
25.74
24.08
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

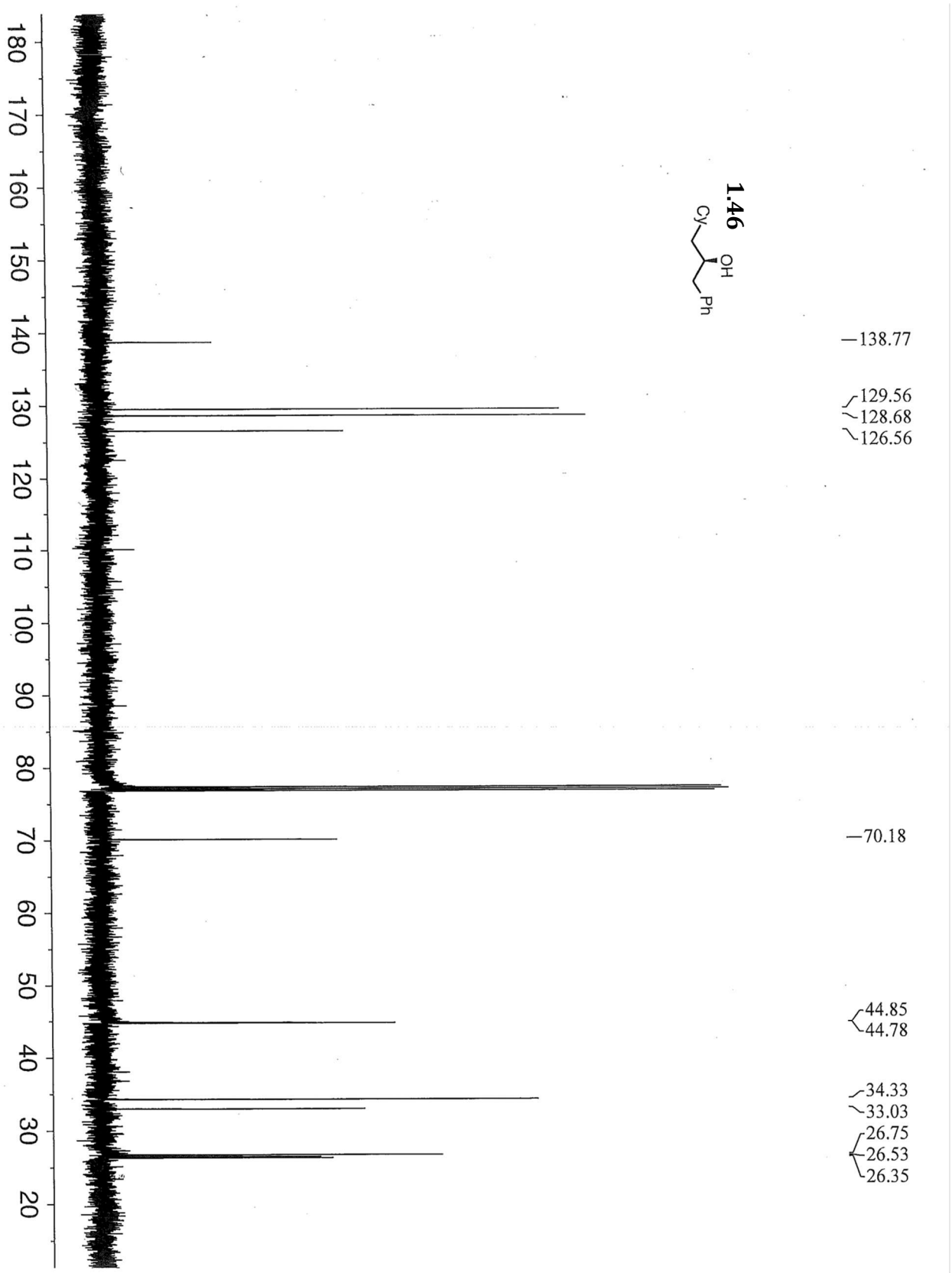

1.45
Cy
OH
Ph
1.82
3.00
1.00
1.00
1.04
15.41
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
7.33
7.32
7.30
7.26
7.25
7.24
7.23
7.21
3.81
3.80
3.80
3.79
3.78
3.77
3.76
2.86
2.85
2.83
2.82
2.67
2.65
2.64
2.62
1.73
1.72
1.70
1.68
1.66
1.64
1.63
1.58
1.57
1.56
1.55
1.54
1.53
1.52
1.51
1.50
1.49
1.48
1.47
1.43
1.41
1.40
1.39
1.38
1.37
1.29
1.27
1.26
1.25
1.24
1.23
1.21
1.18
1.16
1.15
1.14

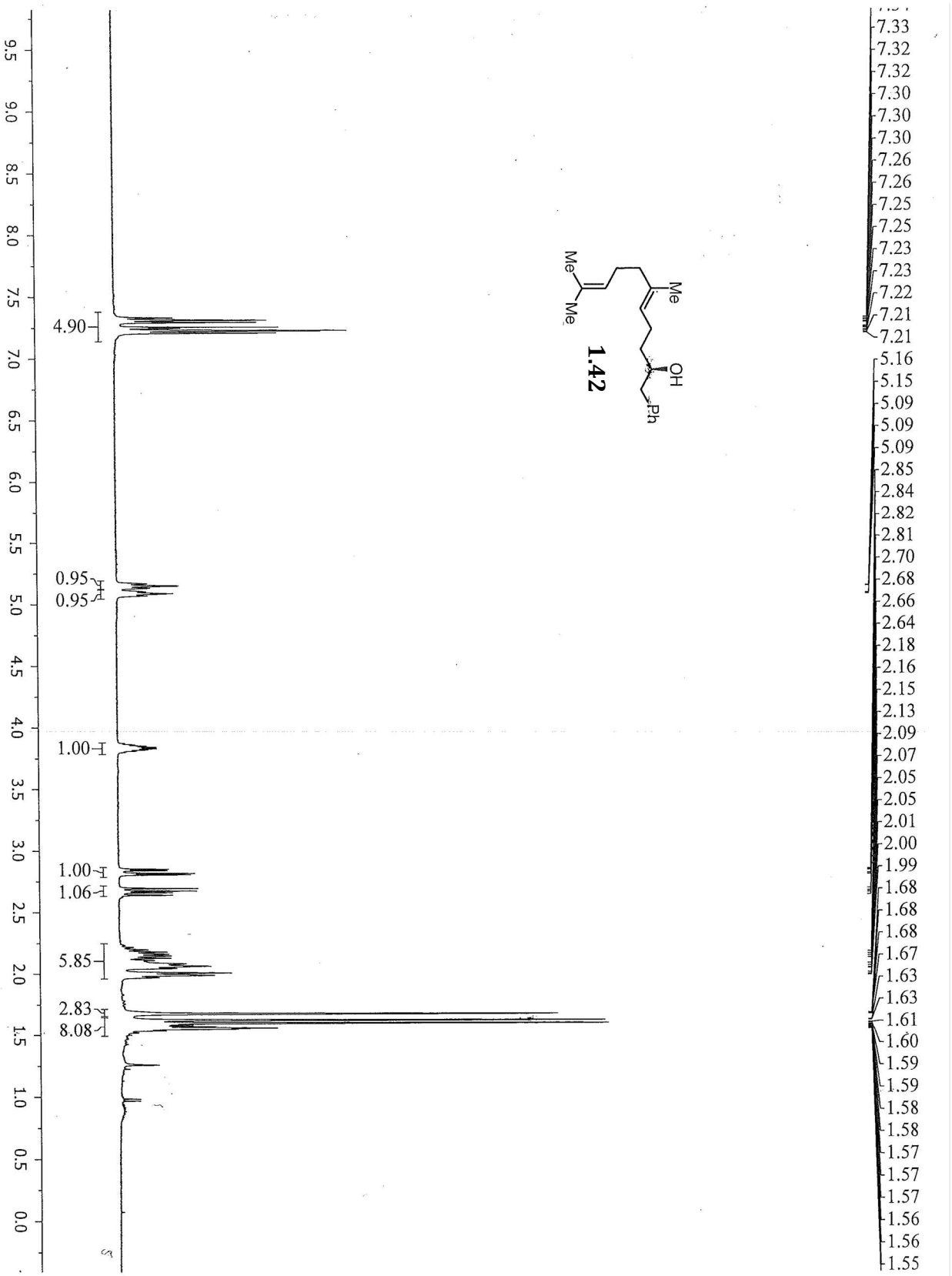

1.45
Cy
OH
Ph
138.81
129.56
129.55
128.68
128.67
126.56
73.18
44.17
37.92
34.33
33.64
33.57
33.46
26.84
26.55
26.53
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

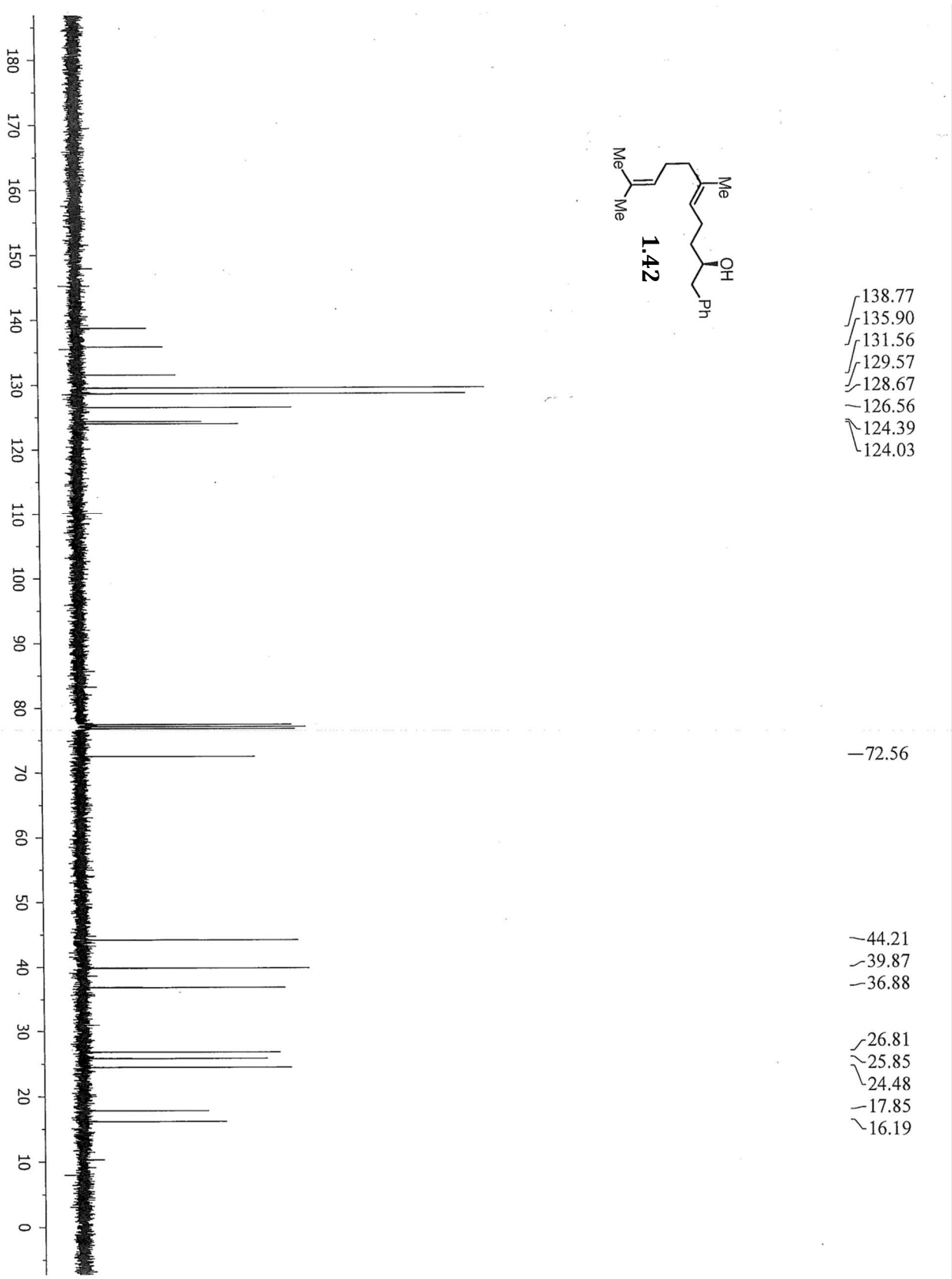

1.47
Cy
OH
Ph
7.33
7.32
7.32
7.32
7.31
7.30
7.26
7.25
7.24
7.23
7.23
7.22
7.22
3.60
3.59
3.58
3.57
2.90
2.90
2.88
2.87
2.62
2.61
2.60
2.58
1.94
1.93
1.93
1.78
1.78
1.78
1.78
1.71
1.70
1.70
1.68
1.68
1.68
1.27
1.26
1.26
1.12
1.11
1.86
2.76
0.95
1.00
1.02
1.09
3.23
1.21
2.13
5.35
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

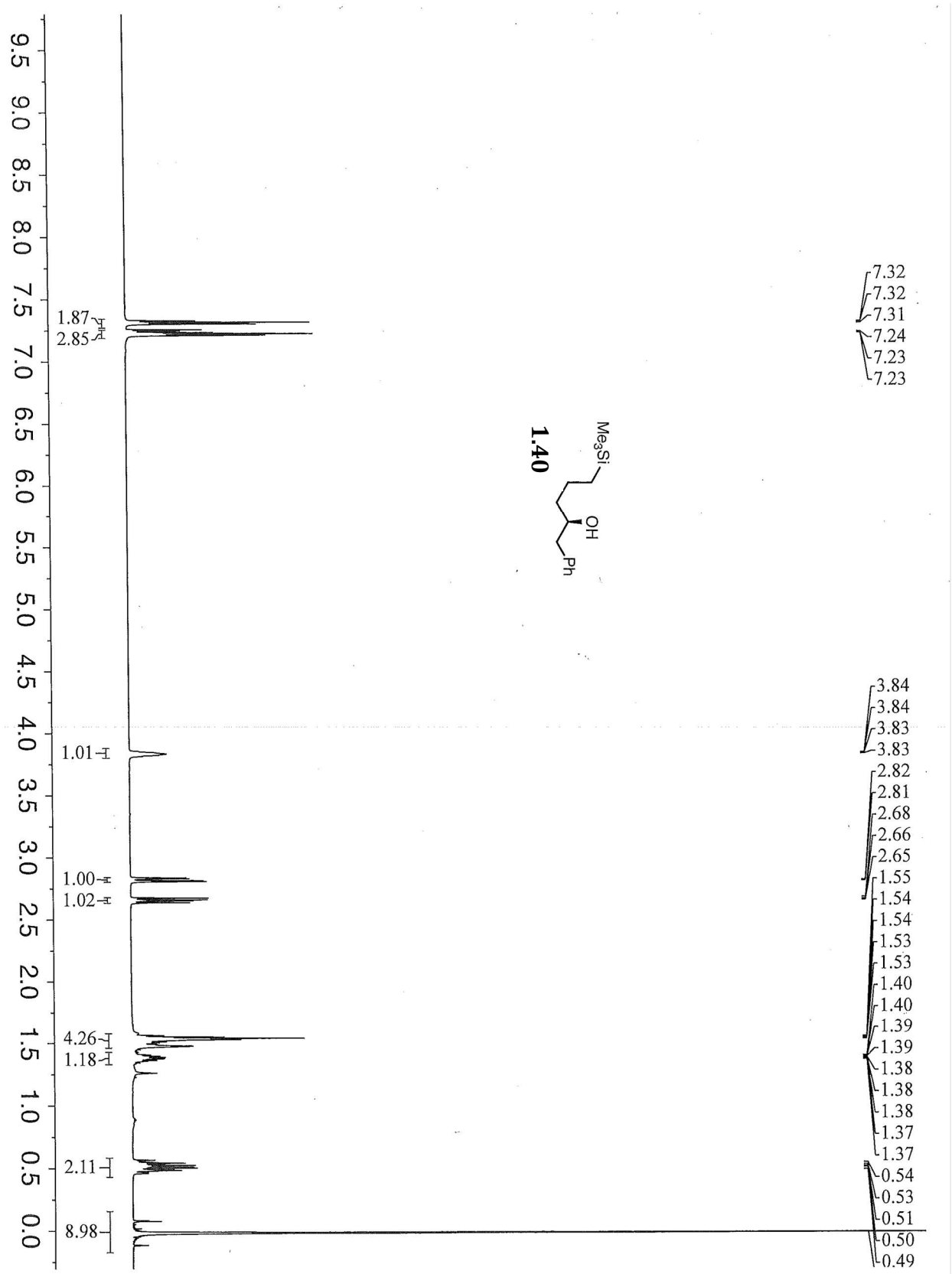

1.47
Cy
OH
Ph
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
139.38
129.52
128.71
126.49
77.05
43.36
40.95
29.50
28.16
26.71
26.47
26.33

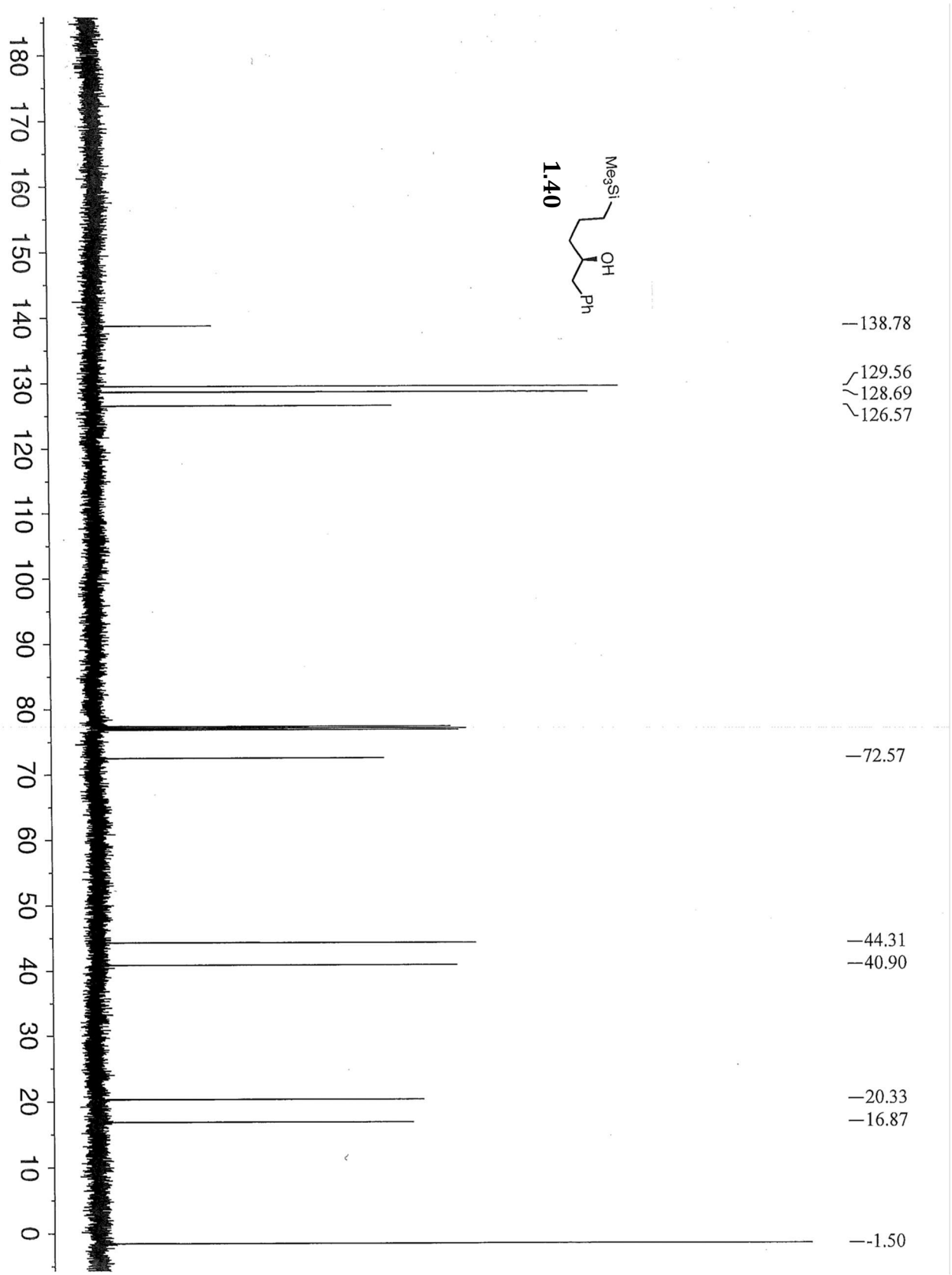

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
4.86
0.95
1.00
1.04
1.09
4.22
8.24
2.31
1.46
Cy
OH
Ph
7.32
7.30
7.26
7.23
7.22
7.21
3.95
3.94
3.93
2.83
2.82
2.80
2.79
2.65
2.64
2.63
2.61
1.71
1.70
1.69
1.69
1.69
1.44
1.43
1.42
1.41
1.37
1.36
1.34
1.26
1.26
1.25
1.25
1.23
1.23
1.23
0.98
0.97
0.97
0.97
0.95
0.95
0.87
0.87
0.87
0.85
0.85

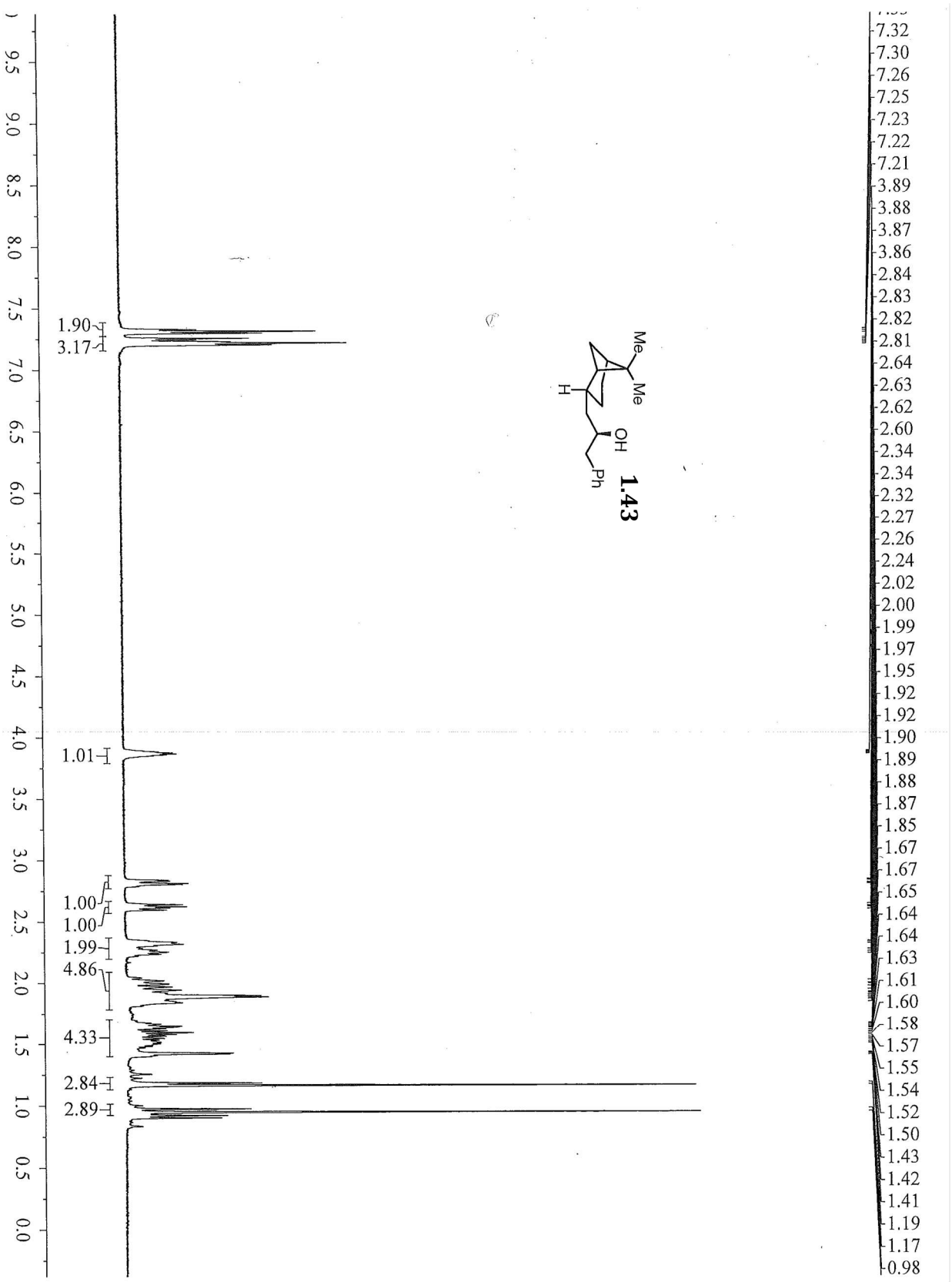

1.46
Cy
OH
Ph
138.77
129.56
128.68
126.56
70.18
44.85
44.78
34.33
33.03
26.75
26.53
26.35
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

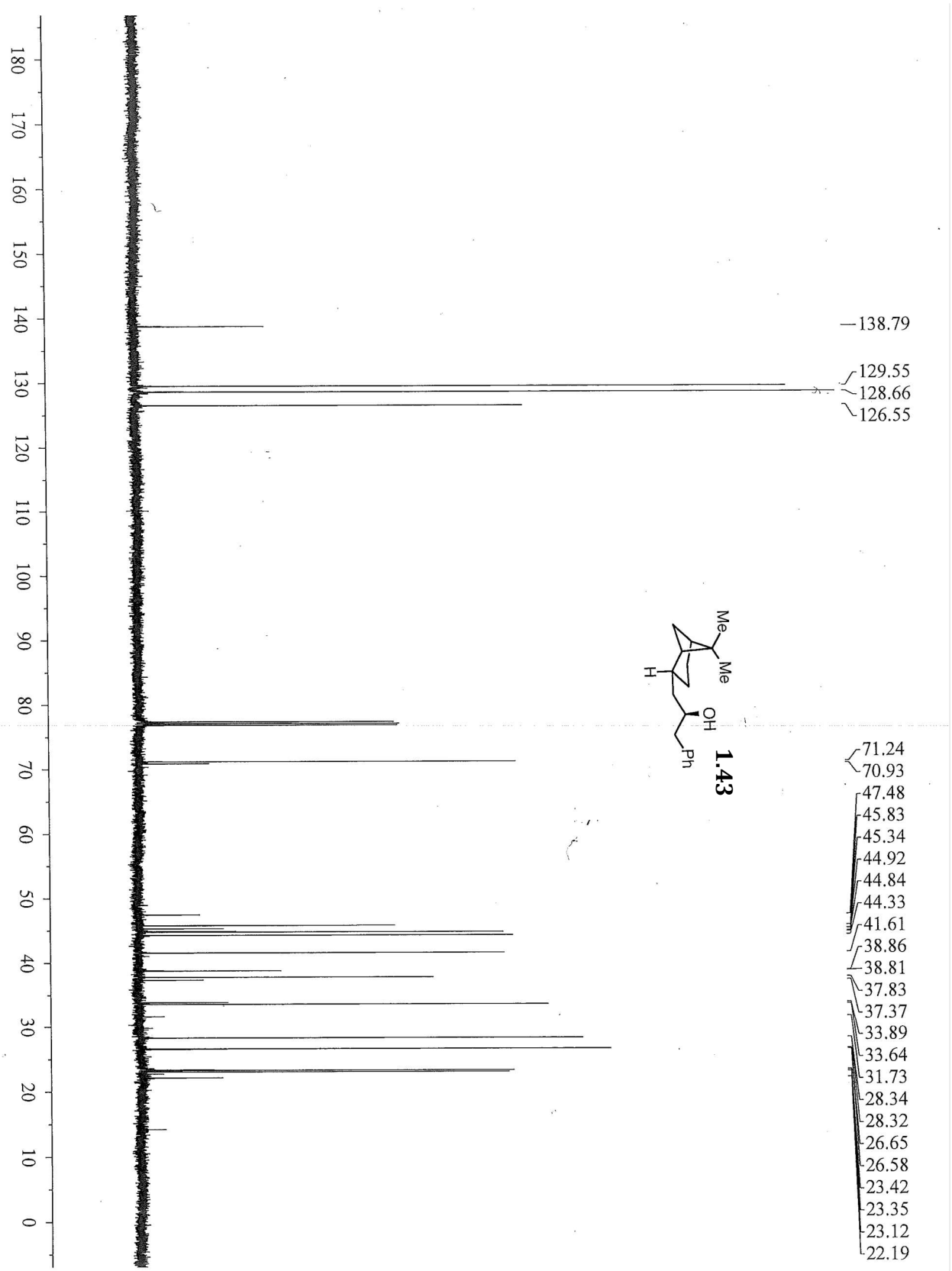

Me
Me
Me
OH
Ph
1.42
4.90
0.95
0.95
1.00
1.00
1.06
5.85
2.83
8.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
7.33
7.32
7.32
7.30
7.30
7.30
7.26
7.26
7.25
7.25
7.23
7.23
7.22
7.21
7.21
5.16
5.15
5.09
5.09
5.09
2.85
2.84
2.82
2.81
2.70
2.68
2.66
2.64
2.18
2.16
2.15
2.13
2.09
2.07
2.05
2.05
2.01
2.00
1.99
1.68
1.68
1.68
1.67
1.63
1.63
1.61
1.60
1.59
1.59
1.58
1.58
1.57
1.57
1.57
1.56
1.56
1.55

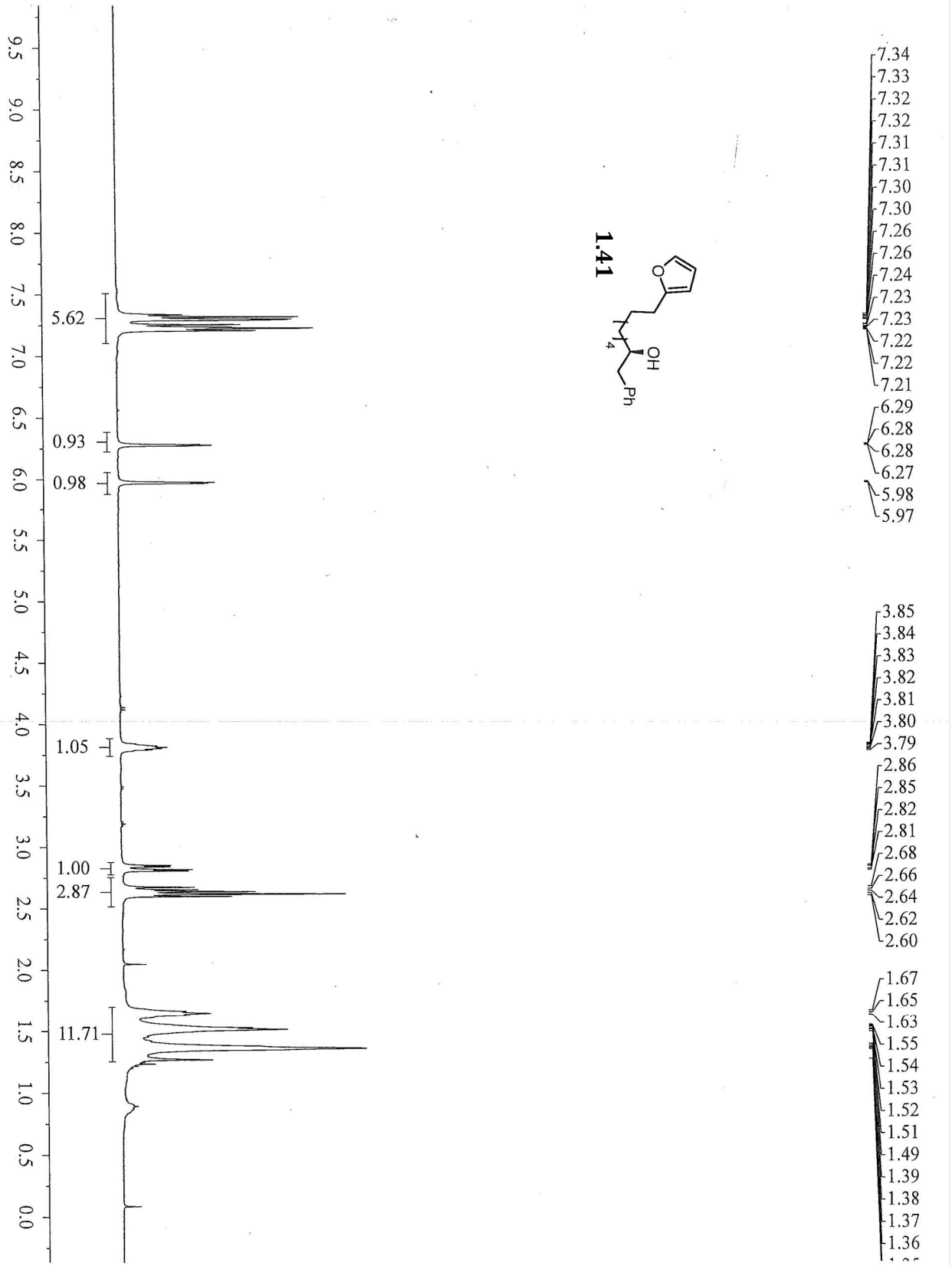

Me
Me
Me
OH
Ph
1.42
138.77
135.90
131.56
129.57
128.67
126.56
124.39
124.03
72.56
44.21
39.87
36.88
26.81
25.85
24.48
17.85
16.19
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

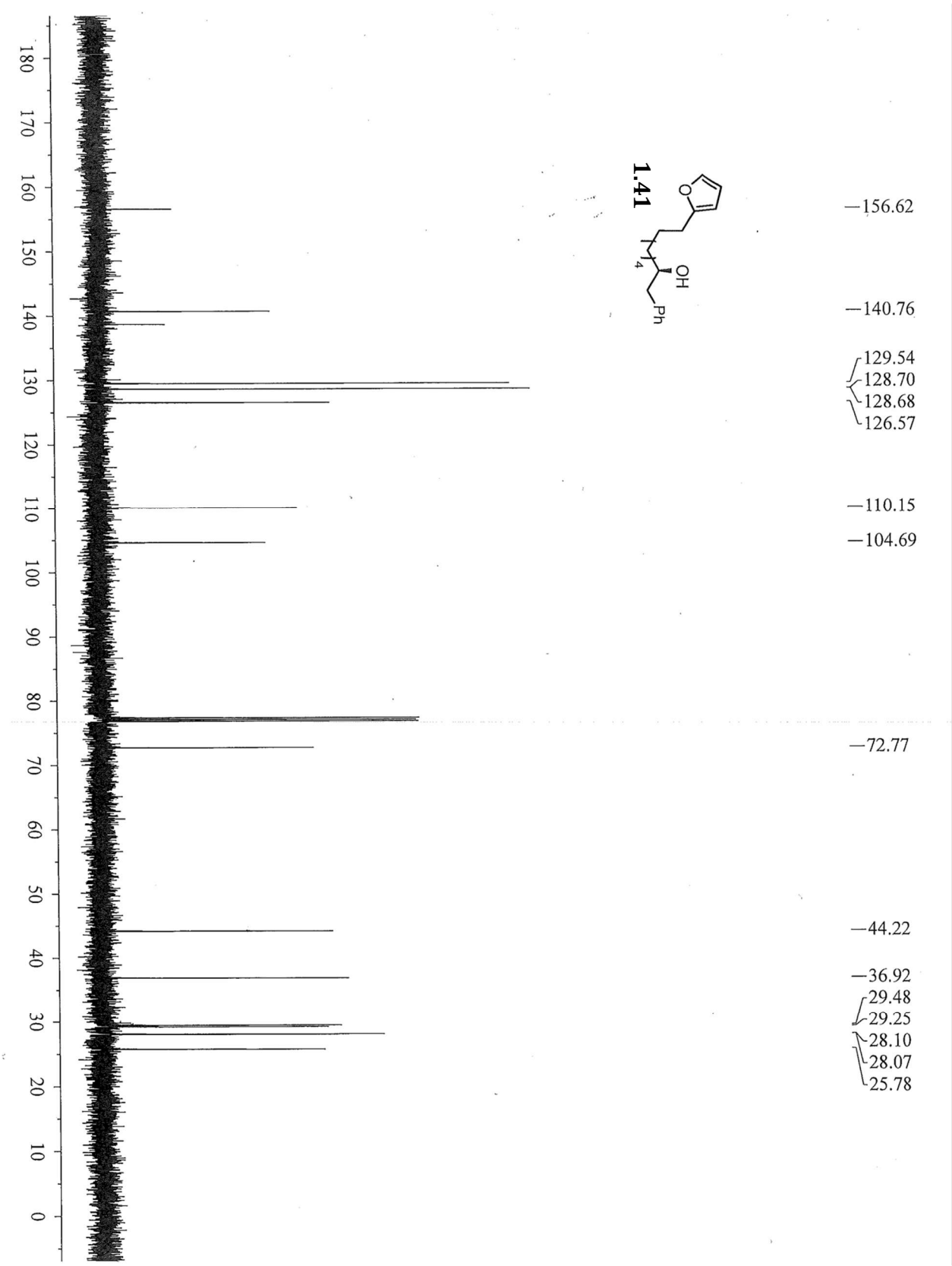

1.40
Me3Si
OH
Ph
7.32
7.32
7.31
7.24
7.23
7.23
3.84
3.84
3.83
3.83
2.82
2.81
2.68
2.66
2.65
1.55
1.54
1.54
1.53
1.53
1.40
1.40
1.39
1.39
1.38
1.38
1.38
1.37
1.37
0.54
0.53
0.51
0.50
0.49
1.87
2.85
1.01
1.00
1.02
4.26
1.18
2.11
8.98
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

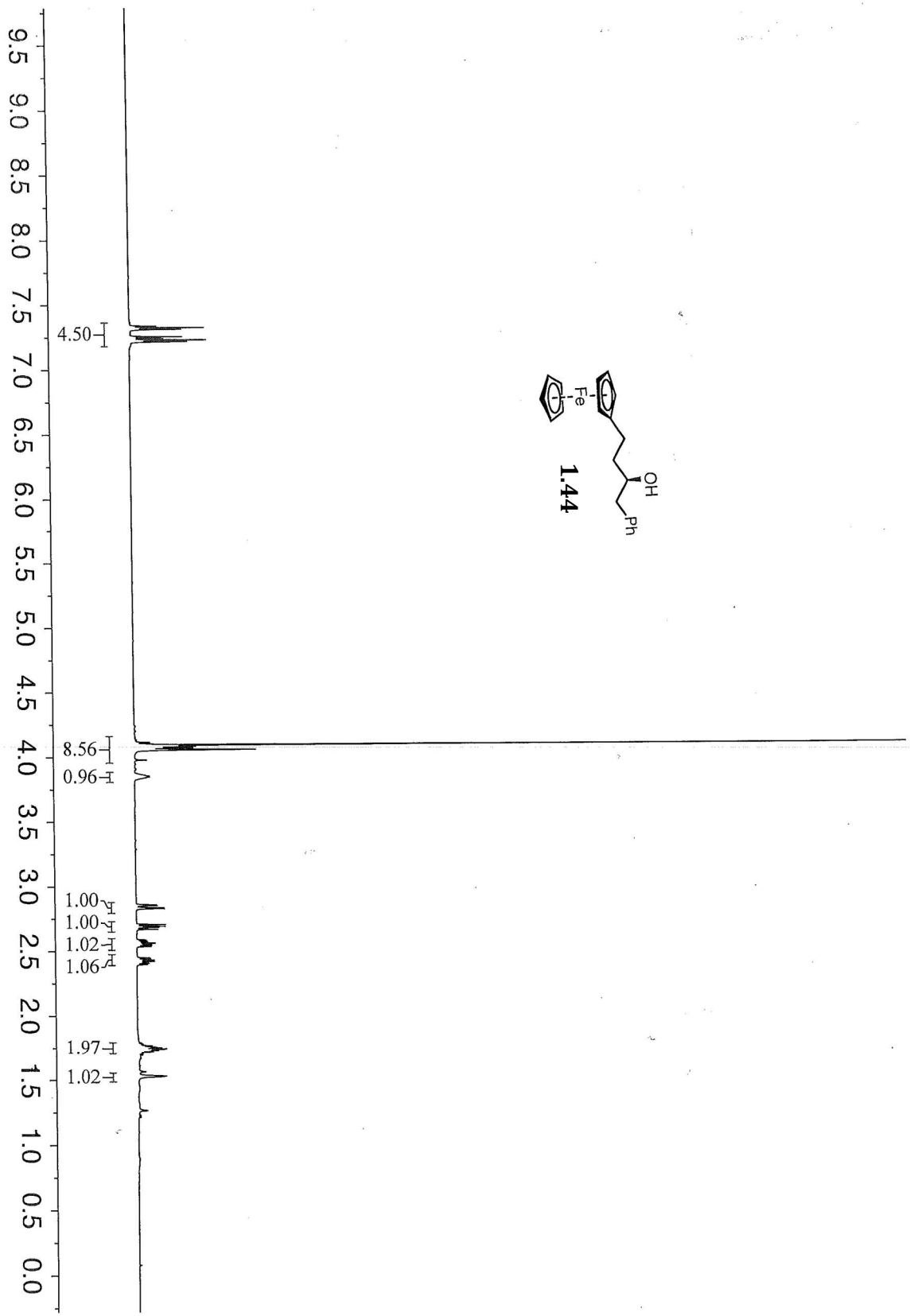

Me3Si
OH
Ph
1.40
138.78
129.56
128.69
126.57
72.57
44.31
40.90
20.33
16.87
-1.50
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

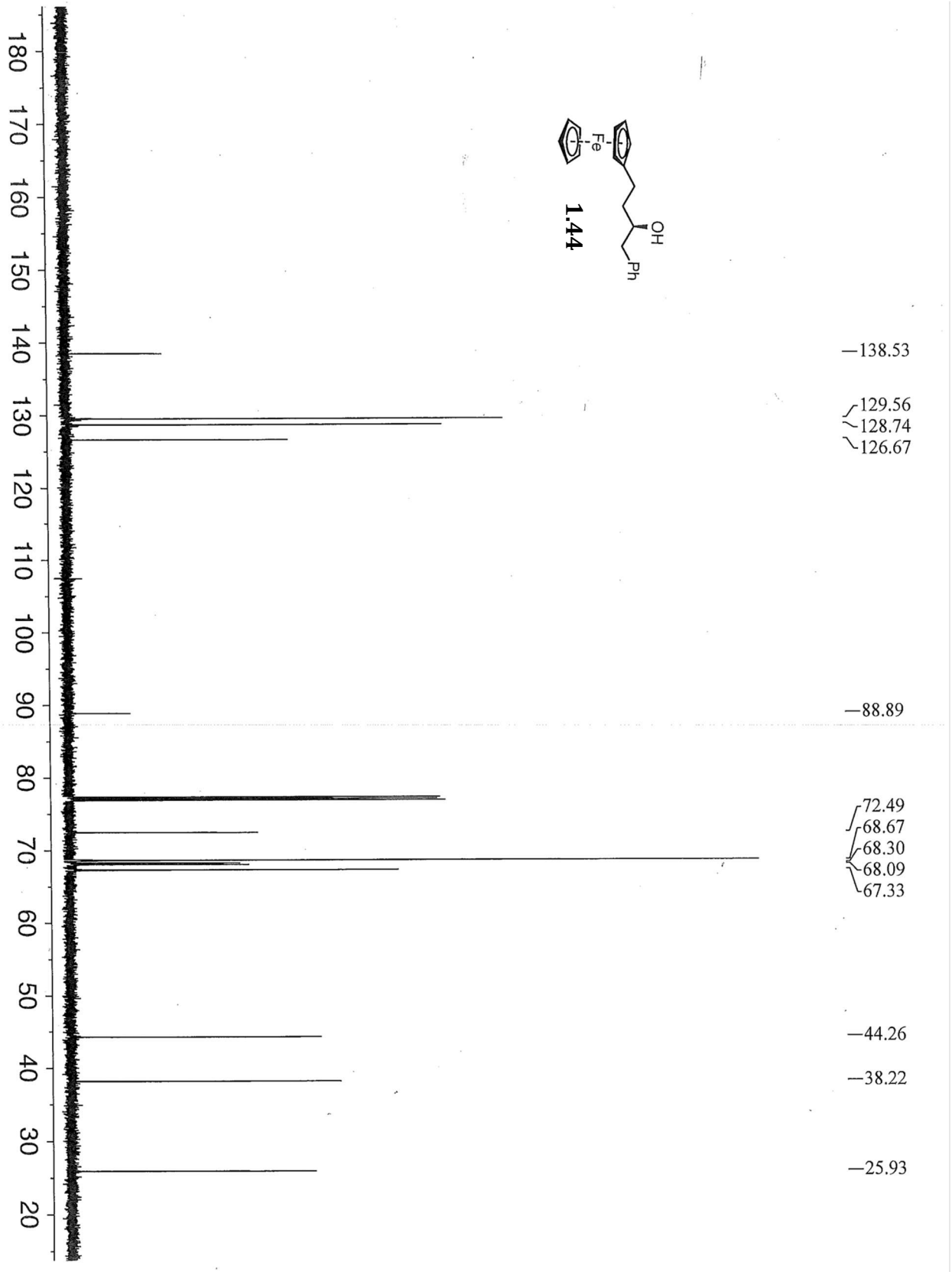

Me
Me
H
OH
Ph
1.43
1.90
3.17
1.01
1.00
1.00
1.99
4.86
4.33
2.84
2.89
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
7.32
7.30
7.26
7.25
7.23
7.22
7.21
3.89
3.88
3.87
3.86
2.84
2.83
2.82
2.81
2.64
2.63
2.62
2.60
2.34
2.34
2.32
2.27
2.26
2.24
2.02
2.00
1.99
1.97
1.95
1.92
1.92
1.90
1.89
1.88
1.87
1.85
1.67
1.67
1.65
1.64
1.64
1.63
1.61
1.60
1.58
1.57
1.55
1.54
1.52
1.50
1.43
1.42
1.41
1.19
1.17
0.98

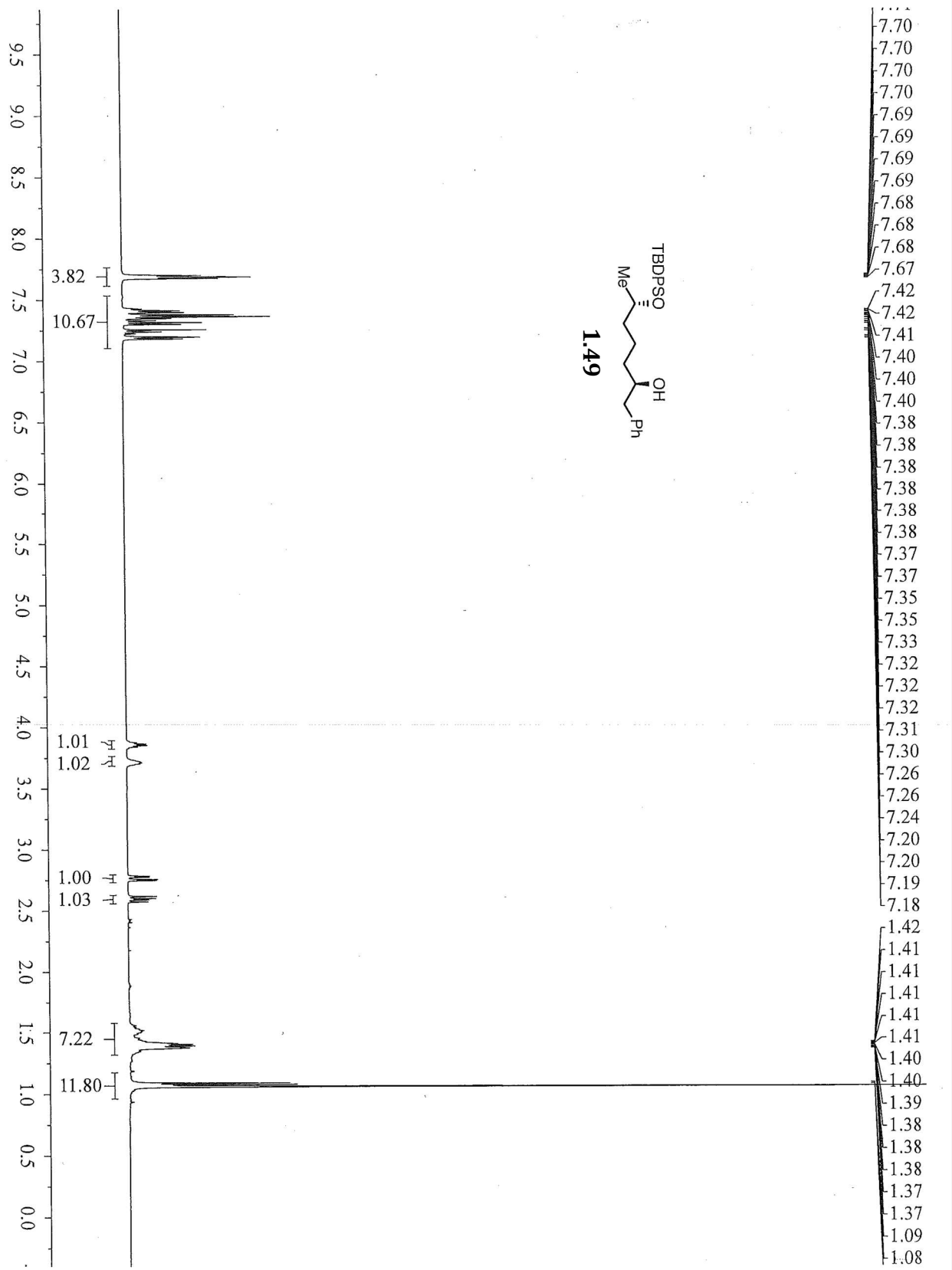

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
138.79
129.55
128.66
126.55
Me
Me
H
OH
Ph
1.43
71.24
70.93
47.48
45.83
45.34
44.92
44.84
44.33
41.61
38.86
38.81
37.83
37.37
33.89
33.64
31.73
28.34
28.32
26.65
26.58
23.42
23.35
23.12
22.19

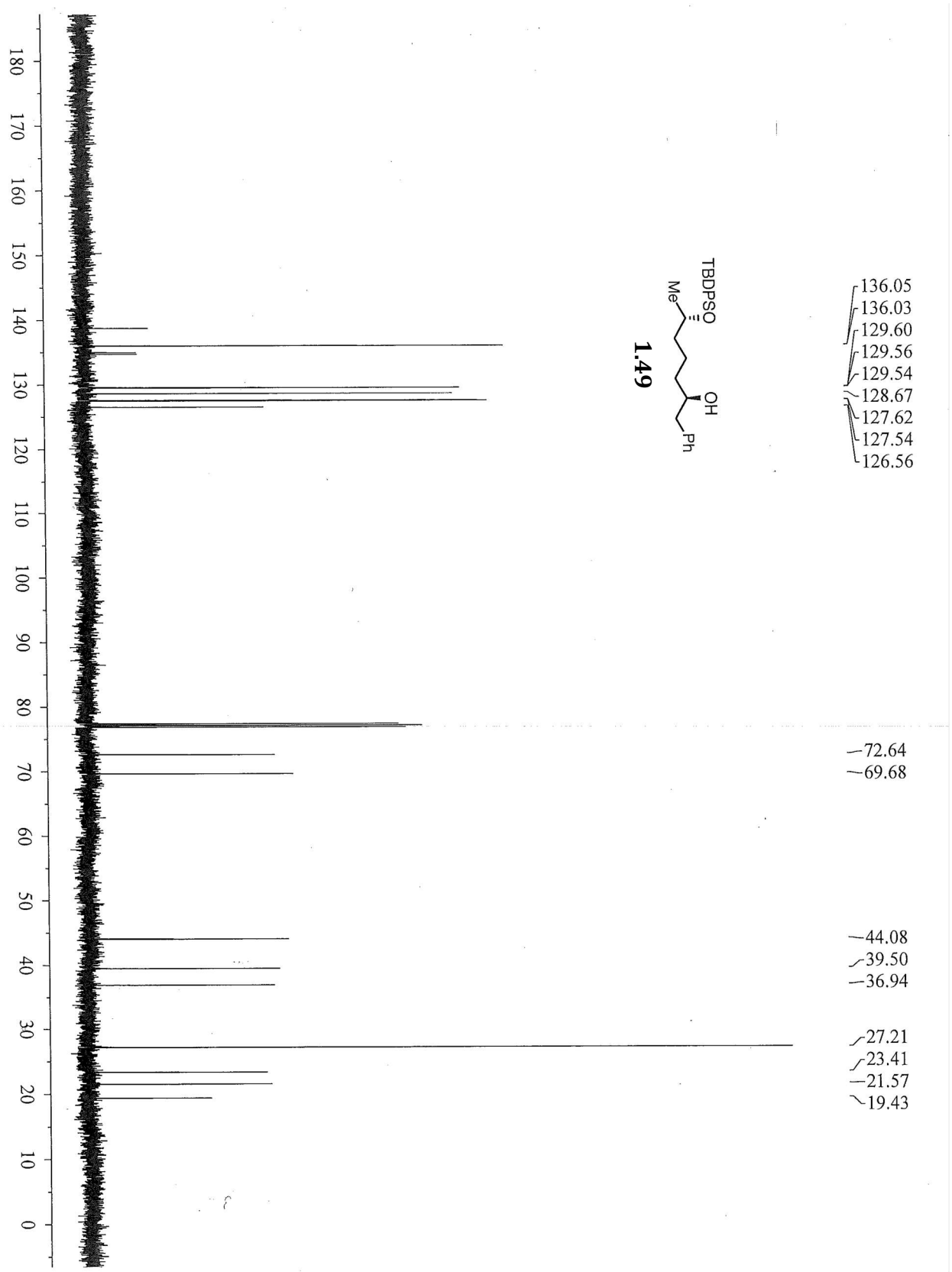

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
5.62
0.93
0.98
1.05
1.00
2.87
11.71
1.41
OH
Ph
4
7.34
7.33
7.32
7.32
7.31
7.31
7.30
7.30
7.26
7.26
7.24
7.23
7.23
7.22
7.22
7.21
6.29
6.28
6.28
6.27
5.98
5.97
3.85
3.84
3.83
3.82
3.81
3.80
3.79
2.86
2.85
2.82
2.81
2.68
2.66
2.64
2.62
2.60
1.67
1.65
1.63
1.55
1.54
1.53
1.52
1.51
1.49
1.39
1.38
1.37
1.36

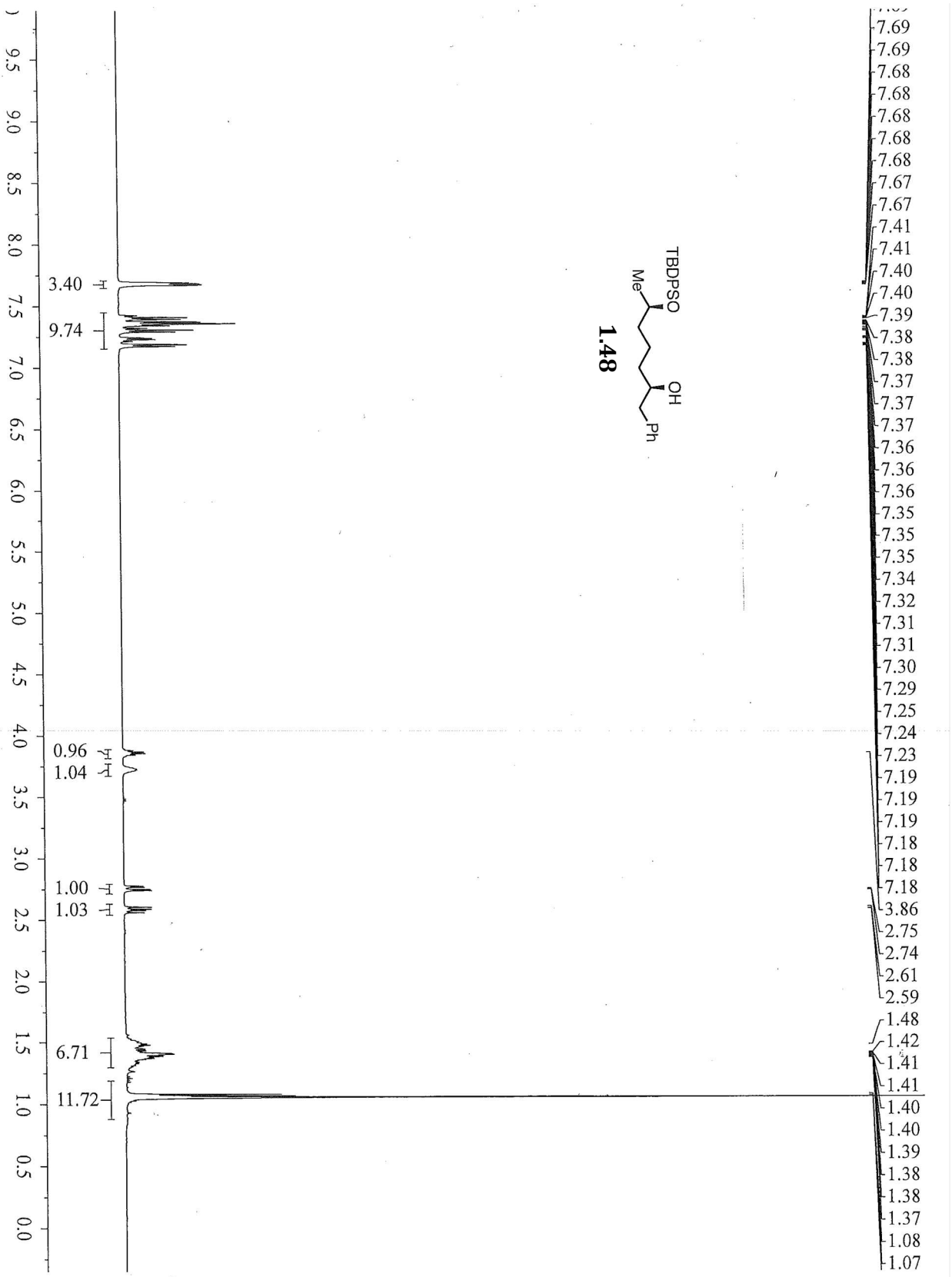

1.41
OH
Ph
156.62
140.76
129.54
128.70
128.68
126.57
110.15
104.69
72.77
44.22
36.92
29.48
29.25
28.10
28.07
25.78
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

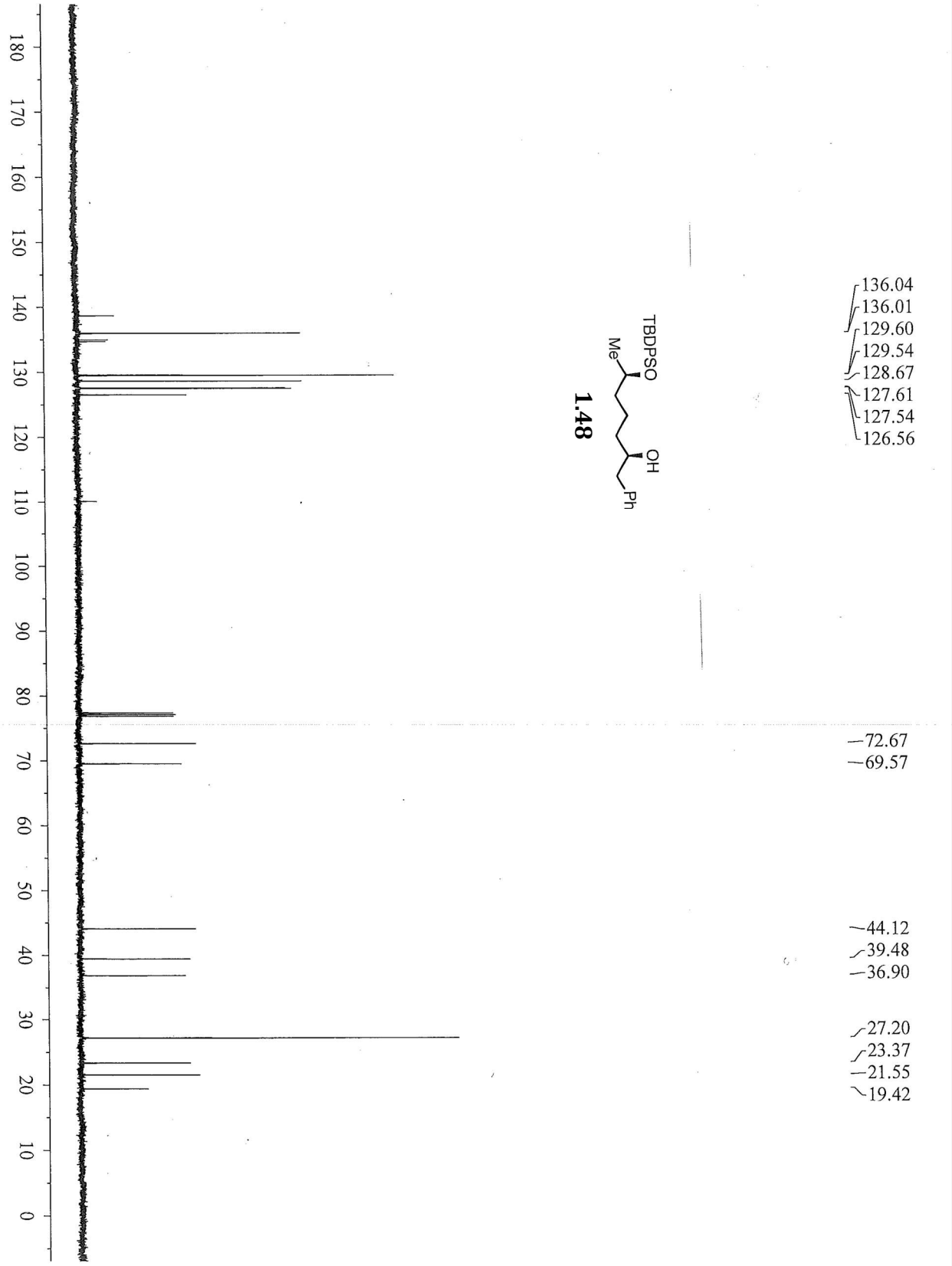

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
4.50
8.56
0.96
1.00
1.00
1.02
1.06
1.97
1.02
Fe
OH
Ph
1.44

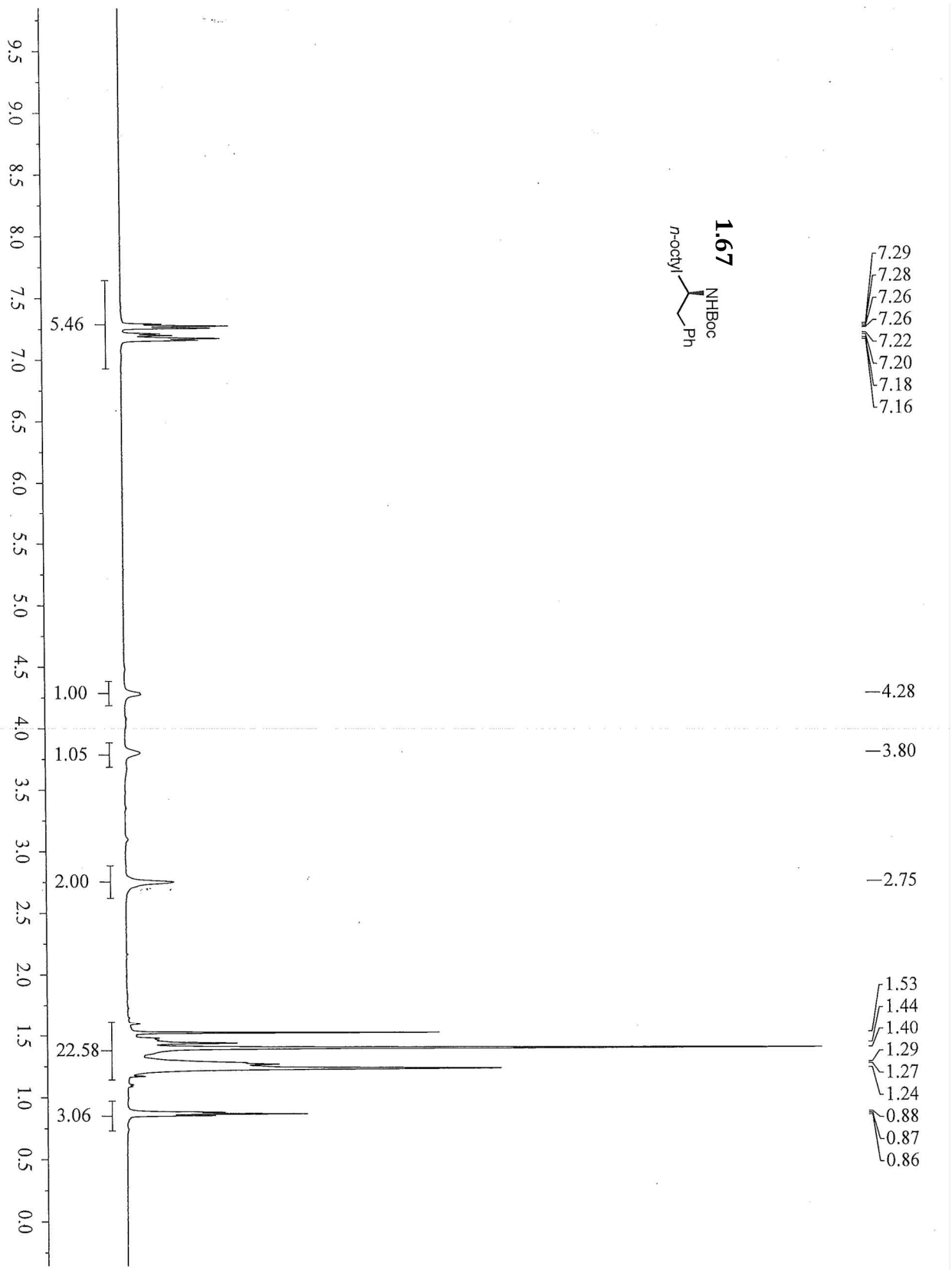

Fe
OH
Ph
1.44
138.53
129.56
128.74
126.67
88.89
72.49
68.67
68.30
68.09
67.33
44.26
38.22
25.93
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

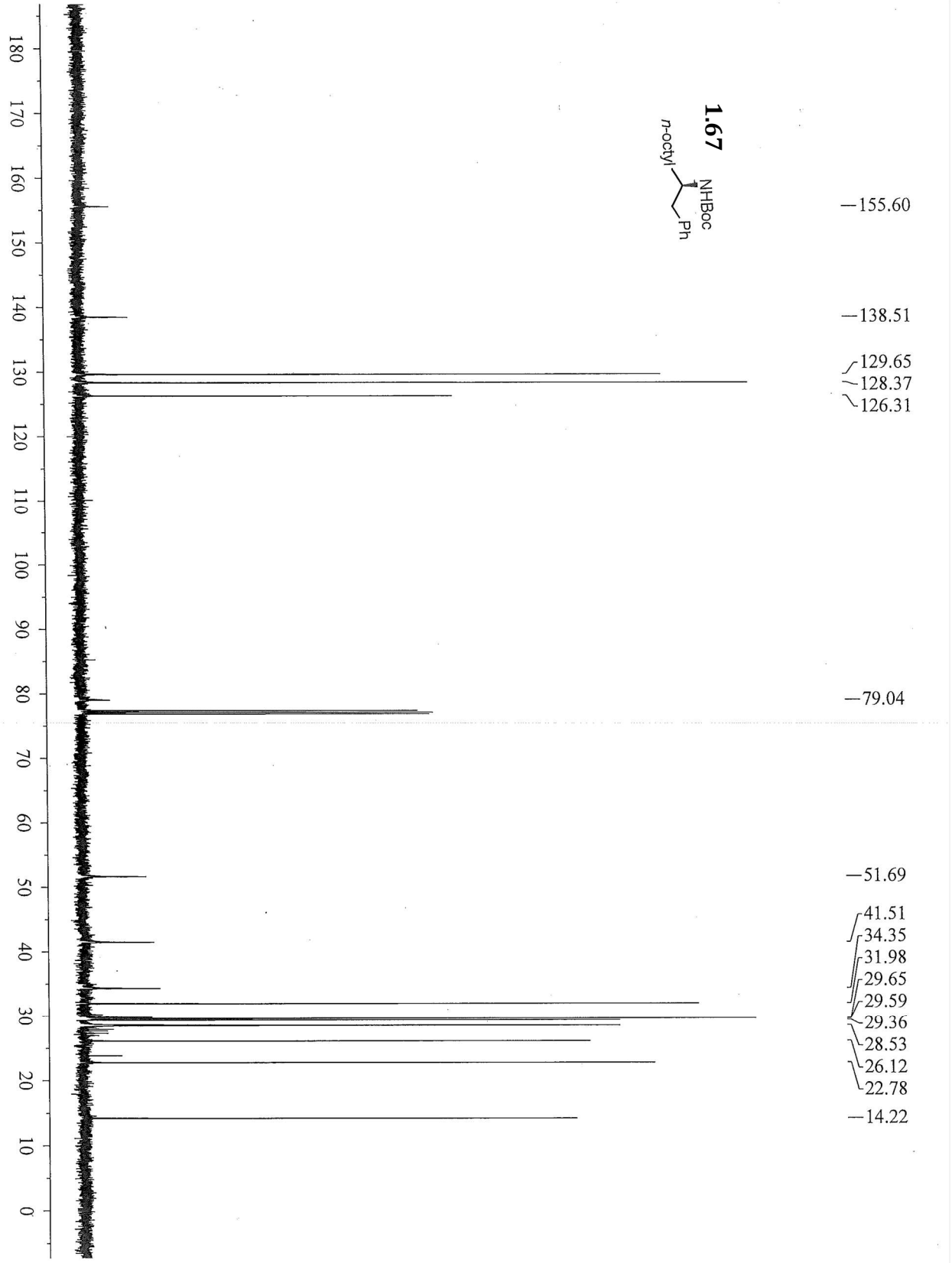

TBDPSO
Me
OH
Ph
1.49
3.82
10.67
1.01
1.02
1.00
1.03
7.22
11.80

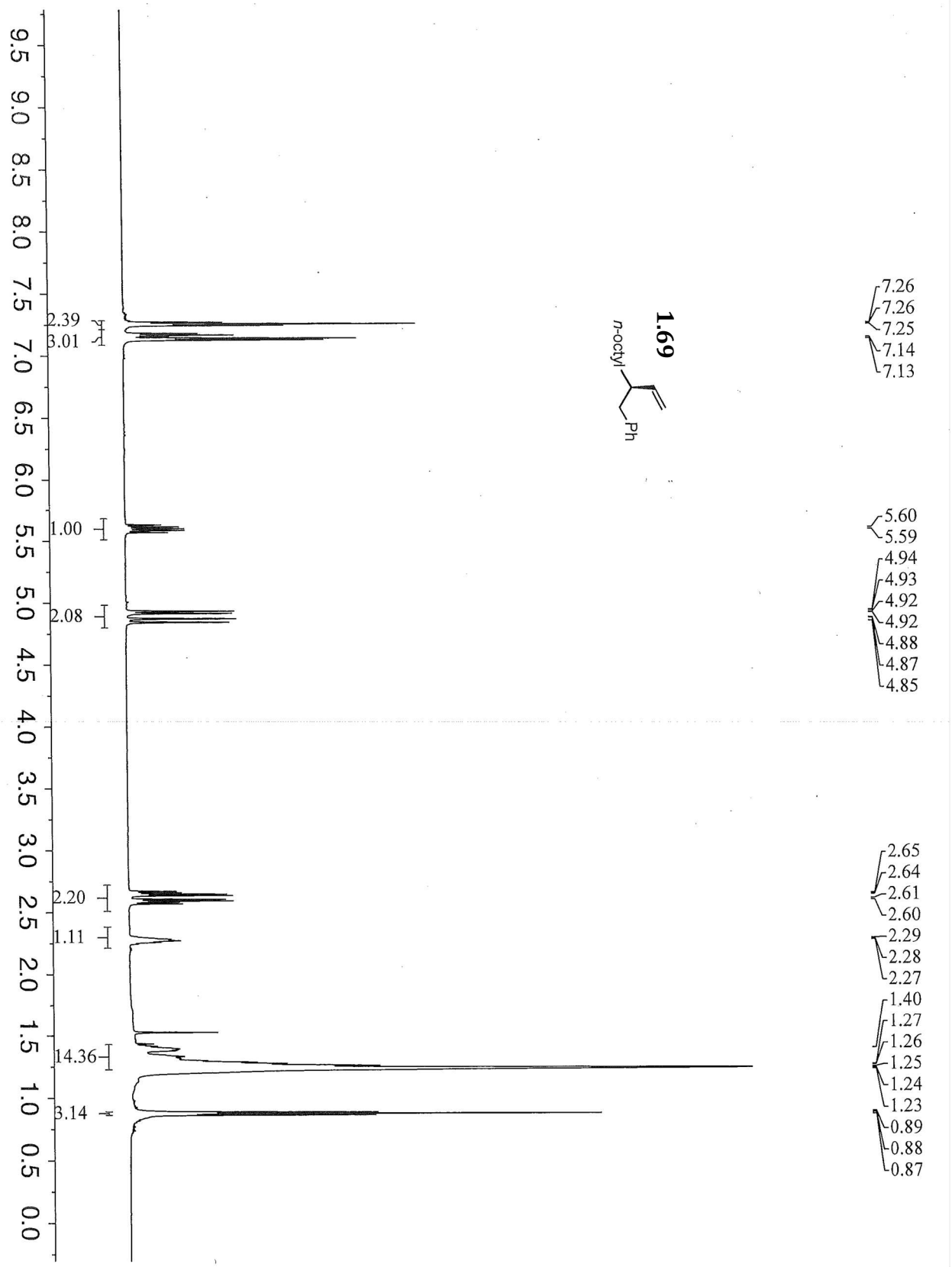

TBDPSO
Me
OH
Ph
1.49
136.05
136.03
129.60
129.56
129.54
128.67
127.62
127.54
126.56
72.64
69.68
44.08
39.50
36.94
27.21
23.41
21.57
19.43
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

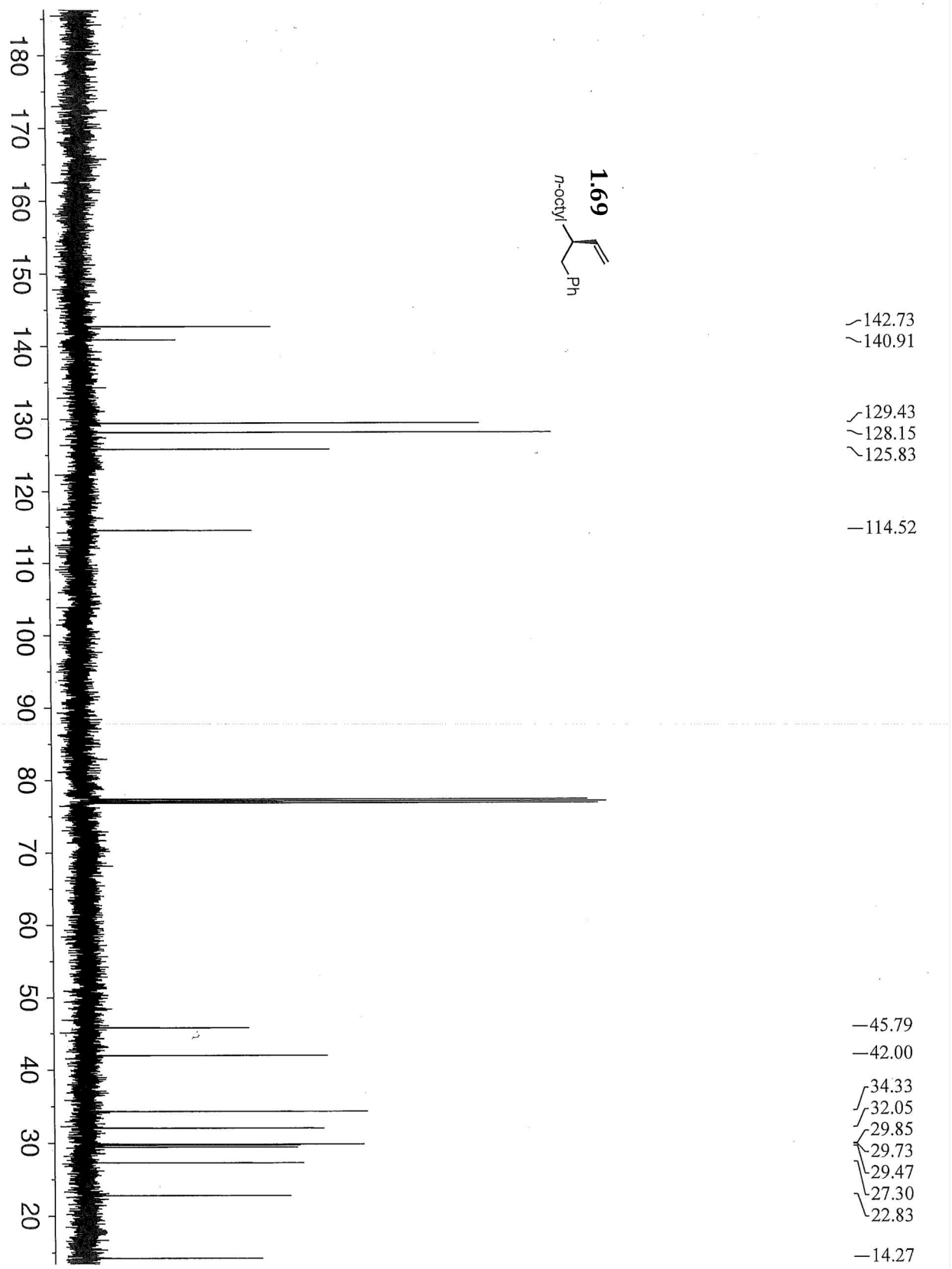

TBDPSO
Me
OH
Ph
1.48
3.40
9.74
0.96
1.04
1.00
1.03
6.71
11.72
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
7.69
7.69
7.68
7.68
7.68
7.68
7.68
7.67
7.67
7.41
7.41
7.40
7.40
7.39
7.38
7.38
7.37
7.37
7.37
7.36
7.36
7.36
7.35
7.35
7.35
7.34
7.32
7.31
7.31
7.30
7.29
7.25
7.24
7.23
7.19
7.19
7.19
7.18
7.18
7.18
3.86
2.75
2.74
2.61
2.59
1.48
1.42
1.41
1.41
1.40
1.40
1.39
1.38
1.38
1.37
1.08
1.07

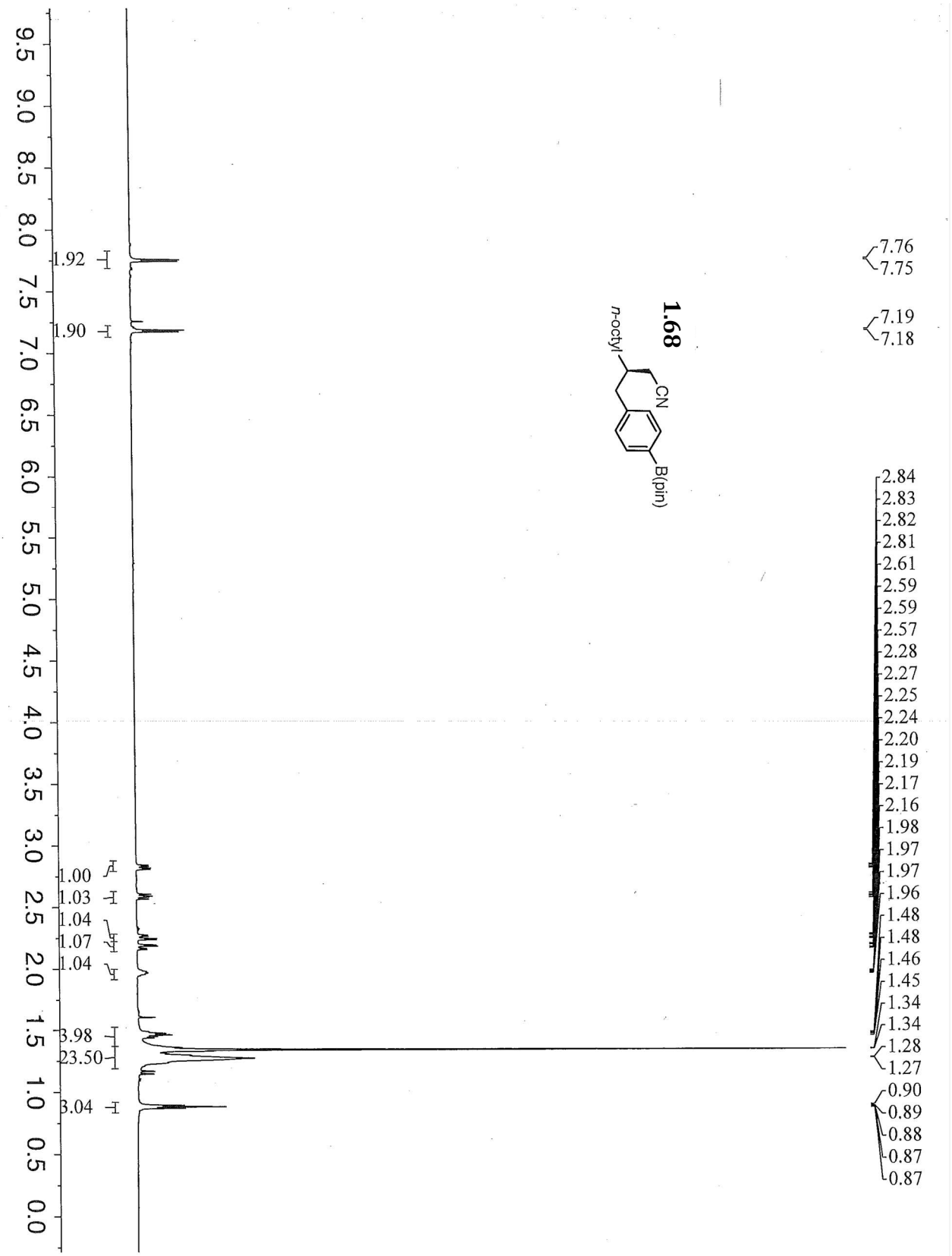

TBDPSO
Me
OH
Ph
1.48
136.04
136.01
129.60
129.54
128.67
127.61
127.54
126.56
72.67
69.57
44.12
39.48
36.90
27.20
23.37
21.55
19.42
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

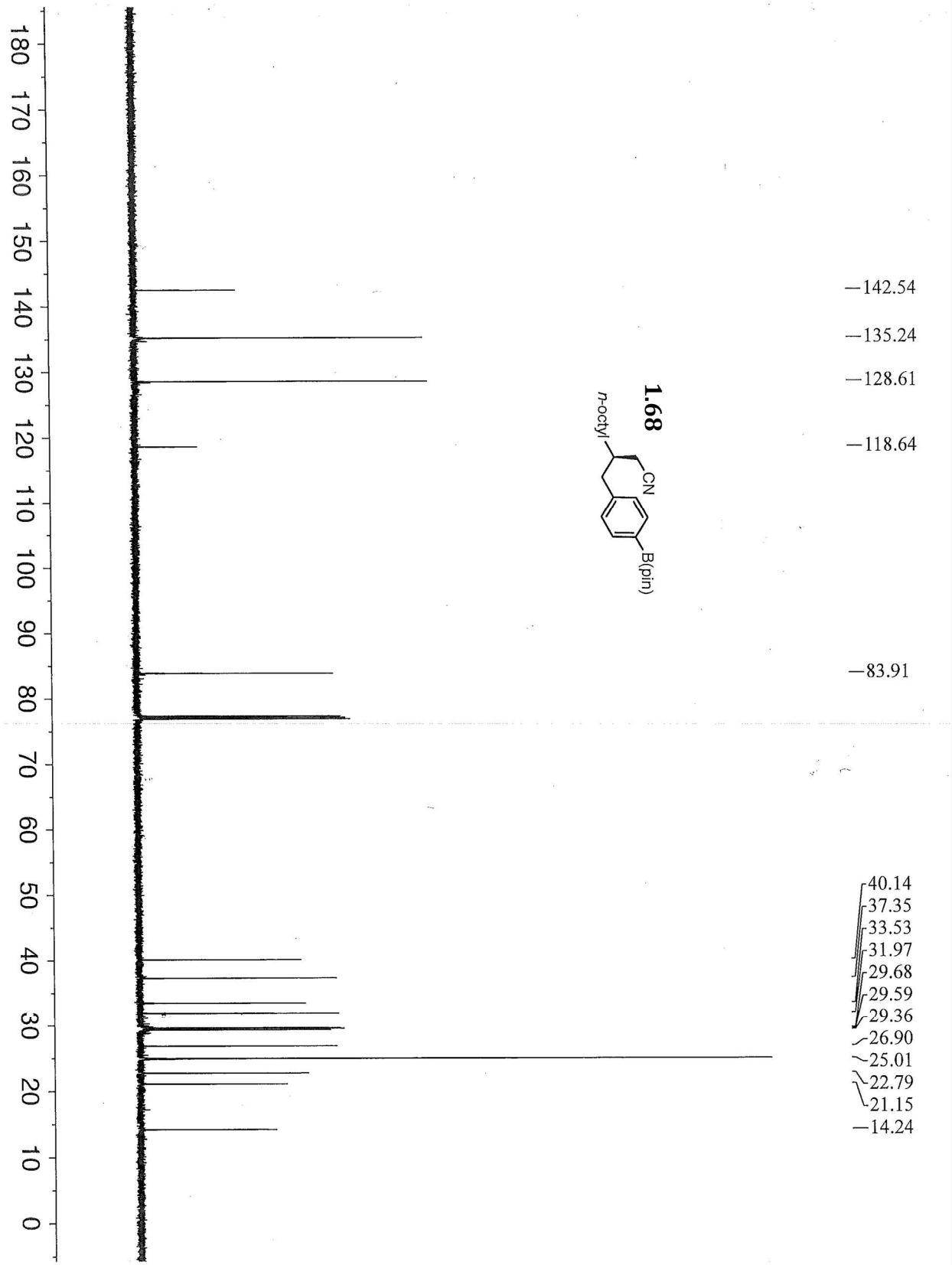

1.67
n-octyl
NHBoc
Ph
7.29
7.28
7.26
7.26
7.22
7.20
7.18
7.16
5.46
1.00
1.05
2.00
22.58
3.06
4.28
3.80
2.75
1.53
1.44
1.40
1.29
1.27
1.24
0.88
0.87
0.86
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


1.67
n-octyl
NHBoc
Ph
155.60
138.51
129.65
128.37
126.31
79.04
51.69
41.51
34.35
31.98
29.65
29.59
29.36
28.53
26.12
22.78
14.22
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


1.69
n-octyl
Ph
2.39
3.01
1.00
2.08
2.20
1.11
14.36
3.14
7.26
7.26
7.25
7.14
7.13
5.60
5.59
4.94
4.93
4.92
4.92
4.88
4.87
4.85
2.65
2.64
2.61
2.60
2.29
2.28
2.27
1.40
1.27
1.26
1.25
1.24
1.23
0.89
0.88
0.87

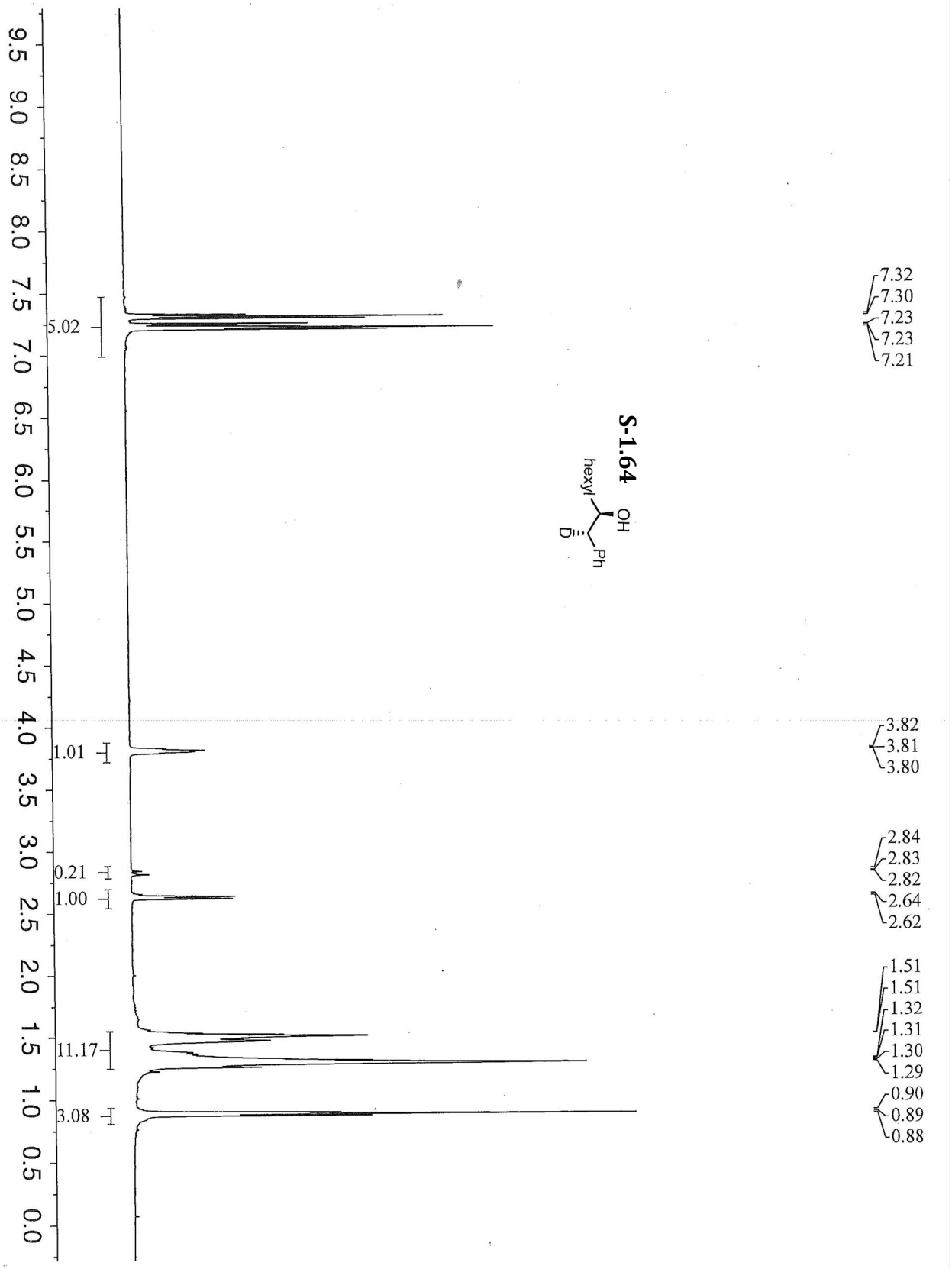

1.69
n-octyl
Ph
142.73
140.91
129.43
128.15
125.83
114.52
45.79
42.00
34.33
32.05
29.85
29.73
29.47
27.30
22.83
14.27
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

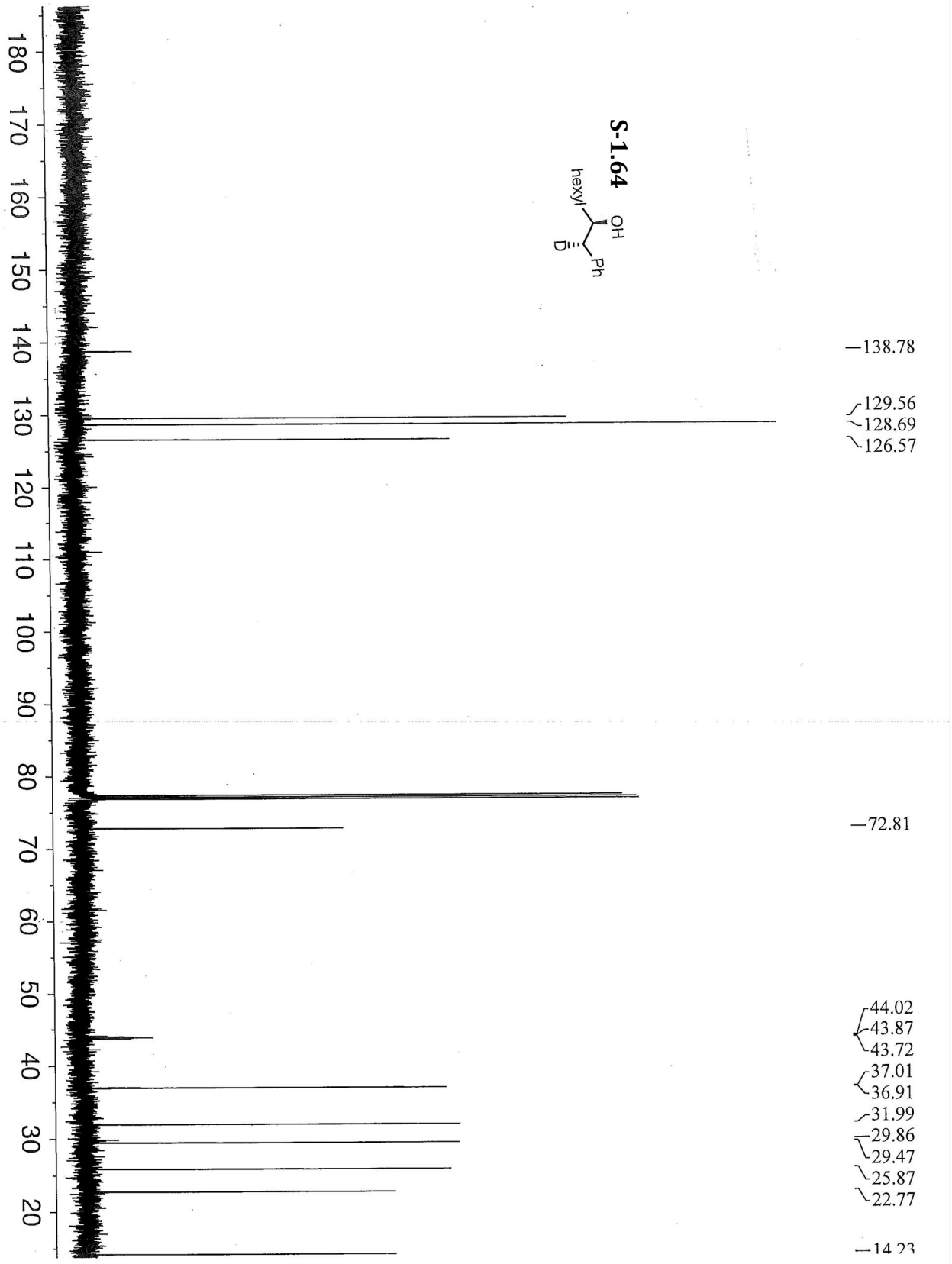

1.68
n-octyl
CN
B(pin)
7.76
7.75
7.19
7.18
2.84
2.83
2.82
2.81
2.61
2.59
2.59
2.57
2.28
2.27
2.25
2.24
2.20
2.19
2.17
2.16
1.98
1.97
1.97
1.96
1.48
1.48
1.46
1.45
1.34
1.34
1.28
1.27
0.90
0.89
0.88
0.87
0.87
1.92
1.90
1.00
1.03
1.04
1.07
1.04
3.98
23.50
3.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

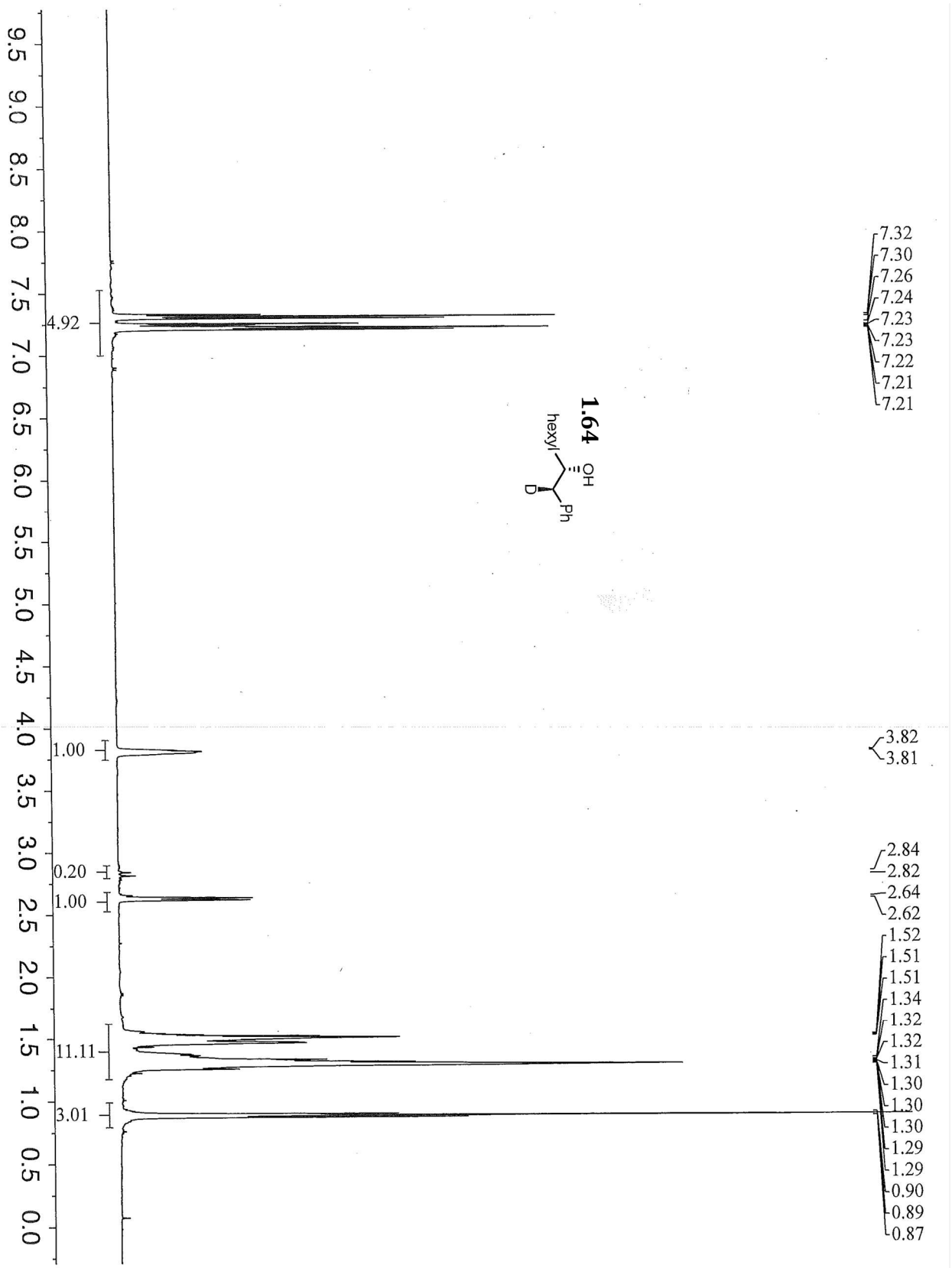

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
142.54
135.24
128.61
118.64
83.91
40.14
37.35
33.53
31.97
29.68
29.59
29.36
26.90
25.01
22.79
21.15
14.24
1.68
n-octyl
CN
B(pin)

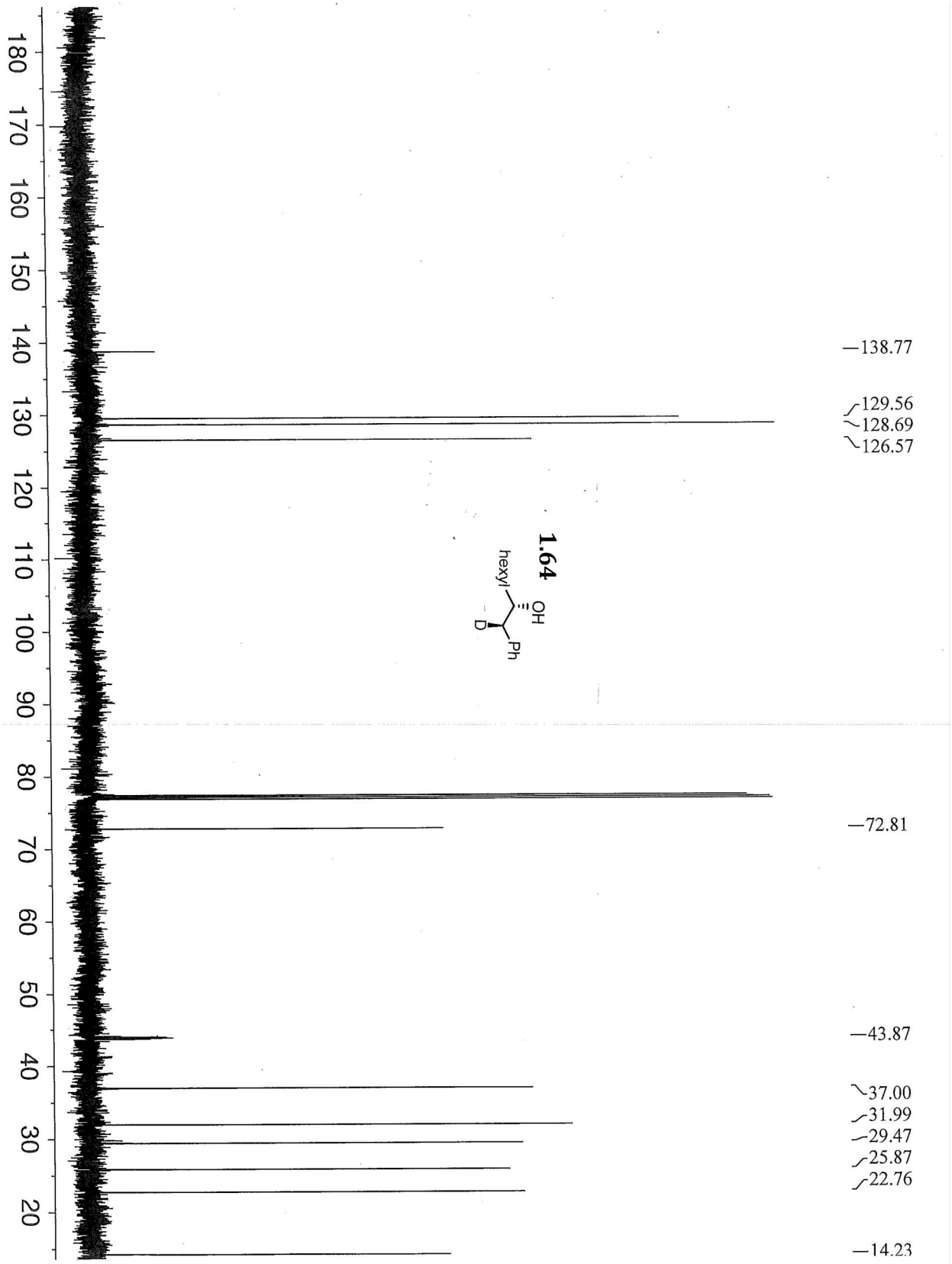
^{11}B NMR

1.68
n-octyl
CN
B(pin)
−30.96
85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25


S-1.64
hexyl
OH
D
Ph
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
5.02
1.01
0.21
1.00
11.17
3.08
7.32
7.30
7.23
7.23
7.21
3.82
3.81
3.80
2.84
2.83
2.82
2.64
2.62
1.51
1.51
1.32
1.31
1.30
1.29
0.90
0.89
0.88


S-1.64
hexyl
OH
D
Ph
138.78
129.56
128.69
126.57
72.81
44.02
43.87
43.72
37.01
36.91
31.99
29.86
29.47
25.87
22.77
14.23


1.64
hexyl
OH
D
Ph
4.92
1.00
0.20
1.00
11.11
3.01
7.32
7.30
7.26
7.24
7.23
7.23
7.22
7.21
7.21
3.82
3.81
2.84
2.82
2.64
2.62
1.52
1.51
1.51
1.34
1.32
1.32
1.31
1.30
1.30
1.30
1.29
1.29
0.90
0.89
0.87


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
138.77
129.56
128.69
126.57
72.81
43.87
37.00
31.99
29.47
25.87
22.76
14.23
1.64
hexyl
OH
D
Ph

2.0 CHAPTER 2

2.0 CHAPTER 2

CATALYTIC CONJUNCTIVE COUPLING OF CARBOXYLIC ACID DERIVATIVES WITH 9-BBN ATE COMPLEXES

2.1 INTRODUCTION

Development of efficient methods for the synthesis of β-hydroxyl carbonyls is an important area of synthetic chemistry, as these are common motifs found in numerous polyketide natural products. Classically, the aldol reaction has been utilized extensively towards the construction of this important motif wherein aldehydes and enolates are employed as the starting materials. Another commonly deployed strategy is the conjugate borylation reaction to afford β-boryl carbonyl compounds. These products unveil β-hydroxyl carbonyls upon oxidative workup.

Carboxylic acids are abundant motifs in natural products and can be easily converted to more reactive carboxylic derivatives. The development of methods that allow transformations of carboxylic derivatives with mild reaction conditions could be advantageous in the context of late-stage functionalization of complex bioactive compounds. Thus, the use of carboxylic derivatives in transition metal catalyzed cross-coupling chemistry has been an important area of research. The key to success of these reactions hinges on the ability of a transition metal to undergo oxidative addition with acyl electrophiles. Depending on the exact reaction conditions, acyl electrophiles have been

demonstrated to yield either ketones through direct coupling with a nucleophilic partner, or decarbonylative products with the loss of carbon monoxide during the course of reaction. Considering the literature precedents of oxidative addition of acyl electrophile to nickel, we investigated the use of these derivatives in our nickel-catalyzed conjunctive coupling reaction. This would provide an alternative synthesis route to afford β-hydroxyl carbonyls. Under the reaction system, simple terminal alkenes can be used as the starting materials and converted to β-hydroxyl carbonyls through a one-pot sequence consisting of hydroboration and conjunctive coupling. This chapter will discuss various approaches to access β-hydroxyl carbonyls, the use of carboxylic derivatives within the realm of catalysis, as well as the development of the nickel-catalyzed conjunctive cross-coupling reaction with carboxylic acid derivatives.

2.2 BACKGROUND

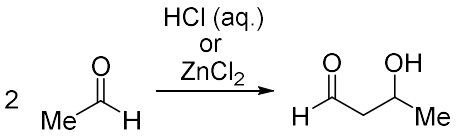
2.2.1 Aldol Reactions to Access β-Hydroxyl Carbonyls

The aldol reaction is one of the most classical reactions in organic synthesis. It was first discovered by A. P. Borodin[67] and C. A. Wurtz[68] in 1872 when they observed the formation of 3-hydroxylbutanal upon mixing acetaldehyde and aqueous sodium hydroxide in the presence of hydrochloric acid or zinc chloride (Scheme 2.1). After its discovery, it was not too long before chemists began to recognize the potential synthetic utility and develop the

[67] Borodin, A. P. *Berichte der deutschen chemischen Gesellschaft* **1869***, 2,* 552.
[68] Wurtz, C. A. *Journal für Praktische Chemie* **1872**, *5*, 457.

aldol reaction further to improve the scope and stereoselectivity of this reaction. Because it is so useful, countless strategies to control the stereoselectivity of this reaction, either with stoichiometric chiral auxiliaries or catalytic means.

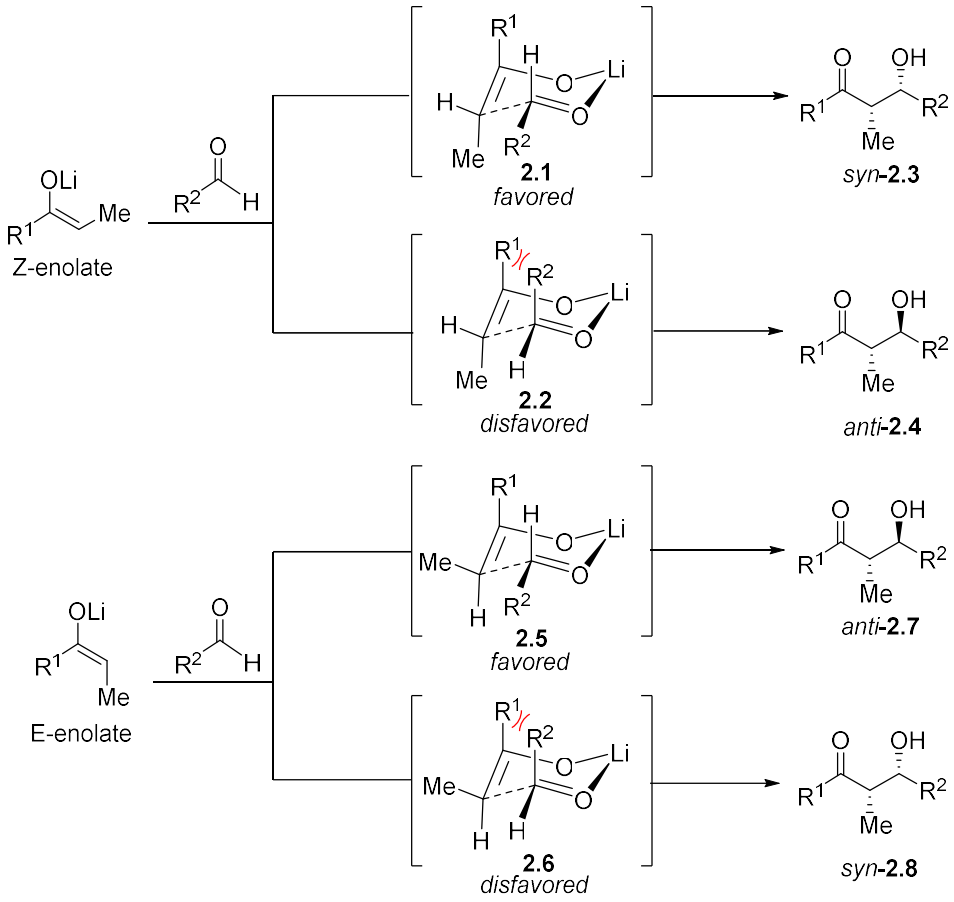
Scheme 2.1 First Reported Aldol Reaction by Borodin and Wurtz.



In cases when the enolate has a β-substitutuent, two vicinal stereocenters would be introduced simultaneously during the aldol reaction. It was found that the geometry of boron enolate would dictate the diastereomeric outcome of the reaction (Scheme 2.2). The outcome can be rationalized by the Zimmerman-Traxler model which invokes a closed chair-like transition state, in which large groups prefer to occupy the equatorial position to minimize 1,3-diaxial repulsion[69].

[69] Zimmerman, H. E.; Traxler, M. D. *J. Am. Chem. Soc.* **1957**, *79*, 1920.

Scheme 2.2 Zimmerman-Traxler Model.

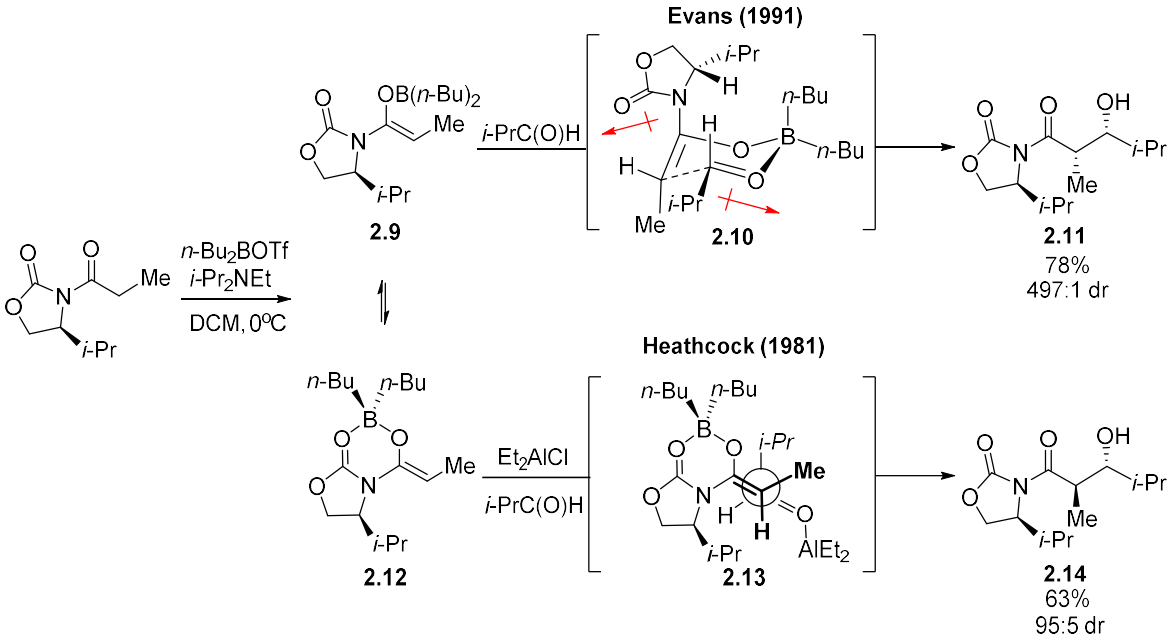


In 1981, Evans reported the first highly enantio- and diastereoselective aldol reaction by the installation of chiral oxazolidinone auxiliaries (Scheme 2.3).[70] The minimization of dipole moments in the chair-like transition state was proposed to be a key factor in the diastereo-differentiation leading to high *syn*-selectivity. Years later, the Heathcock group reported modifications to the system to expand the scope of the reaction to afford "non-Evans" *anti*-aldol products.[71] Under the reaction system, the aldehyde was pre-mixed with one equivalent of bulky Lewis acid before reacting with boron-enolate, forcing the

[70] Evans, D. A.; Takacs, J. M.; McGee, L. R.; Ennis, M. D.; Mathre, D. J.; Bartroli, J. *Pure & Appl. Chem.* **1981**, *53*, 1109.
[71] Walker, M. A.; Heathcock, C. H. *J. Org. Chem.* **1991**, *56*, 5747.

reaction to proceed via the open transition state **2.13**. The chiral auxiliary could then be transformed to either carboxylic acid, amide, aldehyde, or Weinreb amide. Since then, different research groups reported different chiral auxiliaries with varying extent of efficiencies.[72]

Scheme 2.3 Evan's Oxazolidinone Auxiliary in Stereoselective Aldol Reaction.

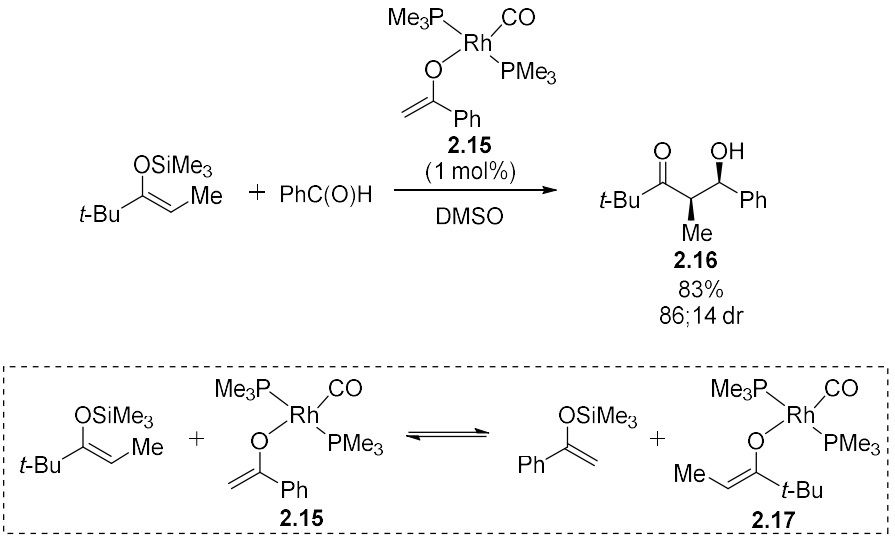


Recent research effort in this field has shifted away from relying on stoichiometric chiral auxiliaries in favor of catalytic methods. Aldol reactions using enol silanes as the nucleophilic partner, also known as the Mukaiyama aldol reaction, have been a great platform for developments of chiral catalysts to afford aldol products with high stereoselectivity. The first transition-metal catalyzed Mukaiyama aldol reaction was

[72] (a) Oppolzer, W.; Blagg, J.; Rodriguez, I.; Walther, E. *J. Am. Chem. Soc.* **1990**, *112*, 2767. (b) Abiko, A.; Liu, J.-F.; Masamune, S. *J. Am. Chem. Soc.* **1997**, *119*, 2586. (c) Masamune, S.; Sato, T.; Kim, B.; Wollmann, T. A. *J. Am. Chem. Soc.* **1986**, *108*, 8279. (c) Reetz, M. T.; Kunisch, F.; Heitmann P. *Tet. Lett.* **1986**, *27*, 4721.

reported by Bergman and Heathcock in 1989 (Scheme 2.4).[73] In this report, rhodium catalyst **2.15** was proposed to undergo metathesis with enol silane to generate an O-bound rhodium enolate, which is the active species and react with aldehyde. However, only non-enolizable aldehyde can be used since the O-bound rhodium enolate has a high basicity and can directly deprotonate an acid aldehyde. No enantioselective variant of this reaction has since been reported.

Scheme 2.4 The First Reported Catalytic Mukaiyama Aldol Reaction.



In 1990, Kobayashi and Mukaiyama reported one of the first enantioselective catalytic Mukaiyama aldol reactions, in which $Sn(OTf)_2$-diamine complex acts as a Lewis-acid catalyst to activate aldehyde for nucleophilic attack by enol silane (eq. 1, Scheme 2.5).[74] The reaction affords the aldol product with high enantioselectivity and *syn* diastereoselectivity. Not too long after this report, Carreira reported the use of Ti(IV) catalyst **2.19** to afford the corresponding β-hydroxyl carbonyls with excellent

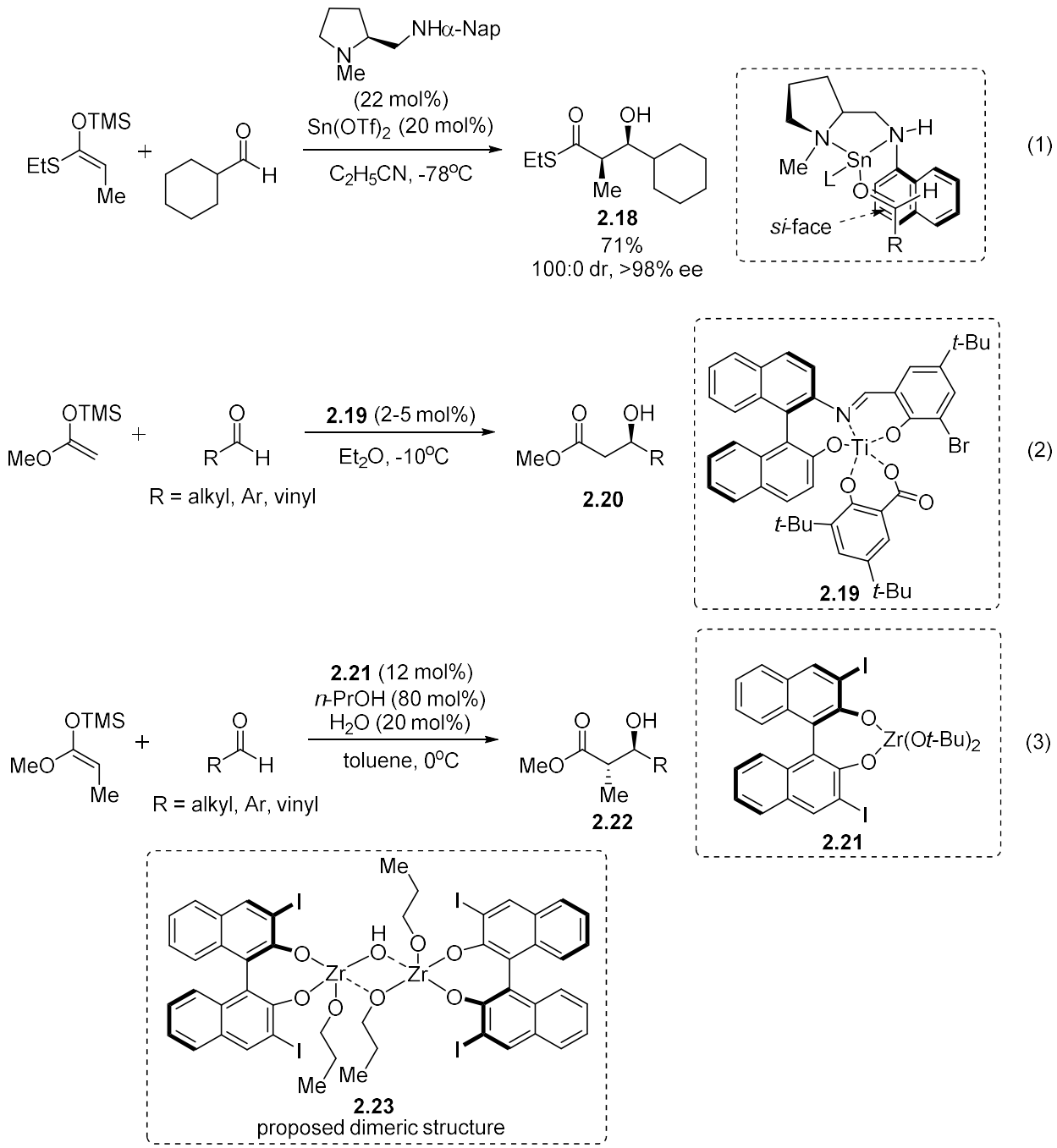
[73] Slough, G. A.; Bergman, R. G.; Heathcock, C. H. *J. Am. Chem. Soc.* **1989**, *111*, 938.
[74] Kobayashi, S.; Fujishita, Y.; Mukaiyama, T. *Chem. Lett.* **1990**, *129*, 1455.

enantioselectivity (eq. 2, Scheme 2.5).[75] The scope of this reaction is broad tolerating both aliphatic as well as aryl aldehyde. To selectively generate the *anti*-aldol product, Kobayashi reported the use of zirconium as Lewis-acid catalyst and ketene silyl acetal as the nucleophile (eq. 3, Scheme 2.5).[76] A positive non-linear effect was observed suggesting a dimeric zirconium structure such as **2.23** may be responsible for the enantioselectivity of the reaction. Since then, other Lewis-acid catalysts including aluminum[77], copper[78], as well as boron-based[79] variants have also been reported.

[75] Carreira, E. M.; Singer, R. A.; Lee, W. J. *Am. Chem. Soc.* **1994**, *116*, 8837.

[76] Yamashita, Y.; Ishitani, H.; Shimizu, H.; Kobayashi, S. *J. Am. Chem. Soc.* **2002**, *124*, 3292.
[77] (a) Furuta, K.; Maruyama, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1991**, *113*, 1041. (b) Parmee, E. R.; Tempkin, O.; Masamune, S.; Abiko, A. *J. Am. Chem. Soc.* **1991**, *113*, 9365. (c) Corey, E. J.; Cywin, C. L.; Roper, T. D. *Tetrahedron Lett.* **1992**, *33*, 6907.
[78] (a) Evans, D. A.; Murry, J. A.; Kozlowski, M. C. *J. Am. Chem. Soc.* **1996**, *118*, 5814. (b) Evans, D. A.; MacMillan, D. W. C.; Campos, K. R. *J. Am. Chem. Soc.* **1997**, *119*, 10859.
[79] (a) Ooi, T.; Tayama, E.; Takahasi, M.; Maruoka, K. *Tetrahedron Lett.* **1997**, *38*, 7403. (b) Ooi, T.; Takahashi, M.; Yamada, M.; Tayama, E.; Omoto, K.; Maruoka, K. *J. Am. Chem. Soc.* **2004**, *126*, 1150. (c) Su, W.; Kim, Y.; Ellern, A.; Guzei, I. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2006**, *128*, 13727. (d) Raders, S. M.; Verkade, J. G. *J. Org. Chem.* **2009**, *74*, 5417.

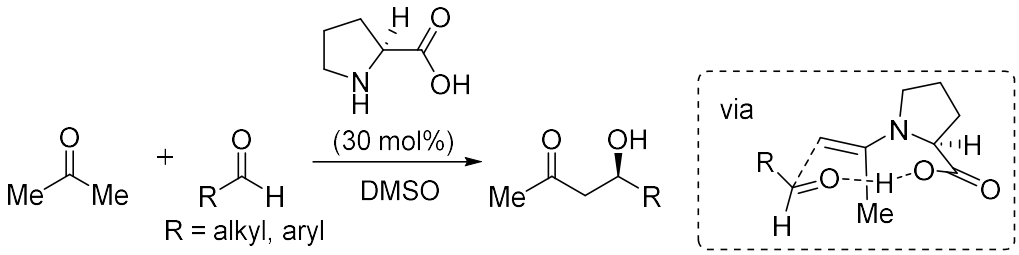
Scheme 2.5 Catalytic Enantioselective Mukaiyama Aldol Reactions.



Asymmetric organocatalytic methods have also been reported, as in the case of proline-catalyzed aldol reaction, in which chiral enamine was formed in-situ as the nucleophile

(Scheme 2.6).[80] Computational work by List suggested that hydrogen-bonding between the aldehyde oxygen and the carboxylate group was an important feature of the transition state, leading to high enantioselectivity of the reaction.[81]

Scheme 2.6 Proline-Catalyzed Aldol Reaction.



2.2.2 Conjugate Borylation Reaction to Access β-Hydroxyl Carbonyls

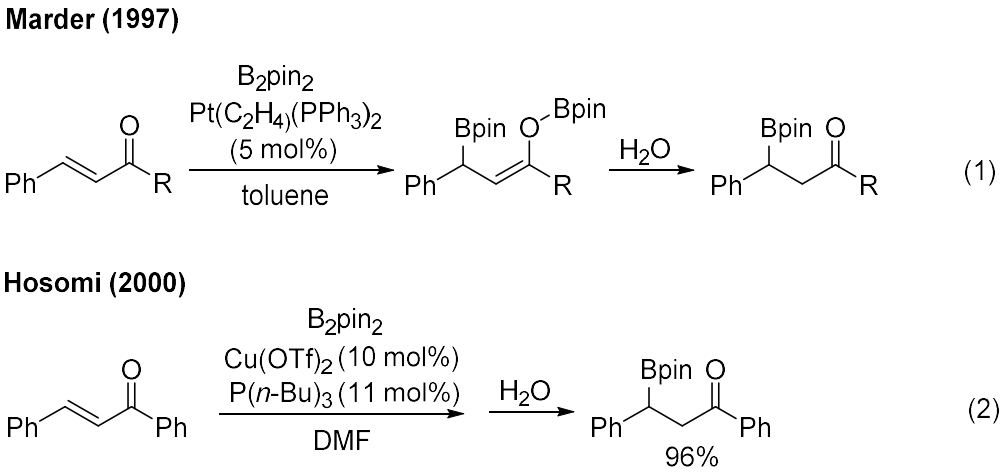
An alternative strategy to access β-hydroxyl carbonyls relies on the efficient synthesis of β-boryl carbonyls, which would unveil the corresponding aldol products upon oxidative workup. The 1,4-addition of nucleophilic boron to α,β-unsaturated carbonyls, known as conjugate borylation, has been a reliable method to generate β-boryl carbonyls. These processes typically require the use of transition metal catalyst to activate the B-B inter-element bond of diboron reagents to form the active M-B species for alkene insertion.

In 1997, Marder and coworkers reported the first example of conjugate borylation with platinum as the metal catalyst (eq. 1, Scheme 2.7).[82] The reaction mechanism was believed to proceed through oxidative addition of B-B bond of B_2pin_2 to the metal enter, followed by coordination of Michael acceptor and β-migratory insertion. Subsequent reductive

[80] List, B.; Lerner, R. A.; Barbas, C. F. III. *J. Am. Chem. Soc.* **2000**, *122*, 2395.
[81] Bahmanyar, S.; Houk, K. N.; Martin, H. J.; List, B. *J. Am. Chem. Soc.* **2003**, *125*, 2475.
[82] Lawson, Y. G.; Lesley, M. J. G.; Marder, T. B.; Norman, N. C.; Rice, C. R. *Chem. Commun.* **1997**, 2051.

elimination would then afford the α-boryl ketone intermediate which then rapidly tautomerizes to the 1,4-bis(boronate) ester product. Finally, the 1,4-bis(boronate) ester then undergoes protodeboronation with the addition of water, and affords the β-boryl ketone. After the report on Pt-catalyzed conjugate borylation, Hosomi reported the first Cu^{I}-catalyzed conjugate borylation reaction (eq. 2, Scheme 2.7).[83] While no effort to engender enantioselectivity was shown in this first report, it spurred the development of numerous enantioselective variants relying on similar reaction conditions years later.

Scheme 2.7 Selected Early Examples of Conjugate Borylation Reactions.

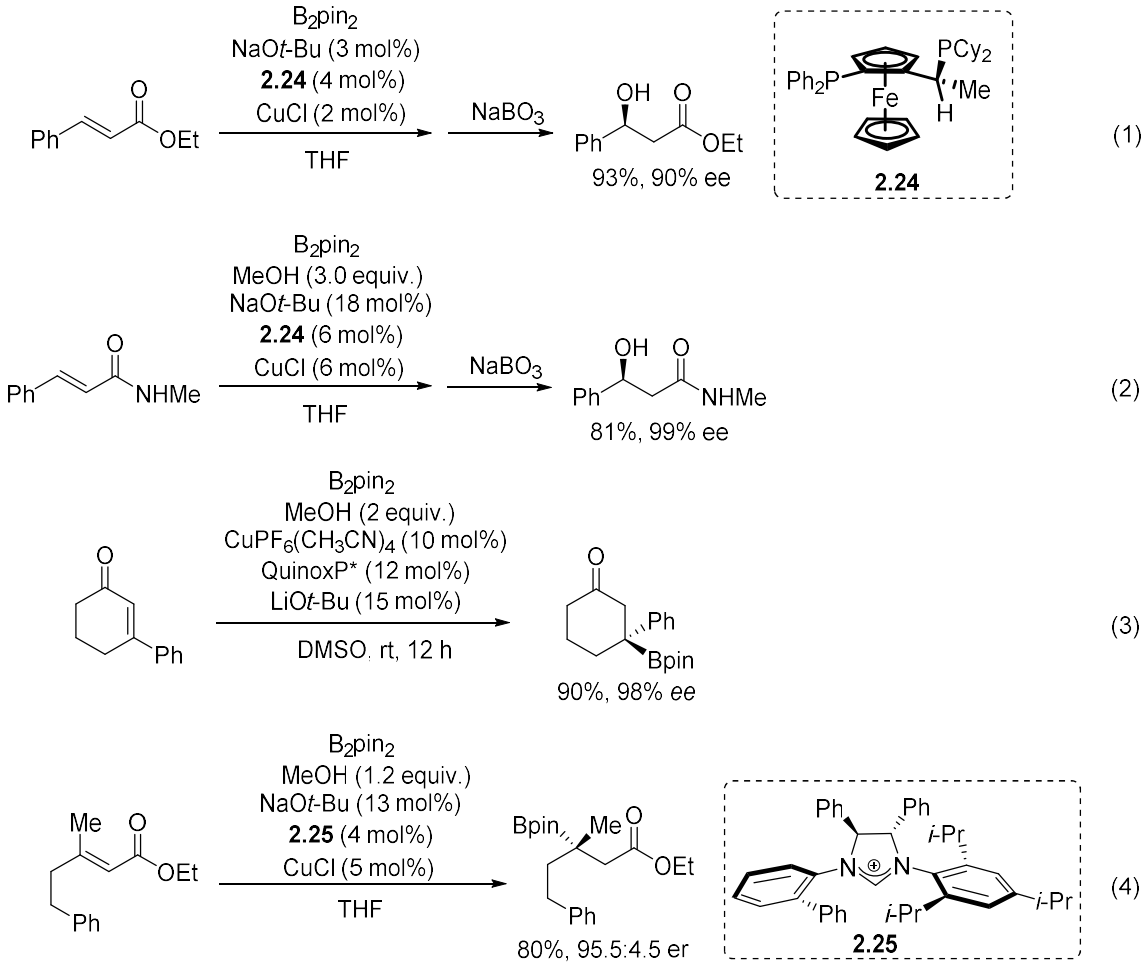


In 2008, Yun used a copper catalyst and Josiphos ligand **2.24** to accomplish the first enantioselective conjugate borylation of α,β-unsaturated esters (eq. 1, Scheme 2.8).[84] The same catalyst system was later shown to be competent with α,β-unsaturated amide substrates (eq. 2, Scheme 2.8).[85] One challenge in this field involves the use of β,β-disubstituted carbonyls as substrates. Due to the increased steric hindrance, coordination

[83] Ito, H.; Yamanaka, H.; Takeiwa, J.-I.; Hosomi, A. *Tetrahedron Lett.* **2000**, *41*, 6821.
[84] Lee. J.-E.;Yun, J.; *Angew. Chem. Int. Ed.* **2008**, *47*, 145.
[85] Chea, H.; Sim, H.-S.; Yun, J. *Adv. Synth. Catal.* **2009**, *351*, 855.

of these substrates to the metal center is more problematic. In addition, achieving high enantioselectivity is inherently more difficult as the chiral metal catalyst would have to differentiate between sterically similar β-substituents. Nonetheless, enantioselective conjugate borylation of both cyclic as well as acyclic β,β-disubstituted carbonyls have been reported independently by both Shibasaki[86] and Hoveyda[87] (eq. 3 & 4, Scheme 2.8).

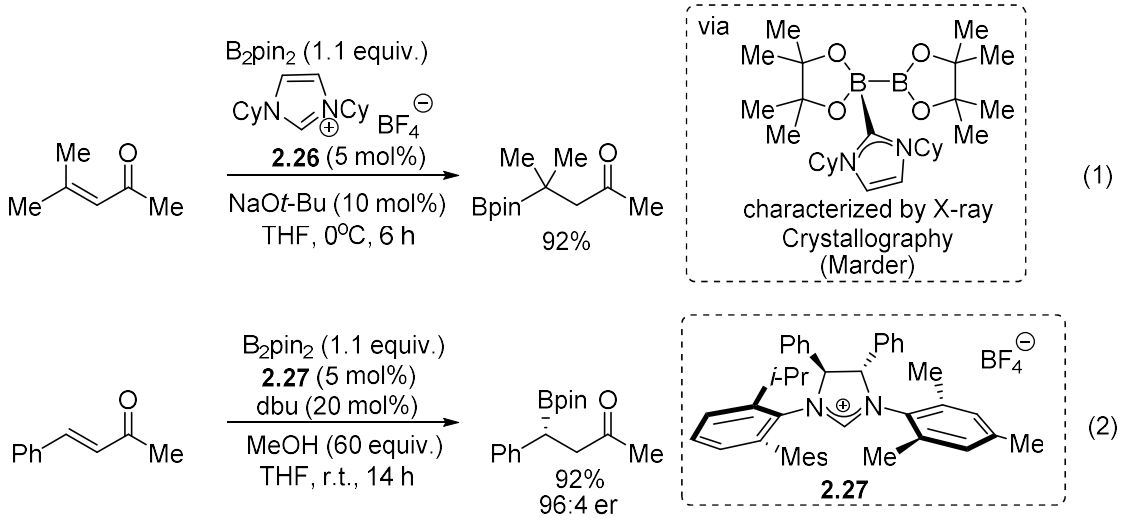
Scheme 2.8 Selected Examples of Enantioselective Conjugate Borylation Reactions.



[86] Chen, I.-H.; Yin, L.; Itano, W.; Kanai, M,; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 11664.
[87] O'Brien, J. M.; Lee, K.-S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10630.

Another breakthrough in this field was achieved by Hoveyda and co-workers when they discovered that a N-heterocyclic carbene alone can be the catalyst without any transition metal (eq. 1, Scheme 2.9).[88] The NHC was proposed to associate with one of the boron groups of B_2pin_2, activating it for nucleophilic attack onto α,β-unsaturated ketones. DFT calculations supported this hypothesis and showed that NHC association would lengthen the B-B bond as well as shift electron density towards the uncomplexed boron atom. Later, Marder provided further support for the proposed mechanism when they determined X-ray crystal structures of the NHC-bound diboron complex.[89] In 2015, Hoveyda and co-workers were able to identify a suitable chiral NHC ligand for enantioselective conjugate borylation reaction.[90] The scope of this reaction was shown to tolerate α,β-unsaturated ketones, esters, amides, and aldehydes (eq. 2, Scheme 2.9).

Scheme 2.9 Metal-Free NHC-Catalyzed Conjugate Borylation Reactions.



[88] Lee, K.-S.; Zhugralin, A. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 7253.
[89] Kleeberg, C.; Crawford, A. G.; Batsanov, A. S.; Hodgkinson, P.; Apperley, D. C.; Cheung, M. S.; Lin, Z.; Marder, T. B. *J. Org. Chem.* **2012**, *77*, 785.
[90] Wu, H.; Garcia, J. M.; Haeffner, F.; Radomkit, S.; Zhugralin, A. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2015**, *137*, 10585.

2.2.3 Carboxylic Acid Derivatives in Catalytic Cross-Coupling Reactions

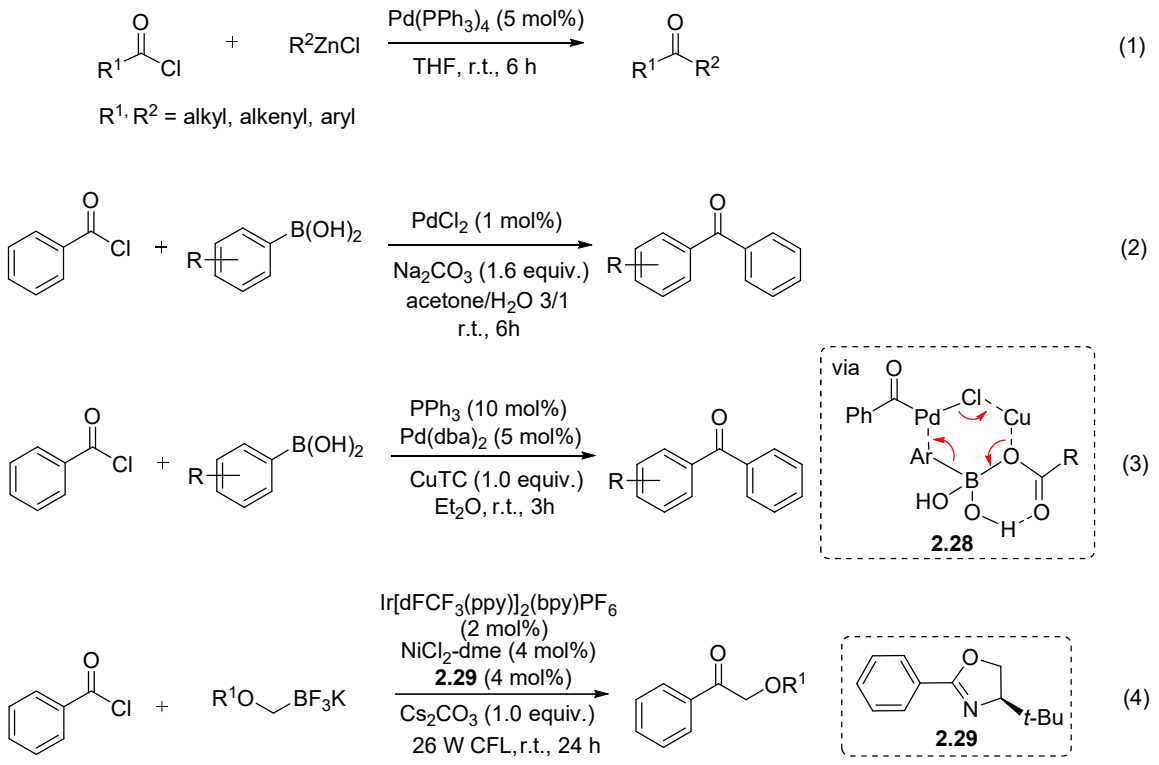
Carboxylic acids are one of the most ubiquitous functional groups in natural products. For this reason, methods to transform this functional group could be of value for the derivatization of natural compounds, and the expansion of new chemical space. Carboxylic acids can be conveniently transformed to activated carboxylic derivatives, such as acyl chlorides, fluorides, anhydrides, esters, or thioesters. In recent years, these carboxylic derivatives have found their use as coupling partners in transition-metal catalyzed cross-coupling reactions. Depending on the specific reaction conditions and ligands being used, these processes may proceed either *via* direct coupling pathway (without decarbonylation) or by a decarbonylative coupling pathway.

Palladium-catalyzed direct cross-coupling reactions of acyl chlorides have been demonstrated as an effective strategy to synthesize unsymmetrical ketones.[91] One of the earliest examples involved the use of acyl chlorides as electrophiles in Negishi cross-coupling reactions (eq. 1, Scheme 2.10).[92] Years later, Bumagin and co-workers first demonstrated the use of acyl chlorides in Suzuki-Miyaura coupling reaction with organoboronic acids as the nucleophilic coupling partner (eq. 2, Scheme 2.10).[93] Since then, Nishihara and co-workers reported modified reaction conditions in which a stoichiometric amount of copper (I) thiophene-2-carboxylate (CuTC) was added as an activator (eq. 3, Scheme 2.10).[94] The new conditions are more tolerant to a wide range of

[91] For a review on Suzuki-Miyaura coupling with acyl electrophiles, see : Blangetti, M.; Rosso, H.; Prandi, C.; Deagostino A.; Venturello, P. *Molecules* **2013**, *18*, 1188.
[92] Negishi, E.-i.; Bagheri, V.; Chatterjee, S.; Luo, F.-T.; Miller, J. A. Stoll, A. T. *Tetrahedron Lett.* **1983**, *24*, 5181.
[93] Bykov, V.V.; Korolev, D. N.; Bumagin, N. A. *Russ. Chem. Bull.* **1997**, *46*, 1631.
[94] Nishihara, Y.; Inoue, Y.; Fujisawa, M.; Takagi, K. *Synlett* **2005**, *46*, 7627.

substrates containing both electron-donating and withdrawing substituents. The enhanced performance was ascribed to a more facile transmetallation, which was proposed to proceed by a six-membered transition state resembling **2.28**. CuTC was proposed to have a dual function of polarizing the Pd-Cl bond while also activating the boronic acid in the transition state of transmetallation. More recently, Molander and co-workers reported the photoredox/nickel dual catalysis coupling a variety of acyl chlorides and potassium alkyltrifluoroboronates under mild conditions (eq. 4, Scheme 2.10).[95]

Scheme 2.10 Utility of Acyl Chlorides in Catalytic Cross-Coupling Reactions.

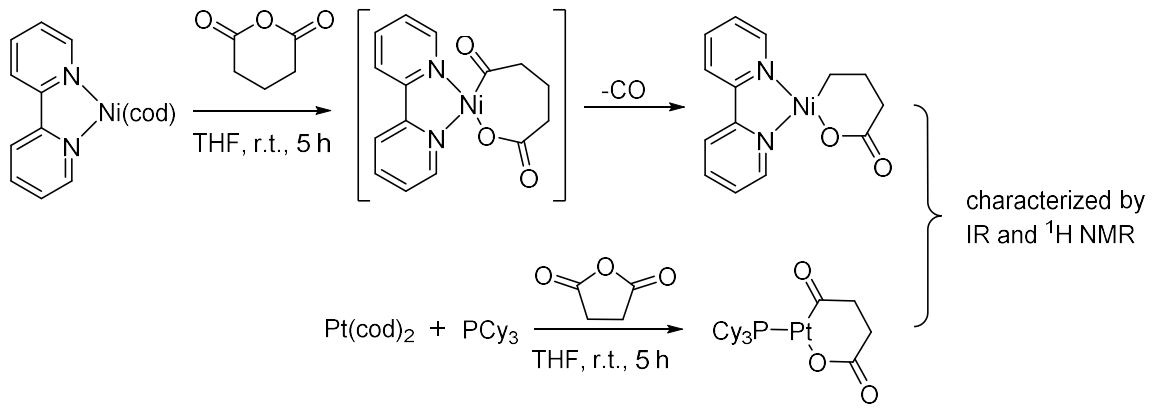


Another class of acyl electrophile that is commonly employed in cross-coupling is the anhydride. Early mechanistic evidence of oxidative addition of anhydrides to transition

[95] Amani, J.; Sodagar, E.; Molander, G. A. *Org. Lett.* **2016**, *18*, 732.

metals was gathered by Yamamoto and co-workers when they isolated and characterized the oxidative addition adduct derived from platinum and the decarbonylated oxidative addition adduct derived from nickel (Scheme 2.11).[96]

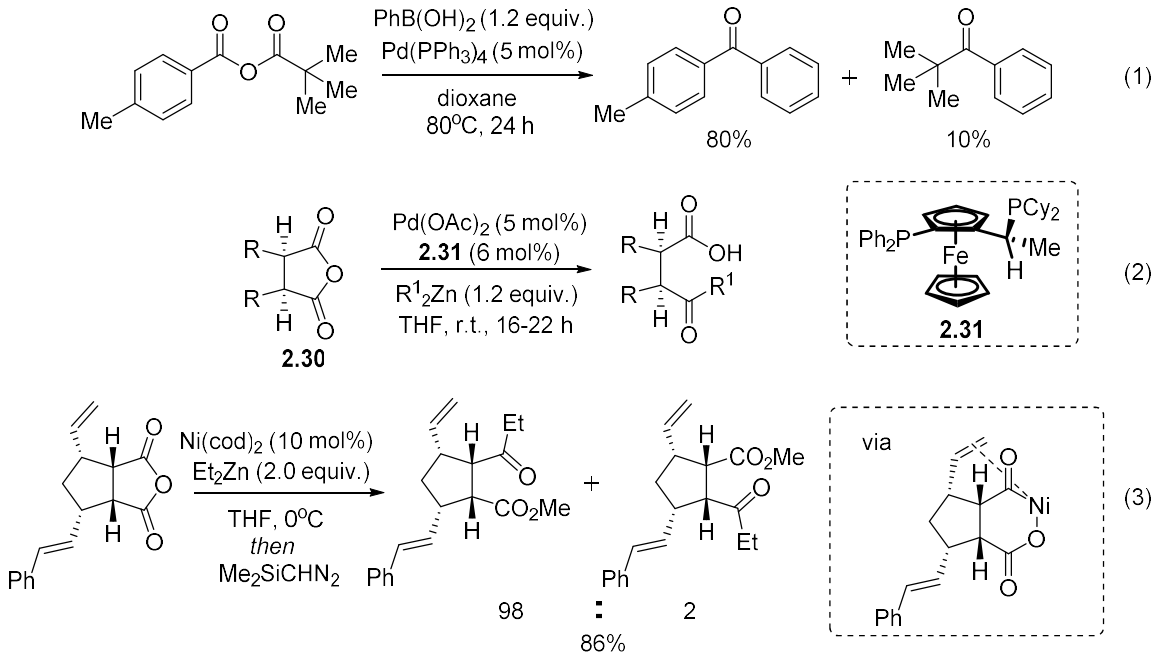
Scheme 2.11 Evidence of Oxidative Addition of Anhydride to Transition Metals.



When unsymmetrical anhydrides were utilized, palladium was shown to undergo oxidative addition selectively at the carbonyl with less steric hindrance (eq. 1, Scheme 2.12).[97] Cyclic anhydrides were also suitable substrates. In cases when substituted *meso*-succinic anhydrides were used as substrates (eq. 2, Scheme 2.12), desymmetrization to afford chiral non-racemic ring-opened products could be achieved, with oxidative addition being the stereochemistry-determining step of the catalytic cycle.[98] Interestingly, an anhydride such as **2.30** exhibits substrate-dependence of regioselectivity when nickel was used as the catalyst (eq. 3, Scheme 2.12).[99] It was proposed to derive from the more facile coordination of terminal alkene as compared to di-substituted *trans*-alkene for directing oxidative addition with the proximal carbonyl of anhydride.

[96] Sano, K.; Yamamoto, T.; Yamamoto, A. *Chem. Lett.* **1983**, 115.
[97] Ryuki, K.; sayaka, Y.; Isao, S.; Akio, Y. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 137.
[98] Bercot, E. A.; Rovis, T. *J. Am. Chem. Soc.* **2004**, *126*, 10248.
[99] Rogers, R. L.; Moore, J. L.; Rovis, T. *Angew. Chem. Int. Ed.* **2007**, 46, 9301.

Scheme 2.12 Utility of Anhydrides in Catalytic Cross-Coupling Reactions.

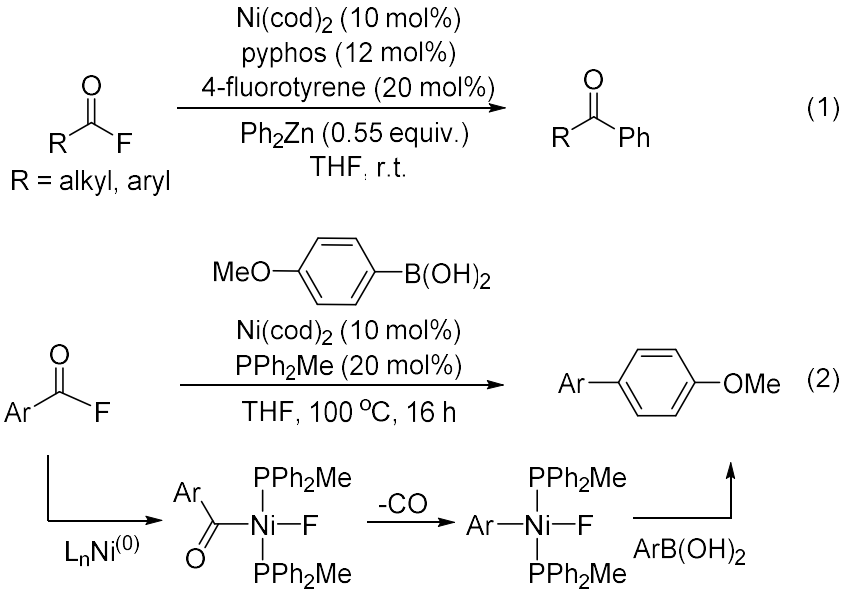


2.2.4 Utility of Acyl Fluoride in Catalytic Cross-Coupling Reactions.

Acyl fluorides can easily be synthesized from the corresponding carboxylic acids, chlorides, as well as anhydrides. In addition, acid fluorides share the advantages of being stable to water and neutral oxygen nucleophiles over acyl chlorides and anhydrides. For this reason, acyl fluorides can often be isolated via aqueous workups and purified by silica gel column chromatography. Because of its ease of preparation, its use in catalytic cross-coupling reactions has been studied by a handful of research groups. Acyl fluorides were first demonstrated to undergo nickel-catalyzed Negishi cross-coupling reaction by Rovis

in 2004 (eq. 1, Scheme 2.13).[100] Remarkably, with the special pyphos ligand, the reaction was found to proceed to full conversion within 30 minutes at room temperature. More recently, Sanford reported a decarbonylative Suzuki-Miyaura coupling of acyl fluorides (eq.2, Scheme 2.13).[101] This reaction offers the advantage of not requiring exogenous base for transmetallation, as Ni(II)-F species generated after decarbonylation is transmetallation-active. For this reason, this reaction is tolerant to a wide variety of base-sensitive organoboronic acids.

Scheme 2.13 Utility of Acyl Fluoride in Catalytic Cross-Coupling Reactions.



[100] Zhang, Y.; Rovis, T. *J. Am. Chem. Soc*. **2004**, *126*, 15964.
[101] Malapit, C. A.; Bour, J. R.; Brigham, C. E.; Sanford, M. S. *Nature*, **2018**, *563*, 100.

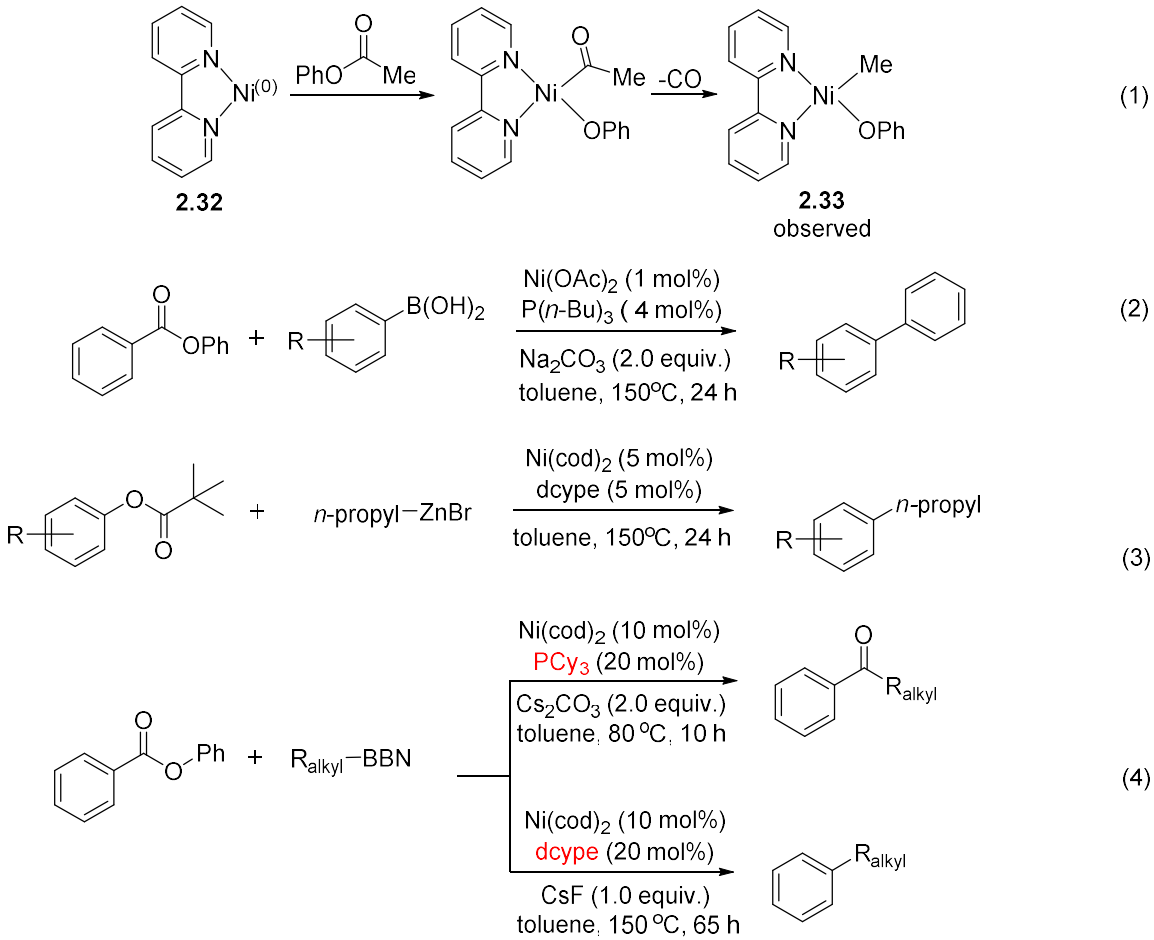
2.2.5 Activation of Ester by Nickel

As mentioned in the previous chapter, the relatively high electropositivity of nickel allows it to undergo oxidative addition with electrophiles that are less reactive with palladium. Esters are among the least reactive electrophiles due to their stabilizing resonance effects. Nevertheless, in 1980, Yamamoto and co-workers reported a stochiometric nickel-mediated decarbonylative coupling reaction with phenyl carboxylates.[102] The oxidative addition/decarbonylation sequence was supported by the observation of (bipy)NiMe(OPh) species **2.33** upon mixing zero-valent nickel **2.32** and aryl phenylcarboxylate. Since this pioneering work by Yamamoto, numerous research groups investigated the use of esters in catalytic cross-coupling reactions with various nucleophilic reagents. For examples, Itami and co-workers reported the use of esters in the decarbonylative coupling reaction with aryl boronic acids (eq. 2, Scheme 2.14).[103] Later, Rueping reported the first nickel-catalyzed alkylation of esters with organozinc reagents (eq. 3, Scheme 2.14).[104] Not long after this report, the same group reported the use of 9-BBN reagents as the coupling partner (eq. 4, Scheme 2.14).[105] They observed a ligand-dependent chemoselectivity under their reaction system. While bidentate dcype ligand selectively gave the decarbonylative coupling product in high yield, the use of monodentate P*n*-Bu$_3$ ligand exclusively gave the direct coupling product. DFT calculations revealed that whereas bidentate ligand would favor bond activation at the C(aryl)-C site, monodentate

[102] Yamamoto, T.; Ishizu, J.; Kohara, T.; Komiya, S.; Yamamoto A. *J. Am. Chem. Soc.* **1980**, *102*, 3758.
[103] Muto, K.; Yamaguchi, J.; Musaev, D. G.; Itami, K. *Nat. Commun.* **2015**, 7508.
[104] Liu, X.; Jia, J.; Rueping, M. *ACS Catal.* **2017**, *7*, 4491.
[105] Chatupheeraphat, A.; Liao, H.-H.; Srimontree, W.; Guo, L.; Minenkov, Y.; Poater, A.; Cavallo, L.; Rueping, M. *J. Am. Chem. Soc.* **2018**, *140*, 3724.

ligand favors oxidative addition at the C(acyl)-O site with no CO extrusion before transmetallation. After the demonstration of decarbonylative coupling reaction of ester with alkyl nucleophiles, this reactivity has since been successfully extended to other nucleophiles to allow for C-CN bond, C-Si bond, and C-B bond forming transformations.[106,107]

Scheme 2.14 Utility of Ester in Nickel Catalyzed Cross-Coupling Reactions.



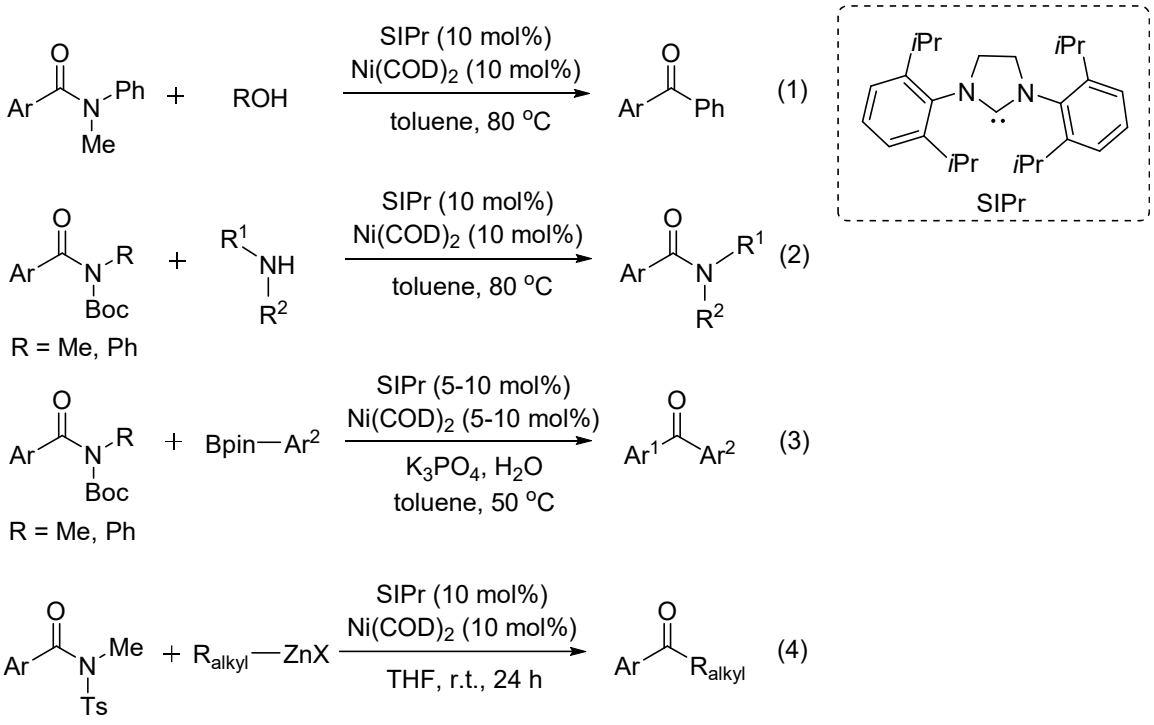
[106] Pu, X.; Hu, J.; Zhao, Y.; Shi, Z. *ACS Catal.* **2016**, *6*, 6692.
[107] Chatupheeraphat, A.; Liao, H.-H.; Lee, S.-C.; Rueping, M. *Org. Lett.* **2017**, *19*, 4255.

2.2.6 Activation of Amides by Nickel

Although amides are traditionally considered to be an inert electrophile due to similar stabilizing resonance effects observed with esters, several research groups managed to activate this electrophile with nickel catalysis. In this regards, Garg and co-workers were among the first to demonstrate the capability of nickel to undergo oxidative addition with amides through a series of cross-coupling reactions. Under the regime of nickel catalysis, they convert amides to esters under milder reaction conditions[108] than are used for classical alcoholysis conditions which require the use of either strong base or acid, as well as excess heat and nucleophiles (eq. 1, Scheme 2.15). Since this first report, the reaction conditions for alcoholysis were applied to trans amidation (eq. 2, Scheme 2.15)[109] as well as coupling reactions with organoboronic esters (eq. 3, Scheme 2.15)[110] and organozinc reagents (eq. 4, Scheme 2.15).[111]

Scheme 2.15 Utility of Amide in Nickel Catalyzed Cross-Coupling Reactions.

[108] Hie, L.; Fine Nathel, N. F.; Shah, T. K.; Baker, E. L.; Hong, X.; Yang, Y.-F.; Liu, P.; Houk, K. N.; Garg, N. K. *Nature* **2015**, *524*, 79.
[109] Dander, J. E.; Baker, E. L.; Garg, N. K. *Chem. Sci.* **2017**, *8*, 6433.
[110] Weires, N. A.; Baker, E. L.; Garg, N. K. *Nat. Chem.* **2015**, *8*, 75.
[111] Simmons, B. J.; Weires, N. A.; Dander, J. E.; Garg, N. K. *ACS Catal.* **2016**, *6*, 3176.



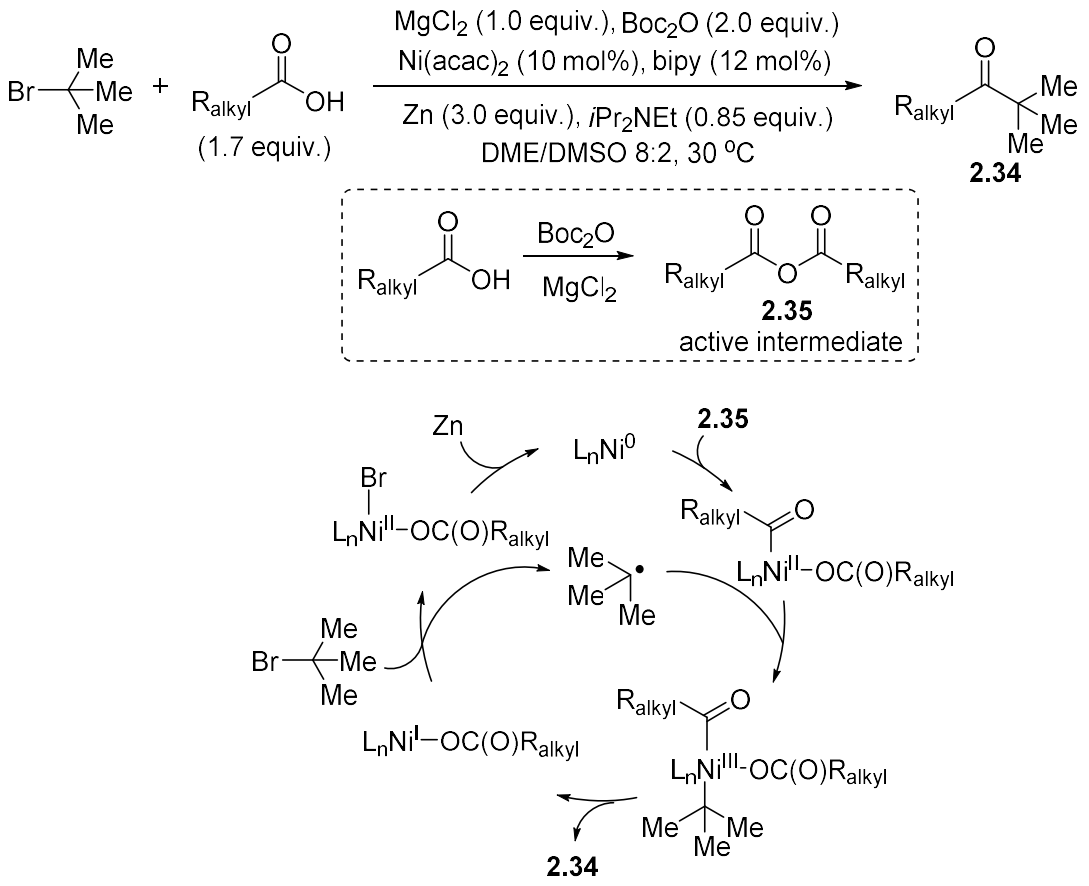
2.2.7 Acyl Electrophiles in Ni-Catalyzed Reductive Cross-Coupling Reactions

As shown in previous sections, both nickel and palladium share comparable capacity to undergo oxidative addition with acyl chlorides and anhydrides. However, unique reactivity of nickel could allow it to engage these same acyl electrophiles in transformations that are not available to palladium. For example, the ability of nickel to engage in non-polar radical reaction pathway allows it to catalyze reductive cross-coupling reaction between an acyl electrophile and another C(sp^3)-electrophile. As reported by Gong and co-workers, anhydrides and tertiary aliphatic bromides can engage in nickel-catalyzed reductive cross-coupling reaction in the presence of a stoichiometric amount of reductant (Scheme 2.16).[112]

[112] Zhao, C.; Jia, X.; Wang, X.; Gong, H. *J. Am. Chem. Soc.* **2014**, *136*, 17645.

Oxidative addition of anhydrides to nickel was proposed to precede radical combination of carbon-centered radical before reductive elimination to generate the ketone product **2.33**.

Scheme 2.16 Nickel-Catalyzed Reductive Cross-Coupling with Anhydrides.

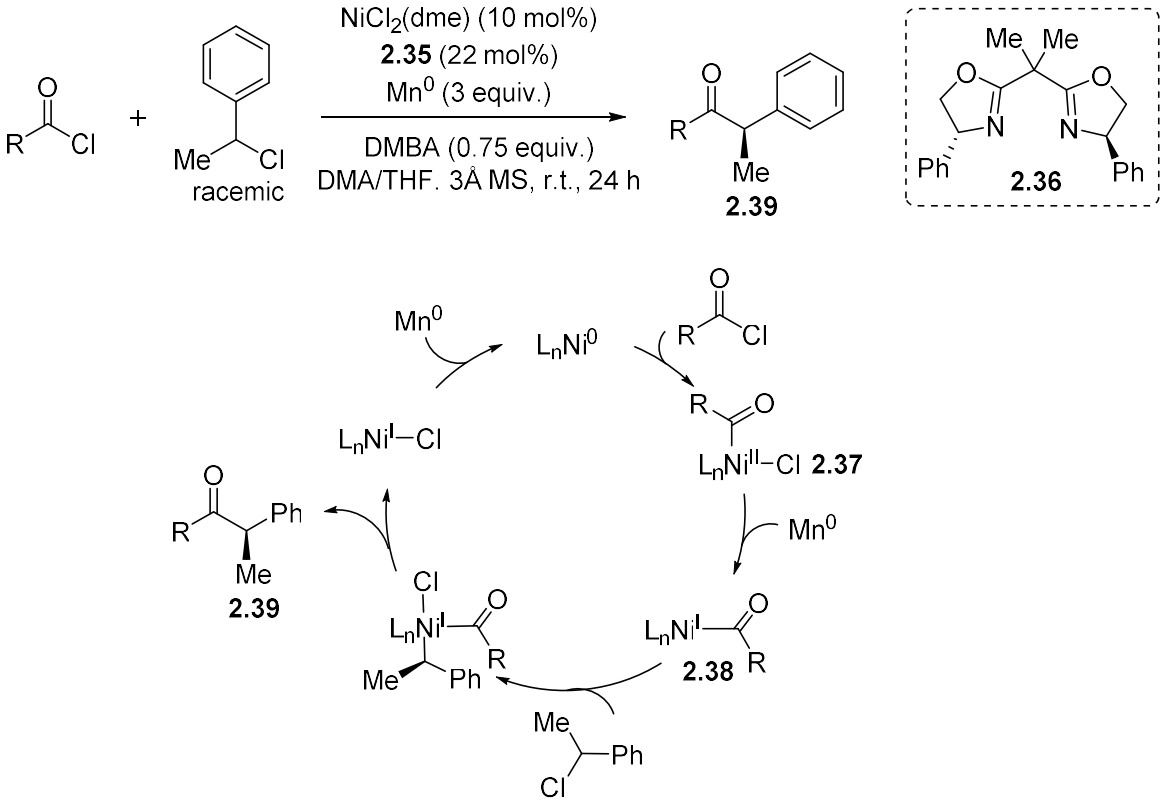


The first enantioselective reductive coupling between acyl chlorides and benzylic chlorides was reported by Reisman in 2013.[113] The mechanism was proposed to proceed with a different mechanism from Gong's reductive coupling with anhydrides. Similar acyl oxidative addition adduct **2.37** would be reduced by Mn^0 to give Ni^I-acyl intermediate **2.38**.

Subsequent enantioconvergent oxidative addition of allylic chloride by a radical pathway followed by reductive elimination would afford the ketone product **2.39**.

[113] Cherney, A. H.; Kadunce, N. T.; Reisman, S. E. *J. Am. Chem. Soc.* **2013**, *135*, 7442.

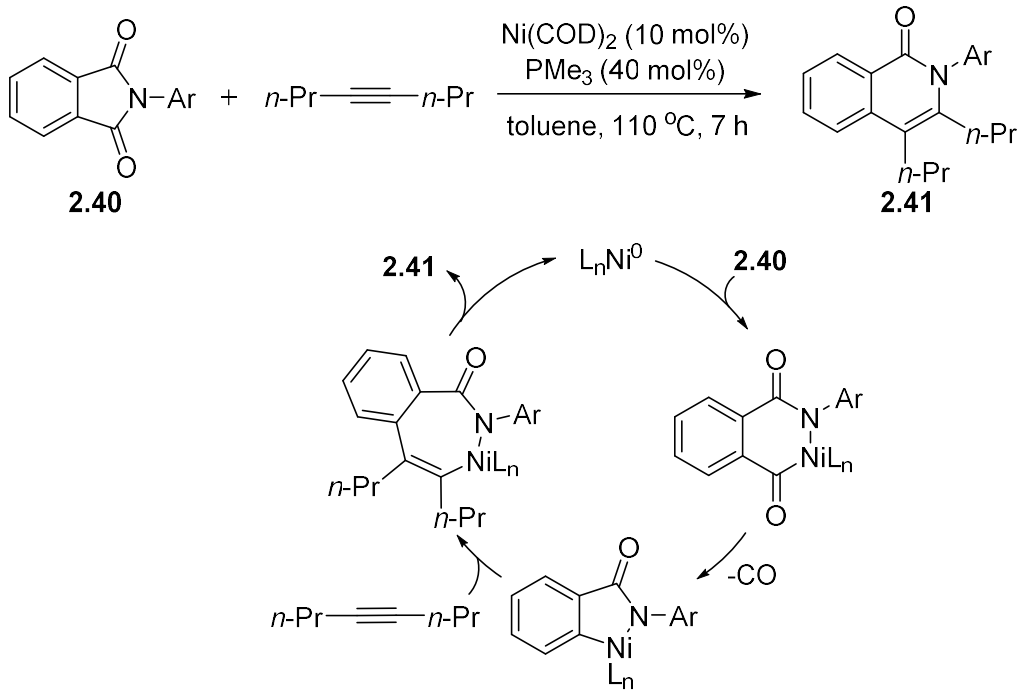
Scheme 2.17 Nickel-Catalyzed Reductive Cross-Coupling with Acyl Chlorides.



Last but not least, the ability of nickel to easily bind to unsaturated molecules also allows for the tandem decarbonylative addition of N-arylphthalimide **2.40** followed by insertion of alkynes to afford isoquinolone **2.41** (Scheme 2.18).[114]

[114] Shiba, T.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2013**, *135*, 13636.

Scheme 2.18 Decarbonylative Addition of Phthalimides to Alkynes.

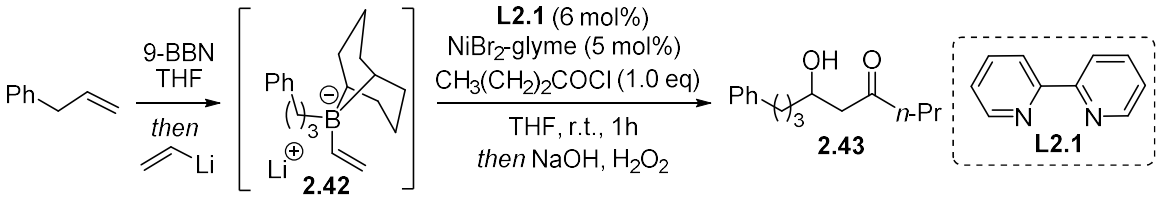


2.3 CATALYTIC CONJUNCTIVE COUPLING OF CARBOXYLIC ACID DERIVATIVES WITH 9-BBN ATE COMPLEXES

2.3.1 Initial Investigations

The idea of developing a conjunctive cross-coupling reaction with acyl electrophiles was inspired by the literature showing that nickel complexes undergo oxidative addition with carboxylic acid derivatives, either in the context of acylative, decarbonylative, or reductive cross-coupling reactions discussed in the previous section. While preliminary experiments with pinacolatoboron-derived reagent yielded a complex mixture with only trace desired product, a promising result was obtained with the corresponding 9-BBN borate complex **2.42** as the nucleophilic partner (Scheme 2.19, entry 1). Reaction between butanoyl chloride and 9-BBN borate complex **2.42** in the presence of $NiBr_2$-glyme and bipyridine ligand **L2.1** afforded the desired β-hydroxy carbonyl **2.43** with 65% yield after oxidative workup. Control experiments showed that background reaction in the absence of nickel precatalyst or bipyridine ligand was minimal, even after stirring at room temperature overnight (Scheme 2.19, entry 2 & 3).

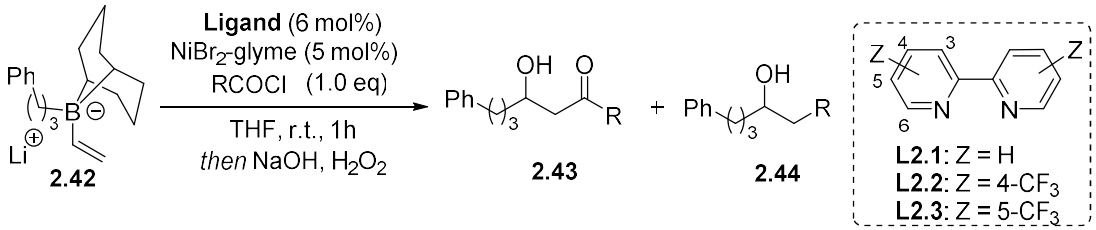
Scheme 2.19. Initial Results of Ni-Catalyzed Conjunctive Coupling of Acid Chloride.



Entry	variation from above	yield (%)
1	none	65
2	no $NiBr_2$-glyme	<5
3	no **L2.1**	<5

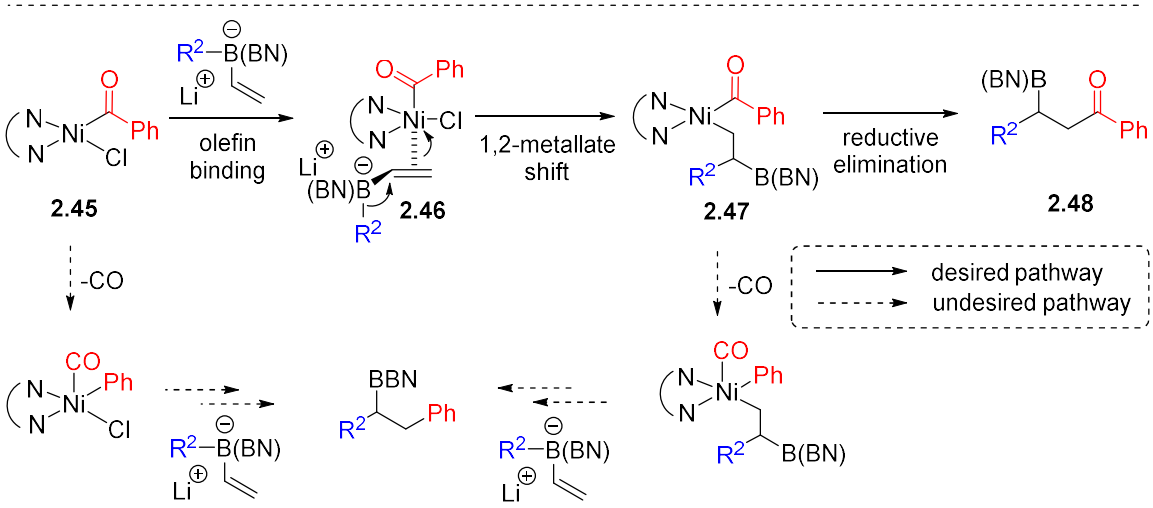
The yield of the desired product was diminished when benzoyl chloride was used instead as the electrophile. In this case, the crude reaction mixture after oxidative workup was found to comprise mostly the desired alcohol **2.43** as well as some decarbonylative coupling product **2.44** (Scheme 2.20, entry 1). We reasoned that the undesired decarbonylation pathway would compete with the elementary steps of 1,2-metallate rearrangement and/or reductive elimination. Thus, we sought to employ a more electrophilic ligand on the nickel catalyst, which should accelerate both the 1,2-metallate rearrangement (**2.45** to **2.46**) and the reductive elimination (**2.47** to **2.48**). Indeed, improved yield of product was observed by installing the electron-withdrawing trifluoromethyl substituent on the backbone of bipyridine (Scheme 2.20, entry 2 & 3). The most generally applicable reaction conditions then employed the use of 5,5'-bis(trifluoromethyl)-2,2'-bipyridine **L2.3** as ligand, which affords high yield of the desired product with both aliphatic and aryl acid chlorides (Scheme 2.20, entry 3 & 4). Remarkably, the reaction in the presence of **L2.3** so highly efficient that it could achieve full conversion within two minutes at room temperature (Scheme 2.20, entry 5).

Scheme 2.20 Results with Ni-Catalyzed Conjunctive Coupling of Benzoyl Chloride.



Entry	R	Ligand	2.43 (%)	2.44 (%)
1	Ph	**L2.1**	40	23
2	Ph	**L2.2**	65	10
3	Ph	**L2.3**	75	12
4	*n*-propyl	**L2.3**	78	<5
5[a]	*n*-propyl	**L2.3**	75	<5

[a] reaction was run for 2 minutes before oxidative workup.



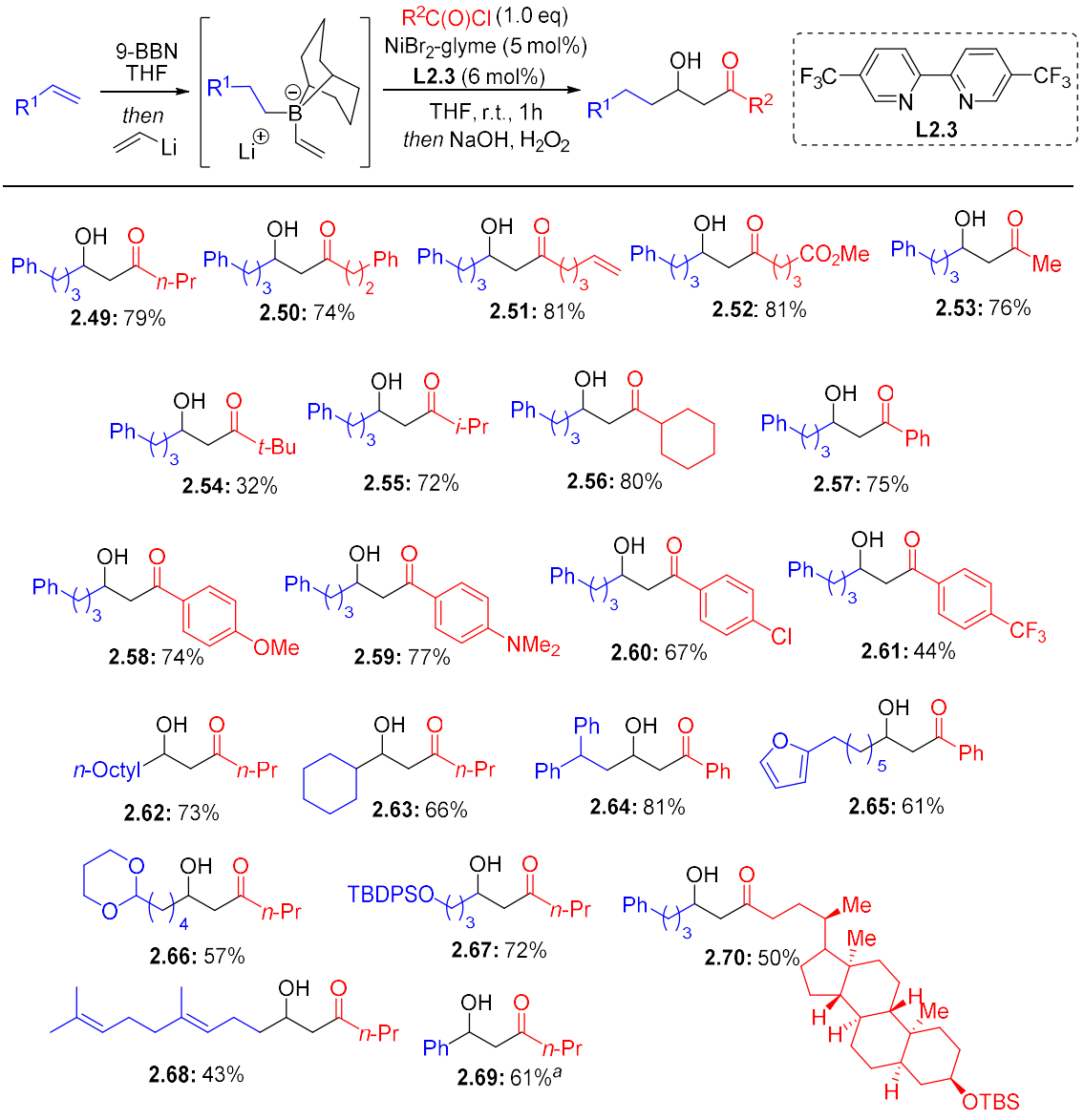
2.3.2 Scope of Ni-Catalyzed Conjunctive Coupling with Acid Derivatives

To survey the substrate scope, a range of 9-BBN derived borate complexes were prepared by the hydroboration of the corresponding alkenes in THF, and treatment with vinyllithium, and then employed in an one-pot reaction (Scheme 2.21). Treatment of the

"ate" complex with pre-mixed $NiBr_2$-glyme and **L3** in the presence of acyl chloride electrophiles, followed by stirring at room temperature for 1 h and oxidative workup afforded the corresponding β-hydroxy ketones. As seen in Scheme 2.21, the reaction with acetyl (**2.53**), linear (**2.49-2.52**), and α-branched (**2.53-2.56**) acyl chlorides afforded products in good yields, although only moderate yield was observed when the sterically demanding pivaloyl chloride (**2.54**) was employed in the reaction. Acyl chloride derived from TBS-protected lithocholic acid (**2.70**) can also be subjected to the reaction conditions to afford the desired product in reasonable yield. Regarding the substrate tolerance with respect to aroyl chloride electrophiles, whereas benzoic chlorides (**2.57**) as well as substrates bearing electron-donating substituents in the *para*-position (**2.58**, **2.59**) reacted in good yields, diminished yield was observed with substrates bearing electron-withdrawing groups (**2.60**, **2.61**) in the same position. Migrating groups derived from various alkenes were also examined in the reaction. Secondary migrating group such as cyclohexyl group (**2.63**) was able to provide the desired product in reasonable yield with no observation of byproducts derived from the migration of the bicyclooctyl ligand of 9-BBN. Migrating groups with appended alkene (**2.68**), acetal (**2.66**), as well as silyl enol ether (**2.67**) can also be tolerated. Lastly, it was shown that the 9-BBN borate complex derived from Ph-BBN (**2.69**) (synthesized from phenylmagnesium bromide and 9-BBN-OMe) can be employed in the reaction to give the corresponding product in good yield. It is worth noting that this method is complementary to the well-precedented aldol reaction. For example, compound **2.52** cannot be accessed with aldol reaction as the enolate of the corresponding methyl ketone is prone to intramolecular Dieckmann cyclization. In the case of compound **2.64**, the requisite aldehyde for an aldol reaction is not commercially

available whereas the corresponding alkene for conjunctive coupling is a cheap commercially available chemical ($3.8/g from Sigma Aldrich).

Scheme 2.21 Scope of Ni-Catalyzed Conjunctive Coupling of Acid Chlorides.

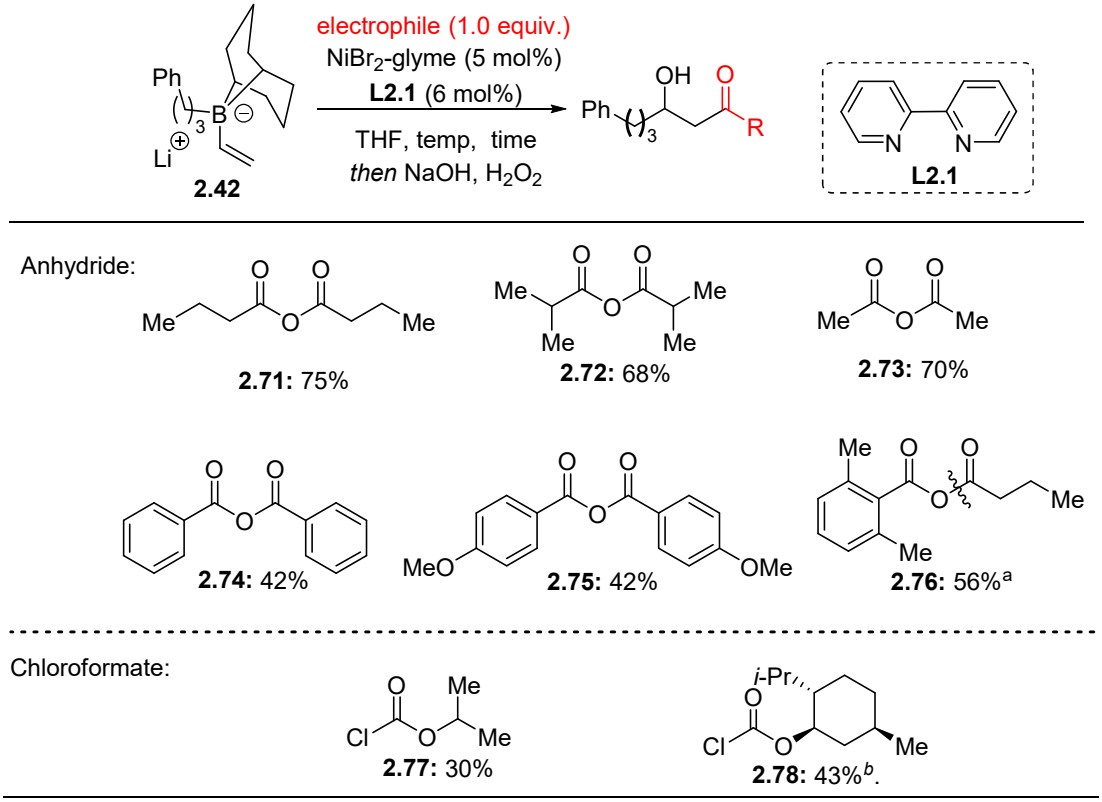


[a] The corresponding 9-BBN starting material was prepared from phenylmagnesium bromide and 9-BBN-OMe.

The compatibility of other classes of acyl electrophiles in conjunctive cross-coupling was also explored. When anhydride **2.71** was subjected to the optimized reaction

conditions for acyl chloride electrophiles, only trace quantity of desired products were observed. We reasoned that the oxidative addition of nickel to the anhydride is less facile as compared to its acyl chloride counterpart and this process should be facilitated by a more electron-rich metal center. Gratefully, the use of bipyridine ligand proved to be effective for conjunctive cross-coupling with anhydrides (Scheme 2.22). Mixed anhydride **2.76** is also an effective electrophile in the reaction, with coupling occurring with the less hindered carbonyl.[115] The same reaction system was also shown to work with moderate efficiency with chloroformates **2.77** & **2.78** to afford the corresponding β-hydroxy esters.

Scheme 2.22 Scope of Ni-Catalyzed Conjunctive Coupling with Acid Derivatives.



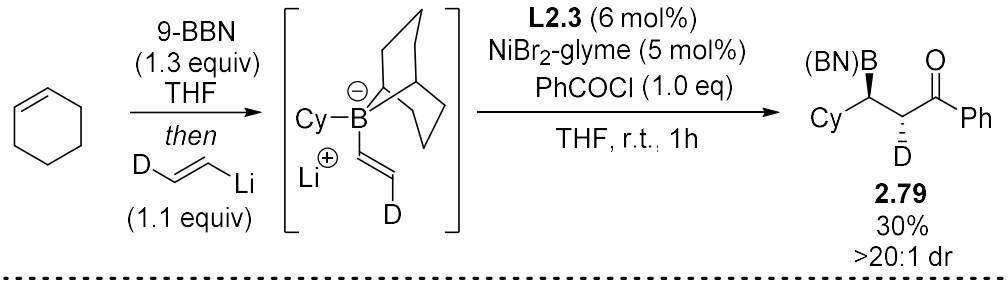
[a] Exclusively selective formation of product derived from the propionyl fragment.
[b] Product is isolated as a equal mixture of diasteromers.

[115] Joe, C. L.; Doyle, A. G. *Angew. Chem. Int. Ed.* **2016**, *55*, 4040.

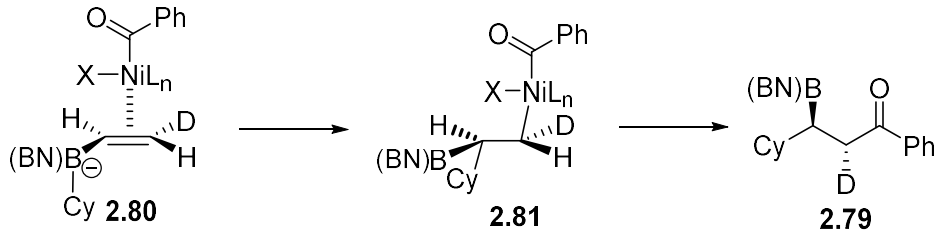
2.3.3 Mechanistic Studies

By subjecting isotopically labelled boron "ate" complex to the reaction conditions (Scheme 2.23), it was found that Ni-catalyzed coupling occurs stereospecifically by *anti* addition across the alkene. This observation is consistent with a mechanism involving nickel-induced metallate shift as opposed to a radical polar cross-over pathway[116], from which an equal mixture of diastereomeric β-boryl ketones would be expected.

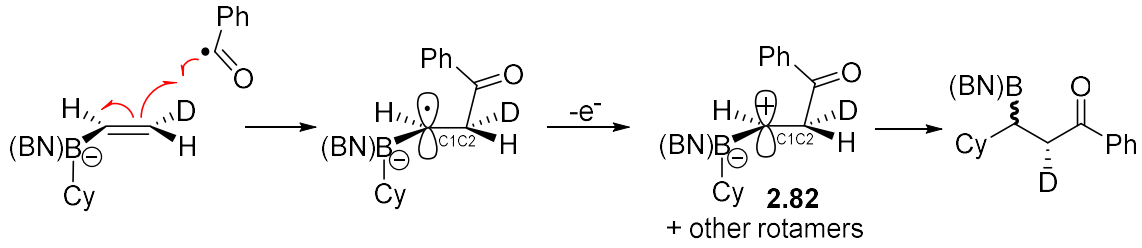
Scheme 2.22 Scope of Ni-Catalyzed Conjunctive Coupling with Acid Derivatives



1,2-metallate shift



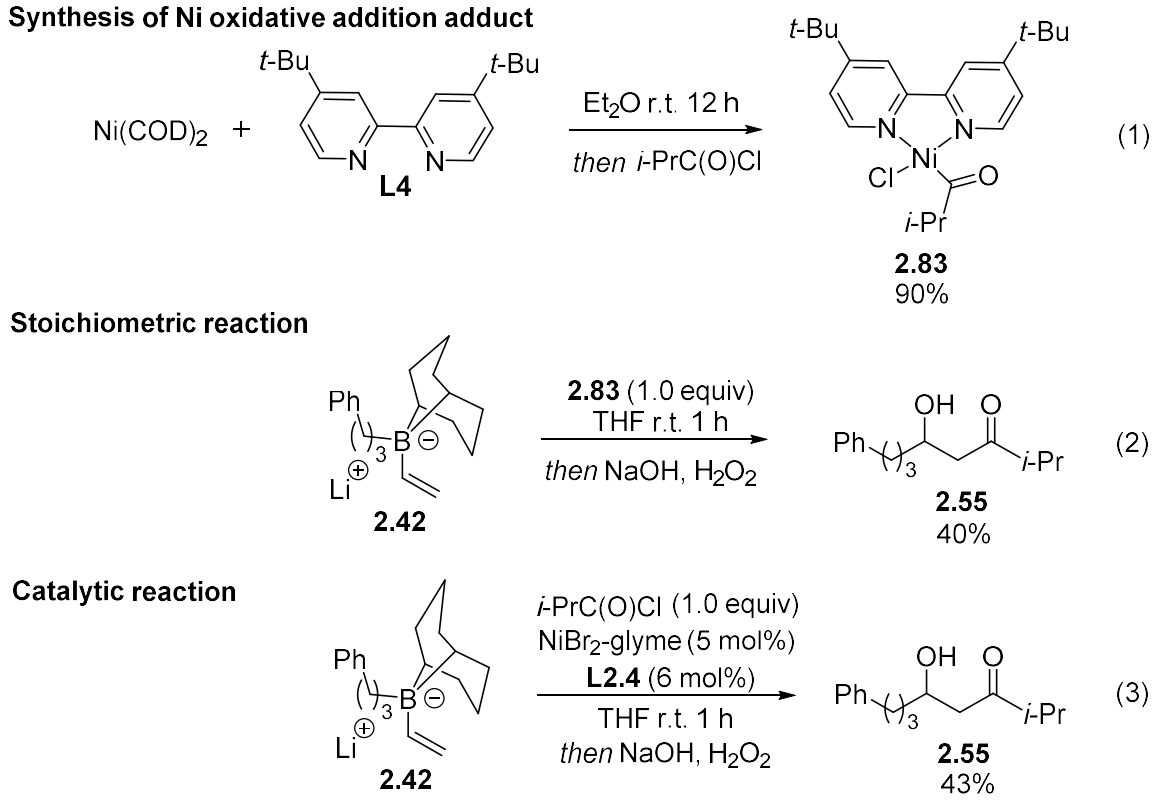
Possible radical polar cross-over pathway



[116] (a) Silvi, M.; Sandford, C.; Aggarwal V. K. *J. Am.Chem.Soc.* **2017**, *139*, 5736. (b) Kischkewitz, M.; Okamoto, K.; Mück-Lichtenfeld, C.; Studer, A. *Science* **2017**, *355*, 936.

To test if the Ni^0-Ni^{II} redox cycle can represent the operative mechanism, the oxidative addition adduct **2.83** was independently synthesized from mixing $Ni(COD)_2$, bipyridine ligand **L4**, and acid chloride.[117] It was then treated with stoichiometric amount of allylbenzene-derived borate complex **2.42**. As depicted in equations (3) and (4), the stoichiometric experiment furnished the conjunctive coupling product **2.55** in comparable yield as that obtained under the catalytic conditions, suggesting that the Ni^{II} oxidative addition adduct may be a competent intermediate in the conjunctive cross-coupling reaction.

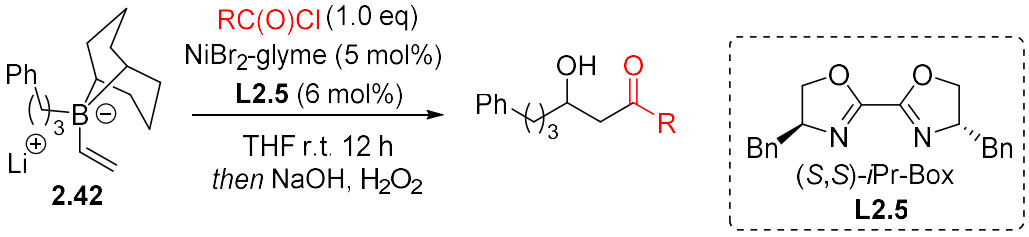
Scheme 2.23 Stoichiometric Experiment.



[117] Zhao, C.; Jia, X.; Wang, X.; Gong, H. *J. Am.Chem. Soc.* **2014**, *136*, 17645.

Lastly, as depicted in Scheme 2.24, a significant dependence of enantioselectivity on the identity of the electrophile was observed when (*S*,*S*)-*i*Pr-Box ligand **L2.6** was used with various acyl chloride electrophiles. We initially considered the possibility of a mechanism proceeding *via a* reversible, and stereo-determining 1,2-metallate shift followed by oxidative addition. However, DFT calculations previously reportd by our group suggests that the elementary step of 1,2-metallate shift is highly exothermic and irreversible under a similar Pd-catalyzed system.[118] We reasoned that the observation is more consistent with a scenario in which the electrophile associates with the Ni center before the stereochemistry-determining, and irreversible 1,2-metallate-shift.

Scheme 2.24 Mechanistic Insights from the Use of Chiral Bis(oxazoline) Ligand.



Entry	RC(O)Cl	Yield[a]	e.r.
1	PhC(O)Cl	36	60:40
2	*t*-BuC(O)Cl	27	51:49
3	*n*-PrC(O)Cl	43	64:36

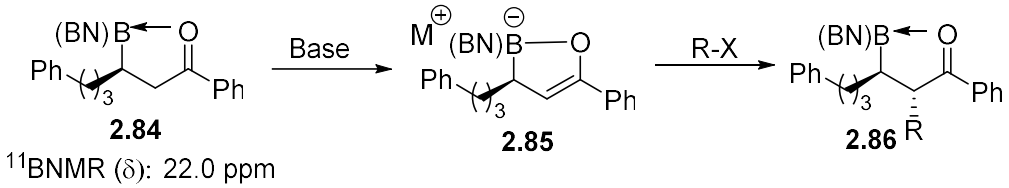
[a] Yield is after isolation by silica gel chromatography.

[118] Myhill, J. A.; Zhang, L.; Lovinger, G. J.; Morken, J. P. *Angew. Chem. Int. Ed.* **2018**, *57*, 12799.

2.3.4 Diasteroselective Boron-Enolate Alkylation

Although β-(pinacolato)boryl ketones have received ample study in the synthesis community, β-trialkyl (boryl)ketones are novel species and a study of their structure and chemistry was of interest. The ^{11}BNMR spectrum of β-boryl ketone **2.84** (δ 22.0 ppm) exhibits a upfield resonance relative to non-functionalized trialkyl borane (δ 70-80 ppm), indicating a tight chelation between boron and carbonyl oxygen atom.[119] We reasoned that this chelation would enhance the acidity of α-protons adjacent to the carbonyl moiety and allow for the formation of a rigid cyclic enolate structure such as **2.85** upon treatment with base, thus providing an opportunity for stereoselective alkylation.[120]

Scheme 2.25 Diastereoselective Boron-Enolate Alkylation.



2.84

^{11}BNMR (δ): 22.0 ppm

2.85

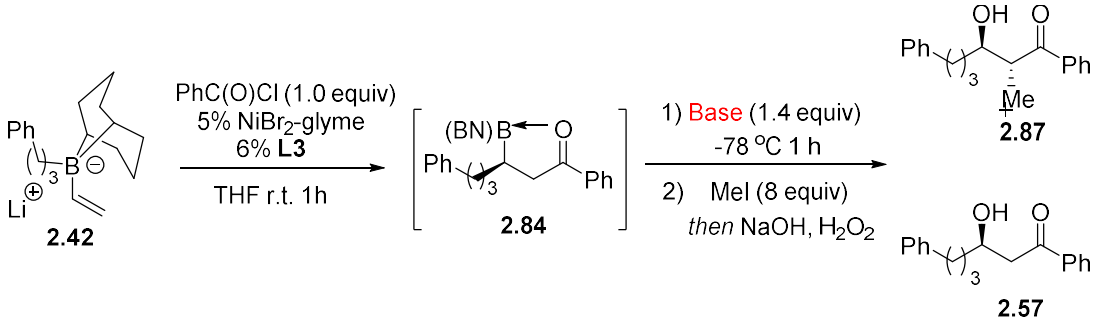
2.86

Our initial investigation commenced with the use of methyl iodide as electrophile and bases such as LDA and DIPEA, which are among the most common bases utilized in enolate alkylation reactions. In both cases, the reaction provided only non-alkylated β-hydroxy ketone **2.57** (derived from oxidation of **2.84**) with no desired alkylation product observed (Scheme 2.26, eq. 1 & 2). In a separate experiment, D_2O was added to the reaction

[119] Wrackmeyer, B.; Annu, Rep. NMR Spectrosc. **1988**, *20*, 61.
[120] Mechanistically related chelation-controlled enolate alkylations: a) Frµter, G.; Müller U.; Günther, W. *Tetrahedron* **1984**, *40*, 1269. b) Seebach, D.;Wasmuth, D. *Helv. Chim. Acta.* **1980**, *63*, 197.

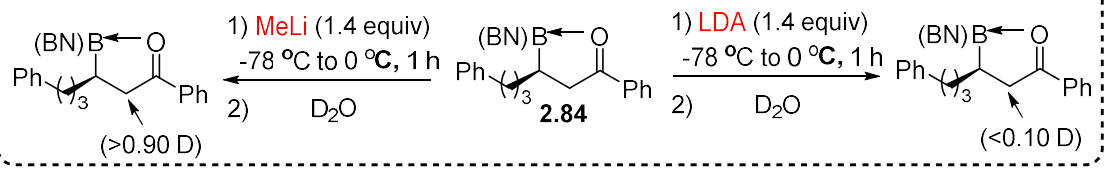
mixture after β-hydroxy ketone **2.84** was treated with LDA, and it was found that no deuterium was observed in the recovered starting material (Scheme 2.26, subtext). In contrast, significant deuterium incorporation at the α-carbon was observed when CH_3Li was used as the base. Thus, it appeared that the initial lack of reactivity observed with LDA could be due to the ineffective enolate formation rather than the inefficient reaction with the electrophile. At this point, we believe the use of less sterically hindered base is needed so as to avoid steric repulsion with the bicyclooctyl ring of **2.84** during deprotonation. Indeed, the desired alkylation product **2.87** could be obtained with reasonable yield and excellent *anti* diastereoselectivity when methyllithium was used as the base (Scheme 2.26, entry 4). Lastly, it is noteworthy that products derived from nucleophilic addition of CH_3Li to the internally activated ketone were not observed in the crude reaction mixture.

Scheme 2.26 Optimization of Bases Employed for Diastereoselective Alkylation.



Entry	Base	**2.87** (%)	**2.57** (%)
1	LDA	0	36
2	*i*-Pr_2NEt	0	27
3	*n*-BuLi	39	5
4	MeLi	45	<5

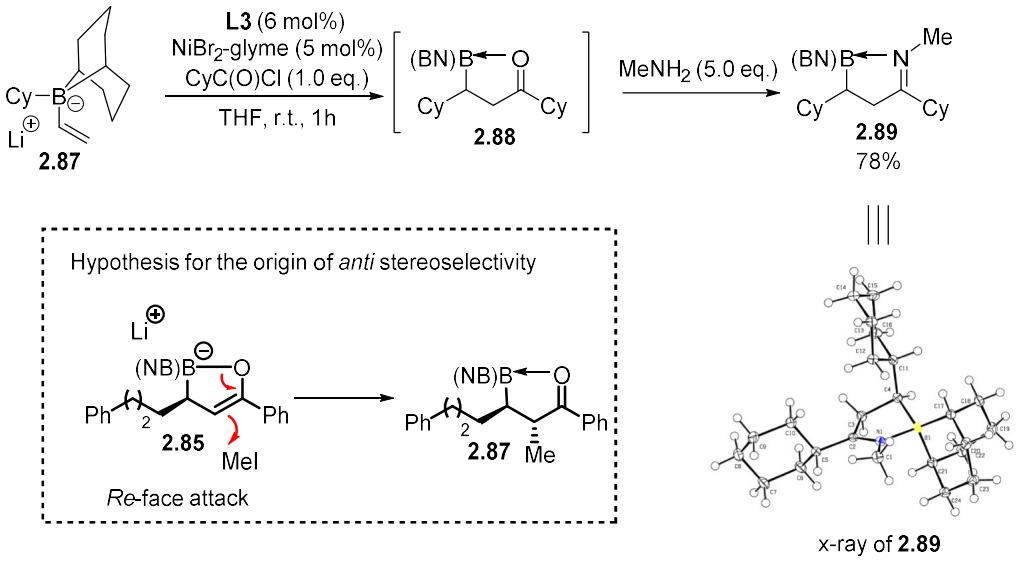
D_2O quenching experiment



Attempts at growing crystals of **2.84** for X-ray diffraction, with the goal of understanding the origin of the diastereoselectivity of alkylation, were not successful. However, to our delight, we found that condensation of **2.84** with methylamine efficiently provided the corresponding Schiff-base **2.89**, from which we were able to grow quality crystals for X-ray diffraction. From the crystal structure of the Schiff base **2.89**, it is obvious there is an internal chelation between boron and the heteroatom of the imine moiety. Due to the steric hindrance of the bicyclooctyl ring system, the cyclohexyl substituent at the stereogenic center points at an axial orientation and appears to block one face of the prochiral α-carbon atom. We reasoned that boron-enolate **2.85** would share a

similar conformation which allows the electrophile to approach only from the less hindered face of the carbonyl and accounts for the excellent *anti* diastereoselectivity.

Scheme 2.28 Synthesis and Structure Elucidation of Schiff-Base Imine.



2.3.5 Conclusion.

In conclusion, we have developed a nickel-catalyzed conjunctive coupling reaction between 9-BBN derived boron "ate" complex and carboxylic acid derivatives. The reaction itself gives β-boryl carbonyls, but subsequent oxidation of the corresponding secondary 9-BBN borates provides the derived alcohol. This method has been shown to be complementary to the well-known aldol reaction for the synthesis of certain β-hydroxy carbonyls. Acyl chlorides, anhydrides, as well as chloroformates are all suitable electrophiles under the reported reaction conditions. Preliminary mechanistic studies suggest that the transformation occurs by a stereospecific *anti*-periplanar metallate shift as

opposed to an alternative one-electron process. It is also shown that, through the intermediacy of a boron-bound enolate generated from the deprotonation of the β-keto boryl motif, a new stereocenter can be generated by alkylation in an one-pot fashion with excellent relative diastereoselectivity.

2.4 Experimental Section

2.4.1 General Information

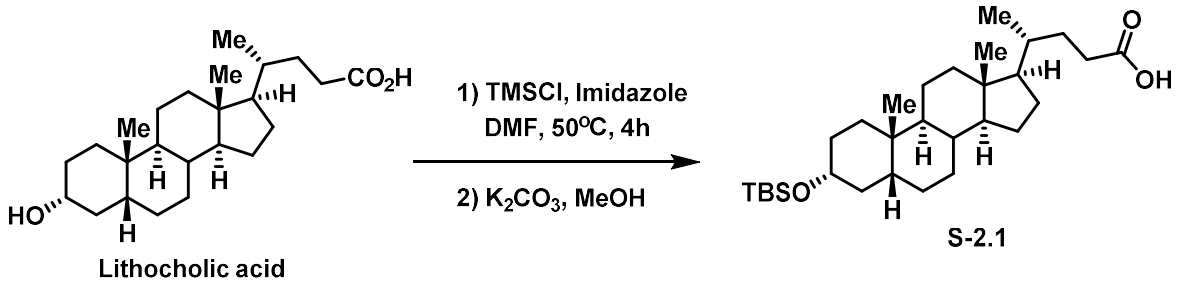
^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.24 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), Varian Gemini-600 (150 MHz) or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). Chemical shifts are reported in ppm using phosphoric acid as the external standard (H_3PO_4: 0.0 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) spectrometer. ^{19}F NMR spectra were recorded on a Varian Gemini-500 (470 MHz) spectrometer. Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART+) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was

performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol or phosphomolybdic acid, and cerium (IV) sulfate in ethanol with sulfuric acid (Seebach).

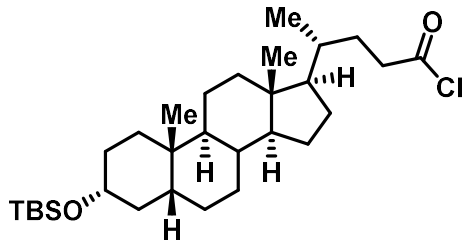
Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol as the modifier.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Nickel(II) bromide-glyme was purchased from Sigma Aldrich, 9-Borabicyclo[3.3.1]nonane 0.5M solution in THF was purchased from Alfa Aesar (of note, cross coupling reactions resulted in slightly diminished yields when a BBN solution from Sigma Aldrich was employed, or when borane reagents were prepared from BBN dimer). All other reagents were purchased from Sigma Aldrich, Alfa Aesar, Oakwood Chemicals, Combi-Blocks, or Acros Organics and used without further purification.

2.4.2 Procedures for Preparation of Acyl Electrophile.



(4*R*)-4-((3*R*,5*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-((tert-butyldimethylsilyl)oxy)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)pentanoic acid (S-2.1). The title compound was prepared according to the procedure reported in literature.[121] All spectral data was in accordance with the literature.

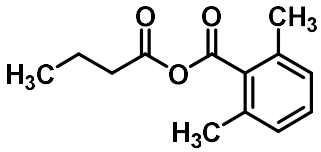


(4*R*)-4-((3*R*,5*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-((tert-butyldimethylsilyl)oxy)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)pentanoyl chloride (S-2.2). To an oven-dried scintillation vial was added **S-6** (500mg, 0.98mmol). The vial was purged with nitrogen for 2 minutes. To it was added THF (1mL) and Et_2O (1mL). The reaction mixture was cooled to 0°C at which point oxalyl chloride (137mg, 1.08mmol) was added followed by 1 small drop of DMF. The reaction mixture was warmed up to room temperature and stirred

[121] C. Joe, A. Doyle, *Angew. Chem. Int. Ed.* **2016**, *55*, 4040.

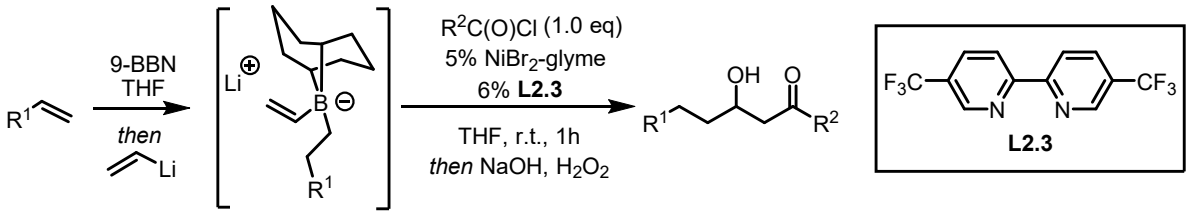
overnight. Solvent was evaporated under vacuum to afford the product as a white solid (394mg, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66-3.49 (m, 1H), 2.96-2.88 (m, 1H), 2.85-2.76 (m, 1H), 1.95-1.02 (m, 26H), 0.92 (s, 3 H), 0.91 (s, 3H), 0.89 (s, 9H), 0.63 (s, 3H), 0.06 (s, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 174.4, 73.0, 56.5, 56.0, 44.6, 42.9, 42.4, 40.34, 40.26, 37.1, 36.0, 35.7, 35.1, 34.7, 31.2, 31.2, 28.3, 27.4, 26.5, 26.1, 24.3, 23.5, 20.9, 18.49, 18.37, 12.17, -4.44. **IR** (neat) ν_{max} 2930 (s), 2863 (s), 1708 (s), 1447 (m), 1249 (m), 1093 (m), 870 (m), 854 (m), 774 (m). **HRMS** (DART) for $C_{30}H_{53}O_2Si$ $(M\text{-}Cl)^+$: Calc'd: 473.3815, found: 473.3753.



butyric 2,6-dimethylbenzoic anhydride (2.76). The title compound was prepared according to the procedure reported in literature. All spectral data was in accordance with the literature.[53]

2.4.3 General Procedure for Conjunctive Cross-Coupling.



In a glovebox, under argon, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with a solution of 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.). The vial was cooled to 0°C, and the olefin (0.26 mmol, 1.30 equiv.) was added. The

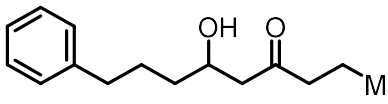
reaction mixture was allowed to warm to room temperature and stir for 3 hours before being cooled back to 0°C. A solution of vinyllithium (for synthesis of halide free vinyllithium see ref) in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.) was added to the reaction mixture which was then warmed to room temperature and stirred for 5 minutes. Meanwhile a solution of $NiBr_2$-glyme (0.010 mmol, 0.050 equiv.) and **L2.3** (see ref[122] for its synthesis) (0.012 mmol, 0.060 equiv.) in THF (0.4 mL) was allowed to complex for 5 minutes under inert atmosphere. The catalyst solution was added to the boron 'ate' mixture at room temperature followed by addition of acyl chloride (0.20 mmol, 1.00 equiv.) The reaction vial was sealed with a septum cap, taken out of the glovebox and stirred at room temperature for 1h, after which point the reaction mixture was cooled to 0°C and 30% H_2O_2 (0.5 mL) were added along with 3 M NaOH (0.5 mL). The reaction mixture was allowed to warm up to room temperature and stirred for 3 hours. Saturated $Na_2S_2O_3$ (1 mL) solution was then added to quench the remaining H_2O_2. The aqueous phase was extracted with EtOAc (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to provide the desired products.

Note: In all cases, a stock solution of 9-BBN derivatives could be prepared and stored in a freezer for as long as one month, before addition of vinyllithium, without a diminished yield.

[122] Y. Forst, S. Becker, P. Caubere, *Tetrahedron*, **1994**, *50*, 11893.

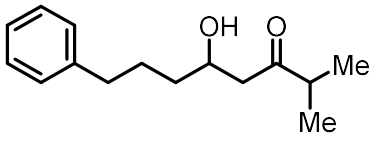
The procedure for conjunctive cross-coupling reaction utilizing anhydrides as electrophiles is identical to the one reported above except the commercially available 2,2'-bipyridine is used as the ligand.

2.4.4 Characterization of Conjunctive Cross-Coupling Products



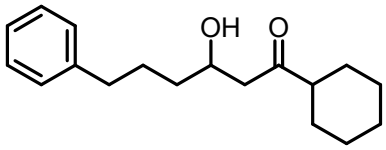
6-hydroxy-9-phenylnonan-4-one (2.49). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), butanoyl chloride (21.3 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (37 mg, 79% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.25 (m, 2H), 7.23-7.14 (m, 3H), 4.11-4.02 (m, 1H), 3.06 (d, J = 3.4 Hz, 1H), 2.68-2.54 (m, 3H), 2.48 (dd, J = 17.6, 9.1 Hz, 1H), 2.39 (t, J = 7.3 Hz, 2H), 1.87-1.74 (m, 1H), 1.73-1.48 (m, 4H), 1.46-1.36 (m, 1H), 0.91 (t, J = 7.4 Hz, 3H).**^{13}C NMR** (150 MHz, $CDCl_3$) δ 212.5, 142.4, 128.5, 128.4, 125.9, 67.6, 49.0, 45.6, 36.1, 35.8, 27.4, 17.2, 13.8. **IR** (neat) ν_{max} 3398 (br, s), 2932 (s), 1707 (s), 1603 (w), 1496 (w), 1408 (m), 1375 (m), 1096 (m), 750 (s), 700 (s) cm^{-1}. **HRMS** (DART) for $C_{15}H_{23}O_2$ $[M+H]^+$: Calc'd: 235.1691, found: 235.1693.



5-hydroxy-2-methyl-8-phenyloctan-3-one (2.55). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), isobutyryl chloride (21.3 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (33.7 mg, 72% yield).

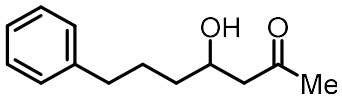
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.25 (m, 2H), 7.20-7.15 (m, 3H), 4.10-3.99 (m, 1H), 3.28-3.01 (br s, 1H). 2.71-2.46 (m, 5H), 1.88-1.73 (m, 1H), 1.72-1.62 (m, 1H), 1.59-1.50 (m, 1H), 1.48-1.38 (m, 1H), 1.10 (d, J = 6.9 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 216.3, 142.4, 128.5, 128.4, 125.9, 67.6, 46.6, 41.6, 36.1, 35.9, 27.4, 18.2, 18.1. **IR** (neat) 3479 (br, m), 2969 (m), 2932 (s), 1706 (s), 1603 (w), 1496 (m), 1094 (m), 1043 (w), 751 (m), 701 (m) cm^{-1}. **HRMS** (DART) for $C_{15}H_{23}O_2$ $[M+H]^+$: Calc'd: 235.1693, found: 235.1703.



1-cyclohexyl-3-hydroxy-6-phenylhexan-1-one (2.56). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060

equiv.) in THF (0.4 mL), cyclohexanecarbonyl chloride (29.3 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (43.9 mg, 80% yield).

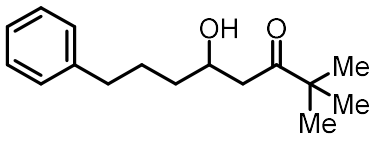
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.33 (m, 2H), 7.28-7.22 (m, 3H), 4.17-4.04 (m, 1H), 3.26 (d, *J* = 3.2 Hz, 1H), 2.74-2.66 (m, 3H), 2.57 (dd, *J* = 17.7, 9.2 Hz, 1H), 2.42-2.34 (m, 1H), 1.96-1.82 (m, 5H), 1.78-1.69 (m, 2H), 1.65-1.57 (m, 1H), 1.55-1.46 (m, 1H), 1.44-1.22 (m, 5H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 215.8, 142.4, 128.6, 128.4, 125.9, 67.6, 51.5, 46.9, 36.1, 35.9, 28.4, 27.4, 25.9, 25.7. **IR** (neat) ν_{max} 3457 (m), 2925 (m), 1670 (s), 1602 (s), 1222 (m), 1023 (m), 969 (m), 827 (s), 613 (w), 580 (w) cm^{-1}. **HRMS** (DART) for $C_{18}H_{27}O_2$ $[M+H]^+$: Calc'd: 275.2006, found: 275.1996.



4-hydroxy-7-phenylheptan-2-one (2.53). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), acetyl chloride (15.7 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (37 mg, 76% yield).

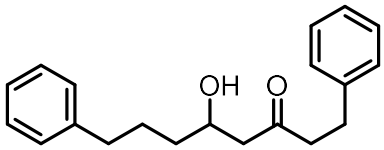
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28-7.24 (m, 2H), 7.20-7.14 (m, 3H), 4.08-4.00 (m, 1H), 3.02-2.94 (s, 1H), 2.66-2.57 (m, 3H), 2.51 (dd, *J* = 17.8, 9.2 Hz, 1H), 2.15 (s, 3H), 1.83-1.74 (m, 1H), 1.70-1.60 (m, 1H), 1.56-1.49 (m, 1H), 1.45-1.38 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 210.1, 142.4, 129.5, 128.4, 125.9, 67.5, 50.1, 36.0, 35.8, 30.9, 27.4. **IR**

(neat) ν_{max} 3457 (m), 2923 (m), 1668 (s), 1596 (s), 1459 (m), 1262 (m), 988 (m), 826 (m), 746 (m), 701 (m), 580 (s), 552 (m). **HRMS** (DART) for $C_{13}H_{19}O_2$ $(M+H)^+$: Calc'd: 207.1380, found: 207.1370.



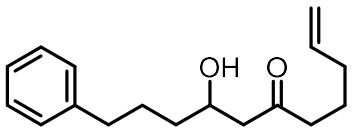
5-hydroxy-2,2-dimethyl-8-phenyloctan-3-one (2.54). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (2.20 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), pivaloyl chloride (24.1 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (15.9 mg, 32% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 (m, 2H), 7.18 (m, 3H), 4.02 (m, 1H), 3.27 (d, *J* = 3.1 Hz, 1H), 2.67 (dd, *J* = 17.8, 2.5 Hz, 1H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.53 (dd, *J* = 17.8, 9.2 Hz, 1H), 1.81 (m, 1H), 1.69 (m, 1H), 1.56 (m, 1H), 1.45 (m, 1H), 1.13 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 218.0, 142.4, 128.54, 128.45, 128.43, 128.41, 125.9, 67.8, 44.5, 43.19, 43.16, 36.1, 35.9, 27.5, 26.44, 26.40, 26.35. **IR** (neat) ν_{max} 3454 (br, w), 3026 (w), 2929 (m), 2861 (m), 1698 (s), 1603 (w), 1496 (m), 1478 (m), 1453 (m), 1394 (w), 1366 (m), 1067 (m), 1030 (w), 1008 (w), 844 (w), 748 (s), 699 (s), 578 (w), 537 (w) cm^{-1}. **HRMS** (DART) for $C_{16}H_{25}O_2$ $[M+H]^+$: Calc'd: 249.1849, found: 249.1840.



5-hydroxy-1,8-diphenyloctan-3-one (2.50). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), hydrocinnamoyl chloride (33.7 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (43.9 mg, 79% yield).

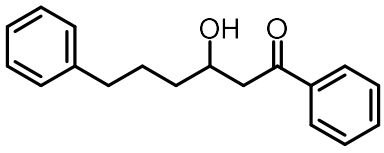
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 (m, 4H), 7.19 (m, 6H), 4.06 (m, 1H), 2.99 (m, 1H), 2.91 (t, *J* = 7.6 Hz, 2H), 2.76 (t, *J* = 7.6 Hz, 2H), 2.64 (t, *J* = 7.7 Hz, 2H), 2.55 (dd, *J* = 17.5, 3.0 Hz, 1H), 2.49 (dd, J = 17.5, 8.9 Hz, 1H), 1.79 (m, 1H), 1.67 (m, 1H), 1.53 (m, 1H), 1.43 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 211.2, 142.3, 140.8, 128.6, 128.6, 128.5, 128.5, 128.40, 128.39, 128.37, 126.3, 125.9, 67.6, 49.4, 45.11, 36.0, 35.8, 29.6, 27.3. **IR** (neat) ν_{max} 3445 (br, w), 3026 (w), 2923 (w), 2856 (w), 1705 (s), 1603 (w), 1496 (m), 1453 (m), 1406 (m), 1371 (m), 1091 (m), 1030 (m), 748 (m), 698 (s), 563 (w) cm^{-1}. **HRMS** (DART) for $C_{20}H_{25}O_2$ $[M+H]^+$: Calc'd: 297.1849, found: 297.1838.



8-hydroxy-11-phenylundec-1-en-6-one (2.51). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme

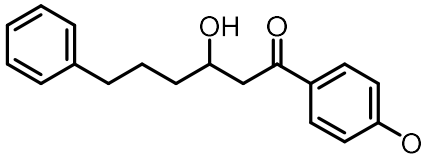
(3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), hex-5-enoyl chloride (26.5 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (42.2 mg, 81% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.24 (m, 2H), 7.19-7.15 (m, 3H), 5.74 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.03-4.95 (m, 2H), 4.11-4.01 (m, 1H), 3.09 (br s, 1H), 2.63 (t, *J* = 7.7,Hz, 2H), 2.55 (dd, *J* = 17.5, 2.8 Hz, 1H), 2.48 (dd, *J* = 17.5, 9.1 Hz, 1H), 2.41 (t, *J* = 7.4 Hz, 2H), 2.04 (q, *J* = 7.1 Hz, 2H), 1.83-1.75 (m, 1H), 1.71-1.62 (m, 3H), 1.57-1.49 (m, 1H), 1.46-1.38 (m, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 212.2, 142.3, 137.9, 128.5, 128.4, 125.8, 115.5, 67.6, 49.2, 42.8, 36.0, 35.8, 33.1, 27.4, 22.6. **IR** (neat) ν_{max} 3448.8 (br, m), 2933 (m), 1705 (m), 1640 (w), 1408 (m), 1276 (w), 1097 (m), 912 (m), 750 (s), 700 (s) cm^{-1}. **HRMS** (DART) for $C_{17}H_{25}O_2$ $[M+H]^+$: Calc'd: 261.1849, found: 261.1853.



3-hydroxy-1,6-diphenylhexan-1-one (2.57). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), benzoyl chloride (28.1 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (40.3 mg, 75% yield).

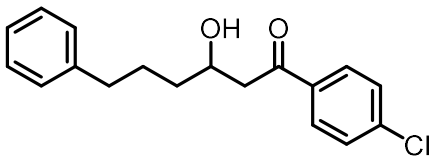
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.4 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 2H), 7.24-7.16 (m, 3H), 4.30-4.19 (m, 1H), 3.28 (d, *J* = 3.3 Hz, 1H), 3.15 (dd, *J* = 17.7, 2.6 Hz, 1H), 3.04 (dd, *J* = 17.9, 9.1 Hz, 1H), 2.68 (t, *J* = 7.6 Hz, 1H), 1.94-1.83 (m, 1H), 1.80-1.71 (m, 1H), 1.71-1.63 (m, 1H), 1.61-1.52 (m, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 201.0, 142.4, 136.9, 133.7, 128.8, 128.6, 128.4, 128.2, 125.9, 67.7, 45.2, 36.2, 35.9, 27.5. **IR** (neat) ν_{max} 3481 (m), 2931 (w), 2901 (w), 1676 (s), 1595 (w), 1219 (w), 1098 (m), 749 (m), 699 (m), 686 (s), 583 (m) cm^{-1}. **HRMS** (DART) for $C_{18}H_{21}O_2$ $[M+H]^+$: Calc'd: 269.1536, found: 269.1545.



3-hydroxy-1-(4-methoxyphenyl)-6-phenylhexan-1-one (2.58). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 4-methoxybenzoyl chloride (34.1 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a white solid (44.1 mg, 74% yield).

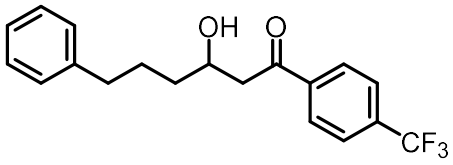
^{1}H NMR (400 MHz, $CDCl_3$) 7.92 (d, *J* = 8.9 Hz, 2H), 7.33-7.24 (m, 2H), 7.21-7.13 (m, 3H), 6.92 (d, *J* = 8.9 Hz, 2H), 4.30-4.10 (m, 1H), 3.86 (s, 3H), 3.41 (br s, 1H), 3.10 (dd, *J* = 17.5, 2.5 Hz, 1H), 2.95 (dd, *J* = 17.5, 9.1 Hz 1H), 2.67 (t, *J* = 7.5 Hz, 2H), 1.93-1.81 (m, 1H), 1.80-1.59 (m, 2H), 1.58-1.46 (m, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 199.6, 164.0, 142.5, 130.5, 130.0, 128.6, 128.4, 125.9, 114.0, 67.9, 55.7, 44.7, 36.2, 35.9, 27.5. **IR** (neat)

ν_{max} 3483 (br, s), 2926 (s), 1709 (s), 1603 (w), 1496 (w), 1168 (m), 1094 (m), 751 (m), 702 cm^{-1}. **HRMS** (DART) for $C_{19}H_{23}O_3$ $[M+H]^+$: Calc'd: 299.1642, found: 299.1649.



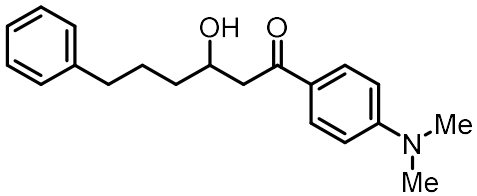
1-(4-chlorophenyl)-3-hydroxy-6-phenylhexan-1-one (2.60). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 4-chlorobenzoyl chloride (35.0 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (40.6 mg, 67% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.28 (t, 2H, *J* = 7.5 Hz, 2H), 7.22-7.16 (m, 3H), 4.28-4.19 (m, 1H), 3.17 (d, *J* = 3.4 Hz, 1H), 3.08 (dd, *J* = 17.7, 2.7 Hz, 1H), 3.01 (dd, *J* = 17.7, 9.1 Hz, 1H), 2.67 (t, *J* = 7.6 Hz, 2H), 1.92-1.84 (m, 1H), 1.78-1.70 (m, 1H), 1.68-1.62 (m, 1H), 1.58-1.51 (m, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 199.7, 142.3, 140.2, 135.2, 129.6, 129.1, 128.6, 128.5, 125.9, 67.6, 45.2, 36.1, 35.9, 27.5. **IR** (neat) ν_{max} 3484 (br, s), 2932 (w), 2901 (w), 1675 (s), 1588 (w), 1494 (m), 1400 (m), 1092 (s), 1039 (m), 986 (m), 832 (m), 817 (s), 733 (s), 534 (s) cm^{-1}. **HRMS** (DART) for $C_{18}H_{21}O_2Cl$ $[M+H]^+$: Calc'd: 303.1146, found: 303.1143.



3-hydroxy-6-phenyl-1-(4-(trifluoromethyl)phenyl)hexan-1-one (2.61). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 4-(trifluoromethyl)benzoyl chloride (41.7 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a white solid (30.0 mg, 44% yield).

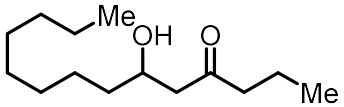
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.6 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 8.0 Hz, 2H), 7.21-7.16 (m, 3H), 4.34-4.22 (m, 1H), 3.14 (dd, *J* = 17.7, 2.9 Hz, 1H), 3.08 (dd, *J* = 17.7, 8.7 Hz, 1H), 3.02 (s, 1H), 2.68 (t, *J* = 7.6 Hz, 2H), 1.93-1.84 (m, 1H), 1.79-1.71 (m, 1H), 1.70-1.63 (m, 1H), 1.60-1.52 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 199.9, 142.3, 139.5, 128.58, 128.56, 128.5, 126.0, 125.9, 125.91, 125.88, 67.6, 45.7, 36.2, 35.9, 27.5. **IR** (neat) ν_{max} 3485 (s), 2931 (w), 2900 (w), 1682 (s), 1579 (w), 1509 (m), 1327 (s), 1169 (m), 892 (m), 844 (m), 703 (w), 606 (w) cm^{-1}. **HRMS** (DART) for $C_{19}H_{20}O_2F_3$ $[M+H]^+$: Calc'd: 337.1410, found: 337.1396.



1-(4-(dimethylamino)phenyl)-3-hydroxy-6-phenylhexan-1-one (2.59). The reaction was performed according to the general

procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 4-(dimethylamino)benzoyl chloride (36.7 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (48.0 mg, 77% yield).

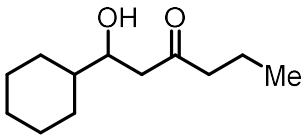
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 9.1 Hz, 2H), 7.34-7.26 (m, 2H), 7.22-7.13 (m, 3H), 6.64 (d, *J* = 9.1 Hz, 2H), 4.24-4.16 (m, 1H), 3.73 (s, 1H), 3.10 (dd, *J* = 17.3, 2.4 Hz, 1H), 3.06 (s, 6H), 2.88 (dd, *J* = 17.3, 9.3 Hz, 1H), 2.67 (t, *J* = 7.6 Hz, 2H), 1.93-1.83 (m, 1H), 1.79-1.70 (m, 1H), 1.69-1.61 (m, 1H), 1.58-1.50 (m, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 199.1, 153.8, 142.5, 130.5, 128.6, 128.4, 125.8, 124.8, 110.7, 68.1, 43.9, 40.1, 36.3, 36.0, 27.5. **IR** (neat) ν_{max} 3468 (br, w), 2926 (w), 1650 (w), 1595 (s), 1530 (w), 1371 (m), 1186 (m), 1169 (m), 819 (w), 750 (m), 700 (w), 579 (w). **HRMS** (DART) for $C_{20}H_{26}NO_2$ $[M+H]^+$: Calc'd: 312.1952, found: 312.1958.



6-hydroxytetradecan-4-one (2.62). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), 1-octene (mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), butanoyl chloride (21.3 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by

column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (33.3 mg, 73% yield).

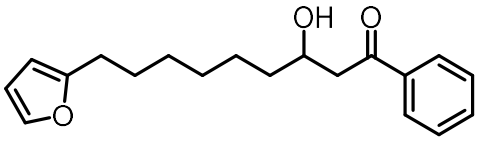
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.05-3.97 (m, 1H), 3.06 (br s, 1H), 2.57 (dd, *J* = 17.5, 2.8 Hz, 1H), 2.47 (dd, 1H), 2.39 (t, *J* = 7.3 Hz, 2H), 1.59 (h, *J* = 7.3 Hz, 2H), 1.52-1.17 (m, 14H), 0.90 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 212.6, 67.8, 49.1, 45.7, 36.6, 32.0, 29.69, 29.67, 29.4, 25.6, 22.8, 17.2, 14.2, 13.8. **IR** (neat) ν_{max} 3244 (br, m), 2957 (m), 2916 (s), 2848 (m), 1701 (s), 1465 (m), 1386 (m), 1132 (m), 1094 (m), 1027 (m), 889 (m), 724 (m), 628 (m). **HRMS** (DART) for $C_{14}H_{29}O_2$ $[M+H]^+$: Calc'd: 229.2162, found: 229.2172.



1-cyclohexyl-1-hydroxyhexan-3-one (2.63). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), cyclohexene (21.4 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), butanoyl chloride (21.3 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (26.2 mg, 66% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 3.79 (m, 1H), 2.97 (s, 1H), 2.58 (dd, *J* = 17.3, 2.4 Hz, 1H), 2.49 (dd, *J* = 17.3, 9.6 Hz, 1H), 2.41 (t, *J* = 7.3 Hz, 2H), 1.85-1.80 (m, 1H), 1.77-1.70 (m, 2H), 1.67-1.56 (m, 4H), 1.36-1.30 (m, 1H), 1.26-1.09 (m, 3H), 1.06-0.95 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 212.9, 71.9, 46.2, 45.8, 43.1, 29.0, 28.4,

26.6, 26.3, 26.2, 17.2, 13.8. **IR** (neat) ν_{max} 3448 (br, w), 2923 (s), 2852 (s), 1703 (s), 1450 (m), 1407 (m), 1371 (m), 1308 (m), 1274 (m), 1127 (m), 1108 (m), 1065 (m), 1027 (m), 989 (m), 957 (w), 892 (w), 531 (w) cm^{-1}. **HRMS** (DART) for $C_{12}H_{23}O_2$ $[M+H]^+$: Calc'd: 199.1693, found: 199.1688.

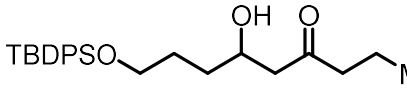


12-(furan-2-yl)-6-hydroxydodecan-4-one (2.65).

The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), **S-1.1** (39.0 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), butanoyl chloride (21.3 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (32.5 mg, 61% yield).

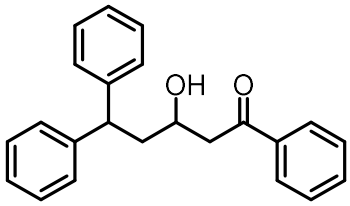
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 8.0 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.29 (s, 1H), 6.29 – 6.24 (m, 1H), 5.97 (d, *J* = 3.1 Hz, 1H), 4.22 (m, 1H), 3.24 (d, *J* = 3.2 Hz, 1H), 3.17 (dd, *J* = 17.6, 2.6 Hz, 1H), 3.04 (dd, *J* = 17.6, 9.0 Hz, 1H), 2.62 (t, *J* = 7.6 Hz, 2H), 1.69-1.58 (m, 3H), 1.56-1.47 (m, 2H), 1.46-1.31 (m, 5H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 201.1, 156.6, 140.8, 136.9, 133.6, 128.8, 128.2, 110.2, 104.7, 67.9, 45.2, 36.6, 29.4, 29.2, 28.11, 28.07, 25.6. **IR** (neat) ν_{max} 3454 (br, w), 2929 (m), 2856 (w), 1677 (s), 1597 (m), 1580 (w), 1507 (w), 1449 (m), 1283 (w), 1210 (s), 1180 (w), 1146 (m), 1072 (w), 1003 (s), 922 (w), 884 (w), 797 (w), 752 (s), 727 (s), 689 (s), 662 (w), 599

(s), 587 (m), 536 (w) cm^{-1}. **HRMS** (DART) for $C_{19}H_{25}O_3$ $[M+H]^+$: Calc'd: 301.1798, found: 301.1796.



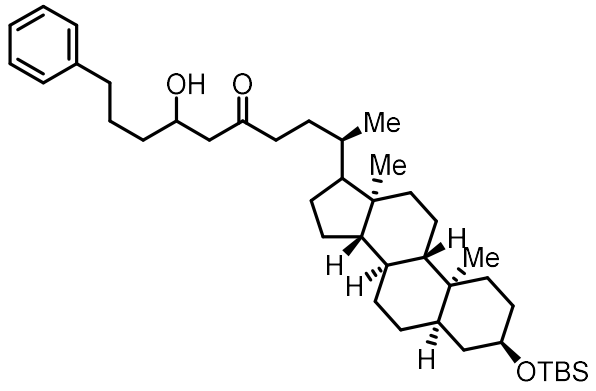
9-((tert-butyldiphenylsilyl)oxy)-6-hydroxynonan-4-one (2.67). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), **S-1.4** (77.1 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (2.20 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), butanoyl chloride (21.3 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (59.4 mg, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.64 (m, 4H), 7.46-7.34 (m, 6H), 4.11-4.01 (m, 1H), 3.69 (t, J = 5.4 Hz, 1H), 3.24 (d, J = 3.2 Hz, 1H), 2.60-2.46 (m, 2H), 2.41 (t, J = 7.3 Hz, 2H), 1.84-1.51 (m, 6H), 1.05 (s, 9H), 0.92 (t, J = 7.4 Hz, 3H). **^{13}CNMR** (126 MHz, $CDCl_3$) δ 212.3, 135.7, 135.7, 129.7, 127.8, 67.6, 64.0, 49.2, 45.7, 33.3, 28.7, 27.0, 19.3, 17.2, 13.8. **IR** (neat) ν_{max} 3399 (br, s), 2938 (s), 2857 (s), 1705 (s), 1472 (w), 1428 (m), 1112 (s), 741 (m), 705 (s), 615 (m) cm^{-1}. **HRMS** (DART) for $C_{25}H_{37}O_3Si$ $[M+H]^+$: Calc'd: 413.2507, found: 413.2505.



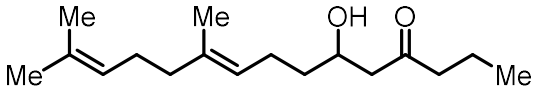
3-hydroxy-1,5,5-triphenylpentan-1-one (2.64). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), 1,1-diphenylethylene (46.9 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), benzoyl chloride (28.1 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (53.5 mg, 66% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.1 Hz, 2H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 2H), 7.28-7.33 (m, 7H), 7.22-7.14 (m, 2H), 4.37 (dd, *J* = 10.4, 5.3 Hz, 1H), 4.06-4.13 (m, 1H), 3.29 (d, *J* = 3.0 Hz, 1H), 3.15 (dd, *J* = 17.7, 3.0 Hz, 1H), 3.09 (dd, *J* = 17.9, 8.6 Hz, 1H), 2.37-2.30 (m, 1H), 2.29-2.22 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 200.8, 145.3, 144.1, 136.8, 133.7, 128.8, 128.7, 128.6, 128.3, 128.1, 127.8, 126.5, 126.3, 65.7, 47.1, 45.4, 42.4. **IR** (neat) ν_{max} 3454 (br, w), 3059 (w), 3026 (w), 2933 (w), 1677 (m), 1597 (m), 1580 (w), 1493 (m), 1449 (m), 1409 (w), 1361 (w), 1280 (w), 1207 (m), 1181 (w), 1158 (w), 1076 (w), 1057 (w), 1031 (m), 1001 (w), 985 (w), 917 (w), 868 (w), 782 (w), 752 (s), 739 (m), 698 (s), 619 (w), 590 (w), 551 (w) cm^{-1}. **HRMS** (DART) for $C_{23}H_{23}O_2$ $[M+H]^+$: Calc'd: 331.1693, found: 331.1695.



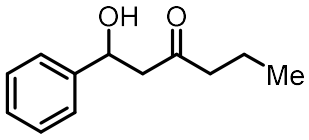
(2*R*)-2-((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*)-3-((tert-butyldimethylsilyl)oxy)-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)-7-hydroxy-10-phenyldecan-5-one (2.70). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), **S-2.2** (101.9 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (63.7 mg, 50% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.24 (m, 2H), 7.21-7.15 (m, 3H), 4.10-3.99 (m, 1H), 3.62-3.53 (m, 1H), 3.09 (dd, *J* = 8.1, 3.4 Hz, 1H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.59-2.39 (m, 3H), 2.37-2.27 (m, 1H), 1.96-1.01 (m, 34H), 0.93-0.85 (m, 15H), 0.62 (s, 3H), 0.06 (s, 6H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 213.1, 142.4, 128.5, 128.4, 125.9, 73.0, 67.63, 67.59, 56.5, 56.1, 49.02, 49.01, 42.9, 42.4, 40.7, 40.4, 40.3, 37.1, 36.1, 36.0, 35.9, 35.7, 35.4, 34.7, 31.2, 29.7, 28.4, 27.43, 27.39, 26.5, 26.1, 24.3, 23.5, 21.0, 18.6, 18.5, 12.2, -4.4. **IR** (neat) ν_{max} 3480 (br, m), 2929 (s), 2854 (m), 1699 (s), 1603 (w), 1496 (w), 1451 (m), 750 (m), 700 (m) cm^{-1}. **HRMS** (DART) for $C_{41}H_{69}O_3Si$ $[M+H]^+$: Calc'd: 637.5016, found: 637.5005.



(E)-6-hydroxy-10,14-dimethylpentadeca-9,13-dien-4-one (2.68). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), **S-1.2** (39.1 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), butanoyl chloride (21.3 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (22.9 mg, 43% yield).

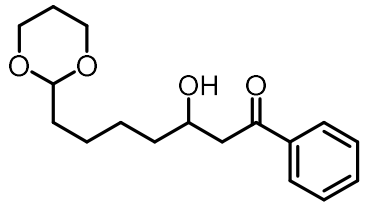
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.14-5.10 (t, J = 6.8 Hz, 1H), 5.09-5.06 (t, J = 6.6 Hz, 1H), 4.07-4.01 (m, 1H), 3.01 (d, J = 3.5 Hz, 1H), 2.59 (dd, J = 17.5, 2.8 Hz, 1H), 2.50 (dd, J = 17.5, 9.1 Hz, 1H), 2.40 (t, J = 7.3 Hz, 2H), 2.17-2.03 (m, 4H), 2.01-1.95 (m, 2H), 1.67 (s, 3H), 1.65-1.52 (m, 9H), 1.45-1.37 (m, 1H), 0.92 (t, J = 7.4 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 212.5, 136.0, 131.5, 124.4, 123.8, 67.4, 49.1, 45.7, 39.9, 36.6, 26.8, 25.8, 24.1, 17.8, 17.2, 16.2, 13.8. **IR** (neat) ν_{max} 3458 (br, m), 2963 (s), 2925 (s), 1707 (s), 1448 (m), 1376 (m), 1127 (w), 1103 (m), 1037 (w), 835 (w) cm^{-1}. **HRMS** (DART) for $C_{16}H_{25}O_3$ $[M+H]^+$: Calc'd: 265.1804, found: 265.1796.



1-hydroxy-1-phenylhexan-3-one (2.69). The reaction was performed according to the general procedure with slight modification. 9-phenyl-9-borabicyclo[3.3.1]nonane (51.5 mg, 0.26 mmol, 1.30 equiv.) was synthesized independently as mentioned above, diluted with 0.5 mL THF, and to it was added halide-

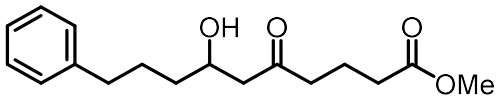
free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (2.20 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), followed by butanoyl chloride (21.3 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (23.5 mg, 61% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.19 (m, 5H), 5.16 (dd, *J* = 8.7, 3.5 Hz, 1H), 3.38 (s, 1H), 2.85 (dd, *J* = 17.4, 8.8 Hz, 1H), 2.78 (dd, *J* = 17.4, 3.6 Hz, 1H), 2.41 (t, *J* = 7.3 Hz, 2H), 1.62 (h, *J* = 7.3 Hz, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). **^{13}CNMR** (150 MHz, $CDCl_3$) δ 211.7, 143.0, 128.7, 127.8, 125.8, 70.1, 51.2, 45.7, 17.2, 13.8. **IR** (neat) ν_{max} 3400 (br, m), 2961 (m), 1702 (s), 1494 (w), 1453 (m), 1370 (m), 1067 (m), 1030 (m), 757 (m), 701 (s) cm^{-1}. **HRMS** (DART) for $C12H20NO_2$ $[M+H]^+$: Calc'd: 210.1489, found: 210.1488.



10-(1,3-dioxan-2-yl)-6-hydroxydecan-4-one (2.66). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), **S-3** (37.0 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), butanoyl chloride (21.3 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (29.5 mg, 57% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.2 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 4.51 (t, *J* = 5.1 Hz, 1H), 4.21 (m, 1H), 4.08 (dd, *J* = 10.7, 5.0 Hz, 2H), 3.74 (td, *J* = 11.0, 2.0 Hz, 2H). 3.26 (m, 1H), 3.14 (dd, *J* = 17.5, 2.5 Hz, 1H), 3.02 (dd, *J* = 17.6, 9.0 Hz, 1H), 2.11-2.01 (m, 1H), 1.67-1.56 (m, 3H), 1.55-1.47 (m, 2H), 1.46-1.35 (m, 3H), 1.33-1.31 (m, 1H). **^{13}CNMR** (126 MHz, $CDCl_3$) δ 201.1, 136.9, 133.6, 128.8, 128.2, 102.4, 67.8, 67.0, 45.1, 36.5, 35.3, 26.0, 25.6, 24.0. **IR** (neat) ν_{max} 3454 (br, w), 2927 (w), 2855 (w), 1678 (m), 1597 (w), 1580 (w), 1449 (w), 1431(w), 1404 (w), 1377 (w), 1283 (w), 1240 (m), 1213 (m), 1181 (w), 1142 (s), 1092 (m), 993 (m), 936 (w), 894 (w), 864 (w), 838 (w), 754 (m), 691 (m), 662 (w), 644 (w), 587 (w), 535 (w) cm^{-1}. **HRMS** (DART) for $C_{17}H_{25}O_4$ $[M+H]^+$: Calc'd: 293.1747, found: 293.1751.

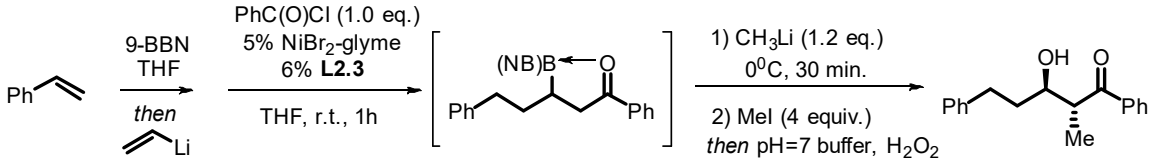


methyl 7-hydroxy-5-oxo-10-phenyldecanoate (2.52). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), methyl 5-chloro-5-oxopentanoate (32.9 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (47.4 mg, 81% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.22 (m, 2H), 7.18-7.13 (m, 3H), 4.07-3.98 (m, 1H), 3.64 (s, 3H), 2.61 (t, *J* = 7.4 Hz, 2H), 2.57-2.43 (m, 4H), 2.31 (t, *J* = 7.4 Hz, 2H), 1.87 (p, *J* = 7.2 Hz, 2H), 1.80-1.71 (m, 1H), 1.70-1.57 (m, 1H), 1.56-1.46 (m, 1H), 1.45-1.34 (m, 1H) .**^{13}C NMR** (126 MHz, $CDCl_3$) δ 211.2, 173.6, 142.3, 128.5, 128.4, 125.9, 77.5, 77.2,

76.8, 67.6, 51.7, 49.2, 42.4, 36.1, 35.8, 33.0, 27.3, 18.7. **IR** (neat) ν_{max} 3407 (br, w), 2937 (m), 1734 (s), 1710 (m), 1603 (w), 1172 (m), 1086 (m), 750 (m), 701 (m) cm^{-1}. **HRMS** (DART) for $C_{17}H_{25}O_4$ $[M+H-H_2O]^+$: Calc'd: 293.1747, found: 203.1737.

2.4.5 Procedure and Characterization for Boron-Enolate Alkylation



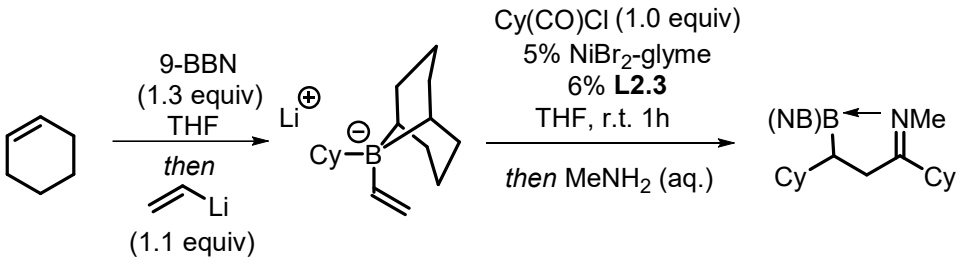
***anti*-3-hydroxy-2-methyl-1,5-diphenylpentan-1-one (2.87).** In a glovebox, under argon, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with a solution of 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.). The vial was cooled to 0°C, and styrene (27.1 mg, 0.26 mmol, 1.30 equiv.) was added. The reaction mixture was allowed to warm to room temperature and stir for 3 hours before being cooled back to 0°C. A solution of vinyllithium (for synthesis of halide free vinyllithium see ref[1]) in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.) was added to the reaction mixture which was then warmed to room temperature and stirred for 5 minutes. Meanwhile a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (see ref[10] for its synthesis) (3.51mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL) was allowed to complex for 5 minutes under inert atmosphere. The catalyst solution was added to the boron 'ate' mixture at room temperature followed by addition of benzoyl chloride (28.1 mg, 0.20 mmol, 1.00 equiv.). The reaction vial was sealed with a septum cap, taken out of the glovebox and stirred at room temperature for 1h, after which point the reaction mixture was cooled to -78°C and

methyllithium in Et_2O (0.15 mL, 1.6M, 0.24 mmol, 1.2 equiv.) was added dropwise through a syringe under inert atmosphere. The reaction mixture was allowed to warm up to 0℃ and stir for 30 minutes. After cooling the reaction mixture back to -78℃, iodomethane (113mg, 0.60 mmol, 4.0 equiv.) was added dropwise. The reaction mixture was then warmed up to room temperature and stir for 2 hours. After cooling the reaction mixture to 0℃, 30% H_2O_2 (0.5 mL) was added along with pH=7 buffer solution (0.5 mL). The reaction mixture was allowed to warm up to room temperature and stir for 3 hours. Aqueous saturated $Na_2S_2O_3$ (1 mL) solution was then added to quench the remaining H_2O_2. The aqueous phase was extracted with EtOAc (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated under reduced pressure, and the crude mixture was purified by 2 runs of column chromatography (1st: 20% EtOAc in hexane, 2nd: 100% chloroform, stain in $KMnO_4$) to afford the product as a colorless oil (24.2 mg, 45% yield, >19:1 d.r.).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.0 Hz, 2H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.29-7.25 (m, 3H), 7.22-7.16 (m, 2H), 3.93-3.85 (m, 1H), 3.59-3.52 (m, 1H), 3.04 (d, *J* = 7.1 Hz, 1H), 2.96-2.88(m, 1H), 2.75-2.69 (m, 1H), 1.91-1.78 (m, 1H), 1.27 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 206.0, 142.2, 136.7, 133.6, 128.9, 128.6, 128.54, 128.52, 126.0, 73.6, 45.9, 37.0, 32.3, 29.9, 15.8. **IR** (neat) ν_{max} 3489 (br, m), 2927 (m), 1678 (s), 1596 (w), 1496 (m), 1454 (m), 1376 (w), 1210 (m), 972 (m), 702 (s) cm^{-1}. **HRMS** (DART) for $C_{18}H_{21}O_2$ $[M+H]^+$: Calc'd: 269.1542, found: 269.1536.

The relative stereochemistry of the product was determined by comparison of ^{1}H NMR spectrum with diastereochemically-enriched authentic sample prepared according to the procedure reported by Evans.[123]

2.4.6 Synthesis and Characterization of 9-BBN-Schiff Base (2.89)

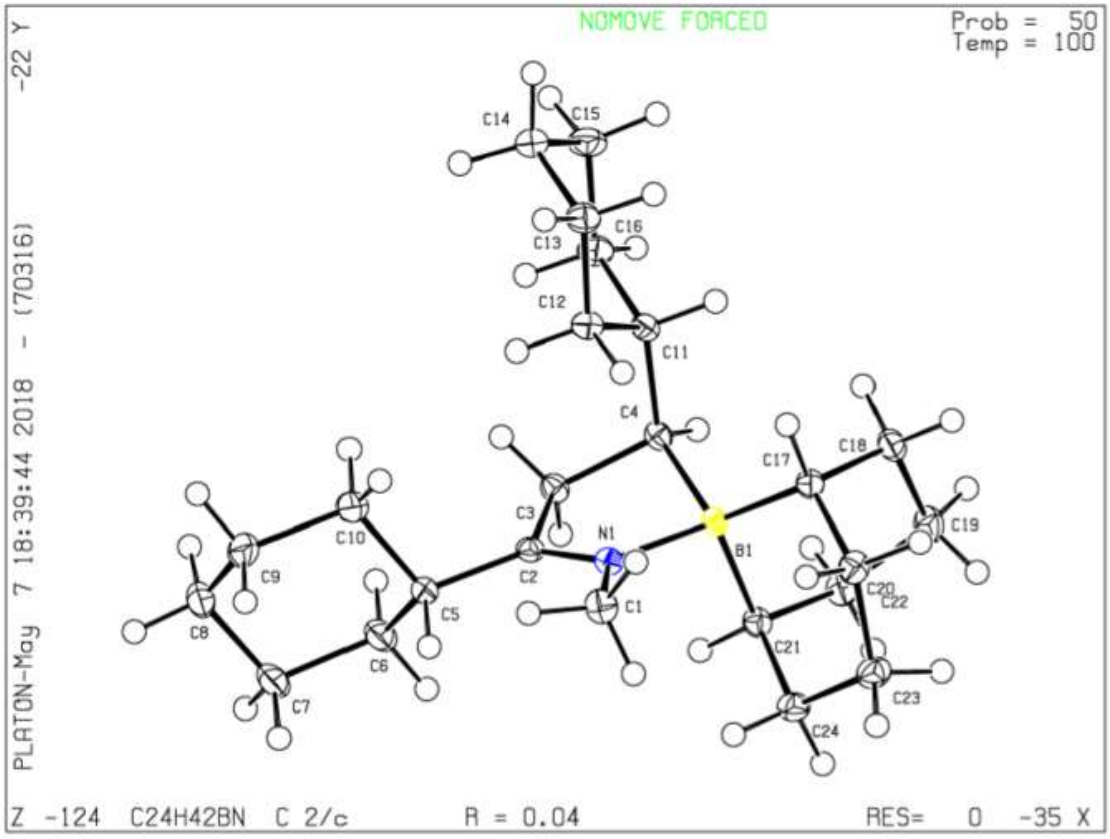


(E)-3-(9-borabicyclo[3.3.1]nonan-9-yl)-1,3-dicyclohexyl-N-methylpropan-1-imine (2.89). In a glovebox, under argon, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with a solution of 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.). The vial was cooled to 0°C, and cyclohexene (21.4 mg, 0.26 mmol, 1.30 equiv.) was added. The reaction mixture was allowed to heat up to 60°C and stir for 3 hours before being cooled back to 0°C. A solution of vinyllithium (for synthesis of halide free vinyllithium see ref[1]) in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.)

[123] D. Evans, J. Tedrow, J. Shaw, C. Downey, *J. Am. Chem. Soc.* **2002**, *124*, 392.

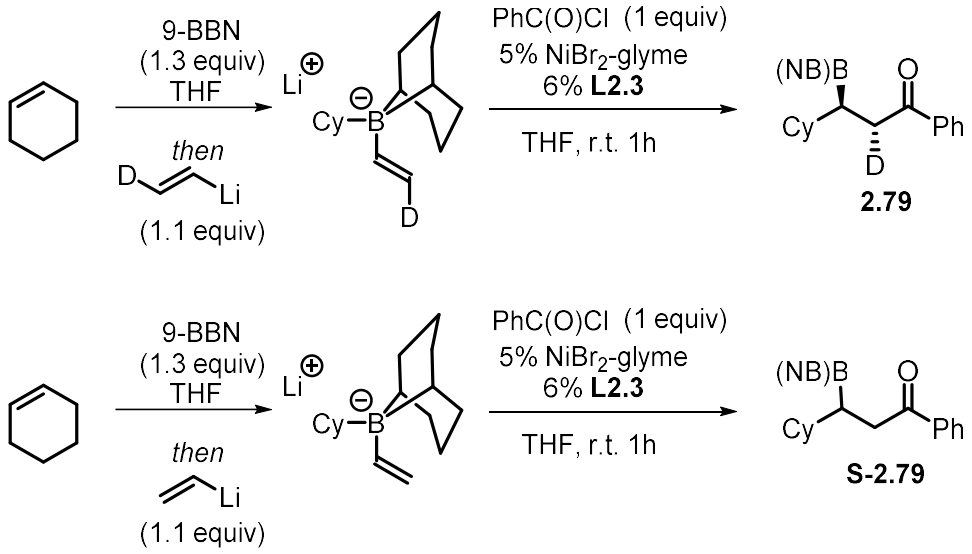
was added to the reaction mixture which was then warmed to room temperature and stirred for 5 minutes. Meanwhile a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (see ref[10] for its synthesis) (0.012 mmol, 0.060 equiv.) in THF (0.4 mL) was allowed to complex for 5 minutes under inert atmosphere. The catalyst solution was added to the boron 'ate' mixture at room temperature followed by addition of cyclohexanecarbonyl chloride (29.3 mg, 0.20 mmol, 1.00 equiv.). The reaction vial was sealed with a septum cap, taken out of the glovebox and stirred at room temperature for 1h, after which point the reaction mixture was cooled to 0°C and 40% methylamine aqueous solution (1mL) was added. The reaction mixture was allowed to warm up to room temperature and stirred for 1h. The aqueous phase was extracted with EtOAc (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography (20% CH_2Cl_2 in hexane, stain in $KMnO_4$) to provide **2.89** as a white solid (55.4 mg, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.28 (s, 3H), 2.61-2.51 (m, 1H), 2.50-2.37 (m, 2H), 2.30-2.18 (m, 1H), 2.10-1.94 (m, 1H), 1.93-0.98 (m, 31H), 0.94 (s, 1H), 0.39 (qd, *J* = 12.3, 3.6 Hz, 1H), 0.31 (s, 1H) .**^{13}C NMR** (126 MHz, $CDCl_3$) δ 189.1, 40.4, 37.7, 36.9, 35.8, 35.1, 34.3, 33.2, 31.9, 30.8, 30.7, 29.5, 29.4, 27.4, 27.3, 27.2, 26.0, 25.9, 25.8, 25.2, 24.2. **IR** (neat) ν_{max} 2917 (s), 2840 (s), 1637 (m), 1447 (m), 1332 (w), 1029 (m), 905 (s), 734 (s) cm^{-1}. **HRMS** (DART) for $C_{24}H_{43}BN$ $[M+H]^+$: Calc'd: 356.3483, found: 356.3489.

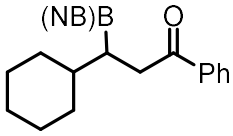


The structure was characterized by X-ray crystallography. Crystals were grown by slow evaporation with Et_2O in a 1-dram vial at room temperature.

2.4.7 Deuterium-Labeling Experiment



The trans-deuterium labeled vinyl lithium was prepared as described in previous reports.[124]



3-(9-borabicyclo[3.3.1]nonan-9-yl)-3-cyclohexyl-1-phenylpropan-1-one (S-2.79). In a glovebox, under argon, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with a solution of 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.). The vial was cooled to 0°C, and cyclohexene (21.4 mg, 0.26 mmol, 1.30 equiv.) was added via syringe. The reaction mixture was heated to 60°C and stir for 3 hours before being cooled back to 0°C. A solution of vinyllithium (for synthesis of halide free vinyllithium see ref[l]) in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.) was added to the reaction mixture which was then warmed to room temperature and stirred for 5 minutes. Meanwhile a solution of $NiBr_2$-glyme (0.010 mmol, 0.050 equiv.) and **L2.3** (see

[124] L. Zhang, G. Lovinger, E. Edelstein, A. Szymaniak, M. Chierchia, J. Morken, *Science* **2015**, *351*, 70.

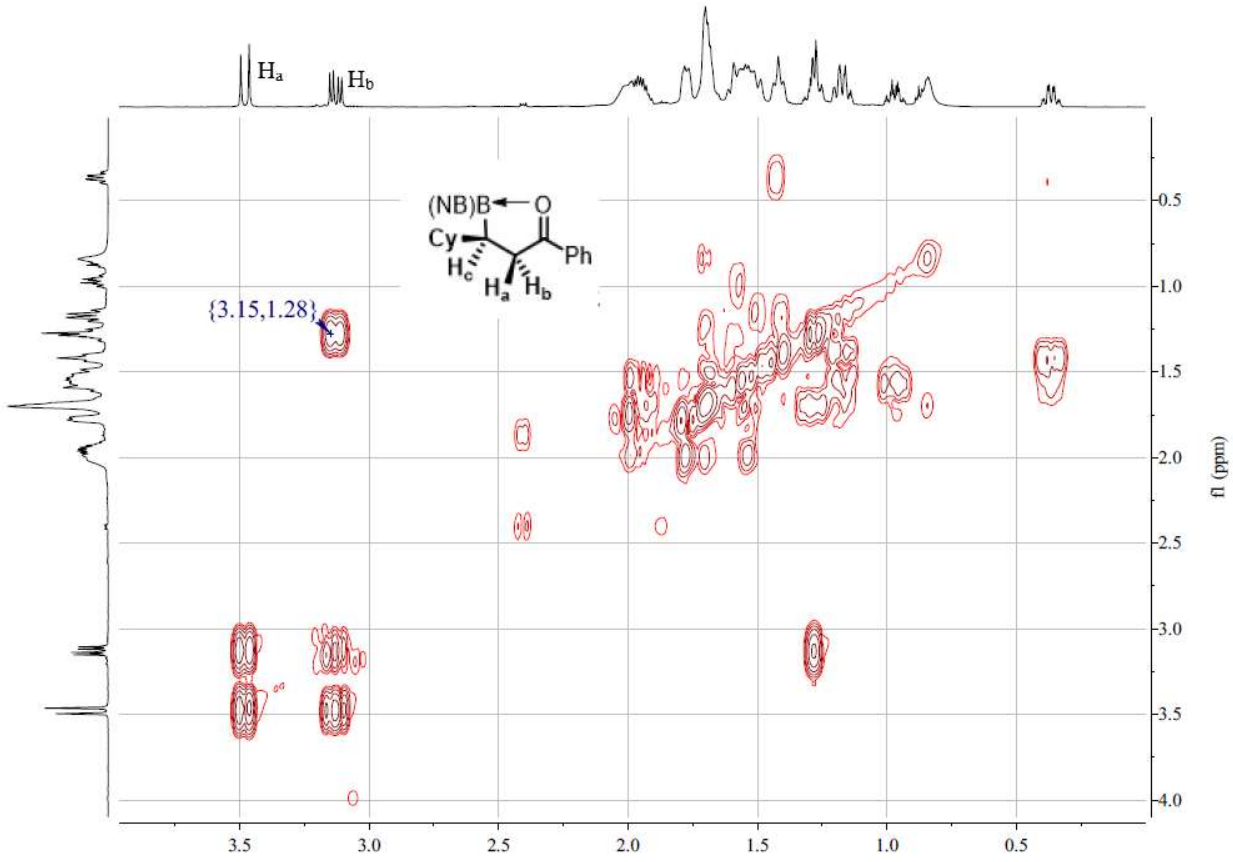
ref[10] for its synthesis) (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL) was allowed to complex for 5 minutes under inert atmosphere. The catalyst solution was added to the boron 'ate' mixture at room temperature followed by addition of benzoyl chloride (28.1 mg, 0.20 mmol, 1.00 equiv.). The reaction vial was sealed with a septum cap, taken out of the glovebox and stirred at room temperature for 1h. The crude mixture was concentrated in vacuo and purified by silica gel column chromatography (20% CH_2Cl_2 in hexane, stain in $KMnO_4$) to afford the product as a yellow oil (37.0 mg, 55% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.1 Hz, 2H), 7,74 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 8.1 Hz, 2H), 3.48 (d, *J* = 19.4 Hz, 1H), 3.15 (dd, *J* = 19.4, 8.3 Hz, 1H), 2.06-1.87 (m, 4H), 1.80-1.12 (m, 18H), 1.02-0.92 (m, 1H), 0.89-0.77 (m, 2H), 0.37 (dq, *J* = 12.2, 3.5 Hz, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 212.9, 136.4, 131.2, 130.9, 129.4, 40.0, 38.1, 33.5, 33.2, 32.6, 30.1, 27.2, 26.82, 26.77, 25.1. **^{11}B NMR** (150 MHz, $CDCl_3$) δ 21.5. **IR** (neat) ν_{max} 2917 (s), 2840 (s), 1637 (m), 1447 (m), 1332 (w), 1029 (m), 905 (s), 734 (s) cm^{-1}. **HRMS** (DART) for $C_{23}H_{34}BO$ $[M+H]^+$: Calc'd: 337.2697, found: 337.2700.

The resonances of the two diastereotopic protons adjacent to the carbonyl group in ^{1}H NMR are identified by a series of COSY NMR and 1D NOE NMR analysis presented below.

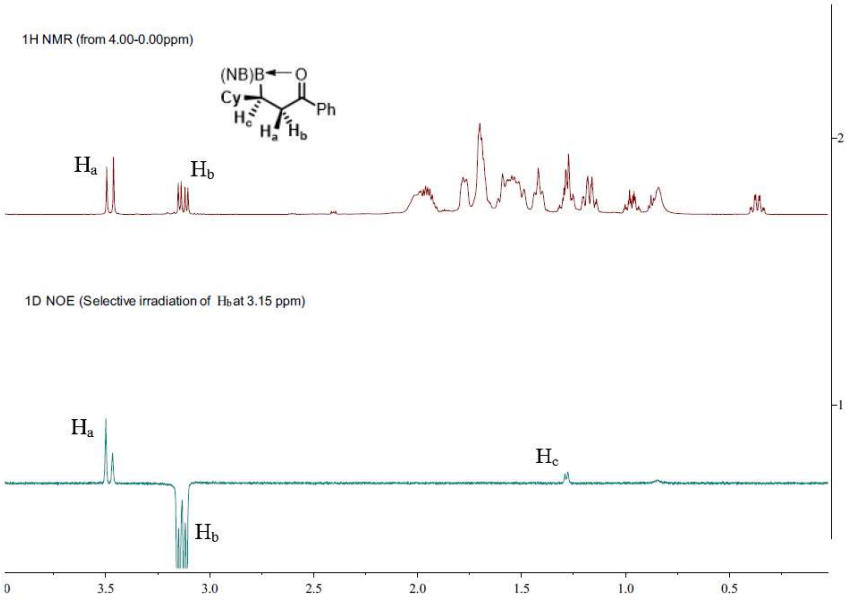
From COSY NMR spectrum, it is clearly seen that the proton with resonance at 3.15 ppm is coupled to H_c (with a resonance at 1.28 ppm), whereas the resonance at 3.48 ppm shows no appreciable coupling with H_c. Therefore, it is determined that the 3.15 ppm resonance corresponds to H_b while the 3.48 ppm resonance corresponds to H_a.

COSY NMR of **S-2.79**

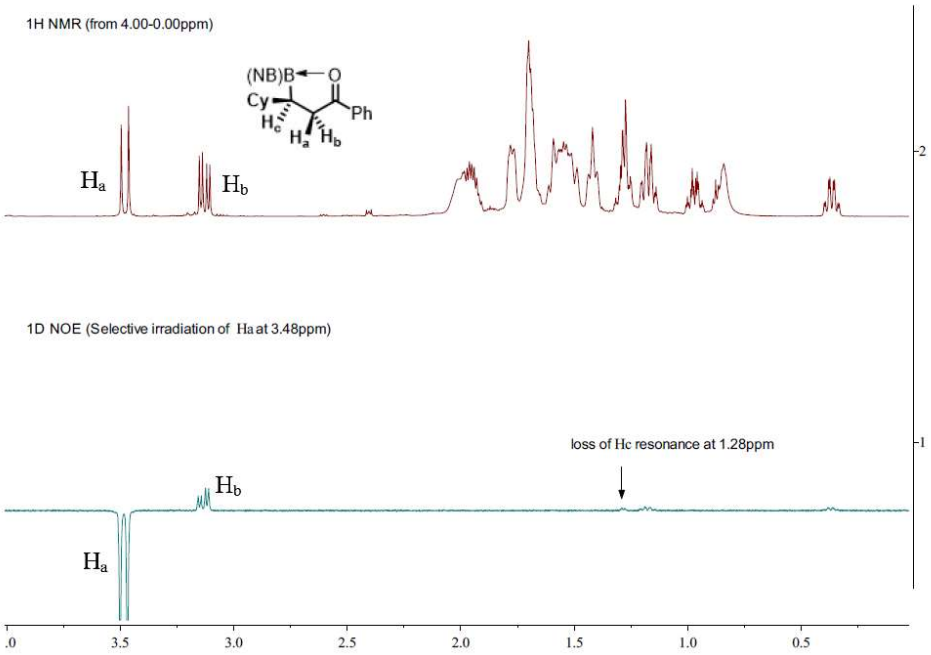


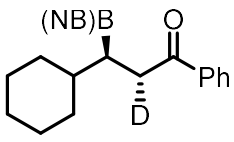
NOESY NMR was also carried out to support the findings about the resonances of the two diasterotopic protons. Selective irradiation of the resonance at 3.15 ppm led to NOE of H_c with resonance at 1.28ppm, whereas selective irradiation of the resonance at 3.48 ppm led to no observable NOE of H_c.

1D-NOE NMR of **S-2.79** (selective irradiation at 3.15 ppm)



1D-NOE NMR of **S-2.79** (selective irradiation at 3.48 ppm)



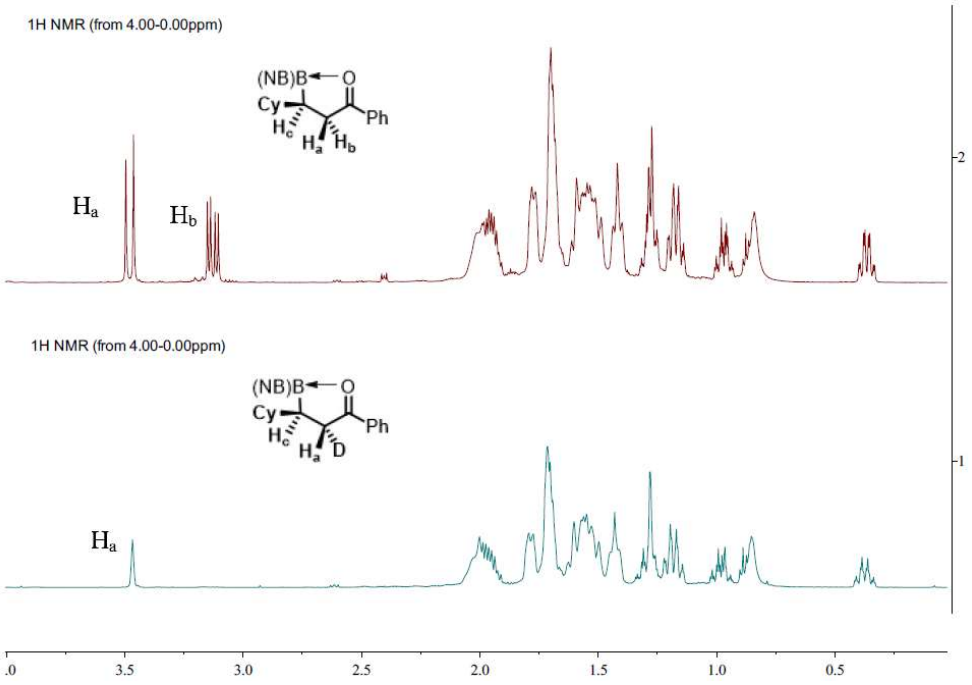


***anti*-3-(9-borabicyclo[3.3.1]nonan-9-yl)-3-cyclohexyl-1-phenylpropan-1-one-2-d (2.79).** The reaction was performed according to the procedure

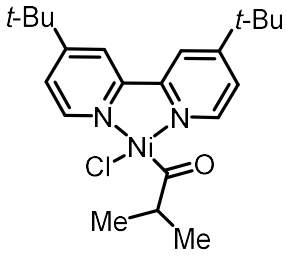
for synthesis of **S-2.79** with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), cyclohexene (21.4 mg, 0.26 mmol, 1.30 equiv.), deuterium labeled vinyl lithium in THF (0.27 mL, 0.82 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.3** (3.51 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), benzoyl chloride (28.1 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% CH_2Cl_2 in hexane, stain in $KMnO_4$) to afford the product as a yellow oil (21.1 mg, 30% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.8 Hz, 2H), 7,75 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.8 Hz, 2H), 3.48 (s, 1H), 2.13-1.88 (m, 3H), 1.81-1.40 (m, 3H), 1.36-1.11 (m, 5H), 1.04-0.94 (m, 1H), 0.91-0.71 (m, 2H), 0.37 (dq, *J* = 12.2, 3.4 Hz, 1H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 213.0, 136.4, 131.3, 130.9, 129.4, 38.1, 33.50, 33.48, 32.6, 30.22, 30.15, 27.2, 26.83, 26.77, 25.1. **^{11}B NMR** (150 MHz, $CDCl_3$) δ 21.5. **IR** (neat) ν_{max} 2922 (s), 2852 (m), 1679 (m), 1598 (w), 1447 (s), 1272 (m), 1206 (m), 746 (s), 689 (s), 651 (w) cm^{-1}.

The relative stereochemistry was determined by comparison of its ^{1}H NMR spectrum with its non-deuterium labeled counterpart (**S-2.79**).



2.4.8 Stoichiometric Experiments



2.83

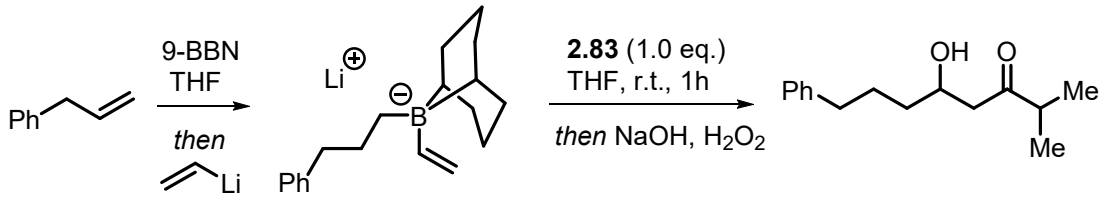
Ni(II) oxidative addition complex (2.83). The title compound was prepared according to the procedure reported by Gong with slight modifications.[125] In an argon filled glovebox, to an oven-dried scintillation vial was

[125] C. Zhao, J. Xiao, X. Wang, H. Gong, *J. Am. Chem. Soc.* **2014**, *136*, 17645.

added $Ni(COD)_2$ (248 mg, 0.90 mmol, 1.0 equiv.) and Et_2O (4 mL). The reaction mixture was allowed to stir for 0.5h at room temperature at which point 4,4'-di-tert-butyl-2,2'-bipyridine (341 mg, 0.90 mmol, 1.0 equiv.) in Et_2O (4 mL) was added dropwise. The resulting mixture was allowed to stir at room temperature, at which point, a solution of *iso*-butyryl chloride (96.0 mg, 0.90 mmol, 1.0 equiv.) in Et_2O (1 mL) was added via a syringe. The mixture was allowed to stir for 1h. The suspension was then allowed to settle and the supernatant was removed via syringe leaving behind red solid which was triturated with Et_2O (2 mL x 4). The red solid was then dried under vacuum, affording **2.83** (351 mg, 90%). All spectral data was in accordance with the literature.[57]

^{1}H NMR (500 MHz, DMF-d_7) δ 8.99 (br s, 1H), 8.72 (br s, 2H), 8.21 (br s, 1H), 7.88 (d, J = 40.3 Hz, 2H), 3.49 (s, 1H), 1.58 (s, 18H), 1.47 (s, 6H). **^{13}CNMR** (150 MHz, DMF-d_7) δ 260.0, 164.2, 163.3, 155.3, 152.2, 150.6, 148.0, 124.2, 123.2, 119.9, 118.7, 45.2, 35.6, 18.5.

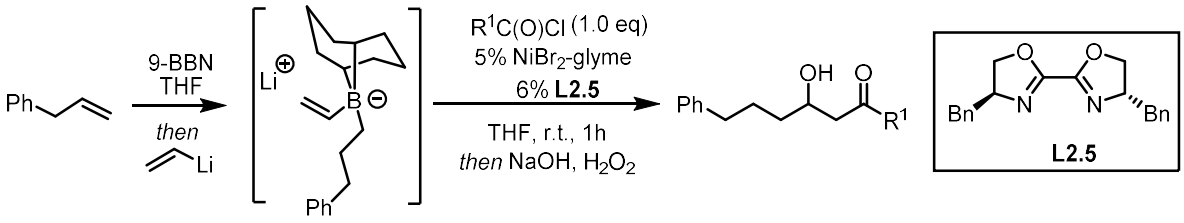
Stoichiometric Conjunctive Cross-Coupling Reaction



In a glovebox, under argon, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with a solution of 9-BBN in THF (0.40 mL, 0.5 M, 0.20 mmol, 1.00 equiv.). The vial was cooled to 0°C, and allylbenzene (23.6 mg, 0.20 mmol, 1.00 equiv.) was added. The reaction mixture was allowed to warm to room temperature and stir for 3 hours before

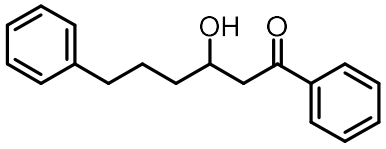
being cooled back to 0°C. A solution of vinyllithium (for synthesis of halide free vinyllithium see ref[1]) in THF (0.15 mL, 1.38 M, 0.22 mmol, 1.00 equiv.) was added to the reaction mixture which was then warmed to room temperature and stirred for 5 minutes. To the vial was added **2.83** (86.7 mg, 0.20 mmol, 1.0 equiv.) in one portion at room temperature. The reaction vial was sealed with a septum cap, taken out of the glovebox and stirred at room temperature for 1h, after which point the reaction mixture was cooled to 0°C and 30% H_2O_2 (0.5 mL) were added along with 3 M NaOH (0.5 mL). The reaction mixture was allowed to warm up to room temperature and stirred for 3 hours. Aqueous saturated $Na_2S_2O_3$ (1 mL) solution was then added to quench the reaction. The aqueous phase was extracted with EtOAc (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to provide **1.55** as a colorless oil (20.2 mg, 43%).

2.4.9 Experiments with Chiral Bis(oxazoline) Ligands.



In a glovebox, under argon, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with a solution of 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.). The vial was cooled to 0°C, and the olefin (0.26 mmol, 1.30 equiv.) was added *via* syringe. The reaction mixture was allowed to warm to room temperature and stir for 3 hours before being cooled back to 0°C. A solution of vinyllithium (for synthesis of halide free

vinyllithium see ref[1]) in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.) was added to the reaction mixture which was then warmed to room temperature and stirred for 5 minutes. Meanwhile a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.5** (0.012 mmol, 0.060 equiv.) in THF (0.4 mL) was allowed to complex for 5 minutes under inert atmosphere. The catalyst solution was added to the boron 'ate' mixture at room temperature followed by addition of the acyl chloride (0.20 mmol, 1.00 equiv.) The reaction vial was sealed with a septum cap, taken out of the glovebox and stirred at room temperature for 1h, after which point the reaction mixture was cooled to 0°C and 30% H_2O_2 (0.5 mL) were added along with 3 M NaOH (0.5 mL). The reaction mixture was allowed to warm up to room temperature and stirred for 3 hours. Aqueous saturated $Na_2S_2O_3$ (1 mL) solution was then added to quench the reaction. The aqueous phase was extracted with EtOAc (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to provide the desired products.



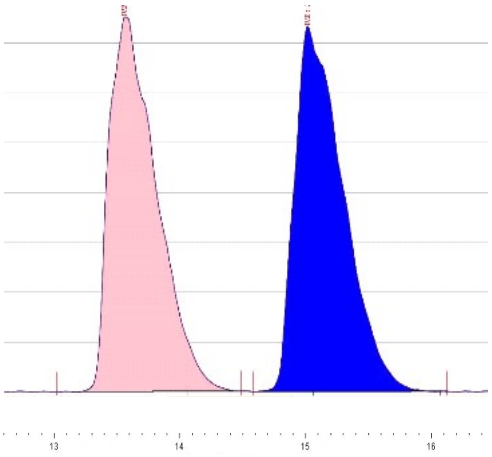
3-hydroxy-1,6-diphenylhexan-1-one (2.57). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.5** (0.012 mmol, 0.060 equiv.) in THF (0.4 mL), benzoyl chloride (28.1 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product

as a colorless oil (19.3 mg, 36% yield). Its corresponding spectral data can be found above in the section **"*Characterization of Conjunctive Cross Coupling Products*"**.

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the general procedure with **L2.3** (6 mol%) as the ligand.

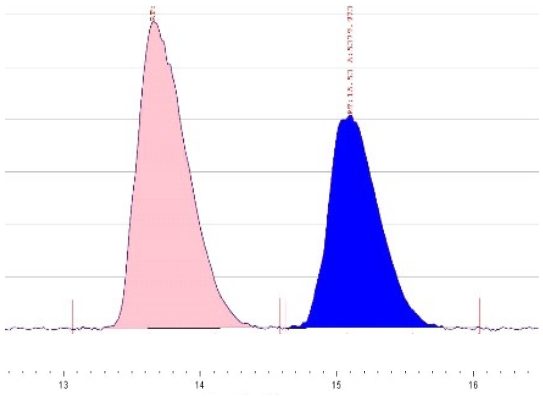
Chiral SFC (Chiracel AS-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)

Racemic material

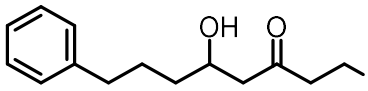


Peak No	% Area	Area	RT (min)
1	49.9903	19738.0387	13.5
2	50.0097	19745.7246	14.95
Total:	100	39483.7633	

Enantioenriched material



Peak No	% Area	Area	RT (min)
1	59.0118	7745.7033	14.03
2	40.9882	5379.9731	15.53
Total:	100	13125.6764	



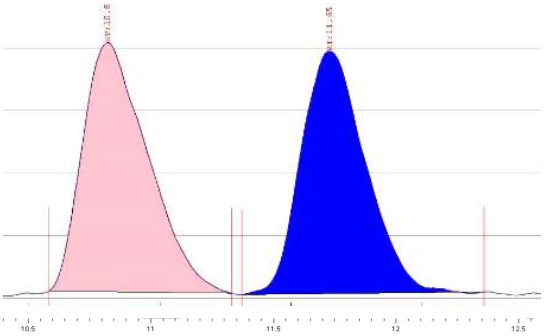
6-hydroxy-9-phenylnonan-4-one (2.49). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (3.09 mg, 0.010 mmol, 0.050 equiv.) and **L2.5** (0.012 mmol, 0.060 equiv.) in THF (0.4 mL), butanoyl chloride (21.3 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the product

as a colorless oil (20.2 mg, 43% yield). Its corresponding spectral data can be found above in the section **"*Characterization of Conjunctive Cross Coupling Products*"**.

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the general procedure with **L2.5** (6 mol%) as the ligand.

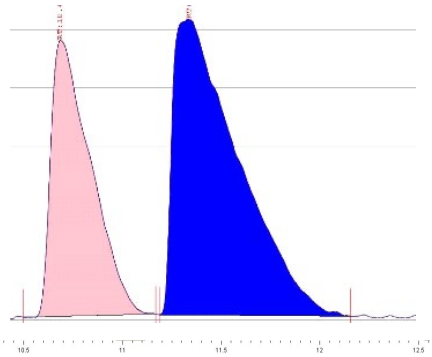
Chiral SFC (Chiracel AS-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)

Racemic material

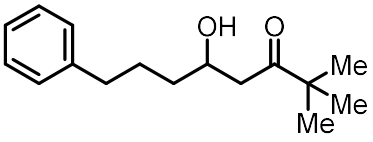


Peak No	% Area	Area	RT (min)
1	51.0302	3457.9941	10.8
2	48.9698	3318.3731	11.65
Total:	100	6776.3672	

Enantioenriched material



Peak No	% Area	Area	RT (min)
1	36.1664	4258.9027	10.41
2	63.8336	7516.955	11.24
Total:	100	11775.8577	



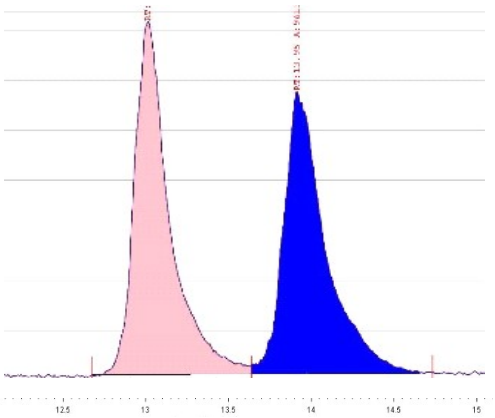
5-hydroxy-2,2-dimethyl-8-phenyloctan-3-one (2.54). The reaction was performed according to the general procedure with 9-BBN in THF (0.52 mL, 0.5 M, 0.26 mmol, 1.30 equiv.), allylbenzene (30.7 mg, 0.26 mmol, 1.30 equiv.), halide-free vinyllithium in THF (0.16 mL, 1.38 M, 0.22 mmol, 1.10 equiv.), a solution of $NiBr_2$-glyme (2.20 mg, 0.010 mmol, 0.050 equiv.) and **L2.5** (0.012 mmol, 0.060 equiv.) in THF (0.4 mL), pivaloyl chloride (24.1 mg, 0.20 mmol, 1.00 equiv.). The crude mixture was purified by column chromatography (20% EtOAc in hexane, stain in $KMnO_4$) to afford the

product as a colorless oil (13.4 mg, 27% yield). Its corresponding spectral data can be found above in the section **"*Characterization of Conjunctive Cross Coupling Products*"**.

Enantioselectivity was determined by chiral SFC. Racemic compound was prepared according to the general procedure with **L2.3** (6 mol%) as the ligand.

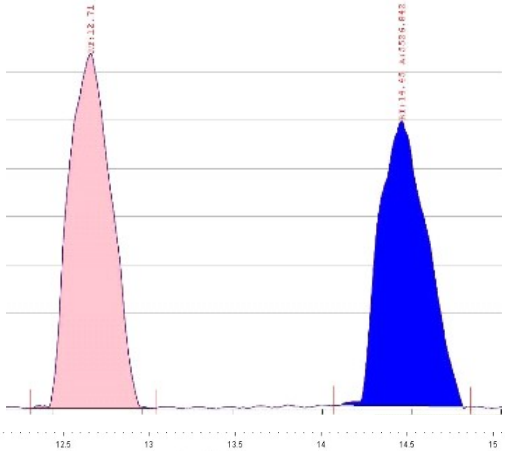
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)

Racemic material



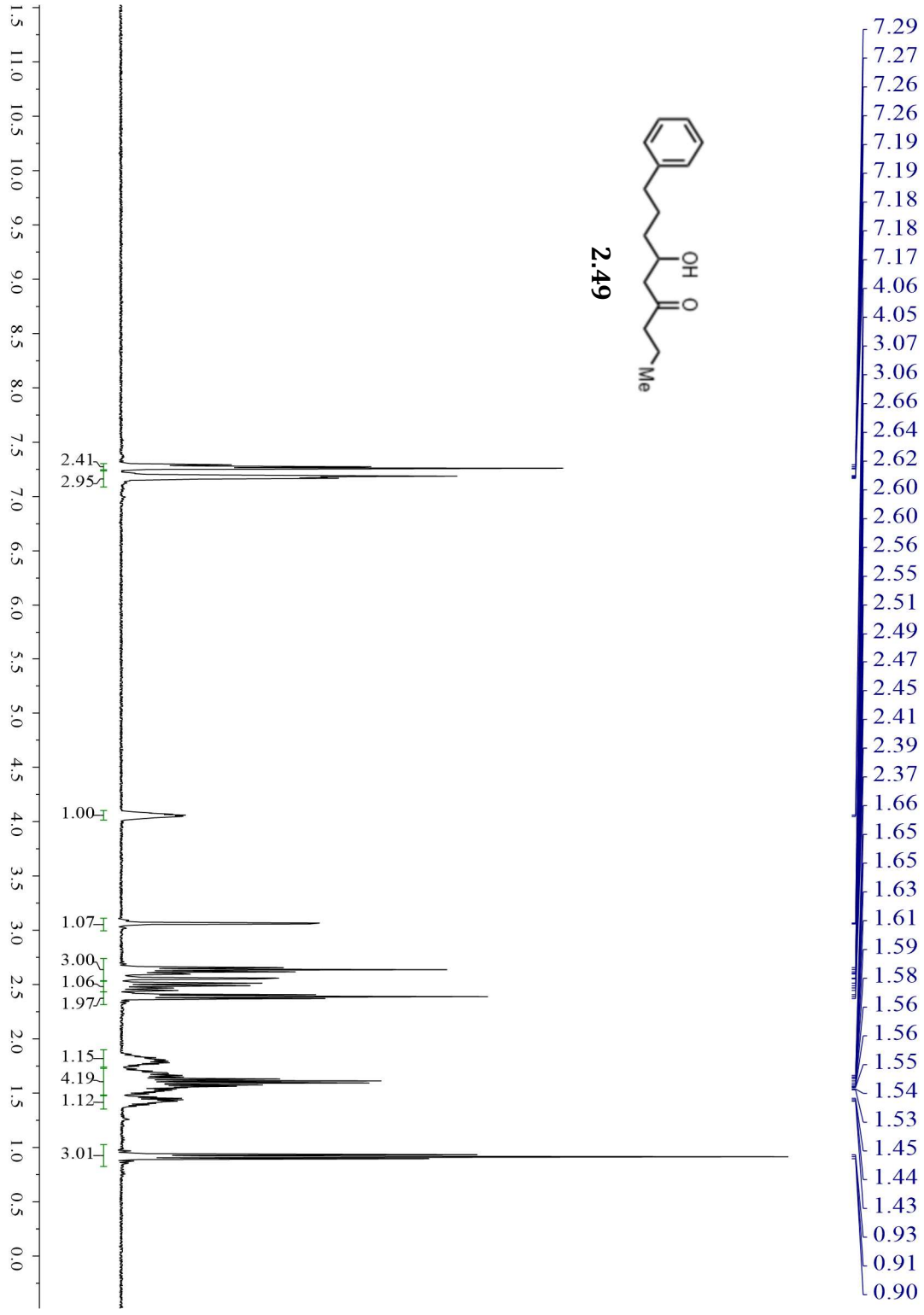
Peak No	% Area	Area	RT (min)
1	51.5896	10244.8632	12.2
2	48.4104	9613.5239	13.95
Total:	100	19858.3871	

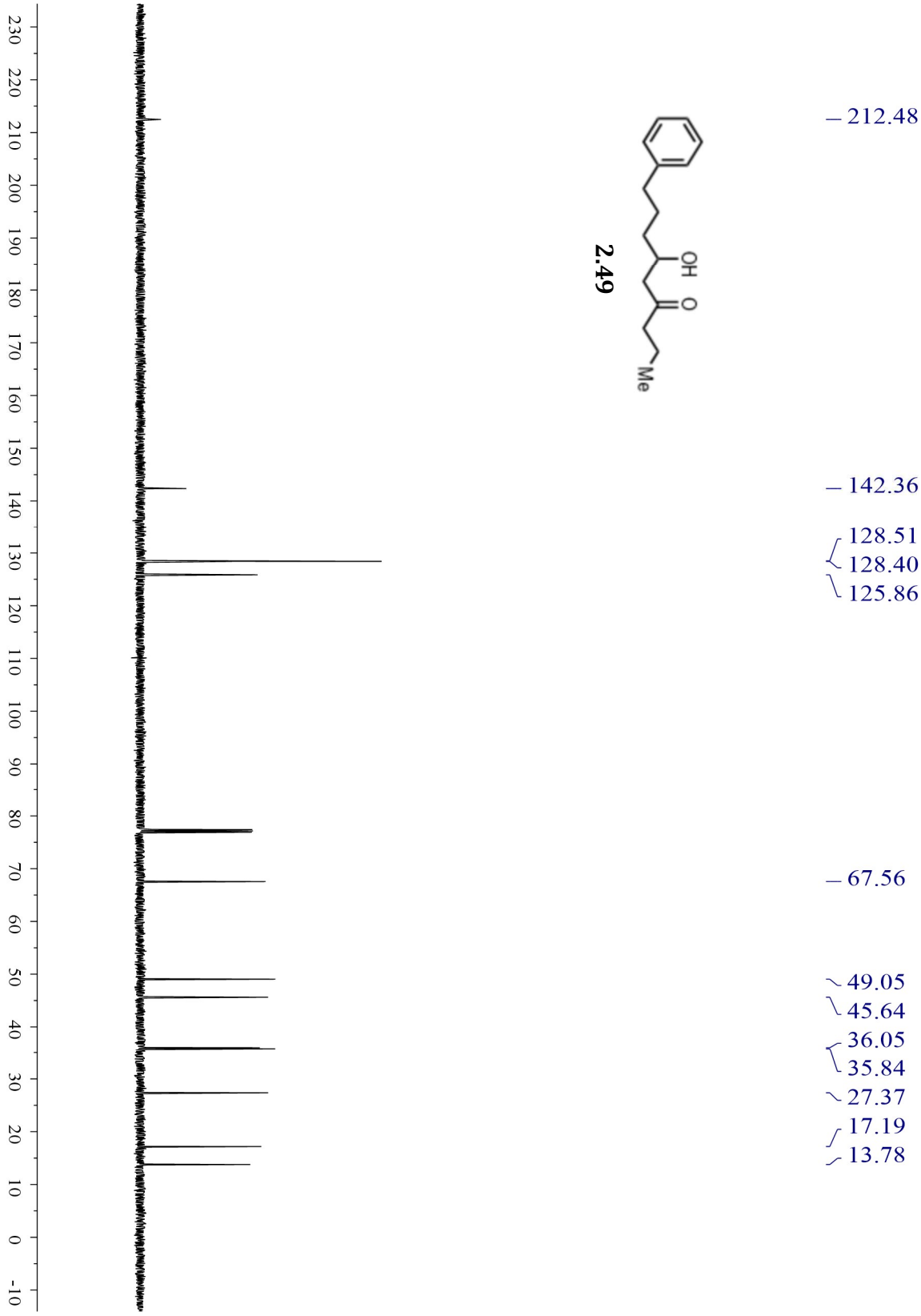
Enantioenriched

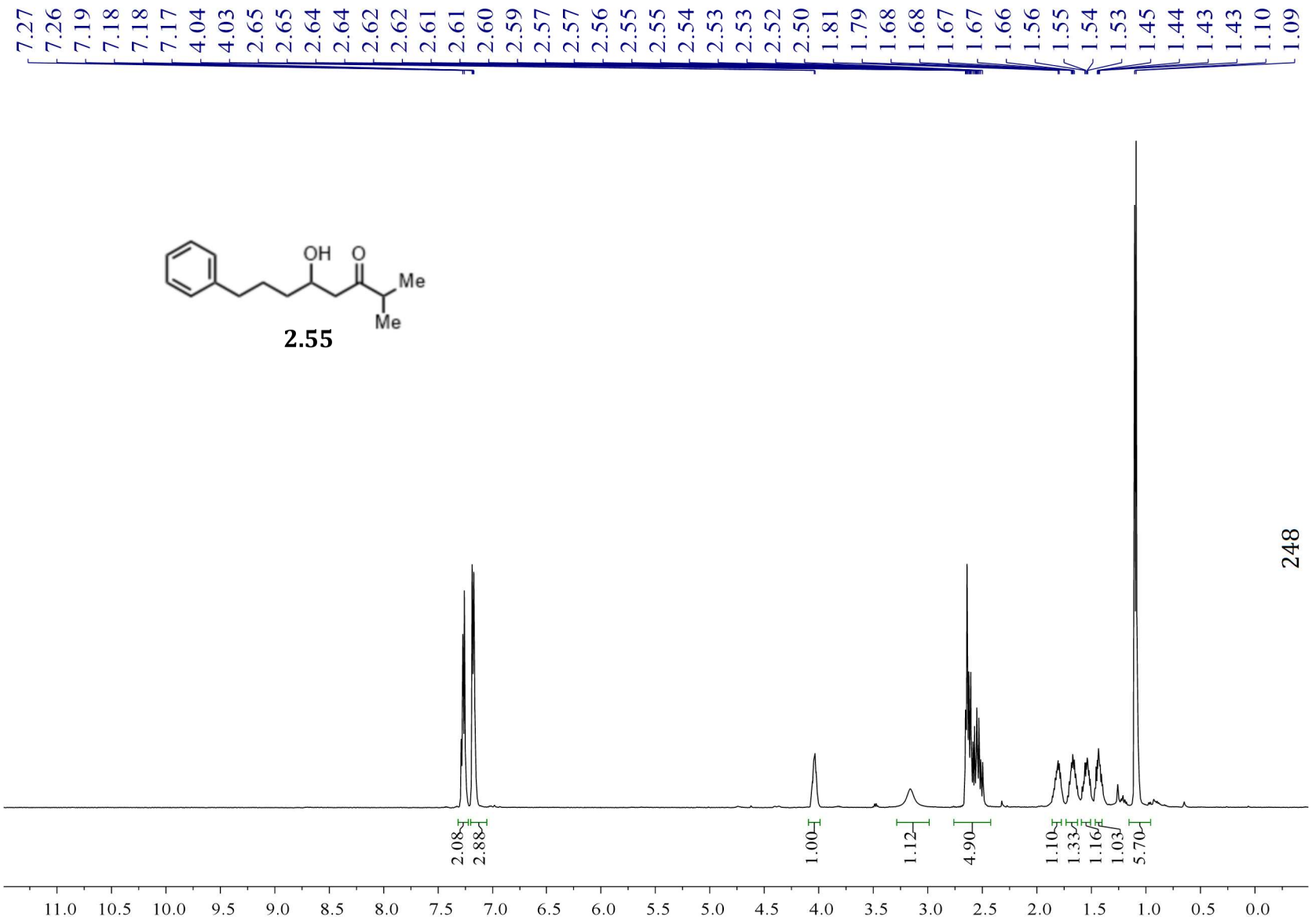


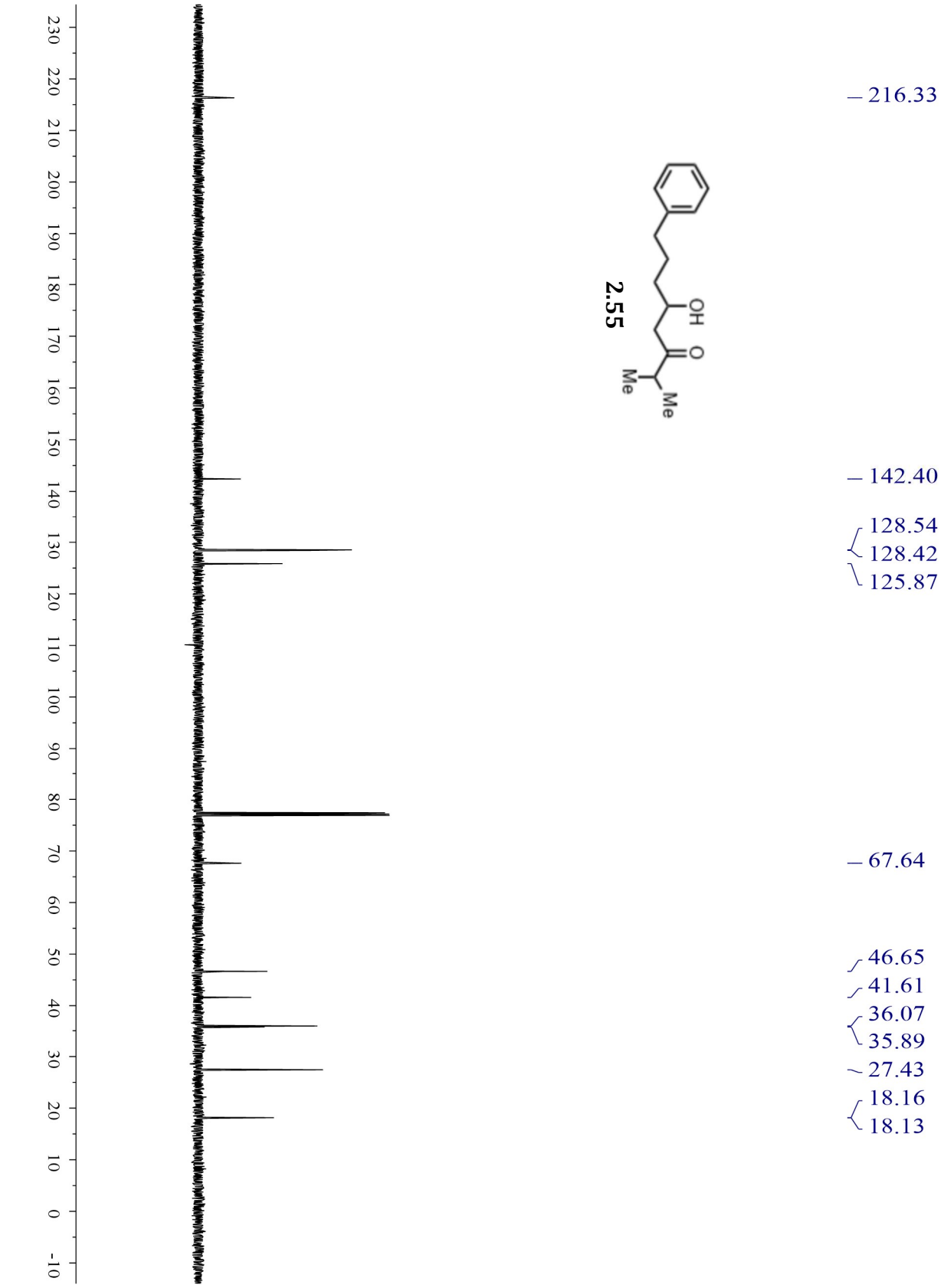
Peak No	% Area	Area	RT (min)
1	52.339	6069.3027	12.71
2	47.661	5526.842	14.45
Total:	100	11596.1447	

2.4.10 Spectral Data



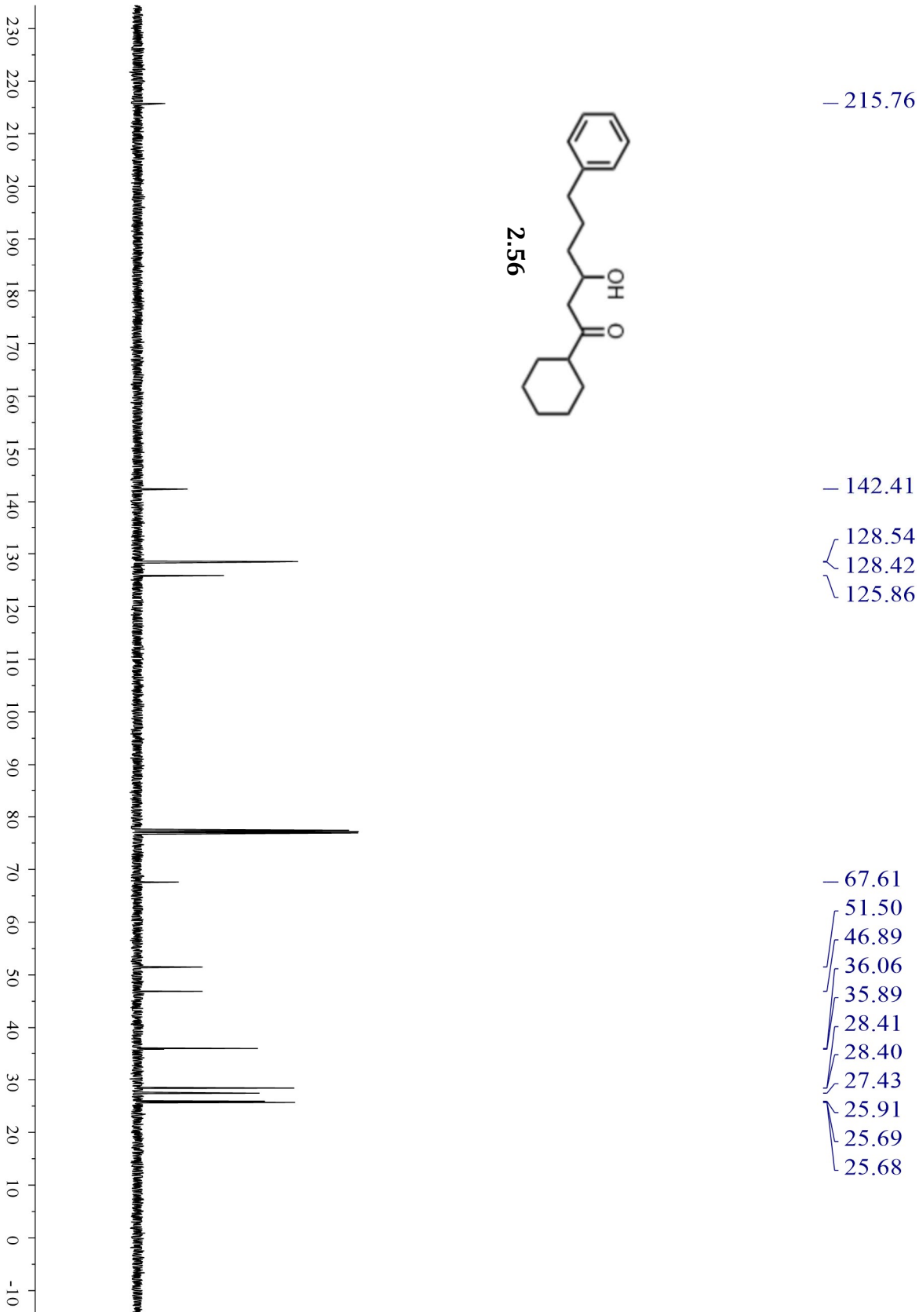

230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
OH
O
Me
2.49
212.48
142.36
128.51
128.40
125.86
67.56
49.05
45.64
36.05
35.84
27.37
17.19
13.78

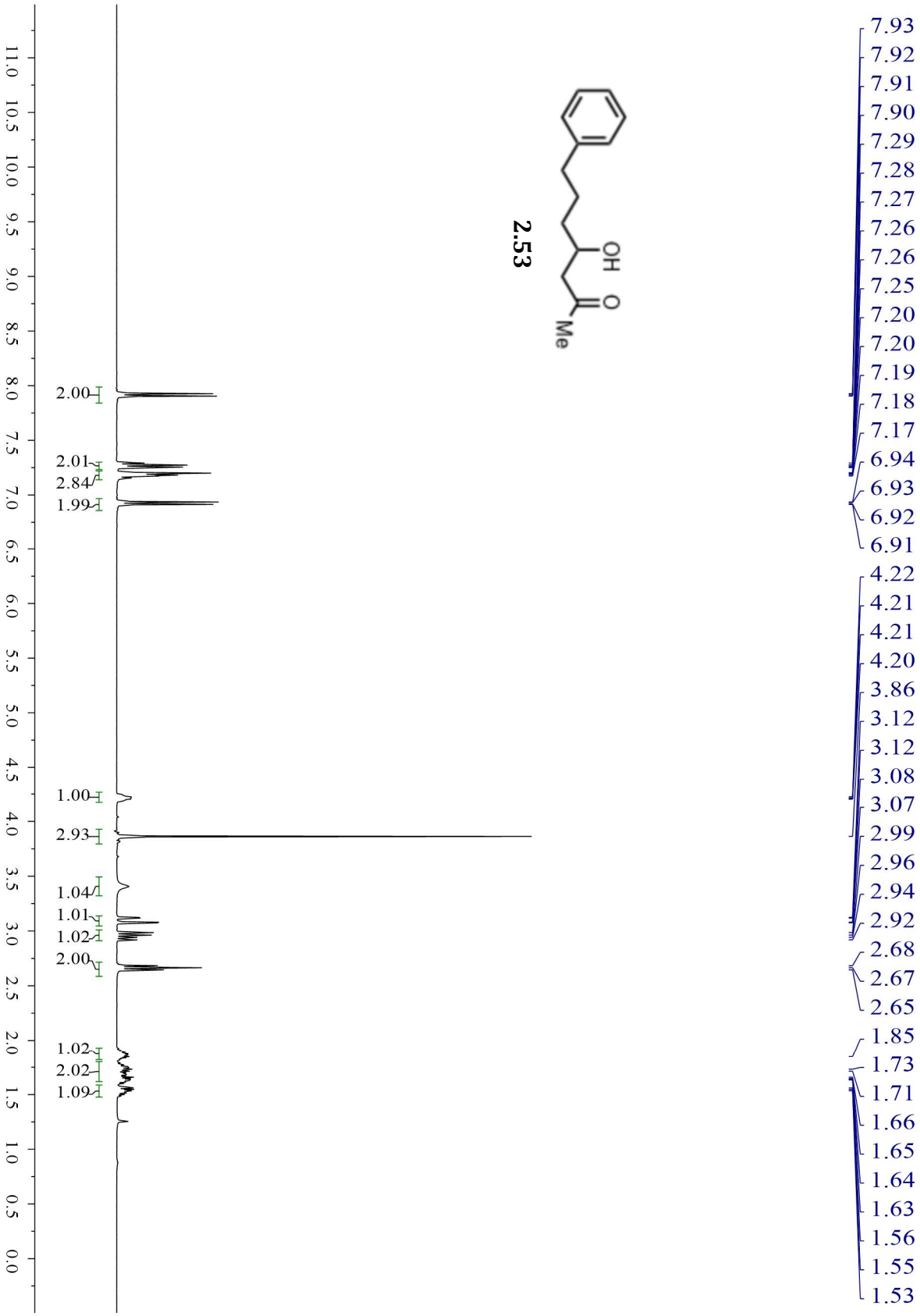

7.27 7.26 7.19 7.18 7.18 7.17 4.04 4.03 2.65 2.65 2.64 2.64 2.62 2.62 2.61 2.61 2.60 2.59 2.57 2.57 2.56 2.55 2.55 2.54 2.53 2.53 2.52 2.50 1.81 1.79 1.68 1.68 1.67 1.67 1.66 1.56 1.55 1.54 1.53 1.45 1.44 1.43 1.43 1.10 1.09
OH
O
Me
Me
2.55
248
2.08
2.88
1.00
1.12
4.90
1.10
1.33
1.16
1.03
5.70
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

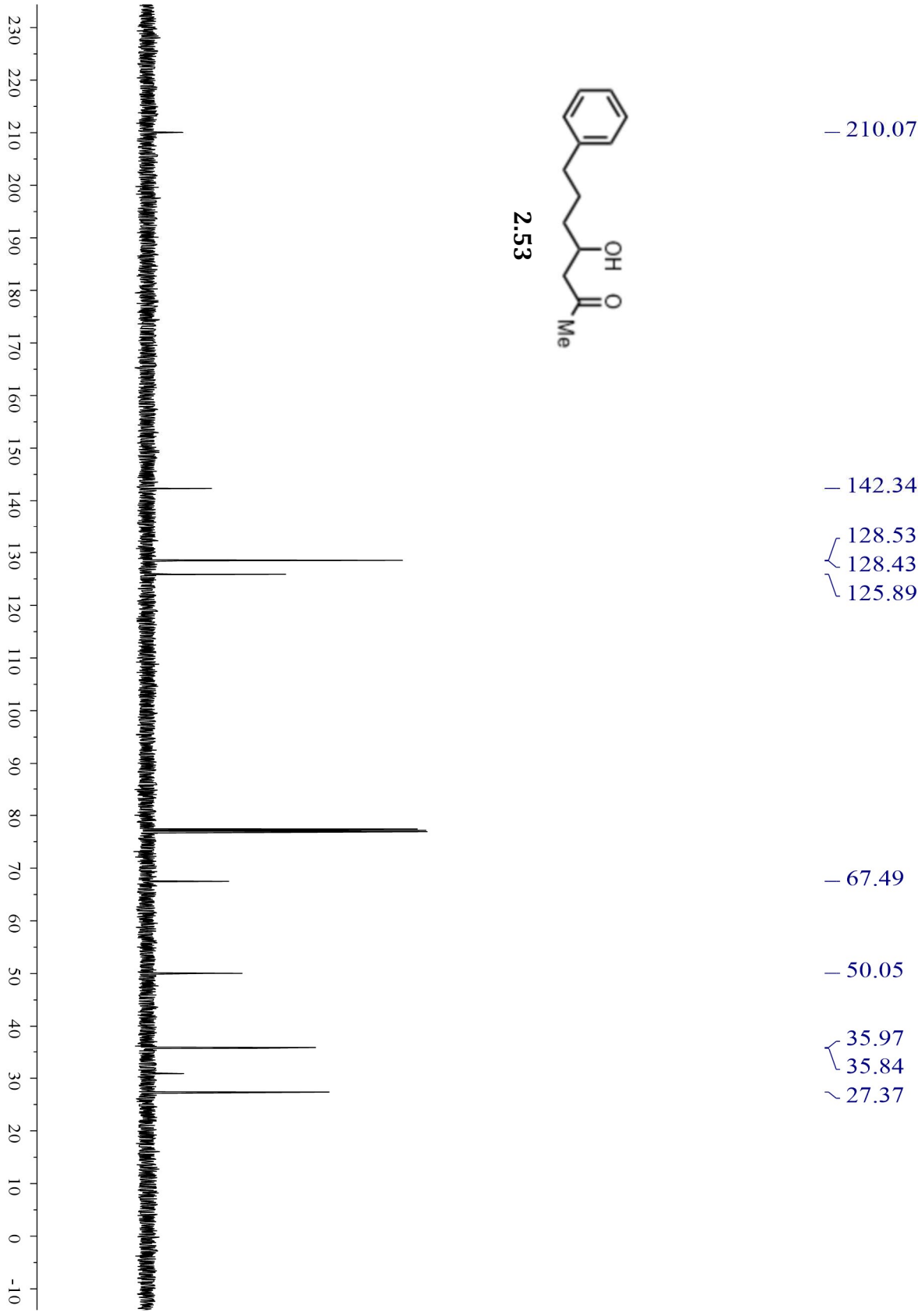

2.55
OH
O
Me
Me
216.33
142.40
128.54
128.42
125.87
67.64
46.65
41.61
36.07
35.89
27.43
18.16
18.13
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

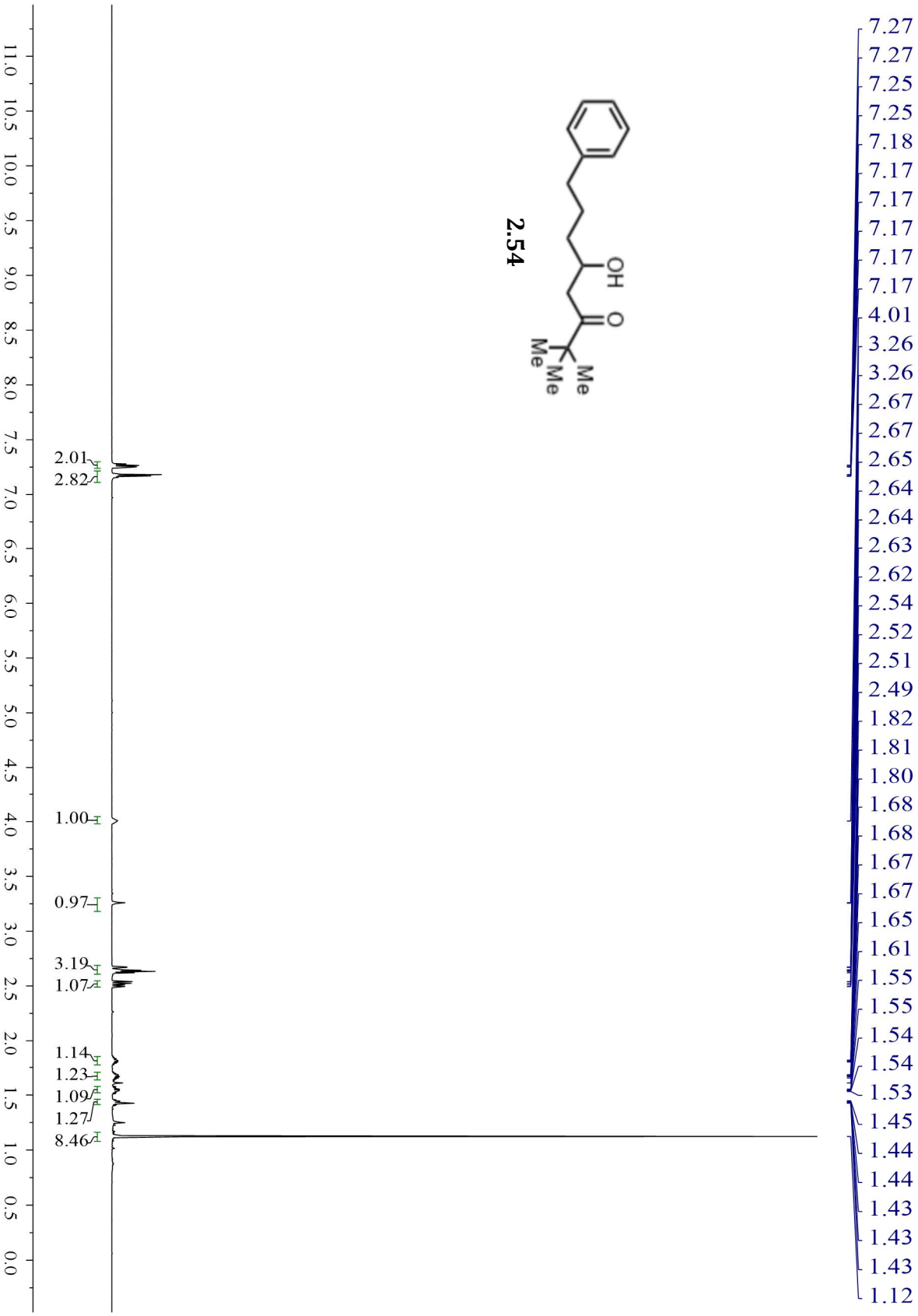
v

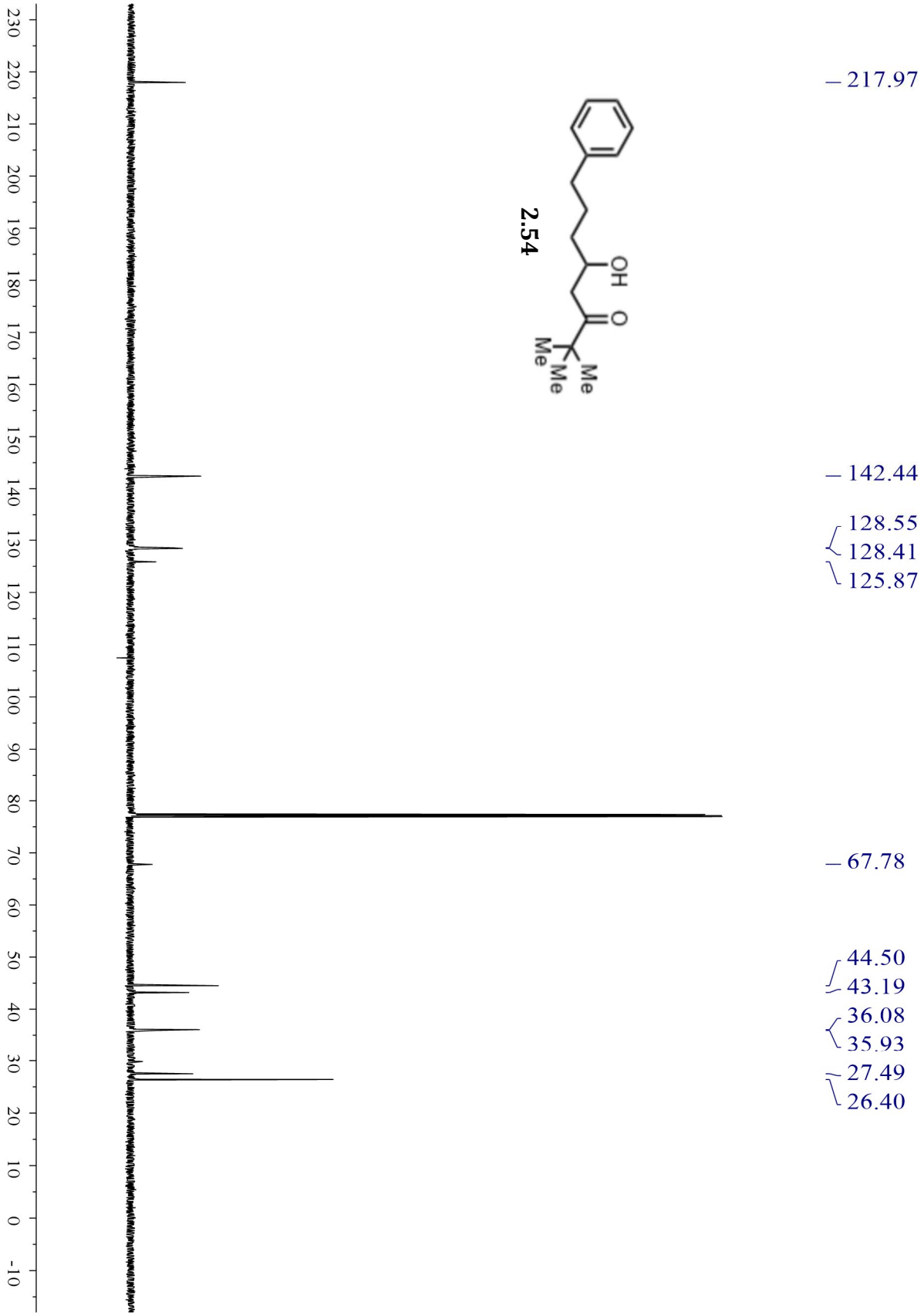
2.56
OH
O
2.25
3.23
1.00
1.09
3.07
1.14
1.16
4.95
2.63
1.32
1.03
5.53
7.36
7.35
7.35
7.33
7.26
7.26
7.25
7.25
7.24
7.24
3.26
3.26
2.72
2.71
2.70
2.69
2.67
2.67
2.60
2.58
1.91
1.91
1.90
1.90
1.89
1.88
1.88
1.87
1.87
1.86
1.86
1.85
1.85
1.84
1.76
1.75
1.74
1.73
1.72
1.40
1.38
1.38
1.35
1.35
1.32

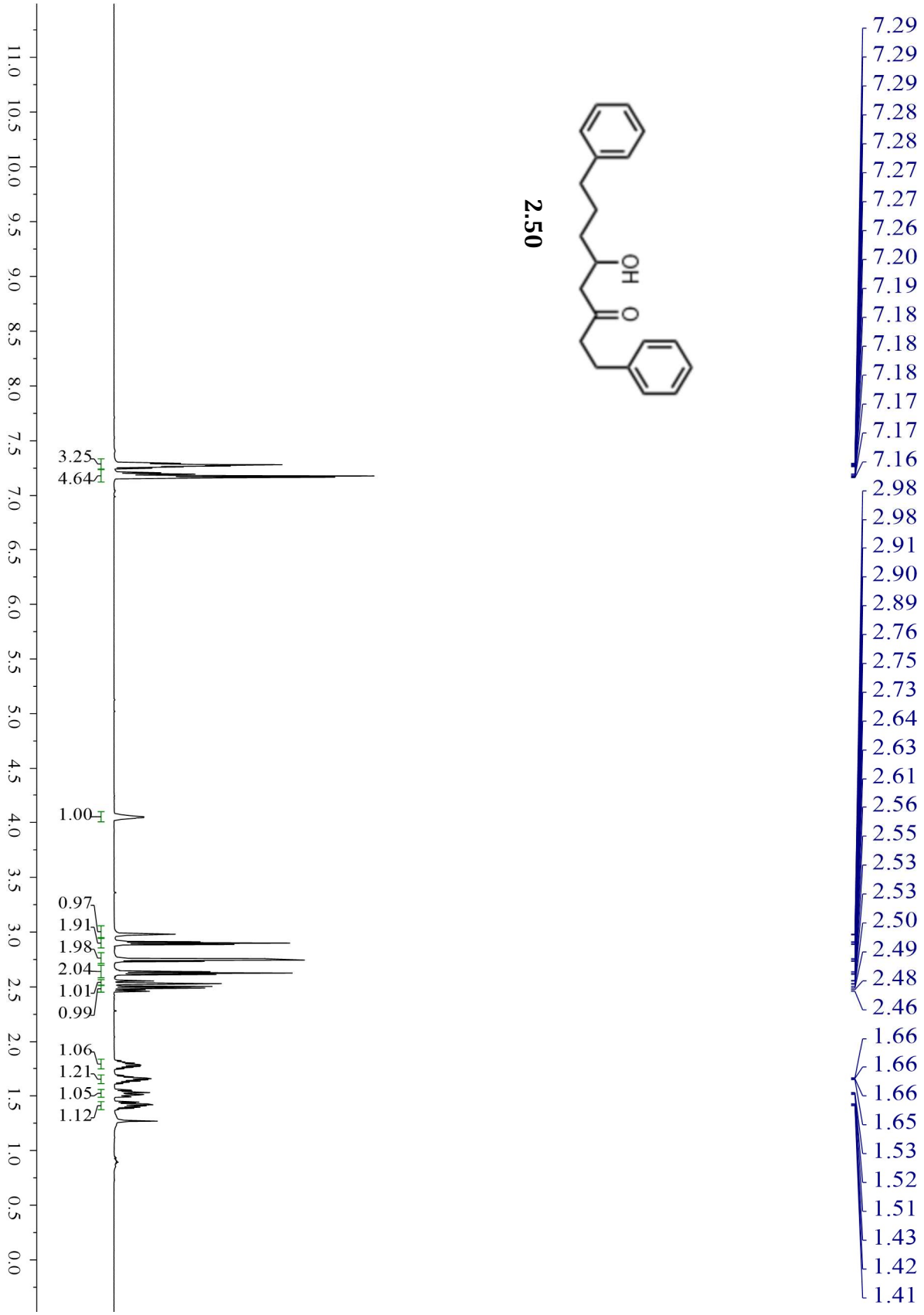

2.56
OH
O
215.76
142.41
128.54
128.42
125.86
67.61
51.50
46.89
36.06
35.89
28.41
28.40
27.43
25.91
25.69
25.68
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

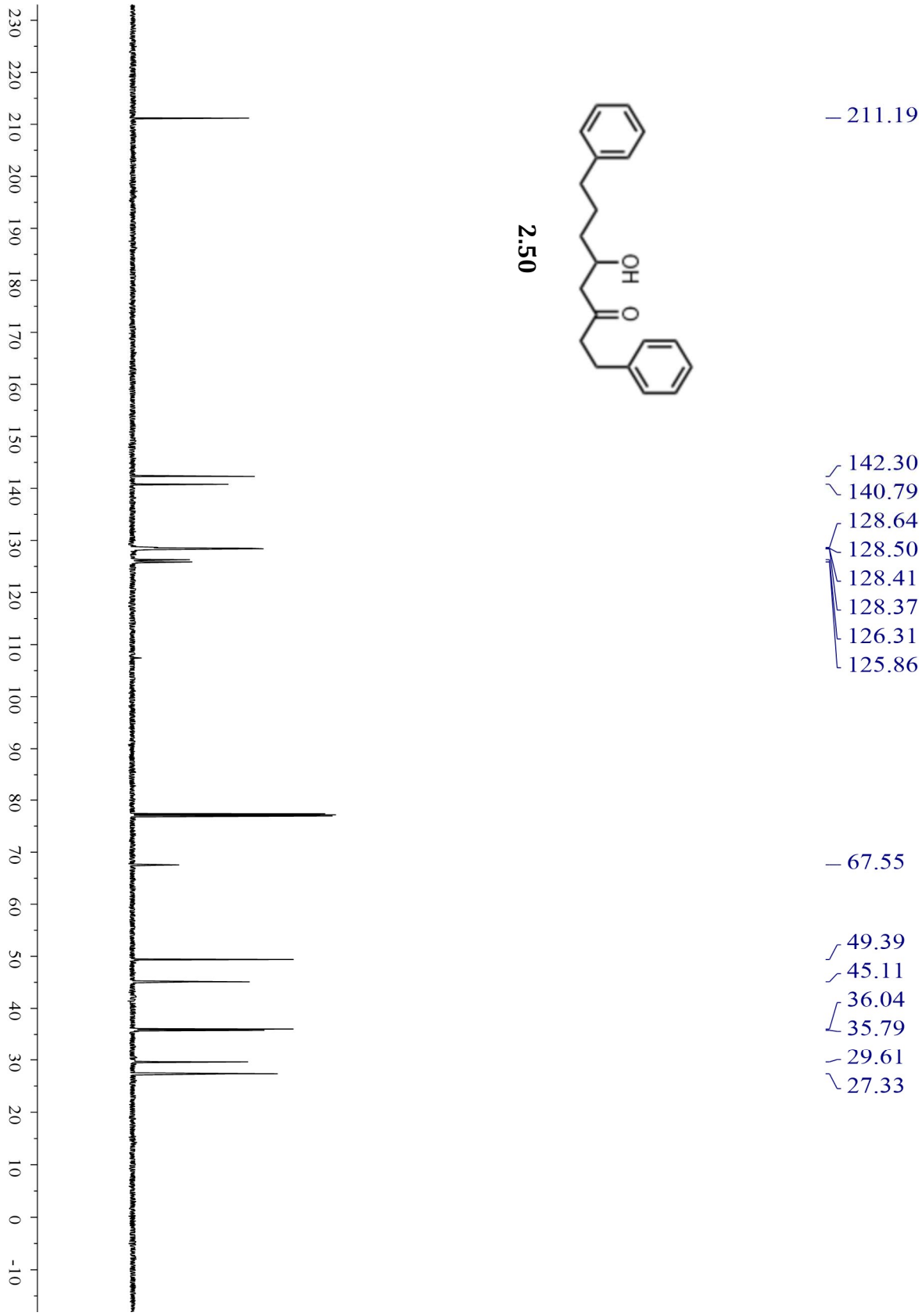

2.53
OH
O
Me
2.00
2.01
2.84
1.99
1.00
2.93
1.04
1.01
1.02
2.00
1.02
2.02
1.09
7.93
7.92
7.91
7.90
7.29
7.28
7.27
7.26
7.26
7.25
7.20
7.20
7.19
7.18
7.17
6.94
6.93
6.92
6.91
4.22
4.21
4.21
4.20
3.86
3.12
3.12
3.08
3.07
2.99
2.96
2.94
2.92
2.68
2.67
2.65
1.85
1.73
1.71
1.66
1.65
1.64
1.63
1.56
1.55
1.53

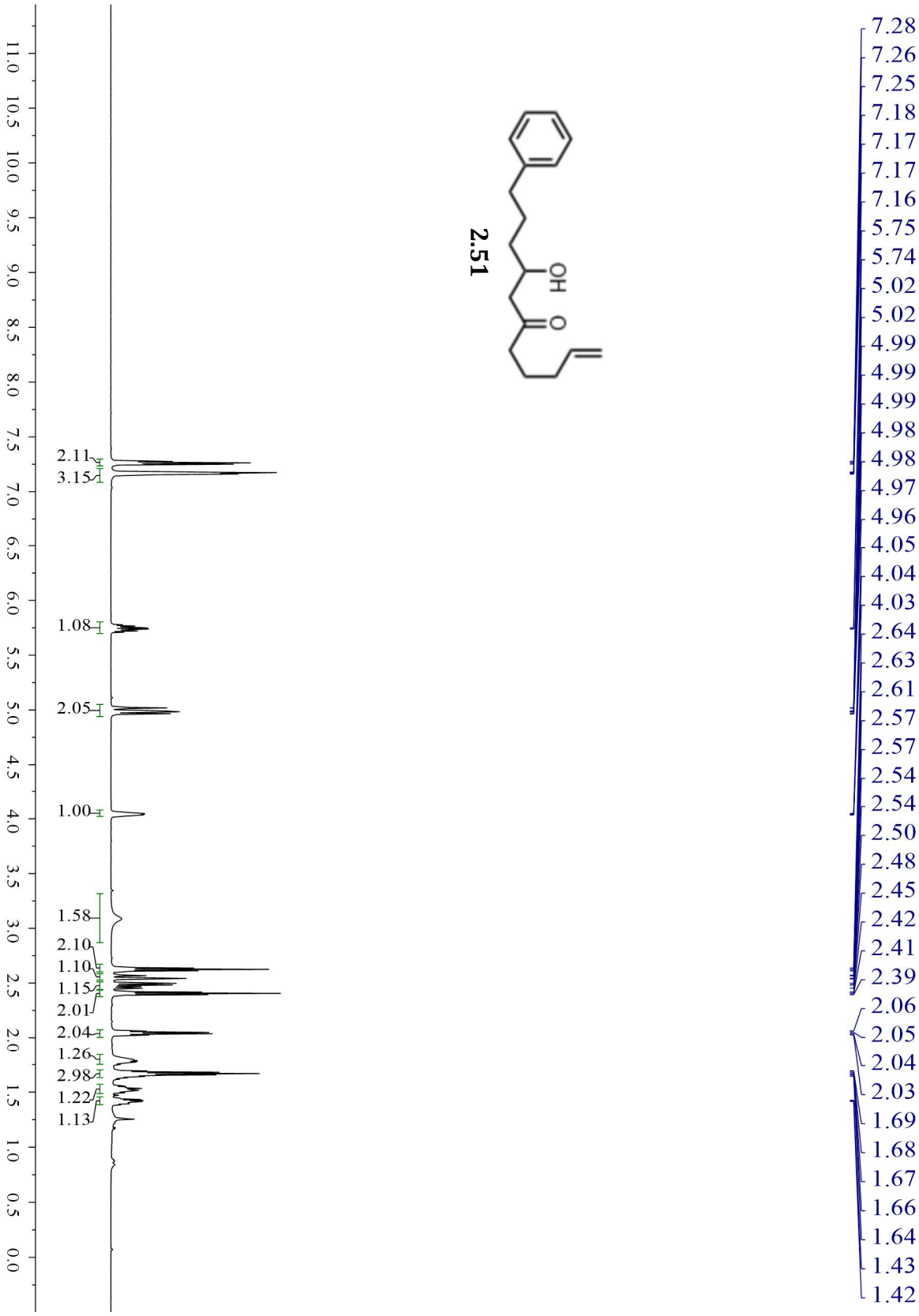

230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
OH
O
Me
2.53
210.07
142.34
128.53
128.43
125.89
67.49
50.05
35.97
35.84
27.37

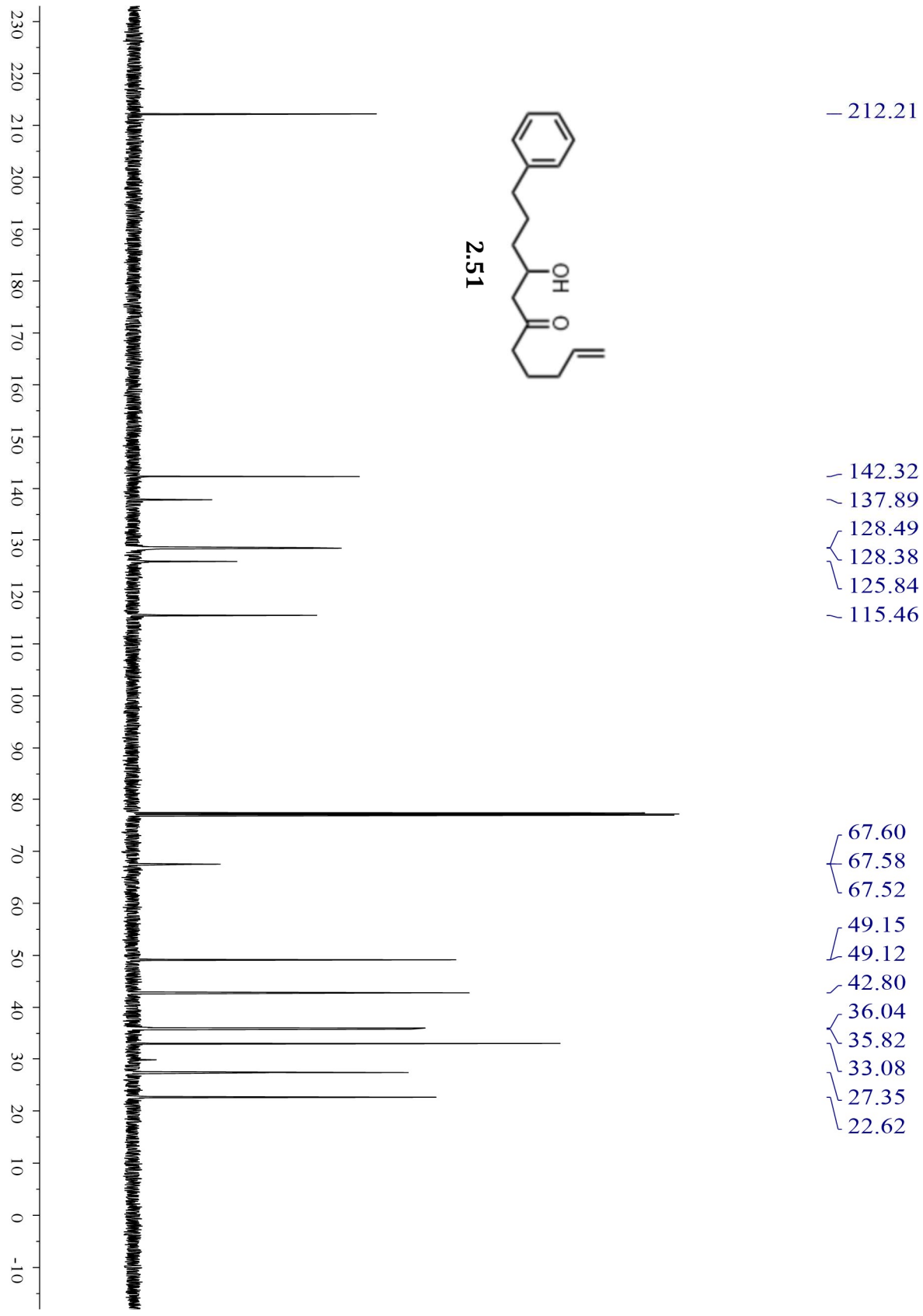

2.54
OH
O
Me
Me
Me
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
2.01
2.82
1.00
0.97
3.19
1.07
1.14
1.23
1.09
1.27
8.46
7.27
7.27
7.25
7.25
7.18
7.17
7.17
7.17
7.17
7.17
7.17
4.01
3.26
3.26
2.67
2.67
2.65
2.64
2.64
2.63
2.62
2.54
2.52
2.51
2.49
1.82
1.81
1.80
1.68
1.68
1.67
1.67
1.65
1.61
1.55
1.55
1.54
1.54
1.53
1.45
1.44
1.44
1.43
1.43
1.43
1.12


2.54
OH
O
Me
Me
Me
217.97
142.44
128.55
128.41
125.87
67.78
44.50
43.19
36.08
35.93
27.49
26.40
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

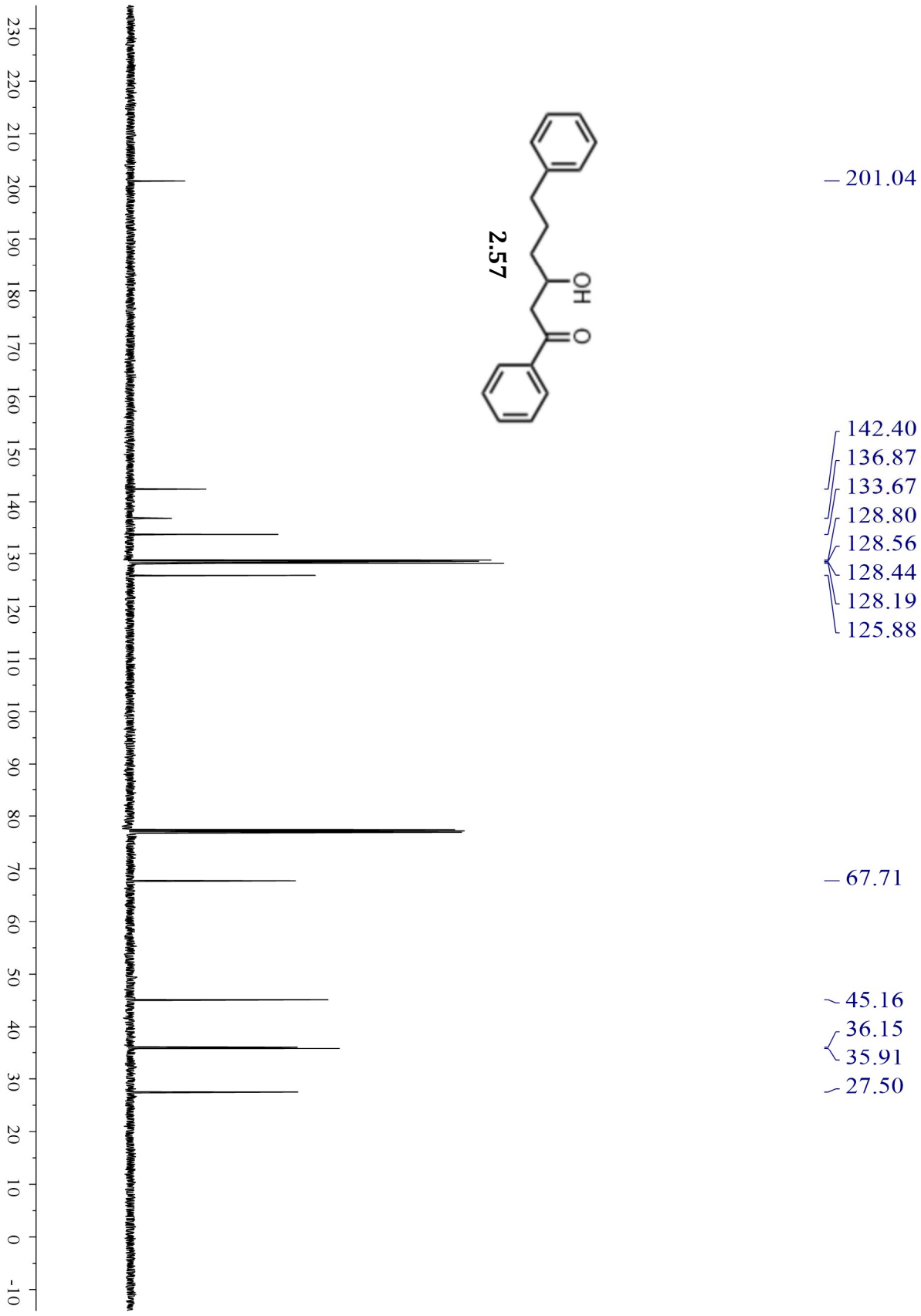

2.50
OH
O
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
3.25
4.64
1.00
0.97
1.91
1.98
2.04
1.01
0.99
1.06
1.21
1.05
1.12
7.29
7.29
7.29
7.28
7.28
7.27
7.27
7.26
7.20
7.19
7.18
7.18
7.18
7.17
7.17
7.16
2.98
2.98
2.91
2.90
2.89
2.76
2.75
2.73
2.64
2.63
2.61
2.56
2.55
2.53
2.53
2.50
2.49
2.48
2.46
1.66
1.66
1.66
1.65
1.53
1.52
1.51
1.43
1.42
1.41

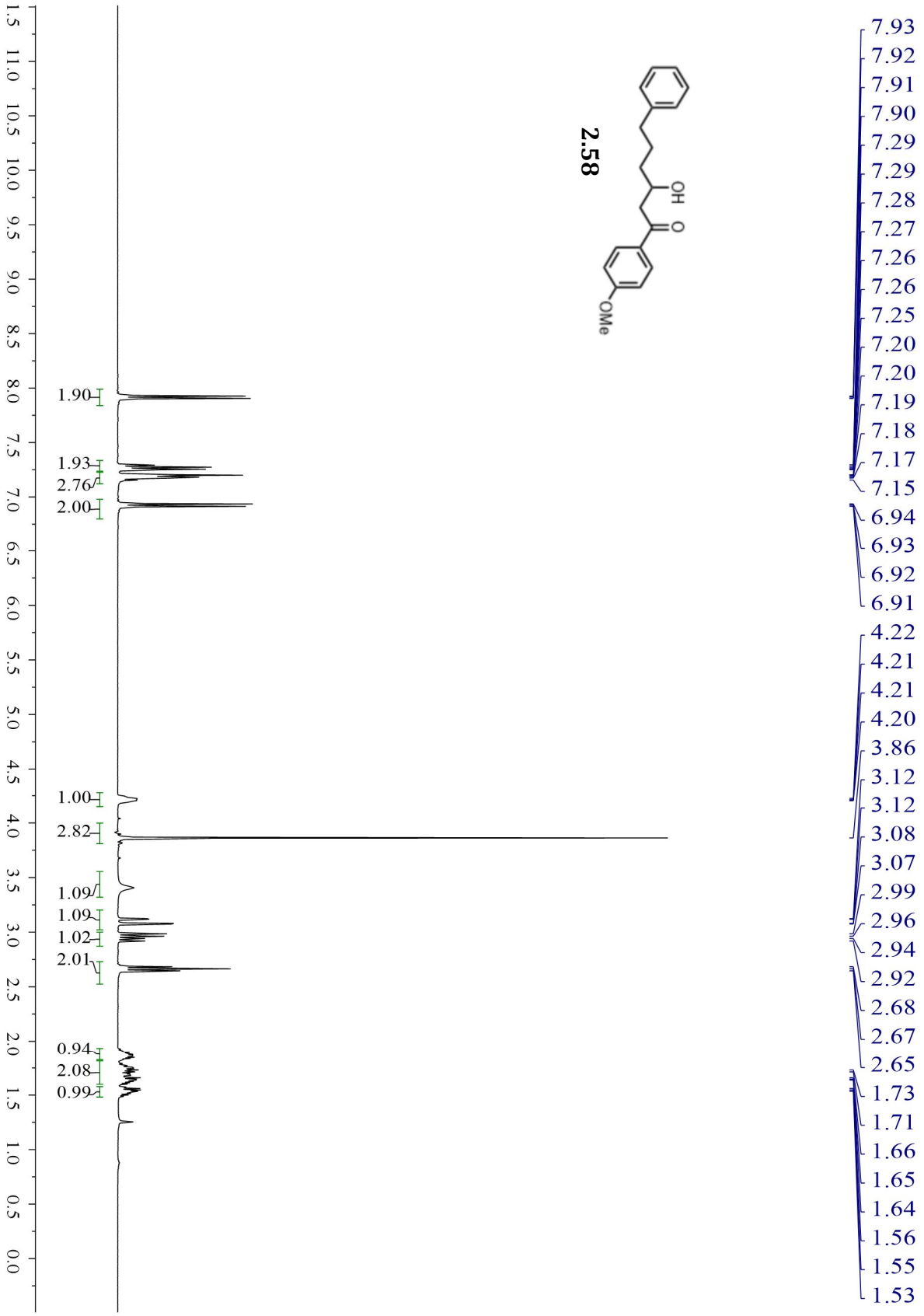

2.50
OH
O
211.19
142.30
140.79
128.64
128.50
128.41
128.37
126.31
125.86
67.55
49.39
45.11
36.04
35.79
29.61
27.33
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

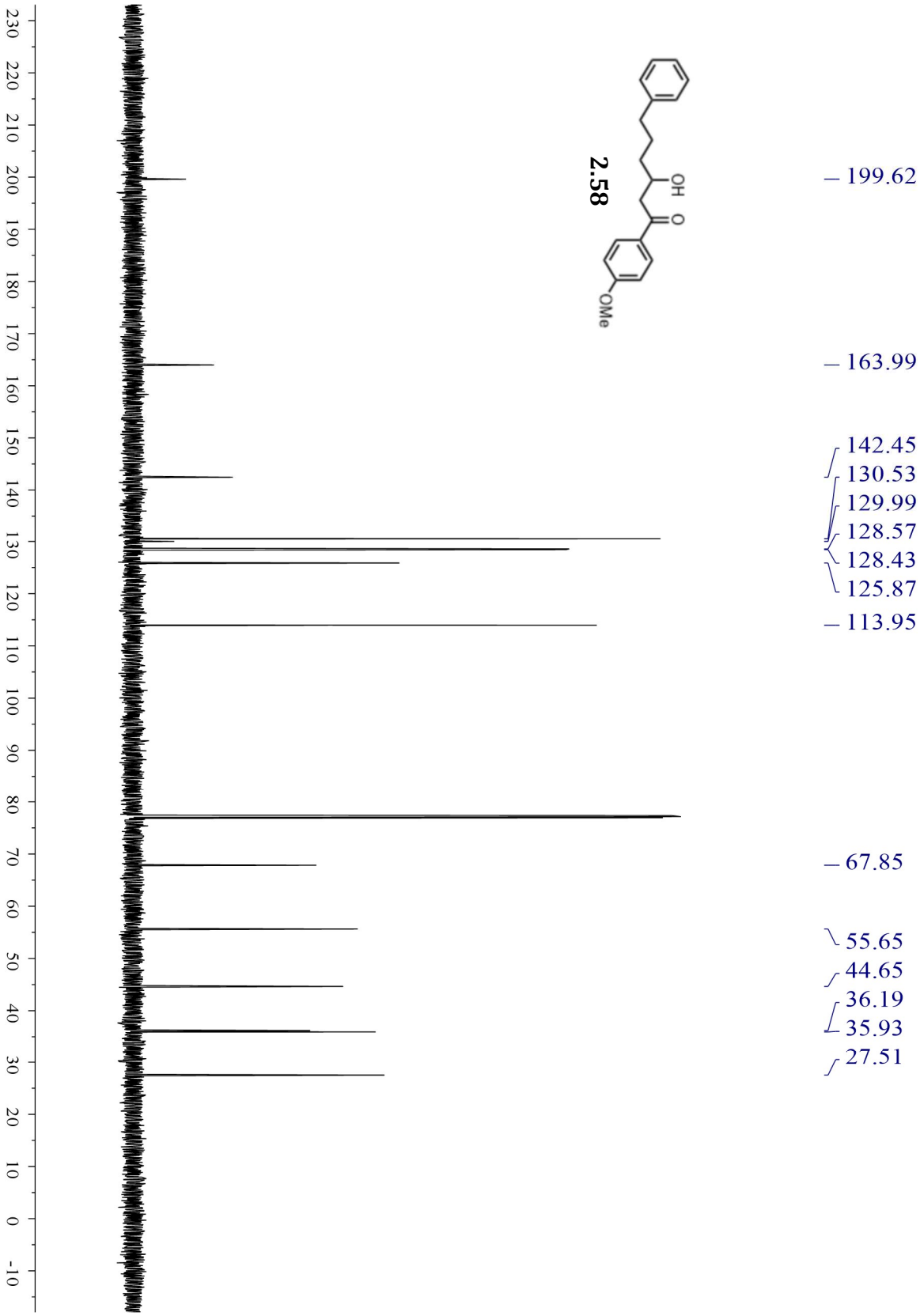

2.51
OH
O
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
2.11
3.15
1.08
2.05
1.00
1.58
2.10
1.10
1.15
2.01
2.04
1.26
2.98
1.22
1.13
7.28
7.26
7.25
7.18
7.17
7.17
7.16
5.75
5.74
5.02
5.02
4.99
4.99
4.99
4.98
4.98
4.97
4.96
4.05
4.04
4.03
2.64
2.63
2.61
2.57
2.57
2.54
2.54
2.50
2.48
2.45
2.42
2.41
2.39
2.06
2.05
2.04
2.03
1.69
1.68
1.67
1.66
1.64
1.43
1.42

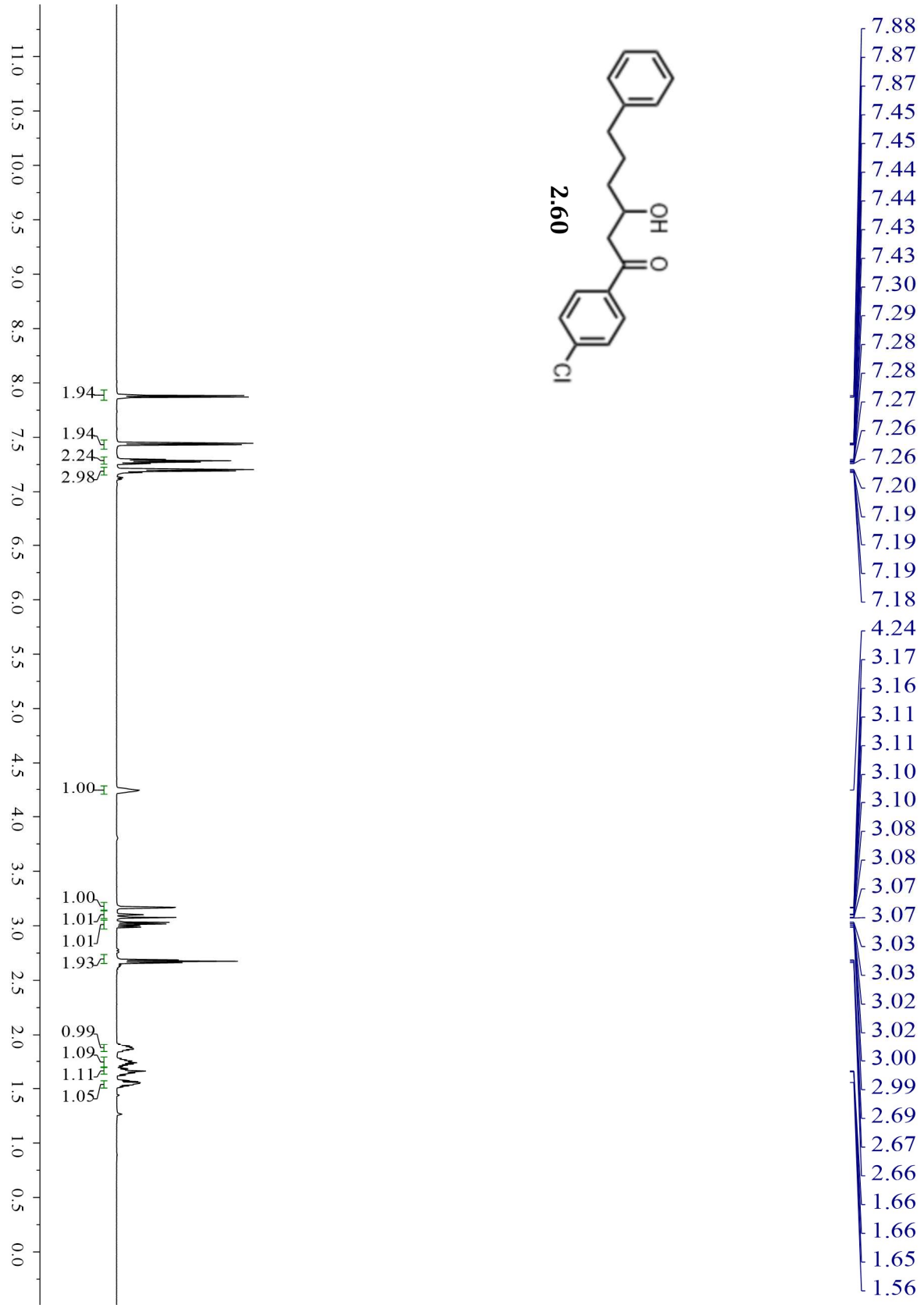

2.51
OH
O
212.21
142.32
137.89
128.49
128.38
125.84
115.46
67.60
67.58
67.52
49.15
49.12
42.80
36.04
35.82
33.08
27.35
22.62
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

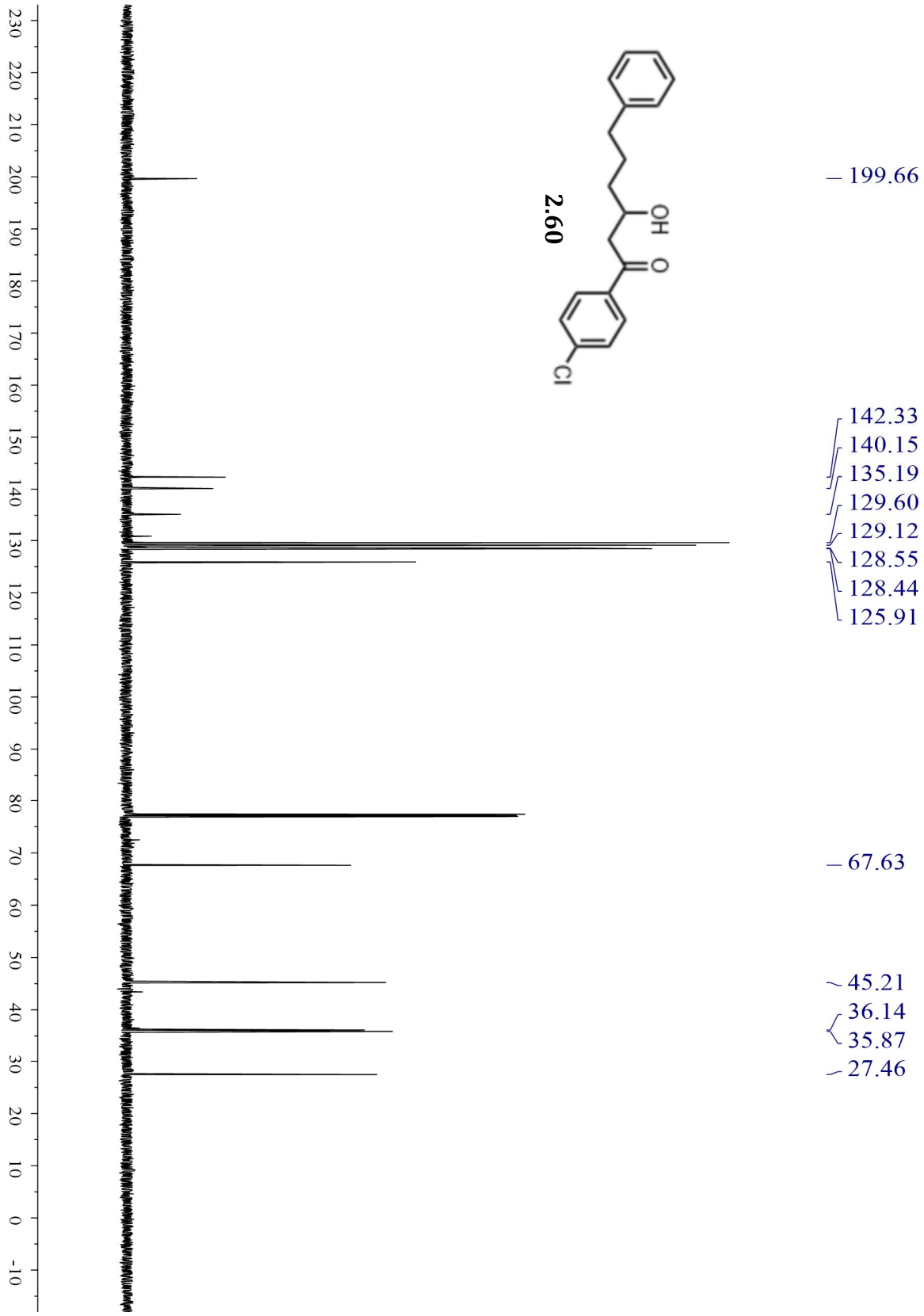
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.01
1.04
1.96
2.12
2.82
1.00
1.04
1.01
1.04
2.00
1.00
2.07
1.02
2.57
OH
O
7.95
7.94
7.94
7.60
7.59
7.58
7.57
7.57
7.49
7.47
7.46
7.30
7.29
7.27
7.26
7.21
7.20
7.20
7.19
7.17
4.26
4.25
4.25
3.29
3.28
3.17
3.17
3.14
3.13
3.06
3.04
3.03
3.01
2.70
2.68
2.67
1.75
1.68
1.67
1.66
1.65
1.65
1.58
1.57
1.56

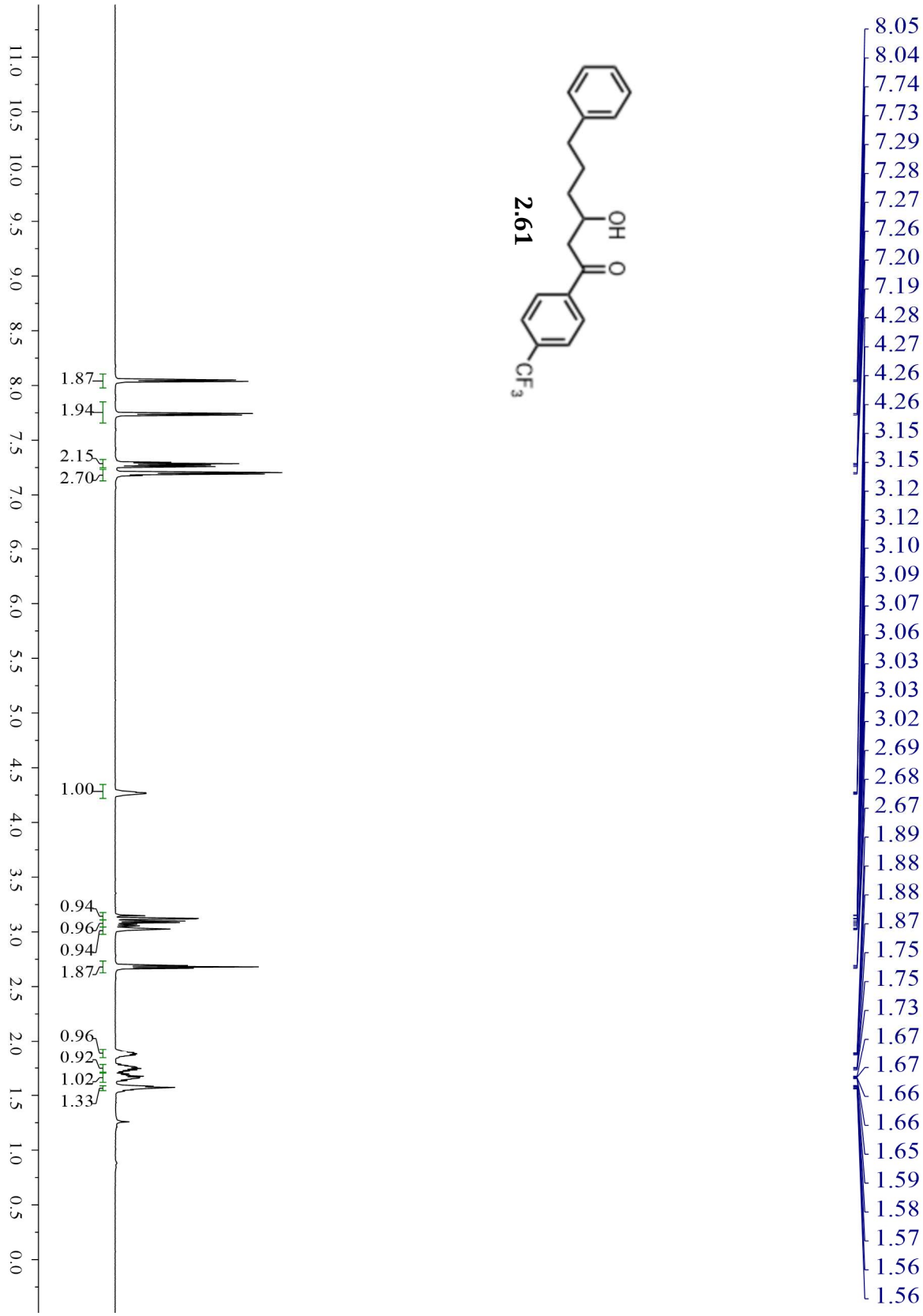

2.57
OH
O
201.04
142.40
136.87
133.67
128.80
128.56
128.44
128.19
125.88
67.71
45.16
36.15
35.91
27.50
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

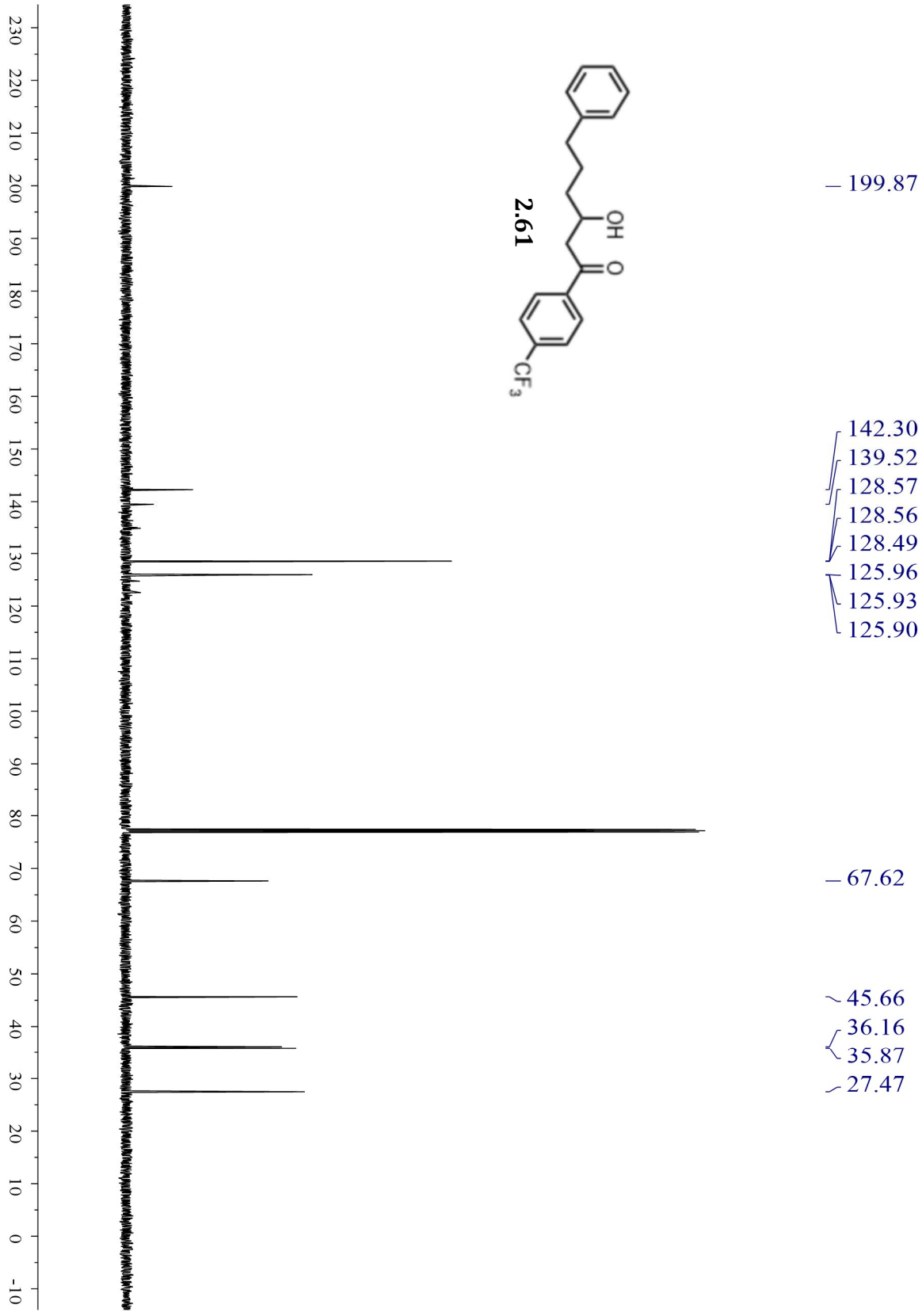

2.58
OH
O
OMe
1.90
1.93
2.76
2.00
1.00
2.82
1.09
1.09
1.02
2.01
0.94
2.08
0.99
7.93
7.92
7.91
7.90
7.29
7.29
7.28
7.27
7.26
7.26
7.25
7.20
7.20
7.19
7.18
7.17
7.15
6.94
6.93
6.92
6.91
4.22
4.21
4.21
4.20
3.86
3.12
3.12
3.08
3.07
2.99
2.96
2.94
2.92
2.68
2.67
2.65
1.73
1.71
1.66
1.65
1.64
1.56
1.55
1.53

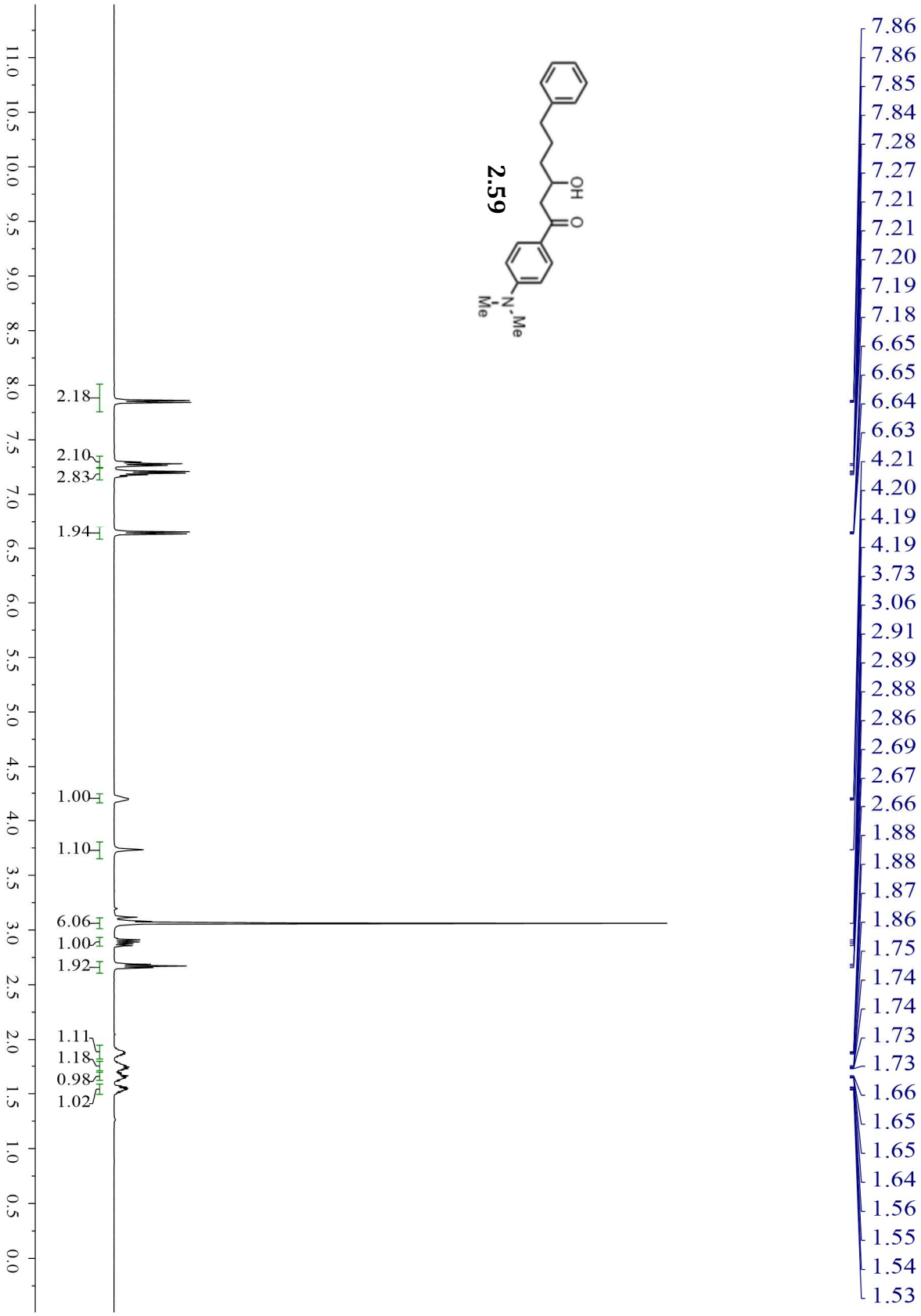

2.58
OH
O
OMe
199.62
163.99
142.45
130.53
129.99
128.57
128.43
125.87
113.95
67.85
55.65
44.65
36.19
35.93
27.51
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

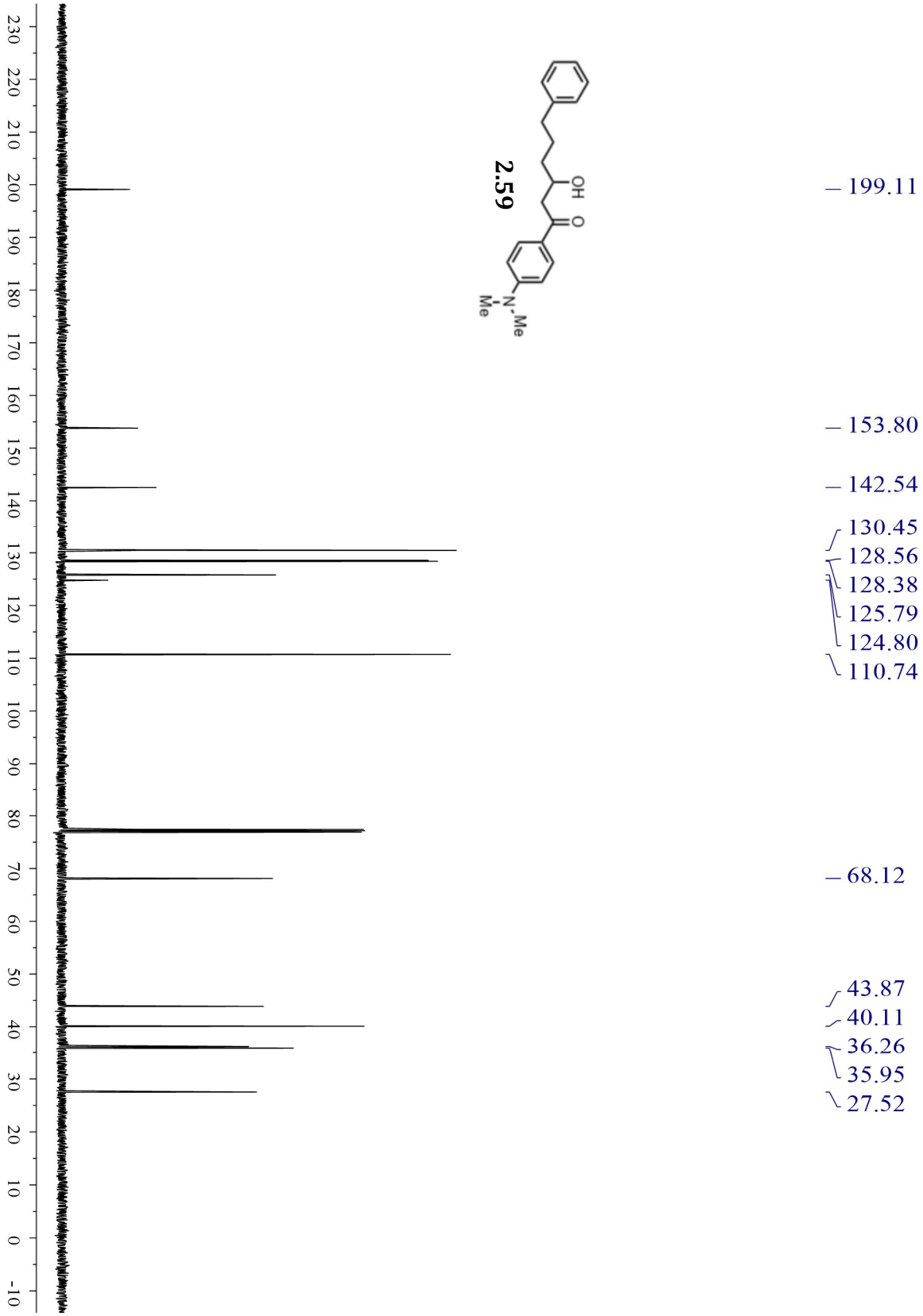

2.60
OH
O
Cl
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
1.94
1.94
2.24
2.98
1.00
1.00
1.01
1.01
1.93
0.99
1.09
1.11
1.05
7.88
7.87
7.87
7.45
7.45
7.44
7.44
7.43
7.43
7.30
7.29
7.28
7.28
7.27
7.26
7.26
7.20
7.19
7.19
7.19
7.18
4.24
3.17
3.16
3.11
3.11
3.10
3.10
3.08
3.08
3.07
3.07
3.03
3.03
3.02
3.02
3.00
2.99
2.69
2.67
2.66
1.66
1.66
1.65
1.56

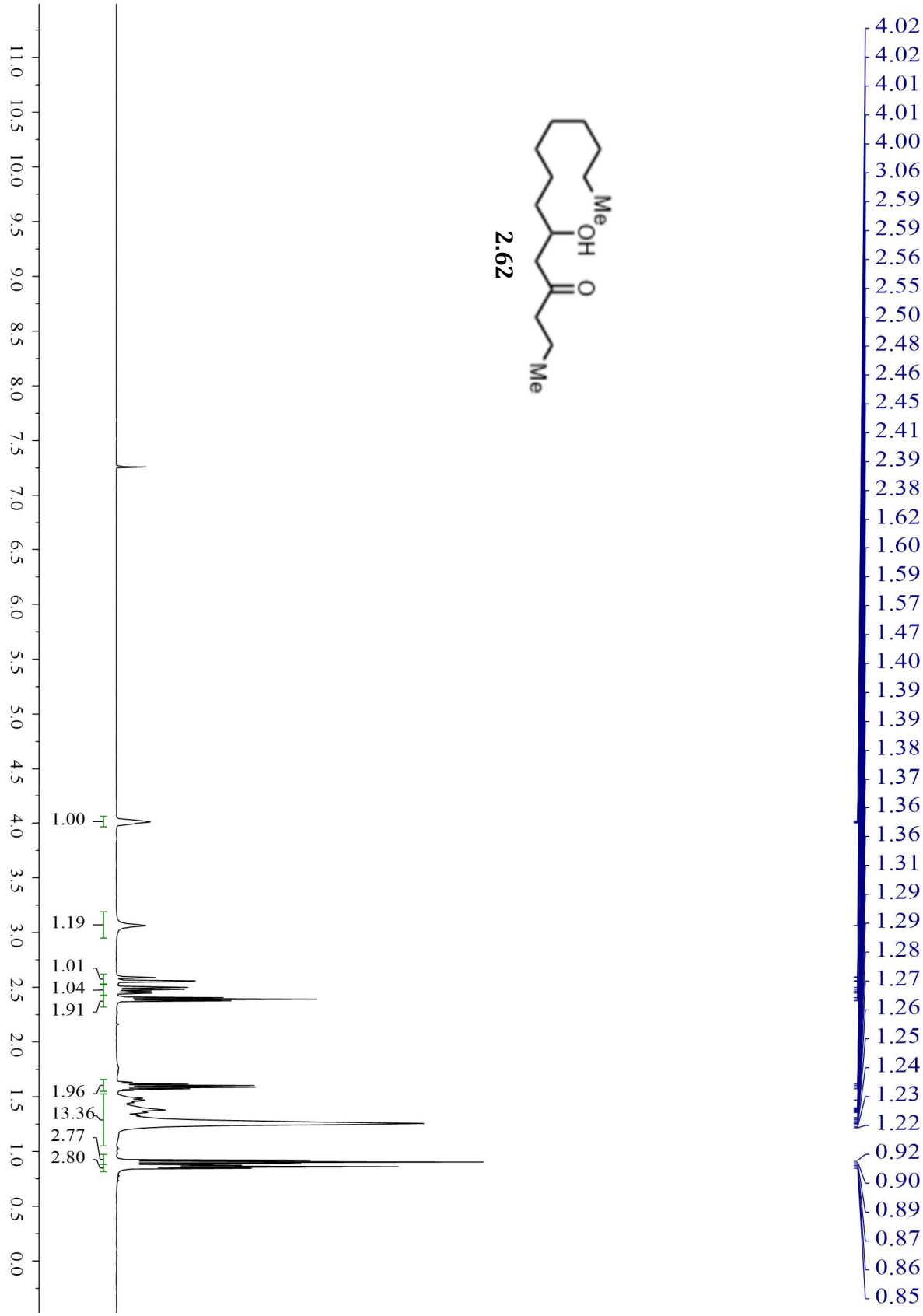

2.60
OH
O
Cl
199.66
142.33
140.15
135.19
129.60
129.12
128.55
128.44
125.91
67.63
45.21
36.14
35.87
27.46
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

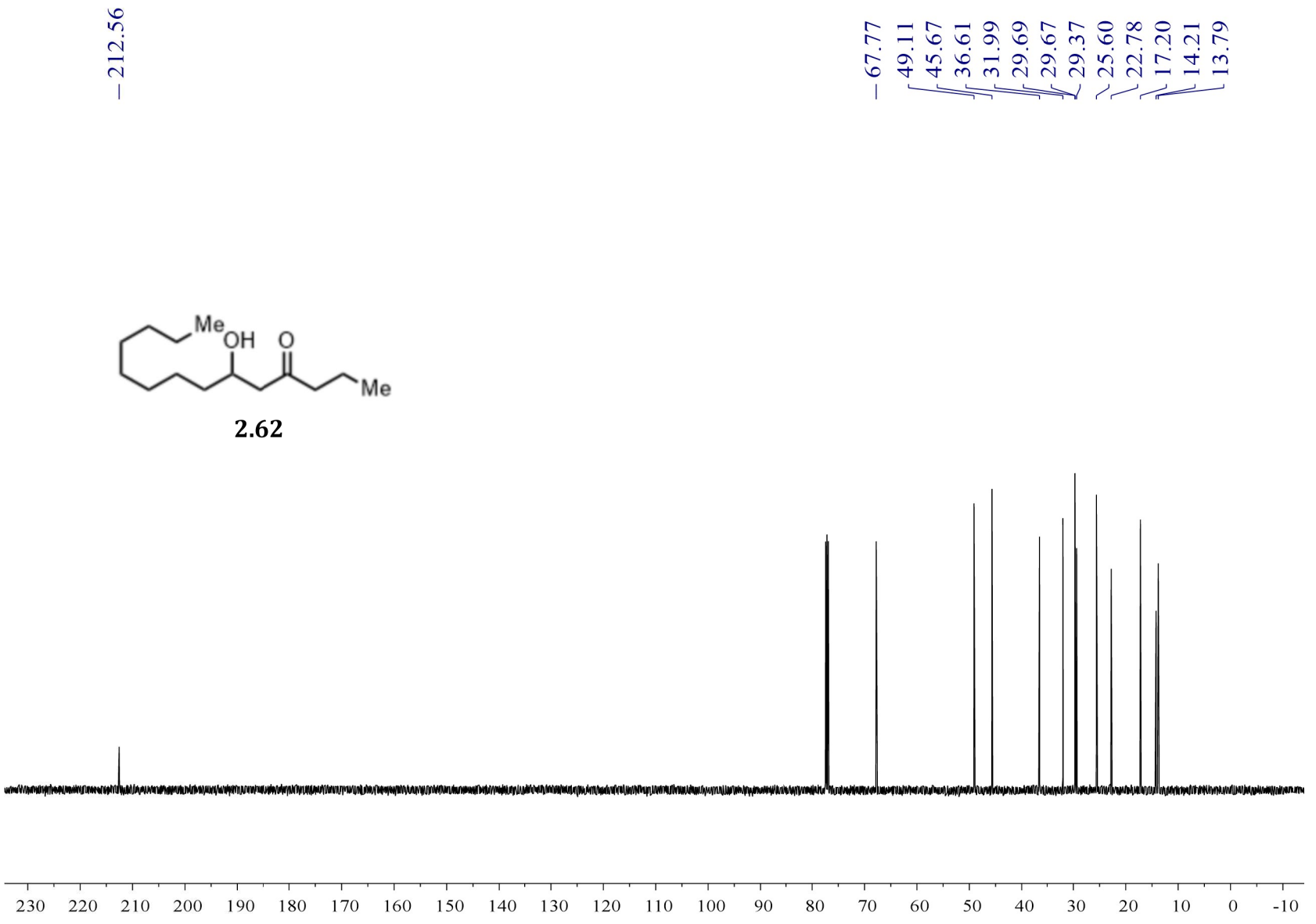

2.61
OH
O
CF3
1.87
1.94
2.15
2.70
1.00
0.94
0.96
0.94
1.87
0.96
0.92
1.02
1.33
8.05
8.04
7.74
7.73
7.29
7.28
7.27
7.26
7.20
7.19
4.28
4.27
4.26
4.26
3.15
3.15
3.12
3.12
3.10
3.09
3.07
3.06
3.03
3.03
3.02
2.69
2.68
2.67
1.89
1.88
1.88
1.87
1.75
1.75
1.73
1.67
1.67
1.66
1.66
1.65
1.59
1.58
1.57
1.56
1.56


2.61
OH
O
CF3
199.87
142.30
139.52
128.57
128.56
128.49
125.96
125.93
125.90
67.62
45.66
36.16
35.87
27.47
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

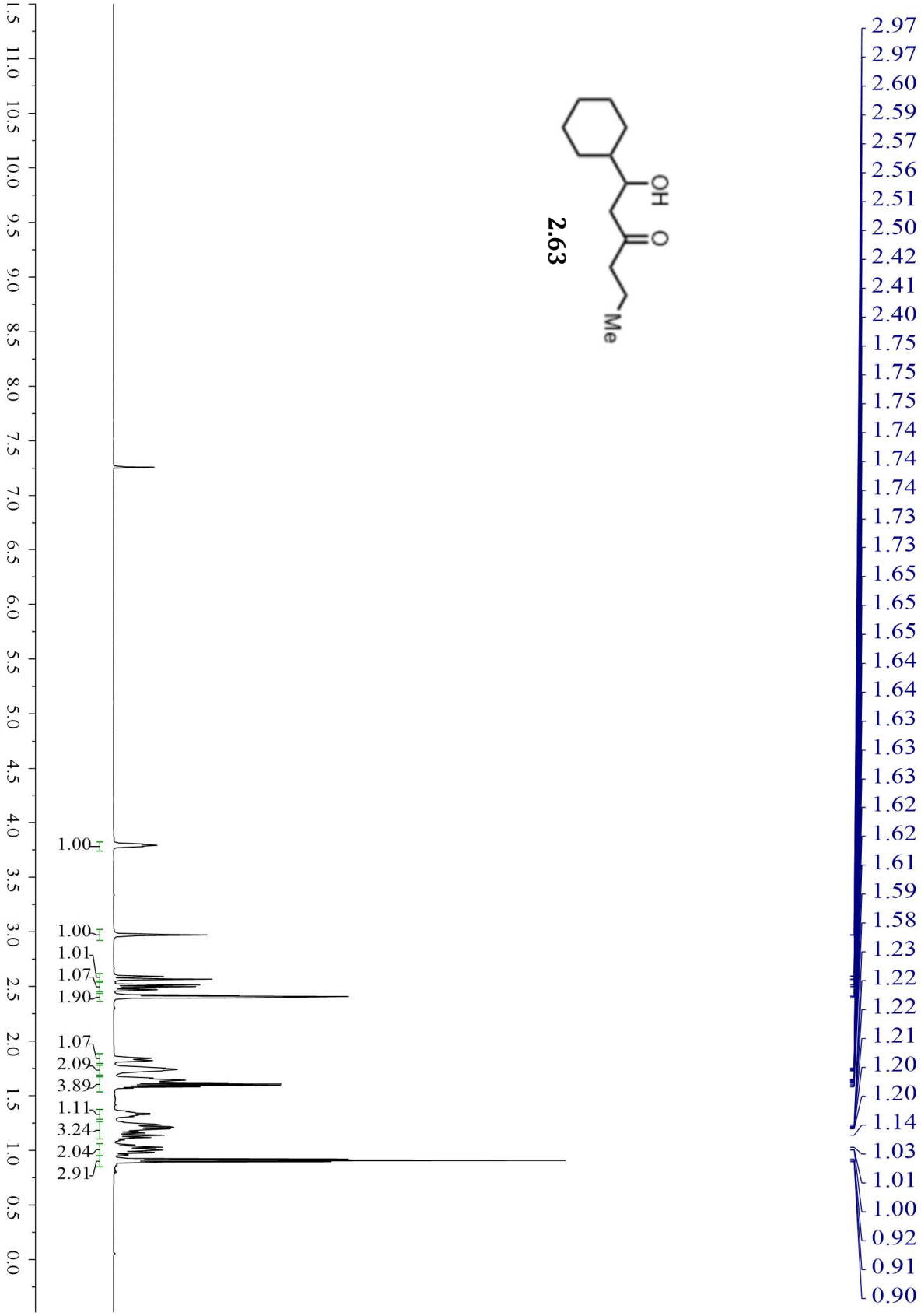

2.59
OH
O
N
Me
Me
2.18
2.10
2.83
1.94
1.00
1.10
6.06
1.00
1.92
1.11
1.18
0.98
1.02
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
7.86
7.86
7.85
7.84
7.28
7.27
7.21
7.21
7.20
7.19
7.18
6.65
6.65
6.64
6.63
4.21
4.20
4.19
4.19
3.73
3.06
2.91
2.89
2.88
2.86
2.69
2.67
2.66
1.88
1.88
1.87
1.86
1.75
1.74
1.74
1.73
1.73
1.66
1.65
1.65
1.64
1.56
1.55
1.54
1.53

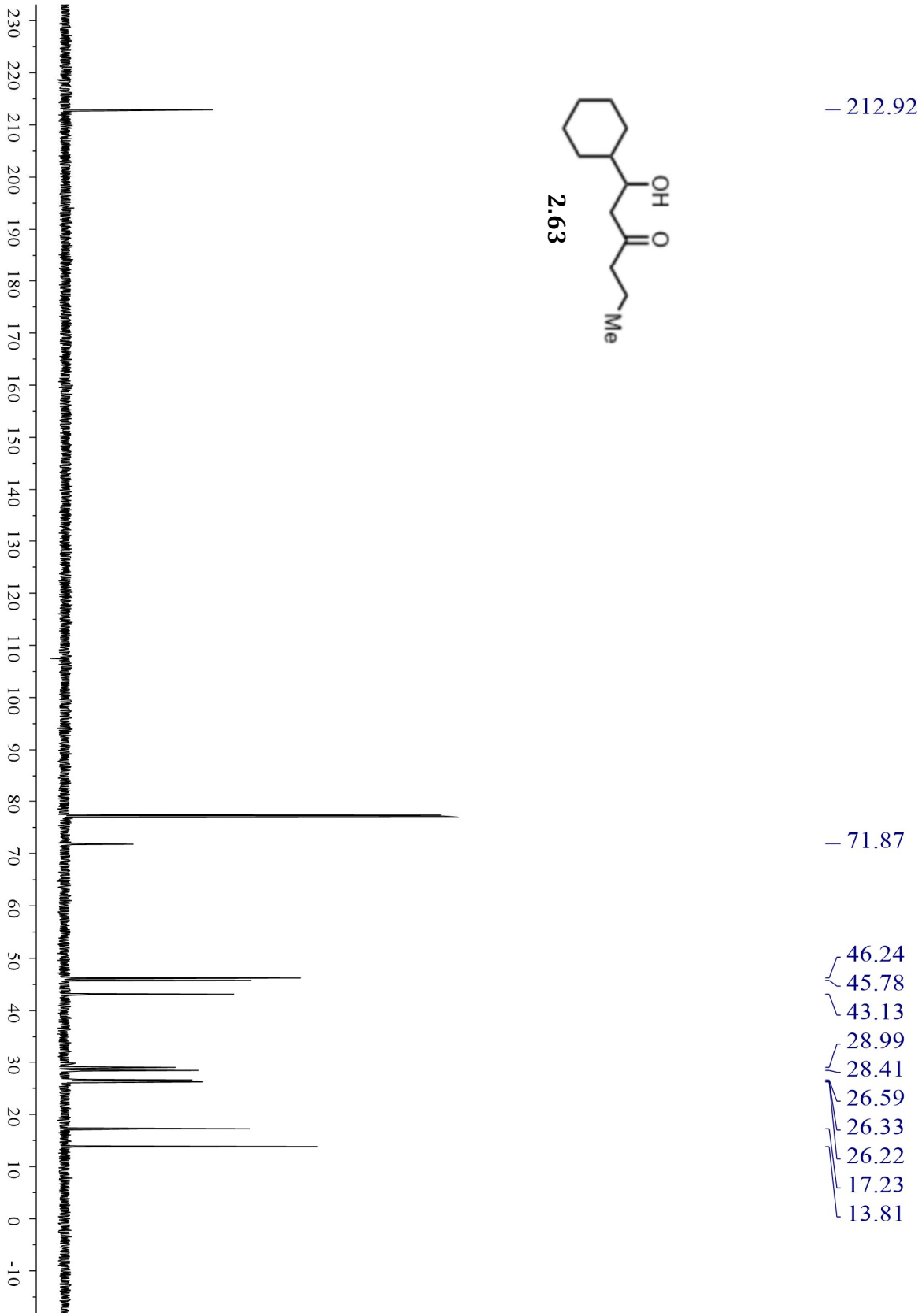

2.59
OH
O
N
Me
Me
199.11
153.80
142.54
130.45
128.56
128.38
125.79
124.80
110.74
68.12
43.87
40.11
36.26
35.95
27.52

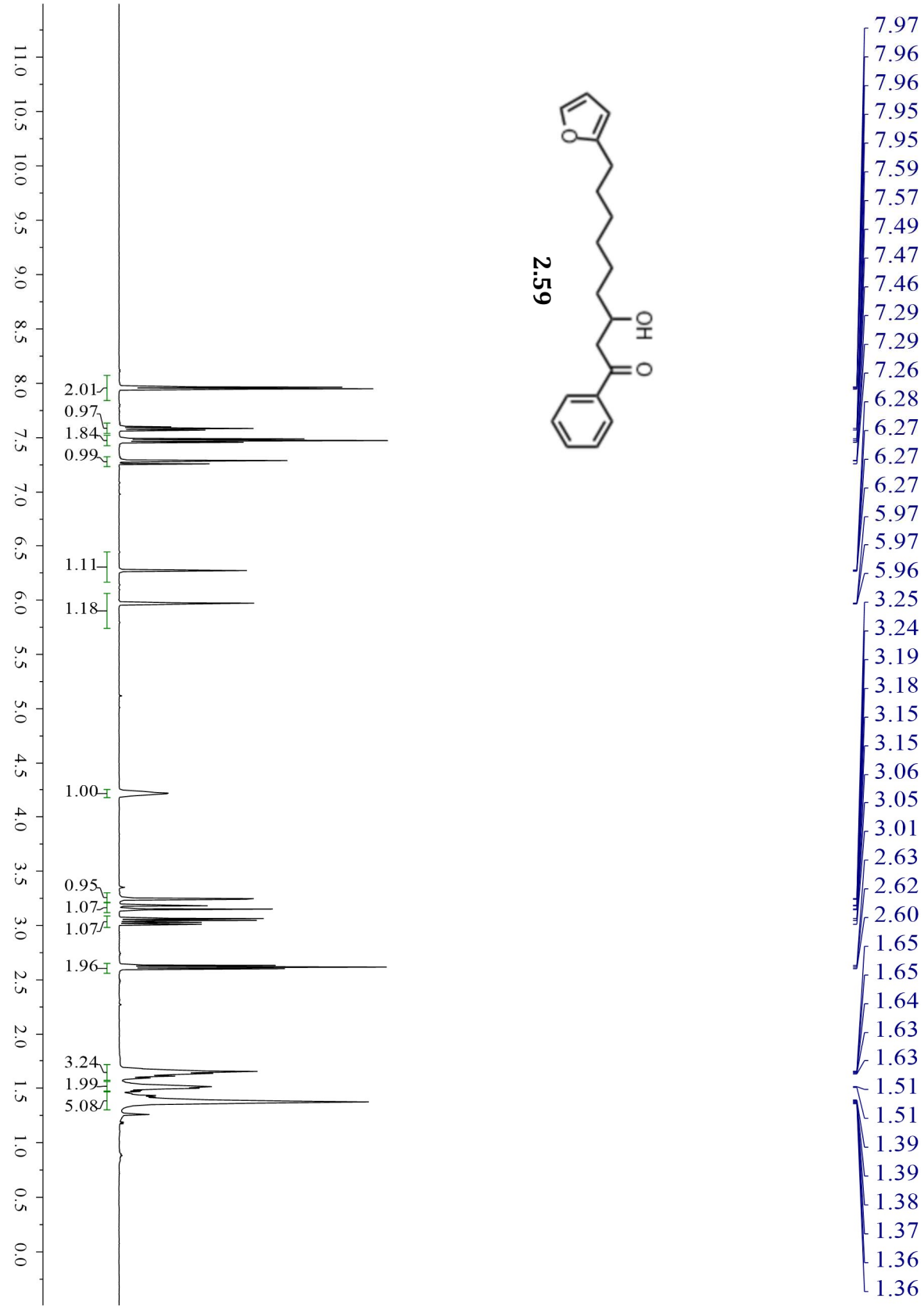

2.62
Me
OH
O
Me
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
1.00
1.19
1.01
1.04
1.91
1.96
13.36
2.77
2.80
4.02
4.02
4.01
4.01
4.00
3.06
2.59
2.59
2.56
2.55
2.50
2.48
2.46
2.45
2.41
2.39
2.38
1.62
1.60
1.59
1.57
1.47
1.40
1.39
1.39
1.38
1.37
1.36
1.36
1.31
1.29
1.29
1.28
1.27
1.26
1.25
1.24
1.23
1.22
0.92
0.90
0.89
0.87
0.86
0.85

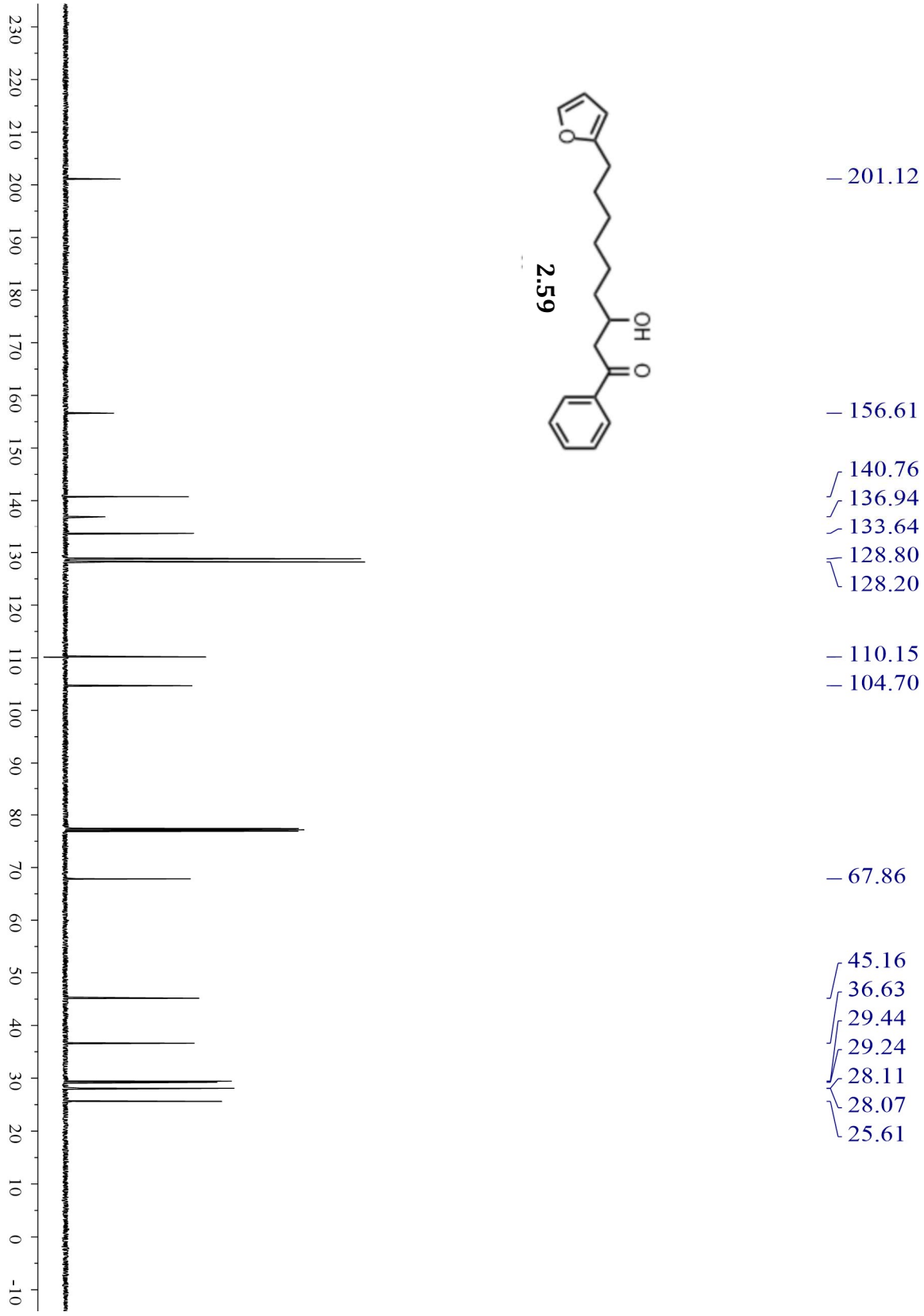

212.56
67.77
49.11
45.67
36.61
31.99
29.69
29.67
29.37
25.60
22.78
17.20
14.21
13.79
Me
OH
O
Me
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

2.62


OH
O
Me
2.63
1.00
1.00
1.01
1.07
1.90
1.07
2.09
3.89
1.11
3.24
2.04
2.91
2.97
2.97
2.60
2.59
2.57
2.56
2.51
2.50
2.42
2.41
2.40
1.75
1.75
1.75
1.74
1.74
1.74
1.73
1.73
1.65
1.65
1.65
1.64
1.64
1.63
1.63
1.63
1.62
1.62
1.61
1.59
1.58
1.23
1.22
1.22
1.21
1.20
1.20
1.14
1.03
1.01
1.00
0.92
0.91
0.90


OH
O
Me
2.63
212.92
71.87
46.24
45.78
43.13
28.99
28.41
26.59
26.33
26.22
17.23
13.81
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
2.01
0.97
1.84
0.99
1.11
1.18
1.00
0.95
1.07
1.07
1.96
3.24
1.99
5.08
2.59
HO
O
7.97
7.96
7.96
7.95
7.95
7.59
7.57
7.49
7.47
7.46
7.29
7.29
7.26
6.28
6.27
6.27
6.27
5.97
5.97
5.96
3.25
3.24
3.19
3.18
3.15
3.15
3.06
3.05
3.01
2.63
2.62
2.60
1.65
1.65
1.64
1.63
1.63
1.51
1.51
1.39
1.39
1.38
1.37
1.36
1.36


2.59
OH
O
201.12
156.61
140.76
136.94
133.64
128.80
128.20
110.15
104.70
67.86
45.16
36.63
29.44
29.24
28.11
28.07
25.61

2.67

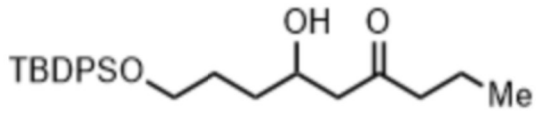
212.31

135.71
135.70
129.74
127.78

67.62
64.03

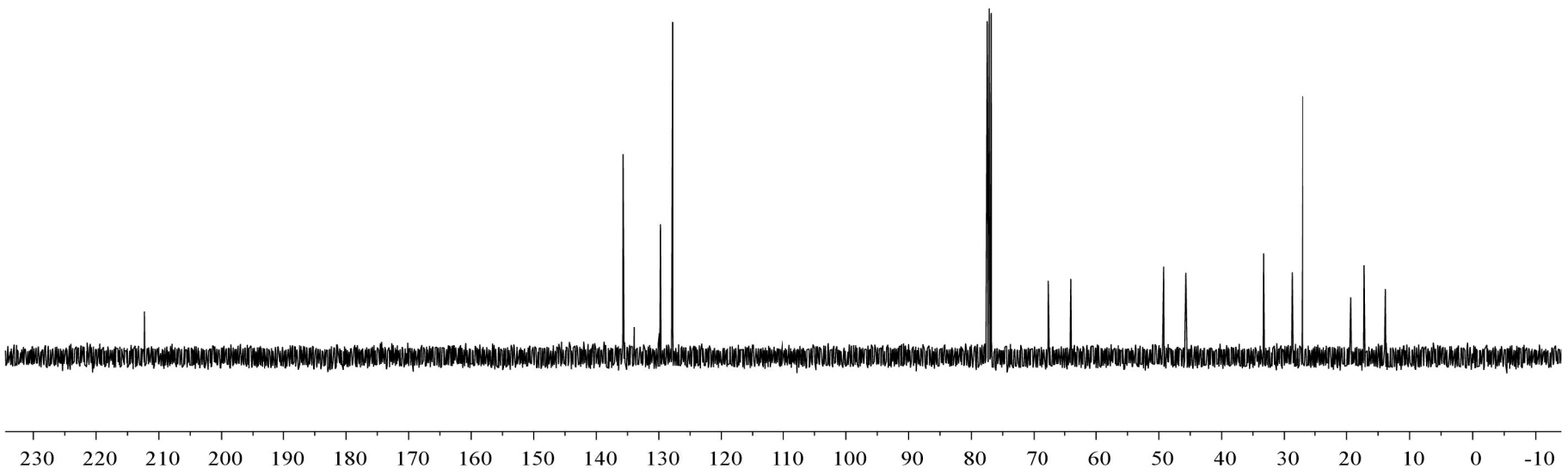
49.23
45.70

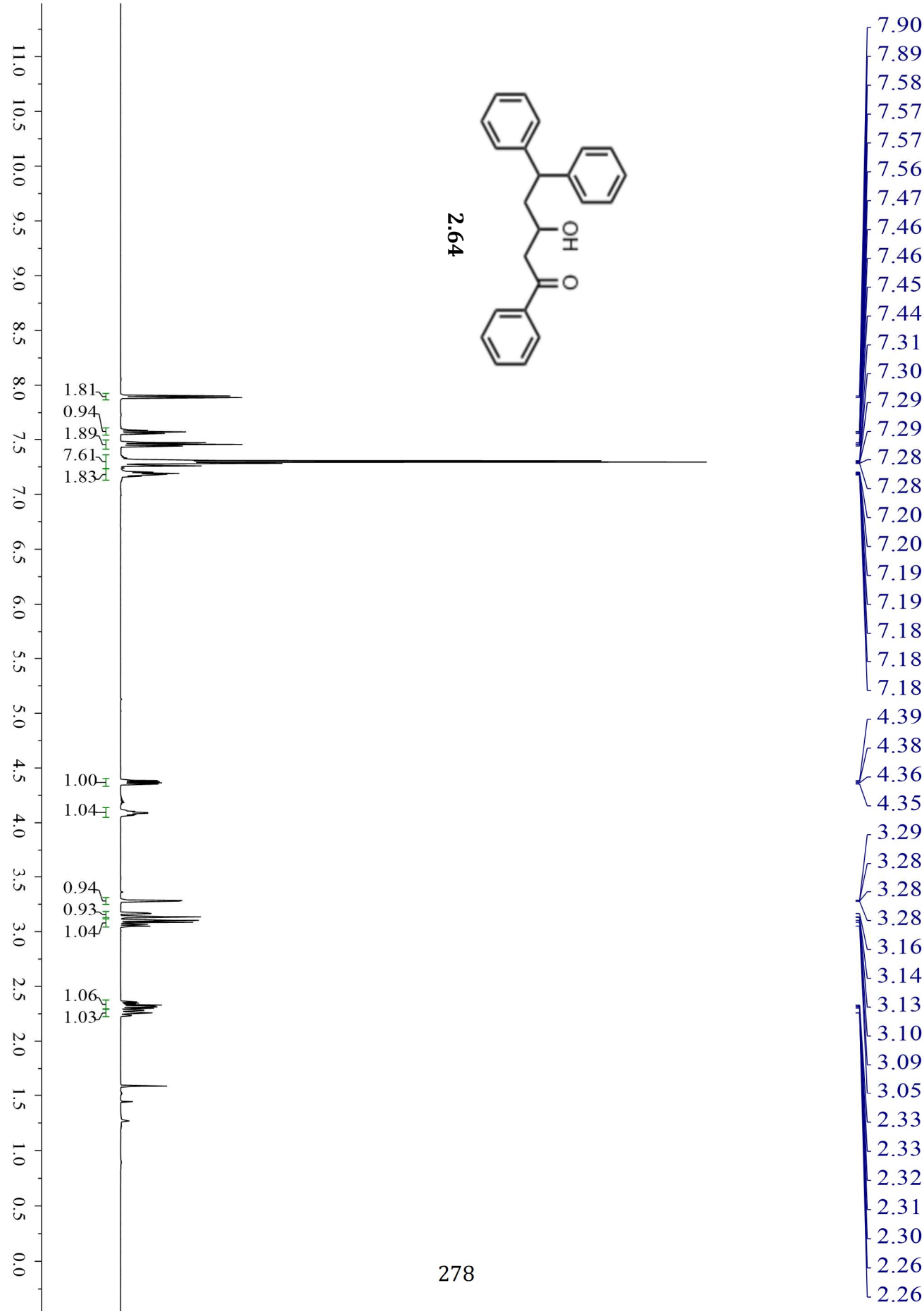
33.30
28.74
27.00
19.34
17.23
13.84

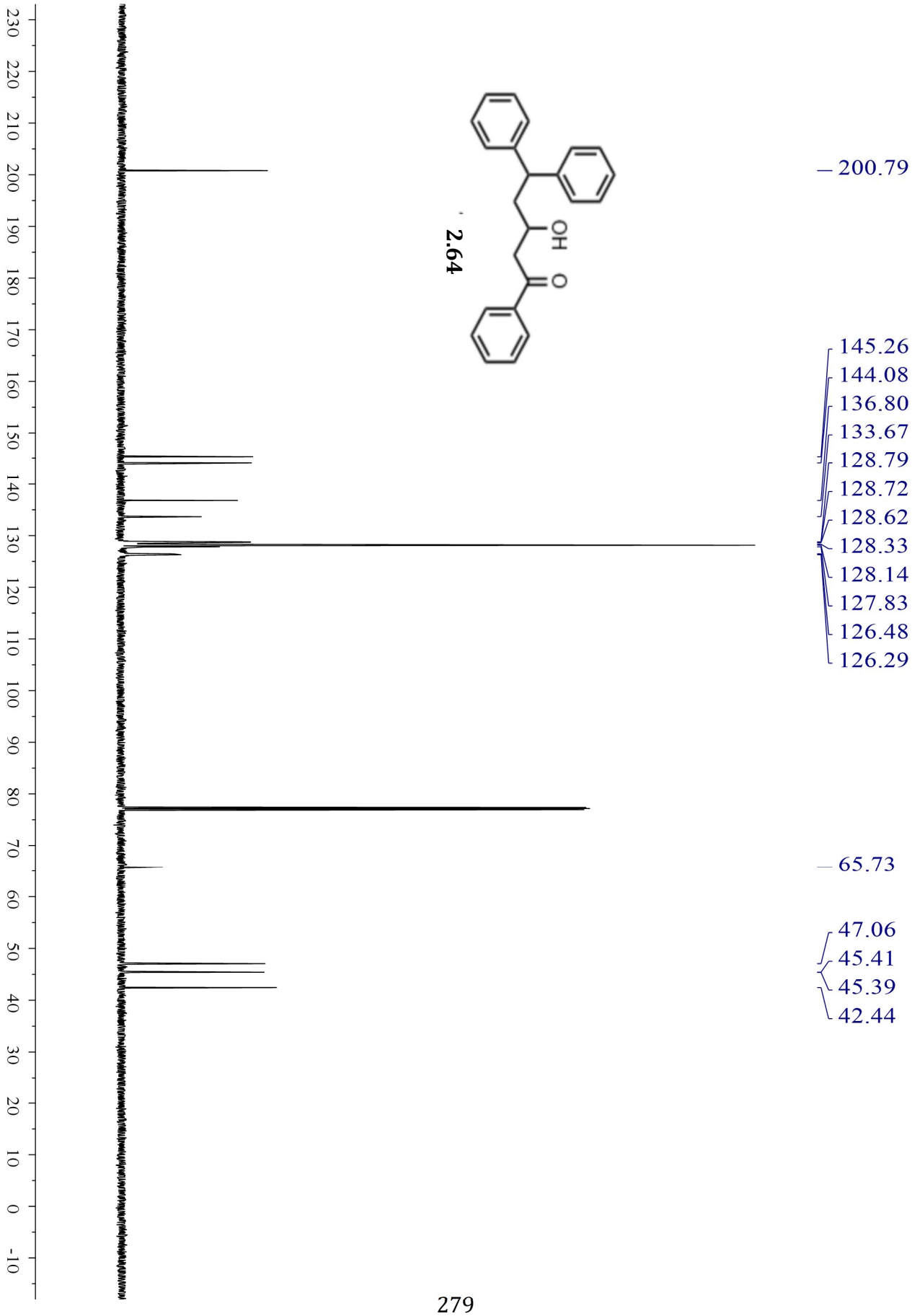


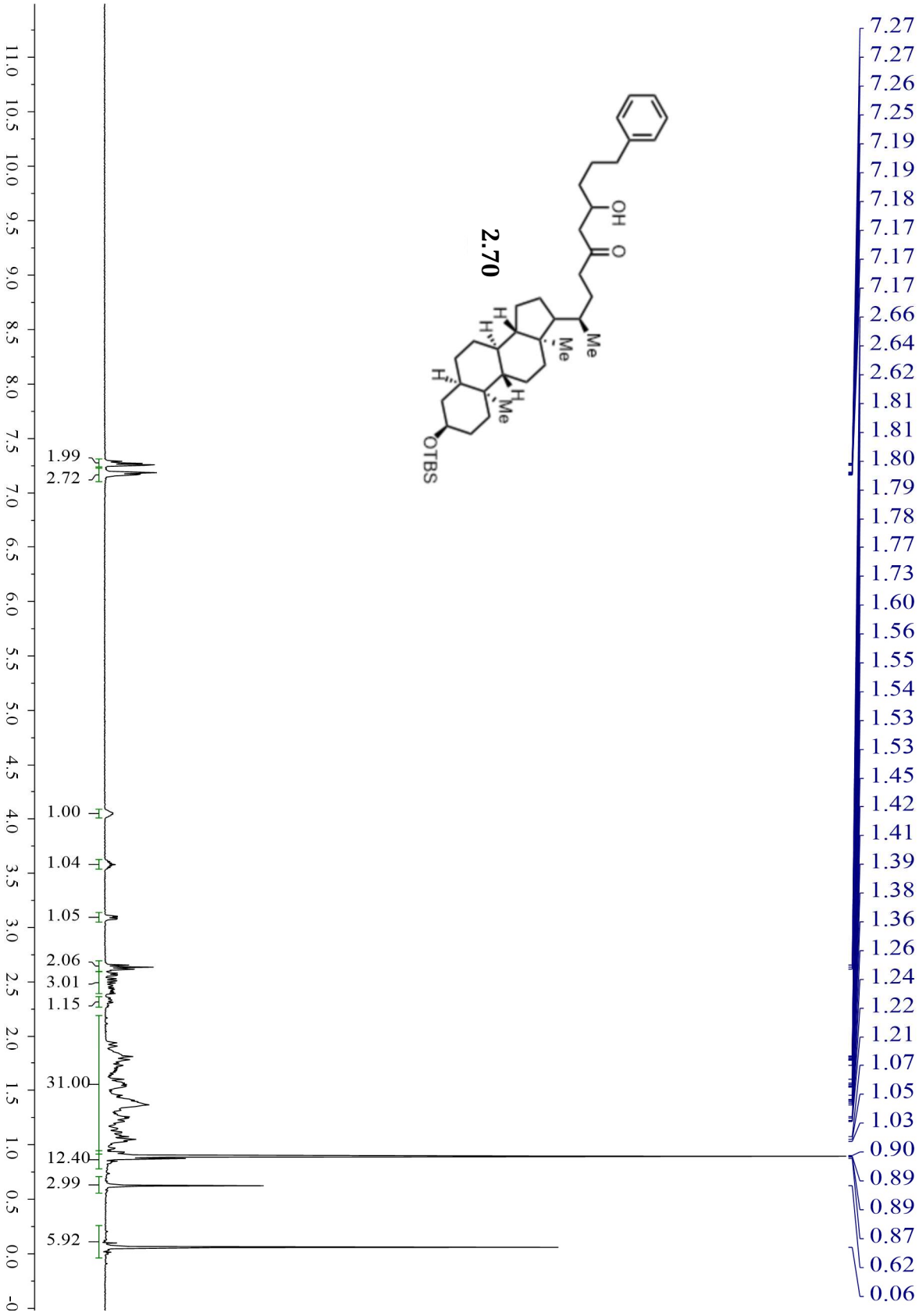
2.67

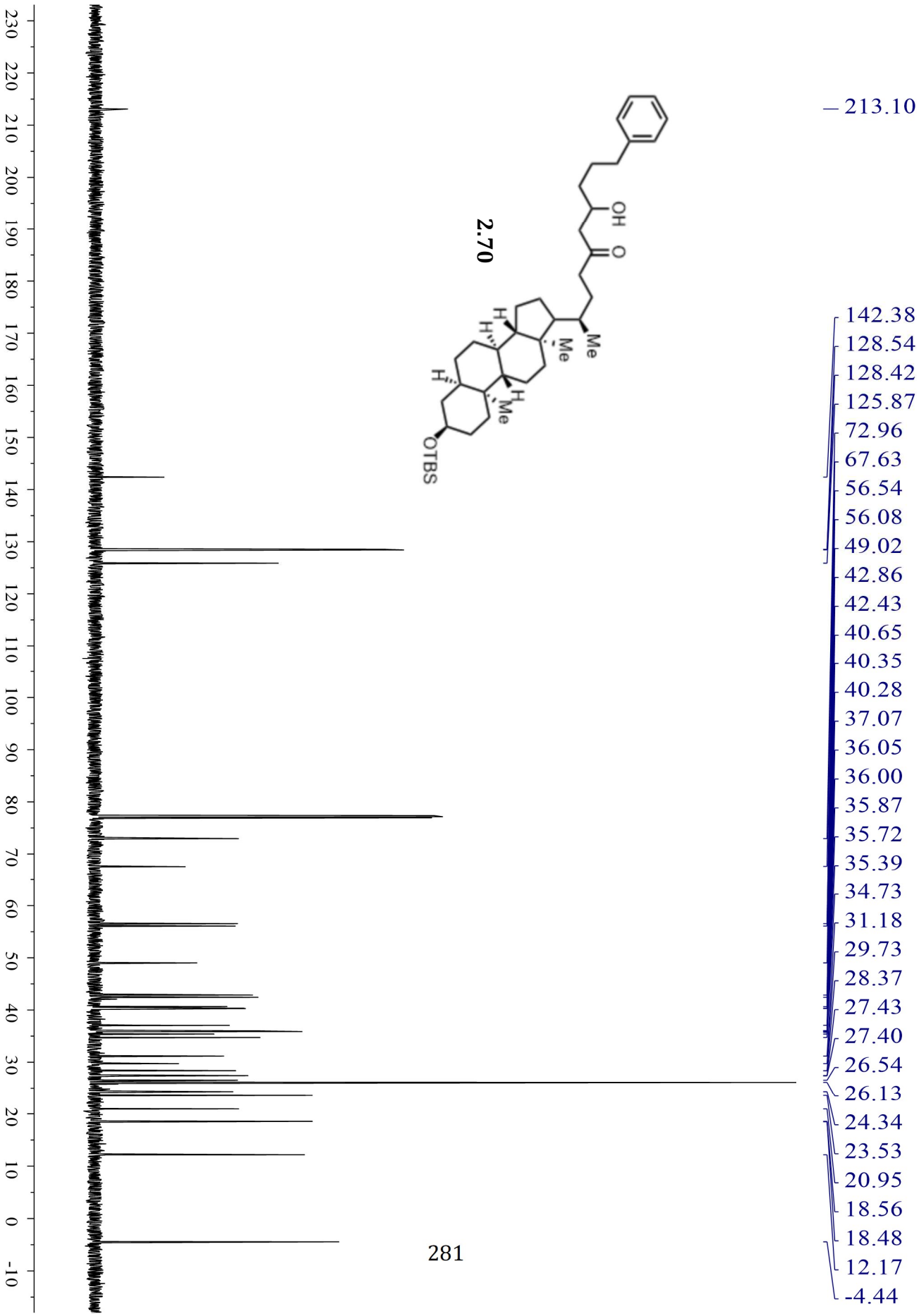
277




2.64
OH
O
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
1.81
0.94
1.89
7.61
1.83
1.00
1.04
0.94
0.93
1.04
1.06
1.03
7.90
7.89
7.58
7.57
7.57
7.56
7.47
7.46
7.46
7.45
7.44
7.31
7.30
7.29
7.29
7.28
7.28
7.20
7.20
7.19
7.19
7.18
7.18
7.18
4.39
4.38
4.36
4.35
3.29
3.28
3.28
3.28
3.16
3.14
3.13
3.10
3.09
3.05
2.33
2.33
2.32
2.31
2.30
2.26
2.26

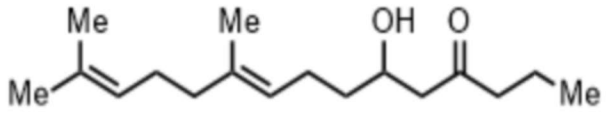

230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
OH
O
2.64
200.79
145.26
144.08
136.80
133.67
128.79
128.72
128.62
128.33
128.14
127.83
126.48
126.29
65.73
47.06
45.41
45.39
42.44


2.70
OH
O
OTBS
Me
Me
Me
H
H
H
1.99
2.72
1.00
1.04
1.05
2.06
3.01
1.15
31.00
12.40
2.99
5.92
7.27
7.27
7.26
7.25
7.19
7.19
7.18
7.17
7.17
7.17
2.66
2.64
2.62
1.81
1.81
1.80
1.79
1.78
1.77
1.73
1.60
1.56
1.55
1.54
1.53
1.53
1.45
1.42
1.41
1.39
1.38
1.36
1.26
1.24
1.22
1.21
1.07
1.05
1.03
0.90
0.89
0.89
0.87
0.62
0.06

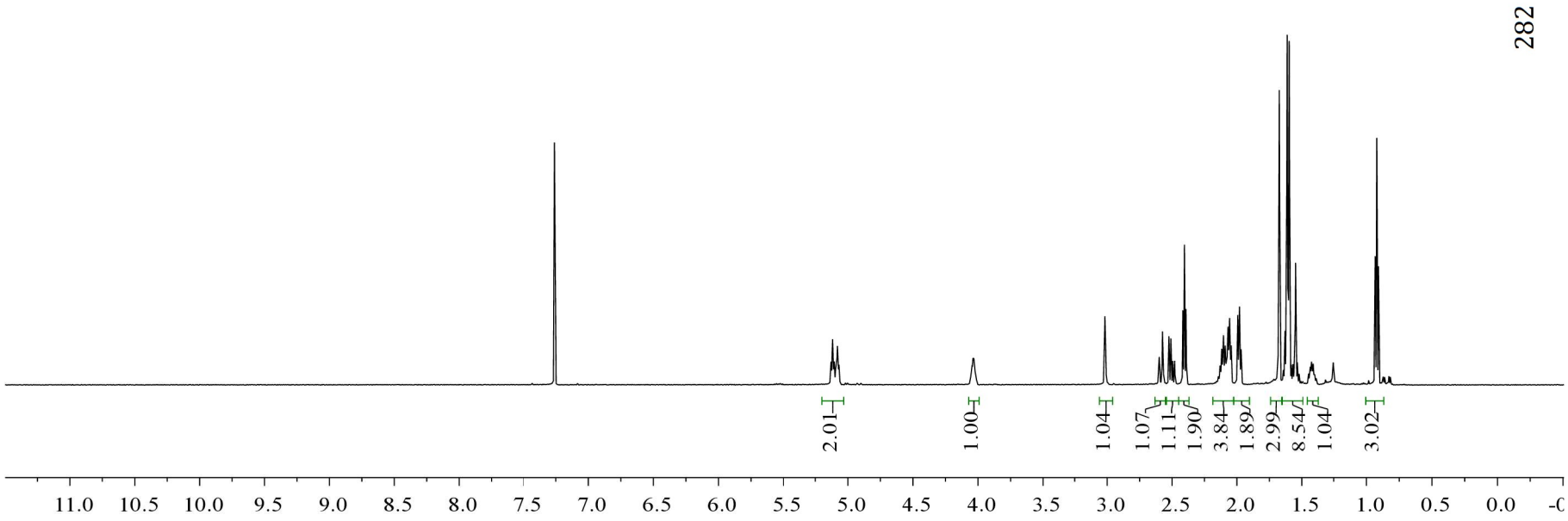

230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
213.10
142.38
128.54
128.42
125.87
72.96
67.63
56.54
56.08
49.02
42.86
42.43
40.65
40.35
40.28
37.07
36.05
36.00
35.87
35.72
35.39
34.73
31.18
29.73
28.37
27.43
27.40
26.54
26.13
24.34
23.53
20.95
18.56
18.48
12.17
-4.44
OH
O
Me
Me
H
H
H
Me
OTBS

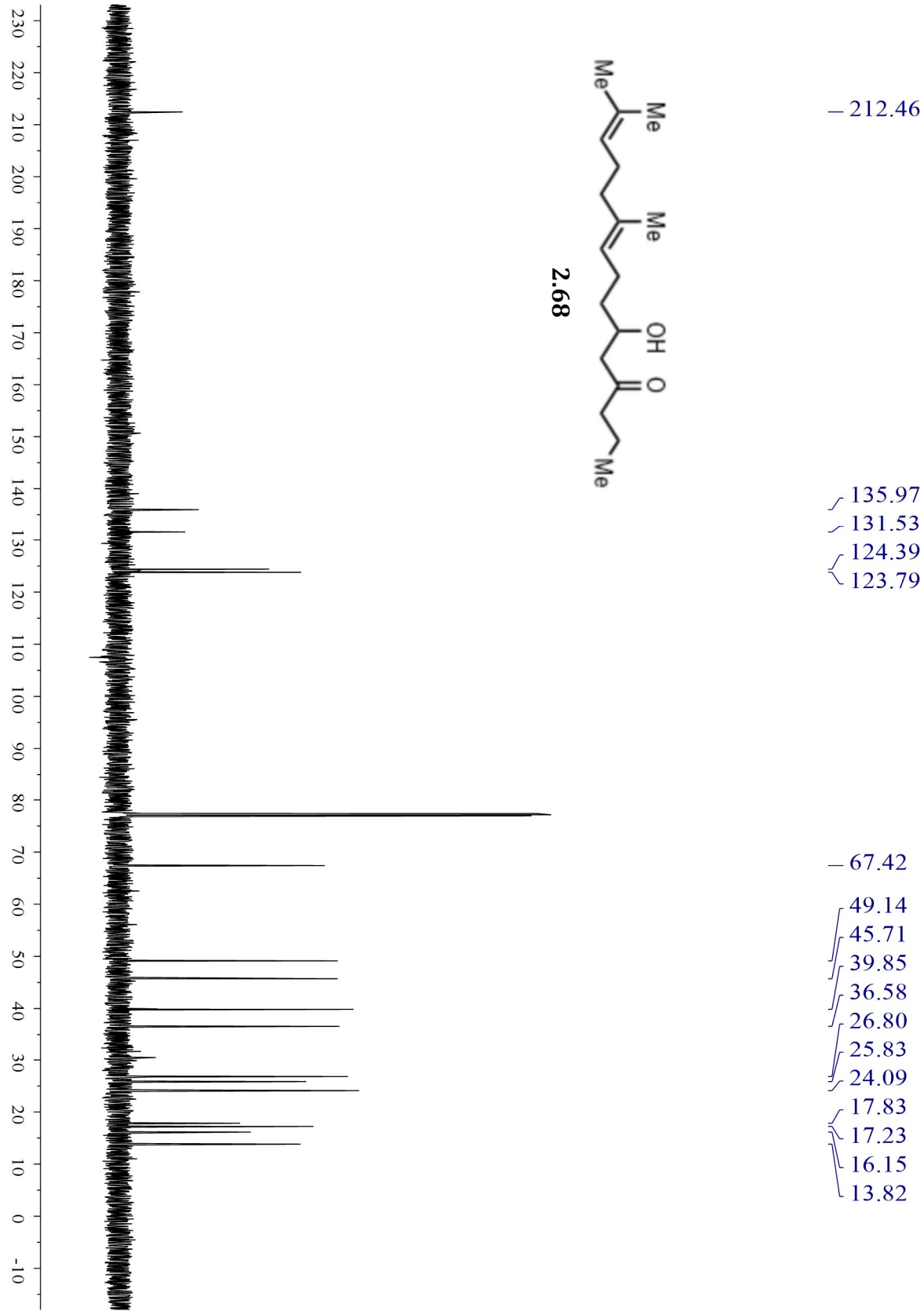
2.70


5.12
5.12
5.12
5.11
5.08
5.08
5.08
5.08
4.04
4.03
3.02
3.01
2.60
2.60
2.57
2.57
2.52
2.51
2.48
2.42
2.40
2.39
2.12
2.10
2.09
2.08
2.07
2.06
2.04
1.99
1.98
1.97
1.68
1.67
1.62
1.61
1.61
1.60
1.55
1.55
0.93
0.93
0.92
0.92
0.91

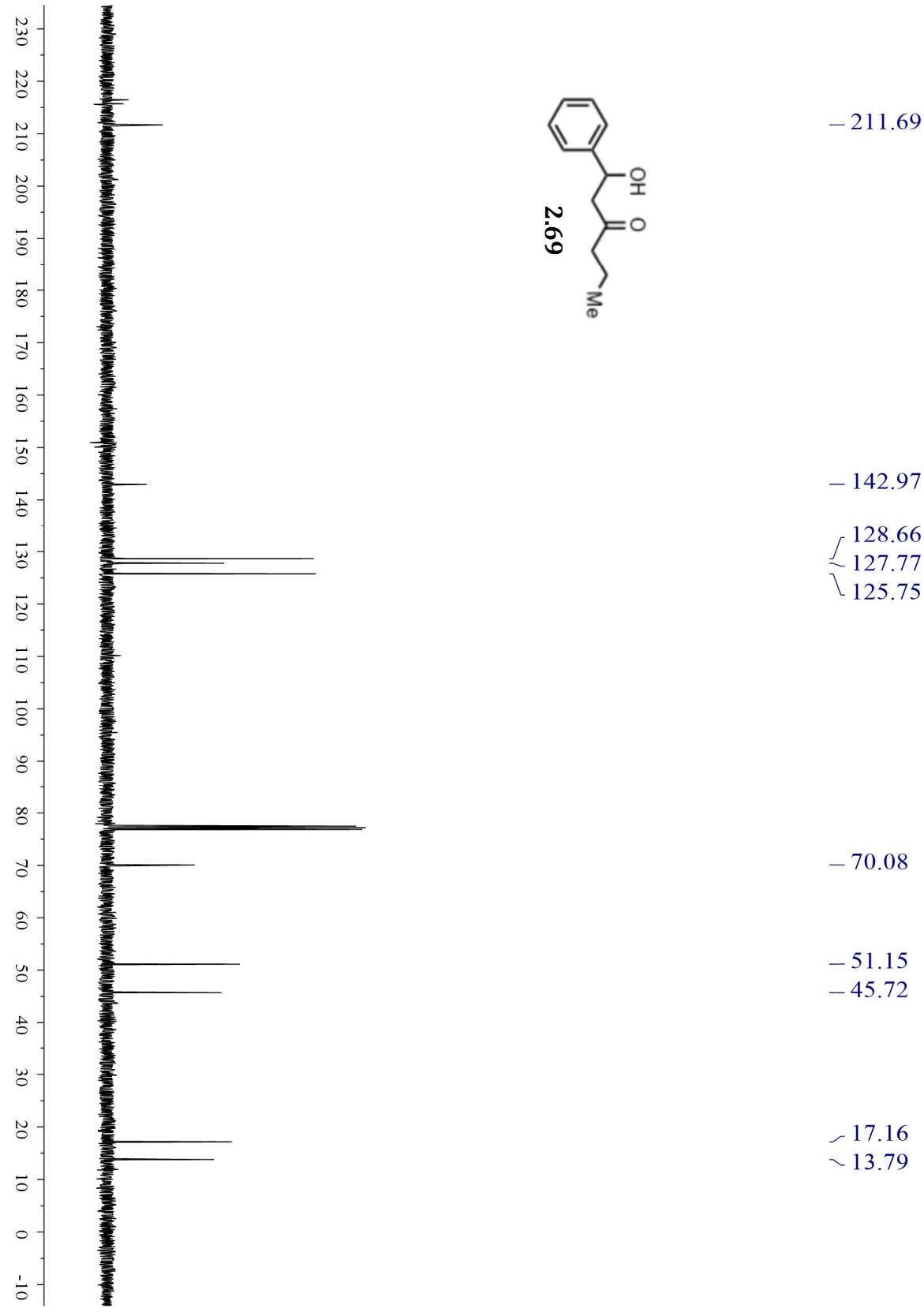

Me
Me
OH
O
Me
Me

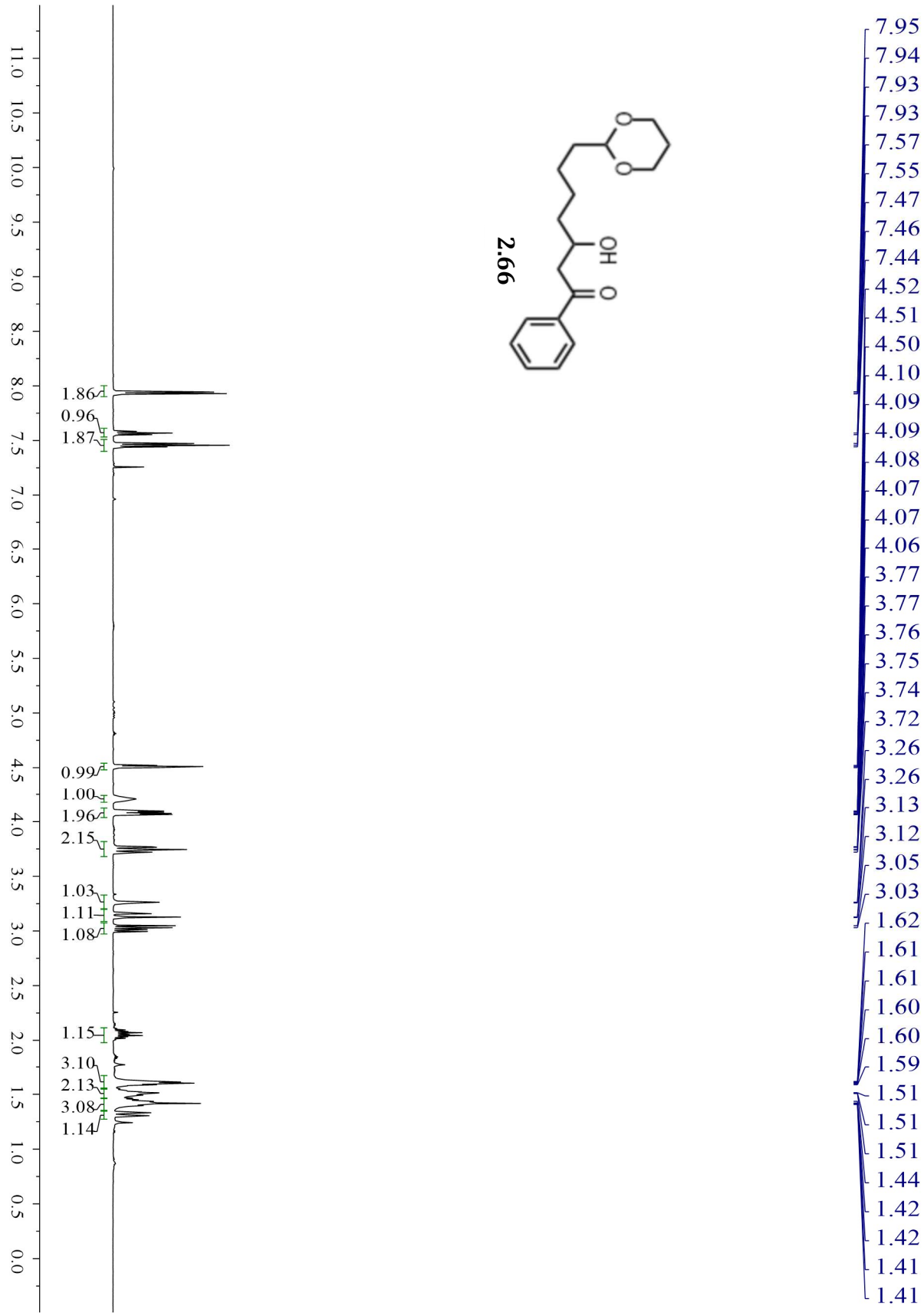
2.68

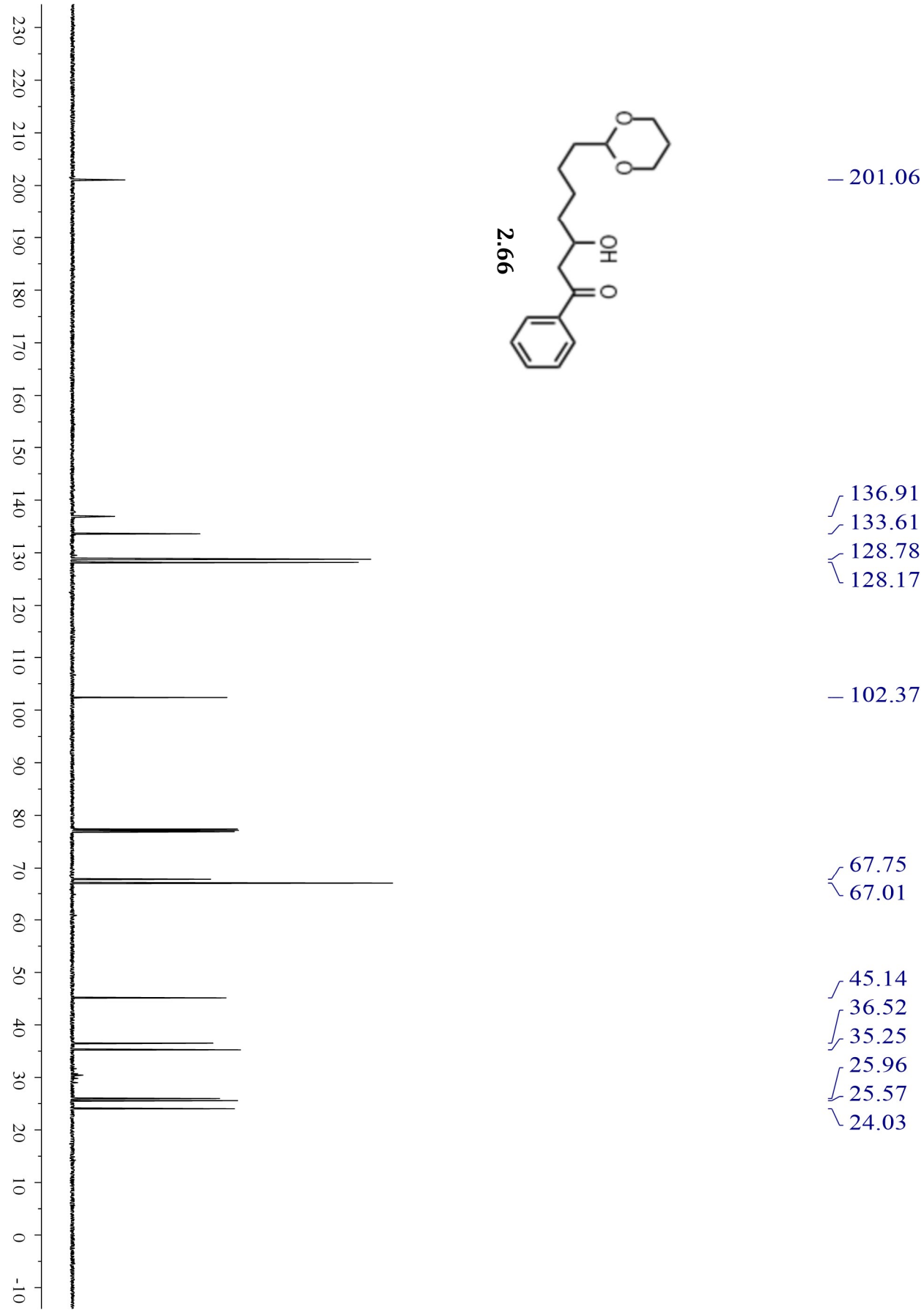

282
2.01
1.00
1.04
1.07
1.11
1.90
3.84
1.89
2.99
8.54
1.04
3.02
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

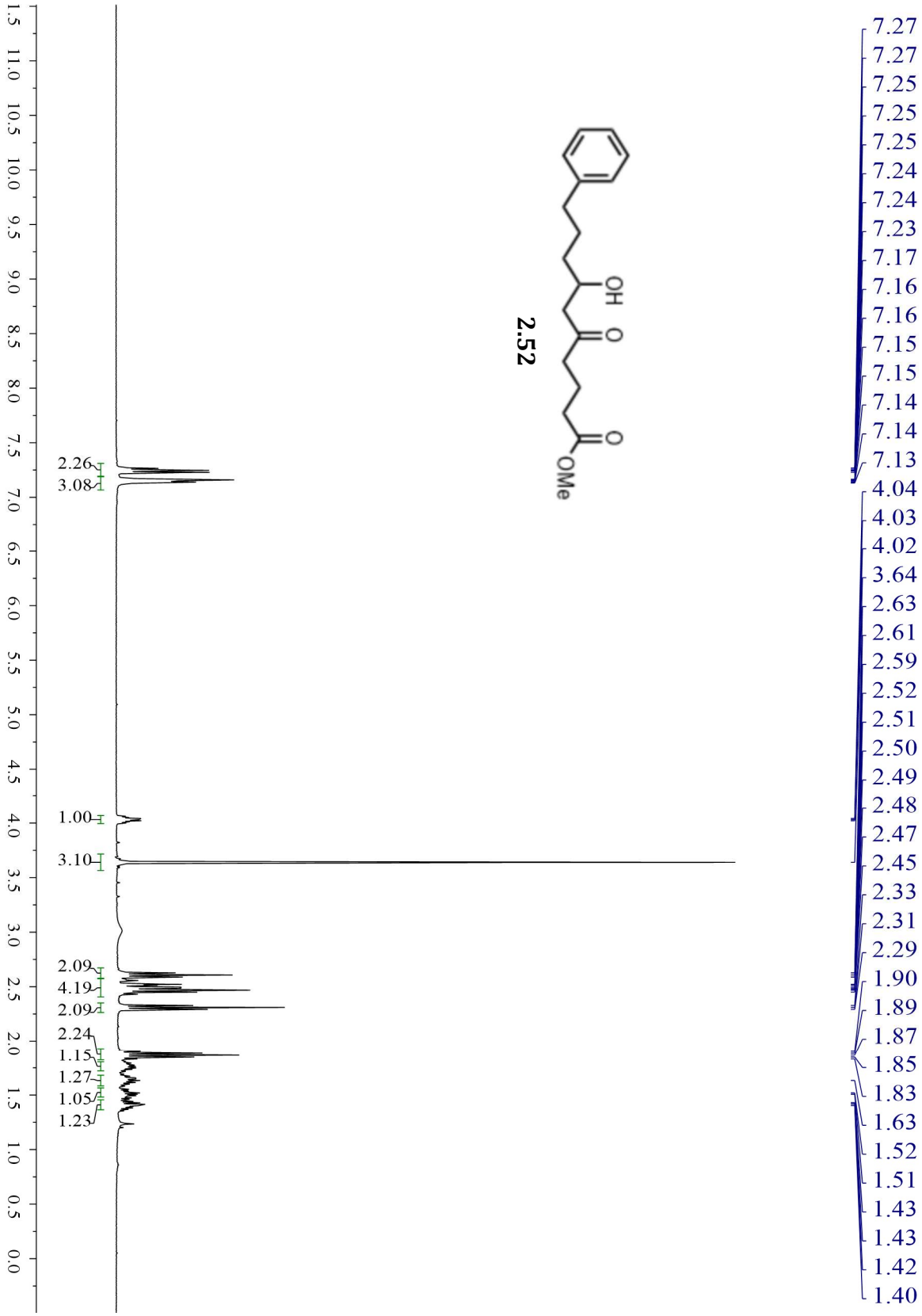

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
Me
Me
Me
OH
O
Me
2.68
212.46
135.97
131.53
124.39
123.79
67.42
49.14
45.71
39.85
36.58
26.80
25.83
24.09
17.83
17.23
16.15
13.82

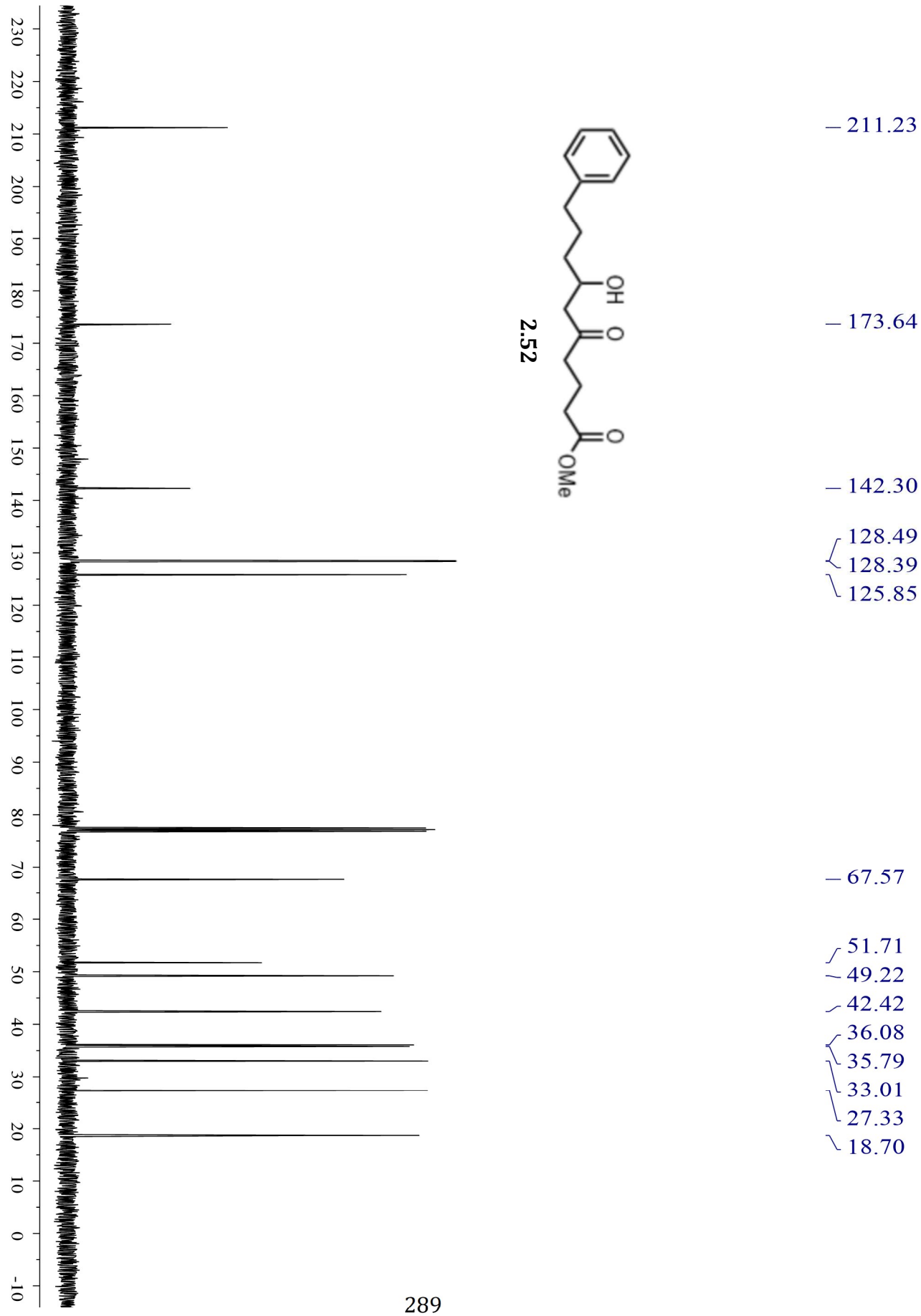
OH
O
Me
2.69
4.95
1.00
1.06
1.99
1.96
2.25
3.13
7.36
7.35
7.35
7.34
7.34
7.33
7.32
7.30
7.29
7.28
7.28
7.27
7.27
7.26
5.17
5.16
5.15
5.14
3.38
2.88
2.86
2.84
2.82
2.81
2.80
2.76
2.76
2.43
2.41
2.40
1.64
1.63
1.63
1.62
1.61
1.59
0.93
0.92

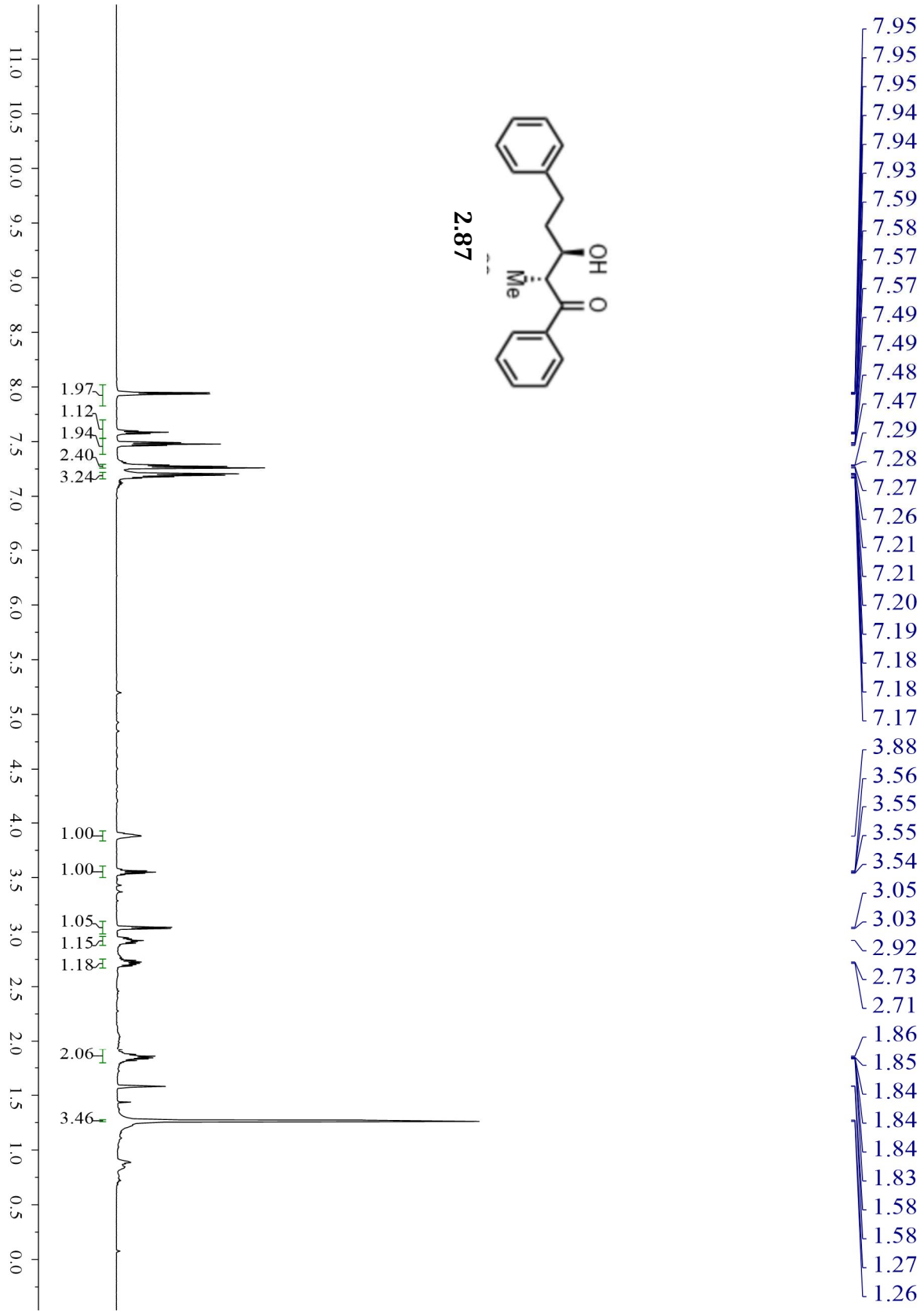

230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
OH
O
Me
2.69
211.69
142.97
128.66
127.77
125.75
70.08
51.15
45.72
17.16
13.79

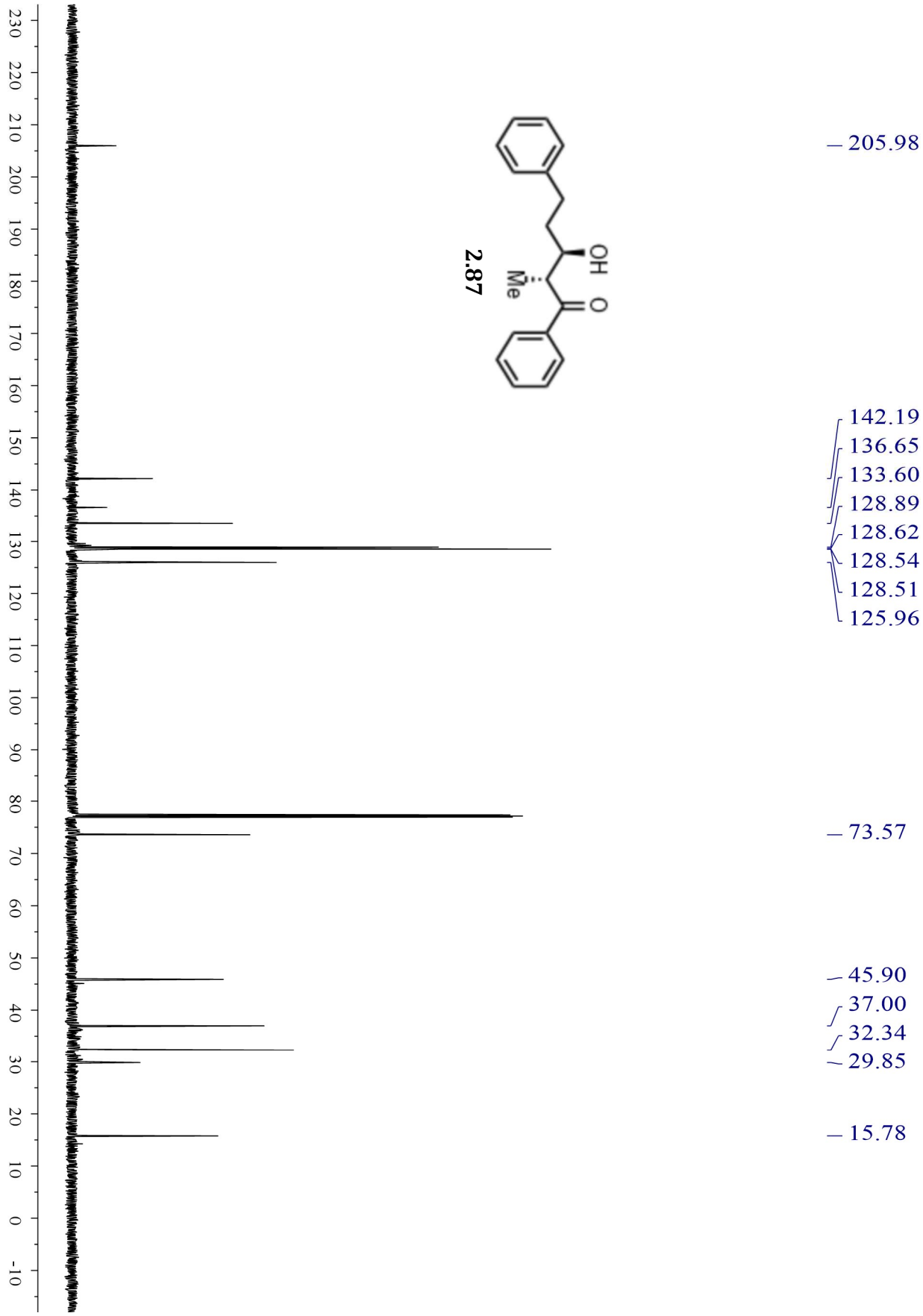

11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
1.86
0.96
1.87
0.99
1.00
1.96
2.15
1.03
1.11
1.08
1.15
3.10
2.13
3.08
1.14
2.66
OH
O
7.95
7.94
7.93
7.93
7.57
7.55
7.47
7.46
7.44
4.52
4.51
4.50
4.10
4.09
4.09
4.08
4.07
4.07
4.06
3.77
3.77
3.76
3.75
3.74
3.72
3.26
3.26
3.13
3.12
3.05
3.03
1.62
1.61
1.61
1.60
1.60
1.59
1.51
1.51
1.51
1.51
1.44
1.42
1.42
1.41
1.41


2.66
OH
O
201.06
136.91
133.61
128.78
128.17
102.37
67.75
67.01
45.14
36.52
35.25
25.96
25.57
24.03
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

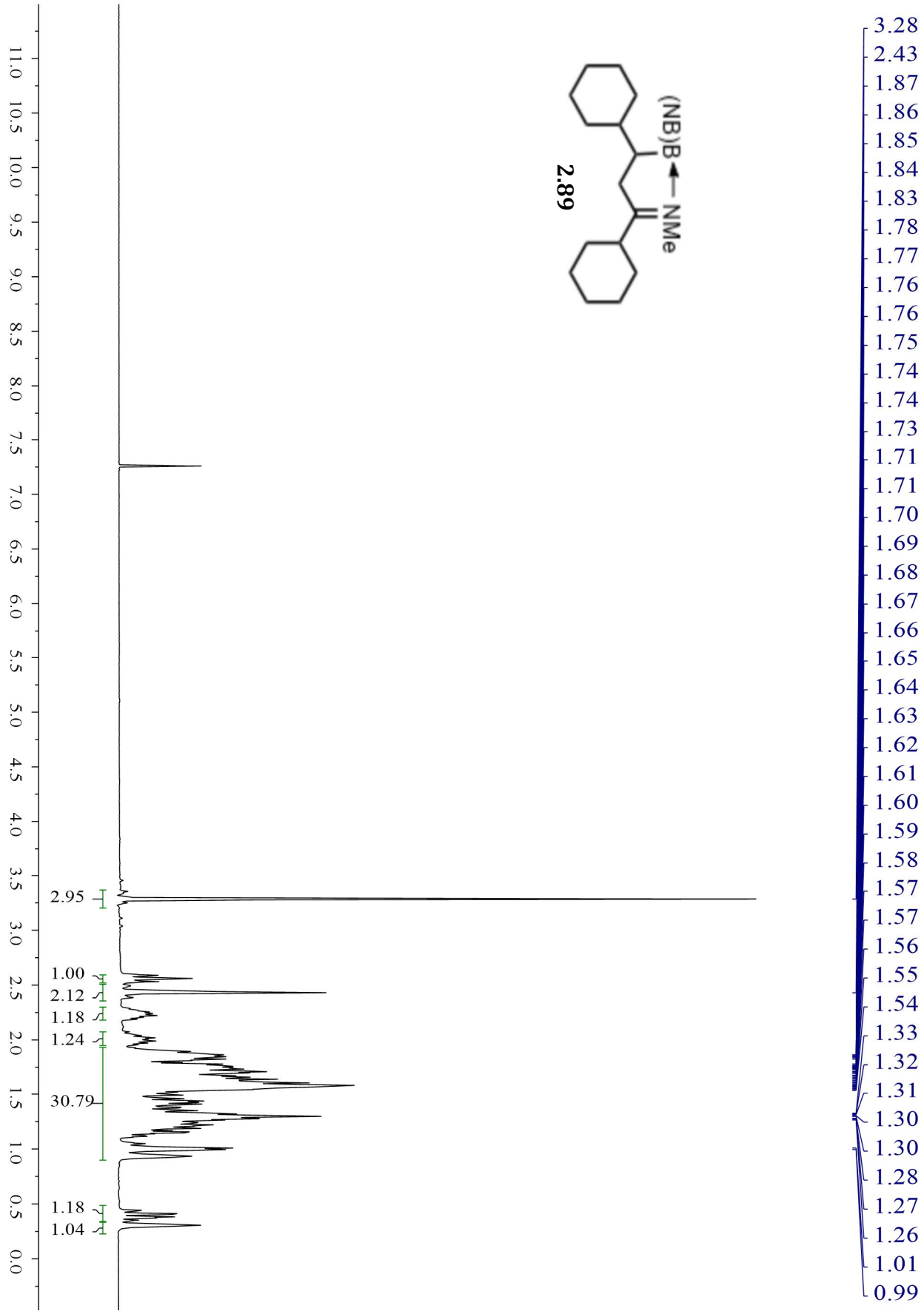

2.52
OH
O
O
OMe
2.26
3.08
1.00
3.10
2.09
4.19
2.09
2.24
1.15
1.27
1.05
1.23
7.27
7.27
7.25
7.25
7.25
7.24
7.24
7.23
7.17
7.16
7.16
7.15
7.15
7.14
7.14
7.13
4.04
4.03
4.02
3.64
2.63
2.61
2.59
2.52
2.51
2.50
2.49
2.48
2.47
2.45
2.33
2.31
2.29
1.90
1.89
1.87
1.85
1.83
1.63
1.52
1.51
1.43
1.43
1.42
1.40


211.23
173.64
142.30
128.49
128.39
125.85
67.57
51.71
49.22
42.42
36.08
35.79
33.01
27.33
18.70
OH
O
O
OMe
2.52

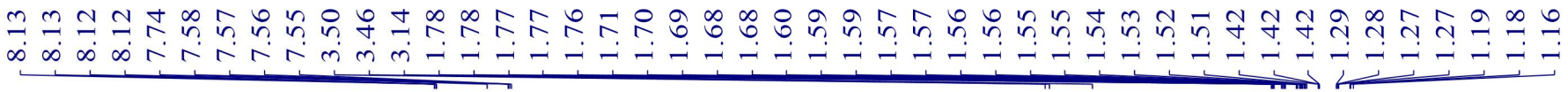

2.87
OH
O
Me
1.97
1.12
1.94
2.40
3.24
1.00
1.00
1.05
1.15
1.18
2.06
3.46
7.95
7.95
7.95
7.94
7.94
7.93
7.59
7.58
7.57
7.57
7.49
7.49
7.48
7.47
7.29
7.28
7.27
7.26
7.21
7.21
7.20
7.19
7.18
7.18
7.17
3.88
3.56
3.55
3.55
3.54
3.05
3.03
2.92
2.73
2.71
1.86
1.85
1.84
1.84
1.84
1.83
1.58
1.58
1.27
1.26

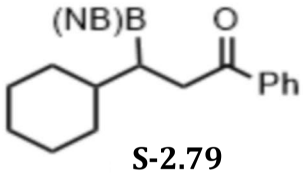

205.98
142.19
136.65
133.60
128.89
128.62
128.54
128.51
125.96
73.57
45.90
37.00
32.34
29.85
15.78
OH
O
Me

2.87

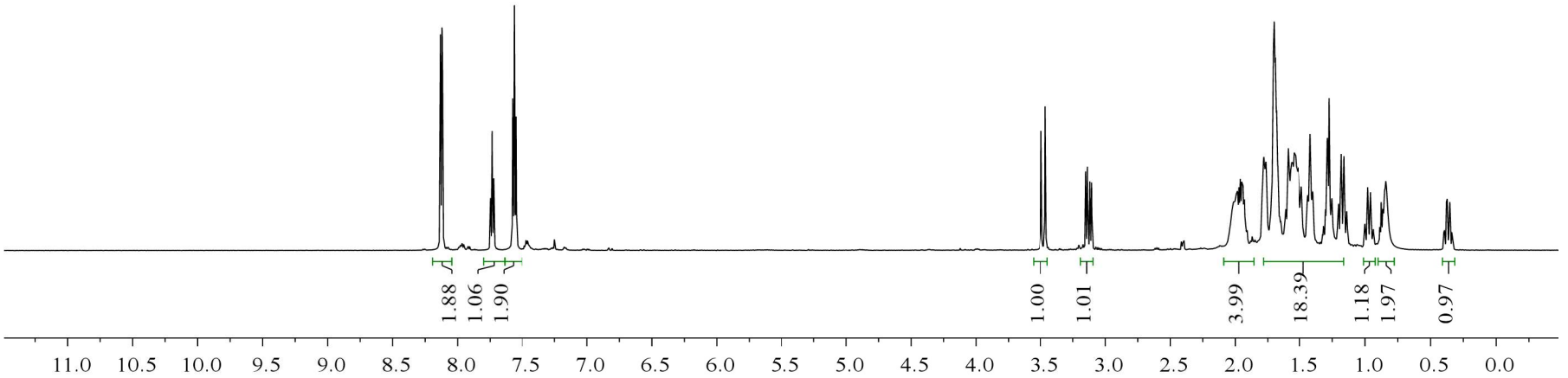

(NB)B NMe
2.89
2.95
1.00
2.12
1.18
1.24
30.79
1.18
1.04
3.28
2.43
1.87
1.86
1.85
1.84
1.83
1.78
1.77
1.76
1.76
1.75
1.74
1.74
1.73
1.71
1.71
1.70
1.69
1.68
1.67
1.66
1.65
1.64
1.63
1.62
1.61
1.60
1.59
1.58
1.57
1.57
1.56
1.55
1.54
1.33
1.32
1.31
1.30
1.30
1.28
1.27
1.26
1.01
0.99

(NB)B← NMe
2.89
189.07
40.42
37.74
36.94
35.78
35.14
34.34
33.24
31.91
30.77
30.65
29.49
29.41
27.39
27.31
27.15
25.95
25.90
25.83
25.24
24.23
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


8.13
8.13
8.12
8.12
7.74
7.58
7.57
7.56
7.55
3.50
3.46
3.14
1.78
1.78
1.77
1.77
1.76
1.71
1.70
1.69
1.68
1.68
1.60
1.59
1.59
1.57
1.57
1.56
1.56
1.55
1.55
1.54
1.53
1.52
1.51
1.42
1.42
1.42
1.29
1.28
1.27
1.27
1.19
1.18
1.16


(NB)B
O
Ph

S-2.79


1.88
1.06
1.90
1.00
1.01
3.99
18.39
1.18
1.97
0.97
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

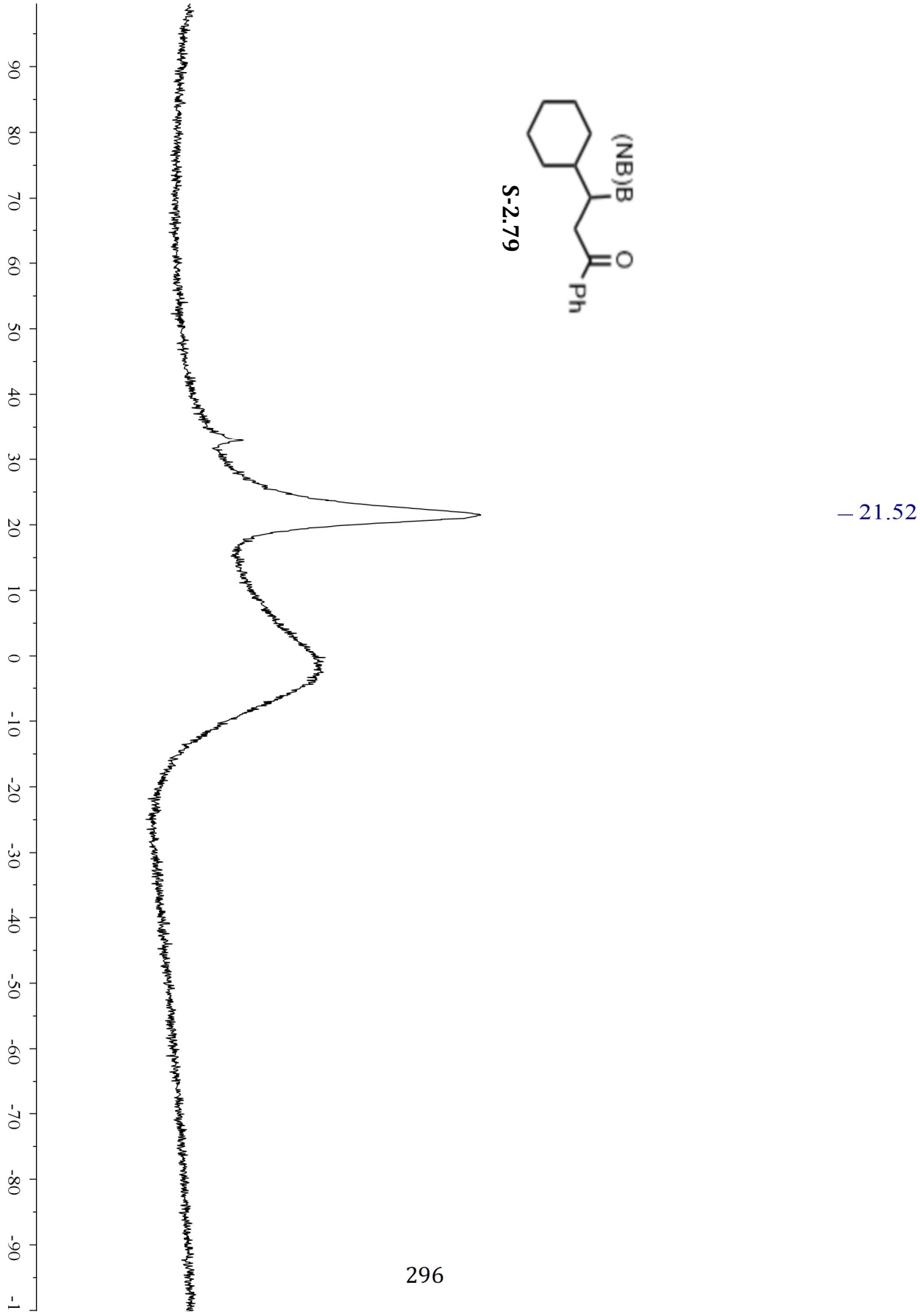
S-2.79

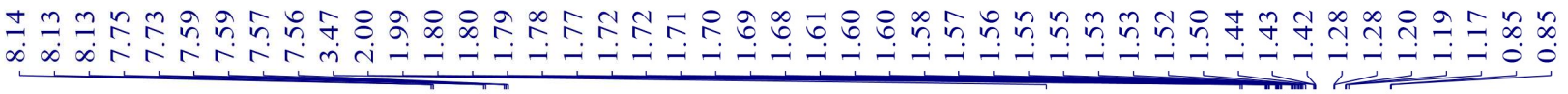
212.92

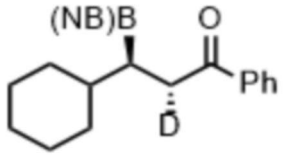
136.40
131.24
130.88
129.37

40.00
38.12
33.48
33.23
32.60
30.13
27.22
26.83
26.77
25.12

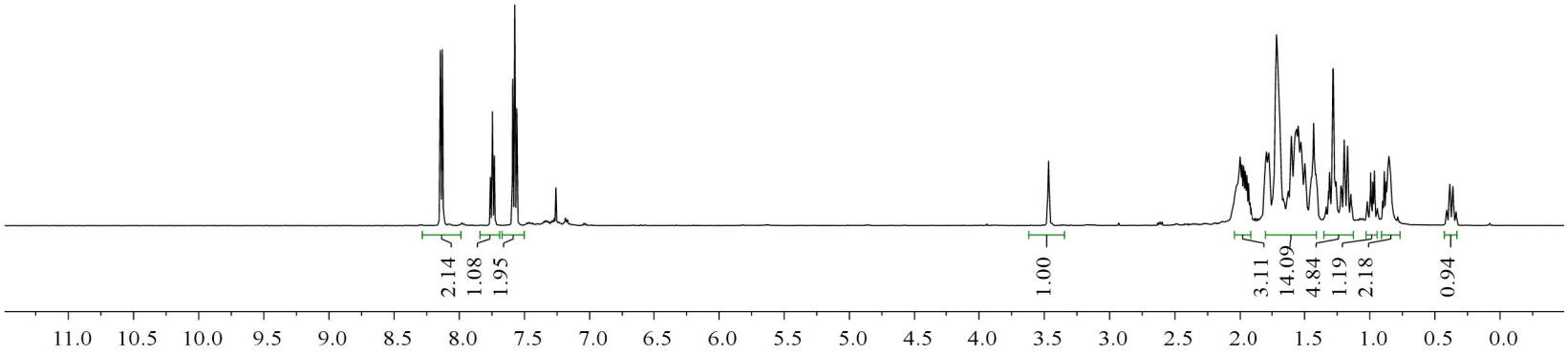
^{11}BNMR of S-2.79

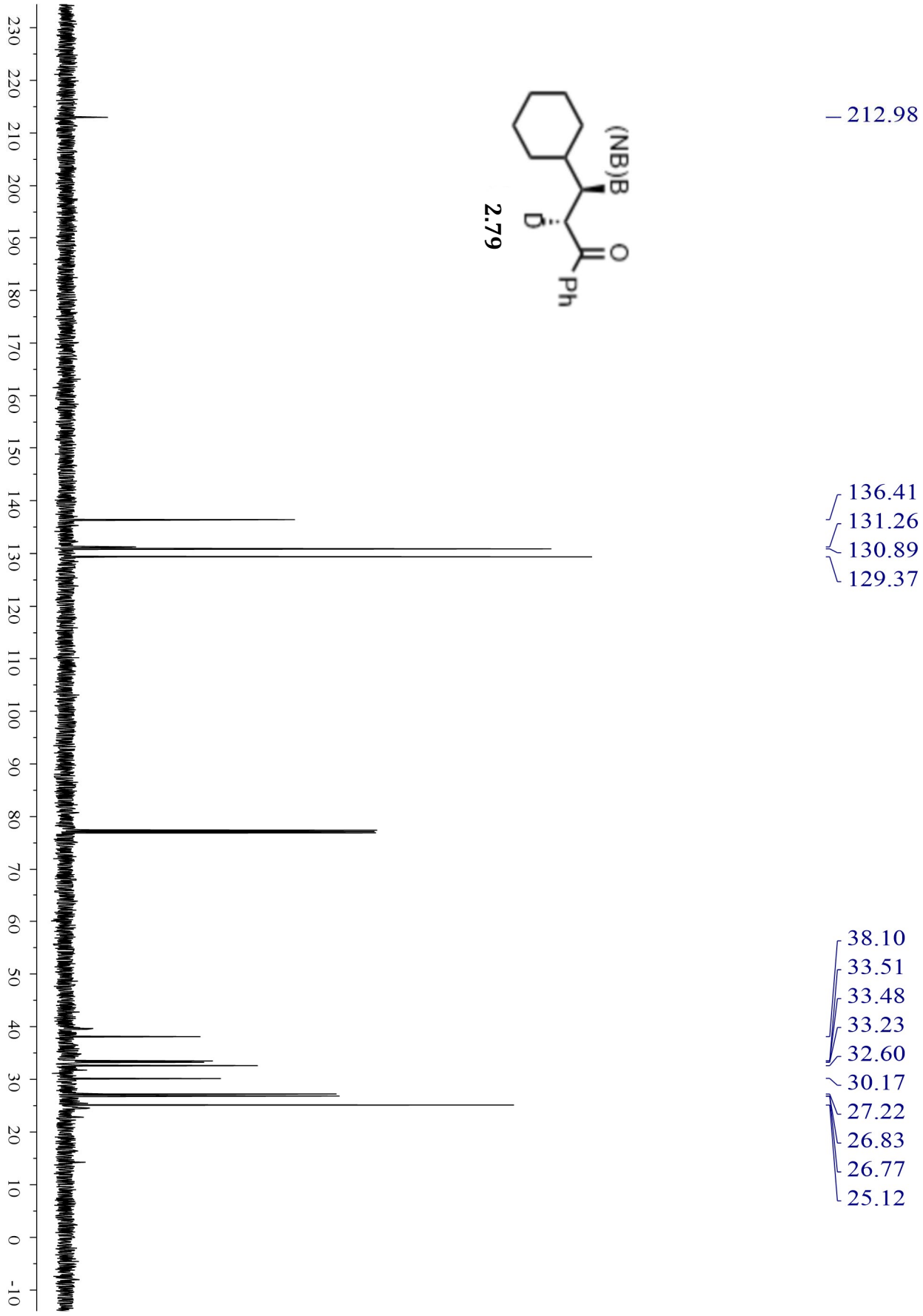



8.14
8.13
8.13
7.75
7.73
7.59
7.59
7.57
7.56
3.47
2.00
1.99
1.80
1.80
1.79
1.78
1.77
1.72
1.72
1.71
1.70
1.69
1.68
1.61
1.60
1.60
1.58
1.57
1.56
1.55
1.55
1.53
1.53
1.52
1.50
1.44
1.43
1.42
1.28
1.28
1.20
1.19
1.17
0.85
0.85

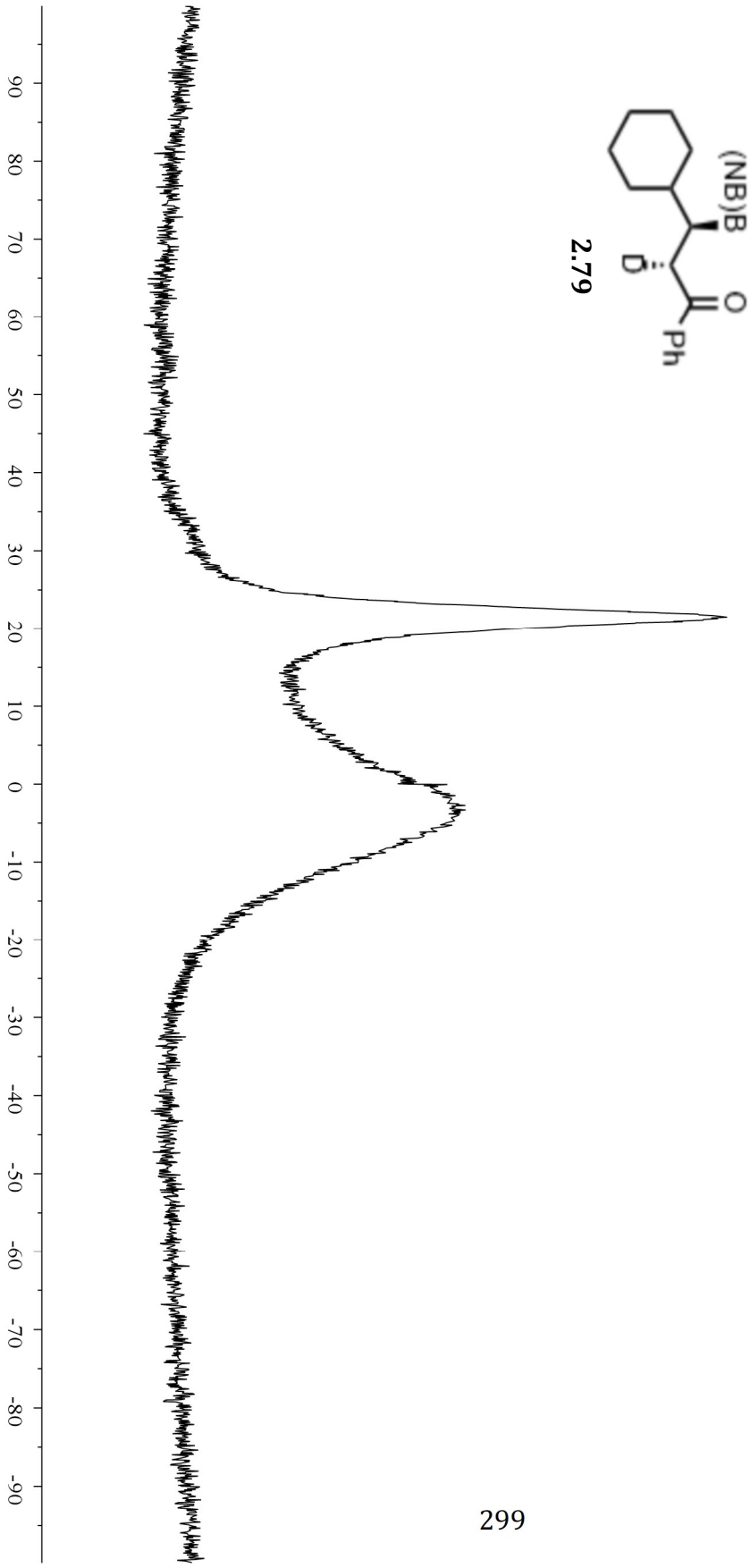

(NB)B
O
Ph
D

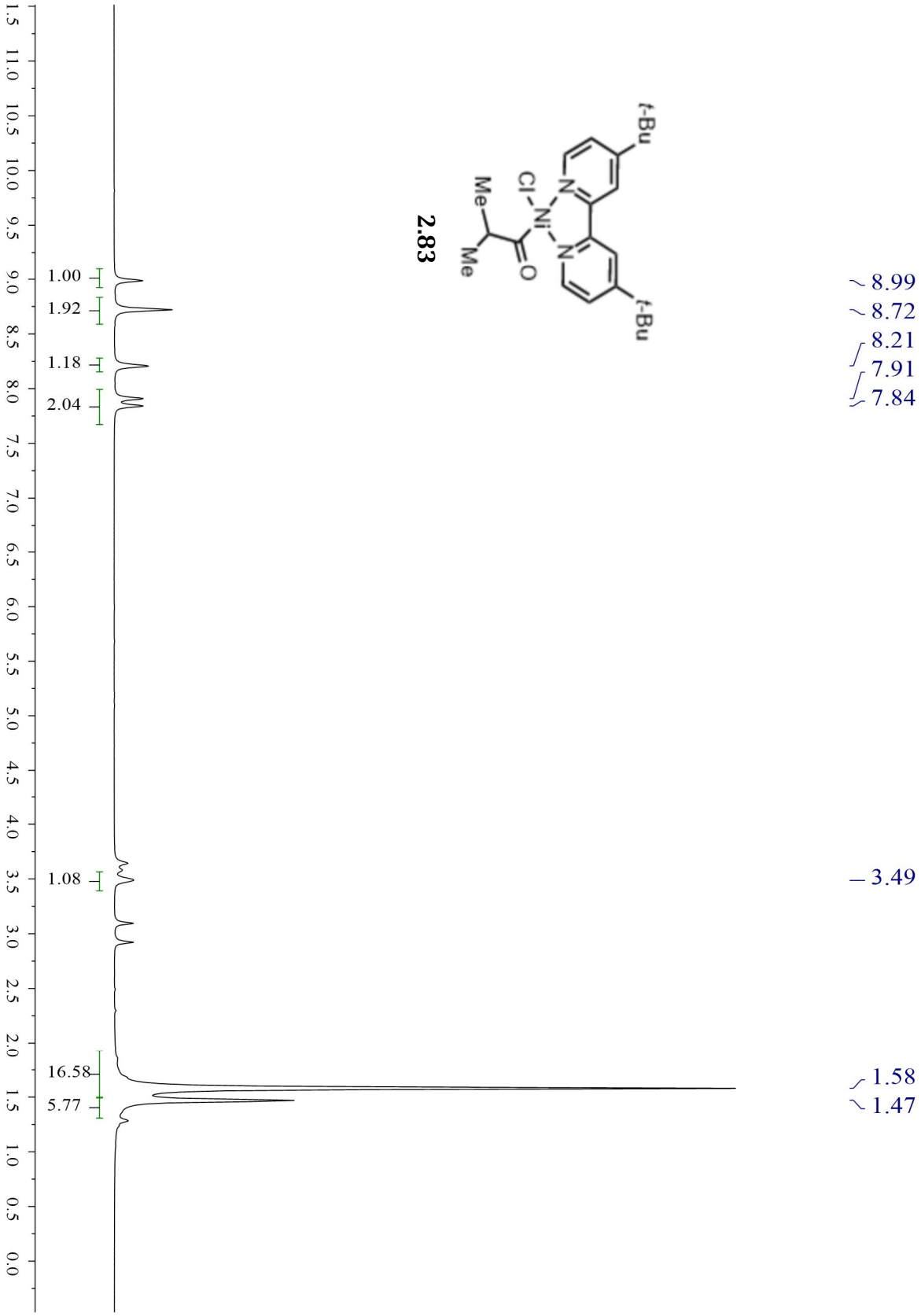
2.79

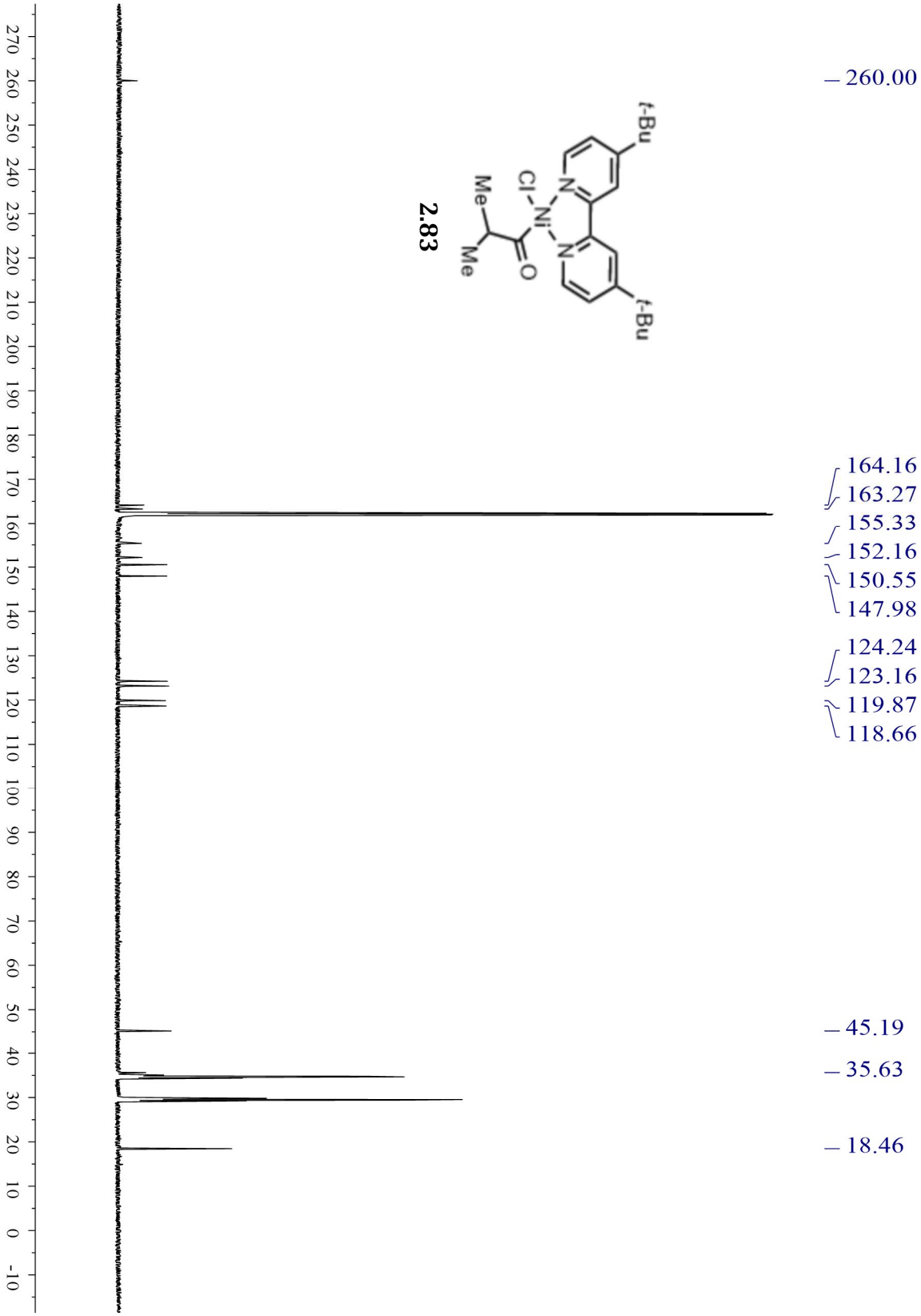

2.14
1.08
1.95
1.00
3.11
14.09
4.84
1.19
2.18
0.94
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


(NB)B
O
Ph
D
2.79
212.98
136.41
131.26
130.89
129.37
38.10
33.51
33.48
33.23
32.60
30.17
27.22
26.83
26.77
25.12

^{11}BNMR of 2.79




2.83
t-Bu
t-Bu
Cl
Ni
N
N
O
Me
Me
1.00
1.92
1.18
2.04
1.08
16.58
5.77
8.99
8.72
8.21
7.91
7.84
3.49
1.58
1.47


270 260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
260.00
164.16
163.27
155.33
152.16
150.55
147.98
124.24
123.16
119.87
118.66
45.19
35.63
18.46
t-Bu
t-Bu
Cl
Ni
N
N
O
Me
Me

2.83

3.0 CHAPTER 3

3.0 CHAPTER 3

Enantioselective and Diastereoselective 1,4-Difunctionalization of Borylenynes by Catalytic Conjunctive Cross-Coupling

3.1 INTRODUCTION

Allenes are important structural motifs found in numerous natural products[126] and, due to their unique reactivity, are frequently used as key synthetic intermediates. In recent years, a substantial body of work has been dedicated to the enantioselective synthesis of axially chiral allenes.[127] In particular, the synthesis of chiral substituted α-allenols has been an area of interest due to their ability to undergo cyclization reactions to afford oxygenated heterocycles of biological and pharmacological relavance. Transition-metal catalyzed cross-coupling reactions of alkynyl oxiranes with organometallic nucleophile remains the most reliable strategy to afford chiral α-allenols. This strategy relies on central-to axial chirality transfer with chiral non-racemic starting materials as an entry to enantioenriched allenes.[128] Recently, Shengming Ma reported an elegant synthesis of α-allenols from the

[126] For selected reviews on allene-containing natural products, see: (a) Krause, N.; Hashmi, A. S. K. *Modern Allene Chemistry*; Wiley−VCH: 2004. (b) Hoffmann-Röder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2004**, *43*, 1196.

[127] For comprehensive reviews on both non-catalytic and catalytic enantioselective synthesis of allenes, see (a) Hoffmann-Röder, A.; Krause, N. *Angew. Chem., Int. Ed*. **2002**, *41*, 2933. (b) Ogasawara, M. *Tetrahedron Asymmetry* **2009**, *20*, 259. (c) Yu, S.; Ma, S. *Chem. Commun.* **2011**, 47, 5384. (d) Ye, J.; Ma, S. *Org. Chem. Front.* **2014**, *1*, 1210. (e) Chu, W.; Zhang, Y.; Wang, J. *Catal. Sci. Technol*. **2017**, *7*, 4570. Huang, X.; Ma, S. *Acc. Chem. Rev*. **2019**, *52*, 1301-1312.

[128] (a) Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, ***31***, 12-21. (b) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701.

corresponding aldehydes with a copper catalyst and a chiral N-PINAP ligand to control the axial chirality.[129] Despite these research efforts towards the synthesis of α-allenols, there is a lack of catalytic methods that allow for their construction from achiral starting materials with simultaneous control of both axial- and central chirality. Indeed, to the best of our knowledge, the alkynylogous Mukaiyama aldol reaction reported by List is the only catalytic method that controls both stereochemical elements during product formation.[130] We report herein the conjunctive cross-coupling reaction towards the enantio- and diastereoselective synthesis of α-borylallenes, which provides α-allenols upon oxidative workup.

3.2 BACKGROUND

3.2.1 Catalytic Enantioselective Syntheses of Chiral Allenes

In addition to being a common moiety in natural products, functionalized allenes are often important synthetic intermediates that engage in complexity-building transformations.[131] These transformations often take advantage of axial-to-central chirality transfer to generate new stereogenic centers. For these reasons, the development of

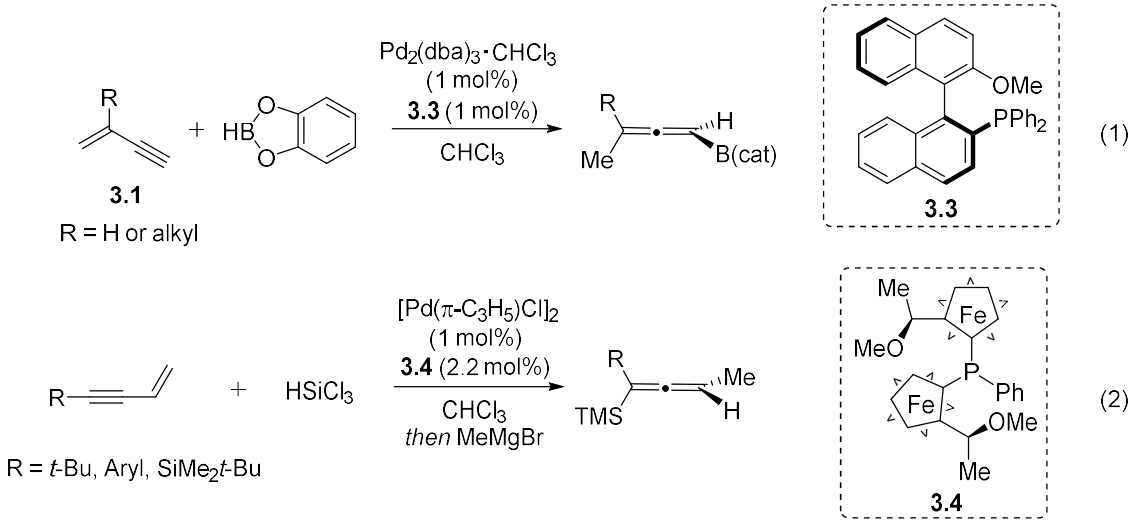
---

[129] Ye, J.; Li, S.; Chen, B.; Fan, W.; Kuang, J.; Liu, J.; Liu, Y.; Miao, B.; Wan, B.; Wang, Y.; Xie, X.; Yu, Q.; Yuan, W.; Ma, S. *Org. Lett.* **2012**, *14*, 1346-1349.
[130] Tap, A.; Blond, A.; Wakchaure, V.; List, B. *Angew. Chem. Int. Ed.* **2016**, *55*, 8962.
[131] For selected reviews on the synthetic utility of allenes, see: (a) Brummond, K. M.; Chen, H. *Modern Allene Chemistry*; Wiley-VCH: 2004. (b) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590. (c) Ma, S. *Chem. Rev.* **2005**, 105, 7, 2829. (d) Ma, S. *Acc. Chem. Res.* **2009**, *42*, 1679. (e) Yu, S.; Ma, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 3074−3112. (f) Neff, R. K.; Frantz, D. E. *Tetrahedron* **2015**, *71*, 7. (g) Alonso, J. M.; Quiros, M. T.; Munoz, M. P. *Org. Chem. Front*. **2016**, *3*, 1186.

enantioselective methods to access axially chiral allenes has been an important area of research. One common strategy to prepare these compounds relies on the use of chiral, non-racemic starting materials wherein central-to-axial chirality transfer, *via* either sigmatropic rearrangement, nucleophilic displacement, or elimination, would generate the chiral allene products.[132] While there are several comprehensive review articles that cover these routes to access chiral allenes, this chapter will focus on catalytic enantioselective reactions to access enantioenriched allenes from achiral or racemic starting materials.

In 1993, Hayashi and co-workers reported one of the first catalytic asymmetric methods to access enantioenriched allenes.[133] In this process, a Pd-catalyzed hydroboration was carried out upon substituted 1,3-enynes to generate the chiral, non-racemic allenylboronic ester (eq. 1, Scheme 3.1). Years later, the same group showed that similar reaction conditions could be successfully extended to hydrosilylation to afford enantioenriched allenylsilane(eq. 2, Scheme 3.1).[134]

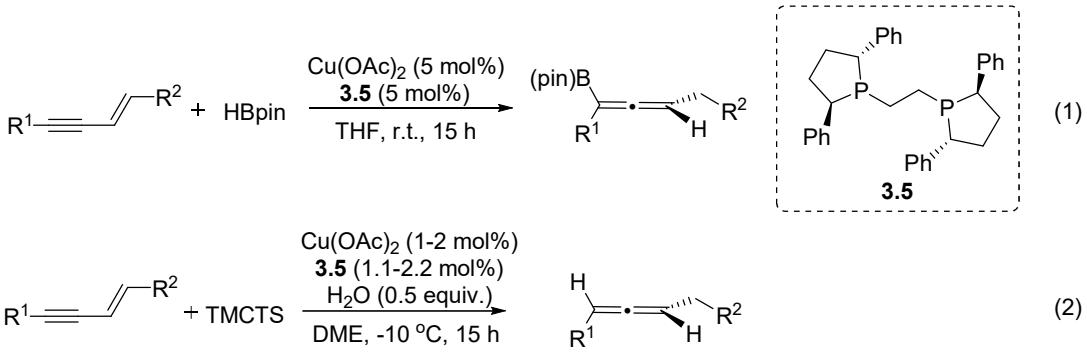
Scheme 3.1 Hayashi's Hydroboration and Hydrosilylation Reactions of 1,3-Enyne.



[132] (a) Brummond, K. M.; DeForrest, J. E. *Synthesis* **2007**, 795. (b) Yu, S.; Ma, S. *Chem. Commun.* **2011**, 47, 5384. (c) Ye, J.; Ma, S. *Org. Chem. Front.* **2014**, 1, 1210.
[133] Matsumoto, Y.; Naito, M.; Uozumi, Y.; Hayashi, T. *J. Chem. Soc., Chem. Commun.* **1993**, 1468.
[134] Han, J. W.; Tokunaga, N.; Hayashi, T. *J. Am. Chem. Soc.* **2001**, *123*, 12915.

The use of 1,3-enynes as starting material, remains to date a popular strategy to access enantioenriched allenes. In 2018, Hoveyda and co-workers reported the enantioselective hydroboration of 1,3-enynes under copper catalysis (eq. 1, Scheme 3.2).[135] The catalytic cycle proceeds via an allenyl copper intermediate which undergoes σ-bond metathesis with HBpin to afford the enantioenriched trisubstituted allenylboronic ester. It is worth noting that the same allenylcopper intermediate was later demonstrated by the Buchwald group to undergo proto-decupration in the presence of water to afford 1,3-disubstituted allenes with high enantioselectivity (eq. 2, Scheme 3.2).[136]

Scheme 3.2 Asymmetric Copper-Catalyzed Syntheses of Allenes.

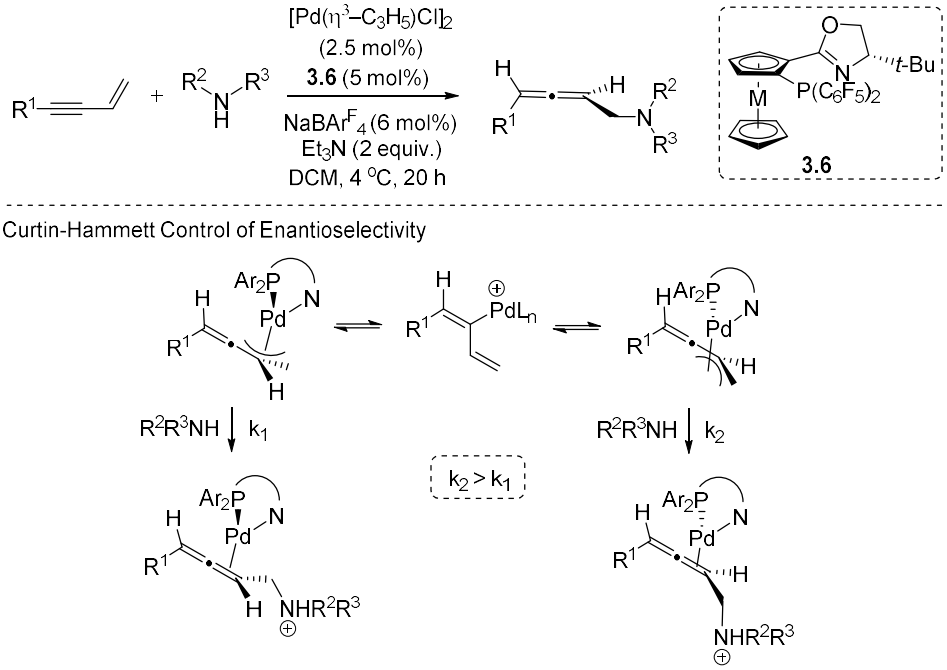


More recently, Malcolmson and co-workers demonstrated the Pd-catalyzed hydroamination of 1,3-enynes as a tool for the synthesis of enantioenrhcied 1,3-disubstituted allenes (Scheme 3.3).[137] The mechanism was proposed to proceed via alkyne insertion to Pd-H species followed by σ-π rearrangement and allylic substitution by the amine. Mechanistic studies point to Curtin-Hammett kinetics being operative, with the step

[135] Huang, Y.; del Pozo, J.; Torker, S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2018**, *140*, 2643.
[136] Bayeh-Romero, L.; Buchwald, S. L. *J. Am. Chem. Soc.* **2019**, *141*, 13788.
[137] Adamson, N. J.; Jeddi, H.; Malcolmson, S. J. *J. Am. Chem. Soc.* **2019**, *141*, 8574.

of allylic substitution rather than the σ-π isomerization as the stereochemistry determining step.

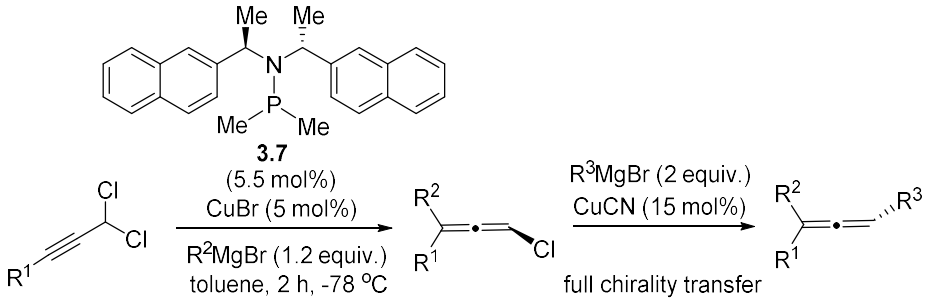
Scheme 3.4 Macolmson's Pd-Catatlyzed Hydroamination of 1,3-Enynes.



In 2012, Alexakis and co-workers reported the use of 1,1-dichloro propargylic compounds as starting materials for the enantioselective synthesis of chloroallenes under copper catalysis (Scheme 3.4).[138] The resulting chloroallenes were then subjected to copper-catalyzed S_N2 substitution reactions with various organomagnesium reagents, and no loss of enantiopurity was observed during the process.

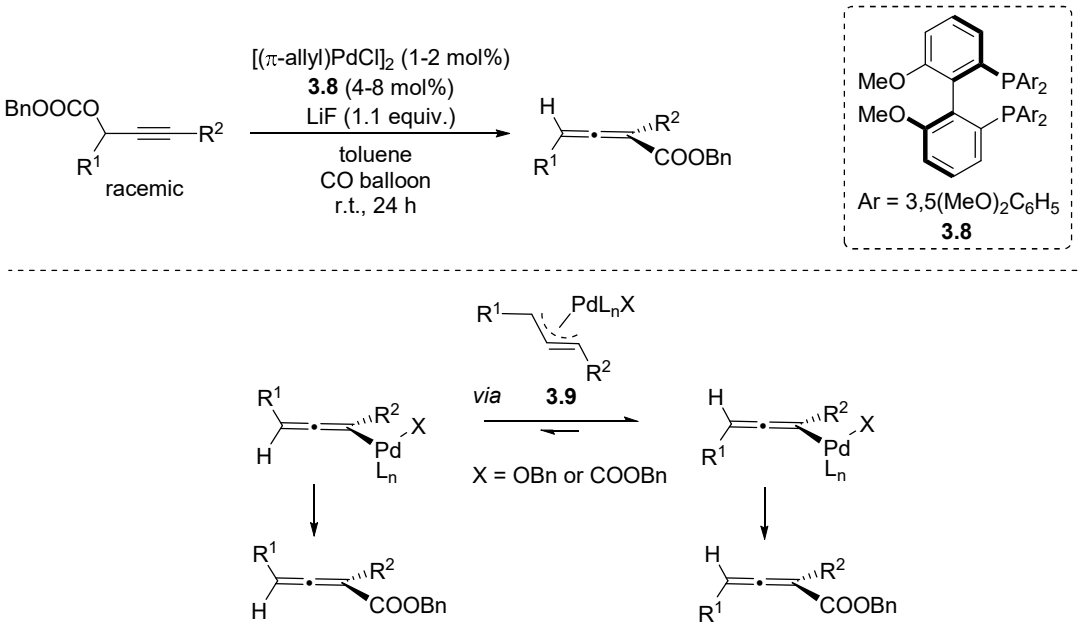
[138] Li, H.; Müller, D.; Guénée, L.; Alexakis, A. *Org. Lett.* **2012**, *14*, 5880.

Scheme3.4 Cu-Catalyzed Enantioselective Substitution with Propagylic dichloride.



Racemic starting materials might also be used to access chiral, non-racemic allenes by using enantioconvergent methods. In 2013, Shengming Ma and co-workers reported the catalytic asymmetric carbonylation of racemic propargylic carbonates to afford enantioenriched allenes (Scheme 3.5).[139] The diastereomic mixture of allenylpalladium species was proposed to undergo diastereo-enrichment by rapid isomerization via the intermediacy of **3.9**.

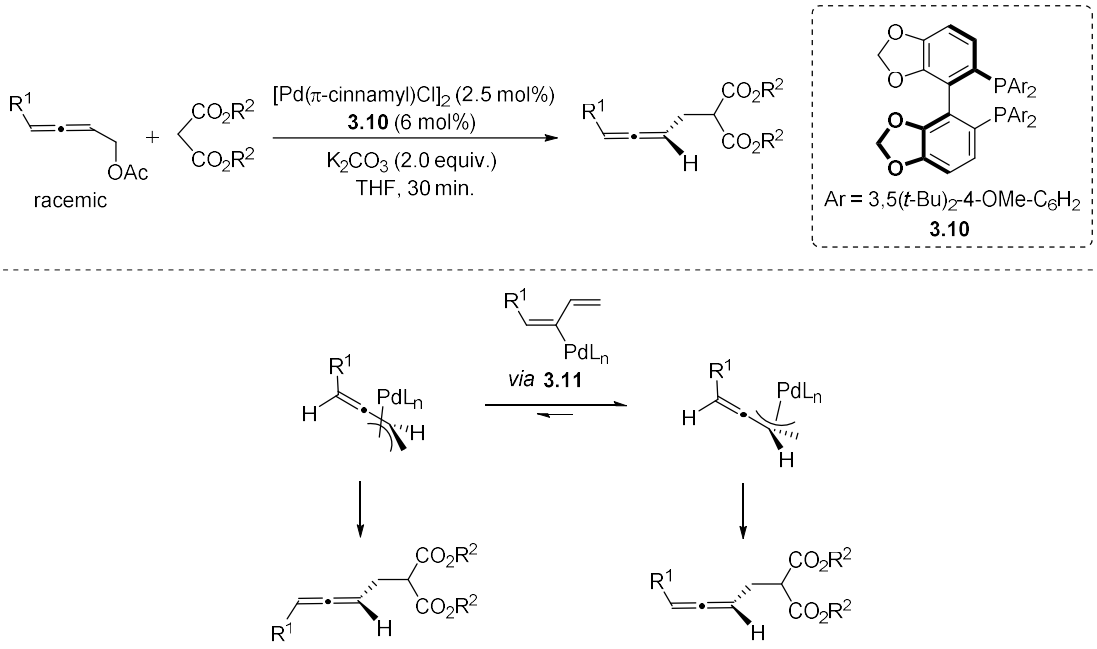
Scheme 3.5 Catalytic Asymmetric Carbonylation of Racemic Propagylic Carbonate.



[139] Wang, Y.; Zhang, W.; Ma, S. *J. Am. Chem. Soc.* **2013**, *135*, 11517.

Later in 2019, the same group reported an asymmetric Pd-catalyzed allylic substitution of malonate to racemic allenic carbonates (Scheme 3.6).[140] The stereoconvergence in this process originates from the generation of achiral η^1-intermediate **3.11** followed by selective σ-π rearrangement to the chiral η^3-intermediate.

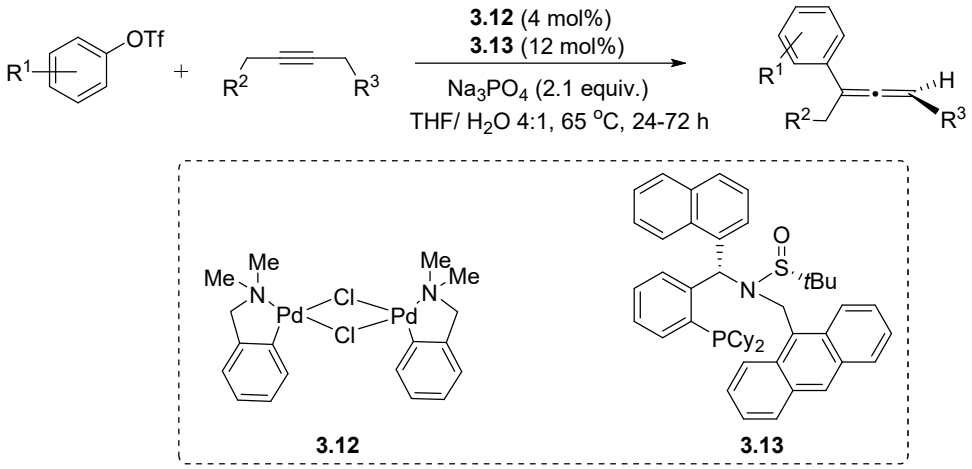
Scheme 3.6 Asymmetric Allylic Substitution to Racemic Allenic Carbonate.



The first enantioselective Heck reaction of alkynes to provide enantioenriched tri-substituted allenes was reported in 2019 by Zhang and co-workers (Scheme 3.7).[141] The selection of the specialized Xu-Phos ligand **3.13** was found to be critical to overcome the high energetic barrier of β-hydride elimination as well as to minimize further isomerization of the allene product to 1,3-diene.

[140] Song, S.; Zhou, J.; Fu, C.; Ma, S. *Nat. Commun.* **2019**, *10*, 507.
[141] Zhu, C.; Chu, H.; Li, G. Ma, S.; Zhang, J. *J. Am. Chem. Soc.* **2019**, *141*, 19246.

Scheme 3.7 Enantioselective Heck Reaction of Alkynes.



3.2.2 Enantioselective Syntheses of α-Allenols

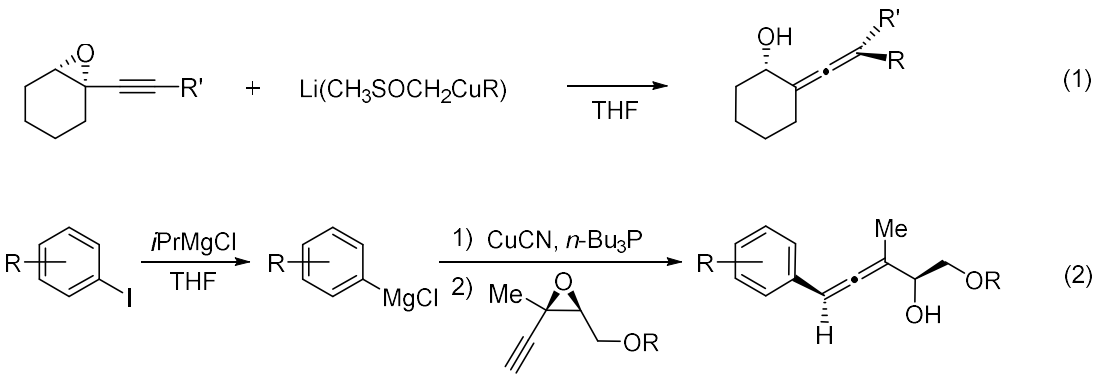
As mentioned in the previous section, the synthesis of chiral substituted α-allenols has been an area of interest in recent years due to their ability to be further transformed to biologically relevant oxygenated heterocycles.[142] One commonly used strategy to access α-allenols possessing both a stereogenic center and an axially chiral allene is by nucleophilic ring opening of chiral alkynyl oxiranes. For example, reaction between alkynyl oxiranes and organocuprates derived from organolithium reagents selectively provides the net *anti* addition product (eq. 1, Scheme 3.8).[143] Later, Krause and co-workers

[142] For reviews and references of α-allenols in nucleophilic cyclization reactions, see (a) Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, ***31***, 12. (b) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701. (c) Ma, S.; Gu, Z. *J. Am. Chem. Soc*. **2005**, *127*, 6182. (d) Alcaide, B.; Almendros, P.; Martinez del Campo, T. *Angew. Chem.Int. Ed.* **2006**, *45*, 4501. (e) Erdsack, J.; Krause, N. *Synthesis* **2007**, 3741. (f) Krause, N.; Belting, V.; Deutsch, C.; Erdsack, J.; Fan, H.-T.; Gockel, B.; Hoffmann-Roder, A.; Morita, N.; Volz, F. *Pure Appl. Chem.* **2008**, *80*, 1063. (g) Deng, Y.; Yu, Y.; Ma, S. *J. Org. Chem.* **2008**, *73*, 585. (h) Deng, Y.; Shi, Y.; Ma, S. *Org. Lett.* **2009**, *11*, 1205.

[143] Johnson, C.; Dhanoa, D. *J. Org. Chem.* 1987, *52*, 1885.

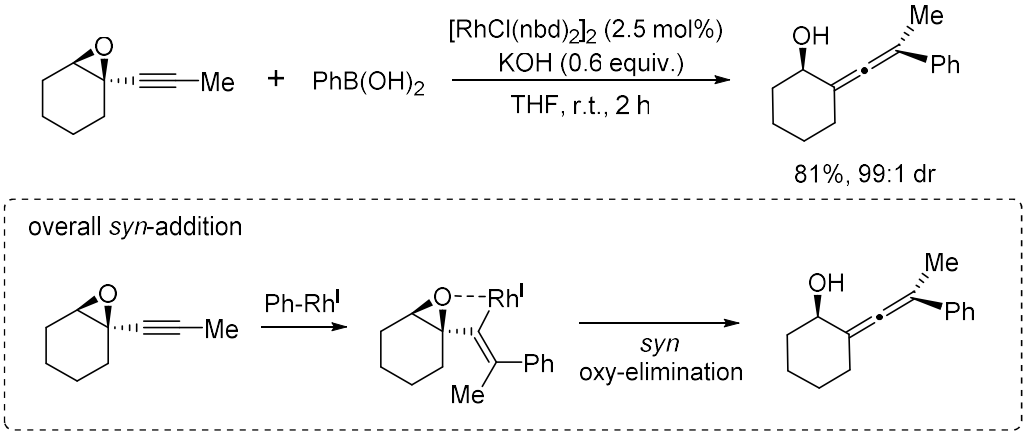
expanded the scope of this reaction by engaging densely functionalized Grignard reagents as nucleophiles (eq. 2, Scheme 3.8).[144]

Scheme 3.8 Copper-Mediated Ring-Opening of Alkynyl Oxiranes.



Milder nucleophilic partners could also be utilized in substitution reactions. In 2005, Ihara and co-workers reported the use of organoboronic acids in cross-coupling reactions with alkynyl oxiranes under rhodium catalysis (Scheme 3.9).[145] The reaction selectively provides the *syn* addition product. A stepwise alkyne insertion to Rh^{I}-R followed by *syn* β-oxygen elimination was proposed to explain the net *syn* selectivity.

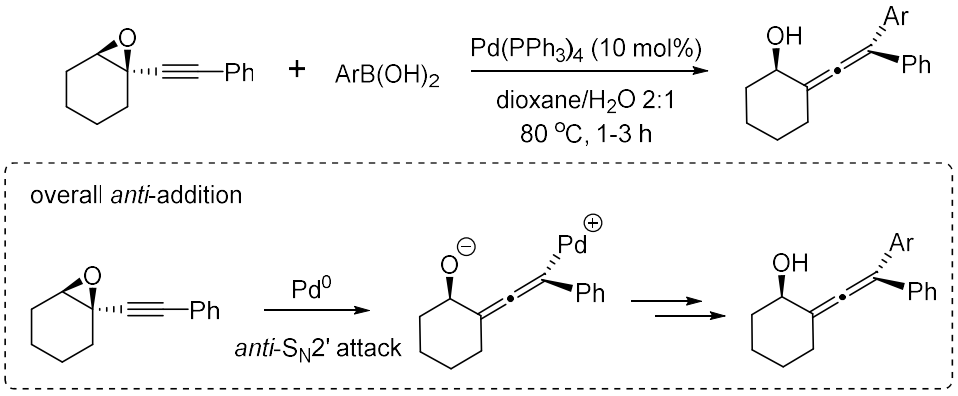
Scheme 3.9 Rh-Catalyzed *Syn*-Selective Ring-Opening of Alkynyl Oxirane.



[144] Deutsch, C.; Hoffmann-Röder, A.; Domke, A.; Krause, N. *Synlett*. **2007**, 737.
[145] Miura, T.; Shimada, M.; Ku,S.-Y.; Tamai, T.; Murakami, M. *Angew. Chem. Int. Ed.* **2007**, *46*, 7101.

Later, Murakami and co-workers reported the selective formation of the *anti* addition product with $Pd(PPh_3)_4$ as the catalyst (Scheme 3.10).[146] Contrary to the report by Ihara, ring-opening proceeds by a concerted *anti* S_N2' attack of Pd(0) on the alkynyl oxirane. The subsequent transmetallation with arylboronic acids followed by reductive elimination would then generate the *anti* addition product selectively.

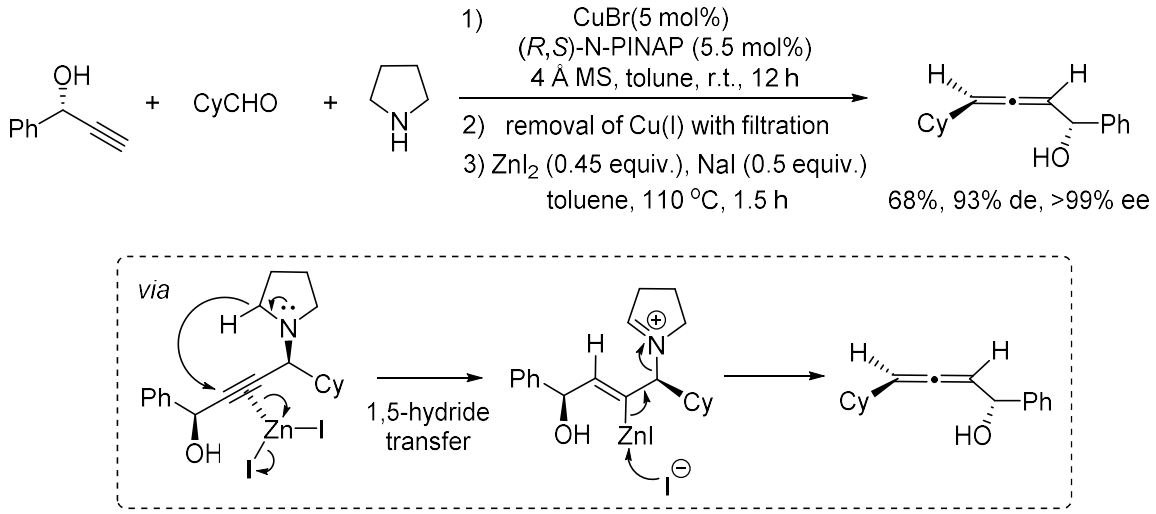
Scheme 3.10 Pd-Catalyzed *Anti*-Selective Ring-Opening of Alkynyl Oxirane.



Aside from alkynyl oxiranes, propargyl alcohols are also suitable starting materials for the synthesis of α-allenols as shown by Shengming Ma (Scheme 3.11).[147] The reaction proceeded by the $CuBr_2$-mediated 1,5-intramolecular hydride transfer to form the allene moiety. Overall, the axial chirality of allene was controlled by the use of chiral N-PINAP ligand on copper.

[146] Yoshida, M.; Ueda, H.; Ihara, M. *Tetrahedron Lett.* **2005**, *46*, 6705.
[147] Ye, J.; Li, S.; Chen, B.; Fan, W.; Kuang, J.; Liu, J.; Liu, Y.; Miao, B.; Wan, B.; Wang, Y.; Xie, X.; Yu, Q.; Yuan, W.; Ma, S. *Org. Lett.* **2012**, *14*, 1346-1349.

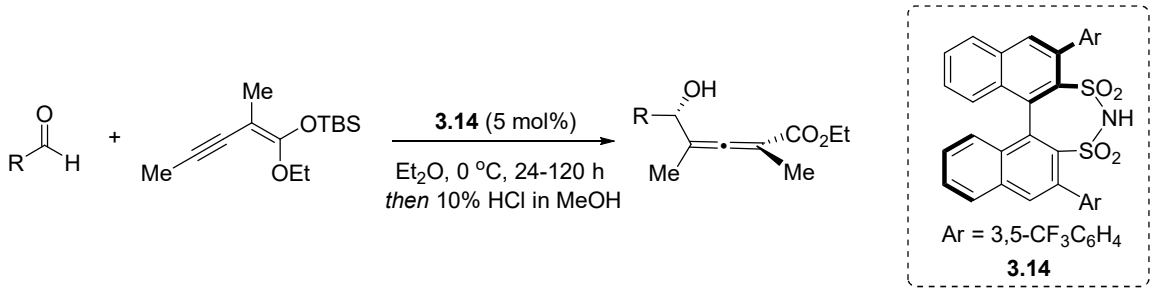
Scheme 3.11 Ma's Catalytic Enantioselective Synthesis of Chiral α-Allenol.



While the aforementioned methods rely on the use of chiral starting materials to access diastereo- and enantioenriched α-allenols, there is a lack of methods that allow for the simultaneous construction of both axial- and central chirality from achiral starting materials. To the best of our knowledge, the alkynylogous Mukaiyama aldol reaction as reported by List is the only existing method that introduces both stereogenic elements of chiral α-allenols from achiral starting materials (Scheme 3.12).[148] Under the reaction system, a variety of alknyl silyl ketene acetals were utilized as the nucleophile with chiral silylated disulfonimide Lewis acid activating the aldehydes.

[148] Tap, A.; Blond, A.; Wakchaure, V.; List, B. *Angew. Chem. Int. Ed.* **2016**, *55*, 8962.

Scheme 3.12 Catalytic Enantioselective Alkynylogous Mukaiyama Aldol Reaction.



3.2.3 Halogen-Mediated 1,4-Addition to 1,3-Enynes

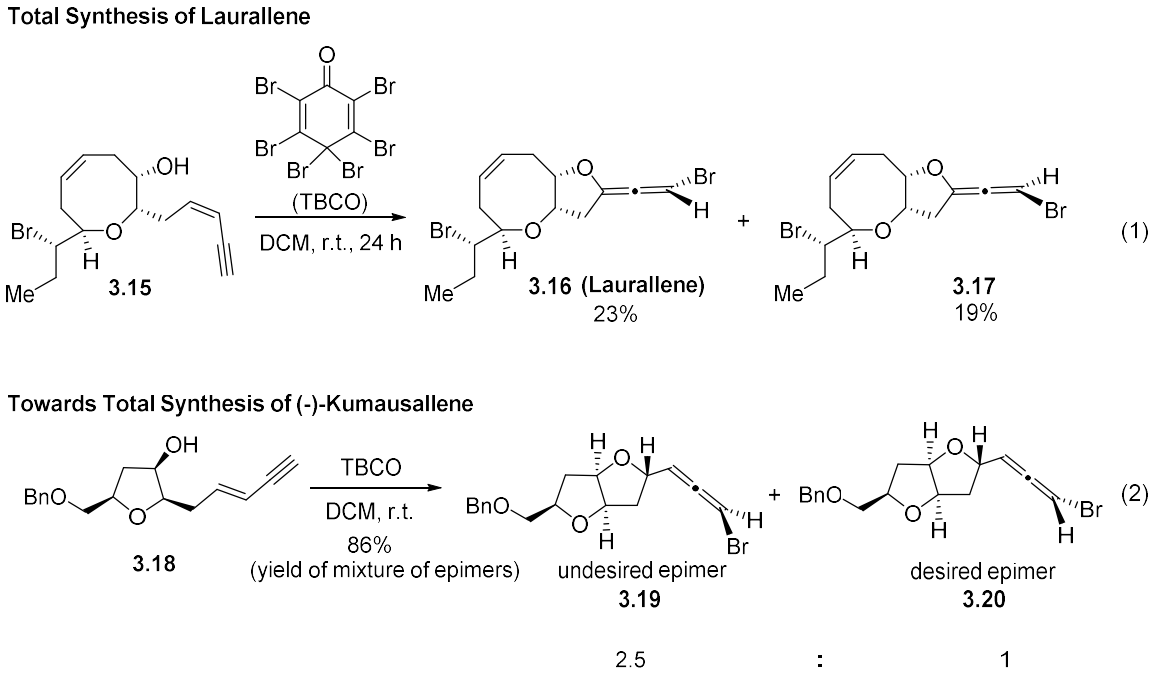
Halogen-mediated 1,4-addition across conjugated enynes has been used as a strategy to synthesize enantioenriched haloallenes, some of which are natural products themselves. An appealing feature of such a reaction is that it allows for the simultaneous formation of C-Nu bond and C-E bond during the formation of the allene moiety. A challenge associated with the 1,4-addition reaction is that it often provides a mixture of *anti* and *syn* addition products, leading to diminished diastereoselectivity.

In the report by Murai, reaction between enyne **3.15** and 2,4,6,6-tetrabromo-2,5-cyclohexadienone (TBCO) provided only a moderate yield of Laurallene **3.16** with significant mass balance consisting of its undesired epimer **3.17** (eq. 1, Scheme 3.12).[149] Later, in an advanced stage of total synthesis towards (-)-kumausallene, treatment of enyne

[149] Ishihara, J.; Shimada, Y.; Kanoh, N.; Takasugi, Y.; Fukuzawa, A.; Murai, A.*Tetrahedron* **1997**, *53*, 8371.

3.18 with TBCO afforded bromoallene with 2.5:1 diastero-ratio favoring the formation of undesired epimer **3.19** (eq. 2, Scheme 3.12).[150]

Scheme 3.13 Halogen-Mediated 1,4-Addition to 1,3-Enynes.

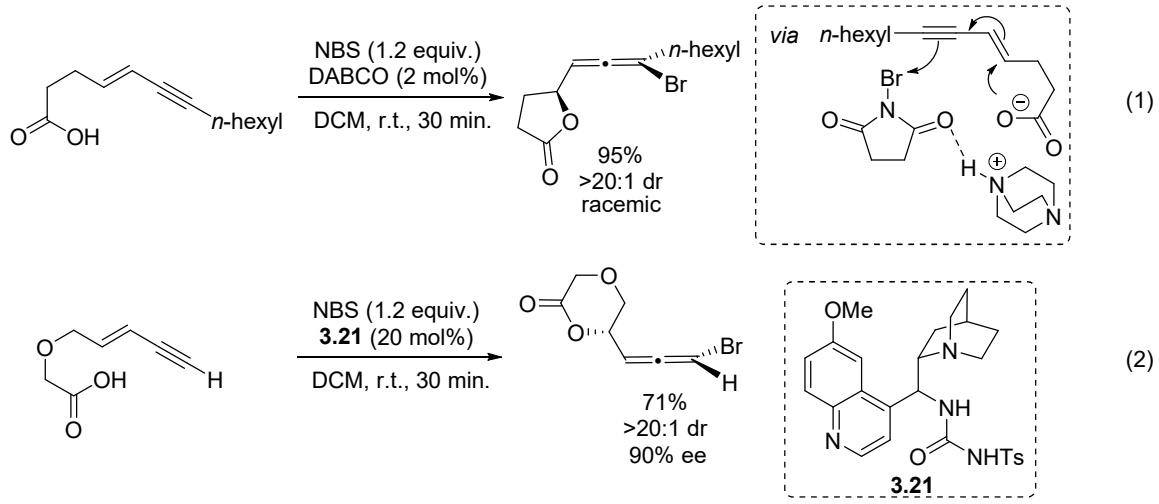


More recently, efforts have been made towards the development of 1,4-addition across 1,3-enynes with catalyst-control of both enatio- and diastereoselectivity. In 2009, Hu and co-workers reported the first highly diasterereoselective *syn* 1,4-bromolactonization of conjugated enynes with catalytic amount of DABCO (eq. 1, Scheme 3.13).[151] The *syn* selectivity was proposed to originate from the composite effect of both ion-pairing between the Bronsted acid-base pair as well as hydrogen bonding between the protonated DABCO and the carbonyl of NBS prior to bond-forming events. Later, the same group was able to achieve this reaction with enantioselectivity by utilizing a derivative of cinchonidine as the

[150] Evans, P. A.; Murthy, V. S.; Roseman, J. D.; Rheingold, A. L. *Angew. Chem. Int. Ed.* **1999**, *38*, 3175.
[151] Zhang, W.; Xu, H. D.; Xu, H.; Tang, W. *J. Am. Chem. Soc.* **2009**, *131*, 3832.

chiral bifunctional catalyst (eq. 2, Scheme 3.13).[152] Aside from carboxylate nucleophile, the reaction system was later shown to be applicable to sulfonamide as nucleophile.[153]

Scheme 3.14 Highly Diastereoselective 1,4-Addition of Conjugated Enynes.



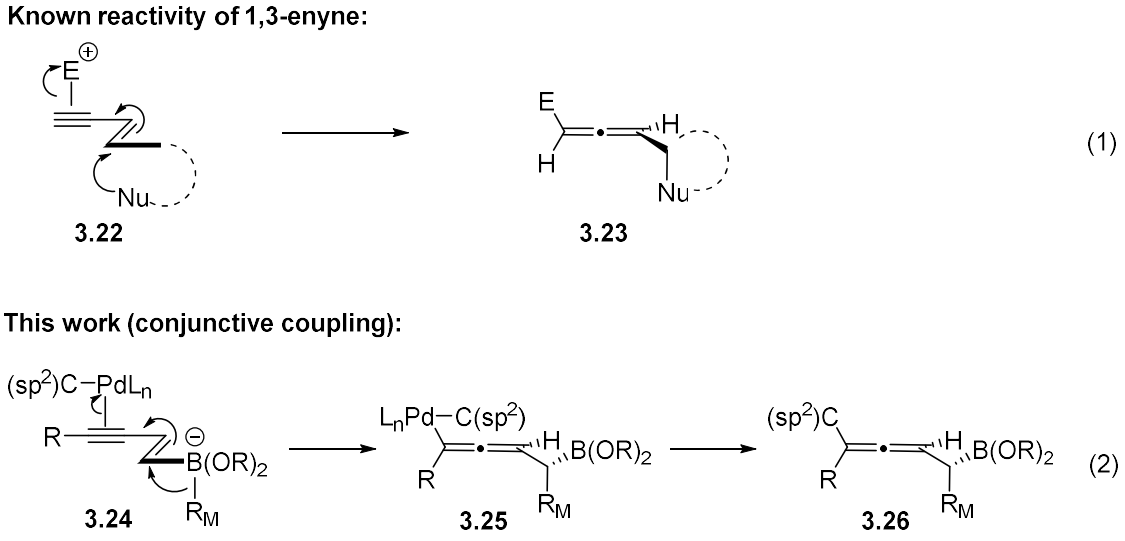
[152] Zhang, W.; Zheng, S.; Liu, N.; Werness, J.; Guzei, I.; Tang, W. *J. Am. Chem. Soc.* **2010**, *132*, 3664.
[153] Liu, N.; Werness, J.; Guzei, I.; Tang, W. *Tetrahedron* **2011**, *67*, 4385.

3.3 DEVELOPMENT OF CATALYTIC CONJUNCTIVE COUPLING OF BORYLENYNES

3.3.1 Reaction Discovery and Optimization.

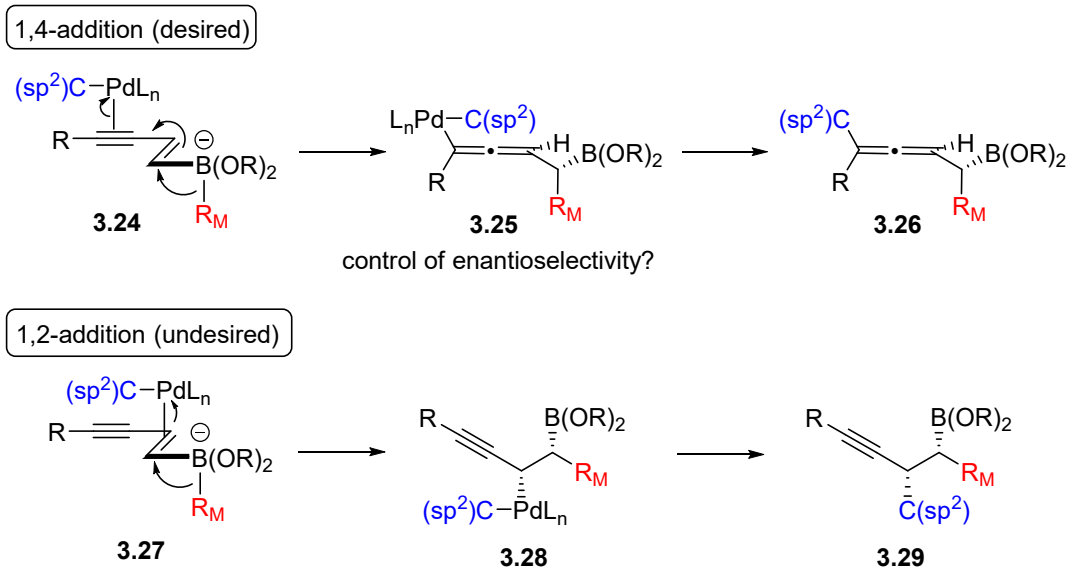
The inspirations for the chemistry in this chapter comes from the above-mentioned intramolecular 1,4-addition of nucleophiles and electrophiles across 1,3-enynes (Scheme 3.15, eq. 2). We sought to merge this known reactivity of 1,3-enynes and the concept of conjunctive coupling developed in our group to engender a new reaction manifold, in which the nucleophile would take the form of a boron "ate" complex, and a cationic Pd would be the electrophile (Scheme 3.15, eq. 2). In this proposed reaction, the Pd catalyst would selectively activate the alkyne unit of the enyne to trigger a boronate rearrangement that forms the allenyl palladium intermediate **3.25**. Upon reductive elimination, allenyl boronic ester **3.26** would then be generated.

Scheme 3.15 Inspiration of Conjunctive Cross-Coupling with Borylenynes.



In practice, selective reaction by this pathway was found to face several challenges: first, while activation of ate complex is proposed to occur by alkyne activation (**3.24**→ **3.25**), activation of the substrate might also occur through alkene association (**3.27**→**3.28**) and this can lead to the competitive formation of **3.29**, leading to lower chemoselectivity. (Scheme 3.16). Second, unlike activation of simple alkenyl boronates where the chiral Pd complex binds to a prochiral alkene substrate, the Pd complex in **3.24** is further situated from the incipient stereogenic center such that effective stereoinduction is more challenging.

Scheme 3.16 Potential Undesired 1,2-Addition Pathway.

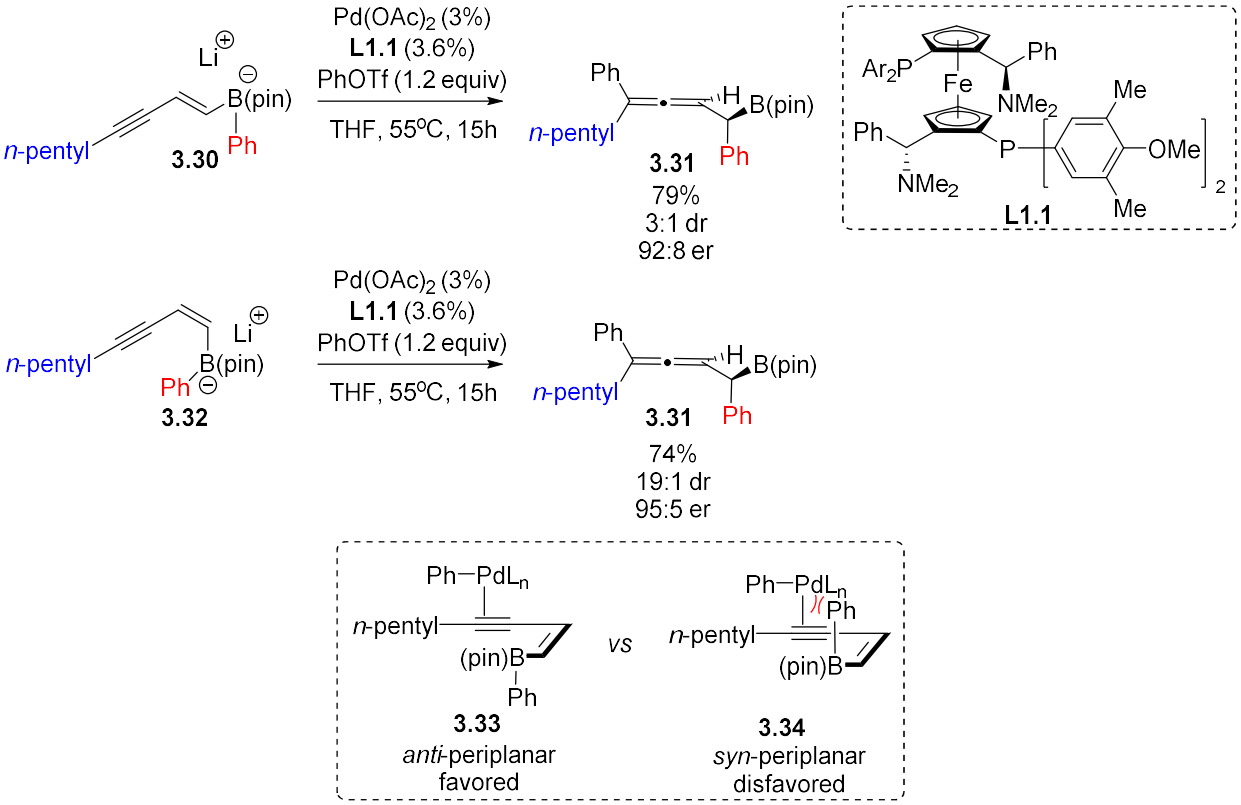


Contrary to the addition of halogen and a nucleophile across olefins, which is known to generate *anti* addition products, 1,4-addition across a 1,3-enyne is known to give a mixture of both *anti*- and *syn*-addition products as shown in the previous section. Indeed, when we commenced our investigations by subjecting *trans*-borylenyne **3.30** to our previously developed conditions for conjunctive coupling reactions, poor diastereoselectivity was

obtained (Scheme 3.17, eq. 1). A survey of various phosphine ligands and solvent systems led to no significant improvements. We reasoned that diastereoselectivity would originate from selectivity between *syn*- and *anti*-periplanar migrations. Our strategy to overcome this challenge of diastereoselectivity was to alter the configuration of the borylenyne from *trans* to *cis* configuration (Scheme 3.17, eq. 2). We reasoned the *cis* configuration would bring the four-coordinate boron center in close proximity to the alkyne-bound palladium catalyst, and that *anti*-periplanar migration should be favored in order to avoid steric repulsions between the migrating group and Pd catalyst (**3.33** *vs* **3.34**). With this idea in mind, we synthesized *cis*-borylenyne **3.32**, which could be easily accessed from 1-bromoheptyne by a stereospecific alkynylboration reaction as reported by Fu.[154] We were delighted to find that the use of *cis*-borylenyne **3.32** led to significantly improved diastereoselectivity while retaining high enantioselectivity and yield of product formation.

[154] For patent on the preparation of (Z)-borylenyne, see: Fu Yao; Yu Shanghai; Zhang Ben; Gong Tianjun. Preparation Method of Alkenyl Alkynyl Boric Acid Ester. CN108503662 (A), July 09, 2018.

Scheme 3.17 Initial Observations with Alteration in Geometry of Borylenynes.

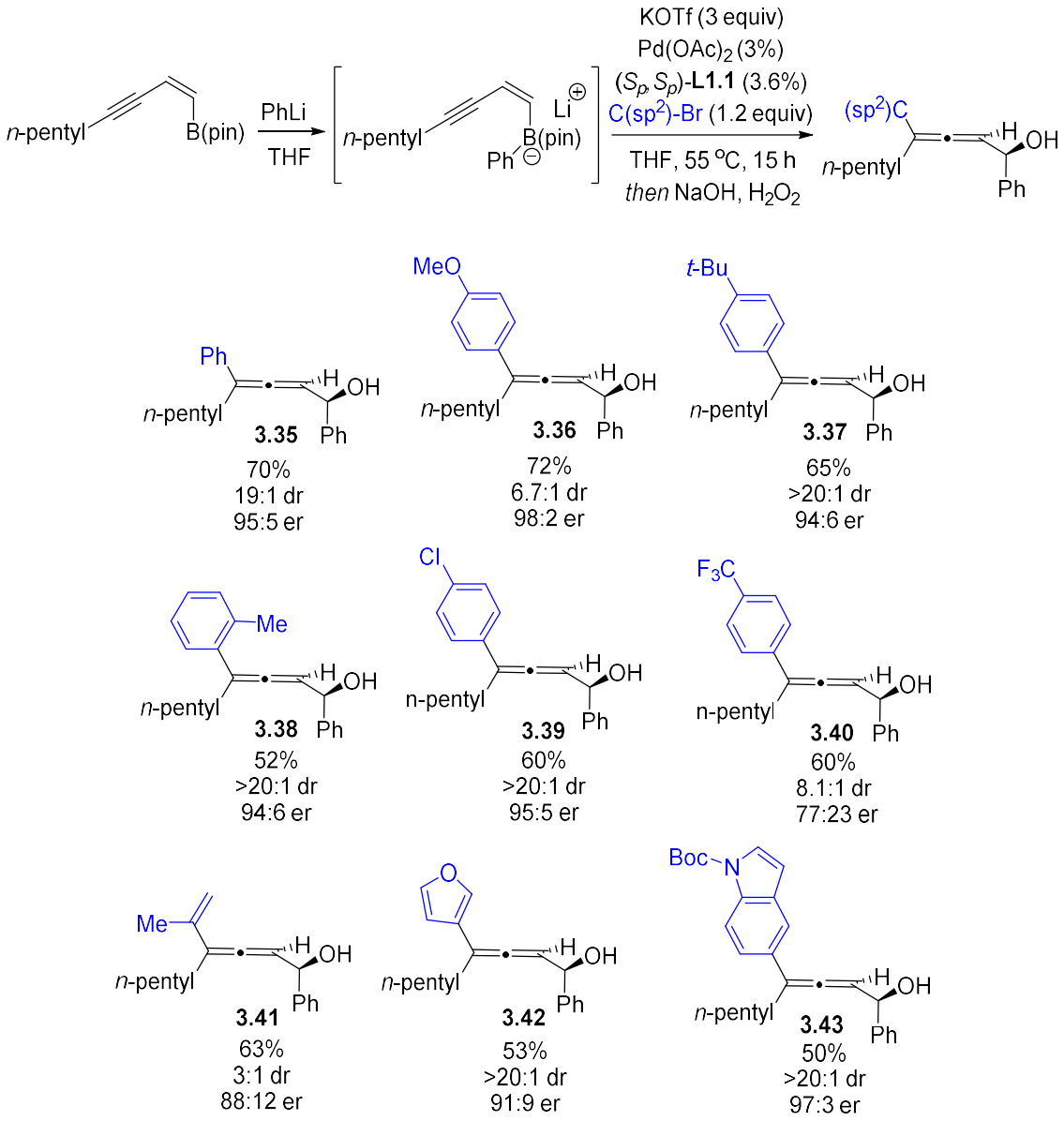


3.3.2 Substrate Scope with Aryl Migration.

With suitable reaction conditions in hand, we examined the scope of the conjunctive coupling reaction with respect to electrophiles (Scheme 3.18). Aryl bromides could be used as the electrophile in the reaction with comparable yields to when aryl triflates were used, as long as KOTf was used as an additive. The reaction is tolerant to both electron-rich (**3.36-3.38**) and electron-poor arene electrophiles (**3.39** & **3.40**), and affords the corresponding α-allenols with high enantio- and diastereoselectivity upon oxidative workup. An alkenyl electrophile with a germinal substituent afforded the desired vinyl allenol (**3.41**) with high yield albeit with diminished stereoselectivity. Heterocycles such

as furan (**3.42**) and N-Boc protected indole (**3.43**) can also be used as electrophiles and perform efficiently in the reaction.

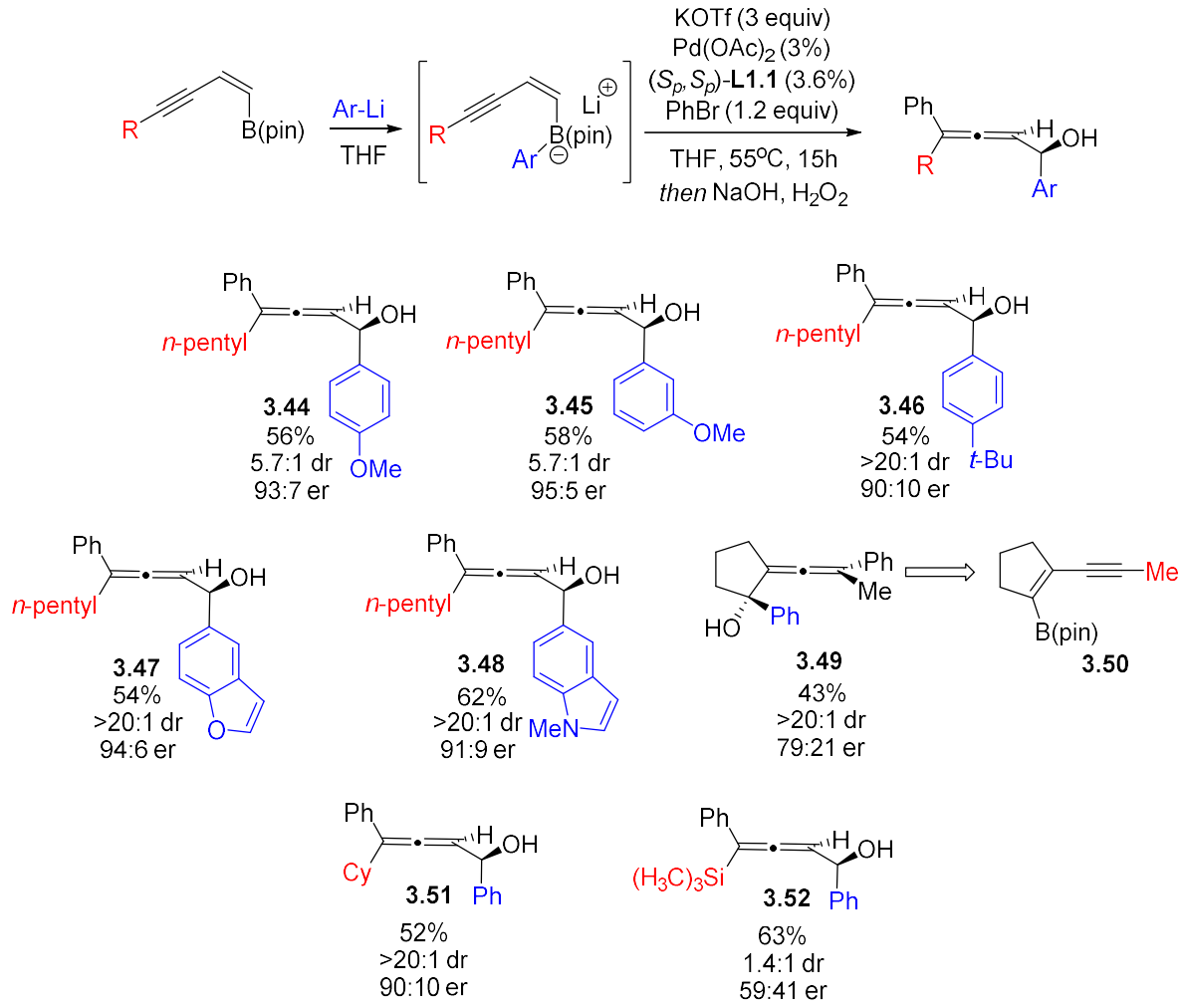
3.18 Scope of Electrophiles in Conjunctive Coupling with *cis*-Borylenynes.



With respect to aryl migrating groups, a range of electron-rich arenes (**3.44-3.46**) were shown to afford the corresponding conjunctive coupling product with high yields and stereoselectivities. Heterocycles such as benzofuran (**3.47**) and N-methylated indole (**3.48**)

can also be incorporated into the migrating group with high efficiencies. We were intrigued by the idea of employing a more hindered cyclic borylenyne such as **3.50** in the reaction. To our delight, the corresponding *tetra*-subtituted allenol **3.49** was obtained with respectable yield and high diastereoselectivity, although enantioselectivity suffers substantially. With regards to alkynyl substitutent, a sterically hindered trimethylsilyl (TMS) substituent is detrimental to both diastereo- and enantioselectivity. And in the case of less sterically hindered cyclohexyl substituent, the reaction affords products with similar yield as when primary alkyl substituent is used; however, significant mass balance was found to be comprised of homopropagylic alcohol **3.52** derived from 1,2-alkene activation (other substrates in the table shows <10% of 1,2-alkene activation product).

3.19 Scope of Migrating Groups and And Alkynyl Substituents.

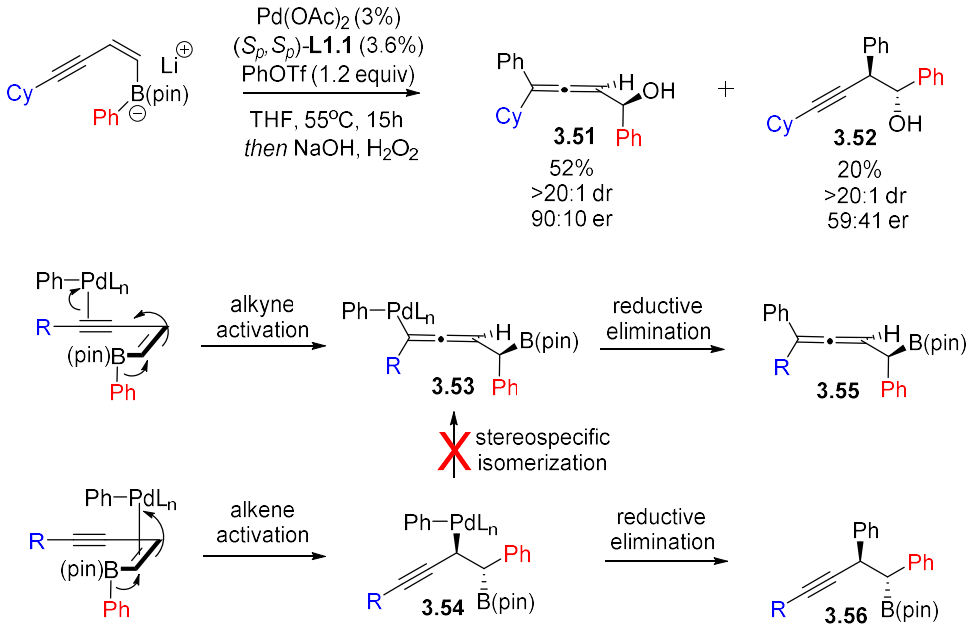


3.3.3 Origin of Chemoselectivity: 1,4- *vs* 1,2-Activation Mode.

The observation of by-product **3.52** provided us an opportunity to interrogate the proposed mechanism involving alkyne activation by Pd (Scheme 3.2.3). An alternative mechanism would proceed through a sequence of alkene activation by Pd followed by a stereospecific isomerization to the same allenylpalladium intermediate **3.53** before

reductive elimination.[155] Presumably, the formation of boronate **3.56** would proceed through the intermediacy of propagylic palladium **3.54**. The fact that the enantioenrichment of propagylic alcohol **3.52** obtained is drastically lower than that of α-allenol **3.51** suggests that the alkene-activation/ stereospecific isomerization sequence is unlikely part of the major pathway towards the formation of the desired α-borylallene **3.55**.

Scheme 3.20 1,4- *vs* 1,2-Activation Mode.



[155] For examples of isomerization of propagylic copper to allenylcopper, see: (a) Huang, Y.; del Pozo, J.; Torker, S.; Hoveyda, A. H. *J. Am. Chem. Soc*. **2018**, *140*, 2643. (b) Bayeh-Romero, L.; Buchwald, S. L. *J. Am. Chem. Soc.* **2019**, 141, 35, 13788. For detailed investigations of interconversion of propagylic platinum and allenylplatinum species, see: (c) Ogoshi, S.; Nishida, T.; Fukunishi, Y.; Tsutsumi, K.; Kurosawa, H. J. Organomet. Chem. **2001**, 620, 190. (d) Ogoshi, S.; Fukunishi, Y.; Tsutsumi, K.; Kurosawa, H. Inorganica. Chim. Acta. **1997**, 265, 9, and references herein.

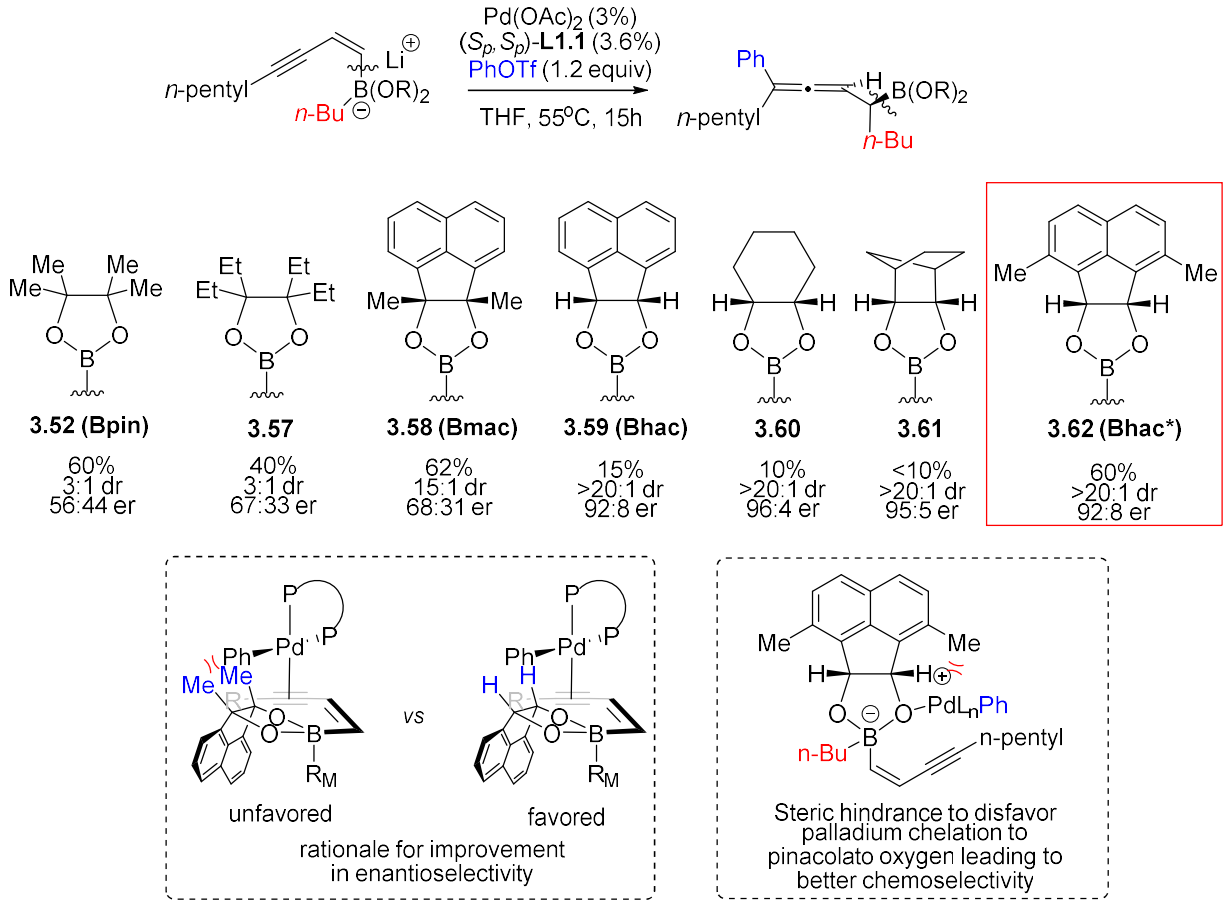
3.3.4 Optimization Studies and Substrate Scope of Alkyl Migration.

Surprisingly, the optimal conditions for aryl migration was found to be suboptimal for alkyl migration in terms of both enantio- and diastereoselectivity (Scheme 3.20). In an attempt to optimize the reaction conditions, we looked into using various chiral phosphine ligands but no significant improvements were observed. Reasoning that the achiral boron ligand could engage in steric interactions with the palladium catalyst and have an effect on stereoselectivity of the process, we chose to focus our attention on boron ligand. Interestingly, we observed a systematic difference in stereoselectivity between tertiary alcohol (**3.52**, **3.57**, **3.58**) and secondary alcohol-derived boronic esters (**3.59**-**3.62**). While it remains to be studied more thoroughly, we believe that the higher enantioselectivity observed with secondary alcohol-derived boronic ester can be due to the mitigation of a steric penalty between the boron ligand and the electrophile-derived ligand on square planar Pd (see subtext of Scheme 3.20). The poor yields observed with boron ligands **3.59**-**3.61** were found to be due to a competitive direct transmetallation reaction pathway leading to Suzuki-Miyaura coupling products. This direct transmetallation pathway has previously been observed in a similar system and it's thought to proceed *via* a pre-transmetallation complex involving chelation of palladium to the oxygen atom of boronic ester.[156] To prevent this, we installed an ortho-substituent on the naphthalene backbone of the ligand (Bhac) for the reason that it could impose steric penalty for palladium chelation to the oxygen atom. To our delight, with the newly designed boron ligand **3.62** (termed 'Bhac*'),

[156] (a) Thomas, A. A.; Denmark, S. E. *Science* **2016**, *352*, 329. (b) Thomas, A. A.; Wang, H.; Zahrt, A. F.; Denmark, S. E. *J. Am. Chem. Soc.* **2017**, *139*, 3805. (c) Thomas, A. A.; Zahrt, A. F.; Delaney, C. P.; Denmark, S. E. *J. Am. Chem. Soc.* **2018**, *140*, 4401.

we obtained the desired product with high yields along with high stereoselectivities. Intriguingly, the use of Bhac* ligand is not suitable for aryl migration as only trace amounts of conjunctive coupling product was observed. We speculate this difference may be due to a ground state stabilization effect of π-π stacking interaction between aryl migrating group and the naphthalene backbone of the Bhac* ligand, leading to an increased kinetic barrier for boronate rearrangement.

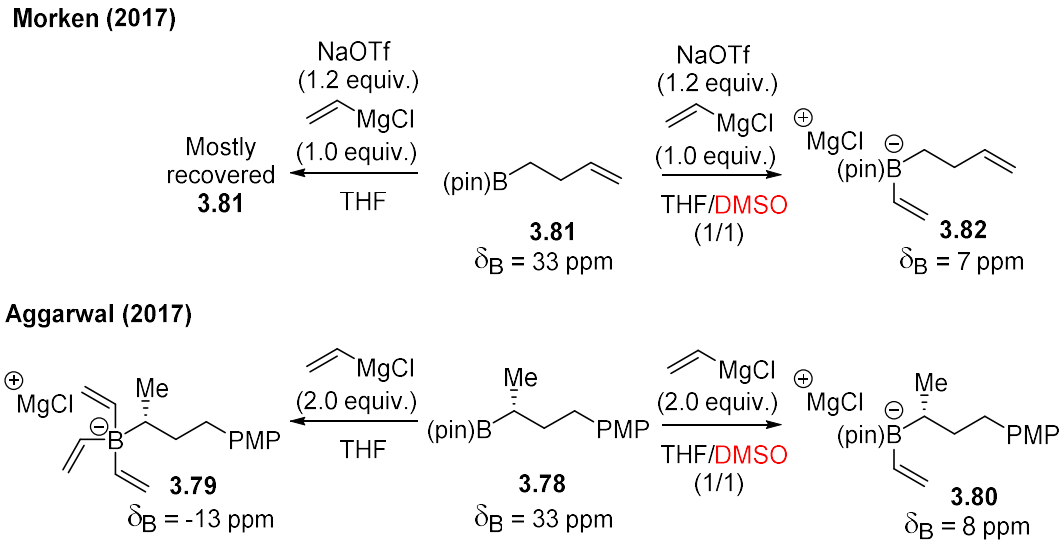
Scheme 3.20 Boron Ligand Optimization for Alkyl Migration.



We recognized the limited number of commercially available alkylorganolithium reagents and the impracticability associated with their preparations on a laboratory scale. Therefore, to expand the scope of alkyl migrating groups, we investigated the use of the

more easily accessible alkyl Grignard reagents as the organometallic reagent in our reaction. Previous studies by both our group[157] as well as Aggarwal[158] demonstrated that addition of DMSO is essential for the stabilization of boron "ate" complex derived from Grignard reagent (Scheme 3.21). In the former case, NaOTf acts as a Lewis base to enhance the nucleophilicity of the Grignard reagent.

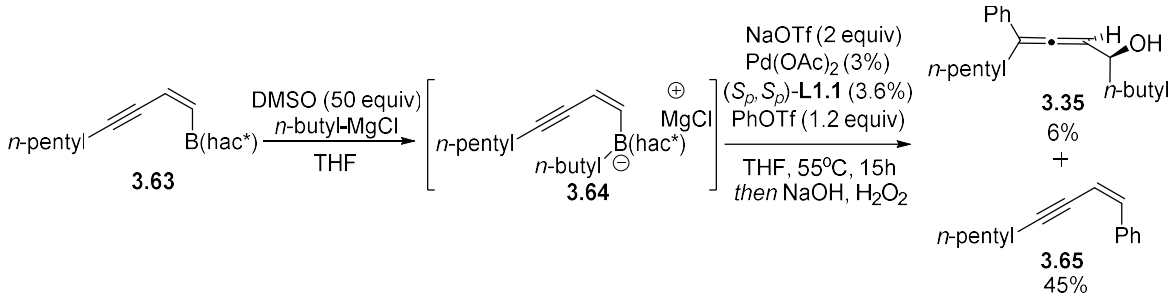
Scheme 3.21 Formation of Boron "Ate" Complex Derived from Grignard Reagents.



In our initial investigations, we added solvent quantity of DMSO (50 equivalents) prior to boron "ate" complex formation (Scheme 3.22). However, with DMSO as solvent, poor yield of desired product **3.35** was obtained with a mixture of by-products containing mostly Suzuki-Miyaura coupling product **3.65**.

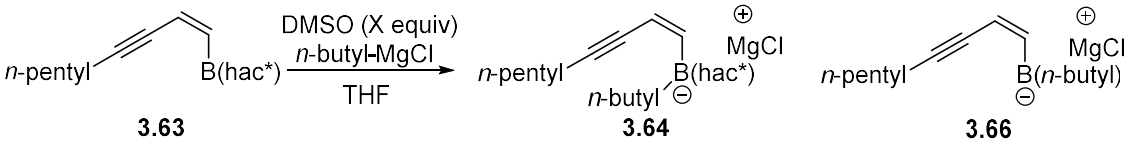
[157] Lovinger, G. J.; Aparece, M. D.; Morken, J. P. *J. Am. Chem. Soc.* **2017**, *139*, 3153.
[158] Armstrong, R.; Niwetmarin, W.; Aggarwal, V. *Org. Lett.* **2017**, *19*, 276.

Scheme 3.22 Initial investigation of Grignard Reagent in Conjunctive Coupling.

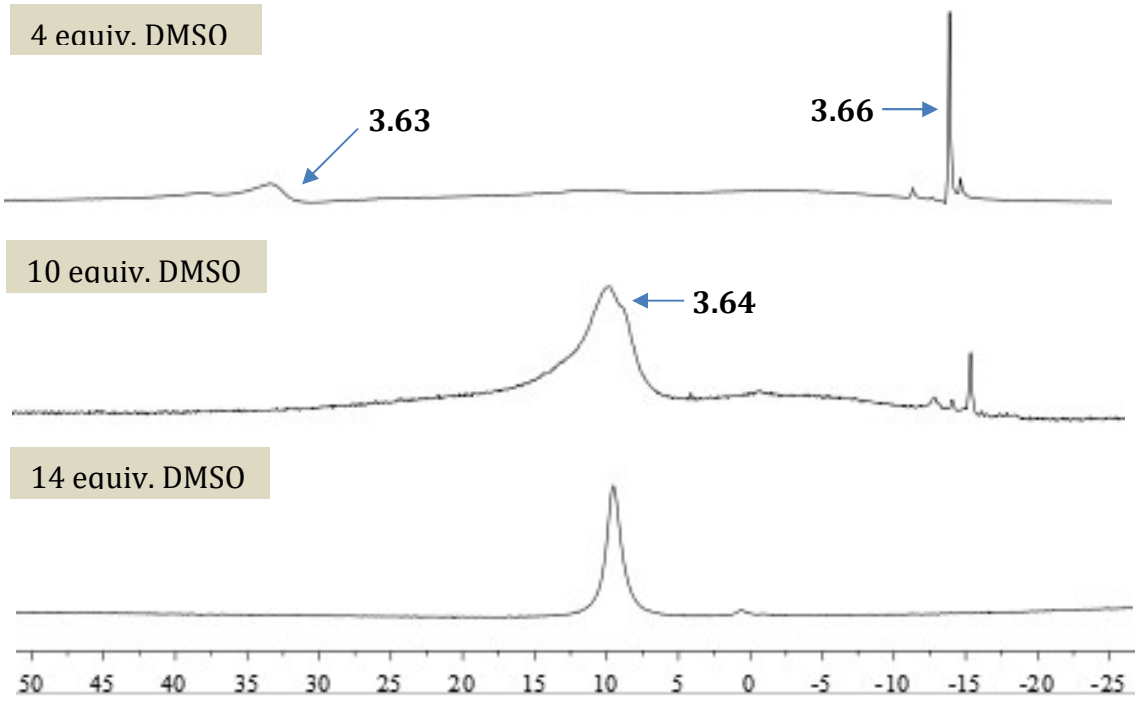


A series of ^{11}B NMR experiments were conducted to test the minimal amount of DMSO required for clean formation of boron "ate" complex (Scheme 3.23). With 3 equivalents of DMSO, no desired boron "ate" complex **3.64** was formed, and only over-addition species **3.66** and unreacted borylenyne **3.63** observed. When the amount of DMSO is increased to ten equivalents, the desired boron "ate" complex **3.35** was the major species with only trace amount of **3.66**. To our delight, 14 equivalents of DMSO cleanly afforded the desired boron "ate" complex.

Scheme 3.23 ^{11}B NMR Studies of Boron "Ate" Complex Formation.

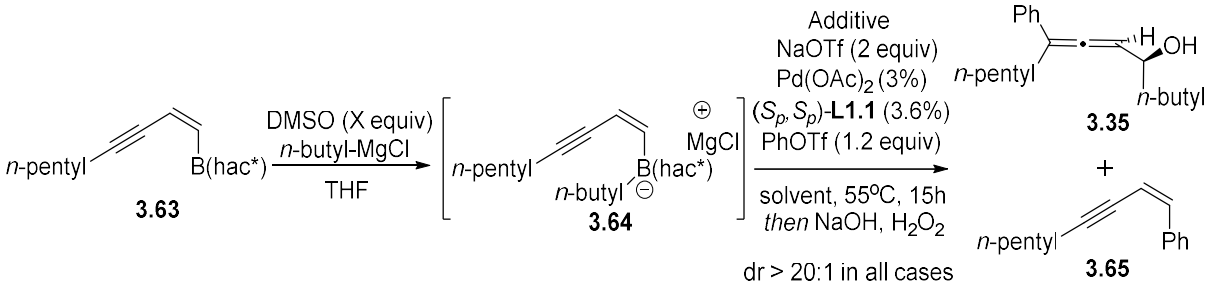


3.63 3.64 3.66



Subsequent to the ^{11}B-NMR studies, we carried out the reaction with 14 equivalents of DMSO and obtained 53% isolated yield of the desired product (Scheme 3.21, entry 4). Further optimization efforts showed that the use of THF/toluene co-solvent system and CsF additive can further enhance the chemoselectivity to afford the conjunctive coupling product in 65% yield (Scheme 3.21, entry 6).

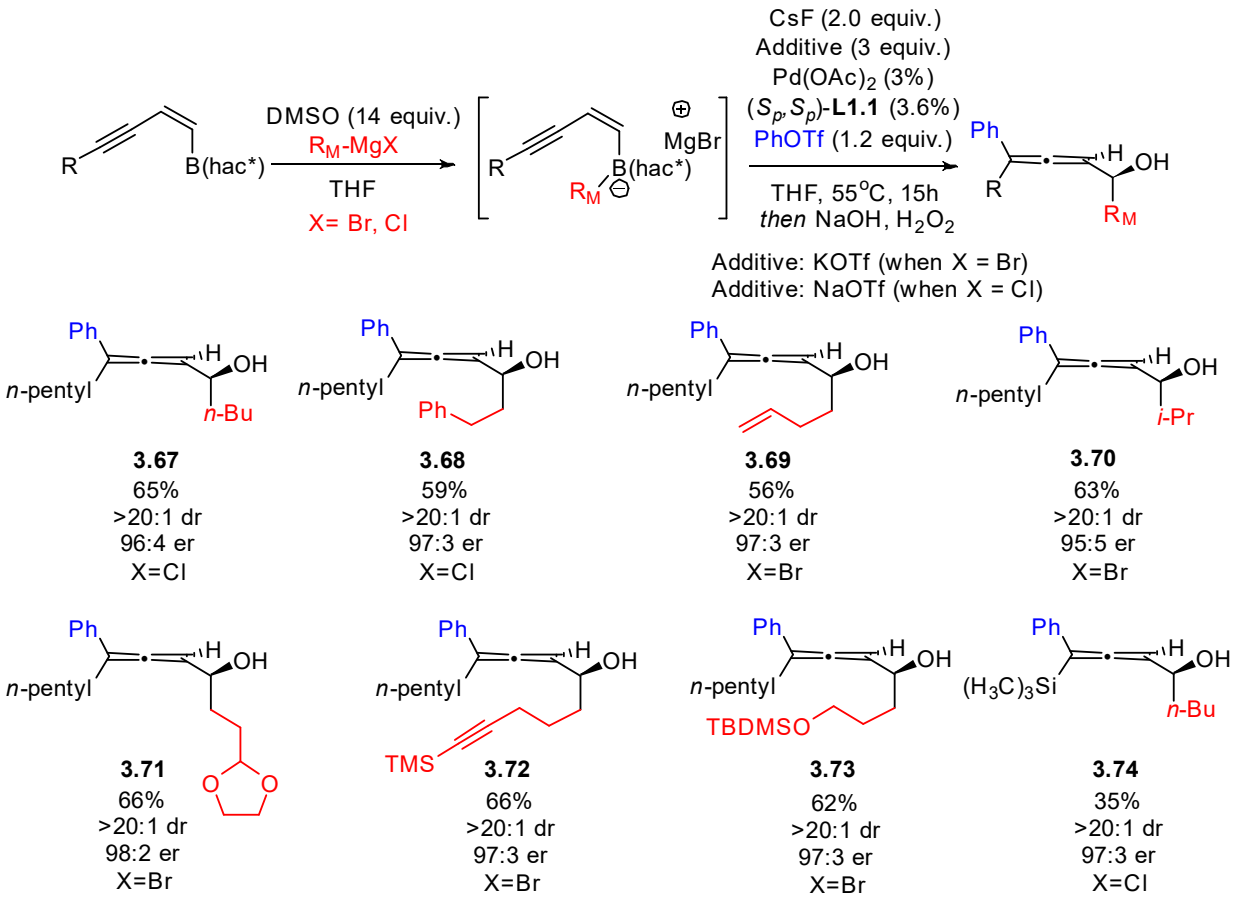
Scheme 3.24 Optimization of Alkyl Migration with the Use of Grignard Reagent.



entry	X (equiv.)	solvent	additive	**3.35** (%)	**3.65** (%)	er
1	50	THF	none	6	45	95:5
2	28	THF	none	23	30	95:5
3	10	THF	none	50	15	96:4
4	14	THF	none	53	17	95:5
5	14	THF	CsF (2 equiv.)	60	10	96:4
6	14	THF/Toluene 1/1	CsF (2 equiv.)	65	7	96:4

Under the new conditions for alkyl migration using Grignard reagents, migrating groups with a variety of functional groups perform well in the conjunctive coupling reaction (Scheme 3.25). Both linear and α-branched migrating groups function smoothly in the reaction. Functional groups such as alkene (**3.69**), acetal (**3.71**), alkynyl-TMS (**3.72**), and silyl ether (**3.73**) are all tolerated in the reaction giving high yields and stereoselectivities. The synthetically useful allenylsilane compound **3.74** can also be synthesized from the corresponding TMS-enyne starting material with high stereoselectivity albeit with diminished yields.

Scheme 3.25 Substrate Scope for Alkyl Migration with Grignard Reagents.



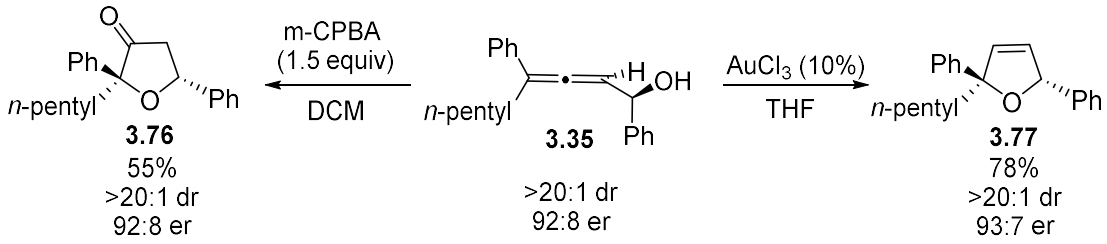
3.3.5 Synthetic Utility of α-Allenols.

To demonstrate the utility of the obtained α-allenols in oxygenated heterocycle synthesis, we first performed a $AuCl_3$-catalyzed cyclization reaction to afford 2,5-dihydrofuran compound **3.77** (Scheme 3.26).[159] In addition, an interesting cascade reaction involving a stereoselective epoxidation followed by intramolecular epoxide opening to

[159] Hoffmann-Röder, A.; Krause, N. *Org. Lett.* **2001**, 3, 2537-2538.

afford tetrahydrofuranone **3.76** was revealed when we treated α-allenol **3.35** with m-CPBA.[160] In both cases, the reactions proceed with transfer of axial chirality to central chirality providing products with high diastereo- and enantioenrichment.

Scheme 3.26 Synthetic Utility of α-Allenols.



3.3.6 Conclusion.

In conclusion, we have reported a catalytic conjunctive cross-coupling reaction that allows for the enantio- and diastereoselective synthesis of α-borylallenes from simple achiral borylenynes. Alkyl- and aryl migrations require different boron ligand design for the realization of both high yield and stereoselectivities. In cases Grignard reagent is the desired organometallic reagent of choice, addition of the right amount of DMSO was found to be crucial for high reactivity. Preliminary experimental evidence points to a mechanism involving the activation of the alkyne by Pd, followed by reductive elimination. The α-allenols obtained upon oxidative workup have been shown to undergo further transformations to biologically relevant oxygenated heterocycles.

[160] For related chemistry of allene oxide, see a) Chan, T.; Ong, B. *Tetrahedron* **1980**, 36, 2269.

3.4 Experimental Section

3.4.1 General Information

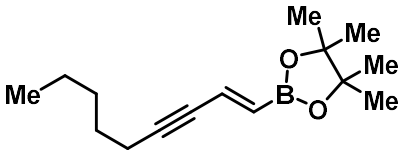
^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.24 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), Varian Gemini-600 (150 MHz) or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). Chemical shifts are reported in ppm using phosphoric acid as the external standard (H_3PO_4: 0.0 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) spectrometer. ^{19}F NMR spectra were recorded on a Varian Gemini-500 (470 MHz) spectrometer. Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART+) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was

performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol or phosphomolybdic acid, and cerium(IV) sulfate in ethanol with sulfuric acid (Seebach).

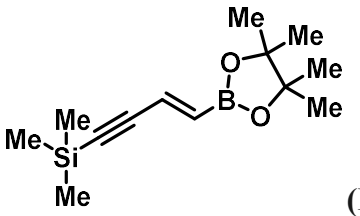
Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol as the modifier.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Palladium (II) acetate, (*Sp*,*Sp*)-, (*Rp*,*Rp*)-**L1.1**, and 1,1'- Bis(dicyclohexylphosphino)ferrocene were purchased from Strem Chemicals, Inc. and used without further purification. Phenyl trifluoromethanesulfonate and cesium fluoride were purchased from Oakwood Chemicals and used without further purification. 3,8-dimethylacenaphthylene-1,2-dione was generously donated by Professor Jay Siegel. Potassium trifluoromethanesulfonate was purchased from Oakwood Chemicals and dried by heating (100 ^{o}C) under vacuum over P_2O_5 overnight.

3.4.2 Procedure for Preparation of Borylenynes



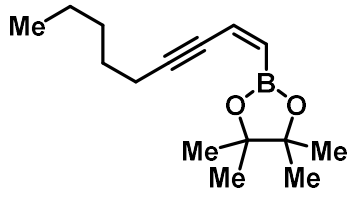
(E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (S-3.1). The title compound was prepared according to the procedure reported in the literature.[161] All spectral data was in accordance with previously published results.[36]



(E)-trimethyl(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yn-1-yl)silane (S-3.2). The title compound was prepared according to the procedure reported in the literature.[36]

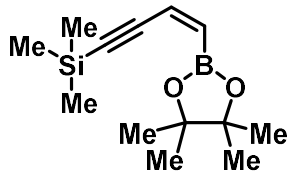
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 – 6.35 (m, 1H), 6.05 (dd, *J* = 18.5, 1.3 Hz, 1H), 1.33 – 1.15 (m, 12H), 0.19 (d, *J* = 1.3 Hz, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 129.3, 104.9, 98.8, 83.7, 24.8, -0.1. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 29.9. **IR** (neat) ν_{max} 2979 (w), 2156 (w), 1593 (m), 1458 (w), 1371 (s) ,1271 (m), 1250 (m), 1166 (s), 1140 (w) cm^{-1}. **HRMS** (DART) for $C_{13}H_{24}BO_2Si$ $[M+H]^+$: Calc'd: 251.1633, found: 251.1638.

[161] Fu Yao; Yu Shanghai; Zhang Ben; Gong Tianjun. Preparation Method of Alkenyl Alkynyl Boric Acid Ester. CN108503662 (A), July 09, 2018.

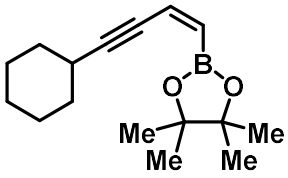


(Z)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (S-3.3). The title compound was prepared according to the procedure reported in the patent literature.[36]

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.27 (d, *J* = 14.1 Hz, 1H), 5.75 (dd, *J* = 14.1, 1.6 Hz, 1H), 2.35 (dt, *J* = 7.2, 1.6 Hz, 2H), 1.59 – 1.54 (m, 2H), 1.44 – 1.38 (m, 2H), 1.37 – 1.26 (m, 14H), 0.91 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 128.5, 96.3, 83.3, 80.1, 31.1, 28.3, 24.9, 22.3, 19.7, 14.0. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 29.7. **IR** (neat) ν_{max} 2957 (s), 2931 (s), 2859 (s), 2207 (w), 1589 (m), 1420 (s), 1257 (s), 1143 (s), 967 (w), 670 (w) cm^{-1}. **HRMS** (DART) for $C_{15}H_{26}BO_2$ $[M+H]^+$: Calc'd: 249.2020, found: 249.2029.

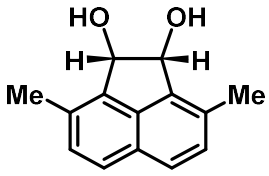


(Z)-trimethyl(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yn-1-yl)silane (S-3.4). The title compound was prepared according to the procedure reported in the patent literature.[1]All spectral data was in accordance with previously published results.[36]



(Z)-2-(4-cyclohexylbut-1-en-3-yn-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (S-3.5). The title compound was prepared according to the procedure reported in the patent literature.[36]

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.29 (d, *J* = 14.1 Hz, 1H), 5.74 (dt, *J* = 14.1, 0.9 Hz, 1H), 2.68-2.51 (m, 1H), 1.81-1.72 (m, 4H), 1.60-1.48 (m, 4H), 1.42 – 1.17 (m, 14H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 128.77, 100.28, 83.29, 80.25, 32.39, 29.87, 26.13, 24.96, 24.64. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 29.9. **IR** (neat) ν_{max} 2977 (s), 2928 (s), 2853 (s),2208 (w), 1588 (m), 1370 (s), 1257 (s), 1142 (s), 858 (w), 578 (w) cm^{-1}. **HRMS** (DART) for $C_{16}H_{26}BO_2$ $[M+H]^+$: Calc'd: 261.2020, found: 261.2020.



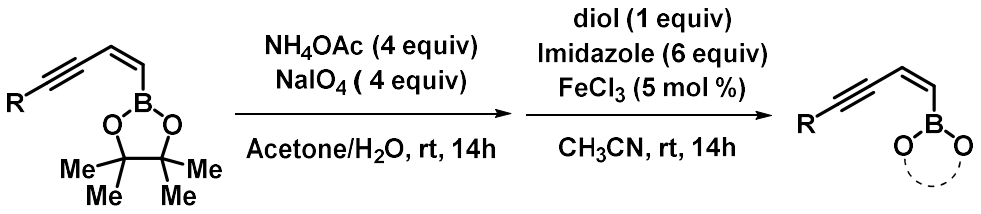
***cis*-3,8-dimethyl-1,2-dihydroacenaphthylene-1,2-diol (S-3.6).** The title compound was prepared according to a modified literature procedure synthesizing a related compound.[162] To a round bottom flask was added 3,8-dimethylacenaphthylene-1,2-dione[163] (5.0 g, 23.8 mmol, 1.0 equiv.) and MeOH (50 mL) followed by the addition of KOH (91.7 mg, 1.19 mmol, 0.05 equiv.). The reaction mixture was cooled to 0 ºC and $NaBH_4$ (1.80 g, 47.6 mmol, 2.0 equiv.) was added in one portion. After being stirred at the same temperature for 15 minutes, the mixture was allowed to warm up to room temperature at which point it was poured into aq. 2M HCl solution (100mL) slowly. The resulting solids

[162] Merz, A.; Dietl, F.; Tomahogh, R. *Tetrahedron* **1984**, *40*, 665.
[163] Butterfield, A. M.; Gilomen, B.; Sigel, J. S. *Org. Process Res. Dev.* **2012**, *16*, 664.

were filtered and rinsed with toluene. The crude product was re-crystallized with toluene by heating the solution to dissolve the solid and letting it slowly cool down to room temperature.

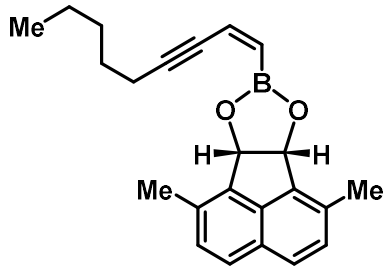
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 5.48 (s, 2H), 2.60 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 137.1, 132.5, 130.1, 129.2, 128.4, 125.8, 81.2, 18.2. **IR** (neat) ν_{max} 3385 (s), 3268 (m), 1743 (w), 1479 (s), 1373 (m), 1095 (m), 1084 (m), 832 (s) cm^{-1}. **HRMS** (DART) for $C_{14}H_{14}O_2$ $[M+H]^+$: Calc'd: 214.0988, found: 214.0985.

General Procedure for the Preparations of cis-Borylenynes with Various Boron Ligands



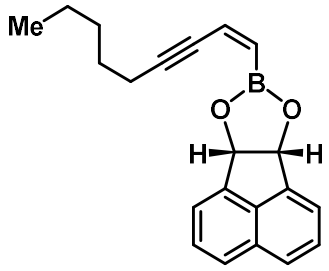
In a round bottom flask was added the corresponding (pinacolato)borylenyne (10 mmol, 1.0 equiv.), NH_4OAC (40 mmol, 4.0 equiv.), and $NaIO_4$ (40 mmol, 4.0 equiv.) in acetone/H_2O mixture (1:1, 50mL). The reaction mixture was allowed to stir vigorously for 14 hours. The reaction mixture was extracted with EtOAc (70mL) and the organic phase was washed with water (2 x 50mL), dried with Na_2SO_4, filtered, and concentrated with rotavap. The residue containing the corresponding boronic acid was then dissolved in CH_3CN (30 mL) in another round bottom flask, followed by sequential addition of the corresponding diol (10 mmol, 1.0 equiv.), imidazole (60 mmol, 6.0 equiv.) and $FeCl_3$ (0.5 mmol, 0.05 equiv.) at room temperature. The reaction mixture was allowed to stir at room

temperature for 14 hours. The crude mixture was then filtered through a plug of silica with Et_2O as the eluent. The crude compound was then purified by column chromatography.



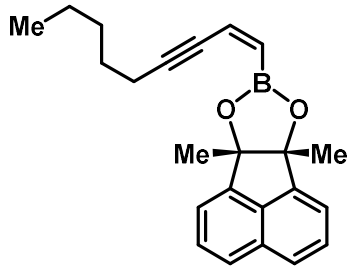
1,6-dimethyl-8-((Z)-non-1-en-3-yn-1-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (S-3.7). The reaction was performed according to the general procedure above with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (3.4 g, 10 mmol), NH_4OAc (3.08 g, 40 mmol), $NaIO_4$ (8.56 g, 40 mmol) in acetone/H_2O mixture (1:1, 50mL), *cis*-3,8-dimethyl-1,2-dihydroacenaphthylene-1,2-diol (**S-3.6**) (2.14 g, 10 mmol), imidazole (2.72 g, 60 mmol), and $FeCl_3$ (81.1 mg, 0.5 mmol) in CH_3CN (30 mL). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a white solid (1.45 g, 42% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.3 Hz, 2H), 6.30 (d, J = 14.1 Hz 1H), 6.10 (s, 2H), , 5.76 (d, J = 14.1 Hz, 1H), 2.42-2.30 (m, 2H), 1.61-1.48 (m, 2H), 1.44– 1.26 (m, 4H), 0.93 (t, J = 7.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 137.7, 137.2, 132.4, 129.99, 129.97, 129.7, 128.3, 125.6, 97.6, 82.1, 80.1, 31.4, 28.5, 22.4, 19.9, 18.2, 14.1. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 29.5. **IR** (neat) ν_{max} 2927 (s), 2860 (m), 1752 (s), 1490 (m), 1447 (m), 1376 (w), 1217 (m), 1105 (s), 758 (s), 702 (s) cm^{-1}. **HRMS** (DART) for $C_{23}H_{26}BO_2$ $[M+H]^+$: Calc'd: 345.2020, found: 345.2039.



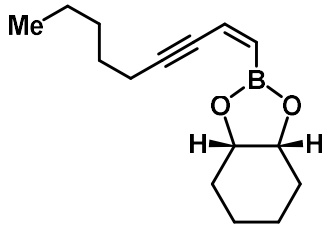
(6b,9a)-8-((Z)-non-1-en-3-yn-1-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (S-3.8). The reaction was performed according to the general procedure above with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (3.4 g, 10 mmol), NH_4OAc (3.08 g, 40 mmol), $NaIO_4$ (8.56 g, 40 mmol) in acetone/H_2O mixture (1:1, 50mL), *cis*-1,2-dihydroacenaphthylene-1,2-diol[2] (**S-3.5**) (1.86 g, 10 mmol), imidazole (2.72 g, 60 mmol), and $FeCl_3$ (81.1 mg, 0.5 mmol) in CH_3CN (30 mL). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a white solid (1.58 g, 50% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 8.1, 2.1 Hz, 2H), 7.69 – 7.55 (m, 4H), 6.30 (d, J = 14.1 Hz 1H), 6.19 (d, J = 2.1 Hz, 2H), 5.74 (dd, J = 14.1, 2.2 Hz, 1H), 2.40 – 2.30 (m, 2H), 1.63 – 1.52 (m, 2H), 1.50 – 1.33 (m, 4H), 0.94 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.0, 137.0, 131.6, 129.8, 128.5, 125.7, 122.0, 97.7, 82.8, 80.1, 31.2, 28.4, 22.4, 19.9, 14.2. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 29.5. **IR** (neat) ν_{max} 2931 (m), 2858 (w), 1589 (m), 1496 (w), 1418 (m), 1364 (m), 1317 (m) ,1252 (m) ,1047 (m) ,983 (w), 823 (m), 643 (w), 548 (w) cm^{-1}. **HRMS** (DART) for $C_{21}H_{22}BO_2$ $[M+H]^+$: Calc'd: 317.1707, found: 317.1702.



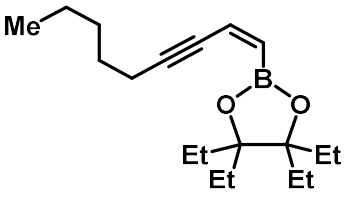
(6b,9a)-6b,9a-dimethyl-8-((Z)-non-1-en-3-yn-1-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (S-3.9). The reaction was performed according to the general procedure above with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (3.4 g, 10 mmol), NH_4OAc (3.08 g, 40 mmol), $NaIO_4$ (8.56 g, 40 mmol) in acetone/H_2O mixture (1:1, 50mL), *cis*-1,2-dimethyl-1,2-dihydroacenaphthylene-1,2-diol (**S-3.5**) (2.14 g, 10 mmol), imidazole (2.72 g, 60 mmol), and $FeCl_3$ (81.1 mg, 0.5 mmol) in CH_3CN (30 mL). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a yellow solid (1.10 g, 32% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, J = 8.1, 0.9 Hz, 2H), 7.63 – 7.54 (m, 4H), 6.21 (dt, J = 14.2, 2.2 Hz, 1H), 5.70 (d, J = 14.2 Hz, 1H), 2.31 (dt, J = 7.2, 2.2 Hz, 2H), 1.83 (d, J = 1.1 Hz, 6H), 1.60 – 1.54 (m, 2H), 1.45 – 1.36 (m, 4H), 0.96 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 144.9, 134.9, 131.5, 128.9, 128.5, 125.3, 119.6, 97.0, 91.9, 80.1, 31.3, 28.4, 22.4, 22.2, 19.8, 14.2. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 29.5. **IR** (neat) ν_{max} 2955 (w),2929 (m), 2857 (w), 2205 (w), 1588 (m), 1498 (w), 1457 (w), 1431 (s), 1372 (m) ,1326 (m) ,1290 (m) ,1210 (w), 825 (s), 598 (w) cm^{-1}. **HRMS** (DART) for $C_{23}H_{26}BO_2$ $[M+H]^+$: Calc'd: 345.2020, found: 345.2025.



(3a,7a)-2-((Z)-non-1-en-3-yn-1-yl)hexahydrobenzo[d][1,3,2]dioxaborole (S-3.10). The reaction was performed according to the general procedure above with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (3.4 g, 10 mmol), NH_4OAc (3.08 g, 40 mmol), $NaIO_4$ (8.56 g, 40 mmol) in acetone/H_2O mixture (1:1, 50mL), *cis*-1,2-cyclohexanediol (1.16 g, 10 mmol), imidazole (2.72 g, 60 mmol), and $FeCl_3$ (81.1 mg, 0.5 mmol) in CH_3CN (30 mL). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a yellow solid (738 g, 30% yield).

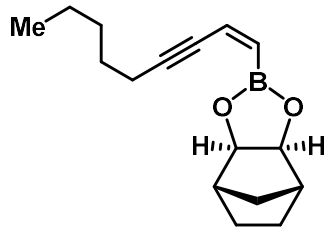
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.29 (dd, J = 14.2, 2.4 Hz, 1H), 5.73 (d, J = 14.2 Hz, 1H), 4.91 – 4.85 (m, 2H), 2.35 (dt, J = 7.1, 2.4 Hz, 2H), 1.99 – 1.90 (m, 2H), 1.74 – 1.51 (m, 6H), 1.46 – 1.26 (m, 4H), 0.90 (t, J = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 129.1, 97.1, 82.4, 80.2, 34.8, 31.2, 28.5, 22.4, 21.6, 19.9, 14.2. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 29.9. **IR** (neat) ν_{max} 2956 (w), 2858 (w), 2204 (w), 1590 (m), 1465 (w), 1435 (m), 1419 (s), 1327 (w), 1283 (s) ,1229 (s) ,1100 (m), 927 (w), 800 (m), 660 (w) cm^{-1}. **HRMS** (DART) for $C_{15}H_{24}BO_2$ $[M+H]^+$: Calc'd: 247.1869, found: 247.1875.



(Z)-4,4,5,5-tetraethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (S-3.11). The reaction was performed according to the general procedure

above with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (3.4 g, 10 mmol), NH_4OAc (3.08 g, 40 mmol), $NaIO_4$ (8.56 g, 40 mmol) in acetone/H_2O mixture (1:1, 50mL), 3,4-diethylhexane-3,4-diol (1.74 g, 10 mmol), imidazole (2.72 g, 60 mmol), and $FeCl_3$ (81.1 mg, 0.5 mmol) in CH_3CN (30 mL). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (1.98 g, 65% yield).

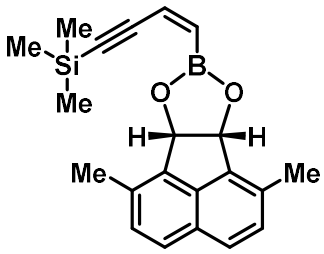
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.28 (dt, J = 14.2, 2.3 Hz, 1H), 5.75 (d, J = 14.2 Hz, 1H), 2.33 (dt, J = 7.2, 2.3 Hz, 2H), 1.78 – 1.61 (m, 8H), 1.58 – 1.51 (m, 2H), 1.44 – 1.27 (m, 4H), 0.91 (m, 14H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 128.8, 96.7, 88.5, 80.3, 31.3, 28.5, 26.5, 22.4, 19.9, 14.1, 9.0. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 29.4. **IR** (neat) ν_{max} 2934 (w), 2887 (w), 1589 (m), 1435 (m), 1419 (w), 1382 (w), 1351 (w), 1257 (s), 1208 (w), 929 (m), 772 (m), 662 (w) cm^{-1}. **HRMS** (DART) for $C_{19}H_{34}BO_2$ $[M+H]^+$: Calc'd: 305.2646, found: 305.2642.



(3a,7a)-2-((Z)-non-1-en-3-yn-1-yl)hexahydro-4,7-methanobenzo[d][1,3,2]dioxaborole (S-3.12). The reaction was performed according to the general procedure above with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (3.4 g, 10 mmol), NH_4OAc (3.08 g, 40 mmol), $NaIO_4$ (8.56 g, 40 mmol) in acetone/H_2O mixture (1:1, 50mL), *cis*-bicyclo[2.2.1]heptane-2,3-diol[5] (1.28 g, 10 mmol), imidazole (2.72 g, 60 mmol), and $FeCl_3$ (81.1 mg, 0.5 mmol) in CH_3CN (30

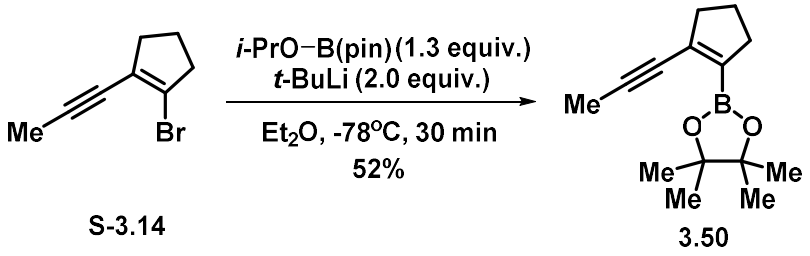
mL). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (929 mg, 36% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.30 (dt, *J* = 14.1, 2.3 Hz, 1H), 5.74 (d, *J* = 14.1 Hz, 1H), 4.27 (d, *J* = 1.4 Hz, 2H), 2.36 (dt, *J* = 7.1, 2.2 Hz, 2H), 2.30 (dq, *J* = 3.2, 1.4 Hz, 2H), 1.66 (dt, *J* = 11.1, 2.0 Hz, 1H), 1.62 – 1.27 (m, 8H), 1.19 (m, 1H), 1.09 – 1.02 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 129.2, 97.2, 83.9, 80.2, 41.1, 31.1, 30.8, 28.4, 23.5, 22.4, 19.9, 14.1. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 29.5. **IR** (neat) ν_{max} 2956 (m), 2873 (w), 1589 (m), 1434 (m), 1382 (w), 1275 (s) ,1258 (s) ,1193 (m), 1027 (m), 1003 (w), 770 (w) cm^{-1}. **HRMS** (DART) for $C_{16}H_{24}BO_2$ $[M+H]^+$: Calc'd: 259.1863, found: 259.1862.



((Z)-4-((6b,9a)-1,6-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)but-3-en-1-yn-1-yl)trimethylsilane (S-3.13). The reaction was performed according to the general procedure above with (Z)-trimethyl(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yn-1-yl)silane (**S-3.3**) (2.50 g, 10 mmol), NH_4OAc (3.08 g, 40 mmol), $NaIO_4$ (8.56 g, 40 mmol) in acetone/H_2O mixture (1:1, 50mL), cis-3,8-dimethyl-1,2-dihydroacenaphthylene-1,2-diol (**S-3.6**) (2.14 g, 10 mmol), imidazole (2.72 g, 60 mmol), and $FeCl_3$ (81.1 mg, 0.5 mmol) in CH_3CN (30 mL). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a white solid (1.49 g, 43% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 2H), 6.32 (d, *J* = 14.4 Hz, 1H), 6.15 (s, 2H), 5.86 (d, *J* = 14.4 Hz, 1H), 2.63 (s, 6H), 0.23 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 137.5, 137.3, 132.5, 130.0, 128.5, 128.3, 125.7, 103.9, 101.3, 82.3, 18.3, -0.01. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 29.3. **IR** (neat) ν_{max} 2930 (s), 2858 (m), 2202 (w), 1590 (s), 1419 (s), 1366 (m), 1254 (s), 1188 (m), 1045 (m), 982 (m), 836 (m), 771 (m) cm^{-1}. **HRMS** (DART) for $C_{21}H_{24}BO_2Si$ $[M+H]^+$: Calc'd: 347.1639, found: 327.1647.



4,4,5,5-tetramethyl-2-(2-(prop-1-yn-1-yl)cyclopent-1-en-1-yl)-1,3,2-dioxaborolane (3.50). In an oven-dried round bottom flask charged with a magnetic stir bar was added 1-bromo-2-(prop-1-yn-1-yl)cyclopent-1-ene (**S-3.14**)[164] (372 mg, 2.01 mmol, 1.0 equiv.) and Et_2O (4 mL). The solution was cooled to -78 °C and added *t*-BuLi in pentane solution (2.4 mL, 4.02 mmol, 1.70M, 2.0 equiv.) dropwise. The reaction mixture was allowed to stir at the same temperature for 30 minutes. Meanwhile, in another oven-dried round bottom flask charged with a magnetic stir bar was added with 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (486 mg, 2.61 mmol, 1.3 equiv.) and Et_2O (4 mL). After being cooled to -78 °C, the solution of organolithium in Et_2O was transferred via syringe. The reaction mixture was allowed to stir at the same temperature for 30 minutes and warm up to room

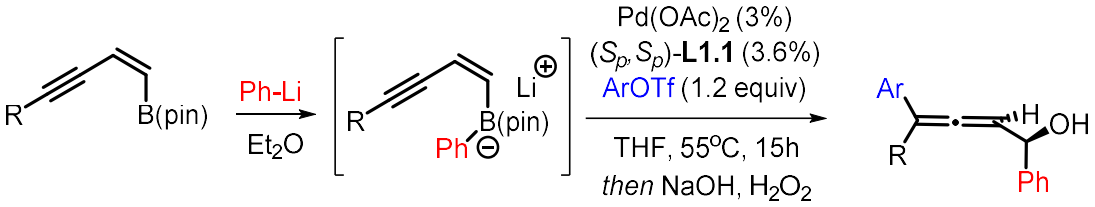
[164] Horino, Y.; Nakashima, Y.; Hashimoto, K.; Kuroda, S. *Synlett* **2010**, *19*, 2879.

temperature at which point it was allowed to stir for an additional 30 minutes. The mixture was cooled to 0 °C and aqueous 1M HCl (4 mL) was added dropwise. After that, it was allowed to warm up to room temperature to stir for 1 hour. The aqueous phase was extracted with Et_2O (3 x 4 mL), dried with sodium sulfate, filtered, and concentrated via rotavap. The crude residue was purified with silica gel column chromatography (5% EtOAc in hexane, stain in $KMnO_4$).

^{1}H NMR (600 MHz, $CDCl_3$) δ 2.48-2.41 (m, 4H), 1.96 (s, 3H), 1.80-1.75 (p, J = 7.5 Hz, 2H), 1.24 (S, 14H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 138.2, 90.7, 83.0, 77.7, 65.8, 39.7, 36.1, 24.8, 23.9, 4.5. **IR** (neat) ν_{max} 3386 (m), 3058 (w), 2957 (m), 2927 (m), 1715 (m), 1683 (m), 1595 (m), 1493 (m), 1446 (m), 1369 (m), 1262 (m), 1228 (s), 1155 (s), 1067 (m), 2017 (s), 956 (s), 910 (s), 803 (m), 758 (s), 696 (s), 593 (w), 546 (w). **HRMS** (DART) for $C_{14}H_{22}BO_2$ $[M+H]^+$: Calc'd: 233.1707, found: 233.1712.

3.4.3 Representative Procedures for Conjunctive Coupling of Borylenynes

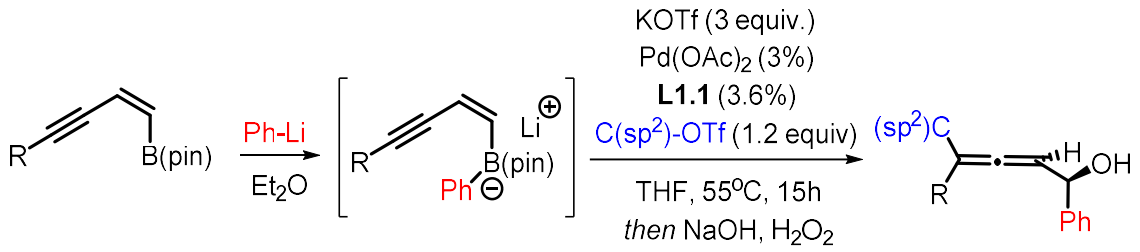
Method A (Use of phenyllithium and triflate electrophile):



To an oven-dried 2-dram vial equipped with a magnetic stir bar was added *cis*-borylenyne (0.20 mmol, 1.0 equiv.) and Et_2O (0.4 mL). The vial was sealed with a septum cap and taken out of the glovebox. The vial was cooled to 0 °C and a solution of phenyllithium in dibutyl ether (0.11 mL, 1.90M, 0.20 mmol, 1.0 equiv.) was added dropwise to the reaction

mixture which was then allowed to warm up to room temperature and stir for 15 minutes. The solvent was carefully removed under reduced pressure after which the reaction vial was brought back into the glovebox and diluted with THF (0.4mL). Meanwhile, a solution of $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.) and (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.) in THF (0.4 mL) was allowed to complex for 10-20 minutes. The catalyst solution was added to the boron "ate" mixture at room temperature under inert atmosphere, followed by the addition of aryl triflate (0.24 mmol, 1.2 equiv.). The reaction vial was sealed with another septum cap and taken out of the glovebox. The reaction mixture was allowed to stir at 55 ^oC for 15 hours and cooled back to room temperature. The crude mixture was filtered through a plug of silica with ether as the eluent and concentrated via rotavap. The crude mixture was diluted with THF (2 mL) and cooled to 0 ^oC before addition of 30% H_2O_2 (0.7 mL) and 3M NaOH (0.7 mL). The mixture was allowed to vigorously stirred for 3 hours, at which point the mixture was cooled back down to 0 ^oC and added sarutared aqueous $Na_2S_2O_3$ solution dropwise. The aqueous phase was extracted with EtOAc (2 mL x3). The combined organic layers were dried over MgSO4, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to provide the desired product.

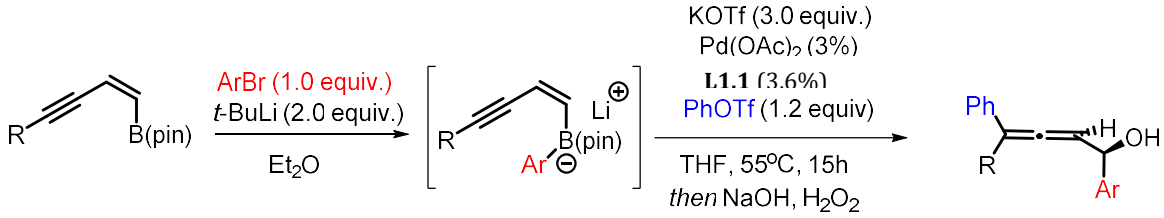
Method B (Use of phenyllithium and bromide electrophile):



To an oven-dried 2-dram vial equipped with a magnetic stir bar was added *cis*-borylenyne (0.20 mmol, 1.0 equiv.) and Et_2O (0.4 mL). The vial was sealed with a septum cap and taken out of the glovebox. The vial was cooled to 0 °C and a solution of phenyllithium in dibutyl ether (0.11 mL, 1.90M, 0.20 mmol, 1.0 equiv.) was added dropwise to the reaction mixture which was then allowed to warm up to room temperature and stir for 15 minutes. The solvent was carefully removed under reduced pressure after which the reaction vial was brought back into the glovebox and diluted with THF (0.4mL). Meanwhile, a solution of $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.) and (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.) in THF (0.4 mL) was allowed to complex for 10-20 minutes. The catalyst solution was added to the boron "ate" mixture at room temperature under inert atmosphere, followed by the addition of potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.) and aryl/alkenyl bromide (0.24 mmol, 1.2 equiv.). The reaction vial was sealed with another septum cap and taken out of the glovebox. The reaction mixture was allowed to stir at 55 °C for 15 hours and cooled back to room temperature. The crude mixture was filtered through a plug of silica with ether as the eluent and concentrated via rotavap. The crude mixture was diluted with THF (2 mL) and cooled to 0 °C before addition of 30% H_2O_2 (0.7 mL) and 3M NaOH (0.7 mL). The mixture was allowed to vigorously stirred for 3 hours, at which point the mixture was cooled back down to 0 °C and added

sarutared aqueous $Na_2S_2O_3$ solution dropwise. The aqueous phase was extracted with EtOAc (2 mL x3). The combined organic layers were dried over MgSO4, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to provide the desired product.

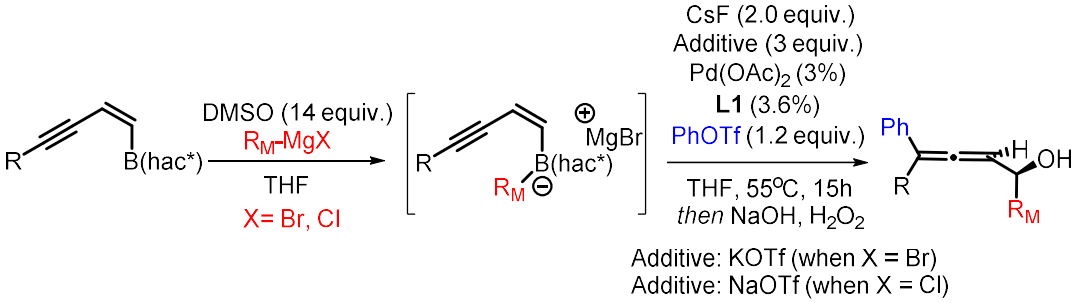
Method C (Lithium-halide exchange with aryl bromide and PhOTf as electrophile



To an oven-dried 2-dram vial equipped with a magnetic stir bar was added aryl bromide (0.20 mmol, 1.0 equiv.) and Et_2O (0.4 mL). The vial was sealed with a septum cap and taken out of the glovebox. The vial was cooled to -78 °C and a solution of *t*-butyllithium in pentane (0.24 mL, 1.70 M, 0.40 mmol, 2.0 equiv.) was added dropwise to the reaction mixture which was then allowed to warm up to room temperature and stir for 15 minutes. At the same temperature, a solution of *cis*-borylenyne (0.20 mmol, 1.0 equiv.) and THF (0.4 mL) was added dropwise. The reaction mixture was allowed to warm up to room temperature and stir for an additional 5 minutes. The solvent was carefully removed under reduced pressure after which the reaction vial was brought back into the glovebox and diluted with THF (0.4mL). Meanwhile, a solution of $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.) and (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.) in THF (0.4 mL) was allowed to complex for 10-20 minutes. The catalyst solution was added to the boron "ate" mixture at room temperature under inert atmosphere, followed by the addition of potassium trifluoromethansulfonate (113 mg, 0.60 mmol, 3.0 equiv.) and phenyl

trifluoromethanesulfonate (54.3 mg, 0.24 mmol, 1.2 equiv.). The reaction vial was sealed with another septum cap and taken out of the glovebox. The reaction mixture was allowed to stir at 55 °C for 15 hours and cooled back to room temperature. The crude mixture was filtered through a plug of silica with ether as the eluent and concentrated via rotavap. The crude mixture was diluted with THF (2 mL) and cooled to 0 °C before addition of 30% H_2O_2 (0.7 mL) and 3M NaOH (0.7 mL). The mixture was allowed to vigorously stirred for 3 hours, at which point the mixture was cooled back down to 0 °C and added sarutared aqueous $Na_2S_2O_3$ solution dropwise. The aqueous phase was extracted with EtOAc (2 mL x3). The combined organic layers were dried over MgSO4, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to provide the desired product.

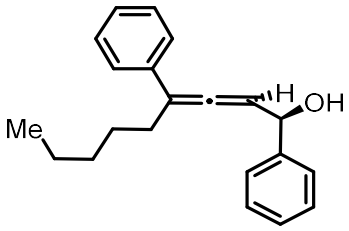
Method D (Use of Alkyl Grignard reagent and PhOTf as electrophile)



To an oven-dried 2-dram vial equipped with a magnetic stir bar was added *cis*-borylenyne (0.20 mmol, 1.0 equiv.), DMSO (219 mg, 14.0 equiv.), and THF (0.4 mL). The vial was sealed with a septum cap and taken out of the glovebox. The vial was cooled to 0 °C and a solution of alkyl Grignard reagent in THF (0.20 mmol, 1.0 equiv.) was added dropwise to the reaction mixture which was then allowed to warm up to room temperature and stir for

15 minutes. The reaction vial was brought back into the glovebox and added cesium fluoride (60.8 mg, 0.6 mmol, 2.0 equiv.). The reaction mixture was allowed to stir for 15 minutes under inert atmosphere. Meanwhile, a solution of $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.) and (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.) in THF (0.4 mL) was allowed to complex for 10-20 minutes. The catalyst solution was added to the boron "ate" mixture at room temperature under inert atmosphere, followed by the addition of potassium/sodium trifluoromethansulfonate (0.60 mmol, 3.0 equiv.) and phenyl trifluoromethanesulfonate (54.3 mg, 0.24 mmol, 1.2 equiv.). The reaction vial was sealed with another septum cap and taken out of the glovebox. The reaction mixture was allowed to stir at 55 ^oC for 15 hours and cooled back to room temperature. The crude mixture was filtered through a plug of silica with ether as the eluent and concentrated via rotavap. The crude mixture was diluted with THF (2 mL) and cooled to 0 ^oC before addition of 30% H_2O_2 (0.7 mL) and 3M NaOH (0.7 mL). The mixture was allowed to vigorously stirred for 3 hours, at which point the mixture was cooled back down to 0 ^oC and added sarutared aqueous $Na_2S_2O_3$ solution dropwise. The aqueous phase was extracted with EtOAc (2 mL x3). The combined organic layers were dried over MgSO4, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to provide the desired product.

3.4.4 Characterization of Conjunctive Cross-Coupling Products



(*P*,1*R*)-1,4-diphenylnona-2,3-dien-1-ol (3.67). The reaction was performed according to the general procedure above (***Method B***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (49.6 mg, 0.20 mmol, 1.0 equiv.), phenyllithium in dibutyl ether (0.11 mL, 1.90M, 0.20 mmol, 1.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and bromobenzene (37.7 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (41 mg, 70% yield).

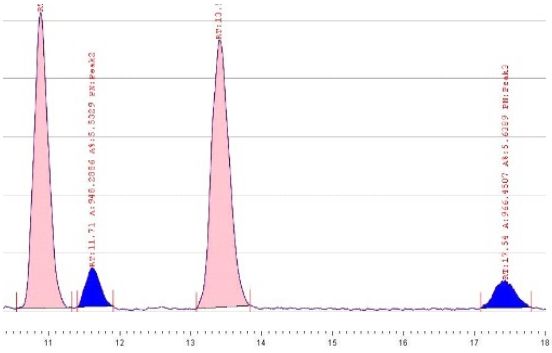
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.5 Hz, 2H), 7.38-7.36 (m, 4H), 7.31 (t, *J* = 7.0 Hz, 3H), 7.22 (t, *J* = 7.5 Hz, 1H), 5.83-5.80 (m, 1H), 5.36 (d, *J* = 6.1 Hz, 1H), 2.49-2.45 (m, 2H), 2.16 (d, *J* = 3.5 Hz, 1H), 1.58-1.53 (m, 2H), 1.40-1.33 (m, 4H), 0.91 (t, *J* = 7.0 Hz, 3H) **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.0, 143.1, 136.2, 128.5, 128.4, 127.7, 127.0, 126.1, 126.1, 110.1, 99.5, 72.5, 31.6, 30.1, 27.8, 22.5, 14.1. **IR** (near) ν_{max} 2954 (s), 2933 (s), 2037 (m), 1915 (m), 1494 (m), 1454 (m), 760 (m), 698 (s), 582 (s). **HRMS** (DART) for $C_{21}H_{24}O$ $(M+H-H_2O)^+$: Calc'd: 275.1794, found: 275.1795. **$[\alpha]_D^{20}$**: +20.3 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Both diastereomic ratio and enantiomeric ratio were determined by chiral SFC. The mixture of racemic diastereomers was prepared by using (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.1**) as borylenyne. Both enantiomers of ligand **L1.1** were used in two separate reactions and equal amount of product from each reaction were mixed together.

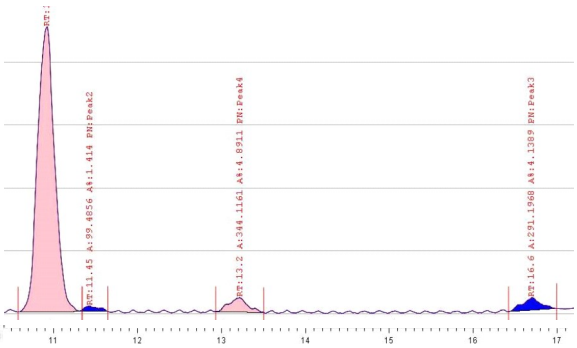
Chiral SFC (Chiralcel OD-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-1,4-diphenylnona-2,3-dien-1-ol.

Mixture of Racemic Diastereomers



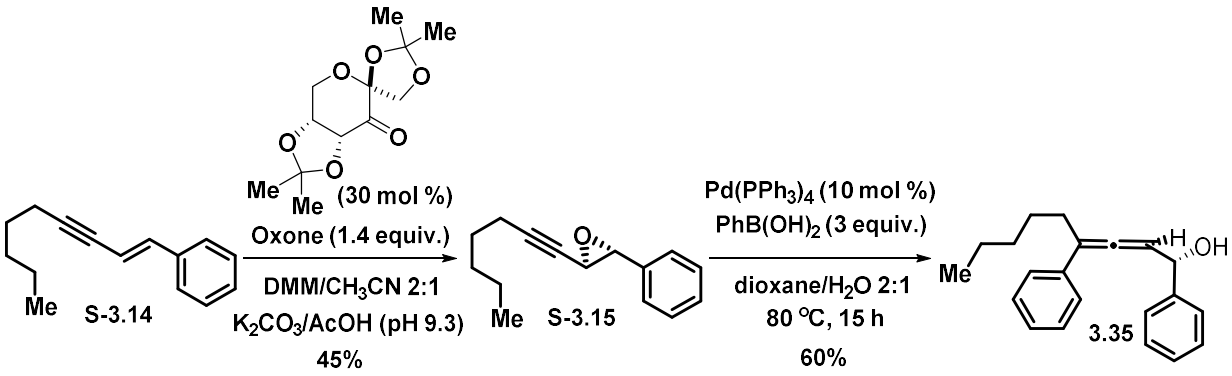
Peak Info			
Peak No	% Area	Area	RT (min)
1	42.168	7227.2016	10.98
2	5.5329	948.2886	11.71
3	46.6603	7997.1374	13.5
4	5.6389	966.4507	17.54
Total:	100.0001	17139.0783	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	89.556	6300.7774	10.95
2	1.414	99.4856	11.45
3	4.8911	344.1161	13.2
4	4.1389	291.1968	16.6
Total:	100	7035.5759	

Structure Proof:

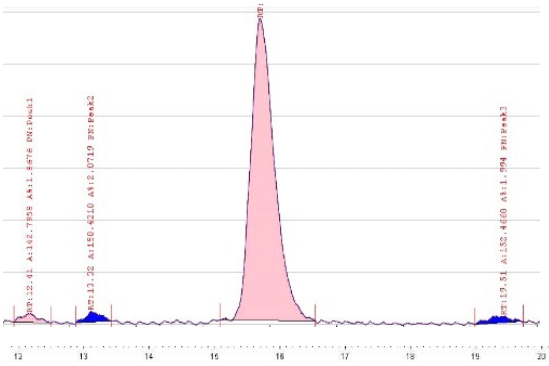


(2*R*,3*R*)-2-(hept-1-yn-1-yl)-3-phenyloxirane (**S-3.15**). The title compound was prepared by asymmetric Shi-epoxidation according to the procedure as reported in the literature.[165] **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H), 3.97 (d, *J* = 1.9 Hz, 1H), 3.33 (d, *J* = 1.9 Hz, 1H), 2.24 (t, *J* = 7.2 Hz, 2H), 1.58-1.51 (m, 2H), 1.40-1.31 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 136.2, 128.69, 128.67, 125.7, 85.5, 76.5, 60.3, 50.0, 31.2, 28.2, 22.3, 18.9, 14.1. **IR** (neat) ν_{max} 2956 (m), 2931 (m), 2242 (w), 1605 (w), 1457 (m), 1334 (w), 869 (m), 843 (m), 743 (m), 696 (s), 621 (m) cm^{-1}. **HRMS** (DART) for $C_{15}H_{19}O$ $(M+H)^+$: Calc'd: 215.1430, found: 215.1424. **$[\alpha]_D^{20}$**: -10.0 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

(1*S*)-1,4-diphenylnona-2,3-dien-1-ol (**3.35**). The title compound was prepared according to the procedure reported in the literature.[8] The reaction would proceed selectively via *anti*-addition resulting in excellent *anti*-diastereoselectivity. The authentic sample is the opposite enantiomer of the major conjunctive coupling product derived from (*Sp*,*Sp*)-**L1.1**.

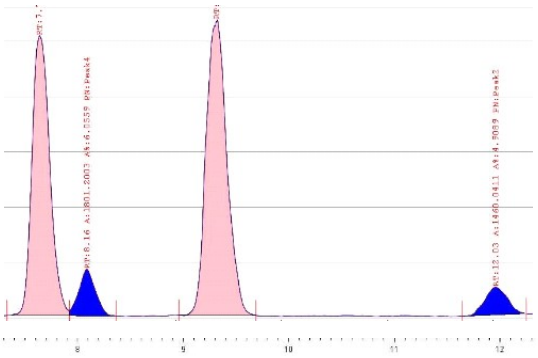
[165] Cao, G.; Wang, Z.; Tu, Y.; Shi, Y. *Tet. Lett.* **1998**, *39*, 4425.

Authentic sample **3.35**

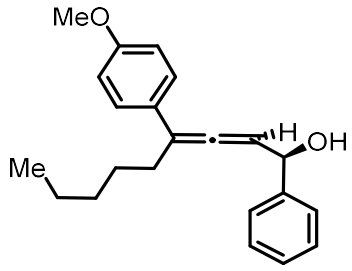


Peak Info			
Peak No	% Area	Area	RT (min)
1	1.8676	142.7958	12.41
2	2.0719	158.4218	13.32
3	94.0665	7192.468	15.86
4	1.994	152.4668	19.51
Total:	100	7646.1524	

Co-injection of authentic product with enantioenriched material derived from conjunctive coupling with (*Sp*,*Sp*)-**L1.1**



Peak Info			
Peak No	% Area	Area	RT (min)
1	39.876	11860.214	7.71
2	6.0559	1801.2003	8.16
3	49.1592	14621.3123	9.39
4	4.9089	1460.0411	12.03
Total:	100	29742.7677	



(*P*,1*R*)-4-(4-methoxyphenyl)-1-phenylnona-2,3-dien-1-ol (3.36). The reaction was performed according to the general procedure above (***Method B***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (49.6 mg, 0.20 mmol, 1.0 equiv.), phenyllithium in dibutyl ether (0.11 mL, 1.90 M, 0.20 mmol, 1.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and 4-bromoanisole (44.9 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (49.6 mg, 72% yield).

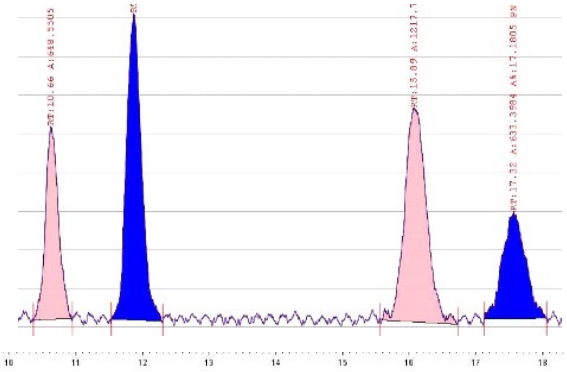
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46-7.44 (m, 2H), 7.39-7.36 (m, 2H), 7.32-7.30 (m, 3H), 6.87-6.85 (m, 2H), 5.81-5.78 (dt, *J* = 6.0 Hz, 3.4 Hz, 1H), 5.38-5.33 (m, 1H), 3.82 (s, 3H), 2.47-2.42 (m, 2H), 2.18 (d, *J* = 3.4 Hz, 1H), 1.58-1.53 (m, 2H), 1.38-1.35 (m, 4H), 0.91 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (500 MHz, $CDCl_3$) δ 201.4, 158.8, 143.2, 128.5, 127.7, 127.2, 126.1, 115.3, 113.9, 109.8, 99.4, 72.6, 55.3, 31.7, 30.3, 27.8, 22.5, 14.1. **IR** (neat) ν_{max} 3393 (m), 2921 (m), 2857 (w), 2137 (w), 1943 (w), 1606 (m), 1511 (s), 1455 (m), 1293 (w), 1250 (s), 1293 (w), 1250 (s), 1178 (m), 1112 (w), 1037 (s), 832 (m), 758 (w), 700 (m), 604 (w) cm^{-1}. **HRMS** (DART) for $C_{22}H_{27}O_2$ $(M+H-H_2O)^+$: Calc'd: 305.1900, found: 305.1900. **$[\alpha]_D^{20}$**: +18.2 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Both diastereomic ratio and enantiomeric ratio were determined by chiral SFC. The mixture of racemic diastereomers was prepared by using (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**3.1**) as borylenyne. Both enantiomers of ligand **L1.1** were used in two separate reactions and equal amount of product from each reaction were mixed together.

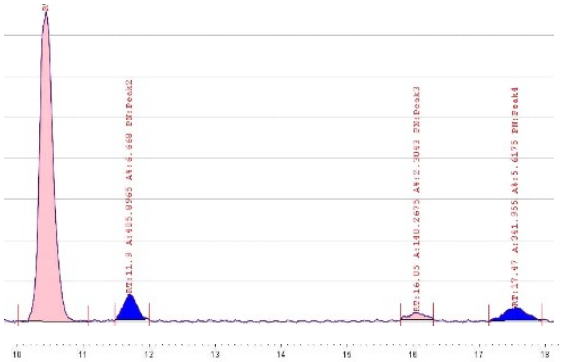
Chiral SFC (Chiralcel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-4-(4-methoxyphenyl)-1-phenylnona-2,3-dien-1-ol.

Mixture of Racemic Diastereomers

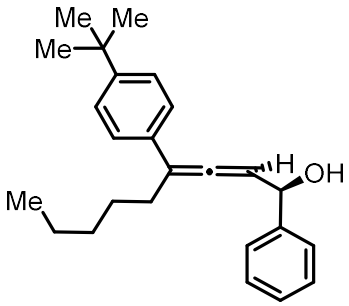


Peak Info			
Peak No	% Area	Area	RT (min)
1	17.5915	648.5505	10.66
2	32.1968	1187.0069	11.85
3	33.0311	1217.7639	15.89
4	17.1805	633.3984	17.32
Total:	99.9999	3686.7197	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	85.4102	5199.1469	10.69
2	6.668	405.8965	11.9
3	2.3043	140.2675	16.05
4	5.6175	341.955	17.47
Total:	100	6087.2659	



(*P*,1*R*)-4-(4-methoxyphenyl)-1-phenylnona-2,3-dien-1-ol (3.37). The reaction was performed according to the general procedure above (***Method B***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (49.6 mg, 0.20 mmol, 1.0 equiv.), phenyllithium in dibutyl ether (0.11 mL, 1.90 M, 0.20 mmol, 1.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and 4-bromoanisole (44.9 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL,

0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (45.3 mg, 65% yield).

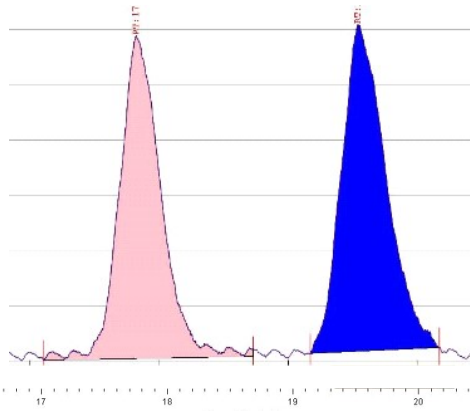
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.3 Hz, 2H), 7.39-7.30, (m, 7H), 5.81-5.78 (m, 1H), 5.36-5.34 (m, 1H), 2.48-2.44 (m, 2 H), 2.16 (d, *J* = 4.0 Hz, 1H), 1.58-1.54 (m, 2H), 1.40-1.30 (m, 4H), 1.32 (s, 9H), 0.91 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 201.8, 150.1, 143.2, 133.2, 128.5, 127.7, 126.1, 125.7, 125.4, 110.0, 99.4, 72.5, 34.5, 31.7, 31.3, 30.1, 27.8, 22.5, 14.1. **IR** (near) ν_{max} 3354 (m), 3019 (w), 2956 (s), 2861 (m), 2165 (s), 1977 (s), 1943 (s), 1652 (s), 1601 (m), 1558 (w), 1511 (m), 1493 (w), 1454 (m), 1376 (w), 1269 (m), 1202 (w), 1025 (s), 836 (s), 700(s), 537 (w). **HRMS** (DART) for $C_{25}H_{33}O$: Calc'd: 349.2526, found: 349.2529. **$[\alpha]_D^{20}$**: +5.3 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

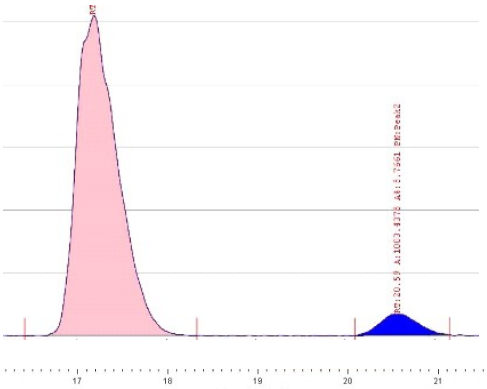
Chiral SFC (Chiralcel OJ-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-4-(4-methoxyphenyl)-1-phenylnona-2,3-dien-1-ol.

Racemic Material

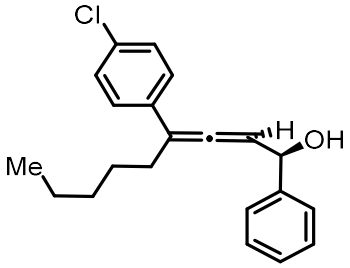


Peak Info			
Peak No	% Area	Area	RT (min)
1	48.0415	2623.6532	17.82
2	51.9585	2837.5737	19.54
Total:	100	5461.2269	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	94.2339	16398.8469	17.18
2	5.7661	1003.4375	20.59
Total:	100	17402.2844	



(*P*,1*R*)-4-(4-chlorophenyl)-1-phenylnona-2,3-dien-1-ol (3.39). The reaction was performed according to the general procedure above (***Method B***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (S-**3.3**) (49.6 mg, 0.20 mmol, 1.0 equiv.), phenyllithium in dibutyl ether (0.11 mL, 1.90 M, 0.20 mmol, 1.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and 1-bromo-4-chlorobenzene (mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10%

EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (39.2 mg, 60% yield).

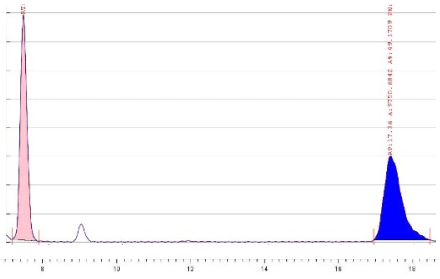
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43-7.22 (m, 9H), 5.82-5.80 (m, 1H), 5.36-5.35 (m, 1H), 2.43-2.39 (m, 2H), 2.13-2.12 (d, J = 4.1 Hz, 1H), 1.53-1.51 (t, J = 7.3, 2H), 1.38-1.32 (m, 4H), 0.91-0.98 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.2, 143.0, 134.8, 132.7, 128.6, 128.5, 127.9, 127.3, 126.1, 109.1, 99.8, 72.5, 31.6, 30.0, 27.7, 22.5, 14.0. **IR** (neat) ν_{max} 3348 (m), 2926 (s), 2857 (s), 2138 (w), 2003 (w), 1946 (m), 1490 (s), 1454 (m), 1093 (m), 1012 (s), 830 (s), 755 (m), 700 (s). **HRMS** (DART) for $C_{21}H_{22}Cl$ (M+H-H_2O): Calc'd: 309.1405, found: 309.1406. **$[\alpha]_D^{20}$**: +7.6 (c = 0.50, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

Chiral SFC (Chiralcel OJ-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-4-(4-chlorophenyl)-1-phenylnona-2,3-dien-1-ol.

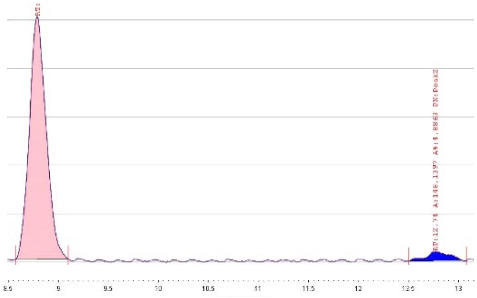
Racemic Material



Peak Info

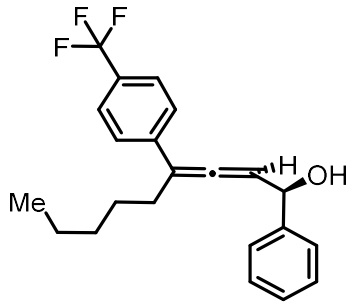
Peak No	% Area	Area	RT (min)
1	50.8291	10079.5154	7.29
2	49.1709	9750.6842	17.36
Total:	100	19830.1996	

Standard Conditions



Peak Info

Peak No	% Area	Area	RT (min)
1	95.1137	2883.6237	8.81
2	4.8863	148.1397	12.74
Total:	100	3031.7634	



(*P*,1*R*)-1-phenyl-4-(4-(trifluoromethyl)phenyl)nona-2,3-dien-1-ol (3.40). The reaction was performed according to the general procedure above (***Method B***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (49.6 mg, 0.20 mmol, 1.0 equiv.), phenyllithium in dibutyl ether (0.11 mL, 1.90 M, 0.20 mmol, 1.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and 4-bromobenzotrifluoride (54.0 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (43.2 mg, 60% yield).

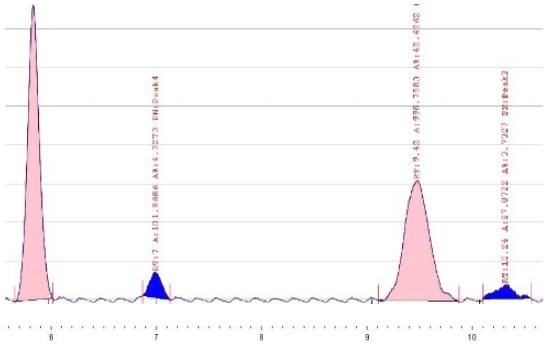
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.44-7.42 (m, 4H), 7.39-7.36 (m, 2H), 7.32-7.30 (m, 1H), 5.87-5.86 (m, 1H), 5.39-5.38 (m, 1H), 2.47-2.42 (m, 2H), 2.10-2.09 (d, *J* = 4.1 Hz, 1H), 1.56-1.54 (m, 2H), 1.39-1.31 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 203.1, 142.9, 140.2, 128.6, 127.9, 126.6, 125.8, 126.2, 126.0, 125.29, 125.26, 109.0, 99.9, 72.5, 31.6, 29.9, 27.6, 22.5, 14.0. **IR** (near) ν_{max} 3649 (m), 2980 (s), 2971 (s), 2359 (m), 2342 (w), 1616 (m), 1456 (m), 1381 (m), 1326 (s), 1251 (w), 1164 (s), 1125 (s), 1069 (s), 1015 (w), 953 (m), 846 (w), 761 (w), 699 (m), 668 (w). **HRMS** (DART) for $C_{22}H_{23}OF_3$ $(M+H-H_2O)^+$: Calc'd: 343.1668, found: 343.1660. **$[\alpha]_D^{20}$**: +8.3 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Both diastereomic ratio and enantiomeric ratio were determined by chiral SFC. The mixture of racemic diastereomers was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

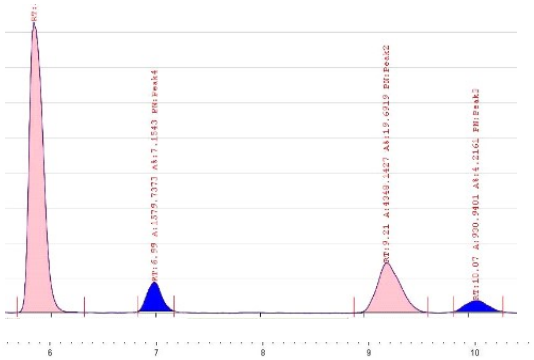
Chiral SFC (Chiralcel OJ-H, 7% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-1-phenyl-4-(4-(trifluoromethyl)phenyl)nona-2,3-dien-1-ol.

Mixture of Racemic Diastereomers

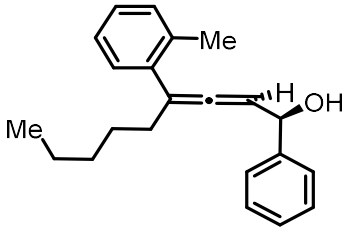


Peak Info			
Peak No	% Area	Area	RT (min)
1	49.5139	1165.6107	5.86
2	4.3273	101.8686	7
3	42.4262	998.7583	9.42
4	3.7327	87.8722	10.24
Total:	100.0001	2354.1098	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	68.9377	15222.0368	5.83
2	7.1543	1579.7373	6.99
3	19.6919	4348.1427	9.21
4	4.2161	930.9401	10.07
Total:	100	22080.8569	



(*P*,1*R*)-1-phenyl-4-(o-tolyl)nona-2,3-dien-1-ol (3.28). The reaction was performed according to the general procedure above (***Method B***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**3.3**) (49.6 mg, 0.20 mmol, 1.0 equiv.), phenyllithium in dibutyl ether (0.11 mL, 1.90 M, 0.20 mmol, 1.0 equiv.),

Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and 2-bromotoluene (41.0 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (31.9 mg, 52% yield).

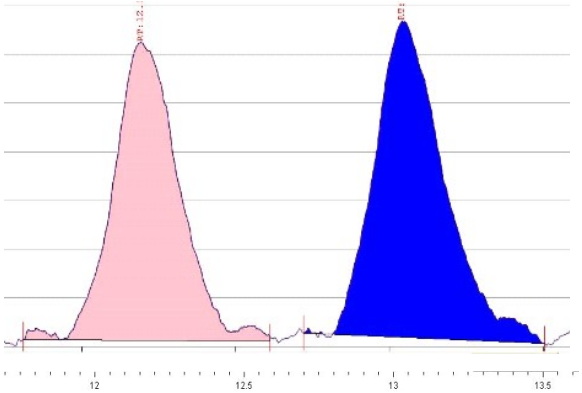
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.32 (m, 4H), 7.28-7.26 (m, 1H), 7.17-7.15 (m, 3H), 7.12-7.10 (m, 1H), 5.55-5.53 (m, 1H), 5.29-5.27 (m, 1H), 2.33-2.29 (m, 2H), 2.29 (s, 3H), 2.17 (s, 1H), 1.49-1.44 (m, 2H), 1.35-1.29 (m, 4H), 0.88 (t, J = 6.9 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 200.7, 143.1, 137.5, 135.8, 130.5, 128.6, 128.3, 127.8, 127.2, 126.4, 125.9, 109.3, 96.7, 72.5, 34.3, 31.7, 27.7, 22.7, 20.4, 14.2. **IR** (neat) ν_{max} 3358 (m), 3062 (w), 3028 (w), 2955 (s), 2926 (s), 2957 (m), 2155 (w), 1956 (w), 1669 (w), 1601 (w), 1489 (m), 1454 (m), 1378 (w), 1330 (w), 1260 (s), 1191 (w), 1029 (s), 914 (w), 846 (w), 803(s), 758 (s), 698 (s), 654 (w), 557 (w). **HRMS** (DART) for $C_{22}H_{26}O$ $(M+H-H_2O)^+$: Calc'd: 289.1952, found: 289.1941. **$[\alpha]_D^{20}$**: +4.5 (c = 0.50, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

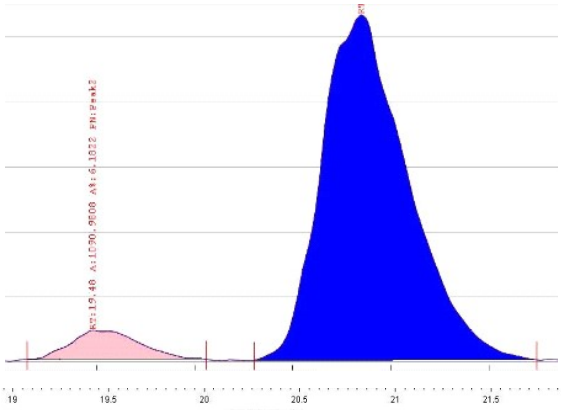
Chiral SFC (Chiralcel OJ-H, 7% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-1-phenyl-4-(o-tolyl)nona-2,3-dien-1-ol.

Racemic Material

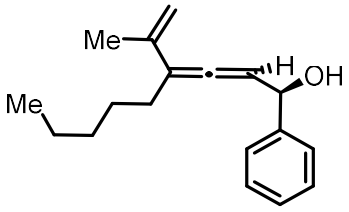


Peak Info			
Peak No	% Area	Area	RT (min)
1	47.1637	919.1641	12.19
2	52.8363	1029.7167	13.04
Total:	100	1948.8808	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	6.2661	1090.9808	19.48
2	93.7339	16319.8484	20.85
Total:	100	17410.8292	



(*P*,1*R*)-1-phenyl-4-(prop-1-en-2-yl)nona-2,3-dien-1-ol (3.41). The reaction was performed according to the general procedure above (***Method B***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**3.3**) (49.6 mg, 0.20 mmol, 1.0 equiv.), phenyllithium in dibutyl ether (0.11 mL, 1.90 M, 0.20 mmol, 1.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and 2-bromopropene (29.0 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (32.3 mg, 63% yield).

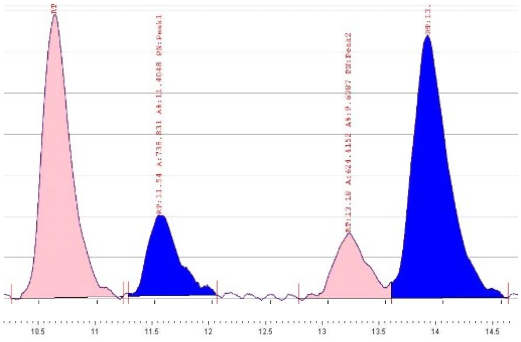
^{1}H NMR (600 MHz, $CDCl_3$) Major diastereomer: δ 7.42-7.33 (m, 4H), 7.31-7.26 (m, 1H), 5.69-5.62 (m, 1H), 5.30-5.24 (m, 1H), 5.00 (s, 1H), 4.92 (d, *J* = 1.5 Hz, 1H), 2.26-2.15 (m, 2H), 2.07 (d, *J* = 3.9 Hz, 1H), 1.79 (s, 3H), 1.52-1.39 (m, 2H), 1,36-1.25 (m, 4H), 0.94-0.85 (m, 3H). Minor diastereomer: δ 7.42-7.33 (m, 4H), 7.31-7.26 (m, 1H), 5.69-5.62 (m, 1H), 5.30-5.24 (m, 1H), 5.00 (s, 1H), 4.94 (d, *J* = 1.5 Hz, 1H), 2.26-2.15 (m, 2H), 2.09 (d, *J* = 3.9 Hz, 1H), 1.87 (s, 3H), 1.52-1.39 (m, 2H), 1,36-1.25 (m, 4H), 0.94-0.85 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) Major diasteromer: δ 203.2, 143.3, 139.8, 128.6, 127.8, 126.2, 111.9, 111.48, 98.9, 72.7, 31.9, 29.4, 28.0, 22.71, 22.2, 14.2. Minor diastereomer: δ 203.1, 143.4, 139.7, 128.6, 127.8, 126.2, 112.1, 111.54, 99.0, 72.66, 31.9, 29.5, 27.9, 22.69, 22.3, 14.20. **IR** (neat) ν_{max} 3650 (w), 2980 (s), 2888 (m), 2361 (m), 2340 (m), 2239 (w), 2223 (w), 2194 (w), 2156 (w), 1472 (w), 1457 (w), 1381 (m), 1251 (m), 1151 (m), 1079 (m), 955 (m), 698 (m), 668 (w), 568 (w), 527 (w). **HMRS** (DART) for $C_{18}H_{24}O$ (M+H-H_2O)$^+$: Calc'd: 239.1794, found: 239.1794. **[α]$_D^{20}$**: +1.2 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Both diastereomic ratio and enantiomeric ratio were determined by chiral SFC. The mixture of racemic diastereomers was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

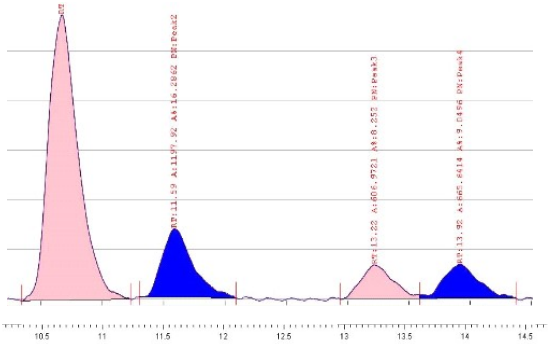
Chiral SFC (Chiralcel AD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-1-phenyl-4-(prop-1-en-2-yl)nona-2,3-dien-1-ol.

Mixture of Racemic Diastereomers

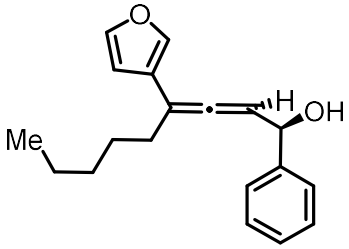


Peak Info			
Peak No	% Area	Area	RT (min)
1	36.6334	2373.1894	10.63
2	11.4048	738.831	11.54
3	9.6387	624.4152	13.18
4	42.3231	2741.7833	13.87
Total:	100	6478.2189	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	66.4122	4884.9125	10.67
2	16.2862	1197.92	11.59
3	8.252	606.9721	13.22
4	9.0496	665.6414	13.92
Total:	100	7355.446	



(*P*,1*R*)-4-(furan-3-yl)-1-phenylnona-2,3-dien-1-ol (3.42).

The reaction was performed according to the general procedure above (***Method B***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**3.3**) (49.6 mg, 0.20 mmol, 1.0 equiv.), phenyllithium in dibutyl ether (0.11 mL, 1.90 M, 0.20 mmol, 1.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and 3-bromofuran (35.3 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (29.9 mg, 53% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.42 (m, 2H), 7.37-7.34 (m, 4H), 7.31-7.28 (m, 1H), 6.29 (dd, *J* = 1.9, 0.9 Hz, 1H), 5.76-5.72 (m, 1H), 5.32 (d, *J* = 6.1 Hz, 1H), 2.36-2.25 (m,

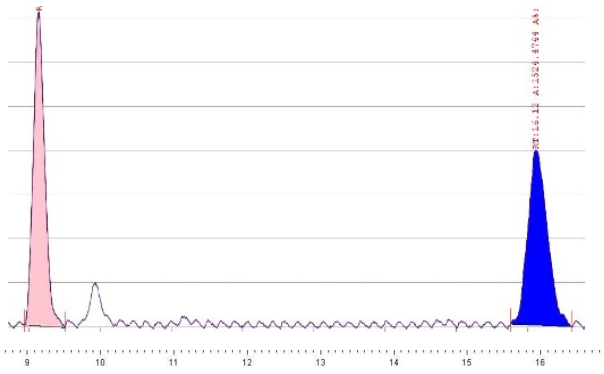
2H), 2.12 (s, 1H), 1.57-1.54 (m, 2H), 1.37-1.30 (m, 4H), 0.92-0.88 (m, 3H). **^{13}C NMR** δ 201.1, 143.34, 143.22, 138.6, 128.7, 127.9, 126.2, 128.1, 109.3, 103.1, 99.3, 72.7, 31.7, 30.7, 27.7, 22.7, 14.2. **IR** (neat) ν_{max} 3346 (m), 3029 (w), 2955 (s), 2927 (s), 2858 (s), 2240 (w), 1948 (w), 1595 (m), 1500 (m), 1454 (s), 1377 (m), 1260 (s), 1155 (s), 1026 (s), 915 (w), 872 (s), 849 (w), 797 (s), 755 (s), 699 (s), 649 (w), 594 (m), 535 (w). **HMRS** (DART) for $C_{14}H_{11}O_2$ $(M\text{-}H+H_2O)^+$: Calc'd: 198.0821, found: 198.0811. **$[\alpha]_D^{20}$**: +5.0 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

Chiral SFC (Chiralcel OJ-H, 6% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-4-(furan-3-yl)-1-phenylnona-2,3-dien-1-ol.

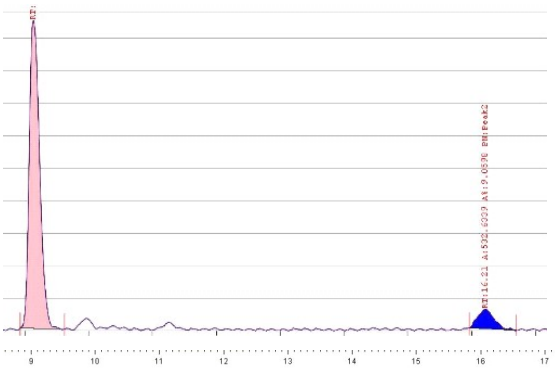
Racemic Material



Peak Info

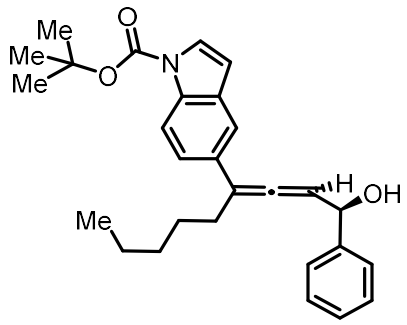
Peak No	% Area	Area	RT (min)
1	51.1321	1595.1052	9.14
2	48.8679	1524.4744	16.12
Total:	100	3119.5796	

Standard Conditions



Peak Info

Peak No	% Area	Area	RT (min)
1	90.9402	5346.4665	9.13
2	9.0598	532.6339	16.21
Total:	100	5879.1004	



tert*-butyl (*P*)-5-((1*R*)-1-hydroxy-1-phenylnona-2,3-dien-4-yl)-1H-indole-1-carboxylate (3.43)**. The reaction was performed according to the general procedure above (Method B***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**3.3**) (49.6 mg, 0.20 mmol, 1.0 equiv.), phenyllithium in dibutyl ether (0.11 mL, 1.90 M, 0.20 mmol, 1.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and *N*-Boc-5-bromoindole (35.3 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (43.2 mg, 50% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 9.1 Hz, 1H), 7.56 (d, *J* = 5.1 Hz, 1H), 7.54 (d, *J* = 1.8 Hz, 1H), 7.47-7.45 (m, 2H), 7.39-7.29 (m, 4H), 6.53-6.52 (d, *J* = 3.7 Hz, 1H), 5.84-5.81 (m, 1H), 5.40-5.37 (m, 1H), 2.58-2.48 (m, 2H), 2.18 (d, *J* = 4.2 Hz, 1H), 1.67 (s, 9H), 1.59-1.54 (m, 2H), 1.43-1.32 (m, 4H), 0.92-0.90 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** δ 201.9, 143.3, 130.8, 129.6, 128.5, 127.7, 126.3, 126.2, 126.1, 123.0, 118.2, 118.1, 115.0, 110.5, 107.4, 99.3, 83.7, 72.6, 31.7, 30.5, 28.2, 27.8, 22.6, 14.1. **IR** (neat) ν_{max} 3650 (m), 2980 (s), 2931 (m), 2361 (m), 2340 (w), 2239 (w), 2225 (w), 2193 (w), 2170 (w), 2156 (m), 1734 (s), 1471 (m), 1371 (s), 1341 (s), 1238 (m), 1163 (s), 1136 (s), 1083 (m), 1024 (w), 956 (w), 821 (w), 765 (m), 727 (m), 699 (m), 668 (w), 576 (w), 536 (m). **HRMS** (DART) for

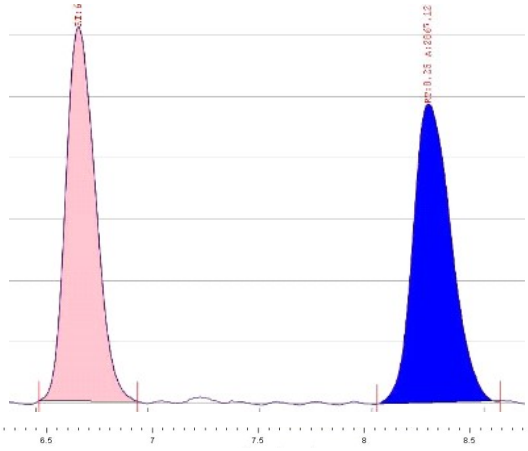
$C_{28}H_{33}NO_3$ $(M+H-H_2O)^+$: Calc'd: 414.2428, found: 414.2428. **[α]D^{20}**: +18.0 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

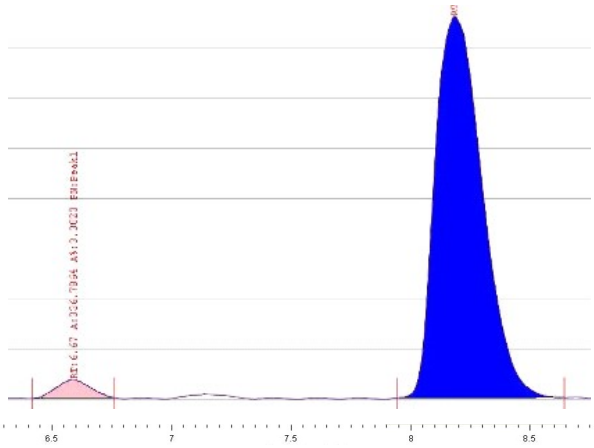
Chiral SFC (Chiralcel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of tert-butyl 5-((1R)-1-hydroxy-1-phenylnona-2,3-dien-4-yl)-1H-indole-1-carboxylate.

Racemic Material

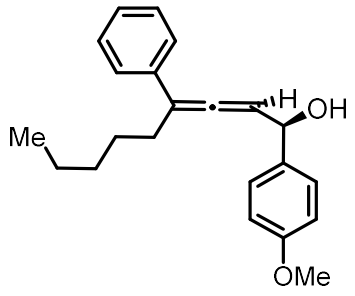


Peak Info			
Peak No	% Area	Area	RT (min)
1	49.4087	2800.1017	6.69
2	50.5913	2867.125	8.25
Total:	100	5667.2267	

Standard Conditions\



Peak Info			
Peak No	% Area	Area	RT (min)
1	3.3023	336.7864	6.67
2	96.6977	9861.904	8.18
Total:	100	10198.6904	



(*P*,1*R*)-1-(4-methoxyphenyl)-4-phenylnona-2,3-dien-1-ol (3.44). The reaction was performed according to the general procedure above (***Method C***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (49.6 mg, 0.20 mmol, 1.0 equiv.), 4-bromoanisole (37.4 mg, 0.20 mmol, 1.0 equiv.), *t*-butyllithium in pentane (0.24 mL, 1.70 M, 0.40 mmol, 2.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0s equiv.), and phenyl trifluoromethanesulfonate (54.3 mg, 0.24 mmol, 1.2 equiv.). in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (36.1 mg, 56% yield).

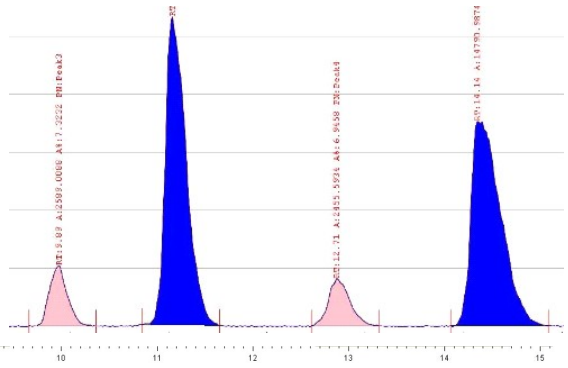
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 4H), 7.31 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.24 – 7.18 (m, 1H), 6.93 – 6.87 (m, 2H), 5.80 (dt, *J* = 6.0, 3.0 Hz, 1H), 5.32 (dd, *J* = 6.0, 3.7 Hz, 1H), 3.82 (s, 3H), 2.49-2.43 (m, 2H), 2.08 (d, *J* = 3.7 Hz, 1H), 1.61 – 1.52 (m, 3H), 1.42 – 1.31 (m, 4H), 0.91 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.1, 159.4, 136.5, 135.5, 128.5, 127.6, 127.1, 126.2, 114.0, 110.2, 99.7, 72.3, 55.5, 31.8, 30.3, 28.0, 22.7, 14.2. **IR** (neat) ν_{max} 3390 (br, w), 2953 (m) ,2925 (m), 2855 (m), 1945 (w), 1610 (m), 1510 (m),1451 (m), 1245 (s) ,1032 (s) ,828 (m) ,763 (w), 544 (w) cm^{-1}. **HRMS** (DART) for $C_{22}H_{25}O$ $[M+H-H_2O]^+$: Calc'd: 305.1898, found: 305.1899. **$[\alpha]_D^{20}$**: +90.0 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Both diastereomic ratio and enantiomeric ratio were determined by chiral SFC. The mixture of racemic diastereomers was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

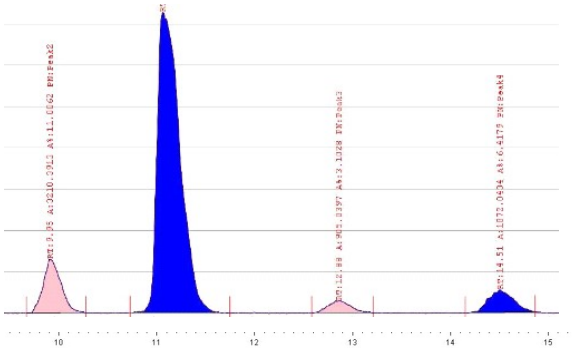
Chiral SFC (Chiralcel OJ-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-1-(4-methoxyphenyl)-4-phenylnona-2,3-dien-1-ol.

Mixture of Racemic Diastereomers

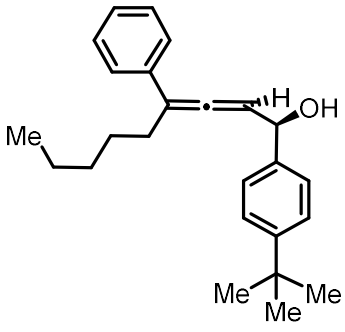


Peak Info			
Peak No	% Area	Area	RT (min)
1	7.3232	2589.0088	9.89
2	43.8937	15518.0113	11.04
3	6.9458	2455.5934	12.71
4	41.8373	14790.9874	14.14
Total:	100	35353.6009	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	11.0062	3210.3913	9.95
2	79.4731	23181.4528	11.09
3	3.1028	905.0397	12.88
4	6.4179	1872.0434	14.51
Total:	100	29168.9272	



(*P*,1*R*)-1-(4-(tert-butyl)phenyl)-4-phenylnona-2,3-dien-1-ol (3.37). The reaction was performed according to the general procedure above (***Method C***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (49.6

mg, 0.20 mmol, 1.0 equiv.), 1-bromo-4-*tert*-butylbenzene (42.6 mg, 0.20 mmol, 1.0 equiv.), *t*-butyllithium in pentane (0.24 mL, 1.70 M, 0.40 mmol, 2.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0s equiv.), and phenyl trifluoromethanesulfonate (51.1 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (37.6 mg, 54% yield).

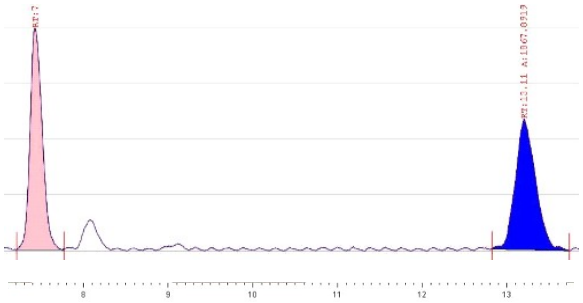
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.36 (m, 5H), 7.32 (ddd, *J* = 8.2, 7.0, 1.9 Hz, 2H), 7.27 – 7.20 (m, 2H), 5.85-5.81 (m, 1H), 5.37-5.33 (m, 1H), 2.52-2.43 (m, 2H), 2.14 – 2.09 (m, 1H), 1.61 – 1.56 (m, 2H), 1.39 – 1.29 (m, 13H), 0.92 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.2, 150.9, 140.3, 136.5, 128.5, 127.1, 126.2, 126.0, 125.6, 110.2, 99.6, 72.4, 34.7, 31.8, 31.5, 30.3, 28.0, 22.7, 14.2. **IR** (neat) ν_{max} 3372 (br, w), 2955 (m) ,2928 (m), 2860 (m), 1945 (w), 1597 (m), 1509 (m),1451 (m), 1268 (m) ,1031 (m) ,824 (m) ,756 (m), 544 (w) cm^{-1}. **HRMS** (DART) for $C_{22}H_{31}$ $[M+H-H_2O]^+$: Calc'd: 331.2424, found: 331.2420. **$[\alpha]_D^{20}$**: +83.7 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

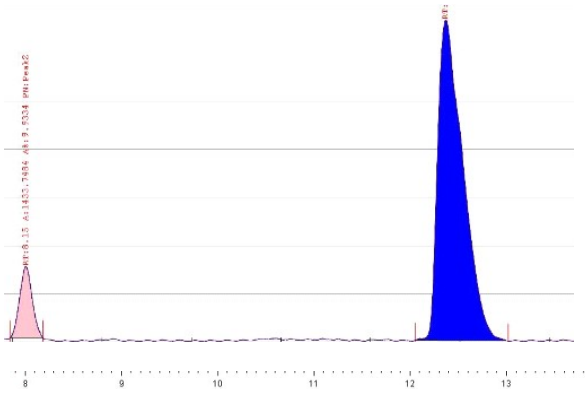
Chiral SFC (Chiralcel OJ-H, 7% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-1-(4-(tert-butyl)phenyl)-4-phenylnona-2,3-dien-1-ol.

Racemic Material

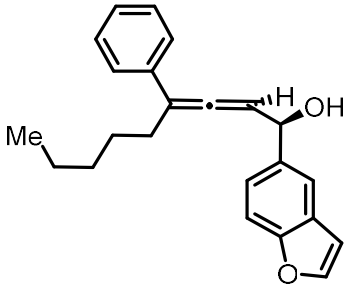


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.3253	1892.3541	7.57
2	49.6747	1867.8919	13.11
Total:	100	3760.246	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	9.9334	1433.7484	8.15
2	90.0666	12999.9045	12.84
Total:	100	14433.6529	



(*P*,1*R*)-1-(benzofuran-5-yl)-4-phenylnona-2,3-dien-1-ol (3.42). The reaction was performed according to the general procedure above (***Method C***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (49.6 mg, 0.20 mmol, 1.0 equiv.), 5-bromobenzofuran (39.4 mg, 0.20 mmol, 1.0 equiv.), *t*-butyllithium in pentane (0.24 mL, 1.70 M, 0.40 mmol, 2.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0s equiv.), and phenyl trifluoromethanesulfonate (51.1 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (35.9 mg, 54% yield).

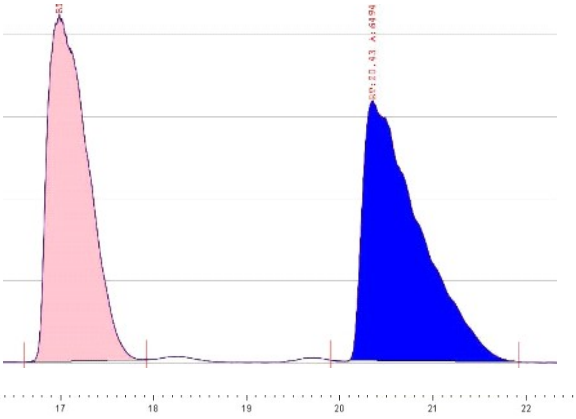
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 2.0 Hz, 1H), 7.65 (d, *J* = 2.0 Hz, 1H), 7.50 (d, *J* = 8.5 Hz, 1H), 7.39 (dq, *J* = 8.3, 2.0 Hz, 3H), 7.32 (dt, *J* = 7.8, 2.0 Hz, 2H), 7.26 – 7.20 (m, 1H), 6.77 (dt, *J* = 3.0, 1.5 Hz, 1H), 5.87 (dt, *J* = 5.9, 3.0 Hz, 1H), 5.48 (dd, *J* = 5.9, 3.6 Hz, 1H), 2.54 – 2.42 (m, 2H), 2.21 (d, *J* = 3.6 Hz, 1H), 1.64 – 1.54 (m, 2H), 1.45 – 1.31 (m, 4H), 0.96 – 0.88 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.1, 154.8, 145.6, 138.1, 136.5, 128.6, 127.7, 127.2, 126.2, 123.0, 119.0, 111.5, 110.3, 106.9, 100.0, 72.8, 31.8, 30.3, 28.0, 22.7, 14.3. **IR** (neat) ν_{max} 3381 (br, w), 3027 (w), 2954 (s) ,2927 (s), 2857 (m), 1946 (w), 1595 (w), 1537 (w), 1466 (s), 1262 (s) ,1031 (m) ,883 (m) ,765 (m), 583 (w) cm^{-1}. **HRMS** (DART) for $C_{23}H_{25}O_2$ $[M+H]^+$: Calc'd: 333.1855, found: 333.1849. **$[\alpha]_D^{20}$**: +77.0 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

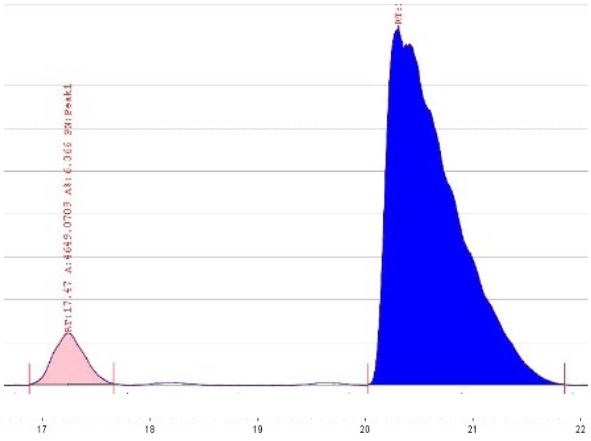
Chiral SFC (Chiralcel OJ-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-1-(benzofuran-5-yl)-4-phenylnona-2,3-dien-1-ol.

Racemic Material

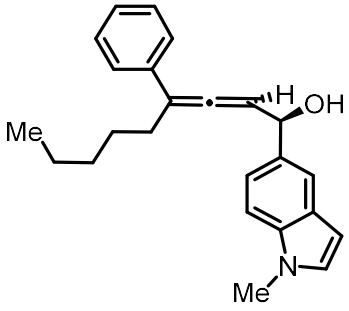


Peak Info			
Peak No	% Area	Area	RT (min)
1	48.7964	61890.1016	17.13
2	51.2036	64943.1582	20.43
Total:	100	126833.2598	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	6.366	4649.0709	17.47
2	93.634	68381.0984	20.44
Total:	100	73030.1693	



(*P*,1*R*)-1-(1-methyl-1H-indol-5-yl)-4-phenylnona-2,3-dien-1-ol (3.48). The reaction was performed according to the general procedure above (***Method C***) with (E)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) (49.6 mg, 0.20 mmol, 1.0 equiv.), 5-bromo-1-methylindole (42.0 mg, 0.20 mmol, 1.0 equiv.), *t*-butyllithium in pentane (0.24 mL, 1.70 M, 0.40 mmol, 2.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0s equiv.), and phenyl trifluoromethanesulfonate (51.1 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25

M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (42.8 mg, 62% yield).

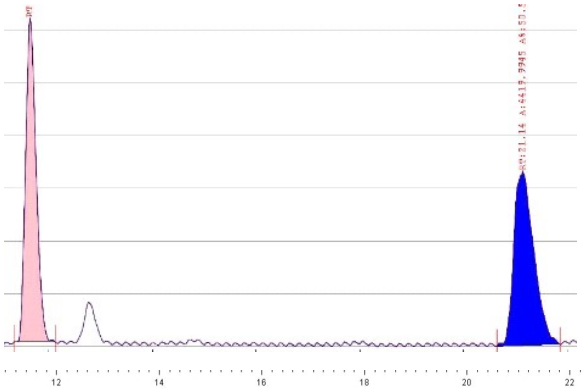
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dt, *J* = 1.7, 0.8 Hz, 1H), 7.46 – 7.37 (m, 2H), 7.36 – 7.28 (m, 4H), 7.25 – 7.20 (m, 1H), 7.08 (d, *J* = 3.1 Hz, 1H), 6.49 (d, *J* = 3.1 Hz, 1H), 5.90 (dt, *J* = 6.0, 3.0 Hz, 1H), 5.48 (dd, *J* = 6.0, 4.0 Hz, 1H), 3.81 (s, 3H), 2.49 (dd, *J* = 14.6, 3.1 Hz, 2H), 2.17 – 2.12 (m, 1H), 1.63 (m, 2H), 1.44 – 1.32 (m, 4H), 0.92 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 201.9, 143.3, 130.8, 129.6, 128.5, 127.7, 126.3, 126.2, 126.1, 123.0, 118.2, 118.1, 115.0, 110.5, 107.4, 99.3, 83.7, 72.6, 31.7, 30.5, 28.2, 27.8, 22.6, 14.1. **IR** (neat) ν_{max} 3650 (m), 2980 (s), 2931 (m), 2361 (m), 2340 (w), 2239 (w), 2225 (w), 2193 (w), 2170 (w), 2156 (m), 1734 (s), 1471 (m), 1371 (s), 1341 (s), 1238 (m), 1163 (s), 1136 (s), 1083 (m), 1024 (w), 956 (w), 821 (w), 765 (m), 727 (m), 699 (m), 668 (w), 576 (w), 536 (m).**HRMS** (DART) for $C_{28}H_{33}NO_3$ $(M+H-H_2O)^+$: Calc'd: 414.2428, found: 414.2428. **$[\alpha]_D^{20}$**: +89.0 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **XX** in two separate reactions and mixing equal amount of product from each reaction.

Chiral SFC (Chiralcel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-1-(1-methyl-1H-indol-5-yl)-4-phenylnona-2,3-dien-1-ol.

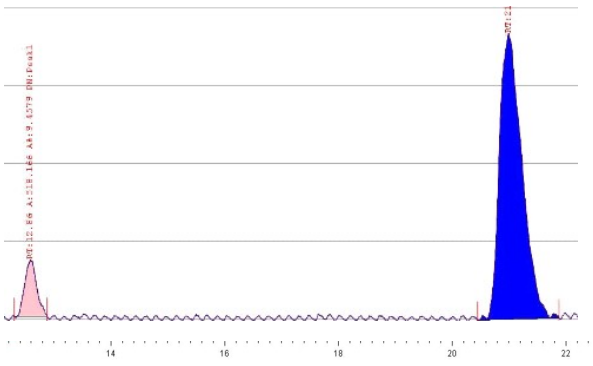
Racemic Material



Peak Info

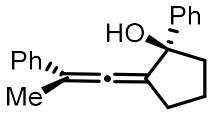
Peak No	% Area	Area	RT (min)
1	49.4212	4318.8294	11.63
2	50.5788	4419.9945	21.14
Total:	100	8738.8239	

Standard Conditions



Peak Info

Peak No	% Area	Area	RT (min)
1	9.4579	518.166	12.86
2	90.5421	4960.5153	21.12
Total:	100	5478.6813	



(*P,R*)-1-phenyl-2-((*S*)-2-phenylprop-1-en-1-ylidene)cyclopentan-1-ol (3.49). The reaction was performed according to the general procedure above (***Method A***) with (E)-4,4,5,5-4,4,5,5-tetramethyl-2-(2-(prop-1-yn-1-yl)cyclopent-1-en-1-yl)-1,3,2-dioxaborolane (**3.50**) (49.6 mg, 0.20 mmol, 1.0 equiv.), phenyllithium in dibutyl ether (0.11 mL, 1.90 M, 0.20 mmol, 1.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), and phenyl trifluoromethanesulfonate (54.3 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (23.8 mg, 43% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55-7.53 (m, 2H), 7.38-7.36 (m, 2H), 7.33-7.28 (m, 4H), 7.25-7.22 (m, 1H), 7.20-7.17 (m, 1H), 2.91-2.86 (m, 1H), 2.74-2.67 (m, 1H), 2.23-2.20 (m, 1H), 2.09-2.09 (m, 2H), 2.02 (s, 1H), 1.95 (s, 3H), 1.89-1.81 (m, 1H), 1.56 (s, 1H). **^{13}C NMR** 199.2, 146.4, 137.3, 128.4, 127.8, 126.8, 126.7, 125.8, 125.4, 114.8, 105.2, 85.1,

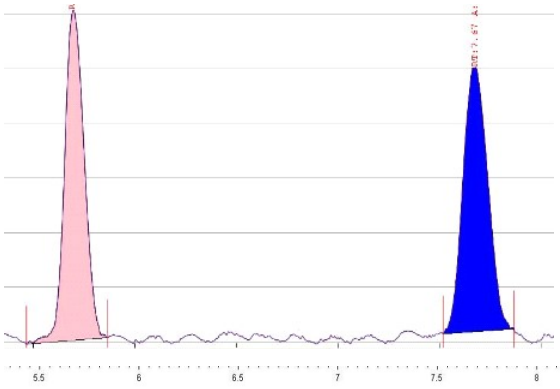
44.5, 30.6, 23.8, 16.3. **IR** (neat) ν_{max} 3507 (m), 3057 (m), 3026 (m), 2960 (s), 2581 (m), 2360 (m), 2342 (m), 2239 (m), 2194 (w), 2155 (w), 1716 (s), 1684 (s), 1598 (m), 1558 (w), 1493 (s), 1683 (s), 1598 (w), 1558 (w), 1493 (s), 1446 (s), 1369 (m), 1237 (w), 1154 (w), 1066 (m), 1027 (m), 955 (w), 909 (w), 759 (s), 698 (s), 668 (w), 622 (w), 594 (w), 568 (w), 558 (w), 534 (w). **HRMS** (DART) for $C_{20}H_{21}O$ $(M+H)^+$: Calc'd: 277.1292, found: 277.1290 $\mathbf{[\alpha]_D^{20}}$: -3.2 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

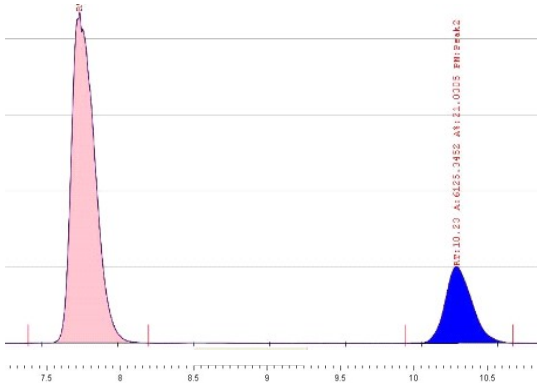
Chiral SFC (Chiralcel OJ-H, 6% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenyl-2-((S)-2-phenylprop-1-en-1-ylidene)cyclopentan-1-ol.

Racemic Material

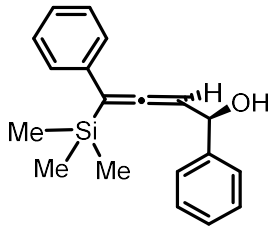


Peak Info			
Peak No	% Area	Area	RT (min)
1	49.6603	806.8995	5.69
2	50.3397	817.9394	7.67
Total:	100	1624.8389	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	78.9695	23000.6936	7.75
2	21.0305	6125.3452	10.23
Total:	100	29126.0388	



(*P*,*R*)-1,4-diphenyl-4-(trimethylsilyl)buta-2,3-dien-1-ol (XX). The reaction was performed according to the general procedure above (***Method C***) with (Z)-4,4,5,5-tetramethyl-2-(non-1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.4**) (50.0 mg, 0.20 mmol, 1.0 equiv.), phenyllithium in dibutyl ether (0.11 mL, 1.90M, 0.20 mmol, 1.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and bromobenzene (37.7 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (37.1 mg, 63% yield).

^{1}H NMR (600 MHz, $CDCl_3$) Major diastereomer: δ 7.44-7.19 (m, 10H), 5.55-5.46 (m, 1H), 5.39-5.34 (m, 1H), 2.07 (d, *J = 4.2* Hz, 2H), 0.19 (s, 9H). Minor diastereomer: δ 7.44-7.19 (m, 10H), 5.55-5.46 (m, 1H), 5.39-5.34 (m, 1H), 2.05 (d, *J* = 4.0 Hz, 1H), 0.22 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) Major diasteromer: δ 206.5, 143.5, 137.0, 128.64, 128.56, 127.8, 126.6, 126.2, 103.9, 92.5, 72.8, -0.3. Minor diastereomer: δ 206.5, 143.4, 137.0, 128.6, 128.5, 127.8, 126.0, 126.2, 104.0, 92.5, 72.7, -0.3. **IR** (neat) ν_{max} 3335 (br, s), 2957 (m), 2361 (w), 1927 (s), 1596 (m), 1491 (s), 1453 (m), 1249 (s), 1030 (m), 972 (m), 763 (s), 670 (s). **HMRS** (DART) for $C_{19}H_{21}Si$ $(M+H-H_2O)^+$: Calc'd: 277.1407, found: 277.1399. **$[\alpha]_D^{20}$**: +1.3 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

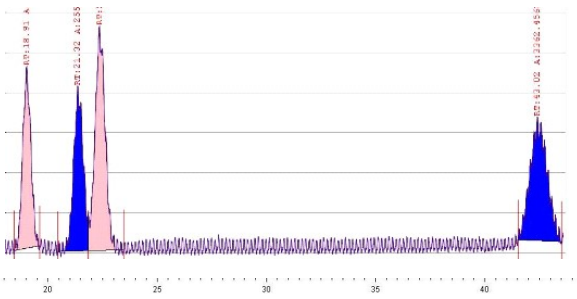
Analysis of Stereochemistry:

Both diastereomic ratio and enantiomeric ratio were determined by chiral SFC. The mixture of racemic diastereomers was prepared by using (E)-4,4,5,5-tetramethyl-2-(non-

1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.3**) as borylenyne. Both enantiomers of ligand **L1.1** were used in two separate reactions and equal amount of product from each reaction were mixed together.

Chiral SFC (Chiralcel ODR-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (E)-trimethyl(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yn-1-yl)silane.

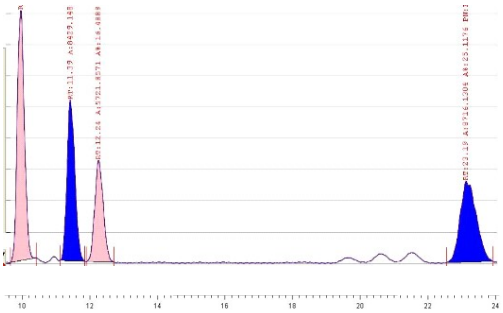
Mixture of Racemic Diastereomers



Peak Info

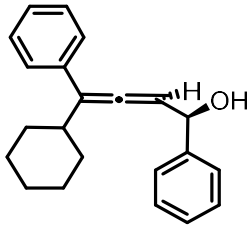
Peak No	% Area	Area	RT (min)
1	19.9167	2397.1738	18.91
2	21.1927	2550.7495	21.32
3	30.9539	3725.6023	22.34
4	27.9367	3362.4563	43.02
Total:	100	12035.9819	

Standard Conditions



Peak Info

Peak No	% Area	Area	RT (min)
1	34.103	11834.1765	9.92
2	24.2906	8429.1483	11.39
3	16.4889	5721.8571	12.24
4	25.1176	8716.1304	23.19
Total:	100.0001	34701.3123	



(*P*,1*R*)-4-cyclohexyl-1,4-diphenylbuta-2,3-dien-1-ol (3.51). The reaction was performed according to the general procedure above (***Method C***) with (Z)-2-(4-cyclohexylbut-1-en-3-yn-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-3.5**) (52.0 mg, 0.20 mmol, 1.0 equiv.), 5-bromo-1-methylindole (42.0 mg, 0.20 mmol, 1.0 equiv.), *t*-butyllithium in pentane (0.24 mL, 1.70 M, 0.40 mmol, 2.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0s equiv.), and

phenyl trifluoromethanesulfonate (51.1 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (31.7 mg, 52% yield).

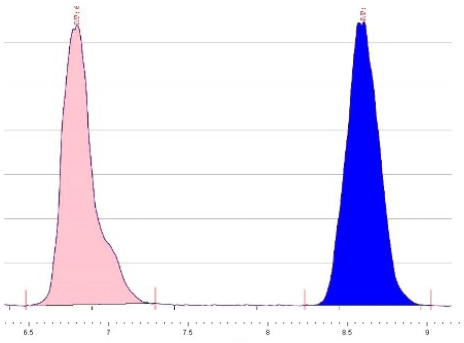
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 2H), 7.39 – 7.28 (m, 7H), 7.23 – 7.19 (m, 1H), 5.83 (d, *J* = 5.8 Hz, 1H), 5.35 (d, *J* = 5.8, 4.0 Hz, 1H), 2.46 (m, 1H), 2.15 (d, *J* = 4.0 Hz, 1H), 1.90 (m, 2H), 1.83 – 1.76 (m, 2H), 1.72 (dtt, *J* = 13.1, 3.4, 1.7 Hz, 1H), 1.41 – 1.33 (m, 2H), 1.25 – 1.12 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 201.8, 143.3, 136.3, 128.7, 128.6, 127.9, 127.2, 126.7, 126.4, 116.6, 100.4, 72.7, 38.2, 33.4, 33.0, 26.83, 26.79, 26.5. **IR** (neat) ν_{max} 3372 (br, w), 3028 (w), 2923 (m), 2850 (m), 1945 (w), 1596 (w), 1448 (m), 1184 (w) ,1030 (m) ,889 (m) ,765 (m), 566 (w) cm^{-1}. **HRMS** (DART) for $C_{22}H_{23}$ $[M+H-H_2O]^+$: Calc'd: 287.1797, found: 287.1794. **$[\alpha]_D^{20}$**: +60.0 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

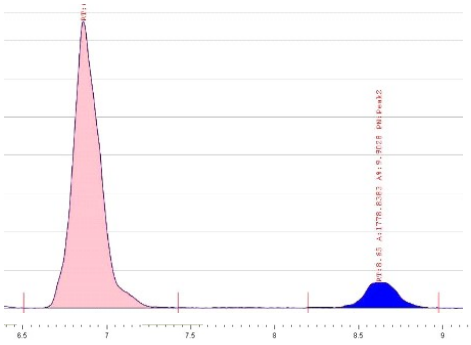
Chiral SFC (Chiralcel ODR-H, 9% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R)-4-cyclohexyl-1,4-diphenylbuta-2,3-dien-1-ol.

Racemic Material

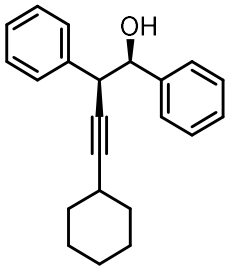


Peak Info			
Peak No	% Area	Area	RT (min)
1	48.3941	16972.1104	6.91
2	51.6059	18098.4743	8.65
Total:	100	35070.5847	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	90.0972	16184.1762	6.93
2	9.9028	1778.8383	8.65
Total:	100	17963.0145	



(1*R*,2*R*)-4-cyclohexyl-1,2-diphenylbut-3-yn-1-ol (3.52). The title compound was observed as a by-product of the reaction above with (Z)-2-(4-cyclohexylbut-1-en-3-yn-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**S-3.5**) (52.0 mg, 0.20 mmol, 1.0 equiv.), 5-bromo-1-methylindole (42.0 mg, 0.20 mmol, 1.0 equiv.), *t*-butyllithium in pentane (0.24 mL, 1.70 M, 0.40 mmol, 2.0 equiv.), Et_2O (0.4 mL), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0s equiv.), and phenyl trifluoromethanesulfonate (51.1 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (12.2 mg, 20% yield).

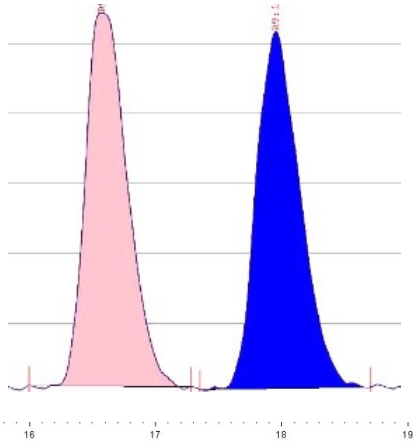
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.13 (m, 10H), 4.72 (dd, *J* = 6.5, 3.7 Hz, 1H), 3.93 (dd, *J* = 6.5, 2.1 Hz, 1H), 2.78 (d, *J* = 3.7 Hz, 1H), 2.49 (m, 1H), 1.84 (m, 2H), 1.72 (m, 2H), 1.57 – 1.47 (m, 3H), 1.35 (d, *J* = 7.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.0, 138.4, 128.5, 128.2, 127.8, 127.6, 127.1, 126.6, 90.9, 78.3, 48.2, 32.9, 30.3, 29.7, 29.2, 25.9, 24.8. **IR** (neat) ν_{max} 3444 (br, w), 3061 (m), 3028 (w), 2926 (s), 2852 (m), 1672 (w), 1601 (w), 1449 (m), 1191 (w), 1028 (w), 889 (w), 754 (m), 541 (w) cm^{-1}. **HRMS** (DART) for $C_{22}H_{25O}$ $[M+H-H_2O]^+$: Calc'd: 305.1907, found: 305.1899. **$[\alpha]_D^{20}$**: +23 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

Chiral SFC (Chiralcel OJ-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R,2R)-4-cyclohexyl-1,2-diphenylbut-3-yn-1-ol.

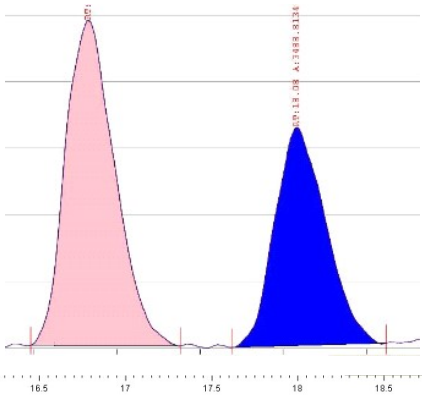
Racemic Material



Peak Info

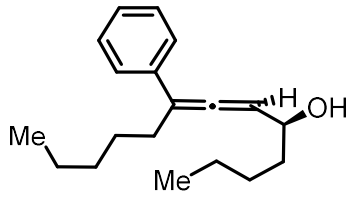
Peak No	% Area	Area	RT (min)
1	50.2604	5857.0688	16.61
2	49.7396	5796.3731	17.91
Total:	100	11653.4419	

Standard Conditions



Peak Info

Peak No	% Area	Area	RT (min)
1	59.0501	5030.8965	16.83
2	40.9499	3488.8134	18.08
Total:	100	8519.7099	



(*P*,5*S*)-8-phenyltrideca-6,7-dien-5-ol (3.67). The reaction was performed according to the general procedure above (***Method D***) with 1,6-dimethyl-8-((Z)-non-1-en-3-yn-1-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole **(S-3.7)** (68.9 mg, 0.20 mmol, 1.0 equiv.), a solution of *n*-butylmagnesium chloride in THF (0.10 mL, 2.0 M, 0.20 mmol, 1.0 equiv.), DMSO (219 mg, 14.0 equiv.), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.6 mmol, 2.0 equiv.), sodium trifluoromethanesulfonate (103 mg, 0.60 mmol, 3.0 equiv.), and phenyl trifluoromethanesulfonate (54.3 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (35.4 mg, 65% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.7 Hz, 2H), 7.32 (t, *J = 7.7 Hz,* 2H), 7.21 (m, 1H), 5.62 (dt, *J* = 6.1, 3.1 Hz, 1H), 4.26 (m, 1H), 2.50-2.41 (m, 1H), 1.73-1.60 (m, 3H), 1.58-1.53 (m, 2H), 0.92 (t, *J* = 7.0 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.0, 136.7, 128.3, 127.0, 126.1, 109.1, 99.3, 70.5, 37.5, 31.8, 30.2, 27.9, 27.8, 22.8, 22.7, 14.21, 14.18. **IR** (neat) ν_{max} 3352 (br, s), 2955 (s), 2859 (s), 1946 (w), 1597 (w), 1494 (m) ,1378 (w), 1009 (m), 805 (w), 693 (s), 648 (w) cm^{-1}. **HRMS** (DART) for $C_{19}H_{29}O$ $(M+H)^+$: Calc'd: 273.2213, found: 273.2234. **$[\alpha]_D^{20}$**: +49.0 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

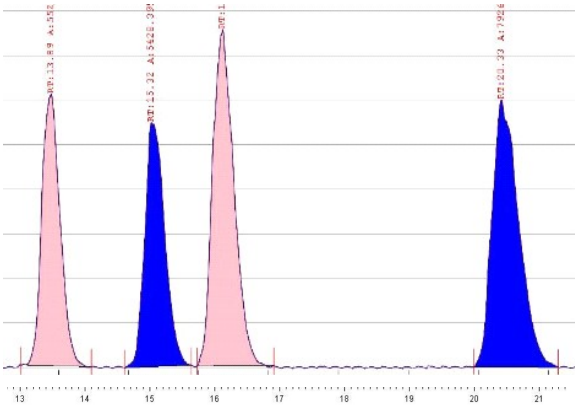
Analysis of Stereochemistry:

Both diastereomic ratio and enantiomeric ratio were determined by chiral SFC. The mixture of racemic diastereomers was prepared by using (E)-4,4,5,5-tetramethyl-2-(non-

1-en-3-yn-1-yl)-1,3,2-dioxaborolane (**S-3.1**) as borylenyne. Both enantiomers of ligand **L1.1** were used in two separate reactions and equal amount of product from each reaction were mixed together.

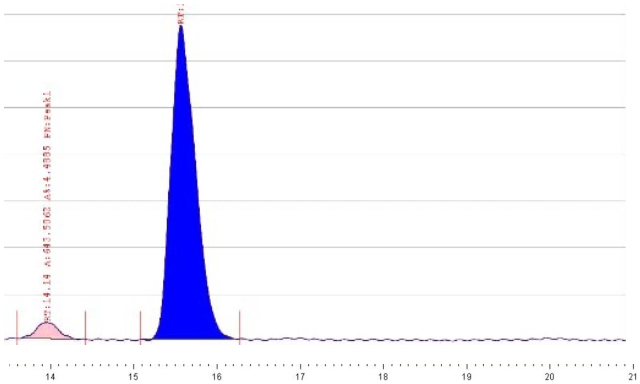
Chiral SFC (Chiralcel OD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (5S)-8-phenyltrideca-6,7-dien-5-ol.

Mixture of Racemic Diastereomers

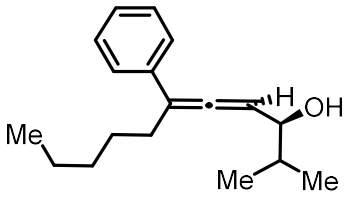


Peak Info			
Peak No	% Area	Area	RT (min)
1	20.5949	5524.7457	13.89
2	20.2358	5428.3956	15.32
3	29.6225	7946.4616	16.34
4	29.5468	7926.1428	20.33
Total:	100	26825.7457	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	4.4885	643.5062	14.14
2	95.5115	13693.3154	15.73
Total:	100	14336.8216	



(*P*,3*S*)-2-methyl-6-phenylundeca-4,5-dien-3-ol (3.70). The reaction was performed according to the general procedure above (***Method D***) with 1,6-dimethyl-8-((Z)-non-1-en-3-yn-1-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole **(S-3.7)** (68.9 mg, 0.20 mmol, 1.0 equiv.), a solution of isopropylmagnesium bromide in THF (0.27 mL, 0.75 M, 0.20 mmol, 1.0 equiv.), DMSO (219 mg, 14.0 equiv.), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.),

cesium fluoride (60.8 mg, 0.6 mmol, 2.0 equiv.), sodium trifluoromethanesulfonate (103 mg, 0.60 mmol, 3.0 equiv.), and phenyl trifluoromethanesulfonate (54.3 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (32.6 mg, 63% yield).

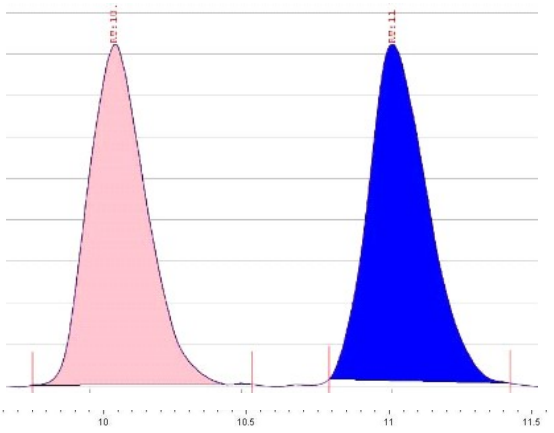
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.17 (m, 5H), 5.63-5.58 (m, 1H), 4.08-4.01 (m, 1H), 2.49-2.38 (m, 2H), 1.82 (hept, J = 6.6 Hz, 1H), 1.62-1.51 (m, 3H), 1.43-1.30 (m, 4H), 1.02-0.97 (m, 6H), 0.89 (t, J = 6.9 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.3, 136.7, 128.5, 127.0, 126.2, 109.3, 97.5, 75.2, 34.4, 31.8, 30.3, 28.0, 22.7, 18.5, 17.9, 14.2. **IR** (neat) ν_{max} 3409 (br, m), 2956 (s), 2928 (s), 2871 (m), 2363 (w), 1944 (w), 1597 (w), 1452 (m), 1379 (w), 1019 (m), 756 (m), 693 (s) cm^{-1}. **HRMS** (DART) for $C_{18}H_{27}O$ $(M+H)^+$: Calc'd: 259.2056, found: 259.2059. **$[\alpha]_D^{20}$**: +33.0 (c = 0.50, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

Chiral SFC (Chiralcel OD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (3S)-2-methyl-6-phenylundeca-4,5-dien-3-ol.

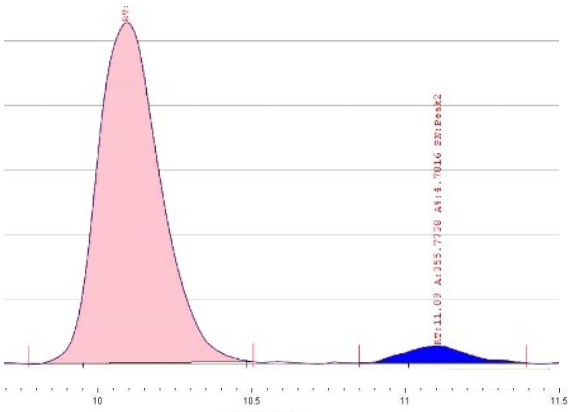
Racemic Material



Peak Info

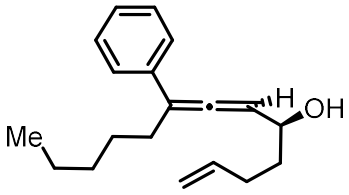
Peak No	% Area	Area	RT (min)
1	49.8562	5488.0228	10.08
2	50.1438	5519.6867	11
Total:	100	11007.7095	

Standard Conditions



Peak Info

Peak No	% Area	Area	RT (min)
1	95.2184	7084.7285	10.13
2	4.7816	355.7738	11.09
Total:	100	7440.5023	



(*P*,5*S*)-8-phenyltrideca-1,6,7-trien-5-ol (3.69). The reaction was performed according to the general procedure above (***Method D***) with 1,6-dimethyl-8-((Z)-non-1-en-3-yn-1-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole **(S-3.7)** (68.9 mg, 0.20 mmol, 1.0 equiv.), a solution of 3-butenylmagnesium bromide in THF (0.40 mL, 0.5 M, 0.20 mmol, 1.0 equiv.), DMSO (219 mg, 14.0 equiv.), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.6 mmol, 2.0 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and phenyl trifluoromethanesulfonate (54.3 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (30.3 mg, 56% yield).

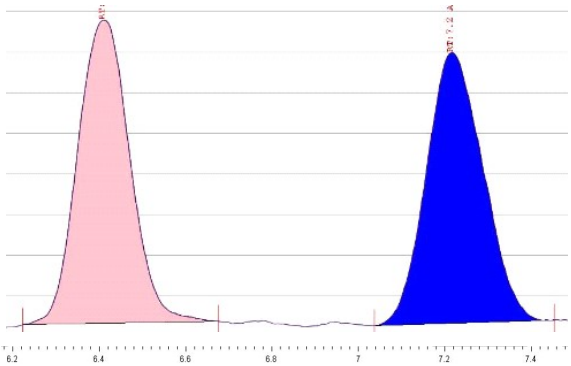
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.39 (m, 2H), 7.34-7.30 (m, 2H), 7.24-7.20 (m, 1H), 5.91-5.80 (m, 1H), 5.64 (dt, *J* = 5.9, 3.0 Hz, 1H), 2.51-2.39 (m, 2H), 2.30-2.17 (m, 2H), 1.81-1.63 (m, 3H), 1.60-1.52 (m, 2H), 1.42-1.30 (m, 4H), 0.91 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.1, 138.4, 136.6, 128.5, 127.0, 126.1, 115.0, 109.4, 99.1, 69.8, 36.9, 31.8, 30.2, 29.9, 27.9, 22.7, 14.2. **IR** (neat) ν_{max} 3356 (br, s), 2955 (m), 2927 (s), 2857 (m), 2360 (w), 1944 (w), 1641 (m), 1450 (m), 1073 (m), 1015 (m), 910 (m), 757 (m), 693 (s), 648 (w) cm^{-1}. **HRMS** (DART) for $C_{19}H_{27}O$ $(M+H)^+$: Calc'd: 271.2056, found: 271.2051. **$[\alpha]_D^{20}$**: +78.0 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

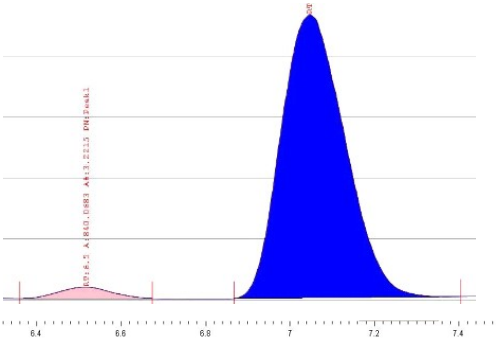
Chiral SFC (Chiralcel OD-H, 6% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (5S)-8-phenyltrideca-1,6,7-trien-5-ol.

Racemic Material

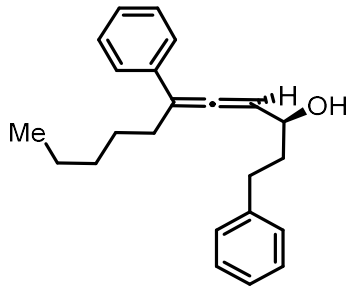


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.6257	3092.7443	6.4
2	49.3743	3016.3007	7.2
Total:	100	6109.045	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	3.2215	840.0683	6.5
2	96.7785	25236.5662	7.05
Total:	100	26076.6345	



(*P*,3*S*)-1,6-diphenylundeca-4,5-dien-3-ol (3.68). The reaction was performed according to the general procedure above (***Method D***) with 1,6-dimethyl-8-((Z)-non-1-en-3-yn-1-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole **(S-3.7)** (68.9 mg, 0.20 mmol, 1.0 equiv.), a solution of phenethylmagnesium chloride in THF (0.20 mL, 1.0 M, 0.20 mmol, 1.0 equiv.), DMSO (219 mg, 14.0 equiv.), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.6 mmol, 2.0 equiv.), sodium trifluoromethanesulfonate (103 mg, 0.60 mmol, 3.0 equiv.), and phenyl trifluoromethanesulfonate (54.3 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (37.8 mg, 59% yield).

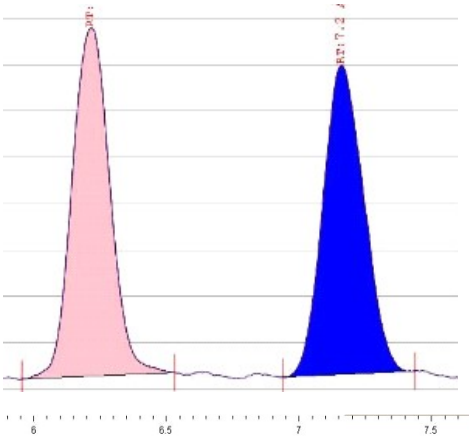
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.09 (m, 10H), 5.68 -5.62 (m, 1H), 4.33-4.24 (m, 1H), 2.86-2.69 (m, 2H), 2.50-2.40 (m, 2H), 1.99-1.89 (m, 2H), 1.64-1.46 (m, 3H), 1.42-1.29 (m, 4H), 0.89 (t, J = 6.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.1, 142.0, 136.6, 128.61, 128.58, 128.5, 127.1, 126.2, 126.0, 109.6, 99.1, 69.6, 39.4, 31.9, 31.8, 30.2, 27.9, 22.7, 14.3. **IR** (neat) ν_{max} 3409 (br, s), 2956 (s), 2928 (s), 2363 (w), 1944 (w), 1597 (m), 1494 (m), 1466 (m), 1379 (m), 1019 (m), 756 (m), 693 (s) cm^{-1}. **HRMS** (DART) for $C_{23}H_{29}O$ $(M+H)^+$: Calc'd: 321.2213, found: 321.2220. **$[\alpha]_D^{20}$**: +82.0 (c = 0.50, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

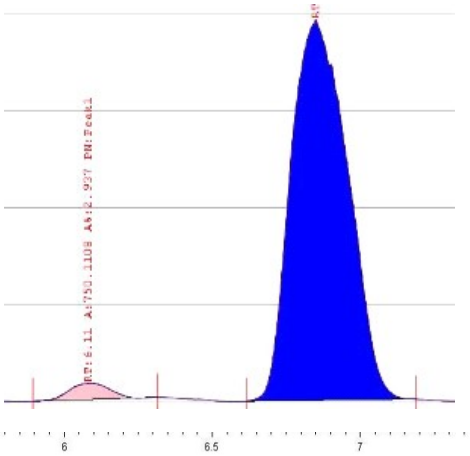
Chiral SFC (Chiralcel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (5S)- (3S)-1,6-diphenylundeca-4,5-dien-3-ol.

Racemic Material

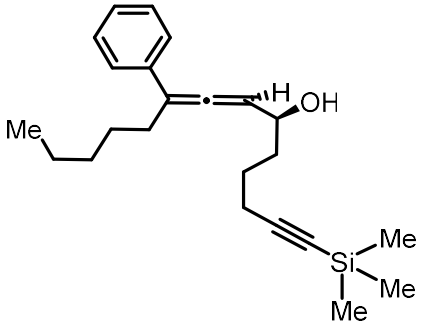


Peak Info			
Peak No	% Area	Area	RT (min)
1	51.0202	3135.5387	6.4
2	48.9798	3010.1391	7.2
Total:	100	6145.6778	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	2.937	750.1108	6.11
2	97.063	24789.4938	6.84
Total:	100	25539.6046	



(*P*,6*S*)-9-phenyl-1-(trimethylsilyl)tetradeca-7,8-dien-1-yn-6-ol (3.72). The reaction was performed according to the general procedure above (***Method D***) with 1,6-dimethyl-8-((Z)-non-1-en-3-yn-1-yl)-6b,9a-dihydroacenaphtho[1,2-

d][1,3,2]dioxaborole (**S-3.7**) (68.9 mg, 0.20 mmol, 1.0 equiv.), a solution of (5-(trimethylsilyl)pent-4-yn-1-yl)magnesium bromide in THF (0.35 mL, 0.57 M, 0.20 mmol, 1.0 equiv.), DMSO (219 mg, 14.0 equiv.), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.6 mmol, 2.0 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and phenyl trifluoromethanesulfonate (54.3 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (46.8 mg, 66% yield).

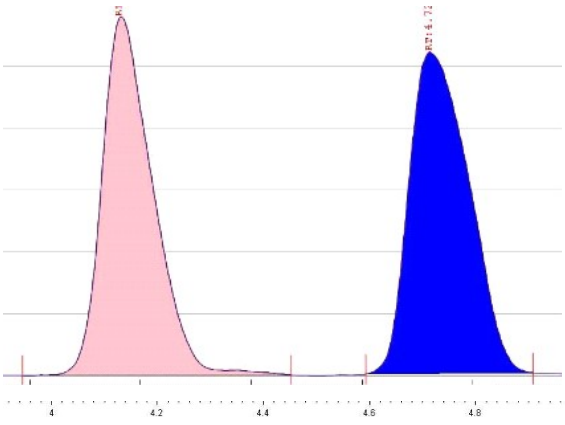
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.38 (m, 2H), 7.34-7.30 (m, 2H), 7.23-7.19 (m, 1H), 5.63 (dt, *J* = 6.0, 3.9 Hz, 1H), 4.33-4.25 (m, 2H), 2.49-2.40 (m, 2H), 2.28 (t, *J* = 7.0 Hz, 2H), 1.79-1.67 (m, 4H), 1.65 (d, *J* = 3.9 Hz, 1H), 1.58-1.53 (m, 2H), 1.42-1.31 (m, 4H), 0.91 (t, *J* = 7.1 Hz, 3H), 0.14 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.0, 136.5, 128.6, 127.1, 126.1, 109.4, 107.2, 99.1, 85.0, 70.0, 36.8, 31.8, 30.1, 27.9, 24.8, 22.7, 19.9, 14.3, 0.3. **IR** (neat) ν_{max} 3356 (br, m), 2956 (m), 2928 (m), 2362 (w), 2173 (m), 1249 (m), 1073 (m), 842 (s), 759 (m), 694 (m) cm^{-1}. **HRMS** (DART) for $C_{23}H_{35}OSi$ $(M+H)^+$: Calc'd: 355.2452, found: 355.2448. **$[\alpha]_D^{20}$**: +92.0 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

Chiral SFC (Chiralcel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (6S)-9-phenyl-1-(trimethylsilyl)tetradeca-7,8-dien-1-yn-6-ol.

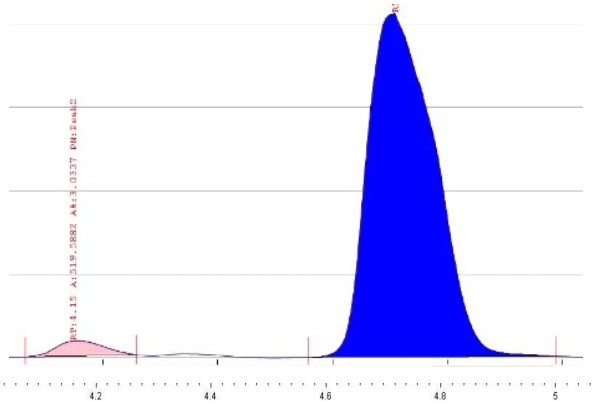
Racemic Material



Peak Info

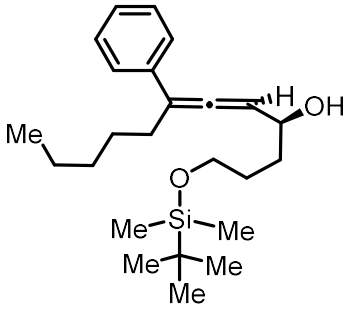
Peak No	% Area	Area	RT (min)
1	48.6434	7334.8164	4.16
2	51.3566	7743.9305	4.72
Total:	100	15078.7469	

Standard Conditions



Peak Info

Peak No	% Area	Area	RT (min)
1	3.0337	519.5882	4.15
2	96.9663	16607.8557	4.71
Total:	100	17127.4439	



(*P*,4*S*)-1-((tert-butyldimethylsilyl)oxy)-7-phenyldodeca-5,6-dien-4-ol (3.73). The reaction was performed according to the general procedure above (***Method D***) with 1,6-dimethyl-8-((Z)-non-1-en-3-yn-1-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (**S-3.7**) (68.9 mg, 0.20 mmol, 1.0 equiv.), a solution of (3-((*tert*-butyldimethylsilyl)oxy)propyl)magnesium bromide in THF (0.44 mL, 0.45 M, 0.20 mmol, 1.0 equiv.), DMSO (219 mg, 14.0 equiv.), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.6 mmol, 2.0 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and phenyl trifluoromethanesulfonate (54.3 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25

M). The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (48.2 mg, 62% yield).

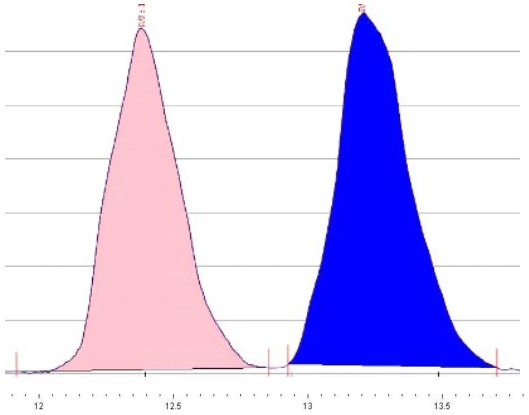
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.38 (m, 2H), 7.33-7.28 (m, 2H), 7.22-7.18 (m, 1H), 5.64 (dt, *J* = 6.0, 4.0 Hz, 1H), 4.32-4.27 (m, 1H), 3.67 (t, *J* = 5.8 Hz, 2H), 2.50 (d, *J* = 4.0 Hz, 1H), 2.47-2.37 (m, 2H), 1.82-1.64 (m, 4H), 1.59-1.51 (m, 2H), 1.41-1.31 (m, 4H), 0.94-0.86 (m, 12H), 0.06 (s, 6H) . **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.1, 136.7, 128.5, 126.9, 126.1, 108.8, 99.3, 70.2, 63.4, 34.5, 31.8, 30.1, 29.1, 27.9, 26.1, 22.7, 18.5, 14.3, -5.2. **IR** (neat) ν_{max} 3409 (br, w), 2954 (s), 2928 (s), 2857 (m), 2363 (w), 1944 (w), 1675 (w), 1463 (m), 1255 (m), 1098 (s), 1006 (m), 835 (s), 775 (m), 693 (m) cm^{-1}. **HRMS** (DART) for $C_{24}H_{39}OSi$ $(M+H-H_2O)^+$: Calc'd: 371.2765, found: 371.2756. **[α]$_D^{20}$**: +70.2 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

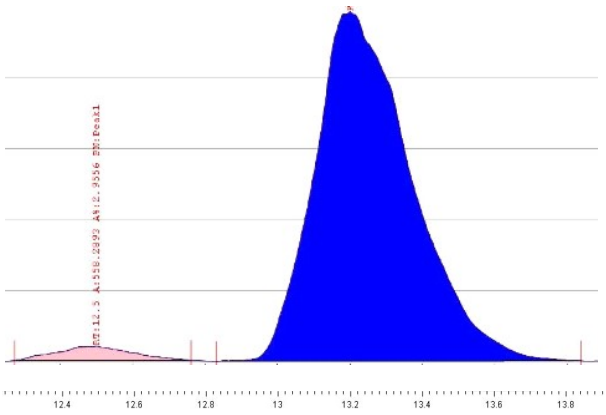
Chiral SFC (Chiralcel OD-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (4S)-1-((tert-butyldimethylsilyl)oxy)-7-phenyldodeca-5,6-dien-4-ol.

Racemic Material

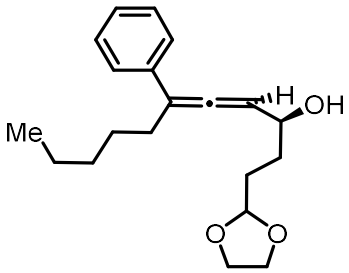


Peak Info			
Peak No	% Area	Area	RT (min)
1	47.2561	5217.2549	12.49
2	52.7439	5823.1315	13.24
Total:	100	11040.3864	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	2.9556	558.2893	12.5
2	97.0444	18330.9869	13.2
Total:	100	18889.2762	



(*P*,3*S*)-1-(1,3-dioxolan-2-yl)-6-phenylundeca-4,5-dien-3-ol (3.71). The reaction was performed according to the general procedure above (***Method D***) with 1,6-dimethyl-8-((Z)-non-1-en-3-yn-1-yl)-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (**S-3.7**) (68.9 mg, 0.20 mmol, 1.0 equiv.), as solution of (1,3-dioxan-2-ylethyl)magnesium bromide solution in THF (0.40 mL, 0.50 M, 0.20 mmol, 1.0 equiv.), DMSO (219 mg, 14.0 equiv.), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.6 mmol, 2.0 equiv.), potassium trifluoromethanesulfonate (113 mg, 0.60 mmol, 3.0 equiv.), and phenyl trifluoromethanesulfonate (54.3 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M).

The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (41.8 mg, 66% yield).

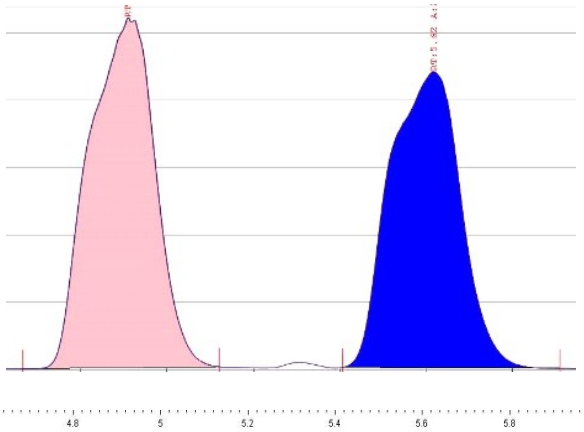
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.19 (m, 2H), 5.68-5.54 (m, 1H), 4.62-4.54 (m, 1H), 4.32-4.23 (m, 1H), 4.10 (dd, *J* = 11.5, 4.8 Hz, 1H), 3.75 (t, *J* = 2.7 Hz, 2H), 2.48-2.39 (m, 2H), 2.32 (s, 1H), 1.84-1.69 (m, 3H), 1.58-1.50 (m, 2H), 1.41-1.29 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 202.1, 136.7, 128.5, 126.9, 109.1, 102.2, 99.1, 70.1, 67.1, 32.0, 31.8, 31.4, 30.1, 27.9, 25.9, 22.7, 14.3. **IR** (neat) ν_{max} 3409 (br, m), 2955 (s), 2927 (s), 2855 (m), 2362 (w), 1944 (w), 1597 (w), 1494 (m), 1140 (s), 1088 (m), 998 (s), 759 (m), 694 (m) cm^{-1}. **HRMS** (DART) for $C_{21}H_{29}O_2$ $(M+H)^+$: Calc'd: 313.2162, found: 313.2160. **$[\alpha]_D^{20}$**: +48.2 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

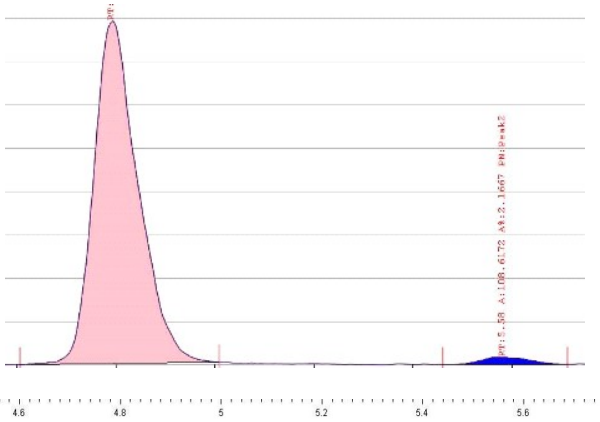
Chiral SFC (Chiralcel OJ-H, 9% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (4S)-1-((tert-butyldimethylsilyl)oxy)-7-phenyldodeca-5,6-dien-4-ol.

Racemic Material

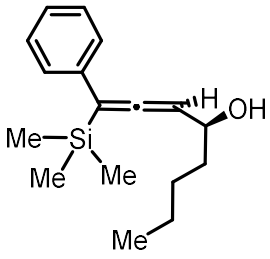


Peak Info			
Peak No	% Area	Area	RT (min)
1	52.3078	27415.8272	4.91
2	47.6922	24996.6702	5.62
Total:	100	52412.4974	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	97.8333	4904.4945	4.79
2	2.1667	108.6172	5.58
Total:	100	5013.1117	



(*P*,4*S*)-1-phenyl-1-(trimethylsilyl)octa-1,2-dien-4-ol (3.74). The reaction was performed according to the general procedure above (***Method D***) with ((Z)-4-((6b,9a)-1,6-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)but-3-en-1-yn-1-yl)trimethylsilane (**S-3.13**) (69.3 mg, 0.20 mmol, 1.0 equiv.), a solution of *n*-butylmagnesium chloride in THF (0.10 mL, 2.0 M, 0.20 mmol, 1.0 equiv.), DMSO (219 mg, 14.0 equiv.), $Pd(OAc)_2$ (1.34 mg, 0.006 mmol, 0.030 equiv.), (*Sp*,*Sp*)-**L1.1** (7.58 mg, 0.0072 mmol, 0.036 equiv.), cesium fluoride (60.8 mg, 0.6 mmol, 2.0 equiv.), sodium trifluoromethanesulfonate (103 mg, 0.60 mmol, 3.0 equiv.), and phenyl trifluoromethanesulfonate (54.3 mg, 0.24 mmol, 1.2 equiv.) in THF (0.80 mL, 0.25 M).

The crude mixture was purified by column chromatography (10% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (19.2 mg, 35% yield).

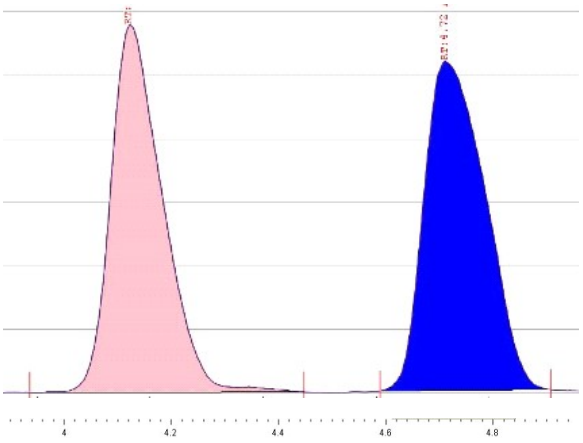
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.27 (m, 4H), 7.23-7.17 (m, 1H), 5.28 (d, *J* = 6.4 Hz, 1H), 4.29-4.21 (m, 1H), 1.66-1.31 (m, 6H), 0.90 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 206.3, 137.2, 128.6, 127.7, 126.5, 103.2, 92.2, 70.5, 37.7, 28.0, 22.7, 14.2, -0.2. **IR** (neat) ν_{max} 3335 (br, m), 2957 (m), 2361 (w), 1927 (m), 1596 (w), 1491 (m), 1453 (w), 1249 (m), 1030 (m), 918 (m), 763 (m), 697 (s), 623 (w) cm^{-1}. **HRMS** (DART) for $C_{17}H_{27}OSi$ $(M+H)^+$: Calc'd: 275.1826, found: 275.1821. **$[\alpha]_D^{20}$**: +39.3 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using both enantiomers of ligand **L1.1** in two separate reactions and mixing equal amount of product from each reaction.

Chiral SFC (Chiralcel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (4S)-1-phenyl-1-(trimethylsilyl)octa-1,2-dien-4-ol.

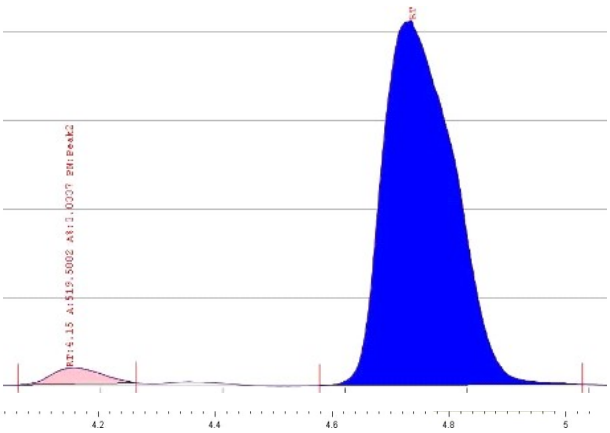
Racemic Material



Peak Info

Peak No	% Area	Area	RT (min)
1	48.6434	7334.8164	4.16
2	51.3566	7743.9305	4.72
Total:	100	15078.7469	

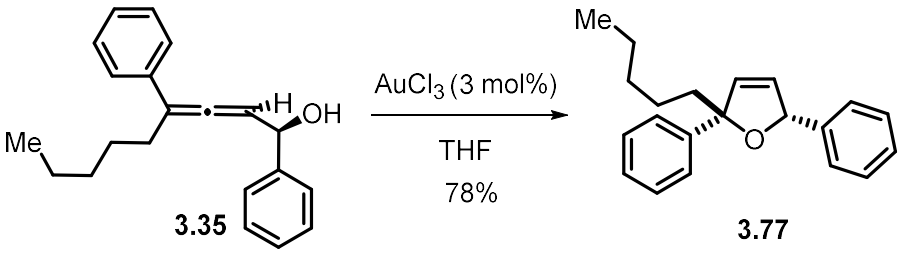
Standard Conditions



Peak Info

Peak No	% Area	Area	RT (min)
1	3.0337	519.5882	4.15
2	96.9663	16607.8557	4.71
Total:	100	17127.4439	

3.4.5 Procedures and Characterization for Transformation of α-Allenols



(2*S*,5*R*)-2-pentyl-2,5-diphenyl-2,5-dihydrofuran (3.77). The title compound was prepared according to the procedure reported in the literature.[166]

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 – 7.27 (m, 10H), 6.23 (dt, *J* = 6.0, 3.0 Hz, 1H), 5.87 (dd, *J* = 6.0, 1.4 Hz, 1H), 5.80 (t, *J* = 2.0 Hz, 1H), 2.06 – 1.93 (m, 2H), 1.46 – 1.34 (m,

[166] Hoffmann-Röder, A.; Krause, N. *Org. Lett.* **2001**, *3,* 2537.

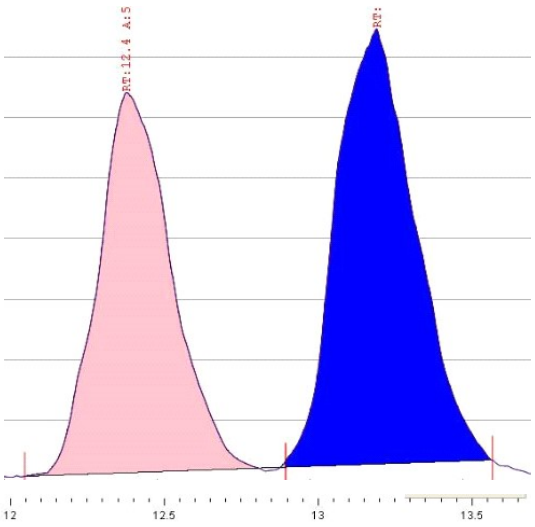
1H), 1.26 (m, 5H), 0.87 – 0.81 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 145.6, 141.3, 133.8, 129.3, 128.4, 128.2, 127.8, 126.9, 126.6, 125.0, 93.8, 86.8, 42.3, 32.1, 24.0, 22.5, 14.0. **IR** (neat) ν_{max} 3335 (br, m), 2957 (m), 2361 (w), 1927 (m), 1596 (w), 1491 (m), 1453 (w), 1249 (m), 1030 (m), 918 (m), 763 (m), 697 (s), 623 (w) cm^{-1}. **HRMS** (DART) for $C_{21}H_{25}O$ $(M+H)^+$: Calc'd: 293.1899, found: 293.1900. **$[\alpha]_D^{20}$**: +92.2 (c = 0.50, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using racemic starting material in the above procedure. The racemic starting material was prepared by using both enantiomers of ligand **L1.1** in two separate conjunctive coupling reactions and mixing equal amount of product from each reaction.

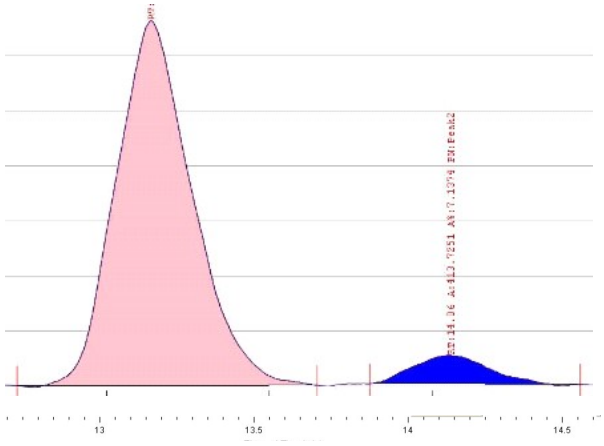
Chiral SFC (Chiralcel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (2S,5R)-2-pentyl-2,5-diphenyl-2,5-dihydrofuran.

Racemic Material

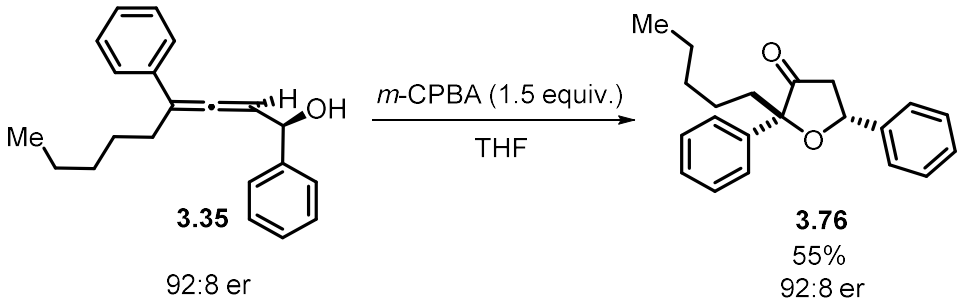


Peak Info			
Peak No	% Area	Area	RT (min)
1	44.8404	5246.6761	12.4
2	55.1596	6454.0995	13.22
Total:	100	11700.7756	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	92.8626	5382.8385	13.14
2	7.1374	413.7251	14.06
Total:	100	5796.5636	



3.35

92:8 er

3.76

55%

92:8 er

(2*R*,5*R*)-2-pentyl-2,5-diphenyldihydrofuran-3(2H)-one (3.76). In an oven-dried 2-dram vial was added (1*R*)-1,4-diphenylnona-2,3-dien-1-ol (**3.35**) (35 mg, 0.12 mmol, 1.0 equiv.) and THF (0.5 mL). The solution was cooled to 0 ºC and *m*-CPBA (31.1 mg, 0.18 mmol, 1.5 equiv.) was added in one portion. The reation mixture was allowed to warm up to room temperature and stir for 5 hours at which point it was quenched with aqueous saturated sodium thiosulfate solution (0.5 mL). The aqueous phase was extracted with Et_2O (3 x 0.5mL). The combined organic phase was dried with magnesium sulfate, filtered, and concentrated in rotavap. The crude mixture was purified by column chromatography (5%

EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (20.4 mg, 55% yield).

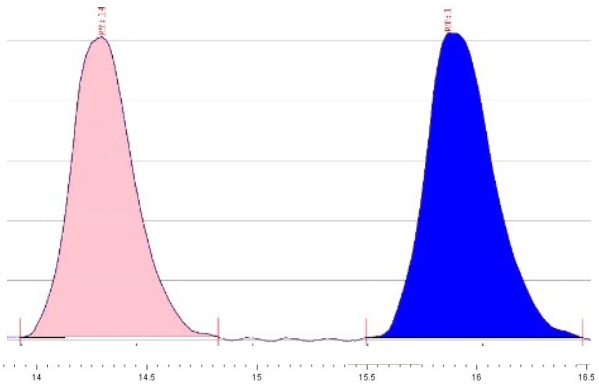
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.27 (m, 10H), 5.18 (dd, *J* = 10.4. 6.1 Hz, 1H), 2.82 (dd, *J* = 18.3, 6.1 Hz, 1H), 2.51 (dd, *J* = 18.3, 10.4 Hz, 1H), 2.04-1.87 (m, 2H), 1.48-1.21 (m, 6H), 0.84 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 214.4, 140.8, 138.3, 128.9, 128.78, 128.75, 128.4, 127.8, 126.2, 87.8, 74.9, 45.4, 40.6, 32.0, 23.8, 22.6, 14.1. **IR** (neat) ν_{max} 2927 (s), 1752 (s), 1600 (w), 1447 (m), 1105 (s), 758 (s), 702 (s) cm^{-1}. **HRMS** (DART) for $C_{21}H_{25}O_2$ $[M+H]^+$: Calc'd: 309.1849, found: 293.1849. **$[\alpha]_D^{20}$**: +80.2 (*c* = 0.50, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The diastereomic ratio was determined by ^{13}C NMR analysis of product to be >20:1 and enantiomeric ratio were determined by chiral SFC. Racemic compound was prepared by using racemic starting material in the above procedure. The racemic starting material was prepared by using both enantiomers of ligand **L1.1** in two separate conjunctive coupling reactions and mixing equal amount of product from each reaction.

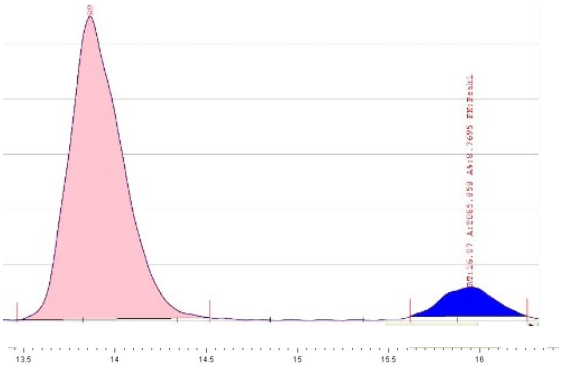
Chiral SFC (Chiralcel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (2R,5R)-2-pentyl-2,5-diphenyldihydrofuran-3(2H)-one.

Racemic Material



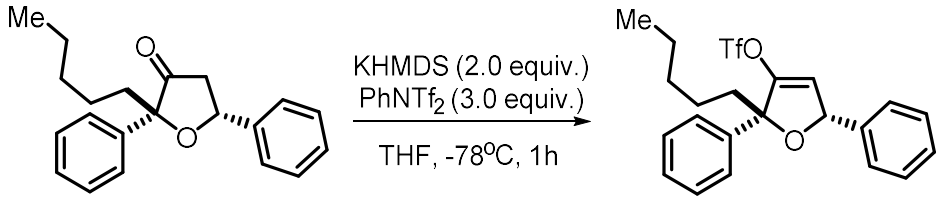
Peak Info			
Peak No	% Area	Area	RT (min)
1	47.5788	4800.9241	14.35
2	52.4212	5289.547	15.85
Total:	100	10090.4711	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	91.2305	21699.4236	14.04
2	8.7695	2085.858	16.07
Total:	100	23785.2816	

Structure Proof:

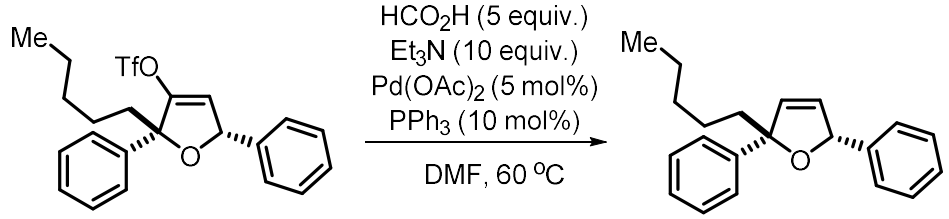


3.76 **S-3.16**

(2*R*,5*R*)-2-pentyl-2,5-diphenyl-2,5-dihydrofuran-3-yl trifluoromethanesulfonate (S-3.15). In a glovebox, to an oven-dried 2-dram vial was added (2*R*,5*R*)-2-pentyl-2,5-diphenyldihydrofuran-3(2H)-one (**3.76**) (16 mg, 0.052 mmol, 1.0 equiv.) and THF (2.5 mL). The solution was cooled to -78 ºC and to it was added a solution of KHMDS (20.7 mg, 0.10 mmol, 2.0 equiv.) in THF (1 mL) dropwise. The reaction mixture was allowed stir at the same temperature for 15 minutes. After that, a solution of $PhNTf_2$ (57.2 mg, 0.16 mmol, 3.0 equiv.) in THF (0.5 mL) was added dropwise at the same temperature. The reaction mixture was stirred at -78 ºC for 1 hour at which point aqueous saturated ammonium chloride solution (2 mL) was added to quench the reaction. The aqueous phase was extracted with EtOAc (3 x 2 mL). The combined organic phase was dried with

magnesium sulfate, filtered, and concentrated in rotavap. The crude mixture was purified by column chromatography (5% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (14.9 mg, 65% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53-7.31 (m, 10H), 5.97 (s, 1H), 5.81 (s, 1H), 2.17-2.08 (m, 1H), 2.06-1.99 (m, 1H), 1.43-1.22 (m, 6H), 0.83 (t, J = 6.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 149.5, 141.7, 139.8, 128.9, 128.81, 128.76, 128.0, 127.2, 125.0, 111.0, 88.9, 83.2, 38.7, 31.9, 23.3, 22.5, 14.1. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -73.2. **IR** (neat) ν_{max} 3498 (br, m), 2926 (s), 2857 (m), 1664 (m), 1431 (s), 1248 (m), 1140 (s), 844 (m), 761 (m), 697 (m), 608 (m) cm^{-1}. **HRMS** (DART) for $C_{22}H_{24}F_3O_4S$ $(M+H)^+$: Calc'd: 441.1347, found: 443.1328. **$[\alpha]_D^{20}$**: +32.0 (c = 0.50, $CHCl_3$, l = 50 mm).



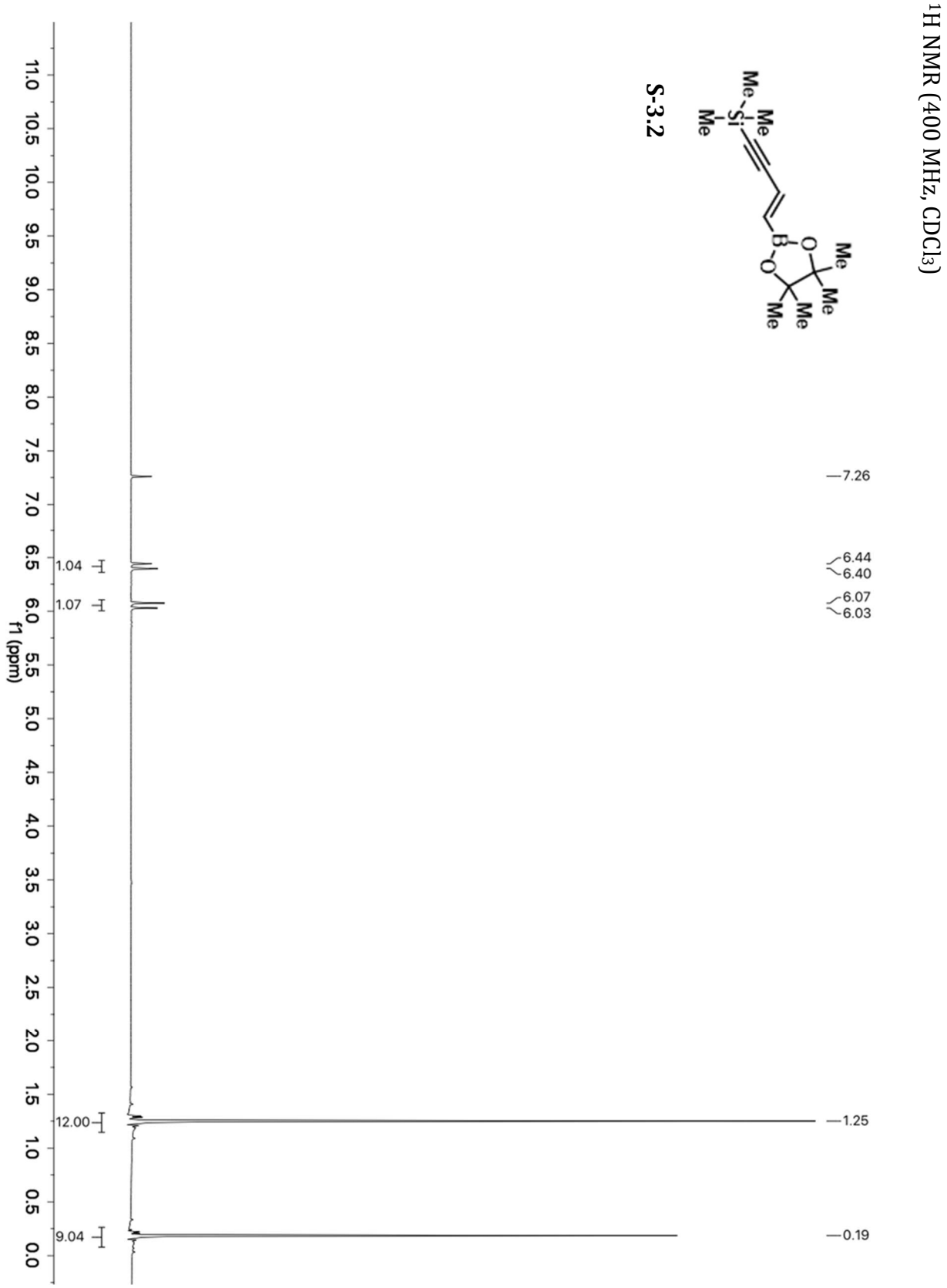
S-3.15 **3.77**

(2*S*,5*R*)-2-pentyl-2,5-diphenyl-2,5-dihydrofuran (3.77). In a glovebox, to an oven-dried 2-dram vial charged with a magnetic stir bar was added (2*R*,5*R*)-2-pentyl-2,5-diphenyl-2,5-dihydrofuran-3-yl trifluoromethanesulfonate (**S-3.15**) (12.0 mg, 0.027 mmol, 1.0 equiv.) and DMF (0.5 mL) at room temperature. After that, to it was added a solution of $Pd(OAc)_2$ (0.30 mg, 1.35 □mol, 0.05 equiv.) and triphenylphosphine (0.71 mg, 2.70□ □mol, 0.10 equiv.) in DMF (0.4 mL), followed by formic acid (6.2 mg, 0.14 mmol, 5.2 equiv.) and triethylamine (27.3 mg, 0.27 mmol, 10 equiv.). The reaction vial was sealed with a septum cap, taken out of the glovebox, and allowed to stir at 60 °C overnight. The resulting suspension was diluted with pentane (3.0 mL), washed with sat. $NaHCO_3$ (1.0

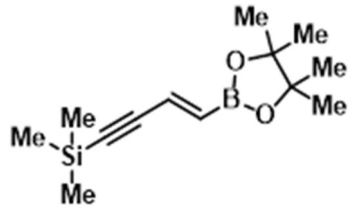
mL), brine (1.0 mL), dried over sodium sulfate, filtered, and concentrated in rotavap. The residue was then purified by silica gel column chromatography (5% EtOAc in hexane, stain in $KMnO_4$) to afford the product as a colorless oil (5.9 mg, 65% yield).

The absolute configuration and relative configuration was assigned by comparison of its ^1H NMR spectrum and SFC trace with the authentic sample synthesized above.

3.4.6 Spectral Data

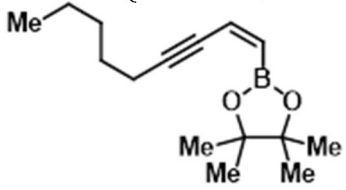


^{13}C NMR (126 MHz, $CDCl_3$)



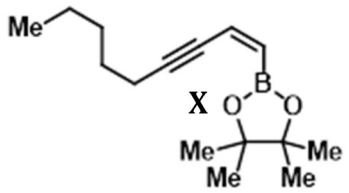
S-3.2

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



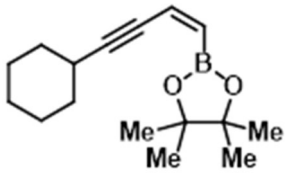
3.3

^{13}C NMR (600 MHz, $CDCl_3$)



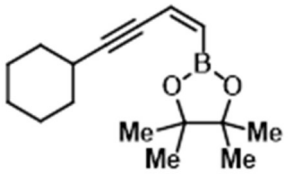
3.3

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



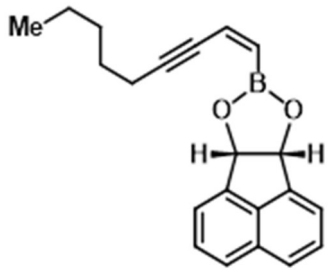
S-3.5

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

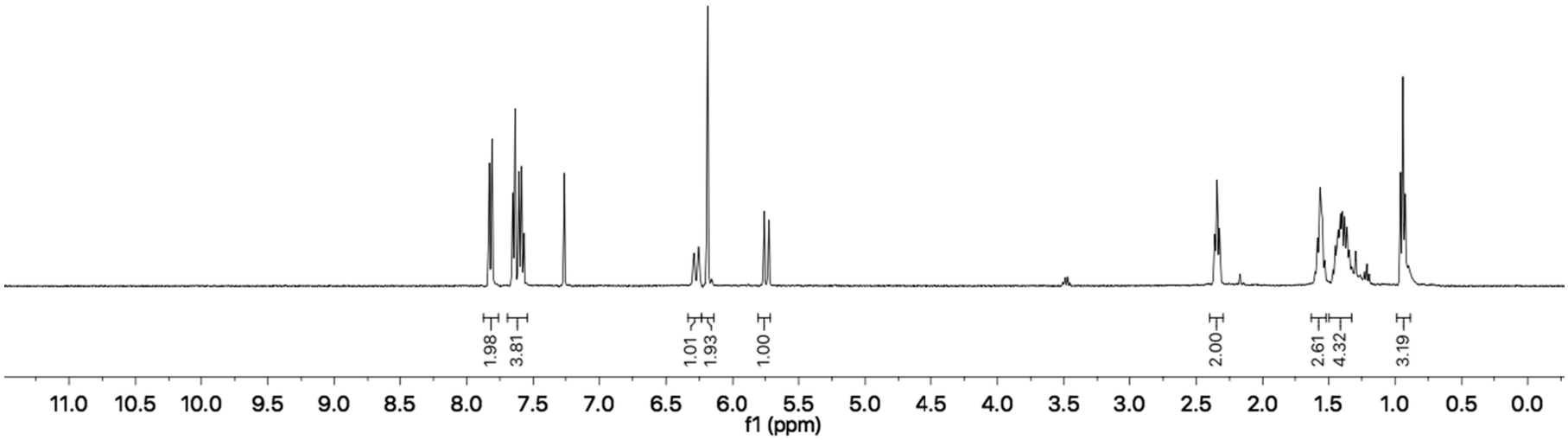


S-3.5

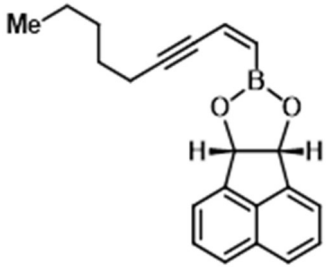
^{1}H NMR (400 MHz, $CDCl_3$)



S-3.8

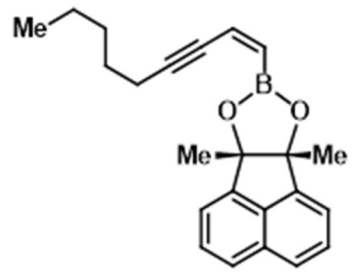


^{13}C NMR (126 MHz, $CDCl_3$)



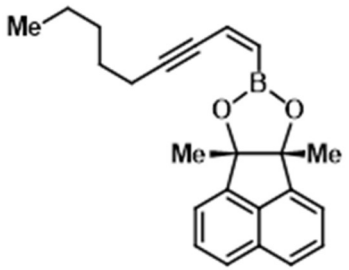
S-3.8

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



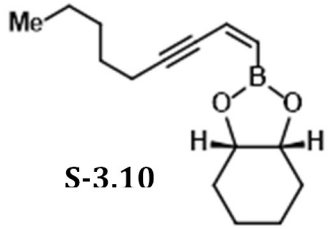
S-3.7

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

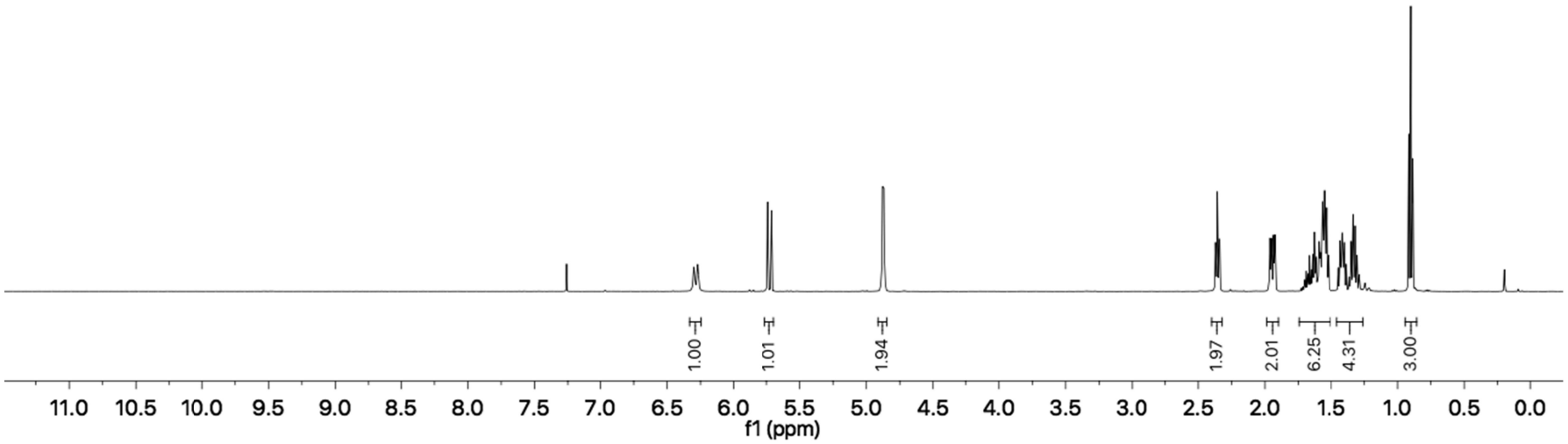


S-3.7

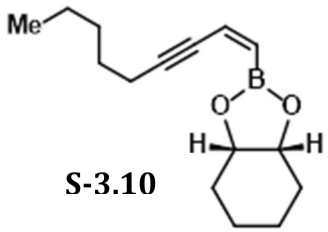
^{1}H NMR (400 MHz, $CDCl_3$)



S-3.10

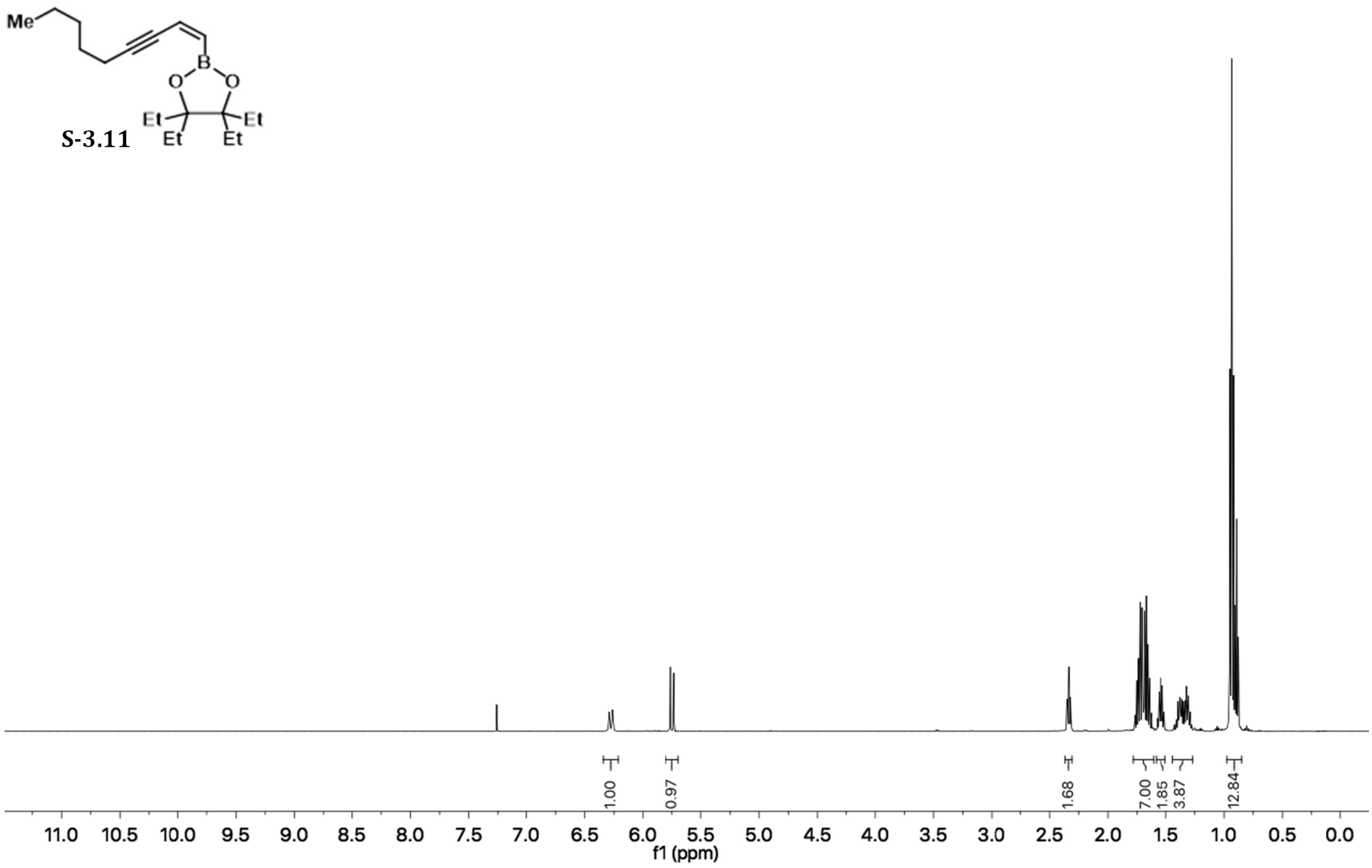


^{13}C NMR (126 MHz, $CDCl_3$)



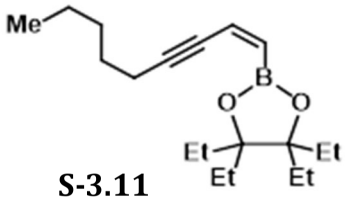
S-3.10

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



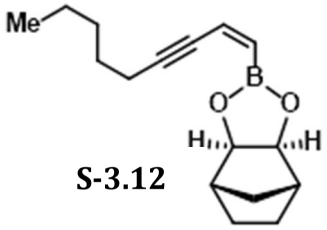
S-3.11

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

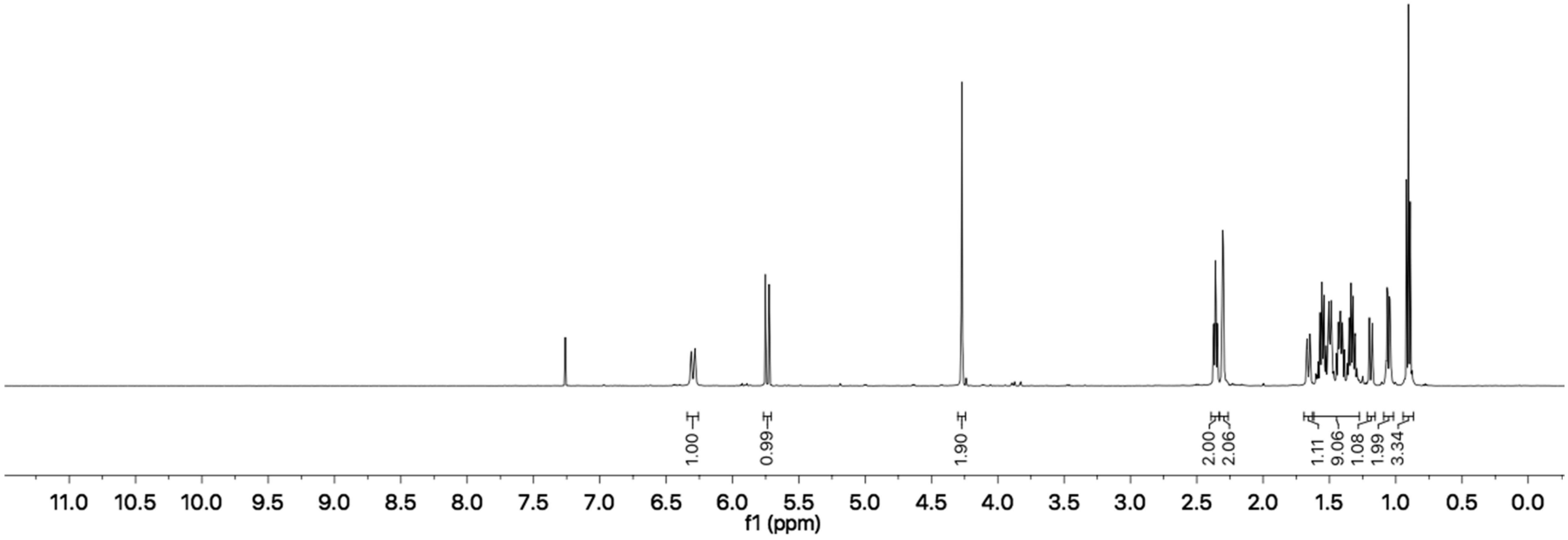


S-3.11

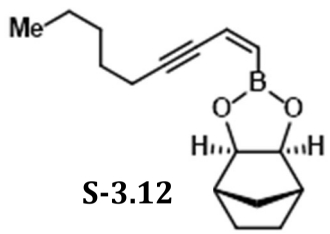
^{1}H NMR (500 MHz, $CDCl_3$)



S-3.12

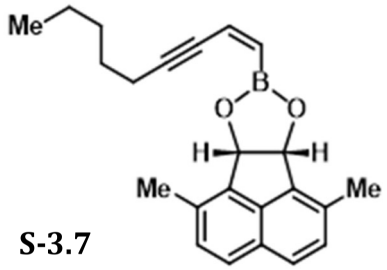


^{13}C NMR (126 MHz, $CDCl_3$)



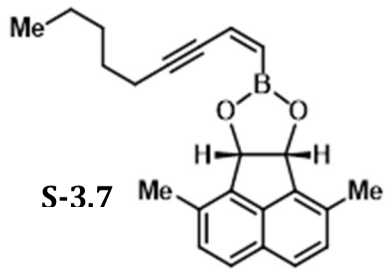
S-3.12

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



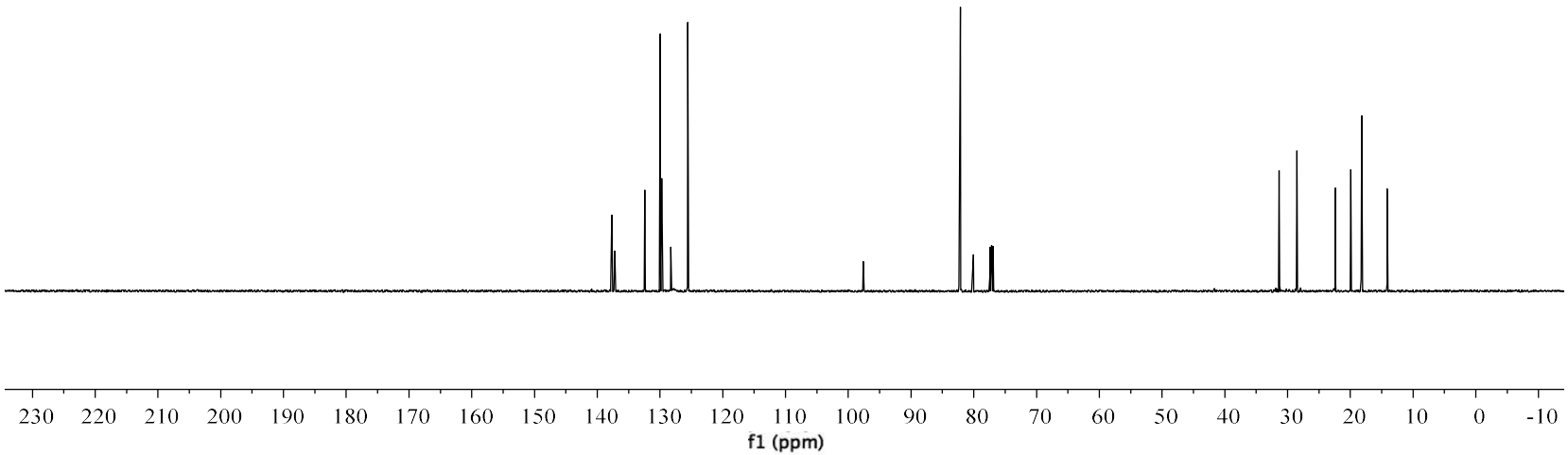
S-3.7

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

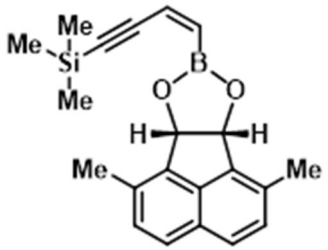


S-3.7

137.68
137.22
132.42
129.99
129.73
128.26
125.60
97.61
82.14
80.08
31.37
31.36
28.50
22.37
19.91
18.19
14.13

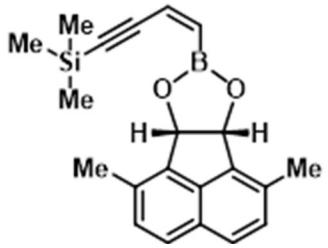


^{1}H NMR (500 MHz, $CDCl_3$)



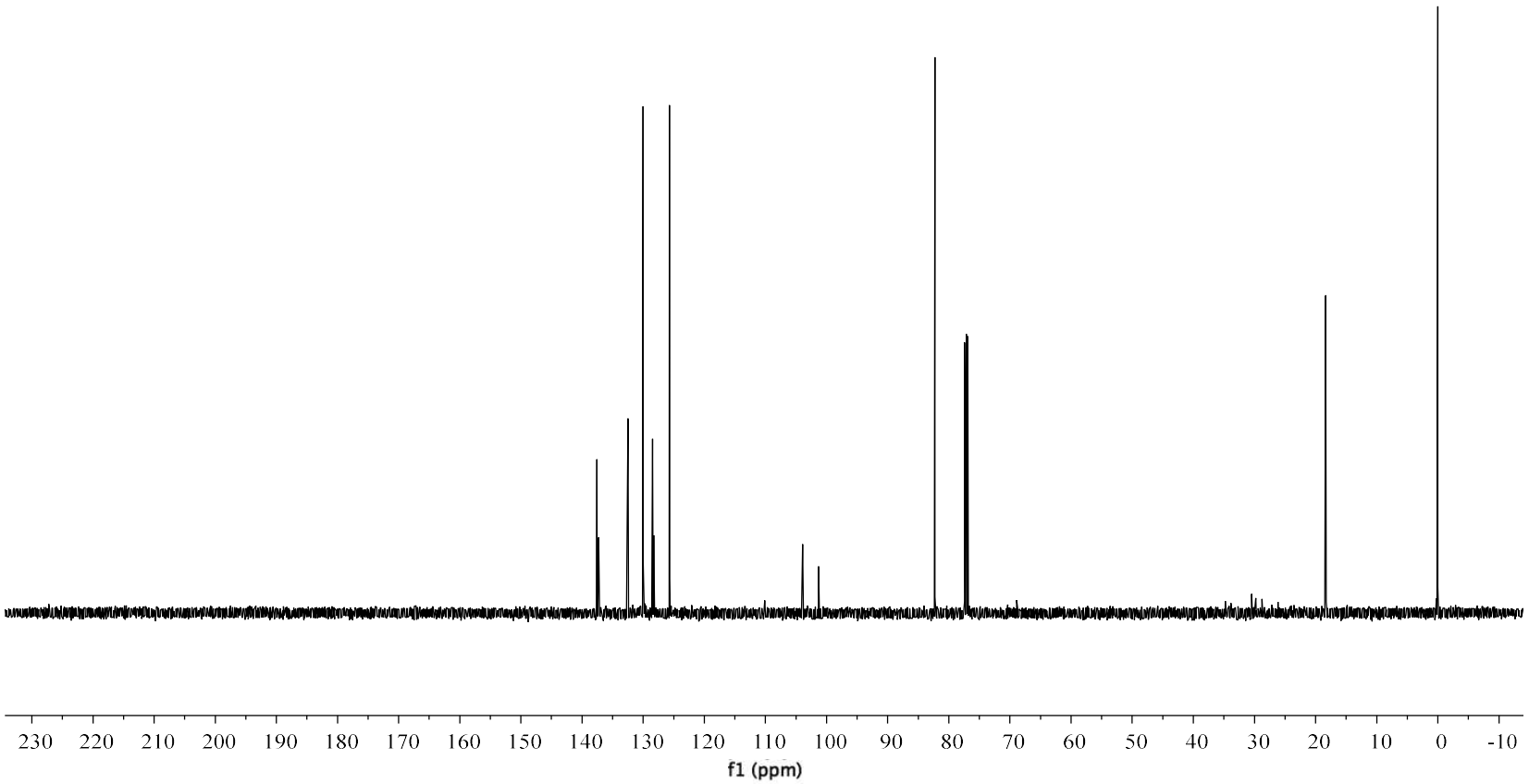
S-3.13

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

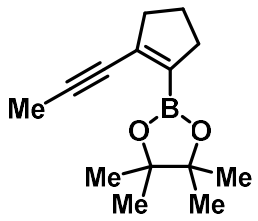


S-3.13

137.55
137.27
132.48
130.01
128.48
128.28
125.68
103.92
101.30
82.28
18.34
0.01

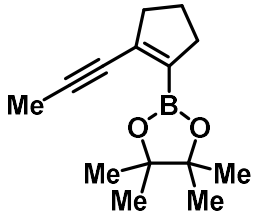


^{1}H NMR (600 MHz, $CDCl_3$)



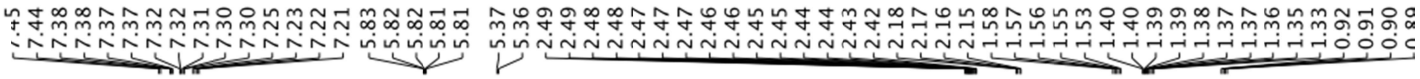
S-3.14

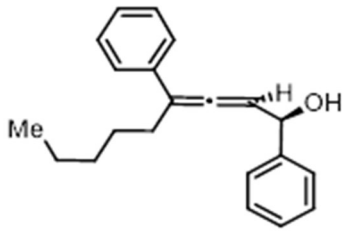
^{13}C NMR (126 MHz, $CDCl_3$)



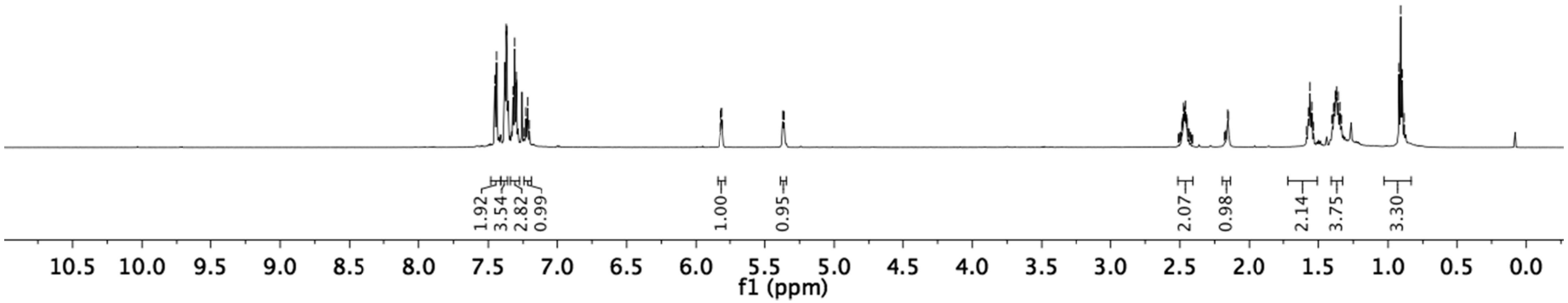
S-3.14

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

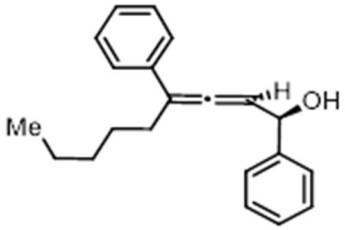




3.35

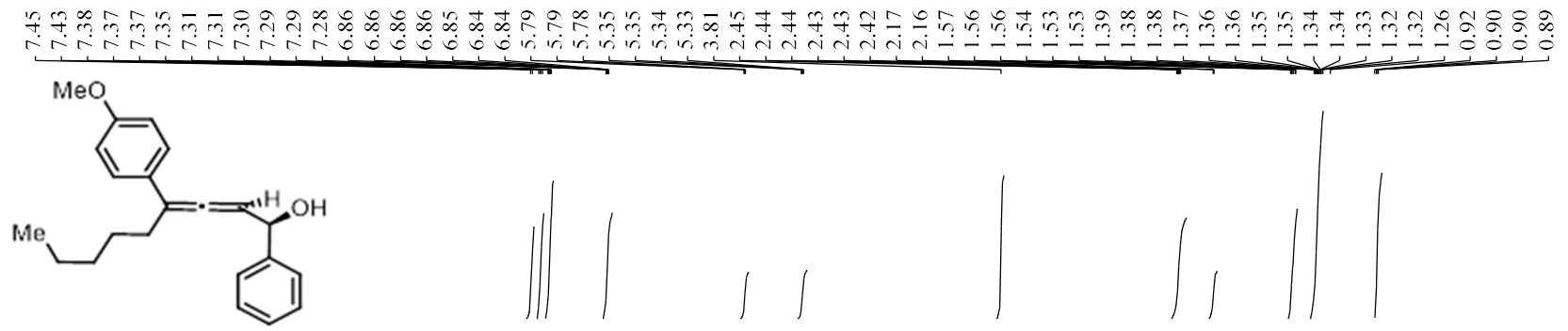


^{13}C NMR (126 MHz, $CDCl_3$)

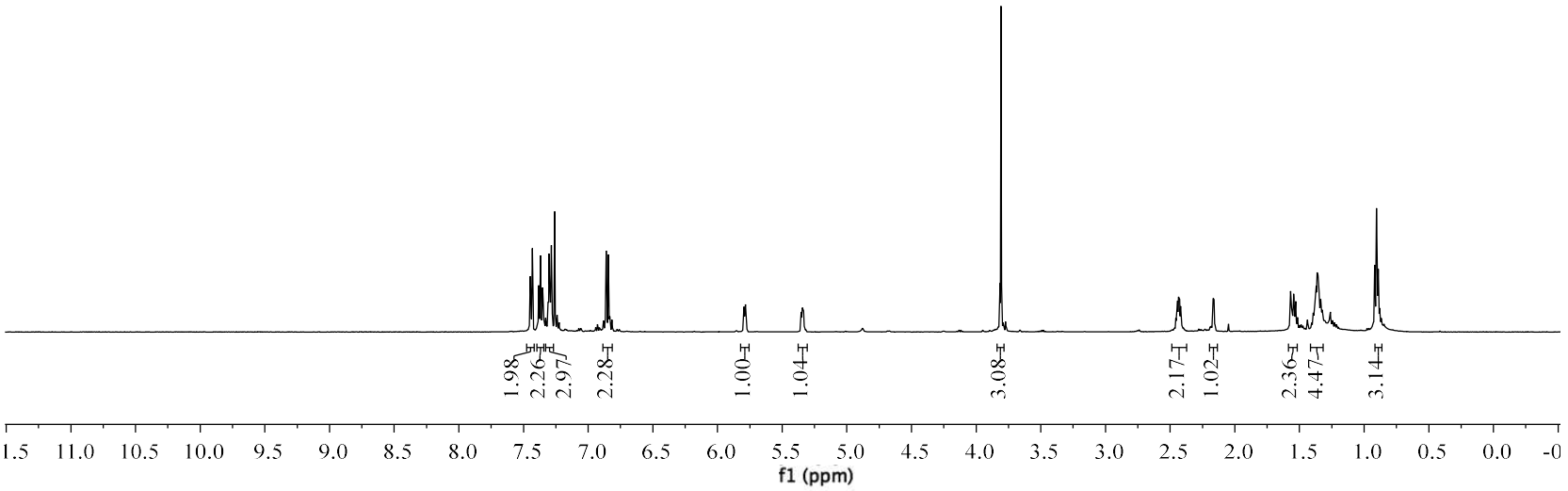


3.35

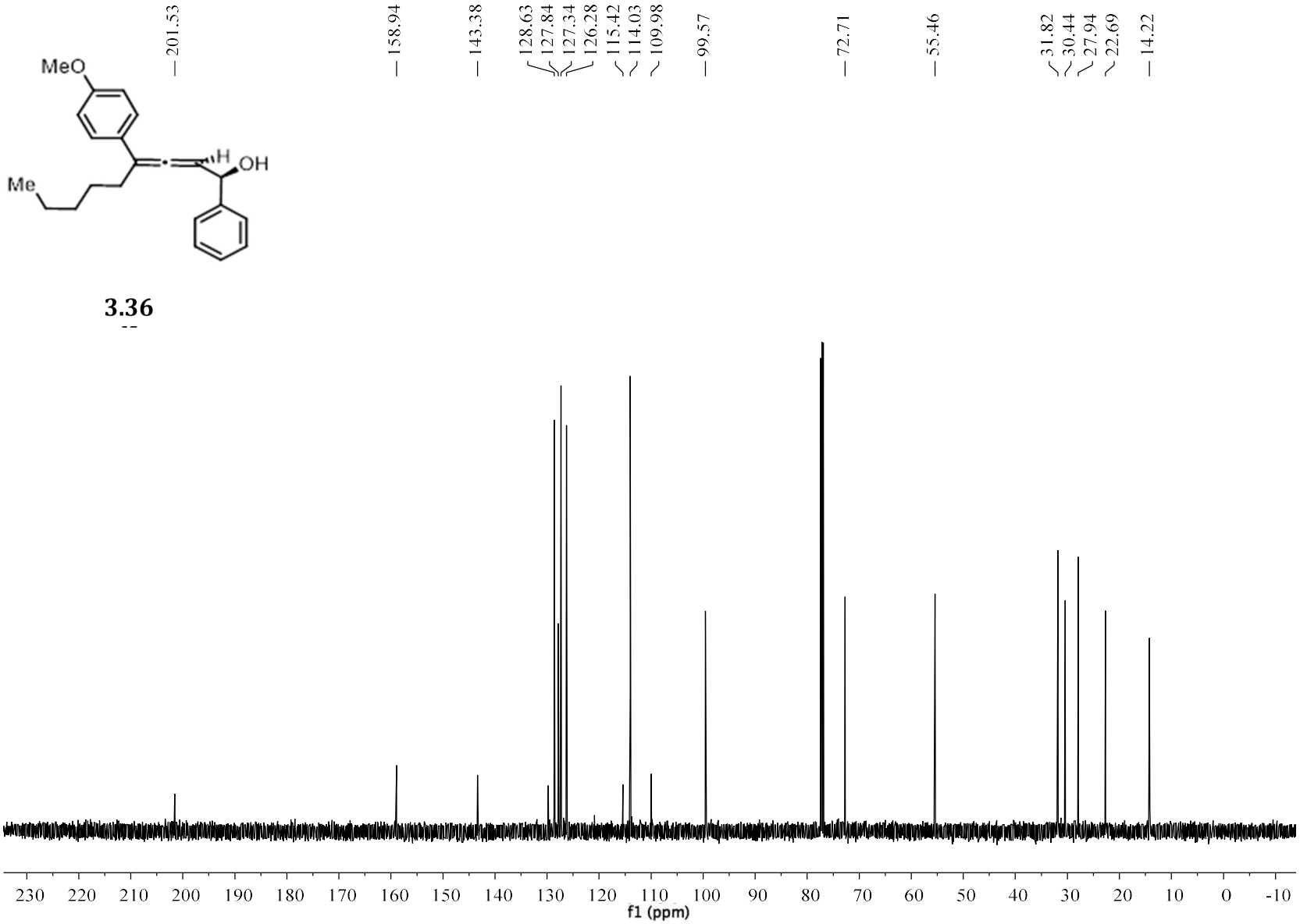
^{1}H NMR (600 MHz, $CDCl_3$)



3.36

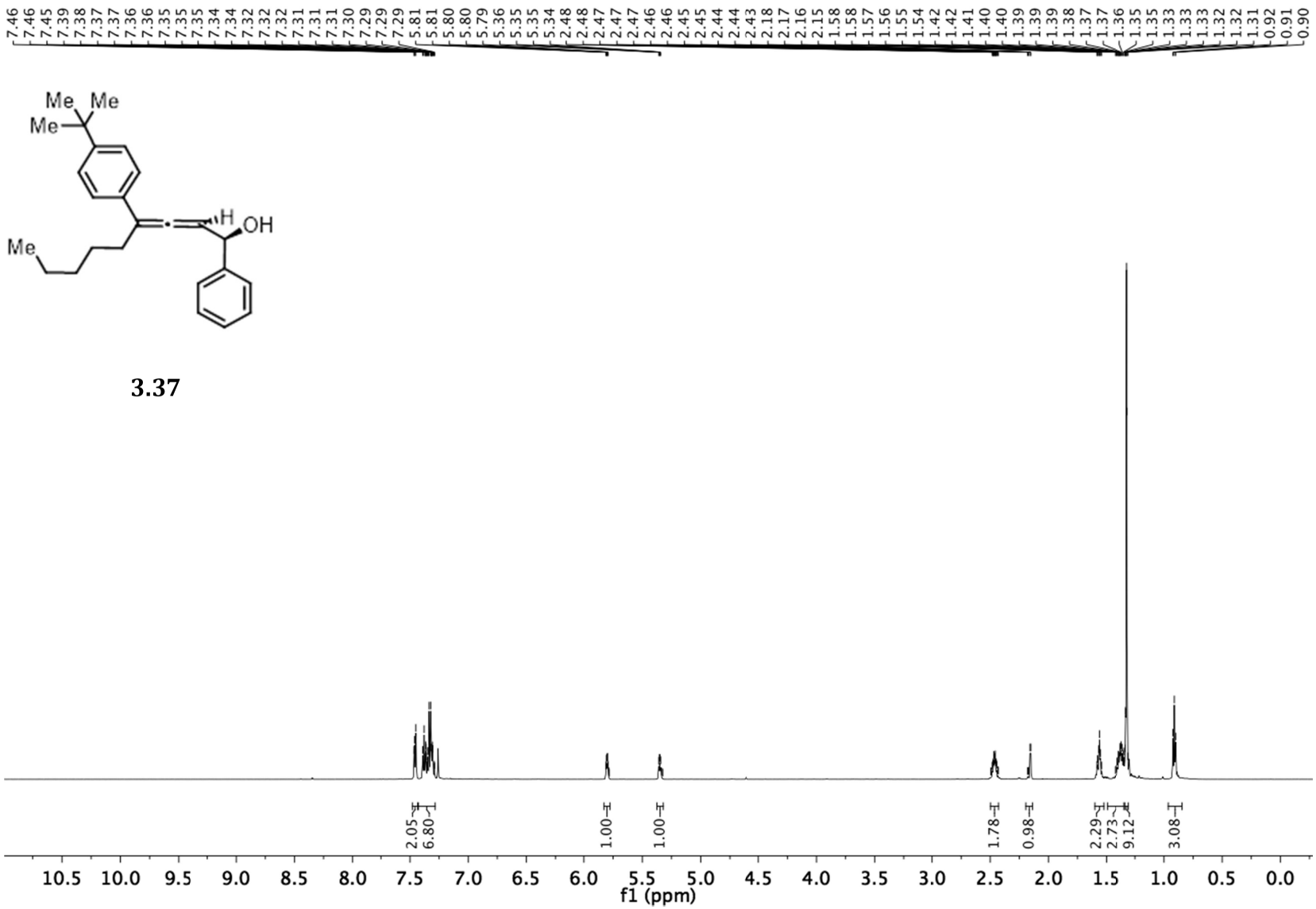


^{13}C NMR (126 MHz, $CDCl_3$)



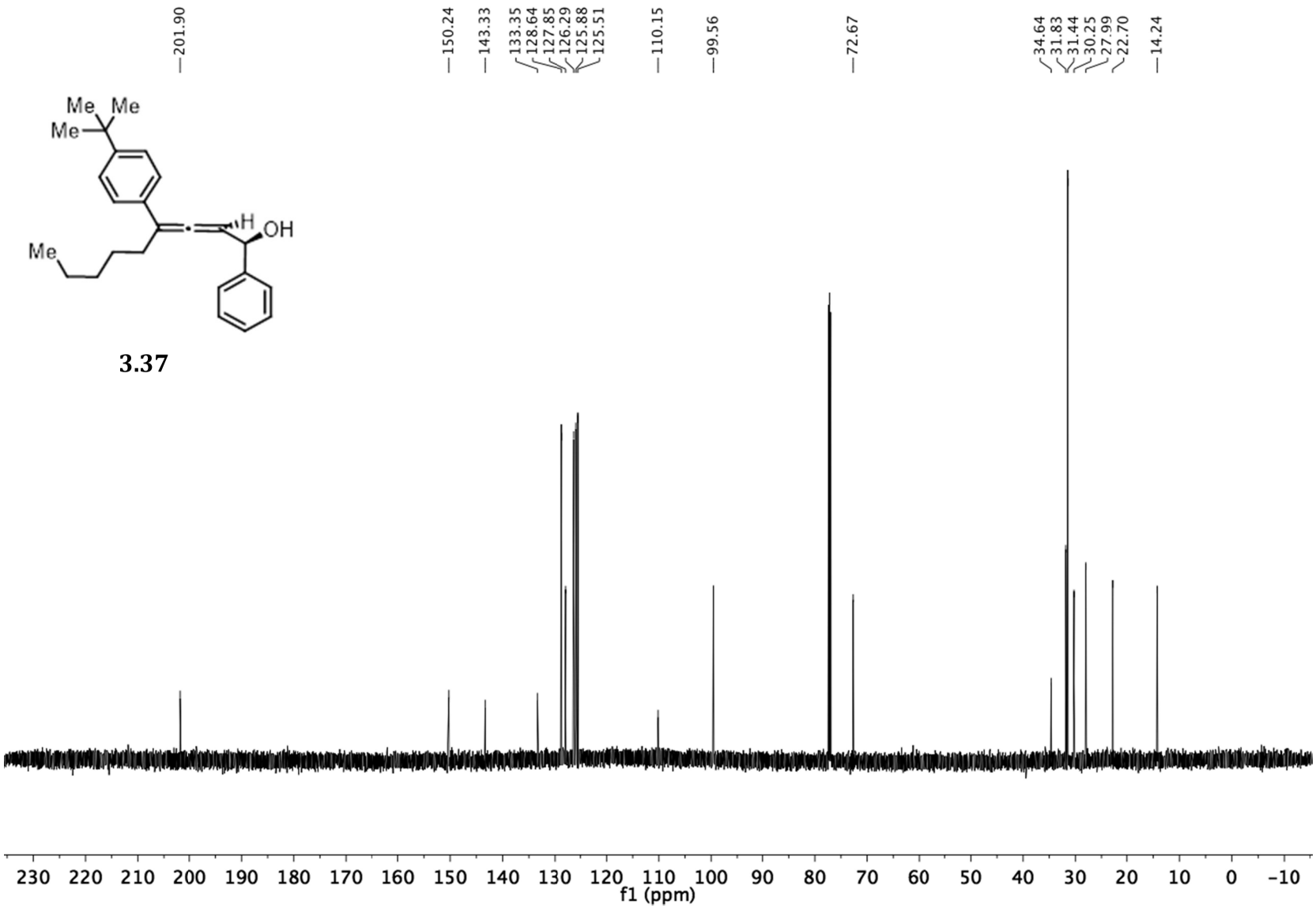
3.36

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



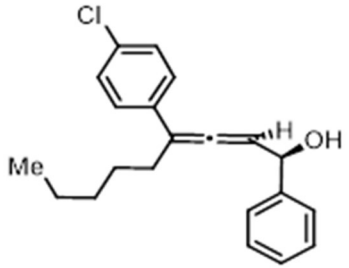
3.37

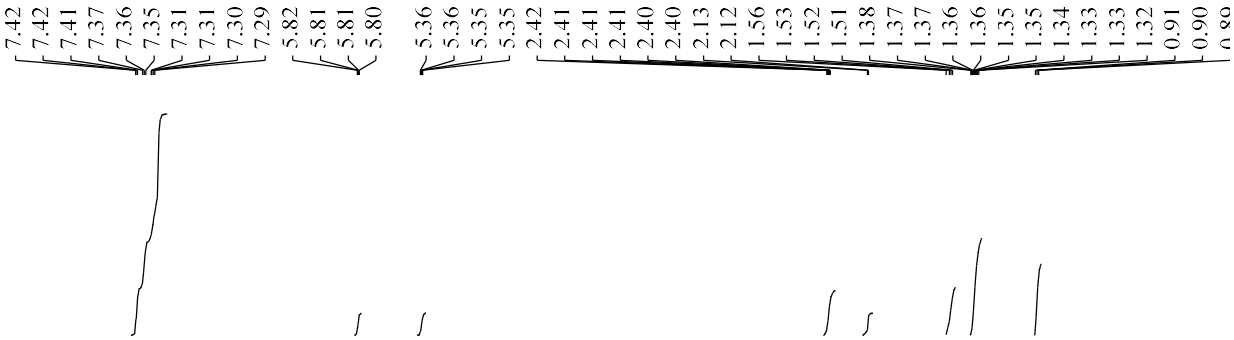
^{13}C NMR (126 MHz, $CDCl_3$)



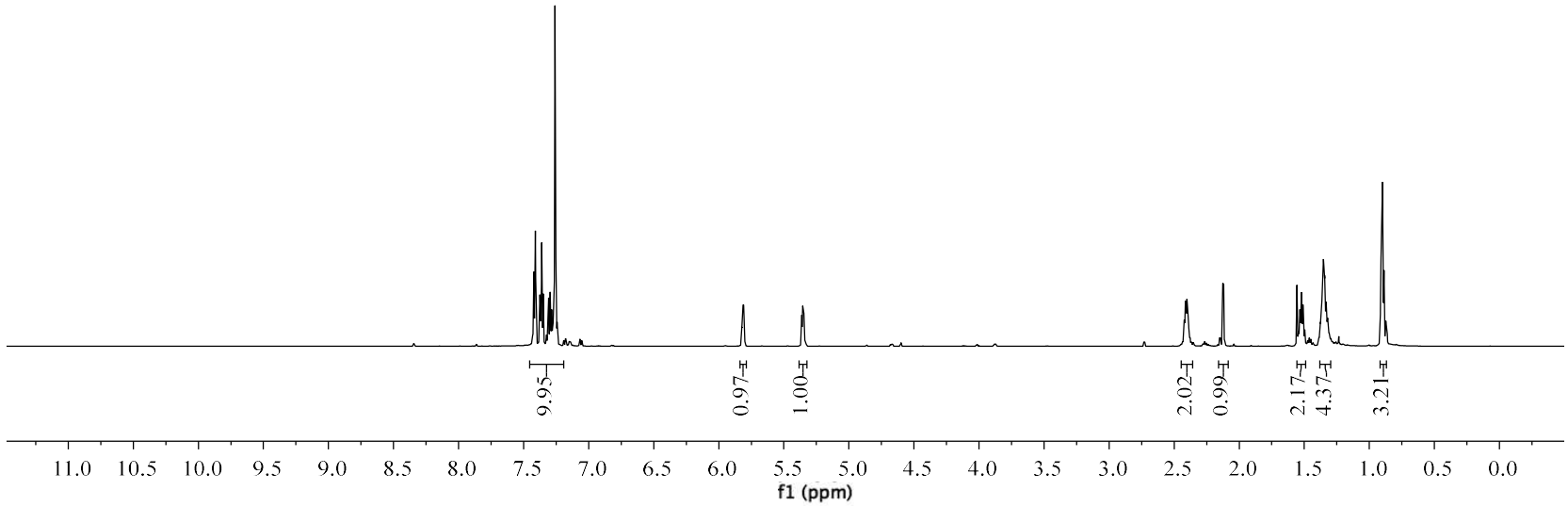
3.37

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

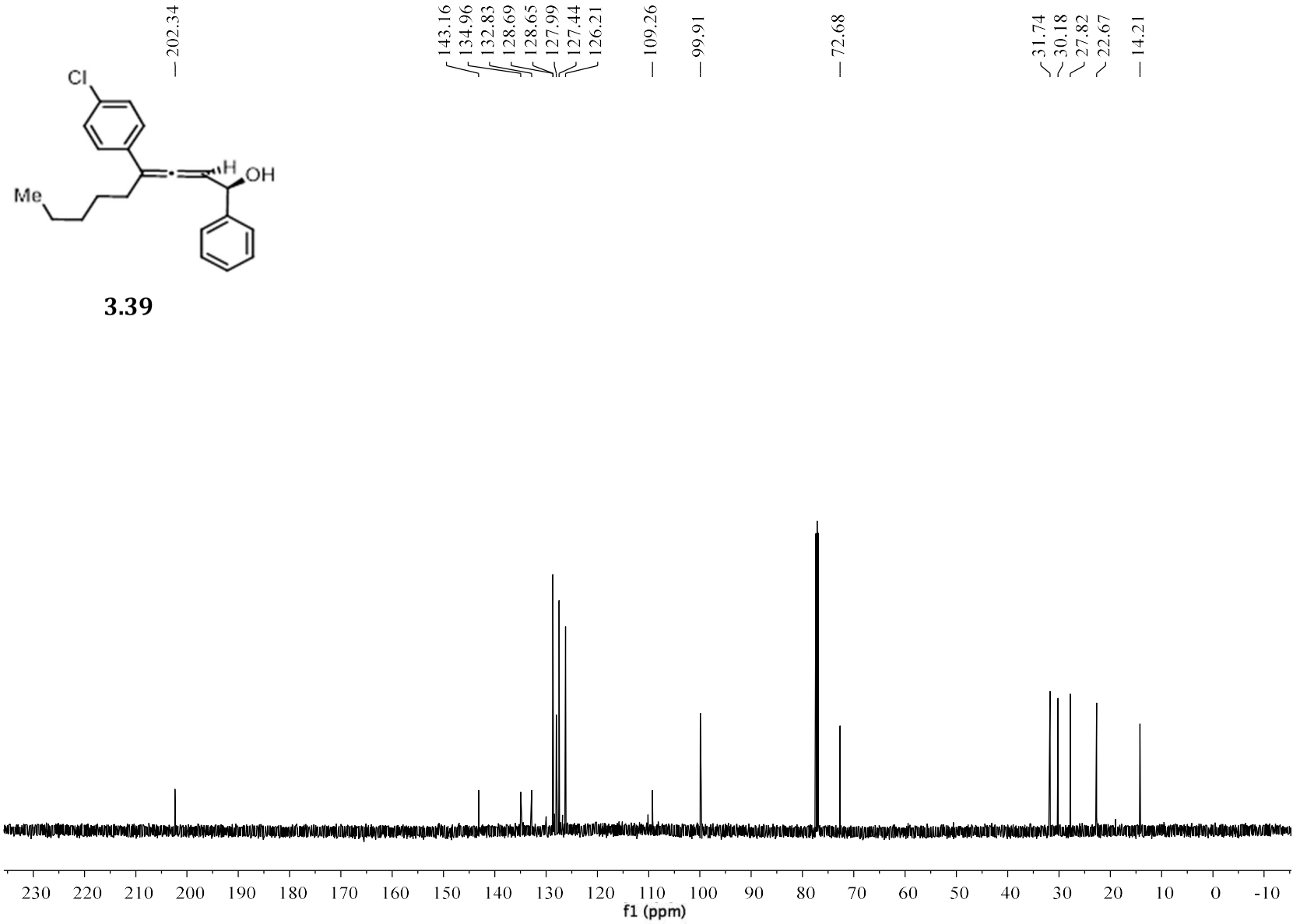




3.39

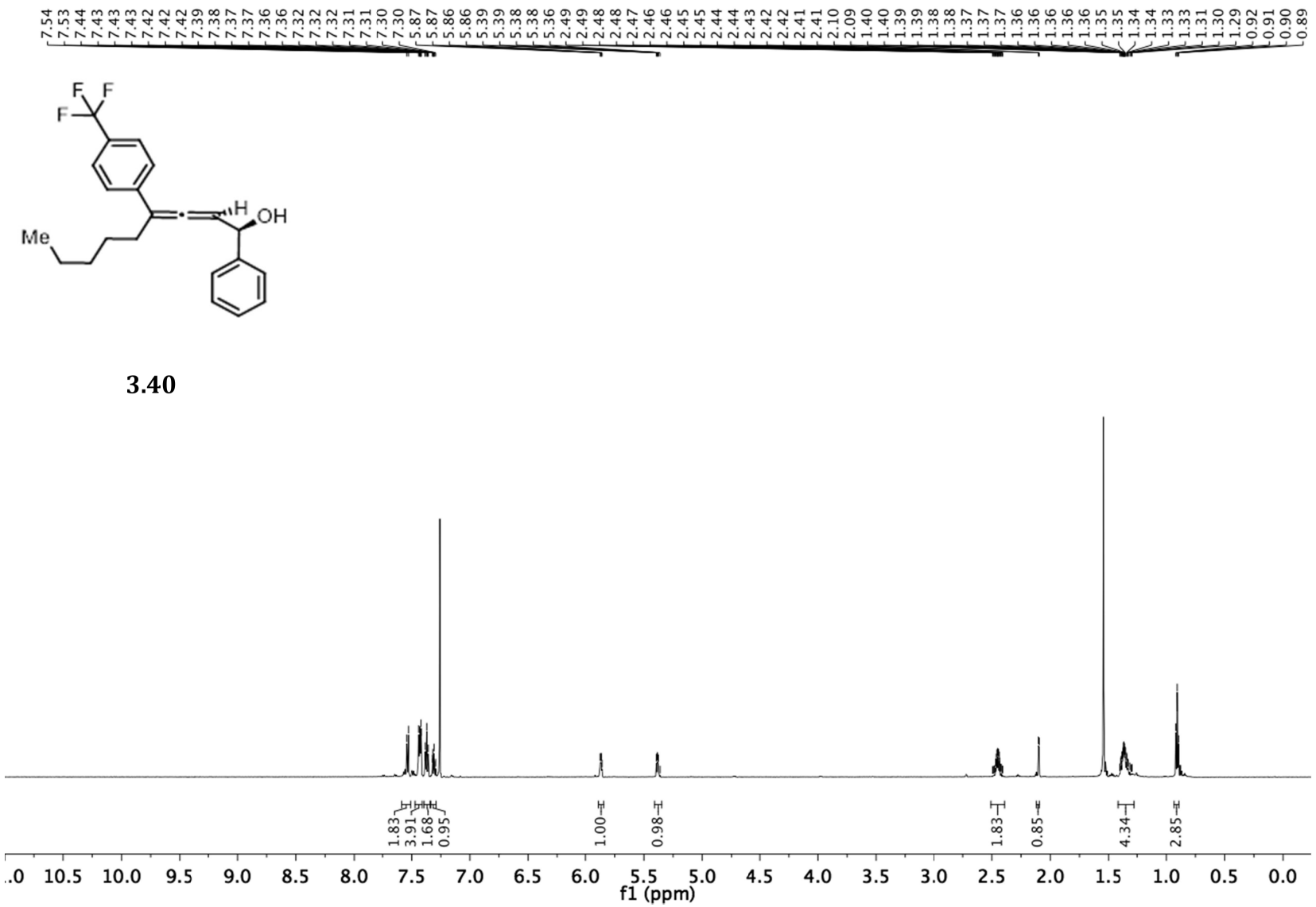


^{13}C NMR (126 MHz, $CDCl_3$)



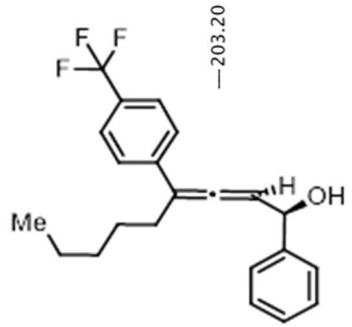
3.39

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



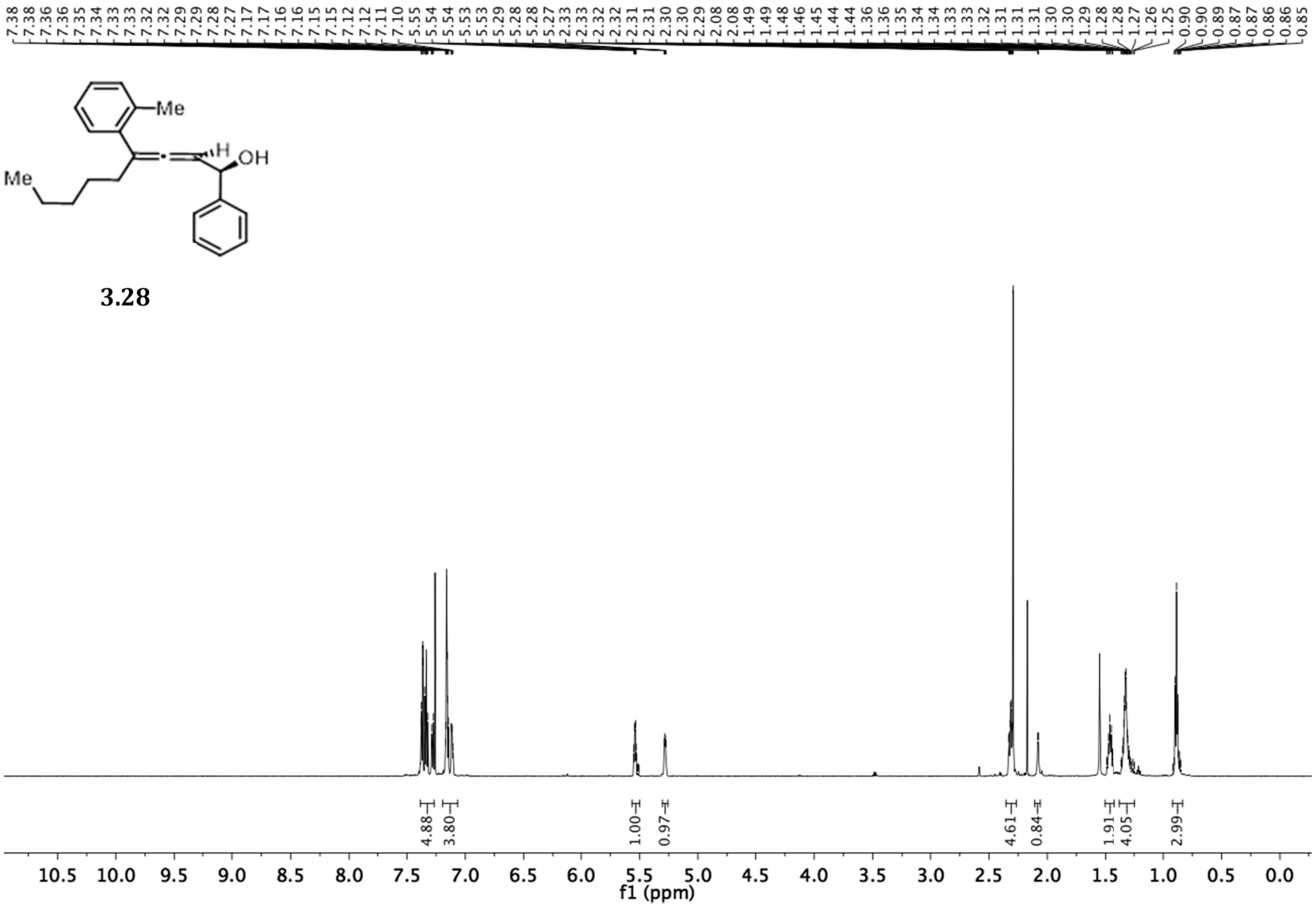
3.40

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



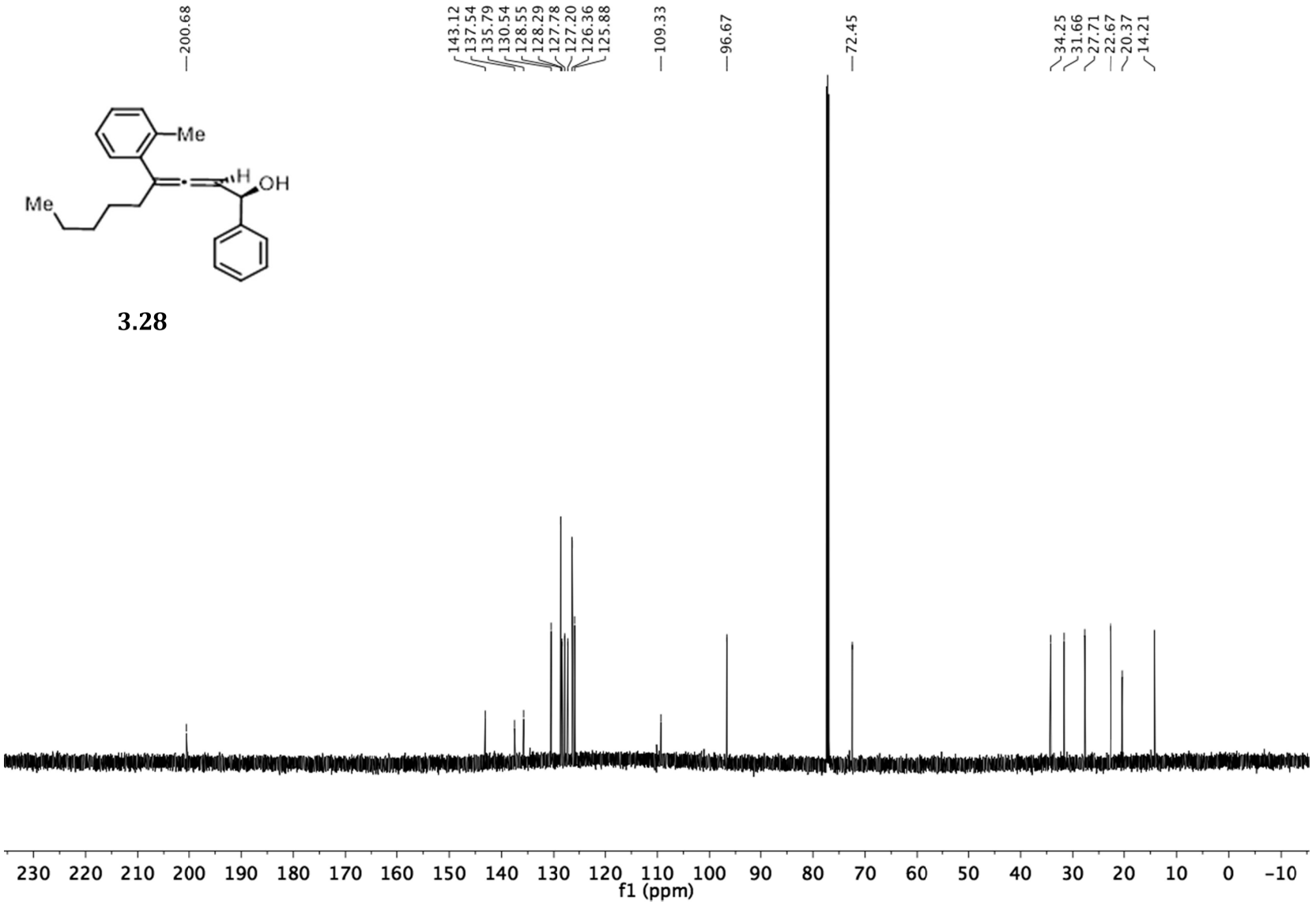
3.40

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



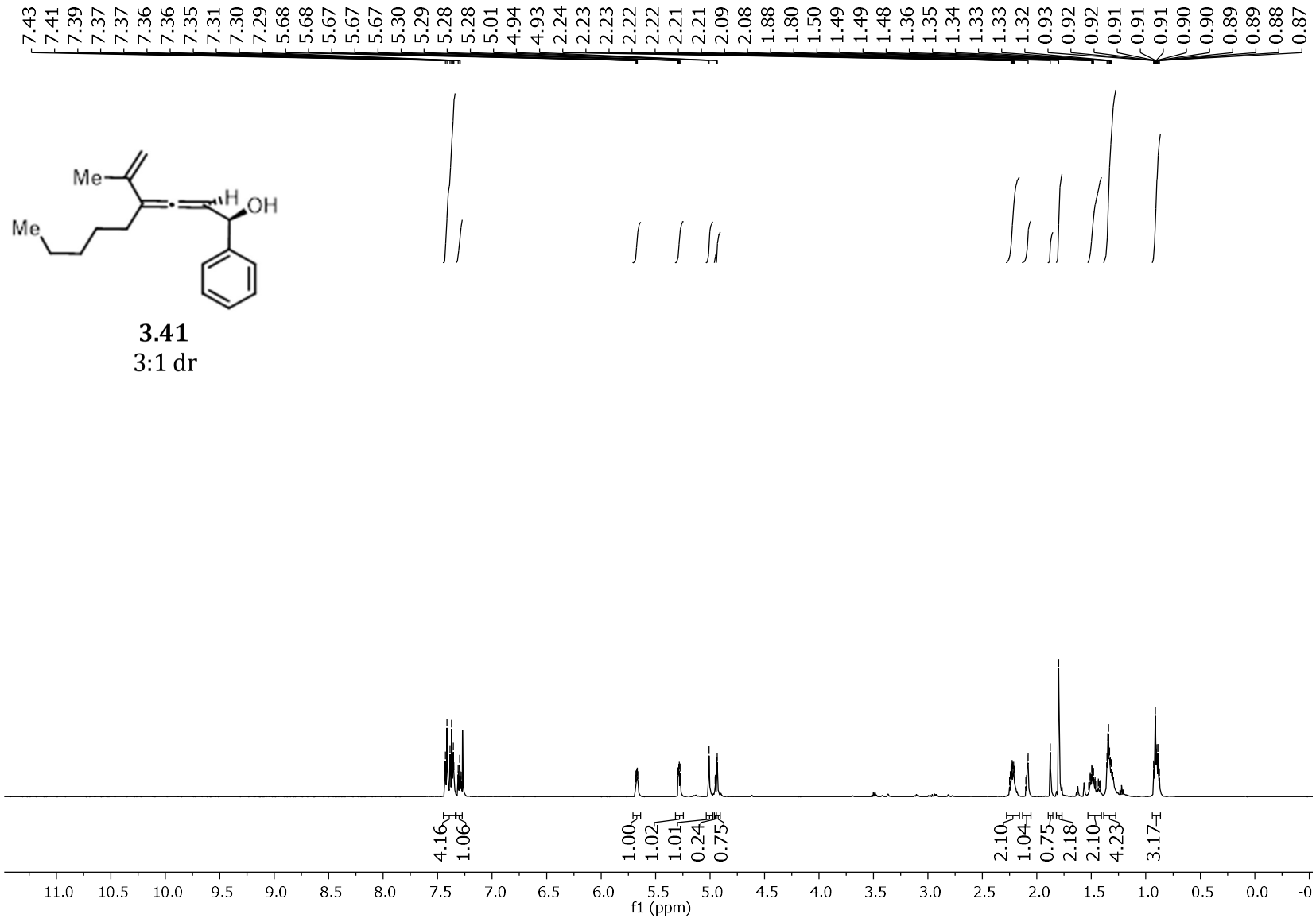
3.28

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



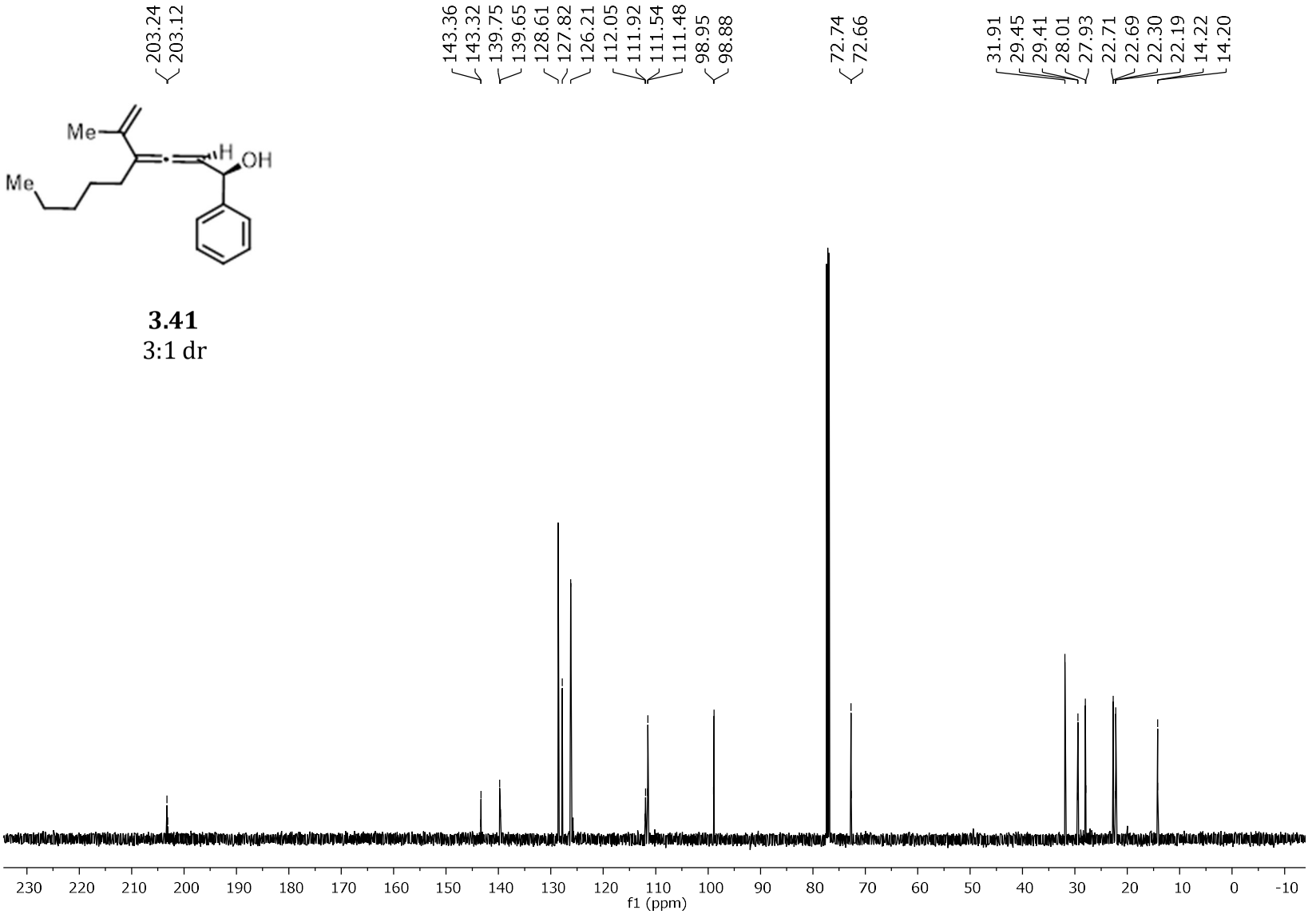
3.28

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



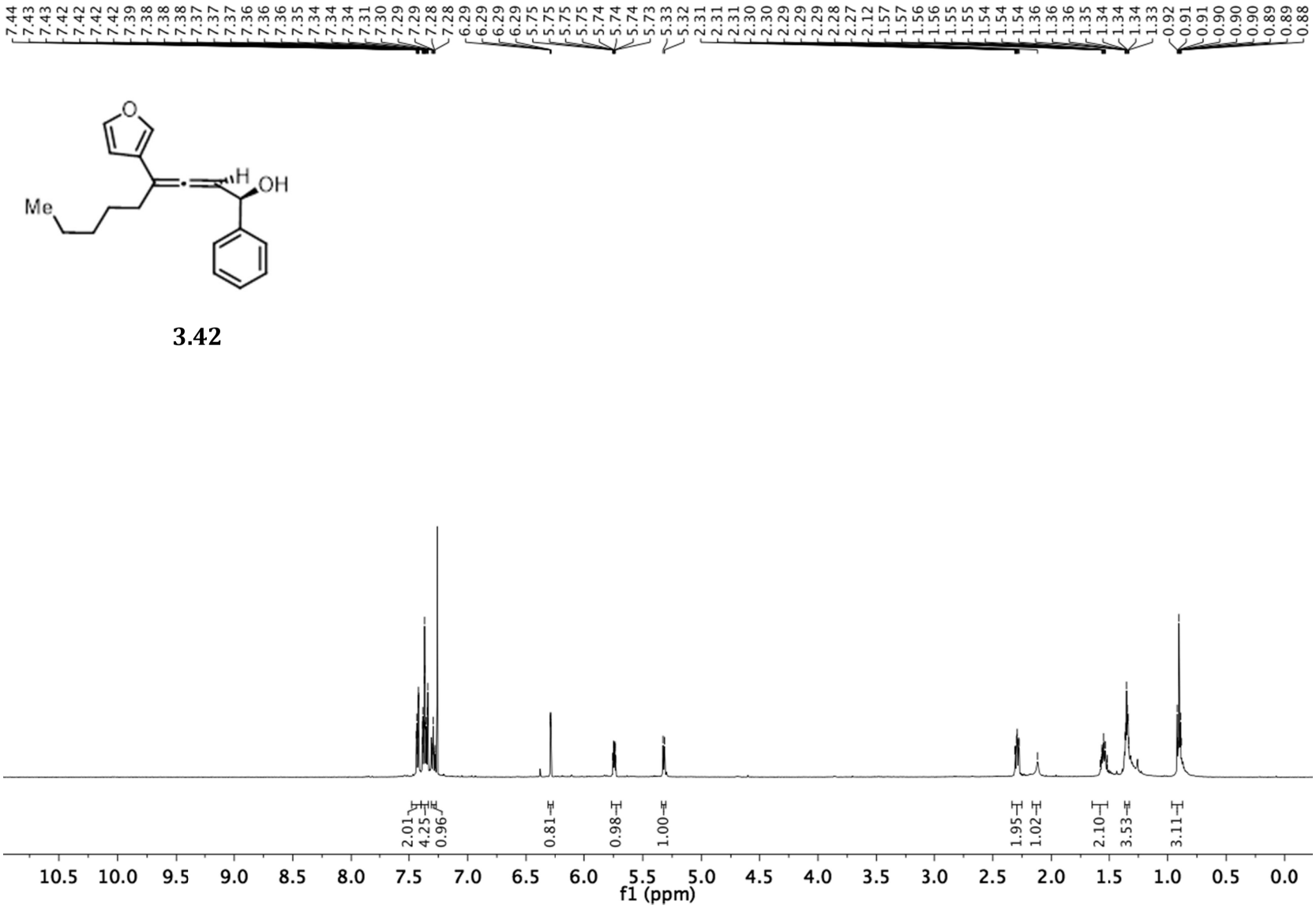
3.41
3:1 dr

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



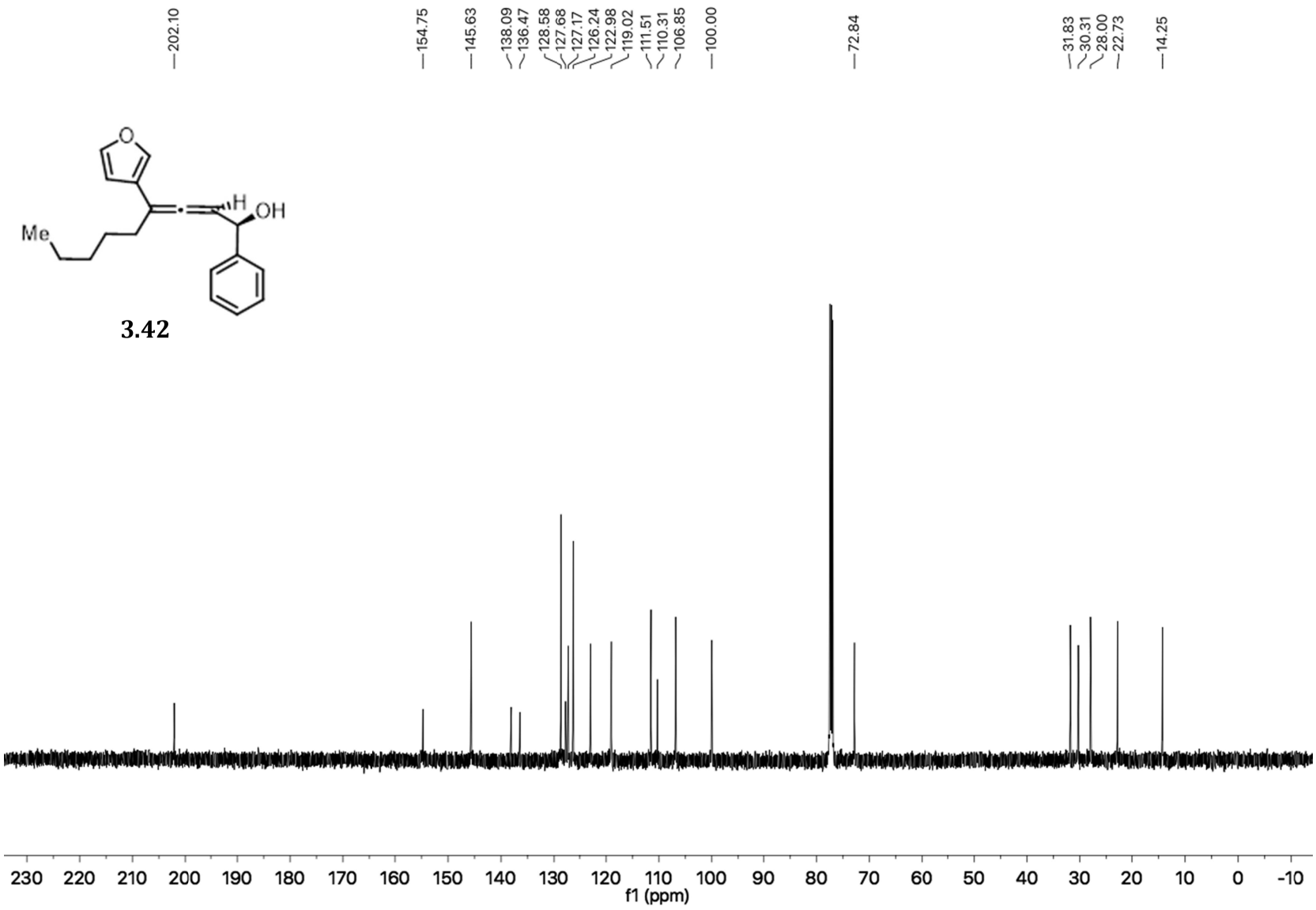
3.41
3:1 dr

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



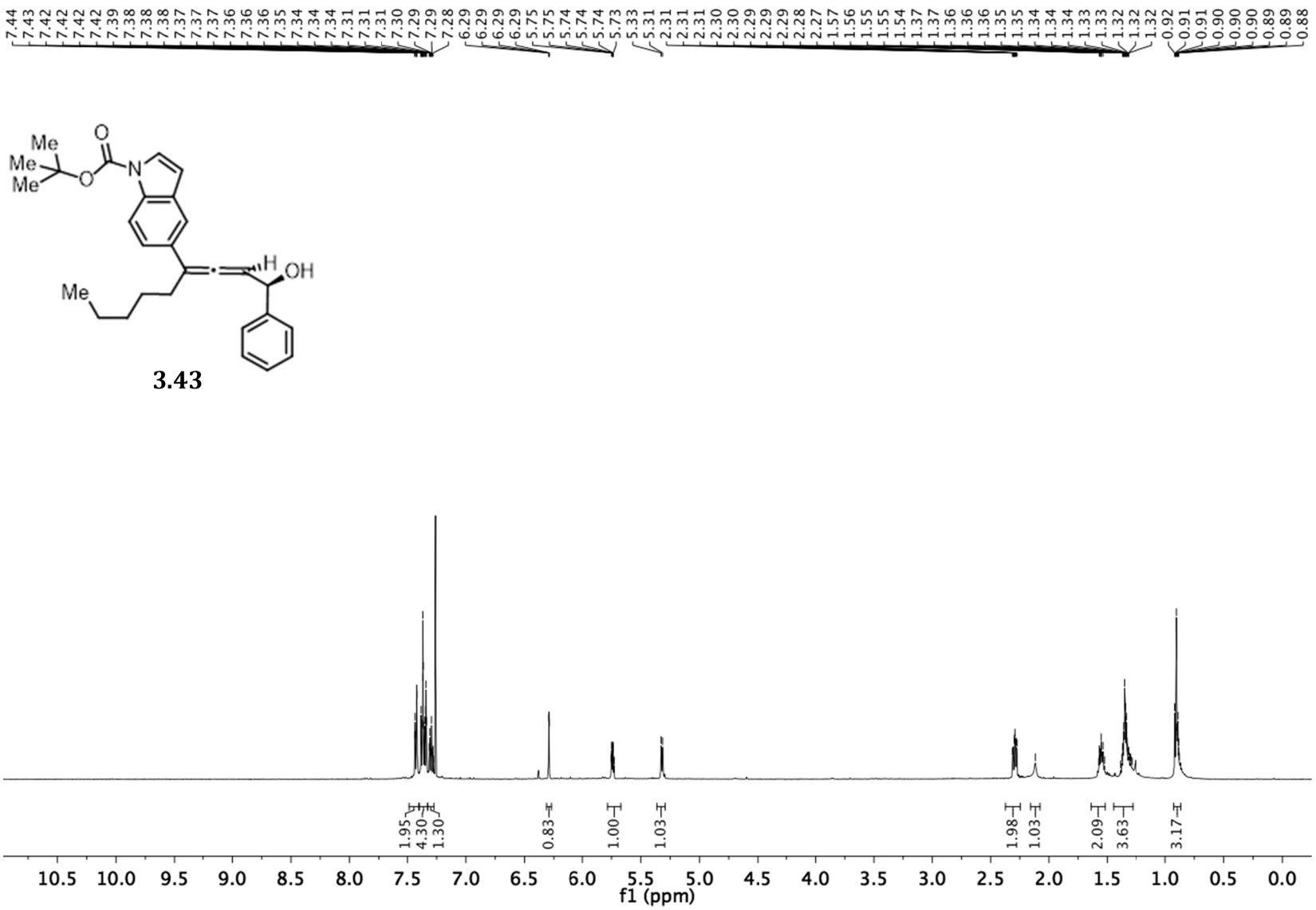
3.42

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



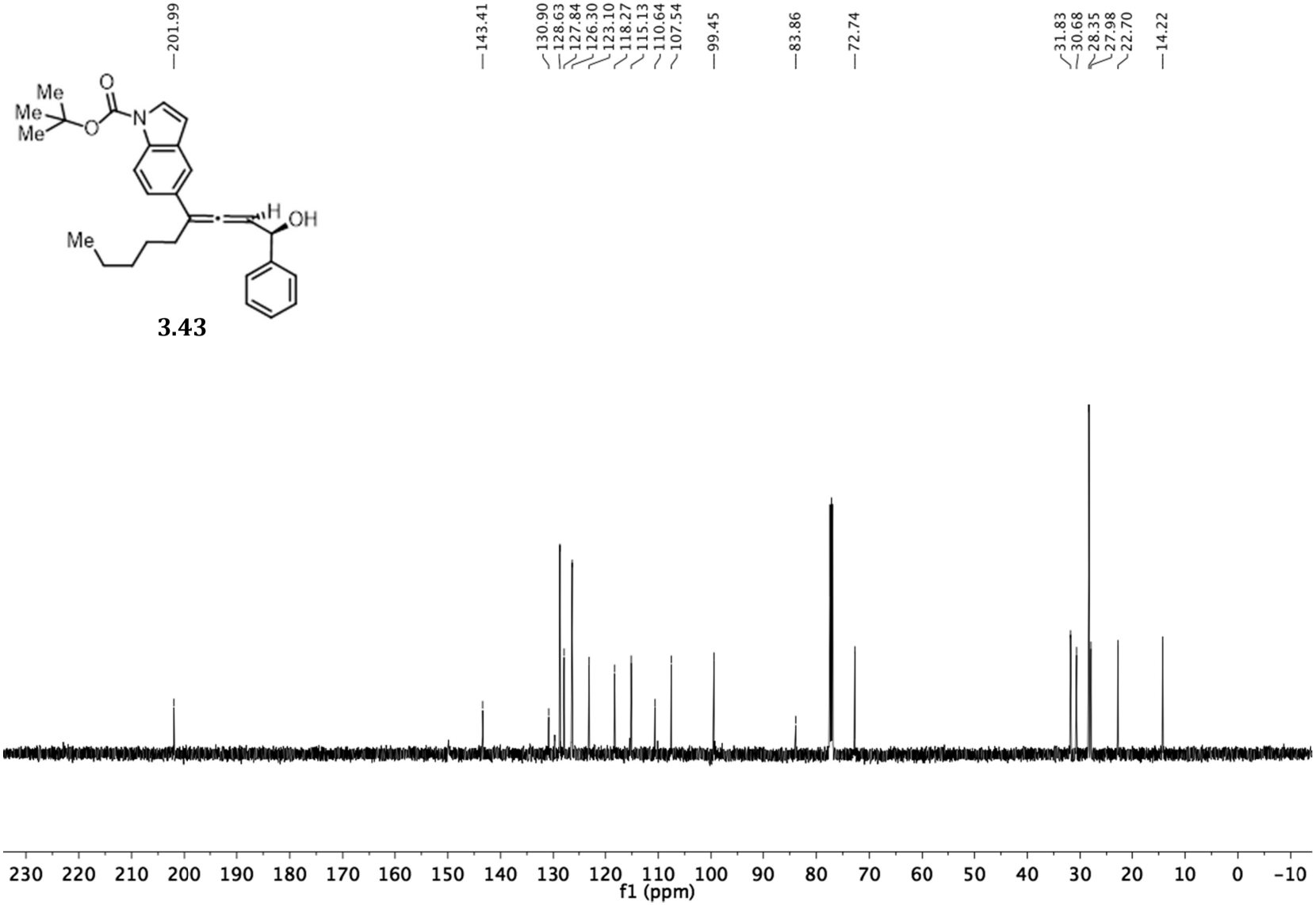
3.42

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



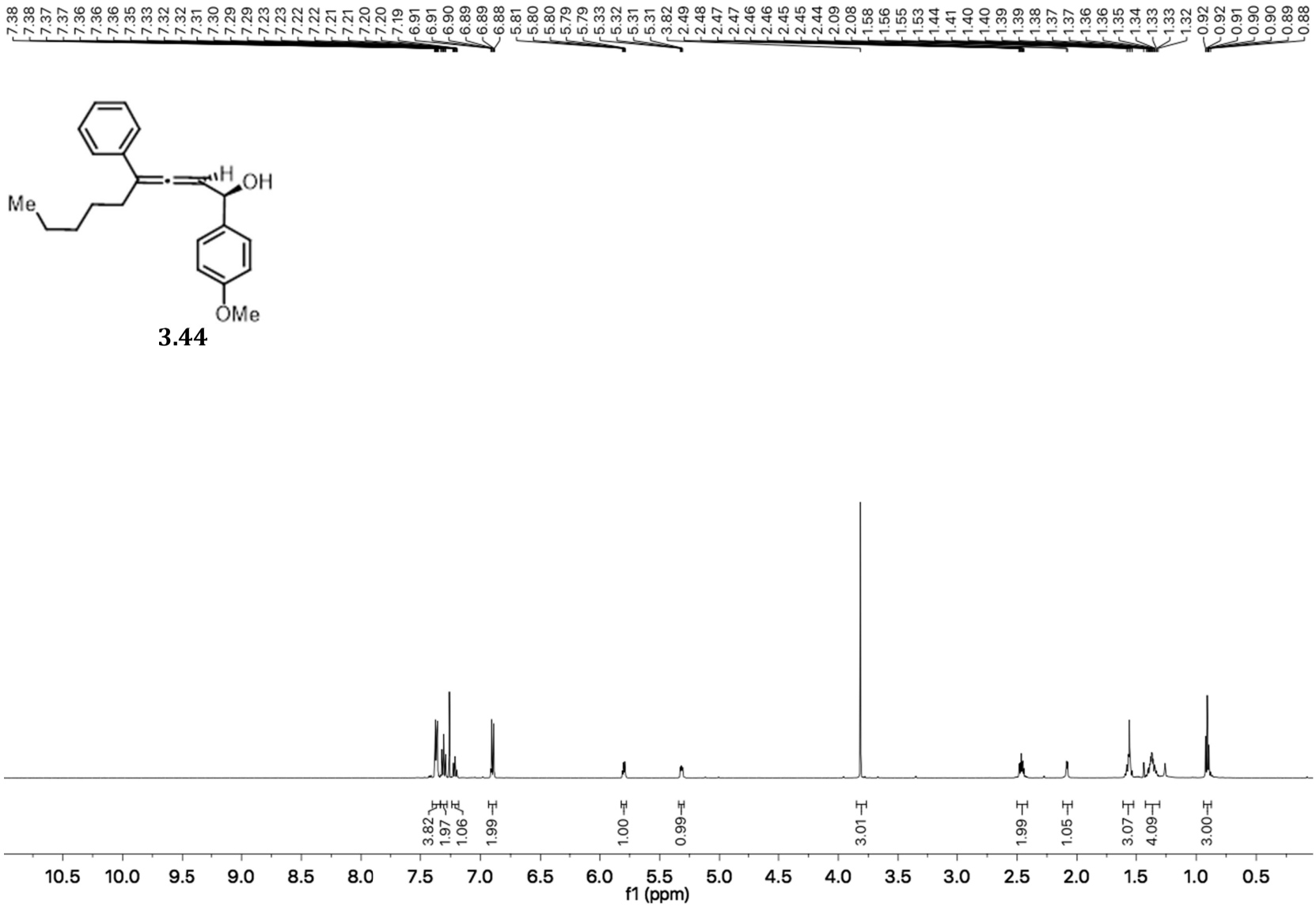
3.43

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



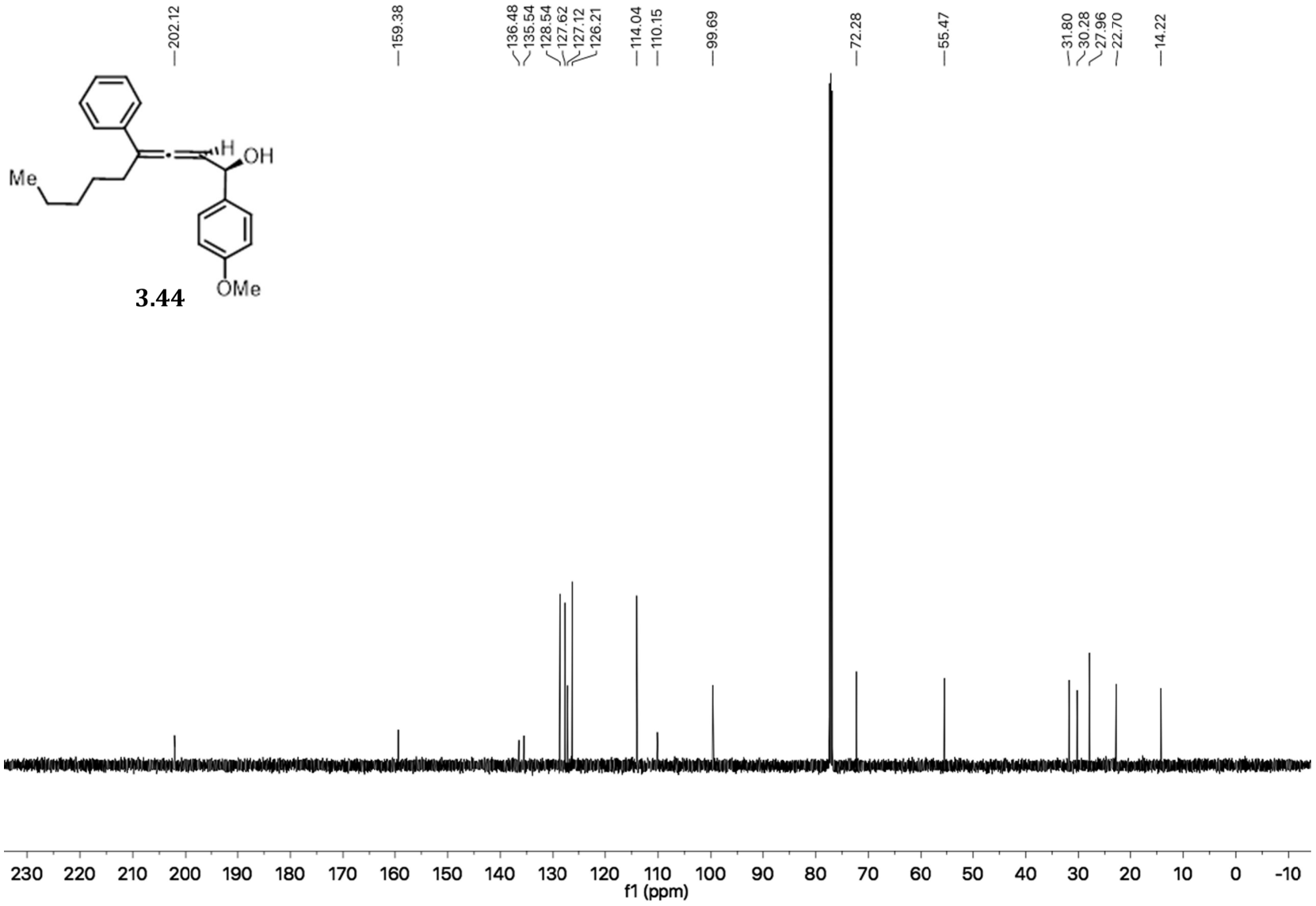
3.43

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

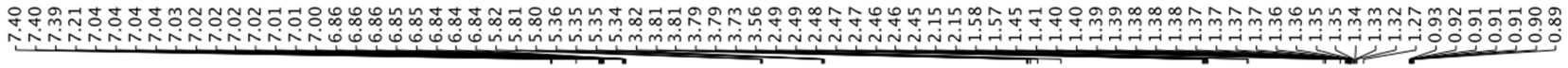


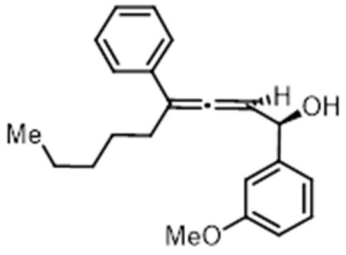
3.44

^{3}C NMR (126 MHz, $CDCl_3$)

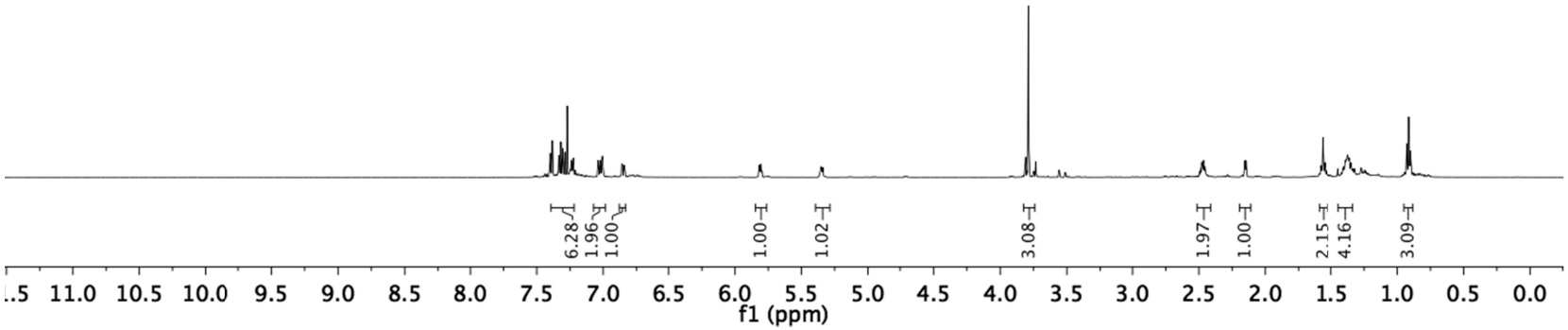


^{1}H NMR (600 MHz, $CDCl_3$)

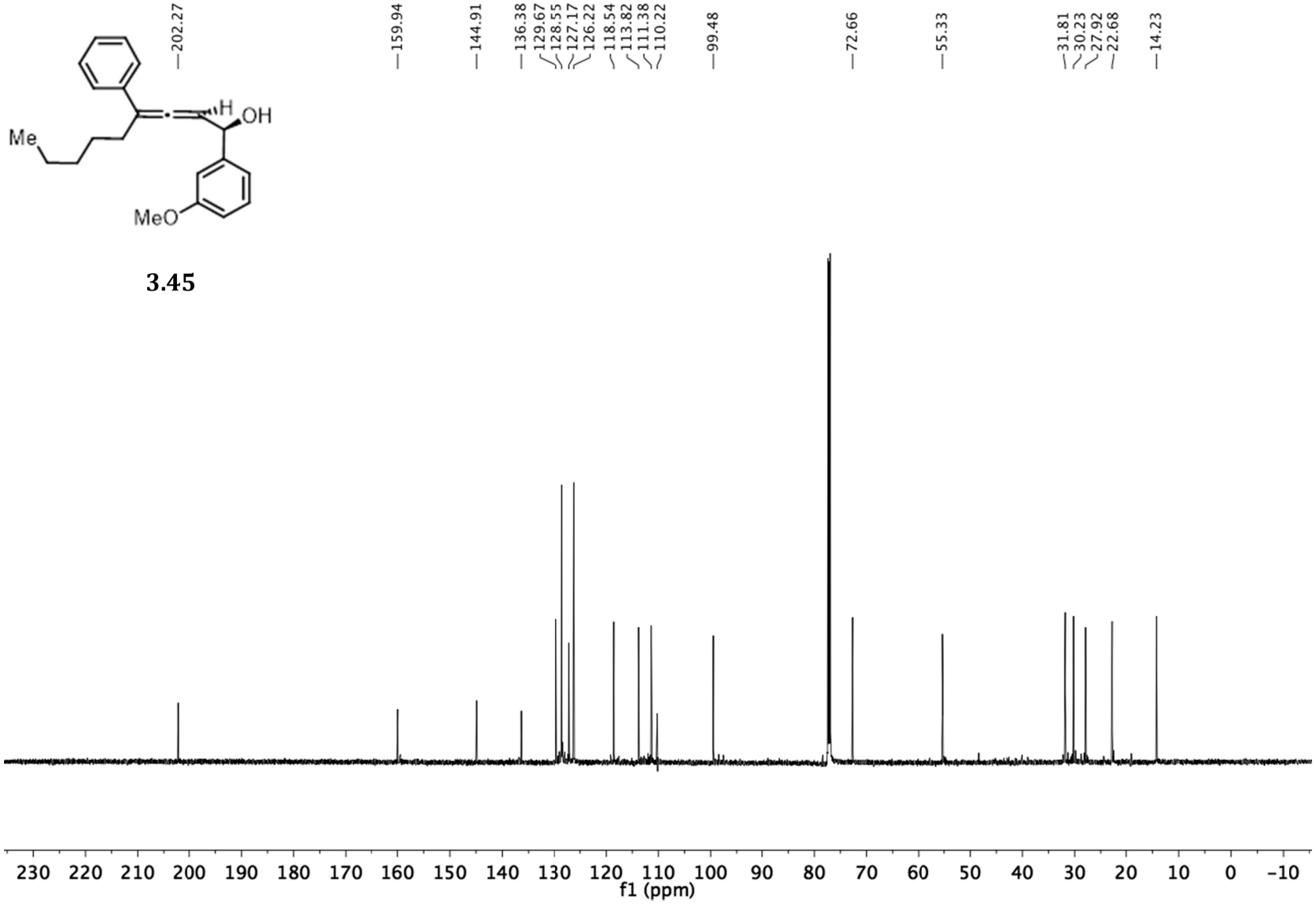




3.45

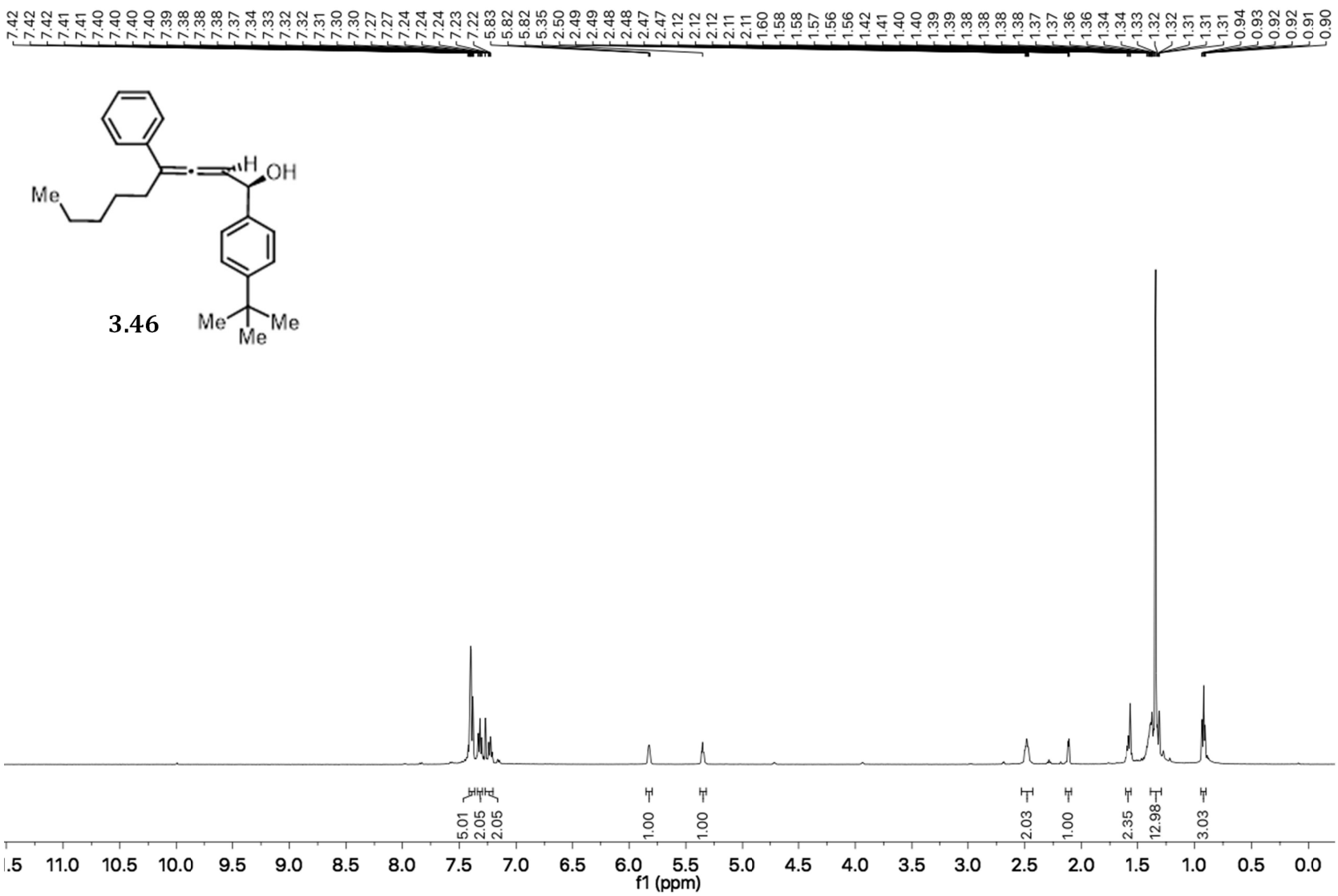


^{13}C NMR (126 MHz, $CDCl_3$)



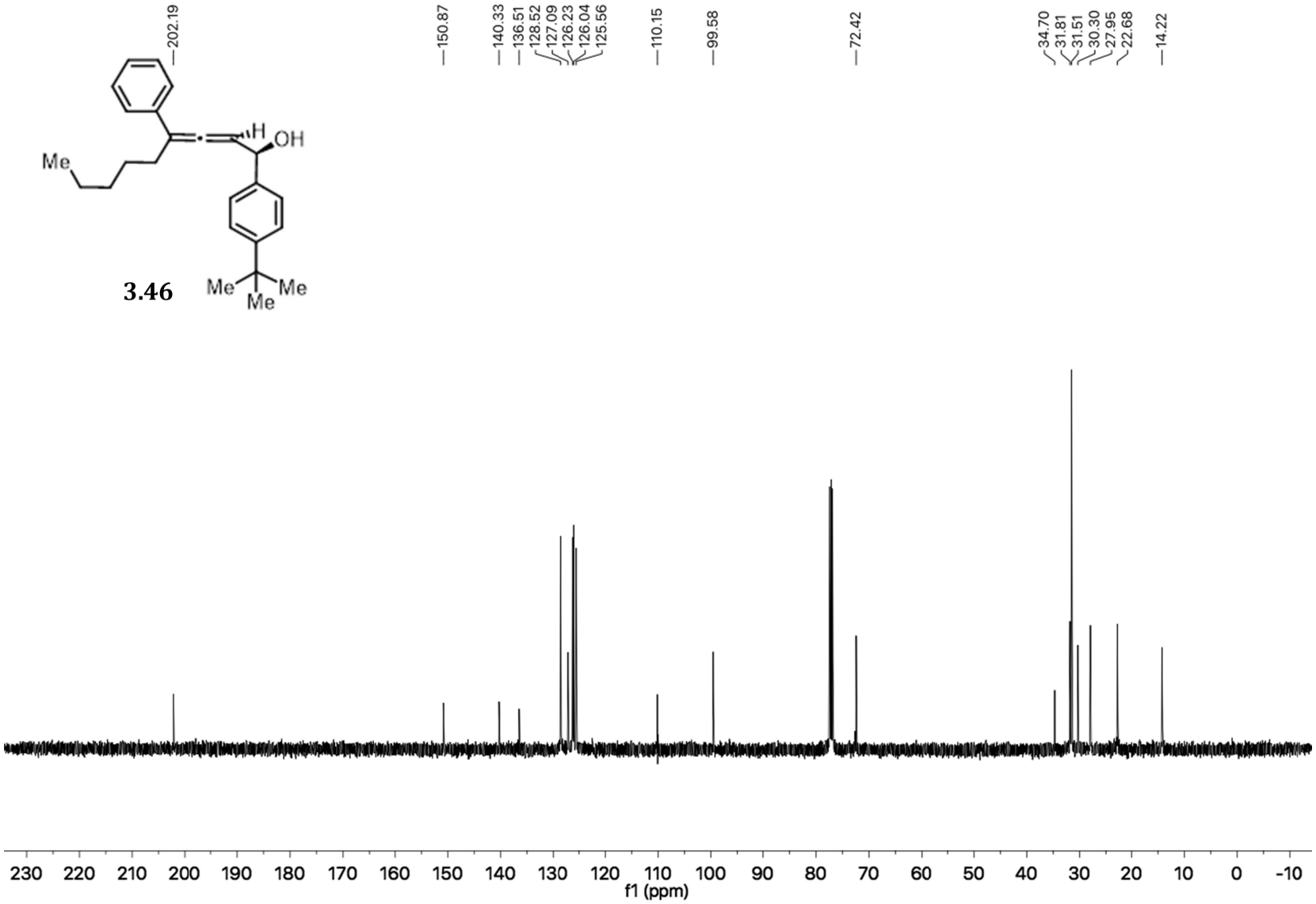
3.45

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

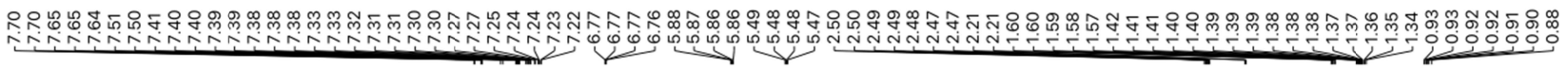


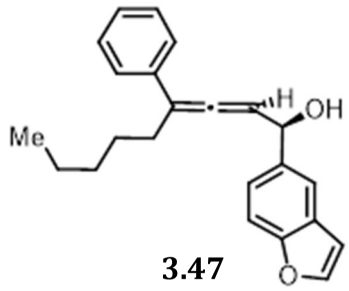
3.46

^{3}C NMR (126 MHz, $CDCl_3$)

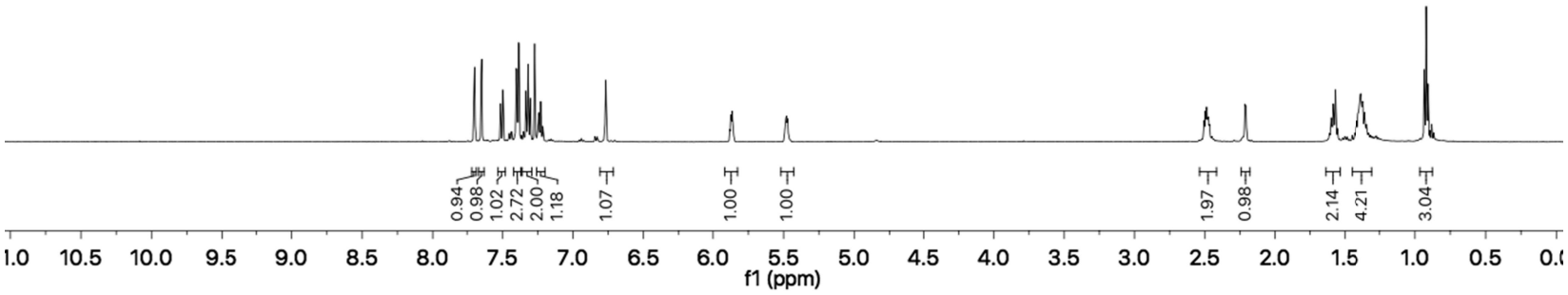


^{1}H NMR (500 MHz, $CDCl_3$)

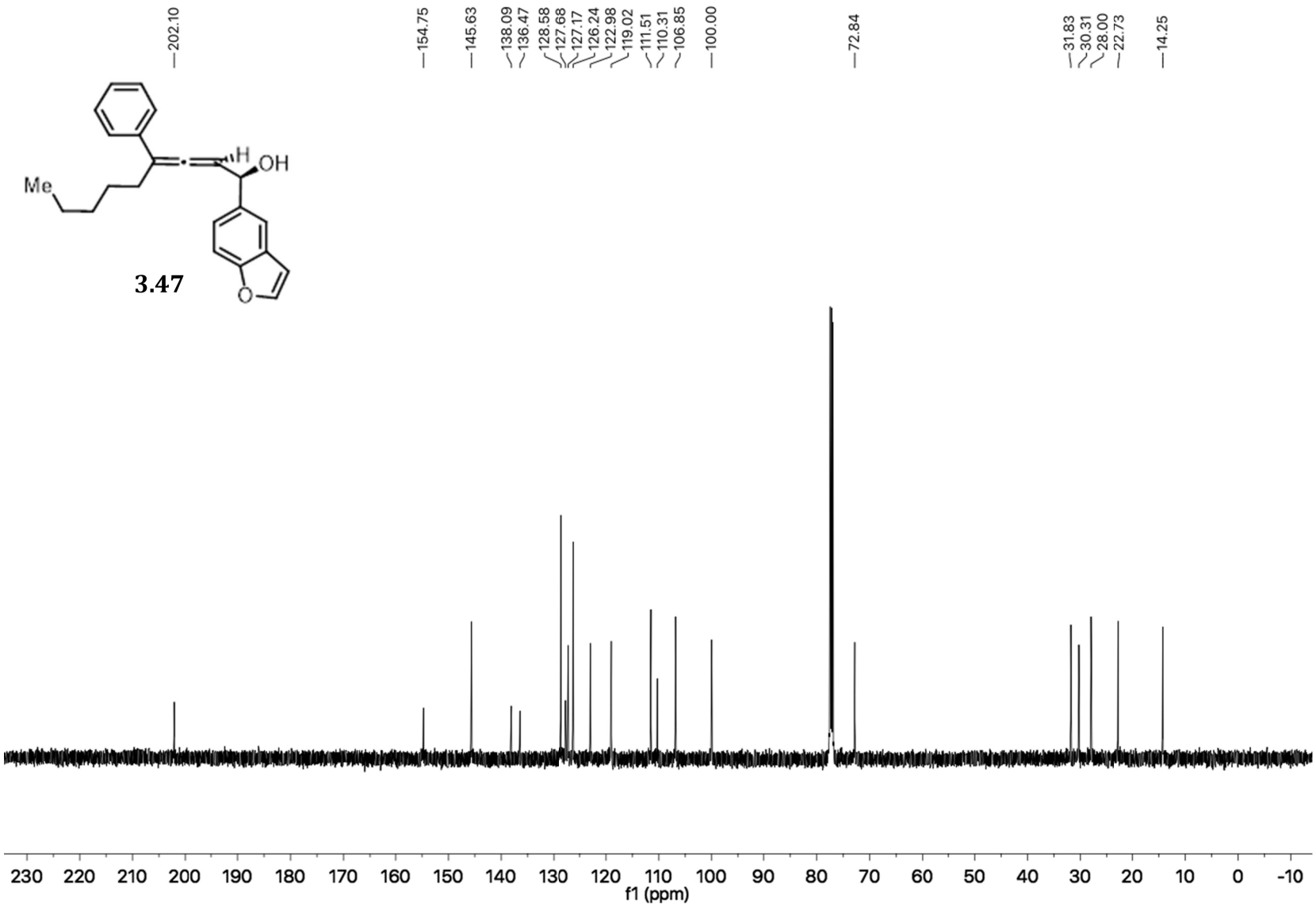




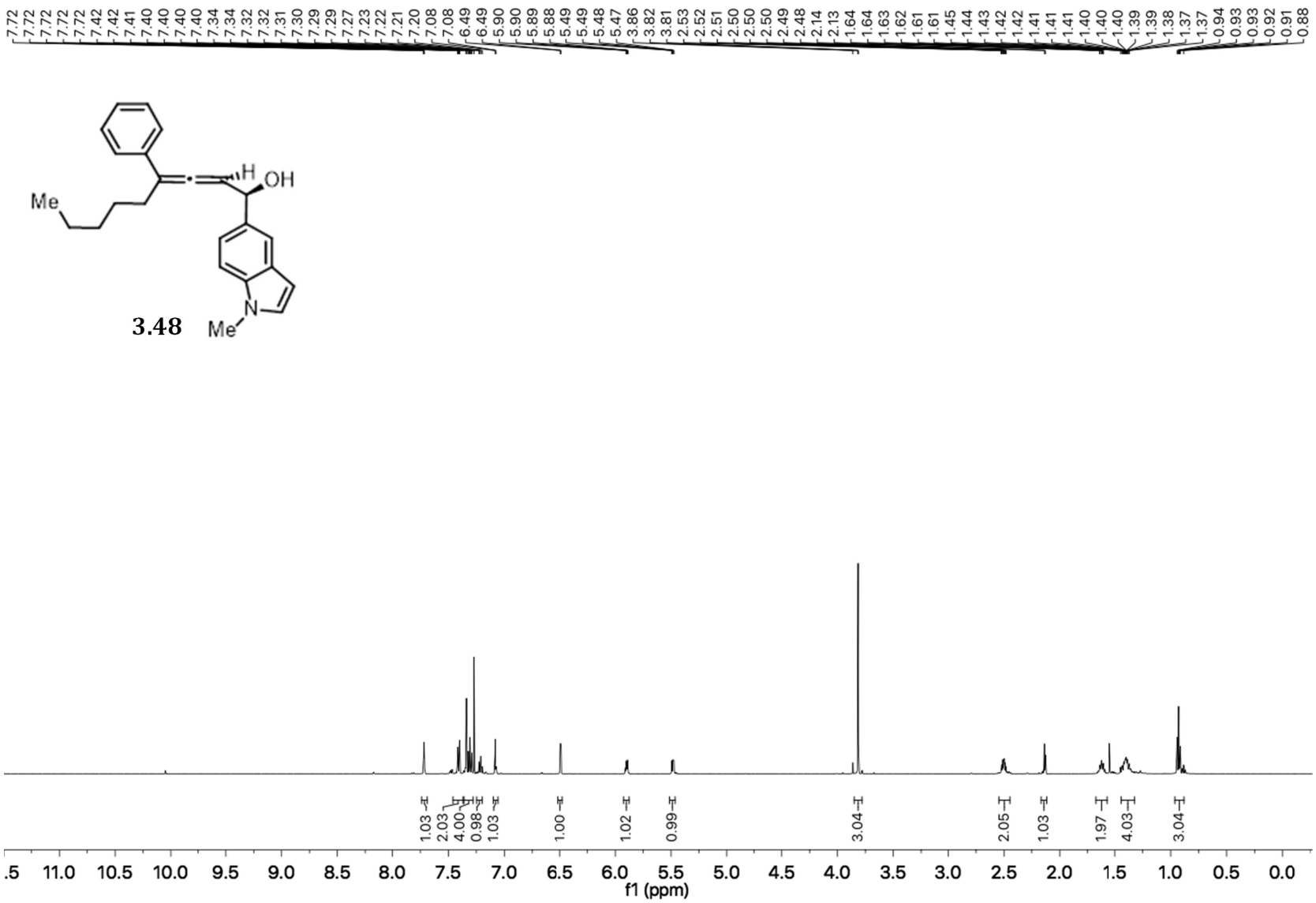
3.47



^{3}C NMR (126 MHz, $CDCl_3$)

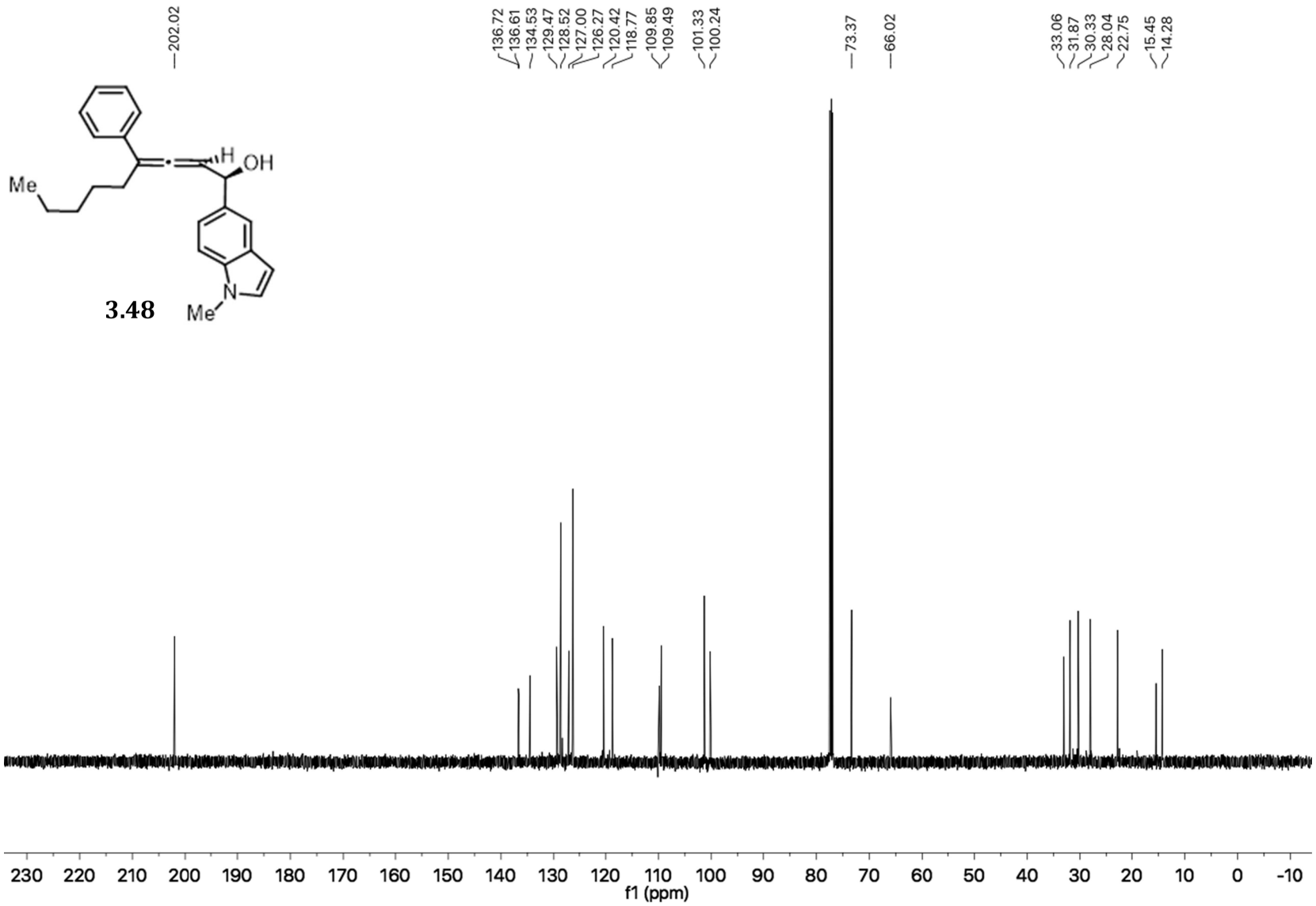


^{1}H NMR (500 MHz, $CDCl_3$)

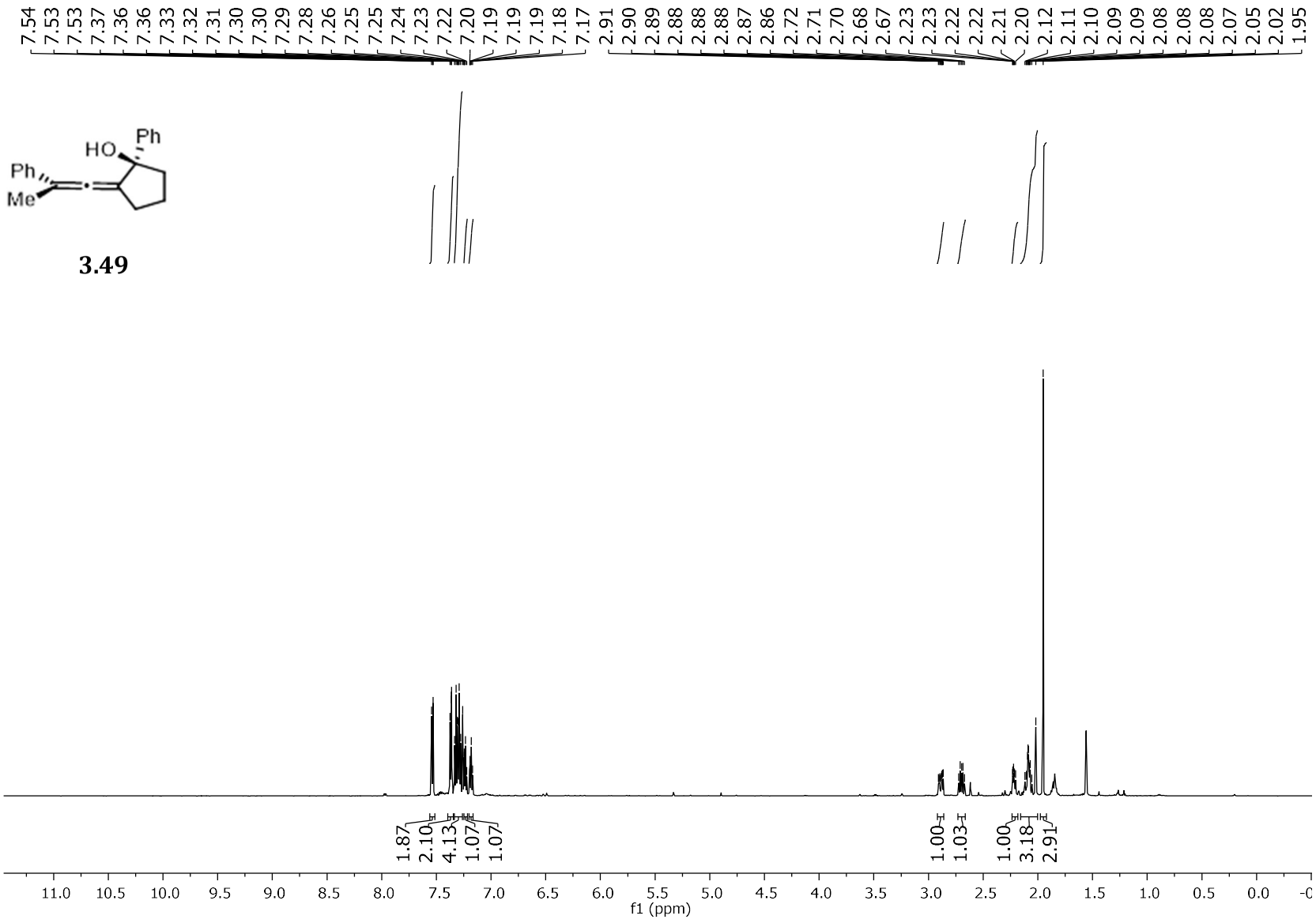


3.48

^{3}C NMR (126 MHz, $CDCl_3$)



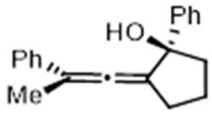
^{1}H NMR (600 MHz, $CDCl_3$)



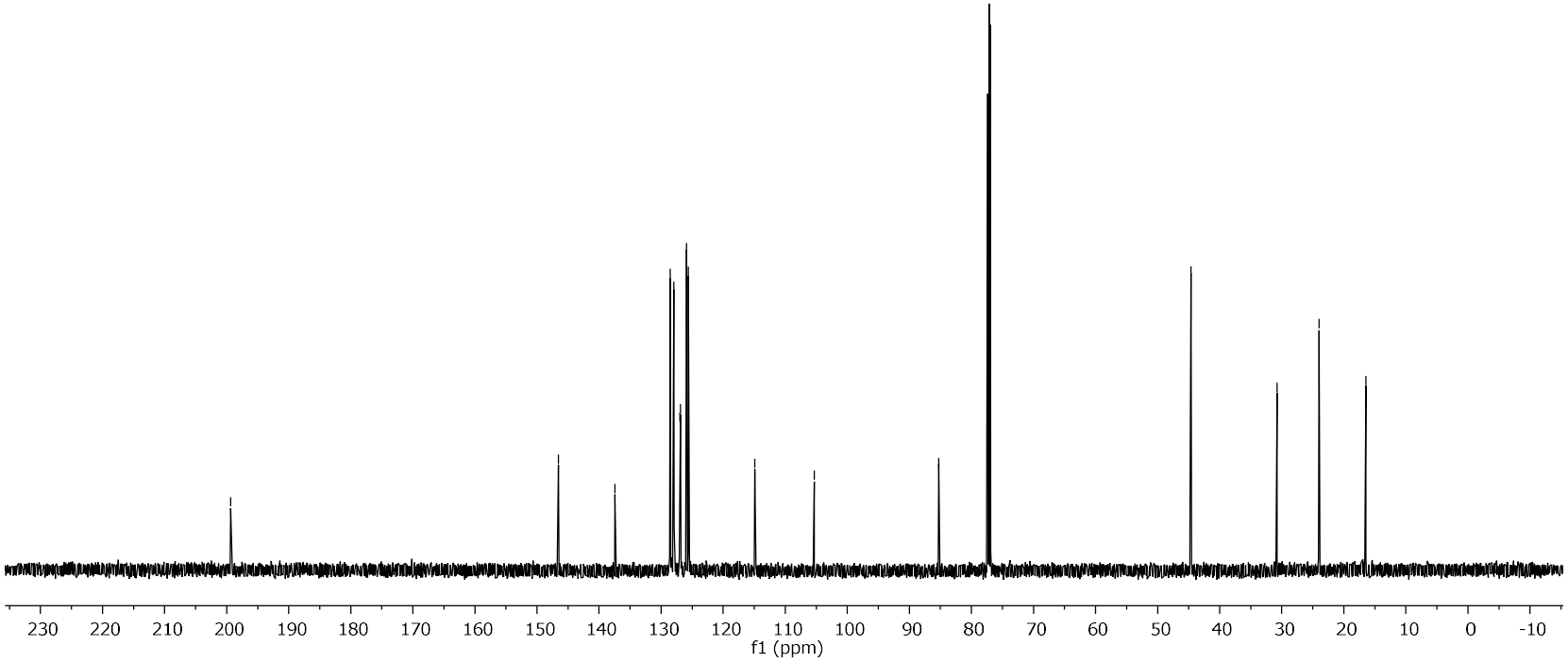
3.49

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

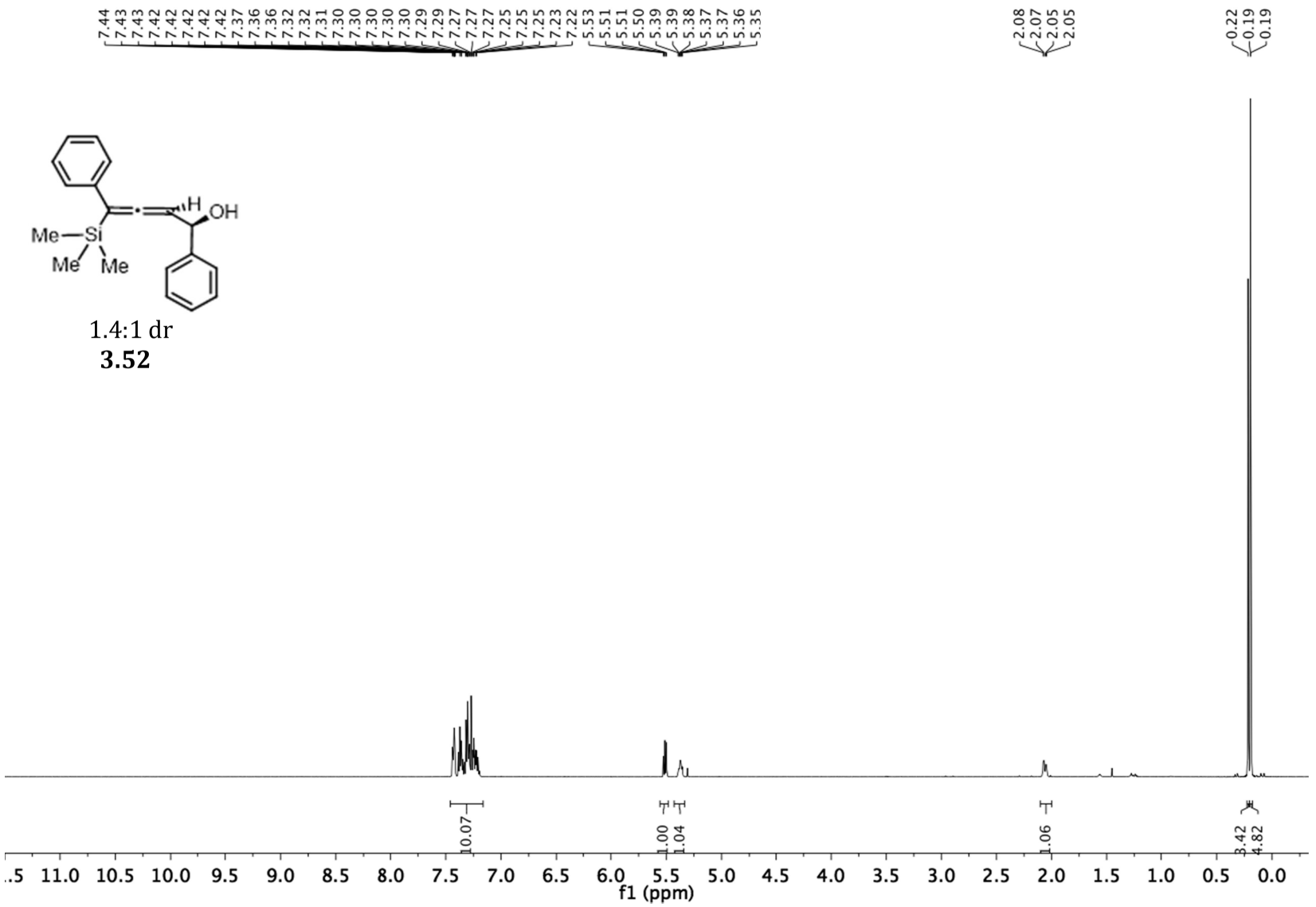
199.37
146.52
137.44
128.54
127.94
126.97
126.88
125.93
125.59
114.92
105.32
85.26
44.63
30.77
23.97
16.45



3.49



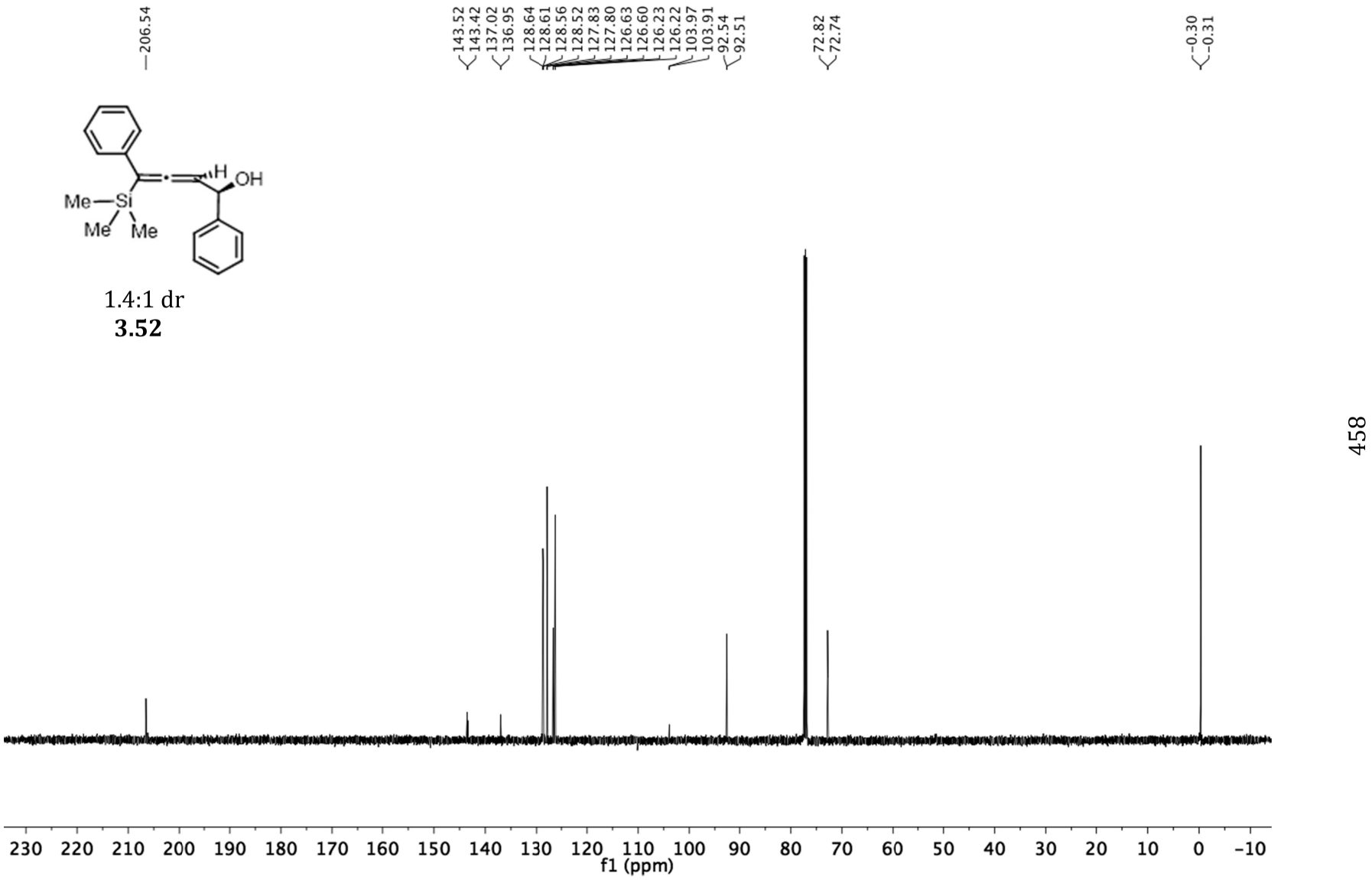
^{1}H NMR (600 MHz, $CDCl_3$)



1.4:1 dr

3.52

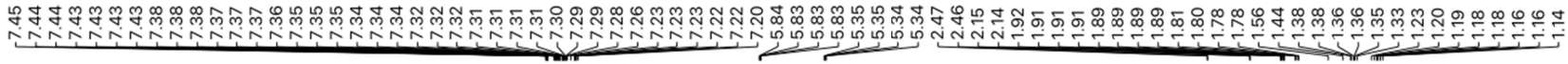
^{13}C NMR (126 MHz, $CDCl_3$)

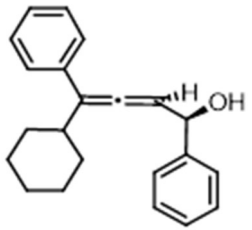


1.4:1 dr

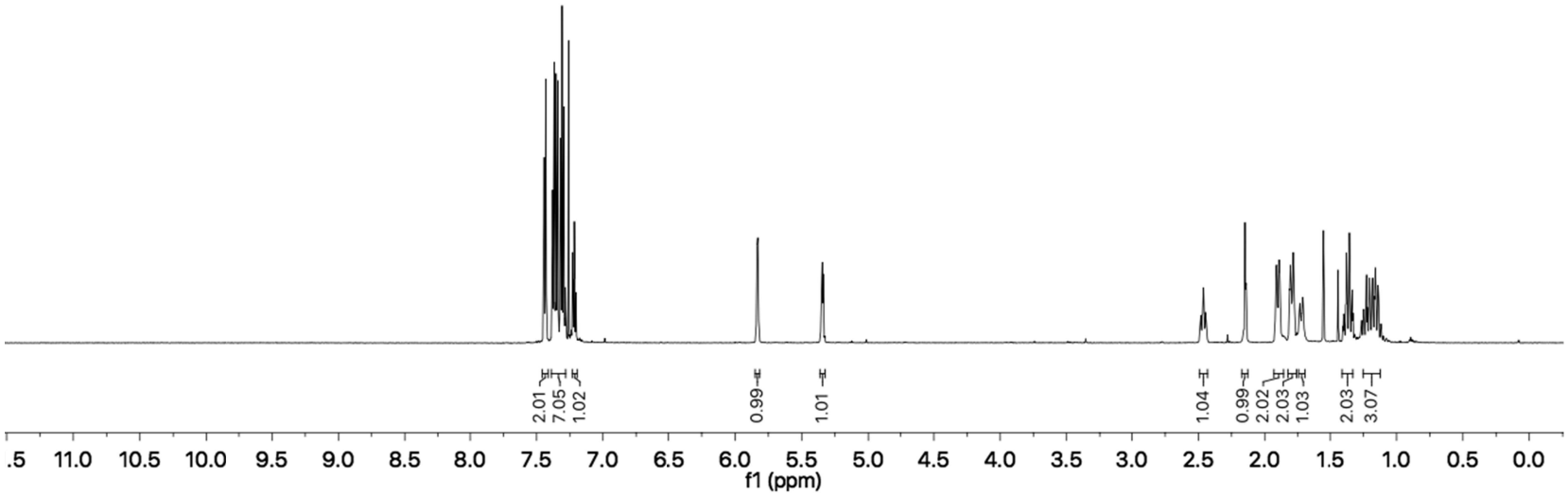
3.52

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

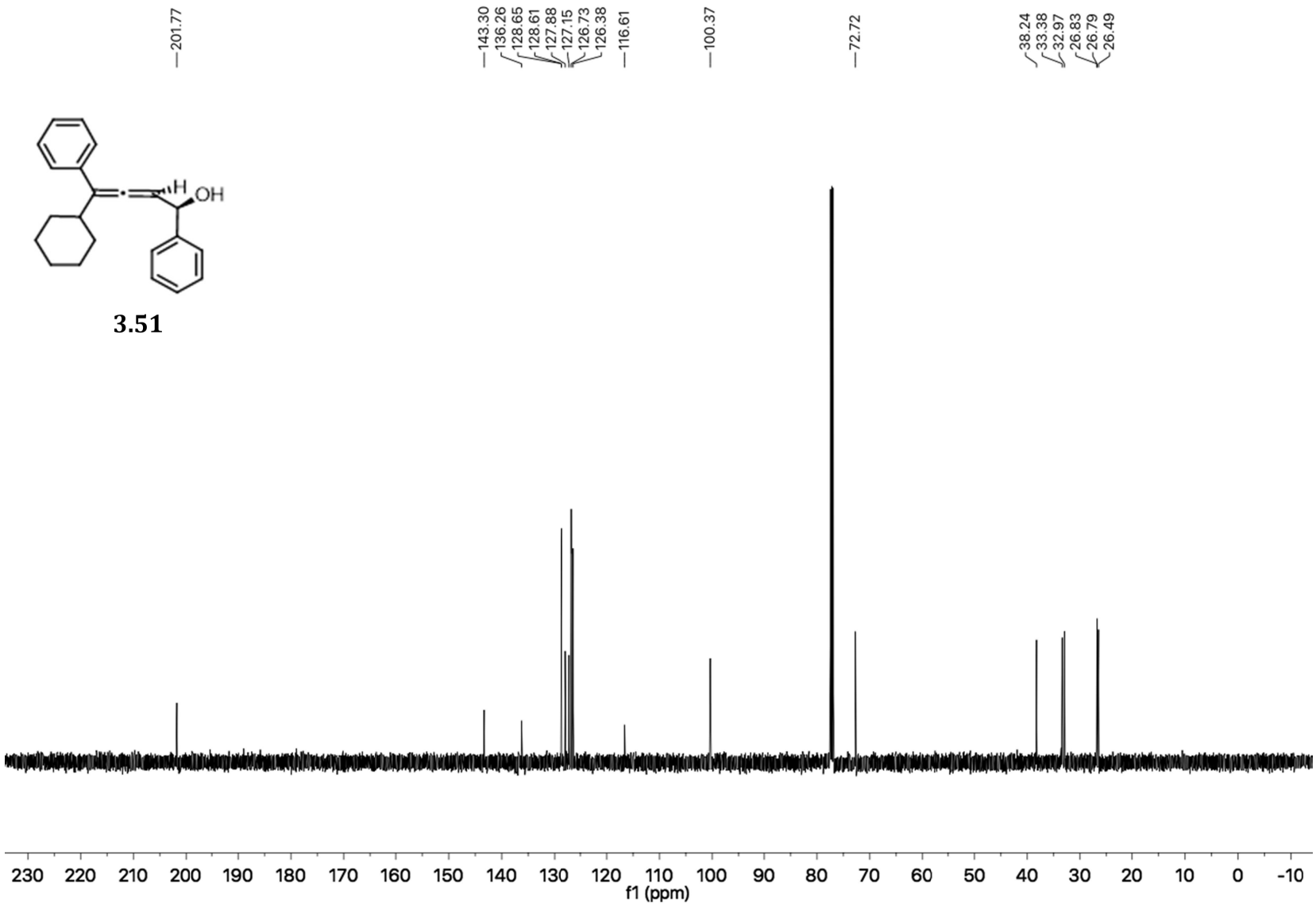




3.51

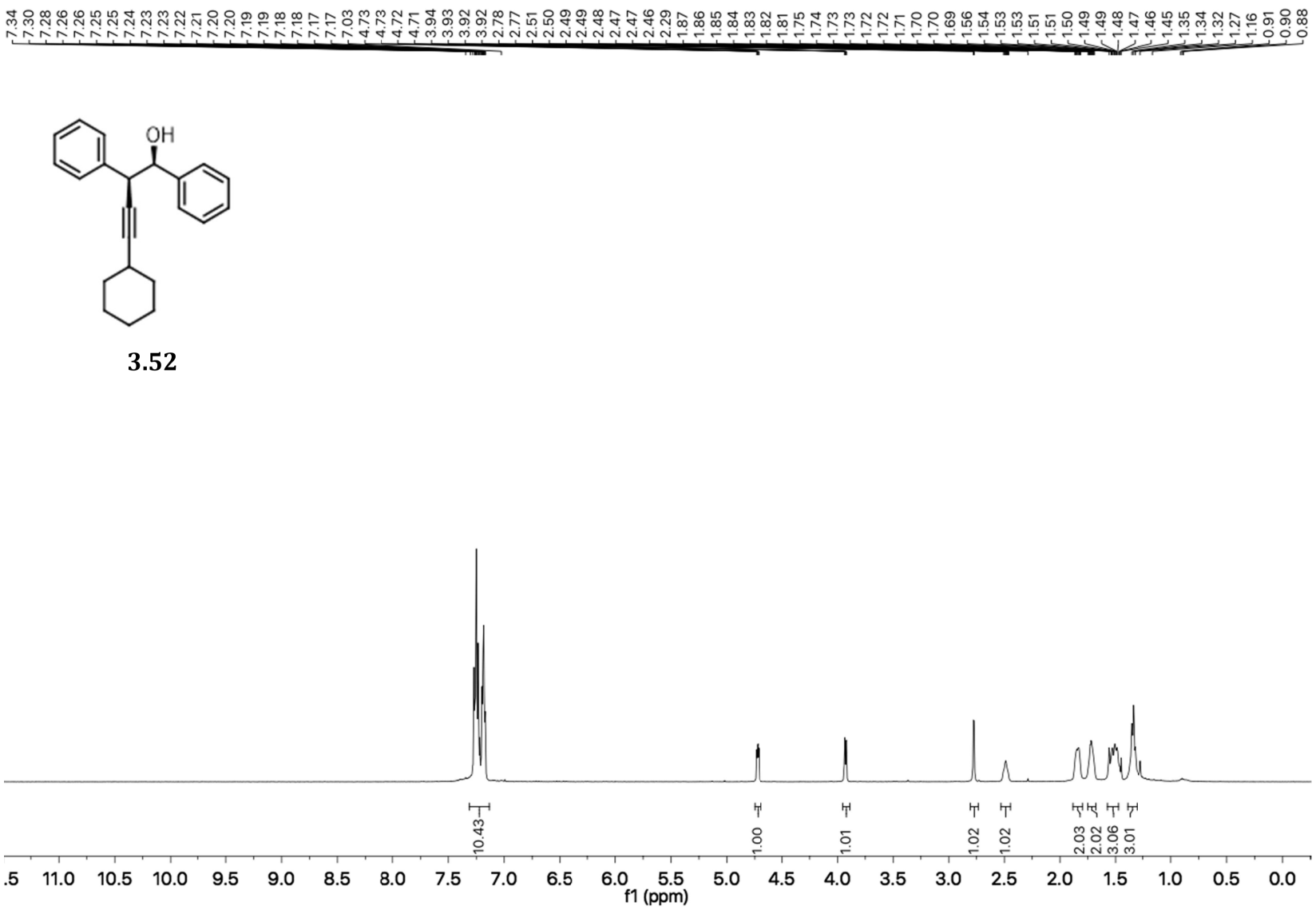


^{13}C NMR (126 MHz, $CDCl_3$)



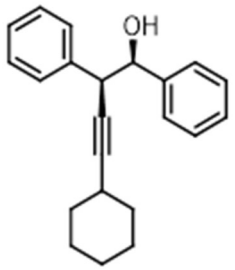
3.51

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



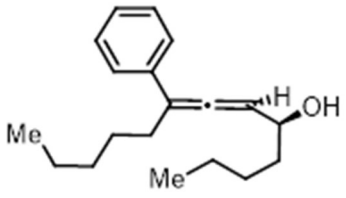
3.52

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

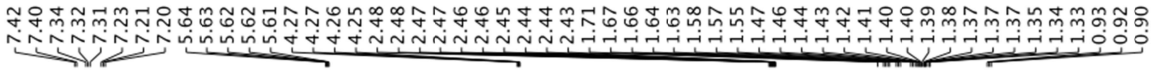


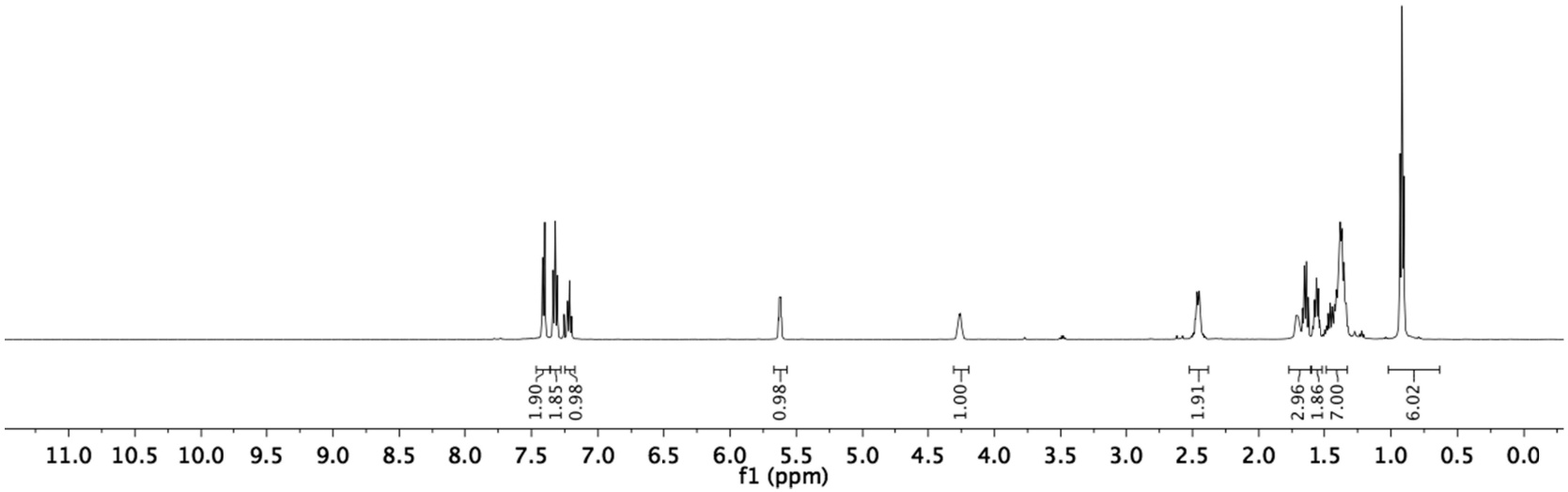
3.52

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

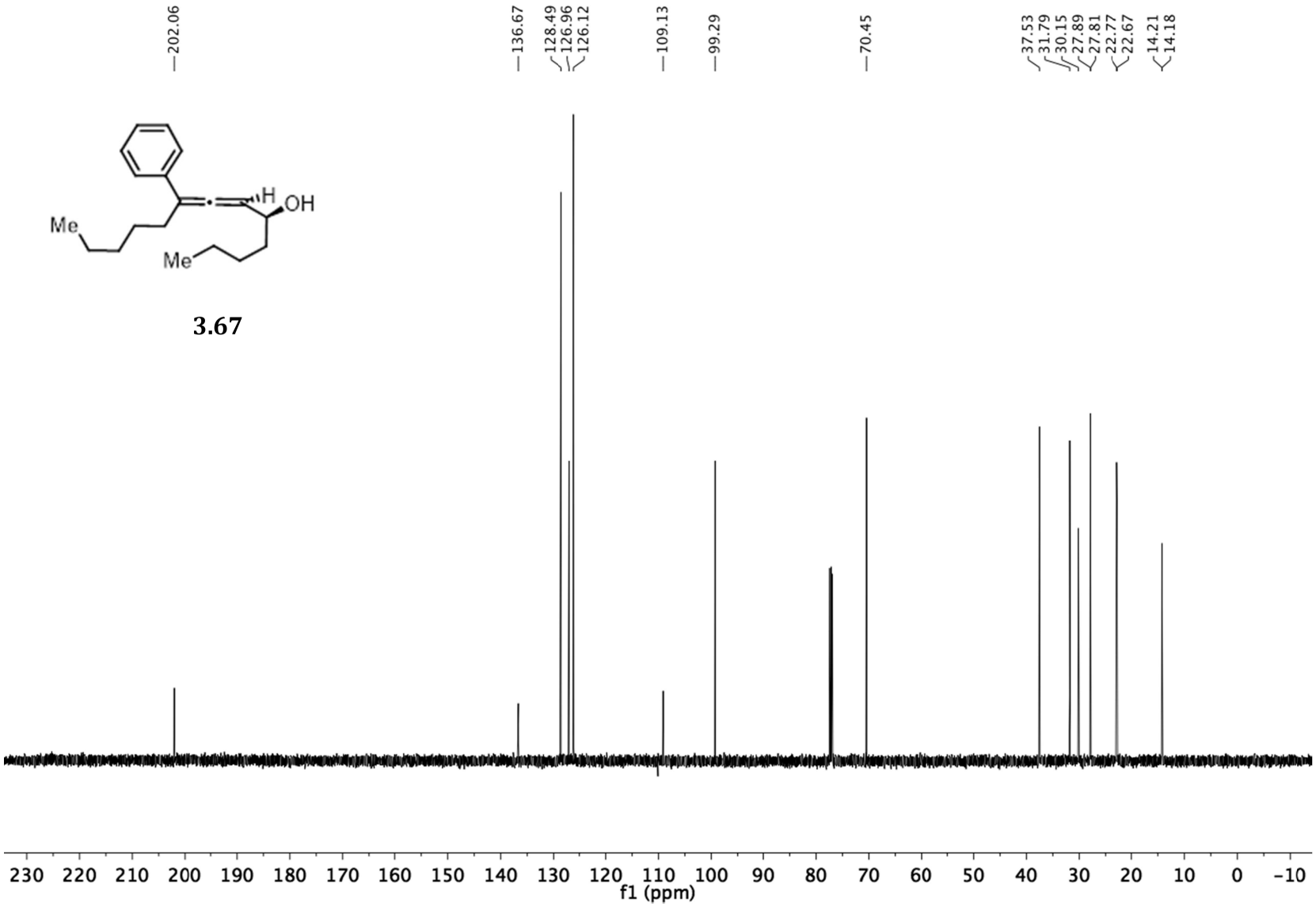


3.67



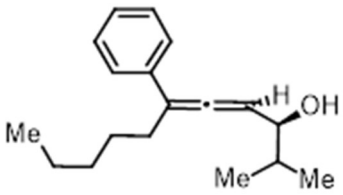


^{13}C NMR (126 MHz, $CDCl_3$)

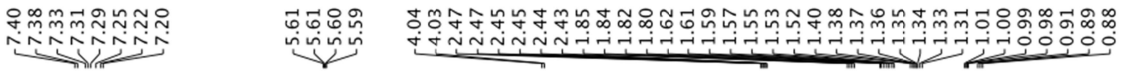


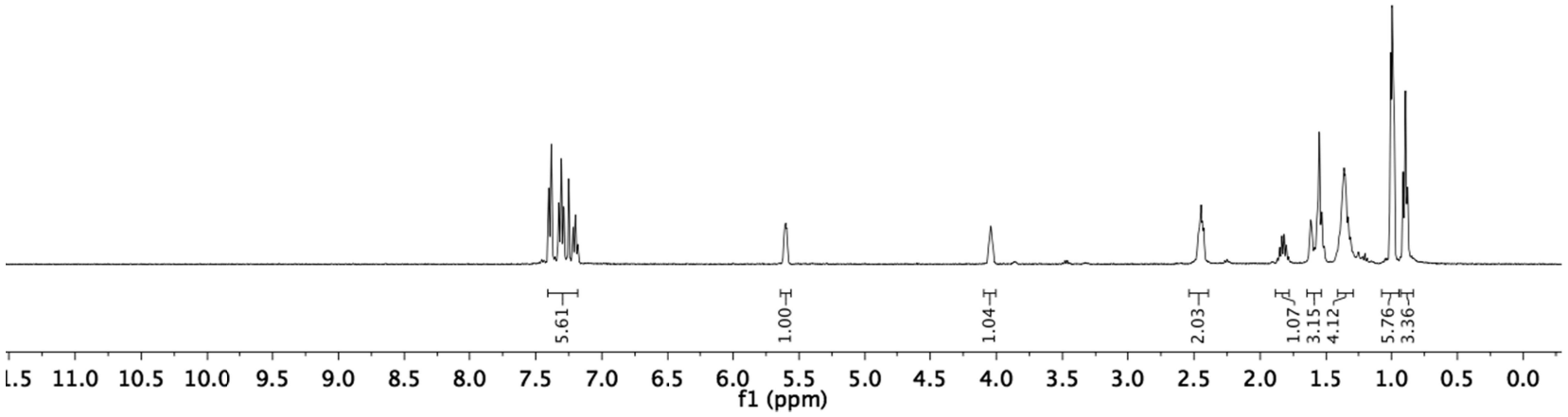
3.67

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



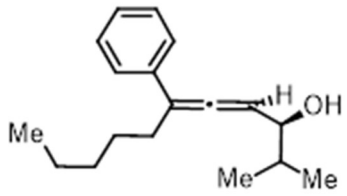
3.70



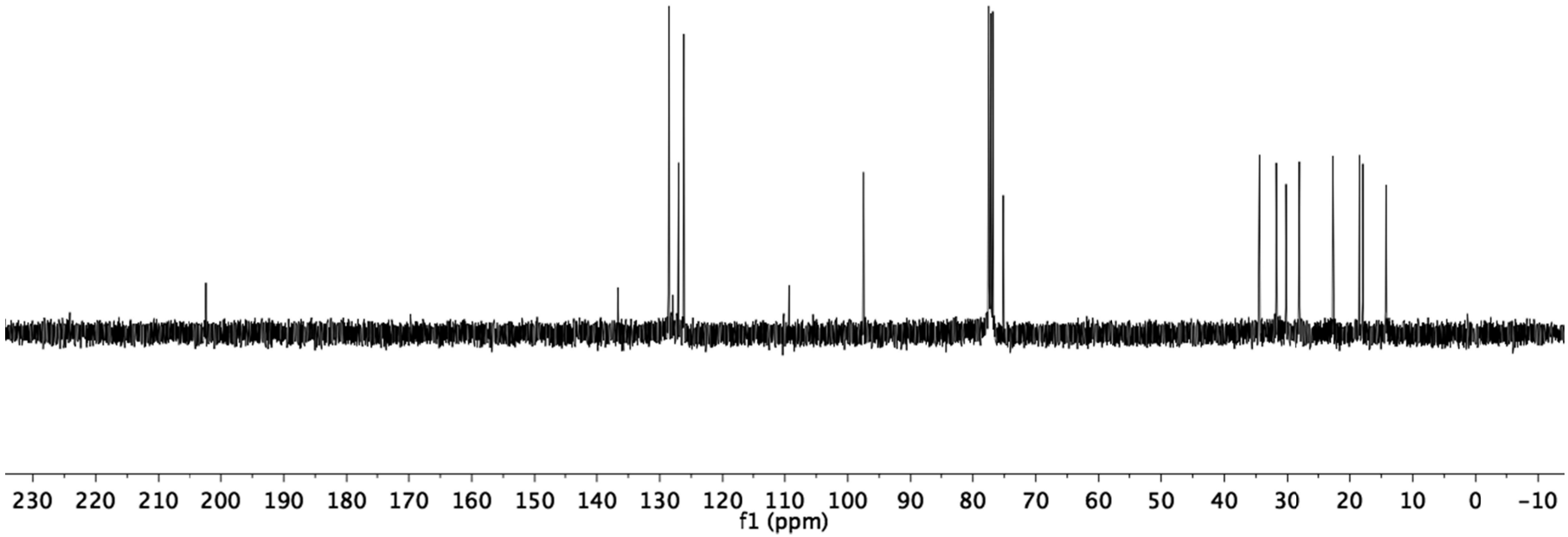


^{13}C NMR (126 MHz, $CDCl_3$)

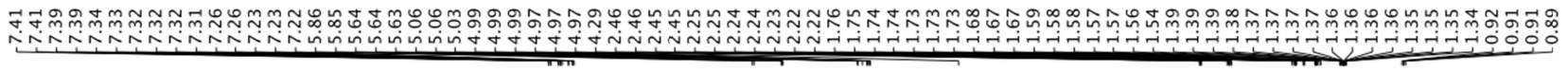
202
136.67
128.52
127.00
126.17
109.33
97.50
75.15
34.45
31.80
30.26
27.99
22.69
18.45
17.94
14.23

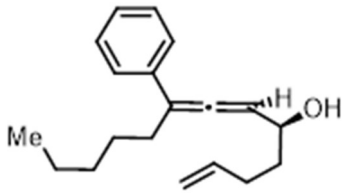


3.70

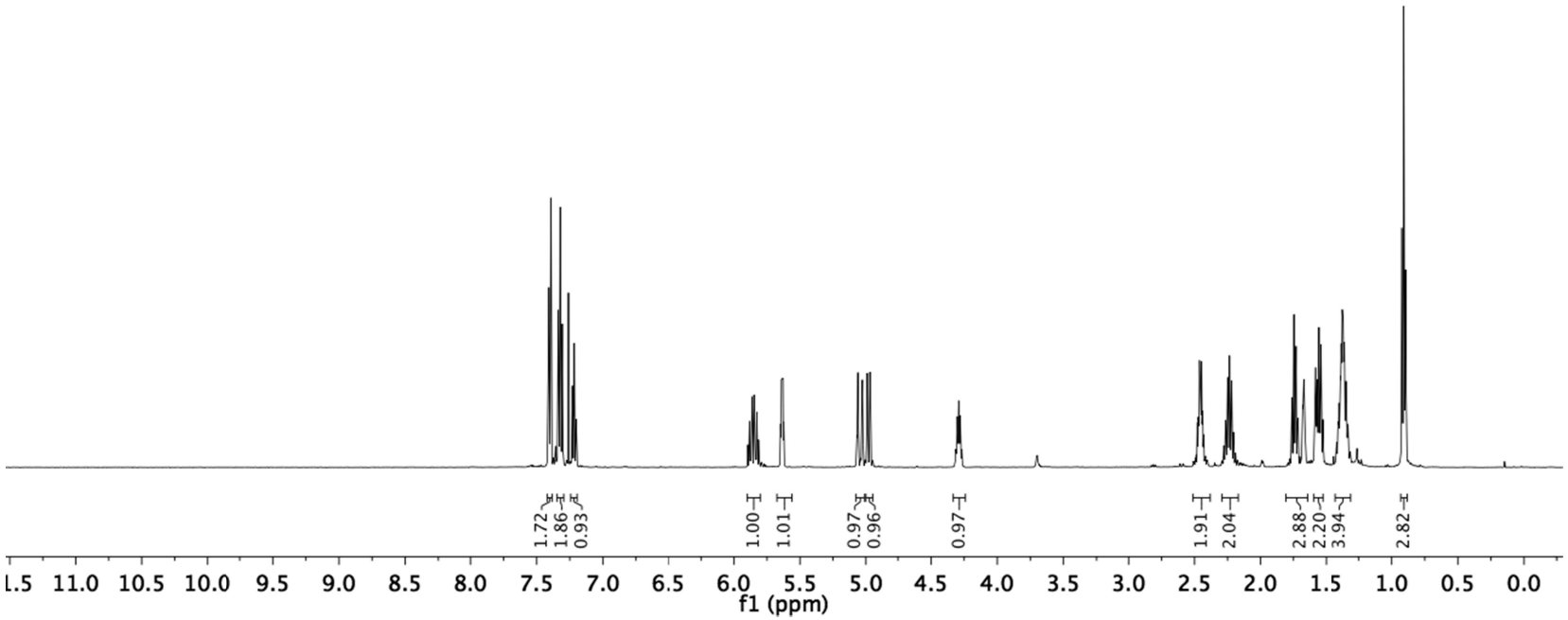


^{1}H NMR (500 MHz, $CDCl_3$)

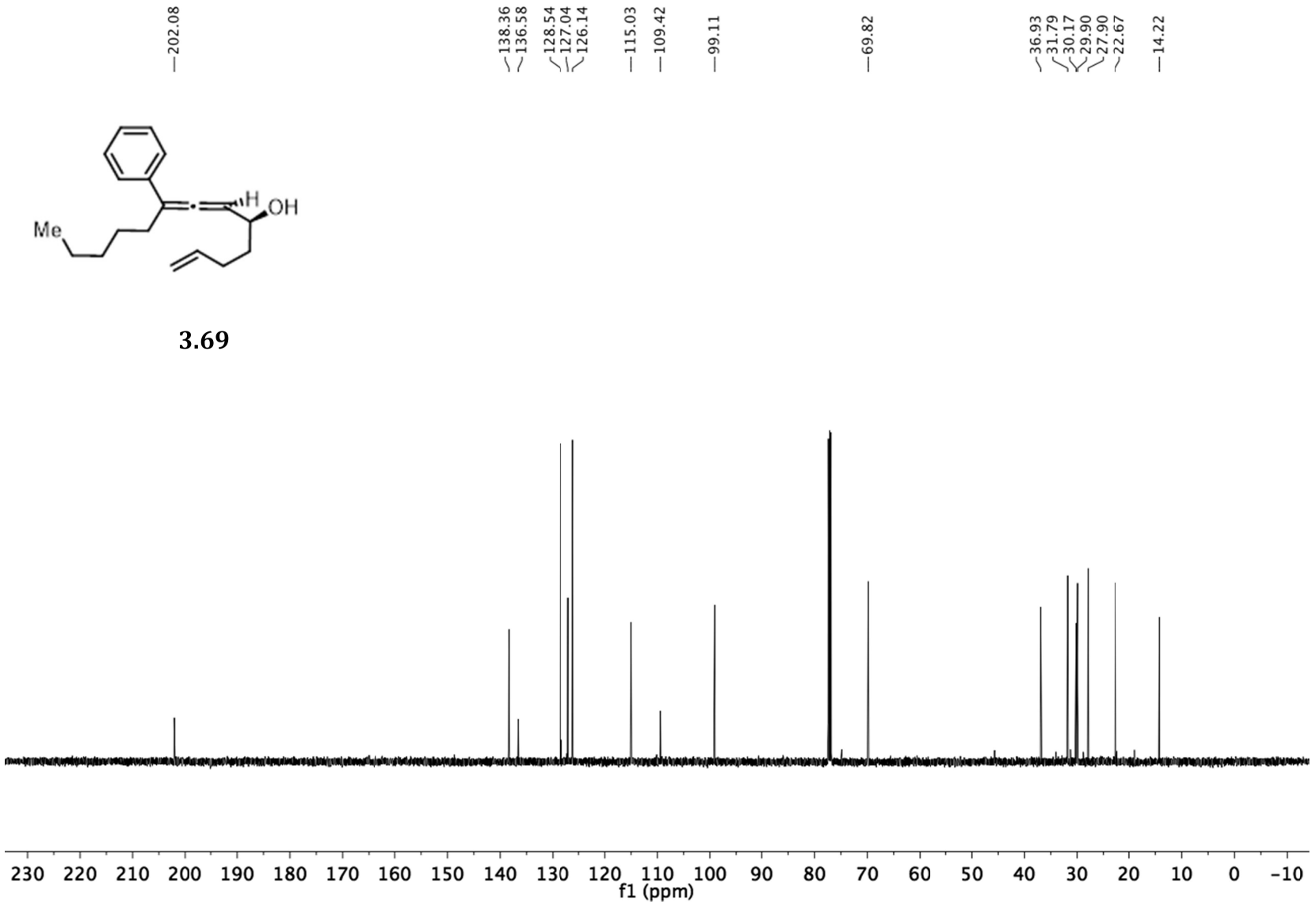




3.69

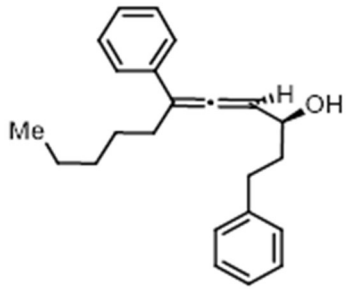


^{13}C NMR (126 MHz, $CDCl_3$)



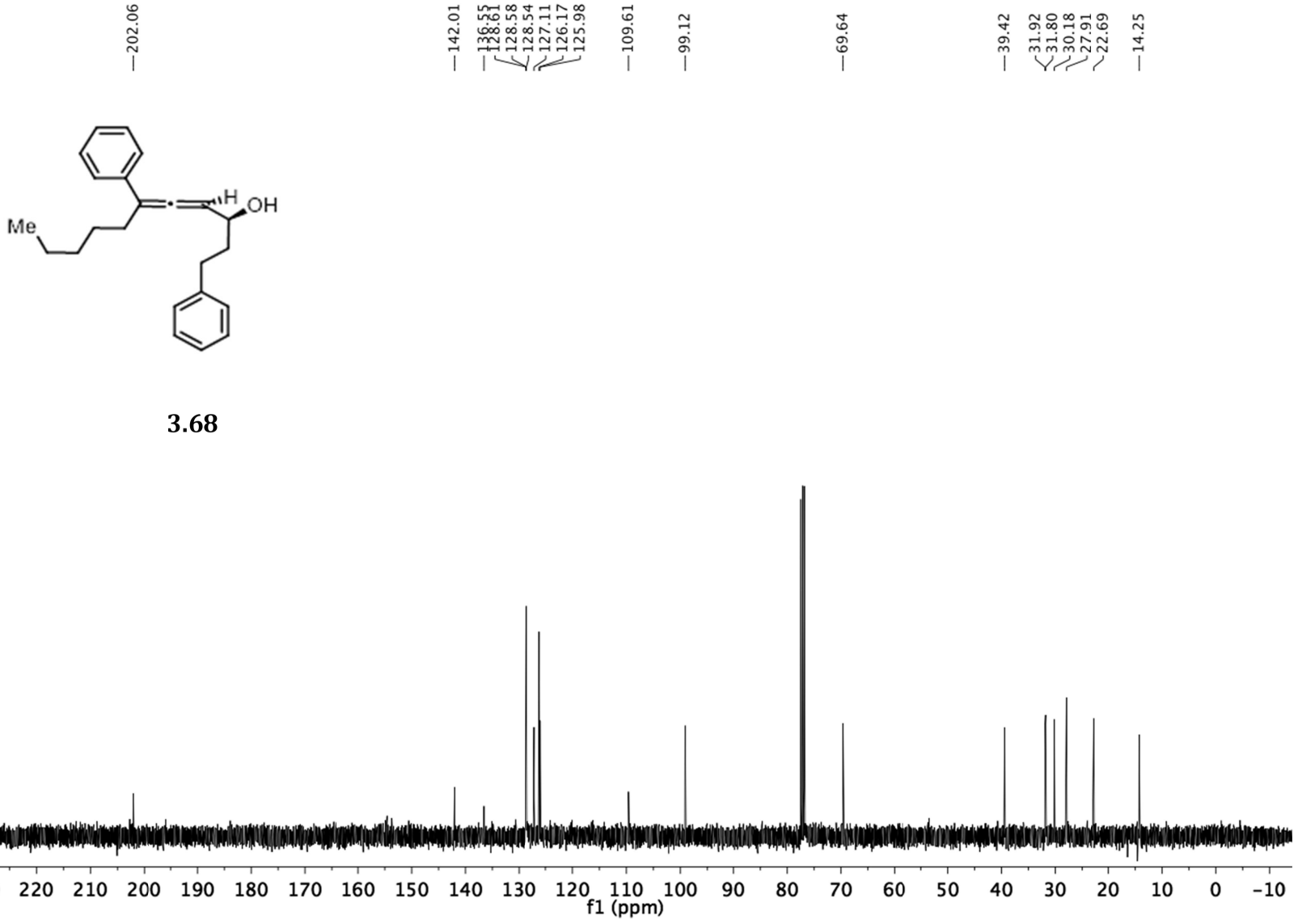
3.69

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



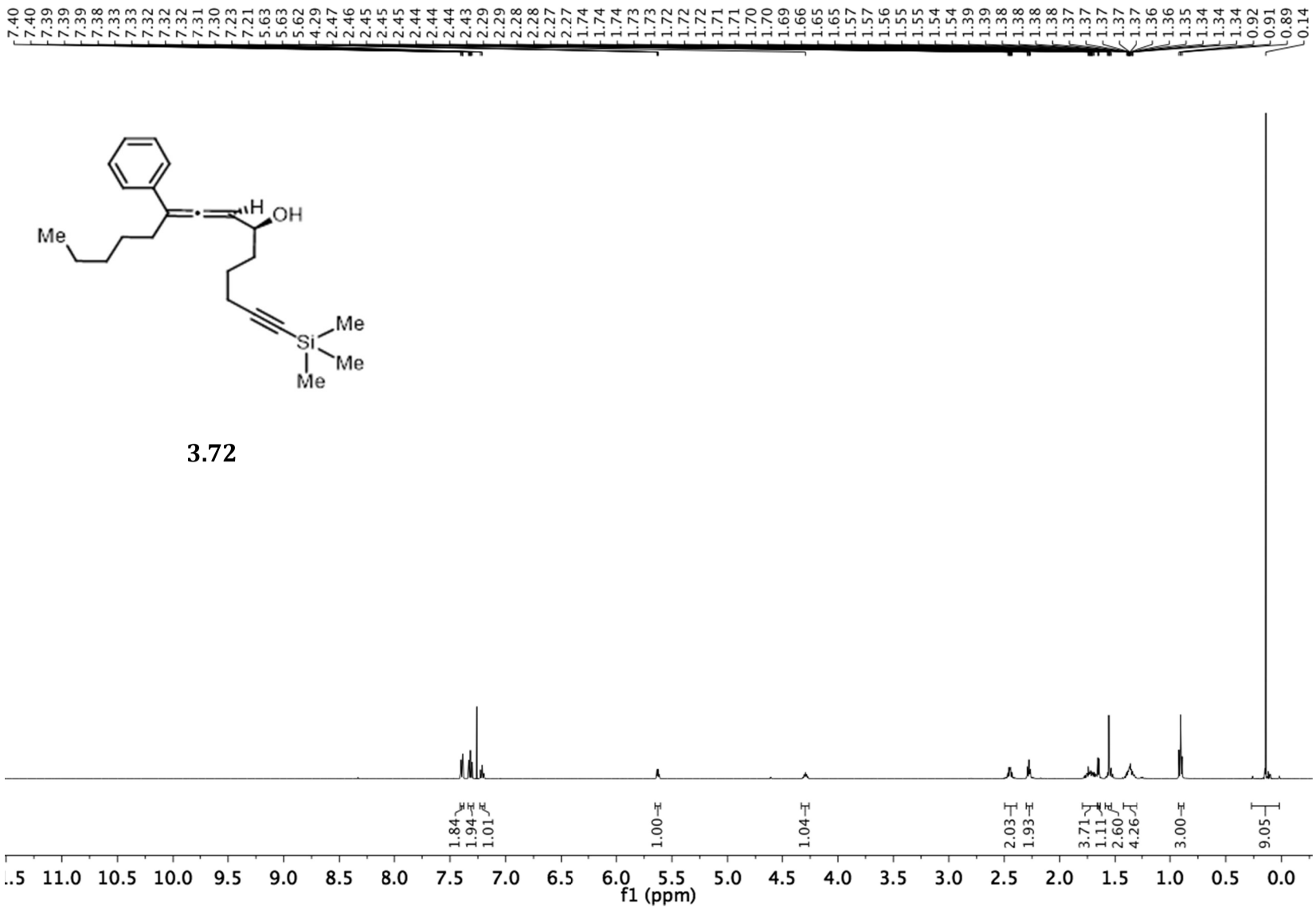
3.68

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



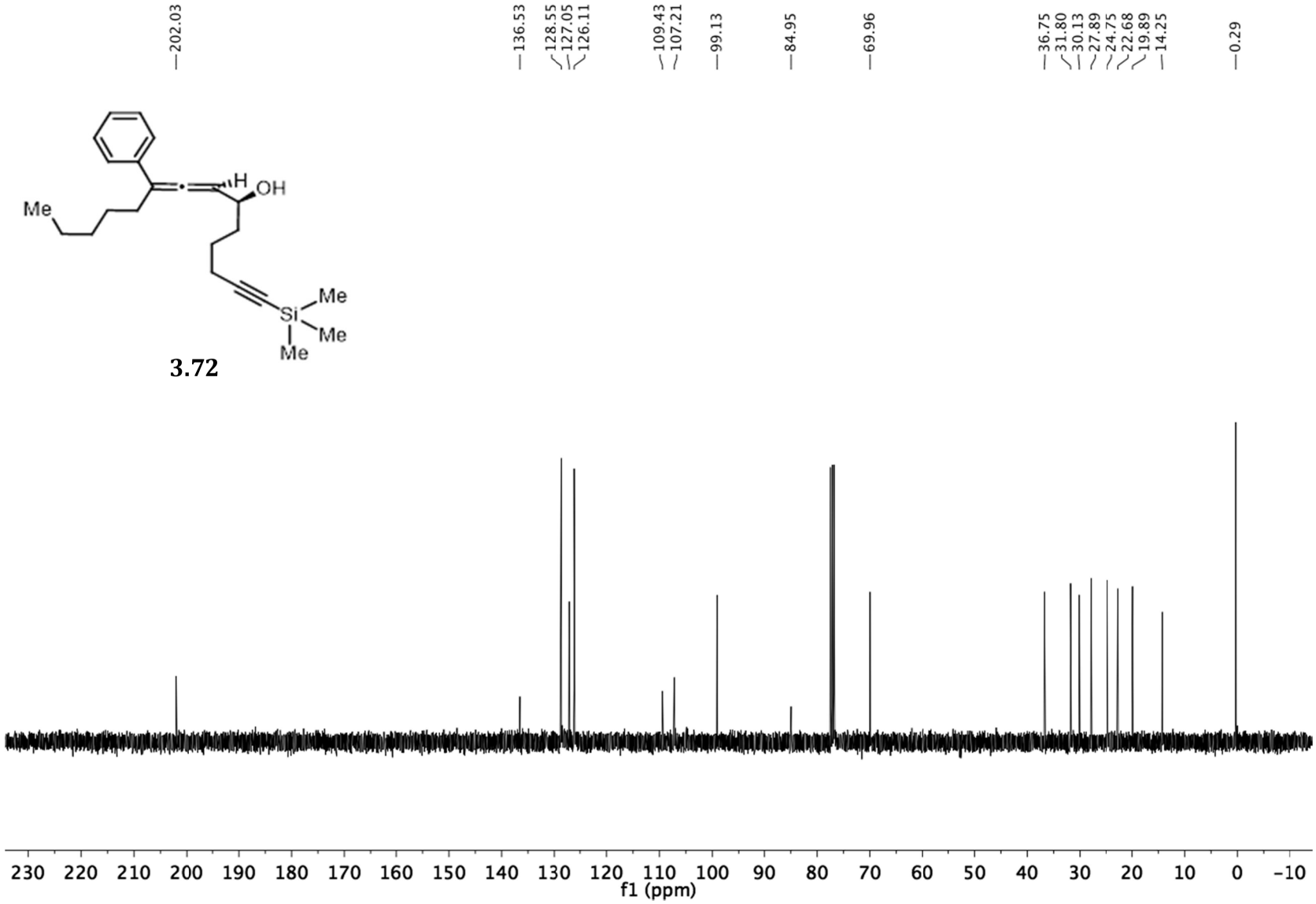
3.68

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



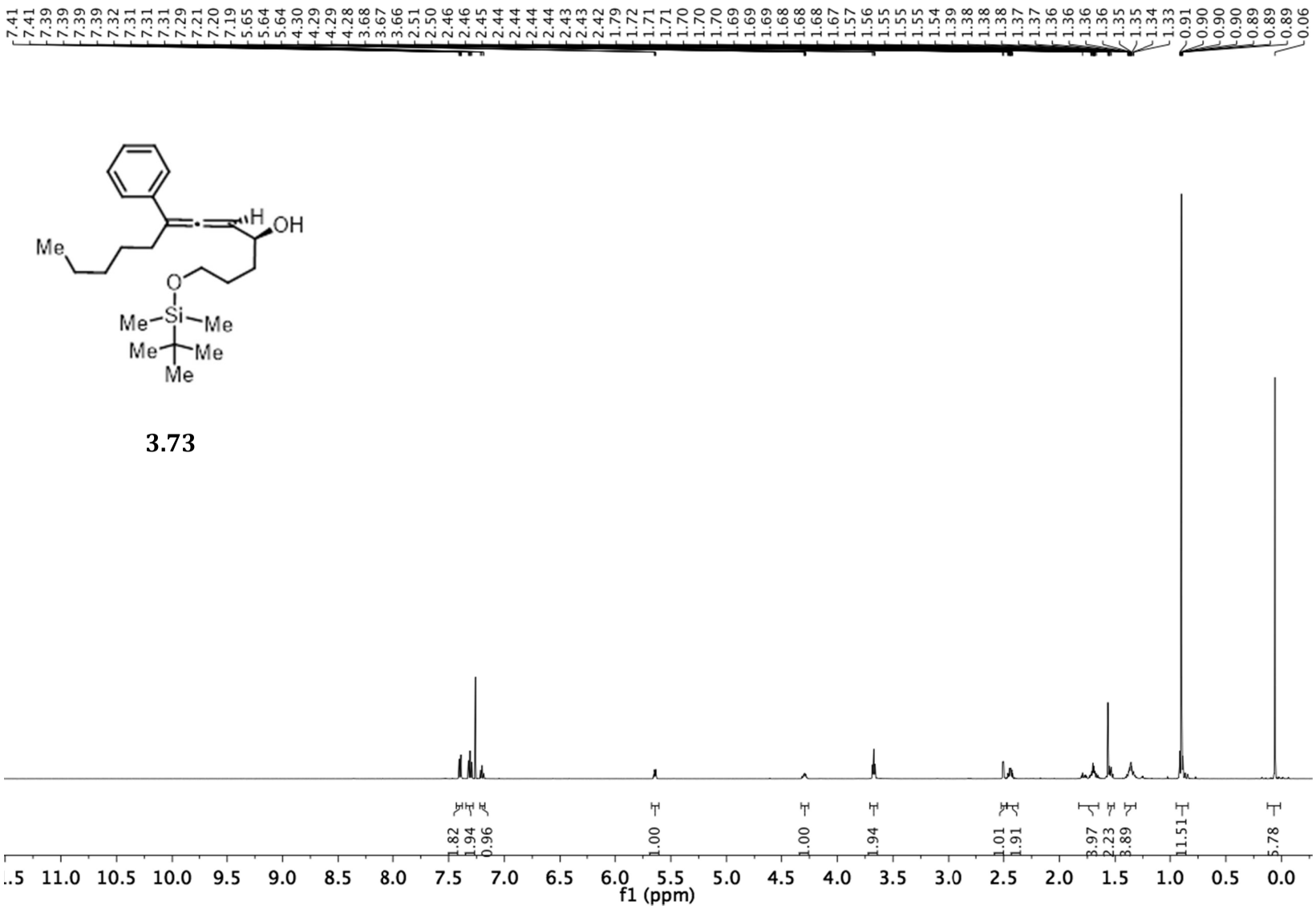
3.72

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



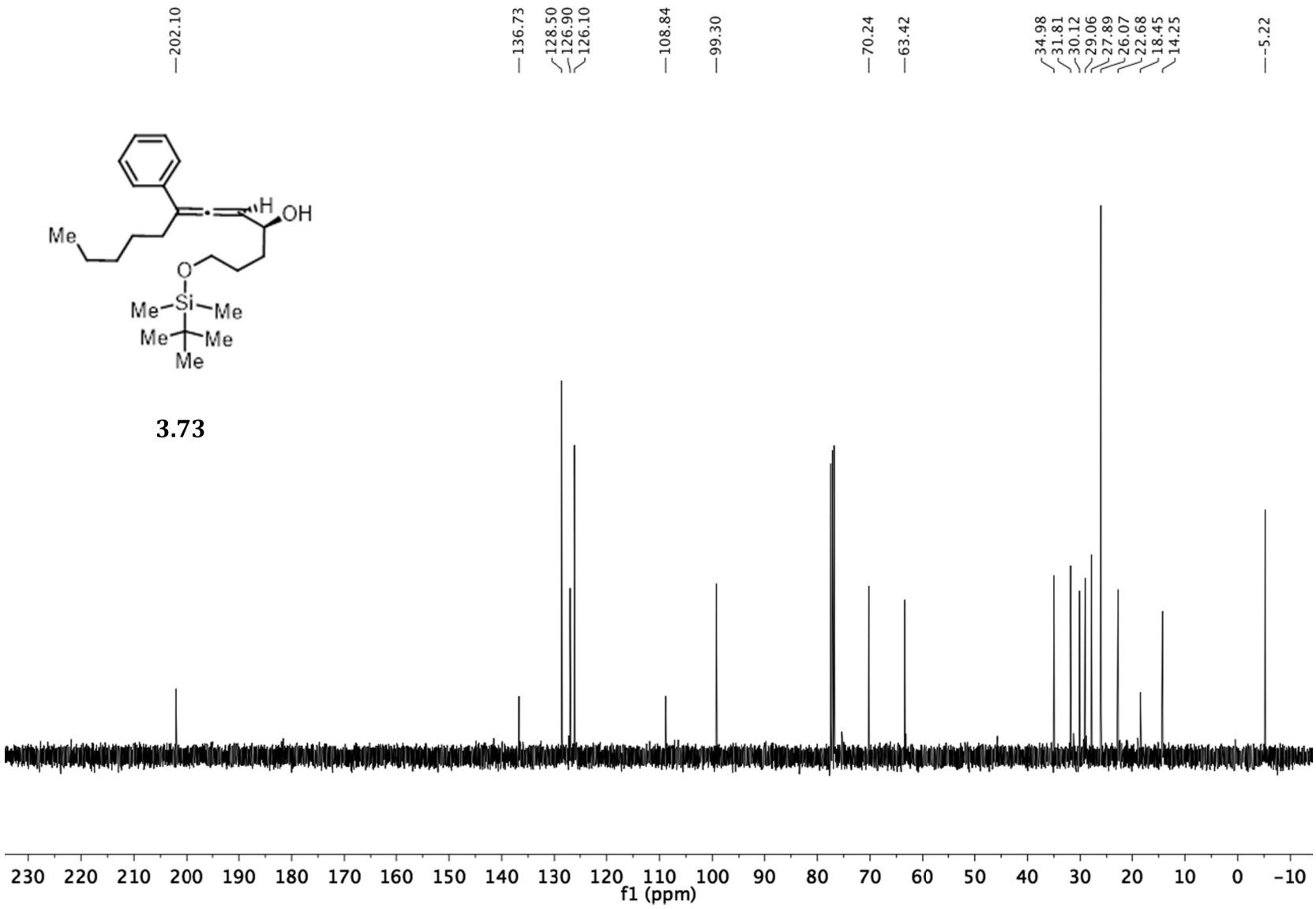
3.72

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



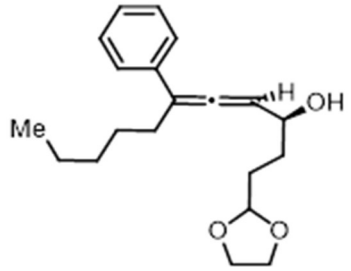
3.73

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

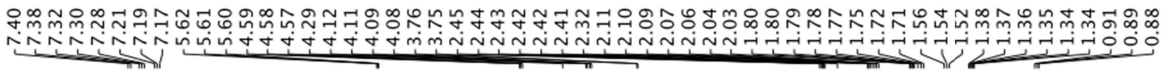


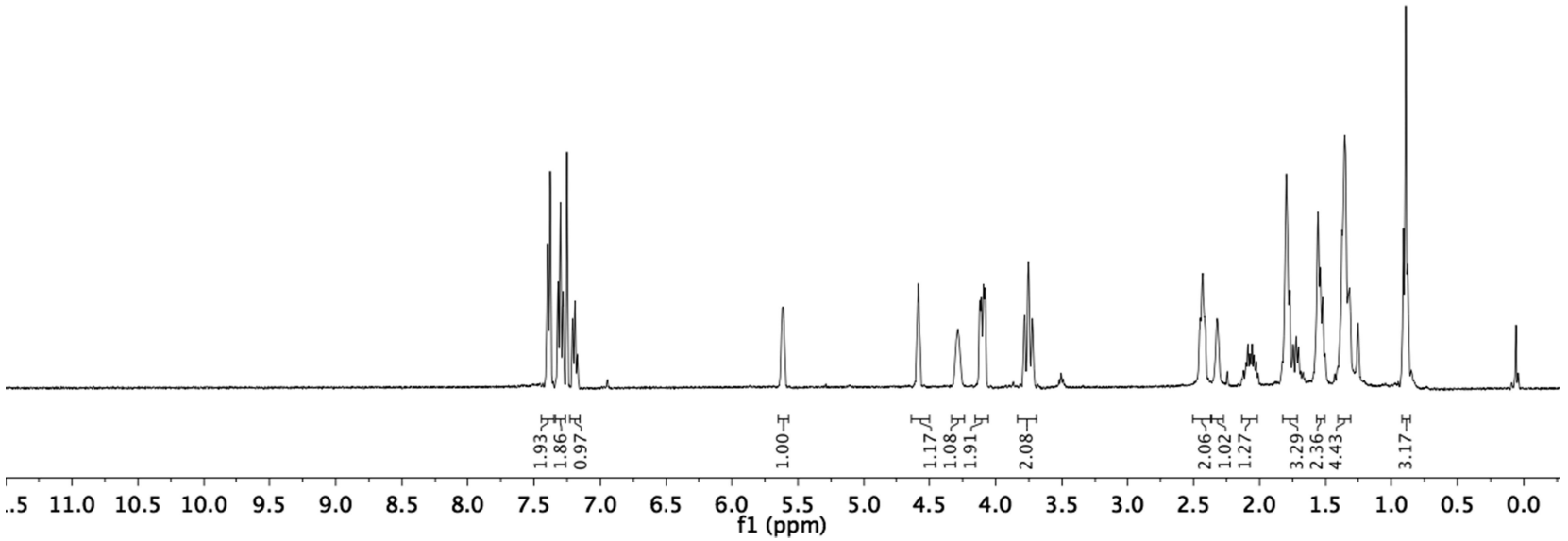
3.73

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

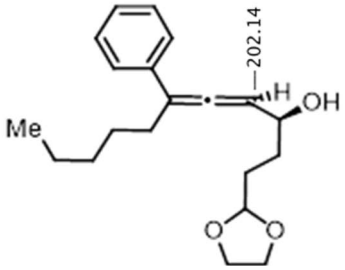


3.71



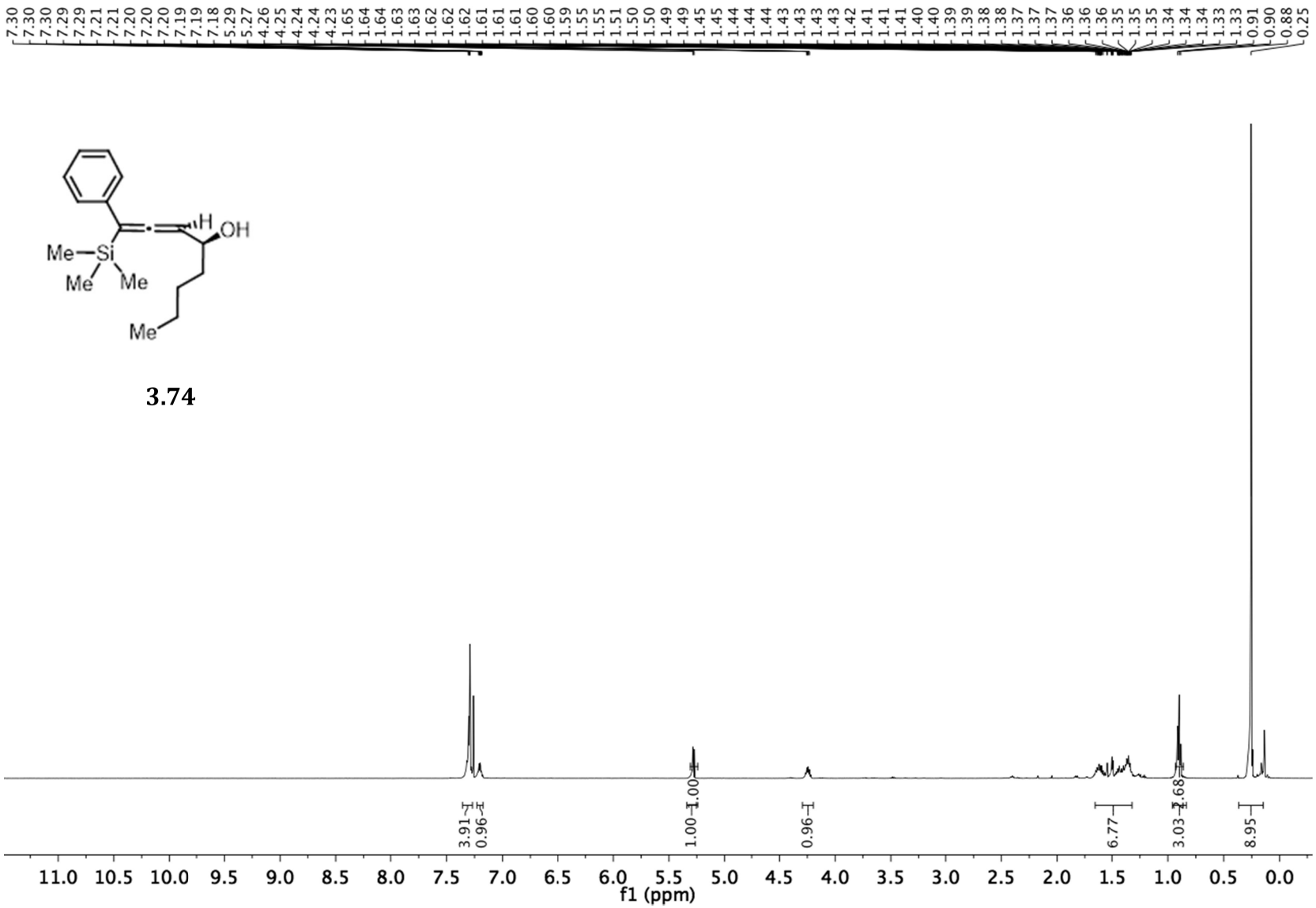


^{13}C NMR (126 MHz, $CDCl_3$)



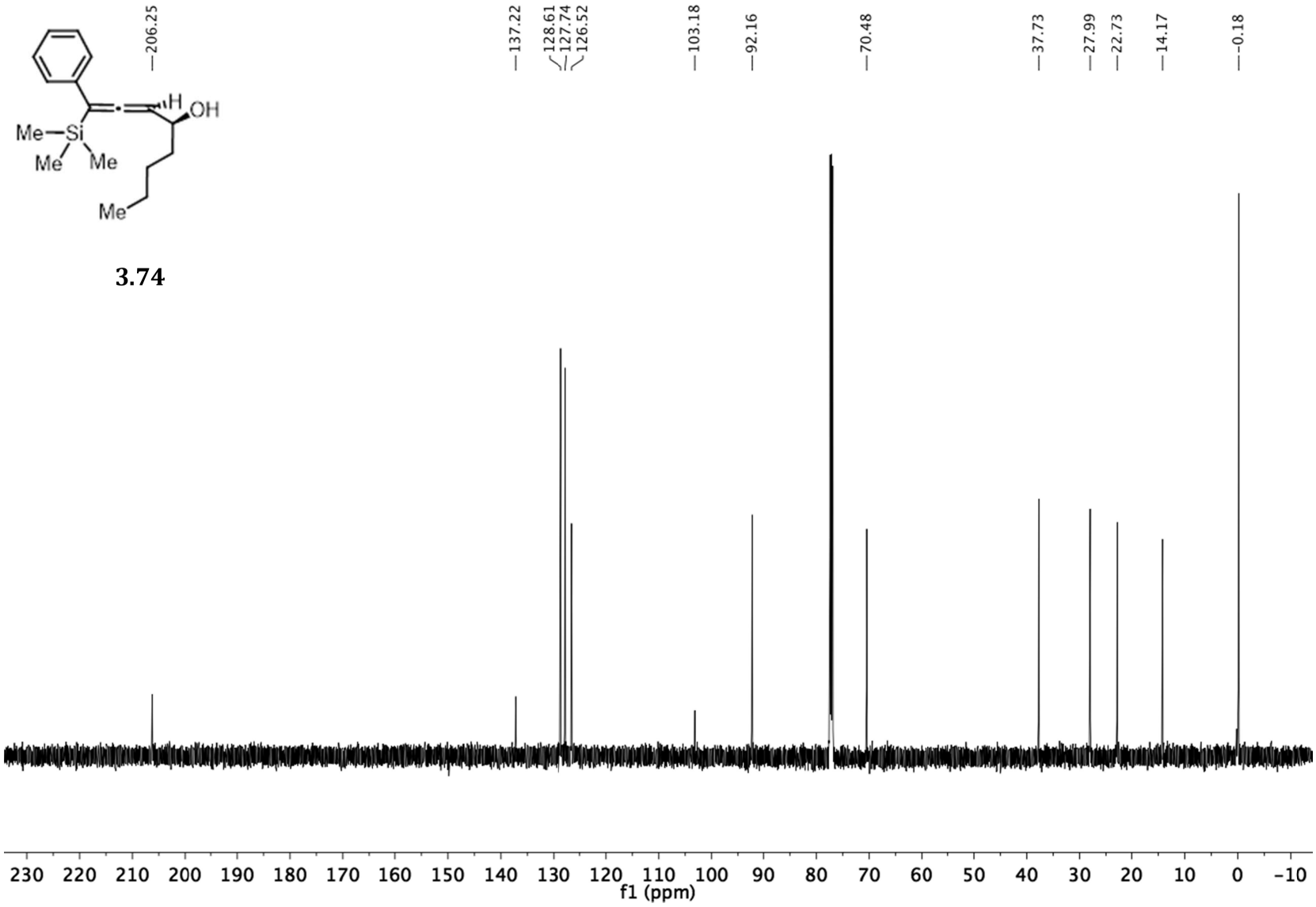
3.71

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



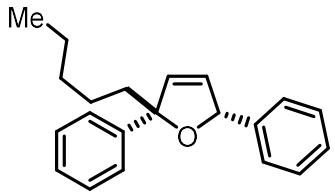
3.74

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

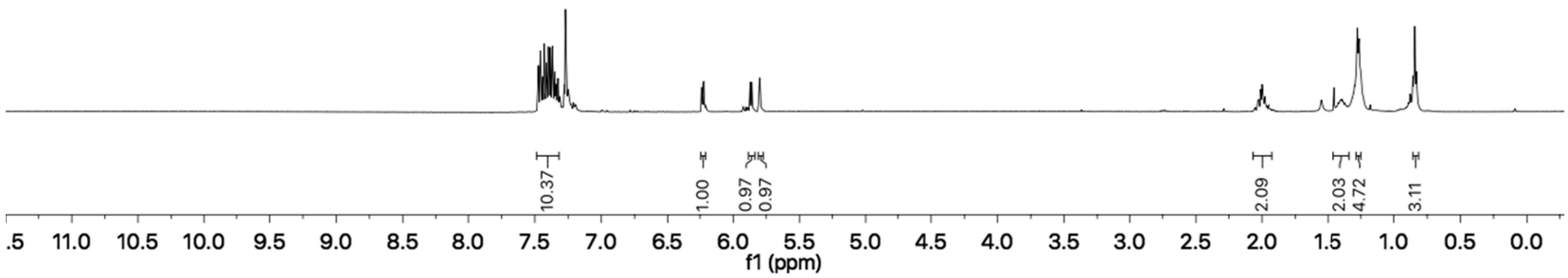


3.74

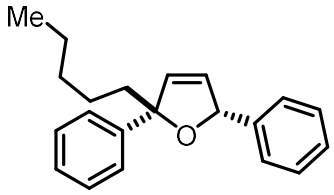
^{1}H NMR (500 MHz, $CDCl_3$)



3.77

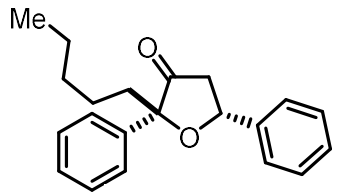


^{13}C NMR (126 MHz, $CDCl_3$)

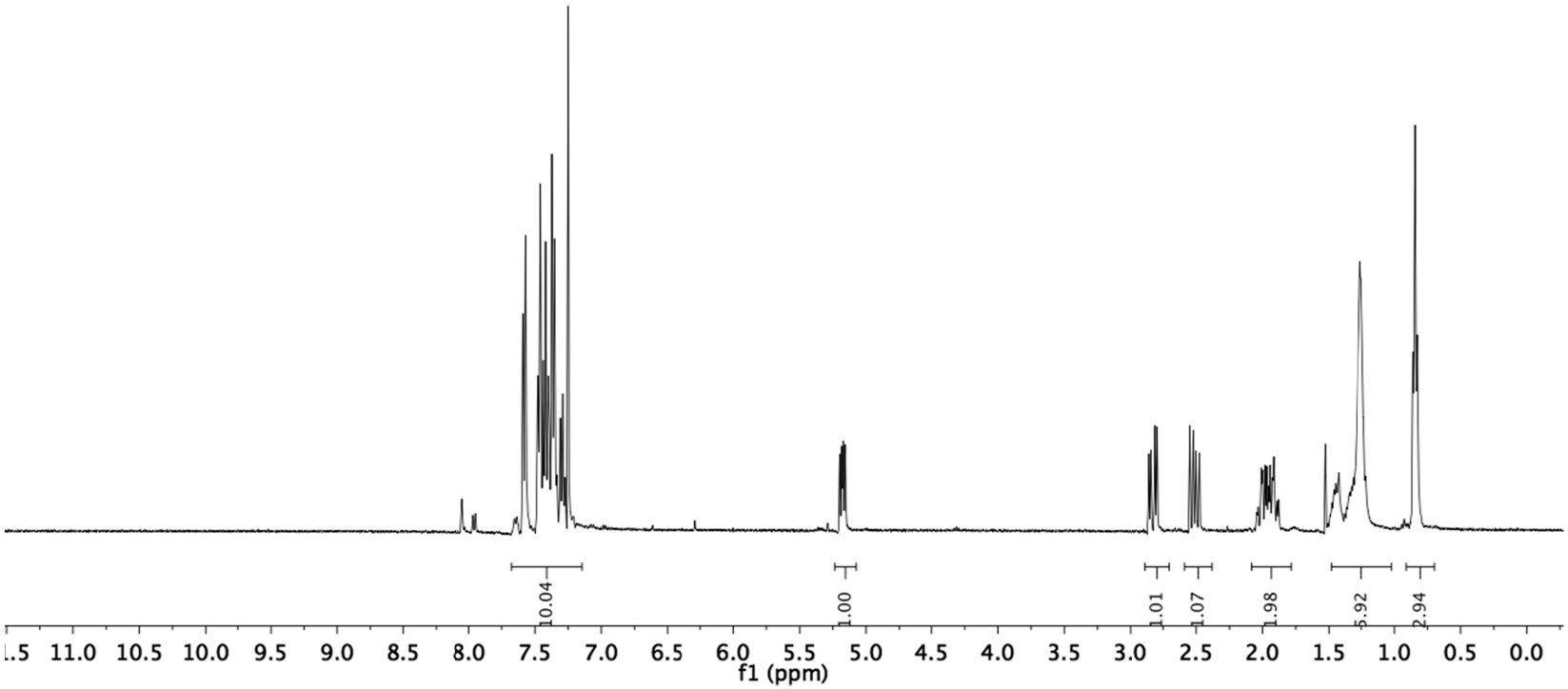


3.77

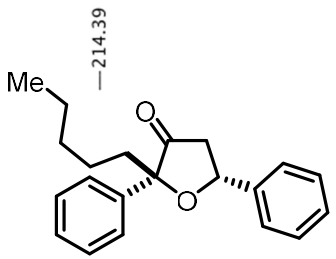
^{1}H NMR (400 MHz, $CDCl_3$)



3.76

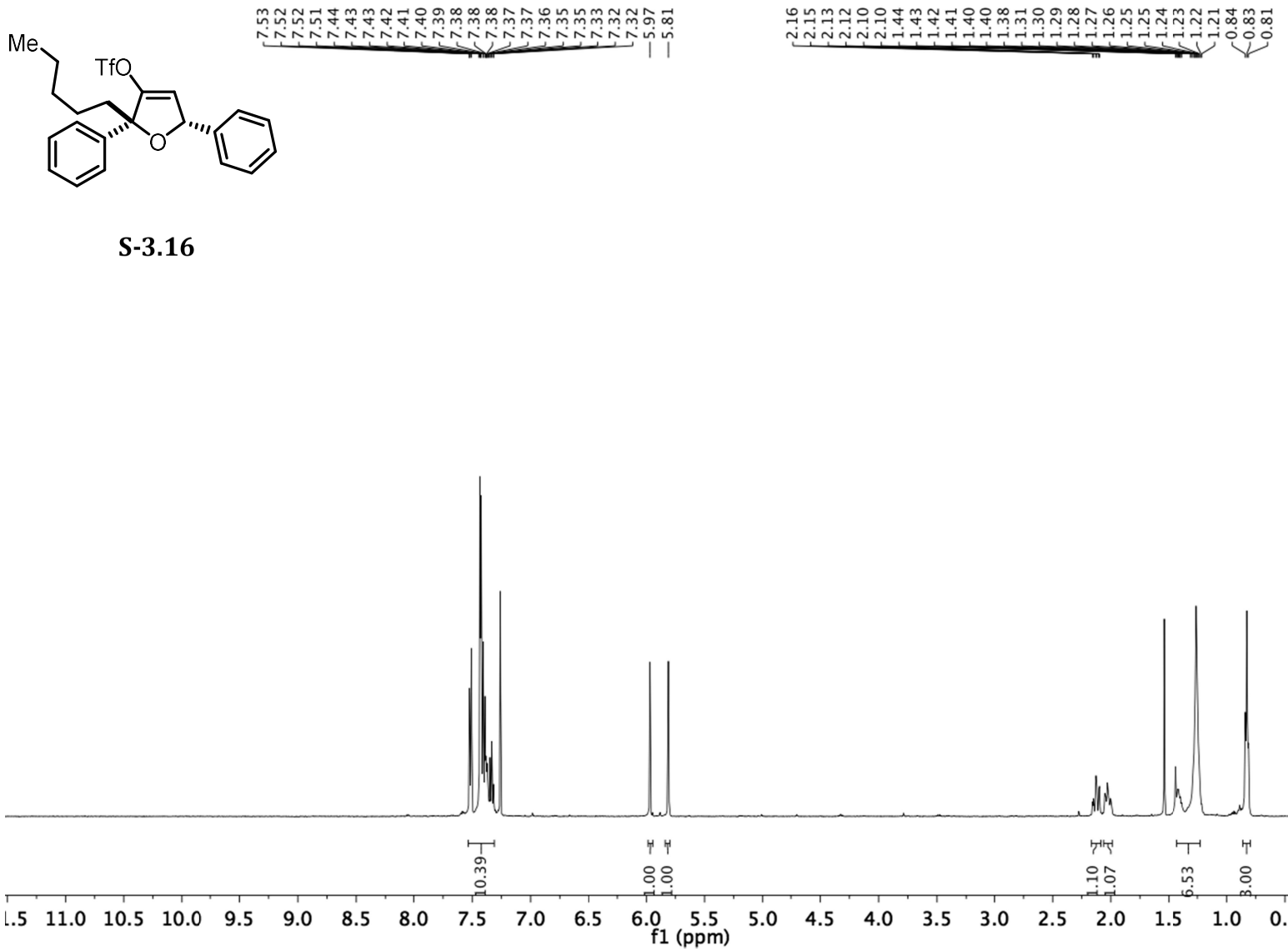


^{13}C NMR (126 MHz, $CDCl_3$)



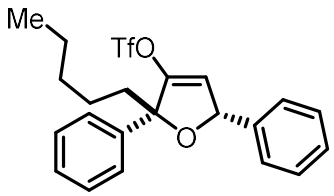
3.76

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



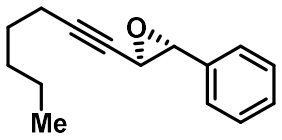
S-3.16

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

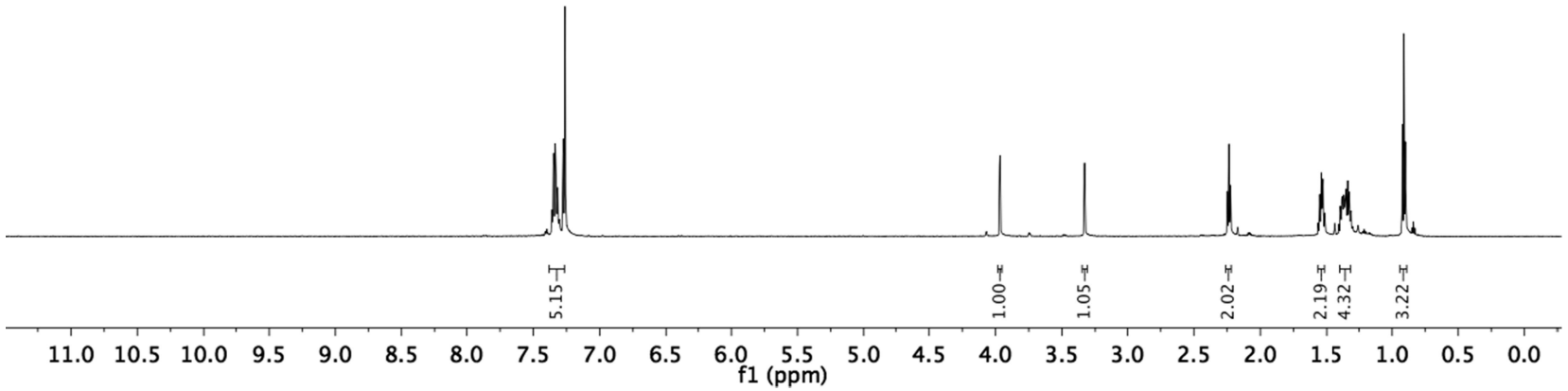


S-3.16

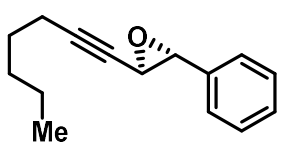
^{1}H NMR (600 MHz, $CDCl_3$)



S-3.15



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



S-3.15