Metal-Catalyzed Enantioselective Dicarbofunctionalization of Alkenylboron Compounds:

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METAL-CATALYZED ENANTIOSELECTIVE DICARBOFUNCTIONALIZATION OF ALKENYLBORON COMPOUNDS

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Abstract: This dissertation will discuss the development of three methodologies for the enantioselective synthesis of organoboron compounds. The first chapter will discuss the initial discovery and development of a palladium-catalyzed reaction that enables the combination of an organolithium, an organoboronic ester and $C(sp^2)$-OTf electrophiles in an enantioselective fashion. This conjunctive cross-coupling takes place through a 1,2-metallate shift which is induced from an alkenylboron 'ate' species through interaction with the palladium catalyst. The second chapter of this manuscript will discuss the development of the first nickel-catalyzed version of the conjunctive cross-coupling reaction, which operates enantioselectively with *in situ* generated 9-BBN boranes. The third and last chapter will discuss the development of complementary method to the conjunctive cross-coupling which enables the enantioselective addition of organozinc reagents and alkyl halides across alkenylboronic esters. This system departs from the metal-induced 1,2-metallate shift mode of reactivity in favor of a Ni-catalyzed radical/addition cross-coupling cascade reaction. This process can be operated in both an inter- and intra-molecular fashion to afford enantiomerically-enriched alkylboronic ester compounds.

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To my parents, my brothers, and to Coralie

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LIST OF ABBREVIATIONS

Å: angstrom

Ac: acetyl

acac: acetylacetonyl

Ad: adamantyl

atm: atmosphere(s)

AQN: anthraquinone

B2(cat)2: bis(catecholato)diboron

B2(pin)2: bis(pinacolato)diboron 9-

BBN: 9-borabicylco[3.3.1]nonane

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

BINAP: 2,2'-bis(diphenylphosphino)-

1,1'-binaphthyl

Bn: benzyl

cat: catechol

CBz: carboxybenzyl

cod: 1,5-cyclooctadiene

conv.: conversion

Cy: cyclohexyl

d: day(s)

DART: direct analysis in real time dba:

dibenzylideneacetone

DCM: dichloromethane

DFT: density functional theory

DHQ: dihydroquinine

DI: deionized

DME: dimethoxyethane

DMF: N,N-dimethylformamide

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

DMPU: 1,3-dimethyl-3,4,5,6-tetrahydro-

2(1H)-pyrimidinone

DMSO: dimethyl sulfoxide

dppb: 1,1'-

bis(diphenylphosphino)butane

DCyPF: 1,1'-

bis(dicyclohexylphosphino)ferrocene

DPPF: 1,1'-

bis(diphenylphosphino)ferrocene

dppm: 1,1'-bis(diphenylphosphino) methane

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

D*i*PrPF: 1,1'-bis(di-*i*-propylphosphino)ferrocene

d.r.: diastereomeric ratio

e.e.: enantiomeric excess

elim.: elimination

eq: equation(s)

equiv.: equivalent(s)

er: enantiomeric ratio

ESI: electrospray ionization

EtOAc: ethyl acetate

GC: gas chromatography

GLC: gas-liquid chromatography

h: hour(s)

HOMO: highest occupied molecular orbital

HPLC: high performance liquid chromatography

HRMS: high resolution mass spectrometry

Hz: hertz

IPA: isopropanol

IR: infrared spectroscopy

KIE: kinetic isotope effect

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

LUMO: lowest unoccupied molecular orbital

M: molar

MALDI: matrix-assisted laser desorption/ionization

MeCN: acetonitrile

min: minutes

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

MS: molecular sieves

MTBE: methyl tbutyl ether

nbd: norbornadiene

NHC: *N*-heterocyclic carbine

NMO: *N*-methylmorpholine *N*-oxide

NMR: nuclear magnetic resonance

neo: neopentylglycol

N.R: no reaction

N.D.: none determined

PHAL: phalazine

pin: pinacol

PMA: phosphomolybdic acid

ppm: parts per million

Pyr: pyrimidine

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

rac: racemic

RCM: ring-closing metathesis

RPKA: reaction progress kinetic analysis

r.r.: regioisomeric ratio

rt: room temperature

SES: 2-(trimethylsilyl)ethanesulfonyl

SFC: supercritical fluid chromatography

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

TBAF: tetrabutylammonium fluoride

tbc: 4-*t*-butylcatechol

TBDPS: *t*-butyldiphenylsilyl

TBS: *t*-butyldimethylsilyl

temp: temperature

TEMPO: 2,2,6,6-tetramethyl-1-piperidinyloxy free radical

TES: triethylsilyl

Tf: trifluoromethanesulfonyl

THF: tetrahydrofuran

TLC: thin layer chromatography

TMEDA: *N*,*N*,*N'*,*N'*-tetramethylenediamine

TMS: trimethylsilyl

tol: toluene

Ts: p-toluenesulfonyl

UV: ultraviolet

xylyl: dimethylphenyl

CHAPTER 1

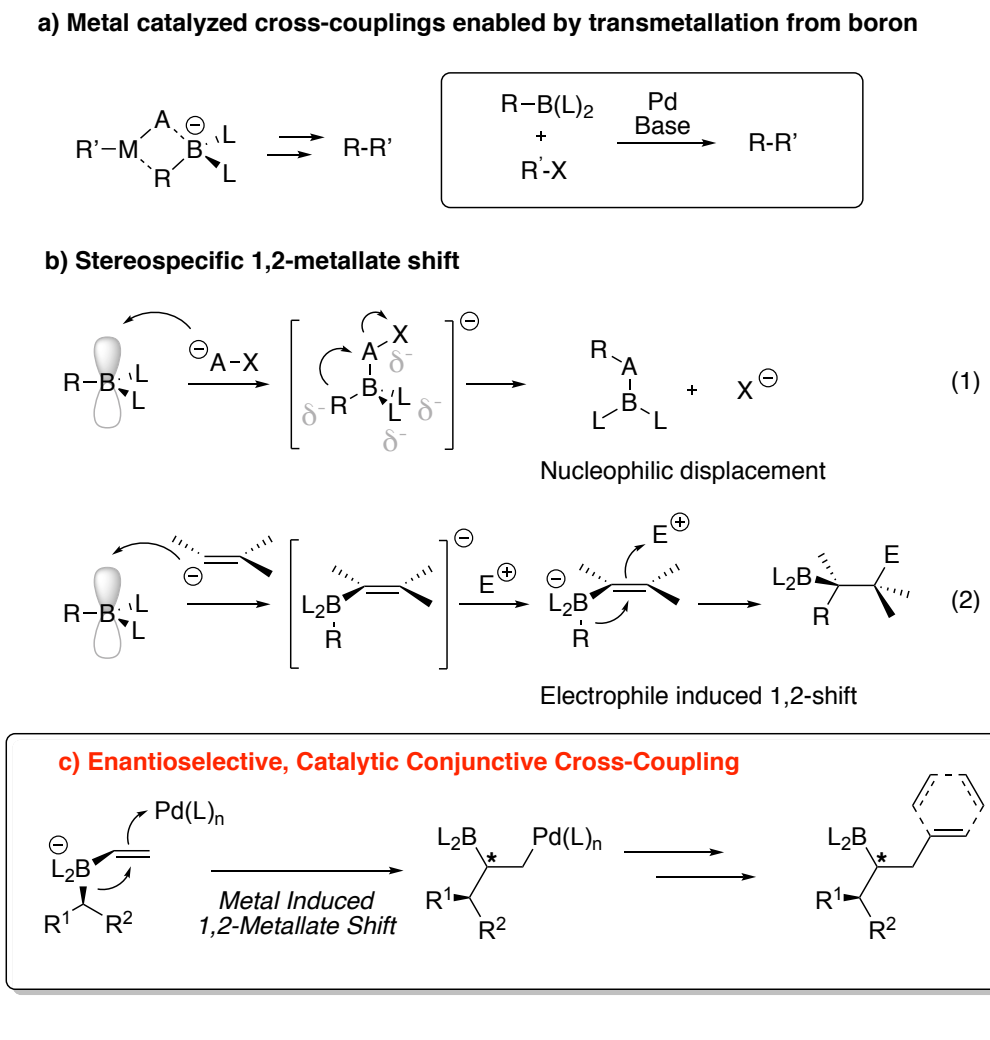
PALLADIUM-CATALYZED CONJUNCTIVE CROSS-COUPLING

1.1 INTRODUCTION

Organoboron compounds are widely available, generally non-toxic, versatile synthetic intermediates. They display remarkable reactivity that can be harnessed to generate new carbon-carbon and carbon-heteroatom bonds through a wide library of processes, many of which are stereospecific. The synthetic utility of organoboron reagents can be ascribed in large part to their ability to engage in a number of transition metal catalyzed cross-coupling reactions including, most famously, the Suzuki-Miyaura cross-coupling (Figure 1.1a). In this context, they act as mild organic nucleophiles through transmetallation with a transition metal catalyst. Moreover, another important mode of reactivity of boron stems from its ability to generate four-coordinate anionic 'ate' species which can readily undergo a stereospecific 1,2-metallate shift. This transformation can take place through the intramolecular displacement of a leaving group α to boron (Figure 1.1b, eq. 1). Alternatively, an external electrophilic activator can trigger a 1,2-metallate shift, often through complexation with a π-system adjacent to boron (Figure 1.1b, eq. 2). From simple oxidation, to amination and homologations, the 1,2-metallate shift mode of reactivity constitutes a powerful tool that enables access to a

wide range of structures and functionalities in a stereospecific fashion. Featured in this chapter is the merger of these two general modes of reactivity: by harnessing a 1,2-metallate shift in a transition metal-catalyzed process, we obtain an enantioselective conjunctive cross-coupling for the synthesis of non-racemic organoboron compounds (Figure 1.1c). In this system, a catalytic palladium complex induces a 1,2-metallate shift from a four-coordinate vinylboron species through a process that formally replaces the canonical transmetallation step common to most metal-catalyzed cross-coupling reactions. Thus, this manifold provides an efficient, modular, and enantioselective method for the synthesis of non-racemic organoboron compounds through the combination of an organolithium, an organoboronic ester, and an C(sp^2) hybridized triflate electrophile.

Figure 1.1. Organoboron reactivity



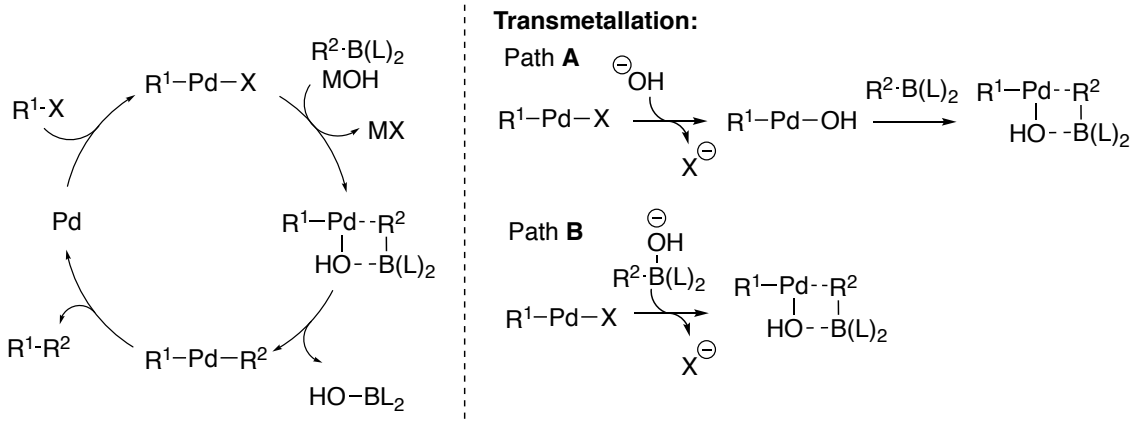
1.2 BACKGROUND

1.2.1 Transmetallation in the Suzuki reaction

The catalytic cycle for the Suzuki cross-coupling involves three steps: oxidative addition into a C-X bond of an electrophile, transmetallation, and reductive elimination (Figure 1.2, left). For palladium catalysis, oxidative addition and reductive elimination

are generally well understood processes, while the mechanistic details surrounding the transmetallation from boron remain the focus of intense research and debate to this day. Thus, a brief discussion of this process is warranted here given that, as alluded to earlier, conjunctive cross-coupling aims to replace this fundamental step with a 1,2-metallate shift, both of which are proposed to take place from a four-coordinate boron 'ate' intermediate.

Figure 1.2. Suzuki-Miyaura cross-coupling mechanism

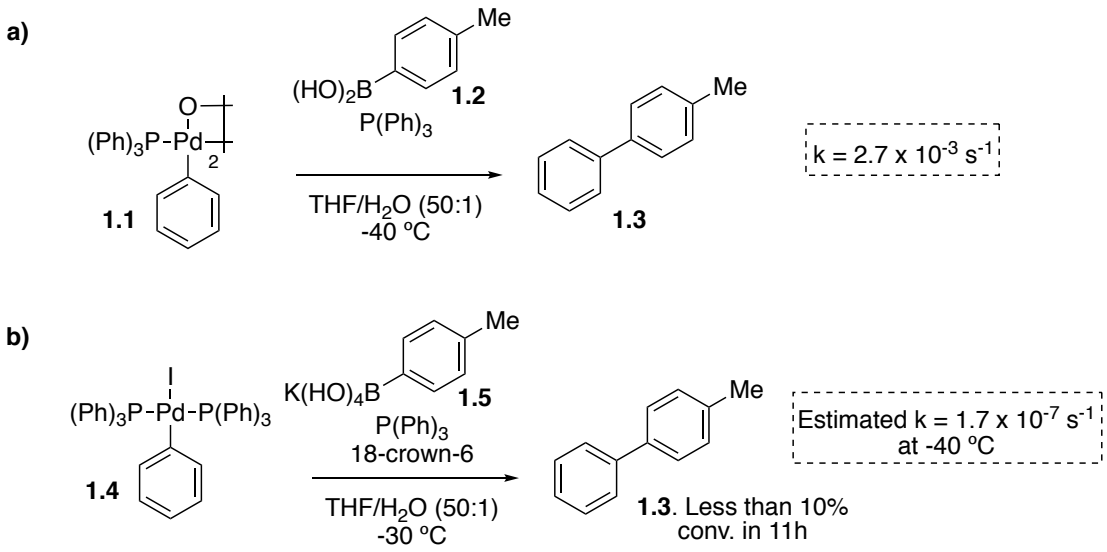


In his studies on the transmetallation of alkyl-9-BBN reagents, Soderquist invoked the intermediacy of a Pd-O-B linkage.[1] However, a source of continued debate regarded the formation of this linkage, which could occur either through the activation of a R-Pd-X oxidative addition adduct by an alkoxide base followed by combination with a three-coordinate boron, (Figure 1.2, path **A**) or by displacement of halide ($^{-}$X) on R-Pd-X by one of the oxygen atoms of a four-coordinate boron 'ate' species (path **B**).[2] In an attempt to answer this question, the Hartwig group studied the rate of biaryl formation in

[1] Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461.
[2] For a brief review: Lenox, A. J. J.; Lloyd-Jones, G. C. *Angew. Chem. Int. Ed.* **2013**, *52*, 7362.

stoichiometric reactions between arylboronic acids and Pd oxidative addition adducts (Figure 1.3). [3]

Figure 1.3. Relative rate of biaryl formation in stoichiometric cross-coupling

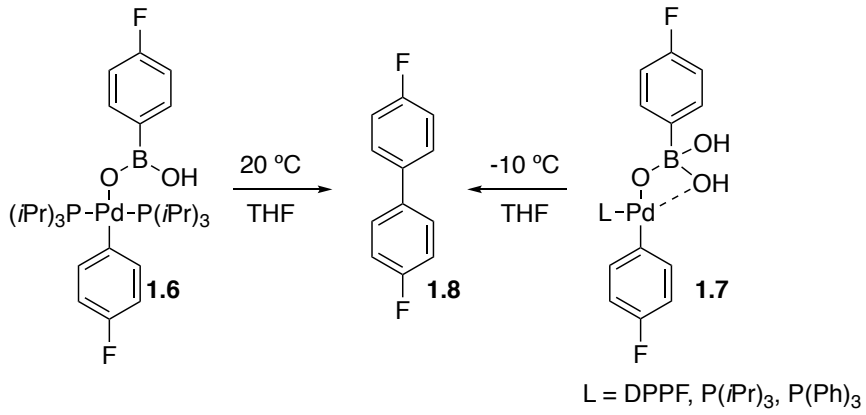


These studies revealed that the stoichiometric reaction between Ar-Pd-OH and a neutral three-coordinate boronic acid proceeded at a rate four orders of magnitude larger than that between Ar-Pd-I and the corresponding tetracoordinate borate. The authors also note that Pd-OH and Pd-X, as well three and four-coordinate boron species tend to equilibrate under catalytically relevant conditions (aqueous solvent mixtures, mild bases). Nevertheless, based on the large difference of reaction rates observed in their low temperature studies they conclude that path **A** is likely the dominant reaction pathway in Suzuki-Myiaura cross-couplings. This hypothesis has been further corroborated through kinetic studies carried out by other groups as well.[4] Path **B** is not ruled out however, and

[3] Carrow, B. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, 133, 2116.
[4] (a) Amatore, C.; Jutand, A.; Le Duc, G. *Chem. Eur. J.* **2011**, 17, 2492. (b) Amatore, C.; Le Duc, G.; Jutand, A. *Chem. Eur. J.* **2013**, 19, 10082. (c) Schmidt, A. F.; Kurokhtina, A. A.; Larina, E. V. *Russ. J. Gen. Chem.* **2011**, 81, 1573.

may be accessed under strongly basic conditions where formation of three-coordinate boron is precluded (such as in examples using trialkylborane reagents).

Figure 1.4. Pre-transmetallation complexes with Pd-O-B linkages



More recently, Denmark characterized both neutral and anionic pre-transmetallation species **1.6** and **1.7** (with DPPF as ligand), containing Pd-O-B linkages (Figure 1.4).[5] These complexes could be seemingly accessed either through path **A** or **B**, and would readily undergo transmetallation and reductive elimination to generate stoichiometric cross-coupling products. Perhaps most surprisingly, it was concluded that both neutral and anionic pre-transmetallation complexes **1.6** and **1.7** could undergo transmetallation, implying that this step may not require an activated four-coordinate boron 'ate'. Finally, based on the results of these studies the authors propose that transmetallation from Pd-O-B complexes requires a mono-ligated Pd species possessing an open coordination site. Thus, direct transmetallation in the case of conjunctive cross-coupling should be diminished by using a bidentate ligand on Pd. Furthermore, formation of a stable four-

[5] (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.

coordinate di-organoboron 'ate' under anhydrous conditions should disfavor equilibration to generate a three-coordinate boron and Pd-OR species that might undergo a rapid transmetallation.

1.2.2 1,2 -Metallate shift

The stereospecific 1,2-metallate shift features in an ever-growing library of transformations of organoboron compounds, which can be used to generate new carbon-carbon and carbon-heteroatom bonds. In this process a four-coordinate, anionic boron 'ate' complex transforms into a three-coordinate neutral species through a 1,2-shift. As alluded to earlier (Figure 1.1b), the rearrangement can take place through the displacement of a leaving group appended α to the boron atom or through addition of an external electrophilic activator. For C(sp^3) acceptors, the 1,2-metallate shift from boron was determined to be stereospecific, proceeding with retention of configuration on the migrating group, and stereoinversion at the migrating terminus.[6] Examples of 1,2-metallate shift have been reported for several atoms including, Al, Zn, Ni, Si, Cd, Cu, Li, Zr.[7] While many atoms capable of reverting between neutral and anionic 'ate' species can, in principle, support a 1,2-metallate shift mode of reactivity, the preponderance of methods in organoboron chemistry that occurs by this mechanism is likely owed to the ease of accessibility and general stability of both neutral and anionic boron atoms.

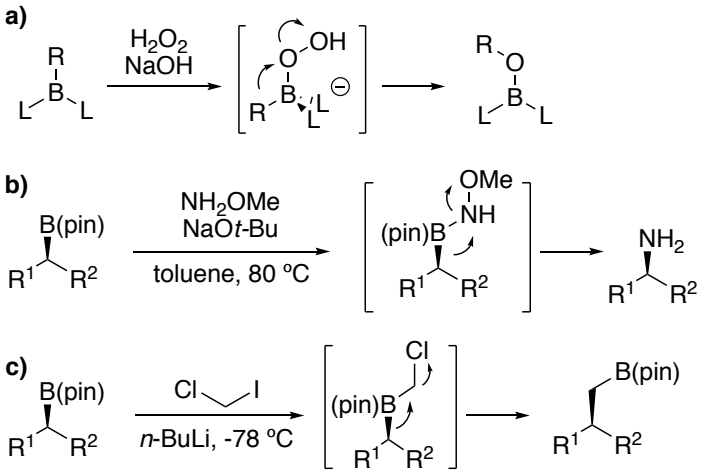
[6] Midland, M. M.; Zolopa, A. R.; Halterman, R. L. *J. Am. Chem. Soc.* **1979**, 101, 248.
[7] (a) Kocienski, P.; Barber, C. *Pure & Appl. Chem*. **1990**, *62*, 1933. (b) Marek, I.; *Tetrahedron*, **2002**, *58*, 9463. (c) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599.

1.2.2.1 1,2-metallate shift to C(sp^3) centers with tethered leaving groups.

One of the earliest, and perhaps most widely employed tranformations of organoboron compounds that involves 1,2-metallate shift, operates in the ionic oxidation of organoboron compounds with hydrogen peroxide to form alcohols (Figure 1.5a).[8] The reaction mechanism at the root of the simple boron oxidation is a continued source of inspiration for new and improved methods aimed at the stereospecific manipulation of organoboron compounds. In fact, 1,2-metallate shift based strategies have been employed to forge a variety of carbon-hetero atom bond. Several stereospecific amination methods have been disclosed throughout the years,[9] including a system developed in our own group (Figure 1.5b),[10] while phosphination and thiolation reactions have been reported as well.[11] Moreover, a prominent application of 1,2-metallate shift based methods is in carbon-carbon bond forming reactions. Since the first observation of this reactivity by Hillman in 1962,[12] a rich literature of methods has been established in this area[13] with important contributions by Matteson, whose homologation method constitutes a seminal and perhaps most famous example of this reactivity[14] (Figure 1.5c).

[8] (a) Zweifel, G.; Brown, H. C. *Org. React*. **1963**, *13*, 1. (b) Brown, H. C.; Snyder, C.; Rao, B. C. S.; Zweifel, G. *Tetrahedron* **1986**, *42*, 5505.
[9] (a) Brown, H. C.; Kim, K.-W.; Srebnik M.; Bakthan, S. *Tetrahedron*, **1987**, *43*, 4071. (b) Brown, H. C. ; Suzui, A.; Sonao, S.; Itoh, M.; Midland, M. M. *J. Am. Chem. Soc.,* **1971**, *93*, 4329 (c) Brown, M. M. Midland, H. C. ; Levy, A. B. *J. Am. Chem. Soc*. **1972**, *94*, 2114
[10] (a) Mlynarski, S. N.; Karns, A. S. Morken, J. P. *J. Am. Chem. Soc*. **2012**, *134*, 16449. (b) Edelstein, E. K.; Grote, A. C.; Palkowitz,M. D.; Morken, J. P. *Syn. Lett.* **2018**, *29*, 1749.
[11] Draper, P. M., Chan, T. H., Harpp, D. N. *Tetrahedron Lett.* **1970**, 11, 1687.
[12] Hillman, M. E. D. *J. Am. Chem. Soc.,* **1962**, 84, 4715.
[13] Sandford C.; Aggarwal V. K. *Chem. Commun.,* **2017**, *53*, 5481.
[14] Sadhu, K. M.;, Matteson, D. S. *Organometallics* **1985**, 4, 1687

Figure 1.5. Examples of 1,2-metallate shift on C(sp^3) migrating termini.

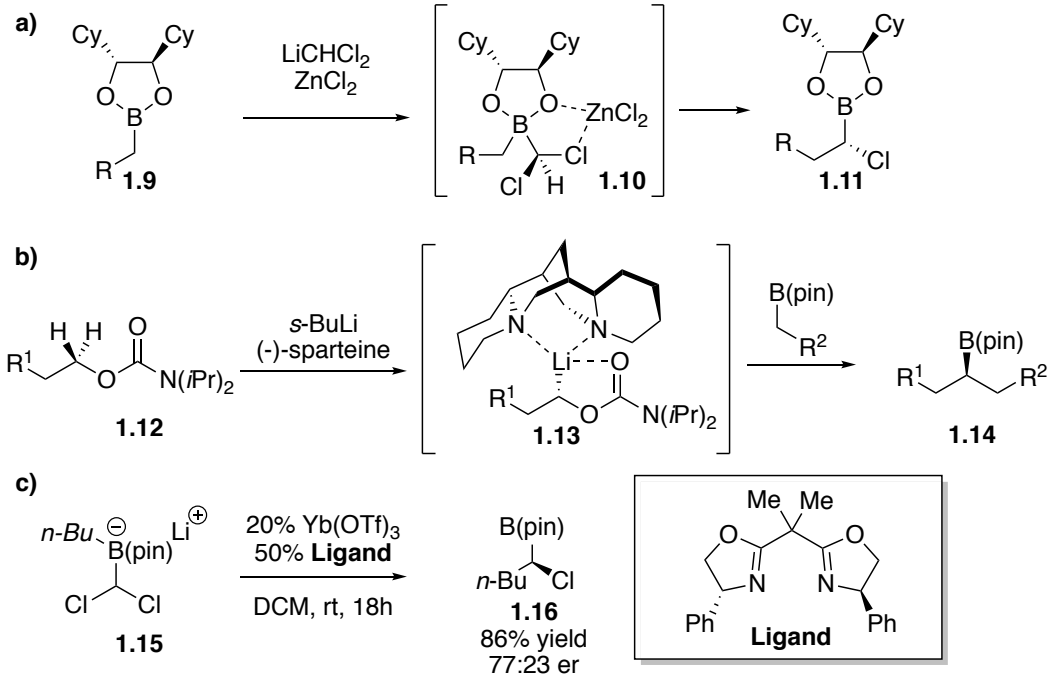


Through the use of stoichiometric chiral reagents, a variant of the Matteson homologation introduced means to operate 1,2-metallate shift based reactions enantioselectively. Specifically, Matteson disclosed a method whereby a chiral diol ligand on boron enabled the distinction between two enantiotopic leaving groups (Figure 1.6a).[15] The use of $ZnCl_2$ as chelating Lewis acid was found to be crucial for obtaining efficient and selective reactions. Aggarwal[16] subsequently built on previous work by Hoppe [17] and developed powerful methods for the asymmetric homologation of organoboranes and boronic esters (Figure 1.6b) using enantiomerically enriched lithiated-carbamates as homologating reagents. The latter reagents are generated via enantioselective deprotonation of the corresponding alkyl carbamate with *s*-BuLi in conjunction with stoichiometric (*S*)-sparteine (Figure 1.6b). In the context of asymmetric synthesis, these methods suffer from the inherent limitation of requiring stoichiometric non-racemic reagents to furnish enantiomerically enriched compounds. The possibility

[15] Matteson, D. S. *Tetrahedron* **1998**, *54*, 10555.
[16] Stymiest, J. L., Dutheuil, G., Mahmood, A., Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2007**, *119*, 7635.
[17] Beckmann, E., Desai, V., Hoppe, D. *Synlett* **2004**, *13*, 2275.

for asymmetric induction through catalysis in a 1,2-metallate shift was demonstrated in one instance by Jadhav, who reported that sub-stoichiometric amounts of a Lewis basic $Yb(OTf)_3$/ligand complex could induce a moderate degree of enantioselectivity in the homologation of boron 'ate' species containing enantiotopic chloride atoms in the migrating terminus (Figure 1.6c). [18]

Figure 1.6. Examples of enantioselective homologations.



1.2.2.2 1,2-metallate shift to C(sp^2)/C(sp) by external electrophilic activation.

While some of the examples discussed above employ Lewis acids to aid 1,2-migration to C(sp^3) centers by activating a leaving group,[15,18] activation of a π-system by an external electrophilic reagent enables homologations to take place without inclusion of any pre-installed functionality.

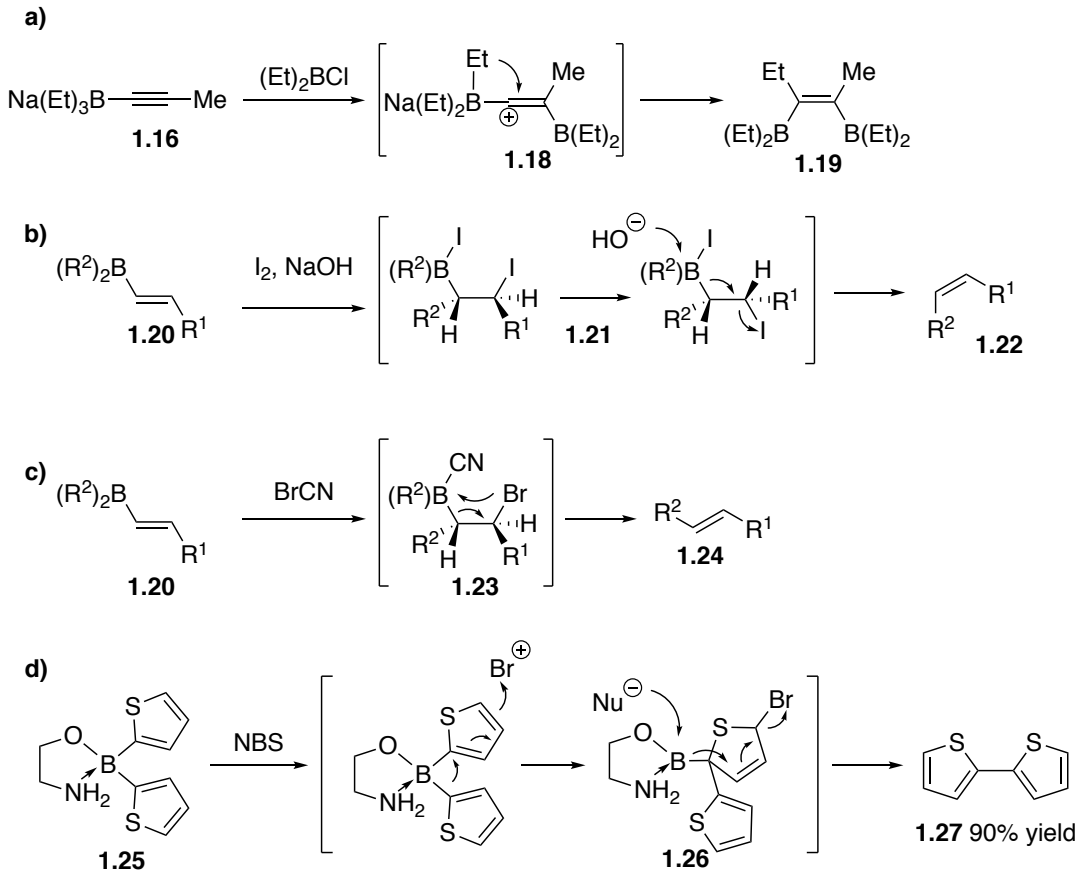
[18] Jadhav, P. K.; Man, P. K. *J. Am. Chem. Soc*. **1997**, *119*, 846.

The first example of a 1,2-metallate shift induced by activation of the π-system on a boron 'ate' was reported by Binger and Koster (Figure 1.7a).[19] In this study, alkynyl borane derived 'ate' species were proposed to undergo a 1,2-metallate rearrangement through a vinyl cation intermediate, generated upon activation by a dialkylchloroborane. Shortly thereafter, Zweifel disclosed the application of this type of process on a C(sp^2)-hybridized carbon. In this seminal report, the olefination of organoborane substrates is carried out through complexation of an alkenylborane with molecular iodine followed by 1,2-migration and boron-iodide elimination (Figure 1.7b).[20] The reaction generates *Z*-olefins from *E*-alkenyl boranes as a result of a stereospecific 1,2-metallateshift followed by hydroxide-promoted *anti*-elimination. This work was expanded on in a later report, in which cyanogenbromide was employed as an electrophilic activator to obtain an *E*-selective olefination starting from *E*-alkenyl boranes (Figure 1.7c). This outcome is proposed to result from the formation of more electrophilic boron species **1.23** after the 1,2-metallate shift, which is then able to accept electrons from the vicinal halide and undergo a *syn*-elimination. Matteson[21] and Evans[22] later expanded the scope of the Zweifel olefination to include boronic esters by using organo lithium reagents to generate four-coordinate complexes. In these examples, iodine induced 1,2-migration is followed by base-induced *anti* iodo-boryl elimination. As recently as 2017, Aggarwal disclosed a method for the use of Grignard reagents in the olefination of boronic esters.[23]

[19] Binger, P.; Koster, R. *Tetrahedron Lett*. **1965**, *6*, 1901.
[20] Zweifel, G.; Arzoumanian, H.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 3652.
[21] Matteson, D. S.; Jesthi, P. K. *J. Organomet. Chem*. **1976**, *110*, 25.
[22] Evans, D. A.; Thomas, R. C.; Walker, J. A. *Tetrahedron Lett*. **1976**, *17*, 1427.
[23] Armstrong, R. J.;Niwetmarin, W.; Aggarwal, V. K. *Org. Lett.* **2017**, *19*, 2762.

The reactivity principles described in these seminal studies have also been applied in methods for the arylation of organoboron species.[24] The general mechanism of these transformations involves an electrophile-induced dearomative 1,2-metallate shift followed by rearomatization through B-X elimination. An example of this reactivity is shown in the seminal work by Levy on borinic esters (Figure 1.7d).

Figure 1.7. 1,2- shift induced by activation of π-system on migrating terminus



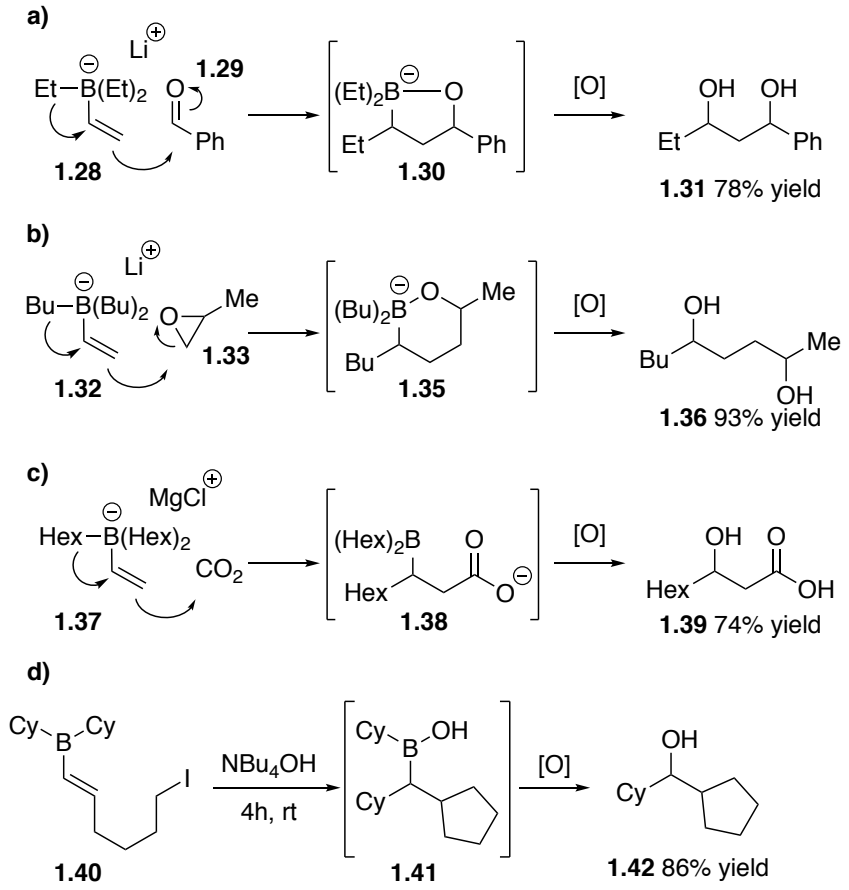
Most of the transformations involving activation of a π-system by stoichiometric electrophiles eventually result in elimination of the boron functionality. However, a

[24] (a) Levy, A. B. *J. Org. Chem.* **1978**, *42*, 4684. (b) Marinelli, E. R.; Levy, A. B. *Tetrahedron Lett.* **1979**, *25*, 2313. (c) Akimoto, I.; Suzuki, A. *Synthesis* **1979**, *2*, 146. (d) Sotoyama, T.; Hara, S.; Suzuki, A. *Bull. Chem. Soc. Jpn*. **1979**, *52,* 1865. (e) Odachowski, M.; Leonori, D.; Essafi, S.; Aggarwal, V. K. *Nat. Chem.* **2014**, *6*, 584.(f) Conti-Ramsden, P.; Harvey, J. N. Leonori, D.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2016**, *138*, 9521.

handful of examples using carbon based electrophiles have been shown to generate product where the boryl functionality is preserved at the end of the reaction. Utimoto disclosed that borane-derived 'ate' complexes undergo 1,2-metallate shift in the presence of aldehydes[25] and epoxides (Figure 1.8a,b).[26] Deng demonstrated a similar process by using CO_2 as the electrophilic activator, which results in the generation of carboxylic acids as products (Figure 1.8c).[27] Finally, Midland reported an example in which alkyl halides, tethered to alkenylboranes, induce an intramolecular alkylation/1,2-metallate shift in the presence of base to afford cyclized alcohol products after oxidation (Figure 1.8d).[28]

[25] Utimoto, K., Uchida, K., Nozaki, H. *Tetrahedron* **1977**, *33*, 1949.
[26] Utimoto, K., Uchida, K., Nozaki, H. *Tetrahedron Lett.* **1973**, *14*, 4527.
[27] Deng, M. Z., Lu, D. A., Xu, W. H. *J. Chem. Soc., Chem. Comm.* **1985**, *21*, 1478.
[28] Hinkens, D. M.; Midland, M. M. *J. Org. Chem.* **2009**, *74*, 4143.

Figure 1.8. Activation of C(sp^2) 'ate' species by carbon electrophiles



1.2.2.3 Metal-induced 1,2-metallate shift.

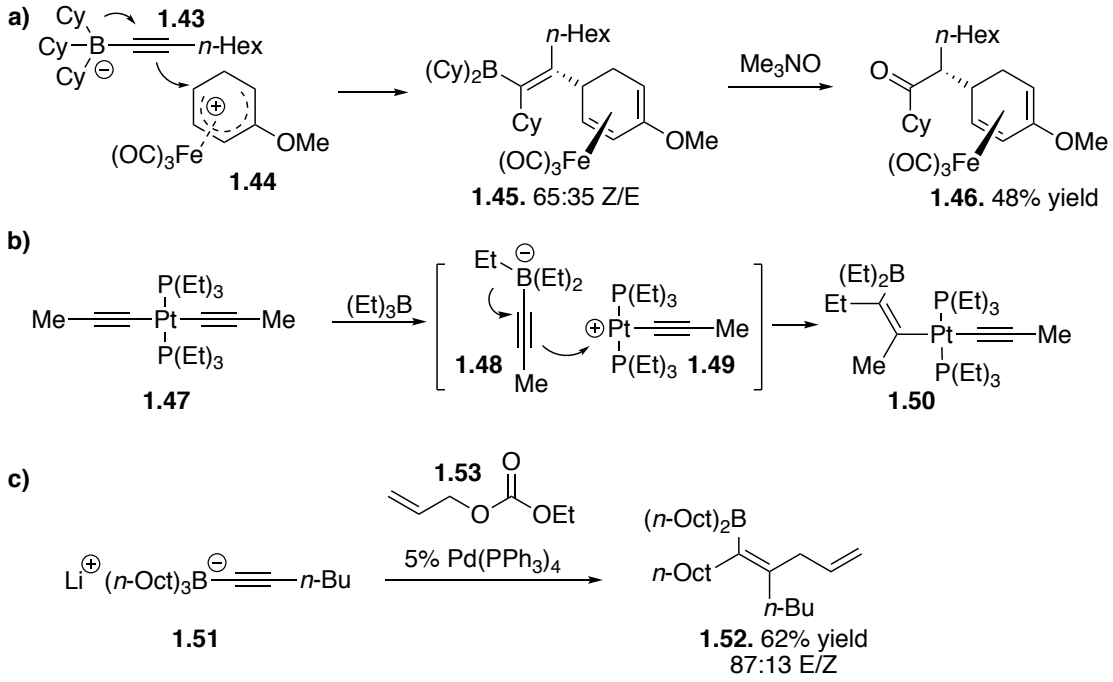
Within the known transformations involving 1,2-metallate shifts from organoboron compounds, methods employing metal catalysts to induce such rearrangements are relatively rare. However, a few important examples of this type of reactivity had been reported prior to the development of our group's conjunctive cross-coupling method. Before considering examples of catalytically-induced 1,2-metallate shift, two early instances of 1,2-metallate rearrangement, induced by the use of stoichiometric transition metals, introduce two distinct mechanistic possibilities for this

type of transformation. In one instance, the 1,2-metallate shift is proposed to take place through an outer-sphere attack of the boron 'ate' onto a transition metal-activated electrophile. This mechanism (Figure 1.9a) was proposed by Pelter,[29] for the coupling of alkynylborane derived 'ate' complexes with iron-bound dienyl cation species **1.44.** The products of these reactions were observed to have an *anti*-relationship between the organoboron moiety and to the iron atom, consistent with an outer-sphere nucleophilic attack of the boron 'ate' on the π-system on the organic electrophile. A second mechanistic scenario for metal-induced 1,2-metallate shift involves direct addition onto the metal atom by the boron 'ate' species. Such an instance has been proposed in a report by Wrackmeyer in which the combination of triethylborane with a bis(acetylide) platinum complex **1.47** results in the formation of platinum complex **1.50**, a structure containing a metallated alkenyl borane ligand (Figure 1.9b).[30] This transformation was proposed to take place by an initial ligand exchange between the Pt complex and the borane resulting in formation of a cationic three-coordinate Pt species **1.49** and a four-coordinate boron 'ate'. The latter complex undergoes a 1,2-metallate rearrangement induced by the cationic Pt species. The earliest catalytic method involving a metal-induced 1,2-metallate shift was reported by Deng (Figure 1.9c).[31] Here, an alkynylborane-derived 'ate' reacts with allyl carbonates in the presence of catalytic palladium salt to generate skipped dienyl boranes. This process was proposed to take place through an outer-sphere addition pathway. In a series of reports by Ishikura,[32a-c]

[29] Pelter, A.; Gould, K. J. *J. Chem. Soc., Chem. Commun*. **1974**, 1029.
[30] Sebald, A.; Wrackmeyer, B. *J. Chem. Soc., Chem. Commun.* **1983**, 309.
[31] Chan, Y.; Li N. S.; Deng, M. Z. *Tetrahedron Lett*. **1990**, *31*, 2405
[32] (a) Ishikura M.; Terashima, M. *J. Chem. Soc., Chem. Commun*. **1991**, 1219. (b) M. Ishikura, M.; Kato, H. *Tetrahedron* **2002**, *58*, 9827. (c) Ishikura, M.; Matsuzaki, Y.; Agata, I.; Katagiri, N. *Tetrahedron* **1998**, *54*, 13929. (d) Panda, S.; Ready, J. M. *J. Am. Chem. Soc*. **2018**, *140*, 13242. (e) Ready, J. M. *J. Am. Chem. Soc.* **2017***, 139*, 6038

the allylation of indole-borane derived 'ate' complexes is also proposed to occur by a similar outer-sphere pathway. This manifold has been recently expanded upon by Ready,[32d,e] who developed an enantioselective system.

Figure 1.9. Metal induced 1,2-metallate shift

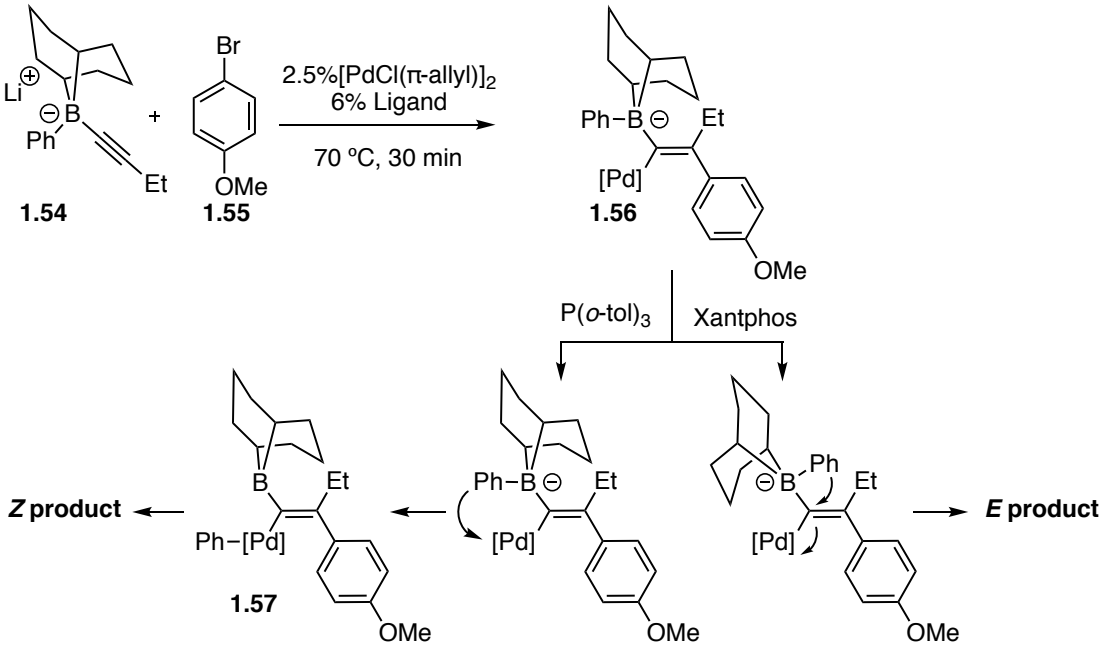


Finally, a series of reports by Murakami detailed the formation of alkenyl boranes through the coupling of alkynyl-derived boron 'ate' species with a variety of electrophiles under palladium catalysis.[33] In these reports, the authors generally put forth a mechanism that is not based on a metal-induced 1,2-metallate shift. Instead, they propose a Heck-type carbopalladation step followed by an intramolecular transmetallation and reductive elimination. Moreover, in a report for the coupling of 9-BBN alkynylboranes, the authors advance an additional mechanistic hypothesis, which is based on the observation that the reaction provides different stereochemical outcomes depending on the choice of

[33] (a) Ishida, N.; Miura, T.; Murakami, M. *Chem. Commun*. **2007**, 4381. (b) Ishida, N.; Narumi, M.; M. Murakami, M. *Org. Lett*. **2008**, *10*, 1279 (c) Ishida, N.; Shimamoto, Y. Murakami, M. *Org. Lett.* **2009**, *11*, 5434. (d) Naoki, I.; Tatsuo, S.; Shota, S.; Tomoya, M. ; Murakami, M. *Bull. Chem. Soc. Jpn.,* **2010**, *83*, 1380. (e) Ishia, N.; Ikemoto, W.; Narumi, M.; Murakami, M. *Org. Lett*. **2011**, *13*, 3008.

phosphine ligand used (Figure 1.10).[33c] Specifically, use of a monodentate tri-*o*-tolyl phosophine ligand yields a *cis*-tetrasubstituted alkenyl boron, whereas use of a wide-bite angle bisphospine Xantphos ligand results in the formation of the corresponding *trans* product. The authors propose that in the case of a *cis*-selective reaction, the reaction operates following their earlier mechanistic hypothesis. After the carbopalladation step, the monoligated Pd should undergo direct transmetallation from intermediate **1.56**. Stereo-retentive reductive elimination results in the observed *E* products. In the second scenario, the bulky bisphophine ligand prevents direct transmetallation from taking place and instead the authors propose that a 1,2-metallate shift ensues from intermediate **1.56**, resulting in a stereo-invertive reductive displacement and formation of *Z*-products. These mechanistic proposals provide compelling alternatives to metal induced 1,2-metallate shift. However, while the carbopalladation pathway accounts for the observed *syn* addition of the electrophile and the migrating group across the alkyne, *anti* addition may also result from a 1,2-metallate shift taking place from alkynyl borate **1.54** upon complexation with the palladium oxidative addition adduct.

Figure 1.10. Murakami's mechanistic proposal for Pd catalyzed alkenylboron synthesis

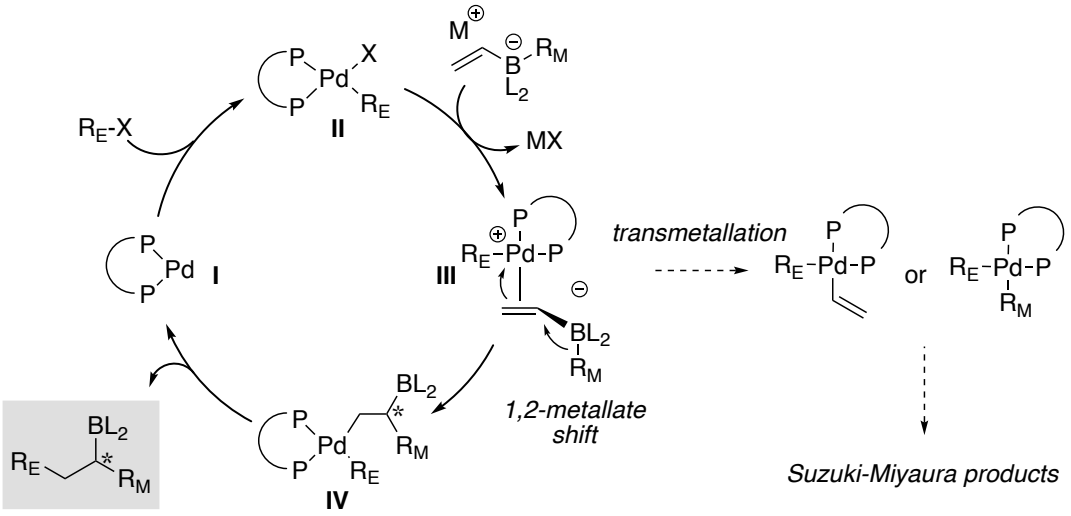


1.3 PALLADIUM-CATALYZED CONJUNCTIVE CROSS-COUPLING[34]

1.3.1 Reaction development.

Considering the proposed pathway of the desired conjunctive cross-coupling reaction, several factors stood out as possible stumbling blocks.

Figure 1.11. Proposed catalytic cycle for Pd-catalyzed conjunctive cross-coupling



In the mechanistic proposal (Figure 1.11), oxidative addition with the electrophilic cross-coupling partner is followed by coordination of Pd with the vinyl boron 'ate' species to generate intermediate **III**. At this point, a metal-induced 1,2-metallate shift would result in complex **IV** that undergoes reductive elimination to deliver the product and restart the cycle. As it was alluded to previously in the chapter, the majority of the steps of the proposed cycle feature common intermediates with the Suzuki-Miyaura

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

cross-coupling, the key point of divergence being the replacement of the transmetallation step by a 1,2-metallate shift. Besides the possible proclivity of this system towards Suzuki-Miyaura cross-coupling, the alkyl-palladium intermediate generated through the proposed metal induced 1,2-metallate shift could be prone to β-hydride or β-boryl elimination. To address these problems it was hypothesized that wide-bite-angle bidentate ligands might increase the rate of reductive elimination from intermediate **IV** and disfavor β-hydride elimination. Moreover, based on the studies by Denmark discussed earlier, the lack of an open coordination site in intermediate **III** should disfavor direct transmetallation from the boron 'ate'. In contrast, we hypothesized that an open coordination site in oxidative addition adduct **II** would favor the complexation with the alkenyl moiety of boron to form the intermediate adduct **III** required for the 1,2-metallate shift. This aim could be accomplished by using aryl triflates as an electrophilic coupling partners, given that the weak coordination ability of the triflate counterion anion should favor formation of a cationic oxidative addition adduct **II**. Finally, we selected unsubstituted vinylboronic esters as initial substrates. We opted for neopentyl glycol as a ligand on boron after considering reports by Mayr and Aggarwal which proposed that neo-pentyl glycolato ligands produced more nucleophilic 'ate' species.[35]

The initial experiments investigating the conjunctive cross-coupling reactivity were carried out largely by Liang Zhang and Gabriel Lovinger. For these studies, a vinylboron 'ate' complex, generated by mixing *n*-butyllithium and vinylB(neo), was combined with phenyl triflate, 5% $Pd(OAc)_2$ and 6% ligand in THF, and heated to 60 ºC. We were

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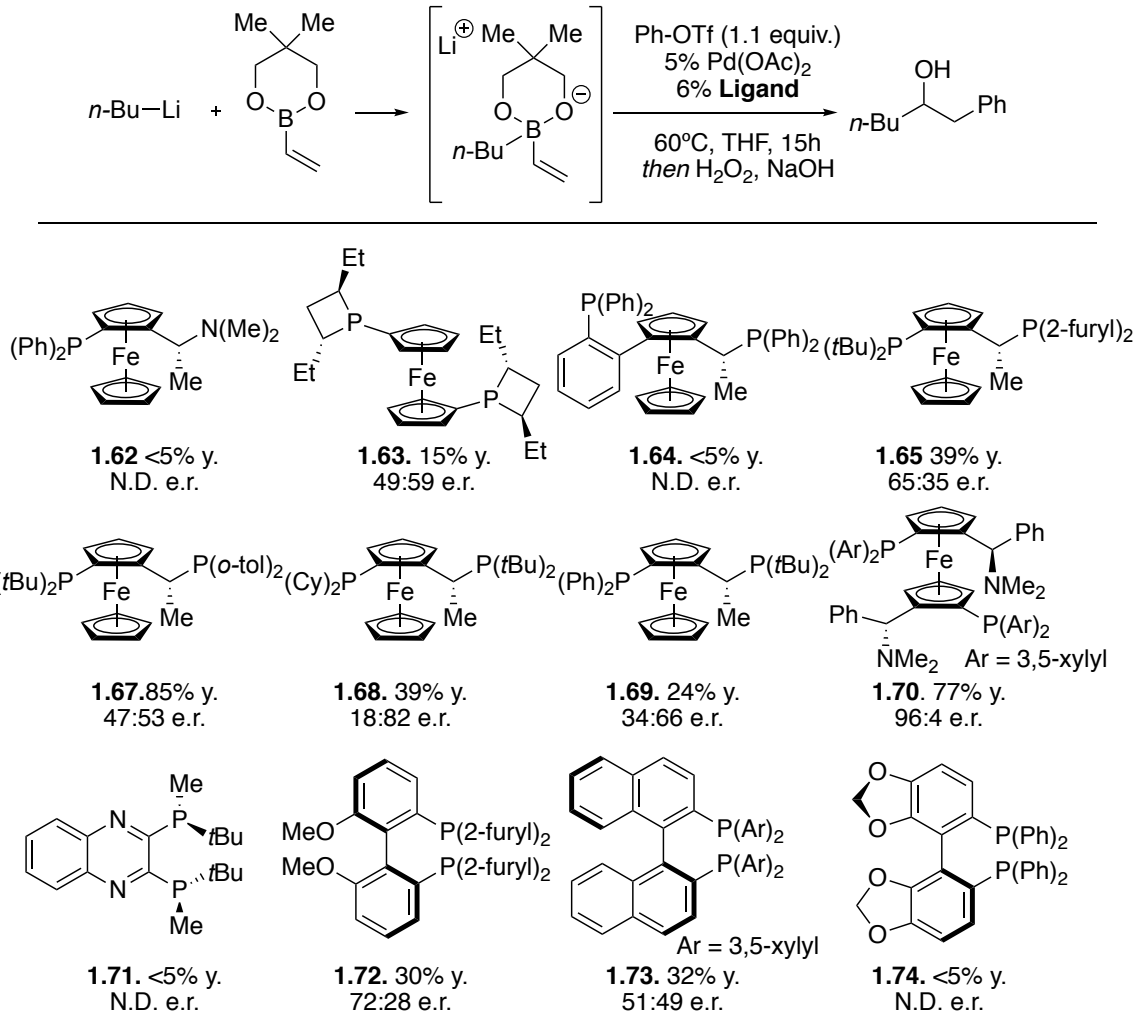
[35] Berionni, G.; Leonov, A. I.; Mayer, P.; Ofial, A. R.; Mayr, H. *Angew. Chem. Int. Ed.* **2015**, 54, 2780. (b) Feeney, K.; Berionni, G.; Mayr, H., Aggarwal, V. K. *Org. Lett.* **2015**, 17, 2614.

excited to discover that the desired reactivity was attainable through the use of (bis)phosphine ferrocenyl ligands D*i*PrPF and DCyPF, which delivered the product in 19% and 31% yield respectively, after peroxide oxidation.

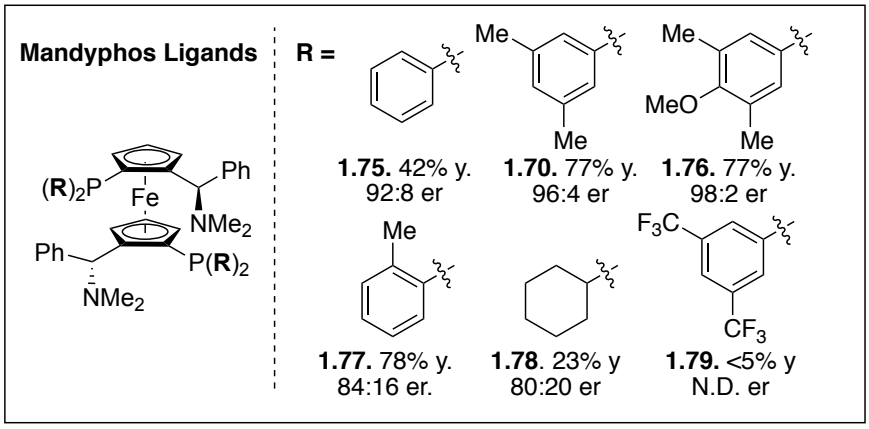
Figure 1.12. Ligand survey for Pd-catalyzed conjunctive cross-coupling



Following these initial results, we sought out related chieral, non-racemic ligand structures to induce enantioselectivity in the reaction (Figure 1.12). Of the ferrocenyl based ligands tested, Ferrotane (**1.63**) and the Josiphos ligand class (**1.64**-**1.69**) were found to deliver product with varying levels of selectivity and efficiency. For the latter ligand class, it was found that the reaction system was fairly responsive to changes on the

phosphine substituents. However, reaction with Josiphos ligands that resulted in improved enantioselectivities were offset by lower reaction efficiencies. The highest enantioselectivity observed was rather modest at 18:82 er (**1.68**) and was paired with a low product yield. Finally, we found that ferrocenyl ligand **1.70** of the Mandyphos[36] class catalyzed the desired reaction efficiently and enantioselectively, delivering product **1.61** in 77% yield and 96:4 er. Other classes of ligands that generated product, albeit inefficiently and with poor enantioselectivities, included atropisomeric biaryl ligands of the Biphep (**1.72**) and Binap (**1.73**) families. Investigating the Mandyphos ligand manifold further (Figure 1.13) we found that *ortho*-tolyl and simple phenyl phosphine substituents resulted in diminished enantioselectivities, and switching to a cyclohexyl group resulted in a dramatic reduction in yield and a substantial loss of selectivity. The use of a bis(3,5-dimethyl-4-methoxyphenyl)phosphine moiety (**1.76**) on the phosphine boosted the enantioselectivity of the product to 98:2 er without affecting the overall efficiency of the reaction in comparison to ligand **1.70**.

Figure 1.13. Survey of Mandyphos ligand class



[36] Perea, J. J. A.; Lotz, M.; Knochel, P. *Tetrahedron: Asymmetry* **1999**, *10*, 375.

Throughout these experiments, the majority of the starting materials were consumed in a competitive Suzuki cross-coupling stemming from direct transmetallation of a C(sp^2) substituent (vinyl or phenyl) from boron. As mentioned earlier, evidence suggests that transmetallation from B to Pd takes place more rapidly upon coordination of Pd-OH to a neutral boron,[2, 3] and that this step may be preceded by intermediates possessing Pd-O-B linkages. The use of anhydrous conditions in this reaction should preclude formation of a Pd-OH intermediate. However, under our reaction conditions, the diol ligand on boron may serve to form a Pd-O-B linkage by coordination to the cationic Pd intermediate, possibly through a pathway involving prior dissociation of one of the oxygen atoms from boron. Then, based on Denmark's studies, the bisphosphine ligand would have to "arm-off" in order to open a coordination site for transmetellation to take place from the Pd-O-B pre-transmetallation intermediate. For transmetallation to take place without dissociation of a phosphine ligand, a substituent on boron would transfer directly onto a three-coordinate cationic Pd intermediate through an outer-sphere process. This should require the Pd to come in close proximity to the boron atom in order for it interact with the C-B σ-bond. In this scenario, either oxygen or olefin binding could lead to Suzuki reactions, as either may function as a directing group for Pd. The Suzuki pathway may ensue if the C-B σ-bond becomes accessible to Pd and non-bonding interactions between the Pd/ligand complex and vinyl boron 'ate' would ultimately dictate which reaction pathway is favored. At this point it is difficult to ascertain whether oxygen binding plays a role in favoring the Suzuki coupling, either as a transient directing group or through the formation of distinct pre-transmetallation intermediates. However, in later works by our

group it has been generally observed that Suzuki cross-coupling does not ensue when using oxygen-free borane-derived 'ate' species as conjunctive coupling reagents.[37]

1.3.2 Scope of conjunctive cross-coupling and halide inhibition effects.

With the optimized conditions in hand, we set out to explore the scope of this transformation (Figure 1.14). A variety of migrating groups were tested by combining commercially available organolithium reagents with vinylB(neo) and PhOTf in the presence of catalytic $Pd(OAc)_2$ and Mandyphos. These studies revealed that both alkyl and aryl migrating groups underwent conjunctive coupling efficiently and selectively. Enantiomerically enriched products could be obtained from primary or secondary alkyl lithium reagents (Figure 1.14, compound **2**, **3**, **4**), and a functionalized methyl-TMS group also migrated effectively (Figure 1.14, compound **5**). As for the scope of the electrophilic component, a range of aryl triflates were generated from the corresponding phenols and examined in the reaction. We found that several electronic profiles were tolerated in the electrophiles, as arenes possessing extended π-systems, electron-withdrawing, and electron-donating functionalities could participate productively in the reaction (Figure 1.14, compounds **6-8**).

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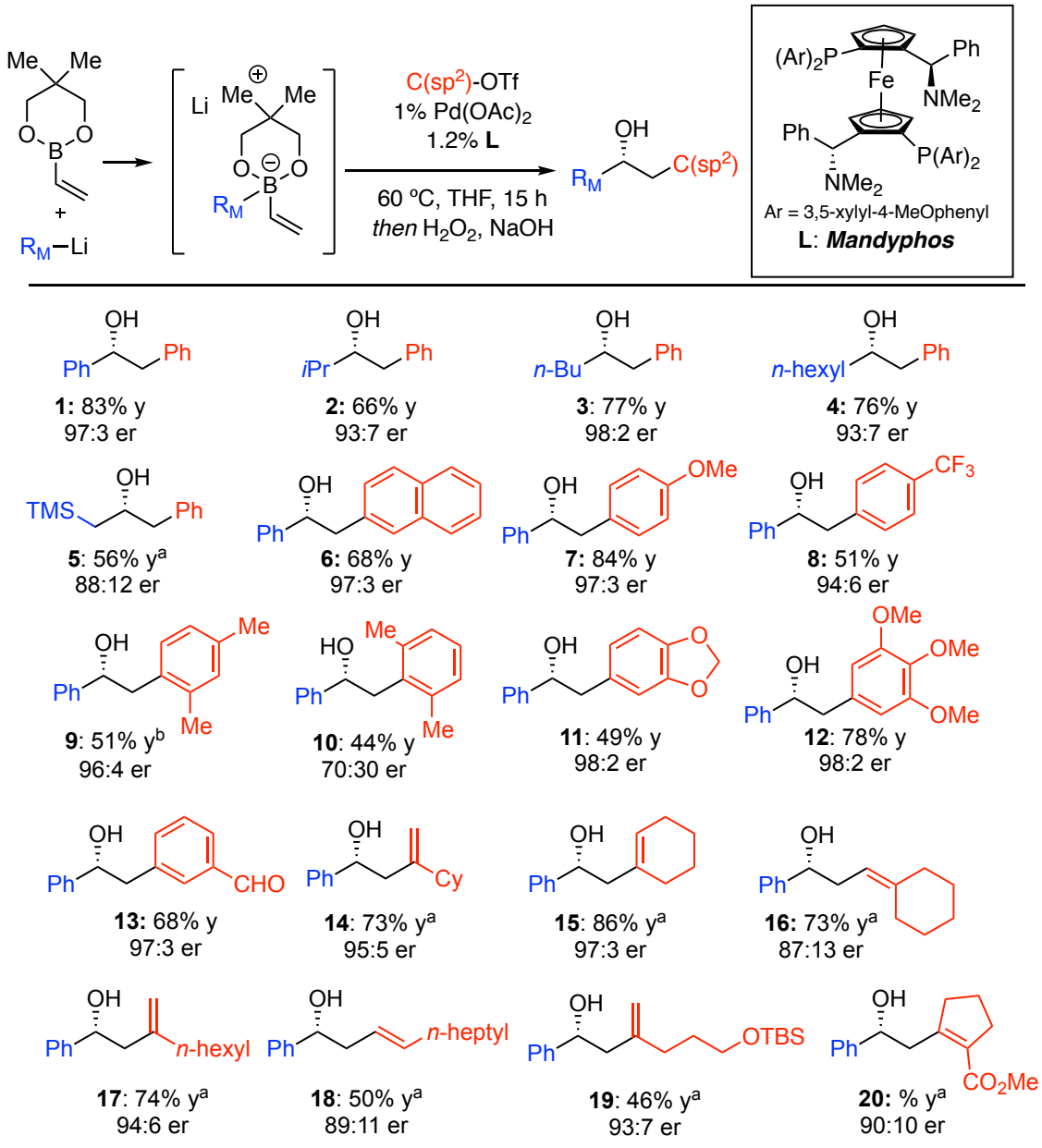
[37] (a) Myhill, J. A.; Wilhelmsen, C. A.; Zhang, L.; Morken, J. P. *J. Am. Chem. Soc.* **2018**, *140*, 15181. (b) Chierchia, M.; Law, C.; Morken, J. P. *Angew. Chem. Int. Ed.* **2017**, *56*, 11870.

Figure 1.14. Substrate scope for the Pd-catalyzed conjunctive cross-coupling



[a] vinyl B(pin) was utilized instead of vinyl B(neo). [b] reaction was performed at 80 °C.

Sterically encumbered *ortho*-substituted arenes could also be used as effective coupling partners, albeit reaction with a di-*ortho*-substituted xylyl triflate required higher temperatures and resulted in diminished enantioselectivity (Figure 1.14, compound **9**, **10**). Sensitive electrophilic functional groups such as aldehydes (**13**) were tolerated in the

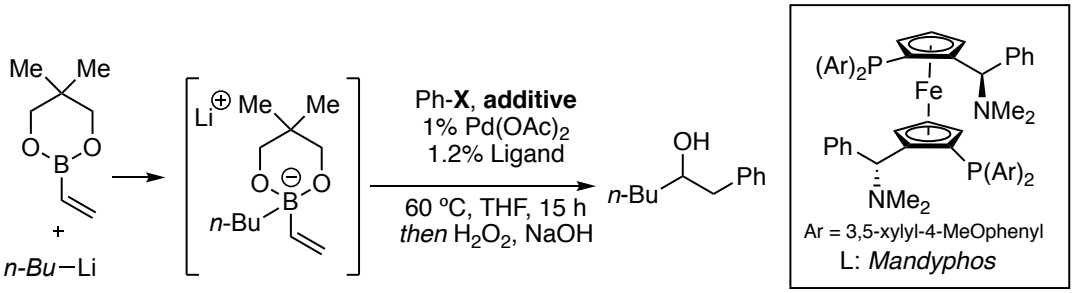
reaction, attesting to the remarkable ability of the boron atom to buffer the nucleophilicity of the organolithium reagents.

It should be noted that, although we set out to explore the reactivity of the conjunctive cross-coupling using neopentyl glycol boronic esters, we also found that pinacol boronic esters generated the desired products efficiently but with diminished enantioselectivities when using aryl electrophiles. However, pinacol boronic ester-derived 'ate' species provided higher enantioselectivities in reactions with alkenyl triflate electrophiles and were therefore used to explore the scope of these substrates. Thus, mono-, di-, and even tri-substituted alkenyl triflates participated in enantioselective reactions (Figure 1.14, compound **14**-**20**), and a stereochemically defined *E*-alkenyl triflate generated product **18** without isomerization.

We were particularly interested in using vinyllithium to generate the reactive boron 'ate' for the reaction, considering the vast number of commercially available boronic esters/acids. However, this required surmounting the non-trivial obstacle of generating a vinyl lithium reagent free of halide salts. In fact, as was alluded to earlier, triflate electrophiles were selected as model substrates due to the non-coordinating nature of the triflate counterion. This feature was estimated to be crucial for maintaining an open coordination site on a putative palladium oxidative addition adduct in order to facilitate the complexation with vinyl boron. The importance of the triflate counterion was confirmed in later studies which revealed that organic halide electrophiles such as iodo-, bromo-, or chlorobenzene were not conducive to generating the desired products efficiently as evidenced by the results in Table 1.1, entries 1-4. Reaction with

iodobenzene generated products in less than 10% yield (while maintaining high enantiomeric purity), and chlorobenzene remained unreacted. Moreover, even the addition of catalytic amounts of exogenous halides resulted in a dramatic inhibition of product formation. In the latter case, the reactivity could be restored if the catalyst loading was increased so as to reach a 2:1 catalyst to free halide ratio. The observed inhibition may be rationalized as a consequence of halide anions binding to the open coordination site on the cationic Pd intermediate. The lack of an open coordination site obstructs the complexation of the vinylboron 'ate' on to the intermediate metal complex which ultimately derails the desired reactivity.

Table 1.1. Halide inhibition in conjunctive coupling

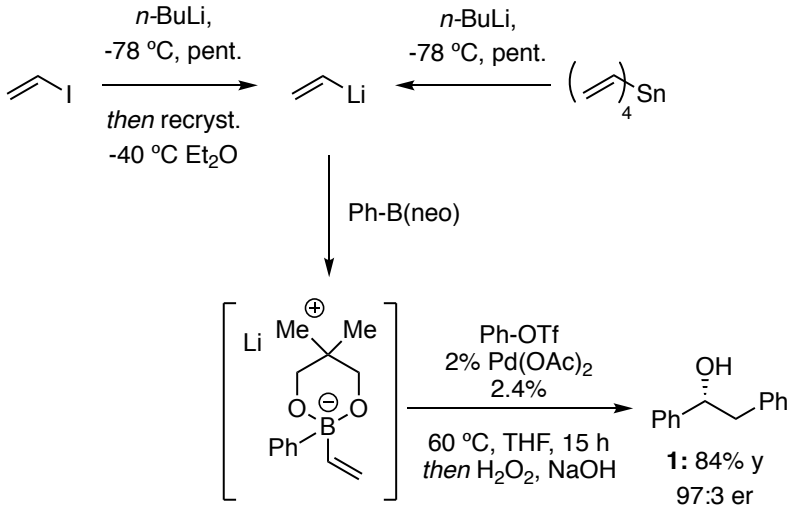


Entry	X	Additive	Yield	er
1	OTf	_	77%	98:2
2	Cl	_	<5%	-
3	Br	_	9%	94:6
4	I	_	9%	94:6
5	OTf	LiBr (0.01 equiv.)	42%	98:2
6	OTf	LiI (0.01 equiv.)	13%	98:2

Therefore, we adopted two separate protocols for the generation of vinyllithium. One protocol involved the recrystallization of vinyl lithium derived through lithium-halogen exchange between vinyl iodide and *n*BuLi. The lithium-halogen exchange for this

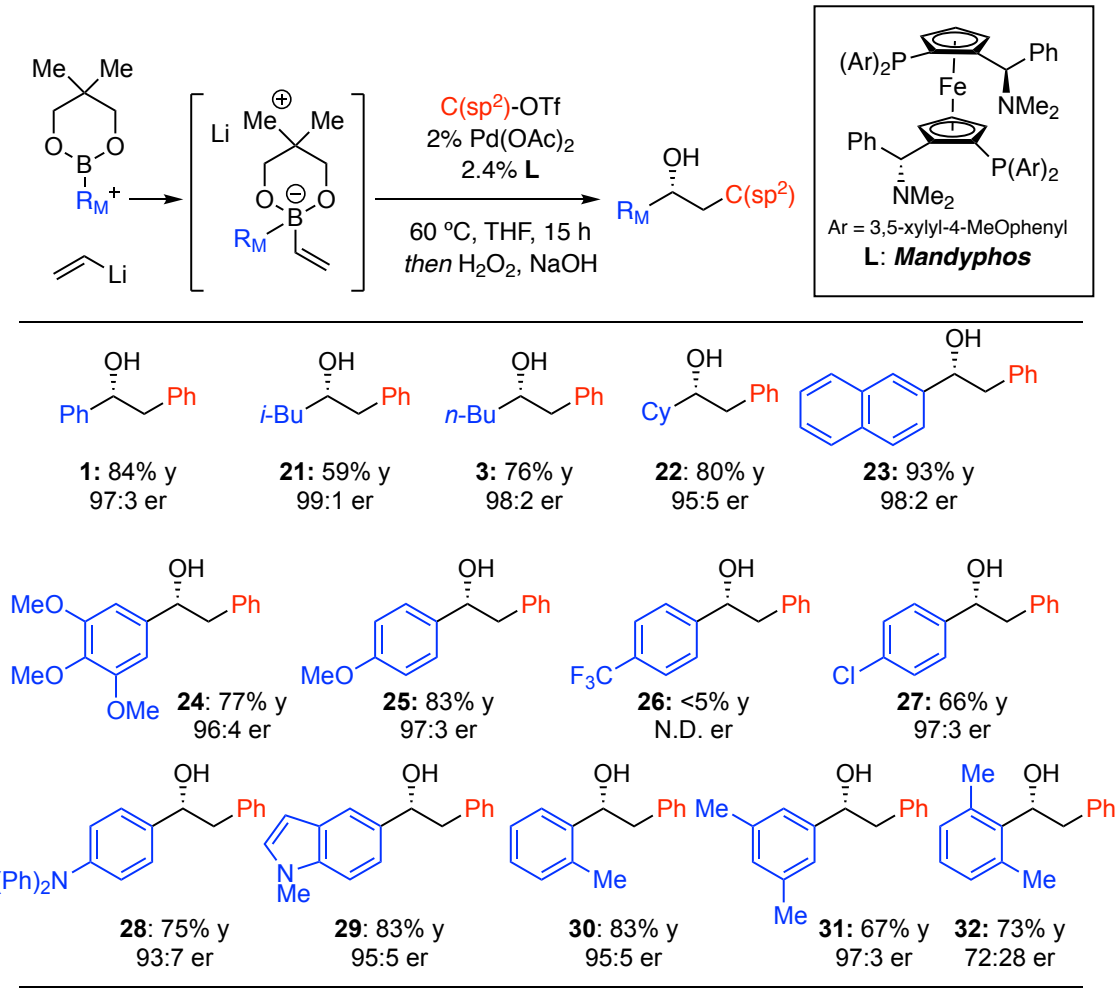
reaction was carried out in pentane, causing the vinyllithium to precipitate out of solution. This solid was collected and recrystallized from Et_2O at -45ºC to remove trace halide impurities. The second protocol involved lithium-tin exchange between *n*BuLi and tetravinyl tin in pentane. Analogously to the previous protocol, the solid vinyl lithium precipitated out of solution, and was collected and dissolved in THF to generate a stock solution. Using either of these reagents with 2% catalyst loading resulted in efficient reactions with yields and selectivities equivalent to those obtained from the reaction of vinylB(neo) and phenyllithium (Figure 1.15).

Figure 1.15. Synthesis of halide free vinyl lithium



The generation of halide-free vinyllithium reagent enabled us to easily study a wide range of migrating groups for the conjunctive coupling manifold, as many commercially available boronic acids could be easily converted to the corresponding neopentyl esters and studied in our system (Figure 1.16). The results obtained previously for reactions with vinylB(neo) and organolithium reagents were reproduced under these conditions with nearly identical results (Figure 1.16, **1, 3**). Secondary alkylB(neo) starting materials participated in the reaction efficiently as well (**21**, **22**).

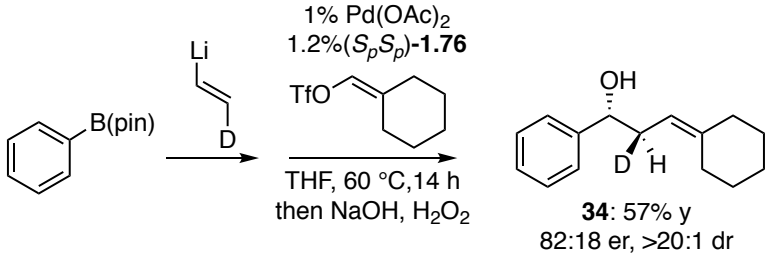
Figure 1.16. Extended substrate scope for the Pd-catalyzed conjunctive cross-coupling



Sterically demanding aromatic migrating groups possessing mono- (**30**) and di-*ortho* (**32**) substituents formed products with good efficiency although with reduced selectivity in the case of di-*ortho* substitution. Electron-rich aromatic substrates (**25**, **28**) worked well, while a *para*-CF_3 substituted phenyl migrating group (**26**) resulted in no product formation, perhaps highlighting the necessity for generating an electron-rich boron 'ate' species to facilitate the 1,2-metallate shift. An arene possessing halide (**27**) substituents underwent efficient migration, and an indole heteroaromatic migrating group (**29**) also formed product under the reaction conditions.

1.3.3 Mechanistic experiments.

Figure 1.17. Deuterium labeling study



As part of the initial investigations into the mechanism of the reaction, we set out to explore the stereochemical outcome of the transformation. Specifically, the 1,2-metallate shift step in this reaction requires an *anti*-periplanar conformation which, combined with a stereoretentive reductive elimination, should result in the overall *anti*-addition of the migrating group and electrophile across the vinyl moiety on boron. A possible alternative mechanism for this transformation could involve an initial carbometallation, followed by transmetallation and reductive elimination to form the product, in line with Murakami's[35] mechanistic hypothesis. This type of dicarbofunctionalization should be stereospecific, but with the expected outcome corresponding to an overall *syn* addition of the coupling partners. To distinguish between these two options, we devised a deuterium labeling study that involved the use of stereochemically-defined deuterated vinyllithium reagent in a conjunctive cross-coupling. Analysis of the reaction outcome revealed that the product, formed in 20:1 dr, possessed stereochemistry consistent with *anti* addition of the coupling partners across the vinyl moiety (Figure 1.17). While this result is consistent with the stereochemical requirements

of a 1,2-metallate shift, the experiment does not rule out the possibility of a carbometallation mechanism followed by a stereo-invertive reductive displacement.[33c]

1.3.4 Conclusion

In summary, herein is described the development of a catalytic conjunctive cross-coupling reaction for the synthesis of enantiomerically enriched alkyl boronic esters in a modular and efficient manner. This method merges two ubiquitous reactivity modes for manipulating organoboron compounds, namely the use of organoboron as nucleophiles in metal catalyzed cross-coupling reactions, and the 1,2-metallate shift mode of reactivity of boron. Thus, in the context of metal-catalyzed cross-couplings, the canonical transmetallation step is replaced by a metal-induced 1,2-metallate shift. The overall process merges an organolithium, an organoboronic ester, and a C(sp^2)-OTf electrophile in a stereospecific and enantioselective process. The reactive vinylboron 'ate' species may be generated in a modular manner by combining either an organolithium reagent with a vinylboronic ester, or an organoboronic ester with a vinyllithium reagent. A wide range of alkyl and aryl migrating groups participated effectively in the reaction, while the triflate electrophiles encompassed a wide scope of aryl and alkenyl substrates. Taken together, these features underscore the potential of the conjunctive cross-coupling manifold as a modular and efficient tool for the generation of enantiomerically enriched organoboron compounds.

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. ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) or Varian Gemini-600 (160 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 or methanol as the modifier.

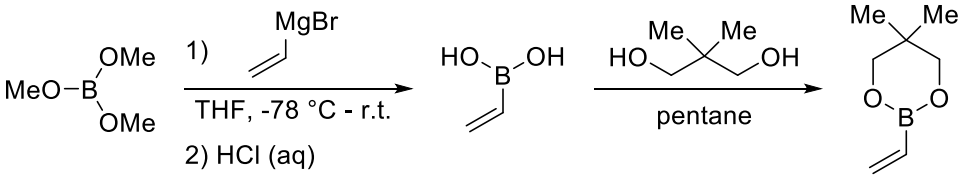
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Palladium (II) acetate, (S_p,S_p)-**L1**, and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene were purchased from Strem Chemicals, Inc. and used without further purification. Vinyl boronic acid pinacol ester was purchased from Combi Blocks and used without further purification. Boronic acids were purchased from Aldrich and used without further purification. Neopentyl glycol was purchased from Aldrich and used without further purification. 4-methoxyphenyltrifluoromethanesulfonate and 2-naphthyl trifluoromethanesulfonate were purchased from Aldrich and used without further purification. Phenyl triflluoromethanesulfonate and Trifluoromethansulfonic anhydride were purchased from Oakwood Chemicals and used without further purification. All other reagents were purchased from either Aldrich, Alfa Aesar or Acros and used without further purification.

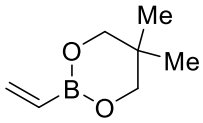
1.4.2. Experimental Procedures

1.4.2.1 Procedures for Preparation of Boronic Esters

General Procedure for the Preparation of Boronic Esters

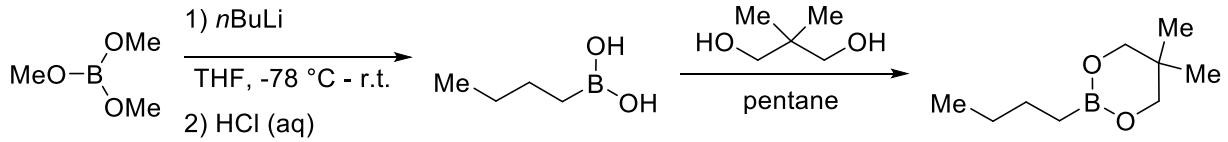
To an oven-dried round bottom flask with magnetic stir bar was added boronic acid (1.0 eq) and pentane. The suspension was cooled to 0°C and 2,2-dimethyl-1,3-propanediol (neopentyl glycol) (1.05 eq) was added neat and the reaction solution was allowed to warm to room temperature and stirred at room temperature for 3 hours. If a water layer was observed it was removed and the resulting pentane solution was dried with over Na_2SO_4, filtered with Et_2O, and the solvent was removed under reduced pressure. The resulting residue was purified on silica gel (plug using CH_2Cl_2 as the eluent).

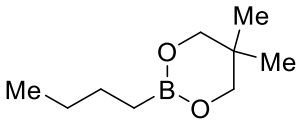




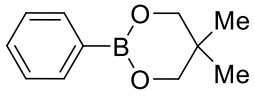
5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (S-1). To an oven-dried 250 mL round bottom flask with magnetic stir bar under N_2 was added trimethylborate (9.95 g, 95.80 mmol, 1.78 eq) and 50 ml of THF. The reaction flask was cooled to -78°C and vinyl magnesium bromide (60 ml, 0.90M, 54 mmol, 1.0 eq) was added over 2 hours via syringe pump. After addition of vinyl magnesium bromide the reaction solution was allowed to warm to room temperature and stir for 8 hours, after which 1M HCl *(aq)* (30 mL) was added followed by 25 mL of deionized water and the reaction solution was allowed to stir at room temperature for 2 hours. The reaction solution was extracted with 6 x 50 mL of Et_2O and the combined organic layers were washed with 50 mL of deionized water, and 50 mL of brine, dried over Na_2SO_4, filtered with Et_2O and the solvent was removed under reduced pressure. The resulting oil was subjected to general procedure for the preparation of boronic esters and the crude product was purified by vacuum distillation (under house vac) while heating to 83°C. The product was

isolated as a clear colorless oil (5.81 g, 77 % yield). All spectral data was in accordance with the literature (*30*).



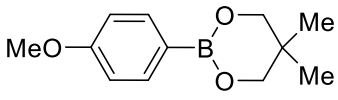


2-butyl-5,5-dimethyl-1,3,2-dioxaborinane (S-2). To an oven-dried 250 mL round bottom flask with magnetic stir bar under N_2 was added trimethylborate (11.21 g, 106.8 mmol, 1.78 eq) and 50 mL of THF. The reaction flask was cooled to -78℃ and *n*BuLi (23.72 mL, 2.53M, 60 mmol, 1.0 eq) was added over 2 hours via syringe pump. After addition of nBuLi the reaction solution was allowed to warm to room temperature and stirred at room temperature for 8 hours, after which 1M HCl *(aq)* (30 ml) was added and the reaction solution was allowed to stir at room temperature for 2 hours. The reaction solution was extracted with 4 x 20 mL of Et_2O and the combined organic layers were washed with brine, dried with sodium sulfate, filtered with Et_2O and the solvent was removed under reduced pressure. The resulting oil was subjected to the general procedure for preparation of boronic esters. The product was isolated as a clear colorless oil (5.26 g, 52% yield). All spectral data was in accordance with the literature (*31*).

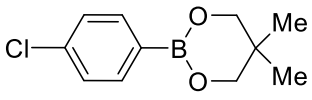


5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane (S-3). Preparted according to the general procedure above with phenylboronic acid (0.268 g, 22.0 mmol), neopenty glycol (2.41 g, 23.1 mmol), and pentane (60 mL). The resulting white solid (4.18 g,

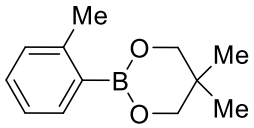
quantitative yield) was used without further purification. All spectral data was in accordance with the literature (*32*). This compound is also commercially available [CAS: 5123-13-7].



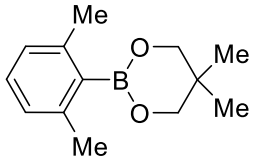
2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (S-4). Prepared according to the general procedure above with 4-methoxyphenylboronic acid (0.4559 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol) and pentane (9.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a white solid (0.650 g, 98%). All spectral data was in accordance with the literature (*33*).



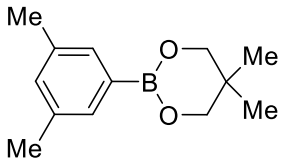
2-(4-chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (S-5). Prepared according to the general procedure above with 4-chlorophenylboronic acid (0.4691 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a white solid (0.667 g, 99% yield). All spectral data was in accordance with the literature (*34*).



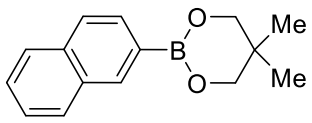
5,5-dimethyl-2-(*o*-tolyl)-1,3,2-dioxaborinane (S-6). Prepared according to the general procedure above with *o*-tolylboronic acid (0.4079 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a colorless oil (0.611 g, quantitative yield). All spectral data was in accordance with the literature (*35*).



2-(2,6-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (S-7). Prepared according to the general procedure above with 2,6-dimethylphenylboronic acid (0.4499 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9.0 mL). The crude residue was purified on silica gel plug with CH_2Cl_2 to afford the product as a white solid (0.558 g, 85%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.09 (1H, t, *J* = 7.8 Hz), 6.93 (2H, d, *J* = 7.8 Hz), 3.78 (4H, s), 2.38 (6H, s), 1.09 (6H, s).). ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.58, 128.59, 126.48, 77.37, 77.16, 76.95, 72.38, 31.79, 22.40, 22.37. ^{11}B NMR (192 MHz, $CDCl_3$) δ 26.25. IR (neat) ν_{max} 3056.7 (w), 2960.3 (w), 2931.5 (w), 1596.3 (w), 1475.0 (m), 1455.3 (m), 1292.4 (s), 1246.2 (m), 1029.0 (w), 768.6 (m), 694.3 (m), 699.1 (m) cm^{-1}. HRMS (DART) for $C_{13}H_{20}BO_2$ $[M+H]^+$ calculated: 219.1556, found: 219.1557.

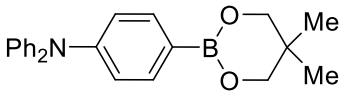


2-(3,5-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (S-8). Prepared according to the general procedure above with 3,5-dimethylphenylboronic acid (0.4499 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9.0 mmol). The crude residue was purified with silica gel plug with CH_2Cl_2 to afford the product as a white solid (0.479 g, 73%). All spectral data was in accordance with the literature (*35*).

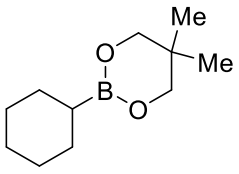


5,5-dimethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborinane (S-9). Prepared according to the general procedure above with 2-napthylboronic acid (2.00 g, 11.6 mmol), neopentyl glycol (1.27 g, 12.18 mmol), and pentane

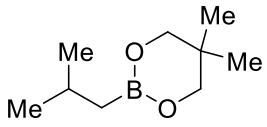
(100.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a white solid (2.79 g, quantitative yield). All spectral data was in accordance with the literature (*35*).



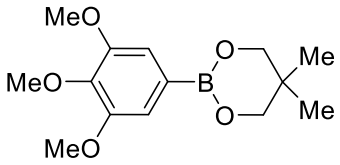
4-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-N,N-diphenylaniline (S-10). Prepared according to the general procedure above with 4-(diphenylamino)phenylboronic acid (0.4935 g, 1.7 mmol, 1 equiv.), neopentyl glycol (0.187 g, 1.79 mmol, 1.05 equiv.), and pentane (10 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a white solid (0.466 g, 77%). All spectral data was in accordance with the literature (*36*).



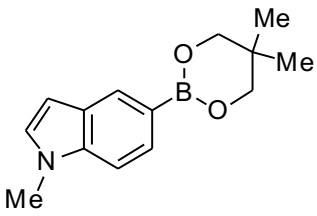
2-cyclohexyl-5,5-dimethyl-1,3,2-dioxaborinane (S-11). Prepared according to the general procedure above with cycylohexylboronic acid (1.98 g, 15.5 mmol), neopentyl glycol (1.70 g, 16.28 mmol), and pentane (100 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a colorless oil (3.00 g, 99% yield). All spectral data was in accordance with the literature (*37*).



2-isobutyl-5,5-dimethyl-1,3,2-dioxaborinane (S-12). Prepared according to the general procedure above with (2-methylpropyl)boronic acid (0.3058 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a colorless oil (0.398 g, 78% yield). All spectral data was in accordance with the literature (*38*).



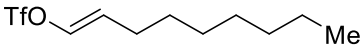
5,5-dimethyl-2-(3,4,5-trimethoxyphenyl)-1,3,2-dioxaborinane (S-13). Prepared according to the general procedure above with 3,4,5-trimethoxyphenylboronic acid (1.91 g, 9.0 mmol), neopentyl glycol (0.984 g, 9.45 mmol), and pentane (100.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a white solid (2.52 g, quantitative yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.04 (2H, s), 3.89 (6H, s), 3.87 (3H, s), 3.76 (4H, s), 1.02 (6H, s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.78, 140.34, 110.31, 72.32, 60.75, 56.02, 31.86, 21.89. ^{11}B NMR (160 MHz, $CDCl_3$) δ 26.49. IR (neat) ν_{max} 29589.0 (w), 2936.7 (w), 2889.3 (w), 1576.9 (m), 1477.2 (m), 1337.3 (s), 1229.9 (s), 1123.4 (s), 1004.0 (m), 688.1 (m) cm^{-1}. HRMS (DART) for $C_{14}H_{22}BO_5$ $[M+H]^+$ calculated: 281.1560, found: 281.1551.



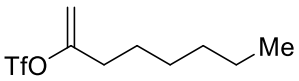
5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1-methyl-1*H*-indole (S-14). Prepared according to the general procedure above with (1-methyl-1H-indol-5-yl)boronic acid (0.500 g, 2.772 mmol), neopentyl glycol (0.306 g, 2.910 mmol), and pentane (100.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a white solid (0.4739 g, 70 % yield). 1H NMR (500 MHz, $CDCl_3$) δ 8.12 (1H, s), 7.65 (1H, d, *J* = 7.0 Hz), 7.29 (1H, d, *J* = 7.0 Hz), 7.00 (1H, d, *J* = 2.5 Hz), 6.48 (1H, d, *J* = 2.5 Hz), 3.78 (4H, s), 3.77 (3H, s), 1.02 (6H, s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.65, 128.85, 128.40, 127.87, 127.07, 108.577, 101.79, 72,52, 32.97, 32.13, 22.16. ^{11}B NMR (160 MHz, $CDCl_3$) δ 27.15. IR (neat) ν_{max} 2960.4 (w), 2939.3 (w), 2895.9 (w), 2874.6 (w), 1608.0 (w), 1513.9 (w),1 4.78.8 (w), 1333.1 (m), 1304.9 (s), 1271.5 (m), 1245.4

(m), 1185.2 (m), 1118.03 (m), 717.99 (w), 692.0 (w), 678.88 (w) cm^{-1} . HRMS (DART) for $C_{14}H_{19}BNO_2$ $[M+H]^+$ calculated: 244.1509, found: 244.1519.

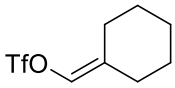
1.4.2.2. Procedures for Preparation of Alkenyl and Aryl Trifluoromethanesulfonates



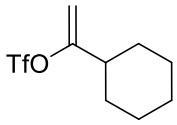
***(E)*-non-1-en-1-yl trifluoromethanesulfonate (S-15).** The title compound was prepared according to a literature precedence with slight modification (*39*). In an Ar-filled glove box, CsF (5.01 g, 33.0 mmol, 3.0 equiv.) and N-Phenyl-bis(trifluoromethanesulfonimide) (7.86 g, 22.0 mmol, 2.0 equiv.) were placed in a large pressure vessel and sealed. Outside the glovebox the flask was briefly opened and a solution of 1-nonen-1-yl trimethylsilyl ether (*40*) (95/5 mixture of E/Z isomers, 2.36 g, 11 mmol) in dimethoxyethane (30 mL) was added. After addition the pressure vessel was quickly sealed with a screw cap. The solution was stirred vigorously at room temperature for 4 hours after which the pressure was released and the reaction mixture was diluted with pentane (100 mL), washed twice with water and once with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude oil was purified by silica gel chromatography (100% pentane) to afford the title compound as a clear colorless oil (1.51 g, 50% yield). All spectral data was in accordance with the literature (*41*).



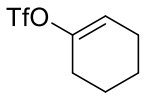
oct-1-en-2-yl trifluoromethanesulfonate (S-16). The title compound was prepared according to the procedure reported in the literature (*42*). All spectral data was in accordance with the literature.



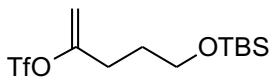
cyclohexylidenemethyl trifluoromethanesulfonate (S-17). The title compound was prepared according to the procedure reported in the literature (*43*). All spectral data was in accordance with the literature.



1-cyclohexylvinyl trifluoromethanesulfonate (S-18). The title compound was prepared according to the procedure reported in the literature (*44*). All spectral data was in accordance with the literature.

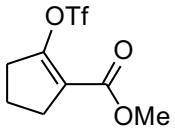


cyclohex-1-en-1-yl trifluoromethanesulfonate (S-19). The title compound was prepared according to the procedure reported in the literature (*45*). All spectral data was in accordance with the literature.



5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-2-yl trifluoromethanesulfonate (S-20). Prepared following a published procedure with slight modifications.[15] 4-Pentyn-1-ol (1.44 mL, 15.5 mmol, 1.0 equiv.) was placed in a flame-dried round bottom flask and dissolved in dry pentane (15 mL). The solution was cooled to - 40℃ and triflic acid (2.5 mL, 27.8 mmol, 1.6 equiv.) was added dropwise with stirring. The mixture was stirred for 10 minutes at -40℃ and allowed to warm to room temperature over 30 minutes. The mixture was quenched with water (10 mL), extracted with diethyl ether and washed with saturated sodium bicarbonate solution and brine. The crude mixture was dried over Na_2SO_4, concentrated under reduced pressure and filtered through a plug of neutral alumina with CH_2Cl_2. The resulting triflate,

obtained as a clear yellow oil (1.84 g, 7.8 mmol, 1 equiv.) was placed in a flame dried round bottom flask with imidazole (1.10 g, 16 mmol, 2 equiv.) and dissolved in CH_2Cl_2 (20 mL). The solution was flushed with N_2 and cooled to 0°C. *tert*-Butyldimethylsilyl chloride (1.18 g, 7.8 mmol, 1.0 equiv.) was added as a solution in CH_2Cl_2 (10 mL). The mixture was stirred at room temperature for 2 hours after which 1M HCl solution (5 mL) were added. The mixture was extracted with CH_2Cl_2 and washed with sodium bicarbonate solution and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (1% ethyl acetate in hexane) to afford the title compound as a clear colorless oil (2.10 g, 40 % yield over two steps). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.11 (1H, d, J = 3.0 Hz), 4.95 (1H, d, J = 3.0 Hz), 3.65 (2H, t, J = 6.0 Hz), 2.44 (2H, t, J = 7.8 Hz), 1.75 (2H, q, J = 6.6 Hz), 0.89 (9H, s), 0.05 (6H, s).^{13}C NMR (125 MHz, CDC_3) δ 156.9, 104.4, 61.4, 30.6, 29.3, 25.7, 18.4, -5.3. IR (neat) ν_{max} 2995.9 (s), 2931.6 (s), 2894.4 (s), 2859.8 (s), 1671.0 (s), 1473.0 (s), 1253.3 (s), 1209.3 (s), 1141.1 (s), 1104.7 (s), 945.0 (s), 835.9 (s), 776.7 (s), 611.56 (s) cm^{-1}. HRMS-(DART) for: $C_{12}H_{24}F_3O_4S_1Si_1$ $[M+H]^+$: calculated: 349.1117, found: 349.1114.

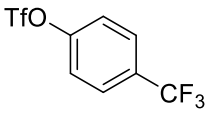


5-hydroxypent-1-en-2-yl trifluoromethanesulfonate (S-21). The title compound was prepared according to the procedure reported in the literature (*46*). All spectral data was in accordance with the literature.

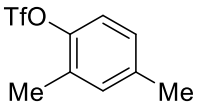
General Procedure for the Synthesis of Aryl Trifluoromethanesulfonates

Aryl Trifluoromethansulfonates were made according to literature procedure with slight modification (*47*). To a solution of the corresponding phenol and pyridine in CH_2Cl_2 at 0°C, a

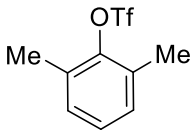
solution of trifluoromethanesulfonic anhydride in CH_2Cl_2 was added dropwise. The mixture was then warmed to room temperature and allowed to stir for 1 hour. The mixture was diluted with Et_2O, quenched with 3M HCl *(aq)* and washed successively with $NaHCO_3$ *(aq, sat.)* and brine. The solution was dried over Na_2SO_4, filtered with Et_2O, and the solvent was removed under reduced pressure. The residue was purified on silica gel chromatography to afford aryl trifluoromethanesulfonates.



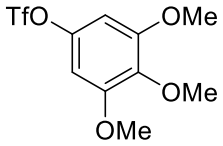
4-(trifluoromethyl)phenyl trifluoromethanesulfonate (S-22). Prepared according to the general procedure above with 4-trifluoromethylphenol (0.630 g, 3.8 mmol), trifluoromethanesulfonic anyhydride (0.774 mL, 4.6 mmol), pyridine (0.615 mL, 7.6 mmol), and CH_2Cl_2 (6.0 mL). The crude residue was purified on silica gel chromatography (10% ethyl acetate in hexanes) to afford the product as a colorless oil (1.180 g, 98% yield). All spectral data was in accordance with the literature (*48*).



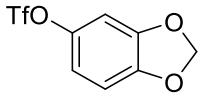
2,4-dimethylphenyl trifluoromethanesulfonate (S-23). Prepared according to the general procedure above with 2,4-dimethylphenol (0.906 mL, 7.5 mmol), trifluoromethanesulfonic anhydride (1.50 mL, 9.0 mmol), pyridine (1.2 mL, 15.0 mmol), and CH_2Cl_2 (13.0 mL). The crude residue was purified with silica gel chromatography (5% ethyl acetate in hexanes) to afford the product as a colorless oil (1.680 g, 88% yield). All spectral data was in accordance with the literature (*49*).



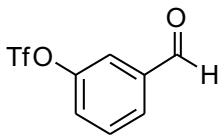
2,6-dimethylphenyl trifluoromethanesulfonate (S-24). Prepared according to the general procedure above with 2,6-dimethylphenol (0.611 g, 5.0 mmol), trifluoromethanesulfonic anhydride (1.0 mL, 6.0 mmol), pyridine (0.809 mL, 10.0 mmol), and CH_2Cl_2 (8.0 mL). The crude residue was purified with silica gel chromatography (17% ethyl acetate in hexanes) to afford the product as a yellow oil (1.124 g, 88% yield). All spectral data was in accordance with the literature (*50*).



3,4,5-trimethoxyphenyl trifluoromethanesulfonate (S-25). Prepared according to the general procedure above with 3,4,5-trimethoxyphenol (0.921 g, 5.0 mmol), trifluoromethanesulfonic anhydride (1.0 mL, 6.0 mmol), pyridine (0.809 mL, 10.0 mmol), and CH_2Cl_2 (8.0 mL). The crude residue was purified with silica gel chromatography (20% ethyl acetate in hexanes) to afford the product as an off white solid (1.552 g, 98% yield). All spectral data was in accordance with the literature (*51*).

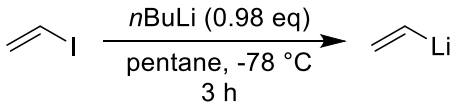


benzo[*d*][1,3]dioxol-5-yl trifluoromethanesulfonate (S-26). Prepared according to the general procedure above with sesamol (1.04 g, 7.5 mmol), trifluoromethansulfonic anhydride (1.5 mL, 9.0 mmol), pyridine (1.2 mL, 15.0 mmol), and CH_2Cl_2 (13.0 mL). The crude residue was purified with silica gel chromatography (5% ethyl acetate in hexanes) to afford the product as colorless oil (1.89 g, 94%). All spectral data as in accordance with the literature (*52*).



3-formylphenyl trifluoromethanesulfonate (S-27). Prepared according to the general procedure above with 3-hydroxybenzaldehyde (916 mg, 7.5 mmol), trifluoromethanesulfonic anhydride (1.5 mL, 9.0 mmol), pyridine (1.2 mL, 15.0 mmol), and CH_2Cl_2 (10 mL). The crude residue was purified by silica gel chromatography (10% ethyl acetate in hexanes) to afford the product as a colorless oil (1.47 g, 77% yield). All spectral data was in accordance with the literature (*47*).

1.4.2.3. *Procedure for Preparation of Vinyllithium*



To an oven-dried 250 mL round bottom flask with magnetic stir bar in an Ar-filled glovebox was added vinyl iodide (12.1670 g, 76.6611 mmol, 1.00 eq) and pentane (35 ml). The reaction flask was sealed with a rubber septa, removed from the glovebox, cooled to -78°C under argon, and maintained at this temperature while *n*BuLi (29.7 ml, 75.1410 mmol, 0.98 eq) was added via syringe pump over two hours. Vinyllithium formation was observed as a white suspension in the reaction flask within 2-3 minutes of initial *n*BuLi addition. Upon completion of slow addition, the reaction solution was allowed to stir for an additional hour at between -50 and -78°C. The vinyllithium suspension was transferred via cannula in two portions to an oven-dried Schlenck filter under argon and filtered, washed with pentane, and dried in the following manner: After transfer of the first half of the vinyllithium suspension in pentane, the pentane was removed under positive pressure by slightly reducing the pressure in the bottom chamber of the filter while

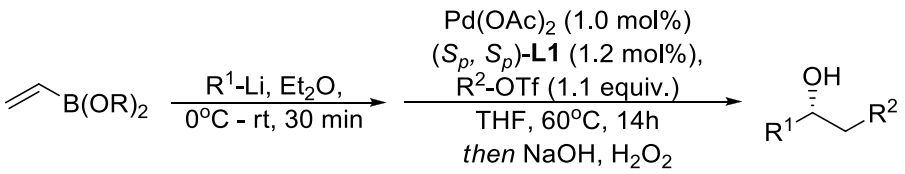
maintaining constant positive pressure of argon in the upper portion of the filter. (Caution, positive pressure must be maintained at all times in the top chamber to prevent air from entering the schlenk filter and reacting with the pyrophoric vinyllithium). After the pentane was removed, a white powdery layer of solid vinyllithium was observed on top of the Schlenk filter frit. The second half of the vinyllithium suspension was transferred and the pentane removed in the same manner. To ensure thorough removal of soluble impurities (*n*-BuLi, *n*-BuI, vinyl iodide) the white powdery pad of vinyllithium left after initial filtration was rinsed three times with 20 mL of dried, distilled, and degassed pentane by adding the pentane to the top chamber of the Schlenk filter and agitating the vinyllithium for two minutes and removal of pentane as described above. The solid vinyllithium was then dried for 15 minutes under positive pressure of argon by reducing the pressure in the bottom chamber of the filter while maintaining positive pressure in the upper chamber of the filter. The receiving 250 ml round bottom flask with pentane washes was replaced via quick-switch with an oven-dried 100 ml 2-neck round bottom flask under argon. The solid vinyllithium was dissolved using 48 ml of diethyl ether and was rinsed into the receiving flask by reducing the pressure of the lower chamber of the filter as described above. The resulting clear yellow solution was titrated using BHT with 1,10-phenanthroline in THF and the yield (72.8280 mmol, 95 % yield) was calculated based on the measured molarity (1.58 M) and the measured volume of the solution upon transfer to a single-necked 100 ml round bottom flask (At this point the vinyllithium can be used directly in a conjunctive coupling with 5 mol % catalyst loading and the coupling product can be obtained in 69% yield, 98:2 er.).

The freshly prepared solution of vinyllithium (1.58 M) was immediately recrystallized three times from diethyl ether by cooling the solution to -45℃ over 1 h using a Cryocool and maintaining this

temperature overnight (10 h) and then reducing the temperature to -78℃ for 6 hours using a dry ice acetone bath. Solid vinyllithium was observed to form as clear, glassy, crystals. After the recrystallization period the supernatant diethyl ether was removed, and the round bottom flask was allowed to warm to room temperature, and 10 ml of fresh diethyl ether was added to the flask. The recrystallization was repeated two more times, resulting in an overall 47 % yield of vinyllithium, evaluated as before, as a clear, nearly colorless solution in diethyl ether.

1.4.2.4. *Procedures for Conjunctive Cross-Coupling*

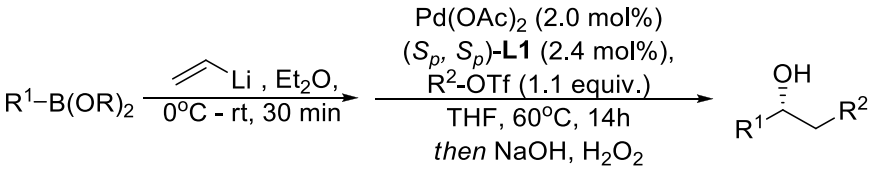
Method A:



To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added vinyl boronic ester (0.30 mmol, 1.00 equiv.) and diethyl ether (0.3 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0℃, and an alkyl/aryl lithium solution (0.30 mmol, 1.0 equiv.) was added at 0℃. 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 stirbar in the glovebox was added $Pd(OAc)_2$ (0.003 mmol, 0.01 equiv.), (S_p, S_p)-**L1** (0.0036 mmol, 0.012 equiv.), and THF (0.3 mL). The $Pd(OAc)_2$/(S_p, S_p)-**L1** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-

L1 solution was transferred into the reaction vial, followed by THF (0.9 mL), and aryl/vinyl triflate (0.33 mmol, 1.10 equiv.). 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, and 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, and subsequently purified via silica gel column chromatography to afford the desired products.

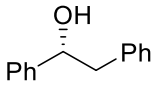
Method B:



To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added alkyl/aryl boronic ester (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 vinyl lithium solution (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 $Pd(OAc)_2$ (0.006 mmol, 0.02 equiv.), (S_p, S_p)-**L1** (0.0072 mmol, 0.024 equiv.), and THF (0.6 mL). The $Pd(OAc)_2$/(S_p, S_p)-**L1** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**L1** 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℃ 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℃, 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℃ 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, and subsequently purified via silica gel column chromatography to afford the desired products.

1.4.2.5. Characterization of Conjunctive Cross Coupling Products and Analysis of Stereochemistry



(R)*-1,2-diphenylethan-1-ol (1).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**S-1**) (42.0 mg, 0.30 mmol, 1.00 equiv.), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol) in THF (1.2 mL, 0.25 M, 0.012 equiv.). The crude mixture was purified by silica gel chromatography (5% ethyl acetate in hexanes, stain in CAM) to afford a white solid (49.37 mg, 83% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26-7.21 (4H, m), 7.20-7.15 (3H, m), 7.14-7.0 (1H, m), 7.10-7.07 (2H, m), 4.78 (1H, ddd, *J* = 6.6, 4.2, 2.4 Hz), 2.93 (1H, dd, *J* = 13.8, 4.8 Hz), 2.87 (1H, dd, *J* = 14.4, 9.0 Hz), 1.84 (1H, br s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.95, 138.17, 129.66, 128.66, 128.56, 127.76, 126.77, 126.04, 75.49, 46.25. HRMS (DART) for $C_{14}H_{13}$ $[M+H-H_2O]^+$ calculated: 181.1017, found: 181.1021. $[\alpha]^{20}_D$: +11.787 (c = 0.635, $CHCl_3$, *l* =50 mm) (lit: $[\alpha]^{20}_D$ = +12.5 (c = 1.01, $CHCl_3$, 98:2 e.r.) (*53*).

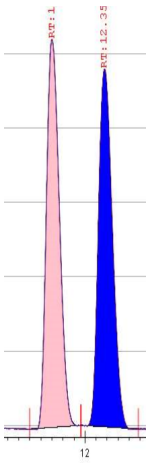
Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with vinyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-

phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was determined by single crystal X-ray diffraction.

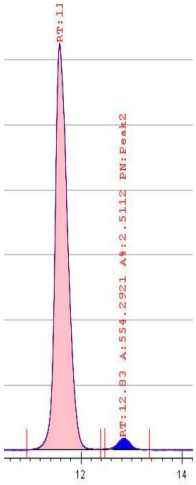
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1,2-diphenylethan-1-ol

Racemic Material



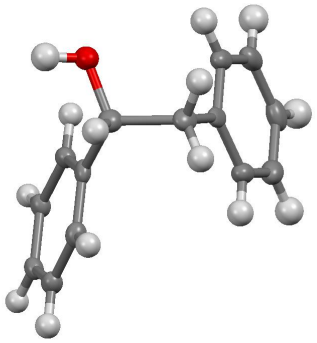
Peak No	% Area	Area	RT (min)
1	50.2599	8450.5728	11.4
2	49.7401	8363.1658	12.35
Total:	100	16813.7386	

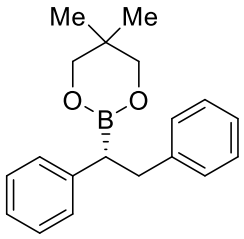
Standard Conditions



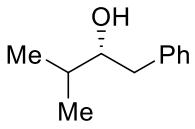
Peak No	% Area	Area	RT (min)
1	97.4888	21518.079	11.58
2	2.5112	554.2921	12.83
Total:	100	22072.3711	

Crystal Structure





(*R*)-2-(1,2-diphenylethyl)-5,5-dimethyl-1,3,2-dioxaborinane (S-28). The reaction was performed according to the general procedure ***(Method A)*** without oxidation step with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**S-1**) (42.0 mg, 0.30 mmol, 1.00 equiv.), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol) in THF (1.2 mL, 0.25 M, 0.012 equiv.). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane, stain in CAM) to afford a colorless solid (67.0mg, 76% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25-7.24 (4H, m), 7.24-7.19 (2H, m), 7.16 (2H, d, J = 7.85 Hz), 7.14-7.10 (2H, m), 3.53 (4H, s), 3.19 (1H, dd, J = 13.2, 9.6 Hz), 2.92 (1H, dd, J = 13.8, 7.2 Hz), 2.57 (1H, t, J = 7.2 Hz), 0.79 (6H, s). ^{11}B NMR (160 MHz, $CDCl_3$) δ 29.47. ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.96, 142.55, 128.98, 128.42, 128.40, 128.19, 125.71, 125.31, 72.27, 38.52, 31.79, 21.88. IR (neat) ν_{max} 3081.9 (w), 3025.2 (w), 2960.3 (w), 1599.6 (w), 1475.8 (m), 1376.3 (m), 1279.3 (m), 1199.7 (s), 1069.8 (s), 770.6 (m), 696.9 (s), 524.5 (m), 493.4 (m) cm^{-1}. HRMS (DART) for $C_{19}H_{24}BO_2$ $[M+H]^+$ calculated: 295.1869, found: 295.1872. $[\alpha]^{20}_D$: -48.214 (c = 2.975, $CHCl_3$, l =50 mm).



(R)*-3-methyl-1-phenylbutan-2-ol (2).** The reaction was performed according to the general procedure **(*Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**S-1**) (42.0 mg, 0.30 mmol), isopropyllithium (0.441 mL, 0.68M in pentane, 0.30 mmol), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol), palladium (II) acetate (0.670 mg, 0.003 mmol), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in hexanes) to afford a yellow oil. (32.5

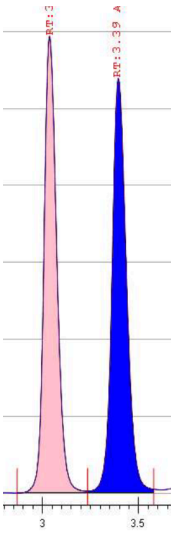
mg, 66% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (2H, t, *J* = 7.2 Hz), 7.21-7.24 (3H, m), 3.57-3.59 (1H, m), 2.84 (1H, dd, *J* = 13.8, 3.0 Hz), 2.32 (1H, dd, *J* = 13.2, 9.0 Hz,), 1.77-1.72 (1H, m), 1.42 (1H, d, *J* = 3.6 Hz), 0.99 (3H, s), 0.98 (3H, s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.39, 129.59, 128.82, 126.62, 77.72, 41.02, 33.37, 19.16, 17.64. IR (neat) ν_{max} 3241 (br), 3027 (w), 2957 (m), 2927 (m), 2981 (m), 1494 (m), 1467 (m), 1031 (m), 995 (s) 741 (m), 698 (s) cm^{-1}. HRMS (DART) for $C_{11}H_{20}NO$ $[M+NH_4]^+$: calculated: 182.1545, found: 182.1547. $[\alpha]^{20}_D$: +15.74 (c = 0.535, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry

Racemic compound was prepared according to the general procedure ***(Method A)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1'-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1, 3,** and **4**).

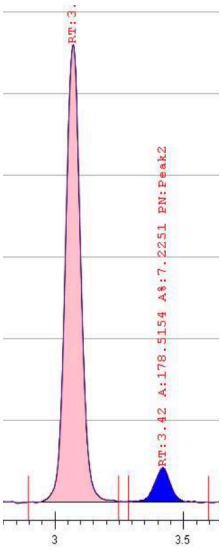
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (R)-3-methyl-1-phenylbutan-2-ol.

Racemic Material

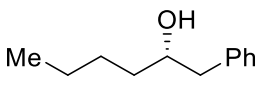


Peak No	% Area	Area	RT (min)
1	49.2988	5449.2883	3.04
2	50.7012	5604.3147	3.39
Total:	100	11053.603	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	92.7749	2292.2693	3.07
2	7.2251	178.5154	3.42
Total:	100	2470.7847	



(S)*-1-phenylhexan-2-ol (3).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**S-1**) (42.0 mg, 0.30 mmol, 1.00 equiv.), *n*-butyllithium (0.120 mL, 2.5M in

hexanes, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (50% CH_2Cl_2 in pentane, stain in CAM) to afford a colorless oil (39.5 mg, 74 % yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (2H, t, *J* = 7.2 Hz), 7.24-7.18 (3H, m), 3.80 (1H, dddd, *J* = 12.6, 8.4, 4.8 Hz), 2.82 (1H, dd, *J* = 13.2, 4.2 Hz), 2.63 (1H, dd, *J* = 13.2, 8.4 Hz). 1.56-1.28 (6H, m), 0.90 (3H, t, *J* = 7.2 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.80, 129.57, 128.69, 126.57, 72.84, 44.20, 36.68, 28.08, 22.85, 14.21. HRMS (DART) for $C_{12}H_{17}$ $[M+H-H_2O]^+$ calculated: 161.1330, found: 161.1335. $[\alpha]^{20}_D$: +14.786 (c = 0.510, $CHCl_3$, *l* =50 mm). (lit: $[\alpha]^{28}_D$: +6.3, c = 1.0, $CHCl_3$, 68:32 e.r.) (*54*).

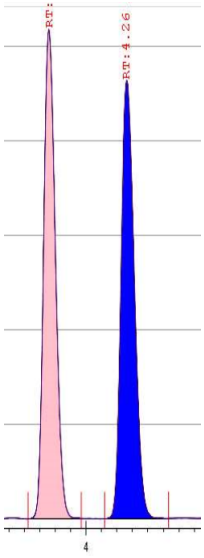
Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with vinyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-

phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was determined by comparison to the literature (*54*).

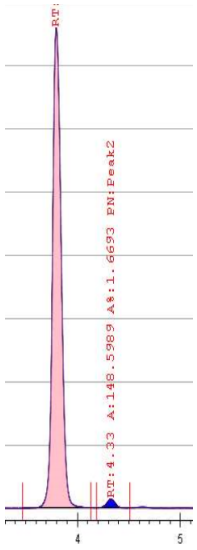
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1,2-diphenylethan-1-ol

Racemic Material

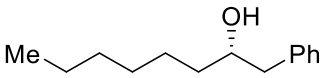


Peak No	% Area	Area	RT (min)
1	49.8946	5442.8203	3.76
2	50.1054	5465.8191	4.26
Total:	100	10908.6394	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	98.3307	8753.1054	3.79
2	1.6693	148.5989	4.33
Total:	100	8901.7043	



(S)*-1-phenyloctan-2-ol (4).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**S-1**) (42.0 mg, 0.30 mmol, 1.00 equiv.), hexyllithium (0.130 mL, 2.3M in hexanes, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel

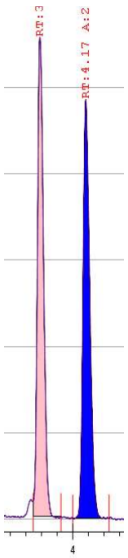
chromatography (50% CH_2Cl_2 in pentane, stain in CAM) to afford a white solid (47.0 mg, 76% yield. HRMS (DART) for $C_{14}H_{26}NO$ $[M+NH_4]^+$ calculated: 224.2014, found: 224.2016. $[\alpha]^{20}_D$: +11.444 (c = 1.645, $CHCl_3$, *l* =50 mm). (lit: $[\alpha]^{20}_D$ = +8.222 (c = 2.043, $CHCl_3$, *l* = 50 mm 96:4 e.r.). All spectral data was in accordance with the literature (*55*).

Analysis of Stereochemistry:

Racemic compound was prepared according to the literature (*55*). Absolute stereochemistry was determined by comparison to the literature (*55*).

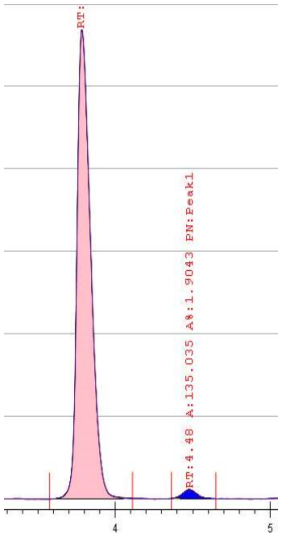
Chiral SFC (Chiracel OD-H, 3% IPA, 5 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-phenyloctan-2-ol

Racemic Material

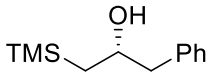


Peak No	% Area	Area	RT (min)
1	50.7244	2991.7195	3.58
2	49.2756	2906.2689	4.17
Total:	100	5897.9884	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	98.0957	6956.0252	3.78
2	1.9043	135.035	4.48
Total:	100	7091.0602	



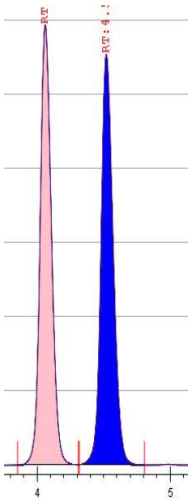
(R)*-1-phenyl-3-(trimethylsilyl)propan-2-ol (5).** The reaction was performed according to the general procedure ***(Method A) with vinyl boronic acid pinacol ester (46.20 mg, 0.30 mmol, 1.00 equiv.), (trimethylsilyl)methyllithium (0.300 mL, 1.0M in pentane, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.6 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (5% ethyl acetate in pentane, stain in CAM) to afford a colorless oil (35.20 mg, 56% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (2H, t, J = 7.2 Hz), 7.24-7.18 (3H, m), 3.98 (1H, ddd, J = 13.2, 13.2, 9.0 Hz), 2.84 (1H, dd, J = 13.8, 4.2 Hz), 2.63 (1H, dd, J = 13.2, 7.8 Hz), 1.44 (1H, br s), 0.96-0.86 (2H, m), 0.06 (9H, s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.98, 129.56, 128.73, 126.63, 71.08, 47.70, 25.99, -0.57. IR (neat) ν_{max} 3582.1 (br), 3441.2 (br) 3062.7 (w), 3028.2 (w), 2951.4 (w), 2917.7 (w), 1495.6 (w), 1454.0 (w), 1247.0 (s), 1076.0 (m), 1056.2 (m), 1018.7 (m), 854.8 (s), 837.4 (s), 743.8 (s), 698.5 (s) cm^{-1}. HRMS (DART) for $C_{12}H_{24}NOSi$ $[M+NH_4]^+$ calculated: 226.1627, found 226.1622. $[\alpha]^{20}_D$: +3.850 (c = 1.135, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (*Method A*) with vinyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1, 3,** and **4**).

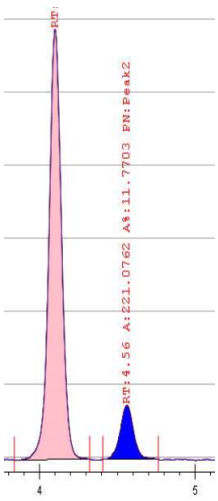
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenyl-3-(trimethylsilyl)propan-2-ol.

Racemic Material

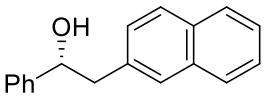


Peak No	% Area	Area	RT (min)
1	49.9308	3484.2905	4.06
2	50.0692	3493.9499	4.52
Total:	100	6978.2404	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	88.2297	1657.1827	4.1
2	11.7703	221.0762	4.56
Total:	100	1878.2589	



(R)*-2-(naphthalen-2-yl)-1-phenylethan-1-ol (6).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**S-1**) (42.0 mg, 0.30 mmol, 1.00 equiv.), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 2-naphthyltrifluoromethanesulfonate (91.20 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv.), (S_p, S_p)-**L1** (3.8 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (50% CH_2Cl_2 in pentane, stain in CAM) to afford a white solid (50.70 mg, 68% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (1H, d, J = 6.6 Hz), 7.78 (1H, d,

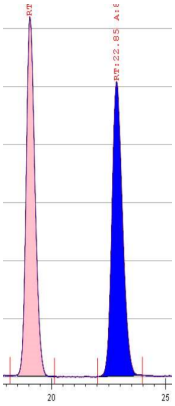
J = 8.4 Hz), 7.48-7.42 (2H, m), 7.38 (2H, d, *J* = 7.2 Hz) 7.30-7.26 (4H, m) 4.99 (1H, ddd, *J* = 7.8, 4.2, 2.4 Hz), 3.20 (1H, dd, *J* = 14.4, 4.8 Hz), 3.15 (1H, dd, *J* = 13.8, 9.0 Hz), 1.99 (1H, d, *J* = 3.0 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.94, 135.68, 133.67, 132.48, 128.61, 128.27, 128.23, 127.92, 127.80, 127.79, 127.71, 126.20, 126.05, 125.69, 75.37, 46.42. IR (neat) ν_{max} 3365.3 (br), 3056.4 (w), 3029.5 (w), 2912.3 (w), 1631.0 (w), 1528.0 (w), 1454.0 (w), 1199.7 (w), 1055.4 (m), 1012.9 (m), 811.1 (s), 747.7 (m), 724.3 (m), 699.4 (s) 478.4 (m) cm^{-1}. HRMS (DART) for $C_{18}H_{15}$ $[M+H-H_2O]^+$ calculated: 231.1174, found 231.1167. $[\alpha]^{20}_D$: -2.8194 (c = 0.770, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

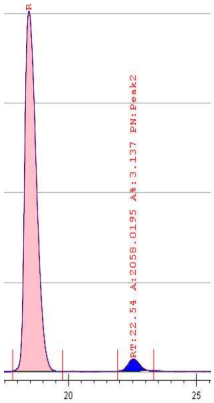
Racemic compound was prepared according to the general procedure (*Method A*) with vinyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

Chiral SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(naphthalen-2-yl)-1-phenylethan-1-ol.

Racemic Material

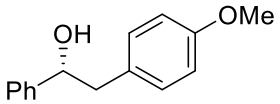


Standard Conditions



Peak No	% Area	Area	RT (min)
1	50.215	8280.1194	19.03
2	49.785	8209.2224	22.85
Total:	100	16489.3418	

Peak No	% Area	Area	RT (min)
1	96.863	63545.7182	18.44
2	3.137	2058.0195	22.54
Total:	100	65603.7377	



(R)*-2-(4-methoxyphenyl)-1-phenylethan-1-ol (7).** The reaction was performed according to the general procedure (Method A***) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**S-1**) (42.0 mg, 0.30 mmol, 1.00 equiv.), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 4-methoxyphenyl

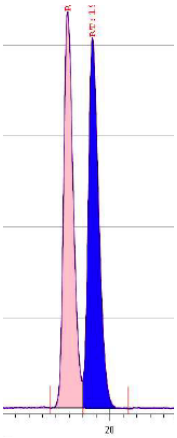
trifluoromethanesulfonate (84.5 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.67 mg, 0.003 mmol, 0.01 equiv.), and (S_p, S_p)-**L1** (3.8 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes) to afford a colorless oil (57.4 mg, 84% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34-7.31 (4H, m), 7.28-7.24 (1H, m), 7.09 (2H, d, J = 9.0 Hz), 6.83 (2H, d, J = 8.4 Hz), 4.84 (1H, ddd, J = 7.8, 4.8, 2.4 Hz), 3.78 (3H, s), 2.98 (1H, dd, J = 13.8, 4.8 Hz), 2.91 (1H, dd, J= 14.4, 9.0 Hz), 1.97 (1H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.6, 144.0, 130.6, 130.1, 128.6, 127.7, 126.0, 114.1, 75.6, 55.4, 45.3; IR (neat) ν_{max} 3407.9 (br), 2999.5 (m), 2834.9 (m), 1611.0 (m), 1583.6 (w), 1510.0 (s), 1453.3 (m), 1242.4 (s), 1176.6 (m), 1031.5 (s), 820.1 (m), 699.1 (s) cm^{-1}; HRMS-(DART) for: $C_{15}H_{15}O_1$ $[M+H-H_2O]^+$: calculated: 211.1123, found: 211.1130. $[\alpha]_D^{20}$ = 4.081 (c = 1.470, $CHCl_3$, l = 50 mm).

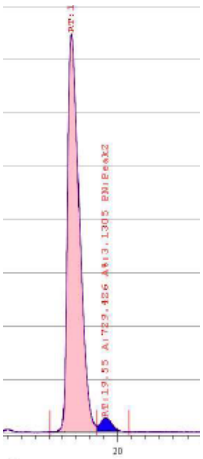
Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-methoxyphenyl)-1-phenylethan-1-ol

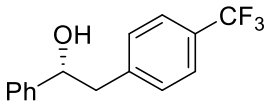
Racemic Material Standard Conditions





Peak No	% Area	Area	RT (min)
1	49.8369	5531.1911	18.43
2	50.1631	5567.3946	19.35
Total:	100	11098.5857	

Peak No	% Area	Area	RT (min)
1	96.8695	22571.4586	18.31
2	3.1305	729.426	19.55
Total:	100	23300.8846	



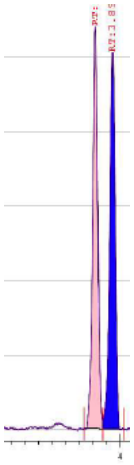
(R)*-1-phenyl-2-(4-(trifluoromethyl)phenyl)ethan-1-ol (8).** The reaction was performed according to the general procedure (Method A***) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**S-1**) (42.0 mg, 0.30 mmol, 1.00 equiv.), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 4-(trifluoromethyl)phenyl trifluoromethanesulfonate (**S-21**) (97.1 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.67 mg, 0.003 mmol, 0.01 equiv.), and (S_p, S_p)-**L1** (3.8 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel column chromatography (5% ethyl acetate in hexanes) to afford a colorless oil (40.9 mg, 51% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (2H, d, J = 8.4 Hz), 7.36-7.27 (6H, m), 4.90 (1H, ddd, J = 8.4, 5.4, 3.0 Hz), 3.08 (1H, dd, J = 13.2, 7.2 Hz), 3.05 (1H, dd, J= 13.2, 5.4 Hz), 1.92 (1H, s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.6, 142.4, 130.1, 129.2, 128.9, 128.7, 128.1, 126.0, 125.4 (q, J = 3.5 Hz), 75.3, 45.7. IR (neat) ν_{max} 3343.5 (br), 2928.8 (w), 1618.3 (w), 1494.5 (m), 1417.9 (m), 1322.6 (s), 1237.4 (m), 1161.6 (m), 1119.4 (s), 1108.1 (s), 1019.1 (m), 841.8 (m), 700.1 (m), 650.7 (m) cm^{-1}. HRMS-(DART) for: $C_{15}H_{12}F_3$ $[M+H-H_2O]^+$: calculated: 249.0891, found: 249.0900. $[\alpha]_D^{20}$ = 5.360 (c = 1.535, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

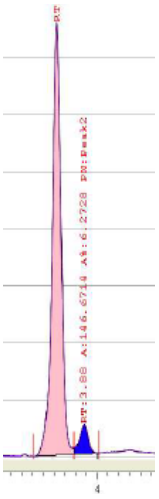
Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenyl-2-(4-(trifluoromethyl)phenyl)ethan-1-ol

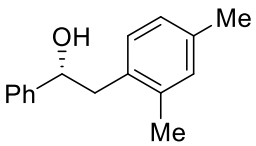
Racemic Material



Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	50.473	557.993	3.64	1	93.7272	2191.5358	3.63
2	49.527	547.5345	3.89	2	6.2728	146.6714	3.88
Total:	100	1105.5275		Total:	100	2338.2072	



(R)*-2-(2,4-dimethylphenyl)-1-phenylethan-1-ol (9).** The reaction was performed according to the general procedure ***(Method A, slight modification at 80°C) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**S-1**) (42.0 mg, 0.30 mmol), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol), 2,4-

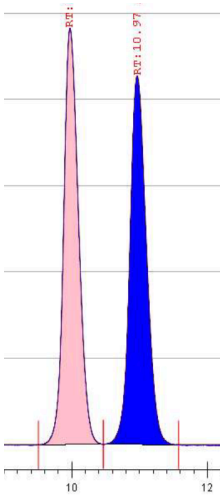
dimethylphenyl trifluoromethanesulfonate (**S-22**) (83.90 mg, 0.33 mmol), palladium (II) acetate (0.670 mg, 0.003 mmol), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in hexanes) to afford a clear oil. (34.6 mg, 51% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33-7.37 (4H, m), 7.27 (1H, t, *J* = 7.2 Hz), 7.04 (1H, d, *J* = 7.8 Hz), 6.98 (1H, s), 6.95 (1H, d, *J* = 7.8 Hz), 4.86-4.86 (1H, m), 3.00 (1H, dd, *J* = 14.4, 4.2 Hz), 2.94 (1H, dd, *J* = 13.8, 9.0 Hz), 2.29 (3H, s), 2.26 (3H, s), 1.92 (1H, d, *J* = 2.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.4, 136.8, 136.5, 133.3, 131.5, 130.4, 128.6, 127.7, 126.9, 125.9, 74.6, 43.2, 21.1, 19.7 IR (neat) ν_{max} 3418 (br), 3027 (w), 3004 (w), 2921 (m), 2856 (w), 1493 (w), 1451 (m), 1026 (s), 805 (s), 699 (s), 567 (m) cm^{-1}; HRMS-(DART): for $C_{16}H_{17}$ [M+H-H_2O]$^+$: calculated: 209.1330, found: 209.1329. $[\alpha]^{20}_D$ = + 3.99 (c = 0.450, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry

Racemic compound was prepared according to the general procedure ***(Method A)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1'-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

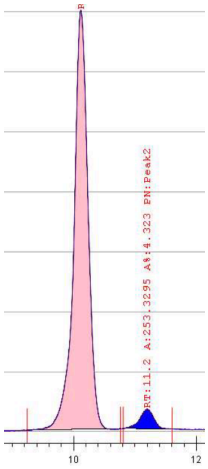
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (R)-2-(2,4-dimethylphenyl)-1-phenylethan-1-ol.

Racemic Material

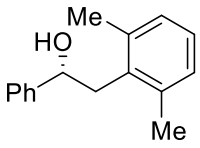


Peak No	% Area	Area	RT (min)
1	50.3811	7320.6585	9.97
2	49.6189	7209.9062	10.97
Total:	100	14530.5647	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	95.677	5606.6891	10.12
2	4.323	253.3295	11.2
Total:	100	5860.0186	



(R)*-2-(2,6-dimethylphenyl)-1-phenylethan-1-ol (10).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**S-1**) (42.0 mg, 0.30 mmol, 1.00 equiv.), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 2,6-dimethylphenyl trifluoromethanesulfonate (**S-23**) (83.90 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane, stain in CAM) to afford a white solid (50.50 mg, 44% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.32 (4H, m), 7.30-7.26 (1H, m), 7.07-7.00 (3H, m), 4.91 (1H, ddd, J = 7.8 4.8, 1.8 Hz). 3.15 (1H, dd, J = 13.8, 9.0 Hz), 2.98 (1H, dd, J = 13.8, 4.8 Hz), 2.31 (6H, s), 1.85 (1H, d, J = 2.4 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.64, 137.58, 135.07, 128.58, 128.53, 127.70, 126.64, 125.70, 74.19,

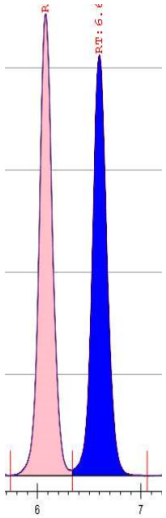
39.96, 20.55. IR (neat) ν_{max} 3534.5 (br), 3416.7 (br), 3064.4 (w), 3027.0 (w), 2956.3 (w), 2921.1 (w), 1550.7 (w), 1493.0 (m), 1379.0 (m), 1049.2 (w), 1024.6 (m), 758.0 (s), 700.2 (s) cm^{-1}. HRMS (DART) for $C_{16}H_{17}$ $[M+H-H_2O]^+$ calcualted: 209.1330, found: 209.1332. $[\alpha]^{20}_D$: +1.419 (c = 0.435, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with vinyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

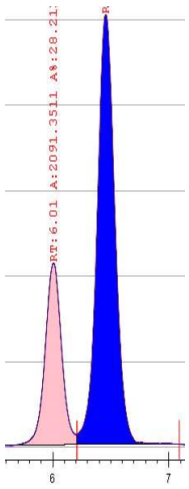
Chiral SFC (Chiracel OD-H, 8% IPA, 3 mL/min, 150 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(2,6-dimethylphenyl)-1-phenylethan-1-ol.

Racemic Material

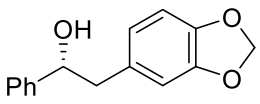


Peak No	% Area	Area	RT (min)
1	49.905	8107.1524	6.08
2	50.095	8138.0096	6.6
Total:	100	16245.162	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	28.2137	2091.3511	6.01
2	71.7863	5321.1889	6.46
Total:	100	7412.54	



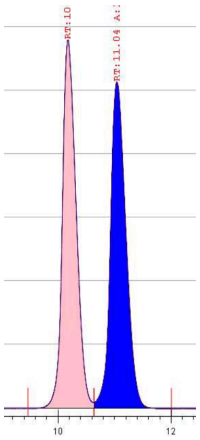
(R)*-2-(benzo[*d*][1,3]dioxol-5-yl)-1-phenylethan-1-ol (11).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**S-1**) (42.0 mg, 0.30 mmol), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol), benzo[d][1,3]dioxol-5-yl trifluoromethanesulfonate (**S-25**) (88.50 mg, 0.33 mmol), palladium (II) acetate (0.67 mg, 0.003 mmol), (S_p, S_p)-**L1** (3.8 mg, 0.0036 mmol) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (5% EtOAc in hexanes) to afford a white solid. (35.6 mg, 49% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (4H, d, *J* = 4.8 Hz), 7.25-7.29 (1H, m), 6.72 (1H, d, *J* = 7.8 Hz), 6.68 (1H, d, *J* = 1.2 Hz), 6.62 (1H, dd, *J* = 8.4, 1.8 Hz), 5.91 (2H, s), 4.82 (1H, dd, *J* = 7.8, 4.2 Hz), 2.94 (1H, dd, *J* = 13.8, 4.2 Hz), 2.88 (1H, dd, *J* = 13.8, 8.4 Hz,), 1.99 (1H, brs,); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.9, 146.5, 143.9, 131.9, 128.6, 127.8, 126.0, 122.6, 110.0, 108.4, 101.1, 75.6, 45.9; IR (neat) ν_{max} 3411 (br), 3062 (w), 3028 (w), 2919 (m), 1607 (w), 1501 (s), 1440 (s), 1243 (s), 1187 (m), 1187 (m), 1036 (s), 928 (s), 699 (s), 537 (m) cm^{-1}; HRMS-(DART): for $C_{15}H_{13}O_2$ $[M+H-H_2O]^+$: calculated: 225.0915, found: 225.0916. $[\alpha]^{20}_D$ = + 1.35 (c = 1.025, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry

Racemic compound was prepared according to the general procedure ***(Method A)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, $Pd(OAc)_2$ (5 mol%) and 1,1'-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

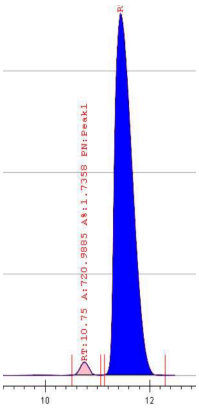
Chiral SFC (Chiracel OJ-H, 8% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (R)-2-(benzo[d][1,3]dioxol-5-yl)-1-phenylethan-1-ol.

Racemic Material

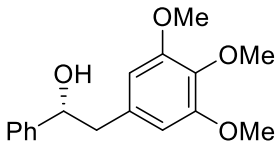


Peak No	% Area	Area	RT (min)
1	50.088	19597.5824	10.18
2	49.912	19528.6842	11.04
Total:	100	39126.2666	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	1.7358	720.9885	10.75
2	98.2642	40816.235	11.44
Total:	100	41537.2235	



***(R)*-1-phenyl-2-(3,4,5-trimethoxyphenyl)ethan-1-ol (12).** The reaction was performed according to the general procedure *(**Method A**)* with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**S-1**) (42.0 mg, 0.30 mmol, 1.00 equiv.), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 3,4,5-trimethoxyphenyl trifluoromethanesulfonate (**S-24**). (104.4 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (15-20% ethyl acetate in pentane, stain in CAM) to afford a white solid (75.20 mg, 87% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37-7.30 (4H, m), 7.28-7.24 (1H, m), 6.35 (2H, s), 4.86 (1H, dd, 8.4, 5.4 Hz), 3.81 (3H, s), 3.78 (6H, s), 2.96 (1H, dd, J = 13.8, 5.4 Hz), 2.90 (1H,

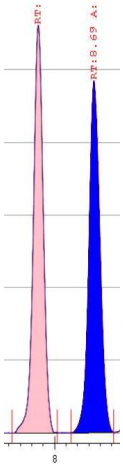
dd, J = 13.2, 7.8 Hz), 2.07 (1H, br s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.26, 143.82, 136.83, 133.64, 128.52, 127.74, 126.05, 106.52, 75.30, 60.95, 56.16, 46.53. IR (neat) ν_{max} 3446.9 (br), 3027.2 (w), 2937.9 (w), 2837.3 (w), 1589.0 (m), 1506.9 (m), 1454.5 (m), 1421.1 (m), 1333.8 (w), 1236.7 (m), 1122.1 (s), 1041.9 (w), 1007.9 (m), 701.5 (m) cm^{-1}. HRMS (DART) for $C_{17}H_{19}O_3$ $[M+H-H_2O]^+$ calcualted: 271.1334, found: 271.1345. $[\alpha]^{20}_D$: +6.128 (c = 2.890, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with vinyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

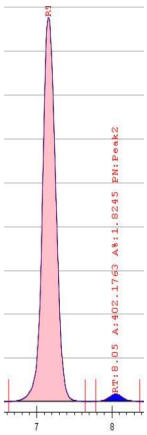
Chiral SFC (Chiracel OD-H, 10% MeOH, 3 mL/min, 150 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenyl-2-(3,4,5-trimethoxyphenyl)ethan-1-ol.

Racemic Material

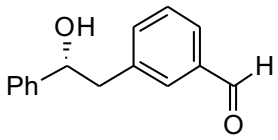


Peak No	% Area	Area	RT (min)
1	50.5474	6748.707	7.71
2	49.4526	6602.5431	8.69
Total:	100	13351.2501	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	98.1755	21641.2099	7.15
2	1.8245	402.1763	8.05
Total:	100	22043.3862	



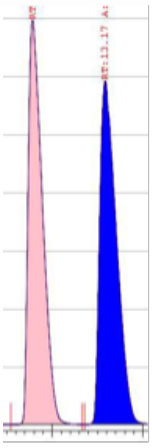
(*R*)-3-(2-hydroxy-2-phenylethyl)benzaldehyde (13). The reaction was performed according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 3-formylphenyl trifluoromethanesulfonate.(**S-27**) (83.9 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (20% EtOAc in Hexanes) to afford a clear colorless oil (45 mg, 66% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.97 (1H, s), 7.48-7.70 (2H, m), 7.46-7.26 (6H, m), 4.94 (1H, t, J = 6.5 Hz), 3.12-3.10 (2H, m), 1.98 (1H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.4, 143.5, 139.3, 136.5, 135.8, 130.6, 129.0, 128.5, 127.9, 125.8, 75.2, 45.4. IR (neat) ν_{max} 3423.5 (br), 3062.1 (s), 3029.5 (s), 2922.1 (m), 2850.5 (s), 1691.3 (s), 1603.0 (d), 1451.7 (s), 1241.1 (s), 1143.8 (s), 1048.0 (s), 698.8 (s) cm^{-1}.HRMS-(DART) for: $C_{15}H_{18}N_1O_1$ $[M+NH_4]^+$: calculated: 244.1339, found: 244.1338. $[\alpha]_D^{20}$: +3.63 (c = 0.84, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with vinyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

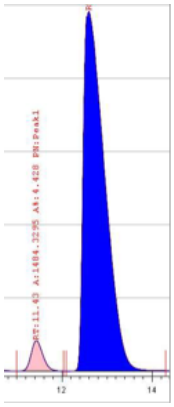
Chiral SFC (Chiracel AS-H, 7% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-(2-hydroxy-2-phenylethyl)benzaldehyde.

Racemic Material

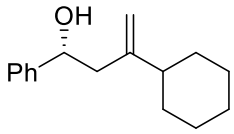


Peak Info			
Peak No	% Area	Area	RT (min)
1	49.9128	15091.73	11.57
2	50.0872	15144.4606	13.17
Total:	100	30236.1906	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	4.428	1484.3295	11.43
2	95.572	32037.2605	12.6
Total:	100	33521.59	



(R)*-3-cyclohexyl-1-phenylbut-3-en-1-ol (14).** The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 1-cyclohexylvinyl trifluoromethanesulfonate (**S-17**) (85.2 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.67 mg, 0.003 mmol, 0.01 equiv.), and (S_p, S_p)-**L1** (3.8 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel column chromatography (5% ethyl acetate in hexane) to afford a colorless oil (50.2 mg, 73% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.32 (4H, m), 7.27-7.24 (1H, m), 4.93 (1H, t, J = 1.2 Hz), 4.88 (1H, d, J = 0.6 Hz), 4.77 (1H, ddd, J = 10.2, 3.6, 2.4 Hz), 2.50 (1H, ddd, J = 13.8, 3.6, 1.2 Hz), 2.36 (1H, dd, J= 13.2, 9.0 Hz), 2.20 (1H, s), 1.88-1.75 (5H, m), 1.70-1.67 (1H, m), 1.29-1.05 (5H, m). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.0, 144.3, 128.5, 127.6, 126.0,

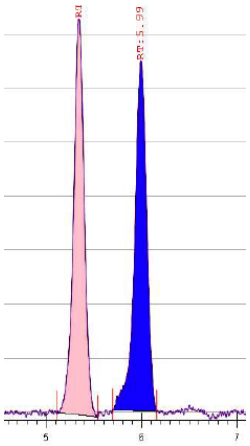
111.1, 71.9, 46.1, 44.0, 32.9, 32.4, 27.0, 26.8, 26.5. IR (neat) ν_{max} 3390.4 (br), 2932.5 (s), 2851.3 (m), 1639.0 (m), 1493.6 (m), 1449.2 (m), 1028.4 (m), 888.1 (m), 755.2 (m), 699.0 (s), 556.4 (m) cm^{-1}. HRMS-(DART) for: $C_{16}H_{21}$ $[M+H-H_2O]^+$: calculated: 213.1643, found: 213.1641. $[\alpha]_D^{20}$ = +44.267 (c = 2.140, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

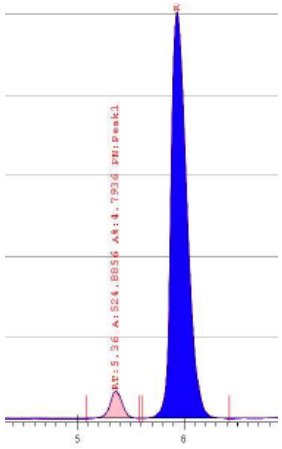
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-cyclohexyl-1-phenylbut-3-en-1-ol

Racemic Material

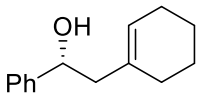


Peak No	% Area	Area	RT (min)
1	50.0769	284.402	5.34
2	49.9231	283.5282	5.99
Total:	100	567.9302	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	4.7936	524.8856	5.36
2	95.2064	10424.8768	5.93
Total:	100	10949.7624	



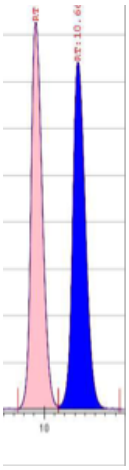
(R)*-2-(cyclohex-1-en-1-yl)-1-phenylethan-1-ol (15).** The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), cyclohex-1-en-1-yl trifluoromethanesulfonate (**S-18**) (76.0 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane) to afford a clear colorless oil (52.3 mg, 86% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39-7.34 (3H, m), 7.28-7.23 (1H, m), 5.60 (1H, s), 4.76 (1H, dd, J = 9.0, 4.2 Hz), 2.36 (1H, m), 2.30 (1H, dd, J = 18.8, 9.6 Hz), 2.17 (1H, s), 2.09-2.05 (3H, m), 1.94-1.92 (1H, m), 1.68-1.64 (2H, m), 1.61-1.57 (2H, m). ^{13}C NMR (125 MHz, CDC_3) δ 144.5, 134.6, 128.5, 127.4, 125.9, 125.9, 71.4, 49.1, 28.4, 25.5, 23.0, 22.4. IR (neat) ν_{max} 3406.1 (br), 3028.27 (m), 2922.0 (s), 2922.5 (s), 2855.4 (s), 2833.9 (s), 1493.2 (s) 1451.1 (m), 1050.2 (m), 1006.6 (s), 753.4 (m), 699.0 (s), 547.2 (s) cm^{-1}. HRMS-(DART) for: $C_{14}H_{17}$ $[M+H-H_2O]^+$: calculated: 185.1330, found: 185.1329. $[\alpha]_D^{20}$: +72.35 (c = 0.74, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

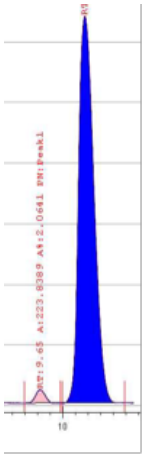
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(cyclohex-1-en-1-yl)-1-phenylethan-1-ol.

Racemic Material

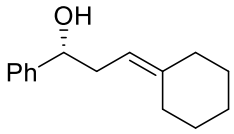


Peak Info			
Peak No	% Area	Area	RT (min)
1	49.6784	6384.9152	9.83
2	50.3216	6467.5726	10.66
Total:	100	12852.4878	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	2.0641	223.8389	9.65
2	97.9359	10620.284	10.35
Total:	100	10844.1229	



(R)*-3-cyclohexylidene-1-phenylpropan-1-ol (16).** The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), cyclohexylidenemethyl trifluoromethanesulfonate (**S-16**) (80.6 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.67 mg, 0.003 mmol, 0.01 equiv.), and (S_p, S_p)-**L1** (3.8 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel column chromatography (3 % ethyl acetate in hexane) to afford a colorless oil (48.5 mg, 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36-7.31 (4H, m), 7.26-7.23 (1H, m), 5.01 (1H, t, J = 7.8 Hz), 4.65 (1H, ddd, *J* = 7.8, 4.8, 3.0 Hz), 2.48 (1H, ddd, *J* = 14.4, 7.8, 7.8 Hz), 2.41 (1H, ddd, *J*= 12.6, 6.0, 6.0 Hz), 2.11-2.07 (4H, m), 2.01 (1H, t, *J* = 3.0 Hz), 1.53-1.49 (4H, m), 1.44-1.36 (2H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.4,

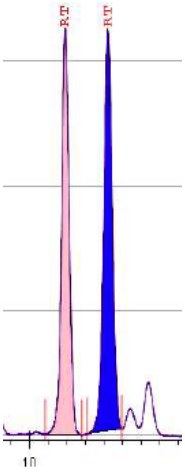
144.3, 128.5, 127.5, 126.1, 116.4, 74.2, 37.5, 29.1, 28.8, 28.0, 27.0; IR (neat) ν_{max} 3343.5 (br), 2923.4 (s), 2851.6 (m), 1494.2 (m), 1447.4 (m), 1266.0 (m), 1232.4 (m), 1027.8 (m), 849.9 (m), 758.2 (m), 698.8 (s), 551.8 (m) cm^{-1}; HRMS-(DART) for: $C_{15}H_{19}$ $[M+H-H_2O]^+$: calculated: 199.1487, found: 199.1496. $[\alpha]_D^{20} = +41.066$ (*c* = 0.540, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

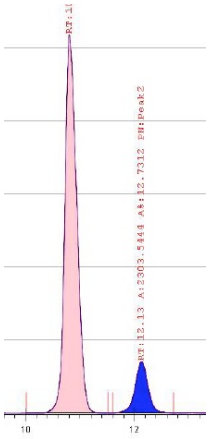
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-cyclohexylidene-1-phenylpropan-1-ol

Racemic Material

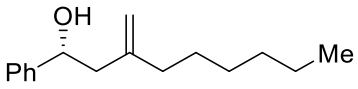


Peak No	% Area	Area	RT (min)
1	47.2345	4658.0381	10.96
2	52.7655	5203.4843	12.11
Total:	100	9861.5224	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	87.2688	15790.1342	10.8
2	12.7312	2303.5444	12.13
Total:	100	18093.6786	



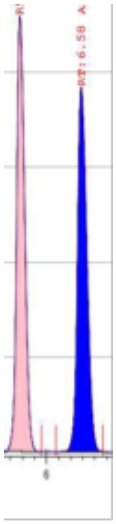
(R)*-3-methylene-1-phenylnonan-1-ol (17).** The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), oct-1-en-2-yl trifluoromethanesulfonate (**S-15**) (85.9 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane) to afford a clear colorless oil (60.0 mg, 86% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39-7.34 (4H, m), 7.29-7.26 (1H, m), 4.94 (1H, s), 4.91 (1H, s), 4.80 (1H, dd, *J* = 1.8, 9.6 Hz), 2.47 (1H, ddd, *J* = 13.8, 4.20 Hz), 2.40 (1H, ddd, *J* = 14.9, 9.6 Hz), 2.17 (1H, d, *J* = 1.8 Hz), 2.08 (1H, t, *J* = 7.8 Hz), 1.51-1.42 (2H, m), 1.34-1.26 (6H, m), 0.90 (3H, t, *J* = 6.6). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.7, 144.24, 128.5, 127.6, 125.9, 125.9, 112.9, 71.7, 46.9, 35.9, 31.9, 30.5, 29.2, 29.2, 27.8, 22.8, 14.2. IR (neat) ν_{max} 3383.7 (w), 2955.3 (s), 2924.0 (s), 2854.0 (s), 1493.7 (s), 1454.3 (m), 1041.5 (m), 968.8 (s), 755.9 (s), 699.1 (s) cm^{-1}. HRMS-(DART) for: $C_{16}H_{23}$ $[M+H-H_2O]^+$: calculated: 215.1800, found: 215.1801. $[\alpha]_D^{20}$: +36.69 (c = 1.23, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

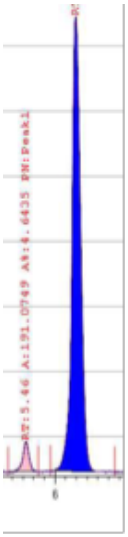
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-methylene-1-phenylnonan-1-ol.

Racemic Material

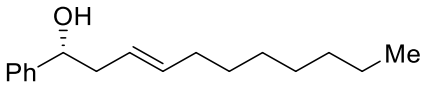


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.4307	4230.6695	5.56
2	49.5693	4158.4116	6.58
Total:	100	8389.0811	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	4.6435	191.0749	5.46
2	95.3565	3923.7903	6.39
Total:	100	4114.8652	



(R,E)*-1-phenylundec-3-en-1-ol (18).** The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), (E)-non-1-en-1-yl trifluoromethanesulfonate (**S-14**) (90.5 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane) to afford a clear colorless oil (39.9 mg, 54% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35-7.345 (4H, m), 7.28-7.26 (1H, m), 5.58 (1H, ddd, J = 14.4, 6.6 Hz), 5.40 (1H, ddd, J = 15.6, 7.2 Hz), 4.69-4.67 (1H, m), 2.47 (1H, ddd, J = 10.8, 5.4 Hz), 2.41 (1H, ddd, J = 14.4, 7.8 Hz), 2.07 (1H, s), 2.02

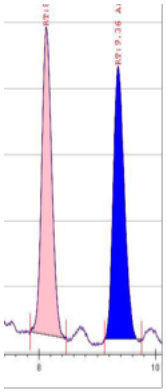
(2H, q, J = 7.2 Hz), 1.37-1.21 (10H, m), 0.89 (3H, t, J = 7.2 Hz,). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.2, 135.5, 128.5, 127.5, 126.0, 125.5, 73.6, 43.0, 32.8, 33.0, 29.6, 29.3, 29.3, 14.3. IR (neat) ν_{max} 3389.8 (w), 3065.9 (s), 3029.0 (s), 2925.9 (s), 2855.9 (s), 1643.6 (s), 1453.3 (m), 1049.7 (m), 889.7 (s), 698.0 (s) cm^{-1}. HRMS-(DART) for: $C_{17}H_{25}$ $[M+H-H_2O]^+$: calculated: 229.1956, found: 229.1953. $[\alpha]_D^{20}$: +26.66 (c = 0.36, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1, 3**, and **4**).

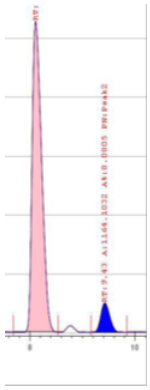
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R,E)-1-phenylundec-3-en-1-ol.

Racemic Material

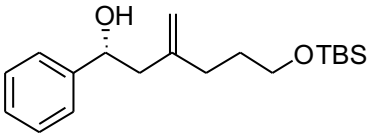


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.3629	557.0803	8.12
2	49.6371	549.0516	9.36
Total:	100	1106.1319	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	91.9195	13242.1375	8.11
2	8.0805	1164.1032	9.43
Total:	100	14406.2407	



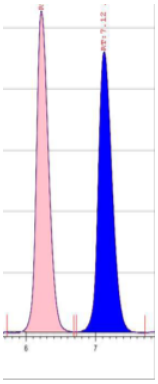
(R)*-6-(*tert*-butyldimethylsilyloxy)-3-methylene-1-phenylhexan-1-ol (19).** The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-2-yl trifluoromethanesulfonate (**S-19**) (115.0 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (3% ethyl acetate in hexanes) to afford a clear colorless oil (43.3 mg, 45% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39-7.31 (4H, m), 7.28-7.22 (1H, m), 4.95 (1H, s), 4.92 (1H, s), 4.81 (1H, dd, J = 9.5, 4.1 Hz), 3.63 (2H, t, J = 6.4), 2.37 (1H, dd, J = 14.1, 4.0 Hz), 2.41 (1H, dd, J = 14.1, 9.5 Hz), 2.16-2.12 (3H, m), 1.74-1.64 (2H, m), 0.90 (9H, s), 0.05 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.2, 144.2, 128.6, 127.6, 125.9, 113.1, 71.7, 62.8, 47.1, 32.1, 31.0, 47.1, 32.1, 31.0, 26.1, 18.52, -5.1. IR (neat) ν_{max} 3438.3(br), 2952.8 (s), 2929.3 (s), 2886.0 (m), 2856.5 (s), 1644.4 (s), 1492.5 (m), 1454.1 (s), 1254.3 (s), 1101.3 (s), 835.4 (s), 775.2 (s), 699.2 (s) cm^{-1}.HRMS-(DART) for: $C_{19}H_{31}O_1Si_1$ $[M+H-H_2O]^+$: calculated: 303.2144, found: 303.2154. $[\alpha]_D^{20}$: +22.00 (c = 0.26, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

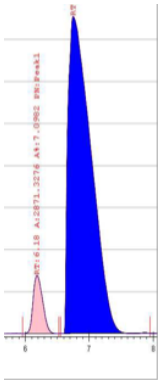
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 6-((tert-butyldimethylsilyl)oxy)-3-methylene-1-phenylhexan-1-ol.

Racemic Material

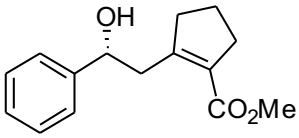


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.0691	3171.9339	6.22
2	49.9309	3163.182	7.12
Total:	100	6335.1159	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	7.0982	2871.3276	6.18
2	92.9018	37580.4402	6.75
Total:	100	40451.7678	



(*R*)-methyl 2-(2-hydroxy-2-phenylethyl)cyclopent-1-enecarboxylate (20). The reaction was performed according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 5-hydroxypent-1-en-2-yl trifluoromethanesulfonate (**S-20**) (90.5 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). Oxidation was performed at pH 7 over 24 hours. A phosphate buffer solution was used instead of 3M NaOH solution. The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in Hexanes) to afford a clear colorless oil (39.9 mg, 54% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (2H, d, J = 12 Hz), 7.34 (2H, t, J = 6.0 Hz,7.27-7.24 (1H, m), 4.91 (1H, m), 3.75 (3H, s), 3.11 (1H, dd, J = 13.2, 3.9 Hz), 2.79 (1H, dd, J= 13.3, 3.9 Hz), 2.66-2.62 (2H, m), 2.54-2.48 (1H, m), 2.32-2.25 (1H, m) 1.81 (2H, q, J = 7.6 Hz). ^{13}C NMR (125 MHz,

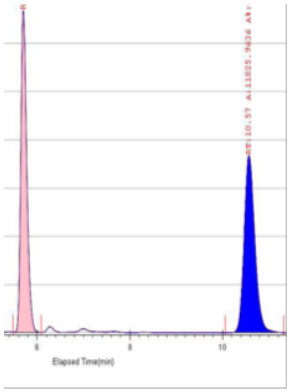
$CDCl_3$) δ 168.0, 157.0, 145.0, 130.3, 128.4, 127.4, 125.6, 125.6, 73.32, 51.6, 40.37, 39.36, 33.60, 21.74. IR (neat) ν_{max} 3451.0 (br), 2952.0 (s), 2924.9 (s), 2854.8 (s), 1705.3 (s), 1636.0 (s), 1434.7 (m), 1266.5 (m), 1198.3 (s), 1116.4 (s), 1054.1 (s), 768.6 (s), 701.9 (s) cm^{-1}. HRMS-(DART) for: $C_{15}H_{17}O_2$ $[M+H-H_2O]^+$: calculated: 229.1230, found: 229.1229. $[\alpha]_D^{20}$: +73.65 (c = 0.68, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

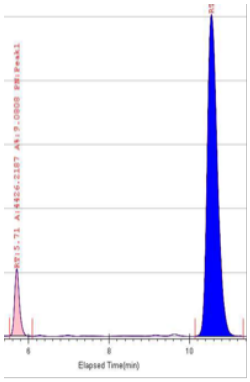
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – Methyl (R)-2-(2-hydroxy-2-phenylethyl)cyclopent-1-ene-1-carboxylate.

Racemic Material

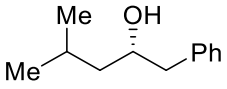


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.236	11938.1215	5.7
2	49.764	11825.9636	10.57
Total:	100	23764.0851	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	9.0808	4426.2187	5.71
2	90.9192	44316.2386	10.55
Total:	100	48742.4573	



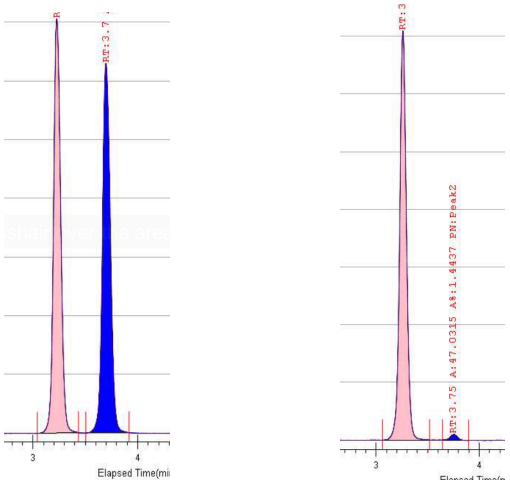
***(S)*-4-methyl-1-phenylpentan-2-ol (21).** The reaction was performed according to the general procedure **(*Method B*)** with 2-isobutyl-5,5-dimethyl-1,3,2-dioxaborinane (**S-12**) (51.0 mg, 0.30 mmol), vinylllithium (0.211 mL, 1.42M in diethyl ether, 0.30 mmol), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol), palladium (II) acetate (1.34 mg, 0.006 mmol), (S_p, S_p)-**L1** (7.60 mg, 0.0072 mmol) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in hexanes) to afford a clear oil. (31.6 mg, 59% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (2H, t, *J* = 7.2 Hz), 7.20-7.24 (3H, m), 3.87-3.89 (1H, m), 2.80 (1H, dd, *J* = 13.2, 3.6 Hz), 2.61 (1H, dd, *J* = 13.2, 8.4 Hz), 1.78-1.85 (1H, m), 1.41-1.48 (2H, m), 1.27-1.31 (1H, m), 0.93 (3H, d, *J* = 6.6 Hz), 0.90 (3H, d, *J* = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.8, 129.6, 128.7, 126.6, 70.9, 46.2, 44.8, 24.8, 23.6, 22.2; IR (neat) ν_{max} 3387 (br), 3027 (w), 2953 (m), 2921 (m), 2868 (w), 2362 (w), 1512 (w), 1466 (m), 1346 (w), 1136 (w), 1078 (m), 1019 (m), 743 (s), 697 (s), 603 (w) cm^{-1}; HRMS-(DART) for $C_{12}H_{17}$ $[M+H-H_2O]^+$: calculated: 161.1330, found: 161.1337. $[\alpha]^{20}_D$ = +4.736 (c = 0.285, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry

Racemic compound was prepared according to the general procedure ***(Method B)*** with $Pd(OAc)_2$ (5 mol%) and 1,1'-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

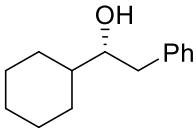
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (*S*)-*4-methyl-1-phenylpentan-2-ol.*

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	50.2125	6624.2856	3.23
2	49.7875	6568.2136	3.7
Total:	100	13192.4992	

Peak No	% Area	Area	RT (min)
1	98.5563	3210.702	3.26
2	1.4437	47.0315	3.75
Total:	100	3257.7335	



(R)*-1-cyclohexyl-2-phenylethan-1-ol (22).** The reaction was performed according to the general procedure (Method B***) with 2-cyclohexyl-5,5-dimethyl-1,3,2-dioxaborinane (S-11) (58.8 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv.), (S_p, S_p)-**L1** (7.60 mg, 0.0072 mmol,0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (5% ethyl acetate in hexanes, stain in CAM) to afford a white solid (49.2 mg, 80% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31-7.28 (2H, m), 7.23-7.18 (3H, m), 3.57 (1H, ddd, J = 9.6, 6.0, 3.6 Hz), 2.87 (1H, dd, J = 13.2, 3.0 Hz), 2.58 (1H, dd, J = 13.2, 9.0 Hz), 1.92-1.88 (1H, m), 1.80-1.62 (3H, m), 1.70-1.64 (1H, m), 1.44-1.38 (2H, m), 1.28-1.04 (5H, m). ^{13}C NMR (150

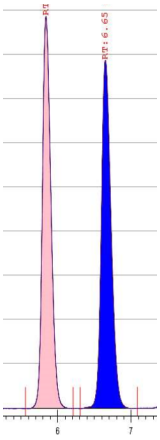
MHz, $CDCl_3$) δ 139.39, 129.53, 128.72, 126.51, 76.95, 43.35, 40.95, 29.49, 28.16, 26.71, 26.47, 26.33. IR (neat) ν_{max} 3327.3 (br), 3024.8 (w), 2923.1 (s), 2852.3 (m), 1493.7 (w), 1444.5 (w), 1401.3 (m), 1085.0 (w), 1059.6 (m), 1001.9 (m), 749.5 (s), 698.2 (s) cm^{-1}. HRMS (DART) for $C_{14}H_{24}NO$ $[M+NH_4]^+$ calculated: 222.1858, found: 222.1858. $[\alpha]^{20}_D$: +23.326 (c = 1.445, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

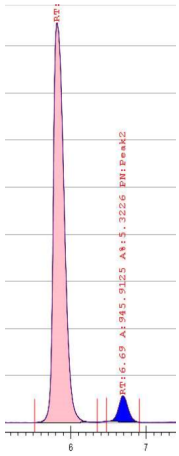
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-cyclohexyl-2-phenylethan-1-ol.

Racemic Material

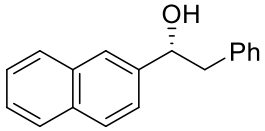


Peak No	% Area	Area	RT (min)
1	49.9353	7108.9938	5.84
2	50.0647	7127.4132	6.65
Total:	100	14236.407	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	94.6774	16825.8605	5.81
2	5.3226	945.9125	6.69
Total:	100	17771.773	



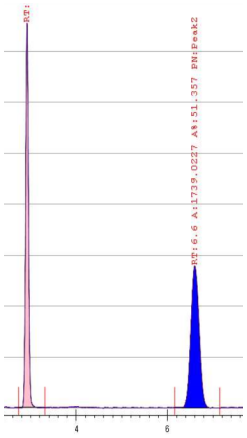
(R)*-1-(naphthalen-2-yl)-2-phenylethan-1-ol (23).** The reaction was performed according to the general procedure (Method B***) with 5,5-dimethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborinane (**S-9**) (72.0 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv.), (S_p, S_p)-**L1** (7.60 mg, 0.0072 mmol,0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford a white solid (69.0 mg, 93% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ7.84-7.78 (4H, m), 7.51-7.45 (3H, m), 7.29 (2H, t, J = 7.2 Hz), 7.23-7.20 (3H, m), 5.06 (1H, dd, J = 7.8, 4.2 Hz), 3.13 (1H, dd, J = 13.2, 4.8 Hz). 3.06 (1H, dd, J = 14.4, 9.0 Hz), 2.04 (1H, br s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.38, 138.14, 133.47, 133.19, 129.72, 128.75, 128.38, 128.16, 127.87. 126.86, 126.31, 126.03, 124.79, 124.28, 75.63, 46.21. IR (neat) ν_{max} 3529.1 (br), 3461.9 (br), 3057.9 (w), 3025.9 (w), 2914.8 (w), 1601.1 (w), 1494.2 (w). 1360.6 (w), 1077.5 (w), 1043.3 (m), 893.2 (m), 818.4 (s), 743.5 (s), 727.6 (s), 698.7 (s), 481.6 (s) cm^{-1}. HRMS (DART) for $C_{18}H_{15}$ $[M+H-H_2O]^+$ calculated: 231.1174, found: 231.1170. $[\alpha]^{20}_D$: -2.515 (c = 1.340, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

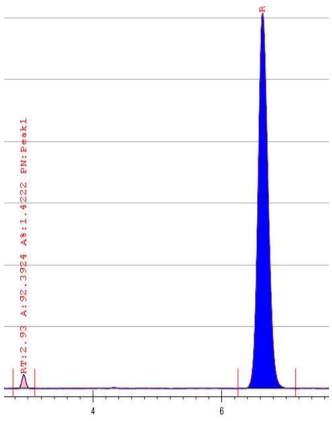
Chiral SFC (Chiracel ODR-H, 15% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-(naphthalen-2-yl)-2-phenylethan-1-ol.

Racemic Material

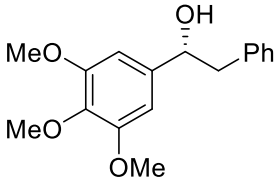


Peak No	% Area	Area	RT (min)
1	48.643	1647.1222	2.92
2	51.357	1739.0227	6.6
Total:	100	3386.1449	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	1.4222	92.3924	2.93
2	98.5778	6404.1044	6.63
Total:	100	6496.4968	



(R)*-2-phenyl-1-(3,4,5-trimethoxyphenyl)ethan-1-ol (24).** The reaction was performed according to the general procedure ***(Method B) with 2-(3,4,5-trimethoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**S-13**) (84.0 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv.), L1 (7.60 mg, 0.0072 mmol, 0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford a white solid (66.70 mg, 77% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31-7.28 (2H, m), 7.24-7.21 (1H, m), 7.20-7.17 (2H, m), 6.54 (2H, s), 4.82 (1H, t, J = 6.6 Hz), 3.82

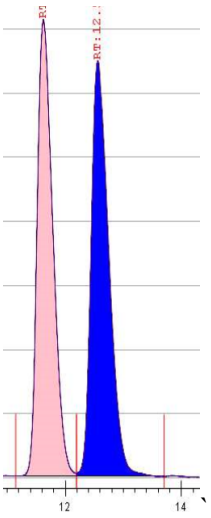
(9H, s), 3.00 (1H, dd, J = 13.2, 5.4 Hz), 2.96 (1H, dd, J = 13.8, 8.4 Hz), 1.94 (1H, d, J = 1.8 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.32, 139.66, 138.05, 137.38, 129.67, 128.65, 126.80, 102.91, 75.63, 60.99, 56.23, 46.26. IR (neat) ν_{max} 3462.0 (br), 2939.3 (w), 2836.6 (w), 1592.2 (m), 1506.7 (m), 1456.5 (m), 1326.3 (m), 1233.5 (m), 1125.3 (s), 1007.6 (s), 701.3 (w) cm^{-1}. HRMS (DART) for $C_{17}H_{19}O_3$ $[M+H-H_2O]^+$ calculated: 271.1334, found: 271.1327. $[\alpha]^{20}_D$: -1.373 (c = 0.510, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

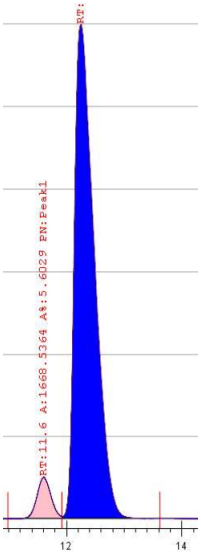
Chiral SFC (Chiracel ODR-H, 6% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-phenyl-1-(3,4,5-trimethoxyphenyl)ethan-1-ol.

Racemic Material

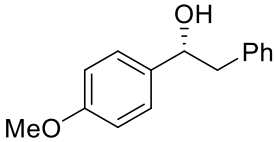


Peak No	% Area	Area	RT (min)
1	49.3717	13286.3101	11.62
2	50.6283	13624.4834	12.56
Total:	100	26910.7935	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	5.6029	1668.5364	11.6
2	94.3971	28111.3344	12.25
Total:	100	29779.8708	



***(R)*-1-(4-methoxyphenyl)-2-phenylethan-1-ol (25).** The reaction was performed according to the general procedure *(**Method B**)* with 2-(4-

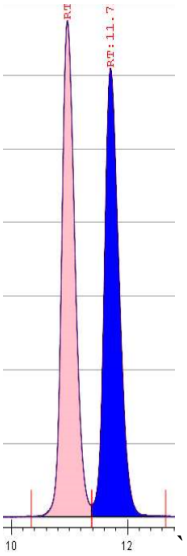
methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**S-4**) (66.0 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv.), (S_p, S_p)-**L1** (7.60 mg, 0.0072 mmol, 0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in pentane, stain in CAM) to afford a white solid (59.60 mg, 87% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31-7.24 (4H, m), 7.23-7.21 (1H, m), 7.17 (2H, d, J = 6.6 Hz), 6.87 (2H, d, J = 9.0 Hz), 4.84 (1H, t, 6.6 Hz), 3.80 (3H, s), 3.02-2.96 (2H, m), 1.92 (1H, br s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.21, 138.29, 136.14, 129.63, 128.60, 127.29, 126.68, 113.91, 75.11, 55.42, 46.15. IR (neat) ν_{max} 3389.0 (br), 3002.2 (w), 2918.0 (w), 2835.9 (w), 1611.4 (m), 1512.2 (s), 1454.2 (w), 1302.3 (w), 1246.0 (s), 1157.1 (m), 1032.9 (m). 831.9 (m), 699.4 (m) cm^{-1}. HRMS (DART) for $C_{15}H_{15}O$ $[M+H-H_2O]^+$ calculated: 211.1123, found: 211.1123. $[\alpha]^{20}_D$: -2.0386 (c = 1.275, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

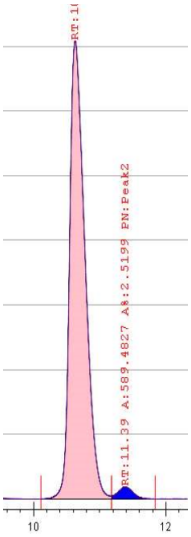
Chiral SFC (Chiracel OD-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(4-methoxyphenyl)-2-phenylethan-1-ol.

Racemic Material

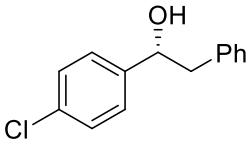


Peak No	% Area	Area	RT (min)
1	49.8119	10639.7812	10.97
2	50.1881	10720.1395	11.71
Total:	100	21359.9207	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	97.4801	22803.3883	10.63
2	2.5199	589.4827	11.39
Total:	100	23392.871	



(R)*-1-(4-chlorophenyl)-2-phenylethan-1-ol (27).** The reaction was performed according to the general procedure ***(Method B) with 2-(4-chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**S-5**) (67.30 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.176 mL, 1.72 M in Et_2O, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv.), (S_p, S_p)-**L1** (7.60 mg, 0.0072 mmol, 0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane, stain in CAM) to afford a clear oil (46.40 mg, 66% yield). ^{1}H NMR (600 MHz, $CDCl_3$)

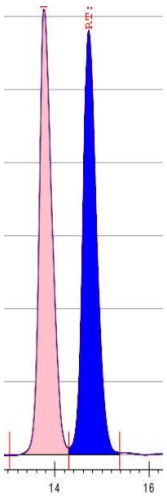
δ 7.30-7.20 (7H, m), 7.13 (2H, d, 6.0 Hz), 4.84 (1H, ddd, *J* = 8.4, 5.4, 3.0 Hz), 2.97 (1H, dd, *J* = 13.8, 4.8 Hz), 2.92 (1H, dd, *J* = 13.8, 8.4 Hz), 1.95 (1H, d, 2.4 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.34, 137.65, 133.36, 129.64, 128.73, 128.65, 127.43, 126.91, 74.78, 46.24. IR (neat) ν_{max} 3389.5 (br), 3085.1 (w), 3062.2 (w), 3027.9 (w), 2851.4 (w), 1600.0 (w), 1492.5 (m), 1453.6 (w), 1089.4 (m), 1013.2 (m), 827.6 (m), 745.7 (m). 699.7 (s), 544.76 (s) cm^{-1}. HRMS (DART) for $C_{14}H_{12}Cl$ $[M+H-H_2O]^+$ calcualted: 215.0628, found: 215.0636. $[\alpha]^{20}_D$: -8.716 (c = 1.845, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

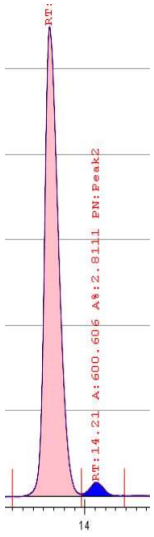
Chiral SFC (Chiracel OD-H, 6% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-(4-chlorophenyl)-2-phenylethan-1-ol.

Racemic Material

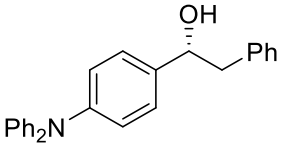


Peak No	% Area	Area	RT (min)
1	49.0709	11621.9899	13.76
2	50.9291	12062.0942	14.72
Total:	100	23684.0841	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	97.1889	20764.8334	13.31
2	2.8111	600.606	14.21
Total:	100	21365.4394	



(R)*-1-(4-(diphenylamino)phenyl)-2-phenylethan-1-ol (28).** The reaction was performed according to the general procedure (Method B***) with 4-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-N,N-diphenylaniline (**S-10**) (107.18 mg, 0.30 mmol, 1.00 equiv), vinyl lithium (0.176 mL, 1.72 M in Et_2O, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (75.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (1.30 mg, 0.006 mmol, 0.02 equiv.), (S_p, S_p)-**L1** (7.60 mg, 0.0072 mmol, 0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in hexanes) to afford a white solid (81.0 mg, 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33-7.31 (2H, m), 7.26-7.22 (10H, m), 7.09-7.06 (5H, m), 7.02-7.00 (2H, m), 4.87-4.84 (1H, m), 3.06 (1H, dd, J = 13.6, 4.6 Hz), 3.01 (1H, dd, J = 13.6, 8.8 Hz), 1.91 (1H, s). ^{13}C NMR (150 MHz,

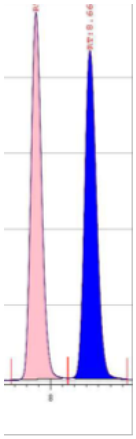
$CDCl_3$) δ 147.9, 147.4, 138.3, 138.1, 129.7, 129.4, 128.7, 127.0, 126.8, 124.3, 124.3, 124.2, 122.9, 75.2, 46.1. IR (neat) ν_{max} 3383.1 (br), 3061.3 (m), 2922.1 (w), 2854.4(w), 1589.0 (s), 1508.9 (s), 1314.1 (m), 1277.3 (s), 752.2 (s), 696.0 (s) cm^{-1}. HRMS-(DART) for: $C_{26}H_{22N}N_1$ $[M+H-H_2O]^+$: calculated: 348.1752, found: 348.1763. $[\alpha]_D^{20}$: -7.79 (c =0 .43, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

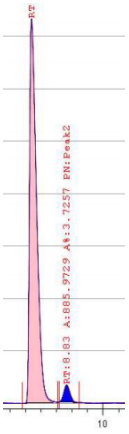
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(4-(diphenylamino)phenyl)-2-phenylethan-1-ol.

Racemic Material

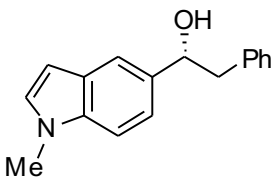


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.0189	6007.4743	7.75
2	49.9811	6002.9239	8.66
Total:	100	12010.3982	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	96.2743	22893.8564	7.7
2	3.7257	885.9729	8.83
Total:	100	23779.8293	



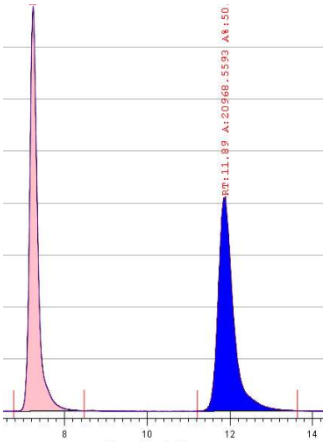
(R)*-1-(1-methyl-1H-indol-5-yl)-2-phenylethanol (29).** The reaction was performed according to the general procedure (Method B***) with 5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1-methyl-1*H*-indole (**S-14**) (75.20 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv.), (S_p, S_p)-**L1** (7.60 mg, 0.0072 mmol, 0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford a white solid (64.8 mg, 86% yield). 1H NMR (500 MHz, $CDCl_3$) δ 7.61 (1H, s), 7.630-7.21 (7H, m), 7.04 (1H, d, J = 3.0 Hz), 6.45 (1H, d, J = 3.0 Hz), 4.99 (1H, t, J = 7.0 Hz), 3.78 (3H, s), 3.09 (2H, d, J = 7.0 Hz), 1.93 (1H, br s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.83, 136.45, 135.12, 129.62, 129.38, 128,49, 128.48, 126.47, 119.99, 118.41, 109.30, 101.15, 76.21, 46.42, 32.97 IR (neat) ν_{max} 2960.4 (w), 3383.6 (w), 3025.8 (w), 2919.9 (w), 1512.4 (m), 1451.7 (w), 1244.5 (w), 1030.9 (w), 721.5 (s), 699.7 (s) cm^{-1} . HRMS-(DART) for $C_{12}H_{18}NO$ $[M+H]^+$ calculated: 252.1379 found: 252.13884. $[\alpha]_D^{20}$: -10.328 (c = 2.08, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

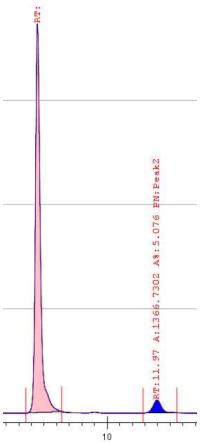
Chiral SFC (Chiracel OJ-H, 30% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(1-methyl-1H-indol-5-yl)-2-phenylethanol.

Racemic Material

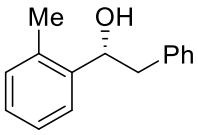


Peak No	% Area	Area	RT (min)
1	49.8909	20877.2269	7.23
2	50.1091	20968.5593	11.89
Total:	100	41845.7862	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	94.924	25558.6592	7.23
2	5.076	1366.7302	11.97
Total:	100	26925.3894	



***(R)*-2-phenyl-1-(o-tolyl)ethan-1-ol (30).** The reaction was performed according to the general procedure *(**Method B**)* with 5,5-dimethyl-2-(o-tolyl)-1,3,2-dioxaborinane (**S-6**). (61.20 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.176 mL, 1.72 M in Et_2O, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.010 equiv.), (S_p, S_p)-**L1** (7.60 mg, 0.0072 mmol, 0.012 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel

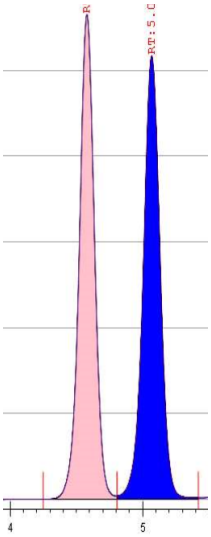
chromatography (2% ethyl acetate in pentane, stain in CAM) to afford a white solid (57.6 mg, 90% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 (1H, d, *J* = 7.8 Hz), 7.36 (2H, t, *J* = 6.6 Hz), 7.33-7.24 (5H, m), 7.18 (1H, d, *J*= 7.2 Hz), 5.17 (1H, ddd, *J* = 5.4, 3.6, 1.8 Hz), 3.06 (1H, dd, *J* = 14.4, 4.8 Hz), 2.97 (1H, dd, *J* = 13.8, 9.0 Hz), 2.33 (3H, s), 1.96 (1H, br s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.17, 138.49, 134.49, 130.41, 129.58, 128.66, 127.43, 126.74, 126.48, 125.37, 71.85, 45.15, 19.12. IR (neat) ν_{max} 3384.9 (br), 3061.3 (w), 2920.4 (w), 2859.95 (w), 1603.1 (w), 1494.1 (m), 1454.0 (m), 1076.0 (m), 1038.8 (m), 755.1 (s). 738.2 (m), 698.4 (s) cm^{-1}. HRMS (DART) for $C_{15}H_{15}$ $[M+H-H_2O]^+$ calculated: 195.1174, found: 195.1181. $[\alpha]^{20}_D$: +30.812 (c = 1.760, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

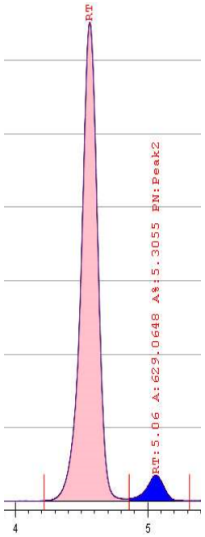
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-2-phenyl-1-(o-tolyl)ethan-1-ol.

Racemic Material

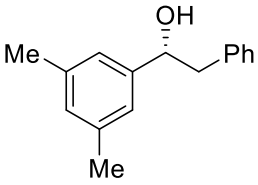


Peak No	% Area	Area	RT (min)
1	49.4517	8989.9843	4.58
2	50.5483	9189.3254	5.07
Total:	100	18179.3097	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	94.6945	11227.6762	4.56
2	5.3055	629.0648	5.06
Total:	100	11856.741	



***(R)*-1-(3,5-dimethylphenyl)-2-phenylethan-1-ol (31).** The reaction was performed according to the general procedure **(*Method B*)** with 2-(3,5-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (65.4 mg, 0.30 mmol) (**S-8**), vinylllithium (0.211 mL, 1.42M in diethyl ether, 0.30 mmol),

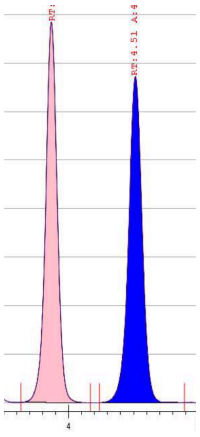
phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol), palladium (II) acetate (1.34 mg, 0.006 mmol), (S_p, S_p)-**L1** (7.60 mg, 0.0072 mmol) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in hexanes) to afford a clear oil. (45.4 mg, 67% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34 (2H, t, J = 7.2 Hz), 7.25-7.28 (3H, m,), 7.02 (2H, s), 6.96 (1H, s), 4.84 (1H, dd, J = 9.0, 4.2 Hz,), 3.05 (1H, dd, J = 14.4, 4.8 Hz,), 2.98 (1H, dd, J = 14.4, 9.6 Hz,), 2.36 (6H, s), 1.98 (1H, s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.0, 138.5, 138.1, 129.6, 129.3, 128.6, 126.7, 123.8, 75.5, 46.2, 21.4. IR (neat) ν_{max} 3404 (br), 3060 (w), 3026 (w), 2941 (m), 2859 (w), 2361 (w), 1603 (m), 1453 (m), 1180 (w), 1051 (m), 849 (s), 748 (m), 698 (s), 507 (m) cm^{-1}; HRMS-(DART): for $C_{16}H_{17}$ $[M+H-H_2O]^+$: calculate: 209.1330, found: 209.1320. $[\alpha]^{20}_D$ = +10.24 (c = 2.835, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry

Racemic compound was prepared according to the general procedure ***(Method B)*** with $Pd(OAc)_2$ (5 mol%) and 1,1'-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

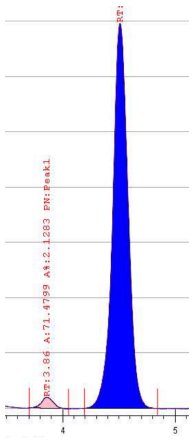
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (R)-1-(3,5-dimethylphenyl)-2-phenylethan-1-ol.

Racemic Material

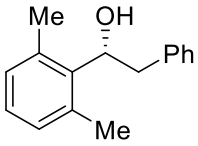


Peak No	% Area	Area	RT (min)
1	49.8529	4861.1049	3.87
2	50.1471	4889.7919	4.51
Total:	100	9750.8968	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	2.1283	71.4799	3.86
2	97.8717	3287.0332	4.51
Total:	100	3358.5131	



(R)*-1-(2,6-dimethylphenyl)-2-phenylethan-1-ol (32).** The reaction was performed according to the general procedure (Method B***) with 2-(2,6-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**S-7**) (65.4 mg, 0.30 mmol,

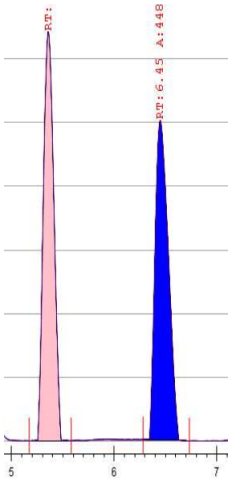
1.00 equiv.), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv.), (S_p, S_p)-**L1** (7.60 mg, 0.0072 mmol,0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in pentane, stain in CAM) to afford a white solid (50.50 mg, 74% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 (2H, t, J = 6.6 Hz), 7.26-7.20 (3H, m), 7.17 (1H, t, J = 7.2 Hz), 7.00 (2H, d, J = 7.8 Hz), 5.32 (1H, ddd, J = 7.8 4.8, 1.8 Hz). 3.22 (1H, dd, J = 13.8, 9.0 Hz), 3.01 (1H, dd, J = 13.8, 5.4 Hz), 2.43 (6H, s), 1.83 (1H, d, J = 2.4 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.90, 138.80, 136.24, 129.55, 129.52, 128.65, 127.30, 126.66, 72.00, 42.33, 20.96. IR (neat) ν_{max} 3549.2 (br), 3429.9 (br), 3062.1 (w), 3025.8 (w), 2925.0 (w), 2864.5 (w), 1601.8 (w), 1495.1 (m), 1468.0 (m), 1453.1 (w), 1045.3 (m) 769.9 (s), 752.6 (s), 700.0 (s) cm^{-1}. HRMS (DART) for $C_{16}H_{17}$ $[M+H-H_2O]^+$ calculated: 209.1330, found: 209.1323. $[\alpha]^{20}_D$: -6.573 (c = 1.660, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

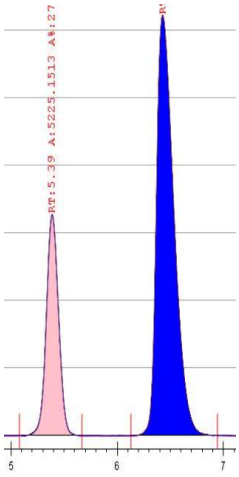
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-(2,6-dimethylphenyl)-2-phenylethan-1-ol.

Racemic Material



Peak No	% Area	Area	RT (min)
1	50.288	4540.9221	5.36
2	49.712	4488.9112	6.45
Total:	100	9029.8333	

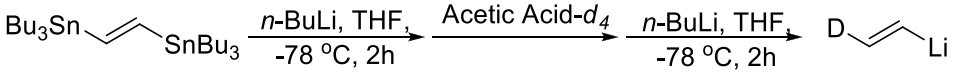
Standard Conditions



Peak No	% Area	Area	RT (min)
1	27.1761	5225.1513	5.39
2	72.8239	14001.8745	6.43
Total:	100	19227.0258	

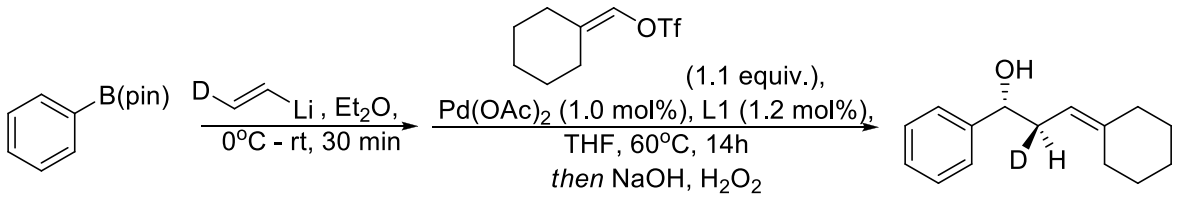
1.4.2.6. Deuterium-labeling Experiment

Procedure for the Preparation of trans-deuterium-labeled vinyl lithium



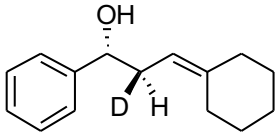
The *trans*-deuterium labeled vinyl lithium was prepared according to the literature procedure with modification (*27*). To an oven-dried 25 mL round bottom flask equipped with a magnetic stir bar in an Ar-filled glovebox was added bis(tributylstannyl)ethylene (1.818 g, 3.00 mmol, 1.0 equiv.), and THF (3 mL), sealed with a rubber septum, and removed from glovebox. The reaction flask was cooled to -78℃, and *n*-butyllithium (3.30 mmol, 1.1 equiv.) was added dropwise. The reaction flask was allowed to stir for additional 2 hours at -78℃. Then acetic acid-d_4 was added dropwise at -78℃. The reaction mixture was allowed to warm to room temperature and quenched with saturated sodium bicarbonate solution. The aqueous layer was extracted with hexanes (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered through a neutral alumina pad, and concentrated under reduced pressure. The result residue was used in next step without further purification. The resulting residue from last step was brought into an Ar-filled glovebox and transferred into an oven-dried 25 mL round bottom flask equipped with a magnetic stir bar, diluted with THF (3 mL), sealed with a rubber septum, and removed from glovebox. The reaction flask was cooled to -78℃, and *n*-butyllithium (3.00 mmol, 1.0 equiv.) was added dropwise. The reaction flask was allowed to stir for additional 2 hours at -78℃. Upon completion, the *trans*-deuterium labeled vinyl lithium solution was allowed to warm to room temperature, titrated with BHT and 1,10-phenanthroline in THF, and used in conjunctive cross coupling.

Procedure for the Conjunctive Cross Coupling with trans-deuterium-labeled Vinyl Lithium



To an oven-dried 2-dram vial equipped with a magnetic stirbar in an Ar-filled glovebox was added 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (61.2 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℃, and *trans*-deuterium labeled vinyl lithium solution (0.30 mmol, 1.0 equiv.) was added at 0℃. The reaction vial was allowed to warm to room temperature and stir for 30 minutes. Over this period, white solid formed. Pentane (2 mL) was added to the reaction mixture by syringe, and the white solid was allowed to settle down to the bottom of the vial. The clear supernatant was removed via syringe. The resulting white solid was suspended in pentane (3 mL), the white solid was allowed to settle down to the bottom of the vial, and the clear supernatant was removed via syringe. The pentane wash process was repeated three times. Then, the solvent was carefully removed under reduced pressure, and the reaction vial was brought back into the glovebox. To a separated oven-dried 2-dram vial equipped with a magnetic stirbar in the glovebox was charged with $Pd(OAc)_2$ (0.67 mg, 0.003 mmol, 0.01 equiv.), (S_p, S_p)-**L1** (3.80 mg, 0.0036 mmol, 0.012 equiv.) and THF (0.6 mL). The $Pd(OAc)_2$/(S_p, S_p)-**L1** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**L1** solution was transferred into the reaction vial, followed by THF (0.6 mL), and cyclohexylidenemethyl trifluoromethanesulfonate (**S-16**) (80.6 mg, 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℃ for 14 hours. The resulting mixture was cooled to room temperature, filtered through a silica gel plug with diethyl

ether, and concentrated under reduced pressure. The reaction mixture was diluted with THF (3 mL), cooled to 0°C and 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 at room temperature 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, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography (5% ethyl acetate in hexanes) to afford the desired product as a colorless oil (37.2 mg, 57% yield).



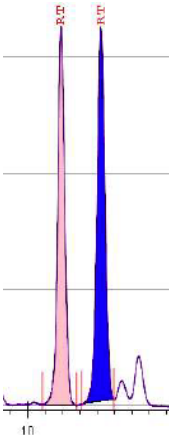
(1*R*,2*R*)-3-cyclohexylidene-1-phenylpropan-2-*d*-1-ol (34). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.31 (4H, m), 7.26-7.23 (1H, m), 5.09 (1H, d, *J* = 7.5 Hz), 4.64 (1H, d, *J* = 5.5 Hz), 2.46 (1H, t, *J* = 7.5 Hz), 2.13-2.05 (4H, m), 2.01 (1H, s), 1.52-1.46 (4H, m), 1.45-1.35 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 144.3, 128.5, 127.5, 126.1, 116.3, 74.2, 37.5, 29.1, 28.8, 28.0, 27.0; IR (neat) ν_{max} 3358.7 (br), 2923.1 (s), 2851.4 (m), 1493.1 (m), 1446.7 (m), 1343.0 (m), 1233.2 (m), 1025.2 (m), 849.3 (m), 755.9 (m), 697.7 (s), 546.8 (m) cm^{-1}; HRMS-(DART) for: $C_{15}H_{18}D_1$ $[M+H-H_2O]^+$: calculated: 200.1550, found: 200.1551. $[\alpha]_D^{20}$ = +40.061 (*c* = 0.640, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **1**, **3**, and **4**).

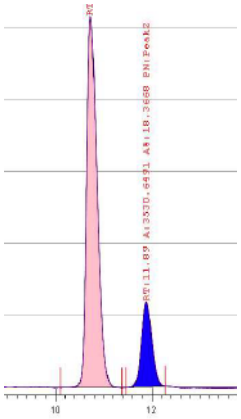
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R,2R)-3-cyclohexylidene-1-phenylpropan-2-d-1-ol

Racemic Material



Peak No	% Area	Area	RT (min)
1	47.2345	4658.0381	10.96
2	52.7655	5203.4843	12.11
Total:	100	9861.5224	

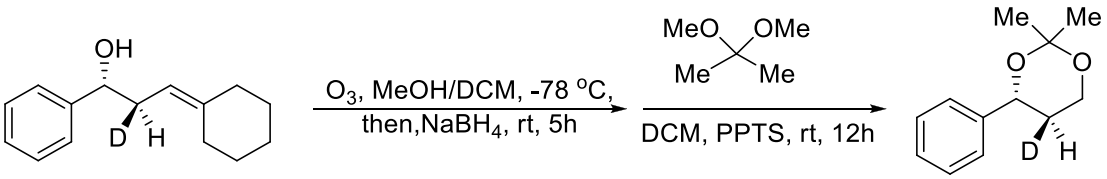
Standard Conditions



Peak No	% Area	Area	RT (min)
1	81.6332	15692.3394	10.72
2	18.3668	3530.6491	11.89
Total:	100	19222.9885	

Proof of Stereochemistry:

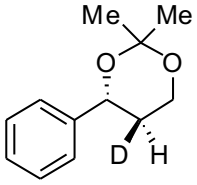
(1*R*,2*R*)-3-cyclohexylidene-1-phenylpropan-2-*d*-1-ol was ozonized, reduced, and cyclized as an acetonide by the sequence shown below. Relative stereochemistry was determined by measuring the coupling constants.



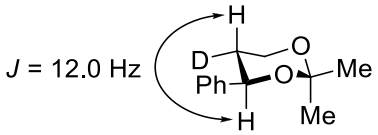
To an oven-dried 6-dram vial equipped with a magnetic stirbar was added (1*R*,2*R*)-3-cyclohexylidene-1-phenylpropan-2-d-1-ol (**34**) (38.2 mg, 0.18 mmol, 1.00 equiv.), dichloromethane (3.0 mL), and methanol (3.0 mL). The reaction mixture was cooled to -78°C, and O_3 was bubbled through the reaction mixture until the solution turned to blue. Then sodium

borohydride (200 mg, 5.3 mmol, 29.4 equiv.) was added, and the reaction mixture was allowed to warm to room temperature and stir for 5 hours. Upon completion, reaction mixture was quenched with water, the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography (30 % ethyl acetate in hexane) to afford (1*R*,2*R*)-1-phenylpropane-2-*d*-1,3-diol as a colorless oil (19.5 mg, 71% yield).

To an oven-dried 6-dram vial equipped with a magnetic stirbar was added (1*R*,2*R*)-1-phenylpropane-2-*d*-1,3-diol (19.5 mg, 0.13 mml, 1.00 equiv.), 2,2-dimethoxypropane (0.3 mL), and dichloromethane (2.0 mL). The reaction mixture was cooled to 0℃, and pyridinium *p*-toluenesulfonate (3.3 mg, 0.013 mmol, 0.10 equiv.) was added. The reaction mixture was allowed to warm to room temperature and stir for 12 hours. Upon completion, the reaction mixture was concentrated under reduced pressure, and subsequently purified via silica gel column chromatography (5 % ethyl acetate in hexane) to afford (4*R*,5*R*)-2,2-dimethyl-4-phenyl-1,3-dioxane-5-*d* as a colorless oil (20.6 mg, 82% yield).



(4*R*,5*R*)-2,2-dimethyl-4-phenyl-1,3-dioxane-5-*d* (S-30). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.32 (4H, m), 7.27-7.24 (1H, m), 4.91 (1H, d, *J* = 12.0 Hz), 4.13 (1H, t, *J* = 12.6 Hz), 3.91 (1H, dd, *J* = 11.4, 4.8 Hz), 1.88 (1H, dt, *J* = 12.6, 5.4 Hz), 2.01 (1H, s), 1.57 (3H, s), 1.49 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.6, 128.6, 127.8, 126.1, 99.0, 71.6, 60.3, 30.3, 19.4; IR (neat) ν_{max} 2992.2 (m), 2938.2 (m), 2866.1 (m), 1452.7 (m), 1378.4 (s), 1368.5 (s), 1223.1 (m), 1195.6 (s), 1163.6 (m), 949.2 (m), 886.8 (s), 698.4 (s), 520.8 (m) cm^{-1}; HRMS-(DART) for: $C_{12}H_{16}D_1O_2$ $[M+H]^+$: calculated: 194.1291, found: 194.1289.



anti-relative stereochemistry was determined
by measuring the coupling constant

1.4.3. References

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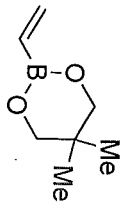
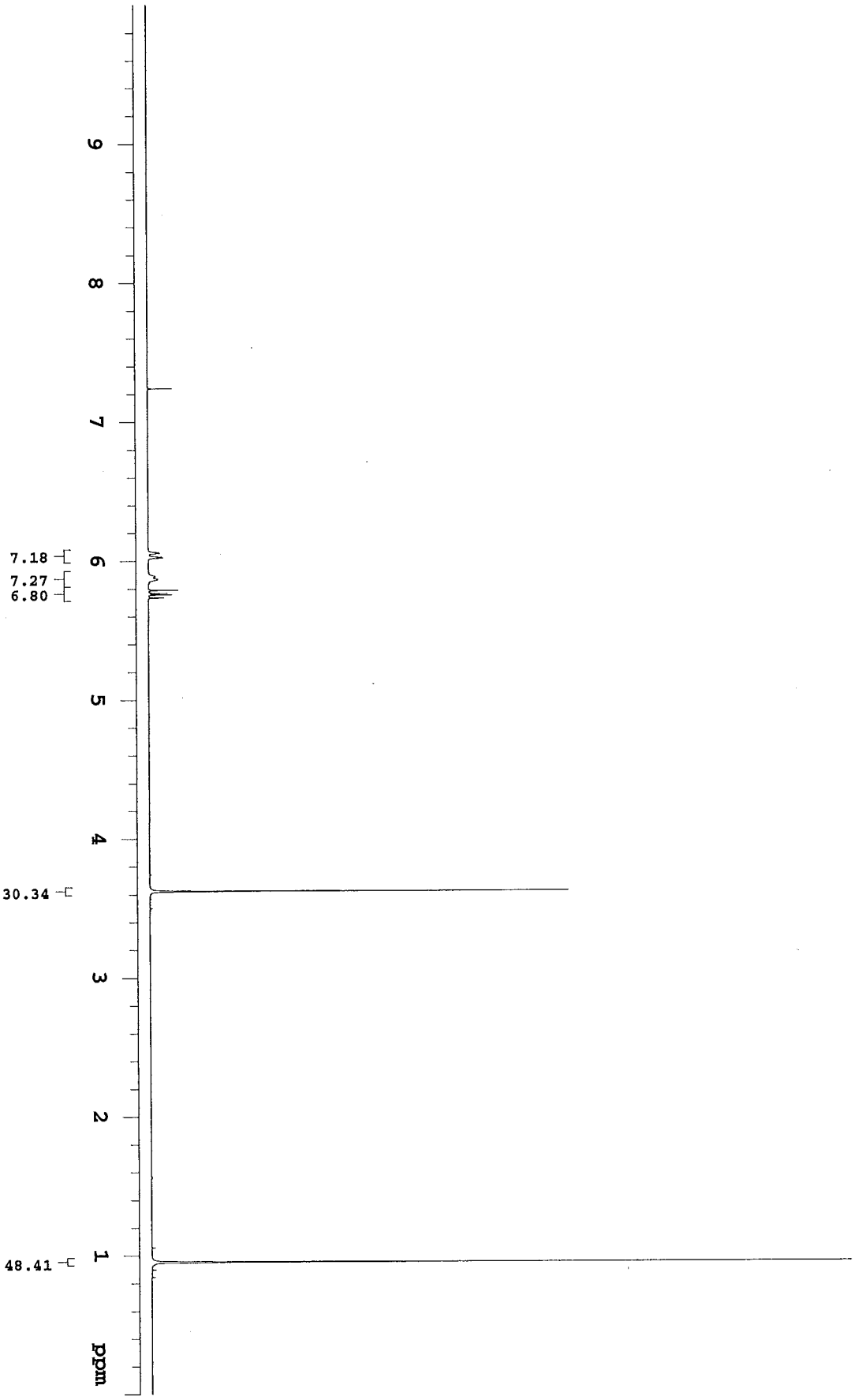
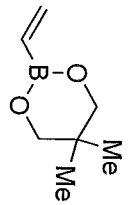
Compound **S-1**





Compound **S-1**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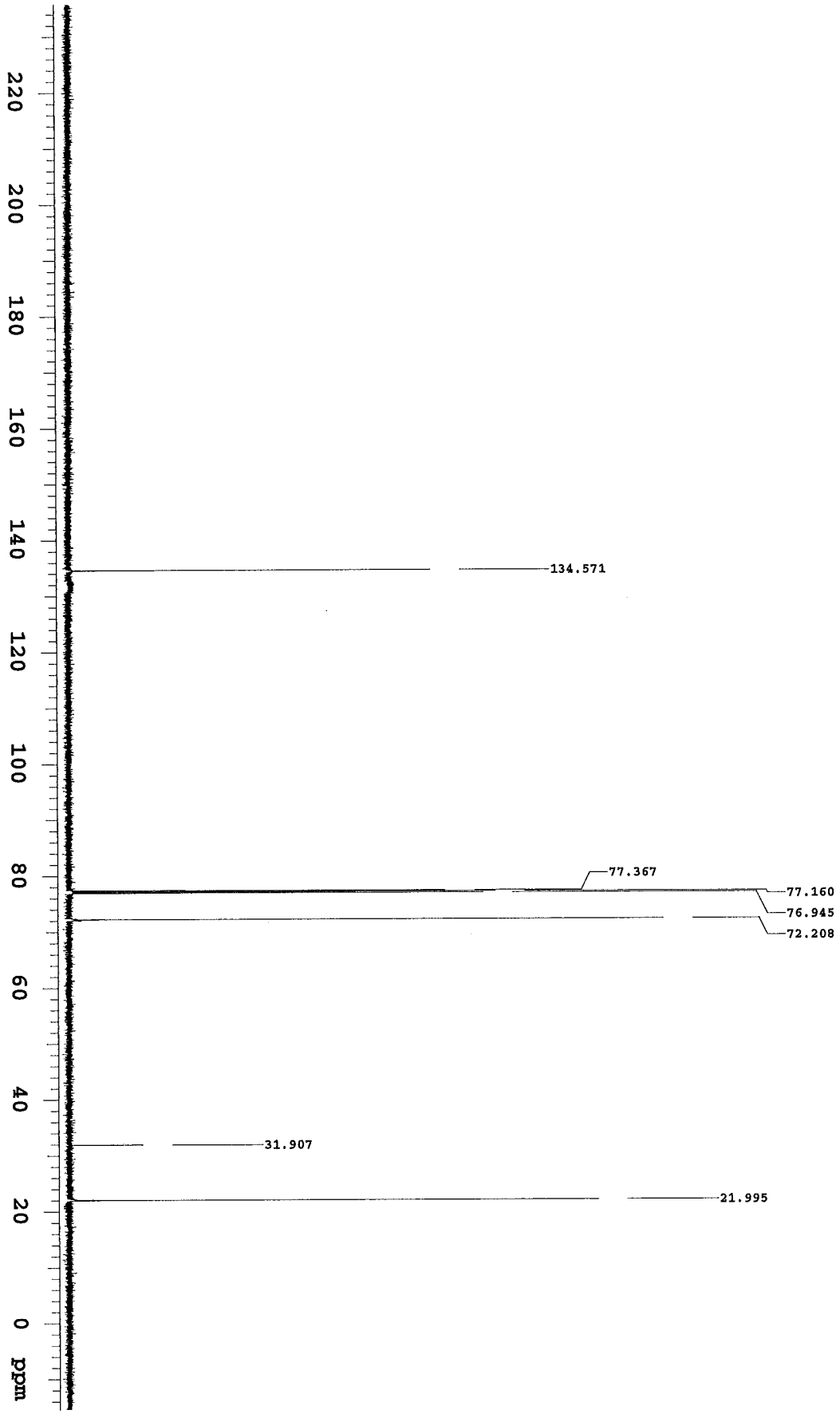
O
O
Me
Me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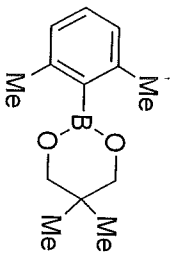

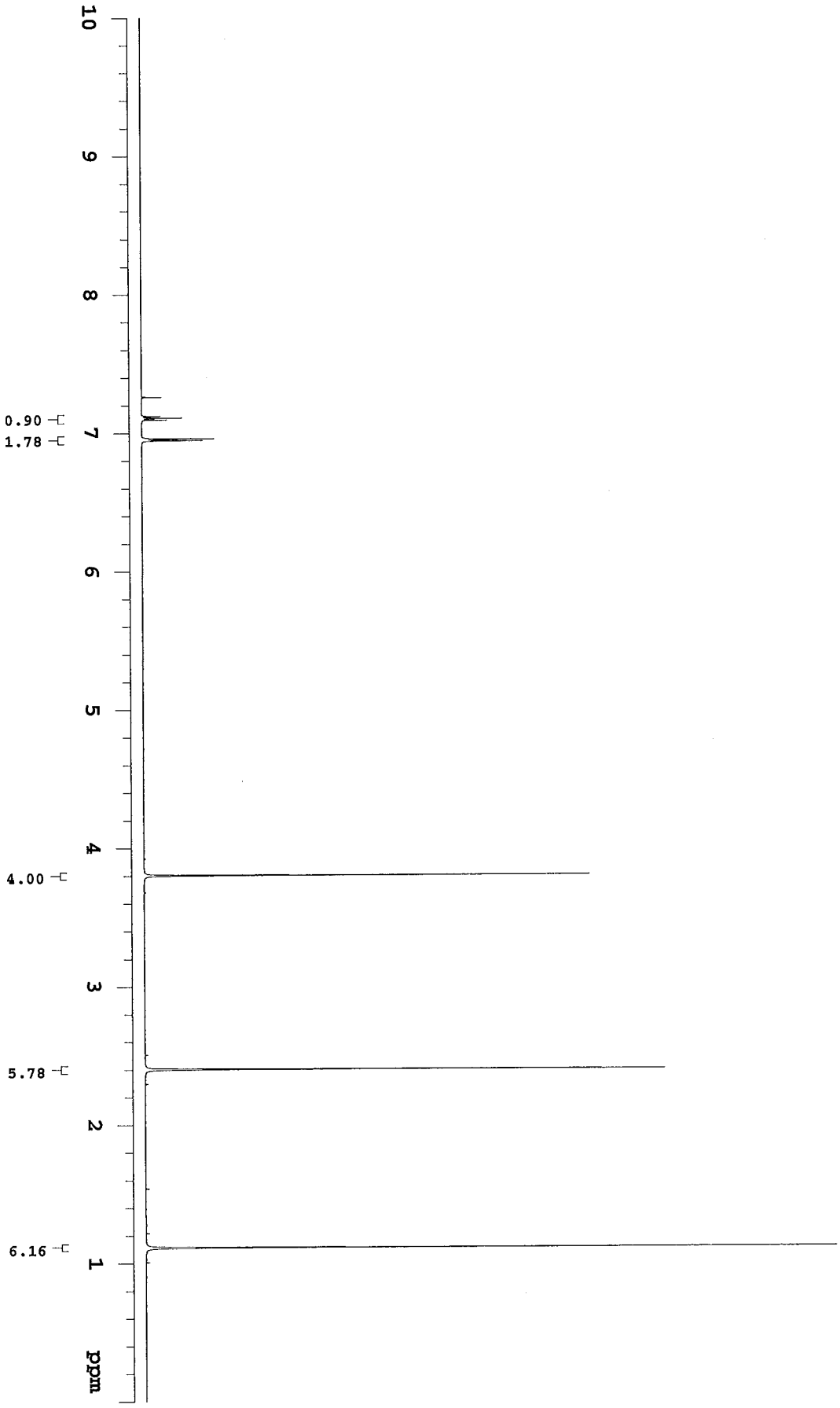

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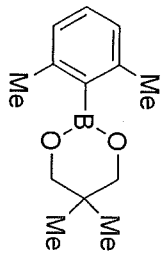
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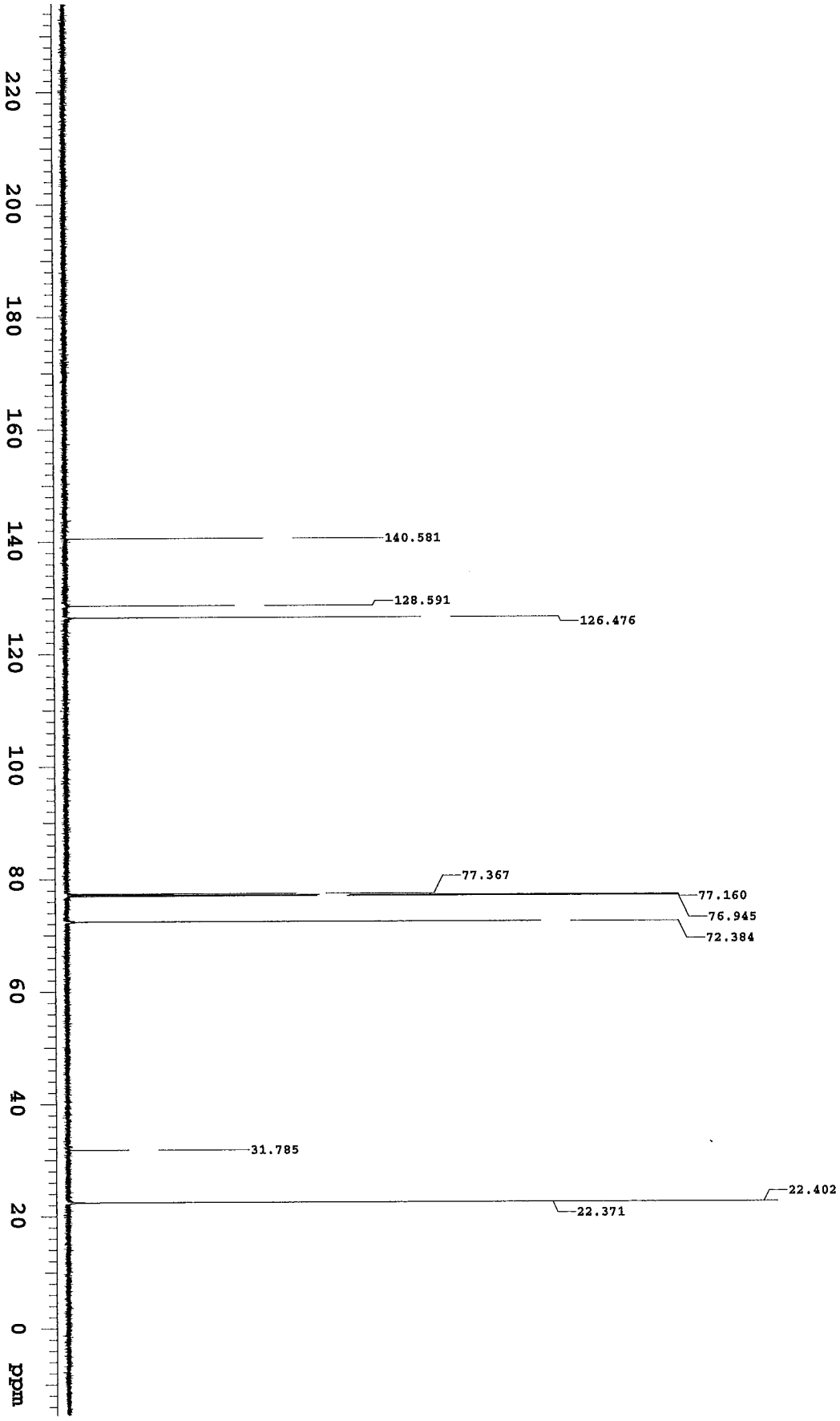
O
Me
Me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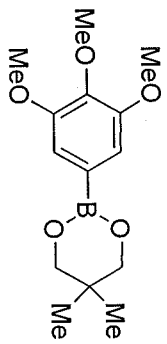

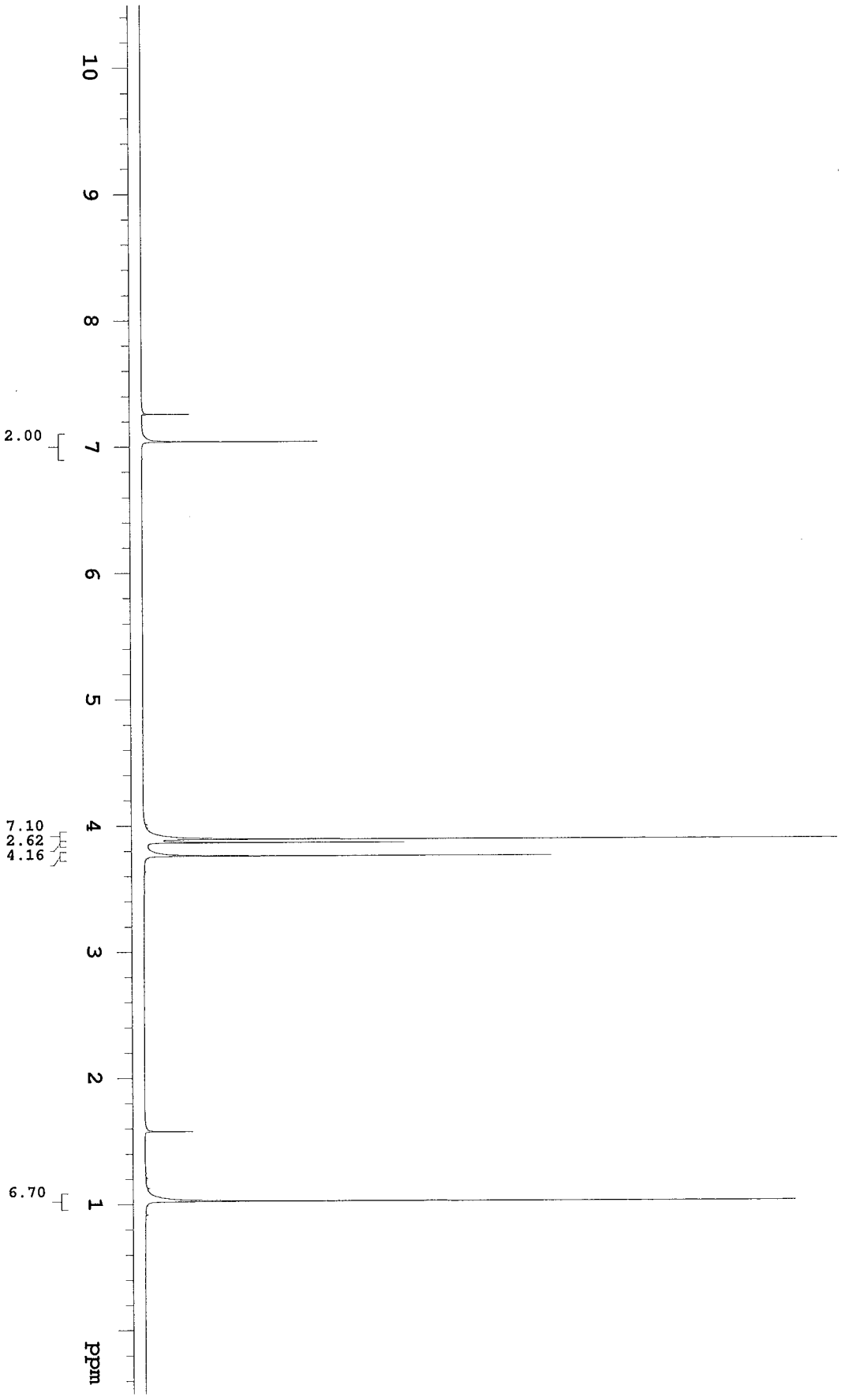

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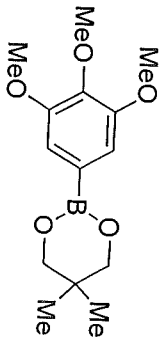

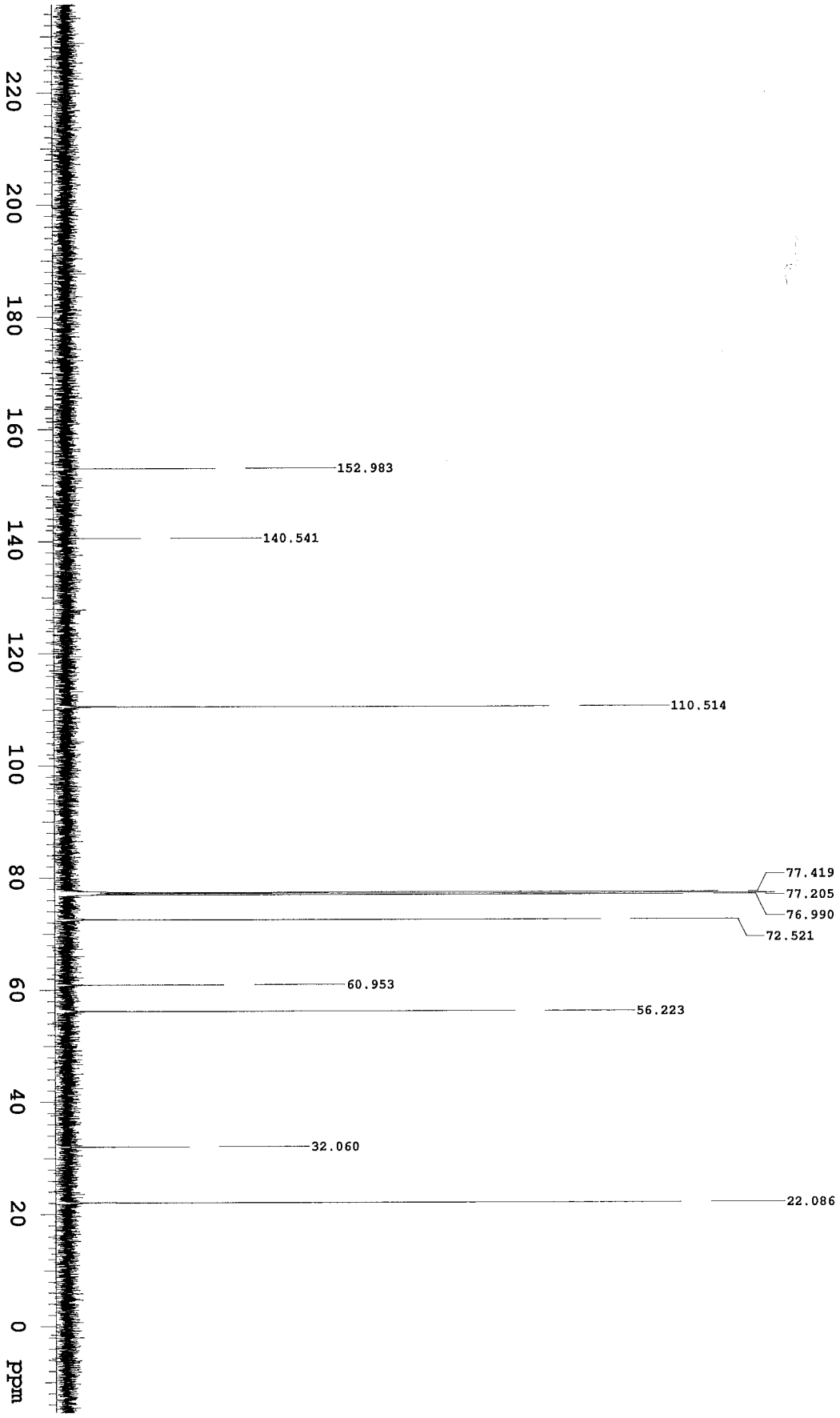

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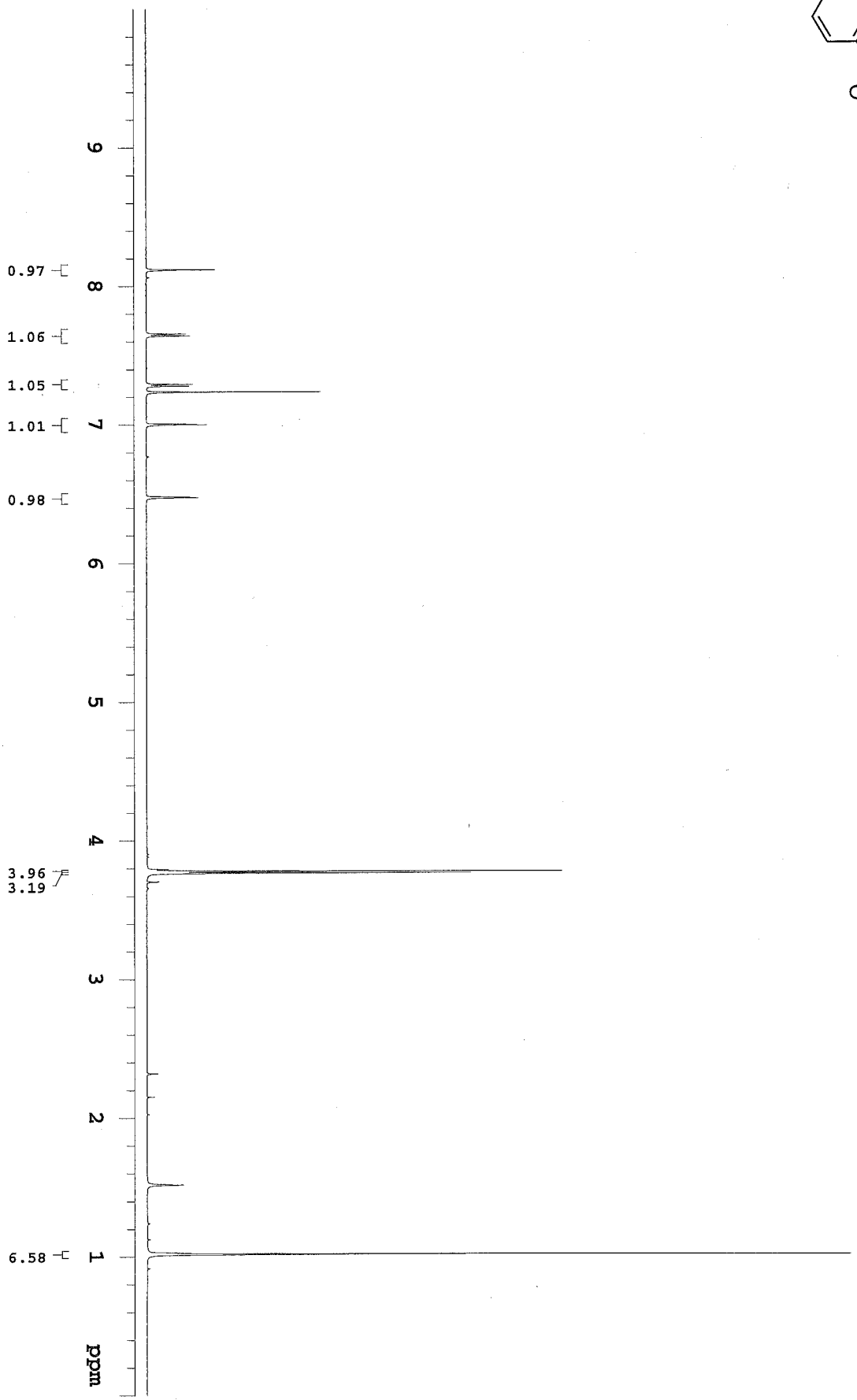

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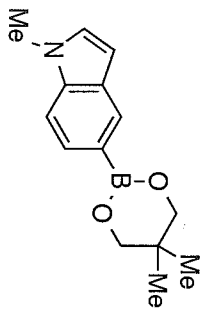

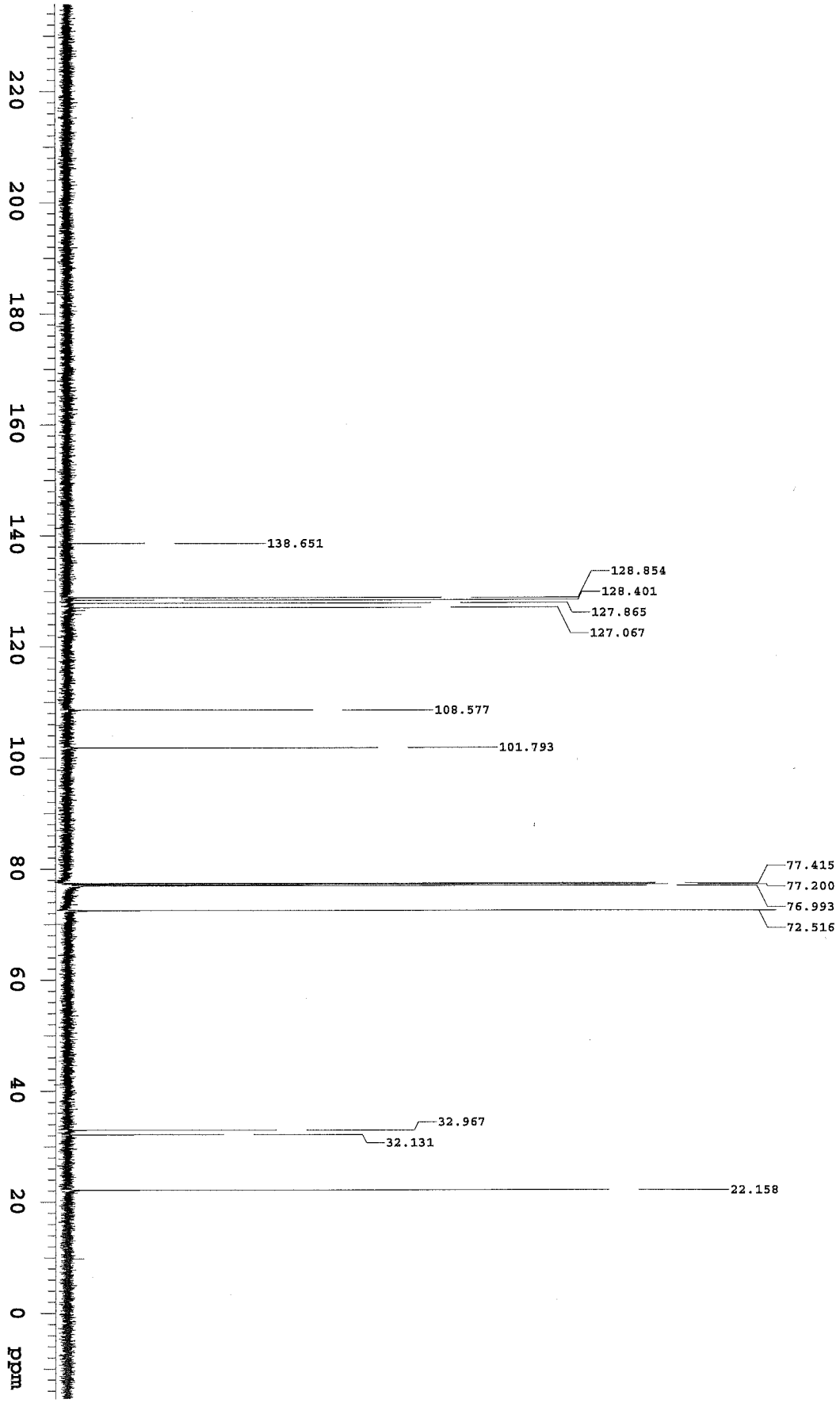

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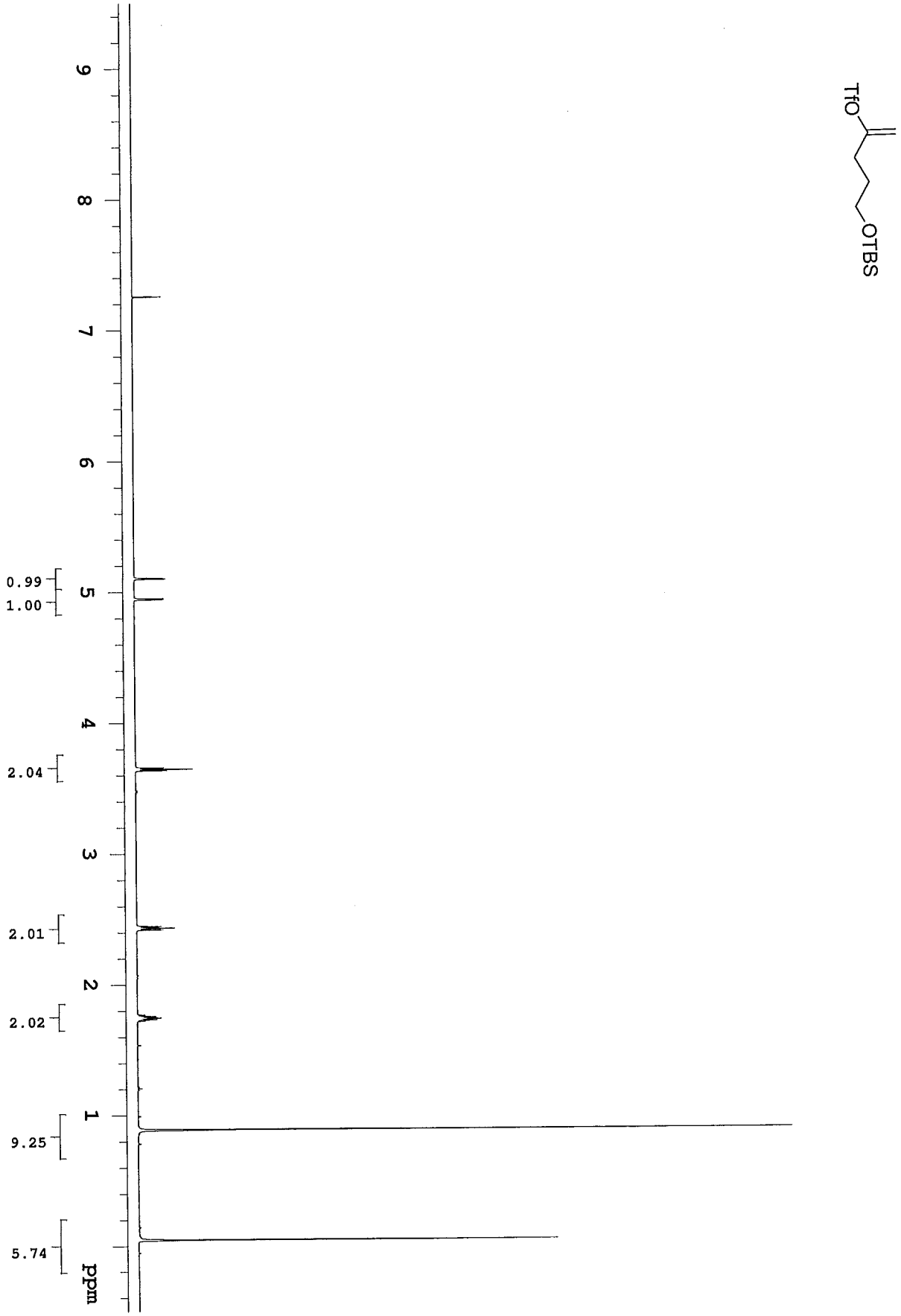

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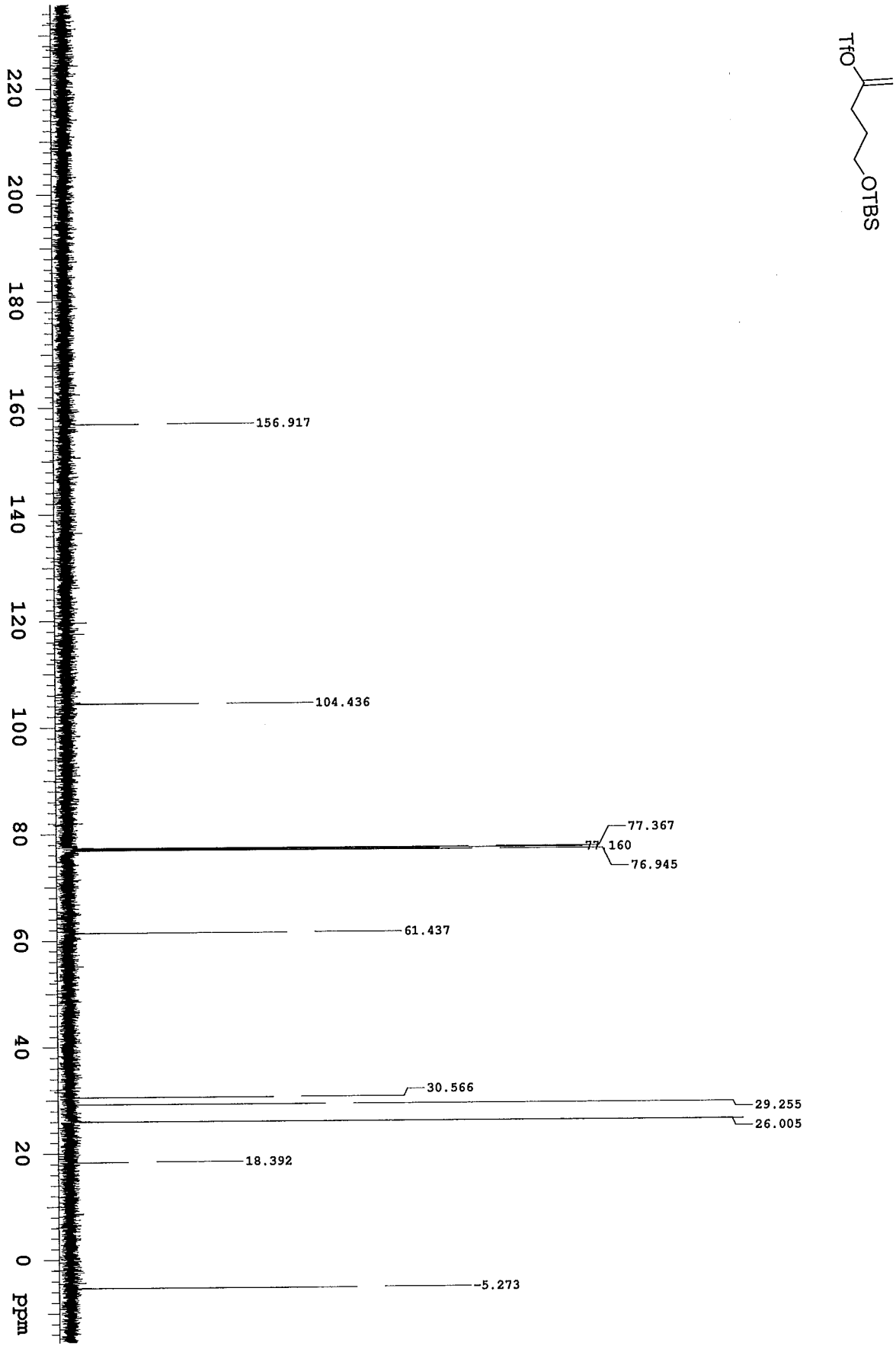

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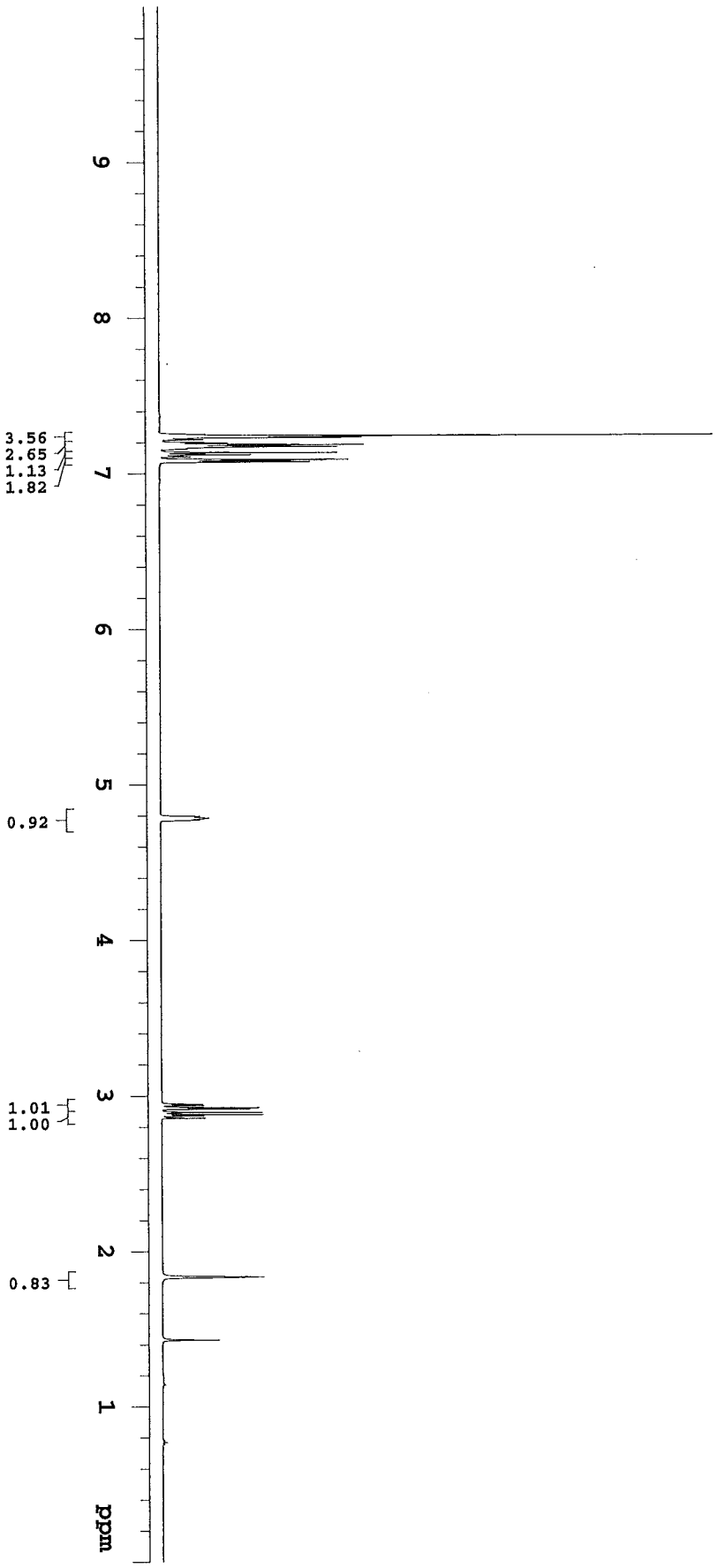

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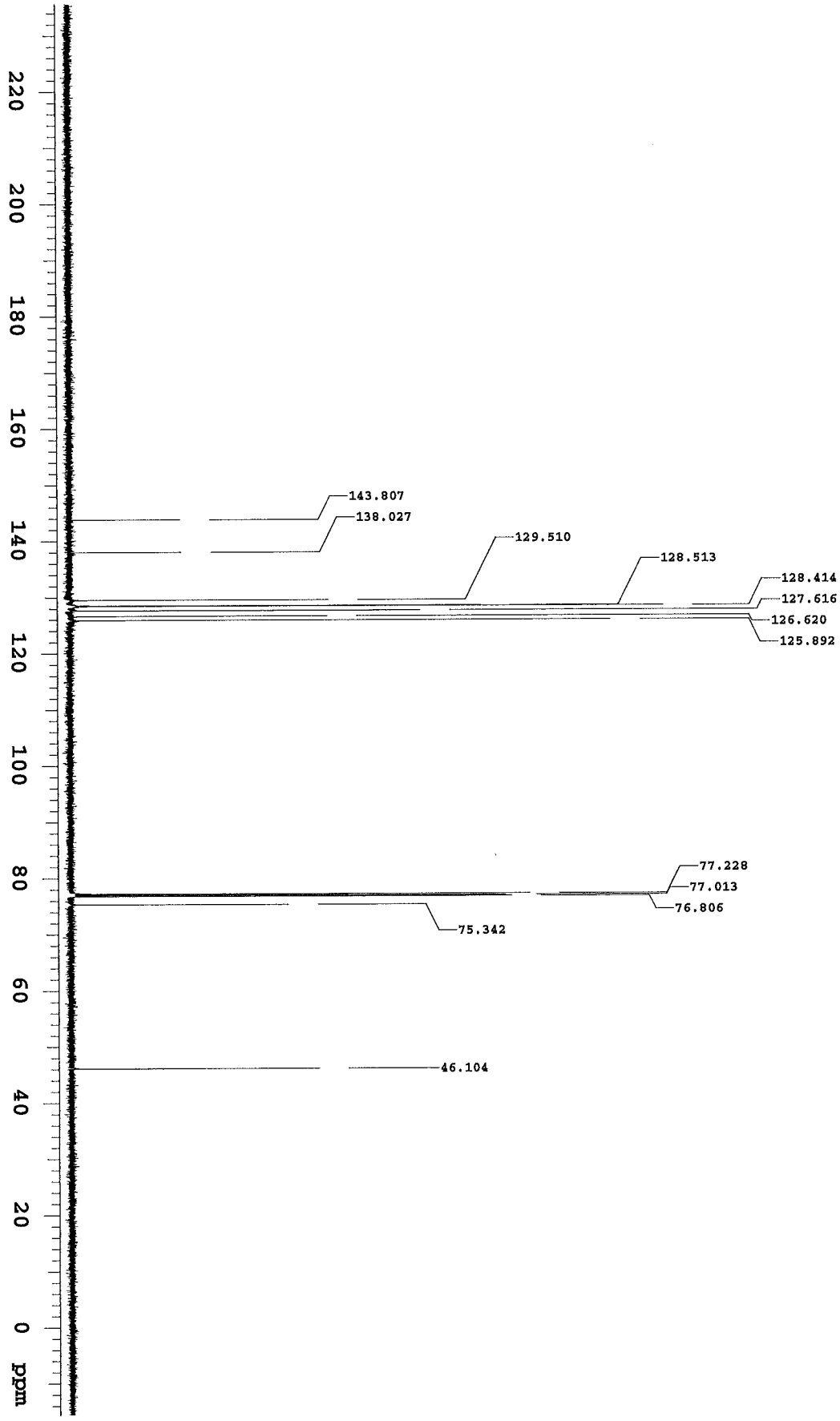
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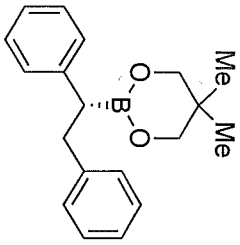
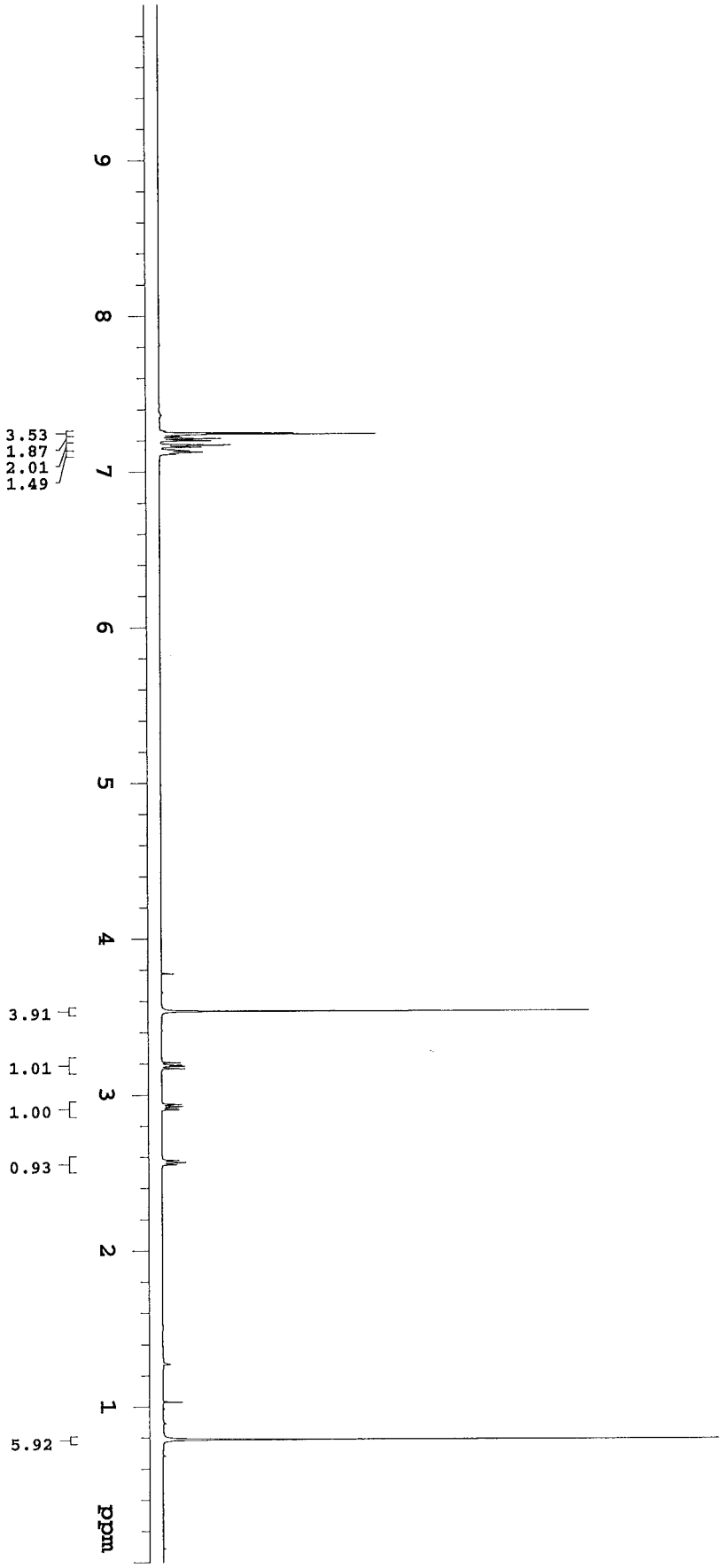
Compound **S-28**





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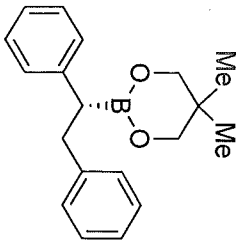

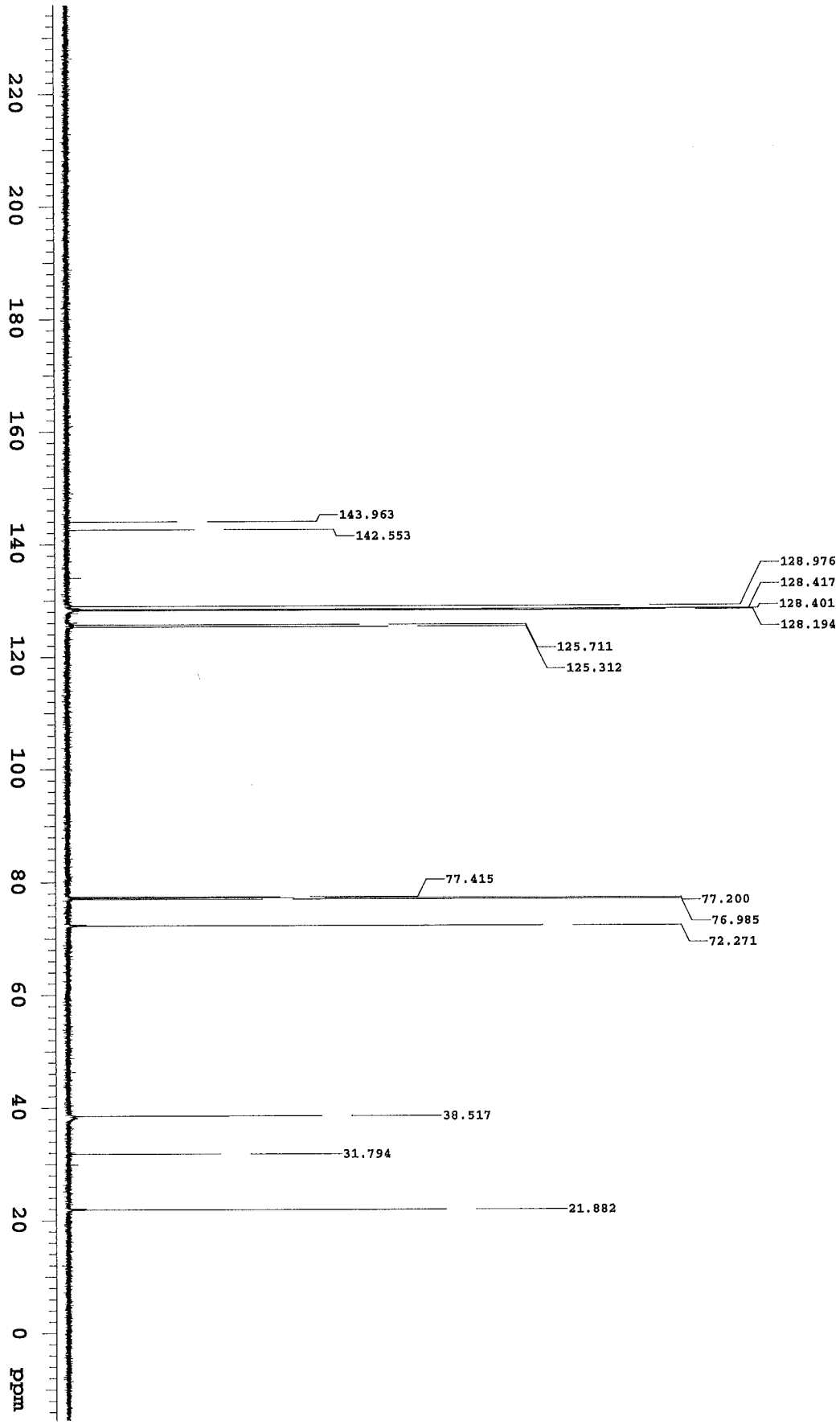

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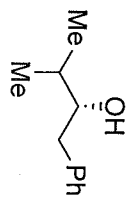

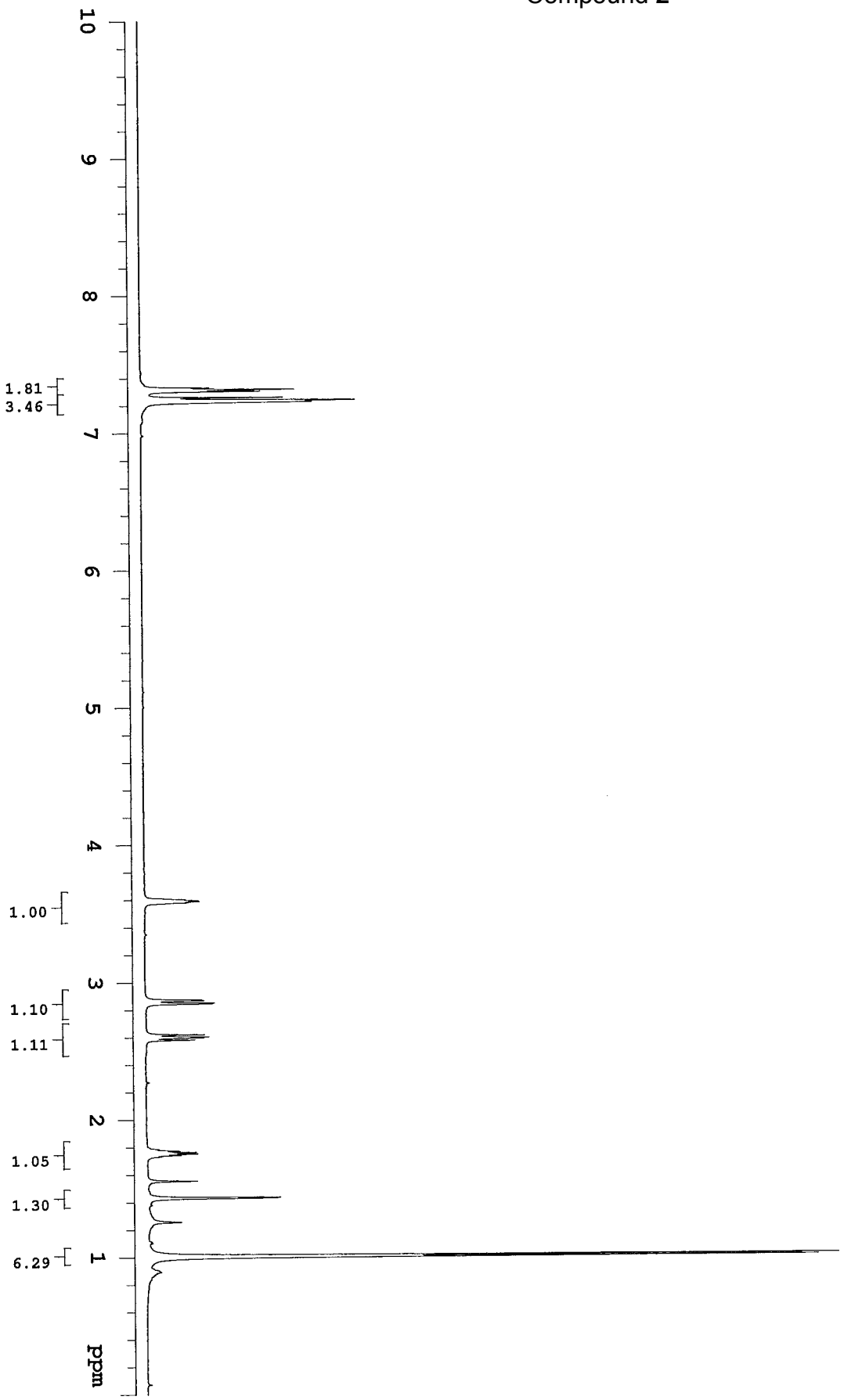

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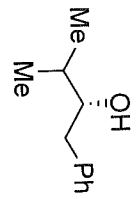
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Me
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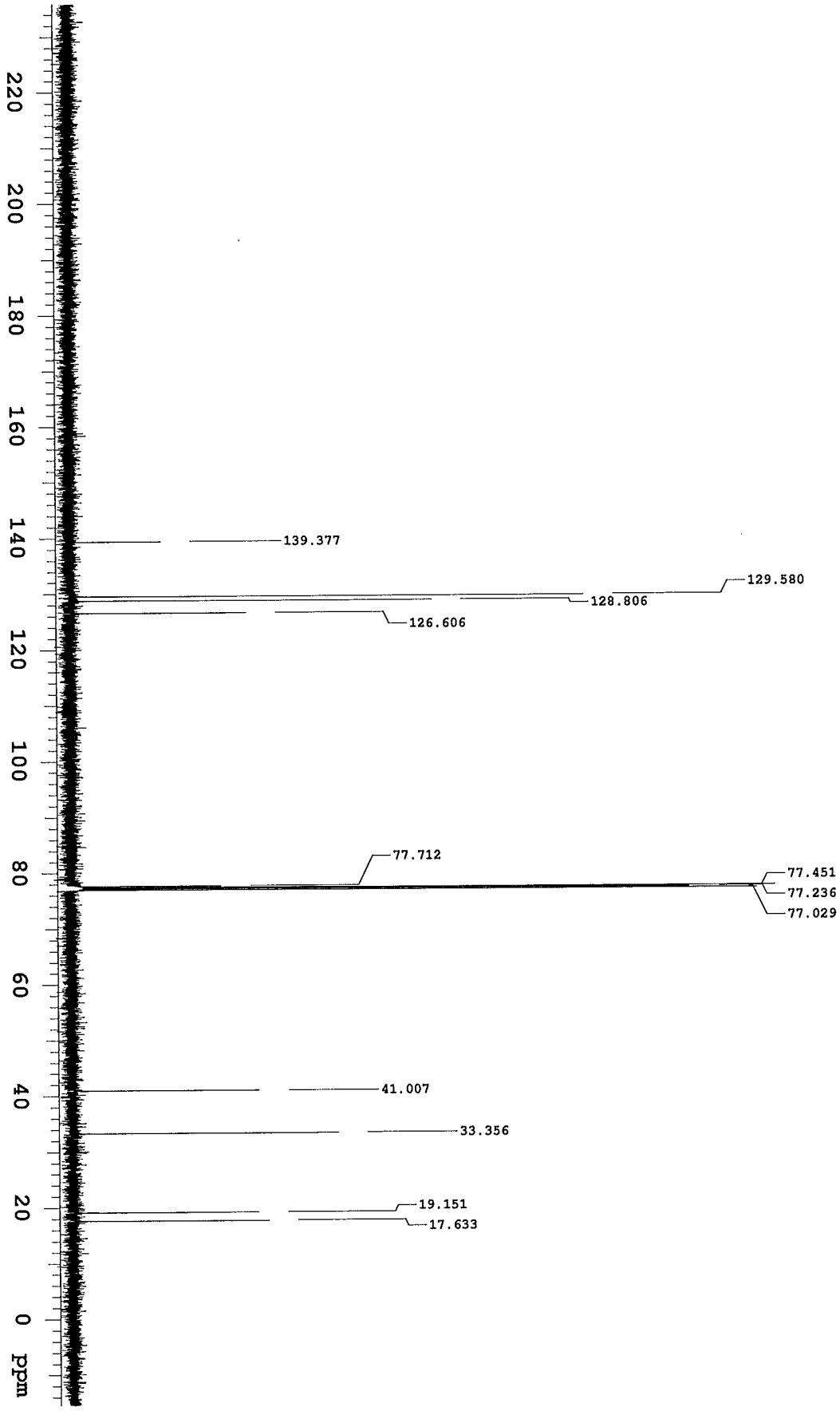
Ph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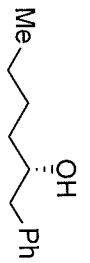

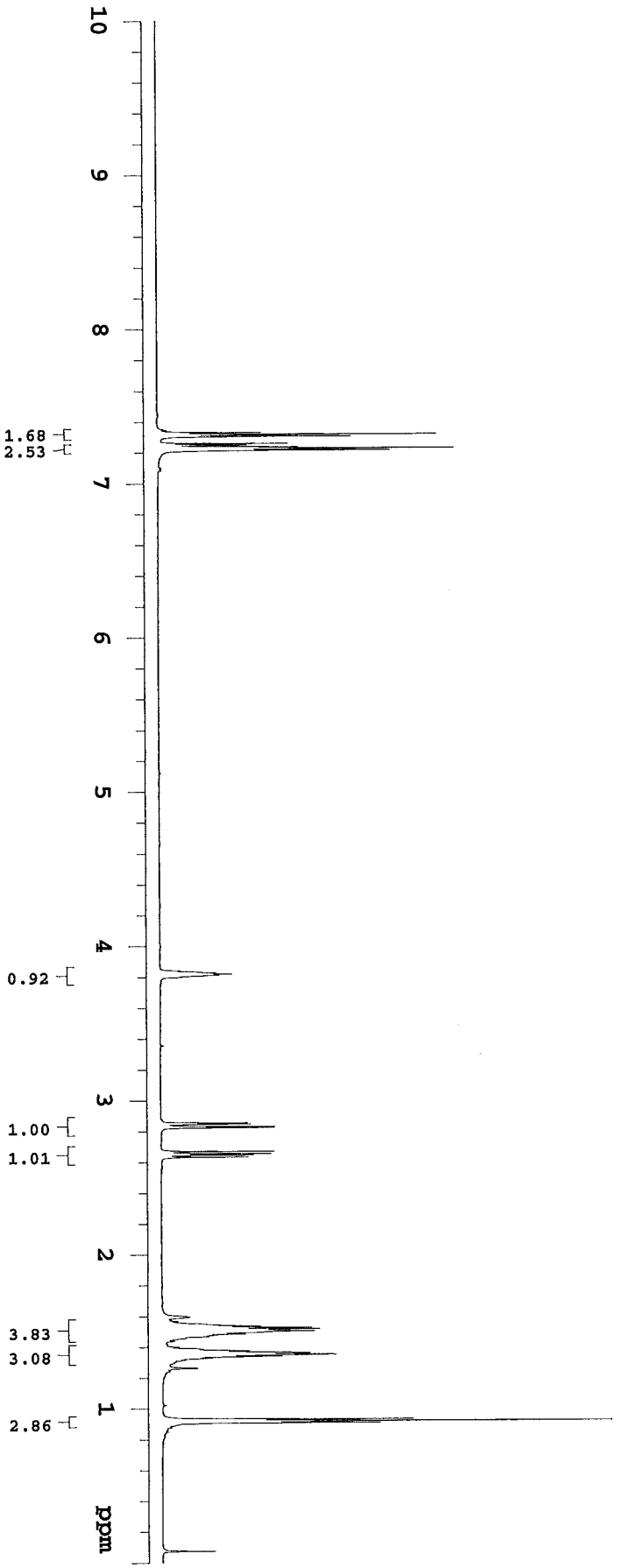

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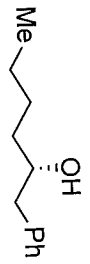
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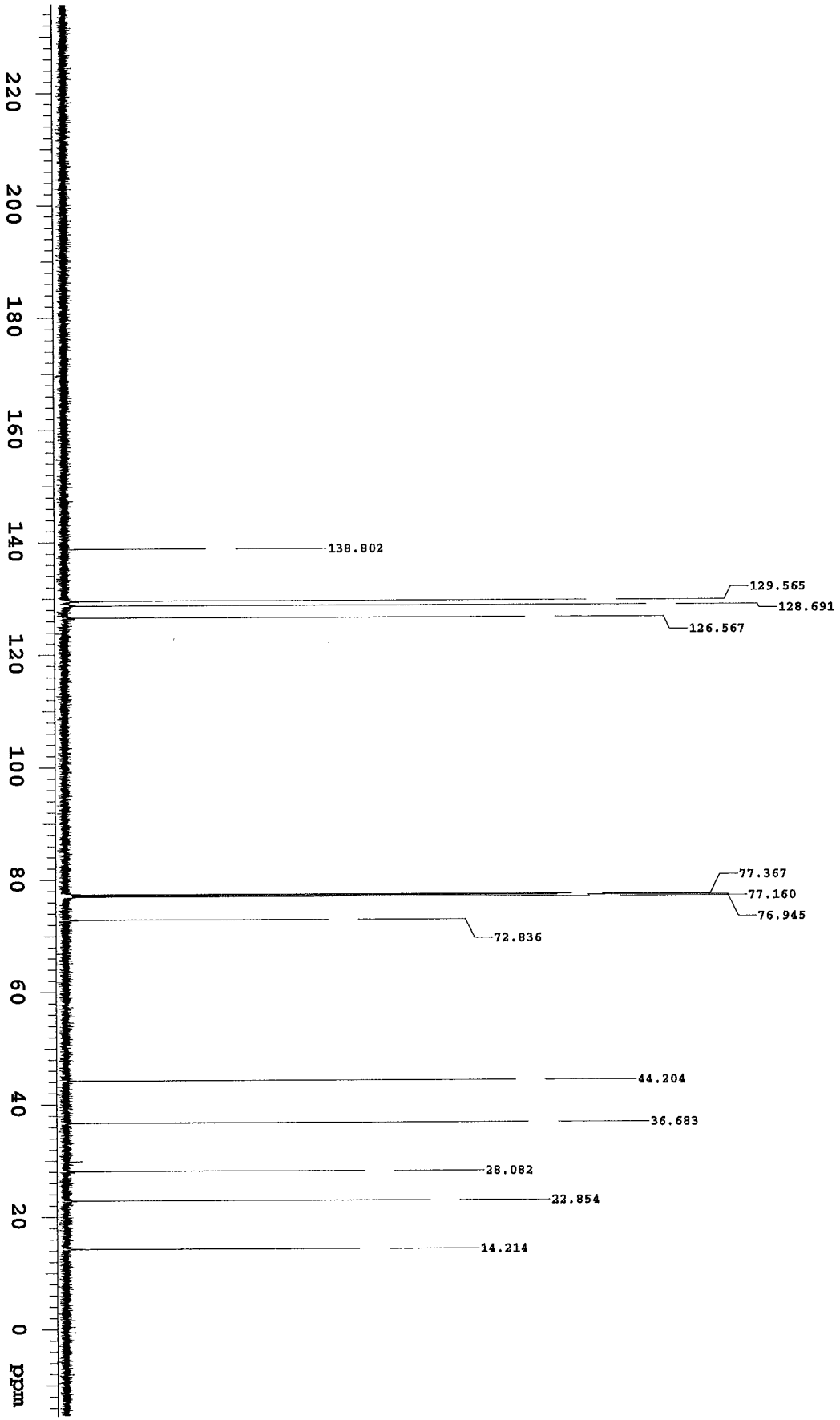
Ph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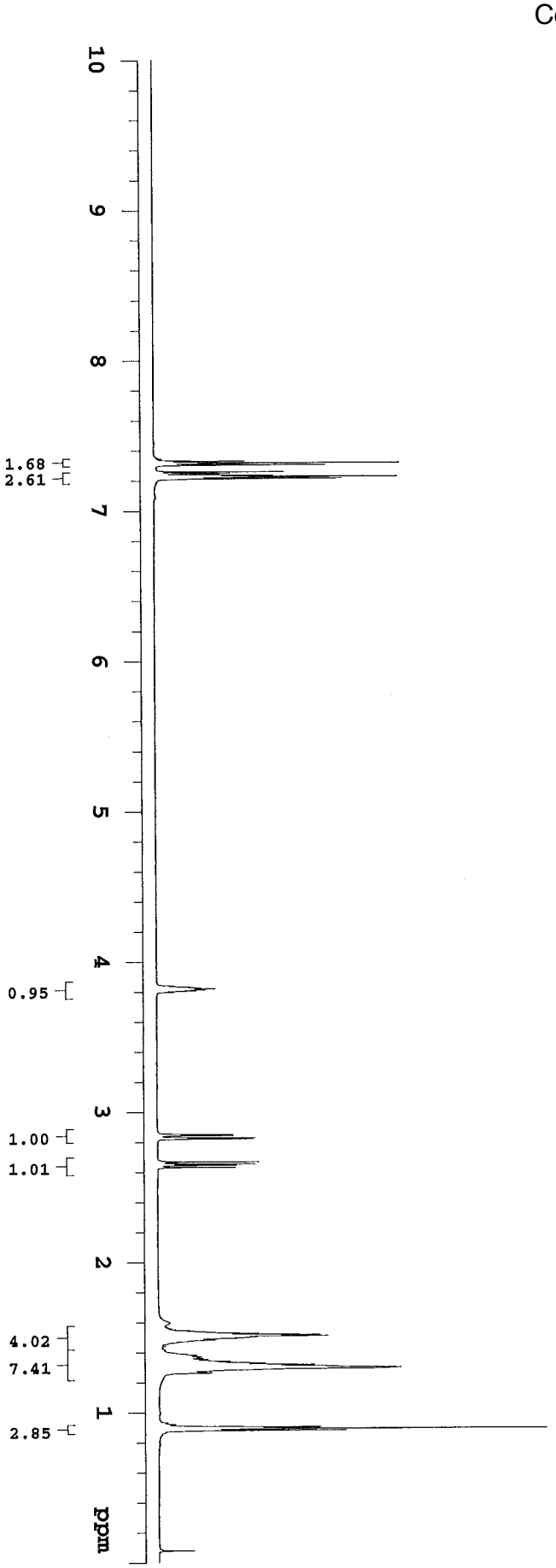

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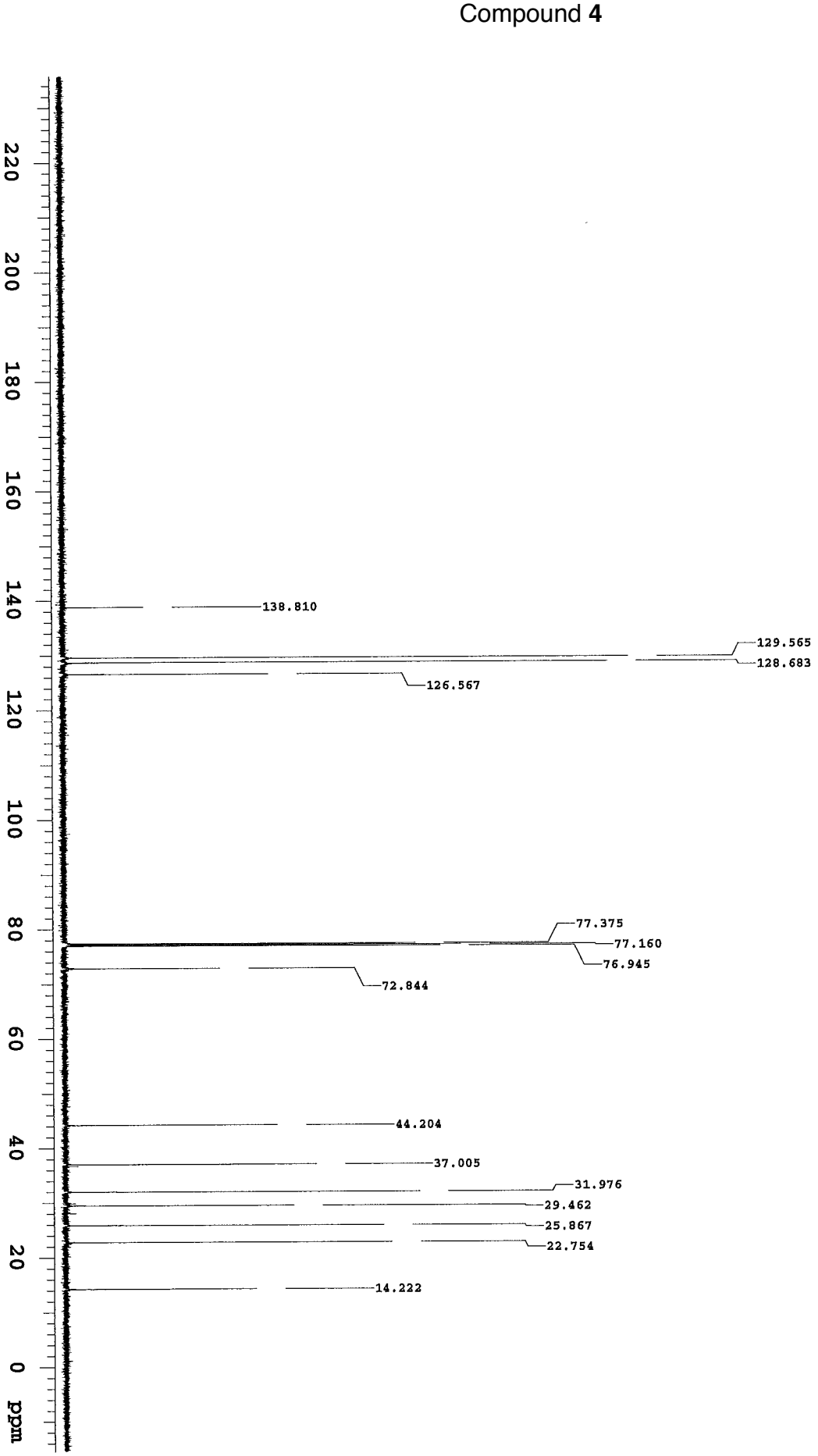
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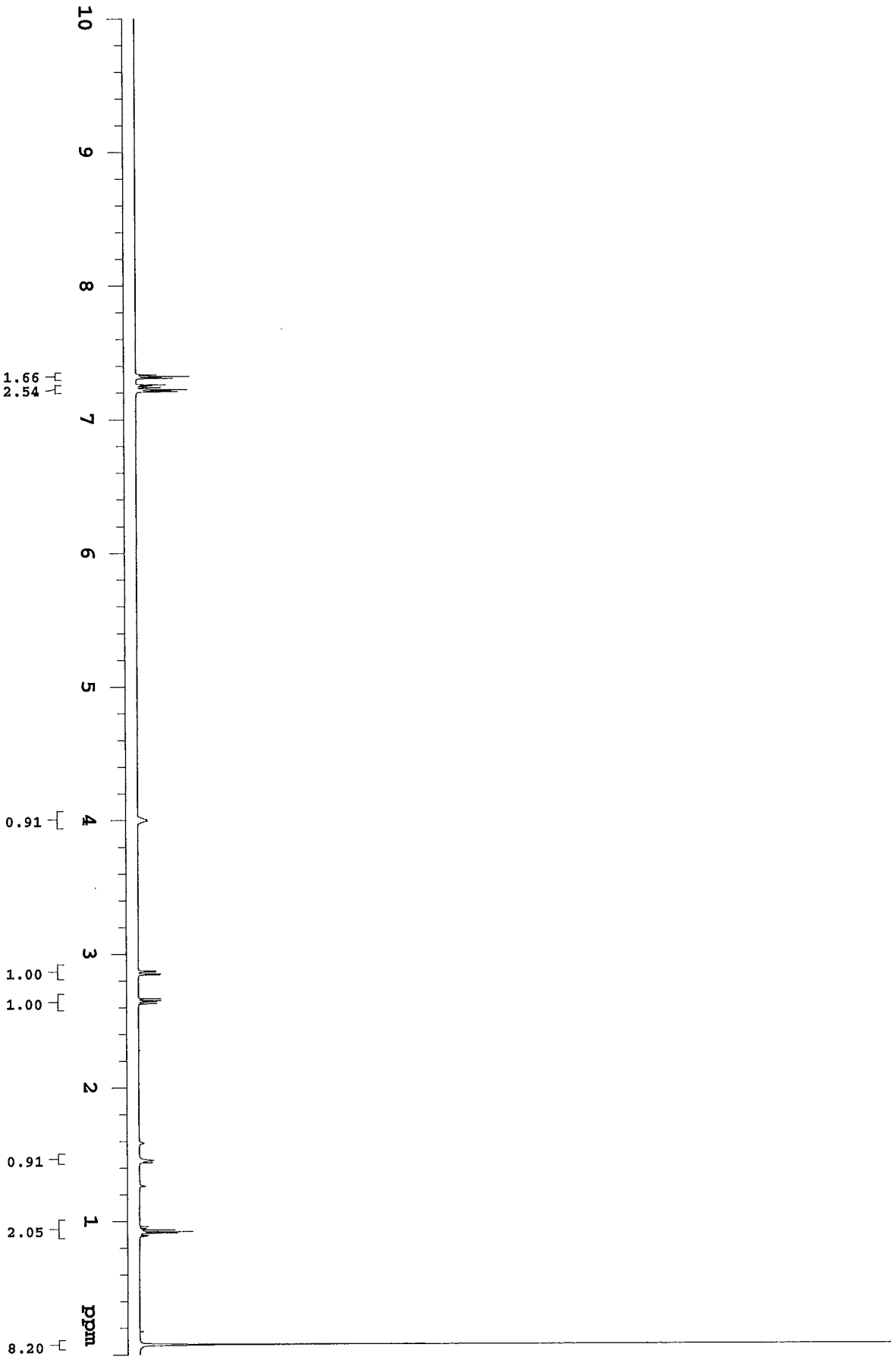

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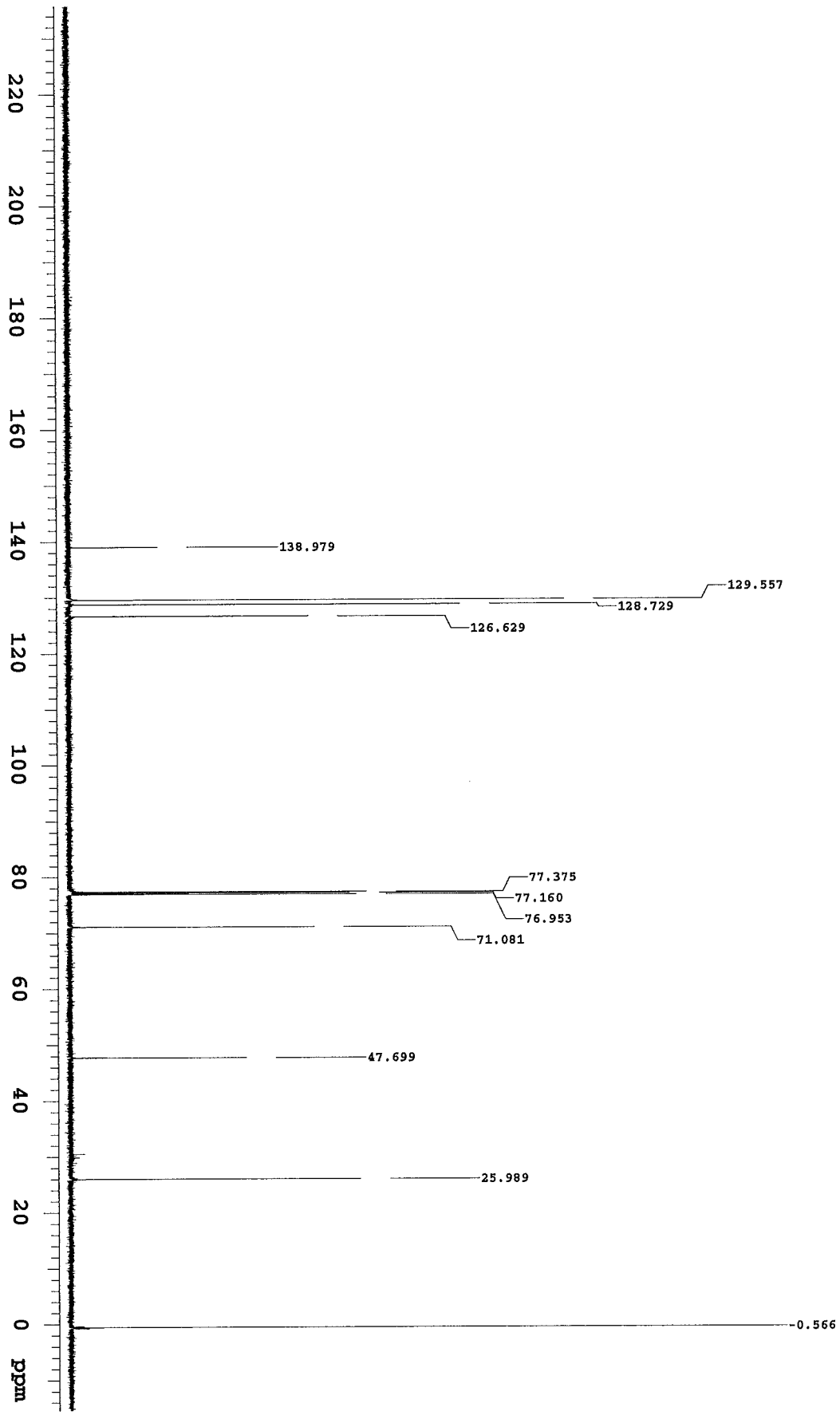
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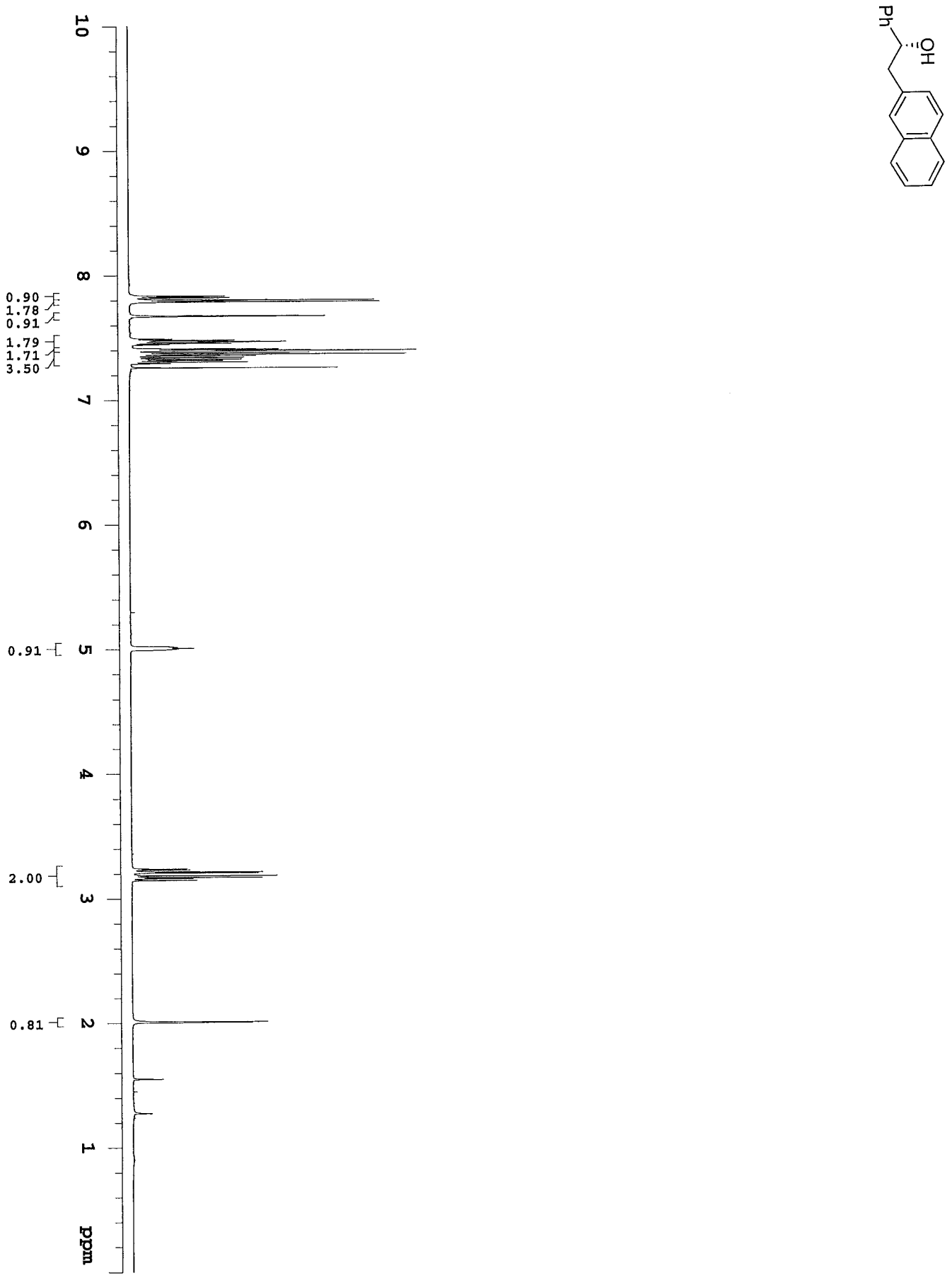

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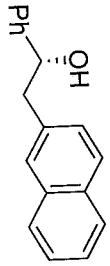
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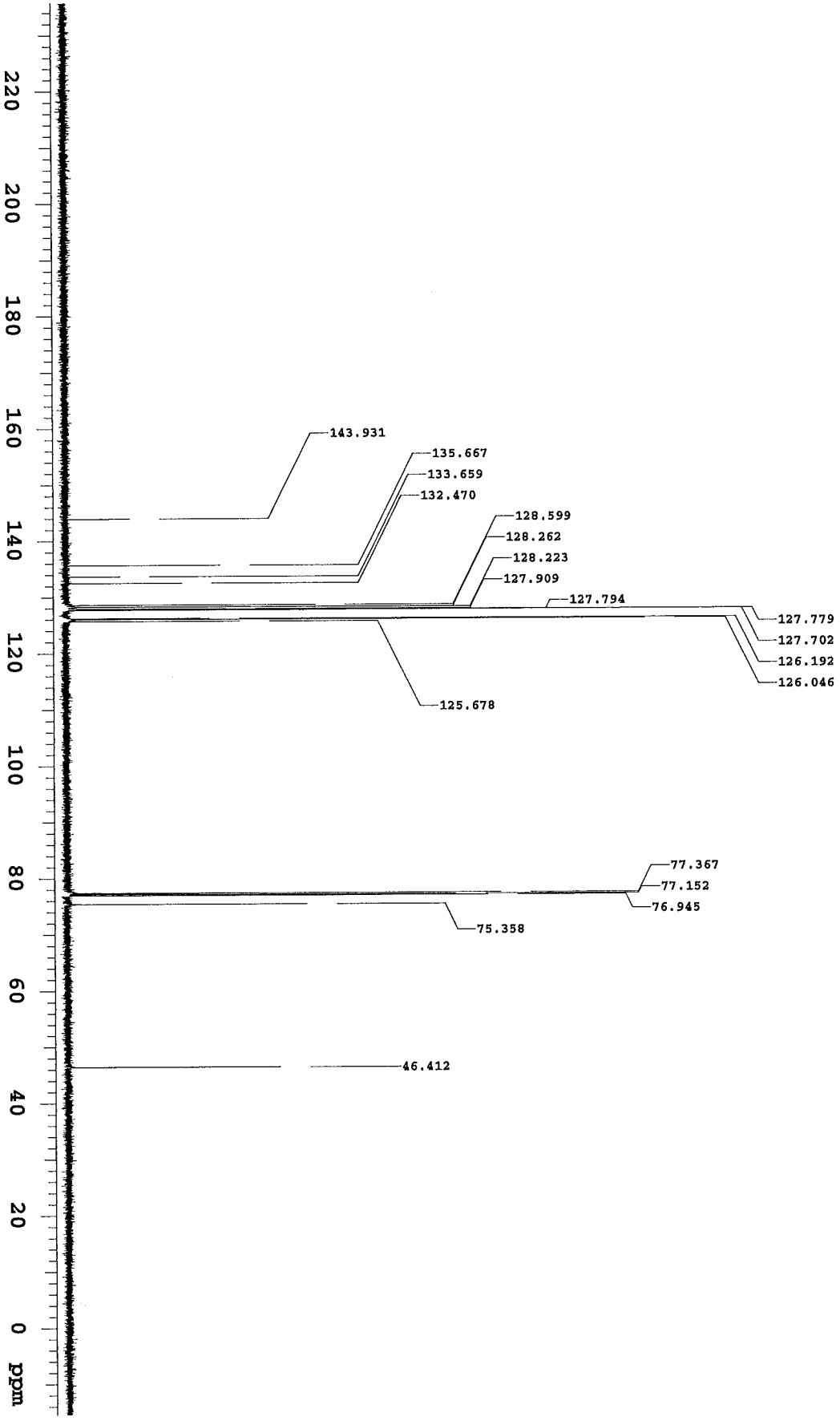
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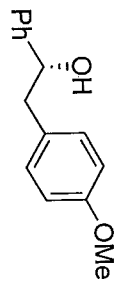
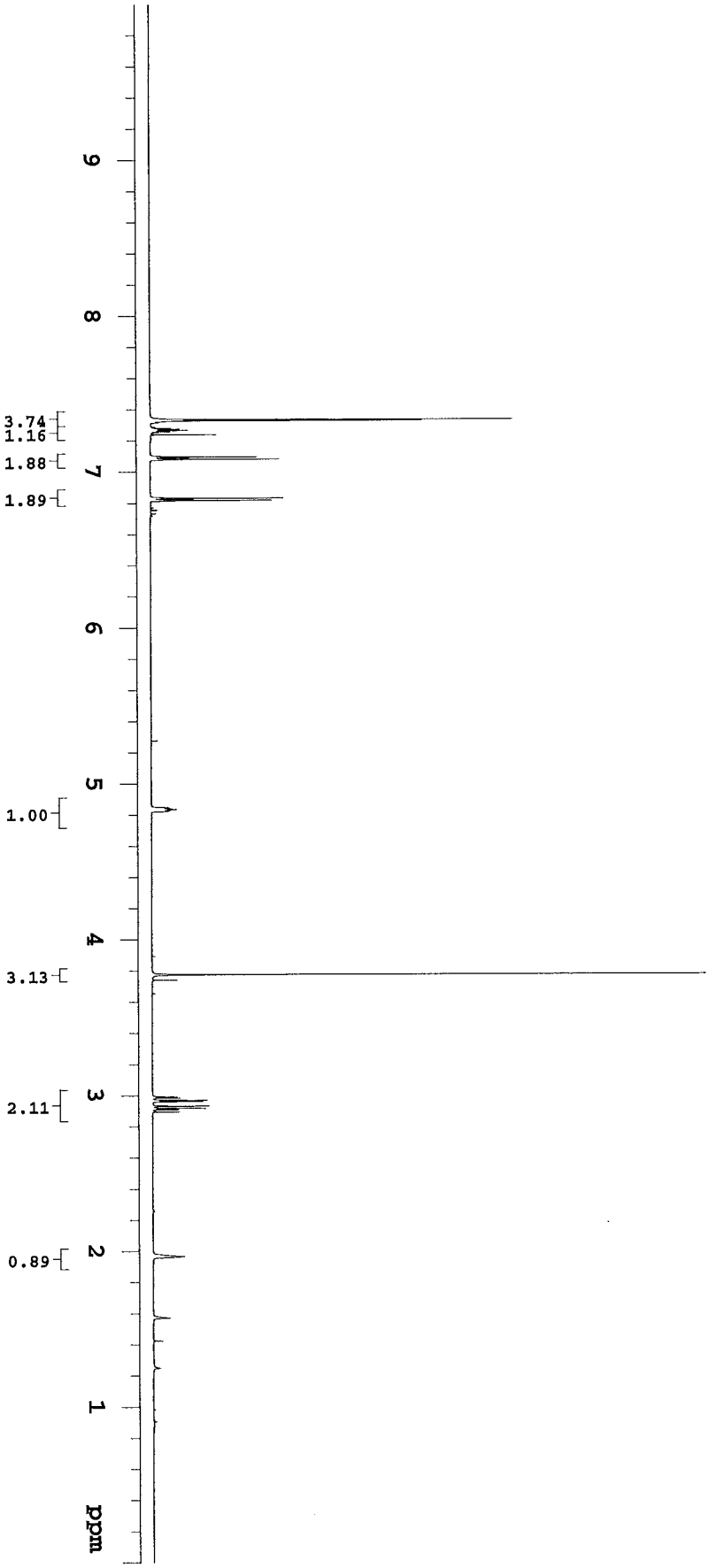
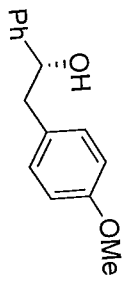
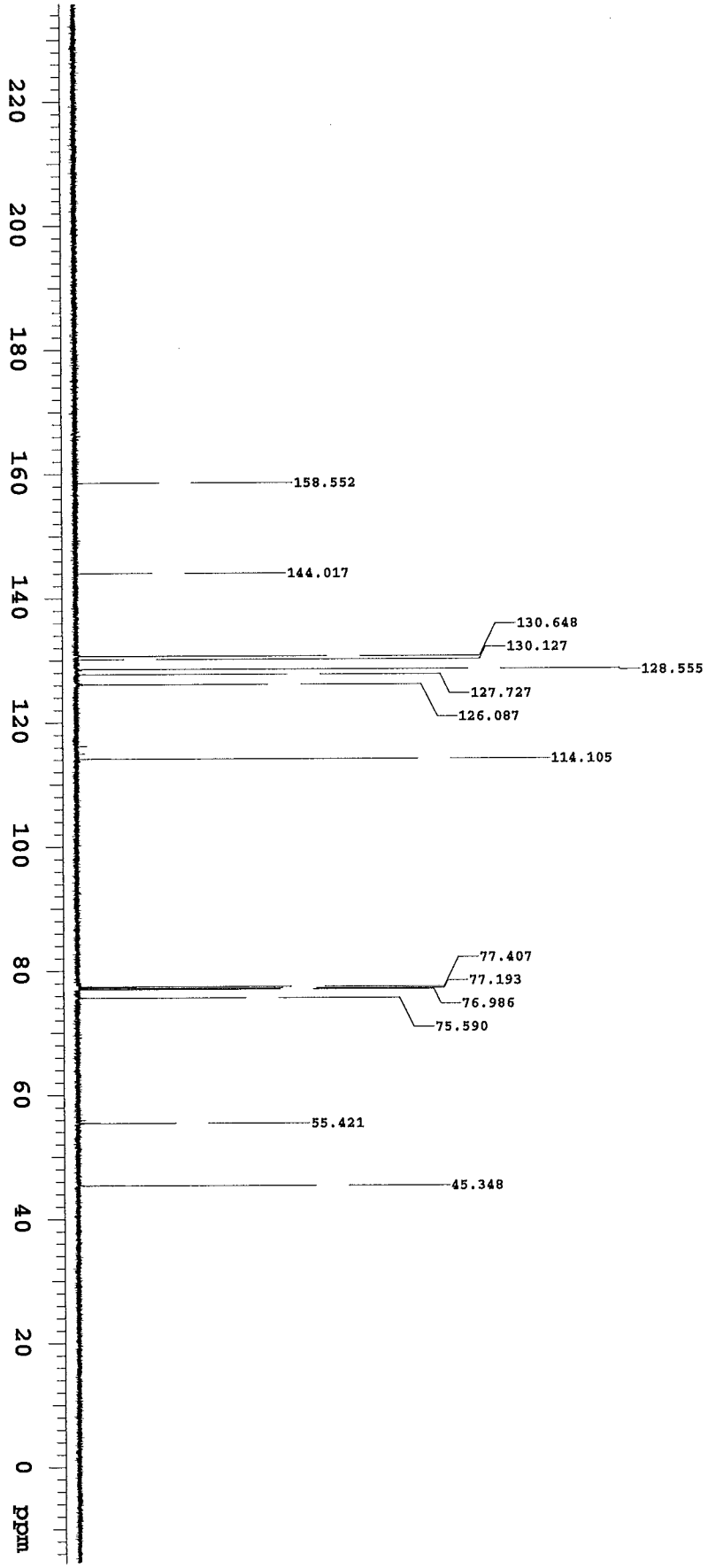
Compound **7**





Compound **7**


Ph
OH
OMe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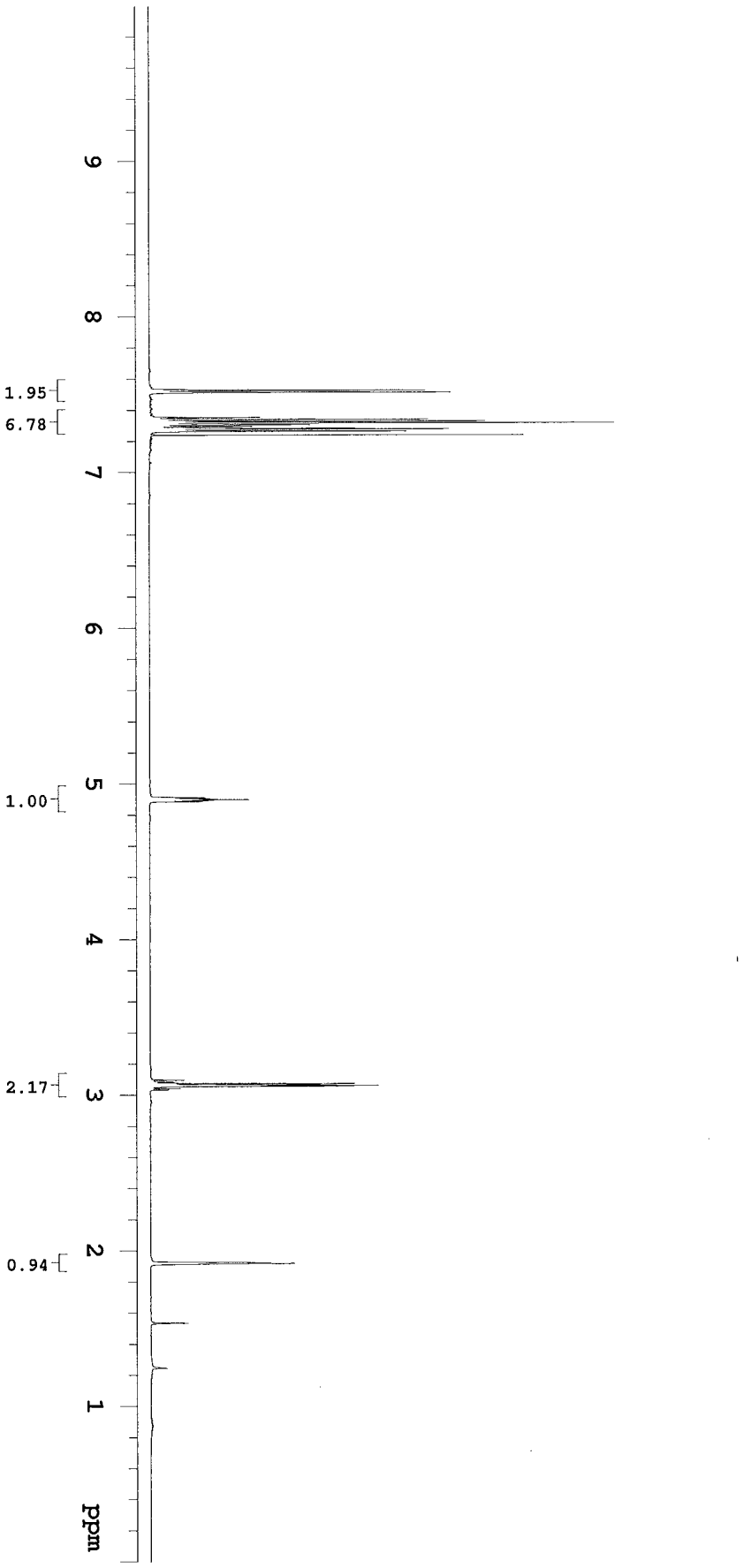
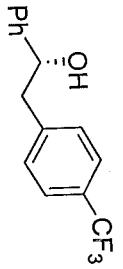
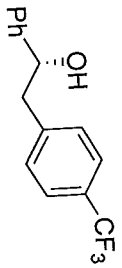
200
180
160
140
120
100
80
60
40
20
0
ppm
158.552
144.017
130.648
130.127
128.555
127.727
126.087
114.105
77.407
77.193
76.986
75.590
55.421
45.348

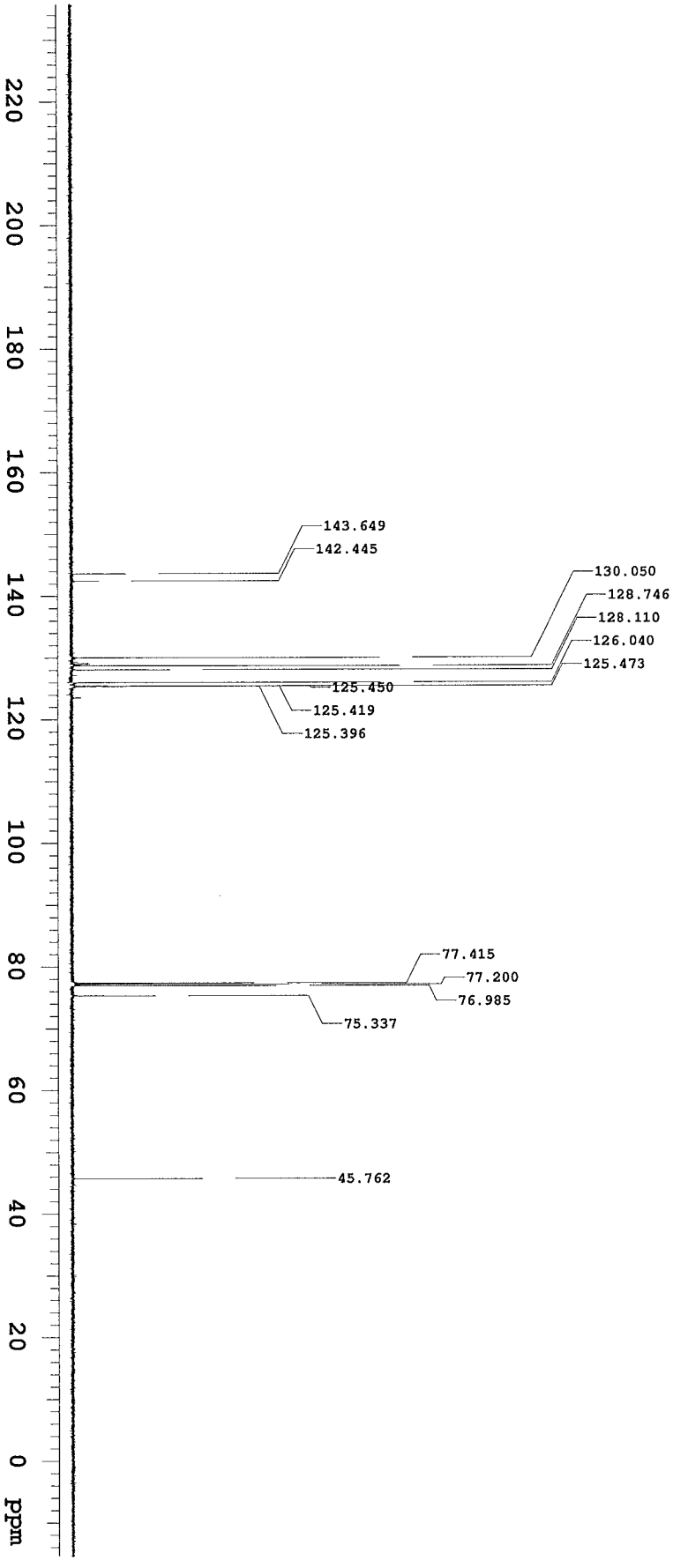
Compound **8**





Compound **8**


Ph
OH
CF3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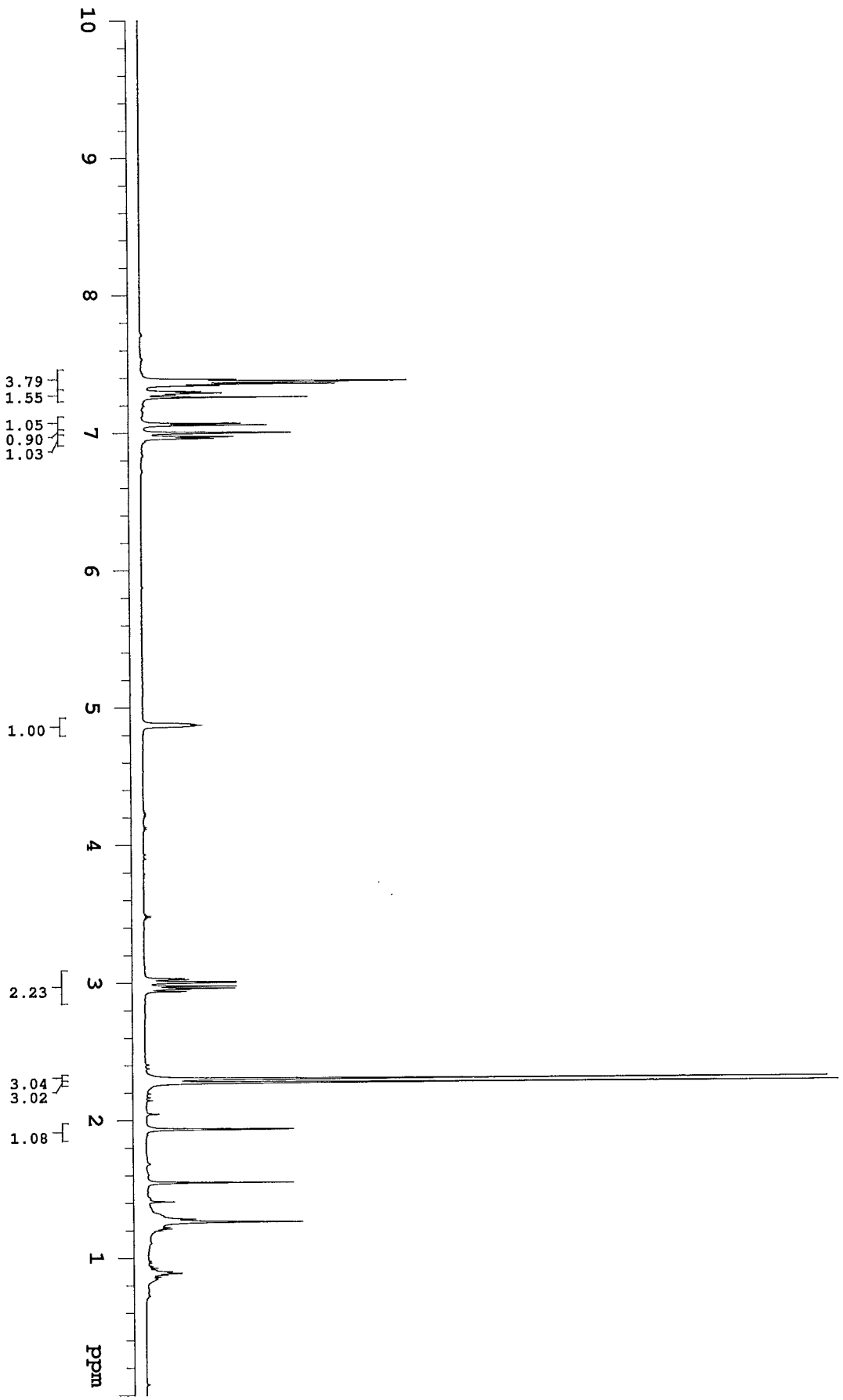
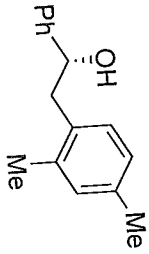
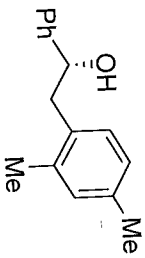
200
180
160
140
120
100
80
60
40
20
0
ppm
143.649
142.445
130.050
128.746
128.110
126.040
125.473
125.450
125.419
125.396
77.415
77.200
76.985
75.337
45.762

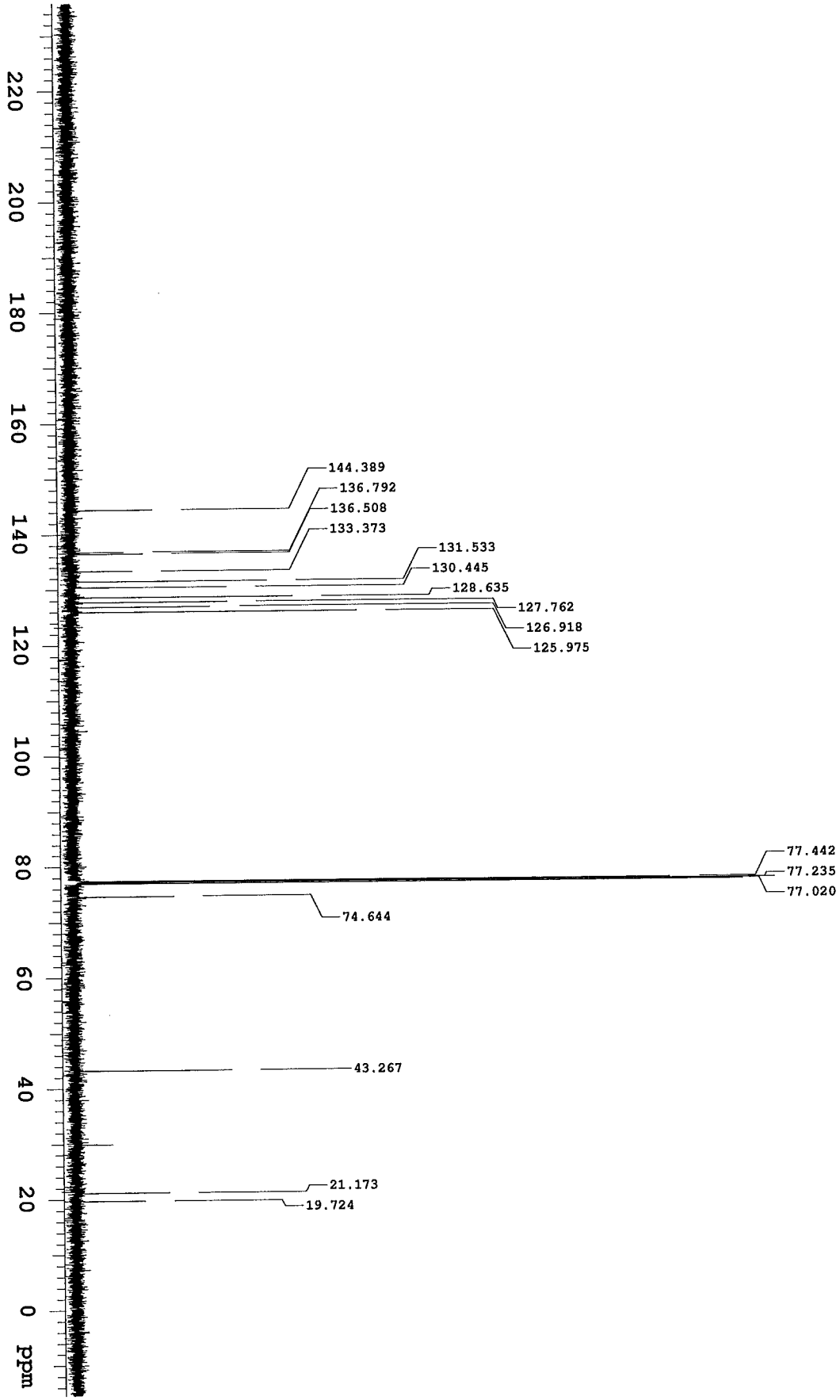
Compound **9**


10
9
8
7
6
5
4
3
2
1
PPm
3.79
1.55
1.05
0.90
1.03
1.00
2.23
3.04
3.02
1.08

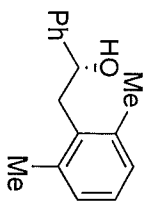

Ph
OH
Me
Me

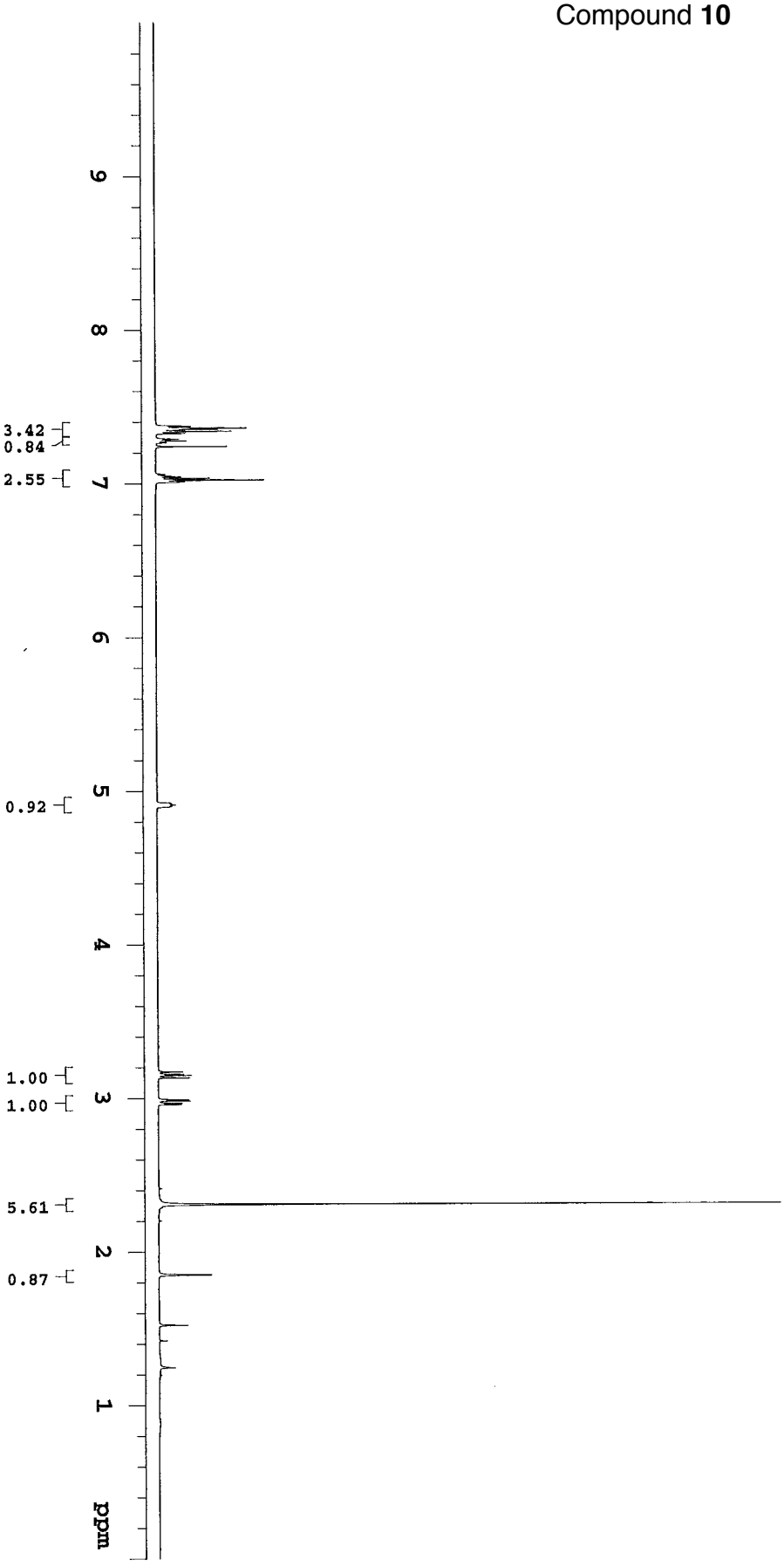
Compound **9**


Ph
OH
Me
Me

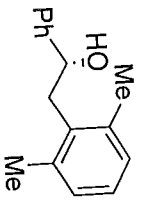

220
200
180
160
140
120
100
80
60
40
20
0
ppm
144.389
136.792
136.508
133.373
131.533
130.445
128.635
127.762
126.918
125.975
77.442
77.235
77.020
74.644
43.267
21.173
19.724

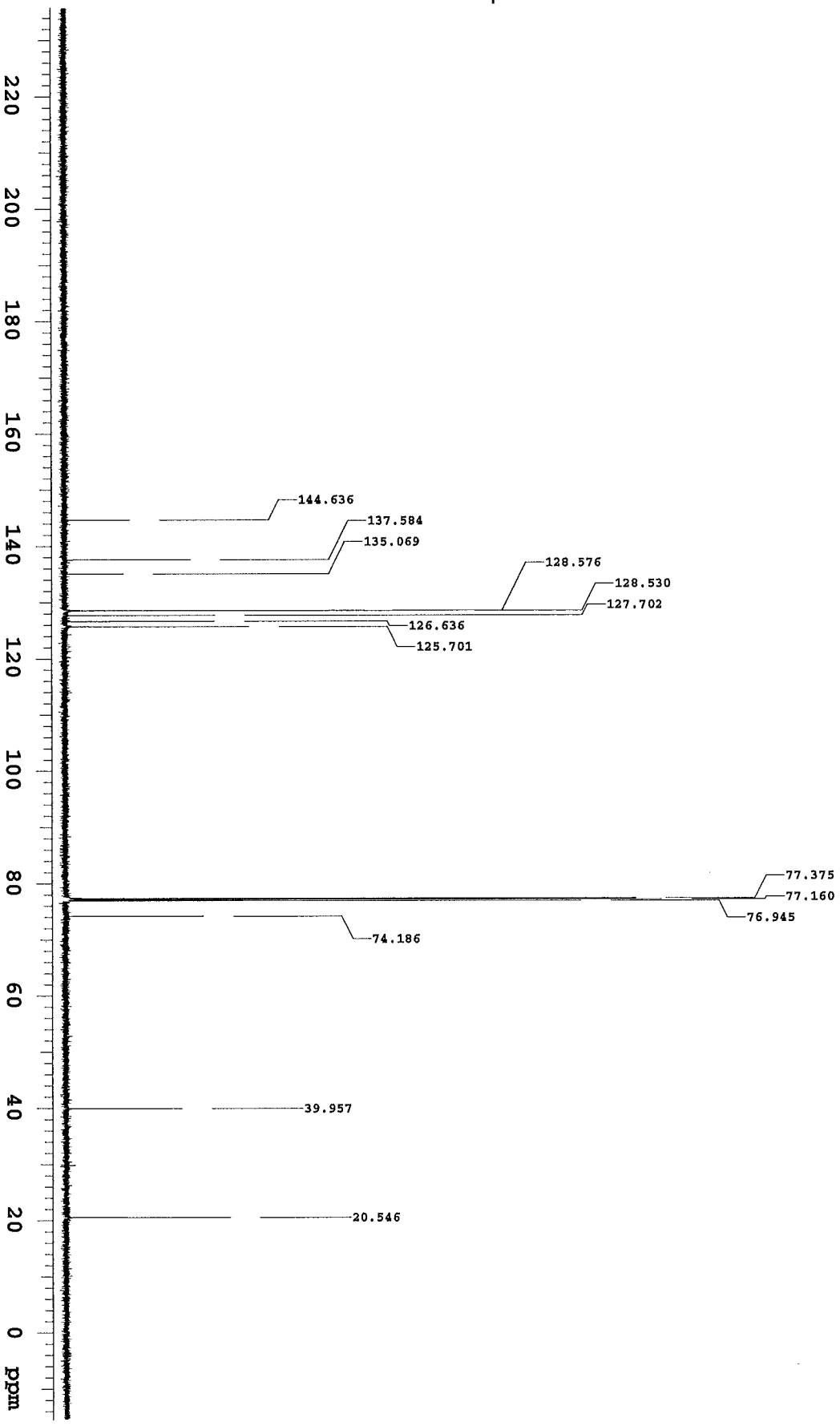
Compound **10**





Compound **10**


Ph
HO
Me
Me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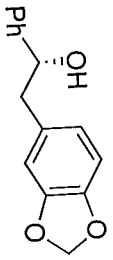
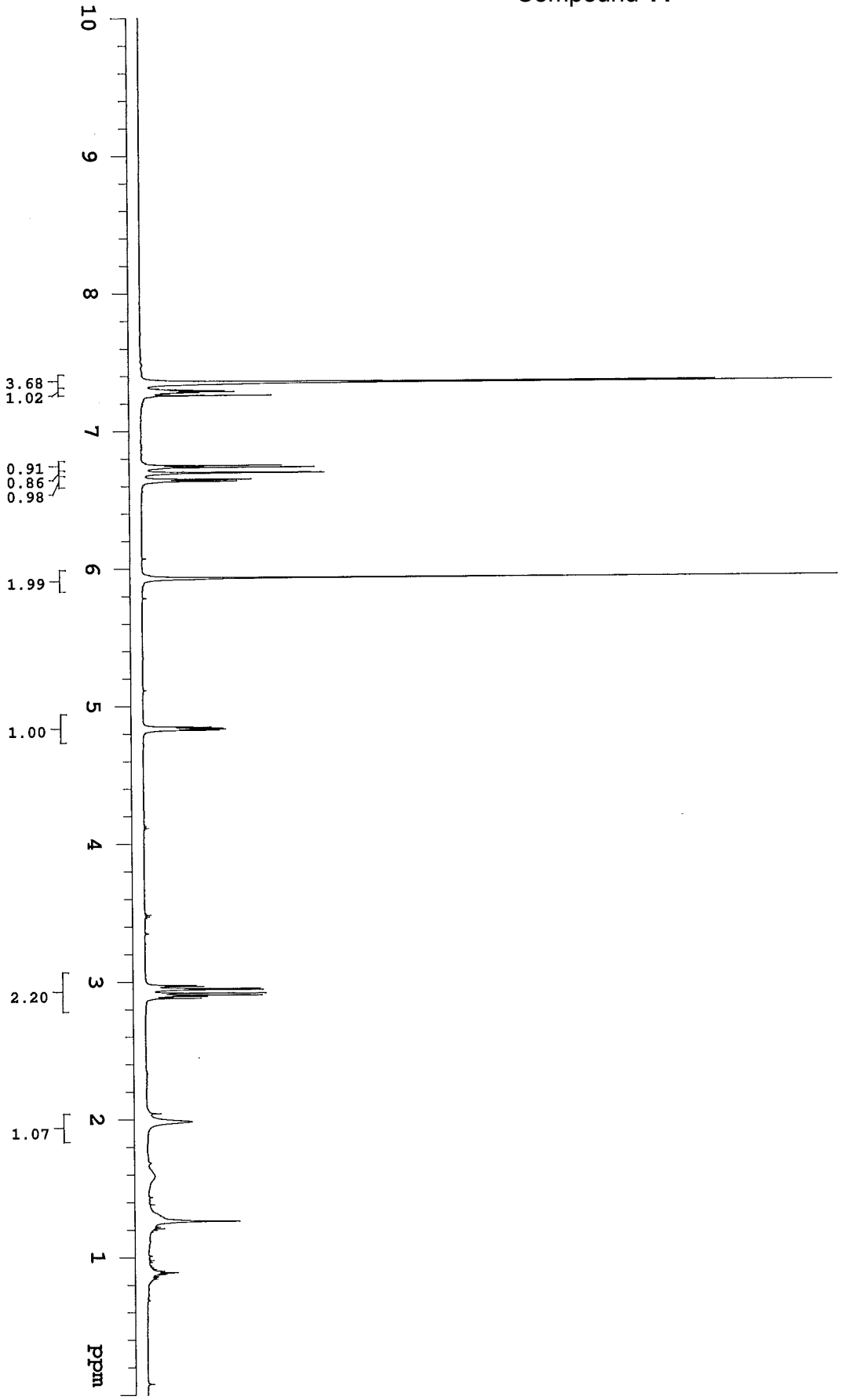
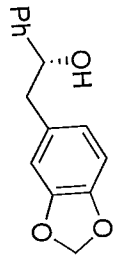
200
180
160
140
120
100
80
60
40
20
0
ppm
144.636
137.584
135.069
128.576
128.530
127.702
126.636
125.701
77.375
77.160
76.945
74.186
39.957
20.546

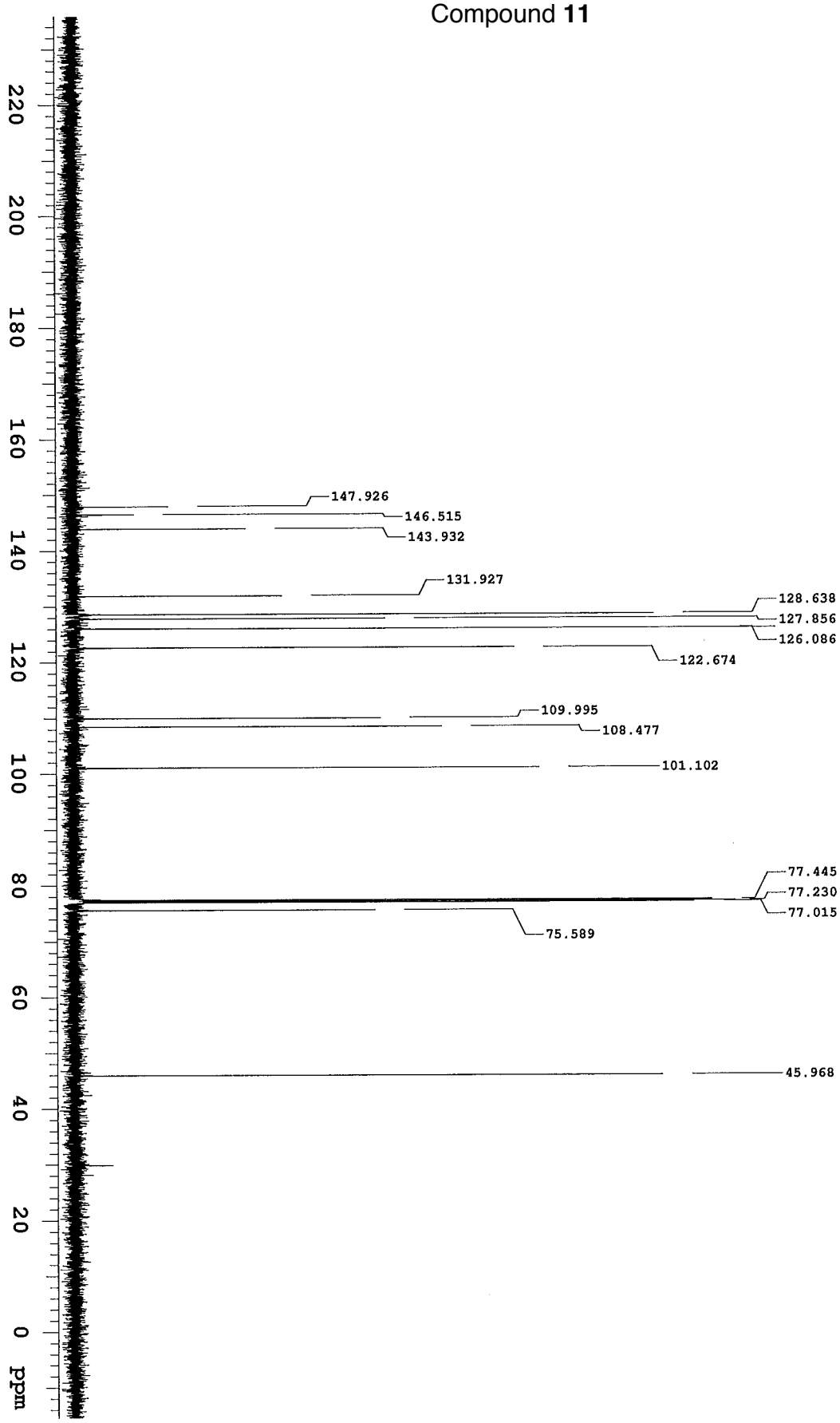
Compound **11**



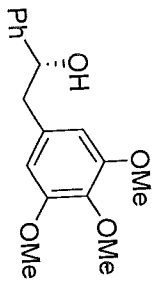


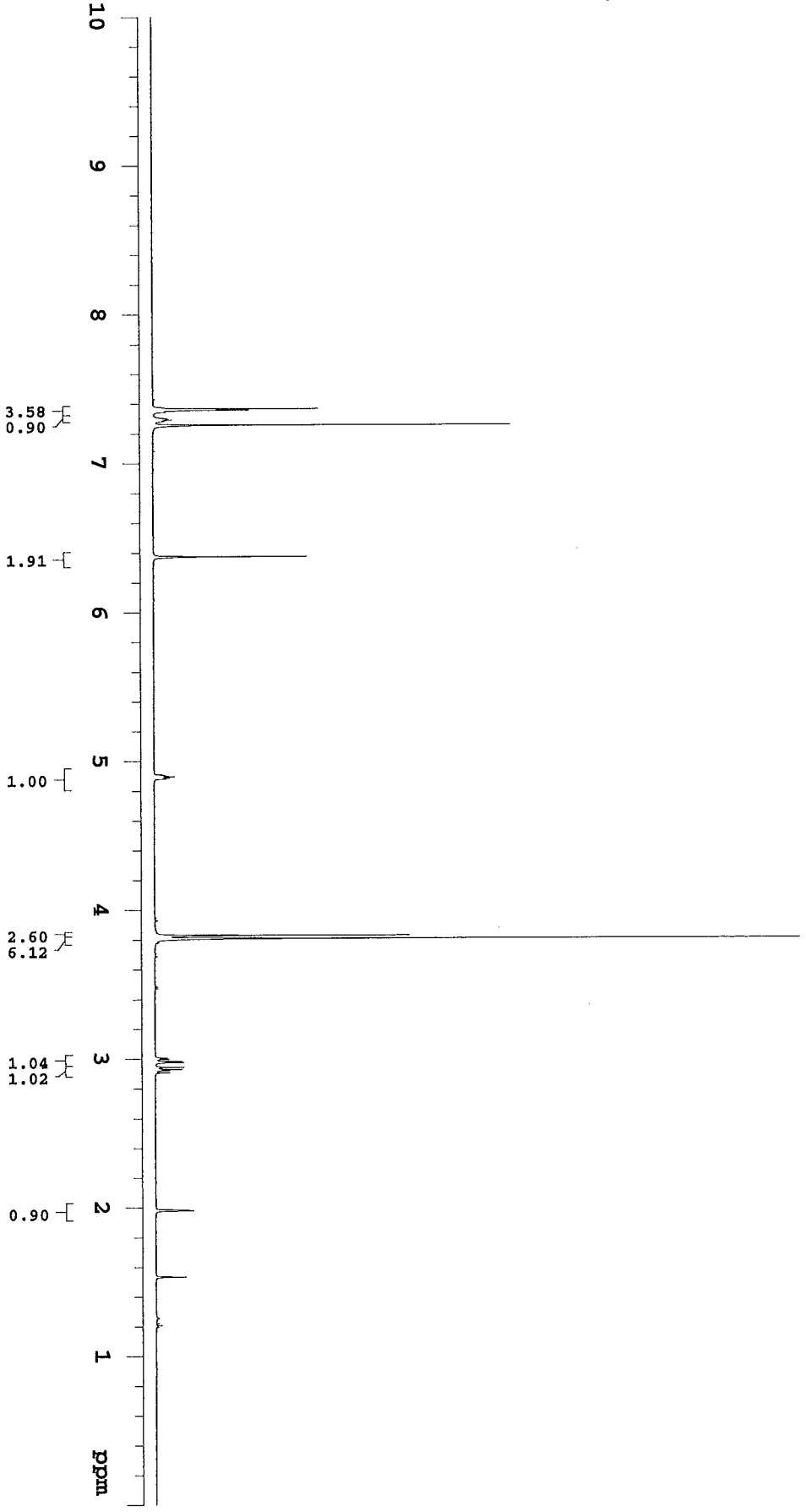
Compound **11**


Ph
OH
O
O

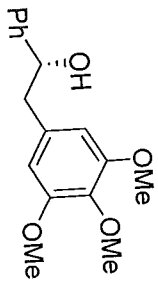

220
200
180
160
140
120
100
80
60
40
20
0
ppm
147.926
146.515
143.932
131.927
128.638
127.856
126.086
122.674
109.995
108.477
101.102
77.445
77.230
77.015
75.589
45.968

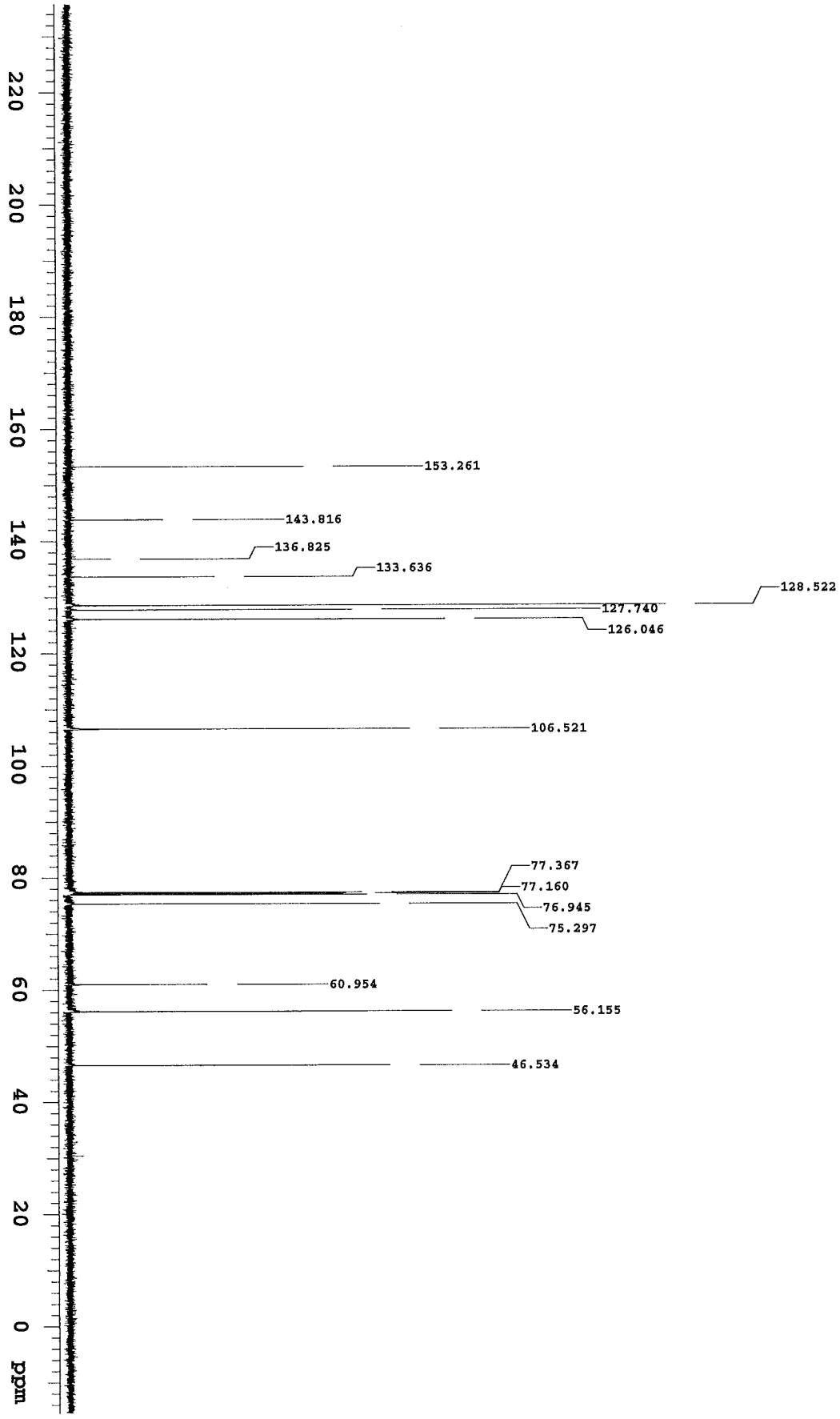
Compound **12**


Ph
OH
OMe
OMe
OMe

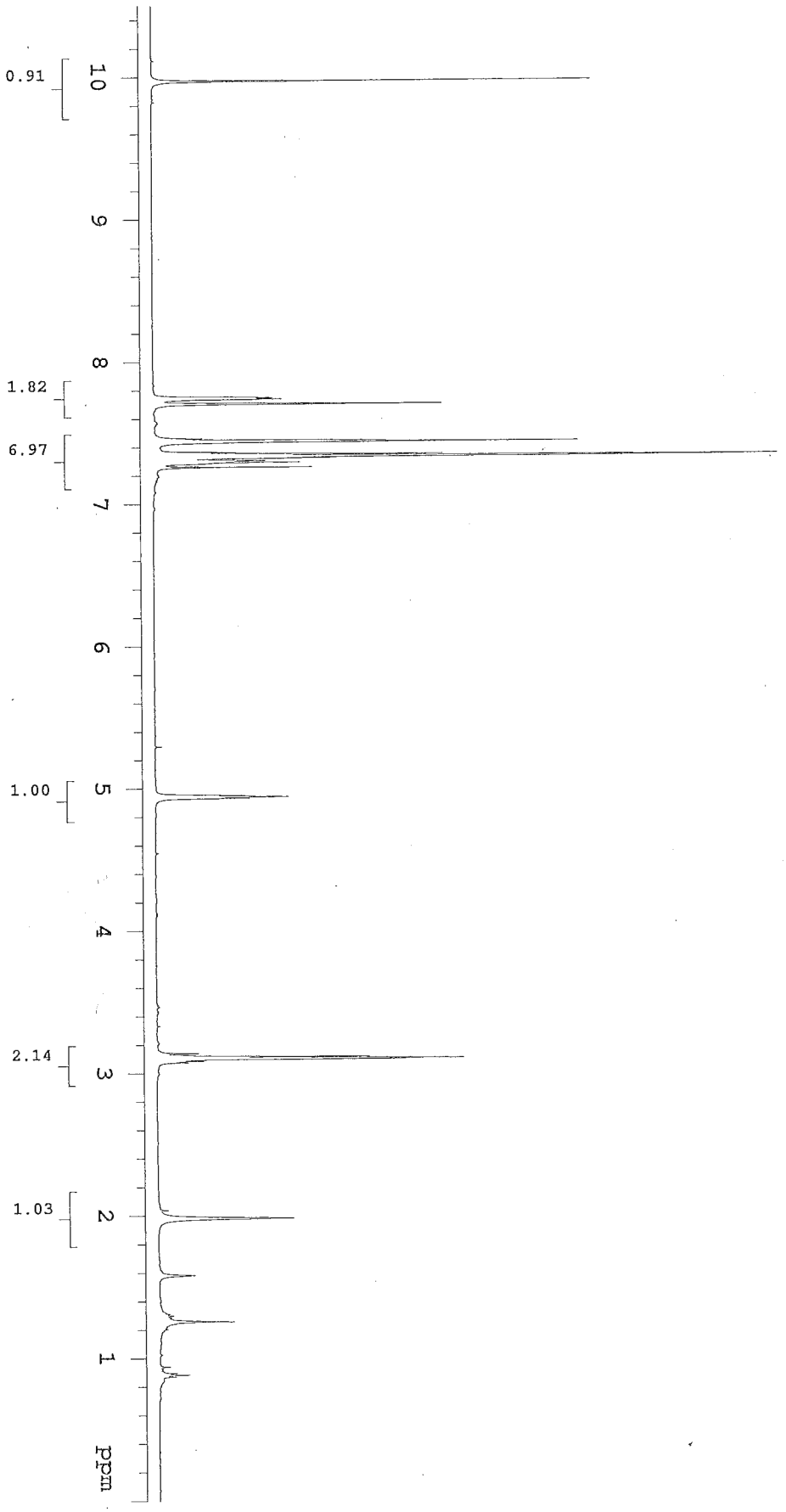

10
9
8
7
6
5
4
3
2
1
ppm
3.58
0.90
1.91
1.00
2.60
6.12
1.04
1.02
0.90

Compound **12**

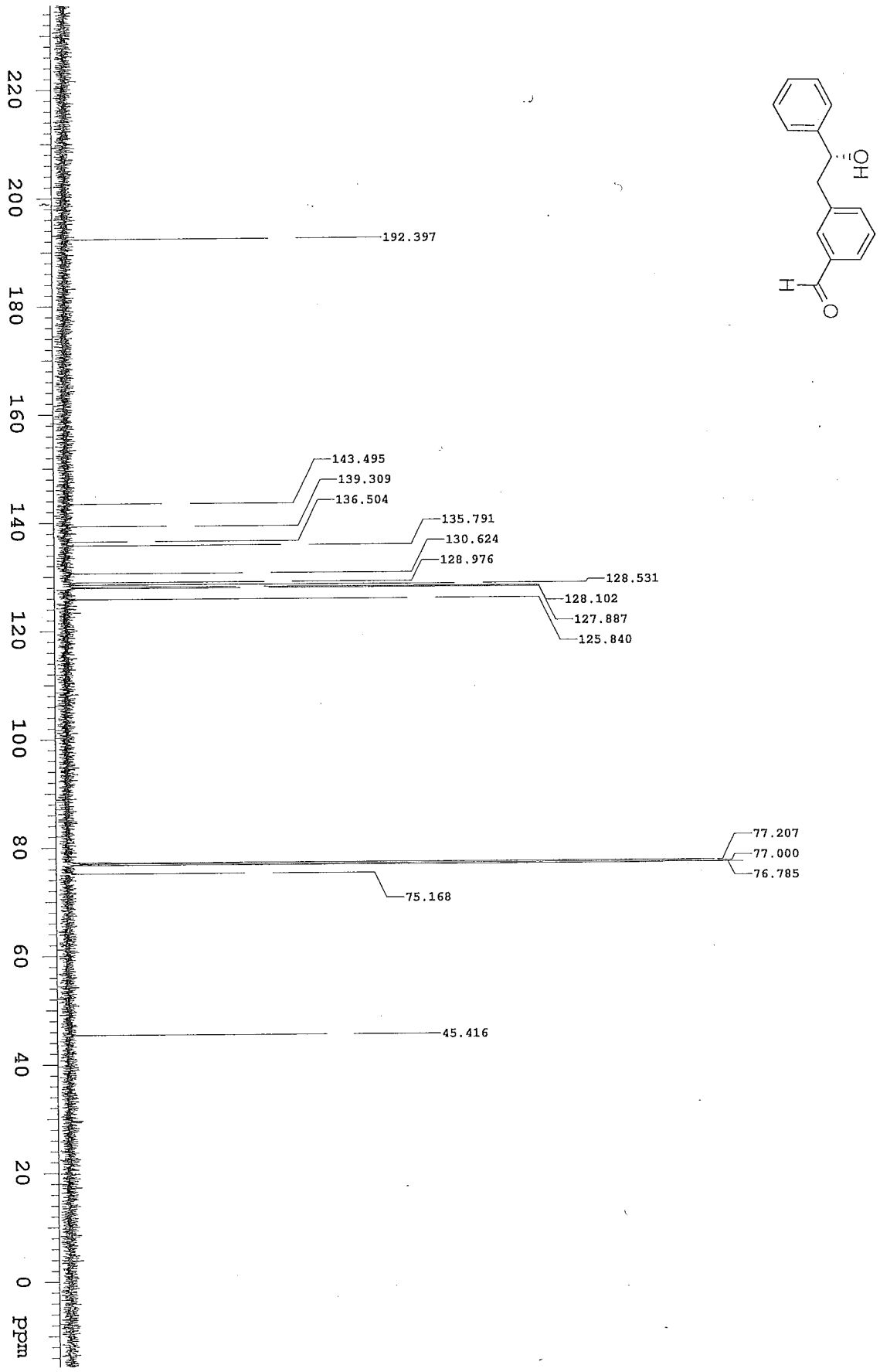

Ph
OH
OMe
OMe
OMe


220
200
180
160
140
120
100
80
60
40
20
0
ppm
153.261
143.816
136.825
133.636
128.522
127.740
126.046
106.521
77.367
77.160
76.945
75.297
60.954
56.155
46.534

Compound **13**



Compound **13**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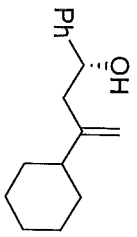
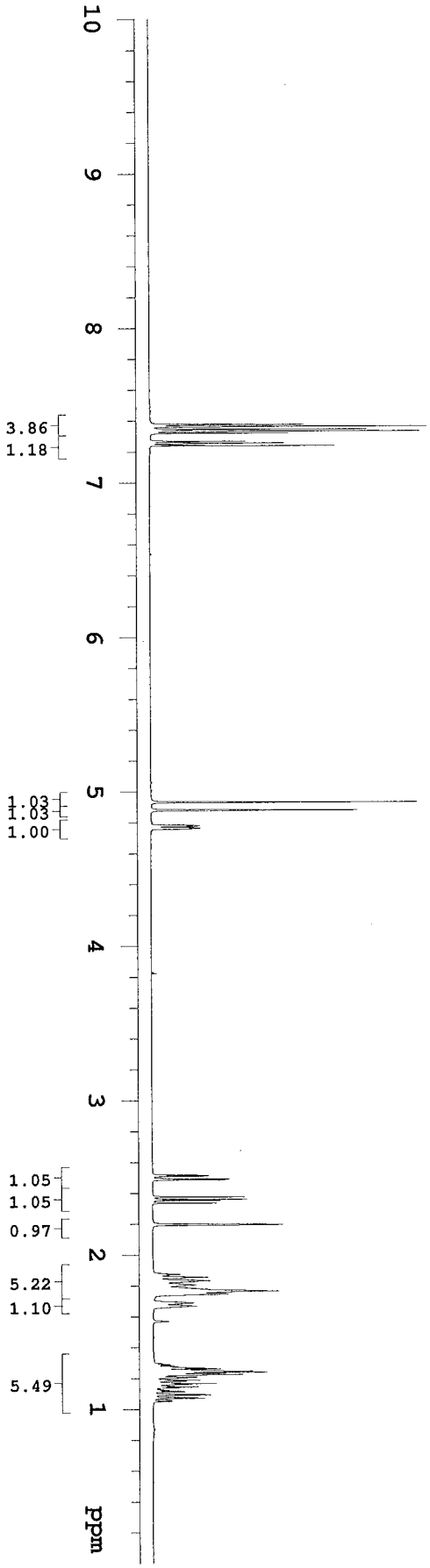
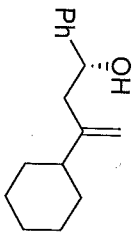
200
180
160
140
120
100
80
60
40
20
0
ppm
192.397
143.495
139.309
136.504
135.791
130.624
128.976
128.531
128.102
127.887
125.840
77.207
77.000
76.785
75.168
45.416
OH
H
O

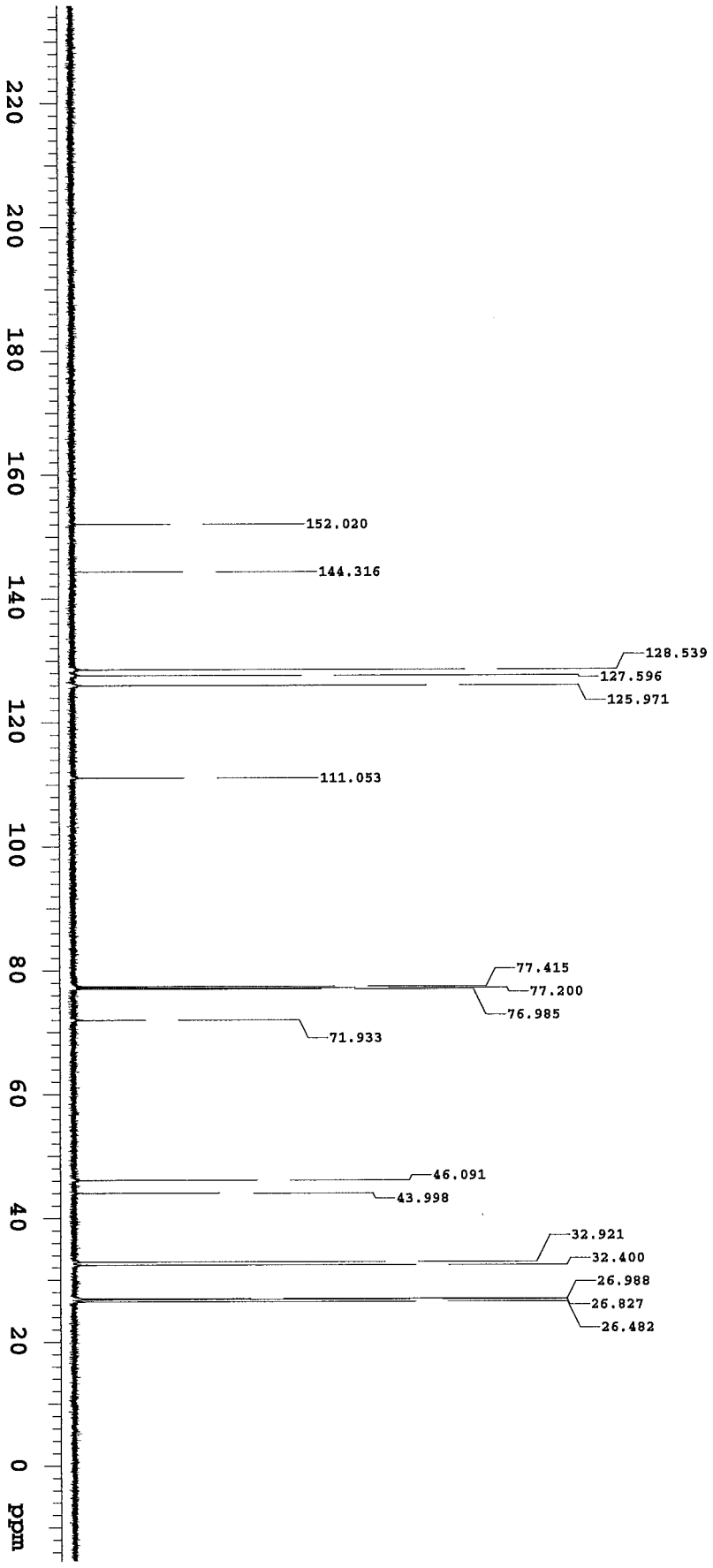
Compound **14**


Ph
OH

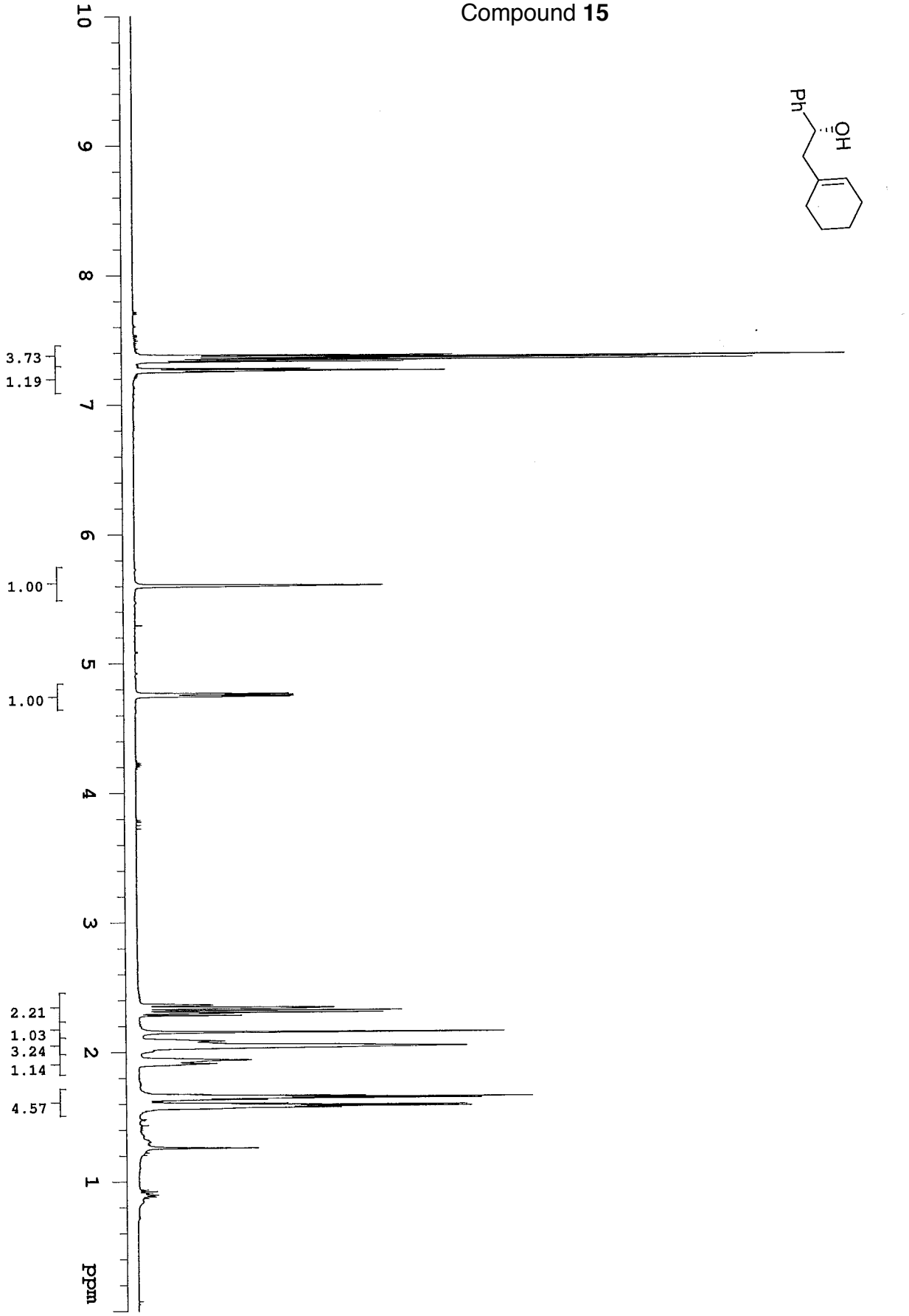

10
9
8
7
6
5
4
3
2
1
ppm
3.86
1.18
1.03
1.03
1.00
1.05
1.05
0.97
5.22
1.10
5.49

Compound **14**

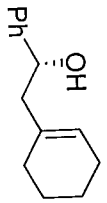

Ph
OH

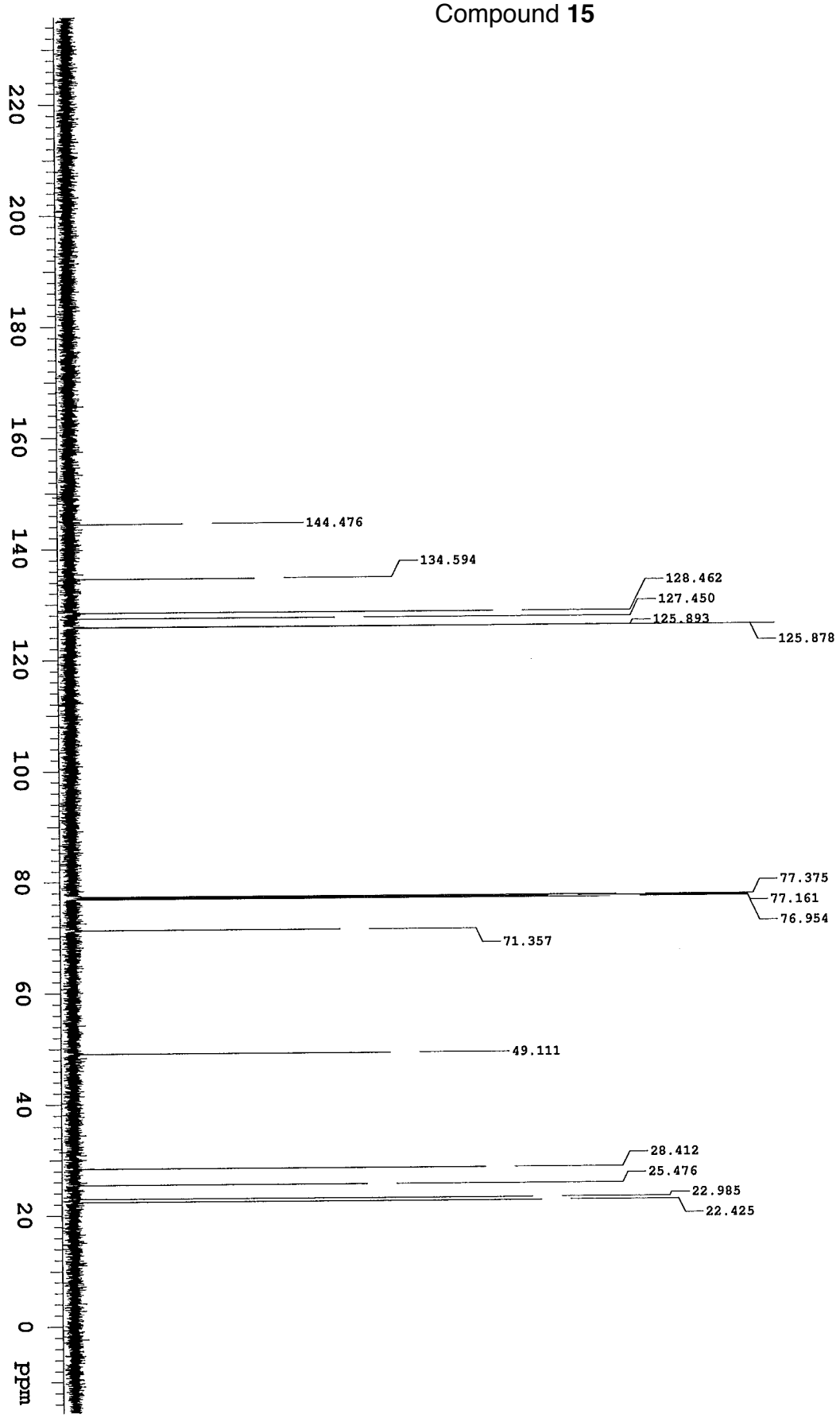

220
200
180
160
140
120
100
80
60
40
20
0
ppm
152.020
144.316
128.539
127.596
125.971
111.053
77.415
77.200
76.985
71.933
46.091
43.998
32.921
32.400
26.988
26.827
26.482

Compound **15**

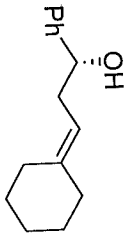


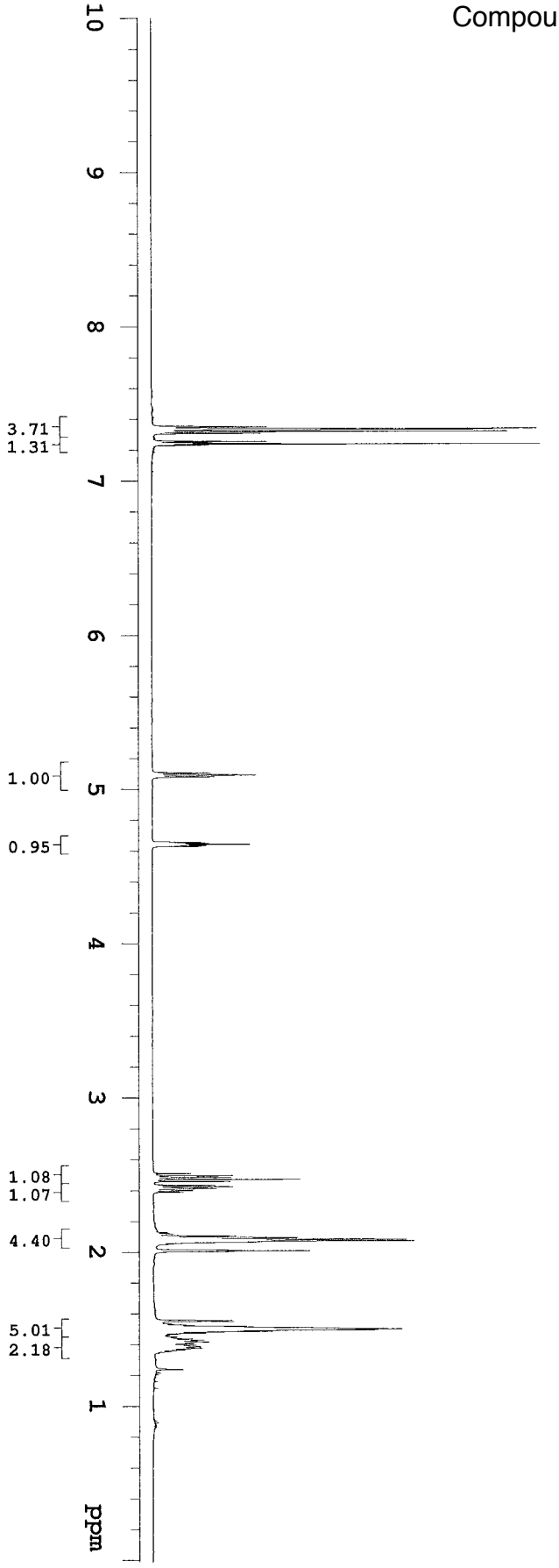
Compound **15**


Ph
OH

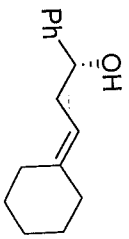

220
200
180
160
140
120
100
80
60
40
20
0
ppm
144.476
134.594
128.462
127.450
125.893
125.878
77.375
77.161
76.954
71.357
49.111
28.412
25.476
22.985
22.425

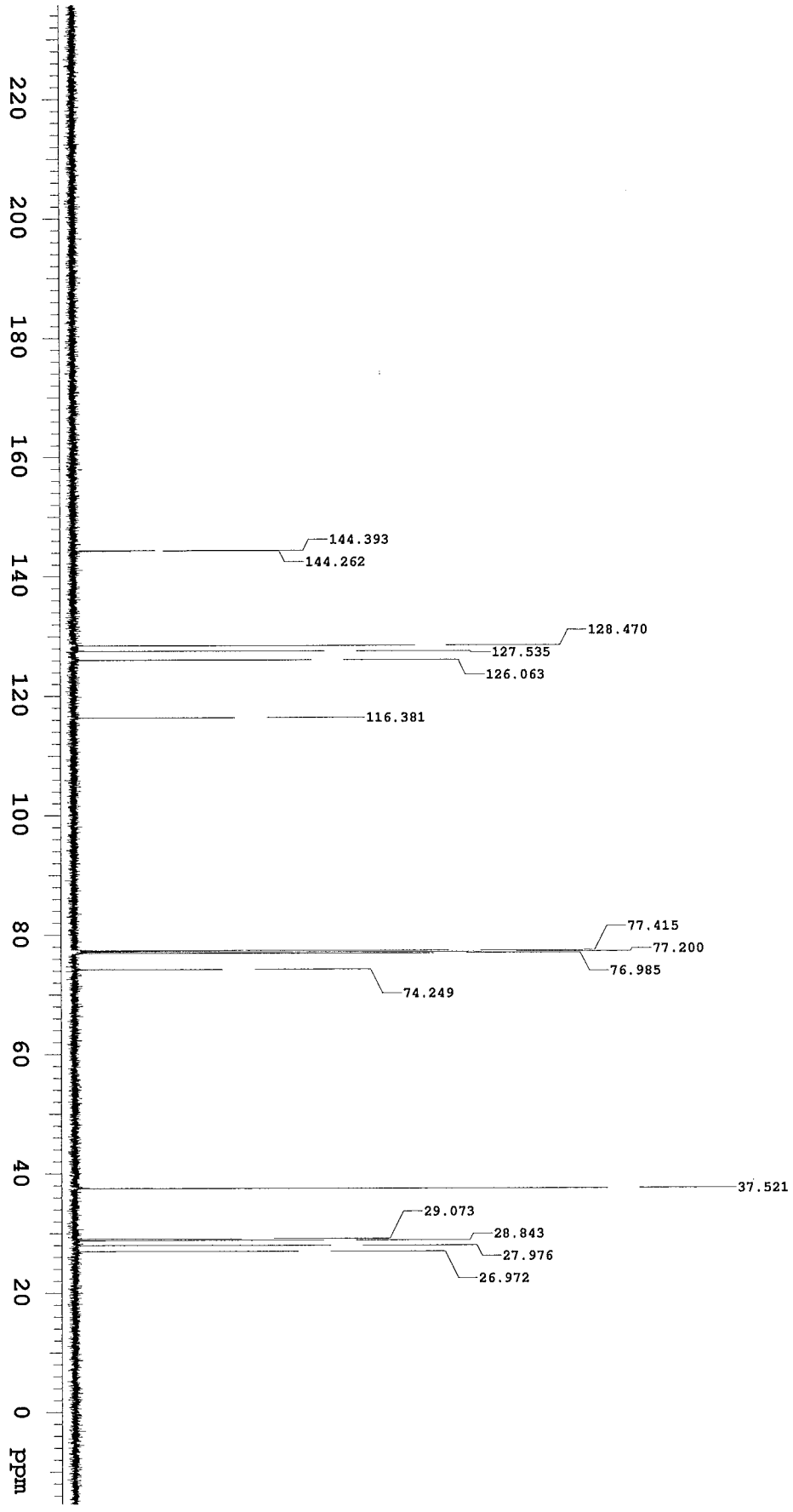
Compound **16**



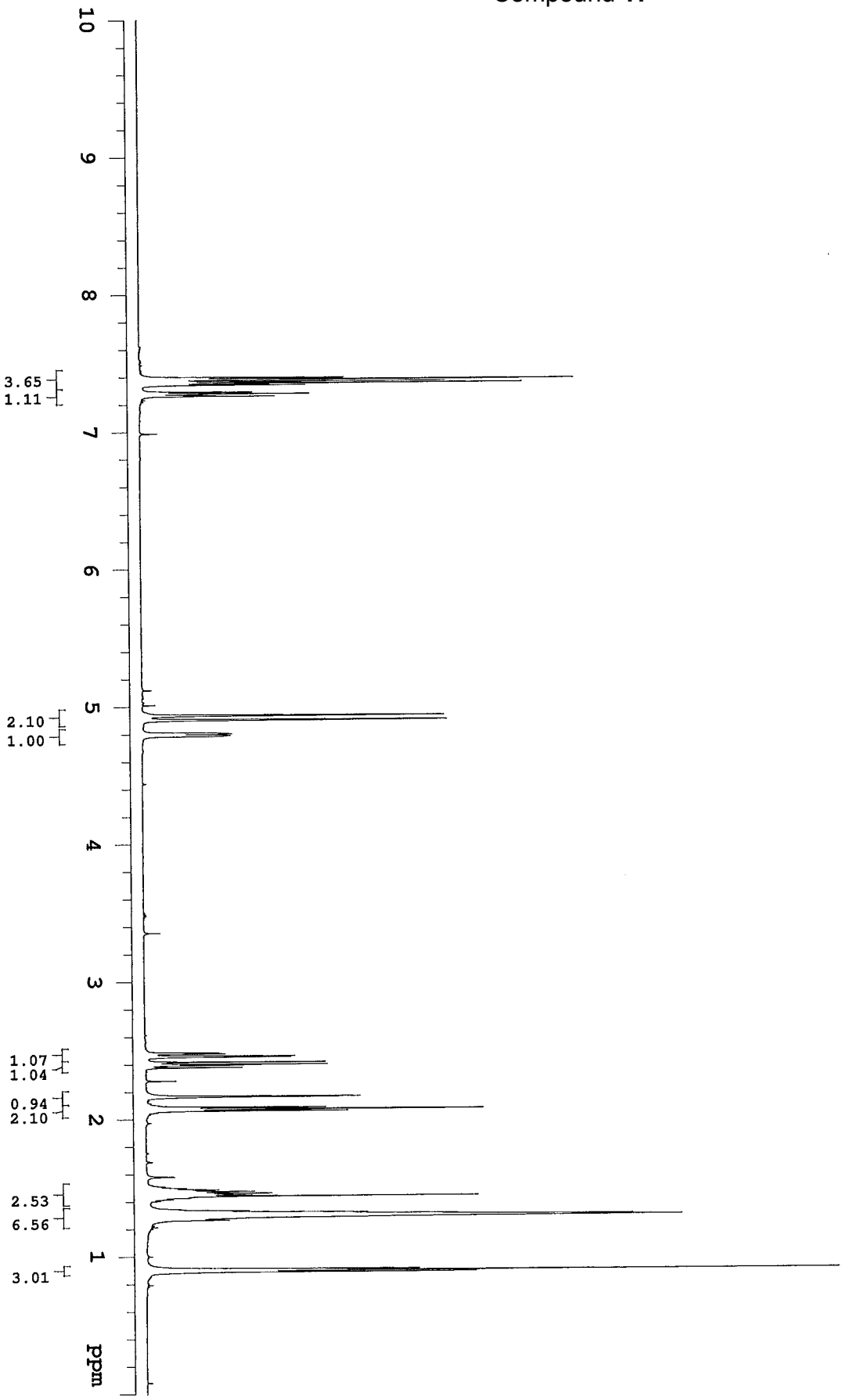


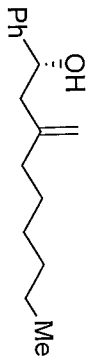
Compound **16**


Ph
OH

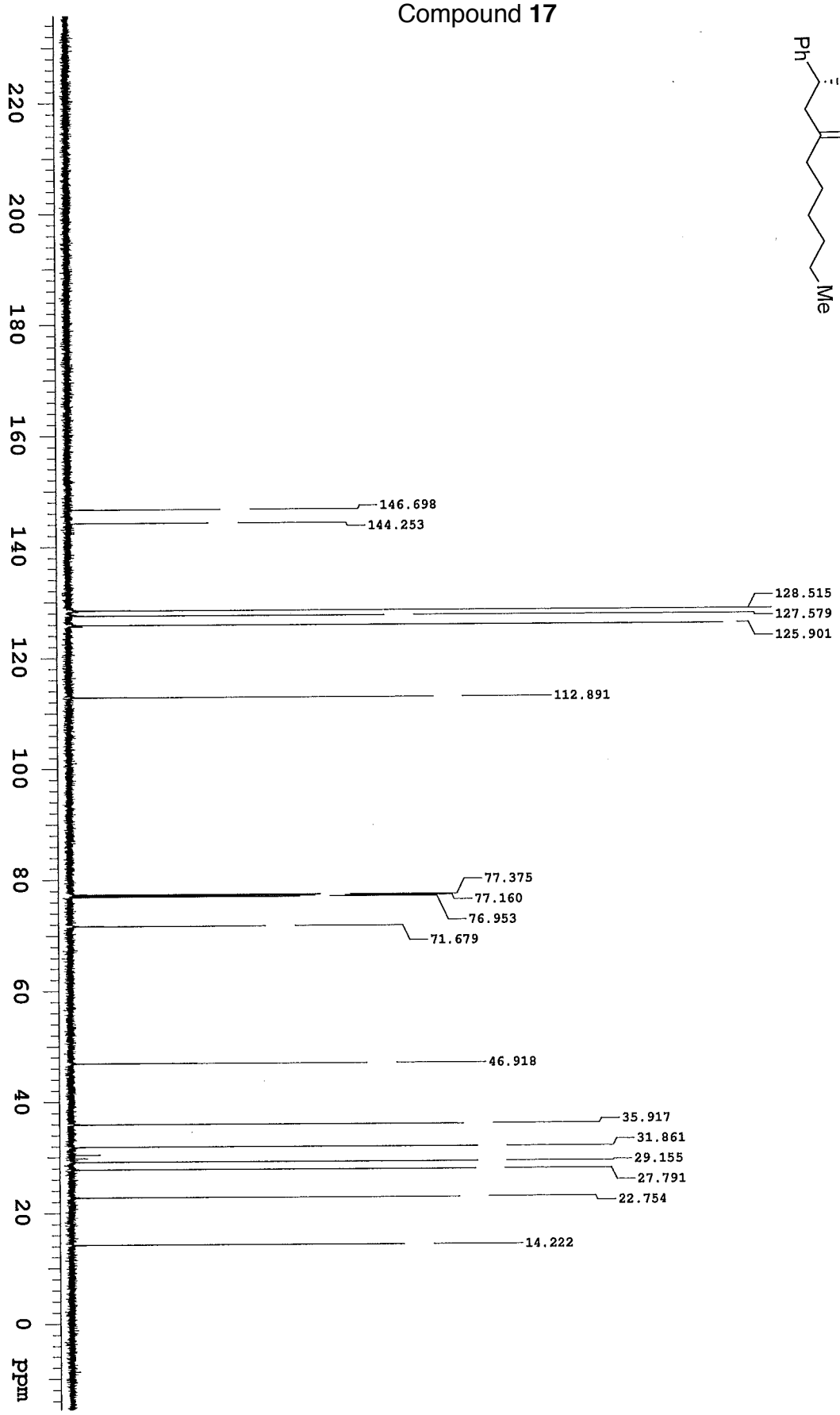

220
200
180
160
140
120
100
80
60
40
20
0
ppm
144.393
144.262
128.470
127.535
126.063
116.381
77.415
77.200
76.985
74.249
37.521
29.073
28.843
27.976
26.972

Compound **17**

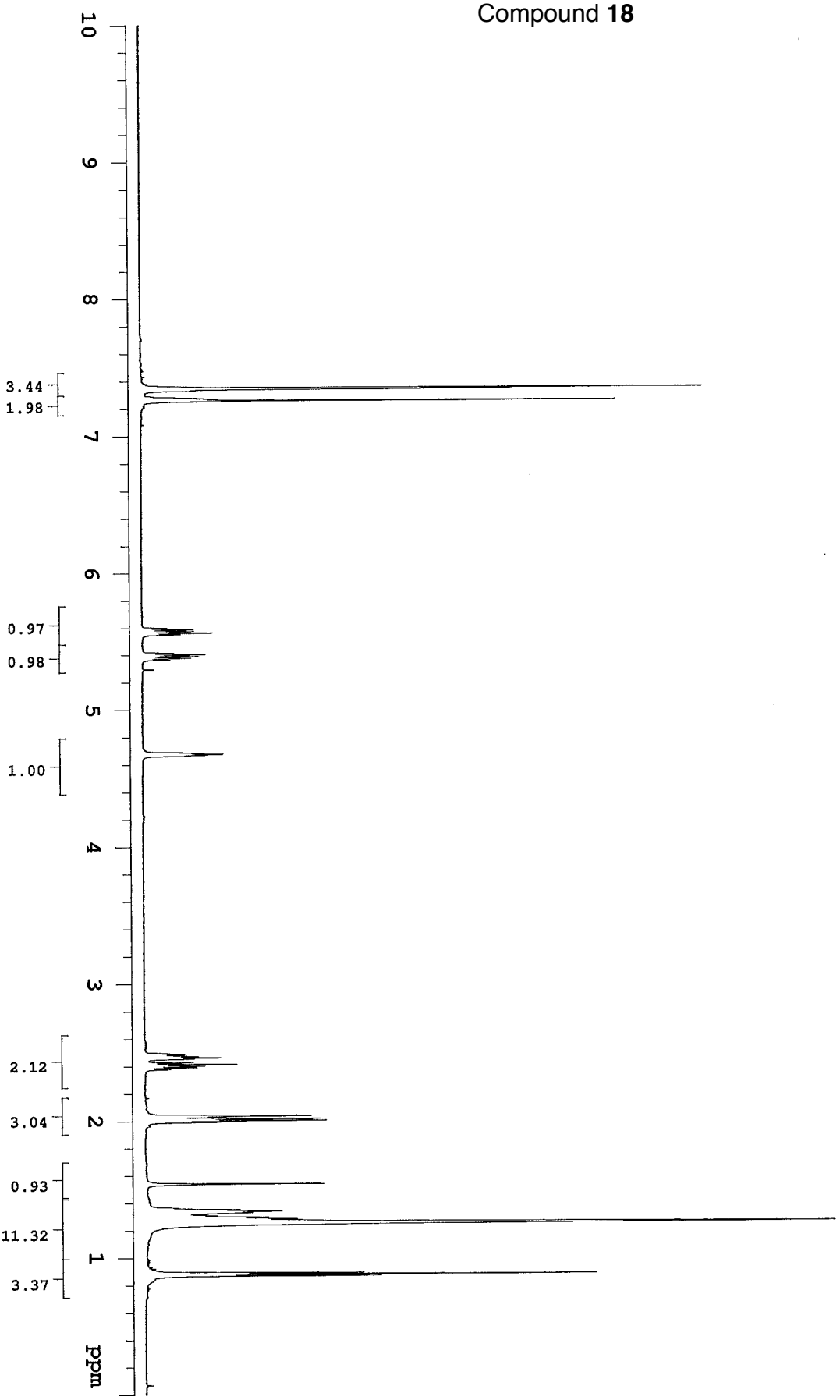

10
9
8
7
6
5
4
3
2
1
ppm
3.65
1.11
2.10
1.00
1.07
1.04
0.94
2.10
2.53
6.56
3.01


Ph
OH
Me

Compound **17**

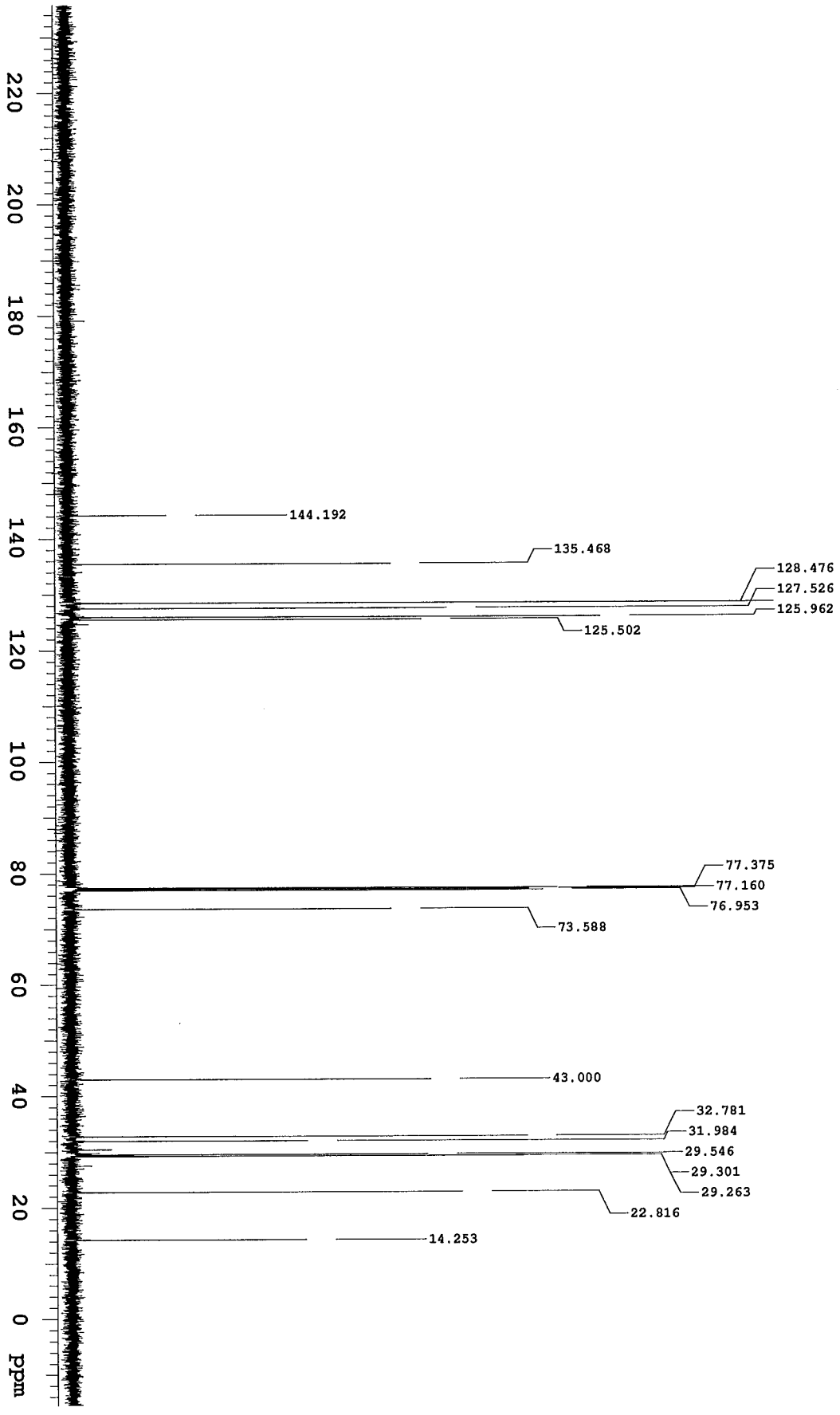

Ph
OH
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm
146.698
144.253
128.515
127.579
125.901
112.891
77.375
77.160
76.953
71.679
46.918
35.917
31.861
29.155
27.791
22.754
14.222

Compound **18**

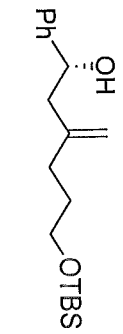

10
9
8
7
6
5
4
3
2
1
ppm
3.44
1.98
0.97
0.98
1.00
2.12
3.04
0.93
11.32
3.37

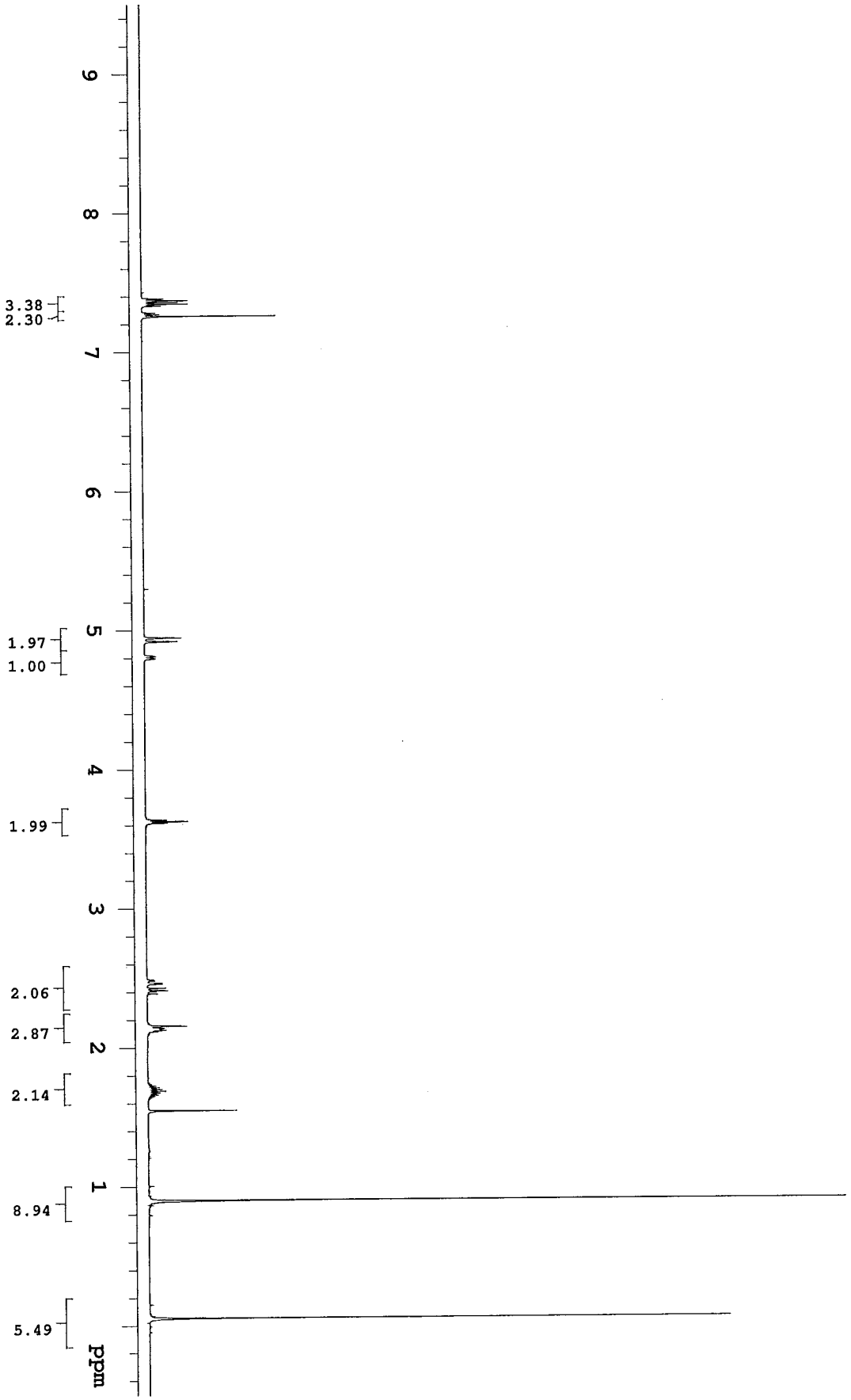

Ph
OH
Me

Compound **18**

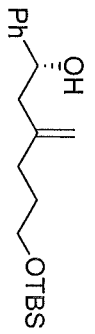

Ph
OH
Me
144.192
135.468
128.476
127.526
125.962
125.502
77.375
77.160
76.953
73.588
43.000
32.781
31.984
29.546
29.301
29.263
22.816
14.253
220
200
180
160
140
120
100
80
60
40
20
0
ppm

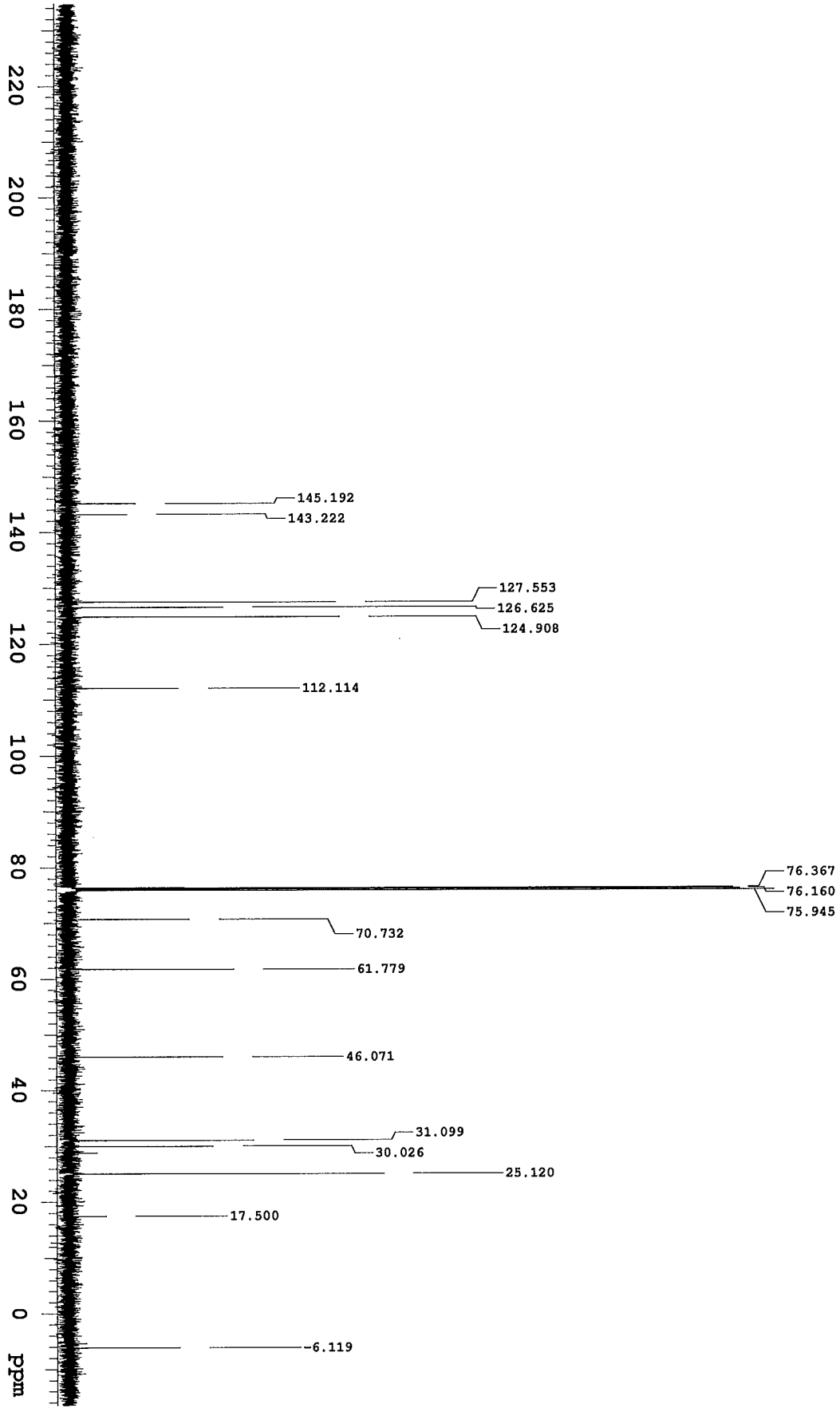
Compound **19**



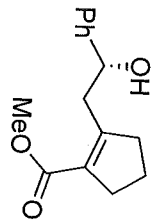


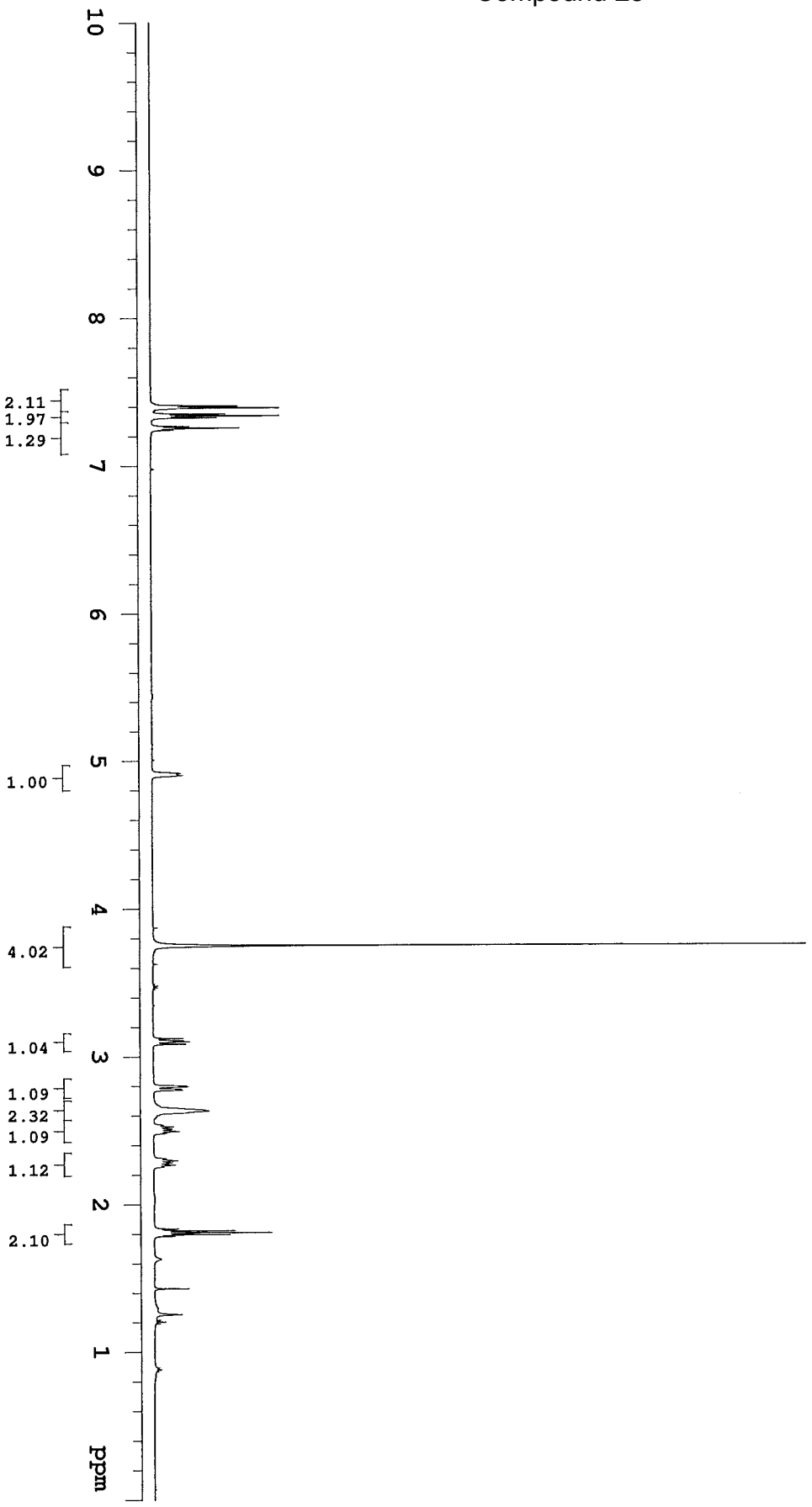
Compound **19**


Ph
OH
OTBS

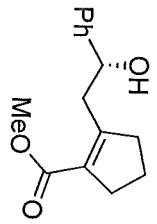

220
200
180
160
140
120
100
80
60
40
20
0
ppm
145.192
143.222
127.553
126.625
124.908
112.114
76.367
76.160
75.945
70.732
61.779
46.071
31.099
30.026
25.120
17.500
-6.119

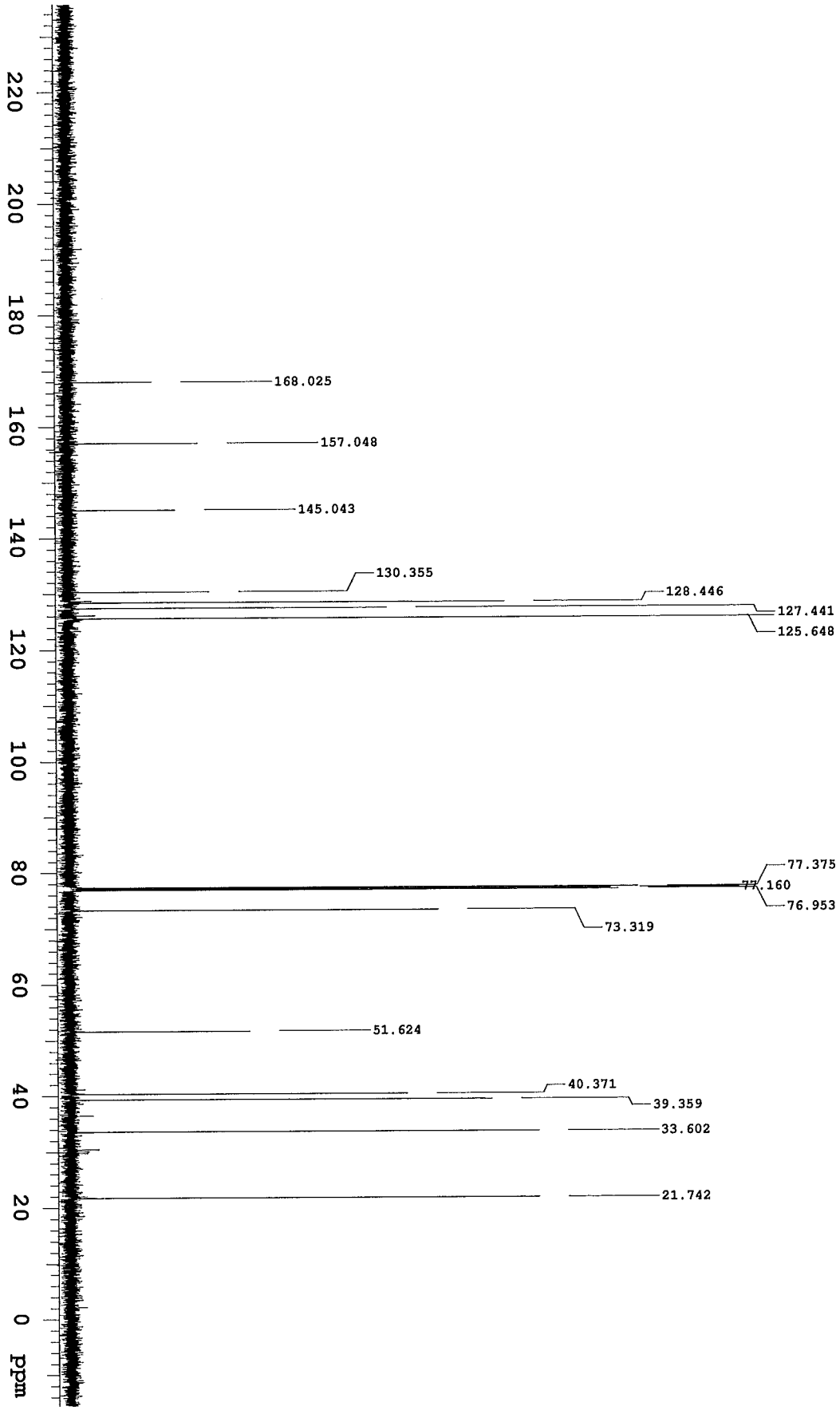
Compound **20**


Ph
OH
MeO
O

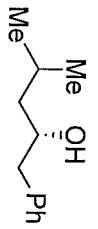

10
9
8
7
6
5
4
3
2
1
ppm
2.11
1.97
1.29
1.00
4.02
1.04
1.09
2.32
1.09
1.12
2.10

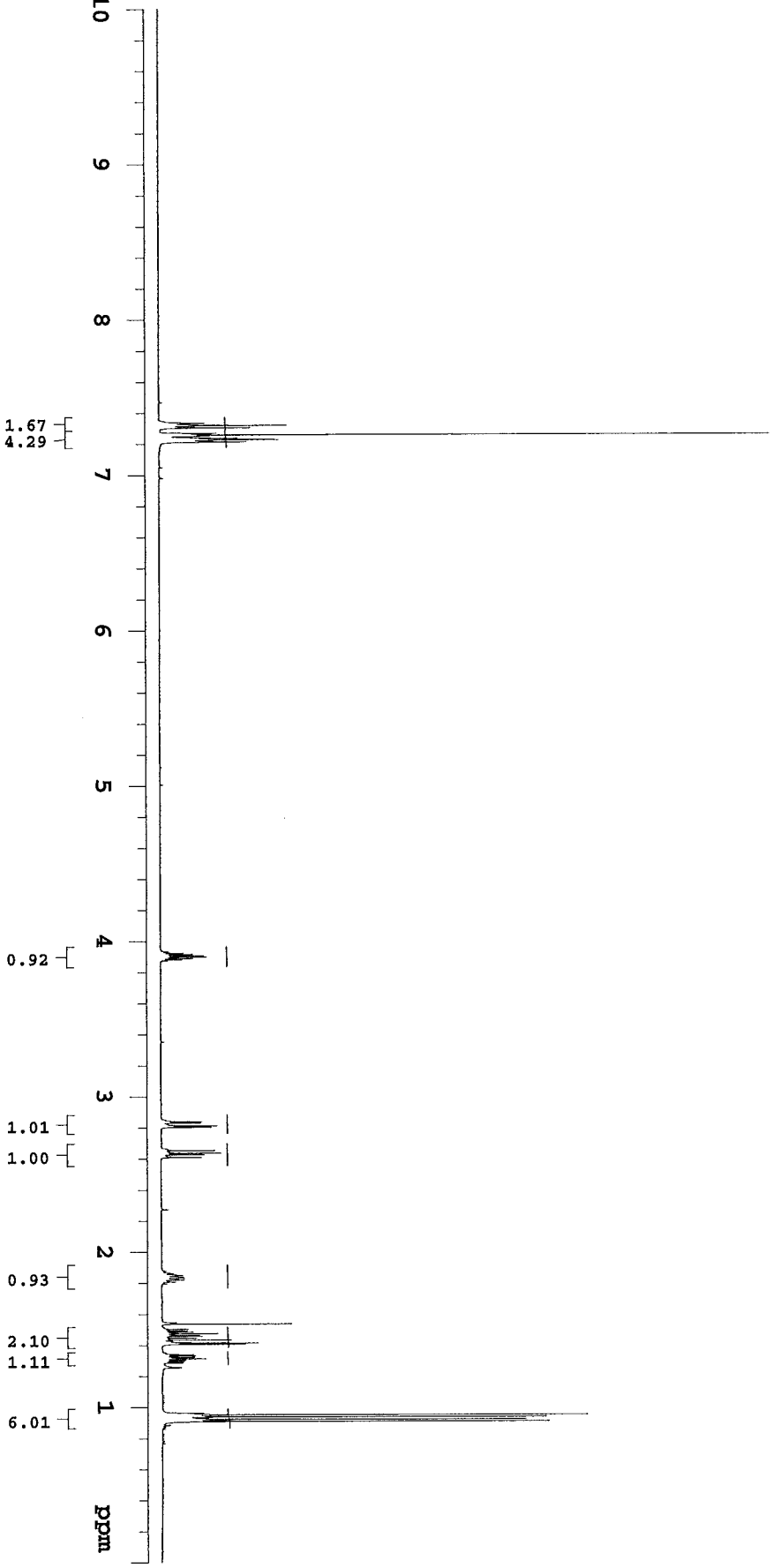
Compound **20**


Ph
OH
MeO
O

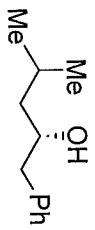

220
200
180
160
140
120
100
80
60
40
20
0
ppm
168.025
157.048
145.043
130.355
128.446
127.441
125.648
77.375
77.160
76.953
73.319
51.624
40.371
39.359
33.602
21.742

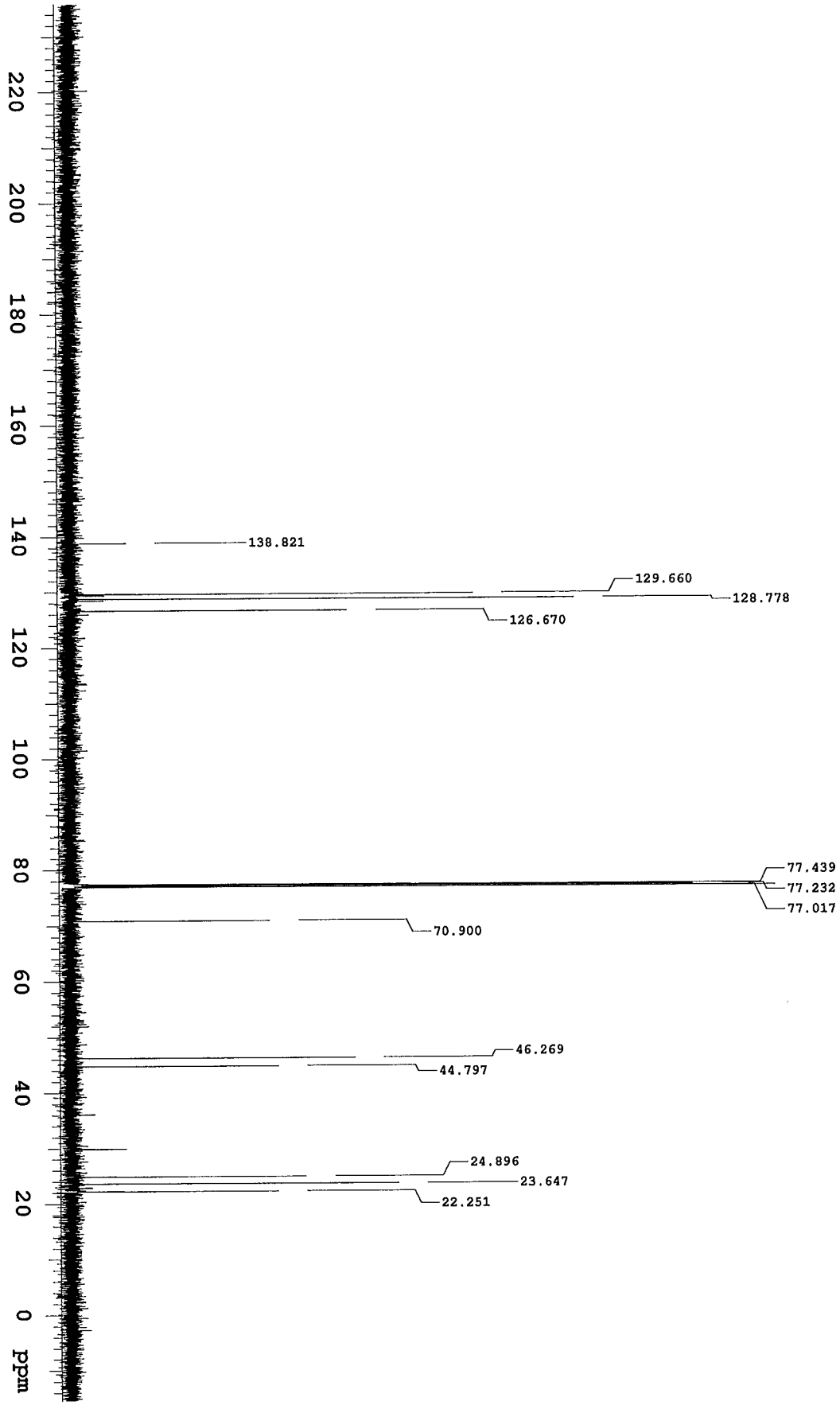
Compound **21**



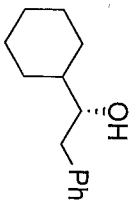


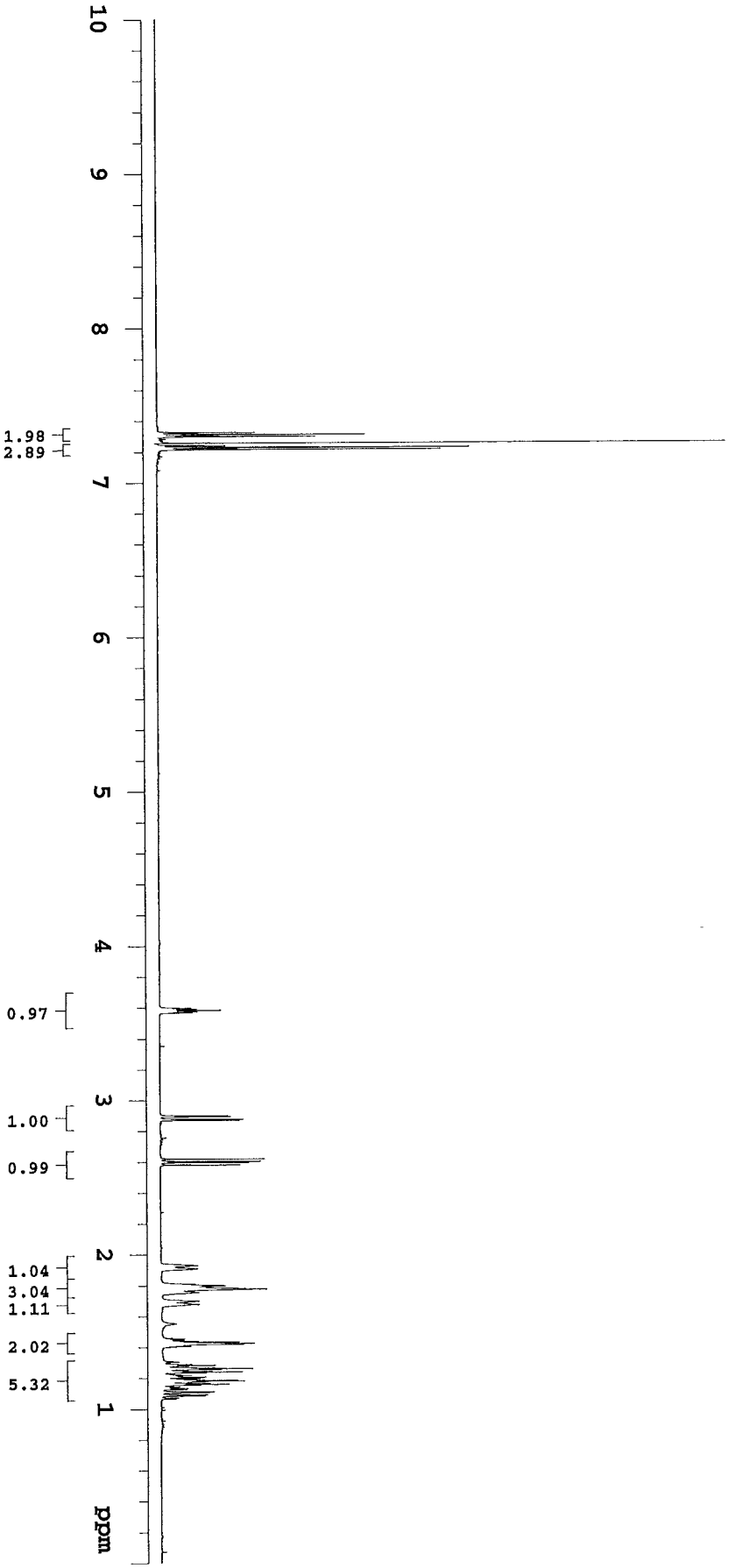
Compound **21**


Me
Me
OH
Ph

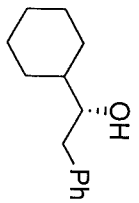

220
200
180
160
140
120
100
80
60
40
20
0
ppm
138.821
129.660
128.778
126.670
77.439
77.232
77.017
70.900
46.269
44.797
24.896
23.647
22.251

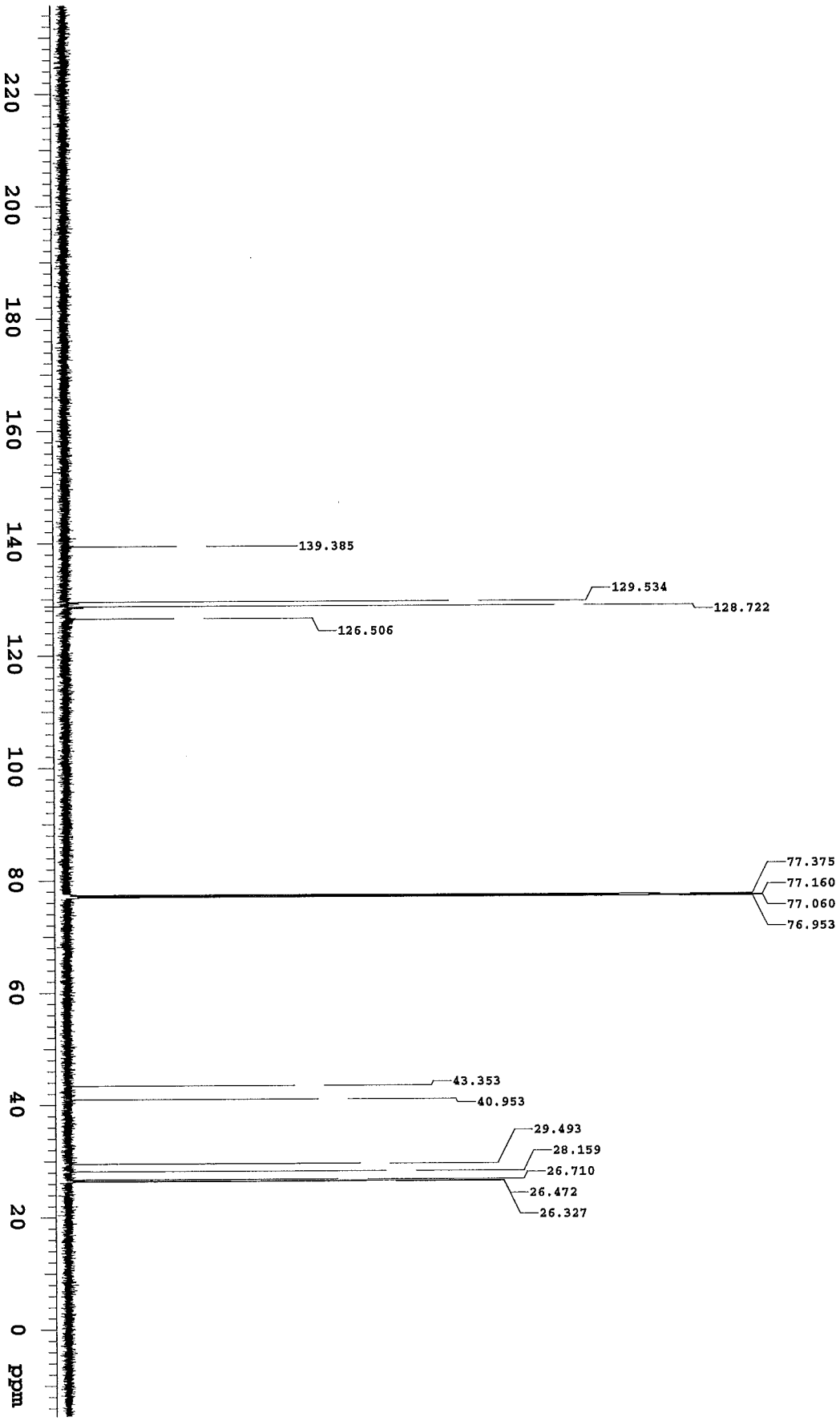
Compound **22**



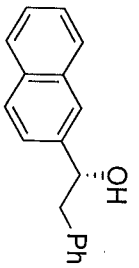


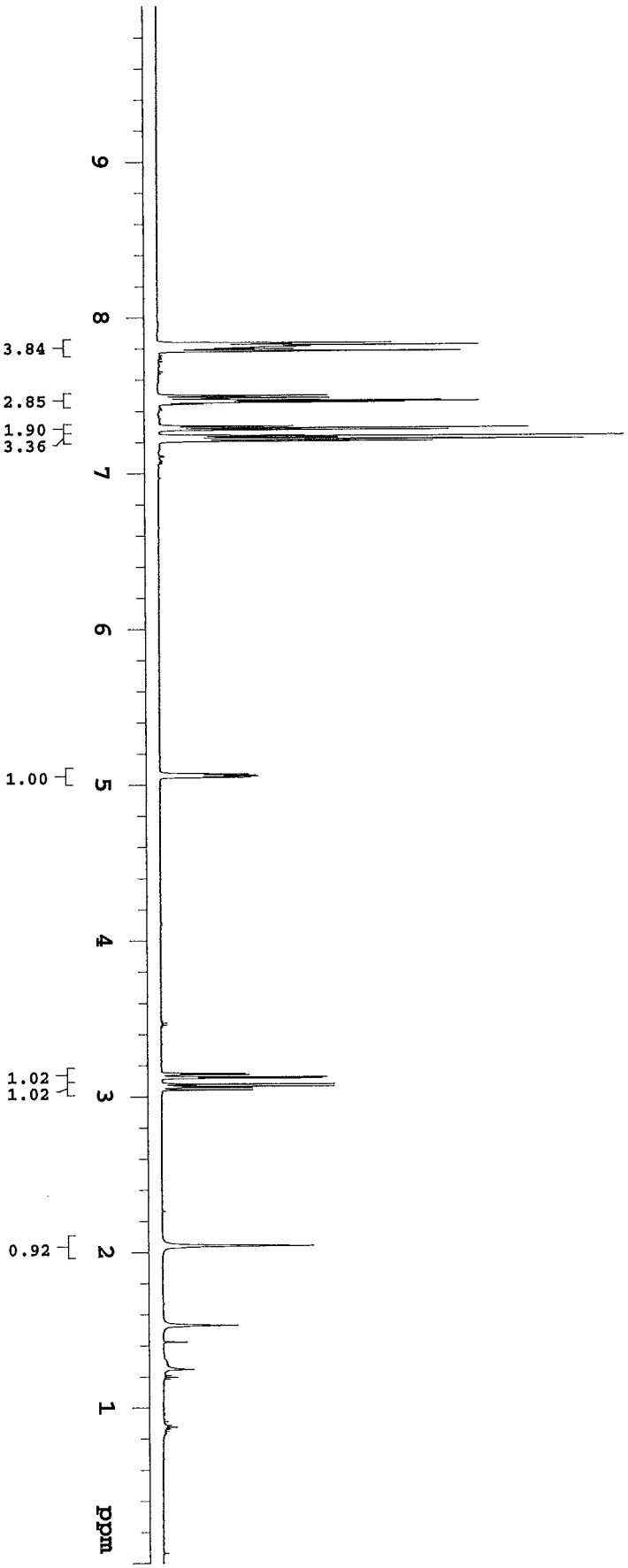
Compound **22**


OH
Ph

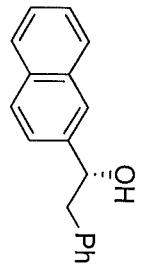

220
200
180
160
140
120
100
80
60
40
20
0
ppm
139.385
129.534
128.722
126.506
77.375
77.160
77.060
76.953
43.353
40.953
29.493
28.159
26.710
26.472
26.327

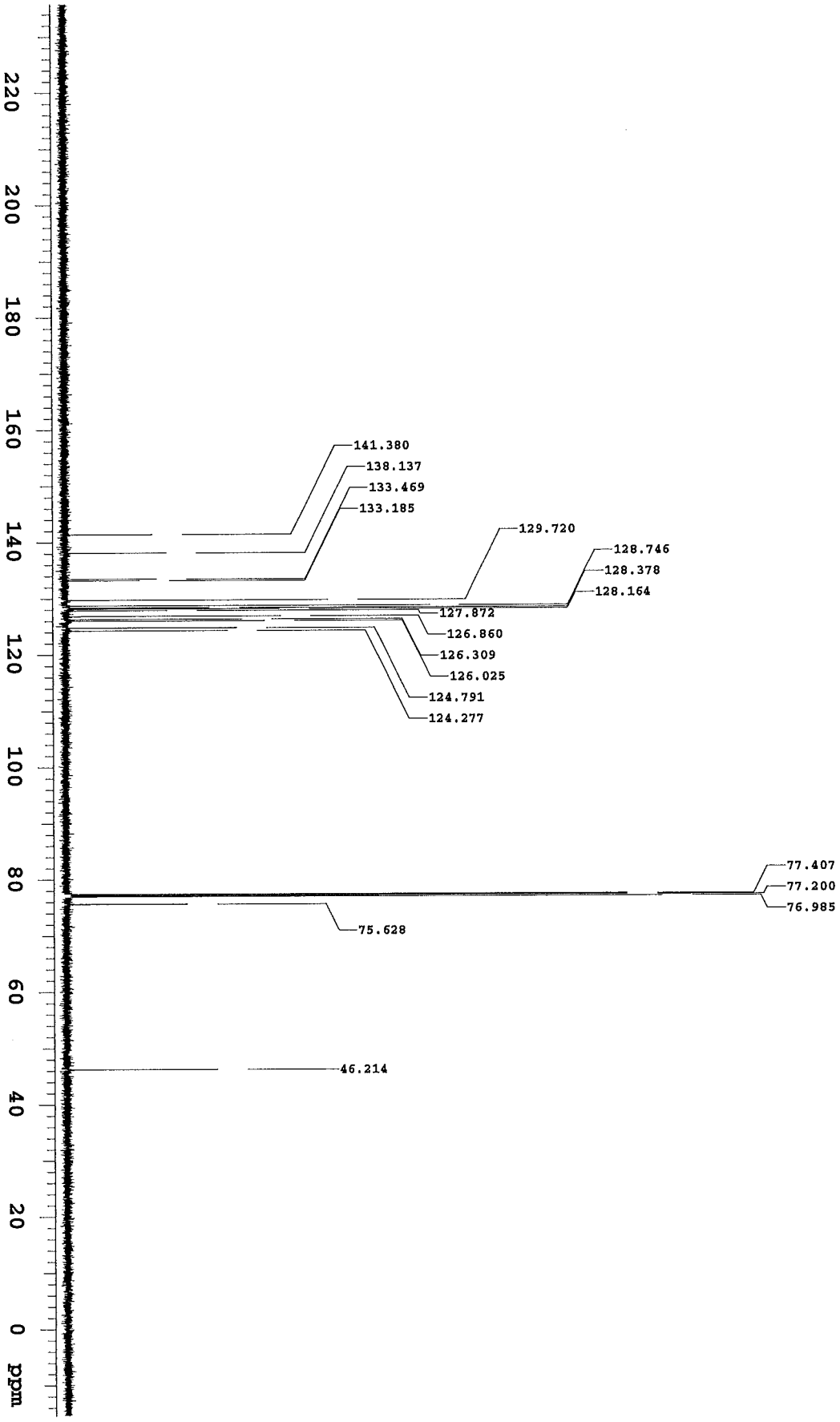
Compound **23**



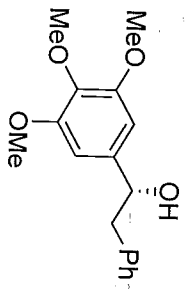


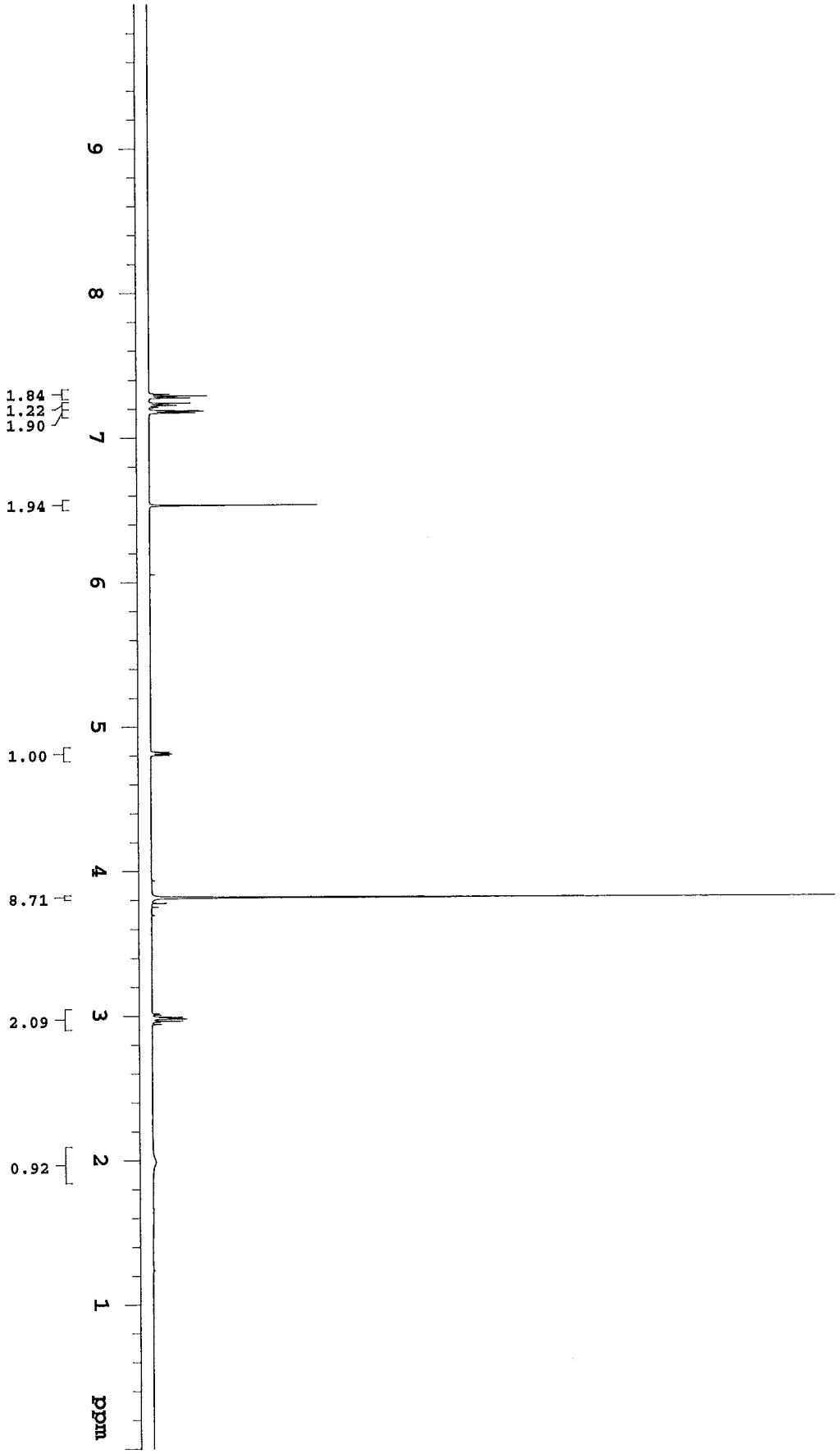
Compound **23**


OH
Ph

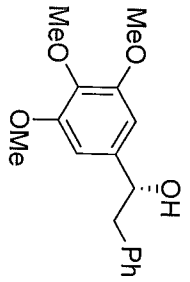

220
200
180
160
140
120
100
80
60
40
20
0 ppm
141.380
138.137
133.469
133.185
129.720
128.746
128.378
128.164
127.872
126.860
126.309
126.025
124.791
124.277
77.407
77.200
76.985
75.628
46.214

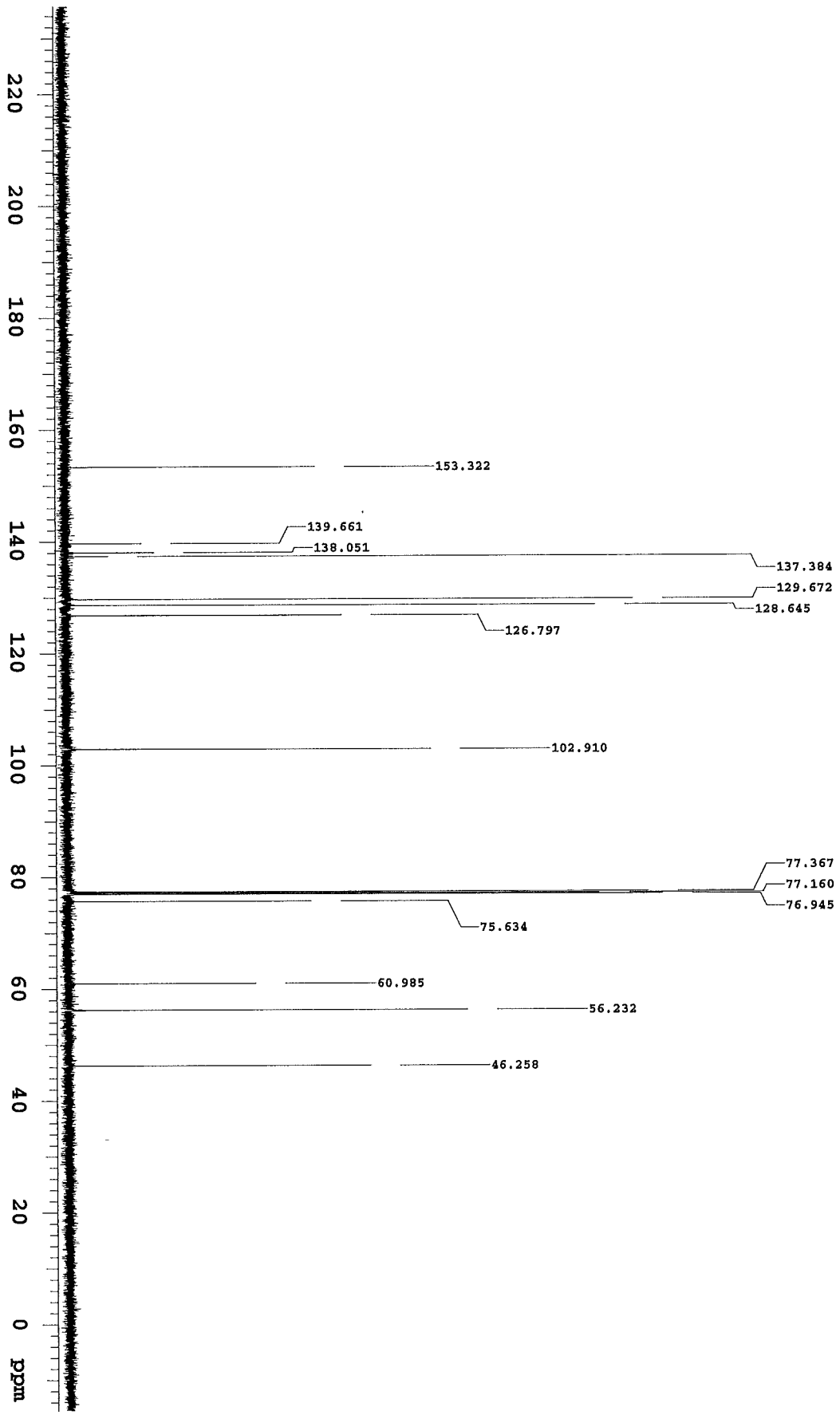
Compound **24**



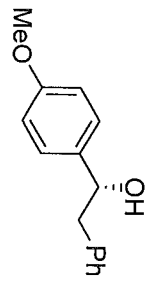


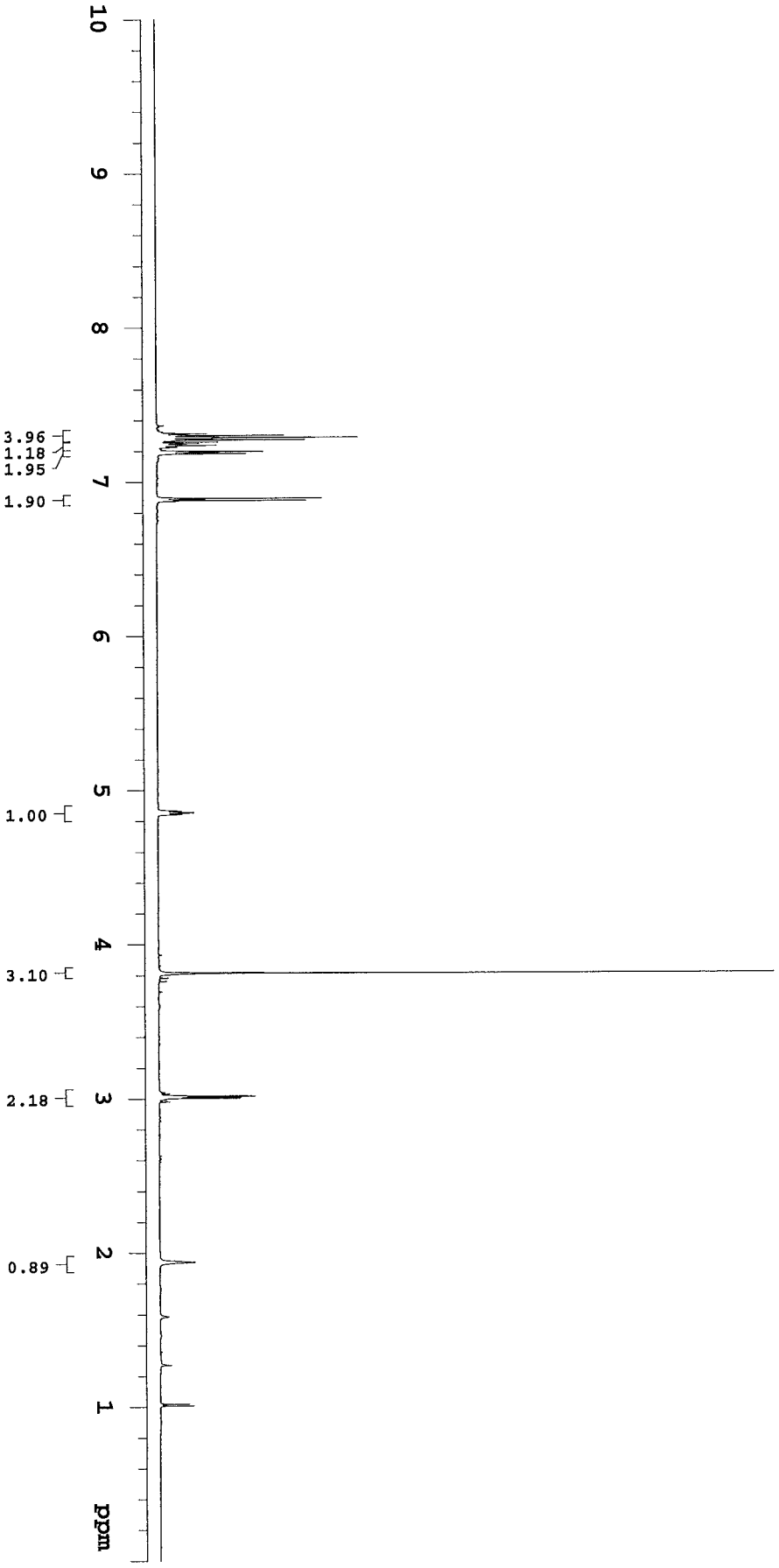
Compound **24**


MeO
MeO
OMe
OH
Ph

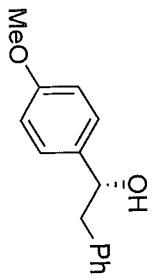

220
200
180
160
140
120
100
80
60
40
20
0
ppm
153.322
139.661
138.051
137.384
129.672
128.645
126.797
102.910
77.367
77.160
76.945
75.634
60.985
56.232
46.258

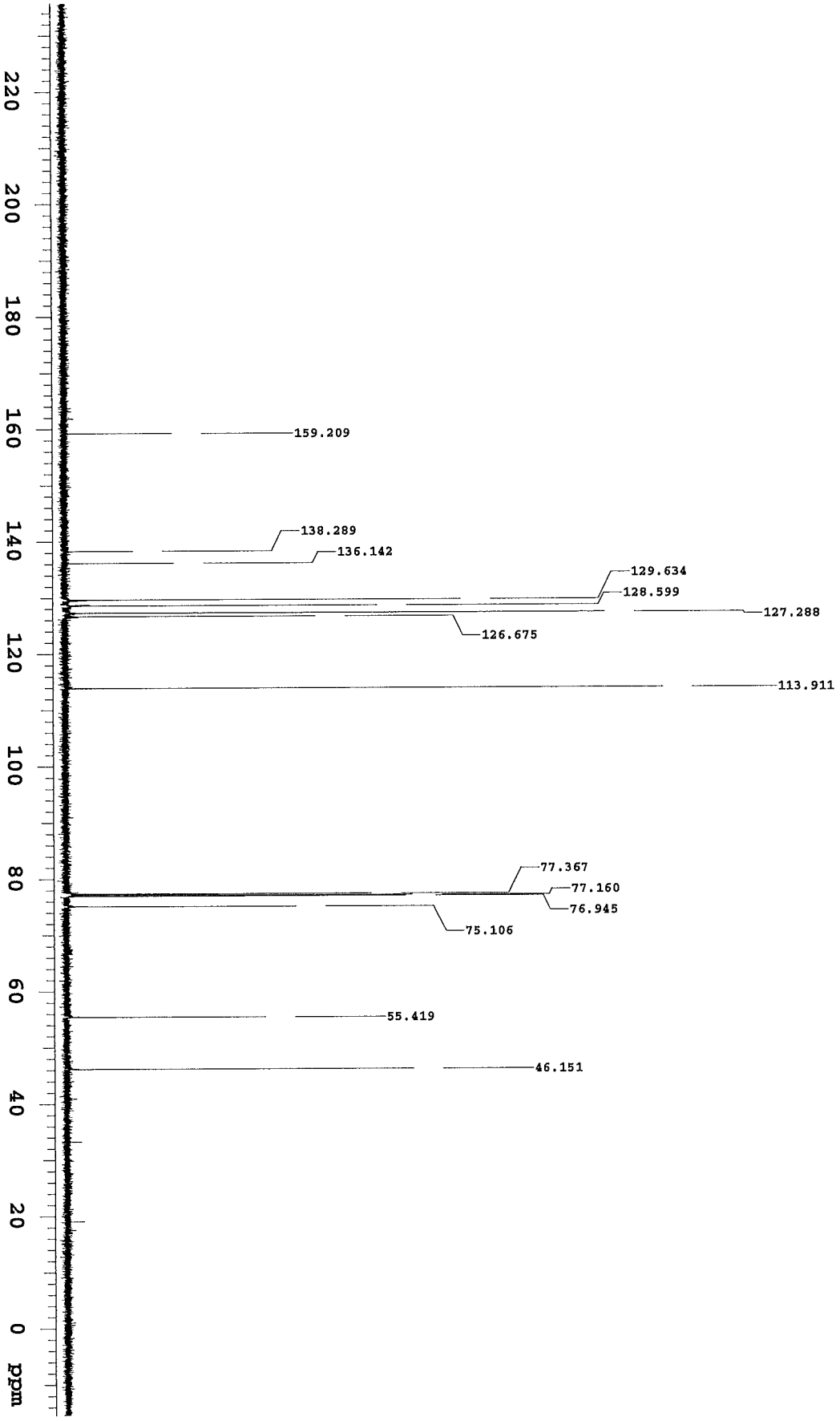
Compound **25**



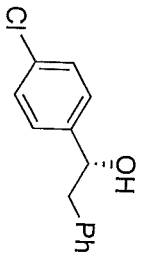


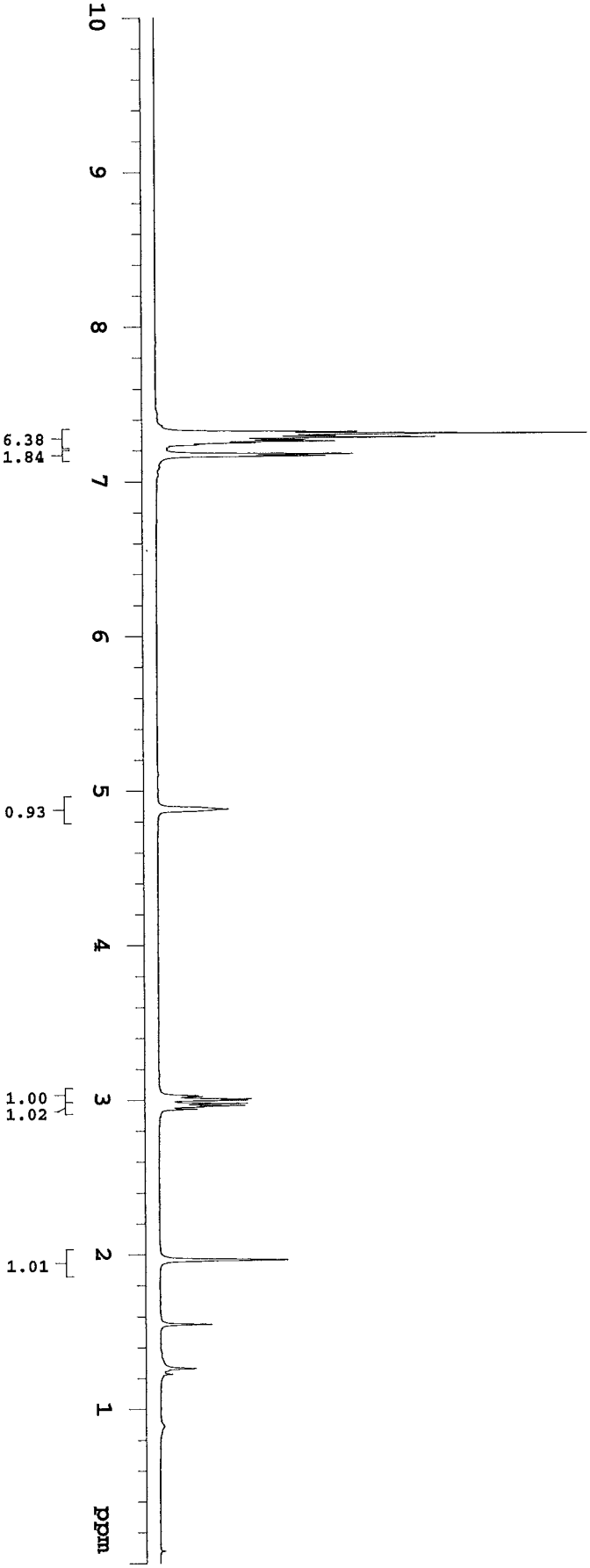
Compound **25**


MeO
OH
Ph

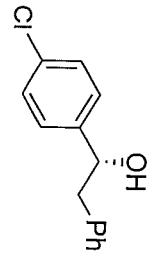

220
200
180
160
140
120
100
80
60
40
20
0 ppm
159.209
138.289
136.142
129.634
128.599
127.288
126.675
113.911
77.367
77.160
76.945
75.106
55.419
46.151

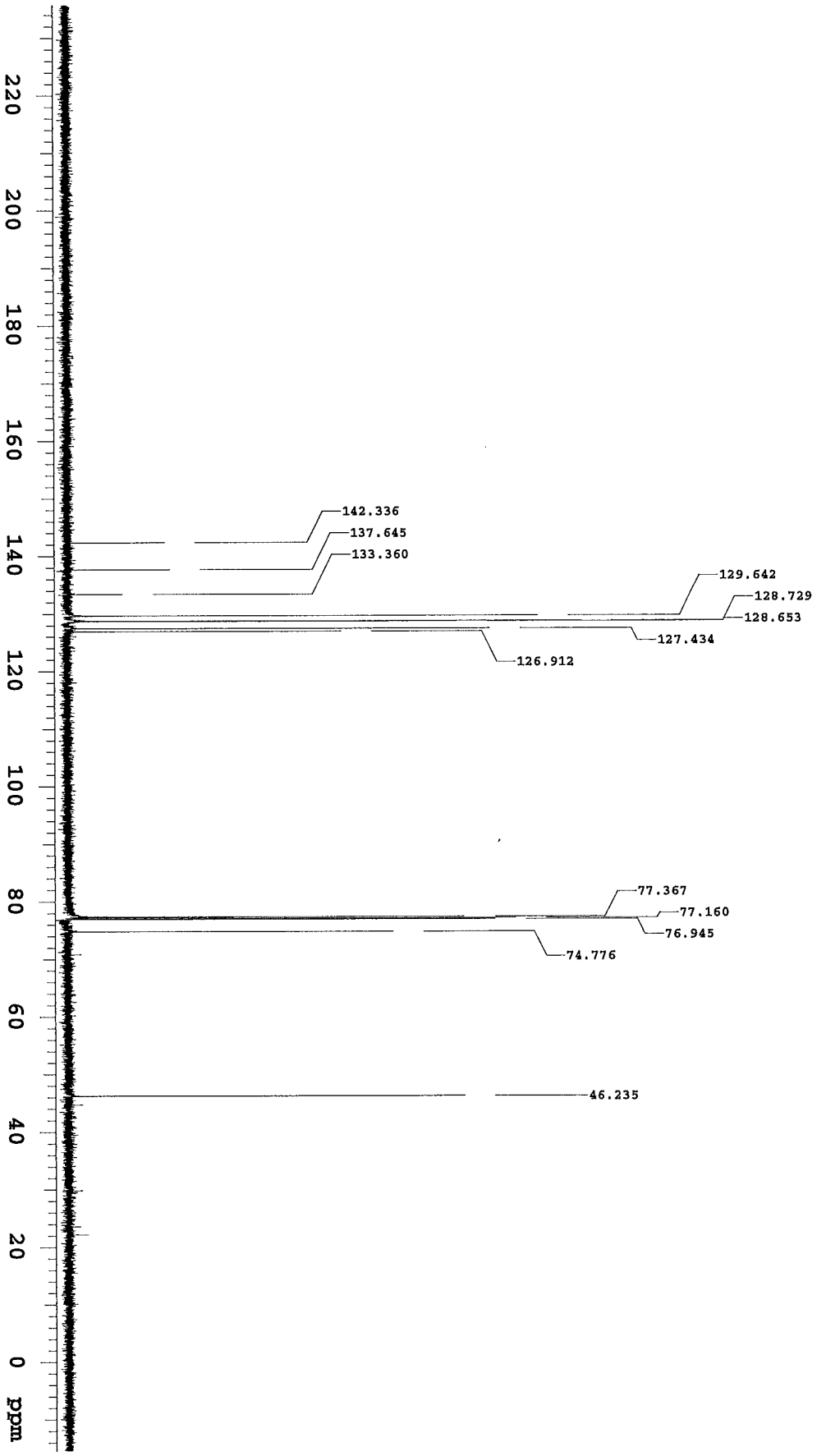
Compound **27**



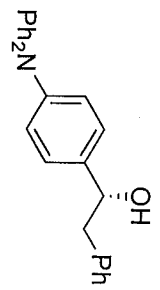


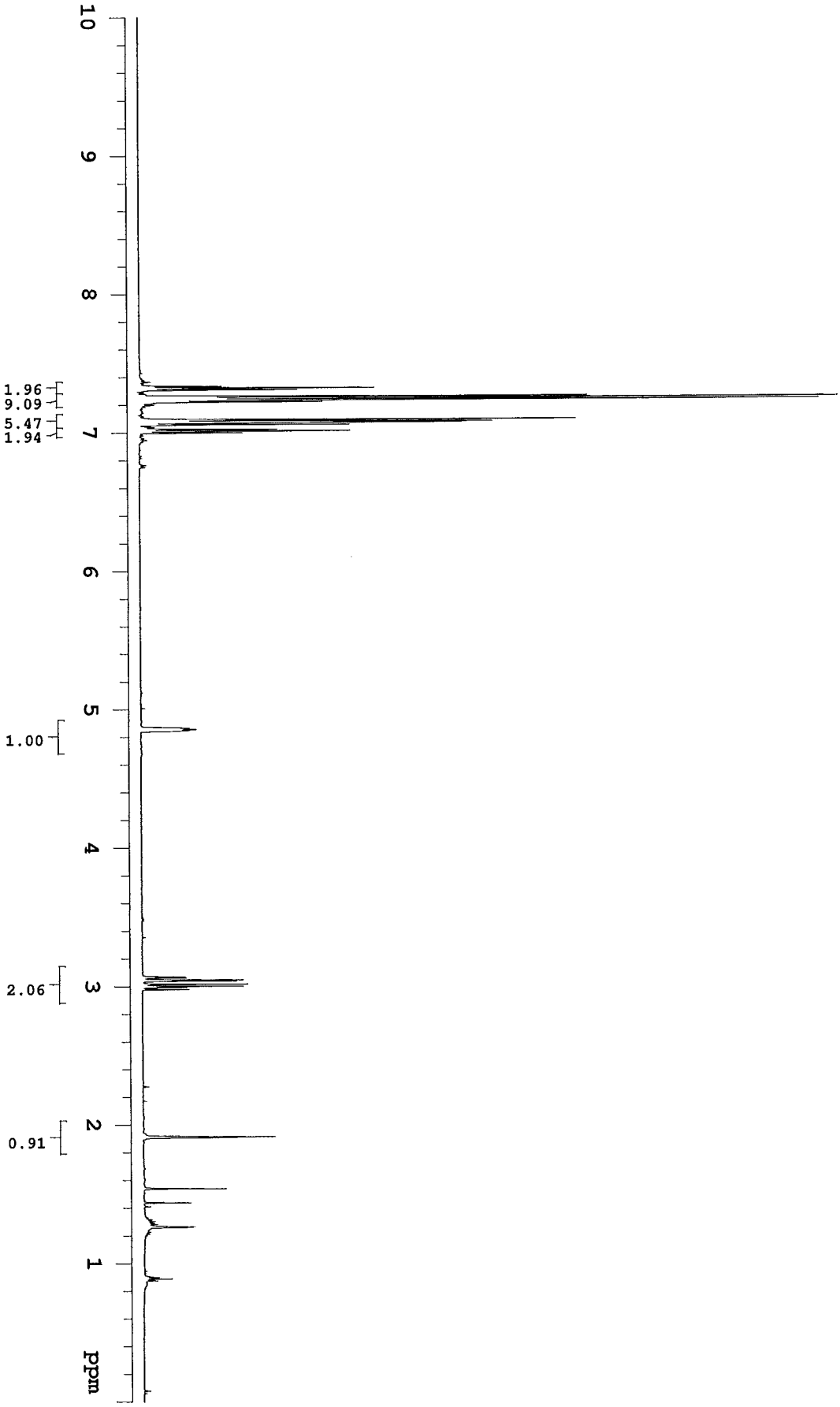
Compound **27**


Cl
OH
Ph

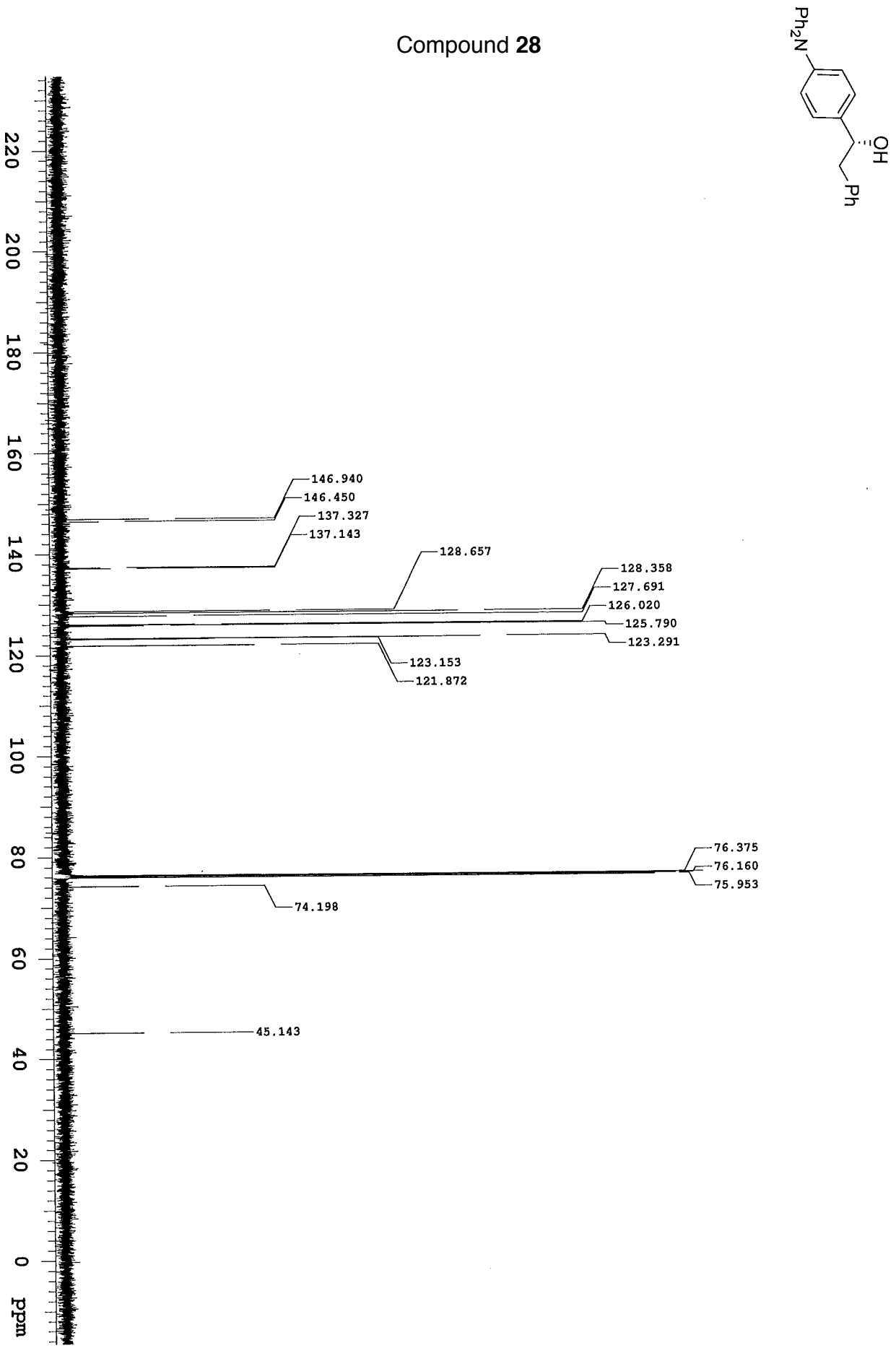

220
200
180
160
140
120
100
80
60
40
20
0
ppm
142.336
137.645
133.360
129.642
128.729
128.653
127.434
126.912
77.367
77.160
76.945
74.776
46.235

Compound **28**

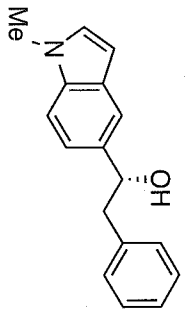


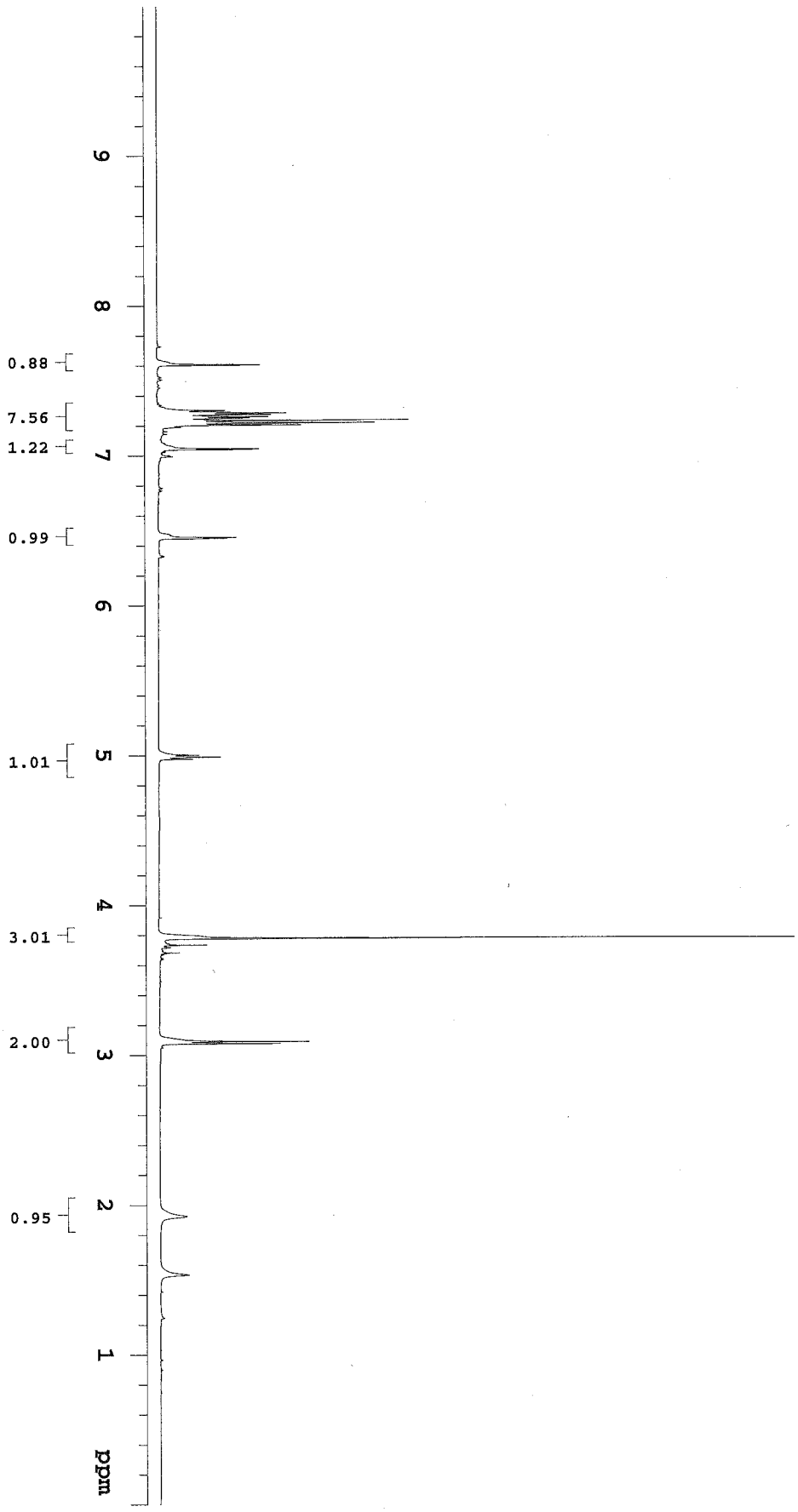


Compound **28**

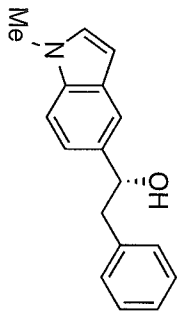

Ph2N
OH
Ph
220
200
180
160
140
120
100
80
60
40
20
0
ppm
146.940
146.450
137.327
137.143
128.657
128.358
127.691
126.020
125.790
123.291
123.153
121.872
76.375
76.160
75.953
74.198
45.143

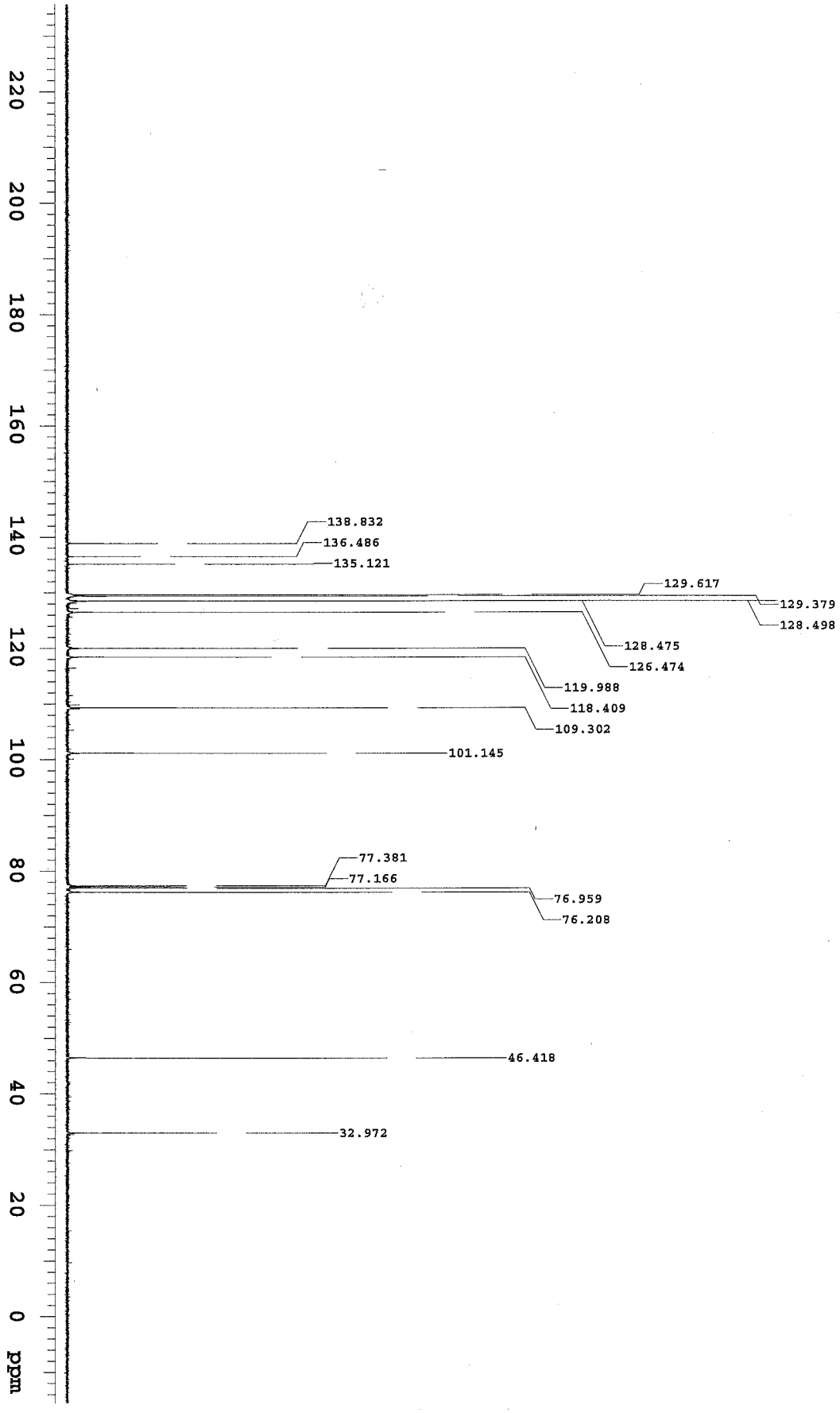
Compound **29**



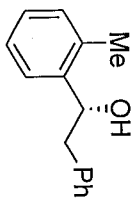


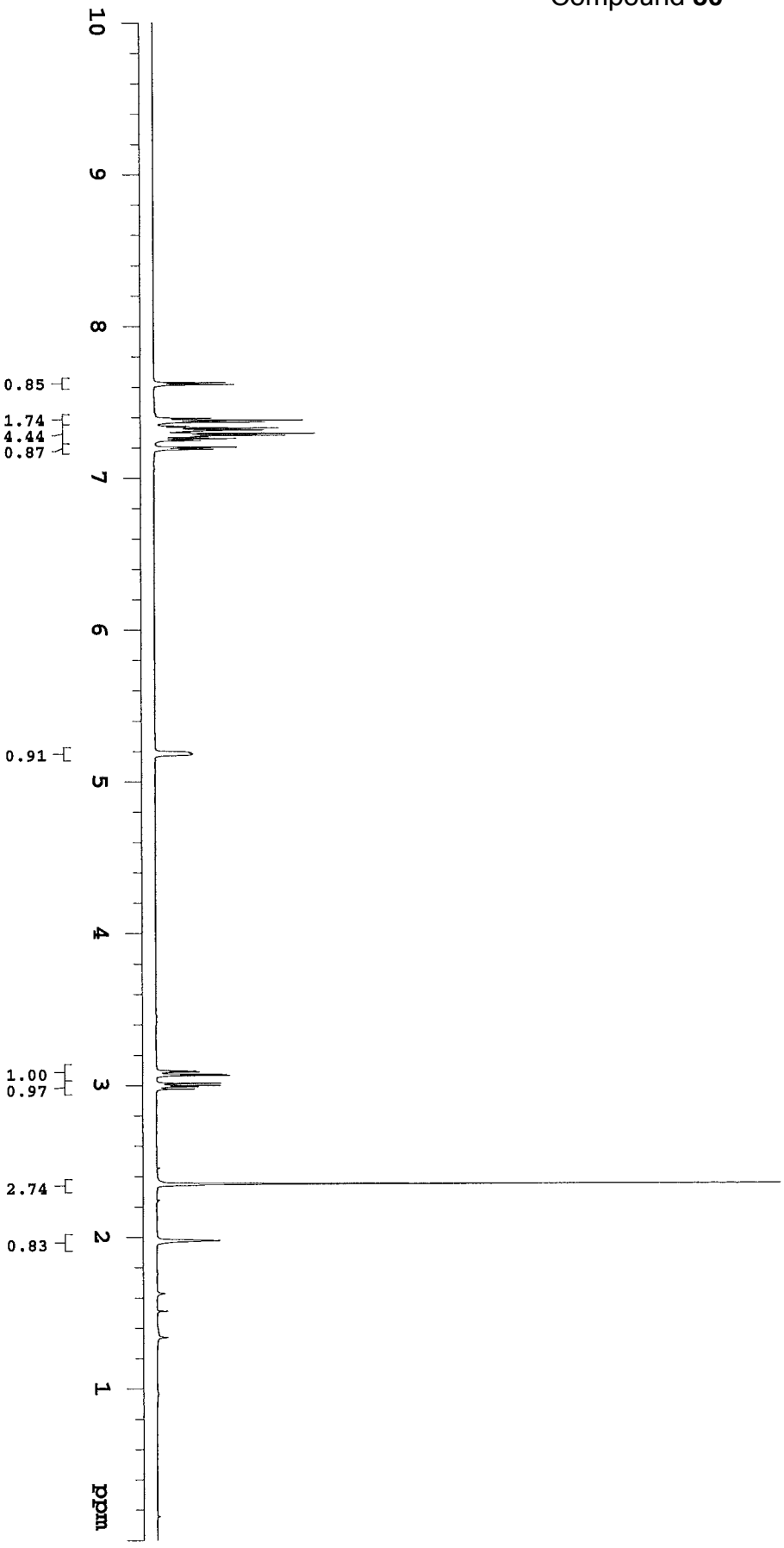
Compound **29**


Me
N
OH


220
200
180
160
140
120
100
80
60
40
20
0
ppm
138.832
136.486
135.121
129.617
129.379
128.498
128.475
126.474
119.988
118.409
109.302
101.145
77.381
77.166
76.959
76.208
46.418
32.972

Compound **30**





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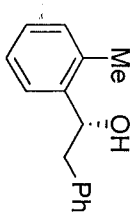
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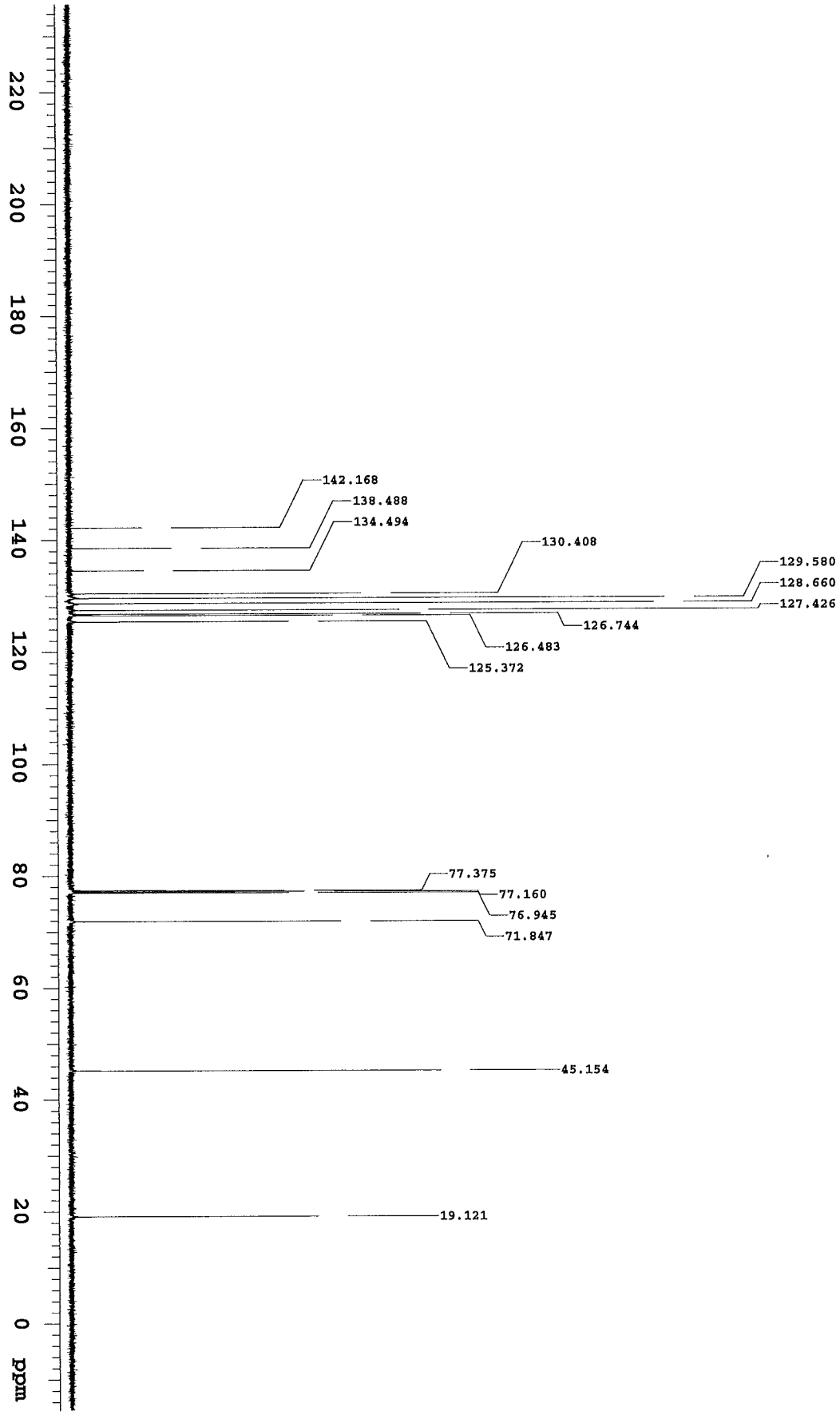
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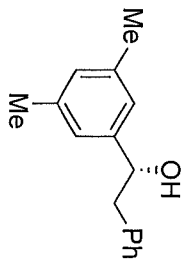
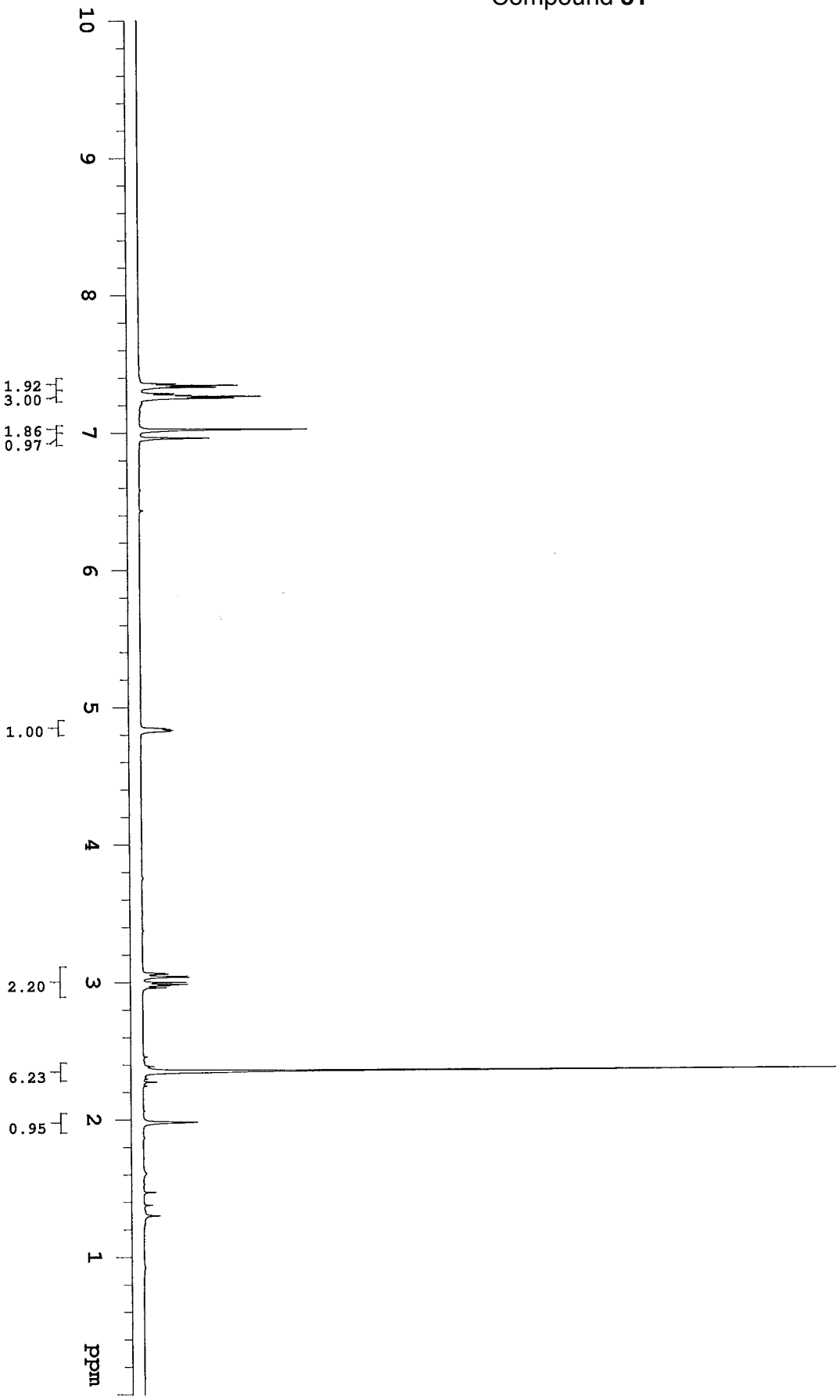
71.847
45.154
19.121

Compound **31**





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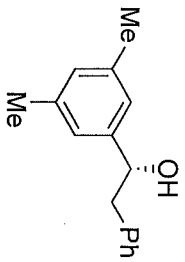
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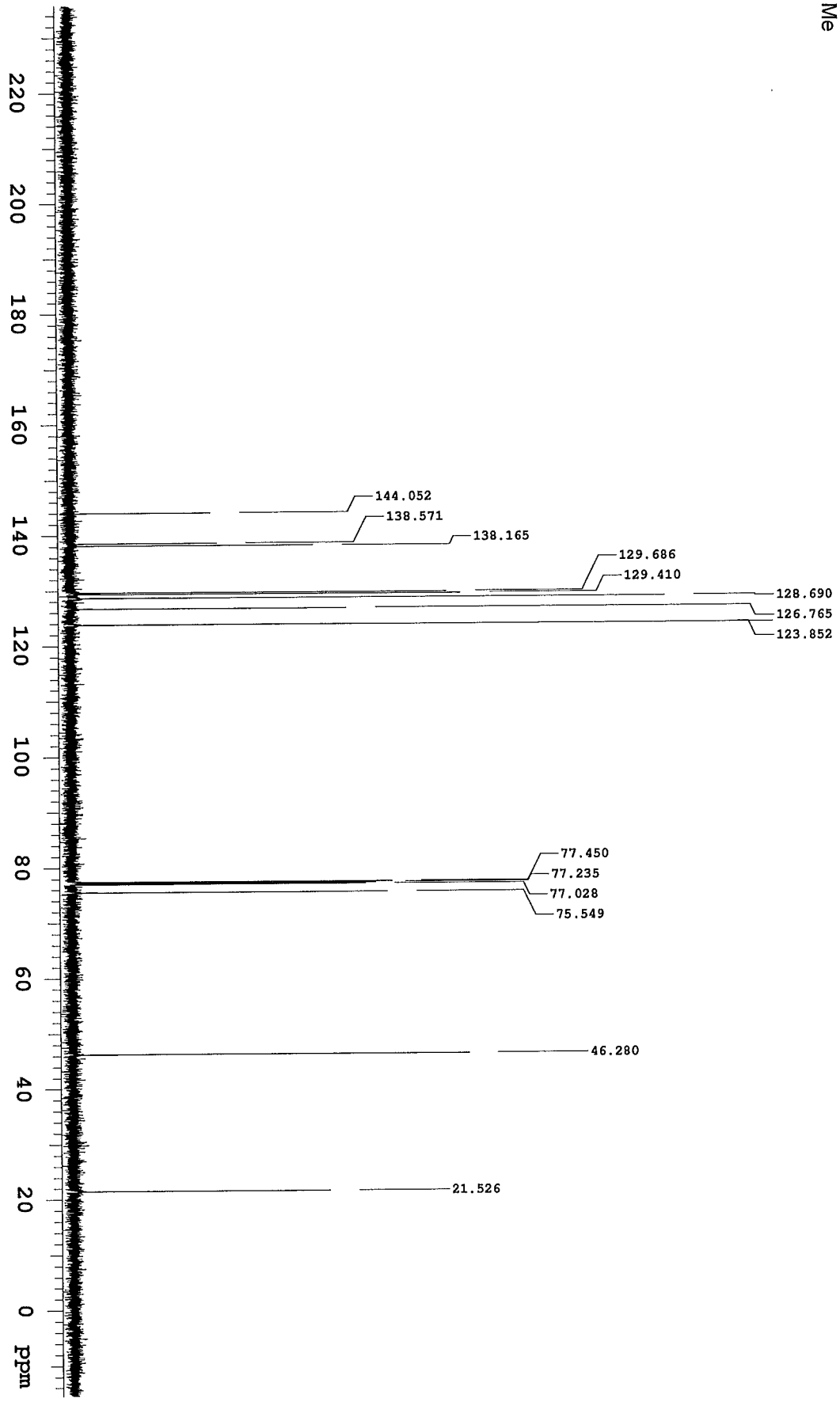
Ph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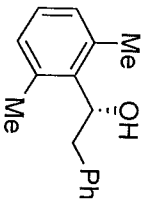
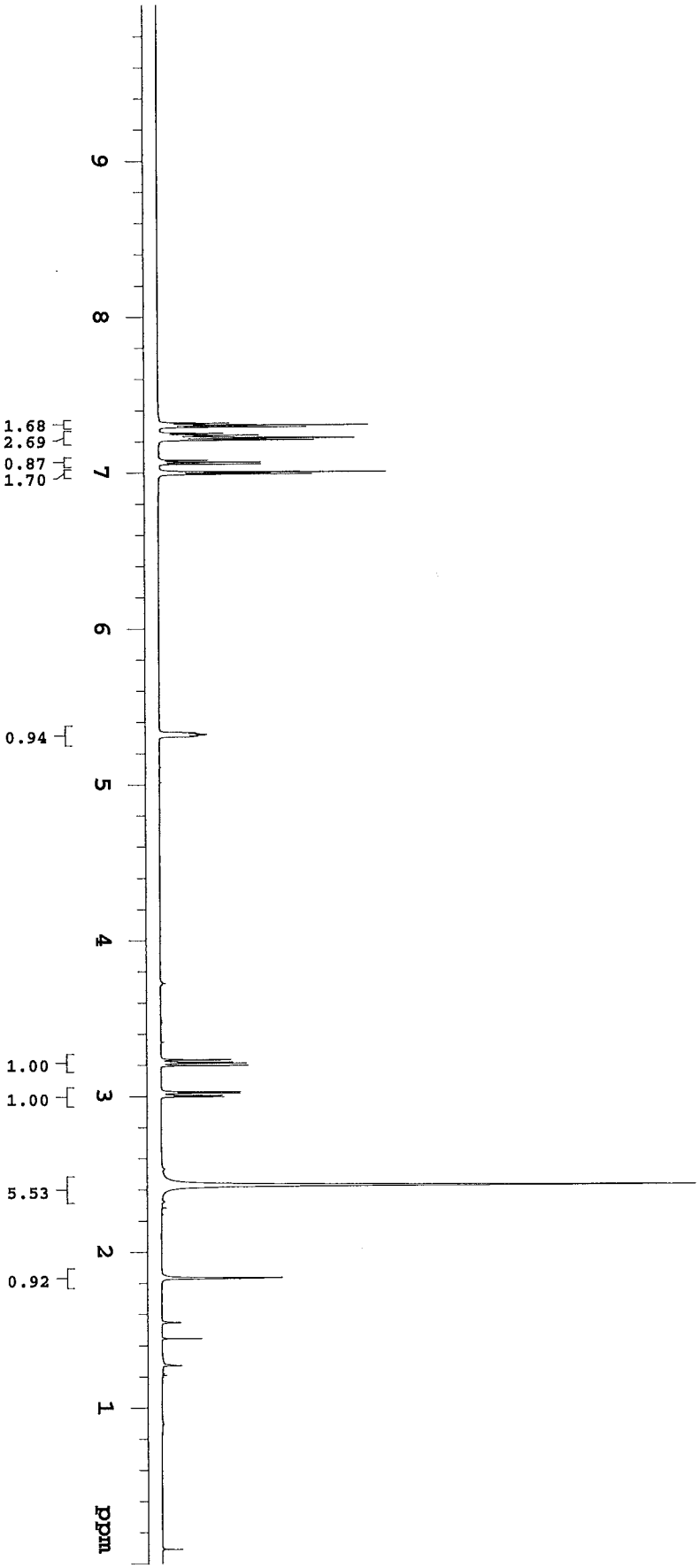
21.526

Compound **32**





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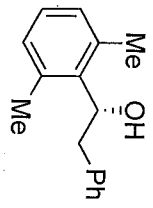
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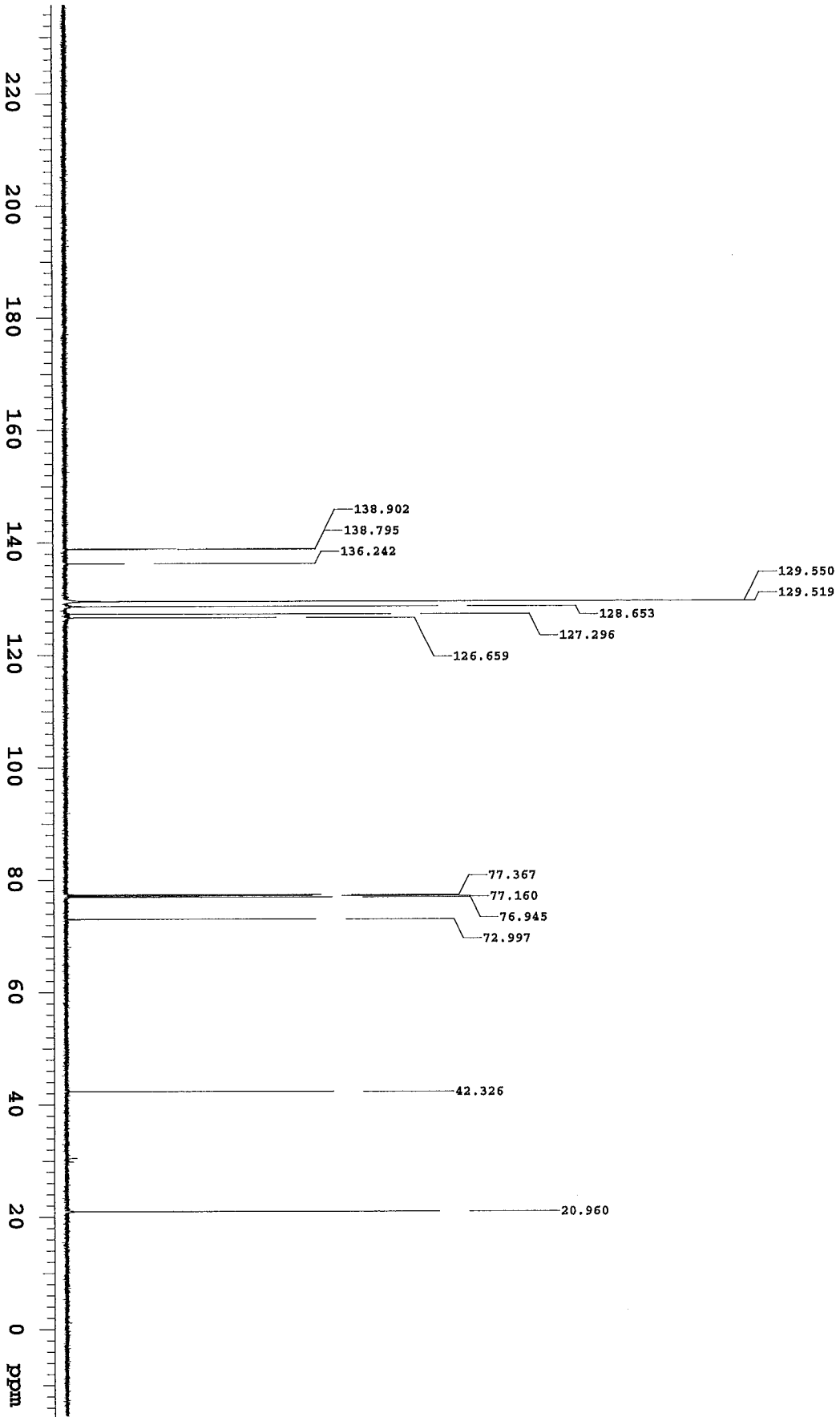
Me
Ph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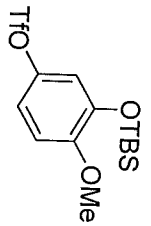
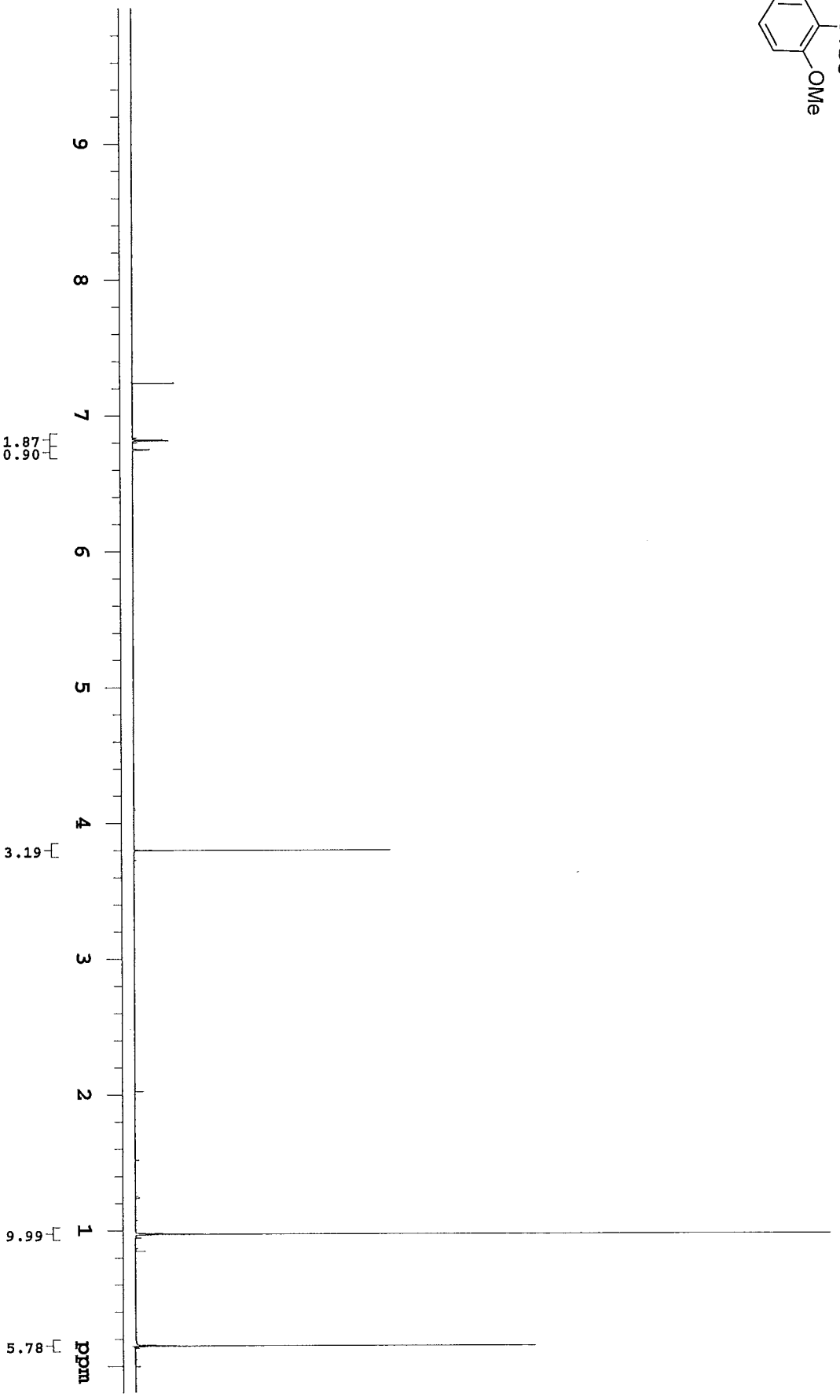
76.945
72.997
42.326
20.960

Compound **S-29**





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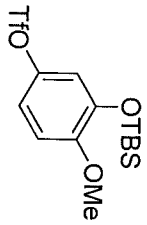

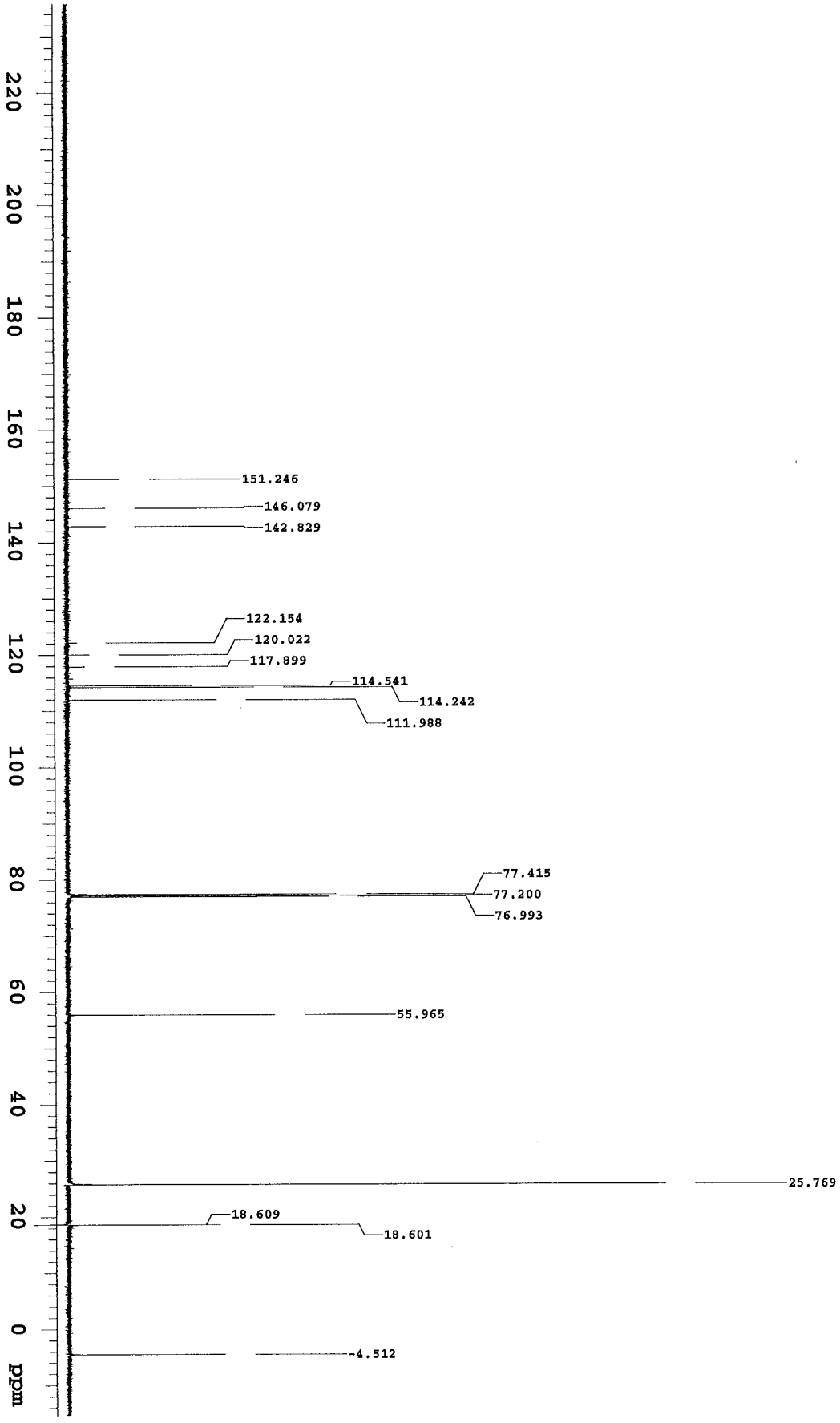

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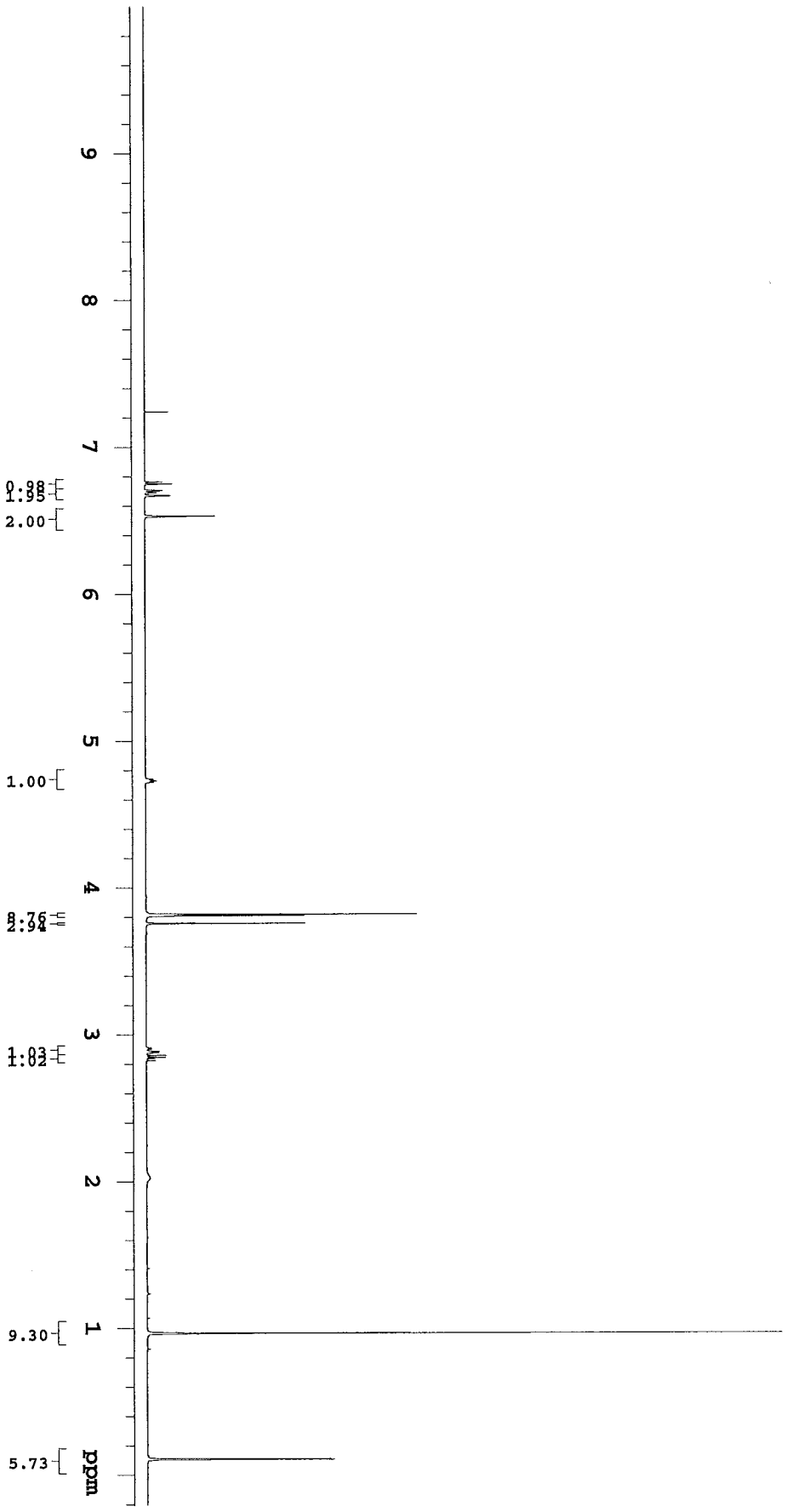
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OH
OTBS
OMe
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8
7
6
5
4
3
2
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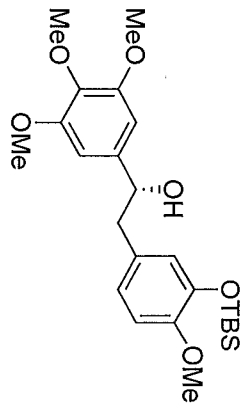
2.94
1.03
1.02
9.30
5.73

Compound **33**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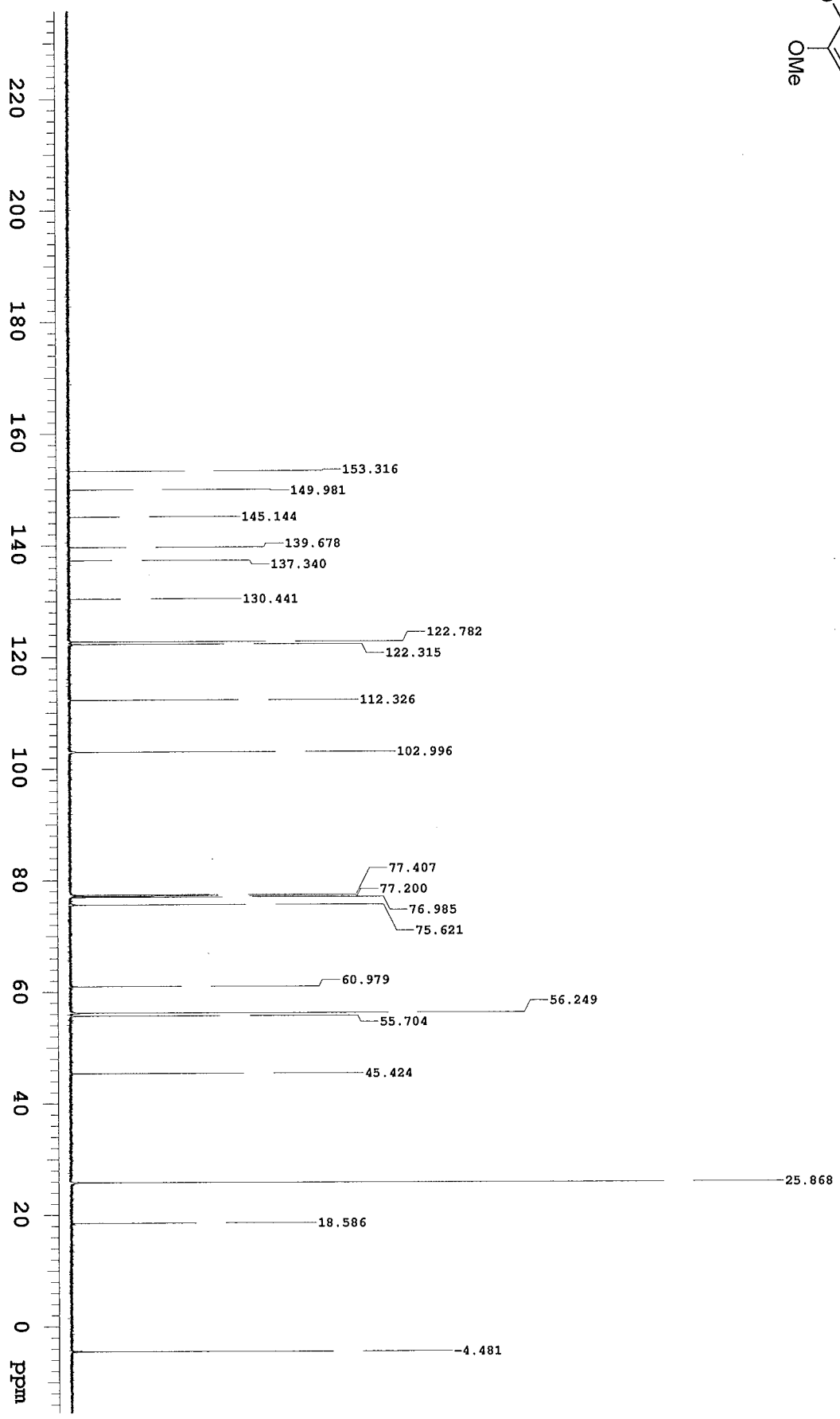
MeO
OMe
OH
OTBS
OMe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137.340
130.441
122.782
122.315
112.326
102.996
77.407
77.200
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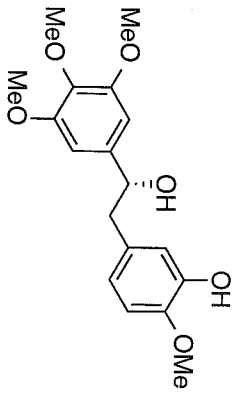
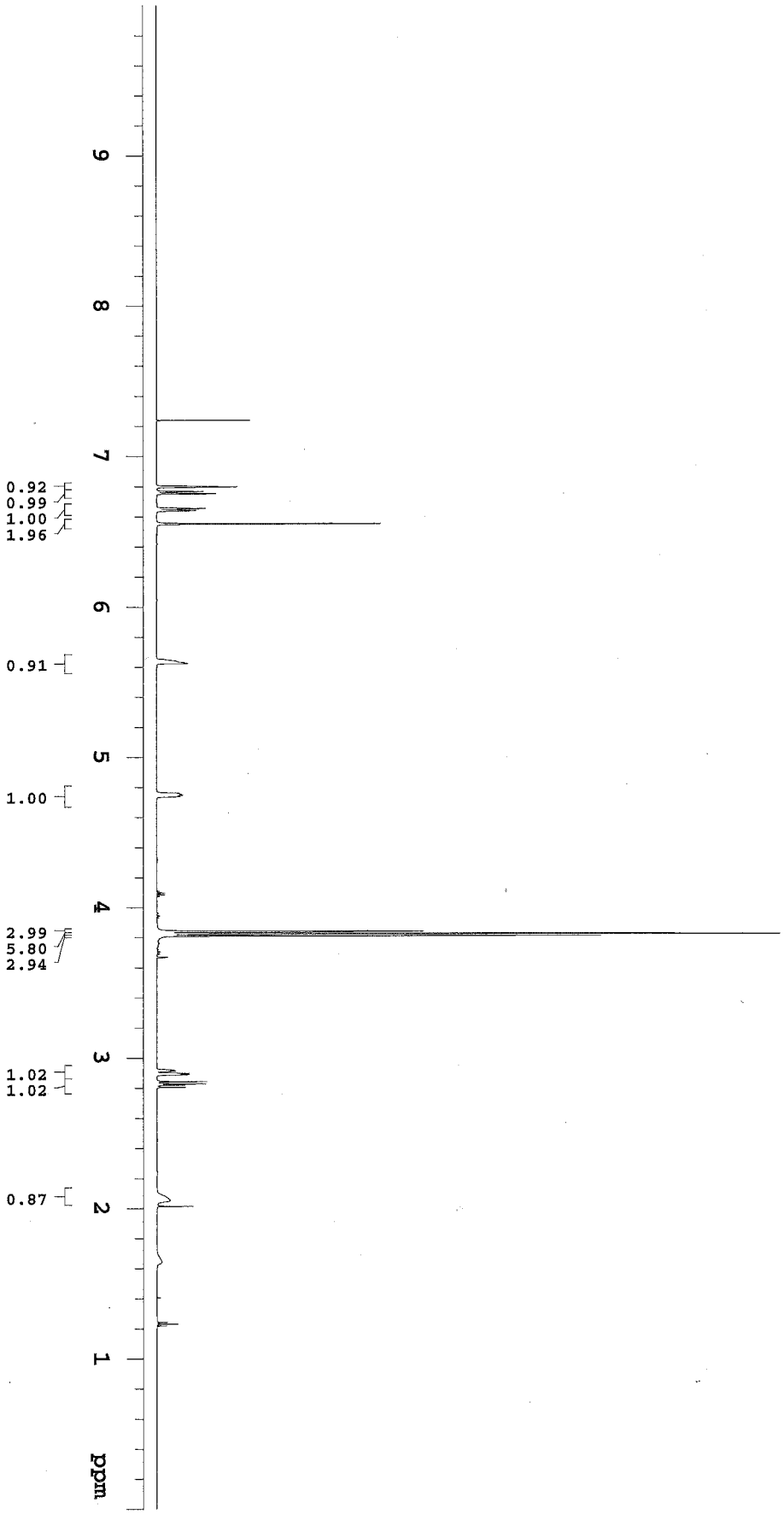
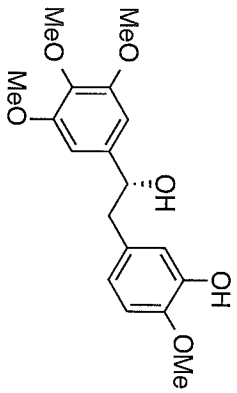
56.249
55.704
45.424
25.868
18.586
-4.481

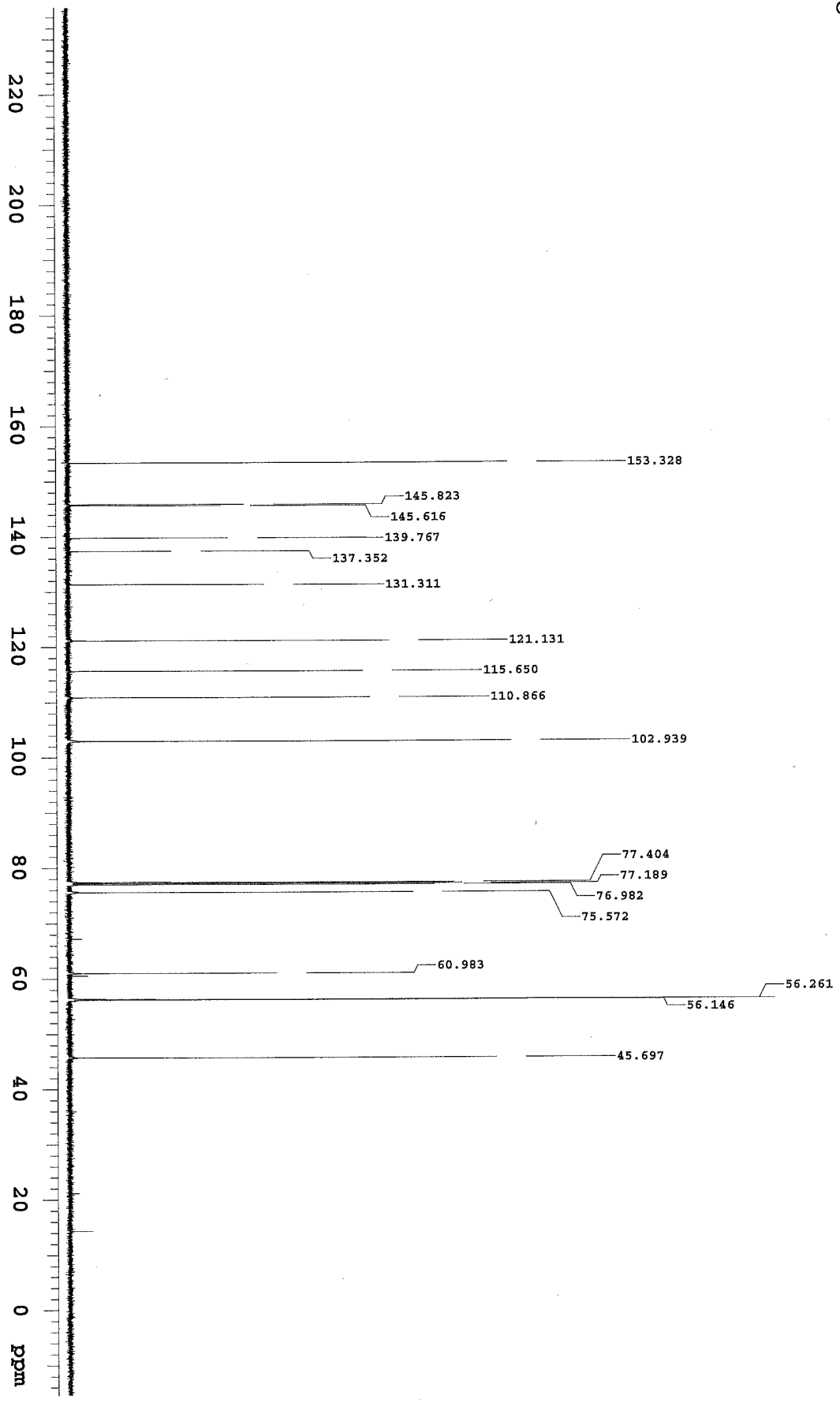
(-)-combretastatin



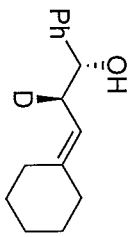


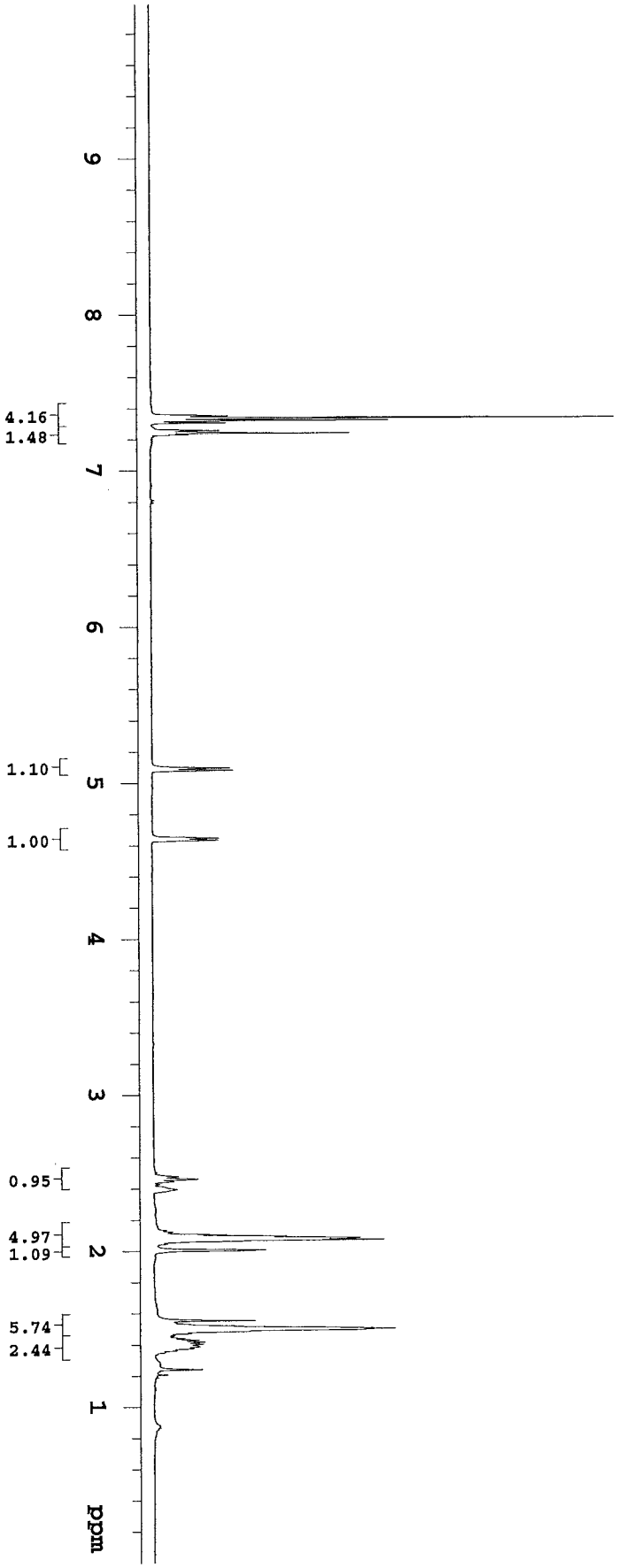
(-)-combretastatin



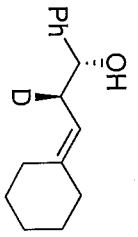


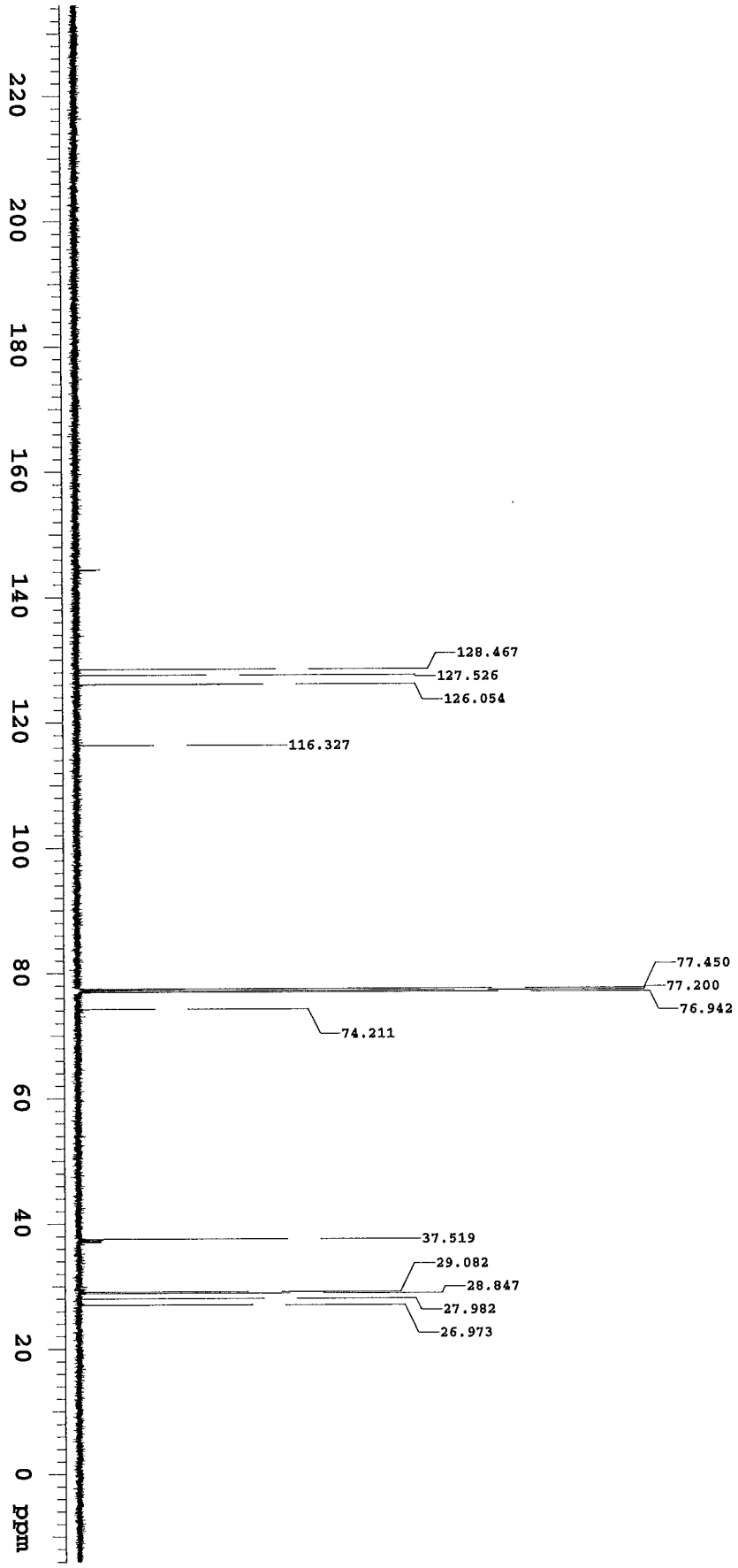
Compound **34**





Compound **34**


Ph
OH
D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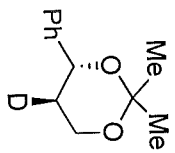
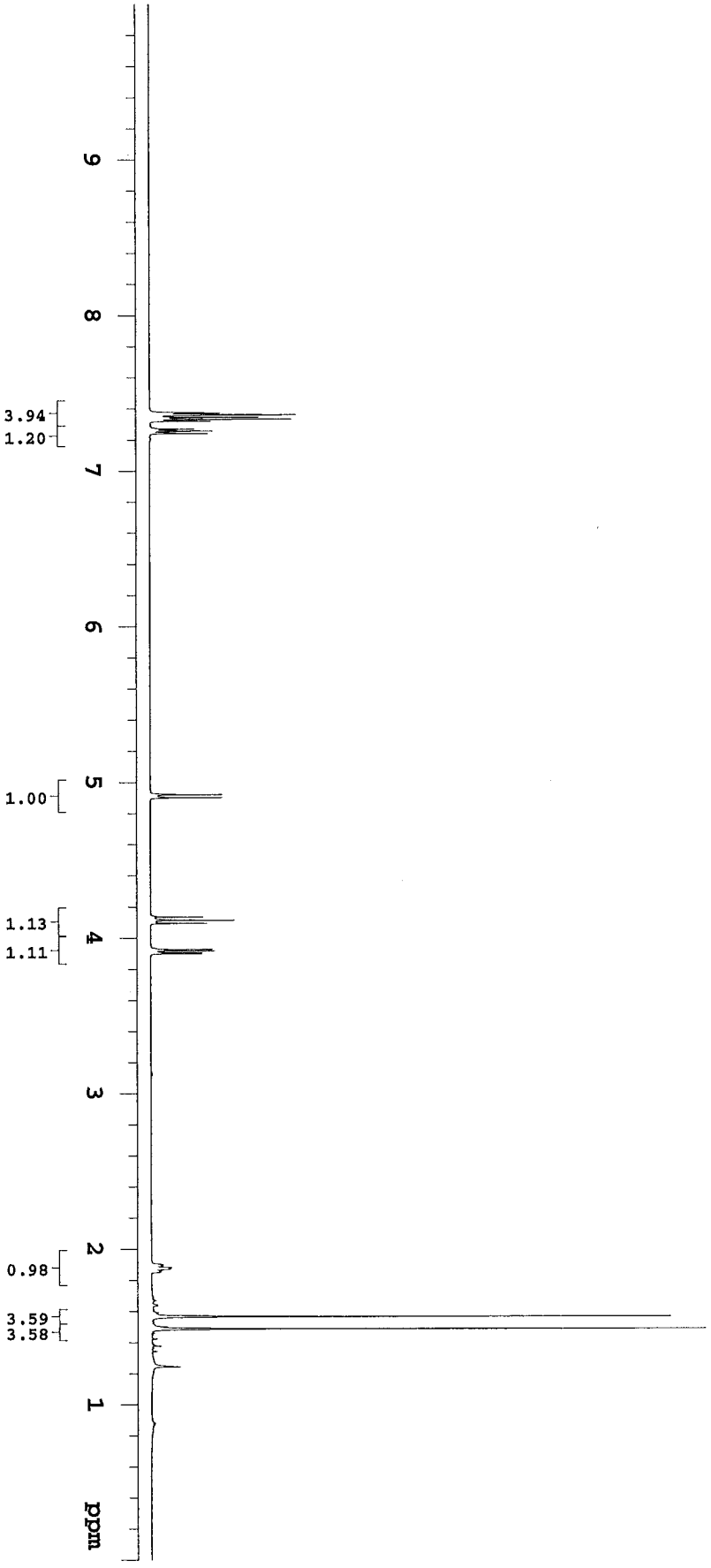
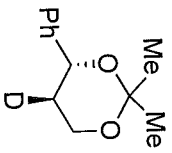
28.847
27.982
26.973

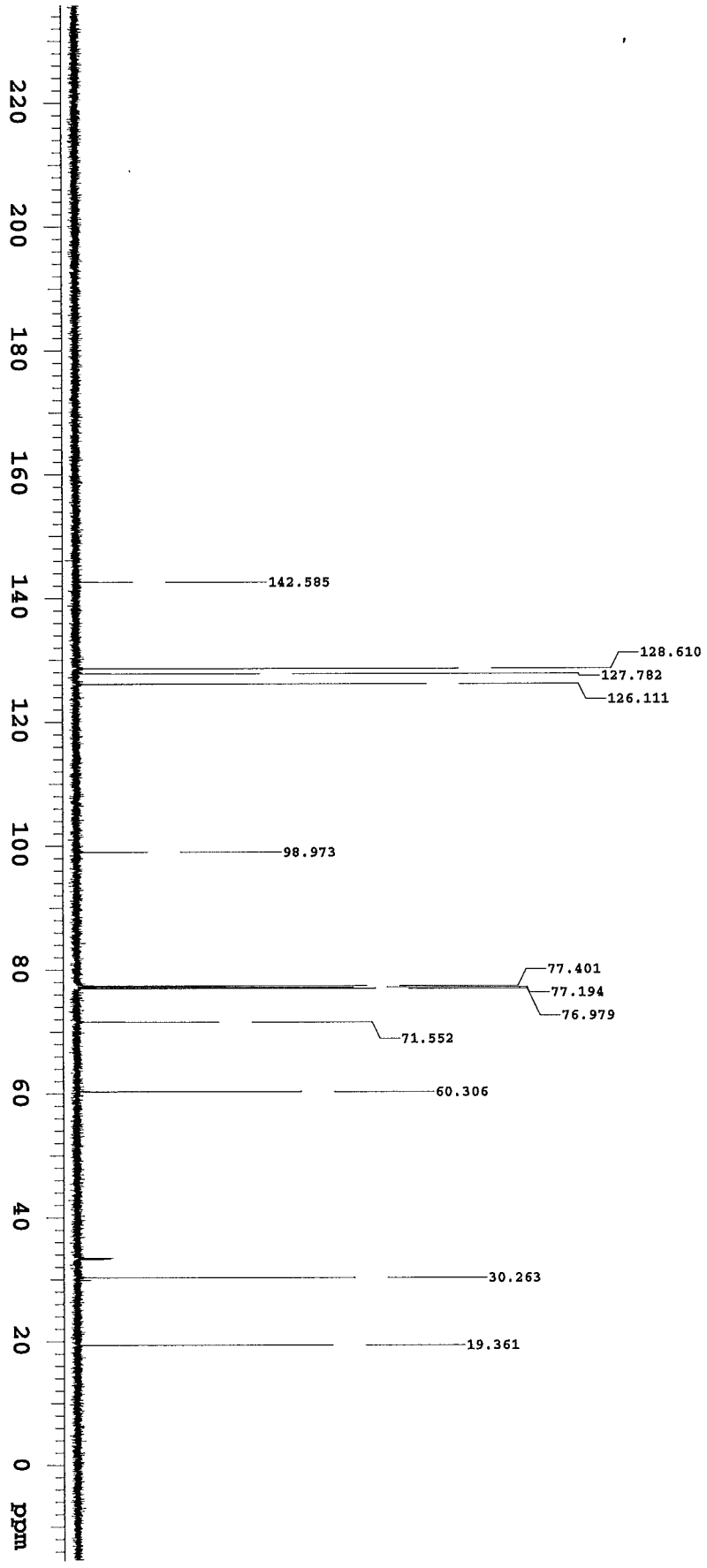
Compound **S-30**





Compound **S-30**





CHAPTER 2

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

2.1 INTRODUCTION

Palladium-catalyzed conjunctive cross-coupling provided a highly modular and efficient method to synthesize enantiomerically enriched alkyl boronates from simple and readily available starting materials. Moreover, this process introduces a metal-induced 1,2-metallate shift as an alternative to the fundamental step of transmetallation between palladium and organoboron species in Suzuki-Miyaura cross-couplings. When the 1,2-rearrangement involves an alkenylboron species, it generates chiral compounds where the absolute configuration can be controlled by a catalyst. Programming a 1,2-metallate shift into processes catalyzed by different metals would provide opportunities to extend the scope and utility of this transformation. For this reason, we set out to explore the possibility of expanding the conjunctive cross-coupling manifold to nickel catalysts. Considering the cost of palladium catalysts, nickel, as an earth abundant metal, provides a sustainable and cheap alternative to precious metal based systems. Outside of cost, the

rich and diverse reactivity of nickel in catalytic systems provides opportunities to develop new types of transformations.[1] To this end, this chapter will discuss the development of the first enantioselective conjunctive cross-coupling with 9-bora-bicyclo[3.3.1.]nonane (9-BBN) reagents using nickel catalysis. Trialkylborane reagents offer distinct advantages over the corresponding boronic esters. Namely, they can be synthesized efficiently and selectively by simple hydroboration of the corresponding alkenes, a feature that has made 9-BBN boranes staples in organic synthesis as textbook reagents for anti-Markovnikov hydroxylation and Suzuki-Miyaura cross-couplings. Moreover, the ability of 9-BBN-derived boranes to participate efficiently in Suzuki cross-couplings is also ascribed to their enhanced reactivity compared to either borinic and boronic ester counterparts.[2] Trialkylboranes are generally more electrophilic than boronic esters in the neutral state, yet highly reactive in the four-coordinate anionic state. These features bestow unique reactivity on the 9-BBN reagents allowing them to participate in a number of transformations that are unavailable to the corresponding boronic esters.[3] While these reagents hold great promise for applications in asymmetric synthesis, no catalytic methods are available for the direct and enantioselective generation of α-chiral 9-BBN containing compounds. With this prospect, we developed a complementary method to palladium catalyzed conjunctive cross-coupling that allows for the direct functionalization of olefin feedstocks through an *in situ* hydroboration and cross-coupling sequence. The system employs a cheap and readily available combination of nickel salts and diamine ligands to engender the enantioselective conjunctive cross-coupling between

[1] For reviews and perspectives: (a) Tasker, S. Z.; Standley, E. A.; Jamison, T. F. *Nature* **2014**, *509*, 299. (b) Hu, X. *Chem. Sci*. **2011**, 2, 1867. (c) Ananikov, V. P. *ACS Catal*. **2015**, *5*, 1964.
[2] Chemler, S. R.; Dirk Trauner, D.; Danishefsky, S. J. *Angew. Chem. Int. Ed*. **2001**, *40*, 4544.
[3] Soderquist, J. A.; Roush, W. R.; Heo, J. "9-Borabicyclo[3.3.1]nonane Dimer" In *Encyclopedia of Reagents for Organic Synthesis*, **2004**.

aryl iodides and alkyl-9-BBN reagents, delivering enantiomerically enriched and synthetically useful trialkylborane products.

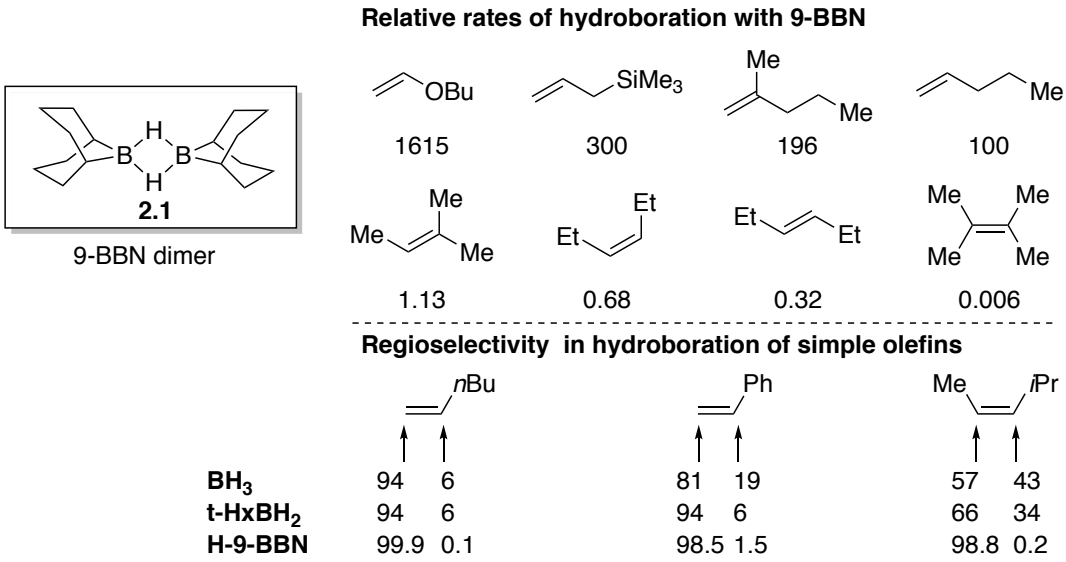
2.2 BACKGROUND

2.2.1 9-BBN reagents, utility and properties.

In 1968 H.C. Brown introduced 9-bora-bicyclon[3.3.1.]nonane (9-BBN) as a highly efficient and selective hydroboration reagent for the synthesis of alkyl boron compounds.[4] 9-BBN was generated from the hydroboration of cyclooctadiene; after isomerization, this provided a stable dimeric structure that was isolated as a crystalline solid (Figure 2.1)**.** Due to its steric bulk, 9-BBN undergoes highly regioselective hydroboration, generally outperforming other common borane reagents (Figure 2.1, bottom).[3] With respect to the alkene substrates, the relative rates of hydroboration are highly sensitive to both steric and electronic parameters, as illustrated in Figure 2.1.[5] These reactivity trends allow for highly selective hydroboration to take place in the context of complex molecule synthesis.

[4] (a) 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.
[5] Nelson, D. J.; Cooper, P. J.; Sounddararajan, R. *J. Am. Chem. Soc*. **1989**, *111*, 1414.

Figure 2.1. Hydroboration of simple olefins with 9-BBN



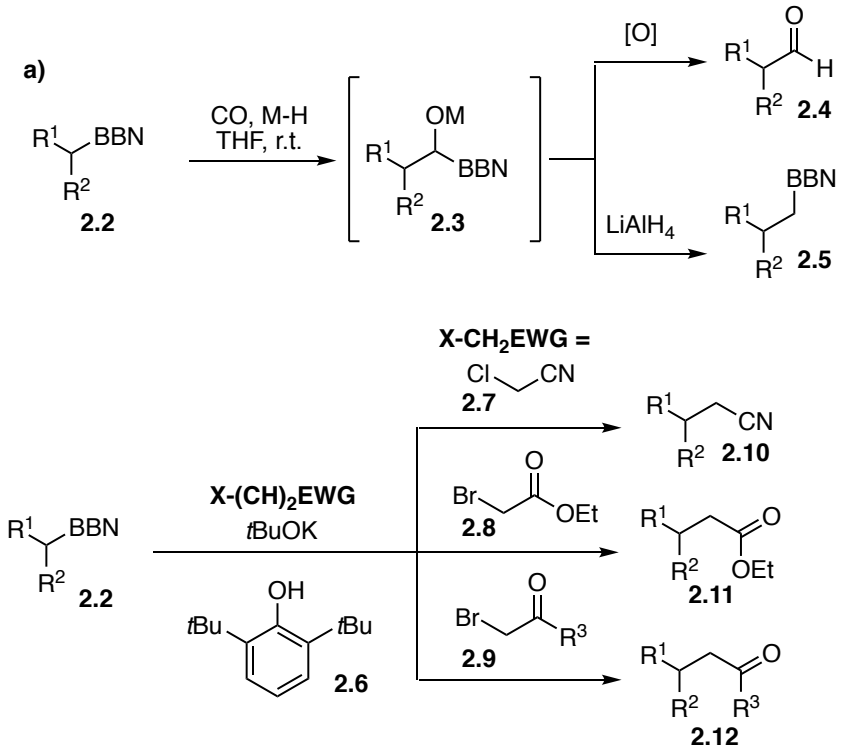
2.1

9-BBN dimer

Trialkylboranes are generally more reactive than the corresponding alkyl boronates, allowing the former to participate in a number of unique transformations that cannot be carried out with the latter. Brown disclosed several stereospecific transformations developed specifically for 9-BBN substrates. These include a series of carbon monoxide based homologations (Figure 2.2a) where, in the presence of reducing agents such as $KHB(OiPr)_3$ or $Li(MeO)_3AlH$, carbon monoxide adds to boron triggering a 1,2-metallate shift that eventually generates α-hydroxyl BBN intermediates such as **2.3**. These compounds can be oxidized to the corresponding aldehyde (**2.4** Figure 2.2a) or further reduced with LAH to yield homologated boranes (**2.5** Figure 2.2a).[6]

[6] (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.

Figure 2.2. Brown's stereospecific functionalization methods for 9-BBN



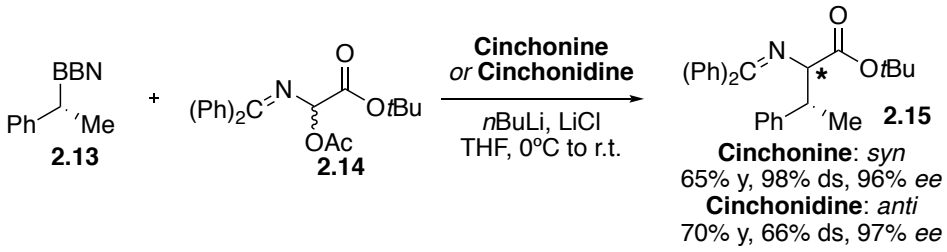
Reaction of 9-BBN reagents with a series of α-halo carbonyl derivatives was also shown to deliver homologated products (isolated after proto-deborylation). This reaction occurs in the presence of *in situ* generated bulky phenoxide bases (Figure 2.2b).[7] More recently, O'Donnel disclosed the enantioselective homologation of 9-BBN reagents with α-acetoxy/imine derivatives of glycine *tert*-butyl ester (**2.14** Figure 2.3). The enantioselectivity in this system arises from the protonation of homologated boryl enol ether intermediates with *Cinchona* alkaloids.[8] Using enantiomerically enriched 9-BBN compounds in this reaction produces products containing two adjacent stereocenters in excellent diastereomeric ratio.[8b] Additional reactions for the stereospecific homologation

[7] (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.

[8] (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.

of 9-BBN reagents include arylations with indoles, furans, and pyrroles, which are available for boronic esters as well.[9]

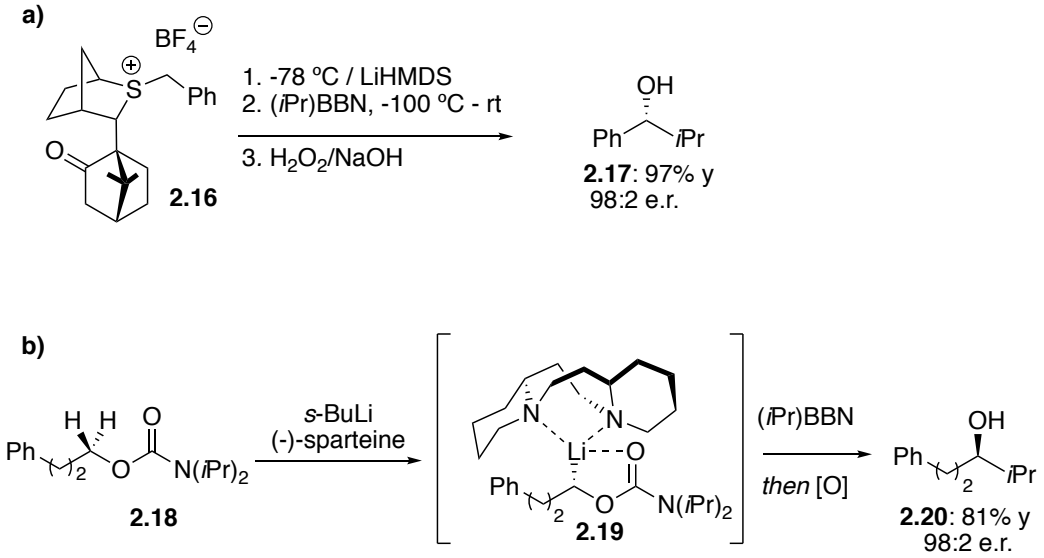
Figure 2.3. O'Donnel enantioselective functionalization of alkyl-9-BBN species



Of note, only two enantiomerically-enriched substrates were tested in O'Donnel's diastereoselective homologations.[8b] Similarly, owing to limited methods for the synthesis of enantiomerically-enriched 9-BBN, a limited number of such substrates were tested by Brown as well.[7d] In both cases, these substrates were generated from reduction of the corresponding boronic esters, followed by hydroboration of cyclooctadiene. In fact, to the best of our knowledge, the only methods available for the direct synthesis enantiomerically enriched 9-BBN compounds were reported years later. These consisted of the powerful lithiation borylation methodologies developed by Aggarwal that proceed with chiral sulfur ylides (Figure 2.4a)[10] and lithiated carbamates (Figure 2.4b).[11]

[9] (a) Levy, A. B. *J. Org. Chem.* **1978**, *43*, 4684. (b) Marinelli, E. R.; Levy, A. B. *Tetrahedron Lett*. **1979**, *20*, 2313.
[10] (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.
[11] (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.

Figure 2.4. Methods for the direct synthesis of non-racemic 9-BBN reagents



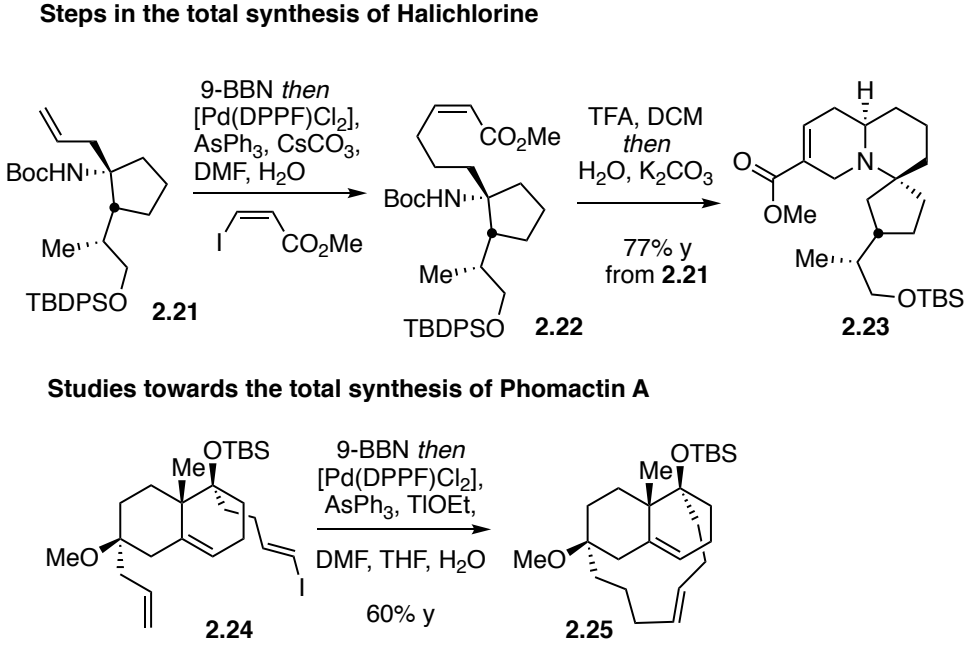
No catalytic enantioselective methods for the synthesis of non-racemic 9-BBN reagents had been disclosed prior to the one reported here. Although 1,2-metallate shift based functionalization with mixed boranes require overcoming issues of unselective migration (which will be discussed in the next section), greater availability of non-racemic 9-BBN reagents may spur the development of stereospecific methods for the functionalization of these substrates.

In addition to homologation based methods, the ease of synthesis and powerful reactivity of alkyl-9-BBN reagents has led to their extensive use as cross-coupling partners in Suzuki-Miyaura reactions. Early on, Suzuki showed that these reagents could be used to furnish alkyl nucleophiles in palladium catalyzed cross-couplings.[12] Since then the synthetic utility of 9-BBN Suzuki reactions has been amply demonstrated in the proving ground of total synthesis, where hydroboration and cross-coupling strategies

[12] Miyaura, N.; Ishiyama, T.; Ishikawa, M.; Suzuki, A. *Tetrahedron Lett*. **1986**, *27*, 6369.

have been adopted to join complex fragments both inter- and intra-molecularly.[2,13] As highlighted below in the examples by Danishefsky[14] (Figure 2.5), 9-BBN hydroboration takes place with exquisite chemo- and regioselectivity on polyolefinated substrates, providing densely functionalized cross-coupling reagents.

Figure 2.5. Alkyl-9-BBN cross-coupling in total synthesis



In this context, the development of an enantioselective conjunctive cross-coupling with 9-BBN reagents could provide a synthetically useful complement to Suzuki-Miyaura reactions for devising total synthesis strategies.

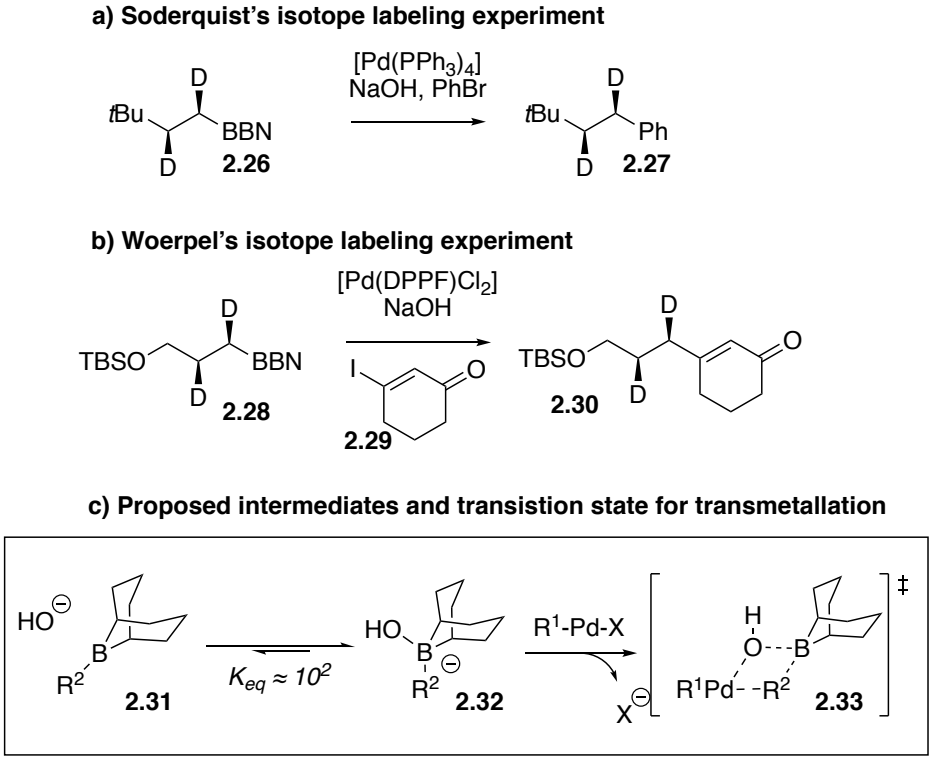
Alkyl-9-BBN compounds were also among the first reagents shown to participate effectively in C(sp^3)-C(sp^3) Suzuki coupling reactions with primary alkyl halides under

[13] Jana, R.; Pathak, T. P.;Sigman, M. S. Chem. Rev. **2011**, *111*, 1417.
[14] (a) Trauner, D. Schwartz, J. B.;Danishefsky, S. J. *Angew. Chem. Int. Ed.* **1999**, 38, 3542. (b) Chemler, S. R.; Danishefsky, S. J. *Org. Lett.* **2000**, 2, 2695.

palladium catalysis,[15] and later on with secondary alkyl halides using nickel catalysis[16]. These reactions will be discussed further in the next section. The mechanism for transmetallation in palladium catalyzed reactions with alkyl-9-BBN reagents was studied early on by Soderquist[17] and Woerpel.[18] In concomitant reports they found that transmetallation proceeded with stereoretention at carbon (Figure 2.6a,b) and proposed a four-member transition state with the intermediacy of a Pd-O-B bound species (**2.33**, Figure 2.6c). Soderquist also observed that alkyl-9-BBN reagents, when mixed with hydroxide base, resulted in rapid and quantitative formation of four-coordinate boron 'ate' species **2.32** (this did not occur with the corresponding borinic esters). Based on this observation and the kinetic profile of the reaction, the authors proposed that transmetallation was rate determining and occurred from the reaction of an alkoxy boron 'ate' complex and Pd-X species.

[15] Ishiyama, T.; Abe, S.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1992**, 691.
[16] Saito, B.; Fu, G. C. *J. Am. Chem. Soc*. **2007**, *129*, 9602.
[17] Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461.
[18] Ridgway, B. H.; Woerpel, K. A. *J. Org. Chem.* **1998**, 63, 458.

Figure 2.6. Mechanistic studies on alkyl-9-BBN transmetallation



2.2.2 Migratory aptitude of 9-BBN reagents.

For organoborane reagents where all the substituents on boron are identical, reactions (whether they involve cross-coupling or 1,2-metallate rearrangements) are often challenged by the fact that upon consumption of each organic moiety, the reactivity of the remaining ones is drastically altered. Thus, poor conversion is often an issue in transformations involving such substrates. This can be especially inconvenient if the substituents on boron constitute valuable organic functionalities. Mixed boranes such as 9-BBN have been introduced in part to circumvent this problem, as the cyclooctane bicycle often acts as an inert spectator ligand. However, especially in reactions that occur

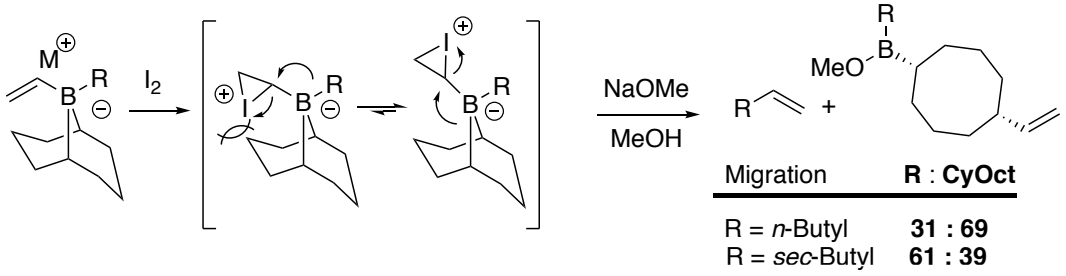
by 1,2-metallate rearrangements, the cyclooctane moiety is often reactive. Electronic and steric factors can play a role in determining the preferred reactivity of the various substituents in organoboron compounds, and the specific reaction conditions and substrates may determine which of these elements will dominate. Considering electronic factors, it has been suggested that in trialkyl boranes, the organic substitutuents that are best able to stabilize a negative charge migrate preferentially (e.g. reactivity follows the order of $C(sp^2)$ > 1º- $C(sp^3)$ > 2º- $C(sp^3)$ > 3º- $C(sp^3)$).[19] However, if this factor was solely responsible for determining the migratory aptitude of alkyl-9-BBN reagents, then only primary alkyl groups could be functionalized efficiently via 1,2-metallate shift. Meanwhile, steric factors have been proposed to play contrasting roles depending on the system in question. In the case of steric crowding around the boron atom, reaction of the most encumbering substituents may be favored as a means to relieve strain.[19, 20] In contrast, steric crowding around a migrating terminus may favor transfer of the least sterically demanding moiety.[20]

Aggarwal has recently reviewed and categorized the various features affecting the migratory aptitudes of mixed boranes in 1,2-metallate shift reactions,[21] and the most relevant will be discussed here. In the case of Brown's 9-BBN reagents, the cyclooctyl group presumably acts as a non-migrating ligand due to torsional strain arising from expansion of the [3.3.1] bicycle to a [3.3.2.] structure. This appears to be the case for several 1,2-metallate shift based transformations of 9-BBN reagents discussed earlier, as in many of these reactions the cyclooctane acts reliably as a spectator ligand.[6-9] However it has been shown in a number of instances that migration of the cyclooctyl moiety can be

[19] Bottoni, A.; Lombardo, M.; Neri, A.; Trombini. C. *J. Org. Chem*. **2003**, *68,* 3397.
[20] Slayden, S. W. *J. Org. Chem.* **1981,** *46*, 2311.
[21] Aggarwal, V. K.; Fang, G. Y.; Ginesta, X.; Howells, D. M.; Zaja, M. *Pure Appl. Chem.*, **2006**, *78*, 215.

competitive if not entirely favored in 1,2-metallate shift-based reactions of 9-BBN boranes. Amination of 9-BBN reagents with organic azides and N-tosyl amines failed due to this reason.[22] Other unsuccessful reactions include homologations with iodonium ylides,[23a] and diazo compounds,[23b] as well as a vinylidenation with α-methoxyvinyl lithium.[23c] Slayden and coworkers reported that Zweifel olefination to a simple vinyl group was impaired by migration of the cyclooctyl ring in competition with a range of other borane substituents.[24] Slayden proposed a reactivity model whereby the outcome of the reaction is dictated by the more stable and accessible conformation of the 'ate' species prior to 1,2-metallate shift (Figure 2.7). Based on this model, subtle non-bonding interactions within the reactive 'ate' species have to be considered on a case by case basis in order to predict the outcome of the reaction.

Figure 2.7. Slayden's model for migration of alkyl-9-BBN in olefination reaction

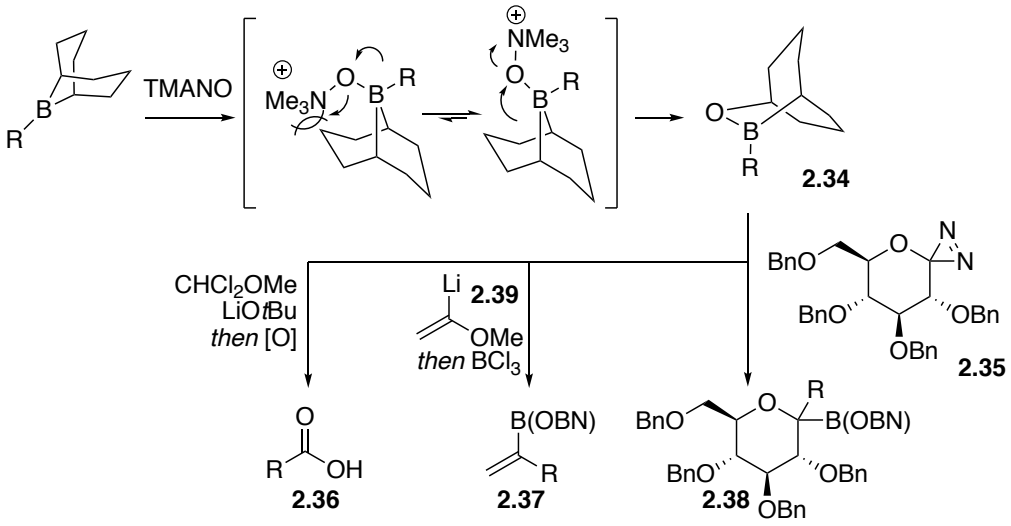


The propensity for migration of the cyclooctyl moiety was exploited by Soderquist in the development of a partial oxidation of 9-BBN boranes to produce

[22] (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.
[23] (a) Ochiai, M.; Tuchimoto, Y.; Higashiura, N. *Org. Lett.* **2004**, *6,* 1505. (b) Hoos, J.; Gunn, D. M. *Tetrahedron Lett*. **1969**, *40*, 3455 (c) Soderquist, J. A.; Rivera, I. *Tetrahedron Lett*. **1989**, *30*, 3919.
[24] Slayden. S.W. *J. Org. Chem.* **1982**, *47*, 2753.

relatively air stable and isolable borinic esters **2.34** (Figure 2.8).[25] A similar argument to that made by Slayden was used to justify the selective mono-oxidation. Later on Soderquist and co-workers disclosed two instances in which the derived cyclic borinic esters could participate in transformations that had not been successful with the parent 9-BBN reagents. These reactions consisted of vinylidenation with α-methoxyvinyl lithium **2.39**[26] and homologation with lithiated dichloromethyl ether[27] (Figure 2.8, bottom). Vasella and coworkers also disclosed a method for carbene-based glycosylation using Soderquist borinic esters.[28] The migratory aptitude of these compounds disfavoring reaction of the cyclooctyl moiety was proposed to result from strain caused by additional ring expansion.

Figure 2.8. Soderquist's borinic ester synthesis and applications



[25] Soderquist, J. A.; Najafi, M. R. *J. Org. Chem*. **1986**, *51*, 1330.
[26] John A. Soderquist, J. A.; Ramos, J.; Matos, K. *Tetrahedron Lett.*, **1997**, *38, 6639.*
[27] Soderquist, J. A.; Martinez, J.; Oyola, Y.; Kock, I. *Tetrahedron Lett*. **2004**, *45*, 5541.
[28] Vasella, A. Wolfgang Wenger, W.; Rajamannar, T. *Chem. Commun*., **1999**, 2215.

2.2.3 Properties of nickel.

As an earth-abundant first row metal, nickel provides a sustainable and much cheaper alternative to palladium in catalytic reactions. Moreover, despite the two compounds being isoelectronic and possessing substantial overlapping reactivity, there are several inherent proprieties that distinguish nickel from palladium and allow for unique synthetic applications. Nickel has a smaller atomic radius than palladium,[29] which is reflected in relatively short Ni-ligand bond lengths. Despite its position in the periodic table, nickel is more electropositive than palladium, which enables it undergo a more facile oxidative addition with a wide range of electrophiles. Increased π-back donation relative to palladium allows nickel to bind olefins more tightly, which in turn results in facile β-migratory insertion.[30] Conversely, the shorter bond lengths in organonickel complexes have been proposed to hinder bond rotation necessary to achieve agostic interactions with β-hydrogens, making nickel-alkyl species less prone to undergo β-hydride elimination.[31] An additional feature of nickel is that it can readily access oxidation states of I, III, and more rarely IV. This ability enables nickel to participate in both polar and radical based catalytic cycles. While catalytic cycles with nickel that alternate between Ni(0) and Ni(II) oxidation states are common, cycles involving Ni(I)/Ni(II)/Ni(III) oxidation states are often invoked.[1] By accessing these diverse manifolds, nickel's reactivity in catalytic processes can be difficult to control, however its

[29] (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.; and Alvarez, S. *Dalton Trans*. **2008**, 2832.
[30] Massera, C.; Frenking, G. *Organometallics* **2003**, *22*, 2758.
[31] Lin, B.-L.; Liu, L.; Fu, Y.; Luo, S.-W.; Chen, Q.; Gu, Q.-X. *Organometallics* **2003**, *23*, 2114 (b) Xu, H.; White, P. B.; Hu, C.; Diao,T. *Angew. Chem. Int. Ed.* **2017**, *56*, 1535.

use in homogenous catalysis has enabled the development of challenging and unique reactions.

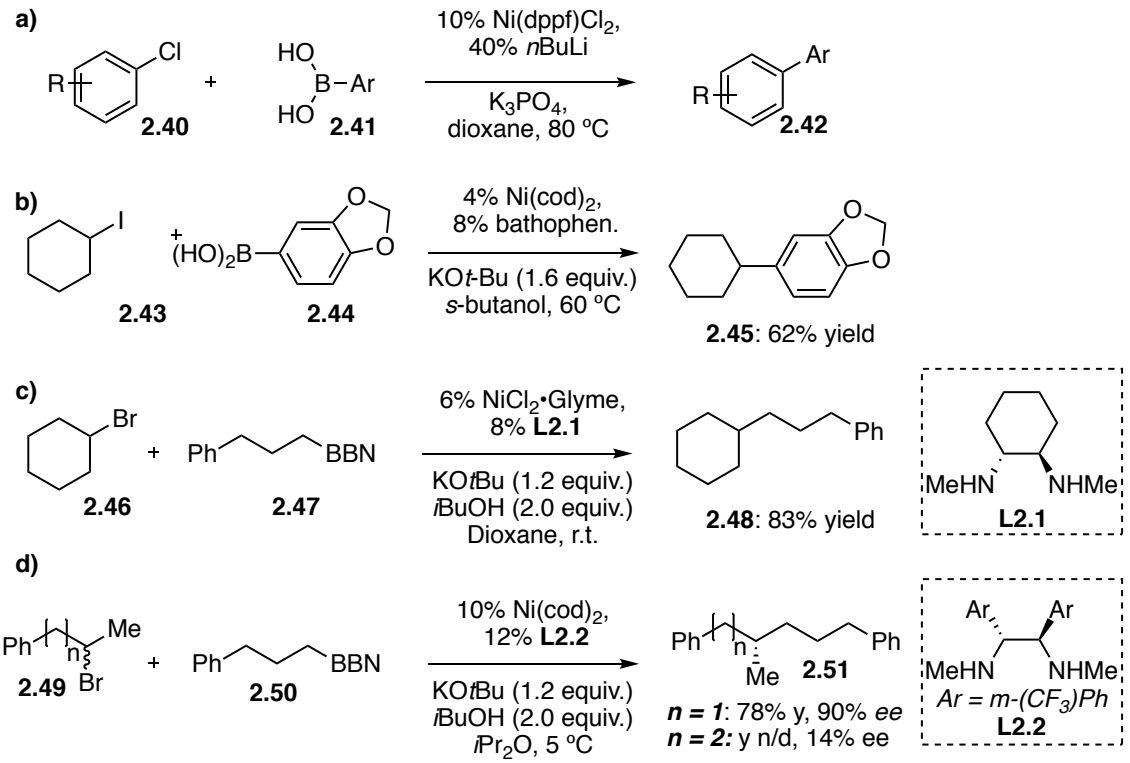
2.2.4 Nickel in Suzuki-Miyaura cross-coupling reactions.

The use of nickel in Suzuki cross-couplings, although not as established as palladium, has seen significant development in recent years. In general, the earliest discoveries on nickel's ability to catalyze cross-couplings between organometallic reagents and organic electrophiles antecede those with palladium and can be traced back to the beginning of the twentieth century.[32] Several important observations that led to the development of modern metal catalyzed cross-couplings were made by studying systems catalyzed by nickel. These include the first isolation of an oxidative addition adduct,[33] and the discovery that phosphine ligands can be used to refine the reactivity of organometallic complexes.[34] However, the predictable behavior of Pd in catalytic processes established it as the metal of choice for Suzuki cross-couplings. Recently a greater understanding of nickel's properties and fundamental reactivity has spurred the development of novel methods that can accomplish unique and challenging transformations. In general, nickel's ability to engage with organoboron nucleophiles in typical Suzuki couplings for biaryl synthesis has been amply demonstrated.[35] Moreover, nickel's ability to undergo a more facile oxidative addition has been harnessed to engage conventionally inert electrophiles. In 1996, Miyaura reported that nickel catalysis enabled

[32] For a historical perspective on metal-catalyzed cross-coupling reactions: Johansson Seechurn, C. C.; Kitching, M. O.; Colacot, T. J.; Snieckus V. *Angew. Chem. Int. Ed*. **2012**, *51*, 5062.
[33] Uchino, M.; Yamamoto, A.; Ikeda, S. *J. Organomet. Chem*. **1970**, *24*, C63.
[34] Tamao, K.; Sumitani, K.; Kumada, M. *J. Am. Chem. Soc*. **1972**, *94*, 4374.
[35] For a review: Han, F. -S. *Chem. Soc. Rev.,* **2013**, *42*, 5270.

Suzuki cross-couplings with aryl chlorides, which at the time were considered unreactive substrates in cross-coupling reactions under palladium catalysis (Figure 2.9a).[36] Since this seminal report, nickel has been used for reactions with increasingly challenging electrophiles such as aryl fluorides, ammonium salts, aryl ethers and more.[35] Nickel has also been used to catalyze cross-couplings with primary and secondary alkyl halides. The first example of Suzuki-Miyaura cross-coupling with secondary alkyl halides was disclosed by Fu using aryl boronic acids (Figure 2.9b).[37] Fu also disclosed the first Suzuki coupling between secondary alkyl halides and alkylborane reagents (Figure 2.9c).[16]

Figure 2.9. Selected examples of Suzuki-Miyaura couplings catalyzed by nickel



[36] Saito, S.; Sakai, M.; Miyaura, N. *Tetrahedron Lett.* **1996**, *37*, 2993.
[37] Zhou, J. Fu, G. C. *J. Am. Chem. Soc*. **2004**, *126*, 1340.

The above examples take advantage of slower β-hydride elimination in alkylnickel intermediates, as well as the ability to access single electron pathways. Moreover, these unique properties have enabled the development of stereoconvergent Suzuki cross-couplings with racemic secondary alkyl halides. In this context, aryl and alkyl-9-BBN have found ample application in enantioselective cross-couplings with a wide range of secondary alkyl halides.[38] Each system in these reactions is typically optimized to achieve high enantioselctivities for specific substrates posessing distinct functionalities and structural motifs. Factors such as the identity of the directing group and its distance from the C-X bond have a large impact on the transformation. This is highlighted in the stereoconvergent coupling with homobenzylic bromides shown in Figure 2.9d, where extending the carbon chain by a single methylene unit results in a dramatic loss of enantioselectivity.[38a] Amines, sulfones, carbonyls, and ethers were among the directing functionalities that enabled enantioselective reactions.

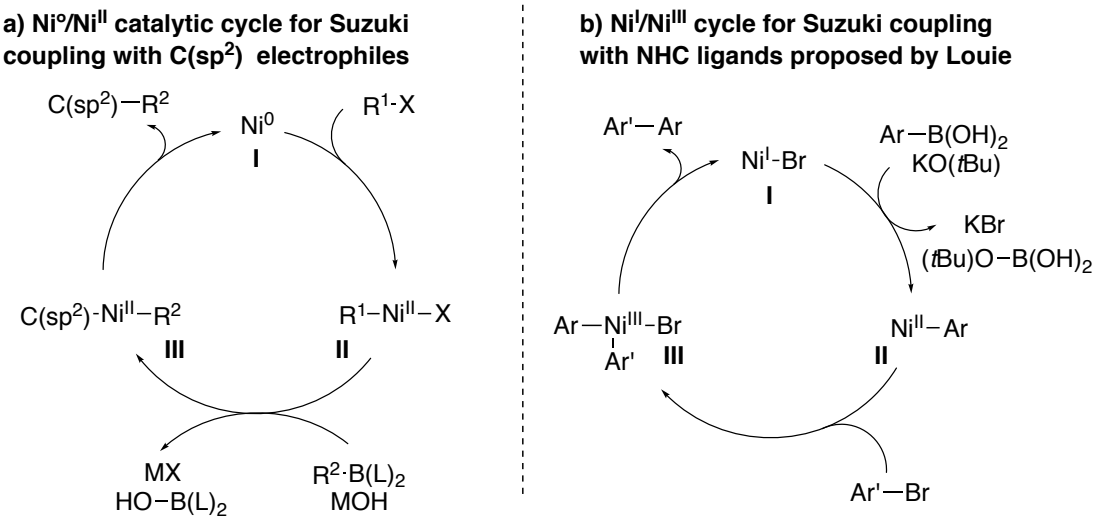
2.2.5 Mechanistic overview of nickel-catalyzed Suzuki cross-couplings.

Mechanistically, the reaction pathways proposed for these transformations are diverse, and warrant a brief discussion given that conjunctive cross-coupling employs reagents and reactive intermediates that are also present in the Suzuki cross-coupling. Nickel-catalyzed reactions often involve sequences of steps that are not aligned with

[38] (a) Lundin P. M.; Fu, G. C. *J. Am. Chem. Soc*. **2010**, *132*, 11027; (b) Zultanski, S. L.; Fu, G. C. *J. Am. Chem. Soc*. **2011**, *133*, 15362. (c) Owston, N. A. ; Fu, G. C. *J. Am. Chem. Soc.* **2010**, *132*, 11908. (d) Lu, Z.; Wilsily, A.; Fu, G. C. *J. Am. Chem. Soc.,* **2011**, *133*, 8154. (e) Wilsily, A.; Tramutola, F.; Owston, N. A.; Fu, G. C. *J. Am. Chem. Soc*., **2012**, *134*, 5794.

those typically reported in palladium-mediated catalytic cycles.[1,39] However, for Suzuki-Miyaura couplings with C(sp^2) electrophiles, mechanisms involving Ni(0)/Ni(II) cycles, akin to those for palladium systems, are generally proposed (Figure 2.10a). In fact, recent studies by Hazari and coworkers found that when using a bisphophine-ligated nickel catalyst, formation of a Ni(I) species (proposed to take place through comproportionation of Ni(II)/Ni(0) intermediates) was detrimental to the reaction.[40] Nevertheless, polar mechanisms that occur through Ni(I)/Ni(III) species have been proposed for reactions with aryl halides. The NHC-catalyzed Suzuki cross-coupling developed by Louie and coworkers was proposed to occur by such a mechanism (Figure 2.10b). Stoichiometric experiments revealed that Ni(I)-X species underwent transmetallation with arylboronic acids, while no reaction took place between the Ni(I)-X and aryl halides.[41]

Figure 2.10. Catalytic cycles for cross-couplings with C(sp^2) electrophiles



[39] For reviews: (a) Li, Z.; Liu L. *Chin. J. Catal.* **2015**, *36*, 3. (b) Diccianni, J. B.; Diao, T. *Trends in Chemistry*, **2019**, *ASAP.*

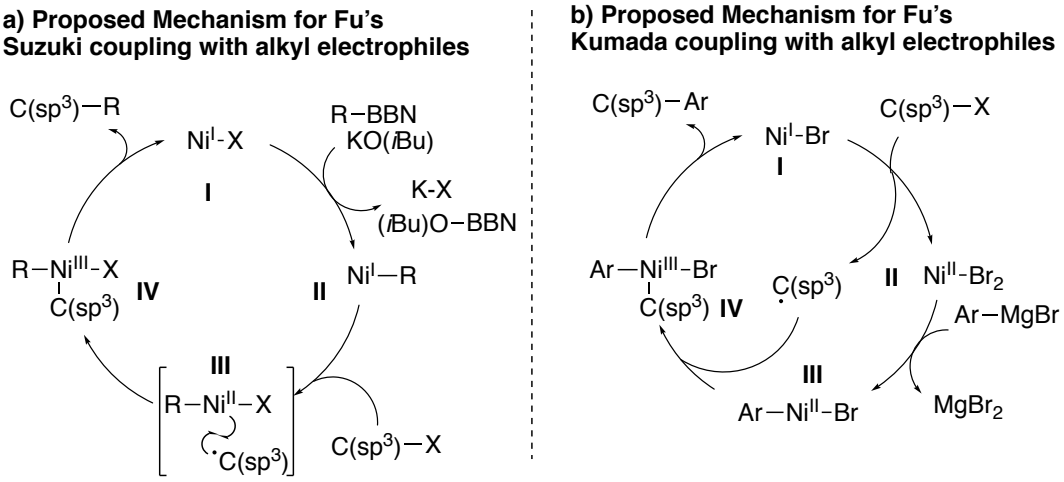
[40] Mohadjer Beromi, M.; Nova, A.; Balcells, D.; Brasacchio, A. M.; Brudvig, G. W.; Guard, L. M.; Hazari, N.; Vinyard, D. J. *J. Am. Chem. Soc.* **2017**, *139*, 922.

[41] Zhang, K.; Conda-Sheridan, M.; Cooke, S. R.; Louie, J. *Organometallics*, **2011**, *30*, 2546.

Couplings with C(sp^3) hybridized electrophiles often involve non-polar mechanisms with radical intermediates. In these reactions Ni(I)/Ni(III) catalytic cycles are generally invoked. An example of such cycle has been proposed by Fu in the cross-coupling between alkyl-9-BBN reagents and secondary alkyl halides (Figure 2.11a).[38d,e] Here a Ni(I)-X species (**I**) is proposed to undergo transmetallation first with the organoboron reagent, forming an alkyl nickel species (**II**). The latter undergoes SET with an alkyl halide to generate a R-Ni(II)-X (**III**) and an alkyl radical that subsequently recombine to form a Ni(III) (**IV**) intermediate from which reductive elimination takes place. This mechanistic proposal was corroborated computationally by professor Yao Fu.[42] "Transmetallation first" mechanisms are common with Ni(I)/Ni(III) mechanisms. However, depending on the system, single-electron-transfer to generate carbon centered radicals may take place before transmetallation, from a Ni(I)-X, or after transmetallation, from a Ni(I)-R species. An example of the former is proposed in a recent mechanistic study by Fu's group on a stereoconvergent Kumada cross-coupling (Figure 2.11b). The authors propose that SET and formation of alkyl radicals takes place from a Ni(I)-Br species (**I**). Subsequent transmetallation takes place between the Grignard reagent and Ni(II)Br_2 intermediate (**II**) prior to recombination with the alkyl radical. In either mechanistic scenario recombination between nickel and the electrophile takes place from a Ni(II) intermediate that has undergone transmetallation.

[42] Li, Z.; Jiang, Y. Y.; Fu, Y. *Chem. Eur. J.* **2012**, *18*, 4345

Figure 2.1. Catalytic cycles for cross-couplings with C(sp^3) electrophiles

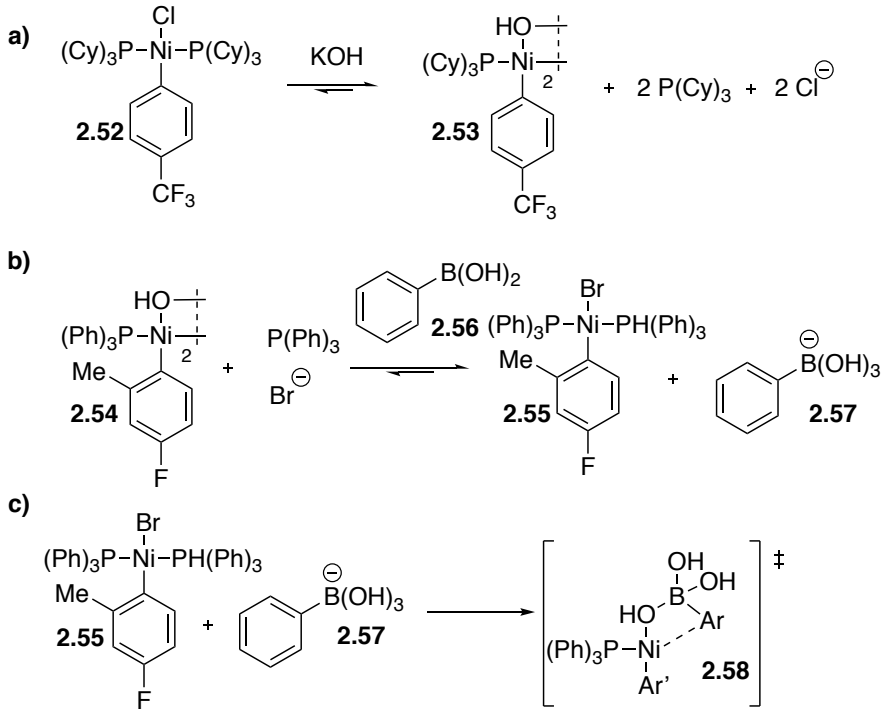


The mechanism of transmetallation in nickel-catalyzed Suzuki-Miyaura reactions has not been investigated as thoroughly as in the palladium-catalyzed counterpart. However, Monfette and coworkers recently studied this step for the Ni-catalyzed cross-coupling of aryl chlorides with arylboronic acids. Specifically, the authors reported that Ar-Ni(II)-Cl oxidative addition adduct **2.52** (Figure 2.12a) dimerized in the presence of hydroxide and proposed that the ensuing nickel-hydroxyl bimetallic species **2.53** was catalytically relevant based on the observation of rapid biaryl formation in reactions between neutral arylboronic acid and stoichiometric amounts of complex **2.53**.[43] This view was challenged later by Grimaud who carried out an in depth experimental and computational study to examine the role of such nickel-hydroxyl dimers in the transmetallation step of Suzuki cross-coupling reactions.[44] Noting the ability of neutral boronic acids to abstract hydroxide from dimer **2.54** and regenerate the monomeric species (Figure 2.12b), as well as rate inhibition resulting from excess hydroxide in cross-

[43] Christian, A. H.; Müller, P.; Monfette, S. *Organometallics* **2014**, *33*, 2134.
[44] Payard, P. -A.; Perego, L. A.; Ciofini, I.; Grimaud, L. *ACS Catal.* **2018**, *8*, 4812.

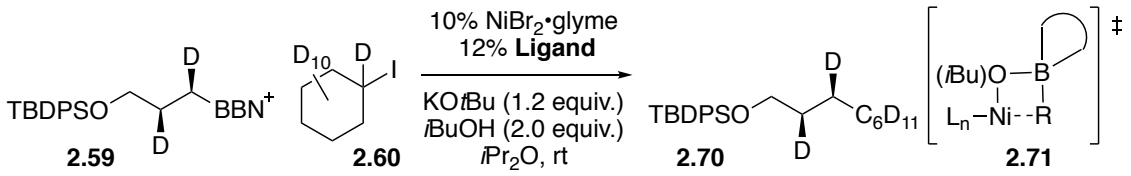
coupling reactions between phenylboronic acid and stoichiometric amounts of dimer **2.54**, the authors concluded that nickel-hydroxyl dimers constituted off-cycle resting states of the catalyst and that transmetallation takes place between Ni-X species such as **2.55** and a four-coordinate boron 'ate' complex (Figure 2.12c). In these studies, the nature of the halide counterion was proposed to play an important role, as nickel's stronger affinity for chloride counterions disfavors formation of hydroxyl dimers, which in turn increases the rate of transmetallation. Conversely a bromide counterion is more easily displaced by hydroxide, leading to the formation of inactive Ni-OH species. Similar to the pre-transmetllation intermediates proposed for palladium, the computational models by Grimaud support the formation of a Ni-O-B linkage with a monoligated nickel oxidative addition adduct as in **2.58** (Figure 2.12c), from which transmetallation ensues through a four-membered transition state.

Figure 2.12. Transmetallation mechanistic studies by Monfette and Grimaud



With regards to transmetallation of 9-BBN reagents, Fu and coworkers carried out isotope labeling experiments using *trans* deuterated alkyl 9-BBN in a cross-coupling with deuterated cyclohexyl bromide (Figure 2.13).[38e] Similar to the corresponding experiments by Woerpel and Soderquist with palladium catalysis, transmetallation was found to take place with retention of configuration at carbon, consistent with a four-membered transition state. KO*i*Bu was shown to form four-coordinate 'ate' complexes with 9-BBN quantitatively, supporting a mechanism whereby transmetallation occurs from the combination of a nickel halide species and oxygen bound borate (**2.71**, Figure 2.13).

Figure 2.13. Transmetallation of alkyl-BBN reagents



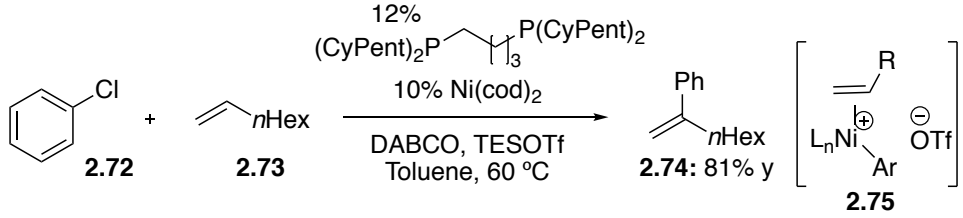
2.2.6 Olefin activation by nickel.

Considering that conjunctive cross-coupling requires activation of an olefin towards carbometallation, nickel's rich history in alkene activation inspired and guided us in developing our reaction. As mentioned earlier in the chapter, the electropositivity of nickel results in increased π-backdonation, and as a consequence, strong olefin binding and activation. This feature has been exploited extensively in industrial and academic research, with a large emphasis on olefin polymerization and oligomerization.[45] As of 2013, Shell's higher olefin process, which is based on homogeneous nickel catalysis,

[45]Speiser, F.; Braunstein, P.; Saussine, L. *Acc. Chem. Res*. **2005**, *38*, 784.

produced α-olefins at over 1 million tons/year.[46] Additionally, the facile nickel insertion into olefins,[30] has led to the development of several methods involving cycloisomerization,[47] and reductive couplings.[48] Heck reactions are relatively uncommon using nickel catalysis. While oxidative addition, olefin binding, and β-migratory insertion should occur more readily with nickel, β-hydride elimination and catalyst regeneration have been proposed to be less facile than with palladium.[31] However, a number of examples have been disclosed throughout the years[49] and recently several advancements have been made in this area through the intermediacy of cationic nickel species.[50] Jamison and coworkers reported methods for highly branch-selective nickel-catalyzed Heck reactions[50c,d] in which silyl triflate species act as halide scavengers (Figure 2.14). The intermediacy of olefin-bound cationic nickel bears resemblance to proposed intermediates in palladium-catalyzed conjunctive couplings.

Figure 2.14. Jamison's Mizoroki-Heck reaction mediated by cationic nickel



Outside of radical addition/cross-coupling cascades (which will be discussed in the next chapter), and methods realized though oxidative cyclization based strategies, a

[46] Keim, W. *Angew. Chem. Int. Ed.* **2013**, *52*, 12492.
[47] Yamamoto, Y. *Chem. Rev.* **2012**, *112*, 4736.
[48] Montgomery, J. *Angew. Chem. Int. Ed.* **2004**, *43*, 3890.
[49] (a) Boldrini, G. P.; Savoia, D.; Tagliavini, E.; Trombini, C.; Ronchi, A. U. *J. Organomet. Chem.* **1986**, *301*, C62. (b) Lebedev, S. A.; Lopatina, V. S.; Petrov, E. S.; Beletskaya, I. P. *J. Organomet. Chem.* **1988**, *344*, 253. (c) Kelkar, A. A.; Hanaoka, T.; Kubota, Y.; Sugi, Y. *Catal. Lett.* **1994**, *29*, 69. (d) Iyer, S.; Ramesh, C.; Ramani, A. *Tetrahedron Lett.* **1997**, *38*, 8533.
[50] (a) Gøgsig, T. M.; Kleimark, J.; Nilsson Lill, S. O.; Korsager, S.; Lindhardt, A. T.; Norrby, P. O.; Skrydstrup, T. *J. Am. Chem. Soc.* **2011**, *134*, 443. (b) Ehle, A. R.; Zhou, Q.; Watson, M. P. *Org. Lett.* **2012**, *14*, 1202. (c) Standley, E. A.; Jamison, T. F. *J. Am. Chem. Soc.* **2013**, *135*, 1585. (d) Tasker, S. Z.; Gutierrez, A. C.; Jamison, T. F. *Angew. Chem. Int. Ed.* **2014**, *53*, 1858.

small number of nickel-mediated dicarbofunctionalization of olefins had been disclosed prior to our investigation into nickel-catalyzed conjunctive cross-couplings. In these methods, Heck-type intermediates obtained through β-migratory insertion are cross-coupled with a second organic moiety, instead of undergoing β-hydride elimination. Early examples of such tandem reactivity were reported by Delgado in cyclization/cyanation and cyclization/carbonylation reactions of olefins with amine tethered alkenyl bromides (Figure 2.15a).[51] These reactions took advantage of the coordinating amine group to stabilize alkyl-Ni species and avoid β-hydride elimination. Murakami showed that nickel catalysis could be used to activate C-C bonds of strained cyclobutanone substrates, and the two fragments could add across an olefin in an intramolecular reaction (Figure 2.15b).[52] The process was rendered enantioselective through the use of a chiral phosphoramidite ligand. Finally, Fu and coworkers disclosed a system for the enantioselective intramolecular cyclization/cross-coupling of aryl-BBN tethered alkenes and alkyl electrophiles enabled by a non-racemic alkyl diamine ligand (Figure 2.15c).[53] The reaction is likely to proceed through a nucleometallation pathway whereby the aryl borane undergoes transmetallation with nickel; subsequent olefin insertion results in a chiral homobenzylic nickel intermediate. The latter is then cross-coupled with an alkyl iodide generating indane and dihydrobenzofuran derived products.

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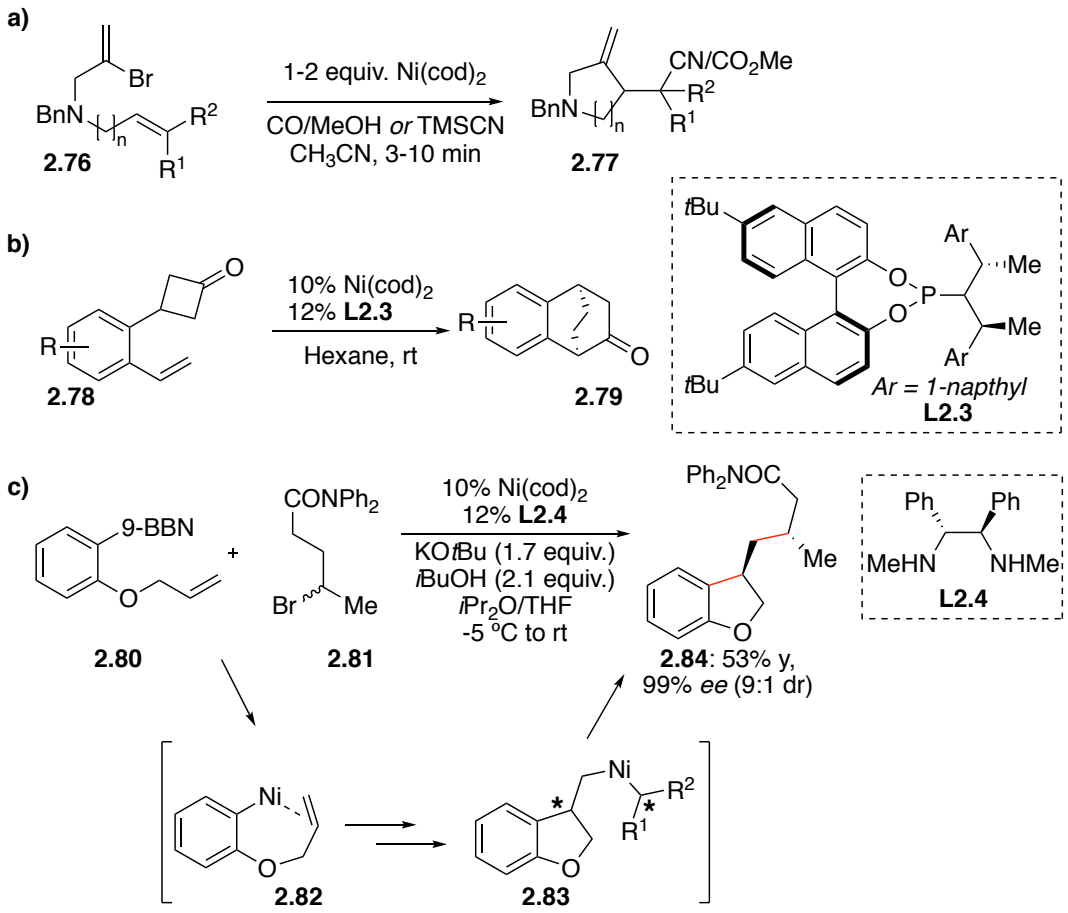
[51] (a) Sole, D.; Cancho, Y.; Llebaria,A.; Moreto, J. M.; Delgado, D. *J. Am. Chem. Soc*. **1994**, *116*, 12133. (b) Sole, D.; Cancho, Y.; Llebaria,A.; Moreto, J. M.; Delgado, D. *J. Org. Chem.* **1996,** *61,* 5895.

[52] Liu, L.; Ishida, N.; Murakami, M. *Angew. Chem. Int. Ed*. **2012**, *51*, 2485.
[53] Cong, H.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 3788.

The catalyst could set multiple stereocenters. Notably, reaction of a racemic secondary alkyl-bromide resulted in formation of product with excellent enantio- and diastereoselectivity. This observation points to a nickel mediated alkyl-alkyl bond forming step and rules out the possibility of a stereoconvergent radical addition/cross-coupling cascade mechanism. Taken together, these precedents pointed to nickel complexes as promising catalysts for activating alkenyl boron 'ate' reagents, and guided us in the development of nickel catalyzed conjunctive coupling.

Figure 2.15. Early examples of Ni-catalyzed dicarbofunctionalization reactions

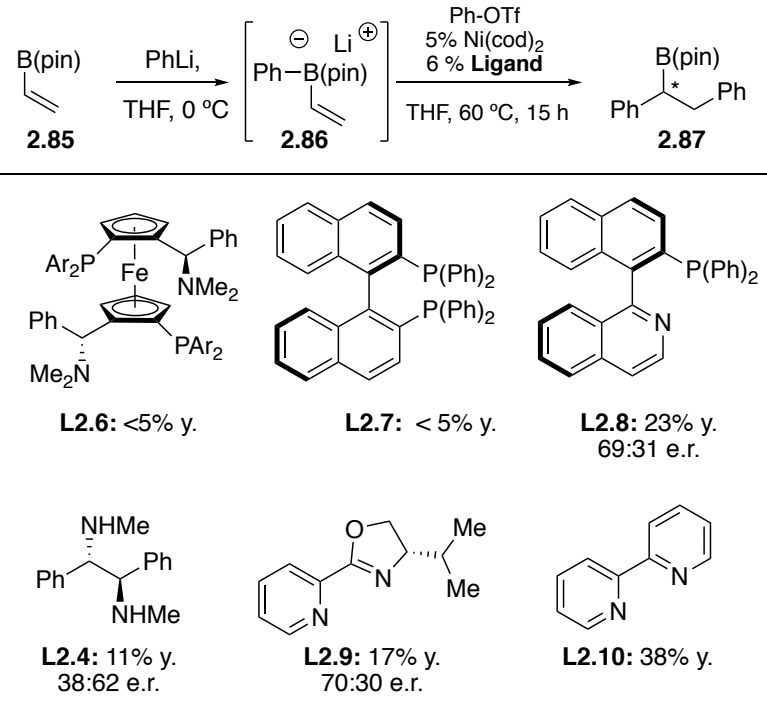


2.3 NICKEL-CATALYZED CONJUNCTIVE CROSS-COUPLING OF 9-BBN BORATES[54]

2.3.1 Reaction development.

In the initial phases of research we sought to obtain a proof of concept for the possibility of inducing a 1,2-metallate shift on a vinylboron 'ate' using nickel catalysis. To this end, we set out to reproduce the reactivity observed in the palladium-catalyzed conjunctive cross-coupling of boronic esters using nickel (Figure 2.16).

Figure 2.16. First discovery of Ni-catalyzed conjunctive coupling with boronic esters

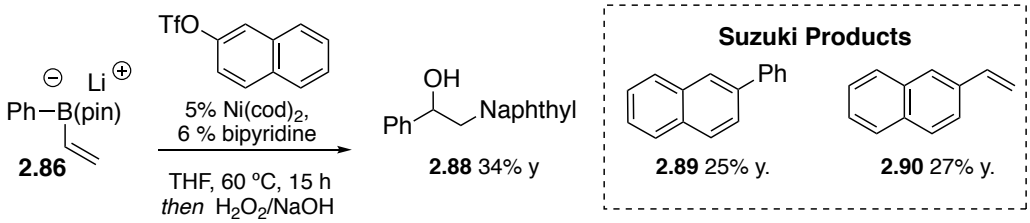


However, treating a vinylboronic acid pinacol ester with phenyl lithium and exposing it phenyl triflate, catalytic Mandyphos ligand **L2.6** and nickel cyclooctadiene in

[54] Chierchia, M.; Law, C.; Morken, J. P. *Angew. Chem. Int. Ed.* **2017**, *56*, 11870.

a manner analogous to the palladium system was not productive. Upon changing the ligands we were pleased to find that while phosphine based ligands did not result in the desired reaction, using ligand **L2.8** provided **2.87** in 23% yield and a 69:31 er, showing that enantioselective conjunctive cross-coupling could be accomplished with nickel. This result led us to explore several amine based ligands, which were found to deliver small amounts of the desired product with modest levels of selectivity. The highest yields were obtained with achiral bipyridine (**L2.10**). Using a larger electrophile in this reaction provided a clearer picture of the product distribution in this transformation, which was found to favor formation of Suzuki cross-coupling products.

Figure 2.17. Ni-catalyzed conjunctive cross-coupling product distribution

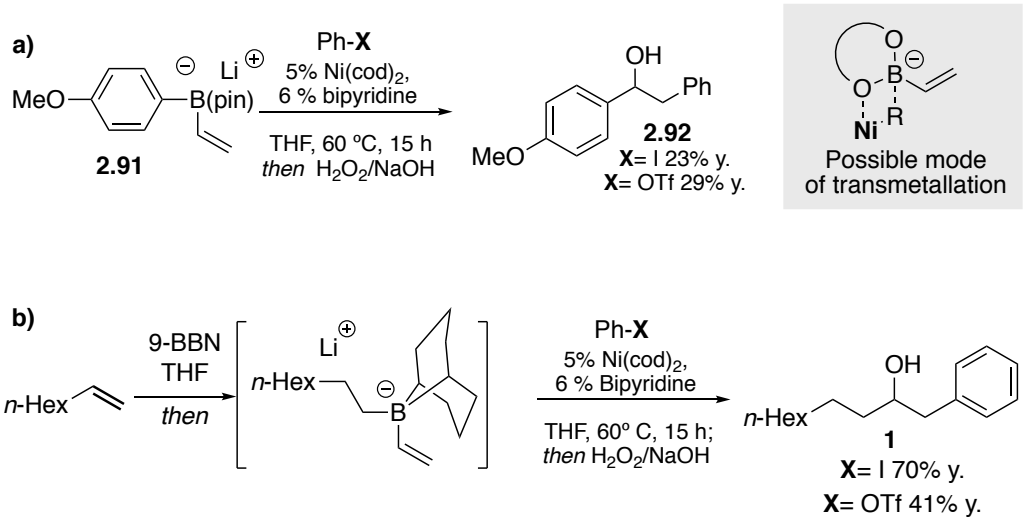


Switching to a more electron-rich aryl migrating group (to promote 1,2-metallate shift by increasing the nucleophilicity of the vinyl boron 'ate'), and exploring different counterions in the electrophiles did not improve the reaction, use of aryl iodides provided similar results as aryl triflates (Figure 2.18a). Based on the hypothesis that transmetallation may be facilitated by oxygen coordination from the pinacol ligand,[55] we examined 9-BBN derived 'ate' species in this transformation since this class of substrates did not possess a coordinating heteroatomic functionality. Thus, hydroboration of 1-

[55] (a) Thomas, A. A.; Denmark, S. C *Science* **2016**, *352*, 329. (b) Thomas, A. A.; Wang, H.; Zahrt, A. F.; Denmark, S. C. *J. Am. Chem. Soc.* **2017**, *139*, 3805. (c) Thomas, A. A.; Zahrt, A. F.; Delaney, C.P.; Denmark, S. C. *J. Am. Chem. Soc.* **2018**, *140*, 4401. See also ref. 38e, 42, 44, 17, 18.

octene followed by addition of vinyllithium and cross-coupling using a nickel/bipyridine catalyst system with phenyl triflate as electrophile provided the product **1** in 41% yield (Figure 2.18b). Switching to iodobenzene increased the product yield to 70% (Figure 2.18b), and Suzuki cross-coupling appeared to be entirely suppressed in this reaction.

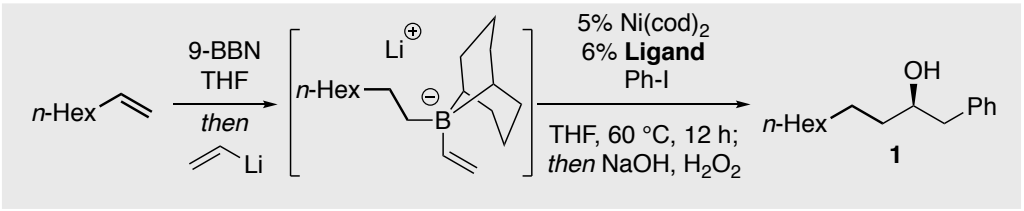
Figure 2.18. Ni-catalyzed conjunctive cross-coupling with 9-BBN



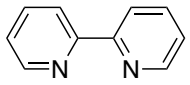
Having established a effective system, we surveyed non-racemic ligands to render the reaction enantioselective (Figure 2.19). In general, reactions with $Ni(cod)_2$ required a diamine ligand to promote the reaction, as none of the desired product was detected in using monodentate, tridentate, or no ligands (Figure 2.19**, L2.13** and **L2.12**). As a chiral analogue of bipyridine, the PyOx ligand class was explored thoroughly and was found to generally deliver products efficiently**, L2.16-L2.20**. However, of the various derivatives tested none exceeded the modest enantioselectivity of 79:21 e.r. obtained with *t*Bu-PyOX **L2.18**. Other bisoxazoline based ligands proved ineffective in delivering products (**L2.14** and **L2.15**). Eventually, aliphatic 1,2-diamine ligand **L2.1** was found to deliver products with good yield and enantioselectivity. Interestingly the reaction was found to be highly sensitive to the substitution pattern on this ligand scaffold, as no products would be

obtained if the amine was completely unsubstituted (**L2.21**), or if branched groups were appended to the nitrogen (**L2.22**). The former resulted in an increase in Ulman coupling of the aryl electrophile, possibly due to the decreased sterics around nickel facilitating bimetallic reactivity, while the latter provided no reaction products. Achiral ligand **L2.24** also resulted in inefficient reactions, highlighting the importance of the substituents on the backbone of the diamine structure. These may promote bidentate ligation. Finally diphenylethylene diamine ligand **L2.4** provided a boost in enantioselectivity for the reaction.

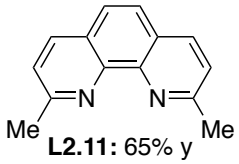
Figure 2.19. Ligand survey for Ni-catalyzed conjunctive coupling with 9-BBN



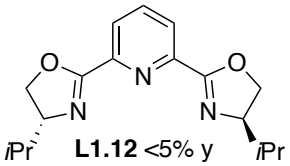
No Ligand: <5% y.



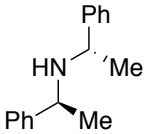
L2.10: 70% y



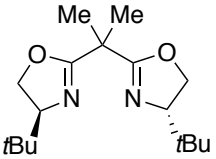
L2.11: 65% y



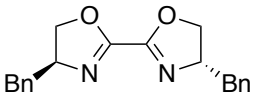
L1.12 <5% y



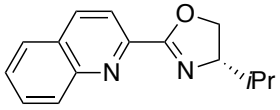
L2.13: <5% y[a]



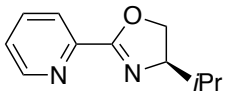
L2.14: <5% y



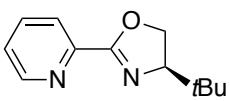
L2.15: <5% y



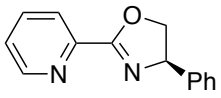
L2.16: 90% y
42:58 er



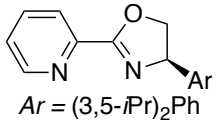
L2.17: 72% y
71:29 er



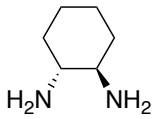
L2.18: 87% y
79:21 er



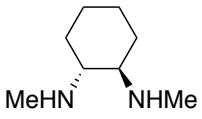
L2.19: 56% y
66:34 er



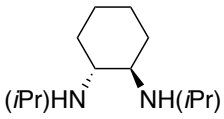
Ar = (3,5-*i*Pr)$_2$Ph
L2.20: 61% y
57:43 er



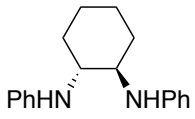
L2.21: <5% y



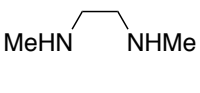
L2.1: 60% y
93:7 er



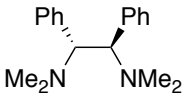
L2.22: <5% y



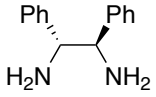
L2.23: <5% y



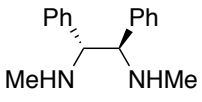
L2.24: 24% y



L2.25: <5% y



L2.26: <5% y



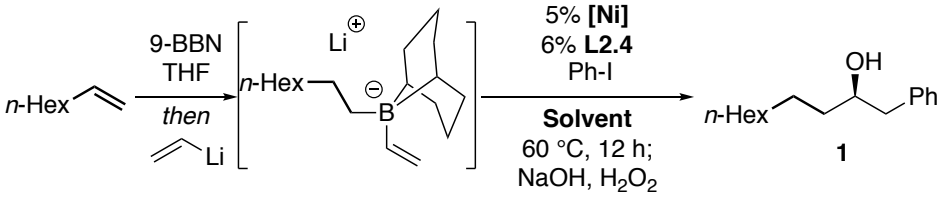
L2.4: 61% y
95:5 er

a: 12% ligand loading

Next, we examined the impact of other parameters in the reaction (Table 2.1). Exploring possible solvent effects (entries 1-6), we found that strongly coordinating solvents such as DMSO and MeCN (entries 1,2) diminished the reactivity, while ether based solvents such as MTBE and 1,4-dioxane (entries 3,4) provided similar results as THF, although with slightly reduced yields and selectivities. Low polarity solvents such

as toluene and cyclohexane (entries 5,6) resulted in markedly decreased selectivities. We then turned our attention to the combination of ligand **L2.4** with different nickel sources (entries 7-10). This was prompted by an NMR experiment which revealed that no complexation took place between $Ni(cod)_2$ and **L2.4** over the course of several hours (conversely mixing $Ni(cod)_2$ and bipyridine in THF results in an immediate color change due to rapid formation of [bipyNi(cod)]). Eventually the nickel plated onto the surface of the NMR tube. Surveying a few common nickel sources, we found $Ni(acac)_2$ provided a slight boost in yield (entry 10). The yield was further improved (entry 11) by adding 10% excess boron 'ate' as sacrificial reductant to generate Ni(0) in account of the switch from a Ni(0) to a Ni(II) precatalyst.

Table 2.1. Effects of solvent and precatalyst on the reaction outcome



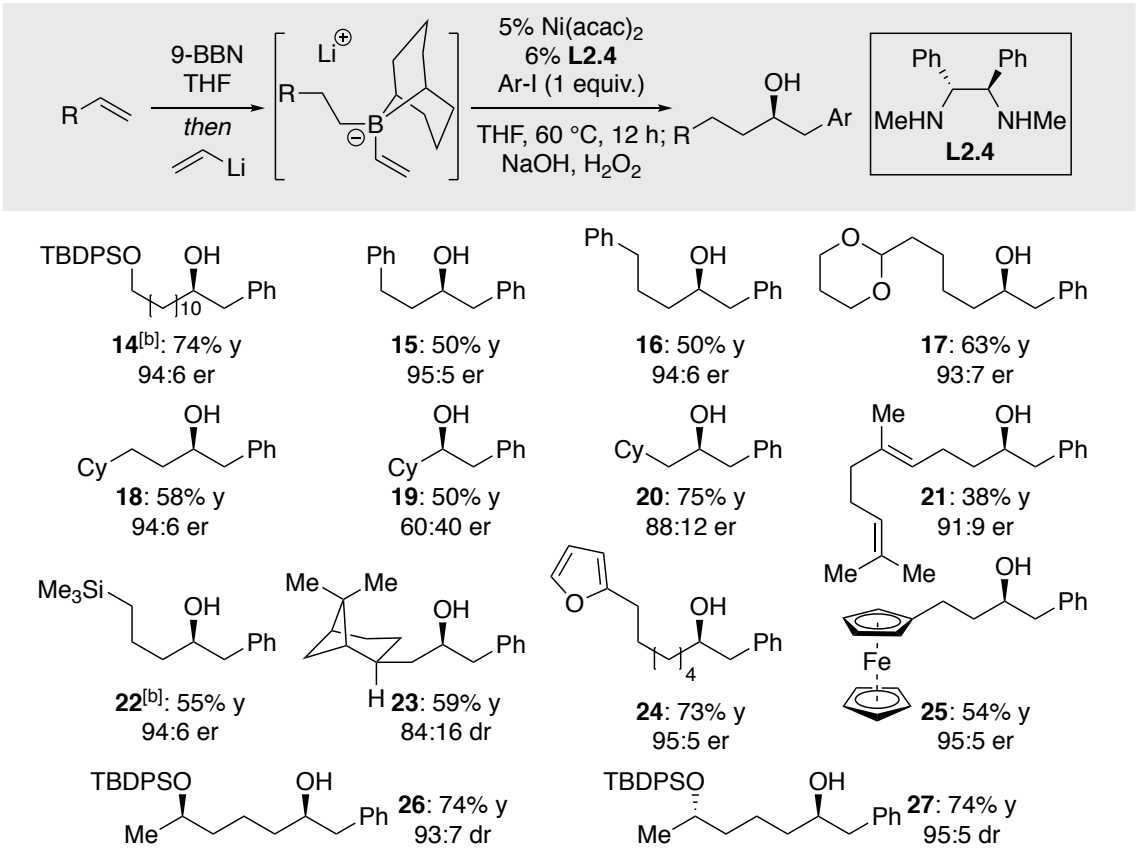
Entry	[Ni]	Solvent	Yield	er
1	$Ni(cod)_2$	DMSO	15%	N.D.
2	$Ni(cod)_2$	MeCN	12%	N.D.
3	$Ni(cod)_2$	1,4-dioxane	51%	93:7
4	$Ni(cod)_2$	MTBE	45%	93:7
5	$Ni(cod)_2$	Toluene	42%	83:17
6	$Ni(cod)_2$	Cyclohexane	32%	79:21
7	$NiBr_2$•glyme	THF	60%	94:6
8	NiI_2	THF	<5%	N.D.
9	$Ni(CO_3)$	THF	<5%	N.D.
10	$Ni(acac)_2$	THF	69%	95:5
11[a]	$Ni(acac)_2$	THF	80%	95:5

(a) 1.1 equiv. of boron 'ate' used.

2.3.2 Substrate scope.

Having identified satisfactory reaction conditions, we explored the scope of the transformation. These studies highlight one of the key advantages of using 9-BBN in the reaction: the reactive boranes can be obtained *in situ* through simple hydroboration of the corresponding alkene. Thus, a wide range of alkenes provided reactive boron 'ate' species that were effectively employed in a one-pot sequence to generate conjunctive cross-coupling products (**Figure 2.19**). Several functional groups, such as protected alcohols (**14, 26, 27**) and aldehydes (**17**), silanes (**22**), furans (**24**), and even a ferrocene (**25**), could be included in the borane substrates without hampering the desired reaction. Regioselective hydroboration of a triene provided dienyl product **21** in excellent enantiomeric ratio. Also of note, pre-installed stereocenters in the migrating group did not affect the selective outcome of the reaction. A limitation in scope of the reaction was found in α and β branched BBN reagents (**19, 20, 23**) which provided products in moderate to good yield, but with decreased selectivity. Nevertheless, it is noteworthy that in all these examples, including in the case of a secondary alkyl-BBN substrate, no migration of the cyclooctyl group was observed.

Figure 2.20. Scope of migrating group in Ni-catalyzed conjunctive coupling of 9-BBN

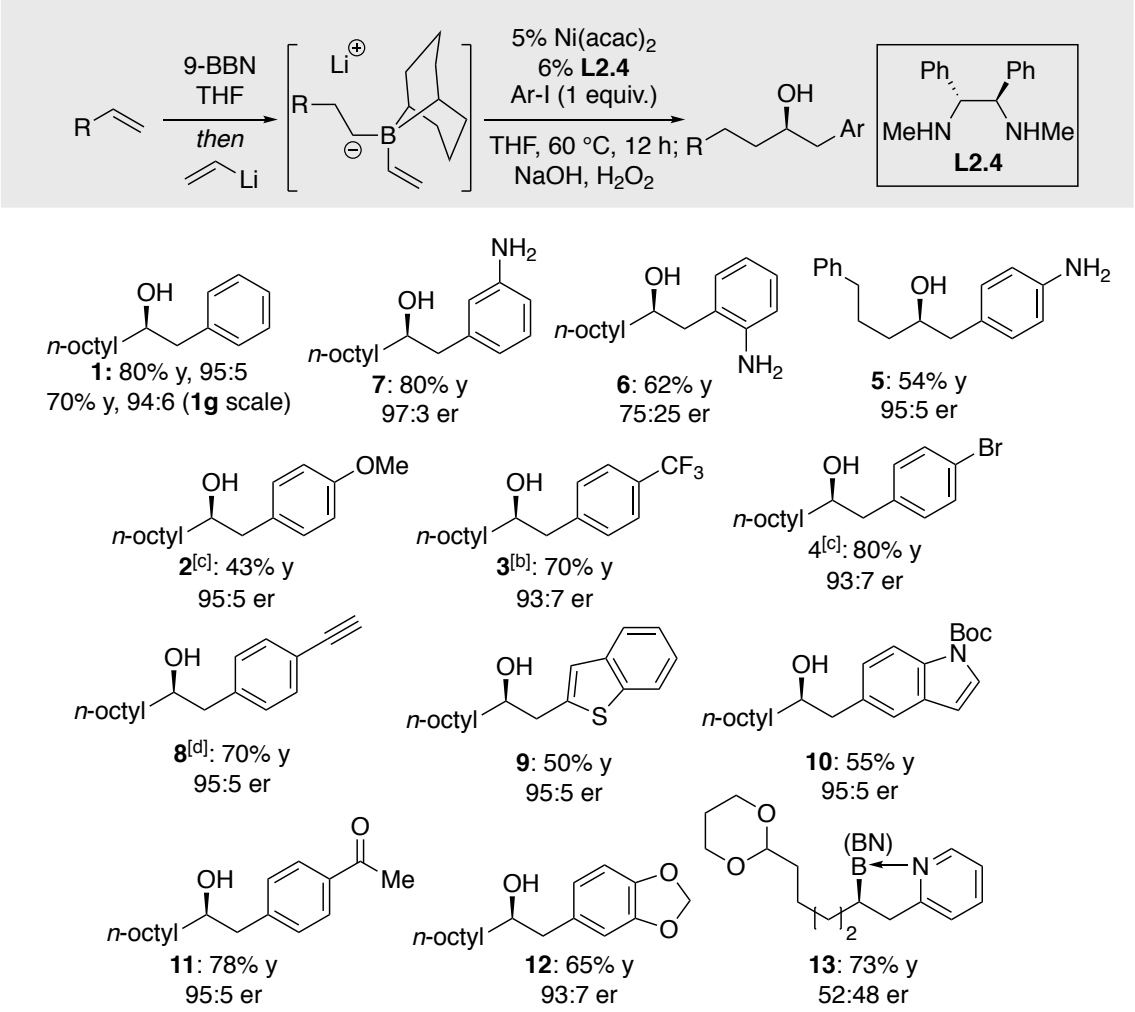


[a] vinyllithium was prepared from *n*-BuLi and tetravinyl stannane. [b] For these experiments, vinyllithium prepared from *n*-BuLi and vinyl iodide.

The scope of the electrophilic coupling partner was examined next, and this was also found to be rather broad, with a variety of iodoarenes participating in the reaction (Figure 2.21). Arenes possessing electron withdrawing (**3**) and electron donating substituents (**2**) as well as sensitive functionalities such as bromides (**3**), alkynes (**8**), ketones(**11**), and even free anilines (**5**, **6**, **7**), underwent the conjunctive cross-coupling to deliver products efficiently and enantioselectively. Indole (**10**), benzodioxole (**12**) and benzothiophene (**9**) heterocycles delivered non-racemic products as well. Interestingly, while sterically demanding *ortho*-substituted electrophiles such as 2-iodotoluene and 2-iodonaphthalene did not generate products efficiently (not shown), electrophiles

possessing coordinating functionality at the ortho position such as 2-iodoaniline (**6**) or 2-iodopyridine (**13**) participated efficiently in the reaction, albeit with greatly diminished enantioselectivity. In the case of 2-iodopyridine, the product **13** was isolated as a stable borane. Intramolecular coordination between boron and nitrogen made the substrate inert even to standard oxidation. Finally, the reaction could be carried out effectively in gram scale.

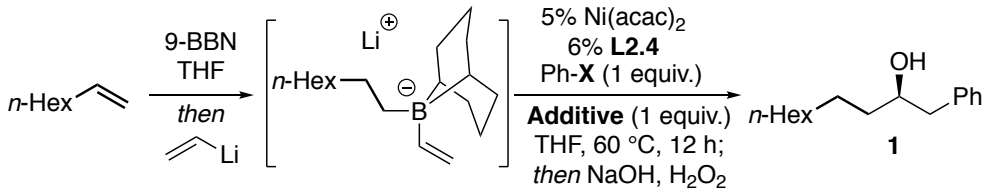
Figure 2.21. Scope of the electrophile in Ni-catalyzed conjunctive coupling of 9-BBN



[a] vinyllithium was prepared from *n*-BuLi and tetravinyl stannane. [b] For these experiments, vinyllithium prepared from *n*-BuLi and vinyl iodide. [c] Reaction conducted at room temperature. [d] Substrate was (4-iodophenyl)triethylsilyl acetylene, which undergoes desilylation during oxidation.

Aryl bromides did not participate effectively in the transformation under standard conditions (Table 2.2, entry 4). Moreover, the reactivity could be reestablished by adding an equivalent of sodium iodide (Table 2.2, entry 7). We also found that there was a significant inhibition of the desired reactivity resulting from the addition either lithium bromide or lithium chloride salts in reactions with iodobonzene (Table 2.2, entries 1-3).

Table 2.2. Halide inhibition in Ni-catalyzed conjunctive coupling



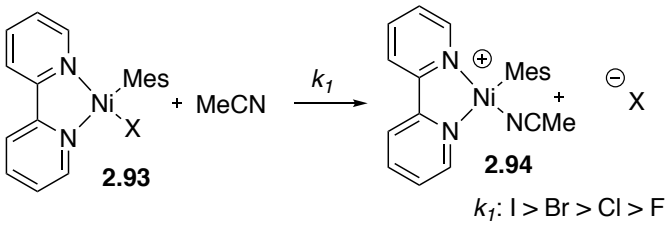
Entry	Ph-X	Additive	Yield	*e.r.*
1	Ph-I	-	80%	95:5
2	Ph-I	LiBr	32%	95:5
3	Ph-I	LiCl	31%	95:5
4	Ph-Br	-	<5%	N.D.
5	Ph-Br	LiI	40%	96:4
6	Ph-Br	KI	43%	96:4
7	Ph-Br	NaI	60%	95:5

This observation underscores the importance of the counterion in this system. It is apparent from these results that oxidative addition of aryl bromides occurs relatively efficiently under the reaction conditions.[56] However, while the bromide counterion seems to derail the desired reaction pathway, the iodide plays an important role in allowing conjunctive cross-coupling to take place. The importance of the iodide anion may result from structural differences in the nickel-halide intermediate, or may be traced to its greater tendency to dissociate from the nickel center. Klein and coworkers reported that Ni/ArX oxidative addition adducts ionized in solution through ligand exchange reactions with the solvent. They found that the rate of exchange in the reaction between [bipyNi(Mes)X] **2.93** and acetonitrile (Figure 2.24) decreased in the order I > Br > Cl >

[56] Cant, A. A.; Bhalla, R.; Pimlott, S. L.; Sutherland, A. *Chem. Commun.* **2012**, *48*, 3993.

F.[57] Thus, the iodide counterion may serve as an effective leaving group that can be easily displaced by THF or by the vinylboron 'ate' itself, opening a coordination site on nickel to facilitate the 1,2-metallate shift.

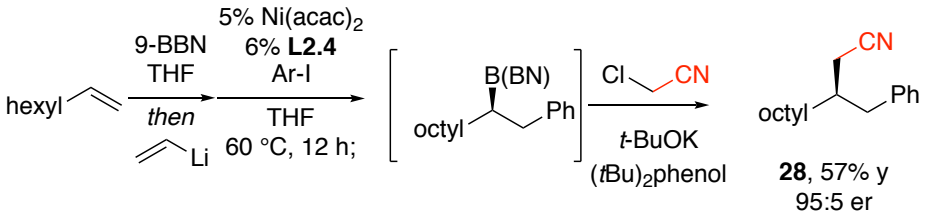
Figure 2.24. Trends in the ionization/ligand exchange in Ni/ArX oxidative addition adducts



2.3.3 Derivatization of the products.

Having explored the substrate scope for the transformation, we investigated means to functionalize the reaction products. To begin, we successfully carried out the stereospecific cyanomethylation developed by H. C. Brown in a one-pot fashion starting from the corresponding alkene(Figure 2.25).[7]

Figure 2.25. One-pot cyanomethylation of 9-BBN products

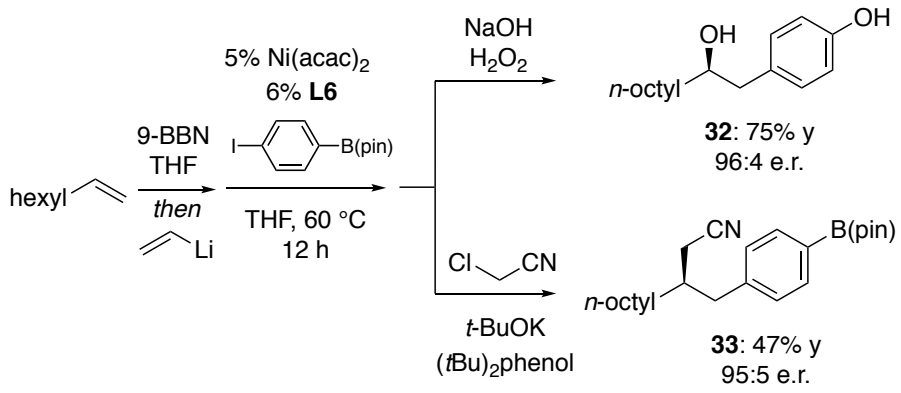


This transformation highlights once more the advantage of using 9-BBN reagents, as their enhanced reactivity enables them to undergo reactions that are not available to boronic esters. In fact, this feature was showcased by carrying out a conjunctive cross-

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

coupling with an aryl iodide containing a boronic ester functionality (Figure 2.26). The product of the reaction could be oxidized to the corresponding diol, or could undergo Brown's cyanomethylation chemoselectively to deliver the corresponding product with perfect retention of stereochemistry and with the boronic ester intact.

Figure 2.26. Chemoselective functionalization of bis-borylated products

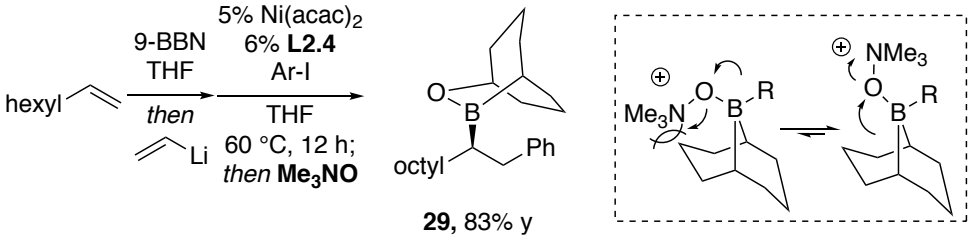


When exploring common reactions such as Evans-Zweifel olefination or our own methoxyamine-based amination method,[58] we were confronted with some of the limitations of 9-BBN mentioned earlier in the chapter: these reactions provided the desired products only in modest yields due to competitive migration of the cyclooctyl ring. Moreover, we found that the partial oxidation developed by Soderquist using trimethyl amine N-oxide (Figure 2.27) resulted in formation of air stable and isolable borinic ester product **29** (we were particularly pleased to note that this reaction could be carried out with hydrated trimethyl amine oxide). Soderquist had detailed the use of these borinic esters in various transformations that could not be carried out directly on the corresponding borane. It was proposed that excessive torsional strain prevented further

[58] (a) Mlynarski, S. N.; Karns, A. S.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 16449. (b) Morken, J.; Edelstein, E.; Grote, A.; Palkowitz, M. *Synlett* **2018**, *29*, 1749.

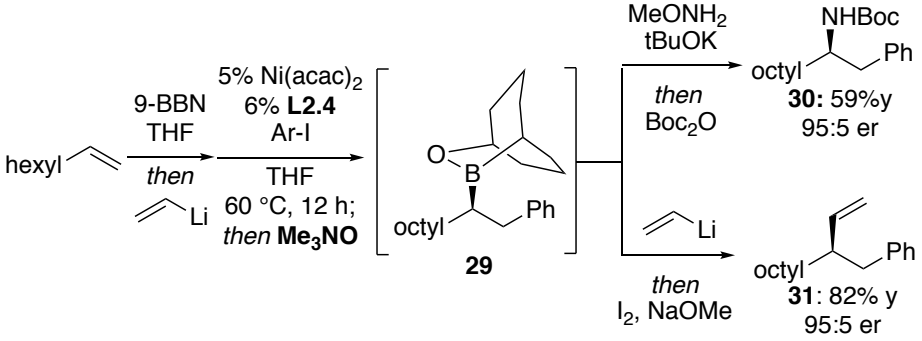
ring expansion of the cyclooctyl moiety. Thus, we sought to explore the possibility of employing such B(OBN) borinic ester substrates in stereospecific functionalization based on 1,2-metallate shift.

Figure 2.27. Soderquist partial oxidation with trimethylamine N-oxide



We were pleased to find that the amination and olefination of derived borinic esters occurred efficiently and without any loss of enantiomeric purity (Figure 2.28). As far as we are aware, no successful stereospecific aminations of 9-BBN or the corresponding borinic ester had been reported in the literature. We think that this functionalization protocol may prove generally useful in the derivatization of 9-BBN reagents, greatly expanding the synthetic utility of this class of reagents.

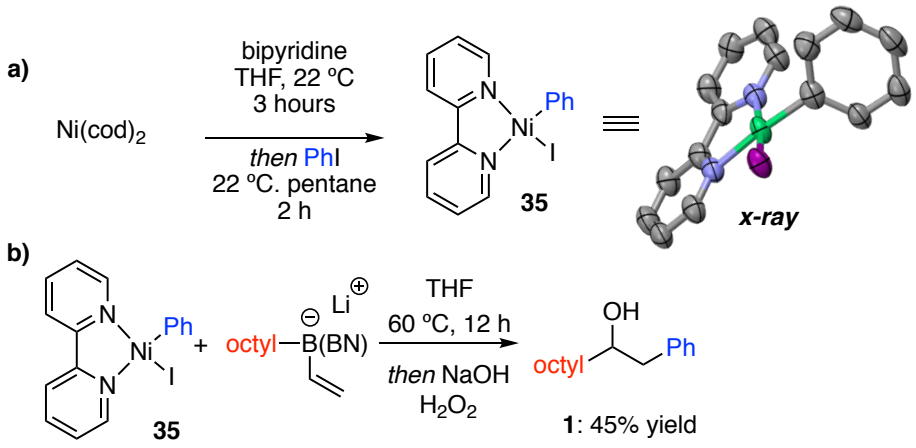
Figure 2.28. One-pot partial oxidation/stereospecific functionalization sequence.



2.3.4 Mechanistic studies and stereochemical model.

A number of experiments aimed at shedding light on the mechanistic details of this transformation were conducted. As per the discussion earlier in this chapter, nickel-catalyzed reactions often involve a mechanism that can widely differ in terms of catalyst oxidation states or the order of the steps in the catalytic cycle. Different systems may employ a Ni(0)/Ni(II) or Ni(I)/Ni(III). Most often, in the Ni(I)/Ni(III) redox couples transmetallation is proposed to take place before oxidative addition. To explore the feasibility of either option we independently synthesized Ni(II) oxidative addition adduct **35** by mixing $Ni(cod)_2$ with bipyridine and then treating it with iodobenzene in pentane. The reaction resulted in immediate precipitation of a dark solid that was then rigorously triturated to remove unreacted iodobenzene (Figure 2.29a). While NMR analysis of the sample proved uninformative, the structure could be confirmed through x-ray crystallography. A stoichiometric reaction between **35** and reactive vinyl boron 'ate' carried out for 1 hour in THF at 60 ºC resulted in product formation (Figure 29b).

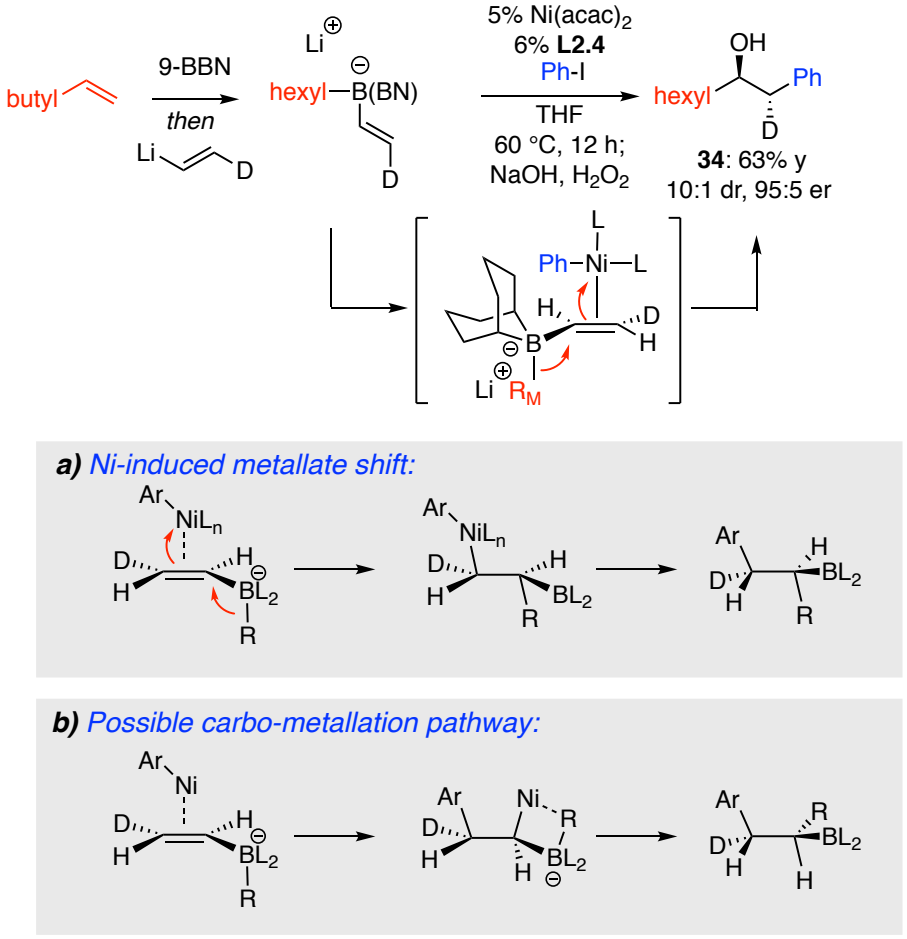
Figure 2.29. Scope of migrating group in Ni-catalyzed conjunctive coupling of 9-BBN



While the identity of the reactive nickel complex cannot be fully elucidated from this experiment (the nickel complex may ionize in solution, and disproportionation of the oxidative addition adduct cannot be excluded), the result of the reaction is in line with a catalytic cycle where oxidative addition takes place before the 1,2-metallate shift.

We then studied the stereochemical outcome of the reaction through a similar isotope labeling strategy as the one employed in the palladium conjunctive coupling system. Carrying out a conjunctive coupling with stereochemically defined, deuterium labeled vinyl lithium resulted in formation of diastereomeric product **34** (Figure 2.30) in 95:5 er and 10:1 diastereomeric ratio. The stereochemistry corresponded to *anti*-addition of the migrating group and the electrophile across the alkene, in-line with the *anti*-periplanar requirement expected in a metal induced 1,2-metallate shift, followed by stereospecific reductive elimination (Figure 2.30a).

Figure 2.30. Deuterium labeling study

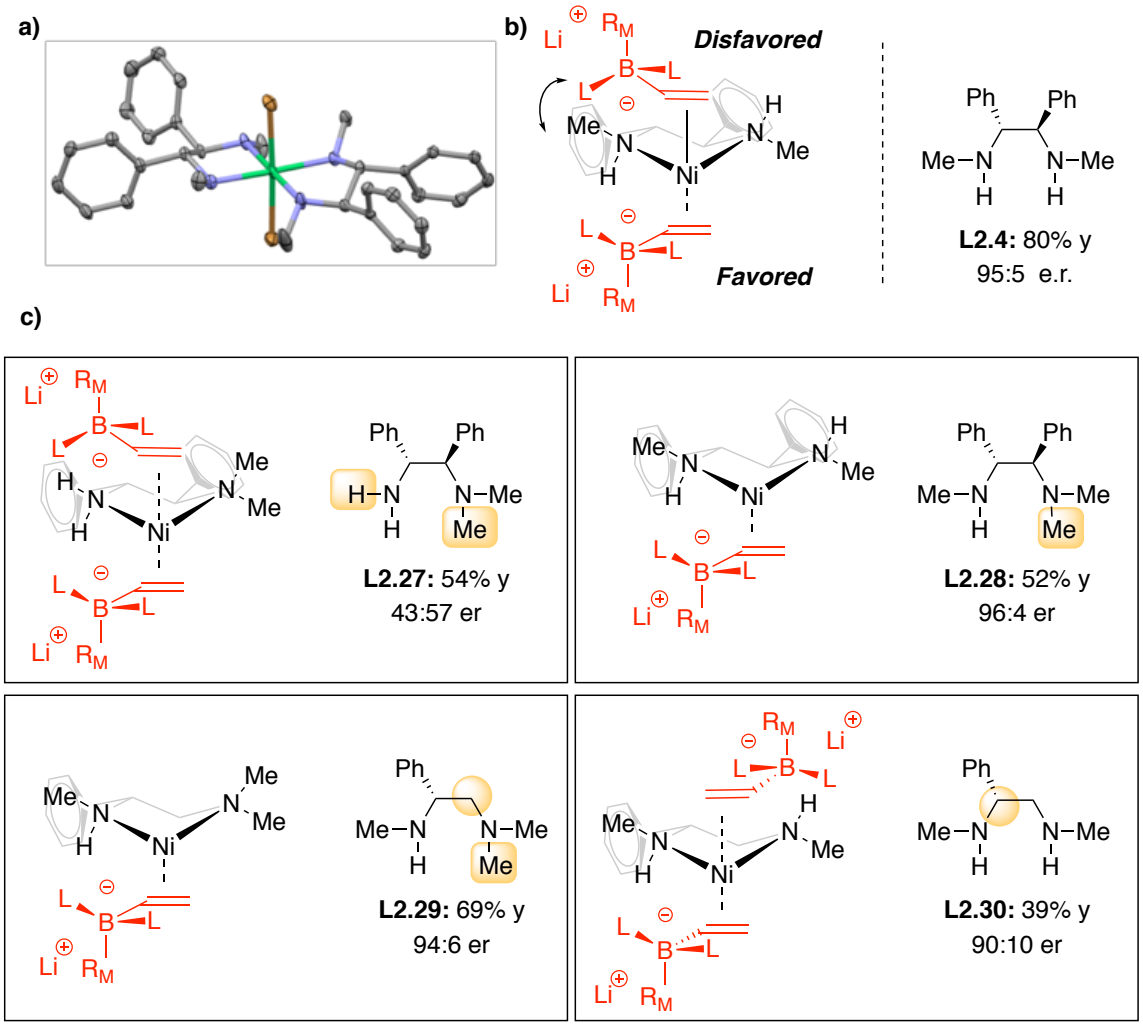


This experiment helps to rule out a mechanistic pathway that involves a carbometallation step followed by transmetallation and reductive elimination (Figure 2.30b). However, at this point we cannot exclude the possibility of carbonickelation followed by a reductive displacement through a 1,2-metallate shift.

By studying a crystal structure we obtained by mixing $NiCl_2$•glyme and ligand **L2.4** (Figure 2.31a), we noted that the methyl groups on the amine tended to adopt a pseudo-equatorial conformation in the metallacycle. The nitrogen atom appears to become stereochemically defined upon coordination with the metal as a result of the influence of the stereocenters in the backbone of the ligand. Thus, we hypothesized that

the stereochemical outcome of the transformation might be determined by the interaction of the substrate with the methyl groups on nitrogen, rather than with the chiral substituents in the backbone (Figure 2.31b). To probe this relationship further, we synthesized the ligand derivatives shown in Figure **2.31**, where the points of deviation from the original ligand structure are highlighted in yellow. The results obtained from testing these ligands in the standard reaction seem to corroborate the initial hypothesis. We found that when one nitrogen had two methyl substituents and the other had none (**L2.27**), the reaction proceeded with almost complete loss of enantioselectivity, consistent with the ability of the vinylboron 'ate' to approach on either side of the metallacycle. Moreover, by reintroducing a methyl substituent on the unsubstituted nitrogen (**L2.28**) selectivity in the reaction is reestablished. Additionally, reaction with ligand **L2.29** showed that a single stereogenic center on the backbone of the ligand was sufficient to effect an enantioselective reaction. This was found to also be the case with ligand **L2.30**, where only one methyl was present on each nitrogen, pointing to the ability of the benzylic stereocenter in the ligand to influence the conformation of the distal methylamine in the metallacycle. It should be noted that we do not know the exact structure of the reactive oxidative adduct. The geometry of the nickel complex and the mechanism of alkene complexation/1,2-metallate shift (the ligand exchange could be associative or dissociative) may determine whether the approach of the vinyl group occurs from the apical position, or in the plane with respect to the metal complex. Nonetheless, the studies on the ligand structure-selectivity relationship outlined here provide insight into the origin of stereoinduction in this system. We hope that these studies will help guide the design of non-racemic ligands for enantioselective catalysis.

Figure 2.31. Ligand survey for Ni-catalyzed conjunctive coupling with 9-BBN



2.3.5 Conclusion.

In conclusion, we have developed the first nickel-catalyzed enantioselective conjunctive cross-coupling using aryl halide electrophiles and 9-BBN borane reagents, generated *in situ* through hydroboration of simple olefins. The reaction proceeds efficiently and enantioselectively across a broad range of substrates, resulting in the formation of non-racemic boranes. The products can be directly derivatized through stereospecific methods

unique to 9-BBN compounds. Moreover, other methods for the functionalization of organoboron that had previously been challenging for 9-BBN compounds, such as olefination and amination reactions, could be implemented effectively and in a one-pot fashion through the intermediacy of borinic esters. Mechanistic studies point to a reaction pathway similar to that of the palladium catalyzed conjunctive cross-coupling, in which the catalyst undergoes oxidative addition with the electrophile, followed by a metal induced 1,2-metallate shift from a vinyl boron 'ate' and subsequent reductive elimination. A model for the origin of enantioselectivity is proposed based on crystallographic and experimental data. This proposal defines the role of each substituent on the diamine ligand used in the reaction and provides a blue print for non-racemic ligand design that may be applicable to other catalytic systems. Finally, we showed that nickel can induce a 1,2-metallate shift from a vinyl boron 'ate' in a catalytic fashion, providing a useful extension to the conjunctive cross-coupling manifold.

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

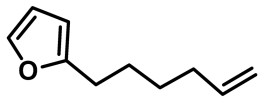
glass backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol or phosphomolybdic acid, and cerium(IV) sulfate in ethanol with sulfuric acid (Seebach).

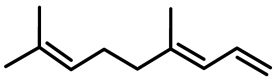
Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol as the modifier.

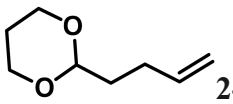
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Nickel(II) acetylacetonate was purchased from Acros Organics, (1*R*,2*R*)-*N*,*N*′-Dimethyl-1,2-diphenylethane-1,2-diamine (***(R,R)*-L2.4**) 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.

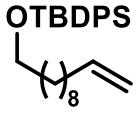
2.4.2 Experimental Procedures

2.4.2.1. Procedure for Preparation of Alkenyl Substrates

 **2-(hex-5-enyl)furan (S-24).** The title compound was prepared according to the procedure reported in the literature.[1] All spectral data was in accordance with previously published results.

 ***(E)*-4,8-dimethylnona-1,3,7-triene (S-21).** The title compound was synthesized in two steps starting with oxidation of geraniol as reported by Stahl *et al.*[2] followed by Wittig olefination. The spectral data was in accordance with the literature.[3]

 **2-(but-3-en-1-yl)-1,3-dioxane (S-13).** Prepared from 4-pentenal according to the procedure reported by Karimi *et al*.[4] The spectral data was in accordance with the literature.[5]

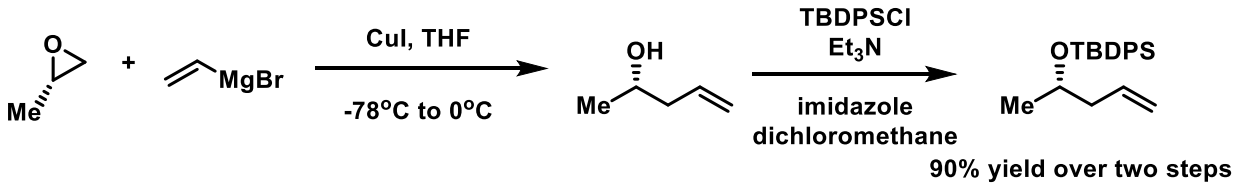


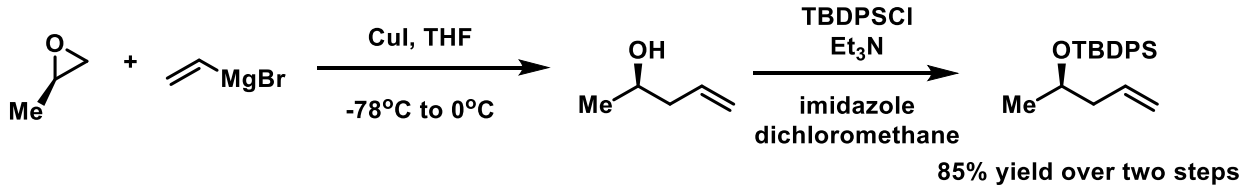
***tert*-butyldiphenyl(undec-10-en-1-yloxy)silane (S-14).** To a flame-dried round bottom flask equipped with a stir bar was added imidazole (1.02g, 15 mmol). The flask was purged with nitrogen for 5 minutes and dichloromethane (20 mL), undec-10-en-ol (10 mmol), and Et_3N (2.09 mL, 15 mmol) were then 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.

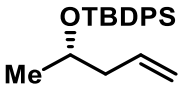
Preparation of (*R*)-tert-butyl(pent-4-en-2-yloxy)diphenylsilane and (*S*)-tert-butyl(pent-4-en-2-yloxy)diphenylsilane.



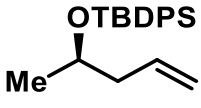


In an argon filled glovebox, a flame-dried round bottom flask equipped with a stir bar was charged with CuI (381mg, 2.0 mmol). The flask was sealed with a rubber septum and taken outside. THF (30 mL) was added under nitrogen. The reaction was cooled down to -78ºC with a dry ice/ acetone bath and vinyl magnesium bromide (1M in THF, 20 mL, 20 mmol) was then added dropwise. The reaction was allowed to stir at -78ºC for another 15 min, and propylene oxide (0.70 mL, 10 mmol) was added in one portion. The reaction was allowed to stir at -78ºC for one hour and at room temperature for another hour. Upon completion the reaction flask was cooled to 0ºC 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.

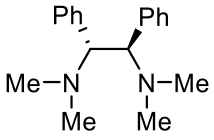


(*R*)-*tert*-butyl(pent-4-en-2-yloxy)diphenylsilane (S-26). The crude material was purified through silica gel column chromatography (hexane, stain in $KMnO_4$) to afford the product as a yellow oil (2.93g, 90% yield over 2 steps). Spectral data were in accordance with previous literature reports.[6]

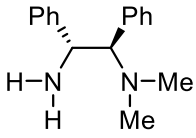


(*S*)-*tert*-butyl(pent-4-en-2-yloxy)diphenylsilane (S-27). The crude material was purified through silica gel column chromatography (hexane, stain in $KMnO_4$) to afford the product as a yellow oil (2.76g, 85% yield over 2 steps). Spectral data were in accordance with previous literature report.[7]

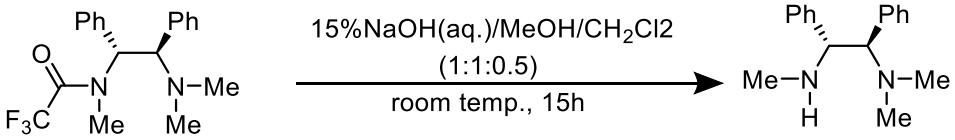
2.4.2.2. Procedures for Preparation of diamine Ligands



(1*R*,2*R*)-N1,N1,N2,N2-tetramethyl-1,2-diphenylethane-1,2-diamine (L). The title compound was prepared according to the procedure reported in the literature.[8] All spectral data was in accordance with the literature.[8]



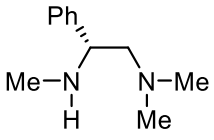
(1*R*,2*R*)-N,N-dimethyl-1,2-diphenylethane-1,2-diamine (L2.27). The title compound was prepared according to the procedure reported in the literature.[9] All spectral data was in accordance with the literature.[10]



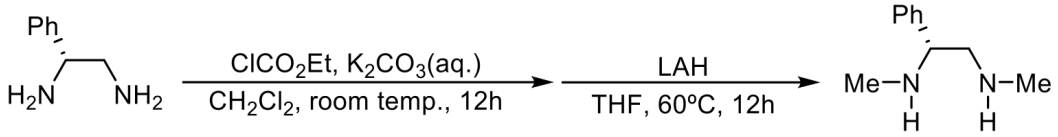
(1*R*,2*R*)-N1,N1,N2-trimethyl-1,2-diphenylethane-1,2-diamine (L2.28). The title compound was prepared from hydrolysis of **S-L2.28**.[9] To a scintillation vial equipped with a magnetic stir bar was added **S-L16** (30mg, 0.0856 mmol, 1.0 equiv.) and CH_2Cl_2 (0.5 mL). 15% aq. NaOH (1 mL) and MeOH (1 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 **L2.28**[11] as a white solid (11 mg, 50% yield).

^{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 (L2.29). The title compound was prepared according to the procedure reported in the literature.[12] All spectral data was in accordance with the literature.[12]



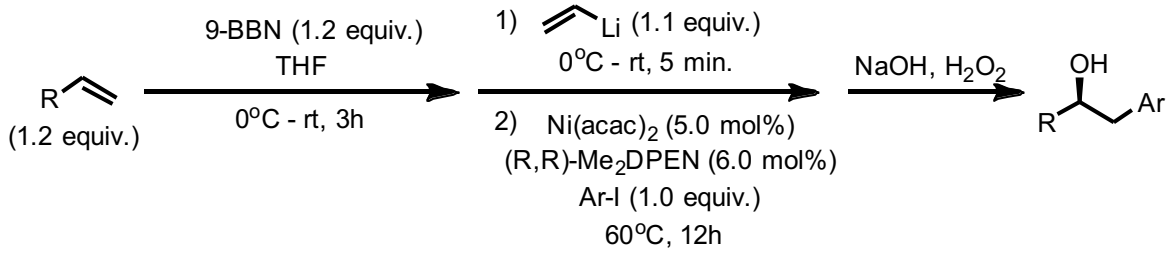
Diamine (L2.30). Diamine **S-L2.30** was prepared by LAH reduction of commercially available D(-)-phenylglycinamide following literature procedures.[13] The yield for the following reactions was not optimized. **S-L2.30** (430 mg, 3.16 mmol) was dissolved in THF (25 mL) in a round bottom flask flushed 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, stained in CAM) to afford ethyl-N-[2-(ethoxycarbonylamino)-1-phenyl-ethyl]carbamate **S2-L2.30** (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. X mL of THF where 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 x mL of H_2O followed by addition of x 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. [14]

2.4.2.3. General Procedure for Conjunctive Cross-Coupling

Procedure A



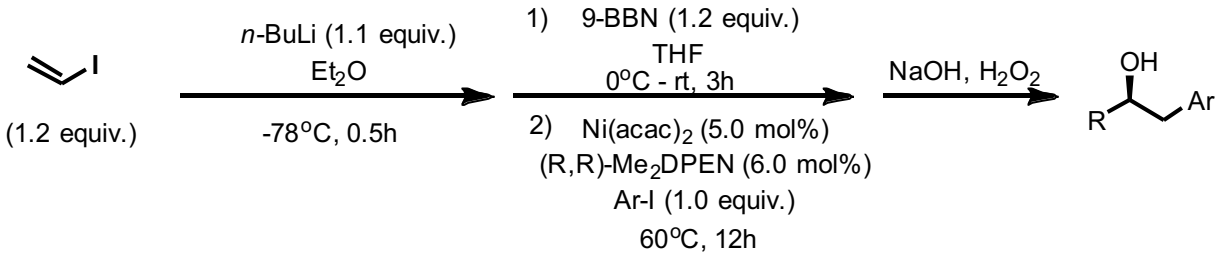
In a glovebox, under argon, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with a solution of 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.). The vial was cooled to 0°C, and the olefin (0.24 mmol, 1.20 equiv.) was added. The reaction mixture was allowed to warm to room temperature and stir for 3 hours before being cooled back to 0°C. Vinyllithium (for synthesis of halide free vinyllithium see ref[15]) 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 ***(R,R)*-L2.4** (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 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℃, 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 ***(R,R)*-L2.4** (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℃, 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.

Procedure for large scale synthesis of *(S)*-1-phenyldecan-2-ol (1).

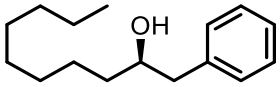
The opposite enantiomer of ligand was used for this reaction, resulting in equal and opposite enantioselectivity in the product.

A 250 mL two-neck round bottom flask equipped with stirbar and reflux condenser was backfilled with N_2, charged with 9-BBN solution in THF (19.2 mL, 0.5 M, 9.6 mmol, 1.20 equiv.) and cooled to 0 ºC. 1-Octene (1.51 mL, 9.60 mmol, 1.20 equiv.) was added and the reaction mixture was warmed to room temperature and stirred for 3 hours. Meanwhile, in an argon filled glove box, $Ni(acac)_2$ (102.76 mg, 0.40 mmol, 0.05 equiv.) and ***(S, S)*-L2.4** (115.36 mg, 0.48 mmol, 0.06 equiv.) were placed in a 20 mL vial, dissolved in 16 mL of THF and allowed to stir for 2 hours at room temperature.

Outside the glove box, the octyl-BBN solution was cooled to 0 ºC and a solution of vinyllithium in THF (4.89 mL, 1.8 M, 8.80 mmol, 1.1 equiv.) was added to the flask drop-wise. The solution was warmed to room temperature and stirred for 20 minutes, after which the catalyst solution was added (the solution should goes from light blue to, yellow/red), followed by addition of iodobenzene (0.90 mL, 8.0 mmol, 1.00 equiv.). The reaction mixture was heated at 60 ºC for 12 hours, then it was cooled to 0º C and 16 mL of aqueous 3M NaOH solution was added, followed by 16 mL of 30% H_2O_2. The biphasic mixture was allowed to warm to room temperature over 4 hoursn with vigorous stirring. The mixture was cooled to 0 ºC once more and 16 mL of aq. saturated $Na_2S_2O_3$ solution was added. The organic layer was extracted twice with 100 mL of Et_2O and twice with 100 mL of EtOAc, dried over Na_2SO_4, filtered and concentrated in vacuo. The crude mixture

was purified by column chromatography (50% DCM in pentane, stain in CAM) to afford the product as a colorless oil (1.31 g, 70% yield).

2.4.2.4. Characterization of Conjunctive Cross Coupling Products and Analysis of Stereochemistry



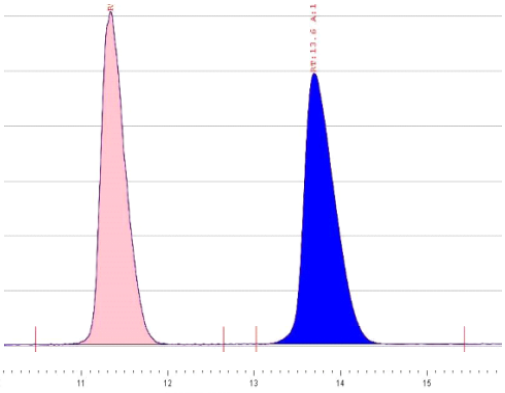
***(R)*-1-phenyldecan-2-ol (1).** The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and ***(R,R)*-L2.4** (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 **34, 19**).

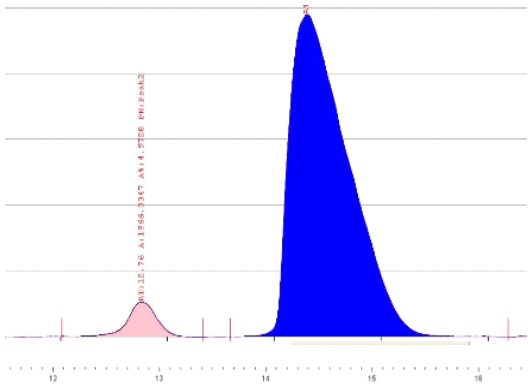
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-phenyldecan-2-ol and (R)-1-phenyldecan-2-ol (from gram scale reaction).

Racemic Material



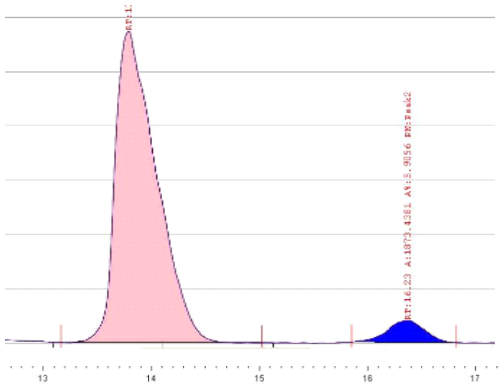
Peak No	% Area	Area	RT (min)
1	49.7027	11395.6892	11.34
2	50.2973	11531.9944	13.6
Total:	100	22927.6836	

Enantioenriched Material

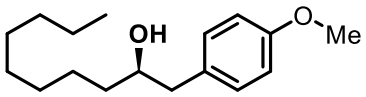


Peak No	% Area	Area	RT (min)
1	4.9728	1966.0347	12.76
2	95.0272	37570.0141	14.3
Total:	100	39536.0488	

Enantioenriched Material from Gram Scale Reaction



Peak No	% Area	Area	RT (min)
1	94.0944	29849.536	13.69
2	5.9056	1873.4381	16.23
Total:	100	31722.9741	



(*R*)-1-(4-methoxyphenyl)decan-2-ol (2). 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 ***(R,R)*-L2.4** (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).

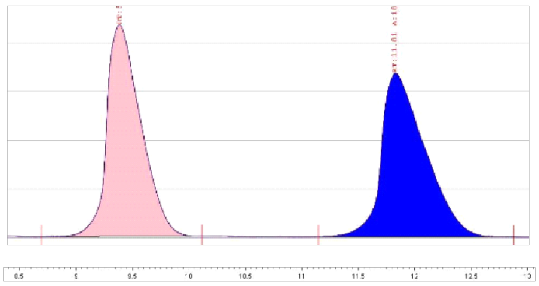
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 3.82-3.73 (m, 4H), 2.78 (dd, *J* = 13.7, 4.2 Hz, 1H), 2.58 (dd, *J* = 13.7, 8.4 Hz, 1H), 1.55-1.22 (m, 14H), 0.88 (t, *J* = 7.0 Hz, 3H).**^{13}C NMR** (150 MHz, $CDCl_3$) δ 158.43, 130.73, 130.51, 114.15, 72.92, 55.41, 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 A** with 2,2'-bipy (6 mol%) as the ligand. Absolute stereochemistry was assigned by analogy (see product **34, 19**).

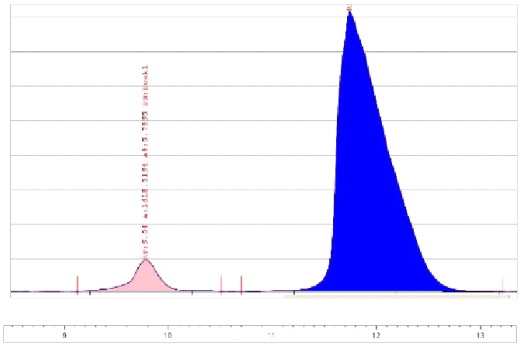
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(4-methoxyphenyl)decan-2-ol.

Racemic Material

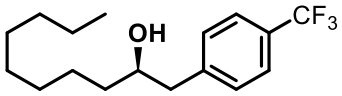


Peak No	% Area	Area	RT (min)
1	50.2402	18343.5134	9.36
2	49.7598	18168.1204	11.81
Total:	100	36511.6338	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	5.7895	1618.3194	9.54
2	94.2105	26334.4714	11.54
Total:	100	27952.7908	



(*R*)-1-(4-(trifluoromethyl)phenyl)decan-2-ol (3). 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.), 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 ***(R,R)*-L2.4** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 4-iodobenzotrifluoride (54.4 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 (42.4 mg, 70% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 3.89-3.80 (m, 1H), 2.87 (dd, *J* = 13.6, 4.3 Hz, 1H), 2.73 (dd, *J* = 13.6, 8.3 Hz, 1H), 1.57-1.22 (m, 14H), 0.88 (t, *J* = 6.3 Hz, 3H).**^{13}C NMR** (150 MHz, $CDCl_3$) δ 129.88, 125.54, 125.50, 125.46, 125.42, 72.64,

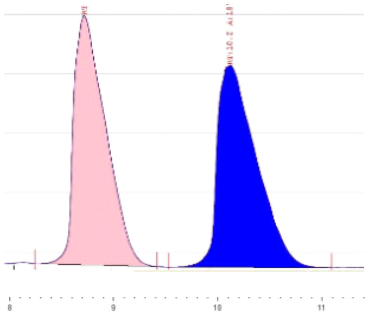
43.90, 37.19, 32.01, 29.74, 29.71, 29.40, 25.84, 22.81, 14.24. **IR** (neat) ν_{max} 3382.00 (br, w), 2923.76 (s), 2853.47 (s), 1612.24 (m), 1511.44 (s), 1464.39 (m), 1441.35 (m), 1299.98 (m), 1245.73 (s), 1177.39 (m), 1038.10 (s), 817.67 (m), 570.95 (w), 521.58 (w) cm^{-1}. **HRMS** (DART) for $C_{17}H_{24}F_3$ $[M+H-H_2O]^+$: Calc'd: 285.183, found: 285.1837. $\mathbf{[\alpha]_D^{20}}$ = -6.195 (*c* = 1.9, $CHCl_3$, *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 **34, 19**).

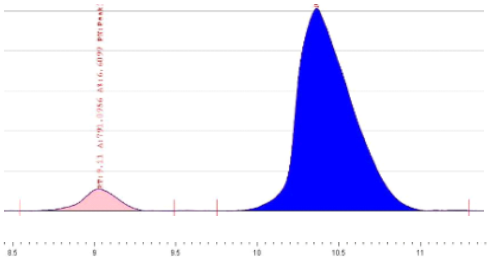
Chiral SFC (Chiracel OJ-H, 0% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(4-(trifluoromethyl)phenyl)decan-2-ol.

Racemic Material

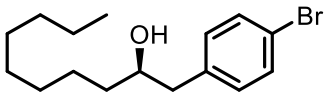


Peak No	% Area	Area	RT (min)
1	50.089	18835.8429	8.72
2	49.911	18768.9061	10.2
Total:	100	37604.749	

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 (4).** 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 ***(R,R)*-L2.4** (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).

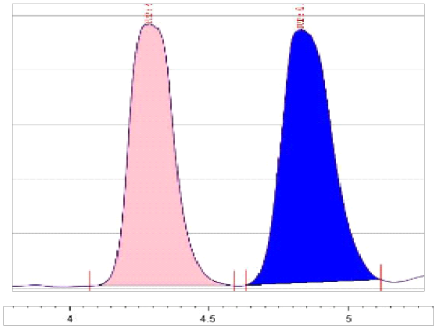
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.7 Hz 2H), 7.10 (d, *J* = 7.7 Hz, 2H), 3.81-3.76 (m, 1H), 2.77 (dd, *J* = 13.7, 4.3 Hz, 1H), 2.61 (dd, *J* = 13.7, 8.2 Hz, 1H), 1.52-1.22 (m, 14H), 0.88 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 137.86, 131.68, 131.30, 120.42, 72.66, 43.51, 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 **34, 19**).

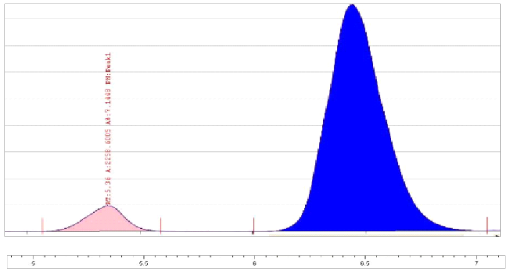
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(4-bromophenyl)decan-2-ol.

Racemic Material

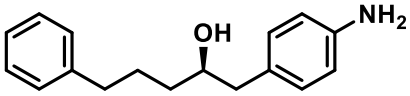


Peak No	% Area	Area	RT (min)
1	47.571	32435.1783	4.17
2	52.429	35747.5313	4.83
Total:	100	68182.7096	

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 (5). 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 ***(R,R)*-L2.4** (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).

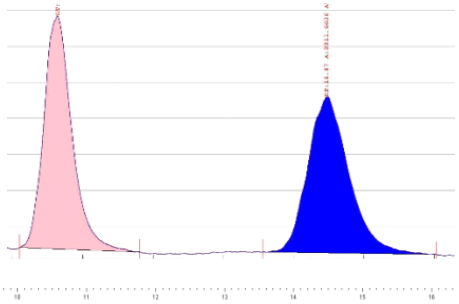
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.15 (m, 5H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.64 (d, *J* = 8.2 Hz, 2H), 3.91-3.29 (m, 3H), 2.72 (dd, *J* = 13.7, 4.1 Hz, 1H), 2.68-2.60 (m, 2H), 2.51 (dd, *J* = 13.7, 8.5 Hz, 1H), 1.90-1.76 (m, 1H), 1.75-1.64 (m, 1H), 1.61-1.48 (m, 2H). **^{13}C NMR** (150 MHz, $CDCl_3$) 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 **34, 19**).

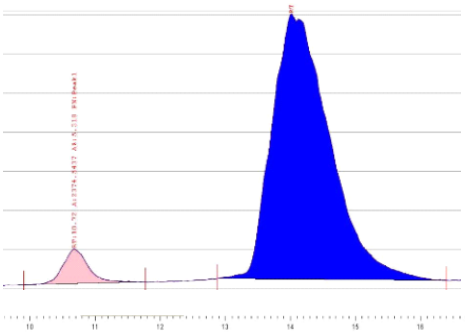
Chiral SFC (Chiracel OJ-H, 20% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(4-aminophenyl)-5-phenylpentan-2-ol.

Racemic Material

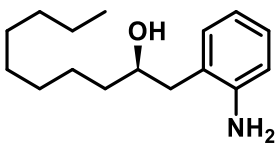


Peak No	% Area	Area	RT (min)
1	50.5473	9006.692	10.64
2	49.4527	8811.6606	14.47
Total:	100	17818.3526	

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 (6). 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 ***(R,R)*-L2.4** (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).

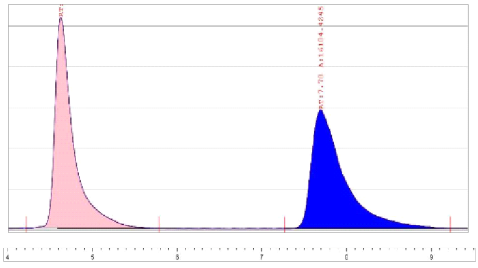
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10-7.01 (m, 2H), 6.81-6.72 (m, 2H), 3.94-3.84 (m, 1H), 3.80-3.44 (br s, 1H). 2.74 (dd, *J* = 14.3, 3.7 Hz, 1H), 2.66 (dd, *J* = 14.3, 8.1 Hz, 1H), 1.58-1.19 (m, 14H), 0.88 (t, *J* = 6.20 Hz, 1H) . **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.73, 131.40, 127.75, 124.92, 119.67, 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 **34, 19**).

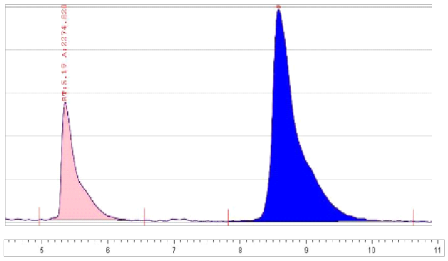
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(2-aminophenyl)decan-2-ol.

Racemic Material

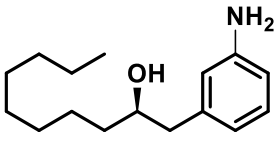


Peak No	% Area	Area	RT (min)
1	50.4002	16364.2842	4.58
2	49.5998	16104.4245	7.78
Total:	100	32468.7087	

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 (7). 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 ***(R,R)*-L2.4** (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).

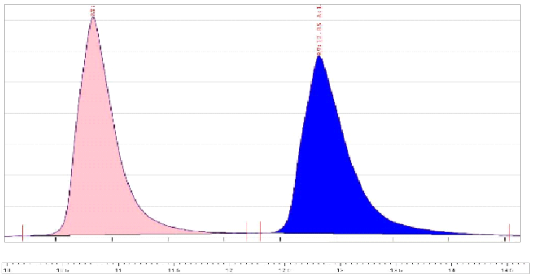
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (t, *J* = 7.6 Hz, 1H), 6.64-6.51 (m, 3H), 3.89-3.36 (m, 3H), 2.75 (dd, *J* = 13.5, 4.0 Hz, 1H), 2.53 (dd, *J* = 13.5, 8.6 Hz, 1H), 1.58-1.18 (m, 14H), 0.89 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 146.74, 140.00, 129.66, 119.76, 116.23, 113.44, 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 **34, 19**).

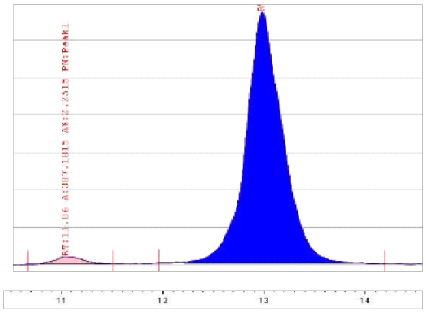
Chiral SFC (Chiracel OJ-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(3-aminophenyl)decan-2-ol.

Racemic Material

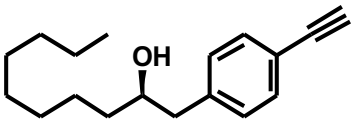


Peak No	% Area	Area	RT (min)
1	50.4733	16097.1974	10.83
2	49.5267	15795.286	12.85
Total:	100	31892.4834	

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 (8). 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 ***(R,R)*-L2.4** (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).

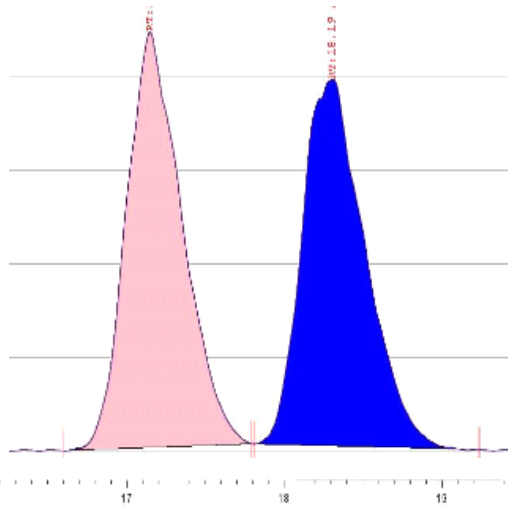
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 3.89-3.75 (m, 1H), 3.05 (s, 1H), 2.82 (dd, *J* = 13.6, 4.3 Hz, 1H), 2.66 (dd, *J* = 13.6, 8.2 Hz, 1H), 1.59-1.18 (m, 14H), 0.88 (t, *J* = 6.7 Hz, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 139.88, 132.40, 129.58, 120.29, 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 **34, 19**).

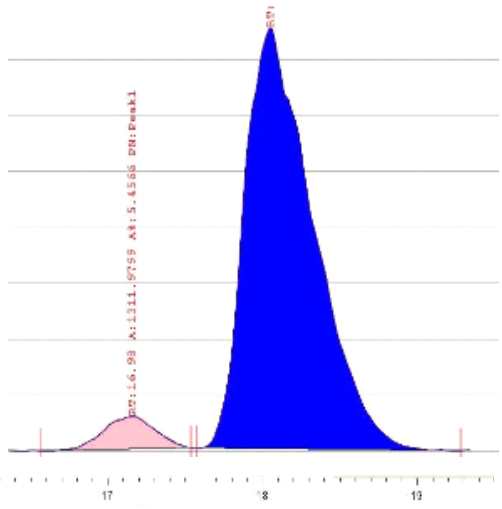
Chiral SFC (Chiracel ODR-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(4-ethynylphenyl)decan-2-ol.

Racemic Material

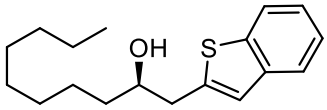


Peak No	% Area	Area	RT (min)
1	50.1087	11087.2775	17.02
2	49.8913	11039.1609	18.19
Total:	100	22126.4384	

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 (9).

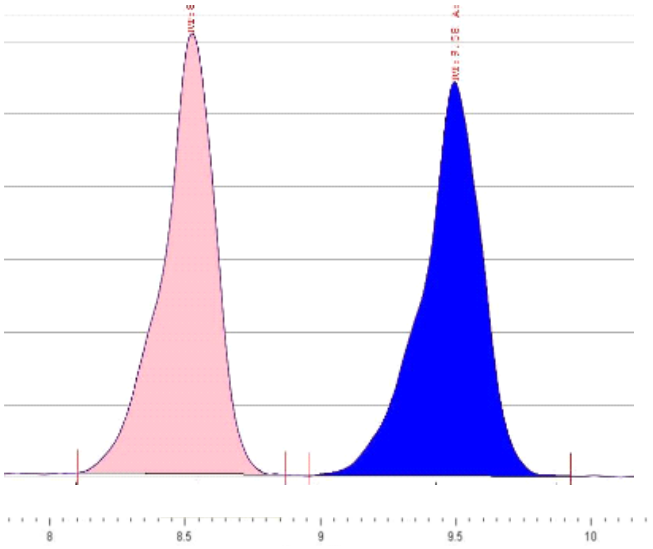
The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), (32.7 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and ***(R,R)*-L2.4** (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 **34, 19**).

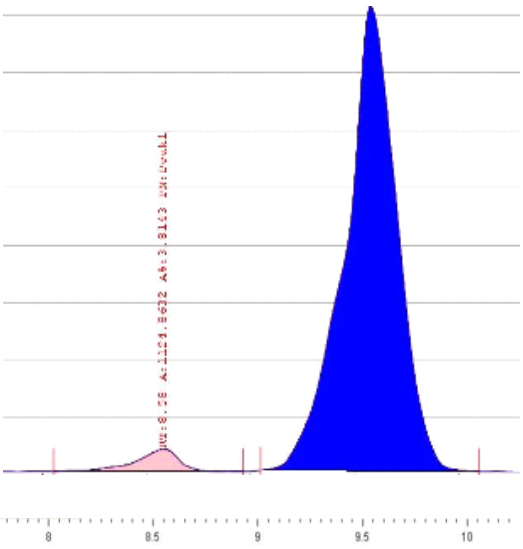
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(benzo[b]thiophen-2-yl)decan-2-ol.

Racemic Material

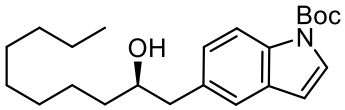


Peak No	% Area	Area	RT (min)
1	49.717	9348.6838	8.48
2	50.283	9455.0956	9.58
Total:	100	18803.7794	

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	



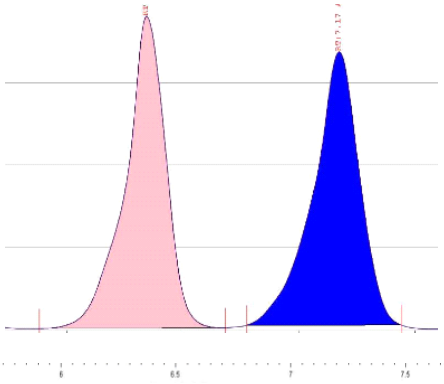
***tert*-butyl (*R*)-5-(2-hydroxydecyl)-1*H*-indole-1-carboxylate (10).** The reaction was performed according to the general **procedure A,** with slight deviation. The reaction was run at room temperature for 12 hours. Reaction was prepared with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 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 ***(R,R)*-L2.4** (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 **34, 19**).

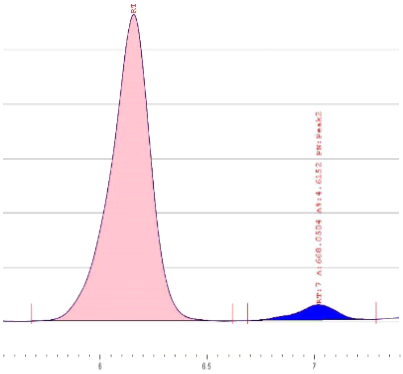
Chiral SFC (Chiracel OJ-H, 6% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of tert-butyl (R)-5-(2-hydroxydecyl)-1H-indole-1-carboxylate.

Racemic Material

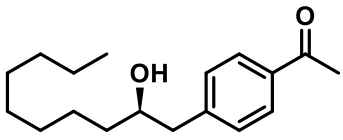


Peak No	% Area	Area	RT (min)
1	49.8935	23002.6909	6.34
2	50.1065	23100.8532	7.17
Total:	100	46103.5441	

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 (11). 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 ***(R,R)*-L2.4** (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).

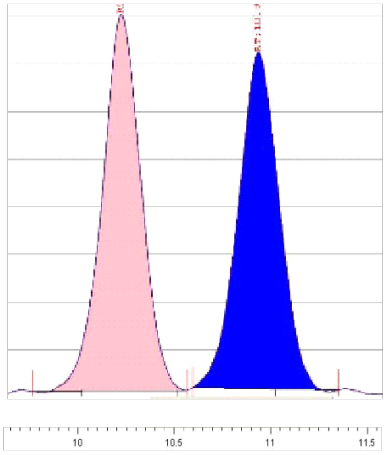
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 3.89-3.82 (m, 1H), 2.88 (dd, *J* = 13.6, 4.3 Hz, 1H), 2.73 (dd, *J* = 13.6, 8.3 Hz, 1H), 2.59 (s, 3H), 1.58-1.20 (m, 14H), 0.88 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 197.95, 144.77, 135.68, 129.79, 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 **34, 19**).

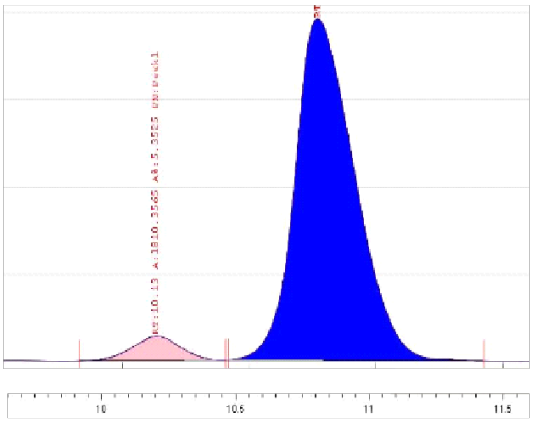
Chiral SFC (Chiracel AD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(4-(2-hydroxydecyl)phenyl)ethan-1-one.

Racemic Material

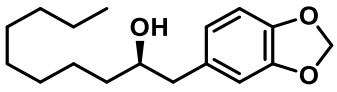


Peak No	% Area	Area	RT (min)
1	51.5576	2225.3493	10.2
2	48.4424	2090.8911	10.91
Total:	100	4316.2404	

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 (12). 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 ***(R,R)*-L2.4** (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).

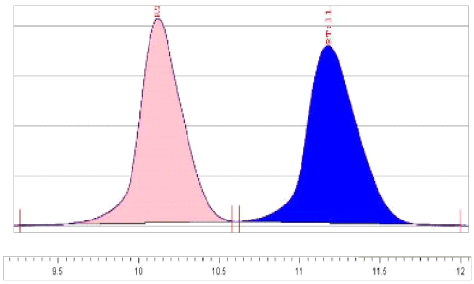
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 (d, *J* = 7.8 Hz, 1H), 6.71 (d, *J* = 1.7 Hz, 1H), 6.66 (dd, *J* = 7.8, 1.7 Hz, 1H), 5.94 (s, 2H), 3.84-3.71 (m, 1H), 2.75 (dd, *J* = 13.7, 4.1 Hz, 1H), 2.55 (dd, *J* = 13.7, 8.5 Hz, 1H), 1.55-1.15 (m, 14H), 0.88 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) 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 **34, 19**).

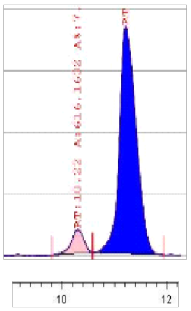
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-(benzo[d][1,3]dioxol-5-yl)decan-2-ol.

Racemic Material

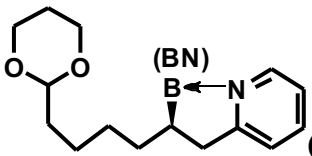


Peak No	% Area	Area	RT (min)
1	49.5546	7242.3644	10.08
2	50.4454	7372.5663	11.11
Total:	100	14614.9307	

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*)-2-(2-(9-borabicyclo[3.3.1]nonan-9-yl)-6-(1,3-dioxan-2-yl)hexyl)pyridine (13). 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-14**) (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 ***(R,R)*-L2.4** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 2-iodopyridine (41.0 mg, 0.20 mmol, 1.00 equiv.)

The crude mixture was purified by silica gel chromatography (15% EtOAc in pentane, stained with CAM) to afford a colorless oil (54.9 mg, 73% yield).

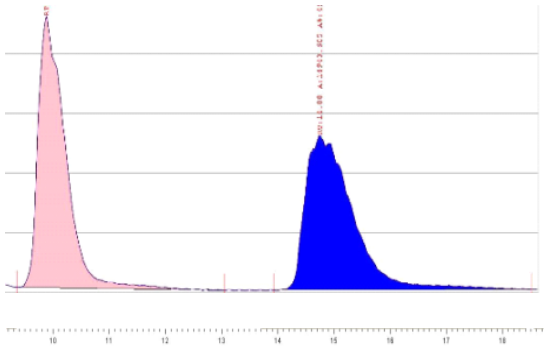
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77 (d, *J* = 5.7 Hz, 1H), 7.74 (td, *J* = 7.7, 1.4 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.26 (m, 1H), 4.47 (t, *J* = 5.2 Hz, 1H), 4.08 (ddd, *J* = 11.2, 5.1, 1.7 Hz, 2H), 3.74 (tdd, *J* = 12.1, 2.6, 1.3 Hz, 2H), 3.14 (dd, *J* = 16.8, 6.2 Hz, 1H), 2.77 (d, *J* = 16.8 Hz, 1H), 2.32 – 2.14 (m, 1H), 2.10 – 1.13 (m, 21H), 1.07 – 0.92 (m, 1H), 0.63 – 0.41 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 164.37, 144.94, 138.42, 123.45, 121.47, 102.76, 67.03, 36.97, 35.71, 34.89, 33.43, 30.83, 30.21 (br) 30.02, 29.34, 28.96, 26.04, 25.10, 24.66, 24.34, 23.93 (br), 22.15 (br **^{11}B NMR** (160 MHz, $CDCl_3$) δ 2.35. **IR** (neat) ν_{max} 2917.5 (s), 2837.1 (s), 1616.6 (s), 1480.3 (s), 1451.1 (s), 1240.4 (s), 1143.1 (s), 1111.5 (m), 993.2 (s), 867.3 (s), 765 (s),723 (s). **HRMS** (DART) for $C_{23}H_{37}NO_2B$ $[M+H]^+$: Calc'd: 370.2917, found: 370.2917.

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 **34, 19**).

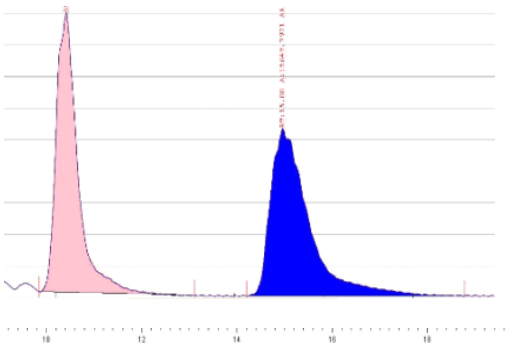
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-2-(2-(9-borabicyclo[3.3.1]nonan-9-yl)-6-(1,3-dioxan-2-yl)hexyl)pyridine.

Racemic Material

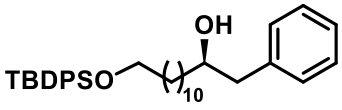


Peak No	% Area	Area	RT (min)
1	50.3138	15132.3538	10.06
2	49.6862	14943.605	14.88
Total:	100	30075.9588	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	48.529	14755.2636	10.25
2	51.471	15649.7971	15.08
Total:	100	30405.0607	



(*R*)-13-((*tert*-butyldiphenylsilyl)oxy)-1-phenyltridecan-2-ol (14).

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-11**) (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 ***(R,R)*-L2.4** (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).

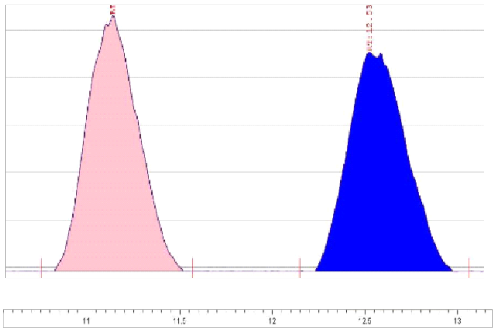
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69-7.65 (m, 4H), 7.44-7.35 (m, 6H), 7.34-7.29 (m, 2H), 7.26-7.20 (m, 3H), 3.86 (m, 1H), 3.65 (t, J = 6.5 Hz, 2H), 2.84 (dd, J = 13.6, 4.2 Hz, 1H), 2.65 (dd, J = 13.6, 8.5 Hz, 1H), 1.59-1.27 (m, 20H), 1.05 (s, 9H). **^{13}C NMR** (150 MHz, CD_3CN) δ 138.94, 134.54, 133.19, 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 **34, 19**).

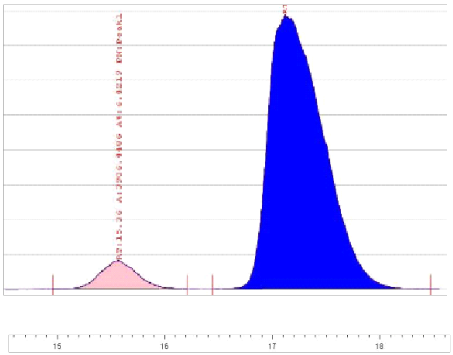
Chiral SFC (Chiracel ODR-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-13-((tert-butyldiphenylsilyl)oxy)-1-phenyltridecan-2-ol.

Racemic Material

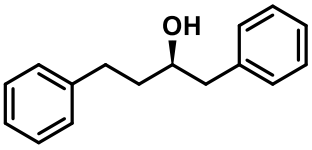


Peak No	% Area	Area	RT (min)
1	50.5346	10304.1582	11.15
2	49.4654	10086.1642	12.53
Total:	100	20390.3224	

Enantioenriched Material



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 (15). 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 ***(R,R)*-L2.4** (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,

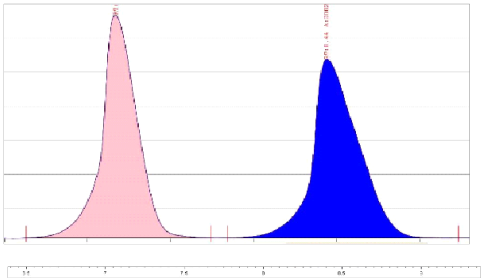
129.58, 128.75, 128.60, 128.56, 126.69, 125.98, 72.10, 44.31, 38.59, 32.27. **IR** (neat) ν_{max} 3405.14 (br,s), 3083.98 (w), 3061.19 (w), 3025.99 (m), 2919.73 (w), 2857.89 (w), 1602.16 (w), 1494.75 (m), 1453.54 (m), 1081.23 (m), 1048.45 (m), 1030.25 (m), 746.25 (s), 698.64 (s), 494.02 (w) cm^{-1}. **HRMS** (DART) for $C_{16}H_{19}O$ $[M+NH_4]^+$: Calc'd: 244.1701, found: 244.1697. $\mathbf{[\alpha]_D^{20}}$ = +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 **34, 19**).

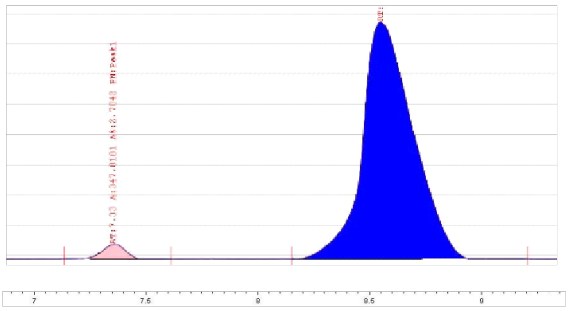
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1,4-diphenylbutan-2-ol.

Racemic Material

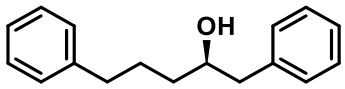


Peak No	% Area	Area	RT (min)
1	49.1242	19332.5243	7.17
2	50.8758	20021.8565	8.44
Total:	100	39354.3808	

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 (16). 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 ***(R,R)*-L2.4** (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).

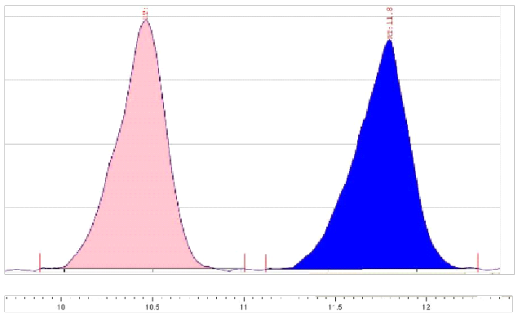
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.14 (m, 10H), 3.90-3.80 (m, 1H), 3.83 (dd, J = 13.6, 4.1 Hz, 1H), 2.69-2.60 (m, 3H), 1.91-1.80 (m, 1H), 1.78-1.65 (m, 1H), 1.64-1.51(m, 2H), 1.48 (s, 1H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.52, 138.65, 129.56, 128.74, 128.57, 128.46, 126.64, 125.89, 72.67, 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 **34, 19**).

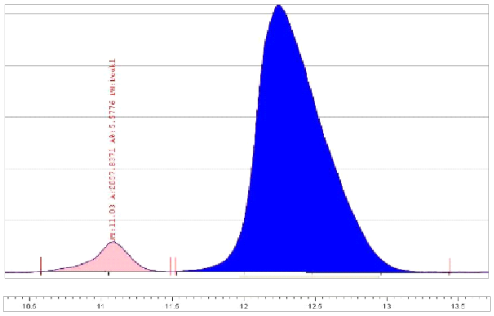
Chiral SFC (Chiracel OJ-H, 9% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1,5-diphenylpentan-2-ol.

Racemic Material

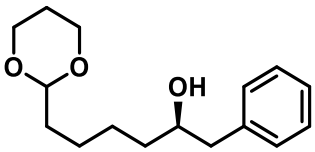


Peak No	% Area	Area	RT (min)
1	49.8175	3788.1127	10.46
2	50.1825	3815.8682	11.85
Total:	100	7603.9809	

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 (17). 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-14**) (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 ***(R,R)*-L2.4** (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).

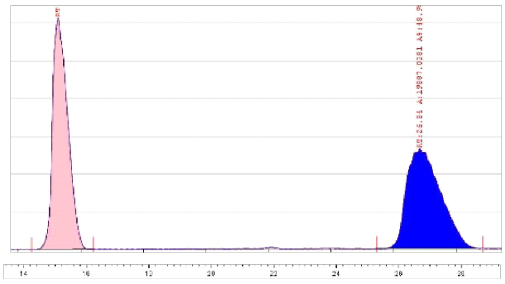
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.12 (m, 5H), 4.51 (t, *J* = 5.1 Hz, 1H), 4.09 (dd, *J* = 12.2, 4.9 Hz, 2H), 3.83-3.72 (m, 1H), 3.75 (td, *J* = 12.2, 2.4 Hz, 2H), 2.81 (dd, *J* = 13.5, 4.2 Hz, 1H), 2.64 (dd, *J* = 13.5, 8.3 Hz, 1H), 2.14-2.01 (m, 1H), 1.73-1.24 (m, 9H).**^{13}(150** MHz, $CDCl_3$) 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 **34, 19**).

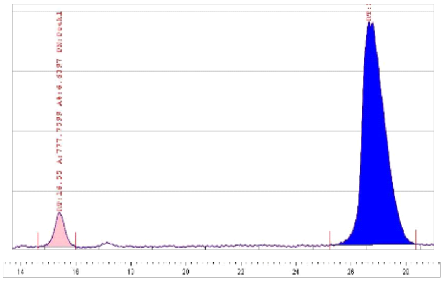
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-6-(1,3-dioxan-2-yl)-1-phenylhexan-2-ol.

Racemic Material

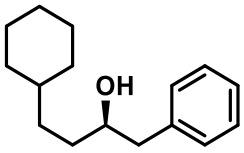


Peak No	% Area	Area	RT (min)
1	51.0169	20712.7843	15.26
2	48.9831	19887.0381	26.84
Total:	100	40599.8224	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	6.6397	777.7599	16.55
2	93.3603	10935.9417	28.09
Total:	100	11713.7016	



(*R*)-4-cyclohexyl-1-phenylbutan-2-ol (18). 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 ***(R,R)*-L2.4** (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).

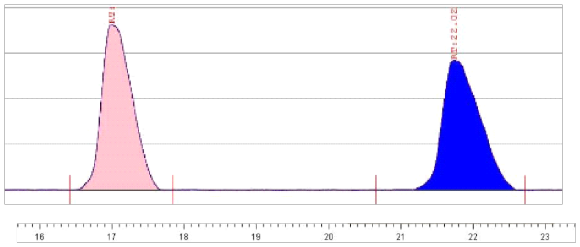
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.20 (m, 5H), 3.82-3.75 (m, 1H), 2.84 (dd, *J* = 13.6, 4.2 Hz, 1H), 2.65 (dd, *J* = 13.6, 8.4 Hz, 1H), 1.75-0.80 (m, 15H).**^{13}C NMR** (150 MHz, $CDCl_3$) δ 138.81, 129.56, 129.55, 128.68, 128.67, 126.56, 73.18, 44.17, 44.15, 37.92, 34.33, 33.64, 33.57, 33.46, 26.84, 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 **34, 19**).

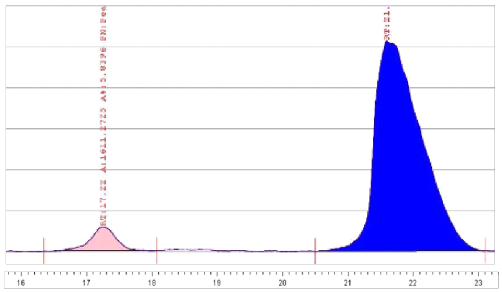
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-4-cyclohexyl-1-phenylbutan-2-ol.

Racemic Material

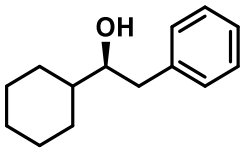


Peak No	% Area	Area	RT (min)
1	50.7312	11138.4917	17.06
2	49.2688	10817.4084	22.02
Total:	100	21955.9001	

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	



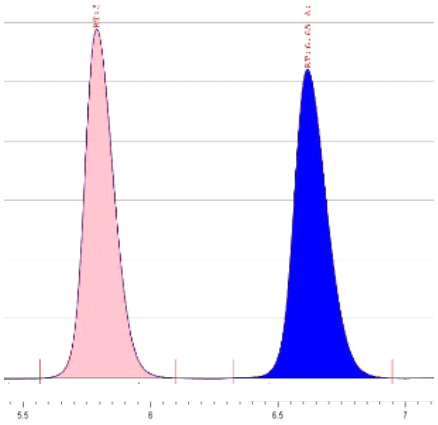
(*R*)-1-cyclohexyl-2-phenylethan-1-ol (19). The reaction was performed according to the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), cyclohexene (19.7 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and ***(R,R)*-L2.4** (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.[16]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 **34, 19**).

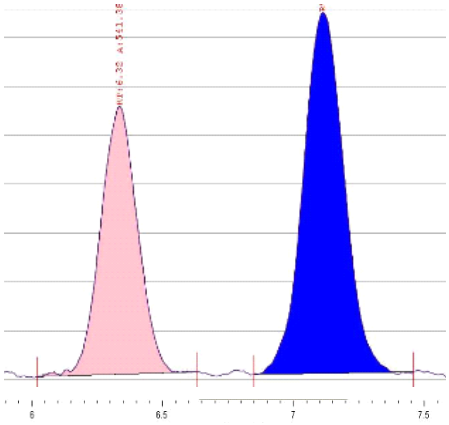
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-cyclohexyl-2-phenylethan-1-ol.

Racemic Material

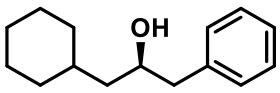


Peak No	% Area	Area	RT (min)
1	50.048	4701.3726	5.84
2	49.952	4692.3455	6.65
Total:	100	9393.7181	

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 (20). 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

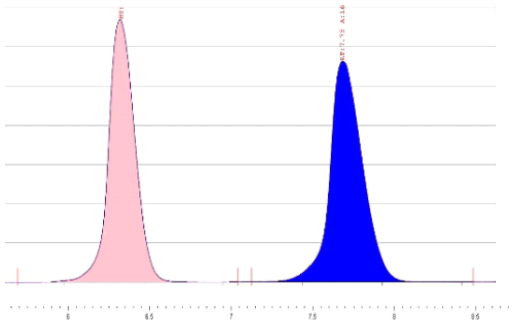
equiv.), methylenecyclohexane (23.1 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and ***(R,R)*-L2.4** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), iodobenzene (40.8 mg, 0.20 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 **34, 19**).

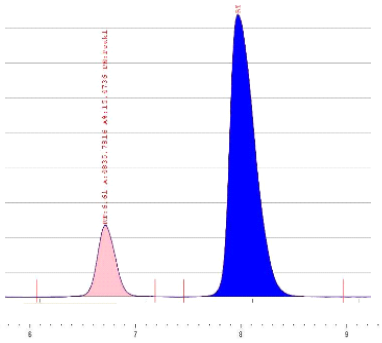
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-4-cyclohexyl-1-phenylbutan-2-ol.

Racemic Material

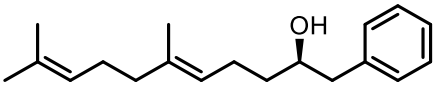


Peak No	% Area	Area	RT (min)
1	49.072	15475.7004	6.36
2	50.928	16061.0519	7.75
Total:	100	31536.7523	

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 (21).**

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-18**) (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 ***(R,R)*-L2.4** (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).

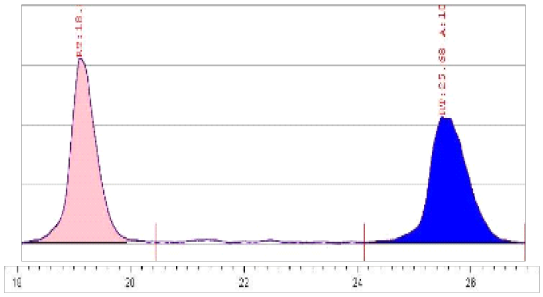
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.20 (m, 5H), 5.18-5.10 (m, 1H), 5.12-5.05 (m, 1H), 3.89-3.79 (m, 1H), 2.83 (dd, *J* = 13.6, 4.3 Hz, 1H), 2.67 (dd, *J* = 13.6, 8.3 Hz, 1H), 2.25-1.97 (m, 6H), 1.68 (s, 3H), 1.64-1.53 (m, 8H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 138.78, 135.91, 131.57, 129.58, 128.67, 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 **34, 19**).

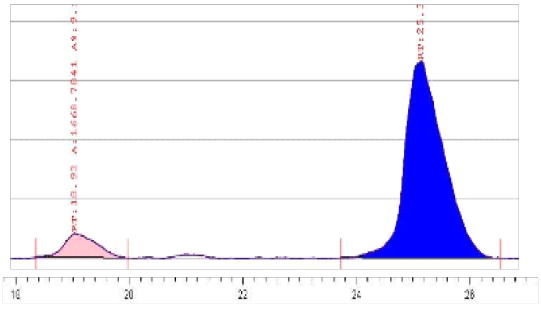
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R,E)-6,10-dimethyl-1-phenylundeca-5,9-dien-2-ol.

Racemic Material

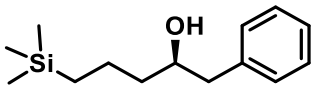


Peak No	% Area	Area	RT (min)
1	50.0529	10620.6165	18.85
2	49.9471	10598.1516	25.68
Total:	100	21218.7681	

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 (22). 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 ***(R,R)*-L2.4** (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).

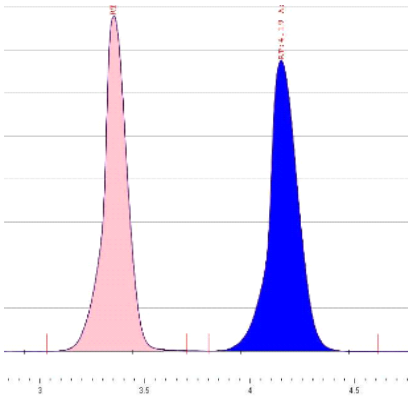
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.7.34-7.30 (m, 2H), 7.25-7.21 (m, 3H), 3.88-3.80 (m, 1H), 2.82 (dd, *J* = 13.6, 4.3 Hz, 1H), 2.66 (dd, *J* = 13.4, 8.4 Hz, 1H), 1.63-1.43 (m, 4H), 1.43-1.34 (m, 1H), 0.66-0.42 (m, 2H), -0.01 (s, 9H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 138.62, 129.40, 128.52, 126.41, 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 **34, 19**).

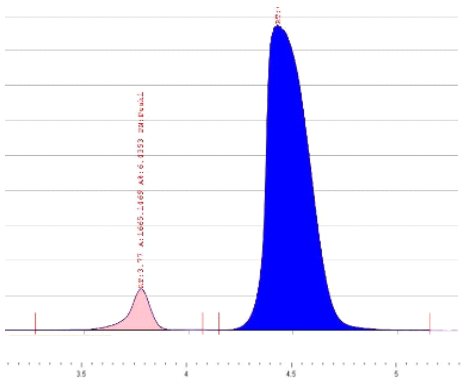
Chiral SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-phenyl-5-(trimethylsilyl)pentan-2-ol.

Racemic Material

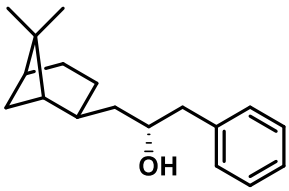


Peak No	% Area	Area	RT (min)
1	48.6805	11888.1196	3.41
2	51.3195	12532.593	4.19
Total:	100	24420.7126	

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 (23). 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 ***(R,R)*-L2.4** (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).

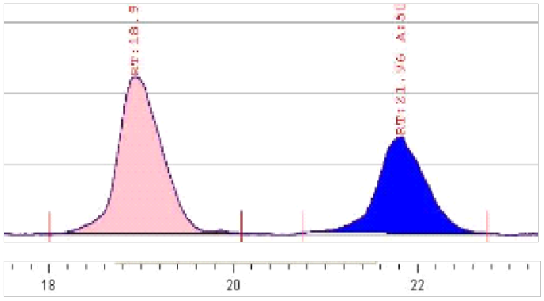
^{1}H NMR (500 MHz, $CDCl_3$) Major diastereomer: δ 7.35-7.19 (m, 5H), 3.91-3.83 (m, 1H), 2.83 (dd, *J* = 13.5, 4.5 Hz, 1H), 2.63 (dd, *J* = 13.5, 8.4 Hz, 1H), 2.37-2.22 (m, 2H), 2.07-1.80 (m, 5H), 1.71-1.39 (m, 4H), 1.18 (s, 3H), 0.96 (s, 3H). Minor diastereomer: δ 7.35-7.19 (m, 5H), 3.91-3.83 (m, 1H), 2.82 (dd, *J* = 13.6, 4.8 Hz, 1H), 2.63 (dd, *J* = 13.6, 8.1 Hz, 1H), 2.37-2.22 (m, 2H), 2.07-1.80 (m, 5H), 1.71-1.39 (m, 4H), 1.20 (s, 3H), 0.99 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) Major diastereomer: δ 138.70, 129.56, 128.67, 126.55, 71.24, 45.83, 44.84, 44.33, 41.61, 38.81, 37.83, 33.64, 28.34, 26.65, 23.35, 23.12. Minor diastereomer: δ 138.70, 129.56, 128.67, 126.55, 70.93, 47.48, 45.33, 44.91, 38.86, 37.37, 33.89, 31.73, 26.57, 23.42, 22.79, 22.19. **IR** (neat) ν_{max} 3357.47 (br, s), 2903.85 (s), 1945.09 (w), 1467.93 (m), 1452.88 (m), 1382.91 (w), 1365.42 (w), 1080.38 (m), 1032.04 (m), 744.04 (s), 698.40 (s), 601.25 (w), 534.46 (w), 493.51 (w) cm^{-1}. **HRMS** (DART) for $C_{18}H_{27}O$ $[M+H-H_2O]^+$: Calc'd: 241.1956, found: 241.196. **$[\alpha]_D^{20}$** = -14.7488 (*c* = 1.92, $CHCl_3$, *l* = 50 mm).

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**.[17]Absolute stereochemistry was assigned by analogy (see product **34, 19**).

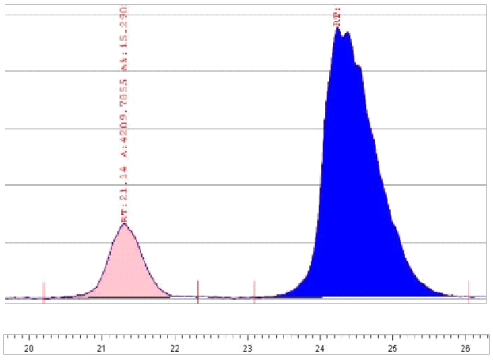
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-((1S,2S,5S)-6,6-dimethylbicyclo[3.1.1]heptan-2-yl)-3-phenylpropan-2-ol.

Diastereomic Mixture

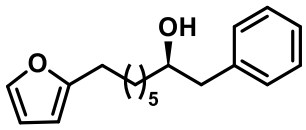


Peak No	% Area	Area	RT (min)
1	60.0783	7660.6494	18.97
2	39.9217	5090.4563	21.96
Total:	100	12751.1057	

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 (24). 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-21**) (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 ***(R,R)*-L2.4** (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).

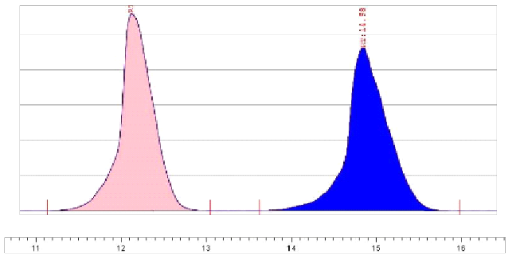
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.06 (m, 6H), 6.28 (dd, *J* = 3.2, 1.9 Hz, 1H), 5.98 (d, *J* = 3.2 Hz, 1H), 3.90-3.77 (m, 1H), 2.83 (dd, *J* = 13.5, 4.2 Hz, 1H), 2.69-2.58 (m, 3H), 1.74-1.25 (m, 10H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 156.63, 140.76, 138.75, 129.55, 128.69, 126.58, 110.16, 104.69, 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 **34, 19**).

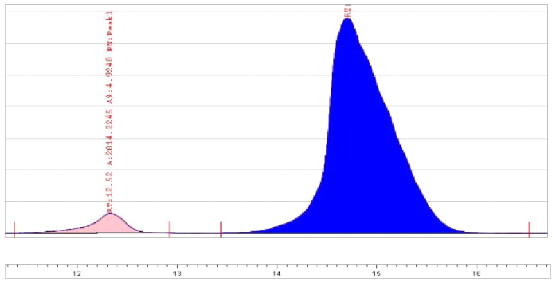
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-8-(furan-2-yl)-1-phenyloctan-2-ol.

Racemic Material

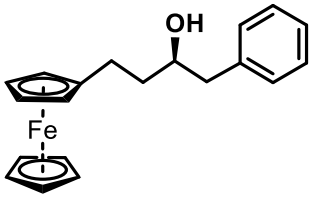


Peak No	% Area	Area	RT (min)
1	49.9478	30493.1904	12.23
2	50.0522	30556.9475	14.98
Total:	100	61050.1379	

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 (25). 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 (50.9mg 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 ***(R,R)*-L2.4** (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).

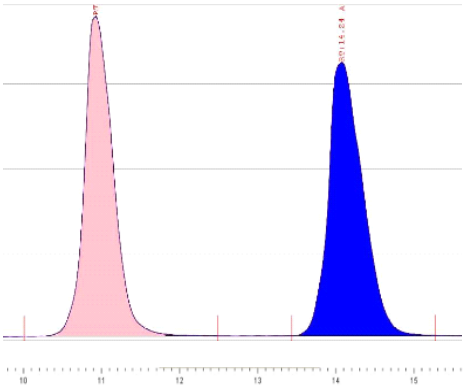
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36-7.30 (m, 2H), 7.25-7.20 (m, 3H), 4.12-4.03 (m, 9H), 3.88-3.81 (m, 1H), 2.85 (dd, *J* = 13.6, 4.3 Hz, 1H), 2.69 (dd, *J* = 13.5, 8.4 Hz, 1H), 2.56 (ddd, *J* = 14.2, 9.8, 5.8 Hz, 1H) 2.42 (ddd, *J* = 14.3, 9.9, 6.4 Hz, 1H), 1.81-1.71 (m, 2H), 1.52 (s, 1H) **^{13}C NMR** (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 **34, 19**).

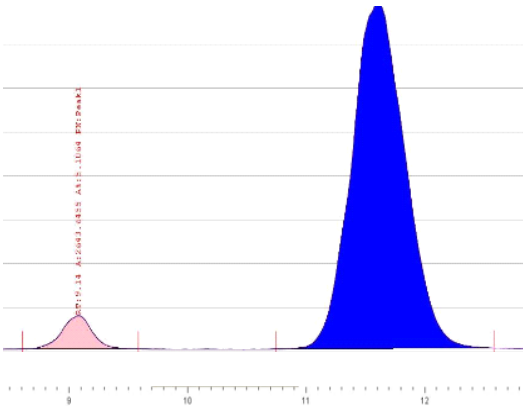
Chiral SFC (Chiracel OJ-H, 13% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-1-phenyl-4-ferrocenylbutan-2-ol.

Racemic Material

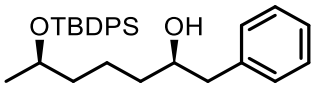


Peak No	% Area	Area	RT (min)
1	49.4303	46023.6816	11.21
2	50.5697	47084.5491	14.24
Total:	100	93108.2307	

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 (26).

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 (**23**) (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 ***(R,R)*-L2.4** (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).

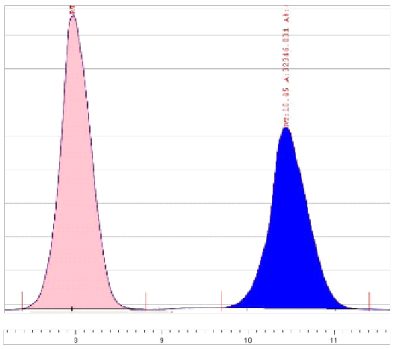
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73-7.67 (m, 4H), 7.45-7.16 (m, 11H), 3.91-3.83 (m, 1H), 3.78-3.69 (m, 1H), 2.77 (dd, *J* = 13.6, 4.2 Hz, 1H), 2.60 (dd, *J* = 13.6, 6.8 Hz, 1H), 1.58-1.29 (m, 8 H), 1.15-1.10 (m, 12H).**^{13}C NMR** (150 MHz, $CDCl_3$) δ 136.04, 136.01, 129.60, 129.54, 128.67, 127.61, 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 **34, 19**).

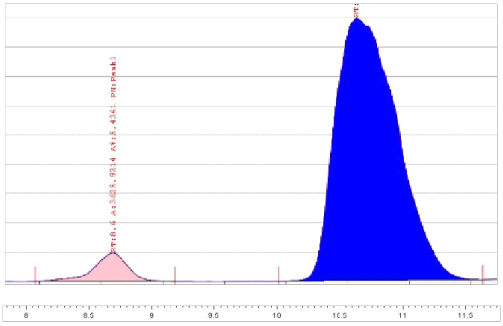
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (2R,6R)-6-((tert-butyldiphenylsilyl)oxy)-1-phenylheptan-2-ol.

Diastereomic Mixture

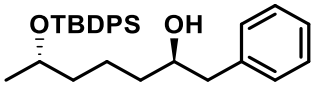


Peak No	% Area	Area	RT (min)
1	57.0781	43014.1003	8.01
2	42.9219	32346.031	10.45
Total:	100	75360.1313	

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 (27).

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 (**24**) (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 ***(R,R)*-L2.4** (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),

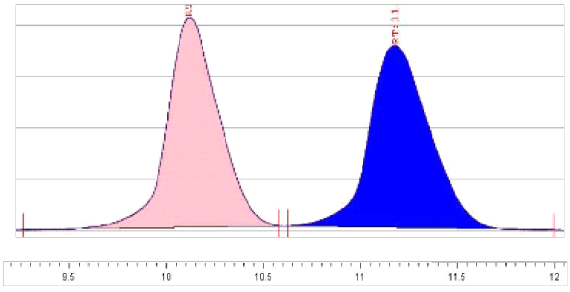
1.11-1.04 (m, 12H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 136.05, 136.04, 129.60, 129.56, 129.54, 128.67, 127.62, 127.54, 126.56, 72.63, 69.67, 44.07, 39.49, 36.93, 27.20, 23.40, 21.56, 19.41. **IR** (neat) ν_{max} 3421.77 (br, w), 2930.61 (m), 2856.83 (m), 1495.23 (w), 1472.11 (w) 1427.36 (m), 1376.40 (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 **34, 19**).

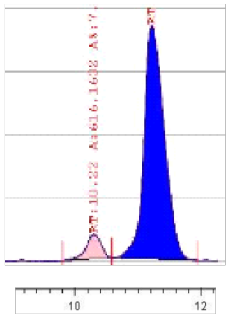
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (2R,6S)-6-((tert-butyldiphenylsilyl)oxy)-1-phenylheptan-2-ol.

Diastereomic Mixture

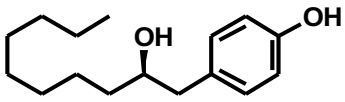


Peak No	% Area	Area	RT (min)
1	49.5546	7242.3644	10.08
2	50.4454	7372.5663	11.11
Total:	100	14614.9307	

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	



(*R*)-4-(2-hydroxydecyl)phenol (32). 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 ***(R,R)*-L14** (2.88 mg, 0.012 mmol, 0.060 equiv.) in THF (0.4 mL), 4-iodophenylboronic acid pinacol ester (66.0 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 white solid (37.8 mg, 75% yield).

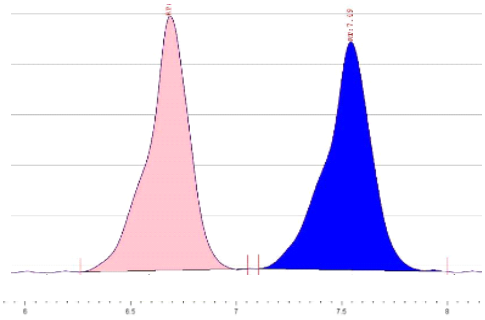
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 2H), 6.09-5.41 (br s, 1H), 4.06-3.55 (m, 1H), 2.77 (dd, *J* = 13.8, 4.2 Hz, 1H), 2.56 (dd, *J* = 13.8, 8.5 Hz, 1H), 1.64-1.06 (m, 14H), 0.88 (t, *J* = 6.5 Hz, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.57, 130.65, 130.36, 115.63, 73.21, 43.11, 36.81, 32.00, 29.78, 29.70, 29.40, 25.90, 22.80, 14.24. **IR** (neat) ν_{max} 3339.98 (br, w), 3212.56 (br, w), 3019.54 (w), 2956.78 (m), 2923.21 (s), 2854.02 (m), 1614.50 (w), 1598.03 (w), 1516.78 (s), 1455.78 (m), 1377.79 (w), 1253.90 (s), 1175.83 (w), 1102.56 (w), 1082.13 (w), 906.34 (s), 812.56 (s), 731.23 (s), 649.33 (w) cm^{-1}. **HRMS** (DART) for $C_{16}H_{30}O_2N$ $[M+NH4]^+$: Calc'd: 268.2277, found: 268.228. **$[\alpha]_D^{20}$** = -20.6985 (*c* = 0.93, $CHCl_3$, *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 **32, 16**).

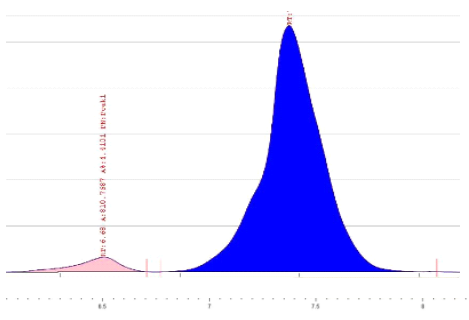
Chiral SFC (Chiracel OJ-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-4-(2-hydroxydecyl)phenol.

Racemic Material



Peak No	% Area	Area	RT (min)
1	50.1544	3558.2552	6.6
2	49.8456	3536.3432	7.49
Total:	100	7094.5984	

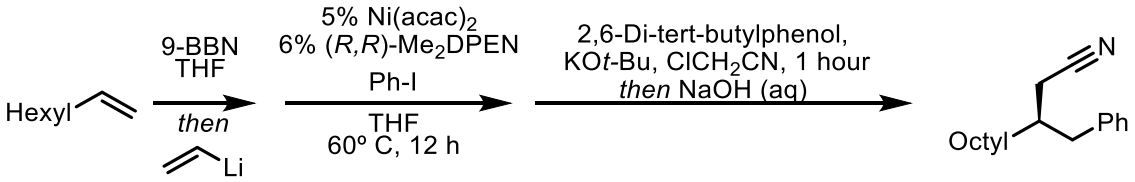
Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	4.4101	810.7687	6.68
2	95.5899	17573.7663	7.46
Total:	100	18384.535	

2.4.2.5. Procedures and Characterization for Transformations of secondary 9-BBN Borates

Cyanomethylation



***(R)*-3-benzylundecanenitrile (28).**

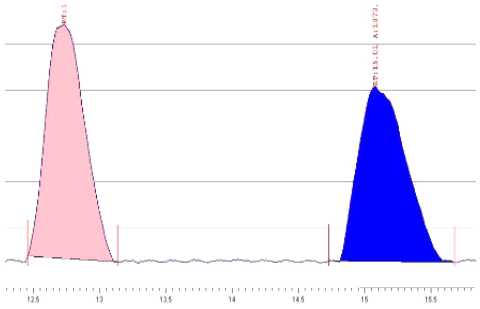
The title compound was prepared from enantiomerically enriched 9-BBN products obtained through the general **procedure A** with 9-BBN in THF (0.48 mL, 0.5 M, 0.24 mmol, 1.20 equiv.), 1-octene (26.9 mg, 0.24 mmol, 1.20 equiv.), halide-free vinyllithium in THF (0.15 mL, 1.47 M, 0.22 mmol, 1.10 equiv.), a solution of $Ni(acac)_2$ (2.57 mg, 0.010 mmol, 0.050 equiv.) and ***(R,R)*-L2.4** (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.), by replacing the oxidation step with a modification of the procedure reported by Brown.[18] After stirring at 60º C overnight the reaction mixture was cooled to 0ºC and a solution of 2,6-di-tert-butylphenol (51.6 mg, 0.25 mmol, 1.25 equiv.) and KO*t*Bu (28.05 mg, 0.25 mmol, 1.25 equiv.) in 400 μL of THF was added to the vial followed by the addition of a solution of $ClCH_2CN$ (18.2 mg, 0.24 mmol, 1.20 equiv.) in 200 μL of THF. The reaction mixture was warmed to room temperature and stirred for 1 hour, after which time 2 mL of a 3M NaOH aqueous solution was added. The biphasic mixture was stirrged for 30 minutes and the organic layer was extracted with Et_2O 3 times, dried over $MgSO_4$ and concentrated in vacuo. The crude mixture was purified by silica gel chromatography (15% DCM in pentane, stain in PMA) to afford a yellow oil (27.7 mg, 57% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.56 – 6.88 (m, 5H), 2.83 (dd, *J* = 13.8, 5.7 Hz, 1H), 2.57 (dd, *J* = 13.8, 9.1 Hz, 1H), 2.28 (dd, *J* = 16.9, 5.3 Hz, 1H), 2.20 (dd, *J* = 16.8, 5.6 Hz, 1H), 2.01 – 1.92 (m, 1H), 1.53 – 1.21 (m, 14H), 0.89 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.23, 129.18, 128.76, 126.65, 118.73, 39.99, 37.45, 33.57, 31.99, 29.70, 29.62, 29.39, 26.93, 22.81, 21.16, 14.25. **IR** (neat) ν_{max} 3027 (w, s), 3034.8 (s), 2024.3 (s), 2854.4 (s), 2245.2 (s), 1603.1 (w, m), 1496.6 (s), 1377.3 (w, m), 1079.6 (w), 1030.5 (w), 741.1 (s), 701.8 (s) cm^{-1}. **HRMS** (DART) for $C_{18}H_{31}N_2$ $[M+NH_4]^+$: Calc'd: 275.2487, found: 275.2475. $[\alpha]_D^{20}$ = -21.315 (*c* =1.0, $CHCl_3$, *l* = 50 .

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 **34, 19**).

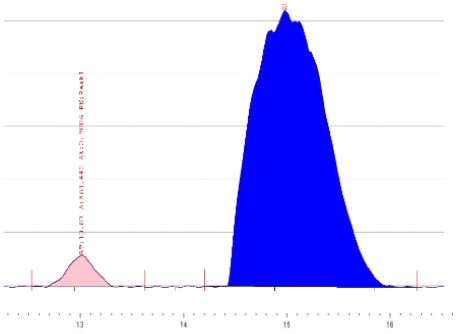
Chiral SFC (Chiracel AD-H, 1 % IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of tert-butyl (R)-3-benzylundecanenitrile.

Racemic material

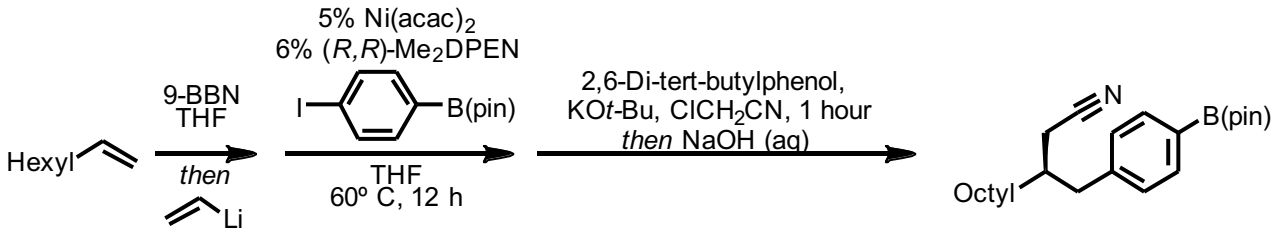


Peak No	% Area	Area	RT (min)
1	52.1976	2045.4617	12.71
2	47.8024	1873.2305	15.01
Total:	100	3918.6922	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	3.9886	563.443	13.07
2	96.0114	13563.0475	15.1
Total:	100	14126.4905	



***(R)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)undecanenitrile* (33).**

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 ***(R,R)*-L14** (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

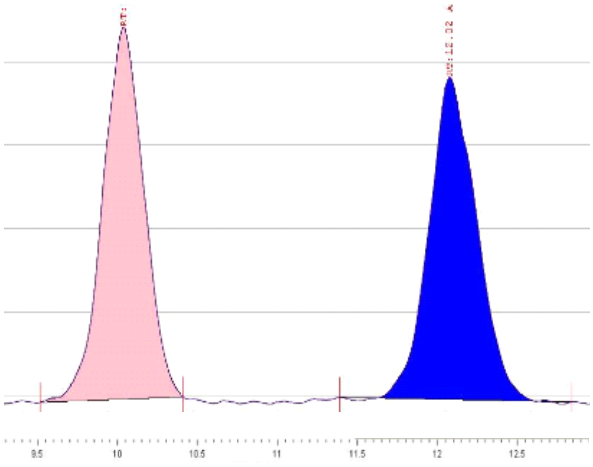
(m), 859.14 (m), 829.74 (w), 736.36 (w), 659.62 (s) cm^{-1}. **HRMS** (DART) for $C_{24}H_{42}N_2O_2B$ $[M+NH_4]^+$: Calc'd: 401.3339, found: 401.3335. $[\alpha]_D^{20}$ = -13.998 (*c* =1.54, $CHCl_3$, *l* = 50 mm).

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 **34, 19**).

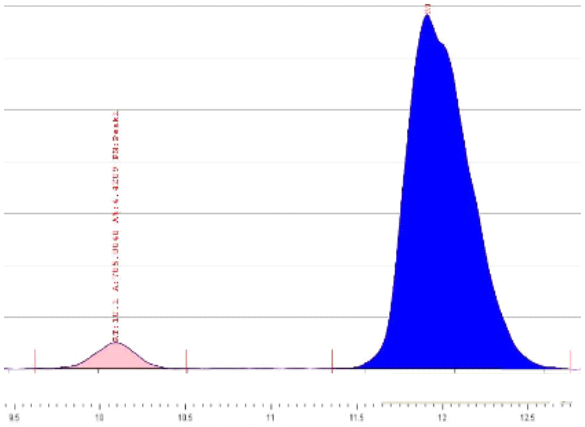
Chiral SFC (Chiracel AD-H, 3 % IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of (R)-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)undecanenitrile.

Racemic material



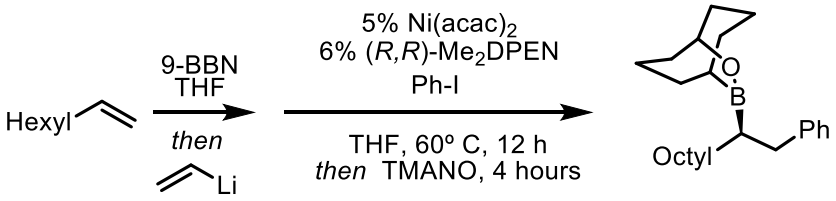
Peak No	% Area	Area	RT (min)
1	49.9809	3793.2285	10.09
2	50.0191	3796.1337	12.02
Total:	100	7589.3622	

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	

Mono-Oxidation

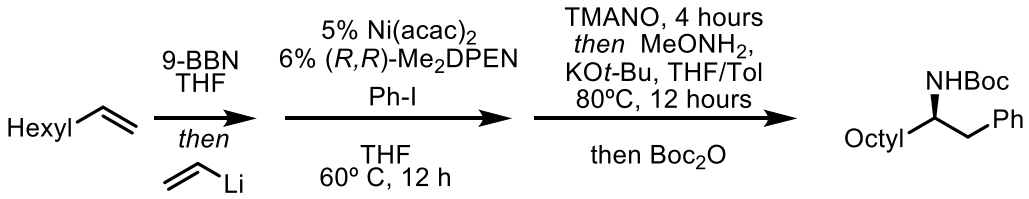


(*R*)-10-(1-phenyldecan-2-yl)-9-oxa-10-borabicyclo[3.3.2]decane (29)

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 ***(R,R)*-L2.4** (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. Afterwards, the mixture was filtered through celite and concentrated in vacuo. The material was purified by neutral alumina column chromatography (pentane, stain in CAM) to afford a colorless oil (58.9 mg, 83% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.27-7.11 (m, 5H), 4.60-4.49 (m, 1H), 2.69 (dd, *J* = 13.8, 7.8 Hz, 1H), 2.58 (dd, *J* = 13.8, 7.3 Hz, 1H), 1.80-1.16 (m, 27H), 0.88 (s, 3H). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.35, 128.99, 128.08, 125.41, 73.39, 37.06, 35.59 (br), 32.11, 32.04, 31.38, 30.78, 30.24, 29.70, 29.65, 29.45, 26.57, 26.36, 24.33 (br), 22.84, 22.34, 22.09, 14.26**. ^{11}B NMR** (160 MHz, $CDCl_3$) δ 53.30. **IR** (neat) ν_{max} 3061.6 (w, m) 3025.0 (w, s), 2919.9

(s), 2851.8 (s), 1602.4 (w, s), 1494.6 (s), 1413.6 (m), 1364.9 (s), 1337.9 (s), 1285.6 (s), 1160.3 (s) 1020.44 (m), 870.9 (w, s), 697.9 (s), 643.4 (s) cm^{-1}. **HRMS** (DART) for $C_{24}H_{40}BO$ $[M+H]^+$, Calc'd: 355.3172, found:355.3186 $[\alpha]_D^{20}$ =10.632 (*c* =1.0, $CHCl_3$, *l* = 50 mm).

Amination



***tert*-butyl (*R*)-(1-phenyldecan-2-yl)carbamate (30)**

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 ***(R,R)*-L2.4** (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.

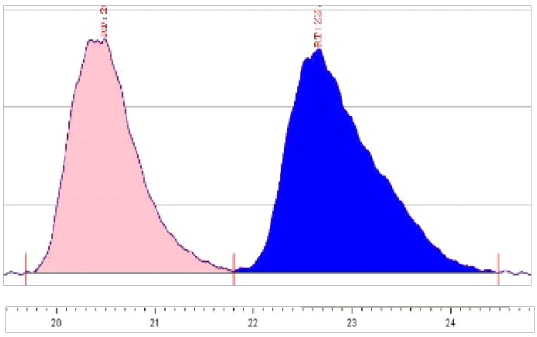
The reaction was stirred at 80°C overnight. Afterwards the mixture was cooled down to room temperature and a solution of di-tert-butyl-dicarbonate in THF (1M solution, 6.5 equiv. 1.3 mL) was added. After having stirred at rt for 4 hours, 1 mL of H_2O was added and the water layer was extracted 4 times 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 by employing the same reaction sequence with 2,2'-bipy (6 mol%) as the ligands. Absolute stereochemistry was assigned by analogy (see product **34, 19**).

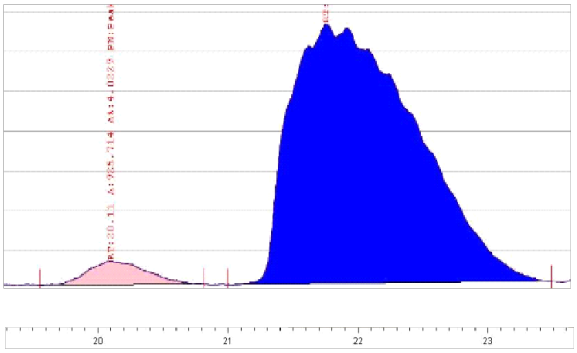
Chiral SFC (Chiracel OD-H, 1 % IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of tert-butyl (R)-(1-phenyldecan-2-yl)carbamate.

Racemic Material



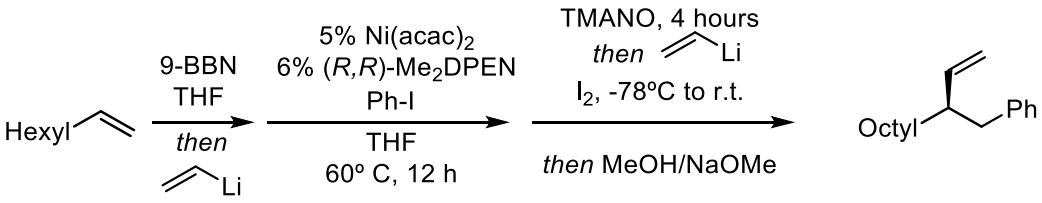
Peak No	% Area	Area	RT (min)
1	45.7469	5763.3965	20.6
2	54.2531	6835.0571	22.78
Total:	100	12598.4536	

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 (*31*)

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 ***(R,R)*-L2.4** (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

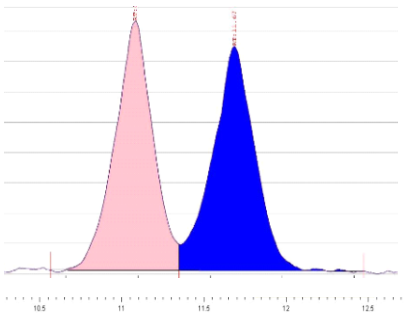
0°C. The water layer was extracted 4 times with Pentane, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (pentane, stain in CAM) to afford a colorless oil (40.2 mg, 82% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.29-7.07 (m, 5H), 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. $[\boldsymbol{\alpha}]_D^{20}$ = 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.

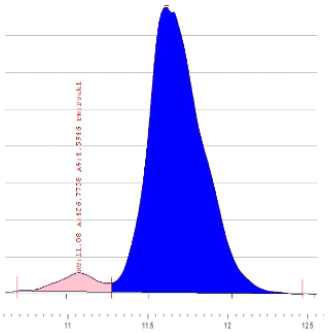
Chiral SFC (Chiracel OJ-H, 2 % IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of tert-butyl (R)-3-benzylundecan-1-ol.

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	

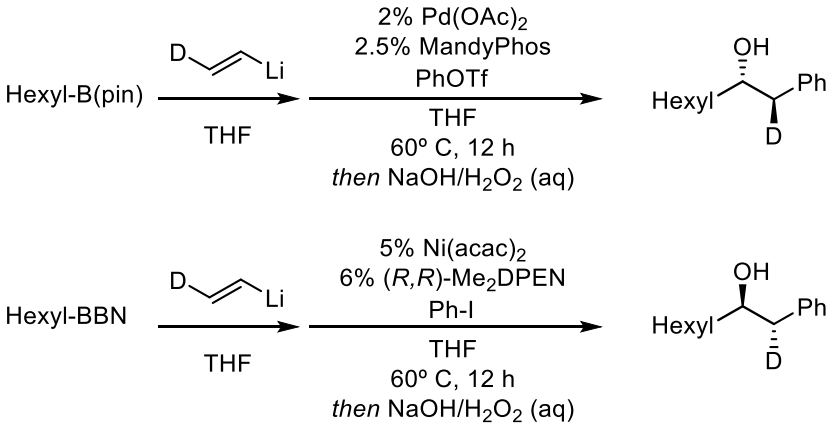
Enantioenriched Material



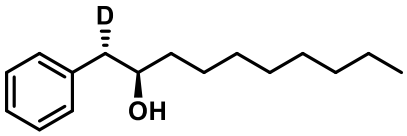
Peak No	% Area	Area	RT (min)
1	4.5946	426.7758	11.08
2	95.4054	8861.79	11.61
Total:	100	9288.5658	

2.4.2.6. Deuterium-labeling Experiment

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



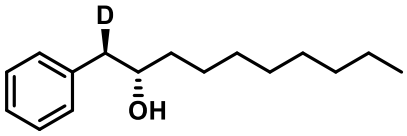
The *trans*-deuterium labeled vinyl lithium was prepared as described in previous reports.[16]



(1*S*,2*R*)-1-phenyldecan-1-*d*-2-ol (34). 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 ***(R,R)*-L2.4** (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). **^{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. $[\alpha]_D^{20}$ -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 .[16]



(1*R*,2*S*)-1-phenyldecan-1-*d*-2-ol (S-34). 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).

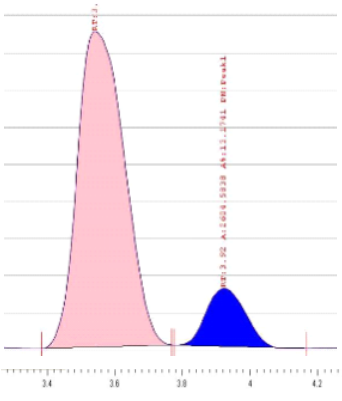
In our previous report,[16] a similar deuterium labelled vinyllithium was used in palladium/Mandyphos catalyzed conjunctive cross-coupling, and it was found to generate products with anti stereochemistry between the hydroxyl group and the deuterium atom, consistent with an anti-migration of the organo lithium 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.

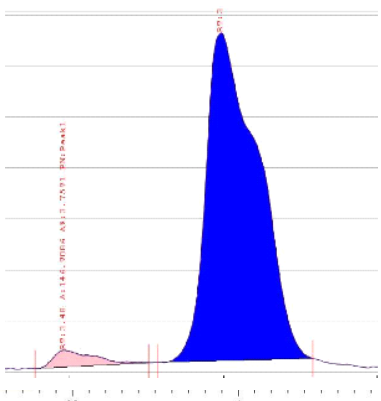
Chiral SFC (Chiracel OD-H, 3 % IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm) – analysis of tert-butyl (1R,2S)-1-phenyldecan-1-d-2-ol.

S-33



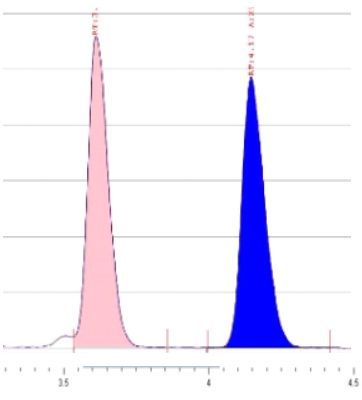
Peak No	% Area	Area	RT (min)
1	86.8259	17165.9122	3.52
2	13.1741	2604.5838	3.92
Total:	100	19770.496	

33



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

Racemic material

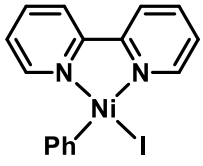


Peak No	% Area	Area	RT (min)
1	50.7244	2991.7195	3.58
2	49.2756	2906.2689	4.17
Total:	100	5897.9884	

Assignment of Absolute Stereochemistry

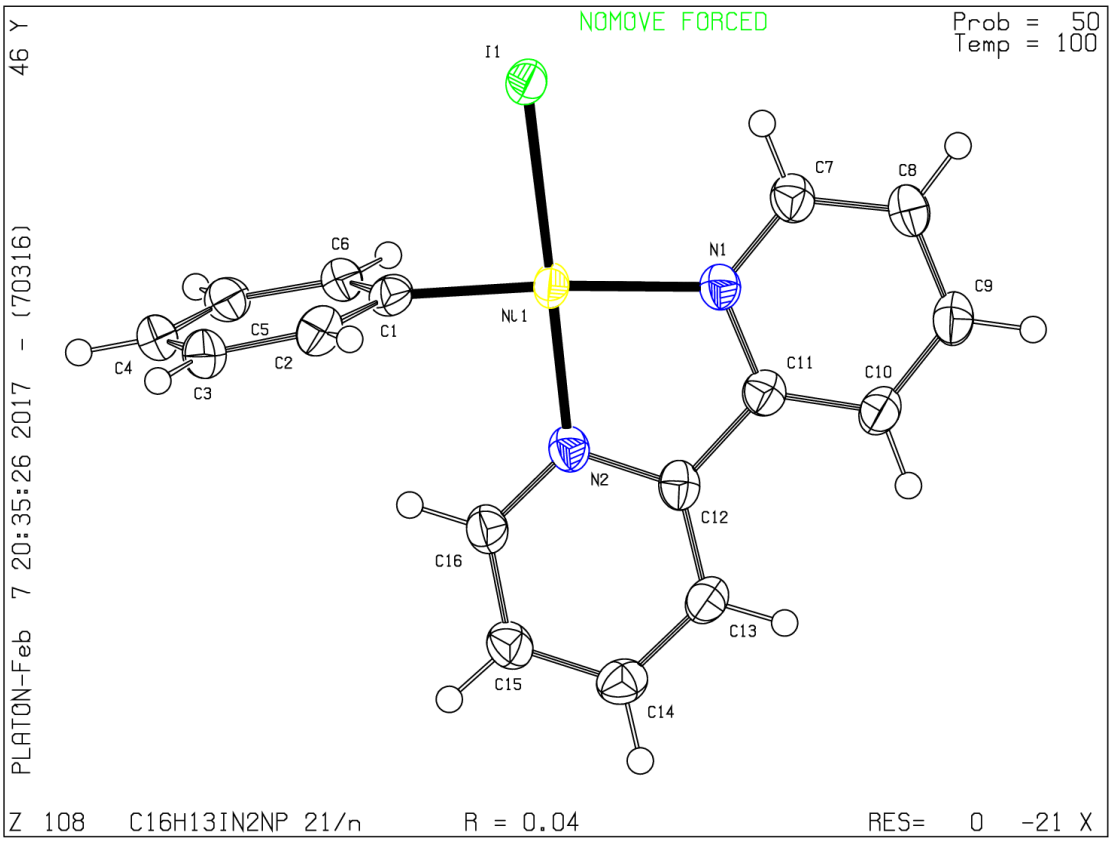
Comparison of the SFC traces and optical rotation of **32** and **S-32** allowed for the assignment of the absolute stereochemistry for the Ni catalyzed conjunctive cross-coupling products. This assignment was also supported by comparison of the SFC trace and optical rotation of the substrate **16**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

2.4.7 ***Stoichiometric experiments.***



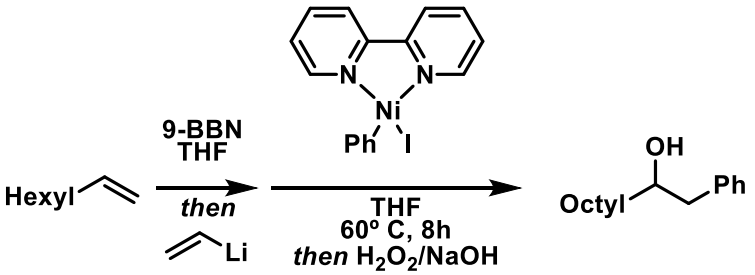
Phenyl(dipyridyl) Nickel Iodide (35)

In an argon filled glovebox, to an oven dried scintillation vial equipped with a magneti 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.

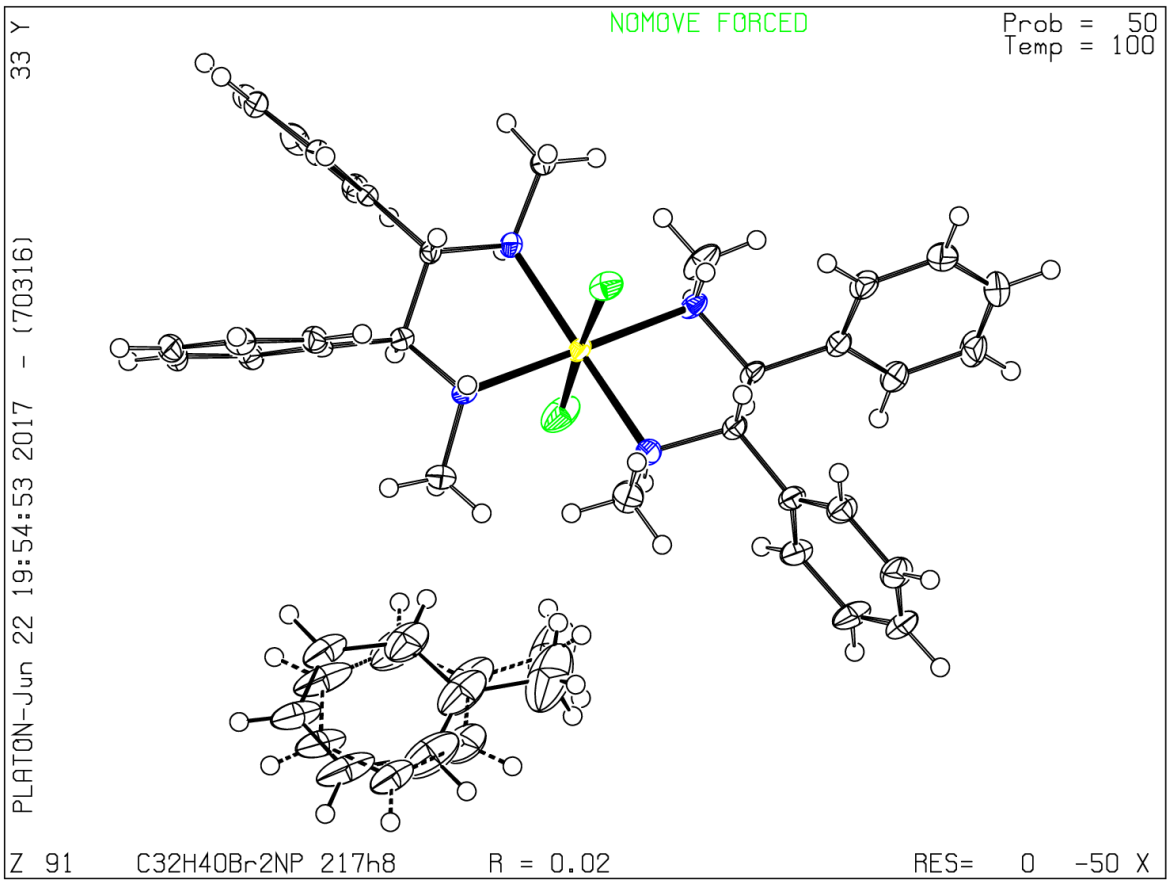


The structure was confirmed through x-ray crystallography. Crystals were grown by vapor diffusion with pentane and 2-methyltetrahydrofuran at -18ºC. The metal complex was dissolved in anhydrous 2-methyltetrahydrofuran in a glovebox, filtered through celite.

Stoichiometric Conjunctive Cross-Coupling Reactions.



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 **(34) (**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*** as a colorless oil (10.5 mg, 45% yield).



Crystal was obtained by vapor diffusion with pentane from a 1:1 metal to ligand solution in toluene. In an argon filled glove box Nickel(II) bromide 2-methoxyethyl ether complex (17.6 mg 0.05 mmol) and (1*S*,2*S*)-*N*,*N*′-Dimethyl-1,2-diphenyl-1,2-ethylenediamine (**L2.4)** (12.0 mg, 0.05 mmol) were placed in a 2-dram vial with 3 mL of toluene. After stirring at r.t. for 2 hours, the solution was filtered through an acro-disk syringe filter in a 1-dram vial which was then placed in scintillation vial filled with 2 mL of dry pentane. The vial was capped and kept at room temperature. Blue crystals were observable after 4 days.

2.4.3 References

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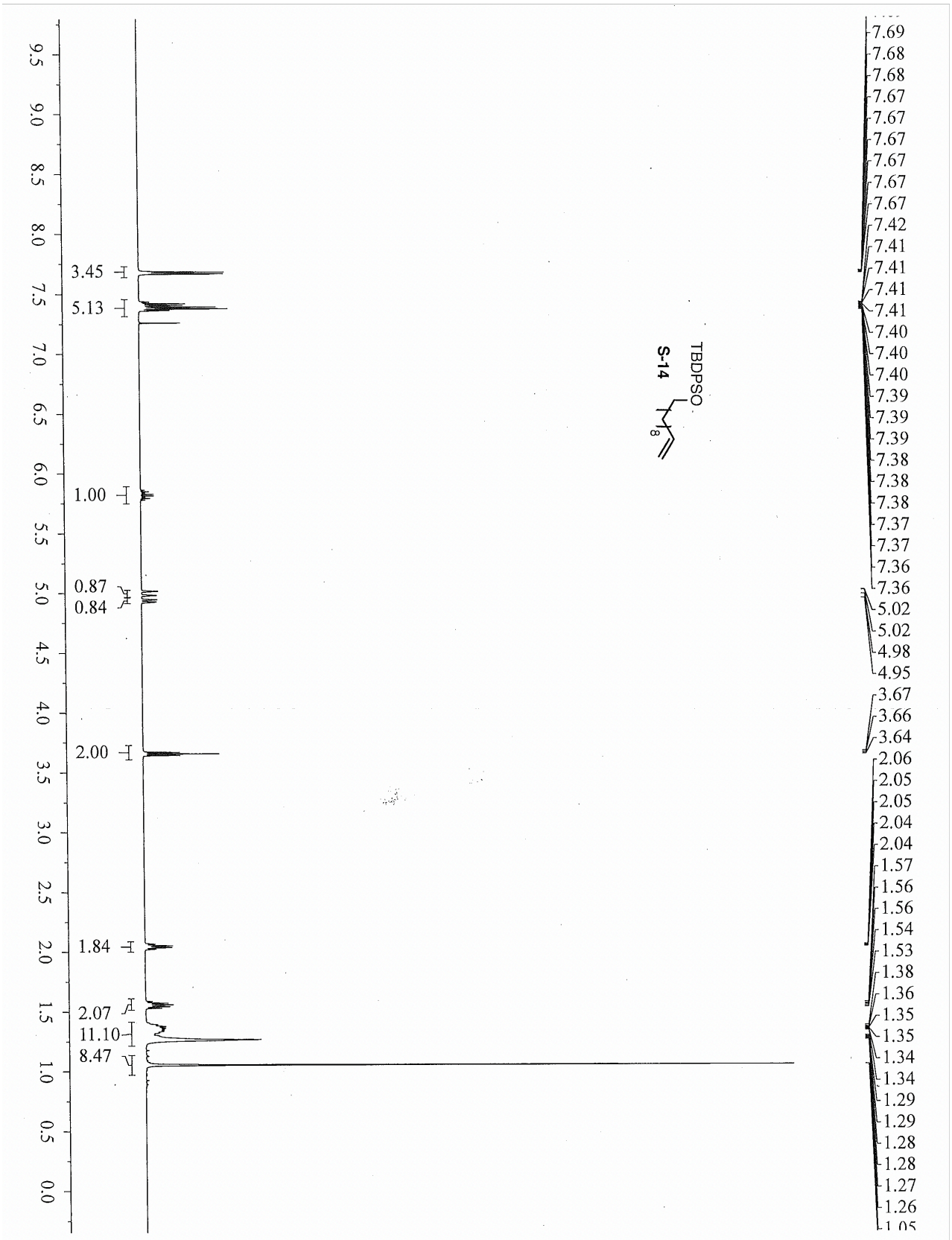
2.4 NMR spectra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8.47
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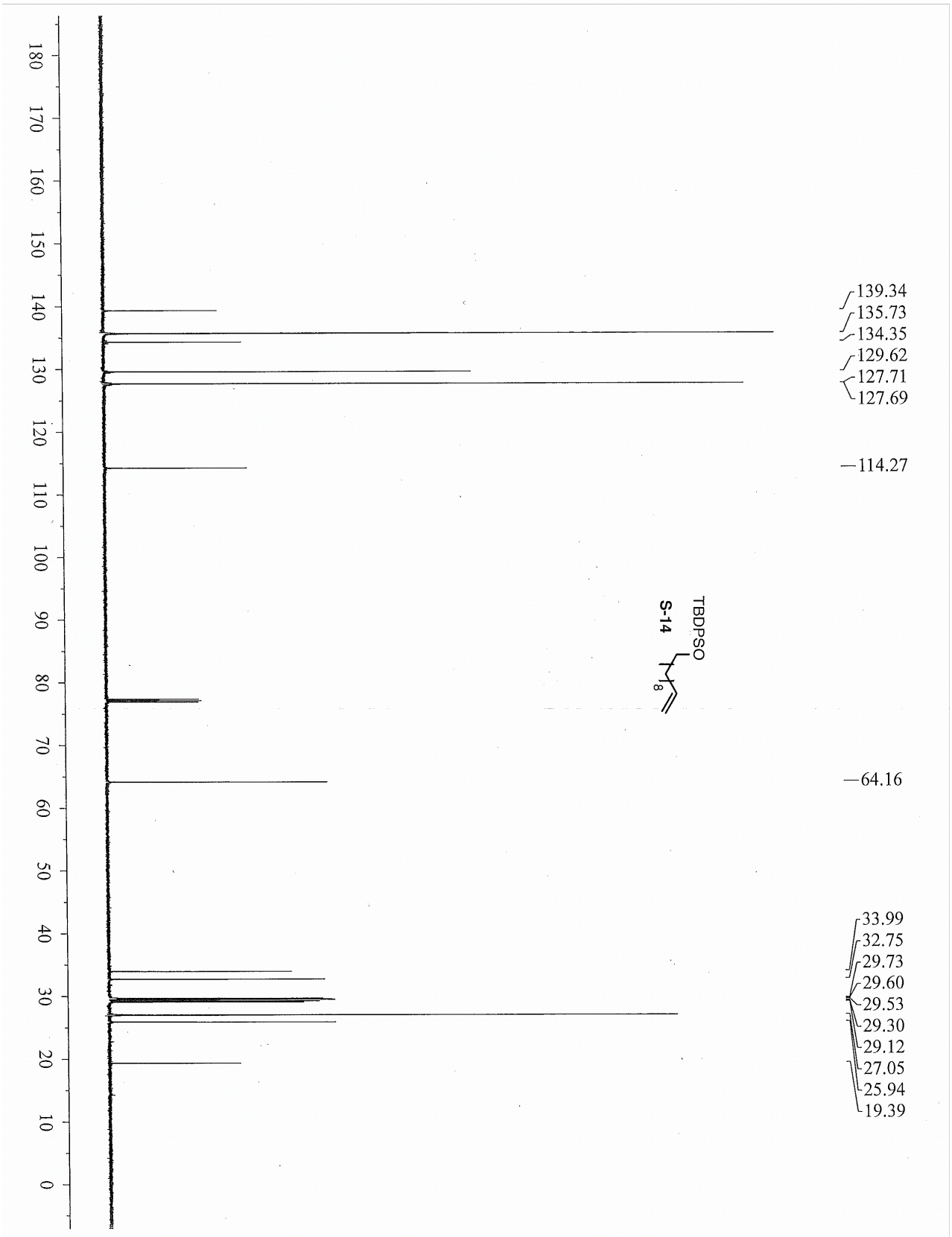
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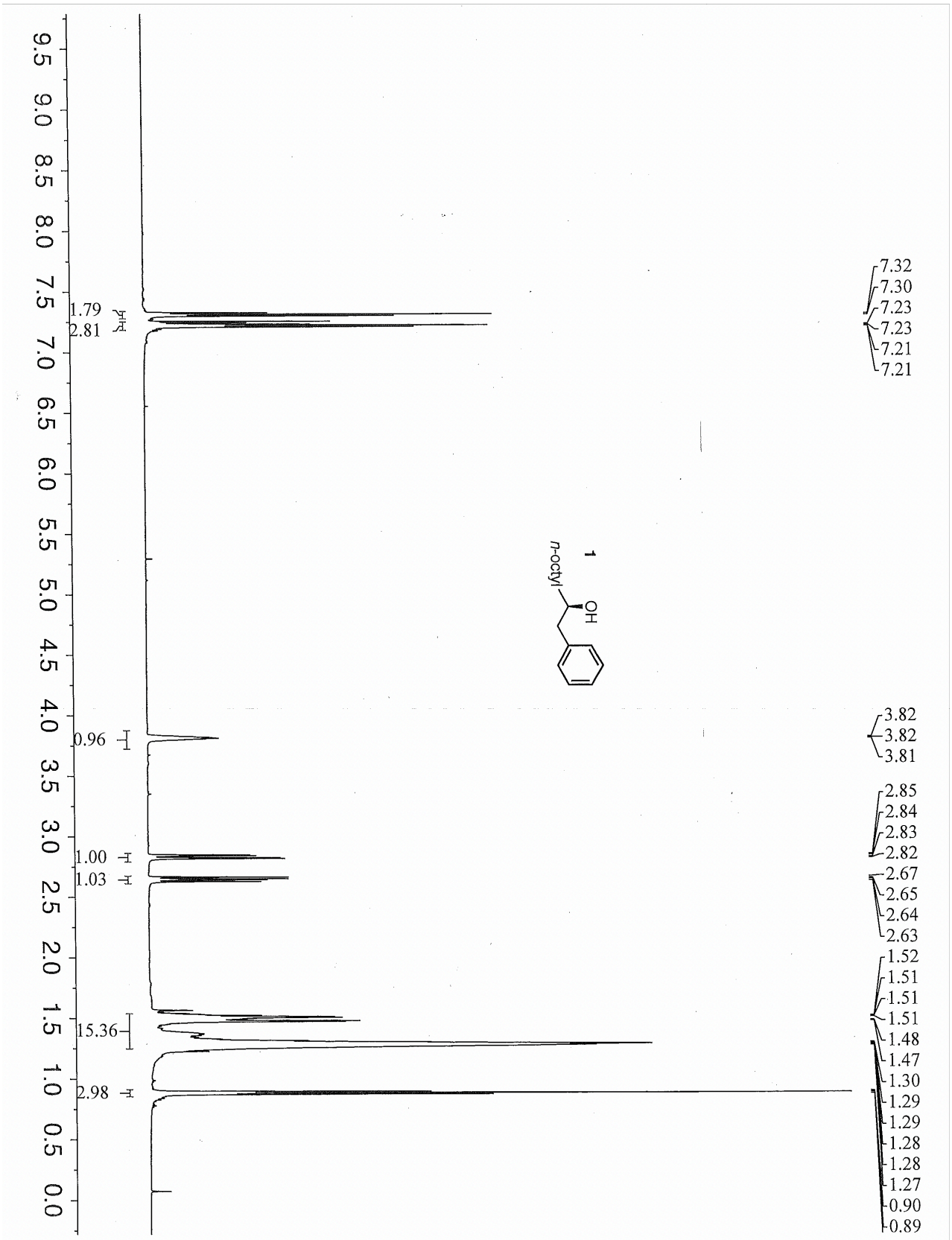
8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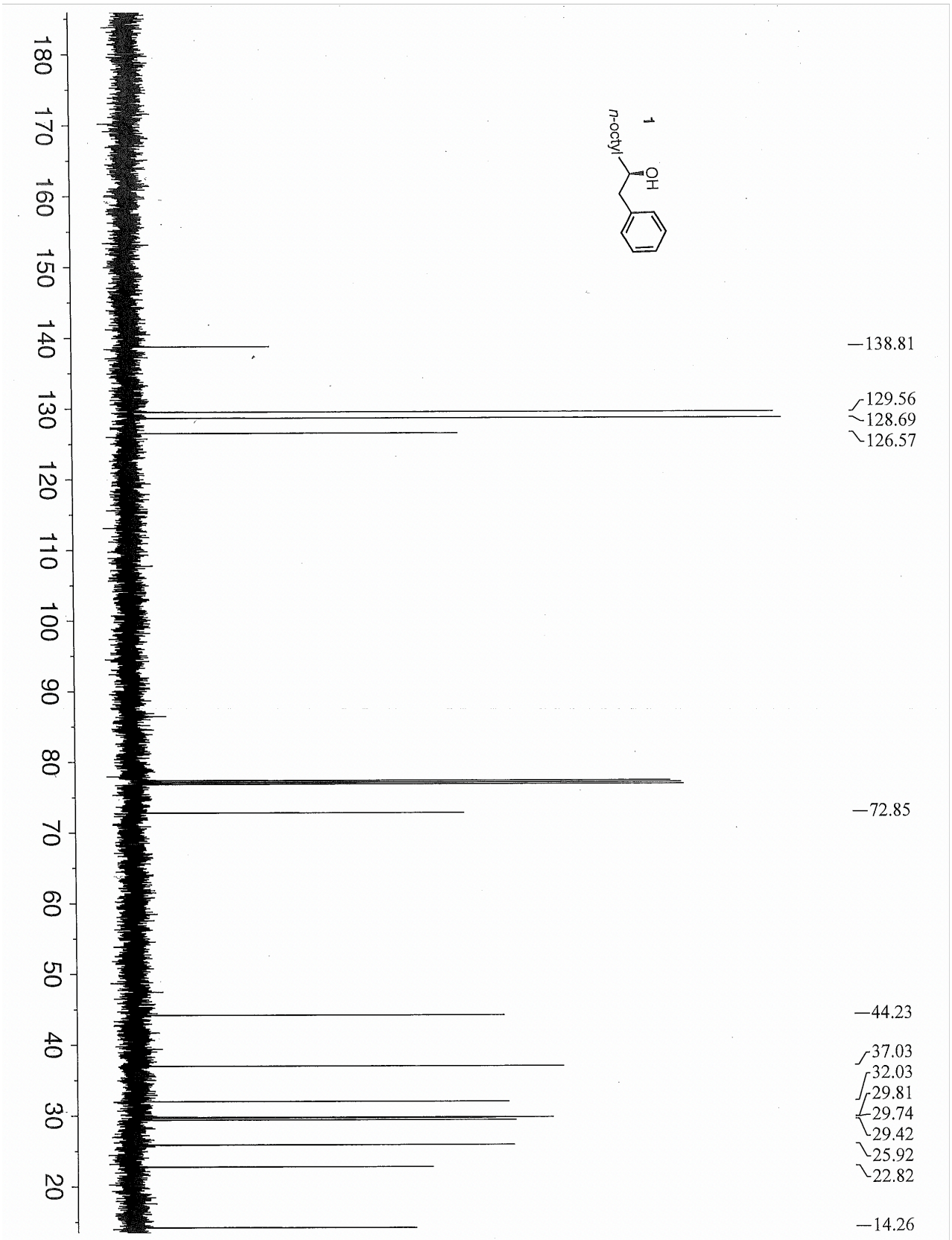
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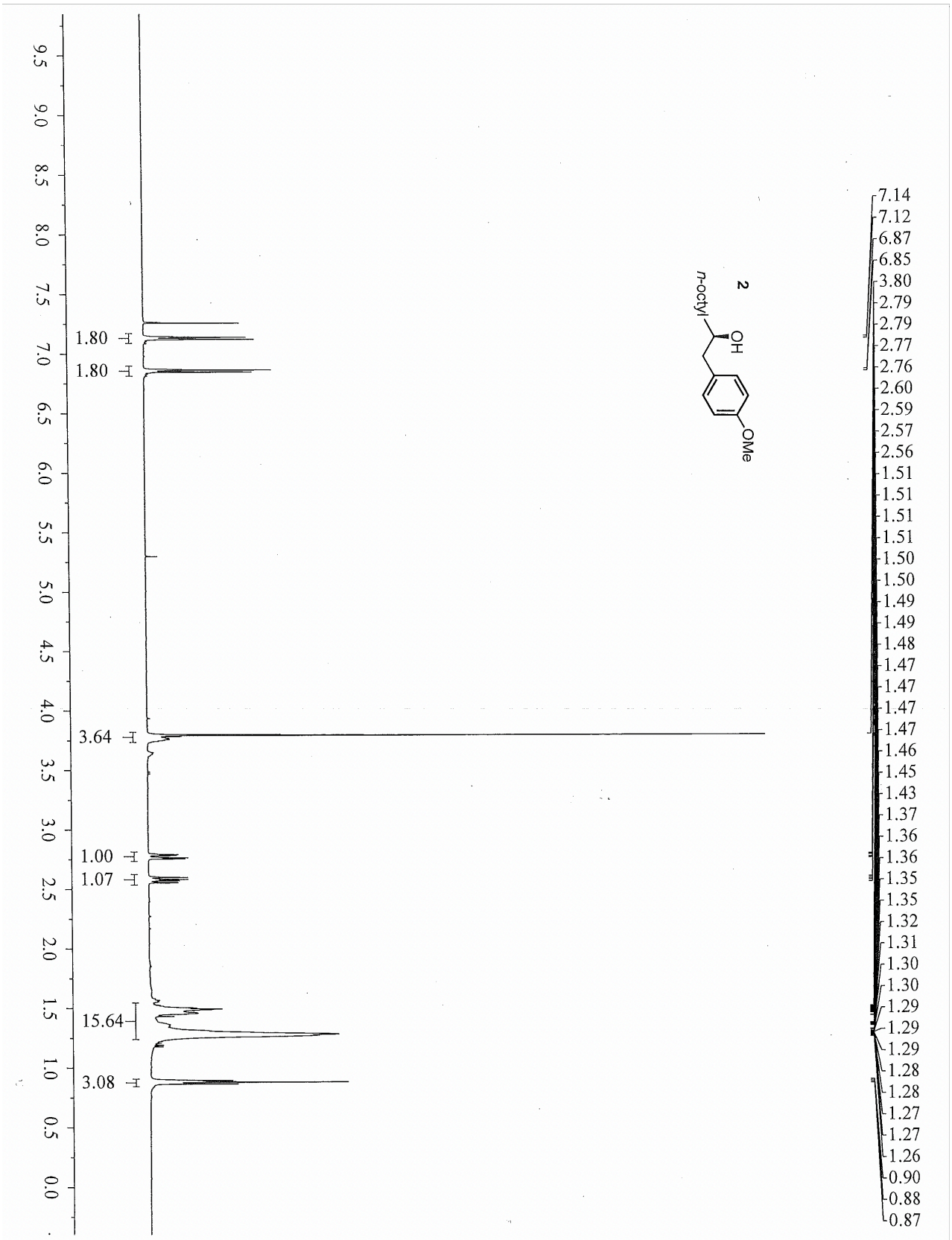
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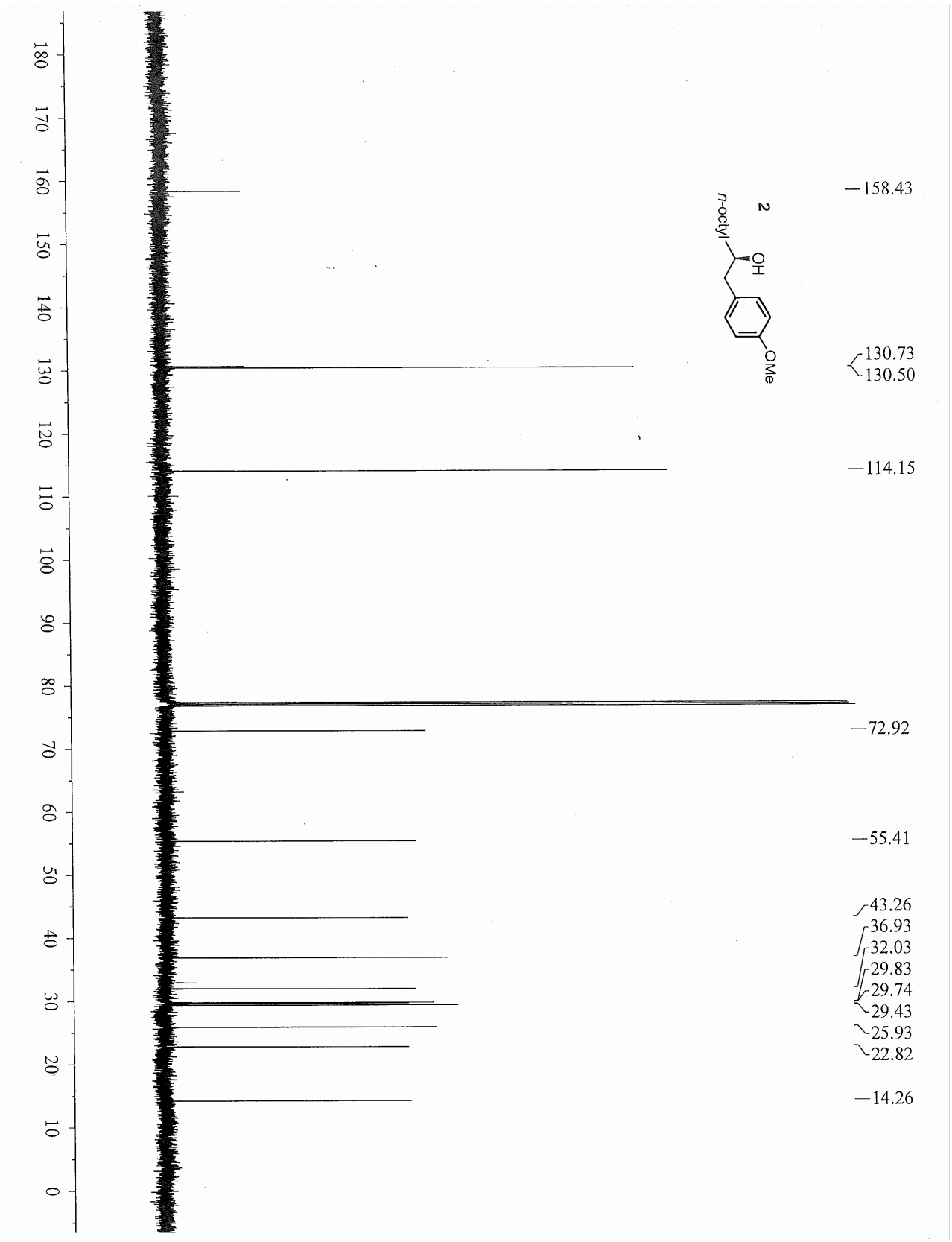
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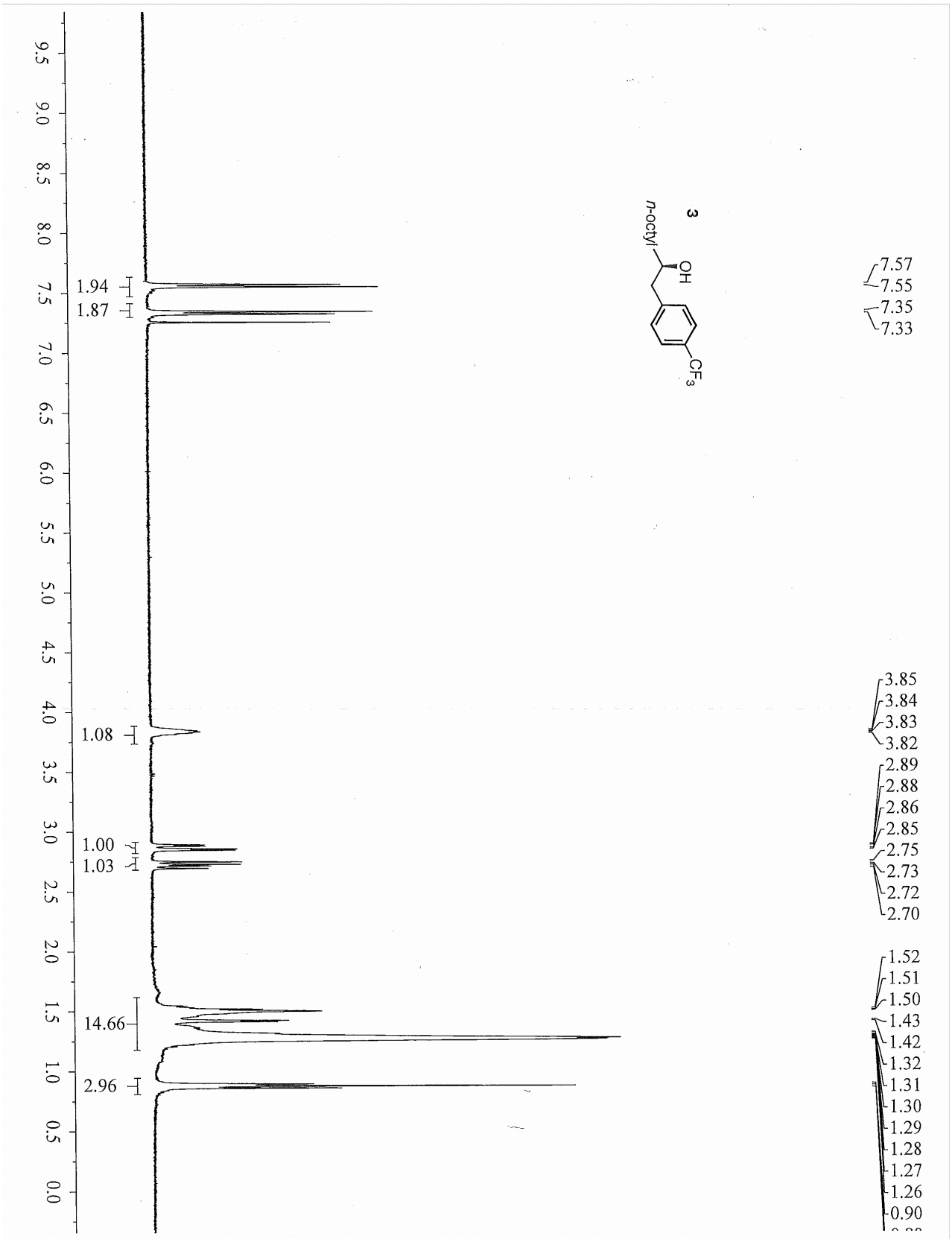
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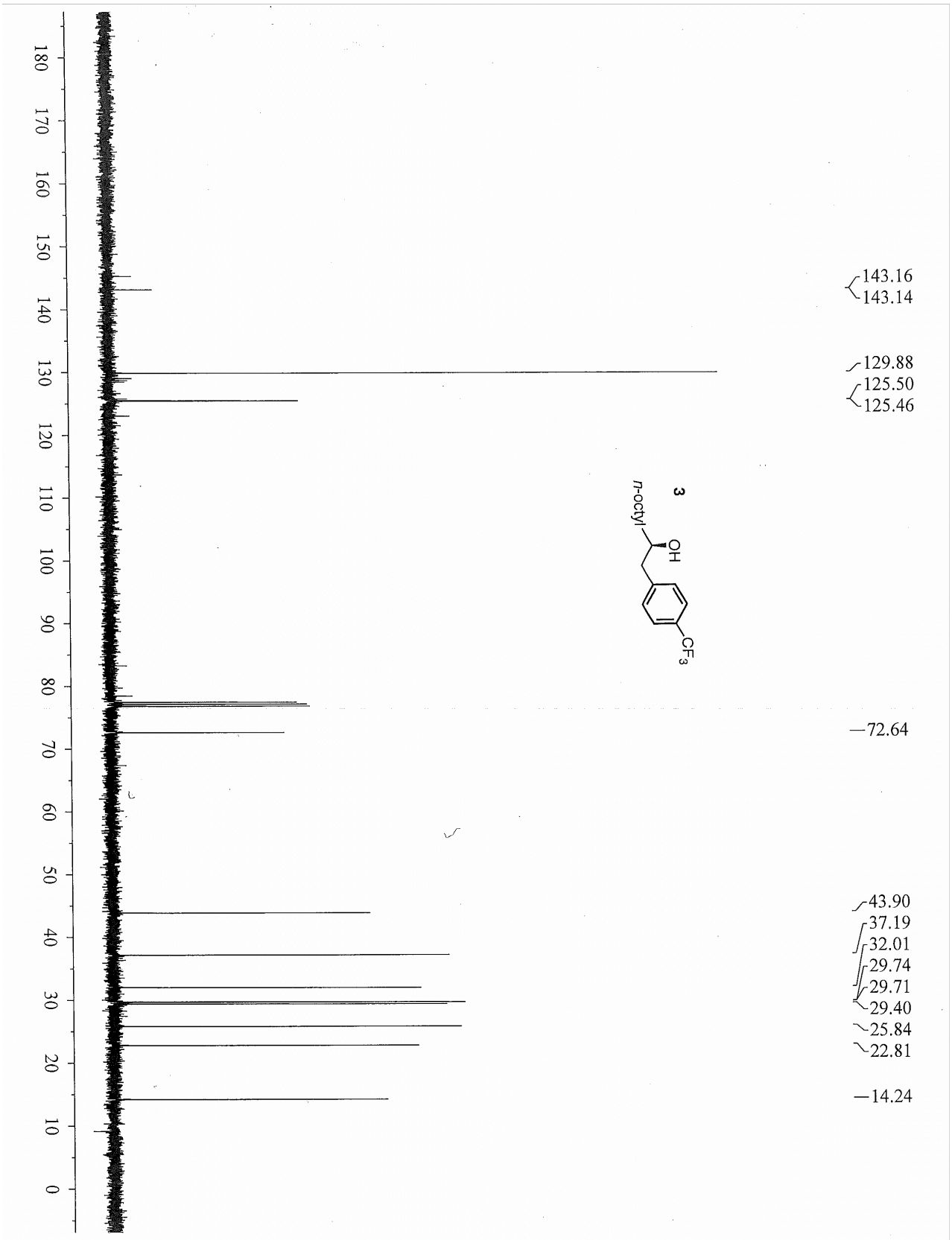
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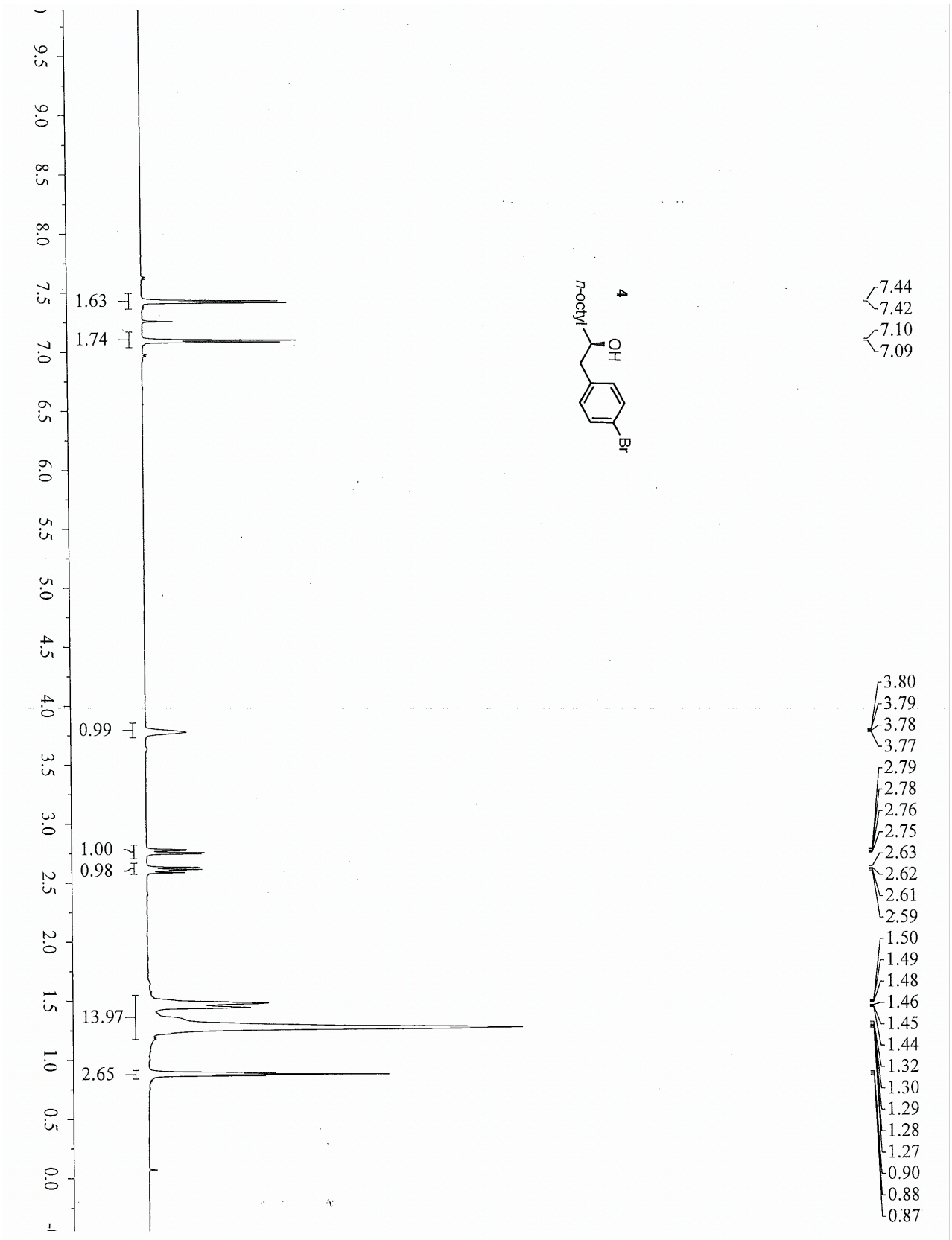
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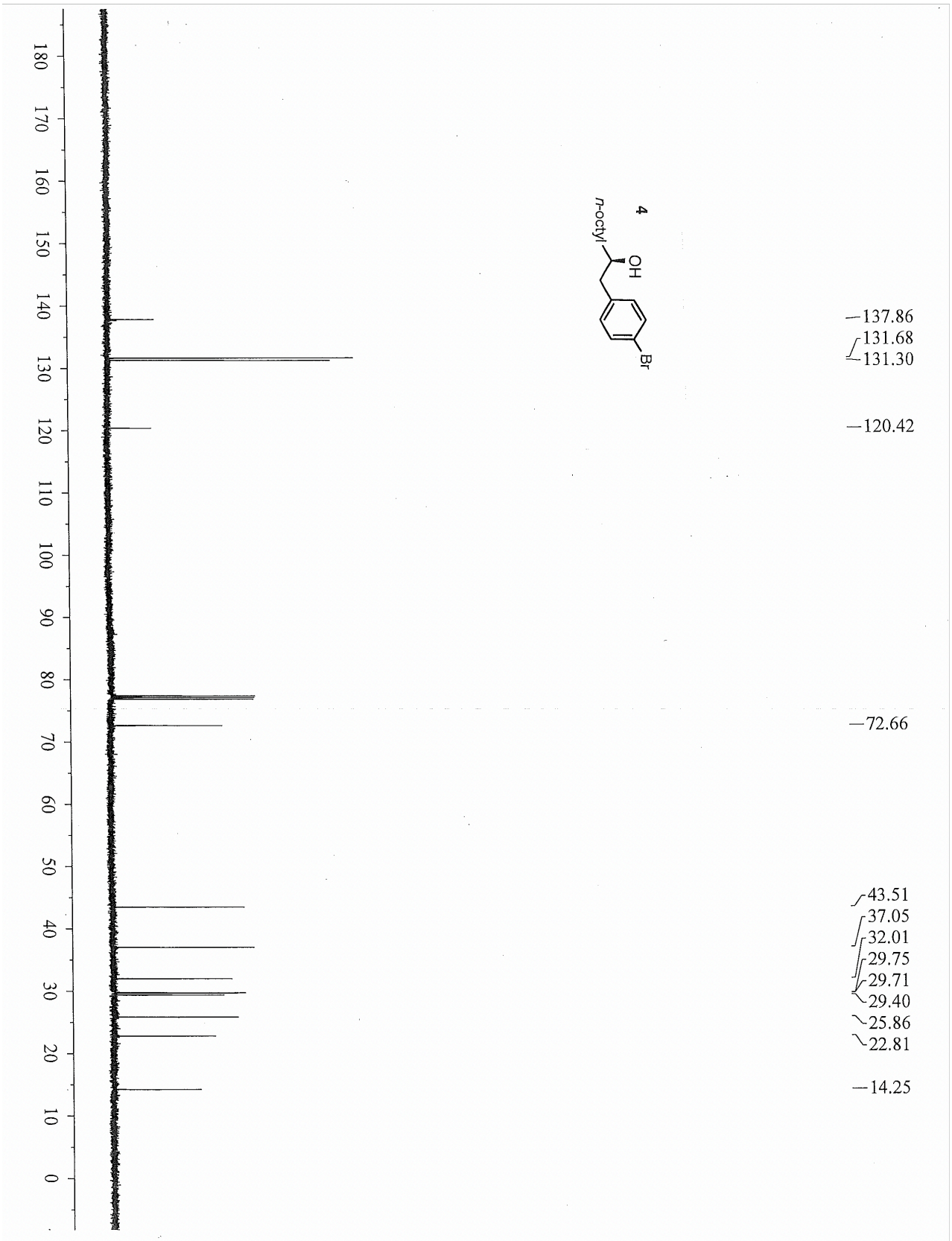
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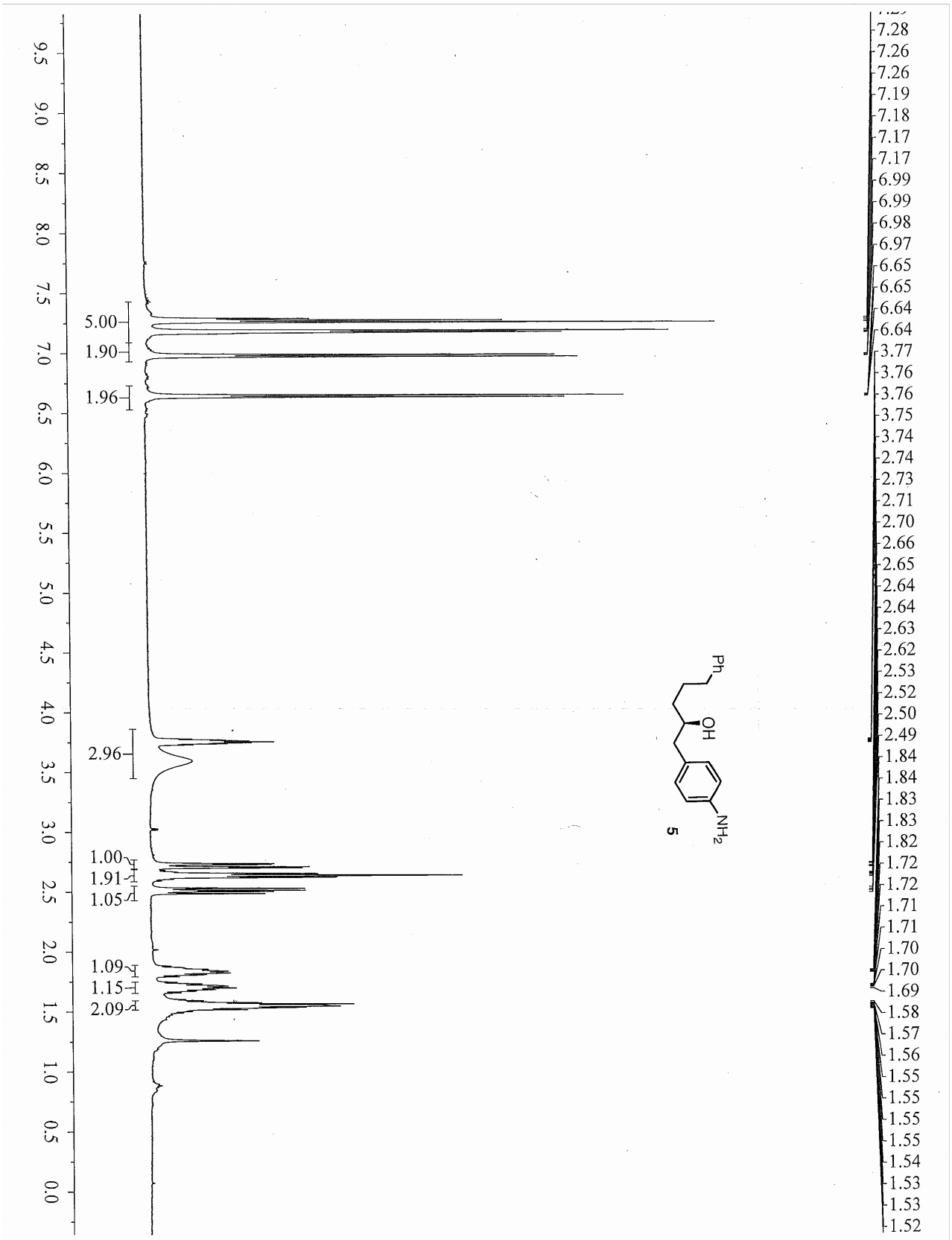
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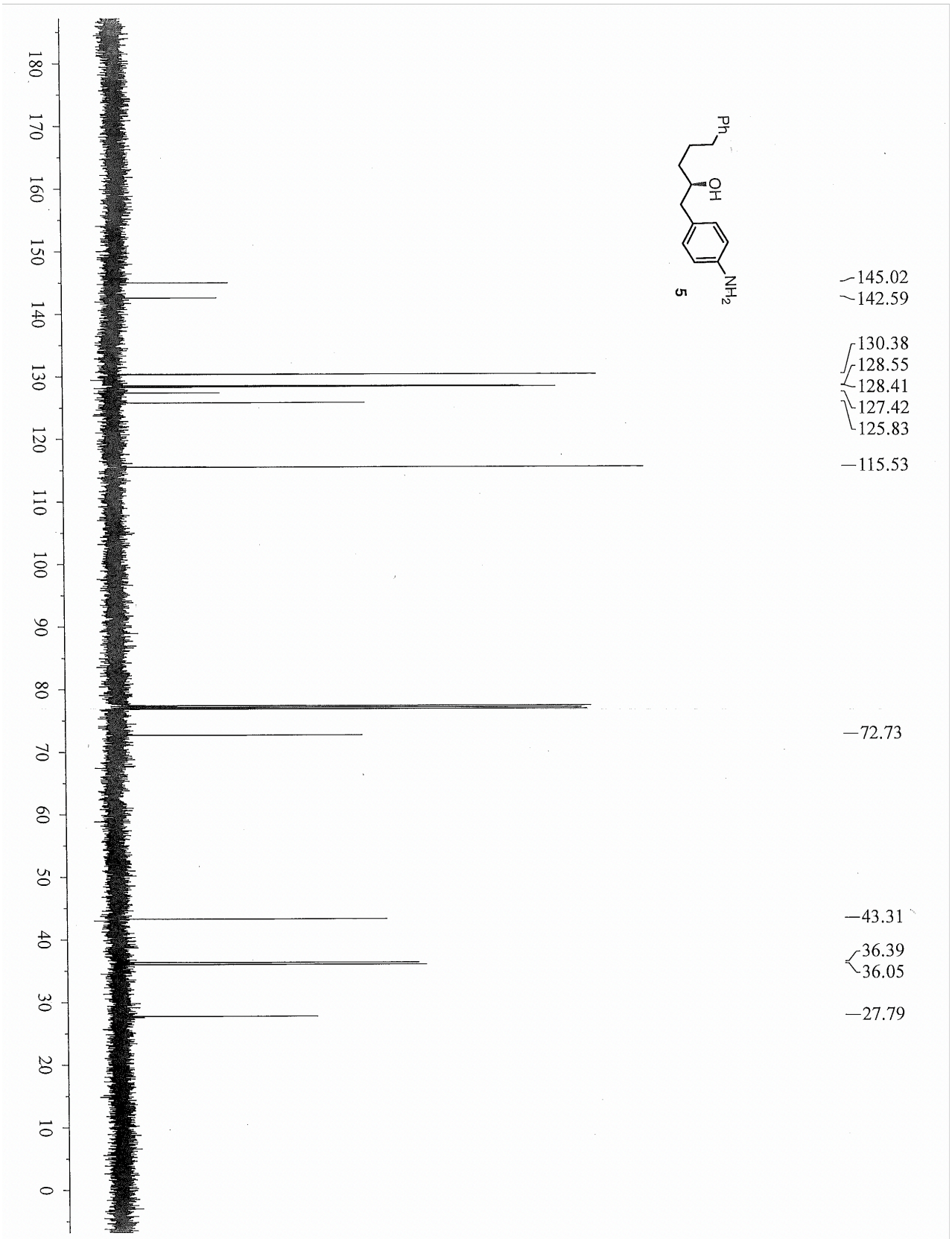
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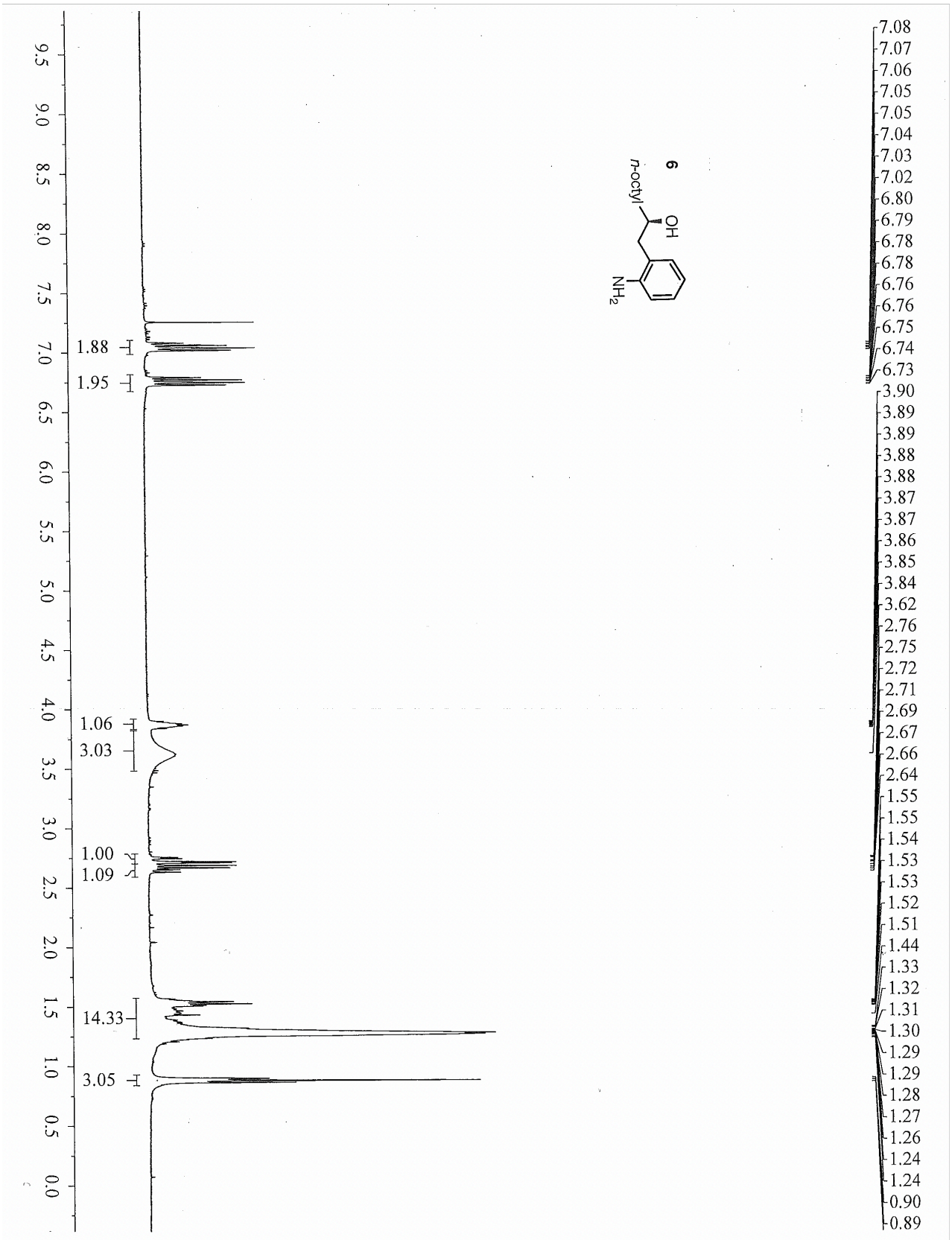
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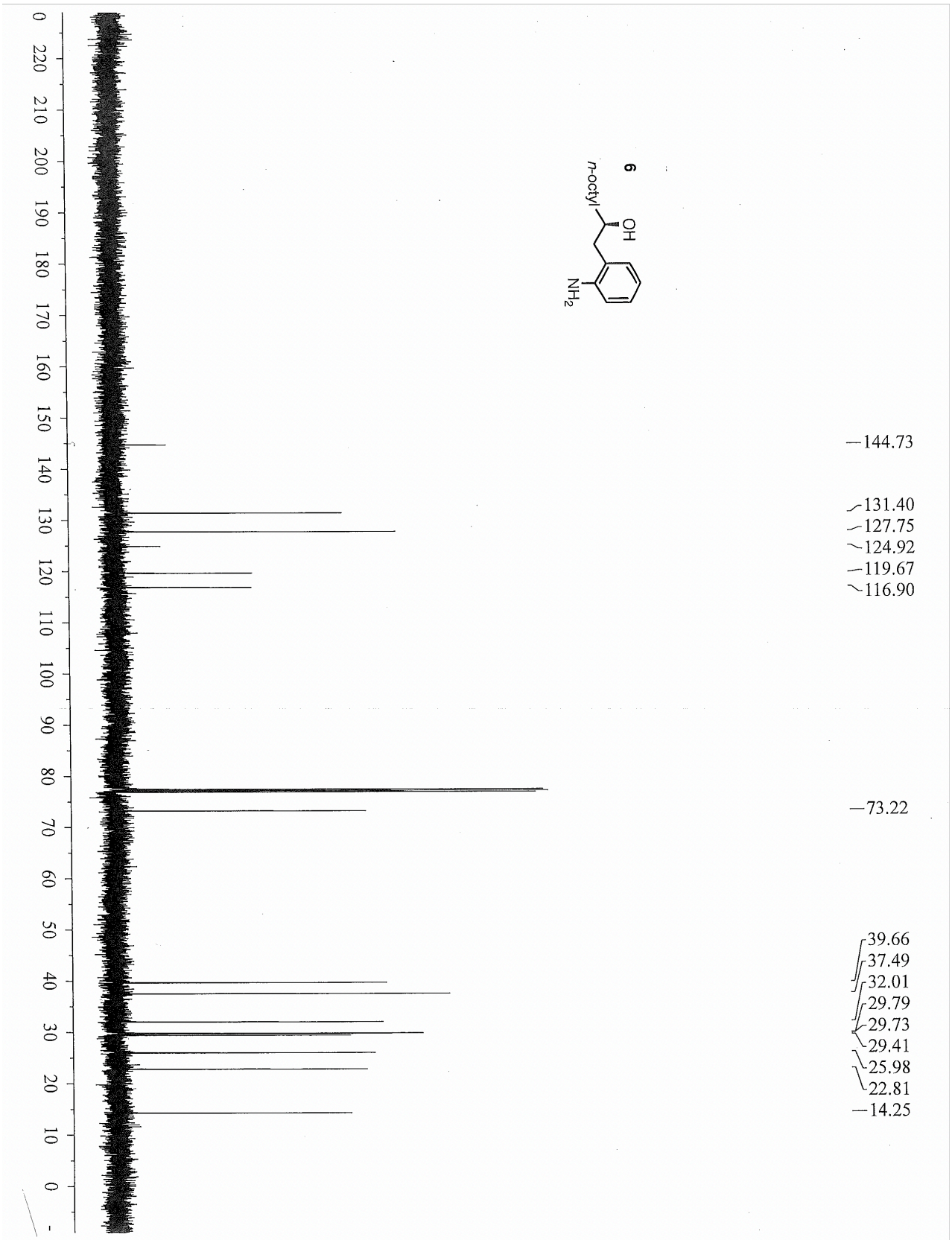
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n-octyl
OH
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124.92
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32.01
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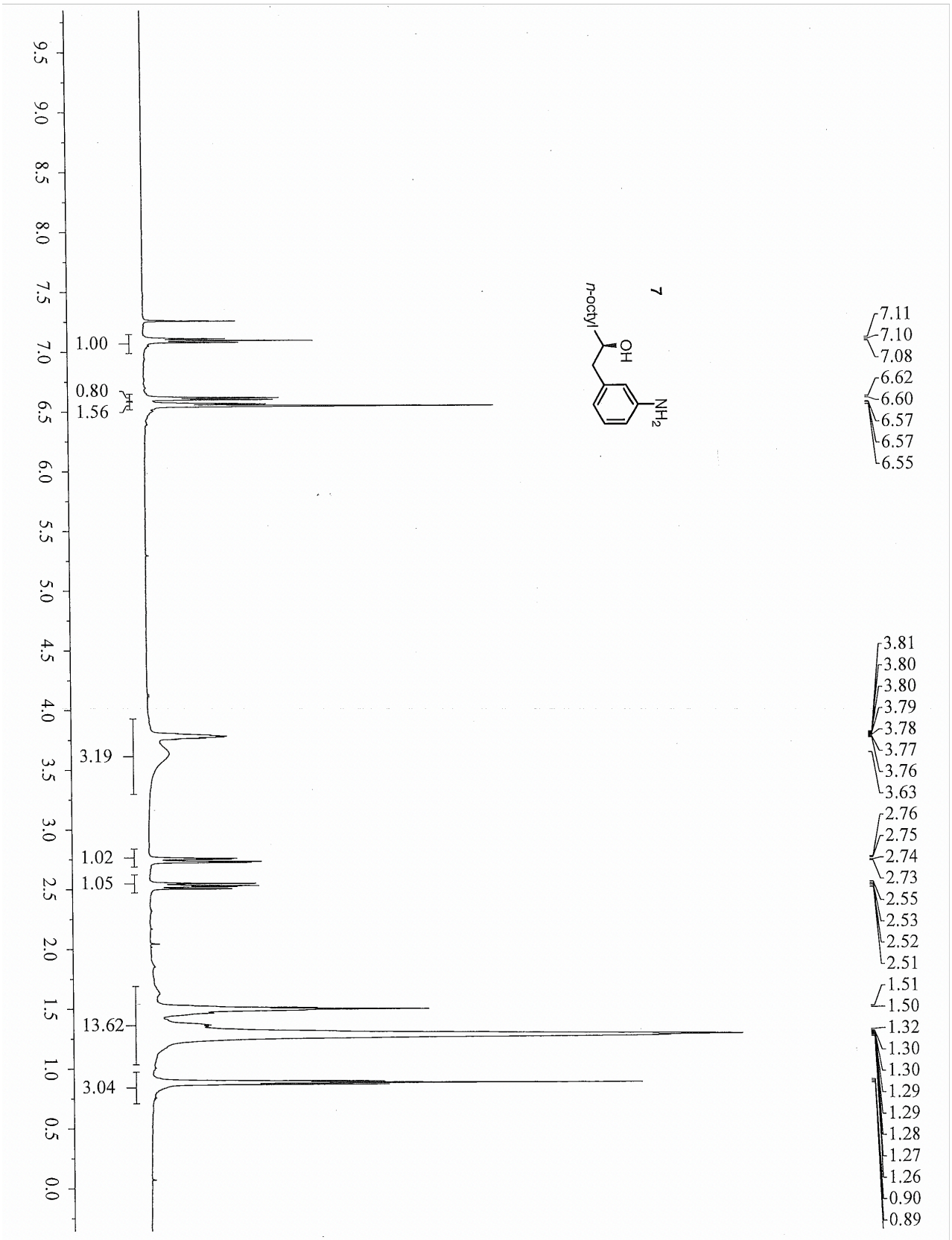
29.73
29.41
25.98
22.81
14.25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n-octyl
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7.10
7.08
6.62
6.60
6.57
6.57
6.55
3.81
3.80
3.80
3.79
3.78
3.77
3.76
3.63
2.76
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2.52
2.51
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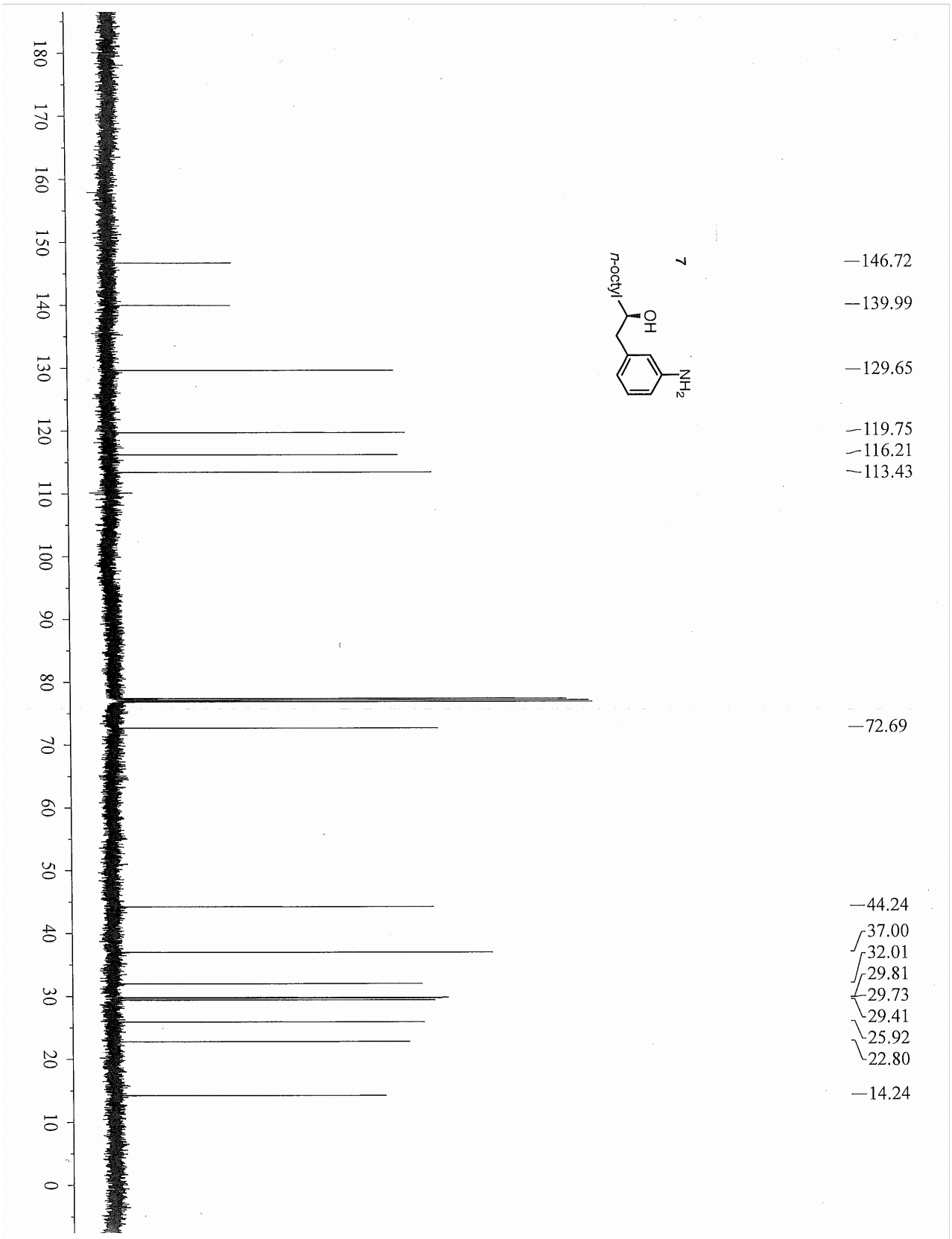
0.89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32.01
29.81
29.73
29.41
25.92
22.80
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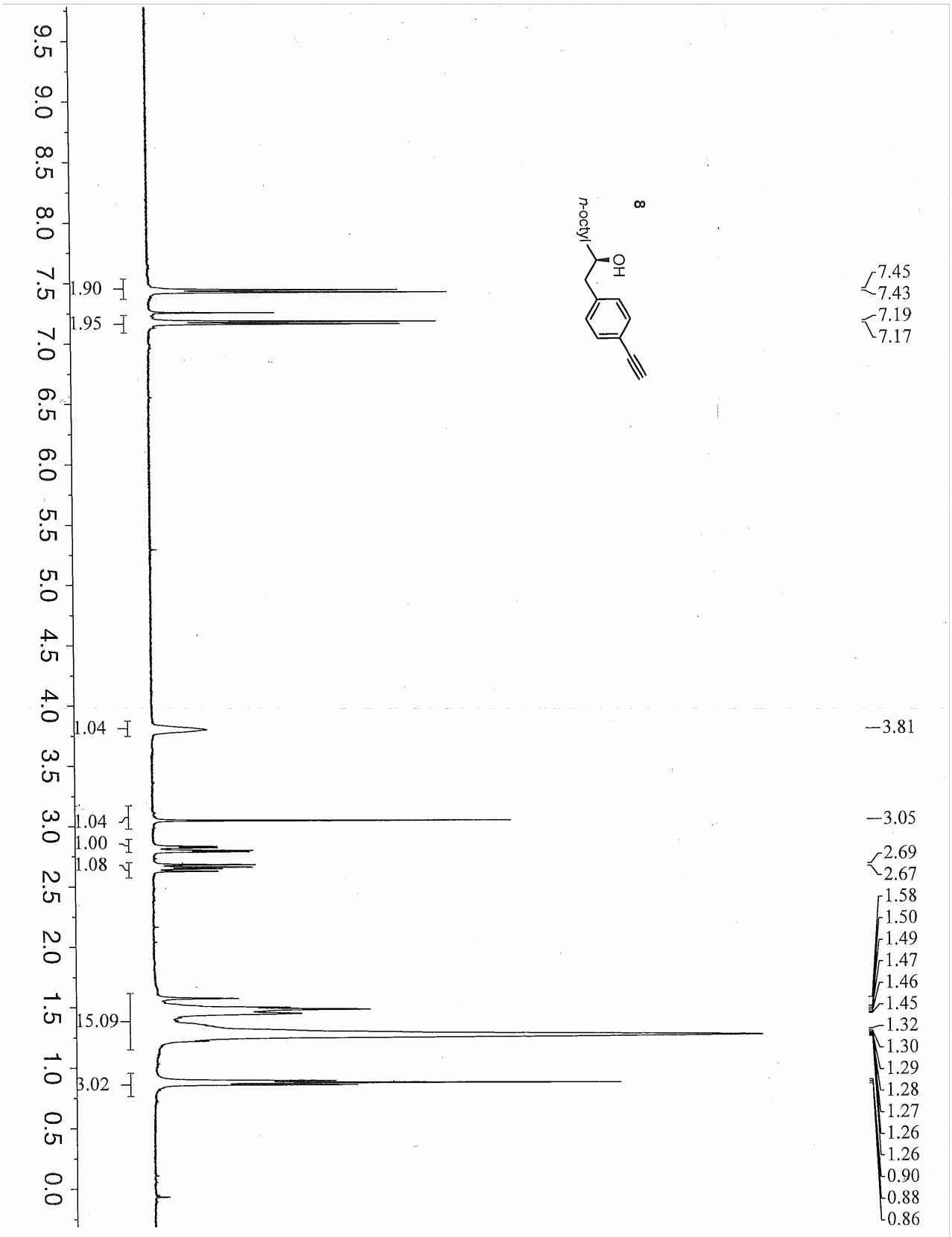
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n-octyl
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1.90
1.95
1.04
1.04
1.00
1.08
15.09
3.02
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7.43
7.19
7.17
3.81
3.05
2.69
2.67
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1.50
1.49
1.47
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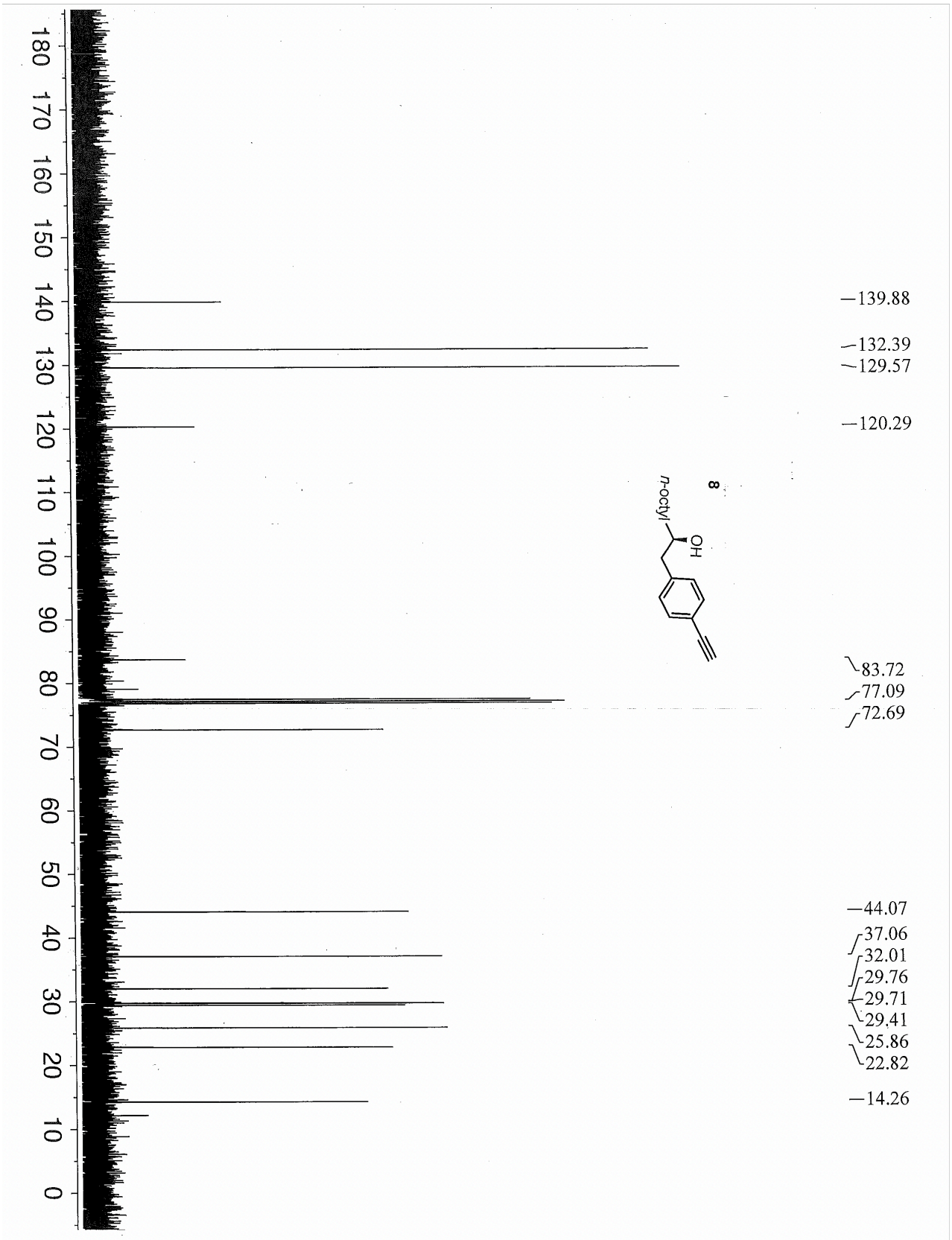
0.86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70
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0
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132.39
129.57
120.29
83.72
77.09
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22.82
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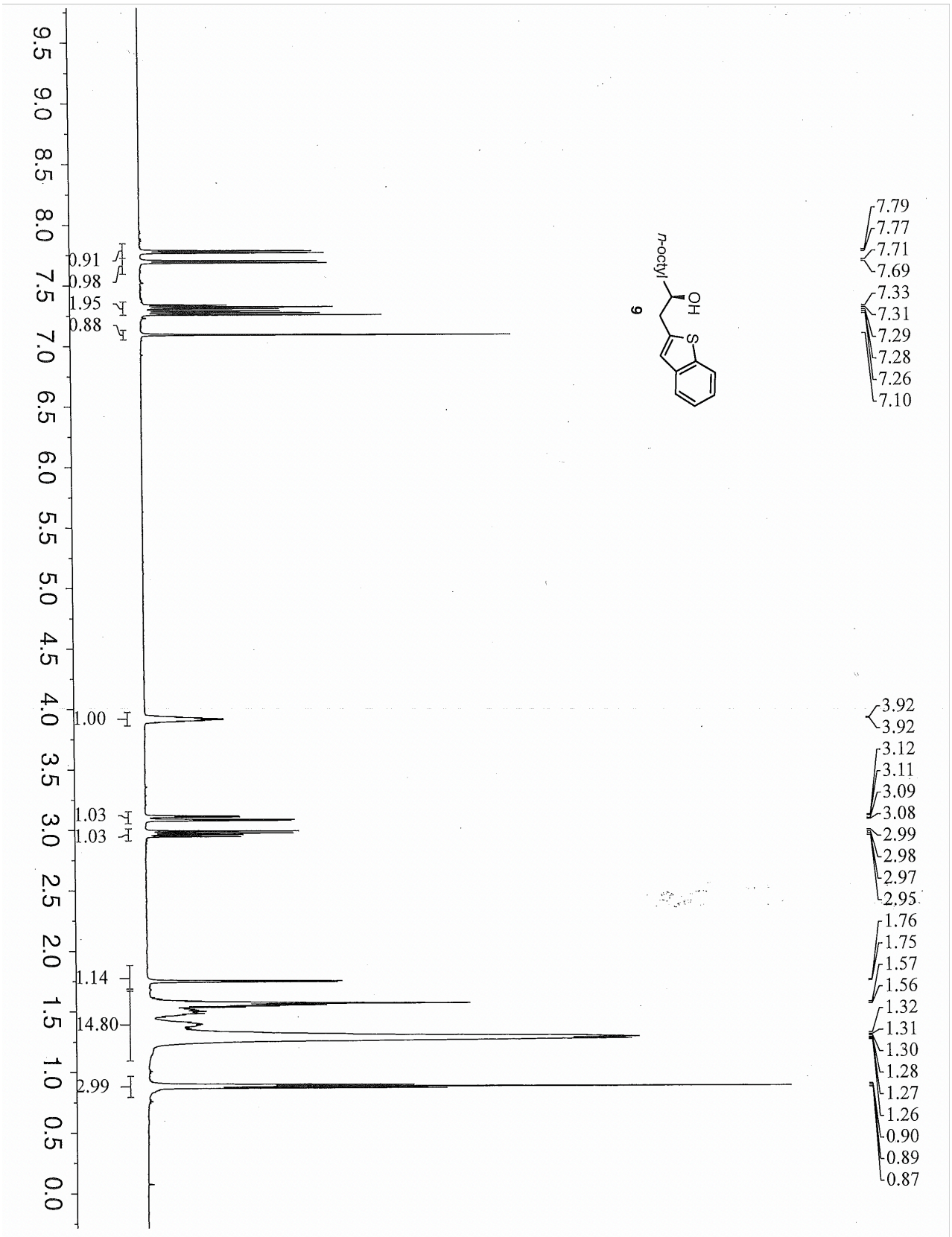
8
n-octyl
OH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0.98
1.95
0.88
1.00
1.03
1.03
1.14
14.80
2.99
n-octyl
OH
S
9
7.79
7.77
7.71
7.69
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7.31
7.29
7.28
7.26
7.10
3.92
3.92
3.12
3.11
3.09
3.08
2.99
2.98
2.97
2.95
1.76
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1.27
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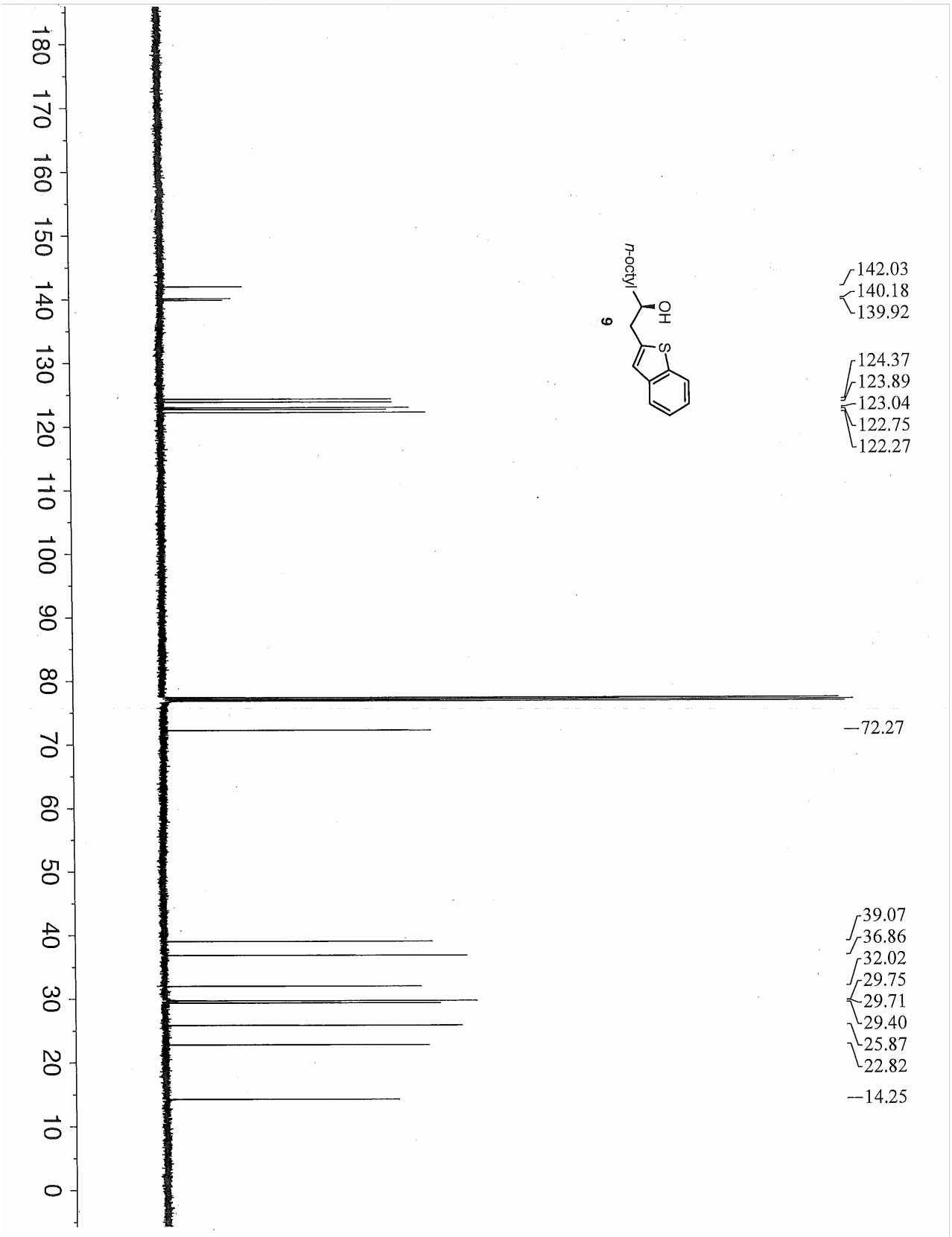
0.87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72.27
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36.86
32.02
29.75
29.71
29.40
25.87
22.82
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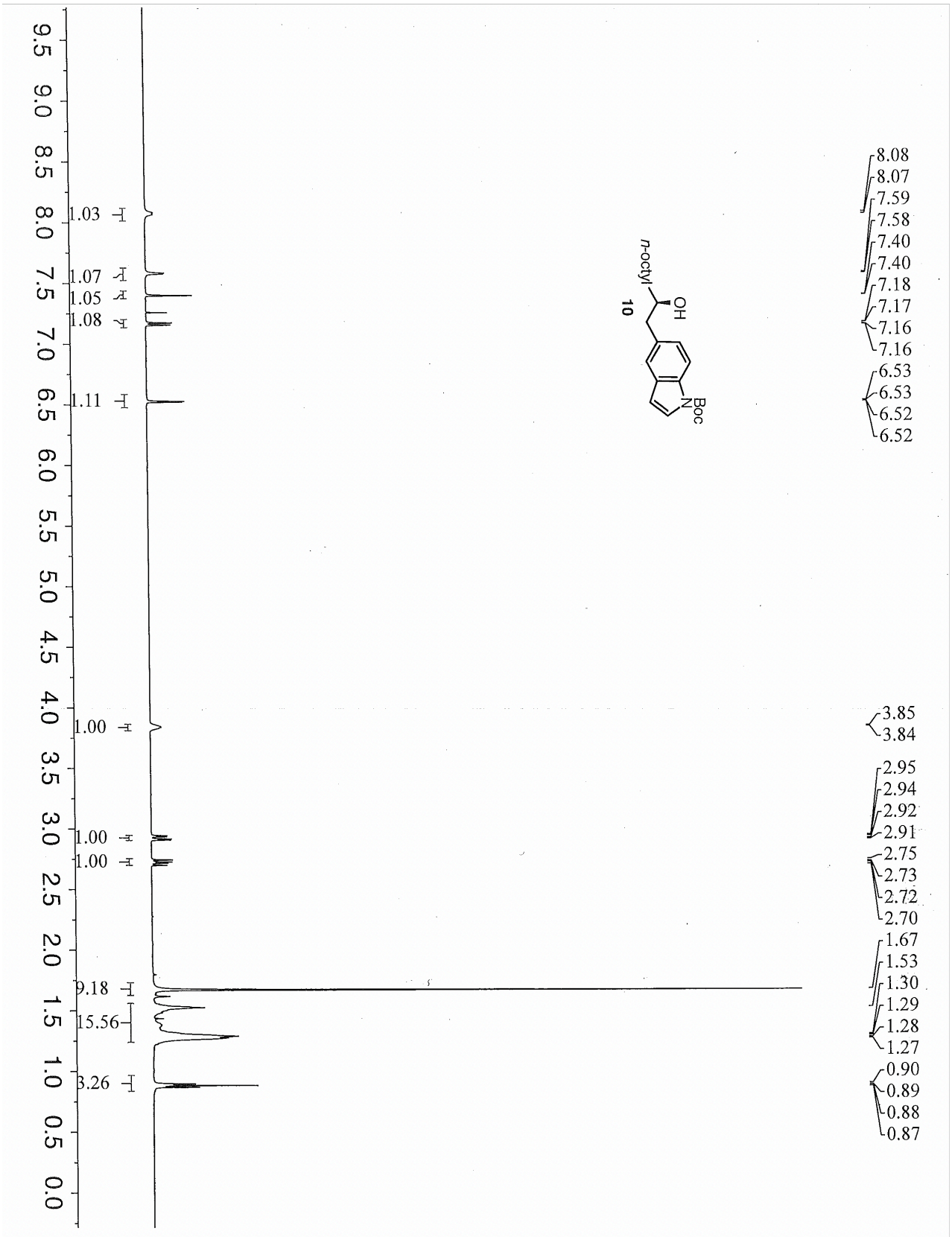
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1.03
1.07
1.05
1.08
1.11
1.00
1.00
1.00
9.18
15.56
3.26
n-octyl
OH
10
Boc
N
8.08
8.07
7.59
7.58
7.40
7.40
7.18
7.17
7.16
7.16
6.53
6.53
6.52
6.52
3.85
3.84
2.95
2.94
2.92
2.91
2.75
2.73
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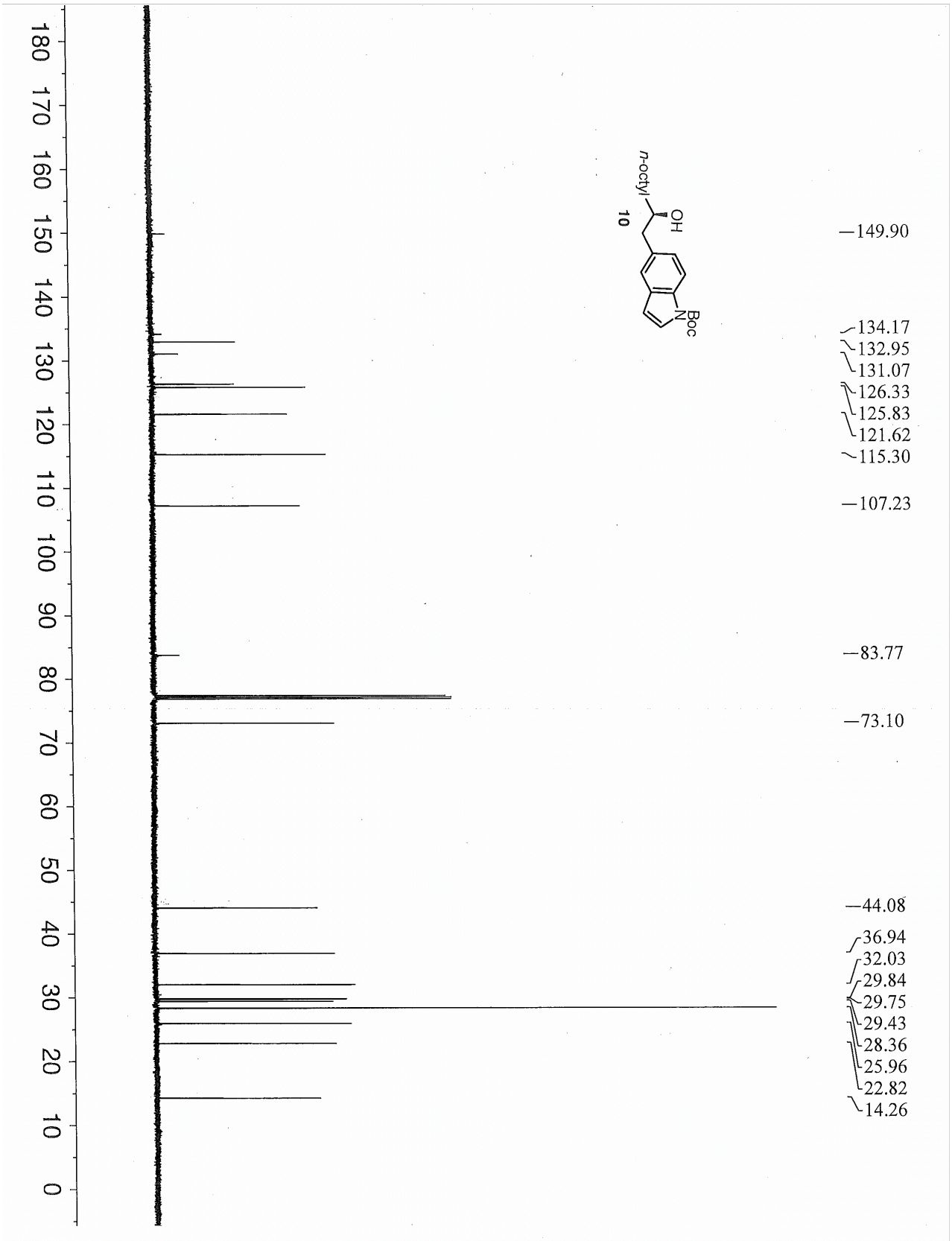
0.87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Boc
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73.10
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36.94
32.03
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29.75
29.43
28.36
25.96
22.82
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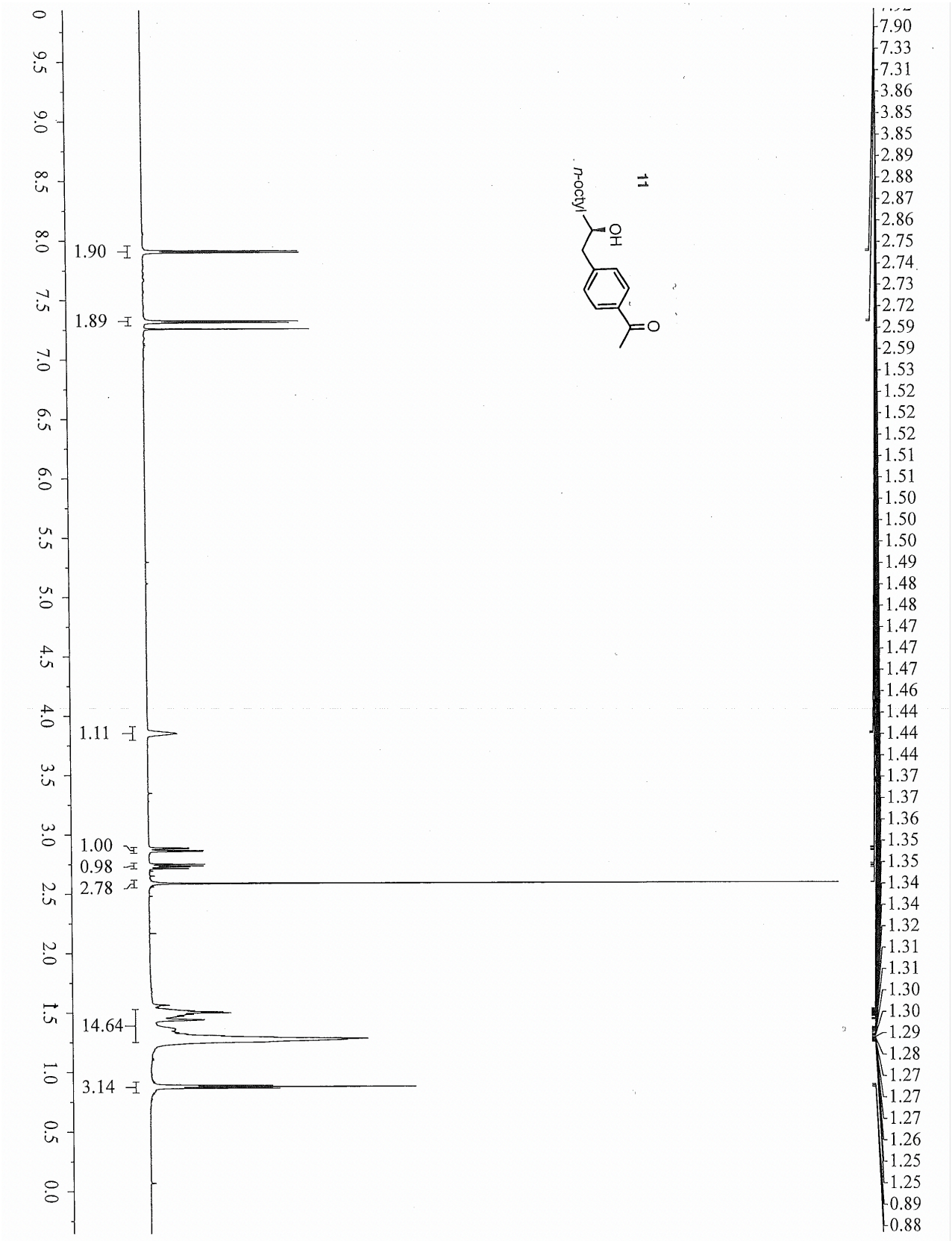
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O
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1.11
1.00
0.98
2.78
14.64
3.14
0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
7.90
7.33
7.31
3.86
3.85
3.85
2.89
2.88
2.87
2.86
2.75
2.74
2.73
2.72
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2.59
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1.52
1.52
1.51
1.51
1.50
1.50
1.50
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1.48
1.47
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1.31
1.31
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1.29
1.28
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1.27
1.27
1.26
1.25
1.25
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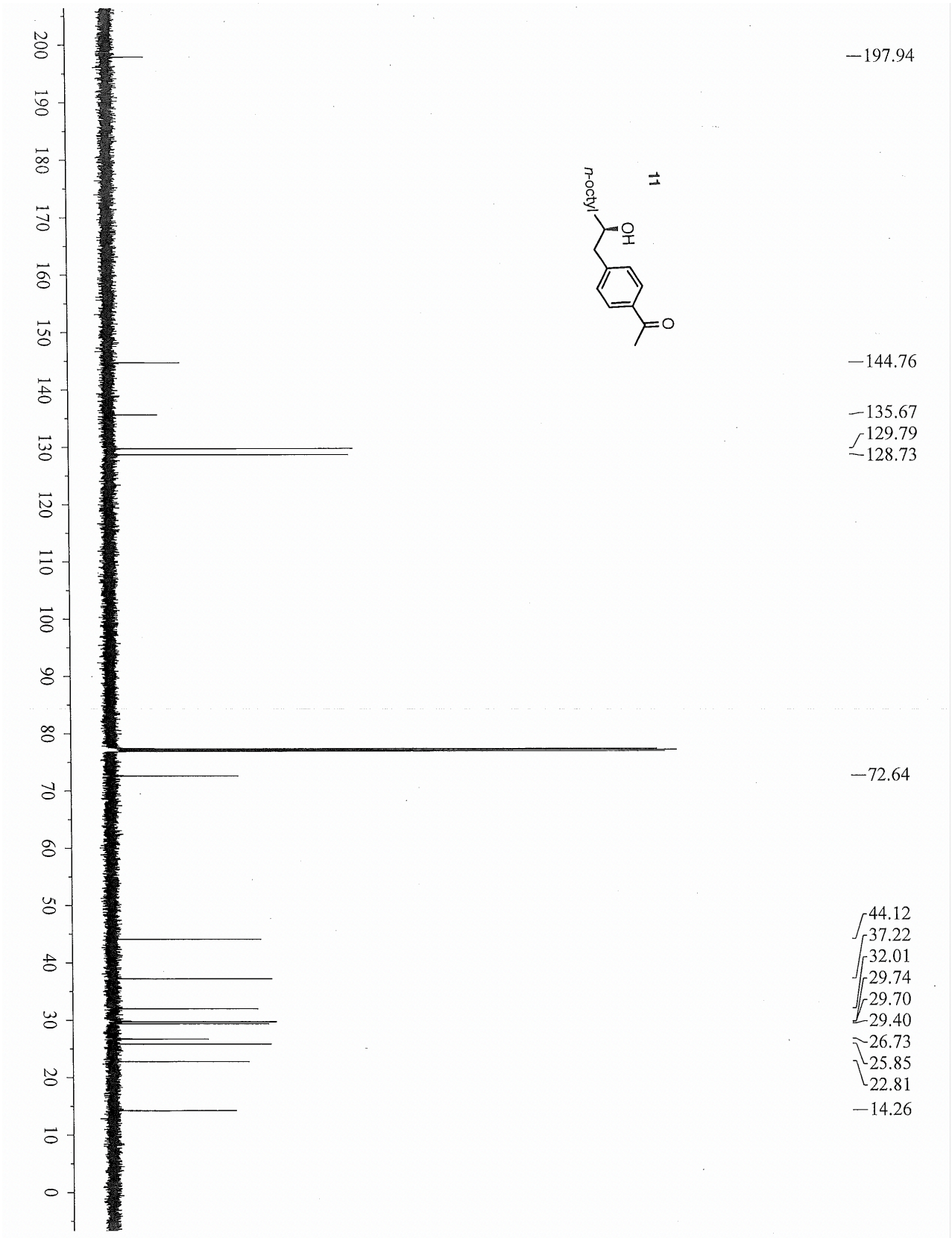
0.88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29.74
29.70
29.40
26.73
25.85
22.81
14.26
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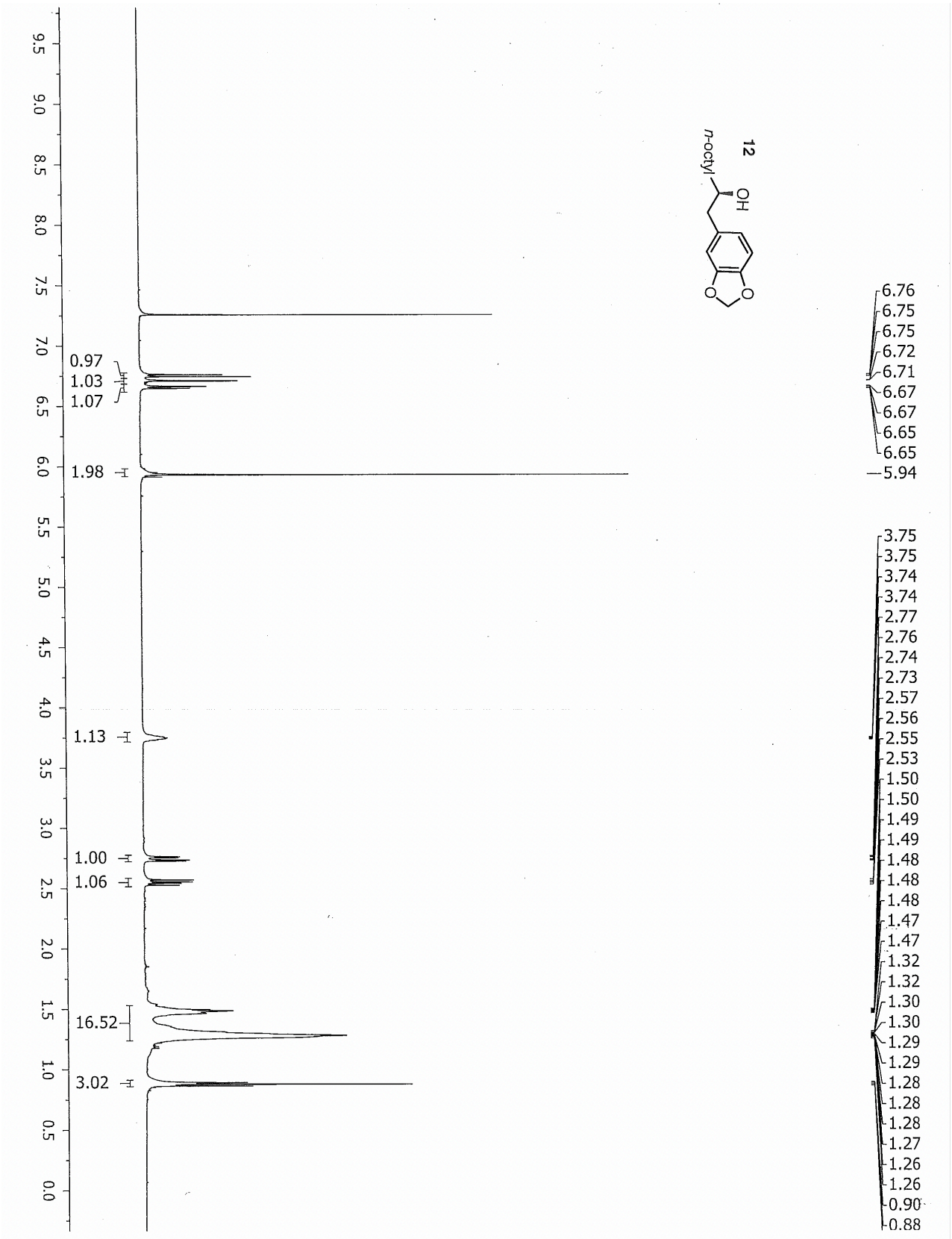
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O
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8.0
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.97
1.03
1.07
1.98
1.13
1.00
1.06
16.52
3.02
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6.75
6.75
6.72
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5.94
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3.75
3.74
3.74
2.77
2.76
2.74
2.73
2.57
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2.53
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1.27
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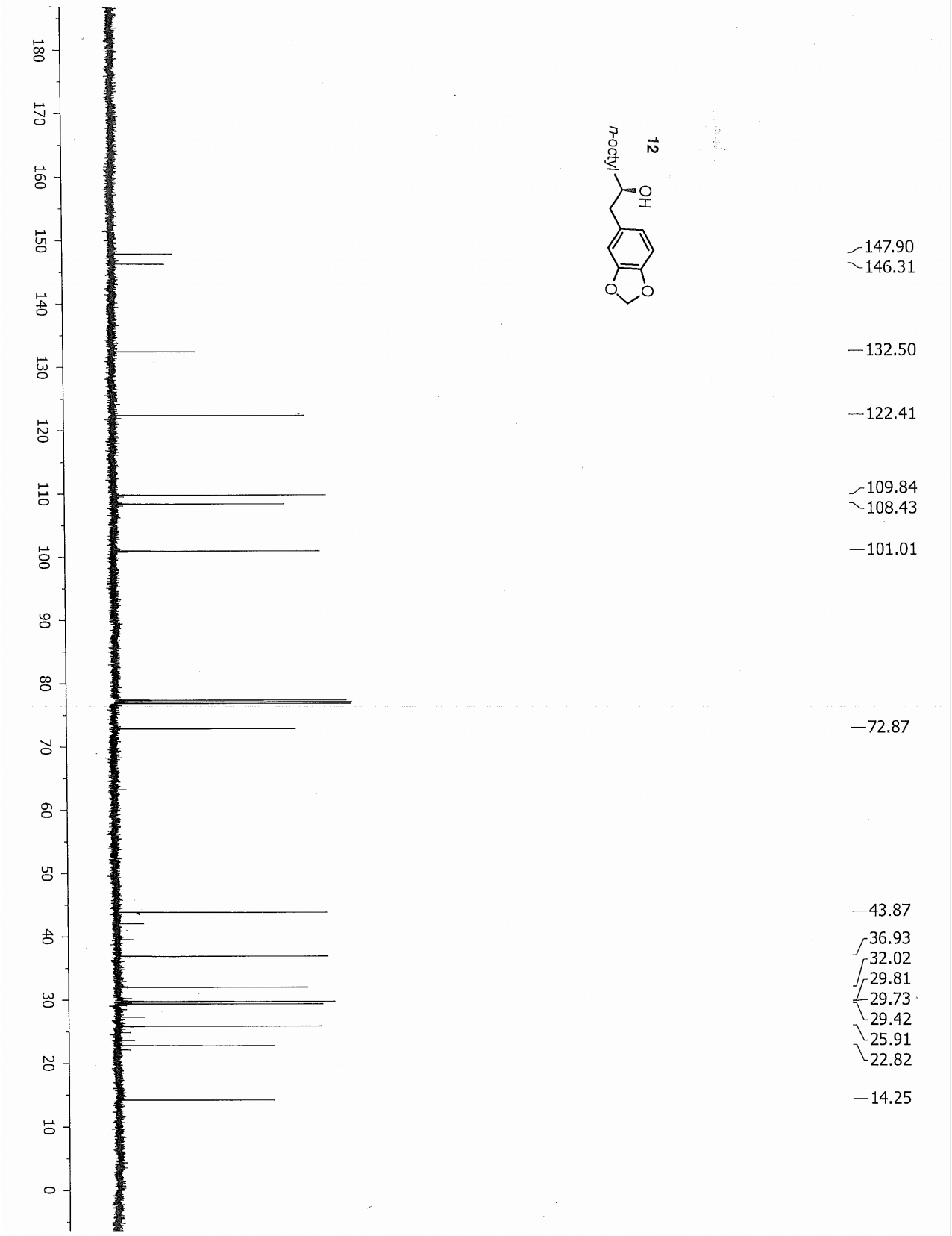
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O
O
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43.87
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32.02
29.81
29.73
29.42
25.91
22.82
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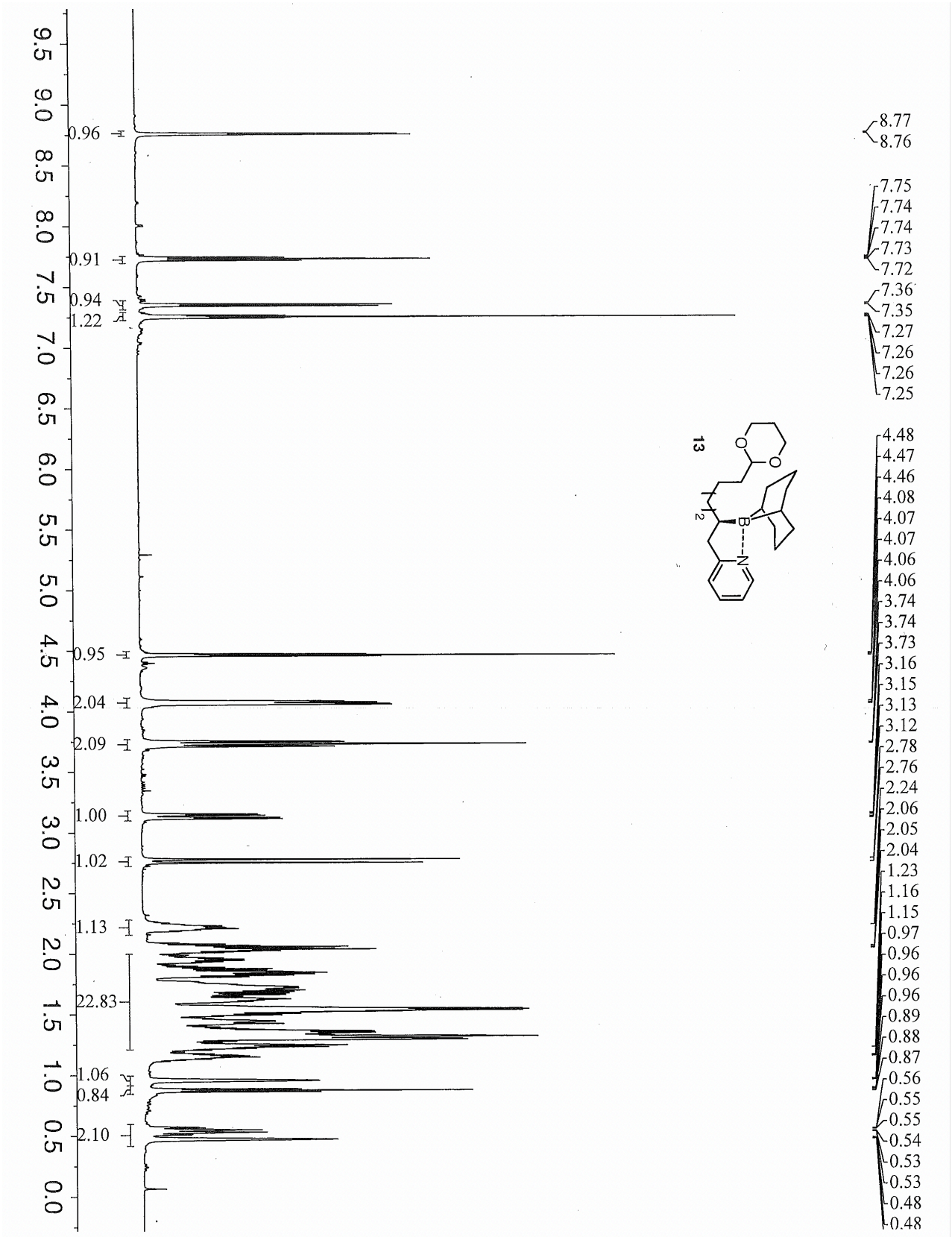
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0.96
0.91
0.94
1.22
0.95
2.04
2.09
1.00
1.02
1.13
22.83
1.06
0.84
2.10
13
8.77
8.76
7.75
7.74
7.74
7.73
7.72
7.36
7.35
7.27
7.26
7.26
7.25
4.48
4.47
4.46
4.08
4.07
4.07
4.06
4.06
3.74
3.74
3.73
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3.13
3.12
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2.76
2.24
2.06
2.05
2.04
1.23
1.16
1.15
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0.96
0.96
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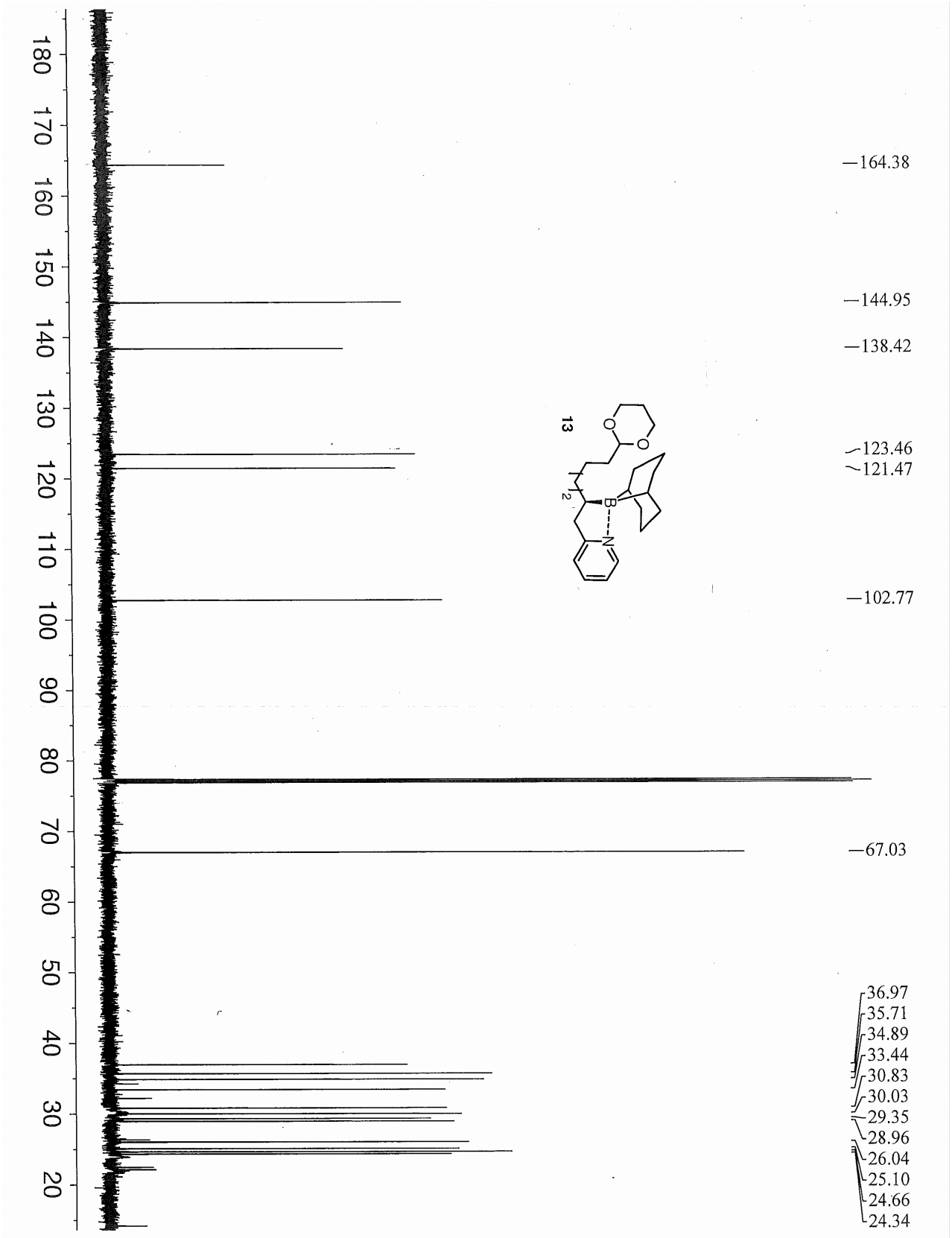
0.48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140
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120
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100
90
80
70
60
50
40
30
20
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144.95
138.42
123.46
121.47
102.77
67.03
36.97
35.71
34.89
33.44
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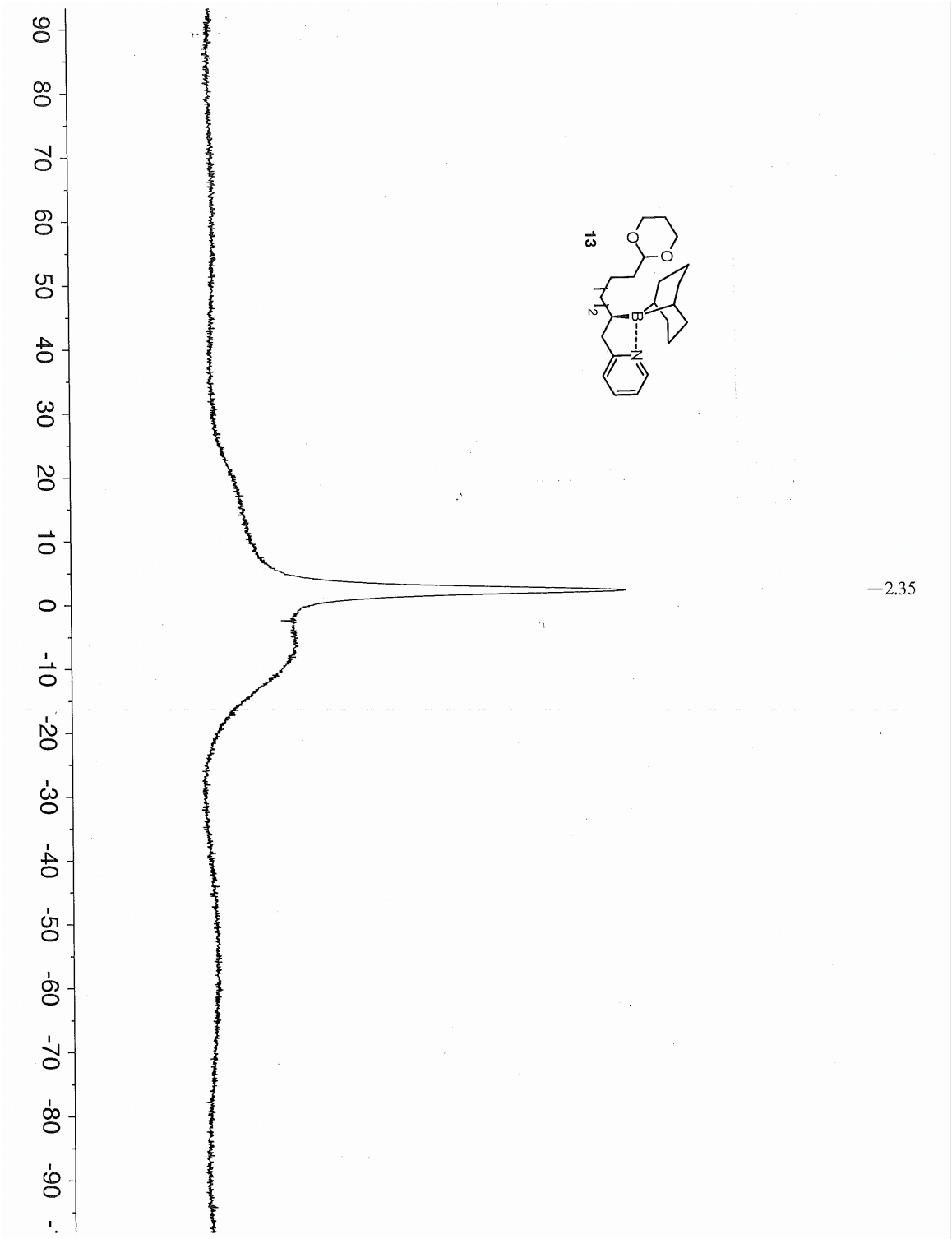
28.96
26.04
25.10
24.66
24.34
13
O
O
B
N

^{11}B NMR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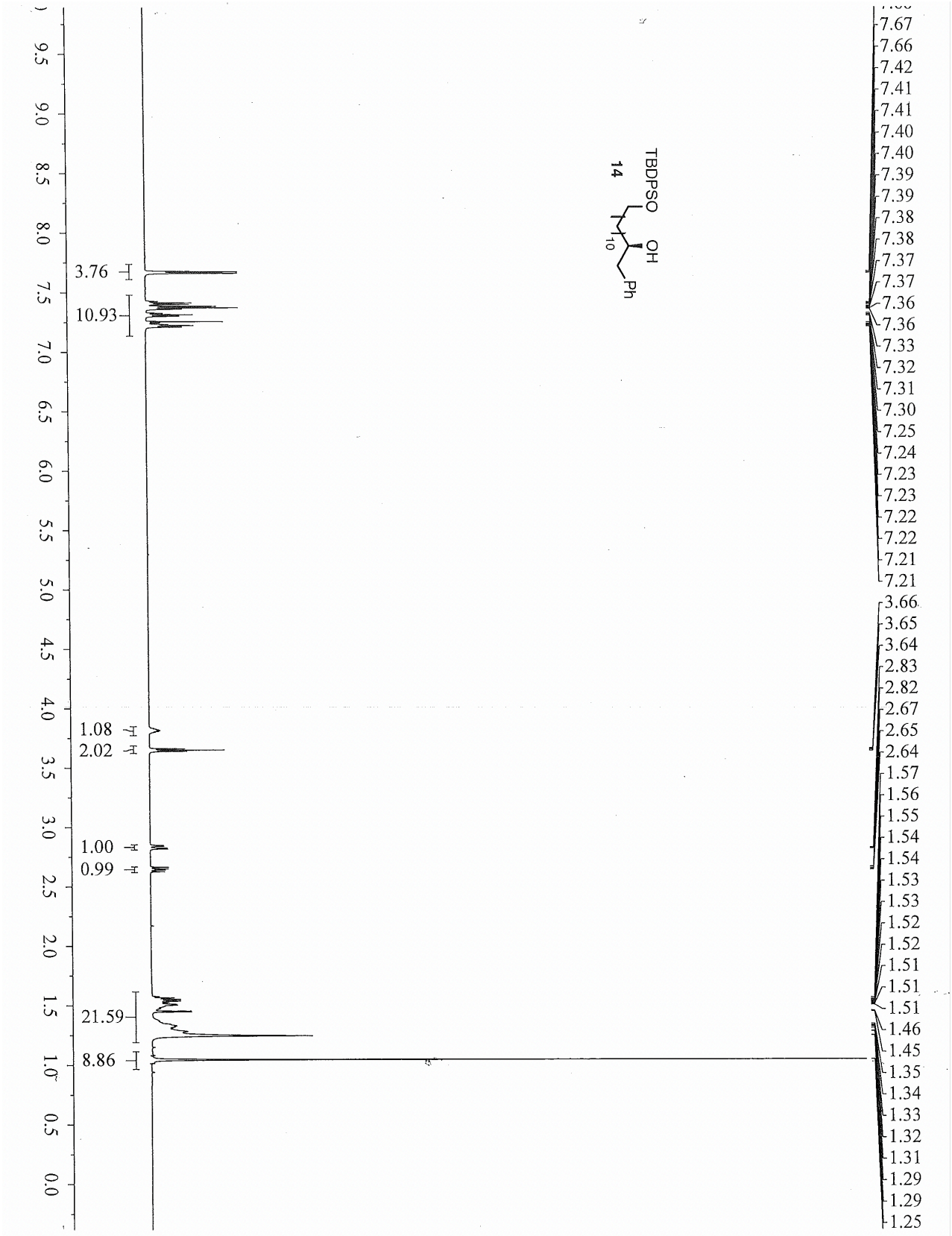
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
13
B
N
2
—2.35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OH
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7.67
7.66
7.42
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7.41
7.40
7.40
7.39
7.39
7.38
7.38
7.37
7.37
7.36
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7.33
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
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1.55
1.54
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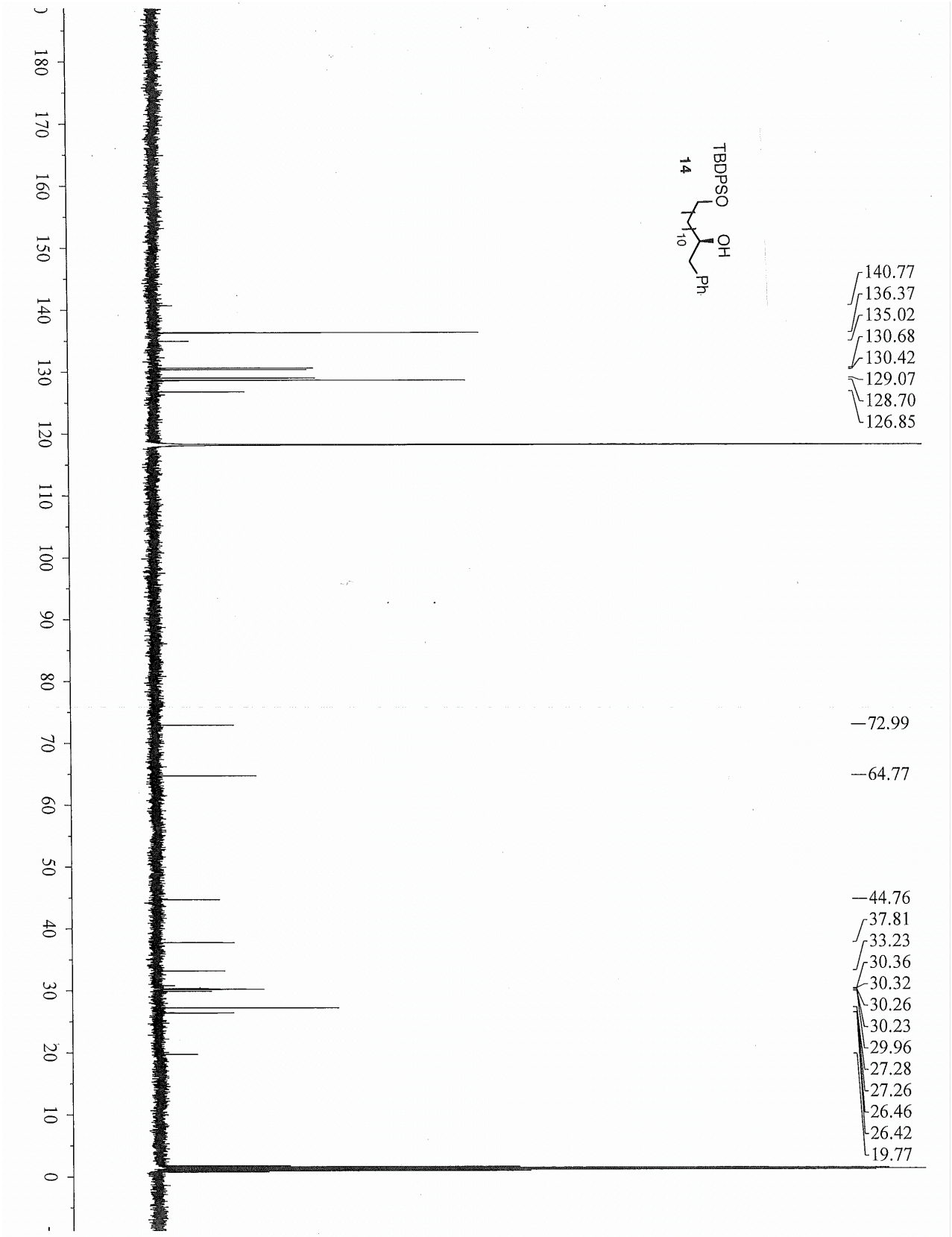
1.25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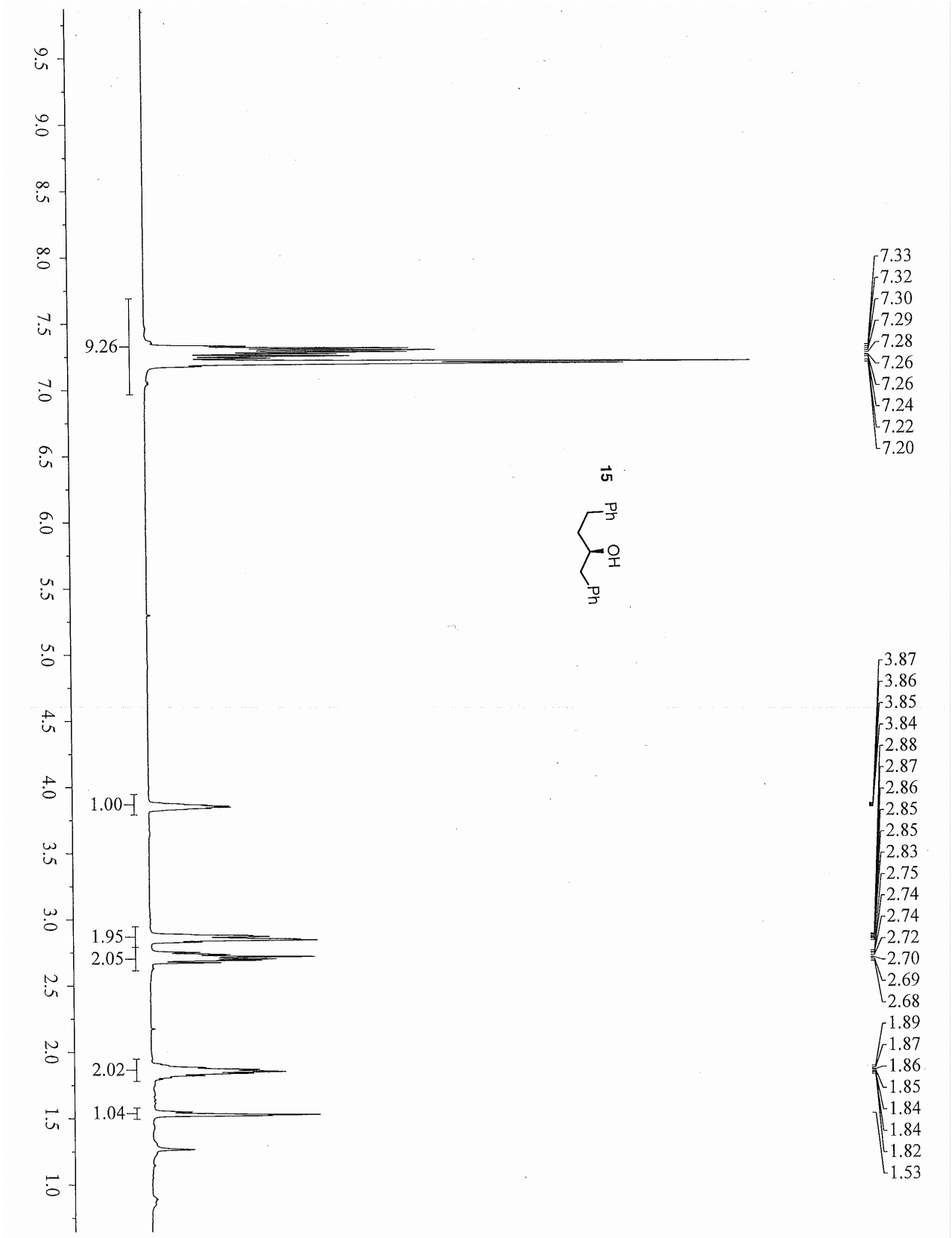
26.42
19.77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6.0
5.5
5.0
4.5
4.0
3.5
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2.5
2.0
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1.0
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2.05
2.02
1.04
7.33
7.32
7.30
7.29
7.28
7.26
7.26
7.24
7.22
7.20
15
Ph
OH
Ph
3.87
3.86
3.85
3.84
2.88
2.87
2.86
2.85
2.85
2.83
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1.85
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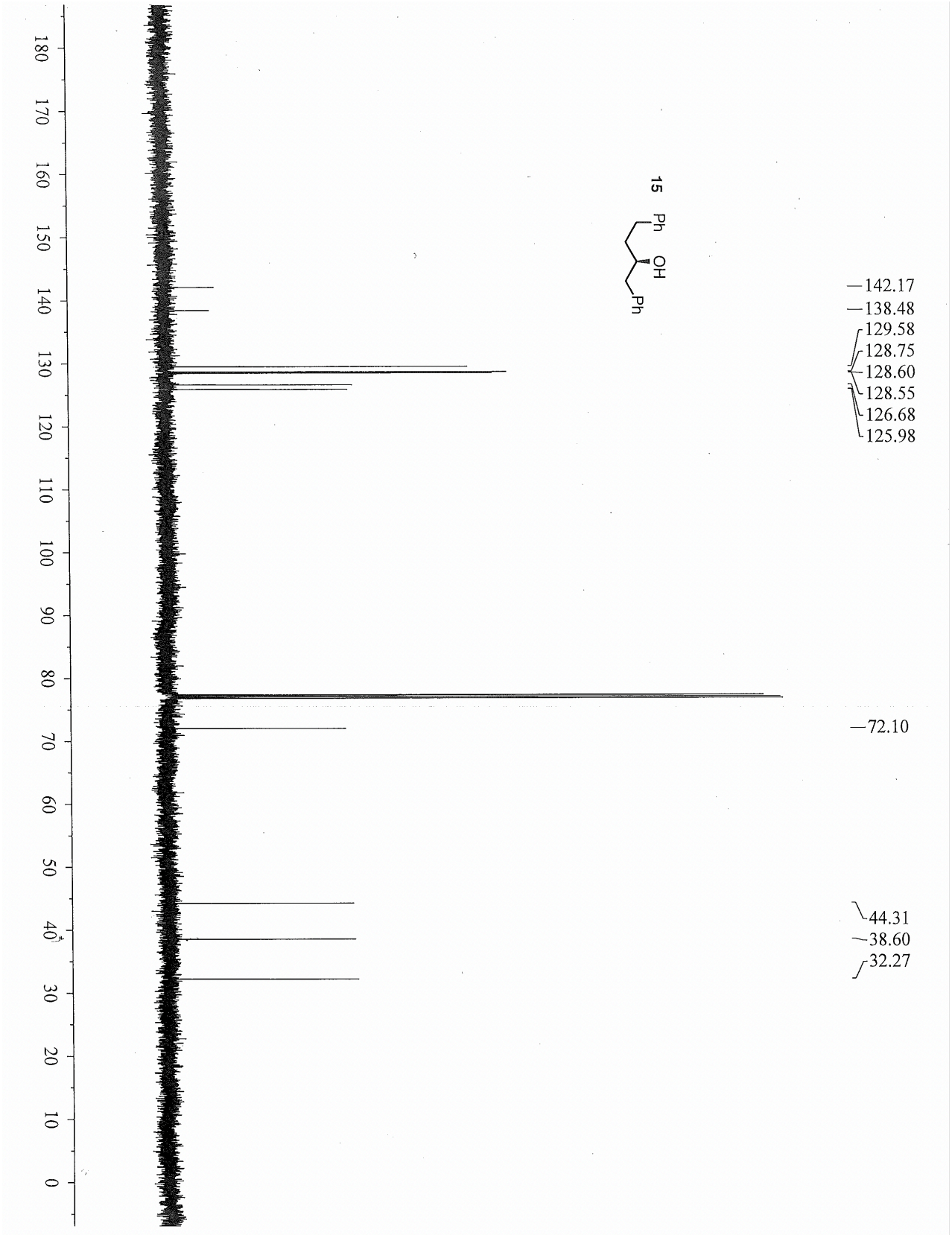
1.82
1.53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Ph
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Ph
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125.98
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38.60
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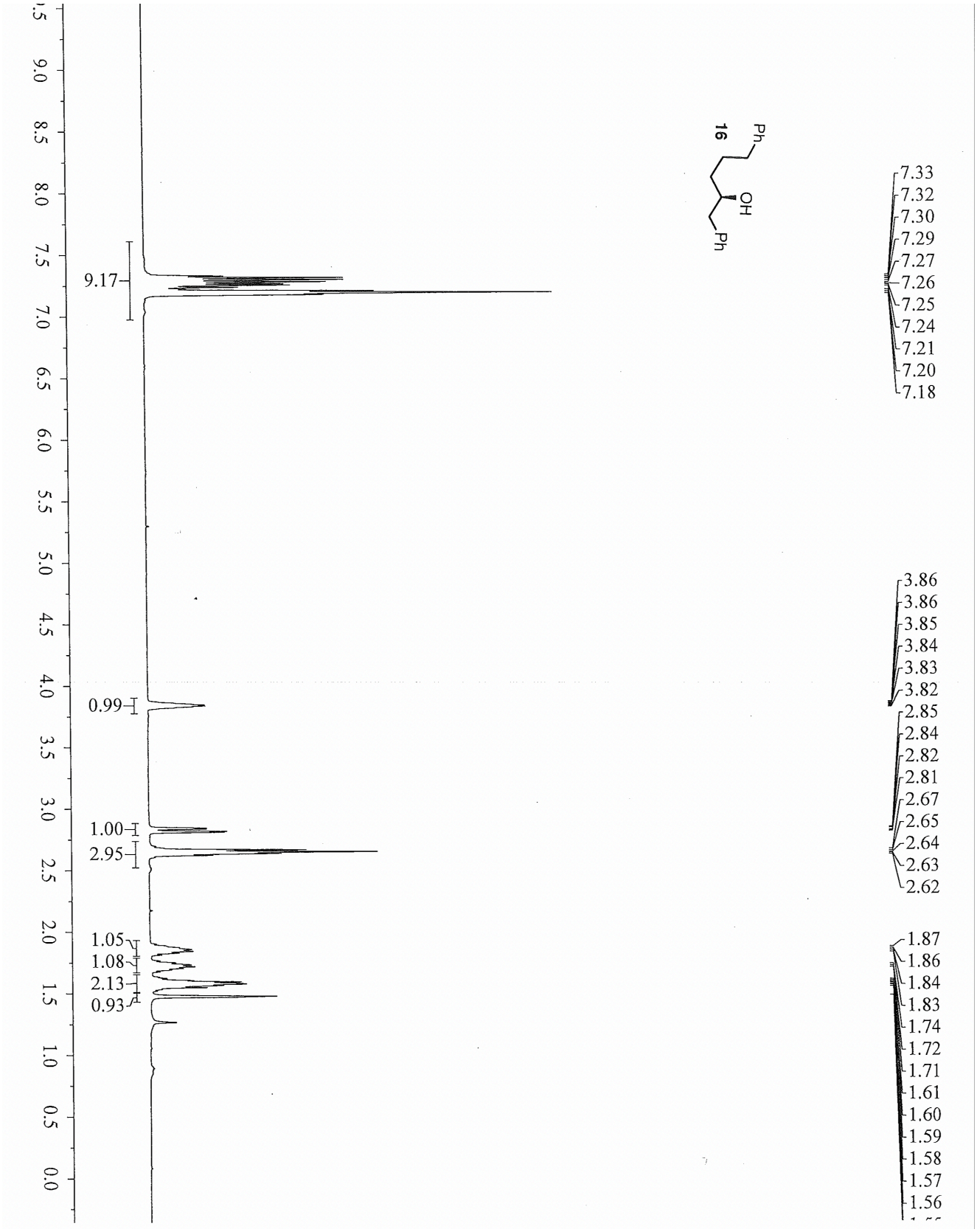
10
0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Ph
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Ph
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1.08
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7.29
7.27
7.26
7.25
7.24
7.21
7.20
7.18
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3.86
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2.62
1.87
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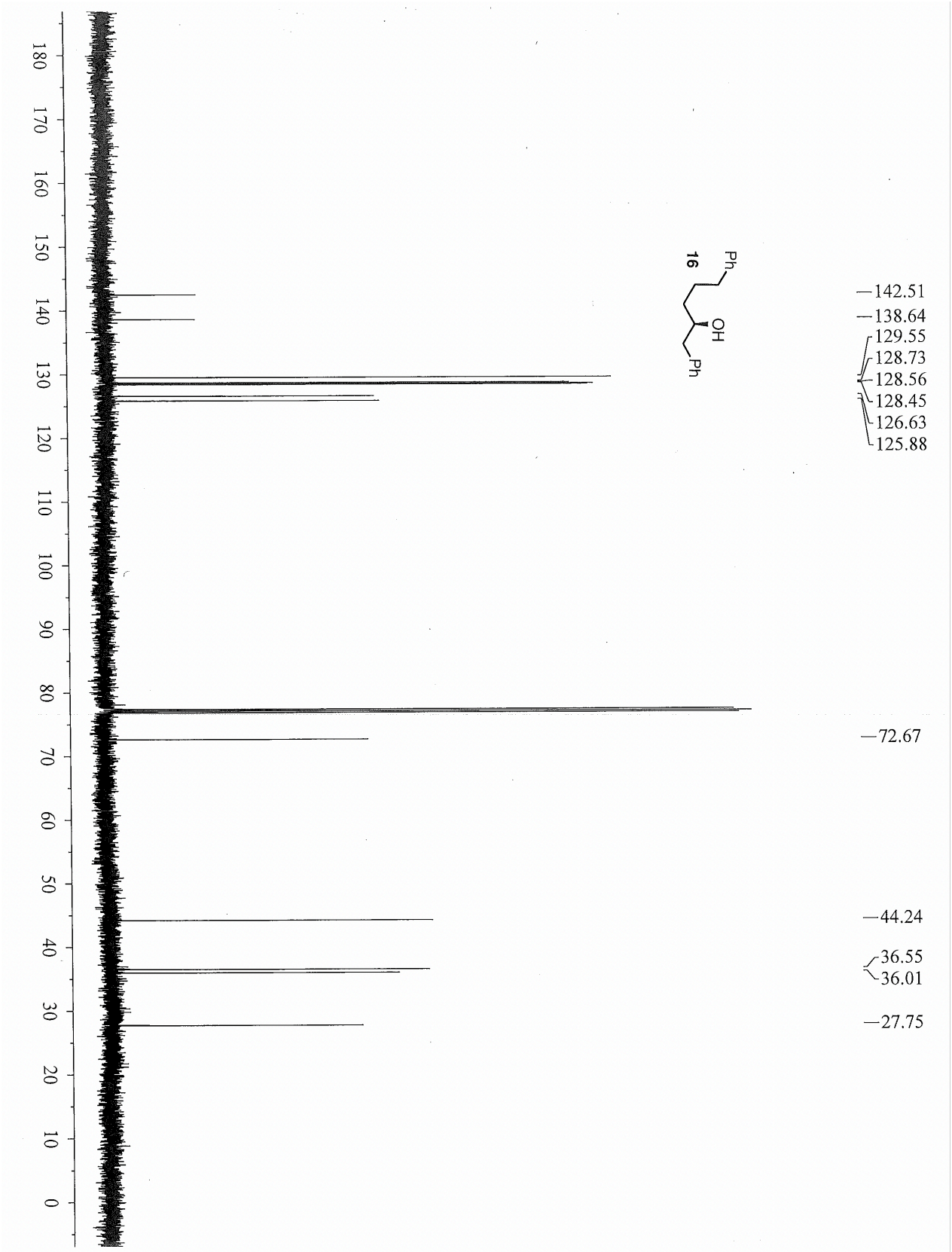
1.56


16
Ph
OH
Ph
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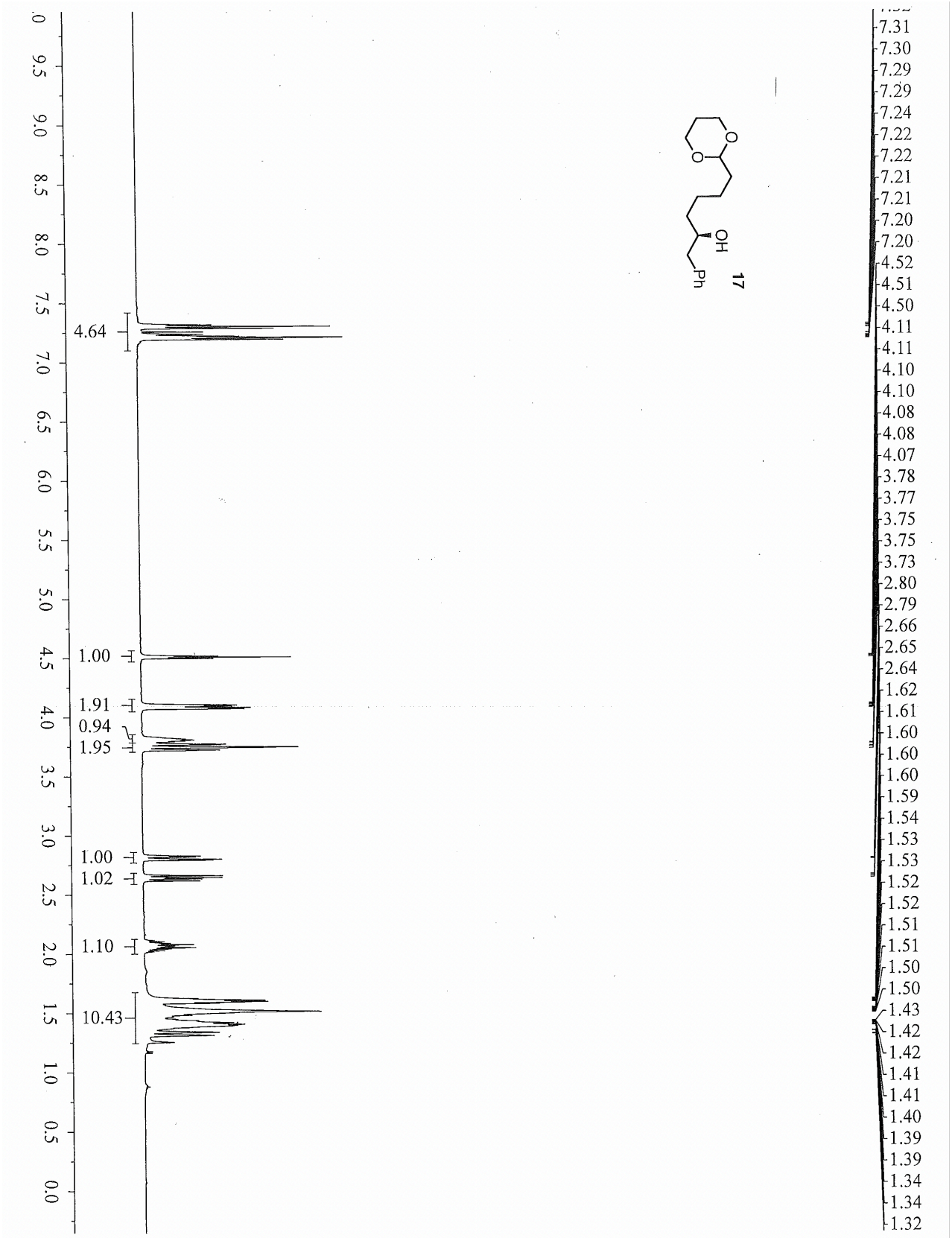
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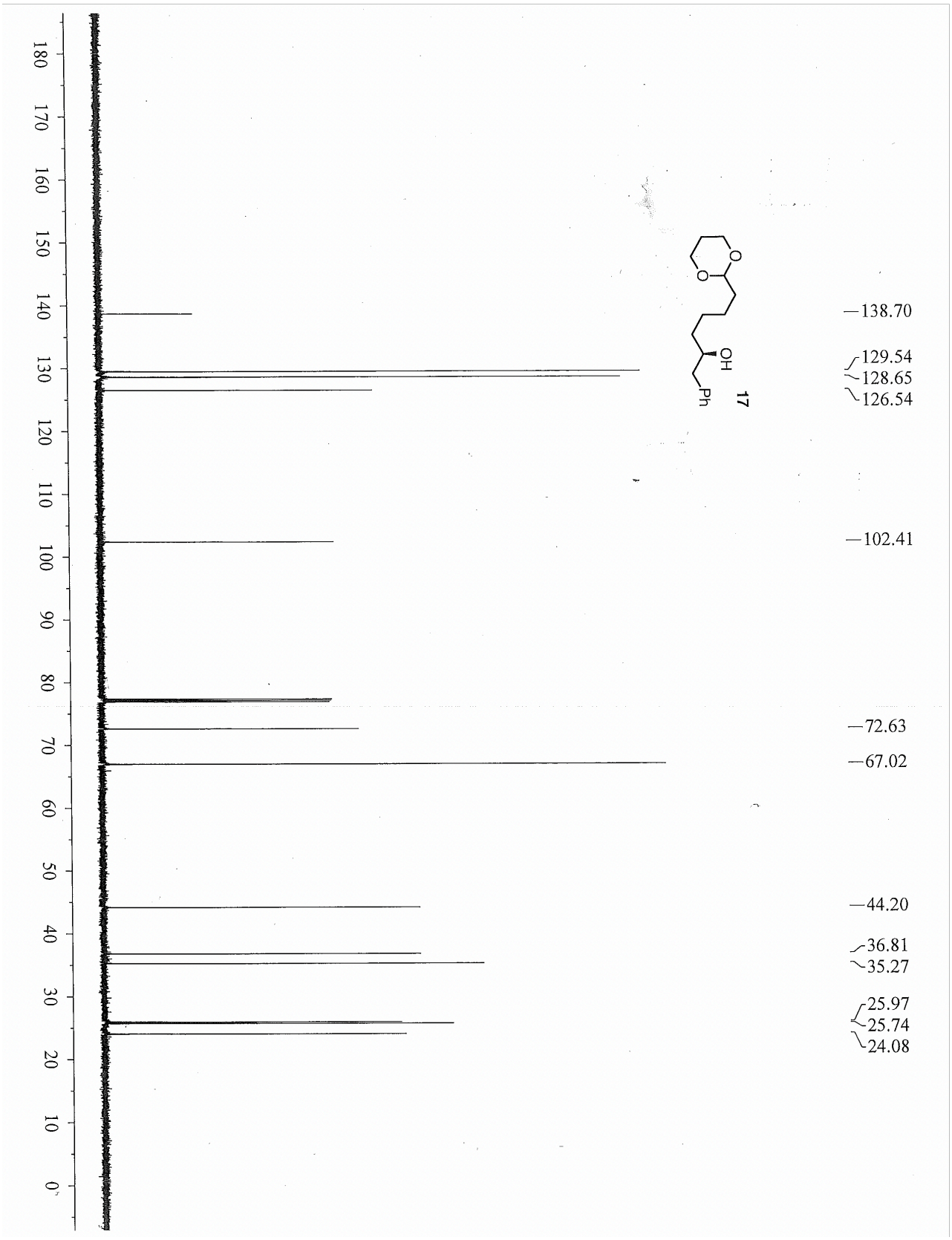
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O
OH
Ph
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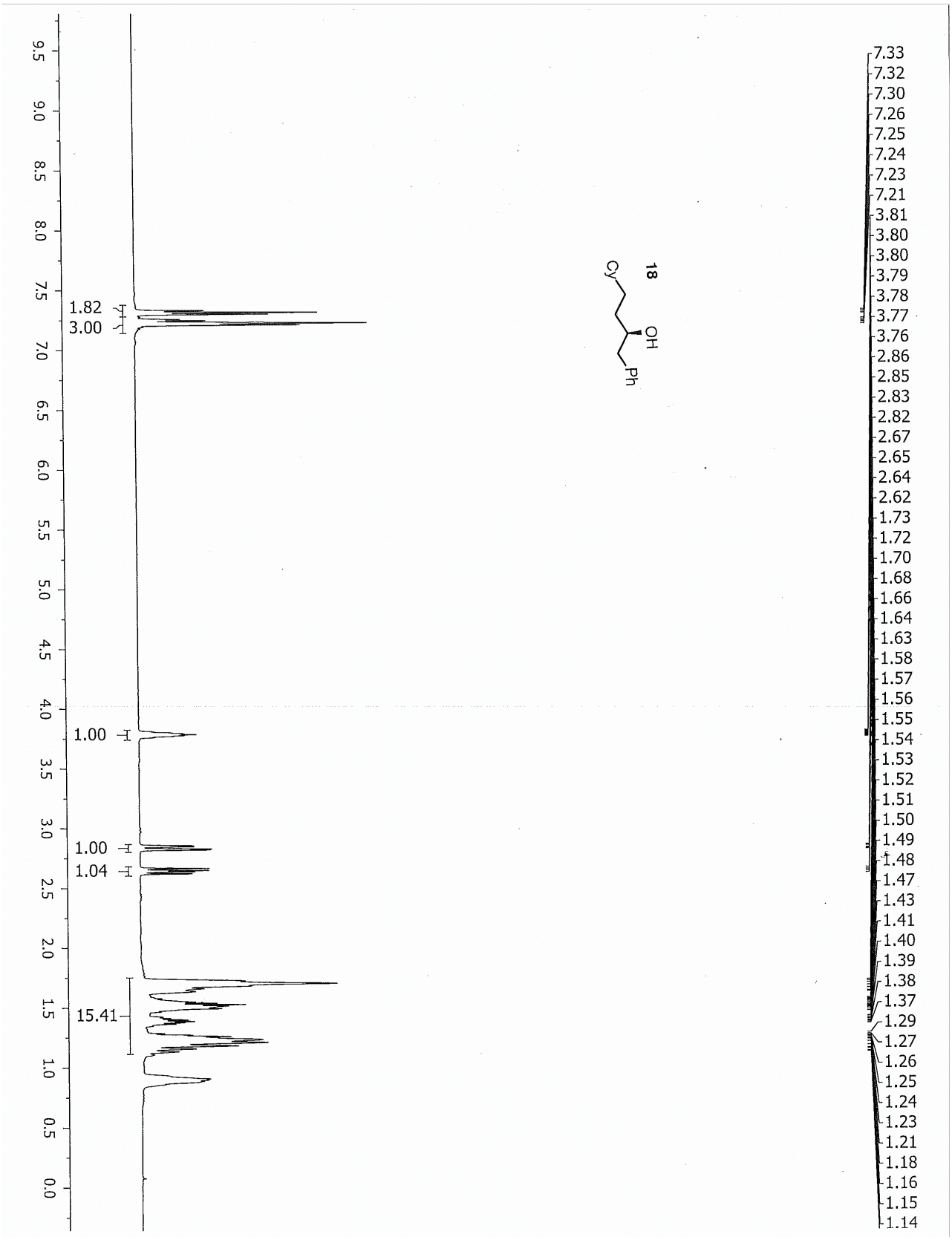
24.08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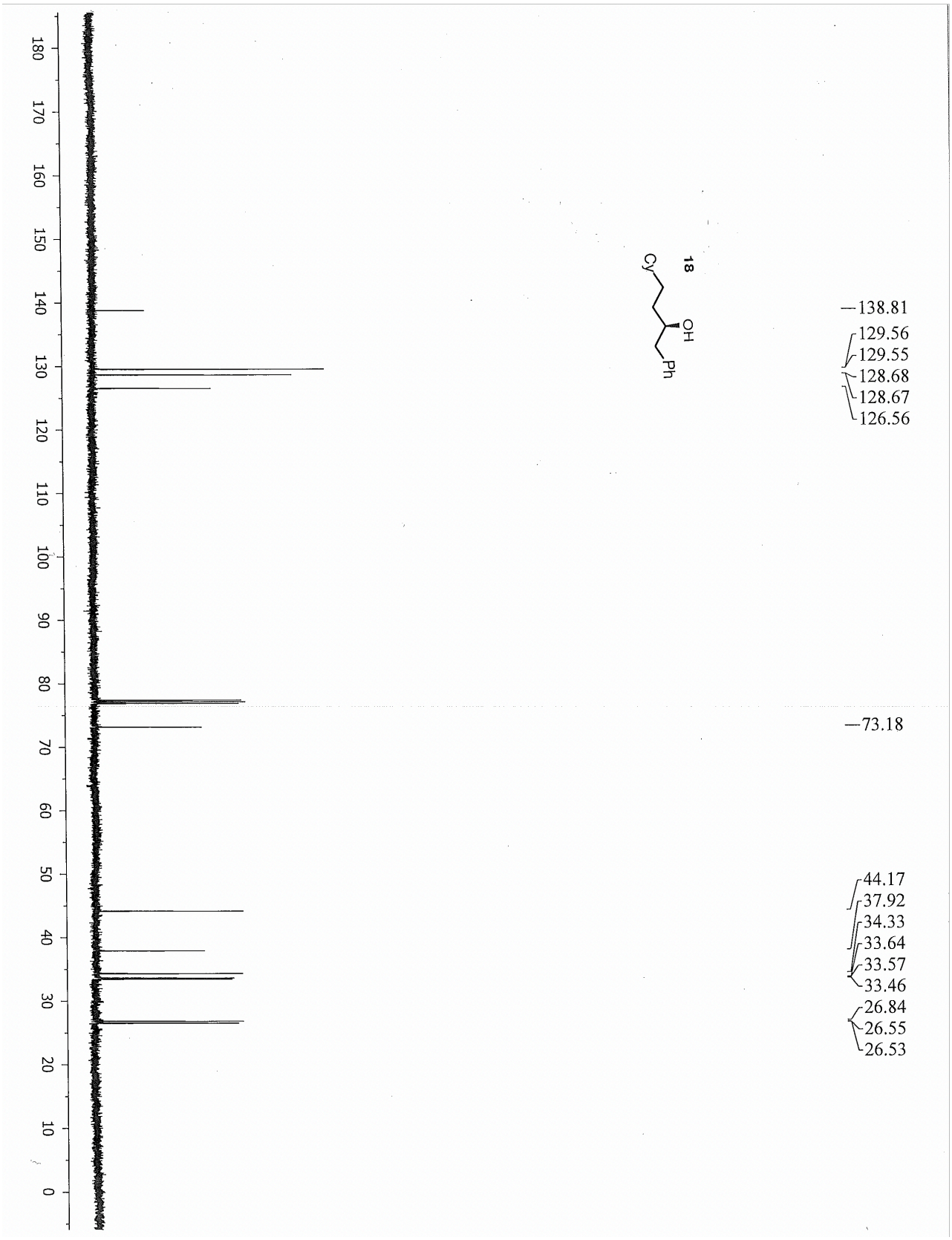
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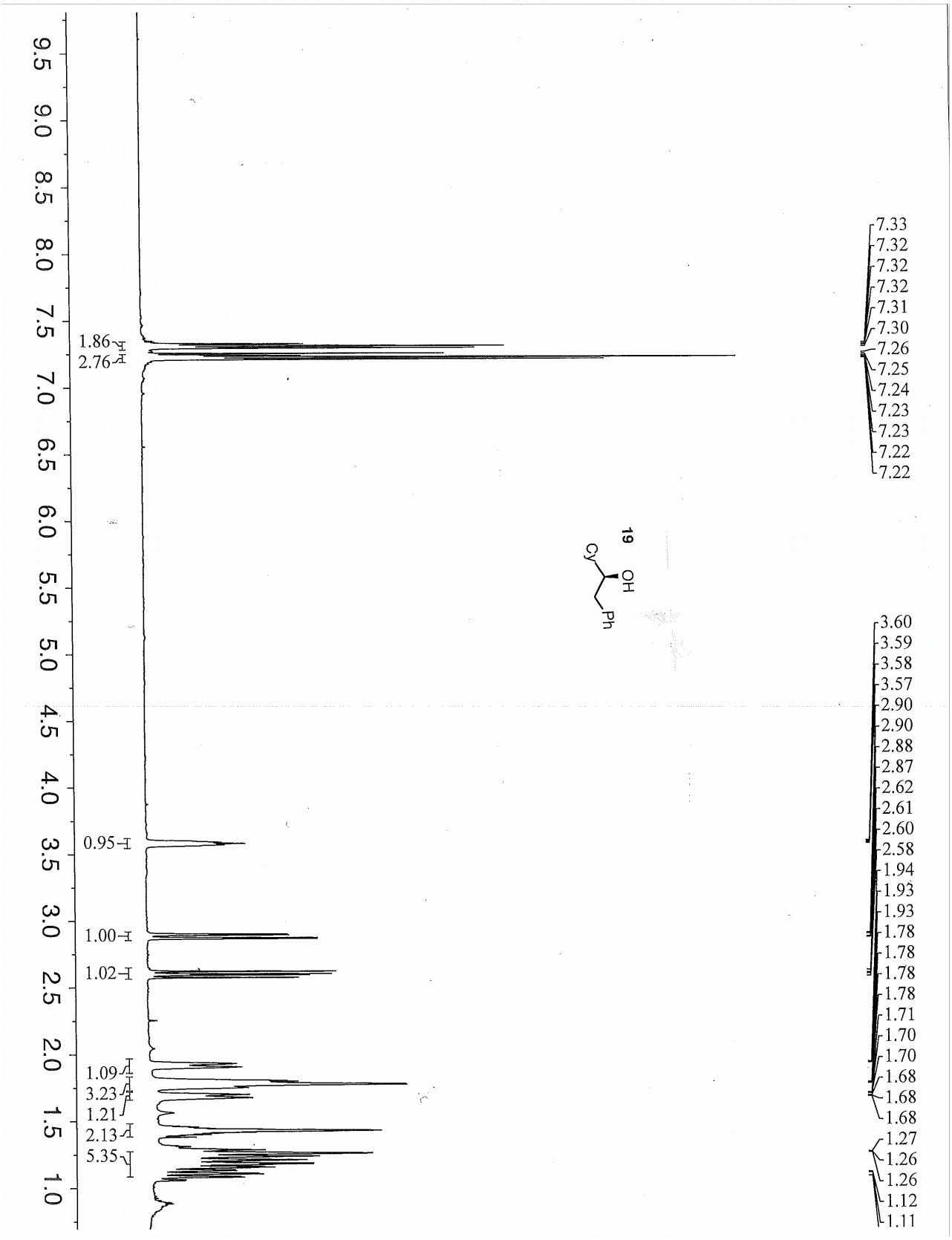
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5.35
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Cy
OH
Ph
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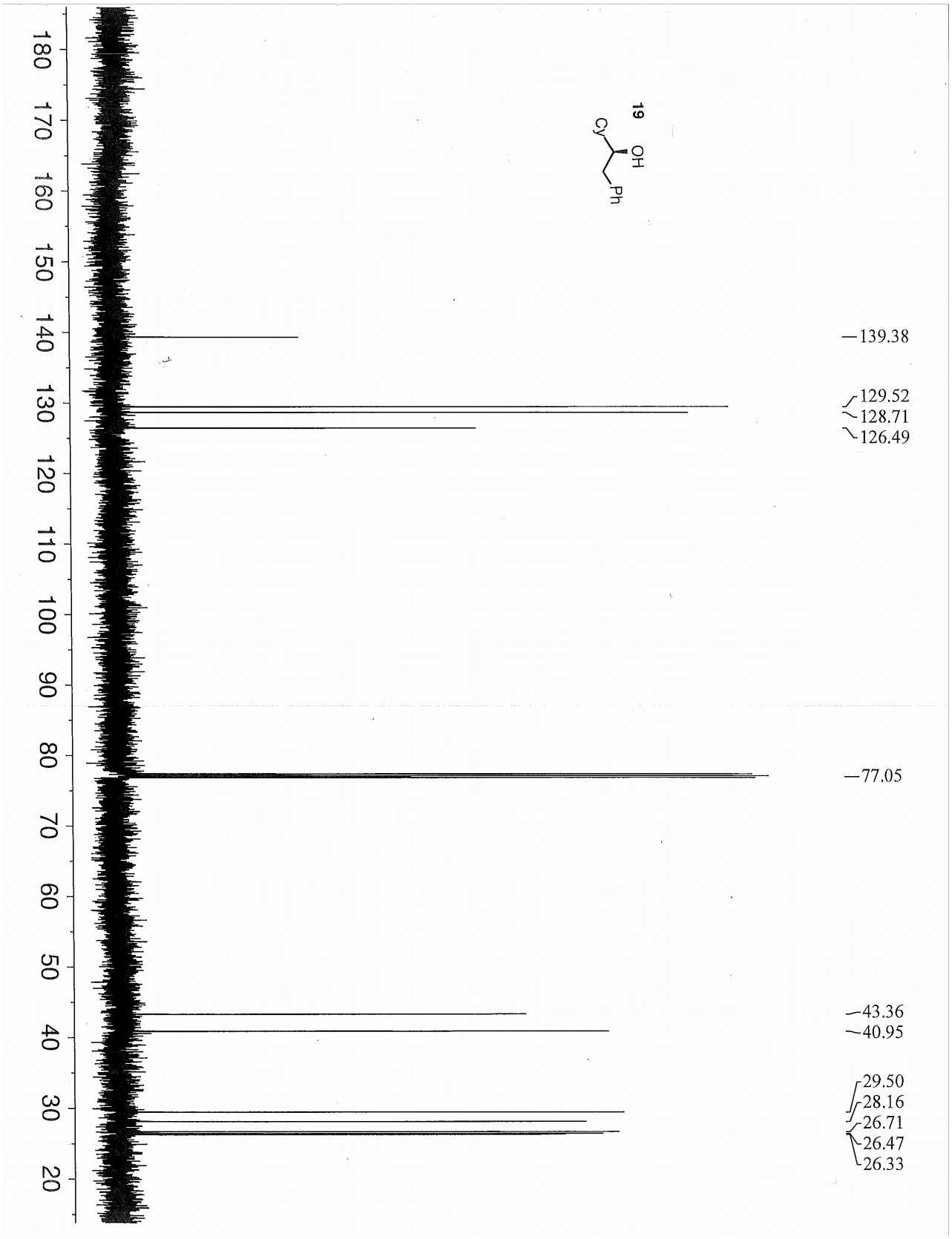
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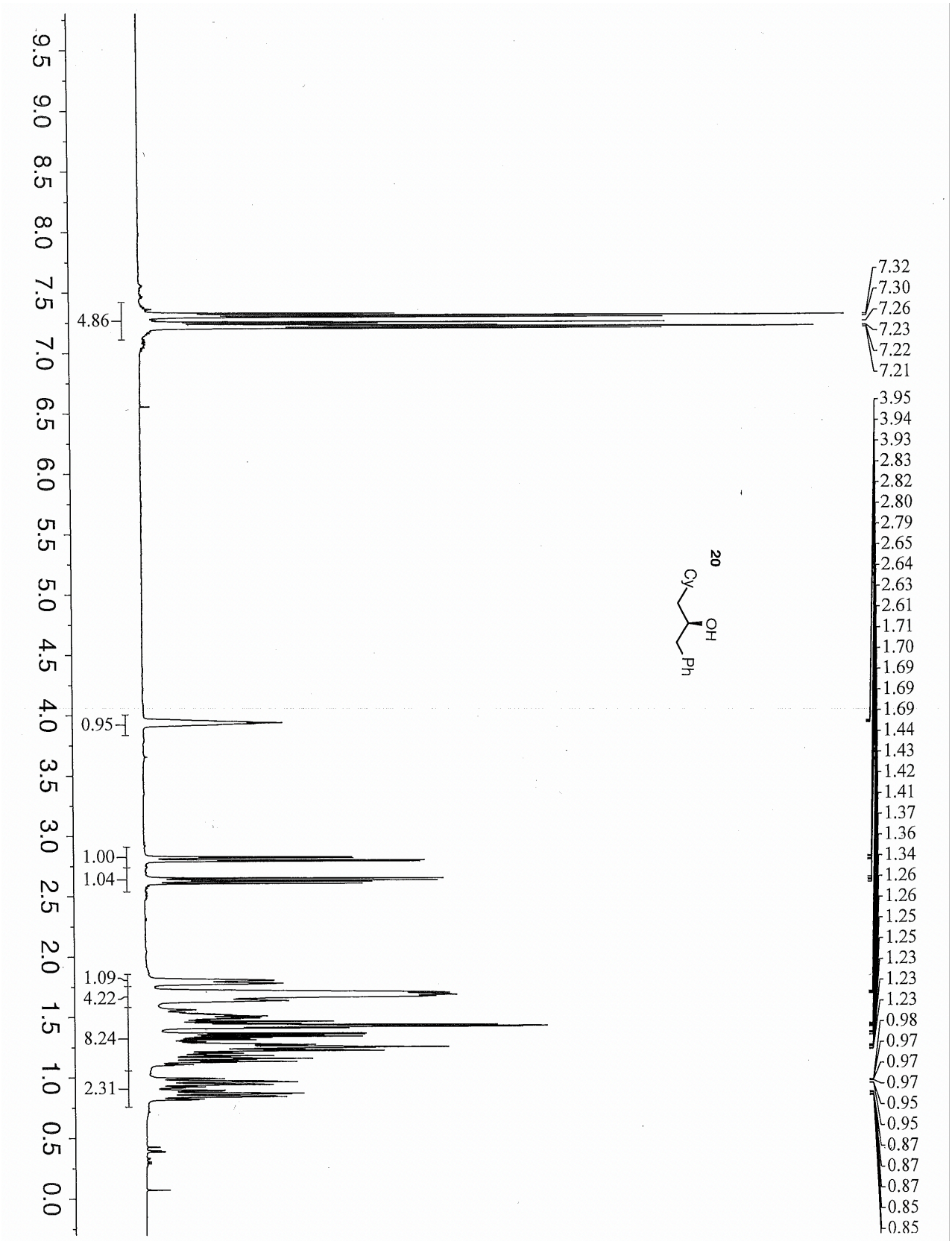
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0.95
1.00
1.04
1.09
4.22
8.24
2.31
20
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OH
Ph
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7.30
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3.94
3.93
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2.82
2.80
2.79
2.65
2.64
2.63
2.61
1.71
1.70
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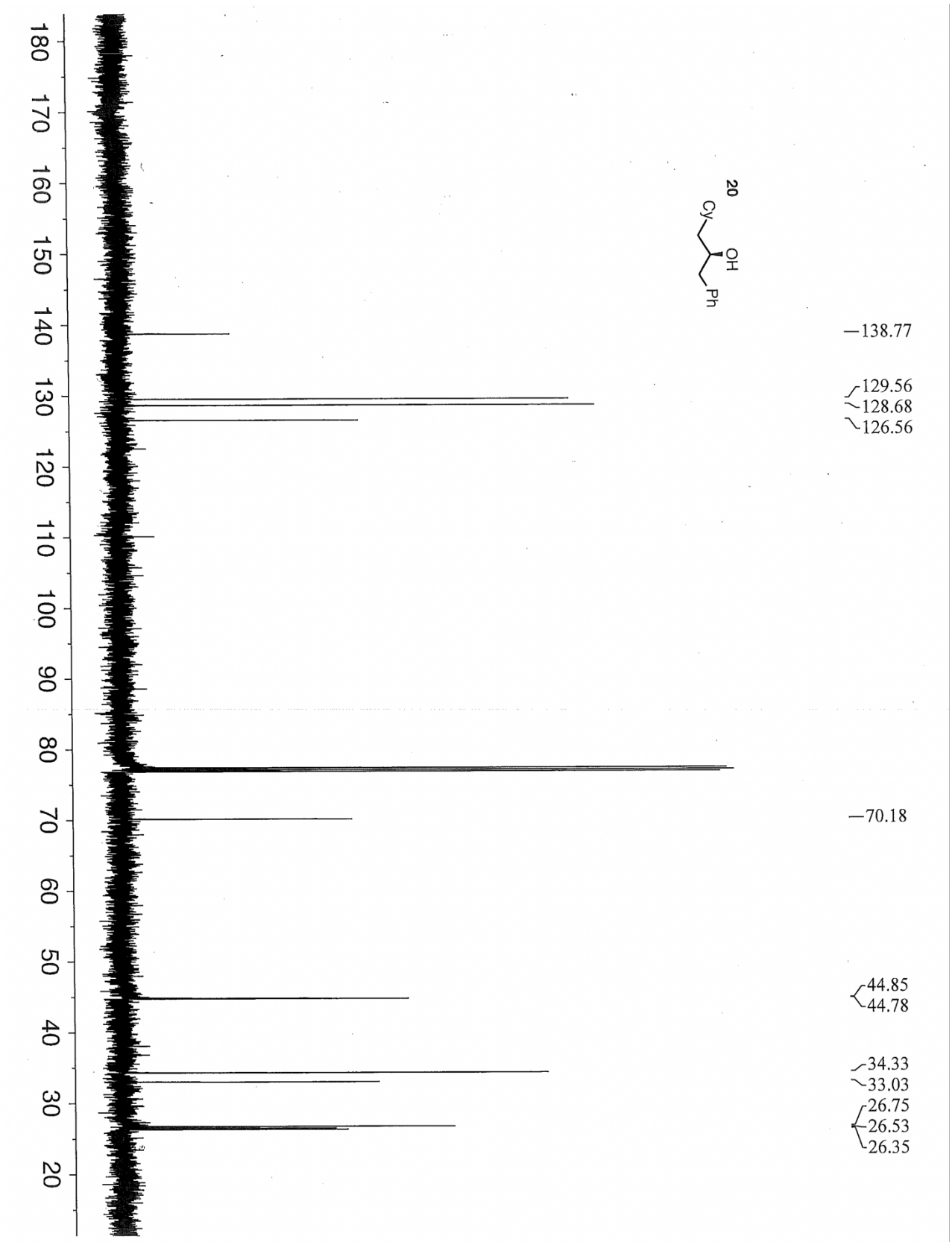
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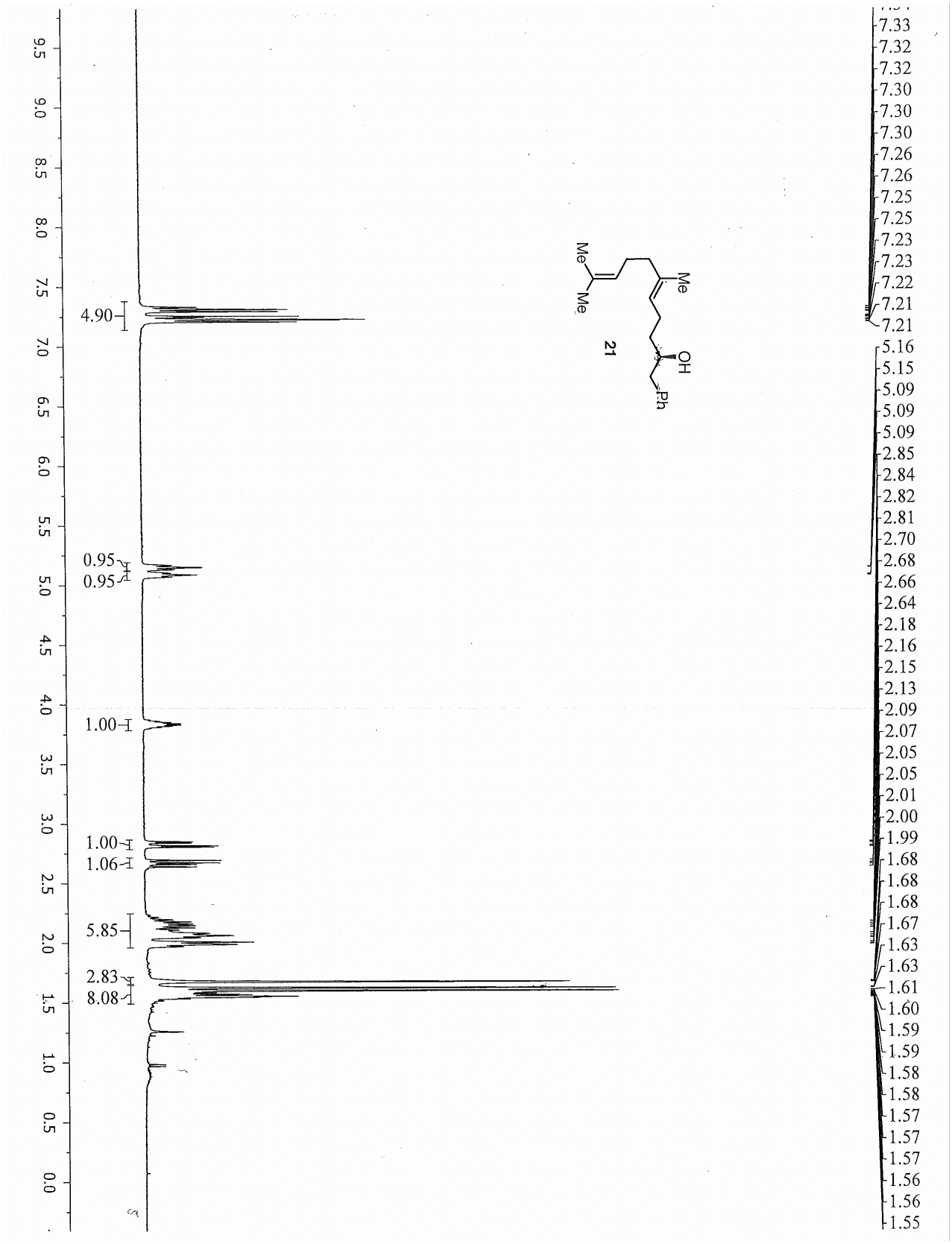
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7.23
7.23
7.22
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7.21
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5.09
5.09
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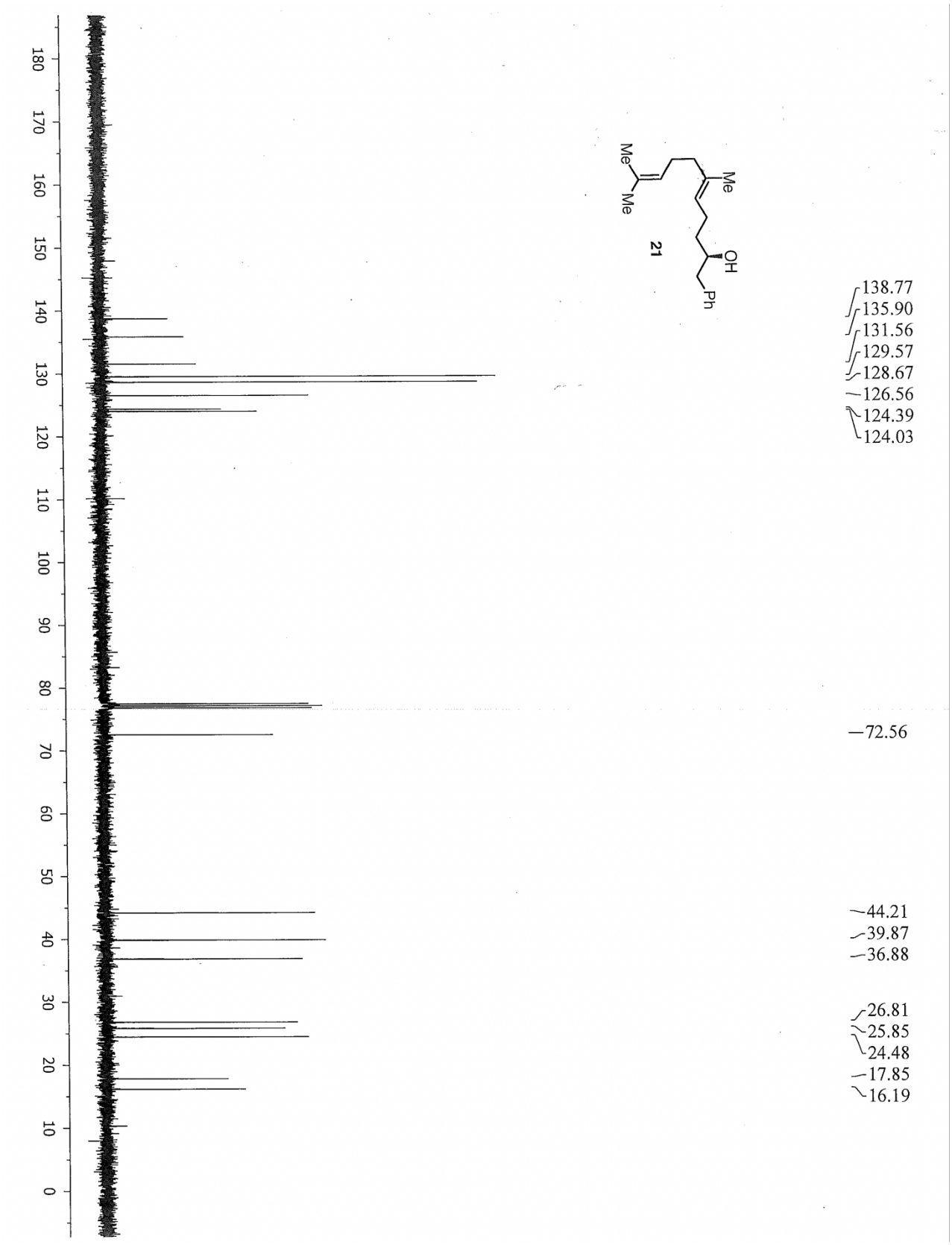
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Me
Me
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124.03
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25.85
24.48
17.85
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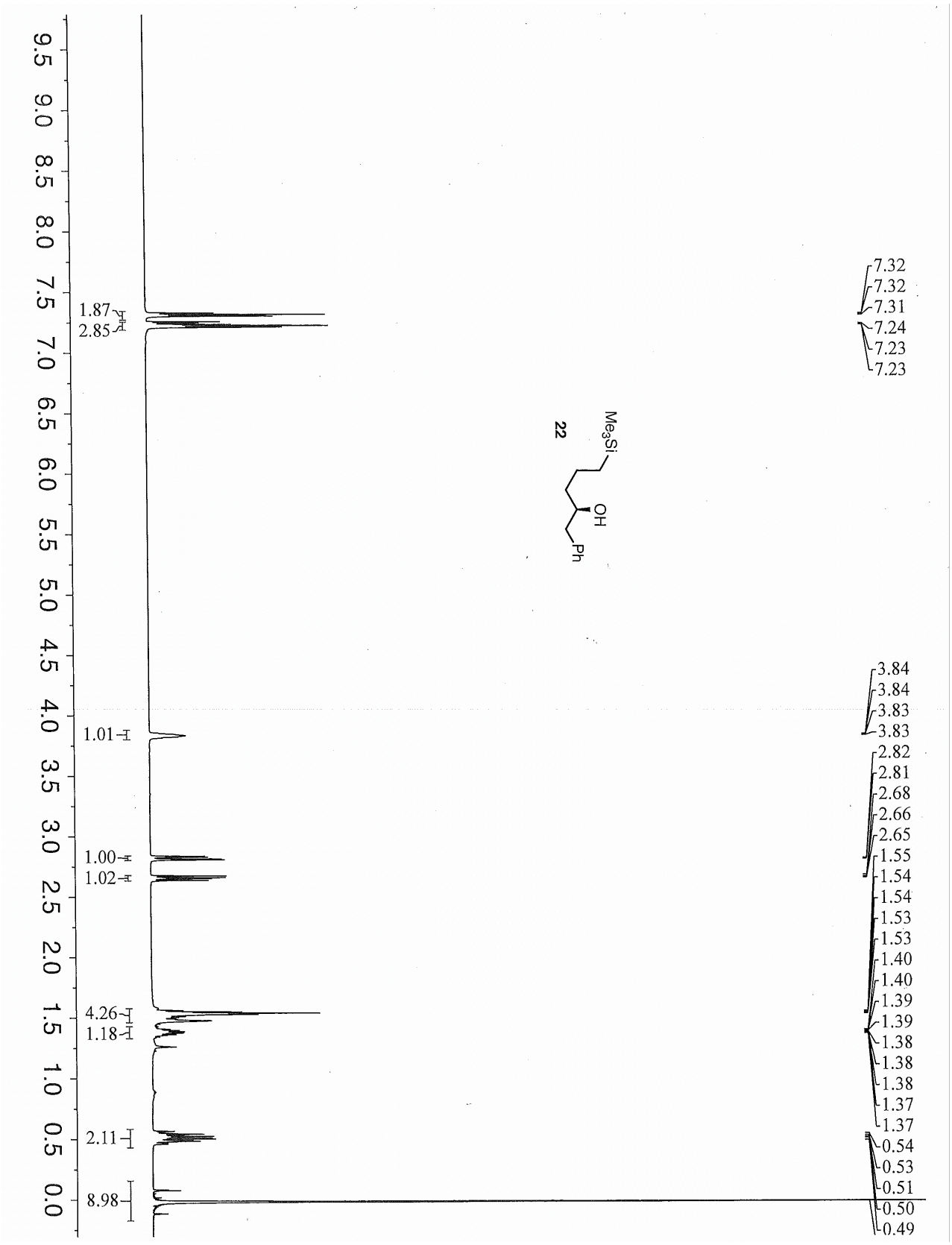
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Me3Si
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2.85
1.01
1.00
1.02
4.26
1.18
2.11
8.98
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7.32
7.31
7.24
7.23
7.23
3.84
3.84
3.83
3.83
2.82
2.81
2.68
2.66
2.65
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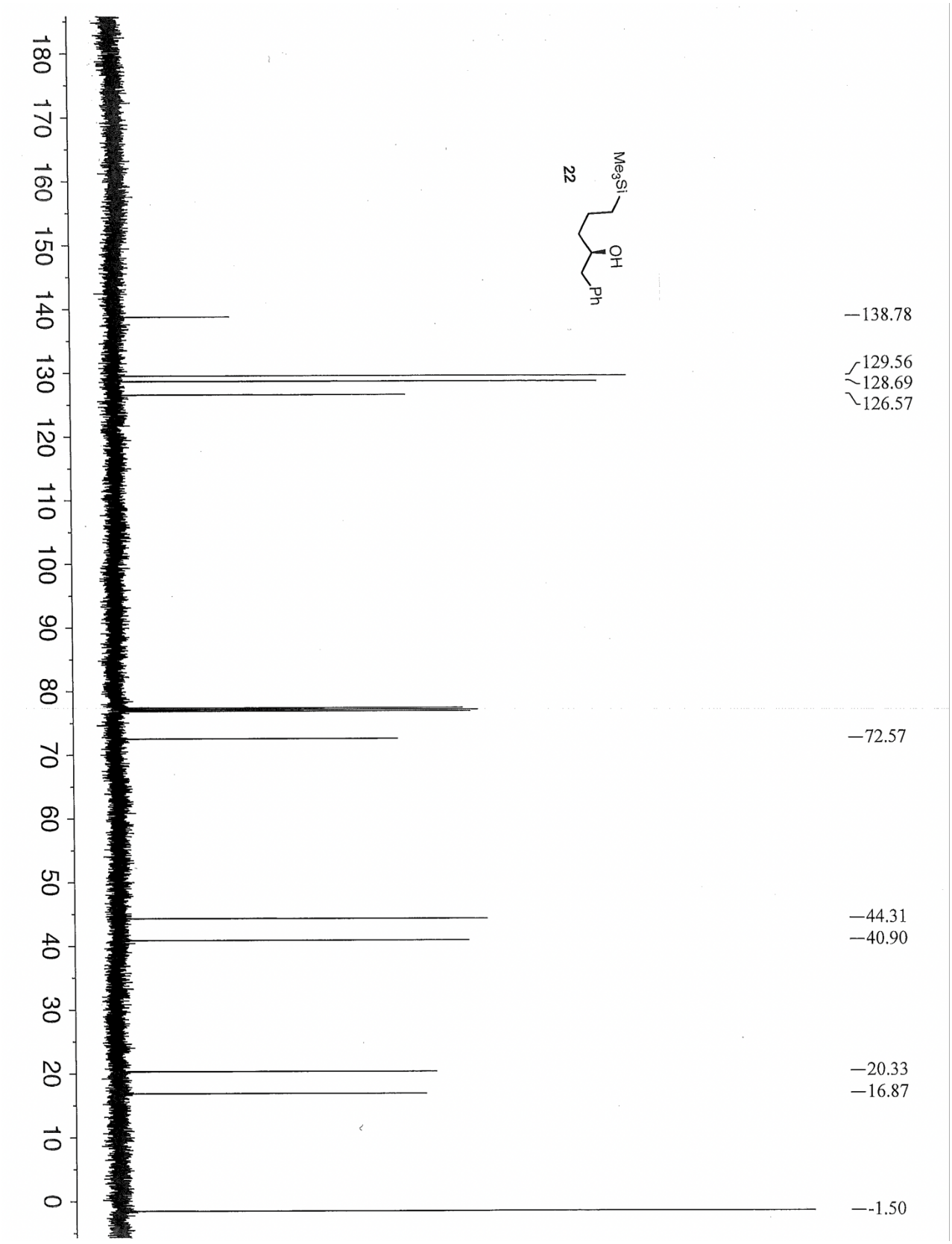
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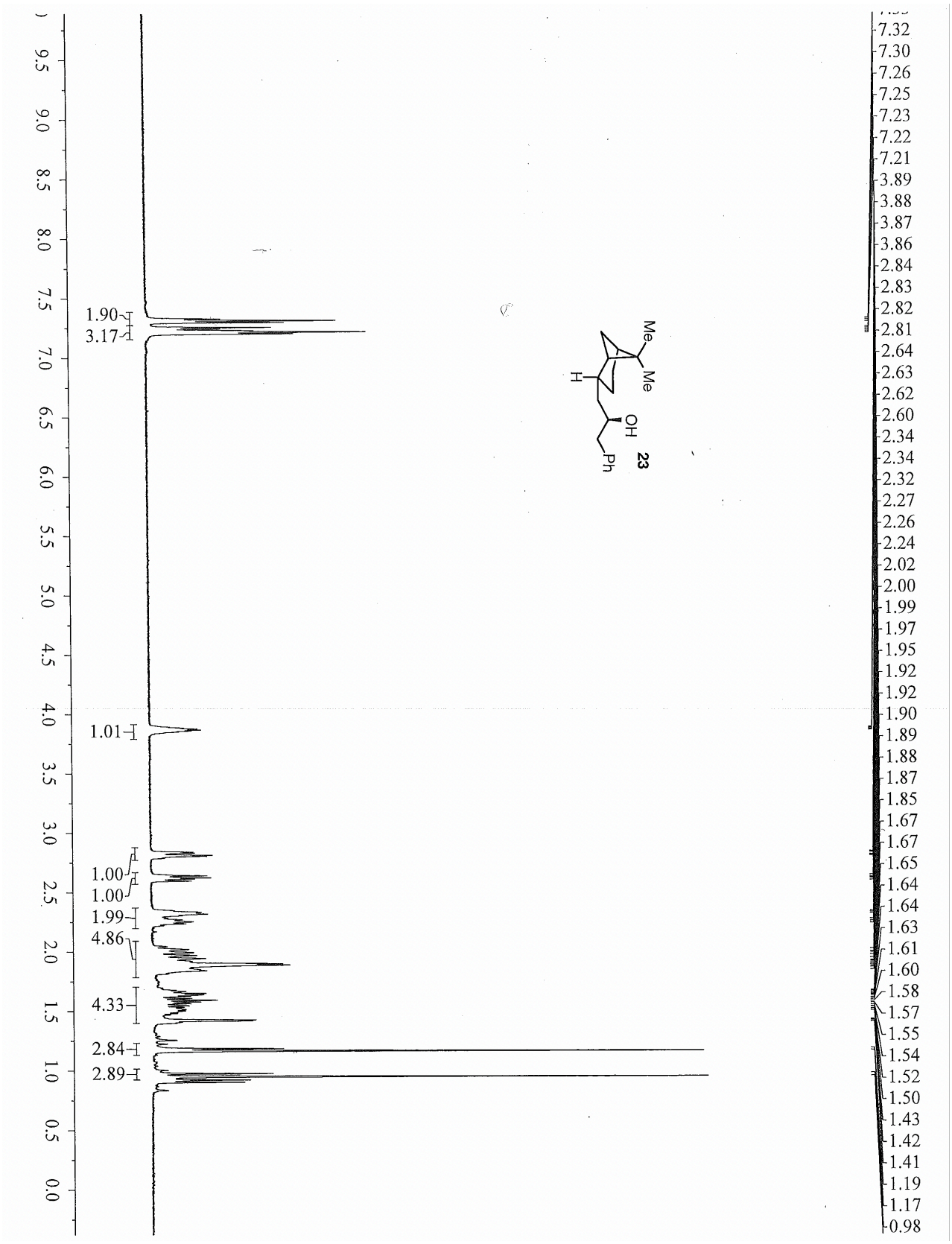
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2.89
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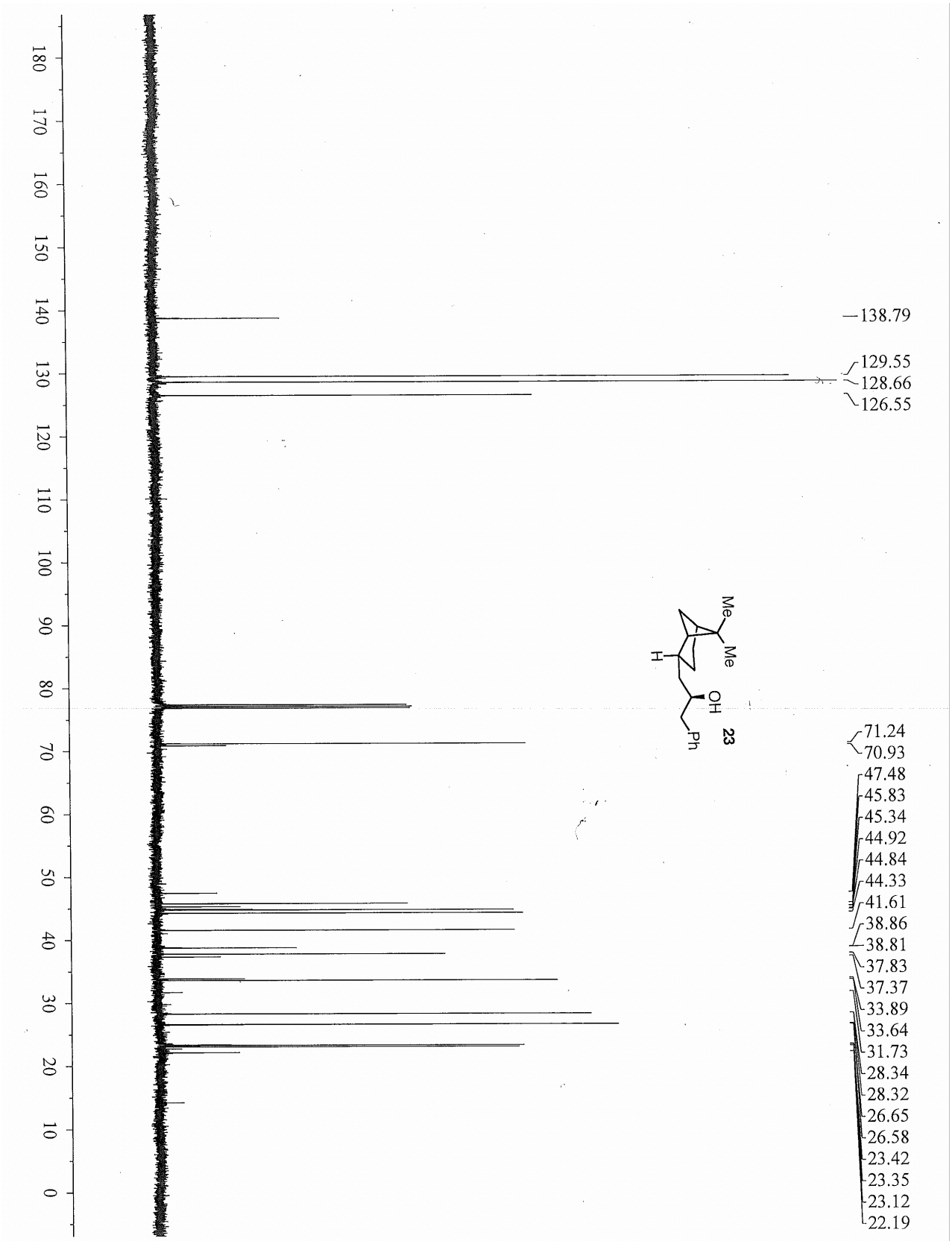
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126.55
Me
Me
H
OH
Ph
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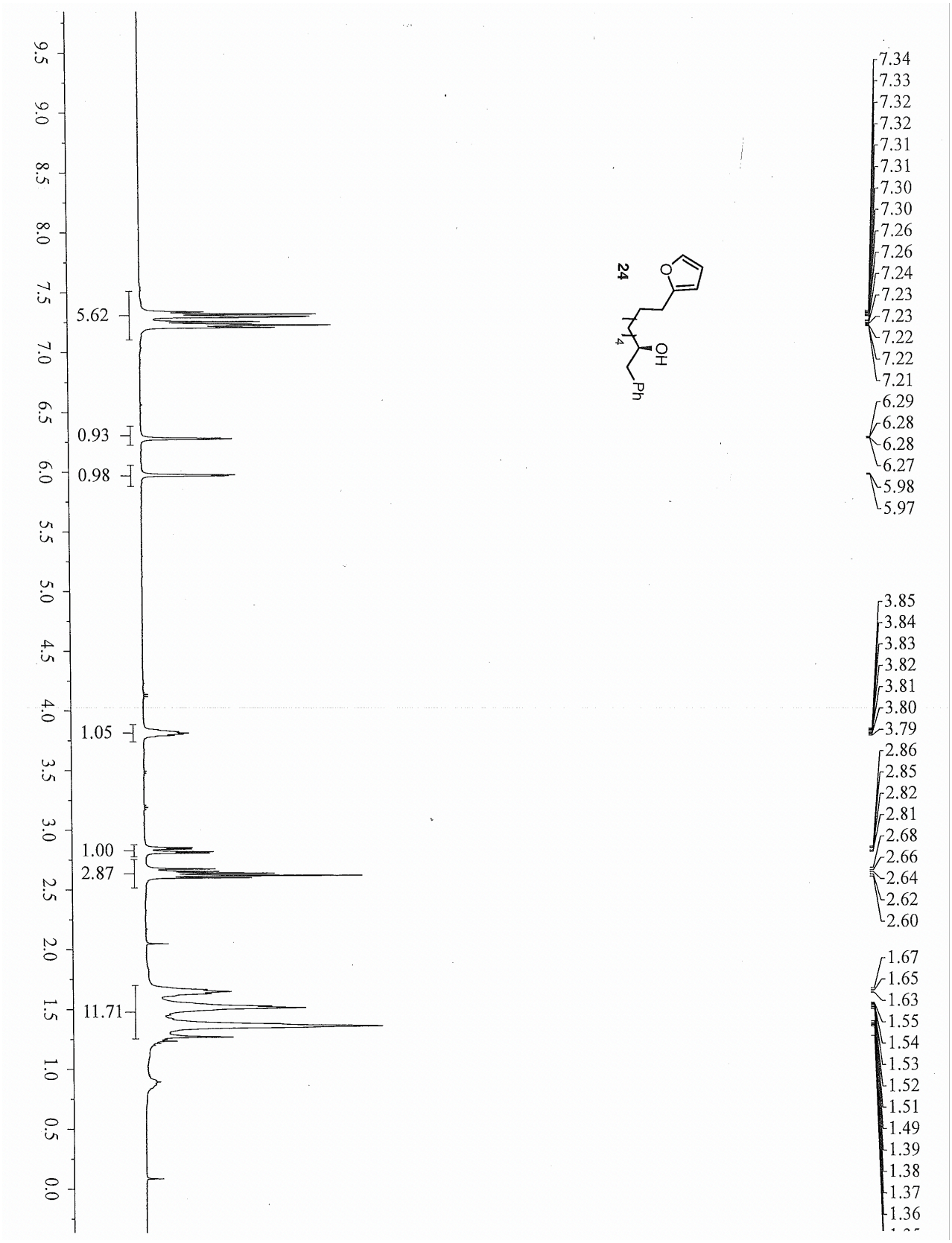
22.19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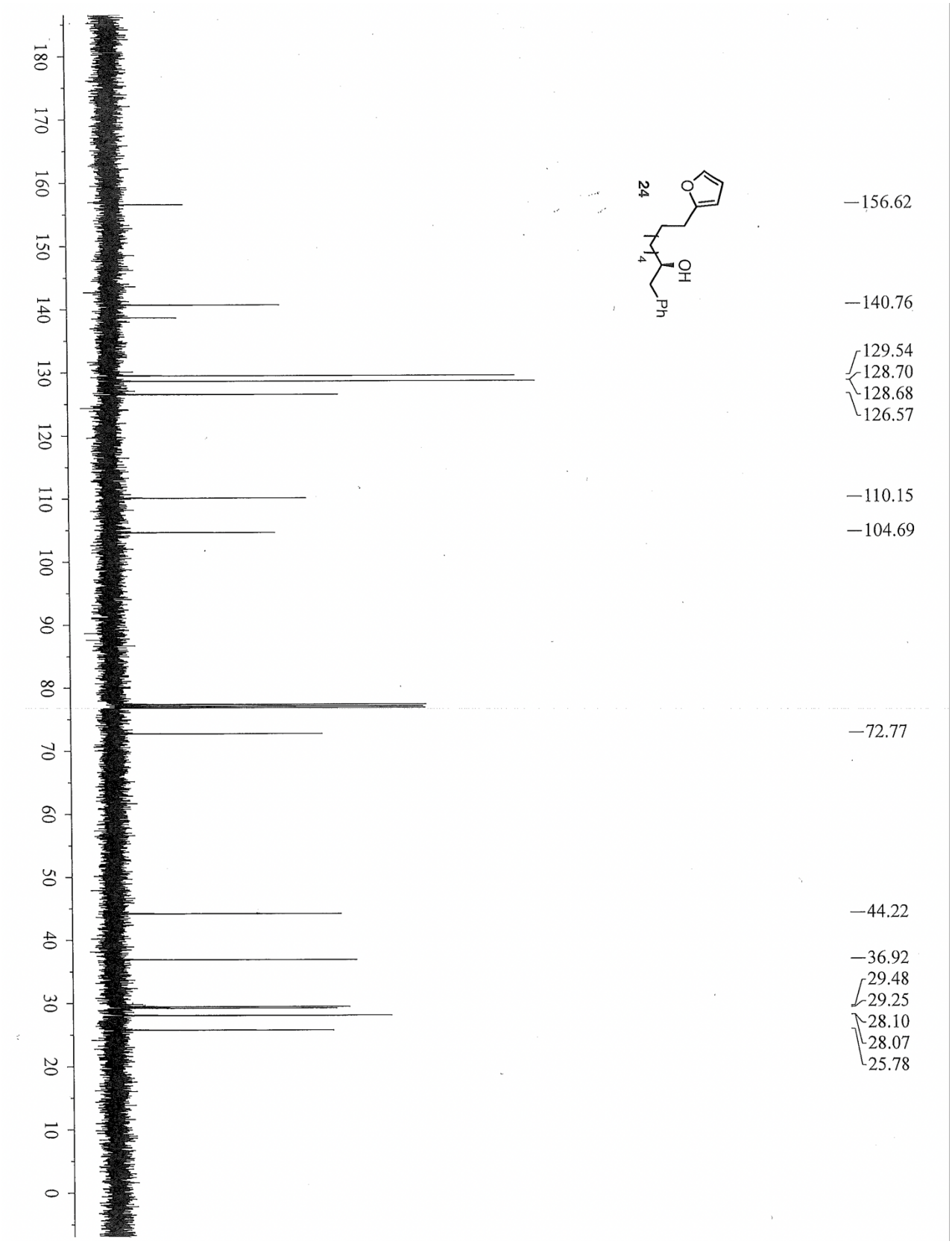
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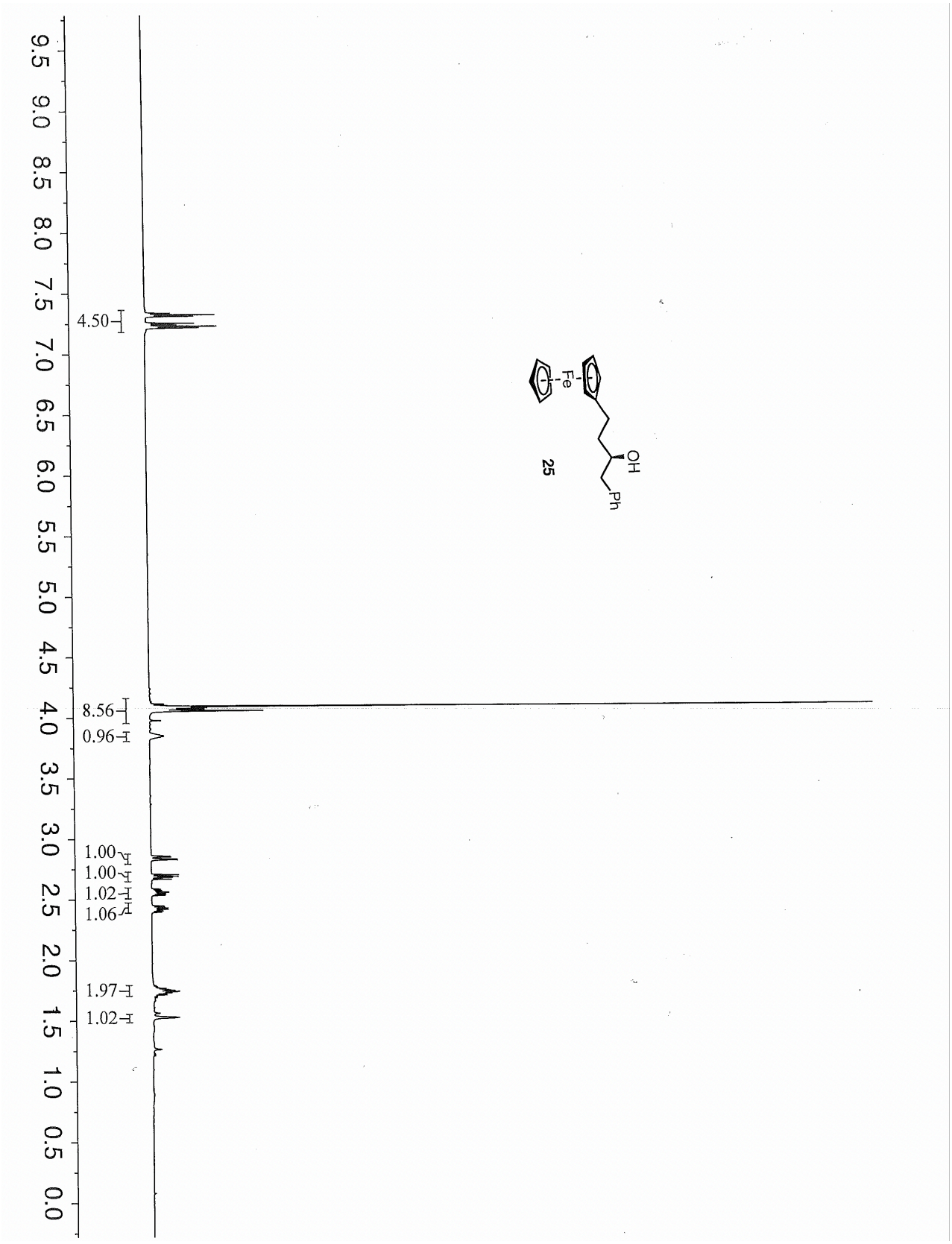
28.07
25.78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1.97
1.02
Fe
OH
Ph
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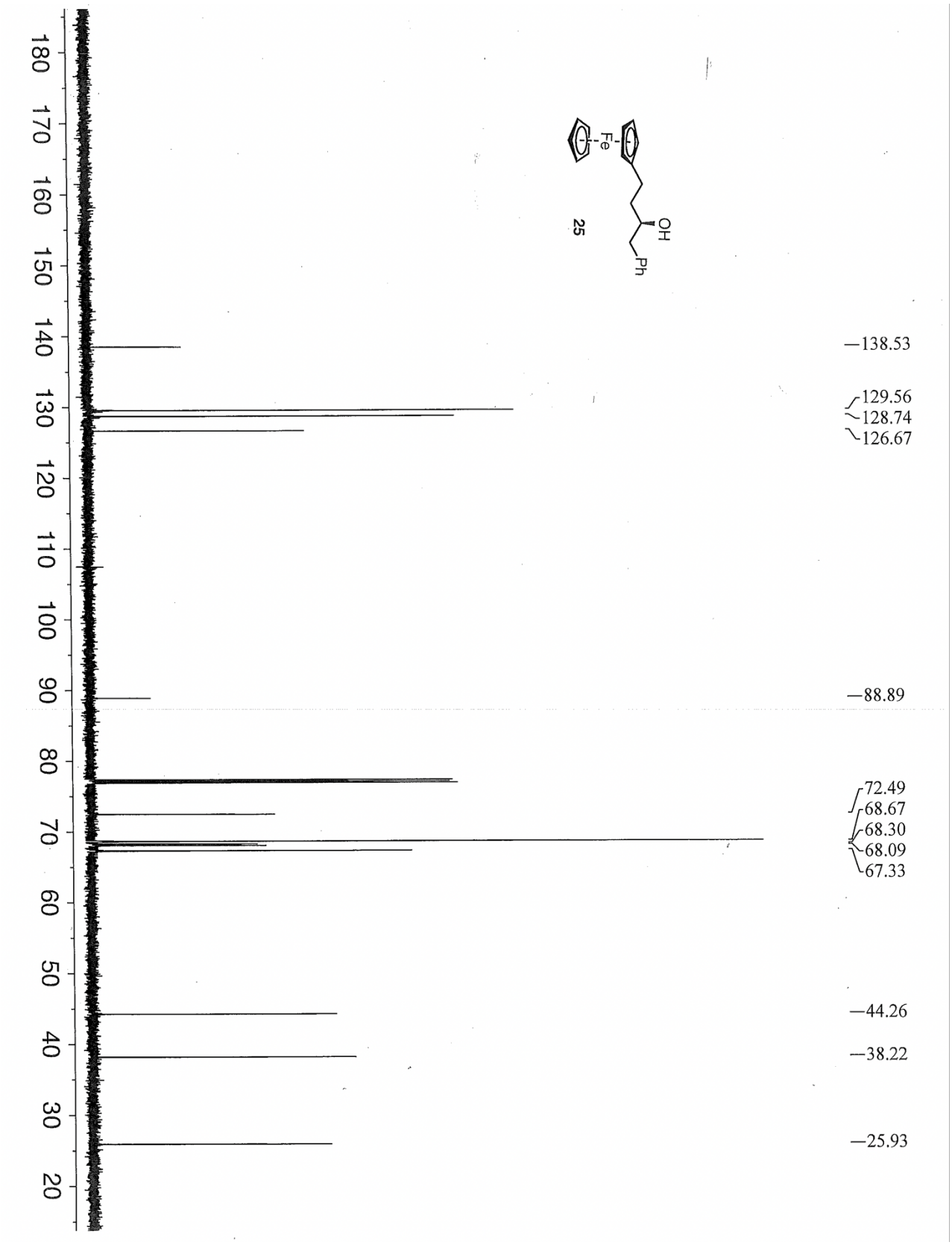
Fe
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20
138.53
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38.22
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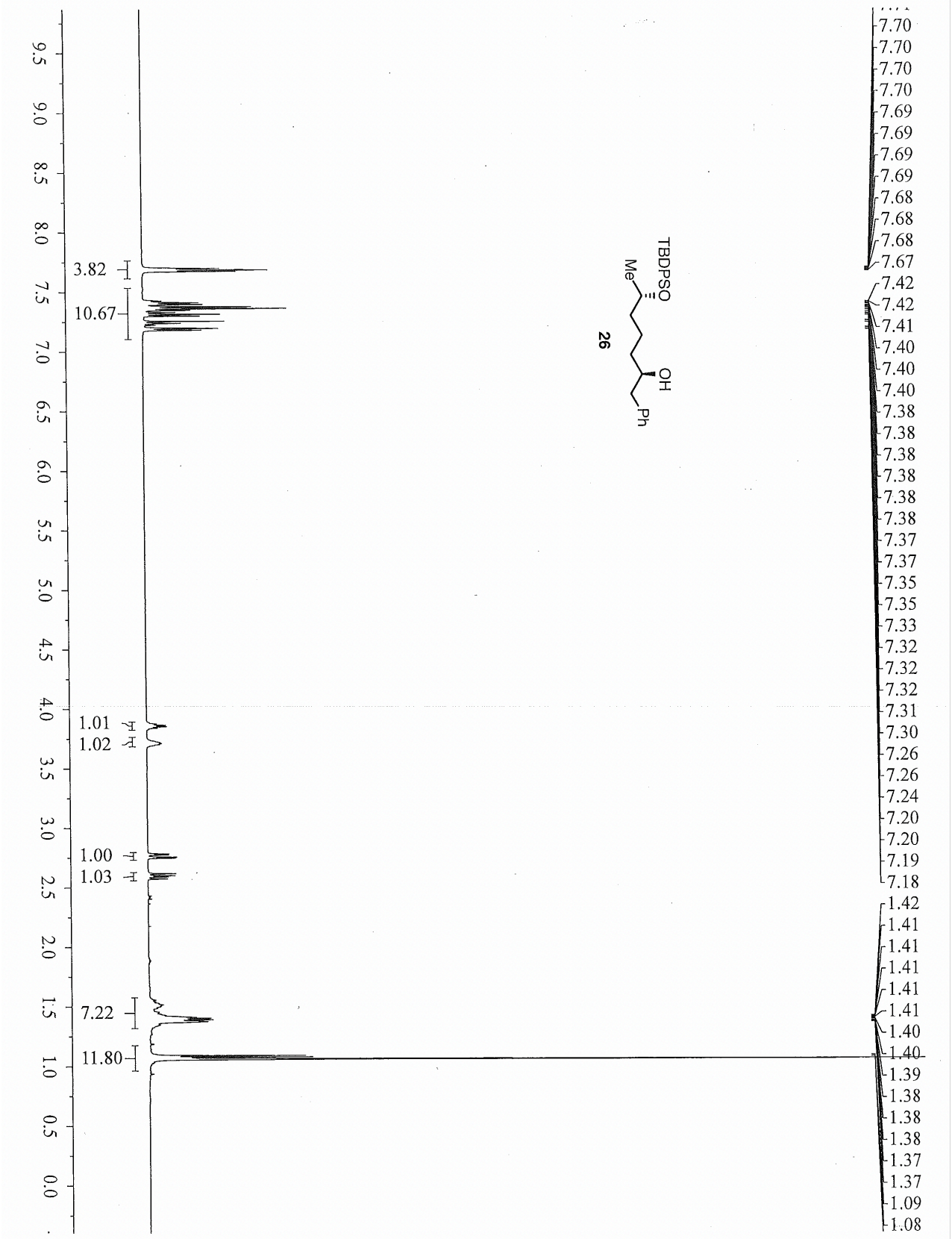
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1.03
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11.80
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7.70 7.70 7.70 7.70 7.69 7.69 7.69 7.69 7.68 7.68 7.68 7.67 7.42 7.42 7.41 7.40 7.40 7.40 7.38 7.38 7.38 7.38 7.38 7.38 7.37 7.37 7.35 7.35 7.33 7.32 7.32 7.32 7.31 7.30 7.26 7.26 7.24 7.20 7.20 7.19 7.18
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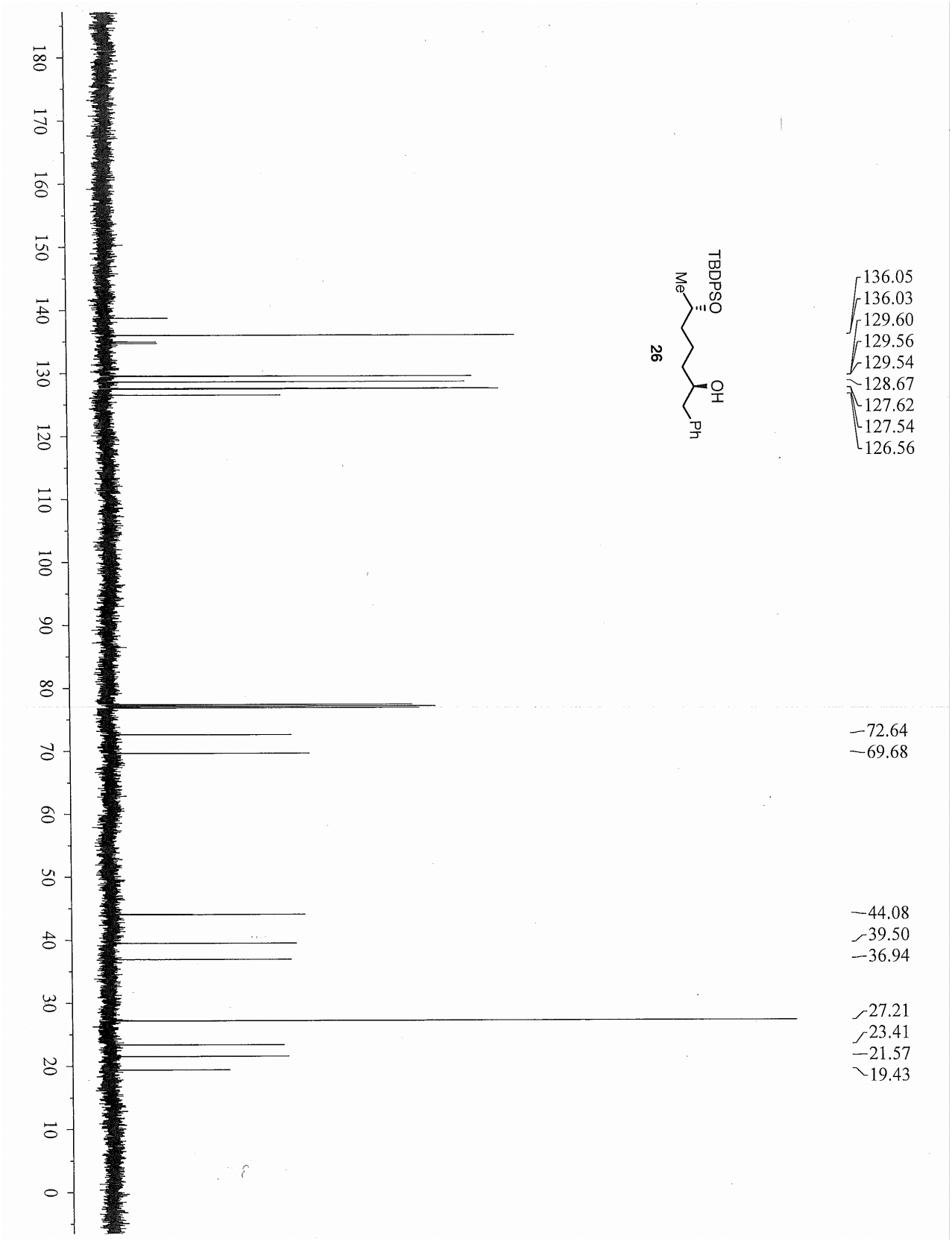
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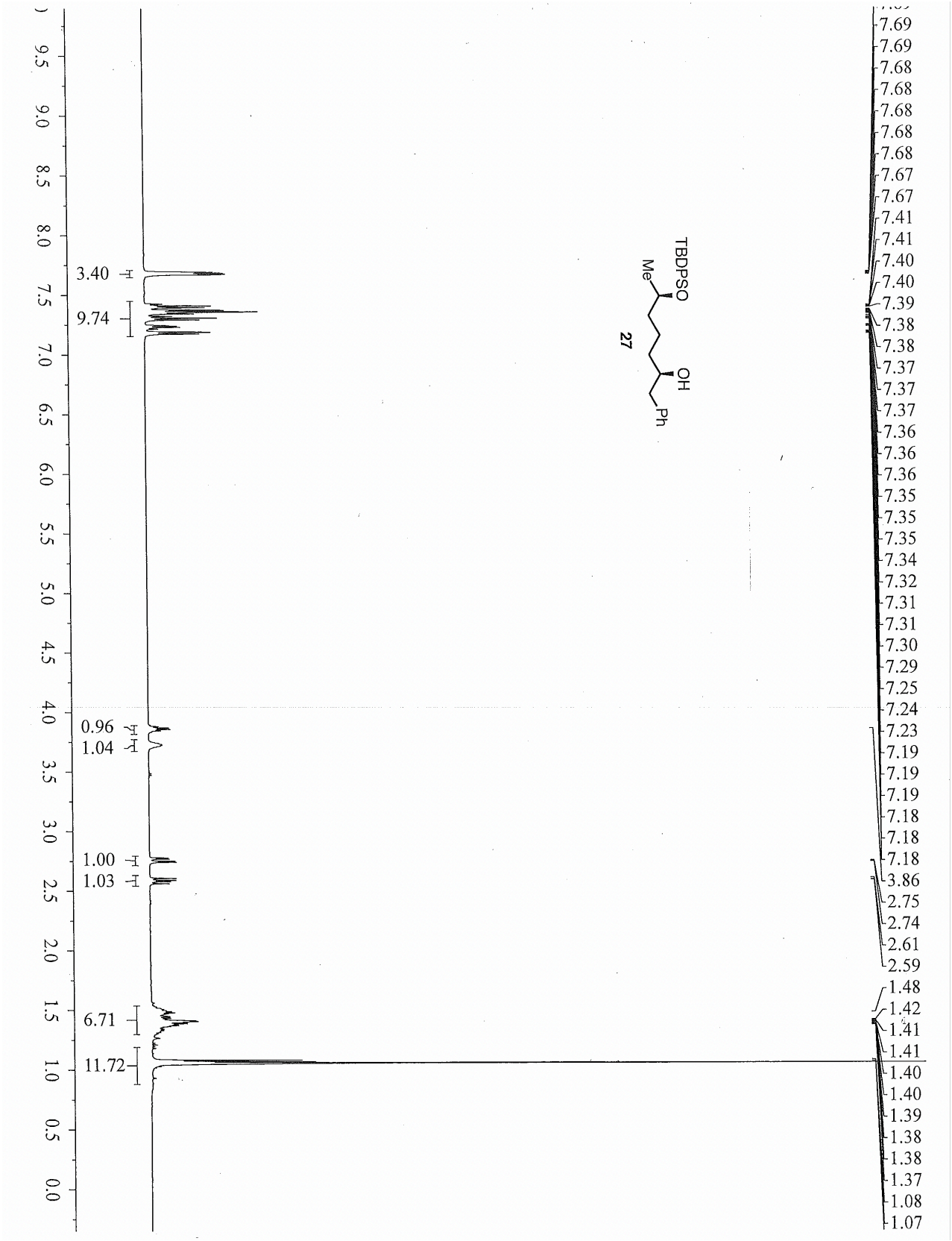
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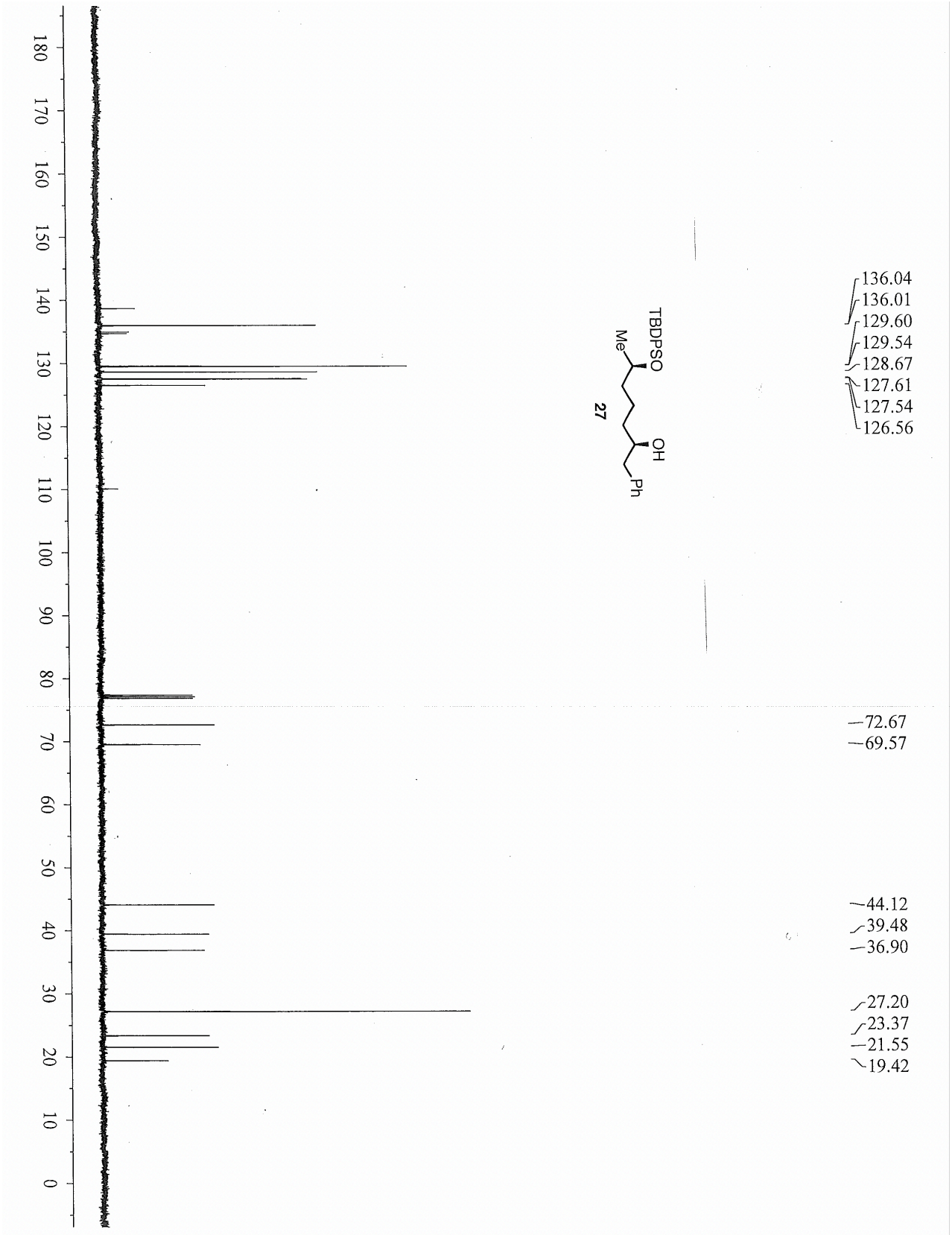
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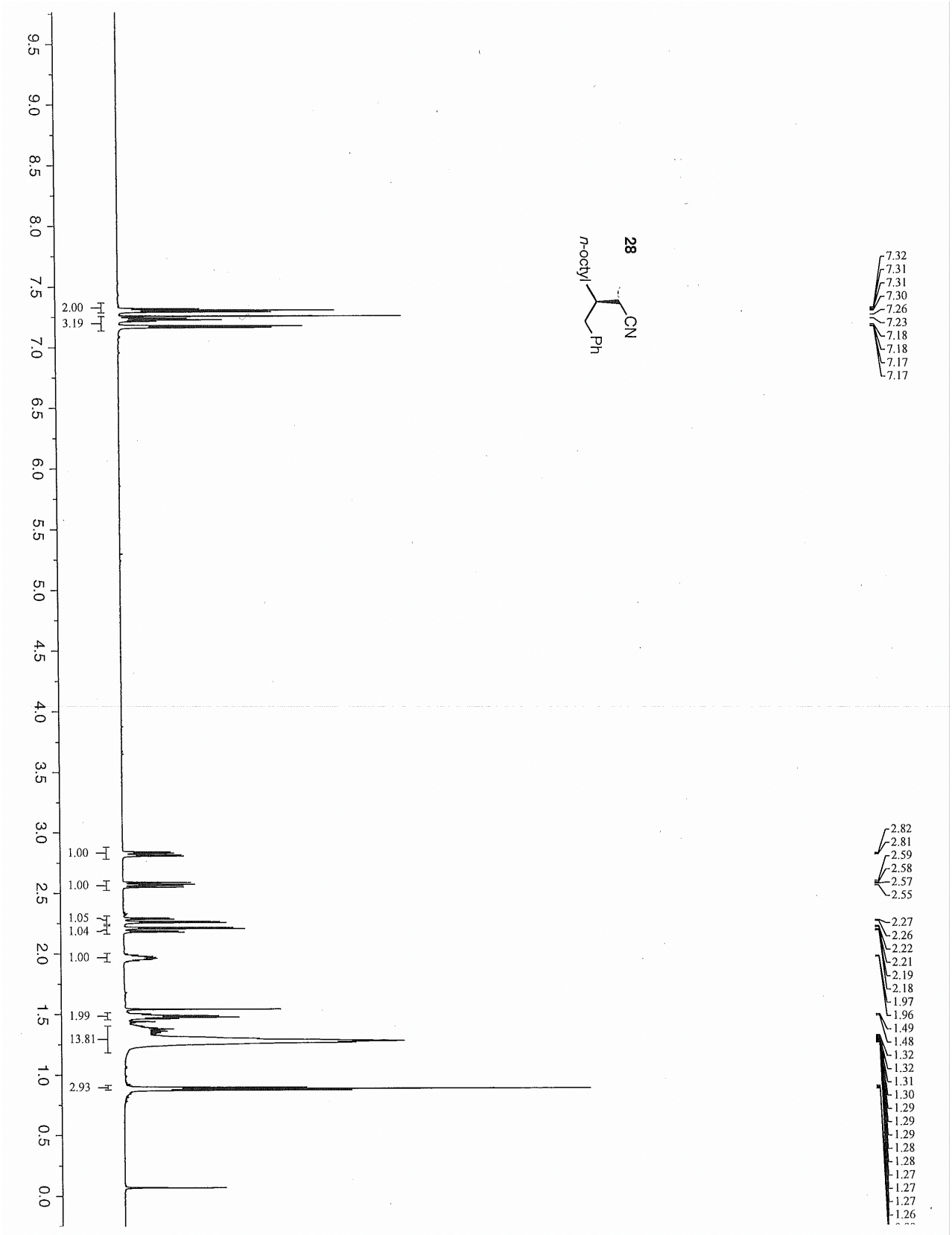
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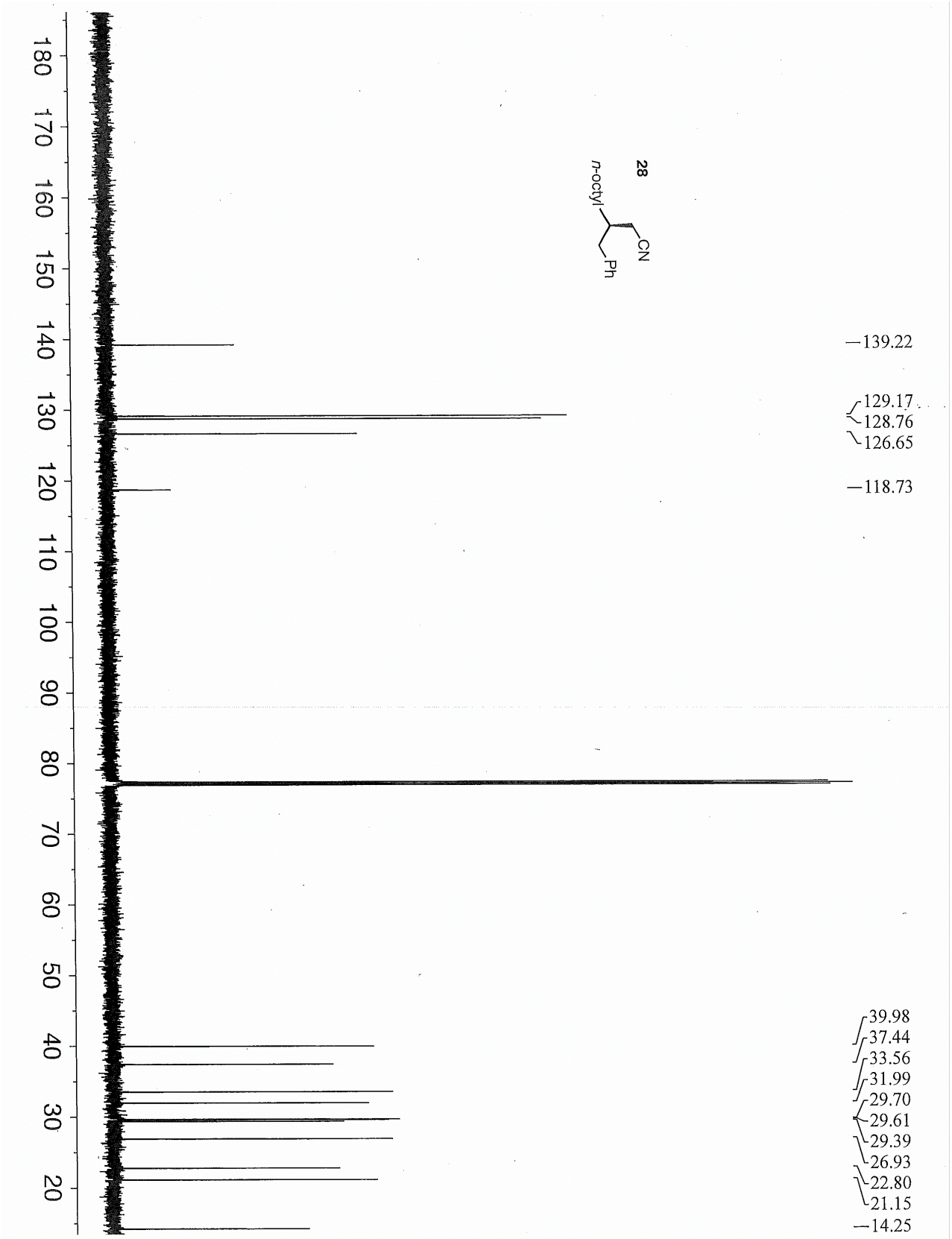
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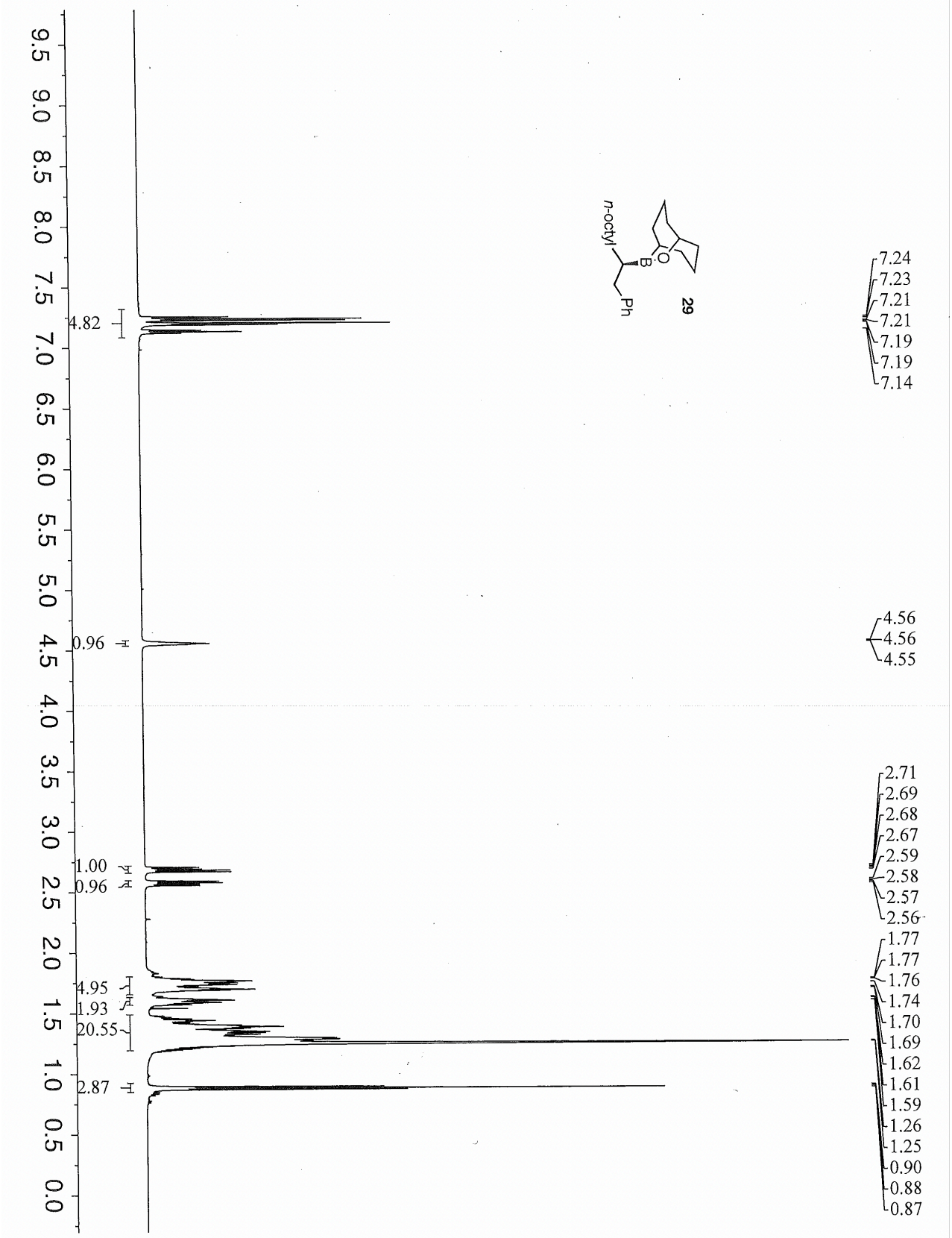
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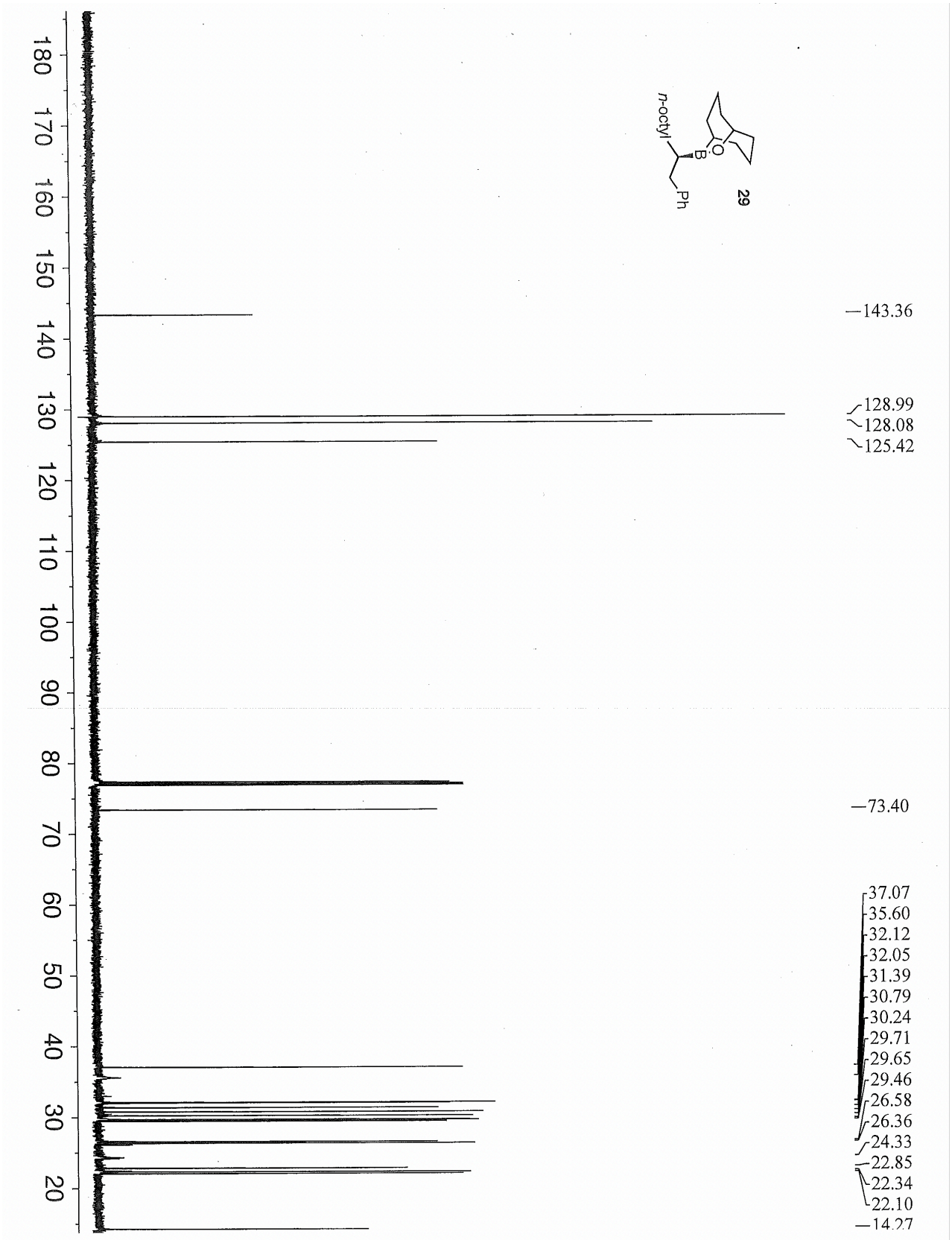
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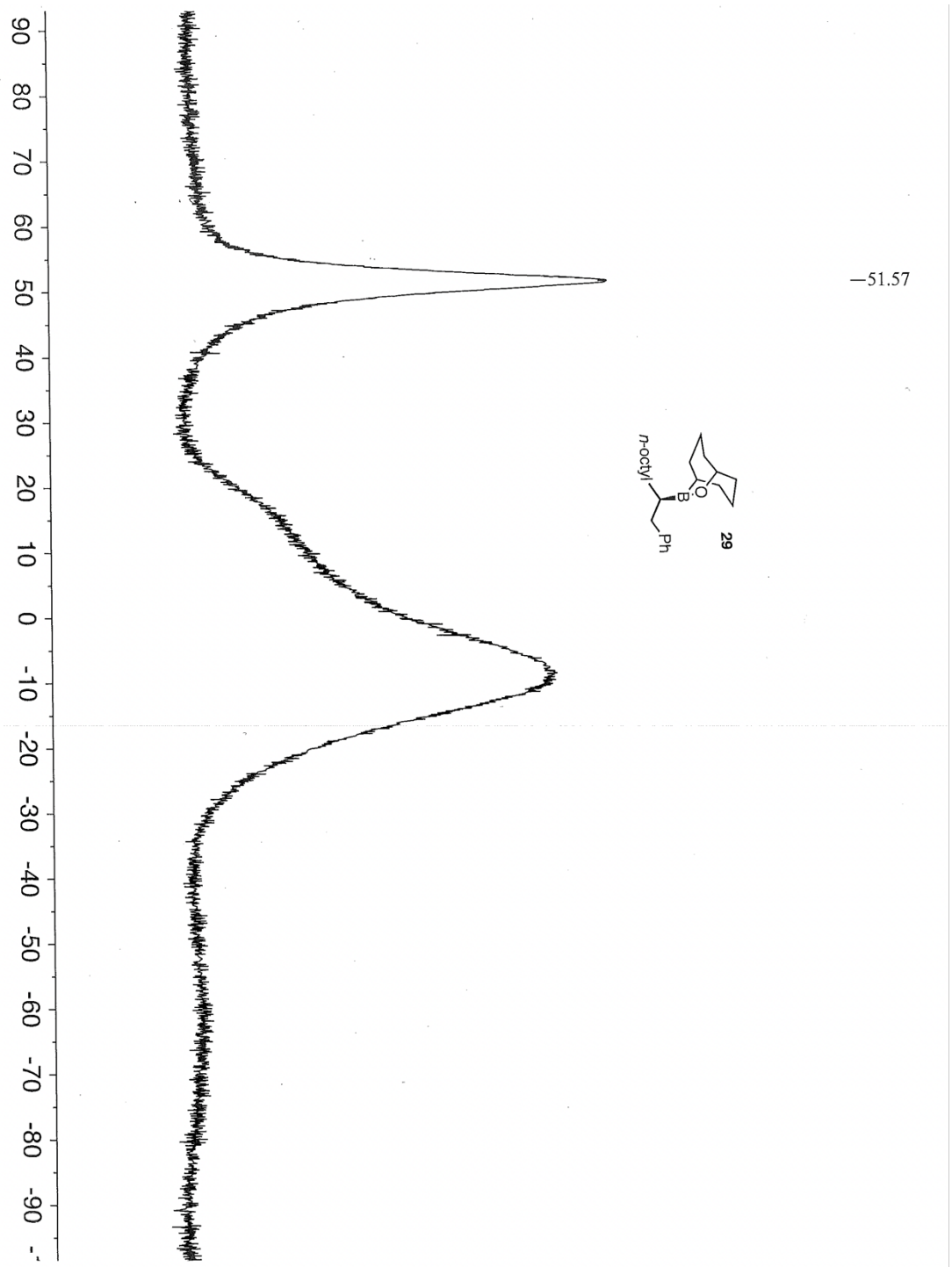
^{11}B NMR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O
Ph
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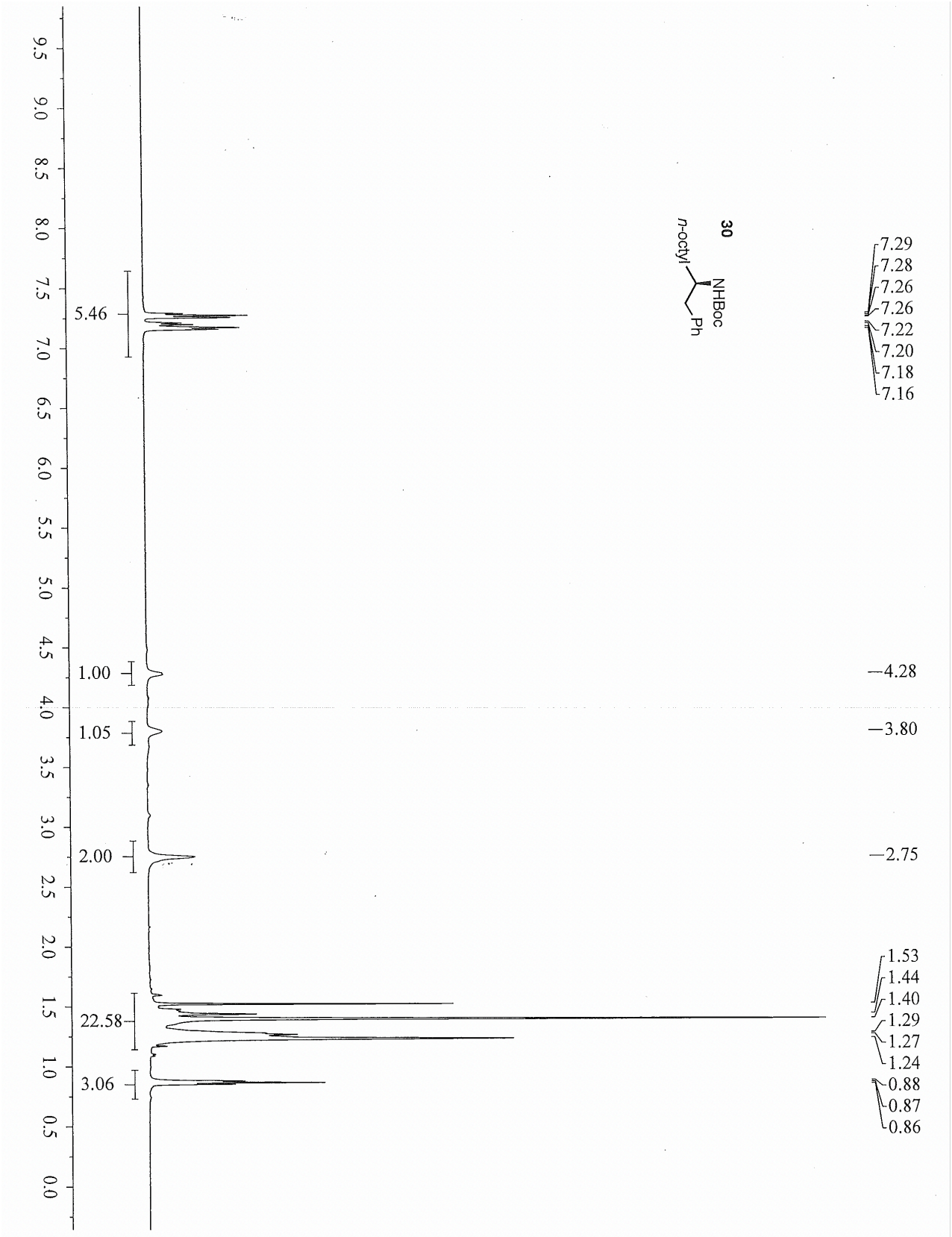
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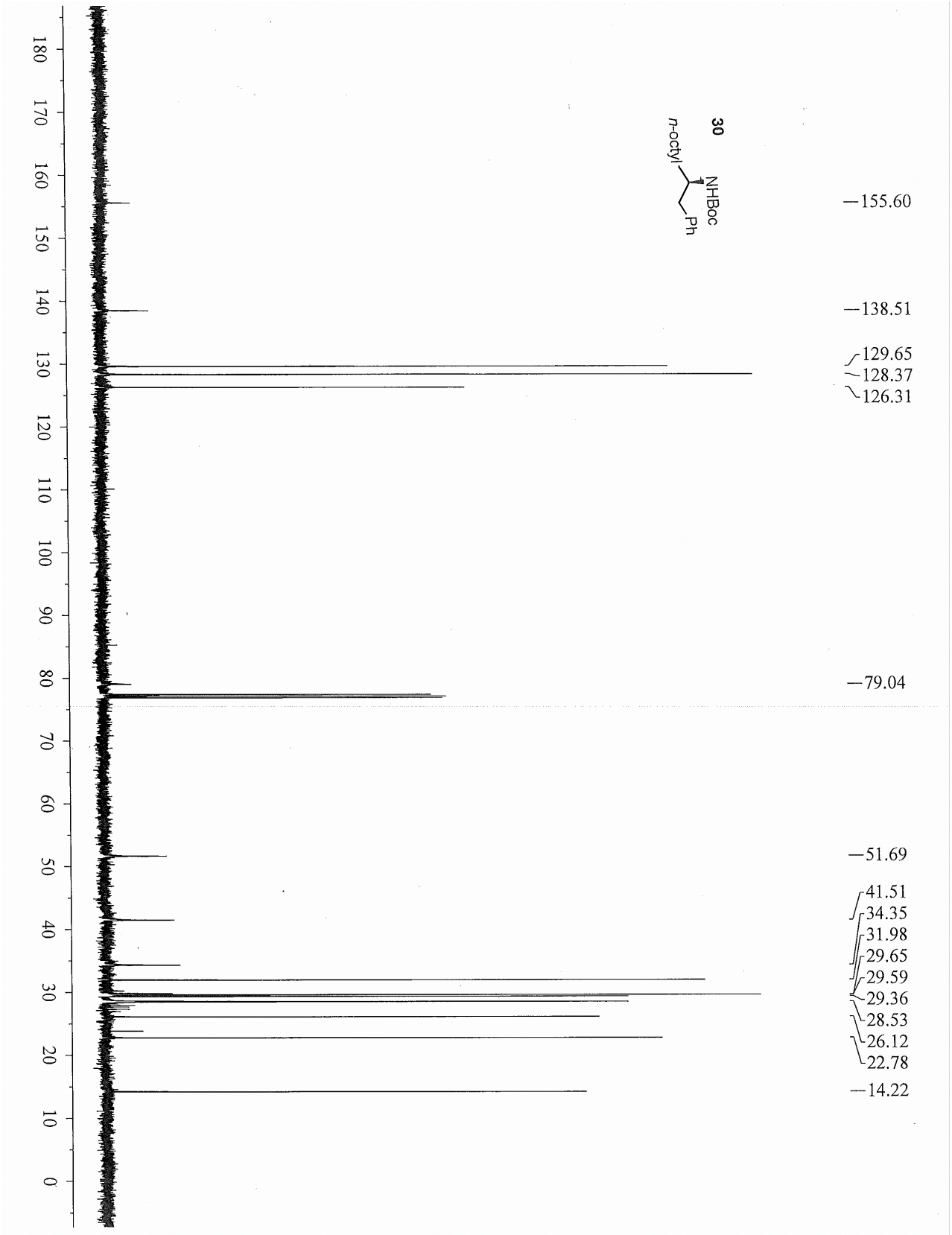
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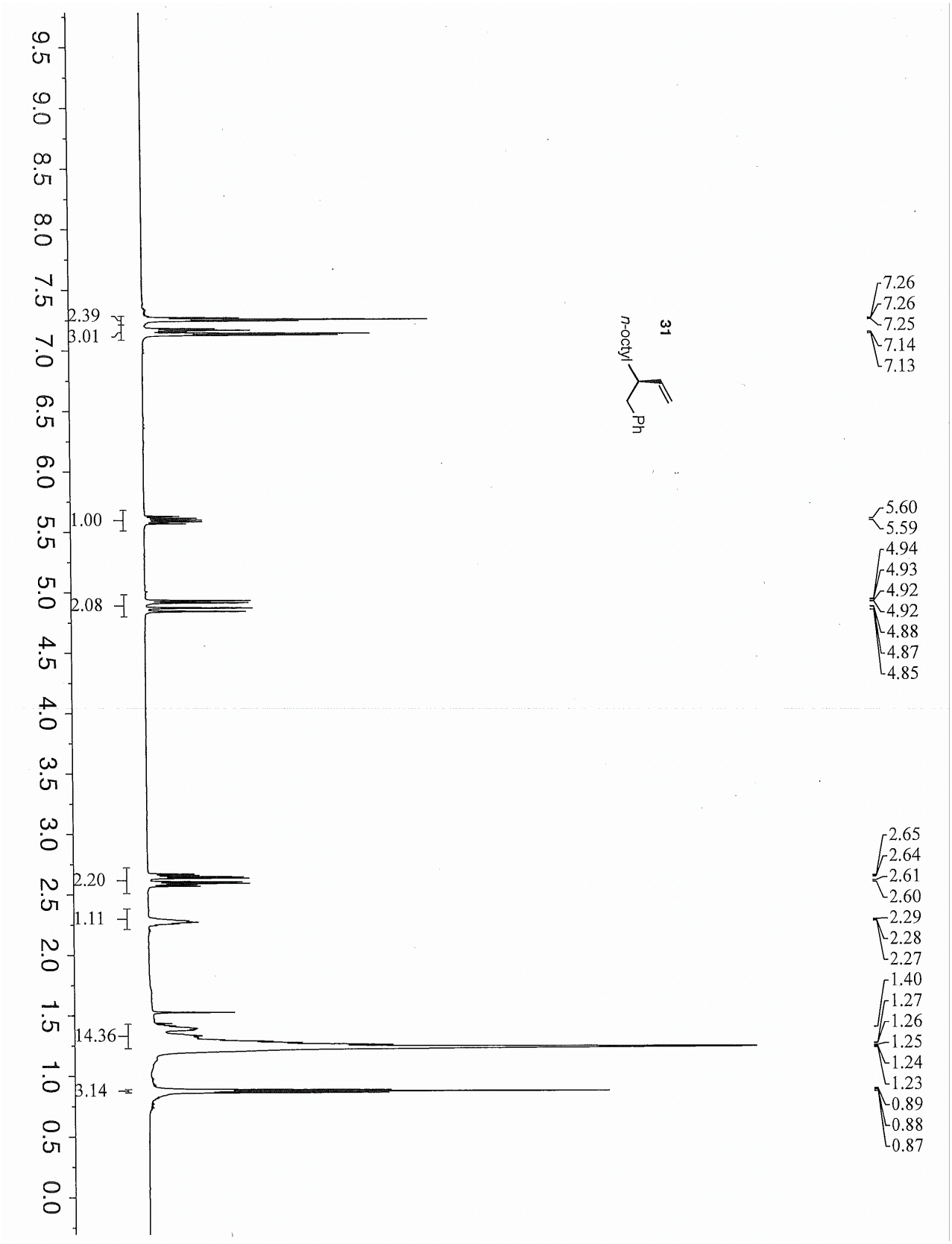
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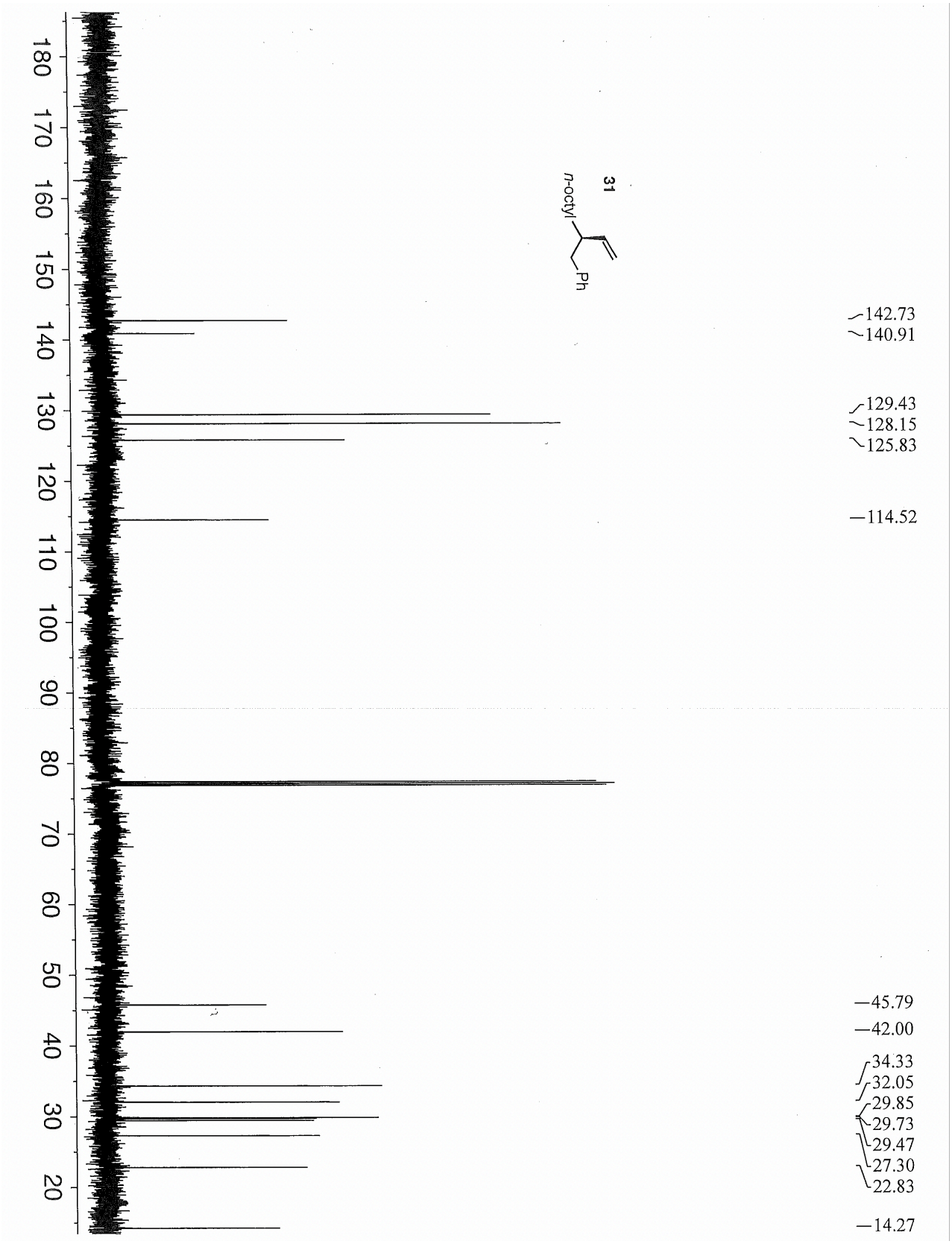
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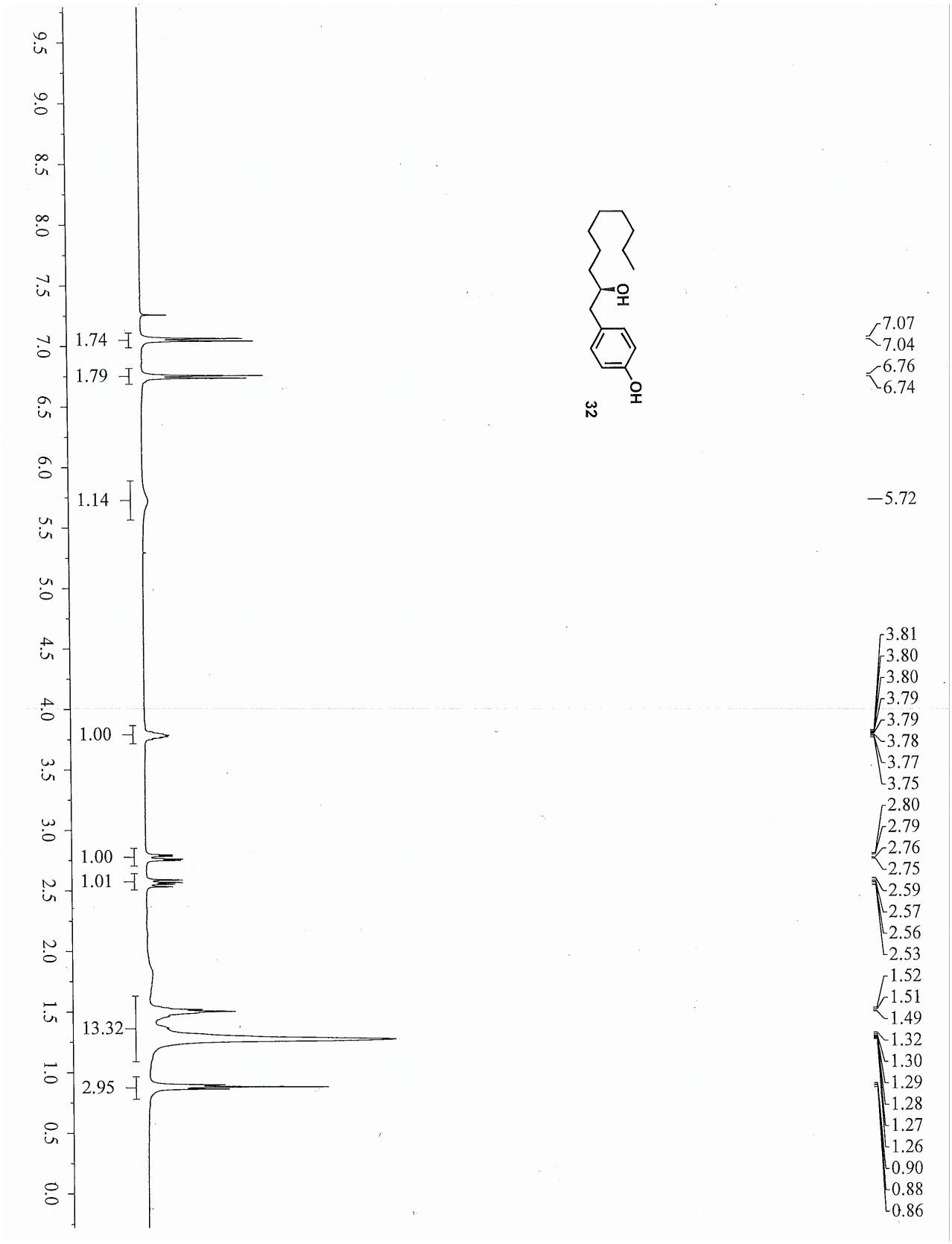
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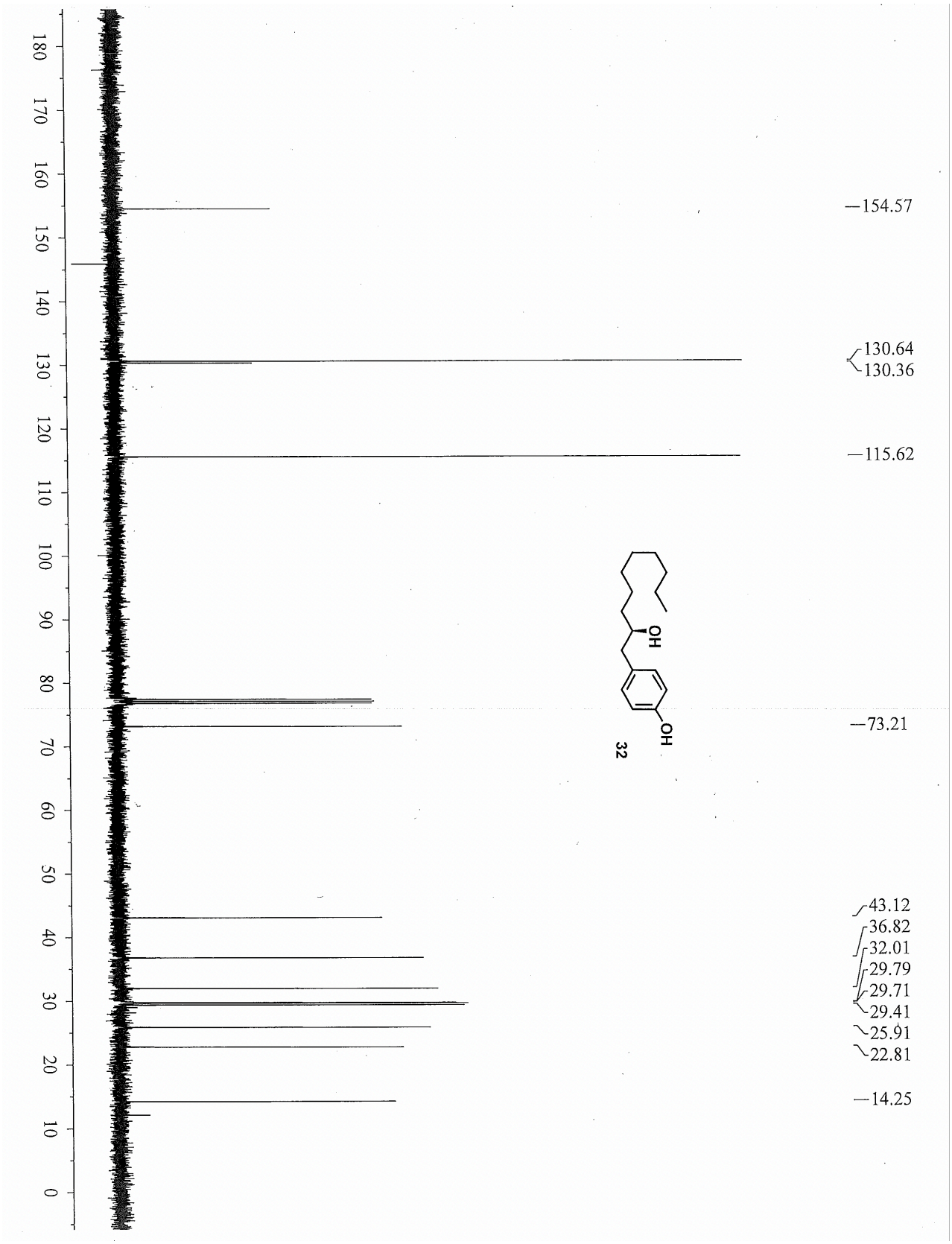
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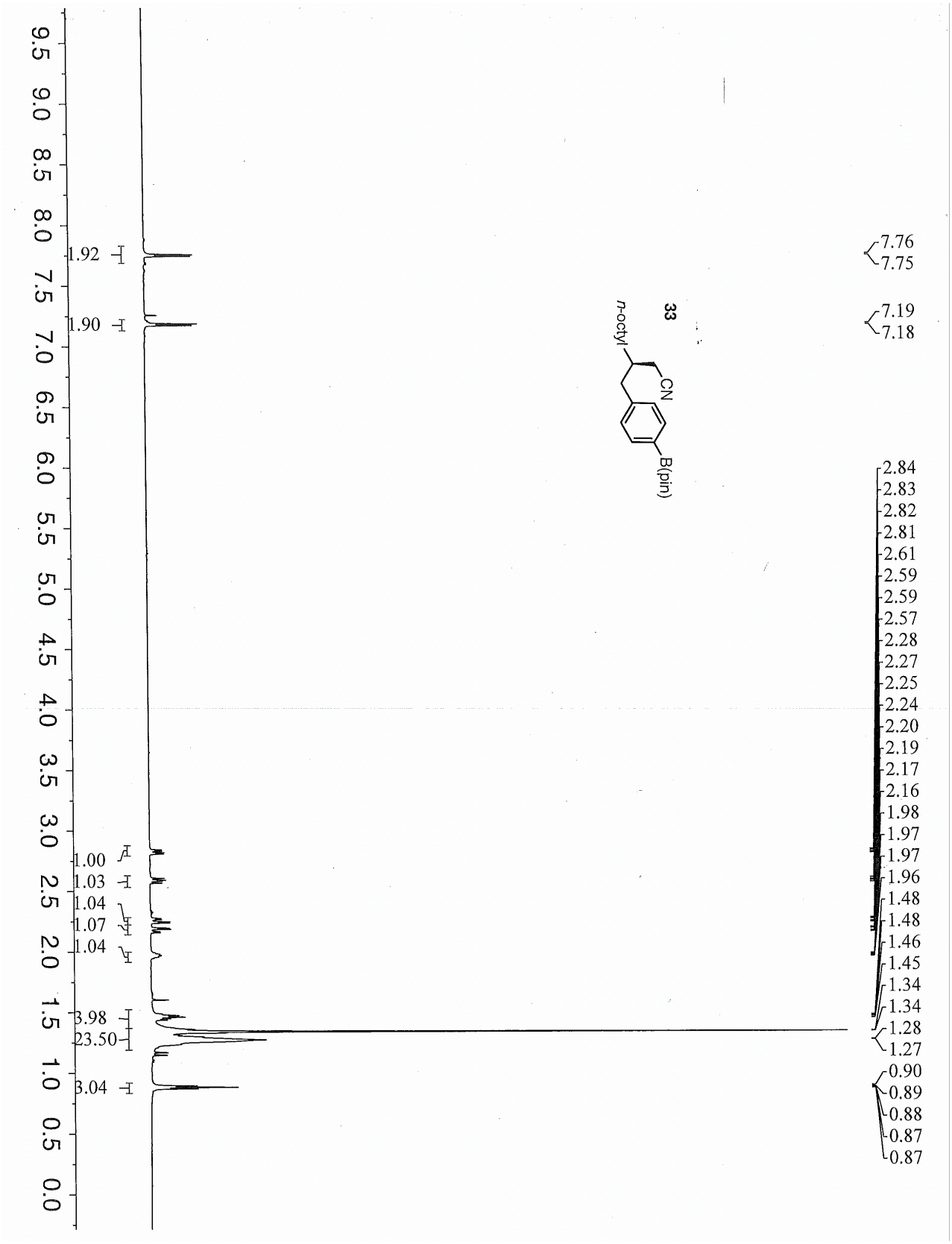
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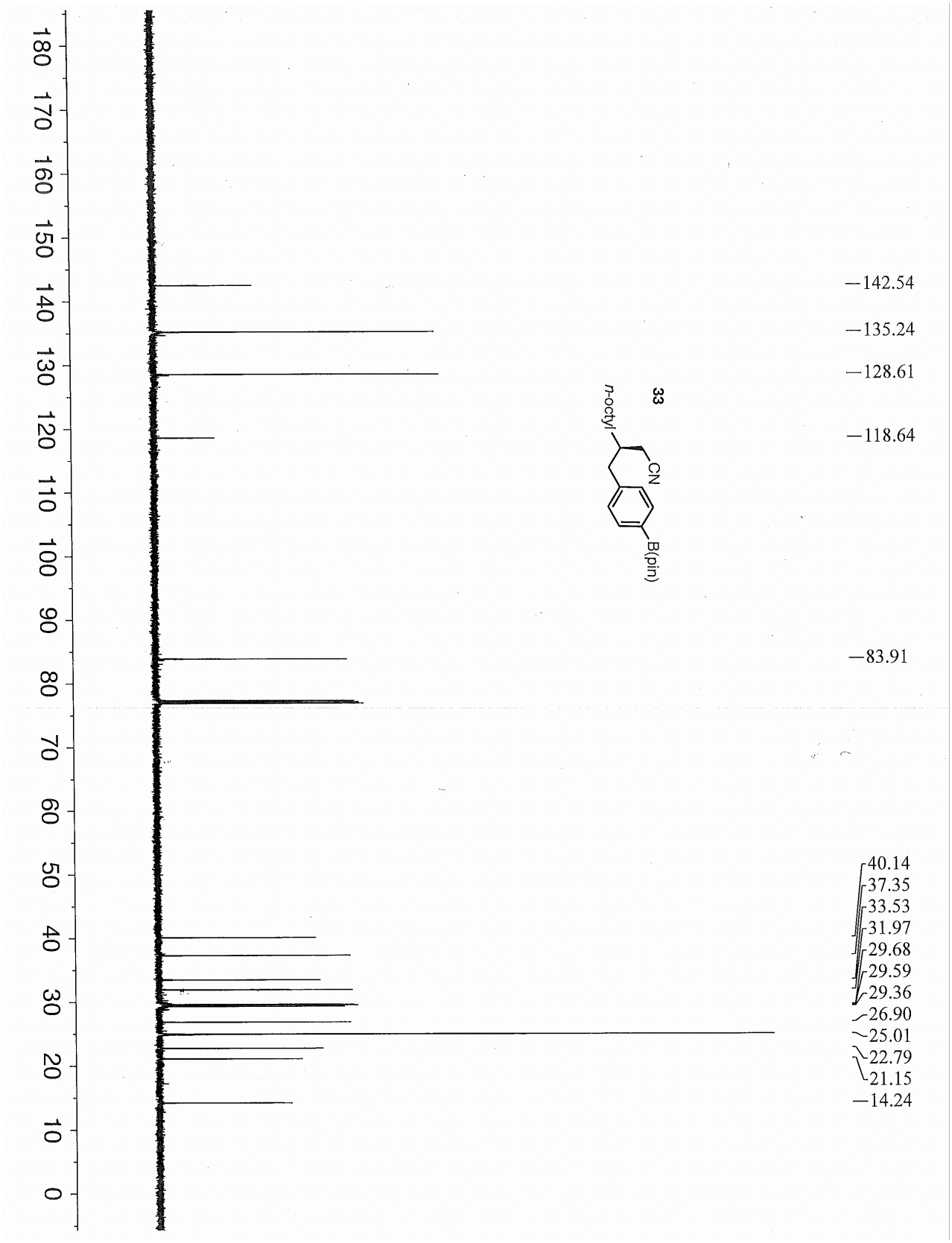
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CN
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22.79
21.15
14.24

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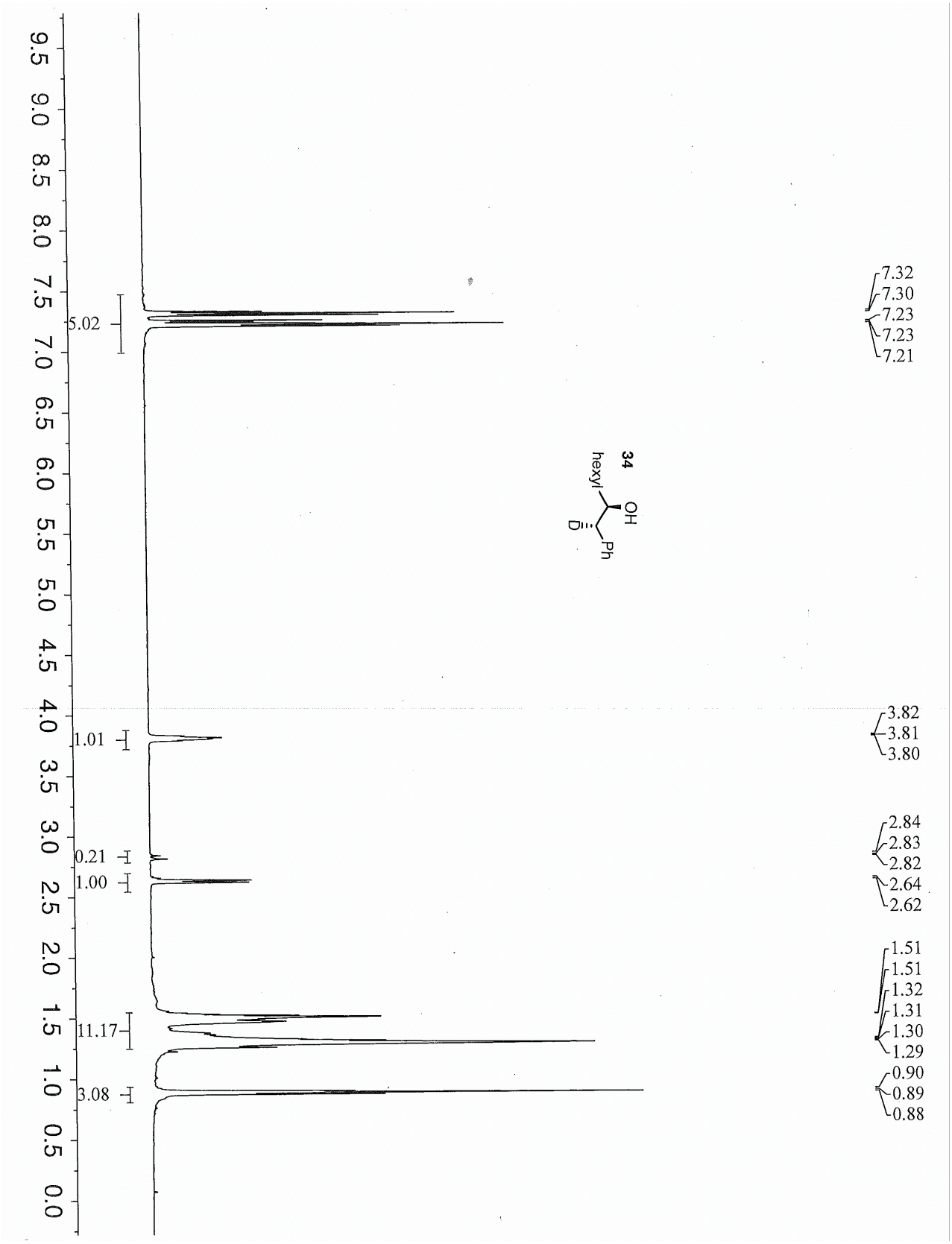
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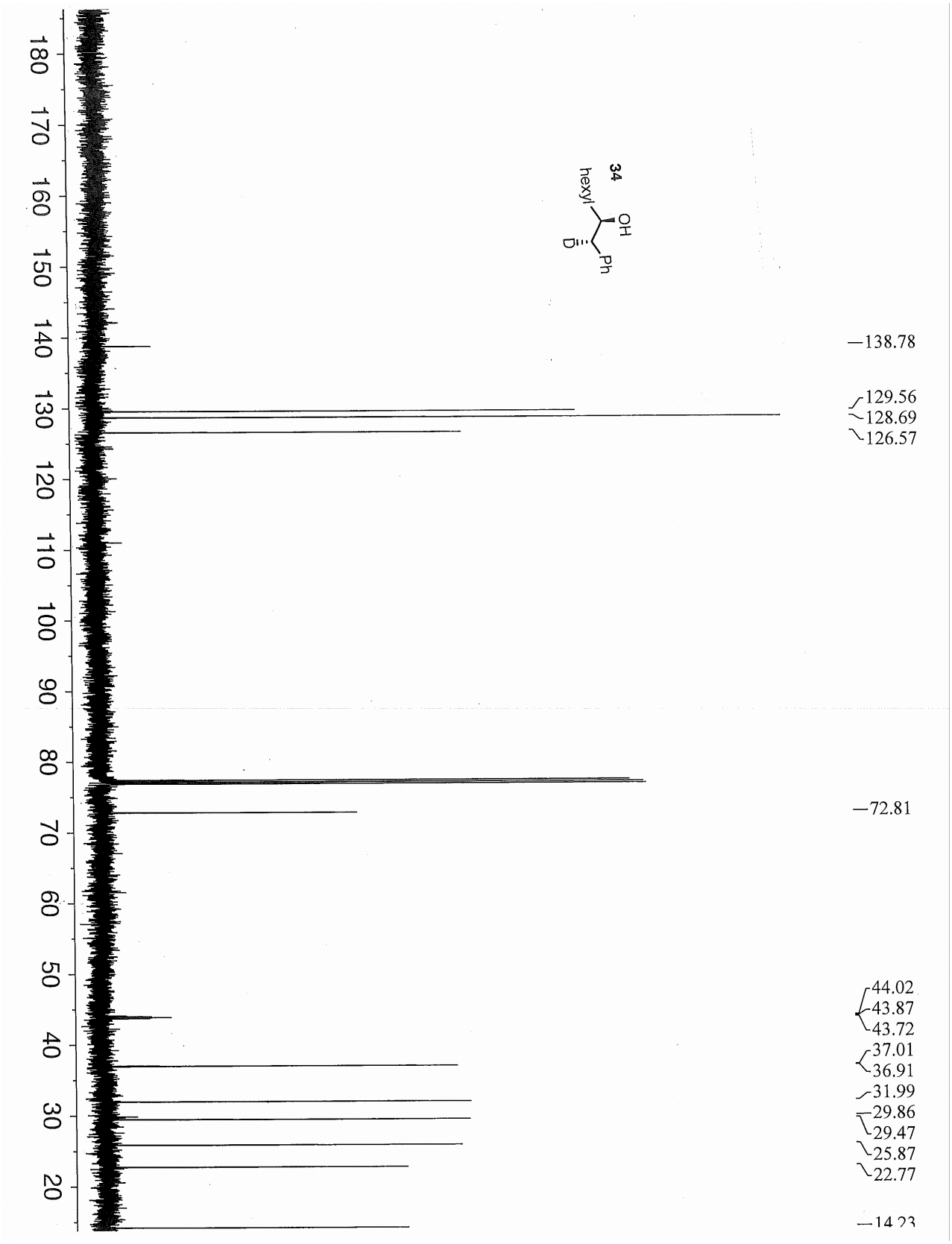
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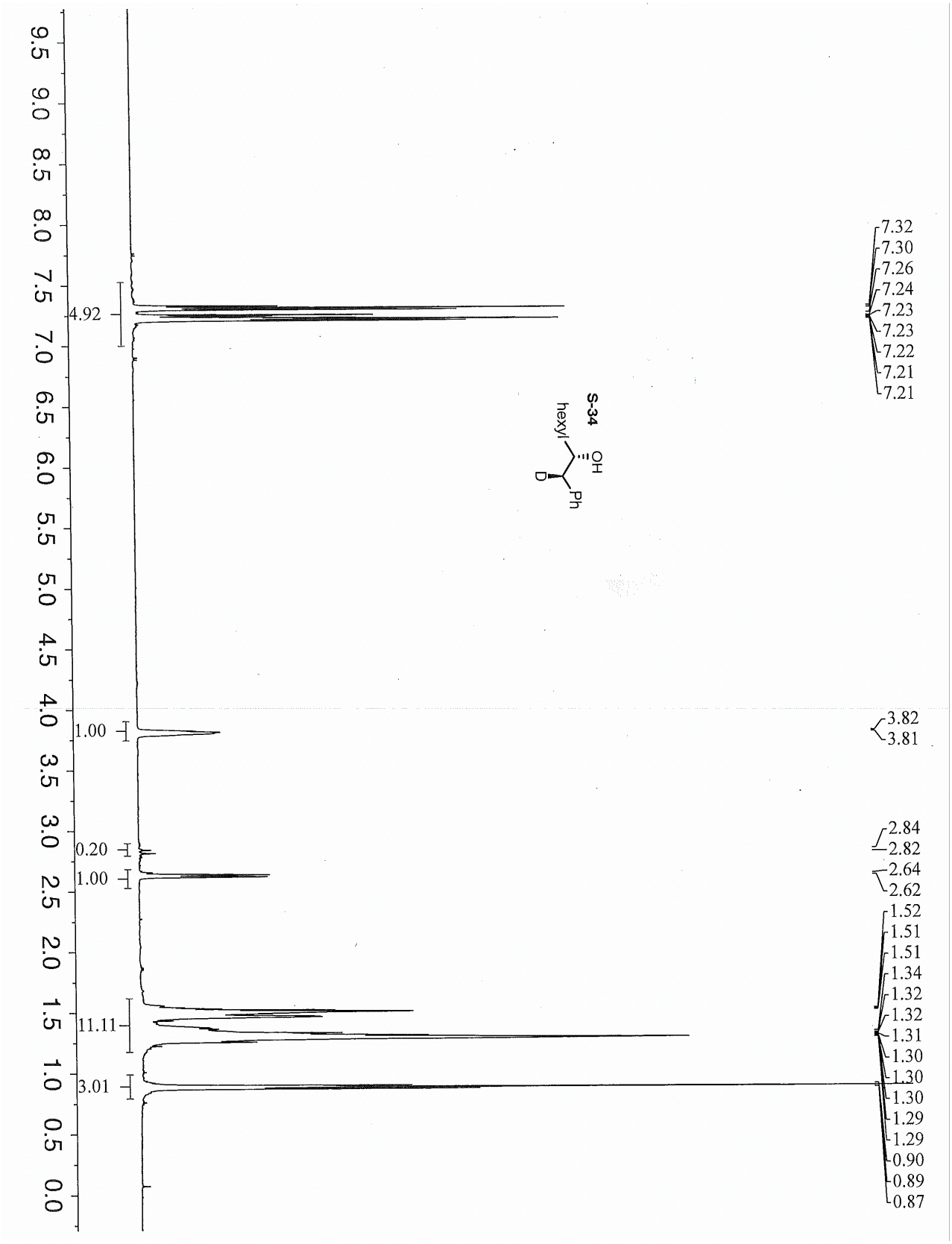
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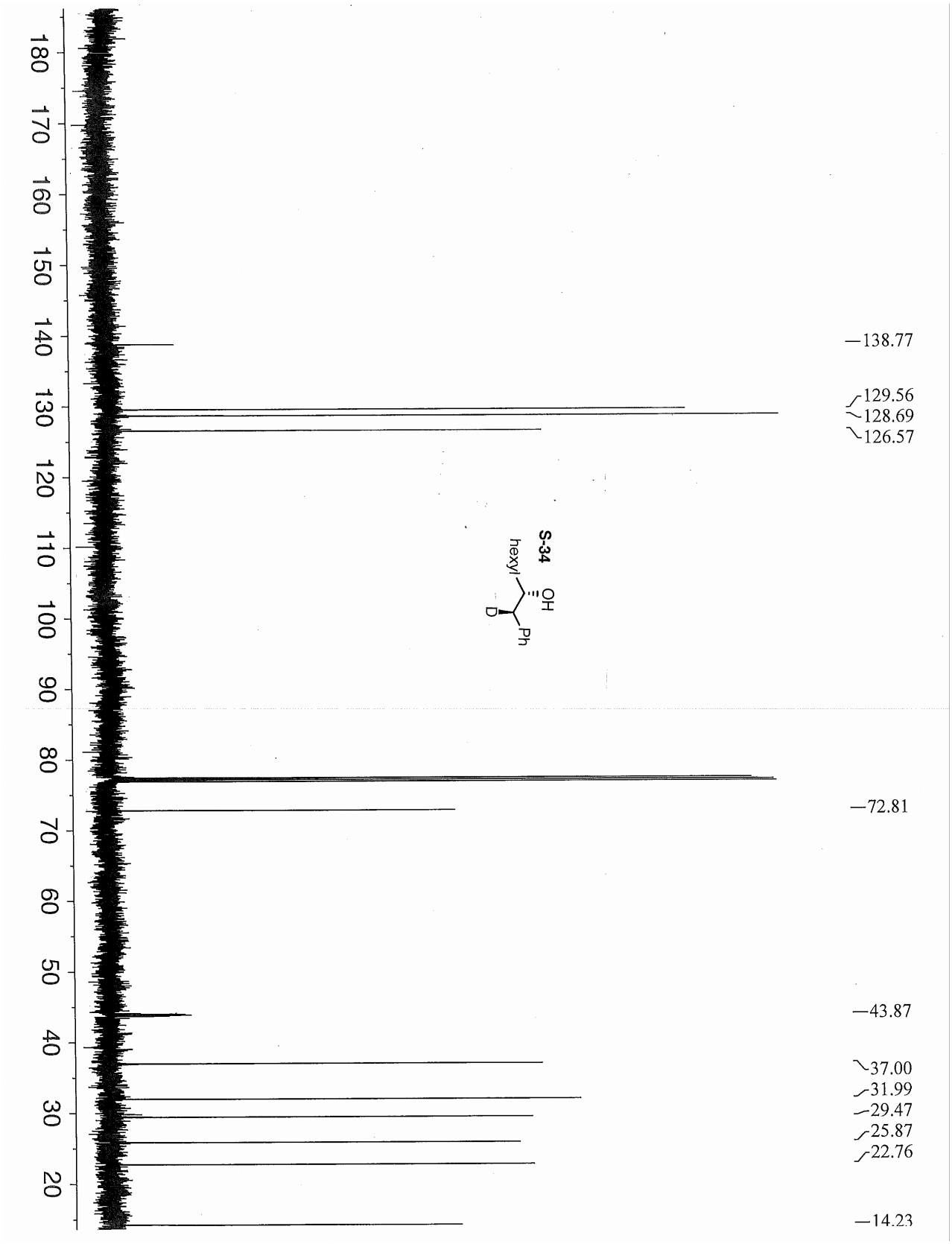
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CHAPTER 3

SYNTHESIS OF NON-RACEMIC ALKYLBORONATES BY NICKEL-MEDIATED RADICAL/ADDITION CROSS-COUPLING CASCADE

3.1 INTRODUCTION

Given the synthetic utility of non-racemic alkyl boronates, methods for their enantioselective synthesis are in high demand. To this end, our laboratory has developed a catalytic conjunctive cross-coupling reaction that merges an organolithium or Grignard reagent, an organoboron compound, and an organic electrophile to accomplish an enantioselective three-component conjunctive cross-coupling process, discussed in the first two chapters (Figure 3.1a).[1] The reaction is proposed to proceed from a four-

[1]Palladium catalyzed conjunctive coupling: (a) Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. *Science*, **2016**, *351*, 70. (b) Lovinger, G. J.; Aparece, M. D.; Morken, J. P. *J. Am. Chem. Soc*. **2017**, *139*, 3153. (c) Edelstein, E. K.; Namirembe S.; Morken, J. P. *J. Am. Chem. Soc*. **2017**, *139*, 5027. (d) Myhill,; J. A.; Wilhelmsen, C. A.; Zhang, L.; Morken, J. P. *J. Am. Chem. Soc.* **2018**, *140*, 15181. (e) Myhill, J. A.; Zhang, L.; Lovinger, G. J.; Morken, J. P. *Angew. Chem. Int. Ed*. **2018**, *57*, 12799.

coordinate vinyl boron 'ate', *via* a 1,2-metallate shift induced catalytically by complexation with a π-acidic transition metal. The initial system was developed using palladium catalysts which enabled enantioselective reactions with aryl, alkenyl or alkyl migrating groups, and aryl or alkenyl electrophiles. Meanwhile, the first system using nickel catalysis, discussed in chapter 2 of this manuscript, enabled the use of alkyl-9-BBN reagents with aryl halide electrophiles.[2a] Following the latter results, the Morken lab expanded on the nickel-catalyzed conjunctive coupling manifold by developing a system for the reaction of aryl boronic esters and alkyl electrophiles.[2b] This system provided enantiomerically enriched products using primary and secondary C(sp^3)-I reagents. However, only aryl migrating groups participated in the transformation. Despite the aforementioned advancements, the enantioselective addition of two alkyl components across an alkenylboron proved elusive, yet this would constitute a powerful tool for asymmetric synthesis. An additional limitation to the use of C(sp^3) electrophiles in conjunctive cross-coupling stems from the fact that highly hindered tertiary substrates do not participate in the transformation. Moreover, nearly concomitant reports by the groups of Studer[3] and Aggarwal[4] described a radical based system that enabled the addition of two alkyl fragments across an alkenylboron reagent, by using stabilized/electron-poor alkyl halides such as haloperfluoroalkanes and α-halocarbonyl compounds as sources of

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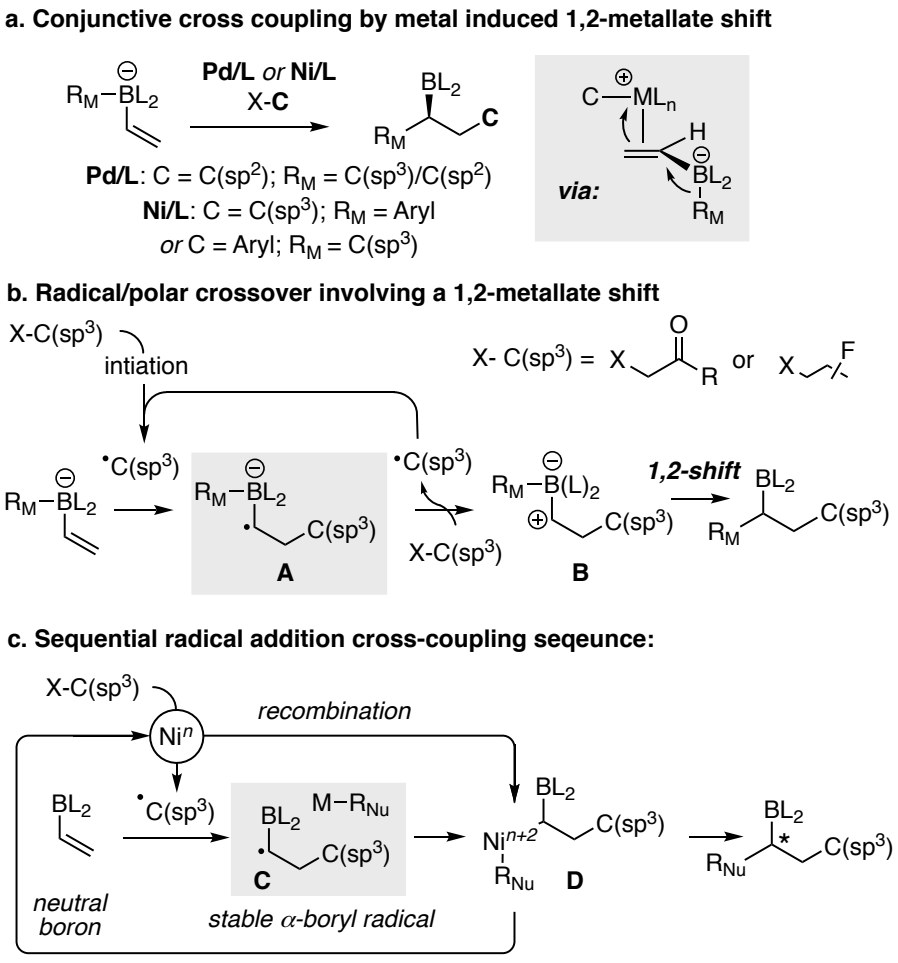
[2]Ni-catalyzed conjunctive coupling: (a) Chierchia, M.; C. Law, C.; Morken, J. P. *Angew. Chem. Int. Ed*. **2017**, *56*, 11870. (b) Lovinger, G. J.; Morken, J. P. *J. Am. Chem. Soc.* **2017**, *139*, 17293. (c) Law, C.; Meng, Y.; Koo, S. M.; Morken, J. P. *Angew. Chem. Int. Ed.* **2019**, *131*, 6726.

[3] (a) Kischkewitz, M.; Okamoto, K.; Mück-Lichtenfeld, C.; Studer, A. *Science* **2017**, *355*, 936. (b) Gerleve, C.; Kischkewitz, M.; Studer, A. *Angew. Chem. Int. Ed.* **2018**, *57*, 2441. (c) Kischkewitz, M.; Gerleve, C.; Studer, A. *Org. Lett.* **2018**, *20*, 3666.

[4] Silvi, M.; Sandford, C.; Aggarwal, V. K. *J. Am. Chem. Soc*. **2017**, *139*, 5736.

electrophilic radicals (Figure 3.1b). These species, upon homolytic cleavage, generate carbon-centered radicals that combine directly with an electron-rich, four-coordinate alkenylboron 'ate' complex to generate α-boryl radical species **A**. Radical anion **A** acts as a powerful oxidant, undergoing single electron transfer to alkyl halides, thus propagating the radical chain reaction and enabling a 1,2-metallate shift from intermediate **B**. Members of our group observed a similar reaction in nickel-catalyzed conjunctive coupling when using activated, electron poor alkyl halides.[2b] Contemporaneously n Renault[5] reported a related reaction.

Figure 3.1. Catalytic and enantioselective dialkylation of alkenyl boronates



[5] Tappin, N. D. C.; Gnägi-Lux, M.; Renaud, P. *Chem. Eur. J.* **2018**, *24*, 11498.

While the radical/polar cross-over transformations are highly efficient, the radical chain nature of the mechanism does not provide straightforward means of catalyst-based stereocontrol. However, noting the seemingly facile radical reaction between alkenylboron species and carbon centered radicals, we became interested in the possibility of harnessing this reactivity in a nickel-catalyzed system. Specifically, an α-boryl radical generated catalytically could recombine with a non-racemic nickel complex to establish an enantioselective transformation. To achieve this, however, recombination with nickel would have to outcompete SET and radical/polar cross-over. Thus, we envisioned a system whereby the organometallic nucleophile component and the vinylboron species would be introduced separately, obviating the possibility of radical/polar cross-over reactions. This proposal led to the implementation of a nickel mediated radical/addition cross-coupling cascade system (Figure 3.1c) in which a catalytically generated alkyl radical adds to an alkenylboronic ester to generate a neutral α-boryl radical **C**. This intermediate is trapped by a nickel catalyst to generate species **D** and is ultimately cross-coupled with an organozinc reagent, generating enantiomerically enriched alkylboron products through a stereoconvergent process. The transformation can be carried out both intermolecularly and intramolecularly, providing a complementary entry to conjunctive cross-coupling based methods for the enantioselective dialkylation of alkenylboronates.

3.2 BACKGROUND

3.2.1 α-Boryl radical synthesis, stability and reactivity.

Historically, several strategies have been employed to generate α-boryl radicals (Figure 3.2). Early reports involved the addition of radicals to alkenylboron species. These will be discussed in depth in the next section.[6] Alternatively α-boryl radical species could be readily accessed from α-halogenated borates through silicon and tin mediated halide abstraction.[7] Finally, formation of α-boryl radical species has been accomplished through C-H abstraction α to boron.[8] This reactivity was demonstrated mainly by means of radical bromination, and proclivity towards C-H abstraction by bromine radicals was found to decrease in the order of boranes > borinates > boronates.[9] Moreover, a recent report by Studer demonstrated that by using four-coordinate 'ate' species derived from boronic esters, hydride abstraction α to boron could be achieved efficiently by trifluoromethyl radicals.[10] The influence of boron atoms on adjacent carbon-centered radicals has been the subject of several mechanistic and computational studies.[11,7b]

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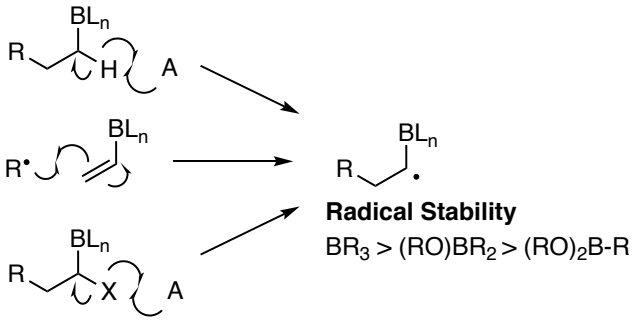
[6] Matteson, D. S. *J. Am. Chem. Soc.* **1960**, *82*, 4228.
[7] (a) Batey, R. A.; Pedram, B.; Yong, K.; Baquer, G. *Tetrahedron Lett.* **1996**, *37*, 6847. (b) Walton, J. C.; McCarroll, A. J.; Chen, Q.; Carboni, B.; Nziengui, R. *J. Am. Chem. Soc.* **2000,** *122,* 5455.
[8] (a) Lane, C. F.; Brown, H. C. *J. Am. Chem. Soc.* **1970**, *92*, 7212. (b) Pasto, D. J.; McReynolds, K. *Tetrahedron Lett*. **1971**, 801.
[9] Pasto, D. J.; Krasnansky, R.; Zercher, C. *J. Org. Chem.* **1987**, *52*, 3062.
[10] Wang, D.; Mück-Lichtenfeld, C.; Studer, A. *J. Am. Chem. Soc*. **2019**, *141*, 14126.
[11] (a) Matteson, D. S. *Prog. Boron Chem.* **1970**, *3*, 117 (b) Grotewold, J.; Lissi, E. A.; Scaiano, J. C. *J. Organomet. Chem.* **1969**, *19*, 431. (c) Lane, C. F.; Brown. H. C. *J. Am. Chem. Soc.* **1970**, *92*, 7212. Grotewold, J. E.; Lissi, E. A.; Scaiano, J. C. *J. Chem. Soc. B* **1971**, 1187. (d) Pasto, D. J. *J. Am. Chem. Soc.* **1988**, *110*, 8164. (e) Coolidge, M. B.; Borden, W. T. *J. Am. Chem. Soc.* **1988**, *110*, 2298. (f) Henry, D. J.; Parkinson, C. J.; Mayer, P. M.; Radom, L. J. *Phys. Chem. A* **2001**, 105, 6750.

Figure 3.2. General strategies for the generation of α-boryl radicals



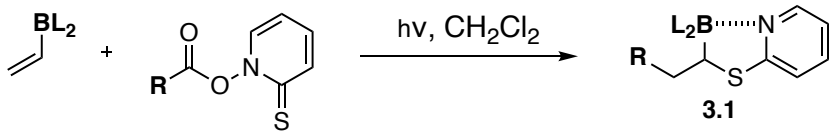
It is generally understood that resonance with the empty p orbital of boron provides a stabilizing effect, the extent of which can vary greatly depending on the nature of the substituents on the boron atom. Atoms capable of donating electrons into boron's empty p-orbital should diminish boron's ability to stabilize vicinal radicals. Thus, as oxygen ligands are added to boron, radical stability is proposed to decrease in the order boranes > borinates > boronates. This trend has been generally supported by experimental and theoretical studies, through which rough estimates of radical stabilization have been determined. Studying the kinetics of gas phase bromination of triethyl borane, Scaiano estimated the BDE of the C-H bond adjacent to boron to be about 80 kcal/mol.[11b] Meanwhile, several computed estimates provide BDE values of about 94-95 kcal/mol (10-11 kcal/mol stabilization) for C-H bonds of methyl boranes such as $H_2B(CH_2\text{-}H)$ and $(Me)_2B(CH_2\text{-}H)$.[7b, 11d-f] Finally, the stabilization provided by boronic esters was calculated by Carboni, who estimated the C-H BDE of $(MeO)_2B\text{-}CH_2\text{-}H$ to be between 98.1-98.7 kcal/mol revealing a rather modest, although not insignificant radical stabilization energy.[7b] Moreover, in these studies Carboni noted that the polarization of the π electrons in vinylboronic esters, resulting from delocalization with boron's p-orbital, played an important role in favoring radical reactions with electron rich silyl and tin based radicals.

3.2.2 Radical additions to neutral alkenylboron species.

Since the earliest studies by Matteson[6] on atom transfer/radical additions to alkenylboronic esters, a number of transformations elaborating on this manifold have been reported. Carboni and coworkers[12] studied the intra- and intermolecular addition of carbon centered radicals to alkenylboranes and boronic esters, highlighting important differences in reactivity between the two. Alkyl radicals were generated either by reactions with alkyl iodides and AIBN/$(Bu)_3SnH$, or through photolysis of O-acyl derivatives of N-hydroxypyridine-2-thione. The reaction outcomes were highly variable (Table 3.1): intermolecular reactions of primary and secondary radicals with vinylB(pin) were found to proceed with much lower efficiency than those of tertiary radicals (entries 2, 3 vs entry 1), while reactions with vinyl(BBN) reagents proceeded efficiently regardless of the substitution on the carbon centered radicals (entries 4,5).

[12] Guennouni, N.; Lhermitte, F.; Cochard S.; Carboni, B. *Tetrahedron* **1996**, *51*, 6999.

Table 3.1. Radical addition on vinylboron by Carboni

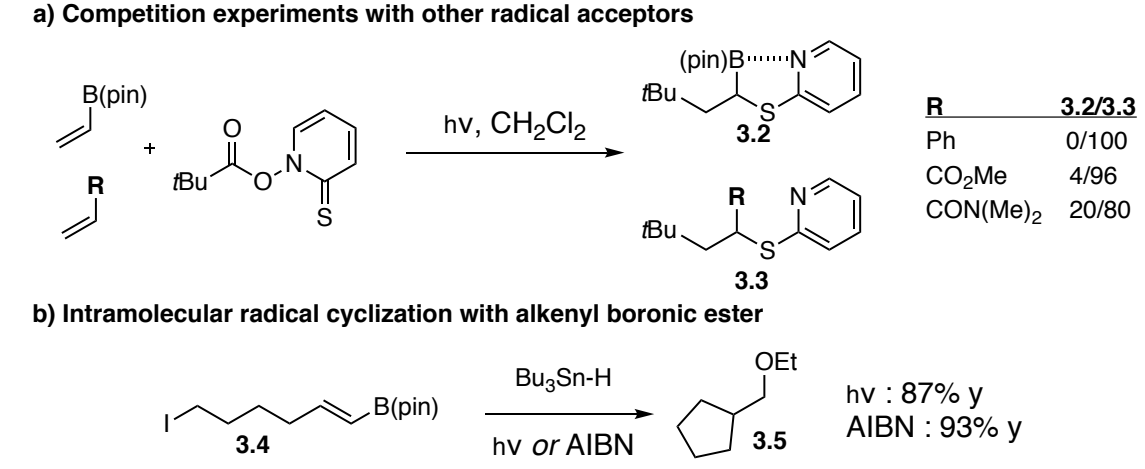


3.1

Entry	BL_2	R	Yield
1	B(pin)	*t*-Bu	58
2	B(pin)	Cy-Hex	36
3	B(pin)	$PhCH_2CH_2$	32
4	9-BBN	*t*-Bu	78
5	9-BBN	Cy-Hex	68

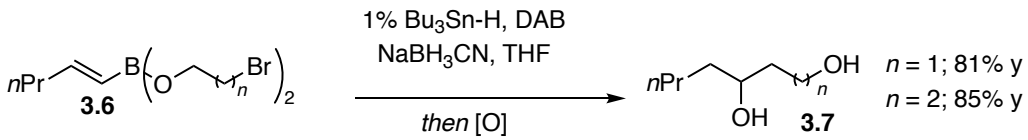
Furthermore, competition studies revealed that boronic esters were generally less efficient radical acceptors than acrylates, acrylamides and styrene (Figure 3.3a). Moreover, intramolecular radical addition to alkenyl boronic esters and boranes proceeded efficiently through 5-exo-trig cyclization in all cases studied (Figure 3.3b). Through these studies it appears that polarity matching and stability of α-boryl radicals are important driving forces in radical addition processes.

Figure 3.3. Radical addition studies by Carboni.



In a later work by Batey, an intramolecular radical cyclization of alkenylboronates with boron tethered alkyl halides provided 1,3- and 1,4- diols (Figure 3.4).[13] The substrates in the reaction underwent 5-exo-trig cyclizations forming β-boryl radicals. Here, the polarization of the alkene and the resonance stabilization provided by the boronic ester at the alpha position appear insufficient to bias the cyclization towards a less favorable 6-endo-trig.[14]

Table 3.4. Batey intramolecular radical cyclization



[13] Batey, R. A.; Smil, D. V. *Angew. Chem. Int. Ed.* **1999**, *38*, 1798.
[14] Bechwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073

In 2014, Baran[15] disclosed a method for hydroalkylation of functionalized olefins by hydrogen atom transfer (HAT) from a catalytically generated iron-hydride species (Figure 3.5). The HAT takes place preferentially between the more electron-rich alkene substrate and the iron-hydride. The resulting alkyl radical is trapped by an electron-poor olefin, generating an electrophilic radical that is subsequently reduced to an anion. The substrates that participate as HAT acceptors include alkenyl-B(pin) (**3.8**, **3.11**, **3.12**), B(dan) (**3.10**, **3.13**), and B(mida) (**3.9**) compounds, which were coupled to acrylates and acrylamides. In the examples shown, reactions with the more electron rich B(dan) species were most efficient, although according to the authors the alkeneylB(mida) suffered from poor solubility. Moreover, the effective participation of alkenylB(pin) in this process underlines once more that the electrophilicity/reduction potential associated with radicals α to boronic esters is less than that of α-carbonyl radical species.

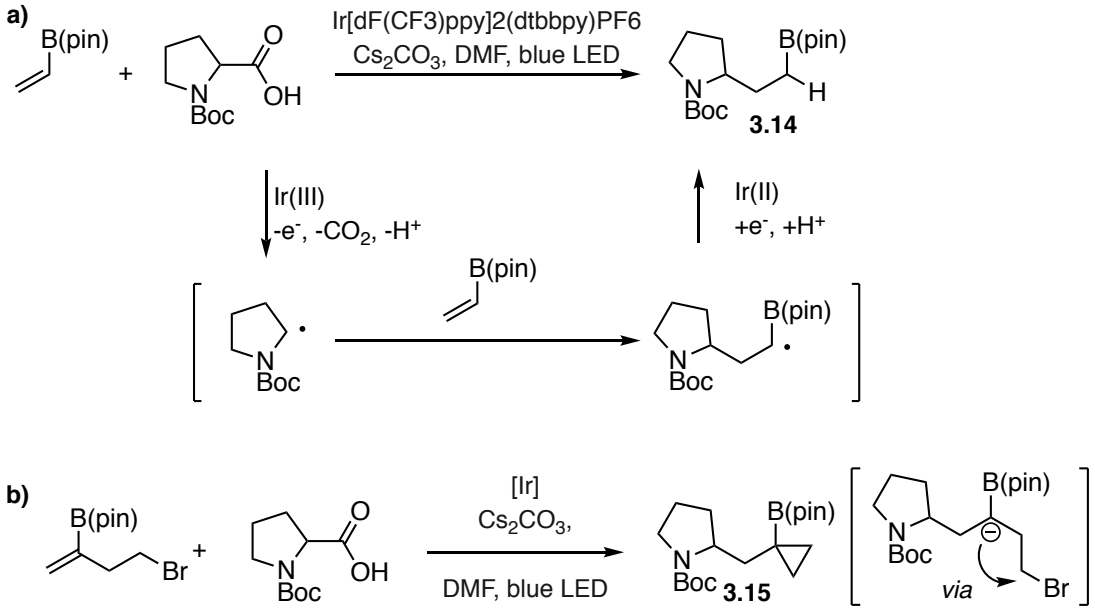
Recently, Aggarwal reported on the decarboxylative addition of carbon-centered radicals to neutral alkenylB(pin) species enabled by photoredox catalysis (Figure 3.6a).[16] In this system, a photochemically excited Ir catalyst generates a radical from an alkyl-carboxylic acid through single electron oxidation. The radical species thus formed adds to a vinylboron to produce an α-boryl radical that is then reduced the corresponding anion by the photocatalyst, reinitiating the catalytic cycle (Figure 3a). Attempts to trap the resulting anion with an electrophile materialized in a subsequent report for the synthesis of functionalized cyclopropanes through radical addition/polar cyclization cascade

[15] Lo, J. C.; Gui, J.; Yabe, Y.; Pan, C. -M. ; Baran, P. S. *Nature* **2014**, *516*, 343.

[16] Noble, A.; Mega, R. S.; Pflästerer, D.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2018**, *57*, 2155.

(Figure 3a).[17] In these systems, reactions with vinylboronates proceeded most efficiently with highly nucleophilic secondary/tertiary alkyl radicals possessing activating α-amine or α-oxygenated functionalities. The only examples involving primary alkyl radicals were carried out with acrylates instead of vinylboronates as radical acceptors.

Figure 3.6. Aggarwal's photoredox enabled decarboxylative radical addition.

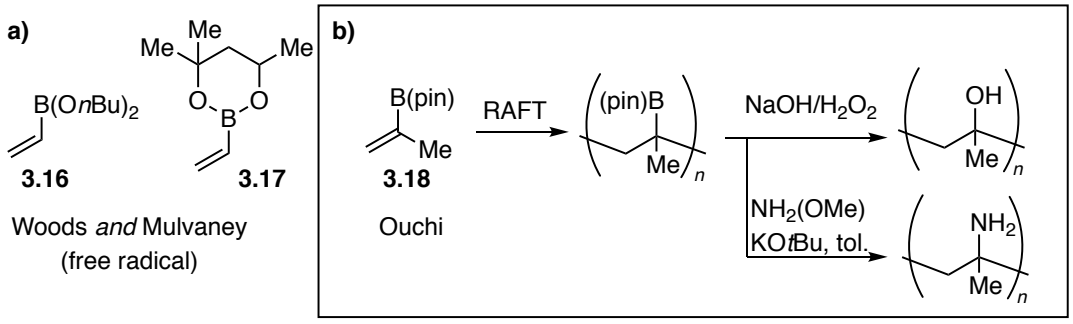


Radical polymerizations of alkenylboron species have also been reported in the literature. Most examples of this reaction have focused on polymerization of vinyl-azaborenes, which function as tunable isosteres of styrene monomers.[18] Klausen highlighted the possibility of tuning the hydroxyl content in azaborene polymers/copolymers through oxidation of the BN ring.[19] Examples of polymerization of

[17] Shu, C.; Mega, R. S.; Andreassen, B. J.; Noble, A.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2018**, *57*, 15430.
[18] For a review: Van De Wouw, H. L.; Klausen, R. S. *J. Org. Chem*. **2019**, *84*, 1117
[19] Van De Wouw, H. L.; Lee, J. Y.; Awuyah, E. C.; Klausen, R. S. *Angew. Chem. Int. Ed.* **2018**, *57*, 1673.

boronic esters are more limited. Early studies on polymerization of vinylboronic esters **3.16** and **3.17** (Figure 3a) were reported by Woods and Mulvaney using free radical polymerization (AIBN/heat).[20] It was found that vinylboronic ester **3.16** cross-linked rapidly upon exposure to oxygen, presumably due to hydrolysis of the labile ligands on boron, while **3.17** generated low molecular weight polymers. Copolymerization was also undertaken between monomer **3.17** and acrylonitrile, styrene, or methyl methacrylate. The reactivity of **3.17** towards copolymerization was found to decrease in the order of acrylonitrile > MMA > styrene. Very recently, Ouchi reported an efficient radical polymerization of isopropenylB(pin) by RAFT radical polymerization.[21] Here, radical stabilization by the empty p-orbital is proposed to provide the driving force in the transformation, as vinylB(mida) did not polymerize under the reaction conditions. The polymerization products could be quantitatively oxidized, and partially aminated.

Figure 3.7. Alkenylboronic esters in radical polymerization

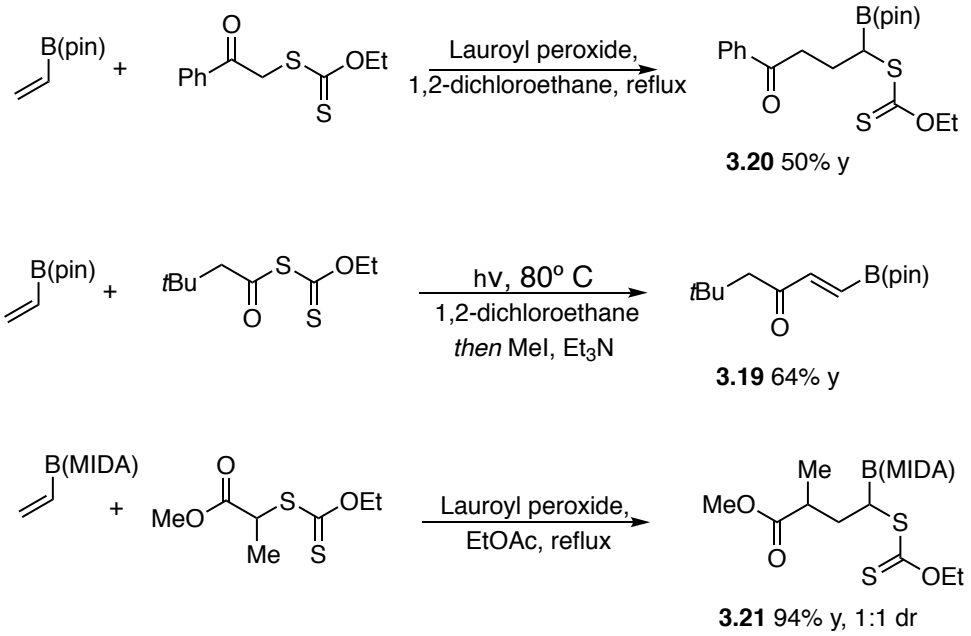


Other instances of radical additions to neutral alkenylboron species include examples by Zard, as part of his studies on Kharasch type atom transfer radical addition

[20] Woods, W. G.; Bengelsdorf, I. S.; Hunter, D. L. *J. Org. Chem.* **1966**, *31*, 2766. (b) Mulvaney, J. E.; Ottaviani, R. A.; Laverty, J. J. *J. Poly. Sci. Poly. Chem. Ed.* **1982**, *20*, 1949.
[21] Nishikawa, T.; Ouchi, M. *Angew. Chem. Int. Ed.* **2019**, *58*, 12435.

using organoxanthates (Figure 3.8a,b).[22] Zard's early examples of this reaction manifold showed the addition of acyl radicals across vinylB(pin) (Figure 3.8b). These reactions proceeded by the addition of the xanthate and acyl moiety which, after elimination of the former, provided corresponding alkenylboron compounds containing a γ-carbonyl group. Prior to this report, the authors had shown two examples of this reaction using alkyl-xanthates with vinylB(pin), which proceeded in moderate yield (Figure 3.8a).

Figure 3.8. Zard's Karasch-type ATRA reaction with vinylboronates



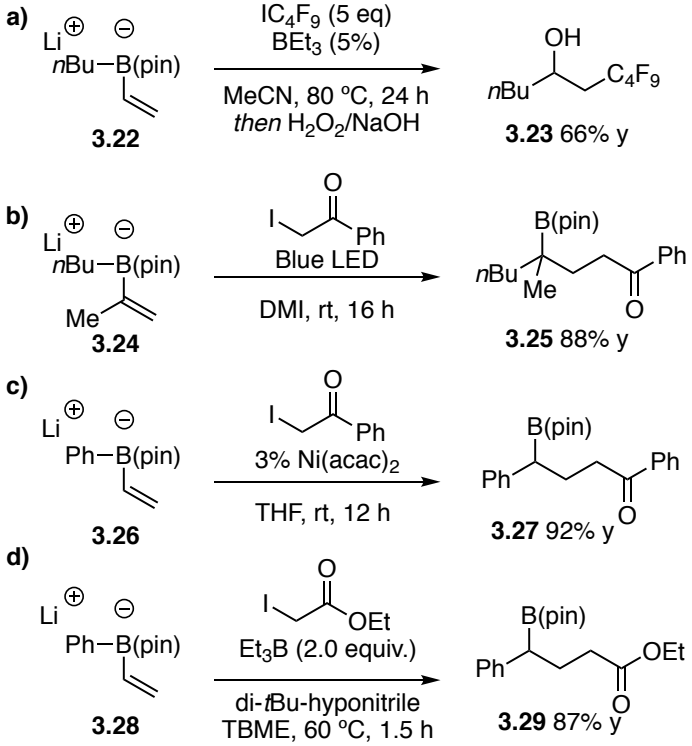
[22] (a) Heinrich, M. R.; Sharp, L. A.; Zard, S. Z. *Chem. Commun*. **2005**, *4*, 3077. (b) Lopez-Ruiz, H.; Zard, S. Z. *Chemical Communications* **2001**, *24*, 2618.

3.2.3 Radical additions to anionic alkenylboron 'ate' species.

Later on, Zard expanded on this reaction scaffold by taking advantage of the electronic tunability of vinylboronates through the use of different ligands on boron (Figure 3.8). Employing vinylB(MIDA) as a radical acceptor, atom transfer radical addition reactions (ATRA) with several electron poor alkyl xanthates are carried out efficiently across several substrates.[23] The authors argue that use of four-coordinate boron 'ate' destabilizes the α-boryl radical with respect to the initial alkyl radical, thus favoring propagation of the radical chain reaction in the xanthate exchange step. Moreover, they also point to polarity matching between more electron rich vinylboronates and electron poor alkyl radical species as a factor that kinetically favors the desired reactivity.

[23] Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2015**, *137*, 6762.

Figure 3.9. Radical/polar cross-over reactions with vinyl boron 'ate' species



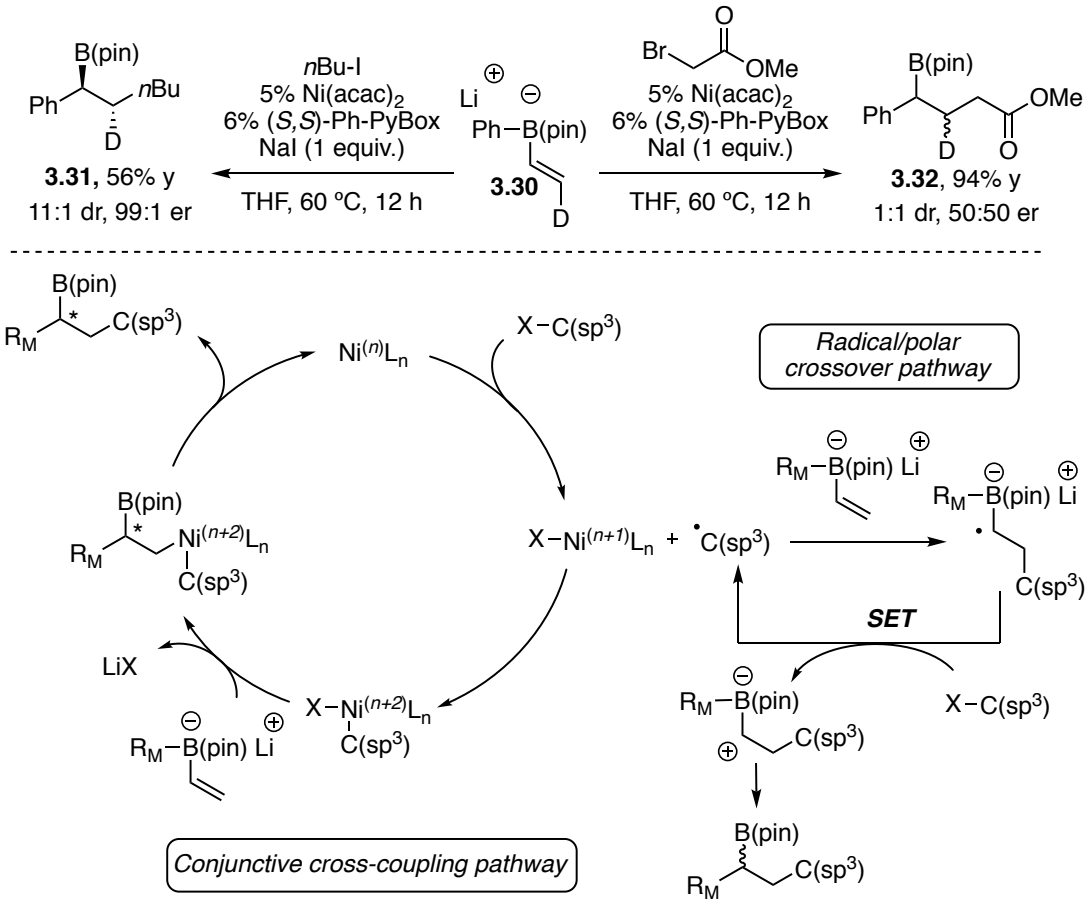
Finally, as mentioned in the introductory section of this chapter, nearly contemporaneous reports by Studer, Aggarwal, Morken and Renaud disclosed radical/polar cross-over methods in which carbon-centered radicals add to a vinyl boron 'ate' species, triggering 1,2-metallate shift (Figure 3.9a-c). The first of a series of reports by Studer[3] (Figure 3.9a) showed that, under radical initiation conditions, several activated/electron-poor alkyl iodides would add to alkenylboron 'ate' species derived from the combination of organolithium and organoboronic acid pinacol esters. The ensuing α-boryl radical anion propagates the radical chain by undergoing a single electron transfer with a second alkyl iodide, thus oxidizing the boron species and triggering a 1,2-metallate shift (the general mechanism is illustrated in Figure 3.1b in the introductory segment). This first report was rapidly followed by Aggarwal's (Figure

3.9b) who showed that the same reaction could be initiated with photoredox catalysis.[4] In their mechanistic proposal, however, the radical/polar cross-over reaction was postulated to occur through oxidation of the α-boryl radical by the photocatalyst, rather than through a radical chain process (although the latter is acknowledged as a possibility). Later on, Renaud disclosed a system to promote the same process (Figure 3.9d).[5] This report included mechanistic experiments that lended credence to Studer's earlier proposal. Overall, these radical/polar cross-over processes appear to be kinetically driven through the use of electronically matched substrates, with electron poor alkyl halides reacting with electron rich alkyl boron 'ates'. Moreover, the ease of oxidation of the anionic α-boryl radical combined with the use of electronically activated alkyl iodides with high reduction potentials ultimately enables propagation of the radical chain.

Finally, our group encountered the radical/polar cross-over mode of reactivity while exploring nickel-catalyzed conjunctive cross-coupling reactions with alkyl iodide electrophiles (Figure 3.9c).[2b] In this study, it was found that while reactions with unactivated alkyl iodides proceeded enantioselectively using a Ni/pyBox catalyst system, reactions with activated/electron-poor alkyl iodides provided entirely racemic products. In fact, these reactions were found to proceed efficiently in the absence of ligands and at room temperature. Deuterium labeling studies revealed that the enantioselective reactions proceeded stereospecifically with *anti*-addition of the electrophile and the migrating group across the alkene, thus outlining a process consistent with our previous conjunctive cross-coupling proposals (Figure 3.10).[1] However, reactions with activated alkyl-iodides proceeded through a non-stereospecific mechanism in line with outer-sphere radical recombination. The latter reactions were therefore proposed to take place through a

radical chain reaction with polar cross-over mechanism as outlined in the Studer/Aggarwal/Renaud reports (Figure 3.10, bottom). The reactivity switch observed in the conjunctive system highlights the large impact that using polarity matched substrates has in determining the favored reactivity pathway, given that both pathways involve radical intermediates but the unactivated alkyl iodides used in this system recombine preferentially with the nickel catalyst, while electrophilic radicals react directly with vinyl boron.

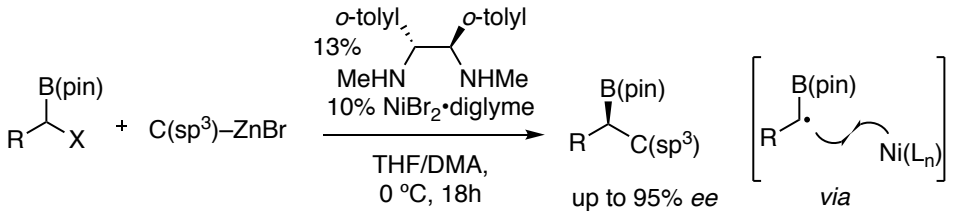
Figure 3.10. Conjunctive coupling to radical/polar cross-over mechanistic switch



3.2.4 α-Boryl radicals in enantioselective catalysis.

A very small number of catalytic enantioselective methods that invoke the intermediacy of an α-boryl radical have been reported. The earliest one was developed by Fu who described stereoconvergent cross-couplings of racemic α-haloboronates (Figure 3.11).[24] Although no mechanistic studies are provided, the work builds upon Fu's nickel-catalyzed stereoconvergent cross-coupling with racemic alkyl halides. Thus, α-haloboronates are proposed to undergo a single electron transfer with the catalyst to generate an α-boryl radical species that subsequently recombines with the chiral catalyst. The latter then orchestrates the coupling with an alkylzinc bromide.

Figure 3.11. Fu's stereoconvergent Negishi coupling of α-haloboronates



The reaction uses $NiBr_2$•diglyme combined with an aliphatic diamine ligand to effect enantioselective cross-couplings that display broad functional group tolerance. α-Bromo, α-chloro- and α-iodoborates all participate in the reaction. By using a weak organometallic nucleophile, the system avoids the 1,2-metallate shift mode of reactivity, providing a catalytic enantioselective alternative to the asymmetric Matteson homologation and other lithiation borylation strategies, all which require use of stoichiometric non-racemic reagents. The main pitfall of this reaction is that it requires

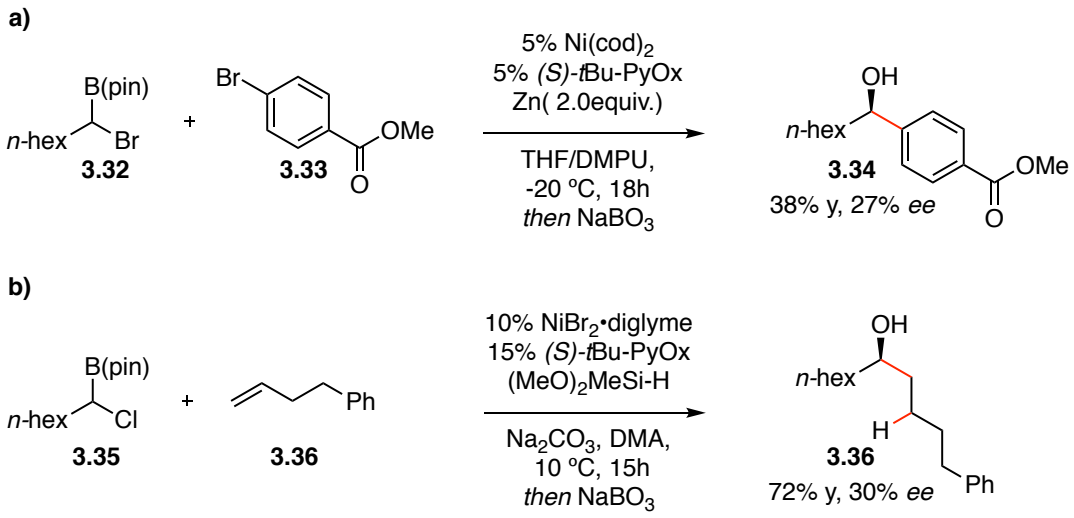
[24] Schmidt, J.; Choi, J.; Liu, A. T.; Slusarczyk, M.; Fu, G. C. *Science* **2016**, *354*, 1265.

synthesis of α-haloboronate starting materials, which can require multiple steps that usually involve the addition of organolithium or Grignard reagents to a boronic ester. Martin and coworkers later reported on a reductive coupling version of Fu's method, coupling α-haloboronates with arylhalides using zinc metal as the stoichiometric reductant (Figure 3.12a). [25] The reaction was carried out using achiral 4,4'-dimethoxybipyridine and delivered racemic products. However, a reaction with *t*Bu-PyOx as ligand generated the corresponding products in modest yield and enantioselectivity, showing the potential for stereoinduction in this method. Shortly after, Martin reported the hydroalkylation of unactivated olefins that also made use of α-haloboronates as cross-coupling partners (Figure 3.12b).[26] This reaction could be used for the remote functionalization of internal alkenes which took place through chain walking of the nickel catalyst. Moreover, the authors showed preliminary results for a stereoconvergent version of the reaction, which proceeded with modest enantioselectivity using *t*Bu-PyOx as a ligand.

[25] Sun, S.-Z.; Martin, R. *Angew. Chem. Int. Ed.* **2018**, *57*, 3622.

[26] Sun, S.-Z.; Börjesson, M.; Martin-Montero, R.; Martin, R. *J. Am. Chem. Soc.* **2018**, *140*, 12765.

Figure 3.12. Martin's preliminary result on stereocovergent couplings of α-haloboronates

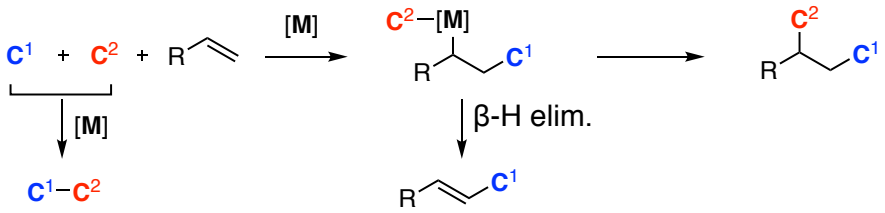


3.2.5 Metal-catalyzed dicarbofunctionalization of olefins

The reaction design proposed in this chapter falls in line with a particular category of cross-coupling processes consisting of metal catalyzed dicarbofunctionalizations of olefins.[27] These reactions take place through the catalytic addition of a carbon fragment and a transition-metal across an olefin, resulting in formation of a C(sp^3)-[M] intermediate that is subsequently cross-coupled with a second organic moiety (Figure 3.13).

[27] For a review: Dhungana, R. K.; Kc, S.; Basnet, P.; Giri, R. *Chem. Rec.* **2018**, *18* , 1314.

Figure 3.13. Metal-catalyzed dicarbofunctionalization

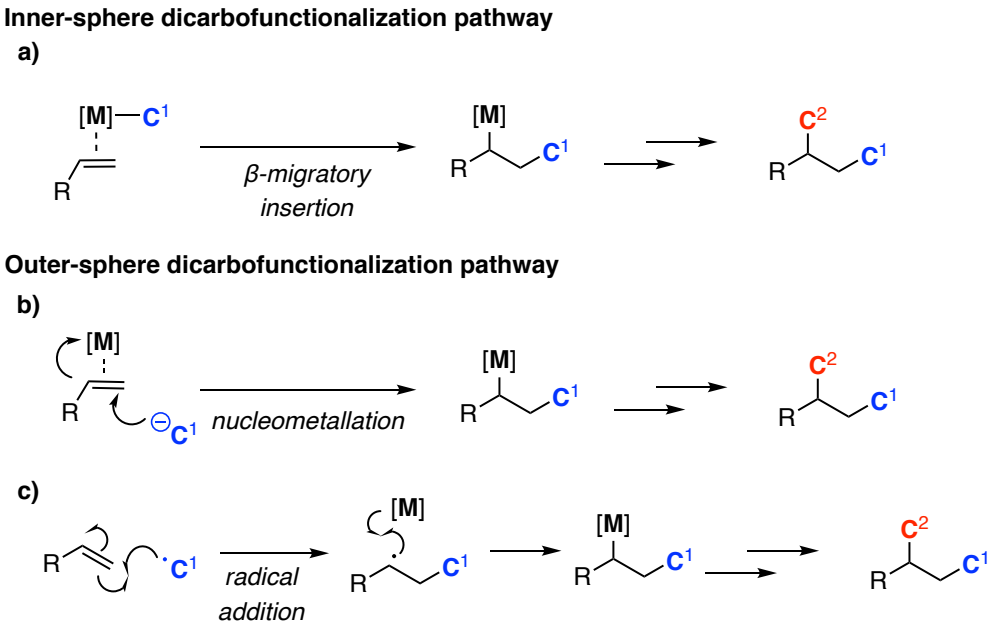


In principle, systems for vicinal difunctionalization are appealing due to the modularity and complexity building capabilities inherent to three-component systems. However, the development of these methods is generally challenging due to the fact C(sp^3)-[M] are prone to undergo β-hydride elimination. In addition, as it is often the case in three-component reactions, olefin difunctionalization has to outcompete direct cross-coupling between two of the organic fragments. Throughout the years, several strategies utilizing Pd, Ni, Pt, Ir, Rh, Mn, Cr, Co catalysis, have been adopted to overcome these challenges and accomplish catalytic dicarbofunctionalizations.[27]

These reactions can be further categorized by their mechanisms of carbometallation, which may involve inner-sphere or outer-sphere processes (Figure 3.14). Inner-sphere carbometallation can take place through the β-migratory insertion of an organometallic species, forming Heck-type intermediates, which instead of undergoing β-hydride elimination, are cross-coupled with an organometallic nucleophile or an organic electrophile depending on the system (Figure 3.14a). Alternatively, an outer-sphere carbometallation can take place through addition of a nucleophile onto a catalytically-activated alkene (Figure 3.14b). Conjunctive cross-coupling can be included in this category. Finally, an outer-sphere carbometallation mechanism may occur through the addition of a carbon centered radical to an olefin, followed by recombination of the

newly generated radical with a transition metal catalyst (Figure 3.14c). The method described herein falls within this category of radical addition/cross-coupling cascade.

Figure 3.14. Mechanistic pathways for metal catalyzed dicarbofunctionalization



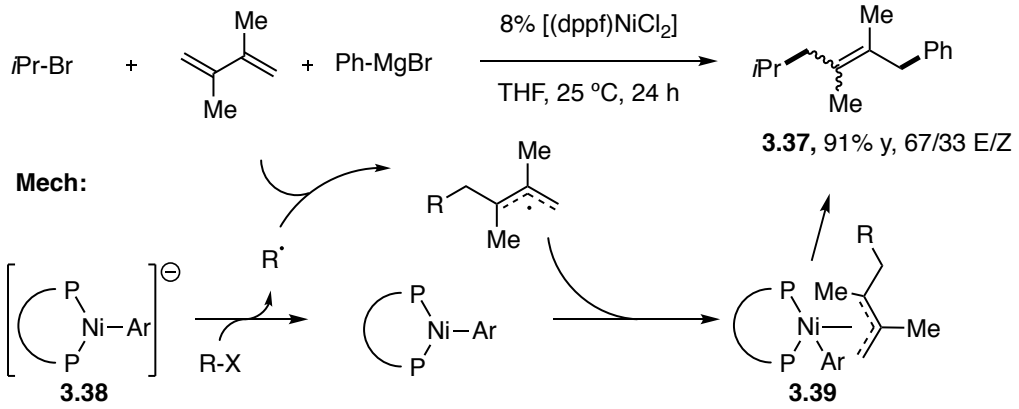
3.2.6 Nickel-catalyzed dicarbofunctionalization with alkyl electrophiles.

The vast majority of nickel-catalyzed dicarbofunctionalization of olefins using alkyl electrophiles rely on one-electron reactions and therefore generally proceed by outer-sphere radical addition/cross-coupling cascades. One of the earliest methods based on this mechanism, consisting of a 1,4-aryl-alkylation of dienes, was reported in 2002 by Kambe.[28] Capitalizing on Ni's propensity to effect single electron transfer with alkyl

[28] Terao, J.; Nii, S.; Chowdhury, F. A.; Nakamura, A.; Kambe, N. *Adv. Synth. Catal.* **2004**, *346*, 905.

halides, Kambe developed a three component coupling between alkyl halides, dienes, and Grignard or organozinc reagents (Figure 3.15).

Figure 3.15. Kambe's 1,4-dicarbofunctionalization of dienes



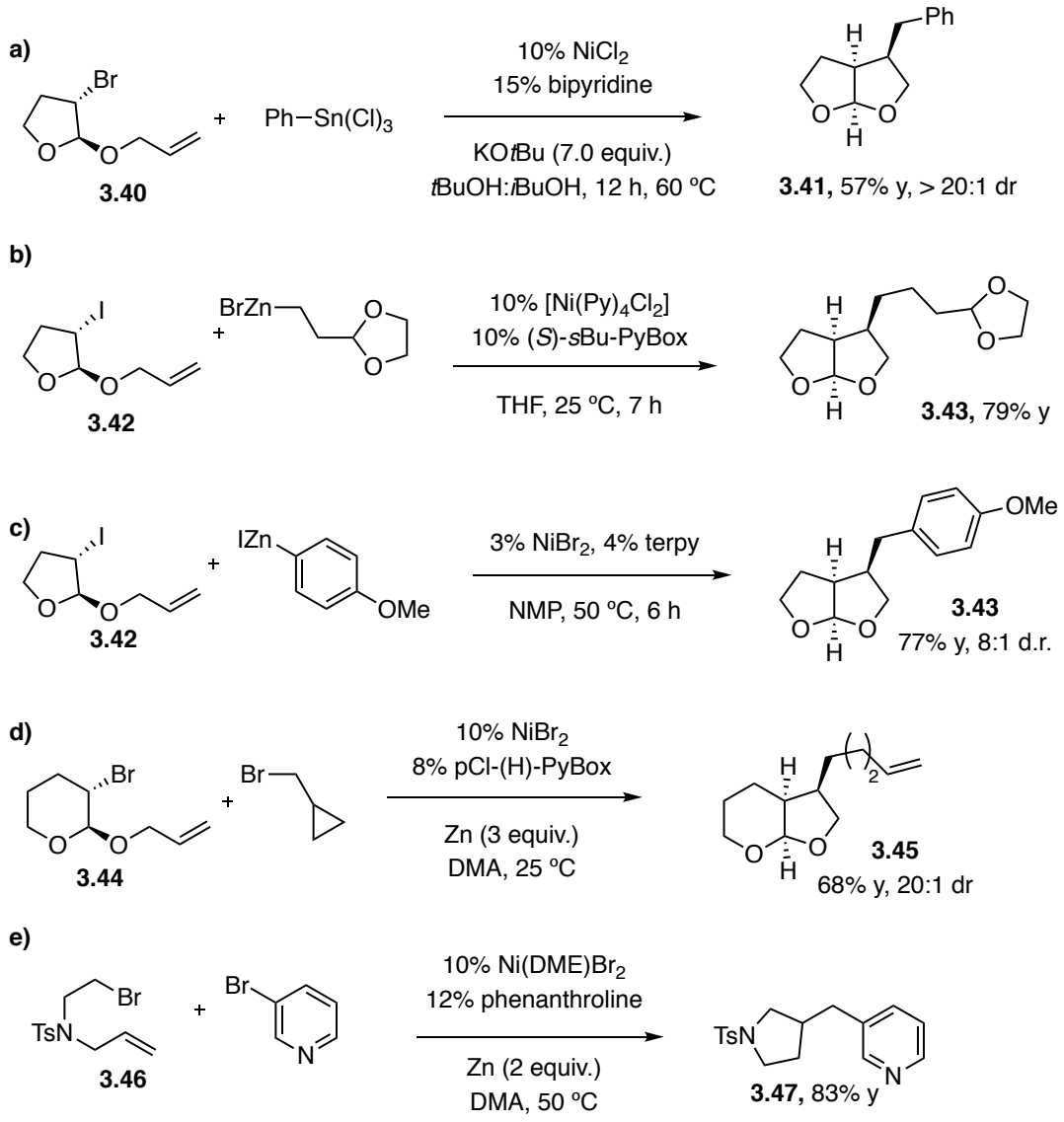
The mechanism of this reaction was proposed to take place through formation of an alkyl radical by SET from a nickel-ate species **3.38**, generated by the combination of the organometallic nucleophile and Ni(0). The carbon-centered radical is trapped by the diene generating an allyl radical that is then trapped the Ni(I)-Ar species to generate **3.39**, which procures 1,4-addition products upon reductive elimination. Following this report, the earliest radical based 1,2-dicarbofunctionalizations using nickel catalysis consisted of isolated examples of intramolecular cyclization/cross-coupling cascade reactions used as a mechanistic probes by Greg Fu in Stille cross-couplings with alkyl radicals (Figure 3.16a).[29] The first methodology devoted to this mode of reactivity consisted of a radical cyclization/cross-coupling cascade reported by Cárdenas in 2007 for the cross-coupling of cyclizing alkyl iodides and alkylzinc halide reagents (Figure 3.16b).[30] The system worked best using $[Ni(py)_4Cl_2]$ and *s*BuPyBox. Radical clock experiments revealed that direct cross-coupling occurred very rapidly and could compete with the radical

[29] Powell, D. A.; Maki, T.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 510.
[30] Phapale, V. B.; Buñuel, E.; García-Iglesias, M.; Cárdenas, D. J. *Angew. Chem. Int. Ed.* **2007**, *46*, 8790.

cyclization process. A related methodology using arylzinc halide nucleophiles and cyclizing alkyl iodide reagents was reported recently by Giri (Figure 3.16c).[31] An example of this reactivity in the context of reductive couplings between alkyl halides was demonstrated by Gong as part of a mechanistic probe (Figure 3.17d).[32] Reductive couplings between cyclizing alkyl halides and aryl iodides were later reported separately by Prof. Wang[33] and Prof. Diao (Figure 3.17e).[34]

[31] Kc, S.; Basnet, P.; Thapa, S.; Shrestha, B.; Giri, R. *J. Org. Chem.* **2018**, *83*, 2920.
[32] Yu, X.; Yang, T.; Wang, S.; Xu, H.; Gong, H. *Org. Lett.,* **2011**, *13*, 2138.
[33] Yan, C.-S.; Peng, Y.; Xu, X.-B.; Wang, Y.-W. *Chem. Eur. J.* **2012**, *18*, 6039.
[34] Kuang, Y.; Wang, X.; Anthony, D.; Diao, T. *Chem. Commun.* **2018**, *54*, 2558.

Figure 3.16. Selected examples of Ni-catalyzed intramolecular dicarbofunctionalization with alkyl electrophiles

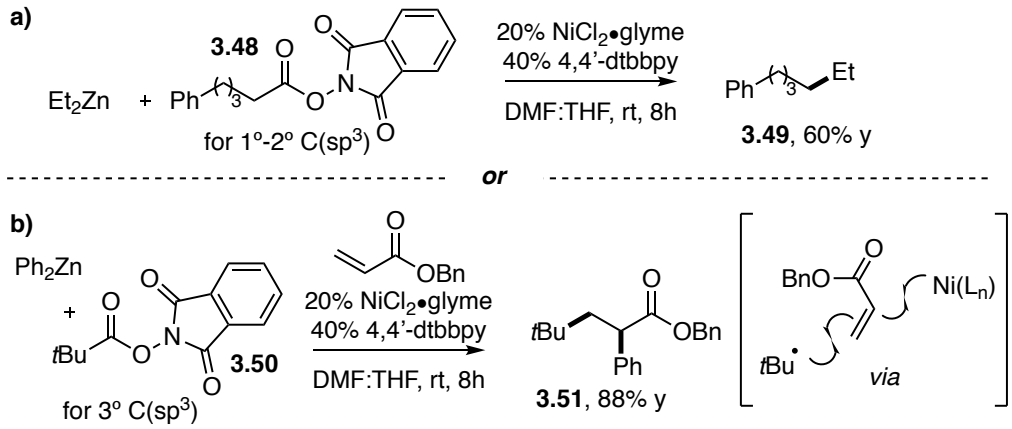


The first example of intermolecular 1,2-dicarbofunctionalization by radical addition/cross-coupling cascade with nickel catalysis was disclosed recently by Baran using redox active esters as electrophiles (Figure 3.17b).[35] In this report, the authors showcased the cross-coupling of dialkylzinc reagent with primary and secondary redox active esters using a Ni/4,4'-(tBu)$_2$bipy (Figure 3.17b). Noting that tertiary redox active

[35] Qin, T.; Cornella, J.; Li, C.; Malins, L. R.; Edwards, J. T.; Kawamura, S.; Maxwell, B. D.; Eastgate, M. D.; Baran, P. S. *Science* **2016**, *352*, 801.

esters could not be coupled directly with the organozinc reagent, presumably due to their increased steric bulk preventing recombination with nickel, they devised a three component cross-coupling solution using benzyl acrylate as a radical trap and PhZnCl as coupling partner. The acrylate intercepts the tertiary carbon centered radical and then recombines with nickel to furnish the overall cross-coupling product.

Figure 3.17. Baran's intermolecular 1,2-dicarbofunctionalization with redox active esters

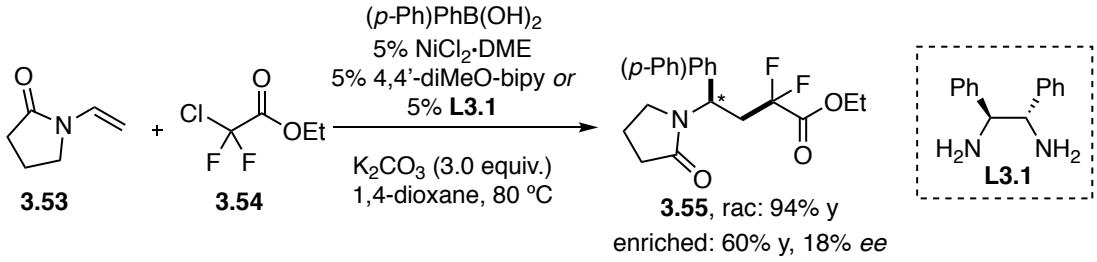


In the same year, Zhang reported the tandem difluoroalkylation-arylation of enamides, using difluoroalkyl bromides and arylboronic acids as cross-coupling partners (Figure 3.17).[36] Enamides furnish highly electron rich radical acceptors to facilitate the recombination with the electron poor difluoroalkyl radicals. Furthermore the amide functionality is proposed to serve as a directing group, coordinating to nickel to accelerate the cross-coupling. Within the same report, the authors disclose preliminary results of an asymmetric version of this transformation by using chiral alkyl diamine ligand **L3.1**. The reaction generates the product in 18% *ee*, establishing the feasibility of developing an enatioselective system. To the best of our knowledge, this is the only

[36] Gu, J.-W.; Min, Q.-Q.; Yu, L.-C.; Zhang, X. *Angew. Chem. Int. Ed.* **2016**, *55*, 12270.

report to date of an enantioselective radical-based dicarbofunctionalization using nickel catalysis.

Figure 3.18. Zhang's difunctionalization of enamines



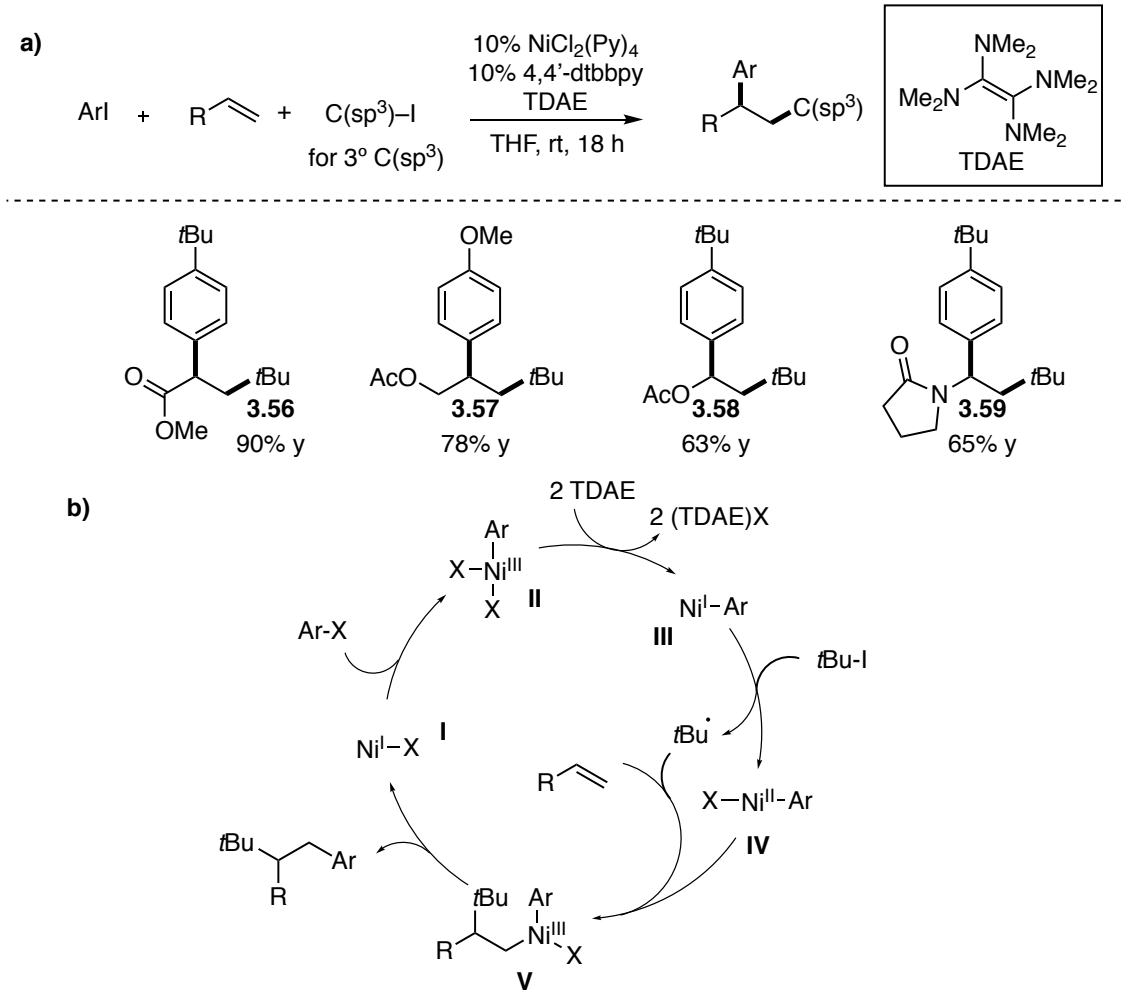
Nevado reported a reductive three component coupling between tertiary alkyl iodides, aryl halides, and a variety of alkenes (Figure 3.19a).[37] These reaction could be realized only through the use of organic reductant tetrakis(dimethylamino)ethylene (TDAE), as all metal based alternatives such as Zn, Mn were found to be ineffective. In the initial communication, a series of electronically biased alkenes, or alkenes possessing directing functionality were difunctionalized efficiently (Figure 3.19a). Of note, both highly electron rich and electron poor alkenes (**3.56-3.59**) furnish products with similar levels of efficiency, perhaps an indication of the importance of coordinating groups (rather than electronic bias) in favoring the desired reactivity in this system. Following up on this initial report, the authors disclosed an updated system with revised reaction conditions that allow for the participation of unactivated terminal olefins.[38] Within this manuscript, the authors examine the mechanism of the reaction through a combination of computational studies and experimentation. They arrive at the mechanistic proposal shown in Figure 3.19b, in which a Ar-Ni(I) species **III**, generated through oxidative

[37] García-Domínguez, A.; Li, Z.; Nevado, C. *J. Am. Chem. Soc.* **2017**, *139*, 6835.
[38] Shu, W.; García-Domínguez, A.; Quirós, M. T.; Mondal, R.; Cárdenas, D. J.; Nevado, C. *J. Am. Chem. Soc.* **2019**, *141*, 13812.

addition followed by TDAE-reduction, undergoes single electron transfer with the tertiary iodide to generate an Ar-Ni(II)-I species **IV** and a carbon centered radical. The latter species is intercepted by a terminal alkene, furnishing a secondary radical which recombines with **IV** and is cross-coupled. The overall chemoselectivity is rationalized through calculations which indicate the activation barrier for the direct recombination of the tertiary radical with Ar-Ni(I)-I **IV** to be nearly twice as high as that for recombination with a secondary radical (10 Kcal/mol vs. 17 Kcal/mol). The authors use computations as the main basis to determine that Ni(I)-I species **I** is more likely to undergo oxidative addition with Ar-I to generate Ar-Ni(III)-I_2 **II** than to undergo single electron transfer with tertiary-iodides. A similar conclusion was reached experimentally by Diao in recent mechanistic studies on the reductive radical cyclization/cross-coupling cascade of aryl halides and cyclizing alkyl bromides.[39] Here, they show that Ni(I)-Br reacts faster with aryl bromides than with primary alkyl bromides by monitoring the rate of consumption of each electrophile.

[39] Lin, Q.; Diao, T. *ChemRxiv.* **2019**.

Figure 3.19. Nevado's reductive intermolecular alkene dicarbofunctionalization

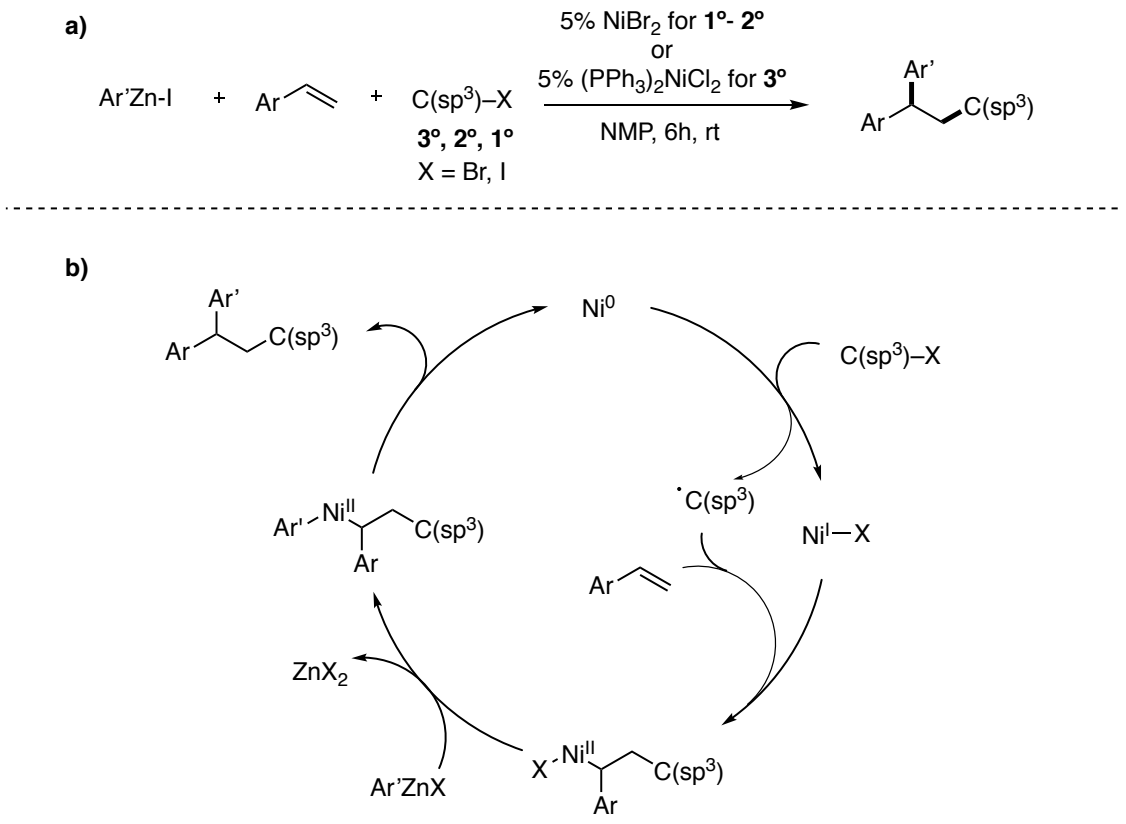


Giri has disclosed the intermolecular dicarbofunctionaliztion of styrenes using arylzinc halides and alkyl-halides electrophiles (Figure 3.19).[40] Remarkably, these reactions proceed with unactivated primary, secondary, and tertiary alkyl bromides and iodides. The reaction proceeds efficiently with simple $NiBr_2$ in the absence of any ligands for primary and secondary halides. Tertiary halides, however, were found to be more challenging and use of a PPh_3 ligated nickel was found to improve those reactions. Mechanistic studies supported the intermediacy of radicals, and revealed that tertiary

[40] Kc, S.; Dhungana, R. K.; Shrestha, B.; Thapa, S.; Khanal, N.; Basnet, P.; Lebrun, R. W.; Giri, R. *J. Am. Chem. Soc.* **2018**, *140*, 9801.

alkyl halides reacted faster than secondary or primary substrates. Based on their studies they propose a Ni(0-II) catalytic cycle shown in Figure 3.19b where SET takes place from a Ni(0) species, and radical recombination precedes transmetallation.

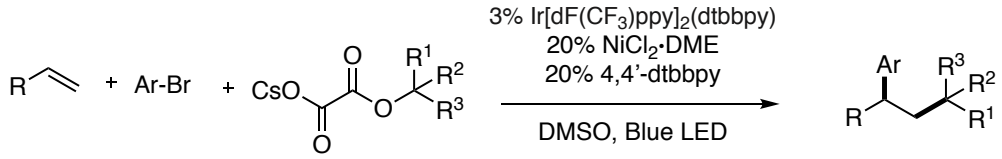
Figure 3.19. Giri's intermolecular aryl-alkylation of styrenes



Finally, a recent example of a radical addition cross-coupling cascade has been disclosed by Chu that combines photoredox and nickel catalysis to achieve the addition of aryl halides and tertiary alkyl oxalates across a range of activated and unactivated olefins (Figure 3.20).[41]

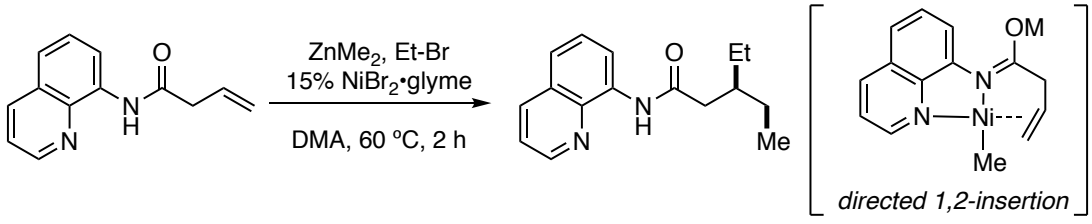
[41] Guo, L.; Tu, H.-Y.; Zhu, S.; Chu, L. *Org. Lett.* **2019**, *21*, 4771.

Figure 3.20. Photoredox/nickel cross-coupling merger for alkene alkyl-arylation with 3° alkyl oxalates



Engle recently disclosed a method for the dicarbofunctionalization of non-conjugated olefins possessing amide directing groups, with alkyl electrophiles and dialkyl zinc reagents (Figure 3.21).[42] The reactions with β,γ unsaturated amides proceed with addition of the nucleophile at the distal position and the electrophile at the proximal position. The regioselectivity is reversed in the case of γ,δ unsaturated amides. The regioselectivity is proposed to arise from nickel mediated β-migratory insertion of the nucleophilic coupling partner resulting in the formation of a metallacycle intermediate (Figure 3.21). Nucleometallation is followed by oxidative addition into the alkyl halide, and reductive elimination to deliver the product. As far as we are aware, this is the only Ni-catalyzed dicarbofunctionalization using alkyl electrophiles that is proposed to go through an inner-sphere mechanism. Moreover, this is also the only Ni-catalyzed method for the addition of two alkyl groups across an olefin thus far.

Figure 3.21. Engle's directed olefin dialkylation



[42] Derosa, J.; Puyl, V. A. V. D.; Tran, V. T.; Liu, M.; Engle, K. M. *Chem. Sci.* **2018**, *9*, 5278.

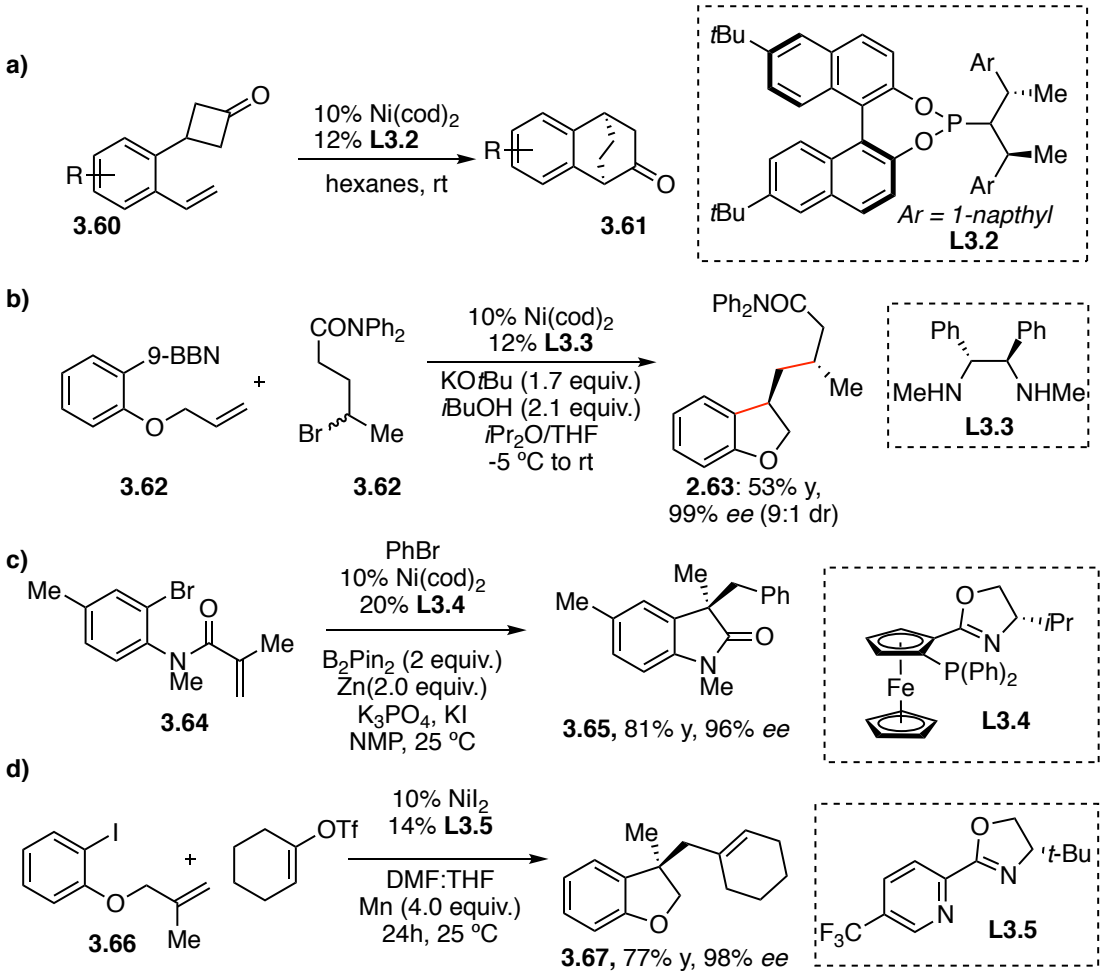
Nickel catalyzed conjunctive cross-coupling with unactivated alkyl iodides can be counted among dicarbofunctionalization reactions that go by a polar outer-sphere pathway, as the 1,2-metallate shift results in the overall nucleometallation of the alkenylboronate.[2b]

3.2.1 Nickel catalyzed enantioselective dicarbofunctionalizations.

Thus far, all the reports of enantioselective nickel-catalyzed dicarbometallation are proposed to proceed through inner-sphere polar mechanism. One of the earliest such systems was reported by Murakami, who showed that a nickel/phosphoramidate complex could add into the strained C-C bond of a cyclobutanone ring (Figure 3.22a).[43] The two carbon fragments would add enantioselectively across an alkene in an intramolecular reaction. Later, Fu reported the intramolecular cyclization/cross-coupling of aryl-BBN tethered alkenes and alkyl electrophiles using a Ni/alkyldiamine complex(Figure 3.22b).[44] The reaction is proposed to proceed through a nucleometallation pathway whereby the arylborane is transmetallated to nickel and subsequently inserted across the olefin in a migratory insertion step, resulting in a stereochemically defined homo benzylic nickel intermediate. The latter is then cross-coupled with an alkyl iodide. Two subsequent reports of enantioselective intramolecular dicarbofunctionazion made use of a reductive coupling strategy. Kong disclosed an enantioselective reductive diarylation of acrylamides using P-N ligand *i*Pr-Phospherrox (Figure 3.22c).[45]

[43] Liu, L.; Ishida, N.; Murakami, M. *Angew Chem. Int. Ed.* **2012**, *51*, 2485.
[44] Cong, H.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 3788.
[45] Wang, K.; Ding, Z.; Zhou, Z.; Kong, W. *J. Am. Chem. Soc.* **2018**, *140*, 12364.

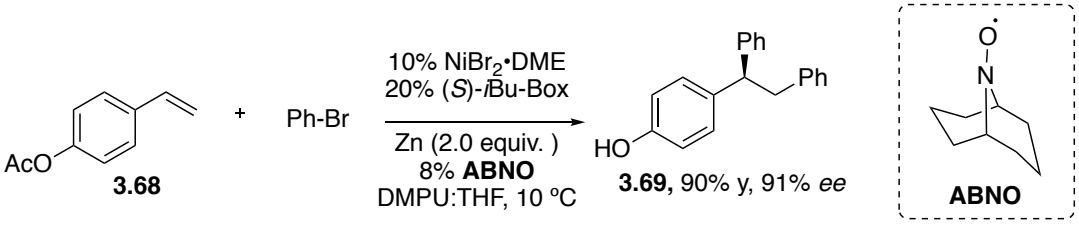
Figure 3.22. Intramolecular examples of Ni-catalyzed enantioselective dicarbofunctionalization of olefins



This system could be used to generate enantiomerically enriched all carbon quaternary stereocenters within oxindole frameworks. Shu later disclosed a reductive coupling system based on a similar manifold as Kong's (Figure 3.22d).[46] In this method, aryl iodide-tethered alkenes are cross-coupled with alkenyl triflates to generate dihydrobenzofuran type products with benzylic all-carbon quaternary stereocenters.

[46] Tian, Z.-X.; Qiao, J.-B.; Xu, G.-L.; Pang, X.; Qi, L.; Ma, W.-Y.; Zhao, Z.-Z.; Duan, J.; Du, Y.-F.; Su, P.; Liu, X.-Y.; Shu, X.-Z. *J. Am. Chem. Soc.* **2019**, *141*, 7637.

Figure 3.23. Diao's enantioselective and intermolecular diarylation of styerenes



An intermolecular enantioselective dicarbofunctionalization of styrenes using nickel catalysis has been recently reported by Diao (Figure 3.23).[47] This transformation avails itself of a bisoxasoline ligand and Zn as reductant to catalyze the addition of two identical arenes across styrenyl substrates. A unique feature of the reaction consists in its use of catalytic 9-azabicyclo[3.3.1]nonane *N*-oxyl radical (ABNO) as an additive. This is proposed to participate as a radical-based ligand in the reaction, providing a dramatic increase in *ee* (from 23% to 91% for product **3.69**).

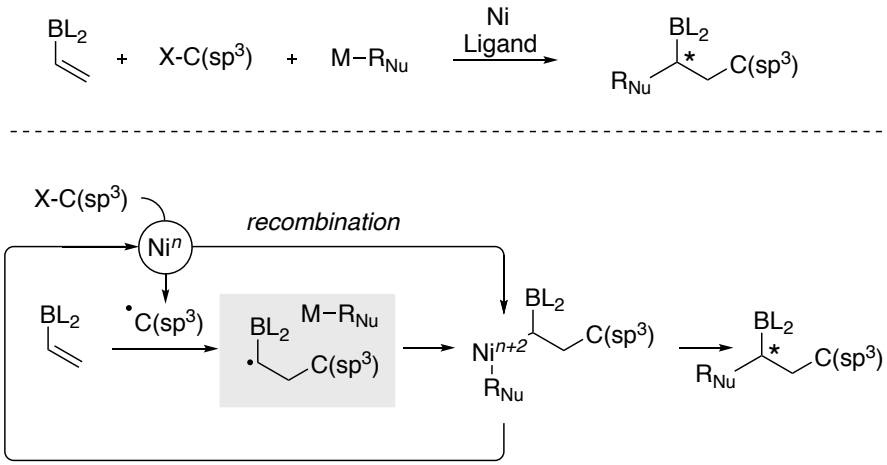
Finally, nickel-catalyzed conjunctive cross-coupling provides a unique example of enantioselective dicarbofunctionalization catalyzed by nickel. Although the 1,2-metallate rearrangement constitutes an intra-molecular process, the overall reaction results in the intermolecular combination of an organolithium, an organoboron and organo halide electrophiles. [2]

[47] Anthony, D. , Lin, Q. , Baudet, J. and Diao, T. *Angew. Chem. Int. Ed.* **2019**, 58, 3198.

3.3 SYNTHESIS OF NON-RACEMIC ALKYLBORONATES BY NICKEL-MEDIATED RADICAL/ADDITION CROSS-COUPLING CASCADE [48]

3.3.1 Reaction development.

Figure 3.24. Proposed reaction design for radical addition/cross-coupling cascade

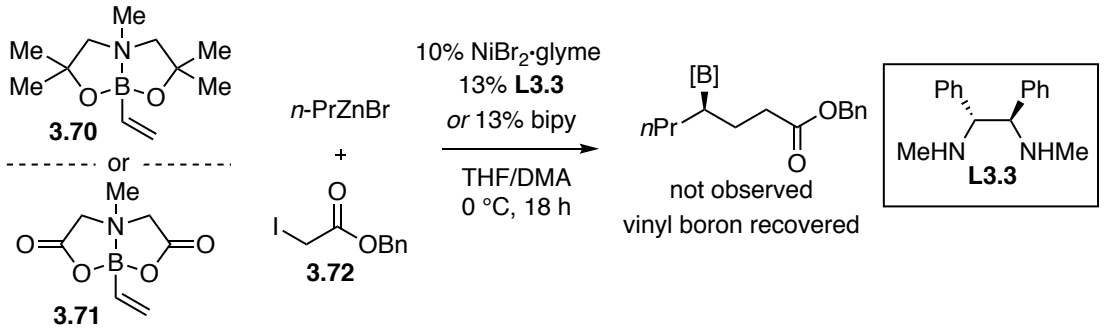


When we set out to explore this three component coupling reaction (Figure 3.24), the first and most important challenge laid in the selection of cross-coupling partners. The reaction required that the organometallic nucleophile component should not complex with the selected vinyl boron reagent and avoid radical/polar cross-over reactivity. Meanwhile the recombination between the alkyl radical and vinyl boron should be sufficiently rapid to outcompete direct cross-coupling with the organic nucleophile. Moreover, the appropriate Ni/ligand combination should play a key role in accessing the desired reactivity. We selected alkylzinc halide reagents as weak organometallic nucleophiles, based on our own observation that these reagents did not generate 'ate'

[48] Chierchia, M.; Xu, P.; Lovinger, G. J.; Morken, J. P. *Angew. Chem. Int. Ed.* **2019**, *58*, 14245.

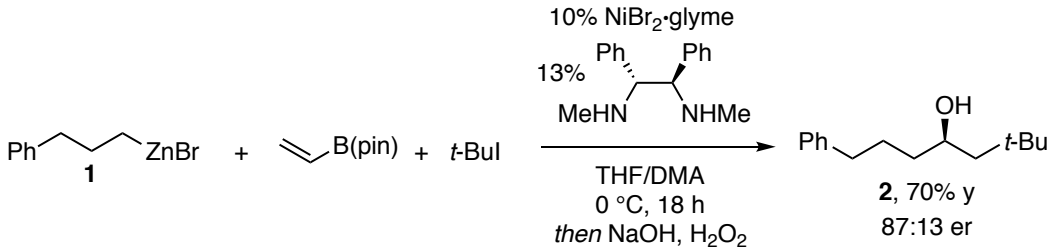
species when combined with a range of organoboron reagents by ^{11}B NMR. We then reasoned that radical recombination between the vinyl boron and the alkyl electrophile should be favored by polarity matched substrates. The importance of this was evidenced by the mechanistic switch observed between conjunctive cross-coupling and radical/polar cross-over mechanisms, when electron poor alkyl halides were used in the transformation.[2b] Thus, for our initial experiments we focused on a narrow scope of diamine ligands commonly used in nickel-catalyzed cross-couplings, namely a bipyridine and alkyl diamine ligand **L3.3** (Figure 3.25). We adapted our initial reaction conditions from Greg Fu's work[24] on stereoconvergent Negishi couplings with α-haloboronates, given that the reaction is also proposed to involve recombination between nickel and an α-boryl radical. Based on the facile recombination observed between electron poor alkyl iodides and vinylboron 'ate' species, we hypothesized that a zwitterionic alkenyl boron possessing MIDA or amine-diol ligands would provide a sufficiently electron rich radical acceptor to facilitate recombination with electrophilic alkyl radicals such as those derived from **3.72** (Figure 3.25). Meanwhile, the α-boryl radical intermediate should be less electron rich than vinyl boron 'ate' species obtained by organolithium addition, and therefore less prone to oxidation via SET. However, no products were observed in the reactions tested and the vinylboron reagents remained unreacted, suggesting that perhaps the electronic bias did not provide a strong enough driving force for radical recombination in this case (Figure 3.25).

Figure 3.25. Attempts of dicarbofunctionalization with electron rich vinylboronates.



We then opted to target a neutral α-boryl radical species which would benefit from resonance stabilization with the empty p-orbital, by using vinylboronic acid pinacol ester as a radical acceptor. In this case however, radical recombination with the electron-poor vinylboron species should be favored by using an electron rich alkyl radical. Thus, we selected *t*-butyl iodide as a source of electron rich radicals and we were pleased to find that we could generate the desired product in 70% yield and 87:13 enantiomeric ratio using **L3.3** as ligand (Figure 3.26). The product could also be generated with bipyridine, albeit only in 23% yield.

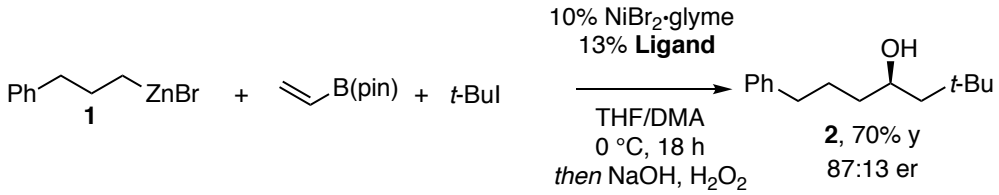
Figure 3.26. Initial results with dicarbofunctionalization of vinylB(pin).

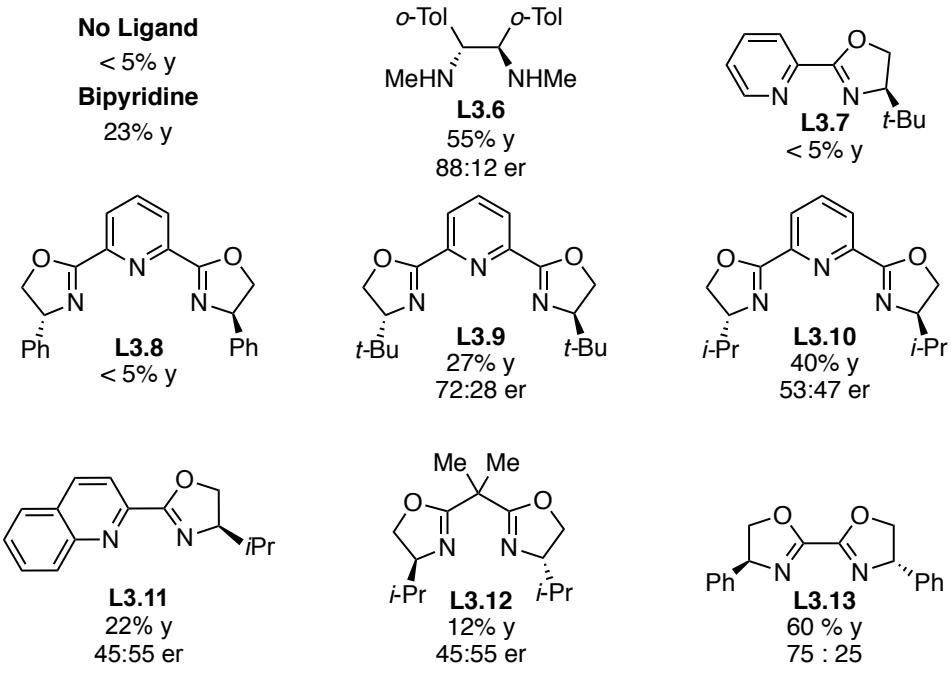


Having identified a productive reaction manifold, we examined several parameters to improve the selectivity and gain a better understanding of the system. Investigating the role of the ligand (Figure 3.27), we found that while ligated nickel was

necessary to obtain product, several ligand classes could achieve the desired reaction. Remarkably both tridentate (**L3.9-3.10**) and bidentate ligands could be used to obtain products, however none of the ligands tested improved the selectivity or yield of the reaction. *o*-Tolyl diamine ligand **L3.6**, employed by Fu in their Ni-catalyzed stereoconvergent coupling with α-boryl radicals did not have a significant impact on the selectivity of the transformation, and provided significantly diminished yield.

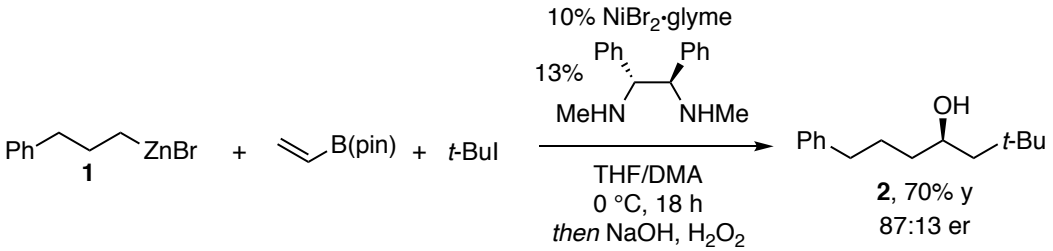
Figure 3.27. Ligand evaluation in Ni-cat. dicarbofunctionalization of vinylB(pin)





Ligands on boron could be changed to affect the reaction outcome as well (**Table 3.2)**. Diol ligands such neopentyl glycol or Morken's lab newly developed mac-diol[1d] resulted in lower selectivities and poor yields suggesting the important impact of the steric environment around the boron atom (entries 2, 3). The more electron rich vinylB(dan) (entry 4) provided a remarkably efficient reaction, albeit with a drastically reduced selectivity, while tetracoordinate vinylB(MIDA) was not consumed in the reaction. These results delineate a requirement for using neutral tricoordinate boron species in the reaction, perhaps underlining the importance that generating a stabilized α-boryl radicals has in driving the reaction.

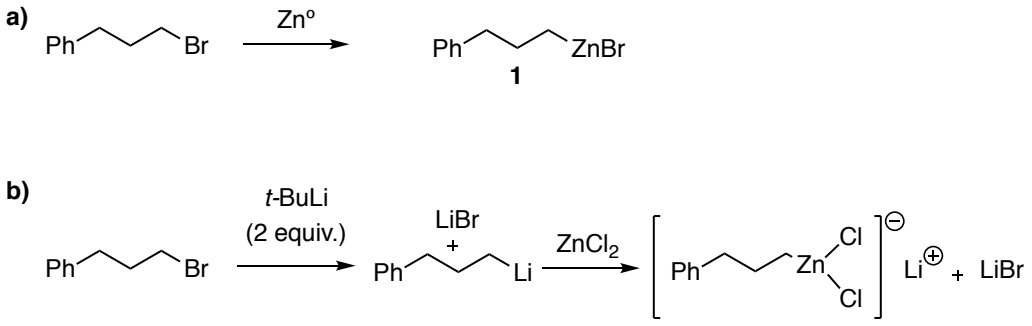
Table 3.2. Evaluation of boron ligands and alkylzinc reagents



Entry	Modification	Yield (%)	er
1	none	71	87:13
2	vinylB(neo)	43	81:19
3	VinylB(mac)	53	62:38
4	vinylB(dan)	80	60:40
5	vinylB(mida)	<5	n/a
6	Et_2Zn	<5	N.D.
7	$PhCH_2CH_2CH_2ZnI$	75	86:14
8	$PhCH_2CH_2CH_2ZnCl•LiCl$	54	95:5
9	$PhCH_2CH_2CH_2ZnBr•2LiCl$	55	95:5

Finally, examining the impact of the organozinc reagent we found that alkylzinc chlorides provided products with diminished yields but with significantly improved enantioselectivity (entry 8). Moreover, the organozinc reagents used in the previous reactions were obtained through direct zinc insertion into the carbon-bromine bond (Figure 3.28a), while the alkyl zinc chloride reagent in question was produced from addition of the corresponding organolithium reagent to $ZnCl_2$, a reaction that generates an additional equivalent of LiCl, as well as an equivalent of LiBr from lithium halogen exchange (Figure 3.28b).

Figure 3.28. Synthesis of alkylzinc halide reagents



Testing the potential impact of these salt additives in the reaction, we found that the outcome of the previous transformation could be reproduced by adding two equivalents of LiCl to an alkylzinc bromide species obtained through direct zinc insertion. It is unclear at this point what the role of these salts may be in affecting the stereochemical outcome of the reaction. It has been well documented that lithium chloride salts can affect the reactivity of organozinc halide reagents by forming organozinc 'ate' species.[49] However these effects should mainly impact the

[49] (a) Zhang, G,; Li, J.; Deng, Y. ;Miller, J. T.; Kropf, A. J.; Bunel, E. E.; Lei, A. *Chem. Commun*. **2014**, *50*, 8709; (b) Fleckenstein, J. E.; Koszinowski, K. *Organometallics* **2011**, *30*, 5018; (c) Hevia, E.; Mulvey,

transmetallation step, which in radical based nickel cross-couplings usually takes place before recombination with the alkyl radical species and therefore before the stereo-determining step. In this case the formation of zinc 'ates' should not have an effect on the selectivity. Instead the salt additives may have a separate effect on the reaction, such as binding to nickel or to boron and affecting the aggregation states of the reactive substrates. If transmetallation takes place after radical recombination in a mechanism akin to the one proposed by Giri (Figure 3.19b) for his dicarbofunctionalization reactions, then the nature of the organozinc halide is more likely to have an impact on the selectivity in the transformation. This mechanistic hypothesis cannot be ruled out at this point, and further experimentation will be required to deconvolute the observed additive effects.

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

Having identified suitable reaction conditions, we explored the scope of the three component cross-coupling reaction with tertiary iodide electrophiles (Figure 3.29**)**. In general, organozinc reagents with varying functional groups and architectures could be used in the transformation, as alkyl chains possessing aryl ether (**3**) and silyl ether (**5**) groups delivered products in good yields and enantioselectivities, and a simple methylzinc chloride could be used as nucleophile as well (**4**). Moreover, we were particularly pleased to find that under the same reaction conditions arylzinc reagents (**7-10**) could participate in the enantioselective cross-coupling to deliver benzylicboronic

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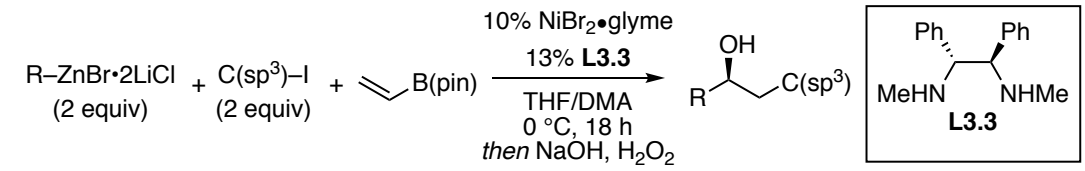
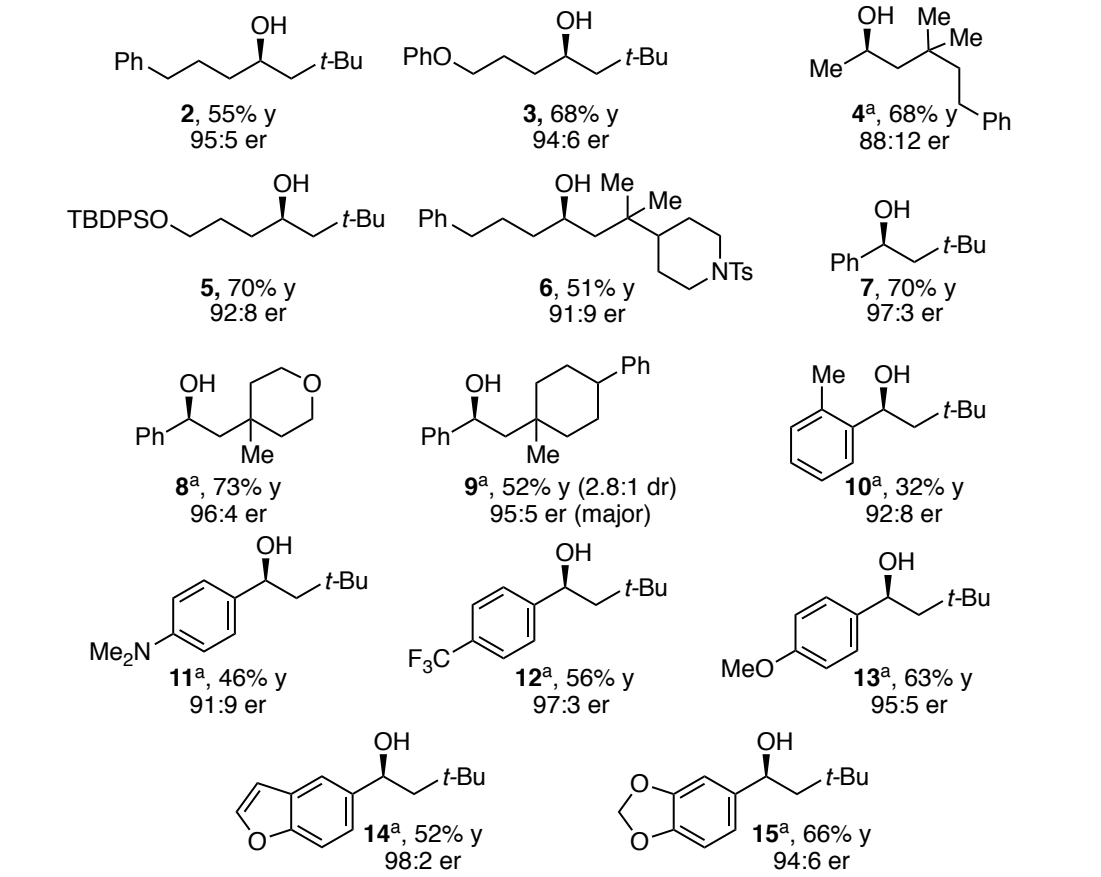
E. *Angew. Chem. Int. Ed.* **2011**, *50*, 6448; (d) Krasovskiy, A.; Malakhov, V.; Gavryushin, A.; Knochel, P. *Angew. Chem. Int. Ed.* **2006**, *45*, 6040

ester products, which were isolated as the corresponding alcohols. Arenes possessing either electron donating (**11, 13**) or electron withdrawing functionalities (**12**) resulted in comparable reaction outcomes. Functionalized arenes such as a benzofuran (**14**), benzodioxole (**15**), and an aniline (**11**) could participate as well. Finally, substrate **9** shows the possibility of controlling diastereoselectivity through substrate control, in reactions where a quaternary stereocenter is formed during the intial radical addition step.

Figure 3.29. Scope of 3-component radical addition cross-coupling cascade

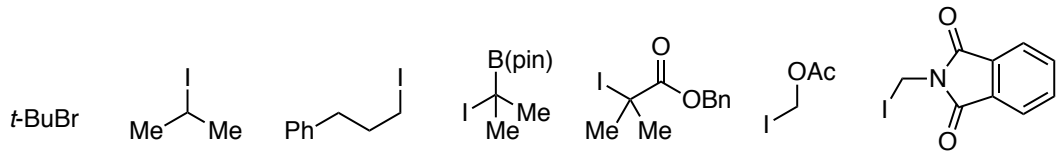




[a] RZnCl•LiCl obtained from addition of RLi to $ZnCl_2$.

A number of substrate classes, however, did not participate efficiently in the reaction (Figure 3.30). The fact that tertiary bromides did not participate in the reaction can be attributed to the stronger C-Br bonds inhibiting radical formation. However, reactions with primary electrophiles did not generate the desired product, while secondary alkyl iodides resulted in very modest yields (**3.74**-**3.75**). Conversely, sterically hindered tertiary iodides possessing electron withdrawing functionalities did not result in consumption of vinylboron (**3.76**, **3.77**). These results point to electronic parameters playing an important role in driving the initial radical recombination step. We speculate that the inherent stability of the radicals generated from **3.76**, **3.77** makes them less reactive, or that the kinetics for recombination are too unfavorable when using electronically mismatched substrates. Moreover, the generation of electron rich/nucleophilic primary/secondary radicals could reestablish the desired reactivity within those substrate classes. Carbon centered radicals can be rendered more nucleophilic through the influence of α-heteroatoms possessing lone pairs, such as oxygen and nitrogen. However, alkyl iodides **3.78** and **3.79** did not participate productively as well. Perhaps more substituted versions of **3.78** and **3.79** are necessary for them to undergo the desired pathway, or perhaps the heteroatoms are too electron-withdrawing to substantially increase the nucleophilicity of the primary radical, as the lone pairs on O and N are delocalized in the carbonyl functionality. However, the alkyl iodide precursors to these radicals are too unstable and could not be accessed. A more thorough examination of electronic effects would require a different source for carbon centered radicals.

Figure 3.30. Ineffective substrates

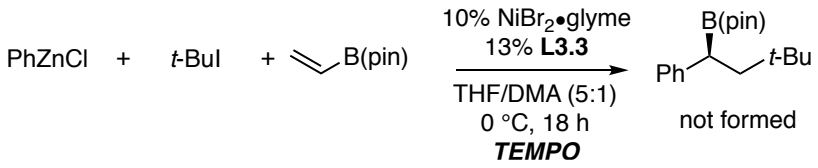


3.73 **3.74** ~20% y **3.75** < 10% y **3.76** **3.77** **3.78** **3.79**

3.3.3 Mechanistic studies.

Having explored the scope of the three component coupling, we were interested in investigating some of the underlying mechanistic details. We found that addition of radical scavenger TEMPO in a standard reaction resulted in complete suppression of product formation, consistent with the intermediacy of radical species in the mechanism (Figure 3.31).

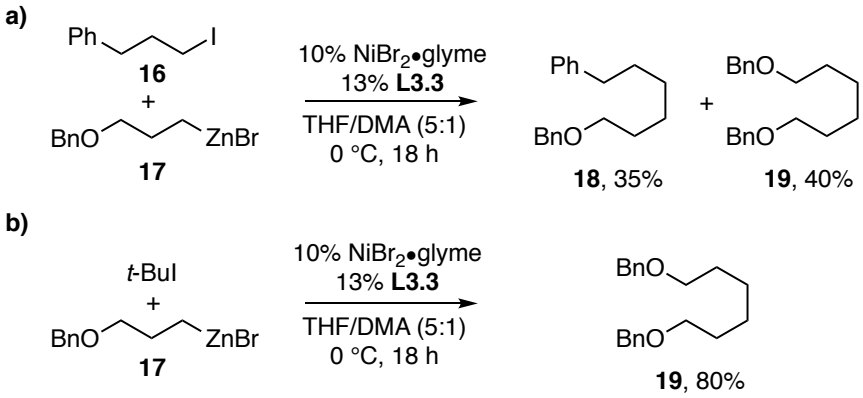
Figure 3.31. TEMPO inhibition



We then set out to investigate the origin of the divergent reactivity between primary and tertiary alkyl iodides. The difference in reactivity could be due to inertness of the primary electrophile due to stronger C-I bonds, or to other competitive side reactions resulting from steric/electronic differences between primary and tertiary alkyl radicals. Thus, we carried out a reaction between a primary alkyl iodide **16** and alkyl zinc reagent **17** in the absence of vinyl boron to gain a better understanding of possible background processes (Figure 3.32a). The reaction between **16** and **17** produced a mixture consisting largely of

homocoupling of the organozinc reagent, as well as alkyl/alkyl cross-coupling products. Based on this result, it is apparent that primary alkyl iodides are reactive under the reaction conditions, as they are able to undergo direct cross-coupling. Moreover, the corresponding experiment carried out using *t*-BuI as electrophile (Figure 3.32b) did not generate any cross-coupled product, instead the alkyl iodide acts as a terminal oxidant enabling the homocoupling of the organozinc reagent.

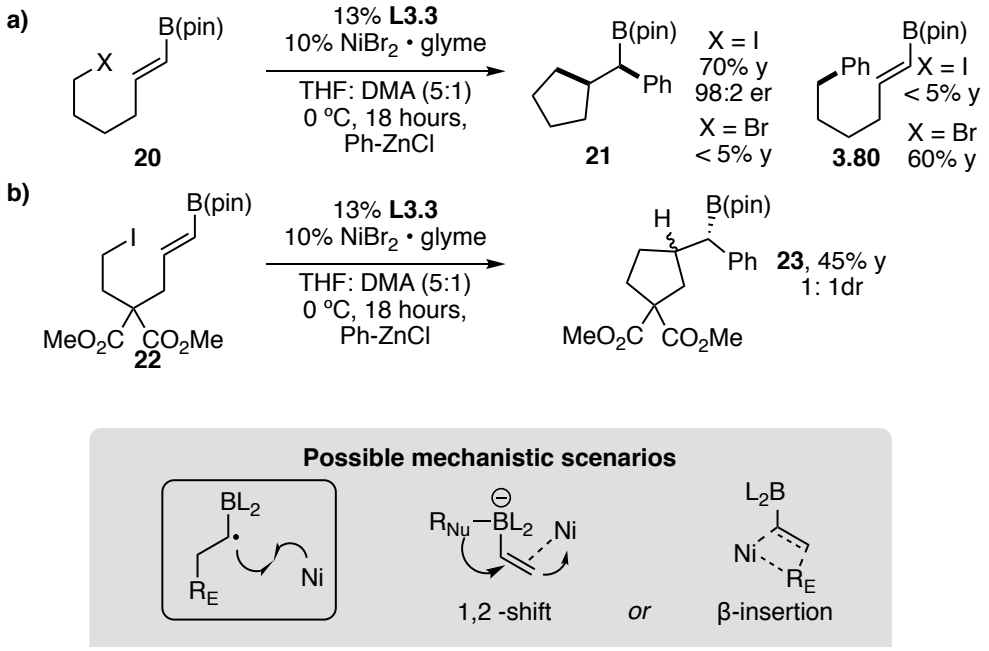
Figure 3.32. Background reaction studies



From these results we surmise that in the case of primary alkyl iodides the direct cross-coupling pathway is accessible under the reaction conditions, whereas with tertiary iodides direct cross-coupling is completely suppressed. This is likely due to the steric difference between the starting materials, which in the case of the bulkier tertiary iodides should inhibit recombination with the nickel, in accordance with observations made by Nevado[37] and Baran.[35] The direct cross-coupling pathway may outcompete radical recombination with vinylboron in the case of primary electrophiles. Radical recombination may be favored kinetically by the use of electronically matched substrates, yet, as discussed in the previous section, we could not generate sufficiently nucleophilic

primary alkyl iodides. We then hypothesized that radical recombination may be accelerated through an intramolecular process. To test this proposal, we generated a primary alkyl iodide tethered to an alkenylboron (**20**) and found that, when used under our standard reaction conditions with phenylzinc chloride, the corresponding cyclized product was generated in good yield and selectivity (Figure 3.33). Interestingly, testing the corresponding boron-tethered alkyl bromide under the same conditions resulted in the direct cross-coupling between the primary alkyl halide and the phenylzinc reagent. No cyclization product was detected. A possible reason for the observed divergence in reactivity could be that a different oxidative addition mechanism is operating in the case of alkyl bromides, since the stronger C-Br bonds may preclude radical formation and instead favor direct insertion or Sn^2 type oxidative addition. This rationale is consistent with the observed inertness of tertiary bromide electrophiles, where non-radical oxidative addition pathways would be inaccessible. Moreover, taking these cyclization studies a step further, we generated substituted cyclizing substrate **22** and tested it in a reaction that resulted in formation of the desired product in 1:1 diastereomeric ratio. This result is consistent with a non-stereospecific radical cyclization followed by recombination of the radical with nickel, as opposed to a possible alternative pathway involving nickel mediated β-migratory insertion followed by cross-coupling, or even a metal induced 1,2-metallate shift resulting from a transiently formed boron 'ate' species.

Figure 3.33. Cyclizing radical probe substrates

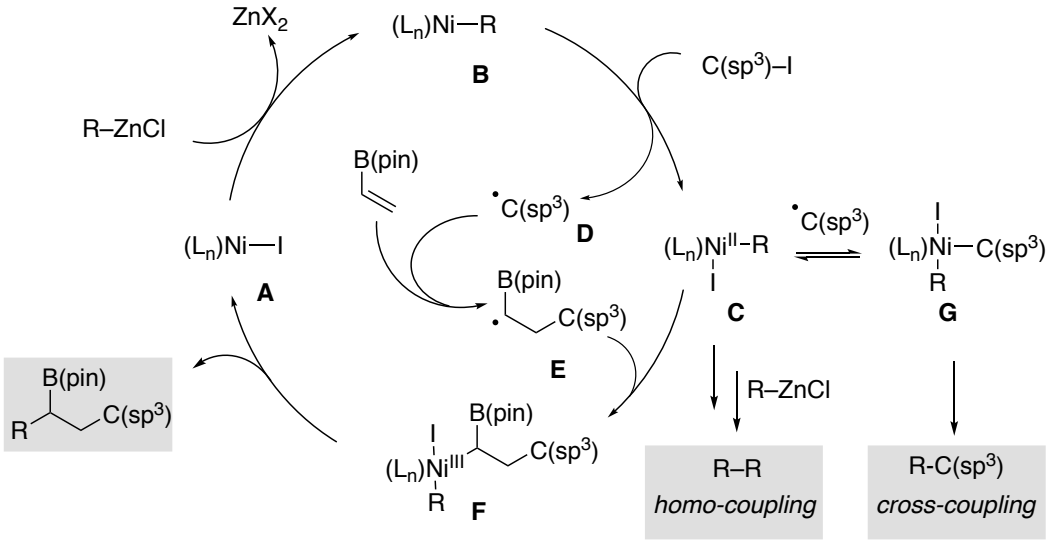


These results help provide a more detailed mechanistic understanding of the transformation. Thus, the proposed catalytic cycle is summarized in Figure 3.34. Based on our results and mechanistic studies done by other groups,[38, 39, 50] we can surmise that nickel(I)-halide species **A** may undergo transmetallation with an organozinc reagent to generate organo-nickel(I) species **B**. Intermediate **B** is oxidized to organo-nickel(II) **C** via single electron transfer with alkyl iodide, resulting in concomitant formation of carbon-centered radical **D** that then adds to vinylboron forming α-boryl radical species **E**. Recombination with organo-nickel(II) **C** to generate a nickel(III) intermediate, followed by reductive elimination generates the products. Meanwhile, prior to recombination with α-boryl radical, the organo-nickel(II) **C** may undergo a second transmetallation event with an organozinc or with another organo-nickel species to generate the homocoupling product. Of note, the exact order of the steps in the catalytic cycle cannot be determined at this point, and other plausible sequences may be proposed. Nickel(I)-X species such as

[50] Diccianni, J. B.; Diao, T. *Trends in Chemistry*, **2019**, *ASAP*. DOI: 10.1016/j.trechm.2019.08.004

A can act as effective SET reductants of alky halides,[51] and the resulting Ni(II)X_2 intermediates may undergo transmetallation with organozinc reagents to generate species **C** in the following steps. Additionally, as in Giri's example, Ni(0)/Ni(I)/Ni(II) cycles have been proposed for similar reactions.[40] We anticipate that future mechanistic studies on the present system as well as on related transformations will shed light over these questions.

Figure 3.34. Mechanistic proposal for radical addition/cross-coupling cascade

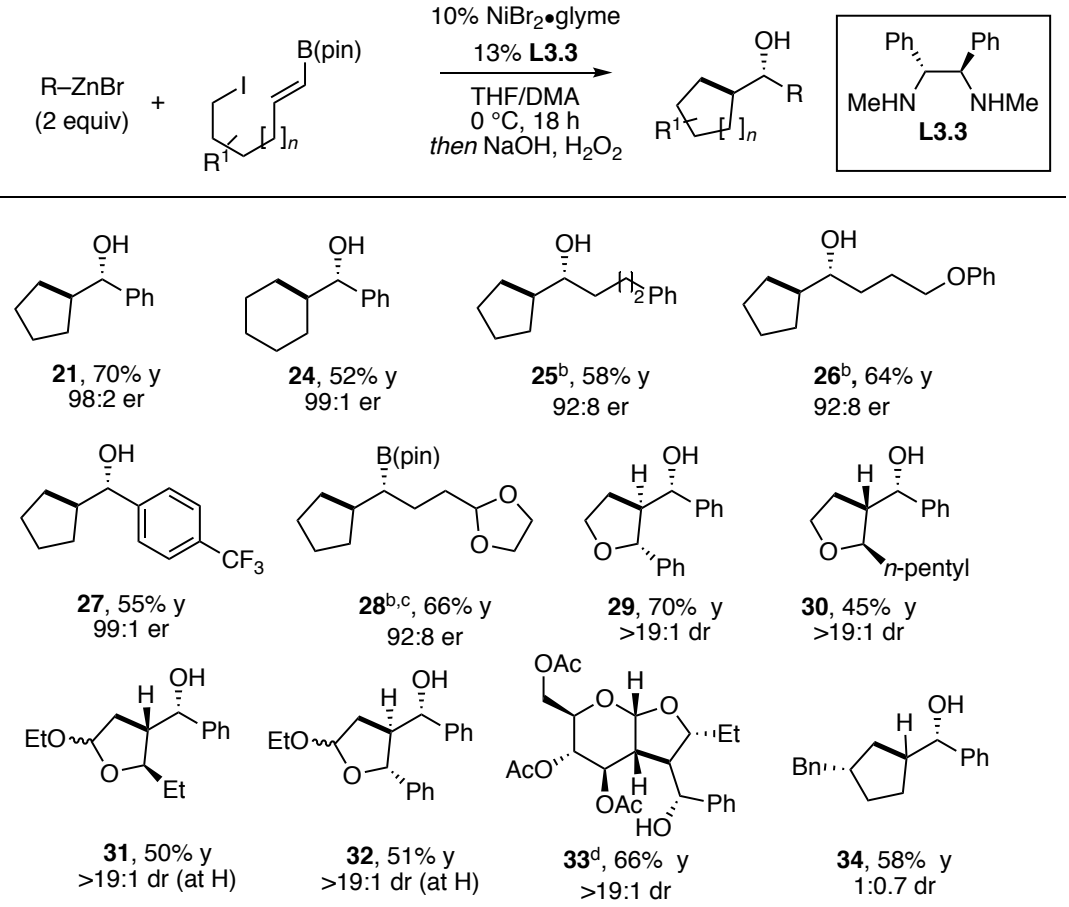


Finally, the intramolecular cyclization/cross-coupling mode of reactivity revealed through our studies furnishes a potentially useful method to generate cyclic scaffolds with exocyclic stereochemically defined boron functionalities. Thus, we set out to explore the scope of this reaction manifold (Figure 3.35). We found that this transformation could be used to generate either five or six membered rings (**21**, **22**) and that either arylzinc or alkylzinc reagents (**25**, **26**, **28**) participated well in the reaction. Of note, the former

[51] Yin, H.; Fu, G. C. *J. Am. Chem. Soc.* **2019**, *141*, 15433.

required slightly modified conditions to proceed efficiently. We then surmised that by combining a diastereoselective cyclization with an enantioselective cross-coupling we may enable access to densely functionalized products. To this end, we developed a number of routes to generate alkenylboron substrates containing non-racemic, chiral functional groups. When tested in the reaction, we were able to obtain the corresponding cyclic scaffolds in moderate to excellent diastereoselectivity (**29**-**34**). This process was tolerant of densely functionalized motifs and enabled the formation of up to three stereocenters in a single operation. The stereochemically defined boron functionality provides an excellent handle for further derivatization. Combined with the possibility of employing a wide range of alkyl and arylzinc cross-coupling partners, this manifold shows promise as a synthetic tool for the generation of complex cyclic scaffolds, particularly in the context of diversity oriented synthesis.

Figure 3.35. Scope of the intramolecular cyclization/cross-coupling cascade



[a] Unless otherwise noted, RZnCl•LiCl obtained from addition of RLi to ZnCl2. [b] RZnBr employed; reaction in dimethylacetamide solvent at room temperature. [c] Because the alcohol derivative was not stable, this compound was isolated as the organoboron. [d] This product was prepared using (*R*,*R*)-**L1** ligand.

3.3.4 Conclusion

In this chapter, we discussed the development and applications of a new method for the enantioselective dicarbofunctionalization of alkenylboronic esters through a nickel mediated radical addition/cross-coupling cascade. In this transformation, catalytic nickel is used to generate an alkyl radical species from an organic halide, which is subsequently

trapped by an alkenylboronic ester to generate an α-boryl radical. The latter species recombines with the nickel catalyst and is ultimately cross-coupled with an organometallic nucleophile to generate enantiomerically enriched products. When operated as an intermolecular process, this reaction enables the addition of tertiary alkyl iodides and alkyl or arylzinc halide reagents across a vinylboronic ester. Moreover, this transformation can be achieved through an intramolecular radical cyclization/cross-coupling process which enables rapid construction of cyclic scaffolds with exocyclic, enantiomerically enriched boron-containing stereocenters. The combination of diastereoselective cyclization with an enantioselective cross-coupling provides a platform for the synthesis of densely functionalized cyclic motifs, underscoring the synthetic utility of this methodology. The system presented here constitutes a complementary method to enantioselective conjunctive cross-coupling, both in terms of scope of the transformation, which can take place with two alkyl coupling partners and with hindered tertiary electrophiles, as well as from a mechanistic standpoint, as the transformation proceeds through a radical based, non-polar pathway. We hope that this reaction design will inspire future studies for the development of asymmetric methodologies.

3.4 EXPERIMENTAL

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

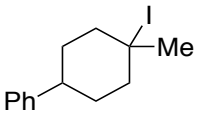
from Silicycle. Visualization was performed using ultraviolet light (254 nm), ceric ammonium molybdate in water/sulfuric acid (CAM), phosphomolybdic acid in ethanol (PMA), phosphomolybdic acid and cerium sulfate in water/sulfuric acid (Seebach), or potassium permanganate ($KMnO_4$). Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol as the modifier.

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

3.4.2 Experimental Procedures

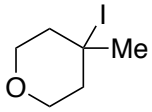
3.4.2.1 Procedure for Preparation of Tertiary Alkyl Iodides

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

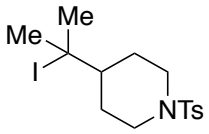


(4-iodo-4-methylcyclohexyl)benzene (SI-1). The title compound was obtained through the general procedure from the corresponding alcohol 1-methyl-4-phenylcyclohexan-1-ol (1.08 g, 5.7mmol). The product was isolated by silica gel chromatography (pentane, stain in CAM) to afford a white solid (1.4 g, 82%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

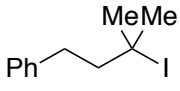
2853.6 (m), 1463.3 (w), 1441.3 (w), 1102.4 (s), 1013.6 (s), 979.7 (s), 775.6 (s), 614.3 (s), 476.6 (s). **HRMS** (DART) for $C_{13}H_{17}$ $(M+H-HI)^+$: Calc'd: 173.1325, found: 173.1318.



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

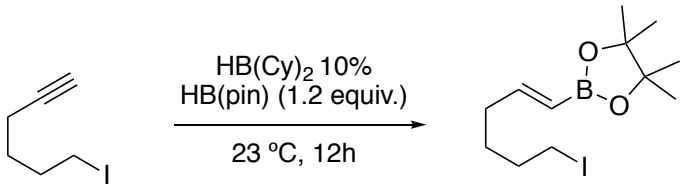


4-(2-iodopropan-2-yl)-1-tosylpiperidine (SI-3). The title compound was synthesized from the corresponding alcohol (2-(1-tosylpiperidin-4-yl)propan-2-ol) which was obtained in turn through standard procedures starting from commercially available ethyl isonipecotate. All spectral data was in accordance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

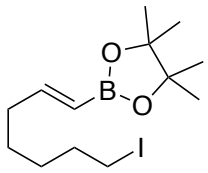


(3-iodo-3-methylbutyl)benzene (SI-4). The title compound was synthesized from the corresponding alcohol 2-methyl-4-phenylbutan-2-ol. All spectral data was in accordance with the literature. [3]

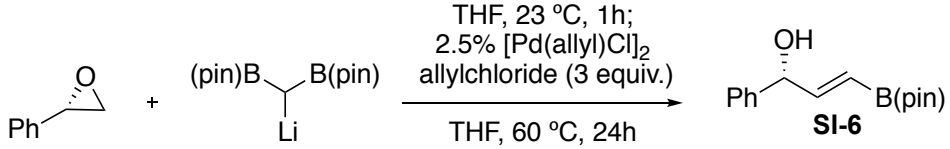
3.4.2.1 Procedure for Preparation of Cyclizing Substrates



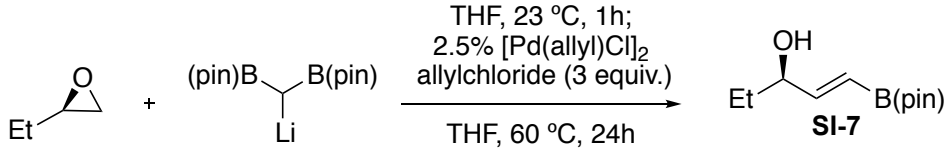
(*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (20). In the glovebox, a 2 dram vial was charged with neat 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.88 g, 22.5 mmol, 1.2 equiv.) and dicyclohexylborane (333.9 mg, 1.87 mmol, 0.10 equiv.). The vial was cooled inside the glovebox freezer for 30 min and 6-iodohex-1-yne (3.90 g, 18.8 mmol, 1.0 equiv.) was added to the cold mixture. The vial was sealed and the mixture was stirred for 12 hours at room temperature. The reaction mixture was quenched by bubbling air through the solution for 2 h at room temperature. to oxidize the dicyclohexylborane. The resulting mixture was diluted with hexanes, washed with water, dried over Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel with 2% ethyl acetate in hexanes as eluent (5.32 g, 84% yield). All spectra for the isolated product was in accordance with the literature. [4]



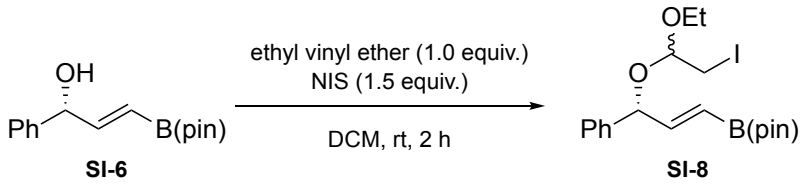
(*E*)-2-(7-iodohept-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SI-5) was synthesized using the same procedure as for substrate **20** from 7-Iodohept-1-yne. The crude product was isolated by silica gel chromatography (2% ethyl acetate in hexanes, stain in CAM), as a colorless oil (78% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.59 (dt, *J* = 17.9, 6.4 Hz, 1H), 5.42 (dt, *J* = 17.9, 1.4 Hz, 1H), 3.16 (t, *J* = 7.1 Hz, 2H), 2.15 (q, *J* = 6.6 Hz, 2H), 1.81 (p, *J* = 7.1 Hz, 2H), 1.47-1.34 (m, 4H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.0, 83.2, 35.6, 33.5, 30.2, 27.2, 24.9, 6.9. **IR** (neat) ν_{max} 2974.1 (w), 2926.4 (w), 2853.3 (w), 1636.4 (m), 1359.4 (s), 1317.2 (s), 1143.0 (s), 994.9 (w), 969.2 (w), 848.5 (w). **HRMS** (DART) for $C_{13}H_{25}BO_2I$ $(M+H)^+$: Calc'd: 351.0987, found: 351.0967.



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

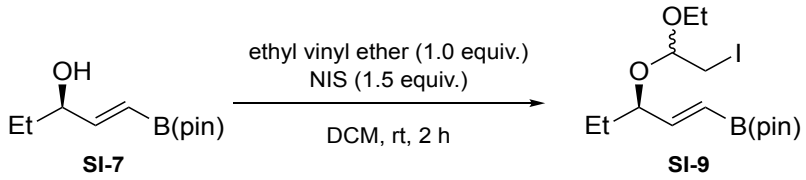


(*R*,*E*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-3-ol (SI-7) was generated from commercial (*R*)-1,2-epoxybutanestyrene (434 mg, 6.00 mmol, 1.0 equiv.) following the method reported by Meek.[5] The product was isolated by silica gel column chromatography (15% ethyl acetate in hexanes,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



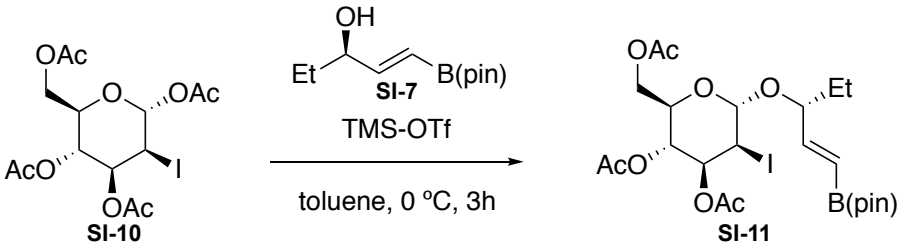
2-((*3R*,*E*)-3-(1-ethoxy-2-iodoethoxy)-3-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SI-8). A mixture of **SI-6** (156.1 mg, 0.6 mmol) and ethyl vinyl ether (43.3 mg, 0.6 mmol) in CH_2Cl_2 (10 mL) was added to a suspension of N-iodosuccinimide (202.5 mg, 0.9 mmol) in CH_2Cl_2 (10 mL) at 0 °C over 5 minutes. After stirring at room temperature for 2 hours, water (10 mL) was added, and the stirring was continued for one additional hour. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2×15 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (10% ethyl acetate in hexanes,

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



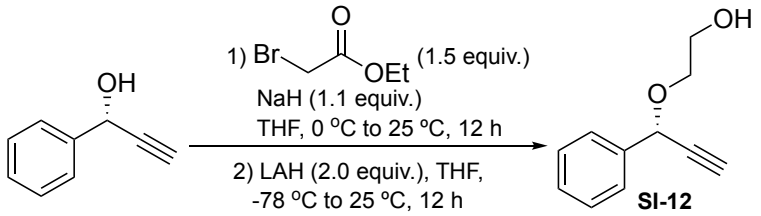
2-((*3R,E*)-3-(1-ethoxy-2-iodoethoxy)pent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3-dioxolane (SI-9) was synthesized using the same procedure for the synthesis of **SI-8** using **SI-7** (200 mg, 0.94 mmol, 1 equiv**.)** as starting material. The product consisting of a 1:1 inseparable mixture of diastereomers was isolated by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) as a clear yellow oil (240 mg, 62% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.46 (ddd, *J* = 45.5, 18.1, 7.1 Hz, 2H), 5.58 (dd, *J* = 18.2, 2.9 Hz, 2H), 4.59 (dt, *J* = 14.7, 5.6, 5.6 Hz, 2H), 3.99 (q, *J* = 6.7, 6.7, 6.7 Hz, 1H), 3.88 (q, *J* = 6.5, 6.5, 6.5 Hz, 1H), 3.69-3.44 (m, 4H), 3.20 (dt, *J* = 5.0, 2.9, 2.9 Hz, 4H), 1.70-1.50 (m, 5H), 1.32-1.24 (m, 24H), 1.22 (t, *J* = 7.0, 7.0 Hz, 3H), 1.17

(t, *J* = 7.0, 7.0 Hz, 3H), 0.92 (t, *J* = 7.5, 7.5 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.1, 152.4, 100.9, 99.6, 83.5, 83.4, 81.2, 80.5, 62.2, 61.5, 28.2, 27.8, 25.0, 24.9, 24.9, 24.8, 15.3, 15.0, 9.8, 9.7, 6.3, 6.3. **IR** (neat) ν_{max} 2972.9 (m), 2927.8 (w), 2874.6 (w), 1639.6 (m), 1365.7 (s), 1323.9 (s), 1141.9 (s), 1101.4 (s), 1047.4 (s), 998.4 (s), 968.6 (s), 847.9 (m), 648.5 (w), 577.4 (w). **HRMS** (DART) for $C_{15}H_{32}BNO_4I$ $(M+NH_4)^+$: Calc'd: 428.1464, found: 428.1467.



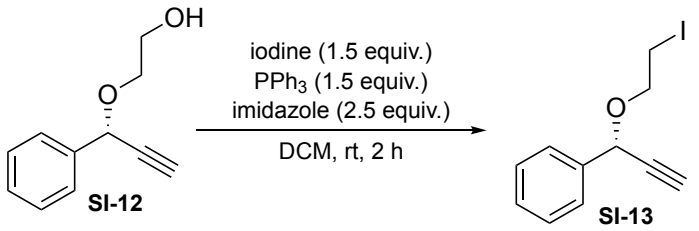
(2*R*,3*R*,4*S*,5*S*,6*S*)-2-(acetoxymethyl)-5-iodo-6-(((*R*,*E*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-3-yl)oxy)tetrahydro-2*H*-pyran-3,4-diyl diacetate (SI-11) was synthesized starting from (2*R*,3*S*,4*S*,5*R*,6*R*)-6-(acetoxymethyl)-3-iodotetrahydro-2*H*-pyran-2,4,5-triyl triacetate (**SI-10**) (1.07 g, 2.34 mmol, 1.1 equiv.) and **SI-7** (452 mg, 2.13 mmol, 1.0 equiv.) following the method described by Wan.[6] The crude product was isolated by silica gel chromatography (30% ethyl acetate in hexanes, UV) to afford a white a solid (1.12 g, 86% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.33 (dd, *J* = 18.1, 7.2 Hz, 1H), 5.59 (d, *J* = 18.1 Hz, 1H), 5.37 (t, *J* = 9.8 Hz, 1H), 5.16 (s, 1H), 4.66 (dd, *J* = 9.5, 4.3 Hz, 1H), 4.50 (d, *J* = 4.3 Hz, 1H), 4.21 (dd, *J* = 12.2, 5.0 Hz, 1H), 4.16-4.12 (m, 1H), 4.08-4.05 (m, 1H), 3.99 (q, *J* = 6.8 Hz, 1H), 2.11 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 1.72-1.50 (m, 4H), 1.28 (d, *J* = 2.5 Hz, 13H), 0.93 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.8, 169.9, 169.7, 150.4, 98.7, 98.6, 83.6, 80.8, 69.4, 69.2, 67.9, 62.5, 30.4, 28.1, 25.0, 24.9, 24.8, 21.1, 20.9, 20.8, 10.2. **IR** (neat) ν_{max} 2973.9

(m), 2933.1 (m), 1744.3 (s), 1641.1 (m), 1453.5 (w), 1366.3 (m), 1328.9 (w), 1222.2 (s), 1142.9 (s), 1114.6 (s), 1030.7 (s). **HRMS** (DART) for $C_{23}H_{40}BNOI$ $(M+NH_4)^+$: Calc'd: 628.1785, found: 628.1779. $[\alpha]_D^{20} = 47.39$ (c =1.0, $CHCl_3$, l = 50 mm).

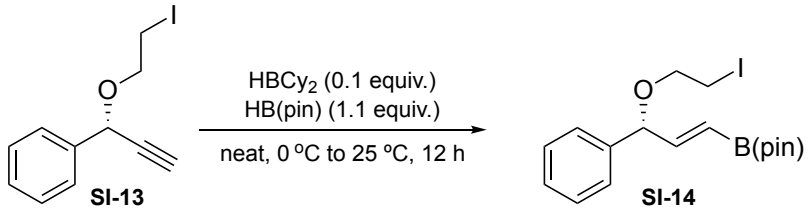


(*R*)-2-((1-phenylprop-2-yn-1-yl)oxy)ethan-1-ol (SI-12). Commercial (*R*)-1-phenylprop-2-yn-1-ol (981.0 mg, 7.42 mmol, 1.0 equiv.) was added dropwise to a suspension of sodium hydride (217.6 mg, 8.16 mmol, 90% purity, 1.1 equiv.) in THF (6 mL) at 0 °C. The mixture was warmed to room temperature and stirred for 1 h. After the mixture was cooled to 0 °C, ethyl 2-bromoacetate (1.86 g, 11.13 mmol, 1.5 equiv.) was added dropwise to the mixture. The mixture was warmed to room temperature and stirred for 12 h. The reaction mixture was quenched by saturated NH_4Cl aq. solution (10 mL) and extracted with Et_2O (3 x 20 mL). The combined organic layer was then dried over anhydrous Na_2SO_4. After filtration, the material was concentrated under reduced pressure. The corresponding crude ether was dissolved in THF (20 mL) and added dropwise to a solution of LAH in THF (1 M, 15.0 mL) at −78 °C under a nitrogen atmosphere. The reaction was allowed to warm to room temperature and stir for 12 h, after which it was cooled to 0ºC and quenched by careful addition of H_2O (1.0 mL) and then aqueous NaOH (3 M, 3.0 mL). After stirring at room temperature for 20 min $MgSO_4$ was added to the reaction mixture and the suspension was filtered through celite. The solvent was removed

in vacuo and the crude product was purified by flash column chromatography (20% ethyl acetate in hexanes) to obtain **SI-12** (0.78 g, 44% yield over two steps) as a colorless oil. All spectral data is in accordance with the literature.[7]

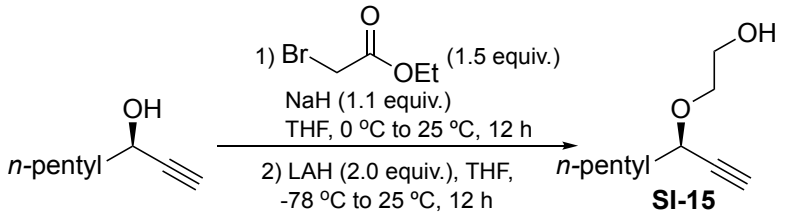


(*R*)-(1-(2-iodoethoxy)prop-2-yn-1-yl)benzene (SI-13). A solution of triphenylphosphine (1.03 g, 3.92 mmol) and iodine (0.99 g, 3.92 mmol) in dichloromethane (20 mL) was allowed to stir for 10 min at ambient temperature. Imidazole (0.44 g, 6.53 mmol) was added to the resulting mixture. After a 10 min stir, **SI-12** (0.46 g, 2.61 mmol) was added and the resulting mixture was stirred for 2 h. The mixture was quenched by the addition of saturated sodium metabisulfite (10 mL). The aqueous and organic layers were separated followed by extraction of the aqueous with dichloromethane (3 x 20 mL). The combined organic extracts were dried (anhydrous Na_2SO_4) and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (5% ethyl acetate in hexanes) to afford the **SI-13** (0.45 g, 60% yield) as a light-yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56-7.54 (m, 2H), 7.44-7.32 (m, 3H), 5.28 (d, J = 2.2 Hz, 1H), 3.95-3.89 (m, 1H), 3.84-3.77 (m, 1H), 3.31-3.28 (m, 2H), 2.69 (d, J = 2.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 137.7, 128.8, 128.7, 127.5, 81.1, 76.4, 71.4, 68.9, 2.5. **IR** (neat) ν_{max} 3284.2 (m), 3059.1 (w), 3027.0 (w), 2914.6 (w), 2850.9 (w), 1491.4 (w), 1451.3 (m), 1261.2 (m), 1189.5 (w), 1170.2 (w), 1094.3 (s), 1054.1 (s), 1027.2 (m), 990.3 (m), 740.0 (m), 696.4 (s), 652.8 (s). **HRMS** (DART) for $C_{11}H_{12}OI$ $(M+H)^+$: Calc'd: 286.9927, found: 286.9929.

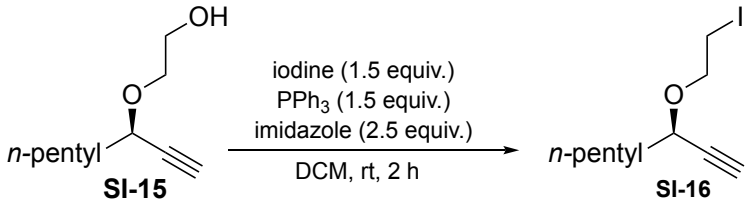


SI-13 SI-14

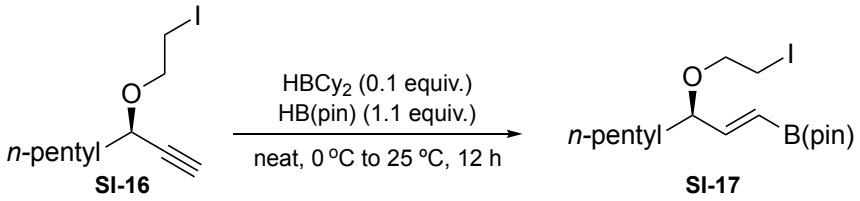
(*R*,*E*)-2-(3-(2-iodoethoxy)-3-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SI-14). In the glovebox a 2-dram vial is charged with neat dicyclohexylborane (19.1 mg, 0.11 mmol), 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (164.5 mg, 1.30 mmol) and **SI-13** (306.4 mg, 1.1 mmol) was added at 0 °C and the mixture was stirred for a 12 hours at room temperature. The reaction mixture was quenched by bubbling air through the solution with tube pump for 2 hours at room temperature to oxidize the dicyclohexylboryl group. The resulting mixture was diluted with hexane, washed with water, dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (5% ethyl acetate in hexanes, stain in CAM) to afford the title compound (0.25 g, 56% yield) as a clear yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H, 6.66 (dd, *J* = 18.0, 5.8 Hz, 1H), 5.70 (d, *J* = 17.8 Hz, 1H), 4.86 (d, *J* = 5.7 Hz, 1H), 3.79-3.71 (m, 2H), 3.67-3.63 (m, 1H), 3.28-3.24 (m, 2H), 1.87-1.84 (m, 1H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 151.9, 140.1, 128.7, 128.0, 127.2, 84.0, 83.5, 69.5, 24.9, 3.0. **IR** (neat) ν_{max} 2974.2 (w), 1637.3 (m), 1355.7 (s), 1355.7 (s), 1265.3 (w), 1142.6 (s), 1106.9 (w), 995.4 (w), 969.3 (w), 847.8 (m), 669.2 (m). **HRMS** (DART) for $C_{17}H_{23}BO_3I$ $(M+H)^+$: Calc'd: 413.0779, found: 413.0788. **$[\alpha]_D^{20}$**= 19.11 (*c* =1.0, $CHCl_3$, *l* = 50 mm).



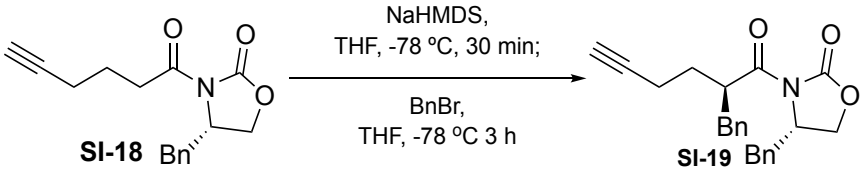
(*R*)-2-(oct-1-yn-3-yloxy)ethan-1-ol (SI-15) was synthesized using the same procedure for the synthesis of **SI-13**, using commercially available (*R*)-oct-1-yn-3-ol. The product was isolated by silica gel chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford a colorless oil (37% yield over two steps). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.08 (td, *J* = 6.7, 6.6, 2.0 Hz, 1H), 3.88-3.83 (m, 1H), 3.80-3.75 (m, 2H), 3.56-3.51 (m, 1H), 2.45 (t, *J* = 1.9, 1.9 Hz, 1H), 1.93 (t, *J* = 6.3, 6.3 Hz, 1H), 1.81-1.69 (m, 2H), 1.50-1.44 (m, 2H), 1.36-1.31 (m, 4H), 0.91 (t, *J* = 7.0, 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 83.0, 74.0, 70.2, 70.1, 62.1, 35.7, 31.6, 25.0, 22.7, 14.1. **IR** (neat) ν_{max} 3423.7 (br), 3306.2 (m), 2950.9 (s), 2927.2 (s), 2858.8 (m), 1460.8 (w), 1333.3 (w), 1105.5 (s), 1070.6 (m), 657.9 (w), 629.3 (w). **HRMS** (DART) for $C_{10}H_{19}O_2$ $(M+H)^+$: Calc'd: 171.1380, found: 171.1376.



(*R*)-3-(2-iodoethoxy)oct-1-yne was synthesized using the same procedure for the synthesis of **2c**. All spectral data is in accordance with the literature.[8]

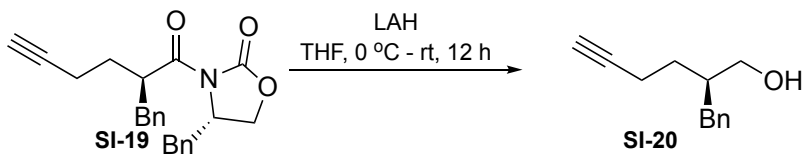


2-((*R*,*E*)-3-(2-iodoethoxy)oct-1-en-1-yl)-4,4,5-trimethyl-1,3,2-dioxaborolane (SI-17) was synthesized using the same procedure for the synthesis of **SI-14**. Isolated by silica gel chromatography (10% ethyl acetate in hexanes, stain CAM) to afford the product as a clear yellow oil (60% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.42 (dd, *J* = 18.1, 6.6 Hz, 1H), 5.57 (d, *J* = 18.1 Hz, 1H), 3.77-3.71 (m, 2H), 3.58-3.46 (m, 1H), 3.21 (t, *J* = 7.0, 7.0 Hz, 2H), 1.59-1.38 (m, 4H), 1.33-1.22 (d, 16H), 0.87 (t, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.2, 83.4, 82.5, 69.7, 35.2, 31.9, 25.2, 24.9, 22.7, 14.2, 3.4. **IR** (neat) ν_{max} 2973.9 (w), 2953.2 (w), 2926.2 (m), 2855.6 (w), 1639.1 (m), 1464.4 (w), 1356.5 (s), 1327.2 (s), 1265.6 (m), 1142.9 (s), 1107.2 (m), 1107.2 (m), 998.2 (m), 968.8 (m), 848.5 (m). **HRMS** (DART) for $C_{16}H_{34}BNO_3I$ $(M+NH_4)^+$: Calc'd: 426.1671, found: 426.1669. **$[\alpha]_D^{20}$** = 26.05 (*c* =1.0, $CHCl_3$, *l* = 50 mm)



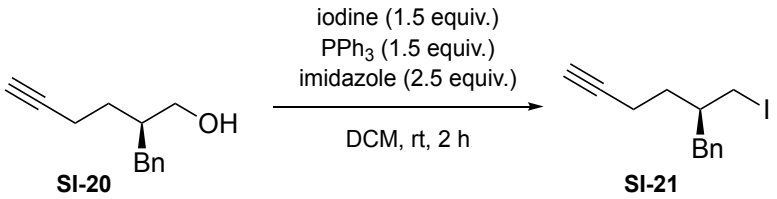
(*S*)-4-benzyl-3-(hex-5-ynoyl)oxazolidin-2-one (SI-18) was synthesized using reported method. All spectral data is in accordance with the literature.[9]

(*S*)-4-benzyl-3-((*R*)-2-benzylhex-5-ynoyl)oxazolidin-2-one (SI-19). In a flame-dried round bottom flask, under an atmosphere of N_2, a solution of sodium bis(trimethylsilyl)amide (11.6 mL, 1.00 M in THF, 11.6 mmol) was further diluted with THF (20 mL) and cooled to -78 °C. To it was added a solution of (4S)-4-benzyl-3-hex-5-ynoyl-oxazolidin-2-one (**SI-18**) (1.8 g, 6.63 mmol) in THF (10 mL) by syringe over 10 min. After stirring for 30 min, benzylbromide (3.40 g, 19.9 mmol) was added neat. The solution was then stirred at -78 °C temperature for 2.5 h at which point the reaction was quenched with 100 mL of 0.5 M HCl (aq.). The mixture was extracted with ethyl acetate (50 mL x 2) and the combined organic extracts were washed with water (100 mL), brine (100 mL) and dried over anhydrous Na_2SO_4. The solution was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (15% ethyl acetate in hexanes, UV active) to afford the product as a colorless oil (1.41 g, 59% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34-7.16 (m, 8H), 7.12-7.03 (m, 2H), 4.66-4.62 (m, 1H), 4.39-4.30 (m, 1H), 4.13 (t, *J* = 8.4 Hz, 1H), 4.07 (dd, *J* = 9.0, 2.6 Hz, 1H), 3.13-3.00 (m, 2H), 2.79 (dd, *J* = 13.4, 7.5 Hz, 1H), 2.46 (dd, *J* = 13.4, 9.6 Hz, 1H), 2.25-2.22 (m, 2H), 2.06-1.99 (m, 1H), 1.94-1.93 (m, 1H), 1.78-1.70 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.4, 153.1, 138.6, 135.3, 129.5, 129.5, 129.0, 128.5, 127.4, 126.7, 83.4, 69.2, 66.0, 55.3, 43.8, 38.8, 37.8, 30.1, 16.6. **IR** (neat) ν_{max} 3284.2 (m), 3059.2 (w), 3025.4 (w), 2921.6 (m), 2856.9 (w), 1772.4 (s), 1691.1 (s), 1385.3 (s), 1348.1 (s), 1239.9 (s), 1210.1 (s), 1193.1 (s), 739.9 (s). **HRMS** (DART) for $C_{23}H_{24}NO3$ $(M+H)^+$: Calc'd: 362.1751, found: 362.1761. **$[\alpha]_D^{20}$** = 18.20 (*c* =1.0, $CHCl_3$, *l* = 50 mm).



SI-19 **SI-20**

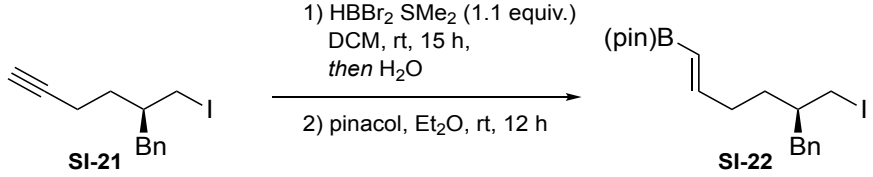
(*R*)-2-benzylhex-5-yn-1-ol (SI-20). To a solution of LAH (220.5 mg, 5.8 mmol) in THF (30 mL) was added a solution of **SI-19** (0.70 g, 1.94 mmol) in 20 mL THF at -78 °C. The mixture was allowed to warm to room temperature over the course of a several hours and stirred for 12 hours. The mixture was cooled to 0 ºC and H_2O (0.6 mL) was carefully added, followed by 3 M NaOH (0.6 mL). The suspension was stirred at room temperature for 20 min after which $MgSO_4$ was added. The resulting mixture was filtered through a pad of celite and concentrated in vacuo. The crude product was purified by silica gel column chromatography (15% ethyl acetate in hexanes) to afford **SI-20** (0.25 g, 68% yield) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32-7.27 (m, 2H), 7.23-7.21 (m, 3H), 3.63-3.53 (m, 2H), 2.67 (d, *J* = 7.3 Hz, 2H), 2.30-2.27 (m, 2H), 2.02-1.97 (m, 2H), 1.72-1.57 (m, 2H), 1.31 (td, *J* = 5.6, 5.6, 2.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.4, 129.3, 128.5, 126.2, 84.5, 68.8, 64.3, 41.6, 37.5, 29.7, 16.4. **IR** (neat) ν_{max} 3288.6 (m), 3023.4 (w), 3025.4 (w), 2921.3 (m), 1600.8 (w), 1493.5 (m), 1451.5 (m), 1029.0 (s), 981.9 (s), 736.3 (s), 699.3 (s), 631.8 (s), 493.4 (w). **HRMS** (DART) for $C_{13}H_{17}O$ $(M+H)^+$: Calc'd:189.1274, found: 189.1268. **$[\alpha]_D^{20}$** = 1.19 (*c* =1.0, $CHCl_3$, *l* = 50 mm).



SI-20 **SI-21**

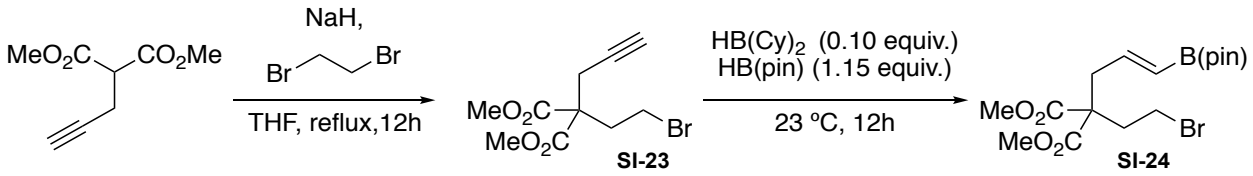
(*R*)-(2-(iodomethyl)hex-5-yn-1-yl)benzene (SI-21). A solution of triphenylphosphine (0.53 g, 2.0 mmol) and iodine (0.51 g, 2.0 mmol) in dichloromethane (5 mL) was allowed to stir for 10 min at ambient temperature. Imidazole (0.23 g, 3.3 mmol) was added to the resulting mixture.

After stirring for 10 min, **SI-20** (.25 g, 1.3 mmol) was added and the resulting mixture was stirred for 2 h. The mixture was quenched by the addition of saturated sodium metabisulfite aq. solution (5 mL). The aqueous and organic layers were separated and the aqueous layer was extracted with dichloromethane (3 x 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (5% ethyl acetate in hexane, stain in CAM) to afford the title compound (0.3 g, 75%) as a light-yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34-7.31 (m, 2H), 7.28-7.24 (m, 3H), 3.27 (dd, *J* = 10.3, 3.1 Hz, 1H), 3.16 (dd, *J* = 10.2, 2.9 Hz, 1H), 2.71 (dd, *J* = 13.8, 4.1 Hz, 1H), 2.56 (dd, *J* = 13.8, 7.6 Hz, 1H), 2.37-2.19 (m, 2H), 2.00 (t, *J* = 2.6, 2.6 Hz, 1H), 1.71-1.56 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.5, 129.3, 128.6, 126.5, 83.4, 69.3, 40.2, 39.1, 33.1, 15.9, 15.5. **IR** (neat) ν_{max} 3290.6 (m), 3058.8 (w), 2920.0 (m), 2851.4 (w), 1601.0 (w), 1493.7 (m), 1451.2 (m), 1220.8 (m), 735.9 (s), 699.1 (s), 634.9 (s), 491.3 (w). **HRMS** (DART) for $C_{13}H_{16}I$ $(M+H)^+$: Calc'd: 299.0291, found: 299.0292. **$[\alpha]_D^{20}$** = -45.02 (*c* =1.0, $CHCl_3$, *l* = 50 mm).



(*R,E*)-2-(5-benzyl-6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (SI-22). To a solution of **SI-21** (0.30 g, 1.0 mmol) in 10 mL of anhydrous dichloromethane was added 1.1 mL of a 1.0 M solution of $HBBr_2$•SMe_2 (1.1 mmol) in dichloromethane. After 15 h at room temperature, the mixture was cooled to 0 ºC and water (5 mL) was slowly added. The aqueous phase was extracted with 2 x 20 mL of ether. Addition of pinacol (0.12 g, 1.0 mmol) to the combined organic phases was followed by stirring for 12 hours at room temperature. The

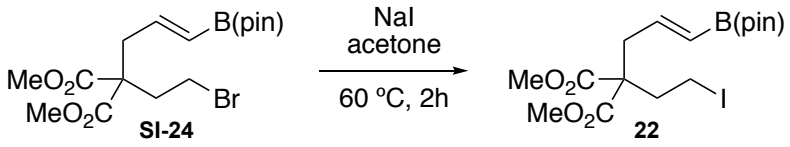
reaction mixture is concentrated under reduced pressure, and purified by flash chromatography (5% ethyl acetate in hexane, stain in CAM) to afford **SI-22** (0.35 g, 82%) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33-7.26 (m, 2H), 7.24-7.19 (m, 3H), 6.63 (dt, *J* = 17.9, 6.4, 6.4 Hz, 1H), 5.49 (d, *J* = 17.9 Hz, 1H), 3.23 (dd, *J* = 10.0, 4.2 Hz, 1H), 3.13 (dd, *J* = 10.0, 3.7 Hz, 1H), 2.67 (dd, *J* = 13.8, 5.5 Hz, 1H), 2.55 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.30-2.21 (m, 1H), 2.18-2.11 (m, 1H), 1.59-1.46 (m, 2H), 1.46-1.37 (m, 1H), 1.29 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.4, 139.7, 129.2, 128.5, 126.4, 83.2, 40.4, 39.9, 33.1, 32.8, 24.9, 15.9. **IR** (neat) ν_{max} 3022.6 (m), 2974.1 (m), 2923.5 (w), 1636.3 (m), 1452.0 (w), 1396.3 (m), 1360.6 (s), 1320.1 (s), 1143.0 (s), 999.4 (w), 969.5 (w), 848.7 (w), 738.3 (w), 699.7 (m). **HRMS** (DART) for $C_{19}H_{29}BO_2I$ $(M+H)^+$: Calc'd: 427.1300, found: 427.1315. **$[\alpha]_D^{20}$** = -18.64 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).



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

concentrated under reduced pressure. The crude material was filtered through a silica plug with 20% ethyl acetate in hexanes and carried to the next step.

Inside an argon filled glovebox a 4 dram vial was charged with neat 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (637.32 mg, 5.00 mmol, 1.15 equiv.) and dicyclohexylborane (77.13 mg, 0.43 mmol, 0.10 equiv.). The vial was placed inside the glove box freezer to cool for 30 minutes. Dimethyl-2-(2-bromoethyl)-2-prop-2-ynyl-propanedioate (**SI-23)** (1.20 g, 4.33 mmol, 1.0 equiv.) was added to the cool suspension and the vial was then sealed and stirred for 12 hours at room temperature. Finally, the reaction mixture was quenched by bubbling air through the solution for 2 hours at room temperature to oxidize the dicyclohexylborane. The resulting mixture was diluted with diethyl ether, washed with water, dried over Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (10% ethyl acetate in hexanes, stain in $KMnO_4$) to afford the product **SI-24** as a colorless oil (862 mg, 49% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.35 (dt, *J* = 17.7, 7.2 Hz, 1H), 5.53 (dt, *J* = 17.7, 1.2 Hz, 1H), 3.74 (s, 6H), 3.34 (t, 2H), 2.76 (dd, *J* = 7.2, 1.3 Hz, 2H), 2.45 (t, 2H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.7, 146.1, 121.9, 83.5, 57.5, 52.9, 40.1, 36.4, 27.2, 24.9. **IR** (neat) ν_{max} 2975.4 (w), 1732.4 (s), 1637.6 (w), 1436.1 (w), 1390.7 (m), 1362.6 (m), 1268.9 (m), 1166.2 (m), 998.4 (w), 970.4 (w), 643.0 (w). **HRMS** (DART) for $C_{16}H_{26}BIO_6$ $(M+H)^+$: Calc'd: 405.1079, found: 405.1075.



Dimethyl(E)-2-(2-iodoethyl)-2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)malonate (22). To a round bottom flask containing **SI-24** (400 mg, 0.99 mmol, 1.0 equiv.) was added a solution of sodium iodide (592.04 mg, 3.95 mmol, 4.0 equiv.) in acetone (22 mL). The reaction mixture was heated to reflux for 2 hours. The mixture was cooled to room temperature, diluted with diethyl ether (100 mL), and washed with water and brine. The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The product was isolated after silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) as a clear yellow oil (395 mg, 89% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.34 (dt, *J* = 17.7, 7.2 Hz, 1H), 5.52 (d, *J* = 17.7 Hz, 1H), 3.73 (s, 6H), 3.14-3.00 (m, 2H), 2.73 (d, *J* = 7.2 Hz, 2H), 2.52-2.38 (m, 2H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.47, 146.12, 83.43, 59.05, 52.85, 39.82, 37.97, 24.88, 2.42. **IR** (neat) ν_{max} 2975.24 (br), 1732.1 (s), 1637.31 (w), 1436.06 (w), 1390.18 (m), 1324.55 (m), 1143.48 (m), 997.73 (w), 970.29 (w), 848.74 (w). **HRMS** (DART) for $C_{16}H_{26}BIO_6$ $(M+H)^+$: Calc'd: 453.0940, found: 453.0949.

3.4.2.3 . Procedures for the Preparation of Organozinc Reagents

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

A 20 mL vial was charged with zinc powder (1.26 g, 19.31 mmol, 2.50 equiv.) and a stir bar. The vial was capped with a PTFE-lined pierceable screwcap and he system was heated at 80 °C under high vacuum for 2 hours with stirring. The vial is then cooled to room temperature and backfilled with N_2. At this point the vial is brought into an Ar filled glove box, a solution of iodine (95.84 mg, 0.38 mmol, 0.02 equiv.) in DMA (1 mL) and the suspension was stirred until the red color subsided. In turn, alkyl bromide (7.60 mmol, 1.00 equiv.) and an additional 4 mL of

DMA were added. The vial was capped with a Teflon screwcap, taped and the suspension was heated at 80 °C for 12 hours. Next, the mixture was cooled to room temperature, brought inside the glovebox and filtered through a syringe filter (pore-size: 0.45 μM, PTFE). The resulting organo-zinc solution was titrated following the Knochel method (I_2 in a 0.5 M THF solution of LiCl).[10]

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

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

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

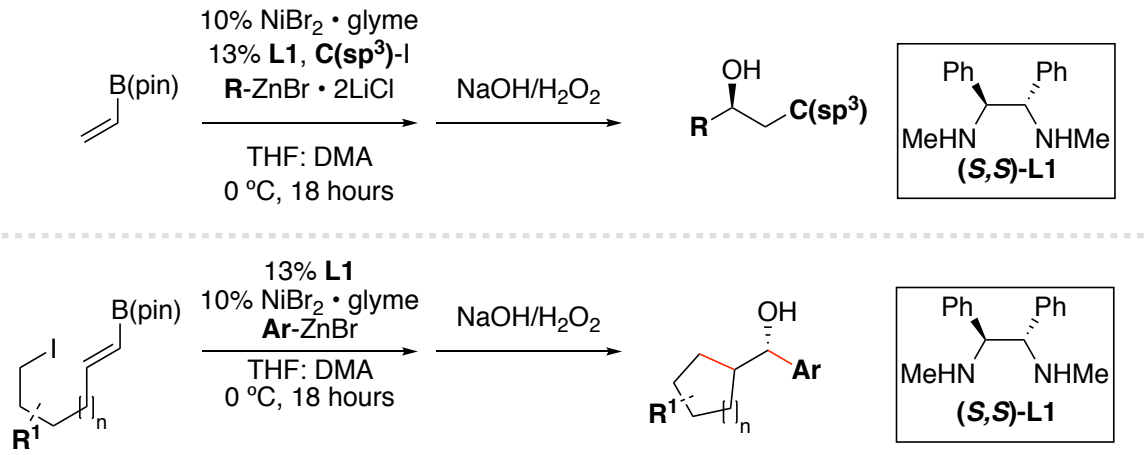
Organolithium reagents were generated by lithium-halogen exchange with *tert*-butyllithium using the following procedure: an aryl bromide or alkyl iodide (1.0 mmol) was placed in a flame-dried 20 mL vial under N_2 atmosphere and dissolved 5 mL of dry diethyl ether. The vial was sealed with a pierceable PTFE-lined cap and a septum was taped over it (this second septum was backfilled with N_2 and creates a buffer zone to prevent air from entering the vial). The solution was cooled to -78 ºC and *tert*-butyllithium (1.18 mL, 1.7 M, 2.0 equiv.) was added dropwise. The solution was stirred at -78°C for 30-40 min after which a solution of $ZnCl_2$ in THF was added

(2.4 mL, 0.5 M, 1.2 equiv.). The mixture was warmed to room temperature and stirred for 45 minutes after which time the solvent was carefully removed under vacuum through the Schlenck line. The concentrated residue was brought inside an argon filled glovebox and re-dissolved in 2 mL of THF. The resulting solution was titrated following the Knochel method.[10]

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

3.4.2.4. Representative Procedure for Cross-Coupling

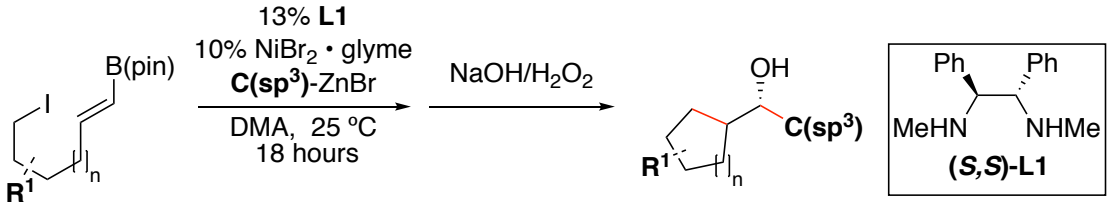
Procedure A, for the three component cross-coupling (alkyl or aryl ZnX) and two component cyclization/cross-coupling with aryl ZnX reagents.



In an argon-filled glovebox, an oven-dried 2 dram vial equipped with a magnetic stirrer was charged with **$NiBr_2$ • glyme** (6.17 mg, 0.02 mmol), (*S*,*S*)-N,N-dimethyl-1,2-diphenyl-ethane-1,2-diamine **(*S,S*)-L1** (6.25 mg, 0.026 mmol) and dissolved in 1.0 mL of THF. The catalyst solution was stirred for 1 hour at ambient temperature. **Vinylboronic acid pinacol ester** (30.80 mg, 0.20 mmol, 1.00 equiv.) and **alkyl iodide** (0.40 mmol, 2.00 equiv.), or **cyclizing alkenyl boron** substrate (0.20 mmol, 1.00 equiv.) were added to the catalyst solution (alternatively, the reactants could be weighed out in a separate vial and the catalyst solution added to the latter). At this point, THF and DMA were added so as to reach a final volume (taking into account the volume of the organozinc solution) of 2.00 mL of THF and 0.40 mL DMA. The vial was sealed with a PTFE-lined pierceable cap, taped, and brought outside the glovebox where it was placed in a CryoCool set at 0 ºC. The vial was cooled for 20-30 minutes before addition of the **organozinc** solution (0.40 mmol, 2.00 equiv.) (***Note:*** for the three component reactions with alkyl-ZnBr reagents, the organozinc reagent was stirred with LiCl (35.6 mg, 0.84 mmol, 4.20 equiv.), in 0.50 mL of THF for 1 hour at room temperature before addition). The puncture hole was taped over and the reaction mixture was stirred at 0 ºC for 18 hours. Oxidation was then carried out by adding 0.50 mL of 30% H_2O_2 and 0.50 mL of 3.0 M aqueous NaOH solution to the cold reaction mixture (the vial was vented to prevent pressure build-up). The mixture was stirred vigorously for 2-3 hours and allowed to slowly warm to room temperature. At this point the reaction mixture was cooled to 0 ºC once more and the oxidation was quenched by addition of 0.50 mL of saturated aqueous $Na_2S_2O_3$ .The organic layer was extracted four times with ethyl acetate, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel chromatography.

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

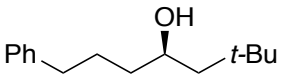
Procedure B, **for intramolecular cyclization/cross-coupling reactions using alkyl-ZnBr.**



In an argon-filled glovebox, an oven-dried 2 dram vial equipped with a magnetic stirrer was charged with **$NiBr_2$ • glyme** (6.17 mg, 0.02 mmol), (*S,S*)-N,N-dimethyl-1,2-diphenyl-ethane-1,2-diamine **(*S,S*)-L1** (6.25 mg, 0.026 mmol) and dissolved in 1.0 mL of DMA. The catalyst solution was stirred for 1 hour at ambient temperature. The **cyclizing alkenyl-boron** substrate (0.20 mmol, 1.00 equiv.) was added to the catalyst solution (alternatively, the substrated could be weighed out in a separate vial and the catalyst solution added to the latter). DMA was added so as to reach a final volume (taking into account the volume of the organozinc solution) of 2.00

mL. The vial was sealed with a PTFE-lined pierceable cap, taped, and brought outside the glovebox where it was placed in an ice-bath. The vial was cooled for a few minutes before addition of the organozinc solution (0.40 mmol, 0.20 equiv.). The puncture hole was taped over and the reaction mixture was taken off the ice bath and stirred at room temperature for 18 hours. Finally, the mixture was cooled to 0 ºC and 0.30 mL of saturated aqueous NH_4Cl solution were added. The mixture was then transferred to a separatory funnel using ethyl acetate and the organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The crude product could then be isolated as the boronic ester by silica gel chromatography, or re-dissolved in 1.0 mL of THF and oxidized following the method outlined in **procedure B**.

3.4.2.5. Procedures and Characterization for Cross-Coupling Product



(*R*)-6,6-dimethyl-1-phenylheptan-4-ol (**2**) The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (3-phenylpropyl)zinc bromide • 2LiCl solution in DMA (0.24 mL, 1.68 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (24.3 mg, 55% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29-7.26 (m, 3H), 7.19-7.18 (m, 2H), 3.80-3.75 (m, 1H), 2.67-2.60 (m, 2H), 1.82-1.69 (m, 1H), 1.7-

1.60 (m, 1H), 1.52-1.42 (m, 2H), 1.38-1.30 (m, 2H), 0.95 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.56, 128.55, 128.44, 125.87, 69.64, 51.49, 39.33, 36.04, 30.41, 30.30, 27.59. **IR** (neat) ν_{max} 3358.9 (br), 3023.7 (w), 2945.4 (s), 2931.7 (s), 2859.3 (m), 1602.2 (w), 1494.4 (m), 1452.2 (m), 1362.2 (m),1089.6 (m), 746.89 (m), 697.6 (s). **HRMS** (DART) for $C_{15}H_{28}NO$ $(M+NH_4)^+$: Calc'd: 238.2165, found: 238.2166. **$[\alpha]_D^{20}$** = 8.60 (*c* =1.0, $CHCl_3$, *l* = 50 mm).

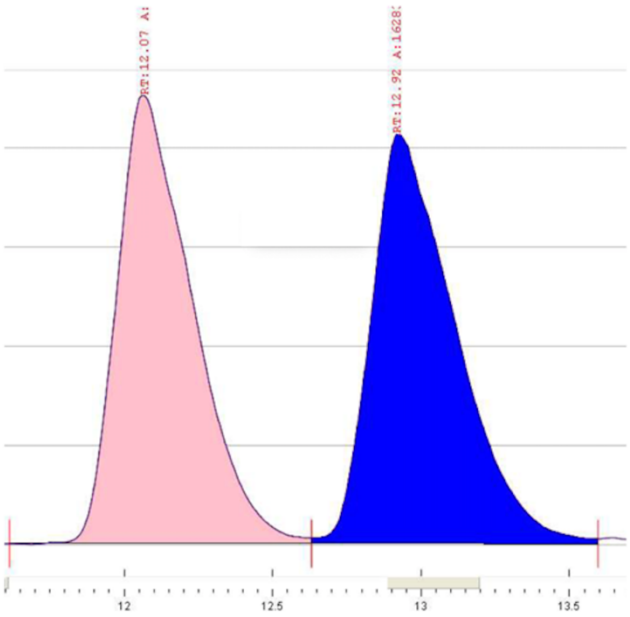
Analysis of Stereochemistry:

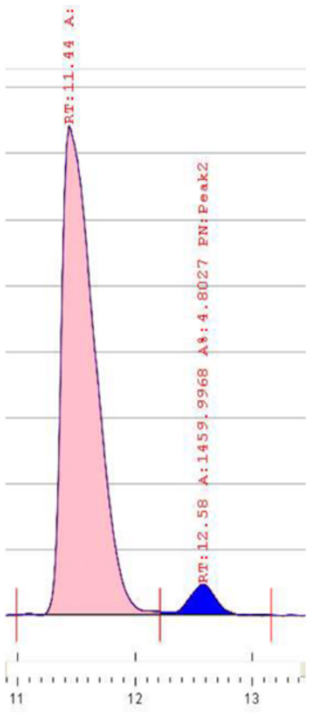
Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned analogy (see product **7** and **21**).

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

Racemic Material

Enantioenriched Material





Peak Info				Peak Info			
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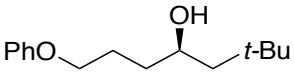
2	50.42	16283.1295	12.92	2	4.8027	1459.9968	12.58
Total:	100	32294.9938		Total:	100	30399.5276	



(*R*)-6,6-dimethyl-1-phenoxyheptan-4-ol (3). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (3-phenoxypropyl)zinc bromide • 2LiCl solution in DMA (0.360 mL, 1.1 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (20% ethyl acetate in hexanes,

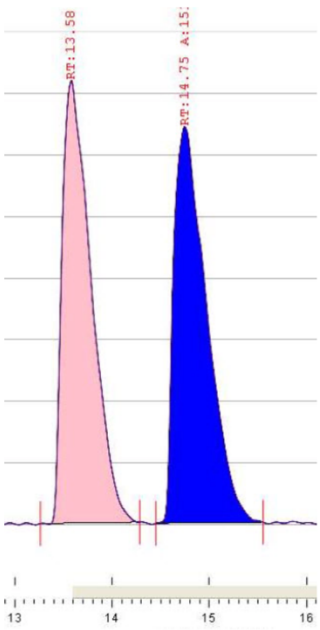
stain in CAM) to afford the product as a colorless oil (33.1 mg,70% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32-7.21 (m, 2H), 6.99-6.84 (m, 3H), 4.08-3.91 (m, 2H), 3.91-3.75 (m, 1H), 2.00-1.76 (m, 2H), 1.71-1.55 (m, 2H), 1.40 (d, *J* = 5.1 Hz, 2H), 0.98 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.0, 129.6, 120.8, 114.6, 69.2, 68.1, 51.5, 36.4, 30.4, 30.3, 25.7. **IR** (neat) ν_{max} 3394.5 (br), 2947.5 (m), 1598.8 (m), 1495.5 (m), 1471.1 (m), 1360.4 (w), 1247.9 (s), 1034.4 (w), 757.1 (m), 690.7 (m). **HRMS** (DART) for $C_{15}H_{25}O_2$ $(M+H)^+$: Calc'd: 237.18491, found: 237.18571. **$[\alpha]_D^{20}$** = -6.898 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).

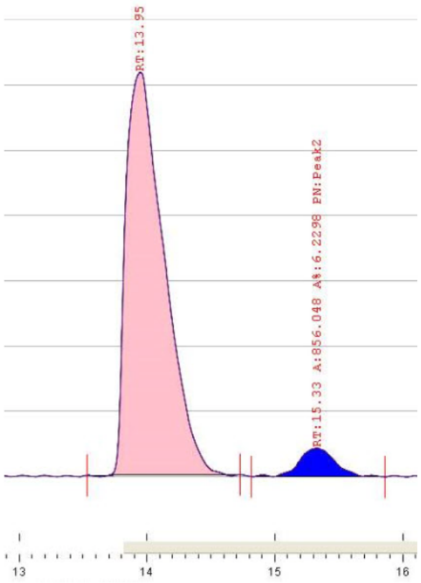
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

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

Racemic Material Enantioenriched Material





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

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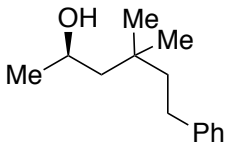
Total:	100	13741.2181	



(*R*)-4,4-dimethyl-6-phenylhexan-2-ol (4). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), (3-iodo-3-methylbutyl)benzene (109.7 mg, 0.40 mmol, 2.0 equiv.), and methylzinc chloride • 2LiCl solution in THF (1.01 mL, 0.40 M, 0.40 mmol, 2.0 equiv.) (**note:** the organozinc reagent was obtained by addition of commercial MeLi (130 µL, 3.1 M in DME, 0.4 mmol, 2.0 equiv.) to $ZnCl_2$ in THF (880 µL, 0.5 M, 0.44 mmol, 2.2 equiv.). After stirring for 30 min at room temperature additional LiCl (18.7 mg, 0.44 mmol, 2.2 equiv.) was added to improve yield and selectivity of the reaction), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg,

0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (48.9 mg, 55% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30-7.23 (m, 2H), 7.21-7.14 (m, 3H), 4.03-4.00 (m, 1H), 2.65-2.50 (m, 2H), 1.65-1.52 (m, 2H), 1.50 (dd, *J* = 14.5, 7.9 Hz, 1H), 1.41 (dd, *J* = 14.6, 2.9 Hz, 1H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.02 (s, 3H), 1.01 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.5, 128.5, 125.7, 65.7, 51.0, 45.3, 33.1, 30.9, 27.9, 27.8, 26.3. **IR** (neat) ν_{max} 3363.6 (br), 3023.3 (w), 2955.9 (s), 2924.5 (s), 2863.2 (m), 1494.9 (m), 1467.25 (m), 1259.0 (m), 1072.9 (s), 1051.5 (s), 1029.7 (s), 737.7 (s) 697.4 (s). **HRMS** (DART) for $C_{14}H_{26}NO$ $(M+NH_4)^+$: Calc'd: 224.2007, found: 224.2009. **$[\alpha]_D^{20}$** = 11.80 (*c* =1.0, $CHCl_3$, *l* = 50 mm).

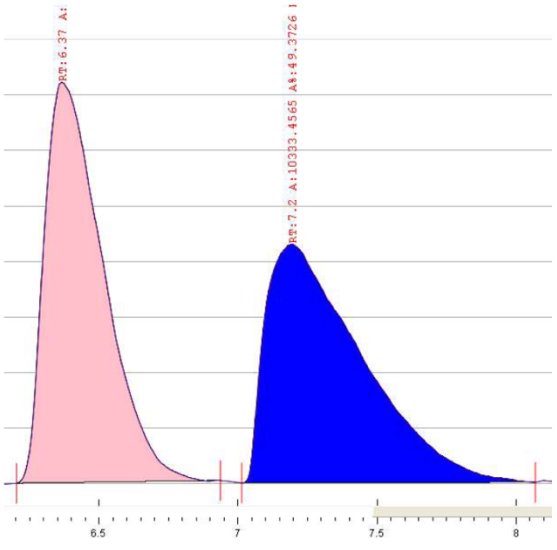
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

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

Racemic Material

Enantioenriched Material



Peak Info			
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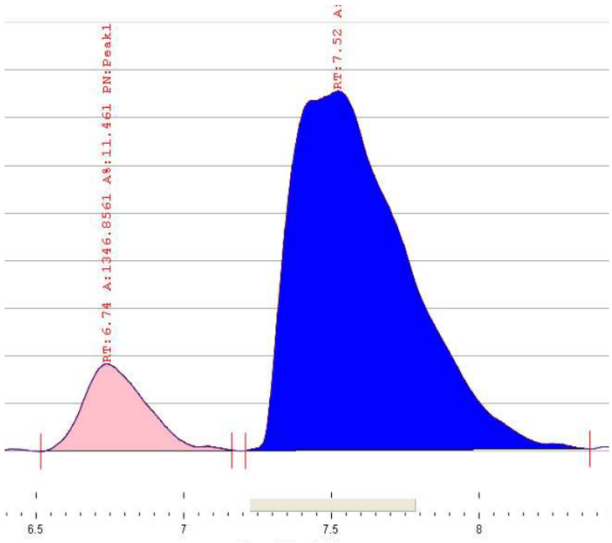

Peak Info			
Peak No	% Area	Area	RT (min)
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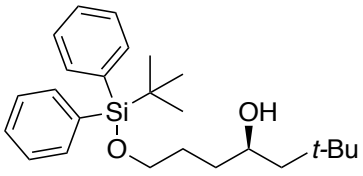
Total:	100	11751.6019	



(*R*)-1-((*tert*-butyldiphenylsilyl)oxy)-6,6-dimethylheptan-4-ol (5).

The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (3-((*tert*-butyldiphenylsilyl)oxy)propyl)zinc bromide• 2LiCl solution in DMA (0.425 mL, 0.94 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (56 mg,

70% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.69-7.67 (m, 3H), 7.48-7.36 (m, 5H), 3.82-3.76 (m, 1H), 3.71-3.68 (m, 2H), 1.83 (s, 1H), 1.73-1.61 (m, 2H), 1.60-1.47 (m, 2H), 1.42 -1.32 (m, 2H), 1.06 (s, 9H), 0.97 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 135.7, 135.7, 133.9, 133.9, 129.8, 127.8, 69.3, 64.3, 51.4, 36.6, 30.4, 30.3, 28.9, 27.0, 19.3. **IR** (neat) ν_{max} 3385.9 (br), 3067.8 (w), 3047.8 (w), 2948.0 (s), 2928.7 (s), 2856.3 (s), 1471.1 (m), 1426.3 (m), 1388.8 (m), 1108.8 (s), 700.3 (s), 613.0 (m), 504.4 (s). **HRMS** (DART) for $C_{25}H_{39}O_2Si$ $(M+H)^+$: Calc'd: 399.2714, found: 399.2723. **$[\alpha]_D^{20}$** = -3.60 (*c* =1.0, $CHCl_3$, *l* = 50 mm).

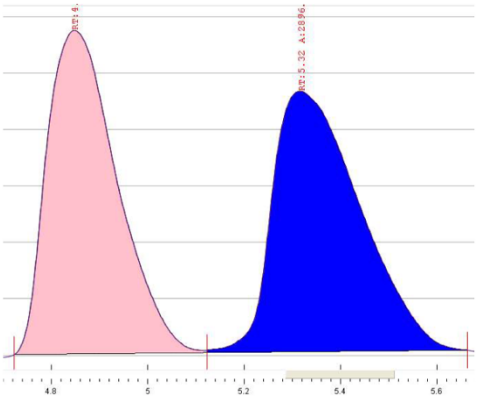
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

Chiral SFC (Chiracel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-1-((*tert*-butyldiphenylsilyl)oxy)-6,6-dimethylheptan-4-ol.**

Racemic Material

Enantioenriched Material



Peak Info			
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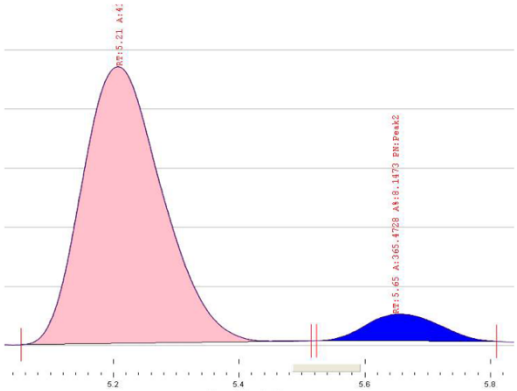

Peak Info			
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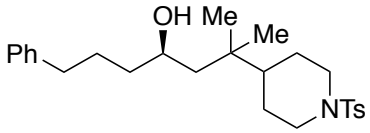
Total:	100	4485.8086	



(*R*)-6-methyl-1-phenyl-6-(1-tosylpiperidin-4-yl)heptan-4-ol (6).

The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), 4-(2-iodopropan-2-yl)-1-tosylpiperidine (162.92 mg, 0.40 mmol, 2.0 equiv.), and (3-phenylpropyl)zinc bromide • 2LiCl solution in DMA (0.24 mL, 1.68 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as white solid (48.9 mg, 55% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65-7.63(m, 2H), 7.33-7.26 (m, 4H), 7.19-7.17 (m, 3H), 3.84 (apparent d, J = 11.2 Hz, 2H), 3.70-3.67 (m, 1H), 2.69-2.55 (m, 2H), 2.43 (s, 3H), 2.20-1.99 (m, 2H), 1.79-1.58 (m, 4H), 1.45-1.25 (m, 6H), 1.11-1.07 (m, 2H), 0.87

(s, 3H), 0.84 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.5, 142.3, 133.2, 129.6, 128.5, 128.4, 127.9, 125.9, 69.0, 47.3, 47.2, 44.7, 39.6, 35.9, 34.7, 27.5, 26.1, 25.3, 25.1, 21.6. **IR** (neat) ν_{max} 3541.5 (br), 3023.0 (m), 2926.1 (s), 2850.8 (m), 1715.6 (w), 1596.4 (w), 1493.2 (m),1464.6 (s), 1450.4 (s), 1353.5 (s), 1334.5 (s), 1303.2 (s), 1054.5 (s), 930.8 (s), 862.3 (s), 813.0 (s), 724.1 (s), 698.9 (s), 649.2 (s), 573.8 (s). **HRMS** (DART) for $C_{26}H_{38}NO_3S$ $(M+H)^+$: Calc'd: 444.2565, found: 444.2567. **$[\alpha]_D^{20}$** = 4.60 (*c* =1.0, $CHCl_3$, *l* = 50 mm).

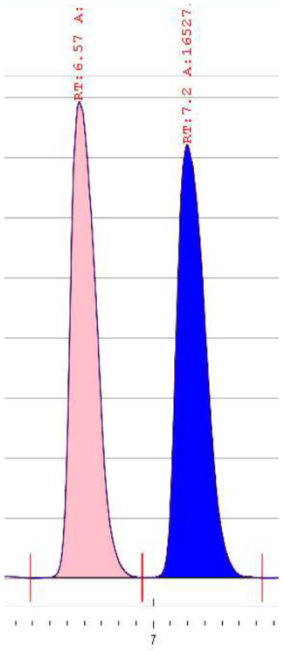
Analysis of Stereochemistry:

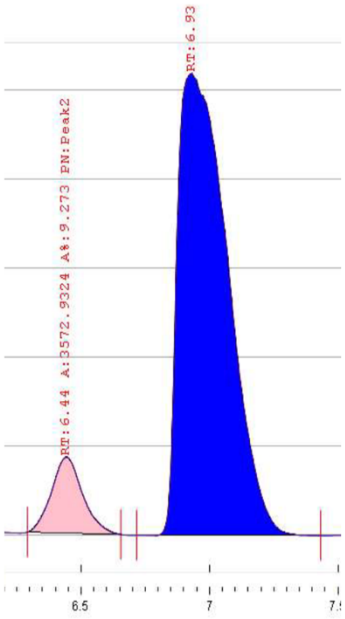
Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

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

Racemic Material

Enantioenriched Material





Peak Info			
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Total:	100	32653.2625	

Peak Info			
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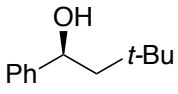


(*S*)-3,3-dimethyl-1-phenylbutan-1-ol (7). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and phenylzinc chloride solution in THF (1.0 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a white solid (25.1 mg, 70% yield). **HRMS** (DART) for $C_{26}H_{38}NO3S$ $(M+H-H_2O)^+$: Calc'd: 161.1321,

found: 161.1325. $[\alpha]_D^{20}$ = -52.39 (*c* = 0.5, $CHCl_3$, *l* = 50 mm). (lit: $[\alpha]_D^{20}$ = -71.2 (*c* = 1.9, THF, *l* = 100mm, ≤ 99% *ee*, (*S*)-enantiomer)). All spectral data was in accordance with the literature. [11]

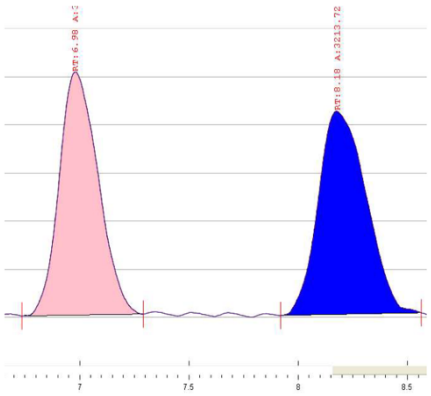
Analysis of Stereochemistry:

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

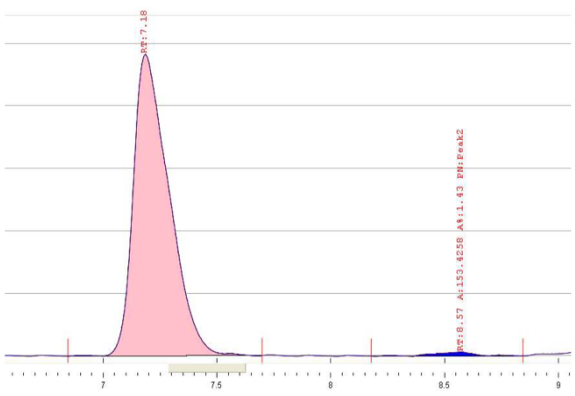
Chiral SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-3,3-dimethyl-1-phenylbutan-1-ol.**

Racemic Material

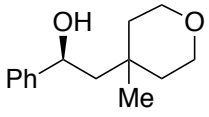
Enantioenriched Material



Peak Info			
Peak No	% Area	Area	RT (min)
1	49.3436	3130.442	6.98
2	50.6564	3213.7248	8.18
Total:	100	6344.1668	



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



(*S*)-2-(4-methyltetrahydro-2*H*-pyran-4-yl)-1-phenylethan-1-ol (8). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), 4-iodo-4-methyltetrahydro-2*H*-pyran (90.0 mg, 0.40 mmol, 2.0 equiv.), and phenylzinc chloride solution in THF (1.0 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (32.2 mg, 73% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36-7.35 (m, 3H), 7.29-7.26 (m, 2H), 4.90 (dd, *J* = 8.8, 3.5 Hz, 1H), 3.84-3.70 (m, 1H), 3.71-3.59 (m, 2H), 1.91 (dd, *J* = 14.7, 8.7 Hz, 1H), 1.75-1.58 (m, 3H), 1.56-1.44 (m, 2H),

1.37-1.30 (m, 1H), 1.26 (s, 1H), 1.14 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 146.4, 128.8, 127.7, 125.8, 71.8, 64.1, 64.0, 51.5, 38.5, 38.4, 31.0, 24.5. **IR** (neat) ν_{max} 3410.3 (br), 2950.7 (s), 2919.2 (s), 2853.8 (s), 1452.7 (m), 1102.3 (s), 1060.0 (m), 1036.0 (m), 1017.1 (m), 699.3 (m). **HRMS** (DART) for $C_{14}H_{19}O$ $(M+H-H_2O)^+$: Calc'd: 203.1424, found: 203.1430. **$[\alpha]_D^{20}$** = 40.78 (*c* = 0.5, $CHCl_3$, *l* = 50 mm).

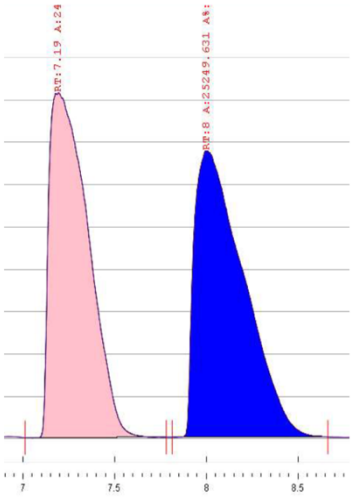
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-2-(4-methyltetrahydro-2*H*-pyran-4-yl)-1-phenylethan-1-ol.**

Racemic Material

Enantioenriched Material



Peak Info

Peak No	% Area	Area	RT (min)
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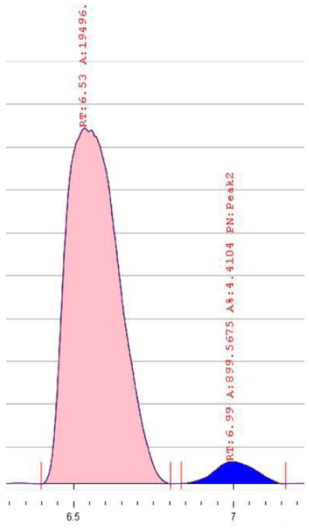
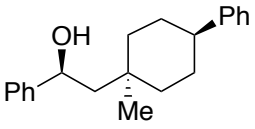
2	51.0988	25249.631	8
Total:	100	49413.3685	

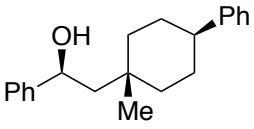


Peak Info

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



and



(*S*)-2-((1*s*,4*R*)-1-methyl-4-phenylcyclohexyl)-1-phenylethan-1-ol (9 and **9')**. The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), (4-iodo-4-methylcyclohexyl)benzene (120.1 mg, 0.40 mmol, 2.0 equiv.), and phenylzinc chloride solution in THF (1.0 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil consisting of a 1:2.7 mixture of diastereomers (30.6 mg, 52% yield). The

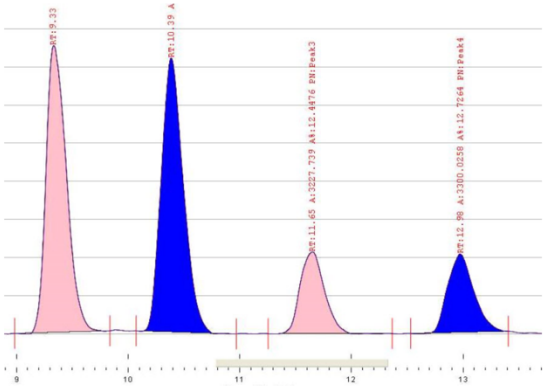
diastereomeric ratio was determined by ^{1}H NMR integration. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44-7.34 (m, 13H), 7.34-7.26 (m, 12H), 7.26-7.16 (m, 11H), 4.97 (dd, *J* = 8.4, 2.9 Hz, 1H, minor diastereomer), 4.88 (dd, *J* = 8.2, 3.2 Hz, 3H, major diastereomer), 2.55-2.37 (m, 5H), 2.00 (m, 4H), 1.94-1.85 (m, 4H), 1.84-1.52 (m, 32H), 1.39-1.24 (m, 9H), 1.14 (s, 3H), 1.09 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.7, 147.6, 146.8, 146.8, 128.7, 128.7, 128.4, 128.4, 127.6, 127.5, 127.0, 126.9, 126.0, 126.0, 125.9, 72.4, 71.8, 55.4, 45.2, 44.7, 44.4, 39.1, 38.7, 38.7, 38.6, 32.8, 32.4, 30.5, 29.9, 29.8, 29.8, 29.7, 22.3. **IR** (neat) ν_{max} 412.6 (br), 2919.3 (m), 2857.4 (w), 1491.2 (w), 1053.4 (w), 718.5 (m), 697.2 (s), 533.78 (w). **HRMS** (DART) for $C_{15}H_{25}O_2$ $(M+H-H_2O)^+$: Calc'd: 277.1951, found: 277.1951.

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

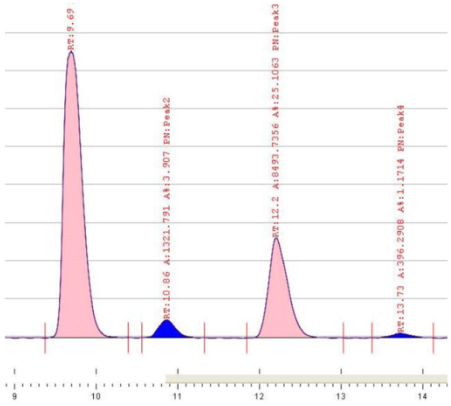
Chiral SFC (Chiracel OJ-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-2-(1-methyl-4-phenylcyclohexyl)-1-phenylethan-1-ol**.

Racemic Material



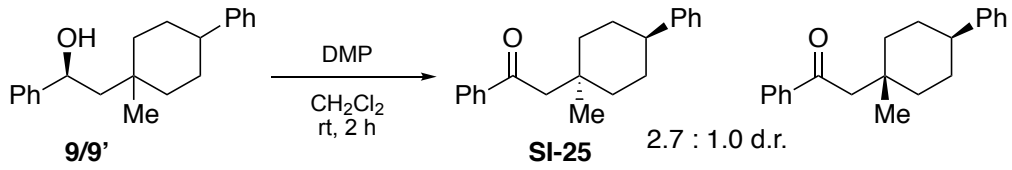
Peak No	% Area	Area	RT (min)
1	36.764	9533.1123	9.33
2	38.062	9869.7005	10.39
3	12.4476	3227.739	11.65
4	12.7264	3300.0258	12.98
Total:	100	25930.5776	

Enantioenriched Material

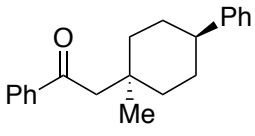


Peak No	% Area	Area	RT (min)
1	69.8153	23619.2332	9.69
2	3.907	1321.791	10.86
3	25.1063	8493.7356	12.2
4	1.1714	396.2908	13.73
Total:	100	33831.0506	

The stereochemical configuration was determined by COSY and NOESY analysis of compound **SI-25** which was isolated as a single stereoisomer from the mixture obtained after oxidation of product **9**.



9/9' **SI-25** 2.7 : 1.0 d.r.

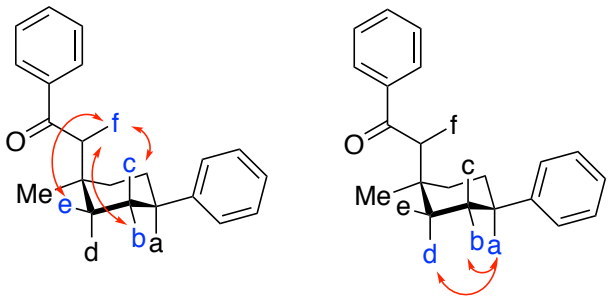


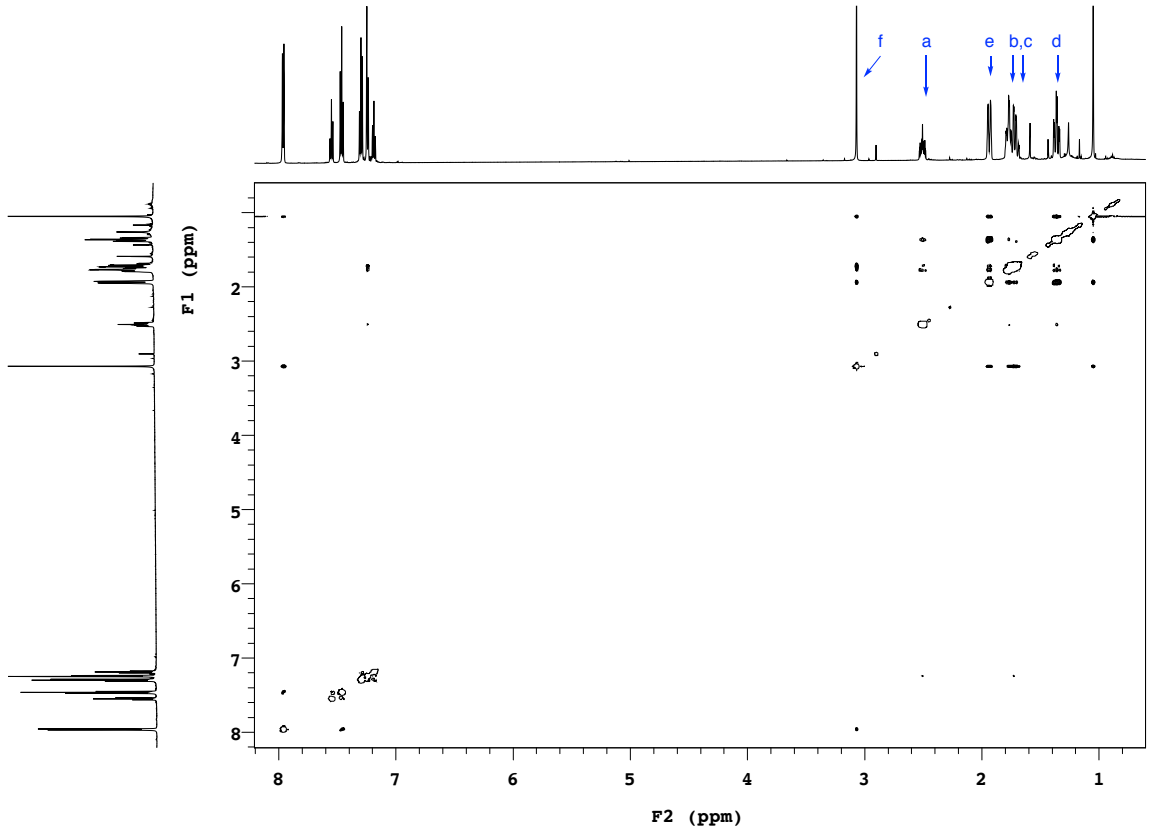
2-((1*s*,4*s*)-1-methyl-4-phenylcyclohexyl)-1-phenylethan-1-one (SI-25)

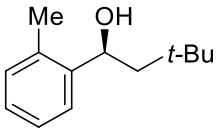
Diastereomeric mixture **9** (40.7 mg, 0.14 mmol, 1.0 equiv.) was placed in a scintillation vial

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

Relevant NOESY correlations are illustrated below.







(*S*)-3,3-dimethyl-1-(o-tolyl)butan-1-ol (10) The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (o-tolyl) zinc chloride (0.89 mL, 0.45 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **(*S*,*S*)-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (27.6 mg, 56% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.7, 1.5 Hz, 1H),

7.23 (t, *J* = 7.4, 7.4 Hz, 1H), 7.17-7.11 (m, 2H), 5.10 (dt, *J* = 9.3, 2.9, 2.9 Hz, 1H), 2.34 (s, 3H), 1.68 (dd, *J* = 14.9, 9.1 Hz, 1H), 1.58 (dt, *J* = 3.5, 1.2 Hz, 1H), 1.51 (dd, *J* = 14.8, 1.4 Hz, 1H), 1.04 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.8, 133.8, 130.5, 127.1, 126.5, 125.3, 68.8, 52.1, 30.9, 30.4, 19.3. **IR** (neat) ν_{max} 2953.0 (m), 2922.3 (s), 2850.9 (w), 1462.4 (w), 1363.0 (w), 1337.35 (w), 1079.7 (w), 1026.27 (w), 425.5 (w). **HRMS** (DART) for $C_{13}H_{19}$ $(M+H-H_2O)^+$: Calc'd: 175.1481, found: 175.1473. $\mathbf{[\alpha]_D^{20}}$ = 17.00 (*c* = 0.20, $CHCl_3$, *l* = 50 mm).

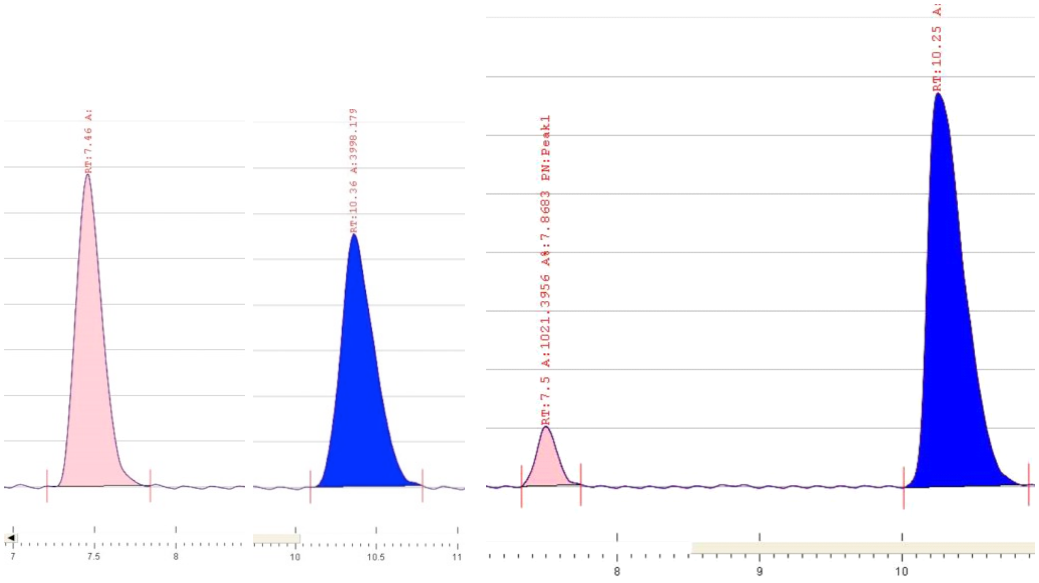
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

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

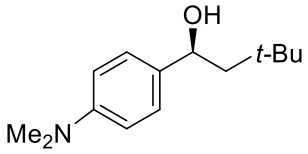
Racemic Material

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	49.0177	3844.1176	7.46
2	50.9823	3998.1798	10.36
Total:	100	7842.2974	

Peak No	% Area	Area	RT (min)
1	7.8683	1021.3956	7.5
2	92.1317	11959.7606	10.25
Total:	100	12981.1562	



(*S*)-1-(4-(dimethylamino)phenyl)-3,3-dimethylbutan-1-ol (11) The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (4-(dimethylamino)phenyl) zinc chloride (1.11 mL, 0.36 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using NiBr2 • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **(*S*,*S*)-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (20.4 mg, 46% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, 2H), 6.72 (d, 2H), 4.74 (dd, *J* = 8.3, 4.1 Hz, 1H), 2.95 (s, 6H), 1.82-1.74 (m, 1H), 1.63-1.54 (m, 2H), 0.97 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.3, 134.6, 127.0, 112.8,

72.4, 52.5, 40.8, 30.5, 30.4. **IR** (neat) ν_{max} 3256.4 (br), 2947.6 (m), 2915.3 (w), 2882.2 (w), 2027.4 (w), 1614.0 (m), 1521.8 (m), 1468.3 (w), 1360.7 (w), 1348.2 (w), 1224.4 (w), 1059.5 (w), 1018.6 (w), 988.7 (w), 819.1 (w). **HRMS** (DART) for $C_{14}H_{22}N$ $(M+H-H_2O)^+$: Calc'd: 204.1747, found: 204.1743. $\mathbf{[\alpha]_D^{20}}$ = 28.98 (*c* = 0.35, $CHCl_3$, *l* = 50 mm).

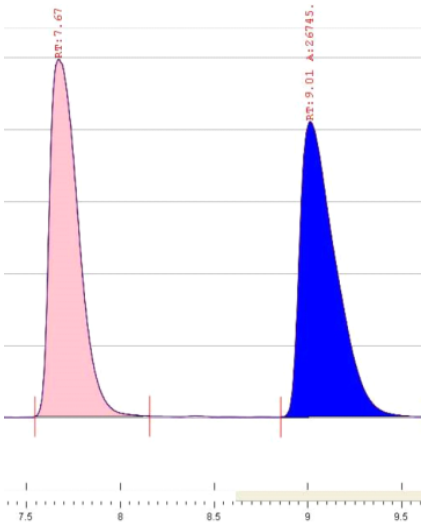
Analysis of Stereochemistry:

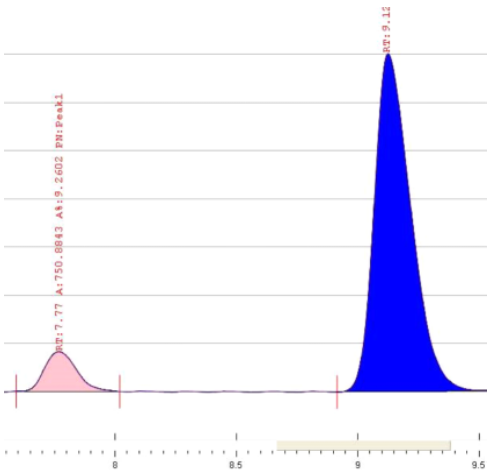
Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-1-(4-(dimethylamino)phenyl)-3,3-dimethylbutan-1-ol.**

Racemic Material

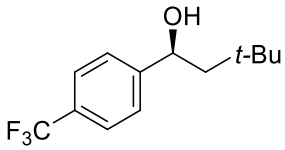
Enantioenriched Material





Peak No	% Area	Area	RT (min)
1	49.3028	26010.3074	7.67
2	50.6972	26745.8883	9.01
Total:	100	52756.1957	

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



(*S*)-3,3-dimethyl-1-(4-(trifluoromethyl)phenyl)butan-1-ol (12). The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and 4-(trifluoromethyl)phenylzinc chloride (0.52 mL, 0.77 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **(*S*,*S*)-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (27.6 mg, 56% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 2H), 4.91 (d, *J* = 8.0 Hz, 1H), 1.77– 1.71 (m, 2H), 1.56 (dd, *J* = 14.7, 3.1 Hz, 1H), 1.02 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.5,

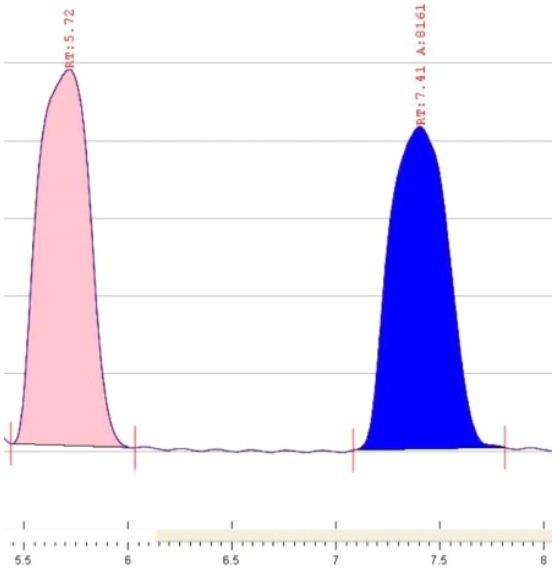
126.1, 125.6, 125.6, 125.6, 125.6, 72.1, 53.3, 30.8, 30.3. **IR** (neat) ν_{max} 3396.7 (br), 2952.3 (m), 2866.9 (w), 1324.8 (s), 1164.2 (m), 1126.6 (m), 1067.7 (m), 1016.6 (w), 843.7 (w). **HRMS** (DART) for $C_{13}H_{16}F_3$ $(M+H-H_2O)^+$: Calc'd: 229.1199, found: 229.1204. $\mathbf{[\alpha]_D^{20}}$ = 28.66 (*c* = 0.30, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

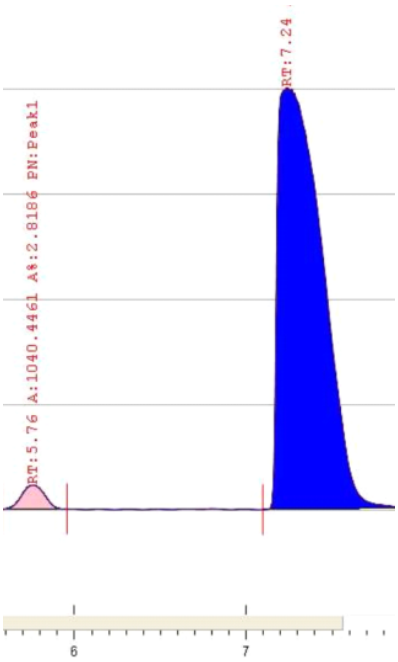
Chiral SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(S)-3,3-dimethyl-1-(4-(trifluoromethyl)phenyl)butan-1-ol**

Racemic Material

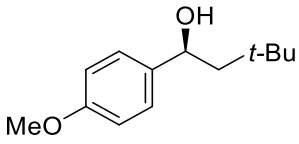


Peak No	% Area	Area	RT (min)
1	50.6036	8360.4958	5.72
2	49.3964	8161.0401	7.41
Total:	100	16521.5359	

Enantioenriched Material



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



(*S*)-1-(4-methoxyphenyl)-3,3-dimethylbutan-1-ol (13). The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (4-methoxyphenyl)zinc chloride (0.23 mL, 1.74 M, 0.4 mmol, 2.0 equiv.), in a mixture of

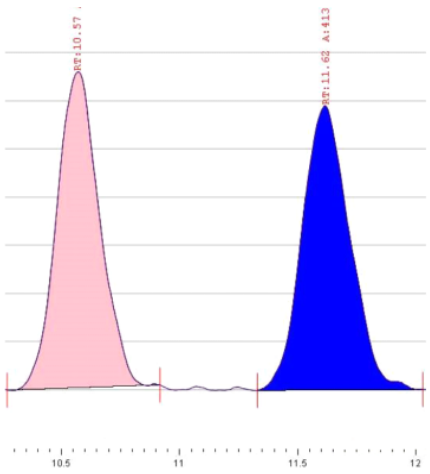
THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **(*S*,*S*)-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product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

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

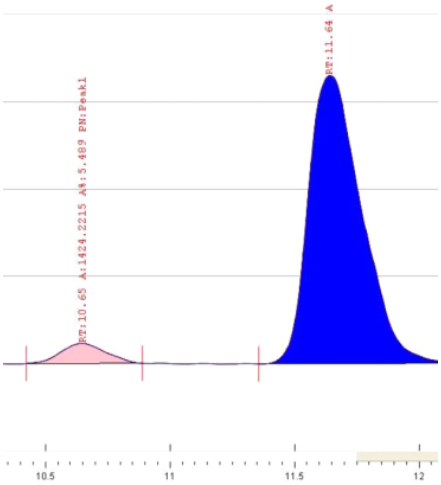
Chiral SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(S)-1-(4-methoxyphenyl)-3,3-dimethylbutan-1-ol.**

Racemic Material

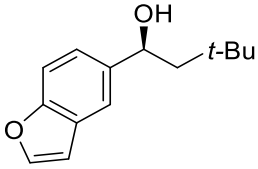


Peak No	% Area	Area	RT (min)
1	49.9828	4128.837	10.57
2	50.0172	4131.6767	11.62
Total:	100	8260.5137	

Enantioenriched Material



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



(S)-1-(benzofuran-5-yl)-3,3-dimethylbutan-1-ol (14). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and (3- benzofuran-5-ylzinc chloride solution in THF (1.0 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, UV

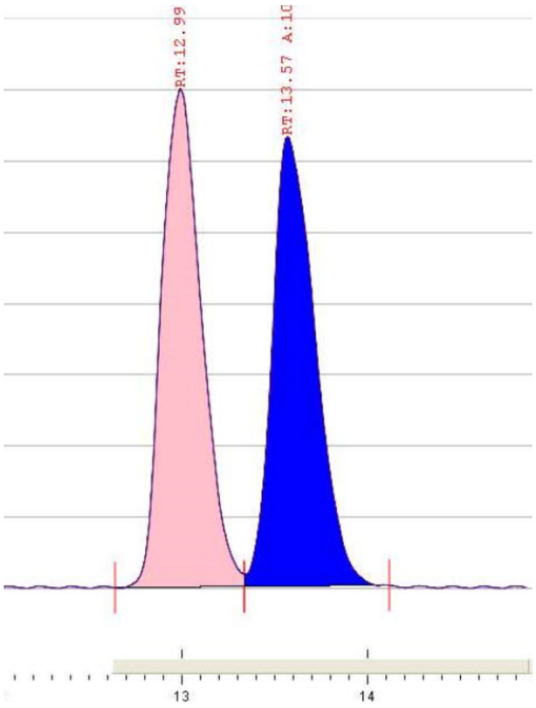
active) to afford the product as a colorless oil (23.1 mg, 52% yield).**^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 2.1 Hz, 1H), 7.59 (s, 1H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.29 (dd, *J* = 8.5, 1.5 Hz, 1H), 6.75 (d, *J* = 2.2 Hz, 1H), 4.93 (dd, *J* = 8.9, 3.3 Hz, 1H), 1.82 (dd, *J* = 14.5, 8.3 Hz, 1H), 1.74 (s, 1H), 1.66 (dd, *J* = 14.5, 3.7 Hz, 1H), 1.00 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.5, 145.6, 141.4, 127.6, 122.54, 118.5, 111.5, 106.8, 72.8, 53.4, 30.7, 30.4. **IR** (neat) ν_{max} 3377.6 (br), 2948.9 (s), 2864.0 (m), 1466.2 (m), 1362.9 (m), 1158.8 (m), 1106.2 (m), 767.5 (m), 747.2 (m), 734.3 (m), 699.5 (m). **HRMS** (DART) for $C_{14}H_{17}O$ $(M+H-H_2O)^+$: Calc'd: 201.1274, found: 201.1268. **$[\alpha]_D^{20}$** = -47.687 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

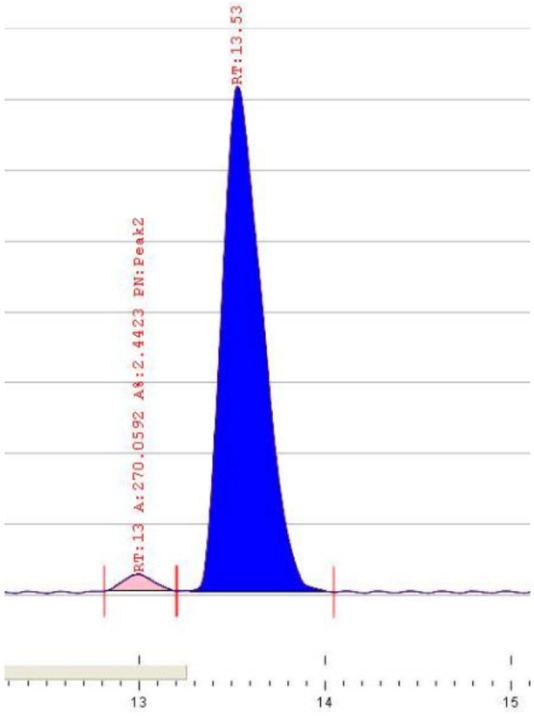
Chiral SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(S)-1-(benzofuran-5-yl)-3,3-dimethylbutan-1-ol**.

Racemic Material

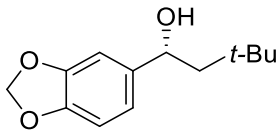


Peak No	% Area	Area	RT (min)
1	50.839	10492.7555	12.99
2	49.161	10146.4396	13.57
Total:	100	20639.1951	

Enantioenriched Material



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



(S)-1-(benzo[d][1,3]dioxol-5-yl)-3,3-dimethylbutan-1-ol (15). The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv.), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv.), and

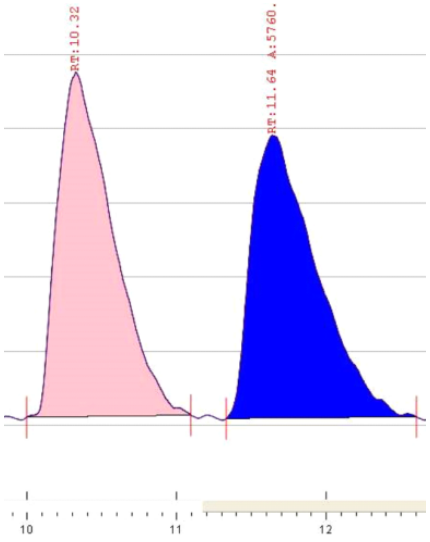
(benzo[d][1,3]dioxol-5-yl) zinc bromide • 2LiCl (1.11 mL, 0.36 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using NiBr2 • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **(*R*,*R*)-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified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

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

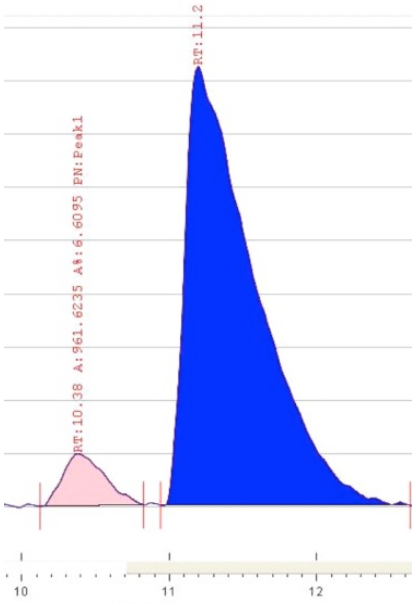
Chiral SFC (Chiracel AS-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-1-(benzo[d][1,3]dioxol-5-yl)-3,3-dimethylbutan-1-ol.**

Racemic Material

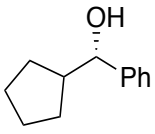


Peak No	% Area	Area	RT (min)
1	50.8722	5964.8104	10.32
2	49.1278	5760.2832	11.64
Total:	100	11725.0936	

Enantioenriched Material



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



(*S*)-cyclopentyl(phenyl)methanol (21). The reaction was performed according to general **procedure A** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using

$NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (24.6 mg, 70% yield). **HRMS** (DART) for $C_{12}H_{15}$ $(M+H-H_2O)^+$: Calc'd: 159.1166, found: 151.1168. $\mathbf{[\alpha]_D^{20}}$ = - 51.03 (*c* = 1.0, $CHCl_3$, *l* = 50 mm (lit: $\mathbf{[\alpha]_D^{20}}$ = - 40.08 (*c* = 0.8, $CHCl_3$, 78% *ee*, (*S*)-enantiomer)). All spectral data was in accordance with the literature.[12]

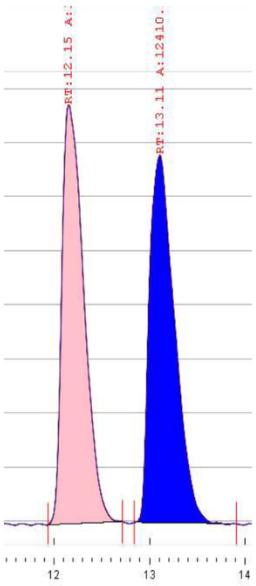
Analysis of Stereochemistry:

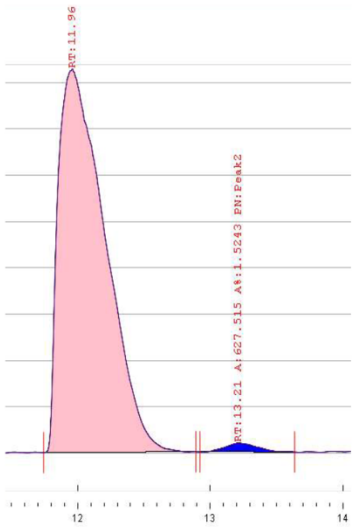
Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by comparison with the optical rotation reported in the literature for the same compound.[12] The stereochemical assignment was found to be in accordance with product **7** (determined through X-ray crystallography).

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

Racemic Material

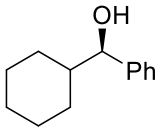
Enantioenriched Material





Peak Info			
Peak No	% Area	Area	RT (min)
1	49.8135	12317.9168	12.15
2	50.1865	12410.1565	13.11
Total:	100	24728.0733	

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



(*R*)-cyclohexyl(phenyl)methanol (24). The reaction was performed according to general **procedure A** with (*E*)-2-(7-iodohept-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (70.0 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(R,R)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (19.0 mg, 52% yield). **HRMS** (DART) for $C_{13}H_{17}$ $(M+H-H_2O)^+$: Calc'd: 173.1325, found: 173.1329. $\mathbf{[\alpha]_D^{20}}$ =

28.27 (*c* = 0.29, $CHCl_3$, *l* = 50 mm (lit: $[\alpha]_D^{20}$ = -21.4 (*c* = 1.01, $CHCl_3$, 91% *ee*, (*S*)-enantiomer)). All spectral data was in accordance with the literature.[13]

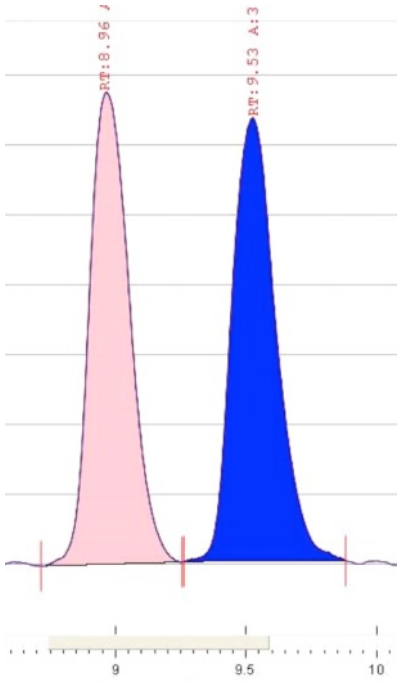
Analysis of Stereochemistry:

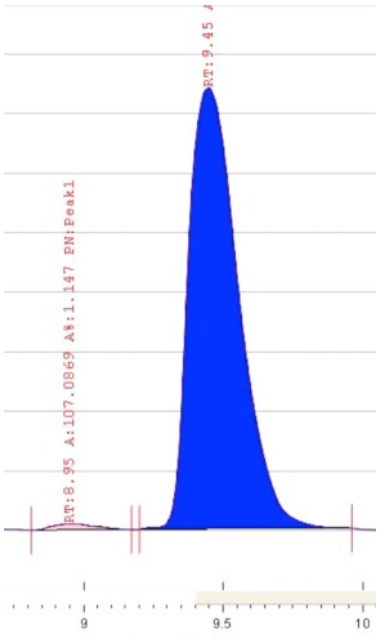
Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**) and comparison of optical rotation reported in the literature for the same compound.[13]

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

Racemic Material

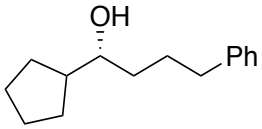
Enantioenriched Material





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

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



(*R*)-1-cyclopentyl-4-phenylbutan-1-ol (25). The reaction was performed according to general **procedure B** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv.), and (3-phenylpropyl)zinc bromide solution in DMA (0.24 mL, 1.68 M, 0.4 mmol, 2.0 equiv.), with (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) in DMA (2.40 mL). The crude mixture was purified by silica gel column

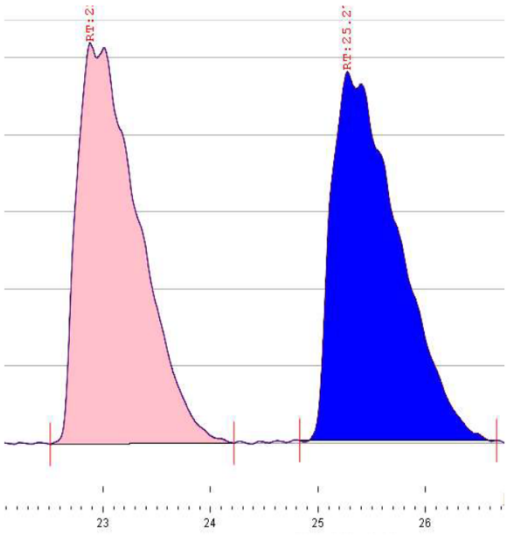
chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (25.3 mg, 58% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29-7.26 m, 2H), 7.20-7.18(m, 3H), 3.43 (td, *J* = 8.0, 3.2 Hz, 1H), 2.72-2.53 (m, 2H), 1.89-1.50 (m, 10H), 1.46-1.28 (m, 2H), 1.29 -1.15 (m, 1H).**^{13}C NMR** (151 MHz, $CDClz_3$) δ 142.6, 128.5, 128.4, 125.8, 75.9, 46.5, 36.1, 35.9, 29.3, 28.6, 27.7, 25.8, 25.7. **IR** (neat) ν_{max} 3357.1 (br), 3082.2 (w), 3057. 3022.8 (w), 2938.7 (s), 2861.2 (s), 1494.2 (m), 1450.8 (m), 1094.4 (m), 1053.8 (m), 1028.9 (m), 920.6 (m), 800.8 (s), 746.5 (s). **HRMS** (DART) for $C_{15}H_{21}$ $(M+H-H_2O)^+$: Calc'd: 201.1634, found: 201.1638. **$[\alpha]_D^{20}$** = -5.66 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

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

Racemic Material



Peak Info			
Peak No	% Area	Area	RT (min)
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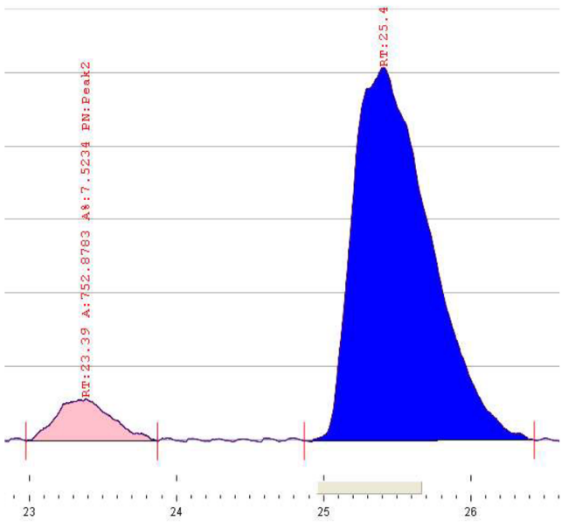
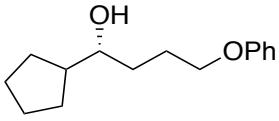
2	49.926	20827.4806	25.27
Total:	100	41716.7121	

Enantioenriched Material



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



(*R*)-1-cyclopentyl-4-phenoxybutan-1-ol (27). The reaction was performed according to general **procedure B** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv.), and (3-phenoxypropyl)zinc bromide solution in DMA (0.360 mL, 1.1 M, 0.4 mmol, 2.0 equiv.), with (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) in DMA (2.40 mL). The crude mixture was purified by silica gel column chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (30.1 mg, 64% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39-7.18 (m, 2H), 7.05-6.76

(m, 3H), 4.00 (ddd, J = 5.8, 3.0 Hz, 2H), 3.59-3.35 (m, 1H), 2.14-1.43 (m, 12H), 1.43-1.30 (m, 1H), 1.27-1.17 (m, 1H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.1, 129.6, 120.8, 114.7, 75.8, 68.1, 46.7, 33.0, 29.3, 28.8, 25.9, 25.8 (one diastereotopic carbon peak not observed). **IR** (neat) ν_{max} 3408.7 (Br), 2946.9 (m), 2865.0 (m), 1598.1 (w), 1495.6 (m), 1299.5 (w), 1244.0 (s), 1040.7 (w), 1012.4 (w), 752.3 (m), 690.7 (m). **HRMS** (DART) for $C_{15}H_{23}O_2$ $(M+H)^+$: Calc'd: 235.1694, found: 235.1704. **$[\alpha]_D^{20}$** = 4.159 (c = 1.0, $CHCl_3$, l = 50 mm).

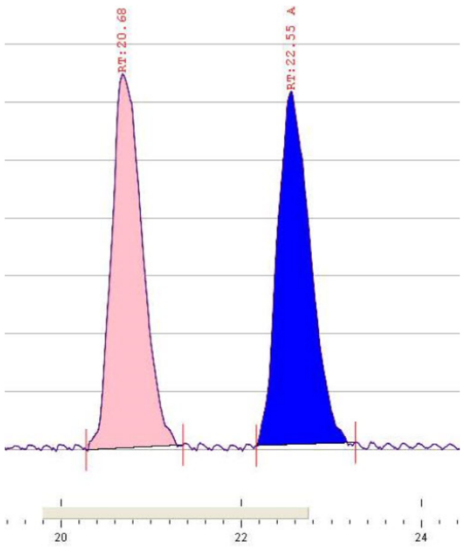
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

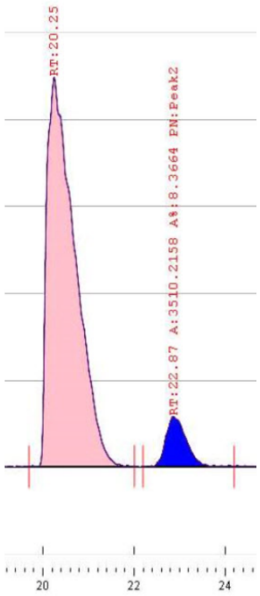
Chiral SFC (Chiracel OJ-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-1-cyclopentyl-4-phenoxybutan-1-ol.**

Racemic Material

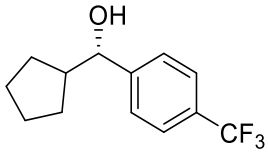
Enantioenriched Material



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



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



(*S*)-cyclopentyl(4-(trifluoromethyl)phenyl)methanol (27). The reaction was performed according to general **procedure A** with (E)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv.), and 4-(trifluoromethyl)phenyl zinc chloride solution in THF (0.52 mL, 0.77 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (27.0 mg, 55% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.9 Hz, 2H), 7.46 (d, *J* = 7.8 Hz, 2H), 4.50 (d, *J* = 8.2 Hz, 1H), 2.18 (h, *J* =

8.9, 8.9, 8.9, 8.3, 8.3 Hz, 1H), 1.93 (dd, *J* = 3.3, 1.2 Hz, 1H), 1.85 (h, td, *J* = 12.4, 12.2, 7.3 Hz, 1H), 1.71-1.55 (m, 3H), 1.55-1.45 (m, 2H), 1.43-1.36 (m, 1H), 1.22-1.14 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 148.5, 126.9, 125.4, 125.4, 125.4, 125.4, 78.4, 47.9, 29.5, 29.2, 25.6, 25.5. **IR** (neat) ν_{max} 3374.5 (br), 2953.1 (w), 2867.0 (w), 1618.6 (w), 1417.4 (w), 1323.9 (s), 1162.2 (m), 1123.4 (s), 1065.9 (s), 1016.1 (w), 836.9 (w), 758.6 (w). **HRMS** (DART) for $C_{13}H_{14}F_3$ $(M+H-H_2O)^+$: Calc'd: 227.1042, found: 227.1048. **$[\alpha]_D^{20}$** = -29.83 (*c* = 1.00, $CHCl_3$, *l* = 50 mm).

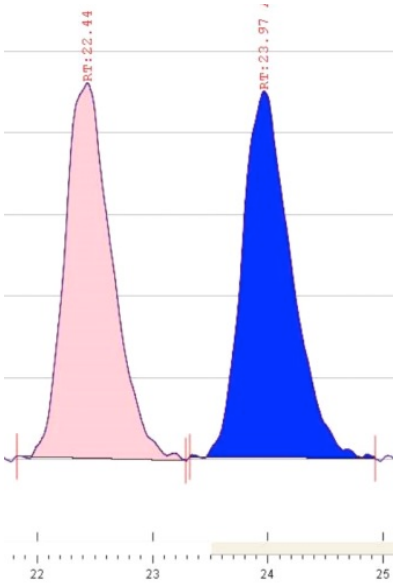
Analysis of Stereochemistry:

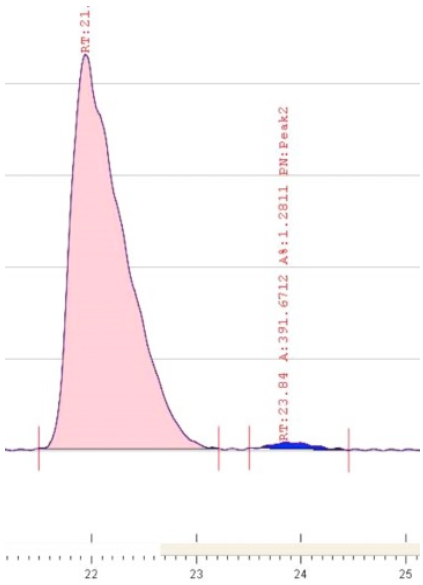
Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

Chiral SFC (Chiracel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-cyclopentyl(4-(trifluoromethyl)phenyl)methanol.**

Racemic Material

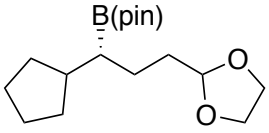
Enantioenriched Material





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

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



(*R*)-2-(1-cyclopentyl-3-(1,3-dioxolan-2-yl)propyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (28). The reaction was performed according to general **procedure B** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv.), and (2-(1,3-dioxolan-2-yl)ethyl)zinc bromide solution in DMA (0.330 mL, 1.23 M, 0.4 mmol, 2.0 equiv.), with (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) in DMA (2.40 mL). ***Note:*** product was isolated and characterized as the boronic ester prior to oxidation since the corresponding alcohol was prone to decomposition. The crude mixture was purified by silica

gel column chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (40.8 mg, 66% yield). **^{1}H NMR** (600 MHz, $CDCl_3$)) δ 4.83 (t, *J* = 4.8 Hz, 1H), 3.99-3.91 (m, 2H), 3.87-3.78 (m, 2H), 1.88-1.77 (m, 2H), 1.77-1.64 (m, 2H), 1.62-1.54 (m, 4H), 1.53-1.40 (m, 3H), 1.24 (s, 12H), 1.17-1.05 (m, 2H), 0.96-0.85 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 104.9, 83.0, 65.0, 42.0, 33.9, 32.6, 32.2, 25.4, 25.3, 25.1, 25.0. **IR** (neat) ν_{max} 2974.1 (m), 2943.9 (m), 2864.7 (m), 1455.5 (w), 1378.4 (m), 1316.5 (m), 1213.3 (w), 1143.8 (s), 1033.6 (w), 966.8 (w), 842.5 (w). **HRMS** (DART) for $C_{17}H_{32}BO_4$ $(M+H)^+$: Calc'd:311.2388, found: 311.2386. **$[\alpha]_D^{20}$** = 6.67 (*c* = 1.0, $CHCl_3$, *l* = 50 mm).

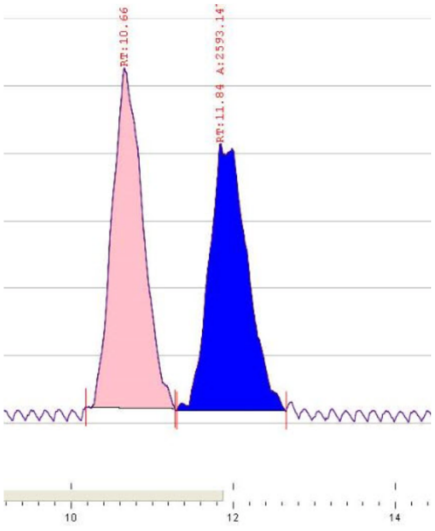
Analysis of Stereochemistry:

Racemic compound was prepared according to the general **procedure A** with racemic **L1** as ligand. Absolute stereochemistry was assigned by analogy (see product **7** and **21**).

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

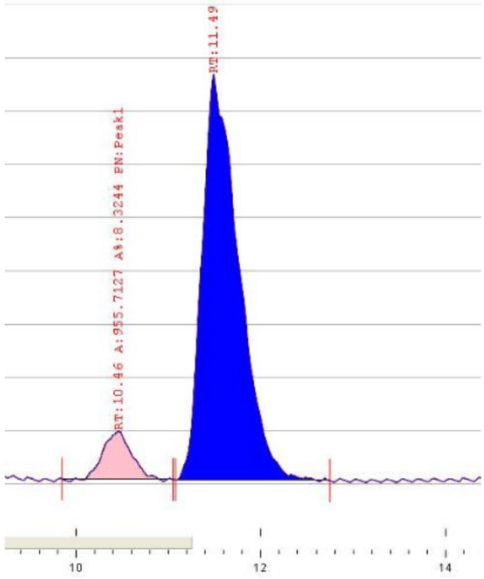
Chiral SFC (Chiracel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-1-cyclopentyl-3-(1,3-dioxolan-2-yl)propan-1-ol**.

Racemic Material

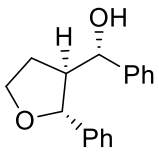


Peak No	% Area	Area	RT (min)
1	50.5782	2653.8255	10.66
2	49.4218	2593.1472	11.84
Total:	100	5246.9727	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	8.3244	955.7127	10.46
2	91.6756	10525.088	11.49
Total:	100	11480.8007	

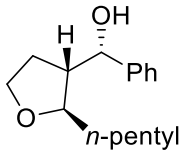


(*S*)-phenyl((*2R*,*3R*)-2-phenyltetrahydrofuran-3-yl)methanol (29). The reaction was performed according to the general **procedure A** with (*R*,*E*)-2-(3-(2-iodoethoxy)-3-

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

Analysis of Stereochemistry:

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

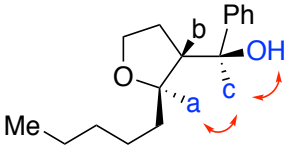


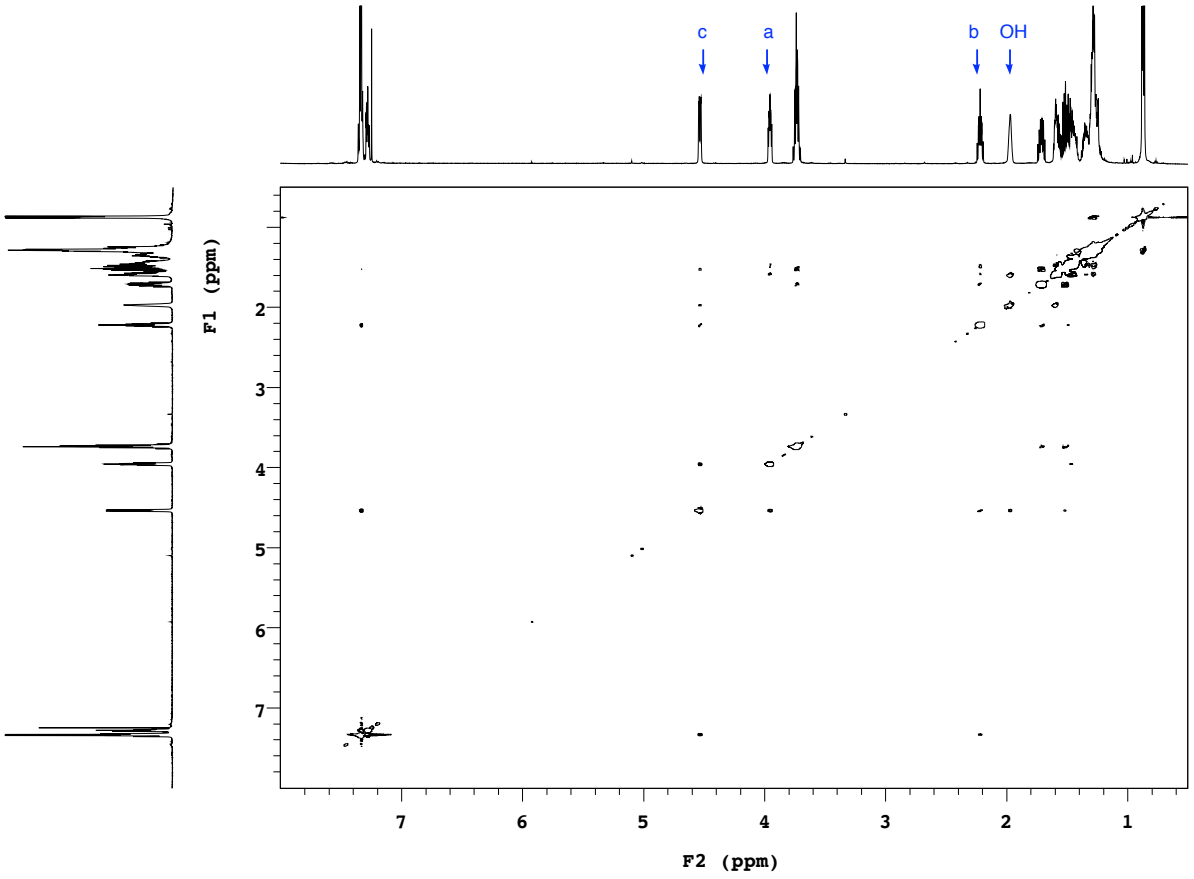
(*S*)-((*2R*,*3R*)-2-pentyltetrahydrofuran-3-yl)(phenyl)methanol (30). The reaction was performed according to the general **procedure A** with (*R*,*E*)-2-(3-(2-iodoethoxy)oct-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (81.6 mg, 0.20 mmol, 1.0

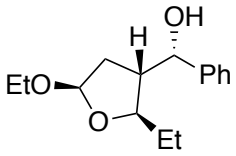
equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using NiBr2 • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **(*S*,*S*)-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified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

Analysis of Stereochemistry:

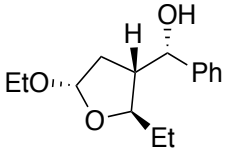
The stereochemistry of the carbon skeleton was assigned through NOESY correlation analysis. The absolute configuration at the B(pin)/OH containing stereocenter was assigned by analogy (see substrates: **7** and **21**). Relevant NOESY correlations are illustrated below.







and

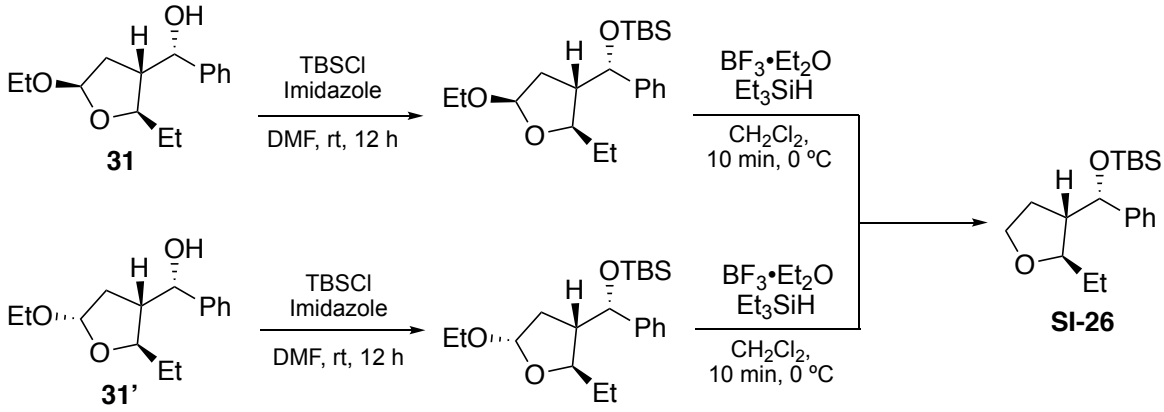


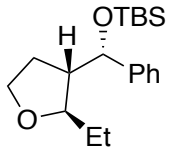
(*1S*)-((*2R*,*3R*)-5-ethoxy-2-ethyltetrahydrofuran-3-yl)(phenyl)methanol (31 and 31'). The reaction was performed according to the general **procedure A** with 2-((3*R*,*E*)-3-(1-ethoxy-2-iodoethoxy)pent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (82.0 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL

DMA overall) using NiBr2 • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **(*S*,*S*)-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel /column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (25.0 mg, 50% yield). The product was obtained as a pair of separable diastereomers. *Diastereomer 1:* **^{1}H NMR** (500 MHz, $CDCl_3$) 7.37-7.36 (m, 2H), 7.33-7.30 (m, 2H), 7.23-7.19 (m, 1H), 5.12 (d, *J* = 4.6 Hz, 1H), 4.90 (d, *J* = 4.3 Hz, 1H), 4.12 (q, *J* = 5.1, 5.1, 4.9 Hz,1H), 4.05 (s, 1H), 3.82 (dq, *J* = 9.3, 7.2, 7.2, 7.1 Hz, 1H), 3.50 (dq, *J* = 9.2, 9.2, 6.1, 6.1 Hz, 1H), 2.28-2.25 (m, 1H), 2.20 (ddd, *J* = 13.3, 11.1, 4.9 Hz, 1H), 1.88 (dd, *J* = 13.5, 2.2 Hz, 1H), 1.26-1.21 (m, 5H), 0.66 (t, *J* = 7.4, 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.6, 128.4, 127.3, 126.1, 102.7, 79.9, 75.4, 62.2, 49.4, 37.7, 28.9, 15.2, 9.5. **IR** (neat) ν_{max} 3423.0 (br), 3059.3 (w), 3026.7 (w), 2968.8 (m), 2920.7 (s), 2873.5 (m), 1492.0 (w), 1452.3 (m), 1202.9 (w), 1082.4 (s), 1072.3 (s), 979.0 (s), 758.2 (w), 701.0 (s). **HRMS** (DART) for $C_{15}H_{21}O_3$ $(M+H)^+$: Calc'd: 249.1485, found: 249.1483. **$[\alpha]_D^{20}$** = 22.40 (*c* =1.00, $CHCl_3$, *l* = 50 mm). *Diastereomer 2:* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33-7.25 (m, 5H), 4.99 (d, *J* = 2.9 Hz, 1H), 4.51 (dd, *J* = 8.5, 3.0 Hz, 1H), 4.03 (ddd, *J* = 9.5, 6.3, 3.7 Hz, 1H), 3.72 (dq, *J* = 9.4, 7.1, 7.1, 7.0 Hz, 1H), 3.36 (dq, *J* = 9.6, 7.2, 7.1, 7.1 Hz, 1H), 2.55-2.46 (m, 1H), 1.90 (d, *J* = 3.4 Hz, 1H), 1.74-1.63 (m, 3H), 1.57 (ddd, *J* = 13.5, 8.6, 6.9 Hz, 1H), 1.14 (t, *J* = 7.1, 7.1 Hz, 3H), 0.99 (t, *J* = 7.4, 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.6, 128.7, 128.1, 126.5, 103.2, 103.2, 85.2, 77.9, 62.4, 49.5, 37.3, 31.1, 15.3, 11.1. **IR** (neat) ν_{max} 3433.0 (br), 2968.7 (m), 2927.1 (m), 2872.2 (m), 1452.9 (m), 1372.2 (w), 1343.9 (w), 1309.5 (w), 1190.3 (w), 1092.5 (s), 1064.9 (s), 1023.0 (s), 971.8 (s), 760.1 (w), 701.4 (s), 624.9 (w). **HRMS** (DART) for $C_{15}H_{21}O_3$ $(M+H)^+$: Calc'd: 249.1485, found: 249.1490. **$[\alpha]_D^{20}$**= -108.38 (*c* = 1.00, $CHCl_3$, *l* = 50 mm).

Analysis of stereochemistry:

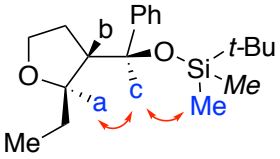
The transformations below were carried out on the isolated compounds **31** and **31'** separately in order to assess the stereochemistry of the isolated compounds. Upon reduction all spectral data of the two separate products was found to be identical. The stereochemical assignment was determined through NOESY correlation analysis of the resulting products. The absolute configuration at the B(pin)/silyl ether containing stereocenter was assigned by analogy (see substrates **7** and **21**).

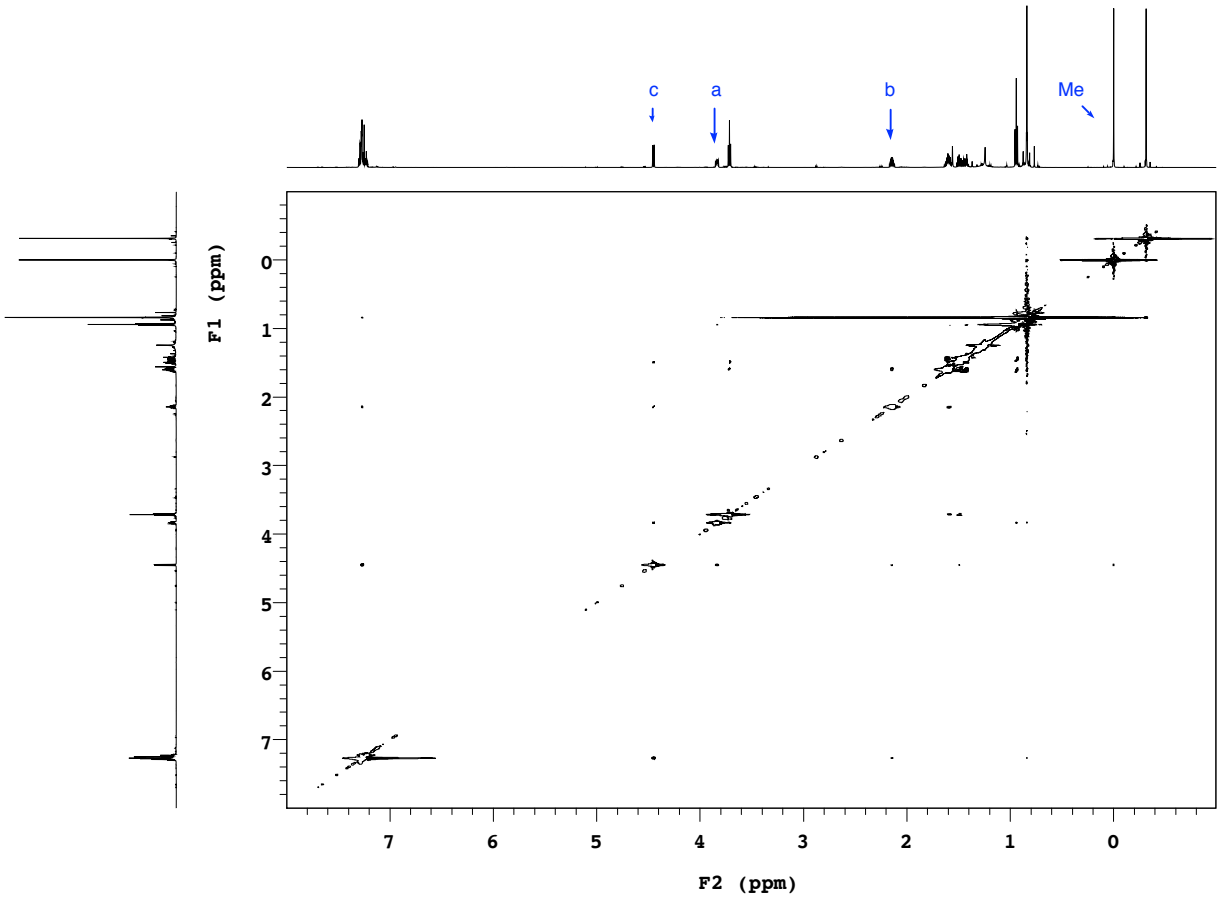


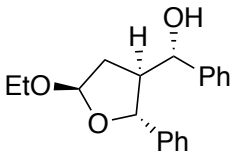


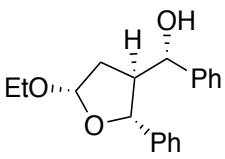
***Tert*-butyl((*S*)-((*2R,3S*)-2-ethyltetrahydrofuran-3-yl)(phenyl)methoxy)dimethylsilane (SI-26)**. Compound **31** (12 mg, 0.048 mmol) was dissolved in anhydrous DMF (4 mL), followed by addition of imidazole (9.8 mg, 0.14 mmol), and TBSCl (5.9 mg, 0.072 mmol). The resulting mixture was stirred overnight at room temperature, diluted with diethyl ether, washed twice with water and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture is filtered through silica gel (3% ethyl in hexanes). The resulting mixture was dissolved in CH_2Cl_2 (5 mL) and triethylsilane (17.5 μL, 0.1 mmol) was added, followed by dropwise addition of BF_3•Et_2O (6.8 μL, 0.055 mmol) at 0 °C. The reaction mixture was stirred for 10 min at the same temperature, then saturated aqueous sodium bicarbonate solution (5 mL) was added, and the mixture was extracted with CH_2Cl_2 (3×10 mL). The combined extracts were dried over anhydrous sodium sulfate and concentrated in vacuo. Purification by flash column chromatography provided **SI-25** (8.2 mg, 93% over two steps) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31-7.19 (m, 5H), 4.45 (d, *J* = 8.5 Hz, 1H), 3.84 (ddd, *J* = 8.3, 5.8, 3.7 Hz, 1H), 3.72 (t, *J* = 6.7, 6.7 Hz, 2H), 2.17-2.12 (m, 1H), 1.65-1.55 (m, 2H), 1.53-1.39 (m, 2H), 0.95 (t, *J* = 7.4, 7.4 Hz, 3H), 0.84 (s, 9H), 0.00 (s, 3H), -0.31 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.4, 128.2, 127.5, 126.9, 84.0, 78.4, 67.0, 52.7, 30.2, 29.0, 25.9, 18.2, 10.8, -4.4, -4.8. **IR** (neat) ν_{max} 2953.9 (s), 2926.3 (s), 2853.9 (s), 1460.2 (w), 1251.7 (m), 1107.9 (m), 1080.2 (m), 851.6 (s), 836.2 (s), 775.0 (s). **HRMS** (DART) for $C_{19}H_{33}O_2Si$ $(M+H)^+$: Calc'd: 321.2244, found: 321.2232. **$[\alpha]_D^{20}$** = -42.66 (*c* = 0.38, $CHCl_3$, *l* = 50 mm).

Relevant NOESY correlations are illustrated below.


Ph
b
O
t-Bu
Si
Me
O
a
c
Me
Me


c
a
b
Me
F1 (ppm)
0
1
2
3
4
5
6
7
7
6
5
4
3
2
1
0
F2 (ppm)



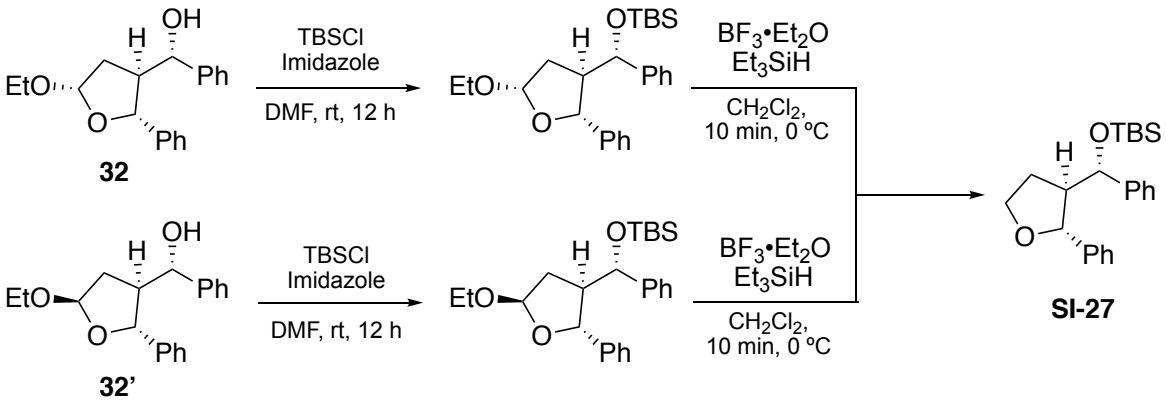
and


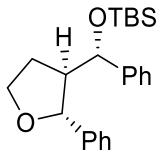
(*1S*)-((*2R*,*3S*)-5-ethoxy-2-phenyltetrahydrofuran-3-yl)(phenyl)methanol (32 and 32') . The reaction was performed according to the general **procedure A** with 2-((*3R*,*E*)-3-(1-ethoxy-2-iodoethoxy)-3-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (91.6 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using NiBr2 • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **(*S*,*S*)-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (30.4 mg, 51% yield). The product is a pair of separable diastereomers. *Diastereomer 1 (up):* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36-7.23 (m, 9H), 7.23-7.18 (m, 1H), 5.34 (d, *J* = 4.9 Hz, 1H), 5.12 (d, *J* = 5.8 Hz, 1H), 4.94 (t, *J* = 4.9, 4.9 Hz, 1H), 3.99 (d, *J* = 5.8 Hz, 1H), 3.93-3.86 (m, 1H), 3.61-3.58 (m, 1H), 2.58-2.54 (m, 1H), 2.12-2.07 (m, 1H), 2.01 (dd, *J* = 14.0, 3.2 Hz, 1H), 1.30 (td, *J* = 7.1, 7.1, 1.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.1, 142.3, 128.7, 128.4, 127.8, 127.2, 126.0, 126.0, 103.3, 103.3, 82.1, 82.1, 73.3, 62.6, 54.1, 33.3, 15.2. **IR** (neat) ν_{max} 3424.6 (br), 3060.1 (w), 3029.2 (w), 2971.0 (w), 2923.0 (w), 1492.5 (w), 1452.4 (w), 1197.7 (w), 1097.0 (m), 1046.2 (s), 1022.8 (s), 759.1 (w), 699.6 (s). **HRMS** (DART) for $C_{19}H_{26}NO_3$ $(M+NH_4)^+$: Calc'd: 316.1907, found: 316.1906. **$[\alpha]_D^{20}$** = 72.04 (*c* =1.00, $CHCl_3$, *l* = 50 mm). *Diastereomer 2 (down):* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.27-7.15 (m, 10H), 5.18 (d, *J* = 5.2 Hz, 1H), 4.91 (d, *J* = 8.9 Hz, 1H), 4.69 (s, 1H), 3.84 (dq, *J* = 9.8, 7.2, 7.1, 7.1 Hz, 1H), 3.47 (dq, *J* = 9.8, 7.1, 7.1, 7.1 Hz, 1H), 2.74-2.69 (m, 1H), 2.32 (ddd, *J* = 12.9, 11.4, 5.3 Hz, 1H), 1.99-1.94 (m, 2H), 1.23 (t, *J* = 7.1, 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.1, 142.3, 128.4, 128.2, 127.7, 127.4, 127.2, 125.9, 103.7, 84.1, 77.3, 77.0, 76.8, 72.7, 62.8, 53.4, 34.3,

15.1. **IR** (neat) ν_{max} 3434.9 (br), 3059.9 (w), 3027.7 (w), 2972.1 (w), 2923.4 (w), 1492.4 (w), 1453.4 (w), 1190.9 (w), 1094.9 (m), 1041.2 (m), 974.1 (m), 908.4 (w), 754.9 (w), 700.6 (s). **HRMS** (DART) for $C_{19}H_{26}NO_3$ $(M+NH_4)^+$: Calc'd: 316.1907, found: 316.1894. $\mathbf{[\alpha]_D^{20}}$ = 57.75 (*c* =1.00, $CHCl_3$, *l* = 50 mm).

Analysis of stereochemistry:

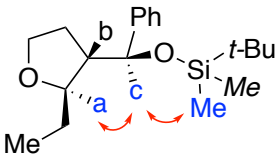
The transformations below were carried out on the isolated compounds **32** and **32'** separately in order to assess the stereochemistry of the isolated compounds. Upon reduction all spectral data of the two separate products was found to be identical. The stereochemical assignment was determined through NOESY correlation analysis of the resulting products. The absolute configuration at the B(pin)/silyl ether containing stereocenter was assigned by analogy (see substrates **7** and **21**).

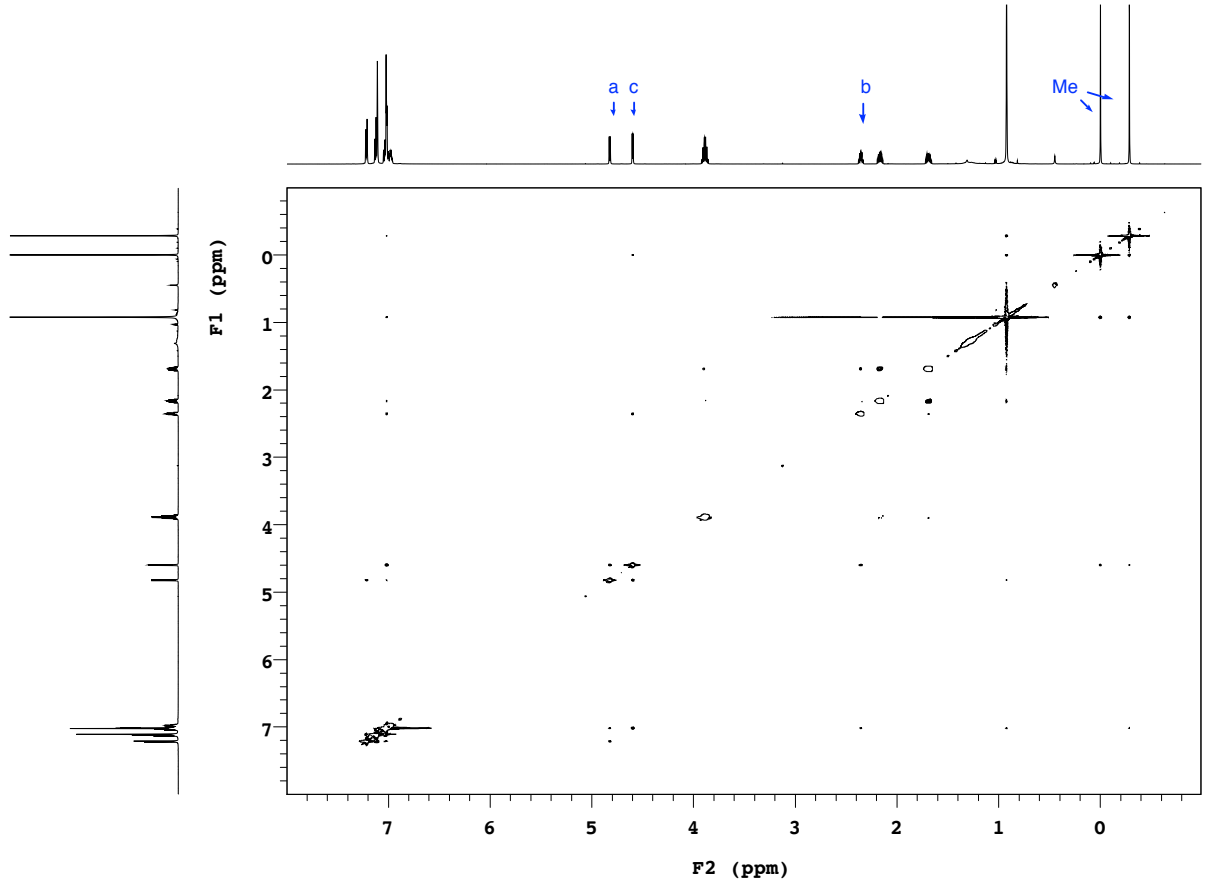


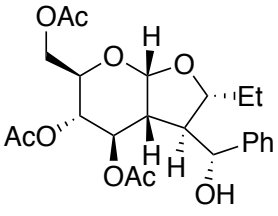


***tert*-butyldimethyl((*S*)-phenyl((*2R,3R*)-2-phenyltetrahydrofuran-3-yl)methoxy)silane (SI-27).** The title compound was generated through the same procedure used to synthesize **SI-25** and isolated by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as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

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







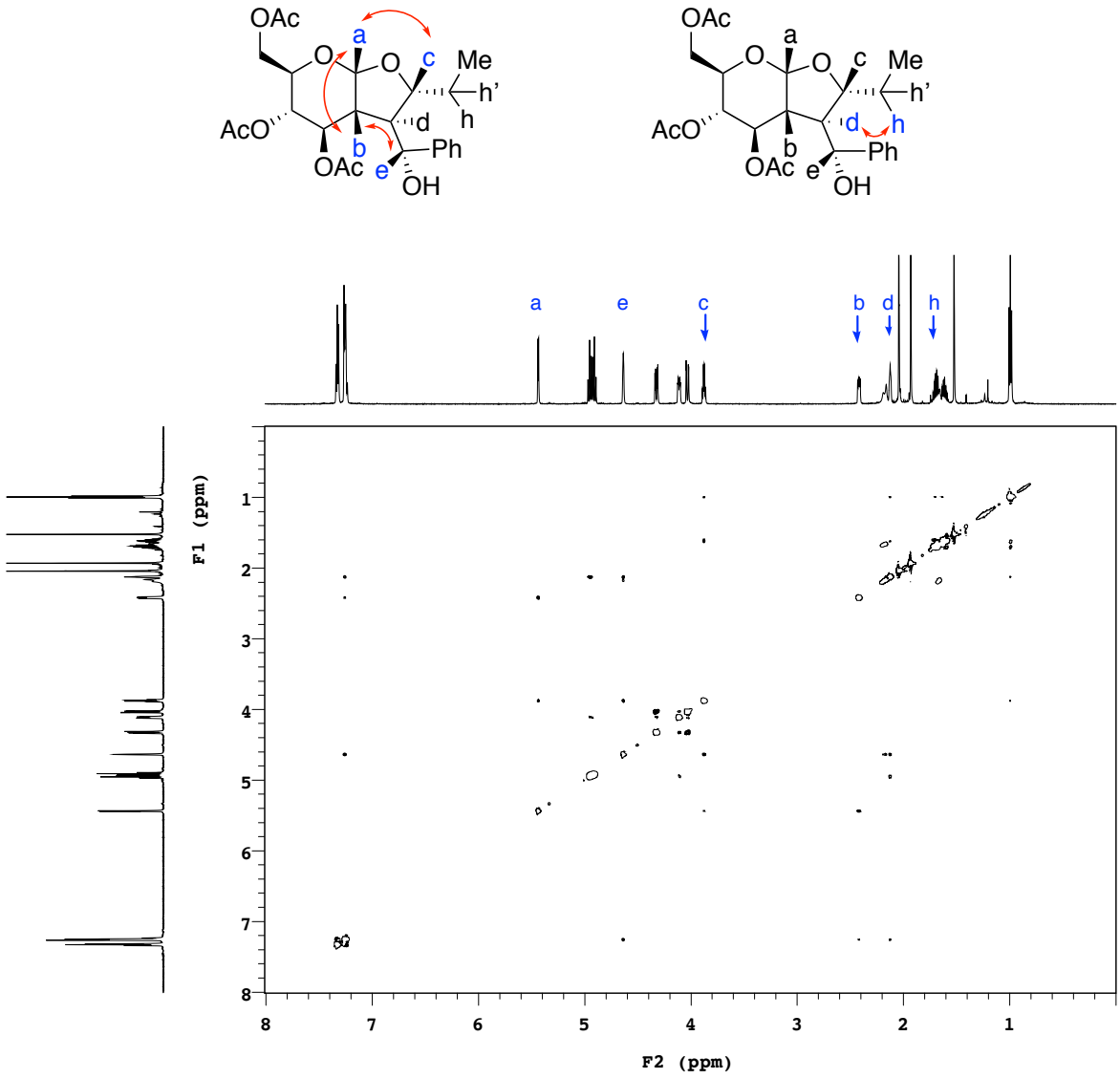
(2*R*,3*R*,3a*R*,4*R*,5*S*,6*R*,7a*S*)-6-(acetoxymethyl)-2-ethyl-3-((*R*)-hydroxy(phenyl)methyl)hexahydro-4*H*-furo[2,3-*b*]pyran-4,5-diyl diacetate (33). The reaction was performed according to general **procedure A** with (2*R*,3*R*,4*S*,5*S*,6*S*)-2-(acetoxymethyl)-5-iodo-6-(((*R*,*E*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-3-

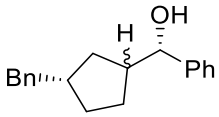
yl)oxy)tetrahydro-2*H*-pyran-3,4-diyl diacetate (122.1 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(R,R)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. ^{1}H NMR of the boronic ester isolated prior to oxidation indicated a 5:1 diastereomeric ratio in the reaction product. ***Note:*** the oxidation was carried out under buffered conditions by using pH7 phosphate buffer solution (0.50 mL) in place of 3M NaOH solution, and carrying out the oxidation for 12 hours. The crude mixture was purified by silica gel column chromatography (30% ethyl acetate in hexanes, stain in CAM) to afford the product as a single diastereomer. White solid (59.6 mg, 66% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37-7.30 (m, 2H), 7.27-7.22 (m, 3H), 5.44 (d, *J* = 4.6 Hz, 1H), 5.00-4.88 (m, 2H), 4.64-4.63 (m, 1H), 4.33 (dd, *J* = 12.3, 4.2 Hz, 1H), 4.11 (ddd, *J* = 9.6, 4.3, 2.2 Hz, 1H), 4.03 (dd, *J* = 12.3, 2.2 Hz, 1H), 3.88 (q, *J* = 6.1 Hz, 1H), 2.42 (ddd, *J* = 9.0, 4.6, 1.8 Hz, 1H), 2.17-2.09 (m, 2H), 2.05 (s, 3H), 1.93 (s, 3H), 1.75-1.56 (m, 2H), 1.53 (s, 3H), 1.00 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDClz_3$) δ 171.0, 170.8, 169.7, 143.0, 128.7, 127.7, 125.6, 100.8, 79.4, 74.3, 73.7, 69.5, 68.2, 62.2, 54.5, 43.1, 28.8, 20 .9, 20.7, 20.5, 10.3. **IR** (neat) ν_{max} 3506.0 (br), 2960.8 (m), 2931.6 (m), 2876.70 (w), 1744.4 (s), 1451.8 (m), 1230.9 (s), 1036.4 (s), 795.2 (w) 763.7 (w). **HRMS** (DART) for $C_{23}H_{34}NO_9$ $(M+NH_4)^+$: Calc'd 468.2228:, found: 468.2248. **$[\alpha]_D^{20}$** = 78.38 (*c* = 0.5, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

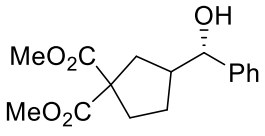
The stereochemistry of the carbon skeleton was assigned through NOESY correlation analysis. The absolute configuration at the B(pin)/OH containing stereocenter was assigned by analogy (see substrates **7** and **21**). Relevant NOESY correlations are illustrated below (assignment of the

^{1}H NMR shifts was aided by COSY analysis. The COSY spectrum is included along with the other spectral data).





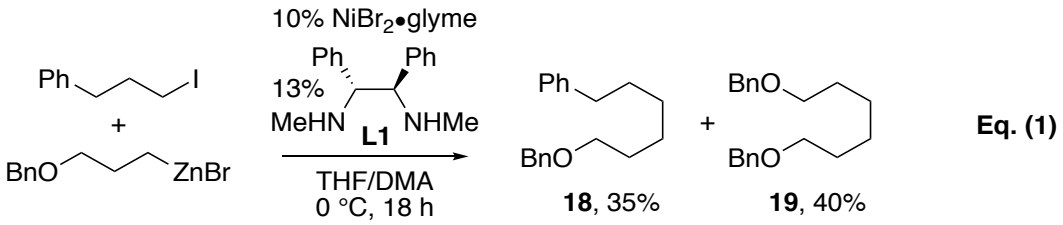
(***1S*)-((*3S*)-3-benzylcyclopentyl)(phenyl)methanol (34).** The reaction was performed according to the general **procedure A** with (*R*,*E*)-2-(5-benzyl-6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (85.2 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using NiBr2 • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and **(*S*,*S*)-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. The crude mixture was purified by silica gel /column chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (30.9 mg, 58% yield). The product is a diastereomeric mixture (d.r. = 1.2:1) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (m, 8H), 7.30-7.24 (m, 7H), 7.19-7.12 (m, 7H), 4.43 (d, *J* = 8.2 Hz, 1H), 4.38 (d, *J* = 8.5 Hz, 1H), 2.68-2.56 (m, 5H), 2.43-2.38 (m, 2H), 2.32-2.23 (m, 2H), 2.14-2.08 (m, 1H), 1.88-1.66 (m, 8H), 1.63-1.43 (m, 5H), 1.39-1.14 (m, 5H), 0.97 (q, *J* = 11.1, 11.1, 11.1 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.3, 144.3, 142.1, 142.0, 128.9, 128.8, 128.5, 128.3, 128.3, 127.7, 127.7, 126.7, 126.6, 125.8, 125.8, 79.3, 79.2, 47.4, 46.3, 42.4, 42.3, 42.1, 41.3, 37.0, 35.1, 32.9, 31.7, 29.6, 28.1. **IR** (neat) ν_{max} 3022.8 (w), 2922.3 (w), 2852.0 (w), 1492.5 (m), 1450.5 (m), 1028.6 (w), 741.5 (m), 697.0 (s), 599.3 (w), 542.1 (w), 479.9 (m). **HRMS** (DART) for $C_{19}H_{21}$ $(M+H-H_2O)^+$: Calc'd: 249.1638, found: 249.1627. **Note**: the product was obtained as a mixture of diastereomers and an optical rotation was not obtained



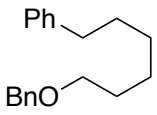
dimethyl 3-((S)-hydroxy(phenyl)methyl)cyclopentane-1,1-dicarboxylate (23). The reaction was performed according to general **procedure A** dimethyl (*E*)-2-(2-iodoethyl)-2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)malonate (90.4 mg, 0.20 mmol, 1.0 equiv.), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv.), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$ • glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and ***(S,S)*-L1** (6.25 mg, 0.026 mmol, 0.13 equiv.) as catalyst. **Note** the oxidation was carried out under buffered conditions by using pH7 phosphate buffer solution (0.50 mL) in place of 3M NaOH solution, and carrying out the oxidation for 12 hours. The crude mixture was purified by silica gel column chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as a colorless oil (36.0 mg, 62% yield).

^{1}H NMR (600 MHz, C_6D_6) δ 7.15-7.12 (m, 2H), 7.10-7.04 (m, 6H), 7.04-6.99 (m, 2H), 4.18 (d, *J* = 7.1 Hz, 1H), 4.11 (d, *J* = 6.7 Hz, 1H), 3.27 (s, 3H), 3.24 (s, 3H), 3.22 (s, 3H), 3.19 (s, 3H), 2.70-2.62 (m, 1H), 2.41-2.36 (m, 1H), 2.35-2.29 (m, 3H), 2.25-2.19 (m, 2H), 2.19-2.12 (m, 1H), 2.12-2.05 (m, 1H), 1.83-1.73 (m, 1H), 1.73-1.63 (m, 1H), 1.35 (s, 1H), 1.35-1.29 (m, 3H), 0.39 (s, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.3, 173.1, 172.9, 172.8, 144.0, 143.8, 128.6, 128.5, 127.80, 127.8, 126.4, 126.3, 77.9, 77.7, 60.2, 60.1, 52.9, 52.8, 52.8, 52.8, 46.9, 46.8, 37.2, 37.2, 34.2, 34.0, 28.8, 28.3. **IR** (neat) ν_{max} 3522.2 (br), 3026.2 (w), 1726.3 (s), 1492.2 (w), 1267.0 (m), 1197.0 (w), 1158.7 (w), 1102.6 (w), 763.8 (w), 702.4 (w). **HRMS** (DART) for $C_{16}H_{19}O_5$ $(M+H)^+$: Calc'd: 291.1227, found: 291.1226. **Note**: the product was obtained as a mixture of diastereomers and an optical rotation was not obtained. The diastereomeric ratio was determined by the integration of the ^{1}H NMR in C_6D_6.

3.4.2.6. Background Reaction Experiments

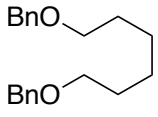


Equation (1). In an argon-filled glovebox, an oven-dried 2 dram vial equipped with a magnetic stirrer was charged with **$NiBr_2$ • glyme** (6.17 mg, 0.02 mmol), (*S,S*)-N,N-dimethyl-1,2-diphenyl-ethane-1,2-diamine (***S,S*)-L1** (6.25 mg, 0.026 mmol) and dissolved in 2.0 mL of THF. The catalyst solution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

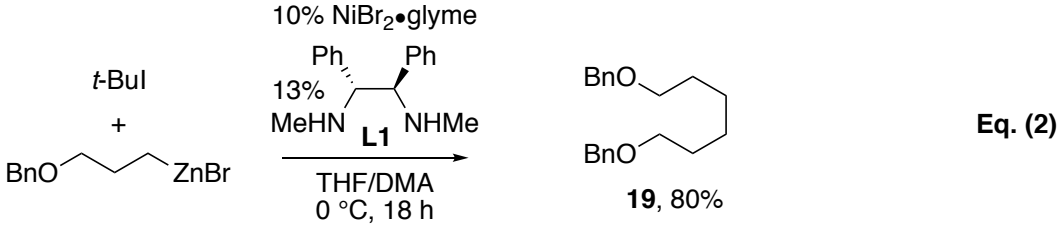


(6-(benzyloxy)hexyl)benzene (18). The product of the reaction was isolated by silica gel column chromatography (25% CH_2Cl_2 in hexane, stain in CAM) as a colorless oil (37.8

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

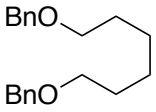


1,6-bis(benzyloxy)hexane (19) was isolated by silica gel column chromatography (40% CH_2Cl_2 in hexane, stain in CAM) as a colorless oil (24.1 mg, 40% yield based on 0.50 equiv. of starting material). All spectral data were in accordance with the literature.[14]

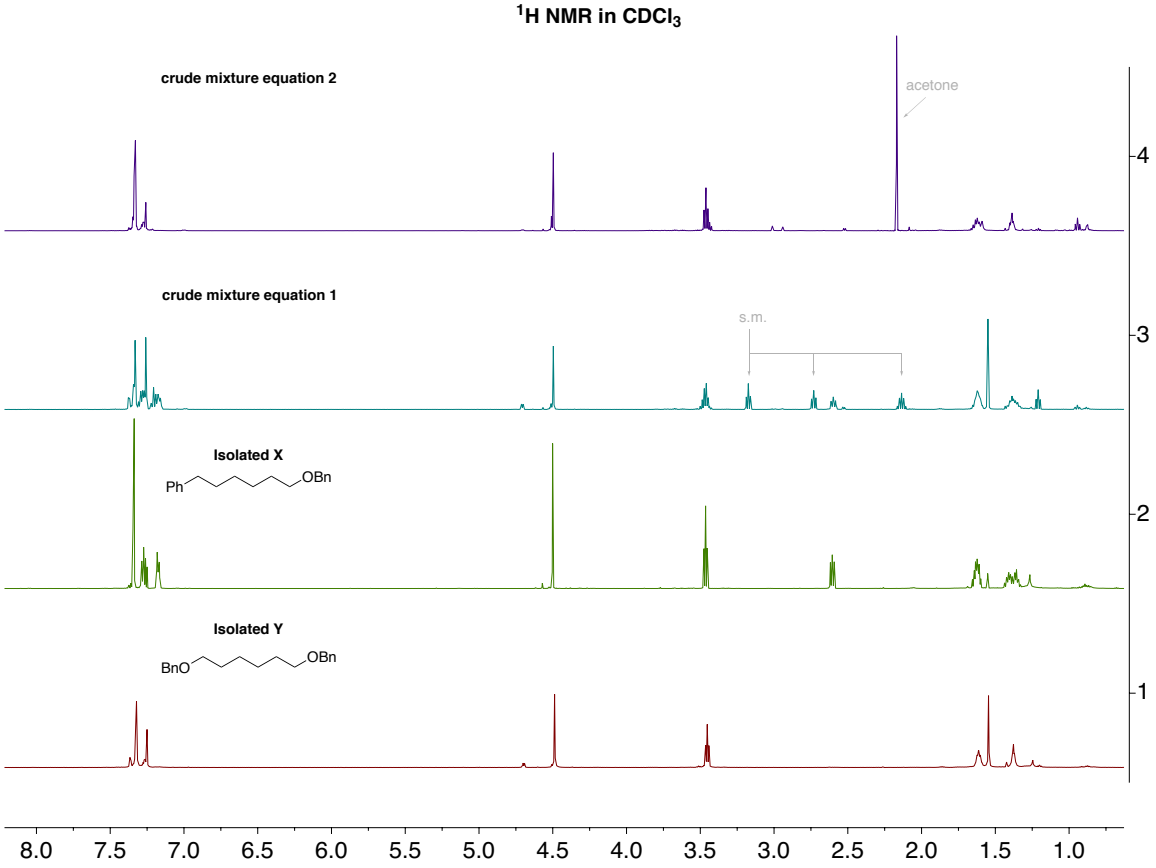


Eq. (2)

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



1,6-bis(benzyloxy)hexane (19) was isolated by silica gel column chromatography (40% CH_2Cl_2 in hexane, stain in CAM) as a colourless oil (47.8 mg 80% yield based on 0.50 equiv. of starting material) All spectral data were in accordance with the literature.[14]



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

3.4.3 References

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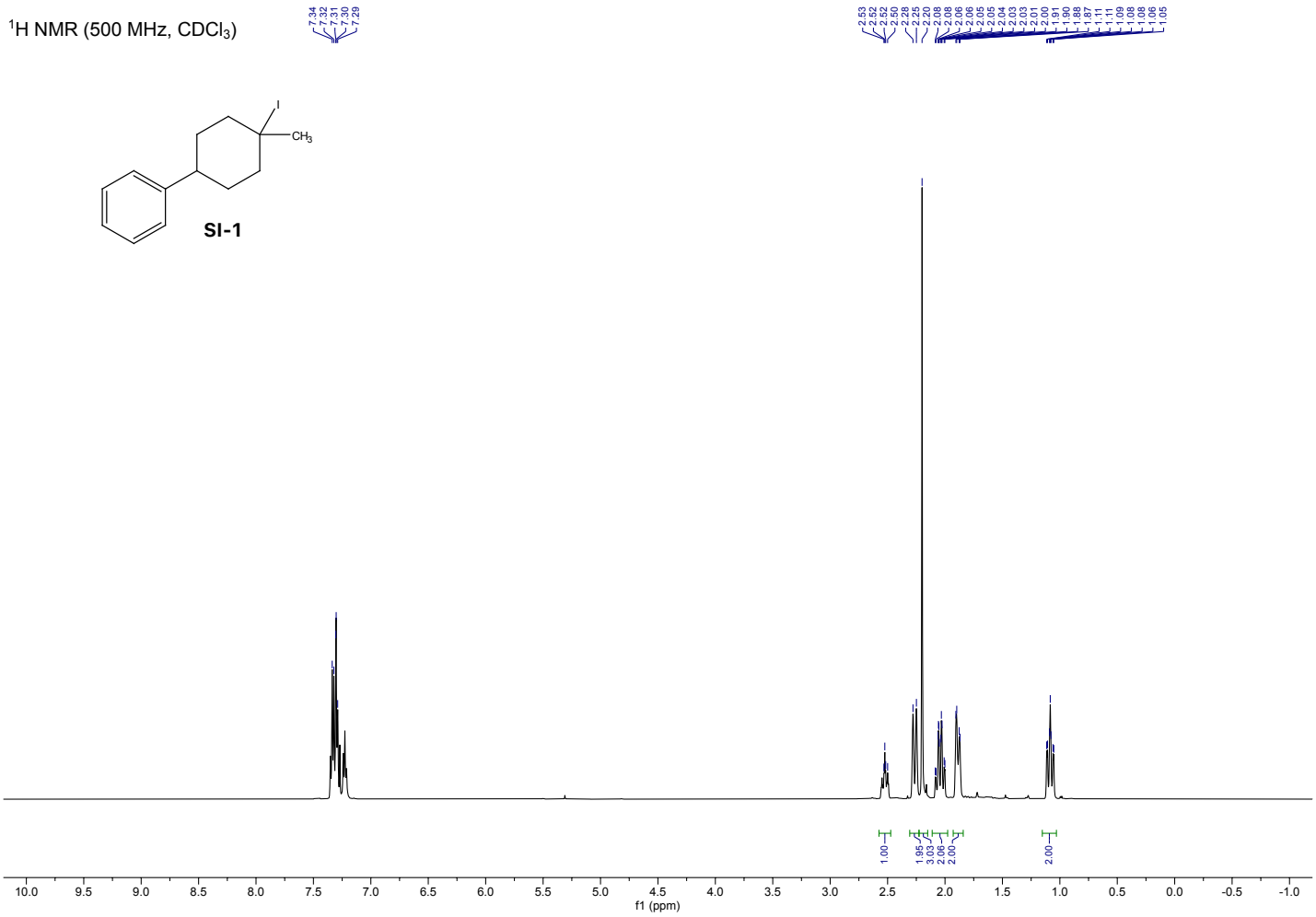
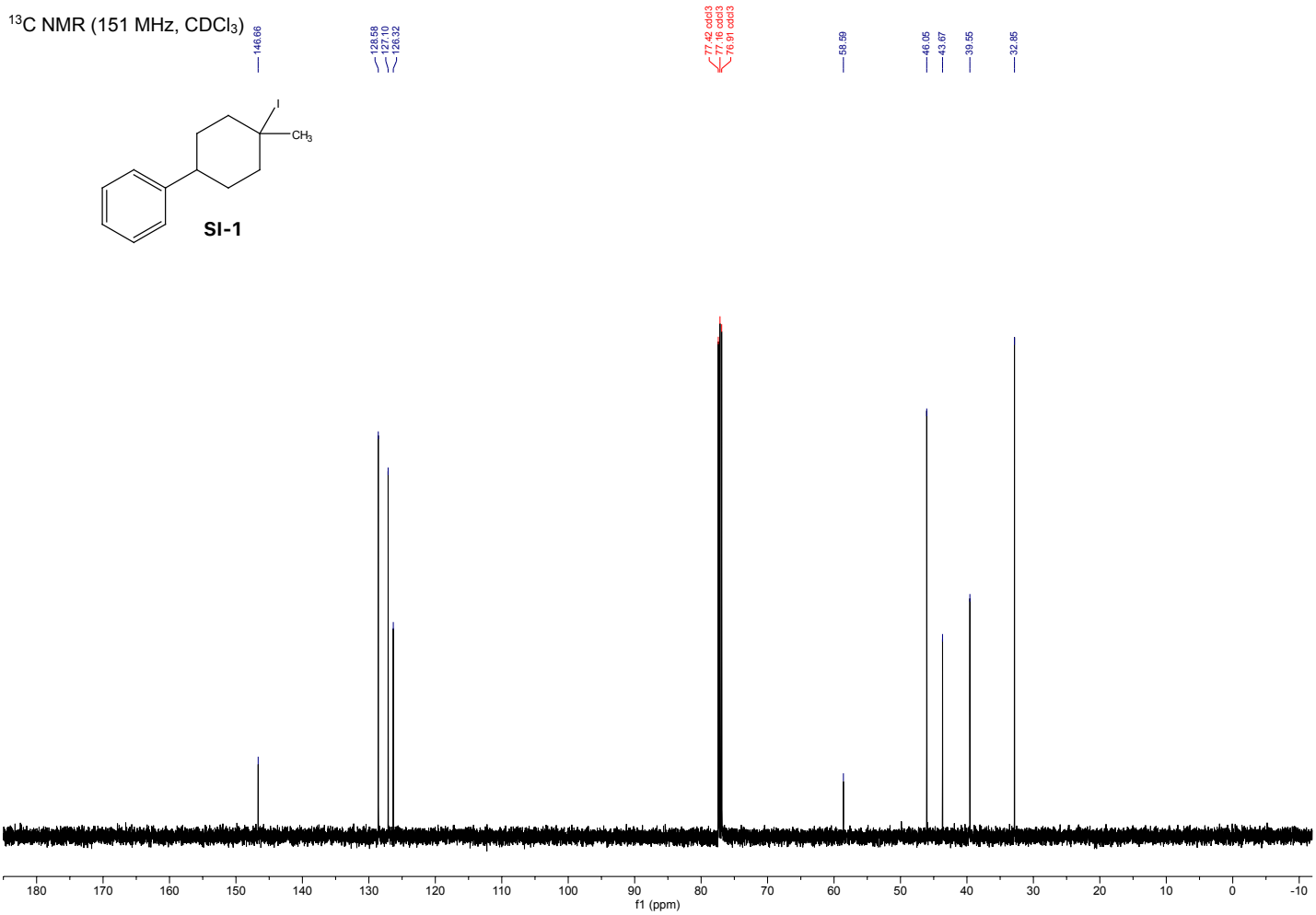
^{1}H NMR (500 MHz, $CDCl_3$)



SI-1

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



SI-1

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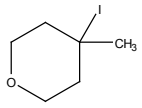

SI-2

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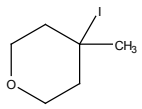
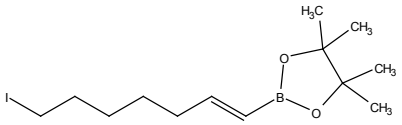


SI-2

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



SI-5

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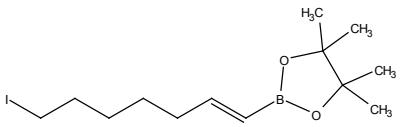

SI-5

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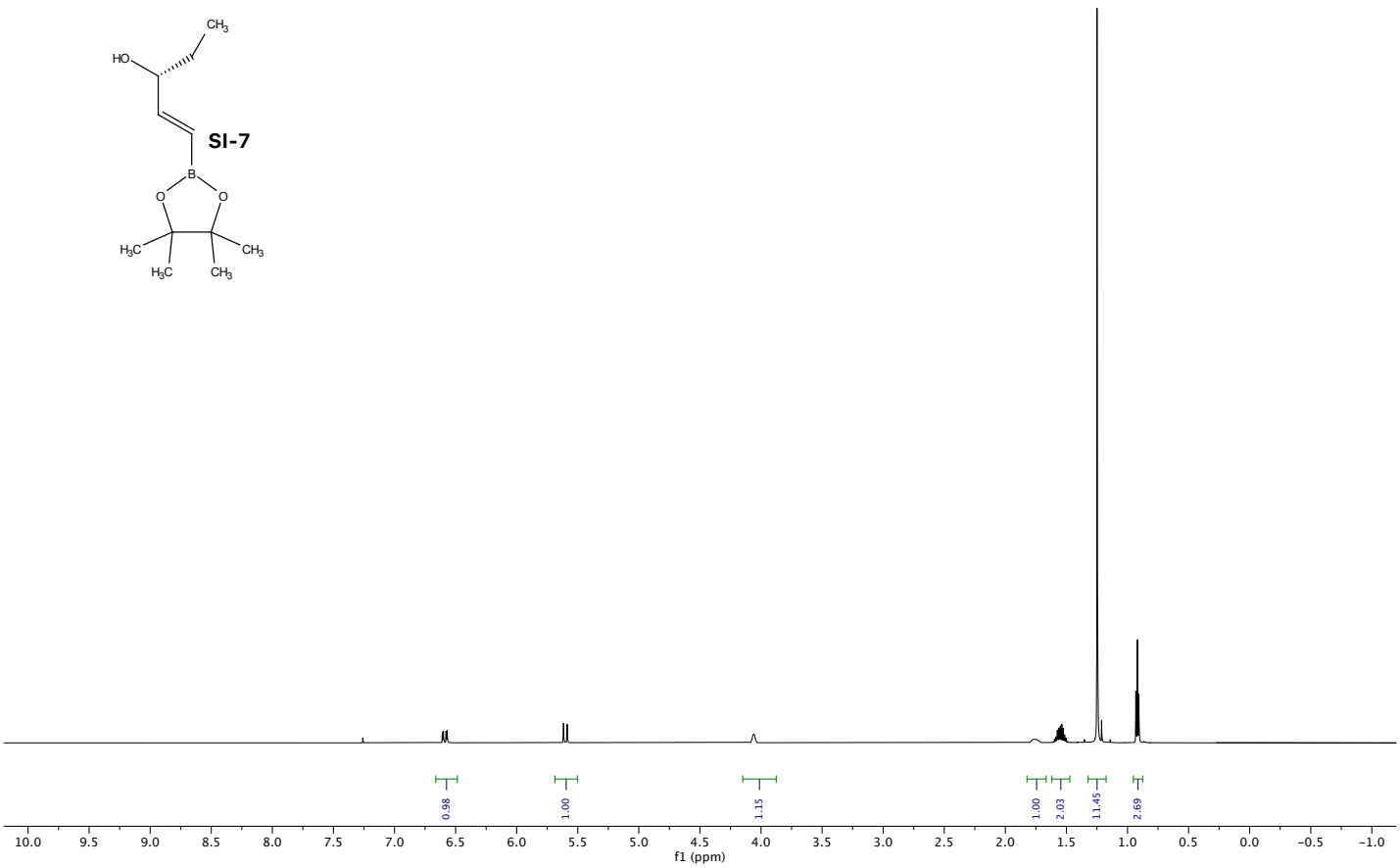

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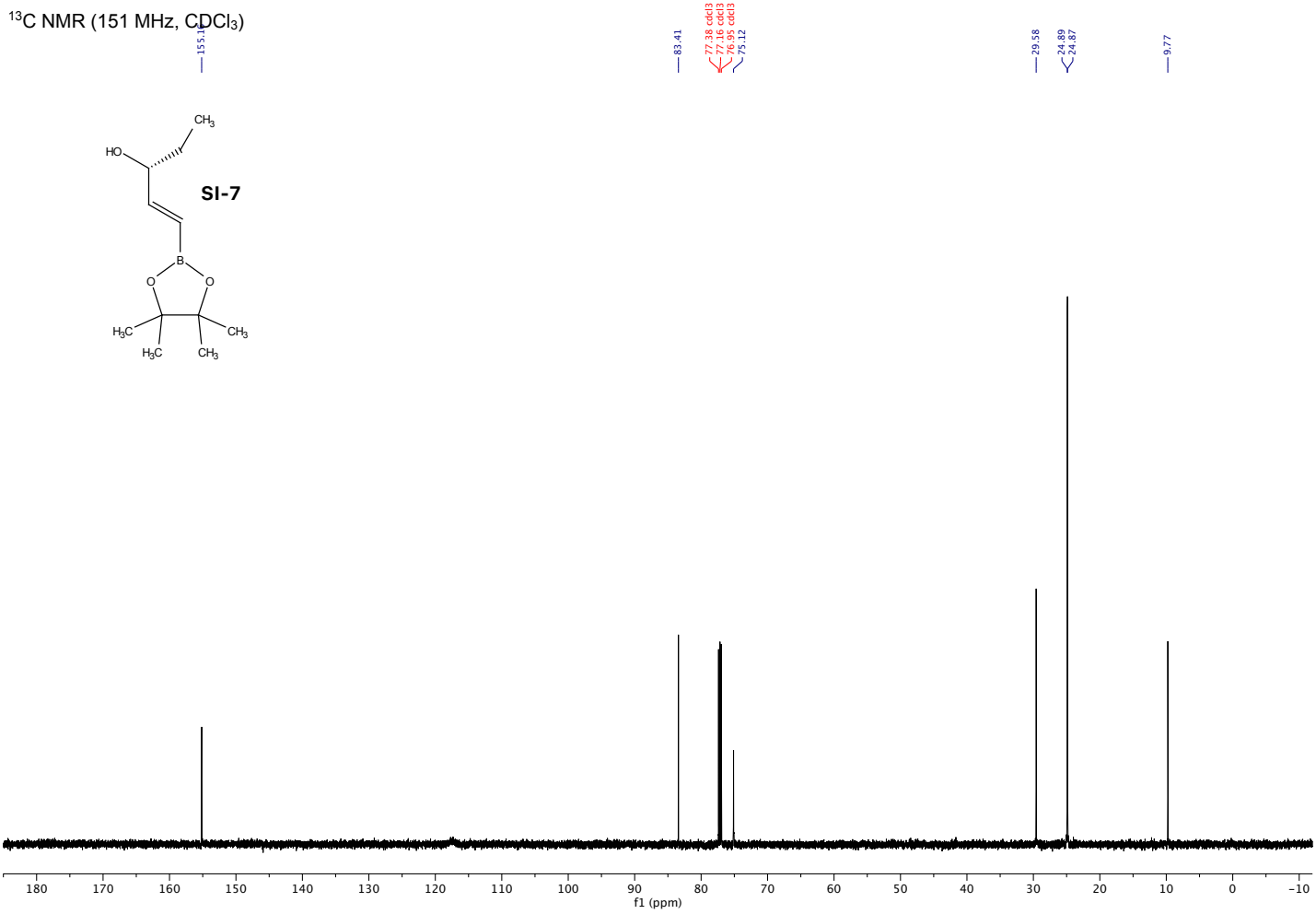

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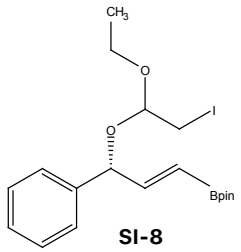
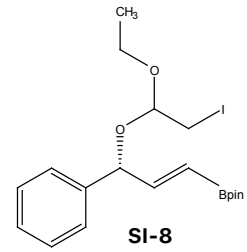


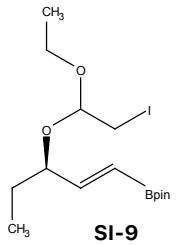
SI-8

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



SI-8

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



SI-9

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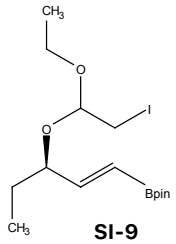

SI-9

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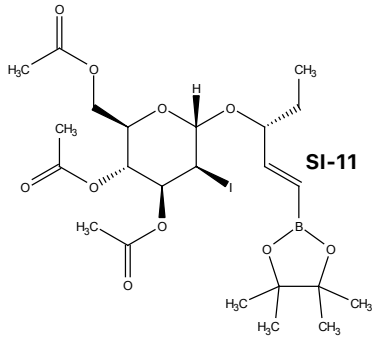

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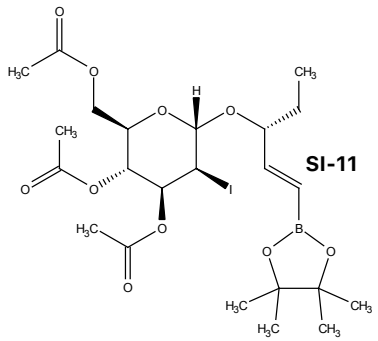

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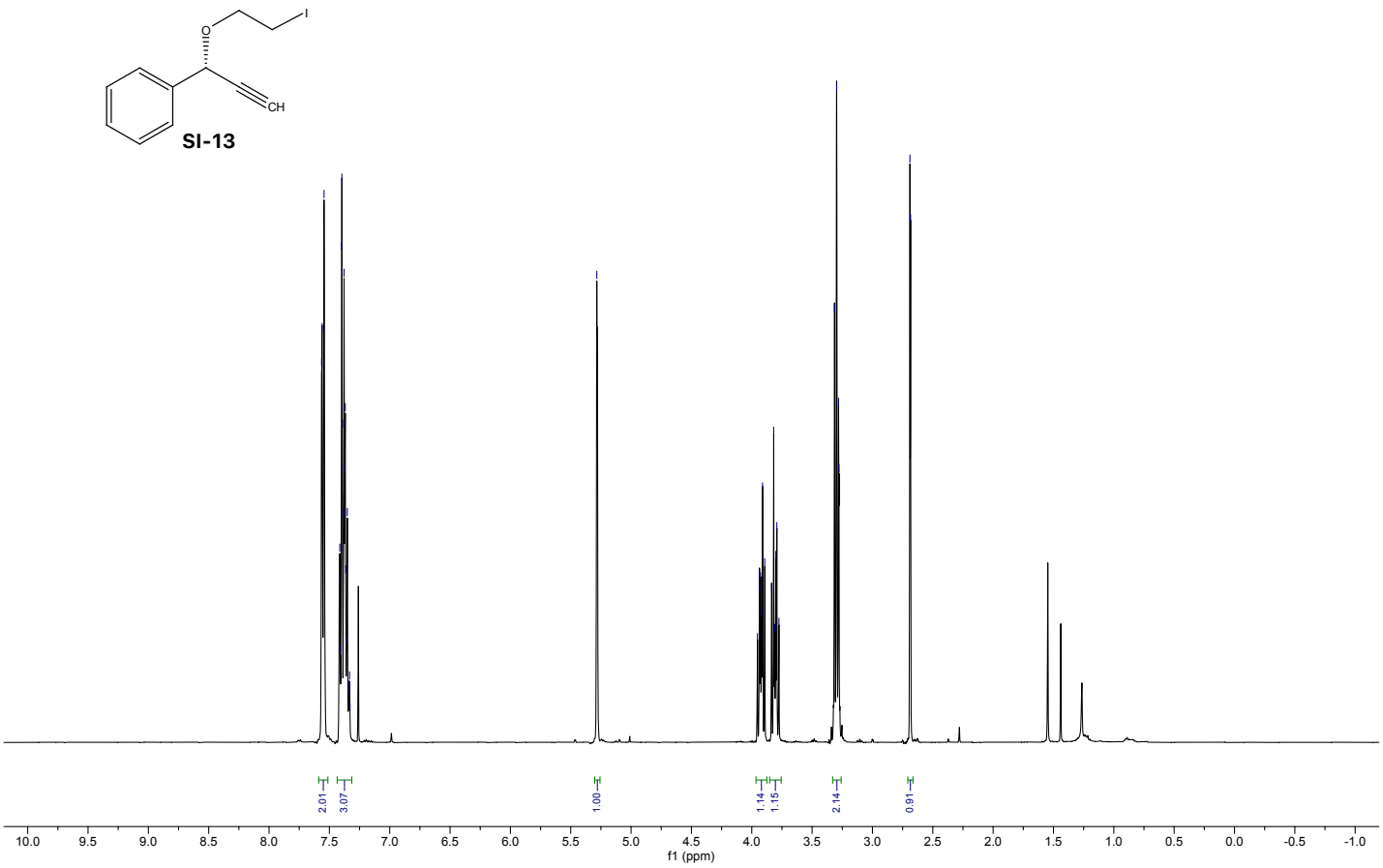

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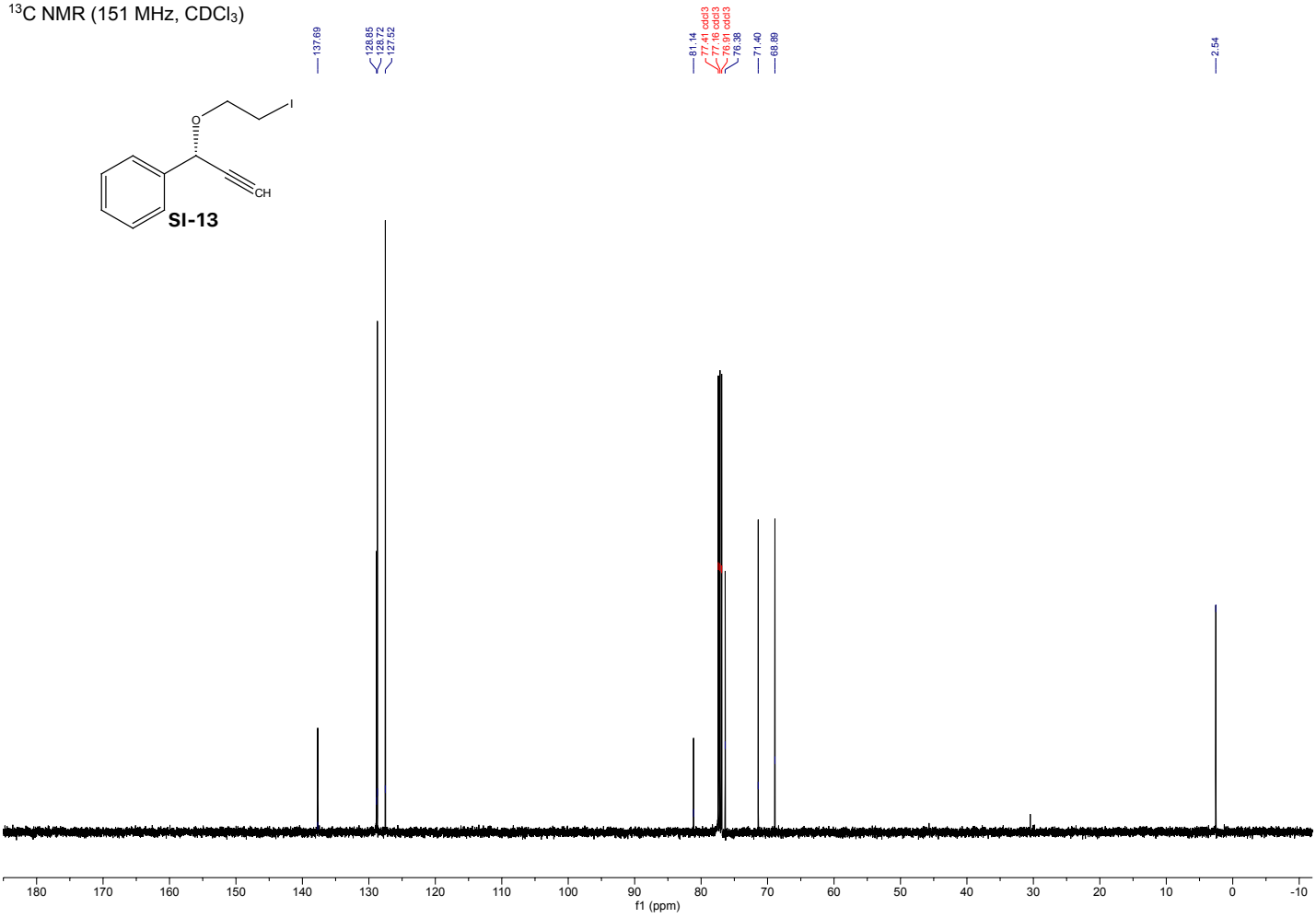

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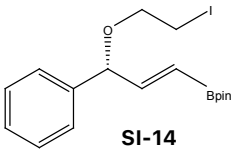
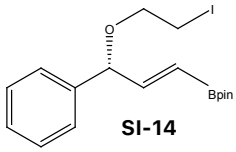


SI-14

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



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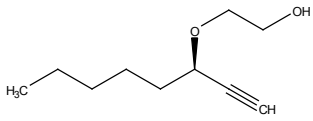
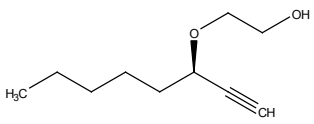


SI-15

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



SI-15

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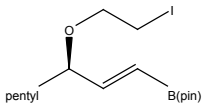

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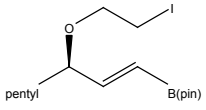
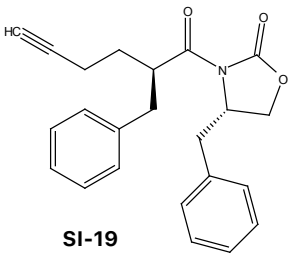


SI-17

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



SI-19

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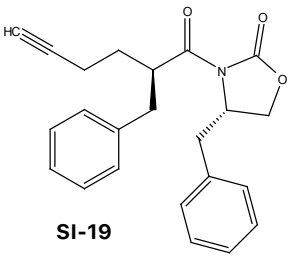

SI-19

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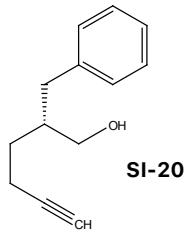

SI-20

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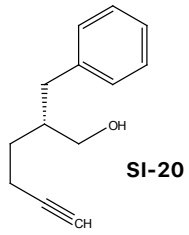

SI-20

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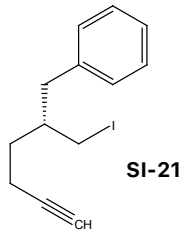

SI-21

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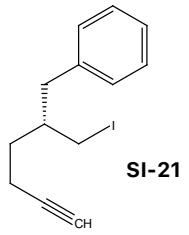

SI-21

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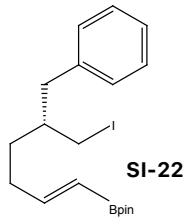

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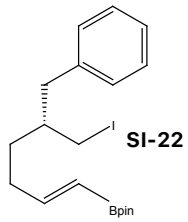
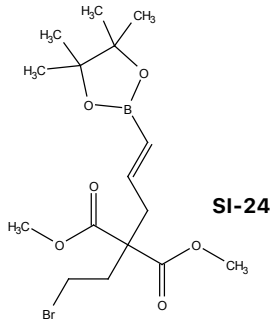
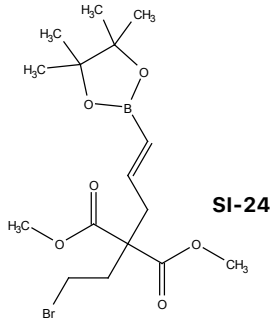


^{1}H NMR (500 MHz, $CDCl_3$)



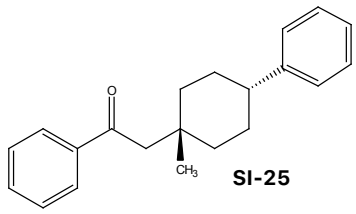
SI-24

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



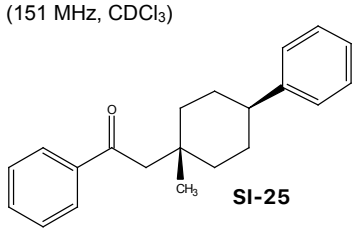
SI-24

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



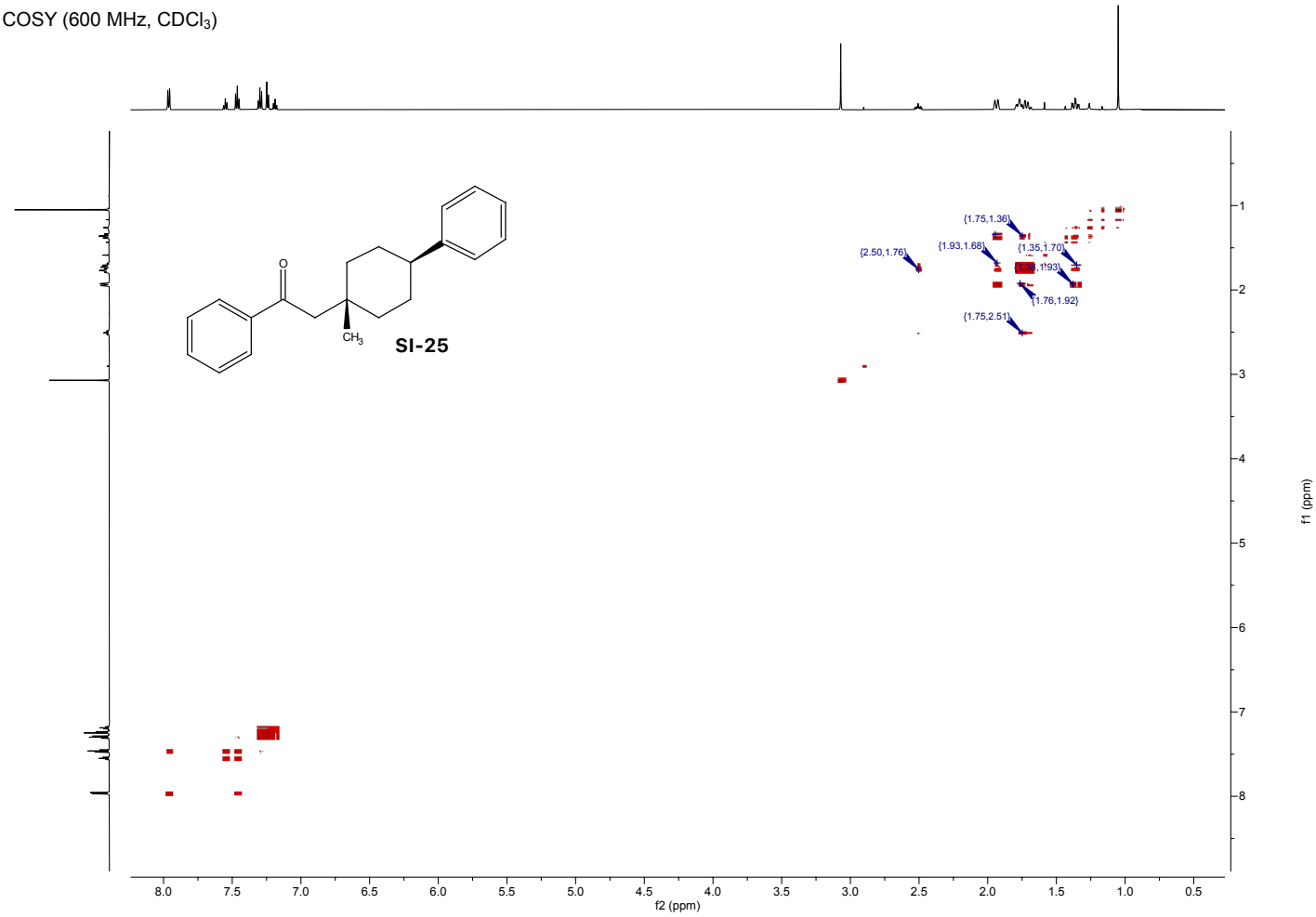
SI-25

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

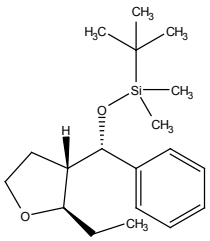


SI-25

COSY (600 MHz, $CDCl_3$)

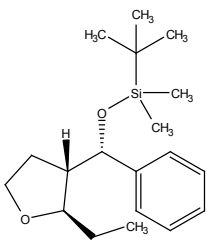


^{1}H NMR (500 MHz, $CDCl_3$)



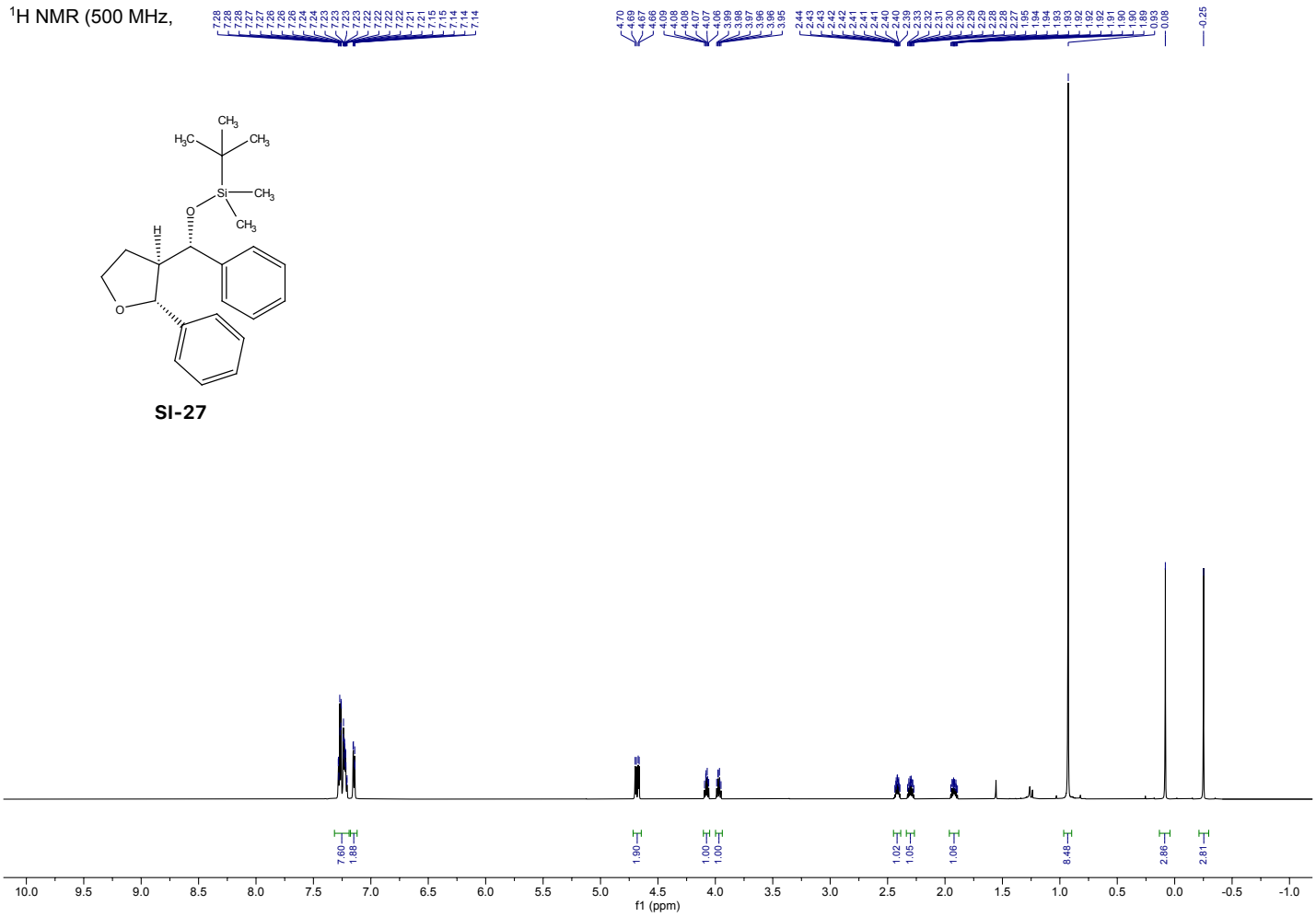
SI-26

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



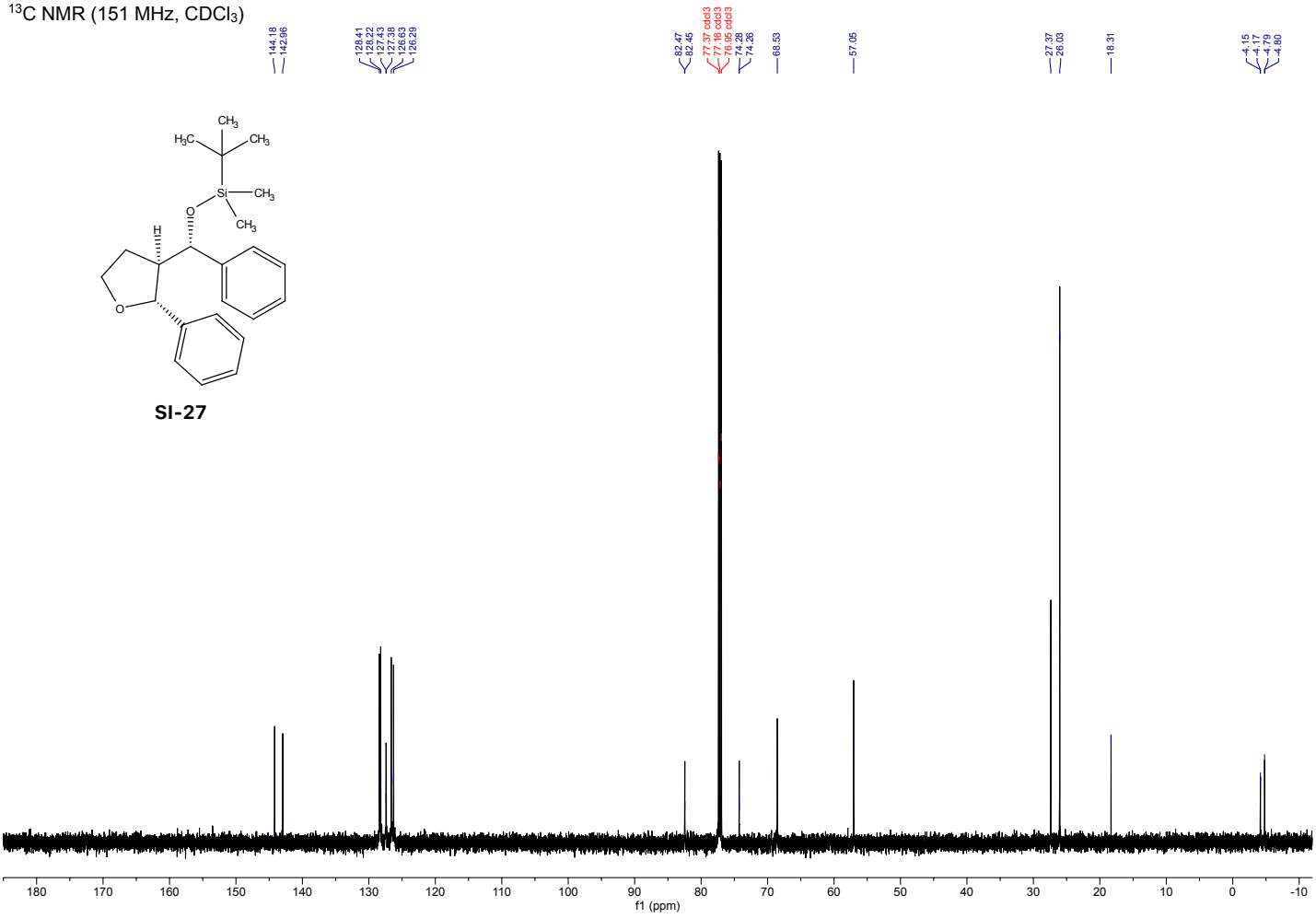
SI-26

^{1}H NMR (500 MHz,



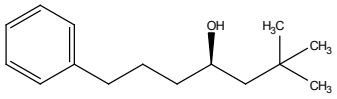
SI-27

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



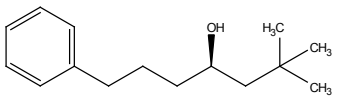
SI-27

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



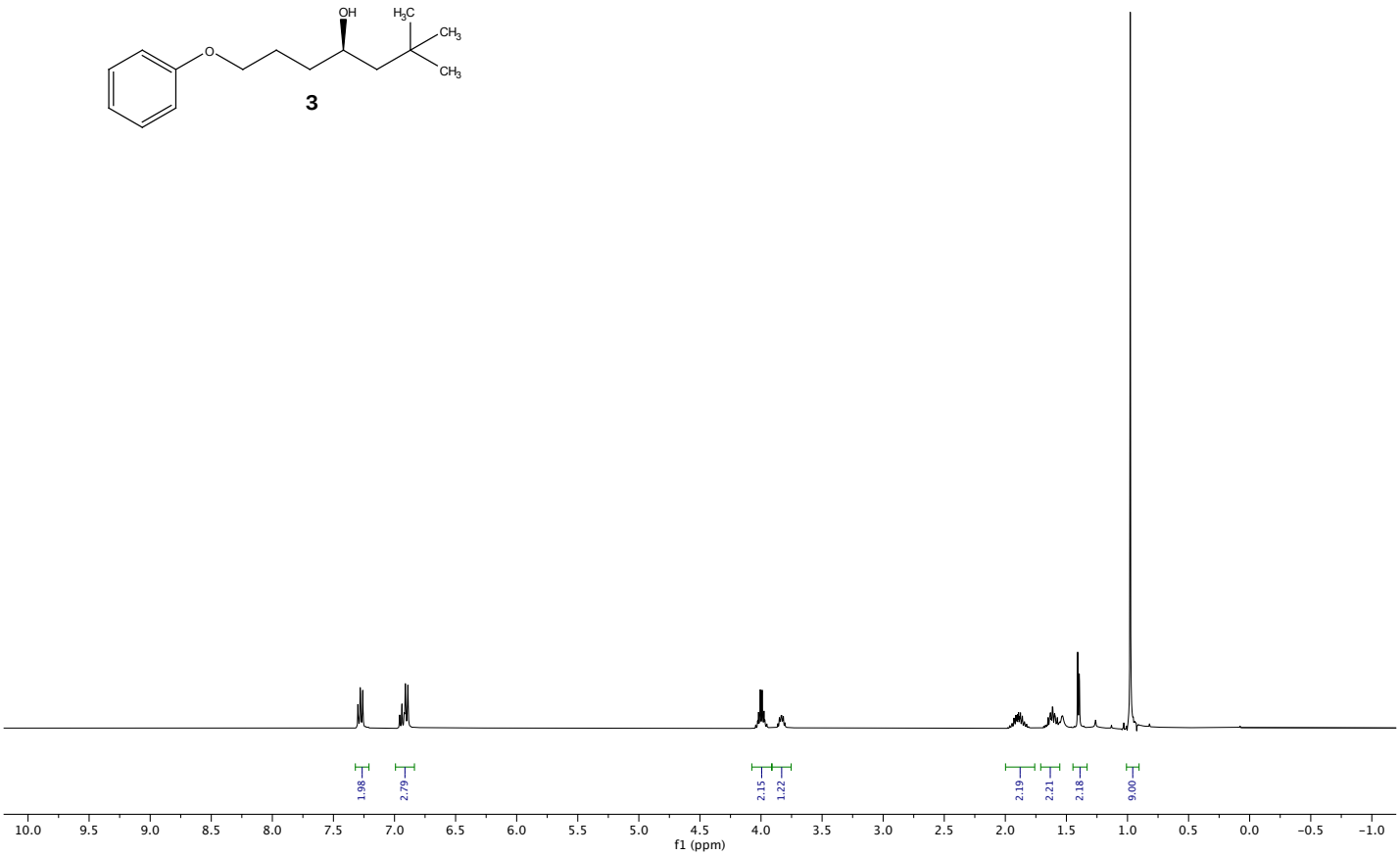
2

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

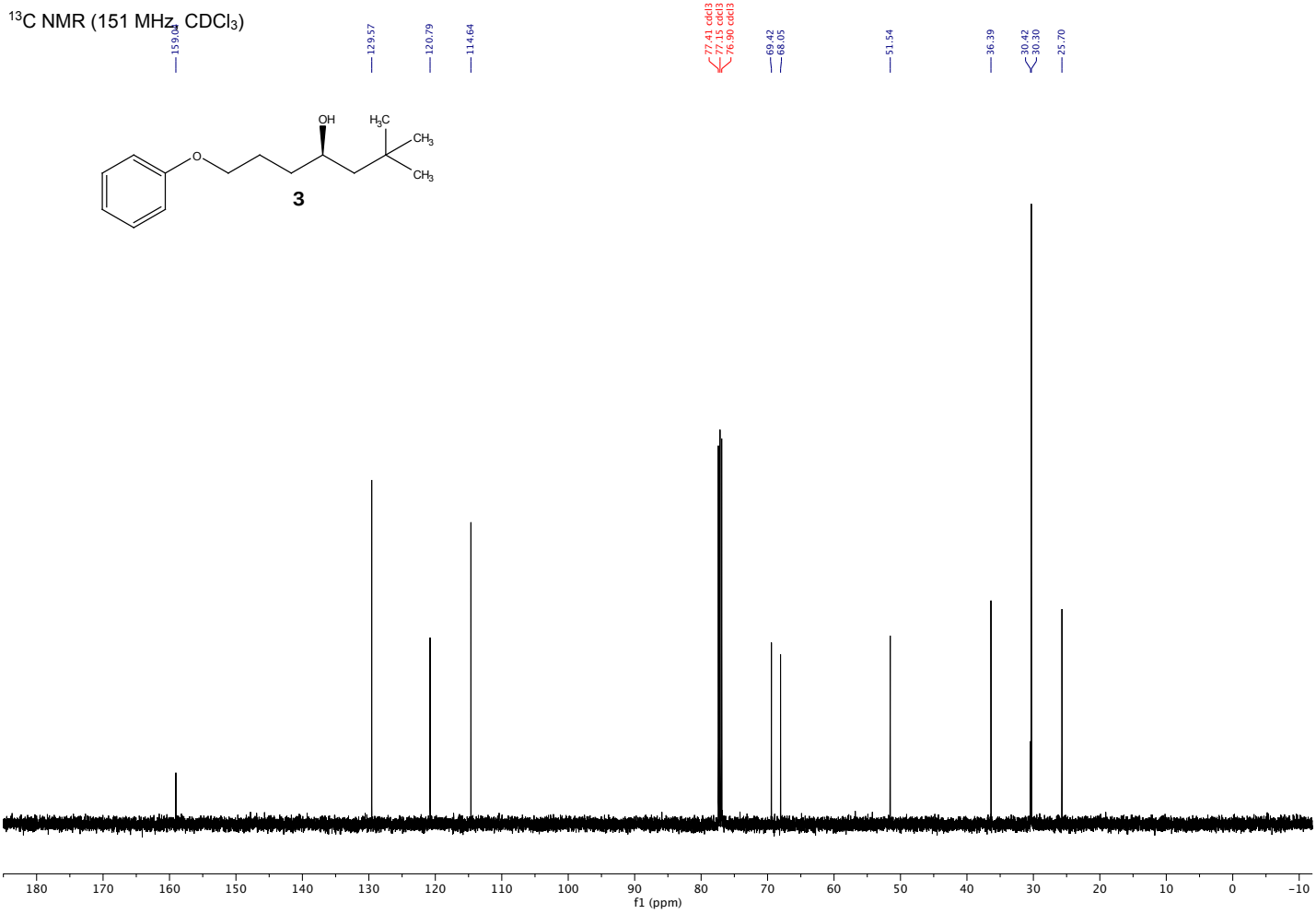


2

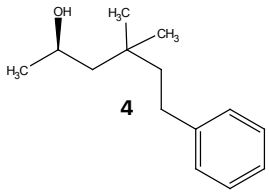
^{1}H NMR (500 MHz, $CDCl_3$)



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

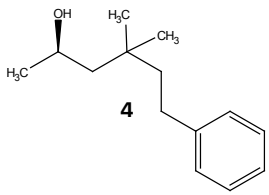


^{1}H NMR (500 MHz, $CDCl_3$)



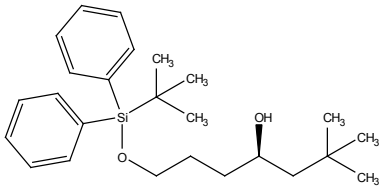
4

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

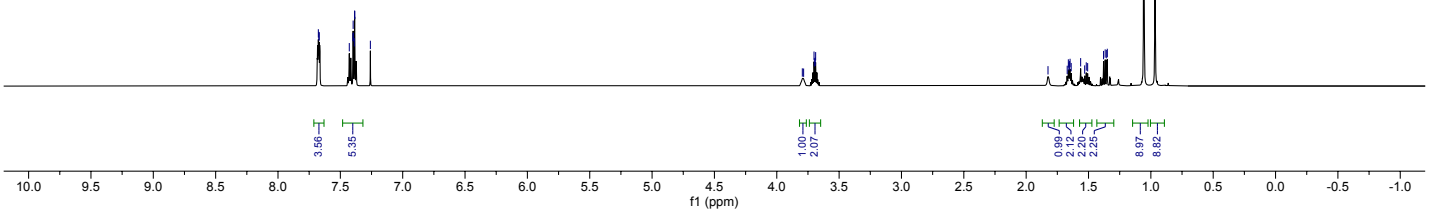


4

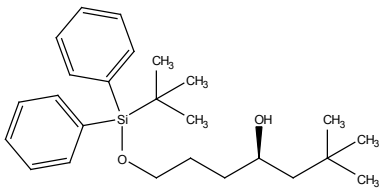
^{1}H NMR (500 MHz, $CDCl_3$)



5

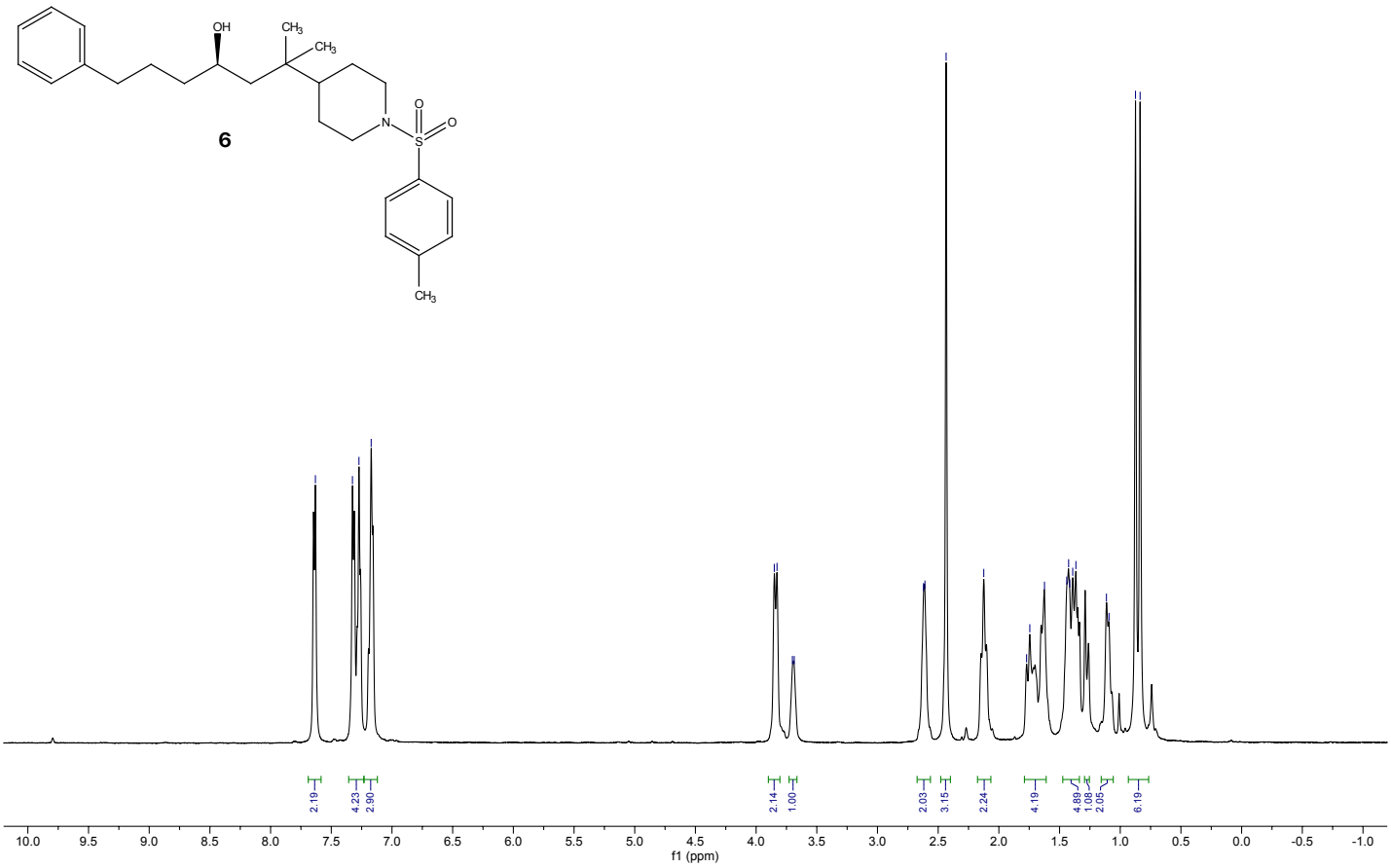


^{13}C NMR (151 MHz, $CDCl_3$)

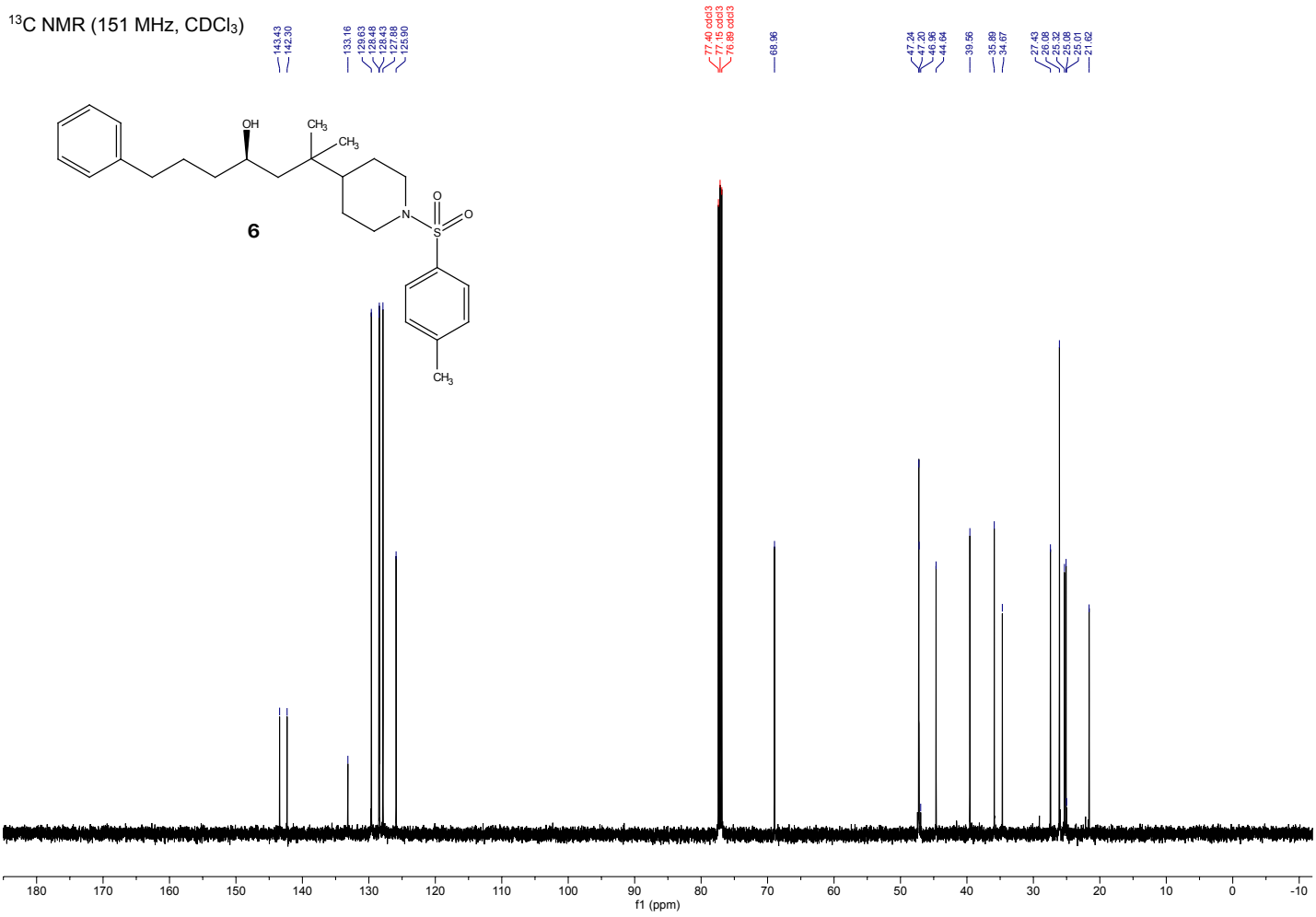


5

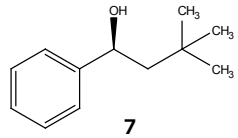
^{1}H NMR (500 MHz, $CDCl_3$)



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

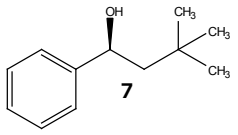


^{1}H NMR (500 MHz, $CDCl_3$)



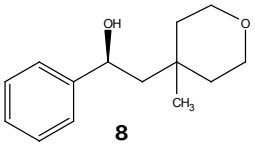
7

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



7

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



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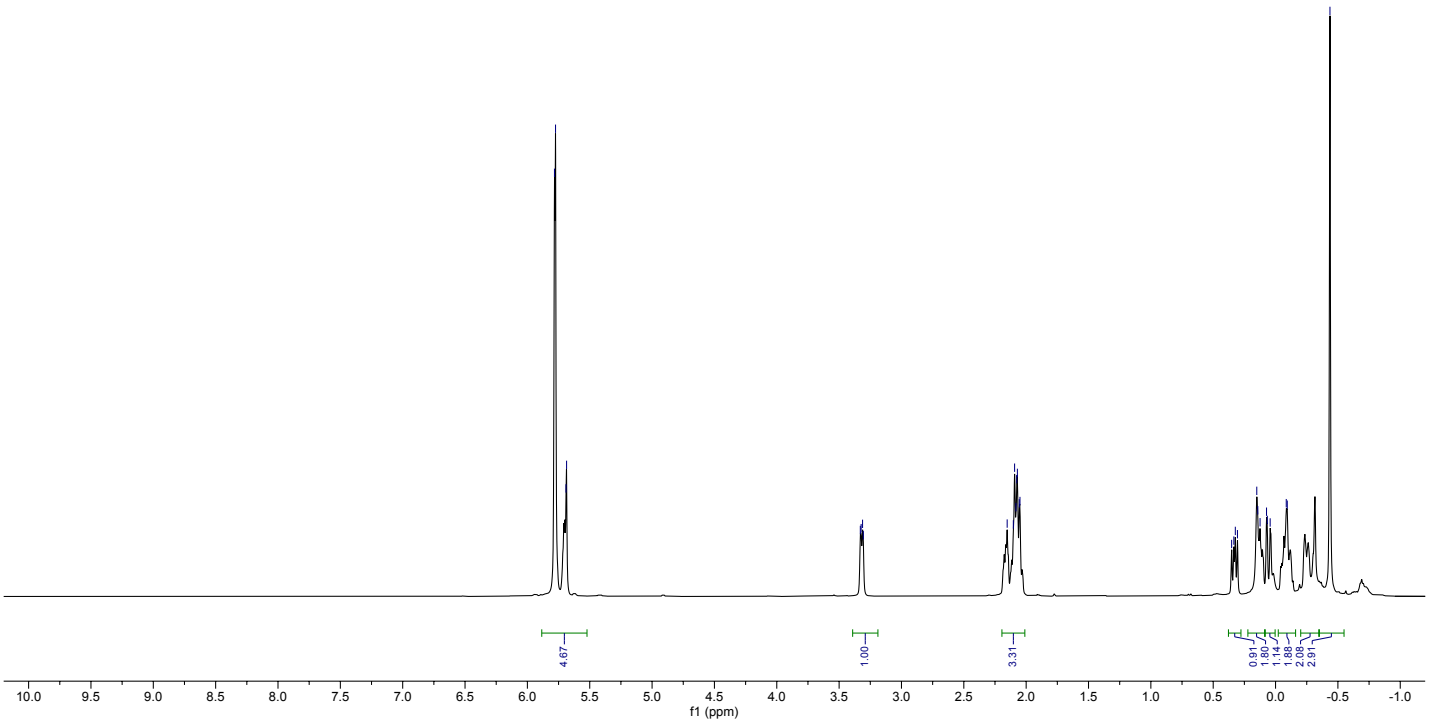
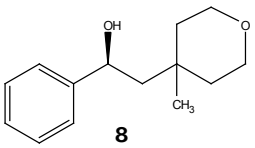
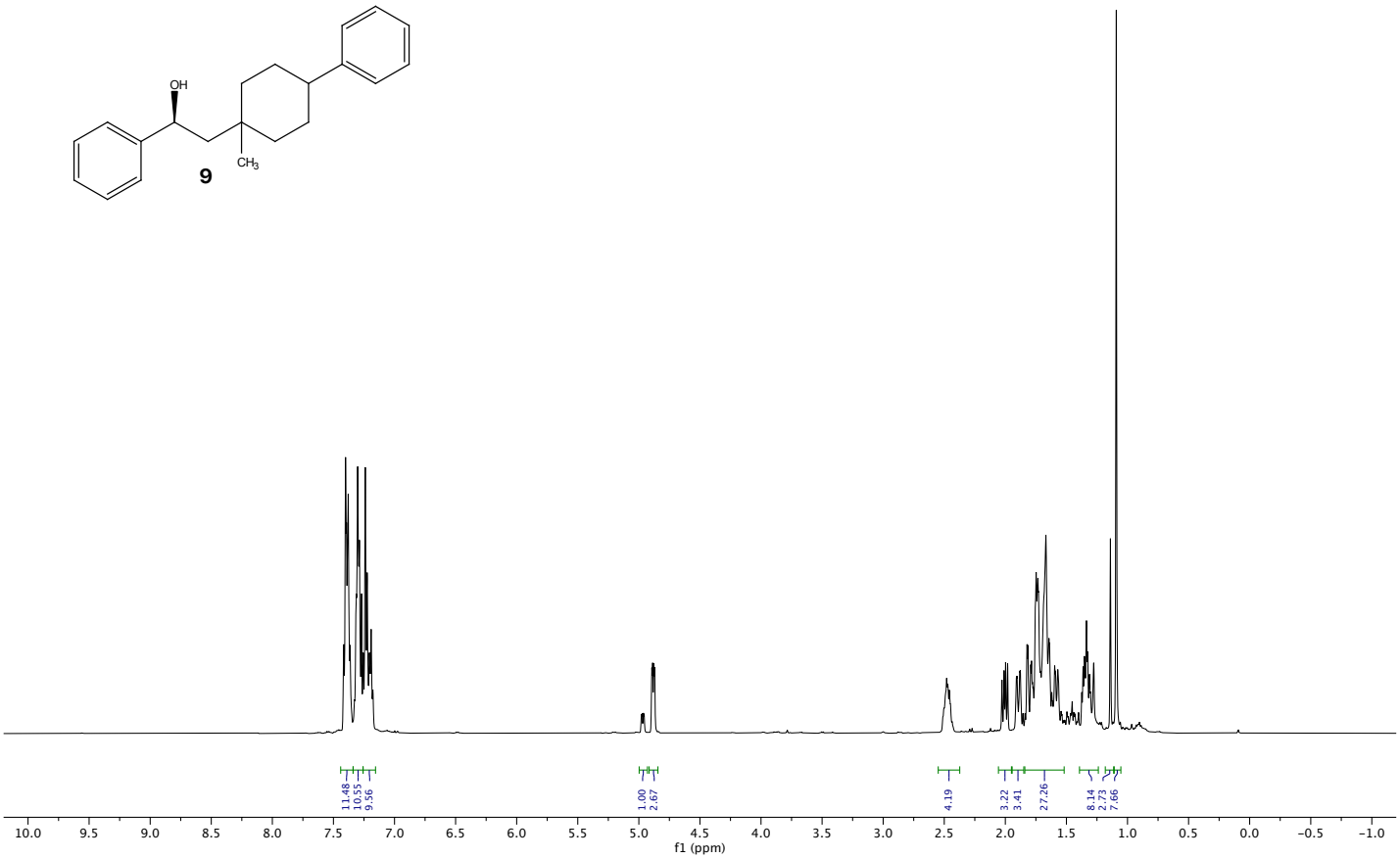


^{13}C NMR (151 MHz, $CDCl_3$)

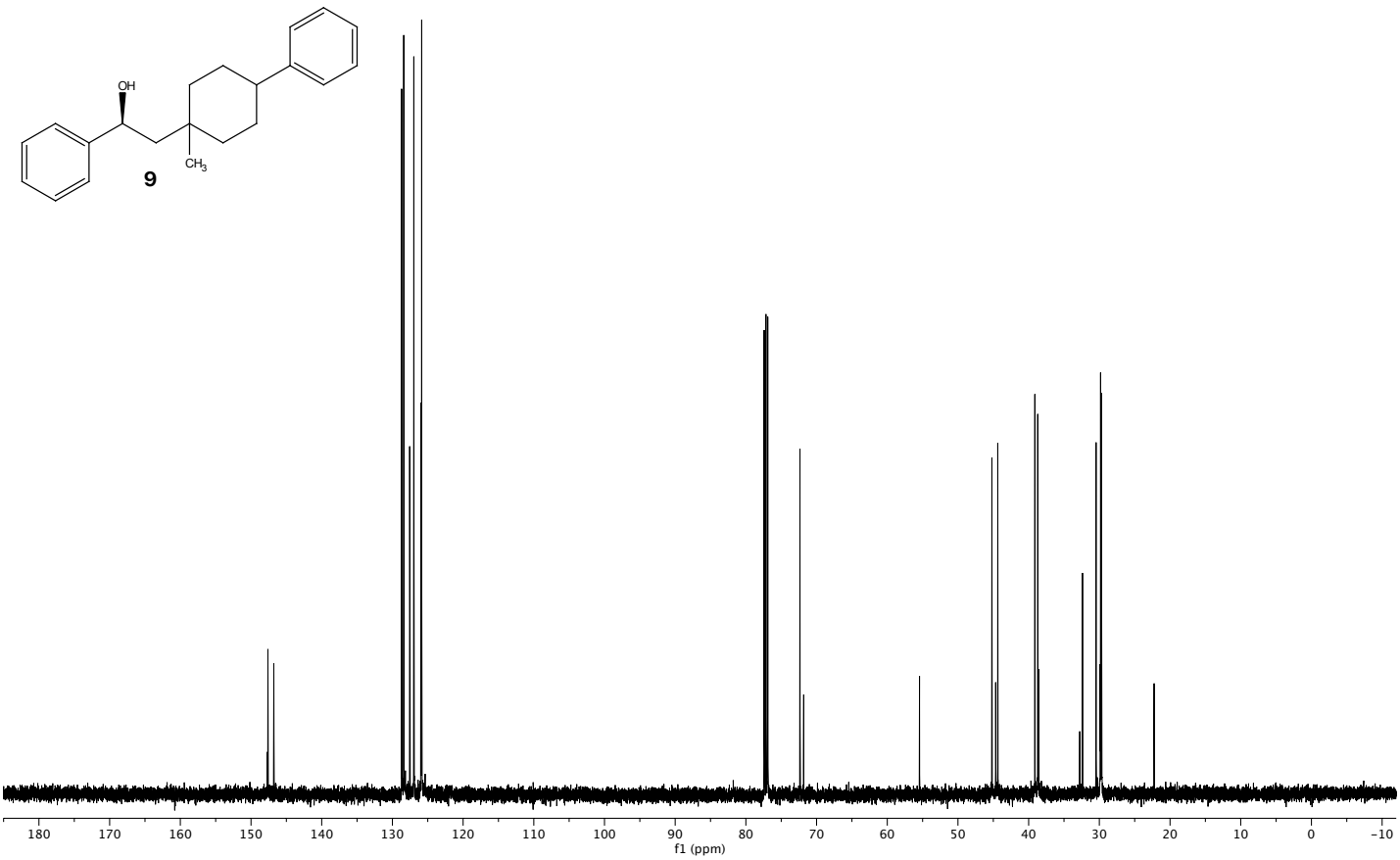


8

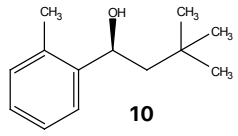
^{1}H NMR (500 MHz, $CDCl_3$)



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

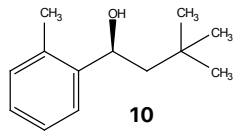


^{1}H NMR (500 MHz, $CDCl_3$)



10

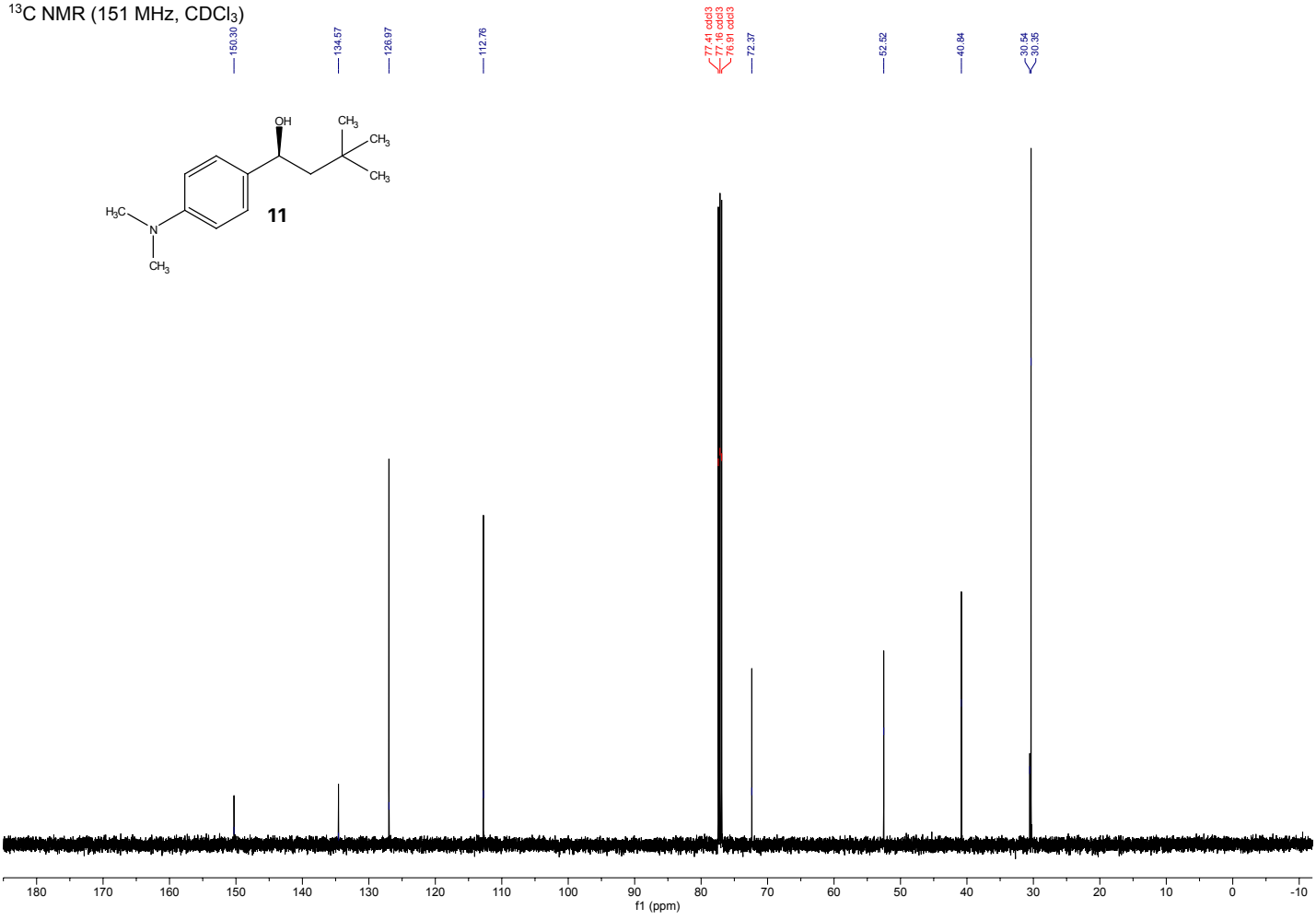
^{13}C NMR (151 MHz, $CDCl_3$)



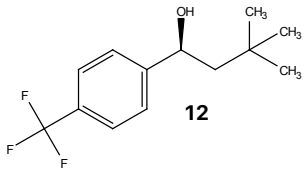
10

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

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

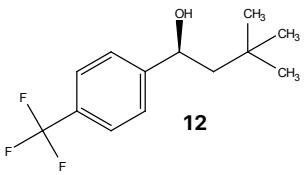


^{1}H NMR (500 MHz, $CDCl_3$)



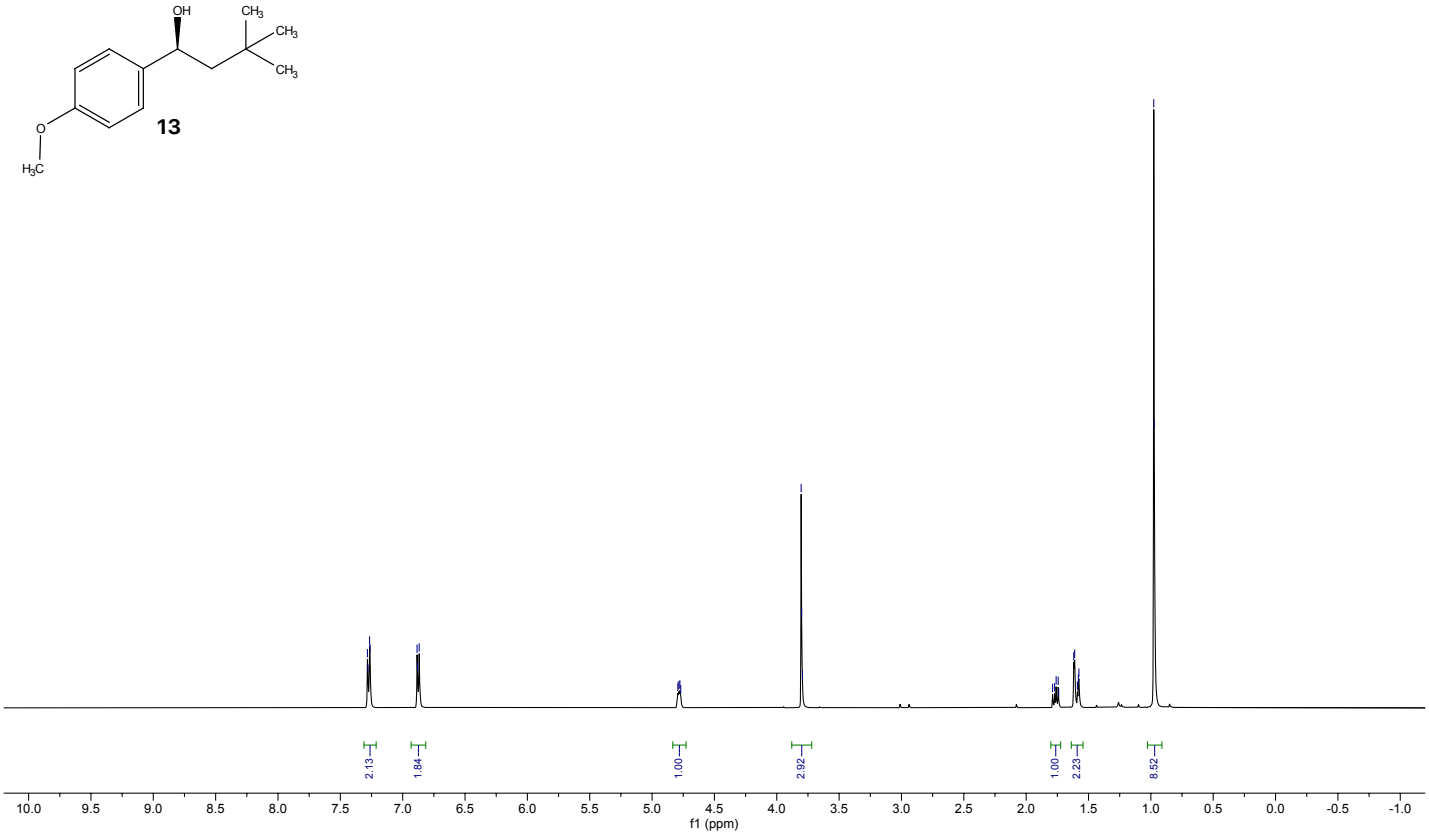
12

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

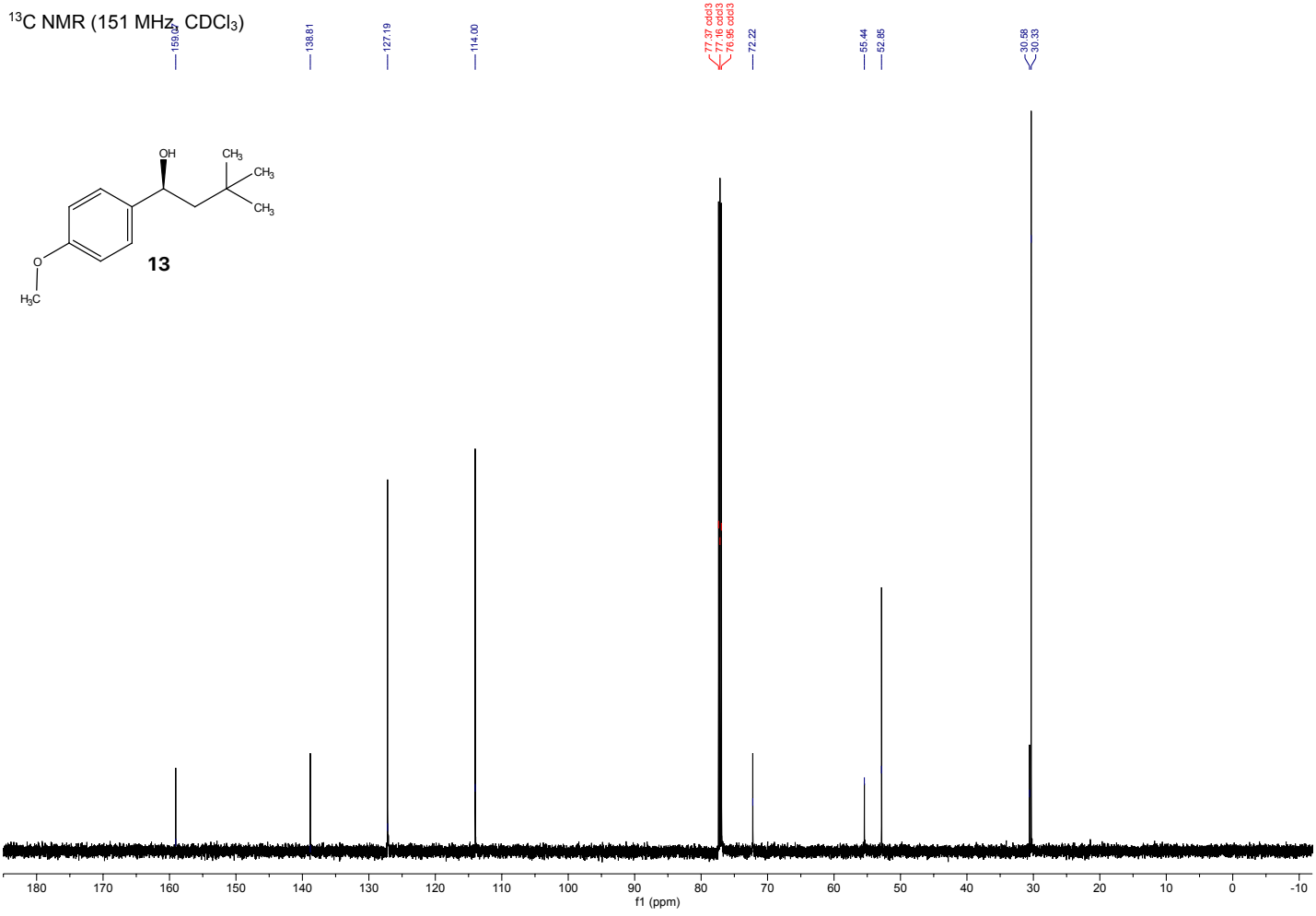


12

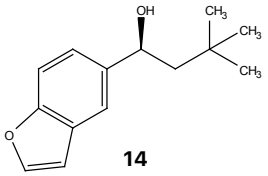
^{1}H NMR (500 MHz, $CDCl_3$)



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

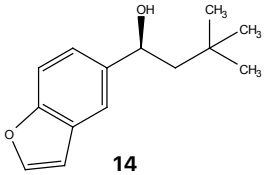


^{1}H NMR (500 MHz, $CDCl_3$)



14

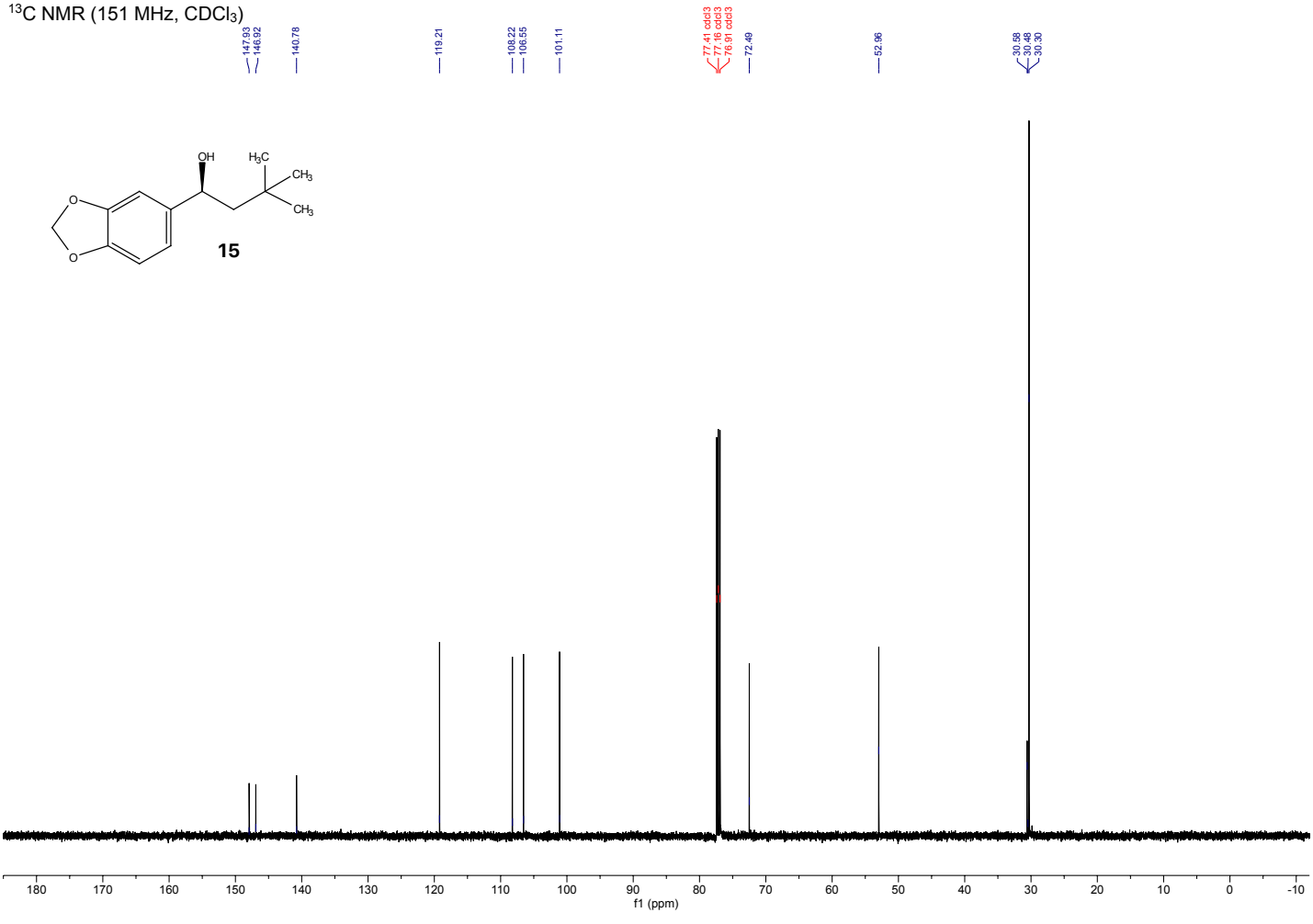
^{13}C NMR (151 MHz, $CDCl_3$)



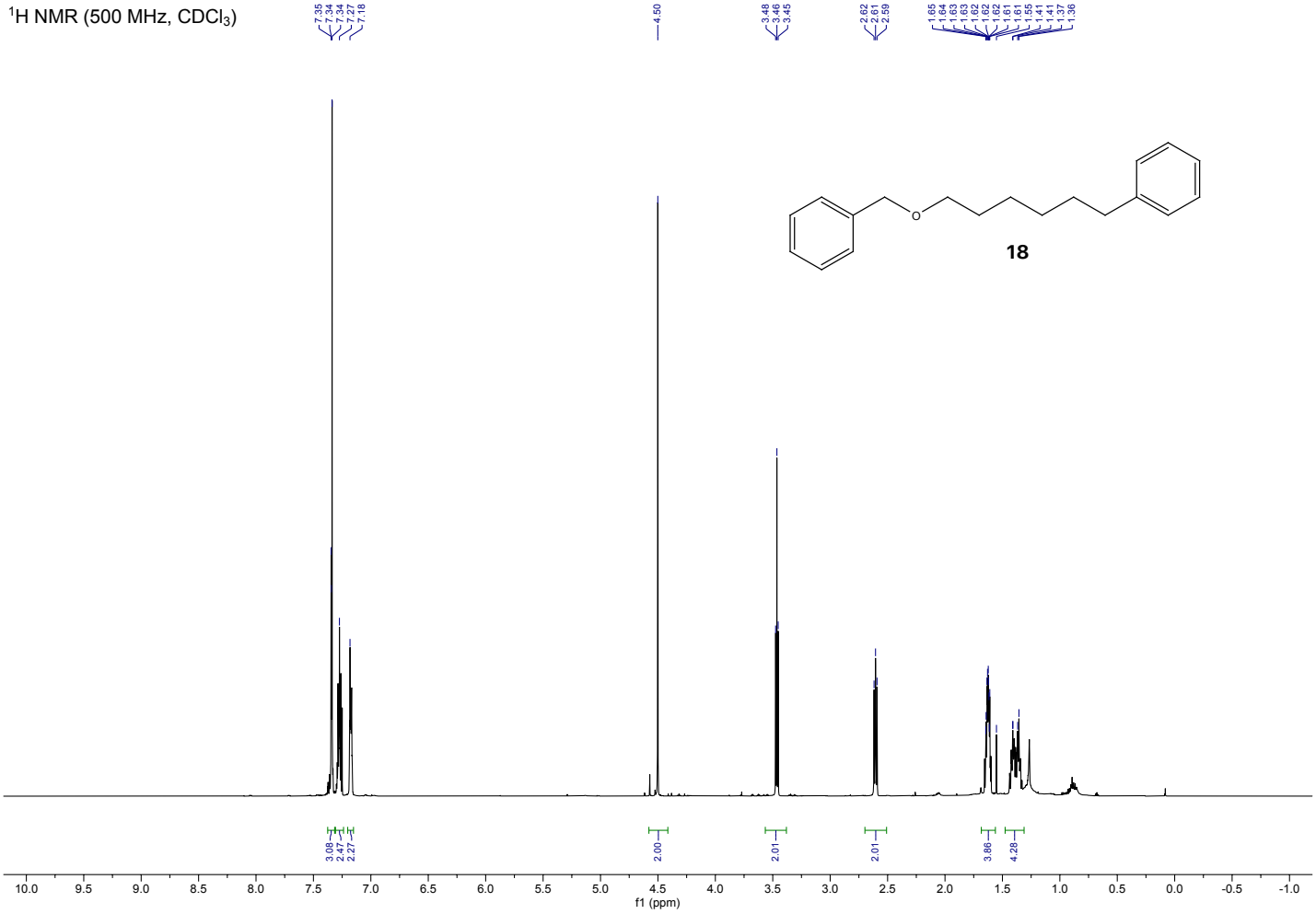
14

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

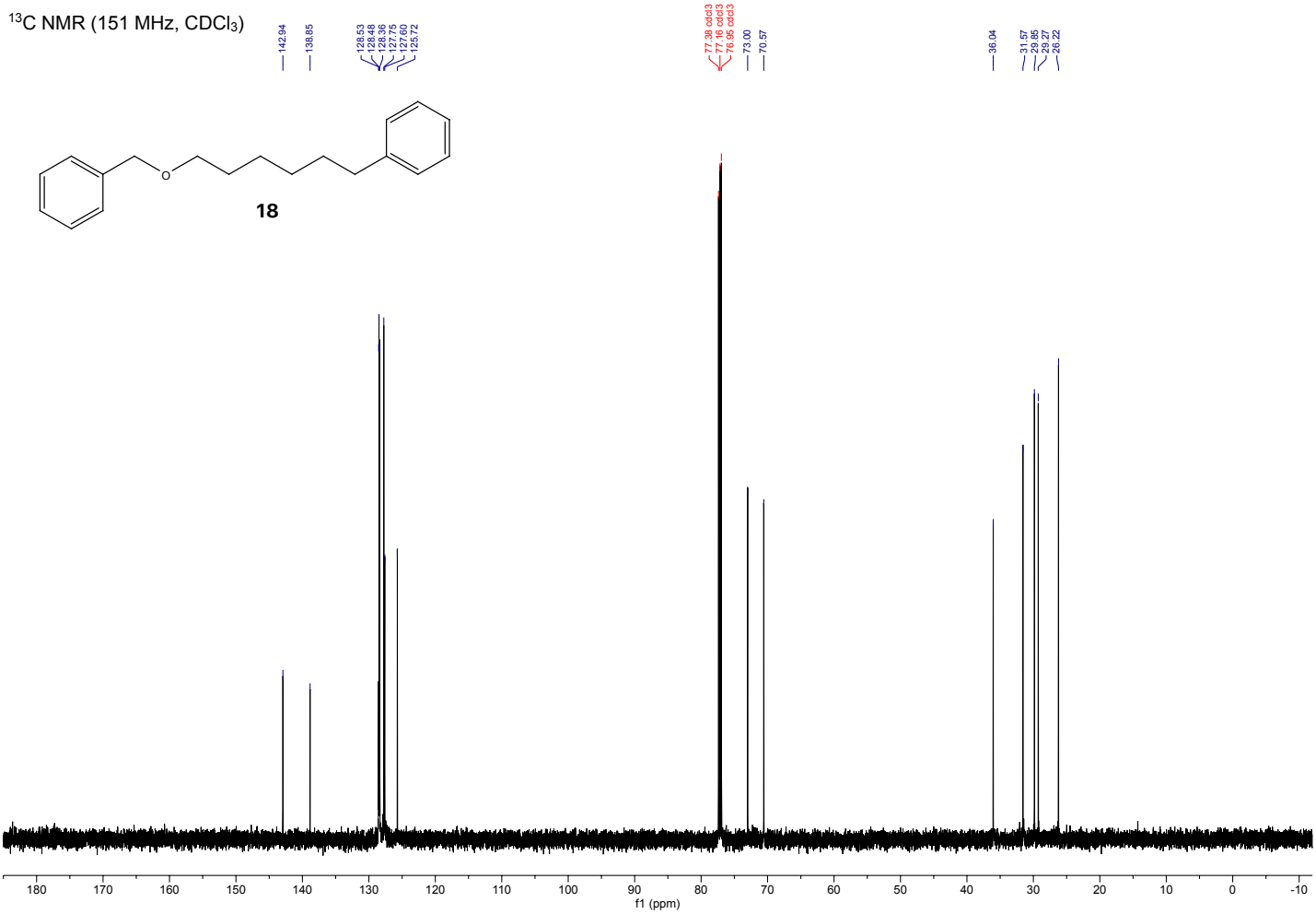
^{13}C NMR (151 MHz, $CDCl_3$)



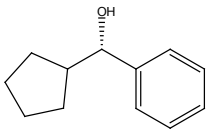
^{1}H NMR (500 MHz, $CDCl_3$)



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

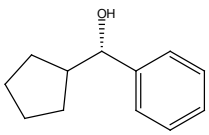


^{1}H NMR (500 MHz, $CDCl_3$)



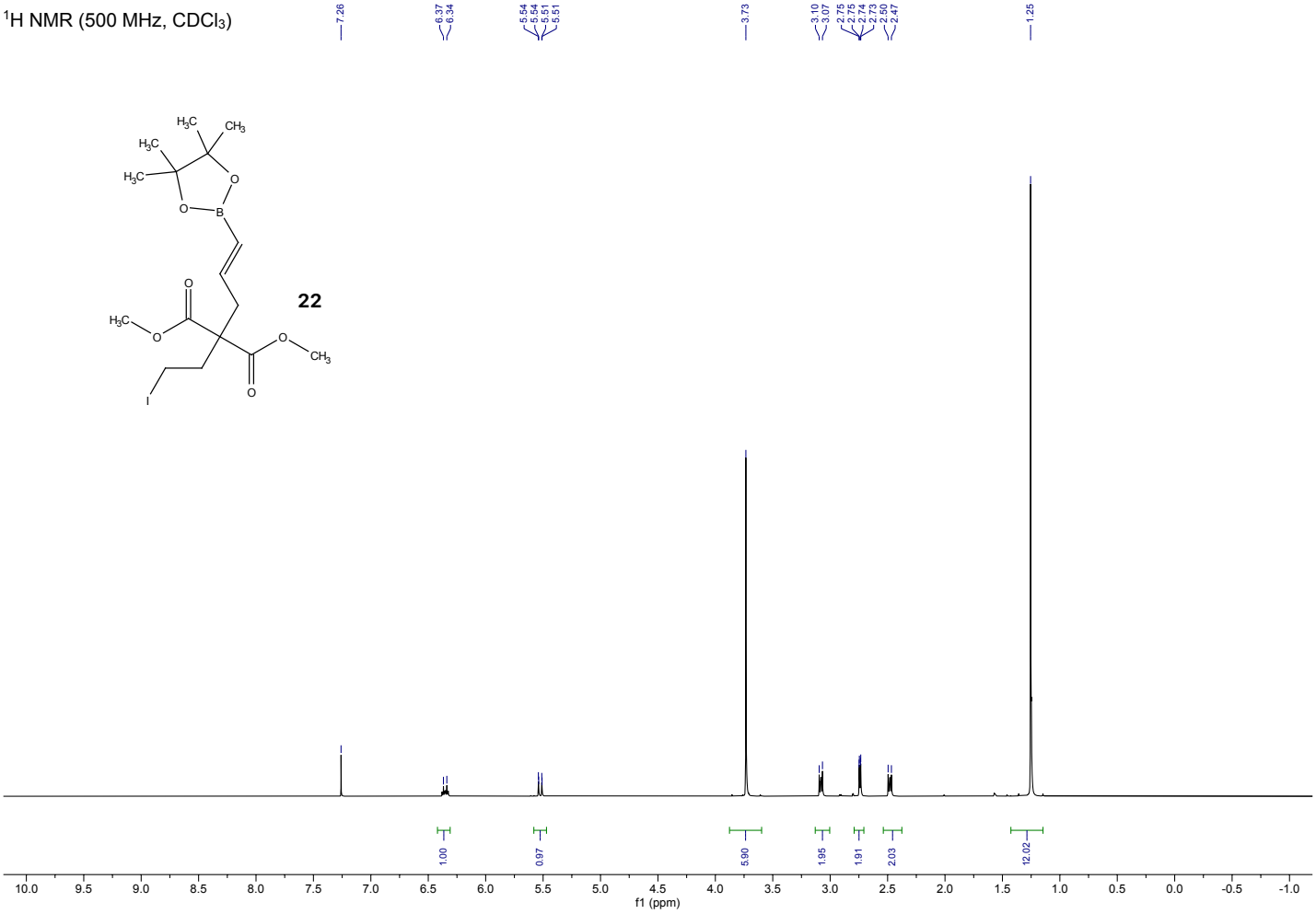
21

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

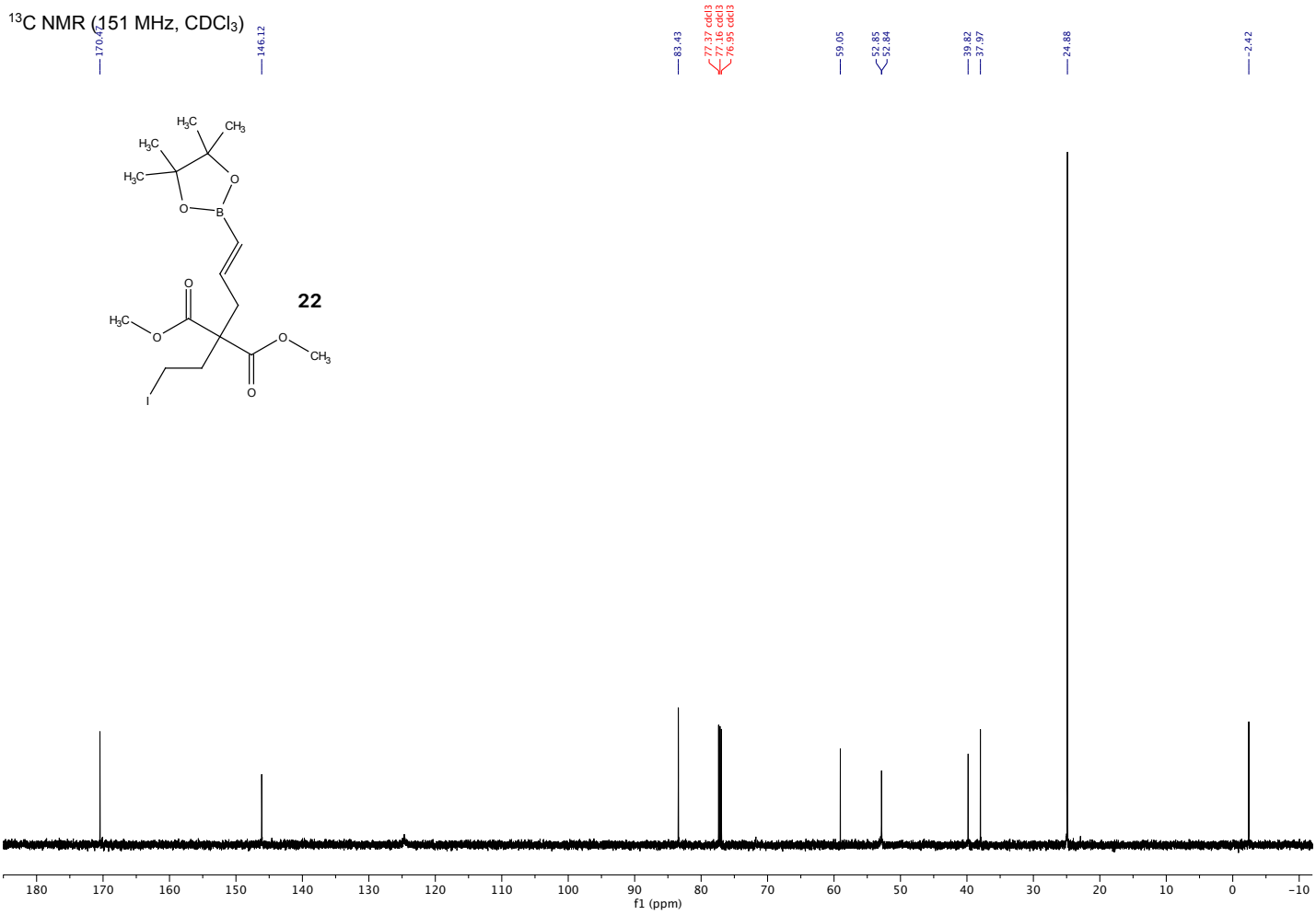


21

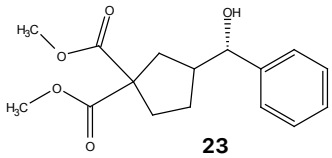
^{1}H NMR (500 MHz, $CDCl_3$)



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

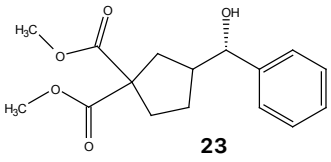


^{1}H NMR (500 MHz, C_6D_6)



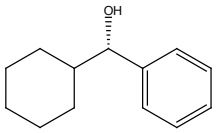
23

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

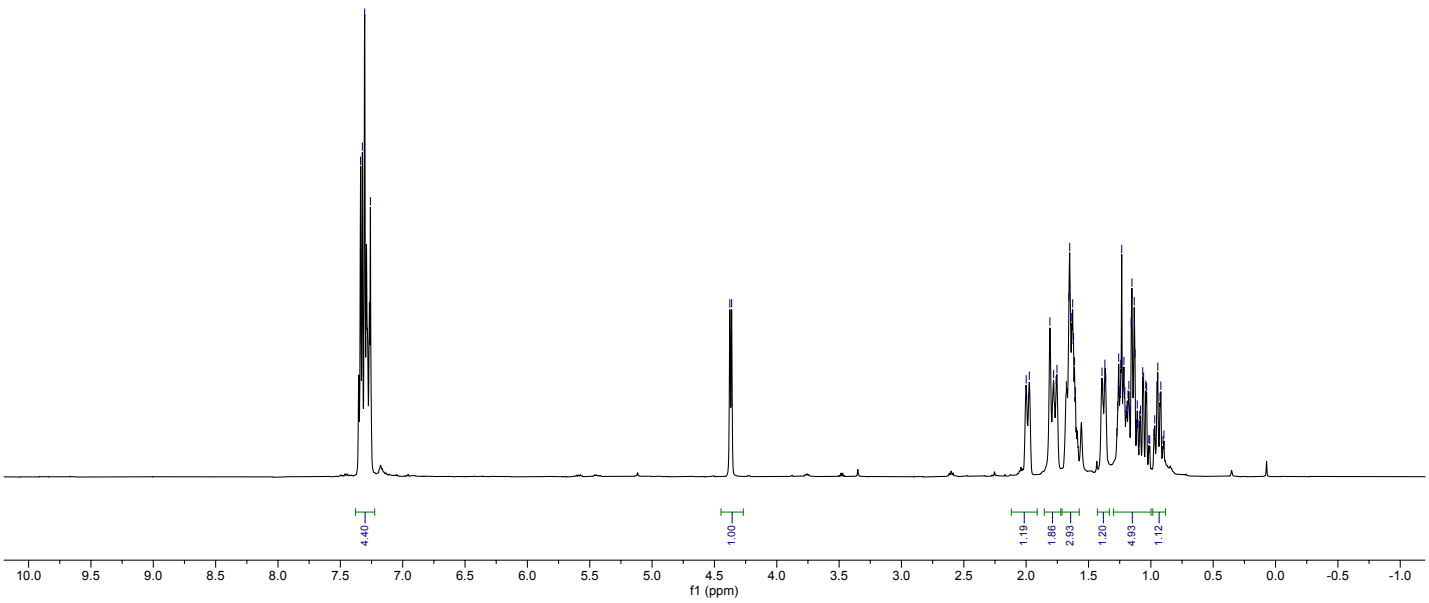


23

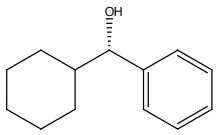
^{1}H NMR (500 MHz, $CDCl_3$)



24

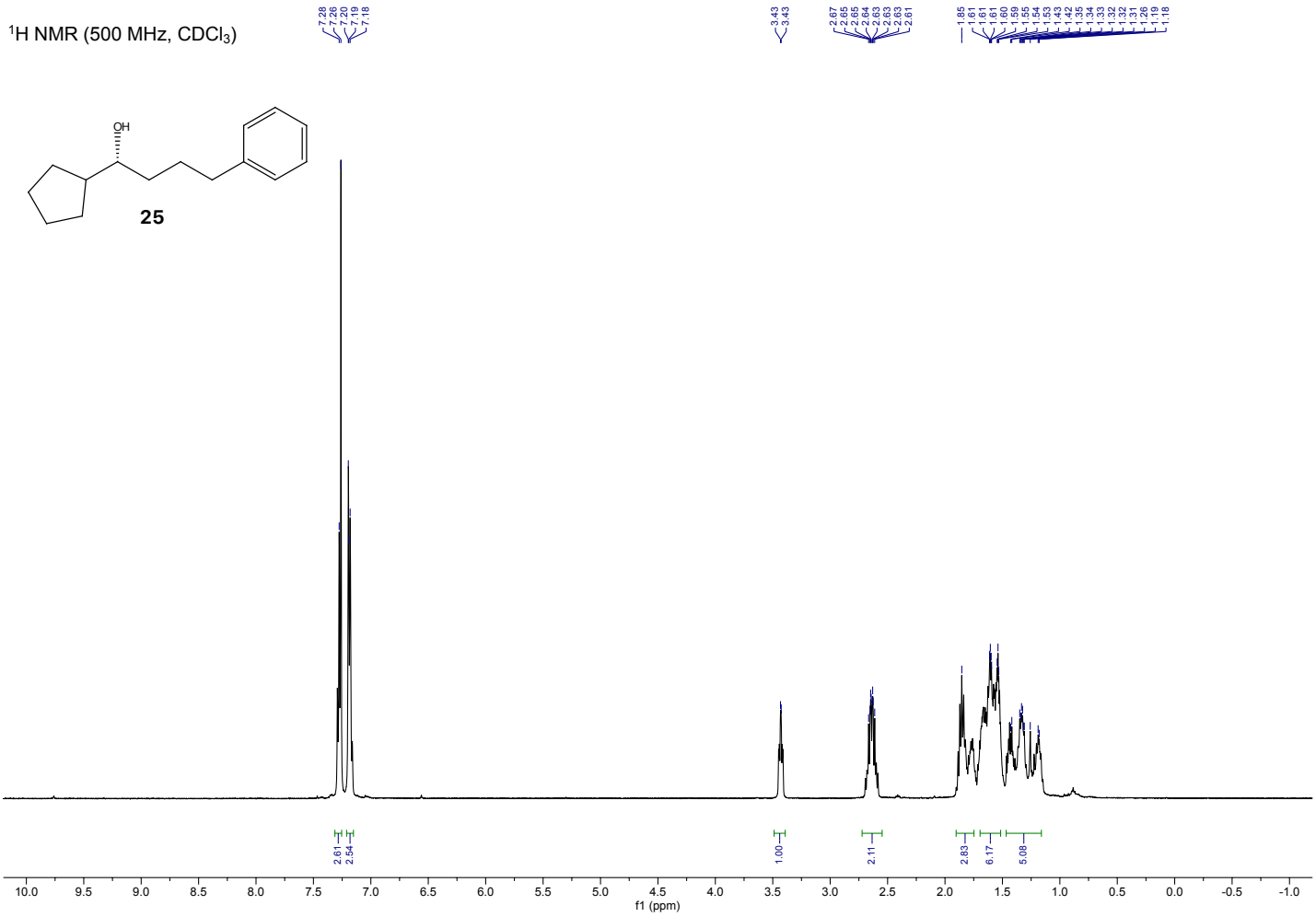


^{13}C NMR (151 MHz, $CDCl_3$)

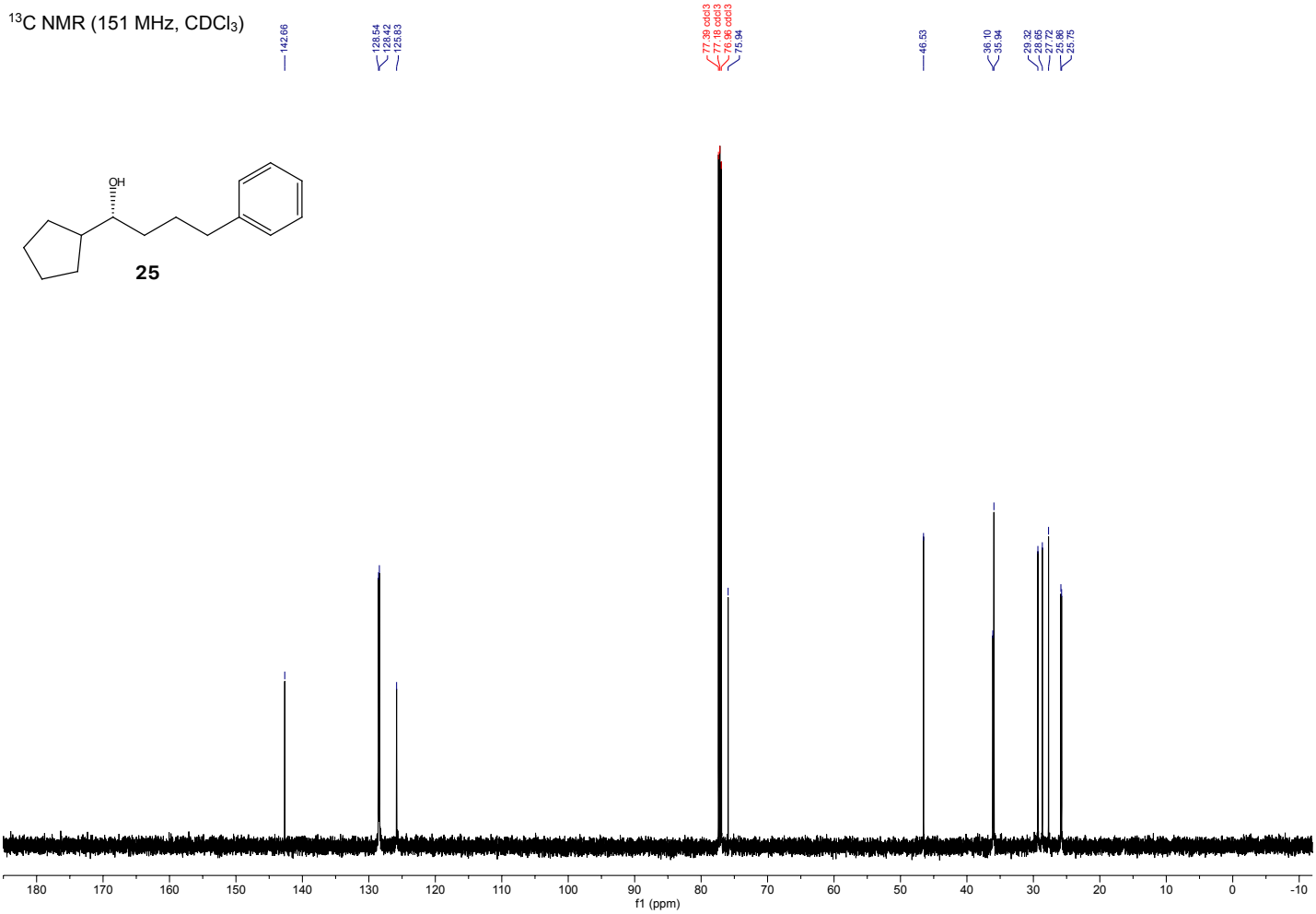


24

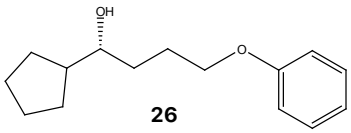
^{1}H NMR (500 MHz, $CDCl_3$)



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

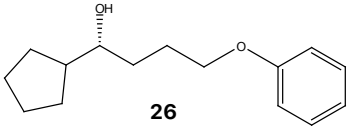


^{1}H NMR (500 MHz, $CDCl_3$)



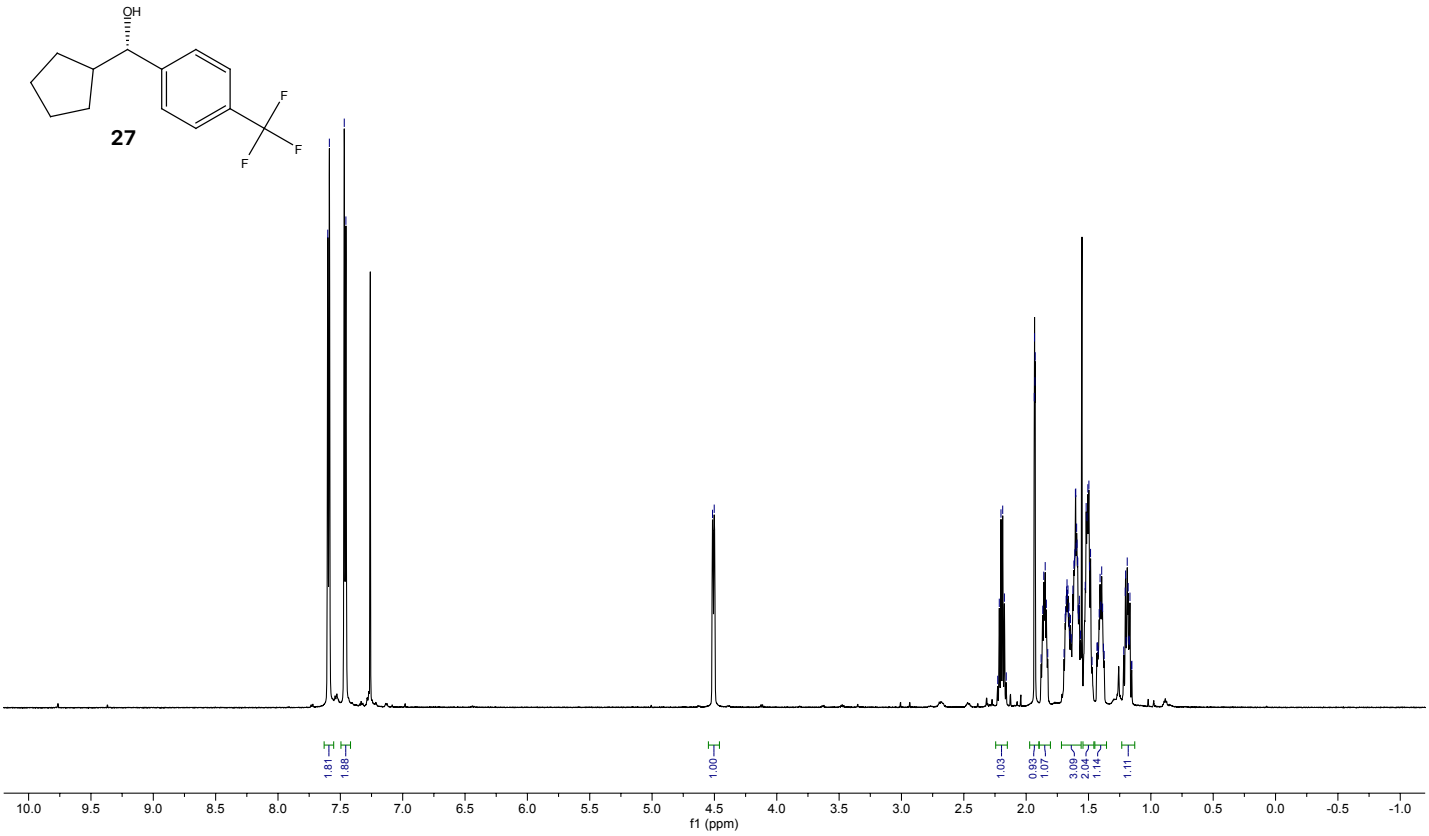
26

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

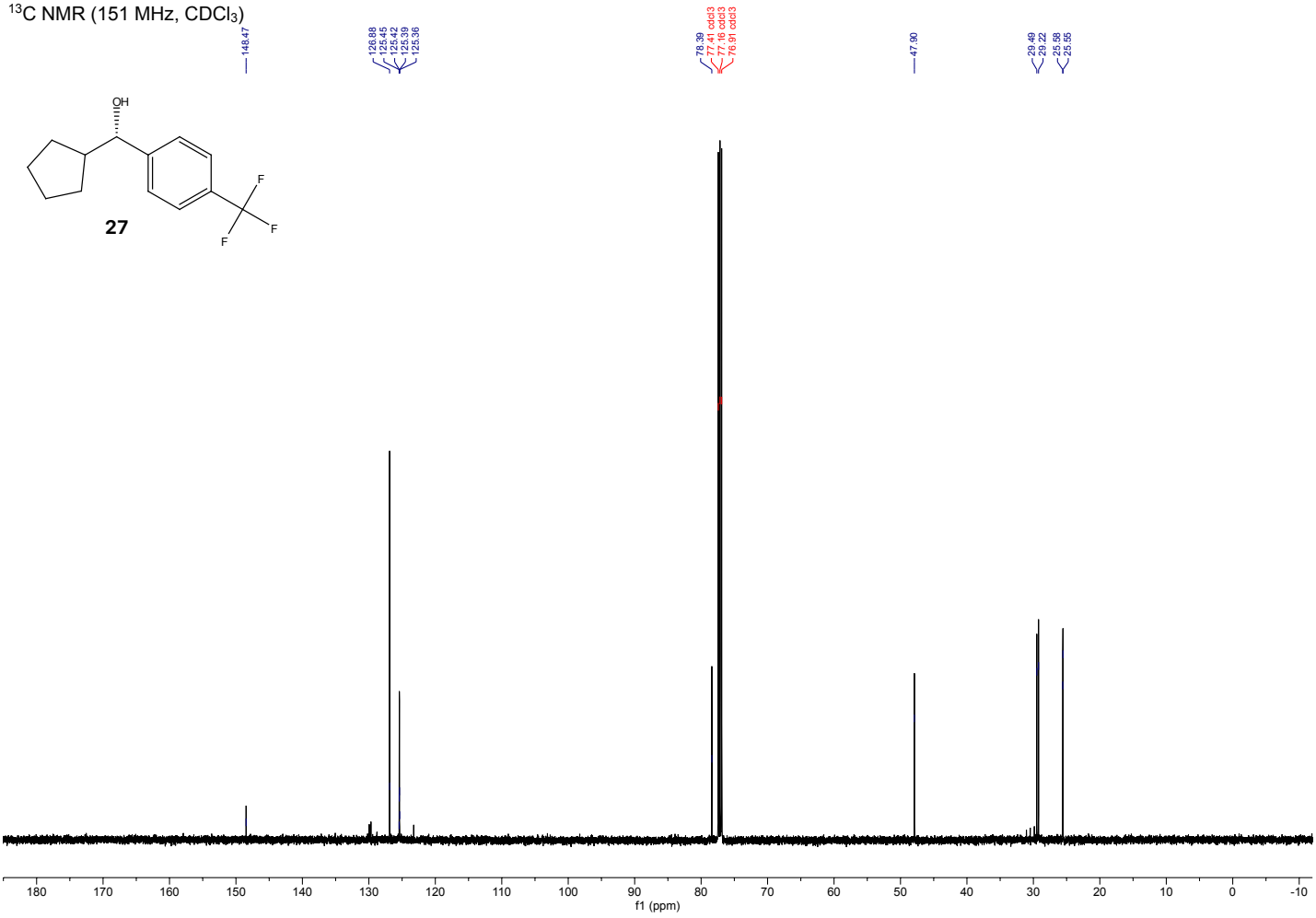


26

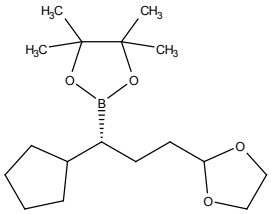
^{1}H NMR (500 MHz, $CDCl_3$)



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

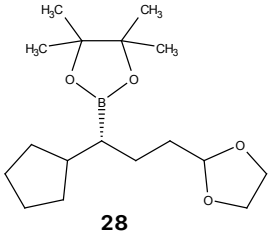


^{1}H NMR (500 MHz, $CDCl_3$)



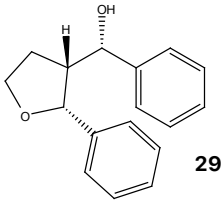
28

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

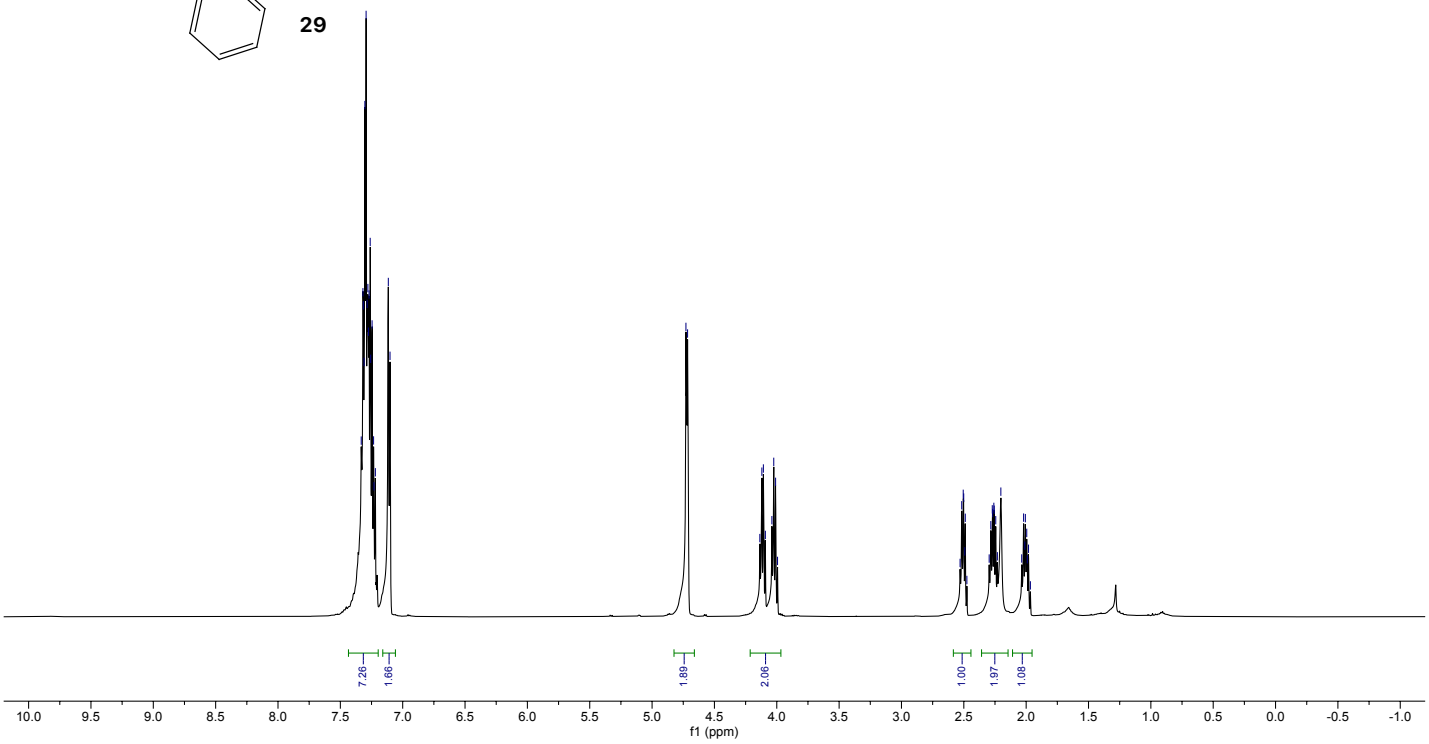


28

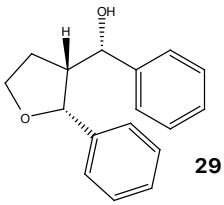
^{1}H NMR (500 MHz, $CDCl_3$)



29

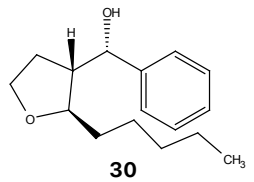


^{13}C NMR (151 MHz, $CDCl_3$)



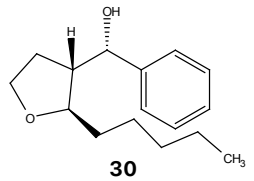
29

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



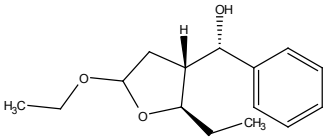
30

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



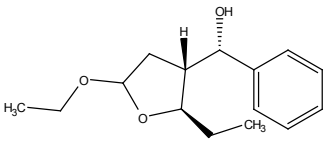
30

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



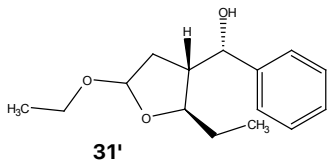
31

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



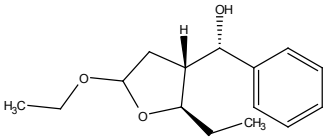
31

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



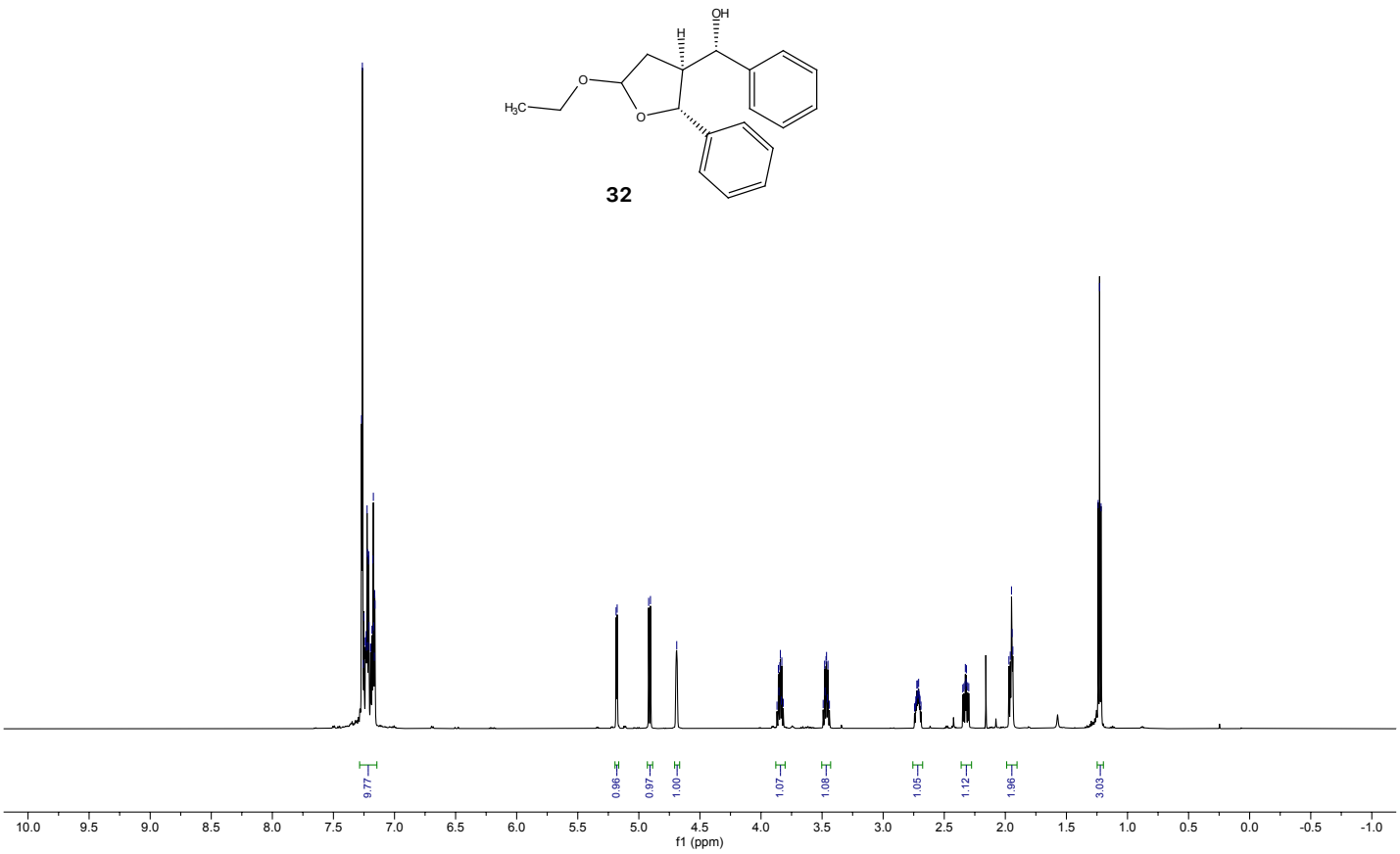
31'

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

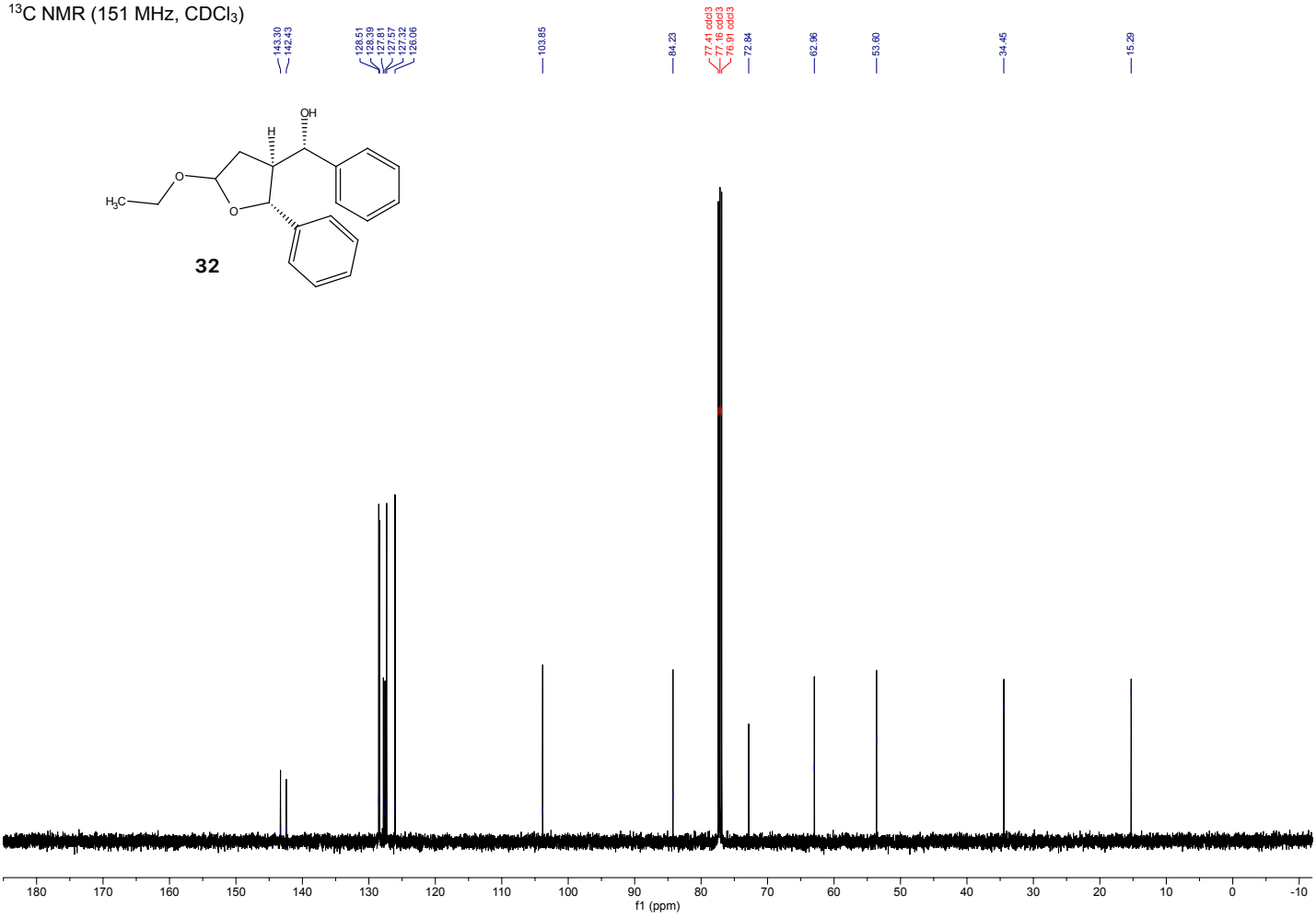


31'

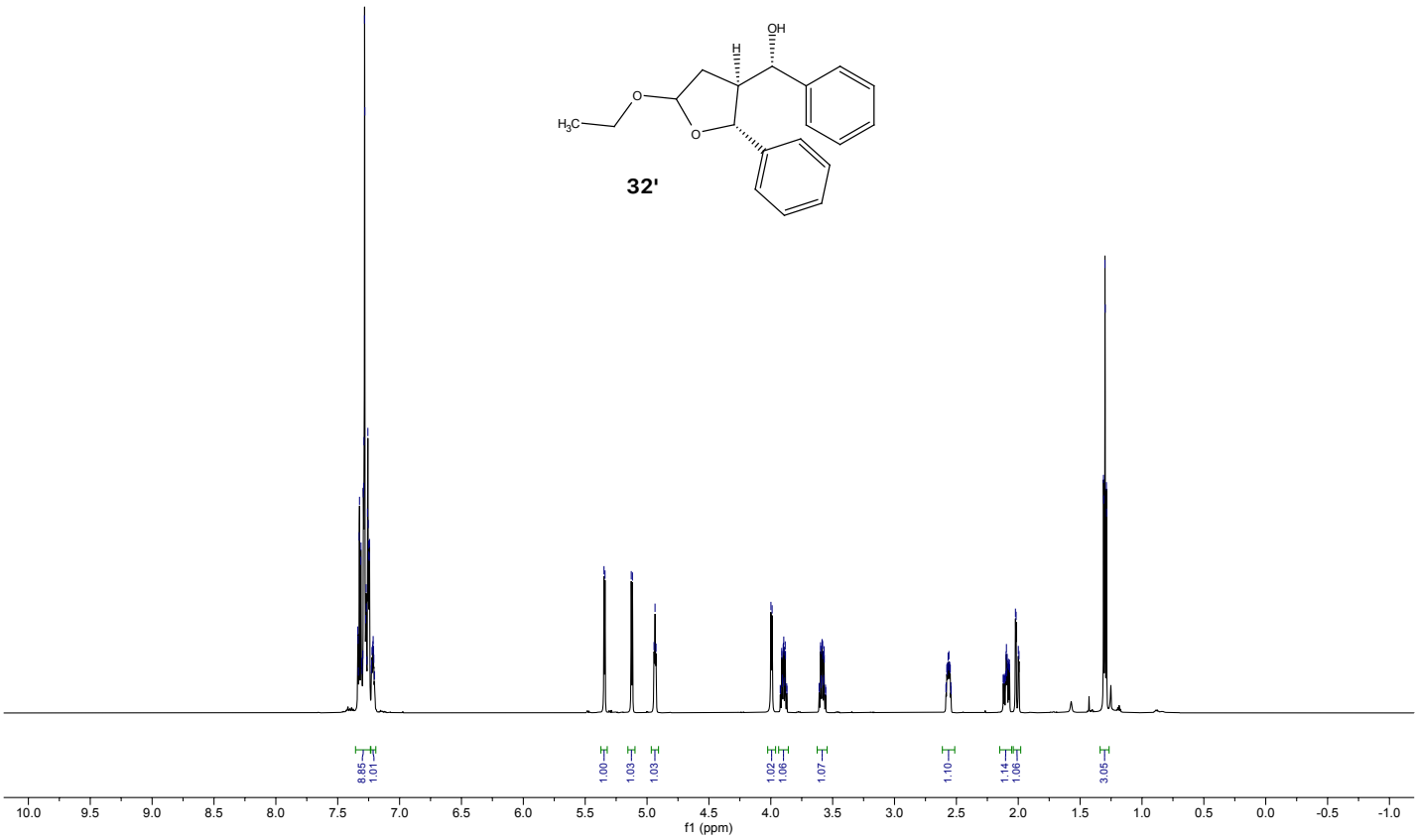
^{1}H NMR (500 MHz, $CDCl_3$)



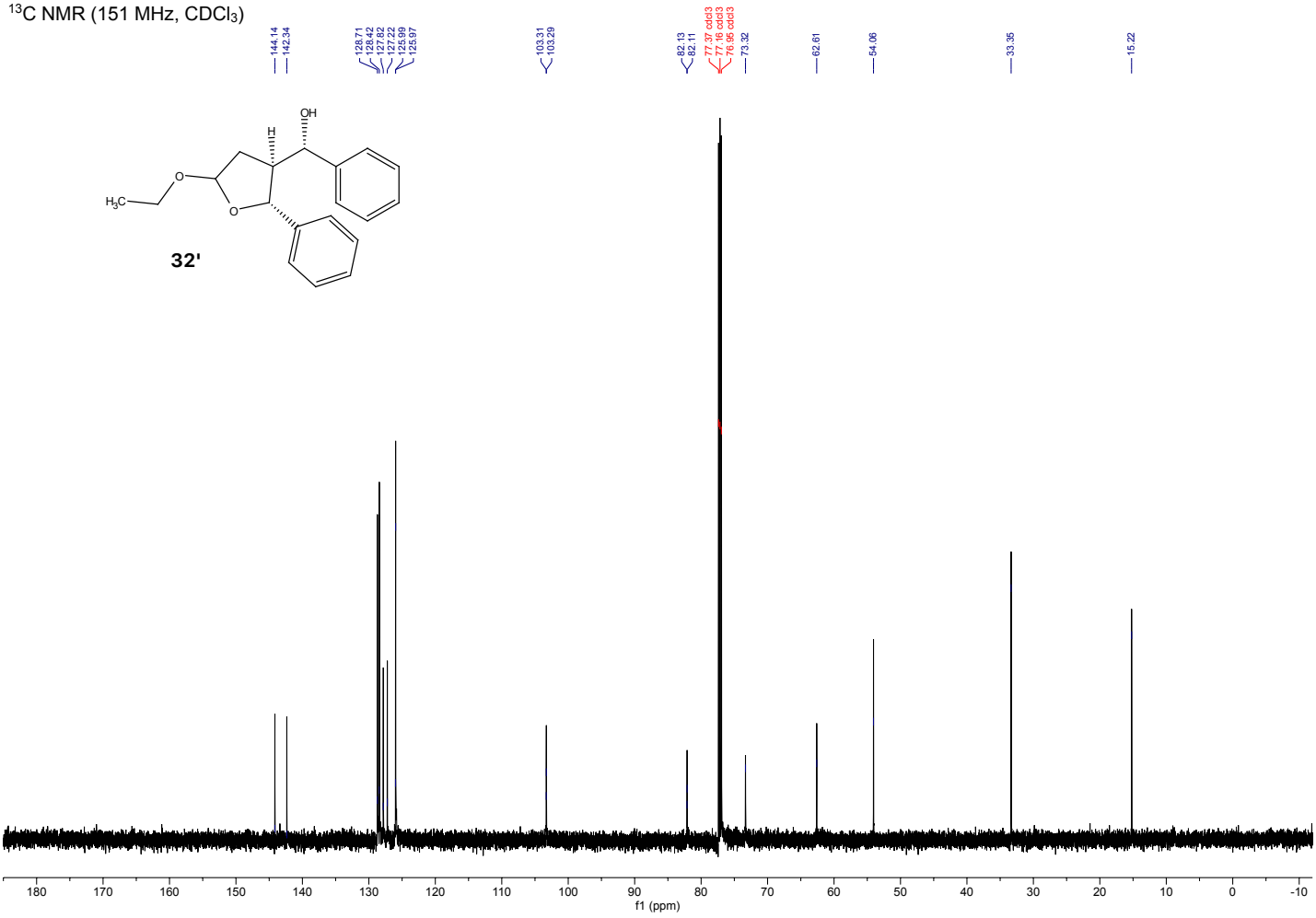
^{13}C NMR (151 MHz, $CDCl_3$)



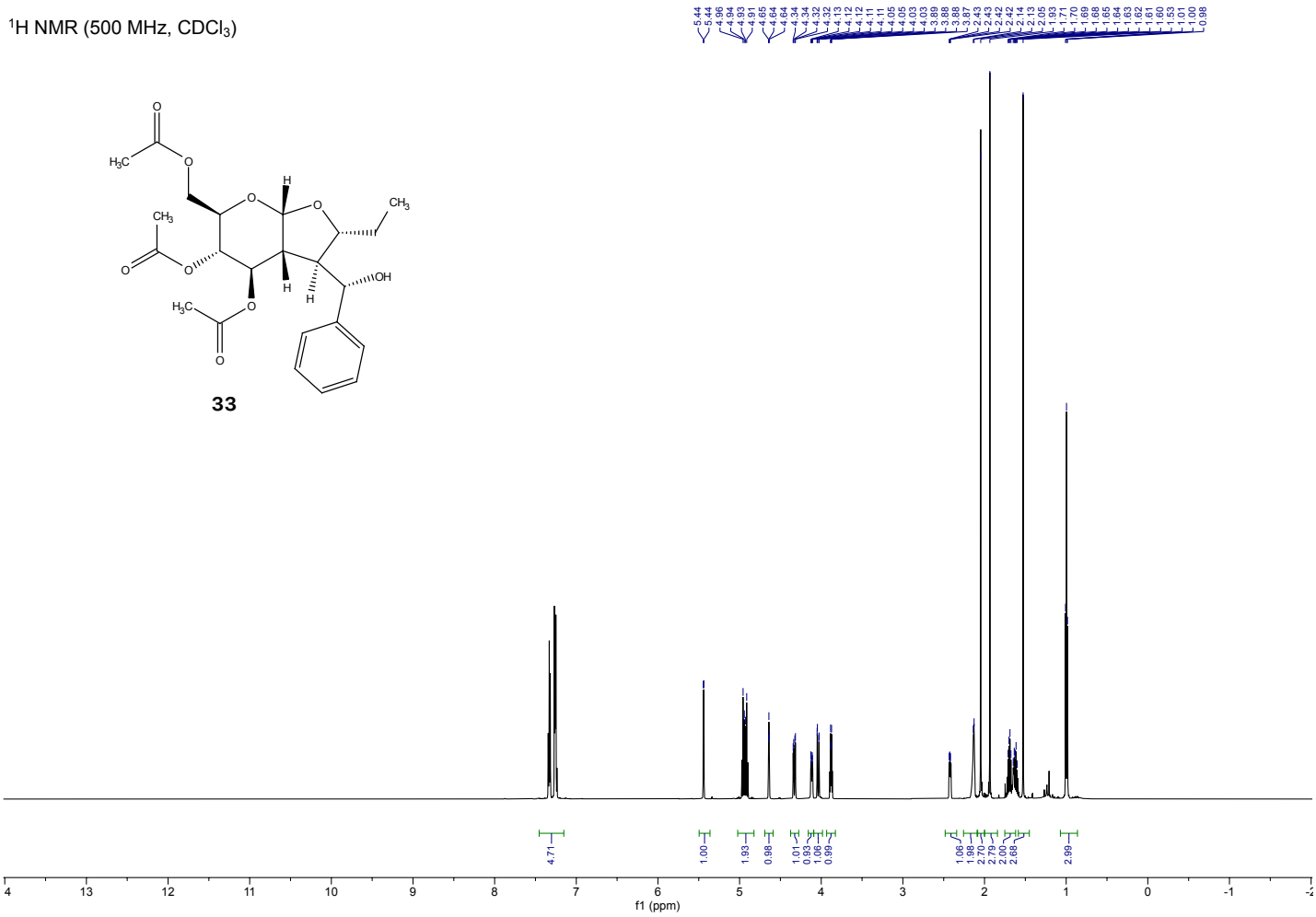
^{1}H NMR (500 MHz, $CDCl_3$)



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

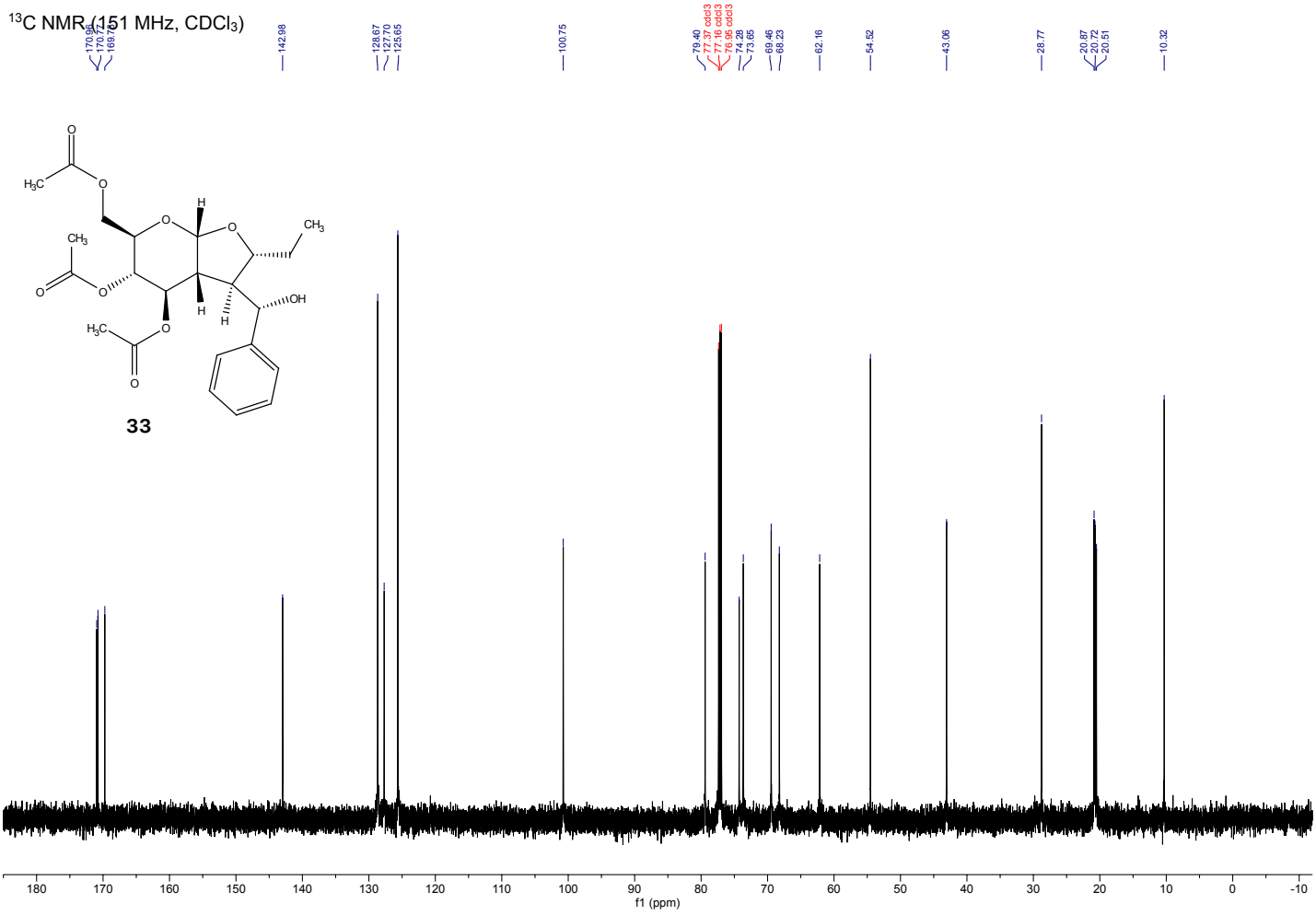


^{1}H NMR (500 MHz, $CDCl_3$)



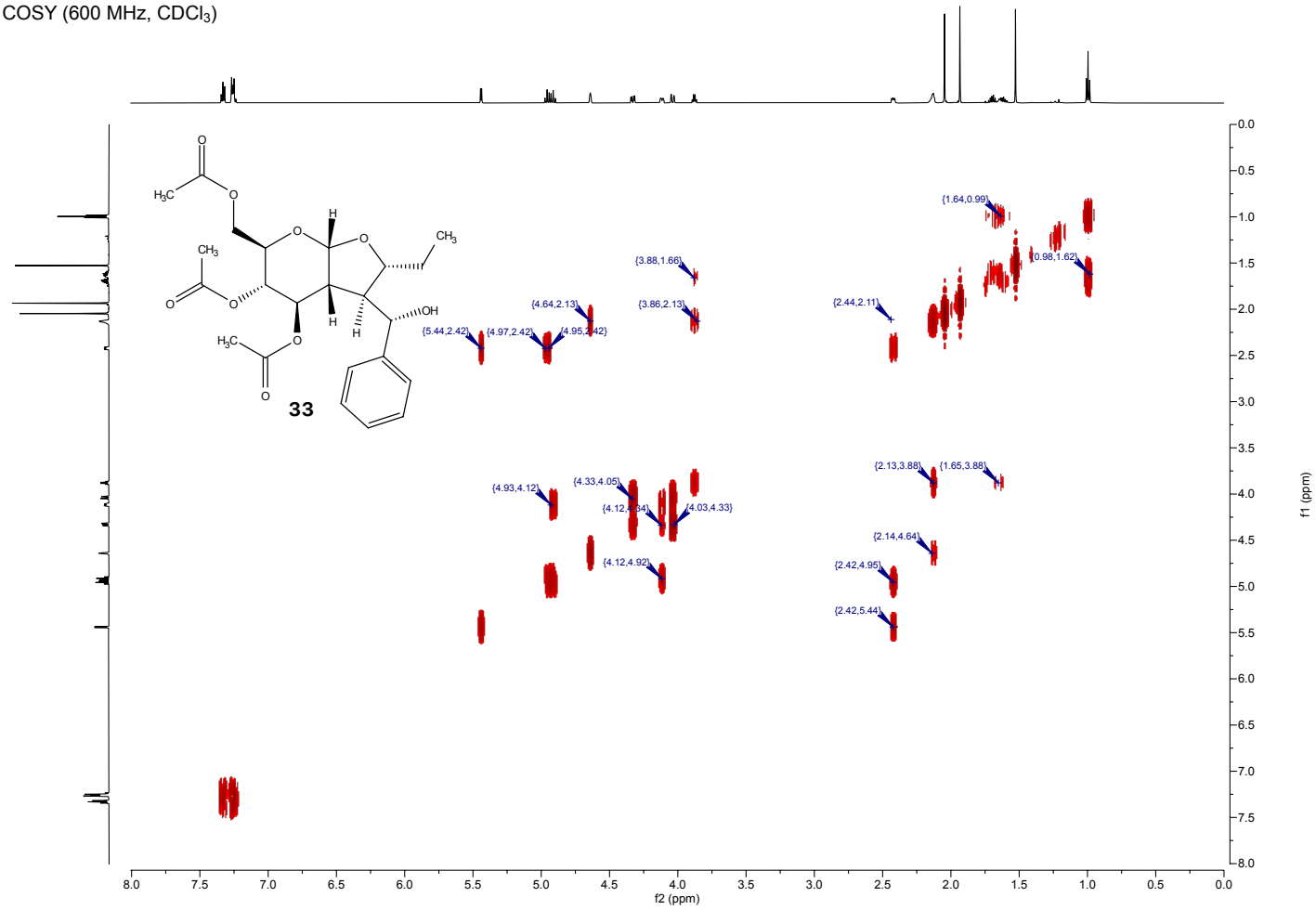
33

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

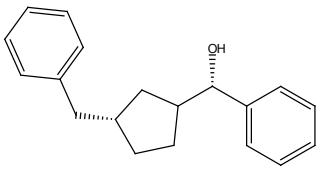


33

COSY (600 MHz, $CDCl_3$)

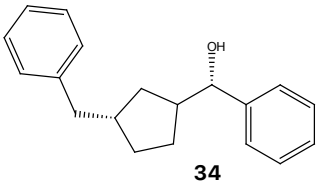


^{1}H NMR (500 MHz, $CDCl_3$)



34

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



34