Catalytic Conjunctive Cross-Coupling and Catalytic Diboration Reactions

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Abstract: This dissertation will present four main projects focused on stereoselective construction of borylated compounds as well as their applications in asymmetric syntheses. The first two projects describe the development of a catalytic conjunctive cross-coupling reaction. By merging three simple starting materials, an organolithium reagent, an organoboronate, and an organic electrophile, a synthetically valuable secondary boronate is furnished by the conjunctive cross-coupling in an efficient and enantioselective fashion. Next, this strategy is expanded to synthesize severely hindered tertiary boronates, a synthetic challenging but powerful building block to access a variety of quaternary stereocenters. The third project presents a platinum-catalyzed enantioselective diboration of alkenyl boronates to furnish a broad range of 1,1,2-tris(boronates) products. A deborylative alkylation of the 1,1,2-tris(boronates) leads to a variety of internal vicinal bis(boronates) with high diastereoselectivity. In the final chapter, a general and practical synthesis of alkenyl boronates via the boron-Wittig reaction is disclosed. Utilizing readily accessible geminal bis(boronates) and aldehydes, a broad range of disubstituted and trisubstituted alkenyl boronates are afforded with good yield and stereoselectivity.

Dedicated to

My love, Shuo Zhou, for the love, comfort, and support she gave me through my life.

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LIST OF ABBREVIATIONS

Å: angstrom

Ac: acetyl

acac: acetylacetonyl

Ad: adamantyl

atm: atmosphere(s)

AQN: anthraquinone

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

$B_2(pin)_2$: 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

DCC: diboration/cross-coupling

DCE: dichloroethane

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

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

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

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

d.r.: diastereomeric ratio

e.e.: enantiomeric excess

elim.: elimination

eq: equation(s)

equiv.: equivalent(s)

e.r.: 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

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Chapter 1

Recent Advances in Catalytic Enantioselective Functionalization of Alkenes via Nucleometallation

1.1. Introduction

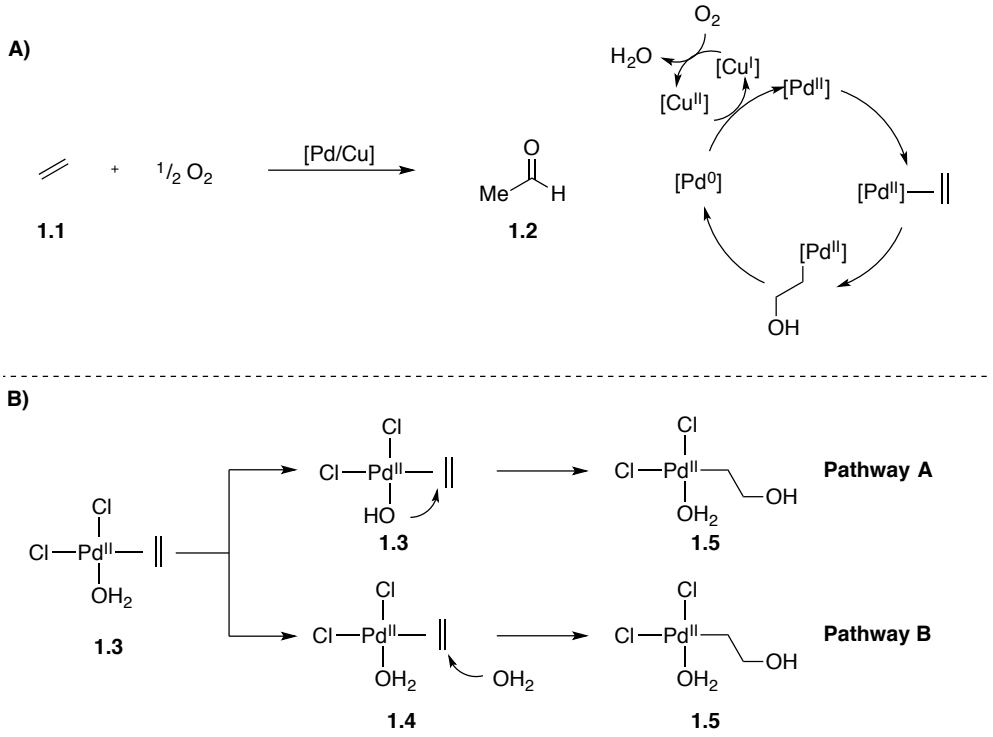
As one of the most readily available feedstock classes in the chemical industry, alkenes are recognized as ideal substrates that can be upgraded to more valuable fine-chemical products. In this context, chemists have done tremendous work to develop catalytic reactions to transform alkenes in a selective and efficient fashion over the past several decades. Representative reactions including hydrogenation, oxidation, hydroformylation, and polymerization have been widely applied in current chemical and pharmaceutical industries.

In 1959, a palladium-catalyzed oxidation reaction was developed by the chemists at Wacker Chemie.[1] In a process referred to as Wacker oxidation (Scheme 1.1.A), ethylene was oxidized to acetaldehyde by water and oxygen in the presence of palladium and a copper co-catalyst in a process referred to as Wacker oxidation. The mechanism of Wacker oxidation was proposed to occur as follows[1(b)]: after ethylene coordination to the palladium catalyst, a hydroxypalladation leads to a β-hydroxyethyl palladium (II) intermediate. This intermediate undergoes β-hydride elimination/reinsertion to release the

[1] (a) Smidt, J., Hafner, W., Jira, R., Sedlmeier, J., Sieber, R., Ruttinger, R., Kojer, H. *Angew. Chem.* **1959**, 71, 176. (b) Smidt, J., Hafner, W., Jira, R., Sieber, R., Sedlmeier, J., Sabel, A. *Angew. Chem. Int. Ed.* **1962**, 1, 80. (c) Jira, R. *Angew. Chem. Int. Ed.* **2009**, 48, 9034.

product and generated palladium (0), which is oxidized to palladium (II) by molecular oxygen and the copper co-catalyst thereby restarting the catalytic cycle.

Scheme 1.1. Wacker oxidation.



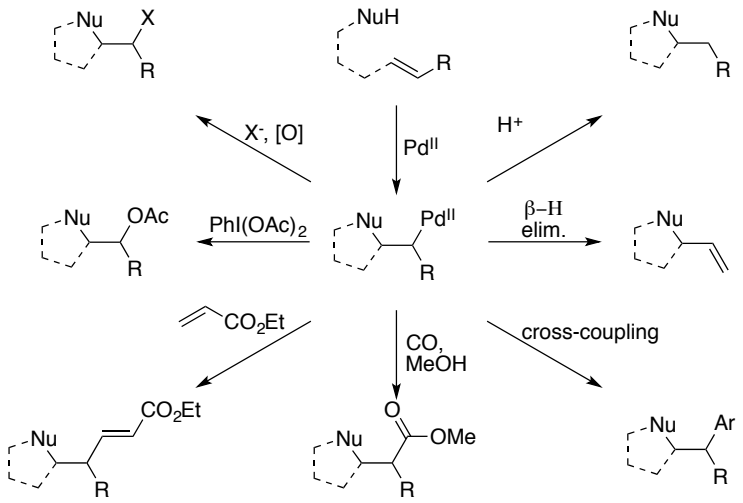
In regard to the hydroxypalladation step, it has been widely debated to occur by one of the two possible pathways.[2] The β-hydroxyethyl palladium (II) intermediate **1.5** could be generated by a *cis*-hydroxypalladation pathway, involving a migratory insertion of a hydroxyl group to ethylene (Scheme 1.1.B, pathway A). On the other hand, a *trans*-hydroxypalladation involving nucleophilic attack of water to palladium coordinated ethylene would also lead to the same β-hydroxyethyl palladium (II) intermediate **1.5** (Scheme 1.1.B, pathway B). Over the past several decades, many mechanistic studies have been conducted to probe the operative pathway. With that the *cis*-

[2] Keith, J. A., Henry, P. M. *Angew. Chem. Int. Ed.* **2009**, 48, 9038.

hydroxypalladation pathway is dominant at low chloride concentration conditions while *trans*-hydroxypalladation is the operative pathway at high concentrations of chloride. More importantly, the Wacker oxidation served as a starting point that inspired chemists to develop a broad range of transition-metal catalyzed alkene functionalization reactions involving a similar nucleometallation key step.

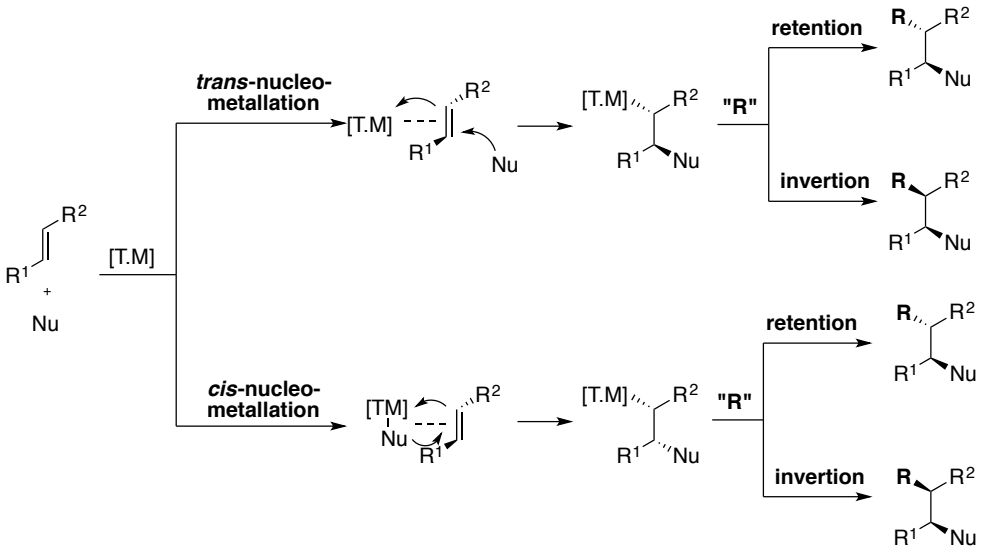
One of the attractive features of developing reactions involving nucleopalladation pathway is that the alkyl-metal intermediate generated by nucleometallation can be engaged in a variety of subsequent transformations (Scheme 1.2). Furthermore, nucleometallation of an alkene often leads to the formation of new stereocenters, where the stereochemical outcome could potentially be controlled by a chiral catalyst. Such features provide an opportunity to develop a broad range of stereoselective alkene functionalization methods to upgrade simple starting materials to valuable fine-chemical products in a catalytic fashion.

Scheme 1.2. Versatility of alkyl-metal intermediate generated by alkene nucleometallation.



In order to develop new catalytic stereoselective reactions via nucleometallation pathways, several challenges need to be addressed by chemists. As demonstrated for the Wacker oxidation, two possible nucleometallation pathways, which lead to diastereomeric intermediates, are operative depending on reaction conditions. The situation is further complicated when the subsequent transformation of the alkyl-metal intermediate can occur in either stereoretentive or stereoinvertive fashions (Scheme 1.3). Moreover, even if the stereochemical pathway of nucleometallation could be controlled by a carefully tuned catalyst system, the competitive β-hydride elimination needs to be suppressed to prevent the newly formed stereocenters from being destroyed.

Scheme 1.3. Stereochemical pathways of nucleometallation and subsequent transformation.



Despite the inherent mechanistic difficulties discussed above, during the past several decades, many catalytic enantioselective reactions have been developed that operate via

nucleometallation pathways. In this chapter, recent progress in transition-metal catalyzed enantioselective reactions involving nucleometallation is summarized.

1.2. Palladium-catalyzed enantioselective reactions

Palladium is one of the most studied transition-metals that is known to catalyze alkene functionalization reactions via nucleometallation. Using palladium complexes, many enantioselective alkene functionalization reactions involving oxy-, amino-, and carbo-palladation have been reported over the past several decades. The detailed history and development of enantioselective alkene functionalization by nucleopalladation has been well documented in an excellent review by Stahl and co-workers in 2011.[3] Here, the more recent developments of enantioselective reactions involving nucleopalladation are summarized.

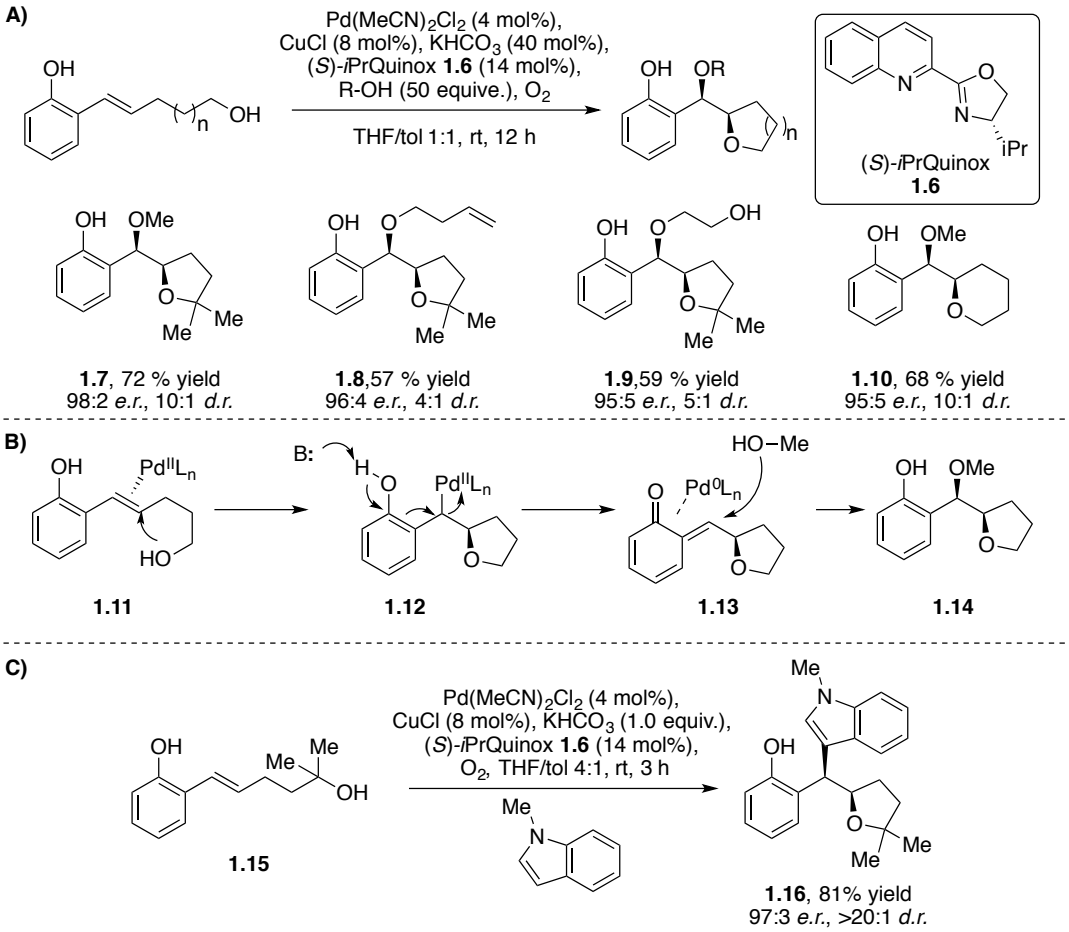
1.2.1. Enantioselective reactions involving oxypalladation

The first enantioselective intramolecular cyclization involving oxypalladation was established by Hosokawa and Murahashi,[4] and further improved by Hayashi[5] and Stoltz,[6] However, the scope of these reactions is typically limited to tri-substituted alkenes, because the presence of a hydrogen atom attached to the newly formed oxygenated stereocenter allows undesired β-hydride elimination. Recently, the challenge of overcoming competitive β-hydride elimination was addressed by Sigman and co-workers

[3] McDonald, R. I., Liu, G., Stahl, S. S. *Chem. Rev.* **2011**, 111, 2981.
[4] Hosokawa, T., Uno, T., Inui, S., Murahashi, S. *J. Am. Chem. Soc.***1981**, 103, 2318.
[5] Uozumi, Y., Kato, K., Hayashi, T. *J. Am. Chem. Soc.* **1997**, 119, 5063.
[6] Trend, R. M., Ramtohul, Y. K., Stoltz, B. M. *J. Am. Chem. Soc.* **2005**, 127, 17778.

with a distinct strategy (Scheme 1.4.A).[7] Employing (*S*)-*i*PrQuinox **1.6** as a chiral ligand, a palladium catalyzed cyclization followed by interception of a second alcohol nucleophile led to a cyclized product where two distinct carbon-oxygen bonds were formed across the alkene in an enantio- and diastereoselective fashion.

Scheme 1.4. Palladium catalyzed enantioselective difunctionalization of alkene.



Regarding the reaction mechanism, the authors proposed that the alkyl-palladium intermediate **1.12** was furnished by an intramolecular oxypalladation. Subsequently, instead of β-hydride elimination, the intermediate **1.12** underwent reductive

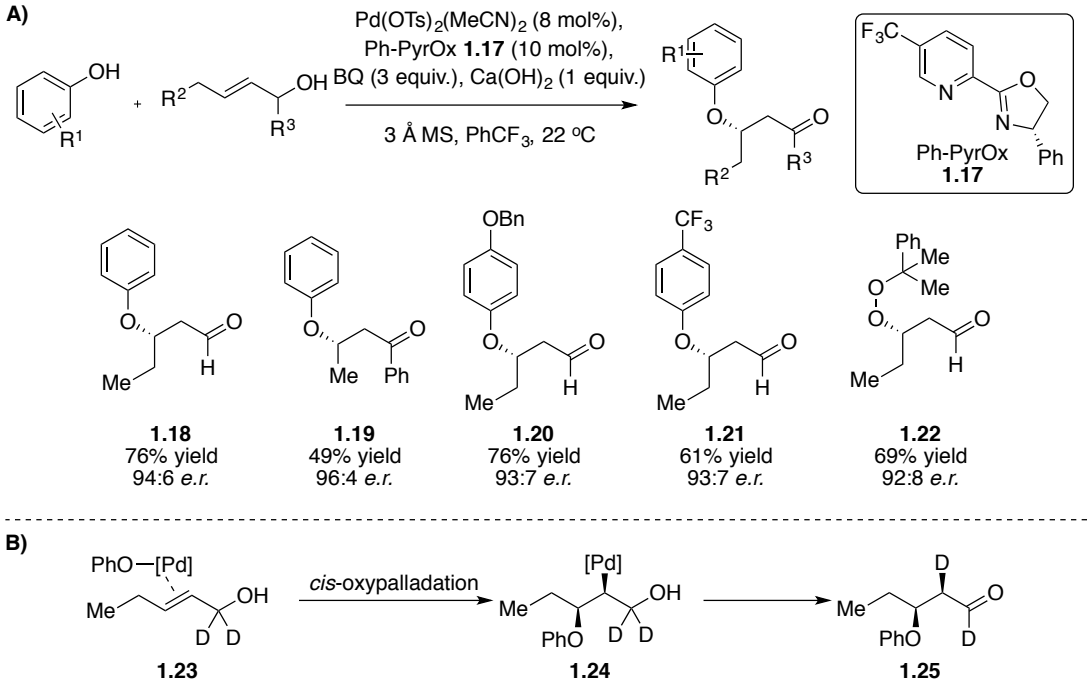
[7] (a) Jensen, K. H., Pathak, T. P., Zhang, Y., Sigman, M. S. *J. Am. Chem. Soc.* **2009**, 131, 17074. (b) Jensen, K. H., Webb, J. D., Sigman, M. S. *J. Am. Chem. Soc.* **2010**, 132, 17471.

decomposition to afford the *ortho*-quinone methide **1.13** and a palladium (0) complex. Finally, an intermolecular attack of a second nucleophile led to the final product **1.14** in a diastereoselective fashion (Scheme 1.4.B). The nucleophile scope of this process was further expanded to include indole derivatives such that a new carbon-oxygen bond and a new carbon-carbon bond were constructed enantioselectively during the process (Scheme 1.4.C). [8]

More recently, Sigman and co-workers described a palladium catalyzed enantioselective intermolecular addition of an oxygen nucleophile to simple 1,2-disubstituted alkenes. [9] Employing allylic alcohols as substrates, phenol derived nucleophiles were added to the alkene in the presence of a palladium catalyst and Ph-PyrOx **1.17** as the ligand to furnish β-aryoxycarbonyl products with good yield and enantioselectivity. It is worthy of note that alkyl peroxides were also suitable nucleophiles in this reaction to afford β-peroxycarbonyl products in an enantioselective fashion (Scheme 1.5.A). A mechanistic study utilizing a deuterium labeled substrate suggested that *cis*-oxypalladation occurred in the reaction conditions (Scheme 1.5.B). Moreover, the authors proposed that the hydrogen attached to the terminal hydroxyl group was more hydridic than the hydrogen attached to the phenoxy group in the structure **1.24**, since the phenol oxygen's lone pair was in conjugation with the aromatic ring. Thus, β-hydride elimination occurred in the direction towards the terminal alcohol instead of destroying the newly formed stereocenter.

[8] Pathak, T. P., Gligorich, K. M., Welm, B. E., Sigman, M. S. *J. Am. Chem. Soc.* **2010**, 132, 7870.
[9] Race, N. J., Schwalm, C. S., Nakamuro, T., Sigman, M. S. *J. Am. Chem. Soc.* **2016**, 138, 15881.

Scheme 1.5. Palladium catalyzed enantioselective intermolecular coupling of oxygen nucleophile and allylic alcohol.

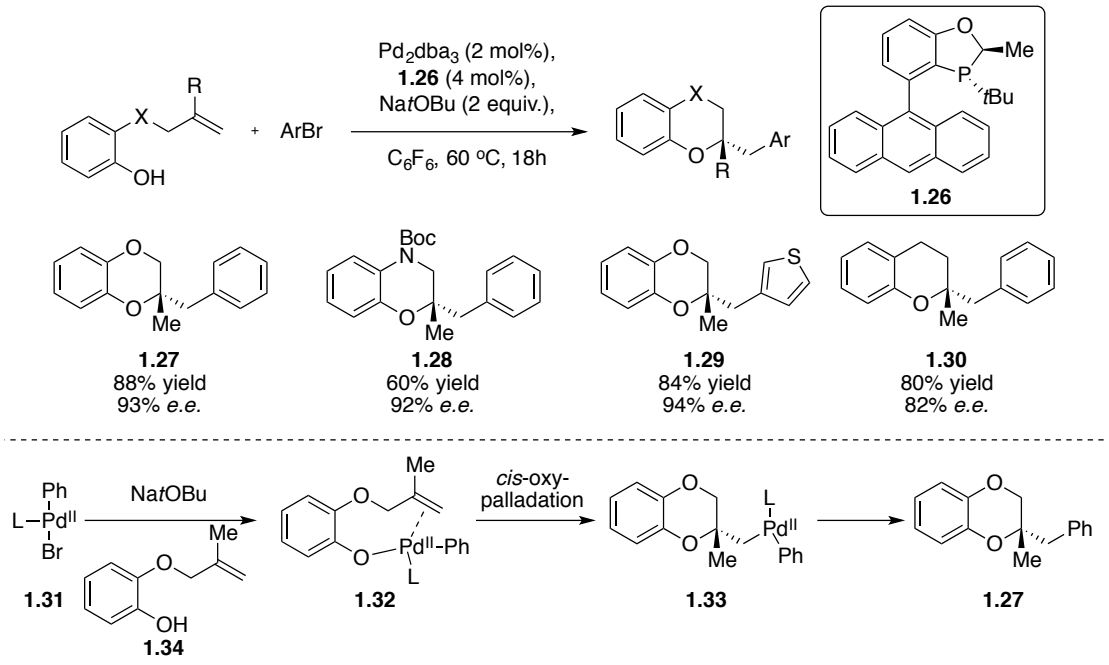


While the alkyl-palladium species generated by oxypalladation underwent β-hydride elimination in most cases, other useful subsequent transformations could also be applied to the alkyl-palladium intermediates. Tietze and co-workers reported that a Heck type migratory insertion occurred to the alkyl-palladium intermediate in the presence of methyl acrylate.[10] Tietze also demonstrated that the alkyl-palladium intermediate furnished by oxypalladation underwent CO insertion to afford carbonylation product.[11] In a process inspired by the studies of Wolfe, Tang and co-workers described a palladium

[10] (a) Tietze, L. F., Sommer, K. M., Zinngrebe, J., Stecker, F. *Angew. Chem. Int. Ed.* **2005**, 44, 257. (b) Tietze, L. F., Stecker, F., Zinngrebe, J., Sommer, K. M. *Chem.-Eur. J.* **2006**, 12, 8770.
[11] (a) Tietze, L. F., Spiegl, D. A., Stecker, F., Major, J., Raith, C., Grosse, C. *Chem.-Eur. J.* **2008**, 14, 8956. (b) Tietze, L. F., Zinngrebe, J., Spiegl, D. A., Stecker, F. *Heterocycles* **2007**, 74, 473.

catalyzed enantioselective cyclization/cross-coupling sequence via oxypalladation.[12] As shown in Scheme 1.6, oxidative addition of an aryl bromide to a palladium (0) catalyst led to the palladium (II) species **1.31**. The palladium (II) intermediate **1.31** reacted with the phenol substrate **1.34** in the presence of sodium *tert*-butyloxide to furnish intermediate **1.32**. *Cis*-oxypalladation of intermediate **1.32** led to alkyl-palladium intermediate **1.33**, and subsequent reductive elimination furnished the cyclized product **1.27** and regenerated the palladium (0) catalyst. Employing the P-chiral ligand **1.26**, the cyclization/cross-coupling sequence furnished a series of 1,4-benzodioxanes, a 1,4-benzooxazine, and chromans containing quaternary stereocenters with high yield and enantioselectivity.

Scheme 1.6. Palladium catalyzed enantioselective alkene aryloxyarylation.



[12] Hu, N., Li, K., Wang, Z., Tang, W. *Angew. Chem., Int. Ed.* **2016**, 55, 5044.

1.2.2. Enantioselective reactions involving aminopalladation

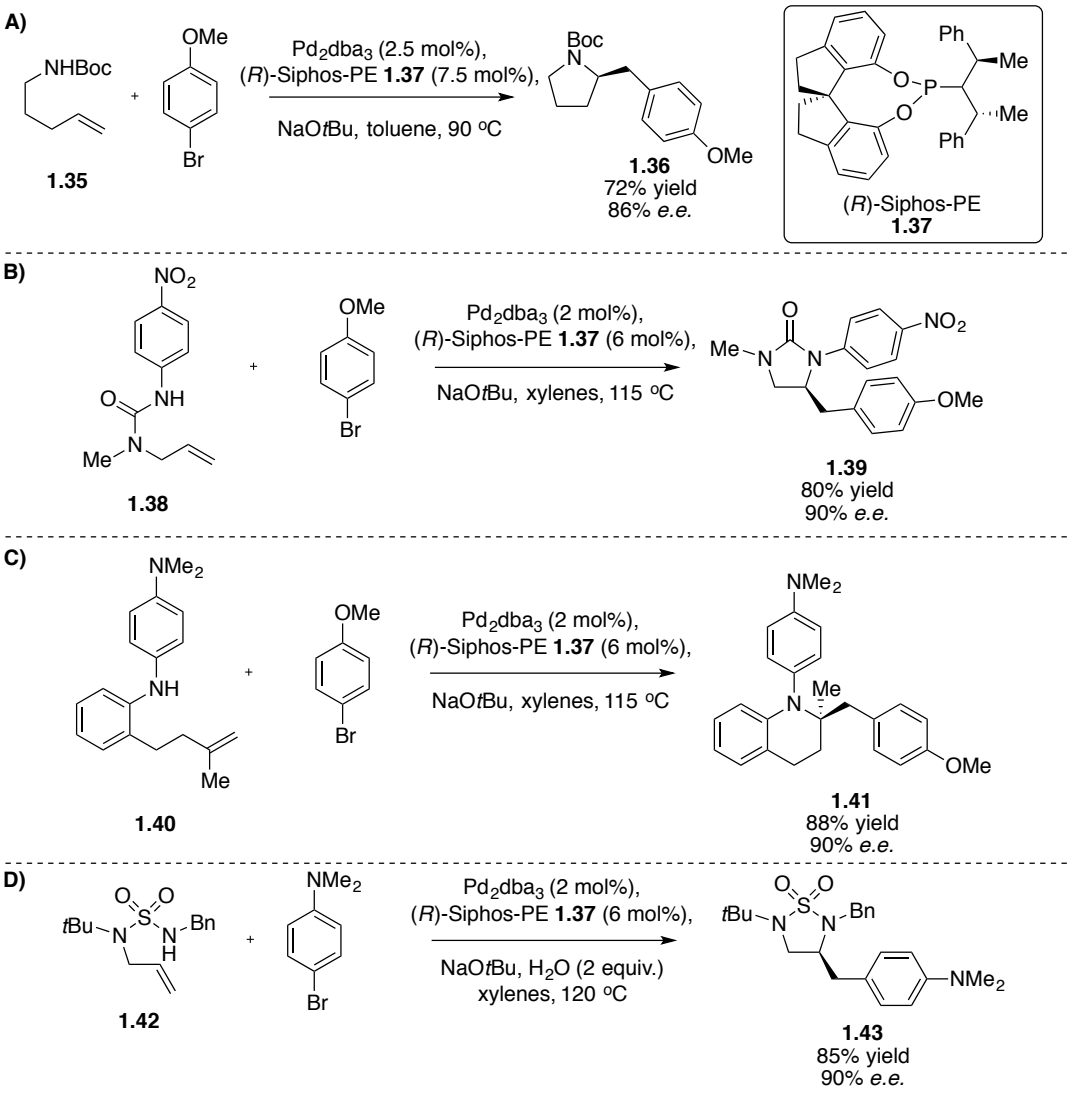
Pioneered by Overman, Wolfe, and Stahl, a broad range of enantioselective alkene functionalization reactions involving aminopalladation have been developed over the past several decades. Recently, Wolfe and co-workers developed an enantioselective aminoarylation of alkenes. As shown in Scheme 1.7.A, employing an alkene with a tethered amine, a palladium-catalyzed intramolecular cyclization/cross-coupling sequence furnished a variety of 2-(arylmethyl)- or 2-(alkenylmethyl)pyrrolidines in an enantioselective fashion.[13] It was demonstrated that Siphos-RE **1.37** was the optimal ligand for this transformation, and both aryl- and alkenyl-halides could be engaged in the reaction. Furthermore, the nature of the tethered amine was not limited to just Boc-protected amines: with a similar strategy, Wolfe and co-workers demonstrated that the scope of substrates could be further expanded to *N*-allyl urea derivatives,[14] aniline derivatives,[15] and *N*-allysulfamide derivatives[16] to afford enantiomerically enriched imidazolidine 2-ones, tetrahydroqunolines, and cyclic sulfamides respectively (Scheme 1.7.B, C, D).

The mechanistic studies conducted by Wolfe deciphered the nature of the key aminopalladation step. Utilizing the *trans*-deuterium-labeled substrate **1.44**, the Wolfe carboamination reaction led to the product **1.45** in which the amine nucleophile and phenyl electrophile had a *cis* relationship. With the assumption that reductive elimination proceeded in a stereoretentive fashion, the stereochemical outcome of product **1.45** suggested that *cis*-aminopalladation occurred under the reaction conditions (Scheme

[13] Mai, D. N., Wolfe, J. P. *J. Am. Chem. Soc.* **2010**, 13, 12157.
[14] Hopkins, B. A., Wolfe, J. P. *Angew. Chem. Int. Ed.* **2012**, 51, 9886.
[15] Hopkins, B. A., Wolfe, J. P. *Chem. Sci.* **2014**, 5(12), 4840.
[16] Garlets, Z. J., Parenti, K. R., Wolfe, J. P. *Chem.-Eur. J.* **2016**, 22(17), 5919.

1.8.A). It is worthy of note that similar *cis*-aminopalladation mechanisms have also been applied to the reactions with *N*-allyl urea derivatives, aniline derivatives, and *N*-allysulfamide derivatives.

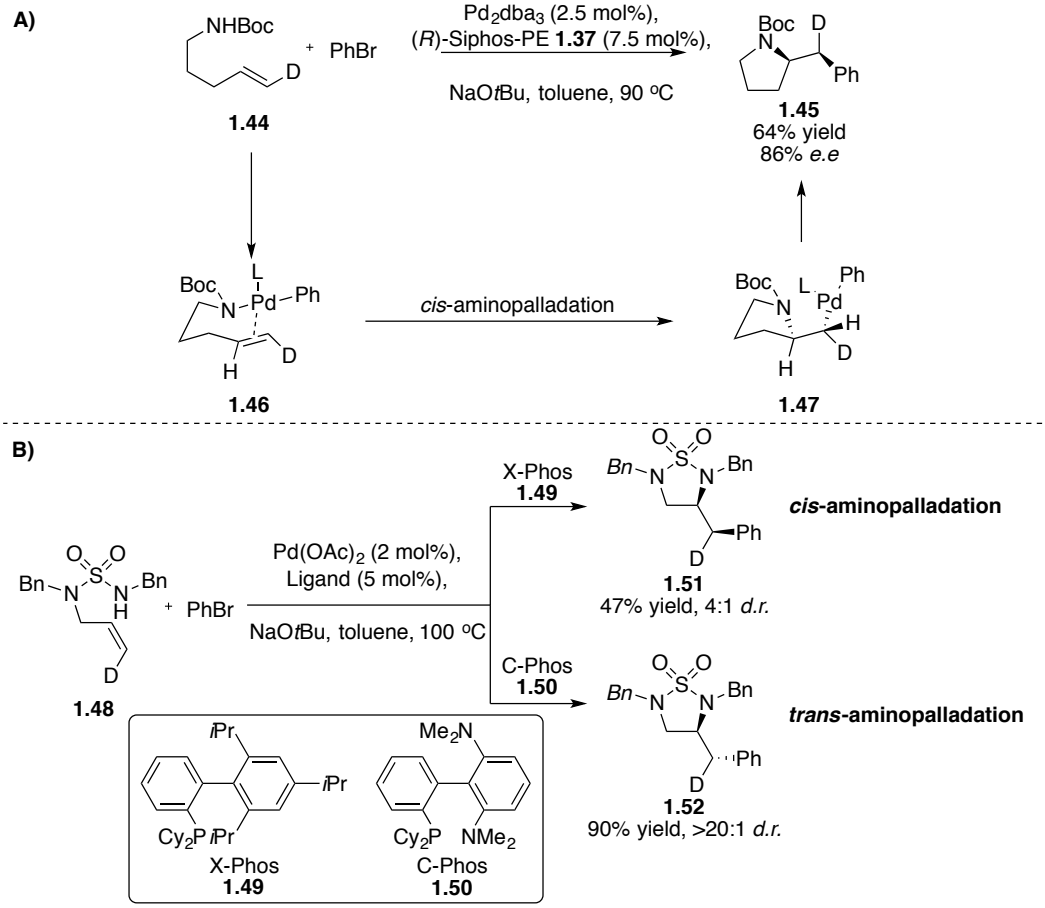
Scheme 1.7. Enantioselective carboamination of alkenes.



Utilizing different ligands for palladium catalyst could influence the stereochemical nature of aminopalladation step. As shown in Scheme 1.8.B, while employing X-Phos **1.49** led to the *cis*-aminopalladation product **1.51**, *trans*-aminopalladation product **1.52**

was isolated exclusively in the presence of C-Phos **1.50** as the ligand.[17] This observation was rationalized by reasoning that the electrophilic or cationic metal center favored the *anti*-addition pathway, whereas ligands containing electron-donating groups, such as C-Phos **1.50**, might better stabilize the cationic intermediate so *trans*-aminopalladation was favored.

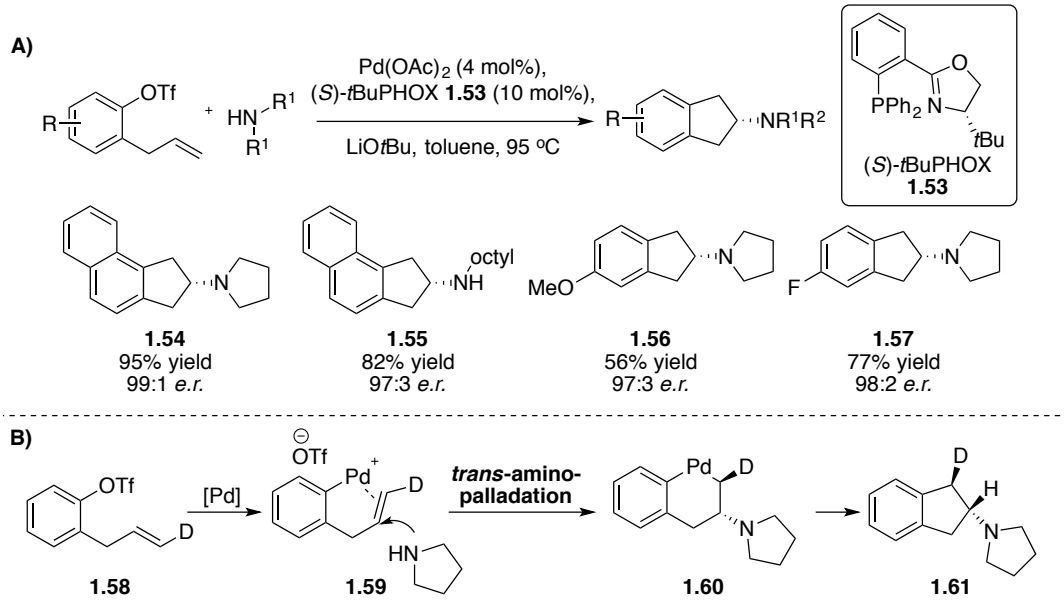
Scheme 1.8. Stereochemical outcome of the carboamination of alkenes.



[17] Fornwald, R. M., Fritz, J. A., Wolfe, J. P. (2014). *Chem. -Eur. J.* **2014**, 20, 8782.

In most alkene carboamination reactions, the amine nucleophile is always tethered to the alkene while the alkyl-palladium intermediate reacts with an external electrophile. In 2015, Wolfe and co-workers reported an asymmetric palladium catalyzed alkene carboamination reaction with an aryl electrophile bearing a tethered alkene and a free amine nucleophile.[18] With such a strategy, a broad range of 2-aminoindane derivatives were synthesized with good levels of enantioselectivity and efficiency (Scheme 1.9.A).

Scheme 1.9. Asymmetric palladium catalyzed alkene carboamination with free amine nucleophiles.



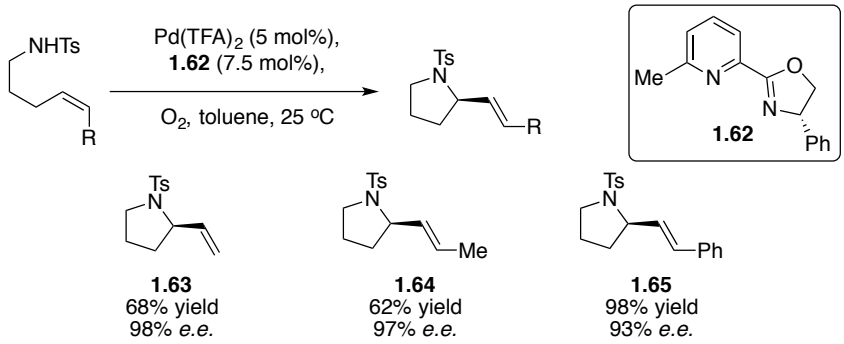
While most enantioselective palladium-catalyzed alkene carboaminations proceeded through a *cis*-aminopalladation pathway, the mechanistic experiment conducted with deuterium labeled substrate **1.58** suggested that the *trans*-aminopalladation dominated under the reaction conditions. Based on this observation, the reaction mechanism was proposed as follows (Scheme 1.9.B): oxidative addition between a palladium (0) catalyst

[18] White, D. R., Hutt, J. T., Wolfe, J. P. *J. Am. Chem. Soc.* **2015**, 137, 11246.

and aryl triflate led to the palladium (II) complex **1.59** where the palladium was coordinated to the tethered alkene. Trans-aminopalladation with external free amine nucleophile afforded the alkyl-palladium intermediate **1.60**. Subsequent reductive elimination furnished the carboamination product and regenerated the palladium (0) catalyst.

Instead of cross-coupling as demonstrated by Wolfe, the alkyl-palladium intermediate can also undergo β-hydride elimination. Utilizing this strategy, Stahl and co-workers reported an enantioselective palladium-catalyzed aerobic oxidative amidation of alkenes.[19] Employing an alkene bearing a tethered protected amine in the presence of a palladium catalyst and chiral PyrOx **1.62** as the ligand, an intramolecular cyclization/β-hydride elimination sequence furnished a range of 2-alkenyl pyrrolidines with good yield and enantioselecitivity (Scheme 1.10).

Scheme 1.10. Enantioselective palladium catalyzed alkene oxidative amidation.

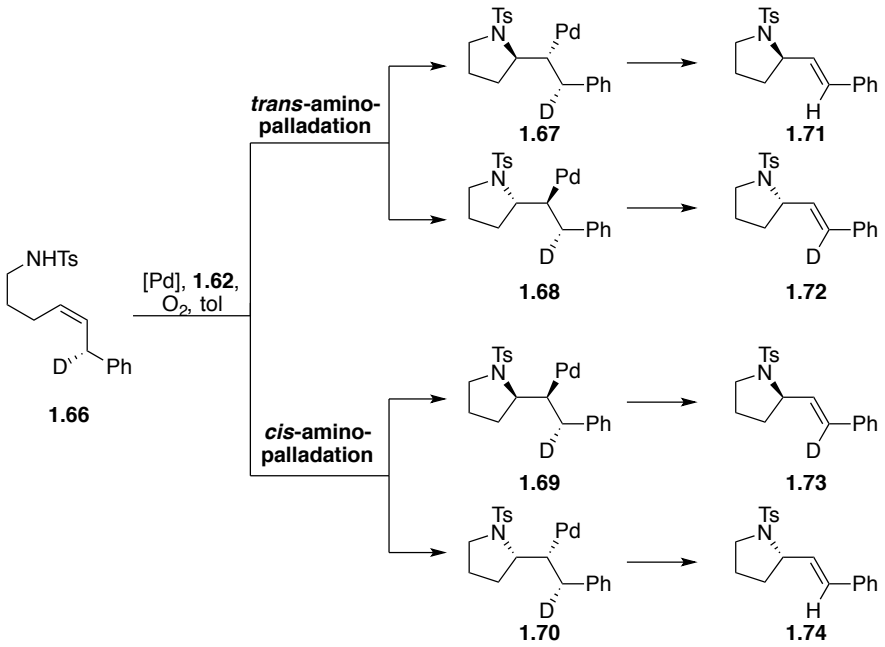


In order to investigate the stereochemical course of the aminopalladation step, the enantiomerically pure deuterium labeled substrate **1.66** was prepared.[20] As shown in Scheme 1.11, if *trans*-aminopalladation occurred to the substrate **1.66**, alkyl-palladium

[19] McDonald, R. I., White, P. B., Weinstein, A. B., Tam, C. P., Stahl, S. S. *Org. lett.* **2011**, 13(11), 2830.
[20] Weinstein, A. B., & Stahl, S. S. *Angew. Chem. Int. Ed.* **2012**, 51(46), 11505.

intermediates **1.67** and **1.68** could be generated. Since it was known that subsequent β-hydride elimination was selective for the *trans*-alkene product, intermediates **1.67** and **1.68** would lead to alkene products **1.71** and **1.72** respectively. On the other hand, if the reaction proceeded through *cis*-aminopalladation pathway, the palladated intermediates **1.69** and **1.70** would be converted to alkene products **1.73** and **1.74** respectively. This means the ratio of *trans*-aminopalladation to *cis*-aminopalladation could be determined by analysis of the ratio of alkene products **1.71** to **1.74**.

Scheme 1.11. Mechanistic study of the stereochemical pathways of aminopalladation.



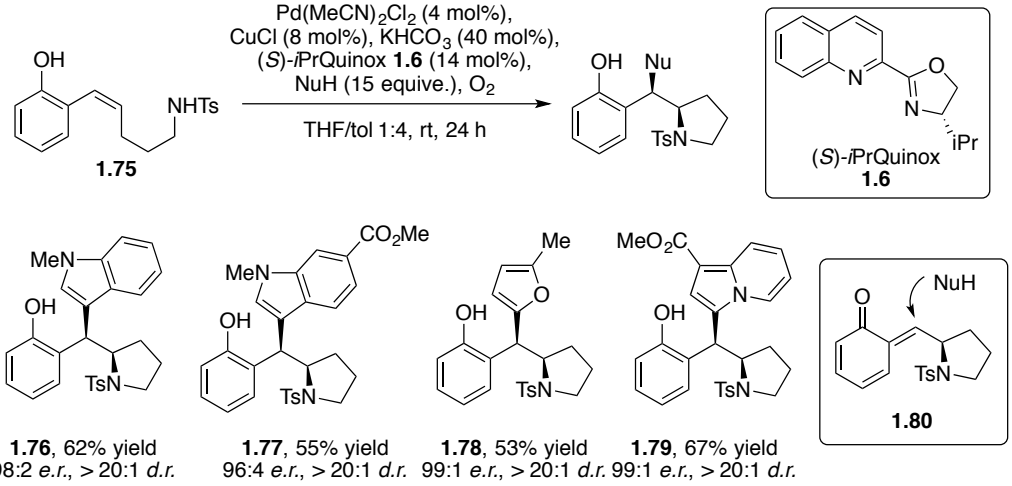
Entry	[Pd]	Yield	*e.e.*	*trans*-aminopalladation/ *cis*-aminopalladation
1	$Pd(TFA_2)$	90 %	96 %	> 9:1
2	$Pd(OAc)_2$	48 %	20 %	1:9

With this strategy, it was determined that the reaction proceeded through *trans*-aminopalladation pathway in the presence of palladium (II) trifluoroacetate to afford the desired product with excellent yield and enantioselectivity. In contrast, employing palladium (II) acetate promoted the *cis*-aminopalladation pathway to furnish the product with diminished yield and poor selectivity. Such an observation was in agreement with the argument that the less coordinating anion promoted the formation of a cationic palladium intermediate, which was thought to favor the *anti*-addition pathway.

As discussed before, Sigman and co-workers developed a palladium catalyzed enantioselective alkene difunctionalization reaction with alkenes bearing tethered alcohol nucleophiles. Utilizing a similar strategy, Sigman further expanded the asymmetric alkene difunctionalization reaction to include alkenes bearing tethered amine nucleophiles in an enantioselective and diastereoselective fashion (Scheme 1.12).[21] Similar to the proposed mechanism involving oxypalladation, the alkyl-palladium intermediate generated by enantioselective intramolecular aminopalladation quickly decomposed to quinone methide intermediate **1.80**. Subsequent diastereoselective nucleophilic attack of the quinone methide intermediate furnished the alkene difunctionalization product with high efficiency and selectivity.

[21] Jana, R., Pathak, T. P., Jensen, K. H., Sigman, M. S. *Org. lett.* **2012**, 14, 4074.

Scheme 1.12. Palladium catalyzed enantioselective synthesis of pyrrolidine derivatives.

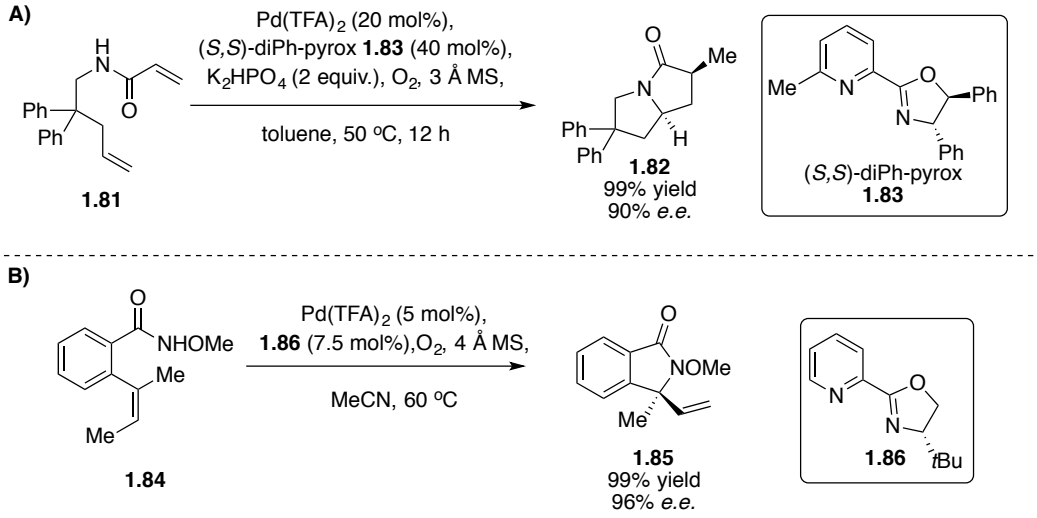


Recently, Yang and co-workers reported a palladium-catalyzed enantioselective oxidative cascade cyclization of aliphatic alkenyl amides.[22] Similar to the oxidative tandem cyclization of unsaturated anilides previously developed by the same group.[23] the aliphatic allenyl amide substrate **1.81** underwent an aminopalladation/alkene insertion sequence to furnish the bicyclic pyrrolidine derivative product **1.82** with excellent yield and enantioselectivity (Scheme 1.13.A). A deuterium labeling experiment suggested that *trans*-aminopalladation occurred under the reaction conditions. Alternatively, similar to the chemistry developed by Stahl, Zhang and co-workers described a palladium-catalyzed enantioselective aza-Wacker type cyclization to synthesize isoindolinones bearing a fully substituted carbon stereocenter.[24] As shown in Scheme 1.13.B, the tri-substituted alkene **1.84** was converted to isoindolinone product **1.85** in the presence of a palladium catalyst

[22] Du, W., Gu, Q., Li, Y., Lin, Z., Yang, D. *Org. Lett.*, **2017**, 19, 316.
[23] He, W., Yip, K. T., Zhu, N. Y., Yang, D. *Org. Lett.* **2009**, 11, 5626. (b) Yip, K.T., Yang, M., Law, K. L., Zhu, N. Y., Yang, D. *J. Am. Chem. Soc.* **2006**, 128, 3130.
[24] Yang, G., Shen, C., Zhang, W. *Angew. Chem. Int. Ed.* **2012**, 51, 9141.

and *t*Bu-PyrOX **1.86** as the ligand. It was proposed that the reaction proceeded through an enantioselective intramolecular cis-aminopalladation/β-hydride elimination sequence.

Scheme 1.13. Palladium catalyzed enantioselective cyclization reactions.



1.2.3. Enantioselective reactions involving carbopalladation

Over the past several decades, a broad range of enantioselective transformations involving carbopalladation have been developed. Similar to oxy- and amino-palladation discussed above, carbopalladation can proceed through two distinct stereochemical courses: *trans*-carbopalladation and *cis*-carbopalladation. The details of the development of enantioselective reactions involving carbopalladation will be further discussed in Chapter 3.

1.3. Gold catalyzed enantioselective reactions

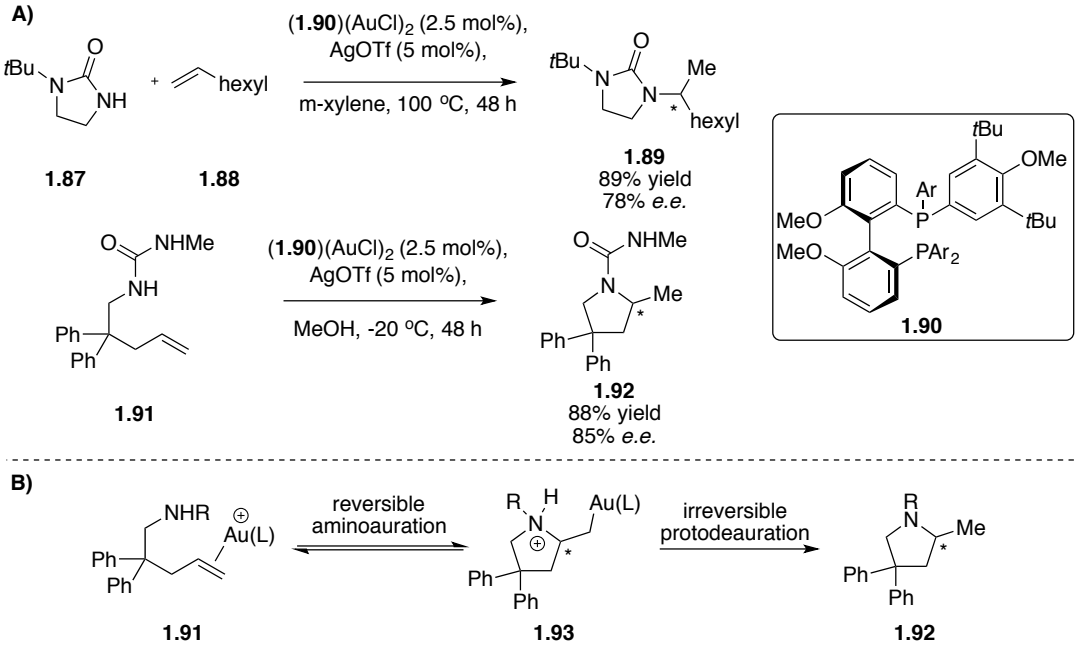
Well-known as a transition-metal that is able to coordinate and activate π-systems, gold complexes have been shown to catalyze a broad range of enantioselective transformations. While most of the recent progress has been focused on alkyne and allene

substrates, enantioselective functionalization of alkenes involving gold catalysts remain underdeveloped. In this context, Widenhoefer and co-workers established a gold (I) catalyzed intermolecular hydroamination of unactivated alkenes. The simple terminal alkene **1.88** was activated by a gold (I) chloride catalyst in the presence of (*S*)-DTBM-MeO-Biphep **1.90** as the ligand.[25] *Trans*-aminoauration followed by protodeauration furnished the hydroamination product **1.89** with good yield and enantioselectivity. Such a strategy was further expanded to intramolecular hydroamination of unactivated alkene **1.91** to construct the cyclized product **1.92** in an enantioselective fashion (Scheme 1.14.A).[26] In contrast to the intermolecular case in which aminoauration was the stereochemistry determining step, DFT studies suggested that the intramolecular reaction proceeded with a reversible aminoauration followed by irreversible enantioselectivity determining protodeauration (Scheme 1.14.B).

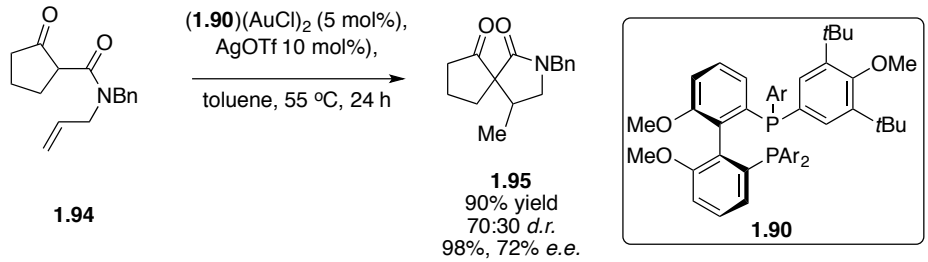
The nucleophile in nucleoauration is not limited to amine derivatives. Gandon and co-workers demonstrated that β-ketoamides could be employed as carbon nucleophiles to attack alkene substrates that were activated by gold (I) catalyst.[27] Although moderate diastereoselectivity was obtained for the intramolecular cyclization of β-ketoamide **1.94**, the enantioselectivities of both diastereomers were high and the reaction occurred with high efficiency (Scheme 1.15).

[25] Zhang, Z., Du Lee, S., Widenhoefer, R. A. *J. Am. Chem. Soc.* **2009**, 131, 5372.
[26] Lee, S. D., Timmerman, J. C., Widenhoefer, R. A. *Adv. Synth. Catal.* **2014**, 356, 3187.
[27] Fang, W., Presset, M., Guérinot, A., Bour, C., Bezzenine-Lafollée, S., Gandon, V. *Org. Chem. Front.* **2014**, 1, 608.

Scheme 1.14. Gold (I) catalyzed enantioselective hydroamination of unactivated alkenes.



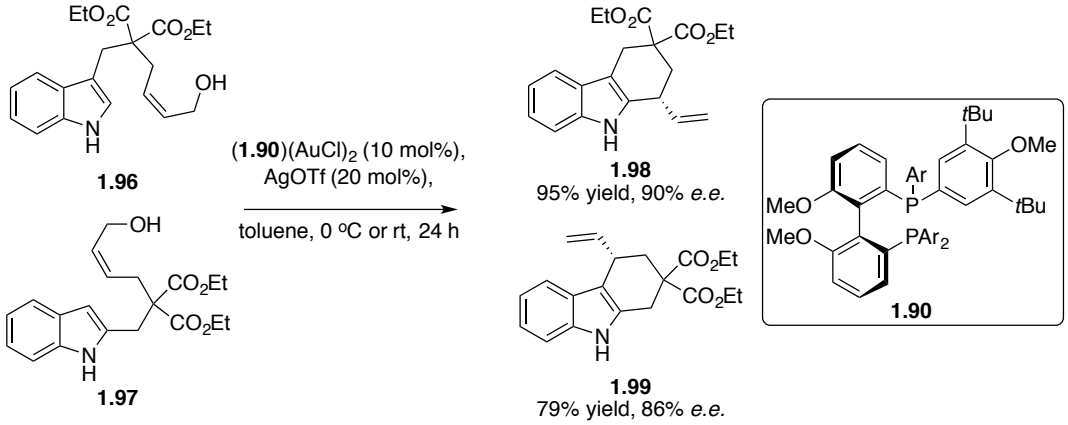
Scheme 1.15. Gold catalyzed enantioselective hydroalkylation.



Compared to simple unactivated alkenes, allylic alcohols show enhanced reactivity towards nucleophilic addition in the presence of gold (I) catalysts. Moreover, the alkyl-gold intermediate derived from nucleoauration undergoes β-hydroxyl elimination instead of protodeauration for simple alkene substrates. Taking the advantage of the inherent features of allylic alcohols, Bandini and co-workers developed a gold-catalyzed

enantioselective intramolecular allylation of indoles bearing tethered allylic alcohols.[28] Both C-2 and C-3 substituted indoles were engaged in the gold catalyzed reaction to furnish the cyclized products **1.98** and **1.99** respectively with good yield and enantioselectivity (Scheme 1.16). The DFT calculations suggested that the reaction proceeded through a *trans*-carboauration/*anti*-β-hydroxyl elimination sequence.[29]

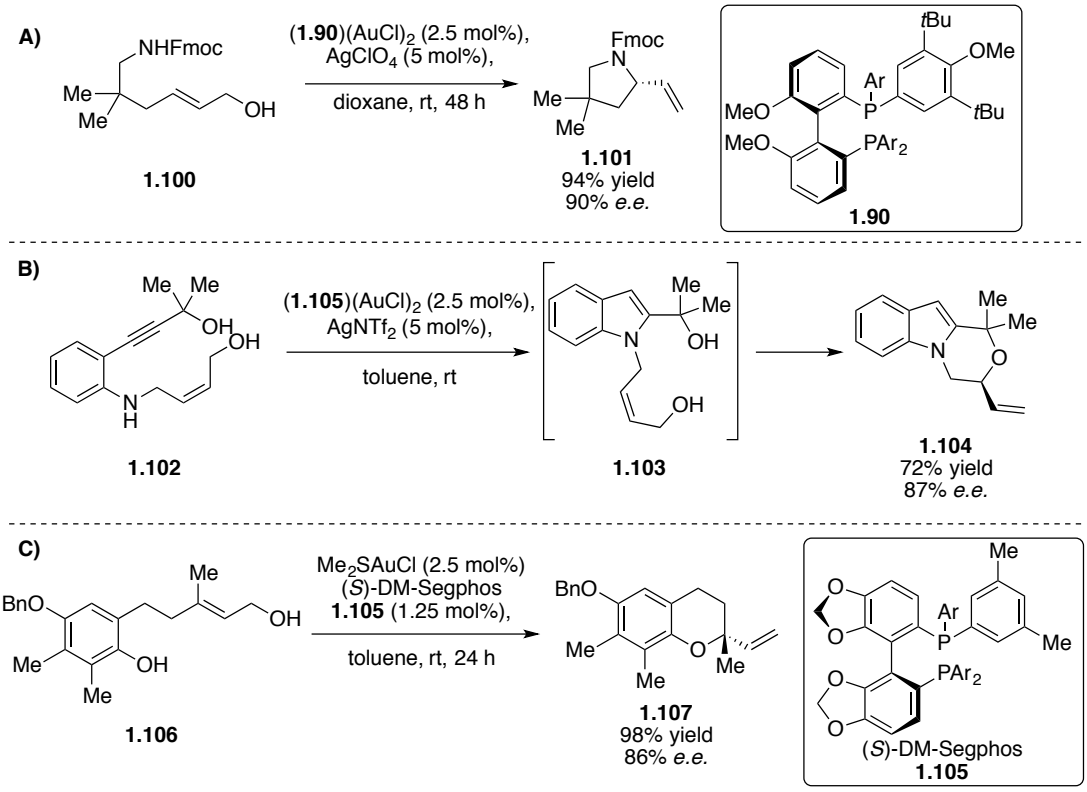
Scheme 1.16. Gold catalyzed enantioselective alkylation of indoles.



In addition to carbon nucleophiles, oxygen and nitrogen nucleophiles can also be engaged in gold catalyzed enantioselective functionalizations of allylic alcohols. Widenhoefer and co-workers described an enantioselective intramolecular amination of allylic alcohols in the presence of a gold (I)/Biphep (**1.90**) complex.[30] The allylic alcohol **1.100** bearing an attached protected amine underwent an aminoauration/β-hydroxyl elimination sequence to furnish the cyclized 2-vinyl pyrrolidine product **1.101** with excellent levels of efficiency and enantioselectivity (Scheme 1.17.A).

[28] Bandini, M., Gualandi, A., Monari, M., Romaniello, A., Savoia, D., Tragni, M. (2011). *J. Organomet. Chem.* **2011**, 696, 338-347.
[29] Bandini, M., Bottoni, A., Chiarucci, M., Cera, G., Miscione, G. P. *J. Am. Chem. Soc.* **2012**, 134, 20690-20700.
[30] Mukherjee, P., Widenhoefer, R. A. *Angew. Chem. Int. Ed.* **2012**, 51, 1405.

Scheme 1.17. Gold catalyzed enantioselective functionalization of allylic alcohols via oxy- and amino-auration.

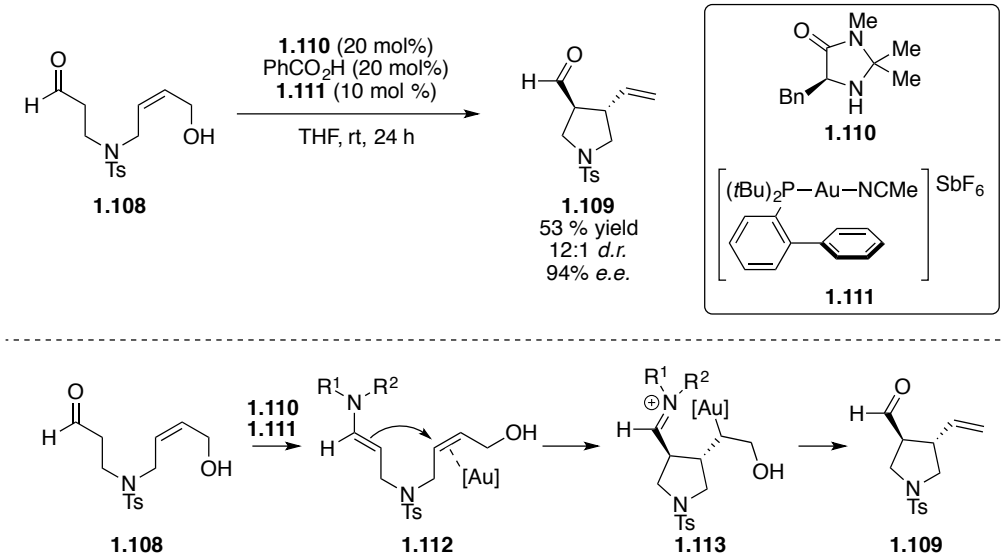


In 2013, Bandini and co-workers established a stereoselective gold catalyzed cascade cyclization to construct oxazino-indole products.[31] Employing ortho-alkynlaniline diol **1.102** as the substrate, a gold catalyzed hydroamination of the alkyne moiety led to the indole intermediate **1.103**. Without isolation, the same gold catalyst, a Segphos **1.105**/gold (I) complex, promoted an oxyauration followed by β-hydroxyl elimination to afford the oxazino-indole product **1.104** with good yield and selectivity (Scheme 1.17.B). Furthermore, Rusping and co-workers demonstrated that the oxyauration/β-hydroxyl

[31] Chiarucci, M., Mocci, R., Syntrivanis, L. D., Cera, G., Mazzanti, A., Bandini, M. *Angew. Chem. Int. Ed.* **2013**, 52(41), 10850.

elimination strategy could also be applied to construct quaternary stereocenters.[32] A gold catalyzed intramolecular oxyauration of **1.106**, including reaction between the phenol nucleophile and tri-substituted allylic alcohol, led to the cyclized product **1.107** bearing a quaternary stereocenter in a highly enantioselective fashion (Scheme 1.17.C).

Scheme 1.18. Gold catalyzed enantioselective α-allylation of aldehyde.



Aside from using a gold/chiral phosphine complex catalyst, Bandini and co-workers reported a tandem gold/organocatalyzed enantioselective α-allylation of aldehydes with allylic alcohols by employing achiral gold complex **1.111** and chiral amine **1.110** as a co-catalyst.[33] As shown in Scheme 1.18, aldehyde substrate **1.108** condensed with chiral amine catalyst **1.110** to form the enamine intermediate **1.112**. Then, a carboauration between the enamine and the gold activated allylic alcohol furnished the alkyl-gold

[32] Uria, U., Vila, C., Lin, M. Y., Rueping, M. *Chem. -Eur. J.* **2014**, 20, 13913.
[33] Chiarucci, M., di Lillo, M., Romaniello, A., Cozzi, P. G., Cera, G., Bandini, M. *Chem. Sci.* **2012**, 3, 2859.

intermediate **1.113**. Subsequent β-hydroxyl elimination and hydrolysis afforded the α-allylated product **1.109** with good diastereo- and enantioselectivity.

1.4. Other transition-metal catalyzed enantioselective reactions

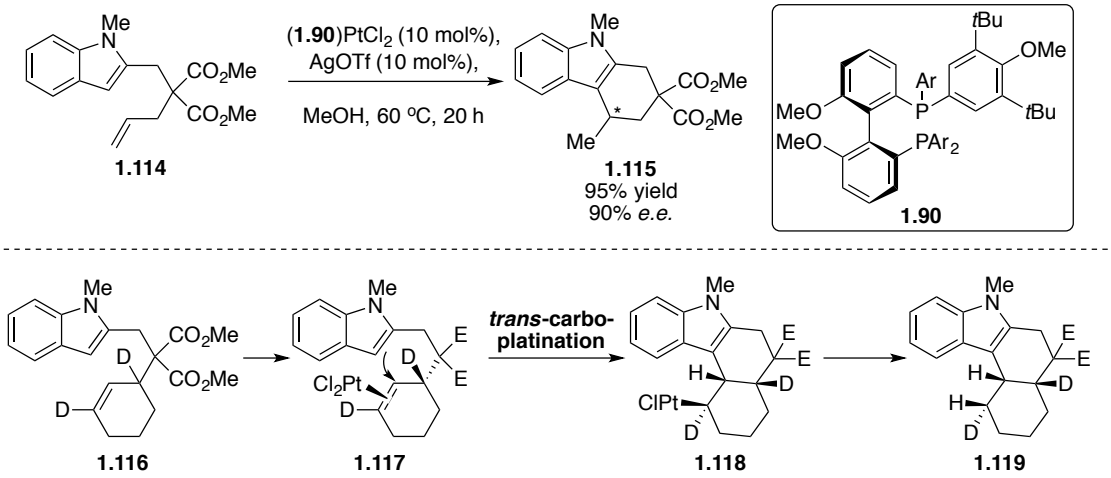
1.4.1. Platinum catalyzed enantioselective functionalization of unactivated alkenes involving nucleoplatination.

In 2006, Widenheofer and co-workers reported a platinum catalyzed enantioselective hydroarylation of unactivated alkenes.[34] As shown in Scheme 1.19, employing platinum/Biphep **1.90** complex as the catalyst, the alkenylindole (**1.114**) underwent an intramolecular cyclization to afford the polycyclic indole derivative **1.115** in excellent yield and enantioselectivity. It was proposed that the reaction proceeded with a carboplatination/protonation sequence. To probe the stereochemical course of the nucleometallation step, the deuterium labeled cyclic substrate **1.116** was prepared and subjected to platinum catalyzed cyclization conditions.[35] The cyclized product **1.119** was isolated with a *cis*-relationship between the indole nucleophile and the deuterium label. This stereochemical outcome suggested that a *trans*-carboplatination occurred to furnish the alkyl-platinum intermediate **1.118**. Subsequent stereoretentive protonation of the alkyl-platinum species led to the cyclized product **1.119** with the observed stereochemistry. It is worthy of note that platinum-catalyzed intramolecular hydroamination[36] and hydroalkoxylation[37] of unactivated alkenes have also been reported

[34] Han, X., Widenhoefer, R. A. *Org. lett.* **2006**, 8, 3801.
[35] Liu, C., Han, X., Wang, X., Widenhoefer, R. A. *J. Am. Chem. Soc.* **2004**, 126, 3700.
[36] Bender, C. F., Widenhoefer, R. A. *J. Am. Chem. Soc.* **2005**, 127, 1070.
[37] Qian, H., Han, X., Widenhoefer, R. A. *J. Am. Chem. Soc.* **2004**, 126, 9536.

by Widenheofer laboratory. However, the platinum catalyzed enantioselective versions of these transformations remain underdeveloped.

Scheme 1.19. Platinum catalyzed enantioselective alkene hydroarylation

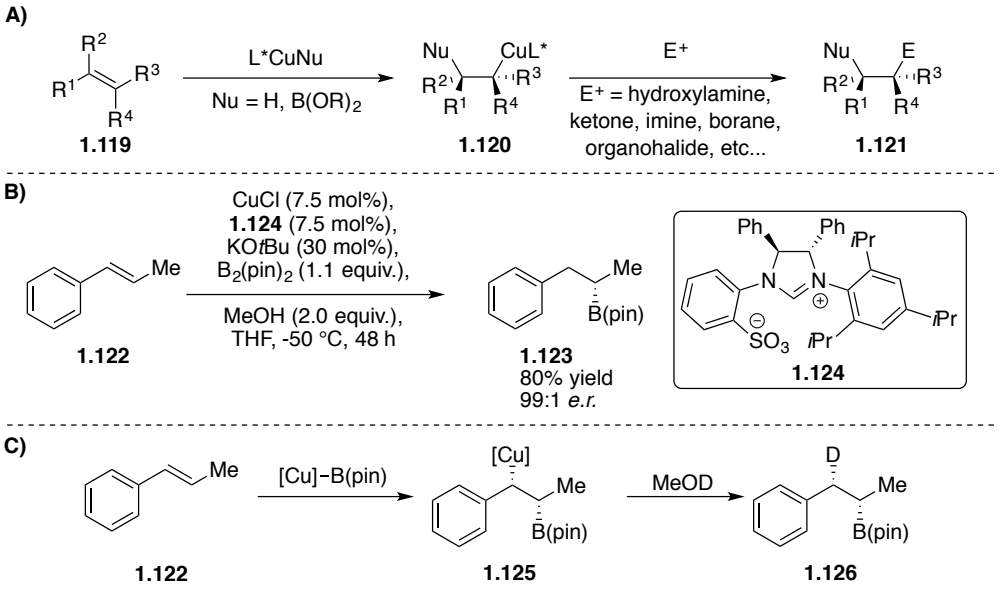


1.4.2. Copper catalyzed enantioselective functionalization of unactivated alkenes involving nucleocupration

The enantioselective functionalization of unactivated alkenes involving copper-hydride or copper-boranyl species has recently been developed and rapidly been expanded upon. Pioneered by Hirano, Miura, and Hoveyda, and further developed by Buchwald, it has been demonstrated that copper-hydride or copper-boranyl species are able to react with unactivated alkenes. Employing chiral ligands for copper catalyst, enantioselective hydrocupration or boracupration affords alkyl-copper intermediates, which can be intercepted by a variety of electrophiles, such as hydroxylamines, ketones, imines, organohalides, and boranes (Scheme 1.20.A). Enantioselective functionalizations of unactivated alkenes involving copper-hydride or copper-boranyl species have been

summarized in a recently published review by Sebesta and co-workers.[38, 39] As in one of the first examples, Hoveyda and co-workers demonstrated an copper-catalyzed enantioselective hydroboration reaction of stryrenes in the presence of chiral NHC **1.124** as the ligand (Scheme 1.20.B).[40] Regarding the mechanism, the authors proposed that a boracupration of the trans-methylstryene **1.222** led to the alkylcopper intermediate **1.125**. Subsequent protonation of the alkylcopper intermediate with methanol furnished the net hydroboration product (Scheme 1.20.C). This proposed mechanism was further supported by the observation that deuterated product **1.126** was isolated as a single diastereomer when the reaction was performed with deuterated methanol.

Scheme 1.20. Enantioselective functionalization of unactivated alkene involving copper-hydride or copper-boranyl species

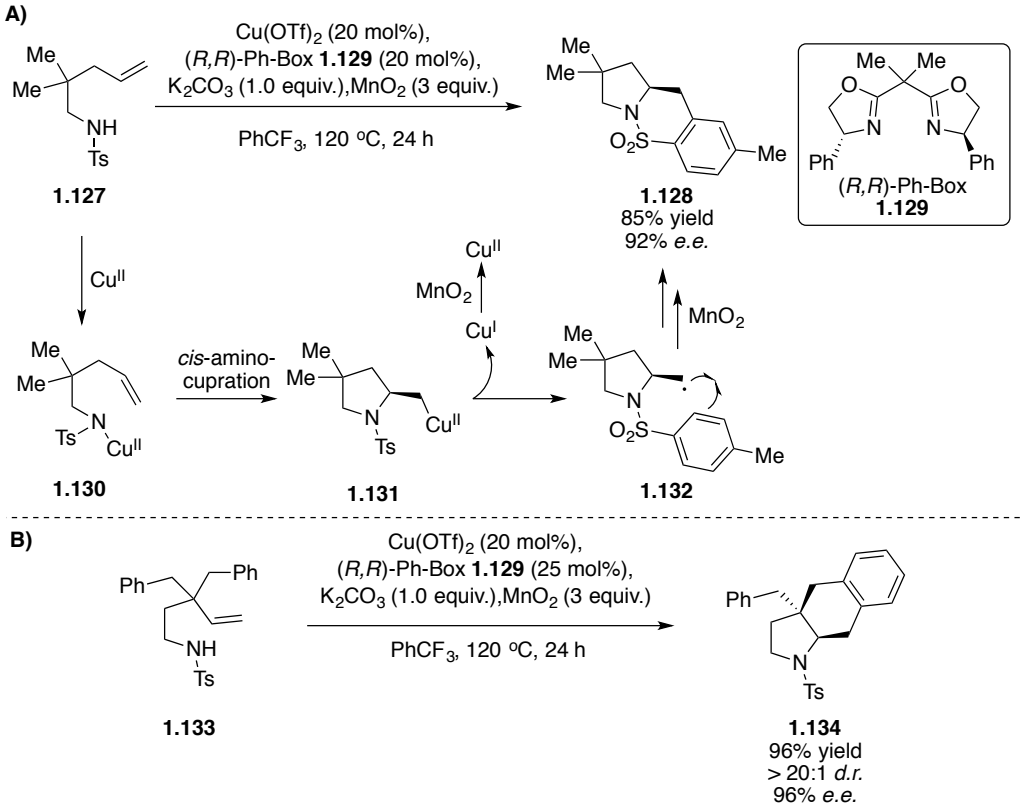


[38] Sorádová, Z., Šebesta, R. *ChemCatChem* **2016**, 8, 2581.
[39] Shimizu, Y., Kanai, M. *Tetrahedron Lett.* **2014**, 55, 3727.
[40] (a) Lee, Y., Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, 131, 3160. (b) Corberán, R., Mszar, N. W., & Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2011**, 50, 7079.

Aside from the well-developed copper-hydride and copper-boranyl chemistry, Chemler and co-workers described a copper catalyzed enantioselective carboamination of unactivate alkenes.[41] Employing copper (II) triflate and Ph-Box **1.129** as the ligand, the terminal alkene substrate **1.127** bearing a tethered protected amine underwent an intramolecular cyclization to furnish the product **1.128** by constructing a new carbon-nitrogen bond and a new carbon-carbon bond across the alkene with high efficiency and enantioselectivity. Systematic mechanistic studies conducted by the same group suggested that the reaction proceeded by the following mechanism:[42] the amine-copper complex formed in the presence of base, then *cis*-aminocupration of complex **1.130** led to the alkyl-copper intermediate **1.131**, which underwent homolytic cleavage to afford alkyl radical **1.132** and a copper (I) species. While the alkyl radical was intercepted by the aryl group in an intramolecular fashion, the copper (I) species was oxidized by MnO_2 to regenerated the copper (II) catalyst (Scheme 1.21.A). This strategy was expanded to enantioselective synthesis of nitrogen containing polycyclic systems bearing vicinal quaternary and tertiary stereocenters.[43] As shown in Scheme 1.21.B, the alkyl radical intermediate, generated by an aminocupration/homolytic cleavage sequence, was intercepted by attached aryl group instead of the *N*-arylsulfonyl group as in the previous example to construct the fused tricyclic product **1.134** with excellent levels of diastereo- and enantioselectivity.

[41] Zeng, W., Chemler, S. R. *J. Am. Chem. Soc.* **2007**, 129(43), 12948.
[42] Paderes, M. C., Belding, L., Fanovic, B., Dudding, T., Keister, J. B., Chemler, S. R. *Chem.-Eur. J.* **2012**, 18, 1711.
[43] Miao, L., Haque, I., Manzoni, M. R., Tham, W. S., Chemler, S. R. *Org. lett.* **2010**, 12, 4739.

Scheme 1.21. Copper catalyzed intramolecular enantioselective carboamination of unactivated alkenes.

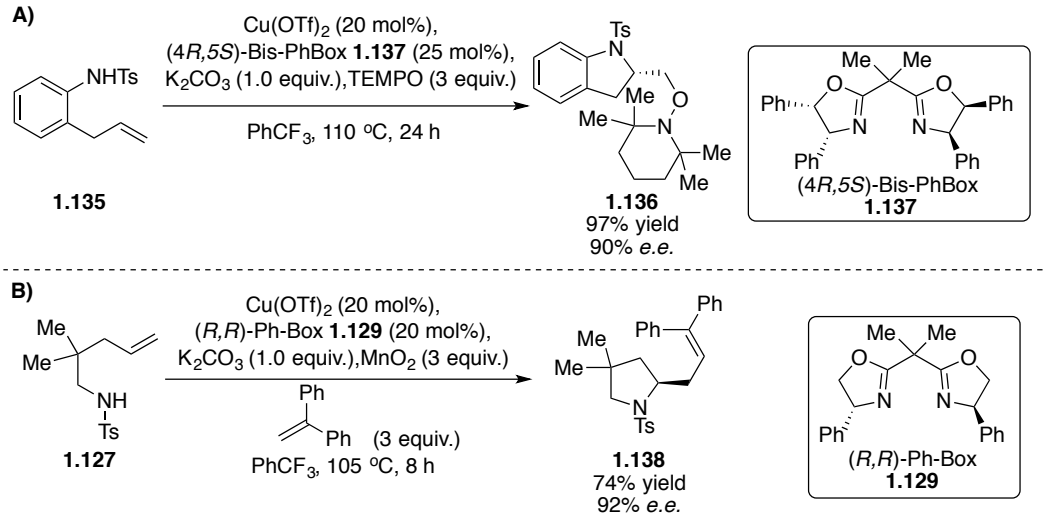


In addition to the intramolecular carboamination reaction discussed above, Chemler and co-workers explored other transformations that could be applied to the alkyl-copper intermediate. By trapping the alkyl radical with a tetramethylaminopiperidinyloxy radical in an intermolecular fashion, a copper catalyzed enantioselective aminooxygenation of unactivated alkenes was established in 2008 (Scheme 1.22.A).[44] This methodology provided efficient access to pyrrolidine and indoline derivatives with high enantioselectivity. Moreover, Chemler also demonstrated that the alkyl radical species generated by the intramolecular aminocupration/homolytic cleavage sequence could also

[44] Fuller, P. H., Kim, J. W., Chemler, S. R. *J. Am. Chem. Soc.* **2008**, 130, 17638.

be engaged in an intermolecular Heck type reaction with an external alkene partner (Scheme 1.22.B).[45] This copper-catalyzed transformation was complementary to Wolfe's palladium catalyzed carboamination reactions.

Scheme 1.22. Copper catalyzed enantioselective aminooxygenation and aminovinylation of unactivated alkenes.

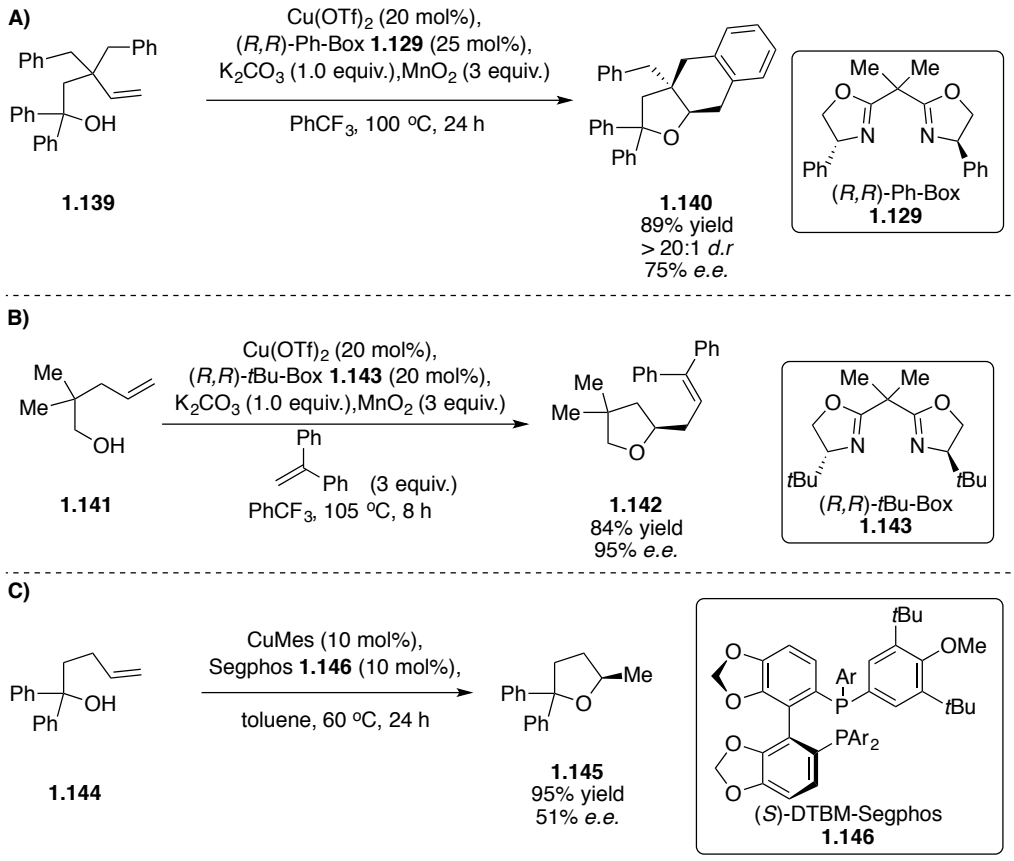


The scope of the copper catalyzed enantioselective intramolecular nucleocupration of unactivated alkenes is not limited to just amine nucleophiles. Recently, Chemler and co-workers demonstrated a copper catalyzed enantioselective intramolecular carboetherification to synthesize tetrahydrofuran derivatives with fused polycyclic systems.[46] Similar to the amine variant of this reaction, it was proposed that an alkyl radical species was generated by *cis*-oxycupration and homolytic cleavage of carbon-copper bond. Subsequently, the alkyl radical was intercepted by the aryl group in an intramolecular fashion (Scheme 1.23.A). It was also demonstrated that the intramolecular

[45] Liwosz, T. W., Chemler, S. R. *J. Am. Chem. Soc*. **2012**, 134(4), 2020.
[46] Miller, Y., Miao, L., Hosseini, A. S., Chemler, S. R. *J. Am. Chem. Soc*. **2012**, 134, 12149.

nucleocupraton/intermolecular Heck type coupling cascade could be applied to alcohol nucleophiles to afford oxyvinylation products with good yield and enantioselectivity (Scheme 1.23.B).[47]

Scheme 1.23. Copper catalyzed enantioselective functionalization of alkene with alcohol nucleophiles.



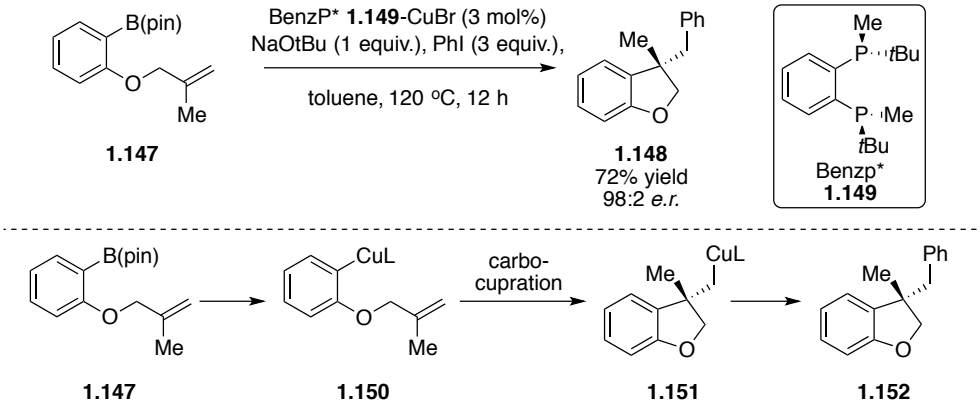
In 2015, Ohimiya and Sawamura reported a copper (I) catalyzed intramolecular hydroalkoxylation of unactiviated alkenes.[48] Employing the terminal alkene bearing an attached alcohol moiety, the 2-methyl tetrahydrofuran derivative **1.145** was obtained with

[47] Bovino, M. T., Liwosz, T. W., Kendel, N. E., Miller, Y., Tyminska, N., Zurek, E., Chemler, S. R. *Angew. Chem. Int. Ed.*, **2014**, 53, 6383.
[48] Murayama, H., Nagao, K., Ohmiya, H., Sawamura, M. *Org. lett.*, **2015**, 17, 2039.

good yield but moderate enantioselectivity in the presence of Segphos **1.146** as the optimal ligand. It was proposed that the reaction proceeded through a *cis*-oxycupration similar to Chemlar's examples, however, instead of homolytic cleavage to generate alkyl radical, the alkyl copper intermediate underwent a protodecupration to furnish the hydroalkoxylation product.

Recently, Brown and co-workers reported a copper-catalyzed enantioselective diarylation of unactivated alkenes.[49] As shown in Scheme 1.24, utilizing the aryl B(pin) bearing a tethered alkene, the 2,3-dihydrobenzofuran bearing a quaternary stereocenter was obtained with good yield and enantioselectivity in the presence of copper (I) bromide and BenzP* **1.149** as the chiral ligand. In regard to the reaction mechanism, the authors proposed that the aryl-copper complex **1.150** was generated by the transmetallation of the aryl B(pin) to the copper catalyst in the presence of sodium *tert*-butoxide. Subsequent carbocupration led to the alkyl-copper complex **1.151**, which underwent cross-coupling with an aryl halide electrophile to furnish the final product.

Scheme 1.24. Copper catalyzed enantioselective diarylation of unactivated alkenes.



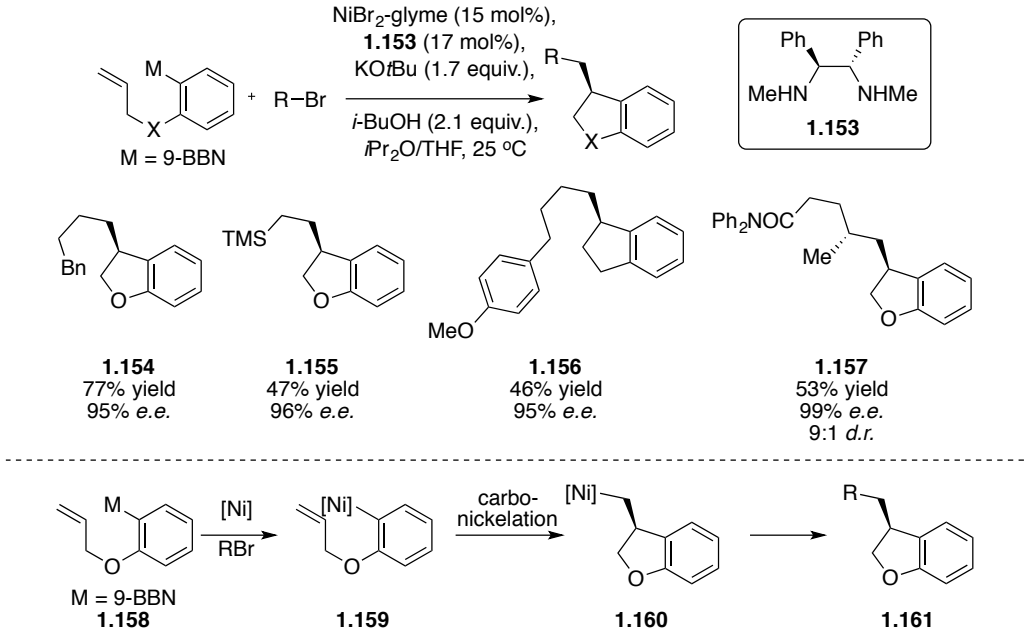
[49] You, W., Brown, M. K. *J. Am. Chem. Soc*. **2015**, 137, 14578.

1.4.3. Nickel catalyzed enantioselective functionalization of unactivated alkene involving nucleonickelation

In 2014, Fu and co-workers reported a nickel catalyzed enantioselective cyclization/cross-coupling reaction with unactivated alkenes and alkyl electrophiles.[50] The Fu group has developed a range of nickel-catalyzed enantioselective cross-coupling reactions between alkyl electrophiles and organometallic reagents, such as organo-9-BBN derivatives. To expand the scope of such nickel-catalyzed cross-coupling reactions, aryl-9BBN compounds bearing an attached alkene were investigated. It was discovered that these organometallic reagents participated in cyclization/cross-coupling cascades to furnish enantioenriched 2,3-dihydrobenzofuran and indane derivatives in the presence of a nickel/diamine **1.153** catalyst (Scheme 1.25). It is worthy of note that racemic γ-bromo-amide could also be engaged in the reaction to construct a cyclization/cross-coupling product containing two stereocenters in an enantio- and diastereoselective fashion. In regard to the reaction mechanism, it was proposed that aryl-nickel complex **1.159** was generated by transmetallation between the aryl-9-BBN and the nickel catalyst. Then, an intramolecular carbonickelation of the tethered alkene led to the alkyl-nickel species **1.160**. Subsequent nickel catalyzed cross-coupling afforded the final product with good yield and enantioselectivity.

[50] Cong, H., Fu, G. C. *J. Am. Chem. Soc*. **2014**, 136, 3788.

Scheme 1.25. Nickel catalyzed enantioselective cyclization/cross-coupling with alkyl electrophiles.



1.5. Conclusion

The methods summarized in this chapter highlight the important recent advances that have been made towards the development of catalytic enantioselective functionalization of unactivated alkenes enabled by nucleometallation. While significant achievements have been made over past several decades, some important challenges that limit the wide application of these strategies in synthetic chemistry remain unsolved. Despite many successful examples involving intramolecular nucleometallation, catalytic enantioselective alkene functionalizations involving intermolecular nucleometallation remain underdeveloped. The factors that control the reactions to proceed through *cis*- or *trans*-nucleometallation pathways are still not well understood, so dictating stereochemical course is relied on substrate control in most cases. More detailed

mechanistic studies to understand the origins of the stereochemical outcomes could lead to the design of new chiral ligands and transformations in the future. The further exploration of more transformations that can be applied to the alkyl-metal intermediates generated from nucleometallation are also desired.

Chapter 2

Catalytic Conjunctive Cross-Coupling Enabled by Metal-induced Metallate Rearrangement

2.1. Introduction

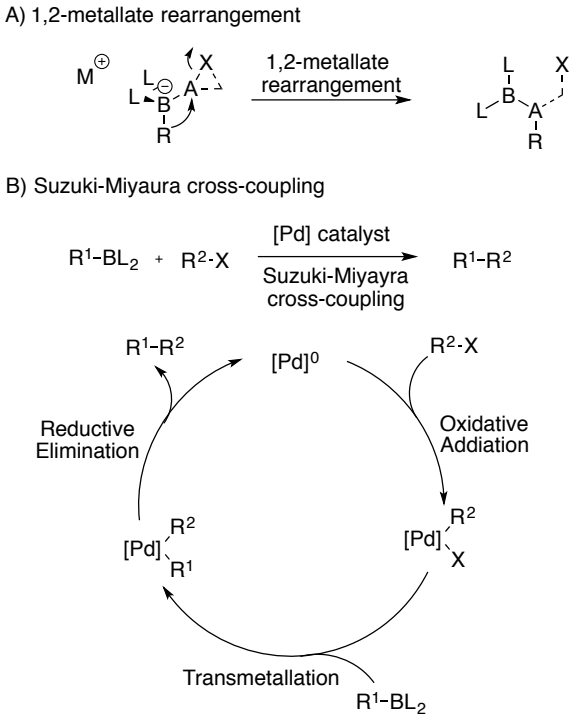
Organoboron compounds are one of the most widely used reagent classes in organic synthesis due to their environmentally benign nature and ready availability.[1] They are one of the few compound classes that show an exceptional balance between stability and reactivity. While organoboron reagents are generally chemically and configurationally stable under a variety of reaction conditions, the carbon-boron bond of these reagents can be also transformed into a broad array of carbon-heteroatom and carbon-carbon bonds, often in a stereoselective or stereosepcefic fashion.

The 1,2-metallate rearrangement, an inherent reactivity mode of organoboron compounds, enables the organoboron reagents to participate in a wide range of carbon-heteroatom and carbon-carbon bond forming reactions.[2] Upon treating a three-coordinated boron compound with stoichiometric amounts of an organometallic reagent, a four-coordinated anionic boron "ate" complex can be generated. Such a boron "ate" complex can undergo a metallate rearrangement by 1,2-carbon shift from the boron center to an adjacent electrophilic center (A) bearing a leaving group (X) (Scheme 2.1.A).

[1] Hall, D. G. Ed., Boronic Acids: Preparation and Applications in Organic Synthesis, Medicine and Materials (Wiley-VCH, Weinheim, Germany, 2011).
[2] (a) Negishi, E. I. *Org. React.* **1985**, 33, 1-246. (b) Aggarwal, V. K., Fang, G. Y., Ginesta, X., Howells, D. M., Zaja, M., *Pure Appl. Chem.* **2006**, 78, 215-229.

This process has been applied to a variety of transformations to construct carbon-carbon, carbon-oxygen, carbon-nitrogen, and other carbon-heteroatom bonds. Of note, metallate rearrangement from boron to *sp* or sp^2 centers are also established, but often require the addition of stoichiometric external electrophile to promote the rearrangement.

Scheme 2.1. 1,2-Metallate rearrangement and Suzuki-Miyaura cross-coupling



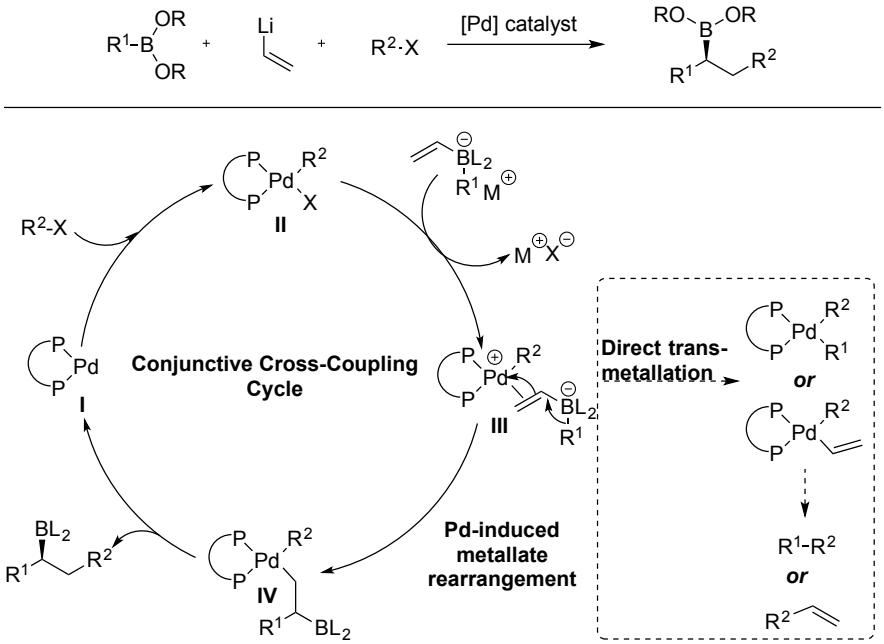
Another common reaction performed on organoboron compounds is the transition-metal catalyzed Suzuki-Miyaura cross-coupling reaction.[3] This Nobel-Prize-awarded reaction, which couples an organoboron nucleophile and an organic electrophile using a transition-metal catalyst, is one of most widely used synthetic tools in both academia and

[3] Miyaura, N., Yamada, K., Suzuki, A. *Tetrahedron Lett*. **1979**, 20, 3437-3440.

industry. In general, the Suzuki-Miyaura reaction proceeds by the following mechanism: first, oxidative addition of the transition-metal catalyst and organic electrophile occurs, which is followed by a transmetallation with the organoboron nucleophile, and the reaction ends by reductive elimination to release the product and close the catalytic cycle (Scheme 2.1.B).

As discussed above, a stoichiometric external electrophile is usually required to promote the 1,2-metallate rearrangement from boron to sp^2 centers. In this context, a π-acidic late transition-metal, such as an electrophilic palladium (II) complex generated by oxidative addition of a palladium (0) complex with an organoelectrophile, might similarly trigger the 1,2-metallate rearrangement of alkenyl boronates to furnish a chiral organometallic intermediate that may then participate in carbon-carbon bond formation by subsequent reductive elimination. In this vein, the metallate shift promoted by transition-metal catalyst can be considered as an alternative to common organometallic transmetallation and employed in a broad variety of ways. When operated as a catalytic process, this sequence constructs a product bearing two new carbon-carbon bonds and a stereogenic organoboronic ester by merging three simple starting materials: an organolithium reagent, an organoboronic ester, and an organic electrophile. This overall reaction is referred to as a "conjunctive cross-coupling" (Scheme 2.2.). In this chapter, the development of the catalytic conjunctive cross-coupling enabled by metal induced metallate rearrangement will be presented.

Scheme 2.2. Conjunctive cross-coupling



2.2. Background

2.2.1. 1,2-Metallate Rearrangement of Organoboron Compounds

2.2.1.1. 1,2-Metallate rearrangement from boron to *sp*^{3} centers

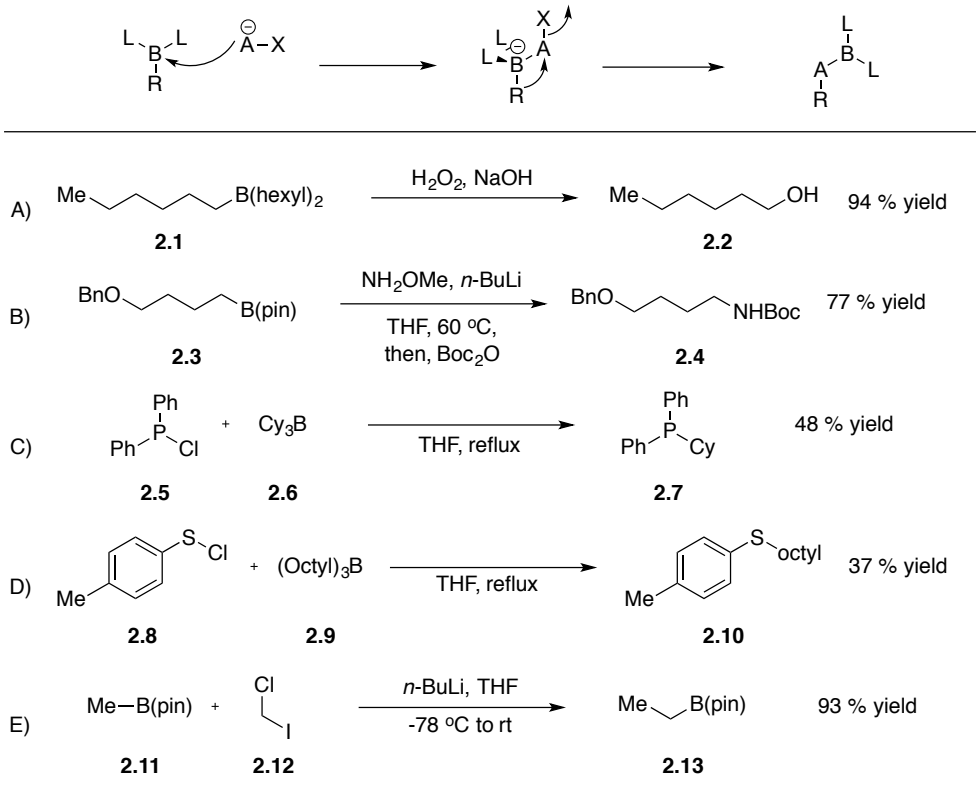
As an inherent reactivity feature, the 1,2-metallate rearrangement enables organoboron compounds to participate in a variety of carbon-boron bond transformations. Oxidizing the carbon-boron bond to the corresponding alcohol is one of the most commonly applied transformations for organoboron compounds. In 1986, H.C. Brown and co-workers[4] showed that organoboranes, boronic acids, and boronic esters could be

[4] Brown, H. C., Snyder, C., Rad, B.C. S., Zweifel, G., *Tetrahedron* **1986**, *42*, 5505.

easily transformed into the corresponding alcohols under hydrogen peroxide and sodium hydroxide conditions with good yield (Scheme 2.3.A).

Not only oxidation, the amination of carbon-boron bond has also been developed for organoboron compounds. Morken and co-workers[5] have shown that methoxyamine and *n*-butyl lithium can react with alkyl boronic acid pinacol ester **2.3** to afford amination product **2.4** in good yield. Of note, aryl, allyl, and benzylic B(pin) substrates can also be converted to the corresponding amines under the same conditions (Scheme 2.3.B).

Scheme 2.3. 1,2-metallate rearrangement from boron to sp^3 centers



[5] Mlynarski, S. N., Karns, A. S., Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 16449-16451.

In contrast to oxygen or nitrogen, sulfur and phosphorus are less common migration termini for 1,2-metallate rearrangement from boron. However, Harpp and co-workers[6] demonstrated that 1,2-metallate rearrangement onto sulfur and phosphorus centers from trialkylborane could also happen to construct new phosphorus- (Scheme 2.3.C) or sulfur-carbon bonds (Scheme 2.3.D).

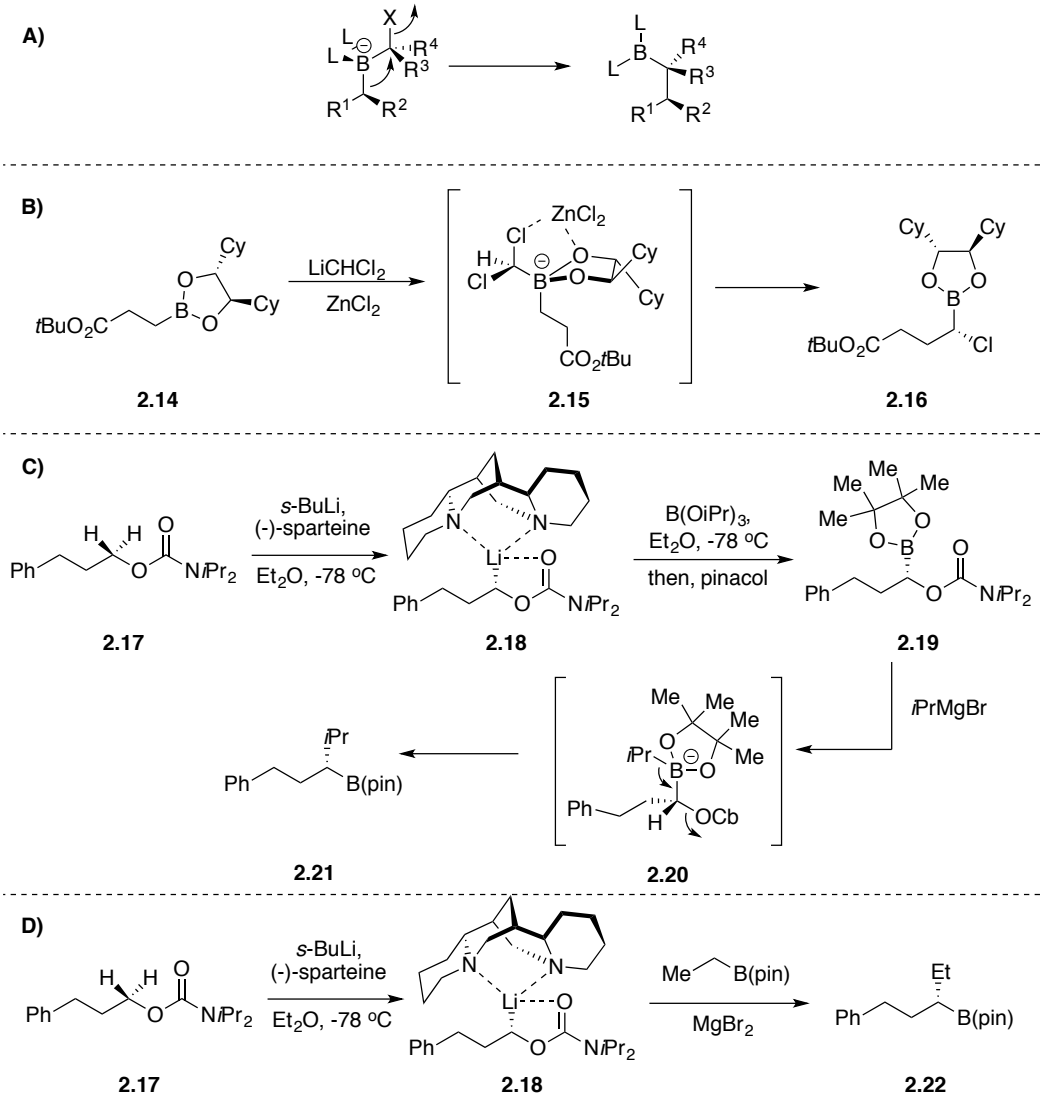
Other than construction of carbon-heteroatom bonds, 1,2-metallate rearrangement of organoboron reagents can be also applied to build new carbon-carbon bonds. Matteson and co-workers[7] contributed much of the seminal work in this field. As shown in Scheme 2.3.E, (chloromethyl)lithium generated by treating iodochloromethane **2.12** with *n*-butyl lithium reacted with methyl boronic acid pinacol ester **2.11** to form an α-chloro-borate complex. Subsequent 1,2-metallate rearrangement led to the homologous boronic ester **2.13** with good yield.

In 1979, the stereochemical outcome of 1,2-metallate rearrangement was studied by Midland and co-workers.[8] According to Midland's research, an *anti*-periplanar arrangement of the migrating carbon atom and the leaving group was required because of the stereoelectronic features of the 1,2-metallate shift. Thus, the overall process is stereoretentive at the migration group but stereoinvertive at the migration terminus (Scheme 2.4.A). Furthermore, stereoselectivity in 1,2-metallate rearrangement is generally dictated by substrate control due to the stereospecific nature of such processes.

[6] Draper, P. M., Chan, T. H., Harpp, D. N. *Tetrahedron Lett.* **1970**, 11, 1687-1688.
[7] Sadhu, K. M., Matteson, D. S. *Organometallics* **1985**, 4, 1687-1689.
[8] Midland, M. M., Zolopa, A. R., Halterman, R. L. *J. Am. Chem. Soc.* **1979**, 101, 248-249.

As an example shown by Matteson and co-workers[9], an enantiopure boronic ester **2.14** reacts with (dichloromethyl)lithium to form a (dichloromethyl)borate complex **2.15**. In the presence of $ZnCl_2$, complex **2.15** undergoes 1,2-metallate shift to afford α-chloroboronic ester **2.16** as a single diastereomer (Scheme 2.4.B).

Scheme 2.4. Stereoselective 1,2-metallate rearrangement



[9] Hiscox, W. C., Matteson, D. S. *J. Organomet. Chem.* **2000**, 614, 314-317.

As an alternative to Matteson's chiral boronic ester backbone strategy, Hoppe and co-workers[10] have shown that an enantioenriched organolithium reagent **2.18** can be generated by asymmetric lithiation of carbamate **2.17** in the presence of (-)-sparteine; subsequent borylation affords the corresponding boronic ester **2.19** with high enantioselectivity. Finally, treatment of isopropyl Grignard reagent leads to boronic ester **2.21** by stereospecific 1,2-metallate rearrangement (Scheme 2.4.C).

Hoppe's method has been further improved by Aggarwal and co-workers. Instead of trapping with borylation reagents after the asymmetric lithiation, Aggarwal has shown that the lithiated cabamate **2.18** directly reacts with ethyl B(pin) to deliver 1,2-metallate shift product **2.22** with excellent yield and enantioselectivity (Scheme 2.4.D).[11]

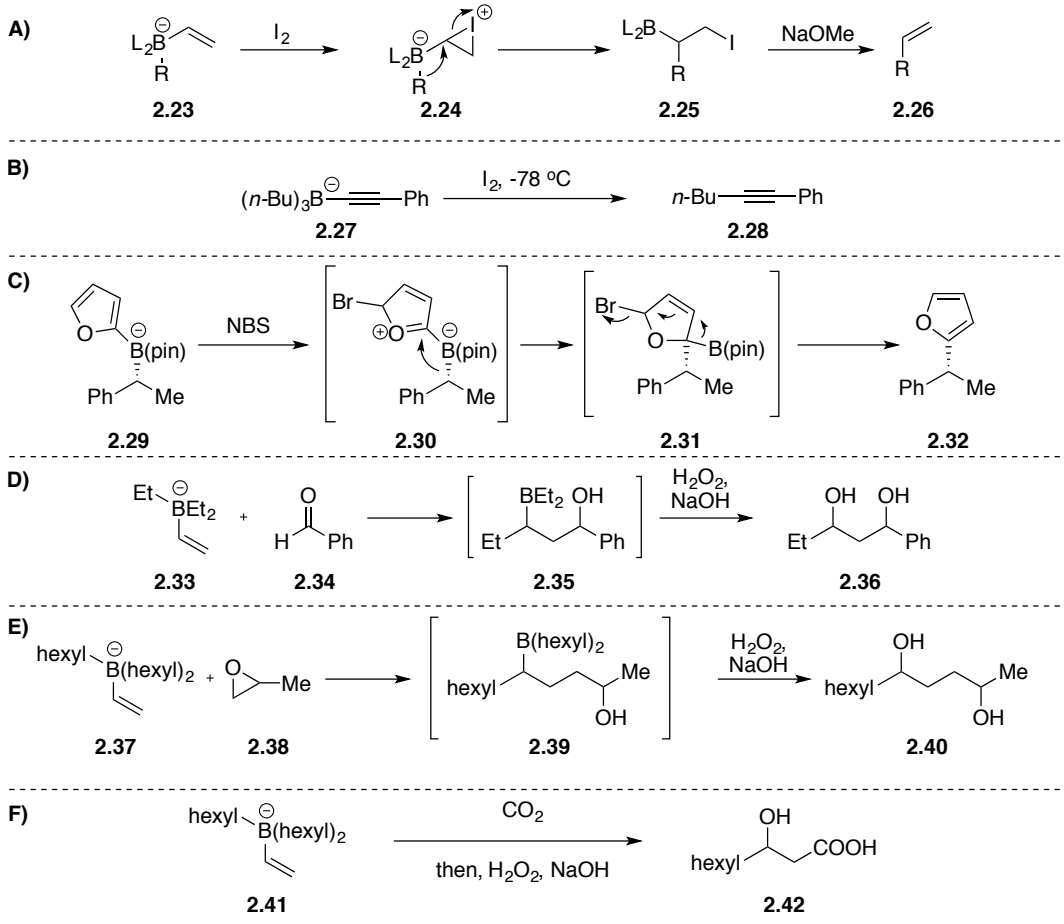
2.2.1.2. 1,2-Metallate rearrangement from boron to sp^2 and sp centers

While the 1,2-metallate rearrangement from boron to sp^3 centers has been well developed over the past several decades to construct a variety of carbon-heteroatom and carbon-carbon bonds from carbon-boron bonds, few examples have been established for the 1,2-metallate shift from boron to sp^2 or sp centers. One of the seminal examples is Zweifel-Evans olefination.[12] When a vinylborate **2.23** is treated with iodine, the π-system is activated by iodine and 1,2-metallate shift is triggered. Under basic conditions, the resulting rearranged product **2.24** undergoes elimination to reestablish unsaturation

[10] Beckmann, E., Desai, V., Hoppe, D. *Synlett* **2004**, 13, 2275-2280.
[11] Stymiest, J. L., Dutheuil, G., Mahmood, A., Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2007**, **119**, 7635-7638.
[12] (a) Zweifel, G., Arzoumanian, H., Whitney, C. C. *J. Am. Chem. Soc.* **1967**, 89, 3652-3653. (b) Evans, D. A., Walker, A. *J. Org. Chem.* **1976**, 16, 5248.

(Scheme 2.5.A). Additionally, Brown and co-workers[13] showed that iodine was also able to trigger 1,2-metallate shift from boron to a *sp* hybridized carbon center, and unsaturation was reestablished similar to Zweifel-Evans olefination (Scheme 2.5.B). Later, Aggarwal and co-workers[14] showed treatment of boron "ate" complex **2.29** with *N*-bromosuccinimide led to a stereospecific coupling product **2.32** through a 1,2-metallate rearrangement following by elimination sequence (Scheme 2.5.C).

Scheme 2.5. 1,2-metallate rearrangement from boron to sp² and sp centers



[13] Suzuki, A., Miyaura, N., Abiko, S., Itoh, M., Brown, H. C., Sinclair, J. A., Midland, M. M. *J. Am. Chem. Soc.* **1973**, 95, 3080-3081.
[14] Bonet, A., Odachowski, M., Leonori, D., Essafi, S., Aggarwal, V. K. *Nat. Chem.* **2014**, 6, 584-589.

As discussed above, 1,2-metallate rearrangements promoted by a halogen electrophile usually undergo β-elimination thereby reestablishing unsaturation. However, a few examples show that the carbon-carbon bond and carbon-electrophile bond constructed by 1,2-metallate shift survive with different classes of electrophiles. In 1977, Utimoto[15] and co-workers showed that the reaction of boron "ate" complex **2.33**, derived from triethylborane and vinyllithium, with benzaldehyde furnished 1,3-diol **2.36** by 1,2-metallate rearrangement followed by oxidation (Scheme 2.5.D). Similarly, Utimoto[16] and Deng[17] also reported that trialkylvinylborate could react with carbon dioxide or epoxides to afford corresponding products (Scheme 2.5.E and F).

2.2.2. Transmetalation in the Suzuki-Miyaura Cross-Coupling Reaction

Suzuki-Miyaura cross-coupling is one of the most important transition-metal catalyzed carbon-carbon bond forming reactions that has been developed. As described above, it proceeds through oxidative addition, transmetallation, and reductive elimination sequence. For the past several decades, a number of studies have been conducted to gain a fundamental understanding of the crucial transmetallation step where carbon migrates from boron to palladium. Two possible pathways that initially were proposed by Soderquist[18] have been considered and widely debated.

Both proposed pathways start with the same palladium (0) complex but differ in the role the hydroxide ion plays in the initial transmetallation step. For pathway A, oxidative

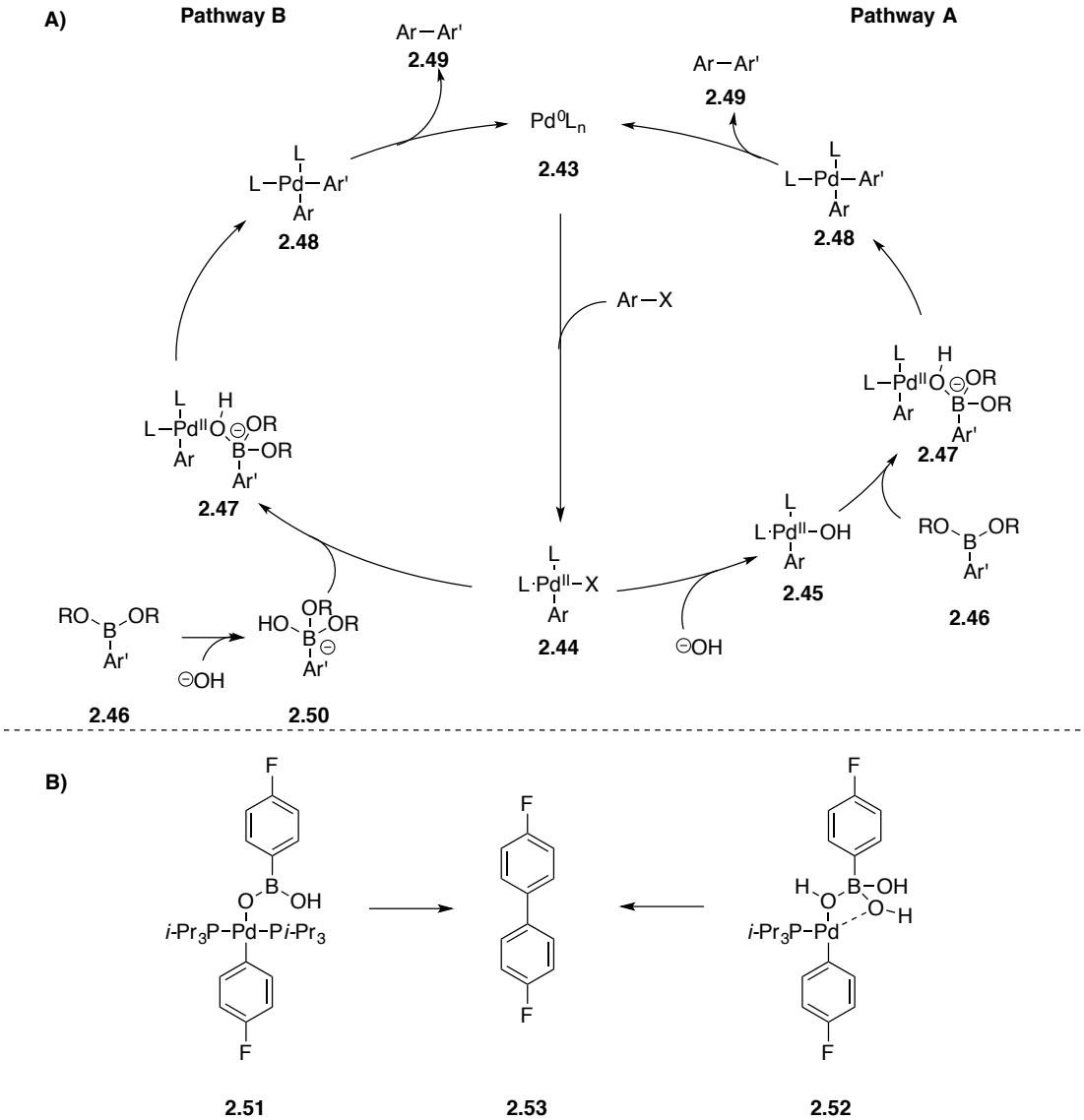
[15] Utimoto, K., Uchida, K., Nozaki, H. *Tetrahedron* **1977**, 33, 1949-1952.
[16] Utimoto, K., Uchida, K., Nozaki, H. *Tetrahedron Lett.* **1973**, 14, 4527-4528.
[17] Deng, M. Z., Lu, D. A., Xu, W. H. *J. Chem. Soc., Chem. Comm.* **1985**, 21, 1478-1479.
[18] Matos, K., Soderquist, J. A. *J. Org. Chem.* **1998**, 63, 461-470.

addition of palladium (0) complex **2.43** and aryl halide electrophile leads to palladium (II) aryl halide complex **2.44**. Then it is proposed that hydroxide ion displaces the halide to form a palladium hydroxide complex **2.45**, which combines with neutral boronic ester **2.46** to generate a Pd-O-B adduct **2.47**. The transmetallation of the Ar' group from boron to palladium is then followed by reductive elimination furnishes the cross-coupling product **2.49**. On the other hand, for pathway B, intermediate **2.44** reacts with organoboron "ate" complex **2.50**, generated by attacking the neutral organoboron reagent **2.46** with hydroxide ion to displace the halide in complex **2.44**. Pathway B furnishes the same intermediate **2.47** as in pathway A. Then similar transmetallation and reductive elimination steps lead to the same cross-coupling product and regenerate the palladium catalyst (Scheme 2.6.A).

Recently, kinetic analysis by the Hartwig laboratory[19] suggested that pathway A is favored over pathway B by more than four orders of magnitude when the cross-coupling reaction was conducted with a weak base such as carbonate or phosphate. It is worthy of note that reactions conducted with stronger base might lead to higher concentration of borate complex **2.50**, and with sufficiently stronger base, pathway B might become competitive with pathway A. Such a conclusion is further reinforced by extensive kinetic studies by Amatore, Jutand, and Schmidt laboratories.[20]

[19] Carrow, B. P., Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, 133, 2116-2119.
[20] (a) Amatore, C., Jutand, A., Le Duc, G. *Chem. Eur. J.* **2011**, 17, 2492-2503. (b) Amatore, C., Le Duc, G., Jutand, A. *Chem. Eur. J.* **2013**, 19, 10082-10093. (c) Schmidt, A. F., Kurokhtina, A. A., Larina, E. V. *Russ. J. Gen. Chem.* **2011**, 81, 1573. (d) Schmidt, A. F., Kurokhtina, A. A. *Kinet. Catal* **2012**, 53, 714-730.

Scheme 2.6. Transmetallation pathways in Suzuki-Miyarua cross-coupling



More recently, Denmark and co-workers [21] unambiguously identified and characterized the pre-transmetalation species **2.51** and **2.52** by spectroscopic analyses and independent synthesis. It was determined that both palladium-boron complexes contain Pd-O-B linkages, where complex **2.51** was constructed with a three coordinate neutral

[21] (a) Thomas, A. A., Denmark, S. E. *Science* **2016**, 352, 329-332. (b) Thomas, A. A., Wang, H., Zahrt, A. F., Denmark, S. E. *J. Am. Chem. Soc.* **2017**, 139, 3805-3821.

boron group, while complex **2.52** contains a four coordinate borate fragment. Furthermore, both pre-transmetlaltion species, complex **2.51** and **2.52**, were able to participate in the Suzuki-Miyaura cross-coupling reaction to afford coupling product **2.53** (Scheme 2.6.B).

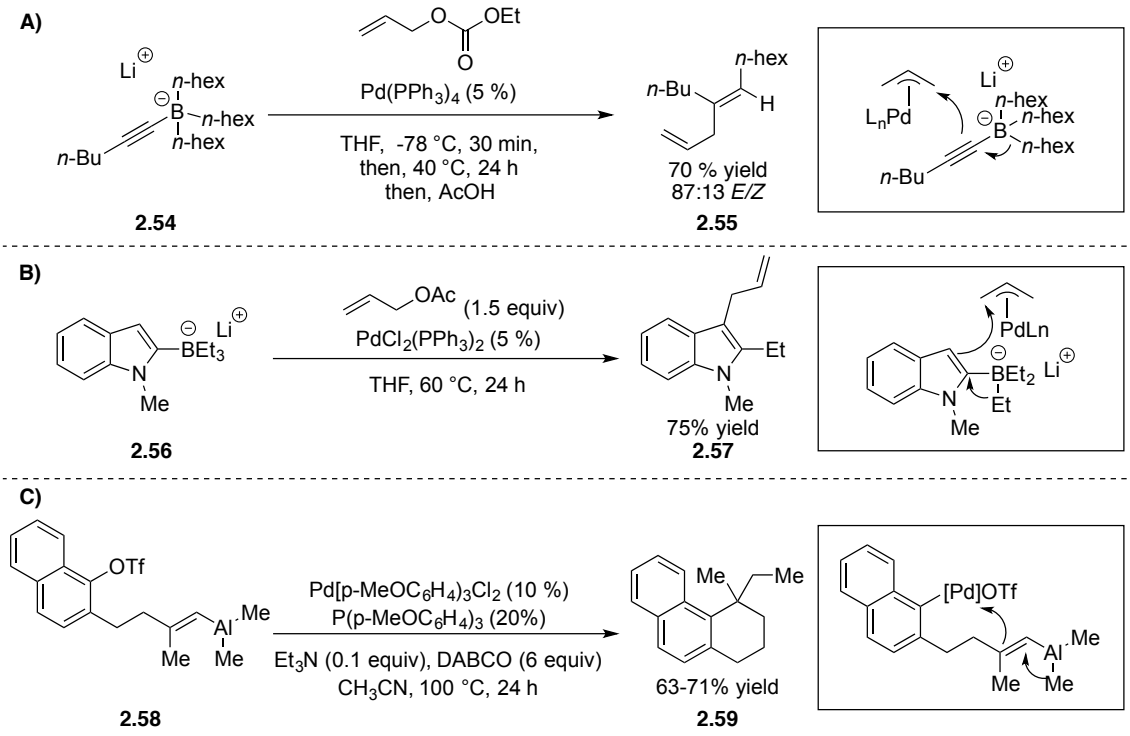
2.2.3. Metal-induced 1,2-Metallate Rearrangement

In comparison to the number of methods involving 1,2-metallate rearrangement triggered by an adjacent leaving group or stoichiometric external electrophile as discussed above, methods involving 1,2-metallate rearrangement induced by catalytic amount of a transition-metal are exceptionally rare. In this context, there are only a few examples reported over the past several decades. In 1990, Deng and co-workers[22] established an allylation reaction of (trialkyl)alkynylborate and allylcarbonate in presence of $Pd(PPh_3)_4$ as catalyst. It was proposed that a π-allylpalladium complex was generated by the reaction between allyl carbonate and $Pd(PPh_3)_4$, and such a complex was able to induce 1,2-metallate shift of (trialkyl)alkynylborate **2.54** to afford the allylation product **2.55** in 70 % yield and 87:13 *E/Z* ratio (Scheme 2.7.A). In addition to Deng's work, Ishikura and co-workers[23] have shown that the π-allyl-palladium complex generated by oxidative addition of allyl acetate to a palladium (0) complex was also a sufficient electrophile to trigger the 1,2-metallate rearrangement of an indoylborate **2.56** derived from triethylborane, and sequential elimination of the borane moiety furnished the rearomatized allylation product **2.57** in 75 % yield (Scheme 2.7.B). Moreover, an

[22] Chen, Y., Li, N. S., Deng, M. Z. *Tetrahedron Lett.* **1990**, 31, 2405-2406.
[23] Ishikura, M., Kato, H. *Tetrahedron* **2002**, 58, 9827-9838.

intramolecular cyclization reaction presented by Fillion and co-workers[24] demonstrated that a palladium (II) complex generated by oxidative addition of organotriflate to palladium (0) complex was able to induce a 1,2-metallate rearrangement from aluminum to carbon instead of from boron to carbon (Scheme 2.7.C).

Scheme 2.7. Early examples of metal induced metallate rearrangement



Lastly, Murakami and co-workers reported a set of studies focused on palladium-catalyzed cross-coupling reactions of organic electrophiles and alkynyltrialkylborates.[25]

[24] Fillion, E., Trépanier, V. E., Heikkinen, J. J., Remorova, A. A., Carson, R. J., Goll, J. M., Seed, A. *Organometallics* **2009**, 28, 3518-3531.

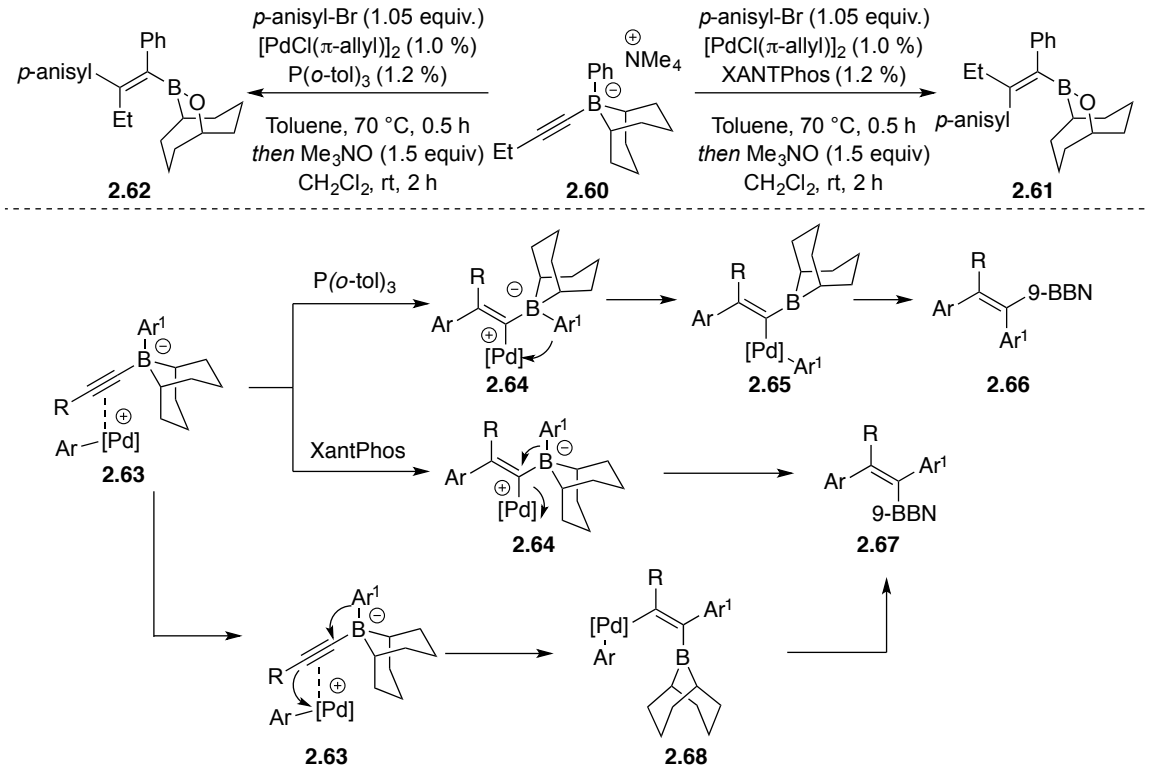
[25] (a) Ishida, N., Miura, T., Murakami, M. *Chem.Commun.* **2007**, 42, 4381-4383. (b) Ishida, N., Narumi, M., Murakami, M. *Org. Lett.* **2008**, 10, 1279-1281. (c) Ishida, N., Narumi, M., Murakami, M. *Helvetica Chimica Acta* **2012**, 95, 2474-2480. (d) Shimamoto, Y., Sunaba, H., Ishida, N., Murakami, M. *Eur. J. Org. Chem.* **2013**, 8, 1421-1424.

In one particular example[26], a palladium-catalyzed stereoselective synthesis of trisubstitued alkenyl 9-BBN compounds with organohalides and alkynylborates **2.60**, derived from aryl 9-BBN reagents, was reported (Scheme 2.8). In this study, the authors showed that ligands on the palladium catalysts were able to dictate stereochemical outcomes of the reactions. While P(*o*-tol)$_3$ ligand led to the *Z*-isomer of the product **2.62** with 97:3 selectivity, utilizing Xantphos as ligand furnished the *E*-isomer of product **2.61** exclusively. To rationalize the ligand dependent stereoselection, the authors proposed the following mechanism for this reaction: an arylpalladium species generated by oxidative addition of arylbromide to palladium (0) complex coordinated to an alkynylborate, subsequent carbopalladation across the carbon-carbon triple bond occurred in a *syn*-selective fashion to afford the alkenylpalladium complex **2.64**. When the relatively less sterically demanding P(o-tol)$_3$ was used as a ligand, enough space was provided around the palladium center to allow the aryl group on the boron to undergo a 1,3-migration to palladium to form intermediate **2.65** which, following reductive elimination, yields the product **2.66** with *syn*-addition of the two aryl groups across the alkyne. On the other hand, a more bulky bidentate ligand, such as Xantphos, occupied the space around the palladium center so that a direct 1,2-migration of the aryl group from boron to the α-carbon occurred instead of 1,3-migration. Such 1,2-migration reduced the palladium (II) species to palladium (0) while inverting the stereochemistry of the α-carbon, this results in the *anti*-addition product **2.67**. However, an alternative mechanism that led to the *anti*-addition product **2.67** was also discussed by the author. Different from the

[26] Ishida, N., Shimamoto, Y., Murakami, M. *Org. lett.* **2009**, 11, 5434-5437.

carbopalladation pathway, 1,2-metallate rearrangement might be induced by the palladium (II) complex after oxidative addition, leading to intermediate **2.68**. Subsequent reductive elimination afforded the same *anti*-addition product **2.67**.

Scheme 2.8. Proposed mechanism for Murakami reaction.



2.3. Development of Catalytic Conjunctive Cross-Coupling

As a relatively novel reaction without extensive precedent, several critical challenges needed to be addressed for the development of catalytic conjunctive cross-coupling. First, the arylpalladium (II) complex generated by oxidative addition of organic electrophile should be sufficiently π-acidic to induce 1,2-metallate rearrangement. The metal induced 1,2-metallate shift should be favored over common direct transmetallation that leads to

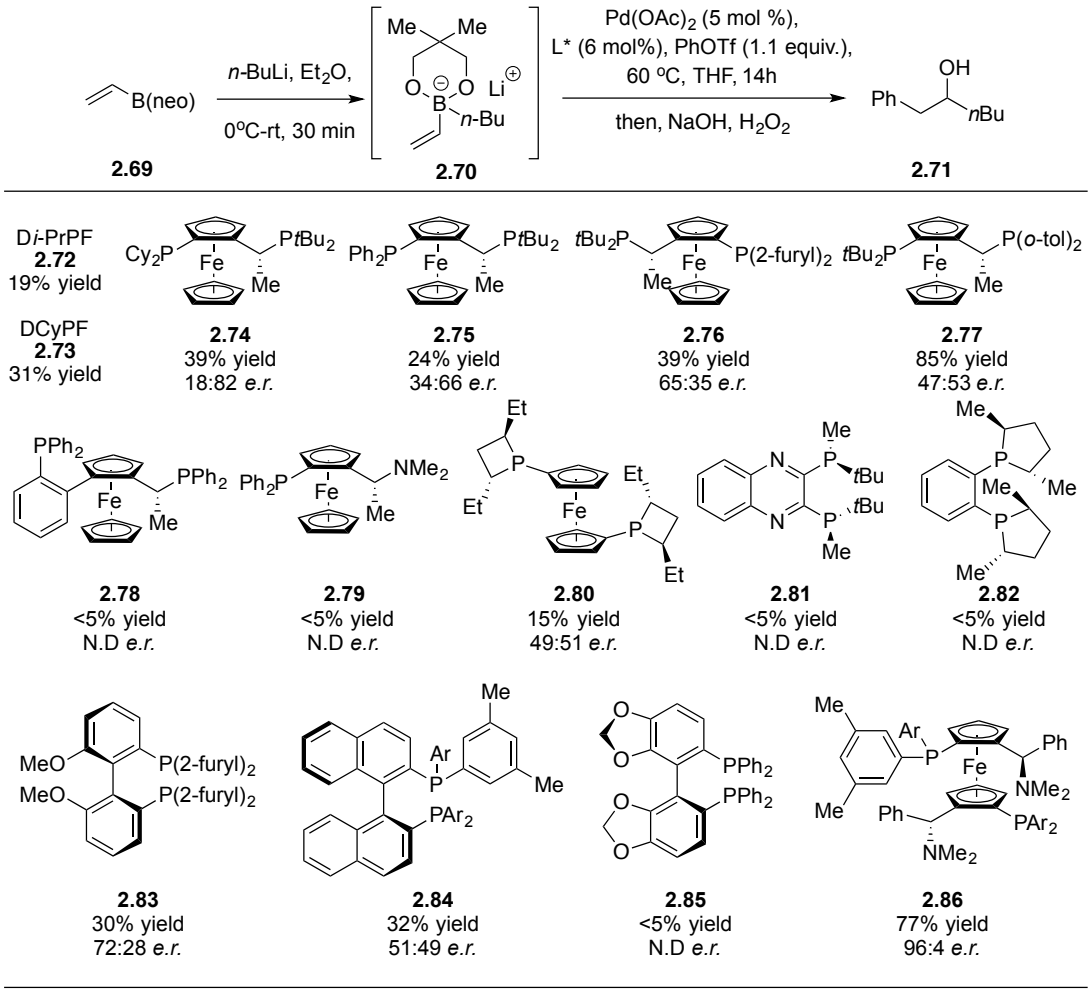
Suziki-Miyaura cross-coupling product. Moreover, the enantionselectivity of 1,2-migration should be well dictated by the facial selectivity of the palladium-olefin binding event. Last but not least, the reductive elimination should outcompete β-hydride or β-boron elimination that would furnish undesired byproducts.

To begin our investigation, phenyl triflate was selected as the model electrophile due to the dissociated nature of the triflate counterion, which would facilitate the formation of an open coordination site on palladium for alkenyl borates to bind. To minimize any possible unfavored steric interaction that might hinder the catalyst-substrate binding, an unsubstituted vinyl group was used to construct the boron "ate" complex. Furthermore, based on the recent studies by Mayr and Aggarwal[27], *neo*-pentylglycol was selected as the ligand for boron because of the higher nucleophilicity of *neo*-pentylglycolato-ligand-derived boron "ate" complex compared to other common choices. With the set of initial reagents in hand, the ligands for palladium catalyst were thoroughly investigated. The vinyl boronic acid neo-pentylglycol ester **2.69** was treated with *n*-butyl lithium to form a vinyl borate complex **2.70**, and this was subjected to 5 mol% $Pd(OAc)_2$ and 6 mol% ligand in the presence of 1.1 equivalents of phenyl triflate at 60 °C for 15 hours, subsequent oxidation furnished the corresponding alcohol **2.71** as the product. To our delight, employing 1,1'-bis(diisopropylphosphino)ferrocene (**2.72**), an electron-rich, wide-bite-angle diphosphine ligand, furnished the desired product **2.71** in 19 % yield while the major byproduct was determined to be direct Suzuki-Miyaura product.

[27] (a) Berionni, G., Leonov, A. I., Mayer, P., Ofial, A. R., Mayr, H. *Angew. Chem. Int. Ed.* **2015**, 54, 2780-2783. (b) Feeney, K., Berionni, G., Mayr, H., Aggarwal, V. K. *Org. Lett.* **2015**, 17, 2614-2617.

Switching to the more sterically hindered 1,1'-bis(dicyclohexylphosphino)ferrocene **2.73** improved the yield to 31% (Scheme 2.9).

Scheme 2.9. Initial ligand screen for conjunctive cross-coupling



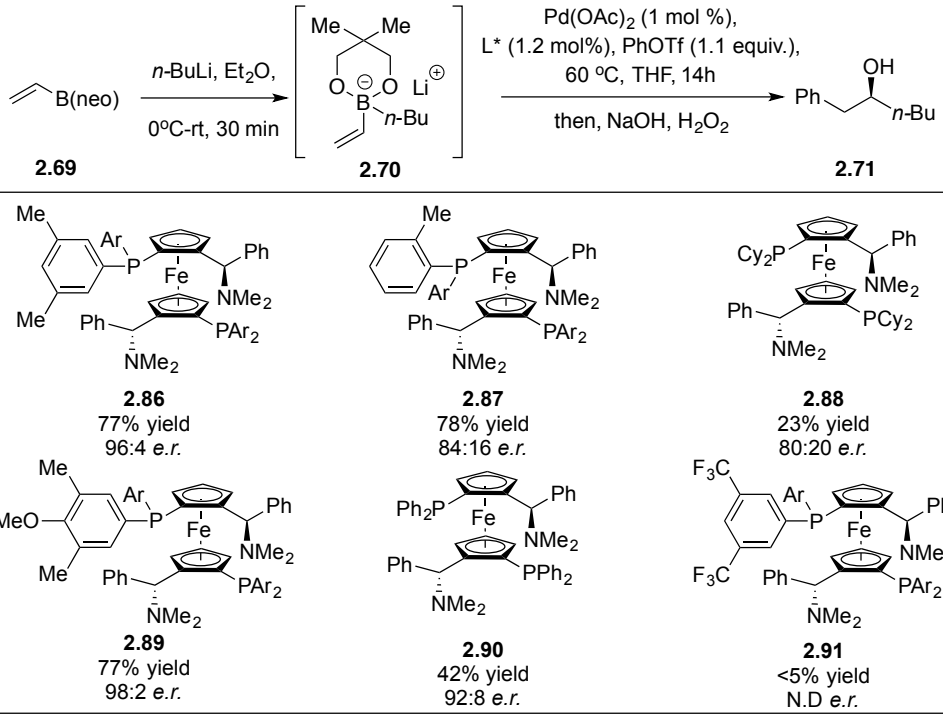
With these encouraging results for achiral ligands, a wide range of chiral ligands were examined to identify a suitable ligand that would be able to promote the conjunctive cross-coupling with good efficiency along with high enantioselectivity. Utilizing Josiphos

ligands **2.74** to **2.77**[28], a common class of ferrocene-based chiral ligands, led to conjunctive coupling product in either moderate enantioselectivity with poor efficiency (**2.74**) or good yield with poor stereoinduction (**2.77**). Other ferrocene-based chiral ligands, such as Walphos (**2.78**), PPFA (**2.79**) and FerroTANE (**2.80**), failed to promote the desired reaction with useful levels of yield and enantioselectivity. A selection of non-ferrocene-based bidentate ligands (**2.81** to **2.85**) was also investigated without any successful results. Fortunately, the desired product was obtained with 77 % yield and 96:4 *e.r.* when Mandyphos[29] **2.86** was employed in the reaction (Scheme 2.9).

With an exciting result in hand, further optimization of conjunctive cross-coupling conditions was then focused on thoroughly investigating available Mandyphos derivatives to achieve higher reaction efficiency and enantioselectivity. As summarized in Scheme 2.10, both more sterically demanding ligand **2.87** and less sterically encumbered ligand **2.90** led to lower enantioselectivity. Dialkyl substituted ligand **2.88** resulted in low reaction efficiency and stereoselectivity. While electron deficient trifluoromethyl substituted ligand **2.91** failed to promoted the conjunctive coupling, more electron rich methyloxy group substituted ligand **2.89** was determined to be the optimal ligand to yield the desire product with 77 % yield and 98:2 *e.r.*.

[28] Togni, A., Breutel, C., Schnyder, A., Spindler, F., Landert, H., Tijani, A. *J. Am. Chem. Soc*. **1994**, 116, 4062-4066.
[29] Perea, J. J. A., Lotz, M., Knochel, P. *Tetrahedron: Asymmetry* **1999**, 10, 375-384.

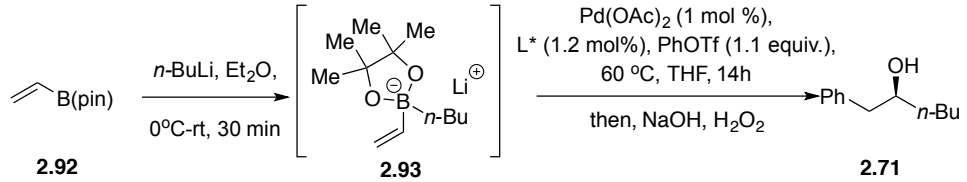
Scheme 2.10. Mandyphos optimization for vinyl B(neo) substrate



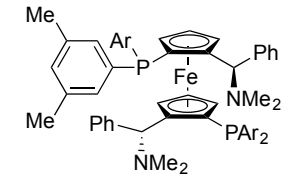
After we identified the optimal ligand for reactions of vinyl B(neo) substrates, we were also curious to see if the less nucleophilic boron "ate" complex **2.93** derived from more commonly used vinyl boronic acid pinacol ester **2.92** was also able to participate in conjunctive cross-coupling (Scheme 2.11). To our surprise, the conjunctive cross-coupling product **2.71** was furnished in moderate-to-good yield in the presence of Mandyphos derivatives as the ligands. Notably, the vinyl B(pin)-derived borate was able to afford the desired product in 22 % yield with electron deficient trifluoromethyl substituted Mandyphos, which failed to promote the desired reaction with the vinyl B(neo) substrate. However, while the reactivity was impressive for vinyl boronic acid

pinacol ester, the enantioselectivity suffered. Even with the optimal Mandyphos ligand **2.89**, only 86:14 e.r. was obtained with 66 % yield.

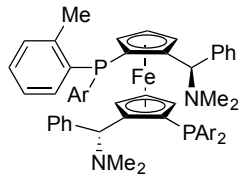
Scheme 2.11. Ligand optimization for vinyl B(pin) substrate.



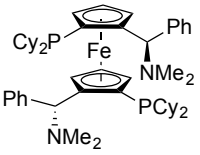
2.92 **2.93** **2.71**



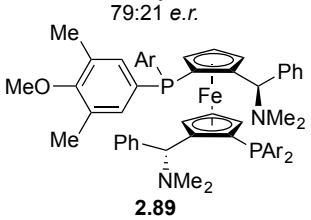
2.86
66% yield
79:21 *e.r.*



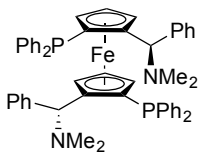
2.87
74% yield
29:71 *e.r.*



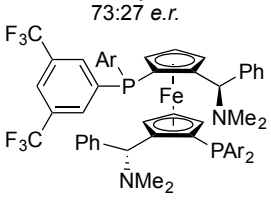
2.88
64% yield
73:27 *e.r.*



2.89
66% yield
86:14 *e.r.*



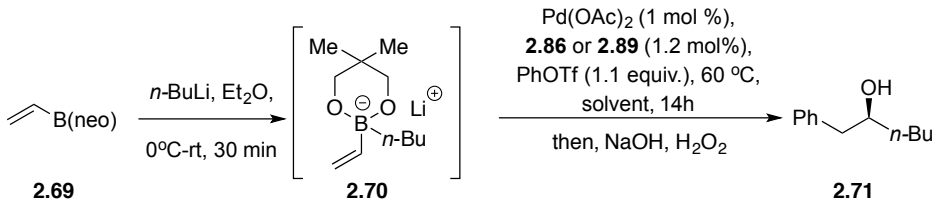
2.90
73% yield
80:20 *e.r.*



2.91
22% yield
68:32 *e.r.*

With the optimal ligands for both palladium and boron in hand, further optimization of the conjunctive cross coupling was focused on evaluating the solvent effect (Table 2.1). Employing a non-polar solvent such as toluene (entry 2) led to racemic product (49:51 e.r) in moderated yield. Non-coordinating polar solvents, such as trifluorotoluene and dichloromethane (entry 3, 4), failed to yield any desired product. The enantioselectivity was also diminished when the reaction was conducted in dioxane or diethyl ether (entry 6, 7). Ultimately, the optimal solvent for conjunctive cross-coupling reaction was determined to be THF (entry 5).

Table 2.1. Solvent optimization of conjunctive cross-coupling



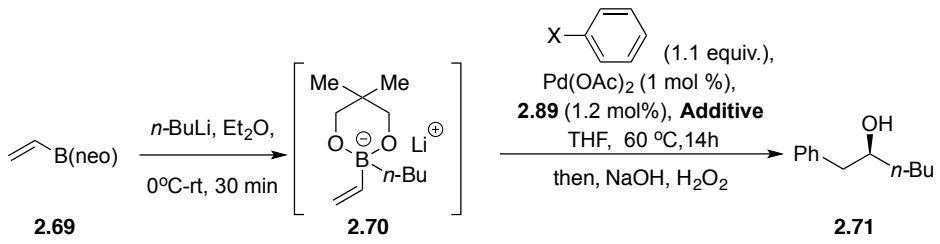
2.69 **2.70** **2.71**

Entry	Ligand	Solvent	Yield	*e.r.*
1	**2.86**	THF	77%	96:4
2	**2.86**	toluene	44%	49:51
3	**2.86**	trifluorotoluene	<5%	N.D.
4	**2.86**	DCM	<5%	N.D.
5	**2.89**	THF	77%	98:2
6	**2.89**	dioxane	65%	90:10
7	**2.89**	Et_2O	48%	92:8

With the optimal conditions determined for organotriflate electrophiles, our focus moved to investigating whether halide electrophiles were also suitable substrates for the conjunctive cross-coupling reaction (Table 2.2). When halide electrophiles, such as chloro-, bromo-, and iodobenzene (entry 1 to 3), were employed in the reaction under standard conditions, reaction efficiencies were dramatically diminished (no desired product for chlorobenzene, 9% yield for bromo- and iodobenzene), but still occurred with high enantioselectivity. The low reaction efficiency was presumably due to the coordinating nature of resulting halide anion that failed to provide an open coordination site on palladium catalyst which was required for catalyst-substrate binding. The halide inhibition effect was further evaluated by treating the standard reaction with halide salt additives. Both efficiency and enantioselectivity were eroded (23% yield, 77:23 *e.r.*,

entry 5) when the reaction was conducted in presence of 1.0 equivalent of lithium bromide, a common impurity when utilizing organolithium reagent generated by lithium halogen exchange reaction. Furthermore, even 1 mol % loading of halide salts was able to severely diminish the conjunctive coupling efficiency while the enantioselectivity remained intact (entry 6 to 8). It was also discovered that the identity of halide salts was also crucial for the inhibition ability. Iodide salts exhibited the most powerful inhibition effect (13% yield with 1 mol% loading) compared to corresponding bromide and chloride variants: the reason might be the higher binding affinity of the iodide towards the palladium catalyst. As a result, organotriflates were determined to be the optimal electrophile for conjunctive cross-coupling.

Table 2.2. Halide electrophiles and halide inhibition effect.



2.69 **2.70** **2.71**

Entry	X	Additive	Yield	*e.r.*
1	Cl	none	<5%	N.D.
2	Br	none	9%	96:4
3	I	none	9%	96:4
4	OTf	none	77%	98:2
5	OTf	LiBr (1.0 equiv.)	23%	77:23
6	OTf	LiI (1 mol %)	13%	98:2
7	OTf	LiBr (1 mol %)	41%	98:2
8	OTF	LiCl (1 mol %)	40%	98:2

2.4. Scope of Catalytic Conjunctive Cross-Coupling

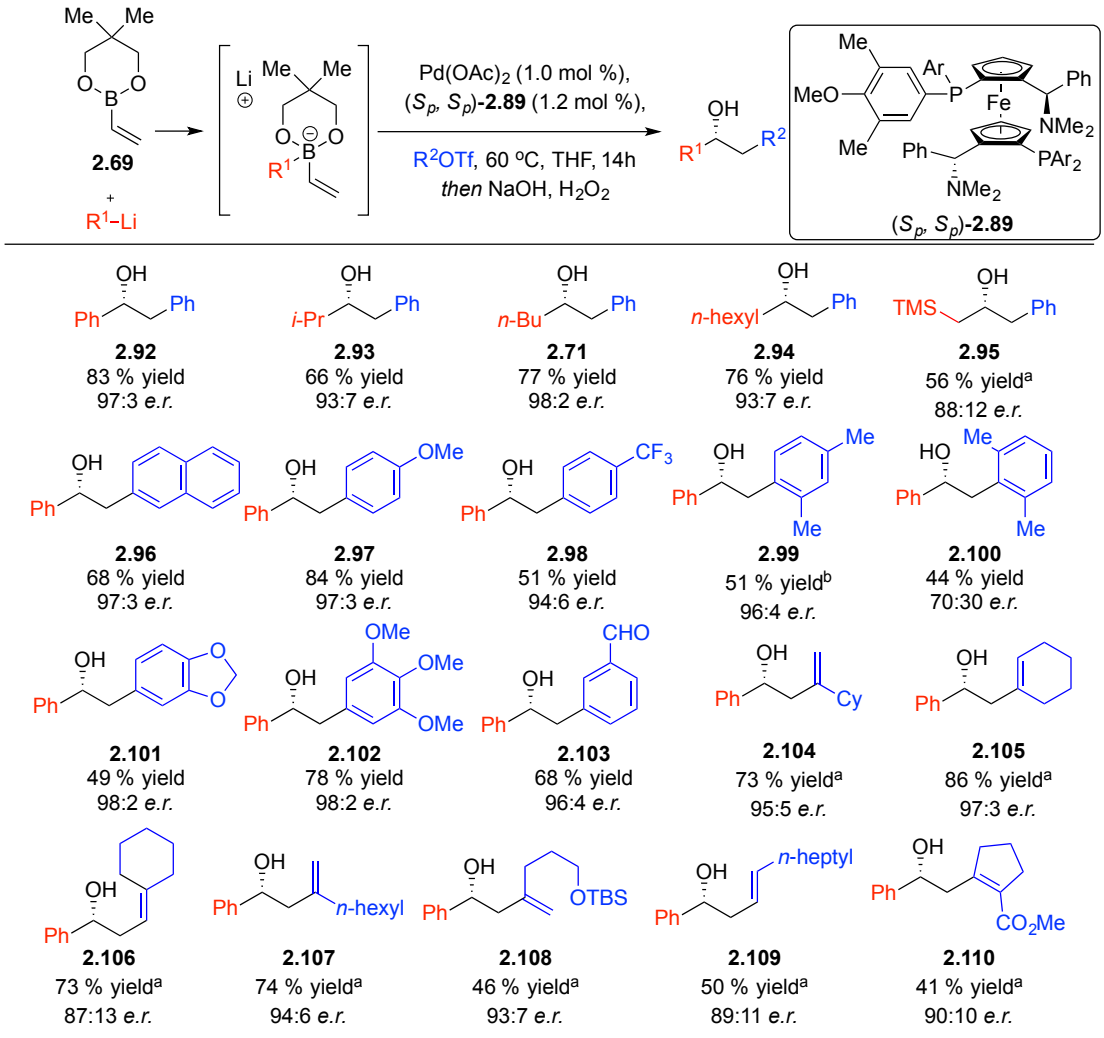
After a thorough optimization, the procedure for conjunctive cross-coupling was identified as follows: the vinyl borate complex that was generated by addition of oganolithium reagents to vinyl boronic acid *neo*-pentylglycolato ester **2.69** was treated with 1 mol% of $Pd(OAc)_2$, 1.2 mol% of Mandyphos ligand **2.89**, and 1.1 equivalents of organotriflate in the presence of THF as the solvent at 60 °C for 14 hours. With this protocol, the scope of the conjunctive cross-coupling was explored with a range of boron "ate" complexes and electrophiles.

As shown in Scheme 2.12, in addition to the test substrate **2.71**, both aryl and alkyl migrating groups behaved well in conjunctive cross-coupling to afford products **2.92** and **2.94** with high yield and enantioselectivity. Secondary alkyl (**2.93**) as well as functionalized alkyl (**2.95**) migrating groups also participated in the reaction. In terms of the electrophile scope, both electron-rich and electron-deficient organotriflates were well tolerated in the reaction. Moderately sterically demanding electrophiles, such as 2,4-dimethylphenyl triflate, could be engaged to furnish desired product **2.99** in useful level of yield and high enantioselectivity at elevated temperature, while the more hindered 2,6-dimethylphenyl derivative suffered from diminished enantioelectivity. Notably, an electrophile bearing a sensitive aldehyde functionality could also be engaged in the conjunctive coupling to afford product **2.103** with high yield and enantioselectivity.

For reactions of alkenyl triflate electrophiles, it was discovered that the reaction selectivity was remarkably improved with boron "ate" complex derived from pinacolato ligands instead of *neo*-pentylglycolato ligands. For example, compound **2.105** was

afforded in 53% yield and 82:18 *e.r.* with *neo*-pentylglycolato ligand derived borate, while 86% yield and 97:3 *e.r.* was achieved with pinacolato-derived boron "ate" complex.

Scheme 2.12. Scope of conjunctive cross-coupling with vinyl-B(neo).



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

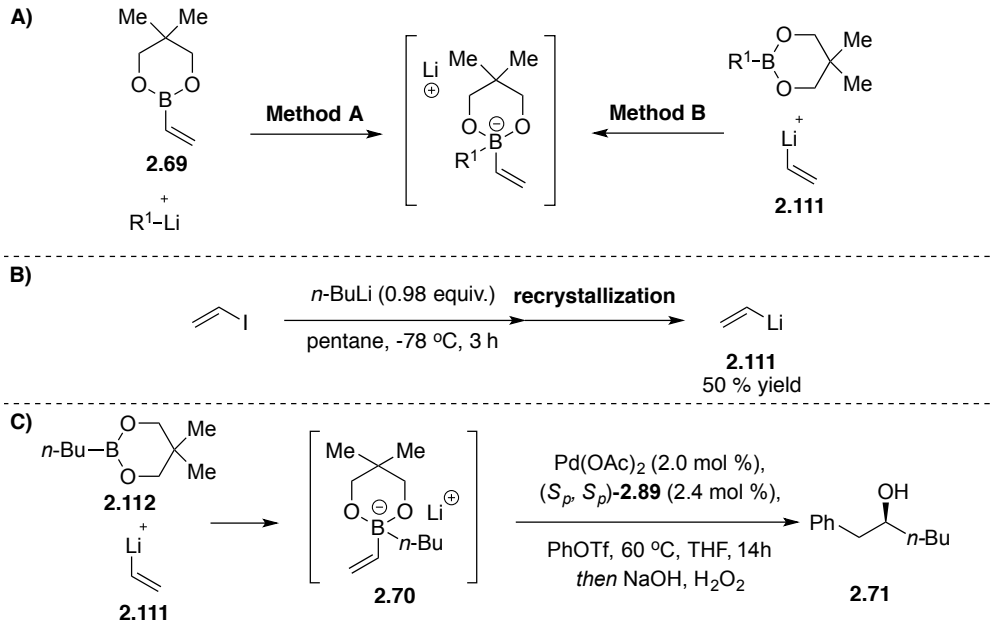
With the vinyl B(pin) as substrate, a range of alkenyl triflate electrophiles were then surveyed (compound **2.104** to **2.110**), and moderate-to-good yield and excellent

enantioselectivity were obtained. Notably, the configuration of the coupled alkene remained intact. Also note, while the organoboronic esters resulting from conjunctive coupling were generally oxidized to the corresponding alcohols for more straightforward purification and analysis, the boronic ester precursor to alcohol **2.92** could also be isolated in 76 % yield by silica gel chromatography.

One distinct advantage of the conjunctive cross-coupling is that the reactive substrate for the palladium-catalyzed process is the four coordinated boron "ate" complex, and such ate complexes can be assembled either by treating the vinylB(neo) with organolithium reagents (Scheme 2.13.A, Method A), or by addition of vinyllithium to organoboronic esters (Scheme 2.13.A, Method B). Even though some organolithium reagents were commercially available, the fact that a much broader scope of organoboronic esters were readily accessible for use in common cross-coupling reactions highlighted the practical feature of Method B. As mentioned above, it was discovered that even traces of halide impurity severely eroded the efficiency of conjunctive cross-coupling. In order to further explore the scope of conjunctive coupling with Method B, developing a synthesis of halide free vinyllithium reagents was critical. To achieve the halide free requirement for conjunctive coupling, the following procedure was developed to yield vinyllithium in high purity. Vinyl iodide was subjected to the lithium-halogen exchange condition with *n*-butyl lithium in pentane at -78 °C for 3 hours to yield vinyllithium without generating stoichiometric iodide salt, and the resulting vinyllithium was further purified by low-temperature recrystallization (Scheme 2.13.B). A test reaction conducted with *n*-butyl B(neo) **2.112** and recrystallized vinyllithium **2.111** led to

product **2.71** in 76% yield and 98:2 *e.r.* at 2 mol% catalyst loading (Scheme 2.13.C, entry 1). In contrast, while utilizing the non-recrystallized vinyllithium with 2 mol% catalyst loading, the desire product was formed in 13% yield, increasing the catalyst loading to 5 mol% restored the majority of reaction efficiency with 98:2 *e.r.* (entry 2, 3).

Scheme 2.13. Formation of the boron "ate" complex and synthesis of halide free vinyllithium

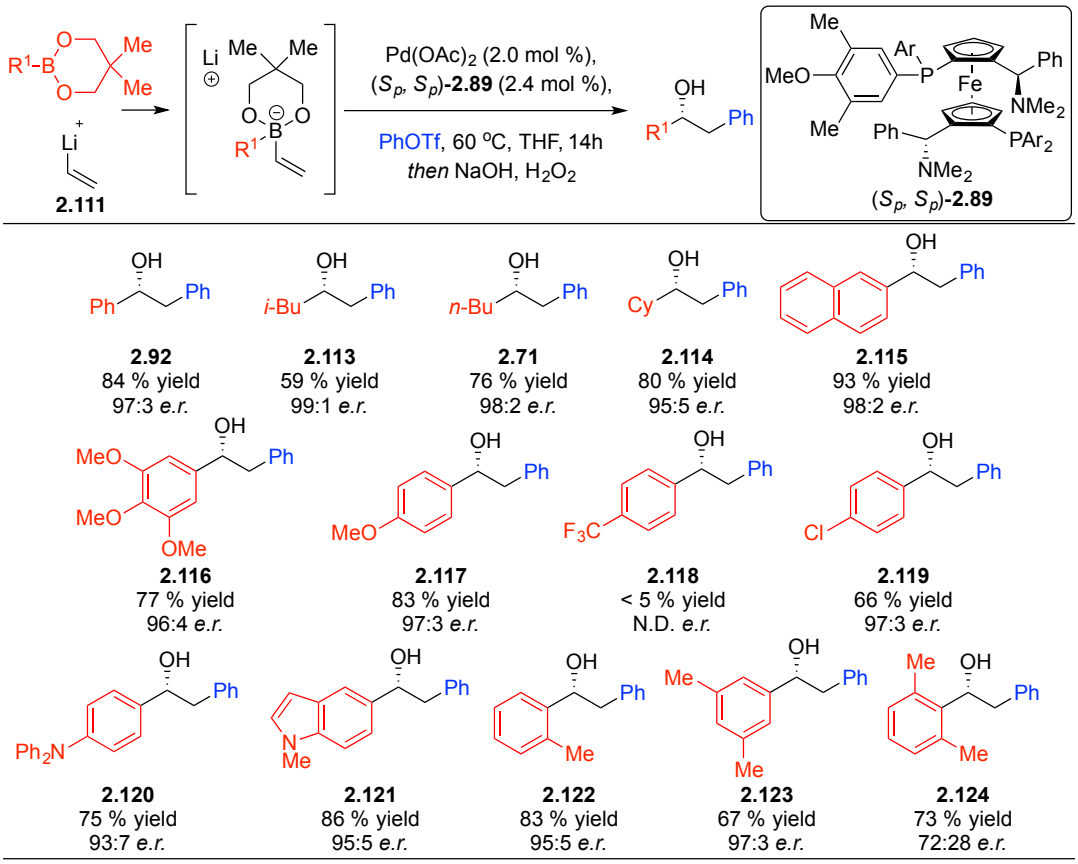


Entry	x mol %	yield	*e.r.*	note
1	2	76 %	98:2	N.A.
2	2	13 %	98:2	vinyllithium without recrystallization
3	5	69 %	98:2	vinyllithium without recrystallization

With pure vinyllithium in hand, a more thorough investigation of the scope was undertaken. It was found that similar yield and enantioselectivity was obtained using organoboronic esters and vinyllithium (Method B) compared to the same boron ate

complex generated from vinyl boronic ester and corresponding organolithium reagents (Method A) (**2.92** and **2.71**). Sterically demanding alkyl (**2.113**, **2.114**) and aryl (**2.122**, **2.123**) migrating groups were well engaged in conjunctive coupling, but highly hindered 2,6-dimethylphenyl group (**2.124**) suffered from lower enantioselectivity. Although electron-deficient migrating group remained a challenge for conjunctive coupling, electron-rich and -neutral substrates behaved well with good efficiency and selectivity. Such an observation was consistent with the initial proposed mechanism that electron-deficient migrating group might be problematic to participate in 1,2-metallate rearrangement. Notably, migrating groups bearing aryl halide (**2.119**) and coordinating functionalities, such as tertiary amine (**2.120**) and indole (**2.121**), were also well tolerated in conjunctive coupling.

Scheme 2.14. Scope of conjunctive cross-coupling with vinyllithium.

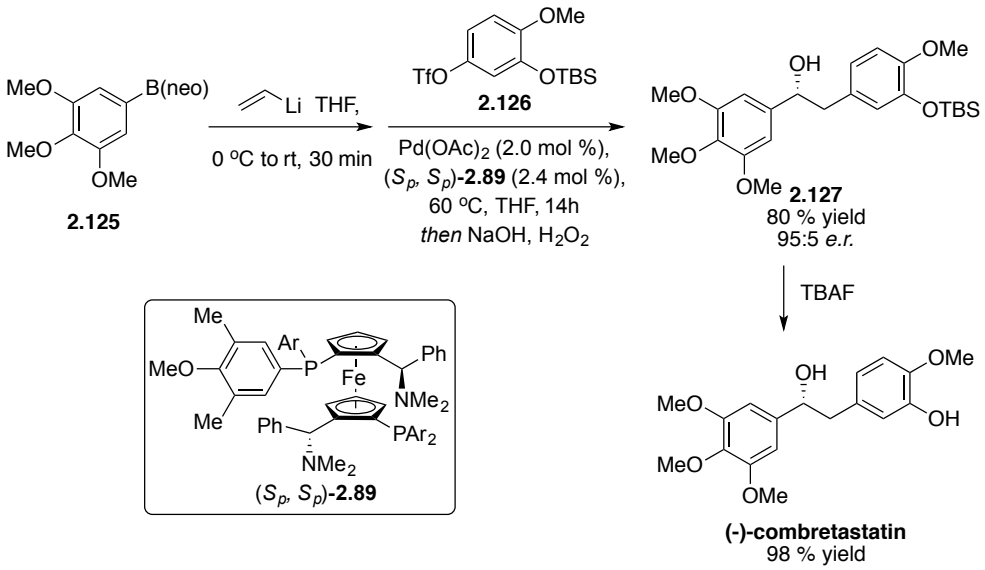


To demonstrate the synthetic utility of conjunctive cross-coupling, a total synthesis of (-)-combretastatin[30] was undertaken. As a member of a family of cytotoxic stilbene derived natural products, many synthetic approaches have been applied to the synthesis of combretastatin.[31] However, the synthesis strategy featuring with conjunctive cross-coupling provided an alternative approach that might be used to efficiently construct a library of combretastatin derivatives by utilizing different simple starting materials. As

[30] Pettit, G. R., Cragg, G. M., Herald, D. L., Schmidt, J. M., Lohavanijaya, P. *Can. J. Chem.* **1982**, 60, 1374-1376.
[31] Singh, R., Kaur, H. *Synthesis* **2009**, 15, 2471-2491.

shown in Scheme 2.15, employing vinyllithium, aryl-B(neo) **2.125** and organotriflate **2.126**, catalytic conjunctive cross-coupling afforded the coupling product **2.127** in 80 % yield and 95:5 *e.r.*. Subsequent deprotection of silyl ether led to the target in an over all a two step sequence with high efficiency and selectivity.

Scheme 2.15. Synthesis of (-)-combretastatin

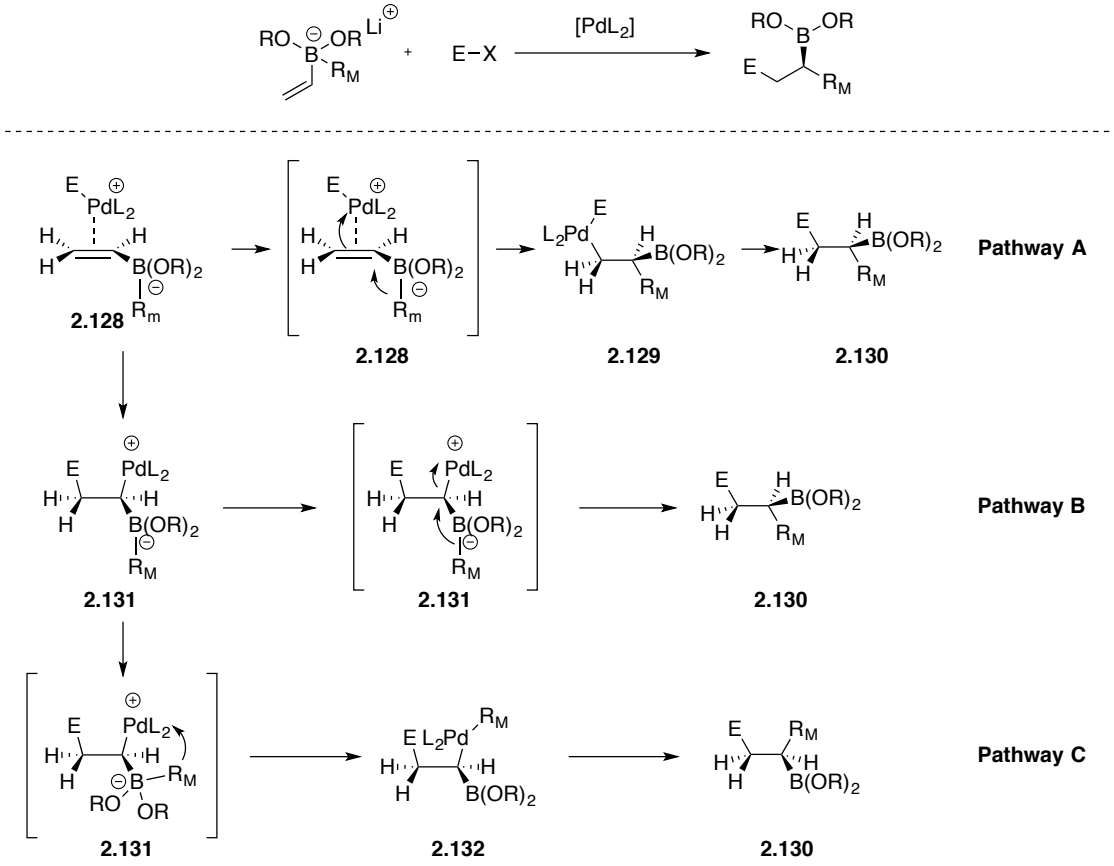


2.5. Mechanistic Discussion of Catalytic Conjunctive Cross-Coupling

Based on experimental observations, the mechanism of conjunctive cross-coupling was proposed as follows: an electrophilic palladium (II) complex generated by oxidative addition of the electrophile to palladium (0) species, coordinated to the alkene of a vinyl boron ate complex to furnish the intermediate **2.128**. This complex then underwent a palladium-induced 1,2-metallate rearrangement to afford the palladated intermediate **2.129**. Subsequent reductive elimination released the product (**2.130**) leading to a reduced palladium (0) species that might restart a new catalytic cycle (Scheme 2.17, pathway A).

In support of this proposed mechanism, it should be noted that electron-rich arenes are much better migrating groups compared to electron-poor arenes. This observation was consistent with the proposed mechanism that electron-deficient group are less prone to migrate in metal induced metallate rearrangements. Furthermore, according to the proposed pathway A, the palladium-induced 1,2-metallate shift would likely to be the stereodetermining step so that all elements that were involved in this step would affect the enantioselectivity. This hypothesis was also in agreement with our observation that the enantioselectivity was dependent on not only the ligand structure of the palladium catalyst, but also on the nature of electrophiles, ligands on the boron ate complex, and the migration groups. However, other possible reaction pathways were also considered. Similar to the mechanism Murakami proposed in his early work, intermediate **2.128** might undergo carbopalladation instead of palladium-induced 1,2-metallate shift to furnish a palladated intermediate **2.131**. The migrating group could then undergo a 1,2-migration from the boron center to the α-carbon to furnish the product **2.130** and reduce the palladium catalyst (Scheme 2.17, pathway B). On the other hand, instead of 1,2-migration, a 1,3-migration from the boron center to palladium might afford an intramolecular transmetallation product **2.132**, and subsequent reductive elimination could lead to the same product **2.130** (Scheme 2.17, pathway C).

Scheme 2.17. Proposed mechanism for conjunctive cross-coupling and possible alternative pathways.



To distinguish these possible pathways, the stereochemical outcome were carefully analyzed. For pathway A, the stereoelectronic requirements of the metallate rearrangement suggested an *anti*-periplanar arrangement of the migrating group R_M and the palladium catalyst. Assuming reductive elimination proceeded with retention of configuration at carbon, such a requirment would lead to an *anti*-addition of the migrating group and the electrophile across the olefin in the product. For pathway B, it can be assumed that the carbopalladation event would occurre through *syn*-addition of the

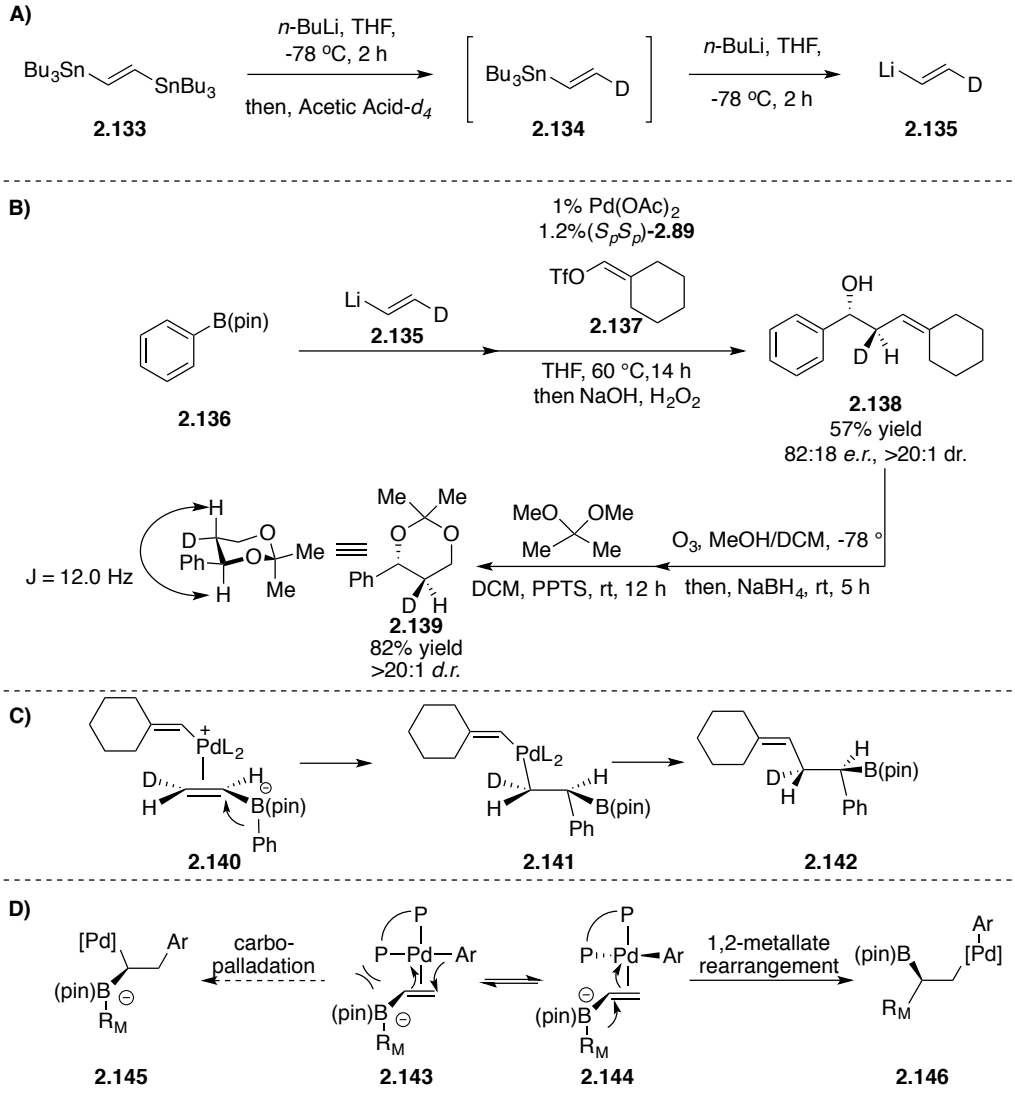
electrophile and palladium catalyst across the olefin. However, the 1,2-migration from boron to α-carbon to reduce the palladium catalyst would lead to a stereoinvertion at the α-carbon so that the overall process would still furnish the final product with an *anti*-addition of the migrating group and the electrophile across the olefin. On the other hand, for pathway C, stereoretentive intramolecular transmetallation followed by stereoretentive reductive elimination would furnish the final product with *syn*-addition of the electrophile and migrating group across the alkene.

To probe the stereochemical outcome of the conjunctive cross-coupling, a reaction with stereochemically defined deuterium-labeled vinyllithium was performed. To synthesize the *trans*-deuterium-labeled vinyllithium **2.135**[32], lithium-tin exchange by treating bis(tributylstannyl)ethylene **2.133** with 1.0 equivalent of *n*-butyl lithium, was followed by quenching with deuterated acetic acid to furnished the *trans*-deuterium-labeled vinylstannyl species **2.134**. Subsequent second lithium-tin exchange afforded the *trans*-deuterium-labeled vinyllithium **2.135** as a single stereoisomer (Scheme 2.18.A). A conjunctive cross-coupling was conducted with *trans*-deuterium-labeled vinyllithium **2.135**, phenyl B(pin) **2.136**, and alkenyl triflate electrophile **2.137** to afford (*1R, 2R*) stereoisomer of product **2.138** with greater than 20:1 diastereoselectivity. To determine the relative stereochemistry, the deuterated product **2.138** was subjected to an ozonolysis/reduction/cyclization sequence to form the cyclic compound **3.139**. The trans-relationship of the two labeled protons in structure **3.139** was determined by measuring the coupling constant in ^{1}H NMR (Scheme 2.18.B). Such a stereochemical outcome is

[32] Hughes, R. P., Trujillo, H. A., Egan, J. W., Rheingold, A. L. *J. Am. Chem. Soc.* **2000**, 122, 2261-2271.

consistent with the prediction that electrophile **2.137** and the migrating phenyl group were added across the alkene in an *anti*-addition fashion so that the pathway C was ruled out (Scheme 2.18.C).

Scheme 2.18. Deuterium labeling experiment and stereochemical outcome of conjunctive cross-coupling.



It is more challenging to differentiate pathway A and pathway B by experimental study, since the same *anti*-addition products were delivered by both pathways. However, a brief DFT calculation study performed in our laboratory suggested that a much higher activation energy barrier was associated with the carbopalladation pathway compared to the palladium induced metallate rearrangement pathway. A disfavored steric interaction between the ligand framework on the palladium catalyst and the sterically bulky boron ate complex was introduced to adopt the required conformation for carbopalladation (Scheme 2.18.D, **2.143**) so that pathway B was disfavored. Alternatively, the disfavored steric interaction could be avoided by rotated the palladium catalyst to orthogonal to the π-system (Scheme 2.18.D, **2.144**) in the transition state for 1,2-metallate rearrangement pathway.

2.6. Conclusion

In summary, a catalytic conjunctive cross-coupling that merges two nucleophiles, an organoboronic ester and an organolithium, with an organotriflate electrophile, was developed to furnish organic boronic ester products in an enantioselective and efficient fashion. Importantly, the conjunctive coupling reaction featured a novel palladium-induced metallate rearrangement step that might potentially be employed as an alternative to the direct transmetallation elementary step. We envision that many other transition-metal catalyzed reactions might be able to adopt this metal induced metallate rearrangement to provide novel approaches for catalytic enantioselective construction of synthetically useful building blocks. Several possible reaction mechanisms have been proposed and preliminary mechanistic experiments are in agreement with our proposed

mechanism. However, to further support the proposed mechanism over other possible pathways, comprehensive mechanistic experiments as well as computational studies will be required. Further studies should also focus on expanding the metal-induced metallate rearrangement to a more broad scope of other distinct transition-metal catalyzed reactions.

2.7. Experimental section

2.7.1. 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.

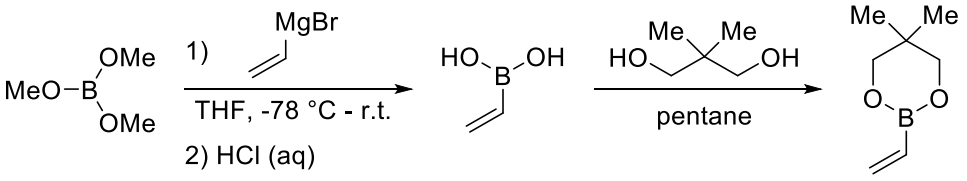
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Palladium (II) acetate, (S_p,S_p)-**2.89**, 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.

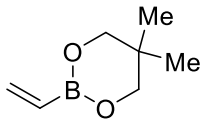
2.7.2. Experimental Procedures

2.7.2.1. Procedures for Preparation of Boronic Esters

General Procedure for the Preparation of Boronic Esters

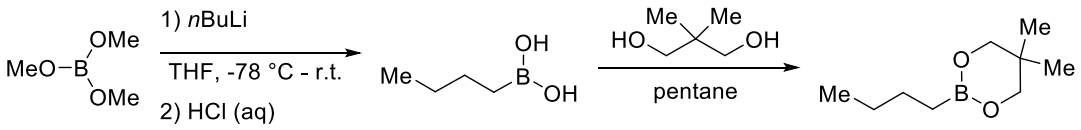
To an oven-dried round bottom flask with magnetic stir bar was added boronic acid (1.0 eq) and pentane. The suspension was cooled to 0 °C and 2,2-dimethyl-1,3-propanediol (neopentyl glycol) (1.05 eq) was added neat and the reaction solution was allowed to warm to room temperature and stirred at room 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).

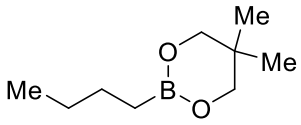




5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (2.69). To an oven-dried 250 mL round bottom flask with magnetic stir bar under N_2 was added trimethylborate (9.95 g, 95.80 mmol, 1.78 eq) and 50 ml of THF. The reaction flask was cooled to -78 °C and vinyl magnesium bromide (60 ml, 0.90M, 54 mmol, 1.0 eq) was 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

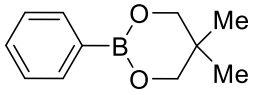
which 1M HCl *(aq)* (30 mL) was added followed by 25 mL of deionized water and the reaction solution was allowed to stir at room temperature for 2 hours. The reaction solution was extracted with 6 x 50 mL of Et_2O and the combined organic layers were washed with 50 mL of deionized water, and 50 mL of 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.



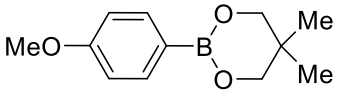


2-butyl-5,5-dimethyl-1,3,2-dioxaborinane (2.112). To an oven-dried 250 mL round bottom flask with magnetic stir bar under N_2 was added trimethylborate (11.21 g, 106.8 mmol, 1.78 eq) and 50 mL of THF. The reaction flask was cooled to -78 °C and *n*BuLi (23.72 mL, 2.53M, 60 mmol, 1.0 eq) was added over 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

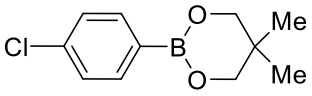
was subjected to the general procedure for preparation of boronic esters. The product was isolated as a clear colorless oil (5.26 g, 52% yield). All spectral data was in accordance with the literature.



5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane (S-1). 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 (*33*). This compound is also commercially available [CAS: 5123-13-7].



2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (S-2). 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[34].

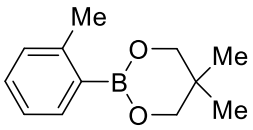


2-(4-chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (S-3). Prepared according to the general procedure above with 4-chlorophenylboronic acid (0.4691 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to

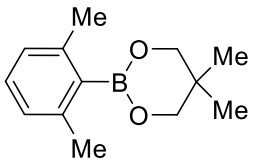
[33] M. Tobisu, H. Kinuta, Y. Kita, E. Rémond, N. Chatani, Rhodium(I)-catalyzed borylation of nitriles through the cleavage of carbon-cyano bonds. *J. Am. Chem. Soc.* **134**, 115–118 (2012). Medline doi:10.1021/ja2095975

[34] B. M. Rosen, C. Huang, V. Percec, *Org. Lett.* **2008**, 10, 2597-2600.

afford the product as a white solid (0.667 g, 99% yield). All spectral data was in accordance with the literature[35].

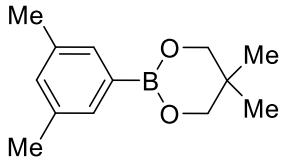


5,5-dimethyl-2-(*o*-tolyl)-1,3,2-dioxaborinane (S-4). Prepared according to the general procedure above with *o*-tolylboronic acid (0.4079 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a colorless oil (0.611 g, quantitative yield). All spectral data was in accordance with the literature[36].

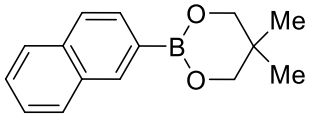


2-(2,6-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (S-5). Prepared according to the general procedure above with 2,6-dimethylphenylboronic acid (0.4499 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9.0 mL). The crude residue was purified on silica gel plug with CH_2Cl_2 to afford 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.

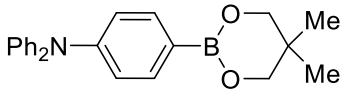
[35] Y. Zhao, V. Snieckus, *Angew. Chem. Int. Ed.* **2014**, 356, 1527-1532.
[36] K. Ukai, M. Aoki, J. Takaya, N. Iwasawa, *J. Am. Chem. Soc.* **2006**, 128, 8706-8707.



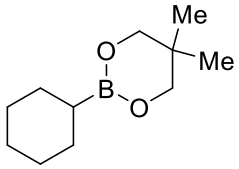
2-(3,5-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (S-5). Prepared according to the general procedure above with 3,5-dimethylphenylboronic acid (0.4499 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9.0 mmol). The crude residue was purified with silica gel plug with CH_2Cl_2 to 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-6). 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] .



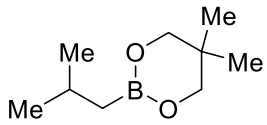
4-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-N,N-diphenylaniline (S-7). Prepared according to the general procedure above with 4-(diphenylamino)phenylboronic acid (0.4935 g, 1.7 mmol, 1 equiv.), neopentyl glycol (0.187 g, 1.79 mmol, 1.05 equiv.), and pentane (10 mL). The crude residue was purified on a silica 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[37].



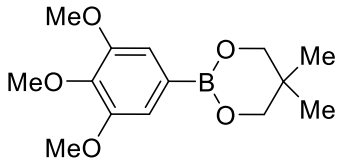
2-cyclohexyl-5,5-dimethyl-1,3,2-dioxaborinane (S-8). Prepared according to the general procedure above with cycylohexylboronic acid (1.98 g, 15.5 mmol), neopentyl glycol (1.70 g, 16.28 mmol),

[37] W. Goodall, J. A. Williams, *Chem. Commun.* **2001**, 23, 2514-2515.

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[38].

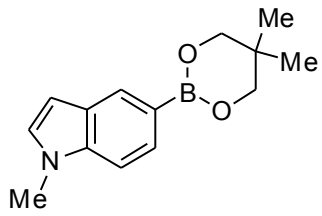


2-isobutyl-5,5-dimethyl-1,3,2-dioxaborinane (S-9). Prepared according to the general procedure above with (2-methylpropyl)boronic acid (0.3058 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a colorless oil (0.398 g, 78% yield). All spectral data was in accordance with the literature[39].



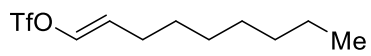
5,5-dimethyl-2-(3,4,5-trimethoxyphenyl)-1,3,2-dioxaborinane (S-10). Prepared according to the general procedure above with 3,4,5-trimethoxyphenylboronic acid (1.91 g, 9.0 mmol), neopentyl glycol (0.984 g, 9.45 mmol), and pentane (100.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 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.

[38] S. K. Bose, K. Fucke, L. Liu, P. G. Steel, T. B. Marder, *Angew. Chem. Int. Ed.* **2014**, 53, 1799-1803.
[39] A. L. Barsamian, Z. Wu, P. R. Blakemore, *Org. Biomol. Chem.* **2015***,* 13, 3781-3786.



5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1-methyl-1*H*-indole (S-11). 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.

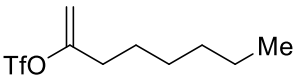
2.7.2.2. Procedures for Preparation of Alkenyl and Aryl Trifluoromethanesulfonates



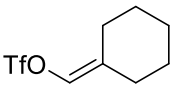
***(E)*-non-1-en-1-yl trifluoromethanesulfonate (S-12).** The title compound was prepared according to a literature precedence with slight modification[40]. In an Ar-filled glove box, CsF (5.01 g, 33.0 mmol, 3.0 equiv.) and N-Phenyl-bis(trifluoromethanesulfonimide) (7.86 g, 22.0 mmol, 2.0 equiv.) were placed in a large pressure vessel and sealed. Outside the glovebox the flask was briefly opened and a

[40] M. S. McCammant, L. Liao, M. S. Sigman, *J. Am. Chem. Soc.* **2013**, 135, 4167-4170.

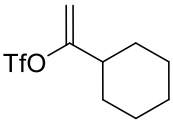
solution of 1-nonen-1-yl trimethylsilyl ether[41] (95/5 mixture of E/Z isomers, 2.36 g, 11 mmol) in dimethoxyethane (30 mL) was added. After addition the pressure vessel was quickly sealed with a screw cap. The solution was stirred vigorously at room temperature for 4 hours after which the pressure was 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[42].



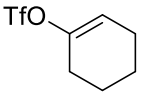
oct-1-en-2-yl trifluoromethanesulfonate (S-13). The title compound was prepared according to the procedure reported in the literature[43]. All spectral data was in accordance with the literature.



cyclohexylidenemethyl trifluoromethanesulfonate (S-14). The title compound was prepared according to the procedure reported in the literature[44]. All spectral data was in accordance with the literature.



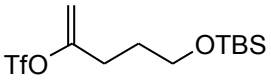
1-cyclohexylvinyl trifluoromethanesulfonate (S-15). The title compound was prepared according to the procedure reported in the literature[45]. All spectral data was in accordance with the literature.



cyclohex-1-en-1-yl trifluoromethanesulfonate (S-16). The title compound was prepared according to the procedure reported in the literature[46]. All

[41] S. Matsuzawa, Y. Horiguchi, E. Nakamura, I. Kuwajima, *Tetrahedron* **1989**, 45, 349-362.
[42] E. Shirakawa, Y. Imazaki, T. Hayashi, *Chem. Commun.* **2009,** 5088-5090.
[43] K. Takai, K. Sakogawa, Y. Kataoka, K. Oshima, K. Utimoto, *Org. Synth.* **1995**, 72, 180.
[44]P. J. Stang, W. Treptow, *Synthesis* **1980**, 283-284.
[45] M. H. Al-huniti, S. D. *Org. Lett.* **2014***,* 16, 4154-4157.

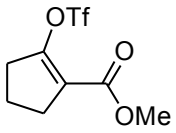
spectral data was in accordance with the literature.



5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-2-yl trifluoromethanesulfo-nate (S-17). Prepared following a published procedure with slight modifications. 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 °C 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°C 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

[46] B. Y. Lim, B. E. Jung, C. G. Cho, *Org. Lett.* **2014**, 16, 4492-4495.

(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.

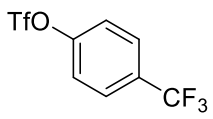


5-hydroxypent-1-en-2-yl trifluoromethanesulfonate (S-18). The title compound was prepared according to the procedure reported in the literature[47]. All spectral data was in accordance with the literature.

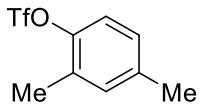
General Procedure for the Synthesis of Aryl Trifluoromethanesulfonates

Aryl Trifluoromethansulfonates were made according to literature procedure with slight modification[48]. 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.

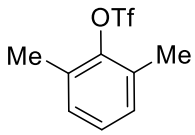
[47] A. W. J. Logan, J. S. Parker, M. S. Hallside, J. W. Burton, *Org. Lett.* **2012**, 14, 2940-2943.
[48] L. J. Goossen, C. Linder, N. Rodríguez, P. P. Lange, *Chem. Eur. J.* **2009**, 15, 9336-9349.



4-(trifluoromethyl)phenyl trifluoromethanesulfonate (S-19). 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[49].



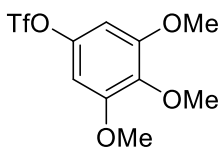
2,4-dimethylphenyl trifluoromethanesulfonate (S-20). Prepared according to the general procedure above with 2,4-dimethylphenol (0.906 mL, 7.5 mmol), trifluoromethanesulfonic anhydride (1.50 mL, 9.0 mmol), pyridine (1.2 mL, 15.0 mmol), and CH_2Cl_2 (13.0 mL). The crude residue was purified with silica 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[50].



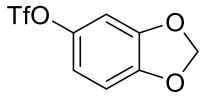
2,6-dimethylphenyl trifluoromethanesulfonate (S-21). Prepared according to the general procedure above with 2,6-dimethylphenol (0.611 g, 5.0 mmol), trifluoromethanesulfonic anhydride (1.0 mL, 6.0 mmol), pyridine (0.809 mL, 10.0 mmol), and CH_2Cl_2 (8.0 mL). The crude residue was purified with silica gel chromatography (17% ethyl acetate in hexanes) to afford the

[49] D. Gill, A. J. Hester, G. C. Lloyd-Jones, *Org. Biomol. Chem.* **2004**, 2, 2547-2548.
[50] G. Radivoy, F. Alonso, M. Yus, *Tetrahedron* **1999**, 55, 14479-14490.

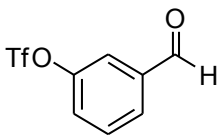
product as a yellow oil (1.124 g, 88% yield). All spectral data was in accordance with the literature[51].



3,4,5-trimethoxyphenyl trifluoromethanesulfonate (S-22). 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[52].



benzo[*d*][1,3]dioxol-5-yl trifluoromethanesulfonate (S-23). 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[53].

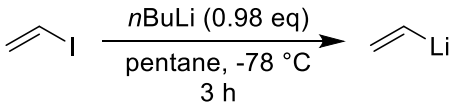


3-formylphenyl trifluoromethanesulfonate (S-24). Prepared according to the general procedure above with 3-hydroxybenzaldehyde (916 mg, 7.5 mmol), trifluoromethanesulfonic anhydride (1.5 mL, 9.0 mmol), pyridine (1.2 mL, 15.0 mmol), and CH_2Cl_2 (10 mL). The crude residue was purified by silica gel chromatography (10% ethyl acetate in hexanes)

[51] H. Mori, T. Matsuo, Y. Yoshioka, S. Katsumura, *J. Org. Chem.* **2006**, 71, 9004-9012.
[52] D. Macmillan, D. W. Anderson, *Org. Lett.* **2004**, 6, 4659-4662.
[53] A. M. Echavarren, J. K. Stille, *J. Am. Chem. Soc.* **1987**, 109, 5478-5486.

to afford the product as a colorless oil (1.47 g, 77% yield). All spectral data was in accordance with the literature[47].

2.7.2.3. 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 (12.2 g, 76.7 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, 75.1 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

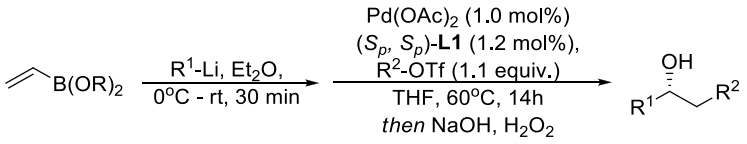
air from entering the schlenk filter and reacting with the pyrophoric vinyllithium). After the pentane was removed, a white powdery layer of solid vinyllithium was observed on top of the Schlenk filter frit. The second half of the vinyllithium suspension was transferred and the pentane removed in the 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 (72.8 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 °C over 1 h using a Cryocool

and maintaining this temperature overnight (10 h) and then reducing the temperature to -78 °C 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.

2.7.2.4. Procedures for Conjunctive Cross-Coupling

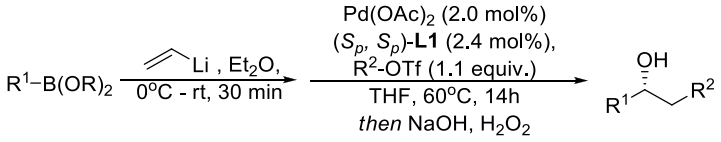
Method A:



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 °C, and an alkyl/aryl 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 stirbar in the glovebox was added $Pd(OAc)_2$ (0.003 mmol, 0.01 equiv.), (S_p, S_p)-**2.89** (0.0036 mmol, 0.012 equiv.), and THF (0.3 mL). The $Pd(OAc)_2$/(S_p, S_p)-**2.89**

solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**2.89** 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.

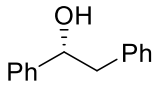
Method B:



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)-**2.89** (0.0072 mmol, 0.024 equiv.), and THF (0.6 mL). The $Pd(OAc)_2$/(S_p, S_p)-**2.89** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**2.89** 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, and subsequently purified via silica gel column chromatography to afford the desired products.

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



(R)*-1,2-diphenylethan-1-ol (2.92).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.69**) (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)-**2.89** (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.)[54].

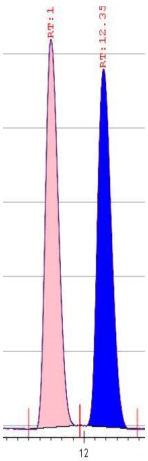
Analysis of Stereochemistry:

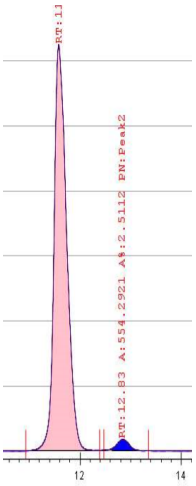
Racemic compound was prepared according to the general procedure (***Method A***) with vinyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was determined by single crystal X-ray diffraction.

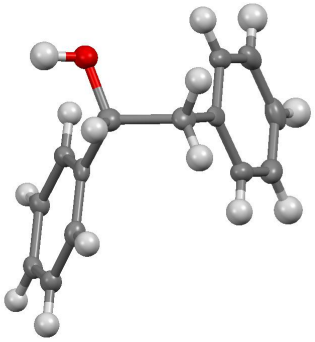
[54] J. Guo, J. Chen, Z. Lu, *Chem. Commun.* **2015**, 51, 5725-5727.

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 Standard Conditions Crystal Structure

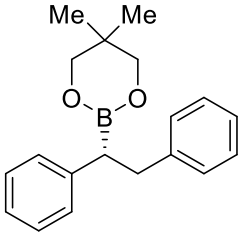






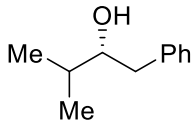
Peak No	% Area	Area	RT (min)
1	50.2599	8450.5728	11.4
2	49.7401	8363.1658	12.35
Total:	100	16813.7386	

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



(*R*)-2-(1,2-diphenylethyl)-5,5-dimethyl-1,3,2-dioxaborinane. The reaction was performed according to the general procedure ***(Method A)*** without oxidation step with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.69**) (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)-**2.89** (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 (2.93).** The reaction was performed according to the general procedure **(*Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.69**) (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)-**2.89** (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)

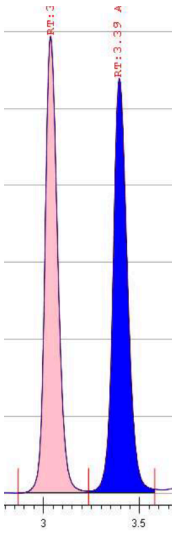
cm^{-1}. HRMS (DART) for $C_{11}H_{20}NO$ $[M+NH_4]^+$: calculated: 182.1545, found: 182.1547. $[\alpha]^{20}_D$: +15.74 (c = 0.535, $CHCl_3$, *l* = 50 mm).

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 **2.71, 2.92, and 2.94**).

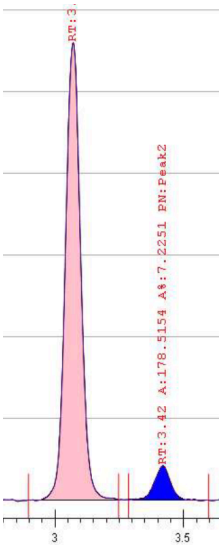
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (R)-3-methyl-1-phenylbutan-2-ol.

Racemic Material

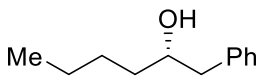


Peak No	% Area	Area	RT (min)
1	49.2988	5449.2883	3.04
2	50.7012	5604.3147	3.39
Total:	100	11053.603	

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 (2.71).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.69**) (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)-**2.89** (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.)[55].

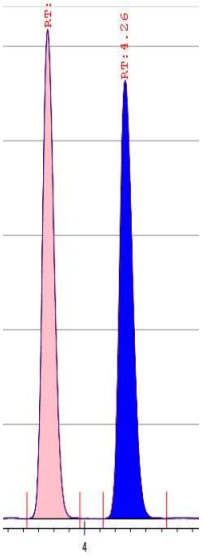
Analysis of Stereochemistry:

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

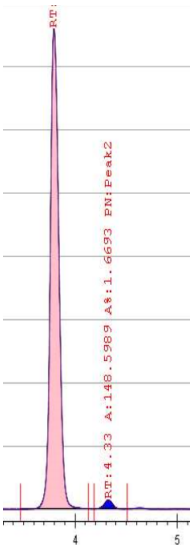
[55] T. Ema, N. Ura, M. Yoshii, T. Korenaga, T. Sakai, *Tetrahedron* **2009**, 65, 9583-9591.

Racemic Material

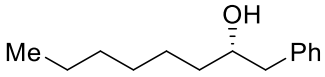


Peak No	% Area	Area	RT (min)
1	49.8946	5442.8203	3.76
2	50.1054	5465.8191	4.26
Total:	100	10908.6394	

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 (2.94).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.69**) (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)-**2.89** (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:

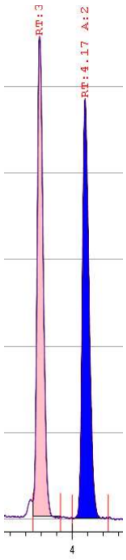
224.2016. $[\alpha]^{20}_{D}$: +11.444 (c = 1.645, $CHCl_3$, *l* =50 mm). (lit: $[\alpha]^{20}_{D}$ = +8.222 (c = 2.043, $CHCl_3$, *l* = 50 mm 96:4 e.r.). All spectral data was in accordance with the literature[56].

Analysis of Stereochemistry:

Racemic compound was prepared according to the literature. Absolute stereochemistry was determined by comparison to the literature.

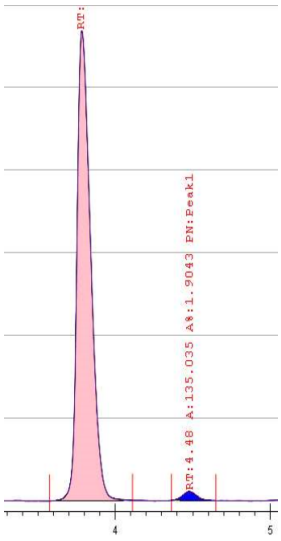
Chiral SFC (Chiracel OD-H, 3% IPA, 5 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-phenyloctan-2-ol

Racemic Material



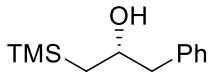
Peak No	% Area	Area	RT (min)
1	50.7244	2991.7195	3.58
2	49.2756	2906.2689	4.17
Total:	100	5897.9884	

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	

[56] S. N. Mlynarski, C. H. Schuster, J. P. Morken, *Nature* **2014**, 505, 386-390.



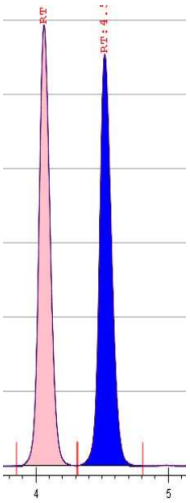
***(R)*-1-phenyl-3-(trimethylsilyl)propan-2-ol (2.95).** The reaction was performed according to the general procedure *(**Method A**)* with vinyl boronic acid pinacol ester (46.20 mg, 0.30 mmol, 1.00 equiv.), (trimethylsilyl)methyllithium (0.300 mL, 1.0M in pentane, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (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)-**2.89** (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 **2.71, 2.92, and 2.94**).

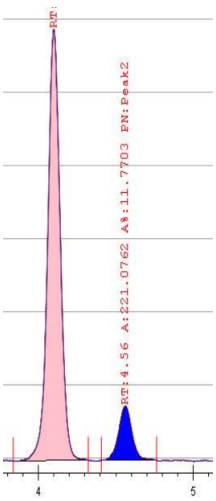
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenyl-3-(trimethylsilyl)propan-2-ol.

Racemic Material

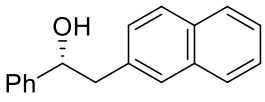


Peak No	% Area	Area	RT (min)
1	49.9308	3484.2905	4.06
2	50.0692	3493.9499	4.52
Total:	100	6978.2404	

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 (2.96).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.69**) (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)-**2.89** (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

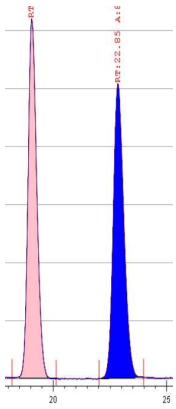
mg, 68% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (1H, d, *J* = 6.6 Hz), 7.78 (1H, d, *J* = 8.4 Hz), 7.48-7.42 (2H, m), 7.38 (2H, d, *J* = 7.2 Hz) 7.30-7.26 (4H, m) 4.99 (1H, ddd, *J* = 7.8, 4.2, 2.4 Hz), 3.20 (1H, dd, *J* = 14.4, 4.8 Hz), 3.15 (1H, dd, *J* = 13.8, 9.0 Hz), 1.99 (1H, d, *J* = 3.0 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 **2.71, 2.92, and 2.94**).

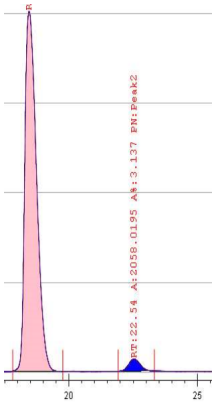
Chiral SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(naphthalen-2-yl)-1-phenylethan-1-ol.

Racemic Material

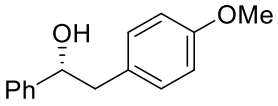


Peak No	% Area	Area	RT (min)
1	50.215	8280.1194	19.03
2	49.785	8209.2224	22.85
Total:	100	16489.3418	

Standard Conditions



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 (2.97).** The reaction was performed according to the general procedure (Method A***) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.69**) (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)-**2.89** (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

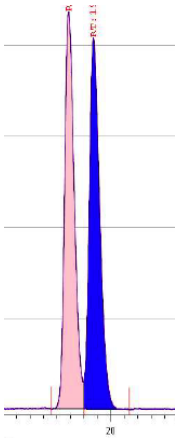
(1H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.6, 144.0, 130.6, 130.1, 128.6, 127.7, 126.0, 114.1, 75.6, 55.4, 45.3; IR (neat) ν_{max} 3407.9 (br), 2999.5 (m), 2834.9 (m), 1611.0 (m), 1583.6 (w), 1510.0 (s), 1453.3 (m), 1242.4 (s), 1176.6 (m), 1031.5 (s), 820.1 (m), 699.1 (s) cm^{-1}; HRMS-(DART) for: $C_{15}H_{15}O_1$ $[M+H-H_2O]^+$: 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 **2.71, 2.92, and 2.94**).

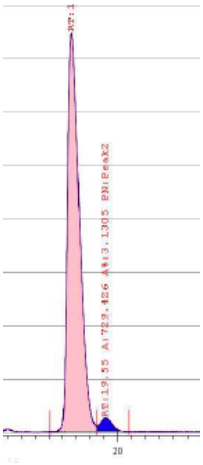
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-methoxyphenyl)-1-phenylethan-1-ol

Racemic Material

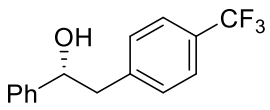


Peak No	% Area	Area	RT (min)
1	49.8369	5531.1911	18.43
2	50.1631	5567.3946	19.35
Total:	100	11098.5857	

Standard Conditions



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



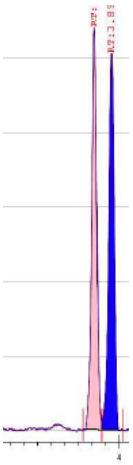
(R)*-1-phenyl-2-(4-(trifluoromethyl)phenyl)ethan-1-ol (2.98).** The reaction was performed according to the general procedure (Method A***) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.69**) (42.0 mg, 0.30 mmol, 1.00 equiv.), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 4-(trifluoromethyl)phenyl trifluoromethanesulfonate (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)-**2.89** (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 **2.71, 2.92, and 2.94**).

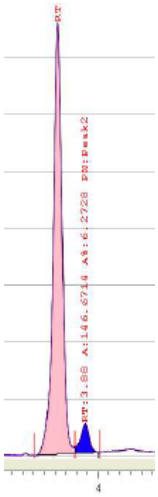
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenyl-2-(4-(trifluoromethyl)phenyl)ethan-1-ol

Racemic Material

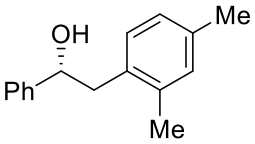


Peak No	% Area	Area	RT (min)
1	50.473	557.993	3.64
2	49.527	547.5345	3.89
Total:	100	1105.5275	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	93.7272	2191.5358	3.63
2	6.2728	146.6714	3.88
Total:	100	2338.2072	



(R)*-2-(2,4-dimethylphenyl)-1-phenylethan-1-ol (2.99).** 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 (**2.69**) (42.0 mg, 0.30 mmol), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol), 2,4-dimethylphenyl trifluoromethanesulfonate (83.90 mg, 0.33 mmol), palladium (II) acetate (0.670 mg, 0.003 mmol), (S_p, S_p)-**2.89** (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

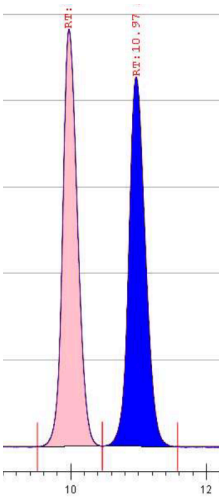
NMR (600 MHz, $CDCl_3$) δ 7.33-7.37 (4H, m), 7.27 (1H, t, *J* = 7.2 Hz), 7.04 (1H, d, *J* = 7.8 Hz), 6.98 (1H, s), 6.95 (1H, d, *J* = 7.8 Hz), 4.86-4.86 (1H, m), 3.00 (1H, dd, *J* = 14.4, 4.2 Hz), 2.94 (1H, dd, *J* = 13.8, 9.0 Hz), 2.29 (3H, s), 2.26 (3H, s), 1.92 (1H, d, *J* = 2.4 Hz); ^{13}C NMR (150 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).

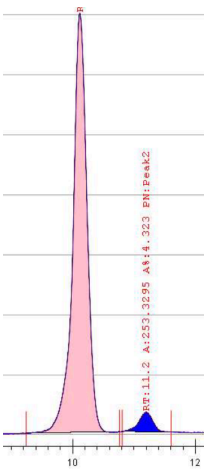
Analysis of Stereochemistry

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 **2.71, 2.92, and 2.94**).

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.

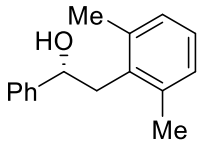
Racemic Material Standard Conditions





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

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 (2.100).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.69**) (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 (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)-**2.89** (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,

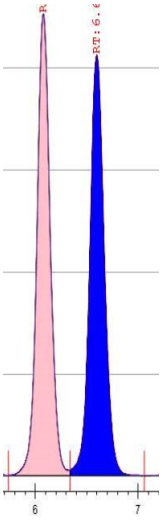
39.96, 20.55. IR (neat) ν_{max} 3534.5 (br), 3416.7 (br), 3064.4 (w), 3027.0 (w), 2956.3 (w), 2921.1 (w), 1550.7 (w), 1493.0 (m), 1379.0 (m), 1049.2 (w), 1024.6 (m), 758.0 (s), 700.2 (s) cm^{-1}. HRMS (DART) for $C_{16}H_{17}$ $[M+H-H_2O]^+$ calcualted: 209.1330, found: 209.1332. $[\alpha]^{20}_D$: +1.419 (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 **2.71, 2.92, and 2.94**).

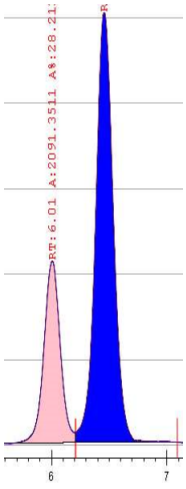
Chiral SFC (Chiracel OD-H, 8% IPA, 3 mL/min, 150 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(2,6-dimethylphenyl)-1-phenylethan-1-ol.

Racemic Material

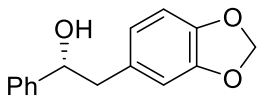


Peak No	% Area	Area	RT (min)
1	49.905	8107.1524	6.08
2	50.095	8138.0096	6.6
Total:	100	16245.162	

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 (2.101).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.69**) (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 (88.50 mg, 0.33 mmol), palladium (II) acetate (0.67 mg, 0.003 mmol), (S_p, S_p)-**2.89** (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).

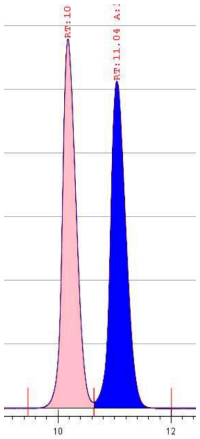
Analysis of Stereochemistry

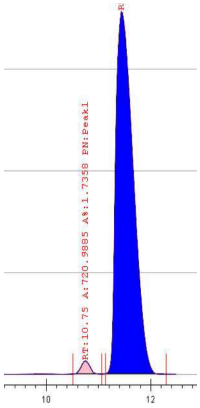
Racemic compound was prepared according to the general procedure ***(Method A)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, $Pd(OAc)_2$ (5 mol%) and 1,1'-

Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.71, 2.92, and 2.94**).

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.

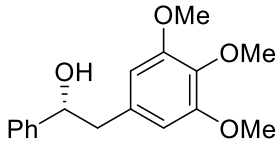
Racemic Material Standard Conditions





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

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 (2.102).** The reaction was performed according to the general procedure *(**Method A**)* with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.69**) (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. (104.4 mg, 0.33

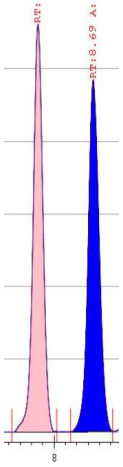
mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv.), (S_p, S_p)-**2.89** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (15-20% ethyl acetate in pentane, stain in CAM) to afford a white solid (75.20 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 **2.71, 2.92, and 2.94**).

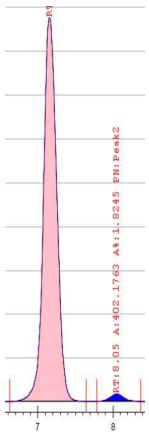
Chiral SFC (Chiracel OD-H, 10% MeOH, 3 mL/min, 150 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenyl-2-(3,4,5-trimethoxyphenyl)ethan-1-ol.

Racemic Material

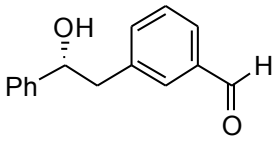


Peak No	% Area	Area	RT (min)
1	50.5474	6748.707	7.71
2	49.4526	6602.5431	8.69
Total:	100	13351.2501	

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 (2.103). 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)-**2.89** (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.

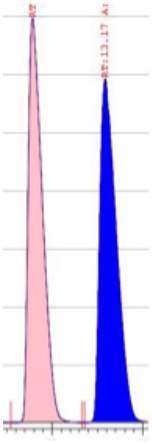
IR (neat) ν_{max} 3423.5 (br), 3062.1 (s), 3029.5 (s), 2922.1 (m), 2850.5 (s), 1691.3 (s), 1603.0 (d), 1451.7 (s), 1241.1 (s), 1143.8 (s), 1048.0 (s), 698.8 (s) cm^{-1}.HRMS-(DART) for: $C_{15}H_{18}N_1O_1$ $[M+NH_4]^+$: calculated: 244.1339, found: 244.1338. $[\alpha]_D^{20}$: +3.63 (c = 0.84, $CHCl_3$, *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 **2.71, 2.92, and 2.94**).

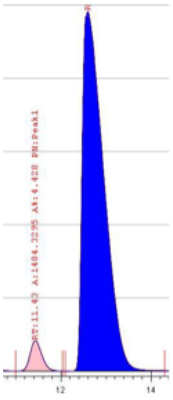
Chiral SFC (Chiracel AS-H, 7% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-(2-hydroxy-2-phenylethyl)benzaldehyde.

Racemic Material

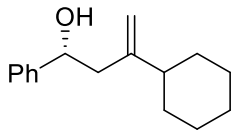


Peak Info			
Peak No	% Area	Area	RT (min)
1	49.9128	15091.73	11.57
2	50.0872	15144.4606	13.17
Total:	100	30236.1906	

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 (2.104).** 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 (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)-**2.89** (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).

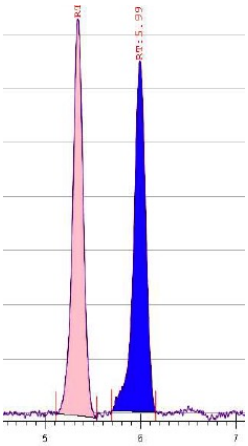
Analysis of Stereochemistry:

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 **2.71, 2.92, and 2.94**).

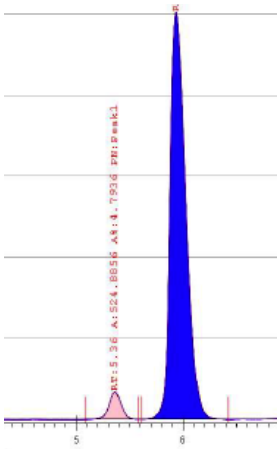
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-cyclohexyl-1-phenylbut-3-en-1-ol

Racemic Material

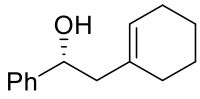


Peak No	% Area	Area	RT (min)
1	50.0769	284.402	5.34
2	49.9231	283.5282	5.99
Total:	100	567.9302	

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 (2.105).** 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 (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)-**2.89** (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),

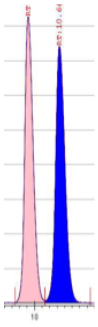
4.76 (1H, dd, J = 9.0, 4.2 Hz), 2.36 (1H, m), 2.30 (1H, dd, J = 18.8, 9.6 Hz), 2.17 (1H, s), 2.09-2.05 (3H, m), 1.94-1.92 (1H, m), 1.68-1.64 (2H, m), 1.61-1.57 (2H, m). ^{13}C NMR (125 MHz, CDC_3) δ 144.5, 134.6, 128.5, 127.4, 125.9, 125.9, 71.4, 49.1, 28.4, 25.5, 23.0, 22.4. IR (neat) ν_{max} 3406.1 (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 **2.71, 2.92, and 2.94**).

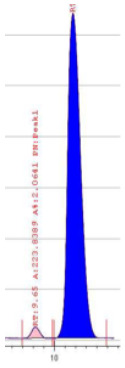
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(cyclohex-1-en-1-yl)-1-phenylethan-1-ol.

Racemic Material

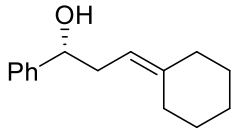


Peak Info			
Peak No	% Area	Area	RT (min)
1	49.6784	6384.9152	9.83
2	50.3216	6467.5726	10.66
Total:	100	12852.4878	

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 (2.106).** 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 (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)-**2.89** (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).

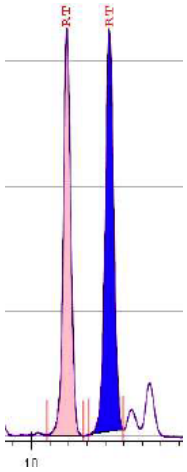
Analysis of Stereochemistry:

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 **2.71, 2.92, and 2.94**).

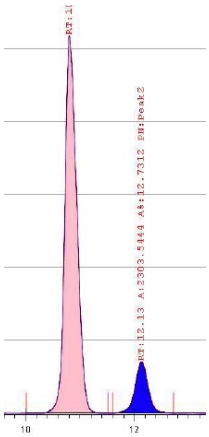
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-cyclohexylidene-1-phenylpropan-1-ol

Racemic Material

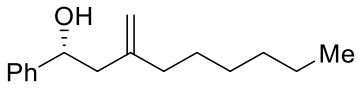


Peak No	% Area	Area	RT (min)
1	47.2345	4658.0381	10.96
2	52.7655	5203.4843	12.11
Total:	100	9861.5224	

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 (2.107).** 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 (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)-**2.89** (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%

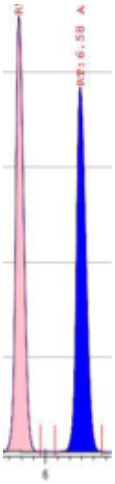
yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39-7.34 (4H, m), 7.29-7.26 (1H, m), 4.94 (1H, s), 4.91 (1H, s), 4.80 (1H, dd, *J* = 1.8, 9.6 Hz), 2.47 (1H, ddd, *J* = 13.8, 4.20 Hz), 2.40 (1H, ddd, *J* = 14.9, 9.6 Hz), 2.17 (1H, d, *J* = 1.8 Hz), 2.08 (1H, t, *J* = 7.8 Hz), 1.51-1.42 (2H, m), 1.34-1.26 (6H, 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:

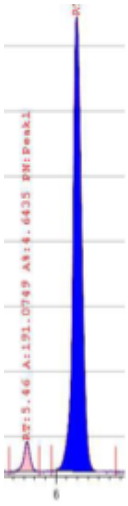
Racemic compound was prepared according to the general procedure (***Method A***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.71, 2.92, and 2.94**).

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.

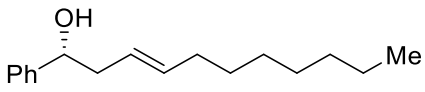
Racemic Material



Standard Conditions



Peak Info				Peak Info			
Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	50.4307	4230.6695	5.56	1	4.6435	191.0749	5.46
2	49.5693	4158.4116	6.58	2	95.3565	3923.7903	6.39
Total:	100	8389.0811		Total:	100	4114.8652	



(R,E)*-1-phenylundec-3-en-1-ol (2.109).** 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)-**2.89** (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,

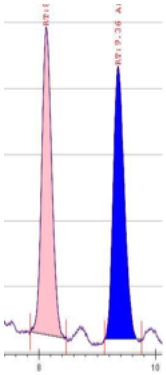
q, J = 7.2 Hz), 1.37-1.21 (10H, m), 0.89 (3H, t, J = 7.2 Hz,). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.2, 135.5, 128.5, 127.5, 126.0, 125.5, 73.6, 43.0, 32.8, 33.0, 29.6, 29.3, 29.3, 14.3. IR (neat) ν_{max} 3389.8 (w), 3065.9 (s), 3029.0 (s), 2925.9 (s), 2855.9 (s), 1643.6 (s), 1453.3 (m), 1049.7 (m), 889.7 (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 **2.71, 2.92, and 2.94**).

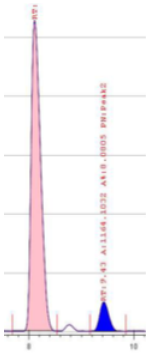
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R,E)-1-phenylundec-3-en-1-ol.

Racemic Material

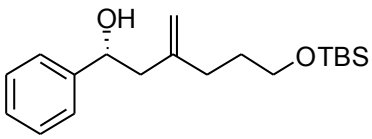


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.3629	557.0803	8.12
2	49.6371	549.0516	9.36
Total:	100	1106.1319	

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	



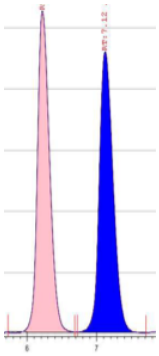
(R)*-6-(*tert*-butyldimethylsilyloxy)-3-methylene-1-phenylhexan -1-ol (2.108).** The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-2-yl trifluoromethanesulfonate (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)-**2.89** (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 **2.71, 2.92, and 2.94**).

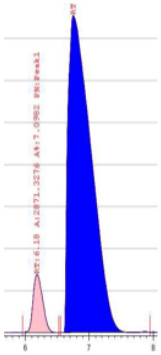
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 6-((tert-butyldimethylsilyl)oxy)-3-methylene-1-phenylhexan-1-ol.

Racemic Material

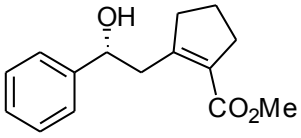


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.0691	3171.9339	6.22
2	49.9309	3163.182	7.12
Total:	100	6335.1159	

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 (2.110). 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

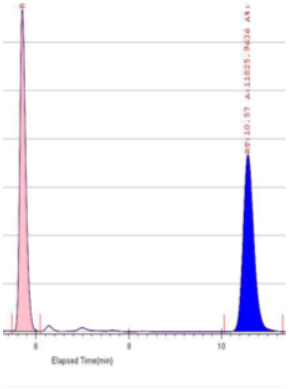
dibutyl ether, 0.30 mmol, 1.00 equiv.), 5-hydroxypent-1-en-2-yl trifluoromethanesulfonate (90.5 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv.), (S_p, S_p)-**2.89** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). Oxidation was performed at pH 7 over 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 **2.71, 2.92, and 2.94**).

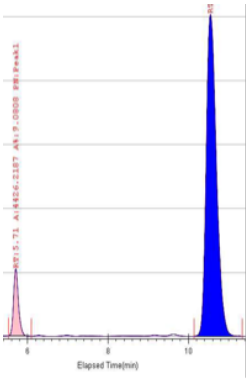
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – Methyl (R)-2-(2-hydroxy-2-phenylethyl)cyclopent-1-ene-1-carboxylate.

Racemic Material

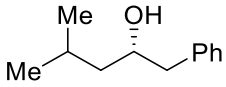


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.236	11938.1215	5.7
2	49.764	11825.9636	10.57
Total:	100	23764.0851	

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 (2.113).** The reaction was performed according to the general procedure **(*Method B*)** with 2-isobutyl-5,5-dimethyl-1,3,2-dioxaborinane (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)-**2.89** (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,

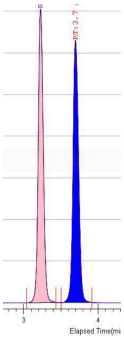
m), 2.80 (1H, dd, J = 13.2, 3.6 Hz), 2.61 (1H, dd, J = 13.2, 8.4 Hz), 1.78-1.85 (1H, m), 1.41-1.48 (2H, m), 1.27-1.31 (1H, m), 0.93 (3H, d, J = 6.6 Hz), 0.90 (3H, d, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.8, 129.6, 128.7, 126.6, 70.9, 46.2, 44.8, 24.8, 23.6, 22.2; IR (neat) ν_{max} 3387 (br), 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).

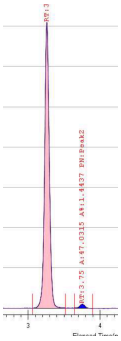
Analysis of Stereochemistry

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 **2.71, 2.92, and 2.94**).

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.

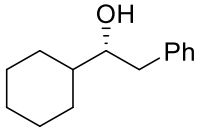
Racemic Material Standard Conditions





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 (2.114).** The reaction was performed according to the general procedure (Method B***) with 2-cyclohexyl-5,5-dimethyl-1,3,2-dioxaborinane (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)-**2.89** (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).

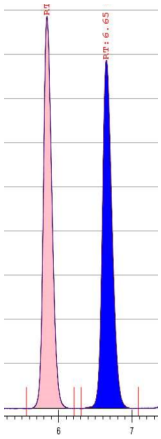
Analysis of Stereochemistry:

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 **2.71, 2.92, and 2.94**).

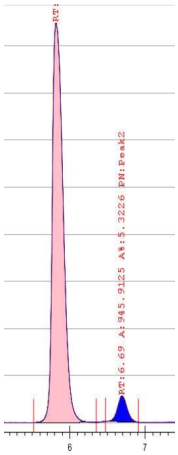
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-cyclohexyl-2-phenylethan-1-ol.

Racemic Material

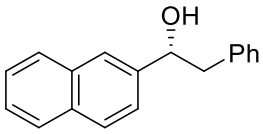


Peak No	% Area	Area	RT (min)
1	49.9353	7108.9938	5.84
2	50.0647	7127.4132	6.65
Total:	100	14236.407	

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 (2.115).** The reaction was performed according to the general procedure (Method B***) with 5,5-dimethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborinane (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)

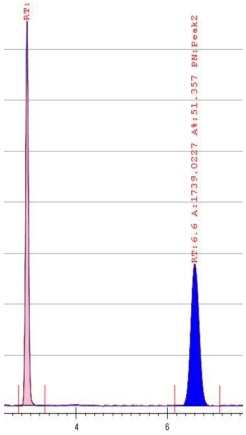
acetate (1.30 mg, 0.0060 mmol, 0.020 equiv.), (S_p, S_p)-**2.89** (7.60 mg, 0.0072 mmol,0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford a white solid (69.0 mg, 93% yield). ^{1}H NMR (600 MHz, $CDCl_3$) 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 **2.71, 2.92, and 2.94**).

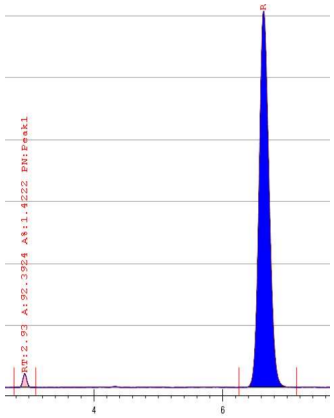
Chiral SFC (Chiracel ODR-H, 15% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-(naphthalen-2-yl)-2-phenylethan-1-ol.

Racemic Material

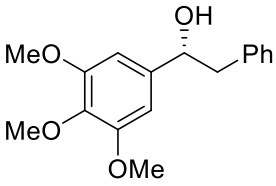


Peak No	% Area	Area	RT (min)
1	48.643	1647.1222	2.92
2	51.357	1739.0227	6.6
Total:	100	3386.1449	

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 (2.116).** 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.), 2.89 (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,

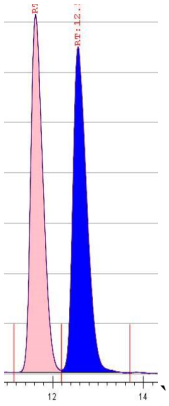
J = 1.8 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.32, 139.66, 138.05, 137.38, 129.67, 128.65, 126.80, 102.91, 75.63, 60.99, 56.23, 46.26. IR (neat) ν_{max} 3462.0 (br), 2939.3 (w), 2836.6 (w), 1592.2 (m), 1506.7 (m), 1456.5 (m), 1326.3 (m), 1233.5 (m), 1125.3 (s), 1007.6 (s), 701.3 (w) cm^{-1}. HRMS (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 **2.71, 2.92, and 2.94**).

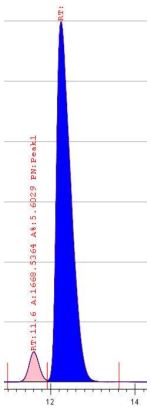
Chiral SFC (Chiracel ODR-H, 6% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-phenyl-1-(3,4,5-trimethoxyphenyl)ethan-1-ol.

Racemic Material

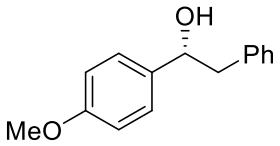


Peak No	% Area	Area	RT (min)
1	49.3717	13286.3101	11.62
2	50.6283	13624.4834	12.56
Total:	100	26910.7935	

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	



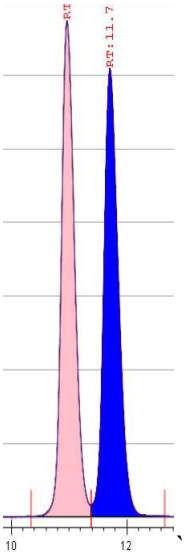
(R)*-1-(4-methoxyphenyl)-2-phenylethan-1-ol (2.117).** The reaction was performed according to the general procedure ***(Method B) with 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (66.0 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (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)-**2.89** (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 **2.71, 2.92, and 2.94**).

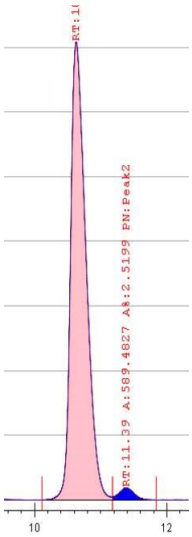
Chiral SFC (Chiracel OD-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(4-methoxyphenyl)-2-phenylethan-1-ol.

Racemic Material

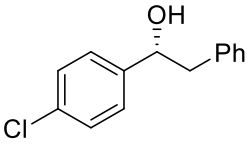


Peak No	% Area	Area	RT (min)
1	49.8119	10639.7812	10.97
2	50.1881	10720.1395	11.71
Total:	100	21359.9207	

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 (2.119).** The reaction was performed according to the general procedure ***(Method B) with 2-(4-chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (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)-**2.89** (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,

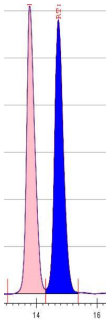
66% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30-7.20 (7H, m), 7.13 (2H, d, 6.0 Hz), 4.84 (1H, ddd, *J* = 8.4, 5.4, 3.0 Hz), 2.97 (1H, dd, *J* = 13.8, 4.8 Hz), 2.92 (1H, dd, *J* = 13.8, 8.4 Hz), 1.95 (1H, d, 2.4 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.34, 137.65, 133.36, 129.64, 128.73, 128.65, 127.43, 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 **2.71, 2.92, and 2.94**).

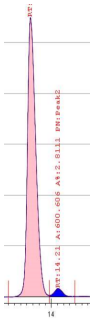
Chiral SFC (Chiracel OD-H, 6% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-(4-chlorophenyl)-2-phenylethan-1-ol.

Racemic Material

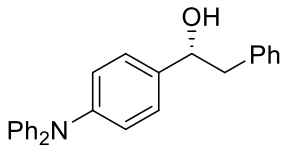


Peak No	% Area	Area	RT (min)
1	49.0709	11621.9899	13.76
2	50.9291	12062.0942	14.72
Total:	100	23684.0841	

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 (2.120).** 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 (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)-**2.89** (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).

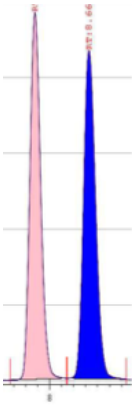
Analysis of Stereochemistry:

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 **2.71, 2.92, and 2.94**).

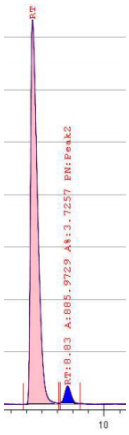
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(4-(diphenylamino)phenyl)-2-phenylethan-1-ol.

Racemic Material

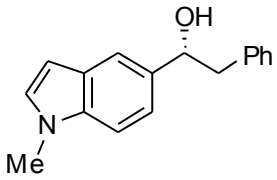


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.0189	6007.4743	7.75
2	49.9811	6002.9239	8.66
Total:	100	12010.3982	

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 (2.121).** 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 (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)-

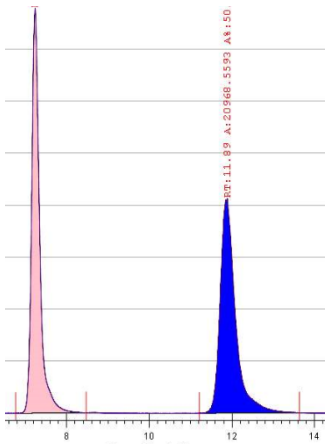
2.89 (7.60 mg, 0.0072 mmol, 0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford a white solid (64.8 mg, 86% yield). 1H NMR (500 MHz, $CDCl_3$) δ 7.61 (1H, s), 7.630-7.21 (7H, m), 7.04 (1H, d, *J* = 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).

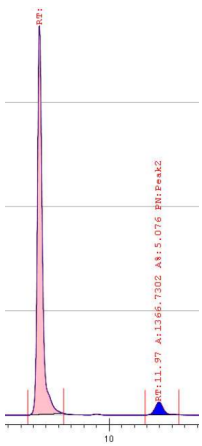
Analysis of Stereochemistry:

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 **2.71, 2.92, and 2.94**).

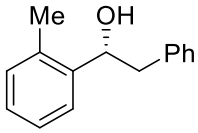
Chiral SFC (Chiracel OJ-H, 30% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(1-methyl-1H-indol-5-yl)-2-phenylethanol.

Racemic Material Standard Conditions





Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	49.8909	20877.2269	7.23	1	94.924	25558.6592	7.23
2	50.1091	20968.5593	11.89	2	5.076	1366.7302	11.97
Total:	100	41845.7862		Total:	100	26925.3894	



(R)*-2-phenyl-1-(o-tolyl)ethan-1-ol (2.122).** The reaction was performed according to the general procedure ***(Method B) with 5,5-dimethyl-2-(o-tolyl)-1,3,2-dioxaborinane (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)-**2.89** (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,

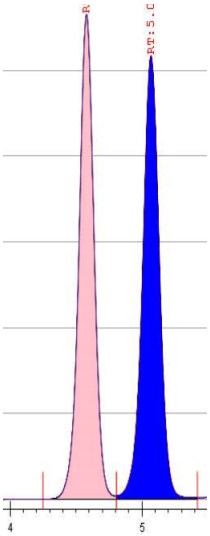
127.43, 126.74, 126.48, 125.37, 71.85, 45.15, 19.12. IR (neat) ν_{max} 3384.9 (br), 3061.3 (w), 2920.4 (w), 2859.95 (w), 1603.1 (w), 1494.1 (m), 1454.0 (m), 1076.0 (m), 1038.8 (m), 755.1 (s). 738.2 (m), 698.4 (s) cm^{-1}. HRMS (DART) for $C_{15}H_{15}$ $[M+H-H_2O]^+$ calculated: 195.1174, found: 195.1181. $[\alpha]^{20}_D$: +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 **2.71, 2.92, and 2.94**).

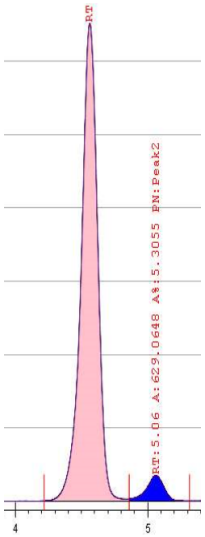
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-2-phenyl-1-(o-tolyl)ethan-1-ol.

Racemic Material

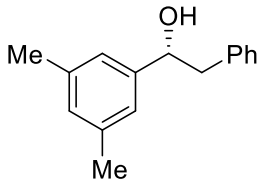


Peak No	% Area	Area	RT (min)
1	49.4517	8989.9843	4.58
2	50.5483	9189.3254	5.07
Total:	100	18179.3097	

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	



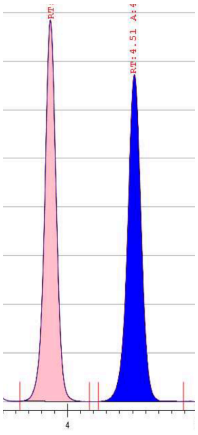
(R)*-1-(3,5-dimethylphenyl)-2-phenylethan-1-ol (2.123).** The reaction was performed according to the general procedure (Method B***) with 2-(3,5-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (65.4 mg, 0.30 mmol), vinylllithium (0.211 mL, 1.42M in diethyl ether, 0.30 mmol), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol), palladium (II) acetate (1.34 mg, 0.006 mmol), (S_p, S_p)-**2.89** (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 **2.71, 2.92, and 2.94**).

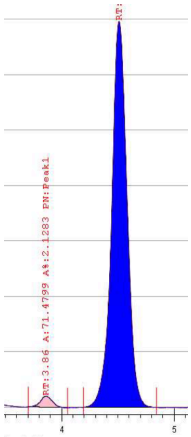
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (R)-1-(3,5-dimethylphenyl)-2-phenylethan-1-ol.

Racemic Material

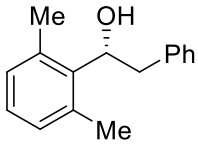


Peak No	% Area	Area	RT (min)
1	49.8529	4861.1049	3.87
2	50.1471	4889.7919	4.51
Total:	100	9750.8968	

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 (2.124).** The reaction was performed according to the general procedure (Method B***) with 2-(2,6-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (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)-**2.89** (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,

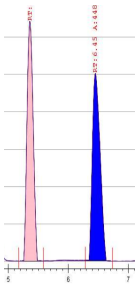
m), 7.17 (1H, t, *J* = 7.2 Hz), 7.00 (2H, d, *J* = 7.8 Hz), 5.32 (1H, ddd, *J* = 7.8 4.8, 1.8 Hz). 3.22 (1H, dd, *J* = 13.8, 9.0 Hz), 3.01 (1H, dd, *J* = 13.8, 5.4 Hz), 2.43 (6H, s), 1.83 (1H, d, *J* = 2.4 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.90, 138.80, 136.24, 129.55, 129.52, 128.65, 127.30, 126.66, 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 **2.71, 2.92, and 2.94**).

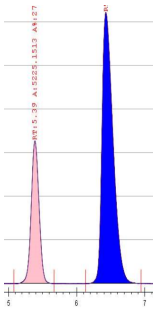
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-(2,6-dimethylphenyl)-2-phenylethan-1-ol

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	

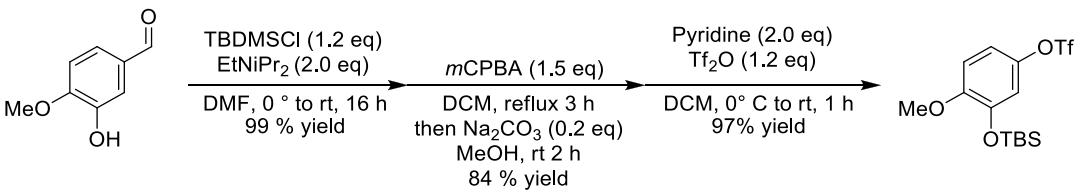
Standard Conditions



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

2.7.2.6. (-)-Combretastatin Synthesis

***Preparation of* 3-(*tert*-butyldimethylsilyloxy)-4-methoxyphenyl trifluoromethanesulfonate**

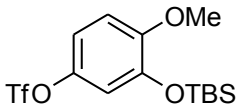


To an oven-dried 100 mL round bottom flask equipped with a magnetic stir bar was added Isovanillin (4.12 g, 28.3 mmol, 1.0 equiv.) and *N,N*-dimethylformamide (30 mL). The solution was cooled to 0 °C under a nitrogen atmosphere, and *N,N*-diisopropylethylamine (6.83 g, 52.8 mmol, 2.0 equiv.) was added and the solution was allowed to stir at 0 °C for 10 minutes. To the cooled reaction solution was added *tert*-Butyldimethylsilyl chloride (4.76 g, 31.6 mmol, 1.2 equiv.) as a 1 M solution in THF over 30 minutes via syringe pump. The reaction solution was allowed to warm to room temperature and stir at room temperature for 12 hours. The solution was diluted with diethyl ether, washed with water and brine, and dried with sodium sulfate. After removing solvent under reduced pressure the residue was purified by flash column chromatography (10% EtOAc in hexane) and the product was obtained as a clear colorless oil (6.89 g, 99% yield). All spectral data was in accordance with the literature[57].

[57] M. V. R. Reddy, M. R. Mallireddigari, S. C. Cosenza, V. R. Pallela, N. M. Iqbal, K. A. Robell, A. D. Kang, E. P. Reddy, Design, *J. Med. Chem.* **2008**, 51, 86-100.

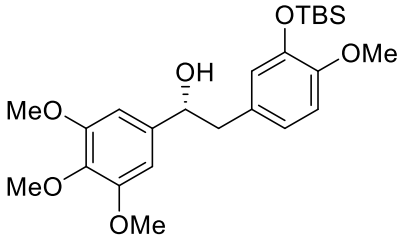
To an oven-dried 250 mL round bottom flask equipped with a magnetic stir bar was added TBS-protected Isovanillin (6.89 g, 26.0 mmol, 1.0 equiv.) and anhydrous CH_2Cl_2 (103 mL), the reaction solution was cooled to 0 °C and placed under nitrogen. To this cooled solution was added 3-chloroperbenzoic acid (13.45 g, 39.0 mmol, 1.5 equiv.), the solution was refluxed for 3 hours, the resulting solution was washed twice with saturated aqueous $NaHCO_3$. The organic phase was dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The resulting residue was dissolved in methanol (150 mL), and to this solution was added Na_2CO_3 (0.64 g, 5.2 mmol, 0.2 equiv.). The reaction mixture was stirred at room temperature for 2 hours, after which the solution was quenched with aqueous NH_4Cl and extracted with CH_2Cl_2 (4x45 mL). The combined organic layers were dried over Na_2SO_4, filtered through a neutral alumina pad, and concentrated under reduced pressure. The resulting residue was used in next step without further purification.

The residue from the last step was subjected to the general procedure for preparation of aryl triflates to afford the product (8.18 g, 97% yield). (81% overall yield over three steps).



3-(*tert*-butyldimethylsilyloxy)-4-methoxyphenyl trifluoromethanesulfon-ate (2.126). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.84-6.80 (2H, m), 6.85 (1H, d, J = 2.4 Hz), 3.80 (3H, s), 0.97 (9H, s), 0.15 (6H, s). ^{13}C NMR (150 MHz, $CDCl_3$) δ 151.2, 146.1, 142.8, 122.2, 120.0, 117.9, 114.5, 114.2, 112.0,

56.0, 25.8, 18.6, -4.5. IR (neat) ν_{max} 2932.6 (w), 1603.6 (m), 1505.0 (s), 1419.9 (m), 1181.4 (s), 1107.9 (s), 882.2 (m), 826.9 (s), 802.1 (s), 693.6 (m), 599.4 (m), 505.6 (s) cm^{-1}. HRMS (DART) for $C_{14}H_{22}F_3O_5S_1Si_1$ $[M+H]^+$ calculated: 387.0909, found: 387.0908.



(R)*-2-(3-((tert-butyldimethylsilyl)oxy)-4-methoxyphenyl)-1-(3,4,5-trimethoxyphenyl)ethan-1-ol (2.127).** The reaction was performed according to the general procedure ***(Method B) with 5,5-dimethyl-2-(3,4,5-trimethoxyphenyl)-1,3,2-dioxaborinane (84.0 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.190 mL, 1.59 M in Et_2O, 0.30 mmol, 1.00 equiv.), 3-((tert-butyldimethylsilyl)oxy)-4-methoxyphenyl trifluoromethanesulfonate (139.0 mg, 0.36 mmol, 1.20 equiv.), palladium (II) acetate (0.67 mg, 0.0030 mmol, 0.010 equiv.), (S_p, S_p)-**2.89** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (15-25% ethyl acetate in hexanes, stain in CAM) to afford a colorless oil (107.0 mg, 80% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.76 (1H, d, *J* = 7.8 Hz), 6.71-6.66 (2H, m), 6.53 (2H, s), 4.73 (t, *J* = 5.4 Hz), 3.82 (6H, s), 3.81 (3H, s), 3.76 (3H, s), 2.90 (1H, dd, *J* = 13.8, 4.8 Hz), 2.84 (1H, dd, 13.8, 8.4 Hz), 2.02 (1H, br s), 0.97 (9H, s), 0.11 (6H, d, *J* = 3.0 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.32, 149.98, 145.14, 139.68, 137.34, 130.44, 122.78, 122.32, 112.33, 103.0, 75.62, 60.98, 56.25, 55.70, 45.42, 25.87, 18.59, -4.48. $[\alpha]^{20}_D$: -6.772 (c = 0.502, $CHCl_3$, *l*

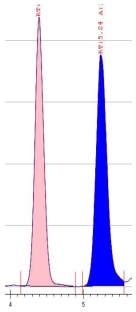
=50 mm). lit: $[\alpha]^{20}_{D}$: -8.51 (c = 2.4, $CHCl_3$) (*58*). All spectral data was in accordance with the literature[57].

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 product **2.71, 2.92, and 2.94**).

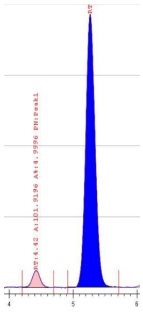
Chiral SFC (Chiracel ODR-H, 10% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(3-((tert-butyldimethylsilyl)oxy)-4-methoxyphenyl)-1-(3,4,5-trimethoxyphenyl)ethan-1-ol.

Racemic Material



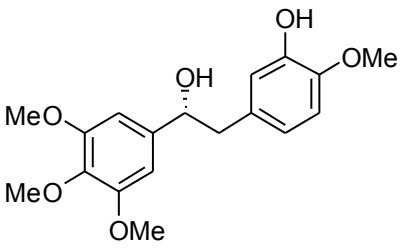
Peak No	% Area	Area	RT (min)
1	48.2262	1848.99	4.39
2	51.7738	1985.0084	5.24
Total:	100	3833.9984	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	4.9996	101.9196	4.42
2	95.0004	1936.6484	5.27
Total:	100	2038.568	

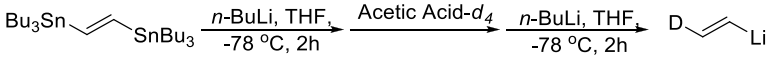
[58] A. Ramacciotti, R. Fiaschi, E. Napolitano, *Tetrahedron Asymmetry* **1996**, 7, 1101–1104.



***(-)*-combretastatin.** Combretastatin was prepared according to the reported procedure to afford the desired product in 97 % yield. $[\alpha]^{20}_{D}$: -5.458 (c = 0.795, $CHCl_3$, *l* =50 mm). All spectral data was in accordance with previous reports[57].

2.7.2.7. Deuterium-labeling Experiment

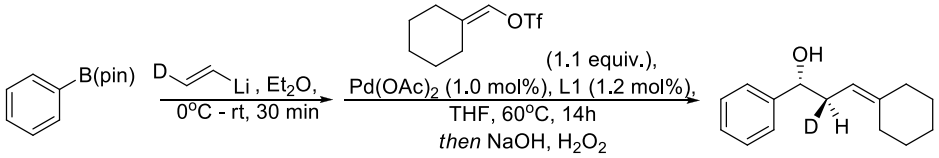
Procedure for the Preparation of trans-deuterium-labeled vinyl lithium



The *trans*-deuterium labeled vinyl lithium was prepared according to the literature procedure with modification. 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 °C, 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 °C. Then acetic acid-d_4 was added dropwise at -78 °C. 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 °C, 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 °C. 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.

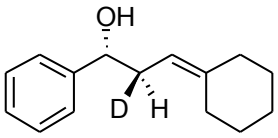
Procedure for the Conjunctive Cross Coupling with trans-deuterium-labeled Vinyl Lithium



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 °C, and *trans*-deuterium labeled 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 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)-**2.89** (3.80 mg, 0.0036 mmol, 0.012 equiv.) and THF (0.6 mL). The $Pd(OAc)_2$/(S_p, S_p)-**2.89** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**2.89** solution was transferred into the reaction vial, followed by THF (0.6 mL), and cyclohexylidenemethyl trifluoromethanesulfonate (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°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 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).



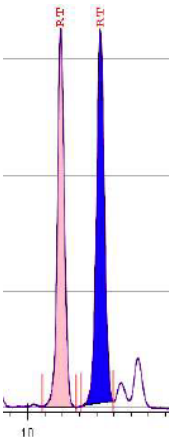
(1*R*,2*R*)-3-cyclohexylidene-1-phenylpropan-2-*d*-1-ol (2.138). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.31 (4H, m), 7.26-7.23 (1H, m), 5.09 (1H, d, *J* = 7.5 Hz), 4.64 (1H, d, *J* = 5.5 Hz), 2.46 (1H, t, *J* = 7.5 Hz), 2.13-2.05 (4H, m), 2.01 (1H, s), 1.52-1.46 (4H, m), 1.45-1.35 (2H, m); ^{13}C NMR (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:

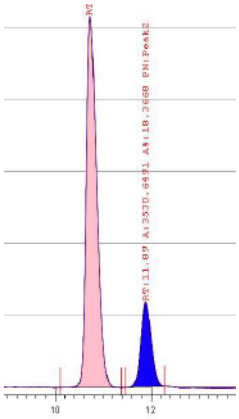
Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.71, 2.92, and 2.94**).

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



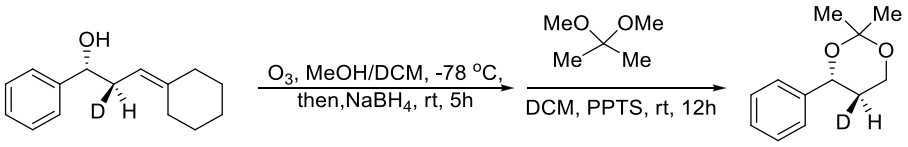
Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	47.2345	4658.0381	10.96	1	81.6332	15692.3394	10.72
2	52.7655	5203.4843	12.11	2	18.3668	3530.6491	11.89
Total:	100	9861.5224		Total:	100	19222.9885	

Proof of Stereochemistry:

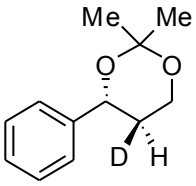
(1*R*,2*R*)-3-cyclohexylidene-1-phenylpropan-2-*d*-1-ol was ozonized, reduced, and cyclized as an acetonide by the sequence shown below. Relative stereochemistry was determined by measuring the coupling constants.



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,

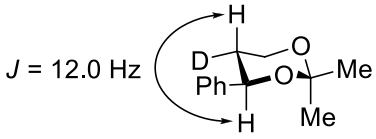
reaction mixture was quenched with water, the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography (30 % ethyl acetate in hexane) 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 °C, 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).



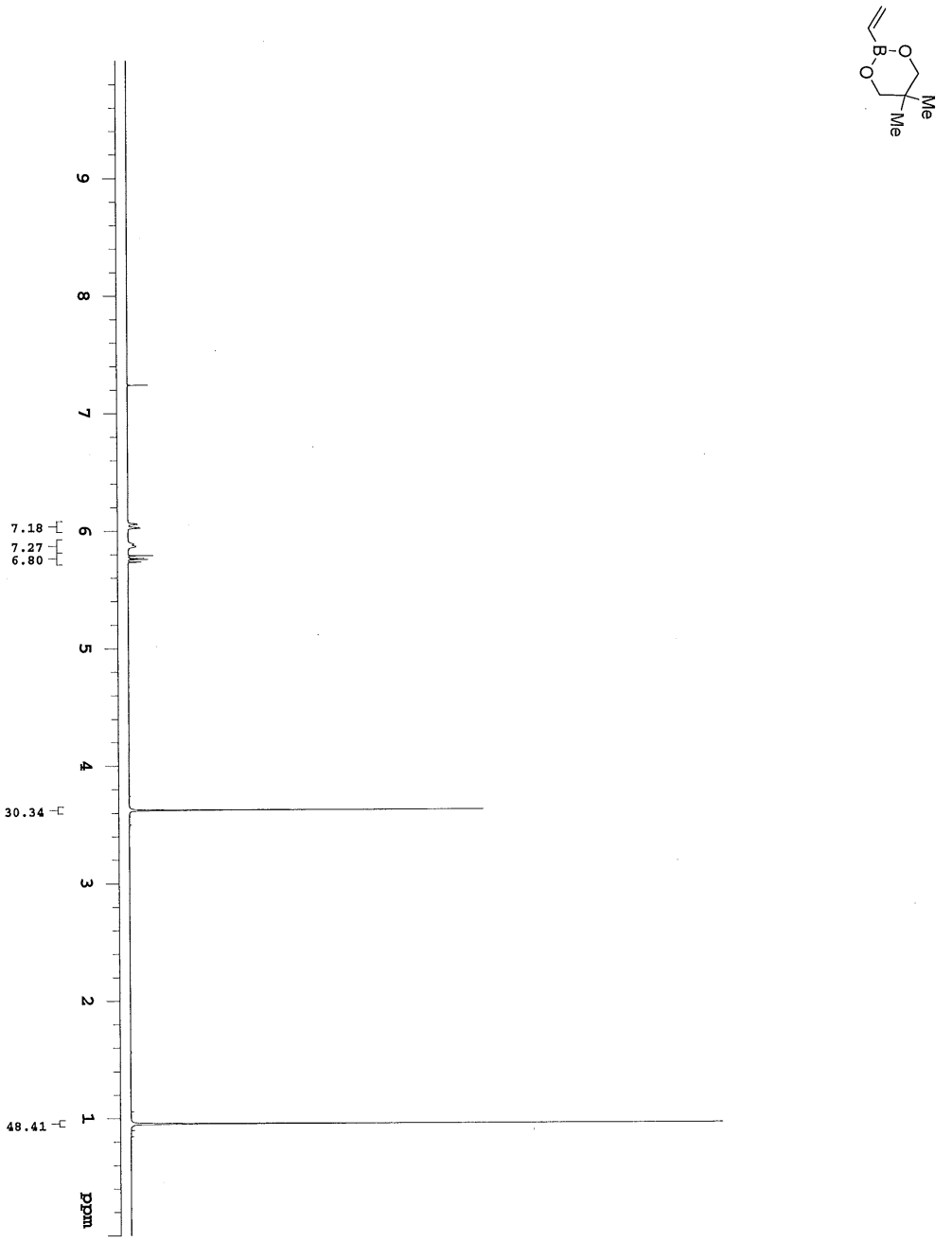
(4*R*,5*R*)-2,2-dimethyl-4-phenyl-1,3-dioxane-5-*d* (2.139). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.32 (4H, m), 7.27-7.24 (1H, m), 4.91 (1H, d, *J* = 12.0 Hz), 4.13 (1H, t, *J* = 12.6 Hz), 3.91 (1H, dd, *J* = 11.4, 4.8 Hz), 1.88 (1H, dt, *J* = 12.6, 5.4 Hz), 2.01 (1H, s), 1.57 (3H, s), 1.49 (3H, s); ^{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

2.7.3. NMR spectra of representative compounds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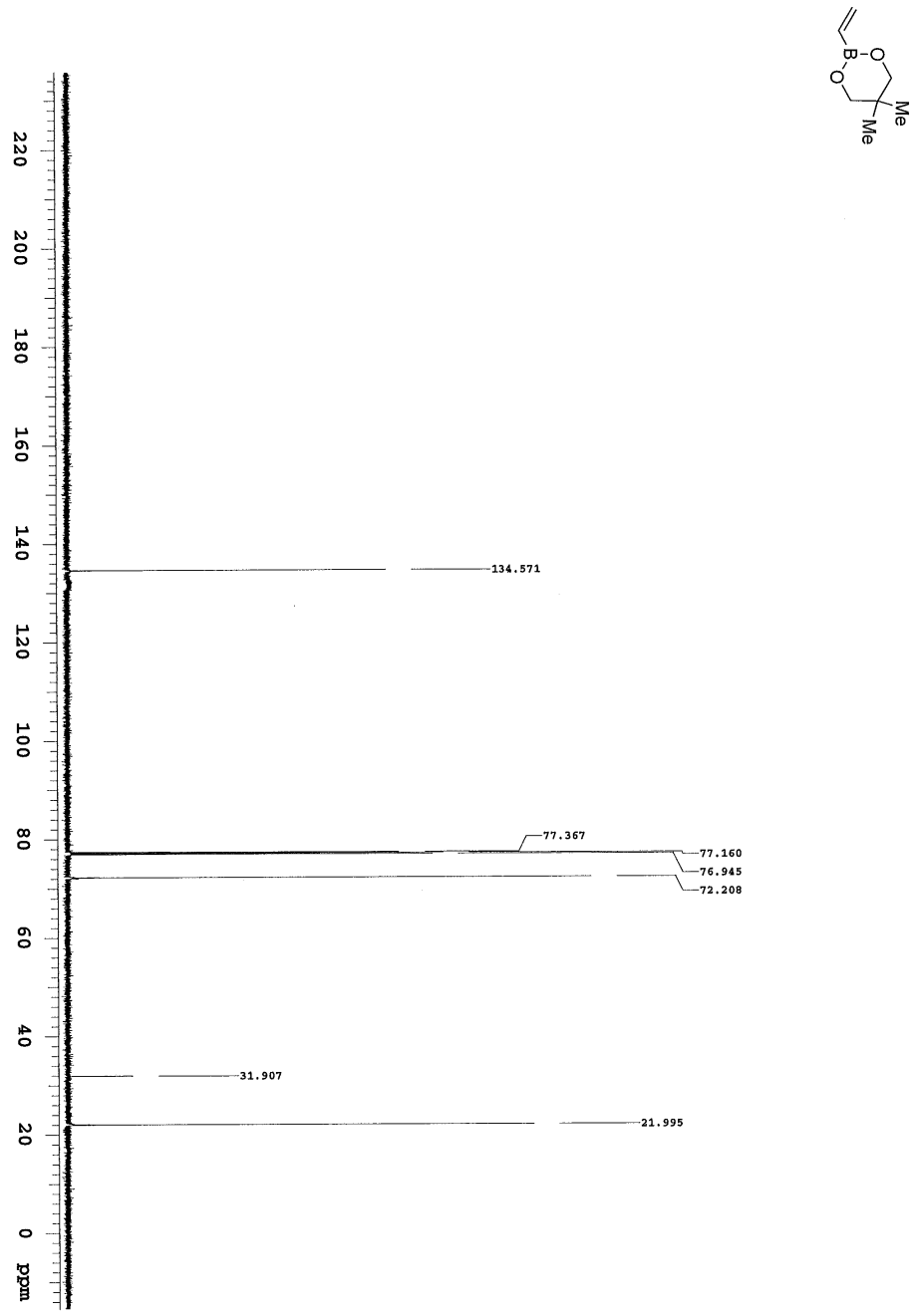
2
1
ppm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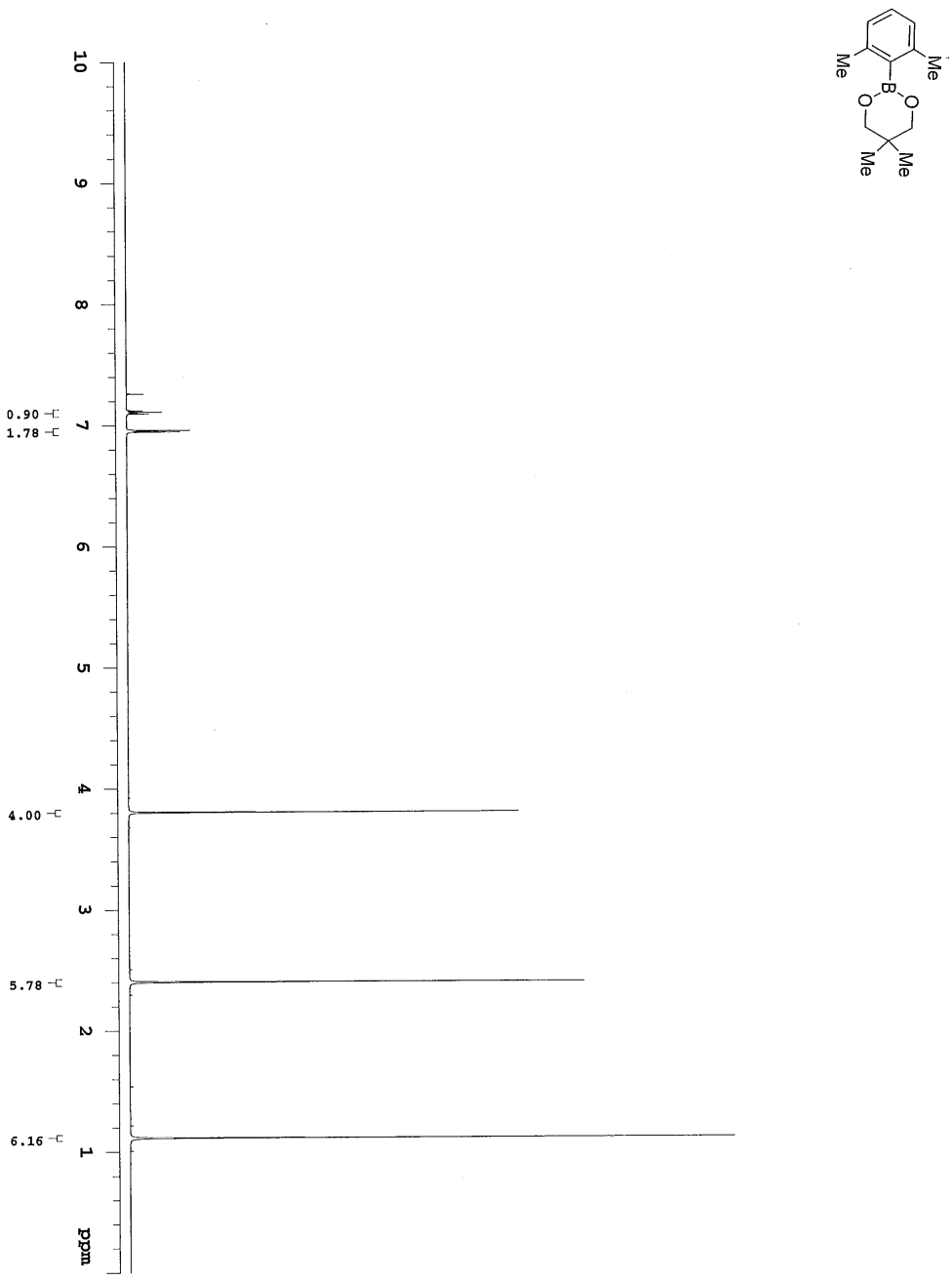
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Me
B
O
O
Me
Me
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9
8
7
6
5
4
3
2
1
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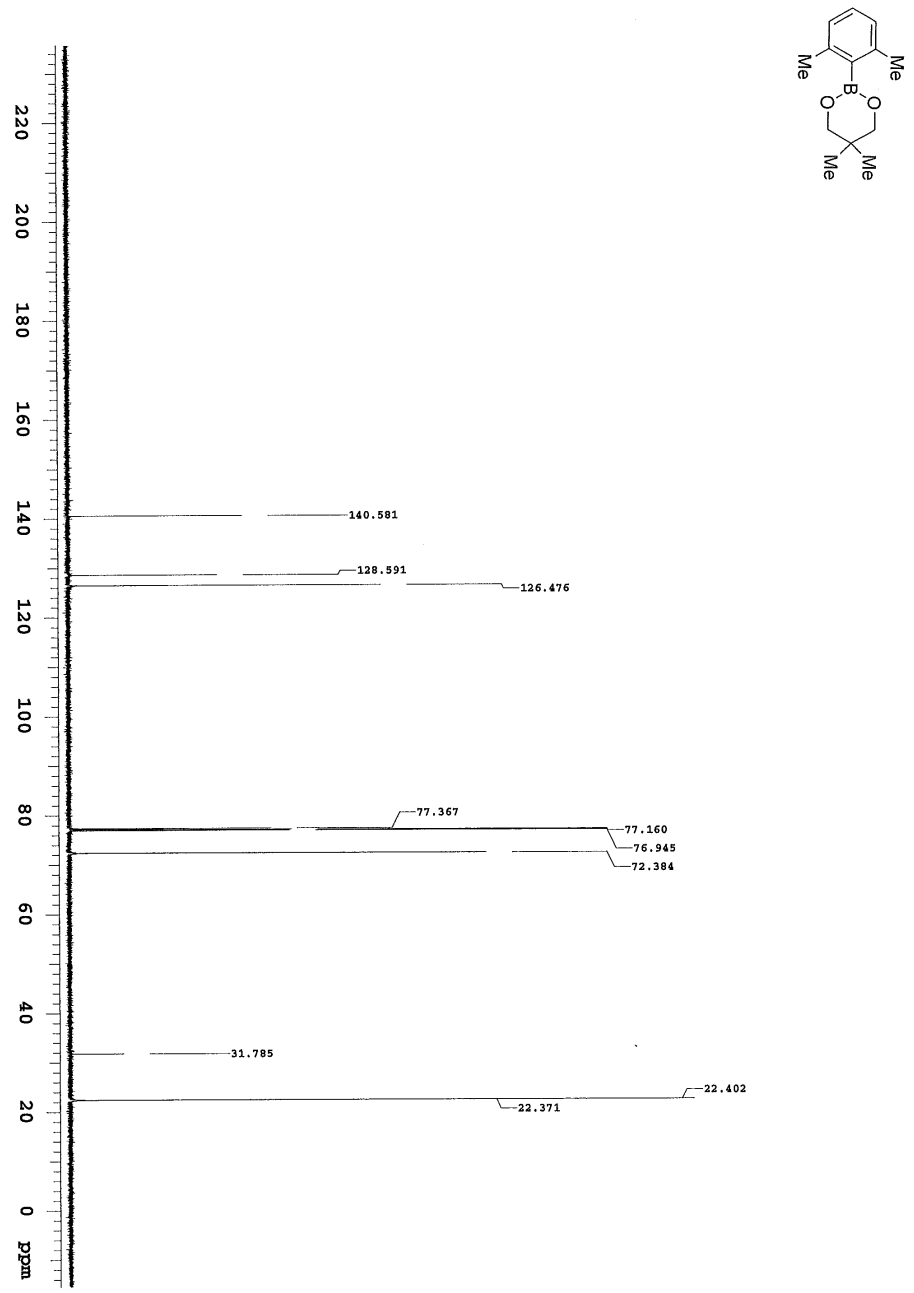
4.00
5.78
6.16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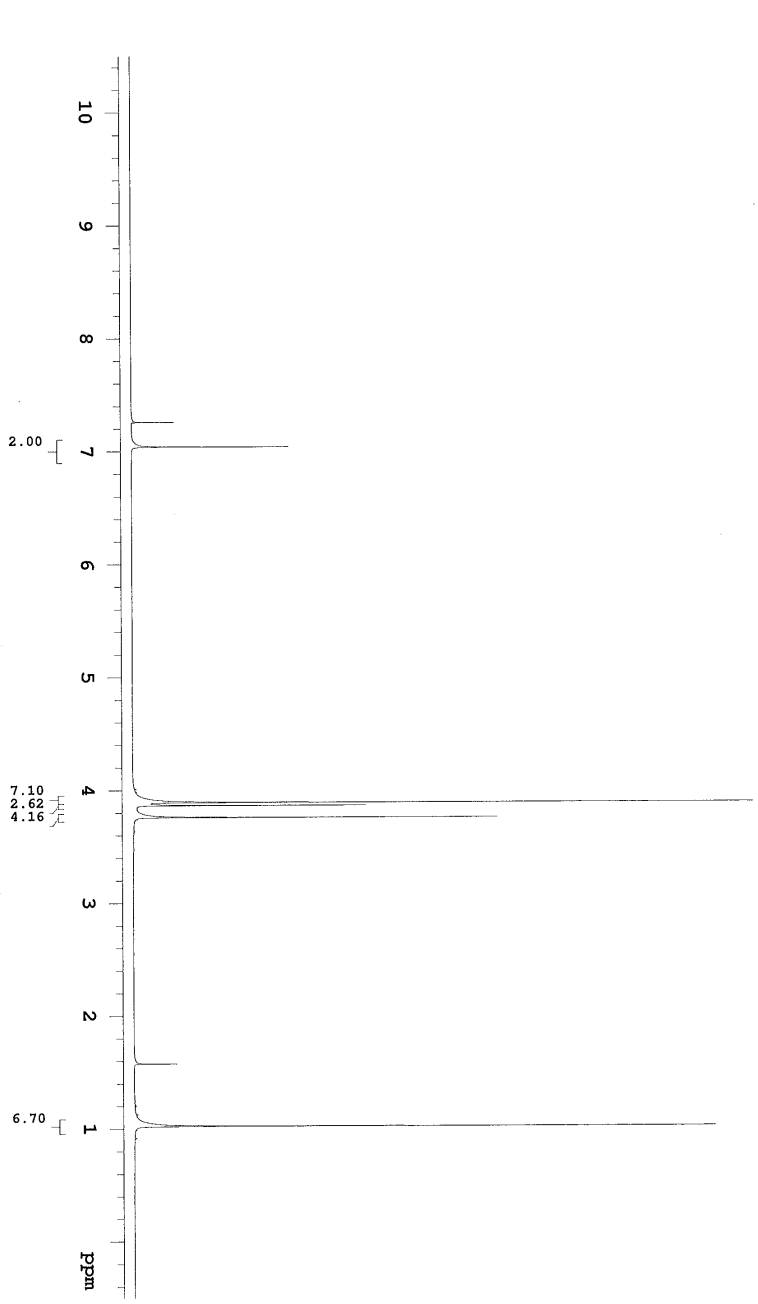
22.371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B
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O
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7
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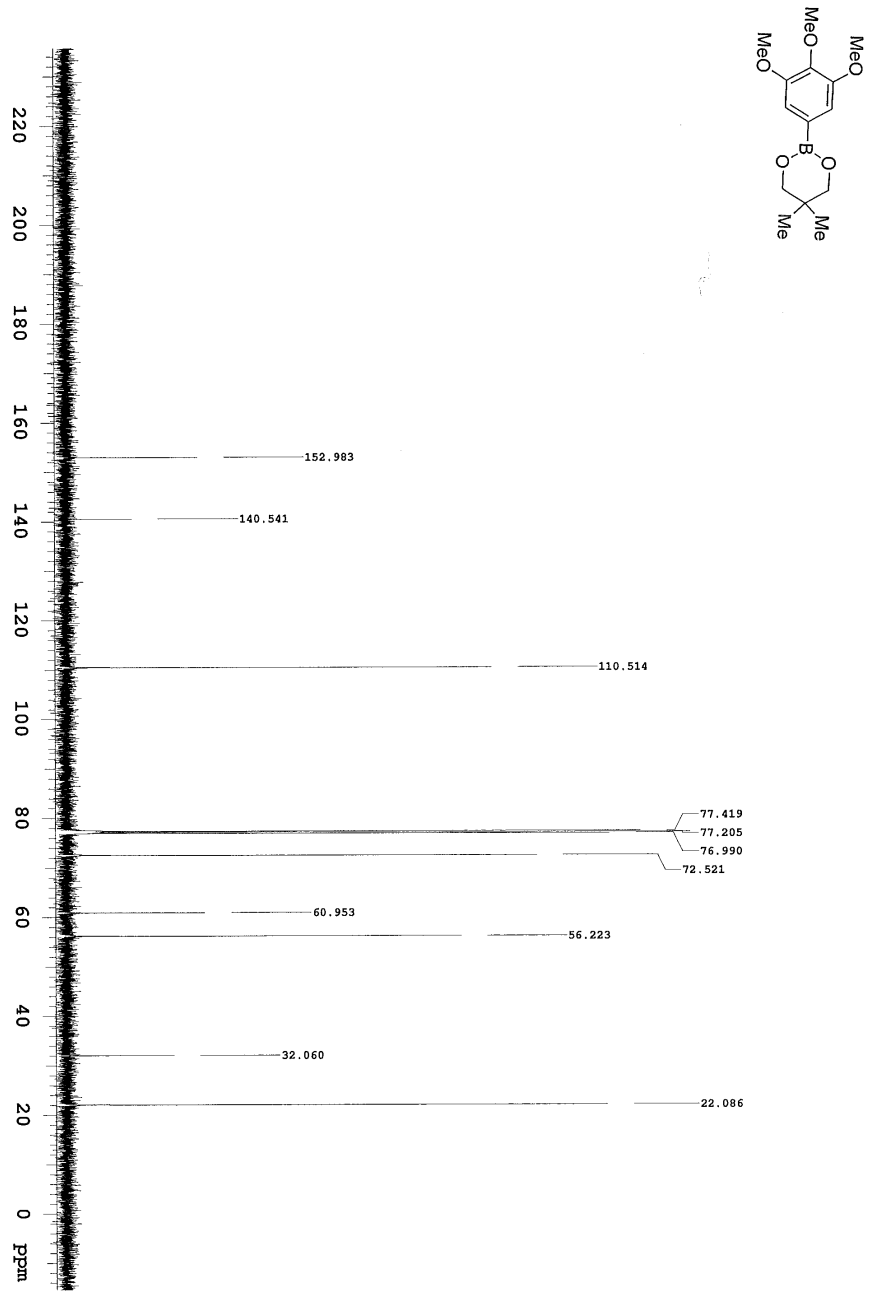
4
3
2
1
ppm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MeO
B
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O
Me
Me
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20
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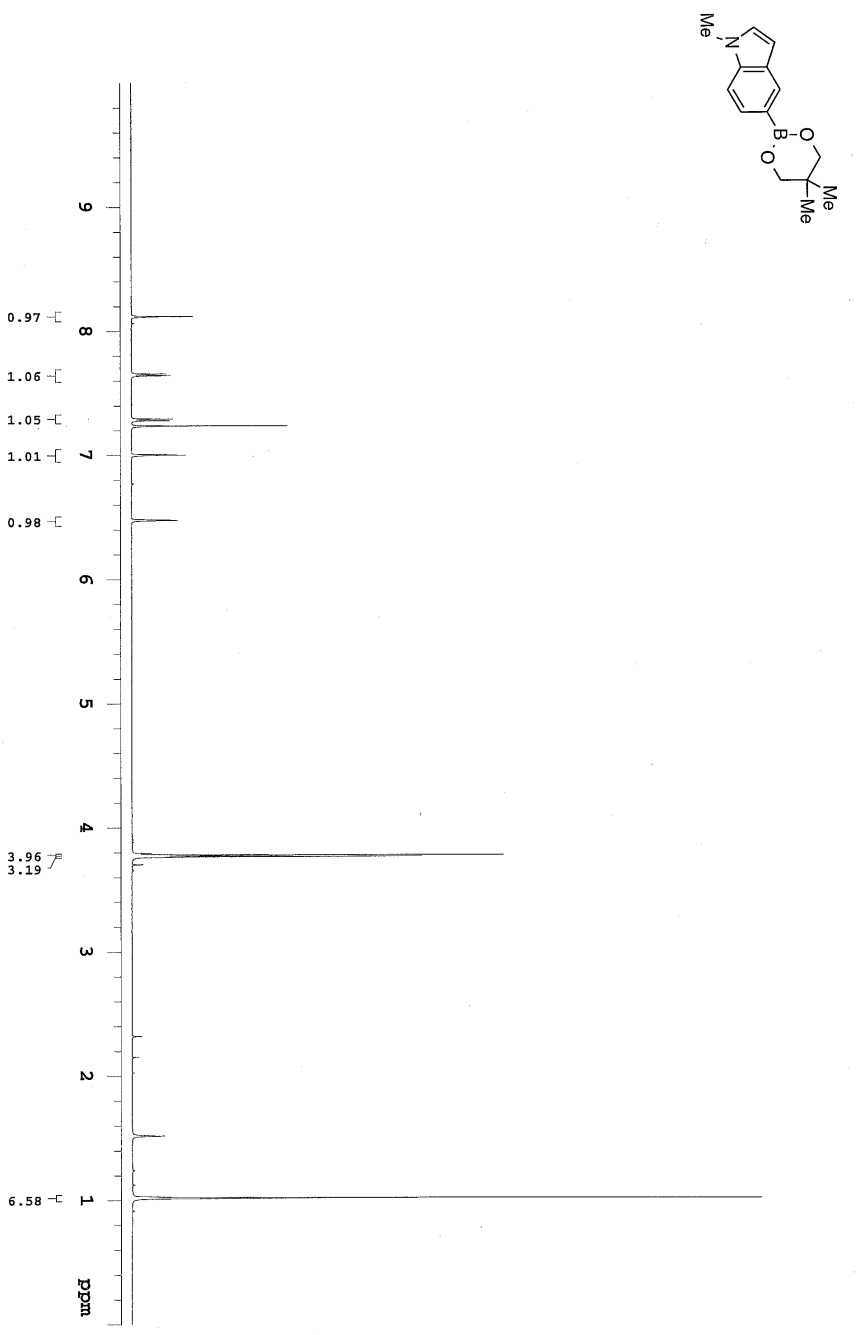
22.086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Me
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7
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4
3
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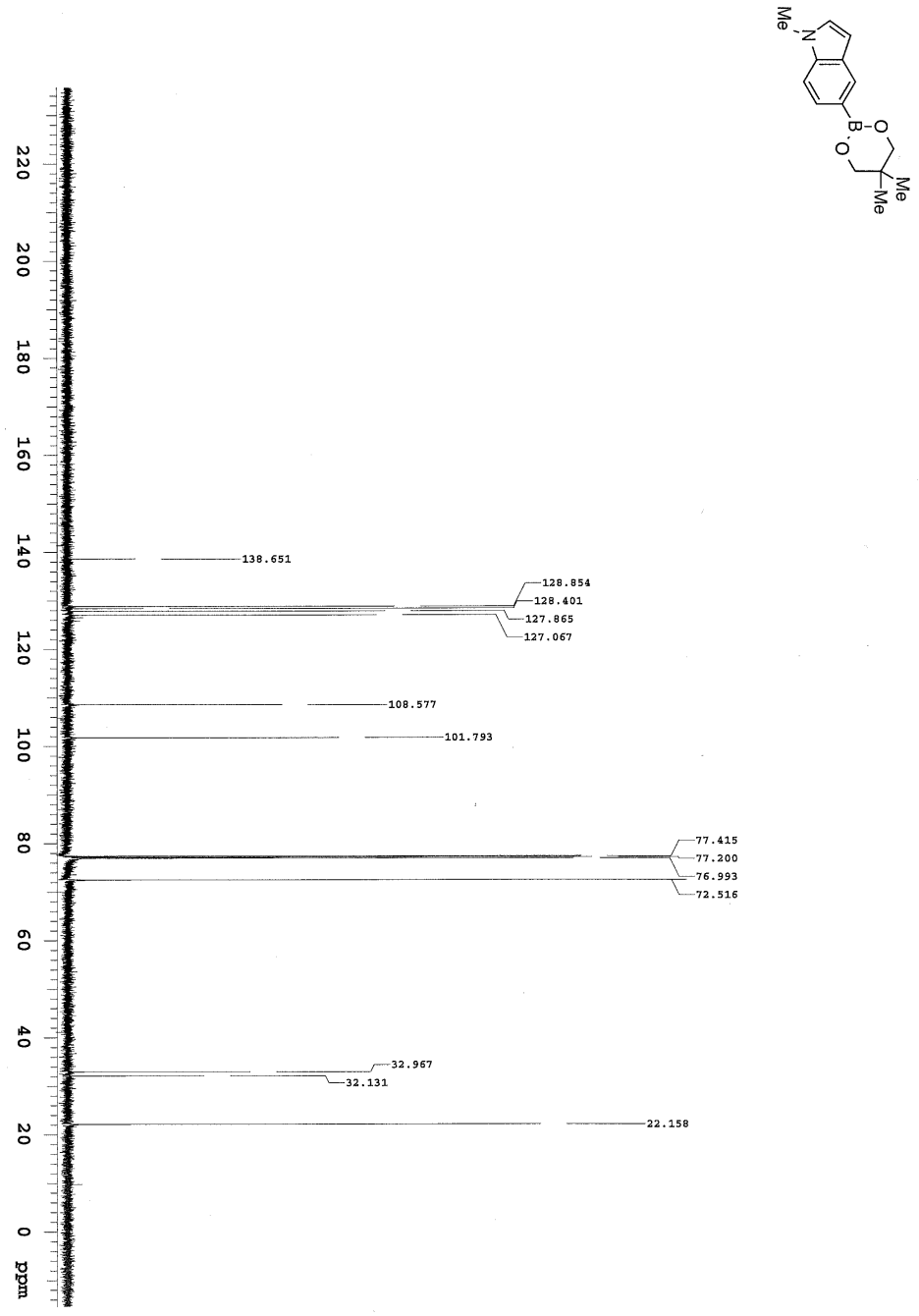
1
ppm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O
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Me
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140
120
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60
40
20
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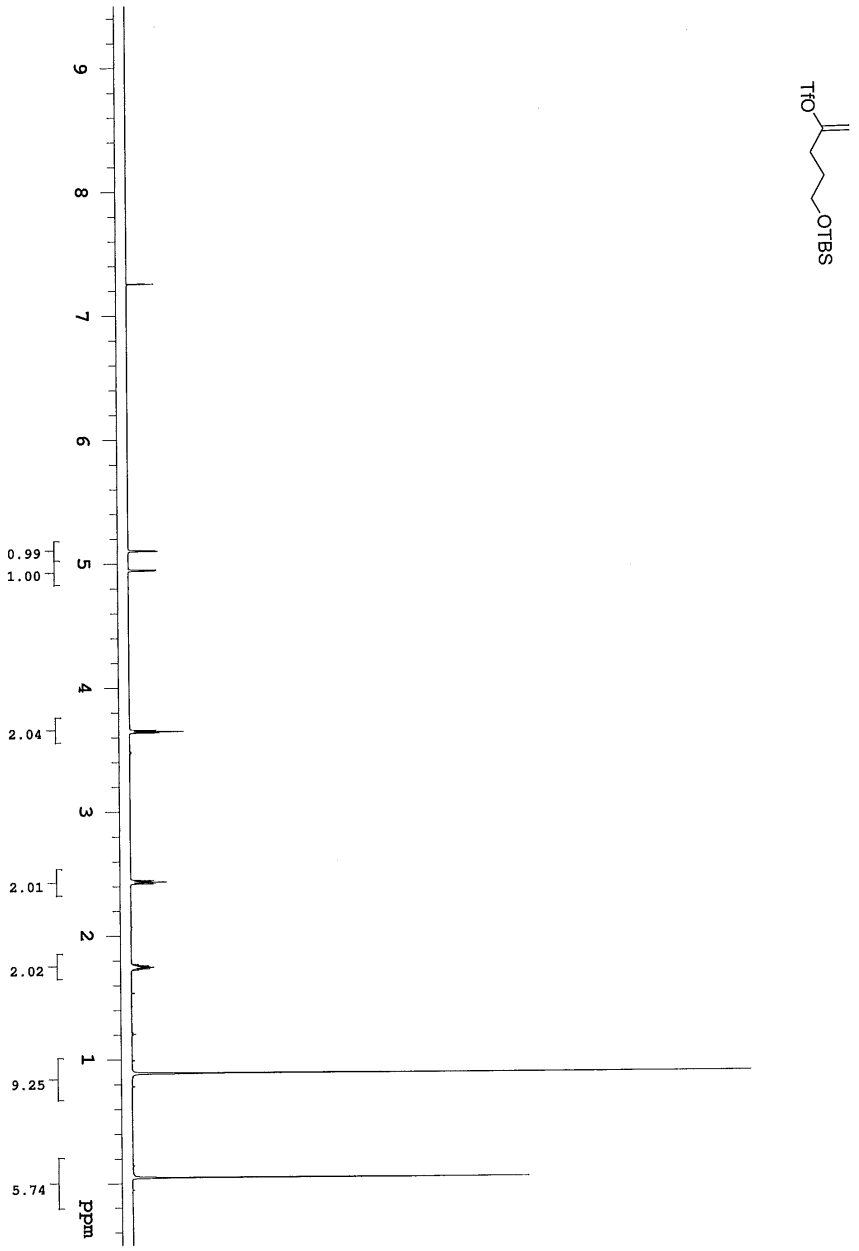
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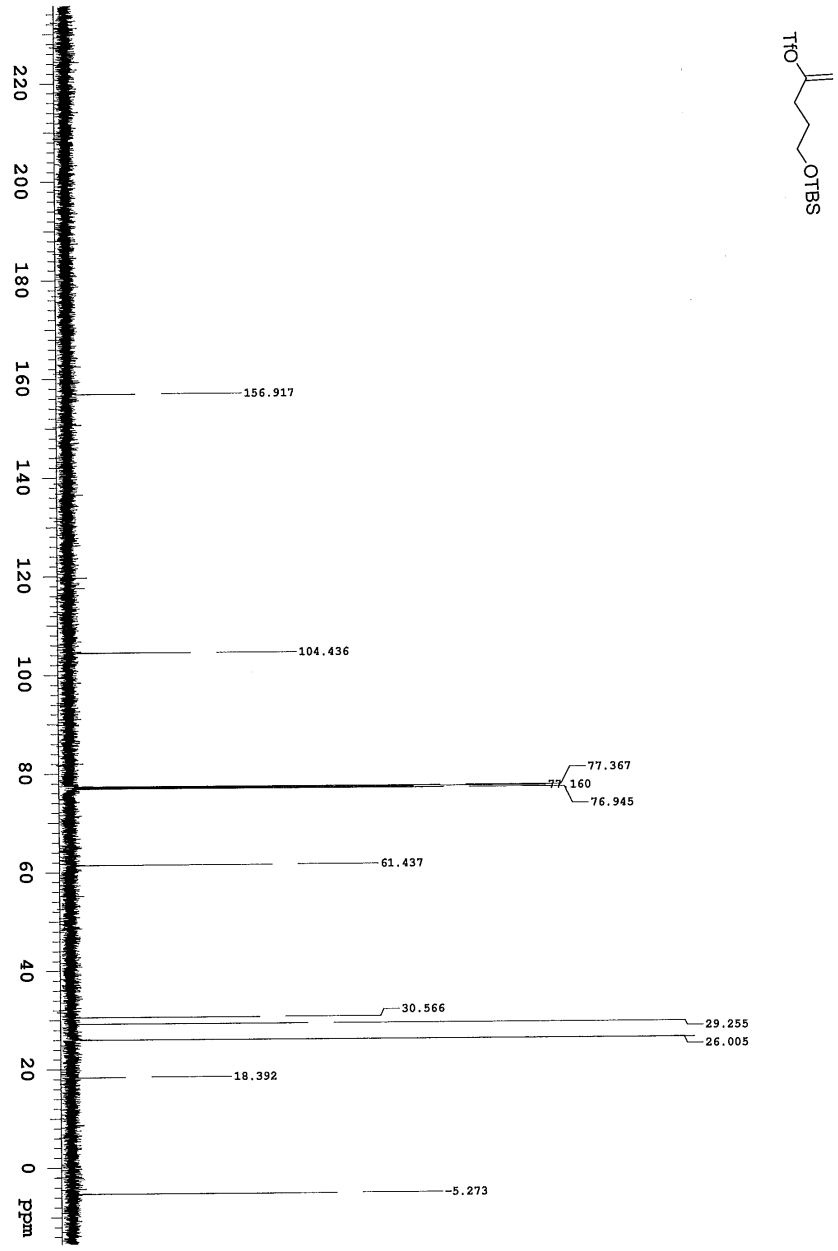
ppm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OTBS
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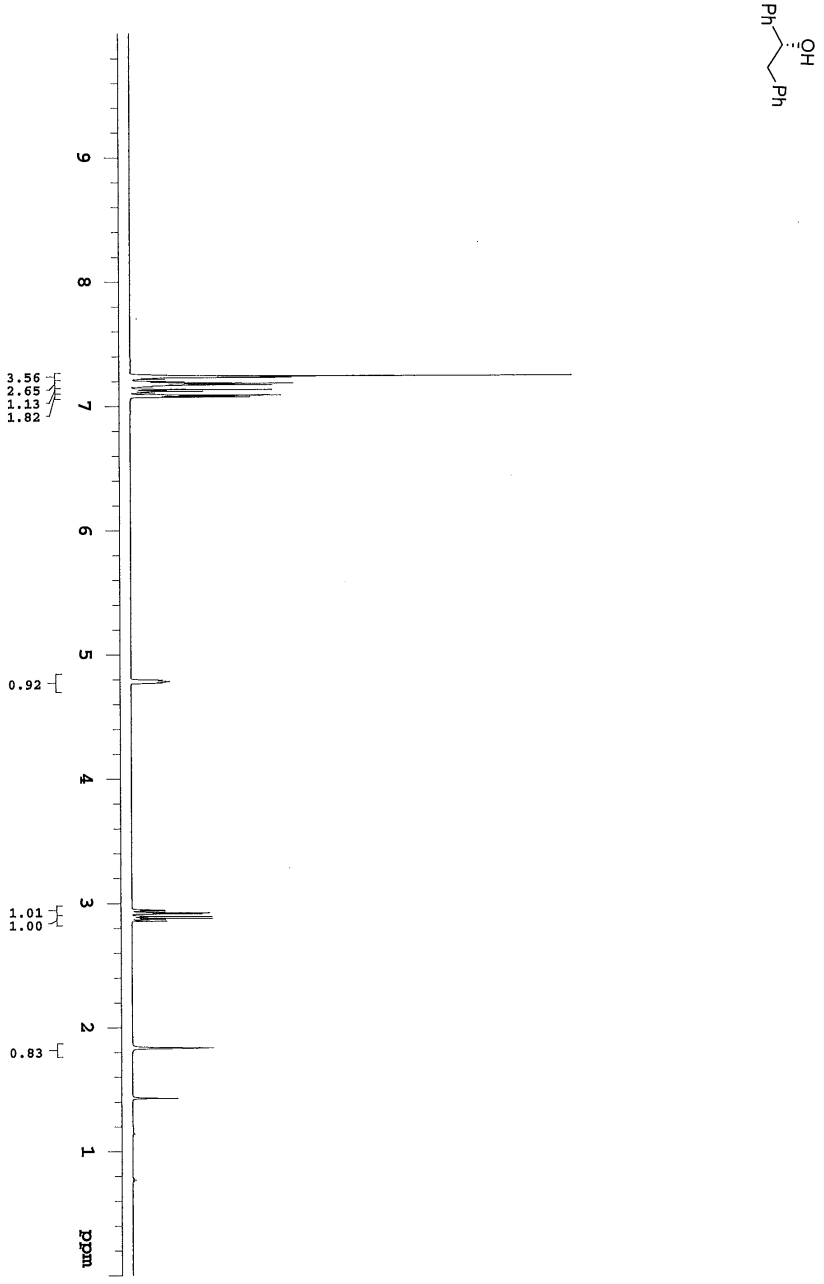
-5.273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3
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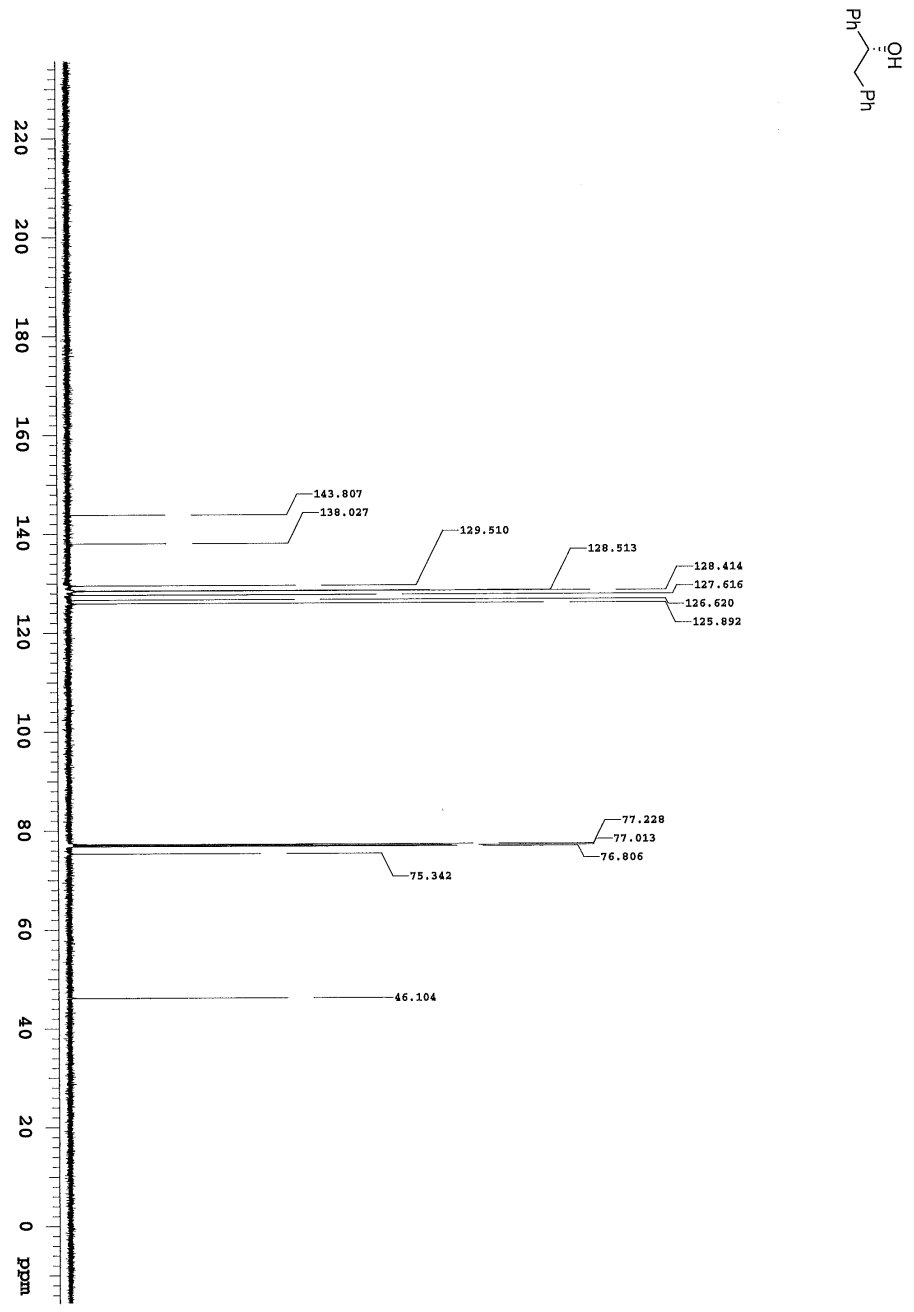
ppm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Ph
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200
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120
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80
60
40
20
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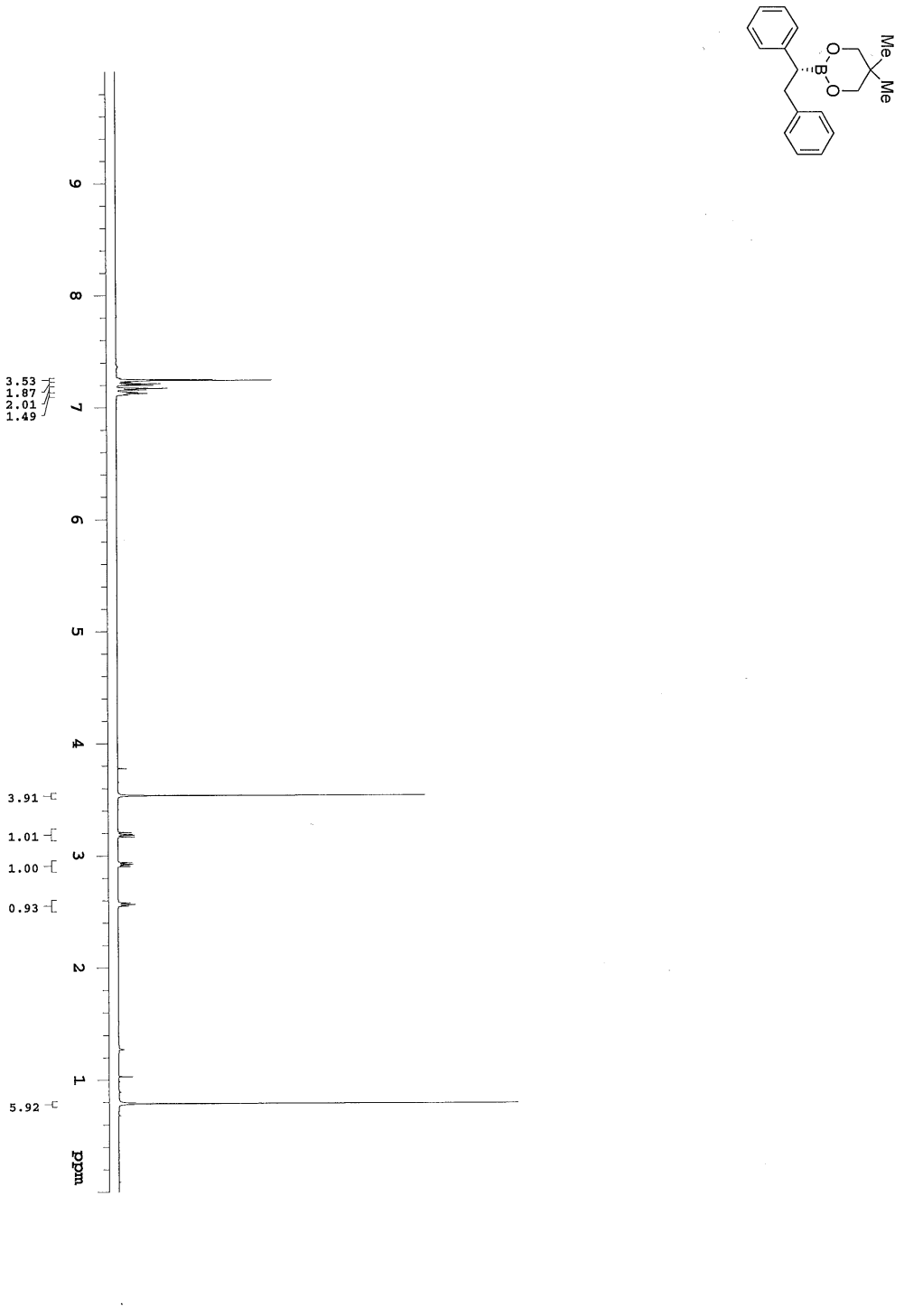
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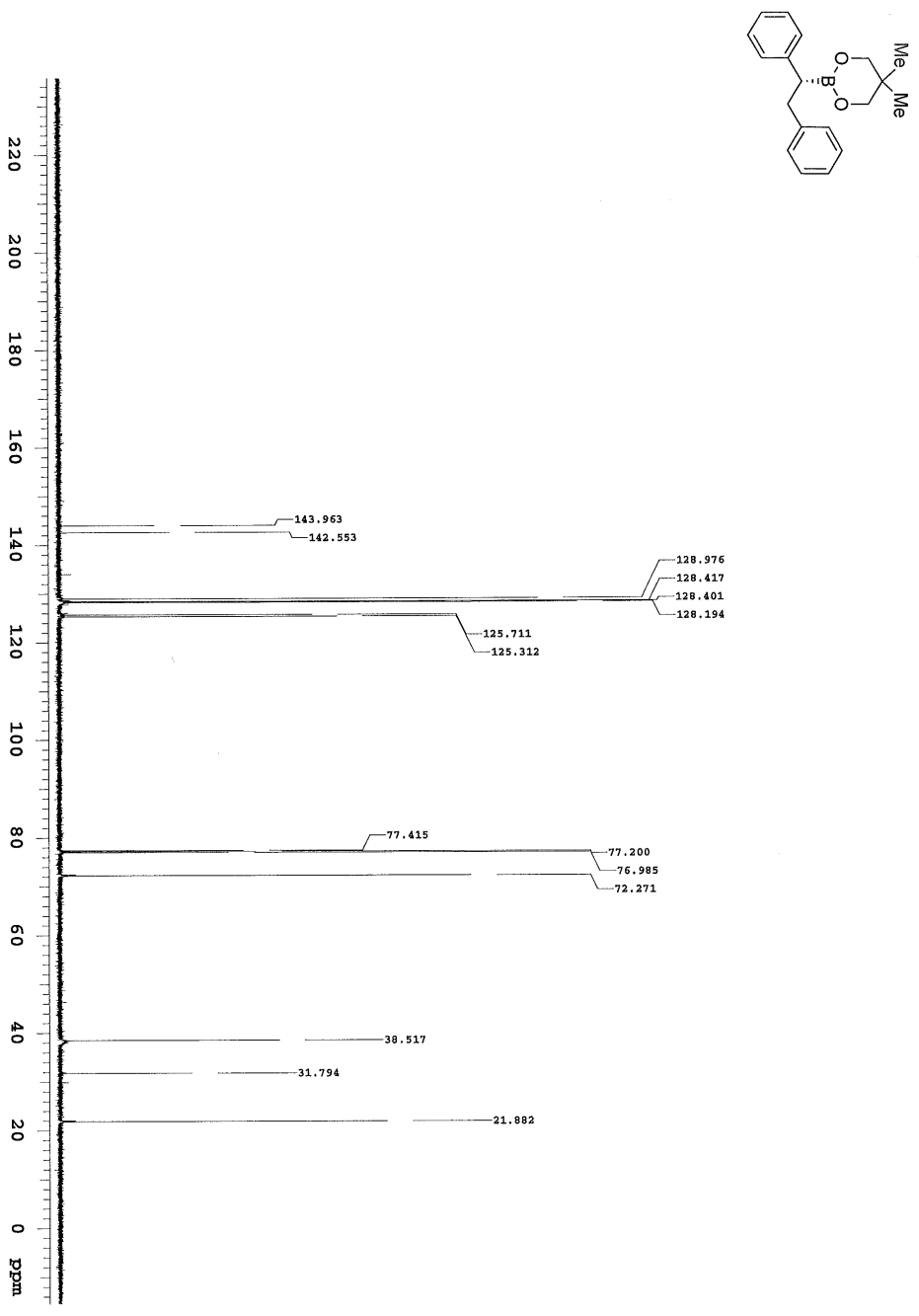
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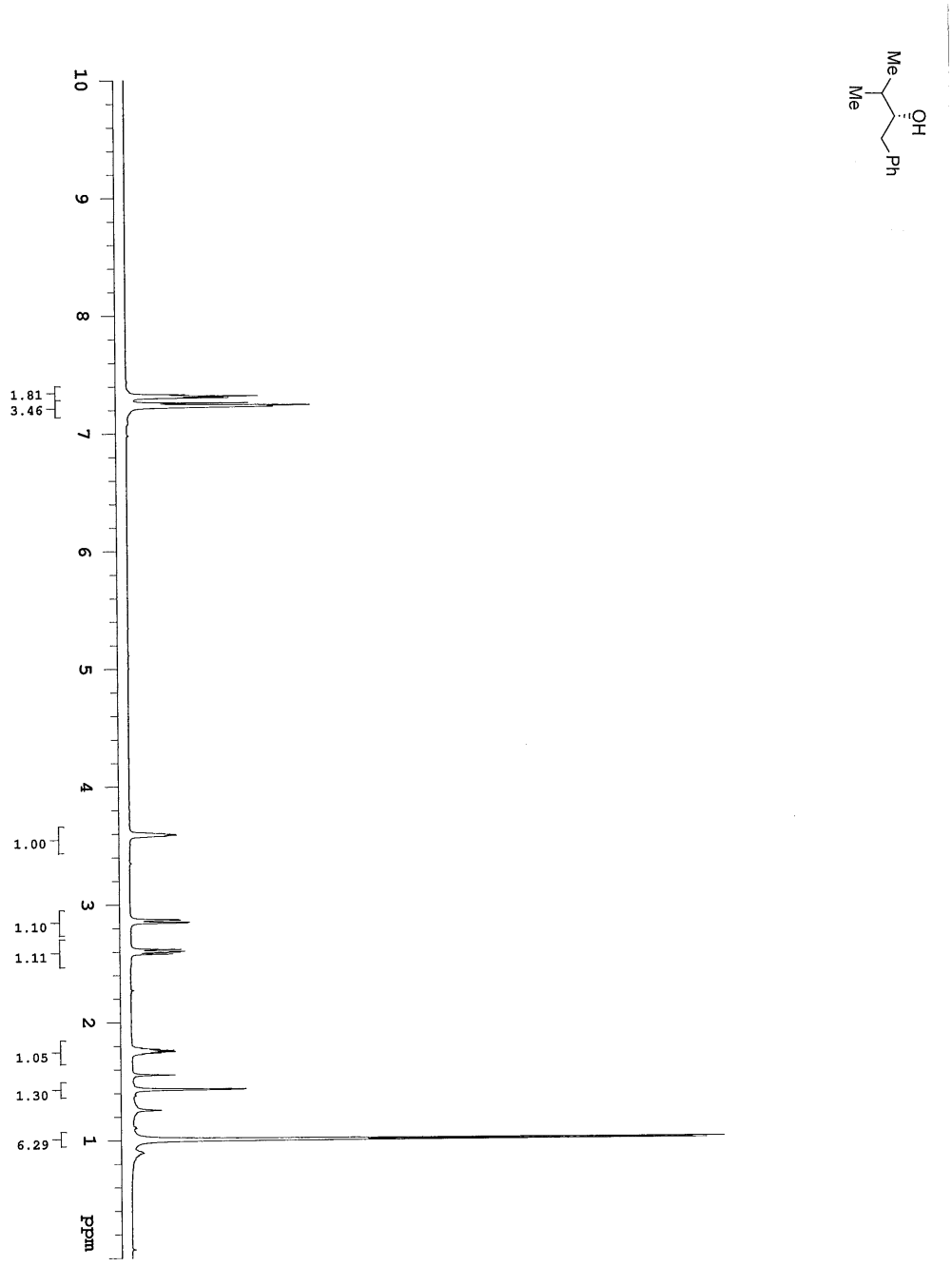
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1.30
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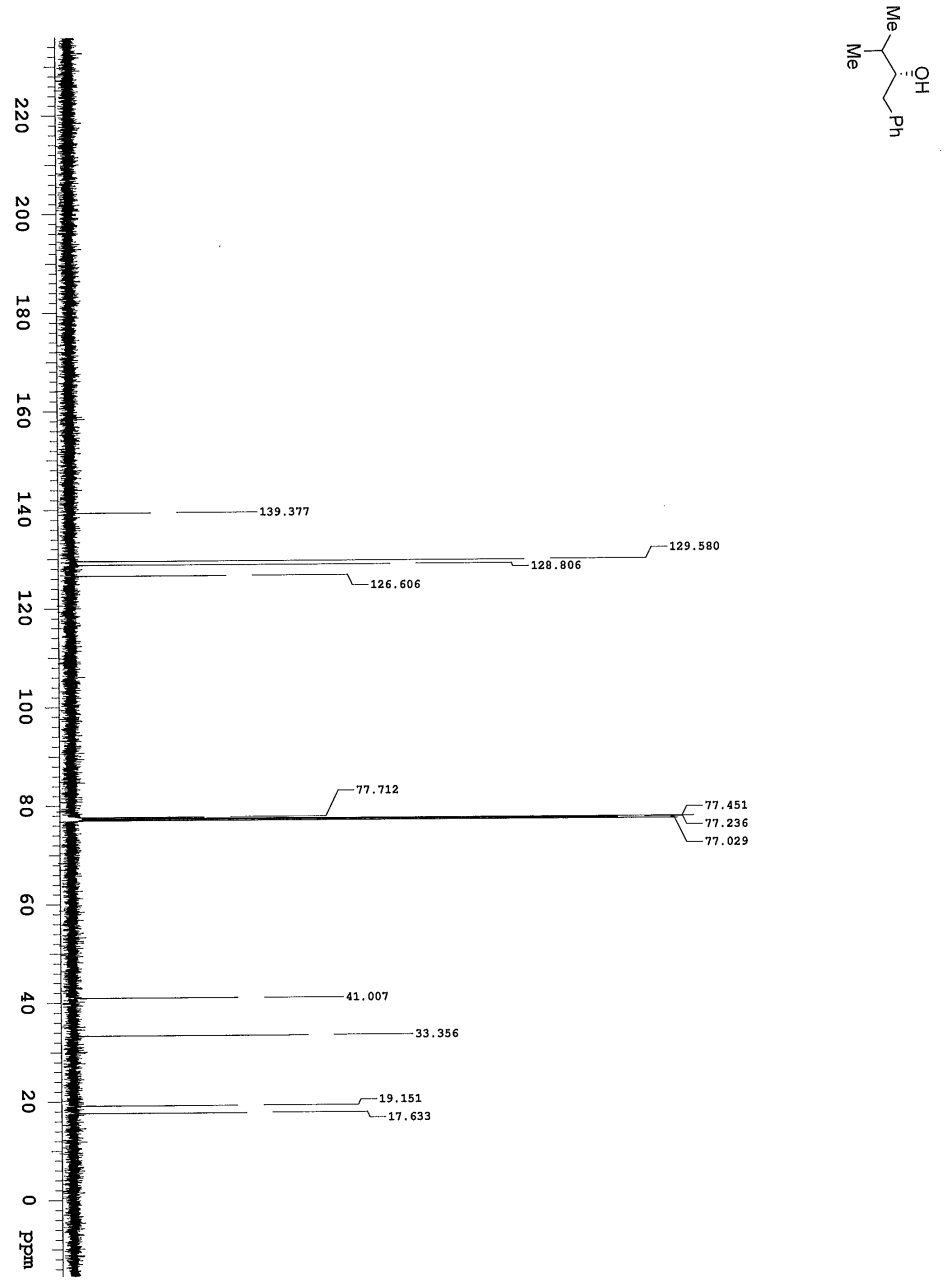
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Ph
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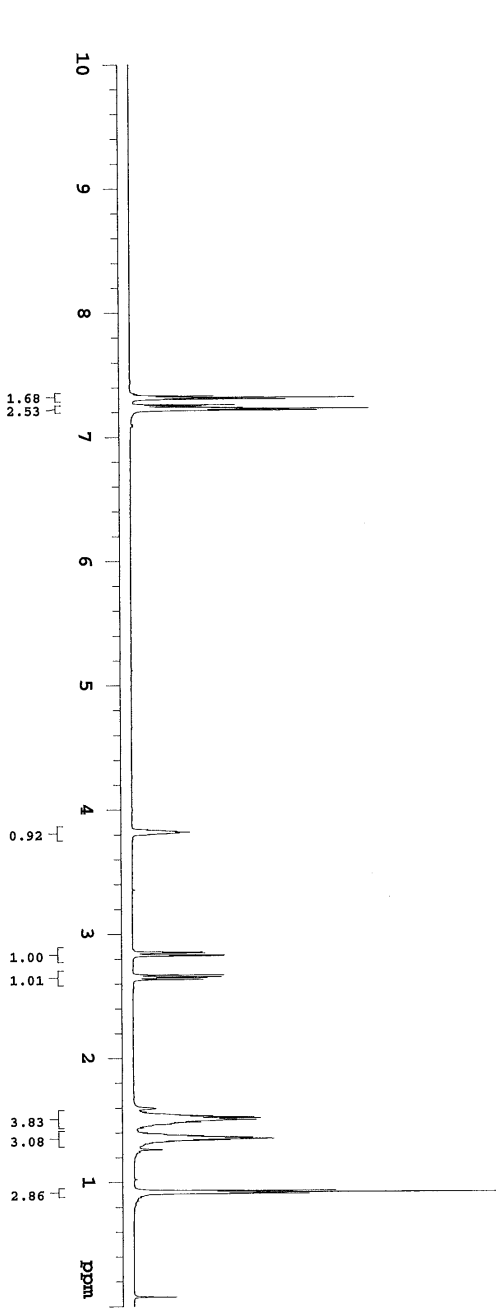
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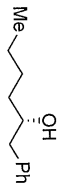
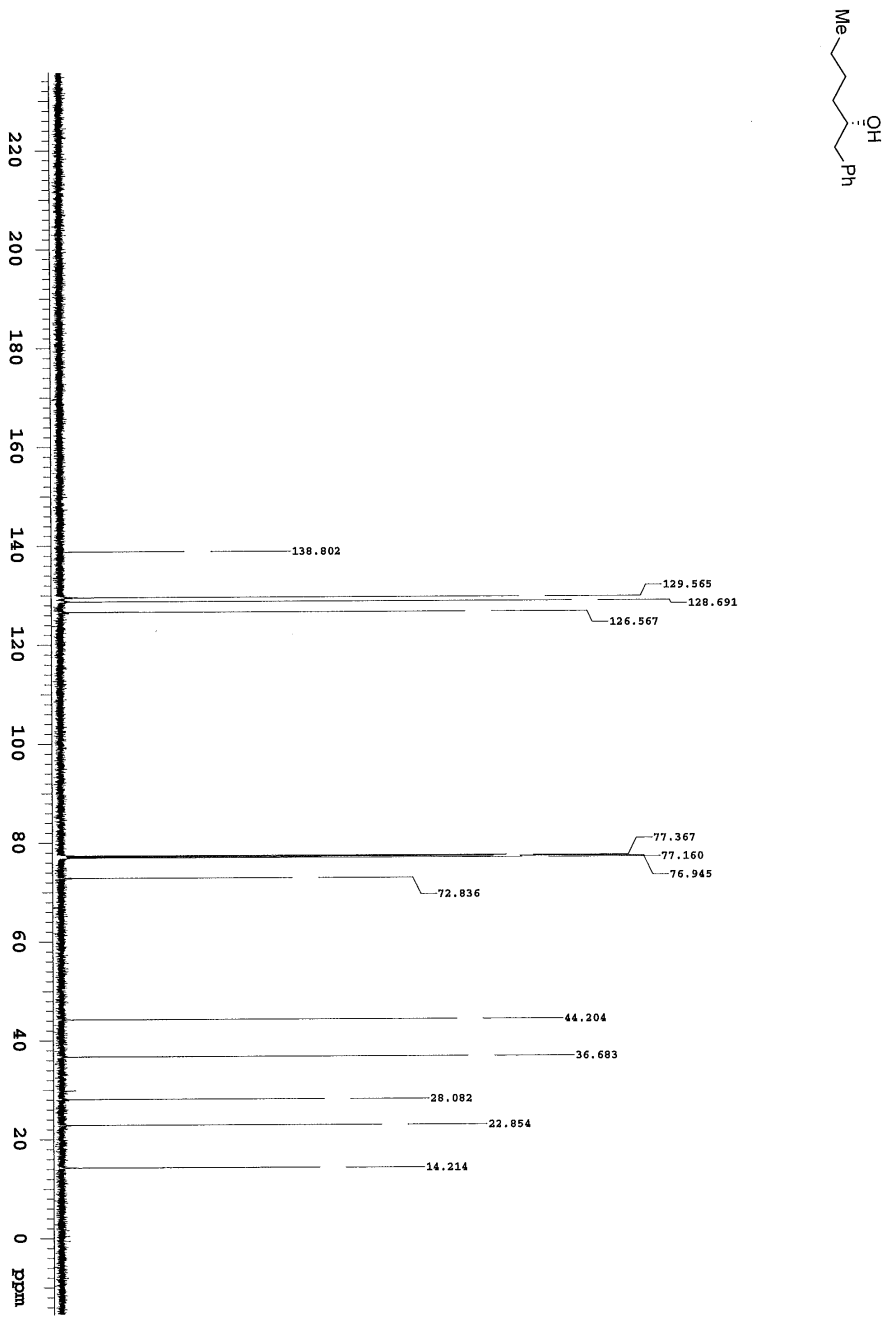

Me
OH
Ph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OH
Ph
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200
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100
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40
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138.802
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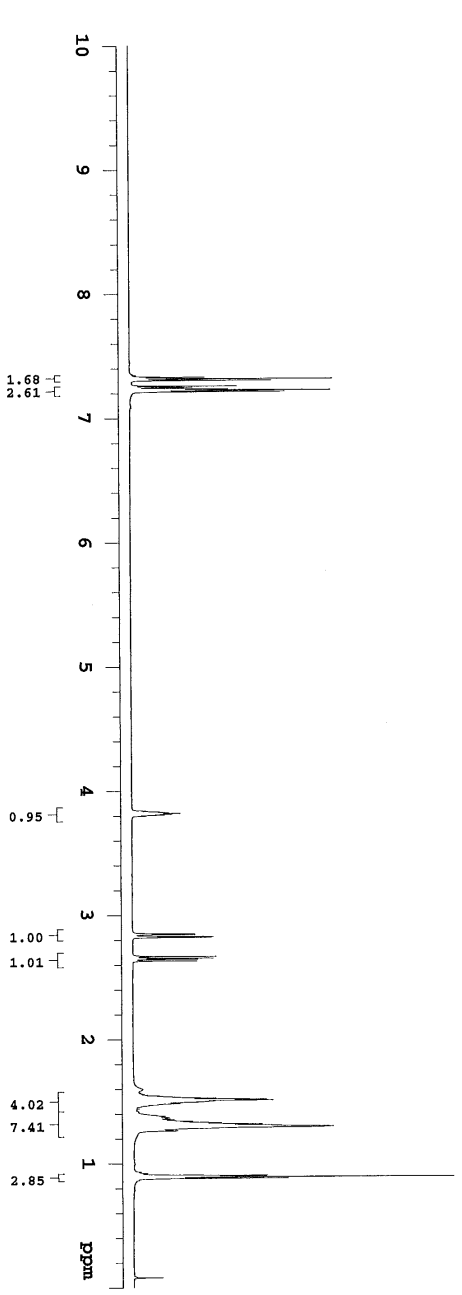
128.691
126.567
77.367
77.160
76.945
72.836
44.204
36.683
28.082
22.854
14.214


10
9
8
7
6
5
4
3
2
1
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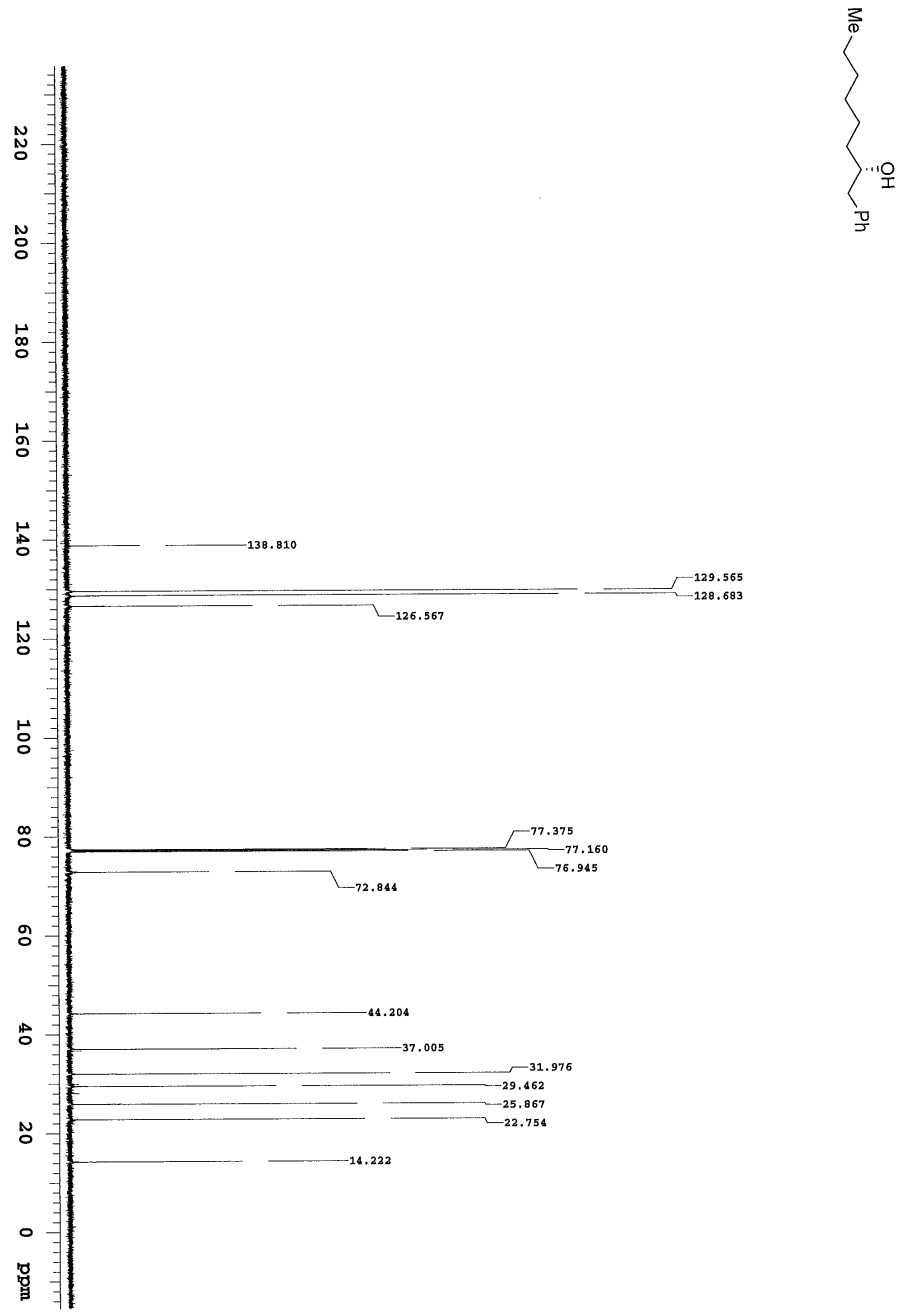
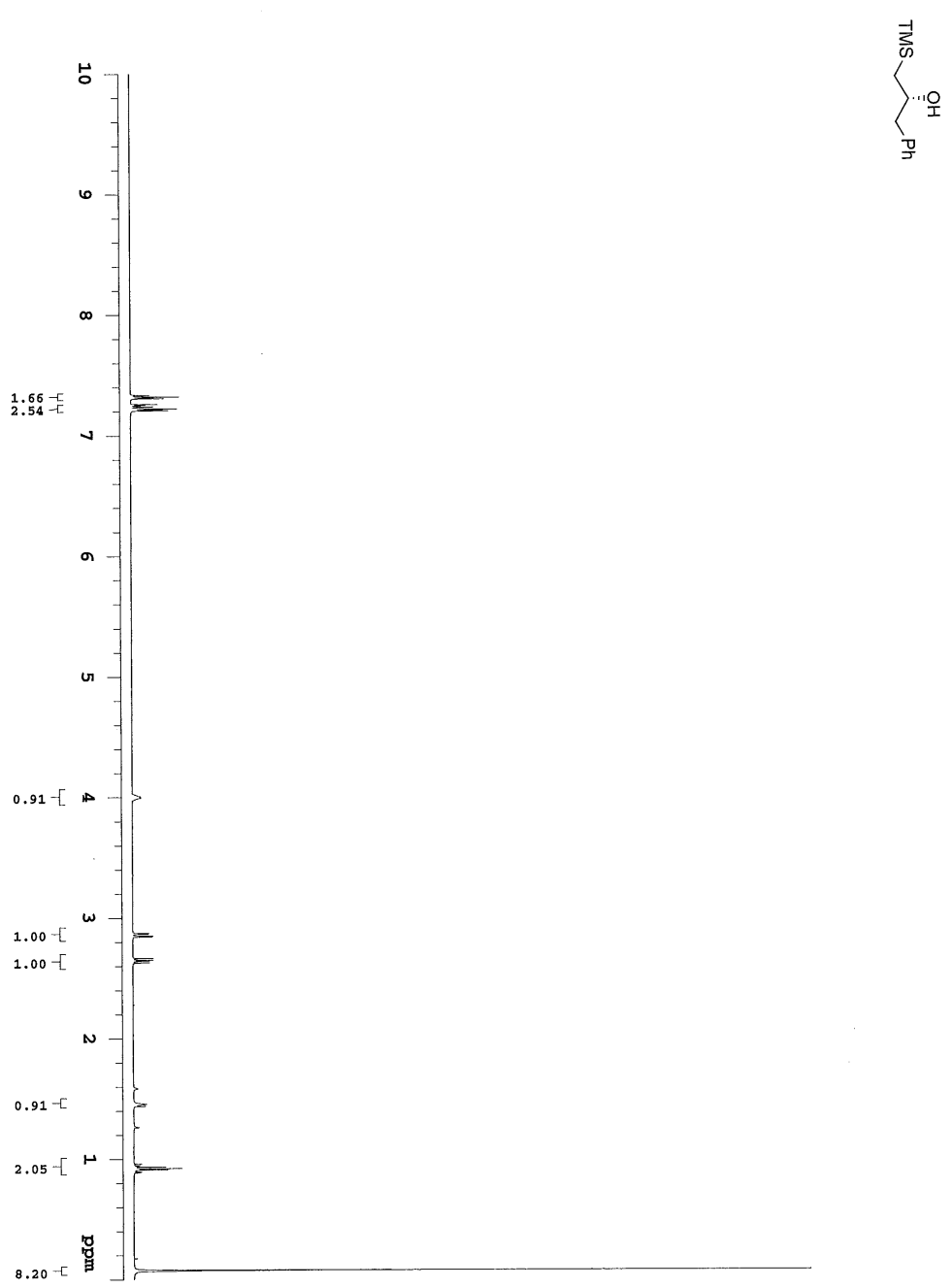
2.61
0.95
1.00
1.01
4.02
7.41
2.85


Me
OH
Ph


Me
OH
Ph
220
200
180
160
140
120
100
80
60
40
20
0
ppm
138.810
129.565
128.683
126.567
77.375
77.160
76.945
72.844
44.204
37.005
31.976
29.462
25.867
22.754
14.222


TMS
OH
Ph
10
9
8
7
6
5
4
3
2
1
ppm
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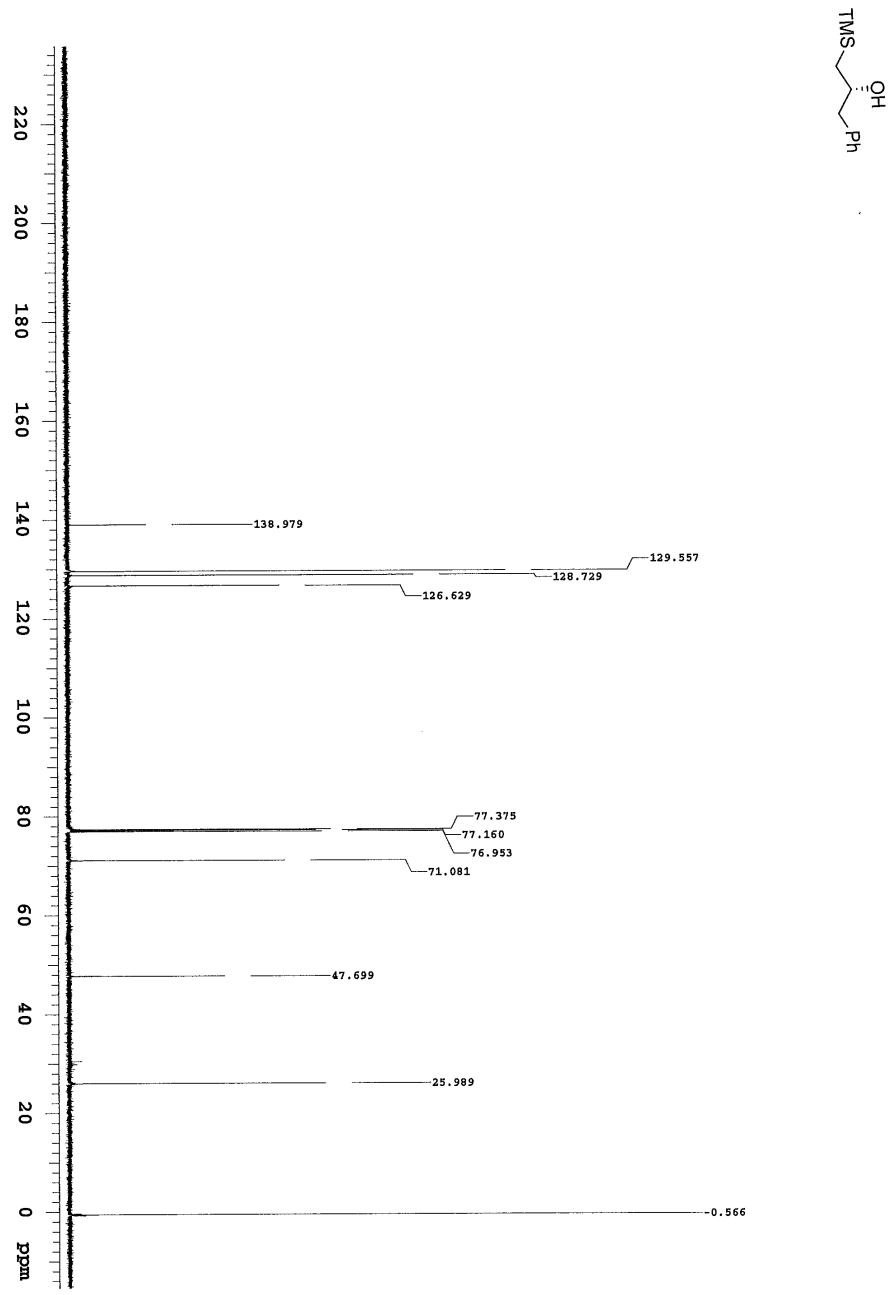
2.54
0.91
1.00
1.00
0.91
2.05
8.20


TMS
OH
Ph
220
200
180
160
140
120
100
80
60
40
20
0
ppm
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128.729
126.629
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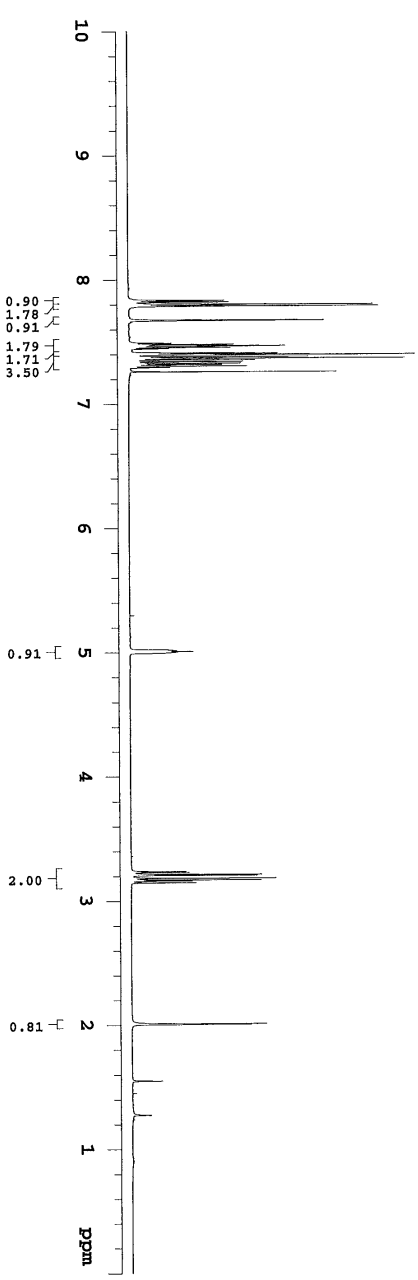
77.160
76.953
71.081
47.699
25.989
0.566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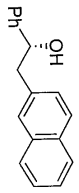
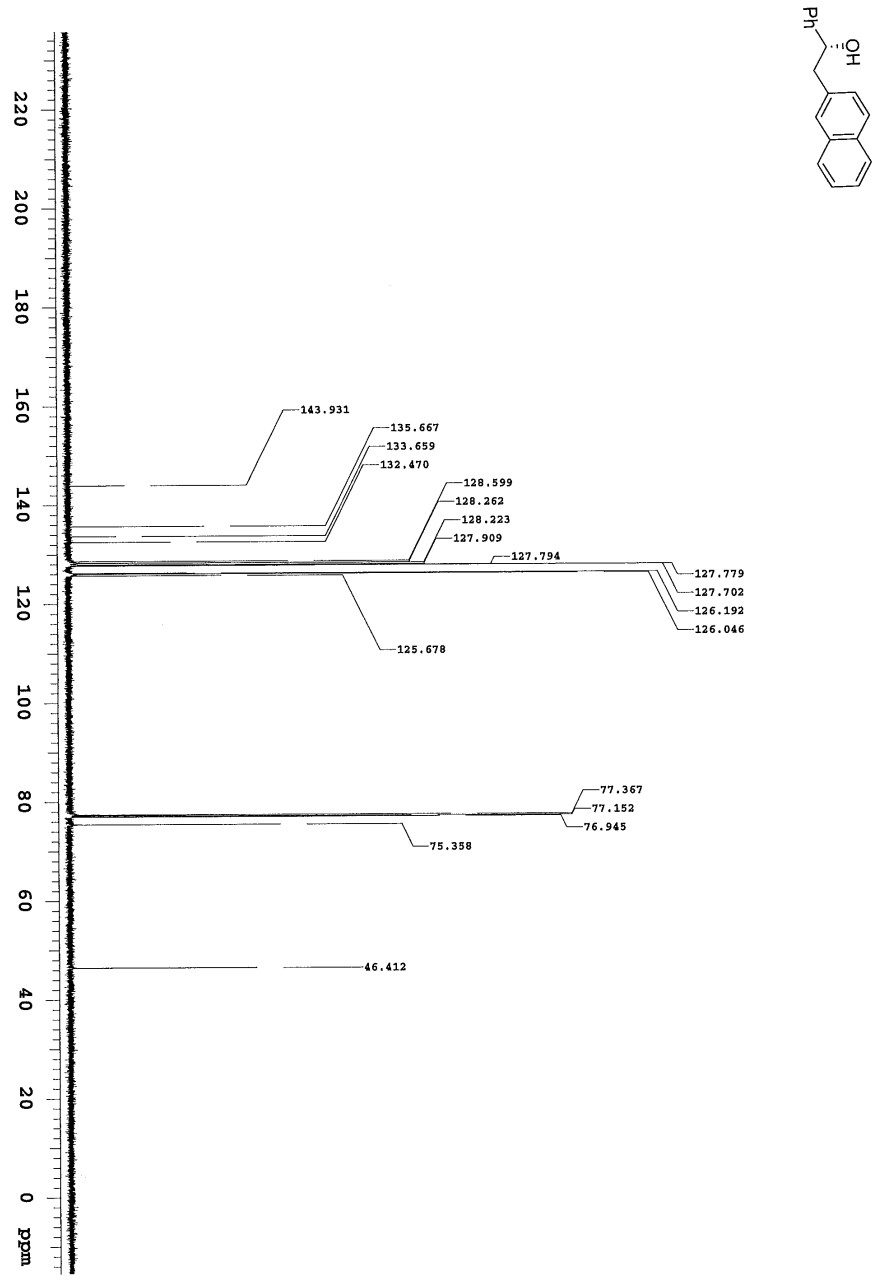
1.78
0.91
1.79
1.71
3.50
0.91
2.00
0.81
10
9
8
7
6
5
4
3
2
1
ppm


Ph
OH


Ph
OH
220
200
180
160
140
120
100
80
60
40
20
0
ppm
143.931
135.667
133.659
132.470
128.599
128.262
128.223
127.909
127.794
127.779
127.702
126.192
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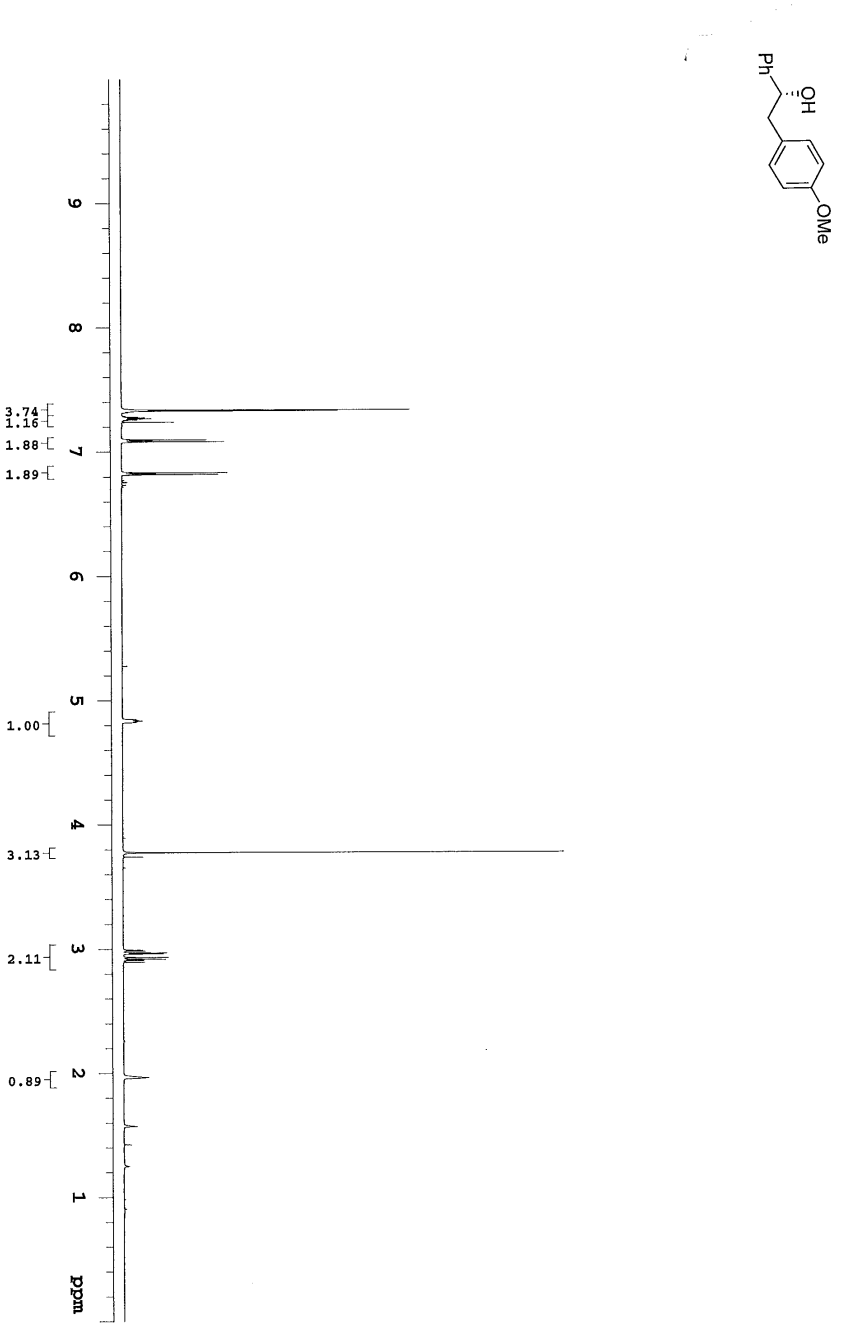
77.367
77.152
76.945
75.358
46.412


Ph
OH
OMe
3.74
1.16
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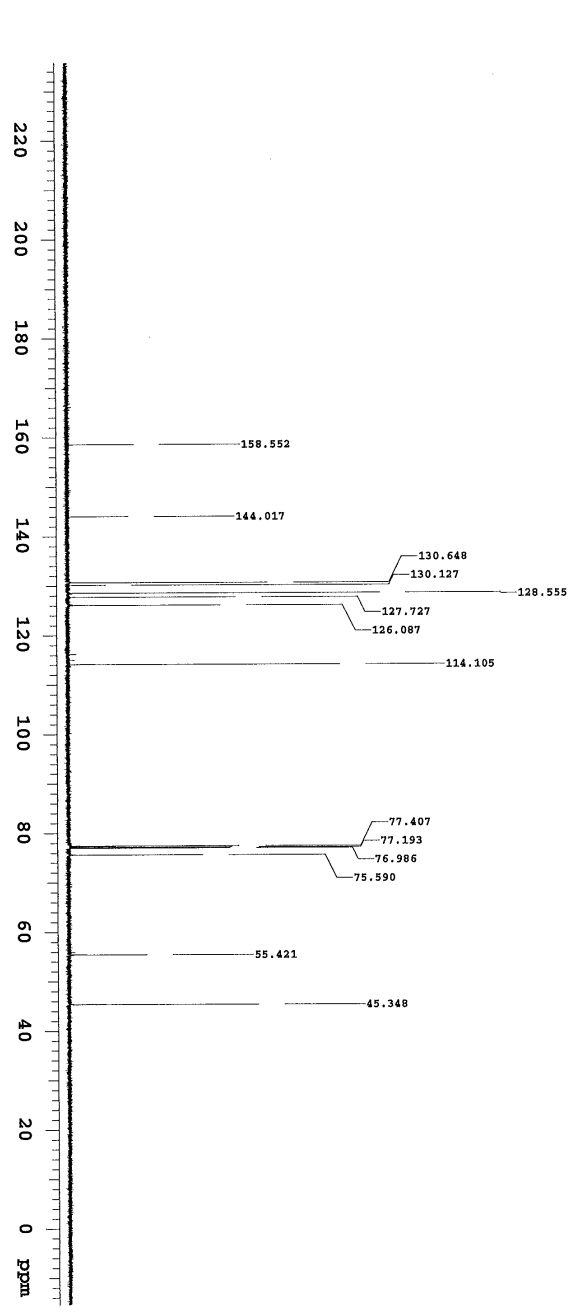
1.00
3.13
2.11
0.89
9
8
7
6
5
4
3
2
1
ppm


Ph
OH
OMe
220
200
180
160
140
120
100
80
60
40
20
0 ppm
158.552
144.017
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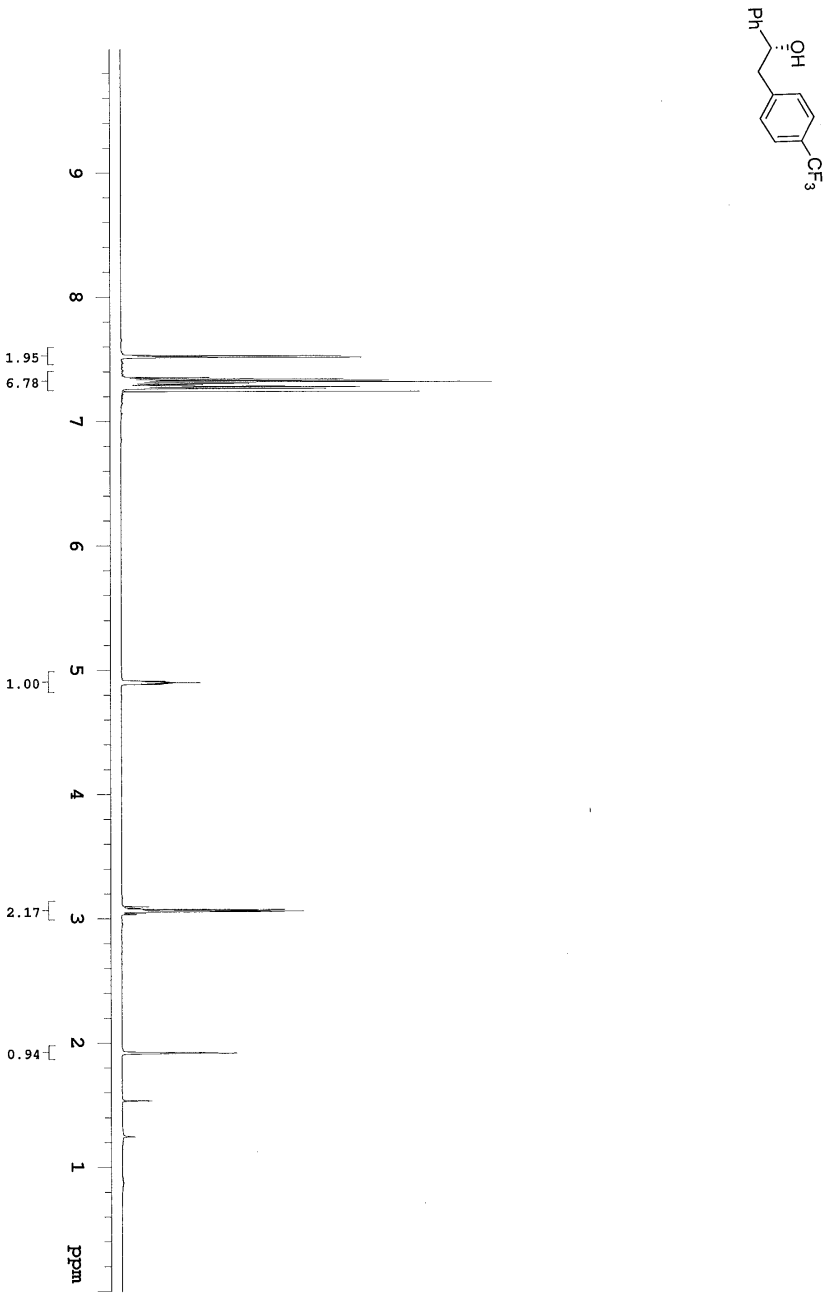
77.193
76.986
75.590
55.421
45.348


Ph
OH
CF3
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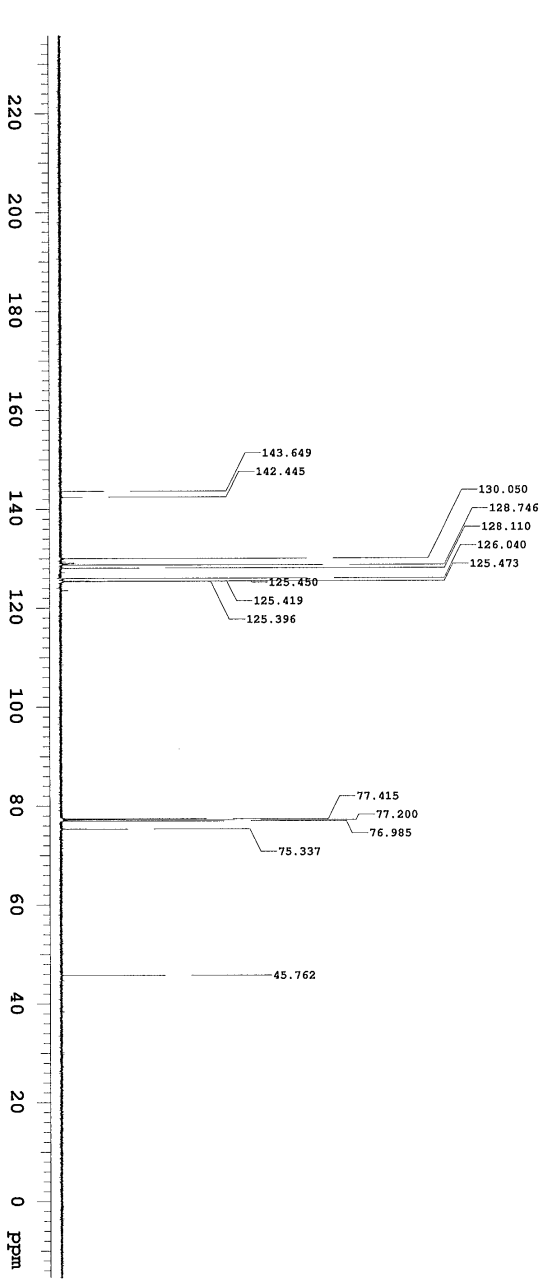
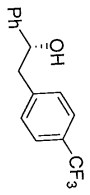
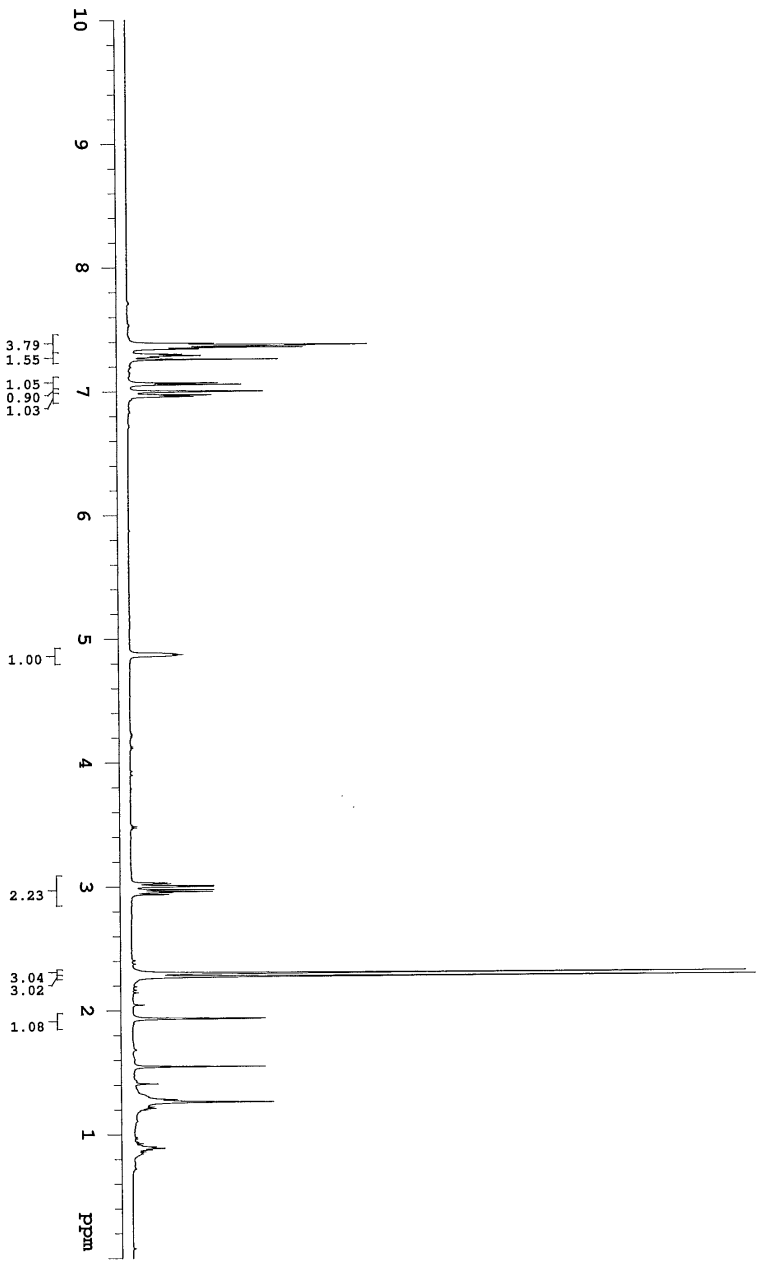
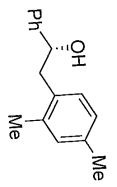
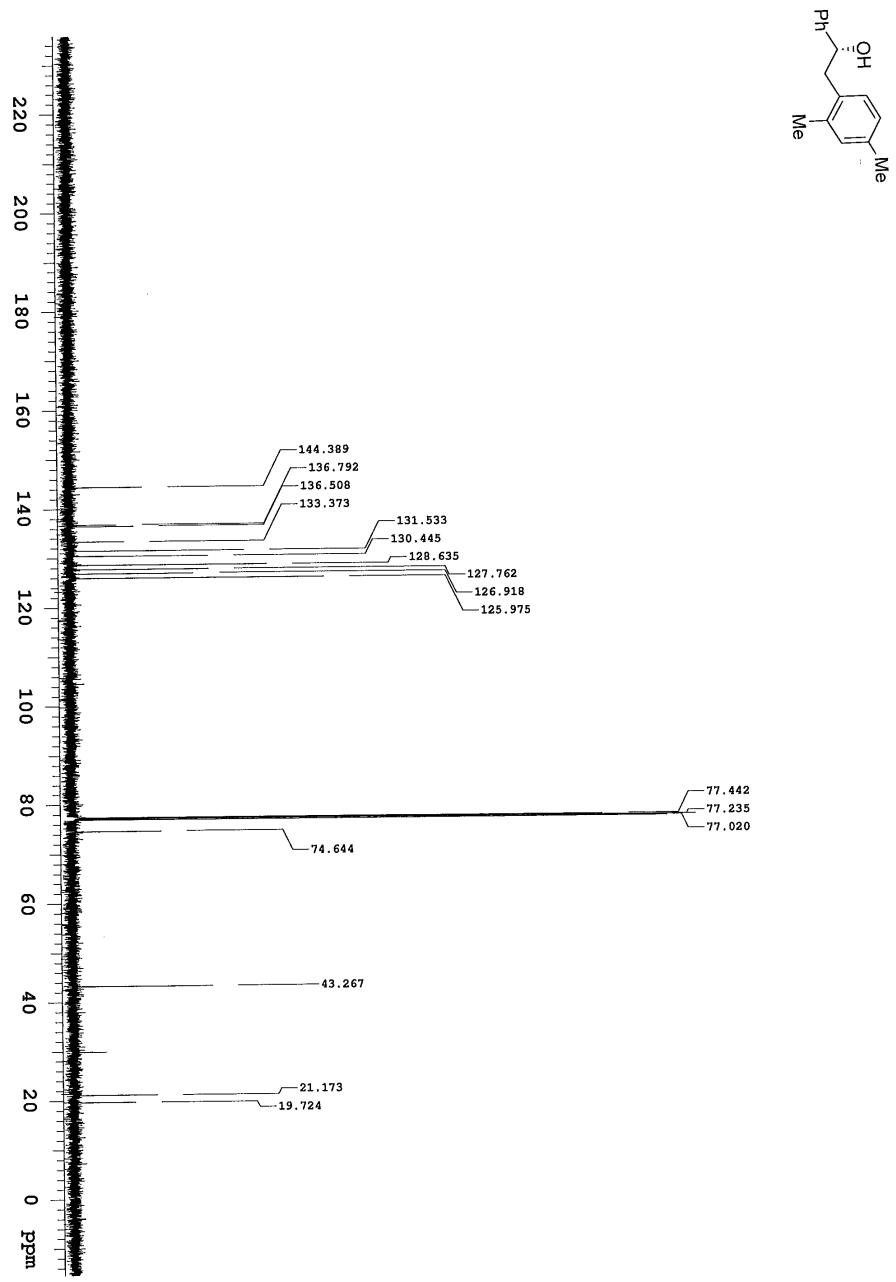
6.78
1.00
2.17
0.94
9
8
7
6
5
4
3
2
1
ppm

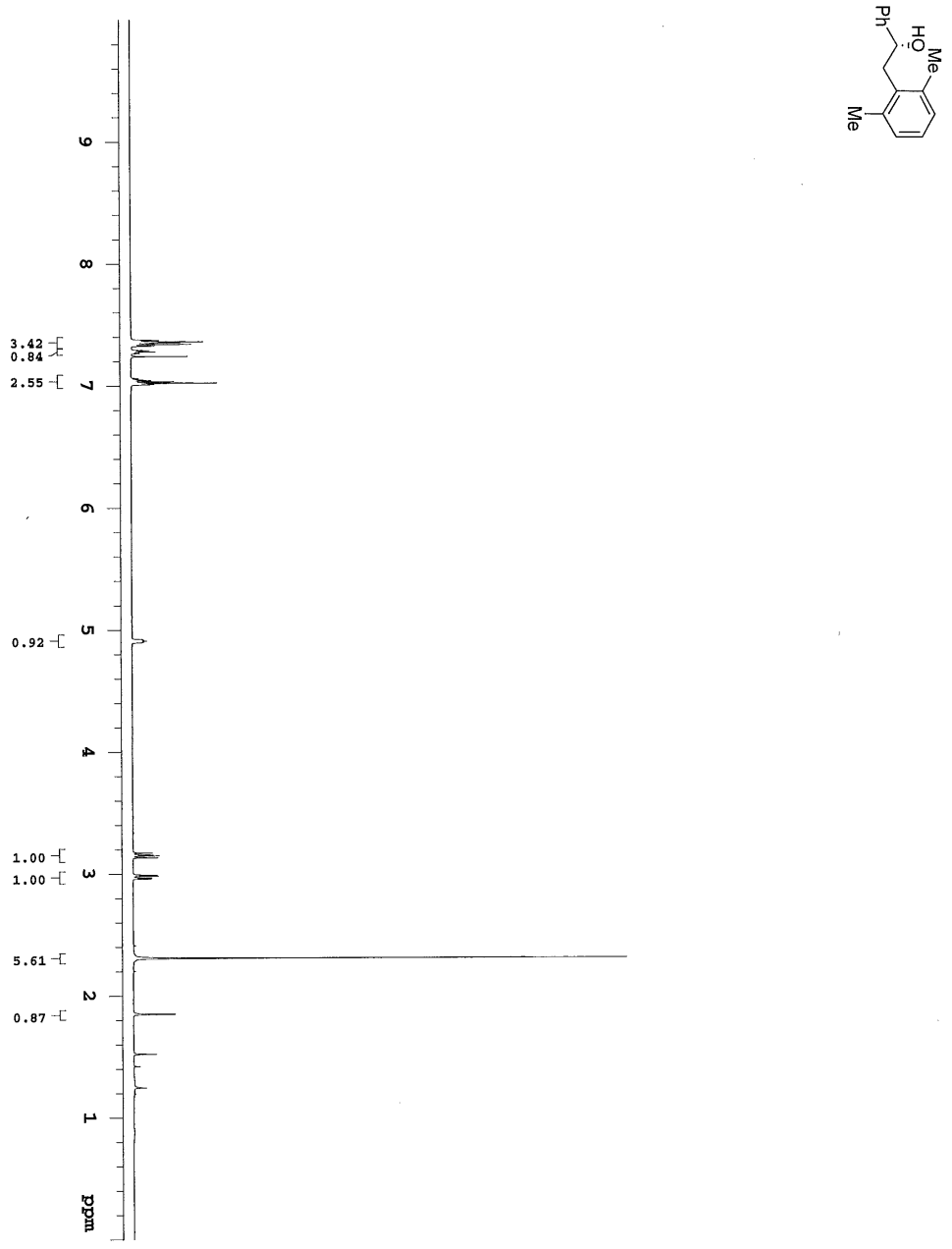

220
200
180
160
140
120
100
80
60
40
20
0
ppm
143.649
142.445
130.050
128.746
128.110
126.040
125.473
125.450
125.419
125.396
77.415
77.200
76.985
75.337
45.762


Ph
OH
CF3


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


Ph
OH
Me
Me
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
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Ph
HO
Me
Me
3.42
0.84
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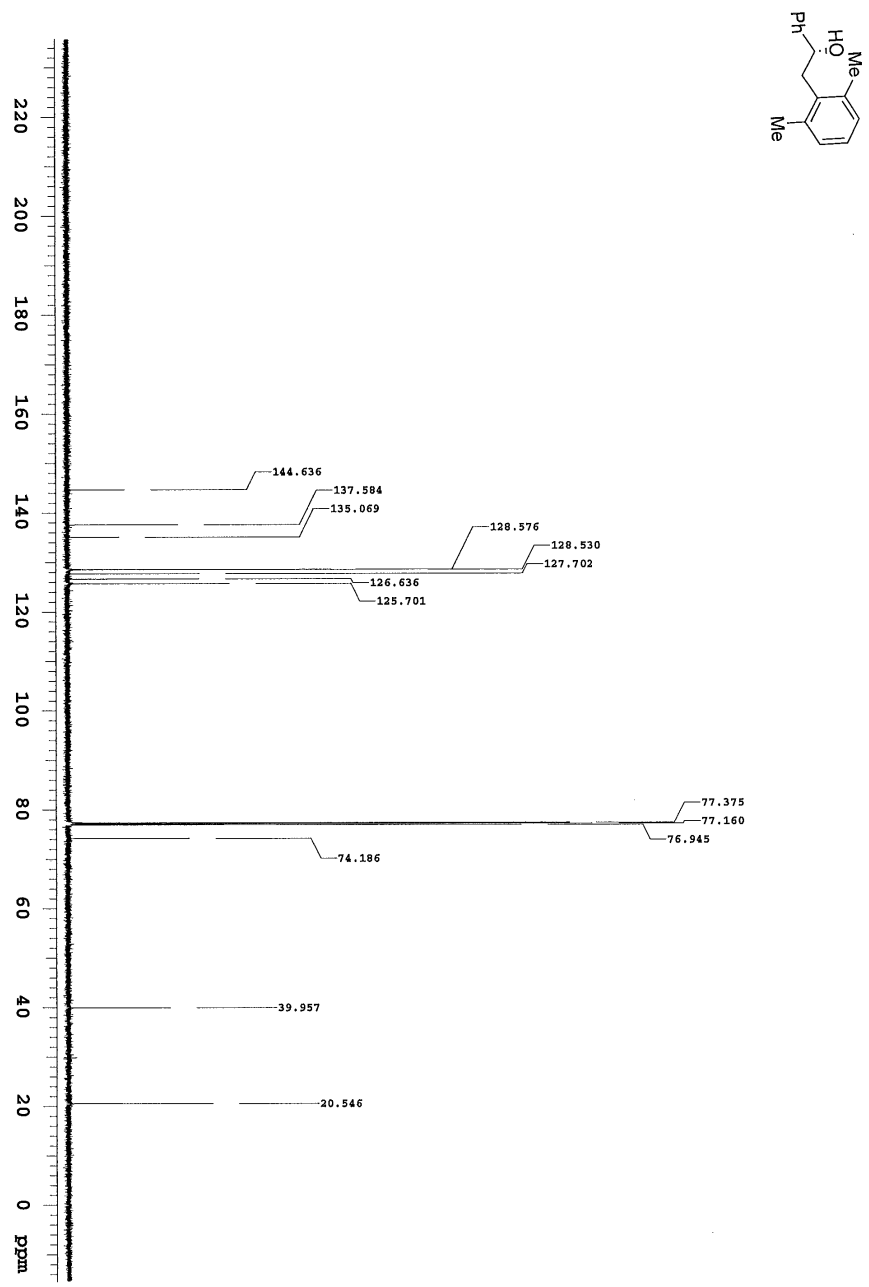
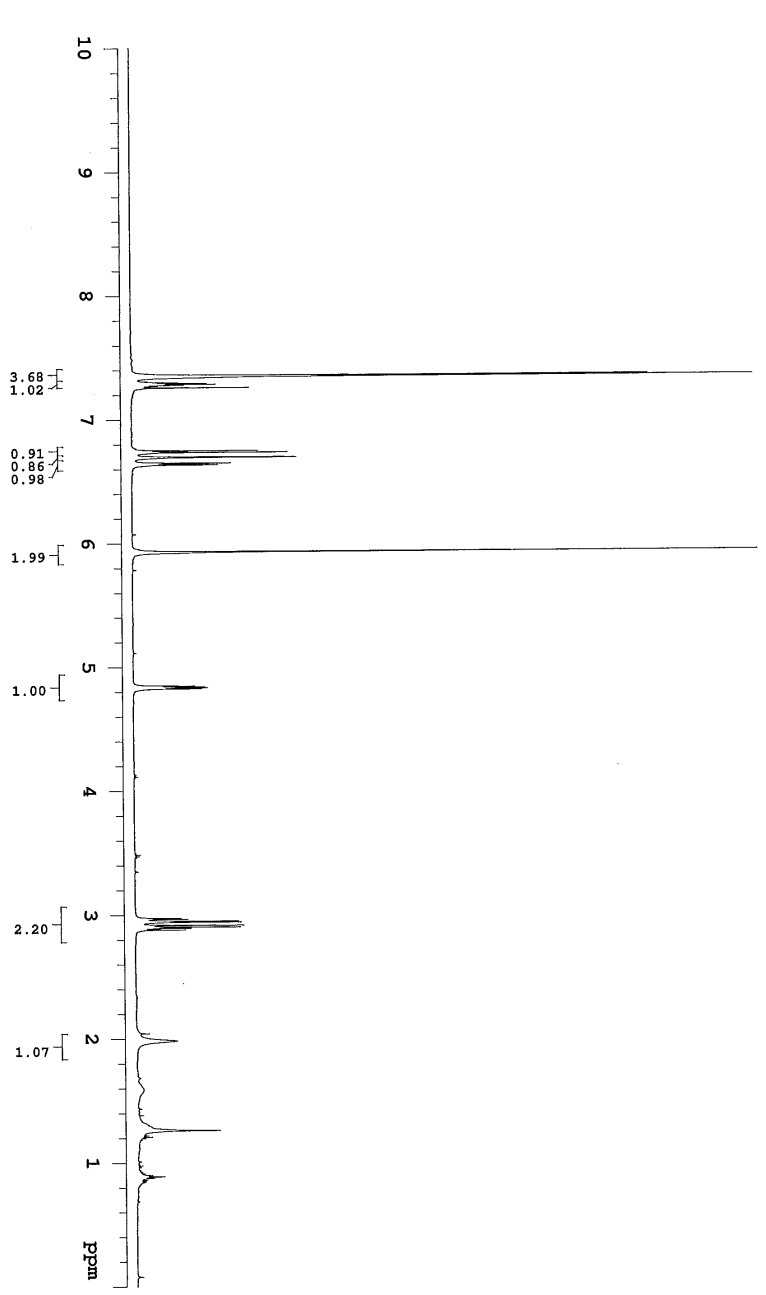
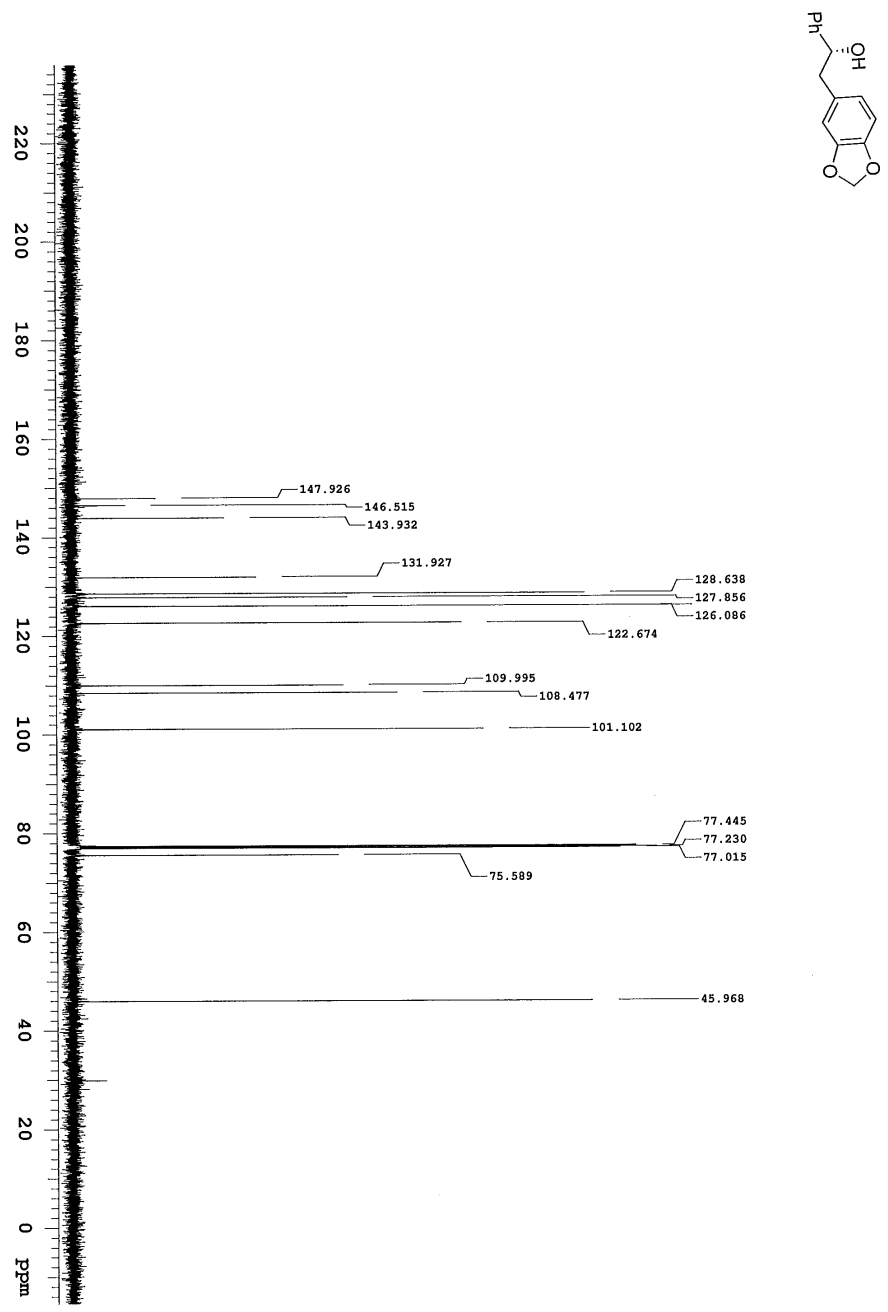
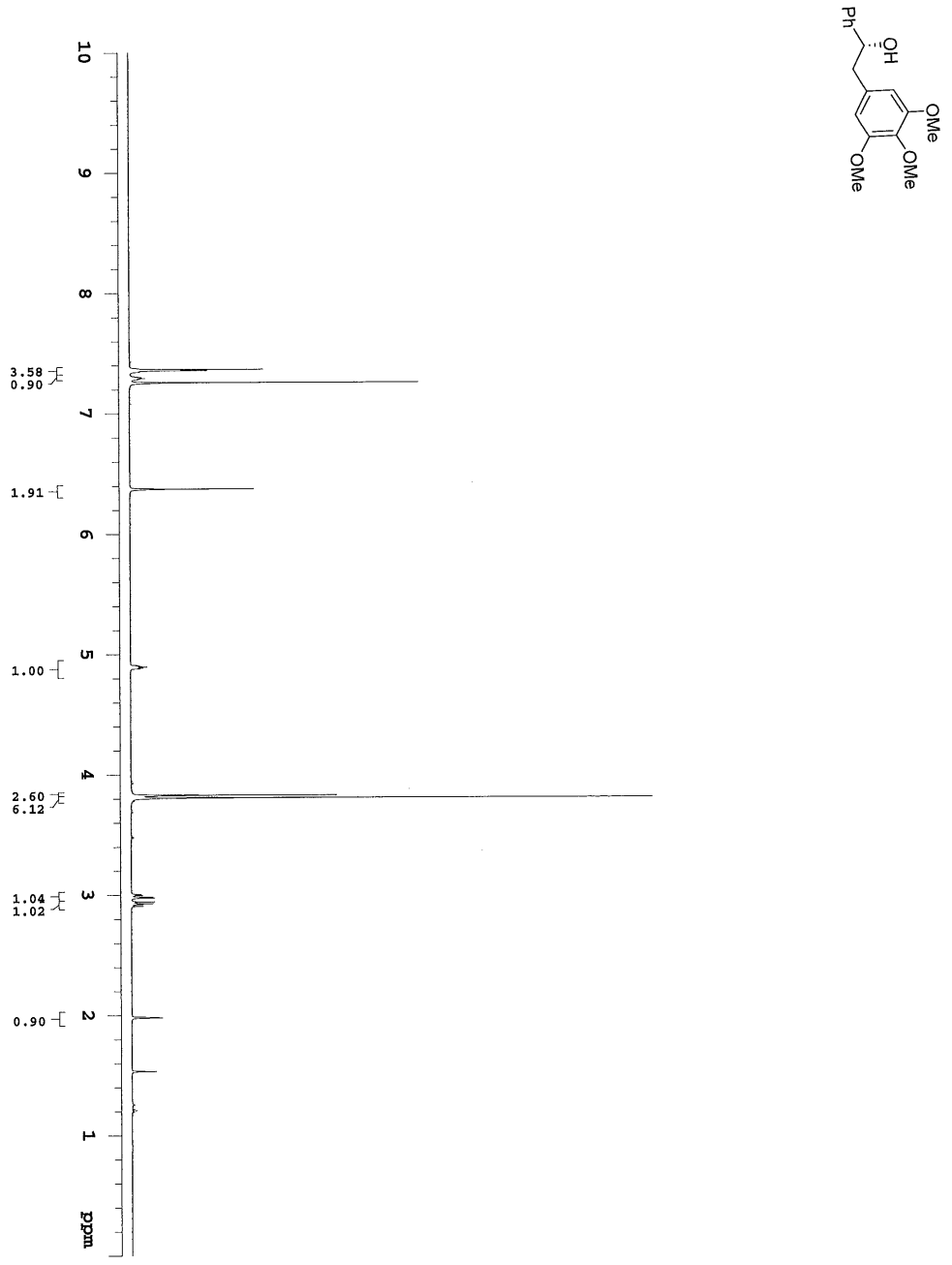
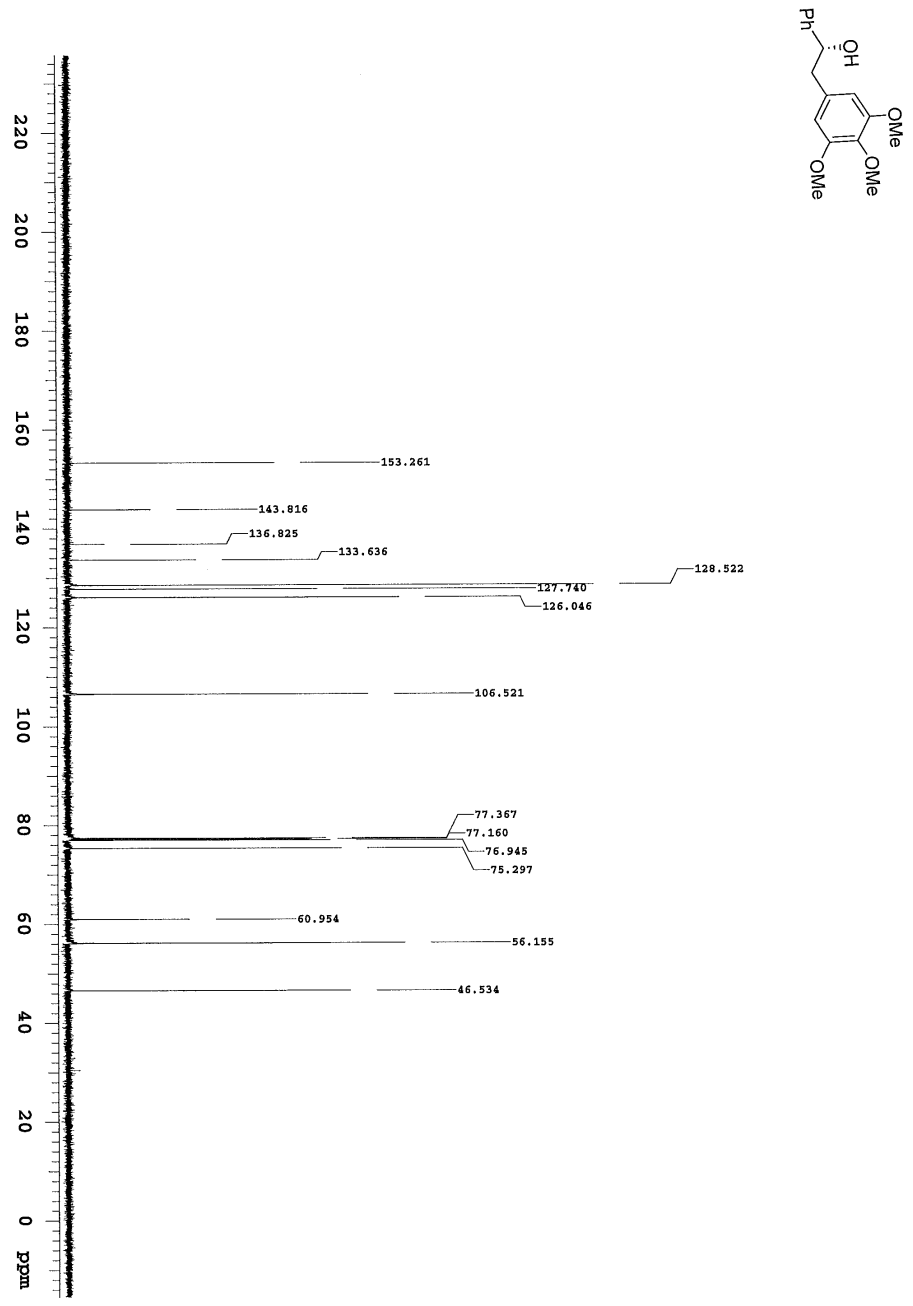
1.00
1.00
5.61
0.87
9
8
7
6
5
4
3
2
1
ppm

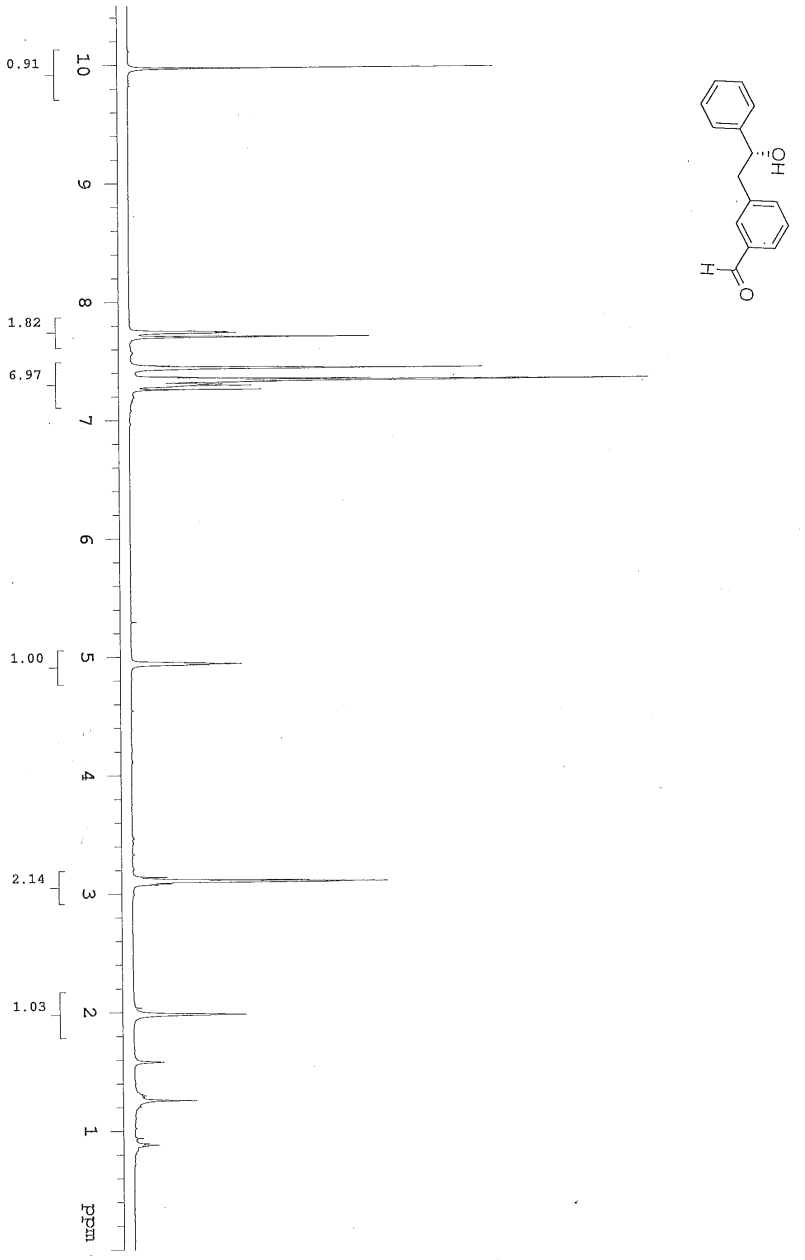

Ph
HO
Me
Me
144.636
137.584
135.069
128.576
128.530
127.702
126.636
125.701
77.375
77.160
76.945
74.186
39.957
20.546
220
200
180
160
140
120
100
80
60
40
20
0
ppm

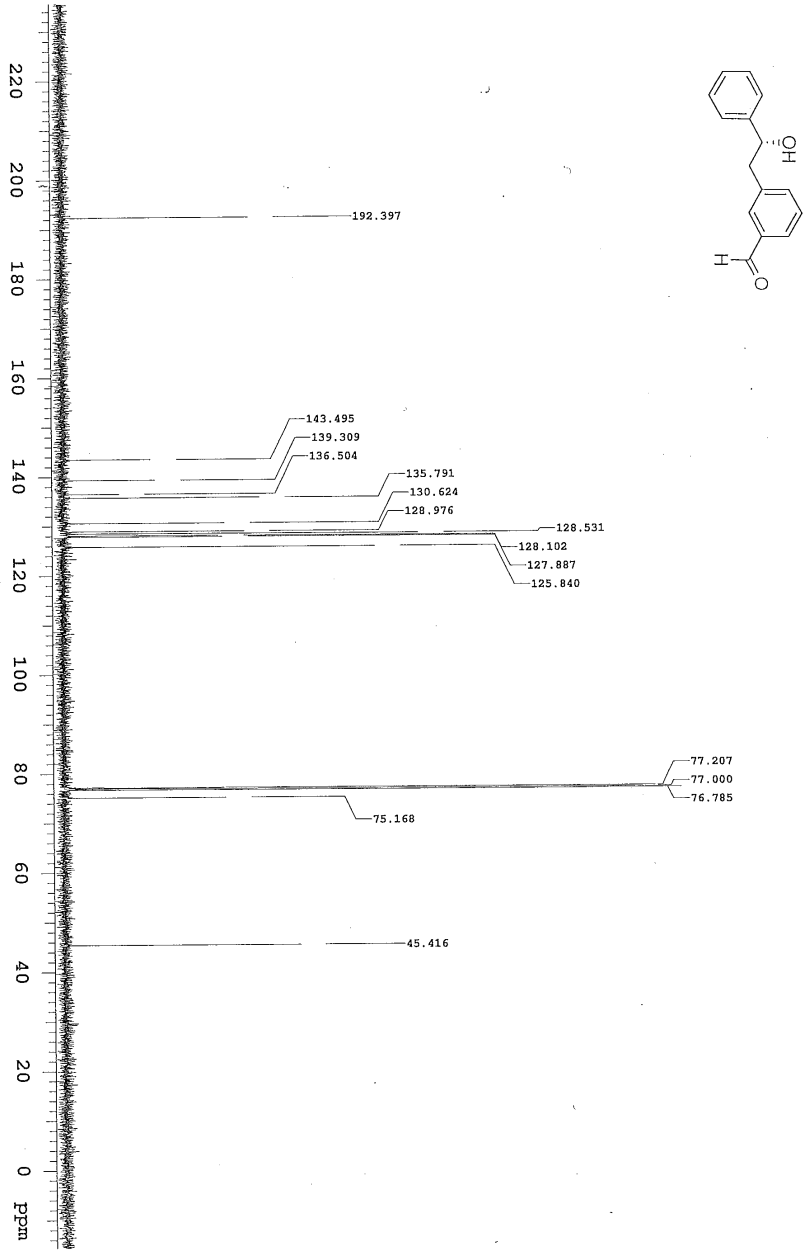

Ph
OH
O
O
10
9
8
7
6
5
4
3
2
1
Ppm
3.68
1.02
0.91
0.86
0.98
1.99
1.00
2.20
1.07


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


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


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


0.91
1.82
6.97
1.00
2.14
1.03
10
9
8
7
6
5
4
3
2
1
ppm
OH
H
O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143.495
139.309
136.504
135.791
130.624
128.976
128.531
128.102
127.887
125.840
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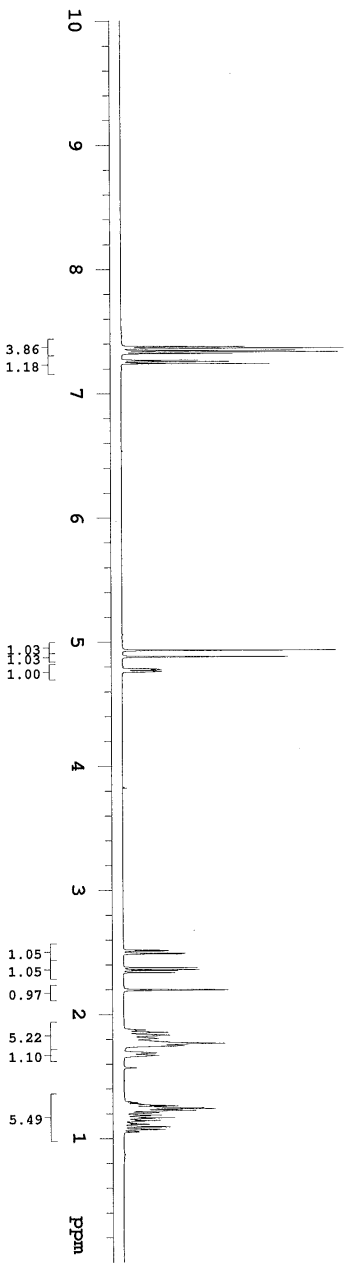
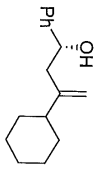
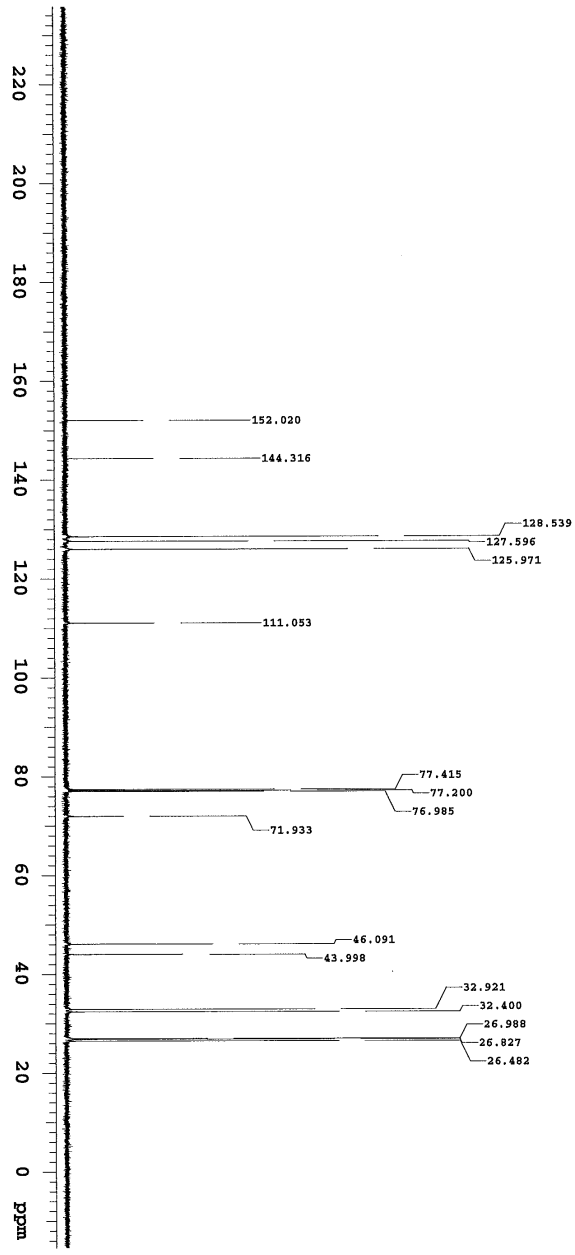
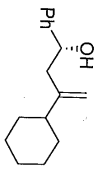
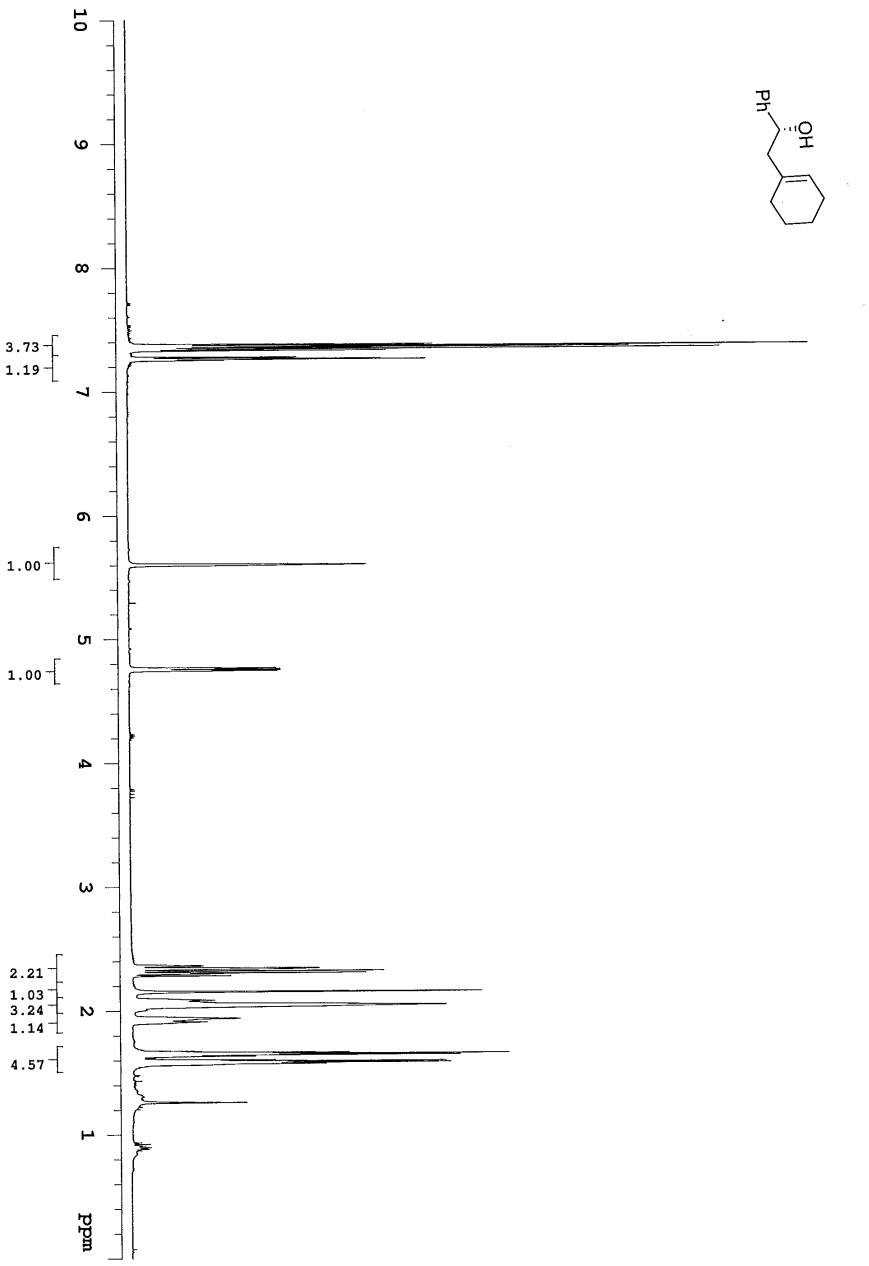
77.000
76.785
75.168
45.416
OH
H
O
220
200
180
160
140
120
100
80
60
40
20
0
ppm

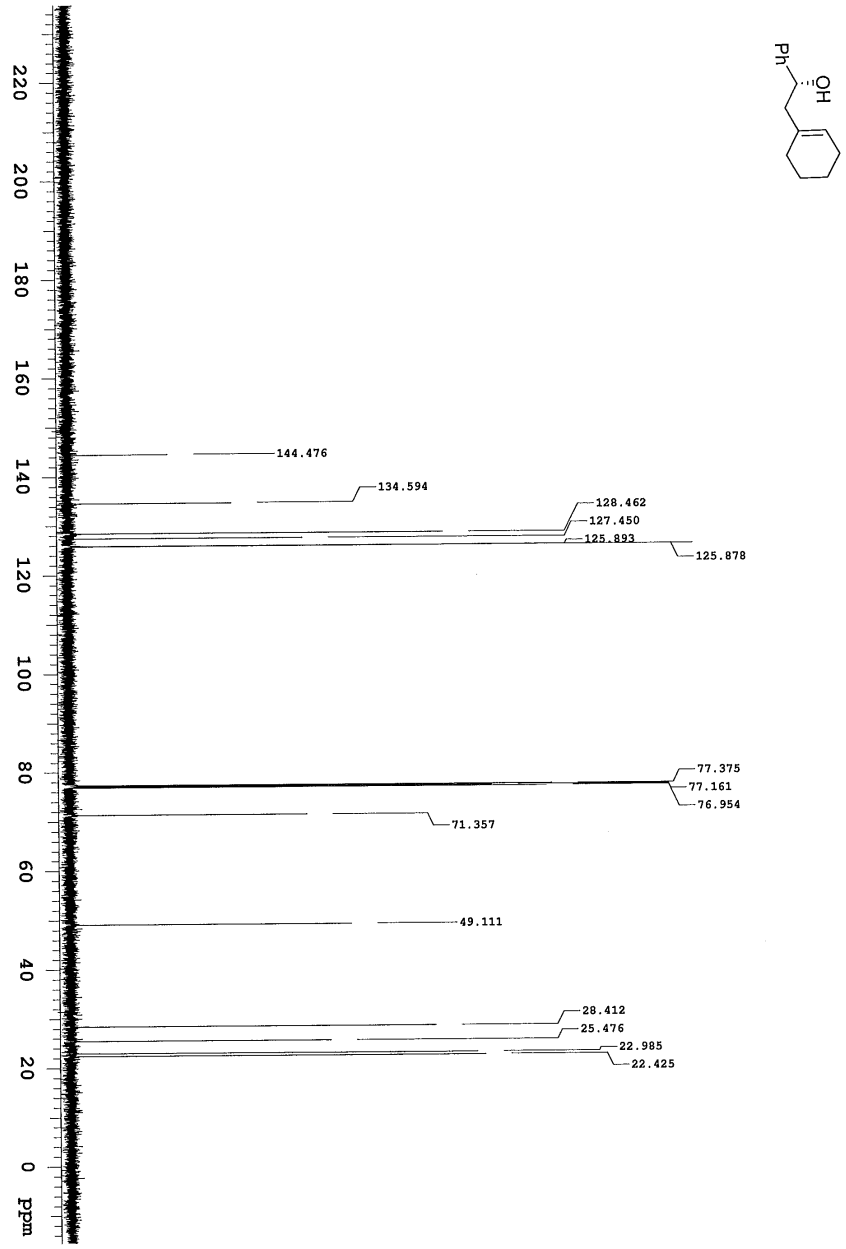

10
9
8
7
6
5
4
3
2
1
ppm
3.86
1.18
1.03
1.03
1.00
1.05
1.05
0.97
5.22
1.10
5.49

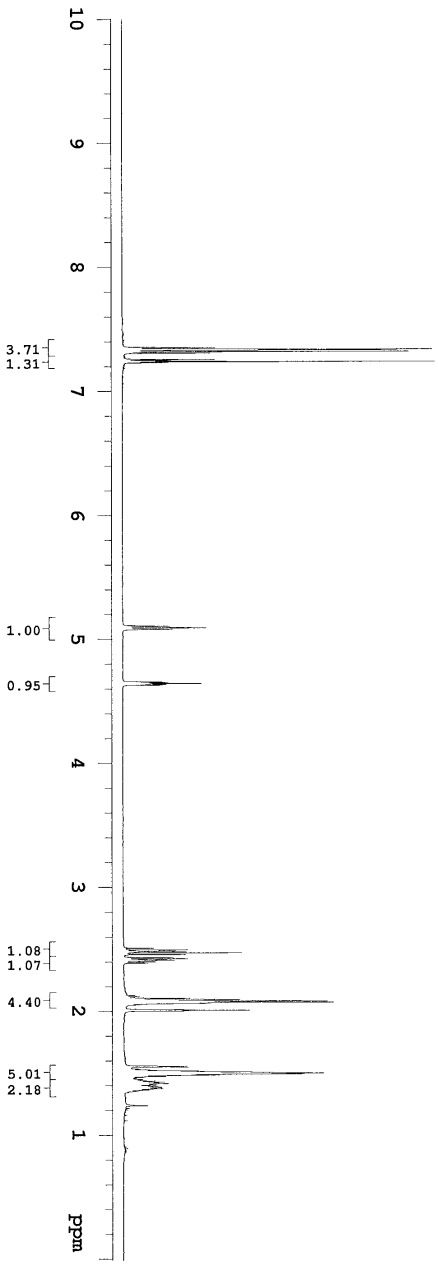

Ph
OH

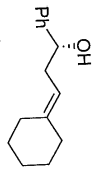

220
200
180
160
140
120
100
80
60
40
20
0
ppm
152.020
144.316
128.539
127.596
125.971
111.053
77.415
77.200
76.985
71.933
46.091
43.998
32.921
32.400
26.988
26.827
26.482

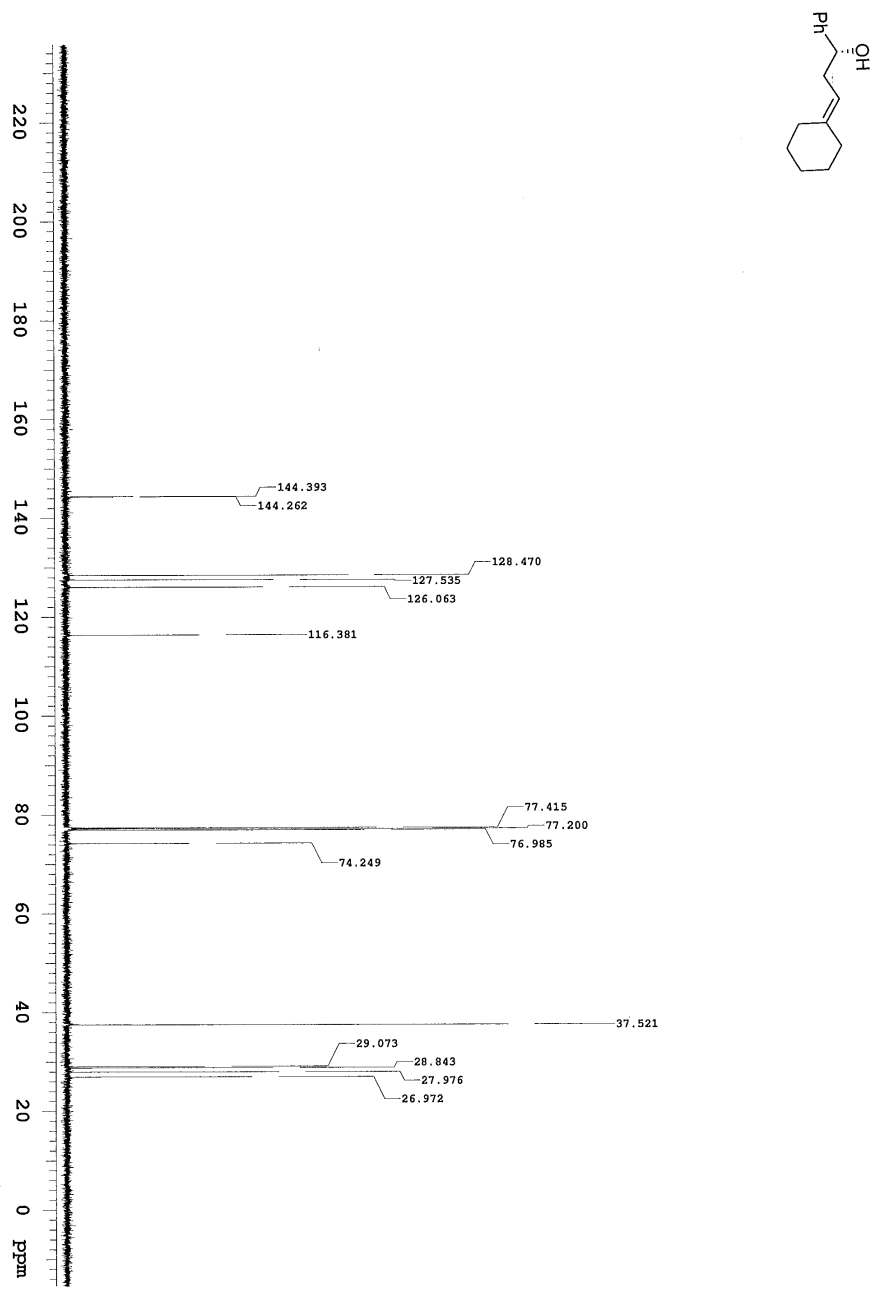

Ph
OH

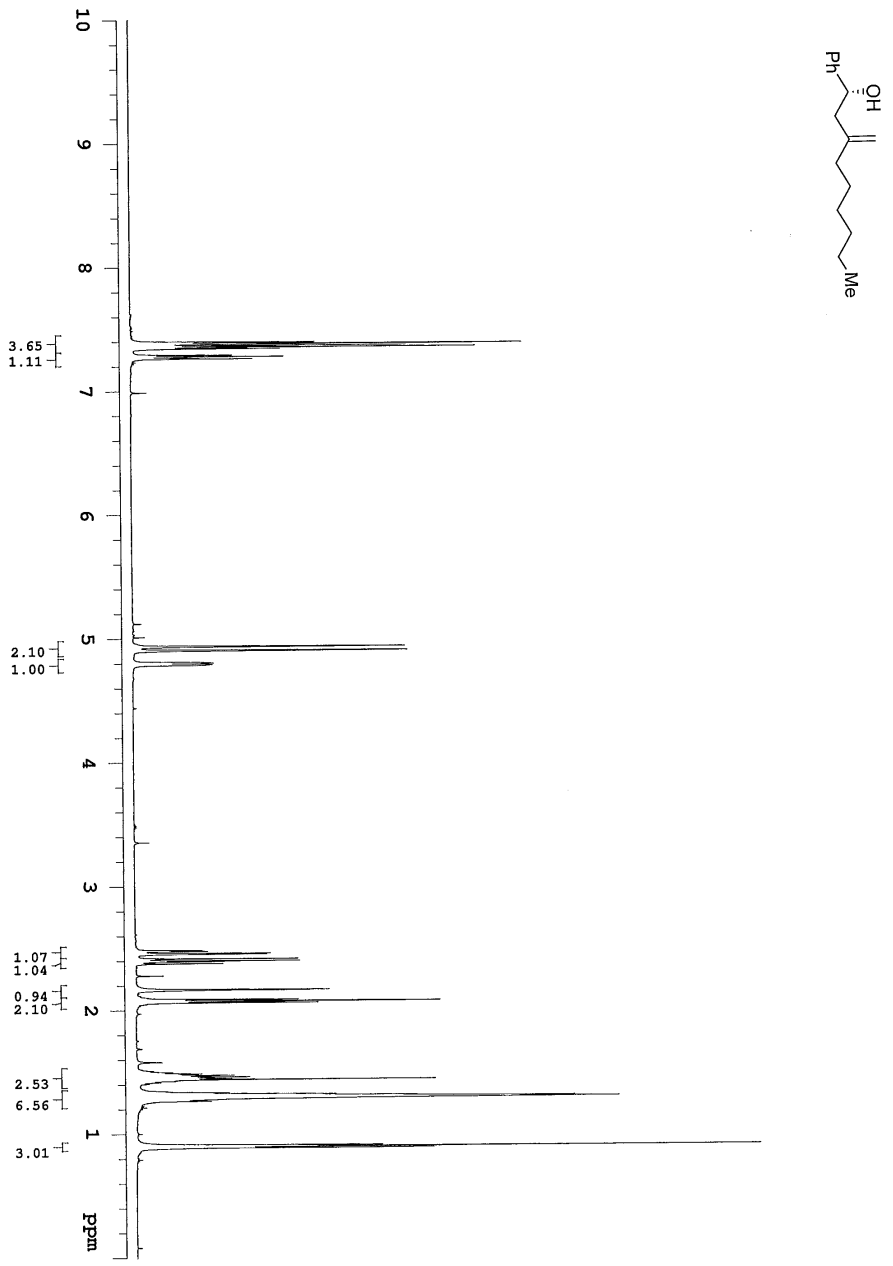

Ph
OH
10
9
8
7
6
5
4
3
2
1
Ppm
3.73
1.19
1.00
1.00
2.21
1.03
3.24
1.14
4.57

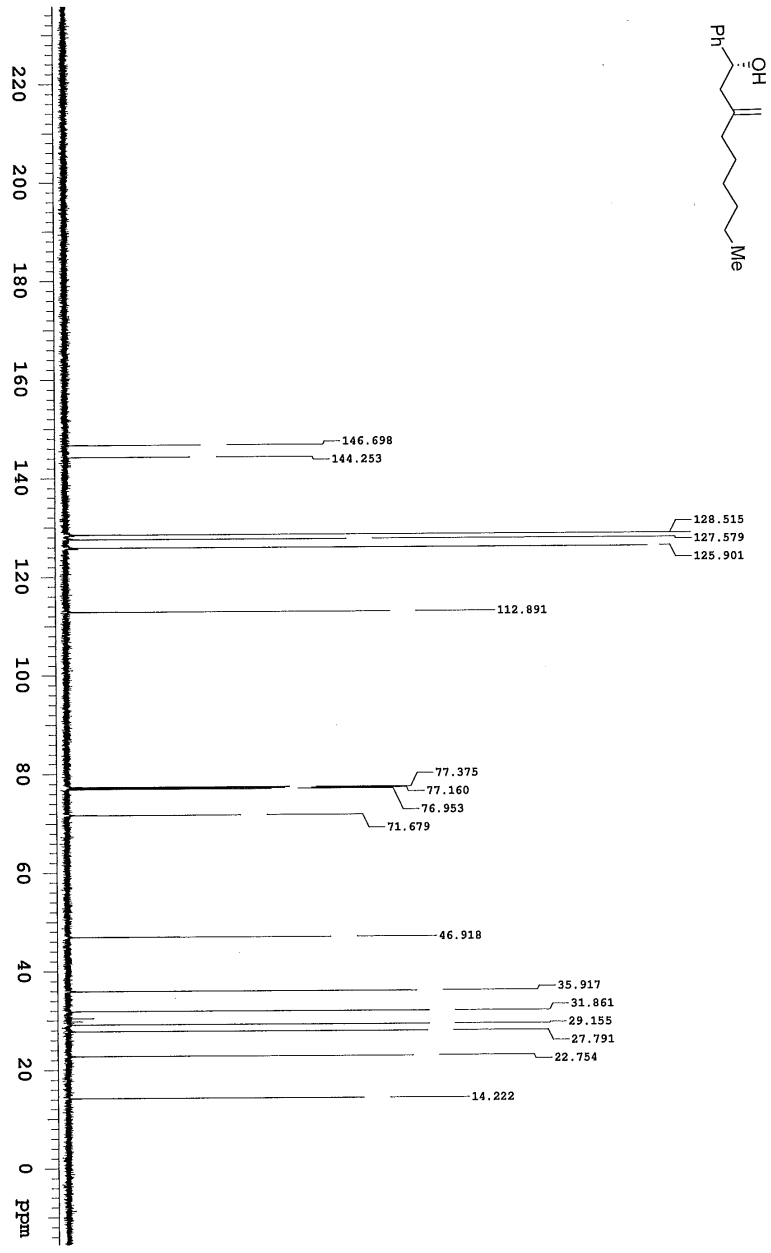

Ph
OH
144.476
134.594
128.462
127.450
125.893
125.878
77.375
77.161
76.954
71.357
49.111
28.412
25.476
22.985
22.425
220
200
180
160
140
120
100
80
60
40
20
0
ppm


10
9
8
7
6
5
4
3
2
1
ppm
3.71
1.31
1.00
0.95
1.08
1.07
4.40
5.01
2.18


Ph
OH


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


Ph
OH
Me
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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OH
Me
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200
180
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140
120
100
80
60
40
20
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ppm
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144.253
128.515
127.579
125.901
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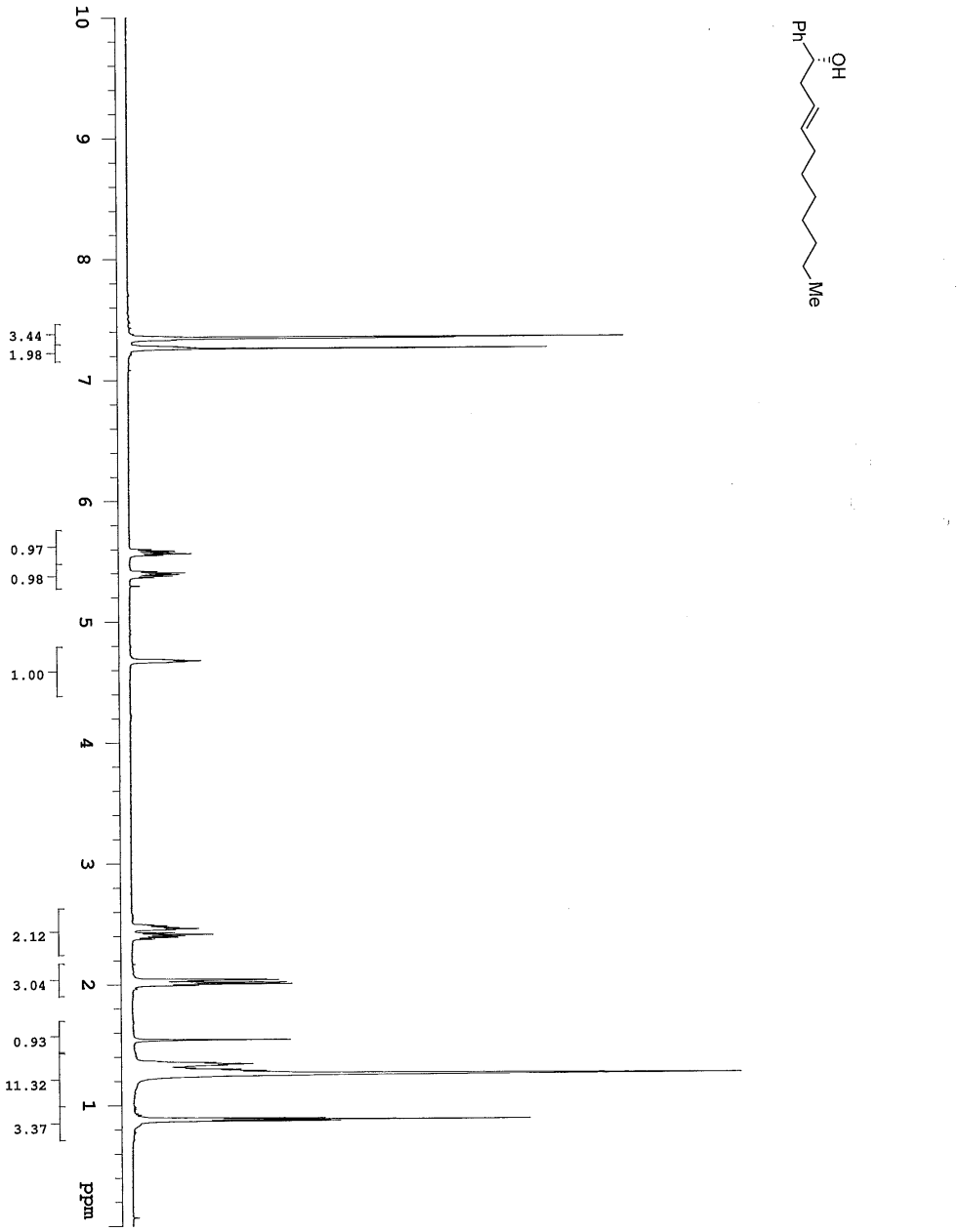
14.222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Me
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9
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5
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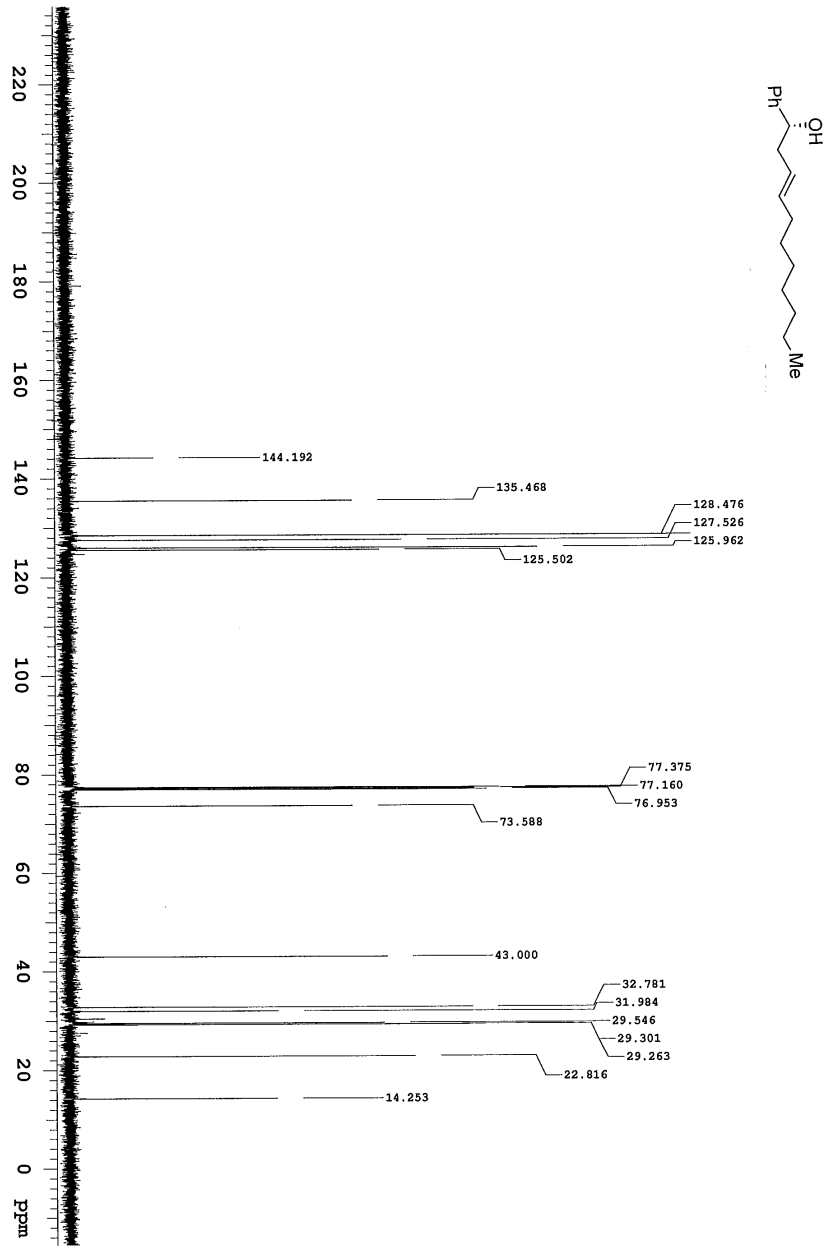
3.37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77.160
76.953
73.588
43.000
32.781
31.984
29.546
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0
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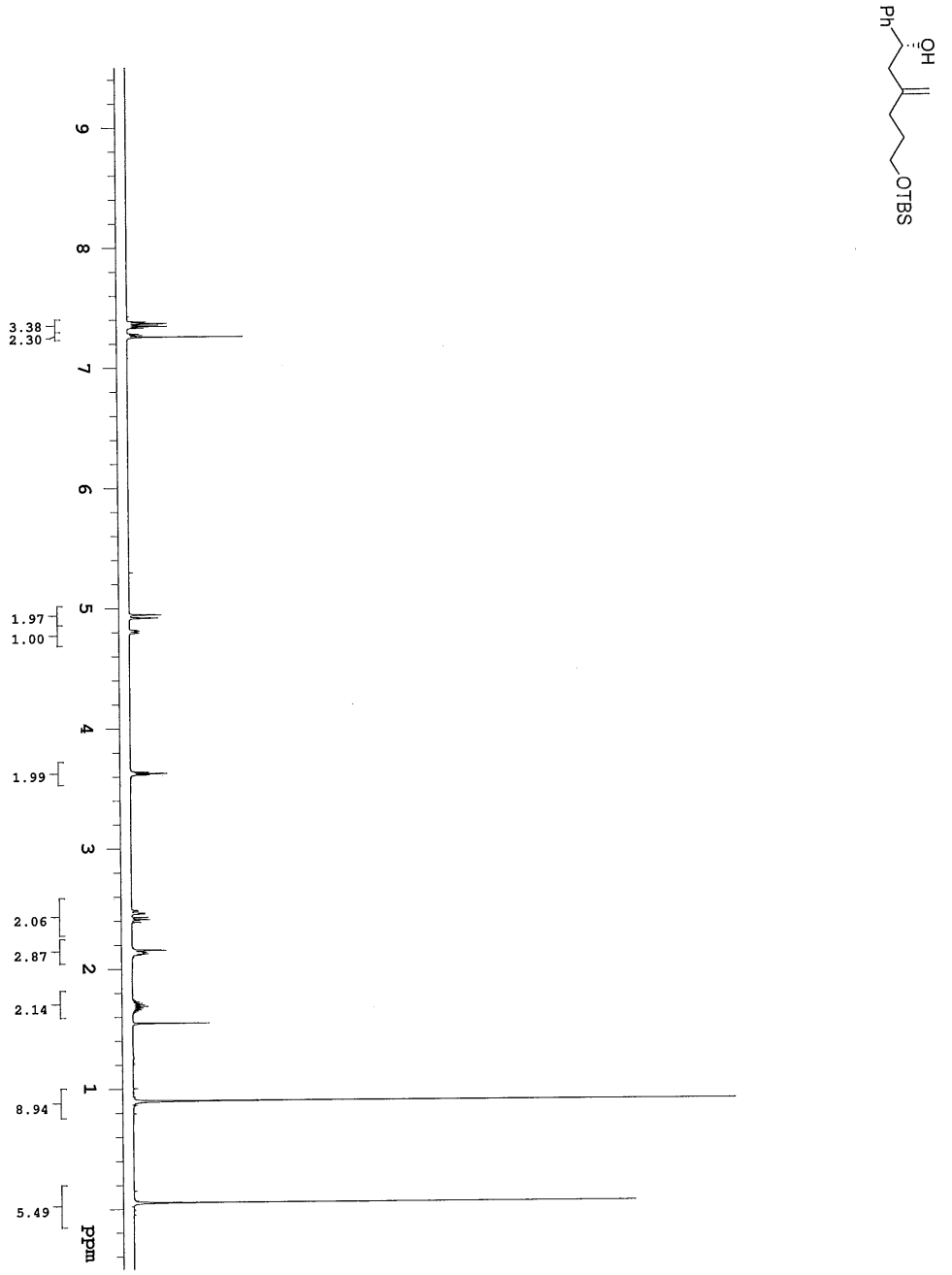
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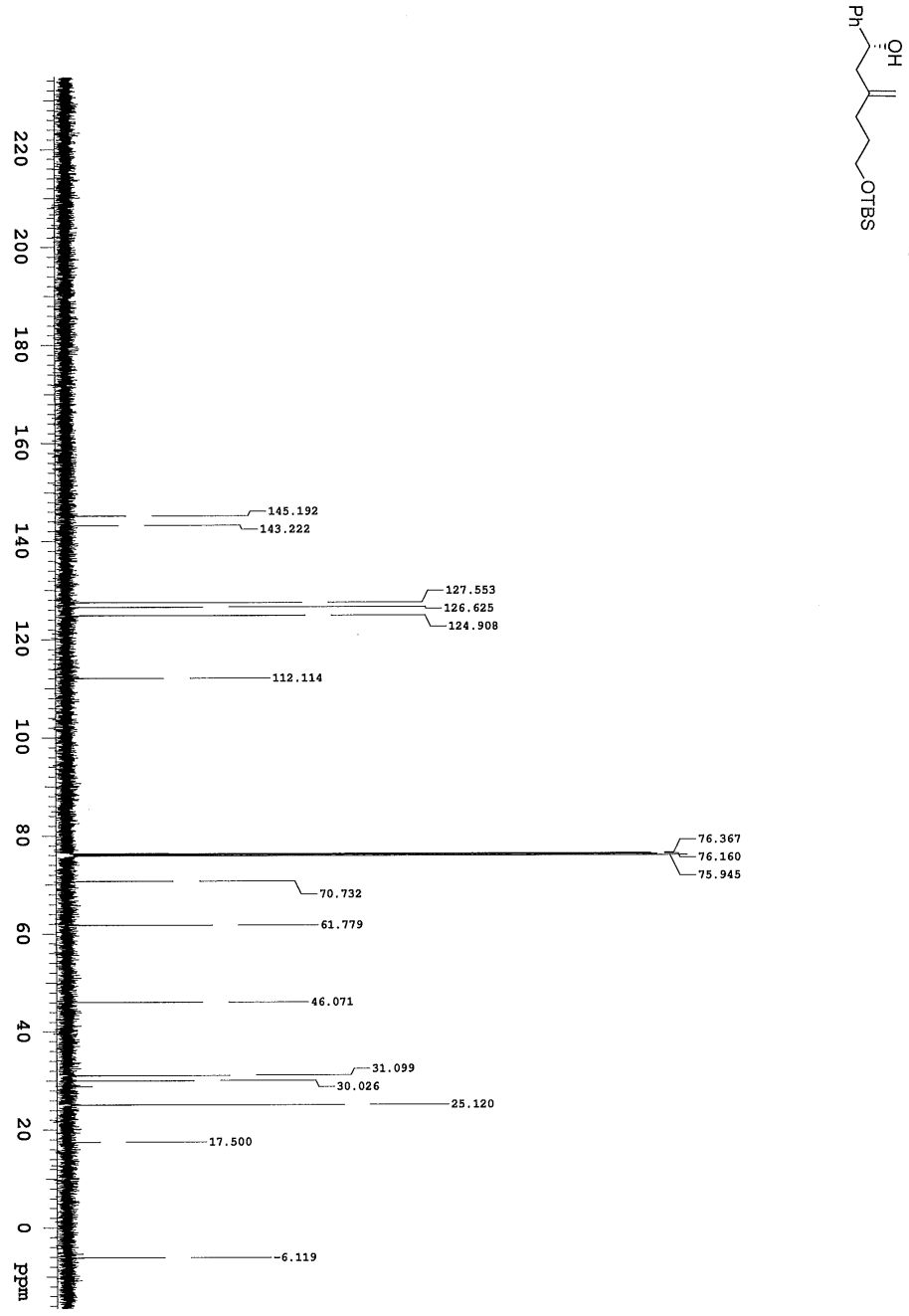
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OH
OTBS
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120
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40
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126.625
124.908
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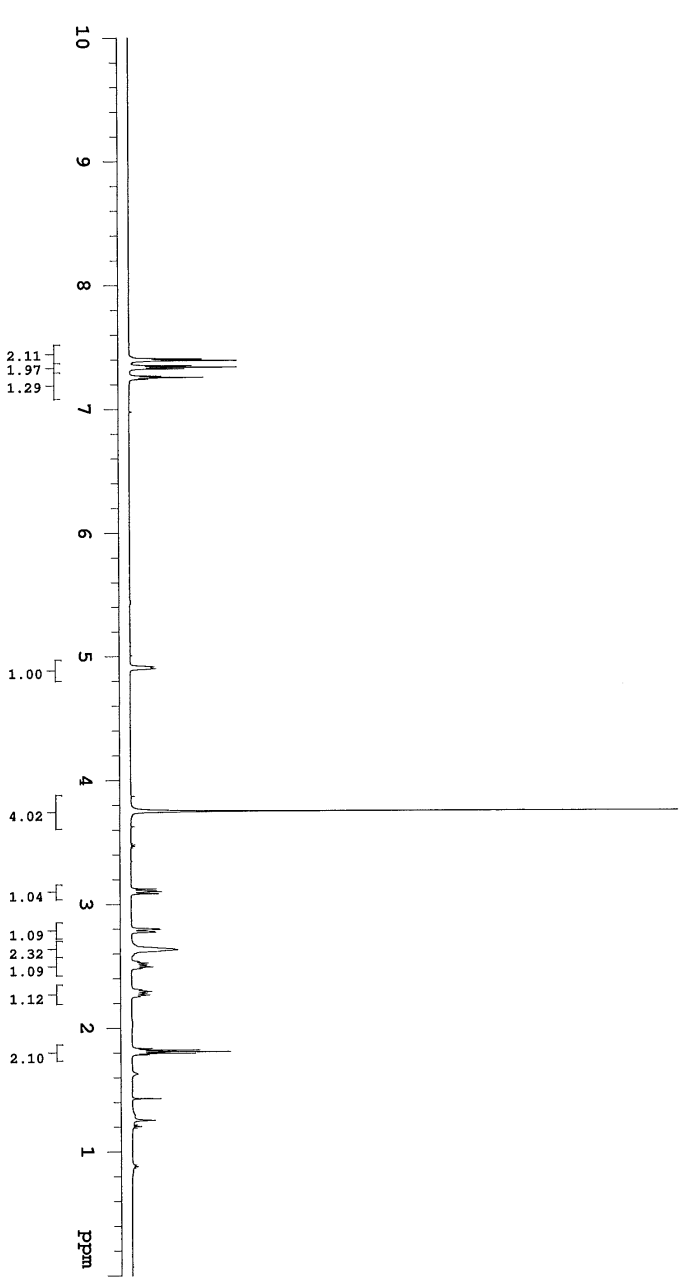
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OH
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O
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9
8
7
6
5
4
3
2
1
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1.00
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1.04
1.09
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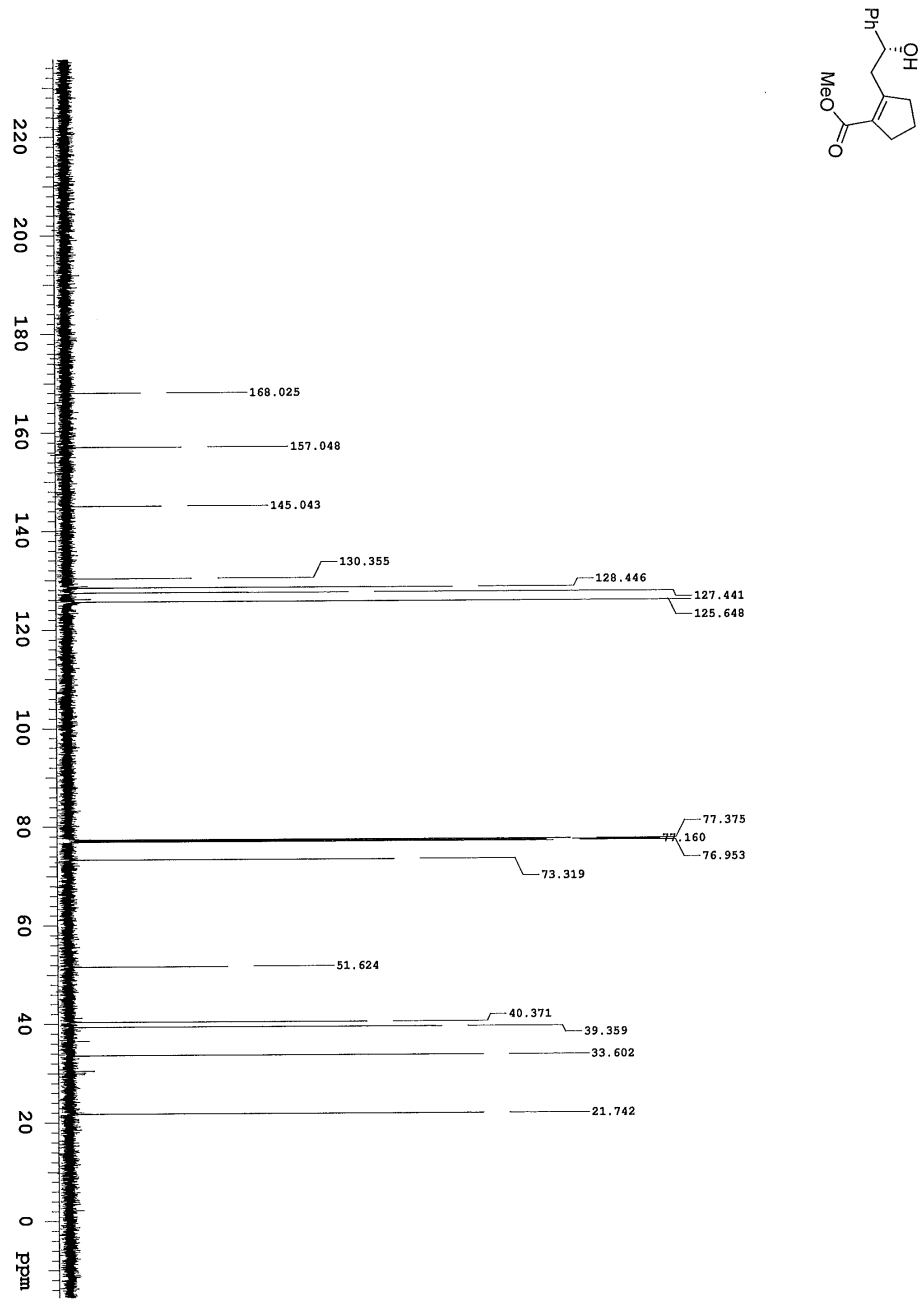
1.12
2.10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OH
MeO
O
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200
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120
100
80
60
40
20
0
ppm
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130.355
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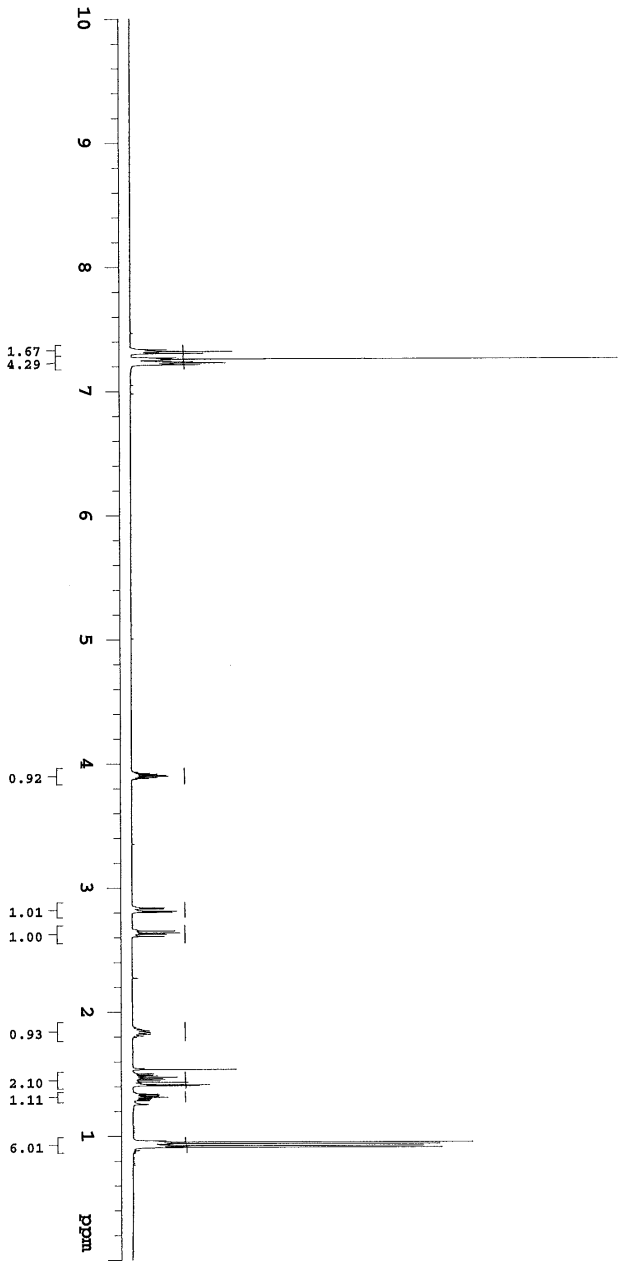
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8
7
6
5
4
3
2
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1.00
0.93
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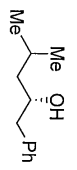
1.11
6.01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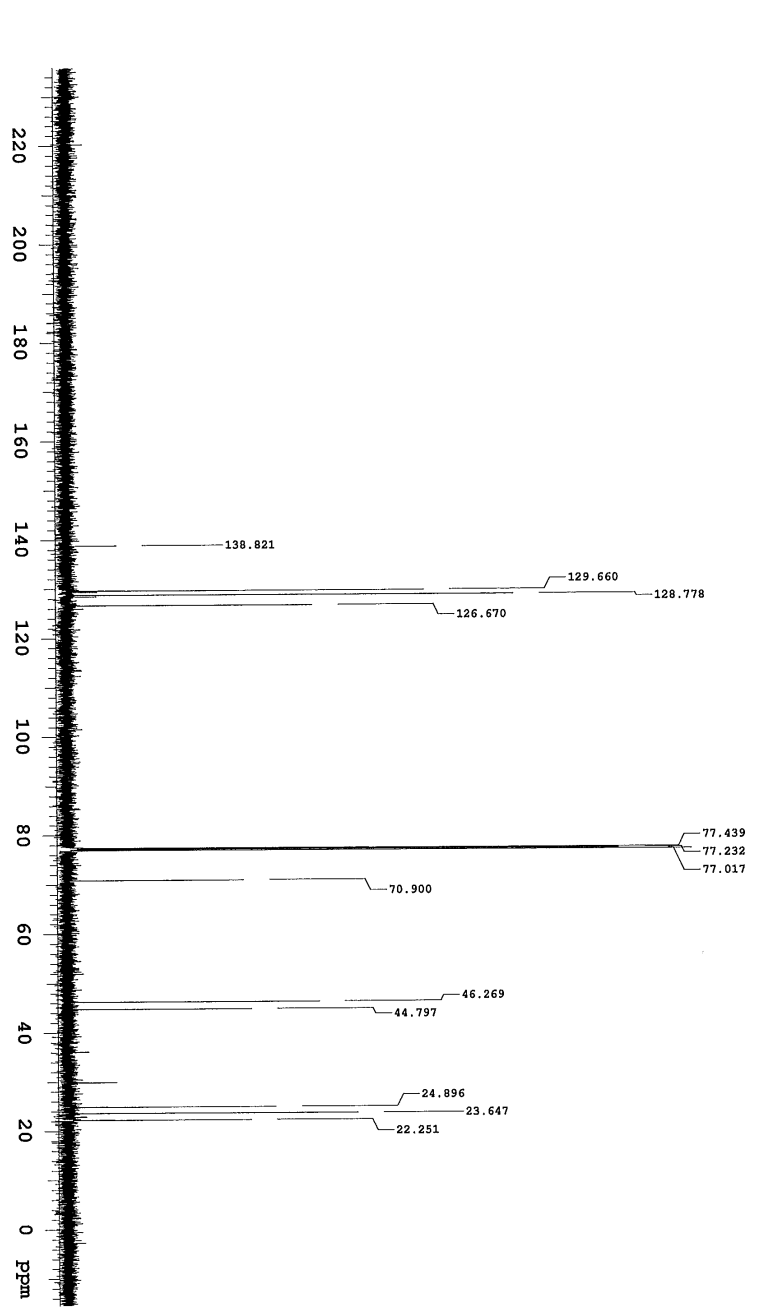
OH
Me
Ph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OH
Ph
Me
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140
120
100
80
60
40
20
0
ppm
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126.670
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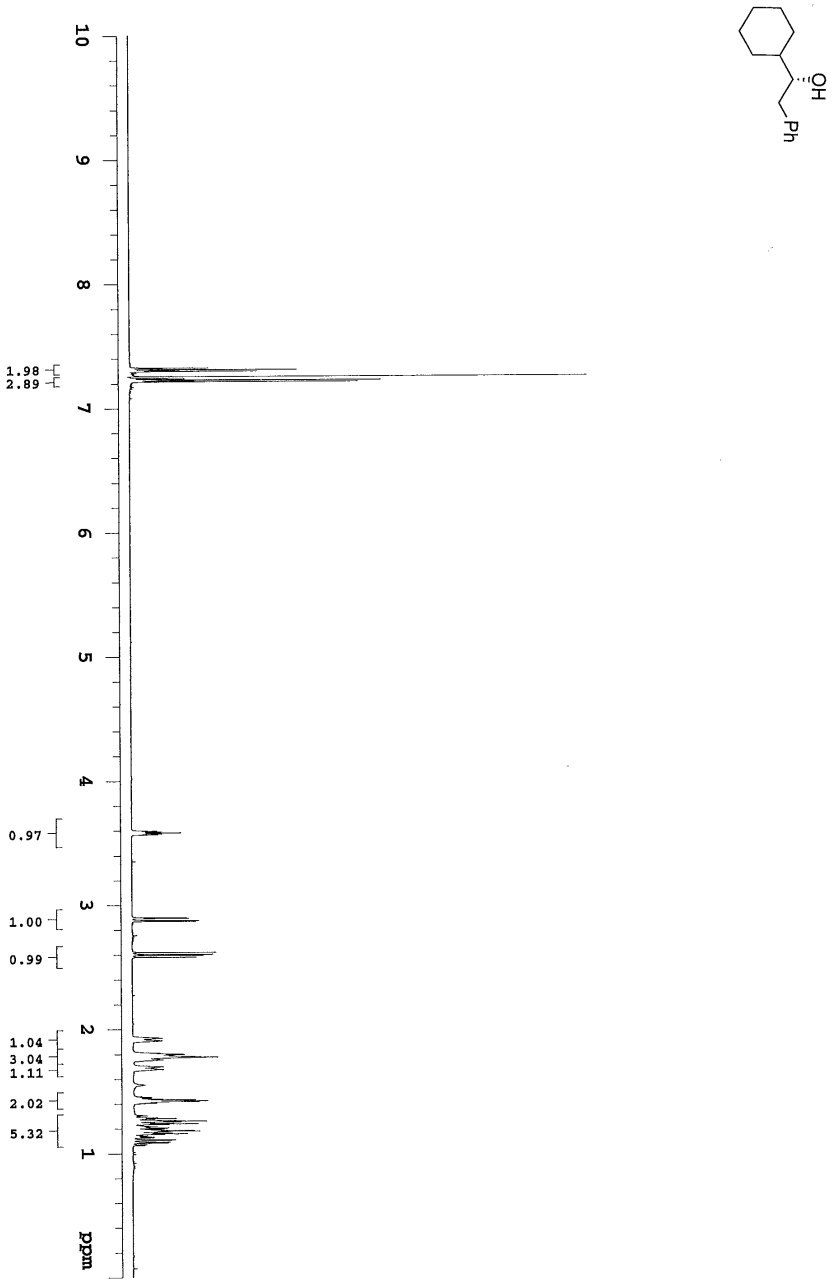
46.269
44.797
24.896
23.647
22.251


OH
Ph
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2.89
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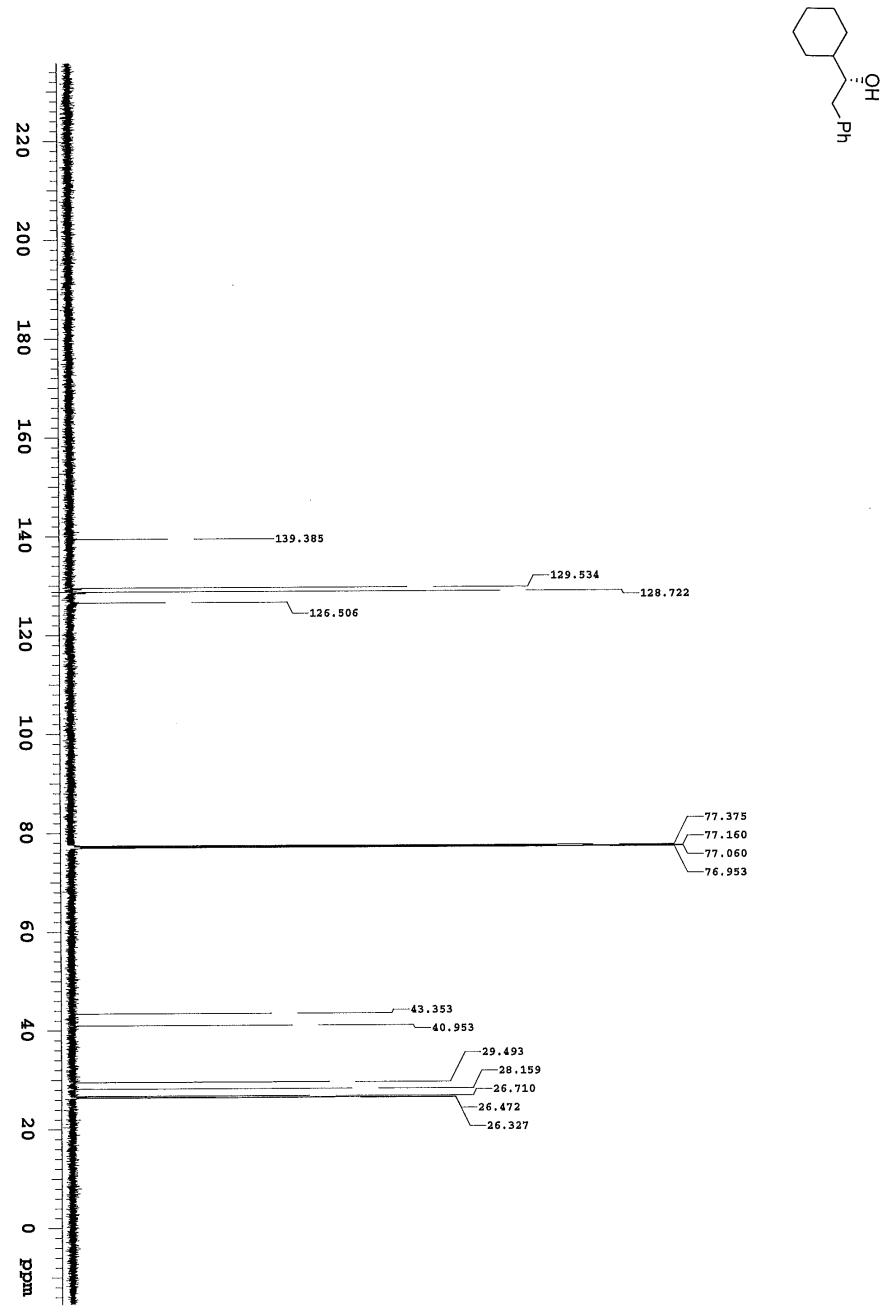
1.00
0.99
1.04
3.04
1.11
2.02
5.32
10
9
8
7
6
5
4
3
2
1
ppm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Ph
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200
180
160
140
120
100
80
60
40
20
0
ppm
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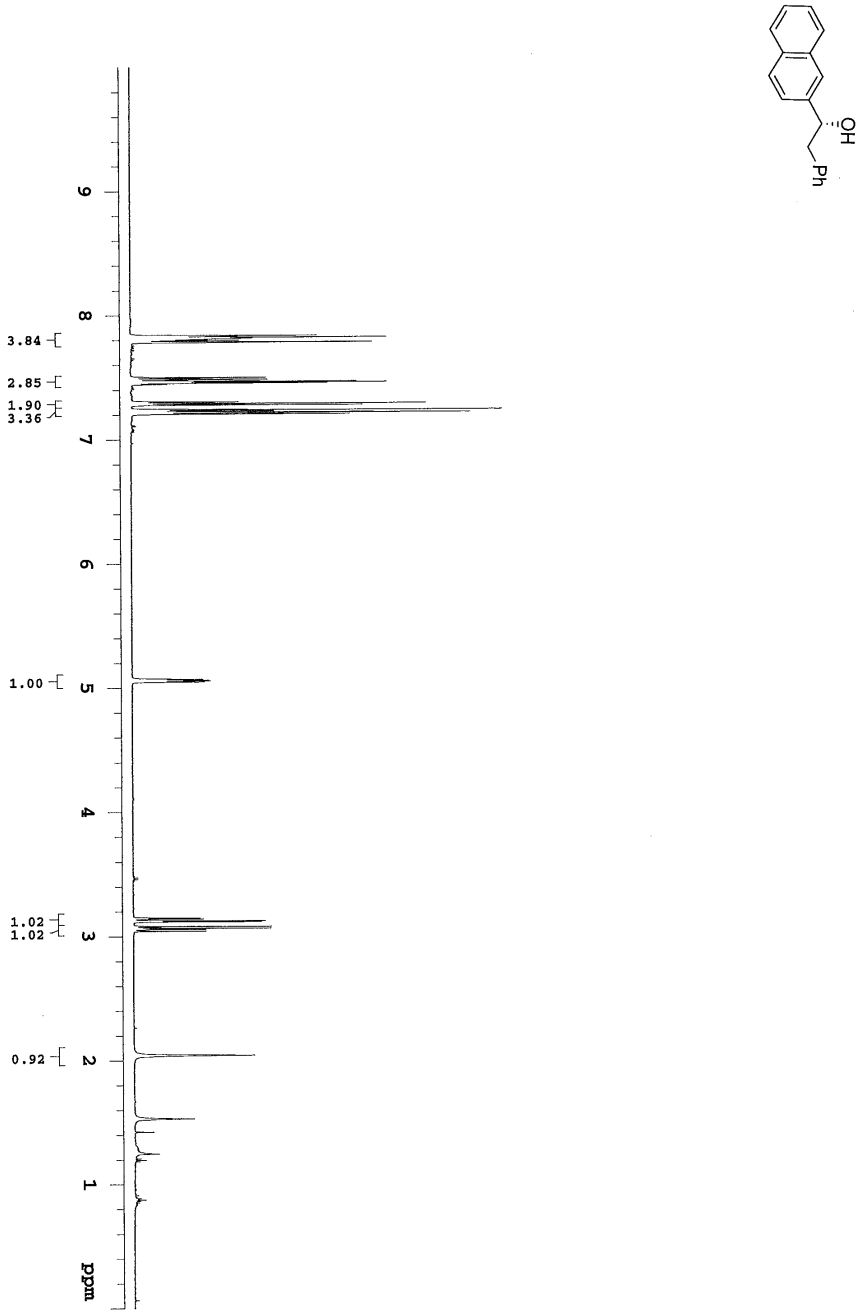
77.160
77.060
76.953
43.353
40.953
29.493
28.159
26.710
26.472
26.327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Ph
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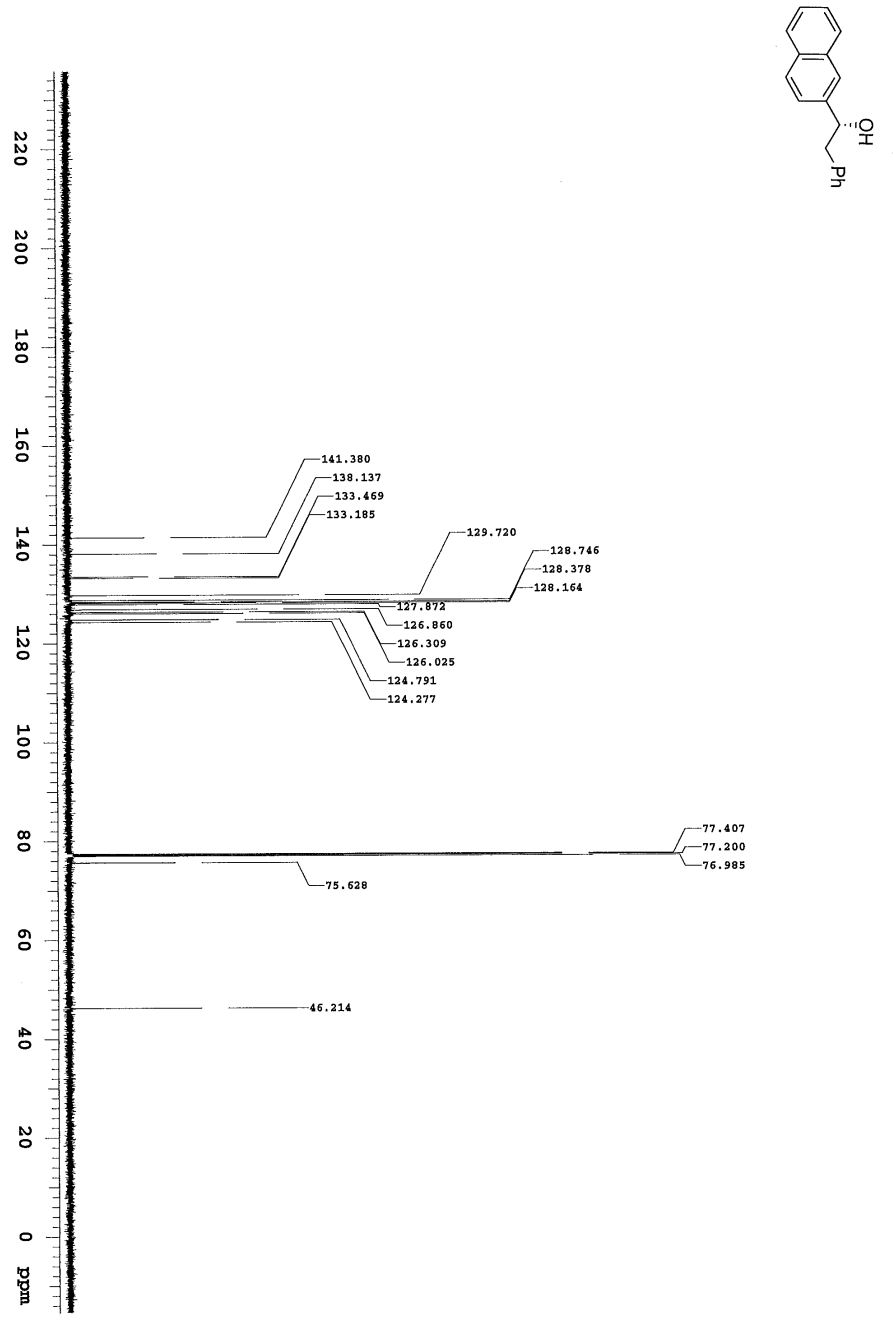
1.02
1.02
0.92
9
8
7
6
5
4
3
2
1
ppm


OH
Ph
220
200
180
160
140
120
100
80
60
40
20
0
ppm
141.380
138.137
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133.185
129.720
128.746
128.378
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126.309
126.025
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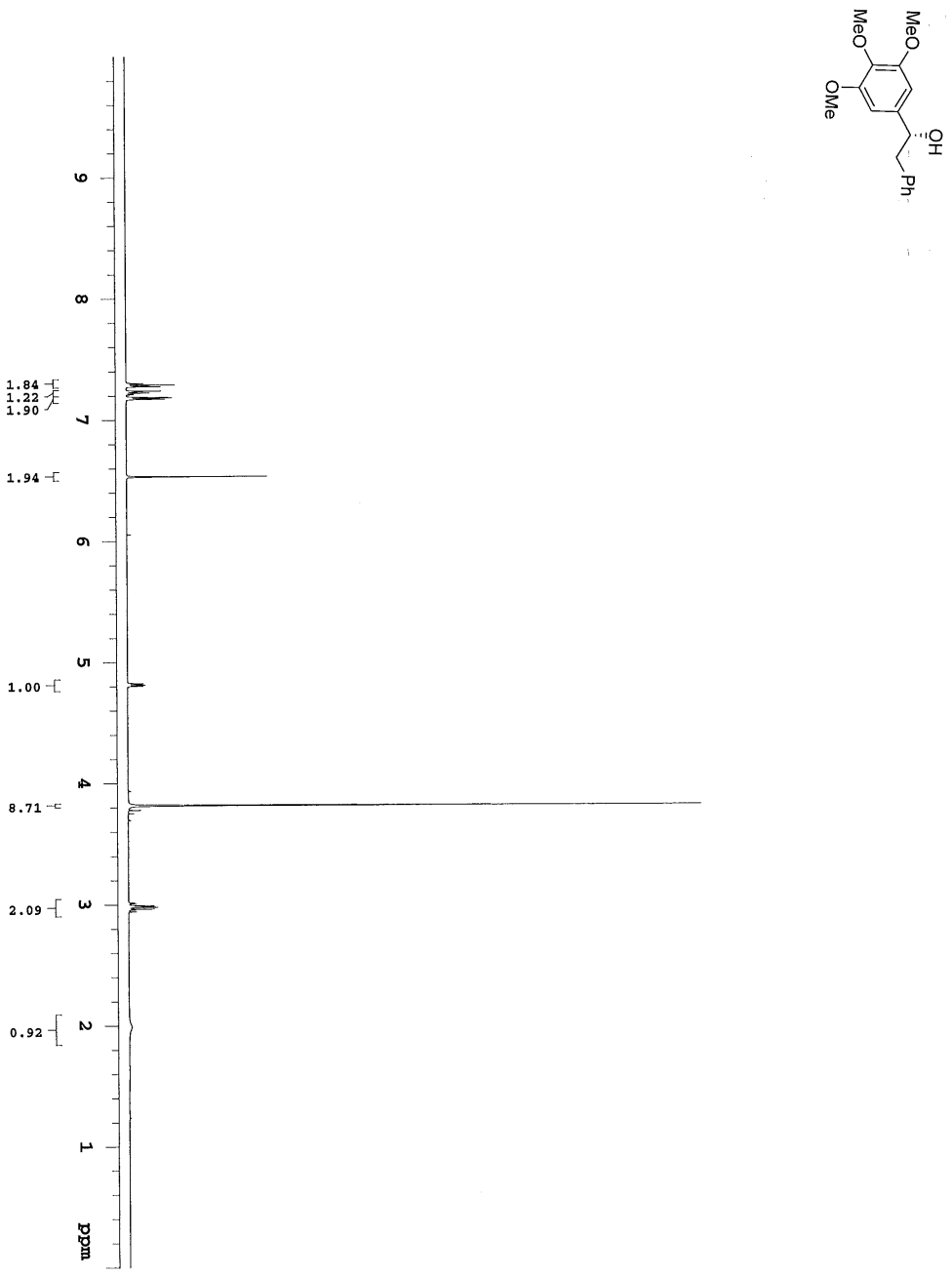
124.277
77.407
77.200
76.985
75.628
46.214


MeO
MeO
OMe
OH
Ph
1.84
1.22
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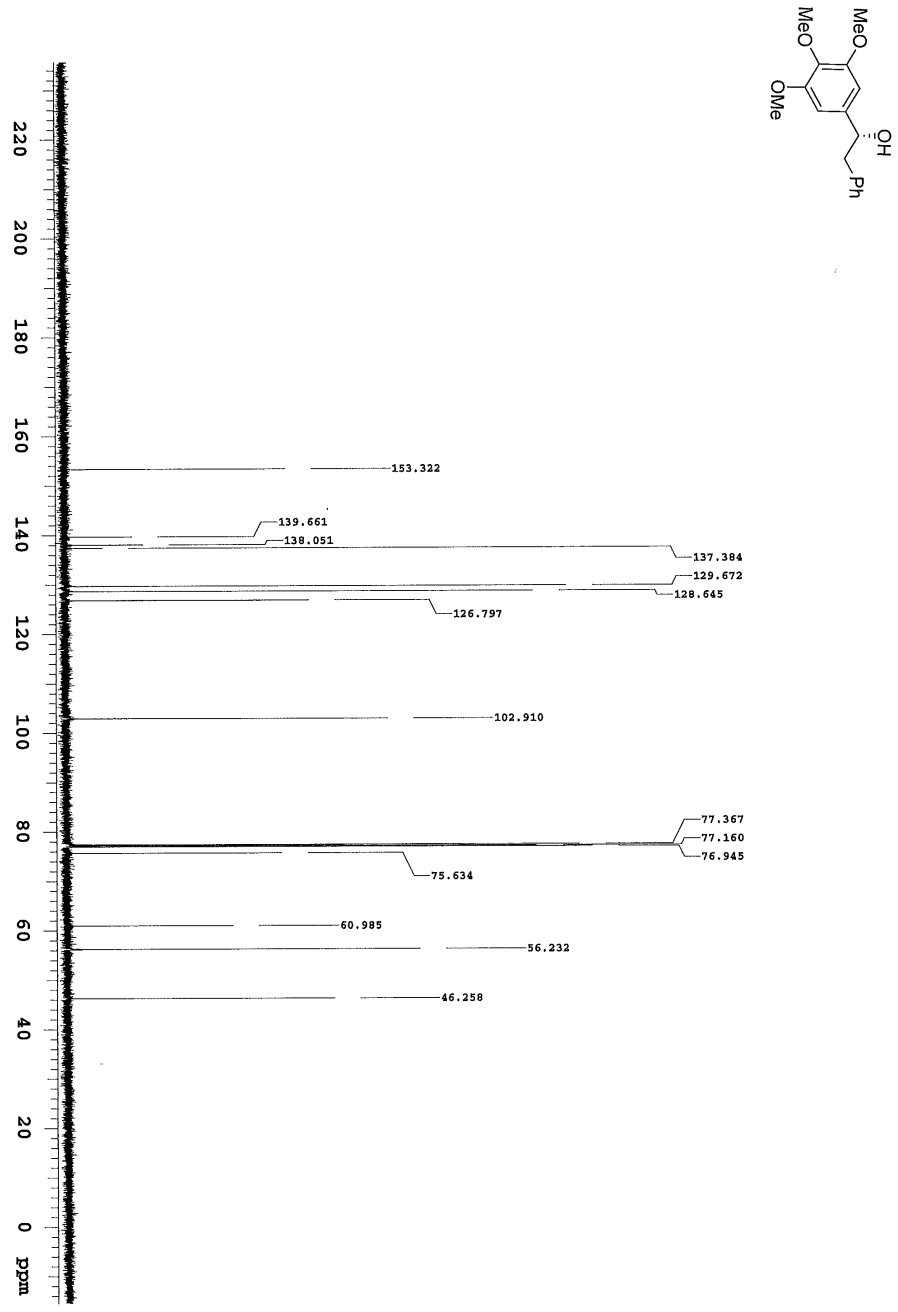
1.94
1.00
8.71
2.09
0.92
9
8
7
6
5
4
3
2
1
ppm


MeO
MeO
OMe
OH
Ph
220
200
180
160
140
120
100
80
60
40
20
0
ppm
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139.661
138.051
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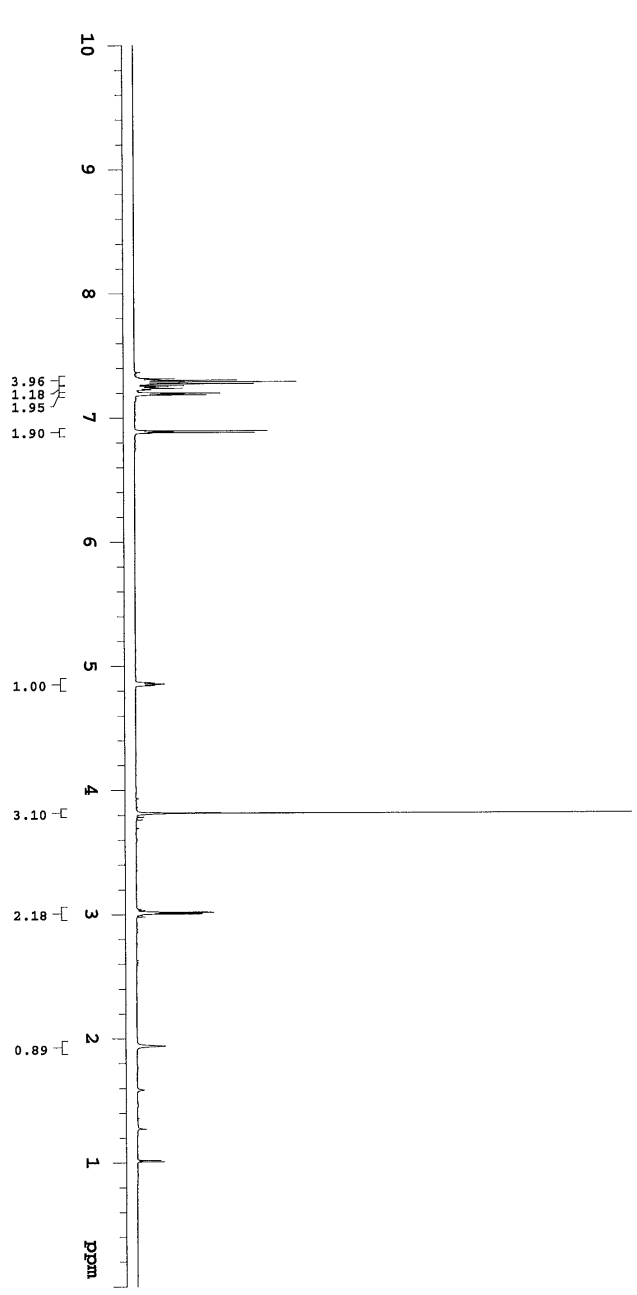
77.160
76.945
75.634
60.985
56.232
46.258


MeO
OH
Ph
10
9
8
7
6
5
4
3
2
1
ppm
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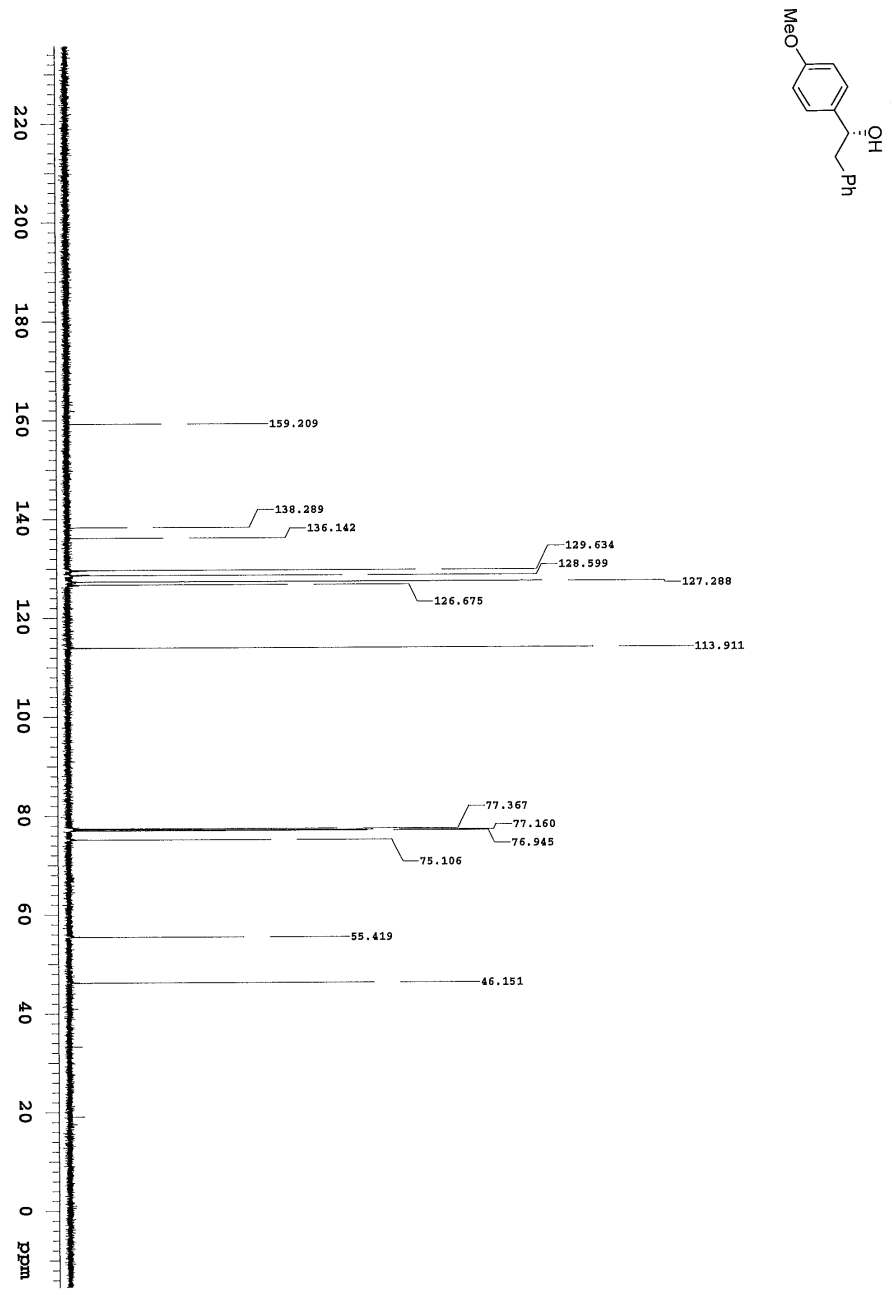
1.90
1.00
3.10
2.18
0.89


MeO
OH
Ph
220
200
180
160
140
120
100
80
60
40
20
0
ppm
159.209
138.289
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113.911
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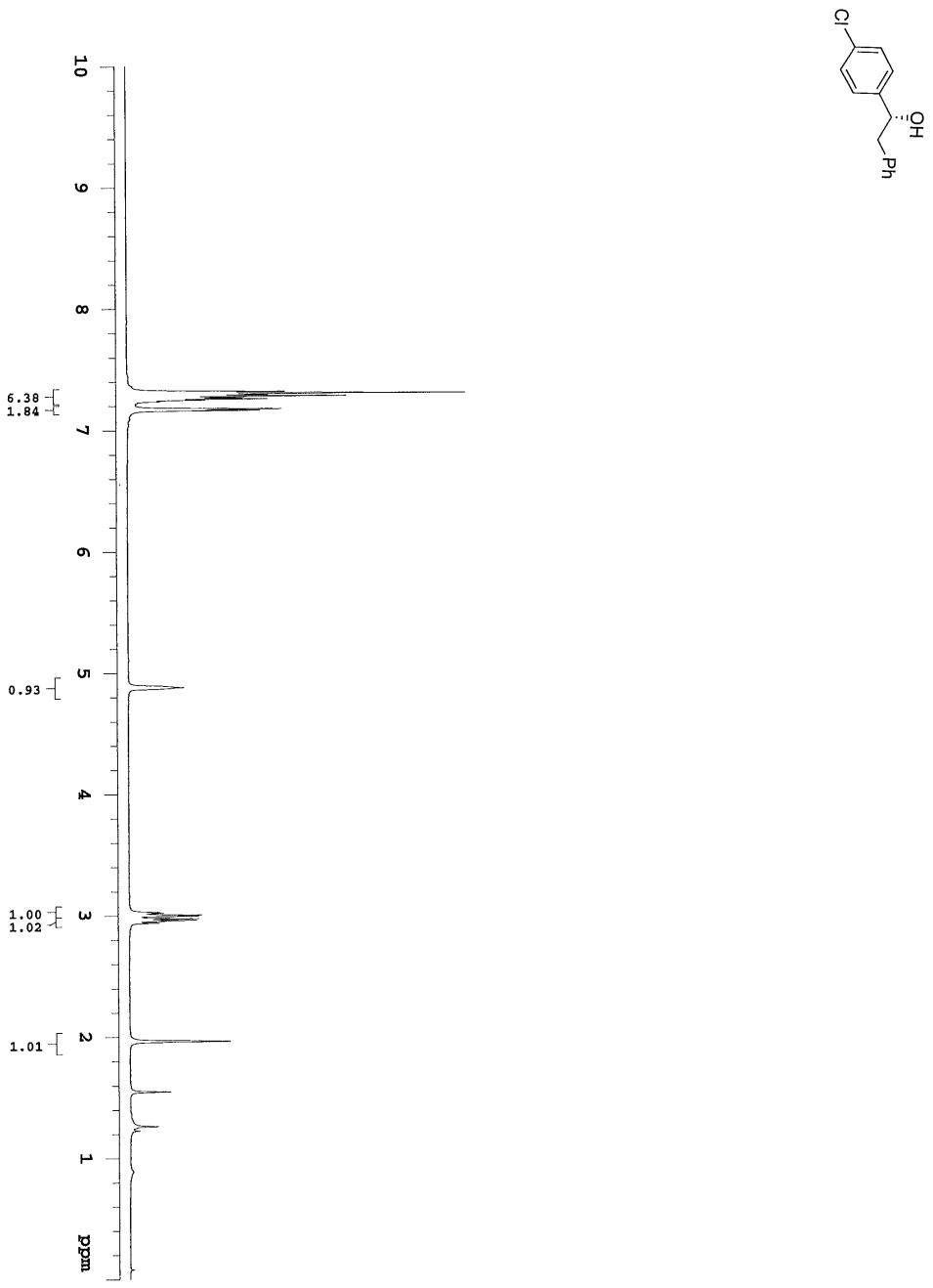
77.160
76.945
75.106
55.419
46.151


Cl
OH
Ph
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9
8
7
6
5
4
3
2
1
ppm
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1.84
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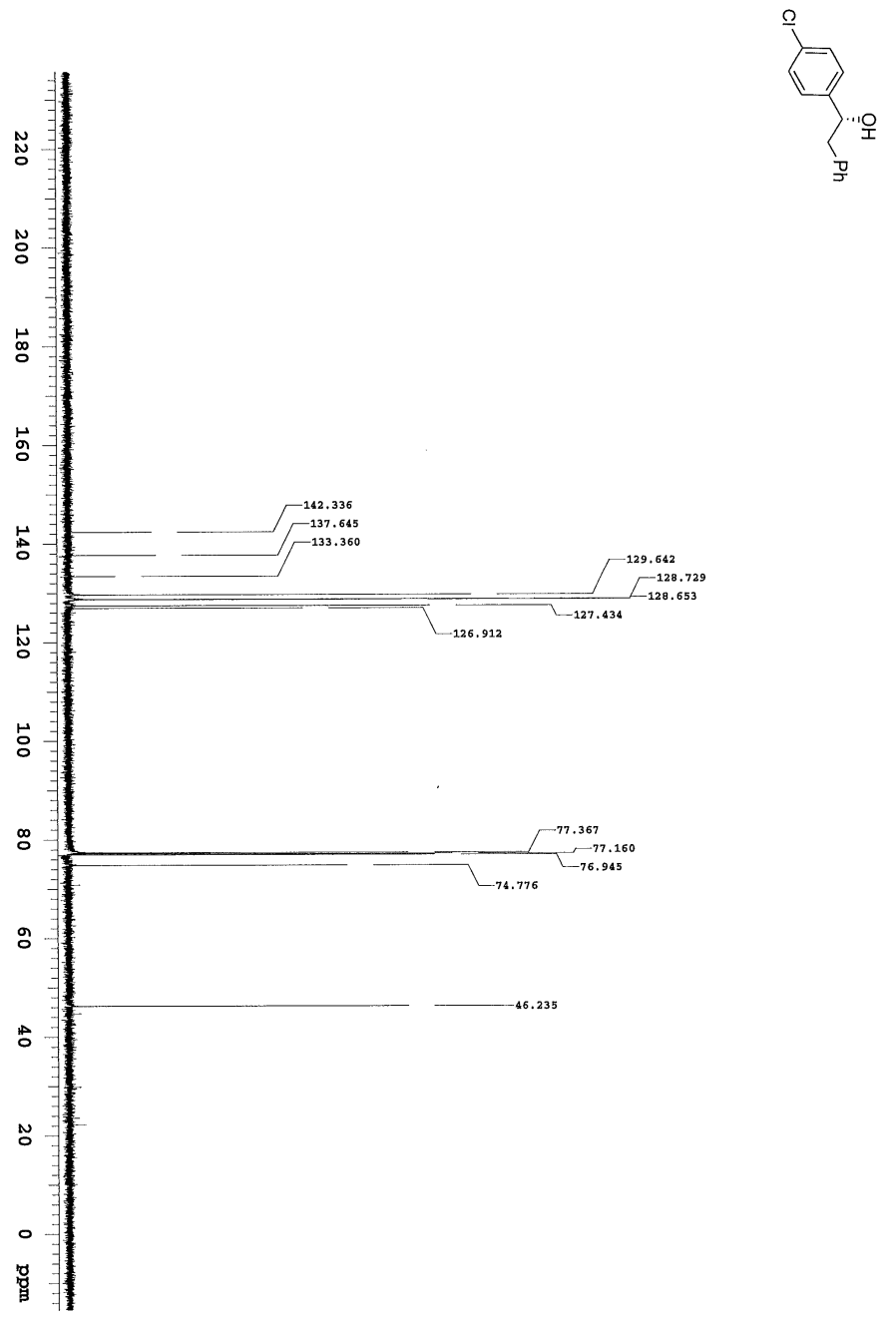
1.01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Ph
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126.912
77.367
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76.945
74.776
46.235
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180
160
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120
100
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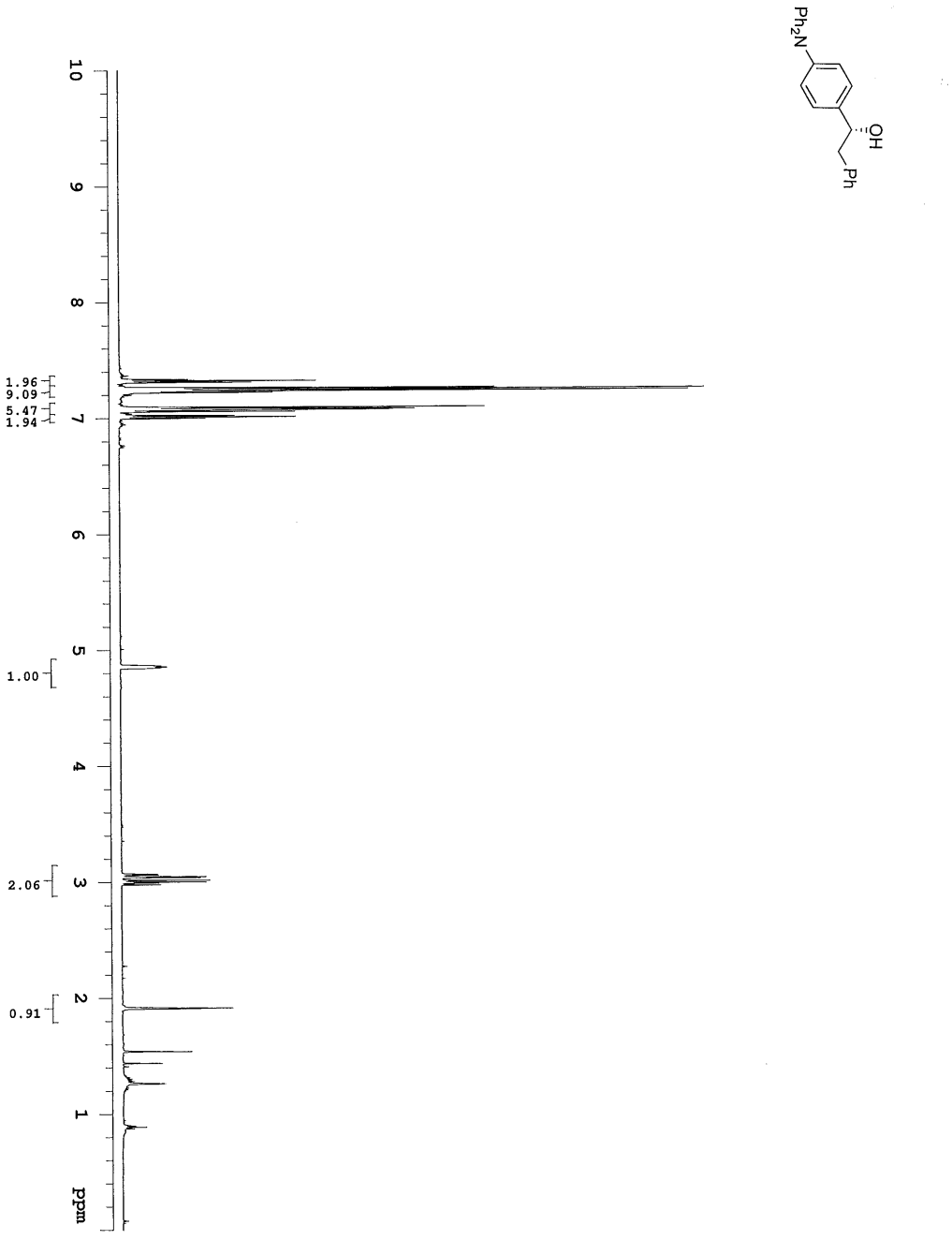
60
40
20
0
ppm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OH
Ph
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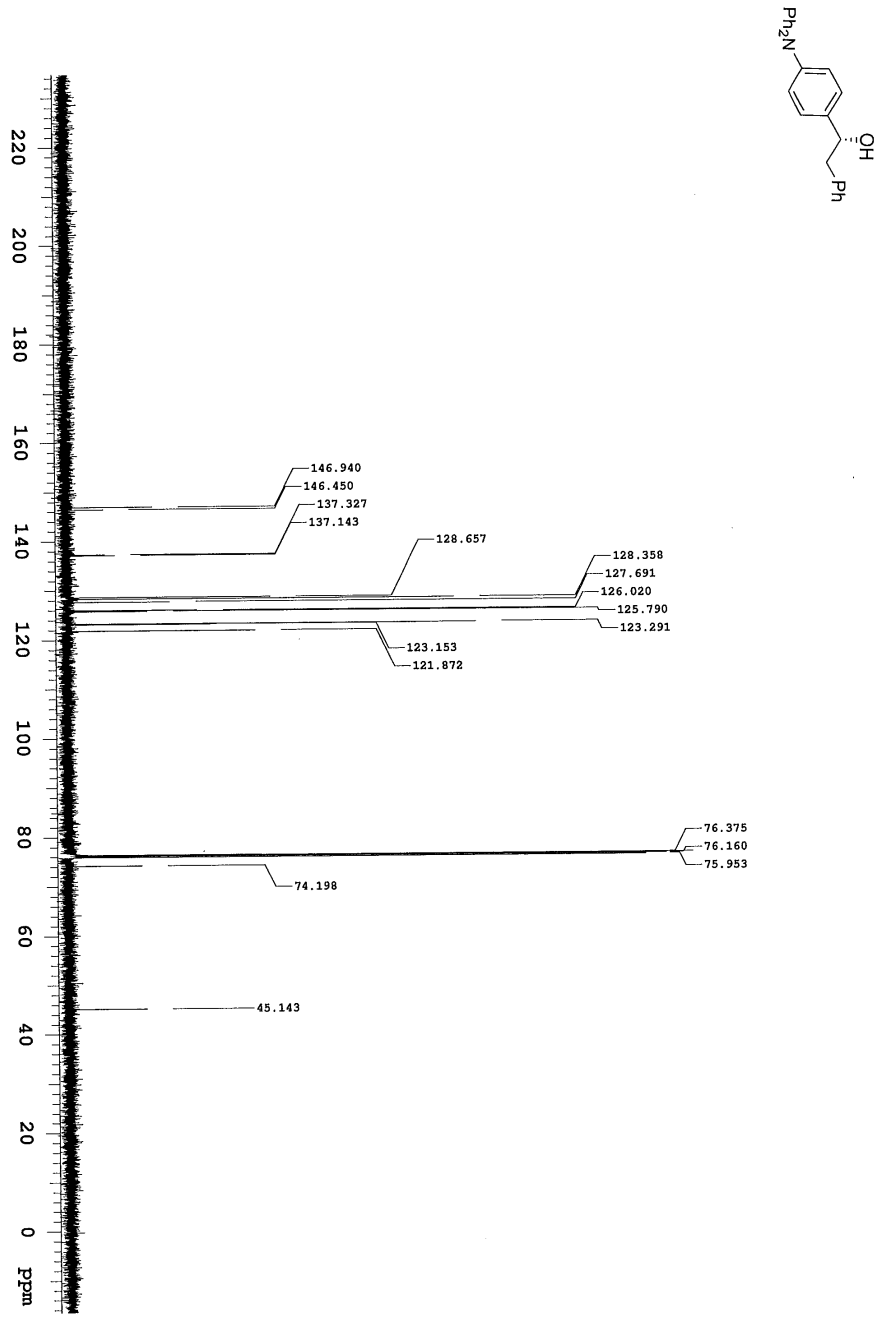
10
9
8
7
6
5
4
3
2
1
ppm


Ph2N
OH
Ph
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140
120
100
80
60
40
20
0
ppm
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146.450
137.327
137.143
128.657
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126.020
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123.153
121.872
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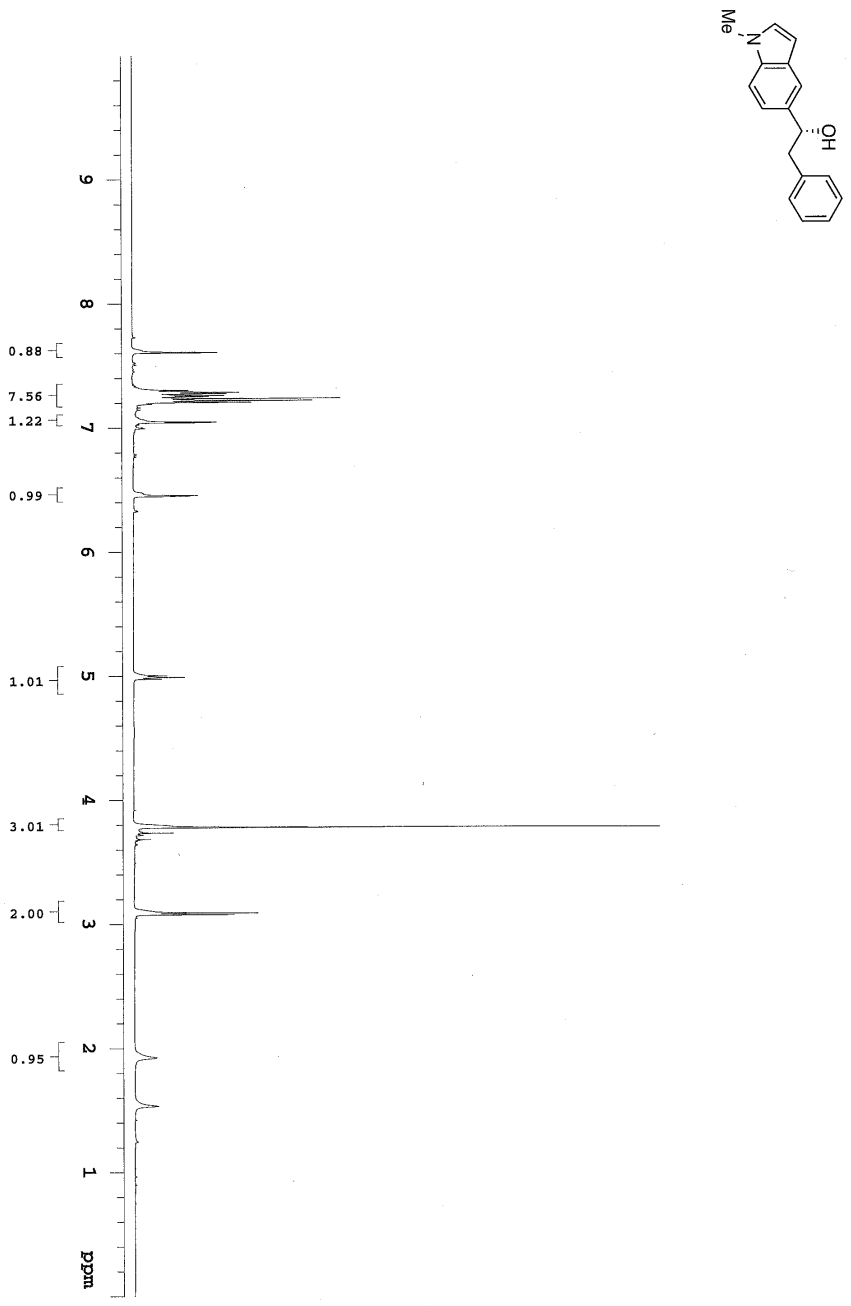
76.160
75.953
74.198
45.143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8
7
6
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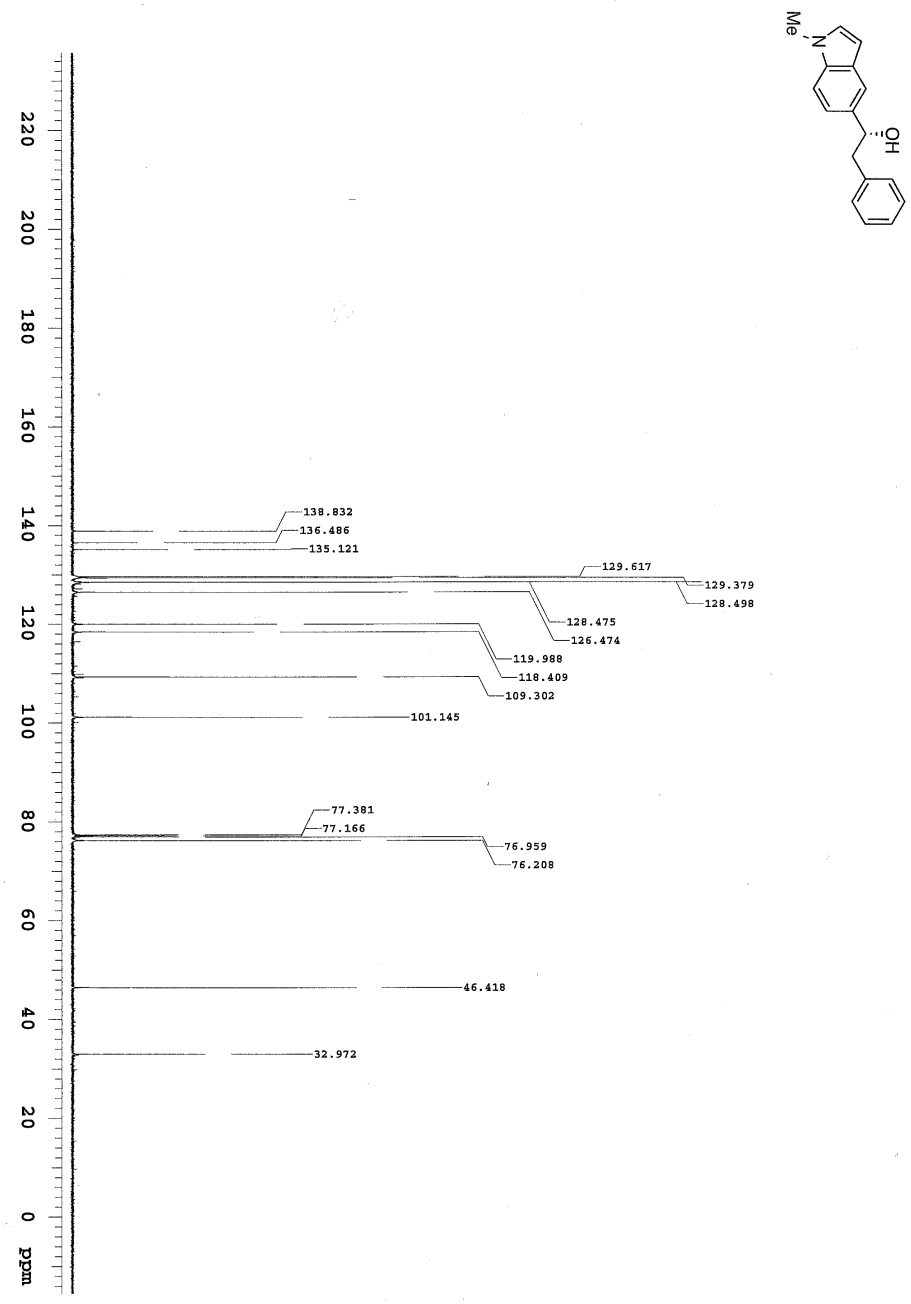
4
3
2
1
ppm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N
OH
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200
180
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140
120
100
80
60
40
20
0
ppm
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136.486
135.121
129.617
129.379
128.498
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101.145
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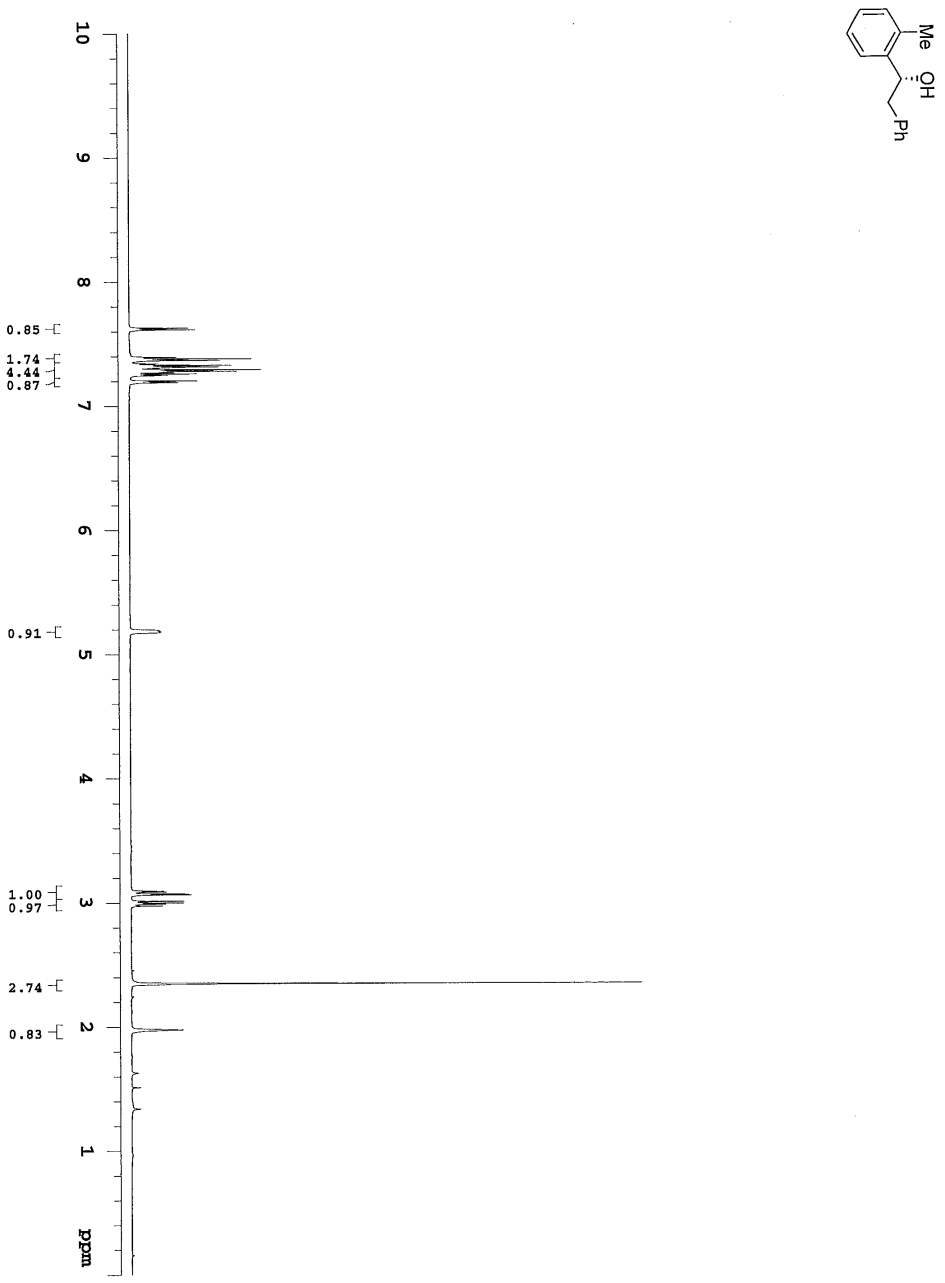
77.166
76.959
76.208
46.418
32.972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Ph
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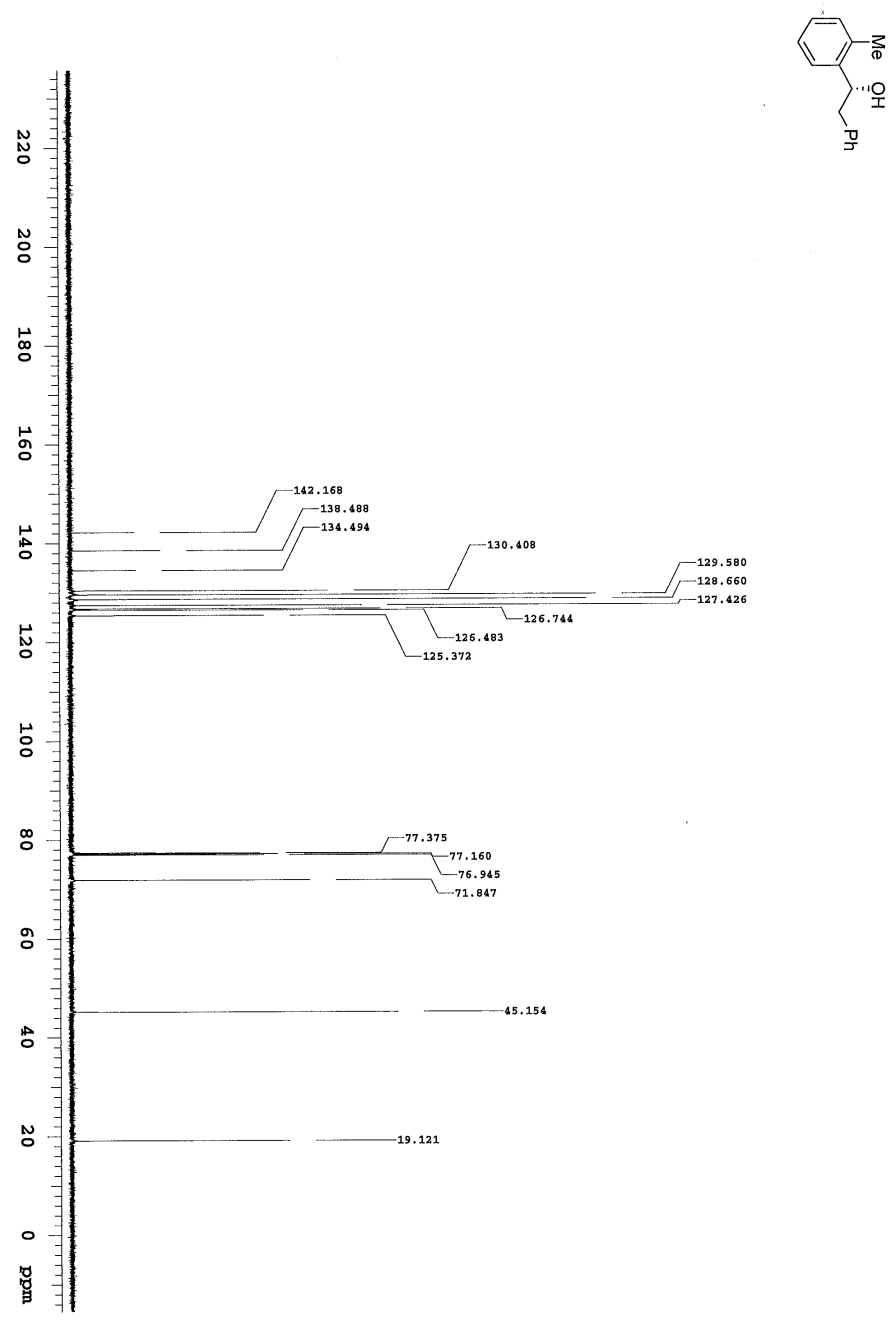
9
8
7
6
5
4
3
2
1
ppm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120
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80
60
40
20
0
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142.168
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134.494
130.408
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125.372
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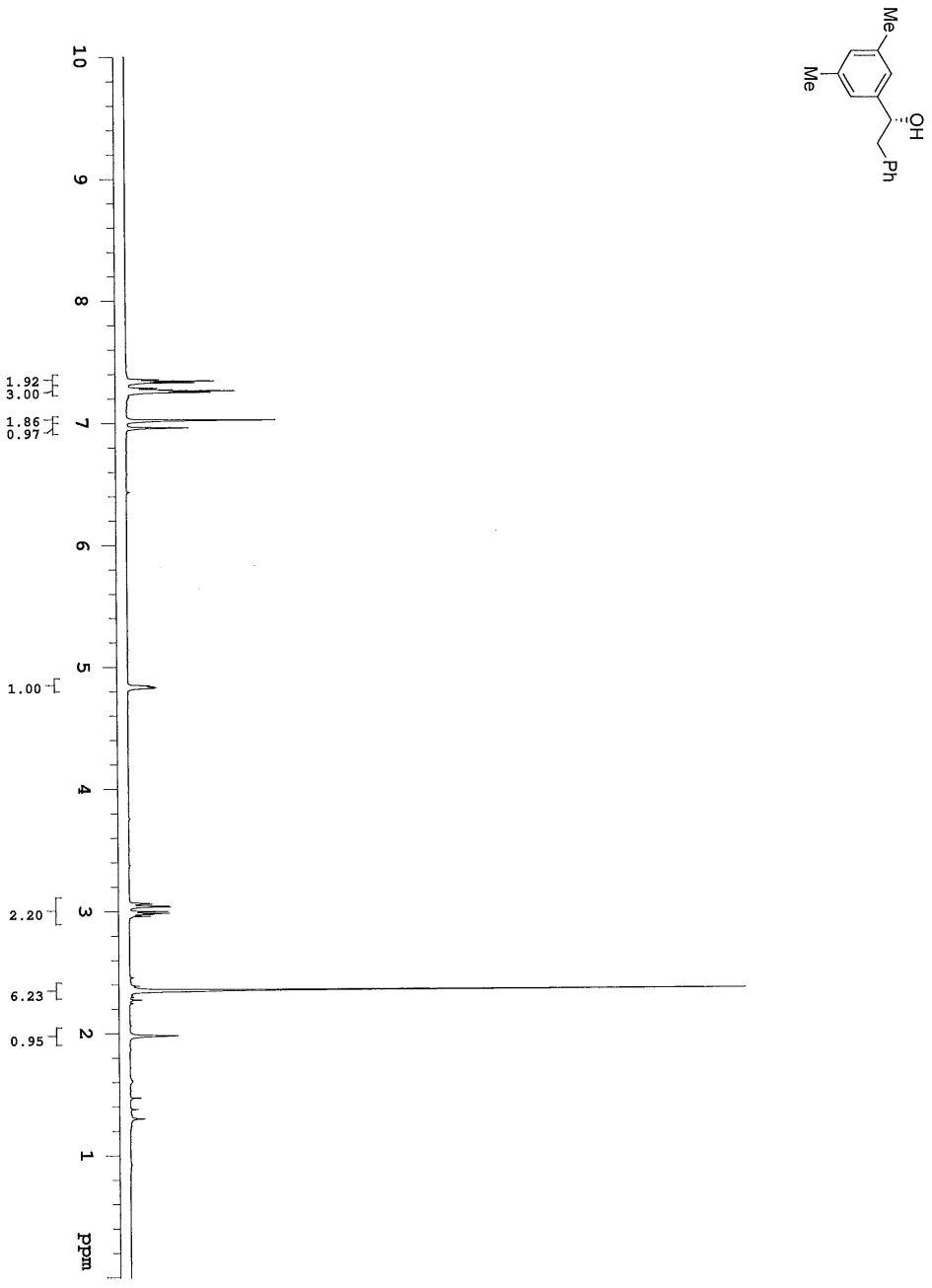
77.160
76.945
71.847
45.154
19.121


Me
Me
OH
Ph
10
9
8
7
6
5
4
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2
1
PPM
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0.97
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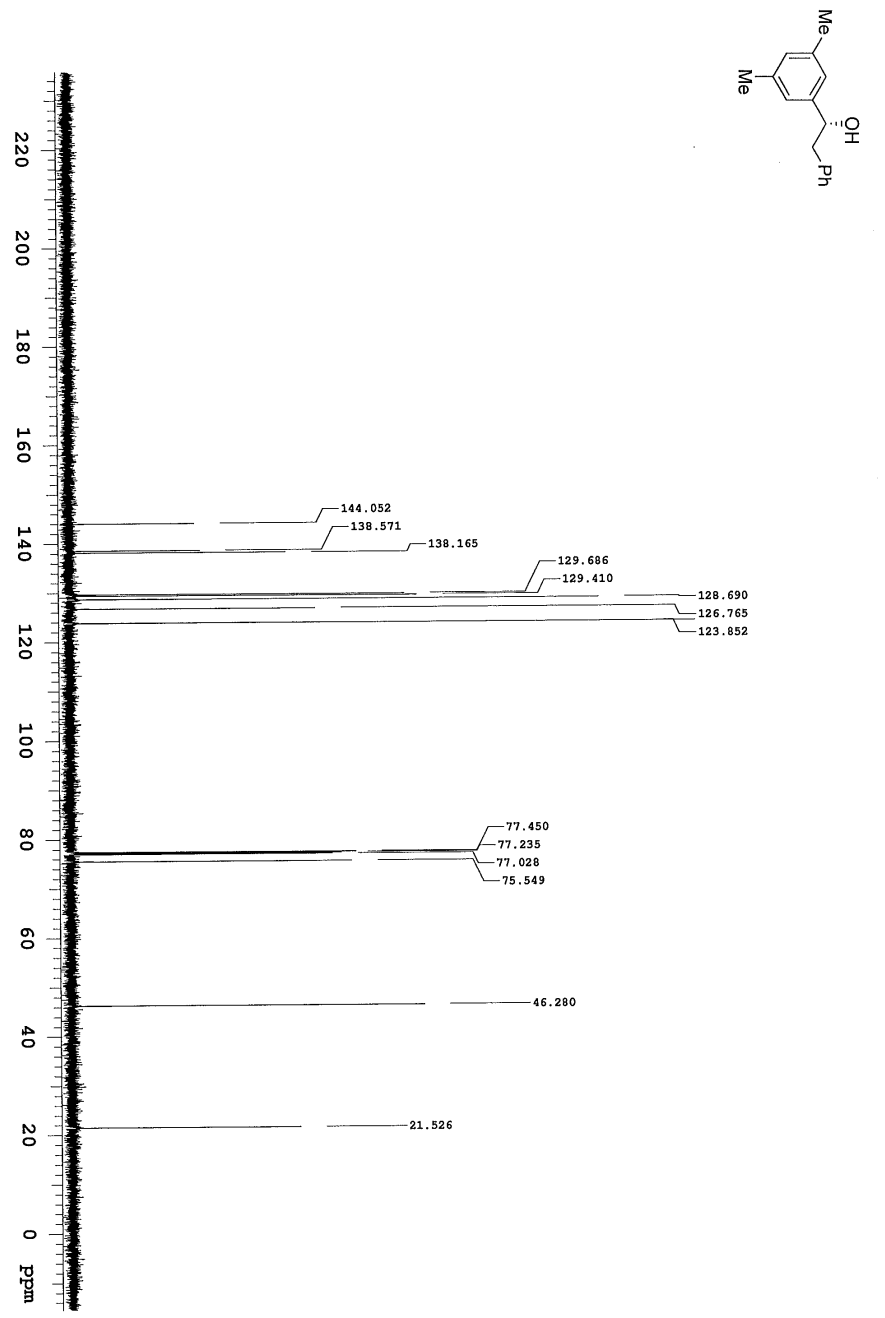
6.23
0.95


Me
Me
OH
Ph
220
200
180
160
140
120
100
80
60
40
20
0
ppm
144.052
138.571
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123.852
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77.235
77.028
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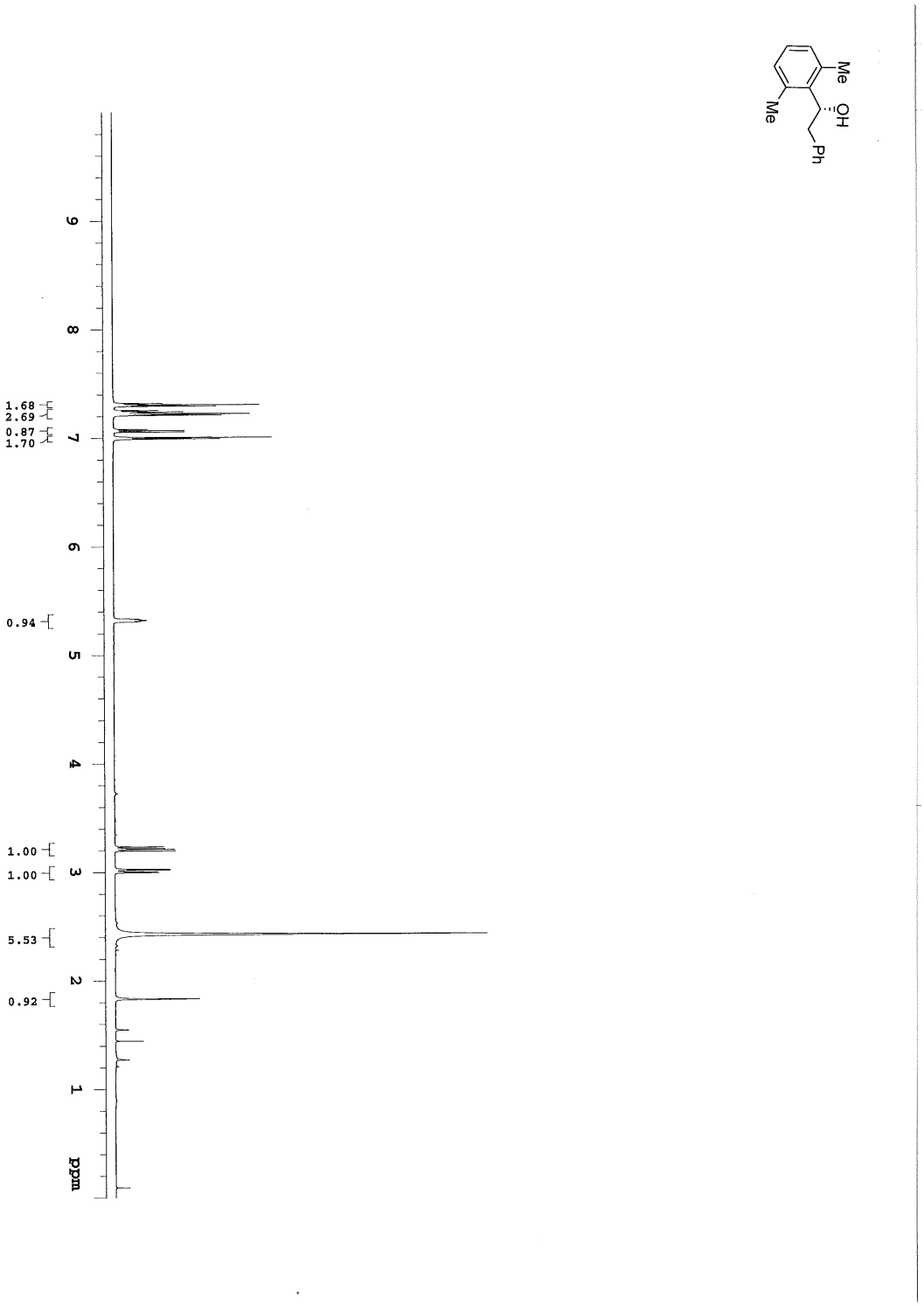
46.280
21.526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Me
Ph
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8
7
6
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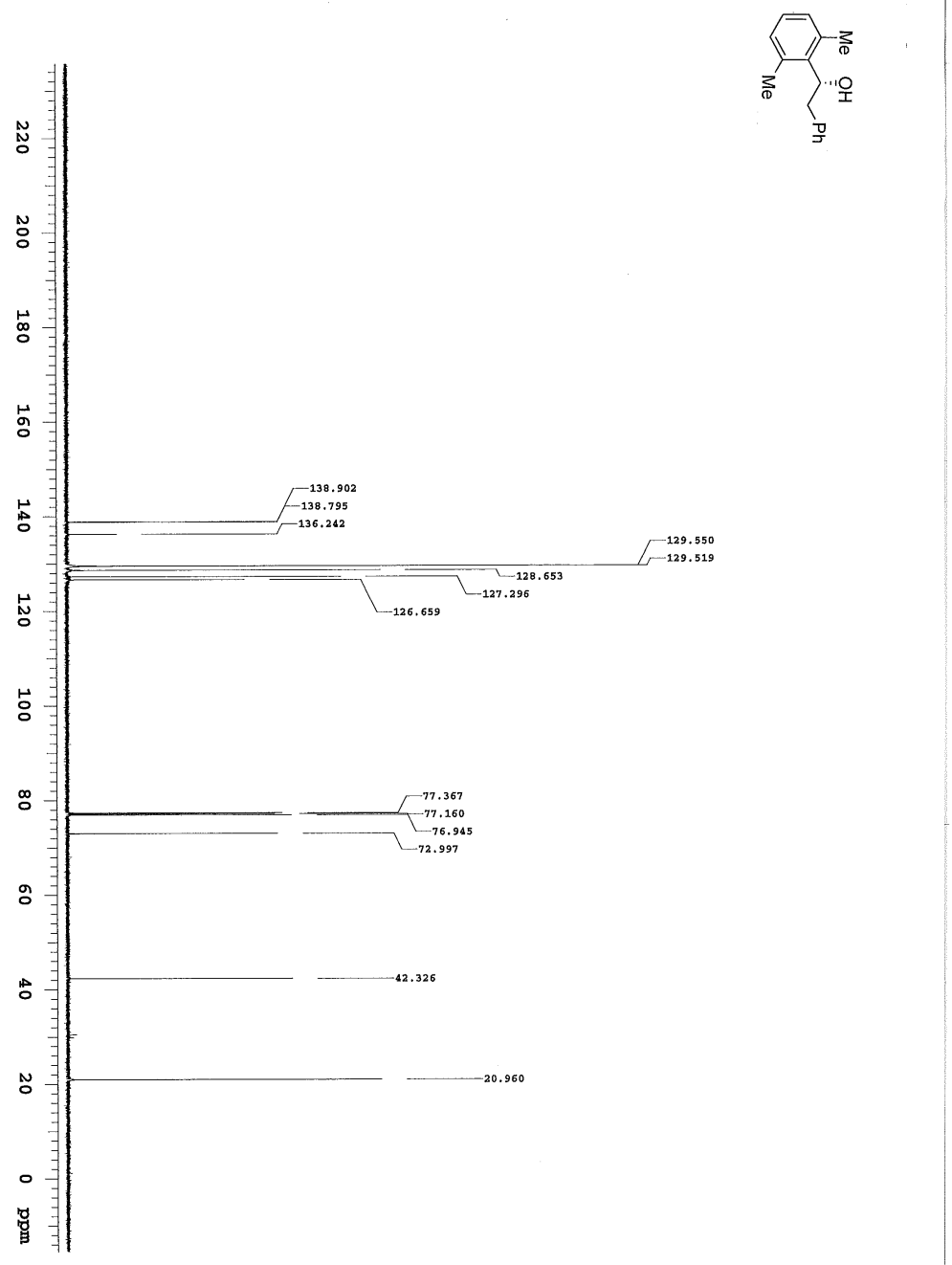
4
3
2
1
ppm


Me
OH
Me
Ph
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140
120
100
80
60
40
20
0
ppm
138.902
138.795
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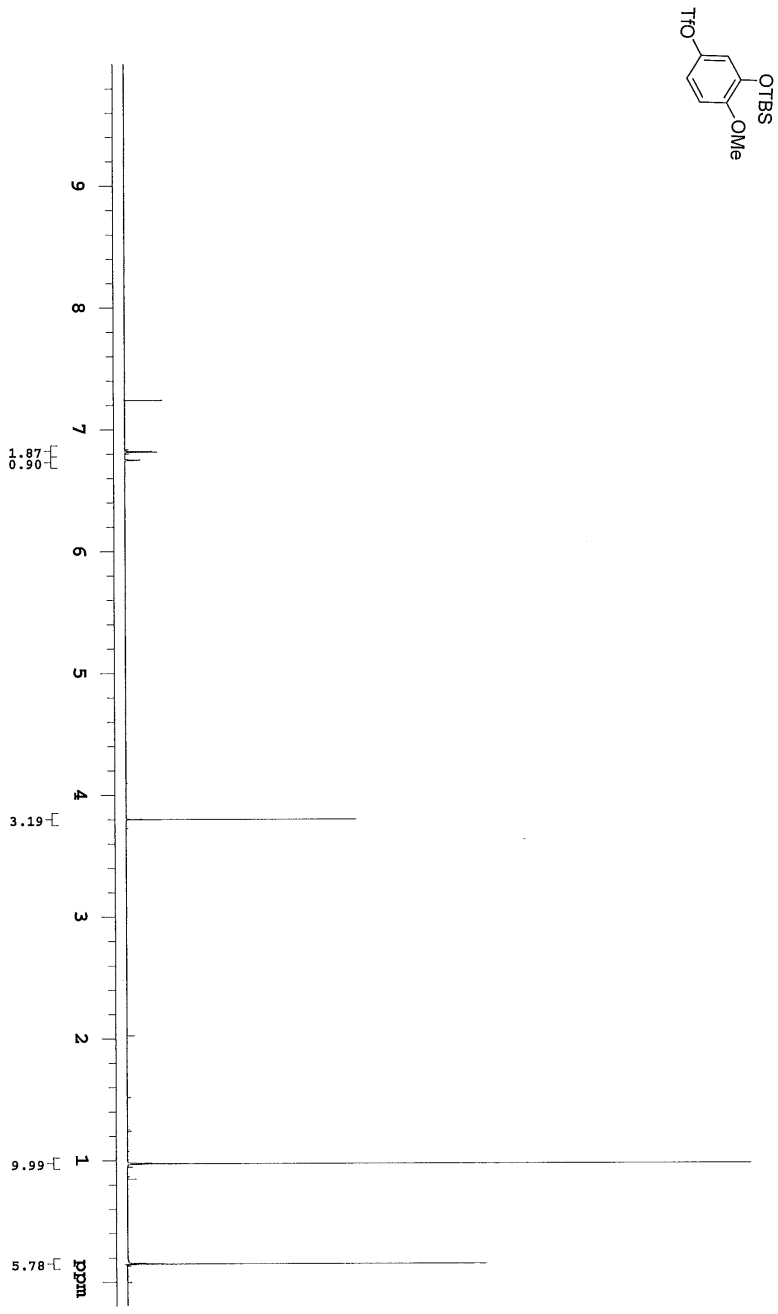
127.296
126.659
77.367
77.160
76.945
72.997
42.326
20.960


TfO
OTBS
OMe
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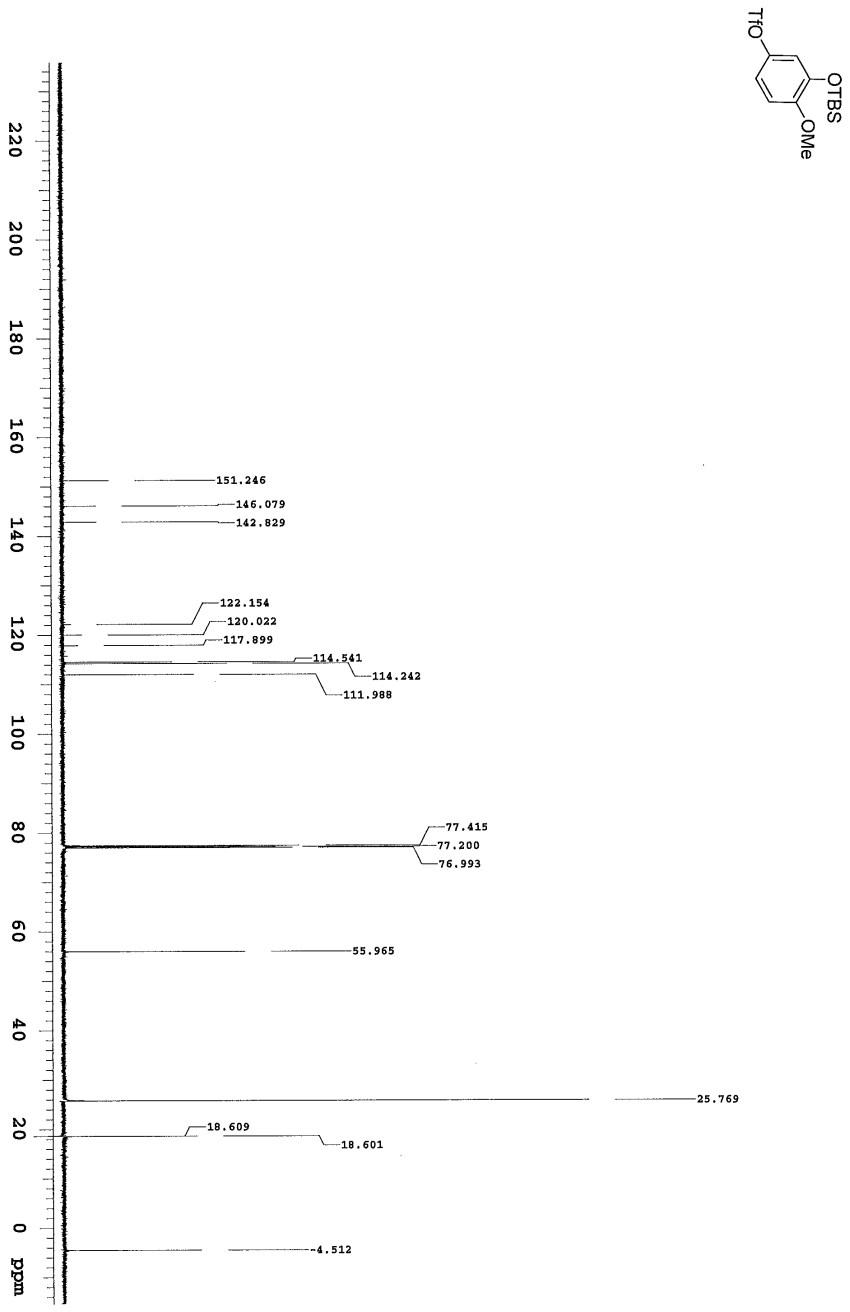
ppm


TfO
OTBS
OMe
220
200
180
160
140
120
100
80
60
40
20
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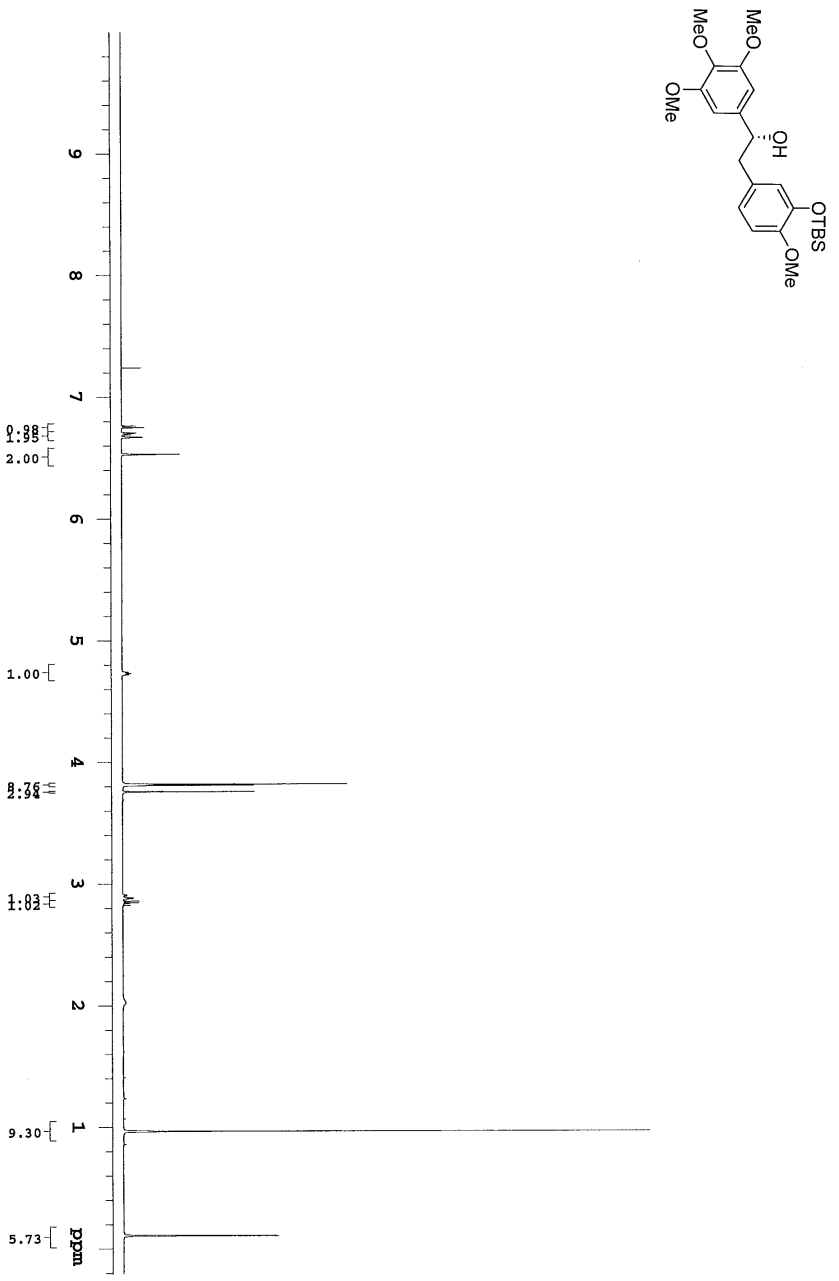
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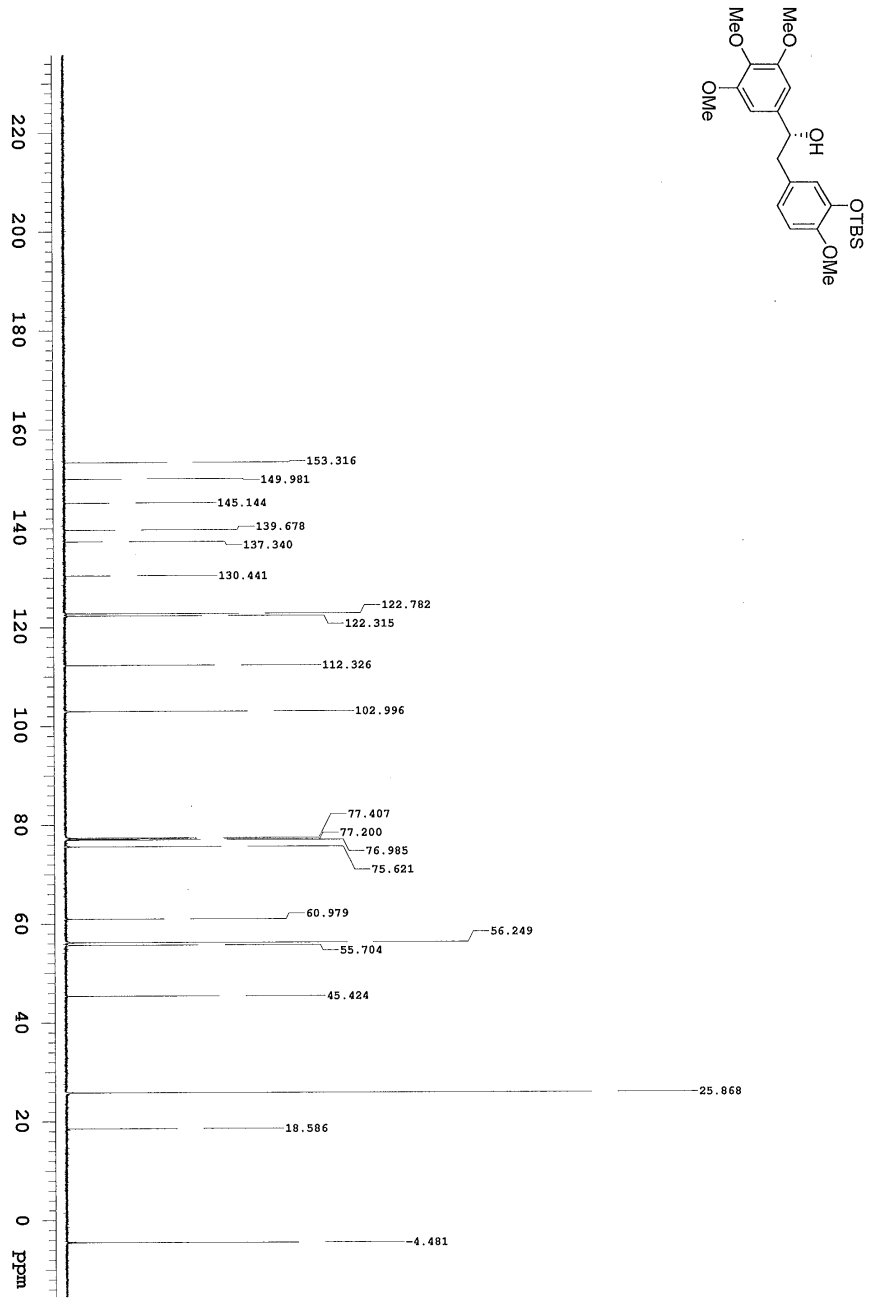
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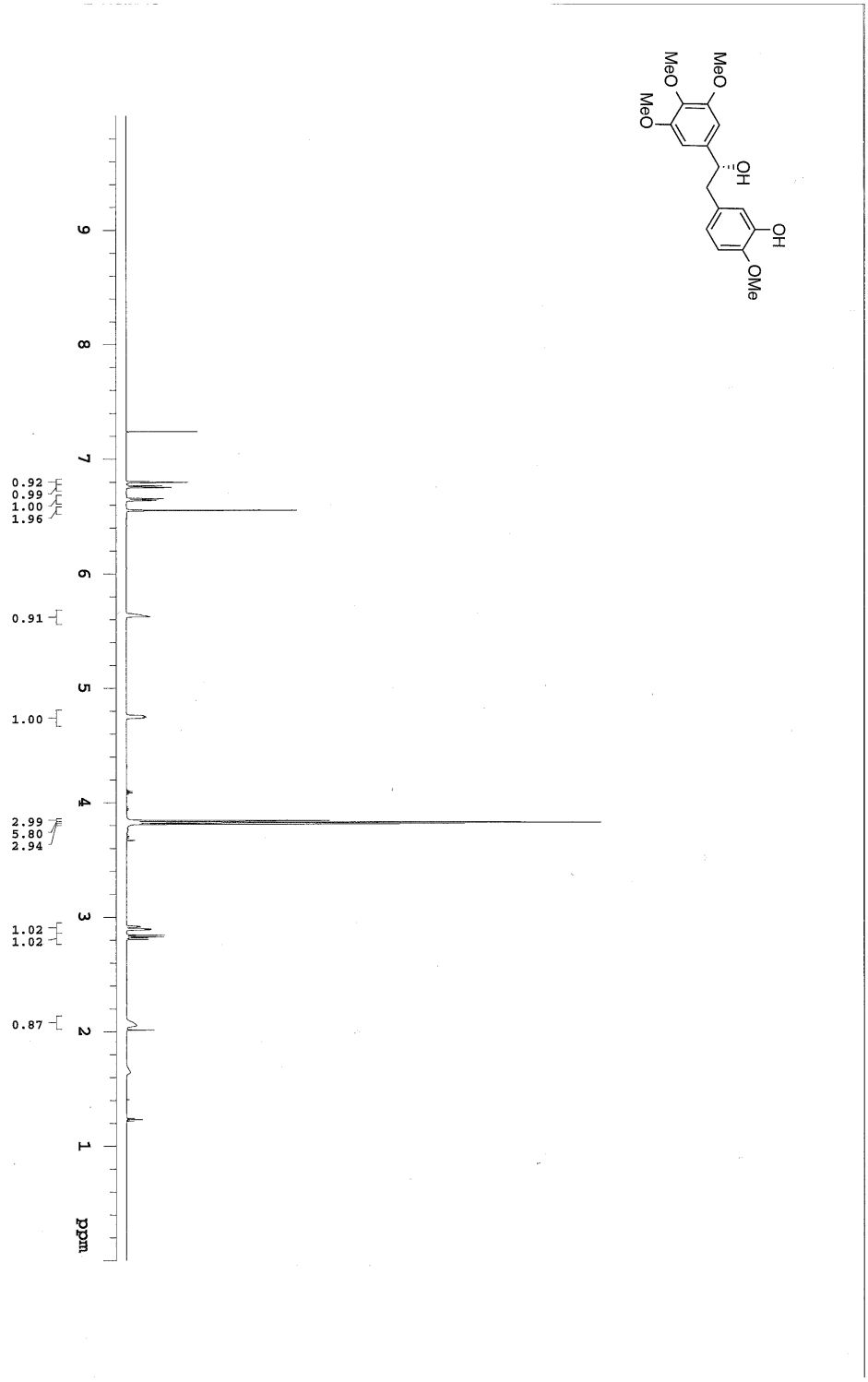
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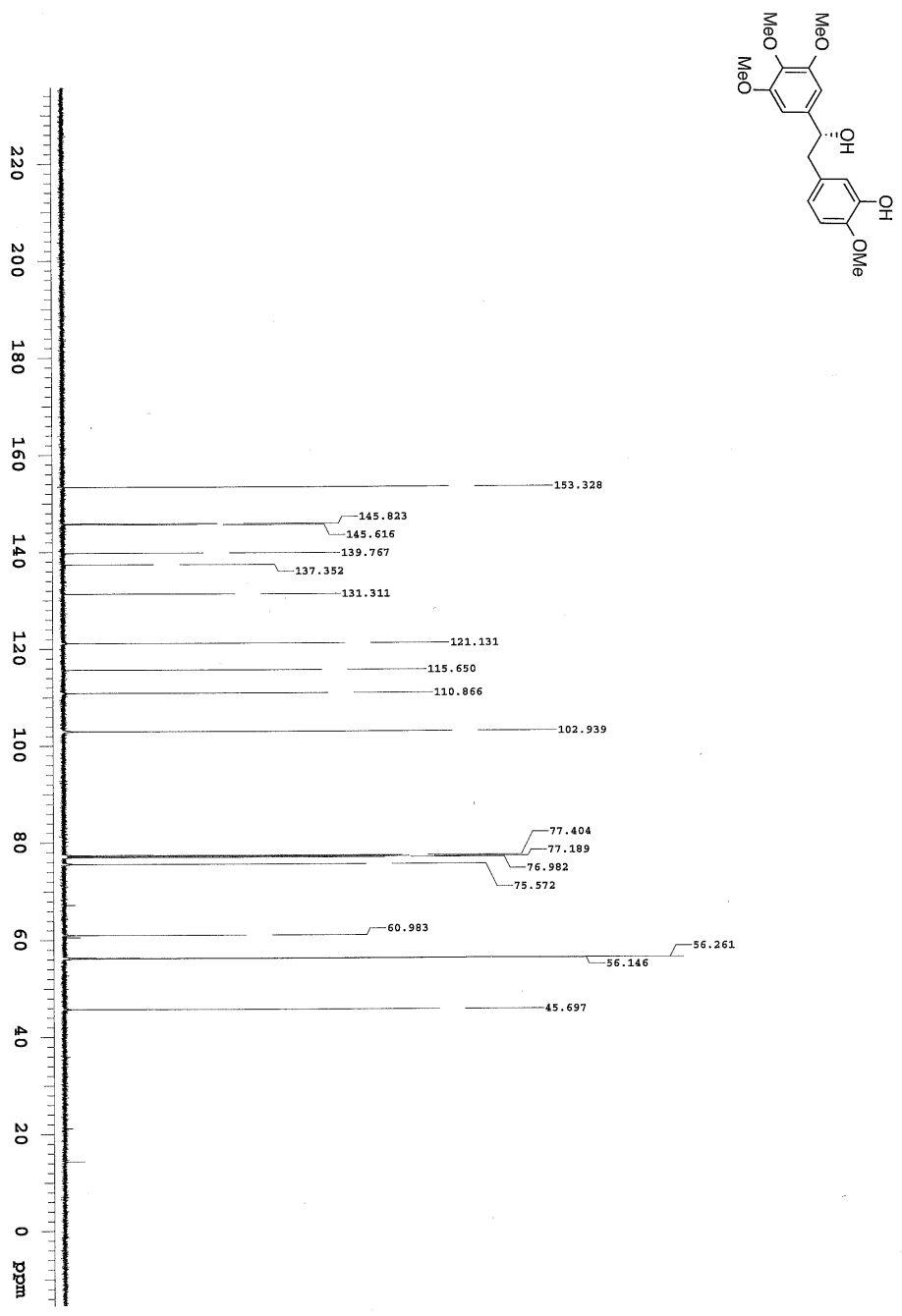
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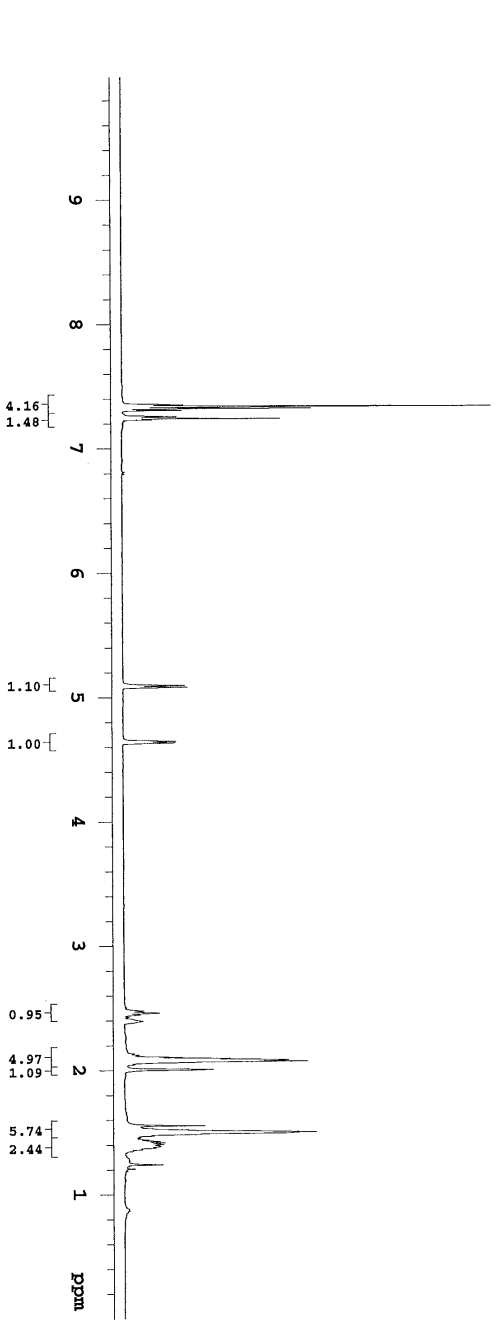
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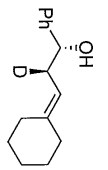
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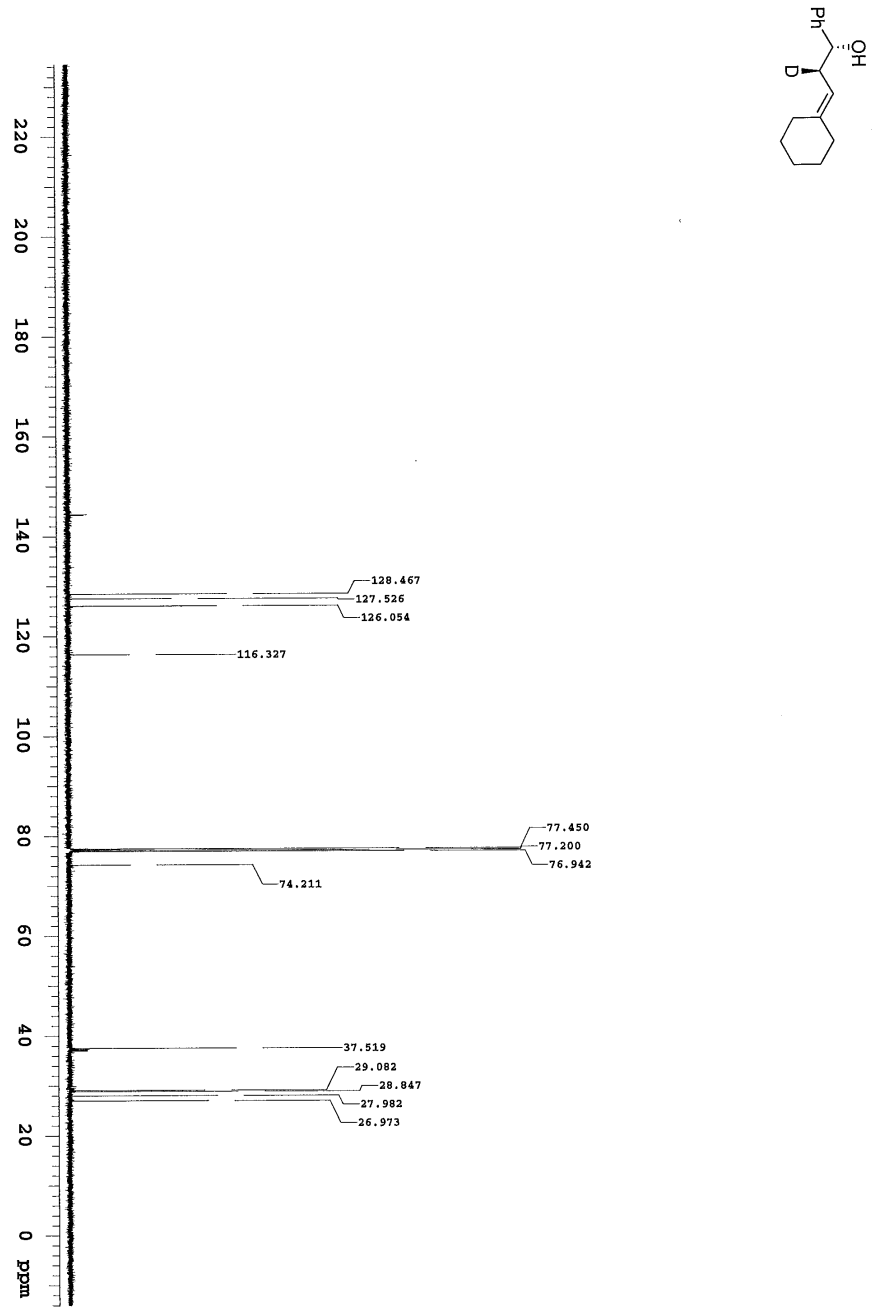
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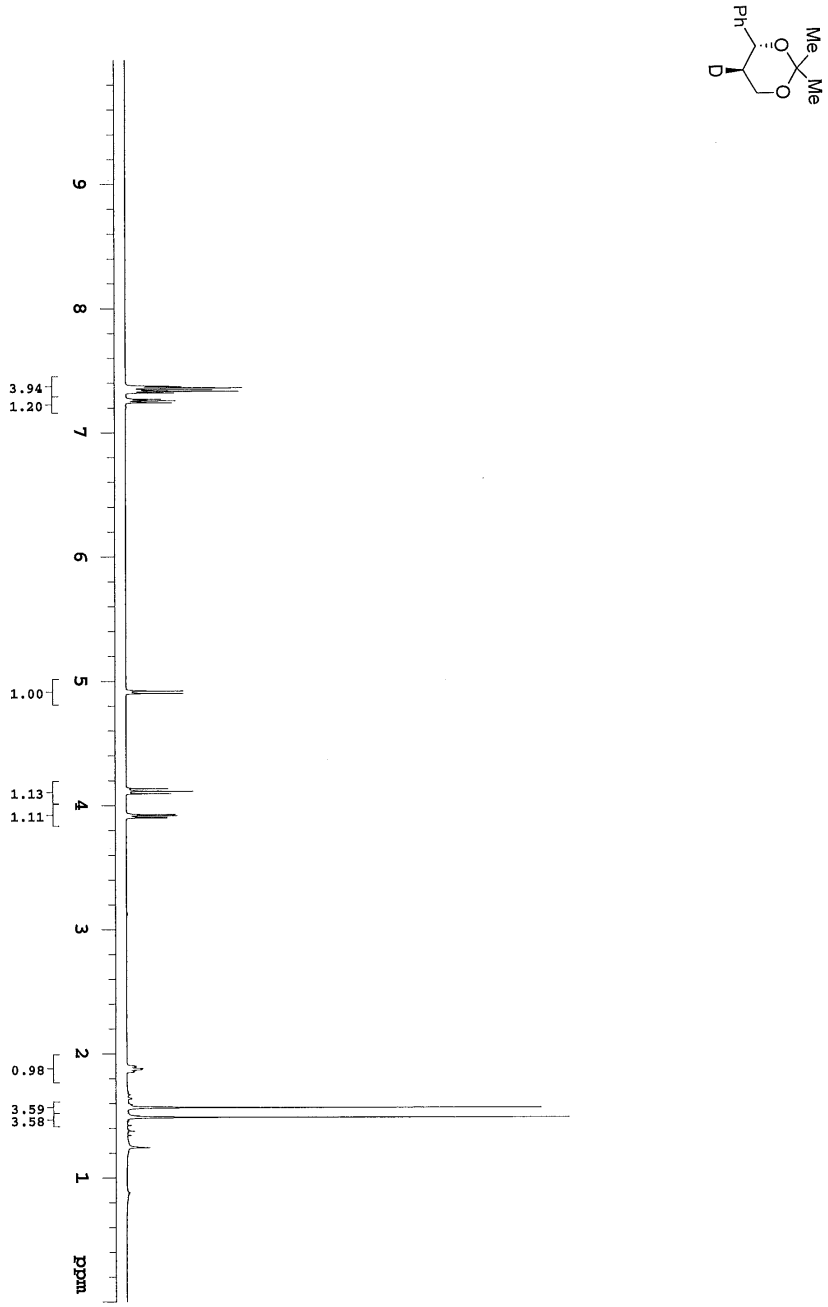
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3
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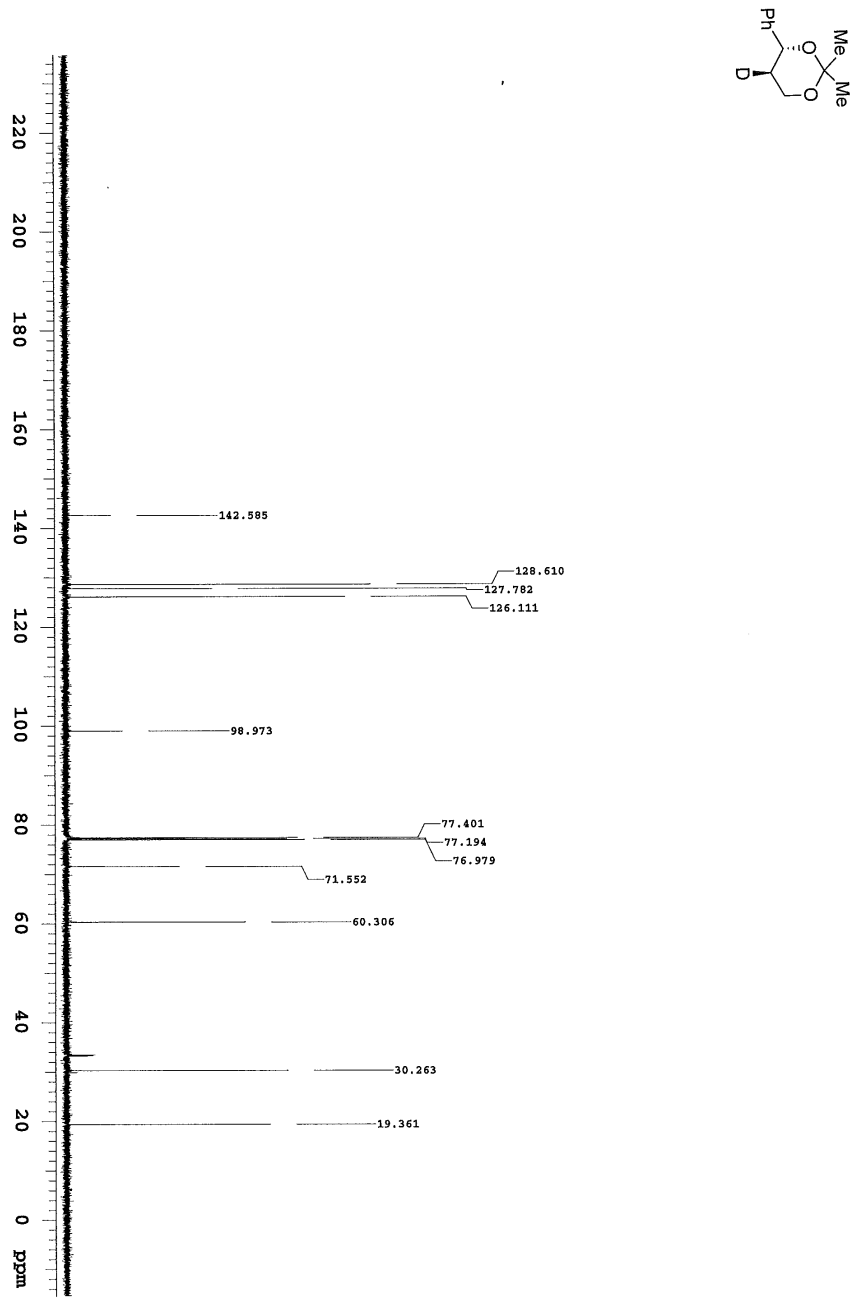
1
ppm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127.782
126.111
98.973
77.401
77.194
76.979
71.552
60.306
30.263
19.361

Chapter 3

Boron-Directed Catalytic Asymmetric Synthesis of Severely Hindered Quaternary Stereocenters

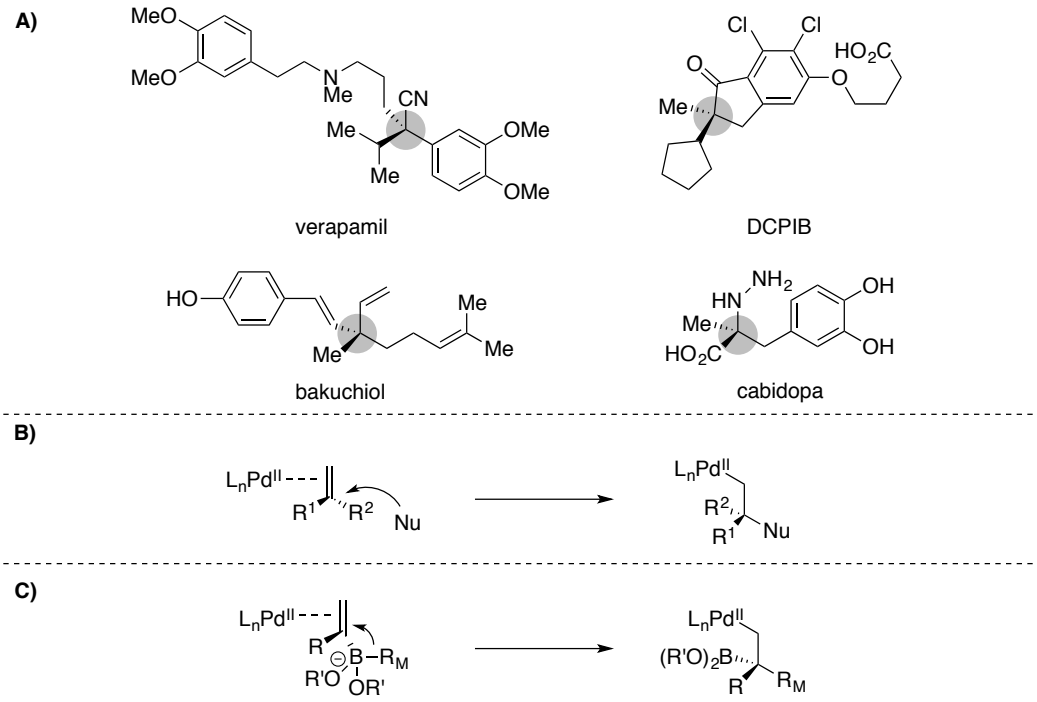
3.1. Introduction

Fully substituted carbon stereocenters, including but not limited to tertiary alcohols, α-tertiary amines, and all-carbon quaternary centers, are one of the most important structural motifs in therapeutic agents, natural products, and other bioactive molecules (Scheme 3.1.A).[1] Despite their wide abundance and structural importance in many useful medicines, agrochemicals and other fine chemicals, catalytic and enantioselective construction of fully substituted carbon stereocenters remains as one of the most difficult challenges for synthetic chemists[2]. In terms of stereocontrol, achieving high enantioselectivity is usually difficult due to the lack of significant structural bias between the prochiral faces of substrates. Furthermore, it becomes even more challenging to assemble acyclic quaternary centers since one cannot take the advantage of the critical conformational constraints offered by cyclic substrates. Besides the difficulty in achieving high enantioselectivity, one of the most significant challenges in constructing fully substituted carbon stereocenters is the sterically hindered environment surrounding the reaction center to which a new bond can form. To address such inherent challenges of

[1] Ley, S. V. (2006). *Quaternary stereocenters: challenges and solutions for organic synthesis*. J. Christoffers, & A. Baro (Eds.). John Wiley & Sons.
[2] (a) Liu, Y., Han, S. J., Liu, W. B., Stoltz, B. M. *Acc. Chem. Res.* **2015**, 48, 740-751. (b) Ling, T., Rivas, F. *Tetrahedron* **2016**, 72, 6729-6777. (c) Quasdorf, K. W., Overman, L. E. *Nature* **2014**, 516, 181-191.

constructing acyclic quaternary centers, several creative strategies have been developed by taking advantage of intramolecular reactions or activating the substrates with specific functional groups. However, the requirement of an intramolecular reaction or pre-functionalized substrate limits more general applications of these synthetic strategies.

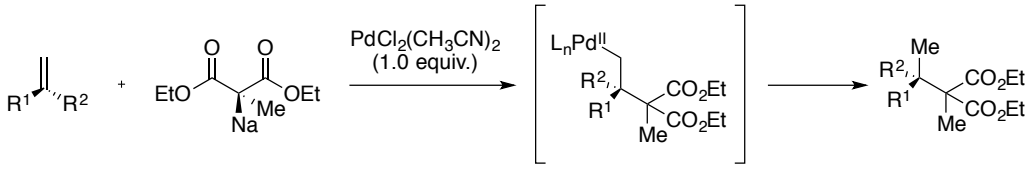
Scheme 3.1 Outer sphere nulceopalladation v.s palladium induced 1,2-metallate rearrangement.



Recently, a catalytic conjunctive cross-coupling has been developed in our laboratory. The conjunctive cross-coupling is a three-component coupling reaction that furnishes chiral organoboronic esters by merging two nucleophiles, an organolithium reagent and an organoboronic ester, and an organotriflate electrophile in an entantioselective and efficient fashion. As discussed in Chapter 2, a featured step in the conjunctive cross-coupling catalytic cycle is proposed to be the palladium-induced 1,2-metallate

rearrangement. A common feature that can be drawn between the metal-induced 1,2-metallate rearrangement and outer-sphere alkene nucleometallation reactions is that both processes occur with *anti*-addition of the transition-metal and the nucleophile across the alkene. This is a consequnence of the π-system being activated by the transition-metal to facilitate nucleophilic attack (Scheme 3.1.B). However, it is known that the efficiency of outer-sphere alkene nucleopalladation is highly depended on the steric nature of the alkene substrates. As an example shown by Hegedus and co-workers[3], *anti*-nucleopalladation proceeded with high efficiency with ethylene as the substrate (95% yield, Scheme 3.2, entry 1), while using a mono-substituted alkene substrate, the yield was diminished to 55%, and the use of 1,1-disubstituted isobutylene only led to trace product (Scheme 3.2, entry 2, 3).

Scheme 3.2. Palladium assisted alkylation of alkenes.



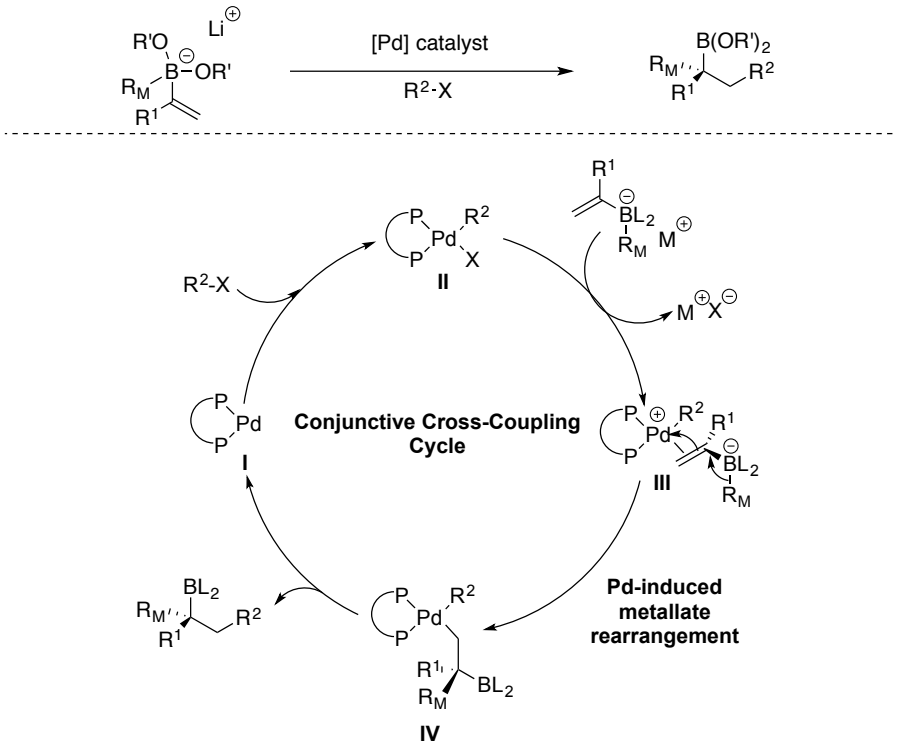
Entry	R^1	R^2	Yield
1	H	H	95%
2	H	*n*-Bu	55%
3	Me	Me	trace

While Hegedus's observations might make one concered about conjunctive coupling with substituted substrates, we envisioned that the challenging nucleopalladation of hindered alkenes might be overcome by employing a metal-induced metallate shift

[3] Hegedus, L. S., Williams, R. E., McGuire, M. A., Hayashi, T. (1980). *J. Am. Chem. Soc.* **1980**, 102, 4973-4979.

strategy via conjunctive cross-coupling. By pre-forming the reactive boron ate complex, the majority of the steric penalty in carbon-carbon bond forming step has been already built into the substrate so that the subsequent palladium induced 1,2-metallate rearrangement might not introduce significant additional strain (Scheme 3.1.C). Taking advantage of this unique mechanistic feature of conjunctive cross-coupling, sterically encumbered tertiary boronic esters might be synthesized in an enantioselective and efficient fashion (Scheme 3.3).

Scheme 3.3. Enantioseletive synthesis of tertiary boronic esters by catalytic conjunctive cross-coupling.



Additionally, the products bearing a useful carbon-boron bond can be readily transformed into corresponding tertiary alcohols, α-tertiary amines and other all-carbon quaternary centers. In this way, conjunctive cross-coupling can be considered as a general

strategy to synthesize a broad range of important fully substituted carbon centers. In this chapter, the development of an enantioselevtive synthesis of tertiary boronic esters by catalytic conjunctive cross-coupling will be presented. Subsequent transformations of the resulting tertiary boronic esters and their synthetic utility will also be demonstrated.

3.2. Background

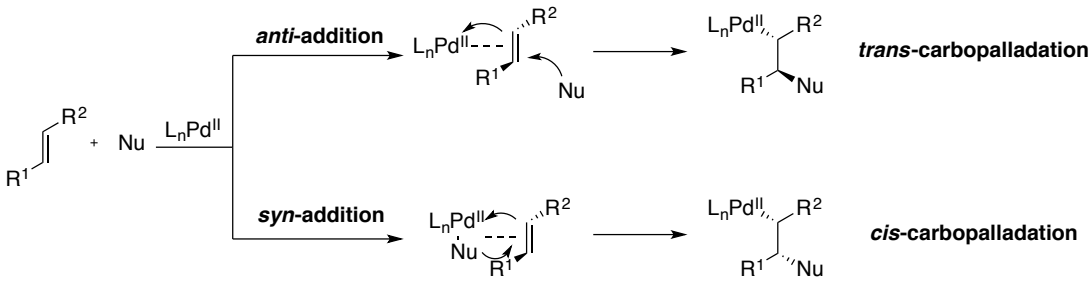
3.2.1. Recent advances in enantioselective carbopalladation of alkenes

As one of the most accessible feedstock chemicals, alkenes are considered as an ideal substrates for chemical synthesis. A tremendous effort has been invested to develop catalytic reactions that transform simple alkenes into a variety of useful fine chemical products. As one of the seminal examples, it has been discovered that palladium (II) is able to catalyze the addition of a range of different nucleophiles to alkenes, and a variety of carbon-oxygen, carbon-nitrogen, and carbon-carbon bond forming reactions have been developed based on this unique reactivity.[4] In terms of carbopalladation, carbon-based nucleophiles react with alkenes in the presence of palladium catalysts to construct a new carbon-carbon bond while also generating an alkyl-palladium (II) intermediate that may engage in a broad range of subsequent transformations. Similar to other nucleopalladation reactions, carbopalladation reactions are capable of proceeding by two distinct pathways: a *trans*-carbopalladation pathway and a *cis*-carbopalladation pathway (Scheme 3.4). For the *trans*-carbopalladation pathway, the alkene is activated by coordination of a palladium catalyst while the nucleophile attacks the alkene from the opposite face of palladium to furnish a carbopalladation product in an *anti*-addition fashion. Alternatively,

[4] McDonald, R. I., Liu, G., Stahl, S. S. *Chem. Rev.* **2011**, 111(4), 2981-3019.

for the *cis*-carbopalladation pathway, the nucleophile can pre-associate with the palladium catalyst. Then, the palladium complex coordinates to the alkene followed by migratory insertion of the nucleophile to alkene substrate to afford the palladated product in a *syn*-addition fashion. According to experimental and computational studies over the past several decades, it has been demonstrated that the energy barriers associated with these two pathways can be very similar, and the operative mechanism for specific reactions needs to be carefully determined case by case.

Scheme 3.4. Stereochemical pathways of carbopalladation.



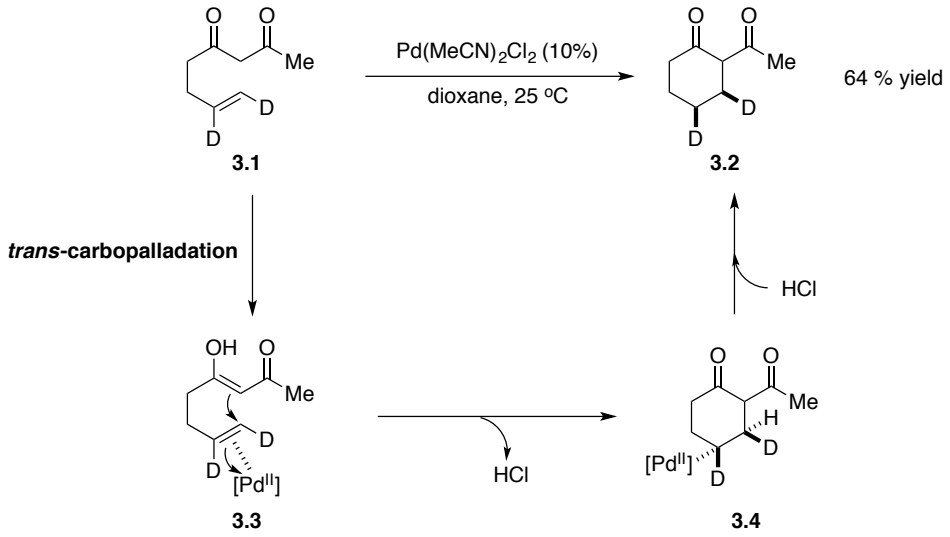
3.2.1.1. Selected examples of reactions involving *trans*-carbopalladation

In 2001, Widenhoefer and co-workers reported a palladium catalyzed intramolecular cyclization reaction of alkenyl β-dicarbonyl compounds.[5] It was proposed that the reaction underwent carbopalladation. Following protonolysis of the resulting palladium-carbon bond, this furnished the cyclized product as a formal hydroalkylation with the enolic C-H bond being added across the alkene. To further understand the key carbopalladation step, a mechanistic experiment employed the *cis*-deuterium labeled alkene substrate **3.1** in the palladium catalyzed reaction, and the *cis*-deuterated isomer of

[5] (a) Pei, T., Widenhoefer, R. A. *J. Am. Chem. Soc.* **2001**, 123, 11290-11291. (b) Pei, T., Widenhoefer, R. A. *Chem. Commun.* **2002**, 6, 650-651.

product **3.2** was isolated exclusively (Scheme 3.5).[6] By assuming that a stereoretentive protonolysis of the palladium-carbon bond occurred under the given reaction conditions, the *cis*-deuterated product isomer **3.2** could only be obtained from the palladated intermediate **3.4**. To furnish the intermediate **3.4**, the enol had to attack the palladium-activated alkene from the opposite face to which palladium was binding. Therefore, the result of this mechanistic experiment indicated the overall process proceeded by a *trans*-carbopalladation pathway.

Scheme 3.5. Palladium catalyzed hydroalkylation and mechanistic study.

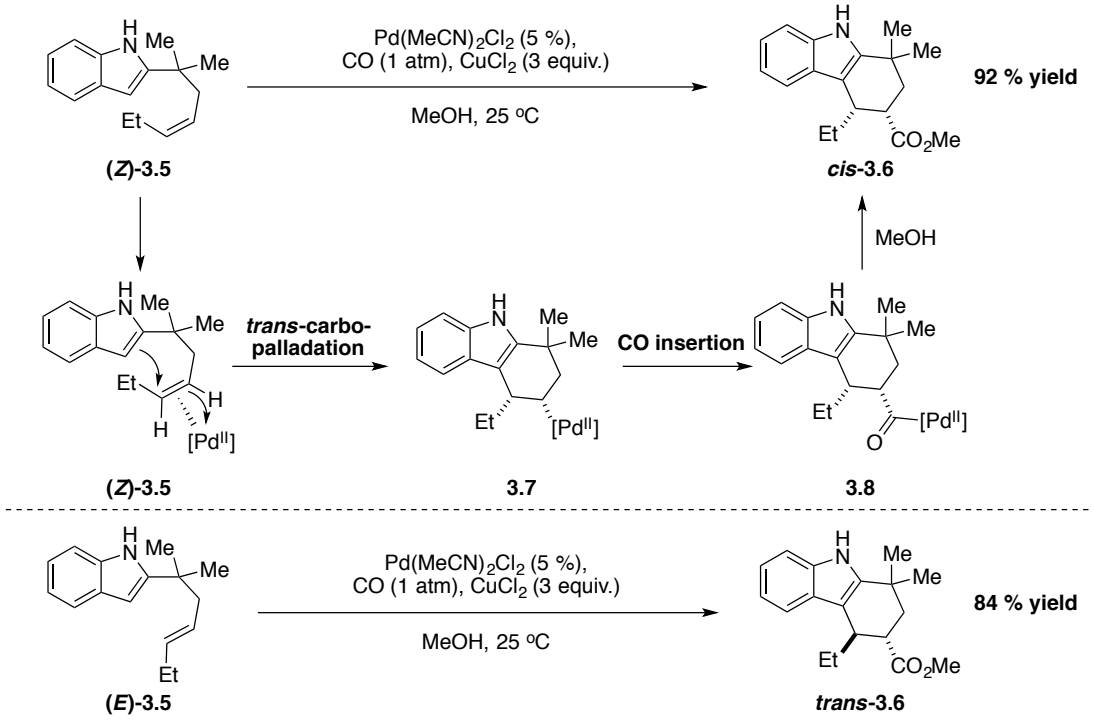


In 2006, a palladium-catalyzed cyclization reaction of alkenyl indole substrates was developed in the Widenhoefer laboratory.[7] An indole with a tethered alkene underwent an intramolecular alkylation/carbonylation in the presence of a palladium catalyst (Scheme 3.6). The reaction was conducted under 1 atm of carbon monoxide and with 3 equivalents of copper (II) chloride as the stoichiometric oxidant. Interestingly, cyclized product ***cis***-

[6] (a) Qian, H., Widenhoefer, R. A. *J. Am. Chem. Soc.* **2003**, 125, 2056-2057. (b) Qian, H., Pei, T., Widenhoefer, R. A. *Organometallics* **2005**, 24, 287-301.
[7] Liu, C., Widenhoefer, R. A. *Chem. Eur. J.* **2006**, 12, 2371-2382.

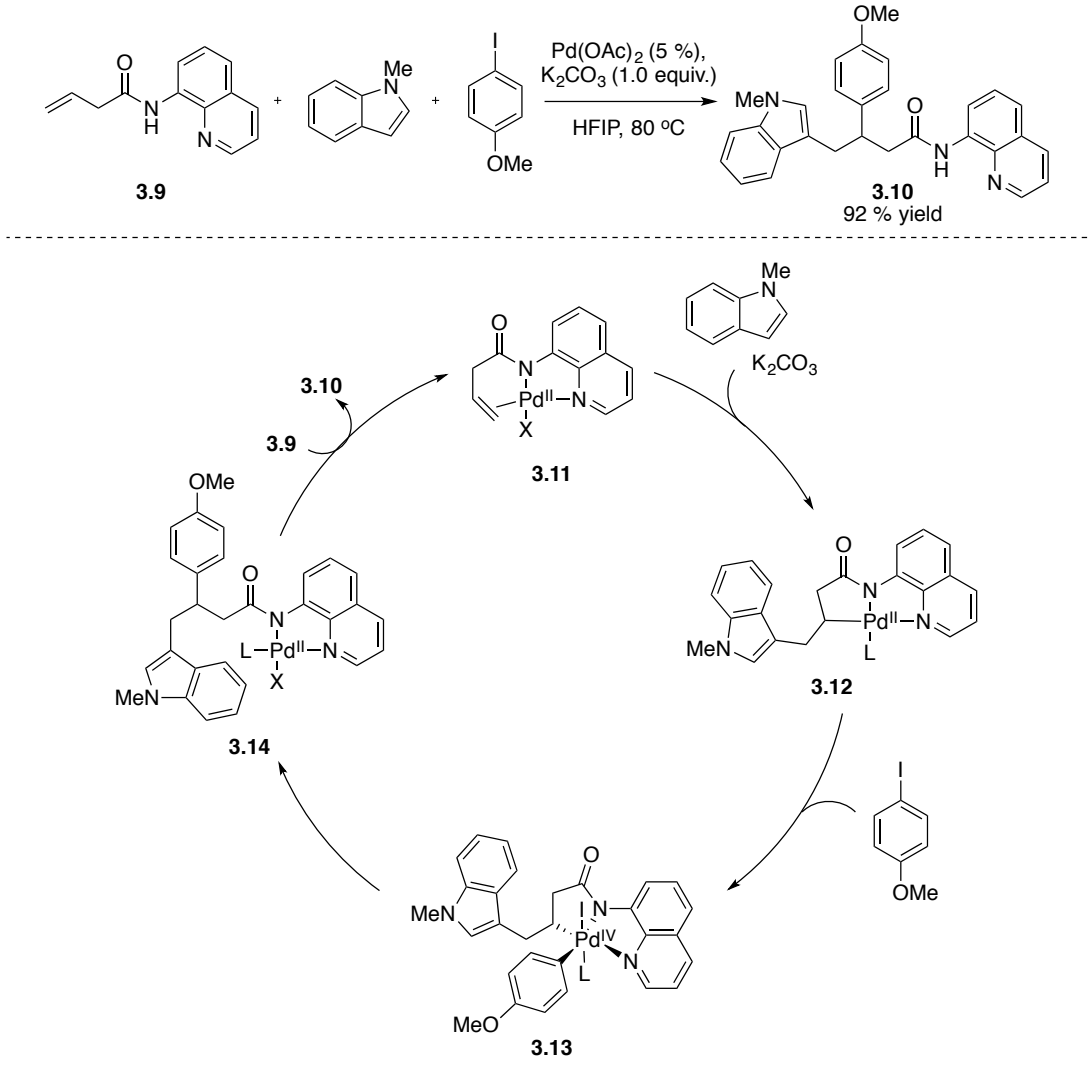
3.6 was isolated exclusively when the *Z*-alkene derived indole **(*Z*)-3.5** was employed in the reaction. Since it was known that α-migatory insertion of CO into palladium-carbon bond occurred with retention of configuration, the mechanism for the stereospecific formation of ***cis*-3.6** from **(*Z*)-3.5** was proposed as follows: starting with the palladium catalyst coordinated to the alkene, a *trans*-carbopalladation led to the alkylpalladium complex **3.7**. Subsequent CO insertion and reductive elimination furnished the alkylation/carbonylation product **3.6** with a *cis*-relationship between the ethyl group and the methyl ester group. The result that the *E*-isomer of the starting material **(*E*)-3.5** led to the *trans*-isomer of the product ***trans*-3.6** further supported the proposed mechanism.

Scheme 3.6. Palladium catalyzed alkylation/carbonylation of alkenyl indoles.



Recently, Engle and co-workers reported a palladium-catalyzed dicarbofunctionalization reaction of unactivated alkenes (Scheme 3.7).[8] By taking advantage of a bidentate directing group near the alkene, the palladium (II) complex was able to catalyze a vicinal difunctionalization of alkenes with a broad range of carbon based nucleophiles and electrophiles.

Scheme 3.7. Dicarbofunctionalization of alkenes via directed nucleopalladation.



[8] Liu, Z., Zeng, T., Yang, K. S., Engle, K. M. *J. Am. Chem. Soc.* **2016**, 138, 15122-15125.

The mechanism of the reaction was proposed as follows (Scheme 3.7): the palladium (II) catalyst coordinated to the bidentate directing group and was delivered to bind to the alkene. Then, a carbon-based nucleophile, such as the *N*-methyl indole, underwent an outer-sphere attack on the palladium-activated alkene to furnish the alkylpalladium (II) intermediate **3.12**. In contrast to the common palladation-β-hydride elimination pathway, the subsequent β-hydride elimination was prevented by the directing group's stabilizing effect so that the long-lived intermediate **3.12** underwent oxidative addition with an aryl iodide to lead to the palladium (IV) complex **3.13**. Finally, sequential reductive elimination and substrate exchange released the product and regenerated the palladium (II) complex **3.11** to turnover the catalytic cycle. Although no detailed stereochemical study was presented by the authors, the proposed outer-sphere attack indicated that the overall process proceeded through a *trans*-carbopalladation pathway.

As discussed above, several useful transformations have been developed that involve a *trans*-carbopalladation pathway. However, to the best of our knowledge, no enantioselective *trans*-nucleopalladation for carbon-based nucleophiles has been reported at this time.

3.2.1.2. Selected examples of enantioselective reactions involving *cis*-carbopalladation

In contrast to the *trans*-carbopalladation, a variety of strategies have been developed to enantioselectively functionalize alkene substrates via a *cis*-carbopalladation pathway. Although the palladium-catalyzed Heck reaction is one of the most widely used alkene functionalization reactions featuring a *cis*-carbopalladation step, it might seem that the

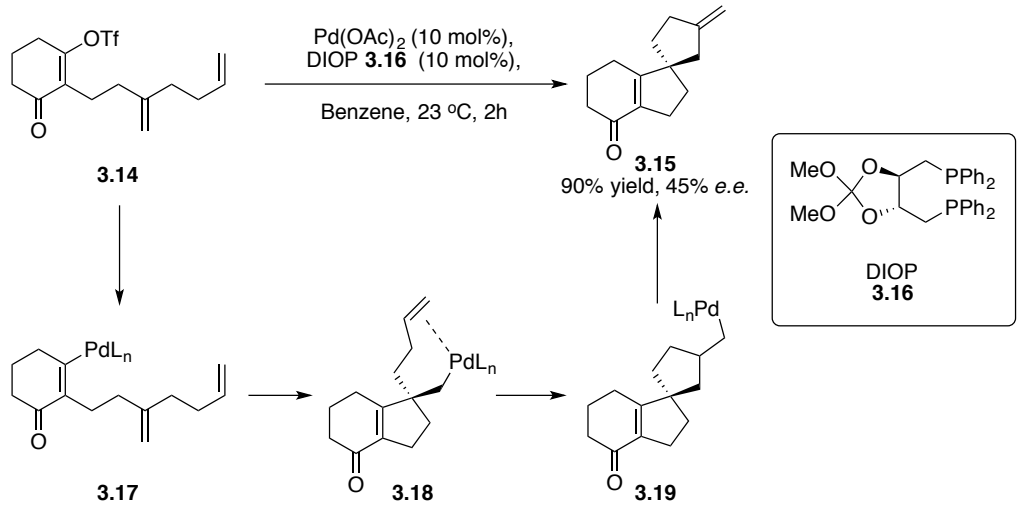
Heck reaction is not a suitable candidate for asymmetric catalysis at first glance. The well accepted mechanism for the Heck reaction includes three key steps: oxidative addition, *cis*-carbopalladation, and β-hydride elimination. Despite a chiral sp^3 carbon center often being generated in the *cis*-carbopalladation step, this stereocenter usually is converted back to a non-stereogenic sp^2 center in the subsequent β-hydride elimination step. Thus, the inherent challenges of an asymmetric Heck reaction are not only achieving high enantioinduction in the carbopalladation step, but also preventing the newly formed stereocenter from being destroyed by the β-hydride elimination step.[9]

In 1989, the first examples of asymmetric intramolecular Heck reactions were reported by Overman and Shibasaki, independently. To address the challenge that the sp^3 stereocenter must survive the β-hydride elimination for an enantioselective processes to result, two distinct strategies were applied by Overman and Shibasaki.

As shown in Scheme 3.8, Overman and co-workers reported the first enantioselective Heck reaction, whereby the alkenyl triflate substrate **3.14** underwent a polyene cyclization in the presence of palladium (II) acetate and (-)-DIOP **3.16**.[10] In this case, the key feature that prevented the sp^3 stereocenter from being destroyed was the lack of a β-hydrogen for β-hydride elimination in the intermediate **3.18**. Instead of β-hydride elimination, the alkylpalladium complex underwent another *cis*-carbopalladation to furnish the alkylpalladium intermediate **3.19**; subsequent β-hydride elimination led to the cyclized product **3.15** with excellent yield but moderate enantioselectivity.

[9] Mc Cartney, D., Guiry, P. J. *Chem. Soc. Rev.* **2011**, 40, 5122-5150.
[10] Carpenter, N. E., Kucera, D. J., Overman, L. E. *J. Org. Chem.* **1989**, 54, 5846-5848.

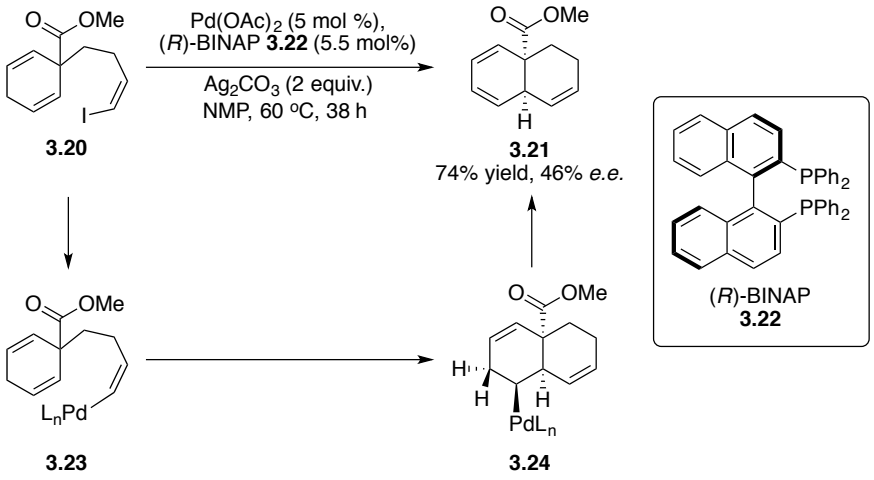
Scheme 3.8. Intramolecular Tandem enantioselective Heck reactions



On the other hand, Shibasaki tackled the challenge by taking the advantage of conformational constraints offered by cyclic substrates. It is known that a *cis*-relationship of the hydrogen and the palladium complex is required for β-hydride elimination event. However, the nature of *cis*-carbopalladation always leads to a *tran*-relationship of the palladium complex and the hydrogen at the newly formed sp^3 stereocenter. When carbon-carbon bond rotation is restricted by the cyclic substrate, the β-hydride elimination can only proceed in the opposite direction from the newly formed stereocenter. In this light, Shibasaki and co-workers demonstrated that cyclic alkenyl iodide **3.20** could undergo a palladium catalyzed enantioselective intramolecular Heck reaction in presence of (*R*)-BINAP **3.22** as ligand to afford the (*Z*)-decalin derivative **3.21** with good efficiency and moderate selectivity (Scheme 3.9).[11]

[11] Sato, Y., Sodeoka, M., Shibasaki, M., *J. Org. Chem.*, **1989**, 54, 4738–4739.

Scheme 3.9. Asymmetric intramolecular Heck reaction of cyclic substrates.

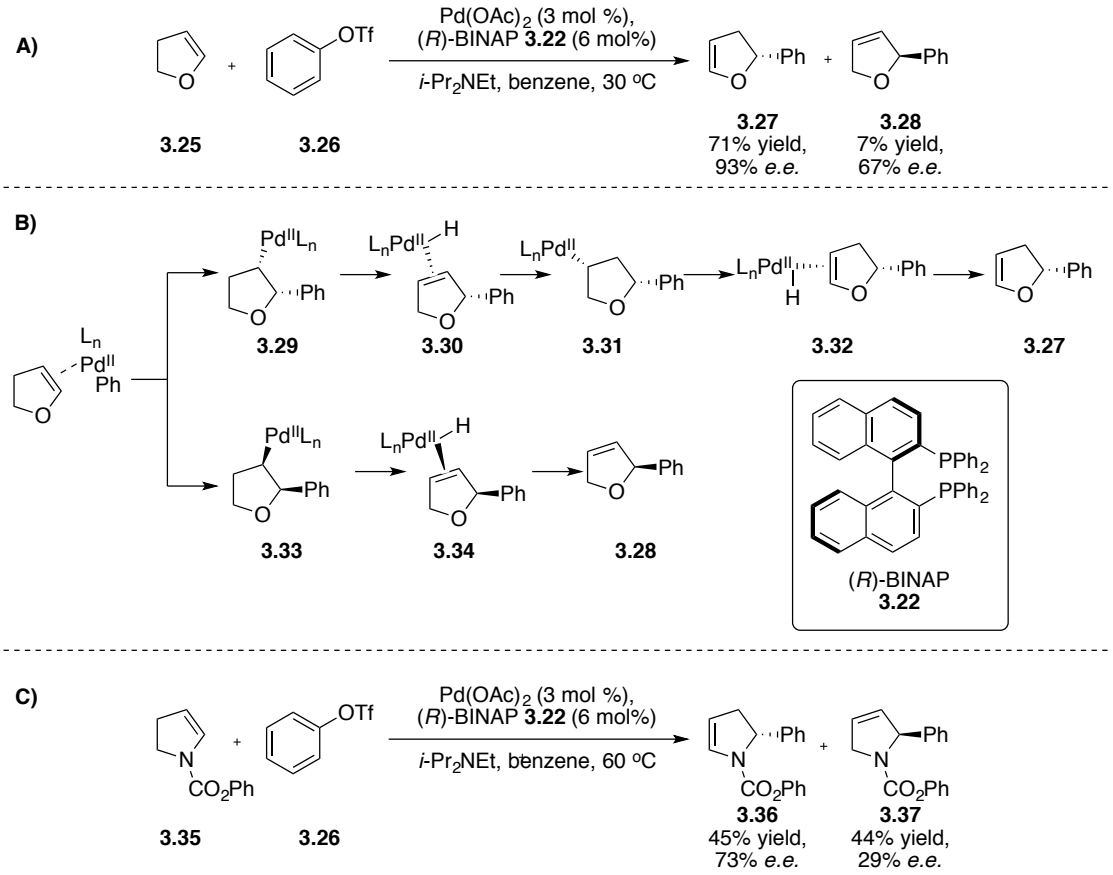


In 1991, the first enantioselective intermolecular Heck reaction was reported by Hayashi and co-workers.[12] Similar to Shibasaki's work, Hayashi showed that asymmetric arylation of 2,3-dihydrofuran **3.25** proceeded with an aryl triflate under palladium and (*R*)-BINAP (**3.22**) catalyzed conditions to furnish the product **3.27** with high enantioselectivity (Scheme 3.10.A). Of note, a minor regioisomer of the product **3.28** with the opposite configuration at the stereocenter was also isolated. It was proposed that the structure of intermediate **3.30** favored the further hydride reinsertion-β-hydride elimination sequence to furnish the major product **3.27**. However, when the arylpalladium complex inserted into the alkene from the other face to generate intermediate **3.33**, the subsequent β-hydride elimination led to the complex **3.34** that prefered to release the minor product **3.28** without the isomerization event (Scheme

[12] Ozawa, F., Kubo, A., Hayashi, T., *J. Am. Chem. Soc.* **1991**, 113, 1417–1419.

3.10.B). Moreover, the intermolecular asymmetric Heck reaction was further expanded to 2,3-dihydropyrrole derivatives with a similar catalytic system (Scheme 3.10.C).[13]

Scheme 3.10. Intermolecular asymmetric Heck reaction



Since the pioneering work of Overman, Shibasaki, and Hayashi, a variety of new ligands have been developed to achieve more efficient and selective asymmetric Heck reactions. It was demonstrated that not only bisphosphine ligands such as BINAP, but also [*P, N*] and [*N, N*] ligands are effective in catalyzing enantioselective Heck reactions[9]. Furthermore, Mikami, Jung, and Gelman[14] developed a range of enantioselective

[13] Ozawa, F., Hayashi, T., *J. Organomet. Chem.* **1992**, 428, 267–277.

[14] (a) K. Akiyama, K. Wakabayashi and K. Mikami, *Adv. Synth. Catal.* **2005**, 347, 1569–1575. (b) H. A. Dieck and R. F. Heck, *J. Org. Chem.* **1975**, 40, 1083–1090. (c) L. Penn, A. Shpruhman and D. Gelman, *J.*

oxidative Heck reactions that utilized organoboronic acids with palladium catalysts in the presence of stoichiometric oxidants. However, while asymmetric Heck reactions have been significantly developed during the past several decades, applying the enantioselective Heck reaction to acyclic, unactivated alkene substrates remained as a daunting challenge for synthetic chemists.[15]

The inherent challenges of engaging acyclic, unactivated alkenes in the asymmetric Heck reaction lie not only in protecting the newly formed stereocenter from β-hydride elimination, but also the absence of adjacent functionalities that polarize the olefin for enhanced regioselectivity. In 2012, Sigman and co-workers described an enantioselective Heck reaction of acyclic alkenyl alcohols using a redox-relay strategy.[16] As shown in Scheme 3.11.A, the homoallylic alcohol **3.38** underwent a palladium-catalyzed enantioselective arylation in the presence of PyrOx **3.40** as the ligand to furnish the carbonyl product **3.41** with good yield and selectivity. Notably, in addition to allylic and homoallylic alcohols as suitable substrates in this reaction, bis-homoallylic alcohols efficiently engaged in the asymmetric arylation reaction to afford the desired products with excellent enantioselectivity. The proposed mechanism was supported by the results of deuterium labeling experiments and computational studies.[17] To initiate the catalytic cycle, *cis*-carbopalladation of the arylpalladium complex to alkenyl substrate afforded the

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Org. Chem. **2007**, 72, 3875-3879. (d) K. S. Yoo, C. P. Park, C. H. Yoon, S. Sakaguchi, J. O'Neil and K. W. Jung, *Org. Lett.* **2007**, 9, 3933-3935. (e) S. Sakaguchi, K. S. Yoo, J. O'Neil, J. H. Lee, T. Stewart and K. W. Jung, *Angew. Chem., Int. Ed.* **2008**, 47, 9326-9329.

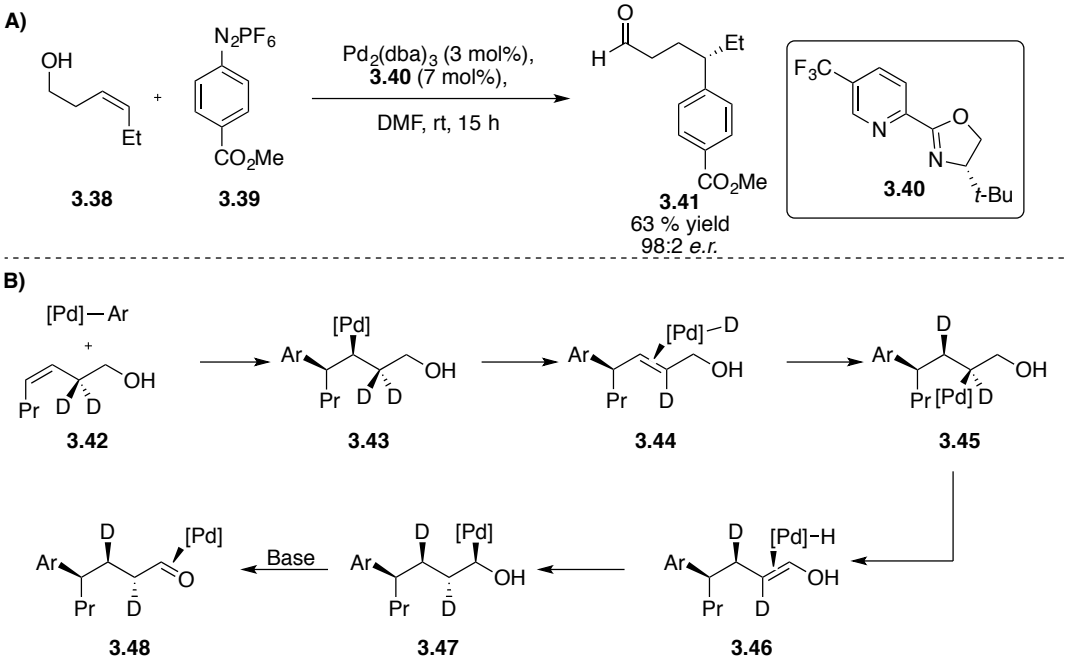
[15] Yonehara, K., Mori, K., Hashizume, T., Chung, K. G., Ohe, K., Uemura, S., *J. Organomet. Chem.* **2000**, 603, 40-49.

[16] Werner, E. W., Mei, T. S., Burckle, A. J., Sigman, M. S. *Science* **2012**, 338, 1455-1458.

[17] (a) Xu, L., Hilton, M. J., Zhang, X., Norrby, P. O., Wu, Y. D., Sigman, M. S., Wiest, O. *J. Am. Chem. Soc.* **2014**, 136(5), 1960-1967. (b) Hilton, M. J., Xu, L. P., Norrby, P. O., Wu, Y. D., Wiest, O., Sigman, M. S. *J. Org. Chem.* **2014**, 79(24), 11841-11850.

alkylpalladium intermediate **3.43**. Successive β-hydride elimination and migratory insertion sequences led to the hydroxyalkyl-palladium intermediate **3.47**. Oxidative deprotonation furnished the carbonyl product and regenerated the palladium (0) species that reengaged in the catalytic cycle (Scheme 3.11.B). The outstanding regioselectivity was rationalized by a remote electronic effect by which the migratory insertion transition state, with developing polarization of the alkene, was stabilized by the carbon-oxygen dipole of the alcohol functionality. Furthermore, computational studies showed that the hydroxyalkyl-palladium species **3.47** served as a thermodynamic sink to drive the reaction toward the carbonyl product.

Scheme 3.11. Enantioselective redox-relay Heck reaction.



Recently, the scope of the enantioselective redox-relay Heck reaction was further expanded by the Sigman laboratory. An oxidative asymmetric Heck reaction was developed utilizing copper (II) triflate as a co-catalyst and oxygen as an oxidant. Aryl

boronic acids were engaged in the redox-relay arylation with alkenyl alcohols to afford carbonyl product with high yield and enantioselectivity.[18] It is worthy of note that remote quaternary stereocenters could also be constructed with high enantio- and regioselectivity when trisubstituted alkenyl alcohols were employed as substrates[19]. Moreover, it was demonstrated that alkenyl triflates were suitable electrophiles to assemble allylic stereocenters by asymmetric redox-relay Heck reaction.[20]

As discussed above, alkylpalladium species generated by *cis*-carbopalladation usually undergo β-hydride elimination to afford alkenes as products in the Heck reaction. Alternatively, protonolysis of the alkypalladium complex leads to net alkene hydroarylation. Such a process has been successfully applied in the development of asymmetric conjugate addition reactions. In 2004, Miyaura and co-workers reported the first example of a palladium-catalyzed enantioselective conjugate addition reaction.[21] It was demonstrated that triarylbismuth reagents reacted with cyclic enones to afford β-arylation product with good efficiency and selectivity. Later on, the scope of palladium-catalyzed enantioselective conjugate addition was further expanded to organoboronic acid nucleophiles. Minnard and co-workers [22] showed that a palladium (II) trifluoroacetate/Me-DuPhos catalyst system was able to catalyze the asymmetric conjugate addition of a variety of aryl boronic acid to α, β-unsaturated ketones with good yield and selectivity (Scheme 3.12.A).

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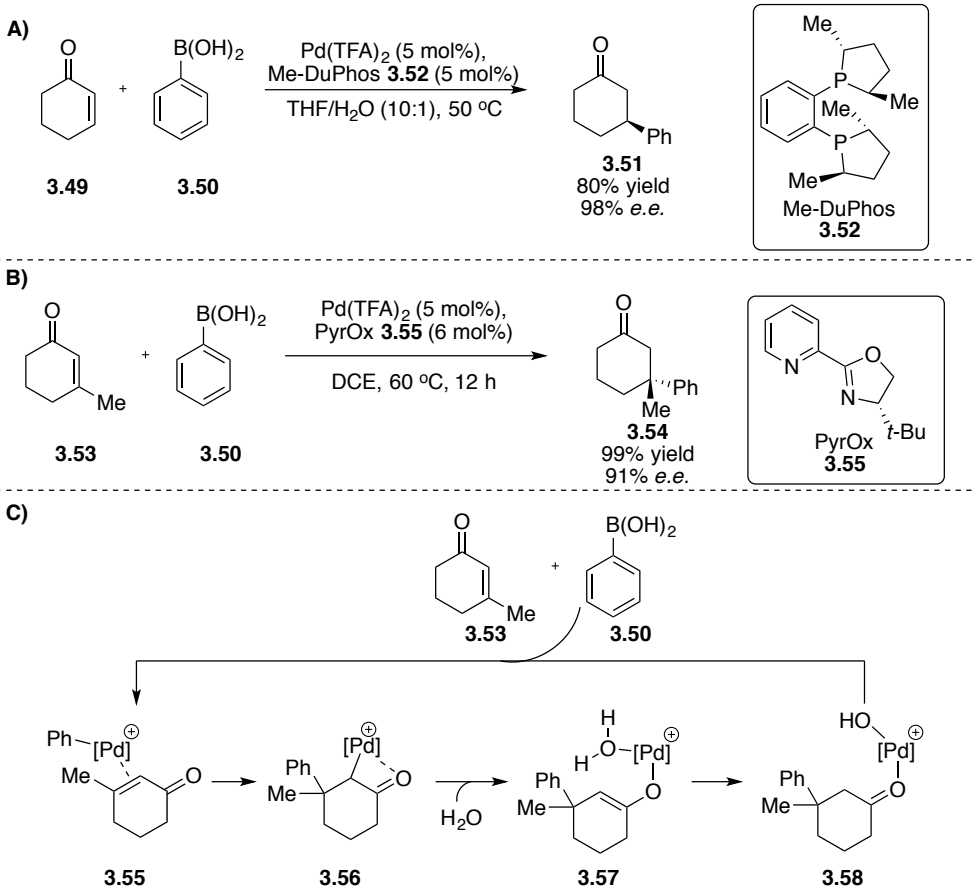
[18] Mei, T. S., Werner, E. W., Burckle, A. J., Sigman, M. S. *J. Am. Chem. Soc.* **2013**, 135, 6830-6833.
[19] Mei, T. S., Patel, H. H., Sigman, M. S. *Nature* **2014**, 508, 340-344.
[20] (a) Patel, H. H., Sigman, M. S. *J. Am. Chem. Soc.* **2015**, *137*(10), 3462-3465. (b) Patel, H. H., Sigman, M. S. *J. Am. Chem. Soc.* **2016**, *138*(43), 14226-14229.
[21] Nishikata, T., Yamamoto, Y., & Miyaura, N. *Chem. Commun.* **2004**, 16, 1822-1823.
[22] Gini, F., Hessen, B., Minnaard, A. J. *Org. Lett.* **2005**, 7, 5309-5312.

Scheme 3.12. Palladium catalyzed asymmetric conjugate addition reactions.



More recently, Stoltz and co-workers established a strategy to enantioselectively construct all-carbon quaternary centers utilizing palladium-catalyzed conjugate addition of aryl boronic acids to β-substituted cyclic enones[23]. As shown in Scheme 3.12.B, the product **3.54** was delivered with excellent yield and enantioselectivity in the presence of a palladium (II) trifluoroacetate catalyst and PyrOx **3.55** as the ligand. Computational studies suggested that, as expected, the asymmetric conjugate addition proceeded through a *cis*-carbopalladation pathway instead of a direct nucleophilic attack by the aryl boronic

[23] Kikushima, K., Holder, J. C., Gatti, M., Stoltz, B. M. *J. Am. Chem. Soc.* **2011**, 133, 6902-6905.

acid with palladium acting as Lewis acid.[24] A *cis*-carbopalladation of complex **3.55** led to the alkyl palladium intermediate **3.56**. Then, coordination of one water molecule delivered the aquo-palladium enolate complex **3.57**. Subsequent protonolysis of intermediate **3.57** yielded the product complex **3.58**. Finally, the product **3.54** was released from the complex **3.58** in the presence of phenyl boronic acid and enone substrate to restart the catalytic cycle.

3.2.2. Enantioselective synthesis of tertiary boronic esters

Tertiary boronic esters are important synthetic building blocks that can be readily transformed into a variety of fully substituted carbon stereocenters. Aggarwal and co-workers[25] showed that enantioenriched tertiary boronic esters could be prepared by a stereospecific 1,2-metallate rearrangement from secondary lithiated carbamate derivatives (Scheme 3.13.A). Enantioenriched carbamate **3.59** was deprotonated with *s*-BuLi at low temperature to generate the lithiated carbamate, which was treated with ethyl B(pin) to afford the boron ate complex **3.60**. Subsequent stereospecific 1,2-metallate shift delivered the tertiary boronic ester product **3.61** with high yield and stereospecificity. To demonstrate the synthetic utility of tertiary boronates, a broad range of transformations were applied to the tertiary boronic ester products. As shown in Scheme 3.13.B, tertiary boronate **3.63** was converted to the corresponding alcohol **3.64**, amine **3.66**, and tertiary alkane **3.67** in an efficient and stereospecific fashion. Furthermore, a variety of all-carbon quaternary centers could be constructed utilizing the homologation protocols from the tertiary boronic esters precursors.

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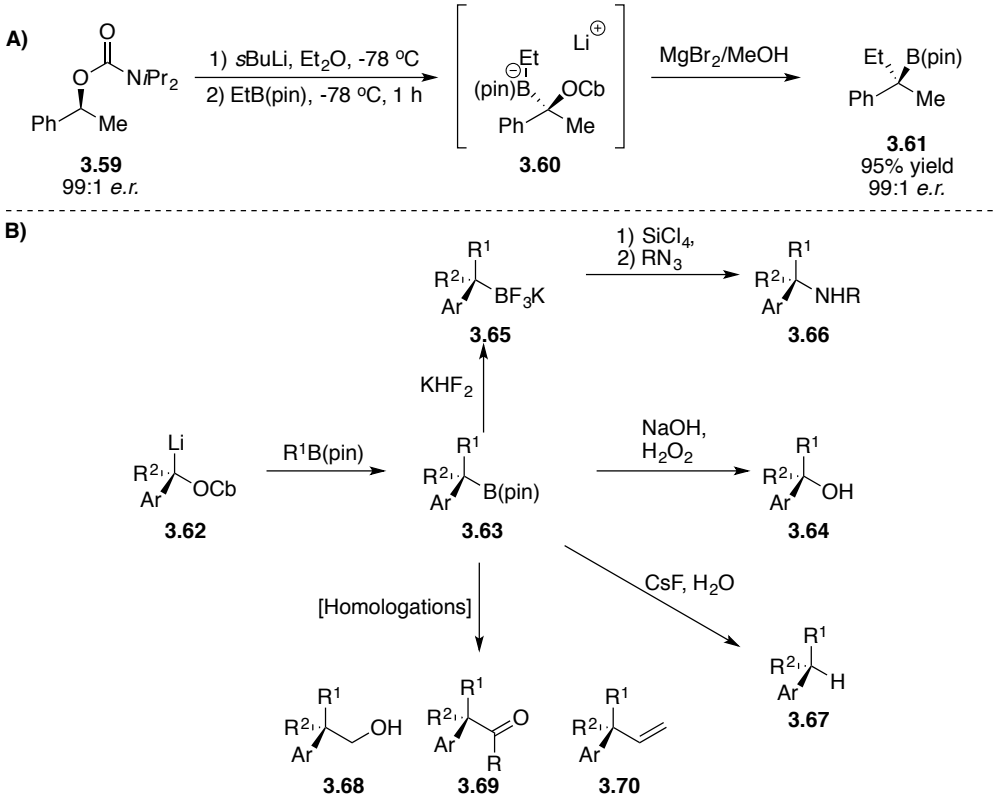
[24] Holder, J. C., Zou, L., Marziale, A. N., Liu, P., Lan, Y., Gatti, M., Stoltz, B. M. *J. Am. Chem. Soc.* **2013**, 135, 14996-15007.
[25] Scott, H. K., Aggarwal, V. K. *Chem.-Eur. J.* **2011**, 17, 13124-13132.

Scheme 3.13. Stereospecific synthesis of tertiary boronic esters.

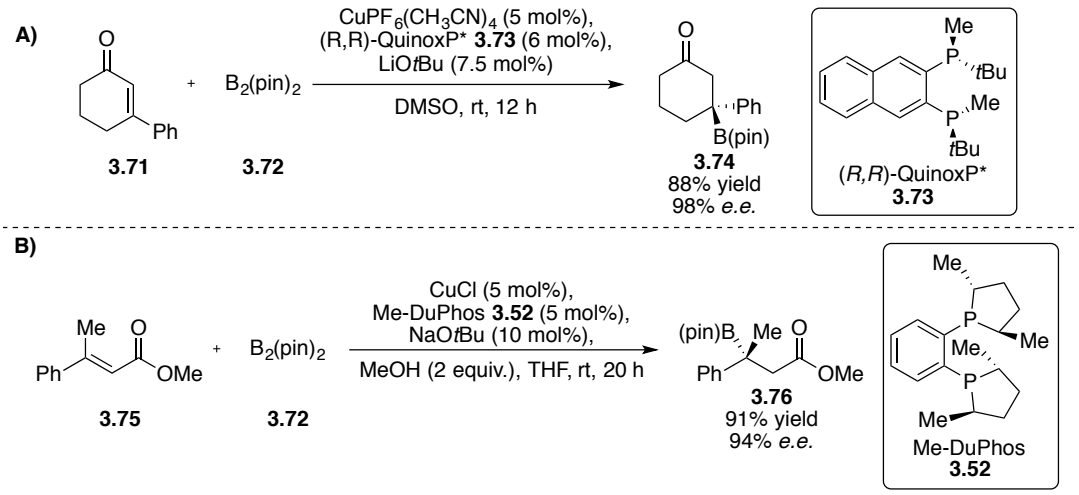


Although Aggarwal's method provides an efficient route to access enantioenriched tertiary boronic esters in a stereospecific fashion, a catalytic enantioselective construction of tertiary boronates would be more desirable. In this light, Shibasaki and co-workers developed a copper-catalyzed asymmetric synthesis of tertiary boronic esters.[26] Utilizing $B_2(pin)_2$ **3.72** as a borylation reagent, Shibasaki showed that β-substituted cyclic enone **3.71** underwent a conjugate borylation reaction to afford tertiary boronic ester product **3.74** with good yield and enantioselectivity in the presence of copper/ QuinoxP* (**3.73**) as the catalyst (Scheme 3.14.A). Similarly, an asymmetric conjugate borylation of acyclic

[26] Chen, I. H., Yin, L., Itano, W., Kanai, M., Shibasaki, M. *J. Am. Chem. Soc.* **2009**, 131, 11664-11665.

enones was reported by Yun and co-workers.[27] Employing copper/Me-Duphos (**3.52**) as the catalyst, the conjugate borylation of enone **3.75** led to the acyclic tertiary boronic ester **3.76** with excellent level of efficiency and selectivity (Scheme 3.14.B).

Scheme 3.14. Synthesis tertiary boronic esters by conjugate borylation.

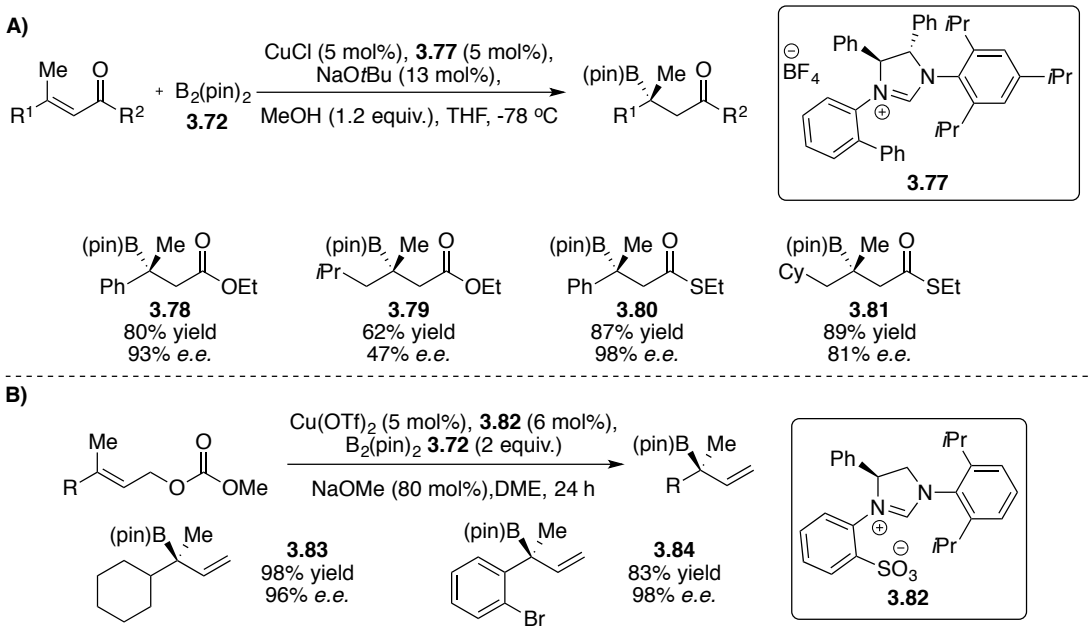


In addition to the copper/bisphosphine catalyst system reported by Shibasaki and Yun, Hoveyda and co-workers developed an *N*-heterocyclic carbene-copper complex that was able to facilitate the asymmetric construction of tertiary boronic esters. Employing copper (I) chloride and imidazolinium salt **3.77**, tertiary boronic esters **3.78** to **3.81** were successfully constructed by boronate conjugate addition in an enantioseletive fashion.[28] It is worthy of note that not only α, β-unsaturated carboxylic esters, but also α, β-unsaturated thioesters and ketones were suitable substrates for this reaction. Furthermore, Hoveyda and co-workers also demonstrated that enantioselective borylation of allylic carbonates were also achieved in the presence of copper (II) triflate and

[27] Feng, X., Yun, J. *Chem.-Eur. J.* **2010**, 16(46), 13609-13612.
[28] O'Brien, J. M., Lee, K. S., Hoveyda, A. H., *J. Am. Chem. Soc.* **2010**, 132, 10630-10633.

imidazolinium salt **3.82** with high efficiency.[29] Alkyl- or aryl substituted allyl boronates, **3.83** and **3.84**, were delivered with excellent yield and enantioselectivity (Scheme 3.15.B).

Scheme 3.15. Asymmetric synthesis of tertiary boronic esters with copper-NHC complex.



3.3. Development of the synthesis of tertiary boronic esters by conjunctive cross-coupling

For the development of the asymmetric synthesis of tertiary boronic esters utilizing conjunctive cross-coupling, several potential challenges had to be addressed. Even through it was proposed that the pre-paid steric penalty for the formation of the boron ate complex might avoid introducing new unfavorable steric interactions during the 1,2-metallate rearrangement step, it was unclear whether such sterically hindered

[29] Guzman-Martinez, A., Hoveyda, A. H., *J. Am. Chem. Soc.* **2010**, 132, 10634-10637.

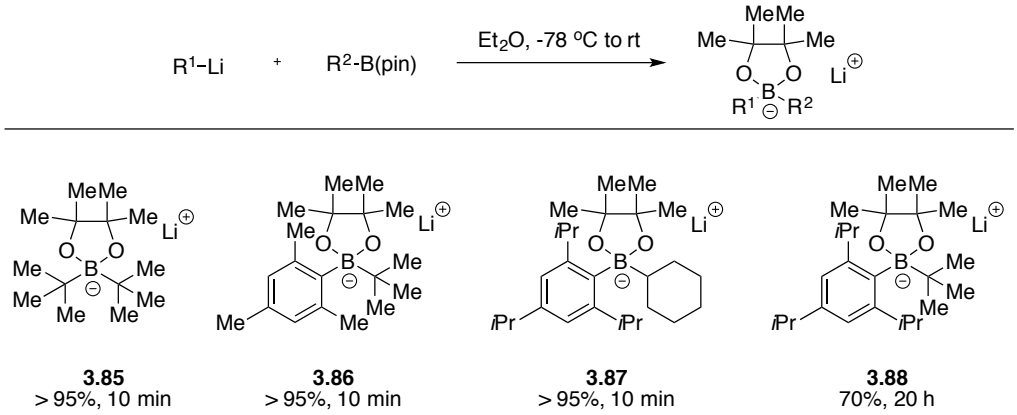
organolithium and organoboronic esters could efficiently form an ate complex. Furthermore, the palladium catalyst must still be able to bind to the sterically hindered alkenyl boron ate complex to induce the 1,2-metallate shift. In terms of enantioselectivity, the chiral palladium ligand complex would have to effectively differentiate the pro-chiral faces of the alkene while the structural bias might be decreased with the additional substitution on the α-position of the alkene.

Althrough Aggarwal and co-workers have shown that hindered boron ate complex could be formed between a tertiary boron species and a tertiary organolithium reagent, the boronic esters were converted to dimethylboranes before the treatment of organolithium reagents.[30] Thus, the effeciency of the formation of boronic esters derived boron ate complex remains unclear. To examine the efficiency of sterically encumbered boron ate complex formation, *tert*-butyl B(pin), a sterically hindered boronic ester, was treated with *tert*-butyl lithium, a sterically encumbered nucleophile, at -78 °C and then allowed to warm to room temperature. ^{11}B NMR analysis suggested that greater than 95% of three coordinated *tert*-butyl B(pin) was converted to four coordinated boron ate complex **3.85** within 10 min. Utilizing a similar protocol, it was determined that both boron ate complex **3.86**, derived from mesityllithium and *tert*-butylB(pin), and complex **3.87**, generated by treating cyclohexylB(pin) with 2,4,6-triisopropylphenyllithium, could also be formed efficiently (>95% conversion). However, it was discovered that reaction between 2,4,6-triisopropylphenyllithium and *tert*-butylB(pin) proceeded sluggishly, and the formation of boron ate complex **3.88** required 20 hours to reach equilibrium, in which

[30] Watson, C. G., Balanta, A., Elford, T. G., Essafi, S., Harvey, J. N., Aggarwal, V. K. *J. Am. Chem. Soc.* **2014**, 136, 17370-17373.

only 70% conversion was obtained. These experimental results suggested that sterically hindered boron ate complexes could be efficiently constructed due to the high electrophilicity of boronic esters combined with the high nucleophilicity of organolithium reagents.

Scheme 3.16. Construction of hindered boron ate complex.

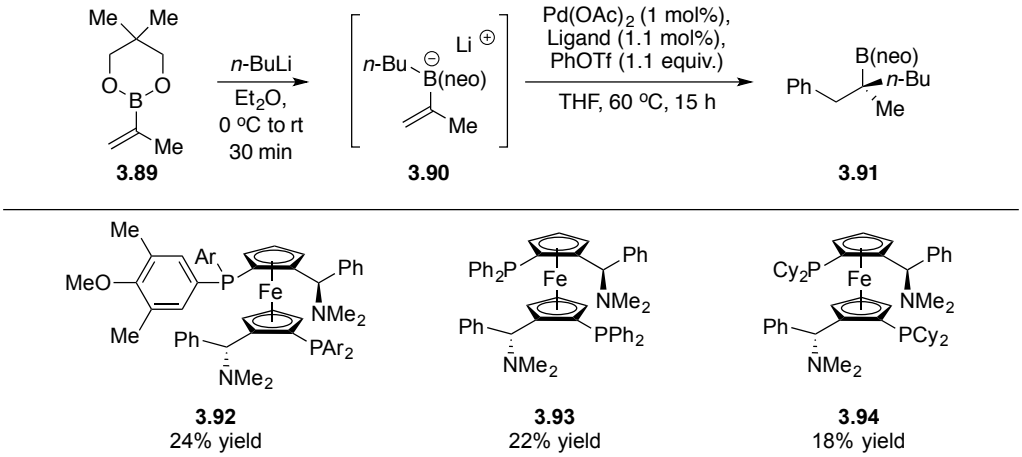


As discussed above, sterically severely hindered boron ate complexes can be constructed efficiently. With this in mind, our focus turned to investigating whether the sterically hindered boron ate complexes are able to participate in the conjunctive cross-coupling. Since the *neo*-pentylglycolato group was determined to be the optimal ligand on boron for conjunctive cross-coupling in previous study[31], *neo*-pentylglycolato derived isopropenyl boronic ester **3.89** was prepared for the investigation of tertiary boronate construction by conjunctive cross-coupling. The boron ate complex **3.90** generated from isopropenyl B(neo) **3.89** and *n*-butyllithium was subjected to the standard conditions for conjunctive cross-coupling of unsubstituted alkenyl boronic esters, and the tertiary boronic ester product **3.91** was afford in only 24% yield in the presence of Mandyphos

[31] Zhang, L., Lovinger, G. J., Edelstein, E. K., Szymaniak, A. A., Chierchia, M. P., Morken, J. P. *Science*, **2016**, 351, 70-74.

ligand **3.92**. The major byproduct was determined to be the direct Suzuki-Miyaura coupling product. As it was suspected that the poor chemoselectivity might due to the increased steric effect of the substituted alkenyl boron ate complex, less sterically demanding Mandyphos derivatives **3.93** and **3.94** were examined. However, it was found that these ligands failed to improve the reaction efficiency significantly.

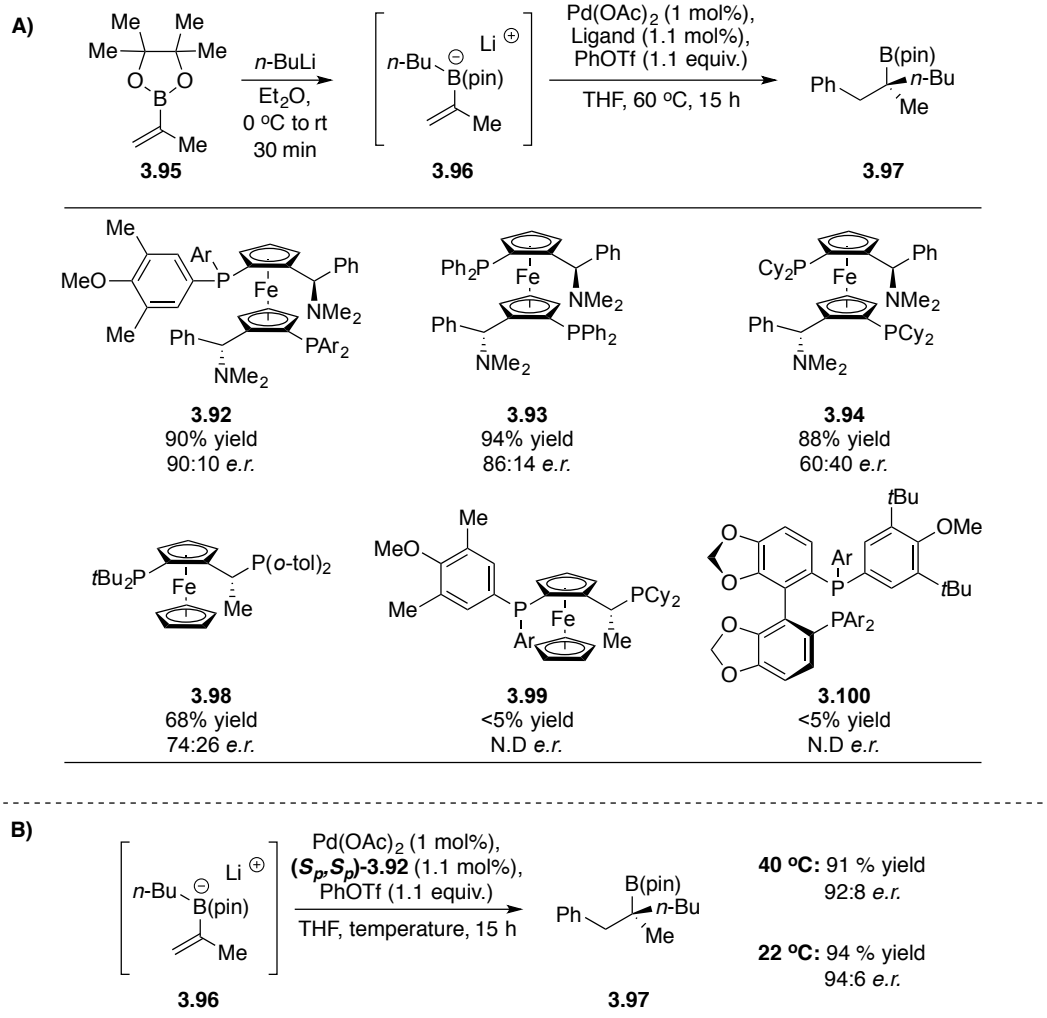
Scheme 3.17. Conjunctive cross-coupling towards tertiary B(neo) products



Since the isopropenyl B(neo)-derived ate complex suffered from low efficiency in conjunctive cross-coupling, our focus moved to the more commonly used pinacol derived alkenyl boron ate complex. The boron ate complex **3.96** generated from isopropenyl B(pin) and *n*-butyllithium was subjected to the conjunctive cross-coupling conditions with 1 mol% palladium (II) acetate, 1.1 mol% Mandyphos **3.92** as the ligand, and phenyl triflate as electrophile. To our delight, the desired coupling product, tertiary boronic ester **3.97**, was isolated with excellent yield and good enantioselectivity (90% yield, 90:10 *e.r*). To further improve the stereoselectivity, other chiral bisphosphine ligands were examined in the reaction. However, neither the less steric demanding Mandyphos derivatives, **3.92**

and **3.94**, nor other commonly used chiral bisphosphine ligand class, such as Josiphos **3.98** and **3.99** and Segphos **3.100** were able to provide improved results (Scheme 3.18.A).

Scheme 3.18. Brief optimization of ligand and reaction temperature



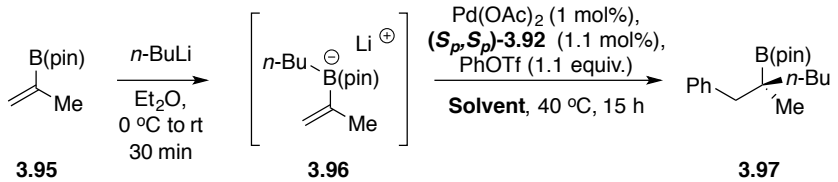
On the other hand, a brief screen of reaction temperature showed that the enantioselectivity was slightly sensitive to the temperature (92:8 *e.r.* at 40 °C, 94:6 *e.r.* at 22 °C), while the reaction efficiency remained excellent (Scheme 3.18.B). Although the reactions performed at room temperature provided higher stereoselection, the reaction could become sluggish when more challenging substrates other than simple *n*-

butyllithium and phenyl triflate were employed. Thus, the standard ligand was decided to be Mandyphos **3.92**, and the reactions would generally be performed at 40 °C.

With the standard ligands for both boron substrate and palladium catalyst in hand, our further optimization was focused on the investigation of solvent effects. As summarized in Table 1, a broad array of common organic solvents was examined. While the reaction conducted in dioxane led to desired product with similar level of yield and selectivity compared to the reaction conducted in THF (Table 1, entry 1,2), less polar ether solvents led to lower reaction efficiency (Table 1, entry 3-5). Nonpolar solvents, such as toluene, or polar but non-coordinating solvents inhibited the conjuctive coupling (Table 1, entry 6-8). Utilizing more polar and coordinated solvents afford the conjunctive coupling product in poor to moderate yield with good level of eneantioselectivity (Table 1, entry 9-12). Accordingly, the standard solvent for the synthesis of tertiary boronate was decided to be THF.

To investigate additive effects of the conjunctive cross-coupling, boron ate complex **3.96** was subjected to the standard conditions in the presence of a variety of triflate salts. While the reaction efficiency and selectivity was not significantly reduced with NaOTf, $Mg(OTf)_2$, and NBu_4OTf, the triflate salts of indium, zinc, and scandium fully inhibited the conjunctive coupling (Table 2).

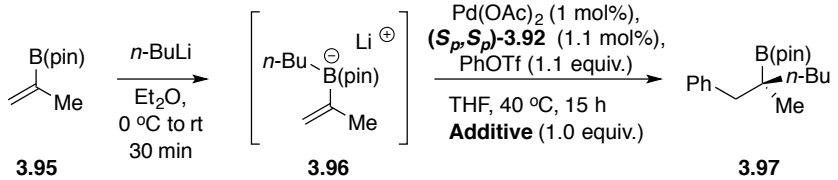
Table 1. Solvent optimization.



3.95 **3.96** **3.97**

Entry	Solvent	Yield	*e.r.*
1	THF	91 %	92:8
2	Dioxane	84 %	92:8
3	Et_2O	50 %	88:12
4	CpME	35 %	92:8
5	MTBE	24 %	88:12
6	DCM	17 %	91:9
7	Toluene	< 5 %	N.D
8	α,α,α-trifluorotoluene	< 5 %	N.D
9	MeCN	20 %	91:9
10	DMSO	45 %	90:10
11	DMF	70 %	92:8
12	DMA	61 %	91:9

Table 2. Additive effect of conjunctive cross-coupling



3.95 **3.96** **3.97**

Entry	Additive	Yield	*e.r.*
1	NaOTf	89 %	91:9
2	$Mg(OTf)_2$	90 %	92:8
3	NBu_4OTf	77 %	92:8
4	$Ca(OTf)_2$	40 %	90:10
5	$In(OTf)_3$	< 5 %	N.D
6	$Sc(OTf)_3$	< 5 %	N.D
7	$Zn(OTf)_3$	< 5 %	N.D

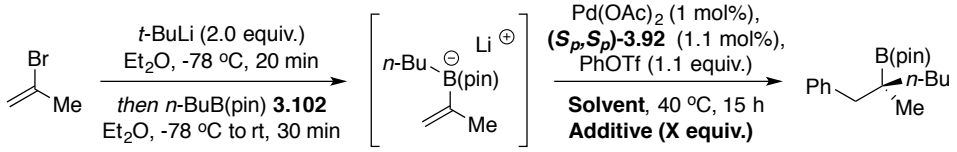
As discussed in Chapter 2, one of the advantages of conjunctive cross-coupling is that the active substrate of the coupling reaction, the boron ate complex, can be assembled by treating an alkenyl boronic ester with an organolithium reagent, or by the combination of an organoboronic ester with an alkenyllithium reagent. However, it is known that conjunctive coupling is significantly inhibited by halide impurities. As a result, the requirement for halogen-free alkenyllithium prevents the conjunctive cross-coupling when utilizing lithium-halogen exchange. While lithium-halogen exchange would be the most straightforward way to generate the alkenyllithium, a full equivalent of lithium halide salt is generated as an inhibitory byproduct. To address this problem, recent studies conducted in our laboratory suggested that potassium triflate could be employed as a halide scavenger in the conjunctive coupling so that the reaction could tolerate up to a full equivalent of halide salt impurity.[32] It was also demonstrated that utilizing a solvent mixture of THF and DMSO could facilitate the conjunctive coupling in the presence of halide inhibitors.

Taking advantage of the recent development in our laboratory, the conditions for conjunctive coupling employing the alkenyllithium generated *in situ* via lithium-halogen exchange were investigated. Isopropenyl bromide **3.101** was treated with *t*-butyllithium to generate isopropenyllithium at low temperature. Subsequent addition of *n*-butyl B(pin) to the isopropenyllithium led to the boron ate complex **3.96**, which was subjected to the conjunctive coupling conditions. While the conjunctive coupling was fully inhibited without any additive, one equivalent of potassium triflate was able to partially overcome the halide inhibition to afford the desired product **3.97** with 49 % yield and 92:8 *e.r.*

[32] Lovinger, G. J., Aparece, M. D., Morken, J. P. *J. Am. Chem. Soc.* **2017**, 139, 3153-3160.

Performing the reaction in THF/DMSO mixture solvent failed to improve the reaction efficiency. However, 70 % yield of product **3.97** was obtained when the reaction was conducted with two equivalents of potassium triflate, and the enantioselectivity remained intact.

Table 3. Additive and solvent optimization for conjunctive coupling with halide inhibitors.



3.101 **3.96** **3.97**

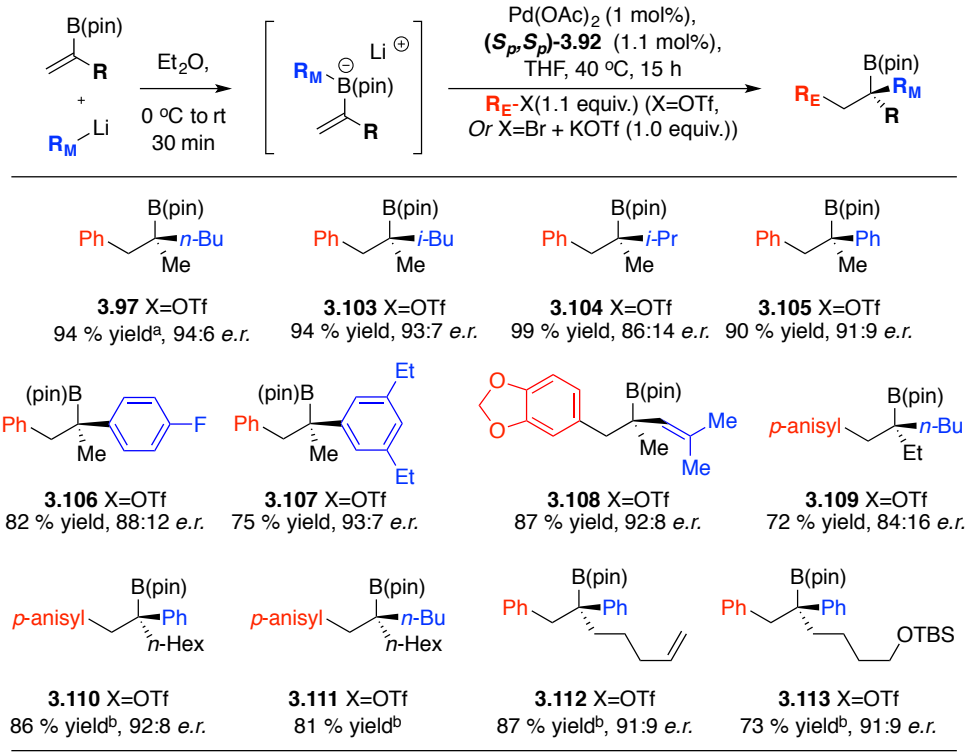
Entry	Additive (X equiv.)	Solvent	Yield	*e.r.*
1	None	THF	< 5 %	N.D
2	KOTf (1.0 equiv.)	THF	49 %	92:8
3	KOTf (1.0 equiv.)	THF/DMSO 1:1	28 %	91:9
4	None	THF/DMSO 1:1	27 %	90:10
5	KOTf (2.0 equiv.)	THF	70 %	92:8

In summary, the standard conditions for the conjunctive cross-coupling with α-substituted alkenyl boron ate complex was determined to be as follow: 1% palladium (II) acetate and 1.1% Mandyphos **3.92** in THF at 40 °C for 15 hours. Two equivalents of potassium triflate were required when the organolithium was generated by lithium-halogen exchange. It is worthy of note that aryl or alkenyl bromides could also be engaged in the reaction as suitable electrophile when 1.0 equivalent of potassium triflate was used as halide scavenger.

3.4. Scope of tertiary boronic esters synthesized by conjunctive cross-coupling

With the optimized conditions in hand, the substrate scope was thoroughly investigated. By employing the boron ate complex constructed from alkenyl B(pin) and organolithium reagents, the scope of the migrating group and the substitution of the alkenyl B(pin) were examined first. As shown in Scheme 3.19, not only alkyl migrating groups, but also aryl groups were tolerated in the reaction. In addition to an *n*-butyl group, more sterically demanding *iso*-butyl and *iso*-propyl groups behaved well in the reaction, such that highly hindered tertiary boronate products **3.103** and **3.104** could be assembled with excellent yield and good enantioselectivity. Other than employing common commercially available organolithium reagents, organolithium generated by lithium-halogen exchange could also be engaged in the reaction in the presence of potassium triflate as halide scavenger. With this method, it was discovered that electron deficient as well as sterically demanding aryl migrating groups led to the corresponding tertiary boronic esters **3.106** and **3.107** with good levels of efficiency and selectivity. It is worthy of note that alkenyl migrating groups were also suitable in conjunctive cross-coupling so that synthetically useful allylic tertiary boronic esters could be easily constructed in an enantioselective and efficient fashion. Furthermore, in addition to isopropenyl B(pin), the tertiary boronic esters derived from more sterically hindered ethyl and hexyl substituted alkenyl B(pin) substrates were afforded in good yield and stereoselection. The alkenyl boronate substrates bearing functional groups, such as an alkene or silyl ether, were also well tolerated in the conjunctive coupling.

Scheme 3.19. Scope of migrating groups and alkenyl B(pin).

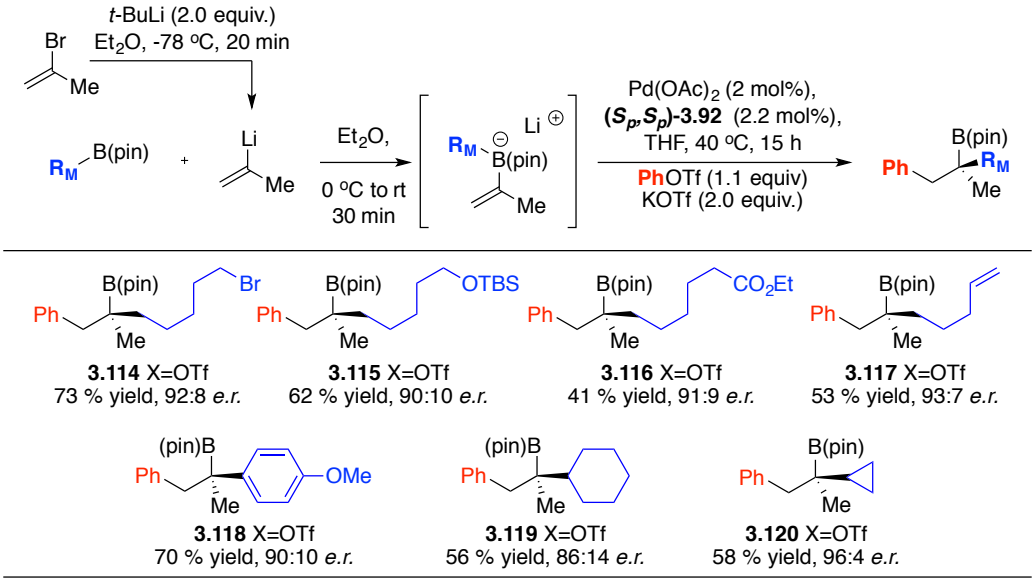


[a] reaction performed at room temperature. [b] reaction performed at 60 °C.

As discussed previously, the boron ate complex that participated in the conjunctive coupling could also be assembled by treating organic boronic esters with alkenyllithium reagents generated by lithium-halogen exchange in the presence of two equivalent of potassium triflate as halide scavenger. With such a strategy, additional migrating groups bearing a variety of functionalities were investigated. To our delight, a broad range of labile functional groups, such as an alkyl halide, a silyl protected alcohol, a ester, and an alkene, not only survived from the ate complex formation step intact, but also engaged in the conjunctive coupling process and led to corresponding tertiary boronate products with high efficiency and selectivity (Scheme 3.20). Moreover, electron-rich arene as well as

synthetically useful cyclopropyl groups were both well-behaved migrating groups for the conjunctive coupling process.

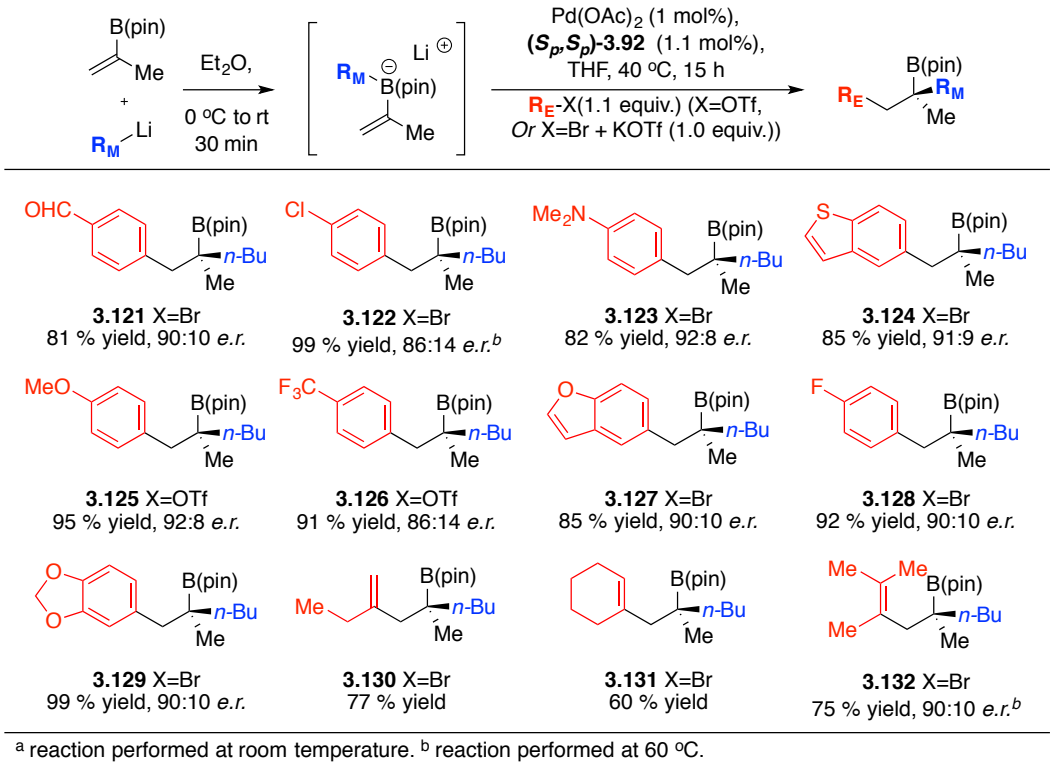
Scheme 3.20. Additional scope of migrating groups.



As shown in Scheme 3.21, the scope of electrophiles was also thoroughly investigated. Electrophiles bearing sensitive functionalities, such as an aldehyde, an aryl halide and a tertiary amine, were well engaged in conjunctive coupling to furnish the corresponding tertiary boronic esters in good yield and enantioselectivity. The tertiary boronates products derived from both electron-rich and electron-deficient electrophiles could be constructed by conjunctive coupling with good efficiency and selectivity. It is worthy of note that heterocyclic electrophiles were suitable substrates for conjunctive coupling to incorporate bioactive heterocyclic motifs into tertiary boronate products. Furthermore, utilizing alkenyl electrophiles, synthetically useful homoallylic tertiary boronic esters could be constructed by conjunctive coupling in an efficient and stereoselective fashion. Importantly, both organotriflates and organobromides could be

engaged in conjunctive coupling as long as potassium triflate was employed as a halide scavenger for organohalide electrophiles.

Scheme 3.21. Electrophile scope of conjunctive cross-coupling.

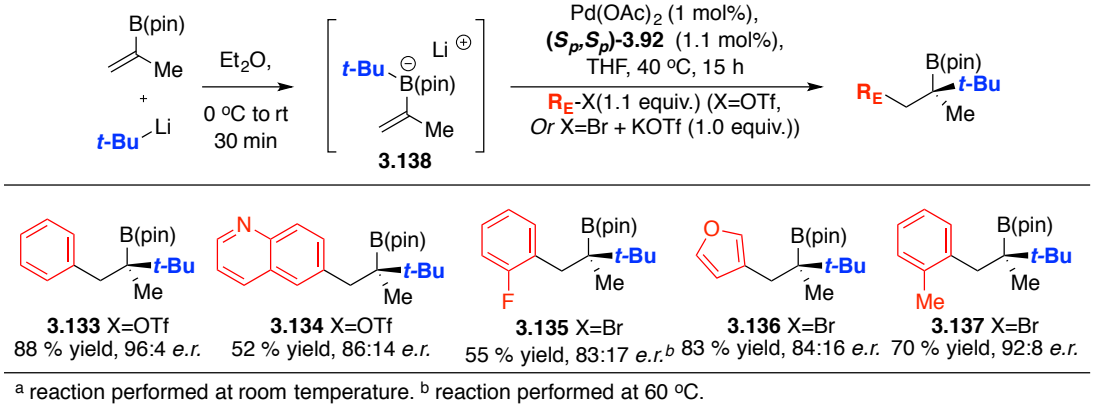


[a] reaction performed at room temperature. [b] reaction performed at 60 °C.

With the knowledge that severely hindered boron ate complex could be formed efficiently, we were curious if a tertiary boronate bearing two contiguous fully substituted carbon centers could be constructed by our conjunctive cross-coupling. To our delight, when the boron ate complex **3.138** derived from *t*-butyllithium and isopropenyl B(pin) was subjected to the standard conjunctive coupling condition, the tertiary boronic ester **3.133**, which was assembled by connecting two fully substituted carbon centers together, was isolated with excellent yield and enantioselectivity. This strategy could be further applied to a broad range of electrophiles. Sterically demanding *o*-methyl substituted aryl

group as well as synthetically challenging heterocyclic substrates were tolerated in the conjunctive coupling to furnish the corresponding tertiary boronates with useful levels of efficiency and selectivity (Scheme 3.22). It is worthy of note that even through the tertiary boronates bearing contiguous fully substituted carbon centers can be furnished with good yield, subsequent oxidation is exceptionally challenging due to the extremely sterically demanding nature.

Scheme 3.22. Scope of conjunctive coupling with tart-butyl migrating group.



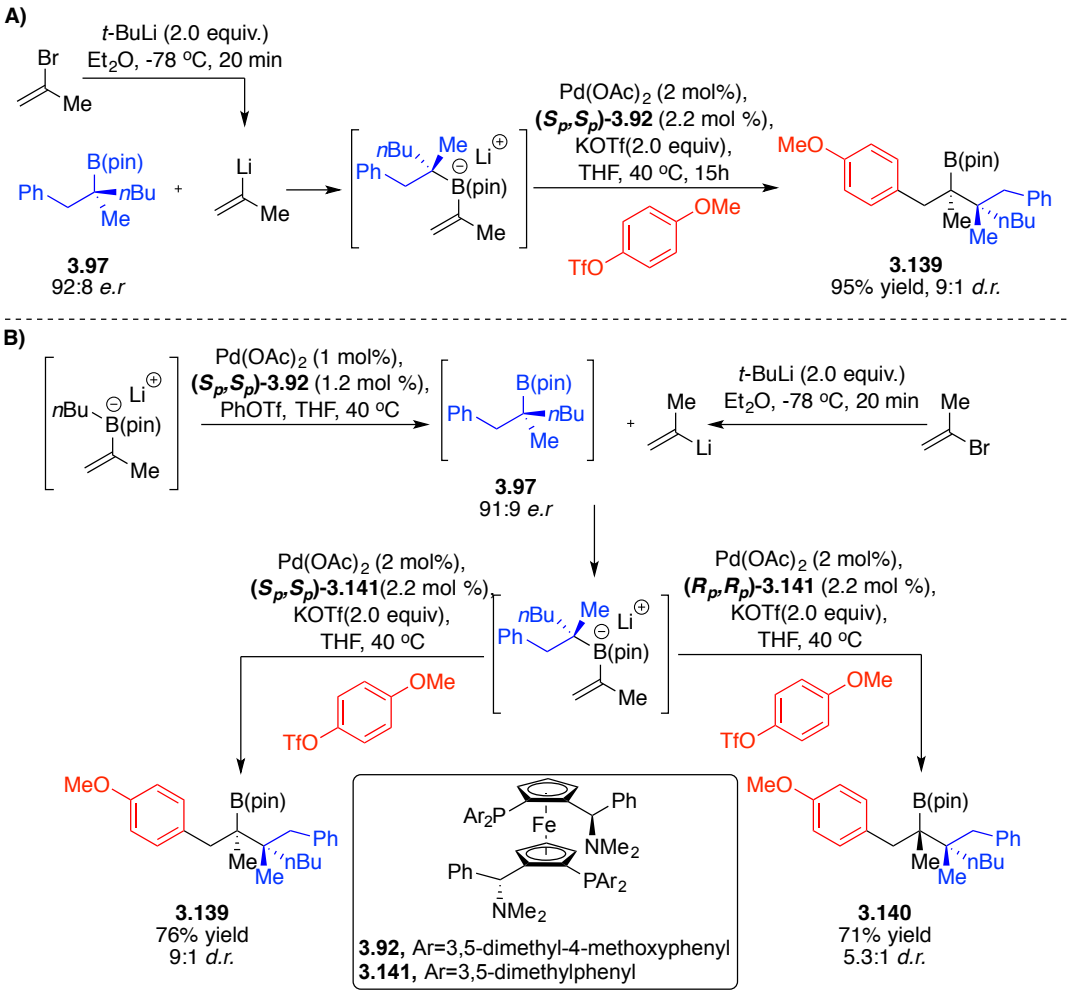
[a] reaction performed at room temperature. [b] reaction performed at 60 °C.

3.5. Synthetic utilities of tertiary boronic esters

As demonstrated above, fully substituted carbon centers, such as a *tert*-butyl group, were suitable migrating group in conjunctive cross-coupling. In this light, we demonstrated that the tertiary boronic ester furnished by conjunctive coupling could participate in a sequential conjunctive coupling to construct a new tertiary boronate product bearing two contiguous stereocenters in an enantio- and diastereo-selective fashion. As depicted in Scheme 3.23, the initial conjunctive coupling product **3.97** was treated with isopropenyllithium to afford a new boron ate complex, and such a boron ate complex could be further coupled to *p*-anisyltriflate under conjunctive coupling condition

to deliver the severely hindered tertiary boronate product **3.139** with excellent yield and high diastereoselectivity (Scheme 3.23.A).

Scheme 3.23. Construction of contiguous fully substituted stereocenters by sequential conjunctive cross-coupling.



More importantly, the sequential conjunctive cross-coupling could be performed in a single flask fashion. The crude material of tertiary boronate **3.97** from the initial conjunctive coupling could be engaged in the subsequent boron ate complex formation step without any further purification, other than simple filtration through a silica gel pad,

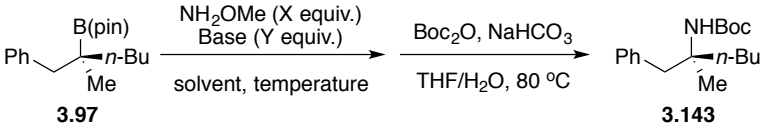
to remove the leftover catalyst. The boron ate complex was then employed in the subsequent conjunctive coupling with **(S_p,S_p)-3.141** and **(R_p,R_p)-3.141** as ligands to afford diastereomeric boronic ester products **3.139** and **3.140** respectively (Scheme 3.23.B). Of note, the observation of a detectable level of difference in diastereoselectivity suggested that stereocontrol of second conjunctive coupling was influenced by not only the chiral ligand on palladium catalyst, but also the chiral migrating group. However, the fact that opposite diastereomers were favored when opposite enantiomers of ligands were employed indicated that the stereocontrol was dominated by the influence of the chiral palladium ligand.

To demonstrate the synthetic utility of tertiary boronic ester products, subsequent transformations of tertiary boronates were investigated. As one attractive advantages of conjunctive cross-coupling, this high yielding process was generally free from complicating by-products that might hinder subsequent transformations so that the tertiary boronate products of conjunctive coupling were able to be directly transformed into other useful functionalities in a single flask fashion. For example, a conjunctive coupling/in situ oxidation sequence led to the tertiary alcohol product **3.142** in excellent yield and enantioselectivity (Scheme 3.24).

In addition to tertiary alcohols, α-tertiary amines are an important but synthetically challenging motif in many therapeutic agents, natural products and other organic compounds. Direct aminiation of tertiary boronic esters constructed by conjunctive coupling would provide an attractive strategy to assemble such a motif in a catalytic, enantioselective, and modular fashion. It is known that an organoboronic acid pinacol ester can be transformed to the corresponding amine in the presence of methoxyamine

and *n*-butyllithium.[33] However, applying this protocol to tertiary boronate **3.97** failed to afford any desired amine product **3.143** (Table 4). Switching the base from *n*-butyllithium to potassium *t*-butyloxide led to 20% desired product at elevated temperature. Further optimization of solvents and equivalents of base improved the amination process to 93% yield. Employing the optimized amination protocol to the conjunctive coupling/amination sequence afforded the tertiary amine **3.143** in 87% yield and 92:8 *e.r* (Scheme 3.24).

Table 4. Optimization of amination of tertiary boronic esters.



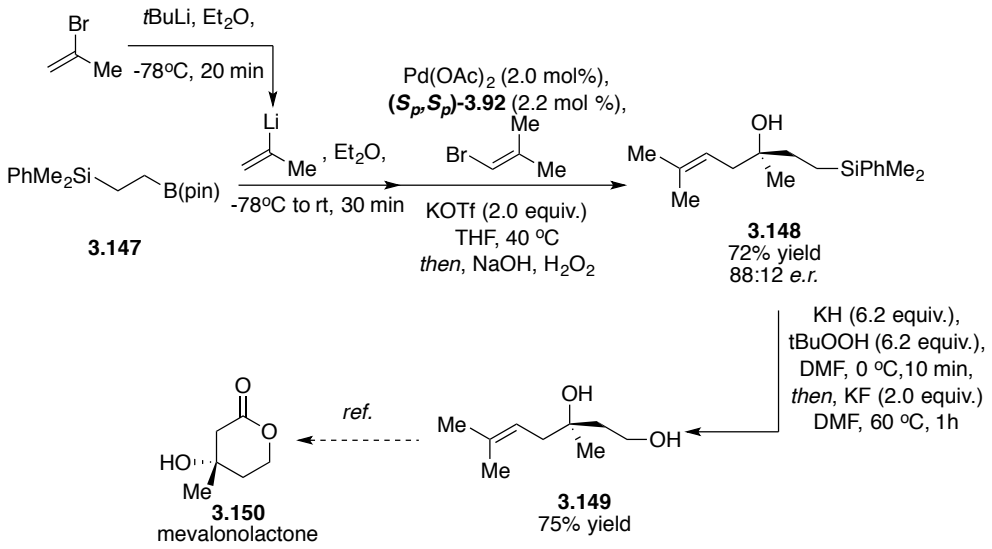
Entry	NH_2OMe (X equiv.)	Base (Y equiv.)	Solvent	Temperature	Yield
1	3 equiv.	*n*BuLi (3 equiv.)	THF	60 °C	< 5%
2	3 equiv.	KO*t*Bu (3 equiv.)	THF	80 °C	20 %
3	3 equiv.	KO*t*Bu (3 equiv.)	Dioxane	80 °C	50 %
4	3 equiv.	KO*t*Bu (3 equiv.)	Toluene	80 °C	70 %
5	3 equiv.	KO*t*Bu (5 equiv.)	Toluene	80 °C	93 %

In addition to transforming the tertiary boronates to corresponding tertiary alcohol and amine, all-carbon quaternary centers could also be efficiently constructed from tertiary boronic ester precursors. While applying Zweifel-Evans olefination to tertiary boronate **3.97** afforded the allylic all-carbon quaternary center in product **3.144**, modified Zweifel-Evans olefination converted the tertiary boronate **3.97** to the methyl ketone

[33] Mlynarski, S. N., Karns, A. S., Morken, J. P. *J. Am. Chem. Soc.* **2012**, 134(40), 16449-16451.

product **3.145** bearing fully substituted α-stereocenter in outstanding level of efficiency. Furthermore, simple Matteson homologation could also be applied followed by oxidation to furnish the primary alcohol **3.146** with high efficiency and stereospecificity (Scheme 3.24).

Scheme 3.24. Direct transformations of conjunctive cross-coupling intermediates.

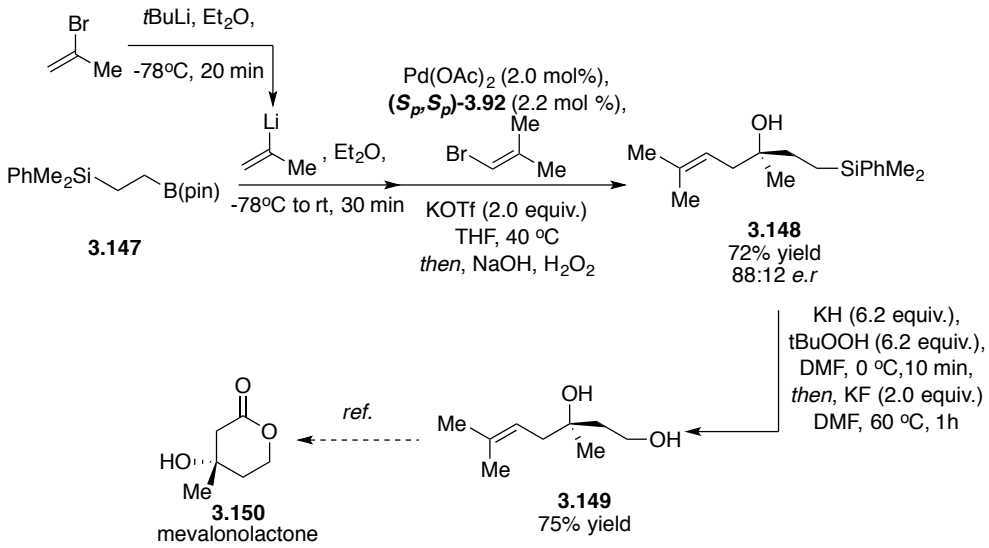


To further probe the synthetic utility of conjunctive cross-coupling and its subsequent transformations, synthesis of the chiral therapeutic agent mevalanolactone[34] **3.150** and the analgesic isoquinolone derivative[35] **3.153** were investigated. In terms of constructing mevalanolactone (**3.150**), the retrosynthetic analysis suggested that engaging an appropriate protected β-hydroxyethyl migration group in conjunctive coupling was required. However, a β-oxygenated migrating group was not tolerated in conjunctive

[34] Scopel, M., Abraham, W. R., Antunes, A. L., Terezinha Henriques, A., Macedo, J., Jose, A. *Med. Chem.* **2014**, 10(3), 246-251.
[35] Vikharev, Y. B., Shklyaev, Y. V., Anikina, L. V., Kolla, V. E., Tolstikov, A. G. *Pharmaceutical Chemistry Journal* **2005**, 39(8), 405-408.

coupling presumably due to the low migratory attitude imparted by inductive effects. It was found that utilizing β-silyl B(pin) **3.147** provided an efficient solution. Employing the organoboronic ester **3.147** in the conjunctive cross-coupling/oxidation sequence afforded the tertiary alcohol intermediate **3.148** where the silyl group served as a masked hydroxyl group.[36] Subsequent Tamao-Fleming oxidation[37] unmasked the silyl group to furnish the 1,3-diol product **3.149**, a known precursor to mevalanolactone **3.150** (Scheme 3.25).[38]

Scheme 3.25. Synthesis towards mevalanolactone.

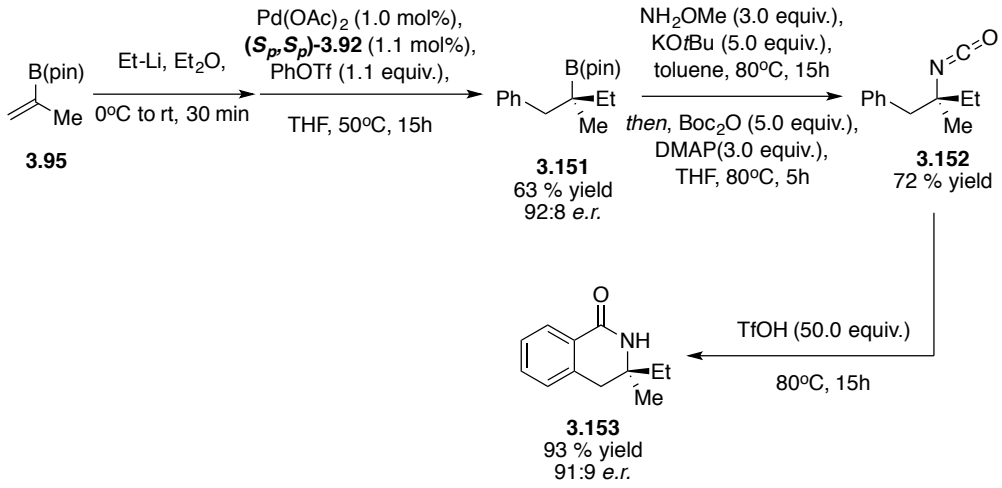


On the other hand, isoquinolone derivative **3.153** was first synthesized in 2005, and moderate anti-inflammatory and analgesic activity was detected for this compound. However, no enantioselective synthesis of **3.153** has been previously reported. Utilizing our conjunctive cross-coupling/amination sequence, the isoquinolone derivative **3.153**

[36] Fleming, I., Henning, R., Parker, D.C., Plaut, H.E. and Sanderson, P.E.J. *J. Chem. Soc., Perkin Trans.* **1995**, 1, 317-337.
[37] Reddy, P. V., Smith, J., Kamath, A., Jamet, H., Veyron, A., Koos, P., Philouze, C., Greene, A. E. and Delair, P. *J. Org. Chem.* **2013**, 78, 4840-4849.
[38] Mori, K. and Okada, K. *Tetrahedron* **1985**, 41, 557-559.

could be easily assembled in an enantioselective and efficient fashion. As shown in Scheme 3.26, conjunctive coupling of ethyllithium, isopropenyl B(pin), and phenyl triflate afforded the tertiary boronic ester intermediate **3.151** with good yield and enantioselectivity. Then, amination and conversion of the resulting amine to an isocyanate were performed in a one-pot fashion to furnish the isocyanate intermediate **3.152** with good efficiency. Finally, acid-induced intramolecular aromatic substitution[39] led to the isoquinolone **3.153** with outstanding efficiency and stereospecificity.

Scheme 3.26. Enantioselective synthesis of anti-inflammatory and analgesic agent 3.153.



3.6. Conclusion

In summary, a palladium catalyzed conjunctive cross-coupling was developed to operate on highly hindered boron ate complexes and furnishes a broad range of severely hindered tertiary boronate products in an efficient and stereoselective fashion. It was also

[39] Kurouchi, H., Kawamoto, K., Sugimoto, H., Nakamura, S., Otani, Y., Ohwada, T. *J. Org. Chem*. **2012**, 77, 9313-9328.

demonstrated that the tertiary boronic ester products could be readily engaged in a variety of subsequent transformations to furnish synthetically important but challenging building blocks, such as tertiary alcohols, α-tertiary amines, and all-carbon quaternary centers. The ability to construct extremely hindered boronic ester products was highlighted by the sequential conjunctive coupling sequence that constructed the tertiary boronic ester products bearing two contiguous fully substituted stereocenter with high efficiency and selectivity. The synthetic utility of such methodology was further demonstrated by enantioselective synthesis of chiral therapeutic agents. The outstanding efficiency of this reaction relied on the pre-formation of sterically encumbered boron ate complex assembled by combination of highly nucleophilic and electrophilic components. Such a concept might be employed in the design of other catalytic processes. Further studies should be focused on discovering possible new ligand scaffolds to further improve the stereoselectivity. Moreover, expanding the scope of conjunctive coupling to alkenyl boronates with other substitution patterns would be ideal to improve the synthetic utility of conjunctive coupling.

3.7. Experimental Section

3.7.1. General Information

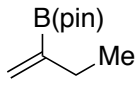
^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.24 ppm). Data are reported as follows: chemical shift, 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 ($CDCl_3$: 77.2 ppm). ^{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)-**3.92**, (S_p,S_p)-**3.141**, (R_p,R_p)-**3.141**, and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene were purchased from Strem Chemicals, Inc. and used without further purification. 2-isopropenyl boronic acid pinacol ester was purchased from Combi Blocks and used without further purification. 4-methoxyphenyltrifluoromethanesulfonate, phenyl trifluoromethanesulfonate, trifluoromethansulfonic acid, and Trifluoromethansulfonic anhydride were purchased from Oakwood Chemicals and used without further purification. All other reagents were purchased from Aldrich, Alfa Aesar, or Acros and used without further purification.

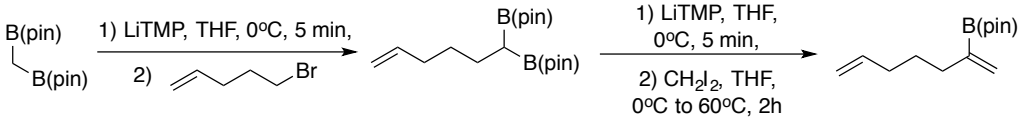
3.7.2. Experimental Procedures

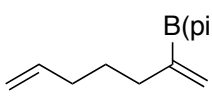
3.7.2.1. Procedures for Preparation of Boronic Esters



2-(but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (S-1). To an oven-dried round bottom flask equipped with a magnetic stir bar under N_2,

2-bromobut-1-ene (5.0 mmol, 1.0 equiv.) and diethyl ether (10.0 mL) were added, and the flask was cooled to -78 °C. Then, a tert-butyl lithium solution (10.0 mmol, 2.0 equiv.) was added at -78 °C dropwise, and the reaction mixture was allowed to stir at -78 °C for 20 minutes. The result solution was transferred to a syringe, and was added to a separated flask with 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (7.5 mmol, 1.5 equiv.) in diethyl ether (10.0 mL) solution by syringe pump over 40 minutes at -78 °C under N_2. Upon completion, the reaction mixture was allowed to warm to room temperature and stir for 1 hour. Then the reaction mixture was cooled to 0 °C, and a 1M HCl (aq.) solution (10.0 mL) was added and stir for additional 1 hour. The reaction mixture was allowed to warm to room temperature and the aqueous layer was extracted with diethyl ether (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 product (630.6 mg, 69% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.72 (s, 1H), 5.58 (s, 1H), 2.14 (q, J = 7.2 Hz, 2H), 1.25 (s, 12H), 0.99 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 127.9, 83.4, 28.4, 24.9, 13.8. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 30.17; IR (neat) ν_{max} 2977.6 (m), 2932.4 (m), 1443.3 (m), 1425.6 (m), 1304.4 (s), 1272.8 (m), 1112.3 (s), 1051.9 (m), 967.3 (m), 737.6 (m), 670.5 (m) cm^{-1}. HRMS (DART) for $C_{10}H_{20}BO_2$ $[M+H]^+$ calculated: 183.1556, found: 183.1554.

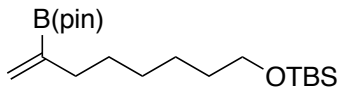




2-(hepta-1,6-dien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (S-2). The title compound was prepared according to the literature

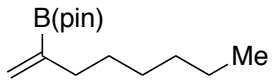
procedure[40]. In the glove box, an oven-dried round bottom flask with magnetic stir bar was charged with LiTMP (4.15 mmol, 1.10 equiv), sealed with a septum, and removed from the glovebox. The reaction flask was cooled to 0 °C, and THF (6.0 mL), and solution of 2,2'-(hex-5-ene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (prepared according to the literature precedence[41] with bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane and 5-bromopent-1-ene) (3.77 mmol, 1.00 equiv) in THF (6.0 mL) were added. The reaction mixture was allowed to stir for 5 minutes at 0 °C. Next, a solution of diiodomethane (7.54 mmol, 2.00 equiv) in THF (3.0 mL) was added dropwise at 0 °C. The reaction vial was allowed to warm to 60 °C and stir for additional 2 hours. Upon completion, the reaction mixture was concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography to afford the title compound (687.2 mg, 82% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.81 (ddt, *J* = 13.2, 10.2, 6.2 Hz1H), 5.75 (d, *J* = 3 Hz, 1H), 5.58 (s, 1H), 4.98 (dd, *J* = 16.8, 1.8 Hz, 1H), 4.91 (dd, *J* = 10.8, 1.2 Hz, 1H), 2.14 (t, *J* = 7.28 Hz, 2H), 2.03 (q, *J* = 7.2 Hz, 2H), 1.50 (p, *J* = 7.2 Hz, 2H), 1.24 (s, 12H. ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.3, 129.3, 114.4, 83.5, 35.0, 33.6, 28.6, 24.9. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 30.07; IR (neat) ν_{max} 2978.1 (m), 2928.7 (m), 1615.4 (w), 1426.2 (m), 1368.4 (s), 1306.5 (s), 1272.2 (m), 1198.1 (s), 1111.9 (m), 990.9 (m), 861.3 (m), 670.4 (w) cm^{-1}. HRMS (DART) for $C_{13}H_{24}BO_2$ $[M+H]^+$ calculated: 223.1869, found: 223.1881.

[40] Coombs, J. R., Zhang, L. Morken, J. P. *Org Lett*. **2015**, 17, 1708-1711.
[41] Hong, K., Liu, X. Morken, J. P. *J. Am. Chem. Soc*. **2014**, 136, 10581-10854.

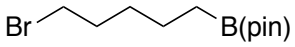


tert-butyldimethyl((7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-7-en-1-yl)oxy)silane (S-3). The title compound was prepared according to a literature procedure with slight modifications[1]. In an Ar-filled glovebox, LiTMP (475.99 mg, 3.23 mmol, 1.0 equiv.) was added to a 50 mL round bottom flask equipped with a magnetic stir bar. The flask was sealed with a rubber septum and removed from the glovebox. Dry THF (8.2 mL, 0.4 M) was added to the reaction vial, and cooled to 0 °C, before a solution of 7,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)heptoxy-tert-butyl-dimethyl-silane (prepared according to the literature precedence[2] with bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane and ((6-bromohexyl)oxy)(*tert*-butyl)-dimethylsilane) (1.56 g, 3.23 mmol, 1.0 equiv.) in THF (9.7 mL, 0.33 M) was added. The reaction mixture was allowed to stir for 5 minutes at 0 °C. Next, a solution of diiodomethane (0.52 mL, 6.47 mmol, 2.0 equiv.) in THF (6.5 mL) was added dropwise at 0 °C. The reaction vial was warmed to 60 °C and stirred for additional 2 hours. Upon completion, the reaction mixture filtered through a plug of silica gel with diethyl ether, then concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (2 % ethyl acetate in hexanes, stain in magic) to afford a colorless oil (830 mg, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.75 (s, 1H), 5.58 (s, 1H), 3.59 (t, *J* = 6.7 Hz, 2H), 2.13 (t, *J* = 7.6 Hz, 2H), 1.56-1.46 (m, 2H), 1.46-1.37 (m, 2H), 1.37-1.23 (m, 16H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 128.67, 83.24, 63.33, 35.27, 32.85, 29.18, 29.05, 25.97, 25.69, 24.72, 18.35, -5.26. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 30.17. IR (neat): ν_{max} 2978.0 (m), 2928.7 (m), 2856.7 (m), 1462.9 (m), 1427.8 (m), 1407.6 (m), 1387.6 (m), 1307.9 (m), 1254.3 (m),

1141.9 (s), 1100.25 (m), 969.1 (m), 834.9 (s), 811.4 (m), 774.5 (m) cm^{-1}. HRMS (DART) for $C_{20}H_{42}BO_3Si[M+H]^+$: calculated: 369.2996, found: 369.3001.

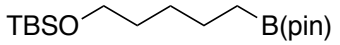


4,4,5,5-tetramethyl-2-(oct-1-en-2-yl)-1,3,2-dioxaborolane (S-4). The title compound was prepared according to a literature procedure with slight modifications[1]. In an Ar-filled glovebox, LiTMP (911 mg, 6.19 mmol, 1.0 equiv.) was added to a 100 mL round bottom flask equipped with a magnetic stir bar. The flask was sealed with a rubber septum and removed from the glovebox. Dry THF (15.5 mL, 0.4 M) was added to the reaction vial, and cooled to 0 °C, before a solution of 2,2'-(heptane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.18 g, 6.19 mmol, 1.0 equiv.) (prepared according to the literature precedence[2] with bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane and 1-bromohexane) in THF (18.8 mL, 0.33 M) was added. The reaction mixture was allowed to stir for 5 minutes at 0 °C. Next, a solution of diiodomethane (1.00 mL, 12.4 mmol, 2.0 equiv.) in THF (12.0 mL) was added dropwise at 0 °C. The reaction vial was warmed to 60 °C and stirred for additional 2 hours. Upon completion, the reaction mixture filtered through a plug of silica gel with diethyl ether, then concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (2 % ethyl acetate in hexanes, stain in magic) to afford a colorless oil (830 mg, 54% yield). All spectral data was in accordance with the literature.



2-(5-bromopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

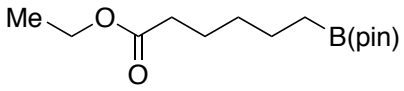
(S-5). The title compound was prepared according to the literature precedence[42]. To an oven-dried 6-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 5-bromo-penten (5.0 mmol, 1.00 equiv.), pinacolborane (6.0 mmol, 1.20 equiv.), $[Ir(cod)Cl]_2$ (0.05 mmol, 0.01 equiv.), 1,1-Bis(diphenylphosphino)methane (0.10 mmol, 0.02 equiv.), and dichloromethane (5.0 mL). The reaction vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at room temperature for 24 hours. The reaction was quenched with methanol (1.0 mL) and water (3.0 mL), and the aqueous layer was extracted with diethyl ether (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 product (1.116 g, 80% yield). All spectral data was in accordance with the literature[43].



***tert*-butyldimethyl((5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)oxy)silane (S-6).** The title compound was prepared according to the literature precedence[3]. To an oven-dried 6-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added *tert*-butyldimethyl(pent-4-en-1-yloxy)silane (5.0 mmol, 1.00 equiv.), pinacolborane (6.0 mmol, 1.20 equiv.), $[Ir(cod)Cl]_2$ (0.05 mmol, 0.01 equiv.), 1,1-Bis(diphenylphosphino)methane (0.10 mmol, 0.02 equiv.), and dichloromethane (5.0 mL). The reaction vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at room temperature for 24

[42] Yamamoto, Y., Fujikawa, R., Umemoto, T. Miyaura, N. *Tetrahedron* **2004**, 60, 10695-10700.
[43] Molander, G. A. & Ham, J. *Org. Lett*. **2006**, 8, 2031-2034.

hours. The reaction was quenched with methanol (1.0 mL) and water (3.0 mL), and the aqueous layer was extracted with diethyl ether (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 product (1.548 g, 94% yield). All spectral data was in accordance with the literature[44].



ethyl 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexanoate (S-7). The title compound was prepared according to a literature procedure with slight modifications[45]. In an Ar-filled glovebox, B_2pin_2 (1.90 g, 7.50 mmol, 1.5 equiv.), lithium methoxide (379.7 mg, 10.00 mmol, 2.0 equiv.), and copper (I) iodide (95.2 mg, 0.50 mmol, 0.10 equiv.) were added to a 100 mL round bottom flask equipped with a magnetic stir bar. The flask was sealed with a rubber septum and removed from the glovebox. Ethyl 6-bromohexanoate (0.89 mL, 5.00 mmol, 1.0 equiv) was added via syringe, followed by DMF (15.00 mL, 0.33 M). Reaction was stirred at room temperature for 15 hours. Then, reaction mixture was passed through a plug of silica gel with diethyl ether. The filtrate was then poured into separatory funnel containing aqueous saturated sodium chloride. The organic layer was separated and the aqueous layer was extracted with diethyl ether (2 x 20 mL). Combined organic layers washed with aqueous saturated sodium chloride, dried over sodium sulfate, then filtered through a plug of cotton and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (2% - 5% ethyl acetate in hexanes, stain in

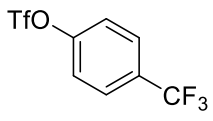
[44] Bedford, R. B., Brenner, P. B., Carter, E., Gallagher, T., Murphy, D. M. Pye, D. R. *Organometallics* **2014**, 33, 5940-5943.
[45] Yang, C., Zhang, Z., Tajuddin, H., Wu, C., Liang, J., Liu, J., Fu, Y., Czyzewska, M., Steel, P. G., Marder, T. B. Liu. L. *Angew. Chem. Int. Ed*. **2012**, 51, 528-532.

magic) to afford a colorless oil (906.0 mg, 67% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.10 (q, *J* = 7.2 Hz, 2H), 2.31-2.22 (m, 2H), 1.67-1.56 (m, 2H), 1.47-1.36 (m, 2H), 1.36-1.27 (m, 2H), 1.27-1.18 (m, 15H), 0.76 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.81, 82.84, 60.05, 34.31, 31.82, 31.29, 24.78, 24.75, 23.60, 14.22. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.17. IR (neat): ν_{max} 2977.9 (m), 2931.2 (m), 2863.6 (m), 1734.6 (s), 1463.7 (m), 1407.9 (s), 1370.8 (m), 1271.4 (m), 1214.5 (m), 1183.6 (m), 1144.1 (s), 968.2 (m), 873.0 (m), 673.2 (m) cm^{-1}. HRMS (DART) for $C_{14}H_{28}BO_4$ $[M+H]^+$: calculated: 271.2081, found: 271.2081.

3.7.2.2. Procedures for Preparation of Aryl Trifluoromethanesulfonates

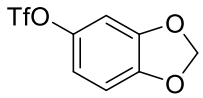
General Procedure for the Synthesis of Aryl Trifluoromethanesulfonates

Aryl Trifluoromethansulfonates were made according to literature procedure with slight modification. 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.



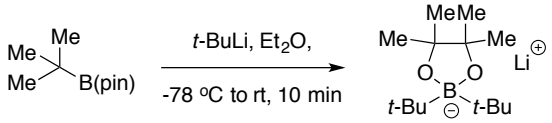
4-(trifluoromethyl)phenyl trifluoromethanesulfonate (S-7). Prepared according to the general procedure above with 4-

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[46].



benzo[*d*][1,3]dioxol-5-yl trifluoromethanesulfonate (S-8). 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[47].

3.7.2.3. Boron "ate" Complex Formation Studies

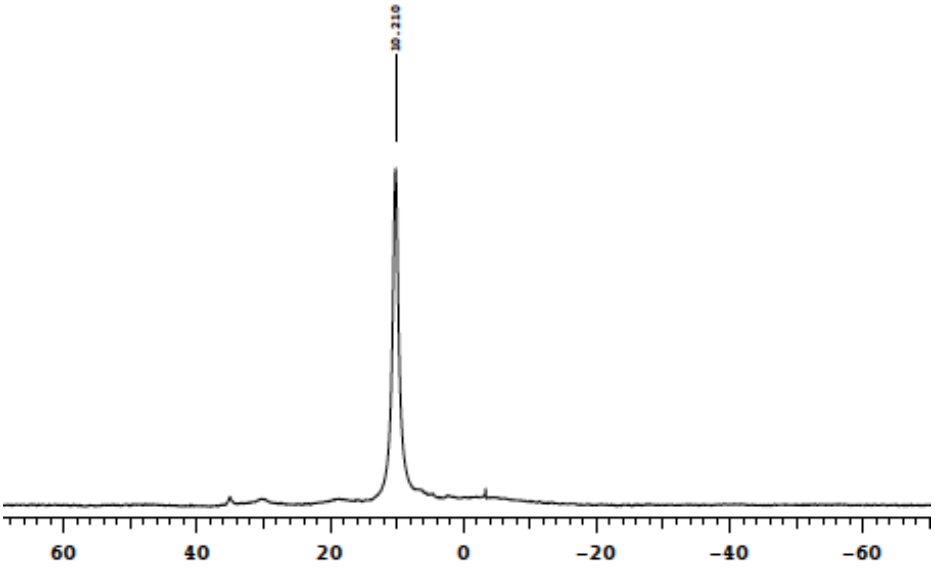


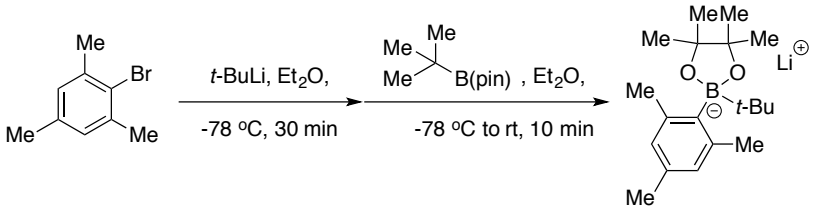
Lithium (I) 2,2-di-*tert*-butyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-uide (3.85). To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added *tert*-butyl boronic acid pinacol ester (36.8 mg, 0.20 mmol, 1.00 equiv.) and diethyl ether (0.2 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to -78 °C, and an *tert*-butyl lithium solution (0.12 mL, 1.7 M in pentane, 0.20 mmol, 1.0 equiv.) was added at -78 °C. The reaction vial was allowed to warm to

[46] Gill, D., Hester, A. J. Lloyd-Jones, G. C. *Org. Biomol. Chem*. **2004**, 2, 2547-2548.
[47] Echavarren, A. M. Stille, J. K. *J. Am. Chem. Soc*. **1987**, 109, 5478-5486.

room temperature, and the reaction vial was brought back into the glovebox, the reaction mixture was was diluted with THF (0.6 mL) and transferred to a NMR tube, sealed and took the ^{11}B NMR.

^{11}B NMR: (160 MHz, $CDCl_3$)

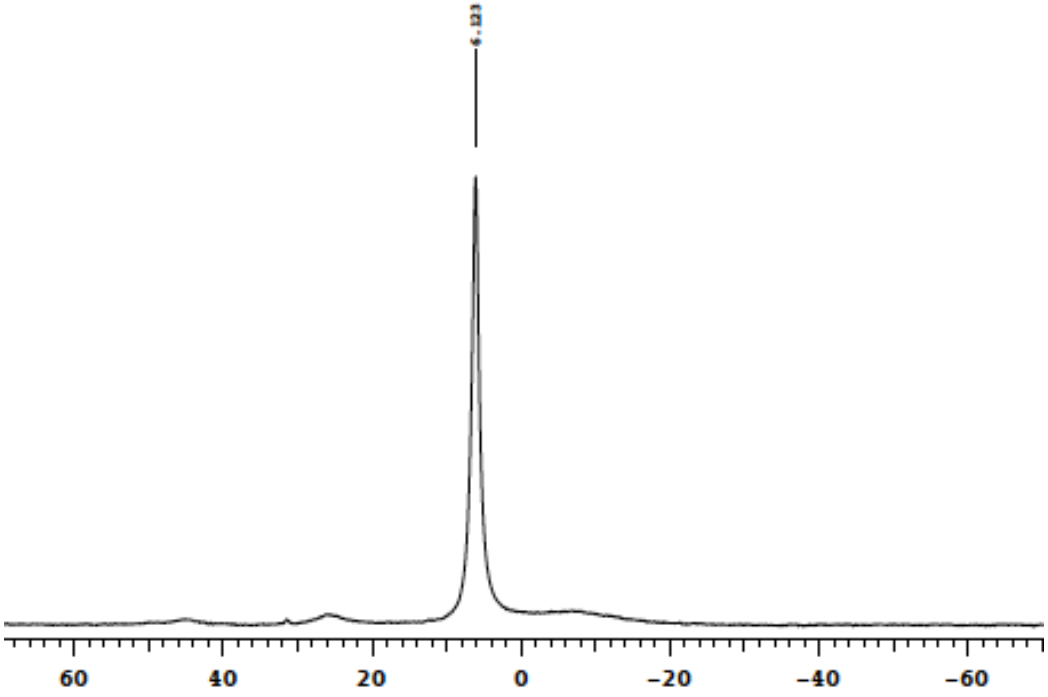




Lithium (I) 2-(*tert*-butyl)-2-mesityl-4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-uide (3.86). To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-bromo-1,3,5-trimethylbenzene (39.8 mg, 0.20 mmol, 1.00 equiv.) and diethyl ether (0.2 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to -78 °C, and a *tert*-butyl lithium solution (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.) was added at -78 °C. The reaction vial was allowed to stir at -78 °C for 30 minutes. Then a *tert*-butyl boronic acid pinacol ester (36.8 mg,

0.20 mmol, 1.00 equiv.) solution in diethyl ether (0.3 mL) was added at -78 °C. The reaction vial was allowed to warm to room temperature, and the reaction vial was brought back into the glovebox, the reaction mixture was diluted with THF (0.6 mL) and transferred to a NMR tube, sealed and took the ^{11}B NMR.

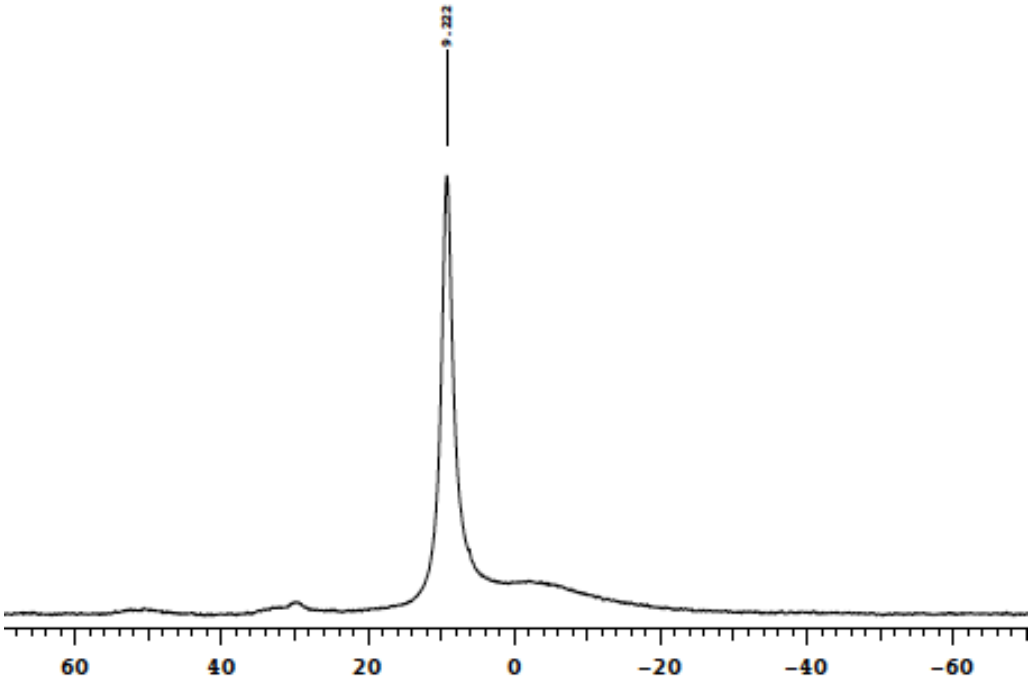
^{11}B NMR: (160 MHz, $CDCl_3$)



Lithium (I) 2-cyclohexyl-4,4,5,5-tetramethyl-2-(2,4,6-triisopropylphenyl)-1,3,2-dioxaborolan-2-uide (3.87). To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-bromo-1,3,5-triisopropylbenzene (56.7 mg, 0.20 mmol, 1.00 equiv.) and diethyl ether (0.2 mL), sealed with a septum cap, and

removed from the glovebox. The reaction vial was cooled to -78 °C, and a *tert*-butyl lithium solution (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.) was added at -78 °C. The reaction vial was allowed to stir at -78 °C for 30 minutes. Then a cyclohexyl boronic acid pinacol ester (42.0 mg, 0.20 mmol, 1.00 equiv.) solution in diethyl ether (0.3 mL) was added at -78 °C. The reaction vial was allowed to warm to room temperature, and the reaction vial was brought back into the glovebox, the reaction mixture was diluted with THF (0.6 mL) and transferred to a NMR tube, sealed and took the ^{11}B NMR.

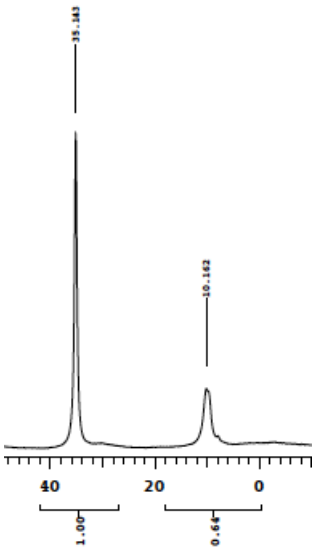
^{11}B NMR: (160 MHz, $CDCl_3$)



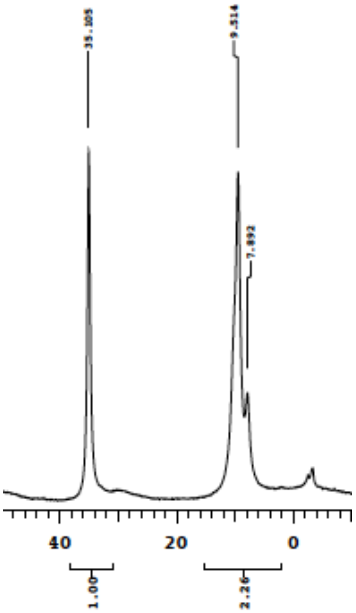
Lithium (I) 2-(*tert*-butyl)-4,4,5,5-tetramethyl-2-(2,4,6-triisopropylphenyl)-1,3,2-dioxaborolan-2-uide (3.88). To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-bromo-1,3,5-triisopropylbenzene (56.7 mg, 0.20 mmol, 1.00 equiv.) and diethyl ether (0.2 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to -78 °C, and a *tert*-butyl lithium solution (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.) was added at -78 °C. The reaction vial was allowed to stir at -78 °C for 30 minutes. Then a *tert*-butyl boronic acid pinacol ester (36.8 mg, 0.20 mmol, 1.00 equiv.) solution in diethyl ether (0.3 mL) was added at -78 °C. The reaction vial was allowed to warm to room temperature, and the reaction vial was brought back into the glovebox, the reaction mixture was diluted with THF (0.6 mL) and transferred to a NMR tube, sealed and took the ^{11}B NMR.

^{11}B NMR: (160 MHz, $CDCl_3$)

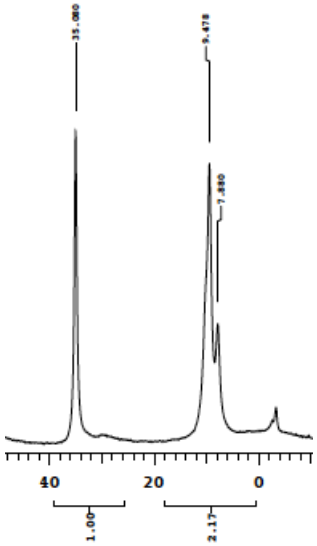
2 hours



20 hours

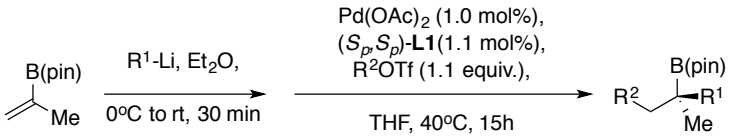


40 hours



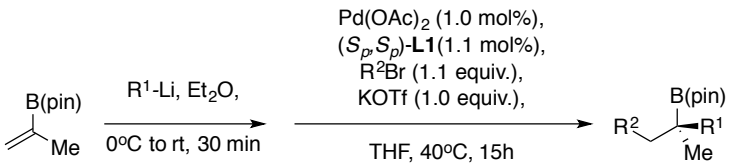
3.7.2.4. Procedures for Conjunctive Cross-Coupling

Method A:



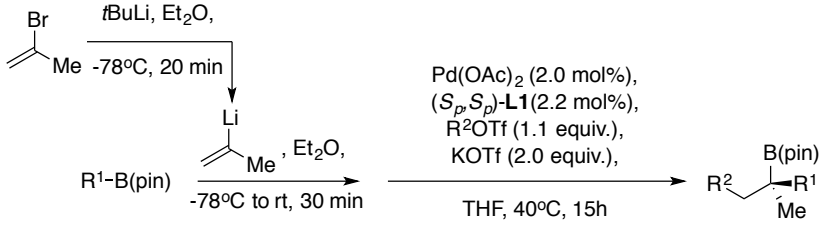
To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-isopropenyl boronic acid pinacol ester (0.20 mmol, 1.00 equiv.) and diethyl ether (0.2 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0 °C, and an alkyl/aryl lithium solution (0.20 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 stirbar in the glovebox was added $Pd(OAc)_2$ (0.002 mmol, 0.01 equiv.), (S_p, S_p)-**3.92** (0.0022 mmol, 0.011 equiv.), and THF (0.2 mL). The $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was transferred into the reaction vial, followed by THF (0.6 mL), and aryl/alkenyl triflate (0.22 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 40 °C for 15 hours. The resulting mixture was cooled to room temperature, filtered through a silica gel plug with diethyl ether, 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 2-isopropenyl boronic acid pinacol ester (0.20 mmol, 1.00 equiv.) and diethyl ether (0.2 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0 °C, and an alkyl/aryl lithium solution (0.20 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 stirbar in the glovebox was added $Pd(OAc)_2$ (0.002 mmol, 0.01 equiv.), (S_p, S_p)-**3.92** (0.0022 mmol, 0.011 equiv.), and THF (0.2 mL). The $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was transferred into the reaction vial, followed by THF (0.6 mL), potassium trifluoromethanesulfonate (0.20 mmol, 1.0 equiv.) and aryl/alkenyl bromide (0.22 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 40 °C for 15 hours. The resulting mixture was cooled to room temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to afford the desired products.

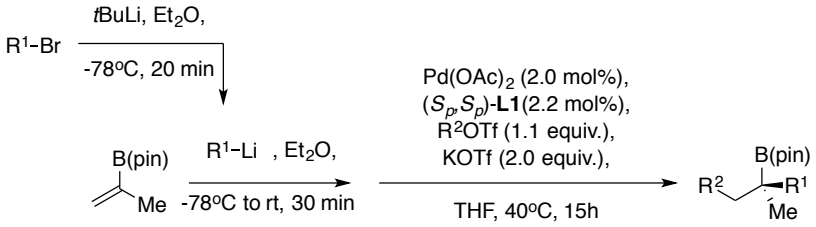
Method C:



To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-isopropenyl bromide (0.20 mmol, 1.00 equiv.) and diethyl ether (0.2 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to -78 °C, and a *tert*-butyl lithium solution (0.40 mmol, 2.0 equiv.) was added at -78 °C. The reaction vial was allowed to stir at -78 °C for 20 minutes. Then an alkyl/aryl boronic acid pinacol ester solution was added at -78 °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 stirbar in the glovebox was added $Pd(OAc)_2$ (0.004 mmol, 0.02 equiv.), (S_p, S_p)-**3.92** (0.0044 mmol, 0.022 equiv.), and THF (0.4 mL). The $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was transferred into the reaction vial, followed by THF (0.4 mL), potassium trifluoromethanesulfonate (0.40 mmol, 2.0 equiv.) and aryl/alkenyl triflate (0.22 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 40 °C for 15 hours. The resulting mixture was cooled to room

temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to afford the desired products.

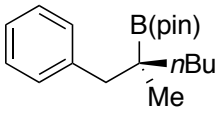
Method D:



To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added aryl bromide (0.20 mmol, 1.00 equiv.) and diethyl ether (0.2 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to -78 °C, and a *tert*-butyl lithium solution (0.40 mmol, 2.0 equiv.) was added at -78 °C. The reaction vial was allowed to stir at -78 °C for 20 minutes. Then a 2-isopropenyl boronic acid pinacol ester solution was added at -78 °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 stirbar in the glovebox was added $Pd(OAc)_2$ (0.004 mmol, 0.02 equiv.), (S_p, S_p)-**3.92** (0.0044 mmol, 0.022 equiv.), and THF (0.4 mL). The $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was transferred into the reaction vial, followed by THF (0.4 mL), potassium trifluoromethanesulfonate

(0.40 mmol, 2.0 equiv.) and aryl/alkenyl triflate (0.22 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 40 °C for 15 hours. The resulting mixture was cooled to room temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to afford the desired products.

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



(*R*)-4,4,5,5-tetramethyl-2-(2-methyl-1-phenylhexan-2-yl)-1,3,2-dioxaborolane (3.97). The reaction was performed according to the general procedure ***(Method A)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (56.6 mg, 94% yield at room temperature; 54.8 mg, 91% yield at 40 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31-7.02 (m, 5H), 2.78 (d, J = 13.1 Hz, 1H), 2.46 (d, J = 13.1 Hz, 1H), 1.51-1.37 (m, 1H), 1.37-1.13 (m, 17H), 0.94-0.82 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 140.38, 130.56, 127.75, 125.77, 83.28, 44.96, 39.43, 28.42, 25.28, 24.98, 23.80, 21.37,

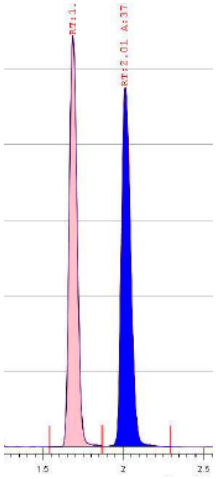
14.35; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.54; IR (neat): ν_{max} 2927.2 (m), 2859.5 (w), 1494.5 (m), 1378.9 (m), 1307.2 (m), 1218.5 (m), 1137.7 (s), 968.1 (m), 852.1 (m), 747.1 (m), 701.6 (m) cm^{-1}. HRMS (DART) for $C_{19}H_{35}BO_2N$ $[M+NH_4]^+$: calculated: 320.2761, found: 320.2763. $[\alpha]^{20}_D$: -5.03 (c = 2.310, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl 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 compounds **3.105, 3.149, and 3.151**).

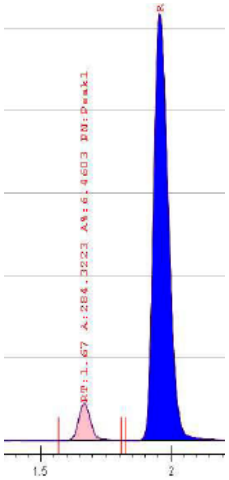
Chiral SFC (Chiracel ODR-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4,4,5,5-tetramethyl-2-(2-methyl-1-phenylhexan-2-yl)-1,3,2-dioxaborolane.

Racemic Material



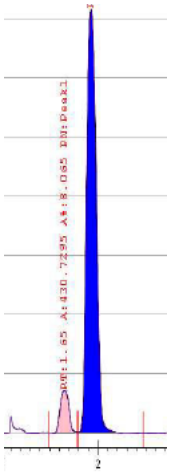
Peak No	% Area	Area	RT (min)
1	49.4079	3701.4525	1.69
2	50.5921	3790.1679	2.01
Total:	100	7491.6204	

Standard Conditions (room temperature)

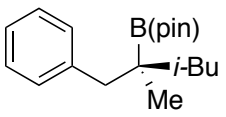


Peak No	% Area	Area	RT (min)
1	6.4603	284.3223	1.67
2	93.5397	4116.729	1.96
Total:	100	4401.0513	

Standard Conditions (40 °C)



Peak No	% Area	Area	RT (min)
1	8.065	430.7295	1.65
2	91.935	4909.9976	1.93
Total:	100	5340.7271	



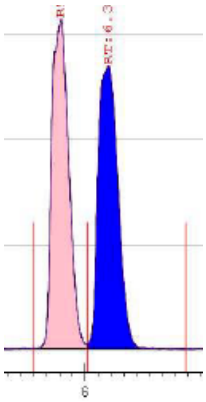
(*R*)-2-(2,4-dimethyl-1-phenylpentan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.103). The reaction was performed according to the general procedure ***(Method A)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), isobutyl lithium (0.12 mL, 1.72 M in heptane, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (56.8 mg, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32-7.10 (m, 5H), 2.80 (d, *J* = 13.1 Hz, 1H), 2.47 (d, *J* = 13.0 Hz, 1H), 1.78-1.65 (m, 1H), 1.52-1.42 (m, 1H), 1.24-1.16 (m, 13H), 1.00-0.86 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.76, 130.63, 127.52, 125.65, 83.15, 48.43, 45.81, 25.75, 25.25, 24.94, 24.72, 24.18, 21.09. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.54. IR (neat) ν_{max} 3062.1 (m), 3028.6 (m), 2954.4 (m), 1602.8 (m), 1467.8 (m), 1378.8 (s), 1371.1 (s), 1336.2 (m), 1307.6 (s), 1250.4 (m), 1136.2 (s), 1084.8 (m), 1031.5 (m), 849.3 (m), 790.8 (m), 701.9 (s), 597.4 (m) cm^{-1}. HRMS (DART) for $C_{19}H_{32}BO_2$ $[M+H]^+$: calculated: 303.2495, found: 303.2291. $[\alpha]^{20}_D$: +4.23 (c = 1.773, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

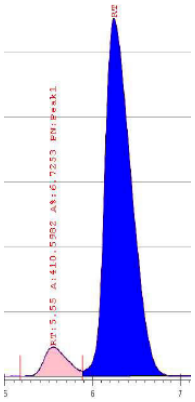
Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)-ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see compounds see compounds **3.105, 3.149, and 3.151**).

Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(2,4-dimethyl-1-phenylpentan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

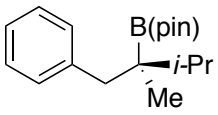
Racemic Material



Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	50.1177	5739.4388	5.62	1	6.7253	410.5982	5.55
2	49.8823	5712.4912	6.36	2	93.2747	5694.6624	6.25
Total:	100	11451.93		Total:	100	6105.2606	



(*S*)-2-(2,3-dimethyl-1-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.104). The reaction was performed according to the general procedure ***(Method A)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), isopropyl lithium (0.36 mL, 0.56 M in pentane, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (54.0 mg, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30-7.19 (m, 4H), 7.18-7.11 (m, 1H), 2.89 (d, J = 12.9 Hz, 1H), 2.46 (d, J = 12.9 Hz, 1H), 1.71 (h, J = 6.9 Hz, 1H), 1.18 (d, J = 54.1 Hz, 12H), 0.97 (dd, J = 31.0, 6.9 Hz, 6H), 0.86 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 140.91, 130.49, 127.55, 125.55, 83.04, 43.27, 35.24, 25.45, 24.81, 19.86,

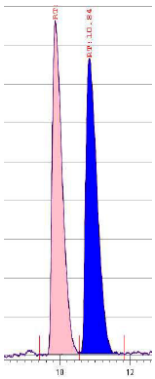
17.73, 17.28. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.31. IR (neat) ν_{max} 2975.5 (m), 2929.6 (m), 2873.5 (m), 1495.0 (m), 1467.6 (m), 1370.7 (s), 1306.9 (s), 1269.1 (m), 1209.4 (m), 1142.2 (s), 1126.5 (m), 1084.1 (m), 967.9 (m), 848.2 (m) cm^{-1}. HRMS (DART) for $C_{18}H_{33}BO_2N$ $[M+NH_4]^+$: calculated: 306.2604, found: 306.2596. $[\alpha]^{20}_D$: -3.83 (c = 1.200, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)-ferrocene (6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

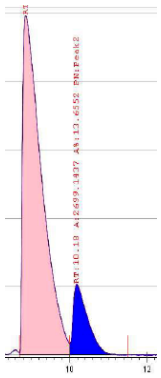
Chiral SFC (Chiracel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2,3-dimethyl-1-phenylbutan-2-ol.

Racemic Material

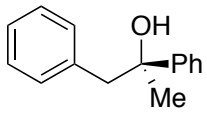


Peak No	% Area	Area	RT (min)
1	49.9738	1729.7895	9.86
2	50.0262	1731.6052	10.84
Total:	100	3461.3947	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	86.3448	17067.2797	8.86
2	13.6552	2699.1437	10.18
Total:	100	19766.4234	



(*R*)-1,2-diphenylpropan-2-ol (3.105). The reaction was performed according to the *conjunctive cross-coupling (**Method A**)/oxidation* procedure with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), phenyl lithium (0.11 mL, 1.9 M in dibutyl ether, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (8.0 % ethyl acetate in hexanes, stain in magic) to afford a colorless oil (35.7 mg, 84% yield at room temperature; 54.8 mg, 91% yield at 40 °C). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (d, J = 7.8 Hz, 2H), 7.36 (t, J = 7.2 Hz, 2H), 7.29-7.23 (m, 4H), 7.03-7.02 (m, 2H), 3.16 (d, J = 13.8 Hz, 1H), 3.06 (d, J = 13.2 Hz, 1H), 1.60 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 147.7, 136.9, 130.8, 128.2, 126.8, 125.1, 74.6, 50.7, 29.6; IR (neat): ν_{max} 3445.6 (br), 3060.1 (m), 3027.5 (m), 2974.3 (m), 2922.5 (m), 2850.4 (m), 1602.1 (m), 1446.7 (m), 1347.0 (m), 1179.0 (m), 1067.5 (m), 946.0 (m), 770.3 (s), 698.9 (s), 573.6 (m) cm^{-1}. HRMS (DART) for $C_{15}H_{15}$ $[M+H-H_2O]^+$: calculated: 195.1174, found: 195.1174. $[\alpha]^{20}_D$: +51.80 (c = 0.905, $CHCl_3$, l = 50 mm).

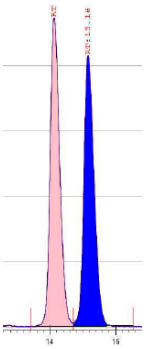
Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl 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 of optical rotation of the product before

the oxidation to the literature[48] (Measured: $[\alpha]^{20}_D$: -51.2 (c = 1.105, $CHCl_3$, l =50 mm), literature: $[\alpha]^{24}_D$: -63.9 (c = 6.2, CH_2Cl_2), 99 % *e.e* for (*S*)-2-(1,2-diphenylpropan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane). And the absolute stereochemistry was assigned to be (*S*)-2-(1,2-diphenylpropan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

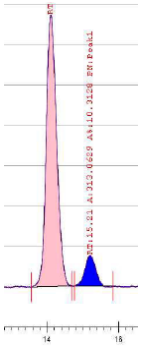
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1,2-diphenylpropan-2-ol.

Racemic Material

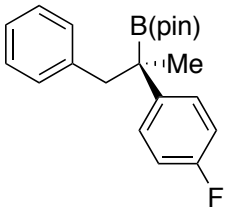


Peak No	% Area	Area	RT (min)
1	51.3279	4756.4478	14.12
2	48.6721	4510.334	15.16
Total:	100	9266.7818	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	89.6872	2722.619	14.1
2	10.3128	313.0629	15.21
Total:	100	3035.6819	



(*S*)-2-(2-(4-fluorophenyl)-1-phenylpropan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.106). The reaction was performed according to the general procedure ***(Method D)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.), 1-bromo-4-fluorobenzene (35.0 mg, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010

[48] Bagutski, V., Ros, A. Aggarwal, V. K. *Tetrahedron* **2009**, 65, 9956-9960.

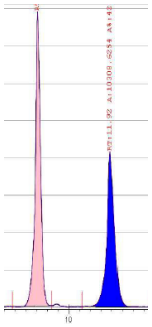
equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (75.2 mg, 0.40 mmol, 2.00 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (55.0 mg, 81% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.28-7.23 (m, 2H), 7.18-7.13 (m, 3H), 7.00-6.94 (m, 4H), 3.15 (d, J = 13.2 Hz, 1H), 2.95 (d, J = 13.1 Hz, 1H), 1.28 (s, 3H), 1.22 (d, J = 17.9 Hz, 12H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.56 (d, $^1J_{C–F}$ = 243.3 Hz), 144.60, 141.89, 133.05, 131.28 (d, $^3J_{C–F}$ = 7.9 Hz) 130.13, 128.50, 117.25 (d, $^2J_{C–F}$ = 20.8 Hz) 86.27, 48.50, 27.53, 27.40, 27.15, 23.33. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 33.83. ^{19}F NMR: (564 MHz, $CDCl_3$) δ -118.61. IR (neat) ν_{max} 2977.0 (m), 2930.9 (m), 1602.5 (m), 1507.4 (s), 1460.1 (m), 1372.2 (m), 1317.7 (s), 1229.6 (m), 1142.8 (s), 1100.9 (m), 1014.4 (m), 966.9 (m), 850.6 (m), 754.7 (m), 579.2 (m) cm^{-1}. HRMS (DART) for $C_{21}H_{30}BFO_2N$ $[M+NH_4]^+$: calculated: 358.2354, found: 358.2350. $[\alpha]^{20}_D$: -39.91 (c = 1.430, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and and $Pd(OAc)_2$ (1.0 mol%), (S_p, S_p)-**3.141** (0.6 mol%), and (R_p, R_p)-**3.141** (0.6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

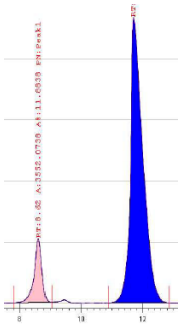
Chiral SFC (Chiracel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-fluorophenyl)-1-phenylpropan-2-ol.

Racemic Material

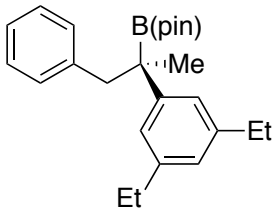


Peak No	% Area	Area	RT (min)
1	57.2278	13792.5788	8.54
2	42.7722	10308.6254	11.92
Total:	100	24101.2042	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	11.8838	3552.0738	8.62
2	88.1162	26337.9331	11.7
Total:	100	29890.0069	



(*S*)-2-(2-(3,5-diethylphenyl)-1-phenylpropan-2-yl)-4,4,5,5-tetra-methyl-1,3,2-dioxaborolane (3.107). The reaction was performed according to the general procedure ***(Method D)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.), 1-bromo-3,5-diethylbenzene (42.6 mg, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (75.2 mg, 0.40 mmol, 2.00 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (56.8 mg, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22-7.09 (m, 3H), 7.09-6.99 (m, 2H), 6.95 (s, 2H), 6.83 (s, 1H), 3.21 (d, J = 13.0 Hz, 1H), 2.87 (d, J = 13.0 Hz, 1H), 2.59 (q, J = 7.6 Hz, 4H), 1.32-1.13 (m, 21H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 146.45, 143.58, 139.87, 130.49, 127.35, 125.63, 124.51, 124.03, 83.40, 45.78, 29.06, 24.85, 24.44, 20.69, 15.74. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 36.60. IR (neat) ν_{max} 2964.7 (m), 2929.4 (m), 2871.9 (m), 1597.5 (m), 1460.2 (m), 1377.9

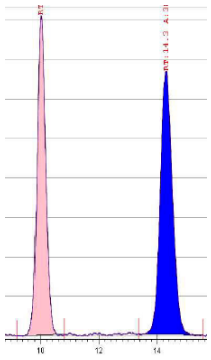
(m), 1350.5 (m), 1312.6 (s), 1271.2 (m), 1212.0 (m), 1145.0 (s), 1098.7 (m), 966.9 (m), 750.7 (m) cm^{-1}. HRMS (DART) for $C_{25}H_{36}BO_2$ $[M+H]^+$: calculated: 379.2808, found: 379.2798. $[\alpha]^{20}_D$: -15.71 (c = 0.60, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)-ferrocene (6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

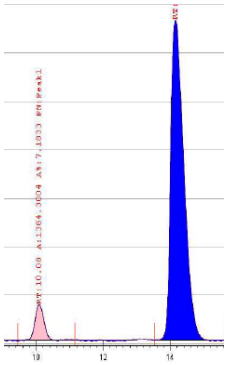
Chiral SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(3,5-diethylphenyl)-1-phenylpropan-2-ol.

Racemic Material

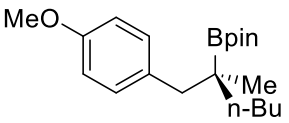


Peak No	% Area	Area	RT (min)
1	45.5526	3254.9697	10
2	54.4474	3890.55	14.3
Total:	100	7145.5197	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	7.1833	1384.3004	10.08
2	92.8167	17886.7192	14.14
Total:	100	19271.0196	



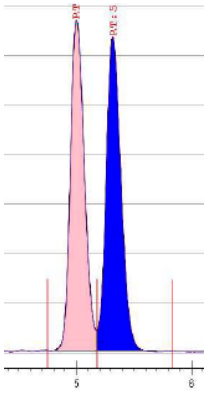
(*R*)-2-(1-(4-methoxyphenyl)-2-methylhexan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.125). The reaction was performed according to the general procedure ***(Method A)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 4-methoxyphenyl trifluoromethanesulfonate (56.4 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), and (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (63.1 mg, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.5 Hz, 2H), 6.77 (t, *J* = 8.5 Hz, 2H), 3.77 (s, 3H), 2.73 (d, *J* = 13.3 Hz, 1H), 2.42 (d, *J* = 13.2 Hz, 1H), 1.48-1.36 (m, 1H), 1.37-1.10 (m, 17H), 0.95-0.79 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.31, 134.94, 133.89, 115.63, 85.70, 57.84, 46.49, 41.78, 30.89, 27.74, 27.45, 26.28, 23.79, 16.81. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.60. IR (neat) ν_{max} 2975.6 (m), 2955.1 (m), 2927.6 (m), 2858.6 (m), 1611.1 (m), 1510.6 (s), 1465.2 (m), 1370.8 (m), 1301.6 (m), 1246.4 (s), 1177.3 (m), 1138.4 (s), 1038.8 (m), 853.2 (m), 823.2 (m) cm^{-1}. HRMS (DART) for $C_{20}H_{34}BO_3$ $[M+H]^+$: calculated: 333.2601, found: 333.2600. $[\alpha]^{20}_D$: -4.66 (c = 0.840, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl 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 compounds **3.105, 3.149, and 3.151**).

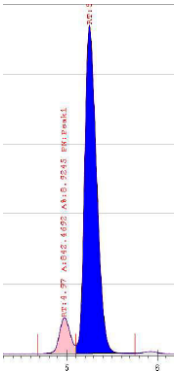
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(4-methoxyphenyl)-2-methylhexan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

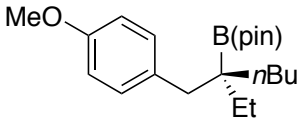


Peak No	% Area	Area	RT (min)
1	49.9848	2823.0389	5
2	50.0152	2824.759	5.32
Total:	100	5647.7979	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	8.9245	842.4692	4.97
2	91.0755	8597.4971	5.25
Total:	100	9439.9663	



(*R*)-2-(3-(4-methoxybenzyl)heptan-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.109). The reaction was performed according to the general procedure ***(Method A)*** with 2-(but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (36.4 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 4-methoxyphenyl trifluoromethanesulfonate (56.4 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (49.7 mg, 72% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.09 (d, J = 8.6 Hz, 2H), 6.76 (d, J = 8.6 Hz, 2H), 3.75 (s, 3H), 2.62 (d, J = 3.0 Hz, 2H), 1.38-1.14 (m, 20H), 0.95-0.81 (m, 6H); ^{13}C NMR

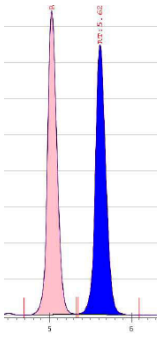
(151 MHz, $CDCl_3$): δ 157.78, 132.44, 131.32, 113.24, 83.20, 55.37, 38.75, 33.88, 27.33, 26.52, 25.29, 25.25, 23.76, 14.42, 9.45; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.45; IR (neat): ν_{max} 2957.5 (m), 2928.9 (m), 2858.5 (w), 1511.3 (m), 1459.8 (m), 1404.2 (m), 1301.3 (m), 1246.7 (s), 1136.9 (s), 1039.3 (m), 837.0 (m), 687.7 (m) cm^{-1}. HRMS (DART) for $C_{21}H_{36}BO_3$ $[M+H]^+$: calculated: 347.2758, found: 347.2745. $[\alpha]^{20}_D$: -1.09 (c = 0.655, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with 2-(but-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the conjunctive cross-coupling/oxidation procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

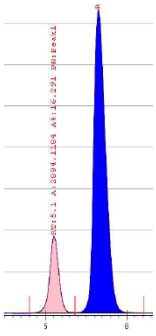
Chiral SFC (Chiracel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-3-(4-methoxybenzyl)heptan-3-ol.

Racemic Material

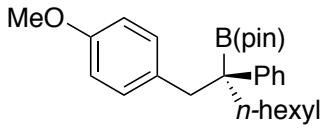


Peak No	% Area	Area	RT (min)
1	50.5891	6807.0834	5.03
2	49.4109	6648.554	5.62
Total:	100	13455.6374	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	16.291	2884.1184	5.1
2	83.709	14819.6338	5.65
Total:	100	17703.7522	



(*R*)-2-(1-(4-methoxyphenyl)-2-phenyloctan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.110). The reaction was performed according to the general procedure ***(Method A)*** with 4,4,5,5-tetramethyl-2-(oct-1-en-2-yl)-1,3,2-dioxaborolane (47.6 mg, 0.20 mmol, 1.00 equiv.), phenyl lithium (0.11 mL, 1.9 M in dibutyl ether, 0.20 mmol, 1.00 equiv.), 4-methoxyphenyl trifluoromethanesulfonate (56.4 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (72.7 mg, 86% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28-7.20 (m, 2H), 7.20-7.14 (m, 2H), 7.11 (td, J = 7.0, 1.3 Hz, 1H), 6.70 (d, J = 8.7 Hz, 2H), 6.62 (d, J = 8.6 Hz, 2H), 3.71 (s, 3H), 3.04 (d, J = 6.9 Hz, 2H), 1.82-1.64 (m, 2H), 1.33-1.15 (m, 22H), 0.85 (t, J = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 157.79, 145.57, 131.57, 131.26, 128.09, 128.00, 125.26, 112.91, 83.60, 55.27, 41.06, 33.59, 31.96, 30.26, 25.56, 25.00, 24.91, 22.83, 14.26; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.12; IR (neat): ν_{max} 2976.5 (m), 2929.3 (m), 2857.3 (w), 1511.0 (s), 1464.4 (m), 1371.2 (m), 1301.6 (m), 1247.7 (s), 1144.4 (s), 1037.8 (m), 852.5 (m), 700.0 (m) cm^{-1}. HRMS (DART) for $C_{27}H_{40}BO_3$ $[M+H]^+$: calculated: 423.3071, found: 423.3078. $[\alpha]^{20}_D$: -28.96 (c = 1.410, $CHCl_3$, l = 50 mm).

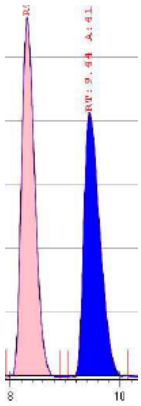
Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with 4,4,5,5-tetramethyl-2-(oct-1-en-2-yl)-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation*

procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

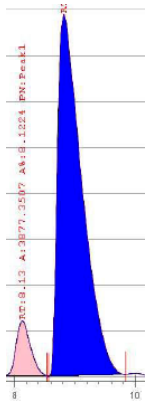
Chiral SFC (Chiracel ODR-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(4-methoxyphenyl)-2-phenyloctan-2-ol.

Racemic Material

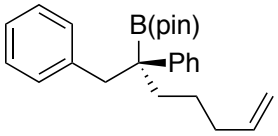


Peak No	% Area	Area	RT (min)
1	52.9461	4708.6986	8.3
2	47.0539	4184.6851	9.44
Total:	100	8893.3837	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	8.1224	3877.3507	8.13
2	91.8776	43859.2344	8.82
Total:	100	47736.5851	



(*S*)-2-(1,2-diphenylhept-6-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.112). The reaction was performed according to the general procedure ***(Method A)*** with 2-(hepta-1,6-dien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (44.4 mg, 0.20 mmol, 1.00 equiv.), phenyl lithium (0.11 mL, 1.9 M in dibutyl ether, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.) in THF (0.8 mL, 0.25 M) at 60 °C. The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (67.5 mg, 89% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ

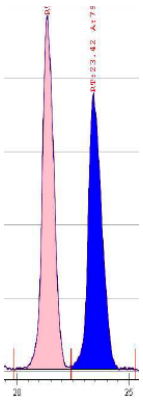
7.35-7.20 (m, 4H), 7.20-7.10 (m, 4H), 6.87 (dd, J = 6.3, 2.9 Hz, 2H), 5.94-5.73 (m, 1H), 5.01 (dd, J = 17.2, 1.8 Hz, 1H), 4.95 (dd, J = 10.3, 2.0 Hz, 1H), 3.16 (s, 2H), 2.16-1.99 (m, 2H), 1.92-1.72 (m, 2H), 1.54-1.39 (m, 2H), 1.24 (d, J = 16.2 Hz, 12H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.31, 139.49, 139.13, 130.39, 128.08, 128.01, 127.55, 125.85, 125.39, 114.45, 83.69, 41.80, 34.63, 33.27, 25.01, 24.99, 24.89; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 33.71; IR (neat): ν_{max} 2977.4 (m), 2932.5 (m), 2862.5 (w), 1496.1 (m), 1454.8 (m), 1371.0 (m), 1313.6 (m), 1142.7 (s), 909.6 (m), 856.4 (m), 700.4 (s) cm^{-1}. HRMS (DART) for $C_{25}H_{34}BO_2$ $[M+H]^+$: calculated: 377.2652, found: 377.2657. $[\alpha]^{20}_D$: -22.05 (c = 1.110, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with 2-(hepta-1,6-dien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (1.0 mol%), (S_p, S_p)-**3.141** (0.6 mol%), and (R_p, R_p)-**3.141** (0.6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the conjunctive cross-coupling/oxidation procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

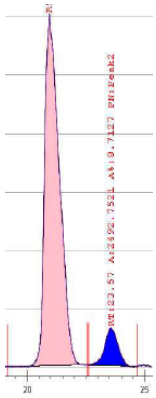
Chiral SFC (Chiracel AD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1,2-diphenylhept-6-en-2-ol.

Racemic Material

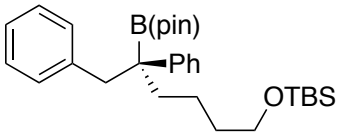


Peak No	% Area	Area	RT (min)
1	52.308	8699.9302	21.36
2	47.692	7932.2036	23.42
Total:	100	16632.1338	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	91.2873	26117.8526	20.94
2	8.7127	2492.7521	23.57
Total:	100	28610.6047	



(*S*)-*tert*-butyl((7,8-diphenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octyl)oxy)dimethylsilane (3.113). The reaction was performed according to the general procedure ***(Method A)*** with *tert*-butyldimethyl((5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-1-yl)oxy)silane (68.1 mg, 0.20 mmol, 1.00 equiv.), phenyl lithium (0.11 mL, 1.9 M in dibutyl ether, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.) in THF (0.8 mL, 0.25 M) at 60 °C. The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (79.0 mg, 76% yield). ^{1}H NMR (600 MHz, $CDCl_3$): 7.27-7.21 (m, 2H), 7.21-7.17 (m, 2H), 7.16-7.11 (m, 1H), 7.11-7.07 (m, 3H), 6.84-6.80 (m, 2H), 3.65-3.52 (m, 2H), 3.12 (s, 2H), 1.83-1.65 (m, 2H), 1.55 -1.44 (m, 3H), 1.36-1.14 (m, 17H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$): 147.90, 142.00, 132.85, 131.35, 130.50, 129.98, 128.27, 127.79, 86.11, 65.89, 44.34,

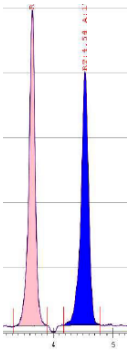
36.08, 35.53, 32.84, 28.65, 28.36, 28.07, 27.47, 27.40, 27.36, 21.03, -2.59. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.10. IR (neat) ν_{max} 2977.8 (m), 2929.6 (m), 2856.6 (m), 1496.3 (m), 1370.9 (m), 1311.3 (m), 1254.5 (m), 1212.9 (m), 1143.1 (s), 1100.1 (s), 1005.8 (m), 835.4 (s), 774.5 (m), 700.7 (m) cm^{-1}. HRMS (DART) for $C_{32}H_{52}BO_3Si$ $[M+H]^+$: calculated: 523.3779, found: 523.3779. $[\alpha]^{20}_D$: -16.61 (c = 0.650, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with *tert*-butyldimethyl((5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-1-yl)oxy)silane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

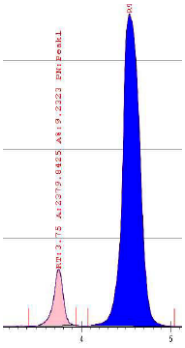
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-6-((tert-butyldimethylsilyl)oxy)-1,2-diphenylhexan-2-ol.

Racemic Material

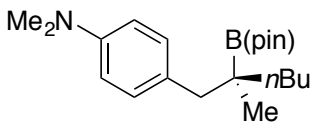


Peak No	% Area	Area	RT (min)
1	50.8847	1836.1111	3.64
2	49.1153	1772.267	4.54
Total:	100	3608.3781	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	9.2323	2379.8425	3.75
2	90.7677	23397.4572	4.54
Total:	100	25777.2997	



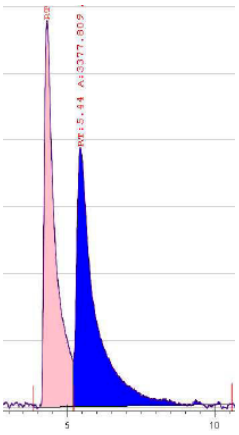
(*R*)-*N,N*-dimethyl-4-(2-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)aniline (3.123). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 4-bromo-*N,N*-dimethylaniline (44.0 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (57.5 mg, 83% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.05 (d, J = 8.7 Hz, 2H), 6.63 (d, J = 8.7 Hz, 2H), 2.88 (s, 6H), 2.68 (d, J = 13.4 Hz, 1H), 2.38 (d, J = 13.3 Hz, 1H), 1.49-1.37 (m, 1H), 1.34-1.12 (m, 17H), 0.94-0.80 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 149.10, 131.15, 128.66, 112.59, 83.16, 43.87, 41.14, 39.24, 28.51, 25.29, 25.01, 23.84, 21.32, 14.37; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.34; IR (neat): ν_{max} 2925.8 (m), 2858.4 (w), 1614.7 (m), 1519.7 (s), 1465.5 (m), 1378.1 (m), 1370.3 (m), 1342.8 (m), 1305.5 (s), 1214.9 (m), 1137.2 (s), 948.1 (m) cm^{-1}. HRMS (DART) for $C_{27}H_{37}BNO_2$ $[M+H]^+$: calculated: 346.2917, found: 346.2905. $[\alpha]^{20}_D$: -3.67 (c = 2.875, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (1.0 mol%), (S_p, S_p)-**3.141** (0.6 mol%), and (R_p, R_p)-**3.141** (0.6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

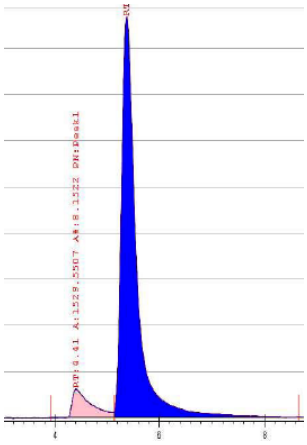
Chiral SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-N,N-dimethyl-4-(2-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)aniline.

Racemic Material

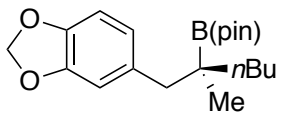


Peak No	% Area	Area	RT (min)
1	47.5159	3058.0657	4.3
2	52.4841	3377.809	5.44
Total:	100	6435.8747	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	8.1522	1529.5507	4.41
2	91.8478	17232.7821	5.37
Total:	100	18762.3328	



(*R*)-2-(1-(benzo[*d*][1,3]dioxol-5-yl)-2-methylhexan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.129). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 5-bromobenzo[*d*][1,3]dioxole (38.5 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (66.4 mg, 96% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.72 (s, 1H), 6.68 (d, J = 7.8 Hz, 1H), 6.64 (d, J = 7.9, 1H), 5.89 (s, 2H), 2.72 (d, J = 13.2 Hz, 1H), 2.37 (d, J =

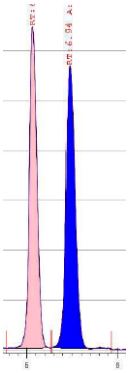
13.2 Hz, 1H), 1.44 (td, J = 11.8, 3.5 Hz, 1H), 1.35-1.15 (m, 17H), 0.97-0.82 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 146.88, 145.40, 134.05, 123.08, 110.75, 107.46, 100.55, 83.10, 44.58, 39.23, 28.17, 25.11, 24.80, 23.60, 21.15, 14.13. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.51. IR (neat) ν_{max} 2956.5 (m), 2927.3 (m), 2870.7 (m), 1503.3 (s), 1488.1 (s), 1467.2 (m), 1440.0 (m), 1371.1 (m), 1274.9 (m), 1246.2 (s), 1164.4 (s), 968.2 (s), 851.3 (m), 770.8 (m), 669.9 (m), 608.6 (m) cm^{-1}. HRMS (DART) for $C_{20}H_{32}BO_4$ $[M+H]^+$: calculated: 347.2394, found: 347.2383. $[\alpha]^{20}_D$: -4.83 (c = 1.605, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)-ferrocene (6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

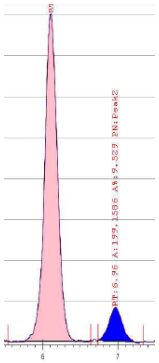
Chiral SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-(benzo[d][1,3]dioxol-5-yl)-2-methylhexan-2-ol.

Racemic Material

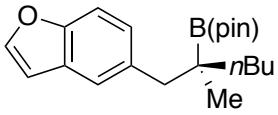


Peak No	% Area	Area	RT (min)
1	50.1598	3855.4563	6.12
2	49.8402	3830.8983	6.94
Total:	100	7686.3546	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	90.471	1890.8774	6.11
2	9.529	199.1586	6.96
Total:	100	2090.036	



(*R*)-2-(1-(benzofuran-5-yl)-2-methylhexan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.127). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 5-bromobenzofuran (43.3 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (63.0 mg, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57 (s, 1H), 7.42 (s, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.15 (d, J = 8.4 Hz, 1H), 6.68 (s, 1H), 2.91 (d, J = 13.2 Hz, 1H), 2.56 (d, J = 13.2 Hz, 1H), 1.50 (t, J = 11.6 Hz, 1H), 1.41-1.13 (m, 17H), 0.96-0.87 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 156.24, 147.37, 137.25, 129.57, 129.53, 125.03, 112.80, 109.00, 85.74, 47.39, 41.98, 30.89, 27.75, 27.47, 26.29, 23.84, 16.82. ^{11}B NMR (160

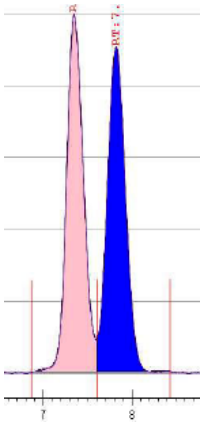
MHz, $CDCl_3$) δ 34.24. IR (neat) ν_{max} 2975.3 (m), 2956.5 (m), 2927.1 (m), 1466.9 (m), 1379.1 (m), 1340.9 (s), 1308.0 (s), 1261.8 (m), 1110.6 (s), 1032.2 (m), 968.4 (m), 851.9 (m), 734.3 (m) cm^{-1}. HRMS (DART) for $C_{21}H_{32}BO_3$ $[M+H]^+$: calculated: 343.2445, found: 343.2436. $[\alpha]^{20}_D$: -8.46 (c = 0.835, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl 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 compounds **3.105, 3.149, and 3.151**).

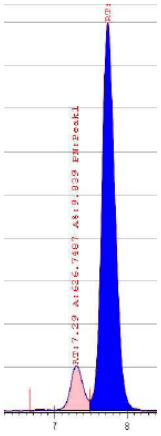
Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(benzofuran-5-yl)-2-methylhexan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

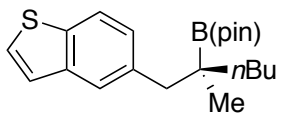


Peak No	% Area	Area	RT (min)
1	50.6292	3309.6612	7.34
2	49.3708	3227.3976	7.82
Total:	100	6537.0588	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	9.839	626.7487	7.29
2	90.161	5743.3208	7.74
Total:	100	6370.0695	



(*R*)-2-(1-(benzo[*b*]thiophen-5-yl)-2-methylhexan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.124). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 5-bromobenzo[*b*]thiophene (46.9 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (61.0 mg, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.3 Hz, 1H), 7.66 (d, *J* = 1.6 Hz, 1H), 7.38 (d, *J* = 5.4 Hz, 1H), 7.30-7.17 (m, 2H), 2.94 (d, *J* = 13.1 Hz, 1H), 2.60 (d, *J* = 13.1 Hz, 1H), 1.54-1.46 (m, 1H), 1.43-1.13 (m, 17H), 0.97-0.85 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.48, 137.15, 136.35, 127.31, 125.95, 124.94, 123.60, 121.36, 83.11, 44.71, 39.34, 28.20, 25.07, 24.84, 23.62, 21.22, 14.15. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.46. IR (neat) ν_{max} 2974.8 (m), 2956.3 (m), 2927.0 (m), 2858.5 (m), 1466.4 (m), 1420.5 (m), 1379.0 (m), 1348.0 (m), 1308.7 (s), 1272.7 (m), 1163.4 (m), 1140.3 (s), 1087.8 (m), 968.4 (m), 832.6 (m), 768.2 (m) cm^{-1}. HRMS (DART) for $C_{21}H_{32}BO_2S$ $[M+H]^+$: calculated: 359.2216, found: 359.2225. $[\alpha]^{20}_D$: -4.10 (c = 1.000, $CHCl_3$, *l* = 50 mm).

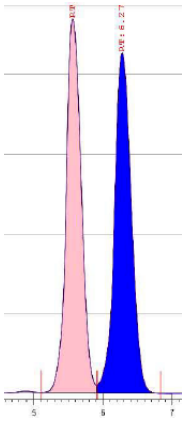
Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl 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 compounds **3.105, 3.149, and 3.151**).

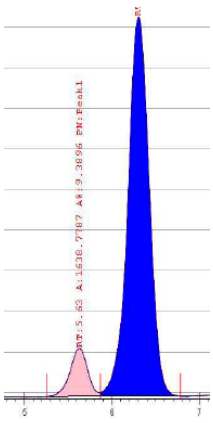
Chiral SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(benzo[b]thiophen-5-yl)-2-methylhexan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

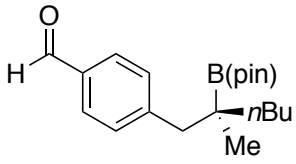


Peak No	% Area	Area	RT (min)
1	49.6956	35515.3238	5.56
2	50.3044	35950.4448	6.27
Total:	100	71465.7686	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	9.3896	1638.7787	5.63
2	90.6104	15814.3513	6.3
Total:	100	17453.13	



(*R*)-4-(2-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)benzaldehyde (3.121). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 4-bromobenzaldehyde (40.7 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to

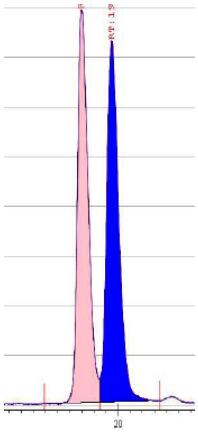
afford a colorless oil (53.4 mg, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ ^{1}H NMR 9.96 (s, 1H), 7.75 (d, *J* = 7.9 Hz, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 2.87 (d, *J* = 12.8 Hz, 1H), 2.54 (d, *J* = 12.8 Hz, 1H), 1.54-1.37 (m, 1H), 1.37-1.12 (m, 17H), 0.95-0.82 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.31, 148.32, 134.54, 131.16, 129.35, 83.48, 45.09, 39.50, 28.28, 25.26, 24.98, 23.73, 21.47, 14.29; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.27; IR (neat): ν_{max} 2975.7 (m), 2928.5 (m), 2858.5 (w), 1700.8 (s), 1605.7 (m), 1466.8 (m), 1380.8 (m), 1309.0 (m), 1214.0 (m), 1139.0 (s), 968.3 (w), 851.4 (m) cm^{-1}. HRMS (DART) for $C_{20}H_{32}BO_3$ $[M+H]^+$: calculated: 331.2445, found: 331.2457. $[\alpha]^{20}_D$: -3.53 (c = 1.090, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diphenylphosphino)ferrocene (6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

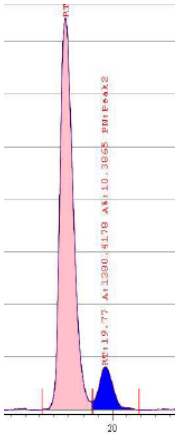
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-4-(2-hydroxy-2-methylhexyl)benzaldehyde.

Racemic Material

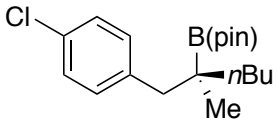


Peak No	% Area	Area	RT (min)
1	49.0217	12179.4416	18.48
2	50.9783	12665.5684	19.74
Total:	100	24845.01	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	89.6135	11910.1133	18.39
2	10.3865	1380.4178	19.77
Total:	100	13290.5311	



(*R*)-2-(1-(4-chlorophenyl)-2-methylhexan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.122). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 1-bromo-4-chlorobenzene (42.1 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M) at 60 °C. The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (64.6 mg, 96% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.19 (d, J = 8.2 Hz, 2H), 7.13 (d, J = 8.2 Hz, 2H), 2.76 (d, J = 13.1 Hz, 1H), 2.43 (d, J = 13.2 Hz, 1H), 1.43 (td, J = 12.1, 3.6 Hz, 1H), 1.36-1.13 (m, 17H), 1.00-0.78 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 141.35, 134.32, 134.04, 130.30, 85.83, 46.65, 41.81, 30.79, 27.72, 27.45,

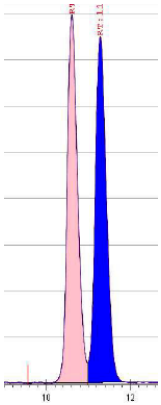
26.23, 23.80, 16.78. ^{11}B NMR: (160 MHz, Chloroform-*d*) δ 34.48. IR (neat) ν_{max} 2976.5 (m), 2957.2 (m), 2859.1 (m), 1490.8 (m), 1466.4 (m), 1378.7 (s), 1309.3 (s), 1272.4 (m), 1164.7 (s), 1092.1 (m), 968.1 (m), 853.4 (m), 787.1 (m), 727.7 (m), 579.2 (m) cm^{-1}. HRMS (DART) for $C_{19}H_{31}BClO_2$ $[M+H]^+$: calculated: 337.2105, found: 337.2114. $[\alpha]^{20}_D$: -3.60 (c = 0.855, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)-ferrocene (6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the conjunctive cross-coupling/oxidation procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

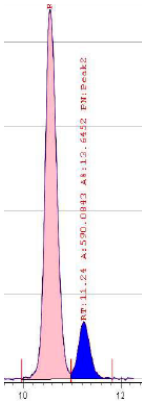
Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-(4-chlorophenyl)-2-methylhexan-2-ol.

Racemic Material

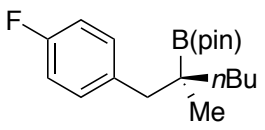


Peak No	% Area	Area	RT (min)
1	49.8201	6885.3541	10.61
2	50.1799	6935.0792	11.28
Total:	100	13820.4333	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	86.3548	3734.3985	10.55
2	13.6452	590.0843	11.24
Total:	100	4324.4828	



(*R*)-2-(1-(4-fluorophenyl)-2-methylhexan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.128). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 1-bromo-4-fluorobenzene (38.5 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (58.8 mg, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.15 (dd, J = 8.3, 5.5 Hz, 2H), 6.91 (dd, J = 10.0, 7.6 Hz, 2H), 2.77 (d, J = 13.3 Hz, 1H), 2.43 (d, J = 13.2 Hz, 1H), 1.43 (dt, J = 12.0, 5.9 Hz, 1H), 1.37-1.12 (m, 17H), 1.01-0.77 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 161.29 (d, $^1J_{C–F}$ = 243.1 Hz), 135.81, 131.60 (d, $^3J_{C–F}$ = 7.6 Hz), 114.22 (d, $^2J_{C–F}$ = 20.7 Hz) 83.12, 43.88, 39.17, 28.14, 25.06, 24.76, 23.58, 21.13, 14.11. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.53. ^{19}F NMR: (470 MHz, $CDCl_3$) δ -118.28. IR (neat) ν_{max} 2977.1 (m), 2957.6 (m), 2928.3 (m), 2859.8 (m), 1602.9 (m), 1508.8 (s), 1466.6 (m), 1379.1 (s), 1309.1 (s), 1157.9 (s), 1112.3 (m), 1093.1 (m), 968.3 (m), 852.98 (m), 767.4 (m), 669.9 (m) cm^{-1}. HRMS (DART) for $C_{19}H_{31}BFO_2$ $[M+H]^+$: calculated: 321.2401, found: 321.2408. $[\alpha]^{20}_D$: -4.21 (c = 1.615, $CHCl_3$, l = 50 mm).

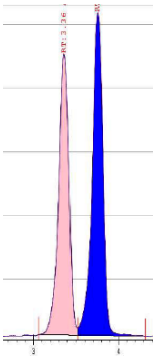
Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (1.0 mol%), (S_p, S_p)-**3.141** (0.6 mol%), and (R_p, R_p)-**3.141** (0.6 mol%) as the catalyst. The product was oxidized with

NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation procedure*, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

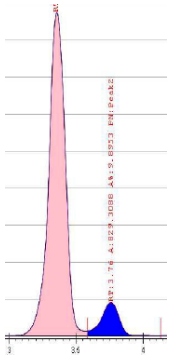
Chiral SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-(4-fluorophenyl)-2-methylhexan-2-ol.

Racemic Material

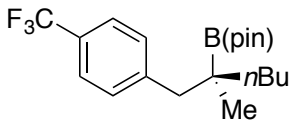


Peak No	% Area	Area	RT (min)
1	44.9309	1850.1542	3.36
2	55.0691	2267.624	3.75
Total:	100	4117.7782	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	90.1047	7551.4868	3.35
2	9.8953	829.3088	3.76
Total:	100	8380.7956	



(*R*)-4,4,5,5-tetramethyl-2-(2-methyl-1-(4-(trifluoromethyl)phenyl)-hexan-2-yl)-1,3,2-dioxaborolane (3.126). The reaction was performed according to the general procedure ***(Method A)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 4-(trifluoromethyl)phenyl trifluoromethanesulfonate (64.7 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (67.4 mg, 91% yield). ^{1}H

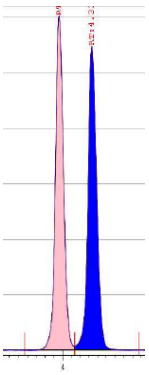
NMR (600 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.9 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 2.85 (d, *J* = 13.0 Hz, 1H), 2.52 (d, *J* = 12.9 Hz, 1H), 1.44 (td, *J* = 11.9, 3.5 Hz, 1H), 1.37-1.10 (m, 17H), 1.01-0.77 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 144.48, 130.54, 127.95 (partially buried, q, $^2J_{C–F}$ = 32.4 Hz), 124. 46 (partially buried, q, $^1J_{C–F}$ = 271.3 Hz), 124.43 (q, $^3J_{C–F}$ = 3.8 Hz), 83.24, 44.41, 39.18, 28.11, 25.02, 24.77, 23.54, 21.19, 14.08. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.39. ^{19}F NMR: ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.28 IR (neat) ν_{max} 2958.8 (m), 2929.4 (m), 2860.9 (m), 1617.9 (m), 1467.6 (m), 1380.4 (m), 1322.7 (s), 1273.4 (m), 1118.7 (s), 1066.7 (s), 1019.7 (m), 968.1 (m), 826.7 (m), 696.3 (m) cm^{-1}. HRMS (DART) for $C_{20}H_{34}BF_3O_3N$ $[M+NH_4]^+$: calculated: 388.2635, found: 388.2656. $[\alpha]^{20}_D$: -1.96 (c = 2.100, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)-ferrocene (6 mol%) as the catalyst.. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

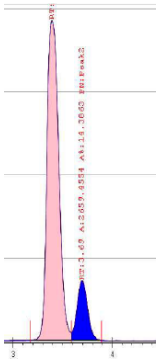
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-2-methyl-1-(4-(trifluoromethyl)phenyl)hexan-2-ol.

Racemic Material

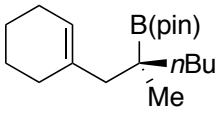


Peak No	% Area	Area	RT (min)
1	50.4514	7738.8905	3.96
2	49.5486	7600.4205	4.33
Total:	100	15339.311	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	85.6137	15826.53	3.39
2	14.3863	2659.4554	3.69
Total:	100	18485.9854	

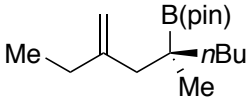


(*R*)-2-(1-(cyclohex-1-en-1-yl)-2-methylhexan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.131). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 1-bromocyclohex-1-ene (35.4 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (47.3 mg, 77% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.37 (s, 1H), 2.14 (d, J = 13.6 Hz, 1H), 2.00-1.82 (m, 4H), 1.76 (d, J = 13.6 Hz, 1H), 1.62-1.43 (m, 4H), 1.43-1.34 (m, 1H), 1.33-1.04 (m, 17H), 0.91-0.80 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 136.91, 123.11, 83.12, 48.18, 40.37, 30.44, 27.99, 25.51, 25.26, 25.09, 23.85, 23.30, 22.62, 21.69, 14.34; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.50; IR (neat): ν_{max} 2925.7 (s), 2857.7 (m), 1461.3 (m),

1386.2 (m), 1304.6 (s), 1224.5 (m), 1140.6 (s), 968.7 (w), 854.5 (m) cm^{-1}. HRMS (DART) for $C_{19}H_{36}BO_2$ $[M+H]^+$: calculated: 307.2808, found: 307.2804. $[\alpha]^{20}_D$: -16.45 (c = 1.120, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

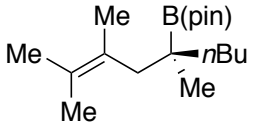


(*R*)-4,4,5,5-tetramethyl-2-(5-methyl-3-methylenenonan-5-yl)-1,3,2-dioxaborolane (3.130). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 2-bromobut-1-ene (29.7 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (43.2 mg, 77% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.72 (d, *J* = 1.8 Hz, 1H), 4.69 (d, *J* = 1.8 Hz, 1H), 2.24 (d, *J* = 14.1 Hz, 1H), 1.96 (d, *J* = 8.6 Hz, 2H), 1.87 (d, *J* = 14.1 Hz, 1H), 1.43-1.37 (m, 1H), 1.34-1.11 (m, 17H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.91-0.81 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 150.40, 109.82, 83.20, 45.96, 40.31, 30.29, 27.94, 25.26, 25.06, 25.05, 23.83, 21.58, 14.33, 12.69; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.60; IR (neat): ν_{max} 2928.4 (m), 2872.7 (w), 1641.4 (w), 1464.2 (m), 1370.8 (m), 1306.3 (m), 1217.0 (m), 1140.0 (s),

889.4 (m), 852.7 (m), cm^{-1}. HRMS (DART) for $C_{17}H_{34}BO_2$ $[M+H]^+$: calculated: 281.2652, found: 281.2663. $[\alpha]^{20}_D$: -8.26 (c = 1.235, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).



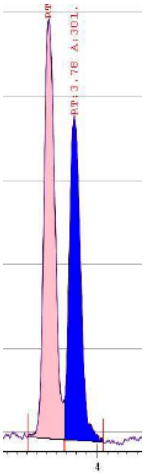
(*R*)-4,4,5,5-tetramethyl-2-(2,3,5-trimethylnon-2-en-5-yl)-1,3,2-dioxaborolane (3.132). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 2-bromo-3-methylbut-2-ene (32.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M) at 60 °C. The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (44.1 mg, 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.14 (d, *J* = 13.4 Hz, 1H), 2.08 (d, *J* = 13.4 Hz, 1H), 1.72-1.55 (m, 9H), 1.51-1.42 (m, 1H), 1.36-1.09 (m, 17H), 0.93-0.79 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 126.90, 125.95, 83.12, 43.74, 40.97, 28.46, 25.36, 25.08, 25.00, 23.93, 21.43, 21.19, 20.99, 20.19, 14.34; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.20; IR (neat): ν_{max} 2926.7 (m), 2860.1 (w), 1466.4 (w), 1370.6 (m), 1305.6 (m), 1141.0 (s), 968.6 (w), 850.7 (w) cm^{-1}. HRMS (DART) for $C_{18}H_{36}BO_2$ $[M+H]^+$: calculated: 295.2808, found: 295.2804. $[\alpha]^{20}_D$: -4.12 (c = 1.055, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and and $Pd(OAc)_2$ (1.0 mol%), (S_p, S_p)-**3.141** (0.6 mol%), and (R_p, R_p)-**3.141** (0.6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

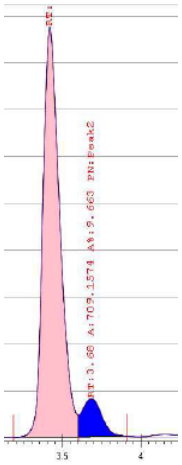
Chiral SFC (Chiracel OD-H, 0% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-2,3,5-trimethylnon-2-en-5-ol.

Racemic Material

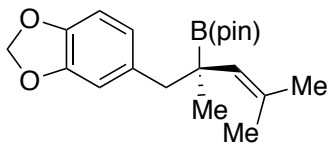


Peak No	% Area	Area	RT (min)
1	55.7398	379.8018	3.52
2	44.2602	301.5819	3.78
Total:	100	681.3837	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	90.337	6629.7175	3.41
2	9.663	709.1574	3.68
Total:	100	7338.8749	



(*S*)-2-(1-(benzo[*d*][1,3]dioxol-5-yl)-2,4-dimethylpent-3-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.108). The reaction was performed according to the general procedure ***(Method D)*** with modification. Using isopropenyl boronic acid pinacol ester (33.6 mg,

0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.), 1-bromo-2-methylprop-1-ene (27.0 mg, 0.20 mmol, 1.00 equiv.), benzo[*d*][1,3]dioxol-5-yl trifluoromethanesulfonate (59.4 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (75.2 mg, 0.40 mmol, 2.00 equiv.) in THF (0.8 mL, 0.25 M). The reaction mixture was allowed to warm to room temperature after adding the *tert*-butyl lithium. The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (60 mg, 87% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.75-6.65 (m, 2H), 6.62 (dd, *J* = 7.9, 1.6 Hz, 1H), 5.94-5.85 (m, 2H), 5.01 (p, *J* = 1.4 Hz, 1H), 2.74 (d, *J* = 13.2 Hz, 1H), 2.64 (d, *J* = 13.2 Hz, 1H), 1.69 (d, *J* = 1.4 Hz, 3H), 1.55 (d, *J* = 1.4 Hz, 3H), 1.24 (d, *J* = 16.6 Hz, 12H), 1.03 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 145.44, 133.60, 131.75, 123.58, 111.11, 107.29, 100.51, 83.24, 44.23, 30.71, 26.51, 25.02, 24.69, 23.53, 20.05. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.06. IR (neat): ν_{max} 2976.0 (m), 2924.6 (m), 1503.0 (m), 1488.4 (s), 1458.0 (m), 1379.4 (m), 1336.9 (m), 1275.6 (m), 1212.0 (s), 1143.4 (m), 1101.9 (s), 1040.3 (m), 933.5 (m), 811.2 (m) cm^{-1}. HRMS (DART) for $C_{20}H_{30}BO_4$ $[M+H]^+$: calculated: 345.2237, found: 345.2249. $[\alpha]^{20}_D$: -48.84 (c = 1.000, $CHCl_3$, *l* = 50 mm).

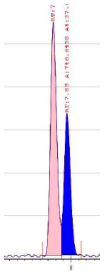
Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (1.0 mol%), (S_p, S_p)-**3.141** (0.6 mol%), and (R_p, R_p)-**3.141** (0.6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure, and

the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

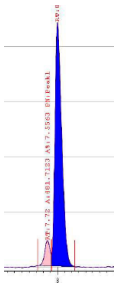
Chiral SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 25 °C, 210-270 nm) – analysis of (R)-1-(benzo[d][1,3]dioxol-5-yl)-2,4-dimethylpent-3-en-2-ol.

Racemic Material

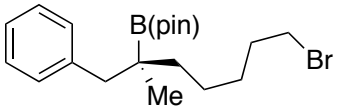


Peak No	% Area	Area	RT (min)
1	62.3105	1234.4004	7.54
2	37.6895	746.6458	7.89
Total:	100	1981.0462	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	7.5563	481.7123	7.72
2	92.4437	5893.2588	8
Total:	100	6374.9711	



(*R*)-2-(7-bromo-2-methyl-1-phenylheptan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.114). The reaction was performed according to the general procedure ***(Method C)*** with 2-bromopropene (24.2 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.), 2-(5-bromopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (55.4 mg, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.90 mg, 0.004 mmol, 0.020 equiv.), (S_p, S_p)-**3.92** (4.60 mg, 0.0044 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (75.2 mg, 0.40 mmol, 2.00 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (57.4 mg, 73% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34-7.04 (m, 5H), 3.40 (t, J = 6.9

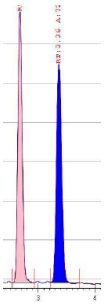
Hz, 2H), 2.77 (d, *J* = 13.0, 1H), 2.49 (d, *J* = 13.0 Hz, 1H), 1.96-1.75 (m, 2H), 1.49-1.12 (m, 18H), 0.88 (s, 3H). ^{13}C NMR (MHz, $CDCl_3$): (151 MHz, $CDCl_3$) δ 142.59, 132.99, 130.26, 128.32, 85.82, 47.37, 41.71, 36.59, 35.36, 31.62, 27.74, 27.71, 27.46, 23.86. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.60. IR (neat) ν_{max} 3028.0 (m), 2976.6 (m), 2929.9 (m), 2857.5 (m), 1494.3 (m), 1380.1 (s), 1371.0 (s), 1309.4 (s), 1250.4 (m), 1228.6 (m), 1164.5 (s), 1109.8 (m), 967.8 (m), 748.1 (m), 670.2 (m) cm^{-1}. HRMS (DART) for $C_{20}H_{33}BBrO_2$ $[M+H]^+$: calculated: 395.1757, found: 395.1751. $[\alpha]^{20}_D$: -7.28 (c = 0.965, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with 2-(5-bromopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

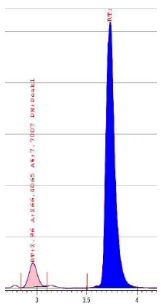
Chiral SFC (Chiracel ODR-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(7-bromo-2-methyl-1-phenylheptan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

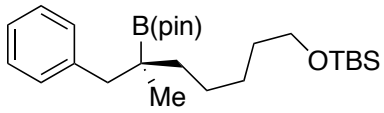


Peak No	% Area	Area	RT (min)
1	50.7099	748.9426	2.67
2	49.2901	727.9746	3.36
Total:	100	1476.9172	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	7.7007	266.4065	2.96
2	92.2993	3193.0848	3.73
Total:	100	3459.4913	



(*R*)-*tert*-butyldimethyl((6-methyl-7-phenyl-6-(4,4,5,5-tetra-methyl-1,3,2-dioxaborolan-2-yl)heptyl)oxy)silane (3.115). The reaction was performed according to the general procedure ***(Method C)*** with 2-bromopropene (24.2 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.), *tert*-butyldimethyl((5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)oxy)silane (65.7 mg, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.90 mg, 0.004 mmol, 0.020 equiv.), (S_p, S_p)-**3.92** (4.60 mg, 0.0044 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (75.2 mg, 0.40 mmol, 2.00 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (55.2 mg, 62% yield). ^{1}H NMR (600 MHz, $CDCl_3$): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24-7.08 (m, 5H), 3.59 (t, J = 6.7 Hz, 2H), 2.79 (d, J = 13.1 Hz, 1H), 2.47 (d, J = 13.1 Hz, 1H), 1.54-1.48 (m, 2H), 1.38-1.12 (m, 20H), 0.94-0.84 (m, 12H), 0.04 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$): (151 MHz, $CDCl_3$) δ 142.78, 133.01, 130.22, 128.25, 85.76, 65.98, 47.40, 42.16, 35.58, 29.36, 28.64, 28.46, 27.73, 27.46, 27.44, 23.84, -2.59. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.27. IR (neat) ν_{max} 2976.0 (m), 2929.4 (m), 2856.9 (m), 1469.9 (m), 1380.5 (m), 1371.1 (m), 1254.2 (m), 1212.4 (m), 1099.7 (s), 968.2 (m), 834.7 (s), 813.3 (m), 775.0 (m), 702.3 (m) cm^{-1}. HRMS (DART) for $C_{26}H_{48}BO_3Si$ $[M+H]^+$: calculated: 447.3466, found: 447.3480. $[\alpha]^{20}_D$: -2.28 (c = 0.800, $CHCl_3$, l = 50 mm).

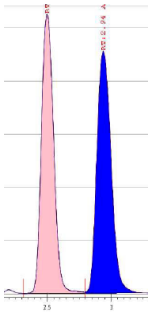
Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with *tert*-butyldimethyl((5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)oxy)silane, and

$Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)-ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

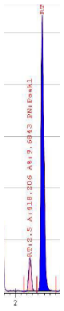
Chiral SFC (Chiracel ODR-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-tert-butyldimethyl((6-methyl-7-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)heptyl)oxy)silane.

Racemic Material

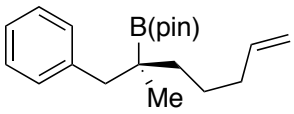


Peak No	% Area	Area	RT (min)
1	49.771	1738.422	2.5
2	50.229	1754.4185	2.94
Total:	100	3492.8405	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	9.6843	418.206	2.5
2	90.3157	3900.2017	2.93
Total:	100	4318.4077	



(*R*)-4,4,5,5-tetramethyl-2-(2-methyl-1-phenylhept-6-en-2-yl)-1,3,2-dioxaborolane (3.117). The reaction was performed according to the general procedure ***(Method C)*** with 2-bromopropene (24.2 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.), 4,4,5,5-tetramethyl-2-(pent-4-en-1-yl)-1,3,2-dioxaborolane (39.2 mg, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.90 mg, 0.004 mmol, 0.020 equiv.), (S_p, S_p)-**3.92** (4.60 mg, 0.0044 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (75.2 mg, 0.40 mmol, 2.00 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel

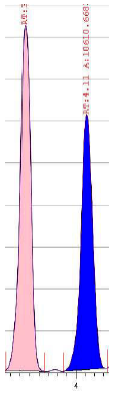
chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (33.4 mg, 53% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30-7.08 (m, 5H), 5.90-5.72 (m, 1H), 5.00 (dd, *J* = 17.5, 1.7 Hz, 1H), 4.94 (d, *J* = 10.3 Hz, 1H), 2.80 (d, *J* = 13.1 Hz, 1H), 2.49 (d, *J* = 13.1 Hz, 1H), 2.11-1.97 (m, 2H), 1.54-1.33 (m, 3H), 1.31-1.17 (m, 13H), 0.90 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): (151 MHz, Chloroform-*d*) δ 142.72, 141.75, 133.01, 130.24, 128.28, 116.83, 85.80, 47.41, 41.69, 37.30, 28.04, 27.75, 27.46, 23.85. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.41. IR (neat) ν_{max} 3062.1 (m), 3028.1 (m), 2929.2 (m), 2861.9 (m), 1640.3 (m), 1494.6 (m), 1380.7 (s), 1371.0 (s), 1349.6 (m), 1309.0 (s), 1212.9 (m), 1142.6 (s), 1031.3 (m), 967.6 (m), 748.4 (m) cm^{-1}. HRMS (DART) for $C_{20}H_{32}BO_2$ $[M+H]^+$: calculated: 315.2495, found: 315.2489. $[\alpha]^{20}_D$: -10.15 (c = 0.650, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with 4,4,5,5-tetramethyl-2-(pent-4-en-1-yl)-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)-ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

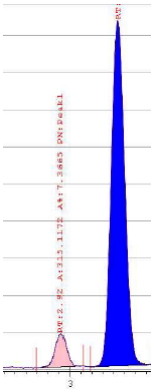
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4,4,5,5-tetramethyl-2-(2-methyl-1-phenylhept-6-en-2-yl)-1,3,2-dioxaborolane.

Racemic Material

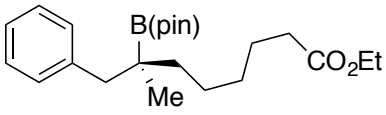


Peak No	% Area	Area	RT (min)
1	54.2936	12604.1579	3.45
2	45.7064	10610.6683	4.11
Total:	100	23214.8262	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	7.3665	315.1172	2.92
2	92.6335	3962.5782	3.44
Total:	100	4277.6954	



ethyl (*R*)-7-methyl-8-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octanoate (3.116). The reaction was performed according to the general procedure ***(Method C)*** with 2-bromopropene (24.2 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.), ethyl 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexanoate (54.0 mg, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.90 mg, 0.004 mmol, 0.020 equiv.), (S_p, S_p)-**3.92** (4.60 mg, 0.0044 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (75.2 mg, 0.40 mmol, 2.00 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (34.0 mg, 44% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.25-7.09 (m, 5H), 4.12 (q, J = 7.1 Hz, 2H), 2.77 (d, J = 13.1 Hz, 1H), 2.48 (d, J = 13.1 Hz, 1H), 2.28 (t, J = 7.6 Hz, 3H), 1.71-1.60 (m, 2H), 1.45 (td, J = 12.5, 3.4 Hz, 1H), 1.40-1.13 (m,

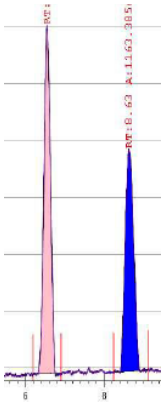
19H), 0.88 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): (151 MHz, Chloroform-*d*) δ 176.52, 142.69, 133.00, 130.23, 128.27, 85.78, 62.79, 47.38, 41.85, 37.04, 32.68, 28.25, 27.73, 27.64, 27.44, 23.83, 16.91. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.82. IR (neat) ν_{max} 3027.8 (m), 2977.3 (m), 2929.9 (m), 2858.6 (m), 1735.0 (s), 1602.9 (m), 1494.4 (m), 1349.0 (s), 1308.4 (s), 1251.8 (m), 1211.5 (m), 1143.1 (s), 1061.4 (m), 968.2 (m), 748.3 (m), 597.6 (m) cm^{-1}. HRMS (DART) for $C_{23}H_{38}BO_4$ $[M+H]^+$: calculated: 389.2863, found: 389.2866. $[\alpha]^{20}_D$: -8.26 (c = 0.690, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with ethyl 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexanoate, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

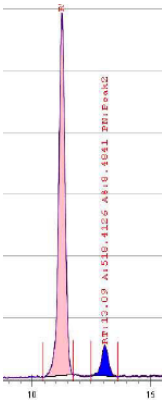
Chiral SFC (Chiracel OD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of ethyl (R)-7-methyl-8-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octanoate.

Racemic Material

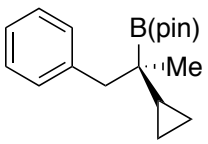


Peak No	% Area	Area	RT (min)
1	55.1931	1433.0577	6.55
2	44.8069	1163.3856	8.63
Total:	100	2596.4433	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	91.5159	5592.0214	11.25
2	8.4841	518.4126	13.09
Total:	100	6110.434	



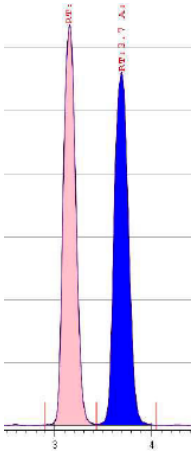
(*S*)-2-(2-cyclopropyl-1-phenylpropan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.120). The reaction was performed according to the general procedure ***(Method C)*** with 2-bromopropene (24.2 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.), 2-cyclopropyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (33.6 mg, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.90 mg, 0.004 mmol, 0.020 equiv.), (S_p, S_p)-**3.92** (4.60 mg, 0.0044 mmol, 0.022 equiv.), and potassium trifluoromethanesulfonate (75.2 mg, 0.40 mmol, 2.00 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (34.8 mg, 60%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31-7.21 (m, 4H), 7.21-7.13 (m, 1H), 2.89 (d, J = 12.9 Hz, 1H), 2.62 (d, J = 12.9 Hz, 1H), 1.22 (d, J = 26.6 Hz, 12H), 0.79 (s, 3H), 0.76-0.69 (m, 1H), 0.47-0.19 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 140.47, 130.63, 127.68, 125.74, 83.29, 45.44, 25.12, 24.91, 24.86, 19.49, 19.15, 1.79, 0.98; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 33.65; IR (neat): ν_{max} 2977.3 (m), 2926.8 (w), 1454.4 (m), 1388.2 (m), 1307.8 (m), 1211.7 (m), 1143.8 (s), 861.0 (m), 701.7 (m) cm^{-1}. HRMS (DART) for $C_{18}H_{28}BO_2$ $[M+H]^+$: calculated: 287.2182, found: 287.2172. $[\alpha]^{20}_D$: -15.27 (c = 0.780, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with 2-cyclopropyl-4,4,5,5-tetramethyl-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 compounds **3.105, 3.149, and 3.151**).

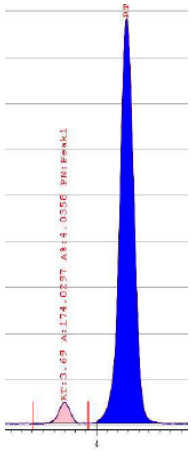
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-2-(2-cyclopropyl-1-phenylpropan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

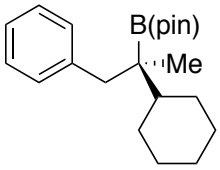


Peak No	% Area	Area	RT (min)
1	49.9977	2852.9164	3.15
2	50.0023	2853.1799	3.7
Total:	100	5706.0963	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	4.0358	174.0297	3.69
2	95.9642	4138.1398	4.28
Total:	100	4312.1695	



(*S*)-2-(2-cyclohexyl-1-phenylpropan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.119). The reaction was performed according to the general procedure ***(Method C)*** with 2-bromopropene (24.2 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.), 2-cyclohexyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (42.0 mg, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.90 mg, 0.004 mmol, 0.020 equiv.), (S_p, S_p)-**3.92** (4.60 mg, 0.0044 mmol, 0.022 equiv.), and potassium trifluoromethanesulfonate (75.2 mg, 0.40 mmol, 2.00 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (45.8 mg, 69%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29-7.17 (m, 4H), 7.17-7.07 (m, 1H),

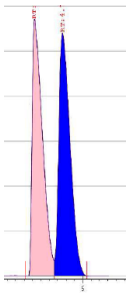
2.85 (d, J = 12.9 Hz, 1H), 2.47 (d, J = 12.9 Hz, 1H), 1.93-1.61 (m, 5H), 1.38-1.06 (m, 17H), 1.01 (qd, J = 12.6, 3.3 Hz, 1H), 0.85 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 141.13, 130.74, 130.73, 127.71, 127.70, 125.71, 83.22, 46.36, 43.10, 30.37, 28.15, 27.99, 27.38, 27.36, 27.32, 27.15, 26.95, 25.67, 24.95, 24.93, 18.08; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.01; IR (neat): ν_{max} 2977.1 (m), 2922.5 (m), 2850.7 (m), 1449.5 (m), 1370.7 (m), 1309.1 (m), 1141.8 (s), 967.5 (m), 854.2 (m), 746.6 (m), 700.6 (m) cm^{-1}. HRMS (DART) for $C_{21}H_{34}BO_2$ $[M+H]^+$: calculated: 329.2652, found: 329.2651. $[\alpha]^{20}_D$: -5.47 (c = 1.650, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with 2-cyclohexyl-4,4,5,5-tetramethyl-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 compounds **3.105, 3.149, and 3.151**).

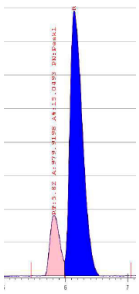
Chiral SFC (Chiracel ODR-H, 0% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-2-(2-cyclohexyl-1-phenylpropan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

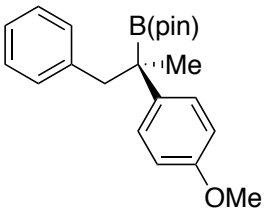


Peak No	% Area	Area	RT (min)
1	49.2909	4858.1719	4.42
2	50.7091	4997.9571	4.76
Total:	100	9856.129	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	15.0493	979.9198	5.82
2	84.9507	5531.4596	6.14
Total:	100	6511.3794	



(*S*)-2-(2-(4-methoxyphenyl)-1-phenylpropan-2-yl)-4,4,5,5-tetramethyl -1,3,2-dioxaborolane (3.118). The reaction was performed according to the general procedure ***(Method C)*** with 2-bromopropene (24.2 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.24 mL, 1.7 M in pentane, 0.40 mmol, 2.00 equiv.), 2-(4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (46.8 mg, 0.20 mmol, 1.00 equiv.), phenyl trifluoromethanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.90 mg, 0.004 mmol, 0.020 equiv.), (S_p, S_p)-**3.92** (4.60 mg, 0.0044 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (75.2 mg, 0.40 mmol, 2.00 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (49.0 mg, 70% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.25-7.20 (m, 2H), 7.20-7.09 (m, 3H), 7.03-6.96 (m, 2H), 6.87-6.77 (m, 2H), 3.80 (s, 3H), 3.16 (d, J = 13.1 Hz, 1H), 2.90 (d, J = 13.1 Hz, 1H), 1.25 (s, 3H), 1.20 (d, J = 20.0 Hz, 12H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 159.91, 142.32, 141.12, 133.09, 130.71, 130.06, 128.35, 116.00, 86.11, 57.83, 48.46, 27.42, 27.14, 23.33. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 33.78. IR (neat) ν_{max} 2976.4 (m), 2932.5 (m), 1606.4 (m), 1509.6 (s), 1495.5 (m), 1372.2 (m), 1290.3 (m), 1247.5 (s), 1183.4 (m), 1165.9 (m), 1143.8 (s), 1093.5 (m), 1033.3 (m), 863.6 (m), 801.8 (m), 701.6 (m) cm^{-1}. HRMS (DART) for $C_{22}H_{33}BO_3N$ $[M+NH_4]^+$: calculated: 370.2553, found: 370.2541. $[\alpha]^{20}_D$: -42.94 (c = 0.950, $CHCl_3$, l = 50 mm).

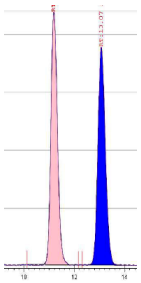
Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with 2-(4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and

1,1′-Bis(diisopropylphosphino)-ferrocene (6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

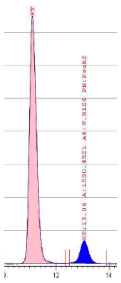
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-methoxyphenyl)-1-phenylpropan-2-ol.

Racemic Material

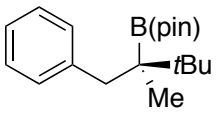


Peak No	% Area	Area	RT (min)
1	50.367	3975.5244	11.18
2	49.633	3917.5846	13.07
Total:	100	7893.109	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	90.1876	13790.9857	11.11
2	9.8124	1500.4521	13.06
Total:	100	15291.4378	



(*S*)-4,4,5,5-tetramethyl-2-(2,3,3-trimethyl-1-phenylbutan-2-yl)-1,3,2-dioxaborolane (3.133). The reaction was performed according to the general procedure ***(Method A)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.12 mL, 1.7 M in pentane, 0.20 mmol, 1.00 equiv.), phenyl trifluoro-methanesulfonate (49.8 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to afford a

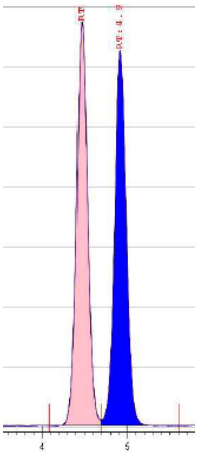
colorless oil (53.4 mg, 88% yield). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.27 (d, *J* = 7.9 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 2H), 7.14 (t, *J* = 7.3 Hz, 1H), 3.09 (d, *J* = 12.5 Hz, 1H), 2.31 (d, *J* = 12.5 Hz, 1H), 1.18 (d, *J* = 85.1 Hz, 12H), 1.01 (s, 9H), 0.82 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 144.11, 133.53, 130.08, 128.10, 85.75, 42.13, 37.65, 29.61, 28.49, 27.27, 19.87. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.36. IR (neat) ν_{max} 3028.4 (m), 2973.9 (m), 2874.3 (m), 1603.7 (m), 1495.1 (m), 1475.1 (m), 1455.6 (m), 1398.9 (m), 1302.8 (s), 1271.1 (m), 1209.5 (m), 1143.8 (s), 1115.5 (m), 872.3 (m), 804.6 (m), 673.5 (m) cm^{-1}. HRMS (DART) for $C_{19}H_{32}BO_2$ $[M+H]^+$: calculated: 303.2495, found: 303.2490. $[\alpha]^{20}_D$: -22.58 (c = 1.500, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)-ferrocene (6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure for 72 hours at room temperature, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

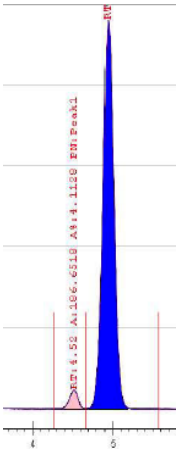
Chiral SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2,3,3-trimethyl-1-phenylbutan-2-ol.

Racemic Material

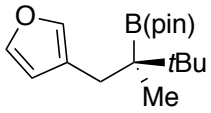


Peak No	% Area	Area	RT (min)
1	49.1983	5781.3223	4.46
2	50.8017	5969.7503	4.91
Total:	100	11751.0726	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	4.1128	186.6518	4.52
2	95.8872	4351.6184	4.94
Total:	100	4538.2702	



(*S*)-2-(1-(furan-3-yl)-2,3,3-trimethylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.136). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.12 mL, 1.7 M in pentane, 0.20 mmol, 1.00 equiv.), 3-bromofuran (32.3 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M) at 60 °C. The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (50.0 mg, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (s, 1H), 7.22 (s, 1H), 6.31 (s, 1H), 2.85 (d, J = 13.3 Hz, 1H), 2.11 (d, J = 13.3 Hz, 1H), 1.17 (d, J = 47.5 Hz, 12H), 0.97 (s, 9H), 0.90 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 141.50, 140.66, 123.47, 113.38, 83.06, 34.72, 28.53, 26.95, 25.70, 24.47, 17.40. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.28. IR

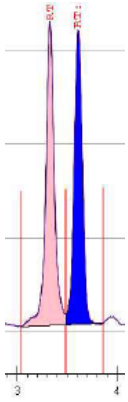
(neat) ν_{max} 2974.6 (m), 2874.2 (m), 1501.0 (m), 1460.8 (m), 1399.6 (m), 1370.5 (m), 1303.4 (s), 1264.5 (m), 1209.8 (m), 1144.0 (s), 1110.9 (m), 1024.9 (m), 967.1 (m), 851.4 (m), 723.0 (m), 635.5 (m) cm^{-1}. HRMS (DART) for $C_{17}H_{30}BO_3$ $[M+H]^+$: calculated: 293.2288, found: 293.2305. $[\alpha]^{20}_D$: -38.79 (c = 1.053, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)-ferrocene (6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

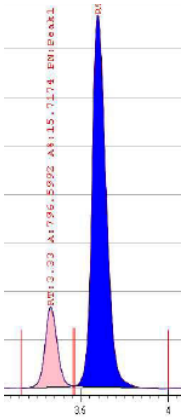
Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(furan-3-yl)-2,3,3-trimethylbutan-2-ol.

Racemic Material

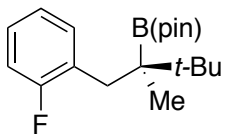


Peak No	% Area	Area	RT (min)
1	52.5426	992.3582	3.33
2	47.4574	896.3136	3.61
Total:	100	1888.6718	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	15.7174	796.5992	3.33
2	84.2826	4271.6557	3.6
Total:	100	5068.2549	



(*S*)-2-(1-(2-fluorophenyl)-2,3,3-trimethylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.135). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *n*-butyl lithium (0.08 mL, 2.5M in hexane, 0.20 mmol, 1.00 equiv.), 1-bromo-2-fluorobenzene (37.6 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M) at 60 °C. The crude mixture was purified by silica gel chromatography (2% ethyl acetate in hexanes, stain in magic) to afford a white solid (52.0 mg, 81% yield). ^{1}H NMR (500MHz, $CDCl_3$): δ 7.43 (td, J = 7.7, 1.8 Hz, 1H), 7.12 (tdd, J = 7.1, 5.0, 1.9 Hz, 1H), 7.06-6.86 (m, 2H), 2.89 (d, J = 13.6 Hz, 1H), 2.66 (d, J = 13.6 Hz, 1H), 1.21 (d, J = 58.2 Hz, 12H), 1.03 (s, 9H), 0.82 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 161.82 (d, $^1J_{C–F}$ = 244.6 Hz), 132.59 (d, $^3J_{C–F}$ = 4.8 Hz) 128.73 (d, $^2J_{C–F}$ = 15.6 Hz) 127.18 (d, $^3J_{C–F}$ = 8.2 Hz), 123.15, 114.86 (d, $^2J_{C–F}$ = 23.4 Hz) 83.17, 35.23, 31.40, 26.94, 25.81, 24.64, 16.13. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.32. ^{19}F NMR: (470 MHz, $CDCl_3$) δ -114.56. IR (neat) ν_{max} 2974.3 (m), 2873.8 (m), 1584.0 (m), 1475.9 (m), 1400.1 (m), 1369.3 (m), 1303.3 (s), 1228.1 (m), 1181.7 (m), 1143.9 (s), 1120.2 (s), 1035.0 (m), 945.3 (m), 754.9 (s), 663.3 (m) cm^{-1}. HRMS (DART) for $C_{19}H_{31}BFO_2$ $[M+H]^+$: calculated: 321.2401, found: 321.2418. $[\alpha]^{20}_D$: -15.88 (c = 2.250, $CHCl_3$, l = 50 mm).

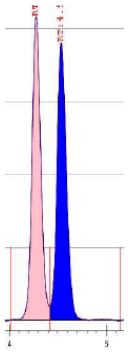
Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-

Bis(dicyclohexylphosphino)-ferrocene (6 mol%) as the catalyst. The product was oxidized with NaOH, and H_2O_2 according to the *conjunctive cross-coupling/oxidation* procedure, and the enantioselectivity was determined on the corresponding alcohol. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

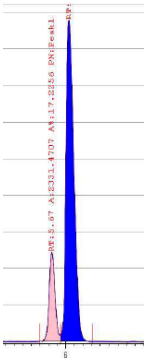
Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(2-fluorophenyl)-2,3,3-trimethylbutan-2-ol.

Racemic Material

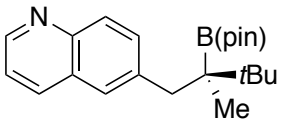


Peak No	% Area	Area	RT (min)
1	50.1737	2607.4373	4.27
2	49.8263	2589.3855	4.53
Total:	100	5196.8228	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	17.2256	2331.4707	5.67
2	82.7744	11203.4438	6.07
Total:	100	13534.9145	



(*S*)-6-(2,3,3-trimethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)quinolone (3.134). The reaction was performed according to the general procedure ***(Method A)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.12 mL, 1.7 M in pentane, 0.20 mmol, 1.00 equiv.), quinolin-6-yl trifluoromethanesulfonate (61.0 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.) in THF (0.8 mL, 0.25 M) at 60 °C. The crude

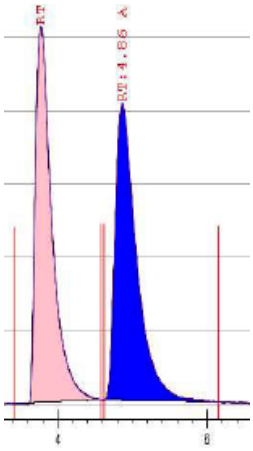
mixture was purified by silica gel chromatography (5-20% ethyl acetate in hexanes, stain in magic) to afford a white solid (39.0 mg, 55% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.83 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.09 – 7.98 (m, 1H), 7.95 (dt, *J* = 8.6, 0.7 Hz, 1H), 7.76-7.61 (m, 2H), 7.34 (dd, *J* = 8.3, 4.2 Hz, 1H), 3.28 (d, *J* = 12.5 Hz, 1H), 2.50 (d, *J* = 12.5 Hz, 1H), 1.25 (s, 6H), 1.12-1.01 (m, 15H), 0.86 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 149.47, 147.04, 140.26, 135.38, 133.61, 128.65, 128.08, 127.83, 120.82, 83.22, 39.43, 35.10, 26.95, 25.78, 24.67, 17.26. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 33.86. IR (neat) ν_{max} 2973.3(m), 2874.1 (m), 1593.7 (m), 1500.3 (m), 1459.4 (m), 1370.6 (m), 1304.5 (s), 1266.8 (m), 1226.9 (m), 1209.5 (m), 1164.4 (m), 1143.3 (s), 1115.8 (m), 841.1 (s), 784.2 (m) cm^{-1}. HRMS (DART) for $C_{22}H_{33}BNO_2$ $[M+H]^+$: calculated: 354.2604, found: 354.2610. $[\alpha]^{20}_D$: -21.96 (c = 0.750, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)-ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

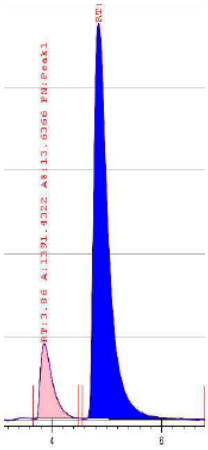
Chiral SFC (Chiracel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-6-(2,3,3-trimethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)quinolone.

Racemic Material

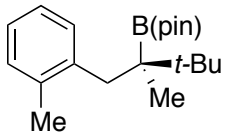


Peak No	% Area	Area	RT (min)
1	49.4414	3945.7417	3.77
2	50.5586	4034.8982	4.86
Total:	100	7980.6399	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	13.6366	1391.4322	3.86
2	86.3634	8812.2584	4.85
Total:	100	10203.6906	



(*S*)-4,4,5,5-tetramethyl-2-(2,3,3-trimethyl-1-(o-tolyl)butan-2-yl)-1,3,2-dioxaborolane (3.137). The reaction was performed according to the general procedure ***(Method B)*** with isopropenyl boronic acid pinacol ester (33.6 mg, 0.20 mmol, 1.00 equiv.), *tert*-butyl lithium (0.12 mL, 1.7 M in pentane, 0.20 mmol, 1.00 equiv.), 1-bromo-2-methylbenzene (37.6 mg, 0.22 mmol, 1.10 equiv.), palladium (II) acetate (0.45 mg, 0.002 mmol, 0.010 equiv.), (S_p, S_p)-**3.92** (2.30 mg, 0.0022 mmol, 0.011 equiv.), potassium trifluoromethanesulfonate (37.6 mg, 0.20 mmol, 1.0 equiv.) in THF (0.8 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (45.3 mg, 71% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (dd, J = 6.8, 2.3 Hz, 1H), 7.10-6.97 (m, 3H), 2.98 (d, J = 13.3 Hz, 1H), 2.51 (d, J = 13.3 Hz, 1H), 2.32 (s, 3H), 1.18 (d, J = 63.8 Hz, 12H), 1.02 (s, 9H), 0.81 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 140.56, 137.58, 130.47, 130.32, 125.60, 125.38, 83.31, 35.70, 35.03, 27.17, 26.03, 24.84, 20.85,

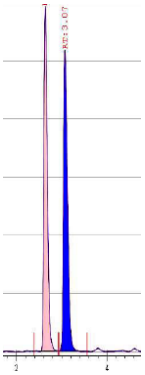
16.54; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.50; IR (neat): ν_{max} 2973.1 (m), 2874.5 (w), 1460.2 (m), 1398.4 (m), 1370.1 (m), 1301.9 (s), 1208.9 (m), 1144.5 (s), 1124.1 (m), 967.5 (m), 852.2 (m), 741.9 (m) cm^{-1}. HRMS (DART) for $C_{20}H_{34}BO_2$ $[M+H]^+$: calculated: 317.2652, found: 317.2661. $[\alpha]^{20}_D$: -13.59 (c = 1.385, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl 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 compounds **3.105, 3.149, and 3.151**).

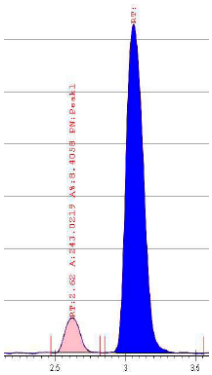
Chiral SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-4,4,5,5-tetramethyl-2-(2,3,3-trimethyl-1-(o-tolyl)butan-2-yl)-1,3,2-dioxaborolane.

Racemic Material



Peak No	% Area	Area	RT (min)
1	50.079	6484.4311	2.63
2	49.921	6463.9835	3.07
Total:	100	12948.4146	

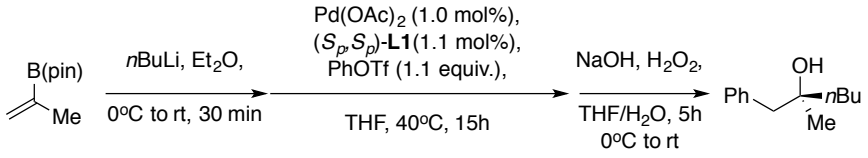
Standard Conditions

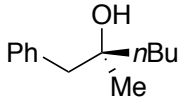


Peak No	% Area	Area	RT (min)
1	8.4058	243.0219	2.62
2	91.5942	2648.1033	3.06
Total:	100	2891.1252	

3.7.2.6. Transformations of Tertiary Boronic Esters

Conjunctive Cross Coupling/Oxidation





(*S*)-2-methyl-1-phenylhexan-2-ol (3.142). To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-isopropenyl boronic acid pinacol ester (0.20 mmol, 1.00 equiv.) and diethyl ether (0.2 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0 °C, and an alkyl/aryl lithium solution (0.20 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 stirbar in the glovebox was added $Pd(OAc)_2$ (0.002 mmol, 0.01 equiv.), (S_p, S_p)-**3.92** (0.0022 mmol, 0.011 equiv.), and THF (0.2 mL). The $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was transferred into the reaction vial, followed by THF (0.6 mL), and aryl/alkenyl triflate (0.22 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 40 °C for 15 hours. The resulting mixture was cooled to room temperature 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 5 hours. The reaction mixture was cooled to 0 °C and saturated aq. $Na_2S_2O_3$ solution (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 product (35.0 mg, 91% yield).

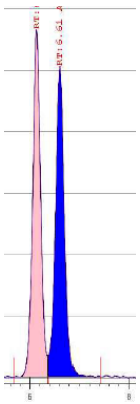
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.29 (m, 2H), 7.29-7.19 (m, 3H), 2.81 (d, *J* = 13.3 Hz, 1H), 2.75 (d, *J* = 13.3 Hz, 1H), 1.57-1.39 (m, 4H), 1.39-1.30 (m, 3H), 1.16 (s, 3H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 137.80, 130.73, 128.34, 126.59, 72.70, 48.14, 41.80, 26.71, 26.42, 23.44, 14.31; IR (neat): ν_{max} 3446.8 (b), 2956.2 (m), 2931.4 (m), 2861.3 (w), 1453.4 (m), 1376.6 (m), 1134.8 (m), 1085.2 (m), 1031.8 (m), 725.7.0 (m), 699.8 (s) cm^{-1}. HRMS (DART) for $C_{13}H_{24}ON$ $[M+NH_4]^+$: calculated: 210.1858, found: 210.1868. $[\alpha]^{20}_D$: +11.29 (c = 1.310, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl 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 compounds **3.105, 3.149, and 3.151**).

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

Racemic Material



Peak No	% Area	Area	RT (min)
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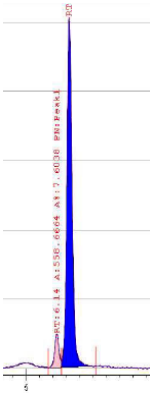
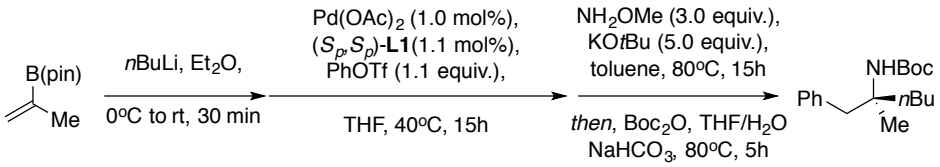
2	49.6297	3156.4811	6.61
Total:	100	6360.067	

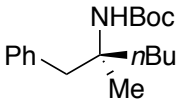
Standard Conditions



Peak No	% Area	Area	RT (min)
1	7.6038	558.6664	6.14
2	92.3962	6788.4942	6.6
Total:	100	7347.1606	

Conjunctive Cross Coupling/Amination





***tert*-butyl (S)-(2-methyl-1-phenylhexan-2-yl)carbamate (3.143).** To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-isopropenyl boronic acid pinacol ester (0.20 mmol, 1.00 equiv.) and diethyl ether (0.2 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0 °C, and an alkyl/aryl lithium solution (0.20 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 stirbar in the glovebox was added $Pd(OAc)_2$ (0.002 mmol, 0.01 equiv.), (S_p, S_p)-**3.92** (0.0022 mmol, 0.011 equiv.), and THF

(0.2 mL). The $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was transferred into the reaction vial, followed by THF (0.6 mL), and aryl/alkenyl triflate (0.22 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 40 °C for 15 hours. The resulting mixture was cooled to room temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure.

To a separate oven-dried 2-dram vial equipped with a magnetic stir bar was added NH_2OMe solution (0.60 mmol, 3.00 equiv.) in THF[49] under N_2. The vial was brought into the glovebox, potassium *tert*-butoxide (1.00 mmol, 5.00 equiv.) was added, followed by the reaction crude mixture for conjunctive cross coupling in toluene (1.2 mL). The reaction vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 80 °C for 15 hours. The reaction mixture was allowed to cool to room temperature, and Boc_2O (1.00 mmol, 5.00 equiv.)solution in THF was added, followed by saturated aq. $NaHCO_3$ solution (2 mL). The reaction vial was sealed with a polypropylene cap, taped, and heated 80 °C for 5 hours. Then the reaction mixture was allowed to cool to room temperature and diluted 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, and concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to afford the desired product (50.5 mg, 87% yield).

^1H NMR (600 MHz, $CDCl_3$) δ 7.28-7.23 (m, 2H), 7.22-7.18 (m, 1H), 7.15-7.11 (m, 2H), 4.13 (s, 1H), 3.09 (d, J = 13.3 Hz, 1H), 2.83 (d, J = 13.3 Hz, 1H), 1.87-1.71 (m, 1H),

[49] Mlynarski, S. N., Karns, A. S. Morken, J. P. *J. Am. Chem. Soc.* **2012**, 134, 16449-16451.

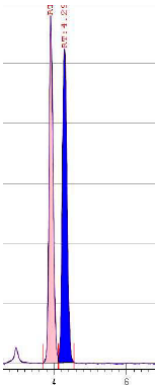
1.49-1.40 (m, 10H), 1.37-1.21 (m, 4H), 1.12 (s, 3H), 0.90 (t, J = 6.9, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 138.23, 130.85, 128.00, 126.30, 55.51, 44.03, 38.80, 28.69, 28.07, 27.60, 26.10, 24.63, 23.22, 14.35; IR (neat): ν_{max} 2958.2 (m), 2929.8 (m), 2860.2 (w), 1716.7 (m), 1494.8 (m), 1364.9 (m), 1239.7 (m), 1163.3 (s), 1077.2 (m), 1030.6 (m), 754.9 (m), 701.5 (s) cm^{-1}. HRMS (DART) for $C_{18}H_{30}O_2N$ $[M+H]^+$: calculated: 292.2277, found: 292.2280.

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl 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 compounds **3.105, 3.149, and 3.151**).

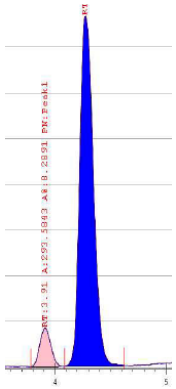
Chiral SFC (Chiracel AD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of tert-butyl (S)-(2-methyl-1-phenylhexan-2-yl)carbamate.

Racemic Material



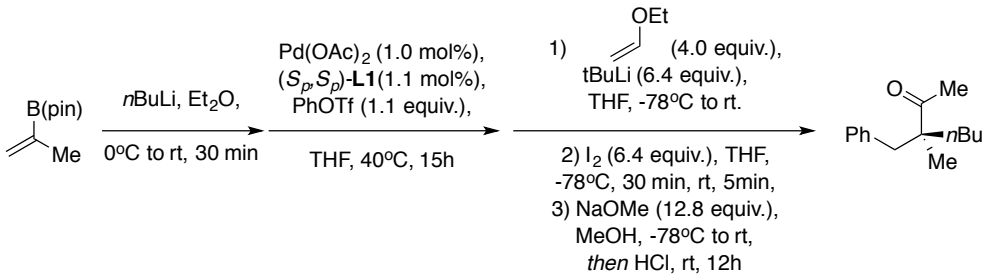
Peak No	% Area	Area	RT (min)
1	49.215	4651.7171	3.91
2	50.785	4800.1101	4.29
Total:	100	9451.8272	

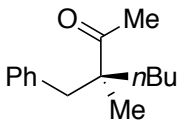
Standard Conditions



Peak No	% Area	Area	RT (min)
1	8.2891	293.5843	3.91
2	91.7109	3248.2234	4.27
Total:	100	3541.8077	

Conjunctive Cross Coupling/Modified Zweifel Olefination





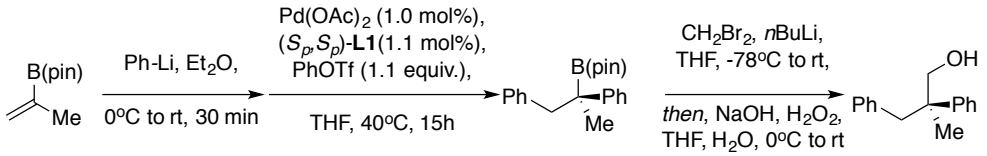
(*S*)-3-benzyl-3-methylheptan-2-one (3.145). To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-isopropenyl boronic acid pinacol ester (0.60 mmol, 1.00 equiv.) and diethyl ether (0.6 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0 °C, and a phenyl lithium solution (0.60 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, 0.01 equiv.), (S_p, S_p)-**3.92** (0.0066 mmol, 0.011 equiv.), and THF (0.6 mL). The $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was transferred into the reaction vial, followed by THF (1.8 mL), and phenyl triflate (0.66 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 40 °C for 15 hours. The resulting mixture was cooled to room temperature, and the crude reaction mixture was used in next step without any further purification.

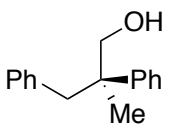
To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added ethyl vinyl ether (0.80 mmol, 4.00 equiv.) and THF (0.4 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to -78 °C, and a *tert*-butyl lithium solution (1.28 mmol, 6.40 equiv.) was added at -78 °C. The resulting solution was stirred at -78 °C for 30 minutes, allowed to warm up to 0 °C, stirred for 30 minutes and cooled back to -78 °C. The crude reaction mixture of conjunctive cross coupling in THF (2.0 mL) was then added dropwise. The resulting solution was stirred at -78 °C for 30 minutes, allowed to warm up to room temperature, stirred for 5 minutes and cooled back to -78 °C. A solution of iodine (1.28 mmol, 6.40 equiv.) in THF (2.0 mL) was then added dropwise. The resulting solution was stirred at -78 °C for 30 minutes, allowed to warm up to room temperature, stirred for 5 minutes and cooled back to -78 °C. A suspension of MeONa (2.56 mmol, 12.80 equiv.) in MeOH (2.5 mL) was then added dropwise and the resulting mixture was stirred for 1 hour at room temperature. A 2M aq. HCl solution (6.0 mL) was then added, the resulting mixture was stirred for 12 hours before a sat. aq. $Na_2S_2O_3$ solution (5.0 mL) was added. The aqueous layer was extracted with diethyl ether (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 product (41.4 mg, 95% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29-7.12 (m, 3H), 7.11-7.03 (m, 2H), 2.93 (d, J = 13.5 Hz, 1H), 2.67 (d, J = 13.5 Hz, 1H), 2.07 (s, 3H), 1.76-1.62 (m, 1H), 1.48-1.35 (m, 1H), 1.33-1.11 (m, 4H), 1.06 (s, 3H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 213.93, 137.95, 130.41, 128.18, 126.49, 52.44, 44.35, 38.65, 30.50, 26.97, 26.83, 23.49, 21.01, 14.14; IR (neat): ν_{max} 2956.8 (m), 2931.0 (m), 2860.7 (w), 1701.7 (s), 1495.1 (m),

1454.5 (m), 1353.8 (m), 1119.3 (m), 752.0 (m), 702.1 (s) cm^{-1}. HRMS (DART) for $C_{15}H_{23}O$ $[M+H]^+$: calculated: 219.1749, found: 219.1752.

Conjunctive Cross Coupling/Homologation





(*R*)-2-methyl-2,3-diphenylpropan-1-ol (3.146). To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-isopropenyl boronic acid pinacol ester (0.60 mmol, 1.00 equiv.) and diethyl ether (0.6 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0 °C, and a phenyl lithium solution (0.60 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, 0.01 equiv.), (S_p, S_p)-**3.92** (0.0066 mmol, 0.011 equiv.), and THF (0.6 mL). The $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was transferred into the reaction vial, followed by THF (1.8 mL), and phenyl triflate (0.66 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 40 °C for 15 hours. The resulting mixture was cooled to room temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure, and

subsequently purified via silica gel column chromatography to afford the desired product (172.1 mg, 89% yield).

Homologation of boronic esters was carried out using the Aggarwal[50] protocol as follows: To a stirred solution of the (*S*)-2-(1,2-diphenylpropan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.36 mmol, 1.00 equiv.) and dibromomethane (0.90 mmol, 2.50 equiv.) in anhydrous THF (1.5 mL) at –78 °C, was added *n*BuLi (0.80 mmol, 2.20 equiv.) dropwise. The resulting mixture was stirred for 10 minutes at –78 °C, warmed to room temperature and stirred for 2 hours. The reaction mixture was then cooled to 0 °C and a solution of 3 M NaOH (2.0 mL) and 30% H_2O_2 (1.0 mL) was added 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. $Na_2S_2O_3$ solution (3.0 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 product (61.9 mg, 76% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ7.41-7.29 (m, 4H), 7.29-7.20 (m, 1H), 7.20-7.11 (m, 3H), 6.93-6.83 (m, 2H), 3.84 (d, *J* = 11.0 Hz, 1H), 3.64 (d, *J* = 11.0 Hz, 1H), 2.95 (s, 2H), 1.28 (s, 4H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 144.80, 137.98, 130.65, 128.61, 127.84, 127.07, 126.57, 126.25, 70.88, 45.05, 44.43, 29.88, 21.86; IR (neat): ν_{max} 3388.9 (b), 3026.6 (w), 2923.3 (m), 2873.8 (w), 1610.2 (w), 1495.9 (m), 1453.2 (m), 1374.2 (w), 1027.3 (m),

[50] Sonawane, R. P., Jheengut, V., Rabalakos, C., Larouche-Gauthier, R., Scott, H. K. Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2011**, 50, 3760-3763.

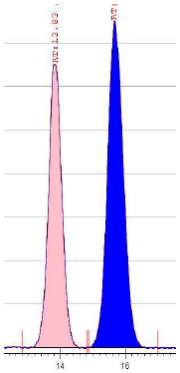
766.8 (m), 698.9 (s) cm^{-1}. HRMS (DART) for $C_{16}H_{22}ON$ $[M+NH_4]^+$: calculated: 244.1701, found: 244.1709. $[\alpha]^{20}_D$: -43.42 (c = 1.310, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the procedure described above with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (1.0 mol%), (S_p, S_p)-**3.141** (0.6 mol%), and (R_p, R_p)-**3.141** (0.6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

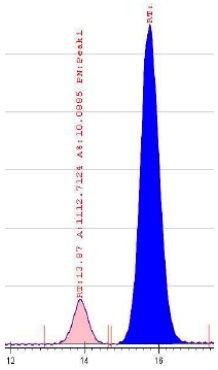
Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-methyl-2,3-diphenylpropan-1-ol.

Racemic Material



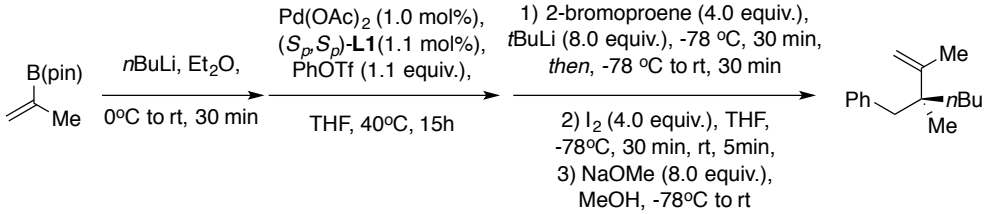
Peak No	% Area	Area	RT (min)
1	42.5096	9469.0126	13.83
2	57.4904	12805.9956	15.67
Total:	100	22275.0082	

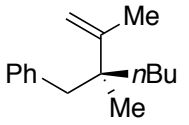
Standard Conditions



Peak No	% Area	Area	RT (min)
1	10.0885	1112.7124	13.87
2	89.9115	9916.8024	15.76
Total:	100	11029.5148	

Conjunctive Cross Coupling/Evans-Zweifel Olefination





(*S*)-(2-methyl-2-(prop-1-en-2-yl)hexyl)benzene (3.144). To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-isopropenyl boronic acid pinacol ester (0.60 mmol, 1.00 equiv.) and diethyl ether (0.6 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0 °C, and a phenyl lithium solution (0.60 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, 0.01 equiv.), (S_p, S_p)-**3.92** (0.0066 mmol, 0.011 equiv.), and THF (0.6 mL). The $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**3.92** solution was transferred into the reaction vial, followed by THF (1.8 mL), and phenyl triflate (0.66 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 40 °C for 15 hours. The resulting mixture was cooled to room temperature, and the crude reaction mixture was used in next step without any further purification.

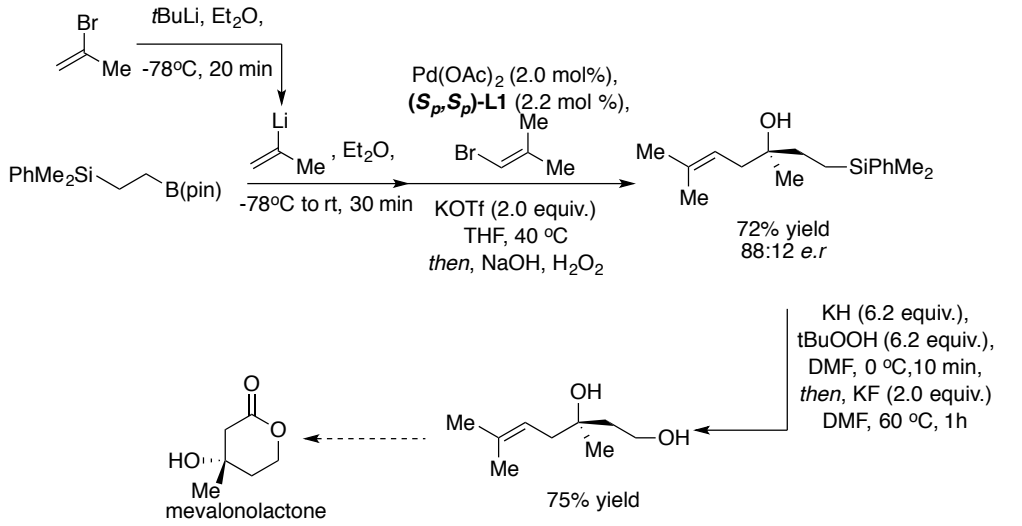
To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-isopropenyl bromide (0.80 mmol, 4.00 equiv.) and THF (0.4 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to -78 °C, and a *tert*-butyl lithium solution (1.60 mmol, 8.00 equiv.) was added at -78 °C. The reaction vial was allowed to stir at -78 °C for 20 minutes. Then crude reaction mixture solution of conjunctive cross coupling in THF was added at -78 °C. The reaction vial was

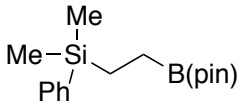
allowed to warm to room temperature and stirred for 30 minutes and cool down to -78 °C. A solution of iodine (0.8 mmol, 4.00 equiv.) in THF (2.0 mL) was added dropwise to the reaction mixture, the result mixture was allowed to stir at -78 °C for 30 minutes, followed 5 minutes at room temperature. Then the reaction mixture was cooled down to -78 °C, and a solution of MeONa (1.60 mmol, 8.0 equiv.) in MeOH (2.0 mL) was added dropwise. The reaction mixture was then allowed to warm to room temperature and stirred for an additional 1 h, diluted with pentane (10 mL) and quenched with a saturated aq. NaS2O3 solution (10.0 mL). The phases were separated, the aqueous layer was extracted with pentane (2 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 product (27.4 mg, 63% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30-7.14 (m, 3H), 7.11-7.03 (m, 2H), 4.81 (q, *J* = 1.4 Hz, 1H), 4.52 (d, *J* = 1.8 Hz, 1H), 2.72 (d, *J* = 13.2 Hz, 1H), 2.56 (d, *J* = 13.3 Hz, 1H), 1.78 (d, *J* = 1.5 Hz, 3H), 1.60-1.46 (m, 1H), 1.34-1.03 (m, 6H), 0.95-0.83 (m, 6H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 149.82, 139.23, 130.66, 127.62, 127.61, 125.94, 112.21, 46.58, 43.34, 39.23, 26.60, 23.62, 22.86, 20.00, 14.34; IR (neat): ν_{max} 2955.9 (m), 2929.0 (m), 2860.2 (w), 1634.3 (w), 1495.6 (w), 1452.4 (m), 1375.8 (m), 891.2 (m), 757.1 (m), 698.5 (s) cm^{-1}. HRMS (DART) for $C_{15}H_{23}O$ $[M+H]^+$: calculated: 217.1956, found: 217.1966.

3.7.2.7. Targets Synthesis

Enantioselective synthesis of (S)- mevalonolactone

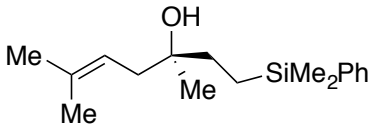




dimethyl(phenyl)(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-silane (3.147). The title compound was prepared according to a literature procedure with slight modification[51]. In an Ar-filled glovebox, B_2pin_2 (1.27 g, 5.00 mmol, 1.0 equiv.), copper (I) chloride (24.8 mg, 0.25 mmol, 0.05 equiv.) 1,1′-bis(diisopropylphosphino)ferrocene (112.1 mg, 0.25 mmol, 0.05 equiv.), and potassium tert-butoxide (673 mg, 6.00 mmol, 1.2 equiv.) were added to 50 mL round bottom flask equipped with a magnetic stir bar. The flask was sealed with a rubber septum and removed from the glovebox. Dry THF (10.00 mL, 0.5 M) was added and reaction mixture was cooled to 0 C before dimethyl-phenyl-vinyl-silane (0.91 mL, 5.00 mmol, 1.0 equiv.) was slowly added, followed by anhydrous methanol (0.81 mL, 20.00 mmol, 4.0 equiv.). Reaction was allowed to warm to room temperature and stirred for 3 hours. Reaction mixture was filtered through a plug of silica gel with diethyl ether, then

[51] Kubota, K., Yamamoto, E. Ito. H. *Adv. Synth. Catal*. **2013**, 355, 3527-3531.

concentrated to afford a yellow oil. The crude mixture was purified by silica gel chromatography (1% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (1.21 g, 83% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56-7.45 (m, 2H), 7.39-7.29 (m, 3H), 1.23 (s, 12H), 0.89-0.68 (m, 4H), 0.26 (d, J = 2.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.39, 133.67, 128.68, 127.61, 82.93, 24.80, 8.46, -3.53. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.06. IR (neat): ν_{max} 2977.7 (m), 2955.3 (m), 1426.0 (m), 1412.8 (s), 1358.9 (m), 1319.1 (m), 1237.7 (m), 1144.6 (m), 1112.8 (m), 996.2 (m), 879.5 (m), 832.9 (s), 811.9 (m), 771.8 (m) cm^{-1}. HRMS (DART) for $C_{16}H_{31}BNO_2Si$ $[M+NH_4]^+$: calculated: 308.2217, found: 308.2217.



(*R*)-1-(dimethyl(phenyl)silyl)-3,6-dimethylhept-5-en-3-ol (3.148). Prepared according to ***Method C***. Upon completion of the reaction, the mixture was cooled to 0 °C, then 3 M aq. NaOH (0.5 mL) was added followed by 30% aq. H_2O_2 (0.5 mL). This solution was stirred vigorously for 3 hours at room temperature then diluted with diethyl ether, cooled to 0 °C and quenched with sat. sodium thiosulfate (0.5 mL). The organic layer was separated, and the aqueous layer was washed with diethyl ether (3 x 20 mL). Combined organic layers were dried over sodium sulfate, then filtered, and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (5% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (80.0 mg, 72% yield). ^{1}H NMR (500 MHz, $CDCl_3$): 7.58-7.46 (m, 2H), 7.41-7.31 (m, 3H), 5.15 (t, 1H), 2.16 (t, J = 8.1 Hz, 2H), 1.73 (s, 3H), 1.63 (s, 3H), 1.52-1.42 (m, 2H), 1.13 (s, 3H), 0.85-0.71 (m, 2H), 0.28 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.11, 135.03, 133.54, 128.85, 127.74, 119.35, 73.73, 39.36, 35.57, 26.20, 26.07, 18.00, 9.35, -3.22, -3.25. IR

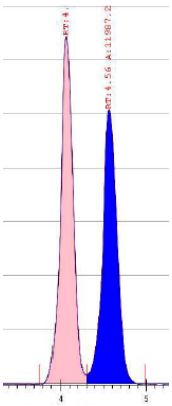
(neat) ν_{max} 3419.9 (br), 3068.7 (m), 2963.7 (m), 2924.3 (m), 2858.1 (m), 1452.9 (m), 1375.2 (m), 1248.0 (m), 1192.4 (m), 1113.1 (s), 1025.3 (m), 878.9 (m), 837.5 (s), 816.2 (s), 699.5 (s), 633.5 (m) cm^{-1}. HRMS (DART) for $C_{17}H_{27}Si$ $[M+H-H_2O]^+$: calculated: 259.1882, found: 259.1870. $[\alpha]^{20}_D$: +3.96 (c = 0.910, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

Chiral SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(dimethyl(phenyl)silyl)-3,6-dimethylhept-5-en-3-ol.

Racemic Material



Peak No	% Area	Area	RT (min)
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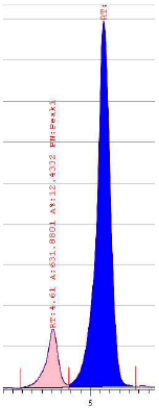
Standard Conditions



Peak No	% Area	Area	RT (min)
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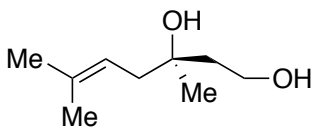
2	87.5668	4450.302	5.14
Total:	100	5082.1821	



(*R*)-3,6-dimethylhept-5-ene-1,3-diol (3.149). The title compound was prepared according to a literature procedure

with slight modification[52]. In an Ar-filled glove-box, neat potassium hydride (79.15 mg, 1.97 mmol, 6.2 equiv.) was added to 20 mL scintillation vial equipped with a magnetic stir bar. The vial was sealed with a rubber septum, and dry DMF (3.8 mL) was added. This solution was cooled to 0 C, then *tert*-butyl hydroperoxide (5.5 M in decane, 358.8 uL, 1.97 mmol, 6.2 equiv.) was added slowly and reaction mixture was stirred for 10 min at 0 °C. Next, (*R*)-1-[dimethyl(phenyl)silyl]-3,6-dimethyl-hept-5-en-3-ol (87.0 mg, 0.32 mmol, 1.0 equiv.) as a solution in DMF (2.5 mL) was added, followed by potassium fluoride (37.0 mg, 0.63 mmol, 2.0 equiv.) in one portion. Reaction was warmed to 60 °C and stirred for 2 hour (caution: gas evolution). Reaction mixture was diluted with ethyl acetate and quenched with H_2O, then poured into a separatory funnel. The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (2 x 20 mL). The combined organic layers were dried over sodium sulfate, then filtered through a plug of cotton, and concentrated under reduced pressure to yield a pale-yellow oil. The crude mixture was purified by silica gel chromatography (20-50% ethyl acetate in hexanes, stain in magic) to afford a colorless oil (38.0 mg, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$): 5.27-5.15 (m, 1H), 3.97-3.77 (m, 2H), 2.79 (br s, 1H), 2.35-2.13 (m, 3H), 1.89-1.71 (m, 4H), 1.71-1.60 (m, 4H), 1.23 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 138.15, 121.63, 76.97, 62.46, 44.08, 43.65, 29.27, 28.73, 20.65. IR (neat) ν_{max} 3336.6 (br), 2968.2 (m), 2917.5 (m), 1451.3 (m), 1375.6 (s), 1296.5 (m), 1252.1 (m), 1125.7 (m), 1096.9 (m), 1056.5 (s), 967.6 (m), 925.4 (m), 880.9 (m), 559.7 (m) cm^{-1}. HRMS (DART) for $C_9H_{19}O_2$

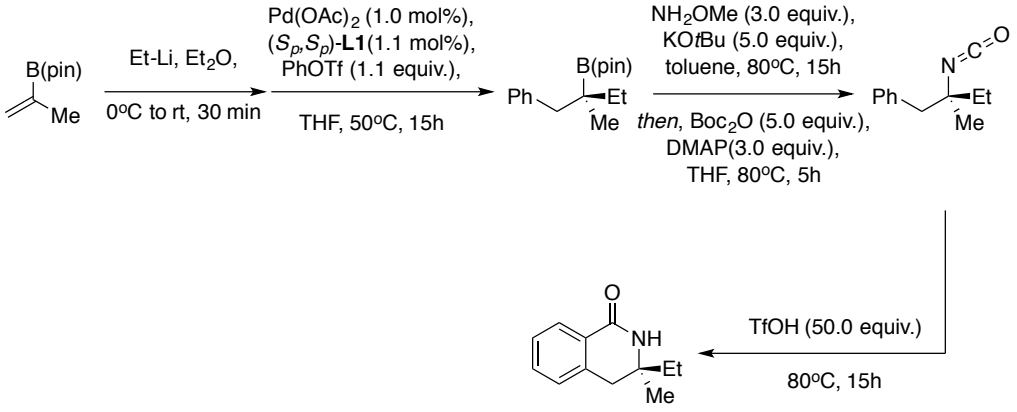
[52] Reddy, P. V., Smith, J., Kamath, A., Jamet, H., Veyron, A., Koos, P., Philouze, C., Greene, A. E. Delair, P. *J. Org. Chem*. **2013**, 78, 4840-4849.

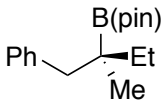
$[M+H]^+$: calculated: 159.1380, found: 159.1380. $[\alpha]^{20}_D$: +1.83 (c = 0.800, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

Absolute stereochemistry was determined by comparison of optical rotation to the literature[53] (Measured: $[\alpha]^{20}_D$: +1.830 (c = 1.300, $CHCl_3$, l =50 mm), literature: $[\alpha]^{20.5}_D$: -2.52 (c = 1.11, $CHCl_3$), 98:2 *e.r* for (*S*)-3,6-dimethylhept-5-ene-1,3-diol). And the absolute stereochemistry was assigned to be (*R*)-3,6-dimethylhept-5-ene-1,3-diol.

Enantioselective synthesis of (S)-3-ethyl-3-methyl-3,4-dihydroisoquinolin-1(2H)-one





(*R*)-4,4,5,5-tetramethyl-2-(2-methyl-1-phenylbutan-2-yl)-1,3,2-dioxaborolane (3.151). The title compound was synthesized according the general procedure (***Method A***) with 2-isopropenyl boronic acid pinacol ester (100.8 mg, 0.60 mmol), ethyllithium (1.20 mL, 0.5M in benzene/cyclohexane, 0.60 mmol),

[53] Mori, K. Okada, K. *Tetrahedron* **1985**, 41, 557-559.

phenyltrifluoromethanesulfonate (149.8 mg, 0.66 mmol), palladium (II) acetate (1.350 mg, 0.006 mmol), (S_p, S_p)-**3.92** (6.90 mg, 0.0066 mmol) in THF (2.4 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2.5% ethyl acetate in hexanes) to afford the desire product as a colorless oil. (104.1 mg, 63% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22-7.17 (m, 4H), 7.15-7.12 (m, 1H), 2.77 (d, *J* = 12.6 Hz, 1H), 2.47 (d, *J* = 13.2 Hz, 1H), 1.54-1.47 (m, 1H), 1.26-1.17 (m, 13H), 0.90 (t, *J* = 7.2 Hz, 3H), 0.86 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ140.3, 130.5, 127.7, 125.8, 83.3, 44.6, 31.9, 25.3, 25.0, 20.9, 10.5. ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.74; IR (neat) ν_{max} 2975.6 (m), 2928.9 (m), 1460.3 (m), 1383.9 (s), 1370.6 (s), 1307.5 (s), 1263.3 (m), 1210.5 (m), 1139.0 (s), 741.7 (m), 701.9 (m), 688.3 (m) cm^{-1}. HRMS (DART) for $C_{17}H_{28}BO_2$ $[M+H]^+$ calculated: 275.2182, found: 275.2187. $[\alpha]^{20}_D$: -4.745 (c = 1.080, $CHCl_3$, *l* =50 mm)

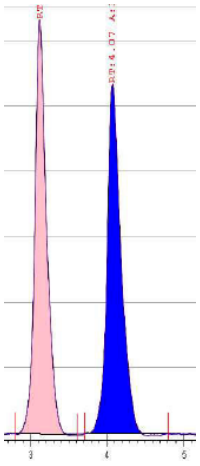
Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with isopropenyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was determined by comparison of optical rotation to the literature[54] after oxidation (Measured: $[\alpha]^{20}_D$: +3.680 (c = 1.300, $CHCl_3$, l =50 mm), literature: $[\alpha]^{24}_D$: -6.5 (c = 1.97, $CHCl_3$), 80% *e.e* for (*R*)-2-methyl-1-phenylbutan-2-ol). And the absolute stereochemistry was assigned to be (*S*)-2-methyl-1-phenylbutan-2-ol.

[54] Doyle, A. G. Jacobson, E. N. *Angew. Chem. Int. Ed*. **2007**, 46, 3701-3705.

Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4,4,5,5-tetramethyl-2-(2-methyl-1-phenylbutan-2-yl)-1,3,2-dioxaborolane.

Racemic Material



Peak No	% Area	Area	RT (min)
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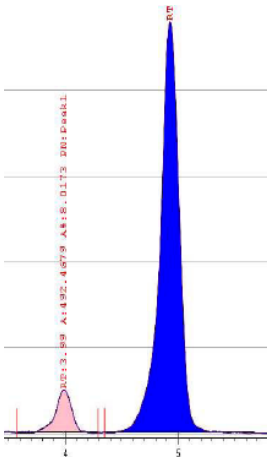
Total:	100	6813.3039	

Standard Conditions



Peak No	% Area	Area	RT (min)
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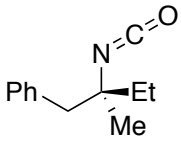
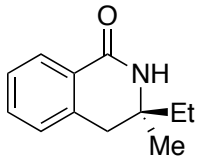
Total:	100	6142.565	



(*S*)-(2-isocyanato-2-methylbutyl)benzene (3.152). To an oven-dried 6-dram vial equipped with a magnetic stir bar was added NH_2OMe solution (1.70 mmol, 3.00 equiv.) in THF[1] under N_2. The vial was brought into the glovebox, potassium *tert*-butoxide (2.84 mmol, 5.00 equiv.) was added, followed by the (*R*)-4,4,5,5-tetramethyl-2-(2-methyl-1-phenylbutan-2-yl)-1,3,2-dioxaborolane (0.56 mmol, 1.00 equiv.) in toluene (3.6 mL). The reaction vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 80 °C for 15 hours. The reaction mixture was allowed to cool to room temperature, and Boc_2O (2.84 mmol, 5.00 equiv.) solution in THF was added, followed by 4-dimethylaminopyridine (1.70 mmol, 3.00 equiv.). The reaction vial was sealed with a polypropylene cap, taped, and heated 80

°C for 5 hours. Then the reaction mixture was allowed to cool to room temperature and diluted with 5% ethyl acetate in hexanes, and passed through a silica gel plug with 5% ethyl acetate in hexanes. The result solution was concentrated under reduced pressure, and subsequently purified via silica gel column chromatography (1% ethyl acetate in hexanes) to afford the desired product as a colorless oil (76.3 mg, 72% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.8 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 2H), 2.76 (d, *J* = 13.8 Hz, 1H), 2.66 (d, *J* = 13.8 Hz, 1H), 1.58-1.46 (m, 2H), 1.18 (s, 3H), 0.94 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ136.7, 130.8, 128.3, 127.0, 61.8, 48.1, 35.2, 27.0, 8.8. IR (neat) ν_{max} 3030.6 (m), 2972.8 (m), 2926.9 (m), 2254.3 (s), 1454.5 (m), 1379.9 (m), 1186.9 (m), 1031.0 (m), 754.3 (m), 619.4 (m) cm^{-1}. HRMS (DART) for $C_{12}H_{16}ON$ $[M+H]^+$ calculated: 190.1232, found: 190.1230. $[\alpha]^{20}_D$: +7.609 (c = 0.680, $CHCl_3$, *l* =50 mm)



(*S*)-3-ethyl-3-methyl-3,4-dihydroisoquinolin-1(*2H*)-one (3.153). To an oven-dried 2-dram vial equipped with a magnetic stir bar was added (*S*)-(2-isocyanato-2-methylbutyl)benzene (0.19 mmol, 1.00 equiv.). The vial was sealed with a septum cap, and purged with N_2. The reaction vial was cooled to 0 °C, and TfOH (9.5 mmol, 50.0 equiv.) was added dropwise under N_2. The reaction vial was heated to 80 °C and allowed to stir for 24 hours, then the reaction mixture was poured into ice-water (20.0 mL), and extracted with dichloromethane (20 mL x3). The organic phase was washed with brine, dried over Na_2SO_4, and the solvent was evaporated under reduced pressure, and subsequently purified via silica gel column chromatography (40 % ethyl acetate in hexanes) to afford the desired product as a white solid (33.6 mg, 93% yield).

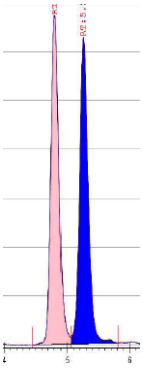
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 5.82 (brs, 1H), 2.95 (d, *J* = 16.0 Hz, 1H), 2.85 (d, *J* = 16.0 Hz, 1H), 1.65-1.51 (m, 2H), 1.23 (s, 3H), 0.91 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.6, 137.7, 132.5, 128.1, 127.1, 54.8, 39.7, 34.1, 26.2, 8.4. IR (neat) ν_{max} 3182.7 (m), 3063.4 (m), 2922.5 (m), 2852.9 (m), 1658.6 (s), 1604.4 (m), 1460.8 (s), 1395.3 (s), 1168.1(m), 820.6 (m), 778.4 (m), 581.7 (m) cm^{-1}. HRMS (DART) for $C_{12}H_{16}ON$ $[M+H]^+$ calculated: 190.1232, found: 190.1233. $[\alpha]^{20}_D$: -11.164 (c = 0.650, $CHCl_3$, *l* =50 mm)

Analysis of Stereochemistry:

Racemic compound was prepared according to the same procedure with racemic (2-isocyanato-2-methylbutyl)benzene. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

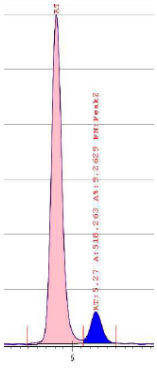
Chiral SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (*S*)-3-ethyl-3-methyl-3,4-dihydroisoquinolin-1(*2H*)-one.

Racemic Material



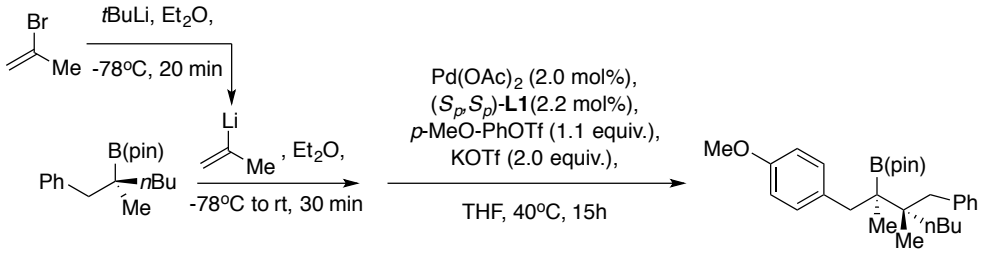
Peak No	% Area	Area	RT (min)
1	49.6255	2981.1745	4.81
2	50.3745	3026.1642	5.25
Total:	100	6007.3387	

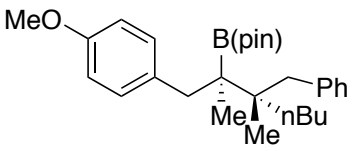
Standard Conditions



Peak No	% Area	Area	RT (min)
1	90.7371	5076.7806	4.82
2	9.2629	518.263	5.27
Total:	100	5595.0436	

3.7.2.8. Sequential Conjunctive Cross Coupling





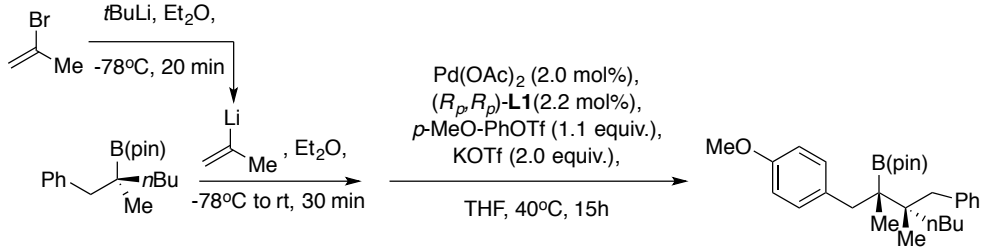
2-((*2S*,*3S*)-3-benzyl-1-(4-methoxyphenyl)-2,3-dimethylheptan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.139). The target product was synthesized according to the General procedure (***Method C***): To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-isopropenyl bromide (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 -78 °C, and a *tert*-butyl lithium solution (0.60 mmol, 2.00 equiv.) was added at -78 °C. The reaction vial was allowed to stir at -78 °C for 20 minutes. Then an (*R*)-4,4,5,5-tetramethyl-2-(2-methyl-1-phenylhexan-2-yl)-1,3,2-dioxaborolane (prepared according to the conjunctive cross coupling general procedure ***Method A***, the crude material was passed through a silica gel plug with diethyl ether, concentrated under reduced pressure, and used without further purification.) diethyl ether solution (0.30 mmol, 1.00 equiv.) was added at -78 °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

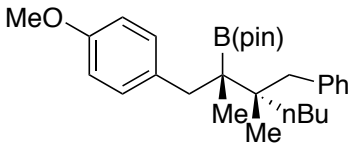
magnetic stirbar in the glovebox was added $Pd(OAc)_2$ (0.006 mmol, 0.02 equiv.), (S_p, S_p)-**3.141** (0.0066 mmol, 0.022 equiv.), and THF (0.6 mL). The $Pd(OAc)_2$/(S_p, S_p)-**3.141** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**3.141** solution was transferred into the reaction vial, followed by THF (0.6 mL), potassium trifluoromethanesulfonate (0.60 mmol, 2.0 equiv.) and 4-methoxyphenyl trifluoromethanesulfonate (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 40 °C for 15 hours. The resulting mixture was cooled to room temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to afford the desired product (102.7 mg, 76% yield, 9:1 *d.r.*).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37-7.16 (m, 6H), 6.81 (d, J = 8.4 Hz, 2H), 3.82 (s, 3H), 3.13 (d, J = 12.7 Hz, 1H), 3.04 (d, J = 13.1 Hz, 1H), 2.67 (d, J = 13.0 Hz, 1H), 2.44 (d, J = 12.7 Hz, 1H), 1.62-1.49 (m, 1H), 1.43-1.08 (m, 17H), 1.03-0.97 (m, 6H), 0.80 (t, J = 6.9 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 157.87, 140.93, 133.30, 132.18, 131.14, 130.96, 127.75, 125.74, 113.08, 83.26, 55.41, 41.56, 38.74, 36.23, 27.62, 26.23, 26.13, 24.87, 23.95, 17.70, 14.26; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 33.91; IR (neat): ν_{max} 2956.1 (m), 2930.4 (m), 2869.9 (w), 1610.1 (w), 1510.5 (s), 1463.8 (m), 1371.6 (m), 1299.2 (m), 1246.4 (s), 1143.0 (s), 1037.9 (m), 967.9 (m), 833.2 (m), 702.5 (m) cm^{-1}. HRMS (DART) for $C_{29}H_{44}BO_3$ $[M+H]^+$: calculated: 451.3384, found: 451.3391. $[\alpha]^{20}_D$: -32.31 (c = 2.060, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

The diastereomer ratio was determined by ^{1}H NMR. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).





2-((*2R*,*3S*)-3-benzyl-1-(4-methoxyphenyl)-2,3-dimethylheptan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.140). The target product was synthesized according to the General procedure (***Method C***): To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 2-isopropenyl bromide (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 -78 °C, and a *tert*-butyl lithium solution (0.60 mmol, 2.00 equiv.) was added at -78 °C. The reaction vial was allowed to stir at -78 °C for 20 minutes. Then an (*R*)-4,4,5,5-tetramethyl-2-(2-methyl-1-phenylhexan-2-yl)-1,3,2-dioxaborolane (prepared according to the conjunctive cross coupling general procedure ***Method A***, the crude material was passed through a silica gel plug with diethyl ether, concentrated under reduced pressure, and used without further purification.) diethyl ether solution (0.30 mmol, 1.00 equiv.) was added at -78 °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

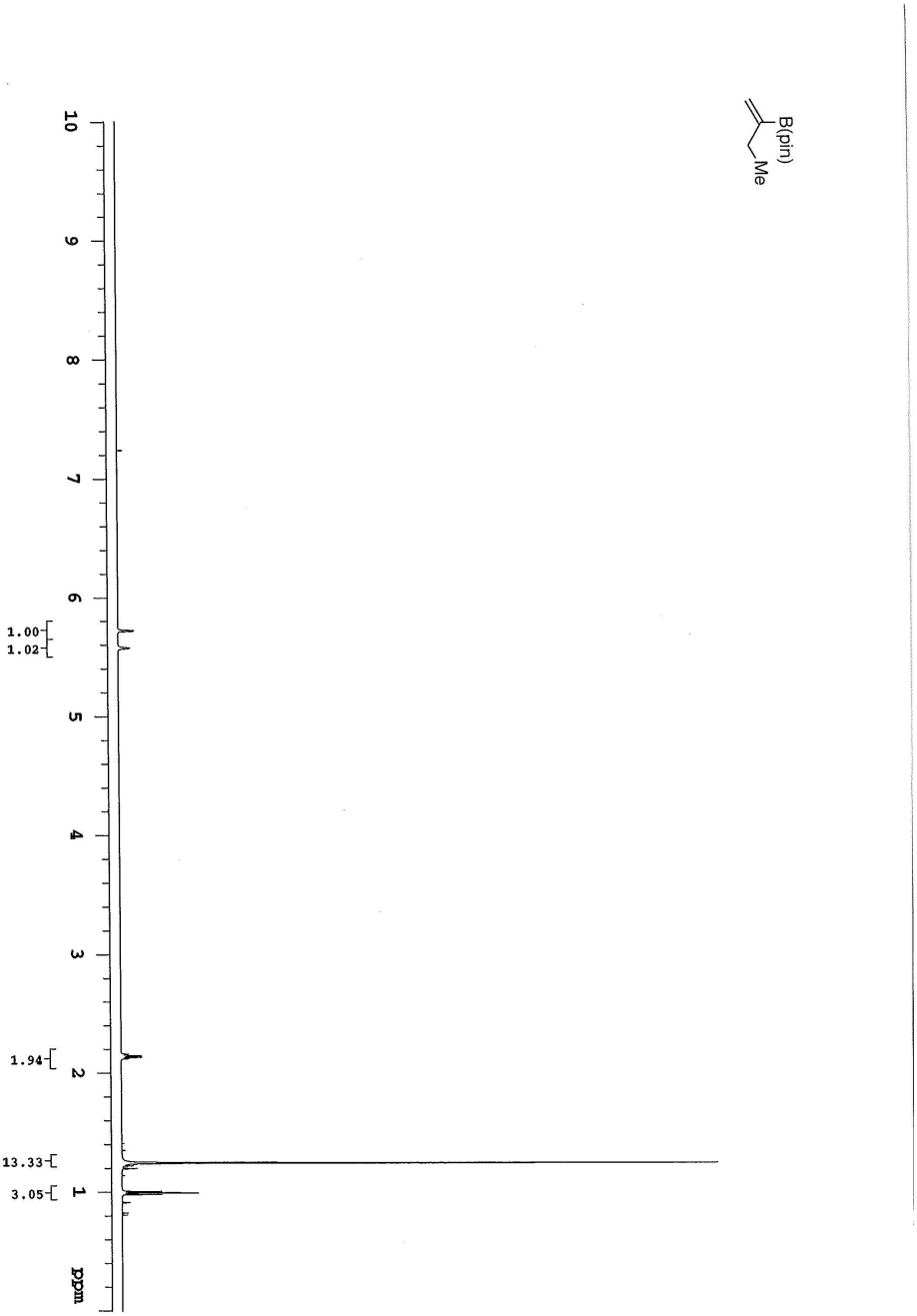
magnetic stirbar in the glovebox was added $Pd(OAc)_2$ (0.006 mmol, 0.02 equiv.), (R_p, R_p)-**3.141** (0.0066 mmol, 0.022 equiv.), and THF (0.6 mL). The $Pd(OAc)_2$/(R_p, R_p)-**3.141** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(R_p, R_p)-**3.141** solution was transferred into the reaction vial, followed by THF (0.6 mL), potassium trifluoromethanesulfonate (0.60 mmol, 2.0 equiv.) and 4-methoxyphenyl trifluoromethanesulfonate (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 40 °C for 15 hours. The resulting mixture was cooled to room temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to afford the desired product (99.1 mg, 73% yield, 5.3:1 *d.r.* diastereoselectivity was determined by ^{1}H NMR).

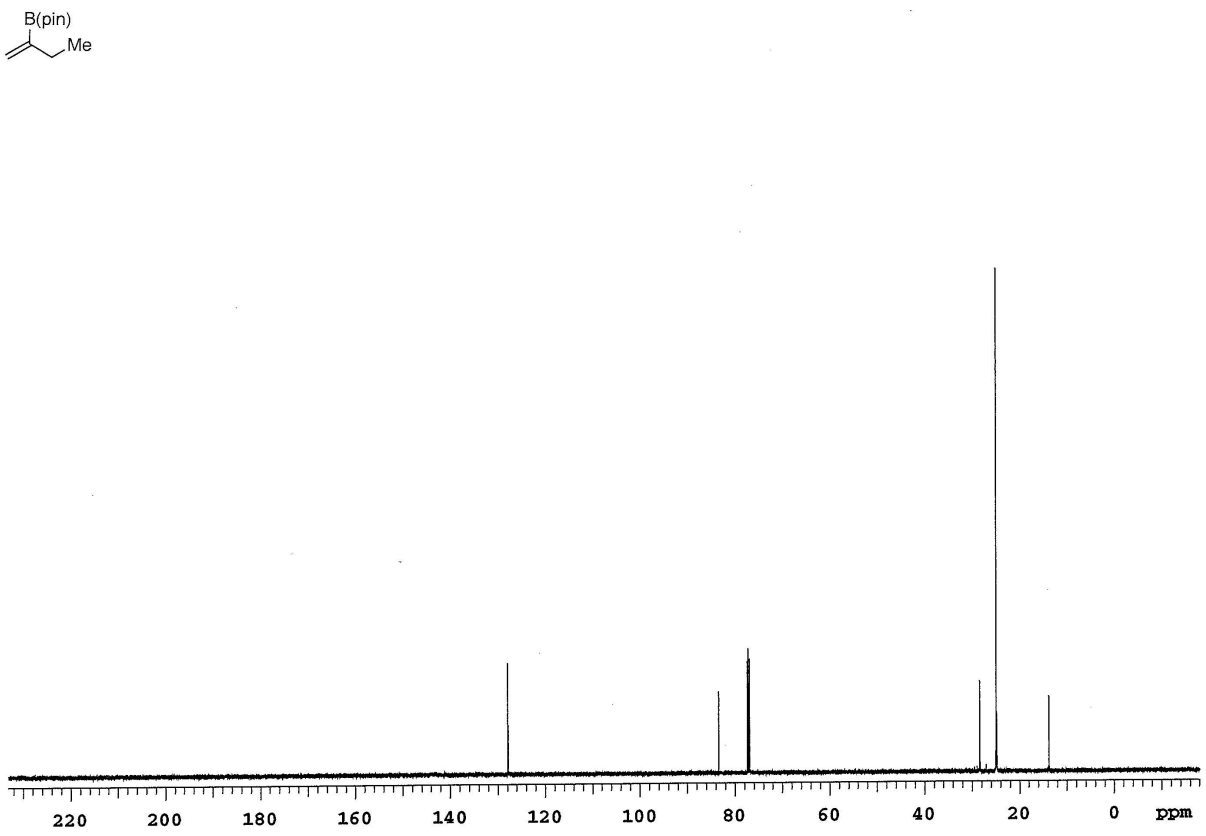
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37-7.18 (m, 7H), 6.83 (d, J = 8.6 Hz, 2H), 3.83 (s, 3H), 3.15 (d, J = 12.7 Hz, 1H), 2.89 (s, 2H), 2.53 (d, J = 12.7 Hz, 1H), 1.52-1.09 (m, 18H), 1.07-0.88 (m, 9H); ^{13}C NMR (151 MHz, $CDCl_3$): δ 157.85, 140.74, 133.30, 132.18, 131.14, 130.95, 127.75, 125.68, 113.07, 113.03, 83.27, 55.39, 41.30, 38.74, 28.16, 26.23, 26.13, 24.87, 24.18, 17.93, 14.35; ^{11}B NMR: (160 MHz, $CDCl_3$) δ 34.03; IR (neat): ν_{max} 2955.9 (m), 2930.8 (m), 2869.9 (w), 1610.3 (w), 1510.3 (s), 1463.9 (m), 1387.1 (m), 1299.3 (m), 1246.4 (s), 1142.9 (s), 1038.2 (m), 967.9 (m), 833.4 (m), 702.5 (m) cm^{-1}. HRMS (DART) for $C_{29}H_{44}BO_3$ $[M+H]^+$: calculated: 451.3384, found: 451.3387. $[\alpha]^{20}_D$: +29.71 (c = 3.745, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

The diastereomer ratio was determined by ^{1}H NMR. Absolute stereochemistry was assigned by analogy (see compounds **3.105, 3.149, and 3.151**).

3.7.3. NMR spectra of representative compounds

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Me
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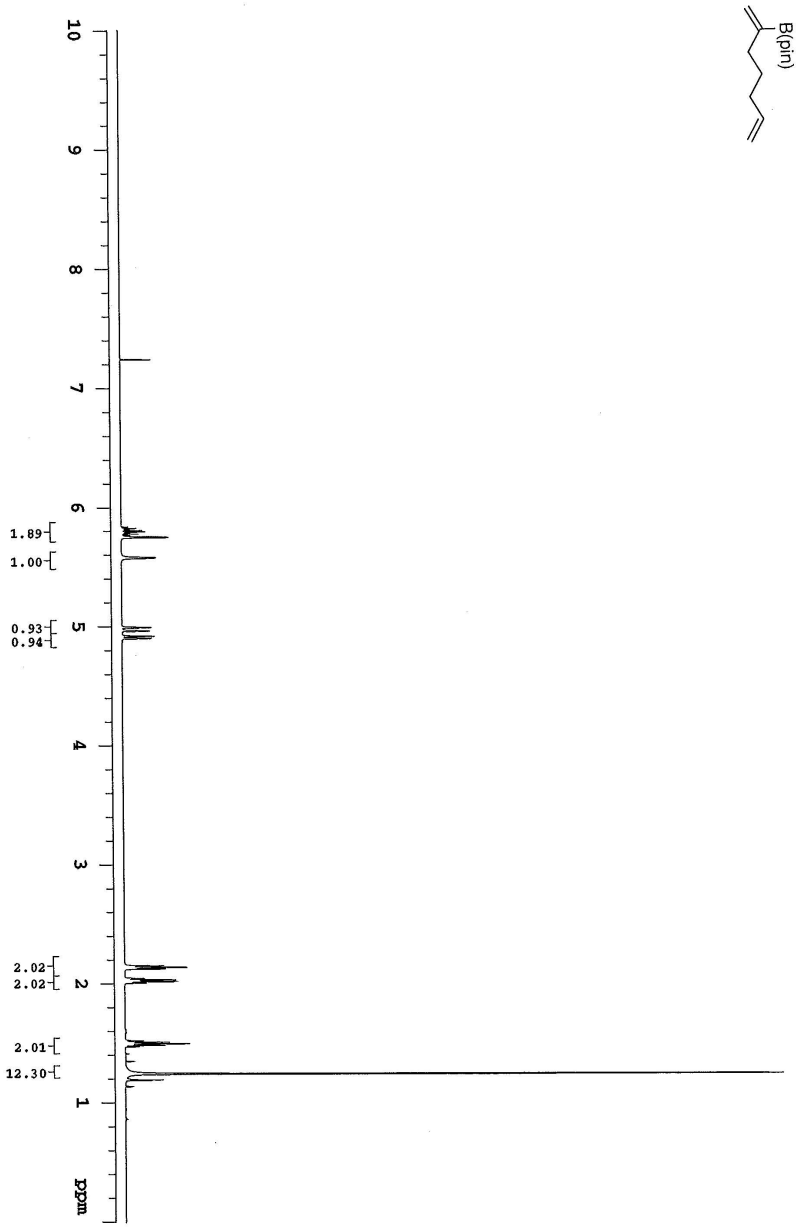
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
10
9
8
7
6
5
4
3
2
1
ppm
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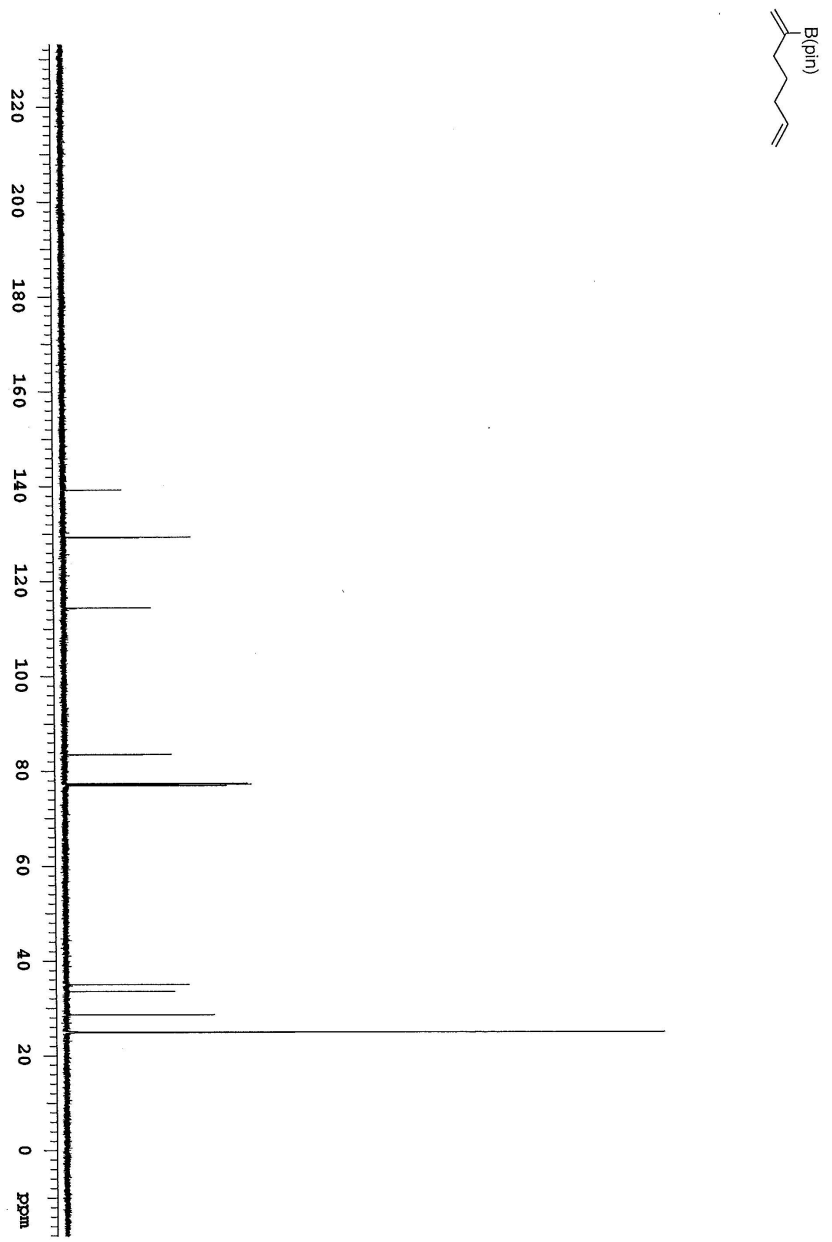
1.00
0.93
0.94
2.02
2.02
2.01
12.30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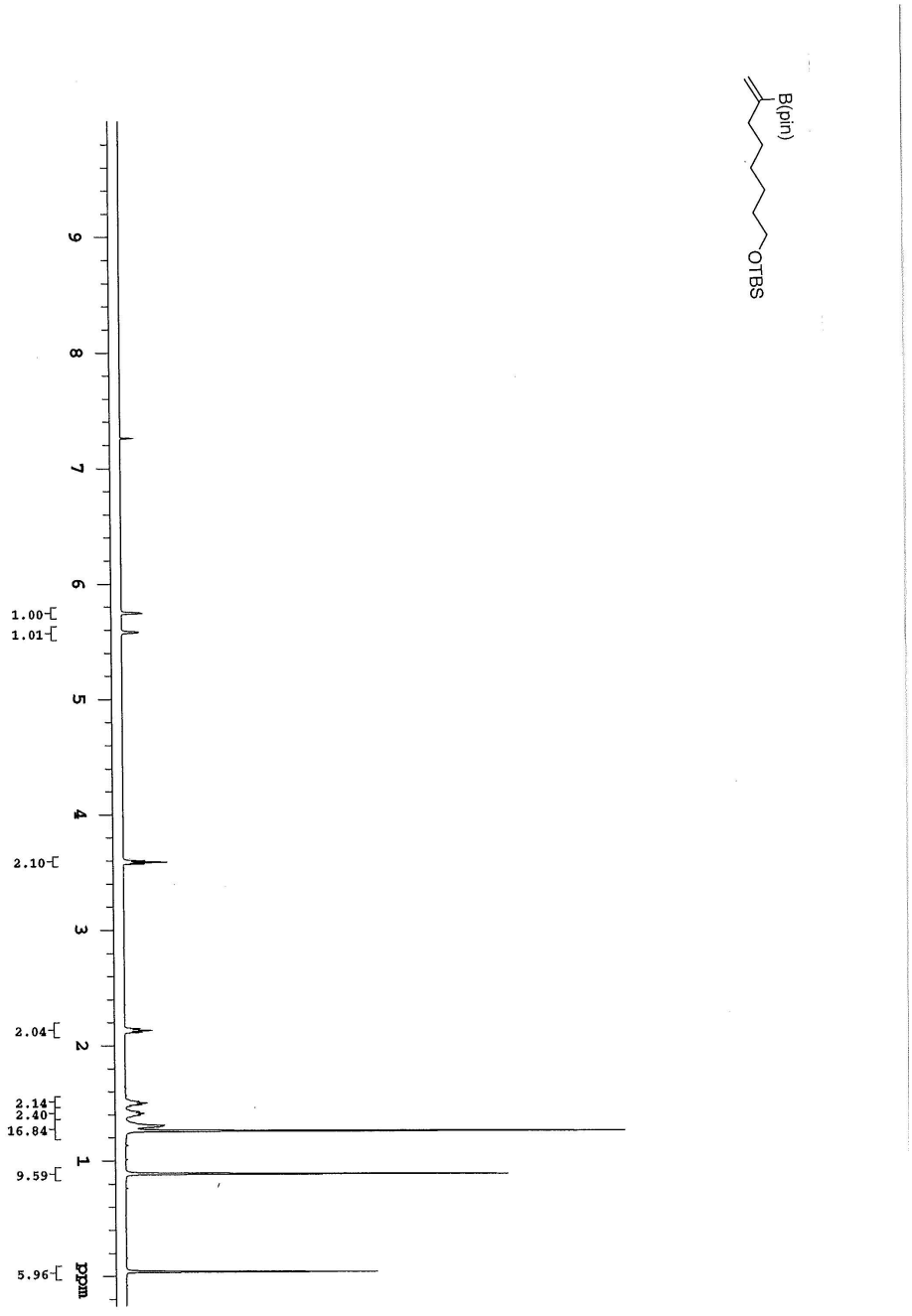
160
140
120
100
80
60
40
20
0
ppm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2.04
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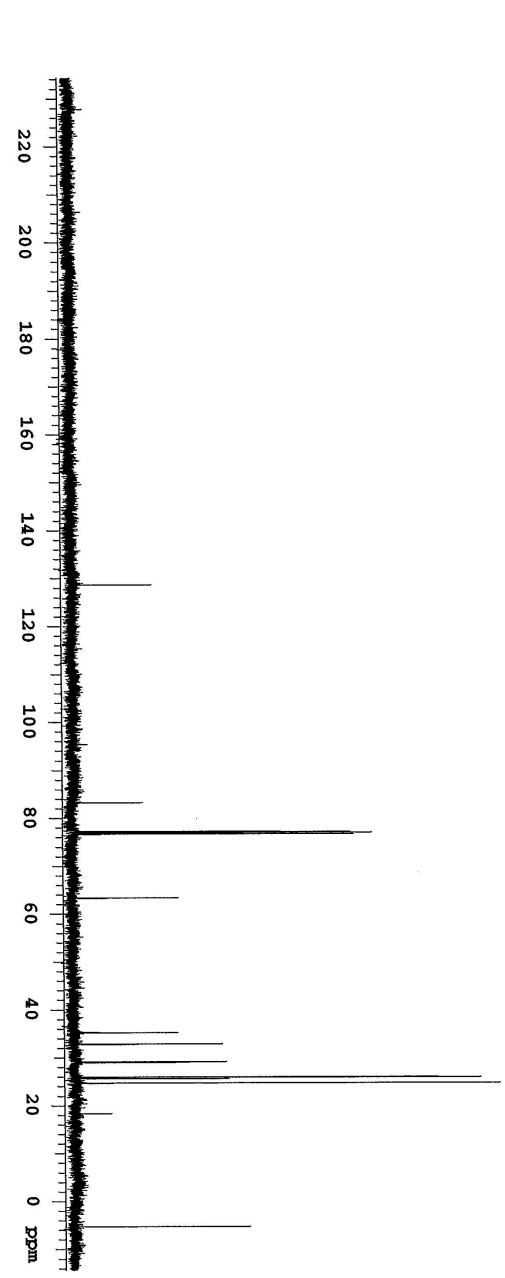
2.40
16.84
9.59
5.96
ppm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OTBS
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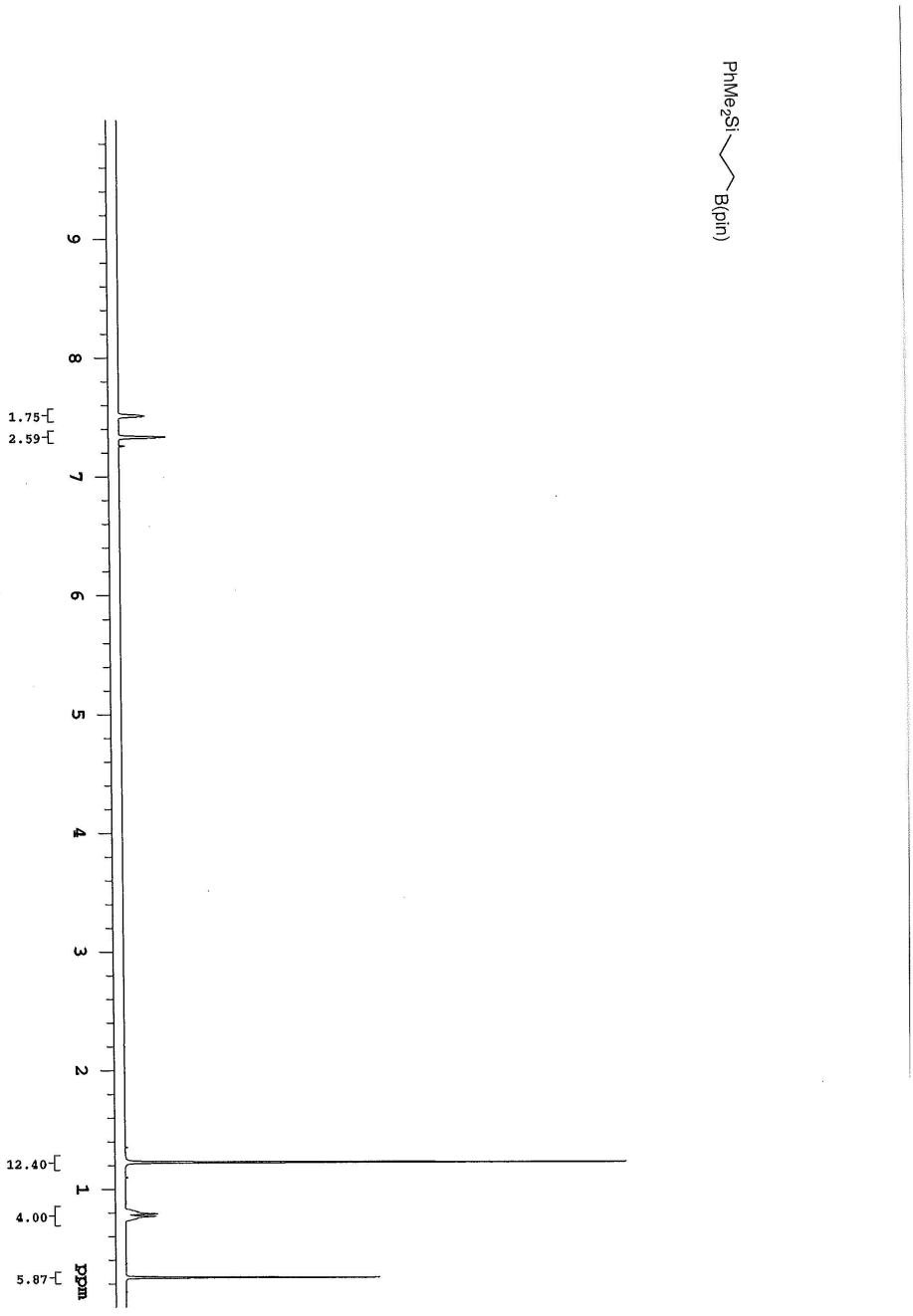
200
180
160
140
120
100
80
60
40
20
0
ppm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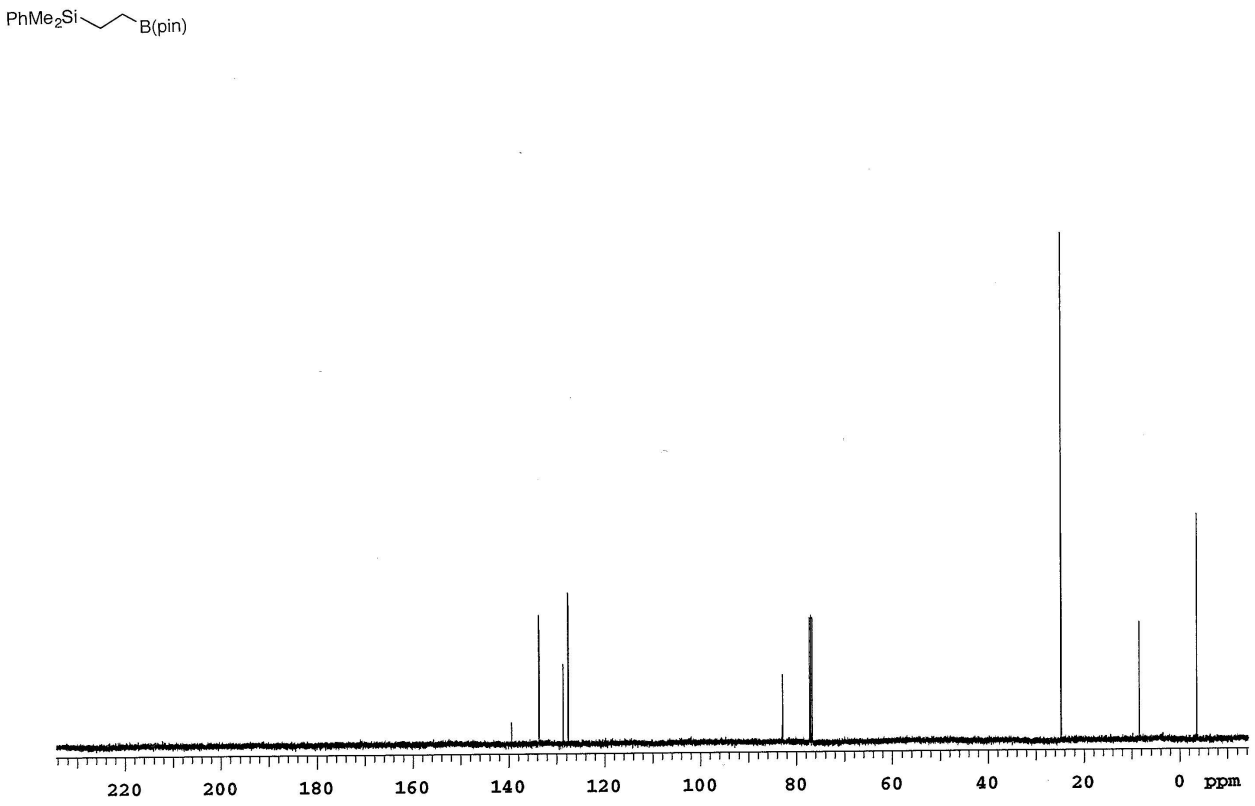
ppm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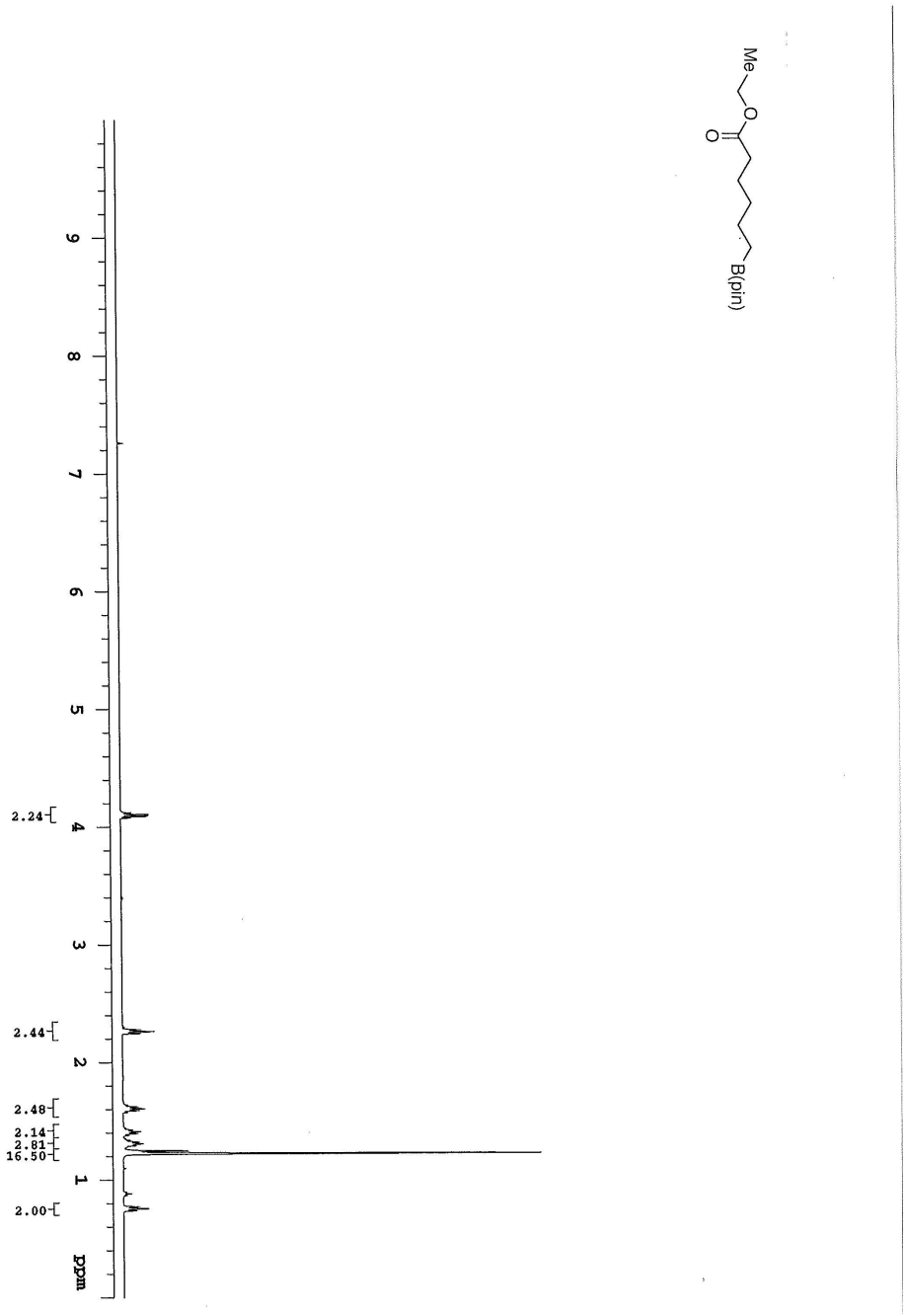
180
160
140
120
100
80
60
40
20
0
ppm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O
O
B(pin)
2.24
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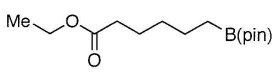
2.48
2.14
2.81
16.50
2.00
9
8
7
6
5
4
3
2
1
ppm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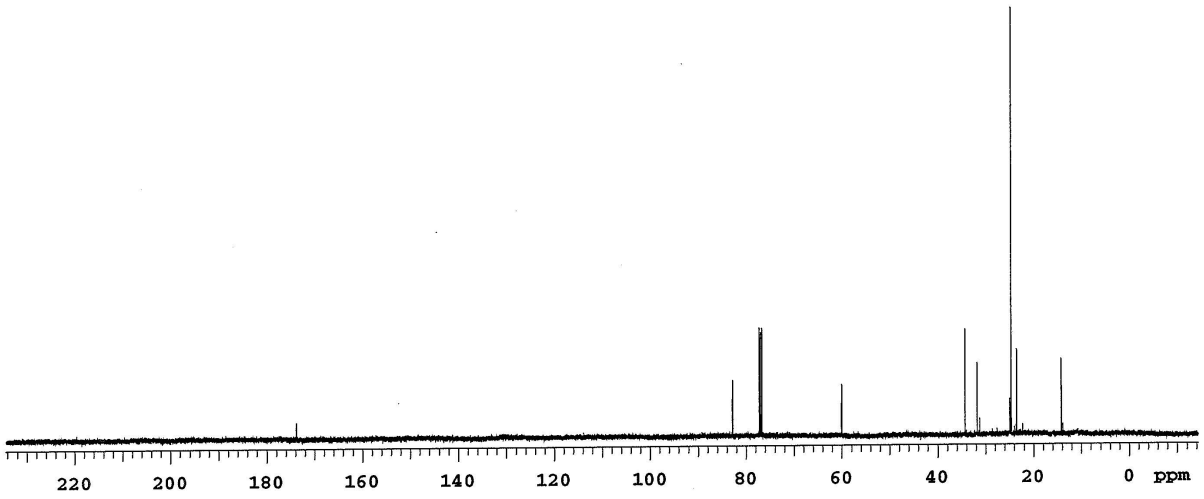
O
O
B(pin)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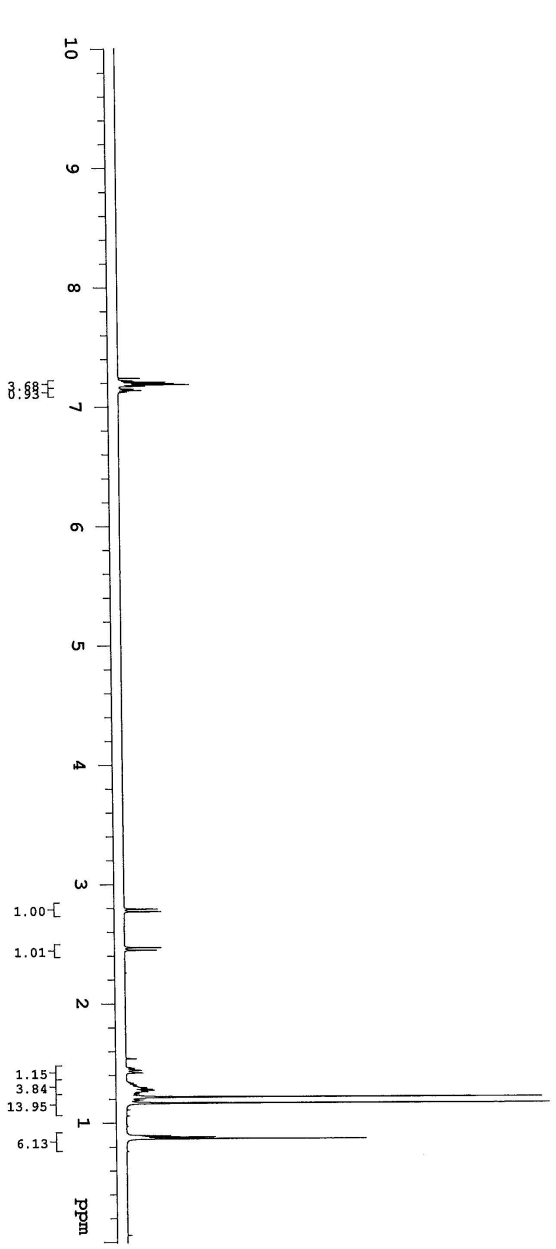
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n-Bu
Me
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8
7
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5
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1.01
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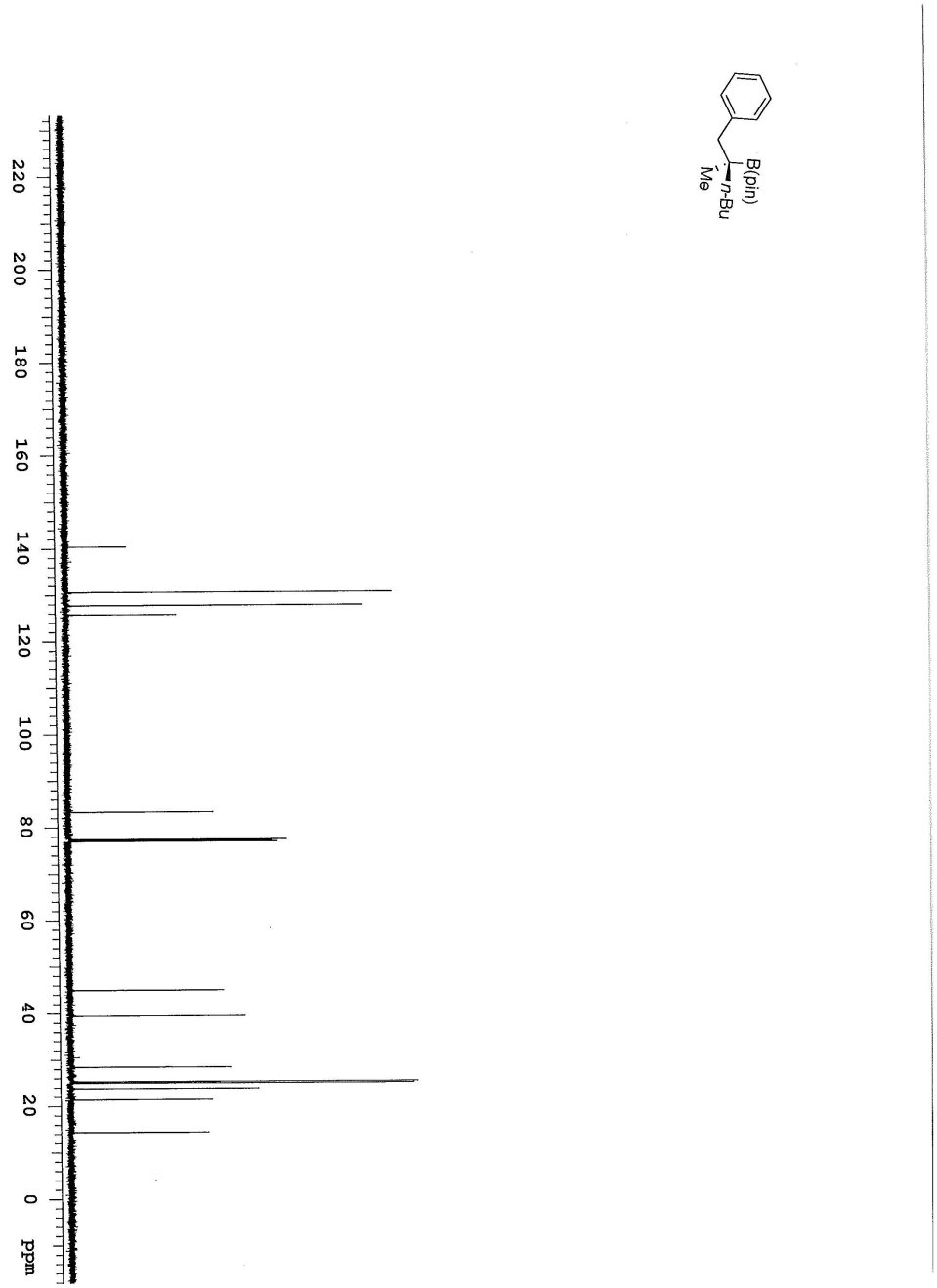
3.84
13.95
6.13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140
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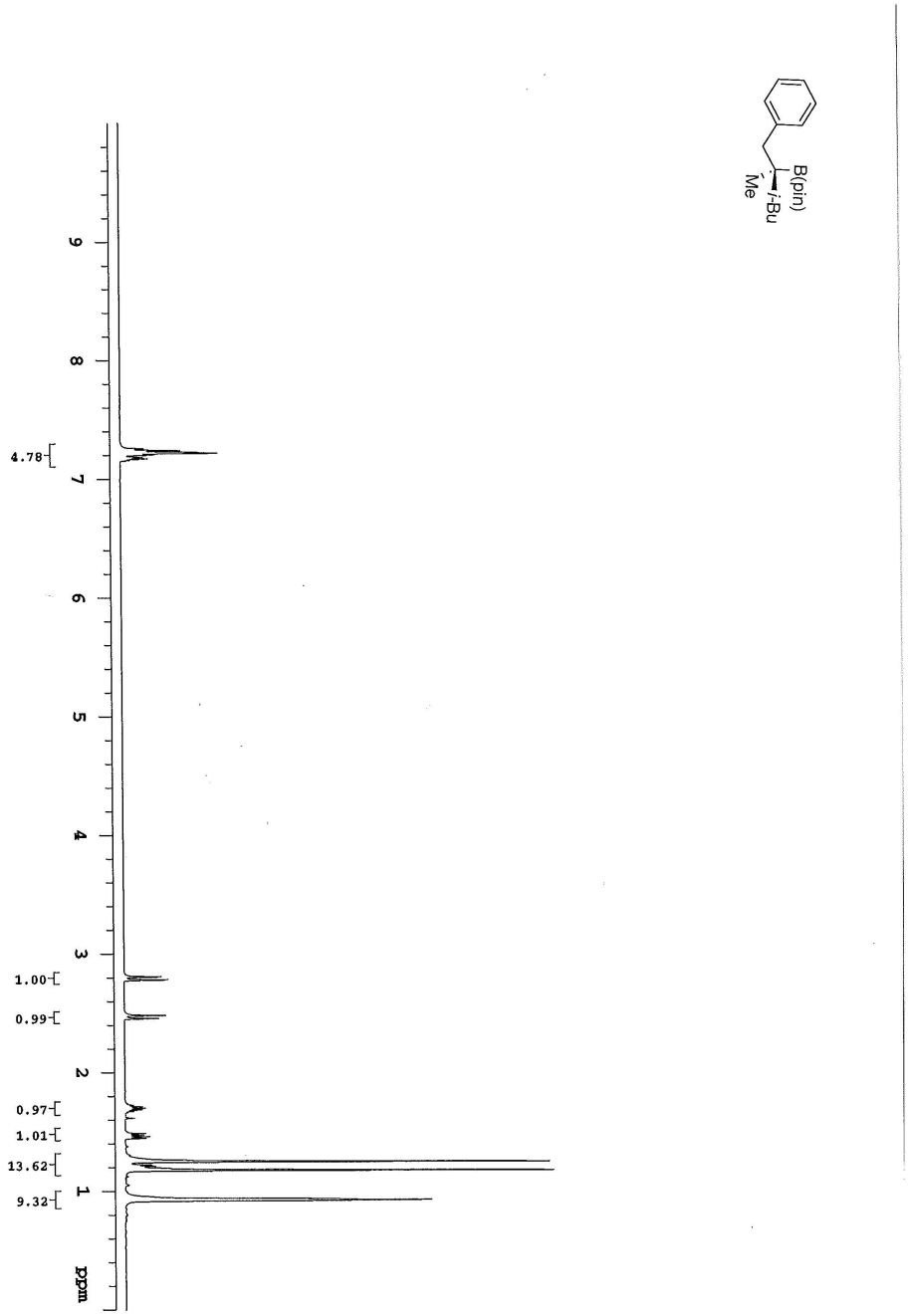
0
ppm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0.97
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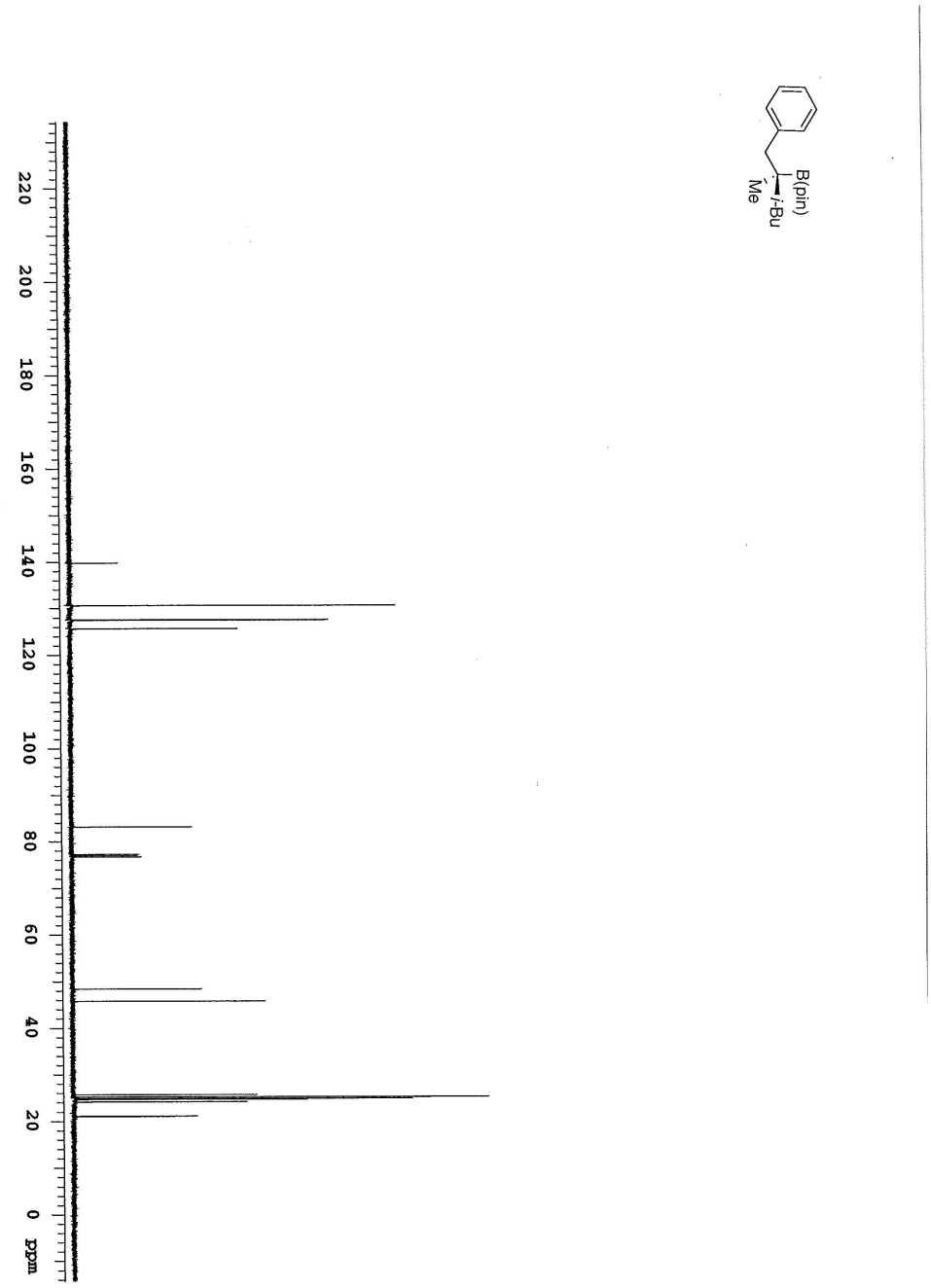
9.32
ppm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i-Bu
Me
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200
180
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120
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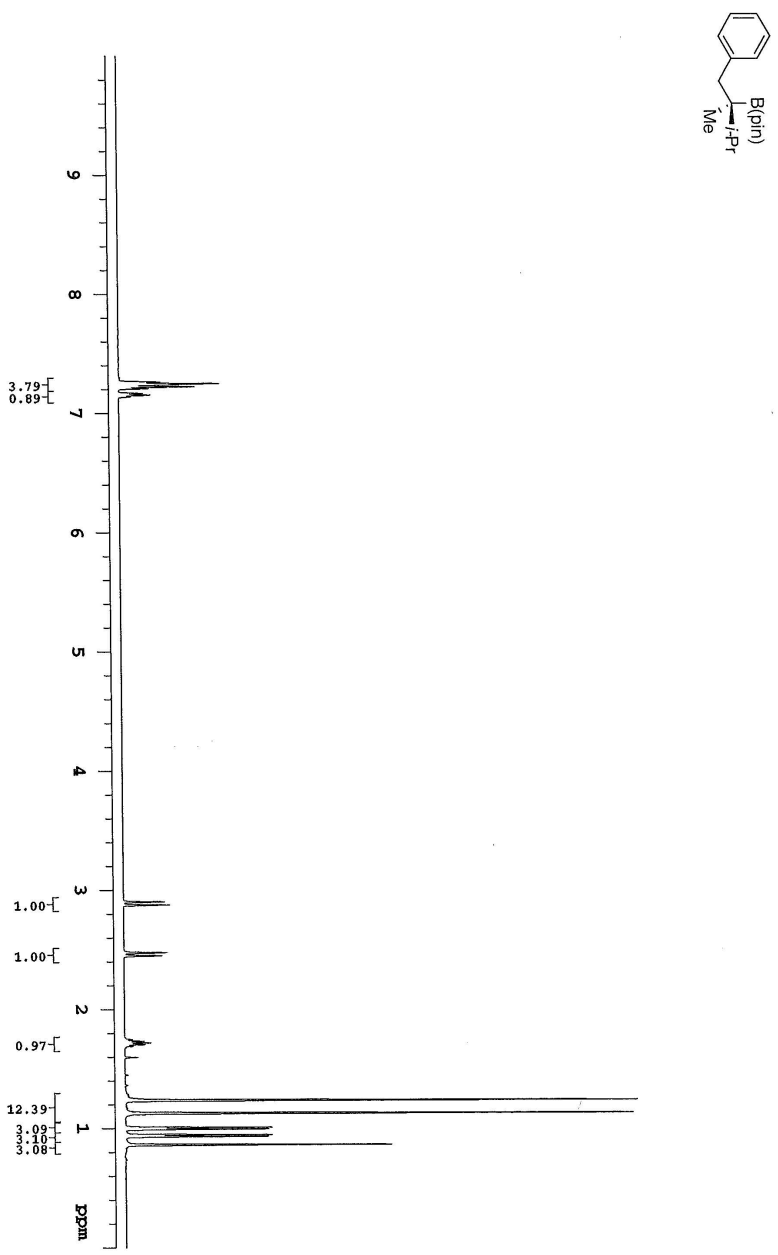
20
0
ppm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1.00
0.97
12.39
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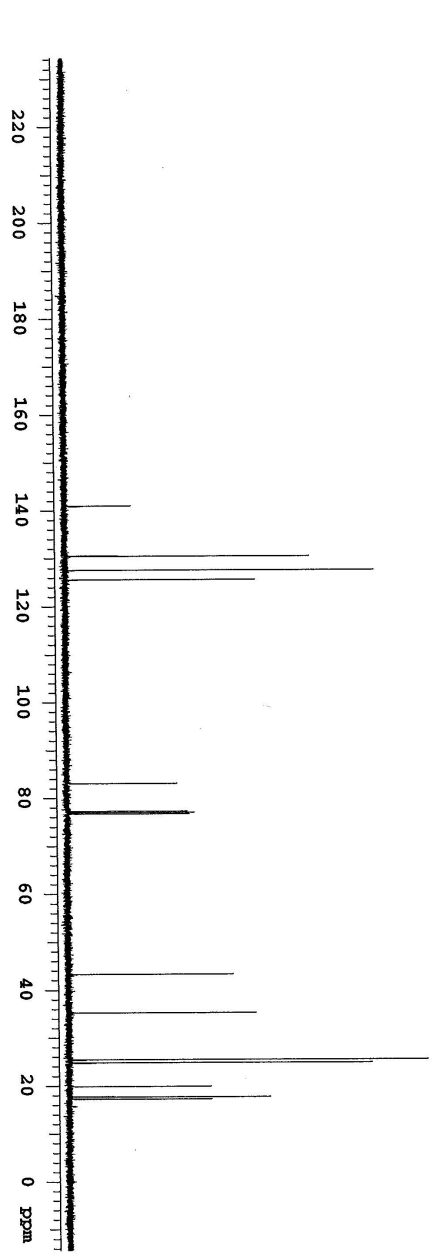
3.10
3.08
ppm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Me
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0
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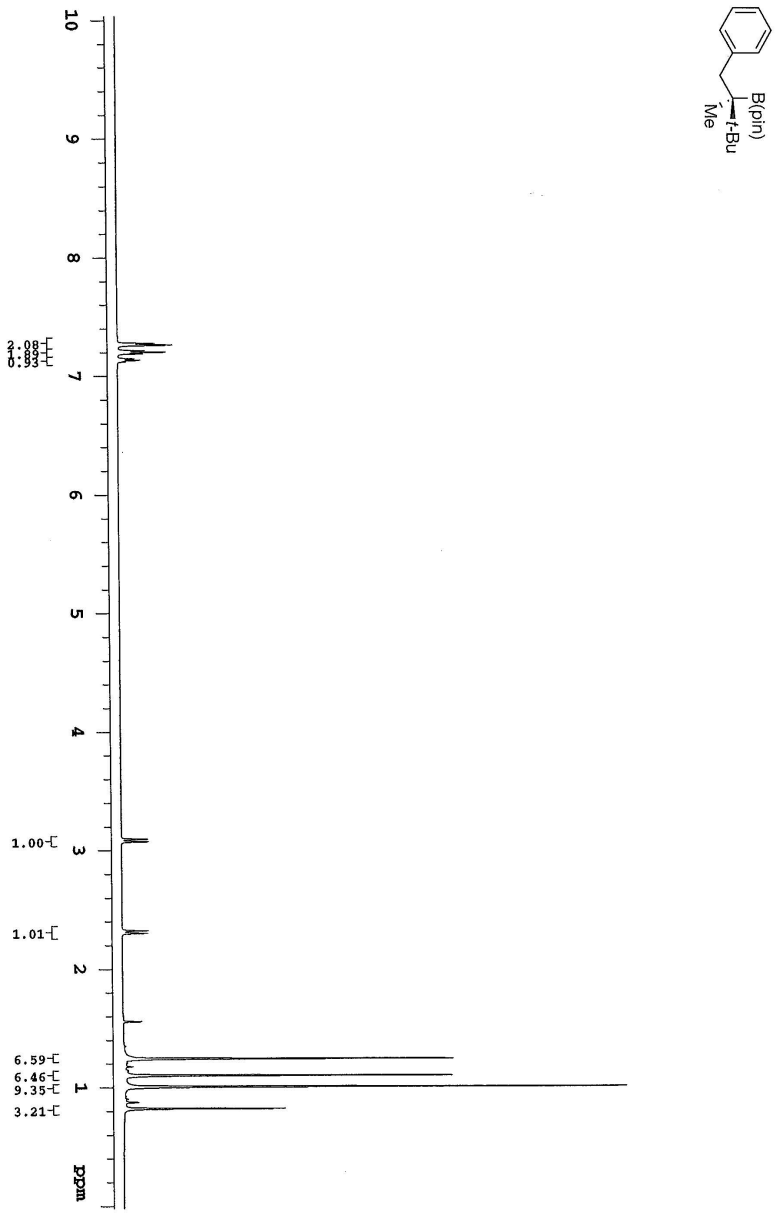
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6
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4
3
2
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ppm
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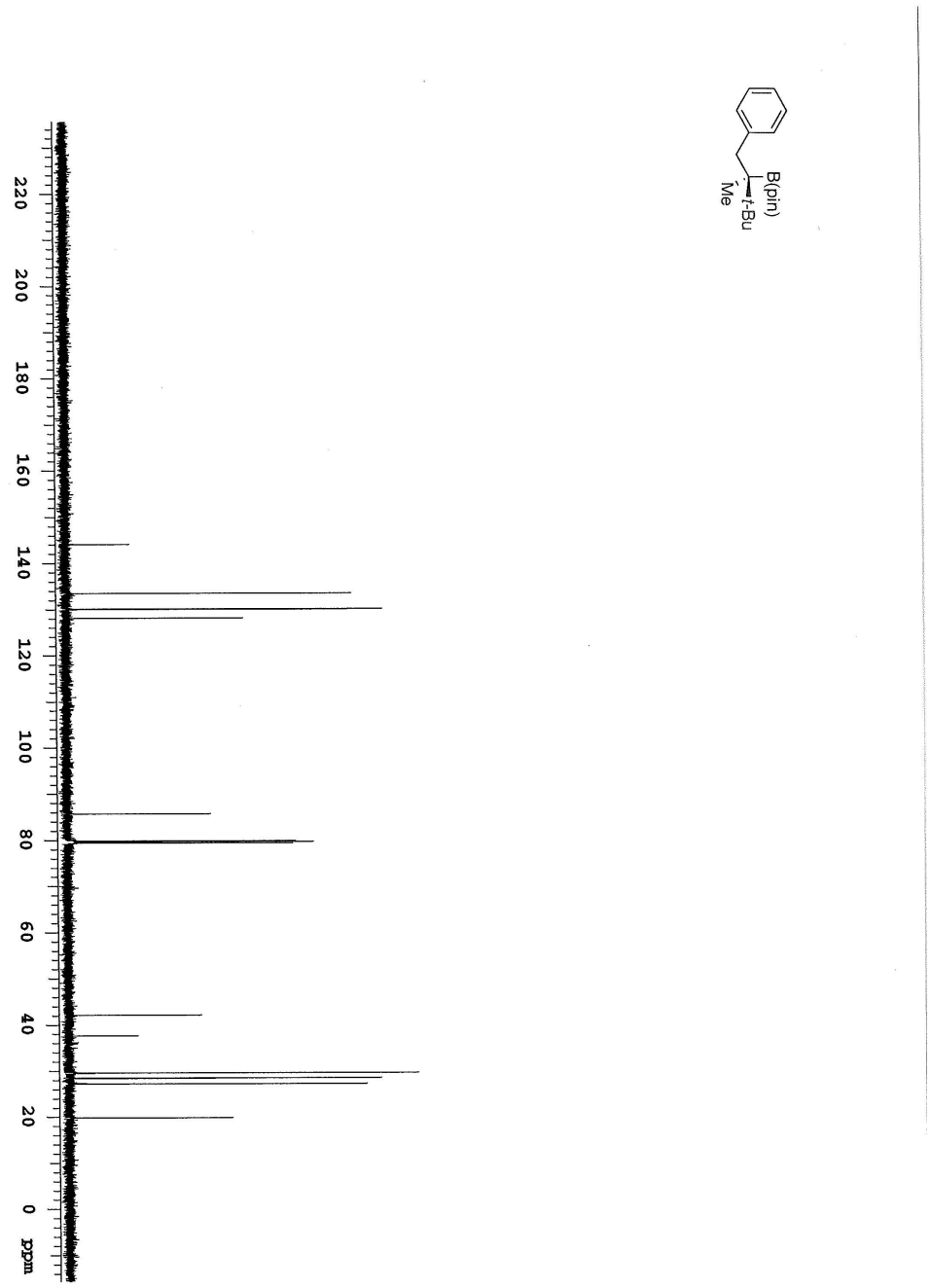
1.00
1.01
6.59
6.46
9.35
3.21


B(pin)
t-Bu
Me
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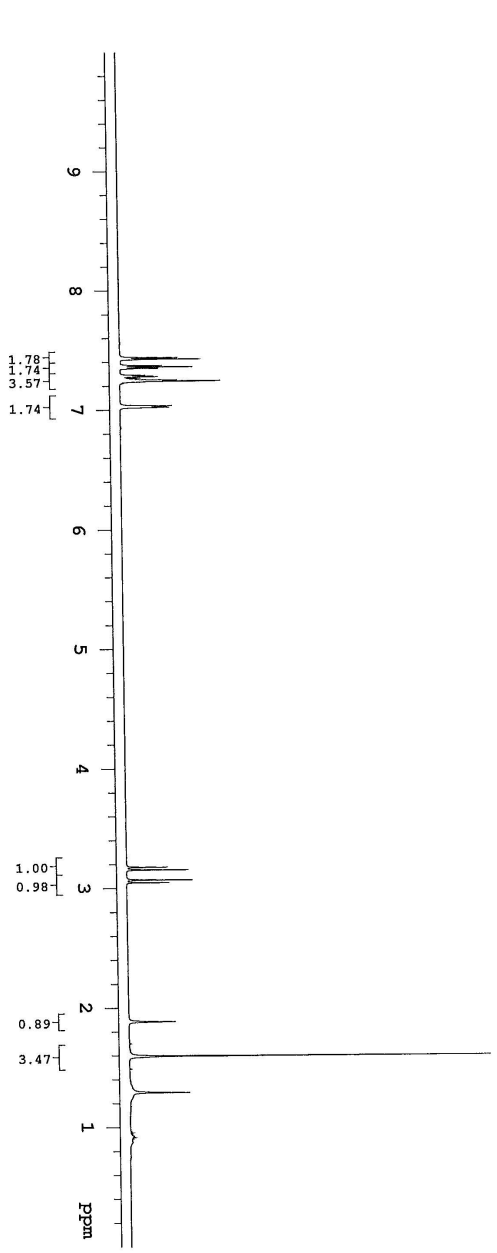
200
180
160
140
120
100
80
60
40
20
0
ppm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Ph
Me
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1.74
3.57
1.74
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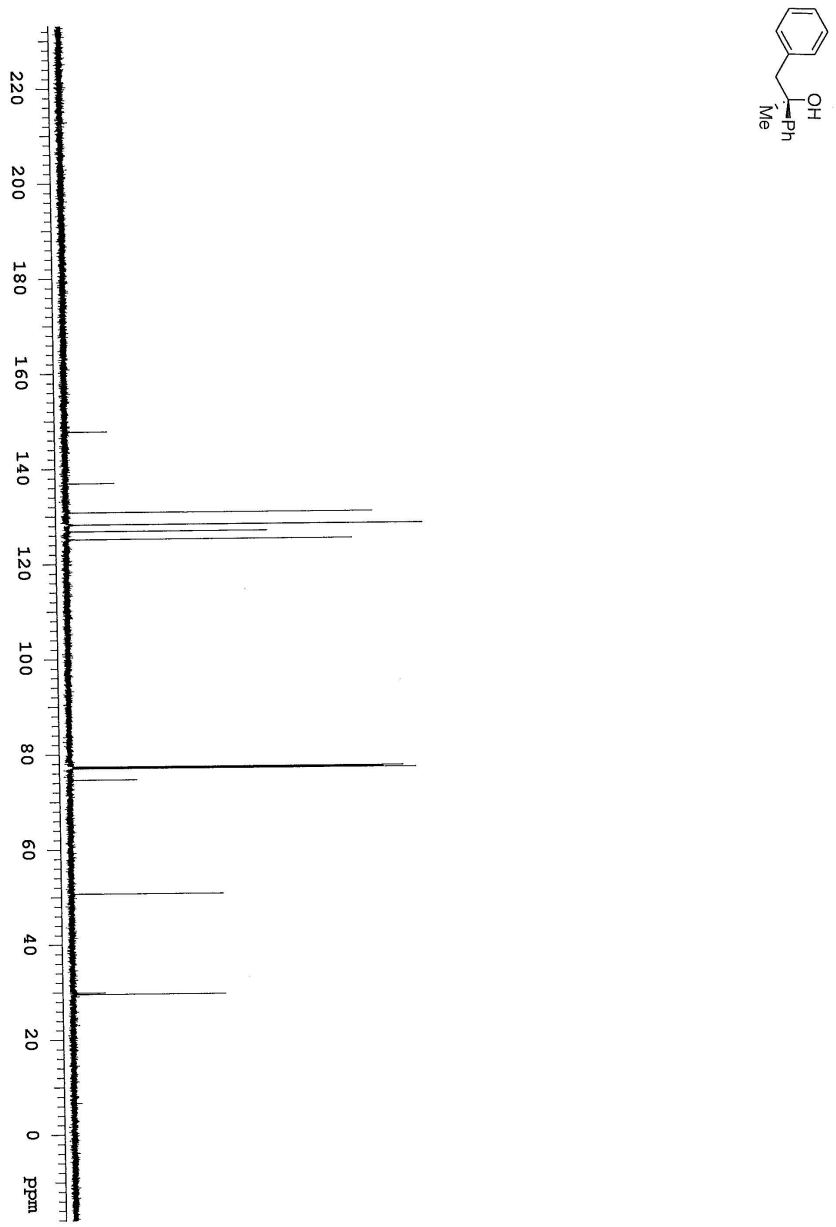
0.98
0.89
3.47
ppm


OH
Ph
Me
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120
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40
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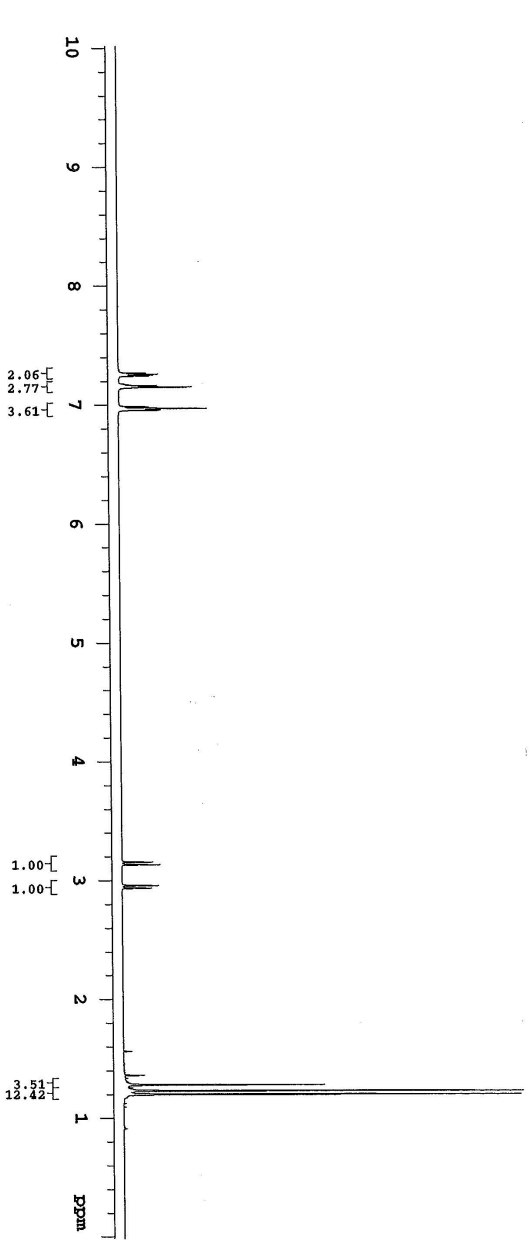
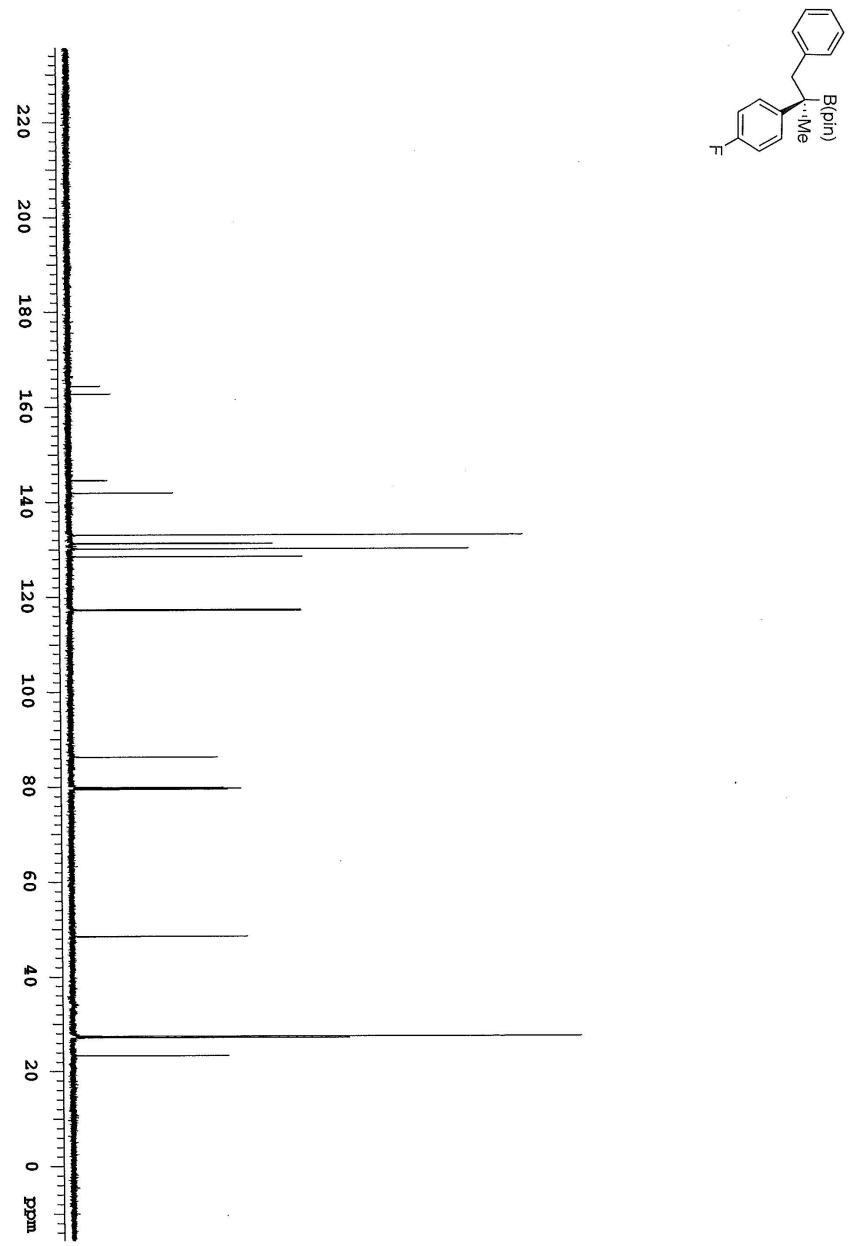

B(pin)
Me
F
10
9
8
7
6
5
4
3
2
1
ppm
2.06
2.77
3.61
1.00
1.00
3.51
12.42


B(pin)
Me
F
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60
40
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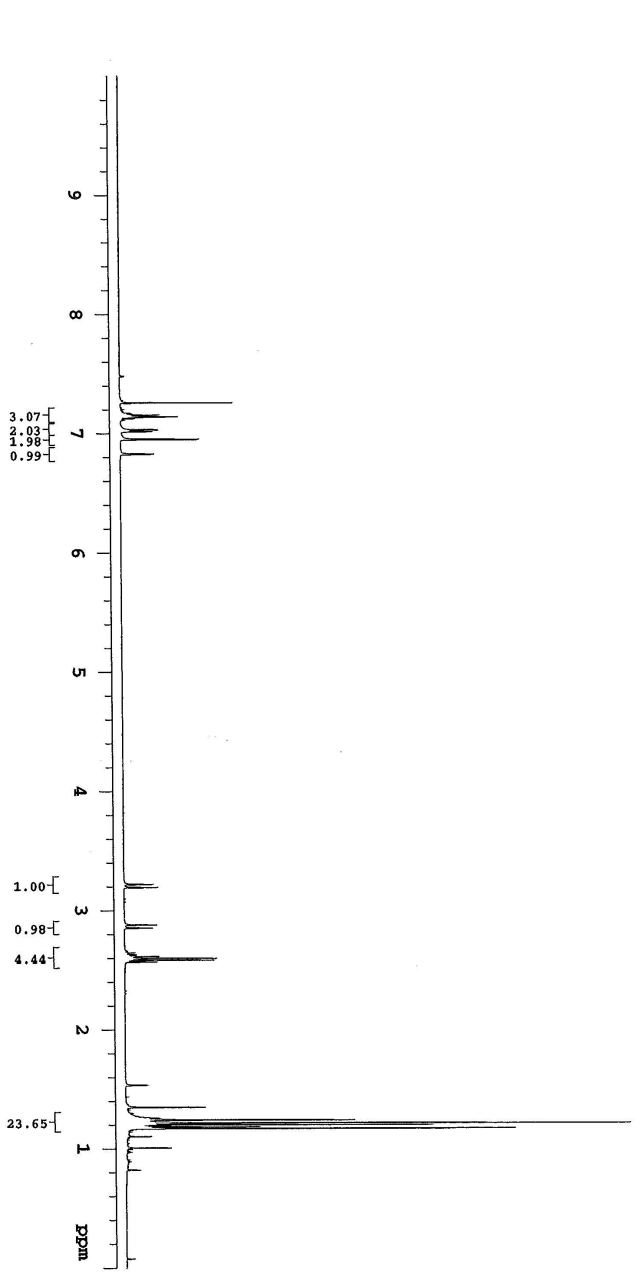
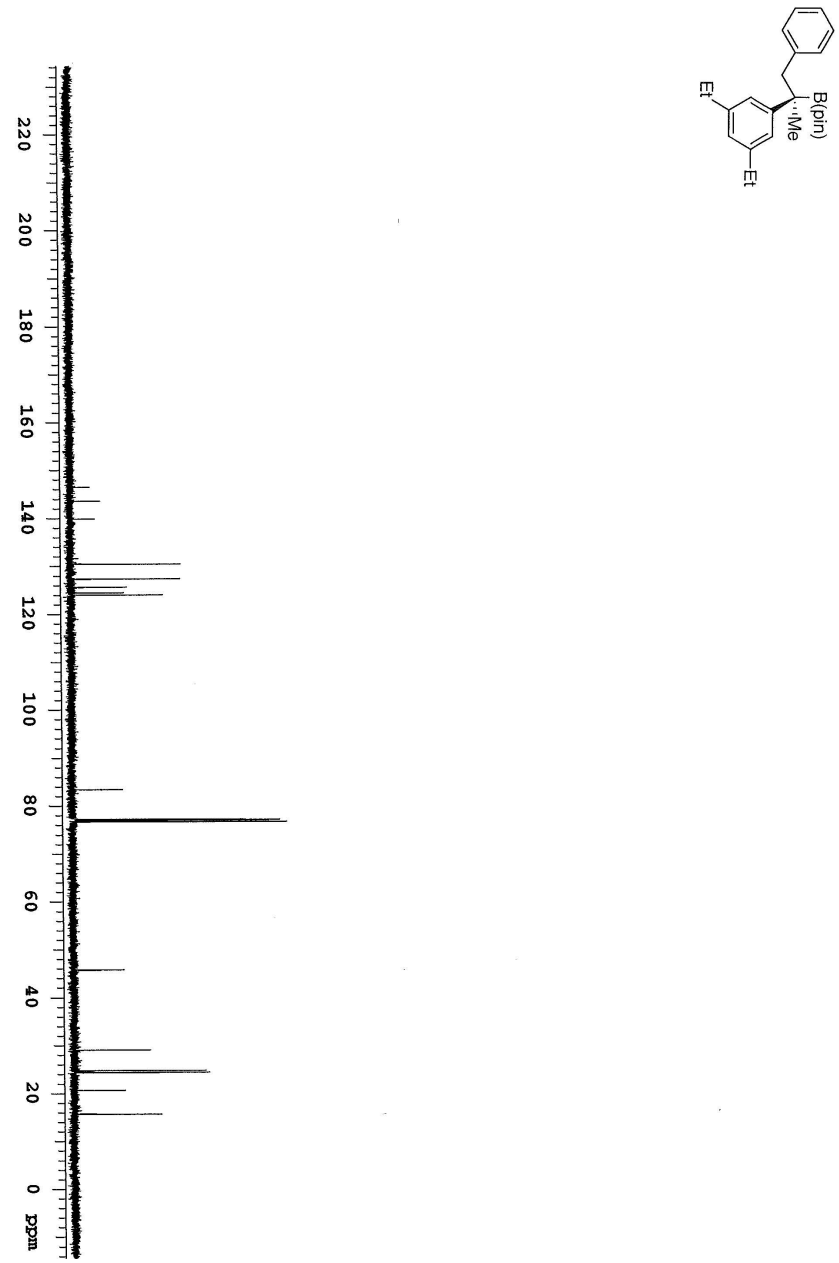
0
ppm


B(pin)
Me
Et
Et
3.07
2.03
1.98
0.99
1.00
0.98
4.44
23.65
9
8
7
6
5
4
3
2
1
ppm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Me
Et
Et
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200
180
160
140
120
100
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60
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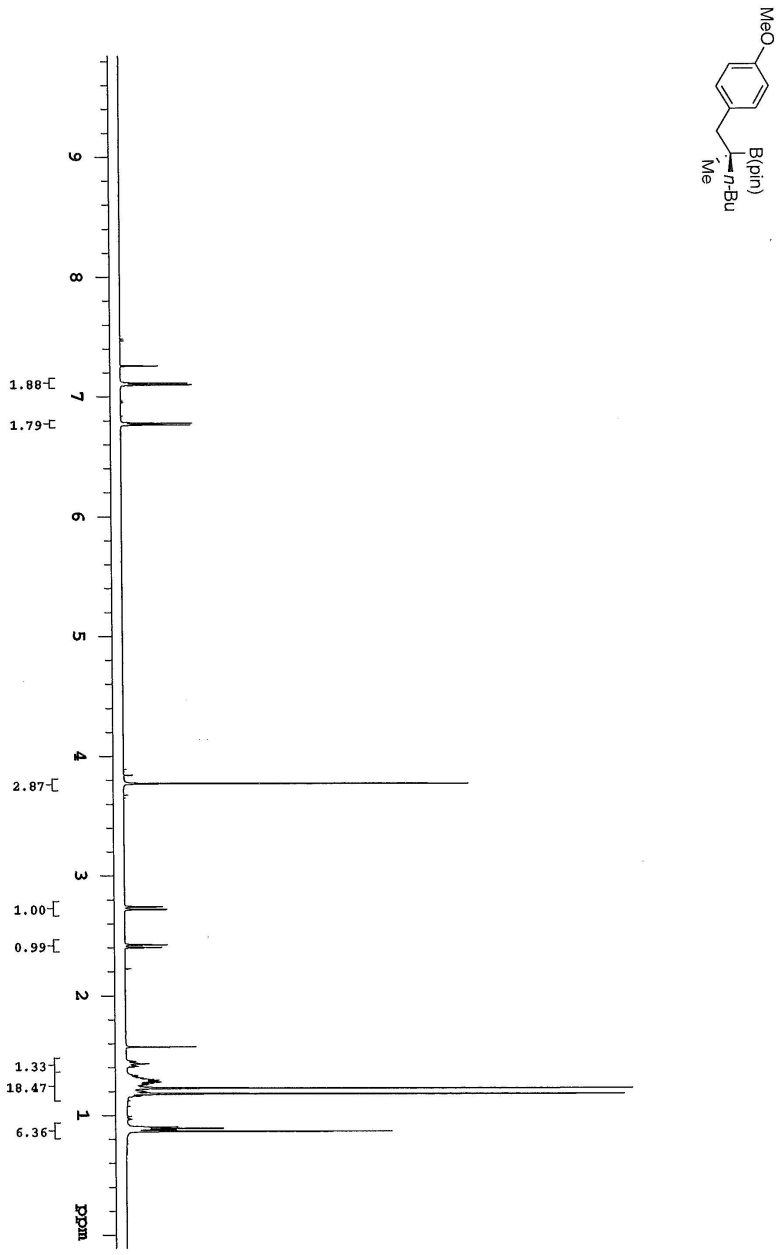
20
0
ppm


MeO
B(pin)
n-Bu
Me
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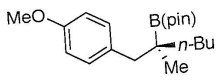
1.79
2.87
1.00
0.99
1.33
18.47
6.36
ppm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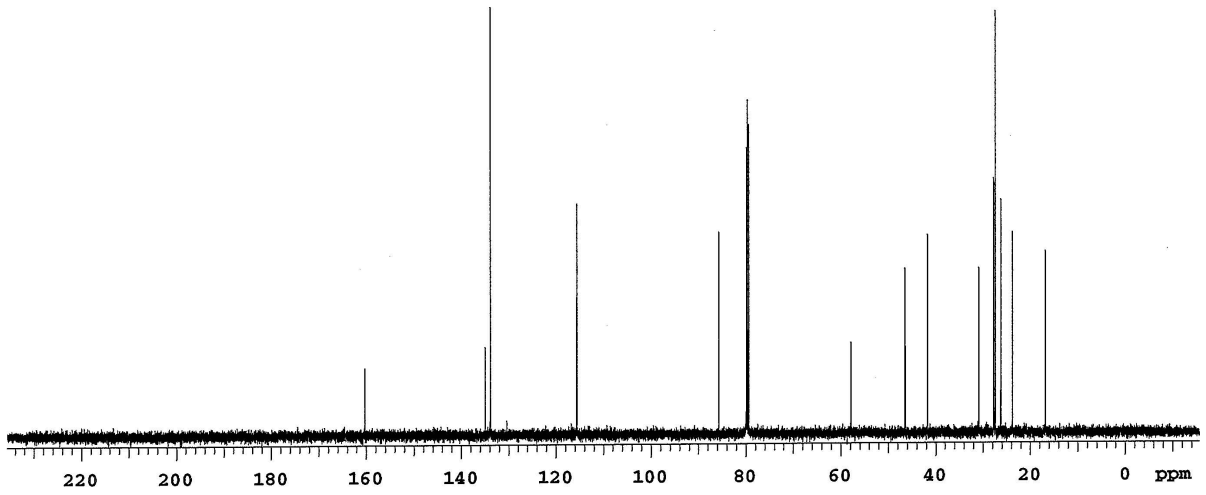
B(pin)
n-Bu
Me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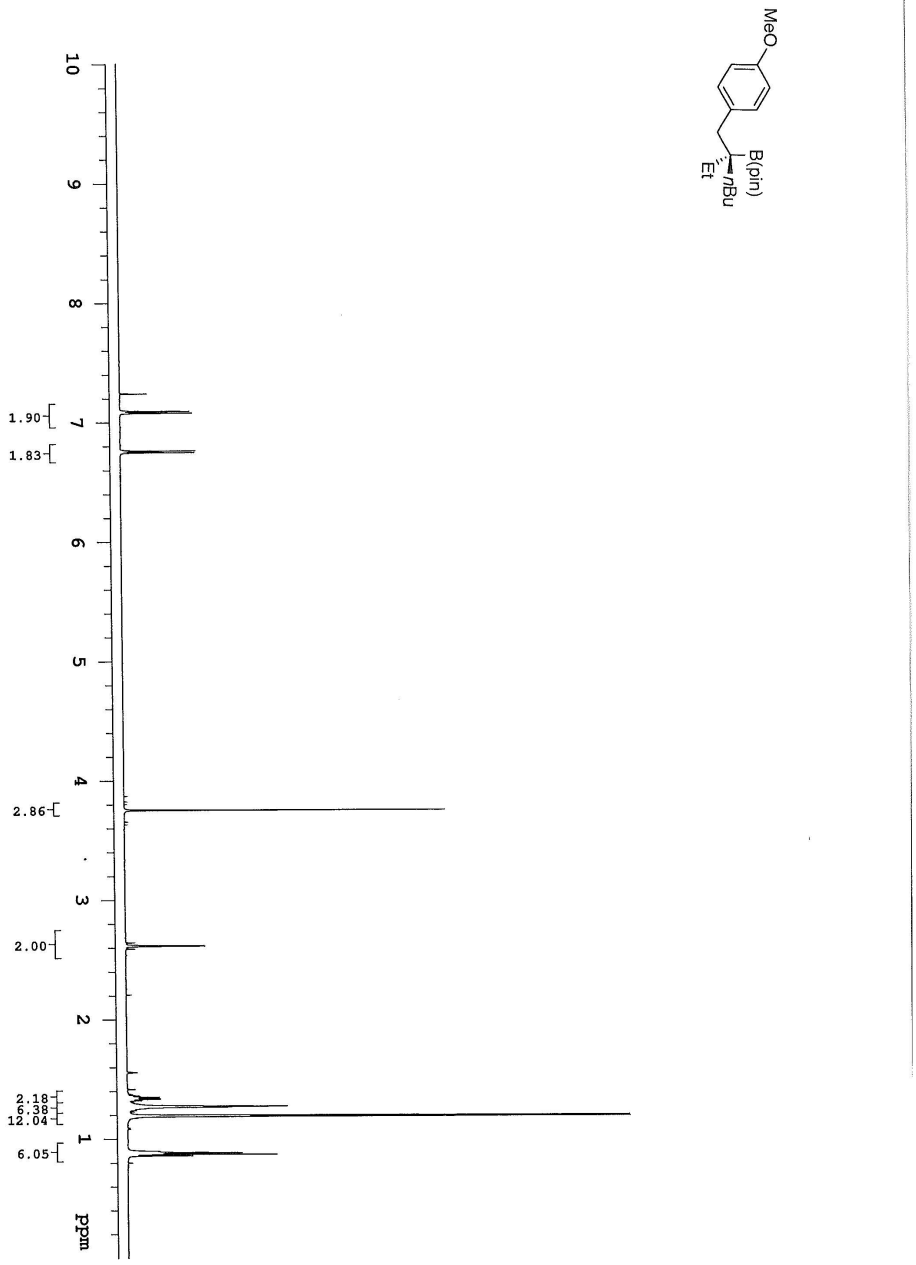
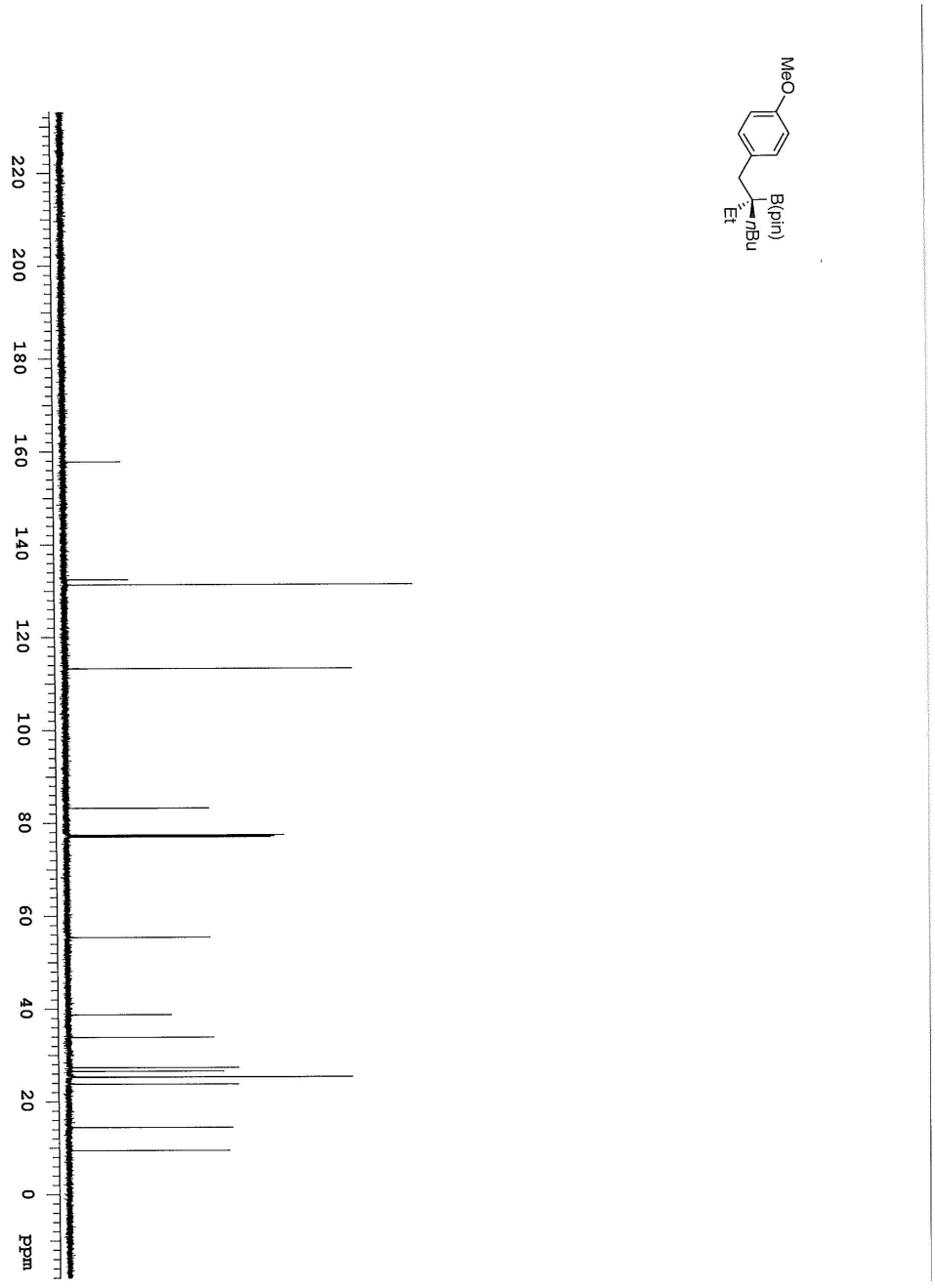
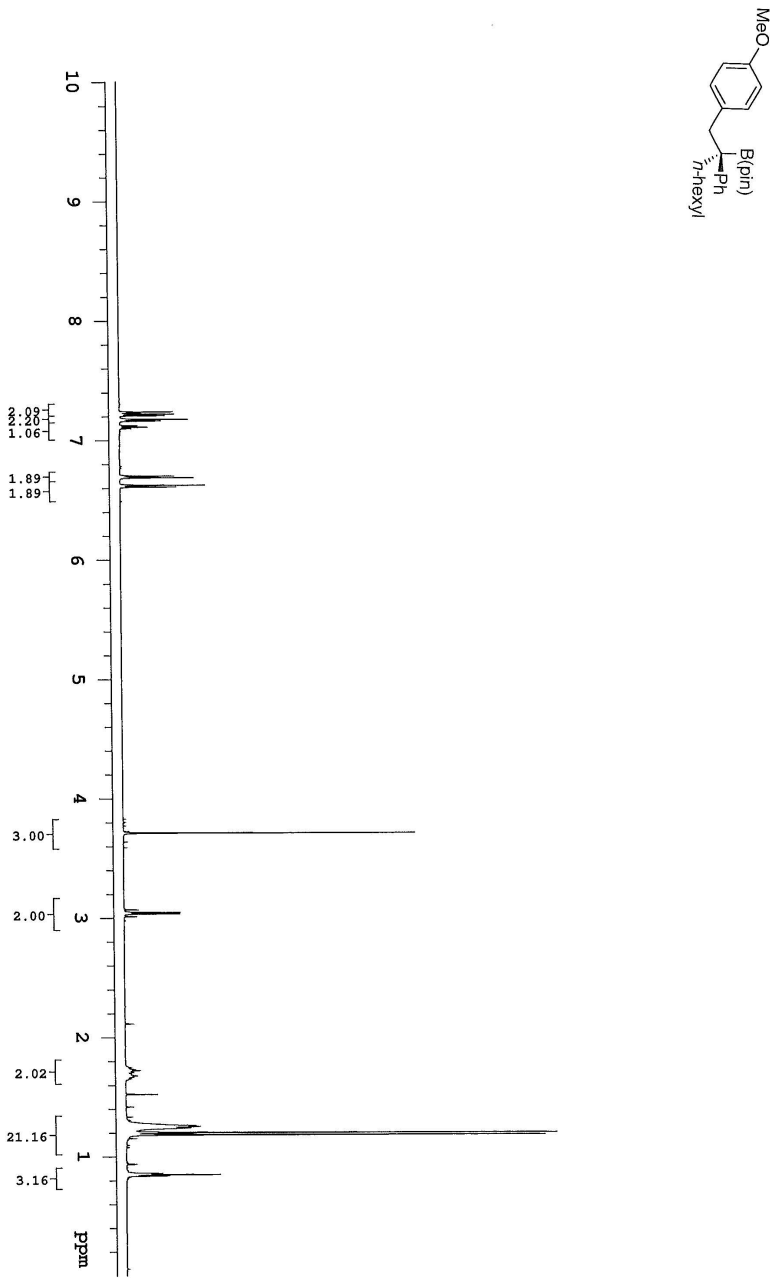
200
180
160
140
120
100
80
60
40
20
0
ppm


MeO
B(pin)
Et
nBu
10
9
8
7
6
5
4
3
2
1
ppm
1.90
1.83
2.86
2.00
2.18
6.38
12.04
6.05


MeO
B(pin)
nBu
Et
220
200
180
160
140
120
100
80
60
40
20
0
ppm


MeO
B(pin)
Ph
n-hexyl
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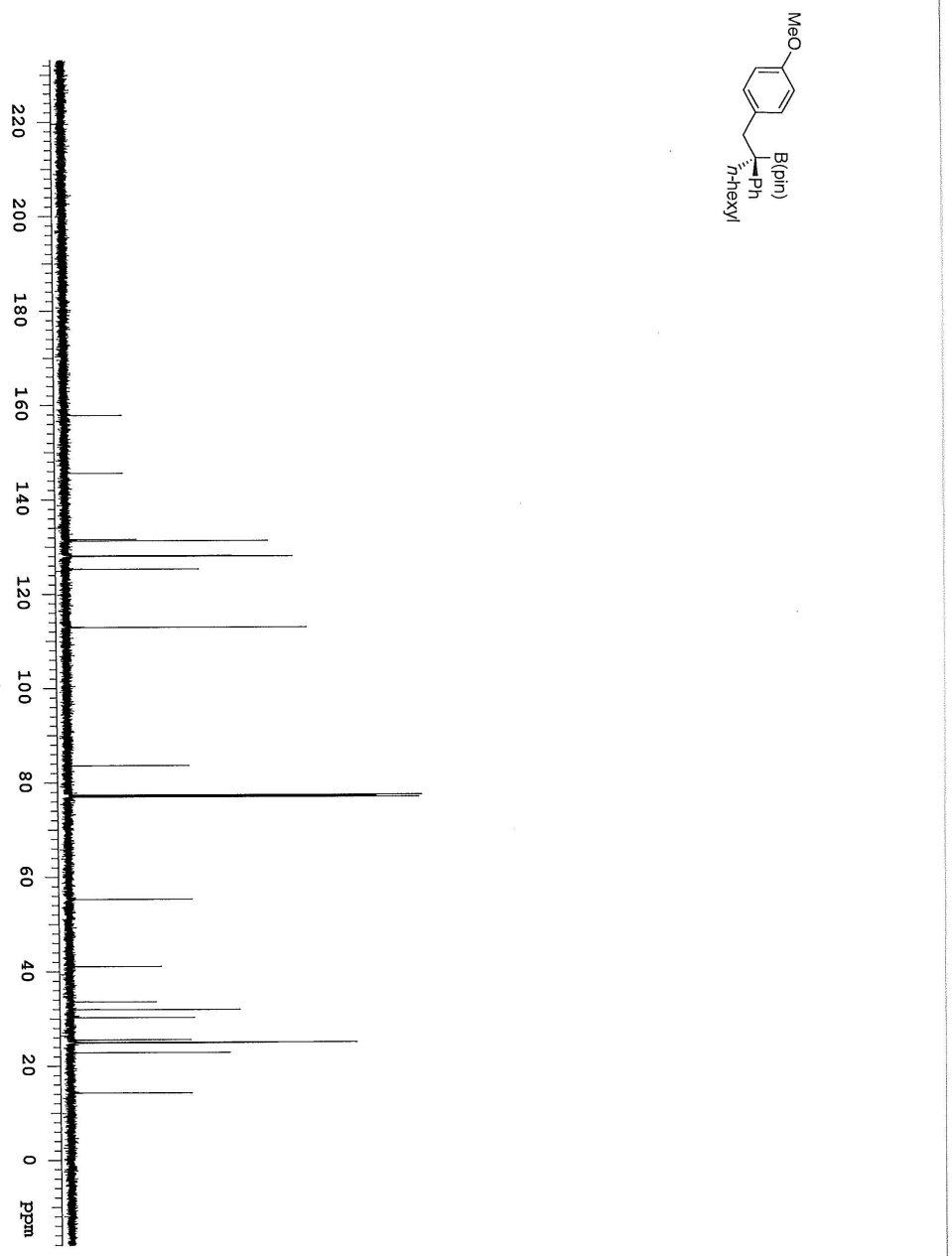
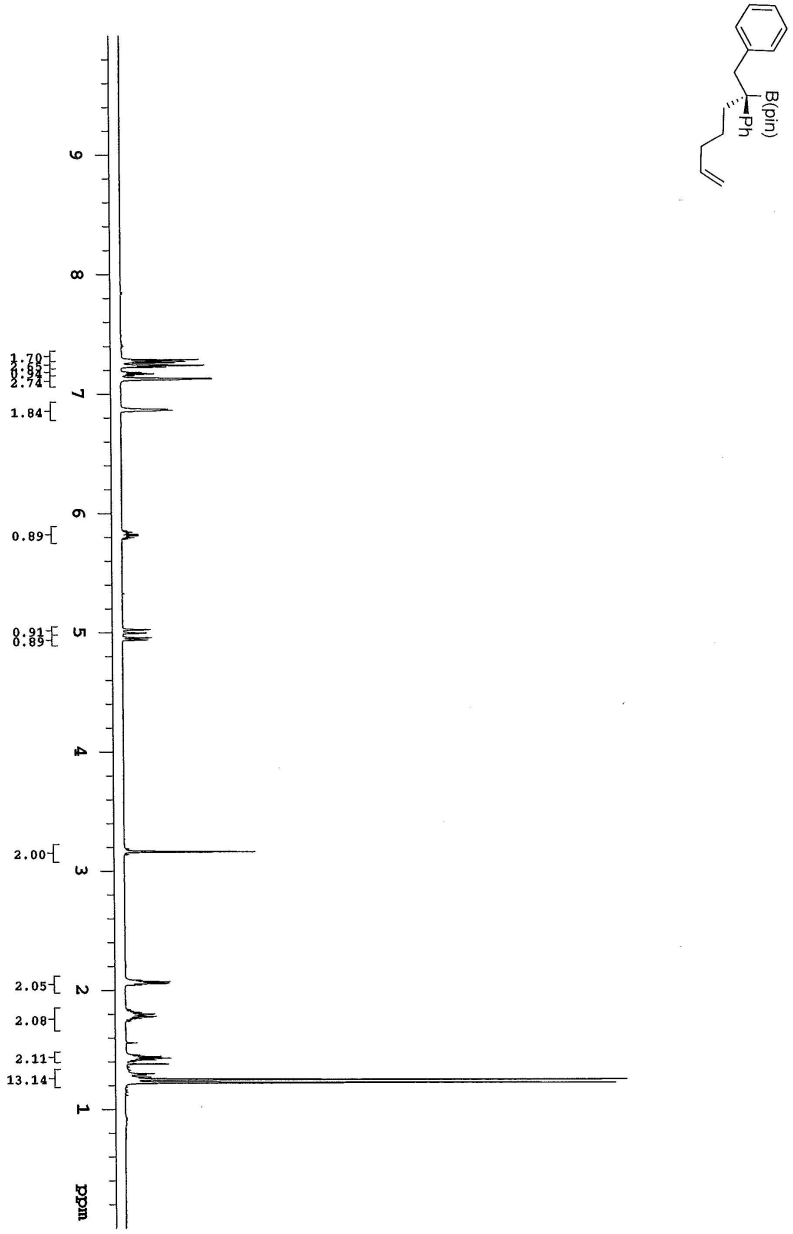
2.20
1.06
1.89
1.89
3.00
2.00
2.02
21.16
3.16
ppm


MeO
B(pin)
Ph
n-hexyl
220
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
Ph
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0.92
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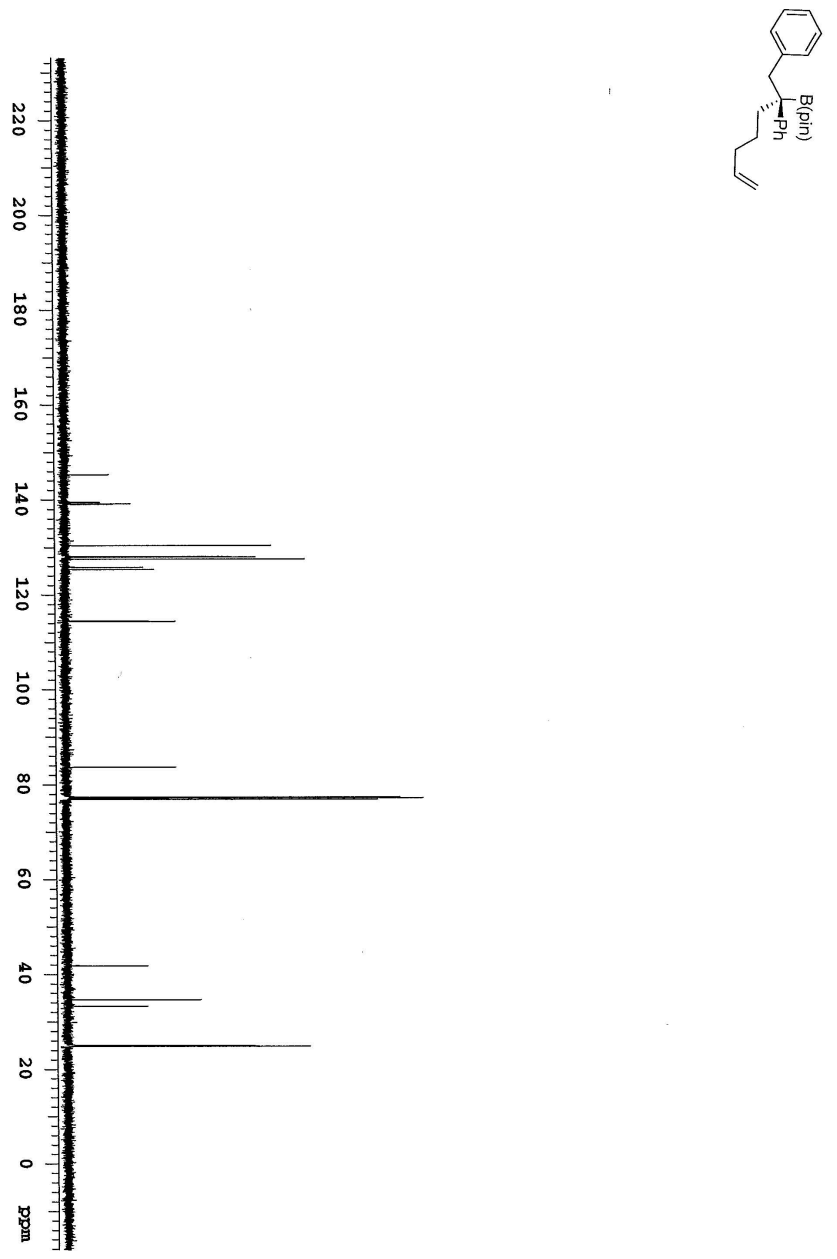
1.84
0.89
0.91
0.89
2.00
2.05
2.08
2.11
13.14
ppm


B(pin)
Ph
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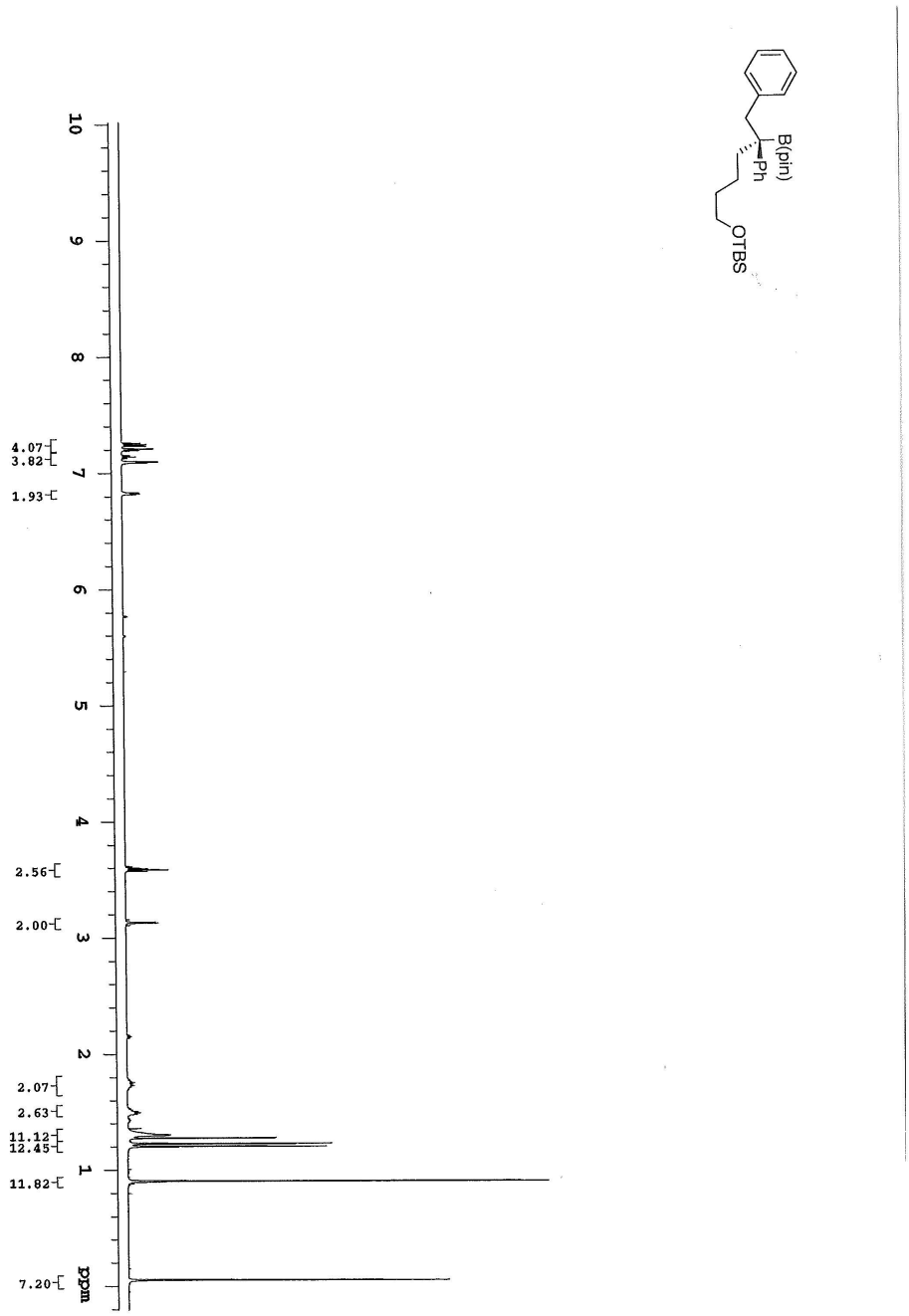
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
Ph
OTBS
10
9
8
7
6
5
4
3
2
1
ppm
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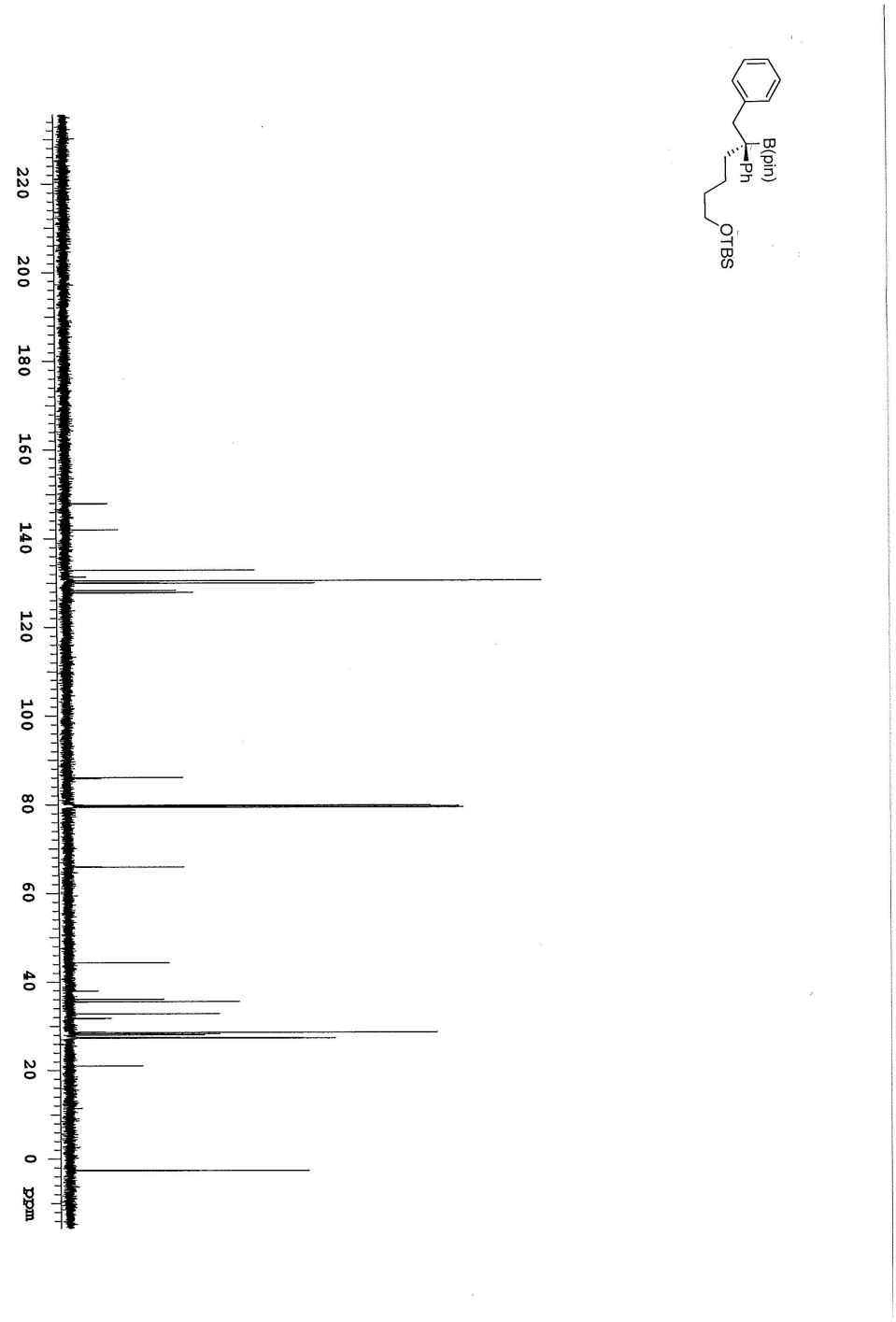
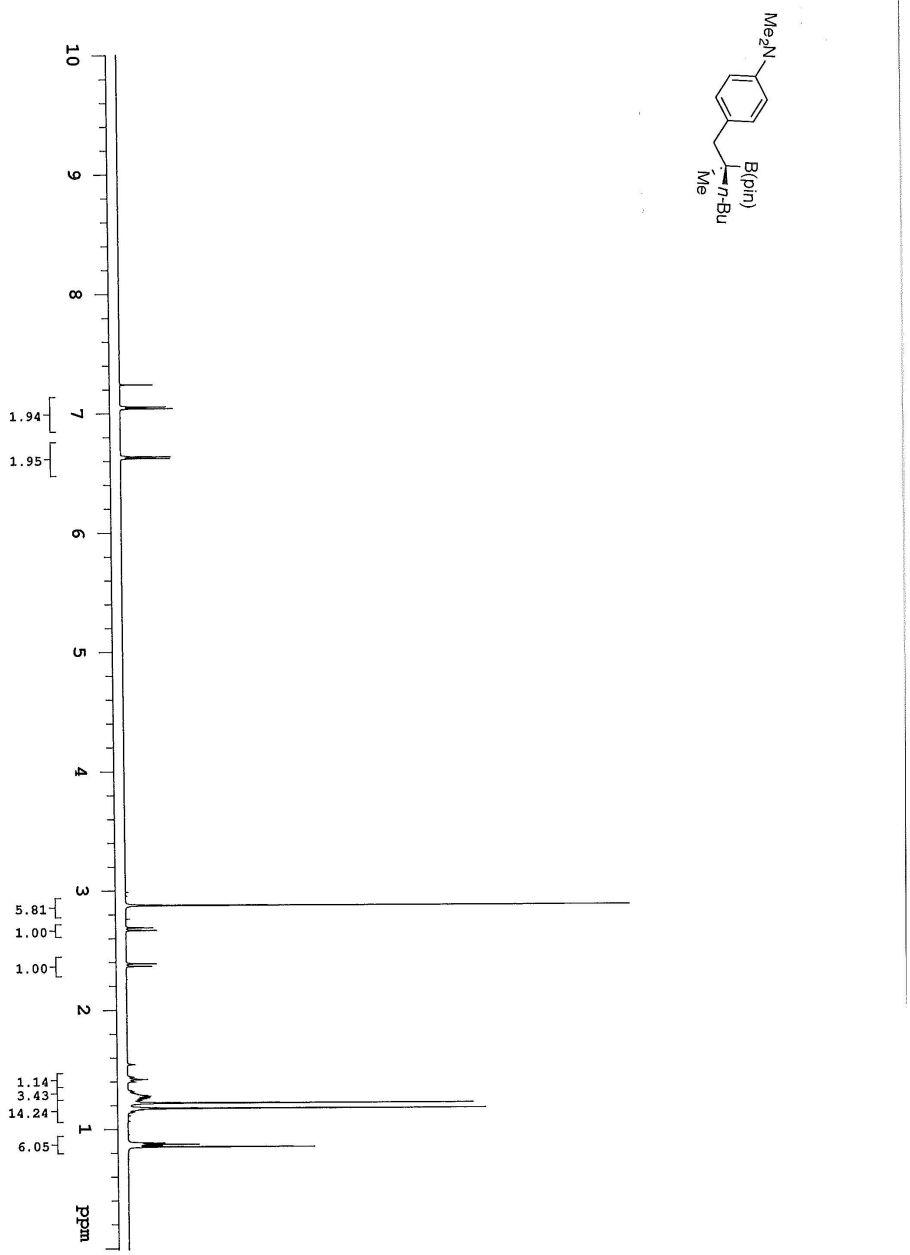
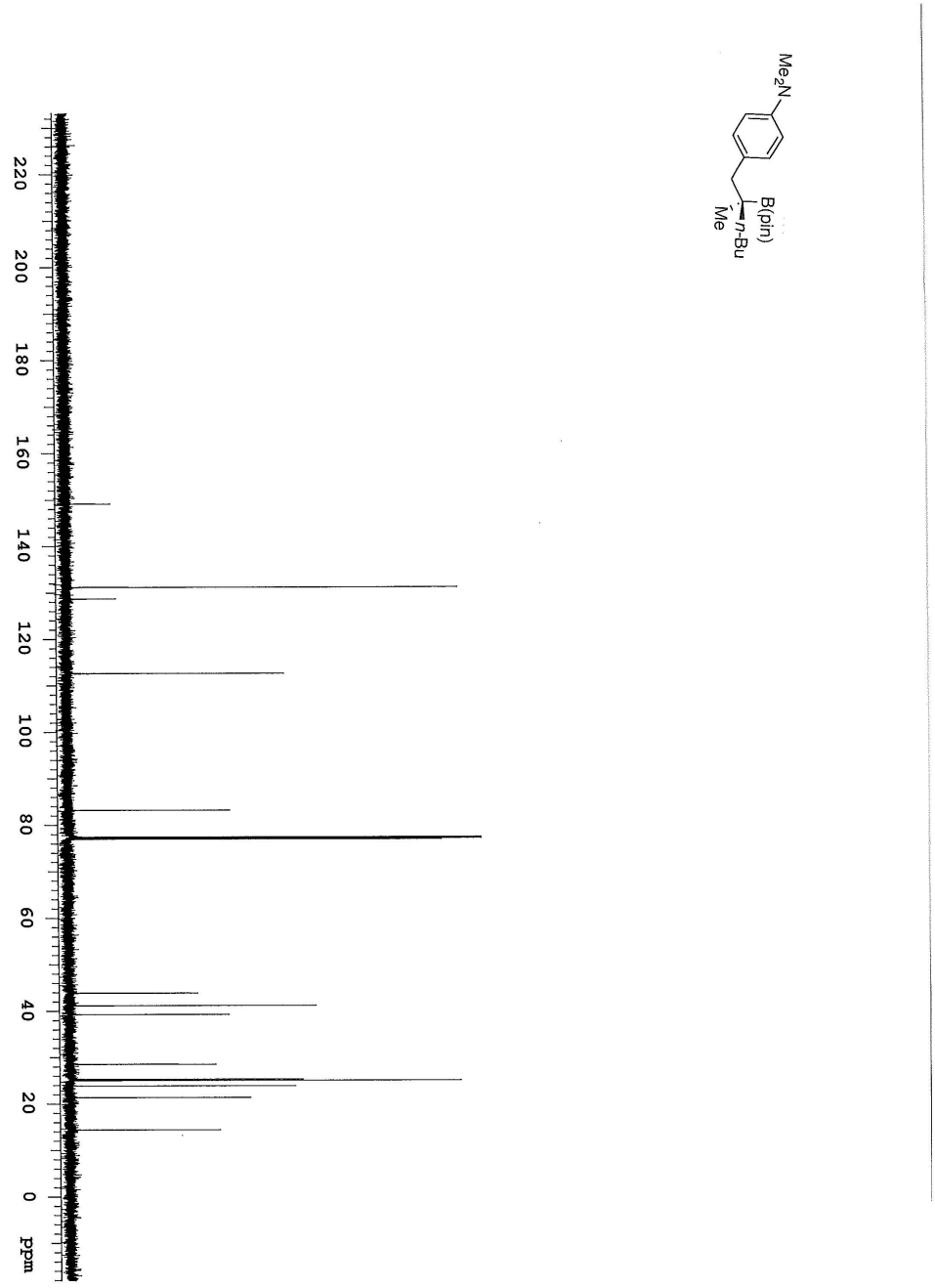
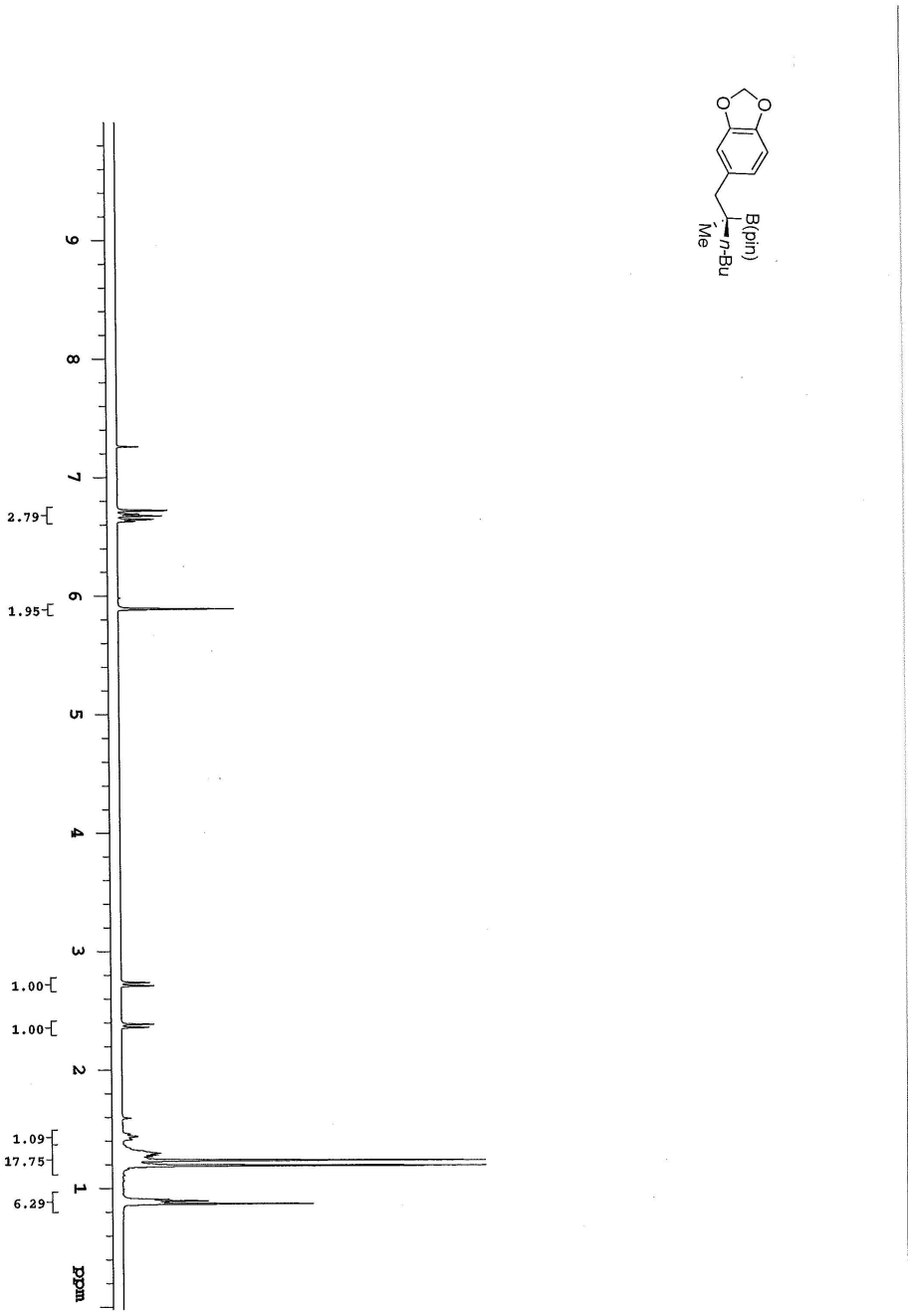
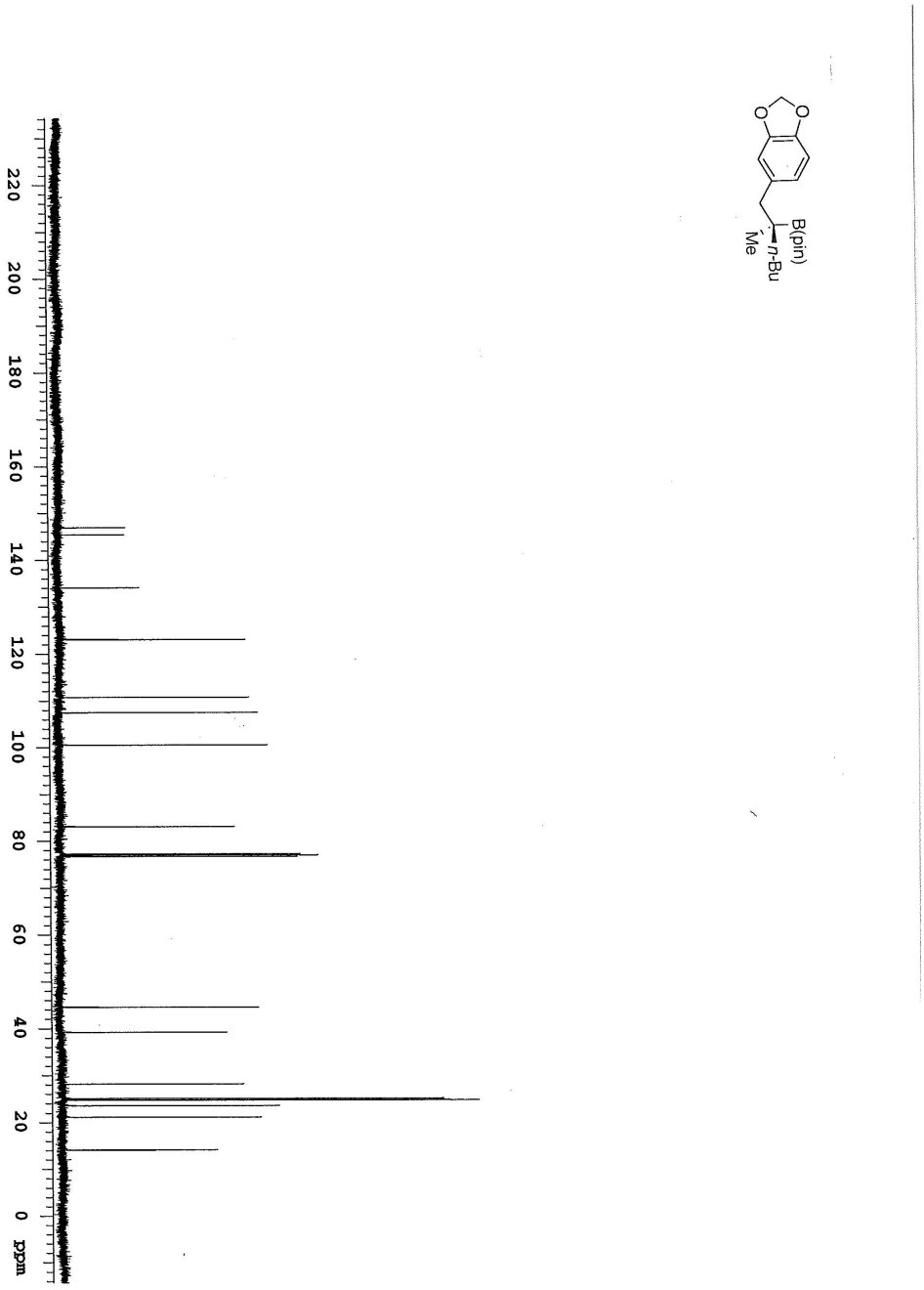
3.82
1.93
2.56
2.00
2.07
2.63
11.12
12.45
11.82
7.20

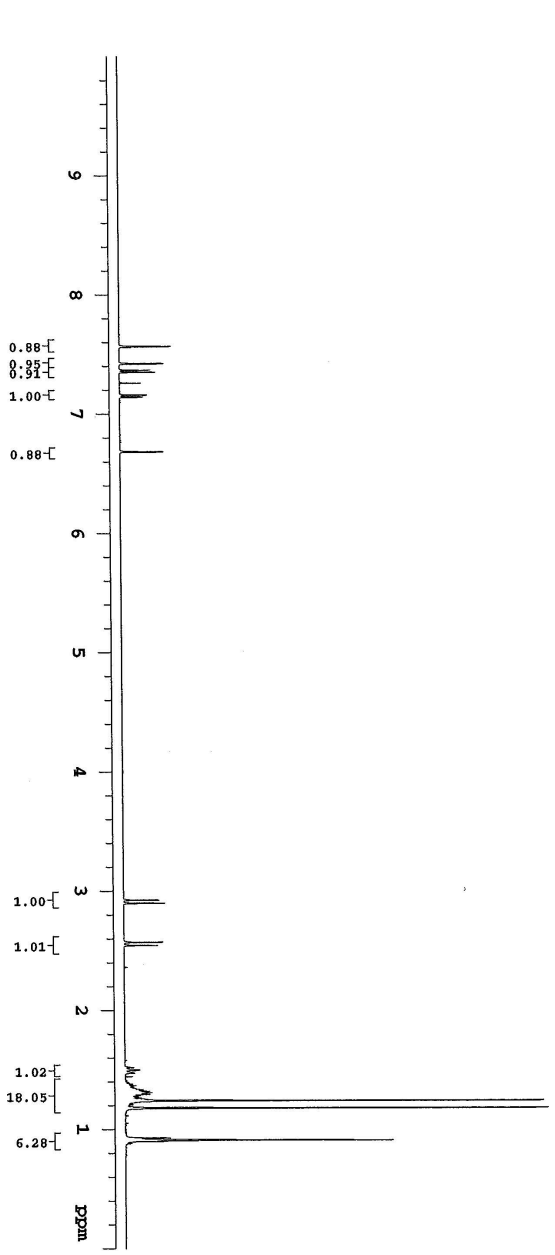

B(pin)
Ph
OTBS
220
200
180
160
140
120
100
80
60
40
20
0
ppm

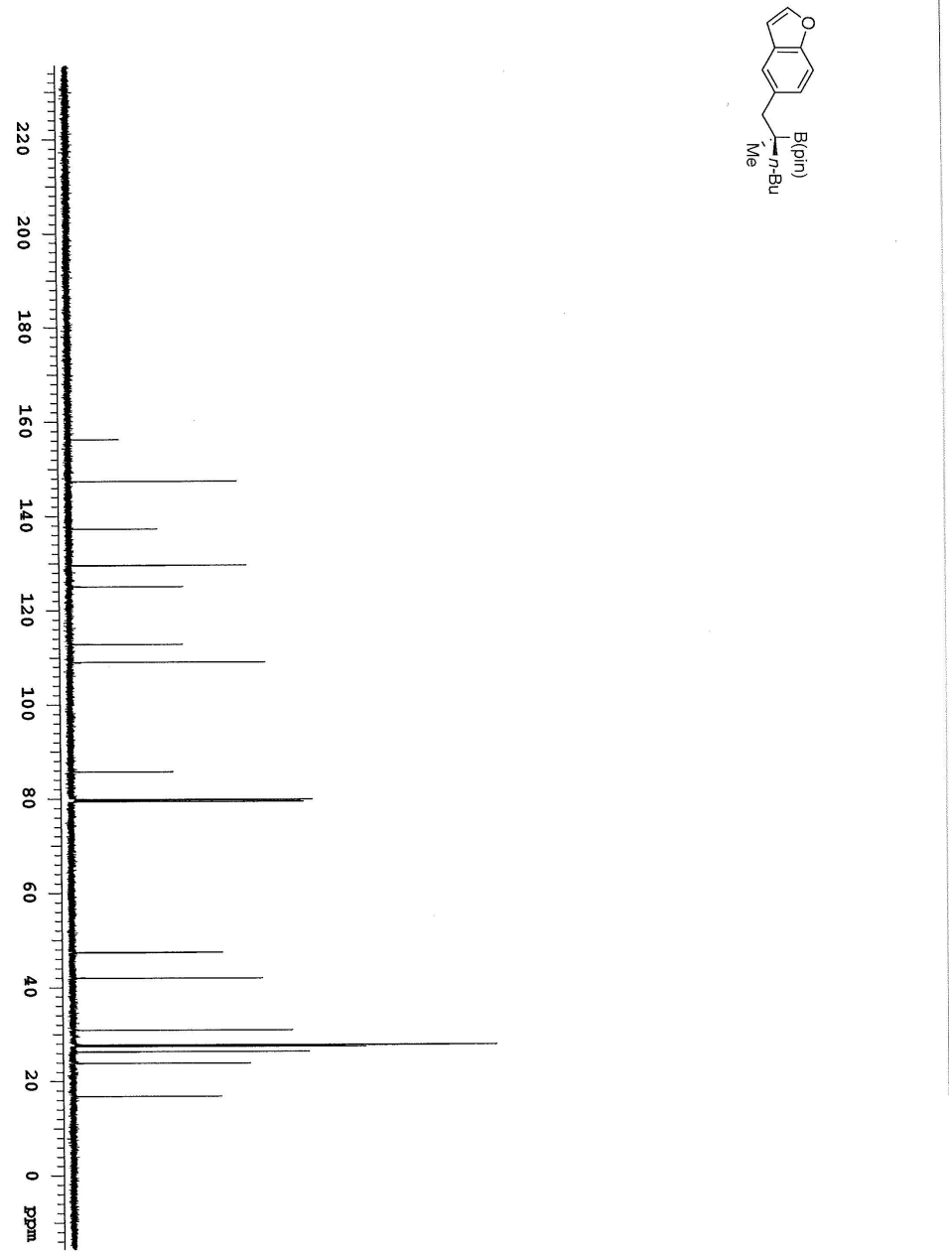

Me2N
B(pin)
n-Bu
Me
10
9
8
7
6
5
4
3
2
1
ppm
1.94
1.95
5.81
1.00
1.00
1.14
3.43
14.24
6.05

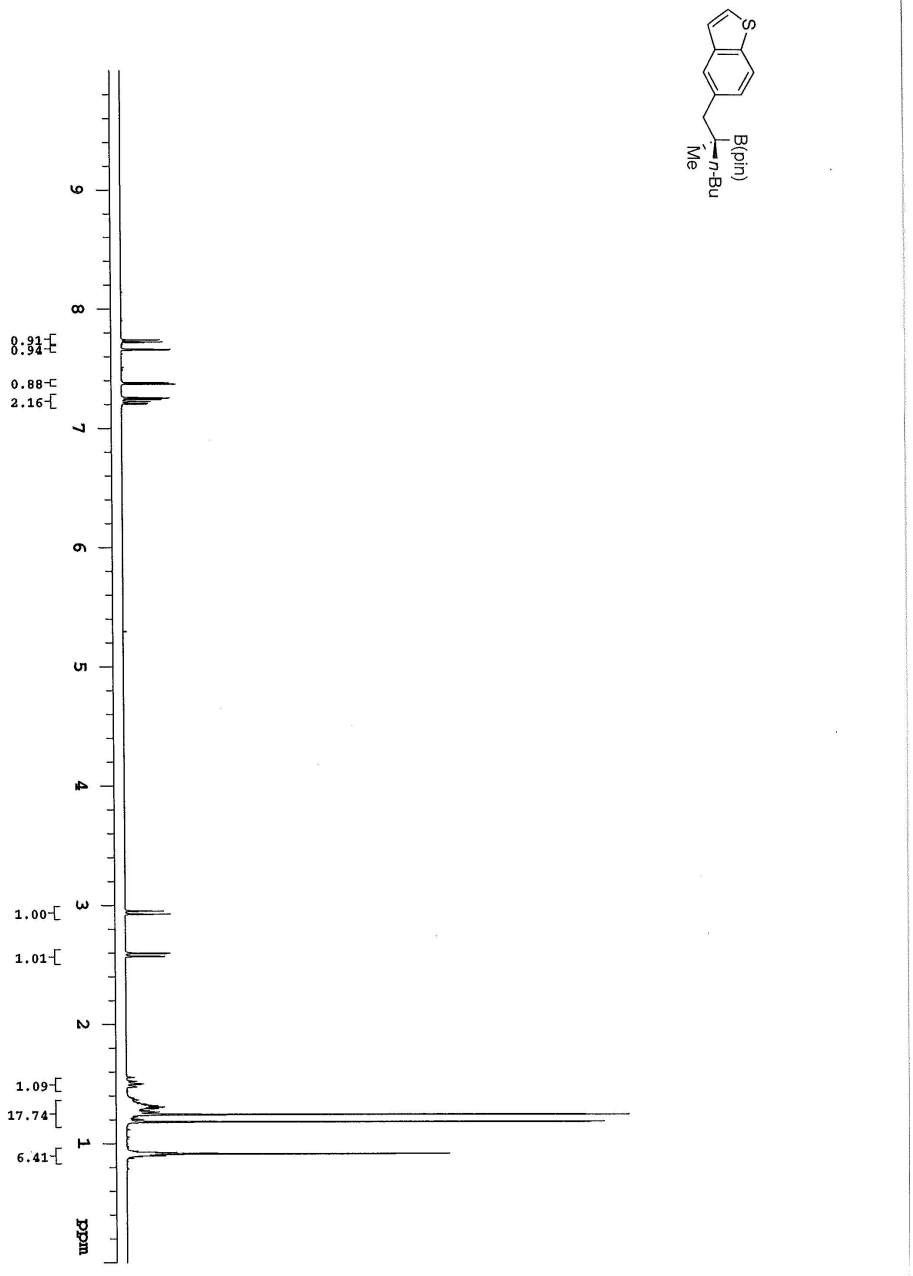

Me2N
B(pin)
n-Bu
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
n-Bu
Me
2.79
1.95
1.00
1.00
1.09
17.75
6.29
ppm


B(pin)
n-Bu
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
n-Bu
Me
0.88
0.95
0.91
1.00
0.88
1.00
1.01
1.02
18.05
6.28
ppm


B(pin)
n-Bu
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


S
B(pin)
n-Bu
Me
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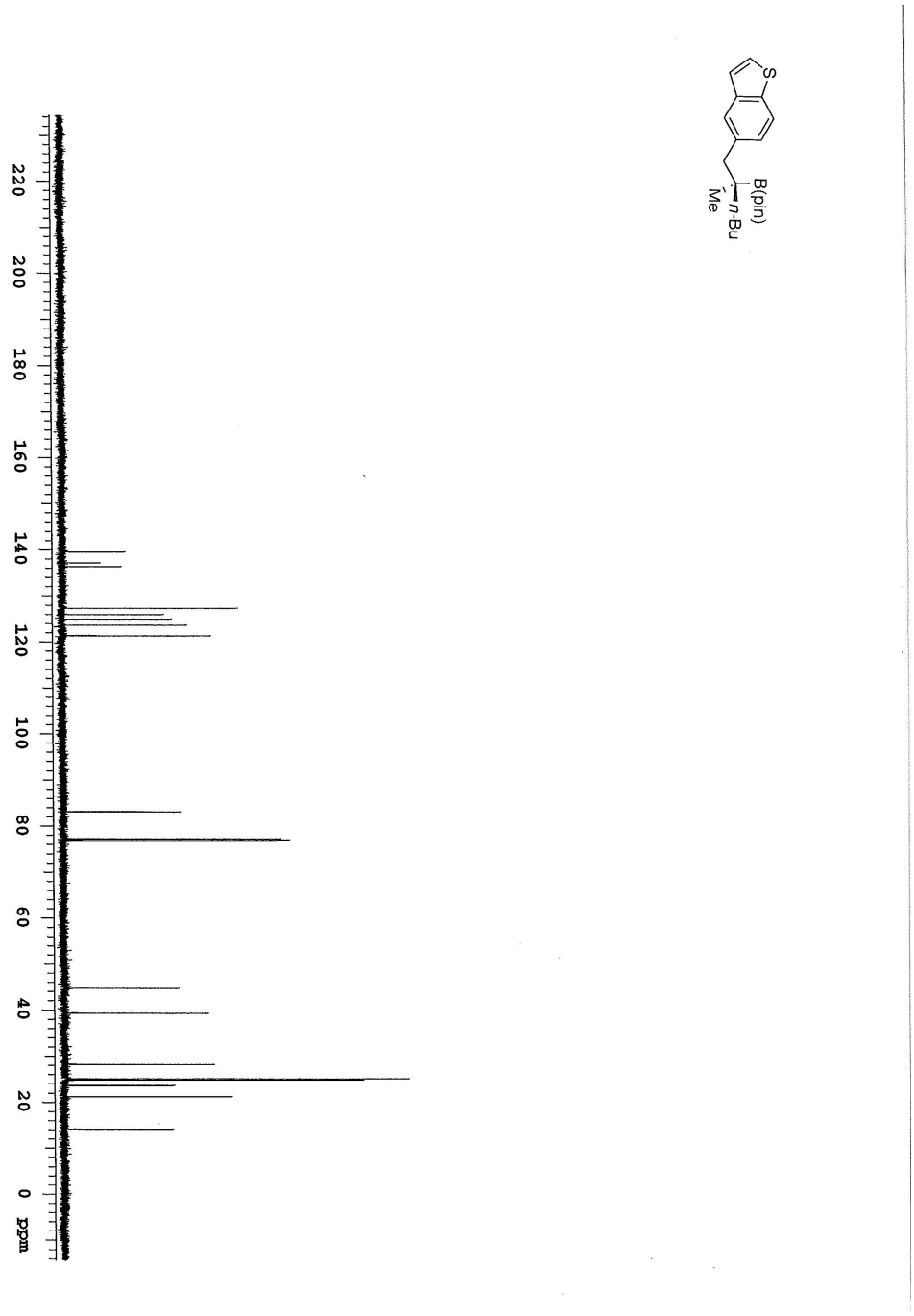
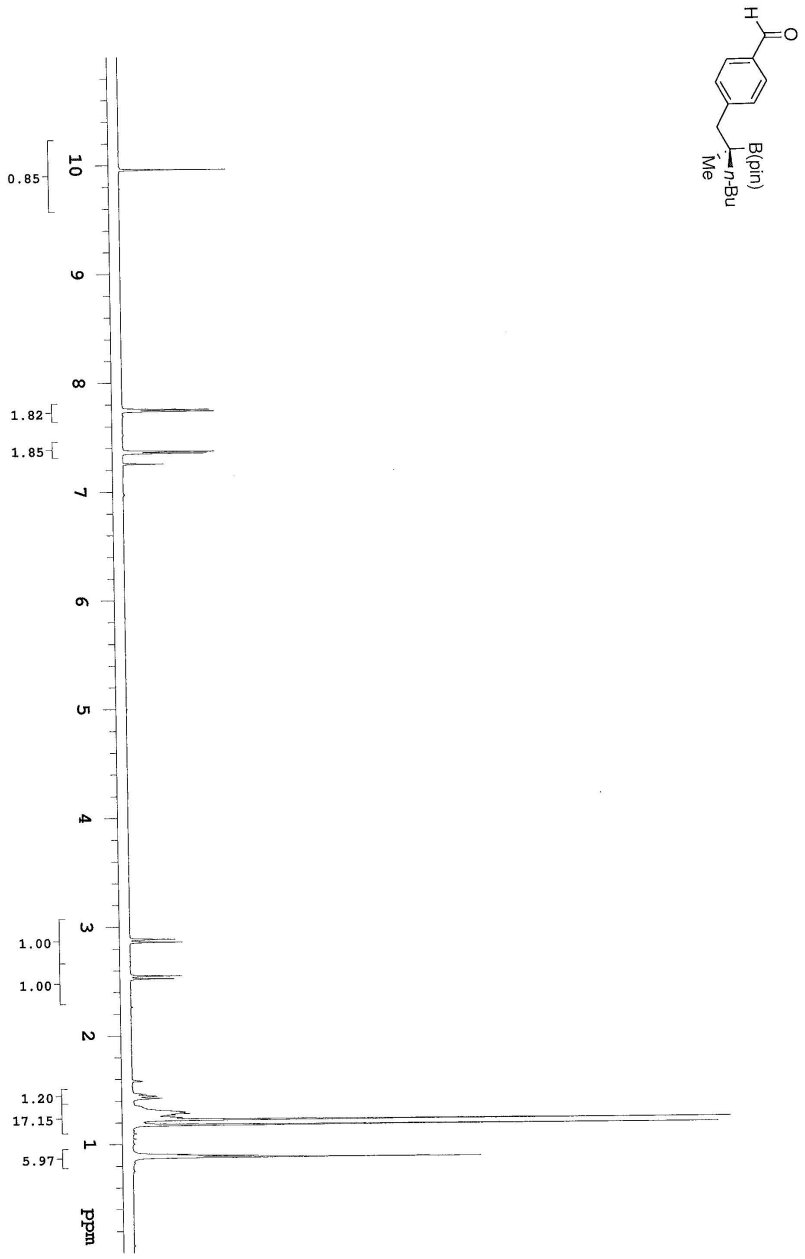
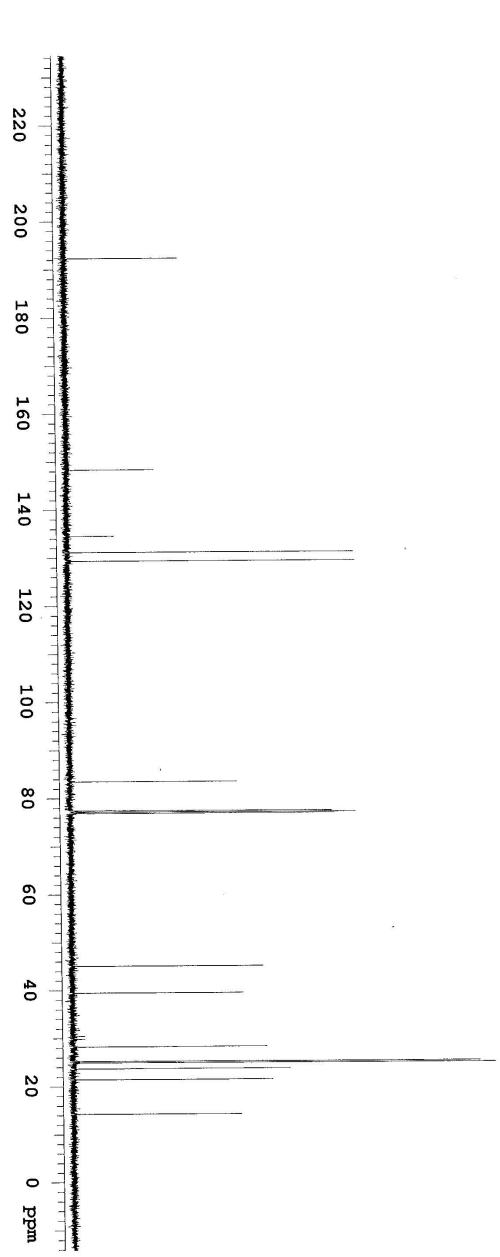
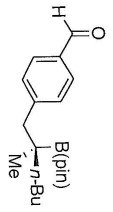
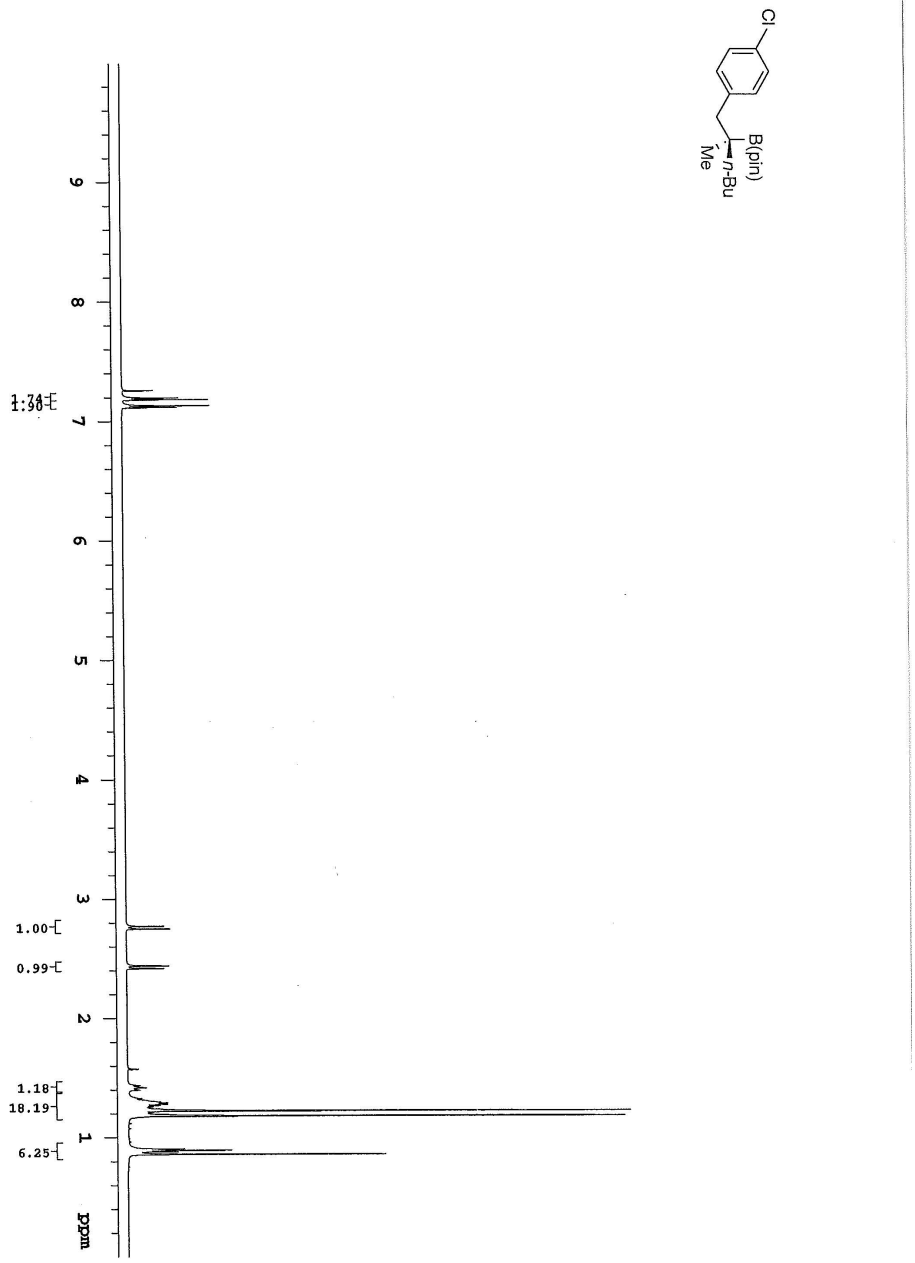
0.94
0.88
2.16
1.00
1.01
1.09
17.74
6.41
ppm


S
B(pin)
n-Bu
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


H
O
B(pin)
n-Bu
Me
0.85
1.82
1.85
1.00
1.00
1.20
17.15
5.97
10
9
8
7
6
5
4
3
2
1
ppm


220
200
180
160
140
120
100
80
60
40
20
0 ppm


H
O
B(pin)
n-Bu
Me


Cl
B(pin)
n-Bu
Me
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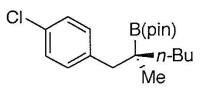
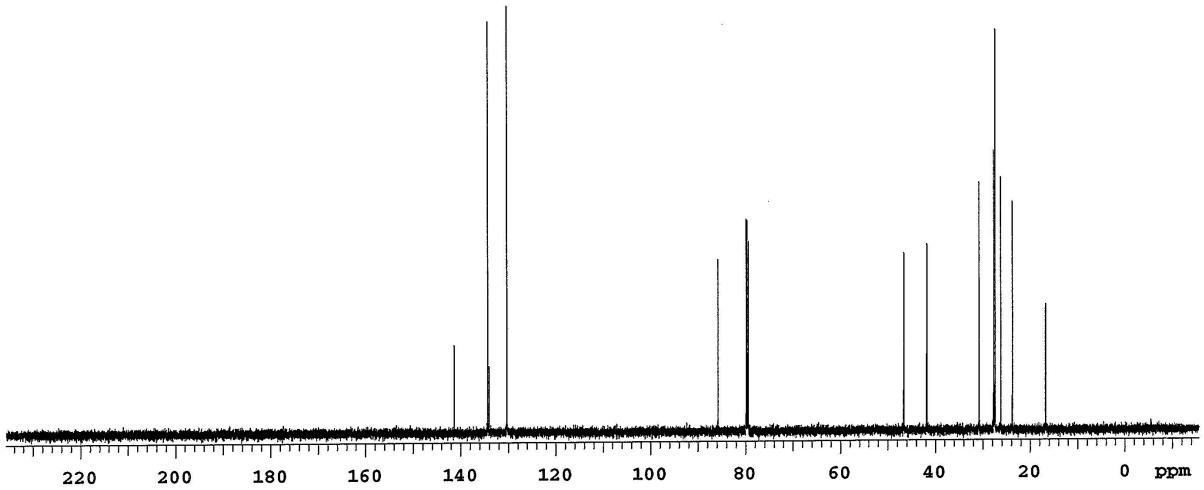
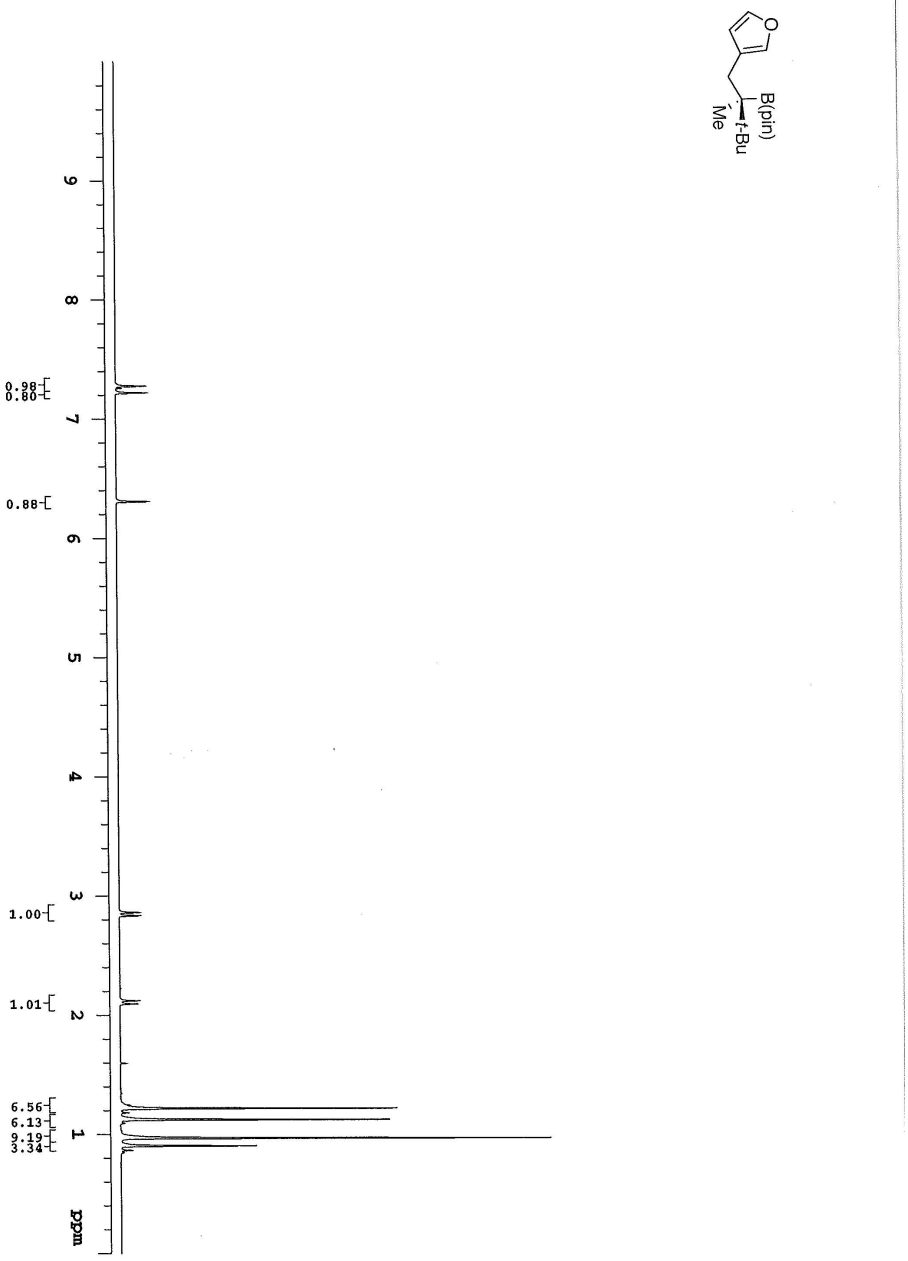
1.00
0.99
1.18
18.19
6.25
ppm


Cl
B(pin)
n-Bu
Me


220
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
t-Bu
Me
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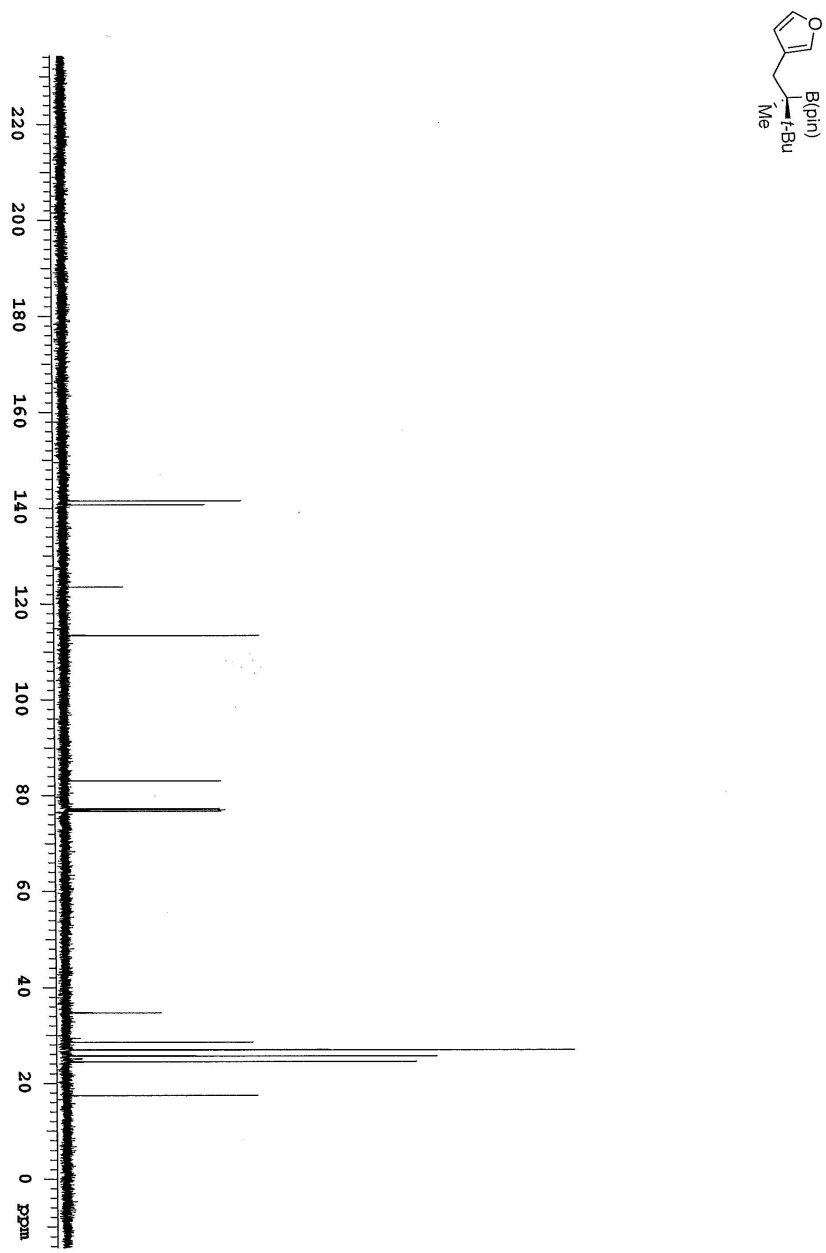
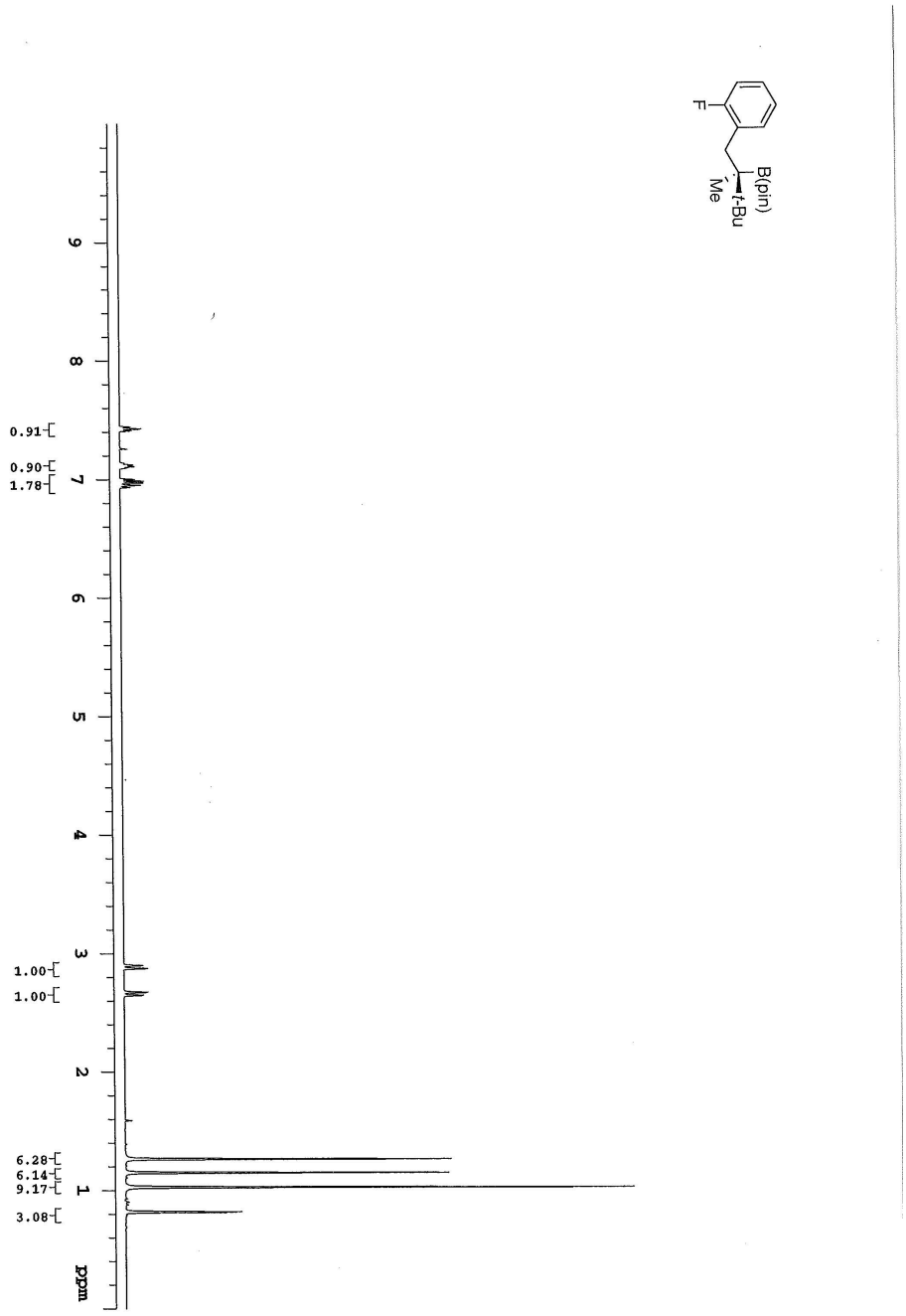
0.80
0.88
1.00
1.01
6.56
6.13
9.19
3.34
ppm


B(pin)
t-Bu
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


F
B(pin)
t-Bu
Me
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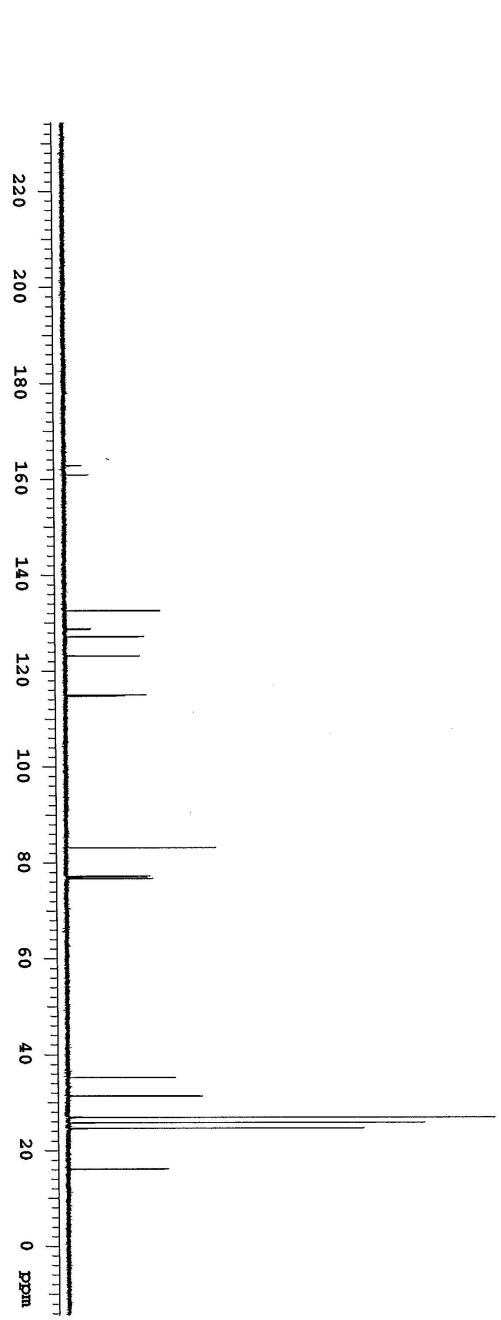
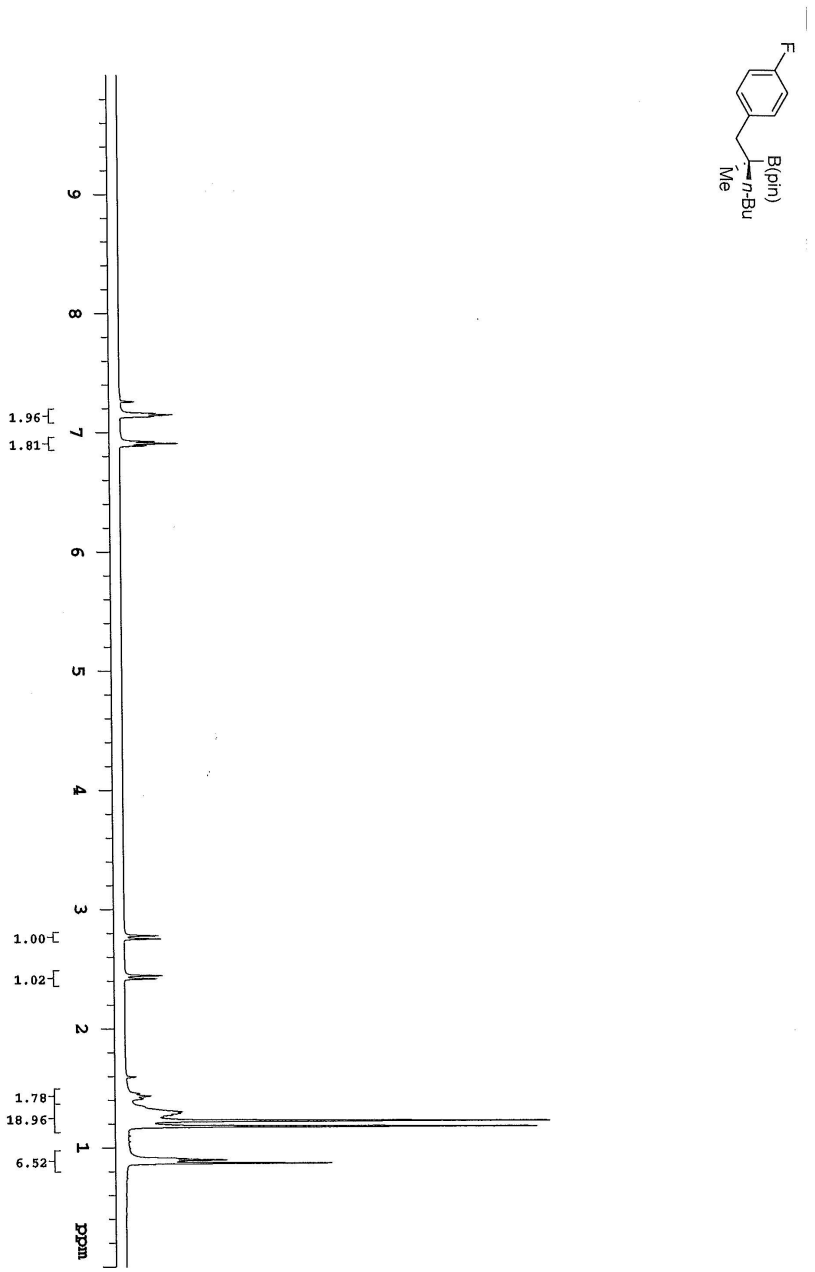
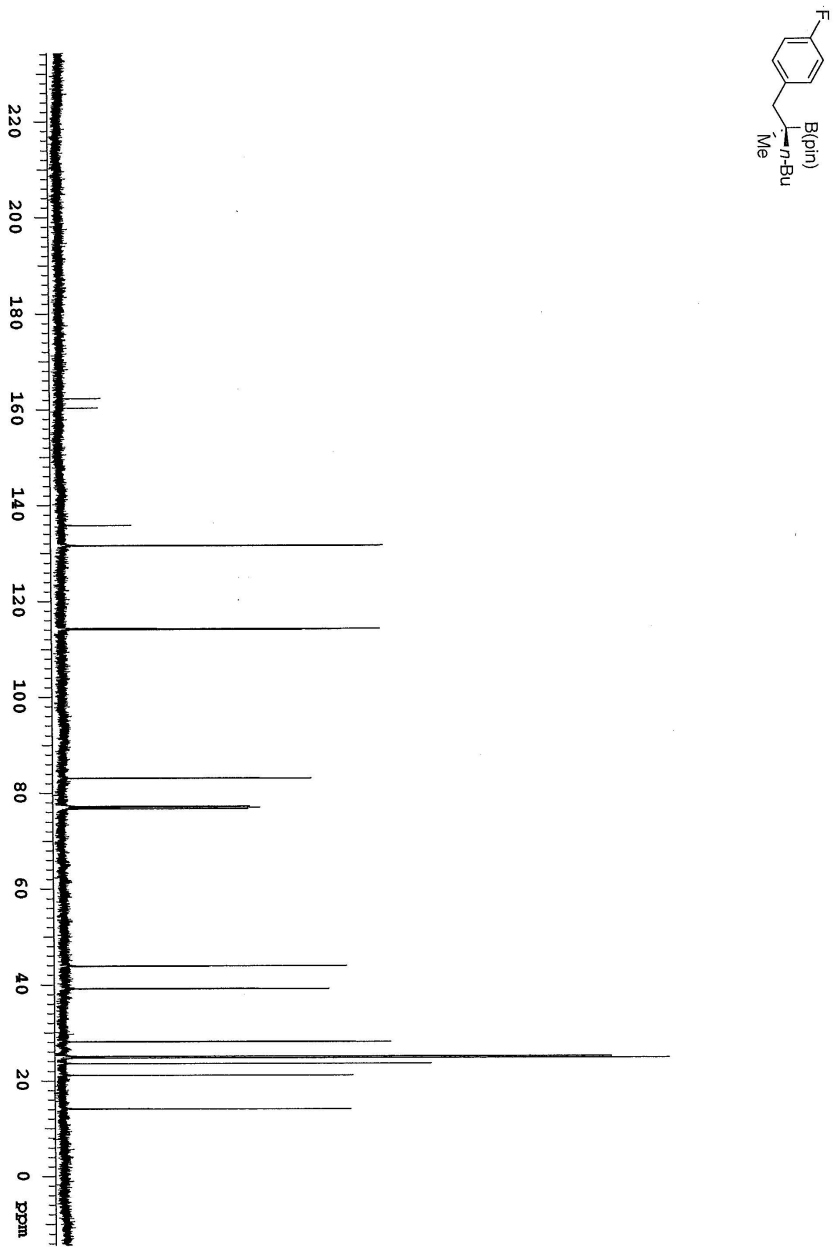
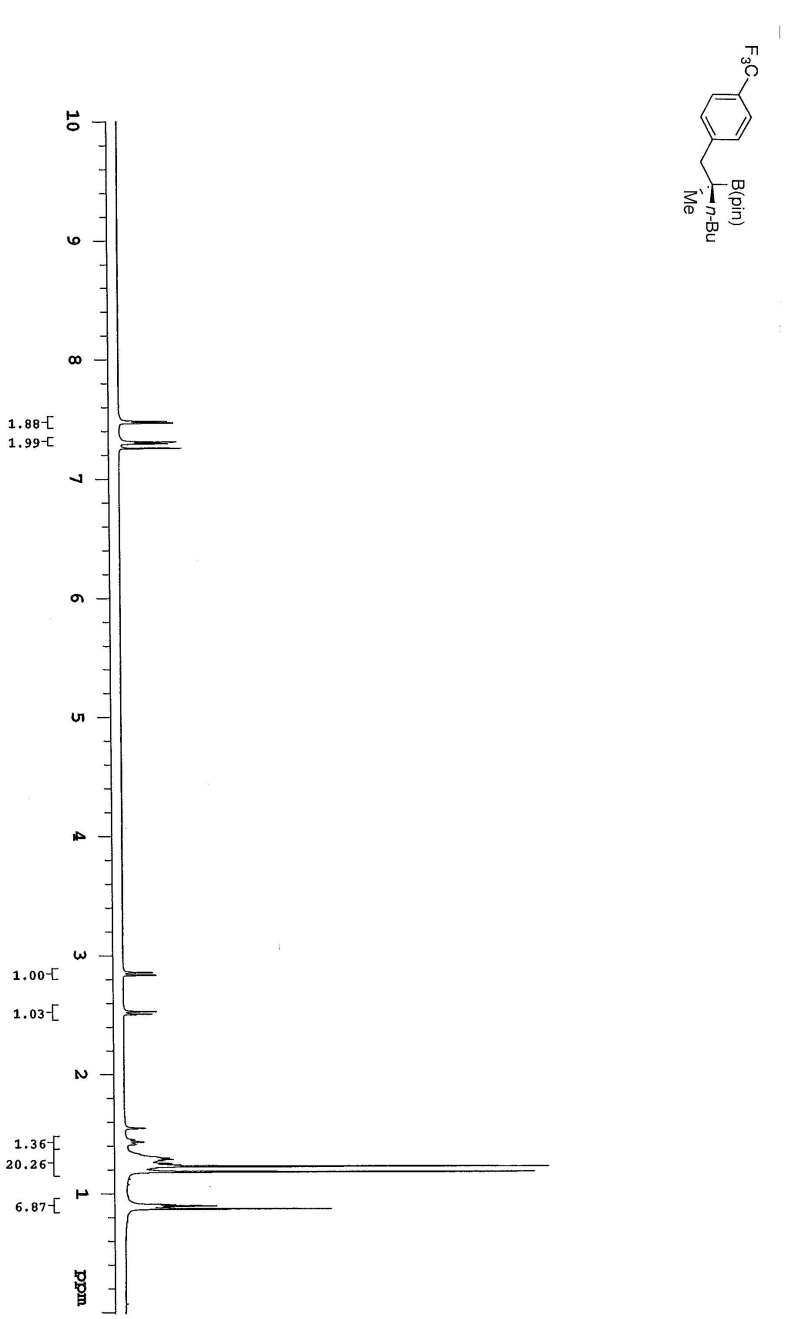
0.90
1.78
1.00
1.00
6.28
6.14
9.17
3.08
ppm


F
B(pin)
t-Bu
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


F
B(pin)
n-Bu
Me
1.96
1.81
1.00
1.02
1.78
18.96
6.52
ppm


F
B(pin)
n-Bu
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


F3C
B(pin)
n-Bu
Me
10
9
8
7
6
5
4
3
2
1
ppm
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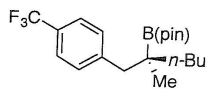
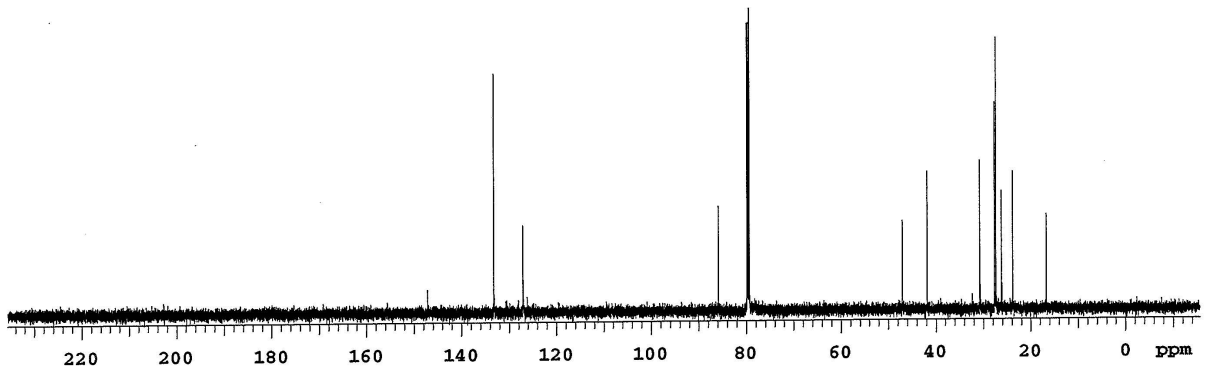
1.99
1.00
1.03
1.36
20.26
6.87


F3C
B(pin)
n-Bu
Me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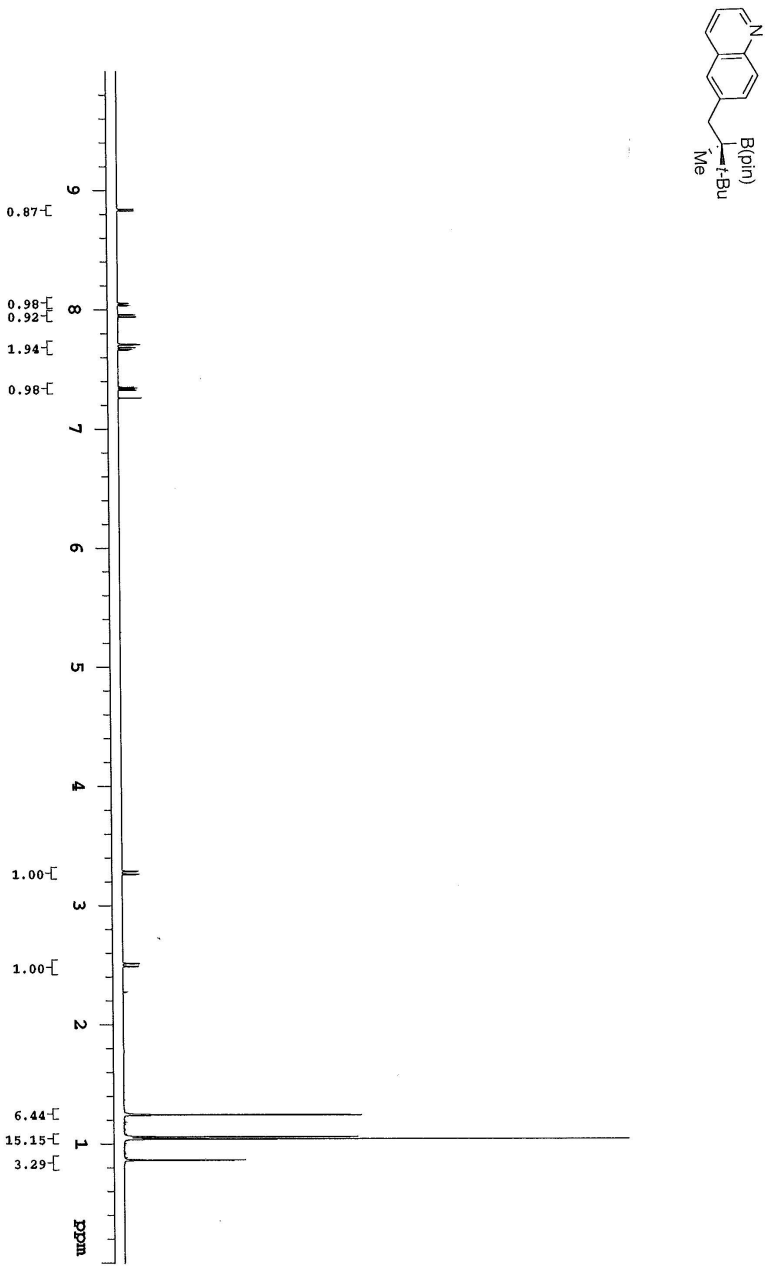
N
B(pin)
t-Bu
Me
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9
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7
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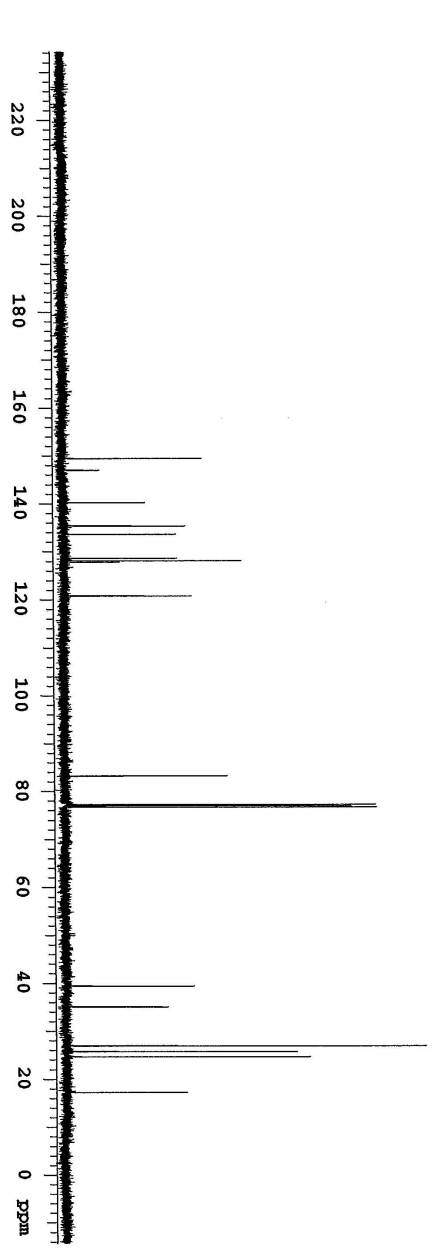
4
3
2
1
ppm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B(pin)
t-Bu
Me
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180
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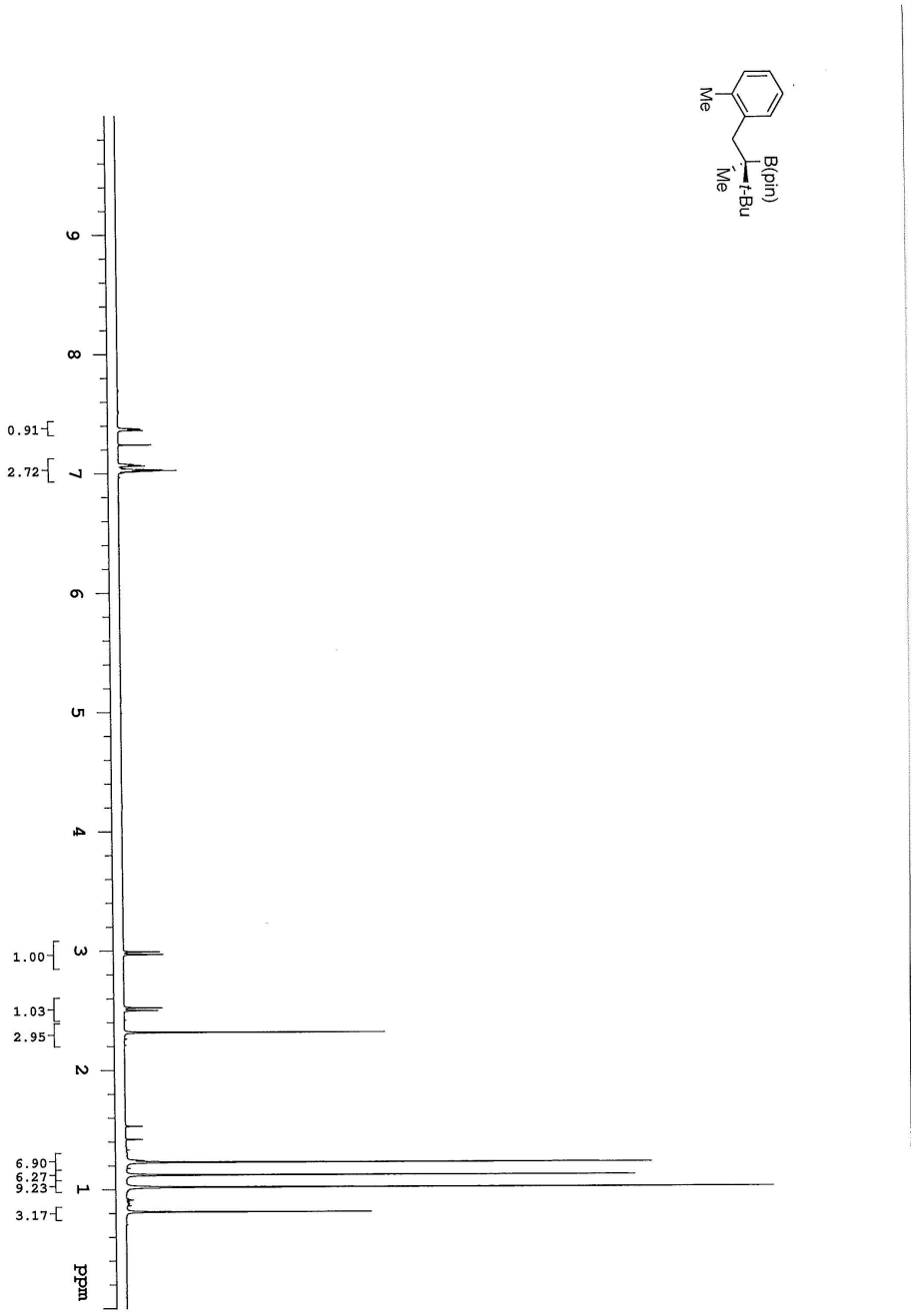
Me
B(pin)
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Me
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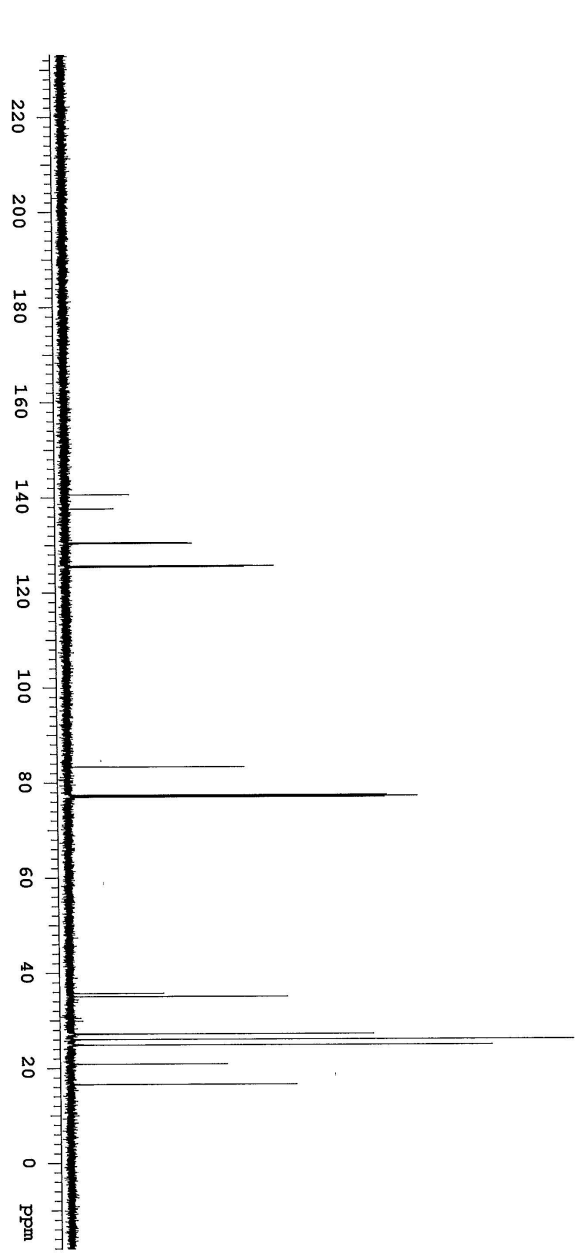
1.03
2.95
6.90
6.27
9.23
3.17
ppm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B(pin)
t-Bu
Me
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200
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160
140
120
100
80
60
40
20
0
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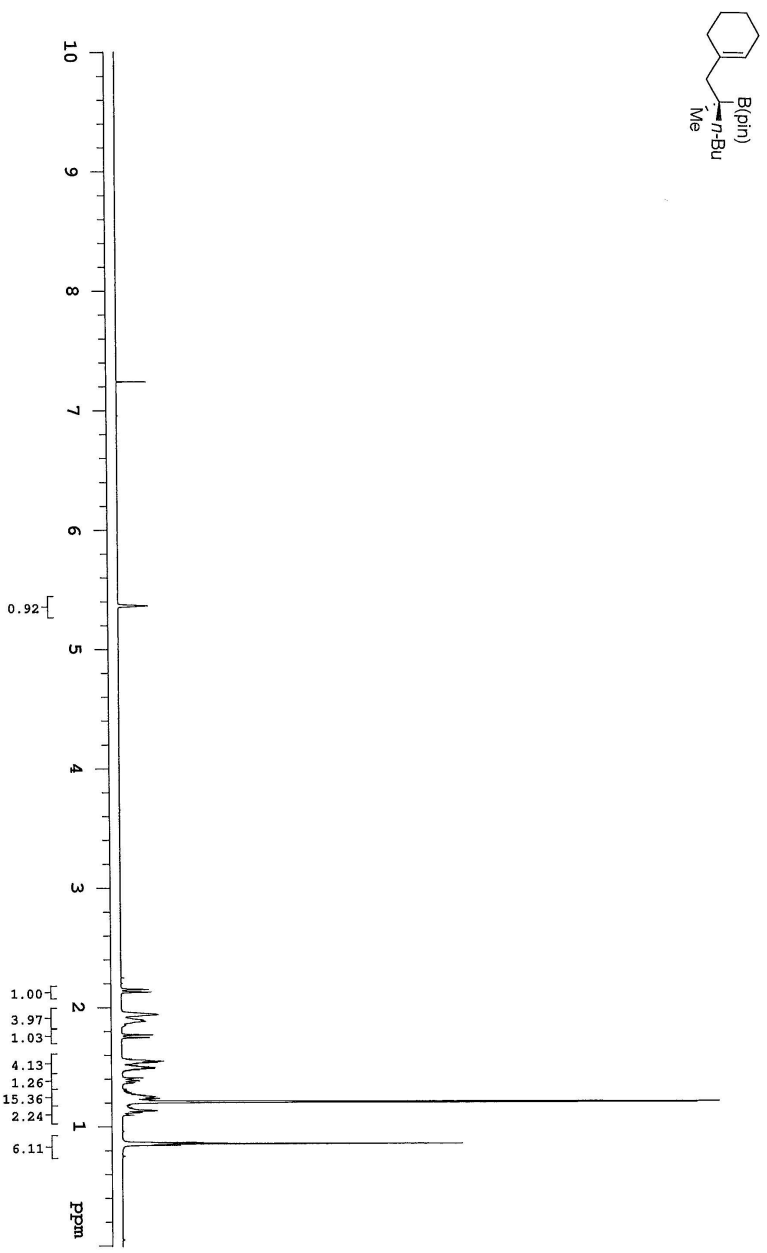
B(pin)
n-Bu
Me
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9
8
7
6
5
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3
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ppm
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1.03
4.13
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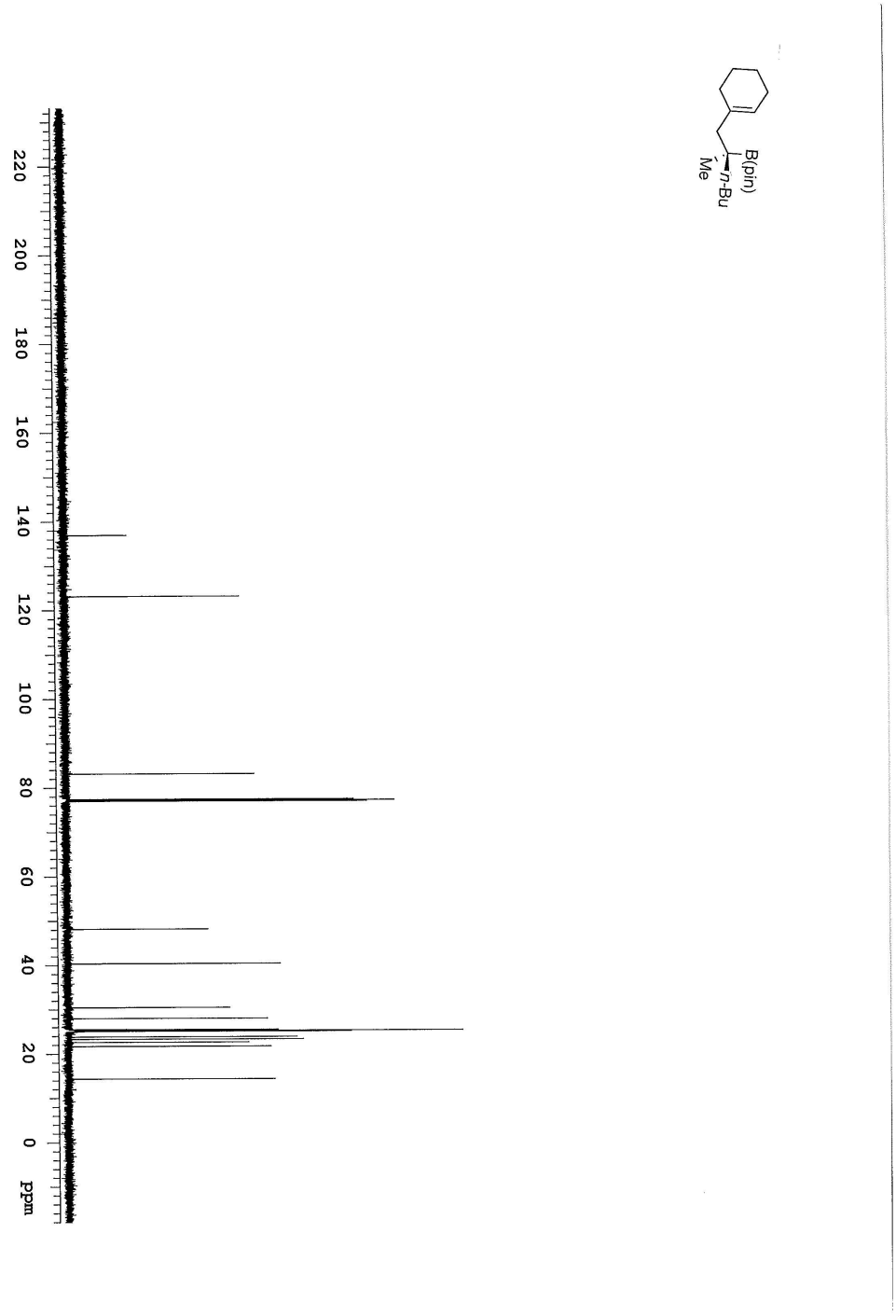
2.24
6.11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n-Bu
Me
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200
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160
140
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100
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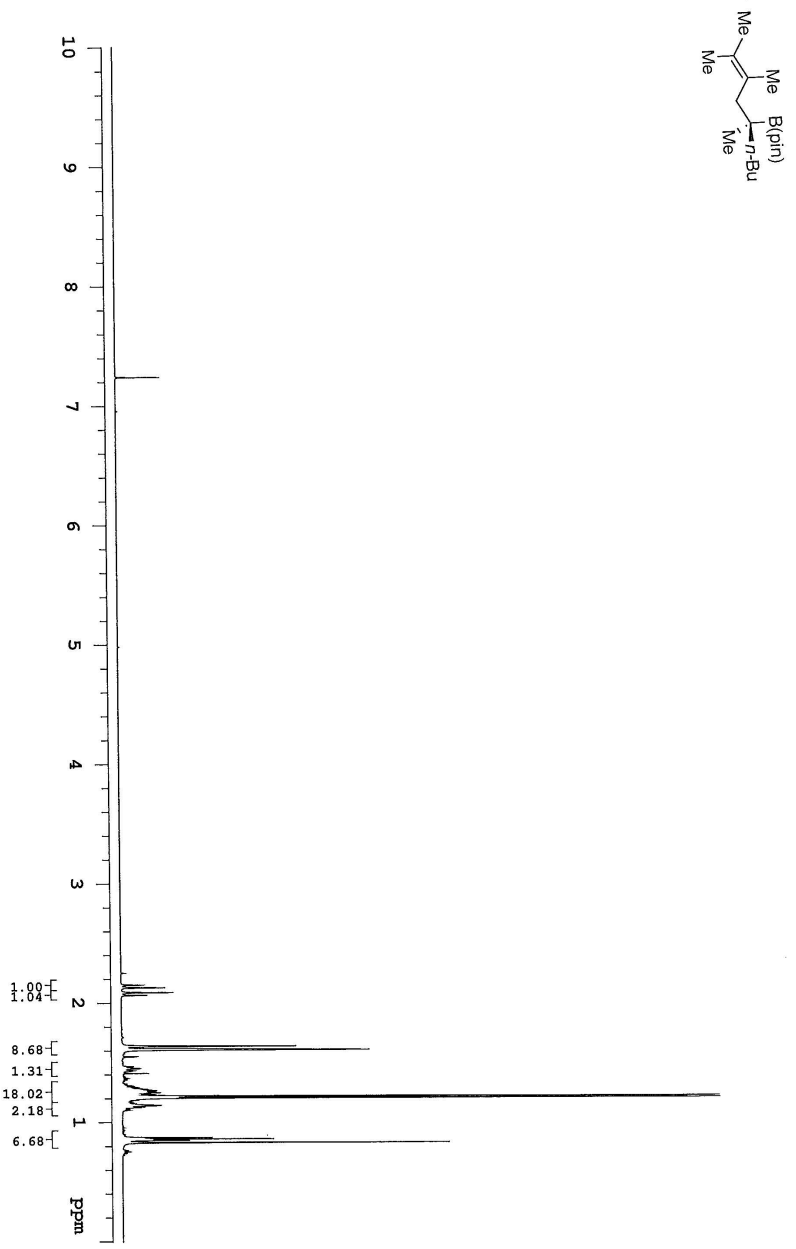
0
ppm


Me
Me
Me
Me
B(pin)
n-Bu
10
9
8
7
6
5
4
3
2
1
ppm
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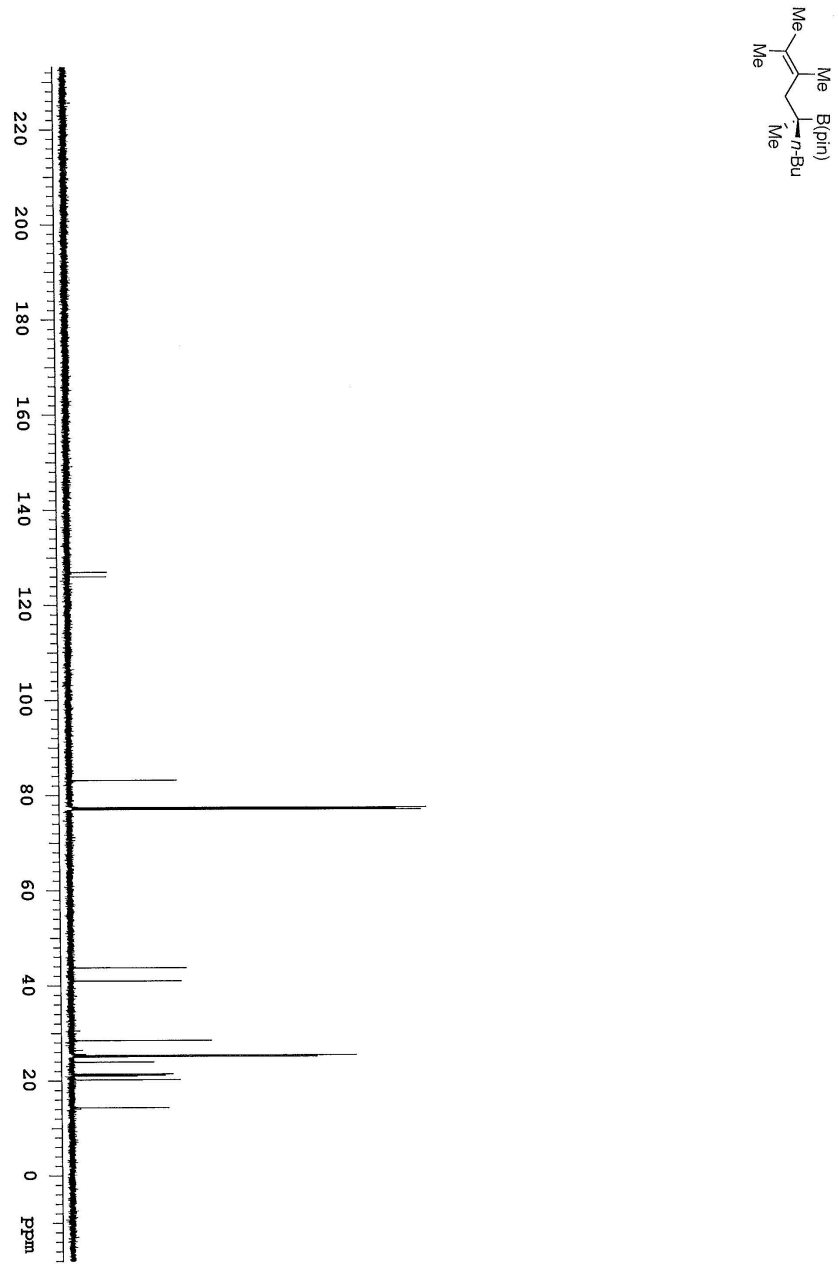
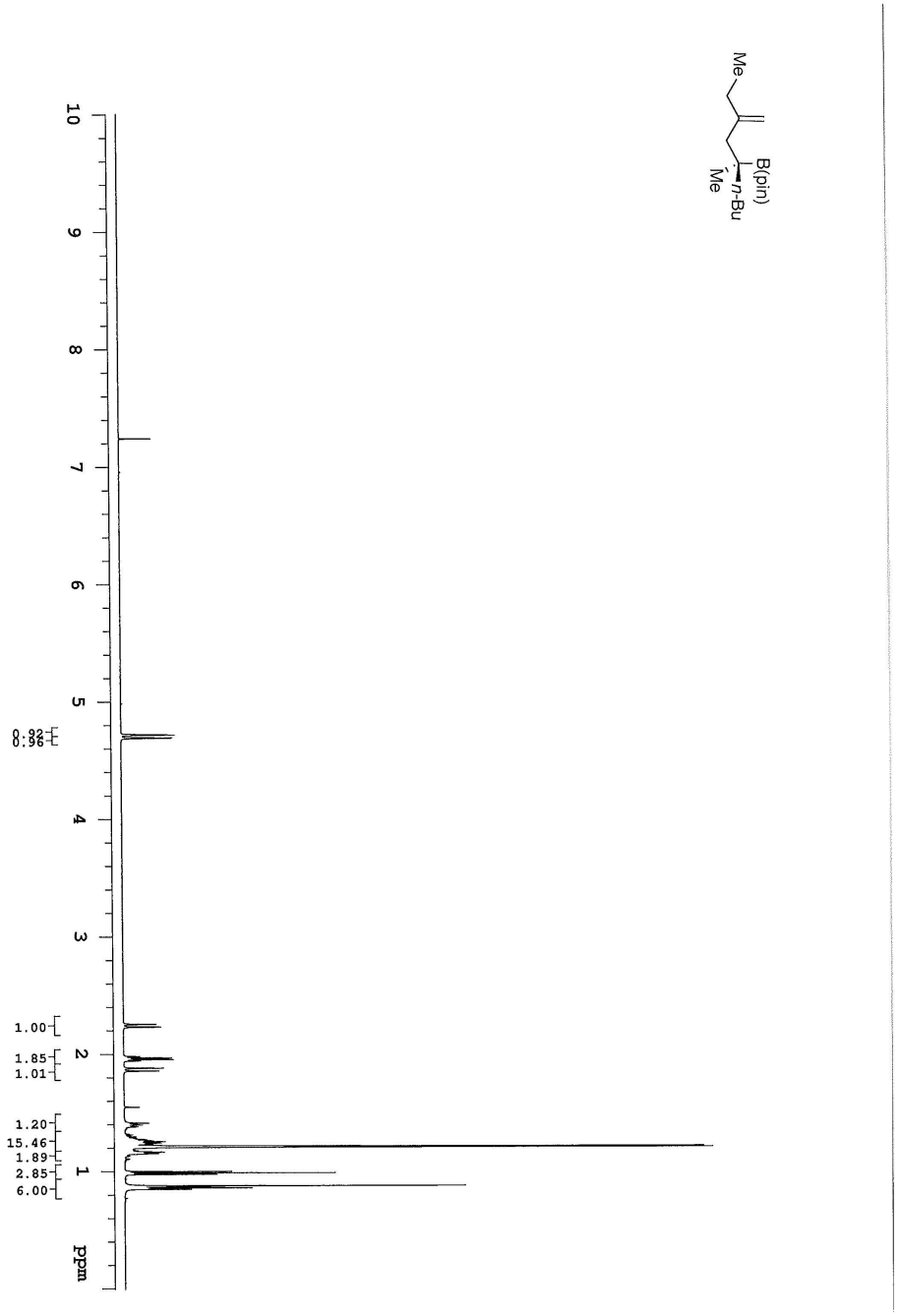
18.02
2.18
6.68


Me
Me
Me
Me
B(pin)
n-Bu
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Me
B(pin)
n-Bu
Me
10
9
8
7
6
5
4
3
2
1
ppm
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0.96
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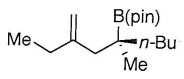
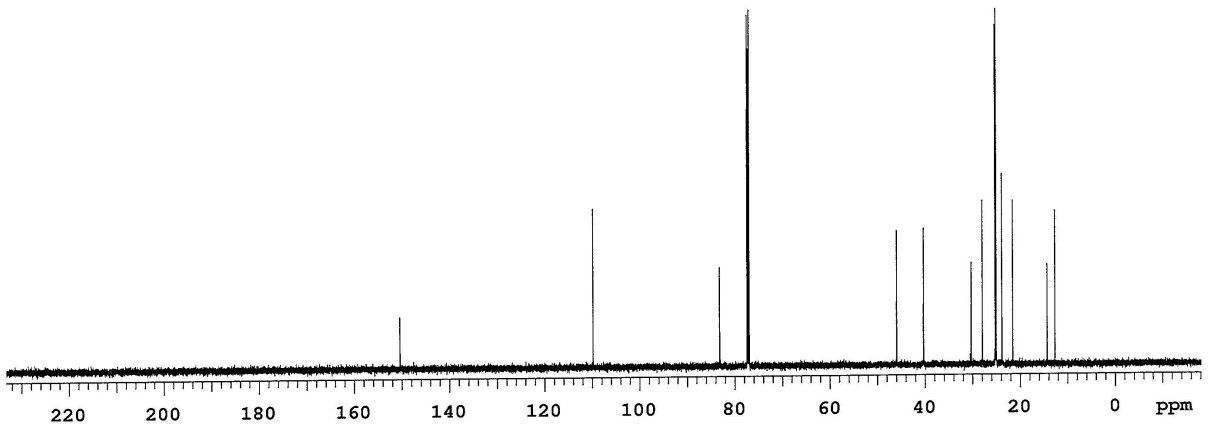
1.85
1.01
1.20
15.46
1.89
2.85
6.00


B(pin)
Me
n-Bu
Me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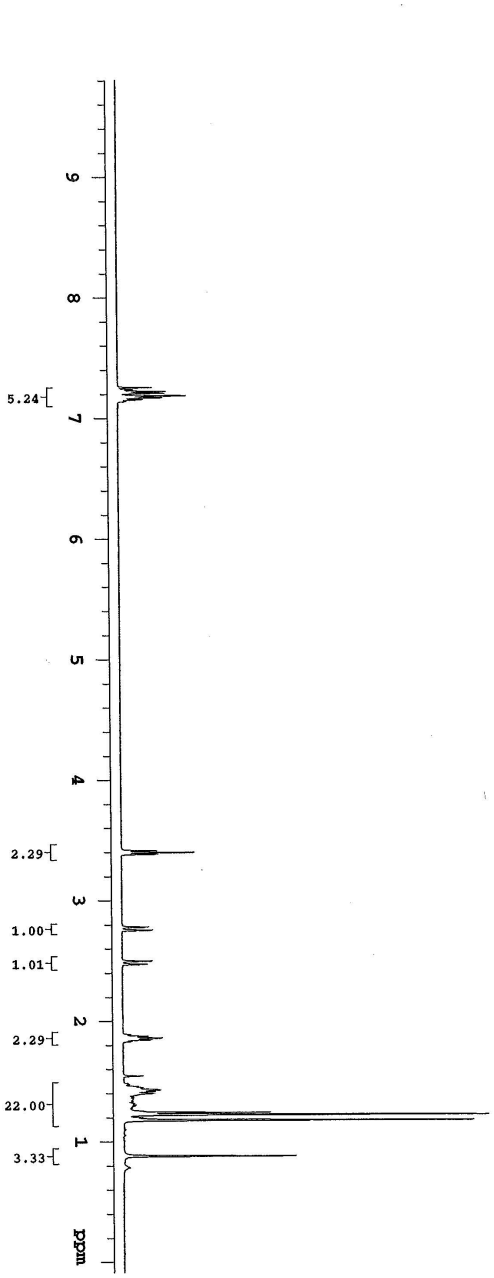
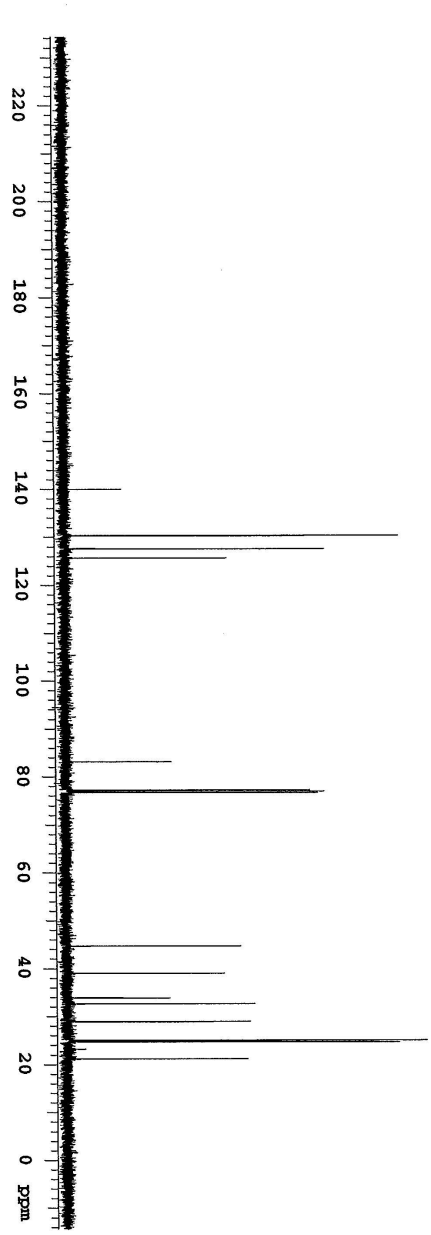
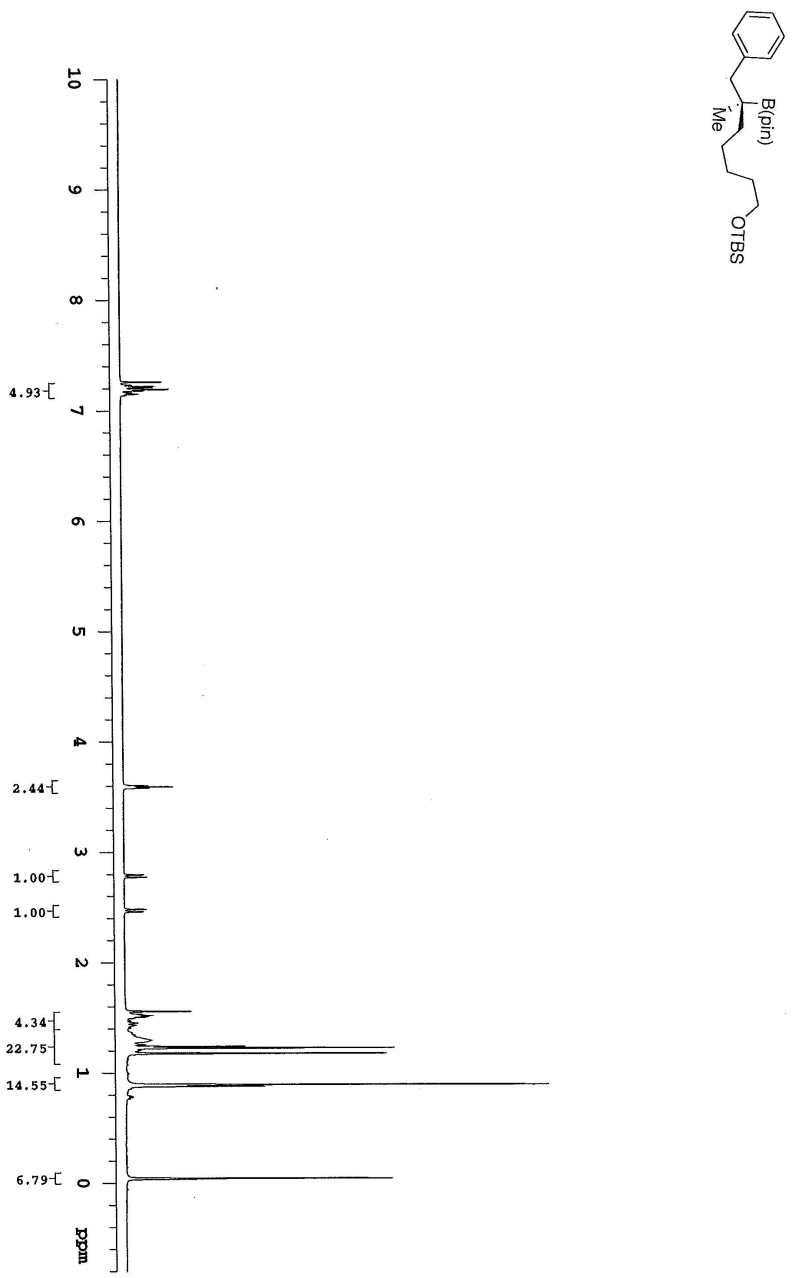
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
Me
Br
5.24
2.29
1.00
1.01
2.29
22.00
3.33
9
8
7
6
5
4
3
2
1
ppm


B(pin)
Me
Br
220
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
Me
OTBS
10
9
8
7
6
5
4
3
2
1
0
ppm
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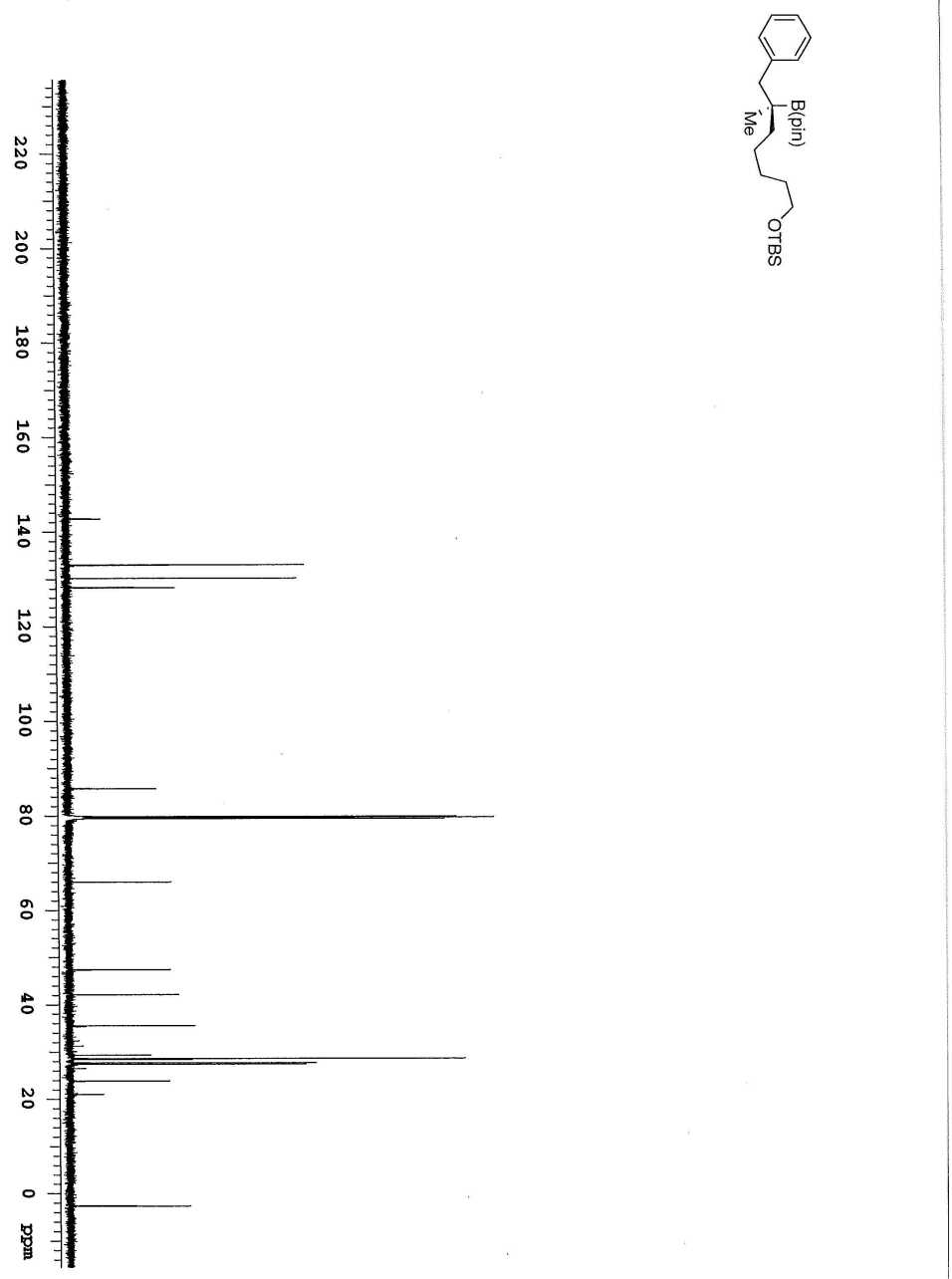
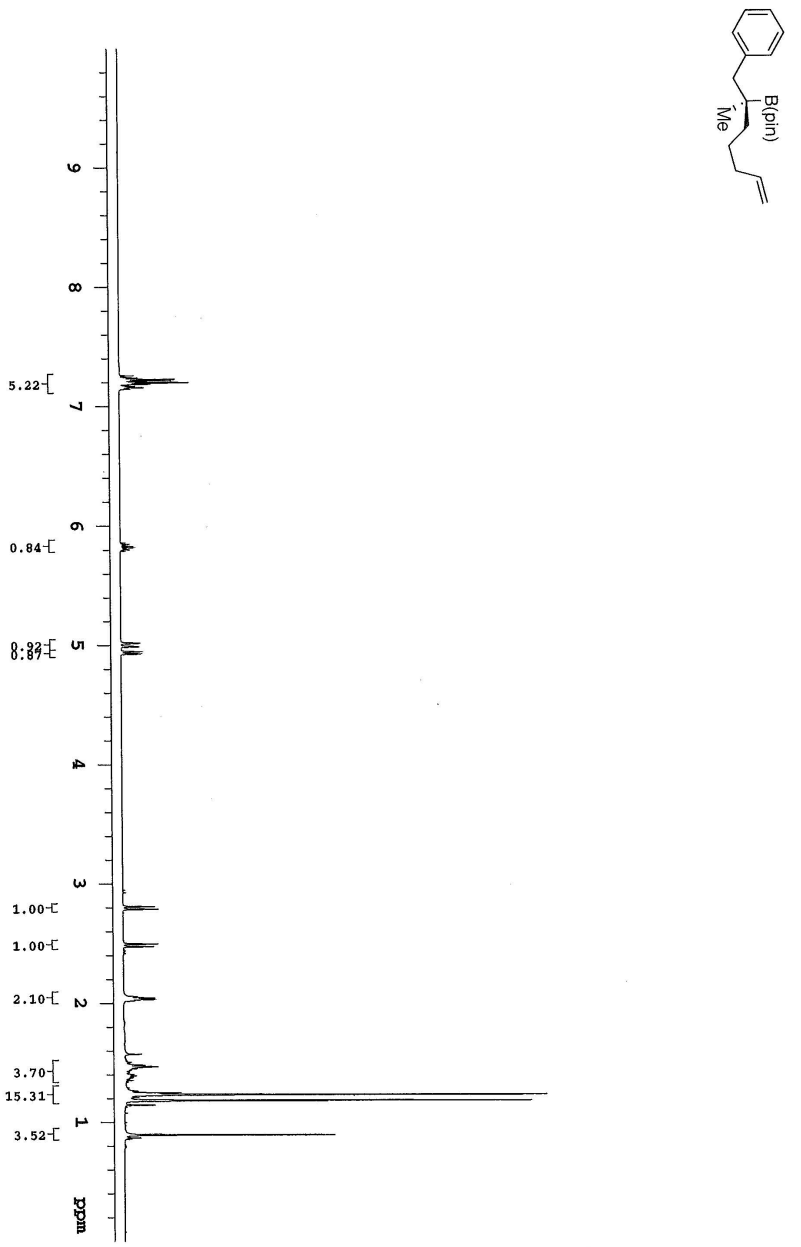
2.44
1.00
1.00
4.34
22.75
14.55
6.79


B(pin)
Me
OTBS
220
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
Me
5.22
0.84
0.92
0.87
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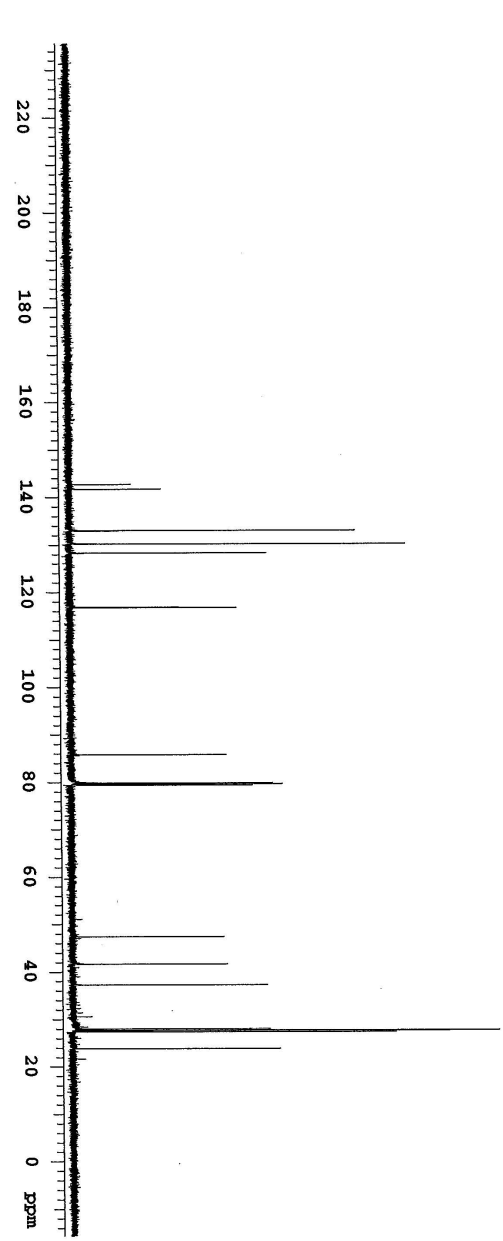
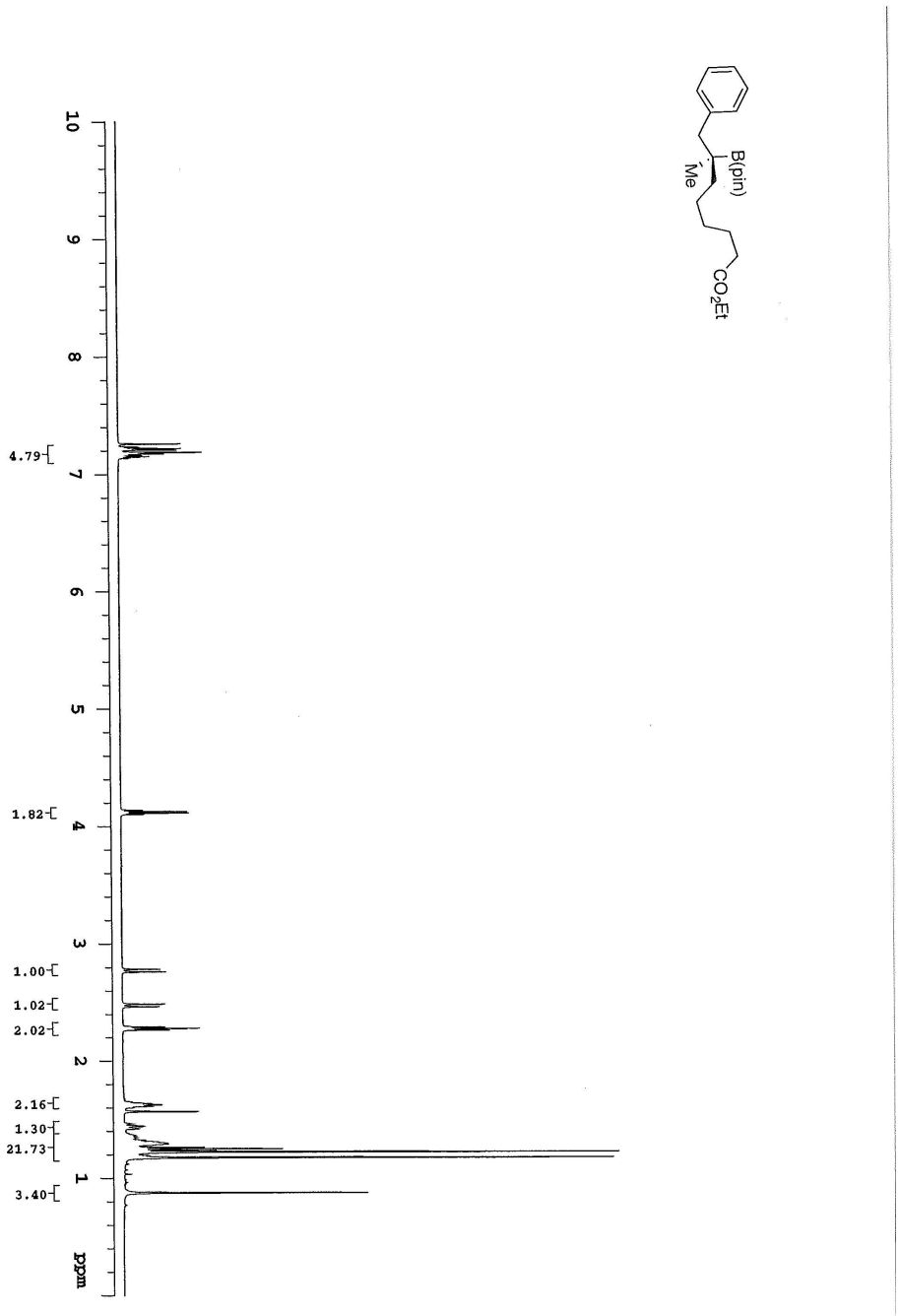
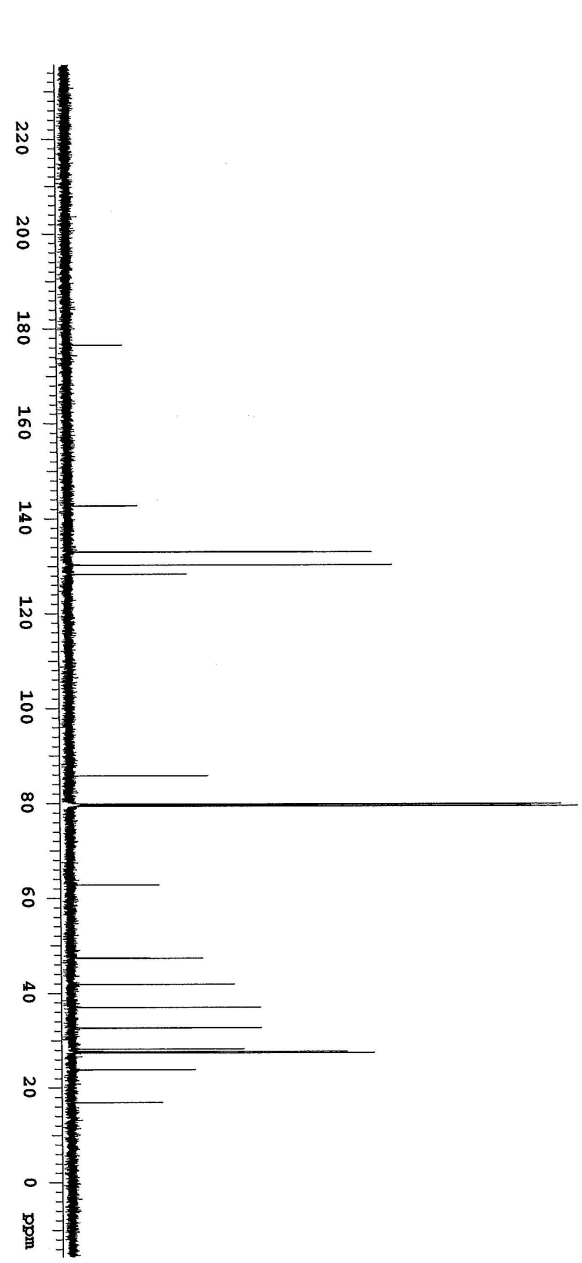
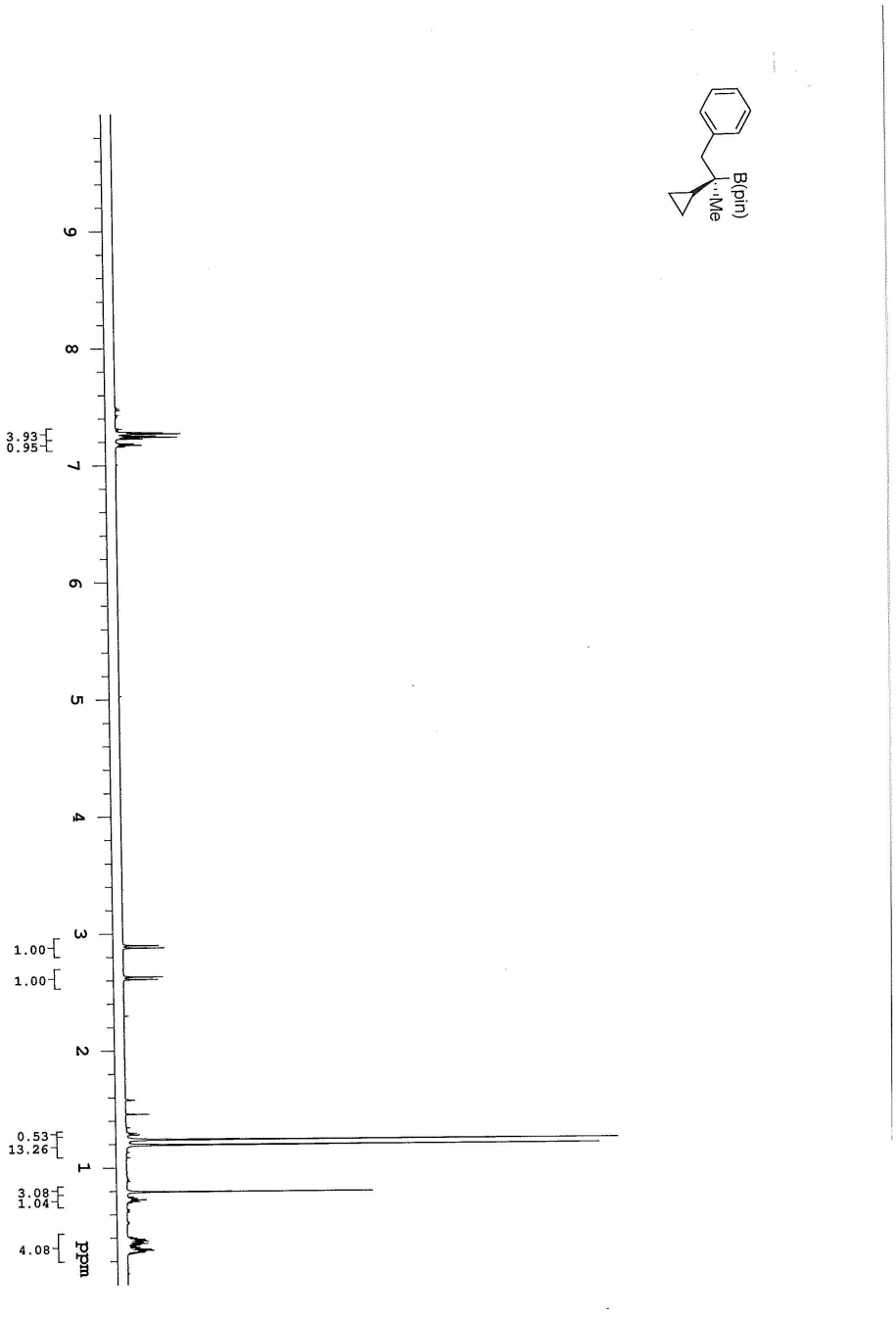
1.00
2.10
3.70
15.31
3.52
9
8
7
6
5
4
3
2
1
ppm


B(pin)
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
Me
CO2Et
4.79
1.82
1.00
1.02
2.02
2.16
1.30
21.73
3.40
10
9
8
7
6
5
4
3
2
1
ppm


B(pin)
Me
CO2Et
220
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
Me
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0.95
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1.00
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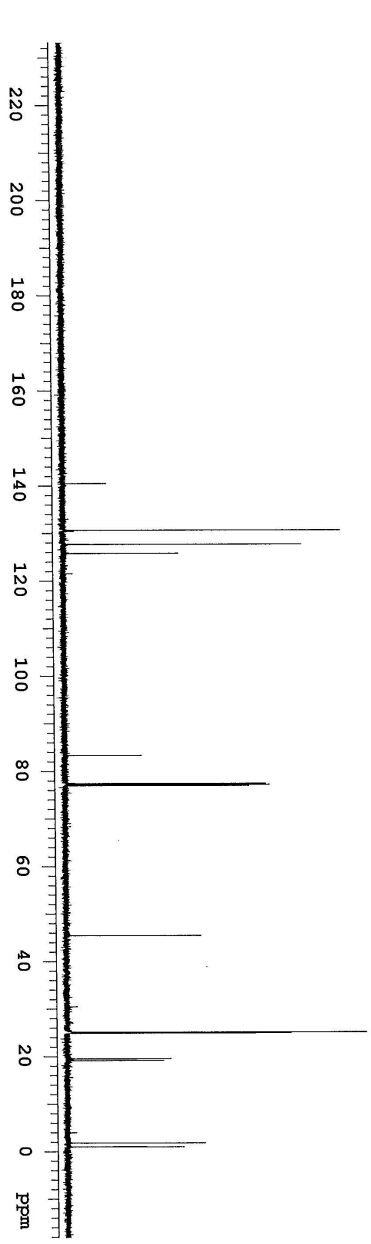
13.26
3.08
1.04
4.08
ppm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200
180
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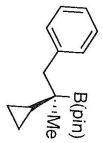
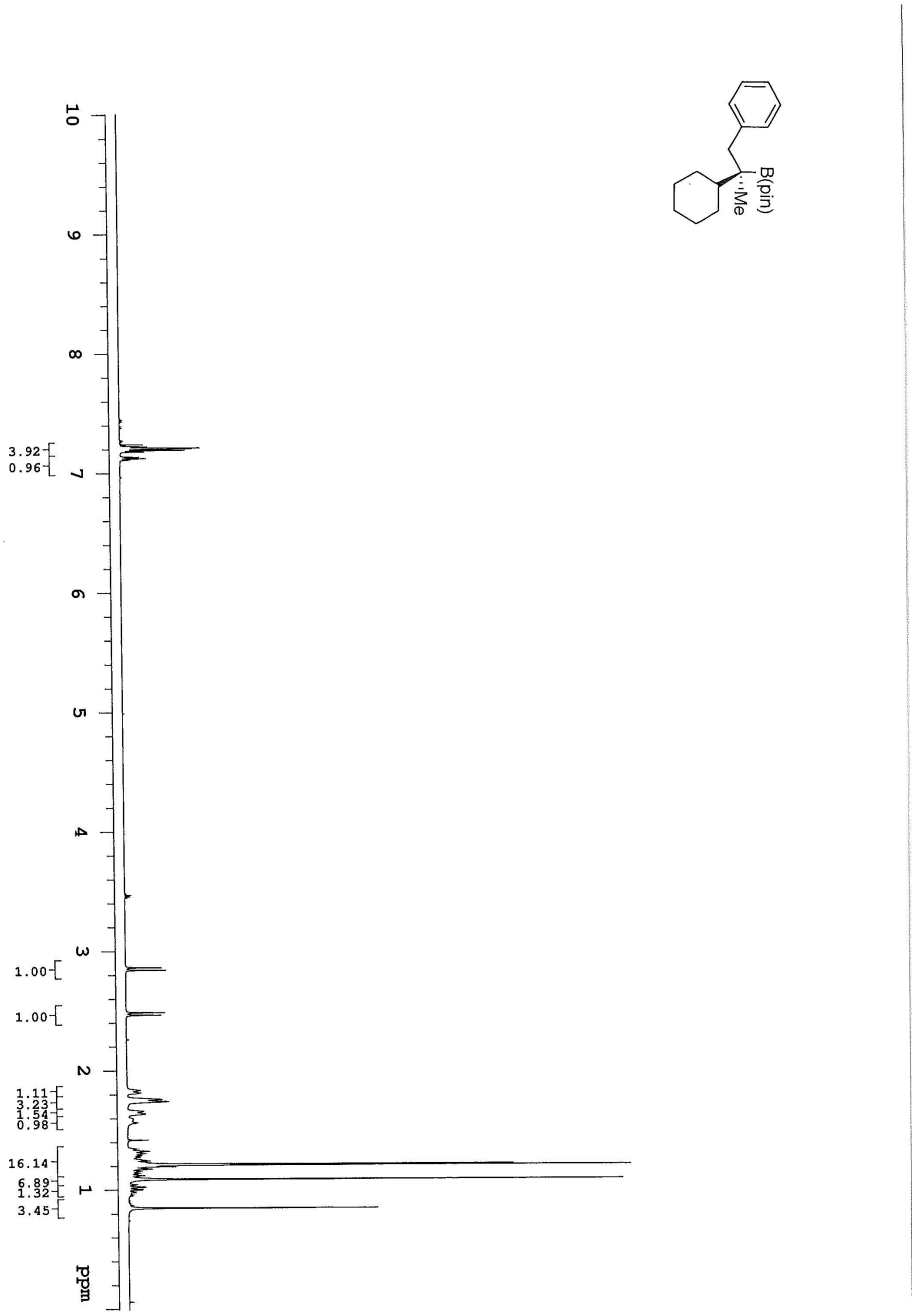
140
120
100
80
60
40
20
0
ppm


B(pin)
Me


B(pin)
Me
10
9
8
7
6
5
4
3
2
1
ppm
3.92
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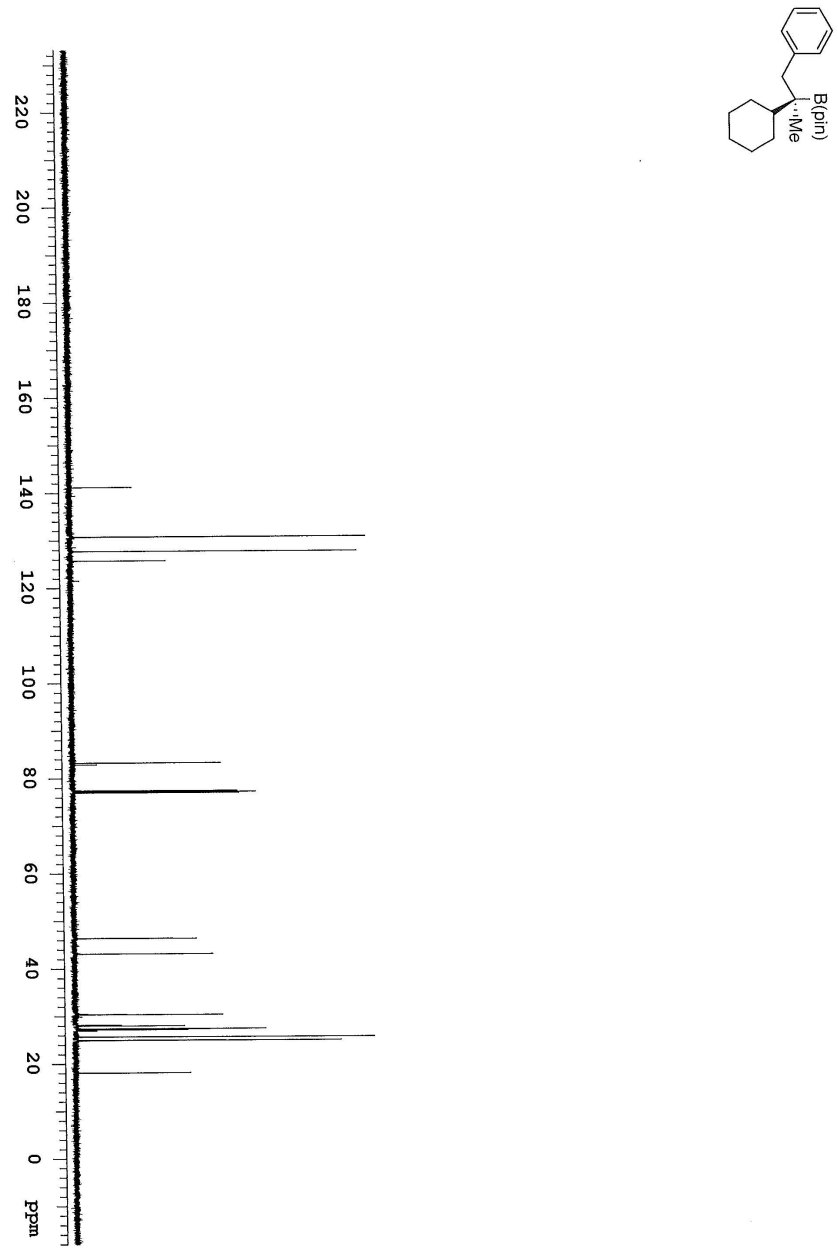
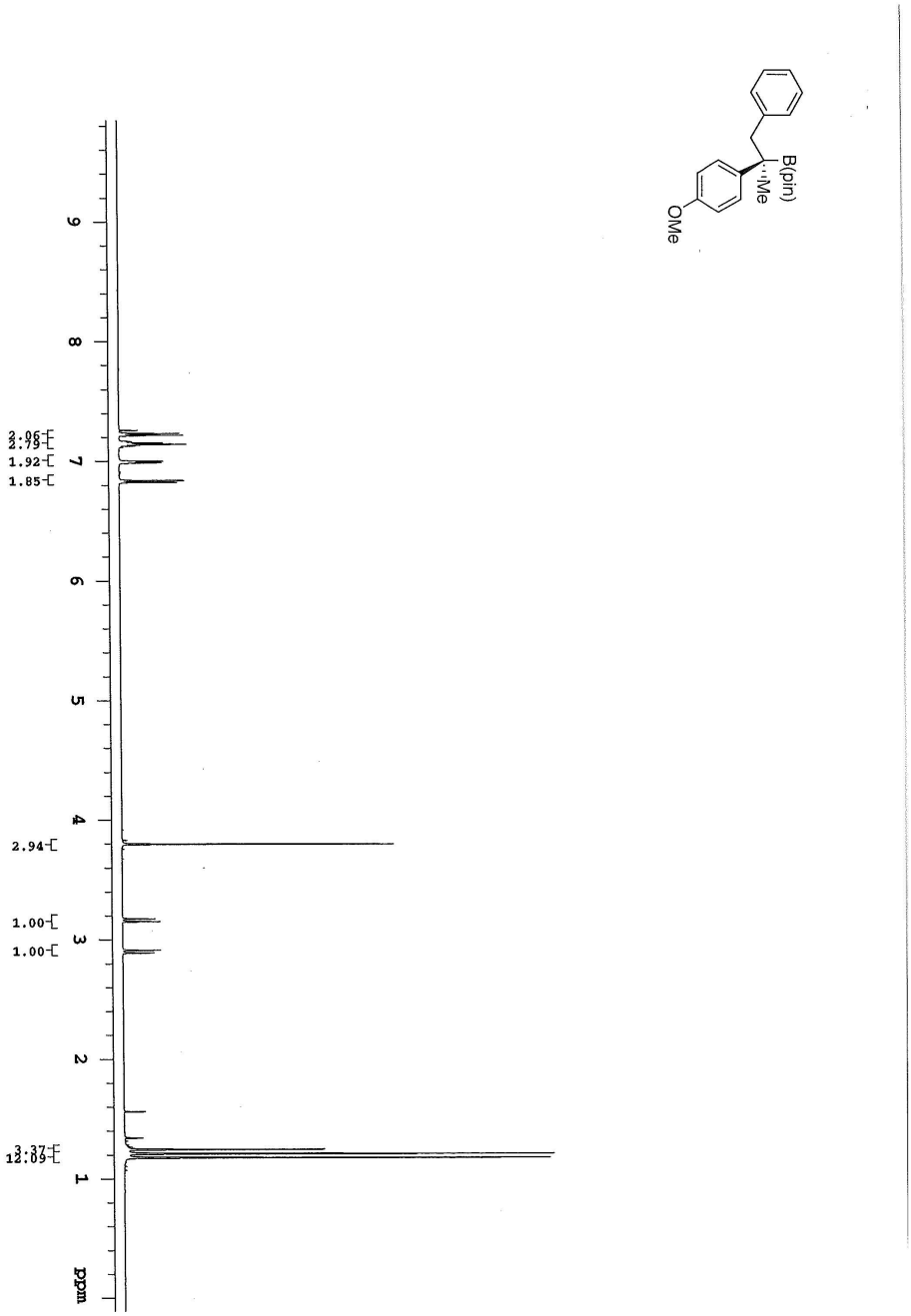
1.00
1.00
1.11
3.23
1.54
0.98
16.14
6.89
1.32
3.45


B(pin)
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
Me
OMe
2.06
2.79
1.92
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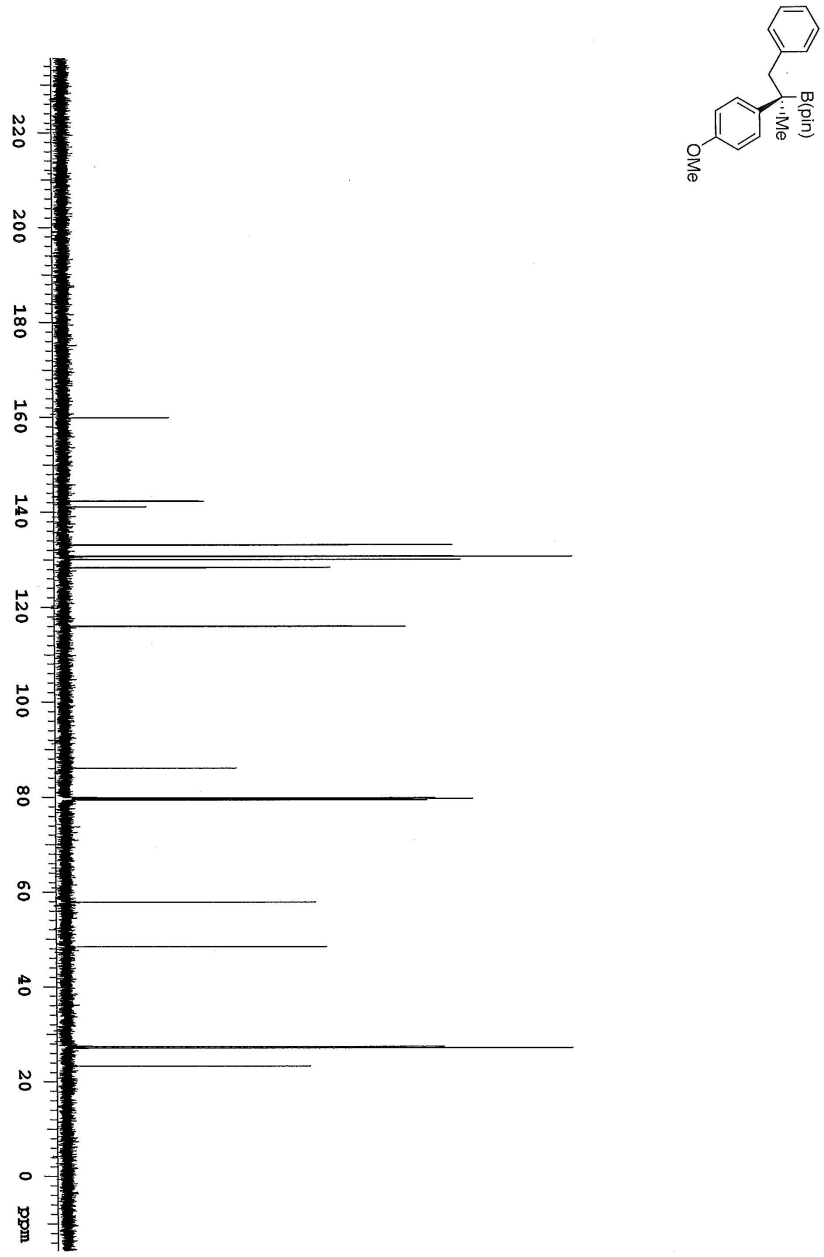
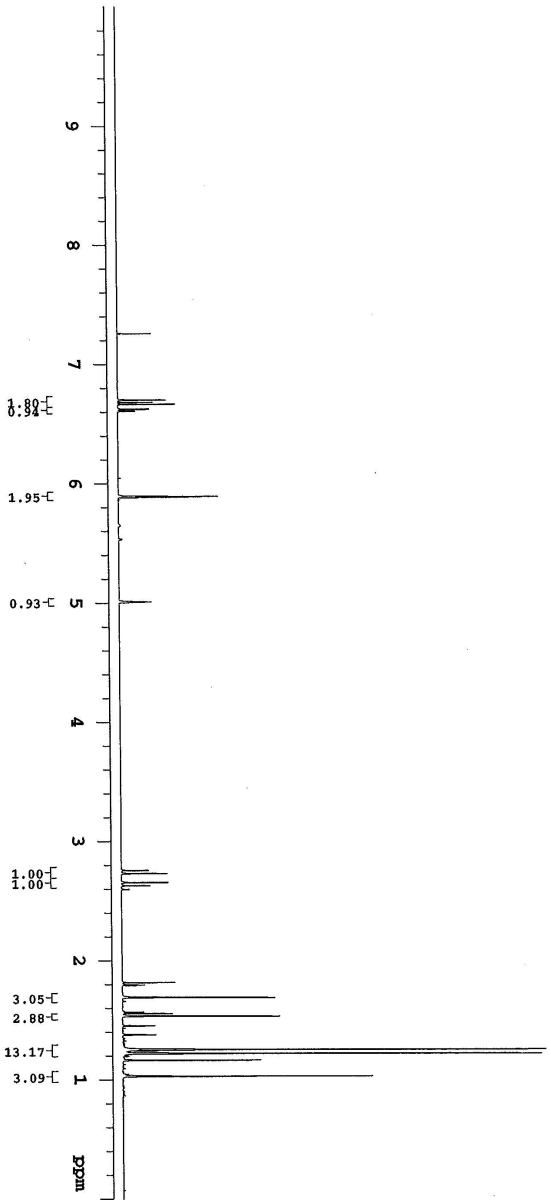
1.00
1.00
3.37
12.09
9
8
7
6
5
4
3
2
1
ppm


B(pin)
Me
OMe
220
200
180
160
140
120
100
80
60
40
20
0
ppm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0.93
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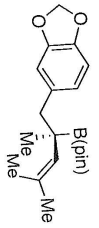
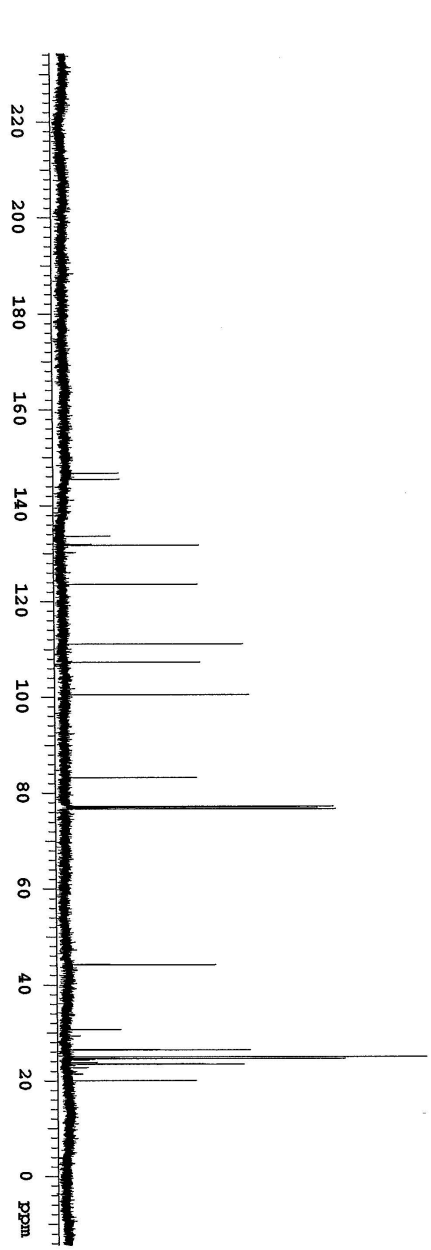
1.00
3.05
2.88
13.17
3.09
ppm


O
O
B(pin)
Me
Me
Me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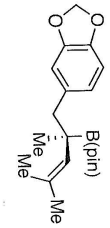
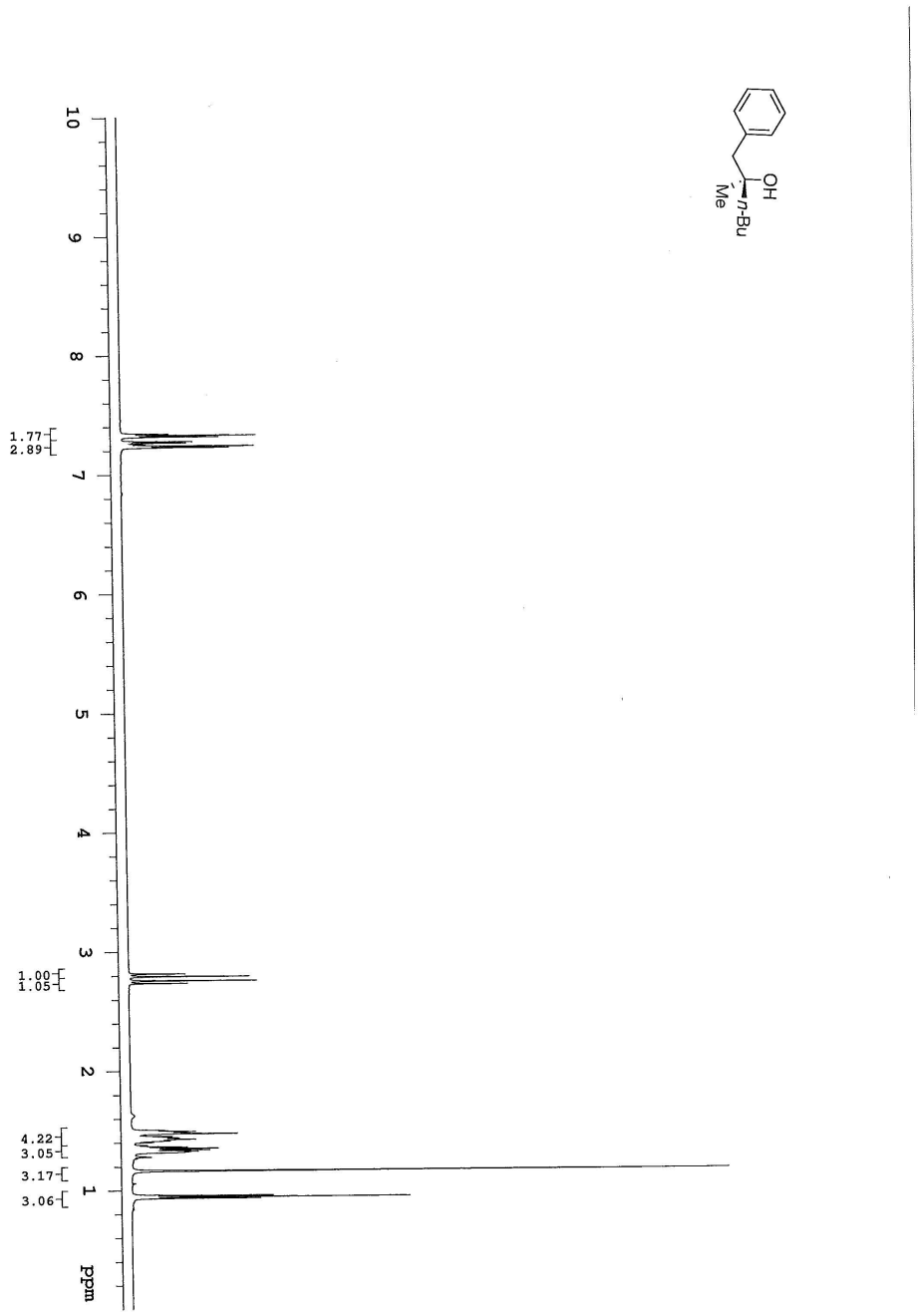
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
Me
Me
Me


OH
n-Bu
Me
10
9
8
7
6
5
4
3
2
1
ppm
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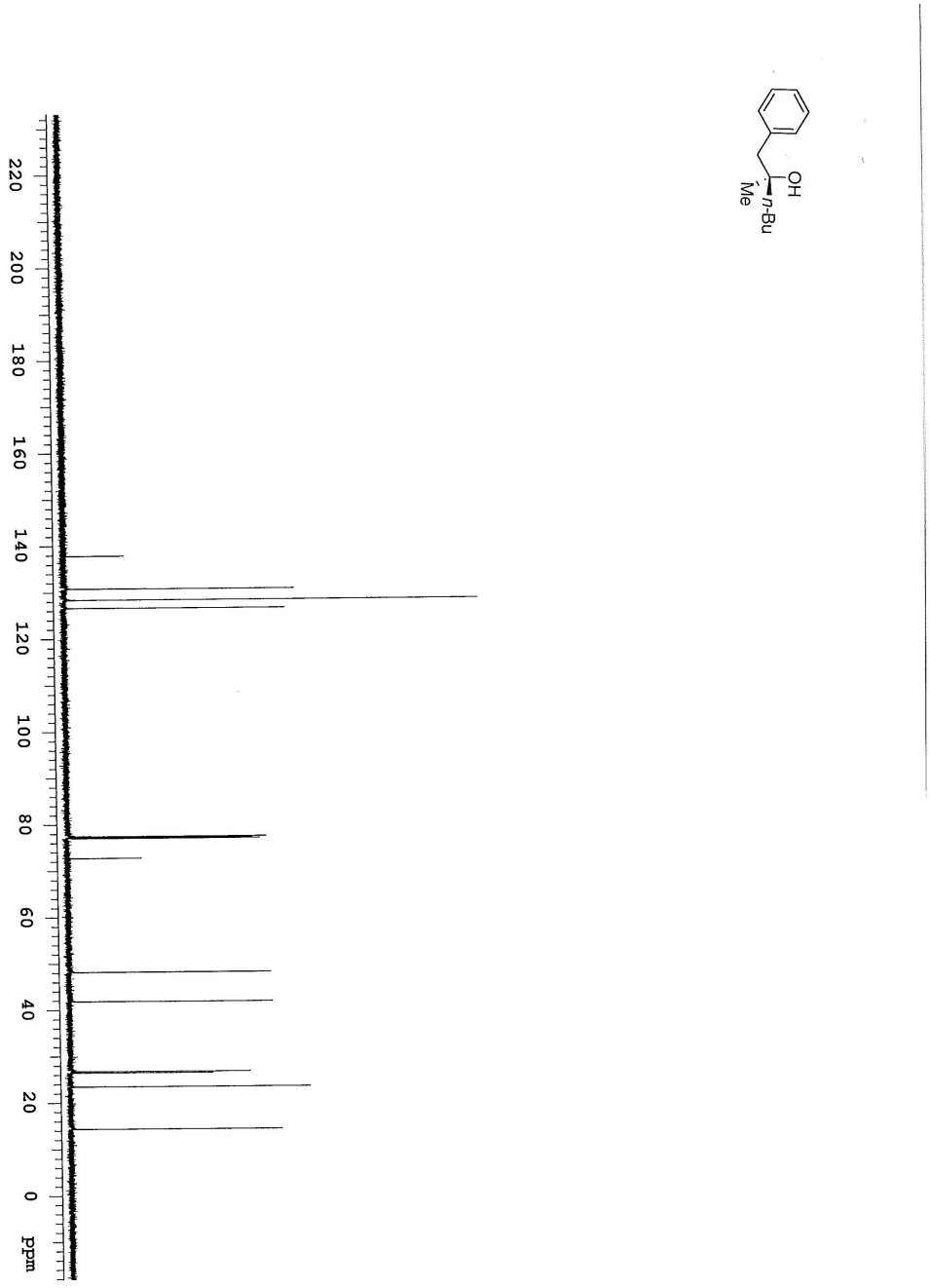
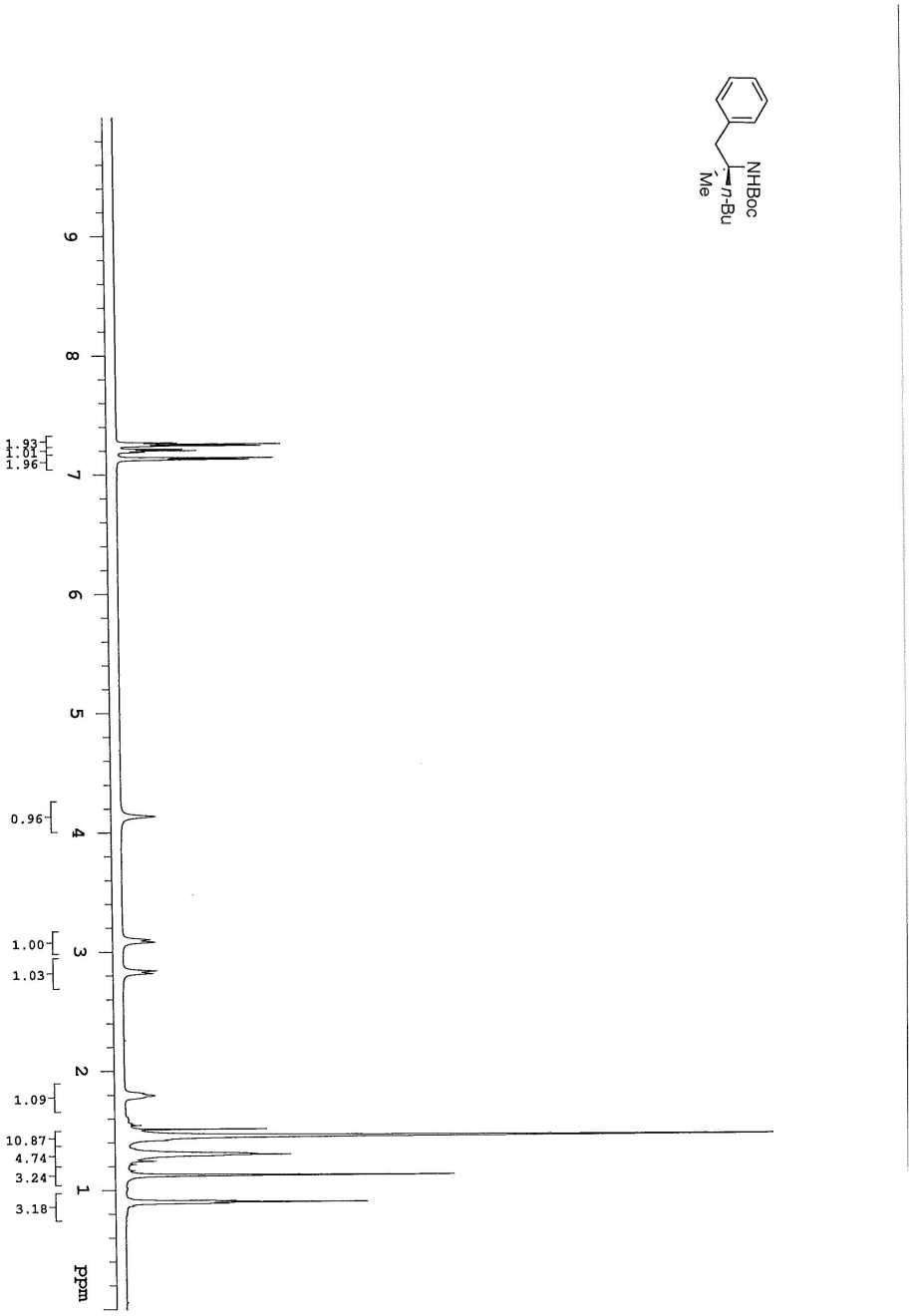
2.89
1.00
1.05
4.22
3.05
3.17
3.06


OH
n-Bu
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


NHBoc
n-Bu
Me
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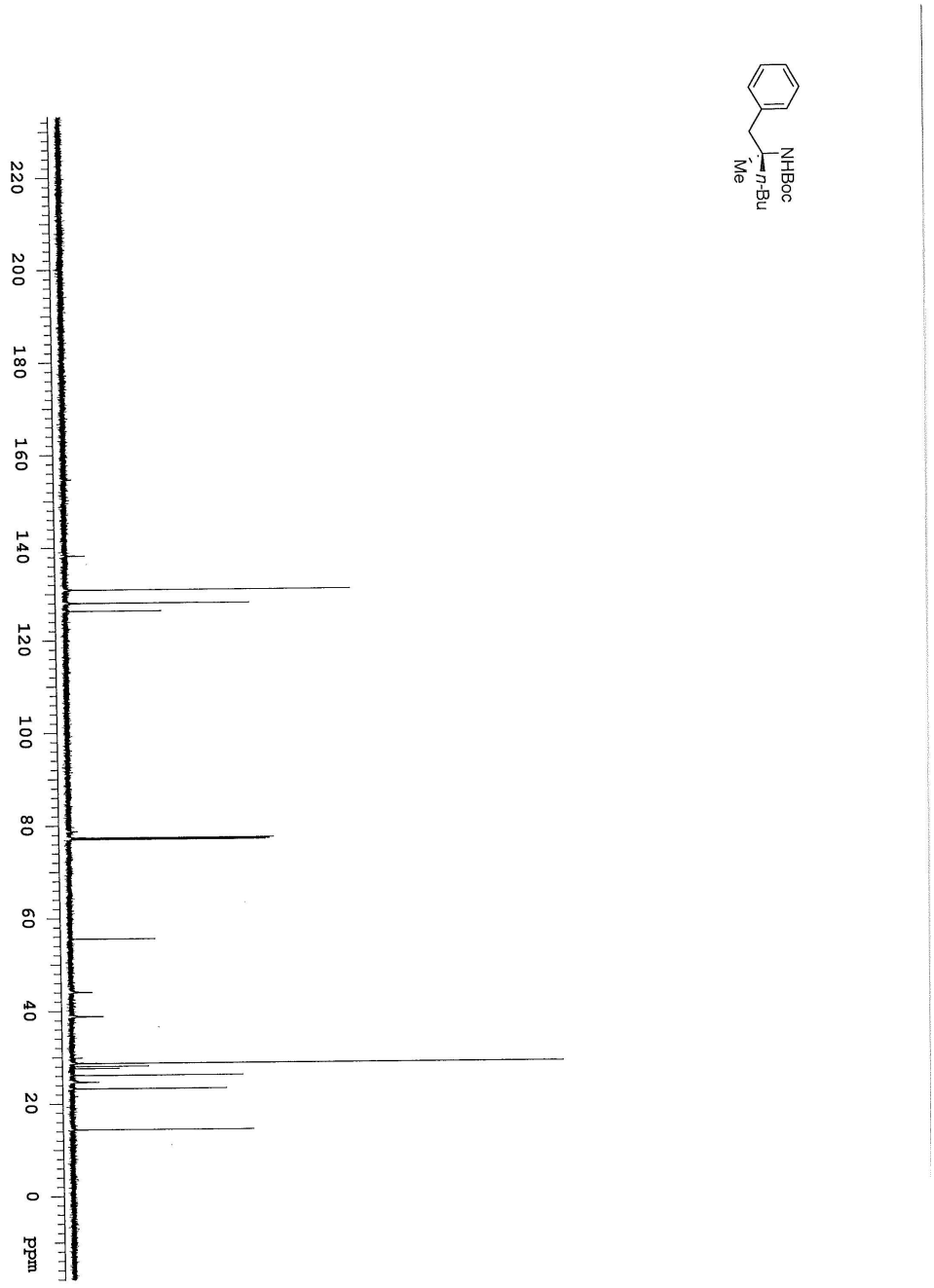
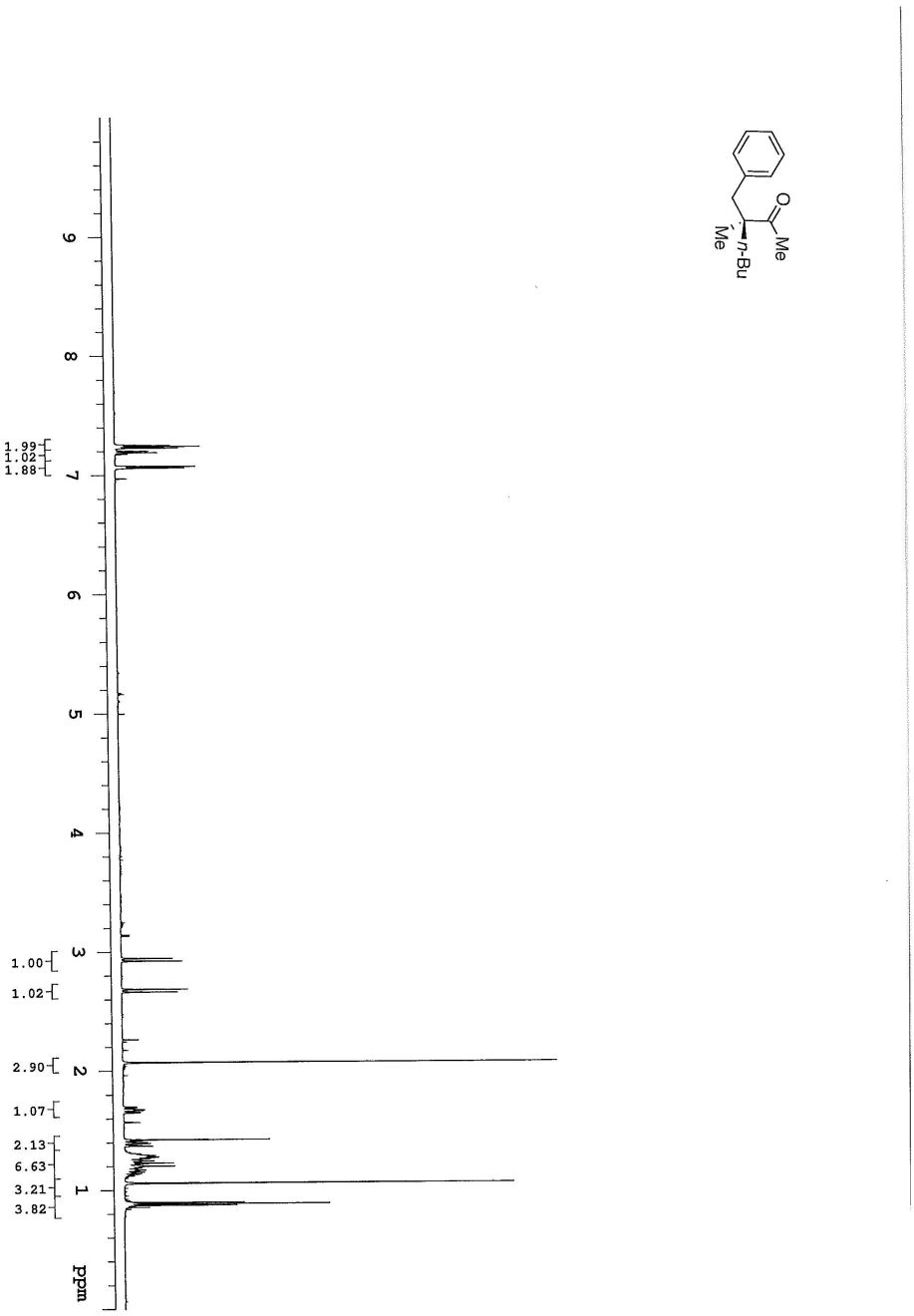
1.96
0.96
1.00
1.03
1.09
10.87
4.74
3.24
3.18
ppm


NHBoc
n-Bu
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


O
Me
n-Bu
Me
1.99
1.02
1.88
1.00
1.02
2.90
1.07
2.13
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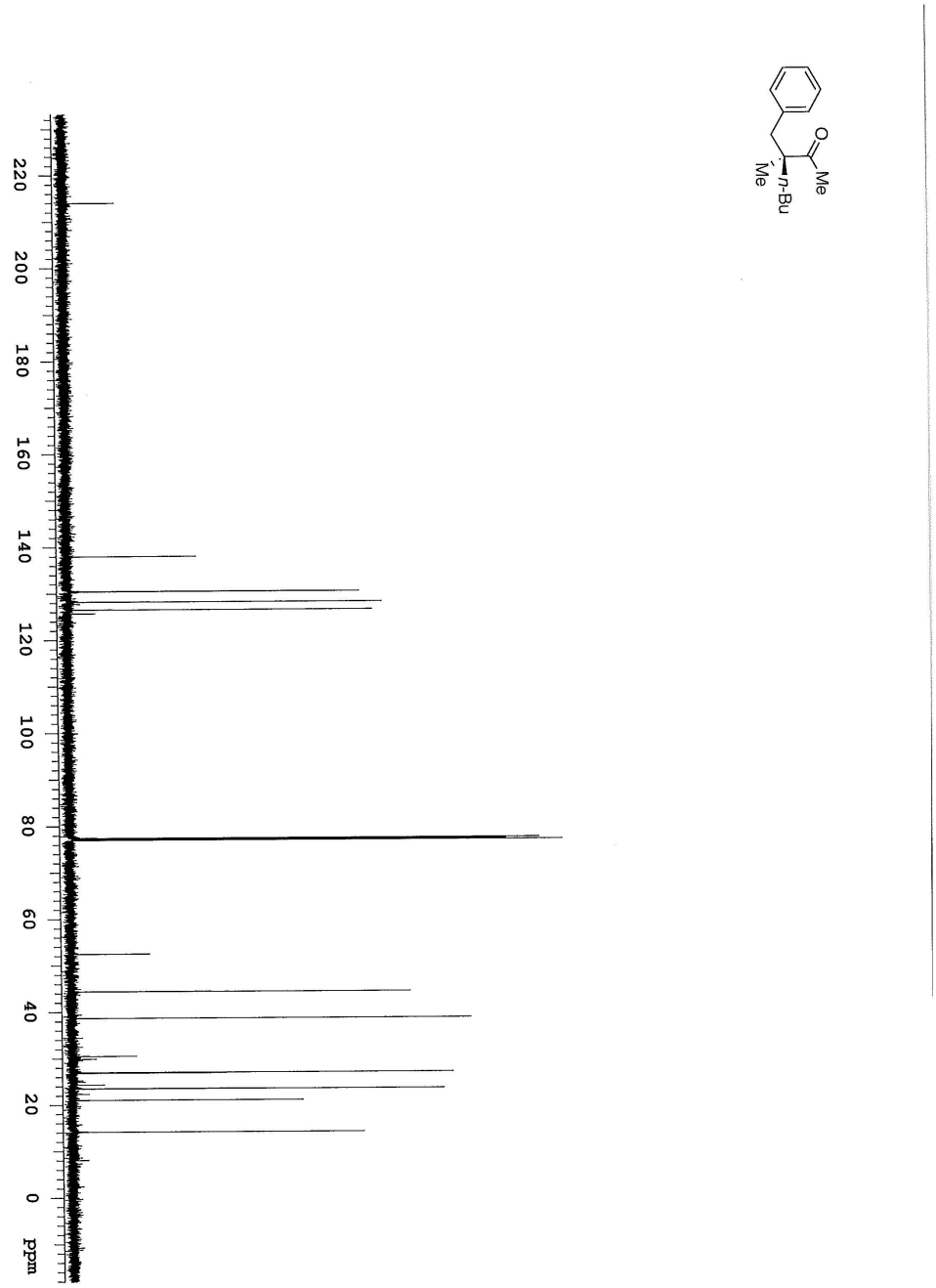
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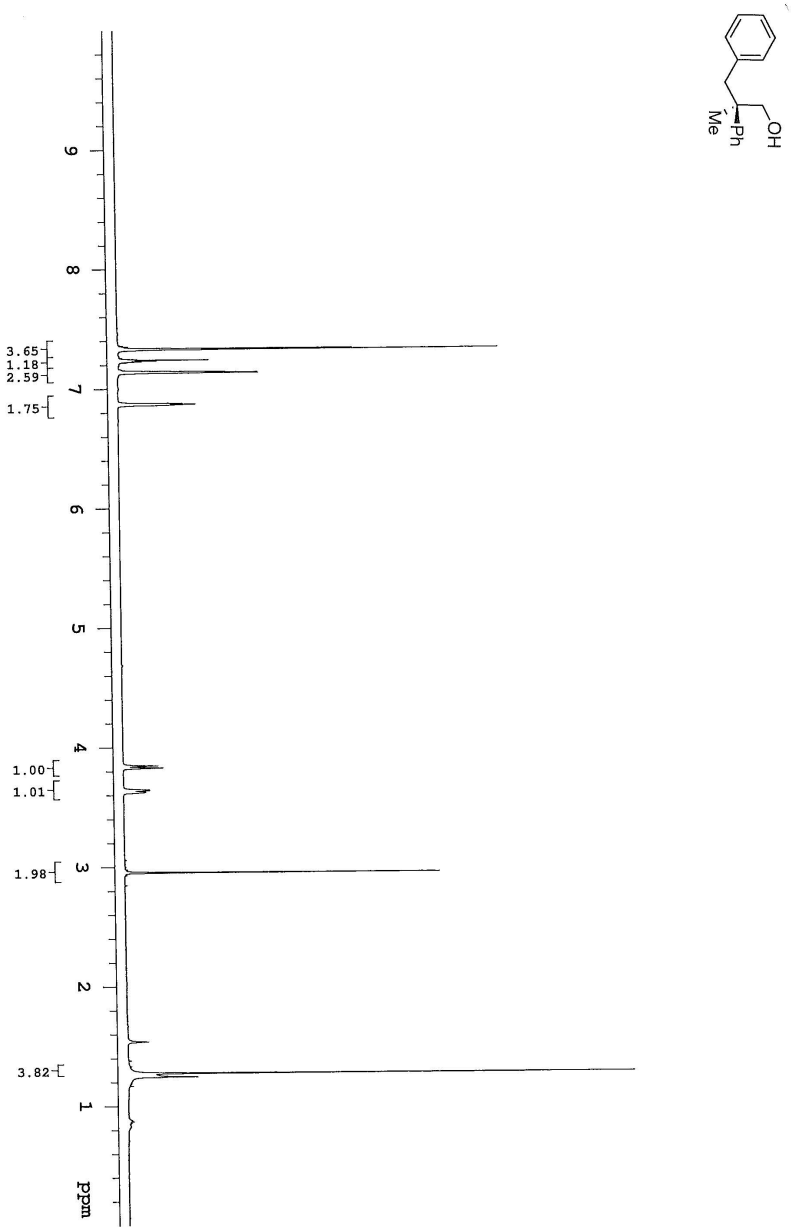
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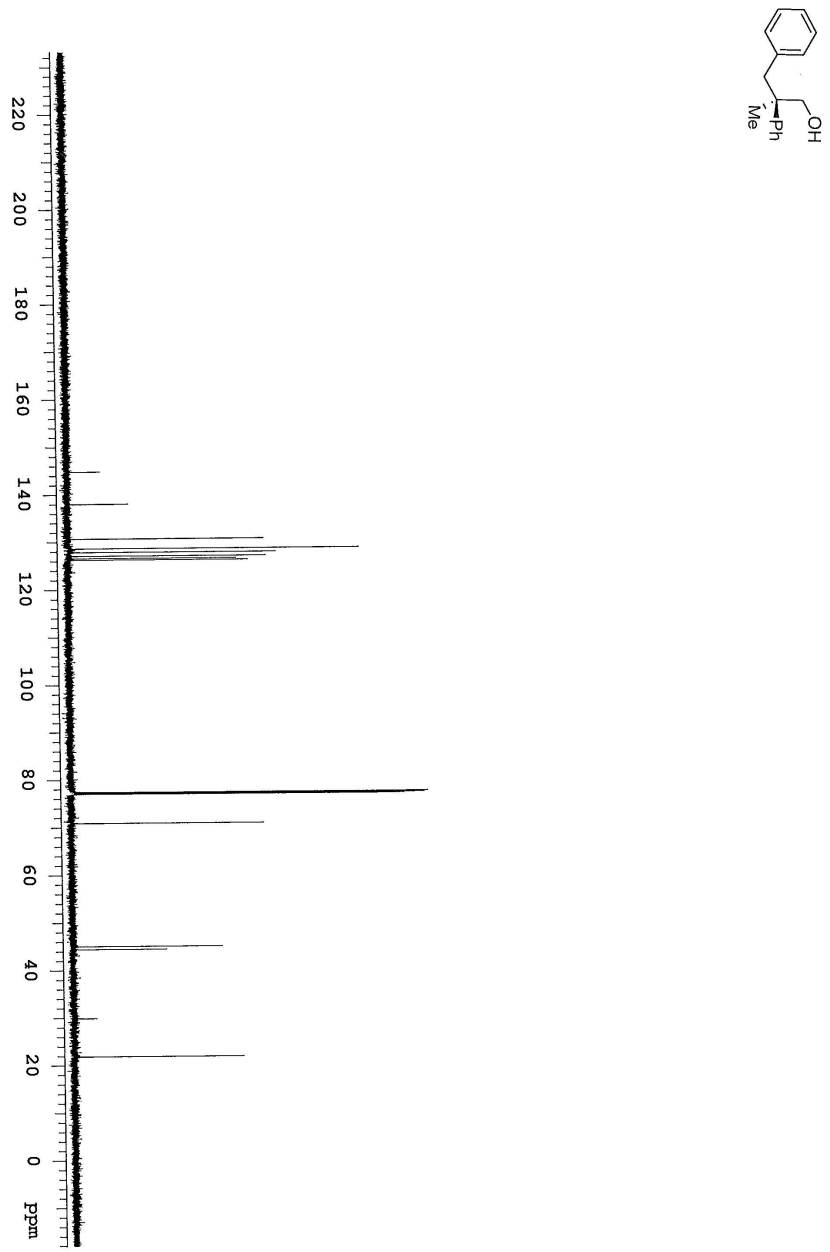
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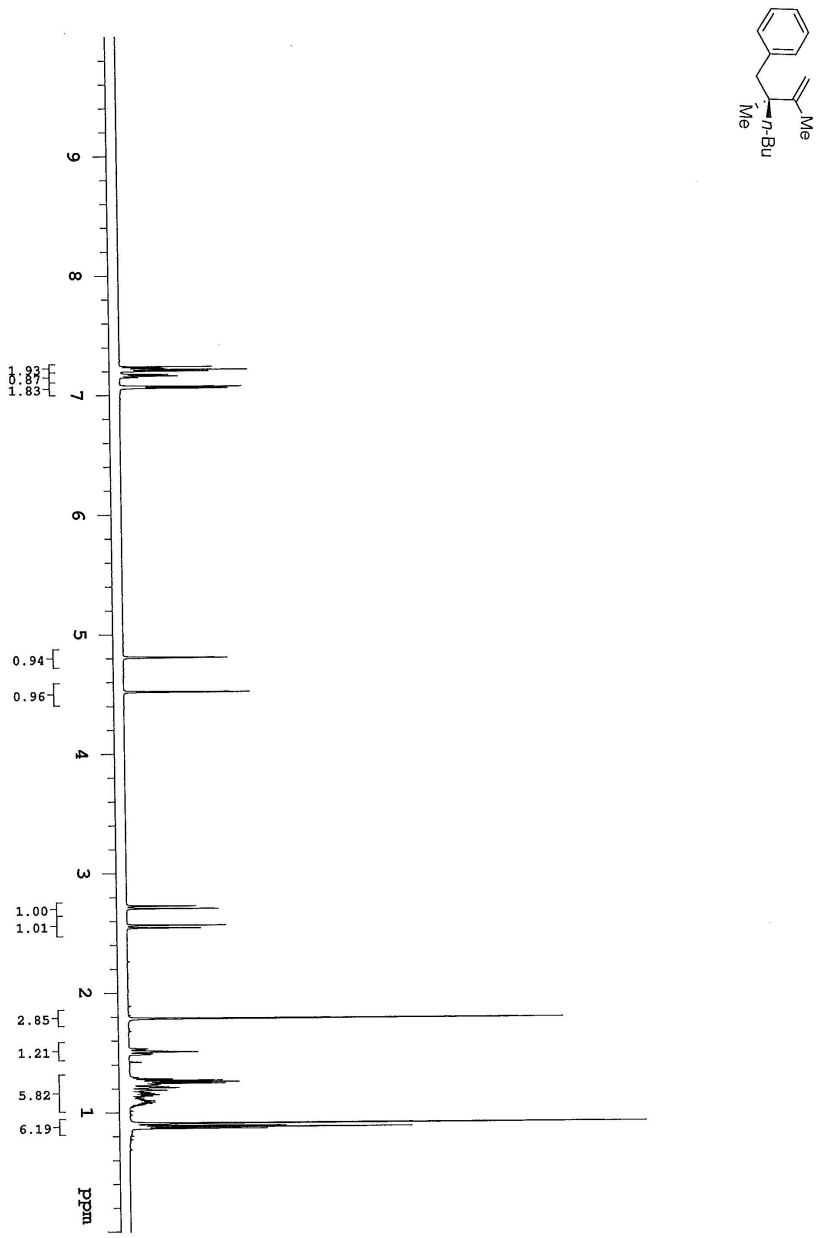
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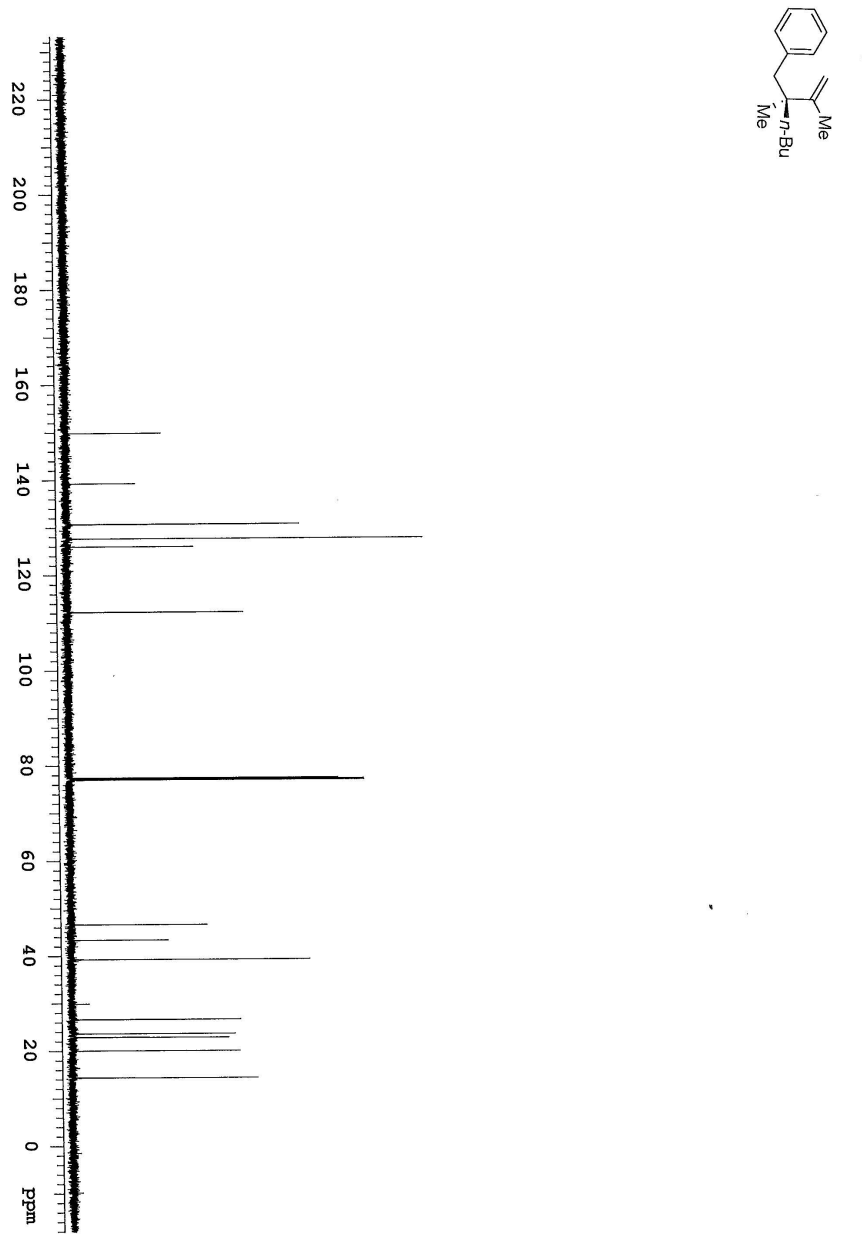
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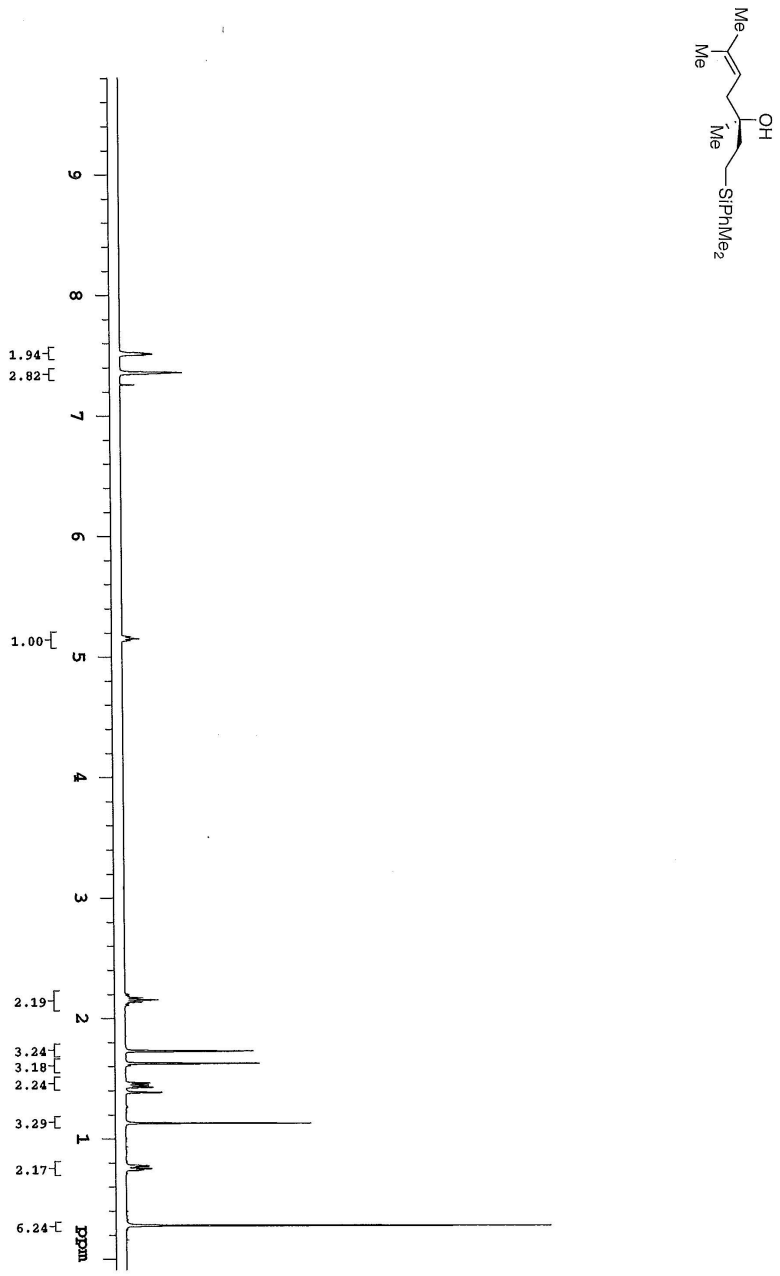
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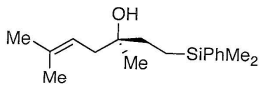
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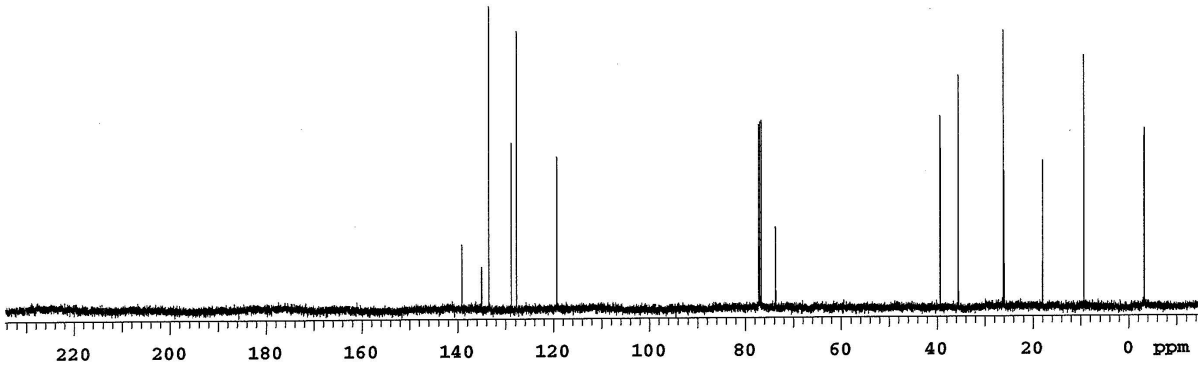
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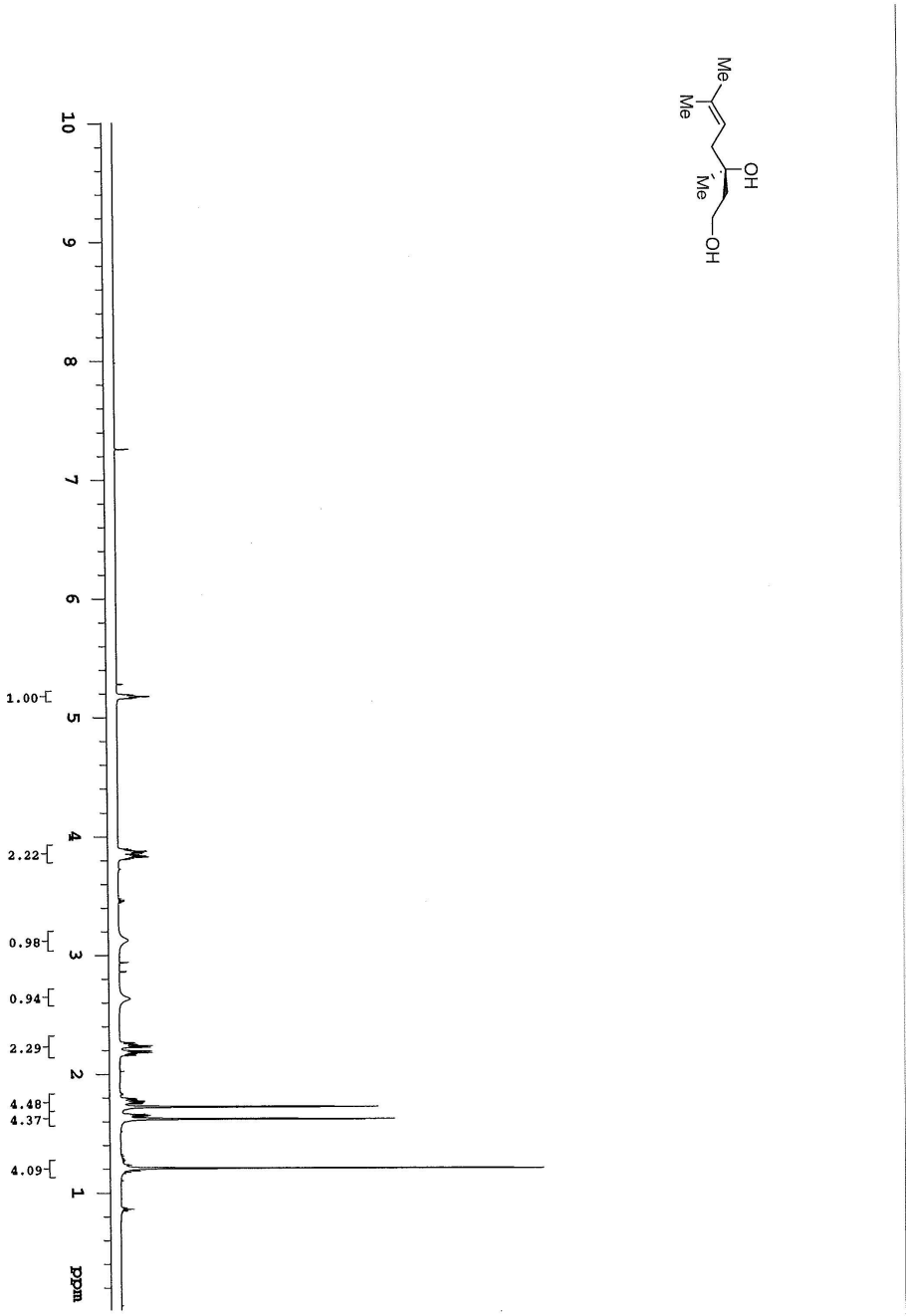
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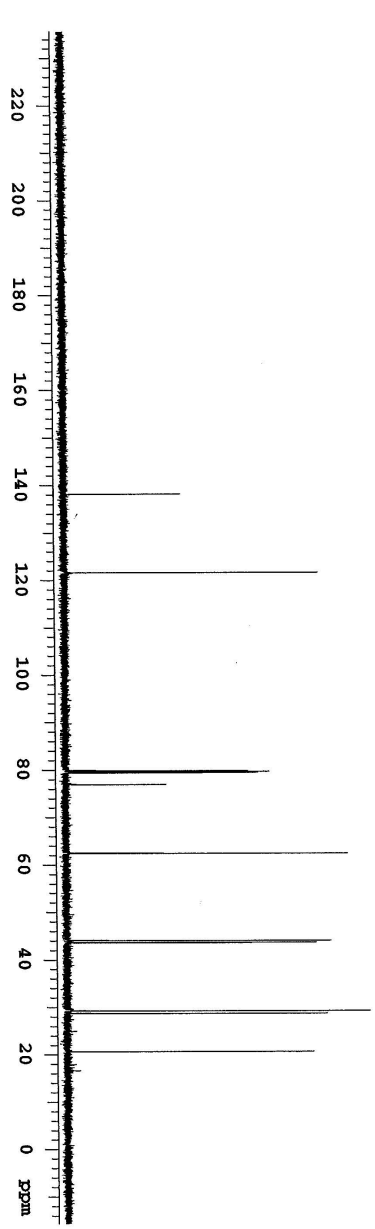
4.09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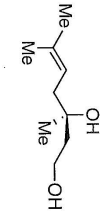
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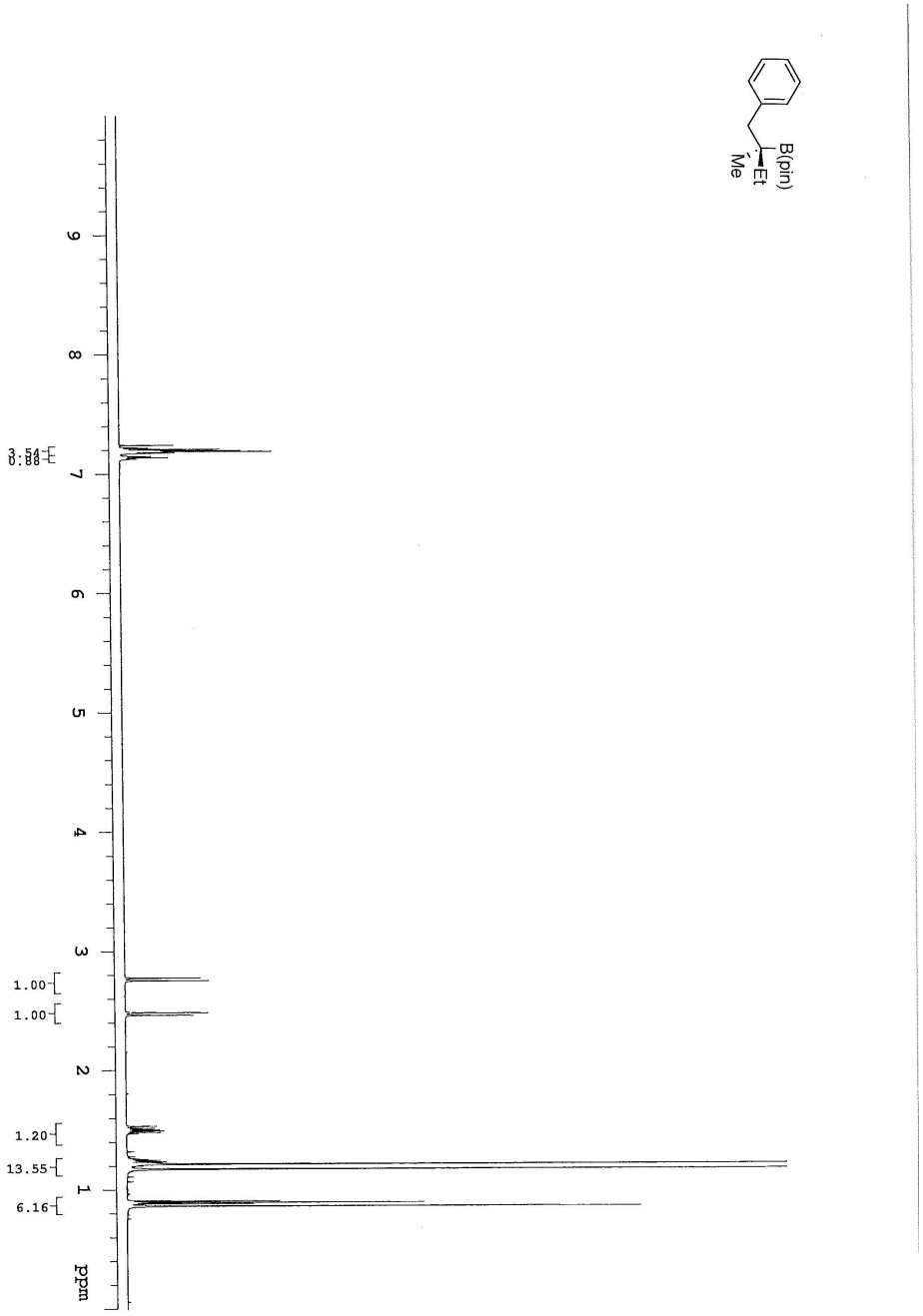
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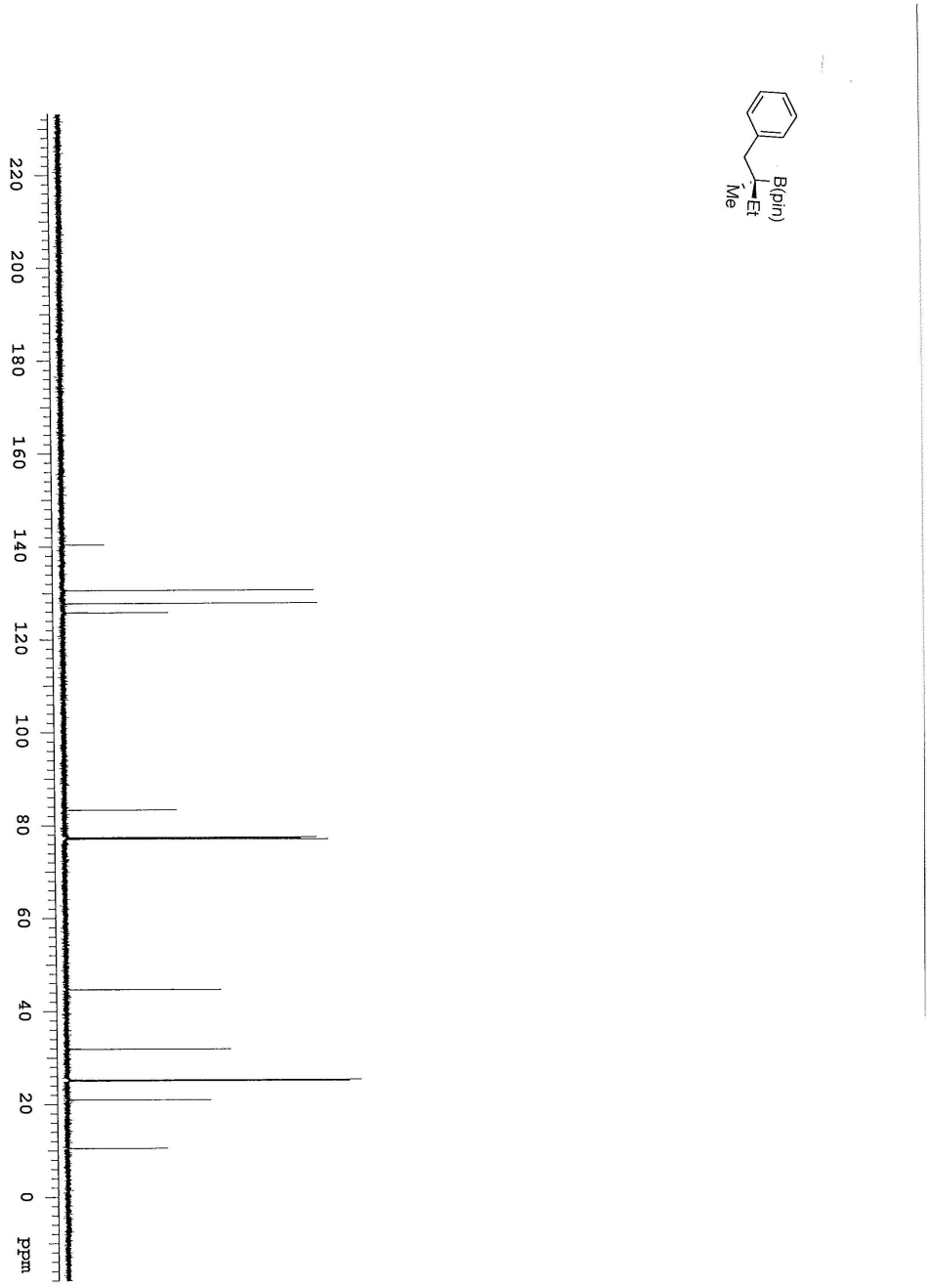
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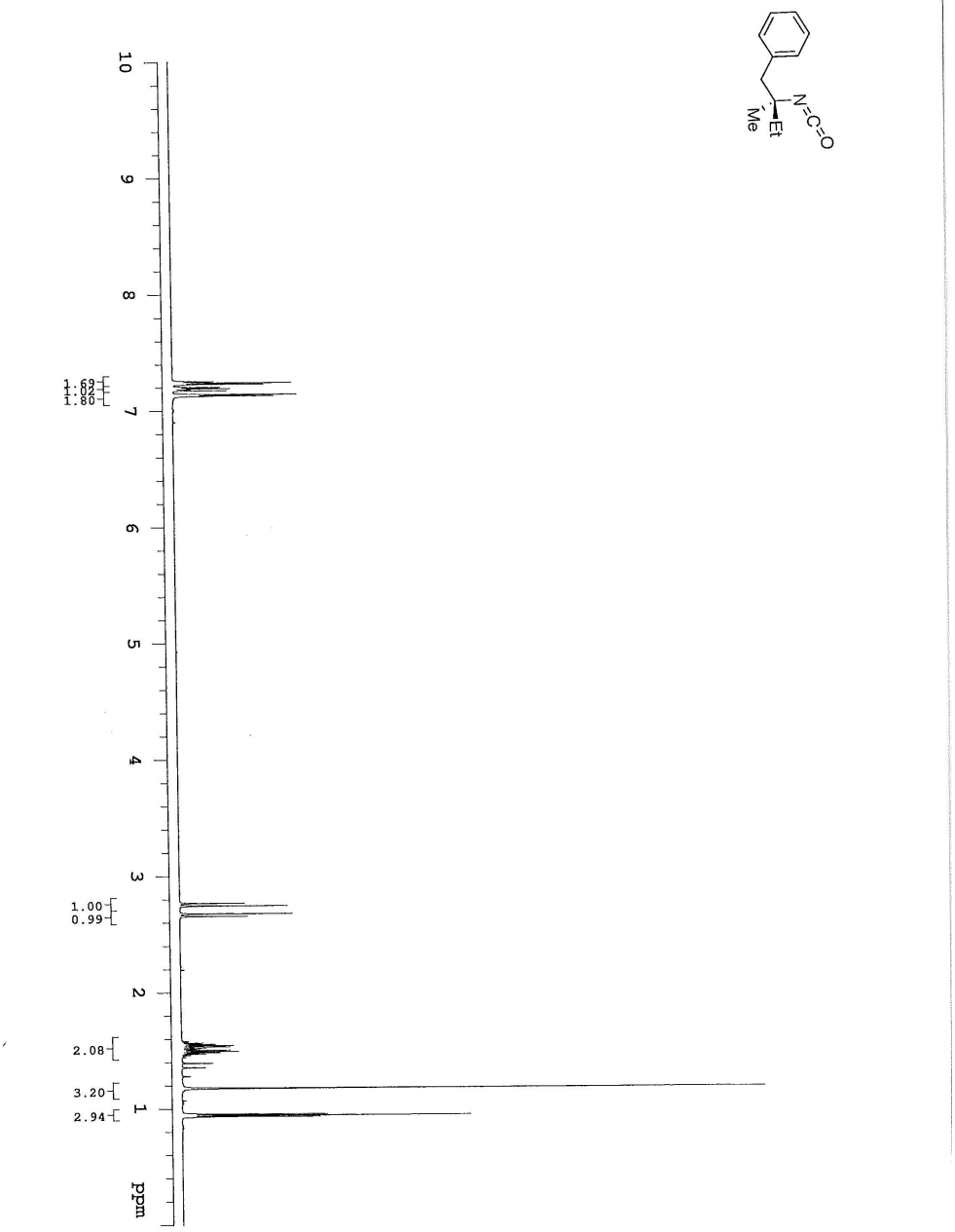
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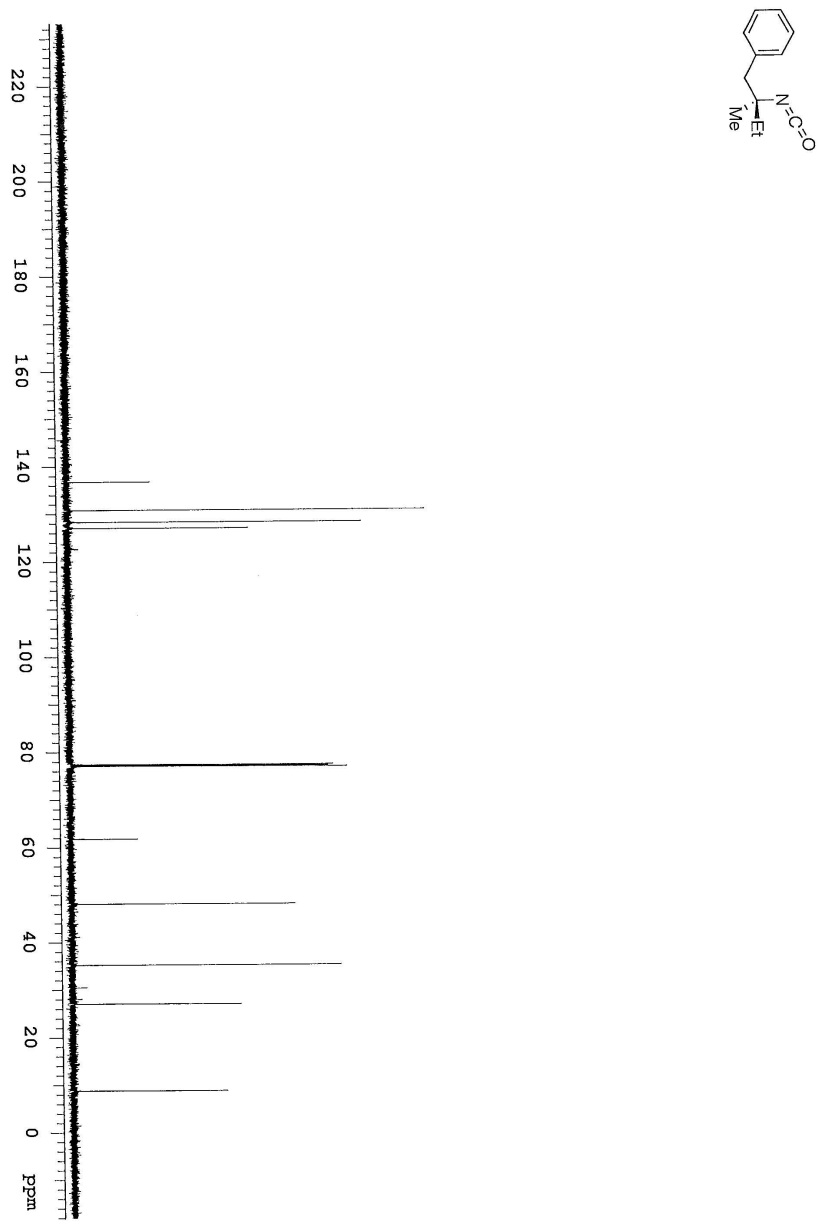
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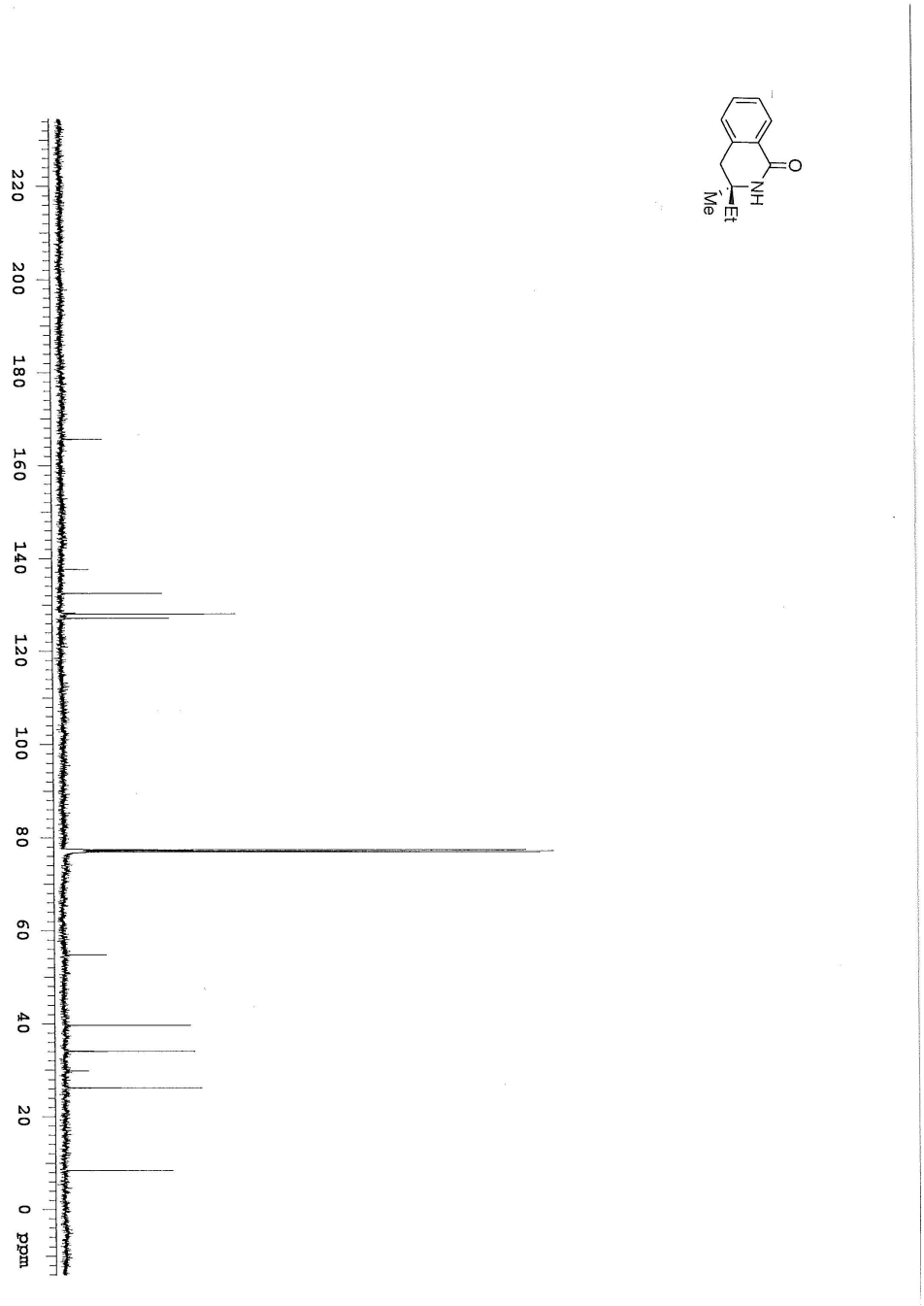
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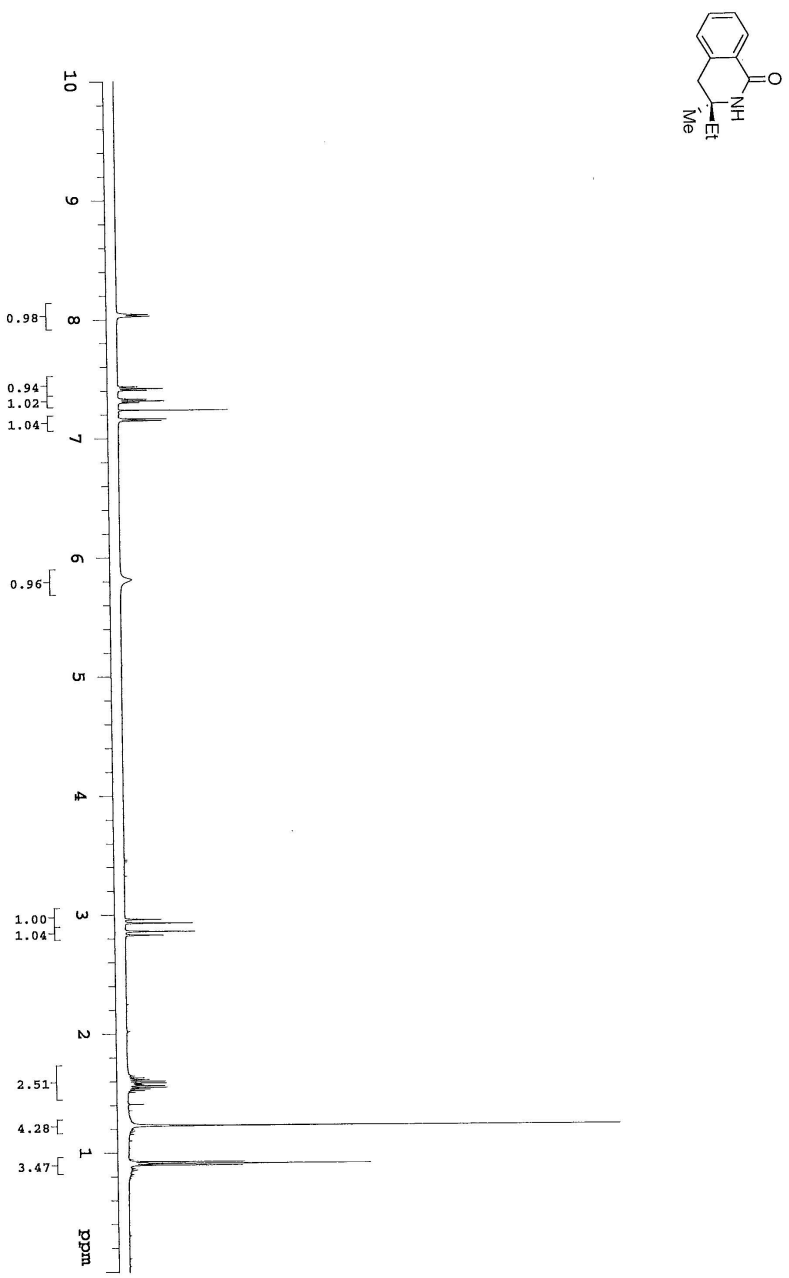
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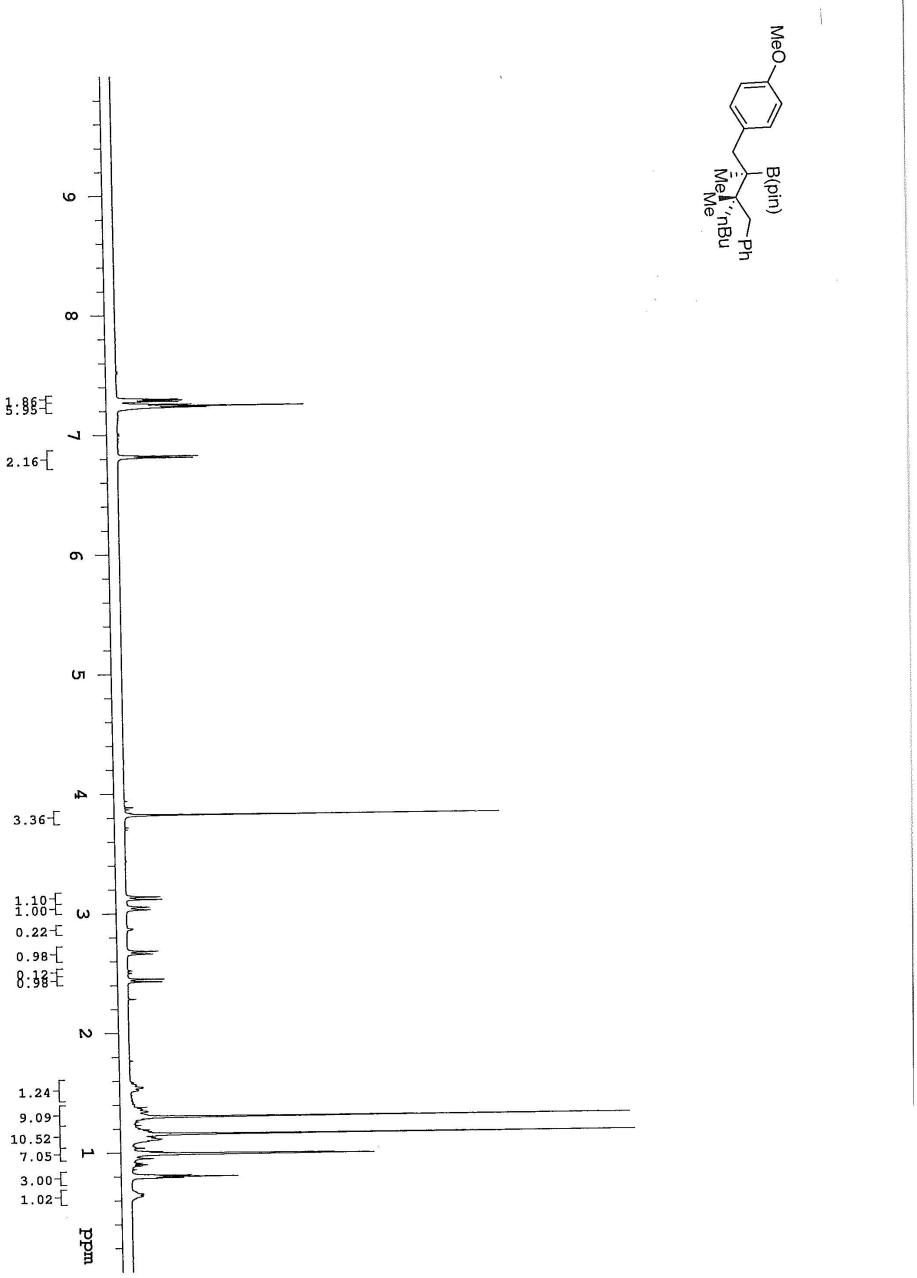
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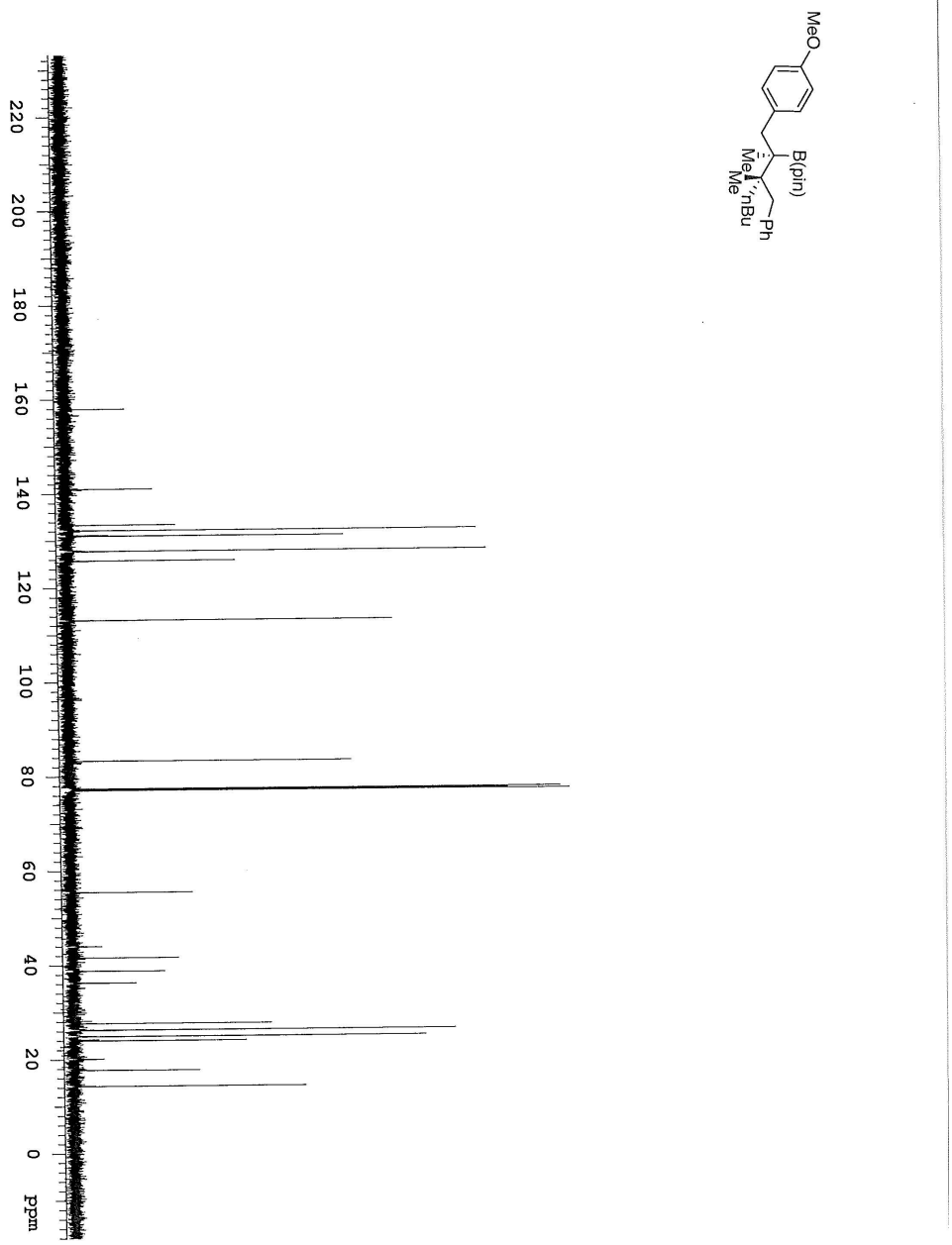
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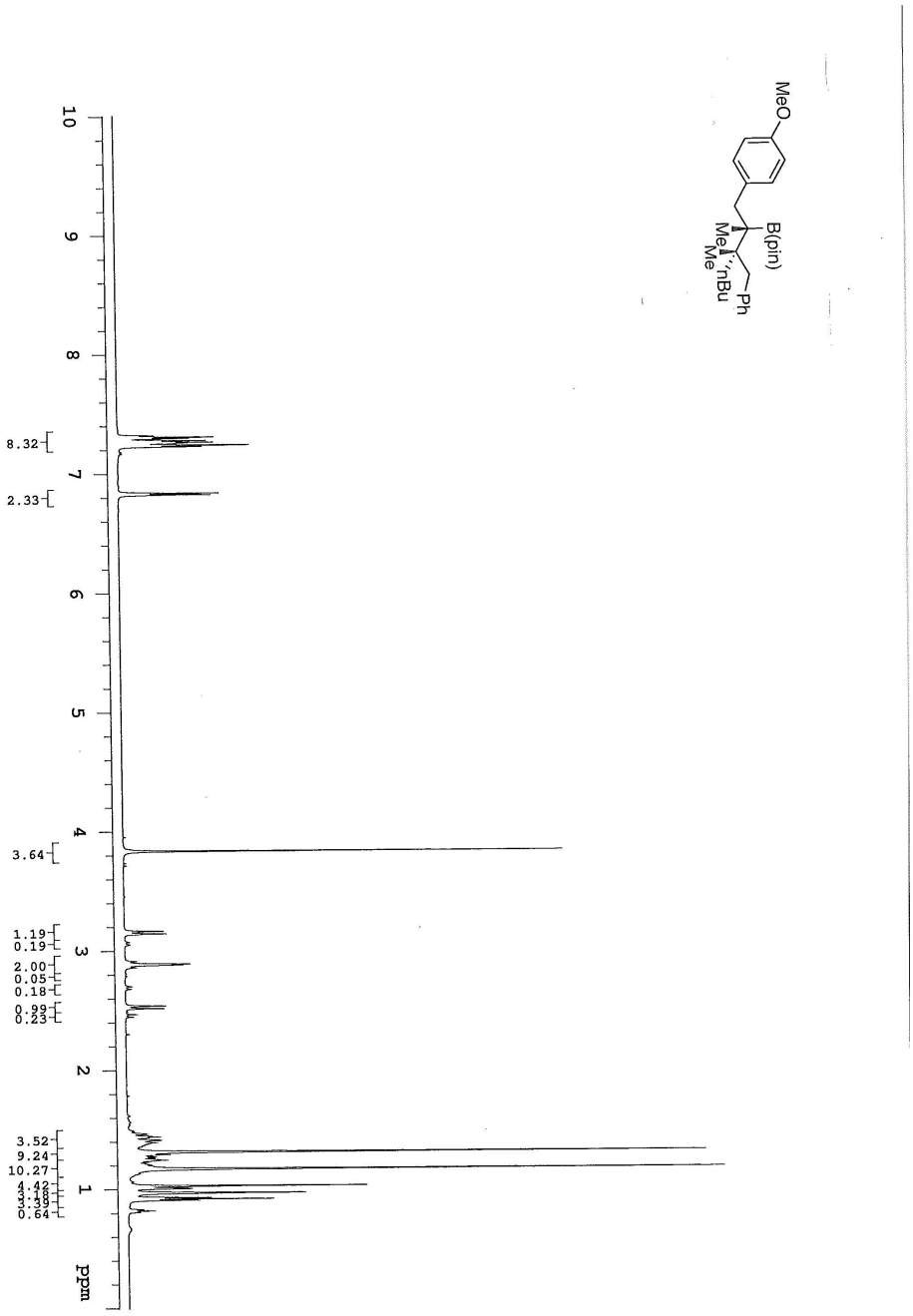
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ppm
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2.33
3.64
1.19
0.19
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0.99
0.23
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10.27
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3.18
3.39
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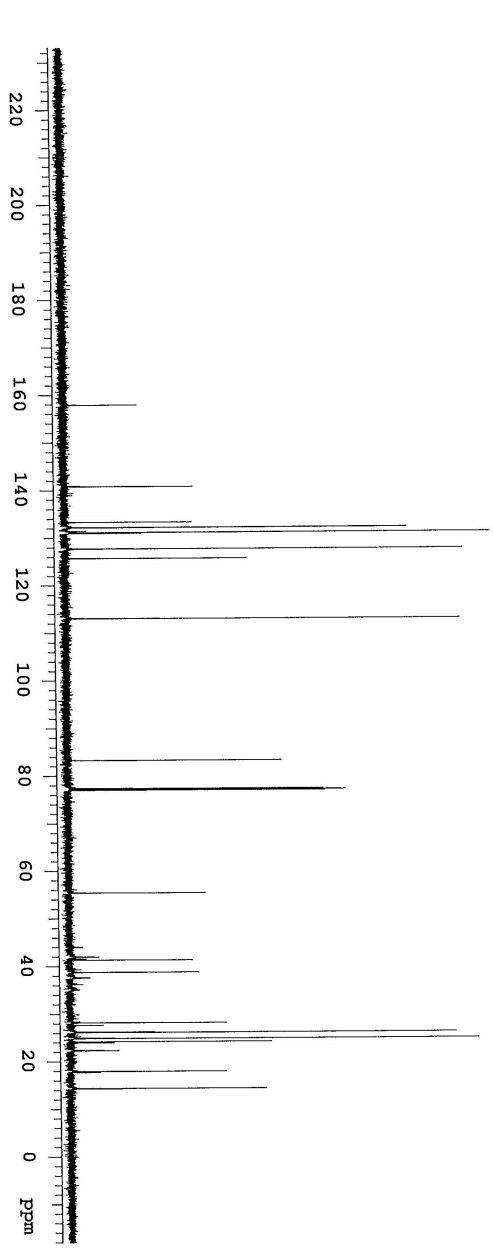
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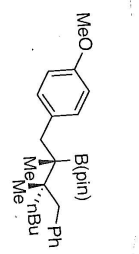
ppm


MeO
B(pin)
Me
nBu
Me
Ph

Chapter 4

Platinum-Catalyzed Enantioselective Diboration of Alkenyl Boronates and Utility of 1,1,2-tris(boronates)

4.1. Introduction

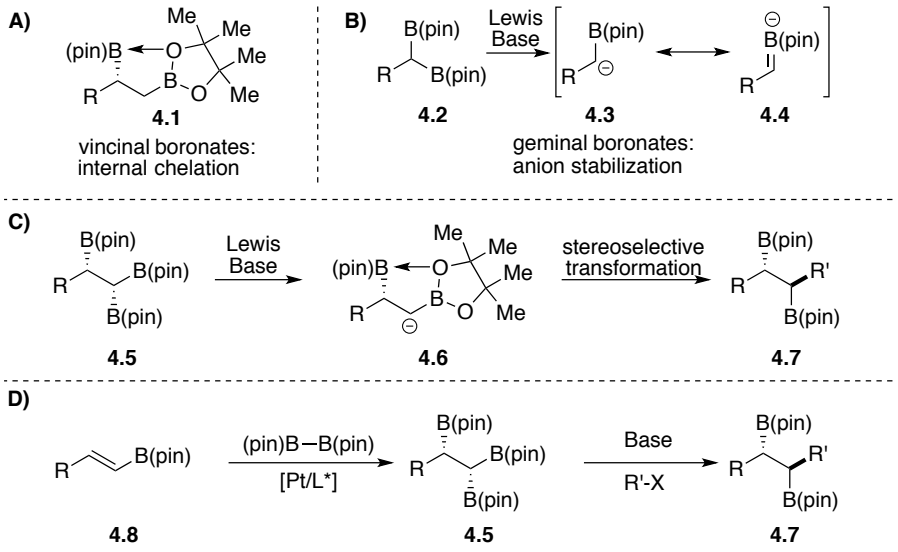
Multiborylated compounds are recognized as powerful building blocks for asymmetric synthesis. They can be synthesized and manipulated in an enantioselective catalytic fashion, and they provide opportunities for multiple sequential carbon-carbon bond or carbon-heteroatom bond constructions. This allows for construction of complex chiral targets from readily available substrates in a stereoselective and efficient manner.

Compared to monoborylated compounds, multiborylated molecules have novel unique reactivity features arising when one organoboron motif can interact with the other. For vicinal bis(boronates) **4.1**, the internal chelation of a pinacol oxygen to the internal boronate moiety is proposed to increase the Lewis acidity of the terminal boronate unit, thus enhancing the efficiency of the Suzuki-Miyaura cross-coupling process (Scheme 4.1.A). On the other hand, the ability of a three-coordinate boron to stabilize an adjacent cabanion is proposed to facilitate the deborylation of geminal bis(boronates). The resulting α-boryl anions efficiently participate in subsequent alkylation reactions with a variety of carbon-based electrophiles (Scheme 4.1.B). In this light, we envision that 1,1,2-tris(boronates) **4.5**, a combination of vicinal and geminal bis(boronates) might be able to generate the internally chelated α-boryl anion **4.6** in the presence of suitable base.

Moreover, the chelation feature of α-boryl anion **4.6** might provide a rigid and organized structure that facilitates subsequent stereoselective transformations (Scheme 4.1.C).

In this chapter, a platinum-catalyzed enantioselective diboration of alkenyl boronates to synthesize 1,1,2-tris(boronates) will be presented. Furthermore, a highly stereoselective deborylative alkylation of 1,1,2-tris(boronates) and its synthetic utility will also be described (Scheme 4.1.D).

Scheme 4.1. Reactivity features of multiborylated compounds.



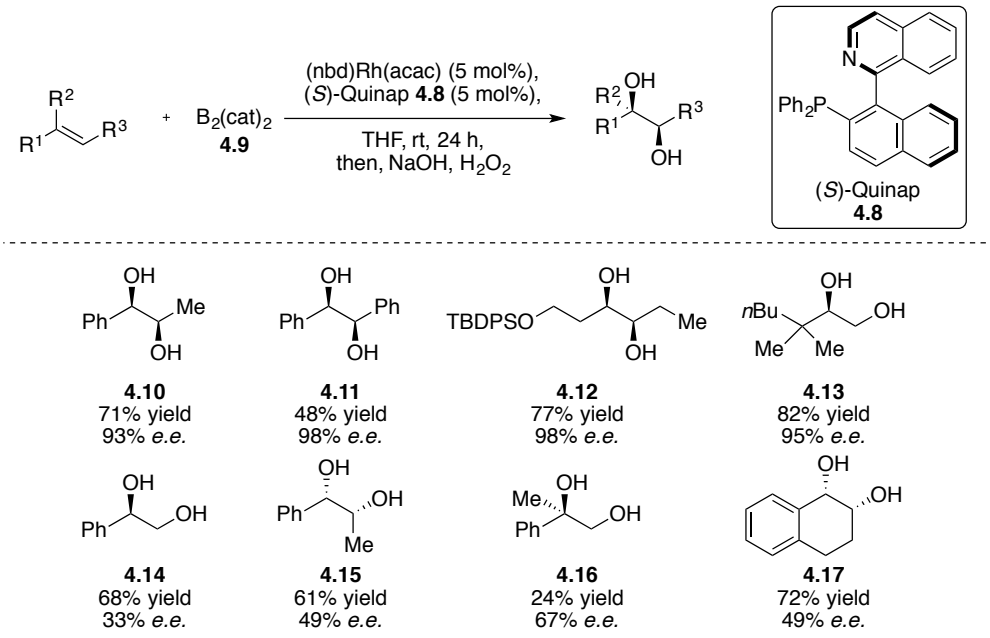
4.2. Background

4.2.1. History of enantioselective diboration of unactivated alkenes

As discussed above, multiborylated compounds, especially vicinal bis(boronates), are powerful building blocks for synthetic chemistry. To synthesize vicinal bis(boronates), one of the most straightforward ways is the enantioselective diboration of unactivated alkenes. Over the past two decades, several important developments have been achieved to synthesize vicinal bis(boronates) from readily available simple alkenes in a catalytic

and enantioselective fashion. In 2003, the first catalytic enantioselective diboration of unactivated alkenes was reported by Morken and co-workers.[1] As shown in Scheme 4.2, $B_2(cat)_2$ **4.9** was added across the alkene under the influence of a rhodium catalyst and (*S*)-Quinap **4.8** as the ligand. Upon oxidation, vicinal diol products were isolated with good yield and enantioselectivity. It is worthy of note that *trans*-substituted alkenes as well as terminal alkenes bearing α-quaternary centers behaved well in this reaction. However, the diol products derived from simple terminal alkenes, *cis*-alkenes, and cyclic alkenes were isolated with diminished selectivity. Furthermore, 1,1-disubstituted alkene substrates also suffered from poor reactivity and enantioselectivity.[2]

Scheme 4.2. The first enantioselective diboration of unactivated alkenes.

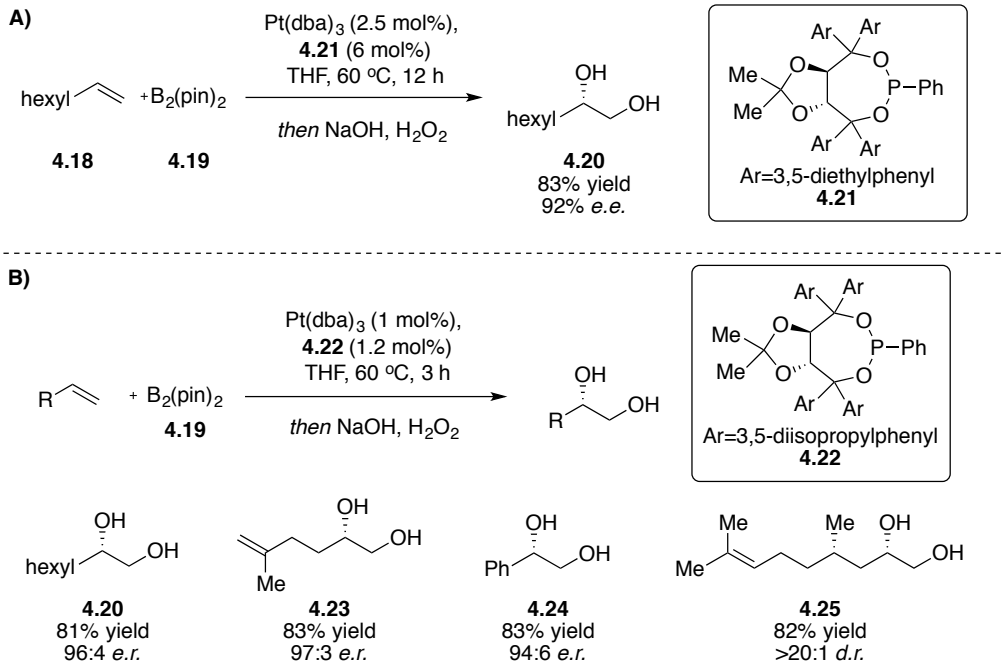


While the rhodium/Quinap system provided an efficient diboration method for *trans*-substituted alkenes with good enantioselectivity, this method could not be expanded to

[1] Morgan, J. B., Miller, S. P., Morken, J. P. *J. Am. Chem. Soc*. **2003**, 125, 8702.
[2] Trudeau, S., Morgan, J. B., Shrestha, M., Morken, J. P. *J. Org. Chem*. **2005**, 70, 9538.

alkenes with other substitution patterns. Most importantly, it could not be applied to terminal alkenes, one of the most readily available feedstock chemicals. To address this challenge, Morken and co-workers developed the first platinum-catalyzed highly enantioselective diboration of terminal alkenes.[3] Instead of $B_2(cat)_2$ **4.9**, which was utilized in the rhodium system, more commonly used and bench stable $B_2(pin)_2$ **4.19** was employed as the diboration reagent in this reaction. With the 3,5-diethylphenyl TADDOL phosphonite derivative **4.21** as a chiral ligand, a platinum-catalyzed diboration of 1-octene **4.18** furnished the vicinal bis(boronates) in an enantioselective fashion. Subsequent oxidation afforded the corresponding 1,2-diol product **4.20** with an excellent level of efficiency and selectivity (Scheme 4.3.A).

Scheme 4.3. Platinum catalyzed enantioselective diboration of terminal alkenes.



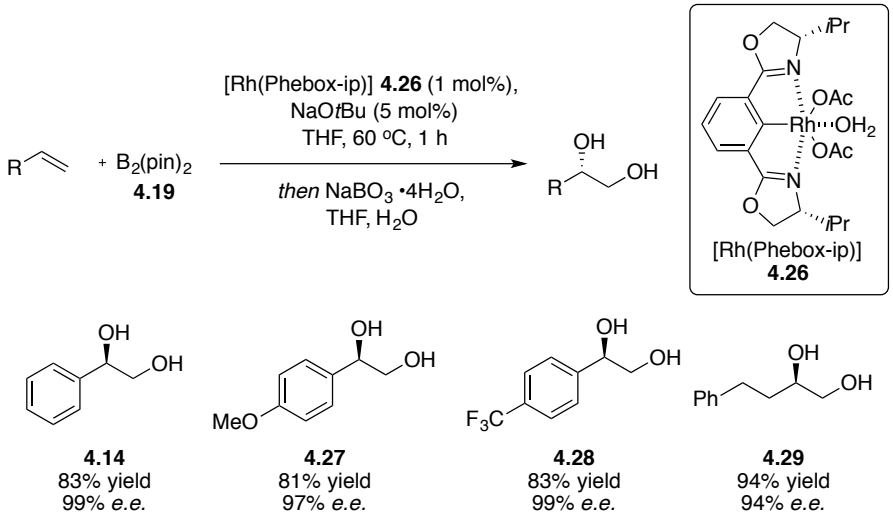
[3] Kliman, L. T., Mlynarski, S. N., Morken, J. P. *J. Am. Chem. Soc.* **2009**, 131, 13210.

In order to promote the further application of the platinum-catalyzed enantioselective diboration for synthetic chemistry, a comprehensive study focused on understanding the reaction mechanism as well as expanding reaction scope was undertaken and published by Morken group in 2013.[4] As shown in Scheme 4.3.B, the reaction conditions were further optimized to only 1% platinum catalyst loading with 3,5-diisopropylphenyl-TADDOL phosphonite derivative **4.22** as the ligand. It was shown that not only alkyl substituted terminal alkenes were suitable substrates for platinum-catalyzed diboration, but also styrene derived alkenes could be engaged in this reaction with good yield and selectivity. Furthermore, α and β stereocenters could be well tolerated in the diboration reaction. It is worthy of note that this platinum-catalyzed diboration was effective only for only terminal alkenes (**4.23**, **4.25**). Alkenes bearing other substitution patterns did not react under the reaction conditions.

As an alternative to the platinum-catalyzed enantioselective diboration developed by the Morken group, Nishiyama and co-workers reported a rhodium-catalyzed enantioselective diboration of terminal alkenes[5]. Utilizing the [Rh(Phebox)] **4.26** as catalyst, the diboron reagent, $B_2(pin)_2$ **4.19**, was added across the terminal alkene in the presence of 5 mol% of sodium *tert*-butoxide to furnish a vicinal bis(boronate) product, which was subsequently oxidized to a 1,2-diol with good yield and enantioselectivity (Scheme 4.4). Similar to platinum-catalyzed diboration reaction, 1,2-disubstituted alkenes were not suitable substrates for the rhodium-catalyzed enantioselective diboration, while both alkyl and aryl substituted terminal alkenes could be well engaged in this reaction.

[4] Coombs, J. R., Haeffner, F., Kliman, L. T., Morken, J. P. *J. Am. Chem. Soc.* **2013**, 135, 11222.
[5] Toribatake, K., Nishiyama, H. *Angew. Chem. Int. Ed.* **2013**, 52, 11011.

Scheme 4.4. Rhodium-catalyzed enantioselective diboration of terminal alkenes.

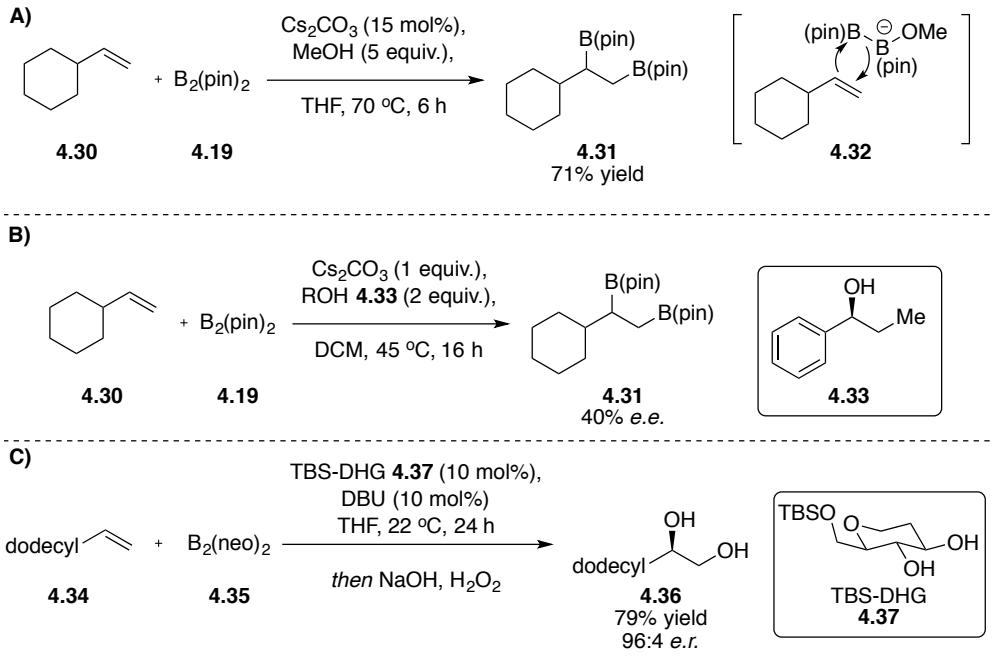


As discussed above, enantioselective diboration of unactivated alkenes could be catalyzed by platinum or rhodium in the presence of chiral ligands. However, utilizing such precious transition-metal catalysts might limit the synthetic application of the diboration reaction on large-scale synthesis. In this context, Fernandez and co-workers developed the first transition-metal free 1,2-diboration protocol that applied to unactivated alkenes.[6] Utilizing catalytic amount of cesium carbonate as base and five equivalents of methanol as an additive, the alkene substrate **4.30** was efficiently diborated with $B_2(pin)_2$ to afford 1,2-bis(boronates) **4.31**. Besides terminal alkenes, this protocol could also be applied to internal alkene substrates. In regard to proposed reaction mechanism, the key reactivity feature of this reaction was that one boron unit of the diboron reagent **4.19** could be activated by the methoxide to from a boron ate complex

[6] Bonet, A., Pubill-Ulldemolins, C., Bo, C., Gulyás, H., Fernández, E. *Angew. Chem. Int. Ed.*, **2011**, 50, 7158.

4.32. Subsequently, the boron ate complex could further react with an alkene to deliver the diboration product (Scheme 4.5.A). While the methoxide activator generated from the methanol additive was involved in the diboration process, it was proposed that a transition-metal free enantioselective diboration reaction might be achieved by employing an appropriate chiral alcohol instead of methanol as additive. Broad ranges of chiral mono-alcohols were investigated by Fernandez and co-workers.[7] However, only moderate enantioselection was obtained even with 200 mol% of chiral alcohol additive (Scheme 4.5.B).

Scheme 4.5. Transition-metal free diboration of alkenes.



To address the challenge that highly enantioselective diboration could only be achieved with non-earth abundant transition-metal catalysts, Morken and co-workers developed the first organocatalyzed diboration of unactivated alkenes with high

[7] Bonet, A., Sole, C., Gulyás, H., Fernández, E. *Org. Biomol. Chem.* 2012, 10, 6621.

enantiomeric excess.[8] Employing TBS-DHG **4.37**, an easily accessible carbohydrate derivative, as catalyst, a broad range of alkenes could participate in the diboration process in the presence of $B_2(neo)_2$ **4.35** as diboron reagent. Subsequent oxidation led to the vicinal diol products with good efficiency and selectivity. Instead of just acting as a alkoxide activator as the chiral mono-alcohol in Fernandez's work, the TBS-DHG **4.37** was proposed to fully exchange onto the $B_2(neo)_2$ **4.35** to form a new diboron reagent with a chiral diol backbone. Thus, this new chiral diboron reagent was the proposed reactive species that participated in the diboration process to yield the 1,2-bis(boronates) with high enantioselectivity.

4.2.2. Enhanced reactivity of Bis(boronates)

4.2.2.1. Enhanced reactivity of vicinal Bis(boronates)

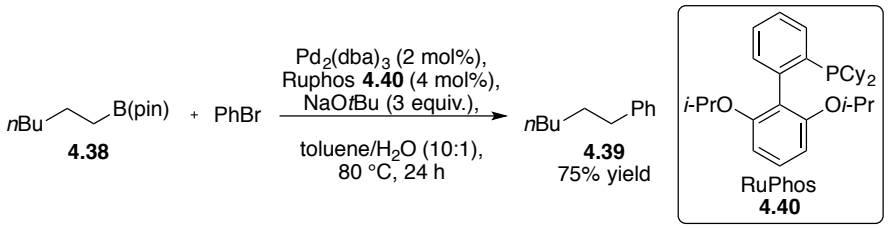
Suzuki-Miyaura cross-coupling has been recognized as one of the most widely applied carbon-carbon bond forming reactions. As one of the key components in Suzuki-Miyaura cross-coupling, a broad range of organoboron reagents have been shown to participate in the cross-coupling process. However, while alkyl boranes and boronic acids show promising reactivity in cross-coupling, their air and moisture sensitive properties limit further applications. On the other hand, alkyl boronic esters, especially the alkyl boronate derived from pinacol, are generally stable under ambient conditions. However, they are also less reactive in the transmetallation step. Only limited examples of Suzuki-Miyaura cross-coupling involving alkyl boronic pinacol esters have been reported. Furthermore, either harsh reaction conditions, such as stoichiometric amounts of toxic

[8] Fang, L., Yan, L., Haeffner, F., Morken, J. P. *J. Am. Chem. Soc.* **2016**, 138, 2508.

thallium reagent[9] or organolithium reagents[10], or specialized substrates[11], such as cyclopropyl- or benzylic boronates, are required to achieve a synthetically useful level of efficiency.

In 2012, Liu and Marder demonstrated that monodendate phosphine ligand RuPhos **4.40**, which was developed by Buchwald, was effective in catalytic Suzuki-Miyaura cross-coupling between alkyl boronic pinacol esters and aryl halides in the presence of palladium catalyst and sodium *tert*-butoxide as base.[12] With this catalytic system, efficient sp^3-sp^2 Sukuzi-Miyaura cross-coupling could be achieved under relatively mild conditions (Scheme 4.6).

Scheme 4.6. Suzuki-Miyaura cross-coupling by Marder and Liu.

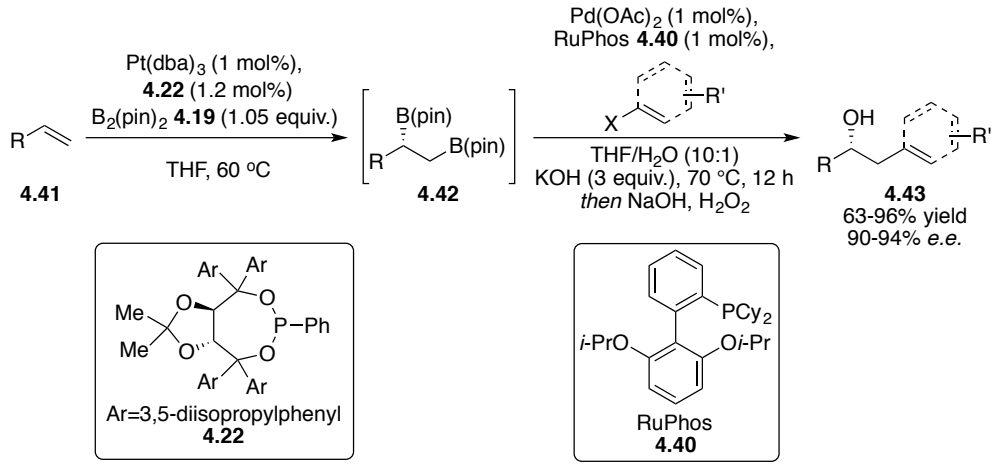


Recently, Morken and co-workers reported a catalytic asymmetric alkene diboration/cross-coupling (DCC) cascade that furnished a broad range of enantioenriched secondary boronic esters in an efficient and modular fashion.[13] Platinum-catalyzed enantioselective diboration of terminal alkenes furnished the 1,2-bis(boronate) product **4.42**. Without any purification, the 1,2-bis(boronate) **4.42** was engaged in the

[9] Sato, M., Miyaura, N., Suzuki, A. *Chem. Lett.* **1989**, 18, 1405.
[10] Zou, G., Falck, J. R. *Tetrahedron Lett.* **2001**, 42, 5817.
[11] (a) Löhr, S., Meijere, A. *Synlett* **2001**, 489. (b) Imao, D., Glasspoole, B. W., Laberge, V. S., Crudden, C. M. *J. Am. Chem. Soc.* **2009**, 131, 5024. (c) Glasspoole, B. W., Oderinde, M. S., Moore, B. D., Antoft-Finch, A., Crudden, C. *Synthesis* **2013**, 45, 1759.
[12] Yang, C.-T., Zhang, Z.-Q., Tajuddin, H., Wu, C.-C., Liang, J., Liu, J.-H., Fu, Y., Czyzeska, M., Steel, P. G., Marder, T. B., Liu, L. *Angew. Chem. Int. Ed.* **2012**, 51, 528.
[13] Mlynarski, S. N., Schuster, C. H., Morken, J. P. *Nature* **2014**, 505, 386.

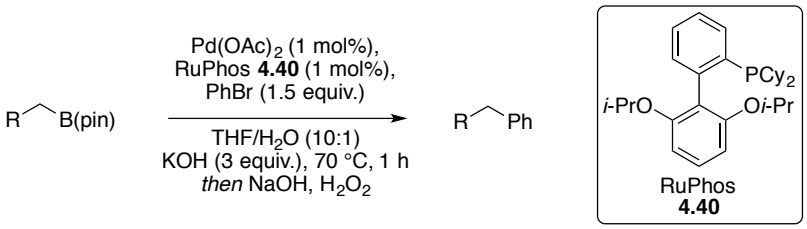
palladium/RuPhos catalyzed cross-coupling in a one-pot fashion. The cross-coupling was exclusively selective for the terminal boronate over the internal boronate with high efficiency under relatively mild conditions (Scheme 4.7).

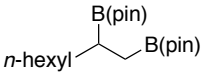
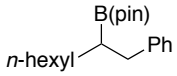
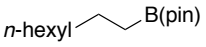
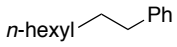
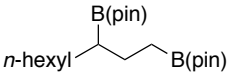
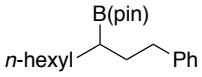
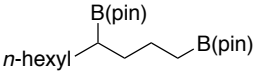
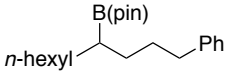
Scheme 4.7. Asymmetric alkene diboration/cross-coupling (DCC) cascade.



Interestingly, it was discovered that vicinal bis(boronates) exhibited enhanced reactivity under Suzuki cross-coupling conditions compared to other alkyl boronates. As summarized in Scheme 4.8, while 91% of 1,2-bis(boronate) **4.44** was converted to cross-coupling product **4.45** in 1 hour under the standard conditions, primary alkyl boronate **4.46** showed very poor cross-coupling reactivity (less than 5% conversion) under identical conditions. Furthermore, 1,3-bis(boronate) **4.48** and 1,4-bis(boronats) **4.50** also failed to provide comparable cross-coupling efficiency with 1,2-bis(boronate) **4.44**.

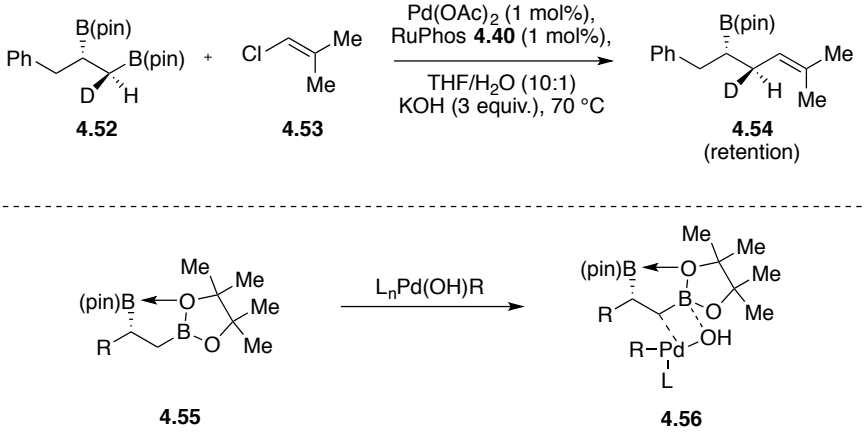
Scheme 4.8. Comparison of the efficiency of alkyl boronates in Suzuki coupling.



entry	R B(pin)	R Ph	conversion
1	 **4.44**	 **4.45**	91%
2	 **4.46**	 **4.47**	<5%
3	 **4.48**	 **4.49**	<5%
4	 **4.50**	 **4.51**	9%

To probe the stereochemical course of the transmetallation step, the deuterium-labeled bis(boronate) **4.52** was prepared and subjected to the standard cross-coupling conditions. The stereoretentive cross-coupling product **4.54** was isolated exclusively. This result indicated that the transmetallation step proceeded through an inner-sphere pathway. Thus, it was proposed that the internal boron atom was acting as a Lewis acid to coordinate with the pinacol oxygen of the terminal boronate moiety, thereby enhancing the Lewis acidity of the terminal boron atom. As a result, the alkyl boronate bearing an adjacent boronate was more reactive in the transmetallation step via association of a palladium-hydroxyide complex with the internally chelated structure **4.55**.

Scheme 4.9. Probe of the stereochemical outcome of transmetallation step.



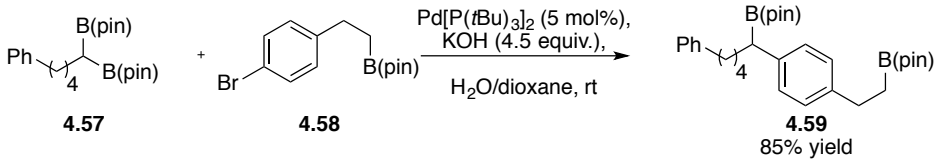
4.2.2.2. Enhanced reactivity of geminal Bis(boronates)

In addition to the vicinal bis(boronate), geminal bis(boronate) also show enhanced reactivity in Suzuki-Miyaura cross-coupling reaction. In 2010, Shibata and co-workers established a Suzuki coupling of 1,1-bis(boronates) under rather mild conditions.[14] Utilizing $Pd[P(tBu)_3]_2$ as the catalyst, a variety of 1,1-bis(boronates) were coupled to a broad range of aryl halides in the presence of hydroxide base with good efficiency. In one example, the aryl bromide bearing a primary boronic acid pinacol ester **4.58** was subjected to the cross-coupling conditions with geminal bis(boronates) **4.57**. The observation that aryl bromide **4.58** was selectively coupled to bis(boronates) **4.57** to afford the product **4.59** in good yield suggested that the 1,1-bis(boronates) was much more reactive compared to the primary alkyl boronate. A computational study and ^{11}B-NMR analysis suggested that *p*-orbital overlap between both geminal bis(boronates) moieties lowered the LUMO by delocalization. Thus, the formation of boron ate complex by coordination of a Lewis base to 1,1-bis(boronates) was facilitated. It is worthy of note

[14] Endo, K., Ohkubo, T., Hirokami, M., Shibata, T. *J. Am. Chem. Soc.* **2010**, 132, 11033.

that enantioselective Suzuki-Miyaura cross-coupling of 1,1-bis(boronates) was developed by Morken and co-workers, recently.[15] It was demonstrated that a broad range of 1,1-bis(boronates) could be coupled to both aryl and alkenyl electrophiles to construct benzylic and allylic secondary boronates in an efficient and enantioselective fashion.

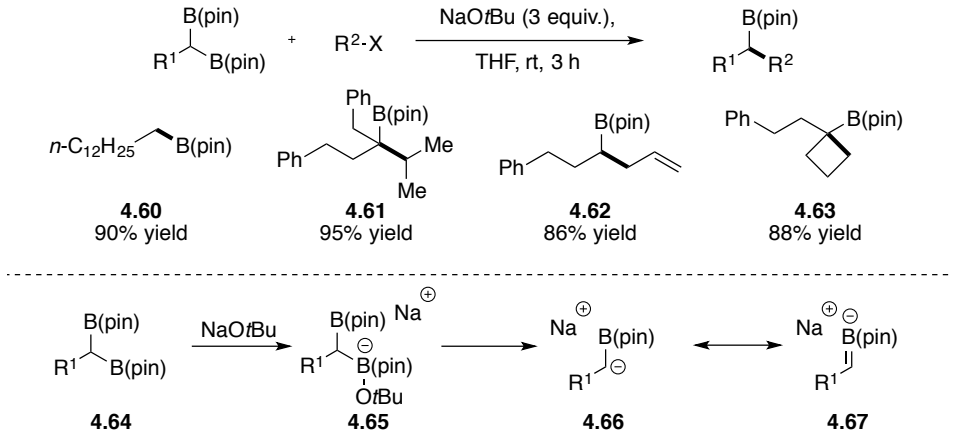
Scheme 4.10. Suzuki-Miyaura cross-coupling of 1,1-bis(boronates).



Besides the enhanced reactive towards palladium-catalyzed Suzuki-Miyaura cross-coupling, the 1,1-bis(boronates) could also be engaged in a deborylation reaction in a transition-metal free fashion. Recently, Morken and co-workers described a deborylative alkylation between geminal bis(boronates) and alkyl electrophiles in the presence of 3.0 equivalents of sodium *tert*-butoxide (Scheme 4.11).[16] It is worthy of note that the deborylation of geminal bis(boronates) proceeded at room temperature with alkoxide base, which was relatively mild conditions compared to the deborylation of a monoborylated alkane. The origin of such enhanced reactivity was rationalized by the ability of the three-coordinate boron to stabilize the α-carbanion. A ^{13}C-NMR study suggested that a full-fledged carbanion **4.66** was generated from boron ate complex **4.65**, which was formed upon treating the 1,1-bis(boronates) with sodium *tert*-butoxide. The α-boryl carbanion **4.66** was stabilized by delocalizing the electron density into the empty *p*-orbital of the adjacent three-coordinate boron (structure **4.67**).

[15] (a) Sun, C., Potter, B., Morken, J. P. *J. Am. Chem. Soc.* **2014**, 136, 6534. (b) Potter, B., Szymaniak, A. A., Edelstein, E. K., Morken, J. P. *J. Am. Chem. Soc.* **2014**, 136, 17918.
[16] Hong, K., Liu, X., Morken, J. P. *J. Am. Chem. Soc.* **2014**, 136, 10581.

Scheme 4.11. Deborylative alkylation of geminal bis(boronates).



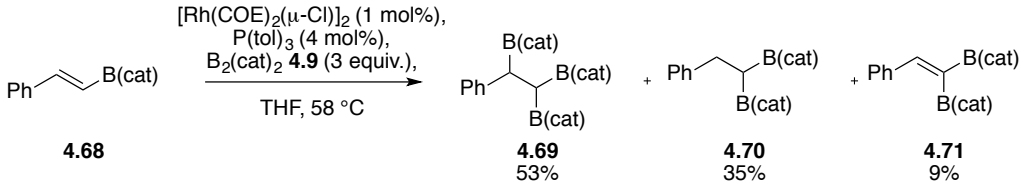
4.2.3. Synthesis of 1,1,2-tris(boronates)

As discussed in Scheme 4.1 previously, 1,1,2-tris(boronates), a structural combination of 1,2-bis(boronates) and 1,1-bis(boronates), potentially inherit both unique reactivity features from the parent structures. To explore the potential reactivity features of 1,1,2-tris(boronates), a straightforward synthetic route to access such a structural motif is highly desired. However, to our best knowledge, Marder and co-workers reported the only method to access 1,1,2-tris(boronates) by a rhodium-catalyzed diboration of alkenyl boronic acid catechol ester (Scheme 4.12).[17] By treating the styrenylboronate **4.68** with rhodium/P(tol)$_3$ catalyst in the presence of $B_2(cat)_2$, the 1,1,2-tris(boronates) product was isolated along with a mixture of hydroboration and β-hydride elimination byproducts. Furthermore, the catchol-derived 1,1,2-tris(boronates) were sensitive to air and moisture so that further purification and applications were limited. Inspired by Marder's work, we considered that applying the platinum-catalyzed diboration to alkenyl boronic acid

[17] Nguyen, P., Coapes, R. B., Woodward, A. D., Taylor, N. J., Burke, J. M., Howard, J. A. K., Marder, T. B. *J. Organomet. Chem.* **2002**, 652, 77.

pinacol esters might provide an efficient route to access potentially stable pinacol derived 1,1,2-tris(boronates) in an enantioselective fashion. Moreover, further exploration of the reactivity of 1,1,2-tris(boronates) might also be facilitated by such methodology.

Scheme 4.12. Rhodium-catalyzed diboration of alkenyl boronates.

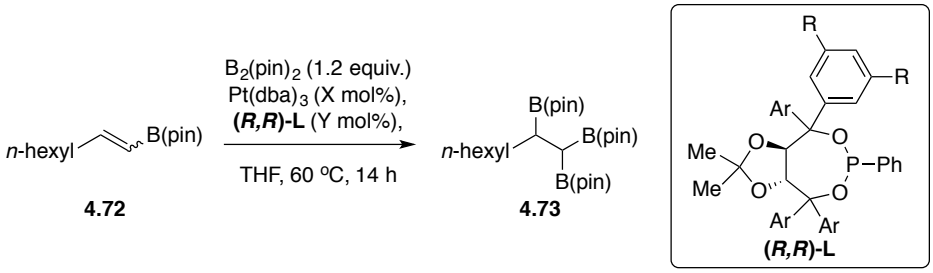


4.3. Development of enantioselective diboration of alkenyl boronates

In order to probe the reactivity of alkenyl boronates towards the platinum-catalyzed enantioselective diboration, the *trans*-octenyl boronic acid pinacol ester **4.72** was treated with 1.2 equivalents of $B_2(pin)_2$ in the presence of 3 mol% of $Pt(dba)_3$ as catalyst. To our delight, the alkenyl boronate substrate was fully converted to 1,1,2-tris(boronates) **4.73** with 81% isolated yield (Table 4.1, entry 1). With this result, we discovered an efficient route to access the racemic 1,1,2-tris(boronates) in a catalytic fashion. However, the fact that $Pt(dba)_3$ was able to catalyze the diboration without any phosphine ligand indicated that significant background reaction might diminish the enantioselectivity if chiral phosphine ligand could not bind to the platinum catalyst properly. Employing 3,5-diethylphenyl-TADDOL derivative **4.21** as a chiral ligand, both *E* and *Z* isomers of alkenyl boronate **4.72** were evaluated (Table 4.1, entry 2, 3). While the *E*-isomer of **4.72** afforded the diborated product with good yield and low enantioselection, the *Z*-isomer of **4.72** furnished the opposite enantiomer of the tris(boronate) product with higher enantioselectivity, but lower efficiency. Thus, further optimization was focused on the *Z*-

isomer of alkenyl boronates. Slightly improved selectivity was obtained when the ligand to platinum ratio was increased from 1.2:1 to 2:1 (Table 4.1, entry 3, 5). Next, the steric effect of the TADDOL-derived ligands was investigated (Table 4.1, entry 4 to 8). While utilizing less sterically hindered ligand **4.74** led to almost racemic product, the enantioselectivity was improved by employing more sterically demanding isopropyl- and isobutyl- derived ligands. However, further increasing the steric bulkiness to *tert*-butyl derived ligand lowered the selectivity. On the other hand, although the stereoselectivity was improved by the sterically demanding isobutyl derived ligand **4.75**, the reaction efficiency was remarkably diminished.

Table 4.1. Initial optimization of platinum-catalyzed diboration of alkenyl B(pin) .



entry	*E* or *Z*	(*R*,*R*)-L	R	X (mol%)	Y (mol%)	conv. (%)	Yield (%)	*e.r.*
1	E	--	--	3	--	>98	81	--
2	E	4.21	Et	3	3.6	>98	85	42:58
3	Z	4.21	Et	3	3.6	>98	59	67:33
4	Z	4.74	H	3	6.0	45	33	51:49
5	Z	4.21	Et	3	6.0	>98	56	72:28
6	Z	4.22	*i*-Pr	3	6.0	93	58	87:13
7	Z	4.75	*i*-Bu	3	6.0	50	46	94:6
8	Z	4.76	*t*-Bu	3	6.0	40	31	81:19
9[a]	Z	4.75	*i*-Bu	3	6.0	55	50	94:6
10[a, b]	Z	4.75	*i*-Bu	3	6.0	>98	71	90:10
11[a]	Z	4.75	*i*-Bu	6	9.0	>98	81	91:9

[a] reaction performed for 48 hours. [b] reaction performed at 70 °C.

To further improve the reaction efficiency, other reaction parameters were investigated. Surprisingly, prolonging the reaction time failed to solve the low conversion issue (Table 4.1, entry 9). This observation suggested that the sluggish reactivity might be due to the active catalyst decomposing over the reaction period. Elevating the reaction temperature to 70 °C led to full conversion with slightly diminished selectivity (Table 4.1, entry 10). Additionally, the reaction efficiency could be improved by increasing the platinum catalyst loading: the 1,1,2-tris(boronates) **4.73** was isolated with good yield and enantioselectivity in the presence of 6 mol% of platinum catalyst and 9 mol% of ligand **4.75** at 60 °C (Table 4.1, entry 11).

With the promising result in hand, we were ready to investigate the alkenyl boronate scope for the 1,1,2-tris(boronates) synthesis. Unfortunately, attempts to reproduce the results under optimal conditions afforded the 1,1,2-tris(boronates) **4.73** with low and inconsistent enantioselectivities. We considered that potential isomerization of *Z*-alkenyl boronates to the more thermodynamically stable *E*-isomer over the reaction period might be the origin of the low and inconsistent enantioselectivity. With the assumption that the chiral catalyst would always recognize the same pro-chiral face of alkenyl boronates, *E*-alkenyl boronate would lead to the opposite enantiomer of the product compared to the *Z*-isomer of the substrate. Thus, the overall enantioselectivity would be significantly diminished even if only small amount of the *E*-alkenyl boronate was generated and engaged in the diboration process over the reaction course (Scheme 4.13.A).

To probe our hypothesis, the *Z*-isomer of alkenyl B(pin) **4.72** was subjected to a variety of potential isomerization conditions (Scheme 4.13.B). No isomerization was observed under simple thermal conditions. However, addition of 6 mol% of $Pt(dba)_3$, the

metal catalyst for the diboration, led to significant amount of the isomerized *E*-alkenyl B(pin) after 12 hours at the reaction temperature. Furthermore, ^{1}H-NMR analysis of the crude reaction mixture under standard conditions indicated that the leftover starting material was a mixture of *E*- and *Z*- isomers. With insight into the origin of low and inconsistent selectivity, it was obvious that the undesired isomerization must be either inhibited or outcompeted by desired diboration. In this light, a more reactive diboron reagent, $B_2(cat)_2$, was tested in the platinum-catalyzed diboration reaction (Scheme 4.13.C). Surprisingly, the 1,1,2-tris(boronates) **4.73** was furnished with 62% yield and 11% enantiomeric excess that favored the opposite enantiomer compared to the reaction performed with $B_2(pin)_2$.

Scheme 4.13. Isomerization of Z-alkenyl boronates.

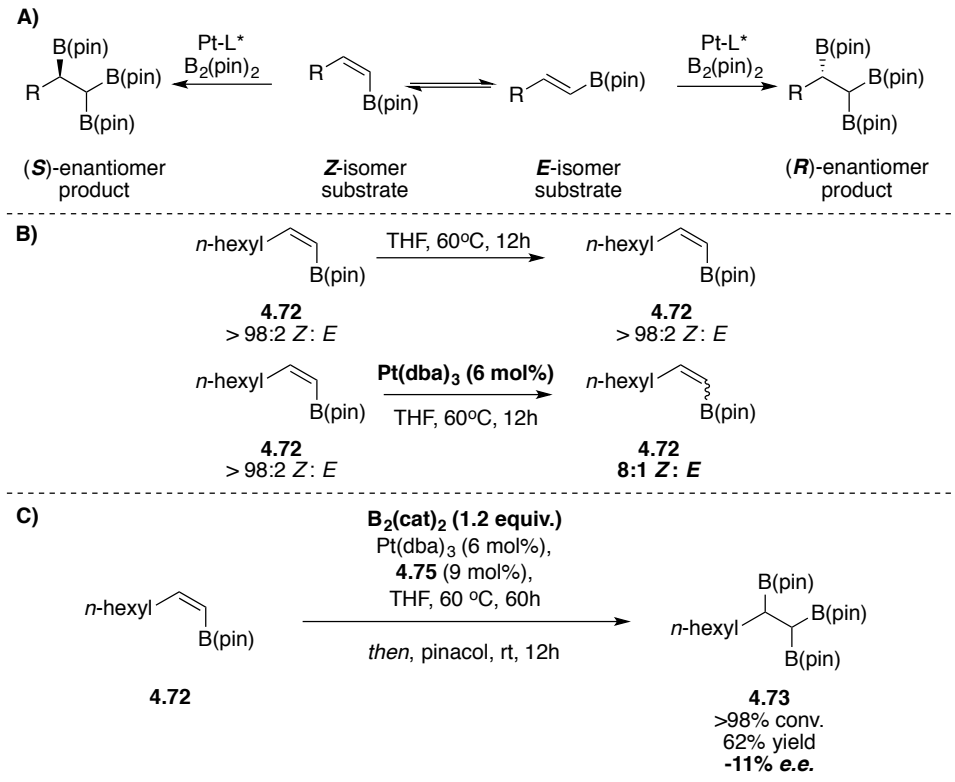
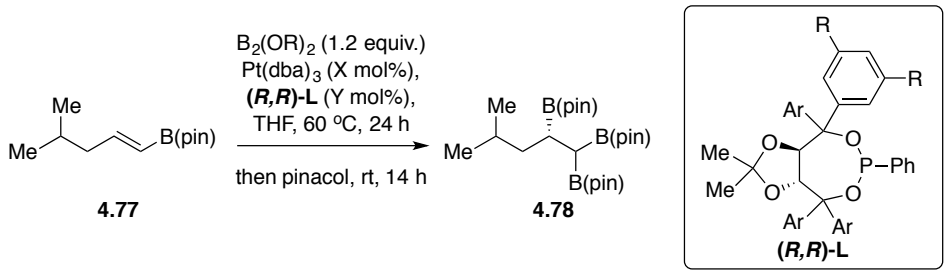


Table 4.2. Optimization of enantioselective diboration for trans-substituted alkenyl boronates.



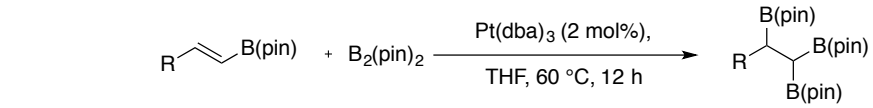
entry	(*R,R*)-L	R	$B_2(OR)_2$	X/Y (mol%)	conv. (%)	Yield (%)	*e.r.*
1	4.75	*i*-Bu	$B_2(pin)_2$	5/10	72	49	68:32
2	4.75	*i*-Bu	$B_2(cat)_2$	5/10	81	50	88:12
3	4.21	Et	$B_2(cat)_2$	5/10	78	43	89:11
4	4.22	*i*-Pr	$B_2(cat)_2$	5/10	80	51	95:5
5[a]	4.76	*t*-Bu	$B_2(cat)_2$	5/10	90	48	94:6
6	4.22	*i*-Pr	$B_2(cat)_2$	6/9	>98	56	94:6
7[b]	4.22	*i*-Pr	$B_2(cat)_2$	3/6	>98	70	92:8

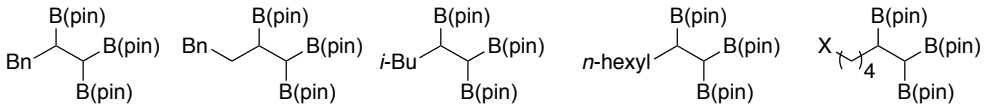
[a] reaction performed for 48 hours. [b] reaction performed at 70 °C with 2 equiv. of $B_2(cat)_2$.

Considering the fact that the reaction between $B_2(cat)_2$ and *Z*-alkenyl boronates favored the same product enantiomer that was favored by the reaction of *E*-alkenyl boronates, the *E*-alkenyl boronates was reevaluated for the diboration with $B_2(cat)_2$. Utilizing the E-alkenyl B(pin) **4.77** as model substrate, it was discovered that $B_2(cat)_2$ furnished the 1,1,2-tris(boronates) **4.78** with remarkably higher enantioselectivity compared to the case where $B_2(pin)_2$ was employed (Table 4.2, entry 1, 2). A brief survey of the steric effect of the ligands identified 3,5-diisopropylphenyl-TADDOL derivative **4.22** as the optimal ligand (Table 4.2, entry 2 to 5). Further optimization of reaction temperature, metal/ligand ratio, and reagent stoichiometry determined the optimal conditions for the platinum-catalyzed asymmetric diboration of alkenyl boronates to be

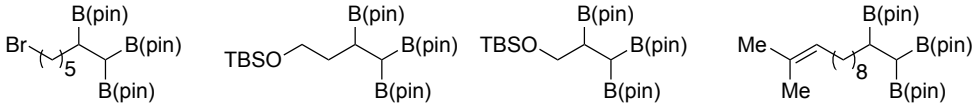
those which employed 3 mol% of $Pt(dba)_3$, 6 mol% of ligand **4.22**, and 2.0 equivalents of $B_2(cat)_2$ at 70 °C for 24 hours. Under such optimal conditions, the 1,1,2-tris(boronates) **4.78** could be furnished with 70% yield and 92:8 *e.r.*.

Scheme 4.14. Scope of racemic synthesis of 1,1,2-tris(boronates) by platinum catalyzed diboration.

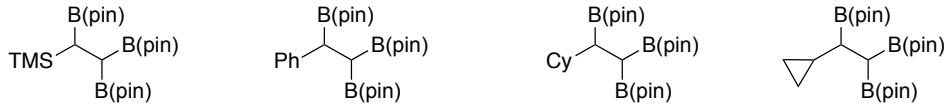




4.79 67% yield | **4.80** 70% yield | **4.78** 71% yield | **4.73** 83% yield[a] | **4.81** X=Cl, 83% yield; **4.82** X=Br, 61% yield



4.83 60% yield | **4.84** 78% yield | **4.85** 81% yield | **4.86** 73% yield



4.87 75% yield | **4.88** 51% yield | **4.89** 48% yield | **4.90** 40% yield

[a] reaction performed on 9.0 mmol scale with 1 mol% of $Pt(dba)_3$ to yield 3.7 g of **4.73**

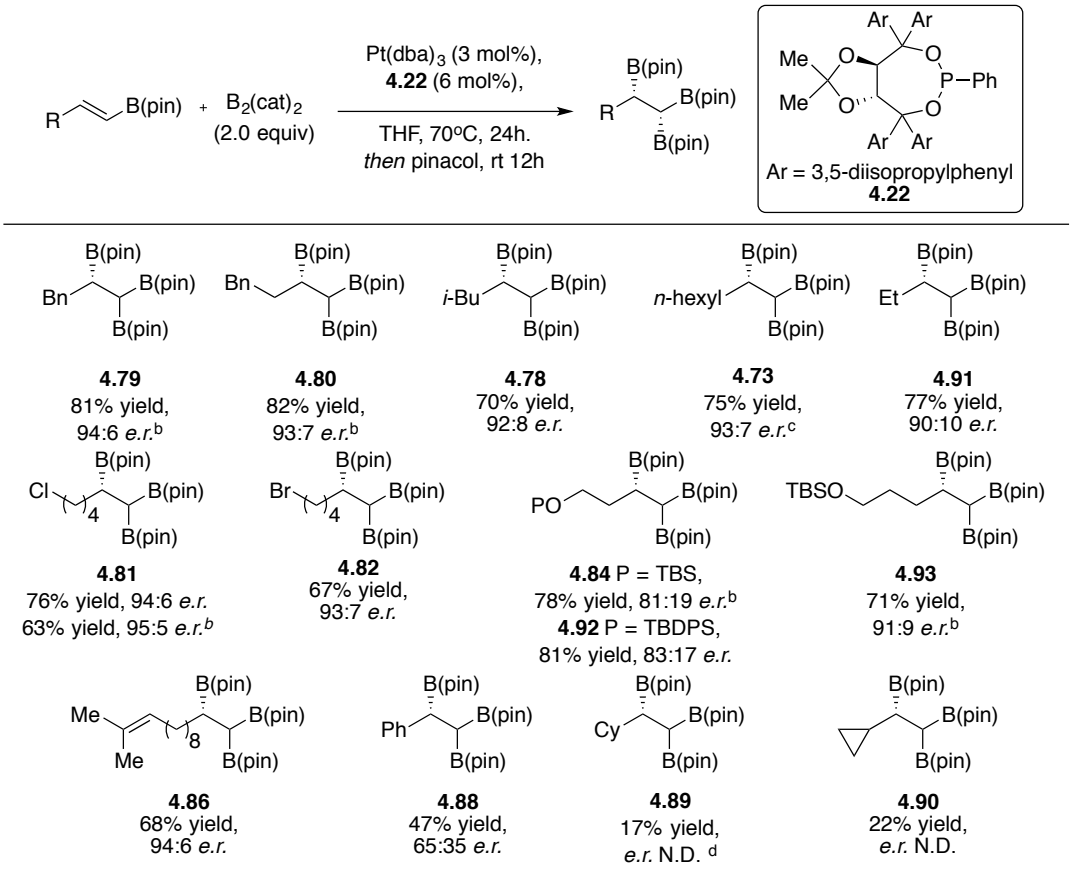
With the optimal conditions in hand, we moved on to explore the substrate scope for the platinum-catalyzed diboration of alkenyl boronates. First, the scope of the racemic synthesis of 1,1,2-tris(boronates) with platinum-catalyzed diboration was investigated. A variety of *E*-alkenyl B(pin) compounds were treated with 1.05 equivalent of $B_2(pin)_2$ in the presence of 2 mol% of $Pt(dba)_3$ catalyst at 60 °C for 12 hours to afford a broad range of 1,1,2-tris(boronates) products with good isolated yields. Notably, this protocol could

be applied on a large-scale synthesis of 1,1,2-tris(boronates) **4.73**: 3.7 gram of diborated product **4.73** was obtained from 9.0 mmol of *E*-alkenyl boronates substrate with only 1 mol% of platinum catalyst. It is worthy of note that alkenyl boronates bearing α-substitution suffered from low conversion in the racemic diboration process. Importantly, this protocol provided a reliable and practical route to access racemic 1,1,2-tris(boronates), which was beneficial towards the further exploration of the synthetic utilities for this novel motif.

To explore the scope of asymmetric synthesis of 1,1,2-tris(boronates) by platinum-catalyzed diboration, a variety of *E*-alkenyl boronates were tested under the optimal conditions (Scheme 4.15). Alkenyl boronates bearing remote aryl groups behaved well in the diboration process to furnish the corresponding tris(boronates) products **4.79** and **4.80** with good yield and enantioselectivity. Alkyl substituted alkenyl boronates could be engaged in the reaction with good level of efficiency and selectivity (**4.73**, **4.78**, **4.91**). Importantly, labile functionalities, such as alkyl halides (**4.81**, **4.82**) and protected alcohols (**4.84**, **4.92**, **4.93**), were well tolerated under the reaction conditions. Additionally, when an alkenyl boronate attached with a remote trisubstituted alkene was subjected to the diboration conditions, the diboration reaction occurred on the boronate-substituted alkene exclusively, while the trisubstituted alkene remained intact (**4.86**). In terms of limitation, poor efficiency and stereoselectivity was observed when a styrenyl boronate was engaged in the platinum-catalyzed diboration conditions. Moreover, alkenyl boronates bearing α-substitution suffered from remarkably diminished reactivity. Of note, the 1,1,2-tris(boronates) constructed by platinum-catalyzed diboration were

sufficiently stable to be purified by silica gel column chromatography, and to be stored under ambient conditions for long periods of time without any significant decomposition.

Scheme 4.15. Scope of asymmetric synthesis of 1,1,2-tris(boronates) by platinum-catalyzed diboration.



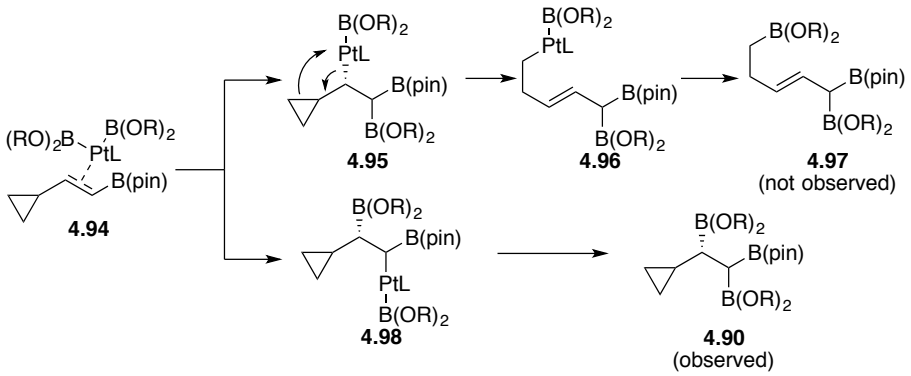
a) Average of 2 or more experiments. Isolated yields are provided. b) Experiment performed with 1.2 equivalents of $B_2(cat)_2$ instead of 2.0 equivalents. c) Reaction run on 1.0 mmol scale with 1.2 equivalents of $B_2(cat)_2$. d) Reaction run at 100 ºC for 24 hours.

Despite the low conversion of 1,1,2-tris(boronate) **4.90**, the observation that cyclopropyl substituted alkenyl B(pin) could participate in the platinum-catalyzed diboration to furnish the desired tris(boronates) product provided important insight into the reaction mechanism. It is known that platinum-catalyzed alkene diboration generally proceeded through an oxidative addition, migratory insertion, and reductive elimination

sequence[18]. As shown in Scheme 4.16, oxidative addition of diboron reagent to the platinum catalyst followed by coordination of the alkenyl boronate substrate to the catalyst furnished the intermediate **4.94**. From here, the migratory insertion of boron to the alkene could proceed with two possible regiochemical outcomes. In one case, the migratory insertion might afford the intermediate **4.95**, with the platinum catalyst located adjacent to the cyclopropyl moiety. It has been documented that this structure would undergo cyclopropyl ring opening to form the intermediate **4.96**.[18] Subsequent reductive elimination would furnish the ring-opened product **4.97**, which was not observed under our reaction conditions. On the other hand, the migratory insertion that placed the platinum catalyst on the α-carbon of boronate moiety would led to the intermediate **4.98**, which could furnish the observed product **4.90** by subsequent reductive elimination. Thus, this experimental result suggested the diboration of alkenyl boronates occurred through an α-boryl alkyl-platinum intermediate that was generated by migratory insertion. Furthermore, such regioselectivity of migratory insertion was also supported by the fact that the carbon-metal bond could be stabilized by α-boryl substitution[19].

[18] Coombs, J. R., Haeffner, F., Kliman, L. T., Morken, J. P. *J. Am. Chem. Soc.* **2013**, 135, 11222.
[19] (a) Nakamyura, M., Hara, K.; Hatakeyama, T., Nakamura, E. *Org. Lett.* **2001**, 3, 3137. (b) Nakamura, M., Hatakeyama, T., Hara, K., Fukudome, H., Nakamura, E. *J. Am. Chem. Soc.* **2004**, 126, 14344. (c) Hatakeyama, T., Nakamura, M., Nakamura, E. *J. Am. Chem. Soc.* **2008**, 130, 15688. (d) Endo, K., Hirokkami, M., Shibata, T. *Synlet*t **2009**, 1331.

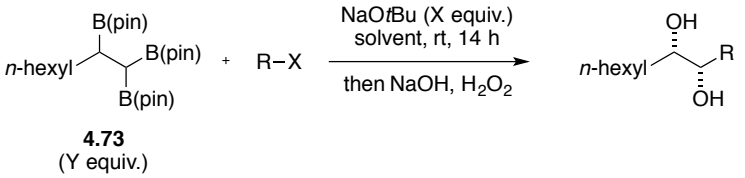
Scheme 4.16. Analysis of migratory insertion step of the platinum catalyzed alkenyl boronates diboration.



4.4. Synthetic utility of enantioenriched 1,1,2-tris(boronates): deborylative alkylation

With a reliable and practical method to access enantioenriched 1,1,2-tris(boronates) in hand, we moved our research focus to the exploration of the potential reactivity of this novel motif. As discussed previously, 1,1,2-tris(boronates) bears both the structural features of vicinal and geminal bis(boronates). The combination of internal chelation of vicinal bis(boronates) and the deborylative alkylation of geminal bis(boronates) might lead to a stereoselective deborylative alkylation of 1,1,2-tris(boronates). If this methodology could be developed, it might provide an alternative route to access enantioenriched internal vicinal bis(boronates) other than the rhodium/Quinap catalyzed asymmetric diboration of internal alkenes. In this light, the conditions for stereoselective deborylative alkylation of 1,1,2-tris(boronates) was investigated.

Table 4.3. Optimization of stereoselective deborylative alkylation of 1,1,2-tris(boronates)



4.73
(Y equiv.)

entry	solvent	NaO*t*Bu (X equiv.)	**4.73** (Y equiv.)	R-X	Yield (conv.) (%)	*d.r.* (syn:anti)
1	THF	4.0	1.3	allyl chloride	93	4.5:1
2	hexane	4.0	1.3	allyl chloride	87	11:1
3	toluene	4.0	1.3	allyl chloride	88	11:1
4	MeCN	4.0	1.3	allyl chloride	<5	N.D
5	pyridine	4.0	1.3	allyl chloride	<5	N.D
6	DMSO	4.0	1.3	allyl chloride	<5	N.D
7	toluene	4.0	1.3	*n*-dodecyl-Br	(82)	>20:1
8	toluene	3.0	1.3	*n*-dodecyl-Br	(72)	>20:1
9	toluene	5.0	1.3	*n*-dodecyl-Br	(92)	20:1
10	toluene	6.0	1.3	*n*-dodecyl-Br	(93)	20:1
11	toluene	5.0	1.5	*n*-dodecyl-Br	93(>98)	18:1
12[a]	toluene	5.0	1.5	*n*-dodecyl-Br	(90)	16:1

[a] KO*t*Bu was employed instead of NaO*t*Bu

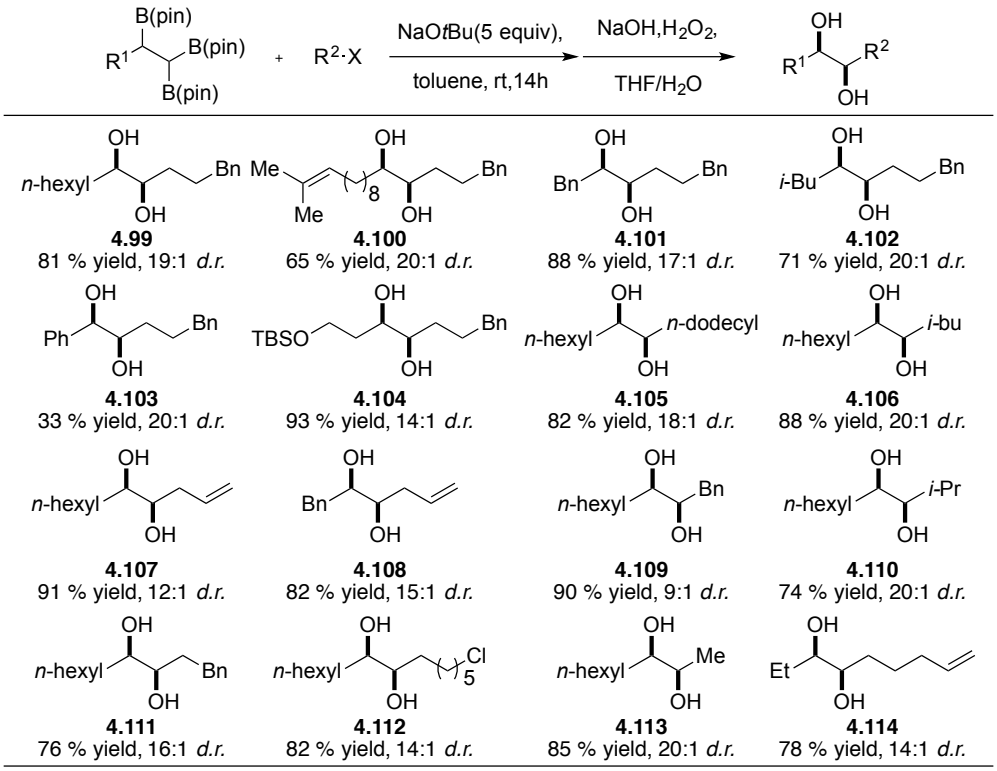
Our initial optimization effort was focused on identifying the optimal solvent for this reaction (Table 4.3, entry 1 to 6). To our delight, employing THF as solvent, the 1,1,2-tris(boronate) **4.73** underwent deborylative alkylation with allyl chloride in the presence of four equivalents of sodium *tert*-butoxide to furnish to desired product with 93% yield and 4.5:1 *d.r.*. The diastereoselectivity was further improved to 11:1 when the reaction was conducted in a non-polar solvent, such as hexane or toluene. On the contrary, utilizing more polar solvents, such as acetonitrile, pyridine, or DMSO, fully inhibited the deborylative alkylation of 1,1,2-tris(boronates). Thus, toluene was identified as the optimal solvent for this reaction. Next, the stoichiometry of reagents was further

optimized. It was found that slightly increasing the equivalents of sodium *tert*-butoxide and tris(boronates) substrate was required to achieve the best conversion (Table 4.3, entry 8 to 11). Furthermore, the diastereoselectivity was slightly diminished when potassium *tert*-butoxide was employed as base instead of sodium *tert*-butoxide. In summary, the optimal conditions for the stereoselective deborylative alkylation of 1,1,2-tris(boronates) was determined to be those which utilized 1.5 equivalents of 1,1,2-tris(boronate), 1.0 equivalent of electrophile, and 5.0 equivalents of sodium *tert*-butoxide in toluene at room temperature for 14 hours. Of note, the *syn*-diastereomer of the deborylative alkylation product was favored in all cases.

With the optimized conditions in hand, the scope for the deborylative alkylation of 1,1,2-tris(boronates) was surveyed (Scheme 4.17). In regard to the scope of 1,1,2-tris(boronates), alkyl substituted tris(boronates) underwent the deborylative alkylation with good yield and diastereoselectivity (**4.99**, **4.101**, **4.102**). Tris(boronates) bearing a protected alcohol (**4.104**) or trisubstituted alkene (**4.100**) functionality were also well tolerated under the reaction conditions. It is worthy of note that low isolated yield was obtained when the benzylic tris(boronates) were employed in the deborylative alkylation (**4.103**). The origin of the low reaction efficiency was due to the competitive substrate decomposition by undesired protodeborylation of the benzylic boronate. In terms of the scope of electrophiles, a broad range of alkyl halides could be engaged in the deborylative alkylation to afford the *syn*-diastereomer of the desired product with high efficiency and selectivity. Importantly, the electrophile scope was not limited to primary halides. The vicinal diols derived from isopropyl bromide and methyl iodide were obtained with good yield and diastereoselection under standard conditions. Of note, when

an electrophile bearing both a primary bromide and chloride was subjected to the deborylative alkylation conditions, the reaction occurred on the primary bromide exclusively. The alkyl chloride remained intact over the reaction course.

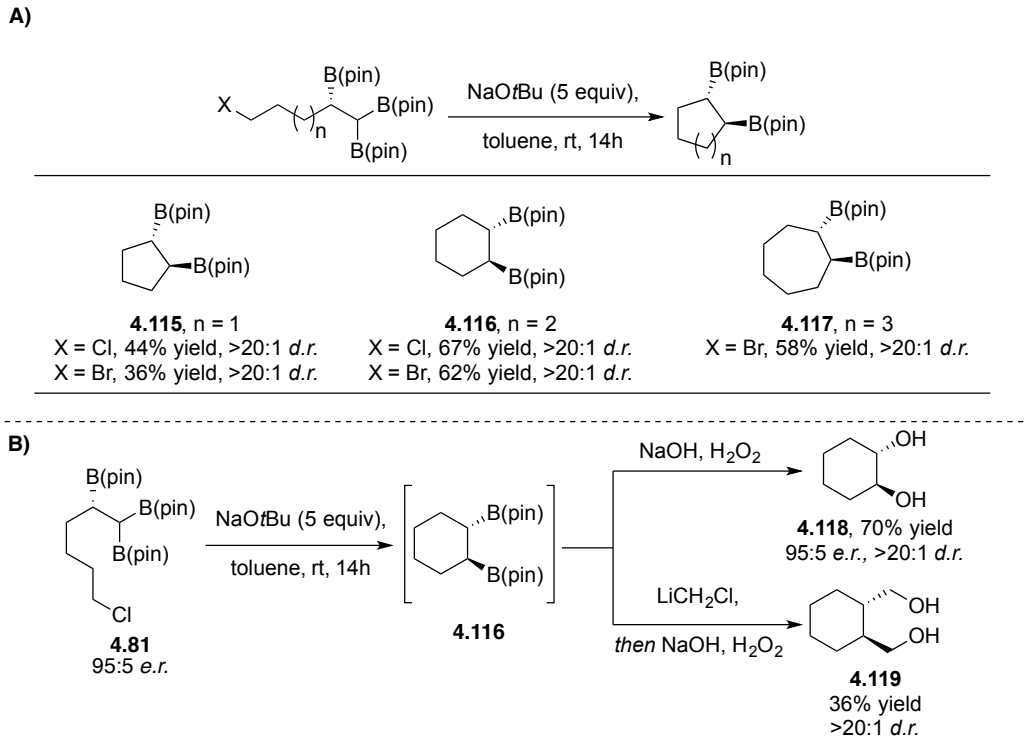
Scheme 4.17. The scope of stereoselective deborylative alkylation of 1,1,2-tris(boronates).



As discussed above, an intermolecular deborylative alkylation between 1,1,2-tris(boronates) and an alkyl halide afforded internal *syn*-bis(boronates) with good yield and stereoselectivity. Alternatively, an intramolecular deborylative cyclization might be developed by subjecting a 1,1,2-tris(boronates) bearing a tethered alkyl halide functionality to the deborylative alkylation conditions in the absence of external electrophile. In this context, a range of 1,1,2-tris(boronates) that contained tethered alkyl

bromide or chloride were tested in the standard deborylative alkylation conditions (Scheme 4.18.A). To our delight, the cyclized products containing five-, six-, and seven membered rings were isolated in moderate yield but excellent diastereoselectivity. Importantly, the resulting cyclic 1,2-bis(boronates) were determined to have an *anti*-relationship. To the best of our knowledge, the platinum-catalyzed asymmetric diboration/deborylative cyclization sequence provided the only route to access cyclic vicinal *anti*-bis(boronates) in a catalytic and enantioselective fashion.

Scheme 4.18. Intramolecular deborylative cyclization and transformations for cyclic anti-bis(boronates).



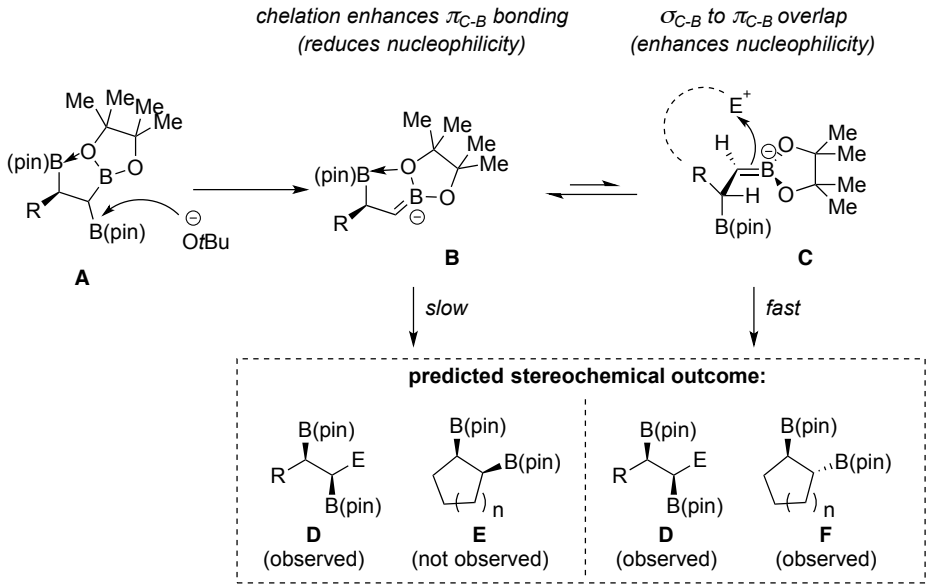
Furthermore, a one-pot deborylative cyclization/oxidation sequence transformed the enantioenriched 1,1,2-tris(boronates) **4.81** to cyclic *anti*-diol **4.118** in 70% yield with excellent level of diastereoselectivity and stereospecificity. Additionally, synthetically

challenging *anti*-1,2-bis(hydroxymethyl)-cyclohexane **4.119** was constructed by a one pot deborylative cyclization/double Matteson homologation/oxidation sequence with moderate yield but excellent stereocontrol (Scheme 4.18.B).

In regards to the mechanism of the deborylative alkylation of 1,1,2-tris(boronates), we propose a stereochemical model that rationalizes the stereochemical outcome in the deborylative alkylation event. The observation that the conditions required for deborylative alkylation of 1,1,2-tris(boronates) were milder than the conditions for geminal bis(boronates) indicated that the Lewis acidity of one of the geminal boronates was enhanced by the chelation between its pinacol oxygen and the internal boronate. Such chelation facilitated the cleavage of the carbon-boron bond by *tert*-butoxide and led to an even more stable α-boryl carbanion **B** compared to the similar moiety derived from geminal bis(boronates). If the α-boryl carbanion **B** was the reactive intermediate, it was reasonable to predict that the electrophile would approach to the α-boryl carbanion **B** from the least-hindered face so that the *syn*-diastereomer **D** would be obtained in the intermolecular case. However, in the intramolecular case, the tethered electrophile would be delivered from the same face as the substitution to furnish the cyclic *syn*-isomer **E**, which was inconsistent to the observed results. On the other hand, the prediction for the reactions through a non-chelated intermediate **C** would be consistent for both inter- and intramolecular reactions. While the bottom face was blocked by the sterically bulky B(pin) group, the electrophile would only be able to approach the carbanion from the top face. Thus, the acyclic *syn*-isomer **D** and cyclic *anti*-isomer **F** would be favored for inter- and intramolecular alkylations respectively. Importantly, in structure **C**, the interaction between the electron-rich carbon-boron σ bond and the adjacent carbon-boron π type

bond (α-boryl carbanion) would enhance the nucleophilicity of the π bond and facilitate the reaction with the electrophile.[20] Overall, the intermediate **B** might be lower energy and occupy the majority of the population compared to intermediate **C**, but the observed stereochemical outcome indicated that the reaction occurred through intermediate **C** due to the much higher reactivity.

Scheme 4.19. Proposed stereochemical model of deborylative alkylation.



4.5. Conclusion

In summary, the first enantioselective synthesis of 1,1,2-tris(boronates) was developed via platinum-catalyzed diboration of alkenyl boronates. Furthermore, the synthetic utility of this novel motif was demonstrated by establishing a diastereoselective deborylative alkylation of 1,1,2-tris(boronates). A broad range of synthetically

[20] Analogous orbital interactions have been claimed to explain the stereoselectivity of reactions of allylsilanes, allylstannanes, and allyl boronates. See: (a) Fleming, I., Lawrence, N. J. *Tetrahedron Lett.* **1988**, 29, 2073. (b) Fleming, I., Lawrence, N. J. *Tetrahedron Lett.* **1988**, 29, 2077. (c) Fleming, I., Lawrence, N. J. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3309. (d) Pelz, N. F., Morken, J. P. *Org. Lett.* **2006**, 8, 4557. (e) Kyne, R. E., Ryan, M. C., Kliman, L. T., Morken, J. P. *Org. Lett.* **2010**, 12, 3796.

challenging 1,2-bis(boronates) could be readily accessed via a platinum-catalyzed diboration/deborylative alkylation sequence in an efficient and stereoselective fashion. Future studies should focus on exploring more transformations for 1,1,2-tris(boronates) other than deborylative alkylation.

4.6. Experimental Section

4.6.1. General Information

^{1}H NMR spectra were measured using a Varian Gemini-500 (500 MHz) spectrometer or a 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, pent= pentet, sept = septet, br = broad, m = multiplet), and coupling constants (Hz). $^{13}C\{^{1}H\}$NMR spectra were measured using a Varian Inova 500 (126 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.0 ppm). $^{31}P\{^{1}H\}$NMR spectra were measured using a Varian Inova 500 (202 MHz) spectrometer. Chemical shifts are reported in ppm using phosphoric acid as the external standard (H_3PO_4: 0.0 ppm). Infrared (IR) spectra were measured using a Bruker a-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). High-resolution mass spectrometry (HRMS) was performed at the chemistry department at 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 was performed on 25 mm silica gel glass backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), phosphomolybdic acid (PMA), potassium permanganate ($KMnO_4$), and Seebach's "magic" stain [21] (phosphomolybdic acid, $Ce(SO_4)_2$, sulfuric acid). Analytical chiral gas-liquid

[21]Seebach, D. *Helv. Chim. Acta.* **1987**, 70, 448

chromatography (GLC) was also performed on an Agilent Technologies 6850 Series chromatograph with a flame ionization detector, and a Supelco β –Dex 120 column with helium as the carrier gas. Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. Analytical chiral supercritical fluid chromatography (SFC) was performed on a Thar Supercritical Fluid Chromatograph equipped with auto sampler and a Waters photodiode array detector with methanol as the modifier.

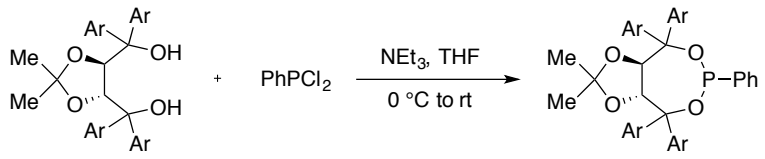
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran, dichloromethane, toluene, and diethyl ether were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after being purged with argon. Dimethylformamide was dispensed from a Glass Contour Solvent Purification System (SG Water, USA LLC). Triethylamine was purchased from Aldrich and refluxed over calcium hydride prior to use. Schwartz's reagent, phenyldichlorophosphine, and sodium *tert*-butoxide were purchased from Strem Chemicals and used as received. 3-Phenyl-1-propyne, imidazole, ethynylcyclohexane, and 1-bromo-2-methylpropane purchased from Alfa Aesar and used as received. $B_2(pin)_2$ was obtained from AllyChem and recrystallized from pentane prior to use. Dibenzylideneacetone and 1-bromo-6-chlorohexane were purchased from Oakwood and used as received. *tert*-Butylchlorodiphenylsilane was purchased from Gelest and used as received. Pinacol borane was purchased from BASF and distilled prior to use. 5-Chloro-1-pentyne was purchased from Chemsampco and used as received. Iodomethane was purchased from Acros and used as received. All other reagents were obtained from Aldrich or Fisher and used as received.

4.6.2. Experimental Procedures

4.6.2.1. Preparation of $Pt(dba)_3$ and phosphonite ligands

Tris(dibenzylideneacetone)platinum(0) was prepared according to the literature procedure.[22] All spectral data and elemental analysis were in accordance with the literature.

Ligands **4.21**[23], **4.22**[24], 4.75[22], and **4.76**[25] were prepared according to the general reaction scheme shown below. All spectral data were in accordance with the literature.

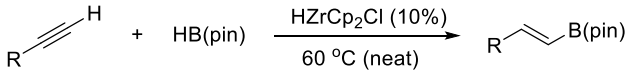


(*R, R*)-**4.21** Ar = 3,5-diethylphenyl
(*R, R*)-**4.22** Ar = 3,5-diisopropylphenyl
(*R, R*)-**4.75** Ar = 3,5-diisobutylphenyl
(*R, R*)-**4.76** Ar = 3,5-di*t*butylphenyl

4.6.2.2. Representative procedure for preparation of trans-vinyl(boronates)

Unless otherwise noted, vinyl boronate starting materials were prepared according to the general method shown below.

General procedure for vinyl(boronate) synthesis

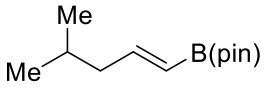


[22] Coombs, J.R., Haeffner, F., Kliman, L.T., Morken, J.P. *J. Am. Chem. Soc.* **2013**, 135, 11222.
[23] Kliman, L.T., Mlynarski, S.N., Ferris, G.E., Morken, J.P. *Angew. Chem. Int. Ed.* **2012**, 51, 521.
[24] Kliman,L.T., Mlynarski, S.N., Morken, J.P. *J. Am. Chem. Soc.* **2009**, 131, 13210.
[25] Burks, H.E., Kliman, L.T., Morken, J.P. *J. Am. Chem. Soc.* **2009**, 131, 9134.

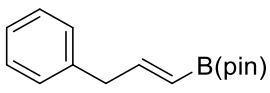
To an oven-dried 2-dram vial equipped with magnetic stir bar in the glovebox was added alkyne (1.10 equiv.) and pinacol borane (1.00 equiv.), followed immediately by Schwartz's reagent (0.10 equiv.). The vial was sealed with a polypropylene cap, taped, and removed from the glovebox. The mixture was heated in an oil bath to 60 °C for 14 hours, at which point it was cooled to room temperature. The pure vinyl(boronate) products were isolated after SiO_2 gel chromatography, unless otherwise noted.

4.6.2.3. Preparation of alkenyl boronate starting materials

The following starting materials were purchased from Aldrich and used without further purification: (*E*)-1-octen-1-ylboronic acid pinacol ester, (*E*)-4-(*tert*-butyldimethylsiloxy)-1-buten-1-ylboronic acid pinacol ester, (*E*)-6-chloro-1-hexen-1-ylboronic acid pinacol ester, (*E*)-2-cyclopropylvinylboronic acid pinacol ester, and (*E*)-2-phenylvinylboronic acid pinacol ester.



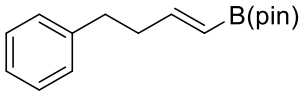
(*E*)-4,4,5,5-tetramethyl-2-(4-methylpent-1-en-1-yl)-1,3,2-dioxaboro-lane (4.77). Prepared according to the general procedure utilizing pinacolborane (1.28 g, 10.0 mmol), Schwartz' reagent (258 mg, 1.00 mmol), and 4-methylpent-1-yne (904 mg, 11.0 mmol). The crude material was purified (SiO_2, 3% ethyl acetate in hexane) to give the desired product as a clear, colorless oil (1.74 g, 83%). All spectral data are in accordance with the literature.[26]



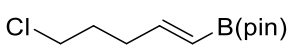
(*E*)-4,4,5,5-tetramethyl-2-(3-phenylprop-1-en-1-yl)-1,3,2-dioxaboro-lane (S1). Prepared according to the general procedure utilizing pinacolborane (1.28 g, 10.0 mmol), Schwartz' reagent (258 mg, 1.00 mmol), and 3-phenyl-1-propyne (1.28 g, 11.0 mmol). The crude material was purified

[26] Yoshida, H., Kageyuki, I., Takaki, K. *Org. Lett.* **2014**, 16, 3512.

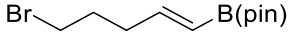
(SiO_2, 3% ethyl acetate in hexane) to give the desired product as a clear, colorless oil (1.94 g, 79%). All spectral data are in accordance with the literature.[27]



(*E*)-4,4,5,5-tetramethyl-2-(4-phenylbut-1-en-1-yl)-1,3,2-dioxaboro-lane (S2). Prepared according to the general procedure utilizing pinacolborane (1.28 g, 10.0 mmol), Schwartz' reagent (258 mg, 1.00 mmol), and 4-phenyl-1-butyne (1.56 g, 12.0 mmol). The crude material was purified (SiO_2, 3% ethyl acetate in hexane) to give the desired product as a clear, colorless oil (2.07 g, 80%). All spectral data are in accordance with the literature.



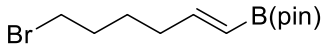
(*E*)-2-(5-chloropent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaboro-lane (S3). Prepared according to the general procedure utilizing pinacolborane (1.28 g, 10.0 mmol), Schwartz' reagent (258 mg, 1.00 mmol), and 5-chloropent-1-yne (1.13 g, 11.0 mmol). The crude material was purified (SiO_2, 3% ethyl acetate in hexane) to give the desired product as a white solid (1.87 g, 81%). All spectral data are in accordance with the literature.



(*E*)-2-(5-bromopent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaboro-lane (S4). To a solution of pent-4-yn-1-ol (1.26 g, 15.0 mmol) in dry dichloromethane (20 mL) were added the tetrabromomethane (7.46 g, 22.5 mmol) and the triphenylphosphine (5.90 g, 22.5 mmol). The mixture was stirred at room temperature for 1 hour. The reaction mixture was directly distilled under vacuum to afford the 5-

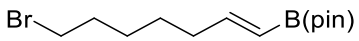
[27] Shimizu, H.; Igasrashi, T.; Miura, T.; Murakami, M. *Angew. Chem. Int. Ed.* **2011**, 50, 11465.

bromopent-1-yne as clear, colorless oil (2.05 g, 93%), which was used in the subsequent step without further purification. Next, (*E*)-2-(5-bromopent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane was prepared according to the general procedure utilizing pinacolborane (1.28 g, 10.0 mmol), Schwartz' reagent (258 mg, 1.00 mmol), and 5-bromopent-1-yne (1.62 g, 11.0 mmol). The crude material was purified (SiO_2, 3% ethyl acetate in hexane) to give the desired product as a white solid (1.32 g, 48%). ^1H NMR (500 MHz, $CDCl_3$): δ 6.55 (1H, dt, *J*=18.0, 6.5 Hz), 5.47 (1H, d, *J*=17.5 Hz), 3.38 (2H, t, *J*=7.0 Hz), 2.29 (2H, q, *J*=7.0 Hz), 1.96 (2H, pent, *J*= 7.0 Hz), 1.24 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ152.1, 83.3, 34.2, 33.3, 31.3, 24.9; IR (neat): 2911.4 (m), 1638.1 (m), 1397.6 (m), 1361.5 (s), 1320.1 (s), 1217.1 (s), 1002.0 (m), 969.4 (m), 849.1 (m); HRMS-(DART+) for $C_{10}H_{21}B_1Br_1O_2$ $[M+H]^+$: calculated: 275.0818, found: 275.0819.



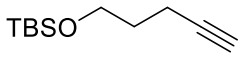
(*E*)-2-(6-bromohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxabor-olane (S5). To a solution of hex-5-yn-1-ol (1.47 g, 15.0 mmol) in dry dichloromethane (20 mL) were added the tetrabromomethane (7.46 g, 22.5 mmol) and the triphenylphosphine (5.90 g, 22.5 mmol). The mixture was stirred at room temperature for 1 hour. The reaction mixture was directly distilled under vacuum to afford the 6-bromohex-1-yne as clear, colorless oil (2.39 g, 99%), which was used in the subsequent step without further purification. Next, (*E*)-2-(6-bromohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane was prepared according to the general procedure utilizing pinacolborane (1.92 g, 15.0 mmol), Schwartz' reagent (387 mg, 1.50 mmol), and 6-bromohex-1-yne (2.66 g, 16.5 mmol). The crude material was purified (SiO_2, 3% ethyl

acetate in hexane) to give the desired product as a white solid (2.17 g, 50%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.58 (1H, dt, *J*= 17.5, 7.0 Hz), 5.43 (1H, d, *J*= 17.5 Hz), 3.38 (2H, t, *J*= 7.0 Hz), 2.16 (2H, q, *J*= 7.5 Hz), 1.85(2H, pent, *J*= 7.0 Hz), 1.56 (2H, pent, *J*= 7.0 Hz), 1.24 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.6, 83.3, 34.7, 33.6, 32.1, 26.7, 24.7; IR (neat):2977.5 (m), 2933.9 (m), 1638.1 (s), 1359.5 (s), 1318.5 (s), 1164.4 (s), 994.8 (m), 969.5 (m), 848.8 (m); HRMS-(DART+) for $C_{12}H_{23}B_1Br_1O_2$ $[M+H]^+$: calculated: 289.09745, found: 289.0980.

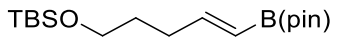


(*E*)-2-(7-bromohept-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dio-xaborolane (S6). To a solution of hept-6-yn-1-ol (1.68 g, 15.0 mmol) in dry dichloromethane (20 mL) were added the tetrabromomethane (7.46 g, 22.5 mmol) and the triphenylphosphine (5.90 g, 22.5 mmol). The mixture was stirred at room temperature for 1 hour. The solvent was removed under reduced pressure. A solution of hexane/ethyl acetate (9:1) was added and the resulting precipitate was filtered and washed abundantly. The filtrate was evaporated and the crude material was purified by silica gel chromatography (SiO_2, 100% hexane) to give 7-bromohept-1-yne as a clear, colorless oil (2.18 g, 83%), which was used in the subsequent step without further purification. Next, (*E*)-2-(7-bromohept-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane was prepared according to the general procedure utilizing pinacolborane (1.08 g, 8.47 mmol), Schwartz's reagent (218 mg, 0.847 mmol), and 7-bromohept-1-yne (1.63 g, 9.32 mmol). The crude material was purified (SiO_2, 3% ethyl acetate in hexane) to give the desired product as a clear, colorless oil (1.85 g, 72%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.59 (1H, dt, *J*= 17.5, 6.5 Hz), 5.41 (1H, d, *J*= 17.5 Hz), 3.37 (2H, t, *J*= 6.5 Hz), 2.14 (2H, q, *J*= 7.0

Hz), 1.83 (2H, pent, *J*= 7.0 Hz), 1.44-1.41 (4H, m), 1.24 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.2, 83.2, 35.7, 33.9, 32.8, 27.9, 27.5, 25.0; IR (neat): 2977.9 (m), 2931.6 (m), 1638.3 (s), 1361.3 (s), 1318.9 (s), 1144.6 (s), 997.2 (m), 970.5 (m), 849.4 (m); HRMS-(DART+) for $C_{13}H_{25}B_1Br_1O_2$ $[M+H]^+$: calculated: 303.1131, found: 303.1134.



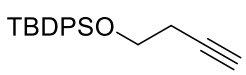
***tert*-butyldimethyl(pent-4-yn-1-yloxy)silane (S7).** To an oven-dried 100 mL round-bottomed flask was added imidazole (4.41 g, 64.2 mmol) followed by CH_2Cl_2 (9.0 mL). To the flask was added pent-4-yn-1-ol (2.21 mL, 23.8 mmol) and the reaction mixture was allowed to stir at room temperature for 5 minutes. To the flask was added *tert*-butyldimethylsilyl chloride (4.96 g, 35.7 mmol) in one portion. The flask wash flushed with nitrogen and the reaction mixture was allowed to stir at room temperature for 18 hours, at which point the mixture was diluted with deionized H_2O (20 mL) and CH_2Cl_2 (20 mL). The crude mixture was extracted with CH_2Cl_2 (3x20 mL), and the organics were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was purified (SiO_2, 3% ethyl acetate in hexane) to give the desired product as a clear, colorless oil (3.54 g, 75%). All spectral data are in accordance with the literature.[28]



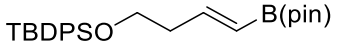
(*E*)-*tert*-butyldimethyl((5-(4,4,5,5-tetramethyl-1,3,2-dioxaboro-lan-2-yl)pent-4-en-1-yl)oxy)silane (S8). Prepared according to the general procedure utilizing pinacolborane (640 mg, 5.00 mmol), Schwartz' reagent (129 mg, 0.500 mmol), and *tert*-butyldimethyl(pent-4-yn-1-yloxy)silane (1.09 g, 5.50 mmol). The

[28] Kleinbeck, F.; Toste, F.D. *J. Am. Chem. Soc.* **2009**, 131, 9178.

crude material was purified (SiO_2, 3% ethyl acetate in hexane) to give the desired product as a clear, colorless oil (1.32 g, 81%). All spectral data are in accordance with the literature.[29]



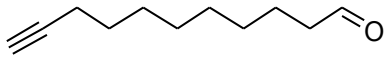
(but-3-yn-1-yloxy)(*tert*-butyl)diphenylsilane (S9). To an oven-dried 100 mL round-bottomed flask was added imidazole (1.09 g, 16.0 mmol) followed by CH_2Cl_2 (20.0 mL). To the flask was added but-3-yn-1-ol (0.610 mL, 8.06 mmol) and the reaction mixture was allowed to stir at room temperature for 5 minutes. To the flask was added *tert*-butyl(chloro)diphenylsilane (2.31 mL, 8.88 mmol) in one portion. The flask wash flushed with nitrogen and the reaction mixture was allowed to stir at room temperature for 18 hours, at which point the mixture was diluted with deionized H_2O (20 mL) and CH_2Cl_2 (20 mL). The crude mixture was extracted with CH_2Cl_2 (3x20 mL), and the organics were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was purified (SiO_2, 3% ethyl acetate in hexane) to give the desired product as a clear, colorless oil (2.28 g, 92%). All spectral data are in accordance with the literature.[30]



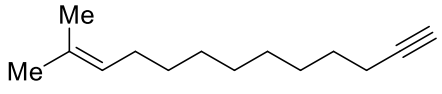
(*E*)-*tert*-butyldiphenyl((4-(4,4,5,5-tetramethyl-1,3,2-dioxaboro-lan-2-yl)but-3-en-1-yl)oxy)silane (S10). Prepared according to the general procedure utilizing pinacolborane (640 mg, 5.00 mmol), Schwartz' reagent (129 mg, 0.500 mmol), and (but-3-yn-1-yloxy)(*tert*-butyl)diphenylsilane (1.70 g, 5.50 mmol). The

[29] Varseev, G.N.; Maier, M.E. *Angew. Chem. Int. Ed.* **2006**, 45, 4767.
[30] Greshock, T.J.; Johns, D.M.; Noguchi, Y.; Williams, R.M. *Org. Lett.* **2008**, 10, 613.

crude material was purified (SiO_2, 2.5% ethyl acetate in hexane) to give the desired product as a clear, colorless oil (1.98 g, 91%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (4H, d, *J*= 6.5 Hz), 7.44-7.36 (6H, m), 6.60 (1H, dt, *J*= 18.0, 7.0 Hz), 5.49 (1H, d, *J*= 18.0 Hz), 3.74 (2H, t, *J*= 7.0 Hz), 2.44 (2H, q, *J*= 7.0 Hz), 1.26 (12H, s), 1.05 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$): δ 150.6, 135.6, 133.9, 129.5, 127.6, 83.0, 62.9, 39.2, 26.8, 24.7, 19.2; IR (neat): 2976.6 (w), 2930.8 (w), 2857.8 (w), 1639.1 (m), 1472.0 (w), 1388.7 (s), 1359.1 (s), 1144.1 (s), 1107.6 (s), 996.3 (m), 849.3 (m), 822.6 (m), 737.6 (s), 612.8 (m), 504.3 (s) cm^{-1}; HRMS-(DART) for: $C_{26}H_{38}BO_3Si$ $[M+H]^+$: calculated: 437.2683, found: 437.2696.

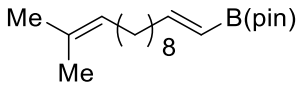


undec-10-ynal (S11). A 50-mL flame-dried round-bottomed flask was charged with a solution of Dess-Martin periodinane (6.36 g) in 20 mL of dichloromethane and then cooled in an ice bath. To the reaction vessel was added undec-10-yn-1-ol (2.87 mL, 15.0 mmol), dropwise over 1 min. The reaction was allowed to stir for 5 min at 0 ^oC, at which point the reaction vessel was allowed to stir for an additionally 3 hours at room temperature. The reaction mixture was washed with saturated $NaHCO_3$, and concentrated under vacuum. The crude was purified by silica gel chromatography (3% ethyl acetate in hexane) to give the desired product as a clear, colorless oil (1.98 g, 80%). All spectral data are in accordance with the literature.



12-methyltridec-11-en-1-yne (S12). A solution of *n*-butyllithium in hexanes (2.48 M, 5.40 mL, 13.4 mmol, 2.0 equiv) was added dropwise via syringe to a stirred suspension of 2-

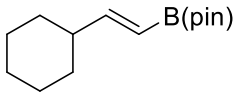
propyltriphenylphosphonium bromide (5.16 g, 13.4 mmol) in tetrahydrofuran (40 mL) at –78 °C. After completion of the addition, the cooling bath was removed and the reaction vessel was placed in an ice bath. The mixture was allowed to stir for 1 hour at 0 °C. The dark red solution that formed was cooled to –78 °C and undec-10-ynal (1.12 g, 6.70 mmol) was added dropwise via syringe over 5 minutes. The reaction mixture was stirred for 1 hour at –78 °C, at which point the vessel was placed in an ice bath. The mixture was allowed to stir for an additional 2 hours at 0 °C. The product mixture was diluted sequentially with saturated ammonium chloride solution (10 mL) and water (30 mL). The diluted product mixture was transferred to a separatory funnel and extracted with ether (3x40 mL). The organic layers were combined and the combined layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The residue obtained was purified by silica gel chromatography (100% hexanes) to afford the desired product as a clear, colorless oil (847.5 mg, 66%). All spectral data are in accordance with the literature.[31]



(*E*)-4,4,5,5-tetramethyl-2-(12-methyltrideca-1,11-dien-1-yl)-1,3,2-dioxaborolane (S13). Prepared according to the general procedure utilizing pinacolborane (640 mg, 5.00 mmol), Schwartz' reagent (129 mg, 0.500 mmol), and 12-methyltridec-11-en-1-yne (1.70 g, 5.50 mmol). The crude material was purified (SiO_2, 2.5% ethyl acetate in hexane) to give the desired product as a clear, colorless oil (1.37 g, 86%). All spectral data are in accordance with the literature. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.61 (1H, dt, *J*= 18.0, 6.5 Hz), 5.40 (1H, d, *J*= 17.5 Hz), 5.10

[31] Li, L., Herzon, S.B. *J. Am. Chem. Soc.* **2012**, 134, 17376.

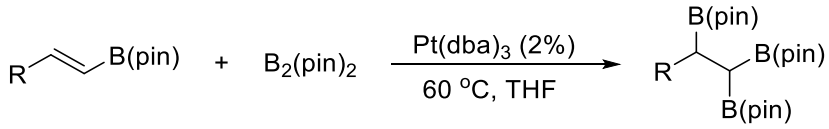
(1H, tt, *J*= 6.0, 1.5 Hz), 2.11 (2H, q, *J*= 7.0 Hz), 1.93 (2H, q, *J*=6.5 Hz), 1.66 (3H, s), 1.57 (3H, s), 1.40-1.36 (2H, m), 1.24-1.22 (22H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.8, 131.1, 124.9, 82.9, 35.8, 29.8, 29.5, 29.3, 29.2, 28.2, 28.0, 25.7, 24.8, 24.7, 17.6; IR (neat): 2977.3 (m), 2923.8 (m), 2853.7 (m), 1637.9 (m), 1360.3.5 (s), 1317.2 (s), 1144.6 (s), 970.6 (m), 849.4 (m); HRMS-(DART+) for $C_{20}H_{38}B_1O_2$ $[M+H]^+$: calculated: 321.2965, found: 321.2961.



(*E*)-2-(2-cyclohexylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (S14). Prepared according to the general procedure utilizing pinacolborane (1.28 g, 10.0 mmol), Schwartz' reagent (258 mg, 1.00 mmol), and ethynylcyclohexane (1.19 g, 11.0 mmol). The crude material was purified (SiO_2, 3% ethyl acetate in hexane) to give the desired product as a white solid (2.00 g, 85%). All spectral data are in accordance with the literature.

4.6.2.4. Representative procedure for Pt-catalyzed vinyl(boronate) diboration

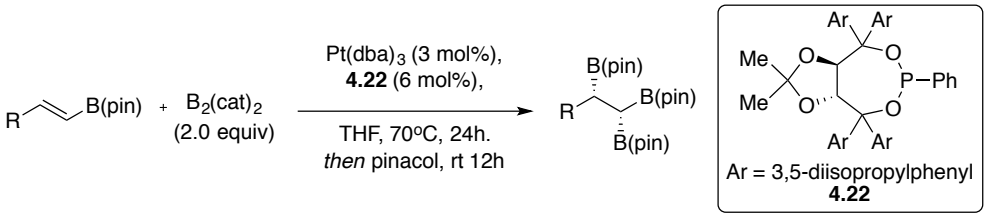
General procedure for racemic Pt-catalyzed vinyl(boronate) diboration



To an oven-dried 6-dram scintillation vial equipped with a magnetic stirbar in the glovebox was added $Pt(dba)_3$ (0.02 equiv.) and $B_2(pin)_2$ (1.05 equiv.), followed by THF (1.0 M in vinyl(boronate)). The mixture was allowed to stir at room temperature for 2

minutes, at which point the vinyl(boronate) (1.00 equiv.) was added all at once. The vial was sealed with a polypropylene cap, taped, brought outside of the glovebox, and heated in an oil bath at 60 °C for 13 hours. The resulting mixture was cooled to room temperature and concentrated under reduced pressure to give the crude material, which was subsequently purified using SiO_2 gel column chromatography.

General procedure for asymmetric Pt-catalyzed vinyl(boronate) diboration

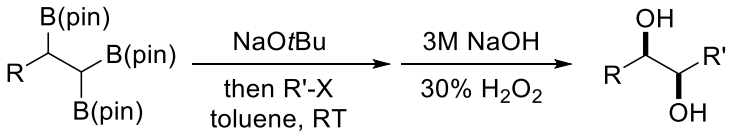


To an oven-dried 2-dram vial equipped with a magnetic stirbar in the glovebox was added $Pt(dba)_3$ (0.03 equiv.), **(*R,R*)-4.22** (0.06 equiv.), and $B_2(cat)_2$ (1.20 *or* 2.00 equiv.), followed by THF (1.0 M in vinyl(boronate)). The vial was sealed with a polypropylene cap, taped, brought outside of the glovebox, and heated to 80 °C for 25 minutes (**Caution:** While we have not experienced any explosions, this reaction involves heating of a closed system, and therefore appropriate safety measures should be followed) . Over this period, the mixture turned from a deep purple solution to a pale yellow solution. The mixture was cooled to room temperature and brought into the glovebox, at which point the vinyl(boronate) (1.00 equiv.) was added all at once. The vial was sealed with a polypropylene, taped, brought outside of the glovebox, and heated to 60 °C for 24 hours. The resulting mixture was cooled to room temperature and brought back into the glovebox, at which point pinacol (7.2 equiv.) was added all at once. The vial was sealed,

taped, brought out of the glovebox, and allowed to stir at room temperature for 14 hours. The resulting mixture was cooled to room temperature, concentrated under reduced pressure, and subsequently purified via SiO_2 gel column chromatography to provide the pure diboration products (**Note:** All tris(boronates) tested are adequately stable to SiO_2 gel column chromatography with minimal degradation observed).

4.6.2.5. Representative procedure for deborylative alkylation of 1,1,2-tris(boronate)esters

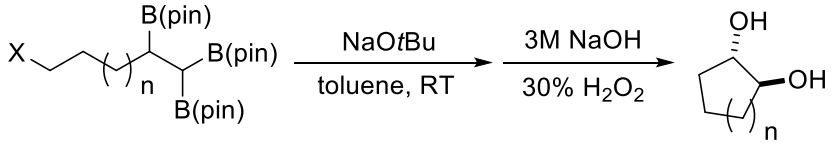
General procedure for deborylative alkylation/oxidation of 1,1,2-tris(boronate)esters



To an oven-dried 2-dram vial equipped with a magnetic stirbar in the glovebox was added 1,1,2-tris(boronate) (1.50 equiv.) and NaO*t*Bu (5.0 equiv.), followed by toluene (0.22 M in tris(boronate)). The mixture was allowed to stir at room temperature for 3-5 minutes, at which point alkyl halide (1.00 equiv.) was added dropwise. The reaction vessel was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at room temperature for 14-18 hours. The reaction mixture was then transferred to a 6-dram vial and diluted with THF (2 mL). The crude mixture was cooled to 0 $^{\circ}$C and 3M NaOH (1.5 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 $^{\circ}$C and saturated aq. $Na_2S_2O_3$ (1.5 mL) was added dropwise. The reaction mixture was

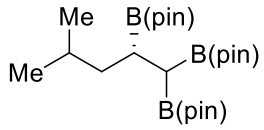
allowed to warm to room temperature and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The pure diol products were isolated after SiO_2 chromatography, unless otherwise noted.

General procedure for deborylative cyclization/oxidation of 1,1,2-tris(boronate)esters



To an oven-dried 2-dram vial equipped with a magnetic stirbar in the glovebox was added 1,1,2-tris(boronate) (1.00 equiv.) and NaO*t*Bu (5.0 equiv.), followed by toluene (0.22 M in tris(boronate)). The reaction vessel was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at room temperature for 14-18 hours. The reaction mixture was then transferred to a 6-dram vial and diluted with THF (2 mL). The crude mixture was cooled to 0 °C and 3M NaOH (1.5 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. $Na_2S_2O_3$ (1.5 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 pure diol products were isolated after SiO_2 chromatography, unless otherwise noted.

4.6.2.6. Full characterization and proof of stereochemistry of 1,1,2-tris(boronate)esters



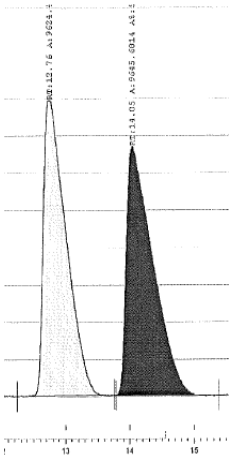
(*R*)-2,2',2''-(4-methylpentane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (4.78). Prepared according to the general procedure utilizing $Pt(dba)_3$ (8.1 mg, 0.0090 mmol), **(*R,R*)-4.22** (16.4 mg, 0.0180 mmol), methylpent-1-en-1-yl)-1,3,2-dioxaboro-lane (63.1 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (425.3 mg, 3.600 mmol). The crude material was purified (SiO_2, 5% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (96.1 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.57-1.53 (1H, m), 1.42-1.31 (2H, m), 1.20-1.12 (37 H, m), 0.84 (3H, d, *J*= 6.0 Hz), 0.81 (3H, d, *J*= 6.5 Hz), 0.78 (1H, d, *J*= 9.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 82.9, 82.8, 82.8, 43.2, 27.2, 25.2, 25.2, 25.0, 24.9, 24.8, 24.8, 23.7, 22.6; IR (neat): 2976.3 (m), 2952.2 (m), 1378.8 (m), 1369.8 (m), 1344.7 (s), 1307.1 (s), 1165.4 (s), 968.6 (m), 848.4 (m) cm^{-1}; HRMS-(DART) for: $C_{24}H_{48}B_3O_6$ $[M+H]^+$: calculated: 465.3730, found: 465.3726. $[\alpha]_D^{20}$ = -12.351 (*c* = 0.340, $CHCl_3$, *l* = 50 mm).

Analysis of stereochemistry:

Racemic compound was prepared according to the general procedure for racemic vinyl boronate diboration utilizing (*E*)-4,4,5,5-tetramethyl-2-(4-methylpent-1-en-1-yl) -1,3,2-dioxaborolane and $Pt(dba)_3$ as the catalyst. The title compound was subjected to the general procedure for deborylative alkylation with (3-bromopropyl)benzene followed by oxidation to give (4*S*,5*S*)-7-methyl-1- phenyloctane-4,5-diol. Further analysis of stereochemistry was performed on (4*S*,5*S*)-7-methyl-1-phenyloctane-4,5-diol. Absolute stereochemistry was assigned by analogy (see product **4.81 and 4.82)**.

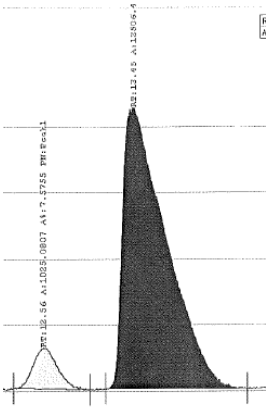
Chiral SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (4S,5S)-7-methyl-1-phenyloctane-4,5-diol

Racemic Material

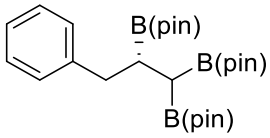


Peak No	% Area	Area	RT (min)
1	49.9449	9624.4423	12.76
2	50.0551	9645.6814	14.05
Total:	100	19270.1237	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	7.5755	1025.0807	12.56
2	92.4245	12506.4458	13.45
Total:	100	13531.5265	

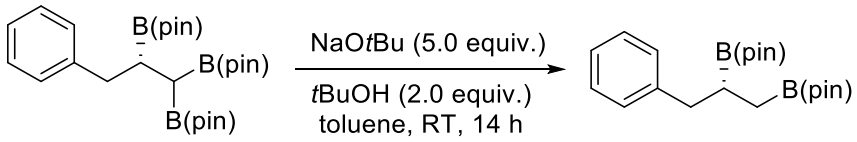


(*R*)-2,2',2''-(3-phenylpropane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (4.79). Prepared according to the general procedure utilizing $Pt(dba)_3$ (8.1 mg, 0.0090 mmol), **(R,R)-4.22** (16.4 mg, 0.0180 mmol), $B_2(cat)_2$ (85.6 mg, 0.360 mmol), (*E*)-4,4,5,5-tetramethyl-2-(3-phenylprop-1-en-1-yl)-1,3,2-dioxaborolane (73.2 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (255.2 mg, 2.160 mmol). The crude material was purified (SiO_2, 5-7% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (121.5 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23-7.17 (4H, m), 7.10 (1H, tt, *J*= 6.5, 2.0 Hz), 2.80 (1H, dd, *J*= 13.5, 7.0 Hz), 2.71 (1H, dd, *J*= 13.5, 8.5 Hz) 1.68 (1H, dt, *J*= 7.0, 9.0 Hz), 1.23 (24 H, s), 1.13 (6H, s), 1.10 (6H, s), 0.85 (1H, d, *J*= 9.0

Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 142.7, 129.3, 127.8, 125.3, 82.8, 82.8, 82.8, 39.2, 25.0, 24.9, 24.8, 24.8, 24.6, 24.6; IR (neat): 2976.6 (m), 2929.1 (w), 1454.9 (w), 1369.8 (s), 1350.4 (s), 1309.6 (s), 1264.6 (m), 1213.7 (w), 1140.0 (s), 969.6 (m), 850.4 (m), 744.7 (w), 699.7 (w), 669.9 (w) cm^{-1}; HRMS-(DART) for: $C_{27}H_{46}B_3O_6$ $[M+H]^+$: calculated: 499.3574, found: 499.3592. $[\alpha]_D^{20} = -15.837$ (*c* = 0.500, $CHCl_3$, *l* = 50 mm).

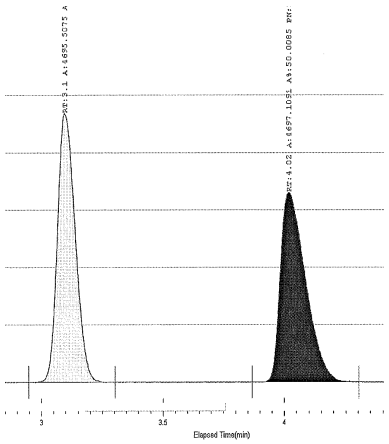
Analysis of stereochemistry:

Racemic compound was prepared according to the general procedure for racemic vinyl boronate diboration utilizing (*E*)-4,4,5,5-tetramethyl-2-(3-phenylprop-1-en-1-yl)-1,3,2-dioxaborolane and $Pt(dba)_3$ as the catalyst. The title compound was subjected to protodeboronation as shown below to give (*R*)-2,2'-(3-phenylpropane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane). Further analysis of stereochemistry was performed on (*R*)-2,2'-(3-phenylpropane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane). Absolute stereochemistry was assigned by analogy (see product **4.81 and 4.82)**.

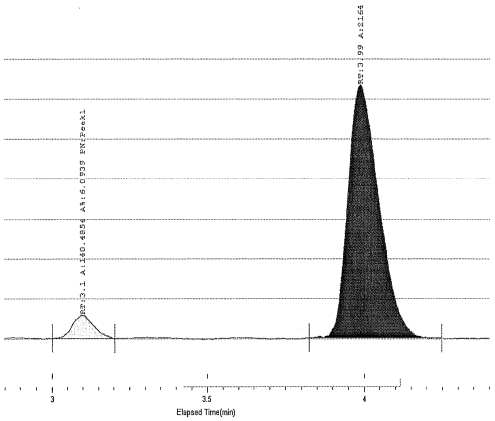


Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2,2'-(3-phenylpropane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

Racemic Material

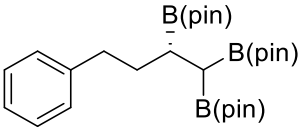


Standard Conditions



Peak No	% Area	Area	RT (min)
1	6.0939	140.4854	3.1
2	93.9061	2164.8638	3.99
Total:	100	2305.3492	

Peak No	% Area	Area	RT (min)
1	49.9915	4695.5075	3.1
2	50.0085	4697.1091	4.02
Total:	100	9392.6166	



(*R*)-2,2',2''-(4-phenylbutane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (4.80). Prepared according to the general procedure utilizing $Pt(dba)_3$ (8.1 mg, 0.0090 mmol), **(*R,R*)-4.22** (16.4 mg, 0.0180 mmol), $B_2(cat)_2$ (85.6 mg, 0.360 mmol), (*E*)-4,4,5,5-tetramethyl-2-(4-phenylbut-1-en-1-yl)-1,3,2-dioxaboro-lane (77.5 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (255.2 mg, 2.160 mmol). The crude material was purified (SiO_2, 5-7% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (121.5 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.22 (2H, m), 7.17 (2H, d, *J*= 7.0 Hz), 7.13 (1H, t, *J*= 7.5 Hz), 2.66 (1H, ddd, *J*= 13.5, 10.5, 6.5 Hz), 2.52 (1H, ddd, *J*= 13.5, 11.0, 6.5 Hz), 1.80-1.70 (2H, m), 1.47-1.43 (1H, m), 1.24-1.21 (36H, m), 0.94 (1H, d, *J*= 10.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 143.7, 128.4, 128.1, 125.2, 82.8, 82.8, 82.8, 35.7, 35.3, 25.1, 25.0, 24.8, 24.7, 24.7, 24.6; IR (neat): 2977.2 (m), 2929.6 (w), 1496.1 (w), 1455.9

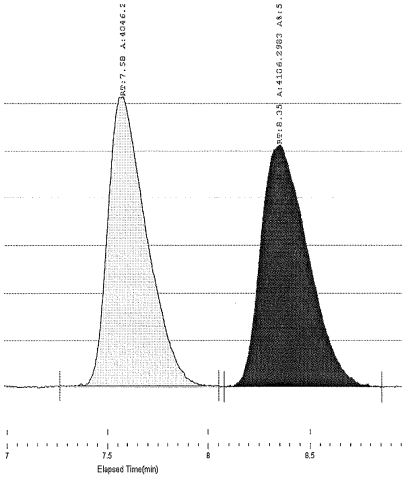
(w), 1378.0 (s), 1370.1 (s), 1348.3 (s), 1312.2 (s), 1267.6 (m), 1214.4 (w), 1141.0 (s), 969.4 (m), 849.0 (m), 699.4 (w) cm^{-1}; HRMS-(DART) for: $C_{28}H_{48}B_3O_6$ $[M+H]^+$: calculated: 513.3730, found: 513.3751. $[\alpha]_D^{20} = -20.472$ (*c* = 0.969, $CHCl_3$, *l* = 50 mm).

Analysis of stereochemistry:

Racemic compound was prepared according to the general procedure for racemic vinyl boronate diboration utilizing (*E*)-4,4,5,5-tetramethyl-2-(4-phenylbut-1-en-1-yl)-1,3,2-dioxaboro-lane and $Pt(dba)_3$ as the catalyst. The title compound was subjected to protodeboronation to give (*R*)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane). Further analysis of stereochemistry was performed on this product. Absolute stereochemistry assigned by analogy (see product **4.81 and 4.82)**.

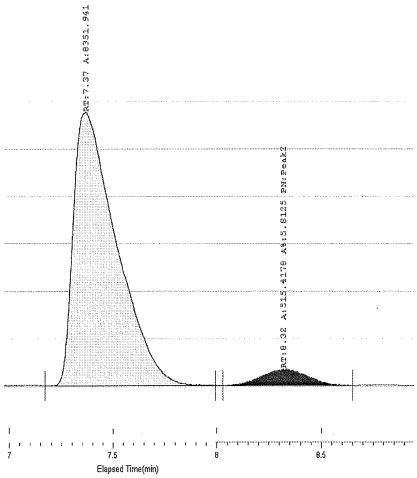
Chiral SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2,2'-(4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

Racemic Material

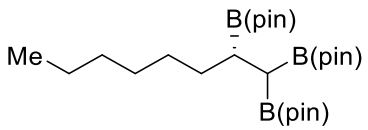


Peak No	% Area	Area	RT (min)
1	49.6317	4046.2516	7.58
2	50.3683	4106.2983	8.35
Total:	100	8152.5499	

Standard Conditions



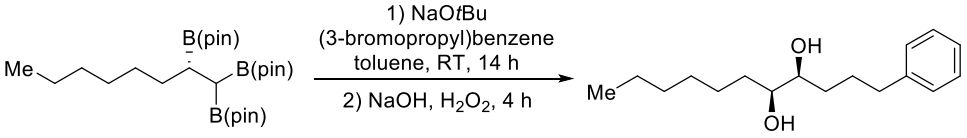
Peak No	% Area	Area	RT (min)
1	94.1875	8351.9413	7.37
2	5.8125	515.4178	8.32
Total:	100	8867.3591	



(*R*)-2,2',2''-(octane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (4.73). Prepared according to the general procedure utilizing $Pt(dba)_3$ (8.1 mg, 0.0090 mmol), **(*R,R*)-4.22** (16.4 mg, 0.0180 mmol), $B_2(cat)_2$ (85.6 mg, 0.360 mmol), (*E*)-1-octen-1-ylboronic acid pinacol ester (71.8 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (255.2 mg, 2.160 mmol). The crude material was purified (SiO_2, 5-7% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (115.6 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.44-1.36 (2H, m), 1.35-1.28 (2H, m), 1.27-1.16 (43H, m), 0.86-0.82 (4H, m); ^{13}C NMR (126 MHz, $CDCl_3$): δ 82.7, 82.6, 82.6, 33.4, 31.8, 29.6, 28.6, 25.0, 24.9, 24.8, 24.7, 24.6, 22.6, 14.1; IR (neat): 2976.0 (m), 2924.6 (m), 2855.2 (w), 1466.8 (w), 1370.1 (s), 1346.7 (s), 1306.2 (s), 1262.4 (s), 1213.3 (w), 1136.1 (m), 876.3 (m), 712.9 (w) cm^{-1}; HRMS-(DART) for: $C_{26}H_{52}B_3O_6$ $[M+H]^+$: calculated: 493.4043, found: 493.4062. $[\alpha]_D^{20}$ = -23.179 (*c* = 1.025, $CHCl_3$, *l* = 50 mm).

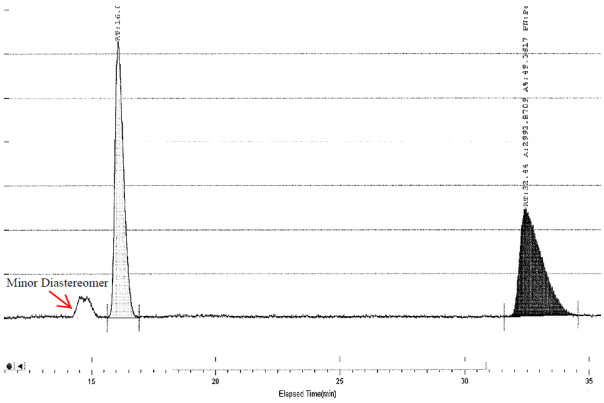
Analysis of stereochemistry:

Racemic compound was prepared according to the general procedure for racemic vinyl boronate diboration utilizing (*E*)-1-octen-1-ylboronic acid pinacol ester and $Pt(dba)_3$ as the catalyst. The title compound was subjected to the general procedure for deborylative alkylation with (3-bromopropyl)benzene followed by oxidation as shown below to give (4*S*,5*S*)-1-phenylundecane-4,5-diol. Further analysis of stereochemistry was performed on (4*S*,5*S*)-1-phenylundecane-4,5-diol. Absolute stereochemistry was assigned by analogy (see product **4.81 and 4.82)**.



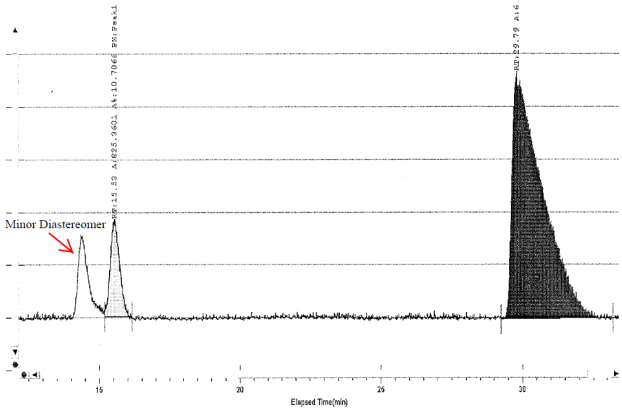
Chiral SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (4S,5S)-1-phenylundecane-4,5-diol

Racemic Material

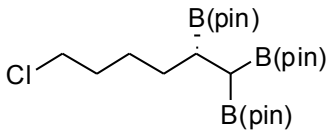


Peak No	% Area	Area	RT (min)
1	50.6383	3071.2958	16.08
2	49.3617	2993.8709	32.44
Total:	100	6065.1667	

Standard Conditions



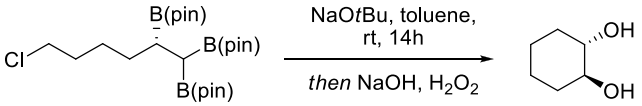
Peak No	% Area	Area	RT (min)
1	10.7066	825.3601	15.53
2	89.2934	6883.5181	29.79
Total:	100	7708.8782	



(*R*)-2,2',2''-(6-chlorohexane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (4.81). Prepared according to the general procedure utilizing $Pt(dba)_3$ (8.1 mg, 0.0090 mmol), **(R,R)-4.22** (16.4 mg, 0.0180 mmol), $B_2(cat)_2$ (142.7 mg, 0.600 mmol), (*E*)-2-(6-chlorohex-1-enyl)-4,4,5,5-tetramethyl-1,3,2 -dioxaborolane (72.9 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (425.3 mg, 3.600 mmol). The crude material was purified (SiO_2, 5% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (114.3 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.49 (2H, t, *J*= 7.0 Hz), 1.74-1.70 (2H, m), 1.46-1.31 (5H, m), 1.20-1.18 (36H, m), 0.83 (1H, d, *J*= 9.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 83.0, 83.0, 82.9, 45.4, 33.1, 32.6, 26.2, 25.2, 25.1, 25.0, 24.9, 24.8, 24.9; IR (neat): 2976.1 (m), 2928.2 (m), 1460.9 (w), 1370.1 (m), 1348.7 (m), 1303.3 (s), 1262.4 (m), 1136.0 (s), 968.6 (m), 846.5 (m) cm^{-1}; HRMS-(DART) for: $C_{24}H_{47}B_3Cl_1O_6$ $[M+H]^+$: calculated: 499.3340, found: 499.3344. $[\alpha]_D^{20}$ = -16.084 (*c* = 0.470, $CHCl_3$, *l* = 50 mm).

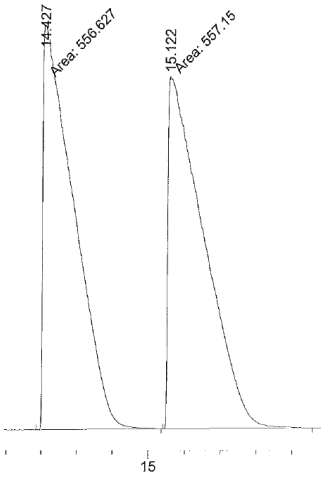
Analysis and Proof of stereochemistry:

Racemic compound was prepared according to the general procedure for racemic vinyl boronate diboration utilizing (*E*)-2-(6-chlorohex-1-en-1-yl)-4,4,5,5-tetramethyl- 1,3,2-dioxaborolane and $Pt(dba)_3$ as the catalyst. The title compound was subjected to the general procedure for deborylative cyclization followed by oxidation to give (1*S*,2*S*)-cyclohexane-1,2-diol. Absolute configuration of stereochemistry was assigned by comparing the prepared (1*S*,2*S*)-cyclohexane-1,2-diol with an authentic sample purchased from Fluka.



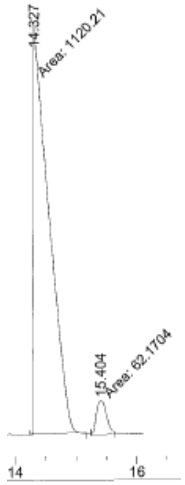
Chiral GLC (β-dex 225, Supelco, 100 °C for 5 min, ramp 3 °C/min to 160 °C, 20 psi) – analysis of (1S,2S)-cyclohexane-1,2-diol

Racemic Material



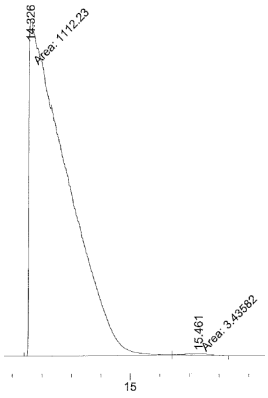
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	14.427	MM	0.1997	556.62695	46.46300	49.97651
2	15.122	MM	0.2298	557.15027	40.40024	50.02349
Totals :				1113.77722	86.86324	

Standard Conditions

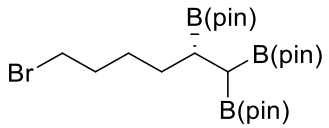


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	14.327	MM	0.2887	1120.20935	64.67873	94.74193
2	15.404	MM	0.1941	62.17039	5.33910	5.25807

Authentic Material



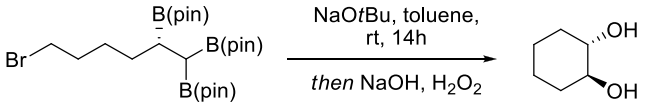
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	14.326	MM	0.2958	1112.23303	62.67395	99.69204
2	15.461	MM	0.1717	3.43582	3.33552e-1	0.30796
Totals :				1115.66886	63.00751	



(*R*)-2,2',2''-(6-bromohexane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (4.82). Prepared according to the general procedure utilizing $Pt(dba)_3$ (8.1 mg, 0.0090 mmol), **(*R,R*)-4.22** (16.4 mg, 0.0180 mmol), $B_2(cat)_2$ (142.7 mg, 0.6000 mmol), (*E*)-2-(6-bromohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (71.8 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (425.3 mg, 3.600 mmol). The crude material was purified (SiO_2, 5-7% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid, which co-eluted with $B_2(pin)_2$ (135.1 mg, product: $B_2(pin)_2$ = 1.00:0.26, 74%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.38 (2H, t, 6.5 Hz), 1.87-1.76 (2H, m), 1.50-1.30 (5H, m), 1.23-1.18 (36H, m), 0.84 (1H, d, *J*= 10.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 82.8, 82.8, 82.7, 34.0, 33.1, 32.3, 27.3, 25.0, 25.0, 24.9, 24.8, 24.7, 24.6**;** IR (neat): 2976.4 (m), 2930.2 (w), 1461.3 (w), 1369.4 (s), 1347.1 (s), 1304.5 (s), 1267.1 (s), 1213.4 (m), 1137.7 (s), 968.9 (m), 848.8 (m), 644.6 (w), 578.2 (w) cm^{-1}; HRMS-(DART) for: $C_{24}H_{47}B_3BrO_6$ $[M+H]^+$: calculated: 543.2835, found: 543.2855. $[\alpha]_D^{20}$ = -16.415 (*c* = 2.975, $CHCl_3$, *l* = 50 mm).

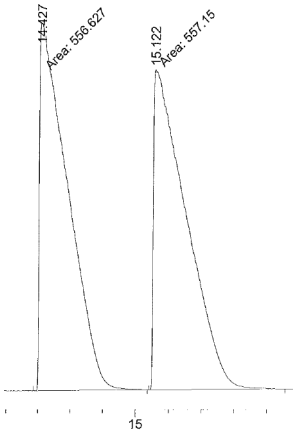
Analysis and Proof of stereochemistry:

Racemic compound was prepared according to the general procedure for racemic vinyl boronate diboration utilizing (*E*)-2-(6-bromohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane and $Pt(dba)_3$ as the catalyst. The title compound was subjected to the general procedure for deborylative cyclization followed by oxidation to give (1*S*,2*S*)-cyclohexane-1,2-diol. Absolute configuration of stereochemistry was assigned by comparing the prepared (1*S*,2*S*)-cyclohexane-1,2-diol with an authentic sample purchased from Fluka.



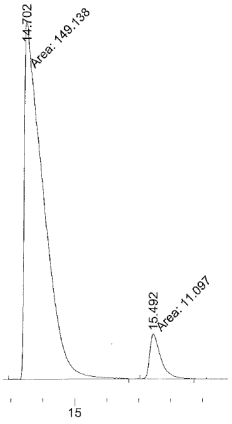
Chiral GLC (β-dex 225, Supelco, 100 °C for 5 min, ramp 3 °C/min to 160 °C, 20 psi) – analysis of (1S,2S)-cyclohexane-1,2-diol

Racemic Material



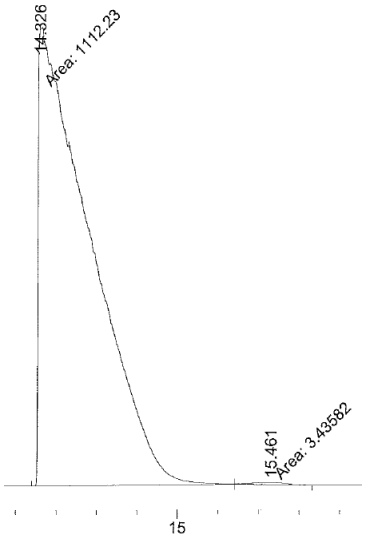
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	14.427	MM	0.1997	556.62695	46.46300	49.97651
2	15.122	MM	0.2298	557.15027	40.40024	50.02349
Totals :				1113.77722	86.86324	

Standard Conditions

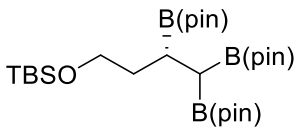


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	14.702	MM	0.1368	149.13812	18.17207	93.07457
2	15.492	MM	0.0809	11.09697	2.28523	6.92543
Totals :				160.23509	20.45730	

Authentic Material



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	14.326	MM	0.2958	1112.23303	62.67395	99.69204
2	15.461	MM	0.1717	3.43582	3.33552e-1	0.30796
Totals :				1115.66886	63.00751	



(*R*)-*tert*-butyldimethyl(3,4,4-tris(4,4,5,5-tetramethyl-1,3,2-dioxa-borolan-2-yl)butoxy)silane (4.84). Prepared according to the general procedure utilizing $Pt(dba)_3$ (8.1 mg, 0.0090 mmol), **(*R,R*)-4.22** (16.4 mg, 0.0180 mmol), $B_2(cat)_2$ (85.6 mg, 0.360 mmol), (*E*)-4-(*tert*-butyldimethylsiloxy)-1-buten-1-ylboronic acid pinacol ester (93.7 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (255.2 mg, 2.160 mmol). The crude material was purified (SiO_2, 5% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (135.4 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.63 (1H, dt, *J*= 6.0, 10.5 Hz), 3.53 (1H, dt, *J*= 6.0, 10.5 Hz), 1.76-1.69 (1H, m), 1.65-1.59 (1H, m), 1.32-1.18 (37H, m), 0.86 (9H, s), 0.80 (1H, d, *J*= 8.5 Hz), 0.02 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$): δ 82.7, 82.7, 82.7, 63.2, 36.4, 26.1, 25.1, 25.0, 24.9, 24.7, 24.7, 24.6, 18.4, -5.1; IR (neat): 2976.8 (m), 2929.5 (m), 2857.2 (w), 1470.1 (w), 1369.6 (s), 1347.5 (s), 1305.9 (s), 1256.4 (m), 1214.7 (m), 1138.8 (s), 1091.2 (s), 1005.4 (m), 846.5 (s), 835.0 (s), 775.0 (m), 668.7 (w), 578.1 (w) cm^{-1}; HRMS-(DART) for: $C_{28}H_{58}B_3O_7Si$ $[M+H]^+$: calculated: 567.4231, found: 567.4257. $[\alpha]_D^{20}$ = -11.340 (*c* = 2.155, $CHCl_3$, *l* = 50 mm).

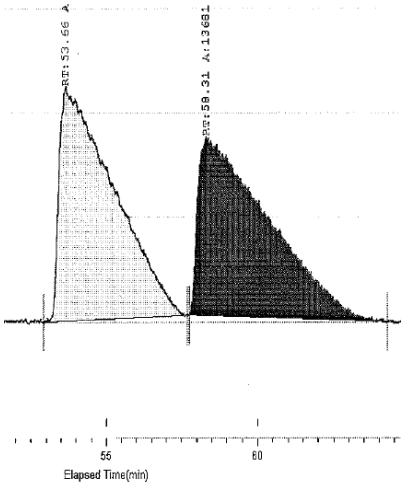
Analysis of stereochemistry:

Racemic compound was prepared according to the general procedure for racemic vinyl boronate diboration utilizing (*E*)-4-(*tert*-butyldimethylsiloxy)-1-buten-1-ylboronic acid pinacol ester and $Pt(dba)_3$ as the catalyst. The title compound was subjected to the general procedure for deborylative alkylation with (3-bromopropyl)benzene followed by oxidation to give (3*S*,4*S*)-1-((tert-butyldimethylsilyl)oxy)-7-phenylheptane-3,4-diol. Further analysis of stereochemistry was performed on (3*S*,4*S*)-1-((tert-

butyldimethylsilyl)oxy)-7-phenylheptane-3,4-diol. Absolute stereochemistry was assigned by analogy (see product **4.81 and 4.82)**.

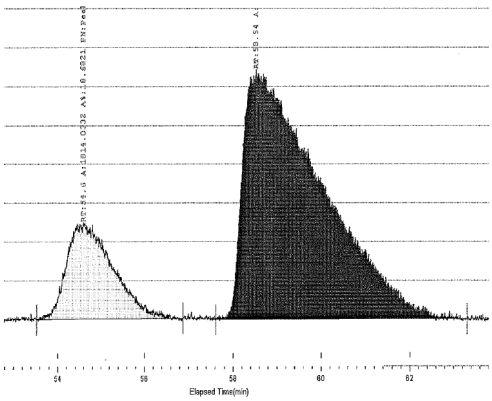
Chiral SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (3S,4S)-1-((tert-butyldimethylsilyl)oxy)-7-phenylheptane-3,4-diol

Racemic Material

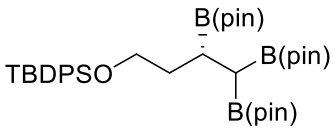


Peak No	% Area	Area	RT (min)
1	50.5769	14000.6213	53.66
2	49.4231	13681.2508	58.31
Total:	100	27681.8721	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	18.6821	1814.0332	54.6
2	81.3179	7895.9517	58.54
Total:	100	9709.9849	



(*R*)-*tert*-butyldiphenyl(3,4,4-tris(4,4,5,5-tetramethyl-1,3,2-dioxa-borolan-2-yl)butoxy)silane (4.92). Prepared according to the general procedure utilizing $Pt(dba)_3$ (8.1 mg, 0.0090 mmol), **(R,R)-4.22** (16.4 mg, 0.0180 mmol), $B_2(cat)_2$ (142.7 mg, 0.6000 mmol), (*E*)-*tert*-butyldiphenyl((4-(4,4,5,5-tetramethyl-1,3,2-dioxaboro-lan-2-yl)but-3-en-1-yl)oxy)silane (130.9 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (425.3 mg, 3.600 mmol). The crude material was purified (SiO_2, 5% ethyl acetate in hexane, UV/magic stain) to give the

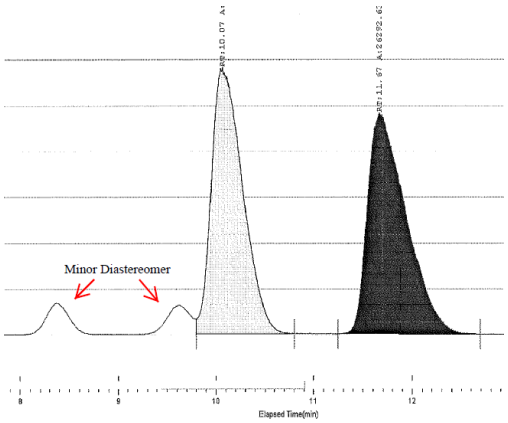
desired product as a white solid, which co-eluted with $B_2(pin)_2$ (203.1 mg, product: $B_2(pin)_2$ = 1.0:0.66, 79%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (4H, dd, *J*= 7.5, 1.5 Hz), 7.39-7.32 (6H, m), 3.71 (1H, dt, *J*= 5.5, 10.0 Hz), 3.63 (1H, dt, *J*= 6.0, 9.5 Hz), 1.89-1.76 (2H, m), 1.40-1.33 (1H, m), 1.21 (12H, s), 1.19 (12H, s), 1.13 (6H, s), 1.12 (6H, s), 1.02 (9H, s), 0.81 (1H, d, *J*= 8.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 135.5, 135.5, 129.2, 127.4, 82.7, 82.7, 82.7, 63.8, 36.1, 25.0, 24.9, 24.9, 24.7, 24.7, 24.6, 19.2; IR (neat): 2977.0 (m), 2930.9 (m), 2858.0 (w), 1469.3 (w), 1348.4 (s), 1308.7 (s), 1279.6 (s), 1213.6 (w), 1139.7 (s), 1124.4 (s), 1109.7 (s), 969.2 (m), 849.0 (m), 742.3 (w), 703.1 (m), 578.7 (w), 505.6 (w) cm^{-1}; HRMS-(DART) for: $C_{38}H_{62}B_3O_7Si$ $[M+H]^+$: calculated: 691.4544, found: 691.4555. $[\alpha]_D^{20}$ = -7.697 (*c* = 1.190, $CHCl_3$, *l* = 50 mm).

Analysis of stereochemistry:

Racemic compound was prepared according to the general procedure for racemic vinyl boronate diboration utilizing), (*E*)-*tert*-butyldiphenyl((4-(4,4,5,5-tetramethyl-1,3,2-dioxaboro-lan-2-yl)but-3-en-1-yl)oxy)silane and $Pt(dba)_3$ as the catalyst. The title compound was subjected to the general procedure for deborylative alkylation with (3-bromopropyl)benzene followed by oxidation to give (3*S*,4*S*)-1-((tert-butyldiphenylsilyl)oxy)-7-phenylheptane-3,4-diol. Further analysis of stereochemistry was performed on (3*S*,4*S*)-1-((tert-butyldiphenylsilyl)oxy)-7-phenylheptane-3,4-diol. Absolute stereochemistry was assigned by analogy (see product **4.81 and 4.82)**.

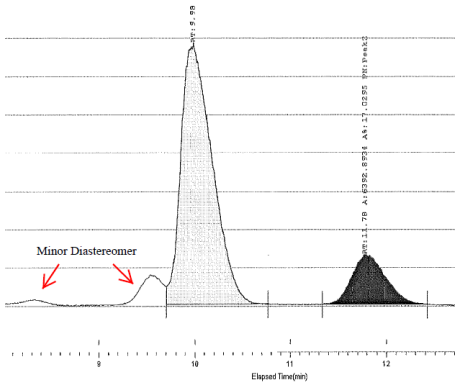
Chiral SFC (Chiracel OD-H, 20% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (3S,4S)-1-((tert-butyldiphenylsilyl)oxy)-7-phenylheptane-3,4-diol

Racemic Material

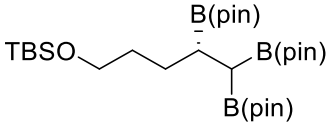


Peak No	% Area	Area	RT (min)
1	49.4598	25730.5679	10.07
2	50.5402	26292.634	11.67
Total:	100	52023.2019	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	82.9705	31147.197	9.98
2	17.0295	6392.8934	11.78
Total:	100	37540.0904	



(*R*)-*tert*-butyldimethyl((4,5,5-tris(4,4,5,5-tetramethyl-1,3,2-dioxa-borolan-2-yl)pentyl)oxy)silane (4.93). Prepared according to the general procedure utilizing $Pt(dba)_3$ (8.1 mg, 0.0090 mmol), **(*R,R*)-4.22** (16.4 mg, 0.0180 mmol), $B_2(cat)_2$ (85.6 mg, 0.360 mmol), (*E*)-*tert*-butyldimethyl((5-(4,4,5,5-tetramethyl-1,3,2-dioxaboro-lan-2-yl)pent-4-en-1-yl)oxy)silane (97.9 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (255.2 mg, 2.160 mmol). The crude material was purified (SiO_2, 5% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (123.6 mg, 71%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.56 (2H, t, *J*= 7.0 Hz), 1.62-1.54 (1H, m), 1.49-1.30 (4H, m), 1.21 (18H, s. overlap), 1.21 (18H, s, overlap), 0.87 (9H, s), 0.88-0.86 (1H, overlaps), 0.02 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$): δ 82.7, 82.7, 64.1, 32.3, 29.6, 26.0, 25.0, 24.9, 24.8, 24.6, 24.6, 24.6, 18.4, -5.2; IR (neat): 2976.8 (m), 2929.5 (m), 2857.1 (w), 1470.4 (w), 1369.7 (s), 1345.8 (s), 1308.6 (s), 1266.0 (m), 1214.4 (m), 1140.3 (s), 1100.5 (m), 1005.4 (w), 969.8 (m), 836.0

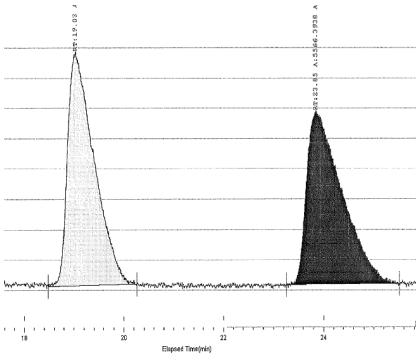
(s), 775.1 (m), 669.3 (w) cm^{-1}; HRMS-(DART) for: $C_{29}H_{60}B_3O_7Si$ $[M+H]^+$: calculated: 581.4388, found: 581.4391. $[\alpha]_D^{20}$ = -15.094 (*c* = 1.060, $CHCl_3$, *l* = 50 mm).

Analysis of stereochemistry:

Racemic compound was prepared according to the general procedure for racemic vinyl boronate diboration utilizing), (*E*)-*tert*-butyldimethyl((5-(4,4,5,5-tetramethyl-1,3,2-dioxaboro-lan-2-yl)pent-4-en-1-yl)oxy)silane and $Pt(dba)_3$ as the catalyst. The title compound was subjected to the general procedure for deborylative alkylation with (3-bromopropyl)benzene followed by oxidation to give (4*S*,5*S*)-1-((tert-butyldimethylsilyl)oxy)-8-phenyloctane-4,5-diol. Further analysis of stereochemistry was performed on (4*S*,5*S*)-1-((tert-butyldimethylsilyl)oxy)-8-phenyloctane-4,5-diol. Absolute stereochemistry was assigned by analogy (see product **4.81 and 4.82)**.

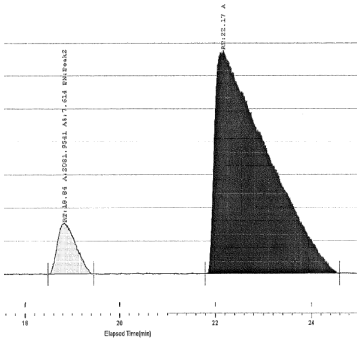
Chiral SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (4S,5S)-1-((tert-butyldimethylsilyl)oxy)-8-phenyloctane-4,5-diol

Racemic Material

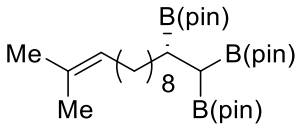


Peak No	% Area	Area	RT (min)
1	50.5133	5681.8675	19.03
2	49.4867	5566.3938	23.85
Total:	100	11248.2613	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	7.614	2081.9541	18.84
2	92.386	25261.846	22.17
Total:	100	27343.8001	



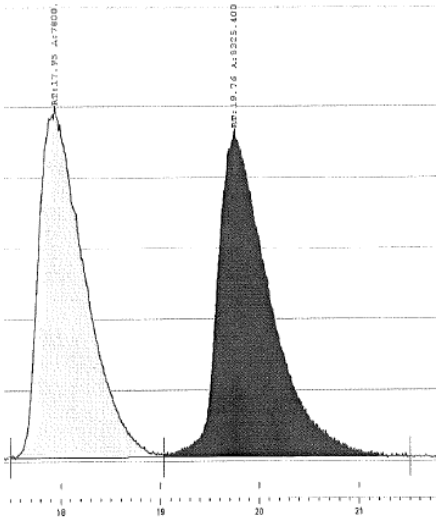
(*R*)-2,2',2''-(12-methyltridec-11-ene-1,1,2-triyl(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (4.86). Prepared according to the general procedure utilizing $Pt(dba)_3$ (8.1 mg, 0.0090 mmol), **(*R,R*)-4.22** (16.4 mg, 0.0180 mmol), $B_2(cat)_2$ (142.7 mg, 0.600 mmol), (*E*)-4,4,5,5-tetramethyl-2-(12-methyltrideca-1,11-dien-1-yl)-1,3,2-dioxaborolane (96.1 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (425.3 mg, 3.600 mmol). The crude material was purified (SiO_2, 5% ethyl acetate in hexane, UV/magic stain) to give the desired product as a clear colorless oil (118.3 mg, 69%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.08 (1H, tt, *J*= 7.0, 1.5 Hz), 1.93-1.89 (2H, m), 1.66 (3H, s), 1.57 (3H, s), 1.40-1.17 (52H, m), 0.84 (1H, d, *J*= 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 131.2, 125.2, 82.9, 82.9, 82.8, 33.6, 30.2, 30.1, 29.7, 29.6, 28.8, 28.3, 25.9, 25.2, 25.1, 25.0, 24.9, 24.8, 24.7, 17.8; IR (neat): 2976.6 (m), 2924.5 (m), 2854.1 (m), 1462.4 (m), 1369.5 (m), 1345.6 (s), 1306.2 (m), 1139.3 (s), 849.3 (m), 756.2 (m) cm^{-1}; HRMS-(DART) for: $C_{32}H_{63}B_3O_6$ $[M+H]^+$: calculated: 575.4826, found: 575.4853. $[\alpha]_D^{20}$ = -16.084 (*c* = 0.470, $CHCl_3$, *l* = 50 mm).

Analysis of stereochemistry:

Racemic compound was prepared according to the general procedure for racemic vinyl boronate diboration utilizing (*E*)-4,4,5,5-tetramethyl-2-(12-methyltrideca-1,11- dien-1-yl)-1,3,2-dioxaborolane and $Pt(dba)_3$ as the catalyst. The title compound was subjected to the general procedure for deborylative alkylation with (3-bromopropyl)benzene followed by oxidation to give (4*S*,5*S*)-15-methyl-1- phenylhexadec-14-ene-4,5-diol. Further analysis of stereochemistry was performed on (4*S*,5*S*)-15-methyl-1-phenylhexadec-14-ene-4,5- diol. Absolute stereochemistry was assigned by analogy (see product **4.81 and 4.82)**.

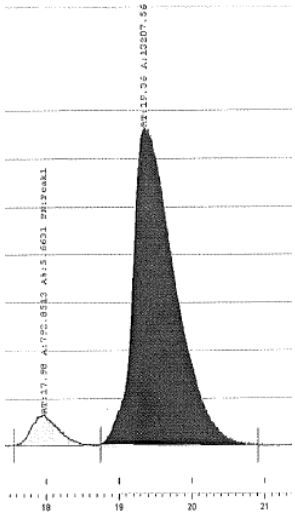
Chiral SFC (Chiracel AD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (4S,5S)-15-methyl-1-phenylhexadec-14-ene-4,5-diol.

Racemic Material

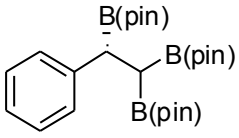


Peak No	% Area	Area	RT (min)
1	48.3725	7800.5002	17.95
2	51.6275	8325.4009	19.76
Total:	100	16125.9011	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	5.6631	792.8513	17.98
2	94.3369	13207.5682	19.36
Total:	100	14000.4195	



(*R*)-2,2',2''-(2-phenylethane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (4.88). Prepared according to the general procedure utilizing $Pt(dba)_3$ (8.1 mg, 0.0090 mmol), **(*R,R*)-4.22** (16.4 mg, 0.0180 mmol), $B_2(cat)_2$ (142.7 mg, 0.600 mmol), (*E*)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane (69.1 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (425.3 mg, 3.600 mmol). The crude material was purified (SiO_2, 5% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (68.7 mg, 47%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19-7.12 (4H, m), 7.02-6.99 (1H, m), 2.64 (1H, d, *J*= 12.5 Hz), 1.42 (1H, d, *J*= 12.5 Hz), 1.21 (6H, s), 1.20 (6H, s), 1.13 (6H, s), 1.11 (6H,

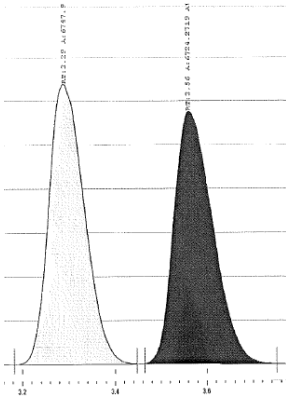
s), 0.92 (6H, s), 0.90 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.5, 128.7, 128.0, 124.8, 83.2, 83.2, 82.8, 25.0, 24.8, 24.6, 24.5, 24.4; IR (neat): 2978.3 (m), 1370.2 (m), 1309.1 (s), 1263.8 (m), 1214.3 (w), 1137.7 (s), 968.0 (m), 908.3 (m), 846.5 (m), 739.4 (s), 668.9 (m) cm^{-1}; HRMS-(DART) for: $C_{26}H_{44}B_3O_6$ $[M+H]^+$: calculated: 485.3417, found: 485.3431. $[\alpha]_D^{20} = -9.267$ ($c = 0.650$, $CHCl_3$, $l = 50$ mm).

Analysis of stereochemistry:

Racemic compound was prepared according to the general procedure for racemic vinyl boronate diboration utilizing (*E*)-4,4,5,5-tetramethyl-2-styryl-1,3,2- dioxaborolane and $Pt(dba)_3$ as the catalyst. The title compound was subjected to protodeboronation to give (R)-2,2'-(1-phenylethane-1,2-diyl)bis(4,4,5,5-tetramethyl- 1,3,2-dioxaborolane). Further analysis of stereochemistry was performed on (R)-2,2' -(1-phenylethane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane). Absolute stereochemistry was assigned by analogy (see product **4.81 and 4.82)**.

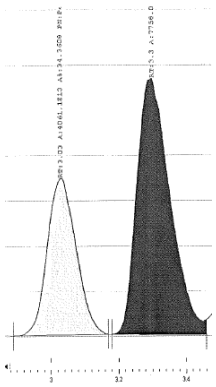
Chiral SFC (Chiracel OD-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2,2'-(1-phenylethane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2- dioxaborolane)

Racemic Material

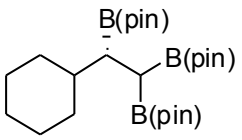


Peak No	% Area	Area	RT (min)
1	50.088	6747.9698	3.29
2	49.912	6724.2719	3.56
Total:	100	13472.2417	

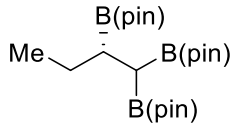
Standard Conditions



Peak No	% Area	Area	RT (min)
1	34.3608	4061.1813	3.03
2	65.6392	7758.0581	3.3
Total:	100	11819.2394	



(*R*)-2,2',2''-(2-cyclohexylethane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (4.89). Prepared according to the general procedure utilizing $Pt(dba)_3$ (8.1 mg, 0.0090 mmol), **(*R,R*)-4.22** (16.4 mg, 0.0180 mmol), $B_2(cat)_2$ (142.7 mg, 0.600 mmol), (*E*)-2-(2-cyclohexylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (70.8 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (425.3 mg, 3.600 mmol). The crude material was purified (SiO_2, 5% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (24.3 mg, 17%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.78-1.57 (5H, m), 1.35-1.30 (2H, m), 1.27-1.02 (42H, m), 0.85-0.79 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 82.9, 82.8, 82.8, 42.6, 33.9, 30.6, 27.4, 27.3, 27.1, 25.5, 25.3, 25.0, 24.9, 24.8, 24.6; IR (neat): 3026.4 (w), 2925.1 (m), 2858.3 (m), 1495.6 (m), 1453.9 (m), 1099.6 (m), 1063.4 (m), 1030.9 (m), 747.3 (m), 699.2 (s) cm^{-1}; HRMS-(DART) for: $C_{26}H_{50}B_3O_6$ $[M+H]^+$: calculated: 491.3887, found: 491.3905.



(*R*)-2,2',2''-(butane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaboro-lane) (4.91). Prepared according to the general procedure in a 15 mL pressure vessel utilizing $Pt(dba)_3$ (80.8 mg, 0.0900 mmol), **(R,R)-4.22** (165 mg, 0.1800 mmol), $B_2(cat)_2$ (1.43 g mg, 6.00 mmol), (*E*)-2-(but-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (546 mg, 3.00 mmol), and THF (3.0 mL), followed by pinacol (4.25 g, 36.0 mmol). The crude material was purified (SiO_2, 5% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid, which co-eluted with $B_2(pin)_2$ (1.46 g, product: $B_2(pin)_2$ = 1.00:0.75, 77%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.63 (1H, dt, *J*= 6.0, 10.5 Hz), 3.53 (1H, dt, *J*= 6.0, 10.5 Hz), 1.76-1.69 (1H, m), 1.49-1.38 (2H, m), 1.33-1.16 (37H, m), 0.89-0.85 (4H, m); ^{13}C NMR (126 MHz, $CDCl_3$): δ

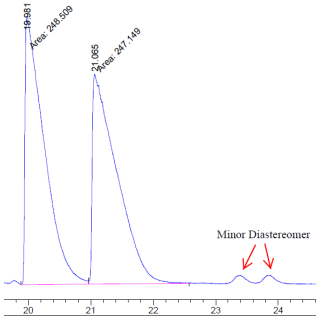
82.7, 82.6, 26.0, 25.0, 24.8, 24.8, 24.6, 24.6, 13.2; IR (neat): 2977.2 (m), 2930.6 (w), 1464.5 (w), 1370.3 (s), 1348.3 (s), 1306.6 (s), 1278.7 (s), 1212.6 (w), 1139.2 (s), 1123.7 (s), 969.1 (m), 848.8 (s), 835.0 (s), 668.4 (w), 555.3 (w) cm^{-1}; HRMS-(DART) for: $C_{22}H_{44}B_3O_6$ $[M+H]^+$: calculated: 437.3417, found: 437.3420. $[\alpha]_D^{20} = -14.107$ (*c* = 1.015, $CHCl_3$, *l* = 50 mm).

Analysis of stereochemistry:

Racemic compound was prepared according to the same procedure utilizing racemic 2,2',2"-(butane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaboro-lane) and 5-bromopent-1-ene. Further analysis of stereochemistry was performed on non-8-ene-3,4-diol. Absolute stereochemistry was assigned by comparing the specific rotation of the title compound to that of (3*R*,4*R*)-non-8-ene-3,4-diol.[34] Diastereoselectivity was determined by both GLC (14:1 *syn:anti*) and 1H NMR (16:1 *syn:anti*) analysis (See spectral data section for NMR analysis).

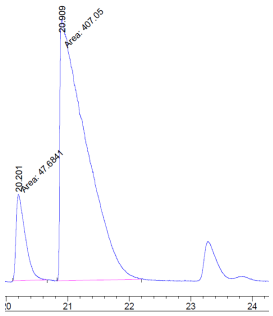
Chiral GLC (β-dex 225, Supelco, 100 °C for 5 min, ramp 3 °C/min to 160 °C, 20 psi) – analysis of (3S,4S)-non-8-ene-3,4-diol

Racemic Material

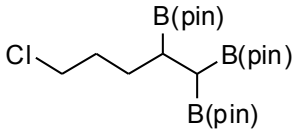


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	19.981	MF	0.3543	248.50932	11.69048	50.13722
2	21.065	FM	0.4503	247.14902	9.14740	49.86278
Totals :				495.65834	20.83788	

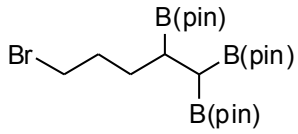
Standard Conditions



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	20.201	MM	0.1734	47.68409	4.58331	10.48614
2	20.909	MM	0.4881	407.05023	13.89834	89.51386
Totals :				454.73433	18.48165	

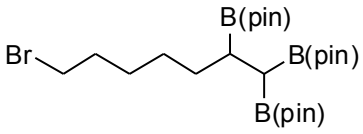


***racemic*-2,2',2''-(5-chloropentane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S15).** Prepared according to the general procedure for racemic vinyl boronate diboration utilizing $Pt(dba)_3$ (26.9 mg, 0.030 mmol), $B_2(pin)_2$ (799.9 mg, 3.150 mmol), (*E*)-2-(5-chloropent-1-en- 1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaboro-lane (691.6 mg, 3.000 mmol), and THF (3.00 mL). The crude material was purified (SiO_2, 5% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (767.1mg, 58%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.50 (2H, t, *J*= 7.0Hz), 1.87-1.80 (1H, m), 1.74-1.67 (1H, m), 1.59-1.51 (2H, m), 1.37-1.32 (1H, m), 1.26-1.21 (36H, m), 0.84 (1H, d, *J*= 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 83.0, 83.0, 45.9, 32.3, 30.9, 25.2, 25.1, 25.1, 25.0, 24.9, 24.8; IR (neat): 2976.9 (m), 1370.1 (m), 1347.4 (m), 1307.4 (s), 1264.8 (m), 1164.5 (m), 1137.1 (s), 1108.0 (m), 847.4 (m), 699.1 (m) cm^{-1}; HRMS-(DART) for: $C_{23}H_{45}B_3Cl_1O_6$ $[M+H]^+$: calculated: 485.3184, found: 485.3181.



***racemic*-2,2',2''-(5-bromopentane-1,1,2-triyl)tris(4,4,5,5-tetramethyl -1,3,2-dioxaborolane) (S16).** Prepared according to the general procedure for racemic vinyl boronate diboration utilizing $Pt(dba)_3$ (26.9 mg, 0.030 mmol), $B_2(pin)_2$ (799.9 mg, 3.150 mmol), (*E*)-2-(5-bromopent-1- en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaboro-lane (824.9 mg, 3.000 mmol), and THF (3.00 mL). The crude material was purified (SiO_2, 5% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (528.9 mg, 36%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.35 (2H, t, *J*= 7.5 Hz), 1.94-1.87 (1H, m), 1.81-1.74 (1H, m), 1.54-1.49 (2H, m), 1.35-1.30 (1H, m), 1.23-1.18 (36H, m), 0.81 (1H, d, *J*= 10.0 Hz); ^{13}C

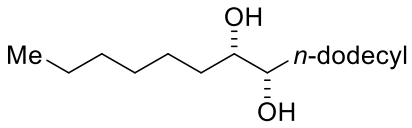
NMR (100 MHz, $CDCl_3$): δ 83.0, 83.0, 45.8, 32.5, 32.2, 25.2, 25.2, 25.1, 25.0, 24.9, 24.8; IR (neat): 2976.6 (m), 1369.5 (m), 1346.5 (m), 1306.5 (s), 1263.8 (m), 1213.5 (m), 1137.3 (s), 968.6 (m), 847.8 (m) cm^{-1}; HRMS-(DART) for: $C_{23}H_{45}B_3Br_1O_6$ $[M+H]^+$: calculated: 529.2679, found: 529.2669.



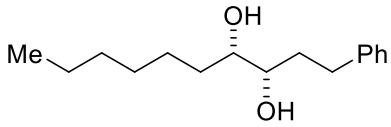
***racemic*-2,2',2''-(7-bromoheptane-1,1,2-triyl)tris(4,4,5,5-tetra-methyl-1,3,2-dioxaborolane) (S17).** Prepared according to the general procedure for racemic vinyl boronate diboration utilizing $Pt(dba)_3$ (26.9 mg, 0.030 mmol), $B_2(pin)_2$ (799.9 mg, 3.150 mmol), (*E*)-2-(7- bromohept-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dio-xaborolane (909.1 mg, 3.000 mmol), and THF (3.00 mL). The crude material was purified (SiO_2, 5% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (1.027g, 60%). ^1H NMR (500 MHz, $CDCl_3$): δ 3.36 (2H, t, *J*= 7.5 Hz), 1.81 (2H, pent, *J*= 7.0 Hz), 1.42-1.31 (7H, m), 1.19-1.18 (36H, m), 0.82 (1H, d, *J*= 10.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 82.9, 82.9, 34.2, 33.1, 32.9, 28.6, 27.9, 25.2, 25.1, 25.0, 24.9, 24.9, 24.8; IR (neat): 2976.5 (m), 2929.4 (m), 1464.7 (w), 1369.5 (m), 1346.0 (m), 1306.2 (s), 1265.9 (m), 1139.2 (s), 1108.1 (m), 969.2 (m), 848.6 (m) cm^{-1}; HRMS-(DART) for: $C_{25}H_{49}B_3Br_1O_6$ $[M+H]^+$: calculated: 557.2992, found: 557.3019.

4.6.2.7. Full characterization and proof of stereochemistry of deborylative alkylation products

Note: For analysis of diastereoselective, see ^{1}H NMR spectra in the Spectral Data section

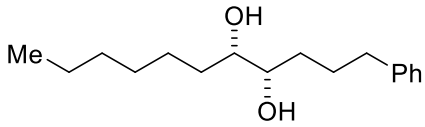


icosane-7,8-diol (4.105). Prepared according to the general procedure for deborylative alkylation utilizing racemic 2,2',2''-(octane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (147.6 mg, 0.3000 mmol), 1-bromododecane (49.8 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (58.6 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 3.44-3.36 (2H, m), 1.98 (2H, br s), 1.52-1.40 (7H, m), 1.38-1.20 (25H, m), 0.90-0.86 (6H, m); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major isomer) 74.5, 33.6, 31.9, 31.8, 29.7, 29.6, 29.6, 29.6, 29.3, 29.3, 25.7, 25.6, 22.7, 22.6, 14.1, 14.1; IR (neat): 3336.9 (br), 2952.6 (m), 2914.2 (s), 2847.0 (s), 1466.3 (s), 1415.2 (w), 1378.1 (w), 1142.1 (m), 1117.1 (m), 1100.3 (m), 1016.7 (m), 850.4 (w), 720.9 (m), 660.7 (w) cm^{-1}; HRMS-(DART) for: $C_{20}H_{41}O$ $[M+H-H_2O]^+$: calculated: 297.3157, found: 297.3145.



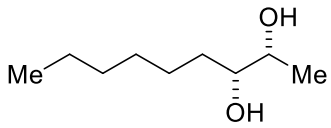
1-phenyldecane-3,4-diol (4.111). Prepared according to the general procedure for deborylative alkylation utilizing racemic 2,2',2''-(octane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (147.6 mg, 0.3000 mmol), (2-bromoethyl)benzene (37.0 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified

(SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (60.4 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.29 (2H, t, *J*= 8.0 Hz), 7.23-7.18 (4H, m), 3.46-3.42 (2H, m), 2.85 (1H, ddd, *J*= 14.0, 9.5, 6.0 Hz), 2.71 (1H, ddd, *J*= 14.0, 9.5, 7.0 Hz) 2.11 (1H, br s), 1.99 (1H, br s), 1.86-1.74 (2H, m), 1.54-1.23 (10H, m), 0.88 (3H, t, *J*= 6.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major isomer) 141.9, 128.4, 125.9, 74.6, 73.8, 35.3, 33.6, 32.0, 31.7, 29.3, 25.5, 22.6, 14.1; IR (neat): 3360.9 (br), 3063.1 (w), 3026.7 (w), 2926.9 (s), 2856.5 (s), 1603.5 (w), 1496.1 (m), 1176.7 (w), 1130.5 (s), 925.5 (w), 747.4 (m), 724.3 (s) cm^{-1}; HRMS-(DART) for: $C_{16}H_{25}O$ $[M+H-H_2O]^+$: calculated: 233.1905, found: 233.1904.

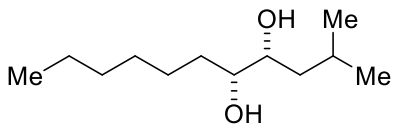


1-phenylundecane-4,5-diol (4.99). Prepared according to the general procedure for deborylative alkylation utilizing racemic 2,2',2''-(octane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (147.6 mg, 0.3000 mmol), (3-bromopropyl)benzene (39.8 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (41.8 mg, 79%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.32-7.29 (2H, m), 7.22 (2H, d, *J*= 7.0 Hz), 3.48-3.40 (2H, m), 2.73-2.63 (2H, m), 2.05 (1H, br s), 1.98 (1H, br s), 1.91-1.82 (1H, m), 1.79-1.70 (1H, m), 1.63-1.42 (6H, m), 1.37-1.27 (6H, m), 0.92 (3H, t, *J*= 5.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major isomer) 142.2, 128.4, 128.3, 125.8, 74.5, 74.3, 35.8, 33.6, 33.2, 31.8, 29.3, 27.4, 25.6, 22.6, 14.1; IR (neat): 3326.9 (br), 3062.1 (w), 3026.9 (w), 2918.3 (s), 2851.8 (s), 1605.3 (w), 1494.5 (m), 1456.4(m), 1334.5 (m), 1286.4 (m), 1226.0 (w), 1067.1 (m), 1019.7 (m),

938.4 (w), 854.6 (m), 746.3 (s), 719.5 (s), 695.9 (s), 491.6 (m) cm^{-1}; HRMS-(DART) for: $C_{17}H_{29}O_2$ $[M+H]^+$: calculated: 265.2168, found: 265.2168.



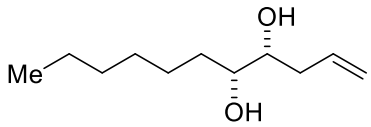
nonane-2,3-diol (4.113). Prepared according to the general procedure for deborylative alkylation utilizing racemic 2,2',2''-(octane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (147.6 mg, 0.3000 mmol), (3-bromopropyl)benzene (39.8 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a clear, colorless oil (41.8 mg, 79%). All spectral data are in accordance with the literature.[32] HRMS-(DART) for: $C_9H_{19}O$ $[M+H-H_2O]^+$: calculated: 143.1436, found: 143.1442.



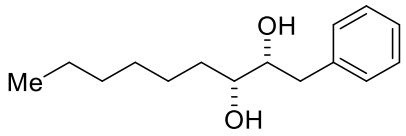
2-methylundecane-4,5-diol (4.106). Prepared according to the general procedure for deborylative alkylation utilizing racemic 2,2',2''-(octane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (147.6 mg, 0.3000 mmol), 1-bromo-2-methylpropane (27.4 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a clear, colorless oil (34.4 mg, 85%). ^1H NMR (500 MHz, $CDCl_3$): δ 3.48 (1H, dt, *J*= 9.0, 4.5 Hz), 3.37-3.34 (1H, m), 2.20 (2H, br s), 1.86-1.78 (1H, m), 1.51-1.20 (12H, m), 0.94 (3H, s, *J*= 7.0 Hz), 0.92 (3H, d, *J*= 6.5 Hz), 0.88 (3H, t, *J*= 6.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 75.0, 72.5, 42.7, 33.6, 31.8, 29.3, 25.6, 25.0, 23.7, 22.6,

[32] Li, X.; Tanasova, M.; Vasileiou, C.; Borhan, B. *J. Am. Chem. Soc.* **2008**, 130, 1885.

21.7, 14.0; IR (neat): 3363.2 (br), 2954.8 (s), 2927.4 (s), 2858.6 (s), 1466.9 (m), 1382.9 (w), 1367.2 (w), 1147.6 (w), 1066.5 (m), 843.5 (w) cm^{-1}; HRMS-(DART) for: $C_{12}H_{25}O$ $[M+H-H_2O]^+$: calculated: 185.1905, found: 185.1904.

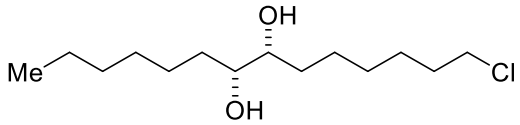


undec-1-ene-4,5-diol (4.107). Prepared according to the general procedure for deborylative alkylation utilizing racemic 2,2',2''-(octane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (147.6 mg, 0.3000 mmol), allyl chloride (15.3 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a clear, colorless oil (34.7 mg, 93%). ^1H NMR (500 MHz, $CDCl_3$): δ (major isomer) 5.85 (1H, ddt, *J*= 17.5, 10.5, 7.5 Hz), 5.17-5.14 (2H, m), 3.51-3.43 (2H, m), 2.38-2.32 (1H, m), 2.26-2.20 (3H, m), 1.53-1.42 (3H, m), 1.37-1.25 (7H, m), 0.87 (3H, t, *J*= 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major isomer) 134.5, 118.1, 73.9, 73.3, 38.3, 33.5, 31.8, 29.3, 25.6, 22.6, 14.0; IR (neat): 3376.1 (br), 3077.3 (w), 2954.8 (s), 2926.9 (s), 2857.1 (s), 1641.4 (w), 1458.7 (m), 1433.6 (m), 1285.7 (w), 1128.9 (w), 1062.5 (m), 996.1 (m), 913.1 (m), 870.4 (w) cm^{-1}; HRMS-(DART) for: $C_{11}H_{23}O_2$ $[M+H]^+$: calculated: 187.1698, found: 187.1692.

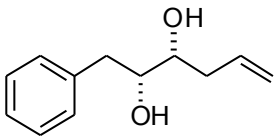


1-phenylnonane-2,3-diol (4.109). Prepared according to the general procedure for deborylative alkylation utilizing racemic 2,2',2''-(octane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaboro-lane) (147.6 mg, 0.3000 mmol), benzyl chloride (25.3 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2,

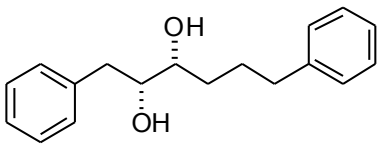
20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (42.6 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.32 (2H, t, *J*= 8.0 Hz), 7.26-7.23 (3H, m), 3.68 (1H, dt, *J*= 8.5, 4.5 Hz), 3.49 (1H, dt, *J*= 8.5, 4.5 Hz), 2.90 (1H, dd, *J*= 13.5, 4.5 Hz), 2.75 (1H, dd, *J*= 13.5, 9.0 Hz), 2.09 (1H, br s), 1.97 (1H, br s), 1.59-1.23 (10H, m), 0.87 (3H, t, *J*= 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (major isomer) 138.1, 129.4, 128.6, 126.6, 75.0, 73.6, 40.3, 33.7, 31.8, 29.3, 25.6, 22.6, 14.1; IR (neat): 3379.6 (br), 3062.4 (w), 2953.6 (s), 2925.7 (s), 2856.0 (s), 1603.8 (w), 1495.7 (m), 1454.9 (m), 1179.7 (w), 1128.8 (m), 1060.7 (m), 747.7 (m), 699.3 (s) 514.4 (w) cm^{-1}; HRMS-(DART) for: $C_{15}H_{23}O$ $[M+H-H_2O]^+$: calculated: 219.1749, found: 219.1751.



1-chlorotetradecane-7,8-diol (4.112). Prepared accord-ing to the general procedure for deborylative alkylation utilizing racemic 2,2',2"-(octane-1,1,2-triyl)tris-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (147.6 mg, 0.3000 mmol), 1-bromo-6-chlorohexane (39.9 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (43.0 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 3.53 (2H, t, *J*= 7.0 Hz), 3.42-3.38 (2H, m), 2.07 (1H, br s), 2.00 (1H, s), 1.78 (2H, dt, *J*= 14.0, 7.0 Hz), 1.52-1.25 (18H, m), 0.88 (3H, t, *J*= 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major isomer) 74.5, 74.4, 45.1, 33.6, 33.5, 32.5, 31.8, 29.3, 28.9, 26.8, 25.6, 25.5, 22.6, 14.0; IR (neat): 3337.8 (br), 2928.4 (s), 2854.7 (s), 1463.4 (m), 1408.1 (w), 1377.5 (w), 1284.1 (w), 1135.0 (m), 1009.7 (m), 724.8 (m), 652.1 (m) cm^{-1}; HRMS-(DART) for: $C_{14}H_{28}ClO$ $[M+H-H_2O]^+$: calculated: 247.1829, found: 247.1820.



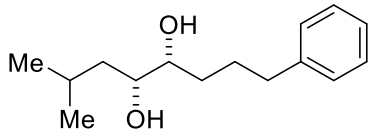
1-phenylhex-5-ene-2,3-diol (4.108). Prepared according to the general procedure for deborylative alkylation utilizing racemic 2,2',2''-(3-phenylpropane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (149.4 mg, 0.3000 mmol), allyl chloride (15.3 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (32.1 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.33-7.30 (2H, m), 7.25-7.22 (3H, m), 5.85 (1H, ddt, *J*= 17.5, 10.5, 7.5 Hz), 5.17-5.13 (2H, m), 3.72 (1H, dt, *J*= 8.5, 4.0 Hz), 3.57 (1H, dt, *J*= 8.5, 4.0 Hz), 2.90 (1H, dd, *J*= 14.0, 5.0 Hz), 2.78 (1H, dd, *J*= 14.0, 9.0 Hz), 2.41-2.29 (2H, m), 2.13 (1H, br s), 2.01(1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$): δ (major isomer) 138.3, 134.6, 129.6, 128.8, 126.8, 118.4, 74.6, 72.4, 40.4, 38.6; IR (neat): 3377.7 (br), 2919.4 (m), 1495.1 (m), 1454.0 (m), 1434.0 (m), 1077.0 (m), 1041.6 (s), 994.8 (m), 914.0 (s), 868.8 (m), 745.1 (m), 698.2 (s) cm^{-1}; HRMS-(DART) for: $C_{12}H_{15}O$ $[M+H-H_2O]^+$: calculated: 175.1123, found: 175.1122. The relative configuration (*syn* diol) was assigned by comparing the ^{1}H and ^{13}C NMR spectra of the prepared sample of the title compound with the spectra of *syn*-1-phenylhex-5-ene-2,3-diol previously reported in the literature.[33]



1,6-diphenylhexane-2,3-diol (4.101). Prepared according to the general procedure for deborylative alkylation

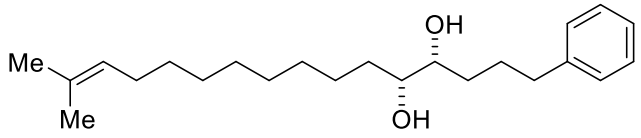
[33] Jiao, P.; Kaasaki, M.; Yamamoto, H. *Angew. Chem. Int. Ed.* **2009**, 48, 3333.

utilizing racemic 2,2',2''-(3-phenylpropane-1,1,2-triyl) tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (149.4 mg, 0.3000 mmol), (3-bromopropyl)benzene (39.8 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (46.5 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.31-7.17 (10H, m), 3.67 (1H, dt, *J*= 9.0, 4.5 Hz), 3.50 (1H, dt, *J*= 8.5, 4.5 Hz), 2.86 (1H, dd, *J*= 14.0, 5.0 Hz), 2.73 (1H, dd, *J*= 14.0, 9.0 Hz), 2.70-2.60 (2H, m), 2.04 (2H, br s), 1.89-1.80 (1H, m), 1.76-1.67 (1H, m), 1.64-1.54 (2H, m) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ (major isomer) 142.4, 138.2, 129.6, 128.9, 128.6, 128.5, 126.8, 126.0, 75.1, 73.5, 40.4, 36.0, 33.4, 27.6; IR (neat): 3377.7 (br), 2976.8 (m), 2924.6 (m), 1312.7 (m), 1264.9 (s), 1137.9 (s), 969.7 (m), 844.5 (m) cm^{-1}; HRMS-(DART) for: $C_{18}H_{21}O$ $[M+H-H_2O]^+$: calculated: 253.1592, found: 253.1587.

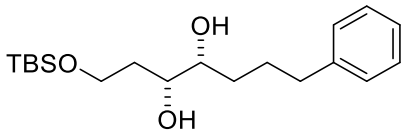


7-methyl-1-phenyloctane-4,5-diol (4.102). Prepared according to the general procedure for deborylative alkylation utilizing racemic 2,2',2''-(4-methylpentane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (139.2 mg, 0.3000 mmol), (3-bromopropyl)benzene (39.8 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (33.6 mg, 71%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.28-7.25 (2H, m), 7.18-7.15 (3H, m), 3.46 (1H, dt, *J*= 8.5, 4.0 Hz), 3.37 (1H, dt, *J*= 8.5, 4.5 Hz), 2.69-2.58 (2H, m), 2.04 (1H, br s), 1.92(1H, br s), 1.85-1.74 (2H, m), 1.72-1.66 (1H, m), 1.58-1.43 (2H, m), 1.39 (1H,

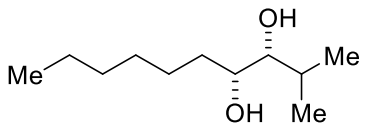
ddd, *J*= 14.5, 10.0, 5.0 Hz), 1.91 (1H, ddd, *J*= 13.0, 9.5, 3.5 Hz), 0.92 (3H, d, *J*= 7.0 Hz), 0.89(3H, d, *J*= 6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (major isomer) 142.4, 128.6, 128.5, 126.0, 75.0, 72.7, 42.9, 36.0, 33.8, 27.6, 24.7, 23.9, 21.9; IR (neat): 3363.5 (br), 2951.6 (m), 2927.7 (m), 2866.8 (m), 1495.9 (m), 1453.4 (m), 1142.1 (m), 1064.1 (m), 1030.3 (m), 746.9 (m), 697.3 (s), 489.6 (m) cm^{-1}; HRMS-(DART) for: $C_{15}H_{23}O$ [M+H-H_2O]$^+$: calculated: 219.1749, found: 219.1951.



15-methyl-1-phenylhexadec-14-ene-4,5-diol. Prepared according to the general procedure for deborylative alkylation utilizing racemic 2,2',2''-(12-methyltridec-11-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2- dioxaborolane) (172.3 mg, 0.3000 mmol), (3-bromopropyl)benzene (39.8 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (46.3 mg, 67%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.27-7.24 (2H, m), 7.17-7.14 (3H, m), 5.10 (1H, tt, *J*= 7.0, 1.5 Hz), 3.43-3.36 (2H, m), 2.68-2.58 (2H, m), 1.94 (2H, q, *J*= 6.5 Hz), 1.85-1.77 (1H, m), 1.72-1.67 (4H, m), 1.65-1.35 (7H, m), 1.30-1.26 (12H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ (major isomer) 142.4, 131.3, 128.6, 128.5, 126.0, 125.1, 74.7, 74.5, 36.0, 33.8, 33.4, 30.1, 29.8, 29.7, 29.7, 29.5, 28.2, 27.6, 25.9, 25.8, 17.9; IR (neat): 3385.0.3 (br), 2925.0 (s), 2854.0 (m), 1603.3 (m), 1496.1 (m), 1454.0 (m), 1376.7 (w), 1313.2 (m), 1069.5 (m), 1030.1 (m), 747.9 (m), 698.8 (m), 558.2 (w) cm^{-1}; HRMS-(DART) for: $C_{23}H_{37}O$ [M+H-H_2O]$^+$: calculated: 329.2844, found: 329.2846.

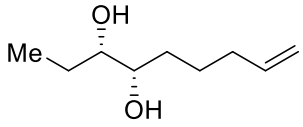


1-((*tert*-butyldimethylsilyl)oxy)-7-phenylheptane-3,4-diol (4.104). Prepared according to the general procedure for deborylative alkylation utilizing racemic *tert*-butyldimethyl(3,4,4-tris-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)silane (169.9 mg, 0.3000 mmol), (3-bromopropyl)benzene (39.8 mg, 0.200 mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a clear, colorless oil (61.2 mg, 94%). Diastereoselectivity was determined by SFC (see spectral data section). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.27 (2H, t, *J*= 7.5 Hz), 7.19-7.16 (3H, m), 3.90-3.82 (2H, m), 3.68 (1H, dt, *J*= 3.0, 7.5 Hz), 3.57 (1H, d, *J*= 7.5 Hz), 3.45 (1H, dt, *J*= 11.0, 5.5 Hz), 2.65 (1H, dt, *J*= 6.5, 8.5 Hz), 2.60 (1H, d, *J*= 5.5 Hz), 1.90-1.63 (4H, m), 1.58-1.51 (2H, m), 0.90 (9H, s), 0.09 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major isomer) 142.4, 128.4, 128.3, 125.7, 74.2, 74.1, 62.0, 35.9, 35.1, 33.1, 27.6, 25.8, 18.1, -5.6, -5.6; IR (neat): 3402.9 (br), 3026.6 (w), 2950.8 (s), 2928.2 (s), 2856.8 (s), 1496.3 (w), 1471.0 (m), 1462.1 (m), 1361.2 (w), 1254.3 (s), 1090.6 (br), 1005.9 (m), 938.0 (m), 834.9 (s), 776.8 (s), 747.9 (m), 698.6 (m), 663.6 (w) cm^{-1}; HRMS-(DART) for: $C_{11}H_{23}O$ $[M+H]^+$: calculated: 339.2356, found: 339.2345.



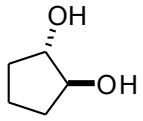
2-methyldecane-3,4-diol (4.110). Prepared according to the general procedure for deborylative alkylation utilizing racemic 2,2',2''-(octane-1,1,2-triyl)tris-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (147.6 mg, 0.3000 mmol), 2-bromopropane (24.6 mg, 0.200 mmol), sodium *tert*-butoxide (96.1

mg, 1.00 mmol) and toluene (1.30 mL). The crude material was purified (SiO_2, 20% ethyl acetate in hexane, UV/magic stain) to give the desired product as a clear, colorless oil (28.5 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 3.59 (1H, dt, *J*= 8.0, 4.5 Hz), 3.13 (1H, t, *J*= 5.0 Hz), 2.14 (1H, br s), 1.79 (1H, sept, *J*= 7.0 Hz), 1.50-1.25 (10H, m), 0.96 (3H, d, *J*= 7.0 Hz), 0.93 (3H, d, *J*= 6.5 Hz), 0.88 (3H, t, *J*= 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major isomer) 79.0, 71.9, 33.9, 31.8, 30.1, 29.3, 25.6, 22.6, 19.7, 17.0, 14.0; IR (neat): 3378.4 (br), 2956.6 (s), 1926.6 (s), 2871.7 (s), 2857.2 (s), 1466.4 (m), 1383.5 (w), 1366.6 (w), 1176.9 (w), 1063.2 (m), 998.9 (m), 725.5 (w) cm^{-1}; HRMS-(DART) for: $C_{11}H_{23}O$ $[M+H-H_2O]^+$: calculated: 171.1749, found: 171.1751.

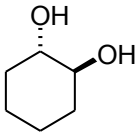


(3*S*,4*S*)-non-8-ene-3,4-diol (4.114). Prepared according to the general procedure for deborylative alkylation utilizing (*R*)-2,2',2''-(butane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaboro-lane) (218.0 mg, 0.5000 mmol), 5-bromopent-1-ene (62.1 mg, 0.417 mmol), sodium *tert*-butoxide (200 mg, 2.08 mmol) and toluene (2.20 mL). The crude material was purified (SiO_2, 30% ethyl acetate in hexane, UV/magic stain) to give the desired product as a clear, colorless oil, which co-eluted with pinacol (166.6 mg, product:pinacol = 1.00:3.31, 73%). All spectral data are in accordance with the literature.[34] HRMS-(DART) for: $C_9H_{19}O_2$ $[M+H]^+$: calculated: 159.1385, found: 159.1385. $[\alpha]_D^{20}$ = -16.200 (*c* = 1.695, $CHCl_3$, *l* = 50 mm).

[34] Page, P.C.B.; Rayner, C.M.; Sutherland, I.O. *J. Chem.Soc. Perkin Trans. I.* **1990**, 5, 1375.



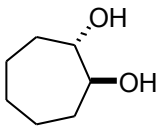
***anti*-cyclopentane-1,2-diol (4.115)**. Prepared according to the general procedure for deborylative cyclization/oxidation utilizing racemic 2,2',2''-(5-chloropentane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (96.9 mg, 0.2000 mmol), or 2,2',2''-(5-bromopentane-1,1,2-triyl)tris(4,4,5,5- tetramethyl-1,3,2-dioxaborolane) (105.8 mg, 0.2000mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (0.87 mL). The crude material was purified (SiO_2, 50% ethyl acetate in hexane, magic stain) to give the desired product as a white solid (9.0 mg, 44% from chloro-1,1,2-tris(boronate)esters, 7.4 mg, 36% from bromo-1,1,2- tris(boronate)esters). All spectral data are in accordance with the literature.[35] The relative configuration (*anti* diol) was assigned by comparing the ^1H and ^{13}C NMR spectra of the prepared sample of the title compound with the spectra of *anti*-cyclopentane-1,2-diol previously reported in the literature.[35]



***anti*-cyclohexane-1,2-diol (4.118).** Prepared according to the general procedure for deborylative cyclization/oxidation utilizing racemic 2,2',2''-(6-chlorohexane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (99.7 mg, 0.2000 mmol), or 2,2',2''-(6-bromohexane-1,1,2-triyl)tris (4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (111.4 mg, 0.2000mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (0.87 mL). The crude material was purified (SiO_2, 50% ethyl acetate in hexane, magic stain) to give the desired product as a white solid (15.6 mg, 67% from chloro-1,1,2-tris(boronate)esters, 14.4 mg, 62% from bromo-1,1,2- tris(boronate)esters). All spectral data are in accordance with the literature.[35] The relative configuration (*anti* diol)

[35] Muller, C.E.; Wanka, L.; Jewell, K.; Schreiner, P.R. *Angew. Chem. Int. Ed.* **2008**, 47, 6180.

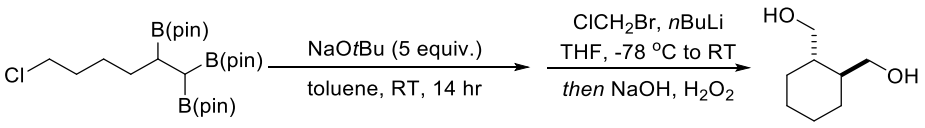
was assigned by comparing the ^{1}H and ^{13}C NMR spectra of the prepared sample of the title compound with the spectra of *anti*-cyclohexane-1,2-diol previously reported in the literature.[35]

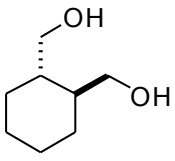


***anti*-cycloheptane-1,2-diol (4.117).** Prepared according to the general procedure for deborylative cyclization/oxidation utilizing racemic 2,2',2''-(7-bromoheptane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (113.4 mg, 0.2000mmol), sodium *tert*-butoxide (96.1 mg, 1.00 mmol) and toluene (0.87 mL). The crude material was purified (SiO_2, 50% ethyl acetate in hexane, magic stain) to give the desired product as a white solid (15.1 mg, 58%). All spectral data are in accordance with the literature.[35] The relative configuration (*anti* diol) was assigned by comparing the ^{1}H and ^{13}C NMR spectra of the prepared sample of the title compound with the spectra of *anti*-cyclohexane-1,2-diol previously reported in the literature.[35]

4.6.2.8. Additional transformations of 1,1,2-tris(boronate)esters

Procedure for deborylative cyclization/homologation/oxidation of 2,2',2''-(6-chlorohexane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)





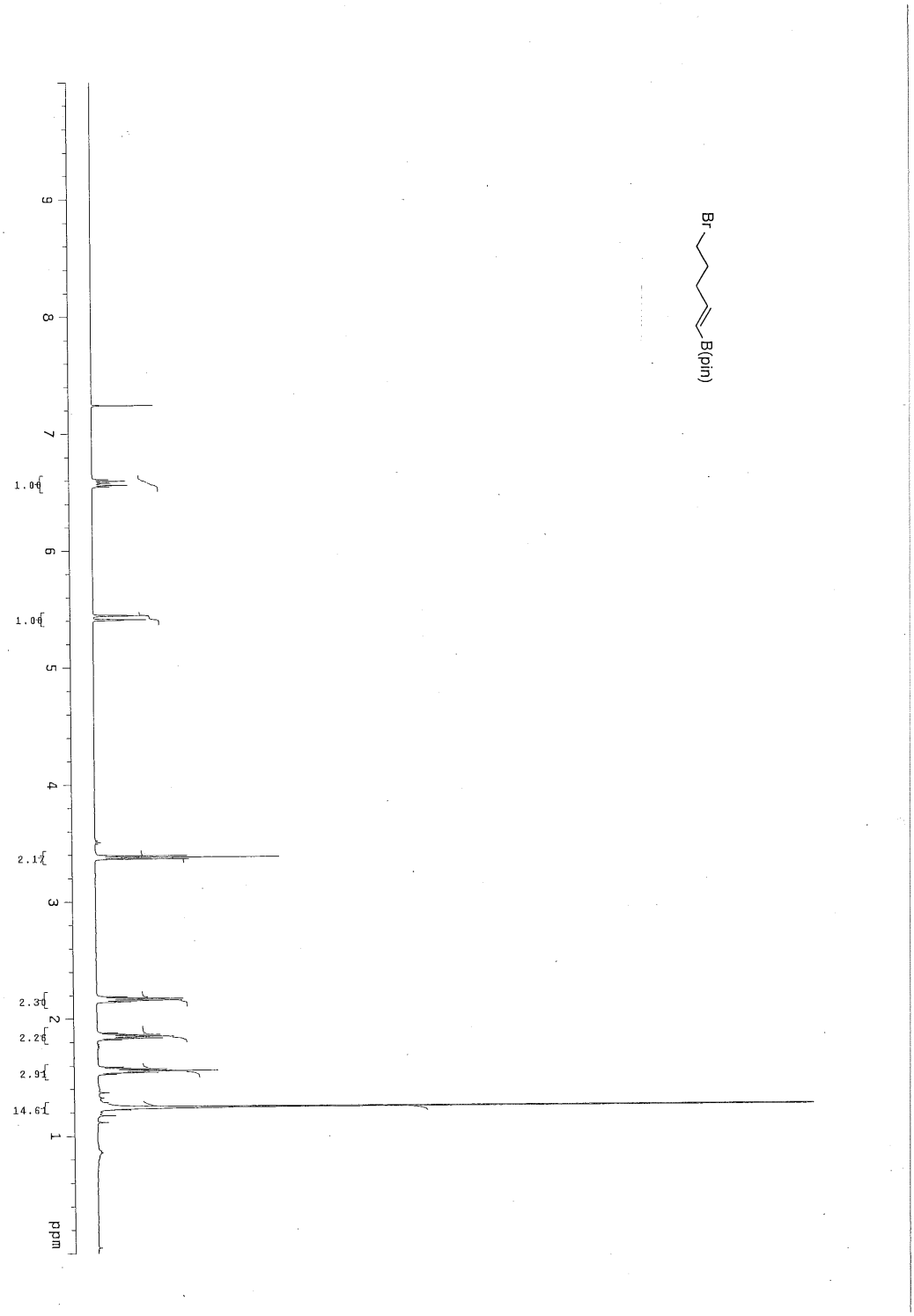
***anti*-cyclohexane-1,2-diyldimethanol (4.119).** To an oven-dried 2-dram vial equipped with a magnetic stirbar in the glovebox was added 2,2',2''-(6- chlorohexane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)

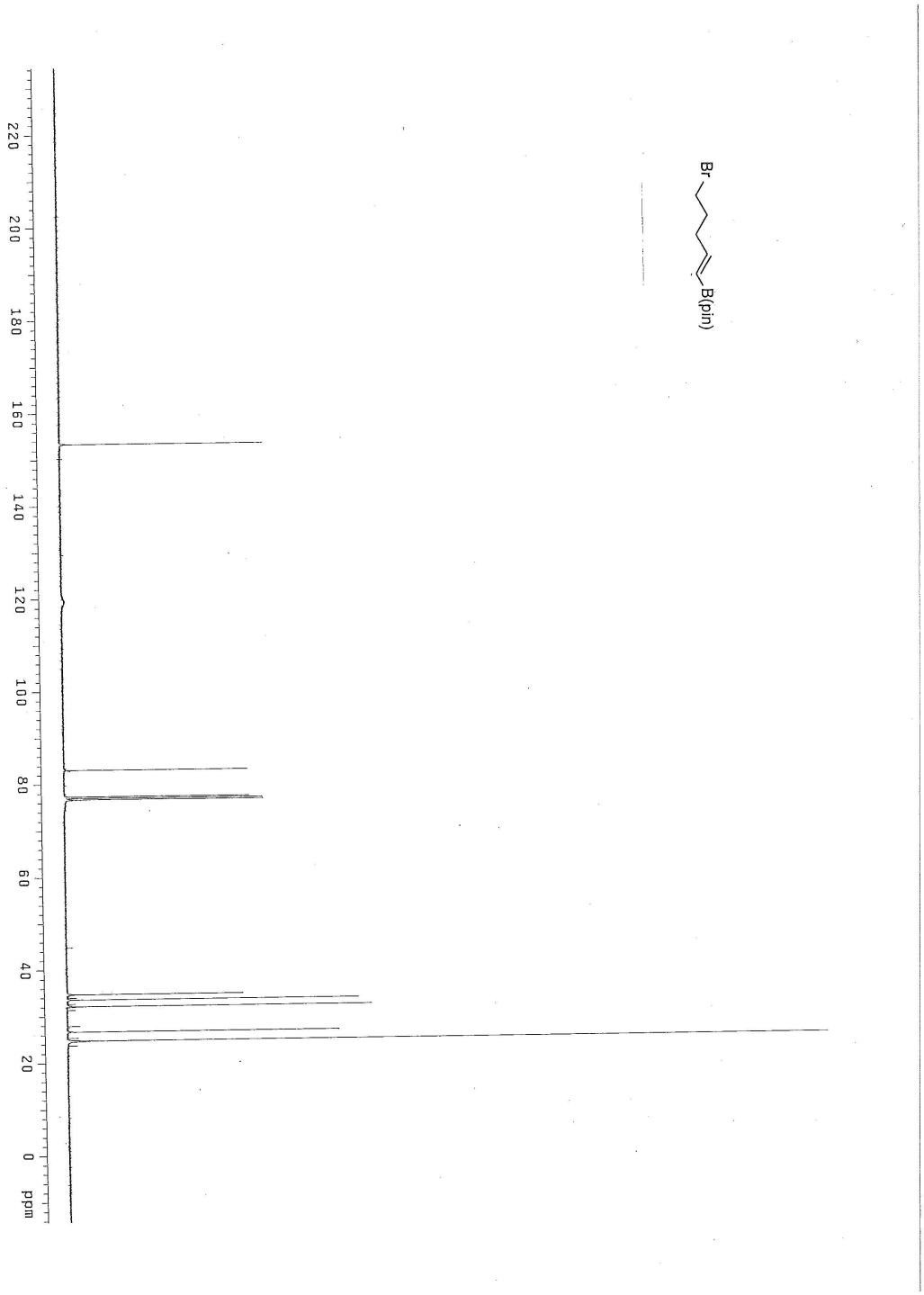
(99.7 mg, 0.2000 mmol) and sodium *tert*-butoxide (96.1 mg, 1.00 mmol), followed by toluene (0.87 mL). The reaction vessel was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at room temperature for 14 hours. The reaction mixture was pushed through a silica gel plug with diethyl ether, and the obtained crude was used in next step without future purification.

To an oven-dried 2-dram vial equipped with a septum cap was added the crude material followed by THF (2.0 mL), and the flask cooled to 78°C. To the reaction vial was added bromochloromethane (28μL, 0.44 mmol) and *n*-BuLi (0.18 mL, 0.44 mmol), sequentially. After 10 min, the cooling bath was removed and the contents stirred for 12 h. The reaction mixture was then transferred to a 6-dram vial and diluted with THF (2 mL). The crude mixture was cooled to 0 °C and 3M NaOH (1.5 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. $Na_2S_2O_3$ (1.5 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 purified by silica gel chromatography (50% ethyl acetate in hexane) give the desired product as a colorless oil (10.4 mg, 36% yield). All spectral data are in accordance with the literature.[36] The relative configuration (*anti*) was assigned by comparing the ^{1}H and ^{13}C NMR spectra of the prepared sample of the title compound with the spectra of *anti*-cyclohexane-1,2-diyldimethanol previously reported in the literature.[36]

[36] Zhang, X.; Huang, K.; Hou, G.; Cao, B.; Zhang, X. *Angew. Chem.* **2010**, *122*, 6565.

4.6.3. NMR spectra of representative compounds

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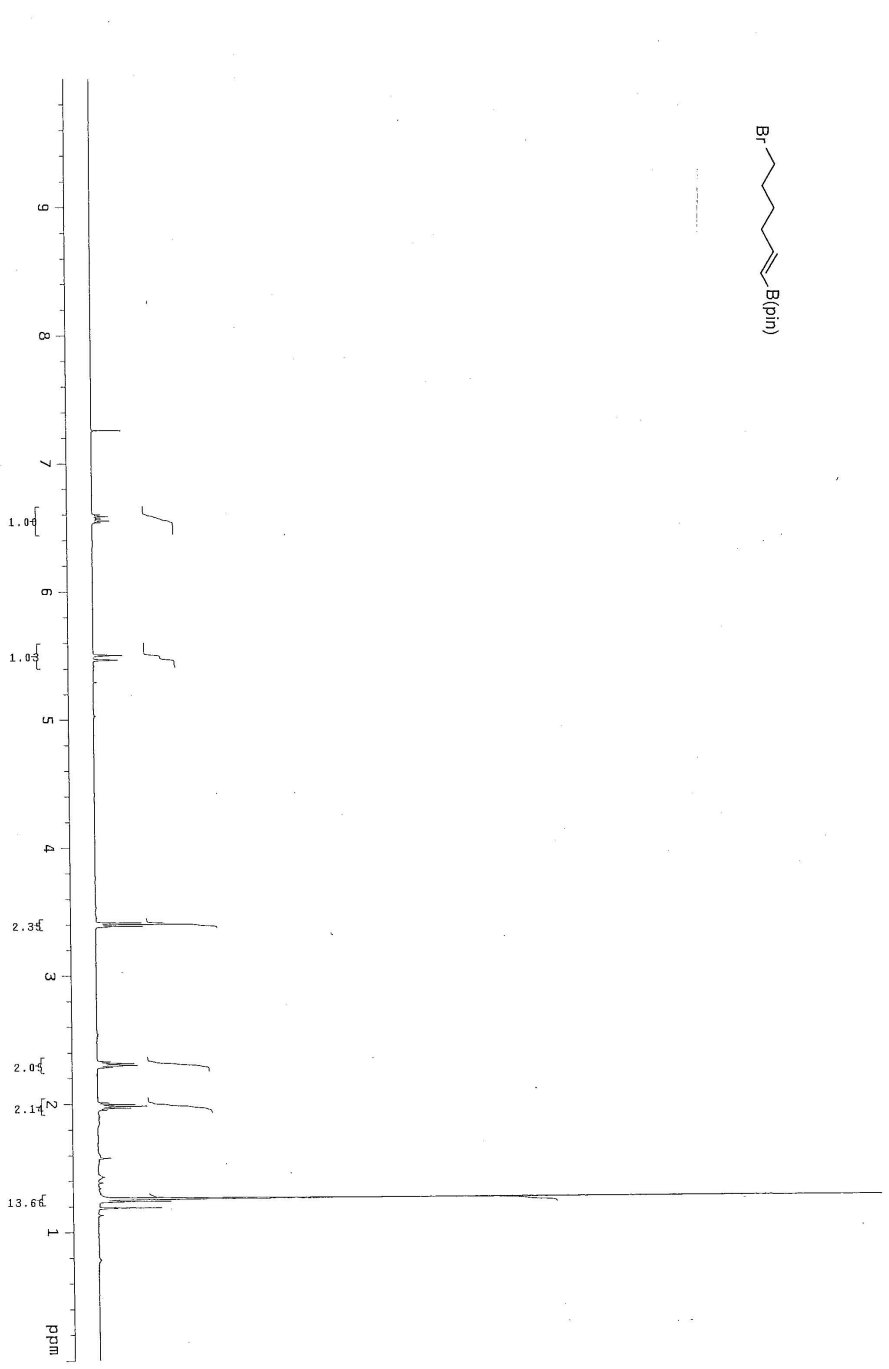
ppm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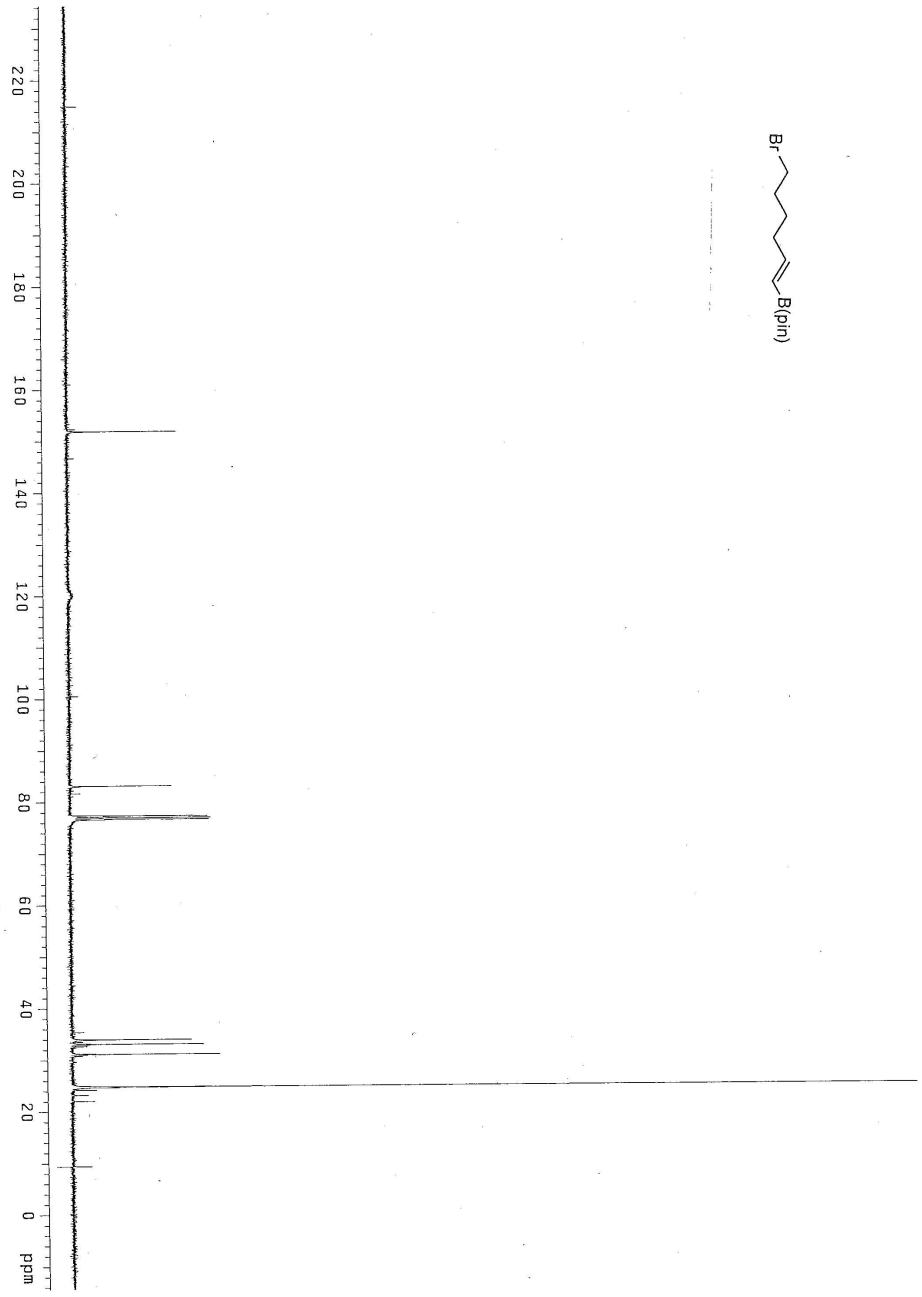
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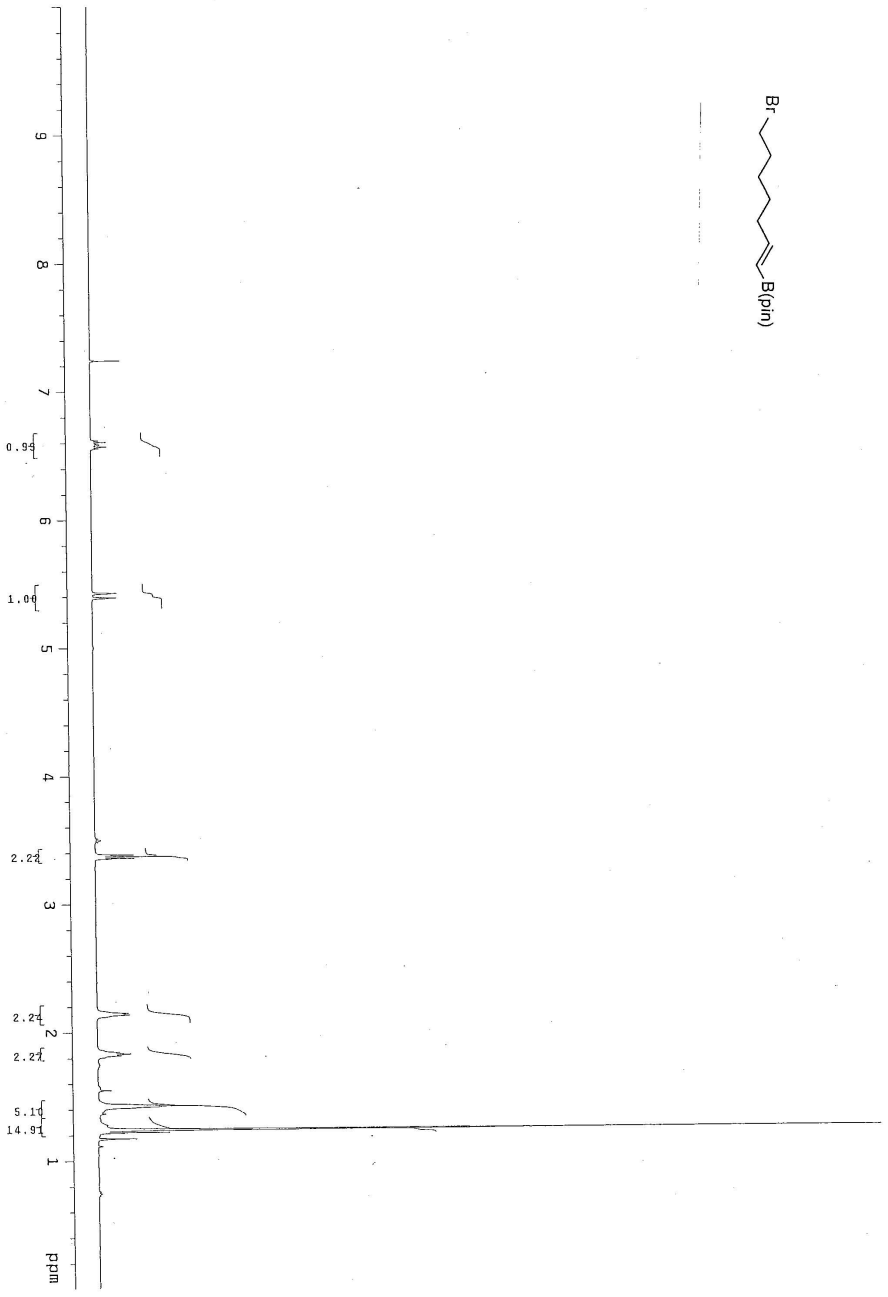
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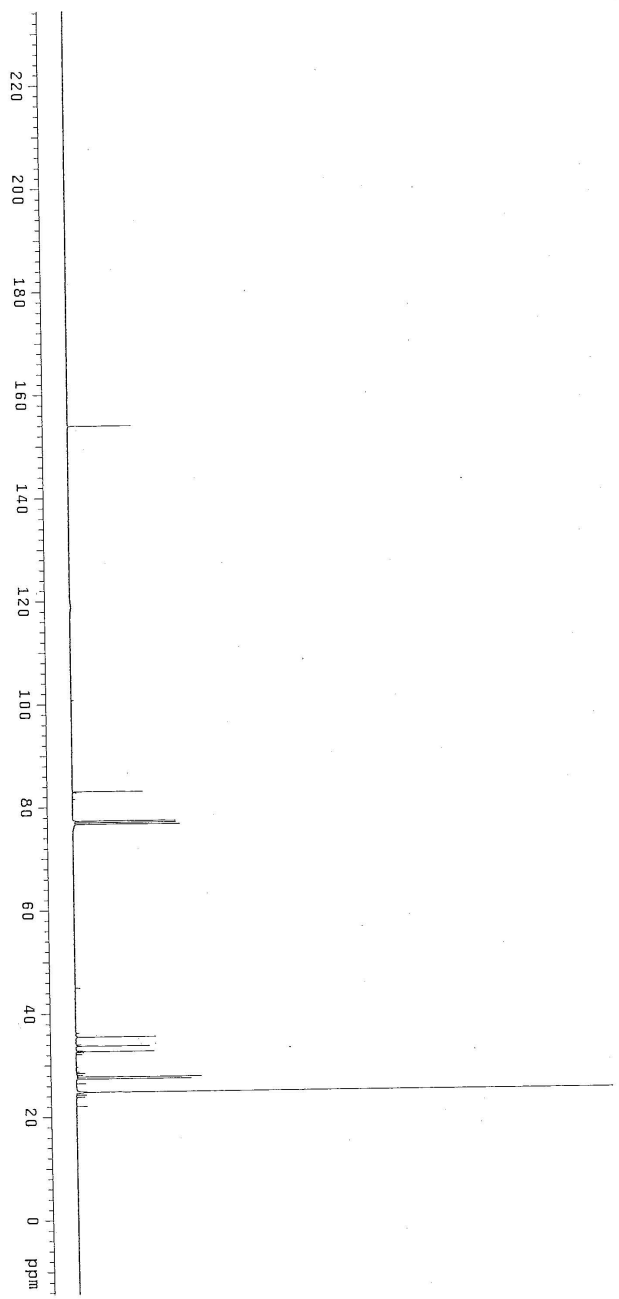
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140
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100
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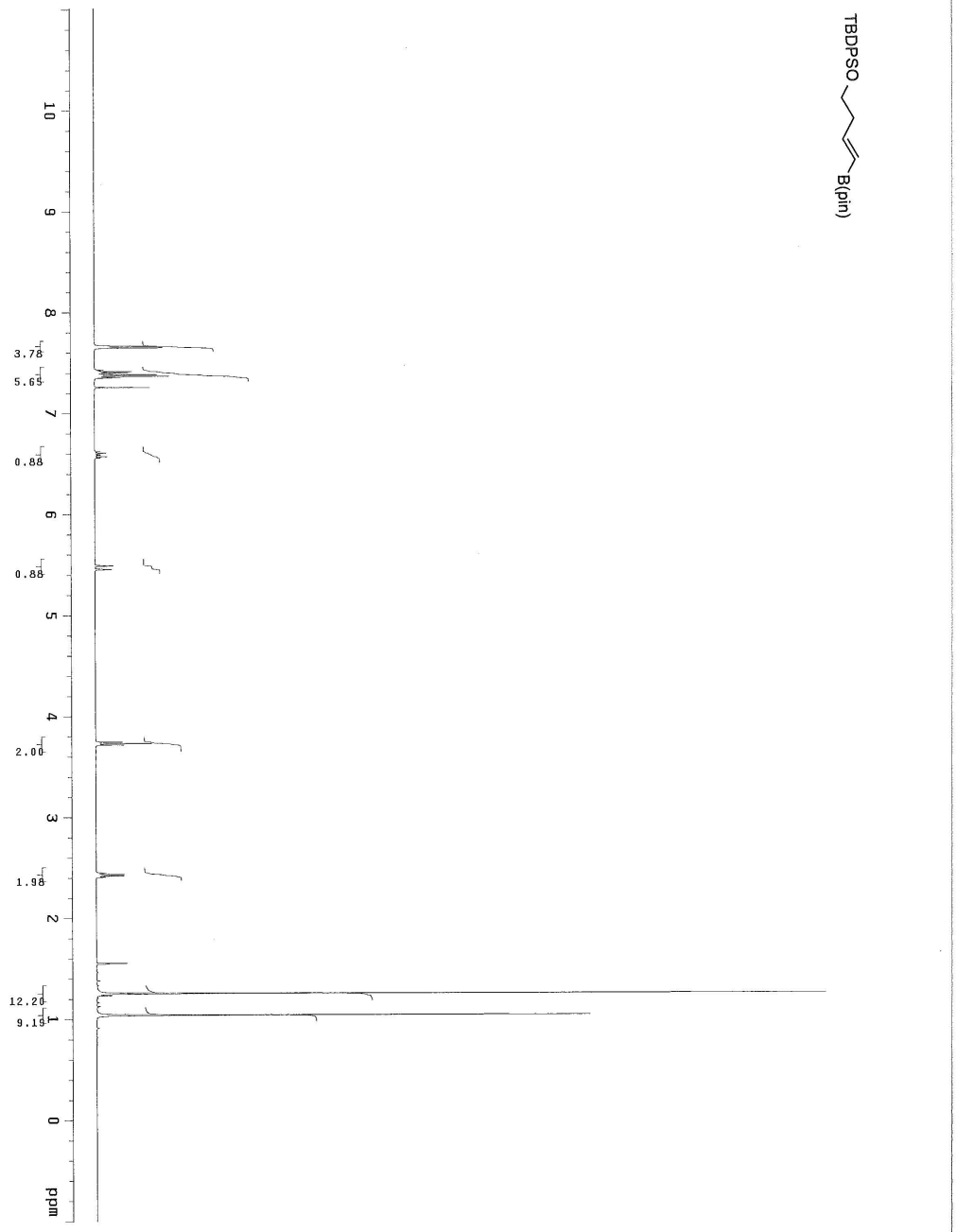
ppm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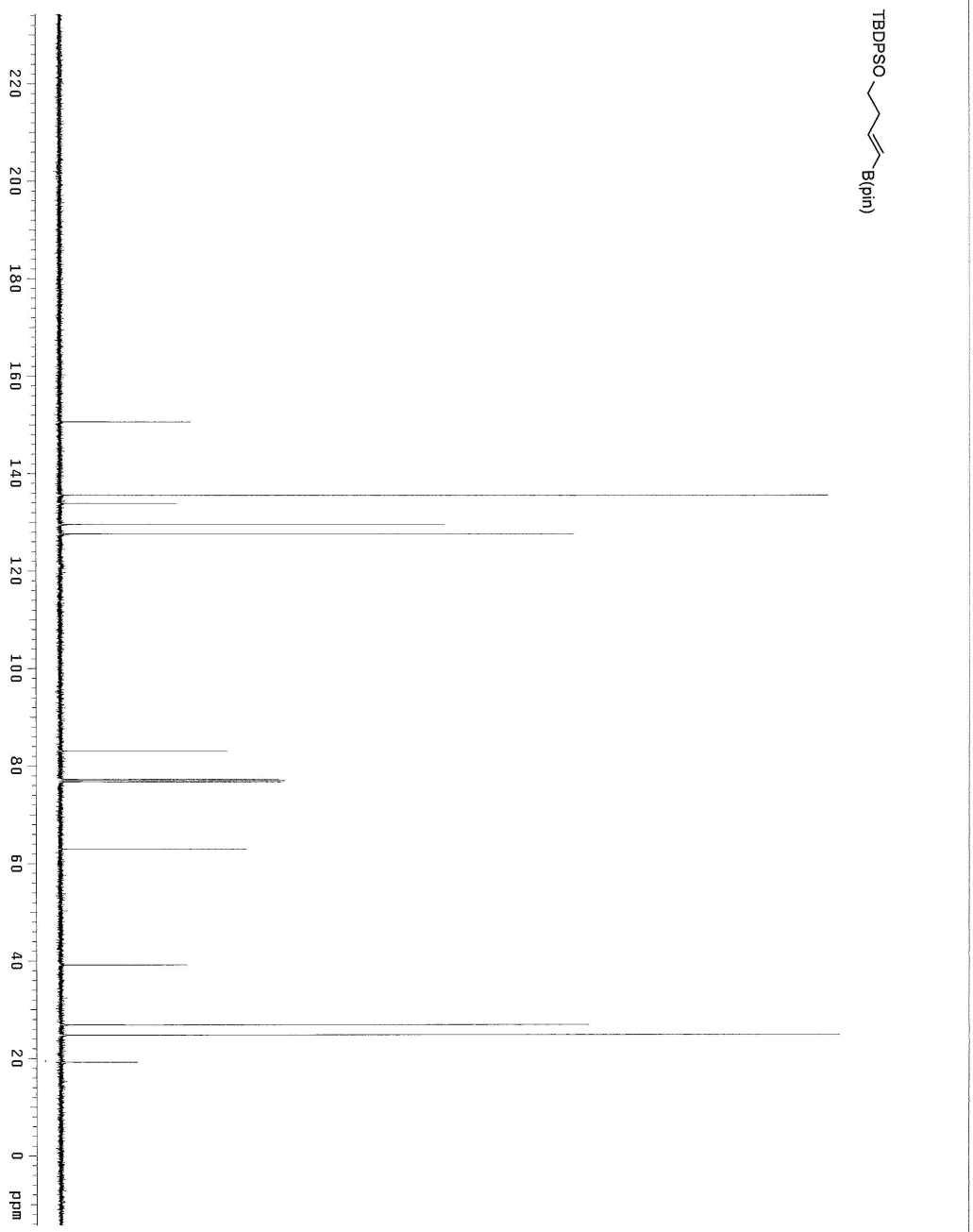
ppm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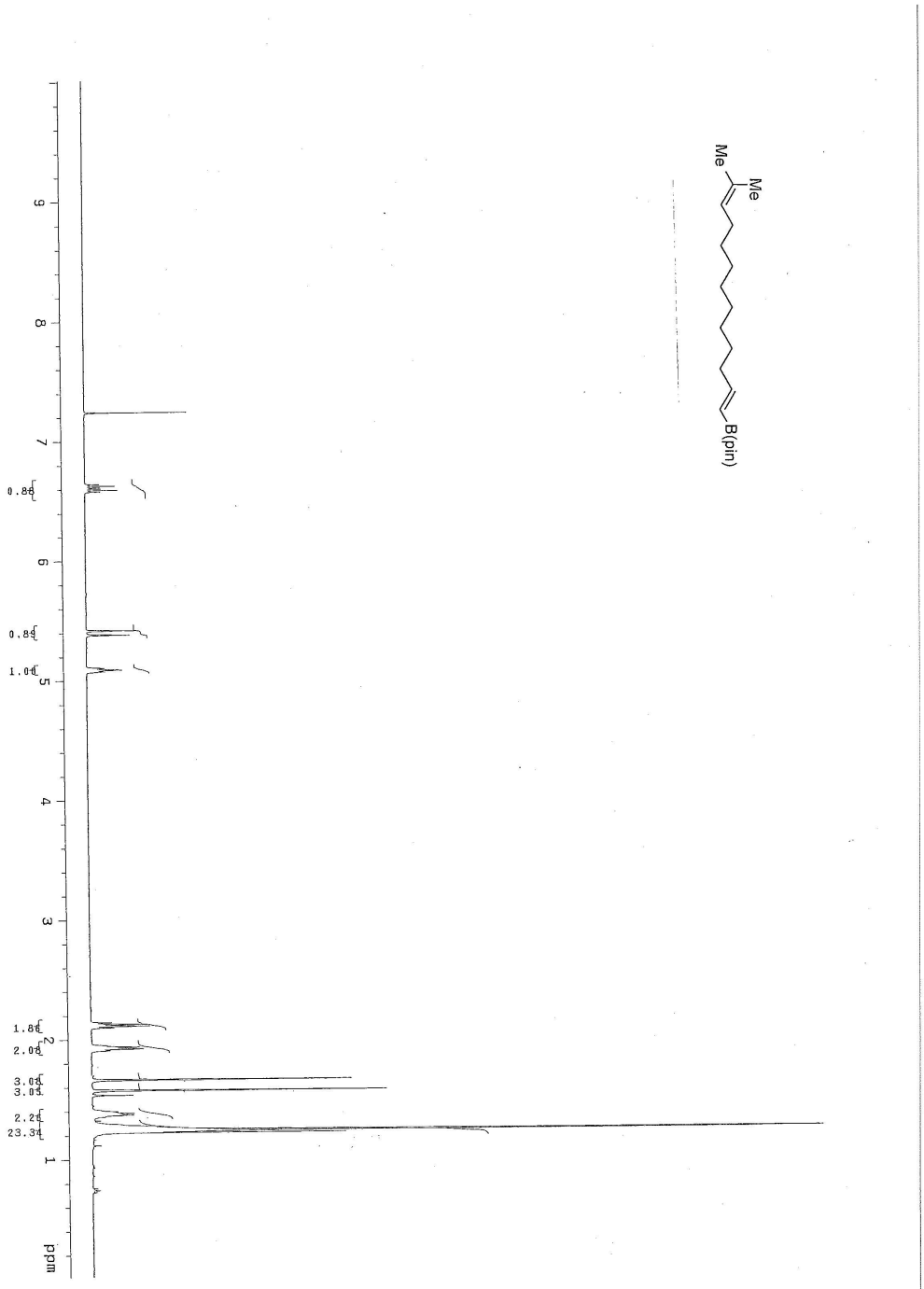
ppm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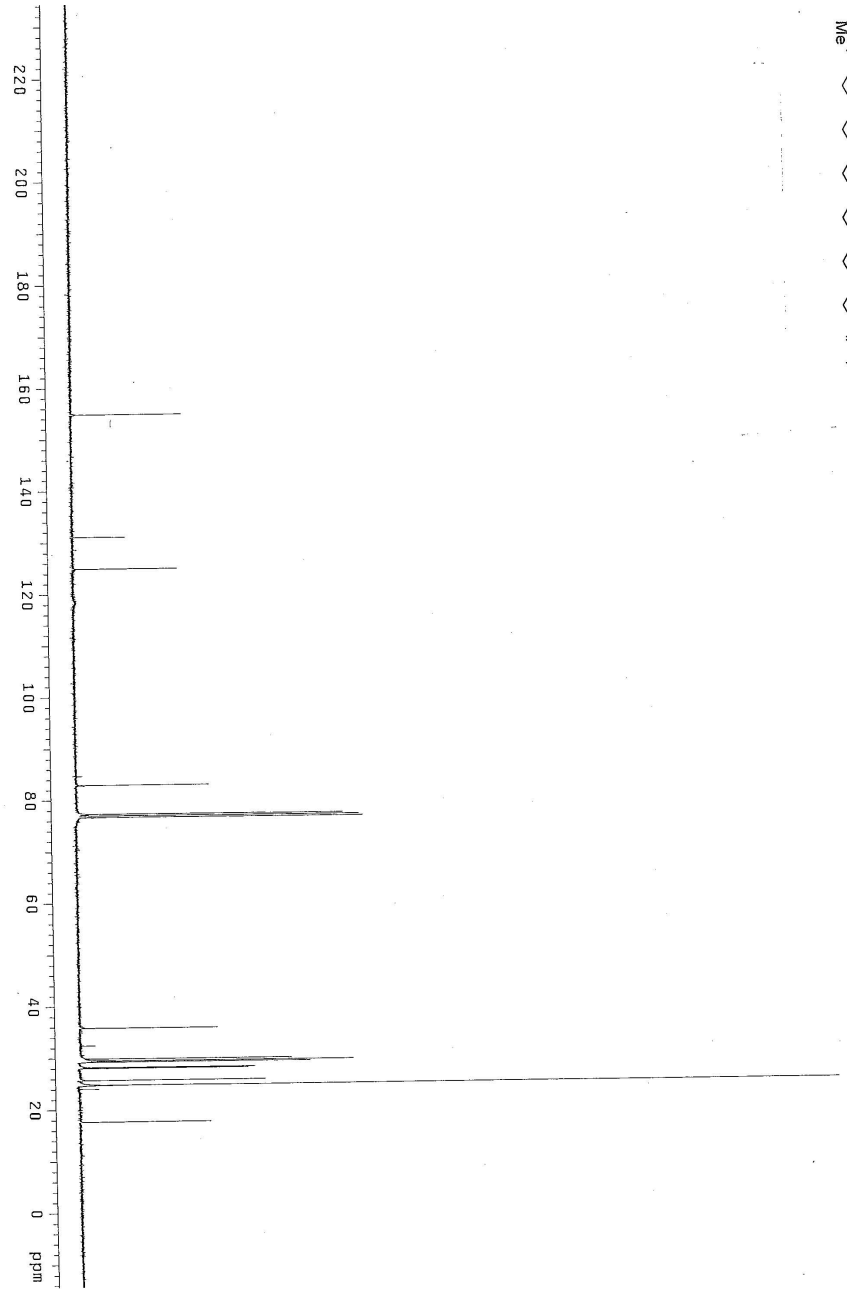
Me
Me
B(pin)
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200
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100
80
60
40
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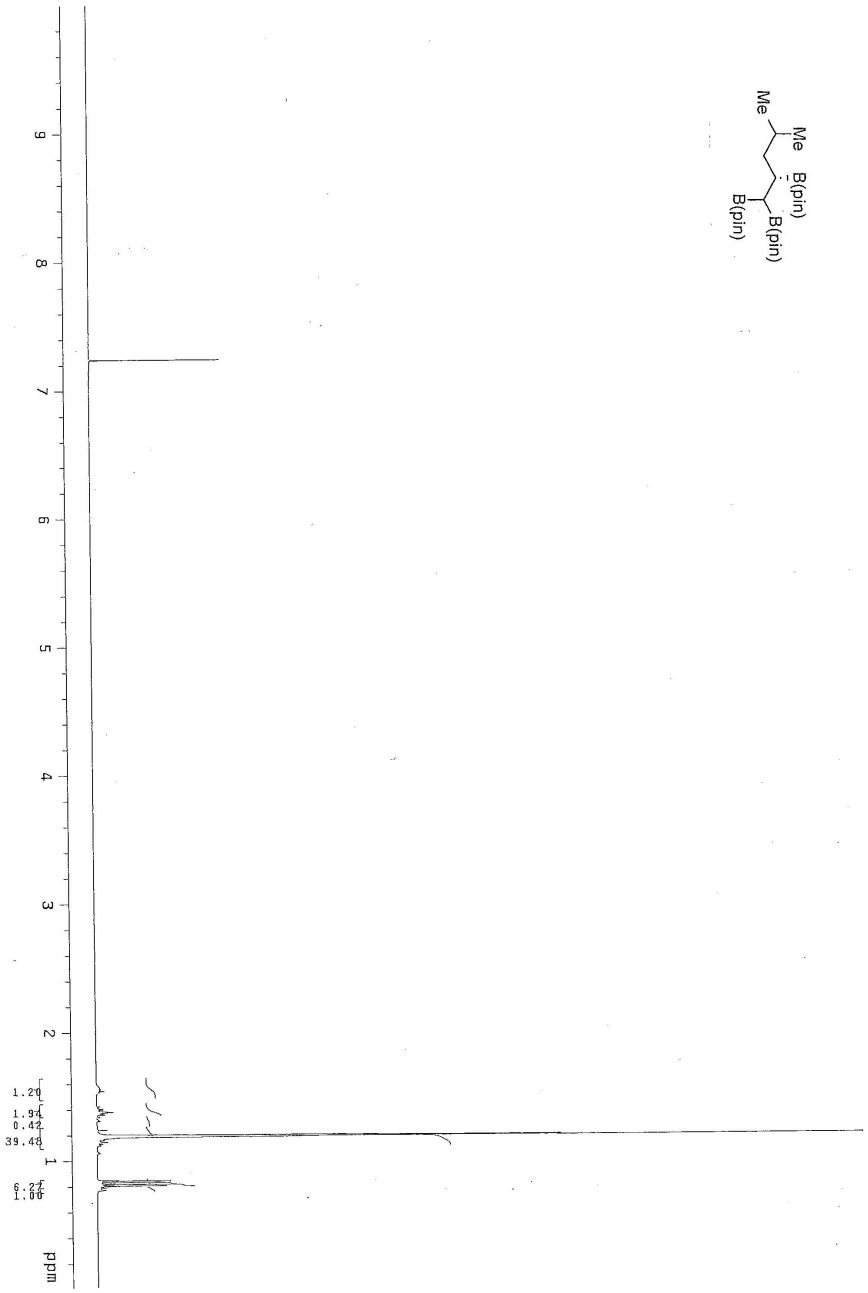
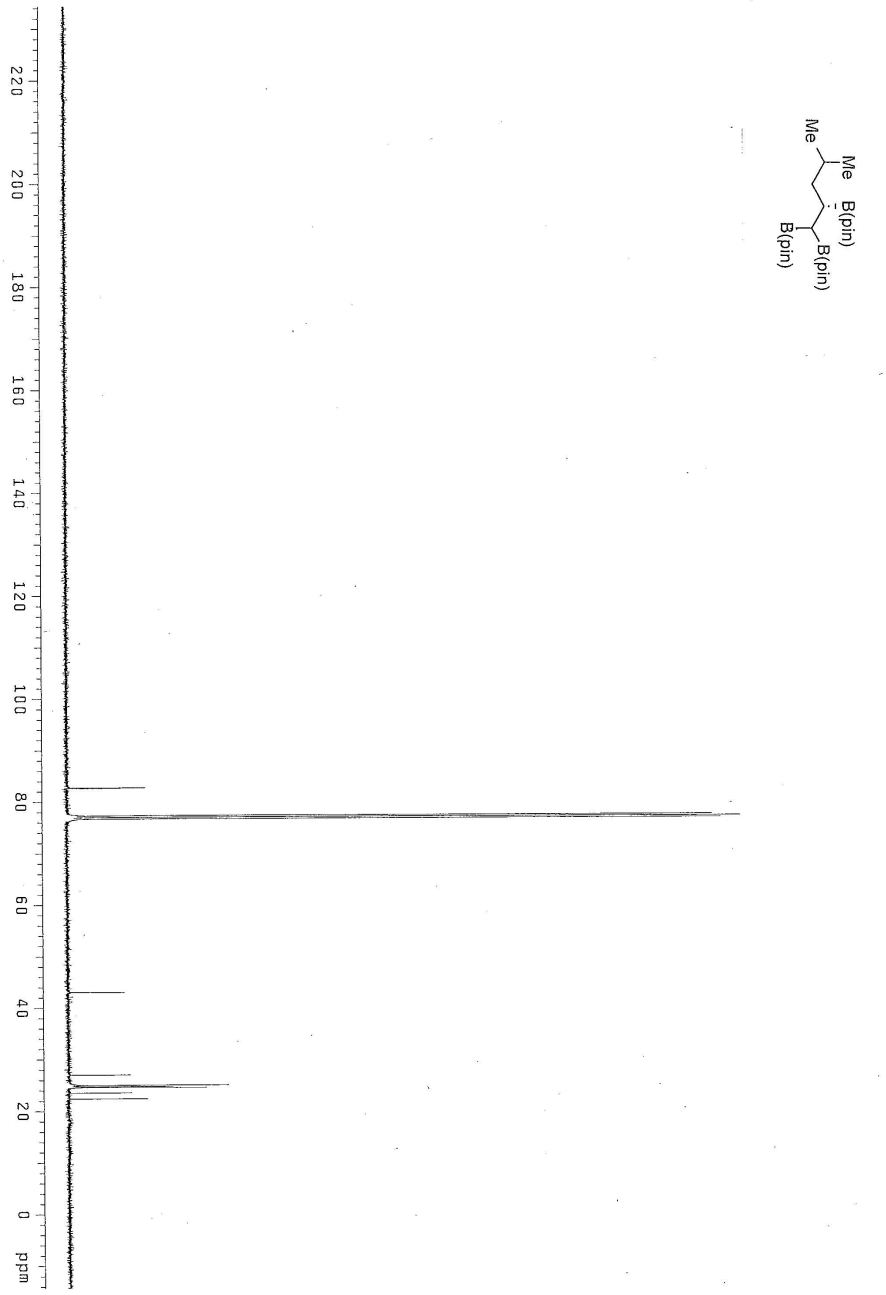
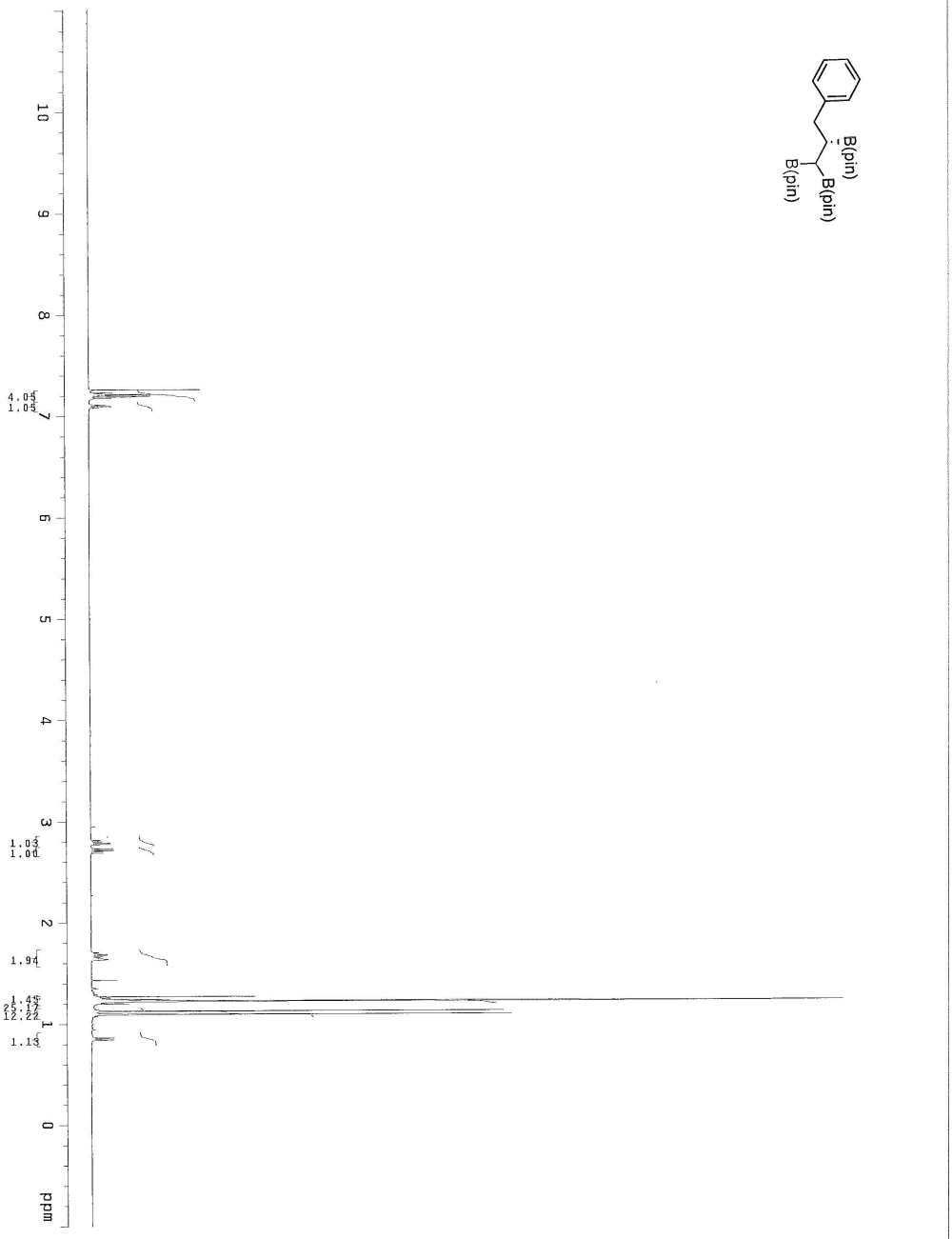
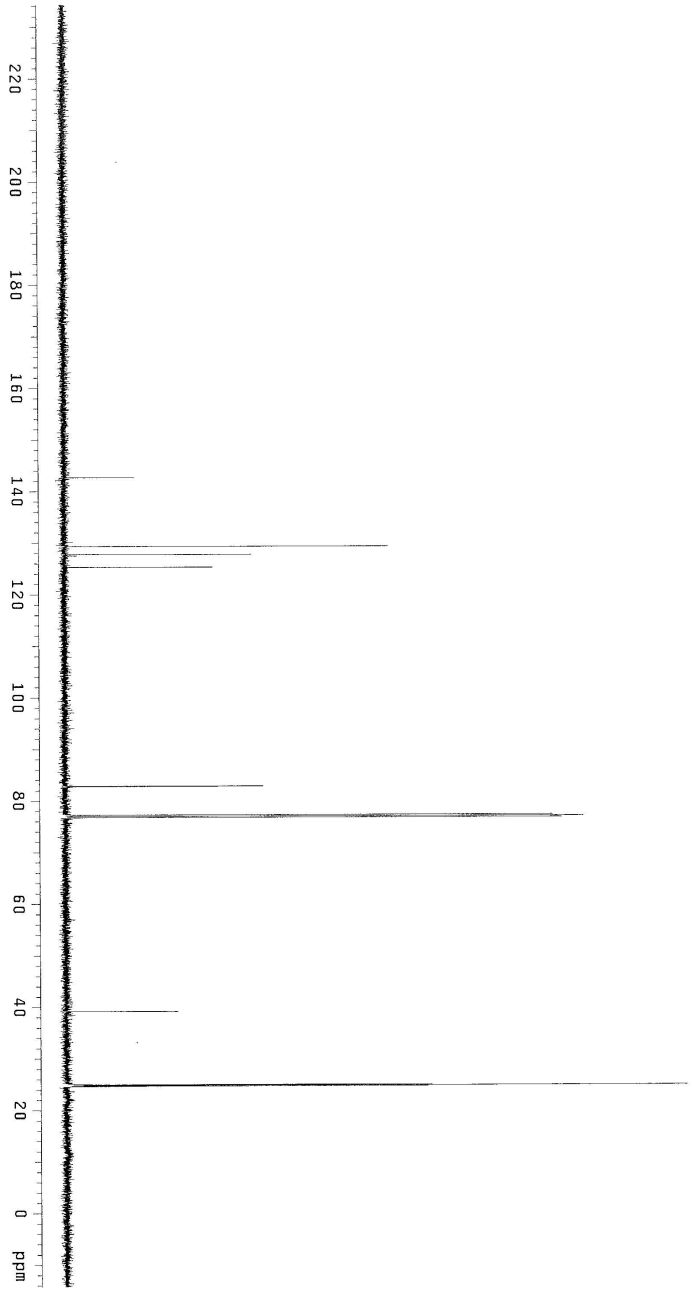
0
ppm


Me
B(pin)
Me
B(pin)
B(pin)
9
8
7
6
5
4
3
2
1
ppm
1.20
1.94
0.42
39.48
6.23
1.00


Me
B(pin)
Me
B(pin)
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
B(pin)
B(pin)
4.04
1.00
1.03
1.00
1.94
1.44
25.17
12.22
1.13
10
9
8
7
6
5
4
3
2
1
0
ppm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B(pin)
B(pin)
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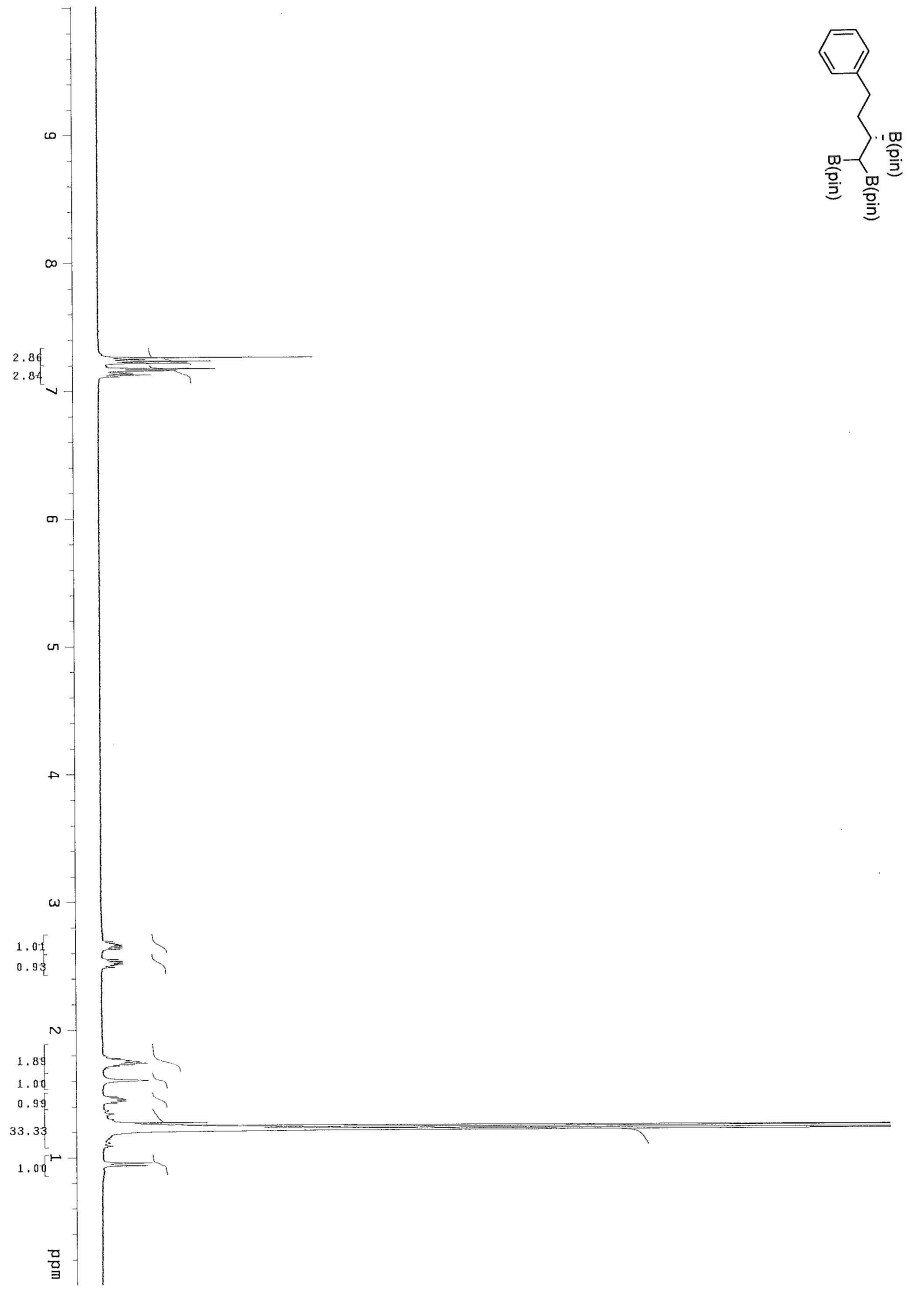
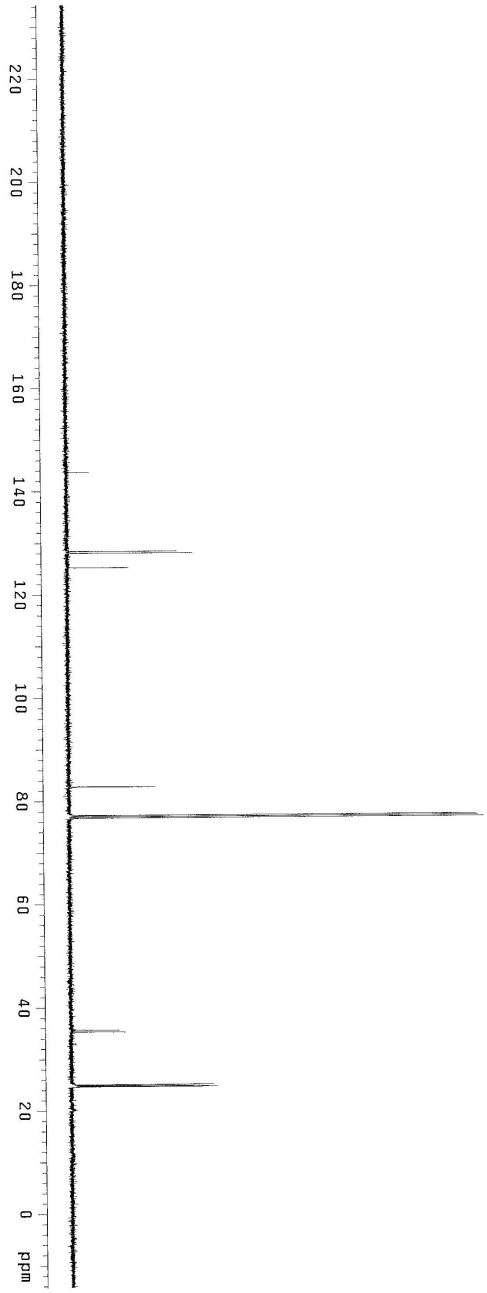
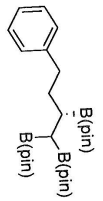
200
180
160
140
120
100
80
60
40
20
0
ppm


B(pin)
B(pin)
B(pin)
2.86
2.84
1.01
0.93
1.89
1.00
0.99
33.33
1.00
9
8
7
6
5
4
3
2
1
ppm


220
200
180
160
140
120
100
80
60
40
20
0
ppm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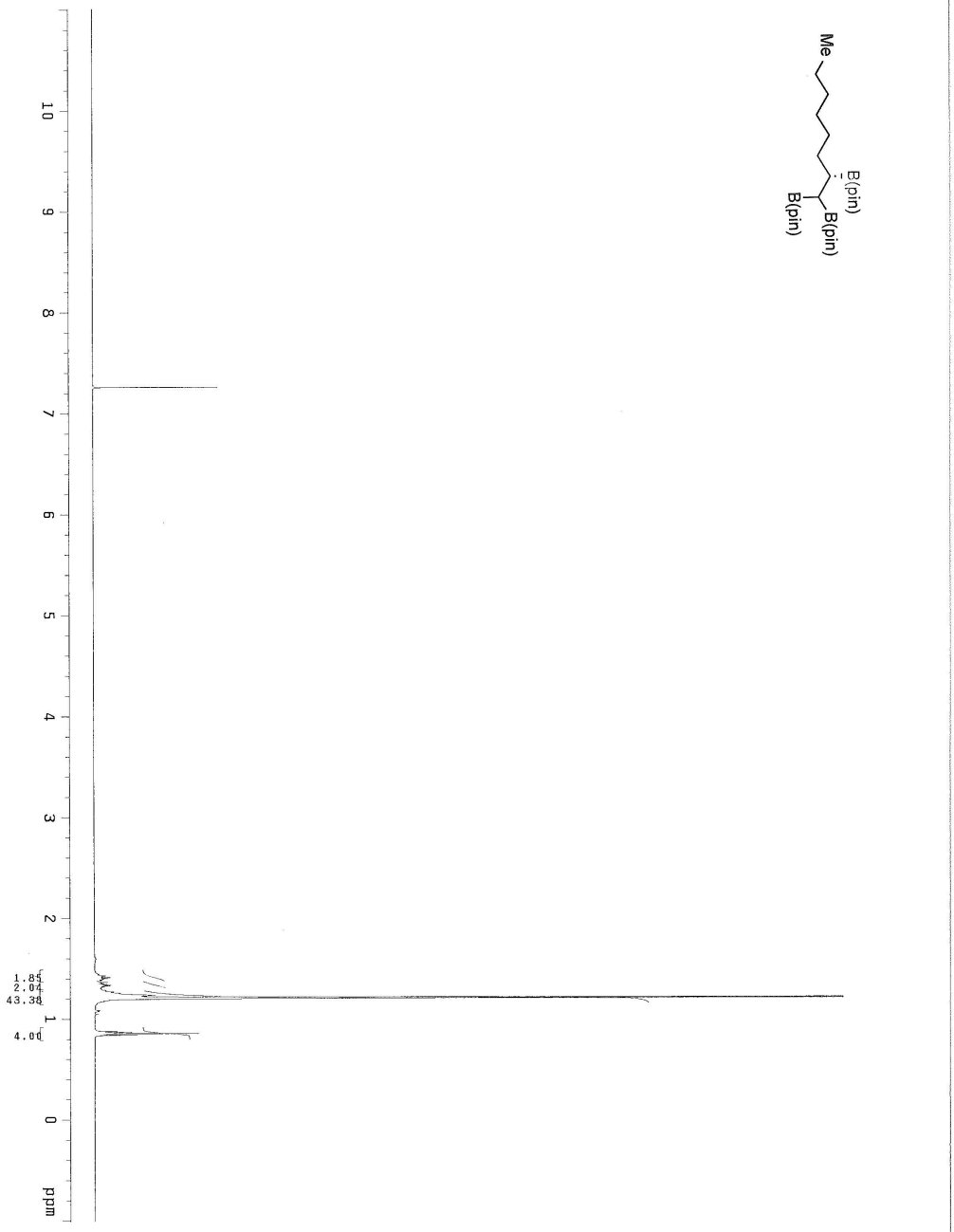
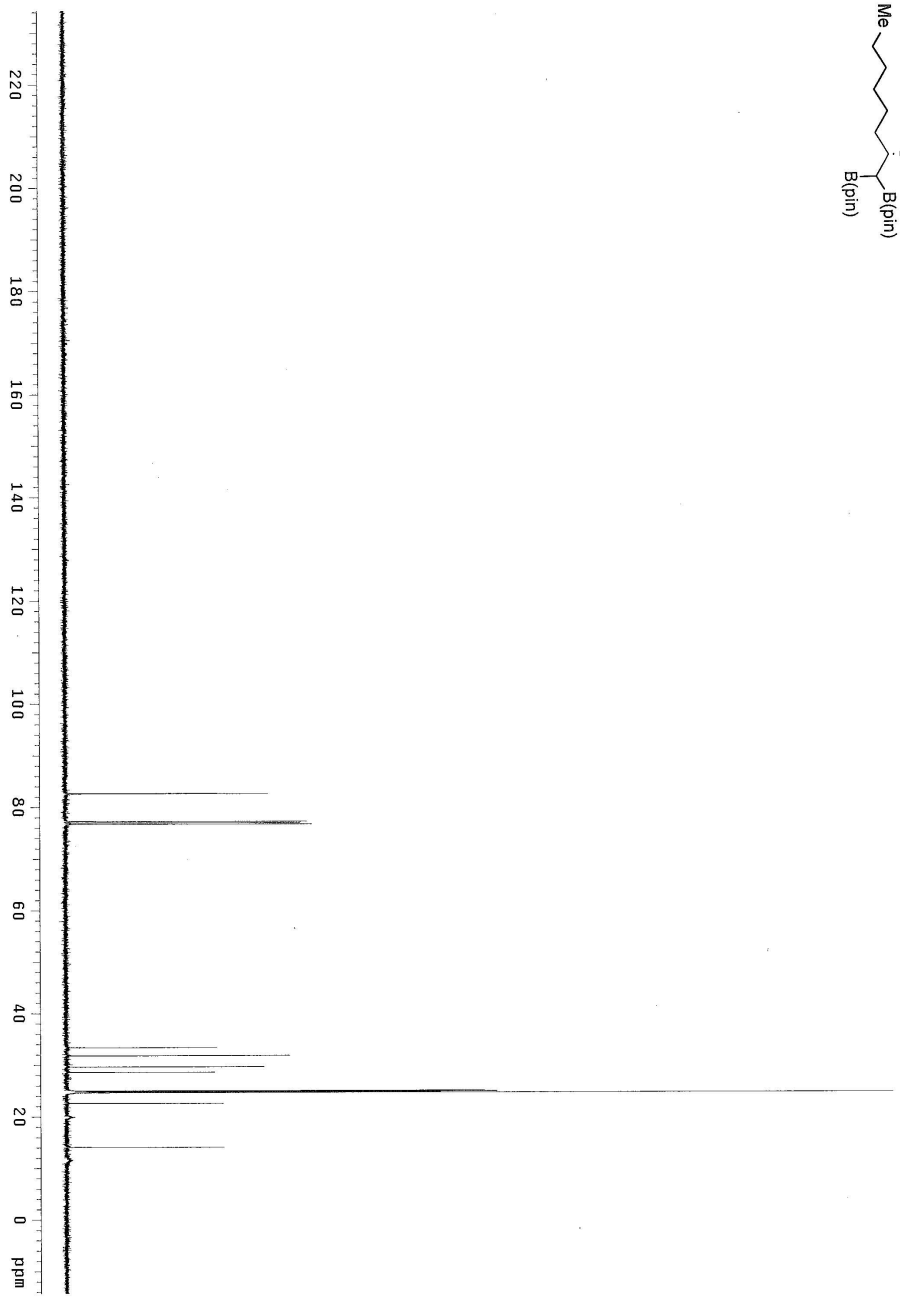
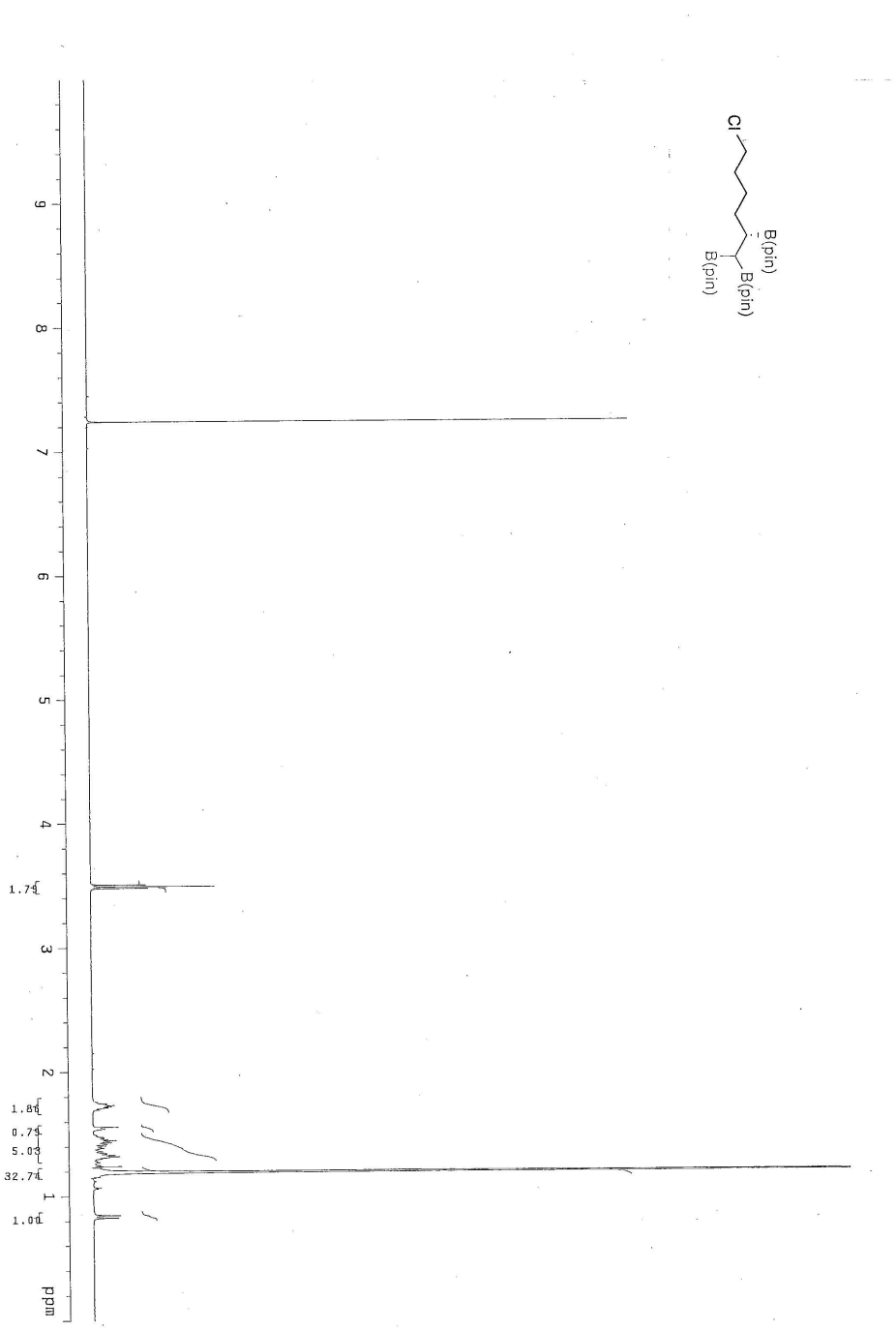
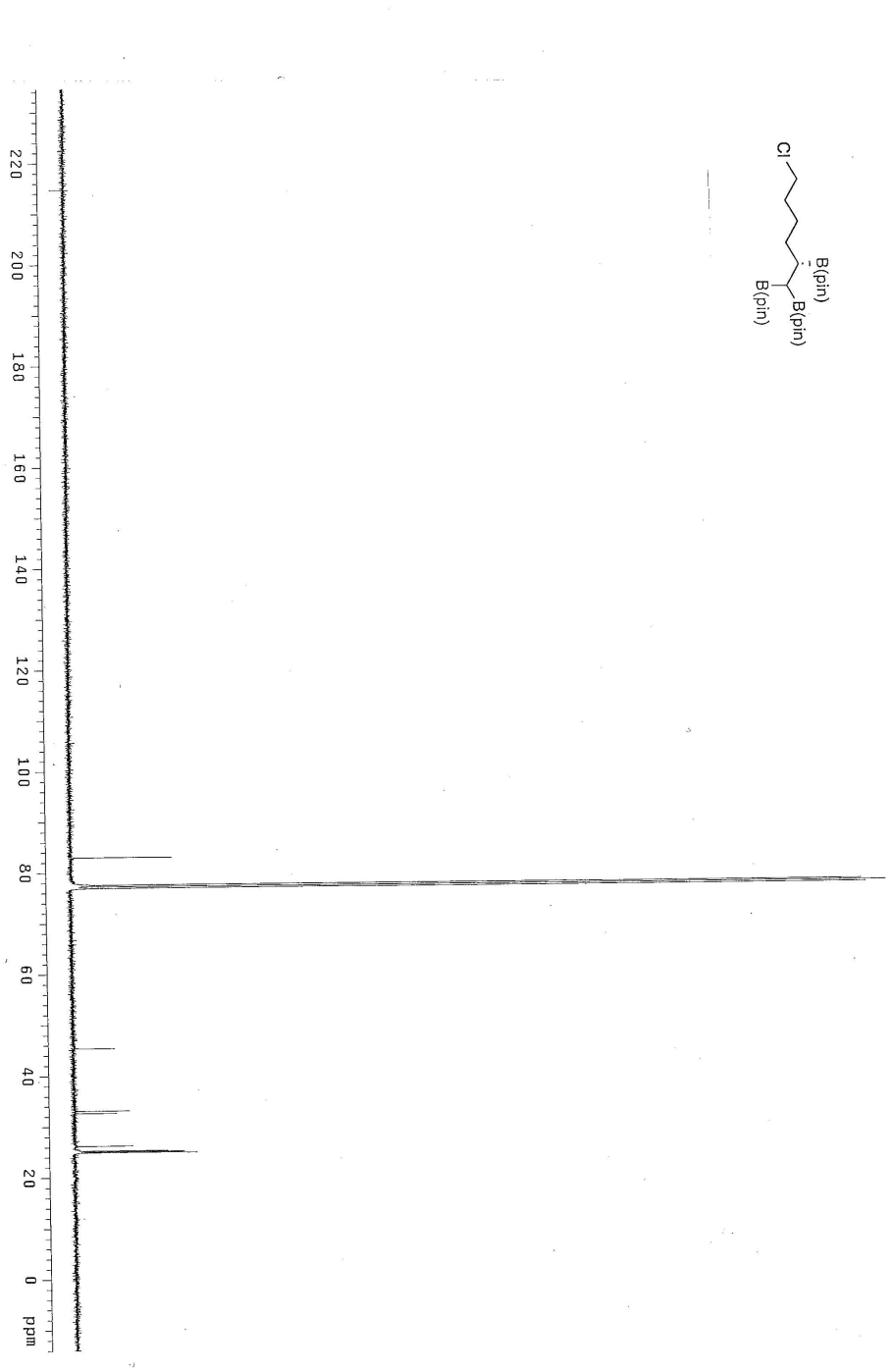
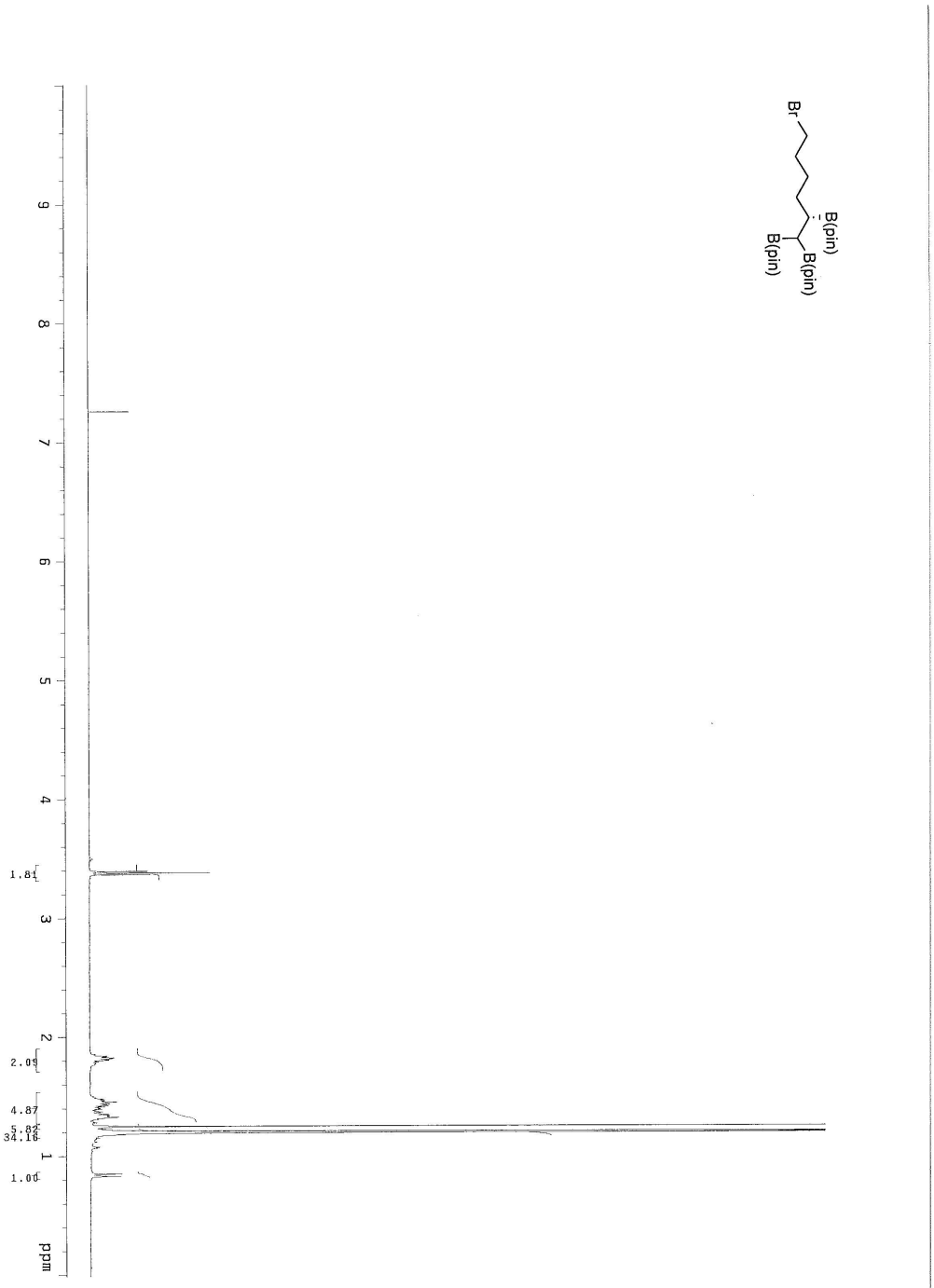
B(pin)
B(pin)

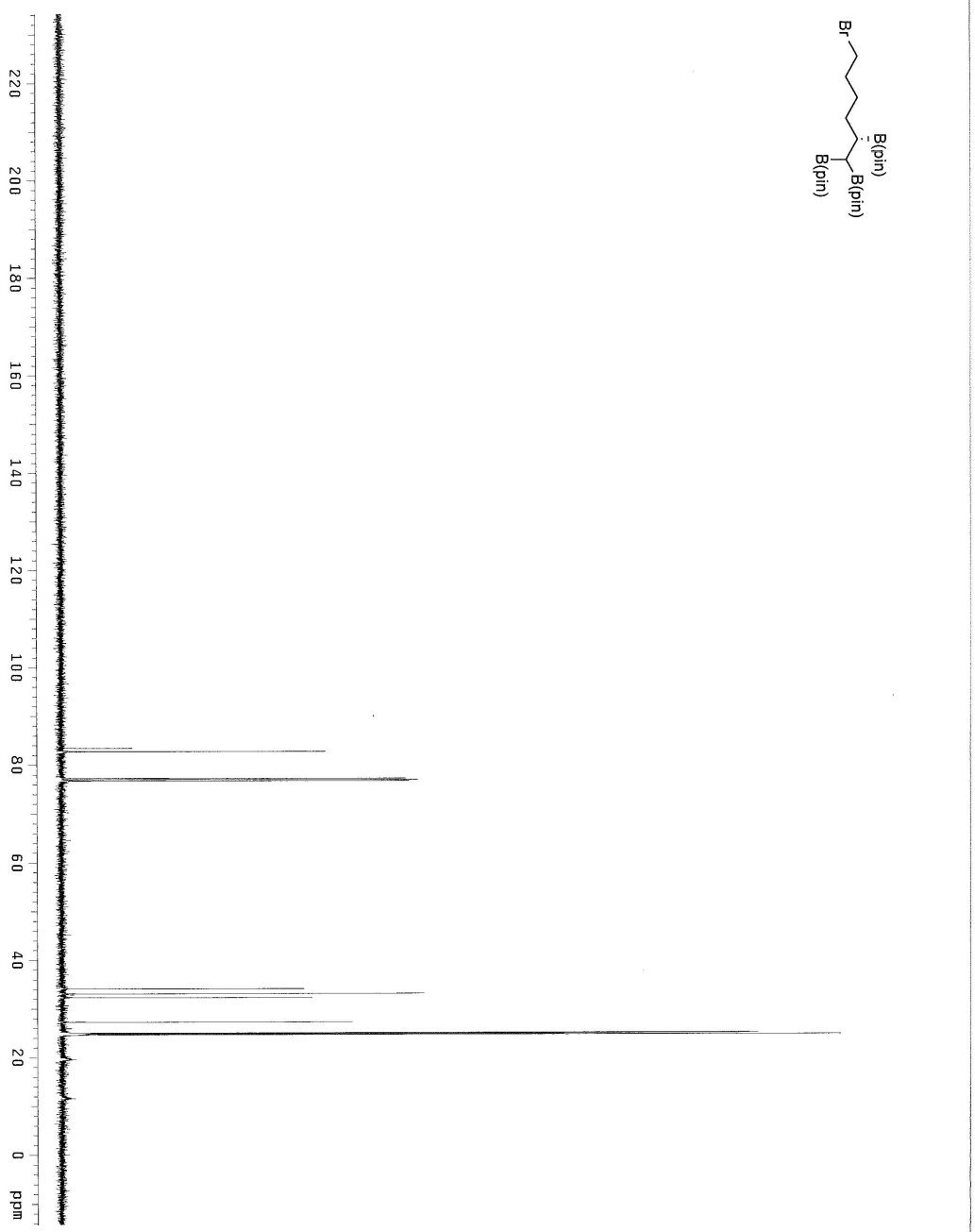

Me
B(pin)
B(pin)
B(pin)
10
9
8
7
6
5
4
3
2
1
0
ppm
1.85
2.04
43.38
4.00

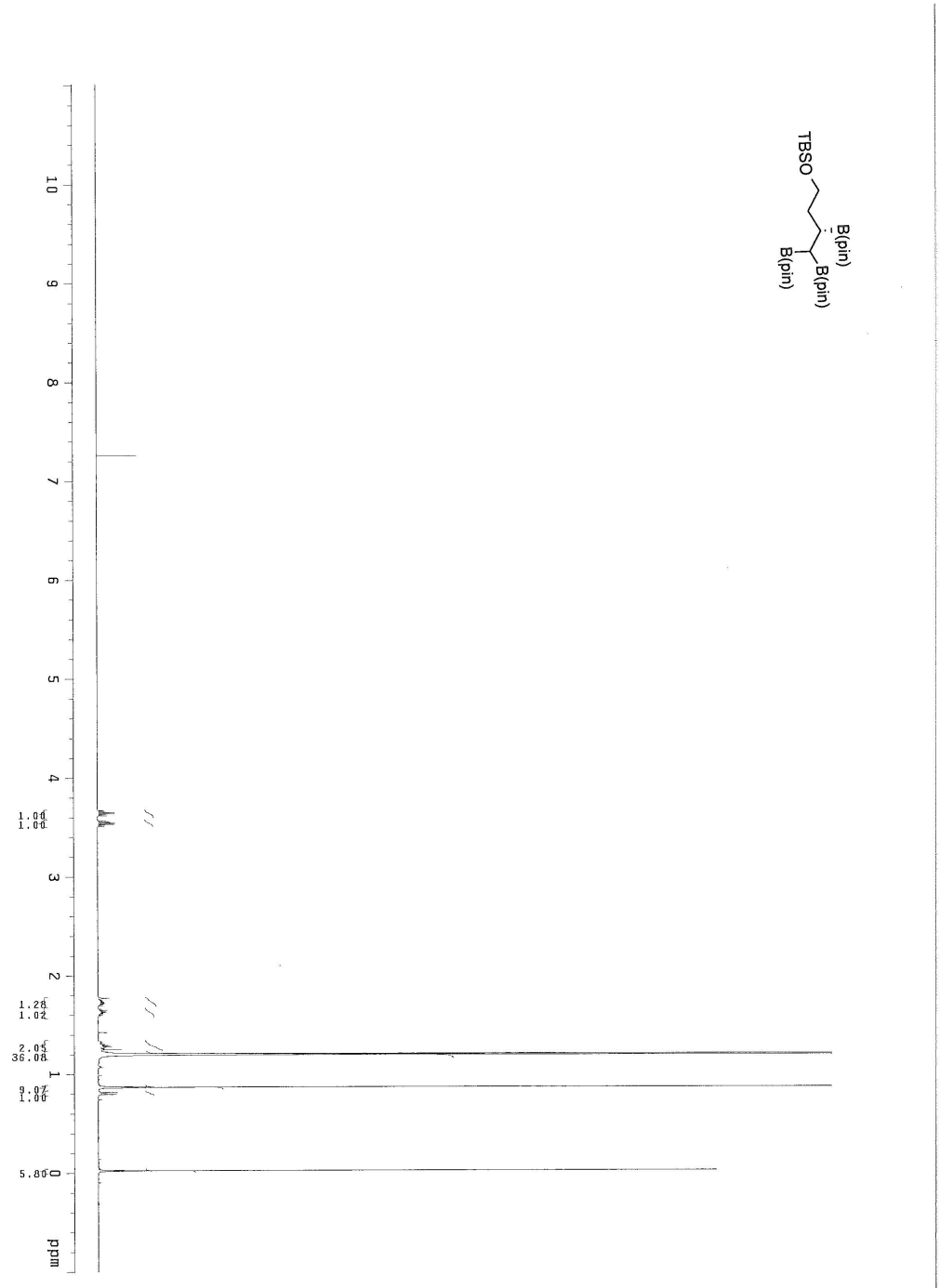

Me
B(pin)
B(pin)
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

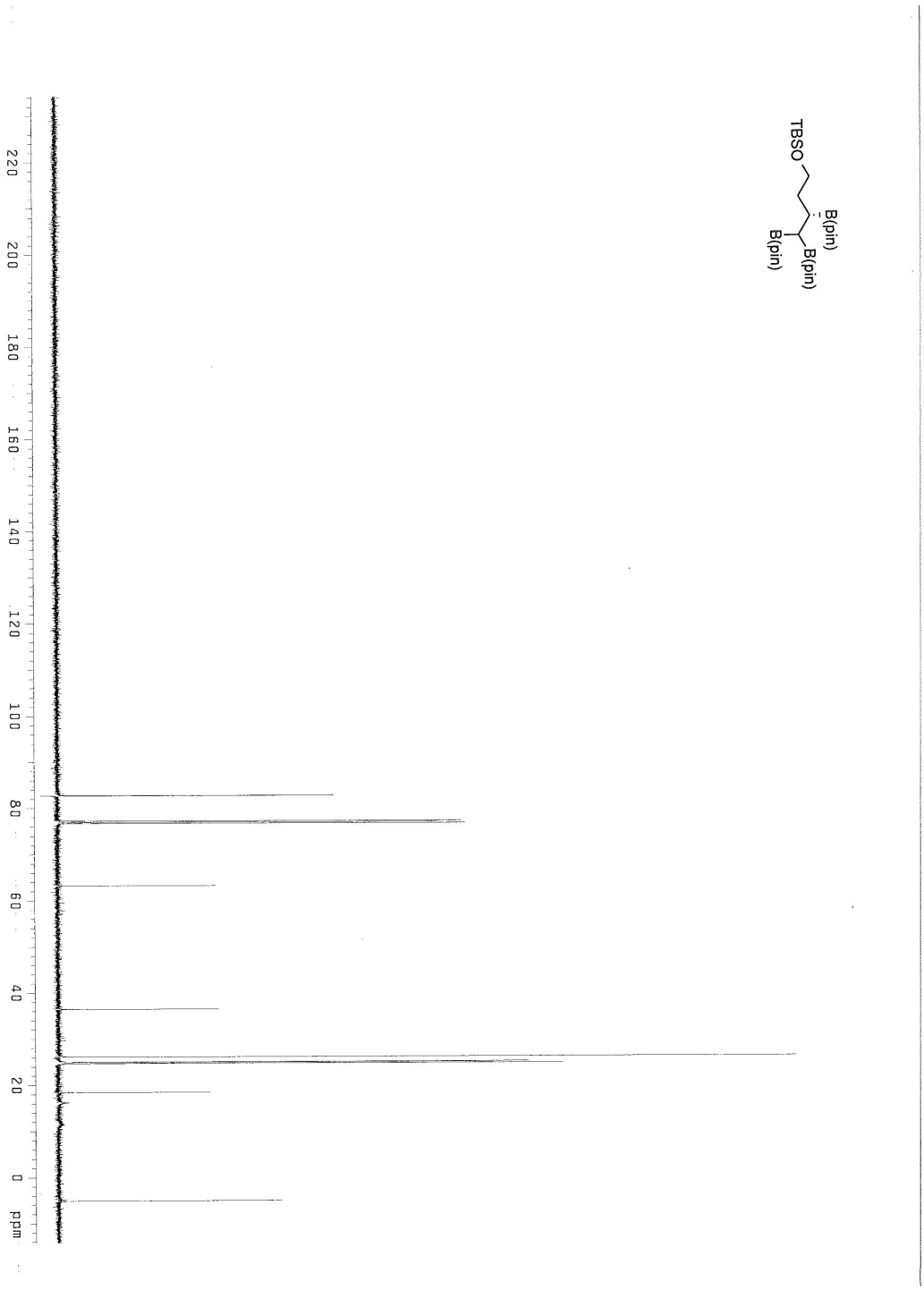

Cl
B(pin)
B(pin)
B(pin)
9
8
7
6
5
4
3
2
1
ppm
1.74
1.84
0.75
5.00
32.74
1.00

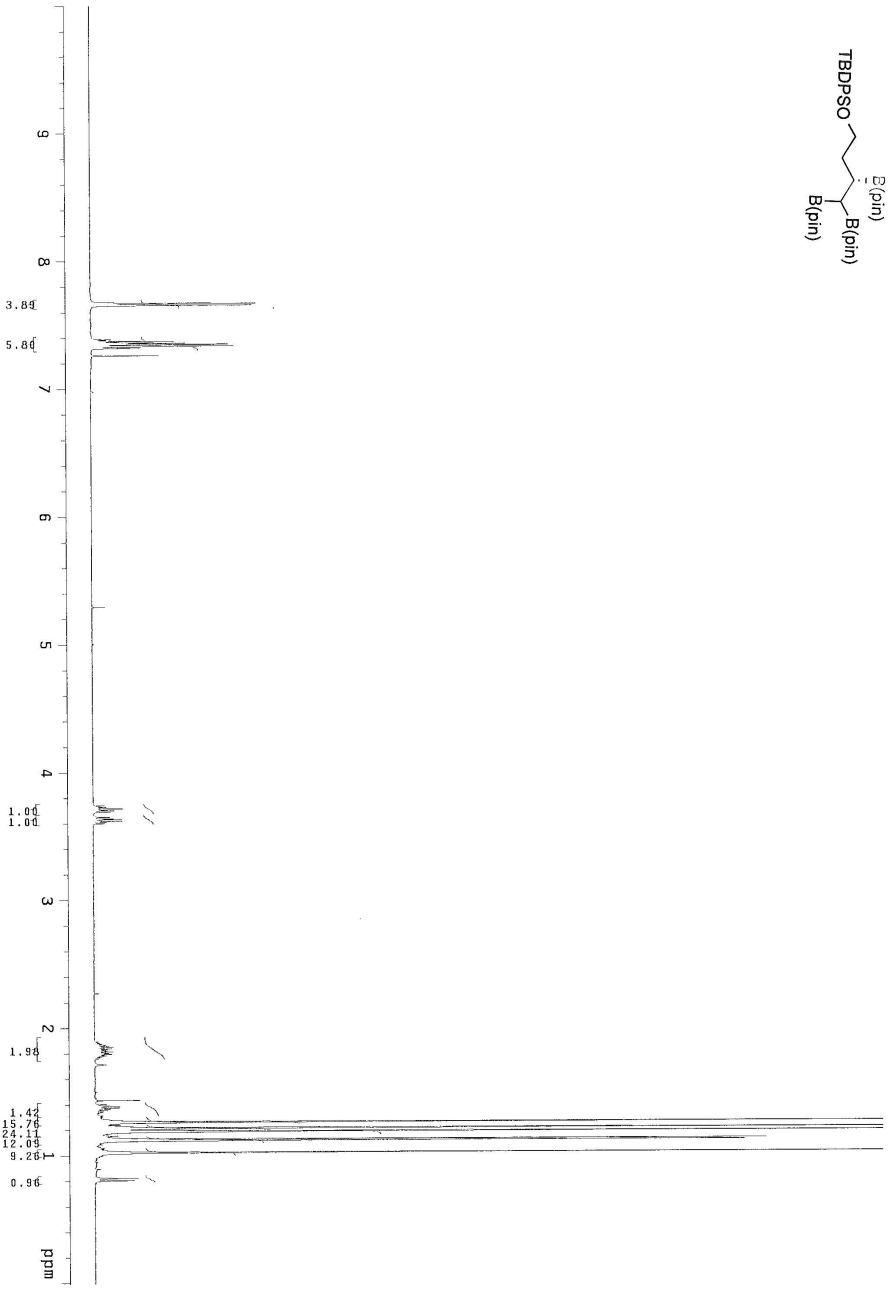

Cl
B(pin)
B(pin)
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

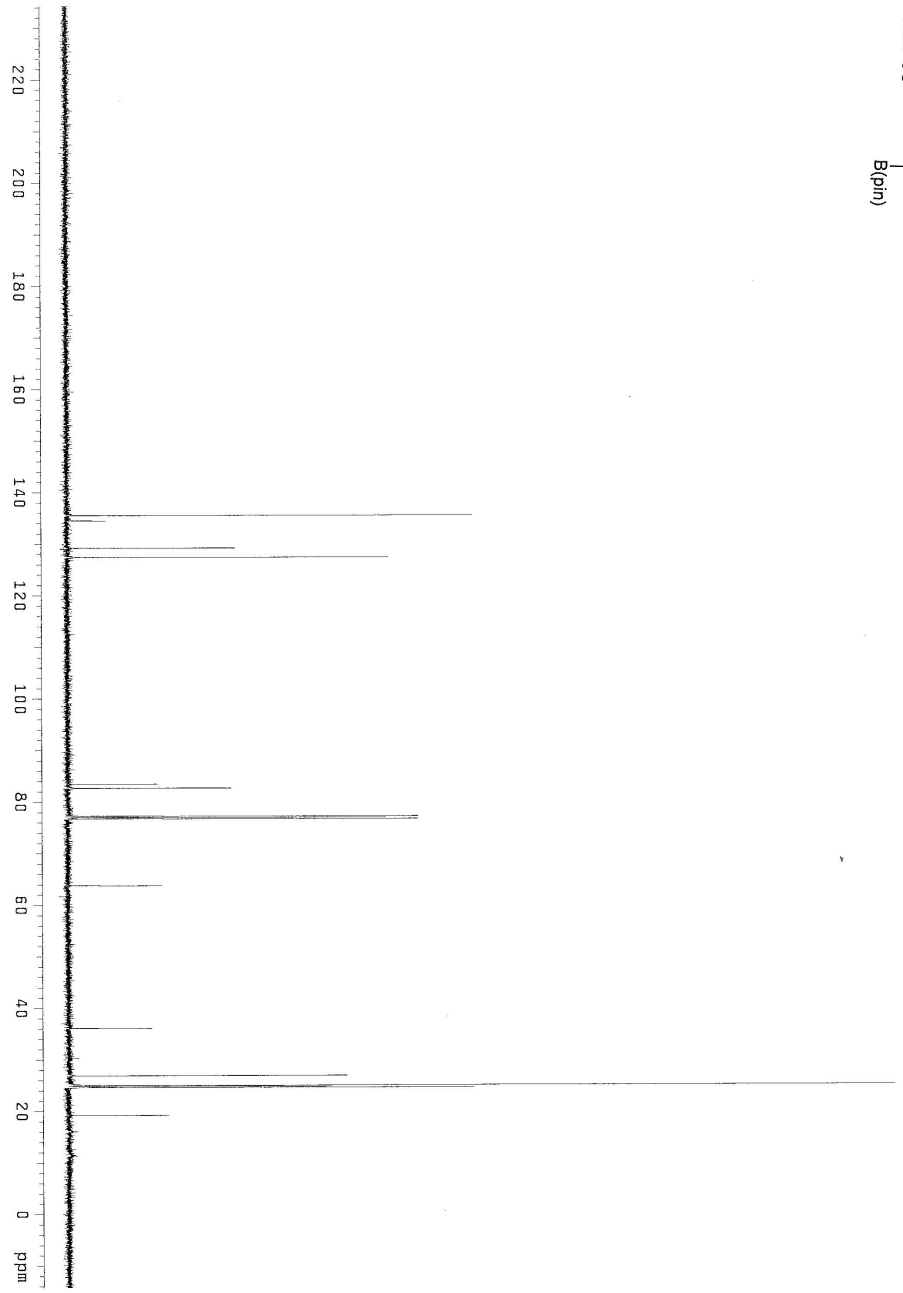

Br
B(pin)
B(pin)
B(pin)
1.81
2.09
4.87
5.82
34.16
1.00
ppm

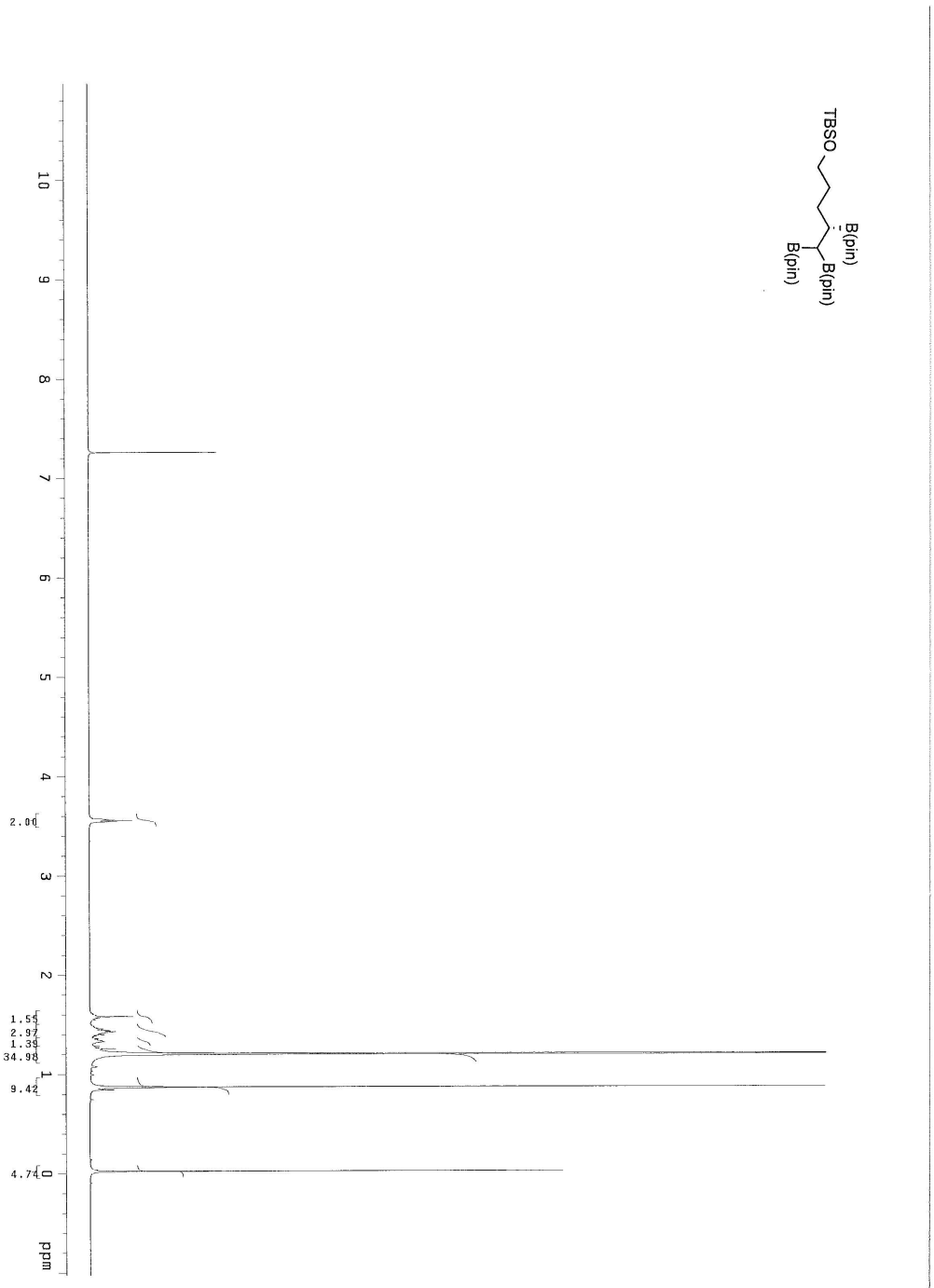

Br
B(pin)
B(pin)
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

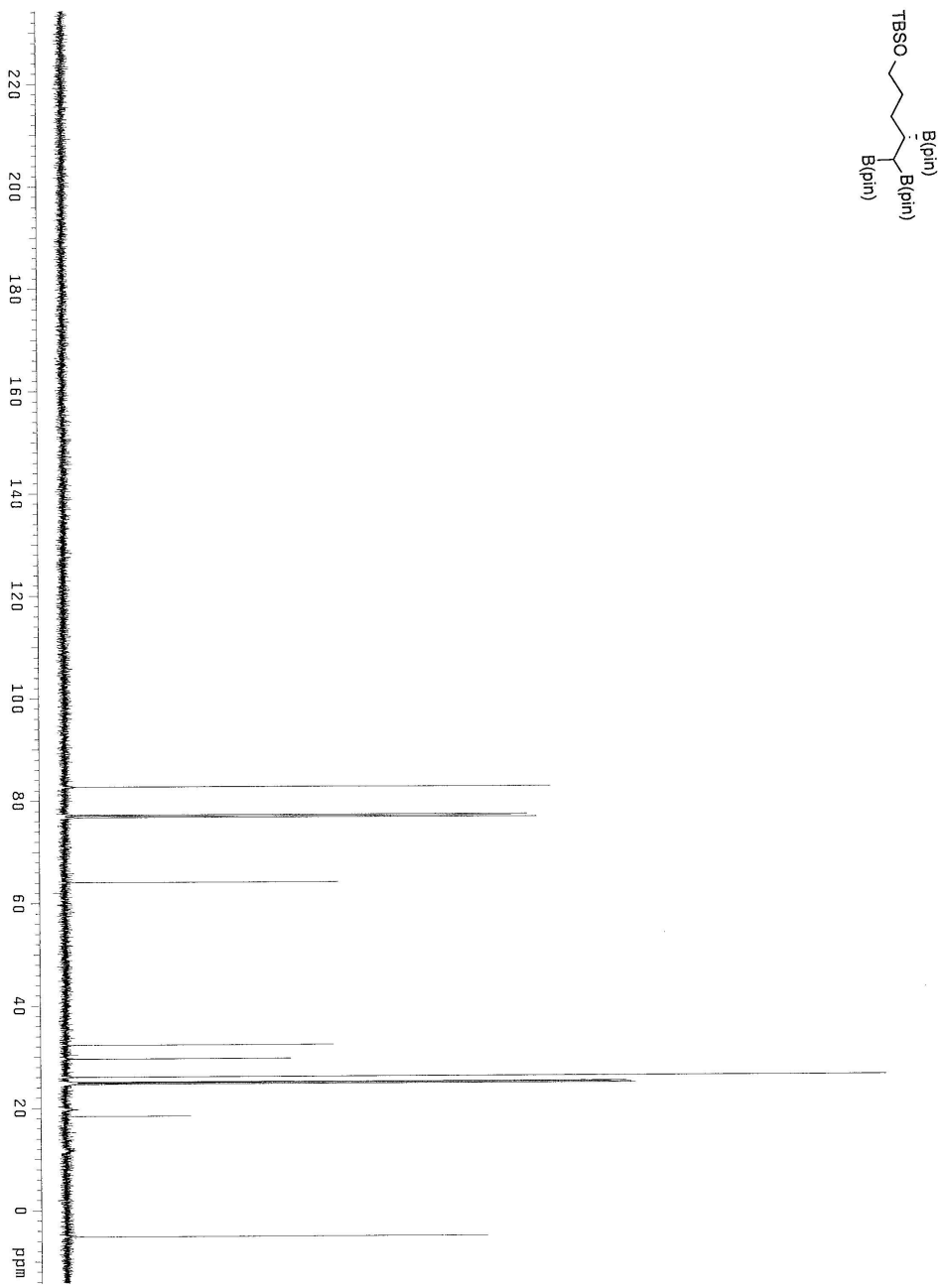

TBSO
B(pin)
B(pin)
B(pin)
10
9
8
7
6
5
4
3
2
1
0
ppm

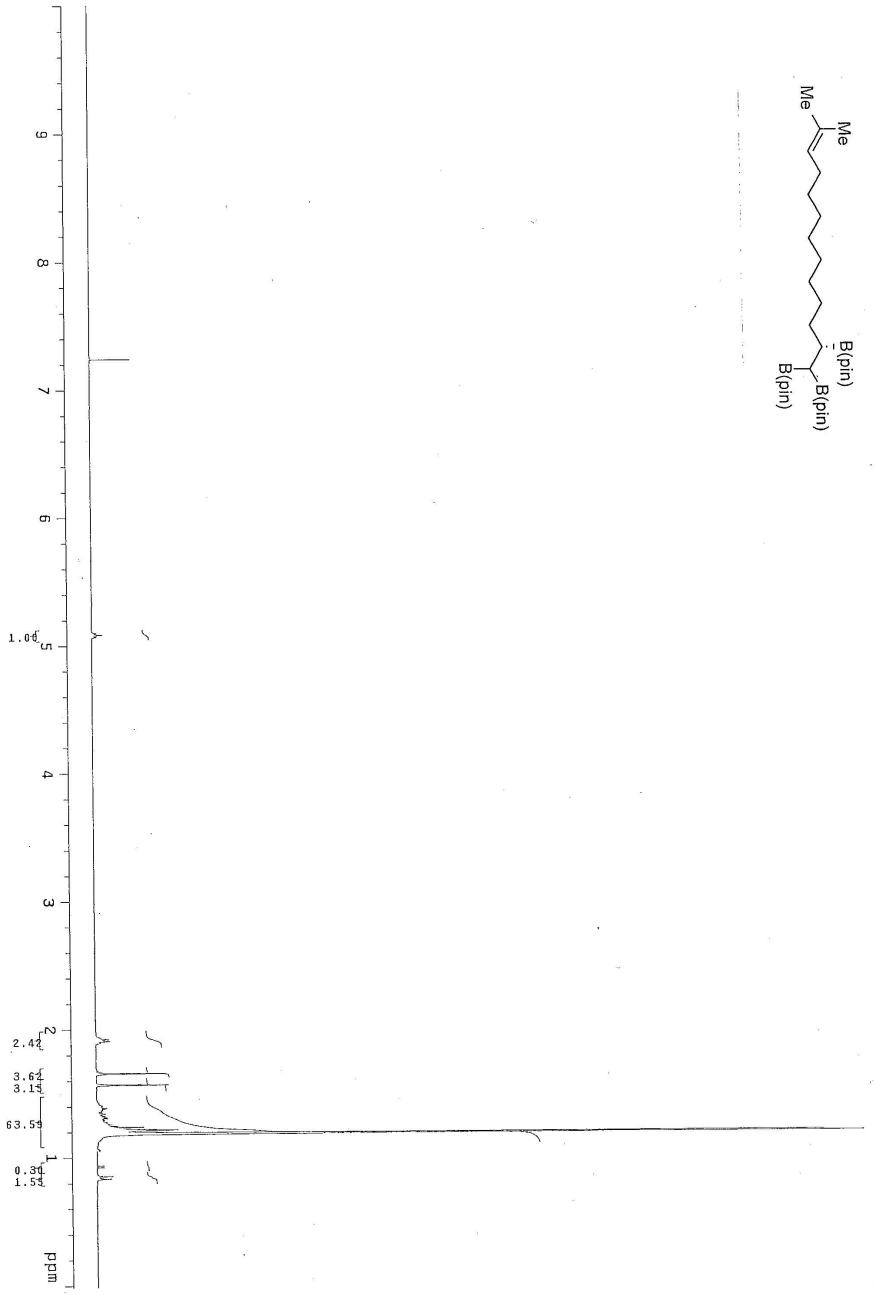

TBSO
B(pin)
B(pin)
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

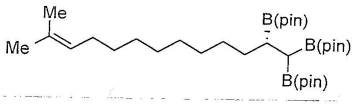

TBDPSO
B(pin)
B(pin)
B(pin)
3.89
5.80
1.00
1.00
1.98
1.42
15.76
24.11
12.09
9.26
0.96
ppm

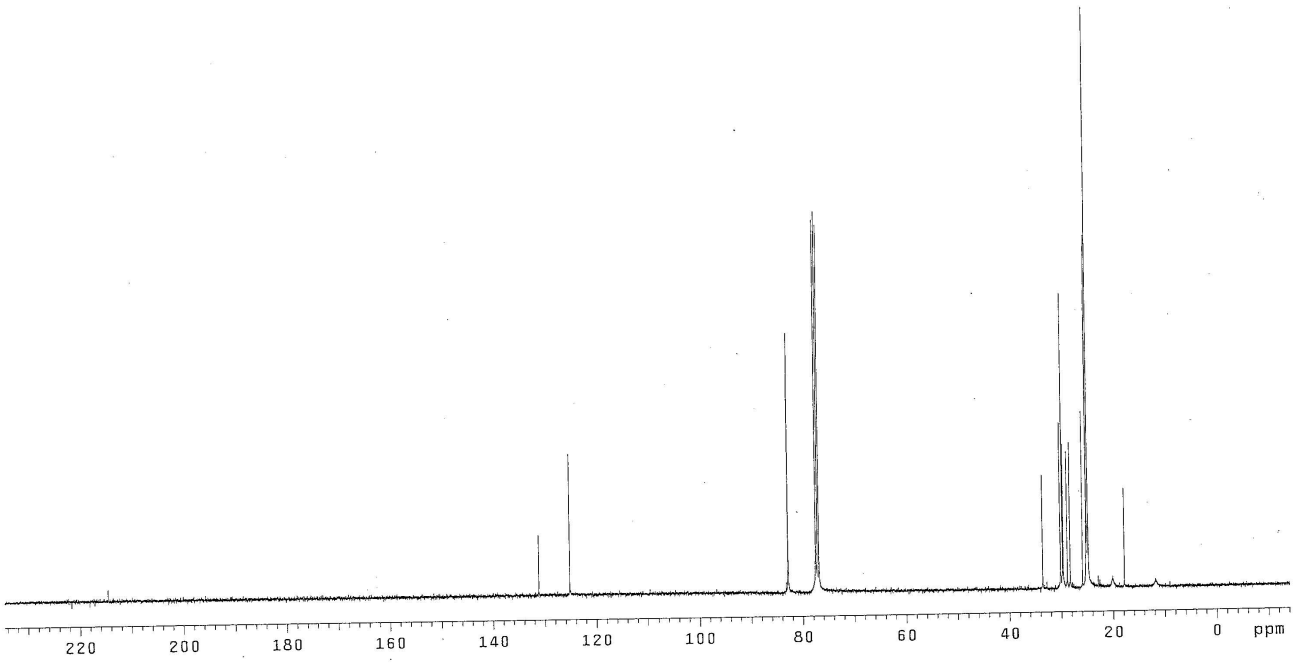

TBDPSO
B(pin)
B(pin)
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

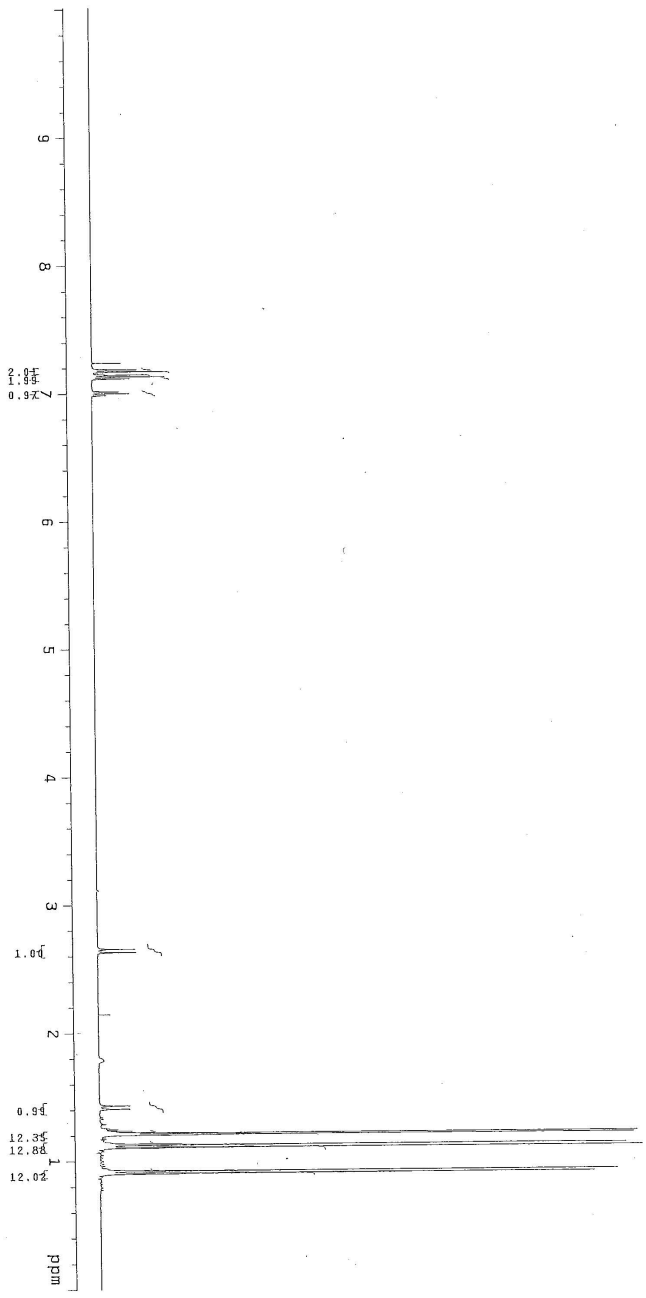

TBSO
B(pin)
B(pin)
B(pin)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.00
1.55
2.97
1.39
34.98
9.42
4.74


TBSO
B(pin)
B(pin)
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

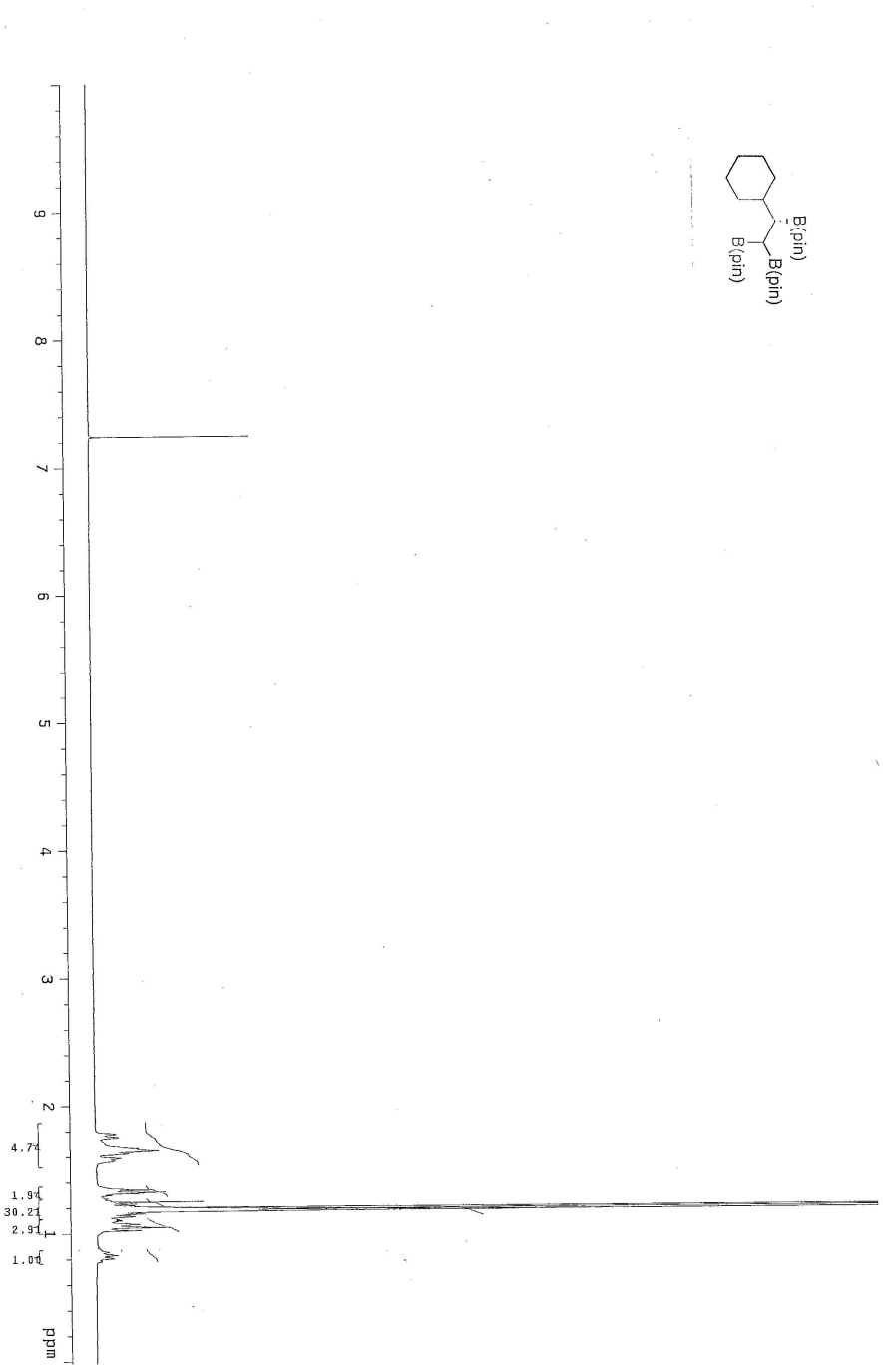

Me
Me
B(pin)
B(pin)
B(pin)
1.00
2.42
3.62
3.14
63.59
0.30
1.54
ppm

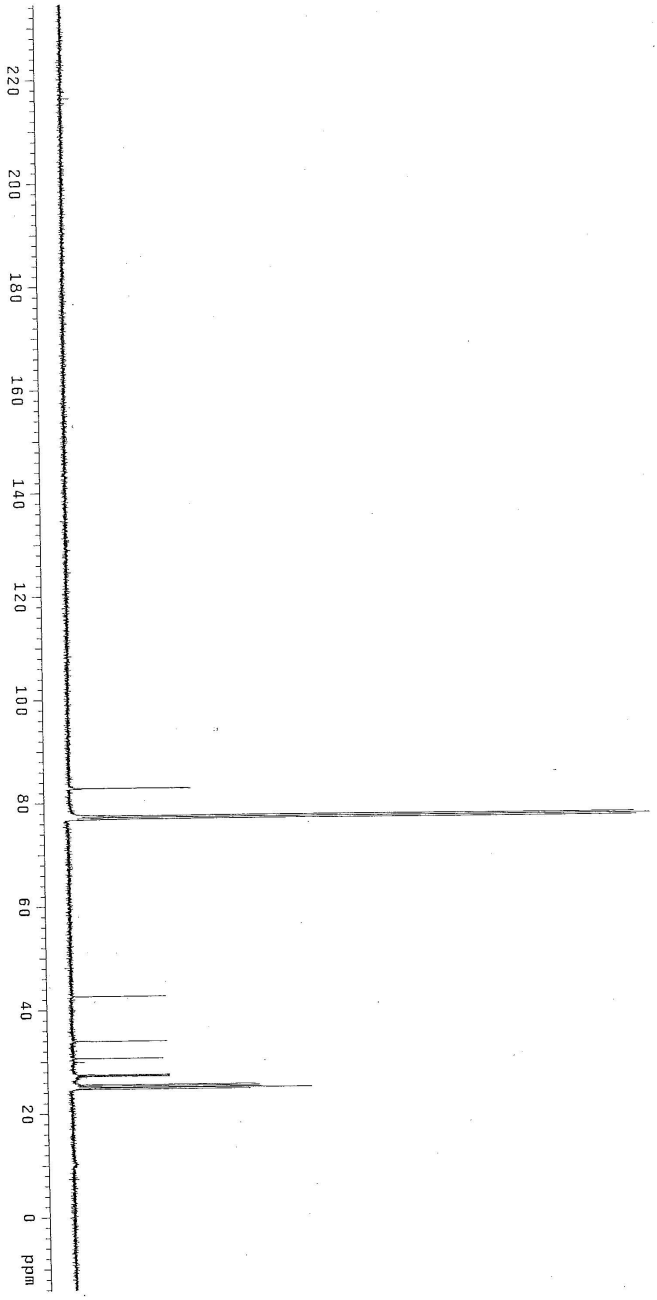

Me
Me
B(pin)
B(pin)
B(pin)

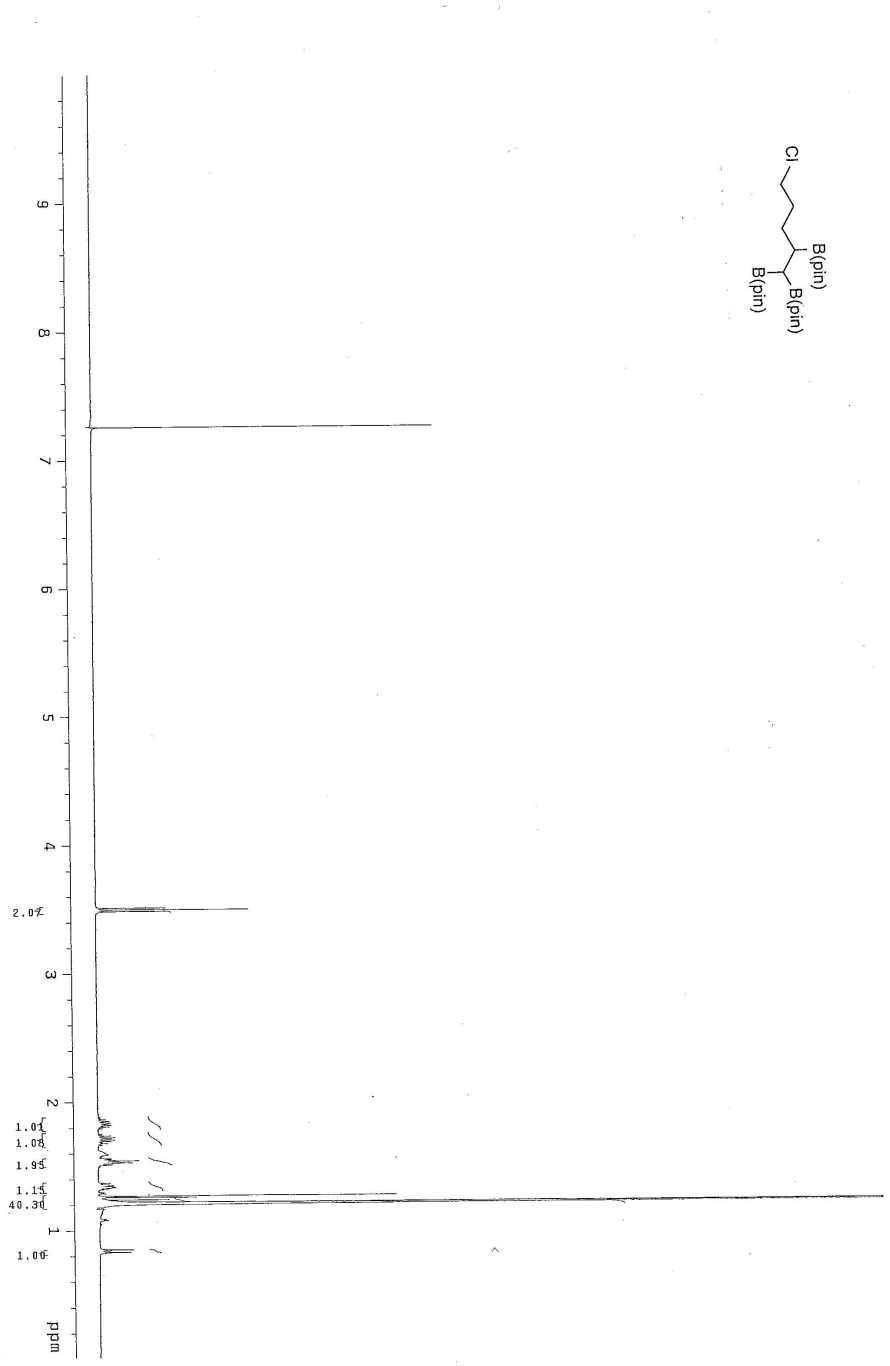

220
200
180
160
140
120
100
80
60
40
20
0
ppm

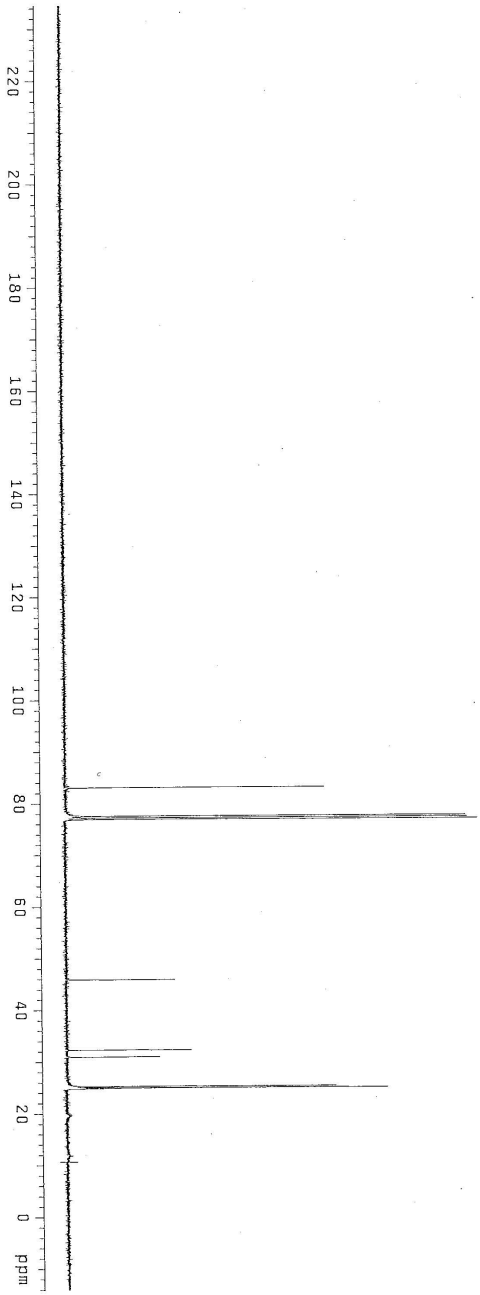

B(pin)
B(pin)
B(pin)
ppm

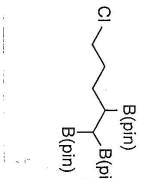
B(pin)
B(pin)
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

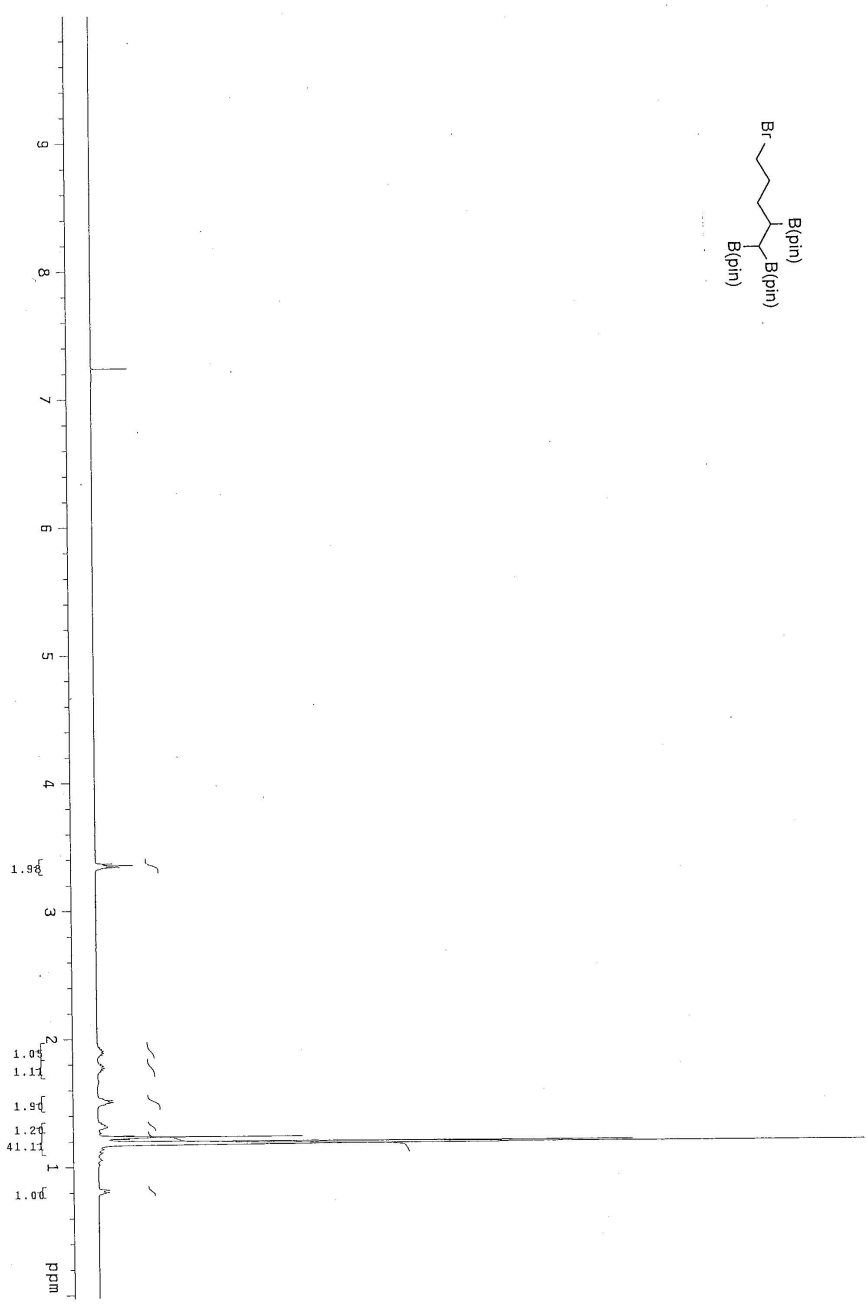

B(pin)
B(pin)
B(pin)
9
8
7
6
5
4
3
2
4.74
1.94
30.21
2.91
1.00
1
ppm

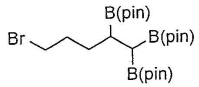

B(pin)
B(pin)
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

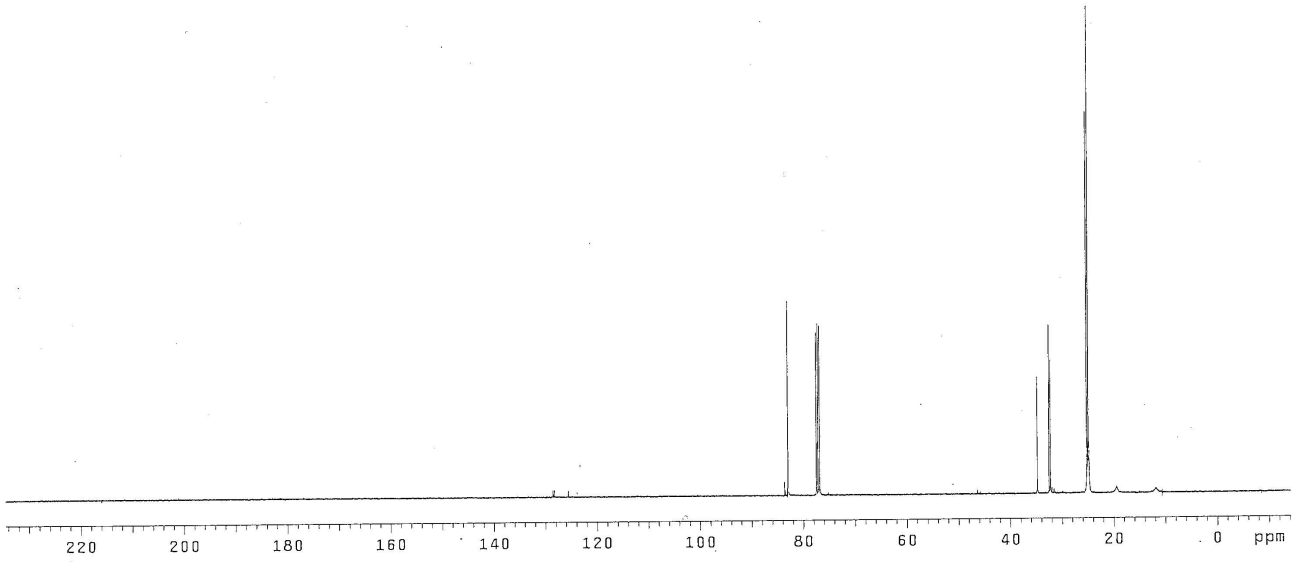

Cl
B(pin)
B(pin)
B(pin)
2.07
1.01
1.08
1.95
1.15
40.30
1.00
ppm

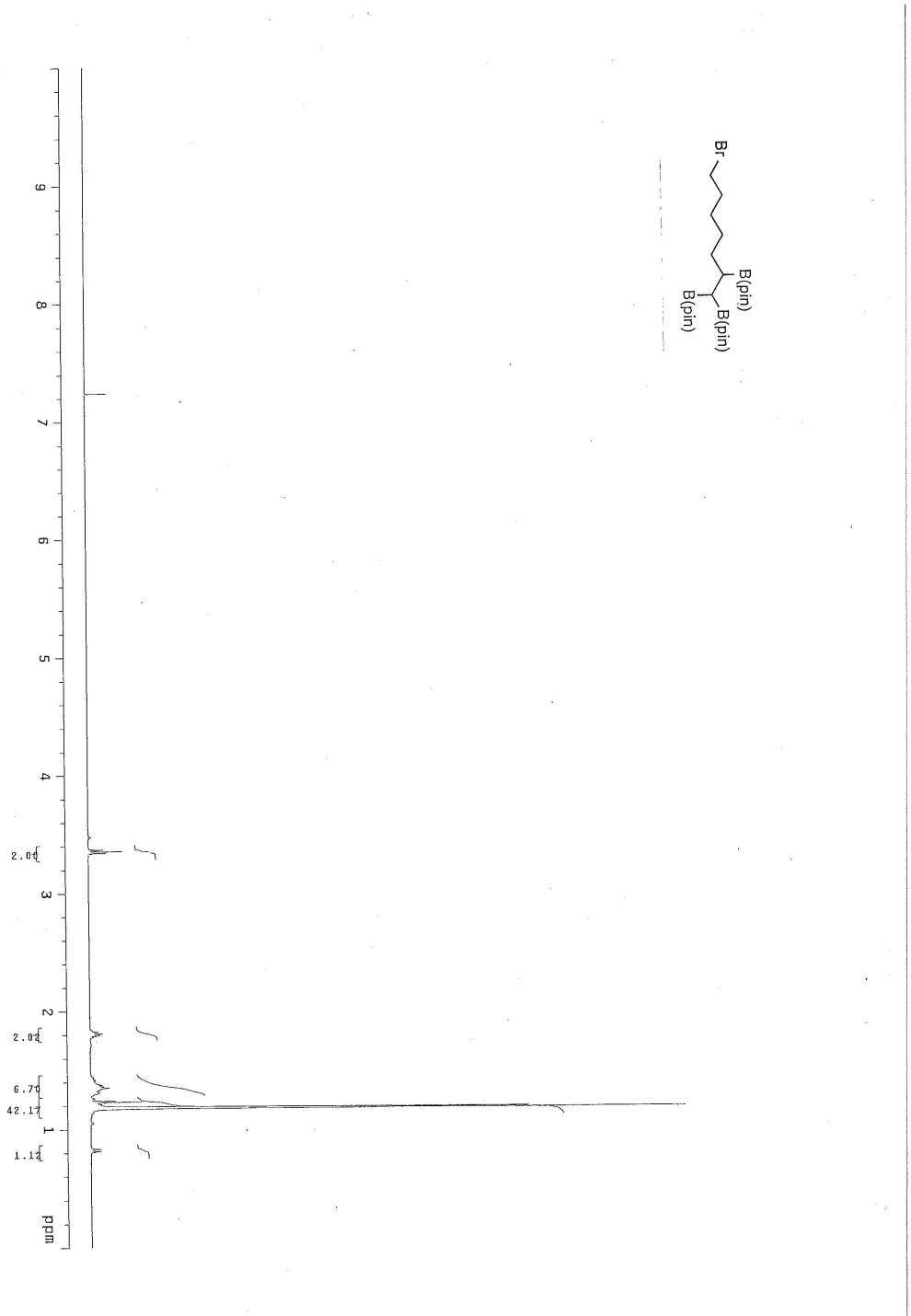

220
200
180
160
140
120
100
80
60
40
20
0
ppm

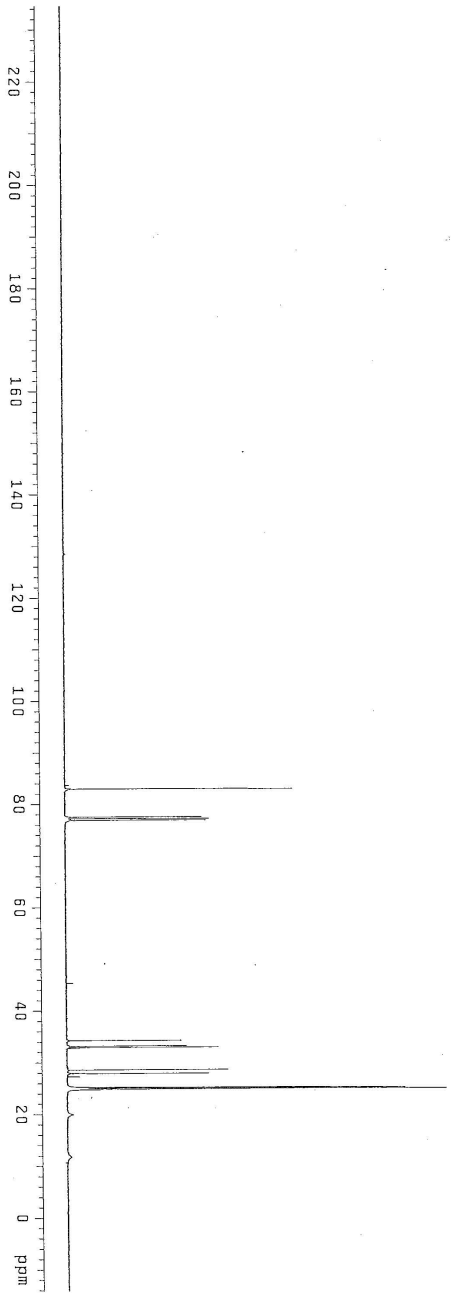

Cl
B(pin)
B(pin)
B(pin)

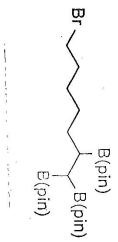

Br
B(pin)
B(pin)
B(pin)
9
8
7
6
5
4
3
2
1
ppm
1.98
1.05
1.11
1.93
1.20
41.11
1.00

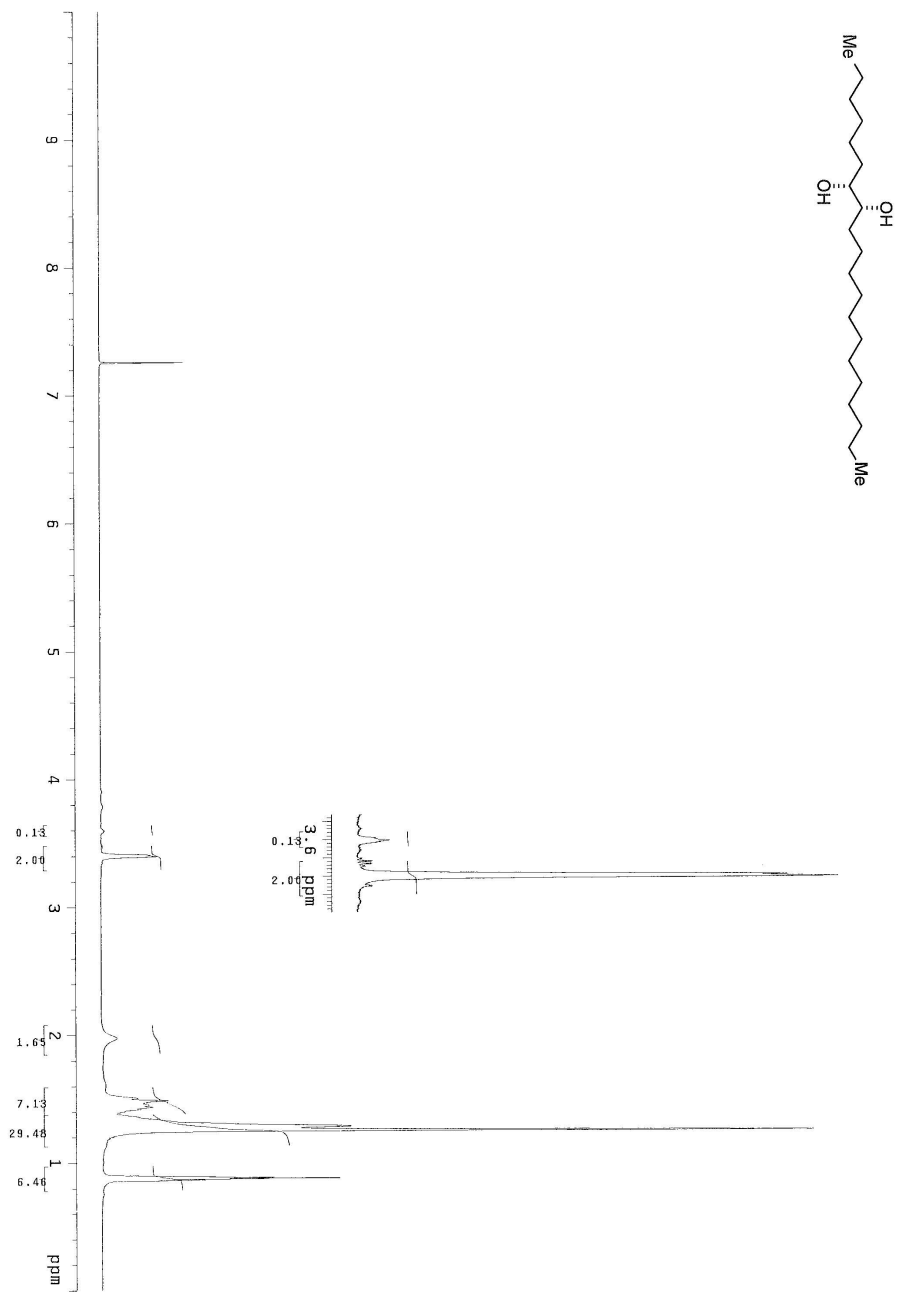

B(pin)
Br
B(pin)
B(pin)

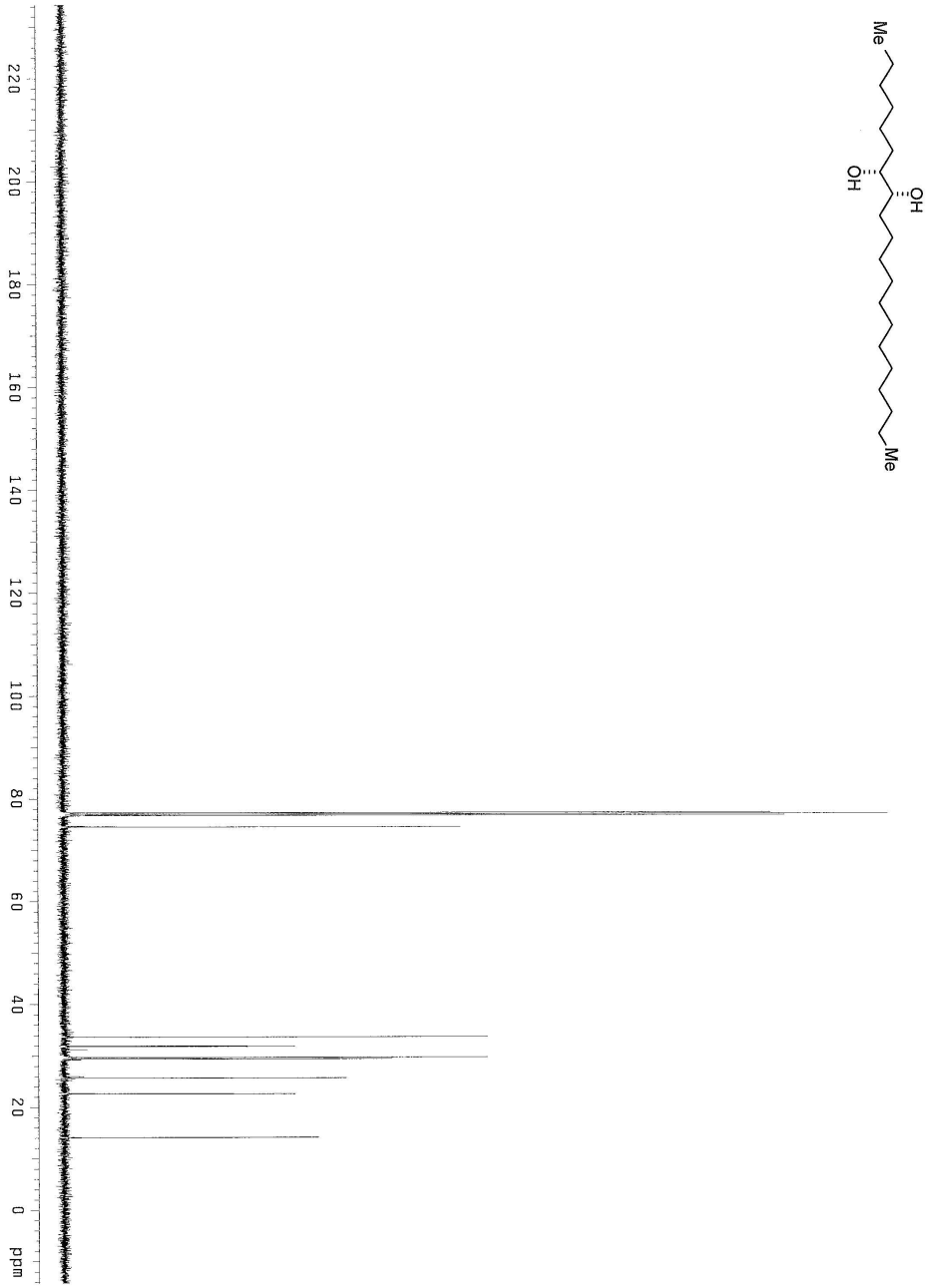

220
200
180
160
140
120
100
80
60
40
20
0
ppm

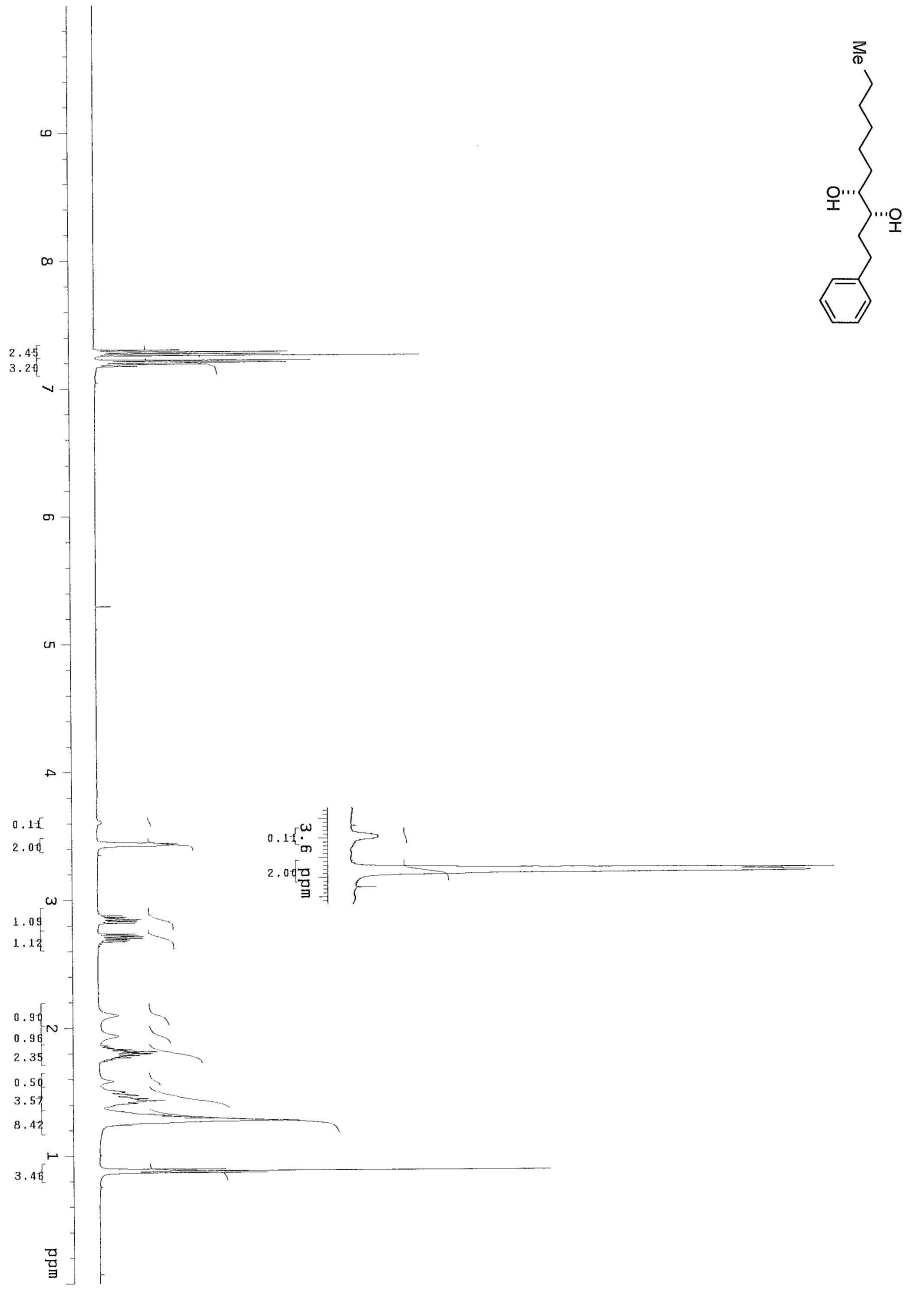

Br
B(pin)
B(pin)
B(pin)
9
8
7
6
5
4
3
2
1
2.04
2.02
6.70
42.17
1.12
ppm

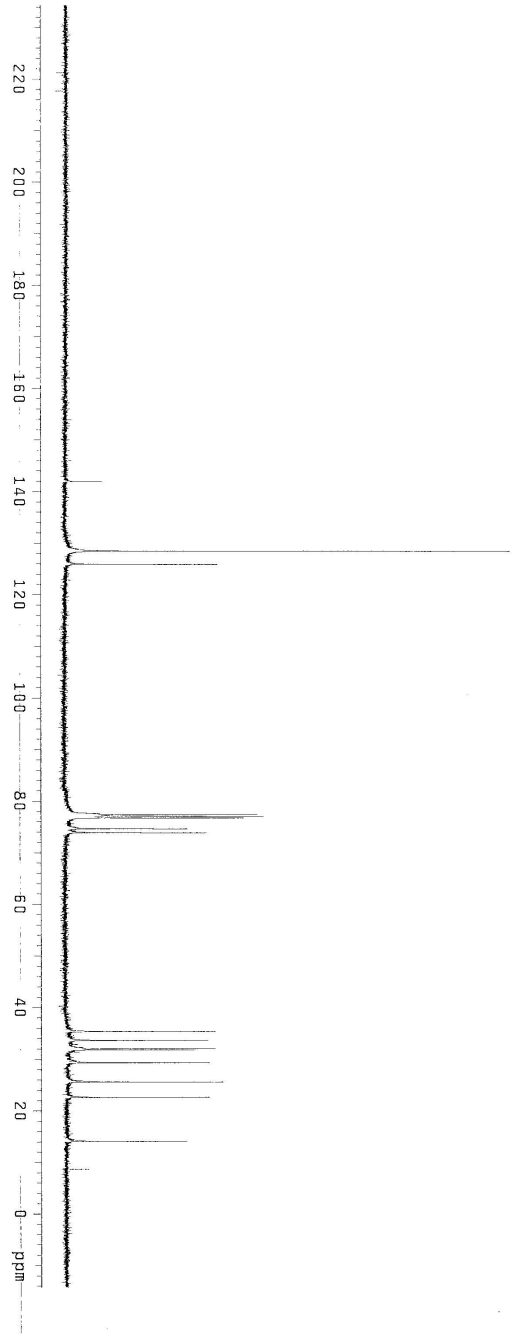

220
200
180
160
140
120
100
80
60
40
20
0
ppm

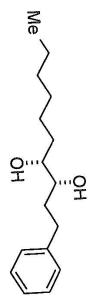

Br
B(pin)
B(pin)
B(pin)

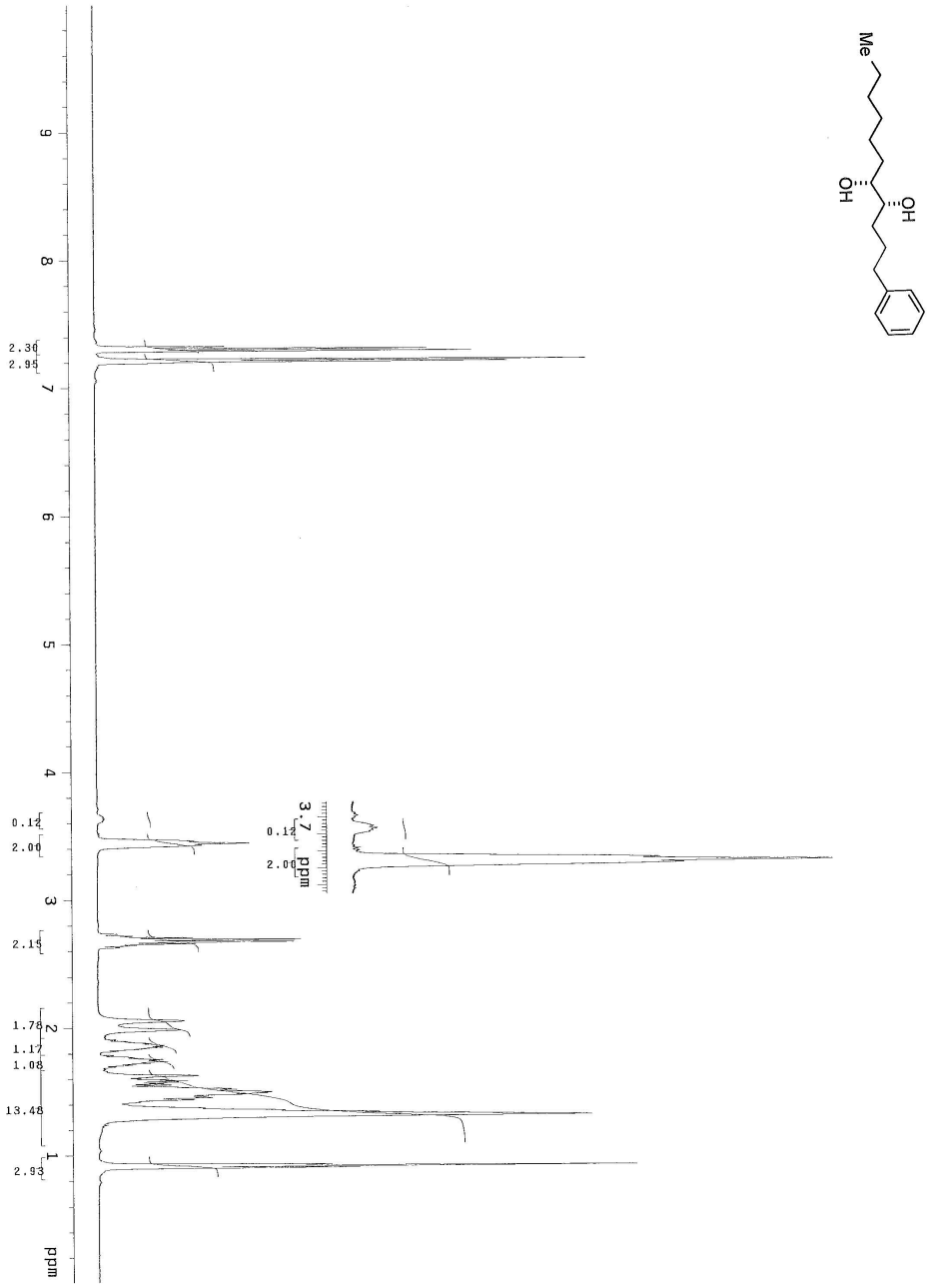

Me
OH
OH
Me
9
8
7
6
5
4
3
2
1
ppm
0.13
2.00
1.65
7.13
29.46
6.46
3.6 ppm
0.13
2.00

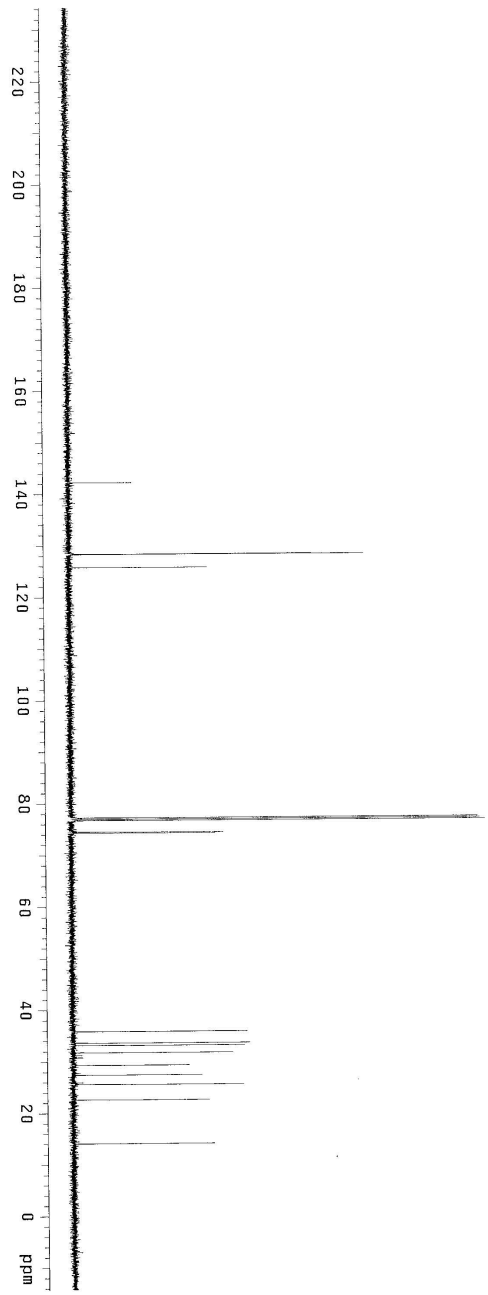

Me
OH
OH
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Me
OH
OH
3.6 ppm
ppm


220
200
180
160
140
120
100
80
60
40
20
0
ppm


Me
OH
OH


Me
OH
OH
2.30
2.95
0.12
2.00
2.15
1.78
1.17
1.08
13.48
2.93
3.7 ppm
0.12
2.00
ppm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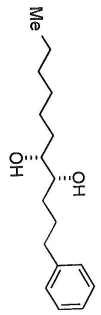
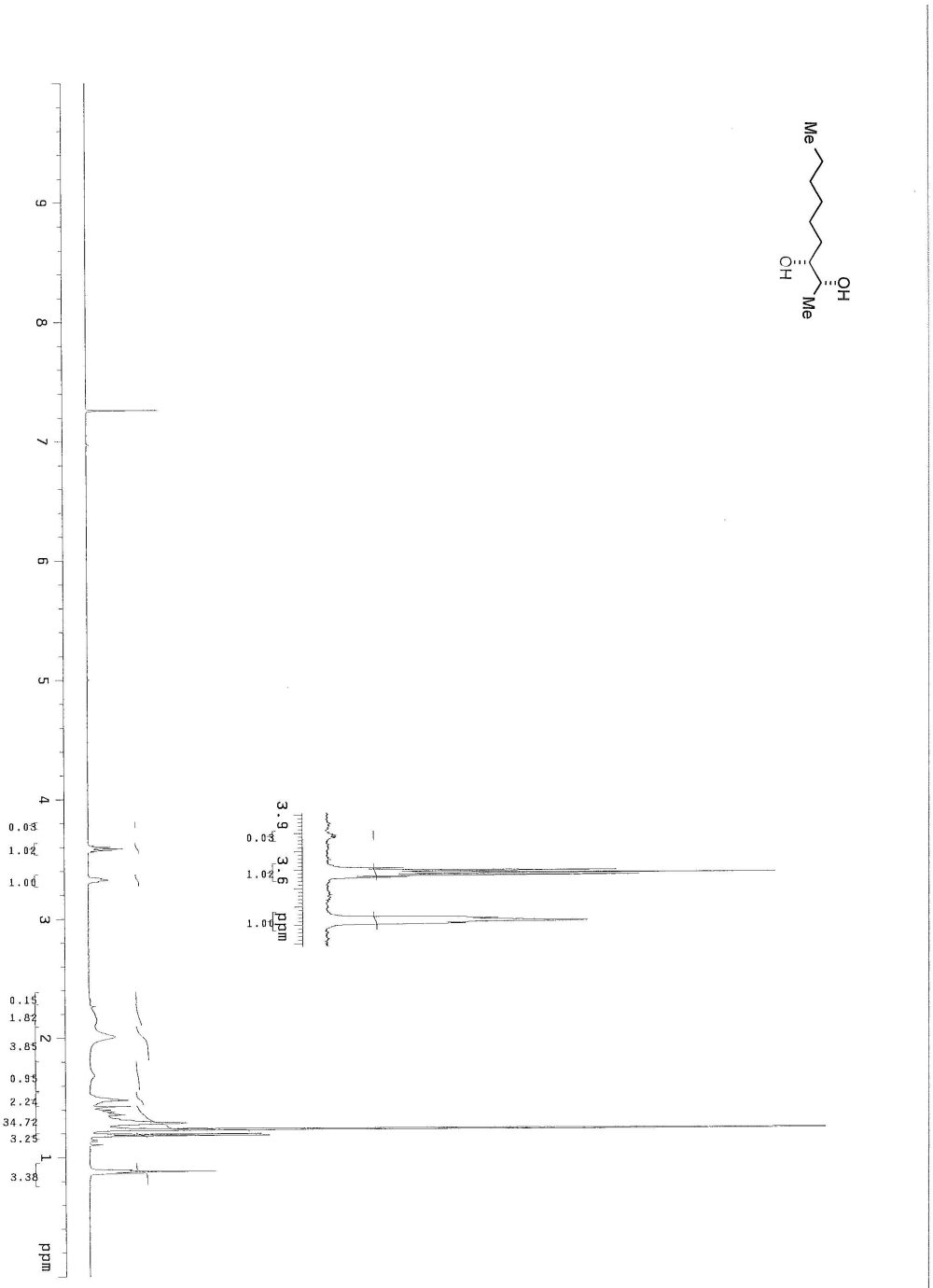
200
180
160
140
120
100
80
60
40
20
0
ppm


Me
OH
OH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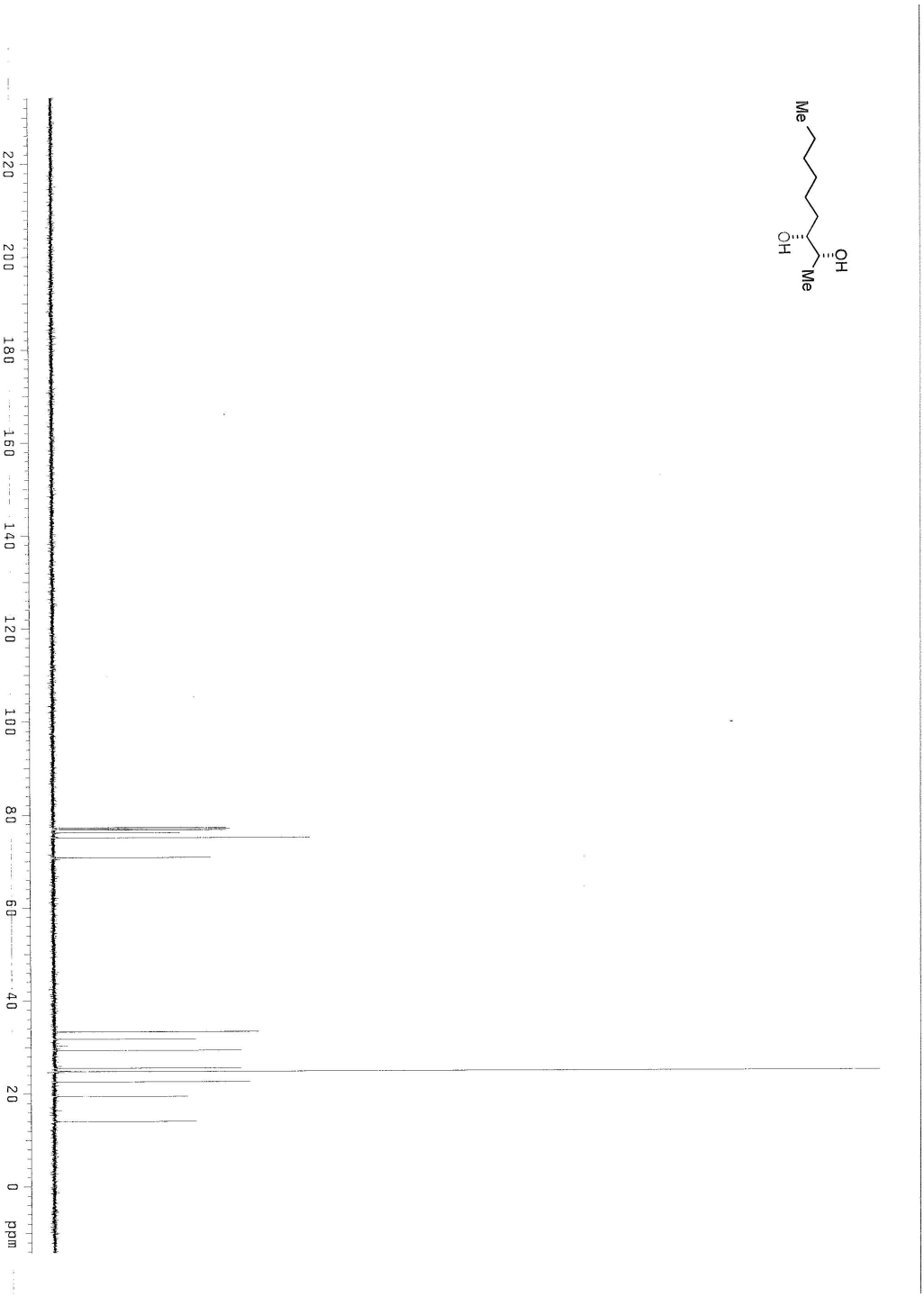
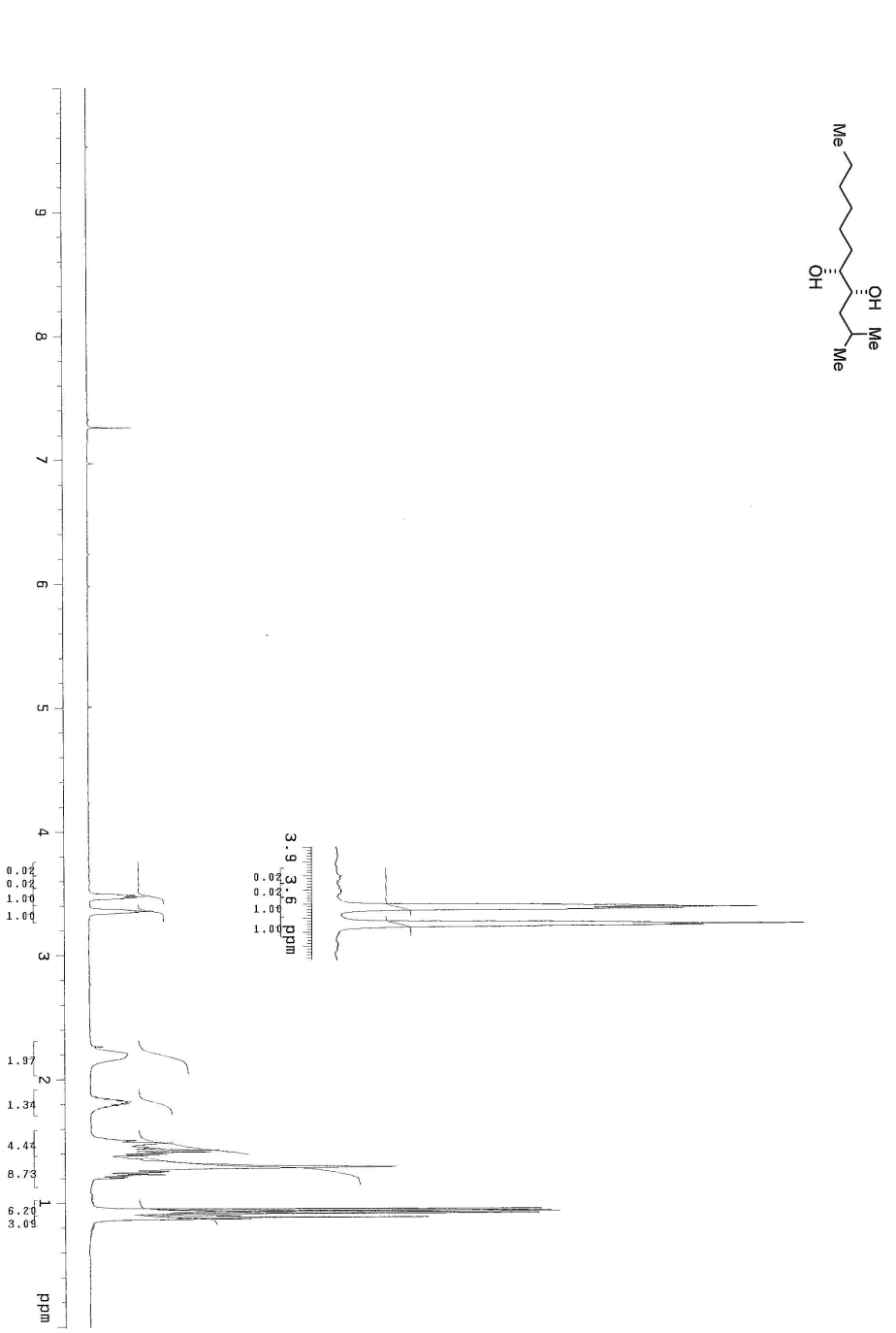
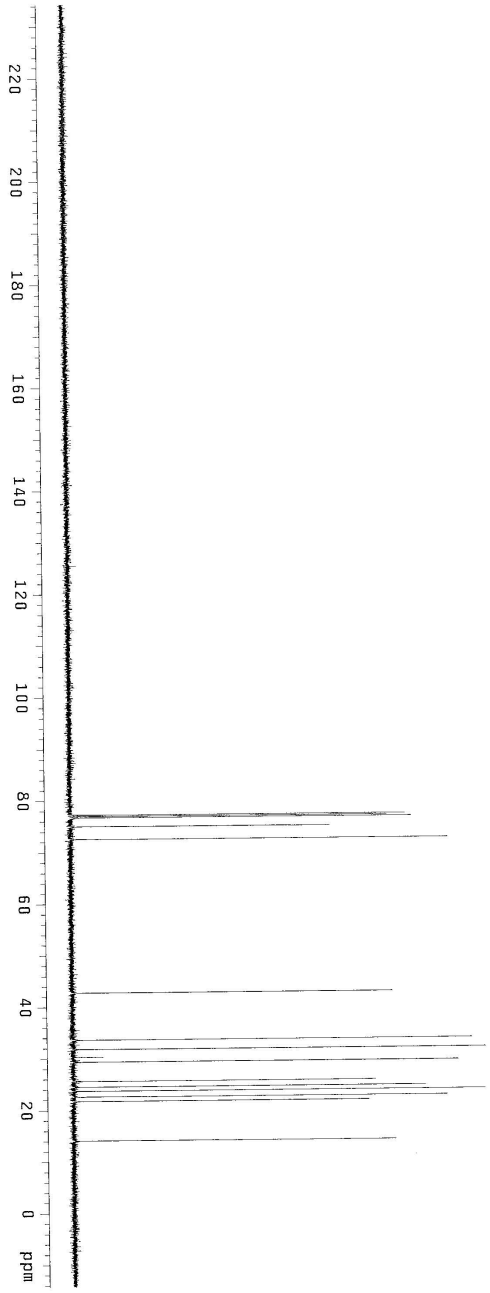
OH
OH
Me
ppm
3.9
3.6
ppm


Me
OH
OH
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Me
OH
Me
OH
Me
9
8
7
6
5
4
3
2
1
ppm
0.02
0.02
1.00
1.00
1.97
1.34
4.44
8.73
6.20
3.09
3.9
3.6
ppm
0.02
0.02
1.00
1.00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200
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100
80
60
40
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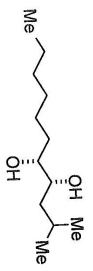
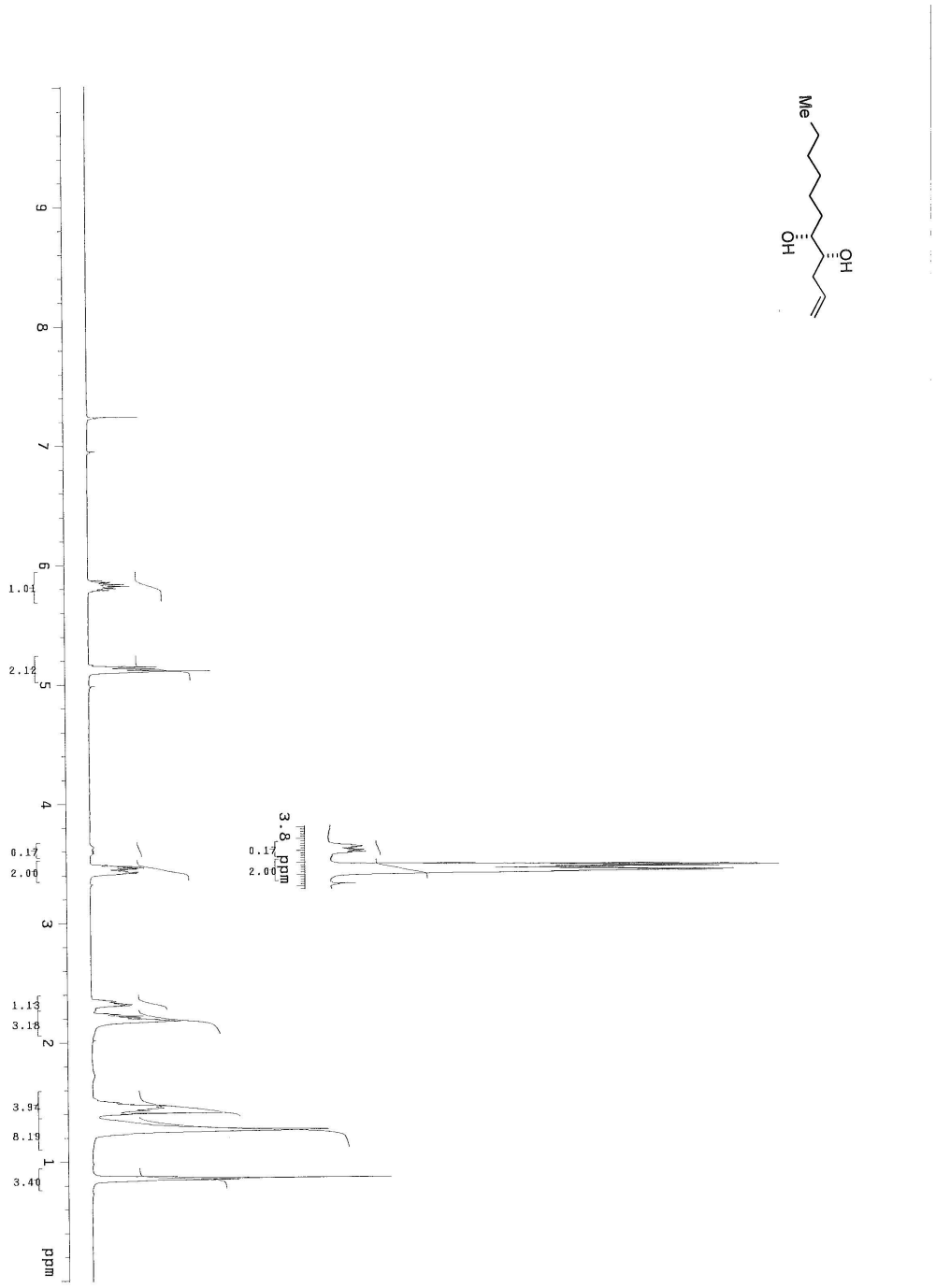
0
ppm


Me
OH
OH
Me
Me


Me
OH
OH
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2.12
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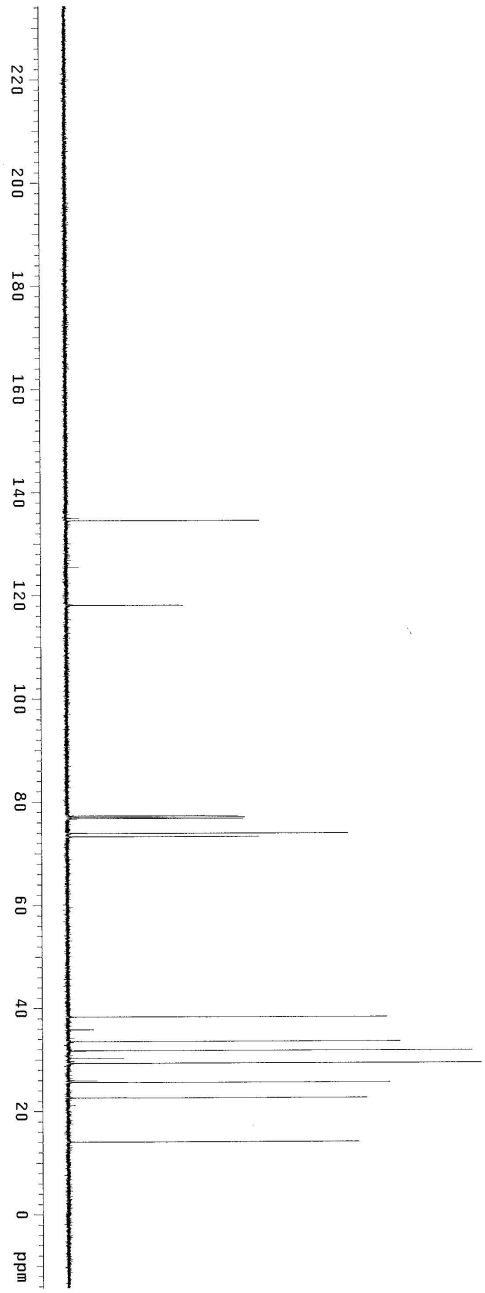
2.00
1.13
3.18
3.94
8.19
3.40
3.8 ppm
0.17
2.00
ppm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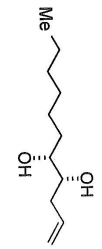
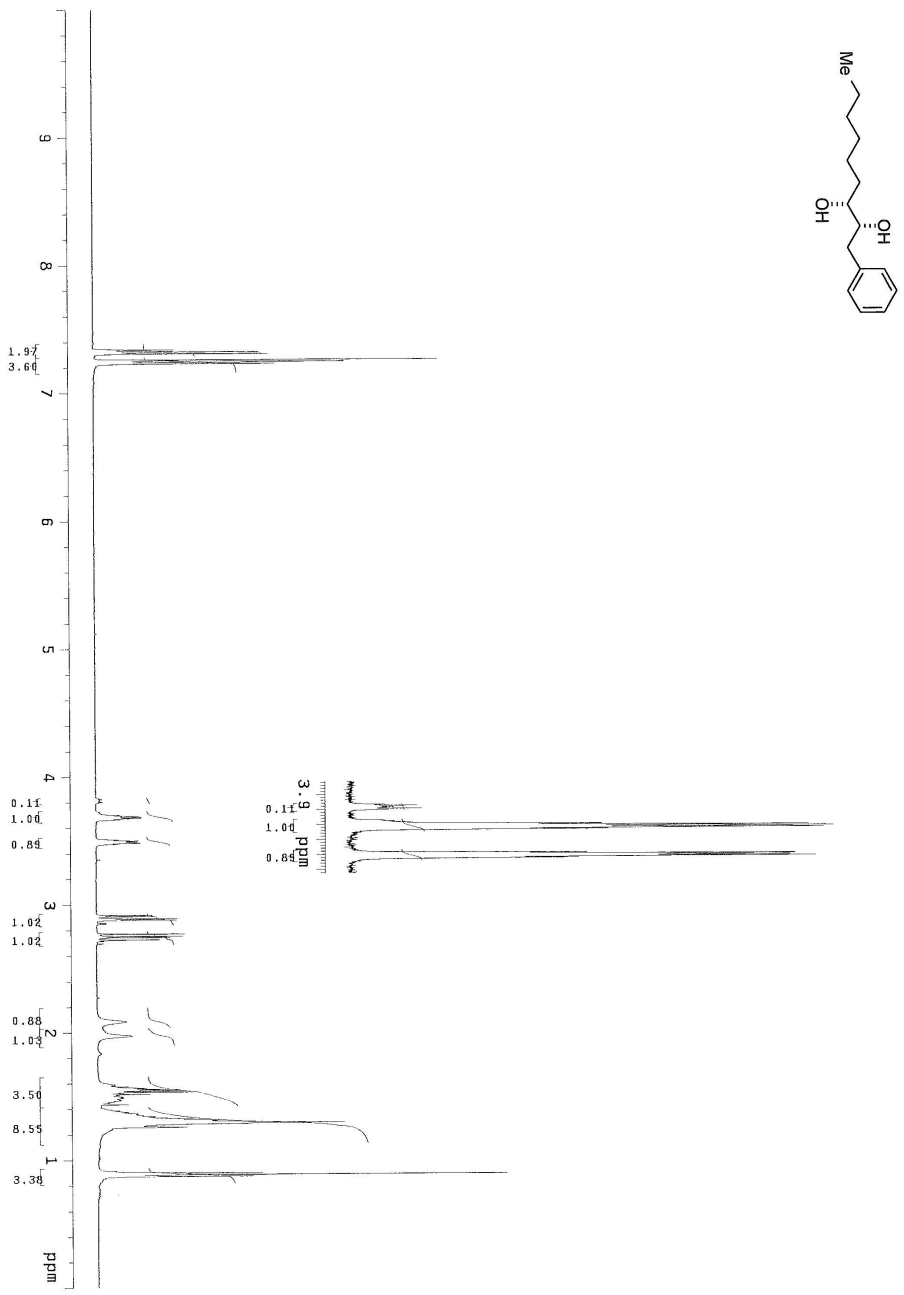
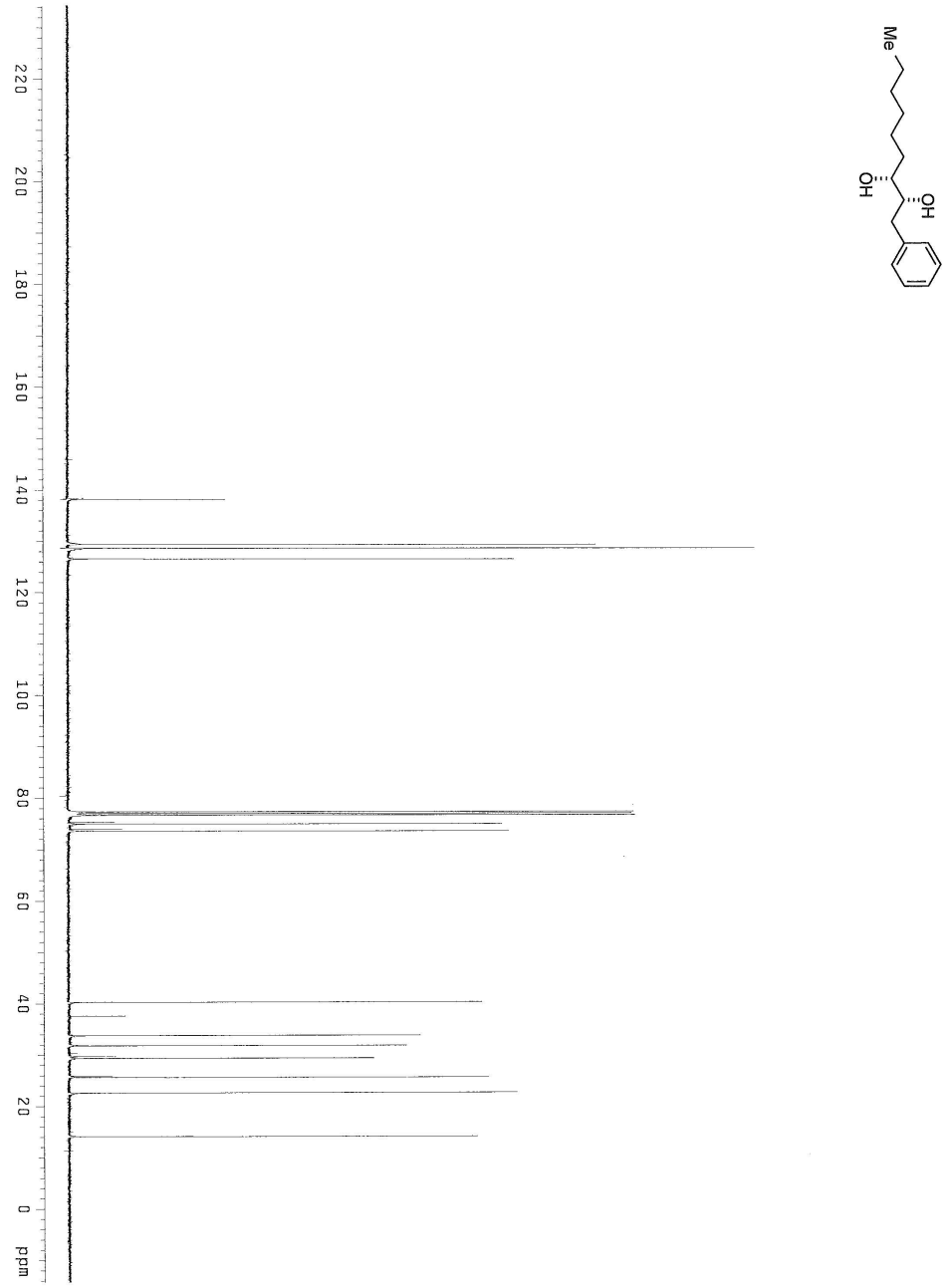
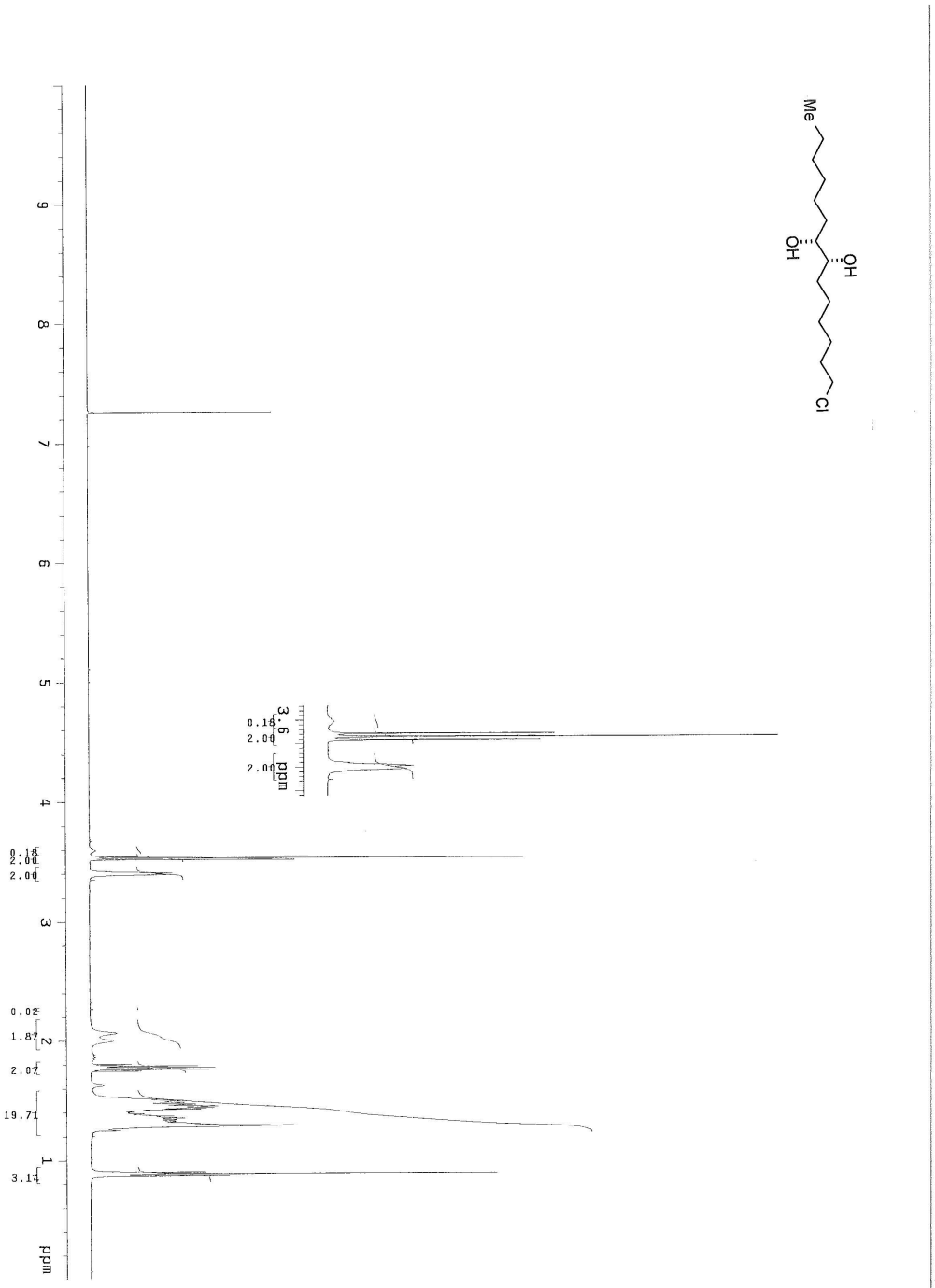
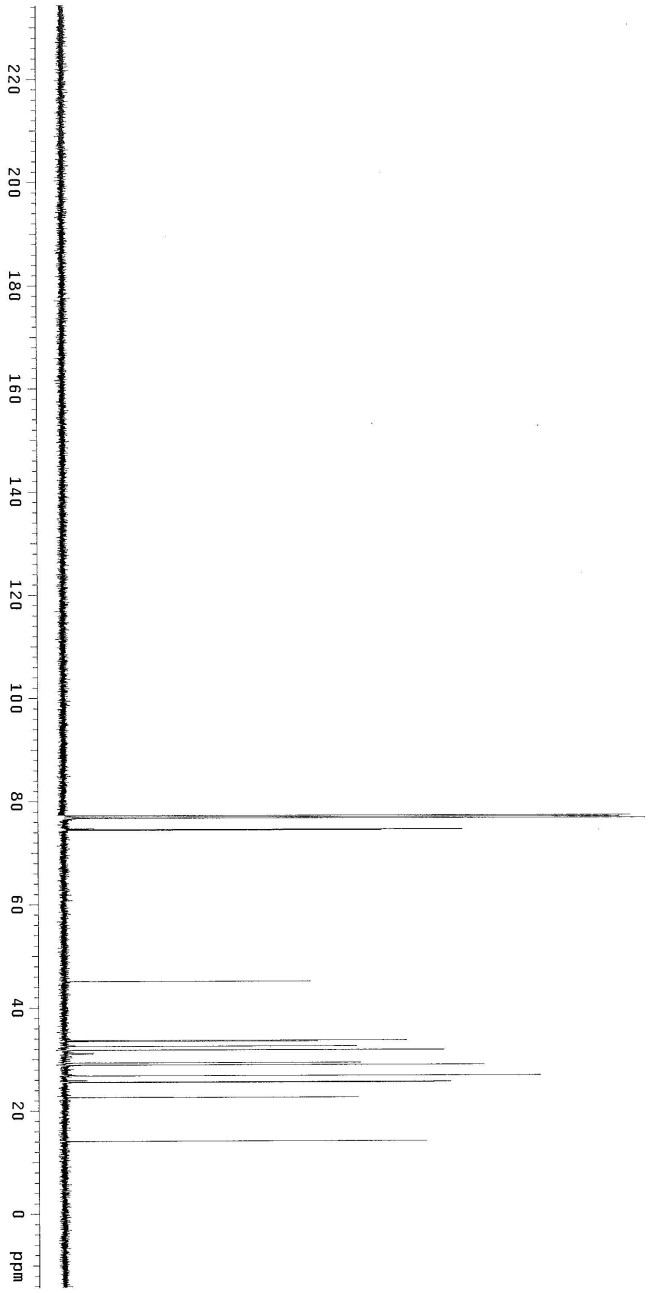
200
180
160
140
120
100
80
60
40
20
0
ppm

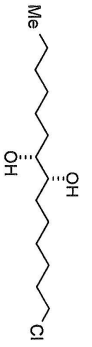

Me
OH
OH

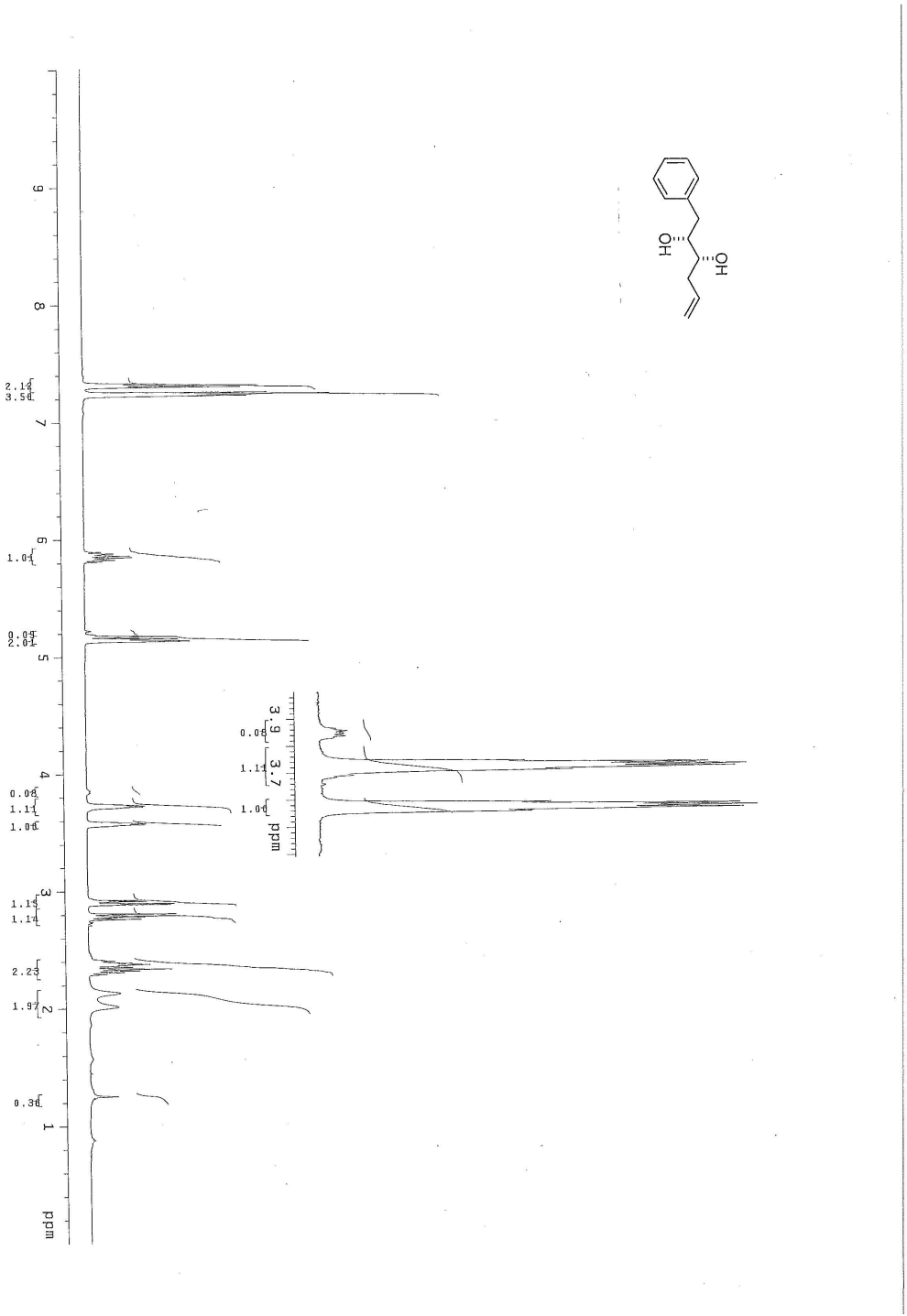

Me
OH
OH
1.97
3.60
0.11
1.00
0.84
1.02
1.02
0.88
1.03
3.50
8.55
3.38
ppm
3.9
ppm

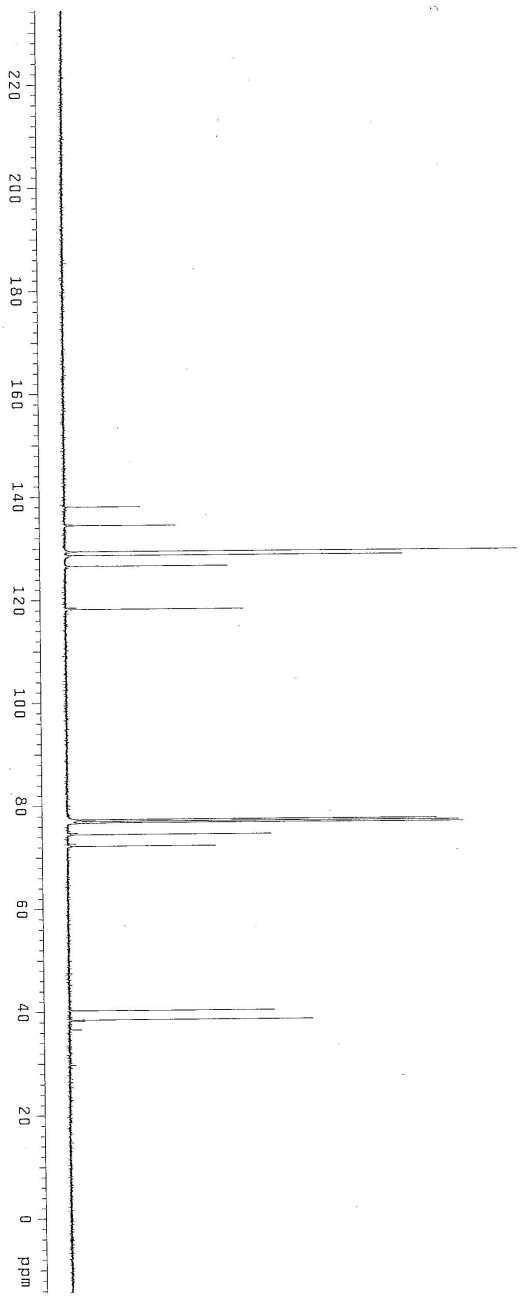

Me
OH
OH
220
200
180
160
140
120
100
80
60
40
20
0
ppm

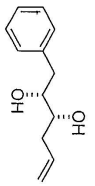

Me
OH
OH
Cl
3.6
ppm
0.16
2.00
2.00
0.02
1.87
2.07
19.71
3.14
ppm

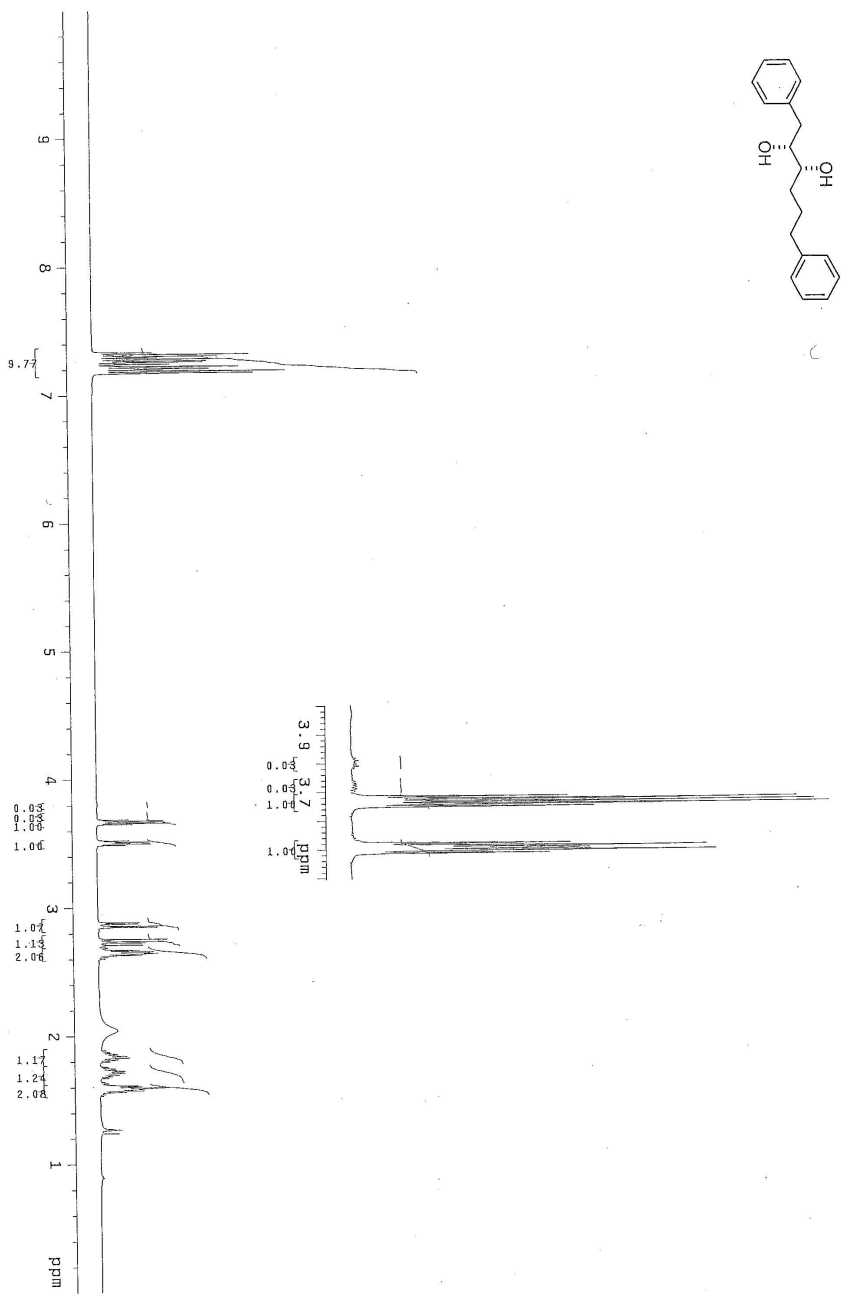

220
200
180
160
140
120
100
80
60
40
20
0
ppm

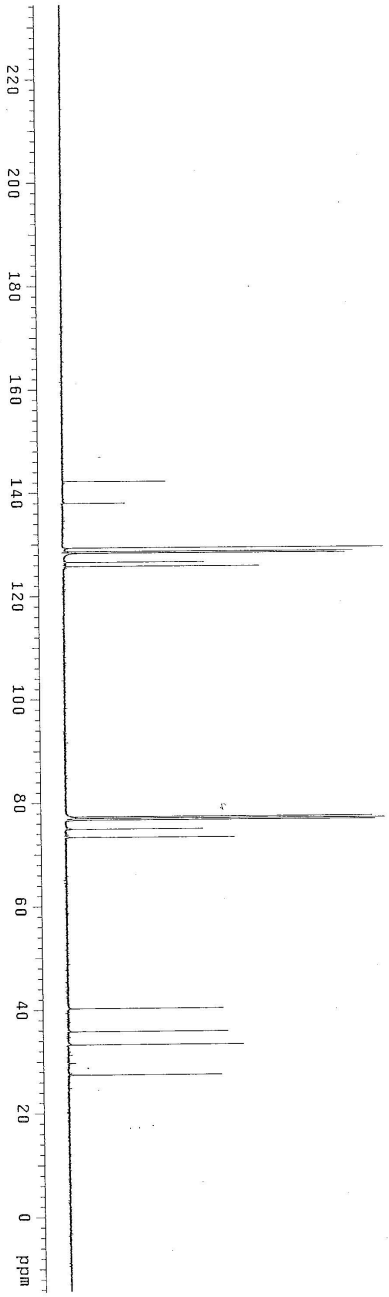

Me
OH
OH
Cl

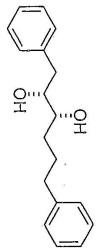

OH
OH
ppm
3.9
3.7
ppm

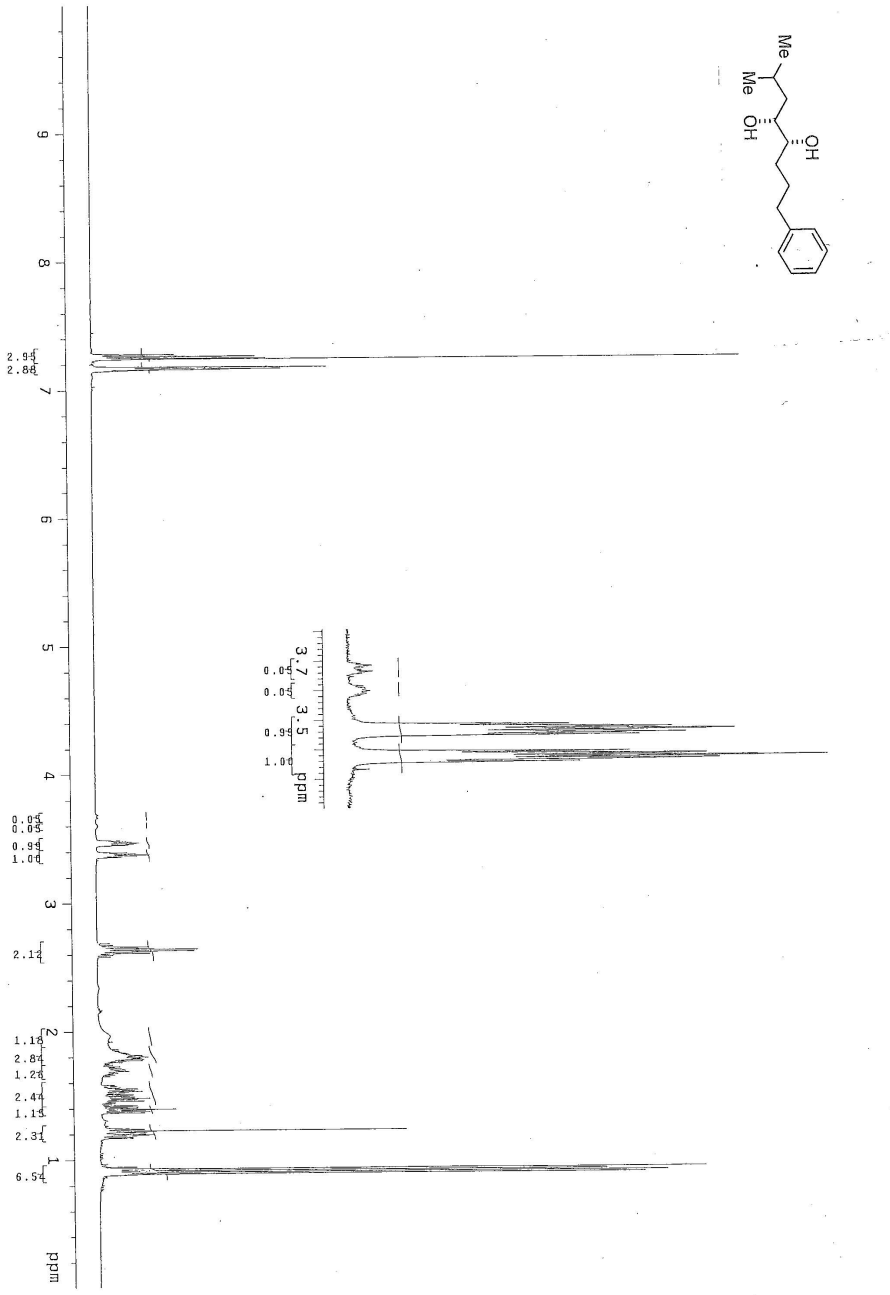

220
200
180
160
140
120
100
80
60
40
20
0
ppm

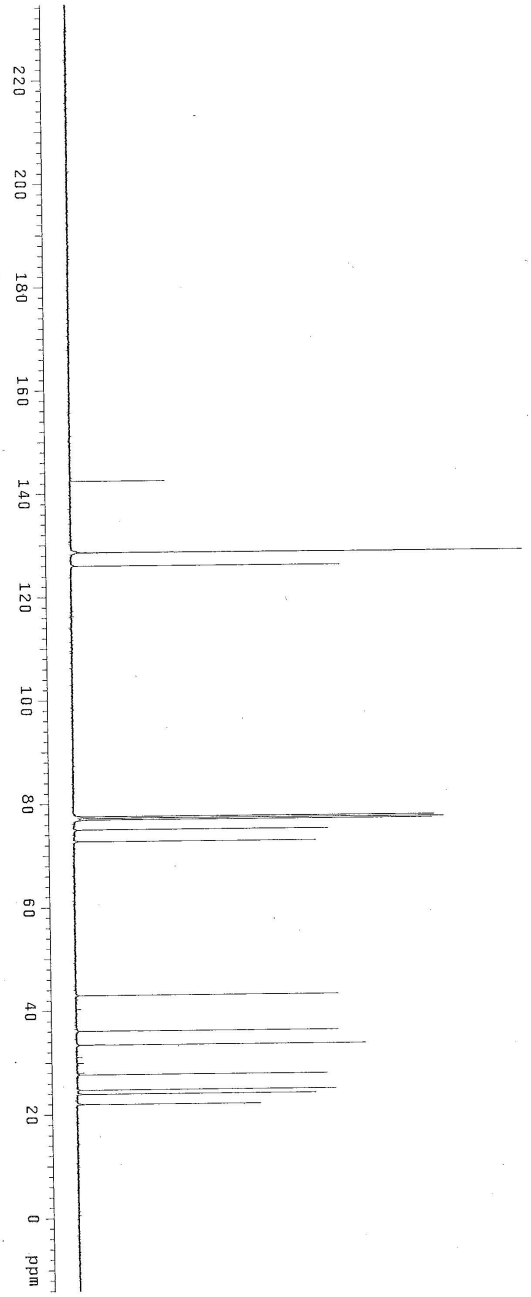

OH
OH

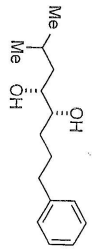

OH
OH
9.77
1.00
1.06
1.00
1.13
2.08
1.17
1.24
2.08
3.9
3.7
ppm
0.00
0.00
1.04
1.04
ppm

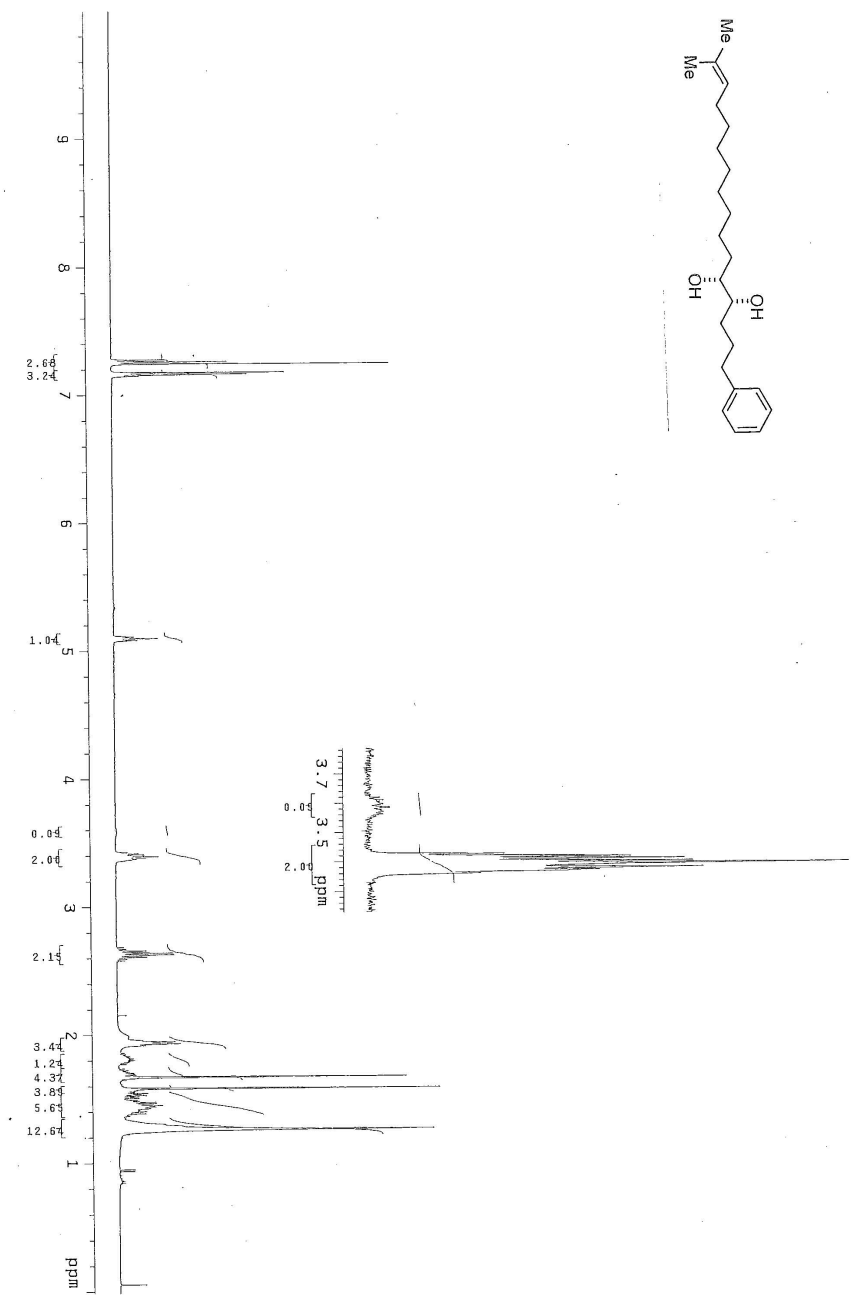

220
200
180
160
140
120
100
80
60
40
20
0
ppm

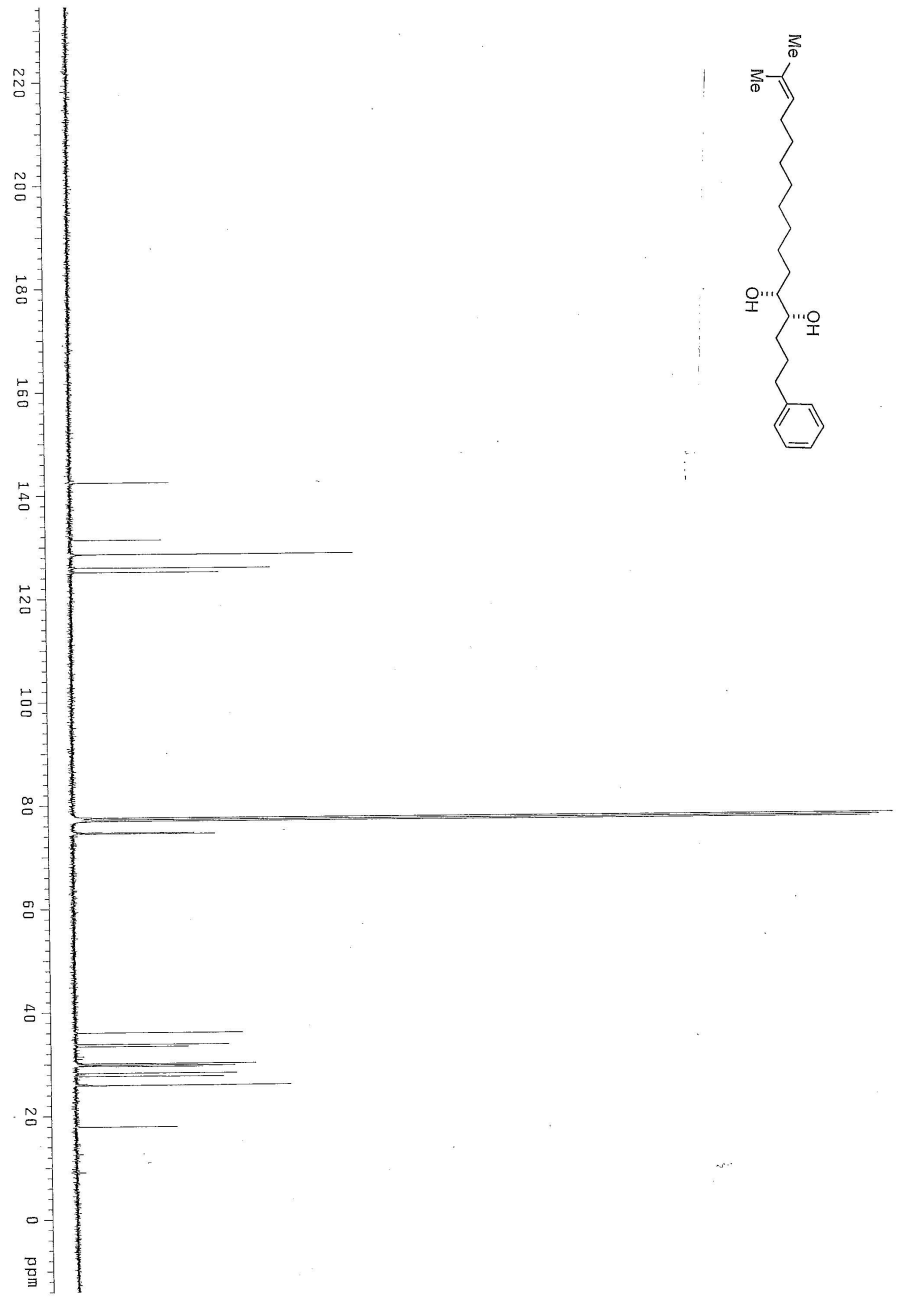

OH
OH

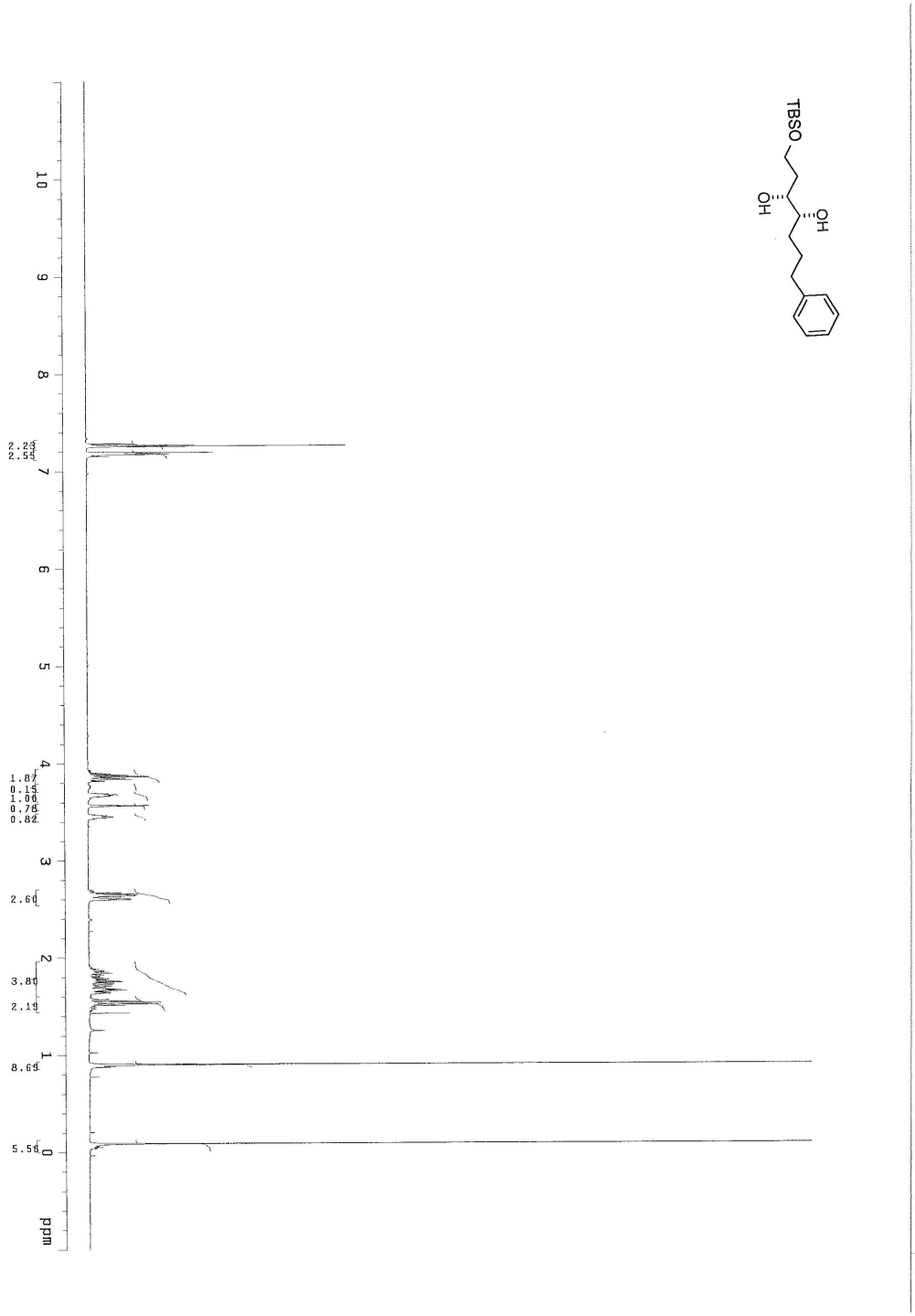

Me
Me
OH
OH
9
8
7
6
5
4
3
2
1
ppm
3.7
3.5
ppm

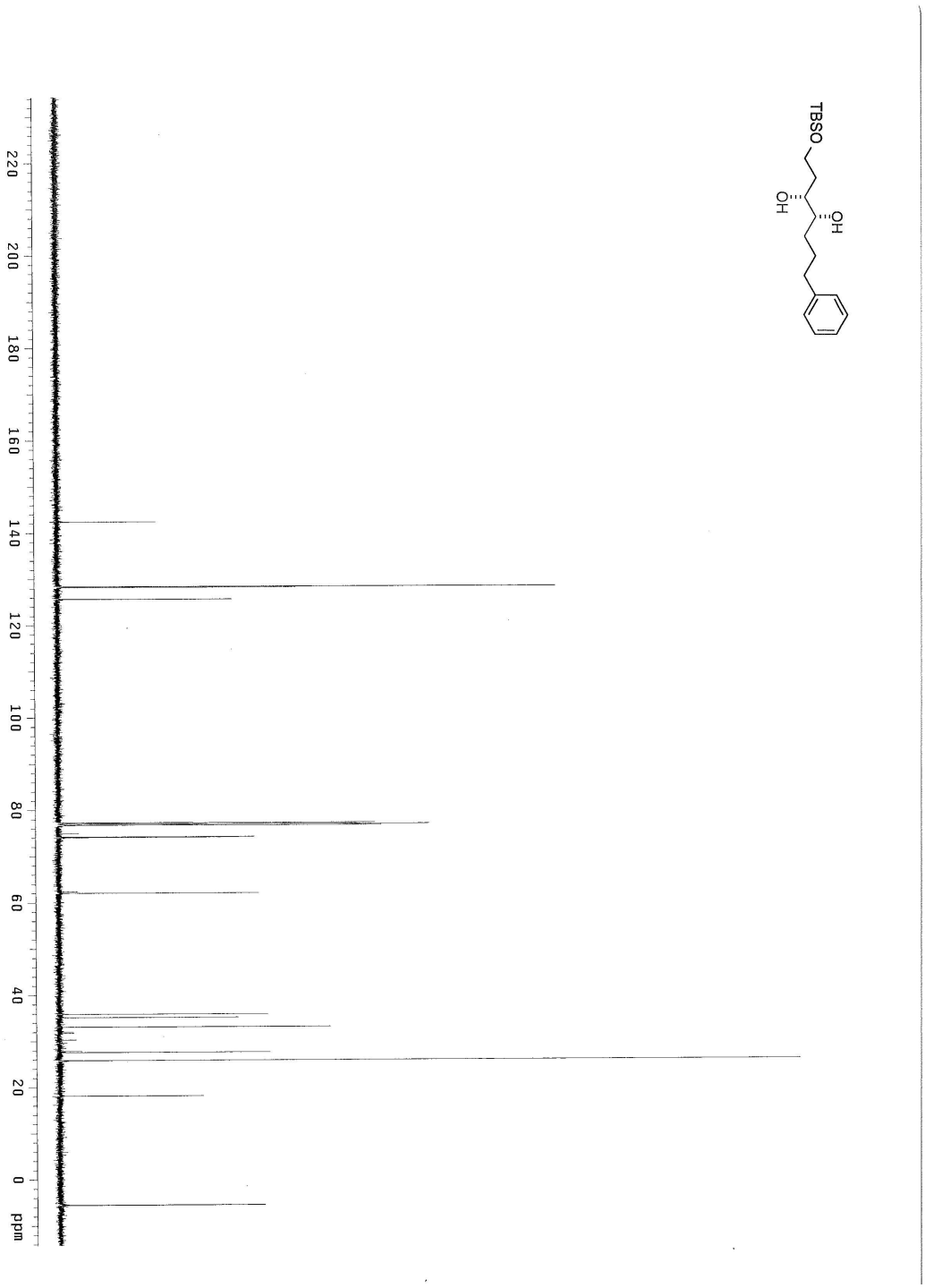

220
200
180
160
140
120
100
80
60
40
20
0
ppm

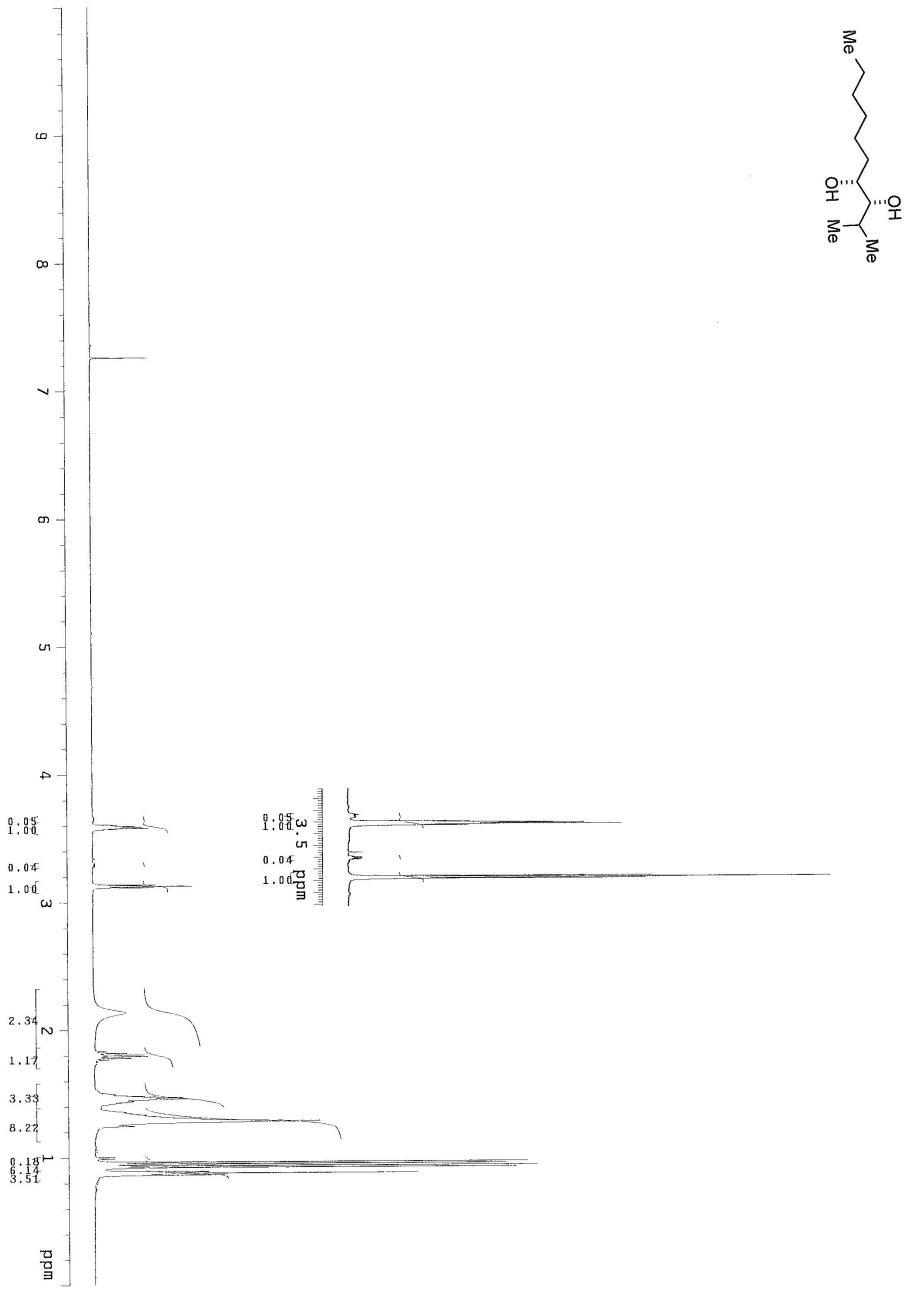

Me
Me
OH
OH


Me
Me
OH
OH
2.68
3.24
1.04
0.04
2.04
2.14
3.44
1.24
4.37
3.84
5.63
12.64
ppm
3.7
3.5
ppm
0.0
2.0


Me
Me
OH
OH
220
200
180
160
140
120
100
80
60
40
20
0
ppm

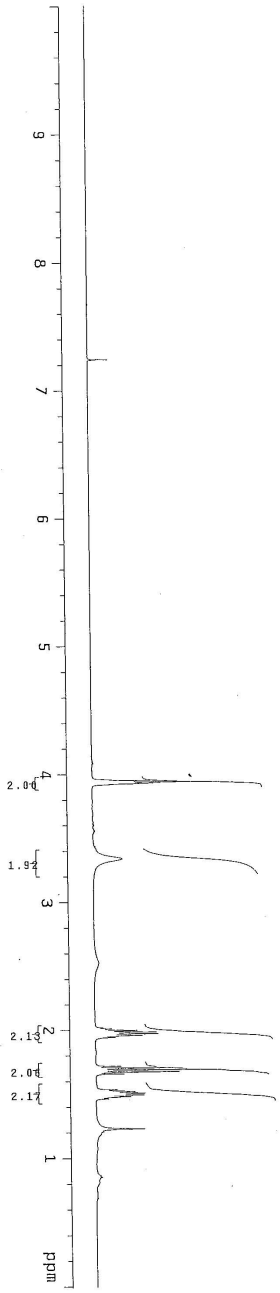

TBSO
OH
OH
ppm

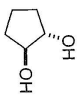

TBSO
OH
OH
220
200
180
160
140
120
100
80
60
40
20
0
ppm

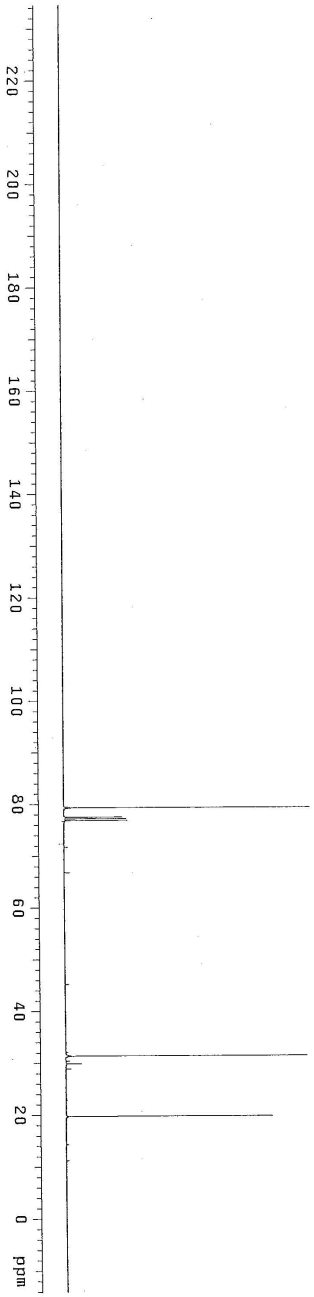

Me
OH
Me
OH
Me
ppm
3.5
ppm

Me
OH
OH
Me
Me

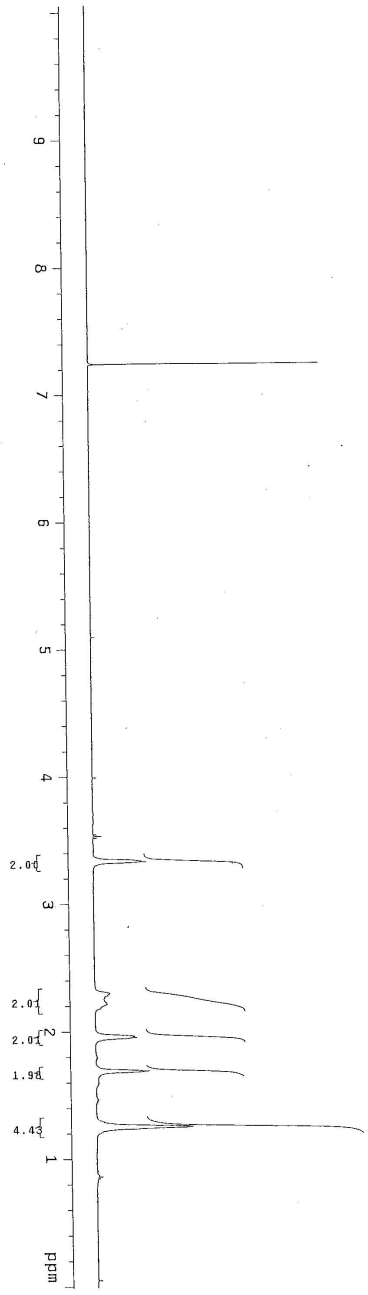
220
200
180
160
140
120
100
80
60
40
20
0
ppm

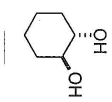

9
8
7
6
5
4
3
2
1
ppm
2.04
1.92
2.13
2.04
2.17

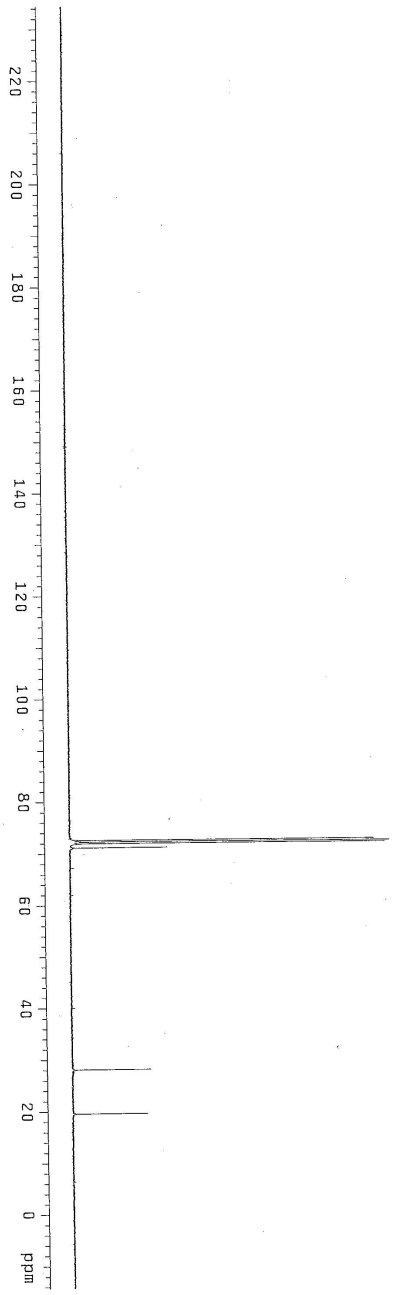

OH
OH

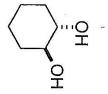

220
200
180
160
140
120
100
80
60
40
20
0
ppm

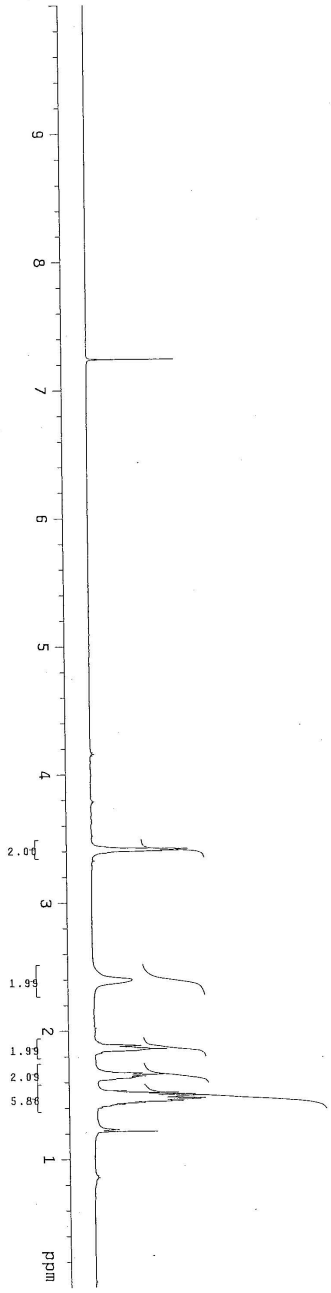

OH
OH


9
8
7
6
5
4
3
2
1
ppm
2.01
2.01
2.01
1.98
4.43


OH
OH


220
200
180
160
140
120
100
80
60
40
20
0
ppm


OH
OH


9
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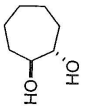
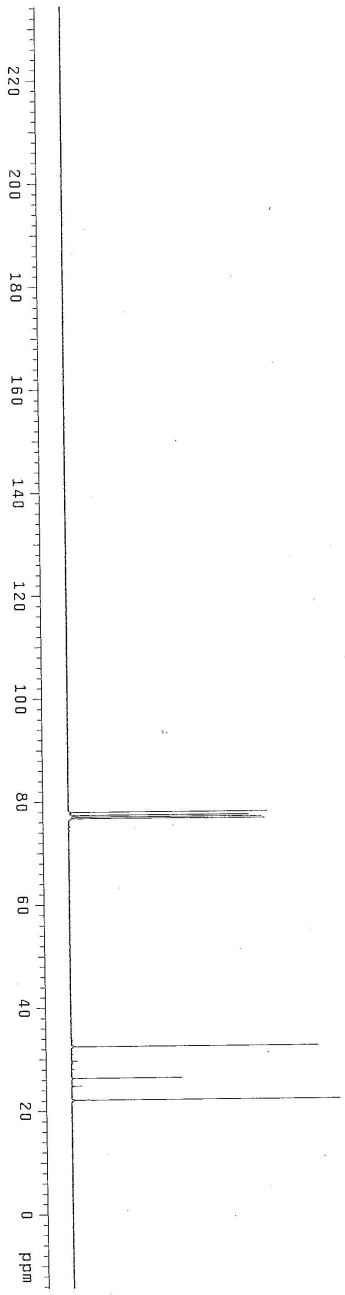
7
6
5
4
3
2
1
ppm
2.04
1.99
1.99
2.09
5.86


HO
HO


220
200
180
160
140
120
100
80
60
40
20
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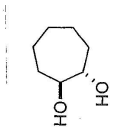
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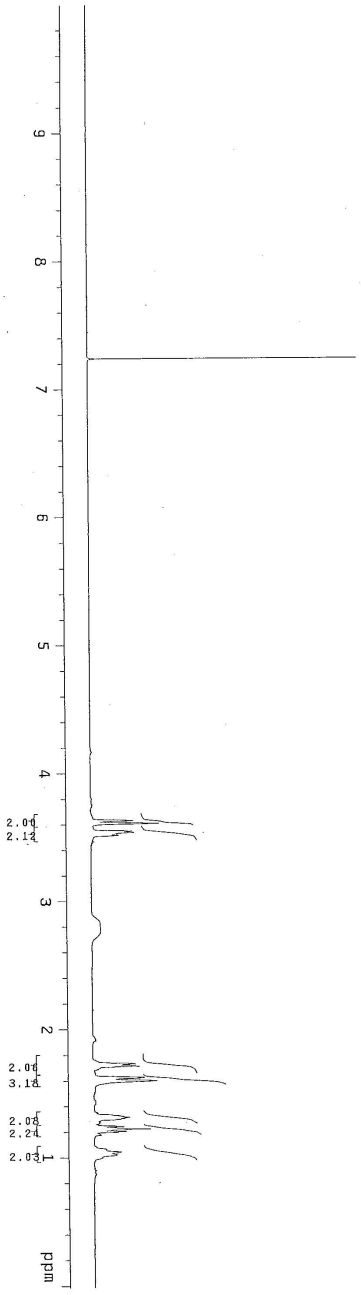
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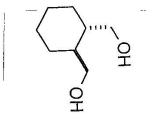
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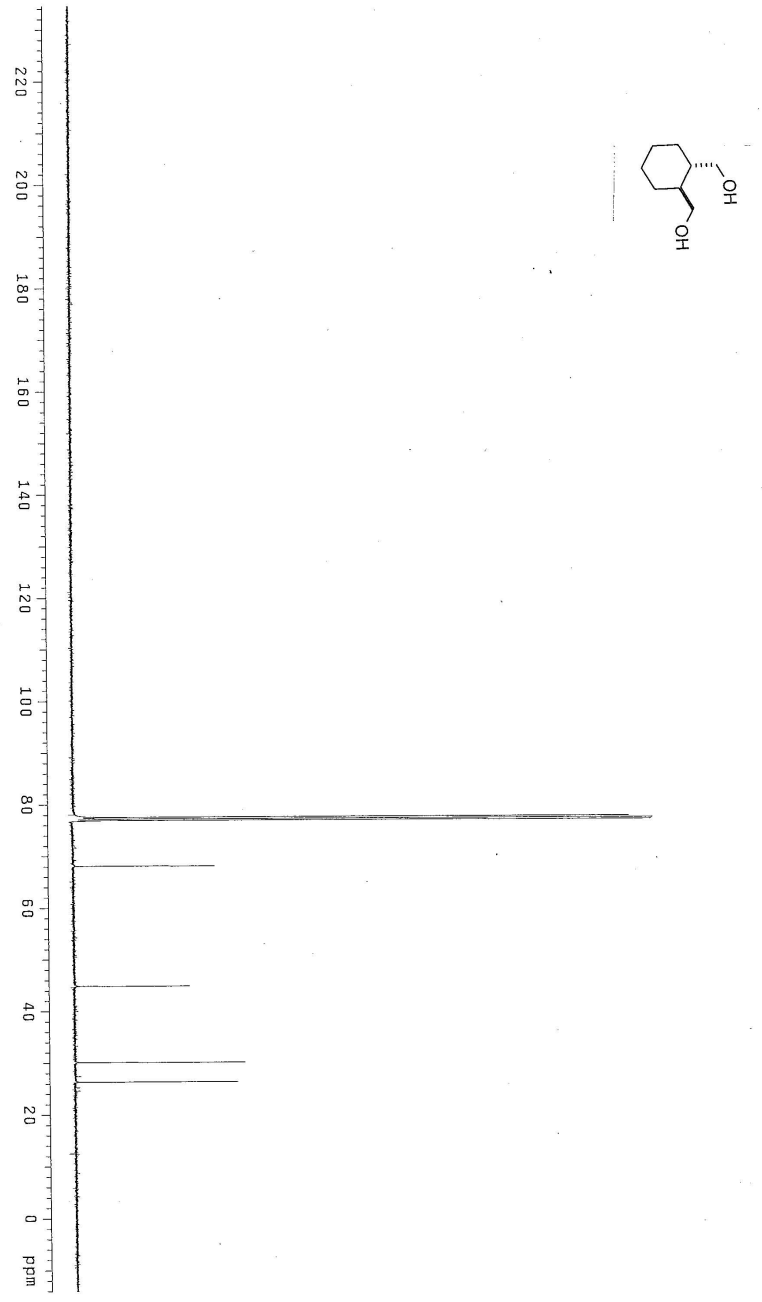
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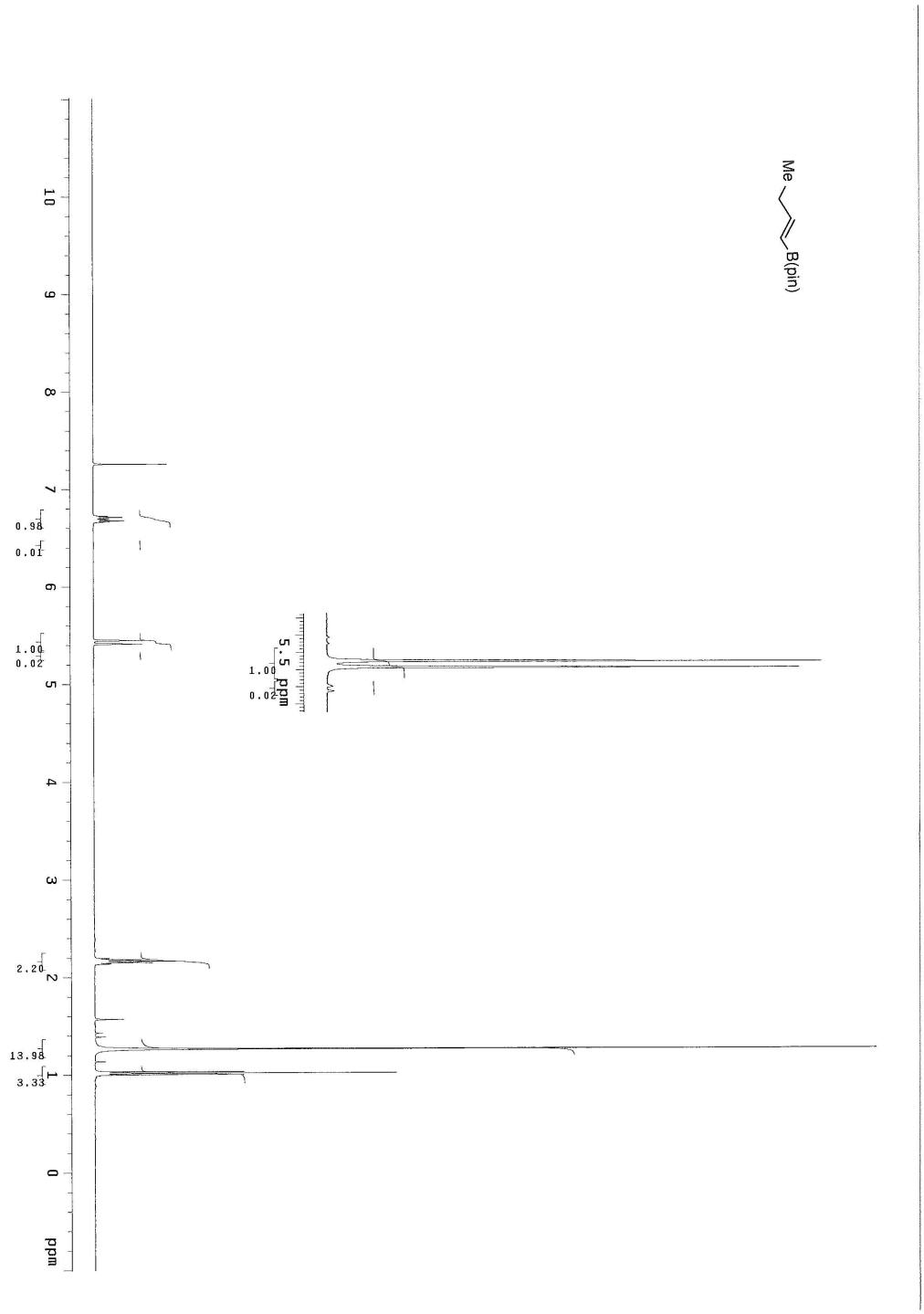
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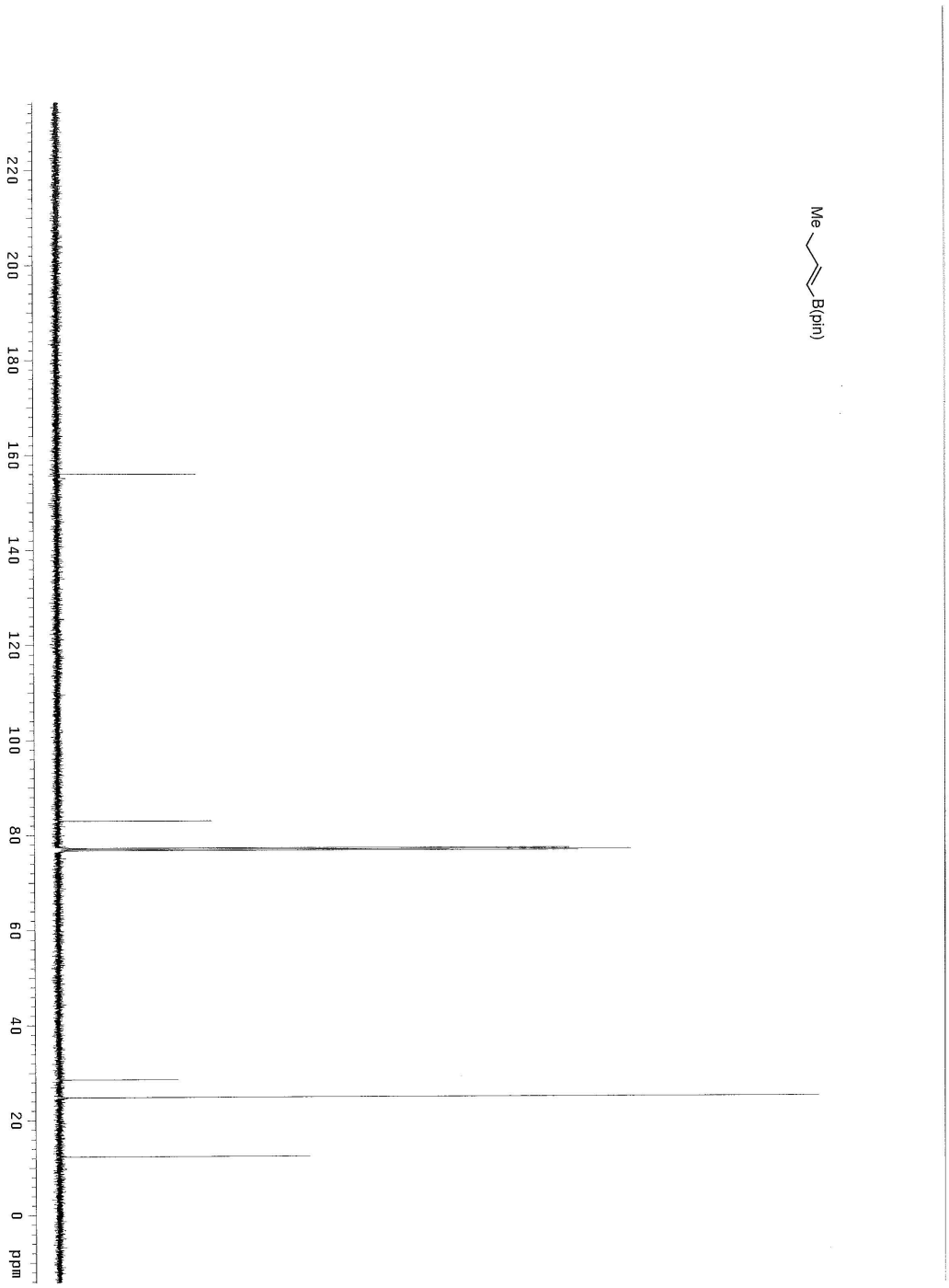
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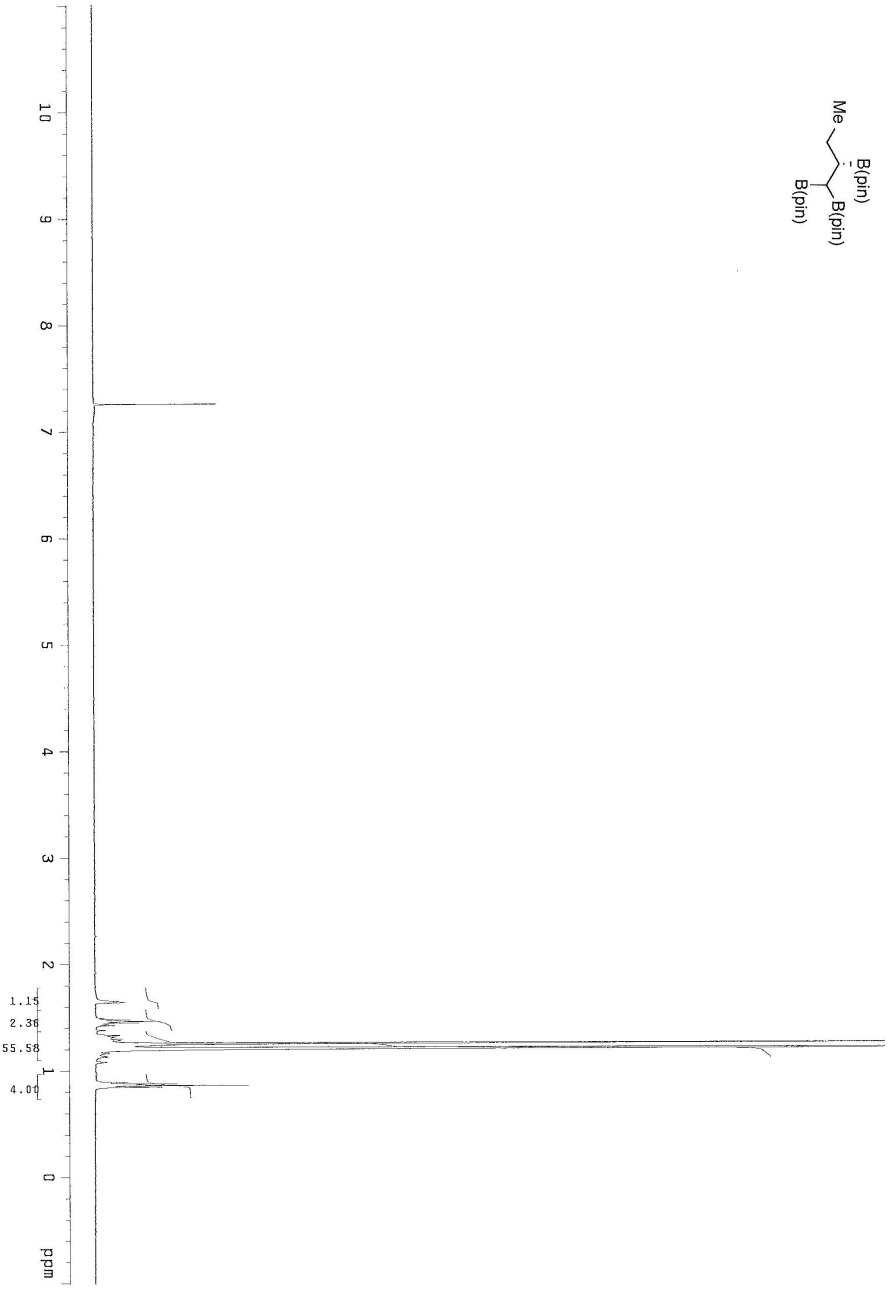
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B(pin)
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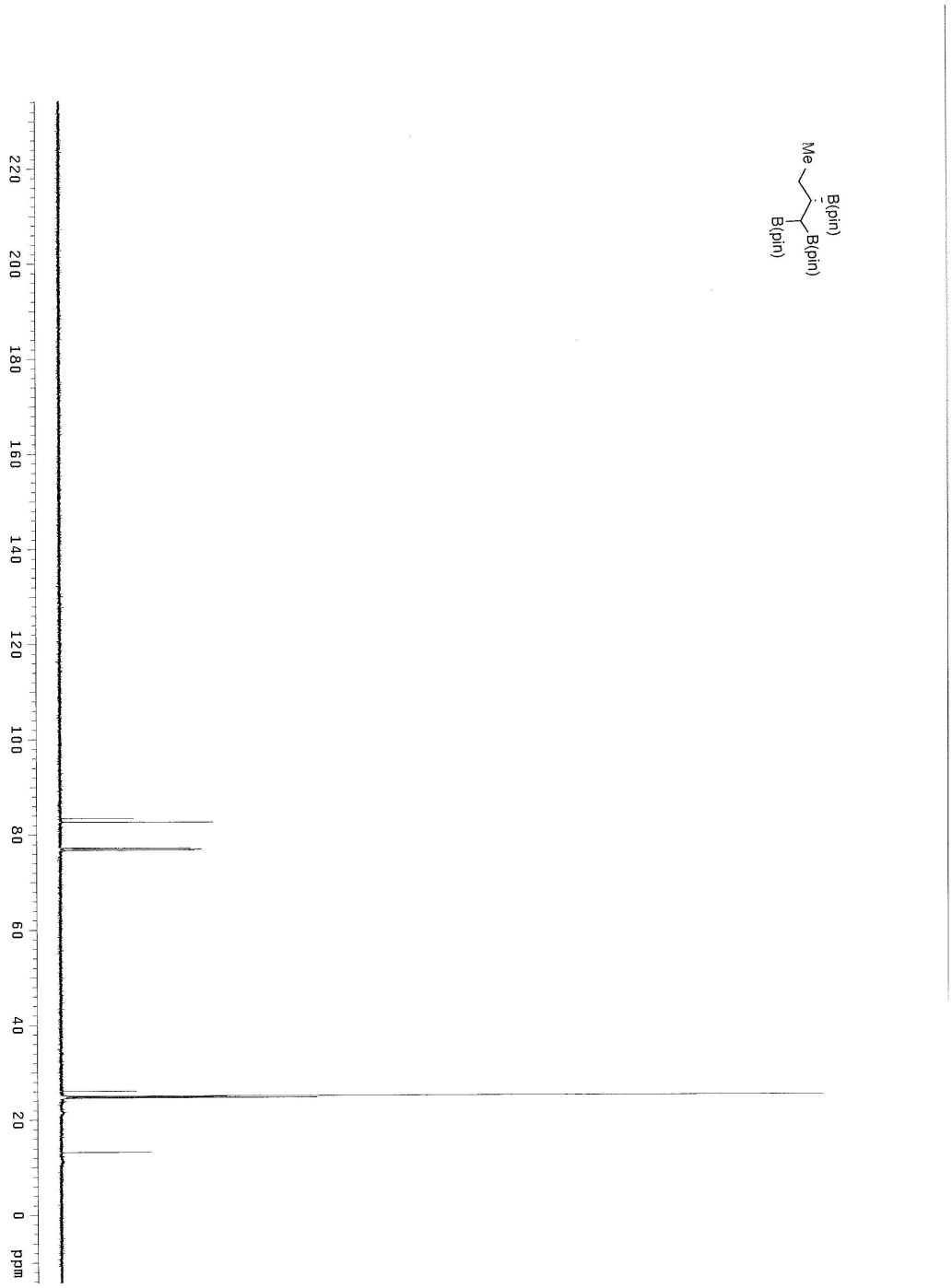
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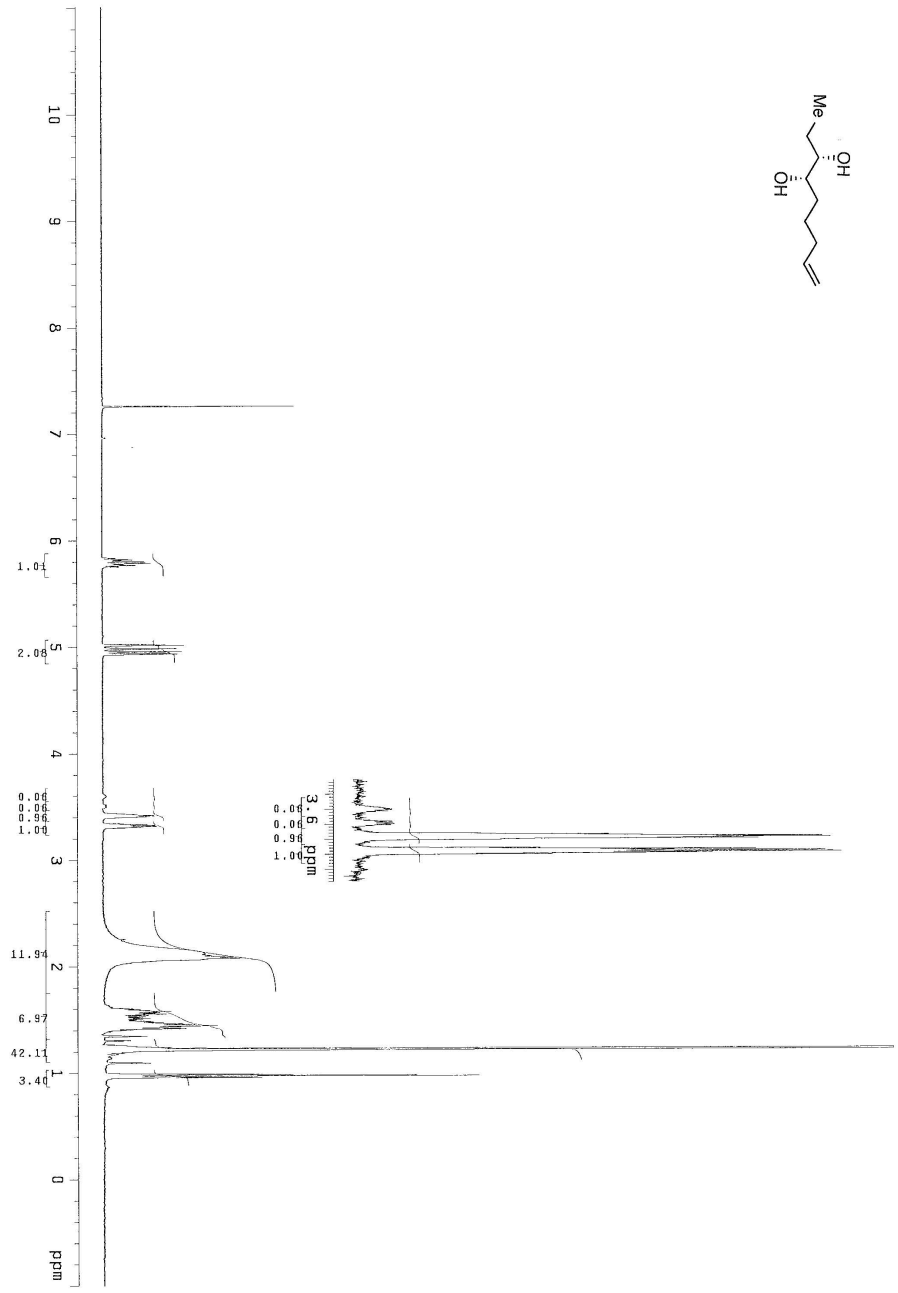
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2
1
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ppm
1.01
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0.06
0.96
1.04
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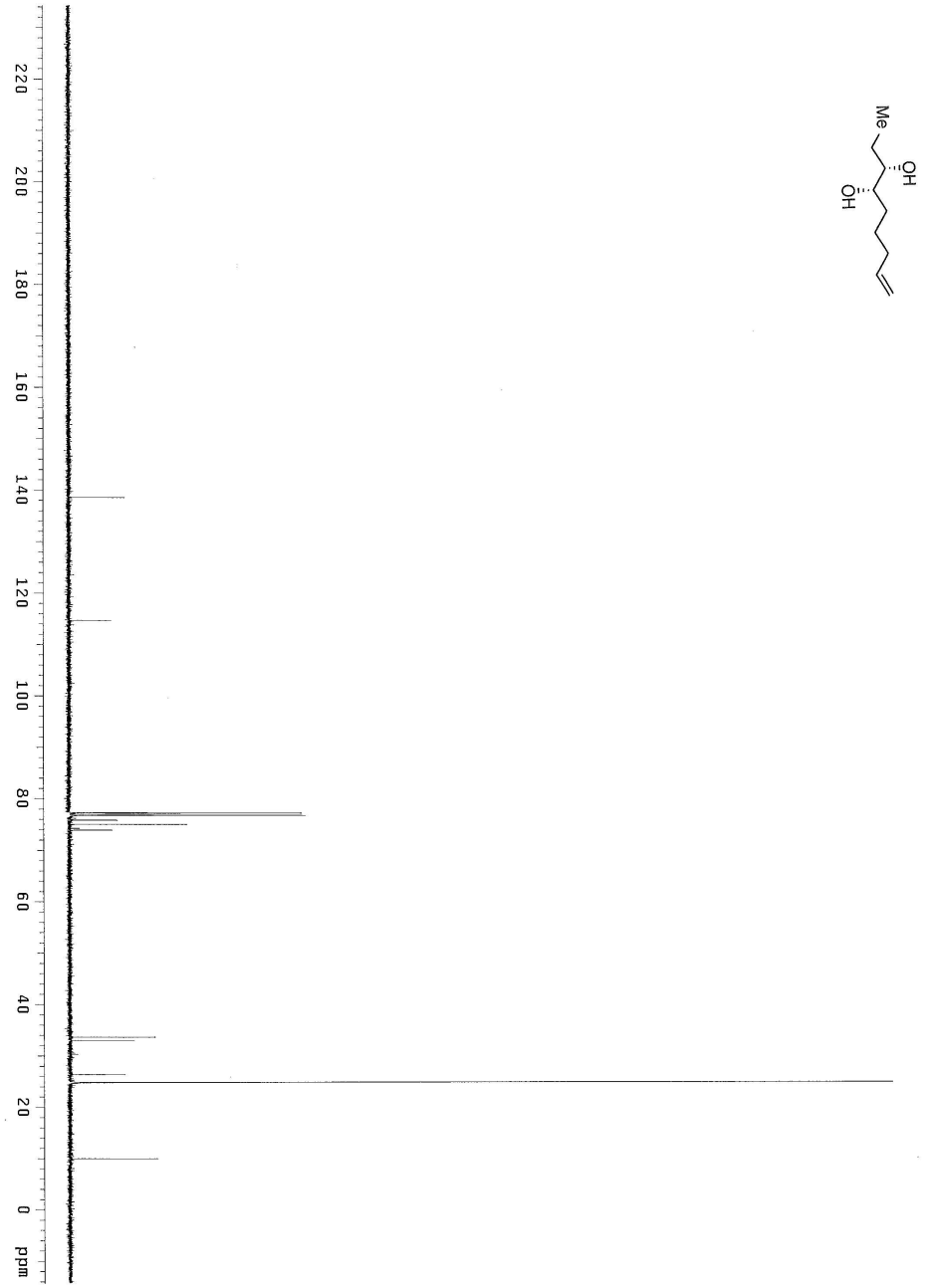
6.97
42.11
3.40
3.6 ppm
0.06
0.06
0.96
1.00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Chapter 5

Synthesis of Alkenyl Boronates from 1,1-bis(boronates) and Aldehydes: A Practical Boron-Wittig Reaction

5.1. Introduction

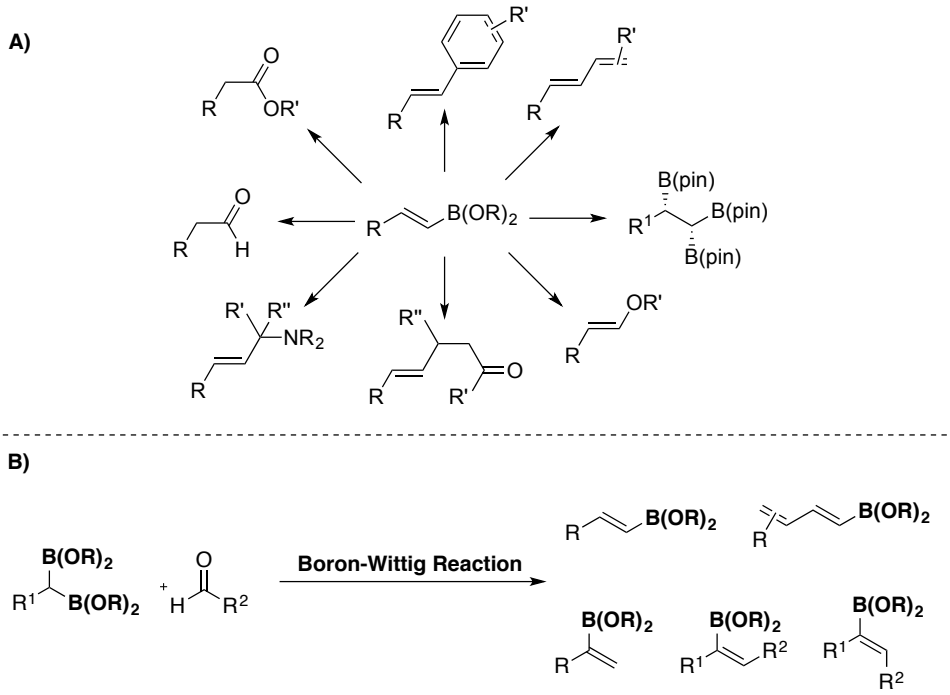
Alkenyl boronates are recognized as powerful building blocks that have been widely used in synthetic organic chemistry. While they are generally chemically stable and environmentally benign, they can be engaged in a variety of transformations (Scheme 5.1.A), including but not limited to Suzuki-Miyaura cross-couplings[1], Chan-Lam couplings[2], Hayashi-Miyaura conjugate additions[3], and Petasis couplings.[4] Their versatility in therapeutic reagents and natural products synthesis makes the development of a practical synthesis of alkenyl boronates highly attractive to synthetic chemists.

In this light, much effort has been invested into this field over past five decades. However, although an abundance of developments regarding the synthesis of alkenyl boronates from alkyne and alkene precusors has been well documented, alternative access to these motifs from readily available reagents, such as aldehydes and ketones, is lacking. Furthermore, while the stereoselective synthesis of *trans*-1,2-disubstituted alkenyl boronates has been well addressed in recent years, highly regio- and stereoselective

[1] (a) Miyaura, N., Suzuki, A. *Chem. Rev.* **1995** 95 , 2457. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, 576,
[2] (a) Shade, R. E., Hyde, A. M., Olsen, J.-C., Merlic, C. A. *J. Am. Chem. Soc.* **2010**, 132, 1202. (b) Winternheimer, D. J., Merlic, C. A. *Org. Lett.* **2010**, 12, 2508.
[3] (a) Takaya, Y., Ogasawara, M., Hayashi, T. *Tetrahedron Lett.* **1998**, 39, 8479. (b) Takaya, Y., Senda, T., Kurushima, H., Ogasawara, M., Hayashi, T. *Tetrahedron: Asymmetry* **1999**, 10, 4047.
[4] (a) Candeias, N. R., Montalbano, F., Cal, P. M. S. D., Gois, P. M. P. *Chem. Rev.* **2010**, 110, 6169. (b) de Graaff, C., Ruijter, E., Orru, R. V. A. *Chem. Soc. Rev.* **2012**, 41, 3969.

synthesis of tri-, *cis*-1,2- and 1,1-disubstituted alkenyl boronates remains challenging. In this context, the development of a practical and highly stereoselective synthesis of alkenyl boronates enabled by the boron-Wittig reaction between readily available aldehydes and geminal bis(boronates) will be presented in this chapter. A broad range of di- and tri-substituted alkenyl boronates can be efficiently furnished by this method in a highly stereoselective and transition-metal-free fashion (Scheme 5.1.B).

Scheme 5.1. Selected transformations of alkenyl boronates and boron-Wittig reaction.



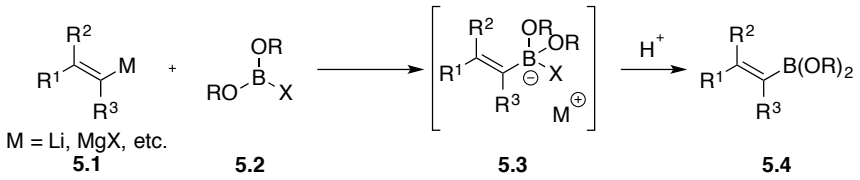
5.2. Background

5.2.1. Representative synthesis of 1,2-disubstituted alkenyl boronates

One of the common methods to synthesize alkenyl boronates involves organometallic reagents. As shown in Scheme 5.2, an alkenyl metal species, such as an alkenyl lithium

or alkenyl Grignard reagent, can be treated with an electrophilic boron species, such as a borate ester, to form a boron ate complex **5.3**. Subsequent protonation of complex **5.3** furnishes alkenyl boronate **5.4**.[5] Thus, the stereoselective synthesis of alkenyl boronate **5.4** relies on a stereoselective synthesis of corresponding alkenyl organometallic reagent **5.1**. Furthermore, employing such route to synthesis alkenyl boronates often requires cryogenic temperatures and reactive organometallic reagents that may not be compatible with sensitive functionalities, so that further application of this synthetic route to scale-up reaction is limited.

Scheme 5.2. Synthesis of alkenyl boronates from alkenyl organometallic reagents.



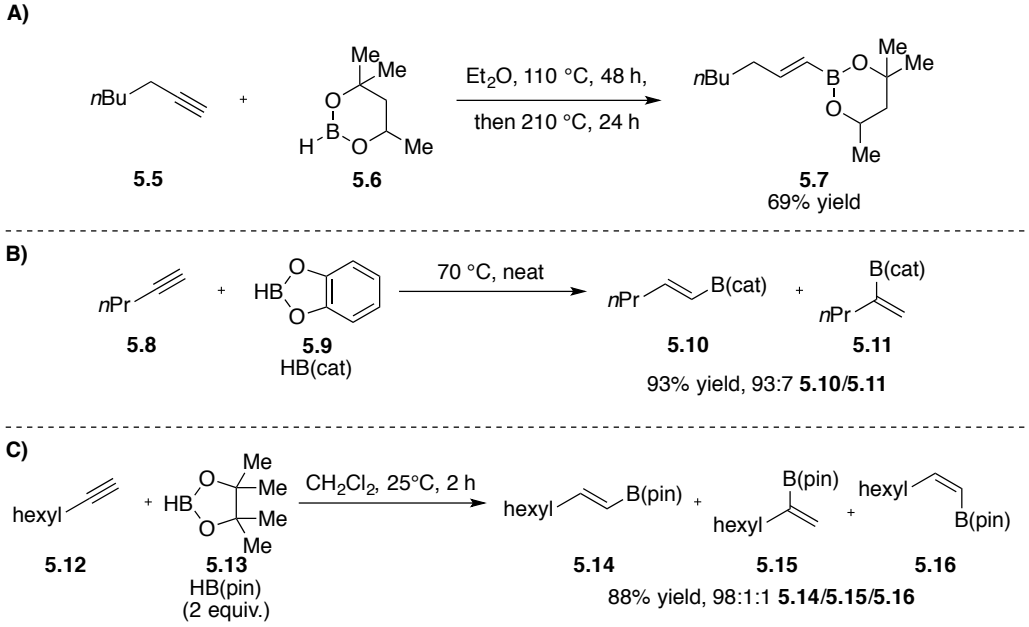
Alternatively, hydroboration of an alkyne with borane provides a mild way to access alkenyl boronates without utilizing reactive organometallic reagents. One of the early examples of alkyne hydroboration was reported by Woods and Strong in 1966.[6] 4,4,6-trimethyl-1,3,2-dioxaborinane **5.6** was synthesized and applied to the alkyne hydroboration reaction. A mixture of 1-heptyne **5.5** and borane **5.6** was heated for a long period of time to afford *trans*-alkenyl boronate **5.7** with moderate yield (Scheme 5.3.A). The observation of exclusively *trans*-isomer of the product suggested a *cis*-hydroboration occurred under reaction conditions. However, the requirement of extremely high

[5] (a) Woods, W. G., Bengelsdorf, I. S., Hunter, P. L. *J. Org. Chem.* **1966**, 31, 2766. (b) Pastro, D. J., Chow, J., Arora, S. K. *Tetrahedron* **1969**, 25, 1557. (c) Schaumber, G. D., Dobovan, S. *J. Organomet. Chem.* **1969**, 20, 261. (d) Mattesson, D. S., Thomas, J. R. *J. Organomet. Chem.* **1970**, 24, 262. (e) Mattesson, D. S. *Acc. Chem. Res.* **1970**, 3, 186.

[6] Woods, W. G., Strong, P. L. *J. Am. Chem. Soc.* 1966, 88, 4667.

temperature and long reaction time indicated the low reactivity of borane **5.6**, which limited the application of such strategy. In this context, Brown and co-workers developed a new hydroboration reagent, catecholborane **5.9**, which was much more reactive in alkyne hydroboration.[7] Treating 1-pentyne **5.8** with catecholborane **5.9** at 70 °C led to the *trans*-alkenyl boronate **5.10** with good yield and regioselectivity (Scheme 5.3.B).

Scheme 5.3. Synthesis of alkenyl boronates via alkyne hydroboration.



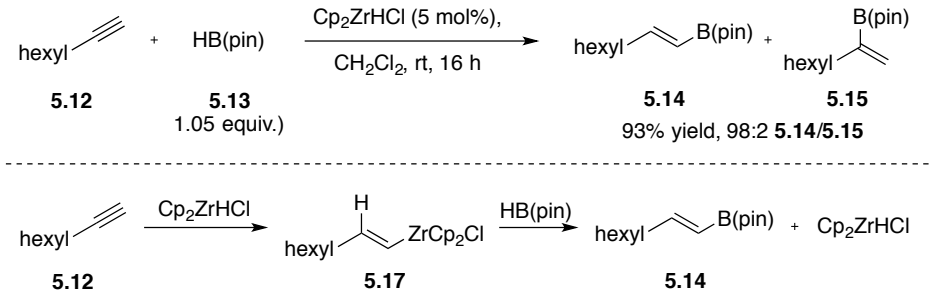
While the catacholborane presented high efficiency in alkyne hydroboration, the hydroborated product, catechol derived alkenyl boronates, were sensitive to air and moisture. Although a catechol derived alkenyl boronate could be converted to more stable pinacol derivative by a simple ligand exchange, the direct formation of alkenyl boronic acid pinacol esters from corresponding alkynes was much more desired transformation. In 1992, Knochel and co-workers reported an alkyne hydroboration with

[7] (a) Brown, H. C., Gupta, S. K. *J. Am. Chem. Soc.* **1972**, 94, 4370. (b) Brown, H. C., Gupta, S. K. *J. Am. Chem. Soc.* **1975**, 97, 5249. (c) Lane, C. F., Kabalka, G. W. *Tetrahedron*, **1976**, 32, 981.

pinacolborane **5.13** (Scheme 5.3.C).[8] It was demonstrated that 1-octyne **5.12** could be converted to *trans*-octenyl-B(pin) **5.14** in the presence of 2.0 equivalent of pinacolborane **5.13** with excellent yield, regio- and stereoselectivity at room temperature in only two hours.

Building on the successful development of non-catalytic alkyne hydroboration, a zirconium catalyzed alkyne hydroboration was established by Srebnik and co-workers.[9] Utilizing just 1.0 equivalent of pinacolborane as hydroboration reagent, 1-octyne **5.12** was engaged in the hydroboration process to furnish the *trans*-alkenyl B(pin) **5.14** with high efficiency and regioselectivity in the presence of Schwartz's reagent as catalyst (Scheme 5.4). Importantly, this process proceeded with exclusive *trans*-selectivity. In terms of reaction mechanism, it was proposed that *cis*-hydrozirconation of the alkyne led to the alkenyl-zirconium intermediate **5.17**. Subsequent σ-bond metathesis between the carbon-zirconium bond and hydrogen-boron bond furnished the hydroborated product **5.14** and regenerated the zirconium-hydride catalyst (Scheme 5.4).

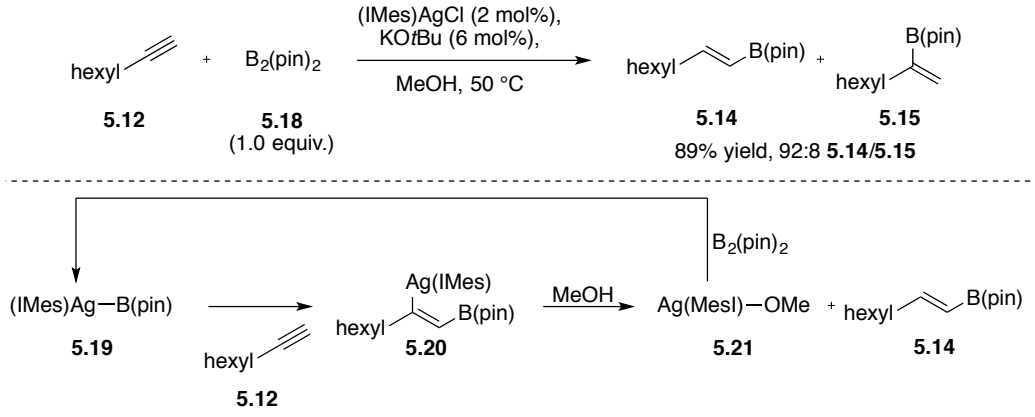
Scheme 5.4. Zirconium-catalyzed alkyne hydroboration.



[8] Tucker, C. E., Davidson, J., Knochel, P. *J. Org. Chem.* **1992**, 57, 3482.
[9] Pereira, S., Srebnik, M. *Organometallics* **1995**, 14, 3127.

Recently, Yoshida and co-workers described a silver-catalyzed hydroboration of alkynes.[10] Employing a silver-*N*-heterocyclic carbene (NHC) complex as catalyst, the *trans*-alkenyl boronate **5.14** was produced from alkyne **5.12** with good yield and regioselectivity in the presence of 1.0 equivalent of $B_2(pin)_2$ and catalytic amount of potassium *tert*-butoxide (Scheme 5.5). While the same products were furnished compared to the zirconium-catalyzed reaction, the proposed mechanism was fundamentally different. Instead of starting with hydroargentation, analogous to the zirconium-catalyzed reaction, a borylargentation between the silver-boron complex **5.19** and alkyne substrate afforded the β-boryl alkenylsilver species **5.20**. Protonation with methanol furnished the hydroboration product **5.14** and silver-methoxide **5.21**, which underwent subsequent σ-bond metathesis with $B_2(pin)_2$ to regenerate the silver-boron complex **5.19**.

Scheme 5.5. Silver-catalyzed alkyne hydroboration.

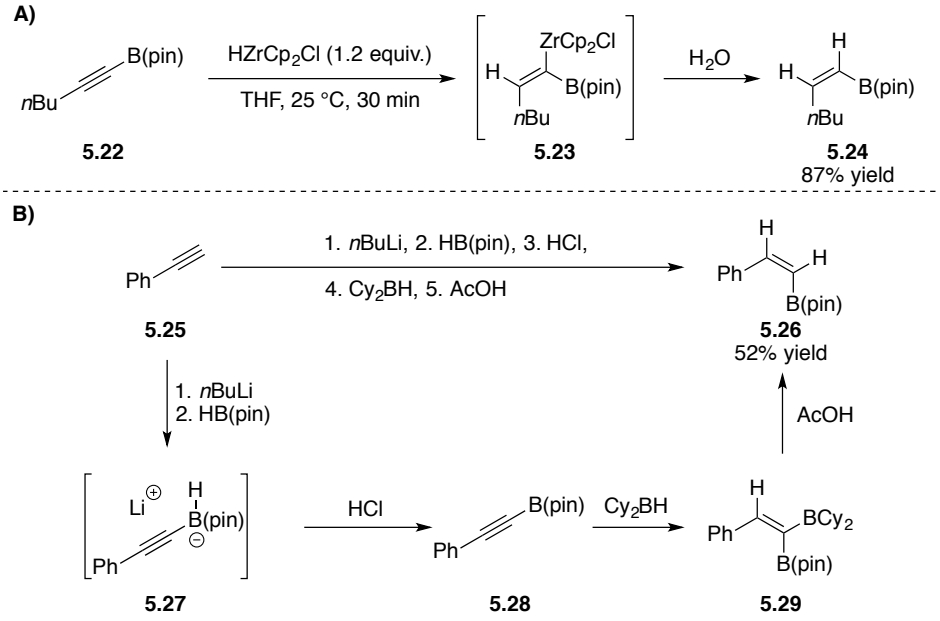


Highly stereoselective synthesis of *cis*-alkenyl boronates is not as straightforward as the synthesis of their *trans*-isomer. The inherent *syn*-addition nature when both hydroboration reagents, such as HB(pin), and metal-hydride or -boryl species react with

[10] Yoshida, H., Kageyuki, I., Takaki, K. *Org. Lett.*, **2014**, 16, 3512.

alkyne makes synthesis of *cis*-alkenyl boronates via alkyne hydroboration exceptionally challenging. One strategy to synthesize *cis*-alkenyl boronates involves a *syn*-reduction of alkynyl boronates. In 1994, Srebnik and co-workers demonstrated that treating the alkynyl B(pin) **5.22** with stoichiometric Schwartz's reagent followed by aqueous workup furnished the *cis*-alkenyl boronate **5.24** with high yield and exclusive stereoselectivity.[11] It was proposed that a *syn*-hydrozirconation of alkynyl B(pin) **5.22** led to the boryl zirconecene 1,1-dimetallic intermediate **5.23**. Subsequent protonation of the zirconium-carbon bond afforded the alkenyl boronate with *cis*-stereochemistry (Scheme 5.6.A).

Scheme 5.6. Synthesis of cis-alkenyl boronates from alkynyl boronates.



Alternatively, Molander and co-workers showed that dicyclohexylborane could conduct the *cis*-reduction of alkynyl boronates.[12] Importantly, they established a

[11] Deloux, L., Srebnik, M. *J. Org. Chem.* **1994**, 59, 6871.
[12] Molander, G. A., Ellis, N. M. *J. Org. Chem.* **2008**, 73, 6841.

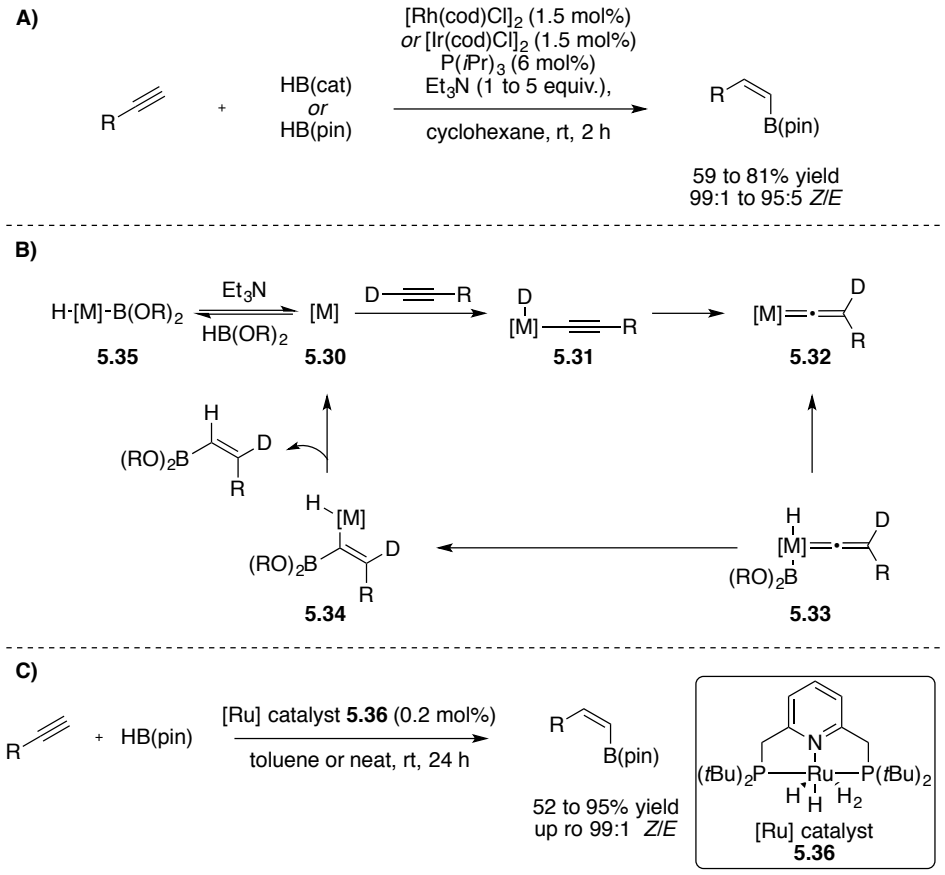
telescope sequence to convert terminal alkyne to *cis*-alkenyl boronates directly. The terminal alkyne **5.25** was treated with *n*-butyllithium and HB(pin) to form the boron ate complex **5.27**, which was converted to alkynyl B(pin) **5.28** with HCl. Subsequent *cis*-hydroboration followed by protodeborylation of dicyclohexylborane furnished the *cis*-alkenyl boronate **5.26** with good yield as single stereoisomer (Scheme 5.6.B).

In 2000, Miyaura and co-workers reported the first *trans*-hydroboration of terminal alkynes to access *cis*-alkenyl boronates.[13] Employing rhodium or iridium as the catalyst, a variety of terminal alkynes underwent *trans*-hydroboration with HB(pin) or HB(cat) to furnish the *cis*-alkenyl boronates with high yield and *Z*/*E* ratio (Scheme 5.7.A). Of note, a deuterium labeled terminal alkyne was subjected to the reaction conditions, and it was found that the deuterium shifted to the internal position in the product. Based on this result, the reaction mechanism was proposed as follows (Scheme 5.7.B): coordination of the transition-metal catalyst to the alkyne followed by carbon-hydrogen bond insertion led to the metal-hydride intermediate **5.31**. A hydride transfer converted the intermediate **5.31** to the metal-alkenylidene **5.32**. Subsequent oxidative addition with borane and 1,2-migration of the boronate moiety furnished the alkenyl metal intermediate **5.34**. The origin of stereoselectivity was due to the formation of the more thermodynamically stable isomer of intermediate **5.34**. Subsequent reductive elimination of intermediate **5.34** afforded the *cis*-alkenyl boronate product and regenerated the transition-metal catalyst. Furthermore, the competitive oxidative addition of borane and catalyst **5.30** was suppressed by the addition of triethylamine. Recently, Leitner and co-workers also

[13] Ohmura, T., Yamamoto, Y., Miyaura, N. *J. Am. Chem. Soc.* **2000**, 122, 4990.

reported a ruthenium-catalyzed *trans*-hydroboration of alkynes (Scheme 5.7.C).[14] It was proposed that the mechanism of the ruthenium-catalyzed reaction was similar to Miyaura's rhodium or iridium-catalyzed reaction.

Scheme 5.7. Rh, Ir, and Ru catalyzed trans-hydroboration of terminal alkynes.



In addition to the rhodium, iridium, and ruthenium-catalyzed *trans*-hydroboration of terminal alkynes, Chirik and co-workers described a cobalt-catalyzed *trans*-hydroboration of terminal alkynes recently (Scheme 5.8.A).[15] Different from Miyaura and Lietner's examples, the metal-akenylidene species was not involved in the proposed

[14] Gunanathan, C., Hölscher, M., Pan, F., Leitner, W. *J. Am. Chem. Soc.* **2012**, 134, 14349.
[15] Obligacion, J. V., Neely, J. M., Yazdani, A. N., Pappas, I., Chirik, P. J. *J. Am. Chem. Soc.* **2015**, 137(, 5855.

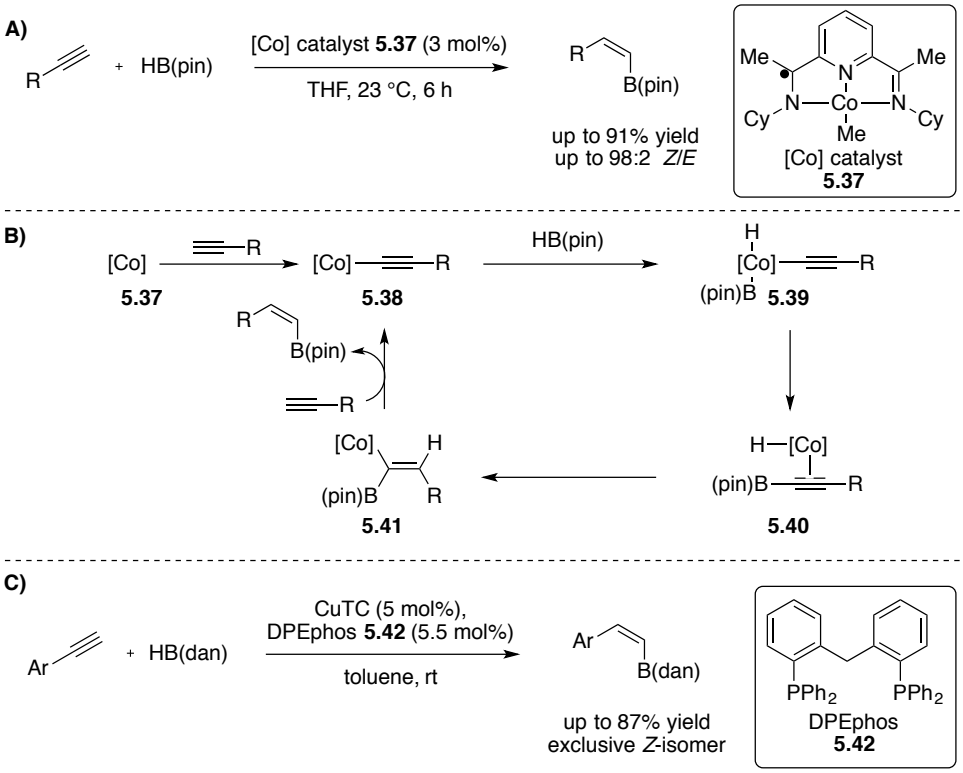
mechanism for cobalt-catalyzed *trans*-hydroboration. Based on the mechanistic experiments performed by the authors, the following possible mechanism was proposed for the reaction. An alkynyl-cobalt complex **5.38** was generated by the reaction between catalyst **5.37** and terminal alkyne substrate. Oxidative addition of HB(pin) to complex **5.38** followed by reductive elimination of the carbon-boron bond furnished the intermediate **5.40**. The cobalt-hydride complex coordinated to the alkynyl boronate, and subsequent *syn*-hydrometallation led to the alkenyl cobalt complex **5.41**, which was protonated by alkyne substrate to release the product and regenerate the alkynyl-cobalt complex **5.38** (Scheme 5.8.B). More recently, a copper-catalyzed hydroboration of aryl substituted alkynes with HB(dan) was developed by Yun and Lee (Scheme 5.8.C). It was demonstrated that both stereoisomers of the alkenyl boronates could be achieved by employing different ligands in the reaction.[16]

In addition to alkenyl boronate synthesis from alkynes by hydroboration, olefin metathesis also has been recognized as a convenient strategy to access alkenyl boronates from readily available starting materials.[17] Compared to alkynes, terminal alkenes are more commonly used feedstock chemical. In 2000, Grubbs and co-workers demonstrated that *trans*-alkenyl boronate **5.45** could be constructed from terminal alkene **5.43** and vinyl B(pin) via ruthenium-catalyzed olefin cross-metathesis strategy.[18] The *trans*-alkenyl boronate **5.45** was isolated with moderate yield but excellent stereoselectivity.

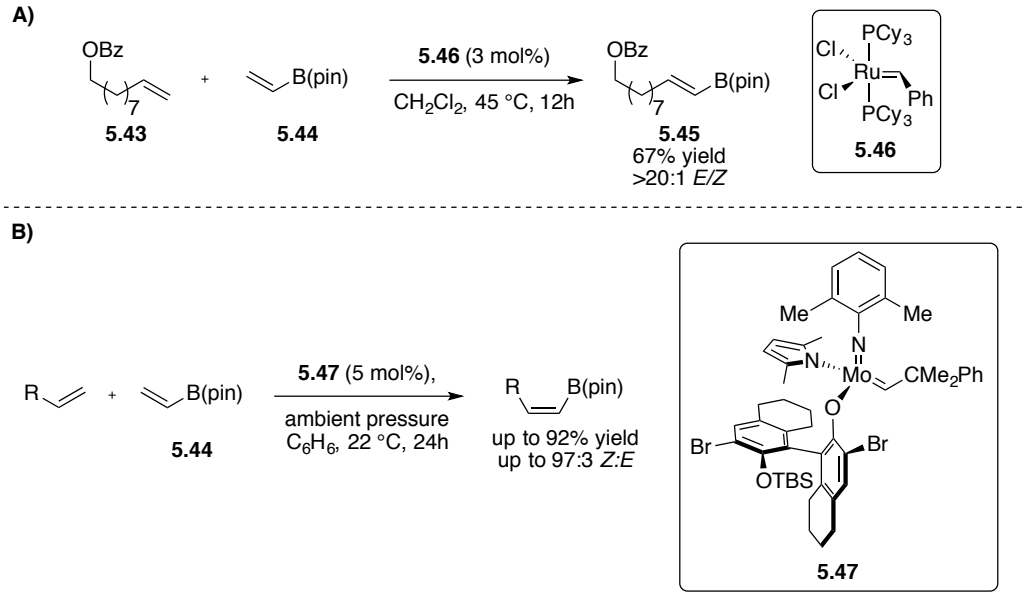
---

[16] Jang, W. J., Lee, W. L., Moon, J. H., Lee, J. Y., Yun, J. *Org. Lett.* **2016**, 18, 1390.
[17] (b) Morrill, C.; Grubbs, R. H. *J. Org. Chem.* **2003**, 68, 6031. (c) Morrill, C.; Funk, T. W.; Grubbs, R. H. *Tetrahedron Lett.* **2004**, 45, 7733. (d) Funk, T. W.; Efskind, J.; Grubbs, R. H. *Org. Lett.* **2005**, 7, 187. (e) McNulty, L.; Kohlbacher, K.; Borin, K.; Dodd, B.; Bishop, J.; Fuller, L.; Wright, Z. *J. Org. Chem.* **2010**, 75, 6001. (f) Hemelaere, R.; Carreaux, F.; Carboni, B. *J. Org. Chem.* **2013**, 78, 6786.
[18] Blackwell, H. E.; O'Leary, D. J.; Chatterjee, A. K.; Washenfelder, R. A.; Bussmann, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, 122, 58.

Scheme 5.8. Cobalt and copper-catalyzed trans-hydroboration of terminal alkynes.



Scheme 5.9. Synthesis of alkenyl boronates by olefin cross-metathesis.



Recently, Hoveyda and co-workers developed a novel molybdenum catalyst **5.47** that was able to catalyze a cross-metathesis reaction between terminal alkenes and vinyl B(pin) to furnish *cis*-alkenyl boronates products with good yield and stereoselectivity.[19] Importantly, this strategy could also be applied to terminal 1,3-diene substrates to afford synthetically challenging *cis*-1,3-dienyl boronates.

5.2.2. Representative synthesis of 1,1-disubstituted alkenyl boronates

While numerous regioseletive syntheses of 1,2-disubstituted alkenyl boronates have been developed, construction of 1,1-disubstituted alkenyl boronates remains a significant challenge in synthetic chemistry. One of the common strategies to synthesize 1,1-disubstituted alkenyl boronates involves organometallic reagents, generated from 2-halo-1-alkene compounds and an electrophilic boron species.[20] However, the scope of such methods is limited by the highly reactive organometallic reagents, such as organolithium or Grignard reagent. Alternatively, 2-halo-1-alkene precursors can also be converted to 1,1-disubstituted alkenyl boronates by palladium-catalyzed Miyaura borylation.[21] However, utilizing such strategies requires a regioselective synthesis of 2-halo-1-olefin precursors, which is often not straightforward.[22]

To address the challenges associated with 1,1-disubstituted alkenyl boronate synthesis, Hoveyda and co-workers have developed a range of catalytic methods involving nickel or copper catalysts. In 2010, the Hoveyda laboratory established a

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[19] Kiesewetter, E. T., O'Brien, R. V., Elsie, C. Y., Meek, S. J., Schrock, R. R., Hoveyda, A. H. *J. Am. Chem. Soc.* **2013**, 135, 6026.

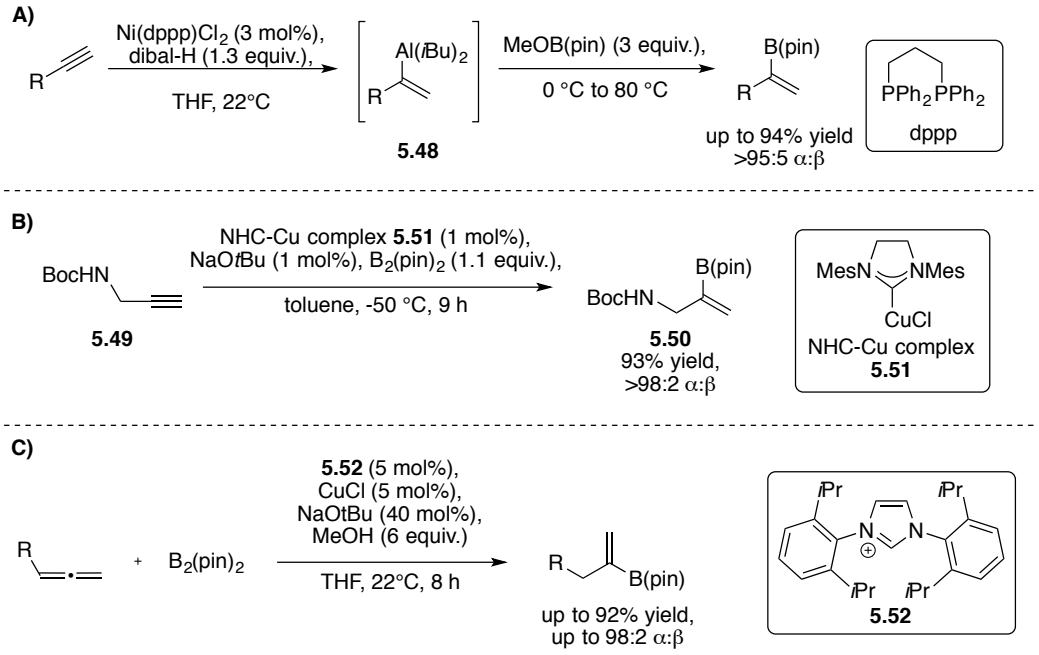
[20] (a) Takahashi, K., Ishiyama, T., Miyaura, N. *J. Organomet. Chem.* **2001**, 47, 625. (b) Takagi, J., Takahashi, K., Ishiyama, T., Miyaura, N. *J. Am. Chem. Soc.* **2002**, 124, 8001. (c) Moran, W. J., Morken, J. P. *Org. Lett.* **2006**, 8, 2413

[21] Takagi, J., Takahashi, K., Ishiyama, T., Miyaura, N. *J. Am. Chem. Soc.* **2002**, 124, 8001.

[22] For selected examples of 2-halo-1-alkene syntheses, see: (a) Spaggiari, A., Vaccari, D., Davoli, P., Torre, G., Prati, F. *J. Org. Chem.* **2007**, 72, 2216. (b) Wang, C., Tobrman, T., Xu, Z., Negishi, E. *Org. Lett.* **2009**, 11, 4092. (c) Pan, J., Wang, X.; Zhang, Y., Buchwald, S. L. *Org. Lett.* **2011**, 13, 4974.

nickel-catalyzed α-selective hydroalumination of aryl and alkyl substituted terminal alkynes.[23] The internal alkenylaluminum **5.48** could be furnished with high regioselectivity in the presence of diisobutylaluminum hydride (dibal-H) and Ni(dppp)Cl_2 catalyst. *In situ* treatment of methoxy(pinacolato)borane with alkenylaluminum intermediate **5.48** led to α-alkenyl boronates with excellent efficiency and selectivity (Scheme 5.10.A).

Scheme 5.10. Catalytic synthesis of 1,1-disubstituted alkenyl boronates.



In 2011, Hoveyda and co-workers demonstrated that a propargyl amine **5.49** could undergo a copper-NHC complex catalyzed α-selective hydroboration to furnish α-alkenyl boronate **5.50** with good yield and regioselectivity (Scheme 5.10.B).[24] More recently, the same group developed an alternative route to access 1,1-disubstituted alkenyl boronates

[23] Gao, F., Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, 132, 10961.
[24] Jang, H., Zhugralin, A. R., Lee, Y., Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, 133, 7859.

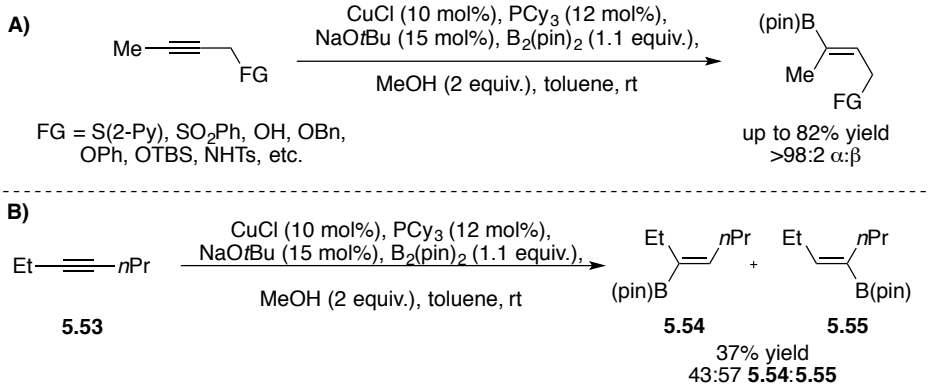
via copper-NHC complex catalyzed site-selective protoboration of allene precousors (Scheme 5.10.C).[25]

5.2.3. Representative synthesis of trisubstituted alkenyl boronates

Although trisubstituted alkenyl boronates have been recognized as very important building blocks in natural products and therapeutic reagents synthesis, a general and practical protocol to synthesize such motifs remains lacking. As part of the reason, achieving high regioselectivity remains a major challenge for hydroboration of internal alkynes. In general, the regioselectivity for internal alkyne hydroboration relies on substrate control so that only the internal alkynes bearing electronically and sterically biased substitution[26], such as 1-phenyl-1-propyne, or bearing prefunctionalized directing groups[27] can be utilized to achieve high site selectivity. In one example, Carreteo and co-workers demonstrated that internal alkynes bearing propargylic functional groups underwent copper-catalyzed hydroboration with excellent regioselectivity (Scheme 5.11.A).[28] However, when 3-heptyne was subjected to the same reaction conditions, a mixture of two regioisomers, **5.54** and **5.55**, was isolated with a ratio of 43:57 (Scheme 5.11.B).

[25] (a) Meng, F., Jung, B., Haeffner, F., Hoveyda, A. H. *Org. Lett.* **2013**, 15, 1414. (b) Jang, H., Jung, B., Hoveyda, A. H. *Org. Lett.* **2014**, 16, 4658.
[26] (a) Semba, K., Fujihara, T., Terao, J., Tsuji, Y. *Chem. -Eur. J.*, **2012**, 18, 4179. (b) Yuan, W., Ma, S. (2012). *Org. Biomol. Chem.* **2012**, 10, 7266.
[27] Park, J. K., Ondrusek, B. A., McQuade, D. T. *Org. Lett.* **2012**, 14, 4790.
[28] Moure, A. L., Gomez Arrayas, R., Cárdenas, D. J., Alonso, I., Carretero, J. C. *J. Am. Chem. Soc.* **2012**, 134, 7219.

Scheme 5.11. Copper-catalyzed hydroboration of internal alkynes.

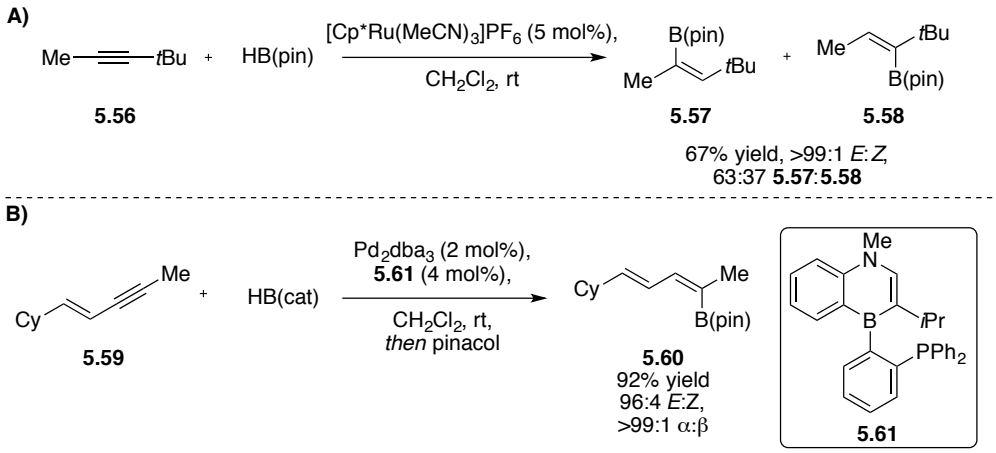


Besides the challenge to achieve high regioselectivity in hydroboration of internal alkynes, *trans*-hydroboration of an internal alkyne, which is required for the synthesis of *E*-trisubstituted alkenyl boronates, remains underdeveloped. In 2013, the first *trans*-hydroboration of internal alkynes was reported by Fürstner and co-workers[29]. Employing $[Cp^*Ru(MeCN)_3]PF_6$ as catalyst, a *trans*-hydroboration of symmetric internal alkynes furnished the *E*-trisubstituted alkenyl boronates with good yield and excellent level of stereoselectivity. However, this method failed to be expanded to non-symmetric internal alkynes. For example, utilizing methyl *tert*-butyl substituted alkyne **5.56**, one of the most sterically biased internal alkynes, led to a mixture of regioisomers **5.57** and **5.58** with a ratio of 63:37 (Scheme 5.12.A). Unfortunately, these regioisomers are often hard to separate. More recently, Liu and co-workers developed a novel monobenzofused 1,4-azaborine phosphine ligand **5.61**, which was able to catalyze a *trans*-hydroboration of terminal and internal 1,3-enynes in the presence of palladium catalyst in a highly stereo-

[29] Sundararaju, B., Fürstner, A. *Angew. Chem. Int. Ed.* **2013**, 125, 14300.

and regio-selective fashion.[30] Importantly, the 1,3-enyne functionality was required to achieve high stereo- and regio-selectivity (Scheme 5.12.B).

Scheme 5.12. Synthesis of trisubstituted alkenyl boronates via trans-hydroboration of internal alkynes.



5.2.4. History of boron-Wittig reaction

Despite the remarkable developments of hydroboration in past several decades, alternative general and practical route to access alkenyl boronates from readily available reagents in a regio- and stereo- selective fashion is still a desirable compliment. We considered that the boron-Wittig reaction, which was pioneered by Pelter and Matteson[31], might be a potential strategy to address these challenges. As shown in Scheme 5.13.A, methylene bis(boronates) **5.62** underwent a deprotonation by lithium tetramethylpiperidide (LiTMP) to generate the α-bis(boronates) anion **5.63**, which attacked carbonyl electrophile to form the intermediate **5.64**. Subsequent boron-oxygen

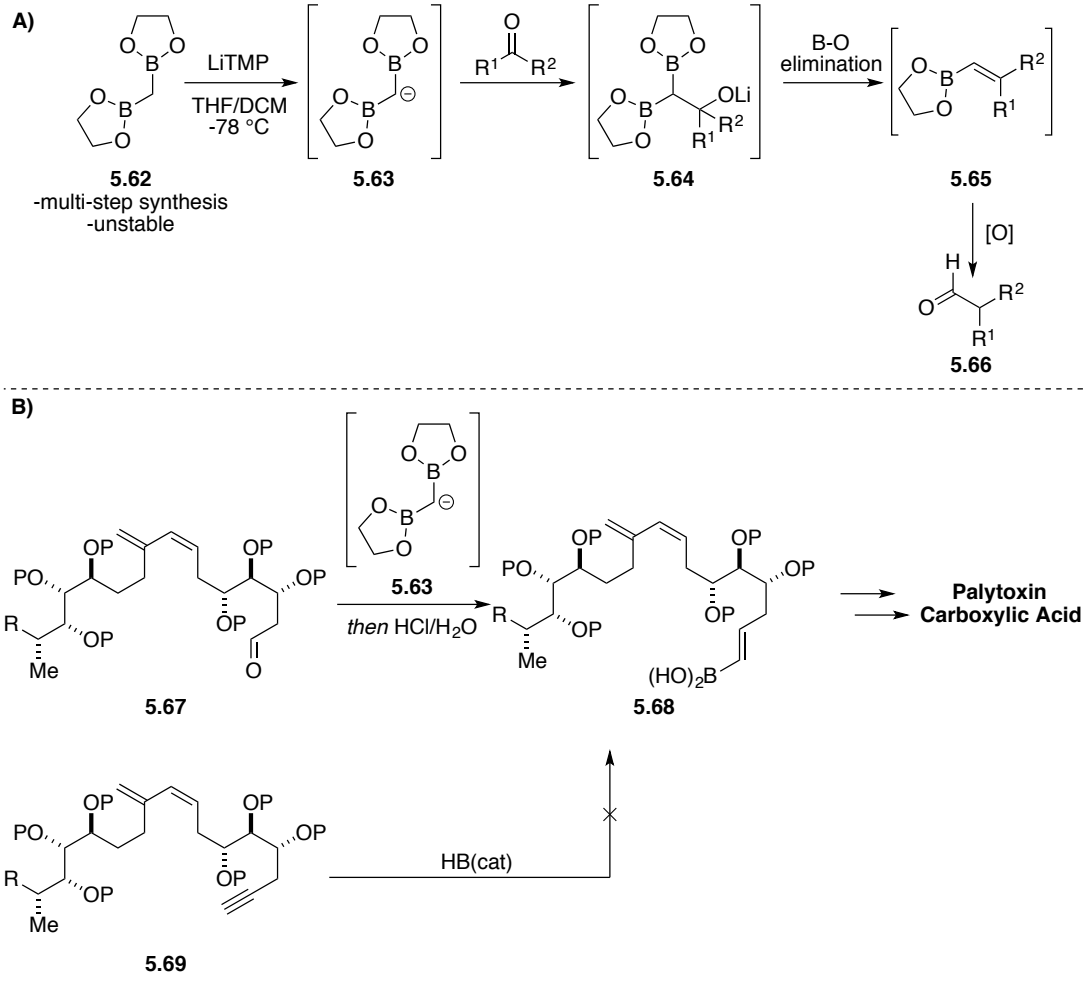
[30] Xu, S., Zhang, Y., Li, B., Liu, S. Y. *J. Am. Chem. Soc.*, **2016**, 138, 14566.

[31] (a) Matteson, D. S., Moody, R. J., Jesthi, P. K. *J. Am. Chem Soc.* **1975**, 97, 5608. (b) Matteson, D. S., Jesthi, P K. *J. Organomet. Chem.* **1976**, 110, 25. (c) Matteson, D. S., Moody, R. J. *J. Am. Chem. Soc.* **1977**, 99, 3196. (d) Matesson, D. S., Moody, R. J. *Organometallics* **1982**, 1, 20. (e) Pelter, A., Buss, D., Colclough, E., Singaram, B. *Tetrahedron* **1993**, 49, 7077.

elimination furnished the alkenyl boronate **5.65**. Compound **5.65** was often oxidized to carbonyl homologation product **5.66** in the early studies conducted by Matteson and co-workers. It is worthy of note that the ethylene glycol derived methylene bis(boronates) **5.62** is unstable under hydrolytic conditions, and the preparation of such reagents is not straightforward. Furthermore, although the authors suggested that the *trans*-isomer of alkenyl boronate **5.65** was favored under reaction conditions, detailed stereoselectivity data and thorough substrate scope investigation was lacking. Moreover, the unstable property of alkenyl boronate **5.65** limited its isolation and utilization in further transformations other than *in situ* oxidation. However, Kishi and co-workers showed that the unstable intermediate **5.65** could be hydrolyzed *in situ* to the boronic acid derivative and engaged in Suzuki-Miyaura cross-coupling (Scheme 5.13.B).[32] During the investigation of the total synthesis of Palytoxin carboxylic acid, an advanced intermediate **5.68**, bearing a *trans*-alkenyl boronic acid, was required for subsequent Suzuki-Miyaura coupling. Unfortunately, an attempt to construct this *trans*-alkenyl boronic acid by HB(cat) hydroboration failed due to side reactions. Instead, utilizing Matteson's protocol, reaction between the aldehyde **5.67** and lithiated bis(boronate) **5.63**, followed by *in situ* hydrolysis furnished the *trans*-alkenyl boronic acid **5.68** with good yield and stereoselectivity. This example demonstrated the potential utility of boron-Wittig reaction, which could be complementary to alkyne hydroboration. More importantly, the regioselectivity issue faced in hydroboration is avoided due to the reaction nature of the boron-Wittig reaction.

[32] Armstrong, R.W., Beau, J.M., Cheon, S.H., Christ, W.J., Fujioka, H., Ham, W.H., Hawkins, L.D., Jin, H., Kang, S.H., Kishi, Y. and Martinelli, M.J., *J. Am. Chem. Soc.* **1989**, 111, 7525.

Scheme 5.13. Early examples of boron-Wittig reaction.

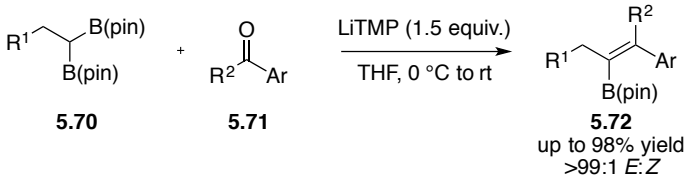


Recently, Shibata and co-workers described an extension of Matteson's work by investigating the reaction between geminal bis(boronates) **5.70** and aryl ketone **5.71** (Scheme 5.14).[33] By utilizing air, moisture, and column stable pinacol derived 1,1-bis(boronate) **5.70**, tetrasubstituted alkenyl boronates **5.72** generated by boron-Wittig reaction could be easily isolated with good yield and excellent stereoselectivity. Of note, the tetrasubstituted alkenyl boronates derived from dialkyl ketones suffered from low

[33] (a) Endo, K., Hirokami, M., Shibata, T. *J. Org. Chem.* **2010**, 75, 3469. (b) Endo, K., Sakamoto, A., Ohkubo, T., Shibata, T. *Chem. Lett.* **2011**, 40, 1440.

stereoselectivity. Furthermore, only tetrasubstituted, but no tri- or disubstituted alkenyl boronate products were surveyed by Shibata.

Scheme 5.14. boron-Wittig reaction by Shibata.



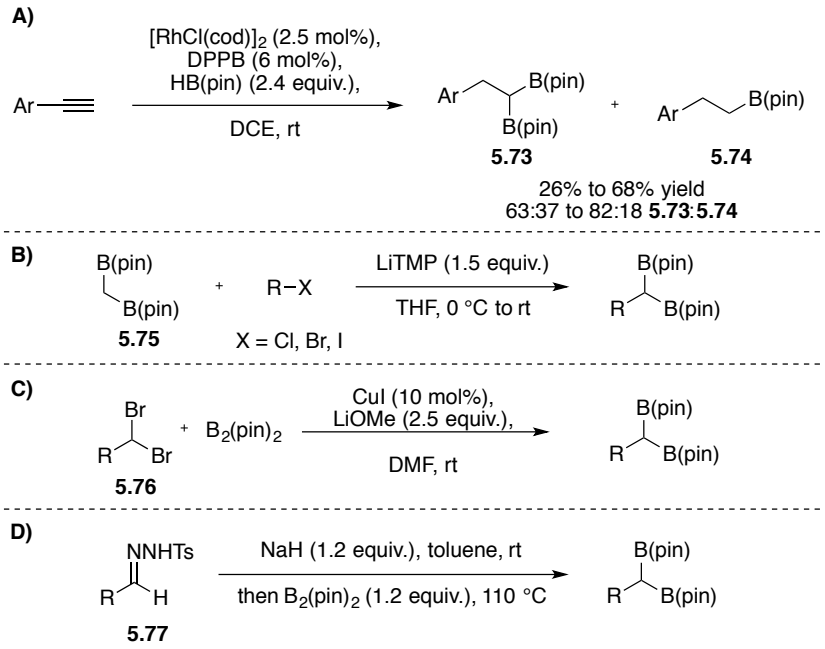
5.70 **5.71** **5.72**
up to 98% yield
>99:1 *E*:*Z*

In order to extensively investigate the scope of boron-Wittig reaction, a general, practical and reliable route to access geminal bis(boronates) is required[34]. In this context, Shibata and co-workers showed that geminal bis(boronates) **5.73** could be constructed by rhodium-catalyzed double hydroboration of terminal alkynes (Scheme 5.15.A). However, the reaction efficiency was often limited by monohydroboration/reduction byproduct **5.74**. Moreover, only aryl substituted alkynes had been examined in Shibata's work. More recently, a handful of practical and general strategies have been developed to synthesize geminal bis(boronates) from a range of readily available starting materials. Some representative examples have been summarized in Scheme 5.15. Alkylation of commercial available pinacol derived methylene bis(boronates) **5.75** furnishes geminal bis(boronate) products with a variety of substitutions (Scheme 5.15.B). Alternatively, diborylation of geminal dibromides **5.76** or *N*-tosylhydrazones **5.77** furnishes 1,1-bis(boronates) efficiently (Scheme 5.15.C and D). Taking advantage of these reliable routes to access stable geminal bis(boronates), we reasoned that an extensive

[34] Representative syntheses of geminal bis(boronates): (a) Endo, K., Hirokami, M., Shibata, T. *Synlett* **2009**, 1331. (b) Sun, C., Potter, B., Morken, J. P. *J. Am. Chem. Soc.* **2014**, 136, 6534. (c) Hong, K., Liu, X., Morken, J. P. *J. Am. Chem. Soc.* **2014**, 136, 10581. (d) Potter, B., Szymaniak, A. A., Edelstein, E. K., Morken, J. P. *J. Am. Chem. Soc.* **2014**, 136, 17918. (e) Ito, H., Kubota, K. *Org. Lett.* **2012**, 134, 10693. (f) Li, H., Shangguan, X., Zhang, Z., Huang, S., Zhang, Y., Wang, J. *Org. Lett.* **2014**, 16, 448.

investigation of the boron-Wittig reaction might provide a general and practical strategy to synthesize alkenyl boronates as an transition-metal-free alternative to alkyne hydroborations.

Scheme 5.15. Representative syntheses of geminal bis(boronates).



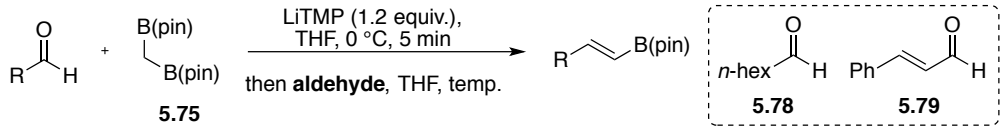
5.3. Development of a practical and general boron-Wittig reaction

5.3.1. Synthesis of 1,2-disubstituted alkenyl boronates via boron-Wittig reaction

Taking the advantage of Matteson's pioneering work on the boron-Wittig reaction between geminal bis(boronates) and aldehydes, the optimization of conditions for synthesis of 1,2-disubstituted alkenyl boronates via the boron-Wittig reaction between methylene bis(boronate) **5.75** and aldehydes was quickly achieved. The deprotonation of bis(boronate) **5.75** was efficiently achieved within 5 minutes, by treatment with 1.2 equivalents of LiTMP at 0 °C. Subsequent addition of hexanal followed by allowing the reaction to warm to room temperature led to the *trans*-alkenyl boronate product with 74%

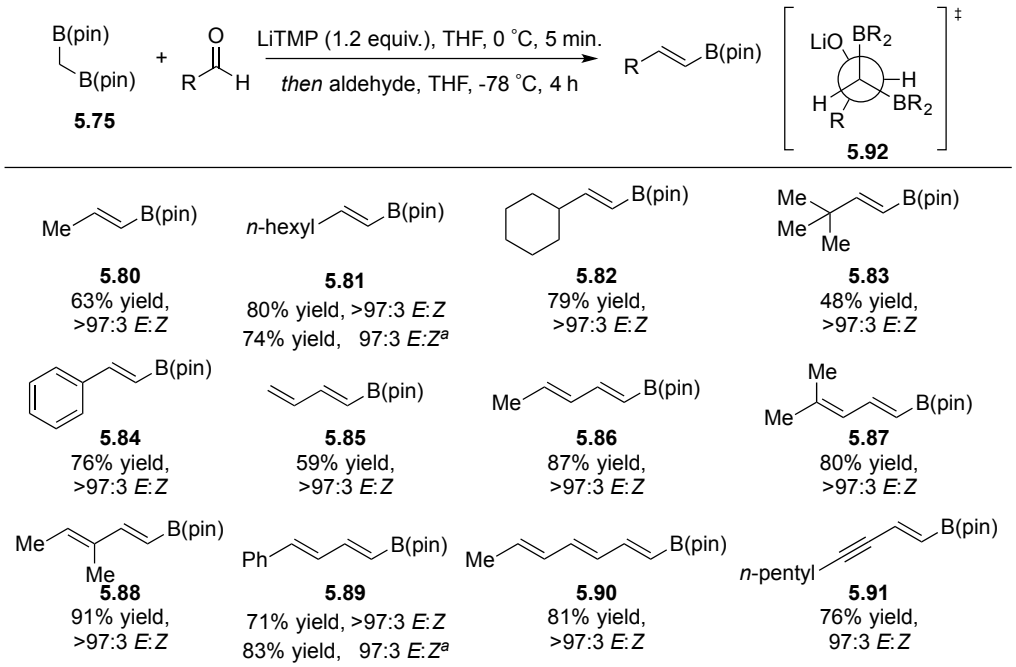
isolated yield and 97:3 *E*/*Z* ratio (Table 1. entry 1). Cooling the reaction temperature to -78 °C resulted a slight enhancement of reaction efficiency and stereoselectivity (Table 1. entry 2). While 1,3-dienes are one of the common motifs in natural products and therapeutic agents, efficient and stereoselective synthesis of 1,3-dienyl boronates remains challenging in synthetic chemistry. In order to explore the synthesis of 1,3-dienyl boronates via the boron-Wittig reaction, α,β-unsaturated aldehyde **5.79** was investigated. To our delight, the boron-Wittig reaction between bis(boronate) **5.75** and cinnamaldehyde **5.79** furnished the *trans*-dienyl boronate product with good yield and 93:7 *E/Z* selectivity (Table 1. entry 3). By lowering the reaction temperature, the stereoselectivity of 1,3-dienyl boronate products was improved to an excellent level (Table 1. entry 4 and 5). In summary, the optimal temperature for the synthesis of *trans*-1,2-disubstituted alkenyl boronates via boron-Wittig reaction was determined to be -78 °C in order to obtain the best stereoselectivity.

Table 1. Optimization for synthesis 1,2-disubstituted alkenyl boronates via boron-Wittig reaction.



entry	aldehyde	temp. (°C)	time (h)	Yield (%)	*E:Z*
1	**5.78**	0 to rt	1.5	74	97:3
2	**5.78**	-78	4.0	80	>97:3
3	**5.79**	0 to rt	1.5	83	93:7
4	**5.79**	0	4.0	60	94:6
5	**5.79**	-78	4.0	71	>97:3

Scheme 5.16. Scope of 1,2-trans-alkenyl boronate synthesis via boron-Wittig reaction.



[a]Reaction performed at 0 °C to room temperature for 1.5 h.

With the optimal conditions in hand, the substrate scope of the synthesis of 1,2-*trans*-alkenyl boronates via boron-Wittig reaction was explored. As summarized in Scheme 5.16, both alkyl and aryl substituted aldehydes could be engaged in the reaction to afford the alkenyl boronates with good yield and excellent stereoselectivity (**5.80** to **5.84**). Sterically hindered substitution, such as cyclohexyl group (**5.82**), was well tolerated in the reaction. However, utilizing an extremely sterically encumbered *tert*-butyl substituted aldehyde led to diminished yield while only *trans*-isomer is observed (**5.83**). Importantly, a broad range of α,β-unsaturated aldehydes participated in the boron-Wittig reaction to furnish the corresponding 1,3-dienyl boronates bearing a variety of substitution patterns with good efficiency and exclusively the *trans*-stereoisomer. It is worthy of note that the

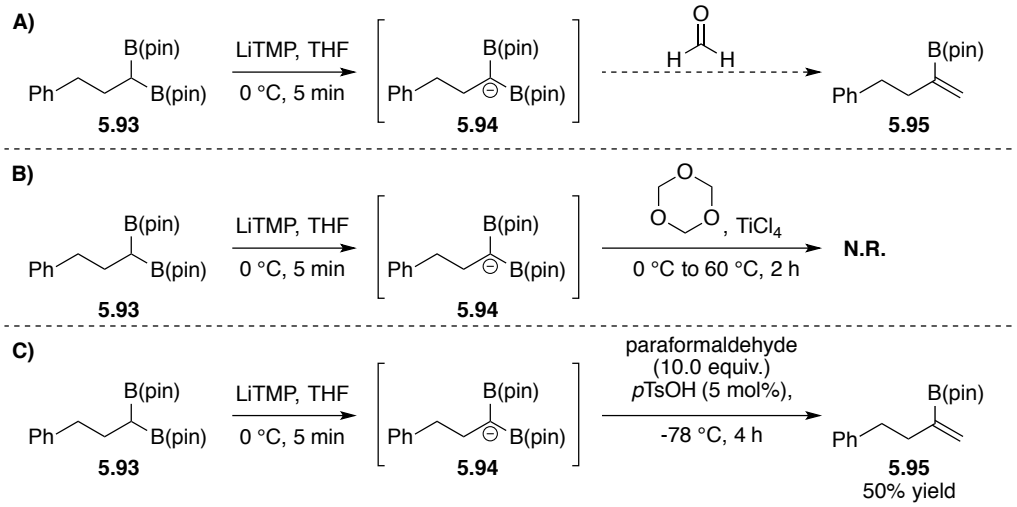
boron-Wittig reaction could also be applied to construct the synthetically challenging trienyl and enynyl boronates with good yield and stereoselectivity. Of note, with the assumption that the boron-oxygen elimination occurred via a *syn*-elimination pathway, the origin of the *trans*-stereoselectivity was proposed to be that the structure **5.92** was adopted to minimize the unfavored steric interaction between the R-group and the boronate group in the boron-oxygen elimination transition state.

5.3.2. Synthesis of 1,1-disubstituted alkenyl boronates via boron-Wittig reaction

With the successfully discovery of a practical protocol for synthesis of 1,2-disubstituted alkenyl boronates via boron-Wittig reaction, we turned our research focus to a more synthetically challenging target, 1,1-disubstituted alkenyl boronates. In order to construct 1,1-disubstituted alkenyl boronates via the boron-Wittig reaction, the lithiated geminal bis(boronates) **5.94** need to react with formaldehyde (Scheme 5.17.A). However, this strategy is unpractical due to the limitation that commercial formaldehyde is only available as an aqueous solution, which is incompatible with the lithiated geminal bis(boronates) intermediate. To address this limitation, we considered use of a Lewis acid, such as $TiCl_4$, that promotes degradation of 1,3,5-trioxane to generate formaldehyde *in situ*. However, no desired product was observed when the lithiated geminal bis(boronate) **5.94** was treated with 1,3,5-trioxane in the presence of $TiCl_4$ (Scheme 5.17.B). A possible explanation was that $TiCl_4$ formed a stable complex with THF instead of promoting trioxane degradation. Alternatively, formaldehyde could also be generated by a *p*-toluenesulfonic acid catalyzed degradation of paraformaldehyde. To adapt this strategy in the boron-Wittig reaction, a special set-up was required. The formaldehyde, which was generated in a separated flask by *p*-toluenesulfonic acid catalyzed degradation

of paraformaldehyde at 80 °C, was transferred to a solution of lithiated geminal bis(boronates) **5.94** at -78 °C via cannula (Scheme 5.17.C). Although 1,1-disubstituted alkenyl boronate **5.95** was obtained with moderate yield, the application of this strategy was significantly limited by the impractical reaction set-up.

Scheme 5.17. boron-Wittig reaction with formaldehyde.

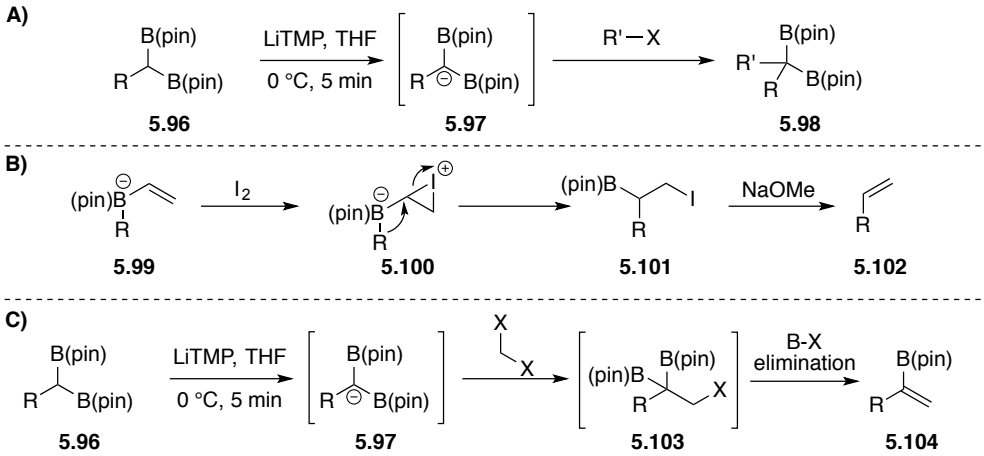


While employing formaldehyde in boron-Wittig reaction proved to be challenging, we considered that utilizing geminal dihalogenated electrophiles might provide an alternative solution. It is known that lithiated geminal bis(boronate) intermediate **5.97** undergoes an alkylation with halogenated electrophile to furnish product **5.98**, efficiently (Scheme 5.18.A). More encouragingly, in the examples of Zweifel-Evans olefination[35], the vicinal boronate-iodide intermediate **5.101**, which was furnished by iodine triggered 1,2-metallate shift, undergoes a boron-iodide elimination to furnish an alkene product **5.102** (Scheme 5.18.B). With this knowledge in mind, it was reasonable to propose that

[35] (a) Zweifel, G., Arzoumanian, H., Whitney, C. C. *J. Am. Chem. Soc.* **1967**, 89, 3652-3653. (b) Evans, D. A., Walker, A. *J. Org. Chem.* **1976**, 16, 5248.

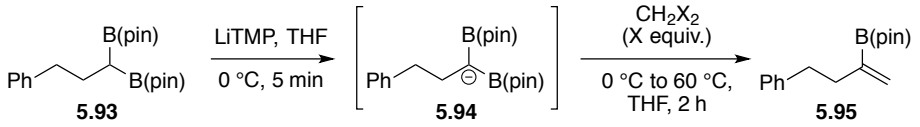
an alkylation between lithiated bis(boronates) **5.97** and dihalogenated methane might lead to the α-halogenated geminal bis(boronates) intermediate **5.103**. Subsequent boron-halogen elimination would furnish the desired 1,1-disubstituted boronate product **5.104** (Scheme 5.18.C).

Scheme 5.18. Potential boron-Wittig reaction with dihalogenated electrophiles.



To our delight, engaging 1.0 equivalent of dibromomethane as electrophile under a modified boron-Wittig reaction conditions with geminal bis(boronates) **5.93** afforded the desired product **5.95** in 65% yield (Table 2. entry 1). Further increasing the amount of electrophile failed to improve the reaction conversion and yield (Table 2. entry 2 to 4). On the other hand, utilizing diiodomethane, a more reactive electrophile compared to dibromomethane, led to a full conversion reaction profile with 87% isolated yield. Thus, the optimal conditions for the synthesis 1,1-disubstituted alkenyl boronates via boron-Wittig reaction was determined as treating the lithiated intermediate with 2.0 equivalent of diiodomethane at 60 °C for 2 hours (Table 2. entry 5).

Table 2. Optimization of boron-Wittig reaction with geminal dihalogenated electrophiles.

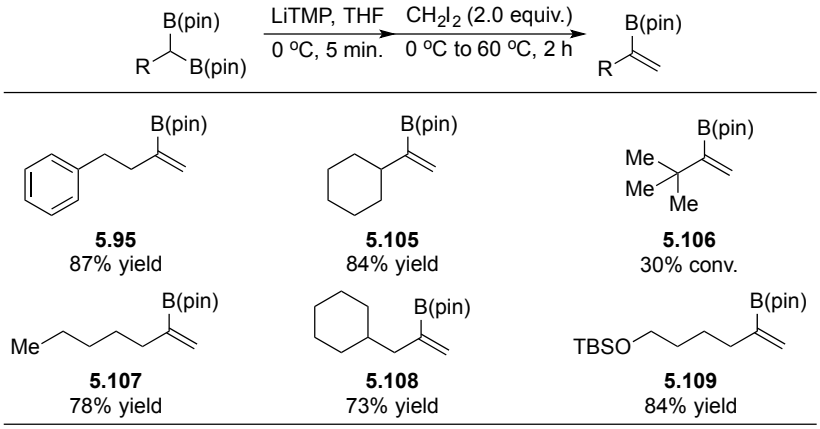


entry	CH_2X_2	X equiv.	conv. (%)	Yield (%)
1	CH_2Br_2	1.0	--[a]	65
2	CH_2Br_2	2.0	80	68
3	CH_2Br_2	10.0	80	65
4	CH_2Br_2	solvent	--	N.R.
5	CH_2I_2	2.0	>95	87
6	CH_2I_2	solvent	--	N.R.

a) 1.1 equiv. of **5.93** was employed for this reaction.

With the optimal conditions in hand, the scope of the synthesis of 1,1-disubstituted alkenyl boronates via boron-Wittig reaction was evaluated. As shown in Scheme 5.19, the substrates bearing straight chain, α-, and β-branching substitution could be engaged in the reaction to furnish corresponding alkenyl boronates with good yield. However, geminal bis(boronates) bearing *tert*-butyl substitution suffered low reaction efficiency due to the steric bulkiness. Of note, silyl ether protected alcohol was also tolerated under reaction conditions.

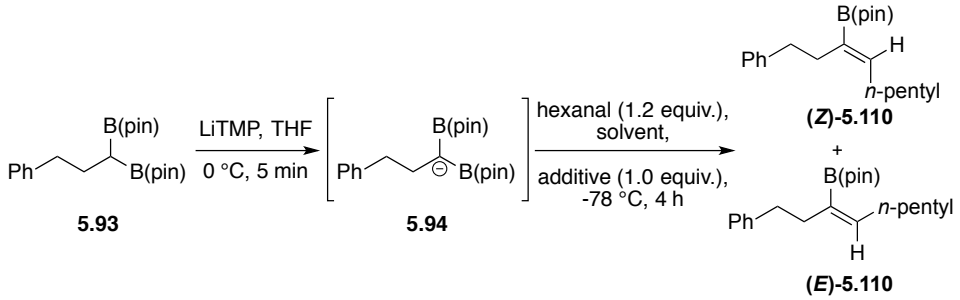
Scheme 5.19. Scope of 1,1-disubstituted alkenyl boronates via boron-Wittig reaction.



5.3.3. Synthesis of trisubstituted alkenyl boronates via boron-Wittig reaction

Encouraged by the successful development of the synthesis of 1,2- and 1,1-disubstituted alkenyl boronates via boron-Wittig reaction, we shifted our focus to one of the most challenging goals: stereo- and regioselective synthesis of trisubstituted alkenyl boronates. We envisioned that a boron-Wittig reaction between substituted geminal bis(boronates) and an aldehyde might enable construction of a trisubstituted alkenyl boronate in a stereo- and regioselective fashion. To test this hypothesis, the lithiated geminal bis(boronates) **5.94** was treated with 1.2 equivalent of hexanal at 0 °C followed by allowing the reaction to warm to room temperature. Upon completion, full conversion to tri-substituted alkenyl boronate product **5.110** was observed in a moderately stereoselective fashion, slightly favoring the *Z*-isomer with a 69:31 ratio (Table 2. entry 1). The stereoselectivity was improved to 88:12 *Z/E* ratio by lowering the reaction temperature to -78 °C (Table 2. entry 2).

Table 2. Optimization of the synthesis of trisubstituted alkenyl boronates via boron-Wittig reaction.



entry	solvent	additive	conversion (yield) (%)	*Z:E*
1[a]	THF	--	>95	69:31
2	THF	--	>95 (88)	88:12
3	THF	$ZnCl_2$	>95	70:30
4	THF	$MgBr_2$	<5	N.D.
5	THF	nBu$_4$NCl	90	63:27
6	THF	DMPU	>95	81:19
7	THF	12-C-4	>95	85:15
8	THF/CH_2Cl_2 (1:1)	--	<5	N.D
9	THF/MeCN (1:1)	--	>95	86:14
10	THF/dioxane (10:1)	--	>95	85:15
11	toluene	--	>95	38:62
12	cyclohexane	--	<5	N.D.
13	diethyl ether	--	>95	32:68
14	diethyl ether	$ZnCl_2$	>95	48:52
15	diethyl ether	nBu$_4$NCl	>95	32:68

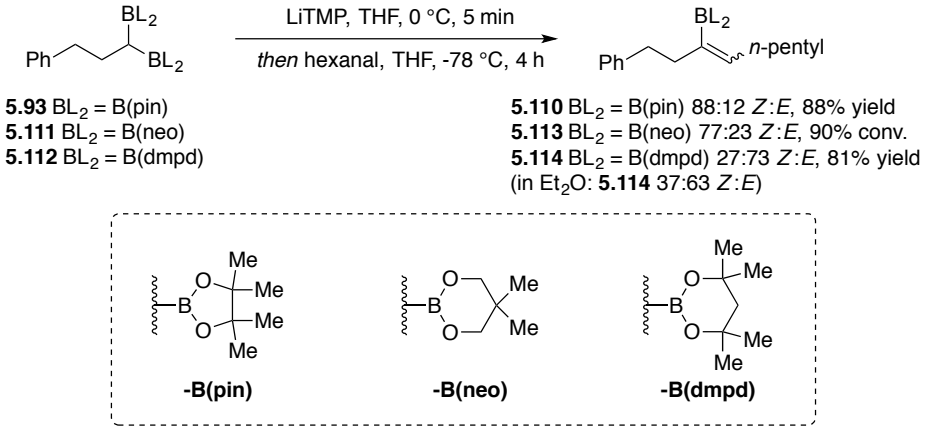
a) reaction was performed from 0 °C to rt for 1.5 hours.

Unfortunately, addition of Lewis acids (Table 2. entry 3 to 5), employing additives to coordinate the cation (Table 2. entry 6, 7), or utilizing mixed solvent systems (Table 2. entry 8 to 10) failed to improve or alter the stereoseletivity. Interestingly, the *E*-isomer of the product **5.110** was slightly favored when the boron-Wittig reactions were performed

in non-polar solvents (Table 2. entry 11 to 15), such as toluene and diethyl ether. However, all attempts to achieve a synthetically useful level of stereoselectivity failed.

While all attempts to improve or alter the stereoselectivity by reaction condition optimization failed, we were delighted to discover that the identity of the ligand on the boron atom had a significant influence on stereoselectivity. As summarized in Scheme 5.20, employing neopentylglycolato-derived geminal bis(boronate) **5.111** led to the corresponding trisubstituted alkenyl boronate product **5.113** with 77:23 *E/Z* ratio. Importantly, engaging the dimethylpentanediolato (dmpd) derived bis(boronate) **5.112** in the boron-Wittig reaction afforded the trisubstituted alkenyl boronate **5.114** that favored the *E*-isomer with 81% yield and 27:73 stereoisomers ratio. Of note, although conducting the reaction in diethyl ether altered the stereoselectivity for pinacol-derived substrate **5.93**, the selectivity was diminished when the reaction was performed in diethyl ether with bis(boronates) **5.112.**

Scheme 5.20. Effects of the ligands for boronates on stereoselectivity.

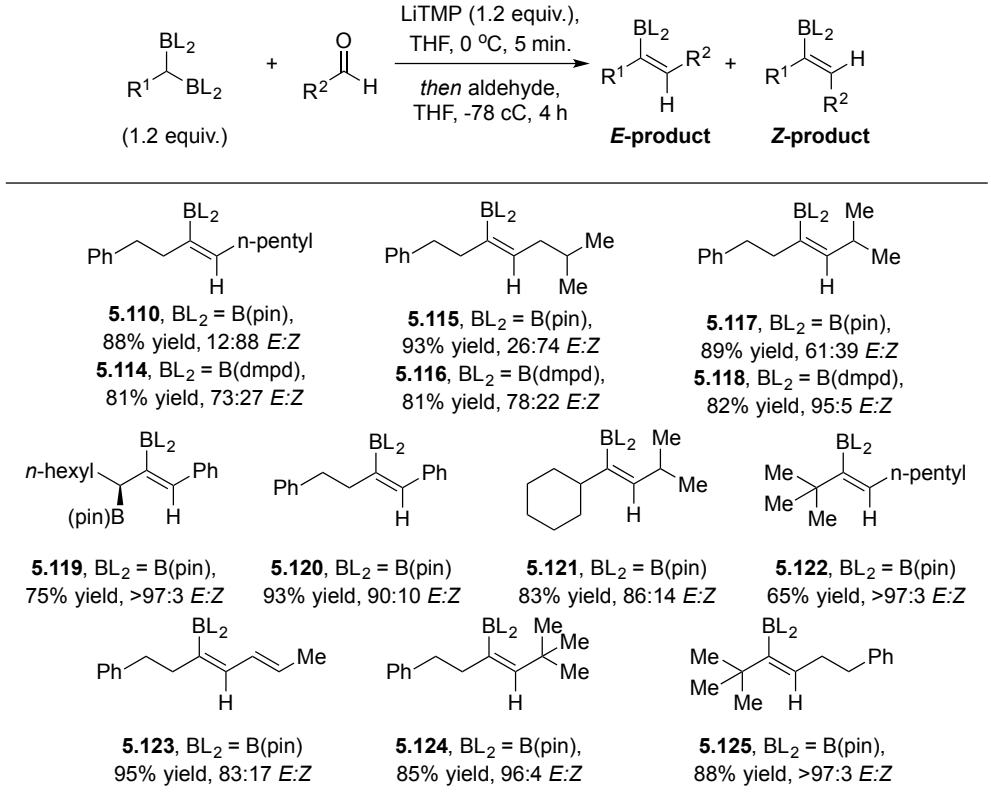


Next, a range of aldehydes and geminal bis(boronates) were evaluated for the synthesis of trisubstituted alkenyl boronates via boron-Wittig reaction. As shown in

Scheme 5.21, by simply switching the diol ligands for geminal bis(boronates), both *E*- and *Z*- isomers derived from hexanal and isobutyl substituted aldehyde were able to be achieved with good yield and synthetically useful level of selectivity (**5.110**, **5.114-5.116**). Notably, when sterically hindered isobutyraldehyde was subjected to the reaction conditions, the *E*-isomer of the product was favored even with B(pin) derived bis(boronates). The stereoselectivity was further improved by employing dmpd as the ligand for the boronates. Moreover, utilizing sterically encumbered geminal bis(boronates) also favored the *E*-isomer of product (**5.121**, **5.122**). Interestingly, a 1,1,2-tris(boronate) substrate and benzylaldehyde could also be engaged in the boron-Wittig reaction to furnish trisubstituted alkenyl boronate **5.119** bearing a α-borylated stereocenter with good yield and stereoselectivity. Synthetically challenging trisubstituted dienyl boronate **5.123** could be constructed with good efficiency and decent selectivity by the boron-Wittig reaction. In summary, the *E*-isomer of the trisubstituted alkenyl boronates was favored when sterically hindered substitution on substrates or sterically demanding diol ligands of boronates were involved in the reaction. On the other hand, a combination of smaller ligand on the boron and linear substrates favored the formation of *Z*-isomer of products. More importantly, the advantage of employing boron-Wittig reaction to overcome the regioselectivity challenge for internal alkyne hydroboration was well demonstrated by the synthesis of trisubstituted alkenyl boronates **5.124** and **5.125**. By simply varying the substitution on geminal bis(boronates) and aldehyde substrates, both regioisomers of trisubstituted alkenyl boronates **5.124** and **5.125** was furnished with good yield, stereoselectivity, and exclusive regioselectivity. Meanwhile, the synthesis of such structures with alkyne hydroboation would require a highly stereo- and regio-

selective *trans*-hydroboration of internal alkynes, which is known to be extremely challenging.

Scheme 5.21. Scope of the synthesis of trisubstituted alkenyl boronates via boron-Wittig reaction.

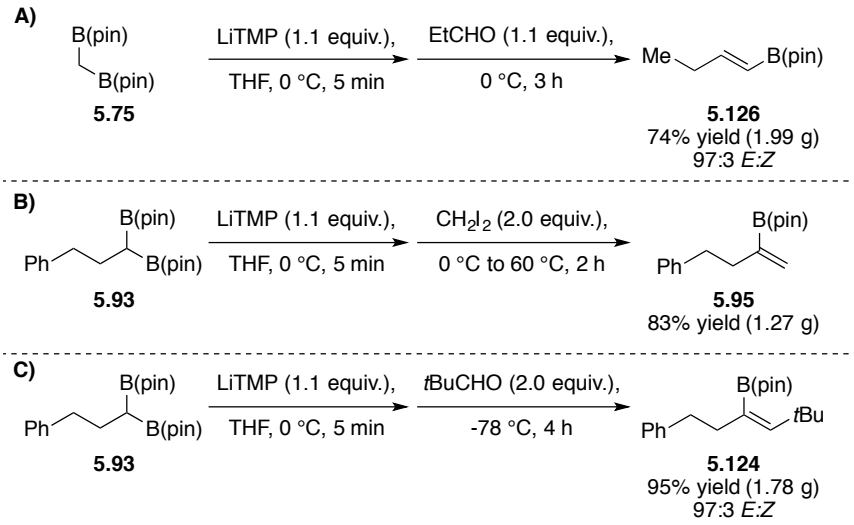


5.3.4. Gram-scale synthesis of alkenyl boronates via boron-Wittig reaction

To demonstrate the synthetic utility and potential application of the boron-Wittig reaction on large-scale operation, gram-scale syntheses of 1,2-disubstituted, 1,1-disubstituted, and trisubstituted alkenyl boronates were examined. As disclosed in Scheme 5.22, high reaction efficiency and excellent stereoselectivity were obtained in all three cases. This study further highlighted that the boron-Wittig reaction is a general and

practical protocol to access synthetically valuable alkenyl boronates from readily available reagents without employing costly transition-metal catalysts.

Scheme 5.22. Gram-scale syntheses of alkenyl boronates via boron-Wittig reaction.



5.4. Conclusion

In summary, a general and practical protocol to construct synthetically valuable alkenyl boronates via the boron-Wittig reaction has been described. The overall transformation engages readily accessible geminal bis(boronates) and aldehydes to stereo- and regioselectively furnish highly complex alkenyl boronates that are often difficult to access via other routes. Furthermore, the fact that the boron-Wittig reaction is free from expensive transition-metals makes such a protocol appealing in large-scale operations. Future studies should focus on understanding the origin of the stereoinduction in trisubstituted alkenyl boronates synthesis as well as exploring further applications of the boron-Wittig reaction in syntheses of natural products and therapeutic agents.

5.5. Experimental Section

5.5.1. General Information

^{1}H NMR spectra were measured using a Varian Gemini-500 (500 MHz) spectrometer or a 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, pent= pentet, sept = septet, br = broad, m = multiplet), and coupling constants (Hz). $^{13}C\{^{1}H\}$NMR spectra were measured using a Varian Inova 500 (126 MHz) or Varian VNMRS 400 (100 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.0 ppm). $^{11}B\{^{1}H\}$NMR spectra were measured using a Varian Inova 500 (160 MHz) spectrometer. Chemical shifts are reported in ppm using boron trifluoride as the external standard ($BF_3 \cdot Et_2O$: 0.0 ppm). Infrared (IR) spectra were measured using a Bruker a-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). High-resolution mass spectrometry (HRMS) was performed at the chemistry department at 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 was performed on 25 mm silica gel glass backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), phosphomolybdic acid (PMA), potassium permanganate ($KMnO_4$), and Seebach's "magic" stain [36] (phosphomolybdic acid, $Ce(SO_4)_2$, sulfuric acid). Analytical chiral gas-liquid chromatography (GLC) was also

[36]Seebach, D. *Helv. Chim. Acta.* **1987**, *70*, 448

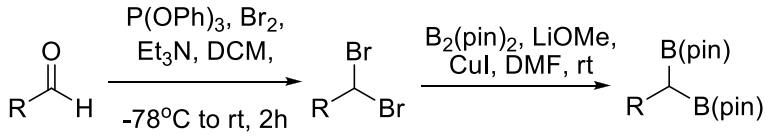
performed on an Agilent Technologies 6850 Series chromatograph with a flame ionization detector, and a Supelco β –Dex 120 column with helium as the carrier gas. Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. Analytical chiral supercritical fluid chromatography (SFC) was performed on a Thar Supercritical Fluid Chromatograph equipped with auto sampler and a Waters photodiode array detector with methanol as the modifier.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran, dichloromethane, toluene, and diethyl ether were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after being purged with argon. Dimethylformamide was dispensed from a Glass Contour Solvent Purification System (SG Water, USA LLC). Triethylamine was purchased from Aldrich and refluxed over calcium hydride prior to use. Copper iodide was purchased from Strem Chemicals and used as received. Triphenyl phosphate, lithium methyloxide, 3-phenylpropionaldehyde, hexanal, benzaldehyde, and crotonaldehyde were purchased from Alfa Aesar and used as received. $B_2(pin)_2$ was obtained from AllyChem and recrystallized from pentane prior to use. Pinacol borane was purchased from BASF and distilled prior to use. Bromine was purchased from Acros and used as received. All other reagents were obtained from Aldrich or Fisher and used as received.

5.5.2. Experimental Procedures

5.5.2.1. Representative procedure for preparation of geminal bis(boronate) esters

Method A:

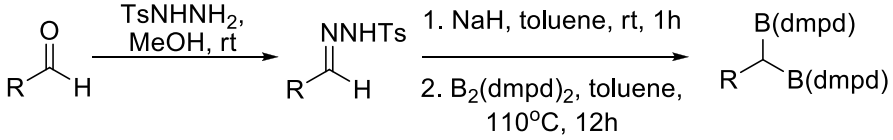


The 1,1-diboronates were prepared according to the literature procedure[37]. To a stirred solution of triphenyl phosphite (1.50 equiv) in anhydrous DCM (1 M) at -78 ℃ under N_2 was added bromine (1.30 equiv) dropwise. Freshly distilled triethylamine (3.00 equiv) and aldehyde (1.00 equiv) were added at -78 ℃. The reaction mixture was allowed to warm to room temperature and stirred for 2 hours. Upon completion, the solvent was evaporated in vacuo and the crude reaction mixture was purified on silica gel (100% hexanes) to afford the 1,1-dibromide.

In the glove box, an oven-dried 100 mL round-bottom flask with a magnetic stir bar was charged with CuI (0.10 equiv), LiOMe (2.50 equiv) and $B_2(pin)_2$ (1.90 equiv). The flask was sealed with a rubber septum, removed from the glove box, and DMF (0.5 M) was added under N_2. After stirring at room temperature for 10 min, a solution of 1,1-dibromide (1.00 equiv) in DMF was added via syringe at room temperature. The reaction mixture was allowed to stir at room temperature for 12 hours. Upon completion, 40 mL DI water was added, and extracted with hexane (3x40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The 1,1-diboronate products were isolated after SiO_2 chromatography, unless otherwise noted.

[37] Hong, K., Liu, X., Morken, J.P. *J. Am. Chem. Soc*. **2014**, 136, 10581.

Method B:

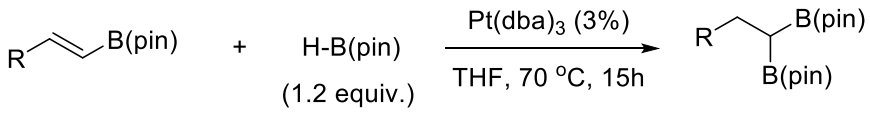


The 1,1-diboronates were prepared according to the literature procedure.[38] A 6-dram vial with magnetic stir bar was charged with aldehyde (1.00 equiv) and tosylhydrazine (1.00 equiv), and methanol (5 mL) was added. The mixture was stirred at room temperature. N-Tosylhydrazone precipitated after 15 minutes or longer and the reaction was monitored by TLC analysis (spot of the carbonyl compound). The precipitate was then collected, washed with pentane (5 mL × 3), and dried under vacuum.

In the glove box, an oven-dried 6-dram vial with a magnetic stir bar was charged with *N*-tosylhydrazone (1.00 mmol, 1.00 equiv), NaH (1.20 mmol, 1.20 equiv), and toluene (8 mL). The mixture was stirred at room temperature for 1 hour. Next, $B_2(dmpd)_2$ (1.20 mmol, 1.20 equiv) in toluene was added, and the vial was sealed, removed from the glovebox and heated at 110℃ for 12 hours. Upon completion, the reaction mixture was allowed to cooled to room temperature, and Et_2O (10 mL) and H_2O (10 mL) were added. The mixture was stirred vigorously for 10 minutes. After separation of the organic layer, the aqueous layer was extracted with Et_2O (2x5 mL). The combined organic layers were washed with saturated brine (10 mL) and dried over anhydrous Na_2SO_4. After the solvent was evaporated, the crude product was purified by silica gel chromatography.

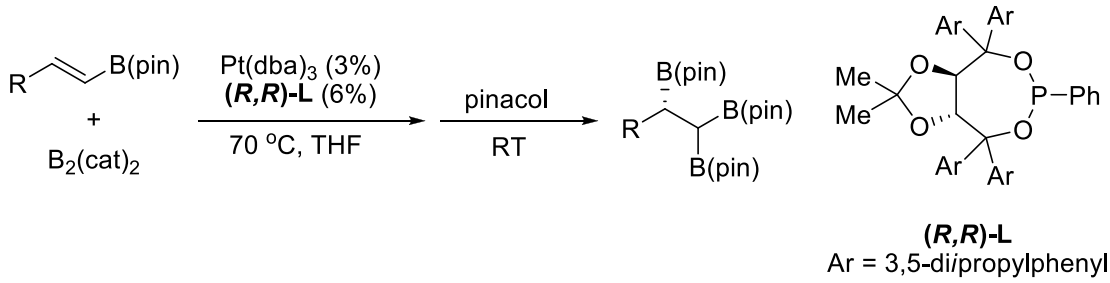
[38] Li, H.; Shangguan, X.; Zhang, Z.; Huang, S.; Zhang, Y.; Wang, J. *Org. Lett*. **2014**, 16, 448.

Method C:



To an oven-dried 2-dram vial equipped with a stir bar in a glovebox was added $Pt(dba)_3$ (3 mol%) followed by THF (1.0 M in vinyl boronate). To the reaction mixture was added pinacolborane (1.20 equiv.) followed by vinyl boronate (1.00 equiv.). The reaction vessel was sealed with a polypropylene cap, brought out of the glovebox, and the reaction mixture was allowed to stir at 70 °C for 15 hours. Upon completion, the solvent was evaporated in vacuo and the crude reaction mixture was purified on silica gel to afford the 1,1-diboronate.

Method D:

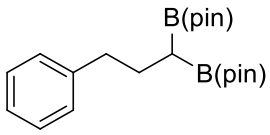


The 1,1,2-tris(boronates) were prepared according to the literature procedure.[39] To an oven-dried 2-dram vial equipped with a magnetic stirbar in the glovebox was added $Pt(dba)_3$ (0.03 equiv.), **(*R,R*)-L** (0.06 equiv.), and $B_2(cat)_2$ (1.20 *or* 2.00 equiv.), followed by THF (1.0 M in vinyl(boronate)). The vial was sealed with a polypropylene cap, taped, brought outside of the glovebox, and heated to 80 °C for 25 minutes. Over this period, the

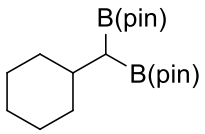
[39] Coombs, J. R., Zhang, L., Morken, J. P. *J. Am. Chem. Soc*. **2014**, 136, 16140.

mixture turned from a deep purple solution to a pale yellow solution. The mixture was cooled to room temperature and brought into the glovebox, at which point the vinyl boronate (1.00 equiv.) was added all at once. The vial was sealed with a polypropylene, taped, brought outside of the glovebox, and heated to 60 °C for 24 hours. The resulting mixture was cooled to room temperature and brought back into the glovebox, at which point pinacol (7.2 equiv.) was added all at once. The vial was sealed, taped, brought out of the glovebox, and allowed to stir at room temperature for 14 hours. The resulting mixture was cooled to room temperature, concentrated under reduced pressure, and subsequently purified via SiO_2 gel column chromatography to provide the pure diboration products

5.5.2.2. Preparation of geminal-bis(boronate) esters

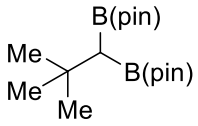


2,2'-(3-phenylpropane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (5.93). Prepared according to the general procedure (Method A) utilizing CuI (166 mg, 0.87 mmol), LiOMe (826 mg, 21.8 mmol), $B_2(pin)_2$ (4.20 g, 16.5 mmol), (3,3-dibromopropyl)benzene (2.43 g, 8.70 mmol) and DMF (15 mL). The crude reaction mixture was purified by column chromatography on silica gel (3% ethyl acetate/hexanes) to afford the desired product as a white solid (2.23 g, 69%). All spectral data are in accord with the literature.

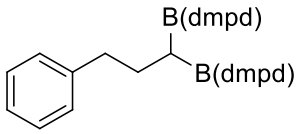


2,2'-(cyclohexylmethylene)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S1). Prepared according to the general procedure (Method A) utilizing CuI (309 mg, 1.62 mmol), LiOMe (1.54 g, 40.5

mmol), $B_2(pin)_2$ (7.80 g, 30.8 mmol), (dibromomethyl)cyclohexane (3.24 g, 16.2 mmol) and DMF (30 mL). The crude reaction mixture was purified by column chromatography on silica gel (3% ethyl acetate/hexanes) to afford the desired product as a white solid (3.74 g, 67%). All spectral data are in accord with the literature.[40]



2,2'-(2,2-dimethylpropane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S2). Prepared according to the general procedure (Method A) utilizing CuI (125.7 mg, 0.66 mmol), LiOMe (627 mg, 16.5 mmol), $B_2(pin)_2$ (3.20 g, 12.6 mmol), 1,1-dibromo-2,2-dimethylpropane (1.54 g, 6.60 mmol) and DMF (15 mL). The crude reaction mixture was purified by column chromatography on silica gel (3% ethyl acetate/hexanes) to afford the desired product as a white solid (1.39 g, 65%). All spectral data are in accord with the literature.

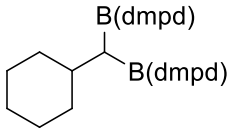


2,2'-(3-phenylpropane-1,1-diyl)bis(4,4,6,6-tetramethyl-1,3,2-dioxa-borinane) (5.114). Prepared according to the general procedure (Method B) utilizing 3-phenylpropanal (1.34 g, 10.0 mmol), tosylhydrazine (1.86 g, 10.0 mmol), and methanol (5 mL). The precipitate was collected, washed with pentane, and dried under reduced pressure to afford 4-*N*′-(3-phenylpropylidene)toluenesulfonohydrazide as a white solid, which was used in the following step without further purification.

The second step of the general procedure (Method B) was performed utilizing the above-synthesized *N*'-(3-phenylpropylidene)toluenesulfonohydrazide (605 mg, 2.00 mmol),

[40] Sun, C.; Potter, B.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 6534.

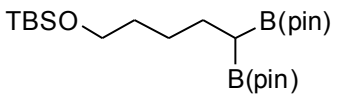
NaH (57.6 mg, 2.40 mmol), $B_2(dmpd)_2$ (677 mg, 2.40 mmol), and toluene (5.0 mL). The crude reaction mixture was purified by column chromatography on silica gel (2.5% ethyl acetate/hexanes) to afford the desired product as a white solid (632 mg, 79%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24 (2H, t, *J*= 7.5 Hz), 7.20 (2H, d, *J*= 7.0 Hz), 7.13 (1H, t, *J*= 7.5 Hz), 2.55 (2H, t, *J*= 8.0 Hz), 1.79-1.72 (2H, m), 1.75 (2H, s), 1.31 (24H, s), 0.47 (1H, t, *J*= 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 144.2, 128.7, 128.0, 125.1, 69.9, 48.9, 39.0, 31.9, 31.8, 28.6; IR (neat): 2072.7 (m), 2931.9 (w), 2862.8 (w), 1495.4 (w), 1453.8 (m), 1355.8 (s), 1300.5 (m), 1255.8 (m), 1196.1 (s), 1140.0 (w), 770.5 (w), 699.1 (w) cm^{-1}; HRMS-(DART) for: $C_{23}H_{39}B_2O_4$ $[M+H]^+$: calculated: 401.3034, found: 401.3048.



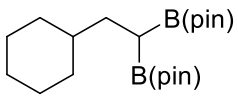
2,2'-(cyclohexylmethylene)bis(4,4,6,6-tetramethyl-1,3,2-dioxaborinane) (S3). Prepared according to the general procedure (Method B) utilizing 3-phenylpropanal (1.34 g, 10.0 mmol), tosylhydrazine (1.86 g, 10.0 mmol), and methanol (5 mL). The precipitate was collected, washed with pentane, and dried under reduced pressure to afford N'-(cyclohexylmethylene)-4-toluenesulfonohydrazide as a white solid, which was used in the following step without further purification.

The second step of the general procedure (Method B) was performed utilizing the above-synthesized *N'*-(cyclohexylmethylene)-4-toluenesulfonohydrazide (561 mg, 2.00 mmol), NaH (57.6 mg, 2.40 mmol), $B_2(dmpd)_2$ (677 mg, 2.40 mmol), and toluene (5.0 mL). The crude reaction mixture was purified by column chromatography on silica gel (2.5% ethyl acetate/hexanes) to afford the desired product as a white solid (646 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.74 (4H, s), 1.78-1.66 (2H, m), 1.65-1.54 (4H, m), 1.32-1.20 (4H,

m), 1.14-1.03 (1H, m), 0.91-0.83 (2H, m), 0.29 (1H, d, *J*= 10.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 69.8, 49.1, 35.7, 25.5, 21.9, 31.8, 26.9, 26.7; IR (neat): 2973.1 (m), 2918.2 (s), 2849.1 (w), 1446.0 (w), 1365.5 (s), 1293.1 (s), 1197.8 (s), 1139.9 (w), 770.2 (w) cm^{-1}; HRMS-(DART) for: $C_{21}H_{41}B_2O_4$ $[M+H]^+$: calculated: 379.3191, found: 379.3206.

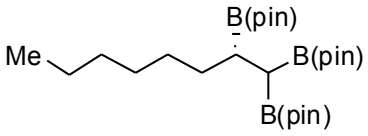


((5,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)-oxy)(*tert*-butyl)dimethylsilane (S4). Prepared according to the general procedure (Method C) utilizing (*E*)-*tert*-butyldimethyl((5-(4,4,5,5- tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-1-yl)oxy)silane (400.0 mg, 1.225 mmol), pinacolborane (188 mg, 1.47 mmol), $Pt(dba)_3$ (33.0 mg, 36.8 mmol) and THF (1.20 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (456 mg, 82%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.57 (2H, t, *J*= 6.5 Hz), 1.57-1.47 (4H, m), 1.35-1.26 (2H, m), 1.22 (12H, s), 1.21 (12H, s), 0.87 (9H, s), 0.71 (1H, t, *J*= 7.5 Hz), 0.02 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$): δ 82.8, 63.4, 33.0, 28.8, 26.0, 25.6, 24.8, 24.5, 18.3, -5.3; IR (neat): 2977.2 (w), 2929.2 (w), 2857.3 (w), 1462.9 (w), 1359.2 (m), 1309.4 (s), 1263.3 (m), 1215.0 (w), 1139.6 (s), 1098.2 (s), 969.1 (m), 834.6 (s), 773.9 (m), 667.0 (w) cm^{-1}; HRMS-(DART) for: $C_{23}H_{49}B_2O_5Si$ $[M+H]^+$: calculated: 455.3535, found: 455.3551.



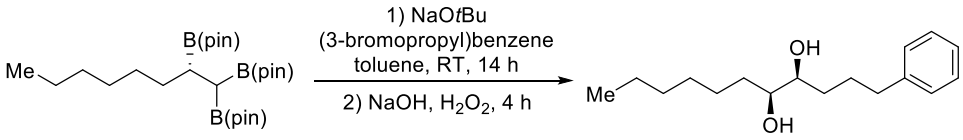
2,2'-(2-cyclohexylethane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxabor-olane) (S5). Prepared according to the general procedure (Method C) utilizing (*E*)-2-(2-cyclohexylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane

(500 mg, 2.12 mmol), pinacolborane (325 mg, 2.54 mmol), $Pt(dba)_3$ (57.0 mg, 63.5 mmol) and THF (2.10 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (473 mg, 61%). All spectral data are in accord with the literature.[41]



(*R*)-2,2',2''-(octane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (S6). Prepared according to the general procedure (Method D) utilizing $Pt(dba)_3$ (8.1 mg, 9.0 μmol), **(*R,R*)-L** (16.4 mg, 0.0180 mmol), $B_2(cat)_2$ (85.6 mg, 0.360 mmol), (*E*)-1-octen-1-ylboronic acid pinacol ester (71.8 mg, 0.300 mmol), and THF (0.30 mL), followed by pinacol (255.2 mg, 2.160 mmol). The crude material was purified (SiO_2, 5-7% ethyl acetate in hexane, UV/magic stain) to give the desired product as a white solid (115.6 mg, 78%). All spectral data are in accord with the literature.[4]

Analysis of stereochemistry:



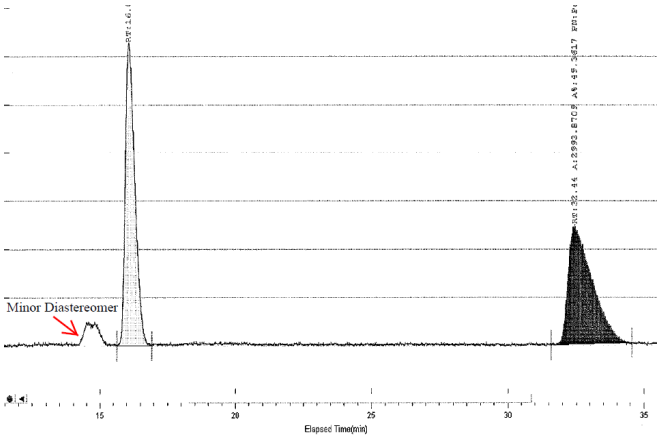
Racemic compound was prepared according to the general procedure for racemic vinyl boronate diboration utilizing (*E*)-1-octen-1-ylboronic acid pinacol ester and $Pt(dba)_3$ as the catalyst. The title compound was subjected to deborylative alkylation condition[4] with (3-bromopropyl)benzene followed by oxidation as shown below to give (4*S*,5*S*)-1-

[41] Lee, S.; Li, D.; Yun, J. *Chem. Asian J.* **2014**, 9, 2440.

phenylundecane-4,5-diol. Further analysis of stereochemistry was performed on (4*S*,5*S*)-1-phenylundecane-4,5-diol. Absolute stereochemistry was assigned by analogy.

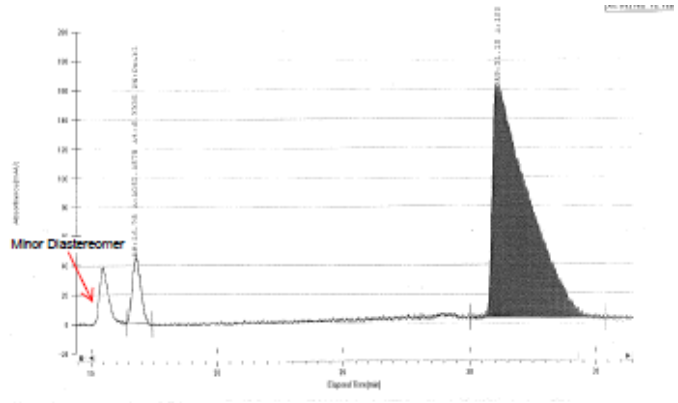
Chiral SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (4S,5S)-1-phenylundecane-4,5-diol

Racemic Material



Peak No	% Area	Area	RT (min)
1	50.6383	3071.2958	16.08
2	49.3617	2993.8709	32.44
Total:	100	6065.1667	

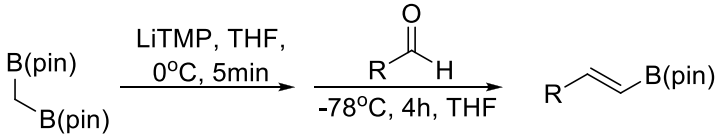
Standard Conditions



Peak Info

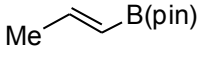
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	6.3335	1052.4575	16.73	45.1627	0.026
2	93.6665	15564.7857	31.12	160.1019	0.0483
Total:	100	16617.2432			

5.5.2.3. Representative procedure for preparation of 1,2-disubtituted vinyl boronates



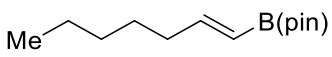
In the glove box, an oven-dried 2-dram vial with a magnetic stir bar was charged with LiTMP (0.30mmol, 1.2 equiv), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0 °C, and THF (0.30 mL), followed by a solution of bis(4,4,5,5-tetramethyl- 1,3,2-dioxaborolan-2-yl)methane (0.30 mmol, 1.2 equiv) in THF (0.60 mL) were added. The reaction vial was allowed to stir for 5 minutes at 0°C. Then the reaction vial was cooled to -78 °C, and a solution of aldehyde (0.25 mmol, 1.0 equiv) in THF (0.30 mL) was added. The reaction vial was allowed to stir at -78 °C for additional 4 hours. Upon completion, the reaction mixture was concentrated under reduced pressure. The 1,2-disubtituted-vinyl boronates products were isolated by SiO_2 chromatography.

5.5.2.4. Full characterization of 1,2-disubtituted vinyl boronates

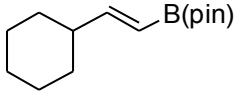


(*E*)-4,4,5,5-tetramethyl-2-(prop-1-en-1-yl)-1,3,2-dioxaborolane (5.80). Prepared according to the representative procedure utilizing LiTMP (162 mg, 1.10 mmol), bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (268 mg, 1.00 mmol), acetaldehyde (5M solution in THF, 0.22 mL, 1.10 mmol), and THF (4.0 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (106 mg, 63%). ^{1}H

NMR (500 MHz, $CDCl_3$): δ 6.64 (1 H, dq, *J* = 18.5, 6.5 Hz), 5.45 (1H, d, *J*= 18.0 Hz), 1.84 (1H, d, *J*= 6.0 Hz), 1.25 (12H, s); ^{13}C NMR (126 MHz, $CDCl_3$): δ 149.6, 82.9, 24.7, 21.6; All additional data are in accord with the literature.[42]



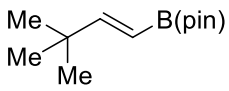
(*E*)-2-(hept-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.81). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (80.4 mg, 0.300 mmol), hexanal (30.0 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2.5% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (47.6 mg, 85%). ^1H NMR (500 MHz, $CDCl_3$): δ 6.63 (1H, dt, *J*= 18.0, 6.0 Hz), 5.42 (1H, d, *J*= 18.0 Hz), 2.14 (2H, q, *J*= 6.5 Hz), 1.42 (2H, pent, *J*= 7.0 Hz), 1.32-1.18 (4H, m), 1.26 (12H, s), 0.88 (3H, t, *J*= 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 154.8, 83.0, 35.8, 31.4, 27.9, 24.8, 22.5, 14.0; IR (neat): 2977.4 (m), 3959.2 (m), 2926.6 (m), 2857.6 (w), 1630.0 (s), 1466.7 (w), 1397.9 (s), 1360.3 (s), 1234.6 (w), 1215.4 (w), 1145.3 (s), 998.8 (m), 972.4 (m), 896.5 (w), 850.4 (m) cm^{-1}; HRMS-(DART) for: $C_{13}H_{26}B_1O_2$ $[M+H]^+$: calculated: 225.2026, found: 225.2037.



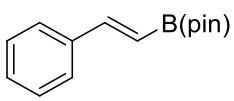
(*E*)-2-(2-cyclohexylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.82). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (80.4 mg, 0.300 mmol), cyclohexanecarbaldehyde (28.0 mg,

[42] Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, 2, 230.

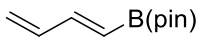
0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (47.2 mg, 80%). All spectral data are in accord with the literature.[43]



(*E*)-2-(3,3-dimethylbut-1-enyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.83). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.3 mmol), bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) methane (80.4 mg, 0.3 mmol), pivalaldehyde (21.5 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (25.1 mg, 48%). All spectral data are in accord with the literature.[44]



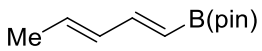
***(E)*-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane (5.84).** Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (80.4 mg, 0.300 mmol), benzaldehyde (26.5 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (43.7 mg, 76%). All spectral data are in accord with the literature.[5]



***(E)*-2-(buta-1,3-dienyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane**

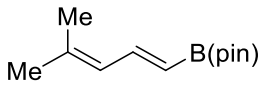
[43] Yoshida, H., Kageyuki, I., Takaki, K. *Org. Lett.* **2014**, 16, 3512.
[44] Shirakawa, K., Arase, A., Hoshi, M., *Synthesis* **2004**, 11, 1814

(5.85). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (80.4 mg, 0.300 mmol), acrylaldehyde (14.2 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (26.8 mg, 59%). ^{1}H NMR (500 MHz, $CDCl_3$): 6.98 (1H, dd, *J*= 17.5 Hz, 10.5 Hz), 6.39 (1H, dt, *J*= 16.5 Hz, 11.0 Hz), 5.55 (1H, d, *J*= 17.5 Hz), 5.36 (1H, d, *J*= 17.0 Hz), 5.23 (1H, d, *J*= 10.0 Hz), δ1.25 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 139.0, 121.2, 83.4, 25.0; IR (neat): 2978.3 (m), 1634.4 (m), 1592.3 (m), 1371.8 (s), 1337.5 (s), 1320.5 (s), 1221.5 (m), 1142.5 (m), 1106.4 (s), 969.7 (m), 913.0 (m) cm^{-1}; HRMS-(DART) for: $C_{10}H_{18}B_1O_2$ $[M+H]^+$: calculated: 181.1400, found: 181.1392.

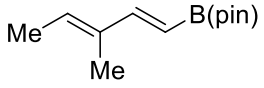


4,4,5,5-tetramethyl-2-((1*E*,3*E*)-penta-1,3-dienyl)-1,3,2-dioxaborolane (5.86). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (80.4 mg, 0.300 mmol), (*E*)-but-2-enal (17.5 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (42.2 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.95 (1H, dd, *J*= 18.0 Hz, 11.0 Hz), 6.12 (1H, t, *J*= 14.5 Hz), 5.84-5.91 (1H, m), 5.38 (1H, d, *J*= 17.5 Hz), 1.76 (3H, d, *J*= 7.0 Hz), 1.24 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 134.3, 134.0, 83.2, 24.9, 18.4; IR (neat): 2978.0 (m), 1645.7 (m), 1603.6 (m), 1392.9 (m), 1378.2 (m), 1350.7 (s), 1319.5 (m), 1264.3 (m),

1106.4 (s), 1006.4 (m), 969.8 (m), 848.6 (m) cm^{-1}; HRMS-(DART) for: $C_{11}H_{20}B_1O_2$ $[M+H]^+$: calculated: 195.1556, found: 195.1556.

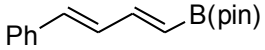


(*E*)-4,4,5,5-tetramethyl-2-(4-methylpenta-1,3-dienyl)-1,3,2-dioxaborolane (5.87). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (80.4 mg, 0.300 mmol), 3-methylbut-2-enal (21.0 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (41.6 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23 (1H, dd, *J*= 18.0 Hz, 11.5 Hz), 5.91 (1H, d, *J*= 11.0 Hz), 5.38 (1H, d, *J*= 17.0 Hz), 1.82 (3H, s), 1.79 (3H, s), 1.25 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.3, 140.7, 128.0, 83.2, 26.4, 24.9, 19.0; IR (neat): 2977.8 (m), 2928.6 (m), 1640.9 (m), 1602.8 (m), 1378.7 (m), 1356.7 (s), 1332.8 (s), 1313.8 (m), 1143.9 (s), 999.5 (m), 970.1 (m), 851.0 (m) cm^{-1}; HRMS-(DART) for: $C_{12}H_{22}B_1O_2$ $[M+H]^+$: calculated: 209.1713, found: 209.1714.

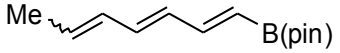


4,4,5,5-tetramethyl-2-((1*E*,3*E*)-3-methylpenta-1,3-dienyl)-1,3,2-dioxaborolane (5.88). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (80.4 mg, 0.300 mmol), (*E*)-2-methylbut-2-enal (21.0 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (47.5 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.02 (1H, d, *J*= 18.5

Hz), 5.76 (1H, q, *J*= 7.0 Hz), 5.42 (1H, d, *J*= 18.0 Hz), 1.74 (3H, d, *J*= 7.0 Hz), 1.72 (3H, s), 1.26 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.7, 136.3, 131.9, 83.2, 25.0, 14.4, 11.5; IR (neat): 2978.0 (m), 2928.7 (w), 1607.7 (m), 1458.6 (m), 1397.8 (m), 1378.5 (s), 1340.1 (m), 1144.2 (s), 1110.3 (m), 1033.9 (m), 993.2 (m), 900.4 (m) cm^{-1}; HRMS-(DART) for: $C_{12}H_{22}B_1O_2$ $[M+H]^+$: calculated: 209.1713, found: 209.1707.

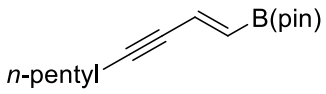


4,4,5,5-tetramethyl-2-((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)-1,3,2-diox-aborolane (5.89). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) methane (80.4 mg, 0.300 mmol), cinnamaldehyde (33.0 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2.5% ethyl acetate/hexanes) to afford the desired product as a clear, pale yellow oil (47.3 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.43 (2 H, d, *J* = 7.5 Hz), 7.32 (2H, t, *J*= 7.5 Hz), 7.25 (1H, t, *J*= 7.5 Hz), 7.18 (1H, dd, *J*= 18.0, 10.5 Hz), 6.85 (1H, dd, *J*= 15.0, 10.0 Hz), 6.70 (1H, d, *J*= 15.0 Hz), 5.68 (1H, d, *J*= 18.0 Hz), 1.30 (12H, s); ^{13}C NMR (126 MHz, $CDCl_3$): δ 149.8, 136.8, 136.1, 130.6, 128.6, 128.1, 126.8, 83.2, 24.8; IR (neat): 3023.7 (w), 2977.6 (m), 2929.5 (w), 1623.2 (m), 1603.4 (s), 1389.7 (m), 1448.0 (w), 1358.6 (s), 1322.5 (s), 1260.0 (s), 1143.6 (s), 1006.6 (m), 969.9 (m), 850.2 (m), 748.3 (w), 691.0 (m), 643.7 (w) cm^{-1}; HRMS-(DART) for: $C_{16}H_{22}B_1O_2$ $[M+H]^+$: calculated: 257.1713, found: 257.1712.



2-((1*E*,3*E*)-hepta-1,3,5-trien-1-yl)-4,4,5,5-tetramethyl-1,3,2-diox-aborolane (5.90). Prepared according to the representative procedure utilizing

LiTMP (44.2 mg, 0.300 mmol), bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) methane (80.4 mg, 0.300 mmol), a 5:1 mixture of (2*E*)-hexa-2,4-dienal and (2*E*,4*Z*)-hexa-2,4-dienal (24.0 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, pale yellow oil (41.6 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.01 (1H, dd, *J*= 17.5, 10.0 Hz), 6.32 (1H, dd, *J*= 14.5, 10.5 Hz), 6.20-6.04 (2H, m), 5.81 (1H, dq, *J*= 14.0, 7.0 Hz), 5.50 (1H, d, *J*= 18.0 Hz), 1.79 (3H, d, *J*= 6.5 Hz), 1.27 (12H, s); ^{13}C NMR (126 MHz, $CDCl_3$): δ 150.0, 136.7, 132.5, 131.9, 131.5, 83.1, 24.8, 18.4; IR (neat): 2977.7 (w), 2930.7 (w), 1615.5 (m), 1584.4 (m), 1358.0 (s), 1320.0 (s), 1270.0 (m), 1214.1 (w), 1142.1 (s), 1106.6 (w), 1008.1 (s), 970.0 (m), 848.7 (m), 645.4 (w) cm^{-1}; HRMS-(DART) for: $C_{13}H_{22}B_1O_2$ $[M+H]^+$: calculated: 221.1713, found: 221.1716.

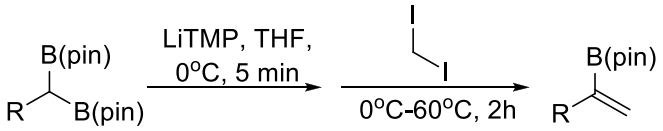


(*E*)-4,4,5,5-tetramethyl-2-(non-1-en-3-ynyl)-1,3,2-dioxaborolane (5.91). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), bis(4,4,5,5-tetramethyl-1,3,2- dioxaborolan-2-yl)methane (80.4 mg, 0.300 mmol), oct-2-ynal (31.0 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (48.7 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.40 (1H, d, *J*= 18.5 Hz), 5.89 (1H, d, *J*= 18.0 Hz), 2.30 (2H, dt, *J*= 7.0 Hz, 1.5 Hz), 1.48-1.54 (2H, m), 1.23-1.36 (16H, m), 0.87 (3H, t, *J*= 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 130.5, 95.5, 83.6, 81.0, 31.2, 28.4, 25.0, 24.9, 22.4, 19.7, 14.2; IR (neat): 2977.8 (m), 2931.5 (m), 2209.2

(w), 1599.8 (s), 1387.0 (m), 1346.8 (s), 1323.3 (s), 1271.0 (m), 1199.0 (m), 1141.5 (s), 980.9 (m), 969.5 (m), 849.8 (m) cm^{-1}; HRMS-(DART) for: $C_{15}H_{26}B_1O_2$ $[M+H]^+$: calculated: 249.2026, found: 249.2031.

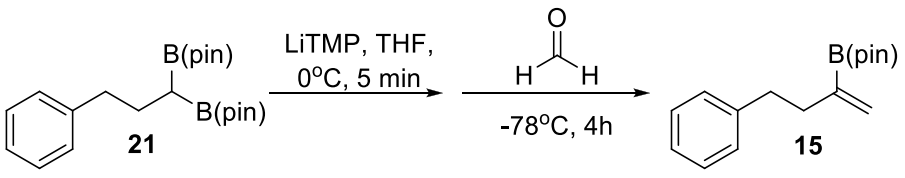
5.5.2.5. Representative procedure for preparation of 1,1-disubtituted vinyl boronates

Method A (with diiodomethane):



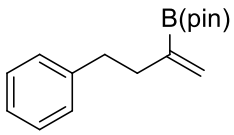
In the glove box, an oven-dried 2-dram vial with magnetic stir bar was charged with LiTMP (0.200 mmol, 1.00 equiv), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0 °C, and THF (0.30 mL), and solution of 1,1-diboronate (0.200 mmol, 1.00 equiv) in THF (0.6 mL) were added. The reaction mixture was allowed to stir for 5 minutes at 0 °C. Next, a solution of diiodomethane (0.400 mmol, 2.00 equiv) in THF (0.4 mL) was added dropwise at 0 °C. The reaction vial was allowed to warm to 60 °C and stir for additional 2 hours. Upon completion, the reaction mixture was concentrated under reduced pressure. The 1,1 disubtituted-vinyl boronate products were isolated by SiO_2 chromatography.

Method B (with formaldehyde):



In the glove box, an oven-dried 2-dram vial with magnetic stir bar was charged with LiTMP (29.4 mg, 0.200 mmol, 1.00 equiv), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0 °C, and THF (0.3 mL), and solution of 2,2'-(3-phenylpropane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (74.4 mg, 0.200 mmol) in THF (0.6 mL) were added. The reaction mixture was allowed to stir for 5 minutes at 0 °C. Then, formaldehyde[45], which was generated by heating a 2-dram vial with paraformaldehyde (60.0 mg, 2.00 mmol, 10.0 equiv) and *p*-toluenesulfonic anhydride (9.8 mg, 0.03 mmol, 0.15 equiv) at 85 °C, was carried by a slow N_2 stream and bubbled through the reaction mixture at -78 °C for 4 hours. Upon completion, the reaction mixture was concentrated under reduced pressure. The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (25.8 mg, 50%). All spectral data are in accord with the literature.[10]

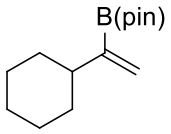
5.5.2.6. Full Characterization of 1,1-disubtituted-vinyl boronates



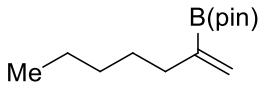
4,4,5,5-tetramethyl-2-(4-phenylbut-1-en-2-yl)-1,3,2-dioxaborolane (5.95). Prepared according to the representative procedure (Method A) utilizing LiTMP (29.4 mg, 0.200 mmol), 2,2'-(3-phenylpropane-1,1-diyl)bis(4,4,5,5- tetramethyl-1,3,2-dioxaborolane) (74.4 mg, 0.200 mmol), diiodomethane (107 mg, 0.400 mmol), and THF (0.9 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to

[45] Schlosser, M., Jenny, T.; Guggisberg, Y. *Synlett*, **1990**, 11, 704.

afford the desired product as a clear, colorless oil (44.9 mg, 87%). All spectral data are in accord with the literature.[46]



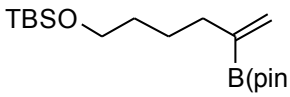
2-(1-cyclohexylvinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.105). Prepared according to the representative procedure (Method A) utilizing LiTMP (29.4 mg, 0.200 mmol), 2,2'-(cyclohexylmethylene)bis(4,4,5,5-tetramethyl-1,3,2 -dioxaborolane) (70.0 mg, 0.200 mmol), diiodomethane (107 mg, 0.400 mmol), and THF (0.9 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (40.3 mg, 85%). All spectral data are in accord with the literature.



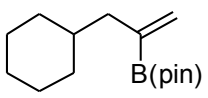
2-(hept-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.107). Prepared according to the representative procedure (Method A) utilizing LiTMP (29.4 mg, 0.200 mmol), 2,2'-(hexane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (67.6 mg, 0.200 mmol), diiodomethane (107 mg, 0.400 mmol), and THF (0.9 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (35.3 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.73 (1H, d, *J*= 3.0 Hz), 5.56 (1H, s), 2.11 (2H, t, *J*= 7.5 Hz), 1.39 (2H, p, *J*= 7.5 Hz), 1.30-1.22 (16H, m), 0.86 (3H, t, *J*= 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 128.8, 83.5, 35.5, 31.7, 29.1, 24.9, 22.8, 14.2; IR (neat): 2978.1 (m), 2958.9 (m), 2926.9 (m), 1425.9 (m), 1368.7 (s),

[46] Ganić, Adnan, and Andreas Pfaltz, *Chem. Eur. J.* **2012**, 18, 6724.

1343.7 (m), 1306.2 (s), 1204.7 (m), 1141.3 (s), 970.4 (m), 860.5 (m), 737.9 (m) cm^{-1}; HRMS-(DART) for: $C_{13}H_{26}B_1O_2$ $[M+H]^+$: calculated: 225.2026, found: 225.2034.



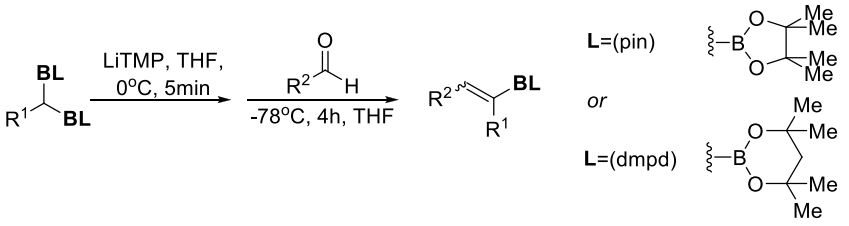
***tert*-butyldimethyl((5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-1-yl)oxy)silane (5.109).** Prepared according to the representative procedure (Method A) utilizing LiTMP (29.2 mg, 0.200 mmol), ((5,5-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)oxy)(tertbutyl) dimethylsilane (90.9 mg, 0.200 mmol), diiodomethane (107 mg, 0.400 mmol), and THF (1.3 mL). The crude reaction mixture was purified by column chromatography on silica gel (2.5% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (57.0 mg, 84%). All spectral data are in accord with the literature.[47]



2-(3-cyclohexylprop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.108). Prepared according to the representative procedure (*Method A*) utilizing LiTMP (29.2 mg, 0.200 mmol), 2,2'-(2-cyclohexylethane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (72.8 mg, 0.200 mmol), diiodomethane (107 mg, 0.400 mmol), and THF (1.3 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (36.1 mg, 72%). All spectral data are in accord with the literature.[12]

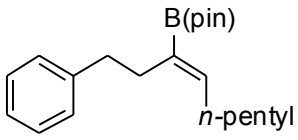
[47] Semba, K.; Shinomiya, M.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. Eur. J.* **2013**, 19, 7125.

5.5.2.7. Representative procedure for preparation of trisubtituted-vinyl boronates



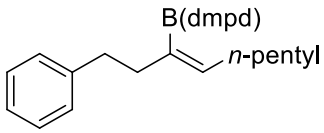
In the glove box, an oven-dried 2-dram vial with a magnetic stir bar was charged with LiTMP (0.300 mmol, 1.20 equiv), sealed with a cap with a septum, and removed from the glovebox. The reaction vial was cooled to 0°C, and THF (0.30 mL), and solution of 1,1-diboronates (0.300 mmol, 1.20 equiv) in THF (0.60 mL) were added. The reaction vial was allowed to stir for 5 minutes at 0°C. Then the reaction vial was cooled to -78°C, and a solution of aldehyde (0.250 mmol, 1.00 equiv) in THF (0.30 mL) was added. The reaction vial was allowed to stir at -78°C for additional 4 hours. Upon completion, the reaction mixture was concentrated under reduced pressure. The trisubtituted vinyl boronate products were isolated by silica gel chromatography.

5.5.2.8. Full characterization of trisubtituted vinyl boronates



(*Z*)-4,4,5,5-tetramethyl-2-(1-phenylnon-3-en-3-yl)-1,3,2-dioxaboro-lane (5.110). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), 2,2'-(3-phenylpropane-1,1-diyl) bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (112 mg, 0.300 mmol), hexanal (25.0 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2.5% ethyl

acetate/hexanes) to afford the desired product as a clear, colorless oil (72.2 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.26 (2H, t, *J*= 8.0 Hz), 7.19 (2H, d, *J*= 7.5 Hz), 7.16 (1H, t, *J*= 7.5 Hz), 6.32 (1H, t, *J*= 7.0 Hz), 2.65 (2H, t, *J*= 7.5 Hz), 2.44 (2H, t, *J*= 7.5 Hz), 2.02 (2H, q, *J*= 7.5 Hz), 1.33-1.22 (6H, m), 1.26 (12H, s), 0.88 (3H, t, *J*= 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major isomer) 146.9, 142.7, 128.6, 128.1, 125.5, 83.0, 36.4, 31.7, 30.6, 28.7, 28.4, 24.7, 22.5, 14.0; IR (neat): 2976.3 (w), 2956.3 (w), 2925.6 (m), 2857.5 (w), 1628.3 (w), 1453.8 (m), 1408.4 (m), 1377.5 (s), 1348.8 (s), 1300.9 (s), 1143.7 (s), 965.6 (w), 856.4 (m), 747.0 (m), 697.3 (s) cm^{-1}; HRMS-(DART) for: $C_{22}H_{35}B_1O_2$ $[M]^+$: calculated: 342.2730, found: 342.2747. (*Note: The olefin geometry was assigned based on analogy to compounds* ***5.114, 5.118, 5.119, and 5.124***.)

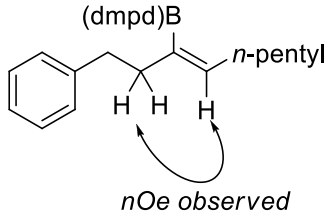


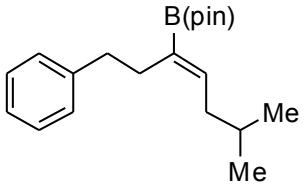
(*E*)-4,4,6,6-tetramethyl-2-(1-phenylnon-3-en-3-yl)-1,3,2-dioxabor-inane (5.114). Prepared according to the representative procedure utilizing LiTMP (35.4 mg, 0.240 mmol), 2,2'-(3-phenylpropane-1,1-diyl)bis(4,4,6,6-tetramethyl-1,3,2-dioxaborinane) (96.1 mg, 0.240 mmol), hexanal (20.0 mg, 0.200 mmol), and THF (0.96 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (55.4 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.28-7.14 (5H, m), 5.90 (1H, t, *J* = 7.0 Hz), 2.65 (2H, t, *J*= 8.0 Hz), 2.35 (2H, t, *J*= 8.0 Hz), 2.27 (2H, q, *J*= 7.0 Hz), 1.84 (2H, d, *J*= 3.0 Hz), 1.38-1.23 (6H, m), 1.37 (12H, s), 0.89 (3H, t, *J*= 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major + minor isomers) 143.5, 143.4, 143.3, 143.1, 128.6, 128.5, 128.1, 128.1, 125.4, 125.3, 70.5, 70.2, 48.8, 39.5, 37.3, 36.7, 31.9, 31.9, 31.8, 31.6, 30.8, 30.7,

29.8, 29.1, 28.4, 22.6, 22.6, 14.1, 14.0; IR (neat): 3025.5 (w), 2972.5 (m), 2923.8 (m), 2855.7 (m), 1672.7 (w), 1495.2 (w), 1453.7 (w), 1384.8 (s), 1366.9 (s), 1323.0 (m), 1257.7 (s), 1169.0 (s), 1204.7 (m), 1098.1 (w), 771.1 (w), 746.2 (w), 697.8 (s) cm^{-1}; HRMS-(DART) for: $C_{21}H_{34}B_1O_2$ $[M+H]^+$: calculated: 329.2652, found: 329.2660.

Determination of Stereochemistry:

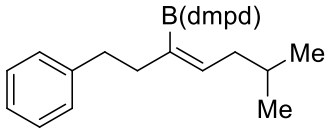
The olefin geometry was determined by 2D NMR (NOESY).





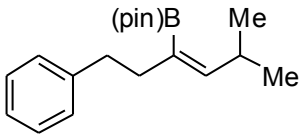
(*Z*)-4,4,5,5-tetramethyl-2-(6-methyl-1-phenylhept-3-en-3-yl)-1,3,2-dioxaborolane (5.115). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), 2,2'-(3-phenylpropane -1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (112 mg, 0.300 mmol), 3-methylbutanal (21.5 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (72.4 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.28-7.14 (5H, m), 6.33 (1H, t, *J*= 7.0 Hz), 2.65 (2H, t, *J*= 7.5 Hz), 2.44 (2H, t, *J*= 8.5 Hz), 1.94 (2H, t, *J*= 7.0 Hz), 1.66-1.55 (1H, m), 1.26 (12H, s), 0.88 (6H, d, *J*= 6.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major + minor isomers) 145.8, 145.5, 142.8, 128.6, 128.1, 125.5, 125.4, 83.0, 82.8, 40.1, 39.1,

37.6, 37.0, 36.3, 30.7, 29.0, 28.3, 24.8, 24.8, 22.6, 22.3; IR (neat): 2976.0 (m), 2953.6 (m), 2929.0 (m), 2867.8 (w), 1628.1 (w), 1495.2 (w), 1453.6 (m), 1407.8 (s), 1378.0 (s), 1350.8 (s), 1268.7 (w), 1142.5 (s), 1030.9 (m), 857.0 (m), 696.7 (s) cm^{-1}; HRMS-(DART) for: $C_{20}H_{32}B_1O_2$ $[M+H]^+$: calculated: 315.2495, found: 315.2498. (*Note: The olefin geometry was assigned based on analogy to compounds* ***5.114, 5.118, 5.119, and 5.124***.)

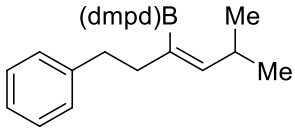


(*E*)-4,4,6,6-tetramethyl-2-(6-methyl-1-phenylhept-3-en-3-yl)-1,3,2-dioxaborinane (5.116). Prepared according to the representative procedure utilizing LiTMP (35.3 mg, 0.240 mmol), 2,2'-(3-phenylpropane-1,1-diyl)bis(4,4,6,6-tetramethyl-1,3,2-dioxaborinane) (96.0 mg, 0.240 mmol), 3-methylbutanal (17.3 mg, 0.200 mmol), and THF (0.96 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (52.9 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.29-7.14 (5H, m), 5.92 (1H, t, *J*= 7.5 Hz), 2.67 (2H, t, *J*= 8.0 Hz), 2.37 (2H, t, *J*= 8.0 Hz), 2.18 (2H, t, *J*= 8.0 Hz), 1.83 (2H, s), 1.70-1.54 (1H, m), 1.37 (12H, s), 0.87 (6H, s, *J*= 7.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major + minor isomers) 143.5, 143.3, 142.1, 141.8, 128.6, 128.5, 128.1, 128.1, 125.4, 125.3, 70.5, 70.2, 48.8, 39.8, 39.6, 37.5, 37.3, 36.6, 31.9, 31.8, 30.8, 29.2, 28.5, 22.7, 22.4; IR (neat): 3025.6 (m), 2972.3 (m), 2927.1 (m), 2867.7 (w), 1627.5 (w), 1495.5 (w), 1453.6 (m), 1384.2 (s), 1316.3 (m), 1301.6 (m), 1281.8 (m), 1204.5 (s), 1097.9 (w), 770.4 (w), 746.0 (w), 698.1 (m) cm^{-1}; HRMS-(DART) for: $C_{21}H_{37}B_1N_1O_2$

$[M+NH_4]^+$: calculated: 346.2917, found: 346.2926. (*Note: The olefin geometry was assigned based on analogy to compounds* ***5.114, 5.118, 5.119, and 5.124***.)



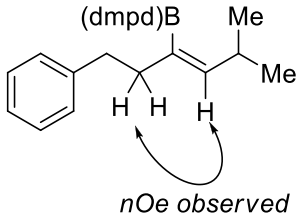
(*E*)-4,4,5,5-tetramethyl-2-(5-methyl-1-phenylhex-3-en-3-yl)-1,3,2-dioxaborolane (5.117). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), 2,2'-(3-phenylpropane -1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (112 mg, 0.300 mmol), isobutyraldehyde (18.0 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (66.9 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.27-7.24 (2H, m), 7.20-7.14 (3H, m), 5.74 (1H, d, *J*= 9.5 Hz), 2.98-2.91 (1H, m), 2.67 (2H, t, *J*= 7.5 Hz), 2.36 (2H, t, *J*= 8.5 Hz), 1.28 (12H, s), 0.91 (6H, d, *J*= 6.5 Hz); (minor isomer) 7.27-7.24 (2H, m), 7.20-7.14 (3H, m), 6.10 (1H, d, *J*= 9.5 Hz), 2.67 (2H, t, *J*= 7.5 Hz), 2.63-2.56 (1H, m), 2.45 (2H, t, *J*= 8.0 Hz), 1.26 (12H, s), 0.88 (6H, d, *J*= 6.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major + minor isomers) 154.4, 153.4, 142.7, 142.7, 128.7, 128.6, 128.1, 128.0, 125.5, 125.4, 83.0, 82.8, 38.8, 36.9, 36.8, 30.7, 29.7, 27.4, 24.8, 24.8, 23.4, 22.6; IR (neat): 2975.5 (m), 2960.9 (m), 2928.6 (m), 2865.6 (w), 1630.2 (w), 1495.5 (w), 1453.7 (m), 1405.3 (s), 1371.6 (m), 1290.7 (s), 1261.2 (s), 1142.9 (s), 966.5 (m), 863.3 (m), 747.2 (w), 698.1 (s) cm^{-1}; HRMS-(DART) for: $C_{19}H_{30}B_1O_2$ $[M+H]^+$: calculated: 301.2339, found: 301.2334. (*Note: The olefin geometry was assigned based on analogy to compounds* ***5.114, 5.118, 5.119, and 5.124***.)

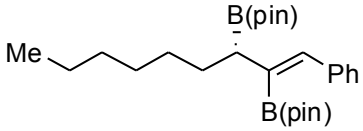


(*E*)-4,4,6,6-tetramethyl-2-(5-methyl-1-phenylhex-3-en-3-yl)-1,3,2-dioxaborinane (5.118). Prepared according to the representative procedure utilizing LiTMP (35.3 mg, 0.240 mmol), 2,2'-(3-phenylpropane -1,1-diyl) bis(4,4,6,6-tetramethyl-1,3,2-dioxaborinane) (96.0 mg, 0.240 mmol), isobutyraldehyde (14.4 mg, 0.200 mmol), and THF (0.96 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (57.3 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (2H, t, *J*= 8.0 Hz), 7.19 (2H, d, *J*= 7.0 Hz), 7.16 (1H, t, *J*= 7.5 Hz), 5.65 (1H, d, *J*= 9.0 Hz), 2.96-2.90 (1H, m), 2.65 (2H, t, *J*= 8.5 Hz), 2.32 (2H, t, *J*= 9.0 Hz), 1.84 (2H, s), 1.37 (12H, s), 0.93 (6H, d, *J*= 6.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 150.7, 143.3, 128.6, 128.0, 125.3, 70.5, 48.8, 39.3, 37.2, 31.9, 29.5, 24.5; IR (neat): 2972.0 (m), 2924.6 (m), 2864.5 (w), 1626.6 (w), 1453.6 (w), 1389.1 (s), 1355.8 (s), 1304.3 (s), 1254.0 (s), 1204.0 (s), 1098.7 (w), 769.9 (w), 746.4 (w), 697.9 (m); HRMS-(DART) for: $C_{20}H_{31}B_1O_2$ $[M]^+$: calculated: 314.2417, found: 314.2412.

Determination of Stereochemistry:

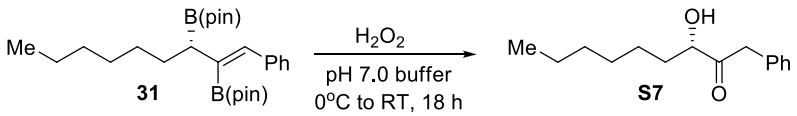
The olefin geometry was determined by 2D NMR (NOESY).



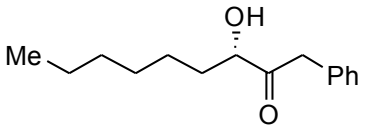


(*S*,*E*)-2,2'-(1-phenylnon-1-ene-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (5.119). To an oven-dried 2-dram vial equipped with a magnetic stirbar in the glovebox was added (*R*)-2,2',2''-(octane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (73.8 mg, 0.150 mmol), and THF (0.25 mL). The reaction vessel was sealed with a polypropylene cap with septum, taped, and brought out of the glovebox where it was cooled to 0 °C. Then LiTMP solution (22.1 mg in 0.44 mL THF, 0.150 mmol) was added dropwise by syringe and the reaction mixture was allowed to stir at 0°C for an additional 5 minutes. Benzaldehyde (10.6 mg in 0.11 mL THF, 0.100 mmol) solution was added dropwise and the reaction mixture was allowed to warm to 60°C and stir for additional 2 hours. Upon completion, the reaction mixture was concentrated under reduced pressure and purificd by silica gel chromatography (2% ethyl acetate/hexane) to give the desired product as a colorless oil (35.0 mg, 77%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (2H, d, *J*= 7.5 Hz), 7.21 (2H, t, *J*= 7.0 Hz), 7.13 (1H, tt, *J*= 7.5, 1.5 Hz), 6.86 (1H, s), 1.99 (1H, t, *J*= 8.0 Hz), 1.70-1.65 (1H, m), 1.57-1.52 (1H, m), 1.36-1.21 (32H, m), 0.85 (3H, t, *J*= 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.8, 138.8, 128.3, 127.9, 126.7, 83.6, 83.3, 32.0, 30.7, 29.6, 29.5, 25.1, 25.0, 24.9, 22.9, 14.3; IR (neat): 2977.5 (m), 2925.9 (m), 2855.4 (m), 1465.2 (m), 1388.6 (m), 1370.5 (m), 1304.6 (s), 1252.3 (m), 1141.8 (s), 966.5 (m), 858.5 (m), 696.2 (m) cm^{-1}; HRMS-(DART) for: $C_{27}H_{45}B_2O_4$ $[M+H]^+$: calculated: 455.3504, found: 455.3518.

Analysis of stereochemistry:



Title compound was oxidized to (*S*)-3-hydroxy-1-phenylnonan-2-one (**S7**). Racemic compound was prepared according to the same procedure utilizing racemic 2,2',2''-(octane-1,1,2-triyl)tris (4,4,5,5-tetramethyl-1,3,2-dioxaborolane) and benzaldehyde. Further analysis of stereochemistry was performed on (*S*)-3-hydroxy-1-phenylnonan-2-one (**S7**). Absolute stereochemistry was assigned by analogy.

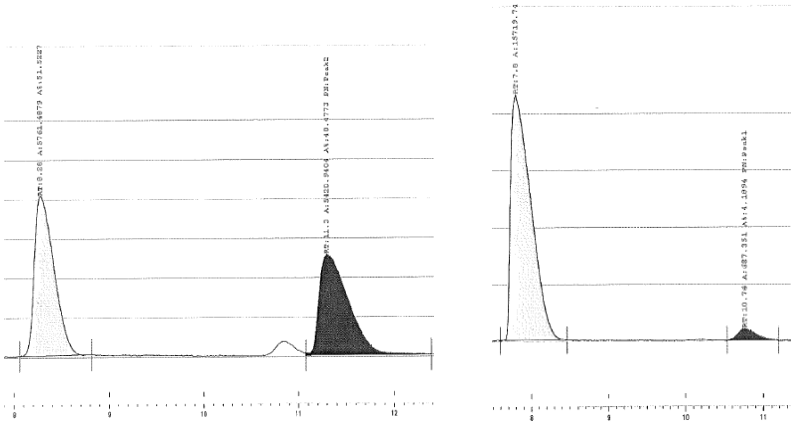


(*S*)-3-hydroxy-1-phenylnonan-2-one (S7). To a 6-dram vial equipped with a magnetic stir bar was added (*S,E*)-2,2'-(1-phenylnon-1-ene-2,3-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (35.0 mg, 0.077mmol), and THF (2.0 mL). The reaction mixture was cooled to 0 °C and pH 7.0 buffer (2.0 mL) was added, 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 18 hours. The reaction mixture was cooled to 0 °C and saturated aq. $Na_2S_2O_3$ (1.5 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. Purification by silica gel chromatography (5% ethyl acetate in hexane) gave the desired product as a colorless oil (13.6 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32(2H, tt, *J*= 7.0, 1.5 Hz), 7.26(1H, tt, *J*= 7.0, 1.5 Hz), 7.18(2H, d, *J*=8.5 Hz), 4.27(1H, dt, *J*=7.0, 3.5 Hz), 3.79(1H, d, *J*=15.5 Hz), 3.74(1H, d, *J*=15.5 Hz), 3.33(1H, d, *J*= 4.0 Hz), 1.88-1.82(1H, m), 1.60-1.53(1H, m), 1.40-1.21(8H, m), 0.87(3H, t, *J*= 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.0, 133.2, 129.6, 129.0, 127.5, 76.2, 45.1, 33.8, 31.8, 29.2, 24.9, 22.7, 14.2; IR (neat): 3470.6(br), 2953.6(m), 2925.1(m), 2856.0(m), 1709.7(s), 1495.6(m), 1454.4(m), 1060.8(m), 1043.9(m), 1031.6(m), 756.5(m), 723.7(m),

698.4(s) cm^{-1}; HRMS-(DART) for: $C_{15}H_{23}O_2$ $[M+H]^+$: calculated: 235.1698, found: 235.1701.

Chiral SFC (Chiracel AD-H, 3% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-3-hydroxy-1-phenylnonan-2-one

Racemic Material Standard Conditions

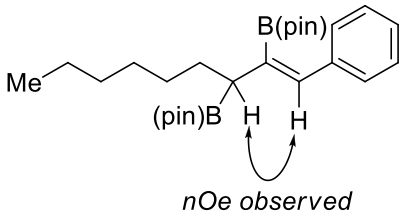


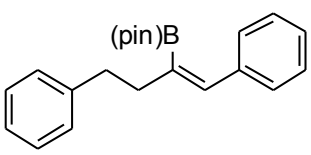
Peak No	% Area	Area	RT (min)
1	51.5227	5761.4879	8.28
2	48.4773	5420.9404	11.3
Total:	100	11182.4283	

Peak No	% Area	Area	RT (min)
1	95.331	14034.101	7.8
2	4.669	687.351	10.76
Total:	100	14721.452	

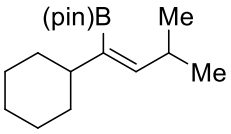
Determination of Stereochemistry:

The olefin geometry was determined by 2D NMR (NOESY).



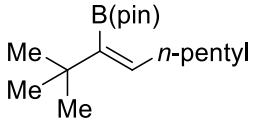


(*E*)-2-(1,4-diphenylbut-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxa-borolane (5.120). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), 2,2'-(3-phenylpropane -1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (112 mg, 0.300 mmol), benzaldehyde (26.5 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (75.0 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.34-7.15 (11H, m), 2.80 (2H, dd, *J*= 10.5, 7.0 Hz), 2.69 (2H, dd, *J*= 10.0, 7.5 Hz), 1.32 (12H, s); ^{13}C NMR (126 MHz, $CDCl_3$): δ (major isomer) 142.6, 142.4, 137.8, 128.8, 128.5, 128.2, 128.1, 127.1, 125.6, 83.4, 36.0, 31.3, 24.8; IR (neat): 3024.9 (w), 2976.9 (m), 2929.6 (w), 1616.4 (w), 1493.4 (m), 1446.3 (m), 1404.7 (s), 1371.4 (s), 1349.4 (s), 1210.9 (m), 1141.6 (s), 963.4 (m), 923.8 (m), 749.5 (s), 697.3 (s), 473.4 (w) cm^{-1}; HRMS-(DART) for: $C_{22}H_{28}B_1O_2$ $[M+H]^+$: calculated: 335.2182, found: 335.2197. (*Note: The olefin geometry was assigned based on analogy to compounds* ***5.114, 5.118, 5.119, and 5.124***.)

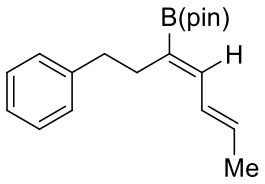


(*E*)-2-(1-cyclohexyl-3-methylbut-1-enyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.121). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), 2,2'-(cyclohexylmethylene)bis(4,4,5,5- tetramethyl-1,3,2-dioxaborolane) (105.0 mg, 0.300 mmol), isobutyraldehyde (18.0 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl

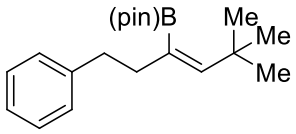
acetate/hexanes) to afford the desired product as a clear, colorless oil (59.3 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.55 (1H, d, *J*= 9.0 Hz), 2.69-2.76 (1H, m), 1.96 (1H, t, *J*= 12.0 Hz), 1.64-1.72 (4H, m), 1.27 (12H, m), 1.11-1.17 (2H, m), 0.93 (6H, d, *J*= 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.4, 83.0, 44.5, 33.5, 30.4, 27.0, 26.5, 25.0, 23.9; IR (neat): 2976.4 (m), 2922.7 (m), 2851.5 (m), 1404.0 (m), 1370.6 (m), 1346.0 (m), 1329.9 (m), 1256.8 (s), 983.8 (m), 714.3 (m) cm^{-1}; HRMS-(DART) for: $C_{17}H_{32}B_1O_2$ $[M+H]^+$: calculated: 279.2495, found: 279.2504. (*Note: The olefin geometry was assigned based on analogy to compounds* ***5.114, 5.118, 5.119, and 5.124***.)



(*E*)-2-(2,2-dimethylnon-3-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.122). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.300 mmol), 2,2'-(2,2-dimethylpropane-1,1-diyl) bis(4,4,5,5- tetramethyl-1,3,2-dioxaborolane) (97.2 mg, 0.300 mmol), hexanal (25.0 mg, 0.250 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (45.5 mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.78 (1H, t, *J*= 7.0 Hz), 2.07 (2H, q, *J*= 7.0 Hz), 1.22-1.36 (18H, m), 1.04 (9H, s), 0.86 (3H, t, *J*= 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.0, 83.3, 35.2, 32.2, 31.8, 30.6, 30.1, 25.2, 22.7, 14.3; IR (neat): 2956.9 (m), 2928.1 (m), 2860.3 (m), 1465.3 (m), 1413.1 (m), 1388.8 (s), 1370.9 (m), 1327.9 (s), 1290.8 (m), 1213.4 (s), 1108.6 (m), 862.4 (m) cm^{-1}; HRMS-(DART) for: $C_{17}H_{34}B_1O_2$ $[M+H]^+$: calculated: 281.2652, found: 281.2666. (*Note: The olefin geometry was assigned based on analogy to compounds* ***5.114, 5.118, 5.119, and 5.124***.)



4,4,5,5-tetramethyl-2-((3*Z*,5*E*)-1-phenylhepta-3,5-dien-3-yl)-1,3,2-dioxaborolane (5.123). Prepared according to the representative procedure utilizing LiTMP (44.2 mg, 0.3 mmol), 2,2'-(3-phenylpropane-1,1-diyl) bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (111.6 mg, 0.3 mmol), (*E*)-but-2-enal (17.5 mg, 0.25 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (70.2 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (major isomer) 7.16-7.30 (5H, m), 6.78 (1H, d, *J*= 11.0 Hz), 6.36-6.41 (1H, m), 5.89 (1H, dq, *J*= 14.0 Hz, 7.0 Hz), 2.69 (2H, t, *J*= 7.0 Hz), 2.56 (2H, t, *J*= 7.0 Hz), 1.80 (3H, d, *J*= 7.0 Hz), 1.25 (12H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.5, 142.8, 134.0, 128.8, 128.3, 127.7, 125.7, 83.3, 36.8, 31.0, 25.0, 18.8; IR (neat): 2976.8 (m), 2930.6 (m), 1640.8 (m), 1594.1 (m), 1406.8 (m), 1379.5 (m), 1371.3 (s), 1345.1 (s), 1301.2 (m), 1213.8 (s), 866.8 (m), 856.1 (m), 675.2 (m) cm^{-1}; HRMS-(DART) for: $C_{19}H_{28}B_1O_2$ $[M+H]^+$: calculated: 299.2182, found: 299.2183. (*Note: The olefin geometry was assigned based on analogy to compounds* ***5.114, 5.118, 5.119, and 5.124***.)

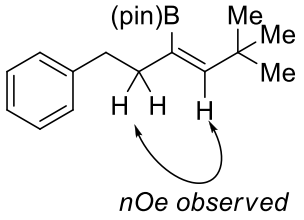


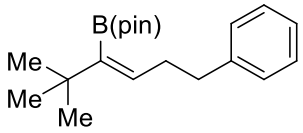
(*E*)-2-(5,5-dimethyl-1-phenylhex-3-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.124). Prepared according to the representative procedure utilizing LiTMP (35.4 mg, 0.240 mmol), 2,2'-(3-phenylpropane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (89.3 mg, 0.240 mmol), pivalaldehyde (17.2 mg, 0.200 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (54.5 mg, 87%). ^{1}H

NMR (500 MHz, $CDCl_3$): δ 7.22-7.26 (2H, m), 7.12-7.16 (3H, m), 5.74 (1H, s), 2.66 (2H, t, *J*= 8.0 Hz), 2.33 (2H, t, *J*= 8.0 Hz), 1.30 (12H, s), 1.03 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.6, 142.7, 128.8, 128.3, 125.7, 83.6, 40.7, 36.9, 34.1, 30.6, 25.0; IR (neat): 2977.2 (m), 2951.9 (m), 1453.7 (m), 1406.6 (m), 1371.0 (s), 1330.8 (m), 1270.2 (m), 1205.5 (s), 1141.1 (m), 965.0 (m), 860.7 (m), 697.9 (m) cm^{-1}; HRMS-(DART) for: $C_{20}H_{32}B_1O_2$ $[M+H]^+$: calculated: 315.2495, found: 315.2511.

Determination of Stereochemistry:

The olefin geometry was determined by 2D NMR (NOESY).

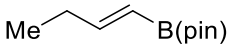




(*E*)-2-(2,2-dimethyl-6-phenylhex-3-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.125). Prepared according to the representative procedure utilizing LiTMP (35.4 mg, 0.240 mmol), 2,2'-(2,2-dimethylpropane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (77.8 mg, 0.240 mmol), 3-phenylpropanal (26.8 mg, 0.200 mmol), and THF (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (2% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (55.2 mg, 88%). ^1H NMR (500 MHz, $CDCl_3$): δ 7.23-7.26 (2H, m), 7.13-7.17 (3H, m), 5.86 (1H, t, *J*= 8.0 Hz), 2.65 (2H, t, *J*= 8.0 Hz), 2.40 (2H, q, *J*= 8.0 Hz), 1.28 (12H, s), 1.05 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.5, 135.1, 128.6, 128.4, 125.8, 83.3, 37.0, 35.4, 34.2,

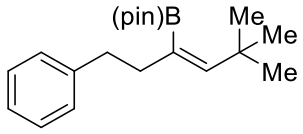
30.5, 25.2; IR (neat): 2976.6 (m), 2950.0 (m), 1454.0 (m), 1412.9 (m), 1388.7 (m), 1378.9 (m), 1325.3 (s), 1291.3 (m), 1268.1 (m), 1141.8 (s), 1108.6 (m), 974.1 (m), 697.8 (m) cm^{-1}; HRMS-(DART) for: $C_{20}H_{32}B_1O_2$ $[M+H]^+$: calculated: 315.2495, found: 315.2506. (*Note: The olefin geometry was assigned based on analogy to compounds* ***5.114, 5.118, 5.119, and 5.124***.)

5.5.2.9. Gram-scale synthesis of vinyl boronates



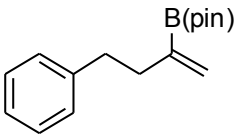
(*E*)-2-(but-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.126). To an oven-dried 250 mL round-bottomed flask equipped with a stirbar was added lithium tetramethylpiperidide (LiTMP, 2.33 g, 15.8 mmol), and the flask was sealed and brought out of the glovebox. To the reaction flask was added THF (40 mL), and the solution was cooled in an ice bath to 0 °C. Once the solution was cooled, a solution of 4,4,5,5-tetramethyl-2-((4,4,5,5-tetramethyl-1,3-dioxolan-2-yl)methyl)-1,3,2-dioxaborolane (3.85 g, 14.4 mmol) in THF (17 mL) was added dropwise, and the reaction mixture was allowed to stir at 0 °C for 5 minutes. Next, propionaldehyde (1.13 mL, 15.8 mmol) was added dropwise at 0 °C, and the mixture was allowed to stir at this temperature for an additional 3 hours. After completion, the reaction mixture was warmed to room temperature, diluted with diethyl ether (50 mL) and run through a pad of silica gel (100% diethyl ether). The resulting mixture was concentrated under reduced pressure and purified using silica gel comlumn chromatography (2.5% ethyl acetate/hexane) to provide the title compound as a clear, colorless oil as a 97:3 mixture of

E:Z isomers (1.99 g, 76%). All spectral data are in accord with the literature.[48] Note: The addition of propionaldehyde can also be performed at -78 °C to provide higher *E*:Z ratios (99:1).



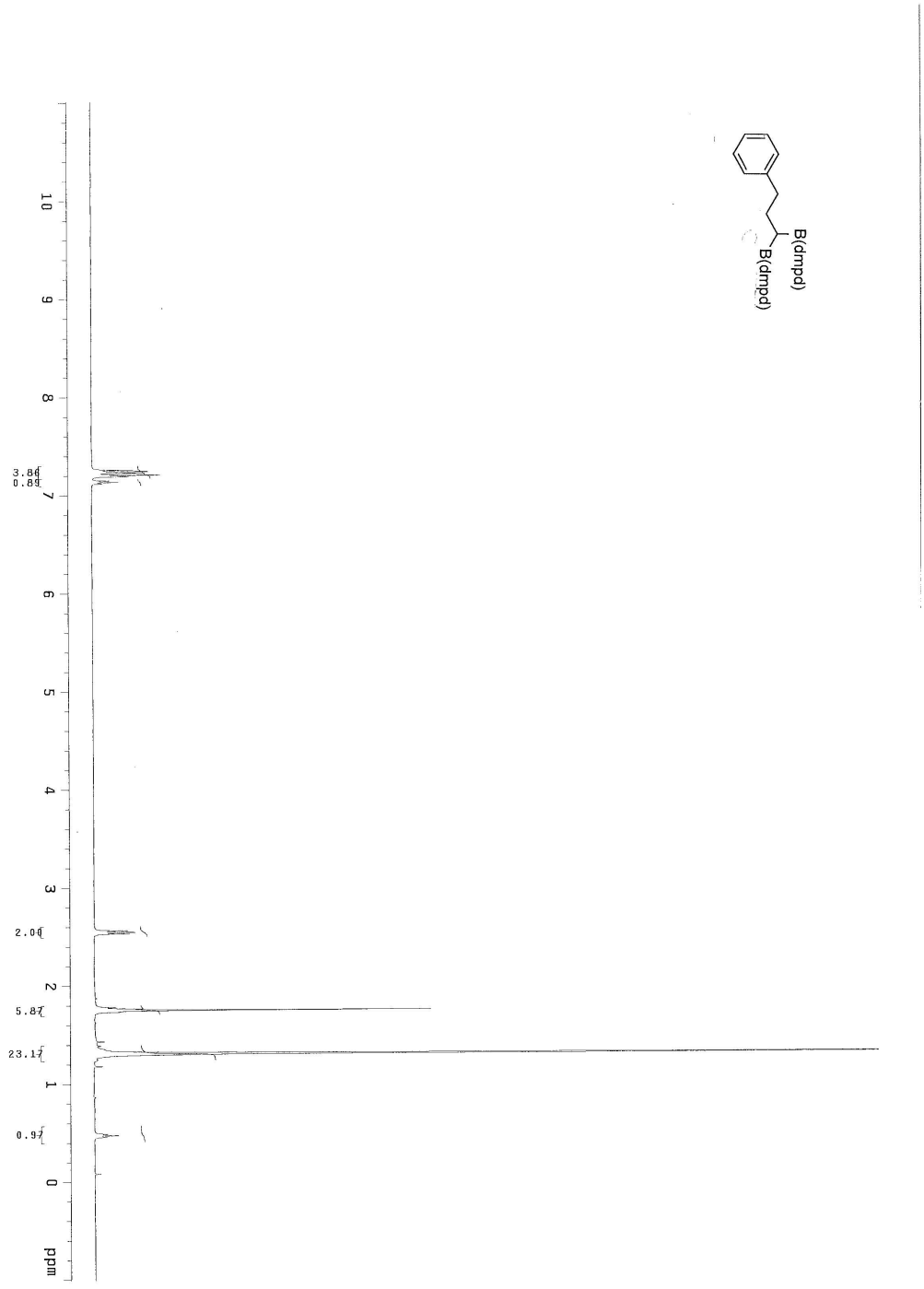
(*E*)-2-(5,5-dimethyl-1-phenylhex-3-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.124). To an oven-dried 50 mL round-bottomed flask equipped with a stirbar was added lithium tetramethylpiperidide (LiTMP, 972 mg, 6.60 mmol), and the flask was sealed and brought out of the glovebox. To the reaction flask was added THF (15 mL), and the solution was cooled in an ice bath to 0 °C. Once the solution was cooled, a solution of 2,2'-(3-phenylpropane-1,1-diyl)bis(4,4,5,5- tetramethyl-1,3,2-dioxaborolane) (2.23 g, 6.00 mmol) in THF (5.0 mL) was added dropwise, and the reaction mixture was allowed to stir at 0 °C for 5 minutes. Next, the reaction mixture was cooled to -78 °C, and pivaldehyde (569 mg, 6.60 mmol) was added dropwise. The reaction mixture was allowed to stir at -78 °C for 4 hours. After completion, the reaction mixture was warmed to room temperature, diluted with diethyl ether (50 mL) and run through a pad of silica gel (100% diethyl ether). The resulting mixture was concentrated under reduced pressure and purified using silica gel column chromatography (2 % ethyl acetate/hexane) to provide the title compound as a clear, colorless oil (1.78 g, 95%).

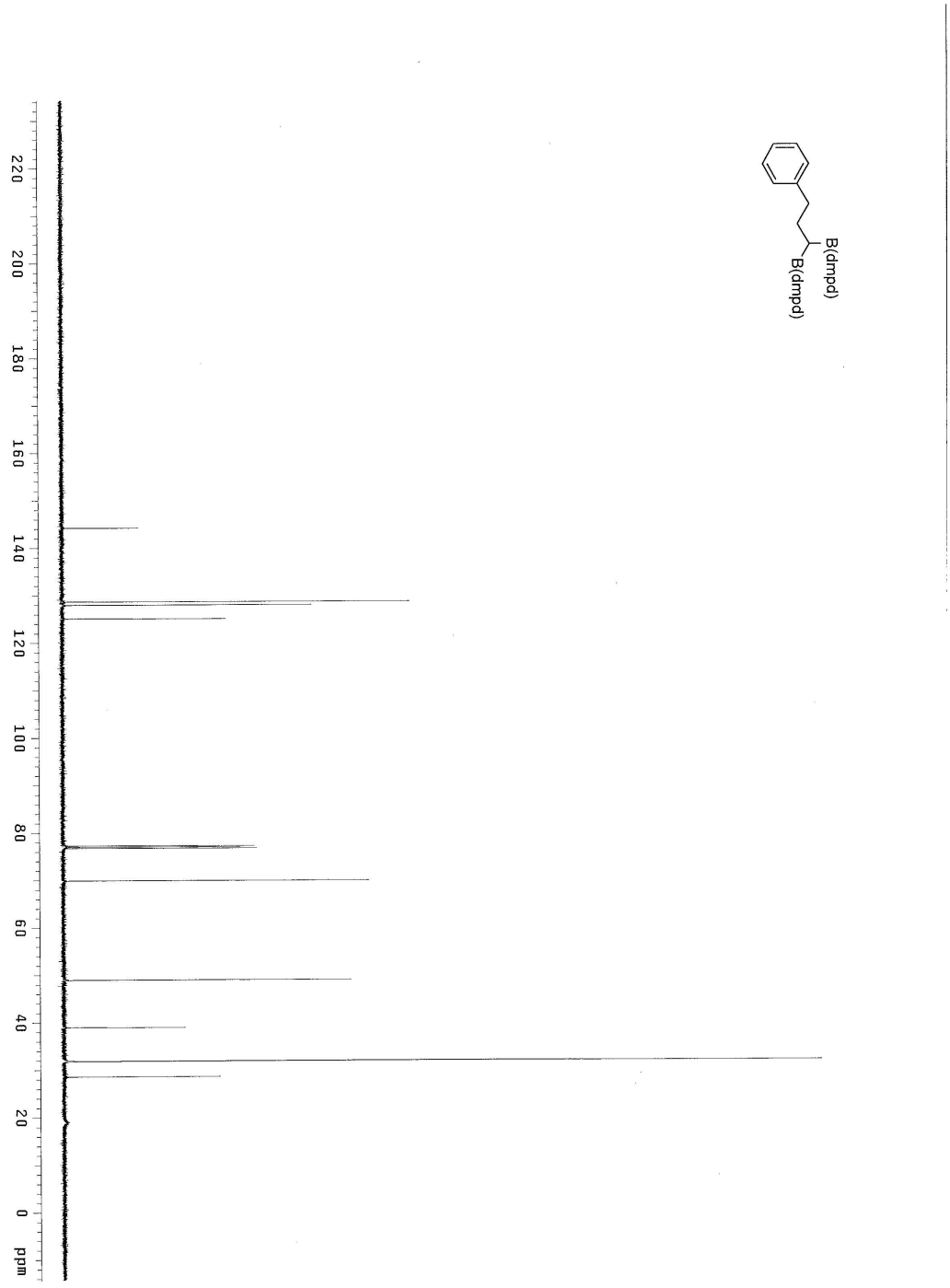
[48] Bruckner, R.; Burghart-Stoll, H. *Org. Lett.* **2011**, *13*, 2730.



4,4,5,5-tetramethyl-2-(4-phenylbut-1-en-2-yl)-1,3,2-dioxaborolane (5.95). To an oven-dried 100 mL round-bottomed flask equipped with a stirbar was added lithium tetramethylpiperidide (LiTMP, 971 mg, 6.60 mmol), and the flask was sealed and brought out of the glovebox. To the reaction flask was added THF (10 mL), and the solution was cooled in an ice bath to 0 °C. Once the solution was cooled, a solution of 2,2'-(3-phenylpropane -1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.23 g, 6.00 mmol) in THF (15 mL) was added dropwise, and the reaction mixture was allowed to stir at 0 °C for 5 minutes. Next, diiodomethane (3.23 g, 12.0 mmol) in THF (5.0 mL) was added dropwise at 0 °C, and the mixture was allowed to stir at this temperature for an additional 15 minutes. Next, the reaction mixture was allowed to warm to 60 °C and stir for 2 hours. After completion, the reaction mixture was cooled to room temperature, diluted with diethyl ether (50 mL) and run through a pad of silica gel (100% diethyl ether). The resulting mixture was concentrated under reduced pressure and purified using silica gel comlumn chromatography (2 % ethyl acetate/hexane) to provide the title compound as a clear, colorless oil (1.28 g, 83%). All spectral data are in accord with the literature.

5.5.3. NMR spectra of representative compounds

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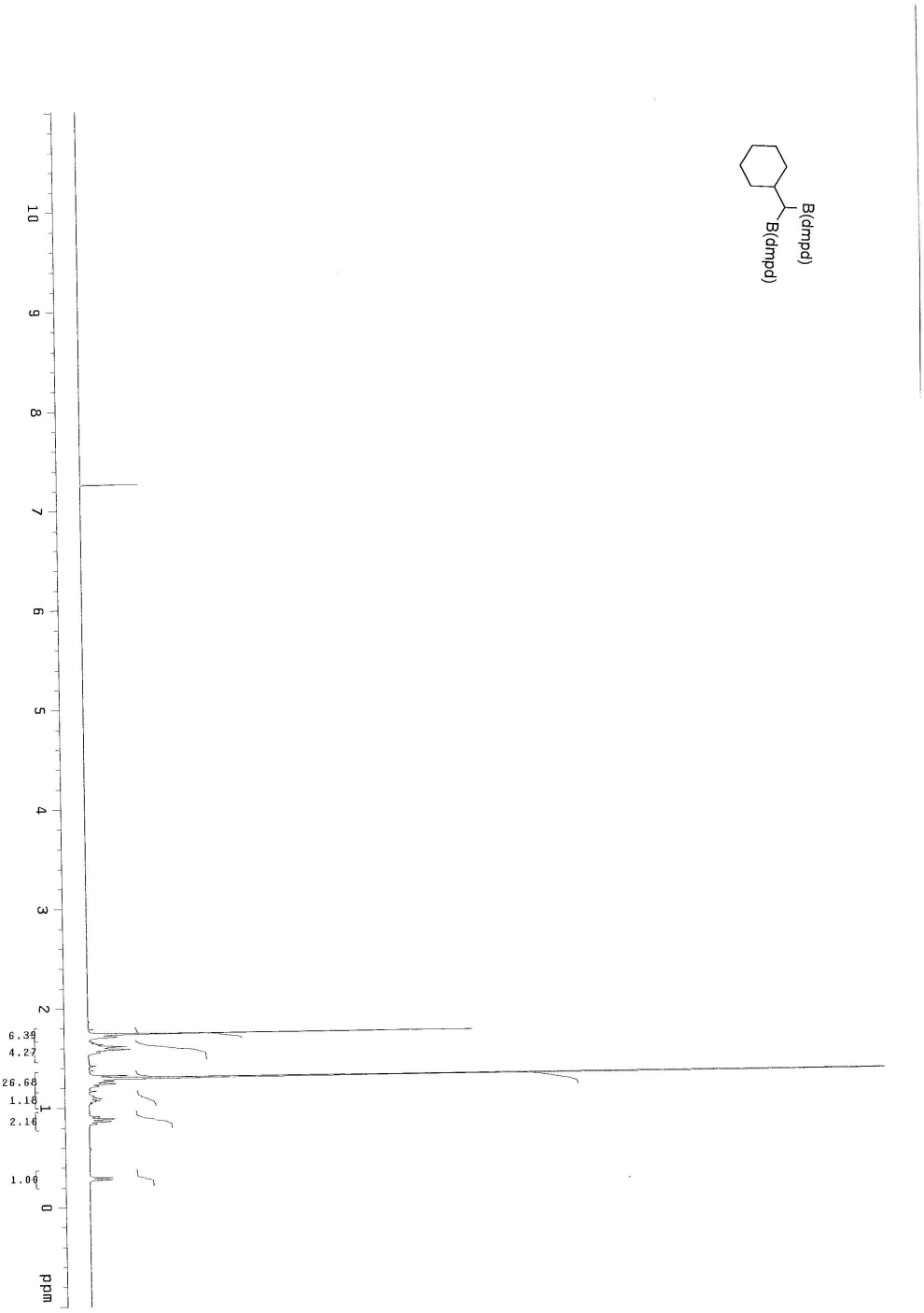
80
60
40
20
0
ppm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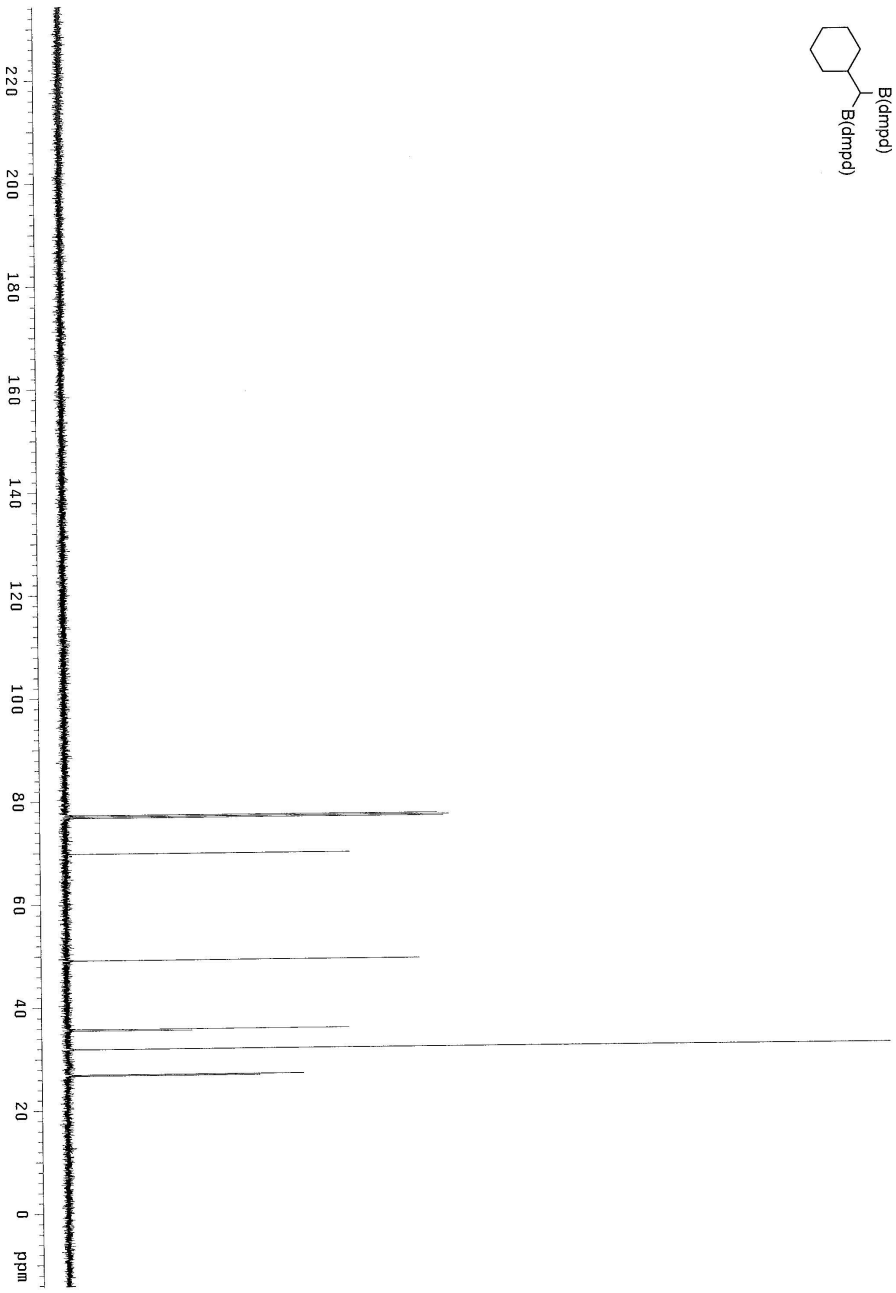
1.00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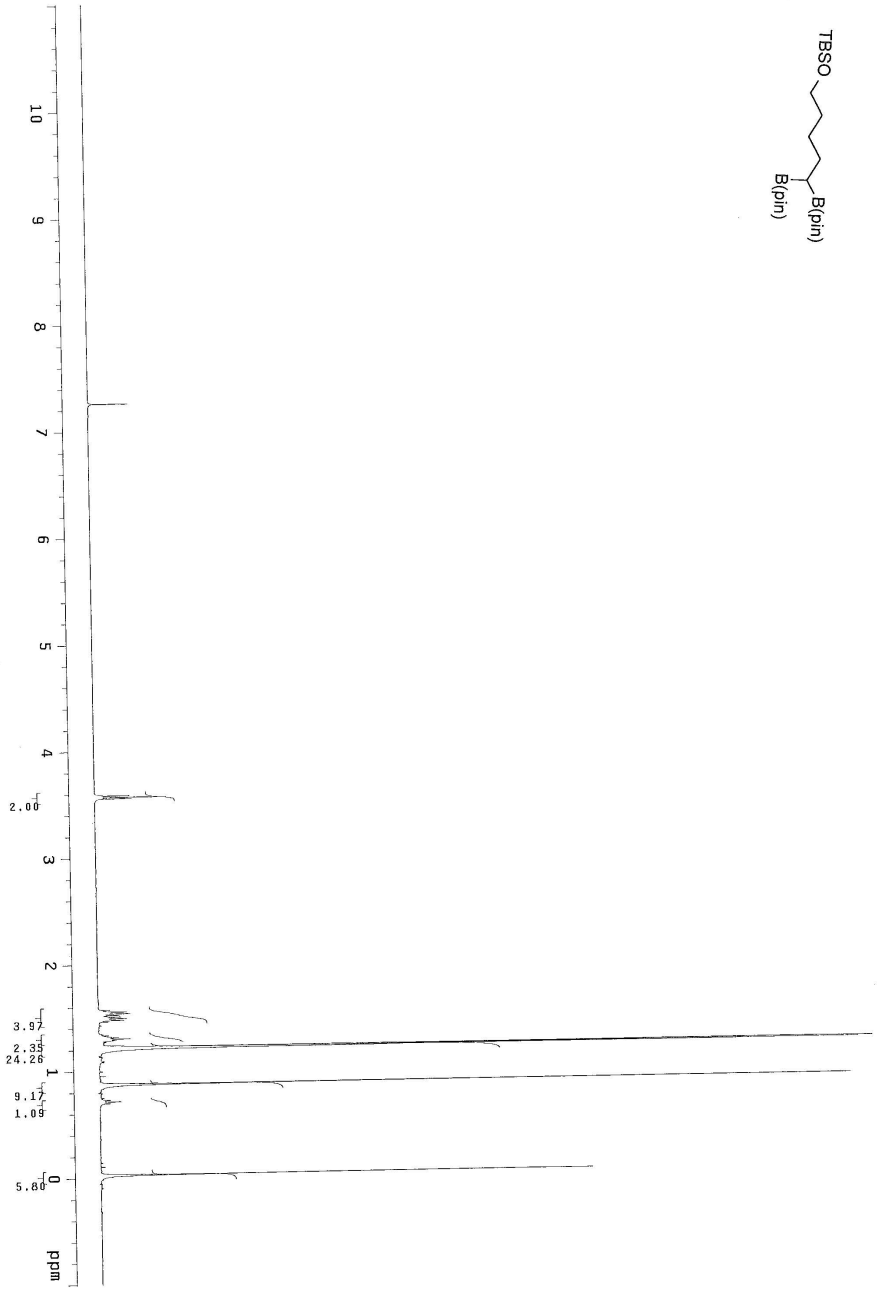
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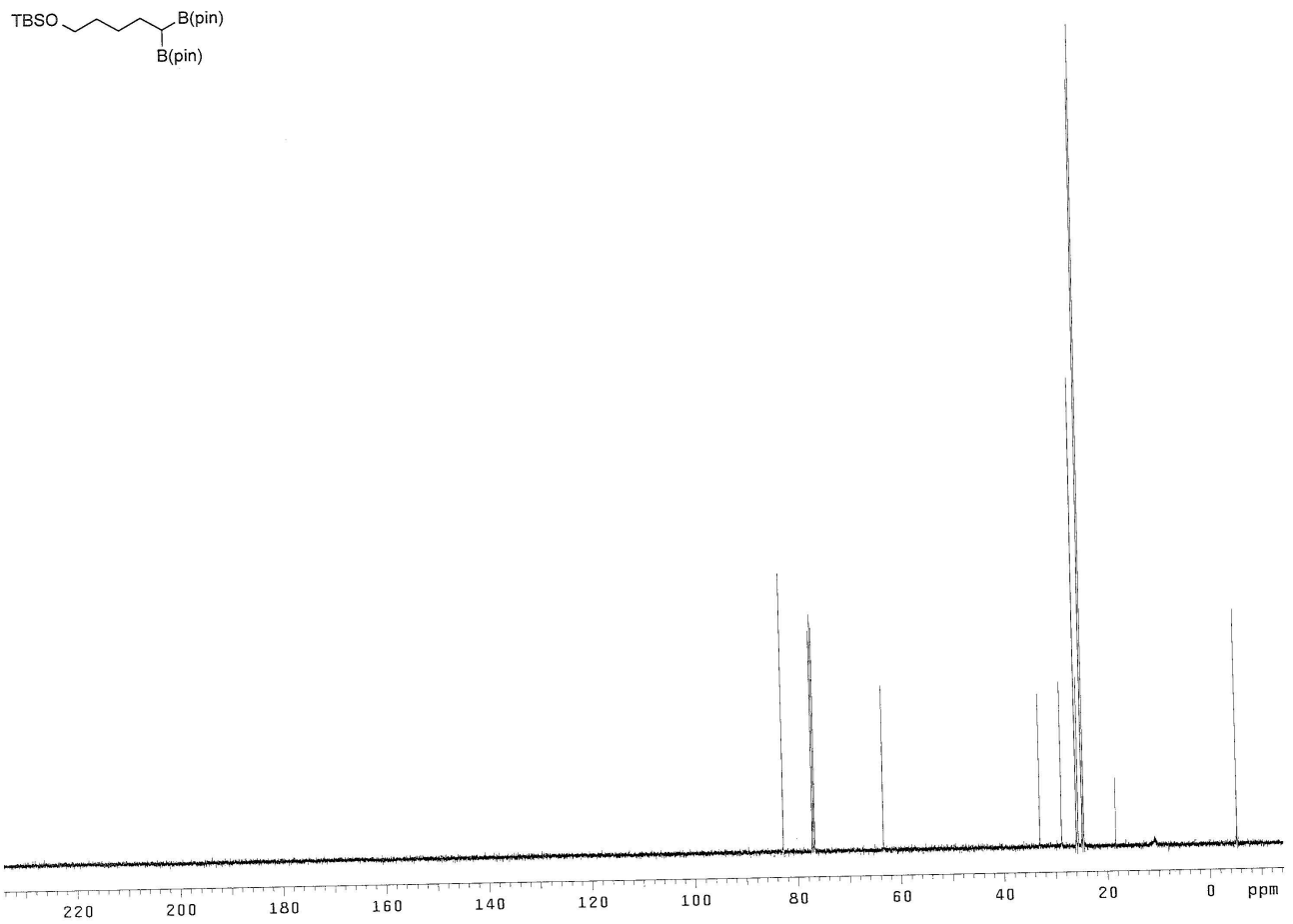
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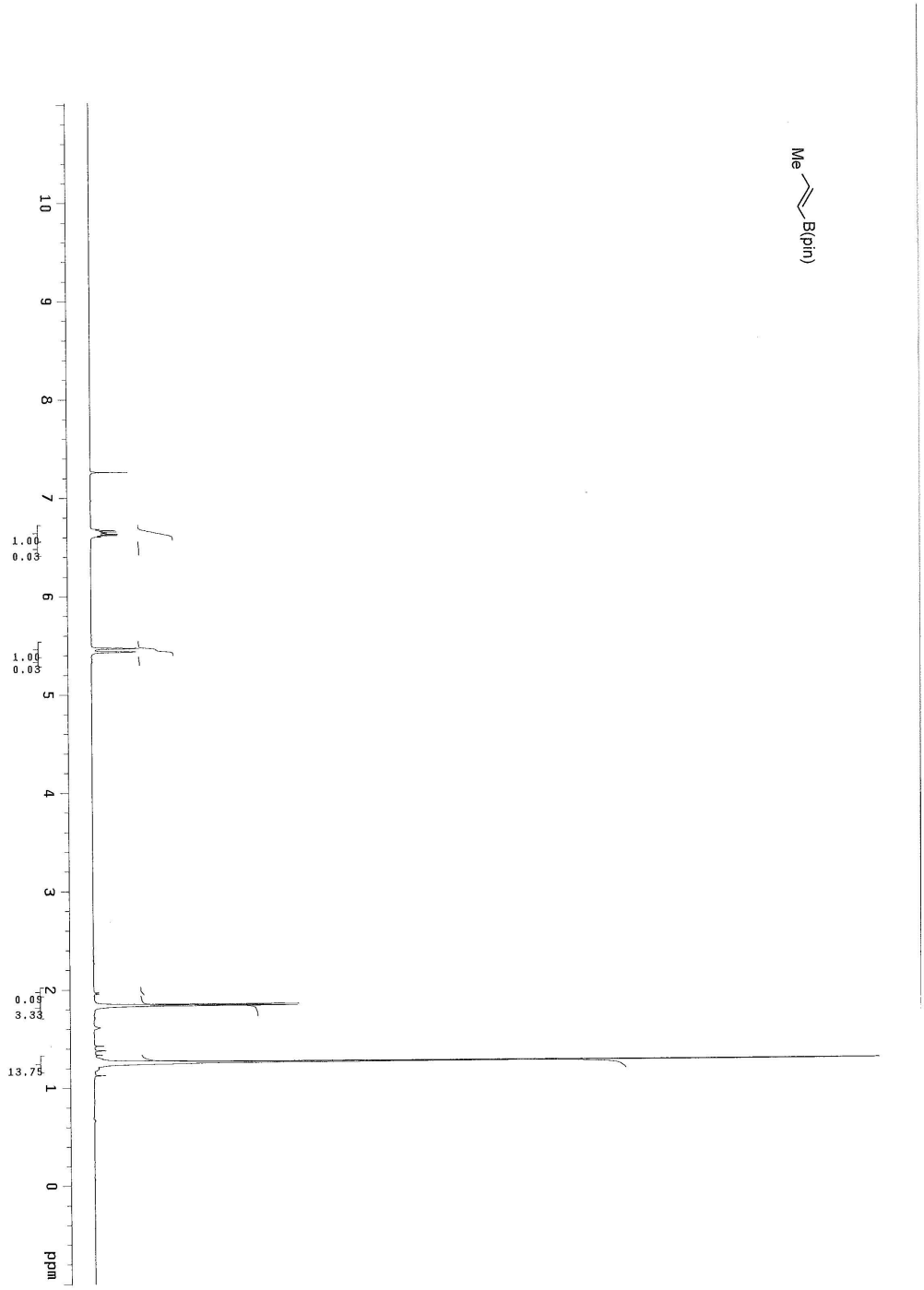
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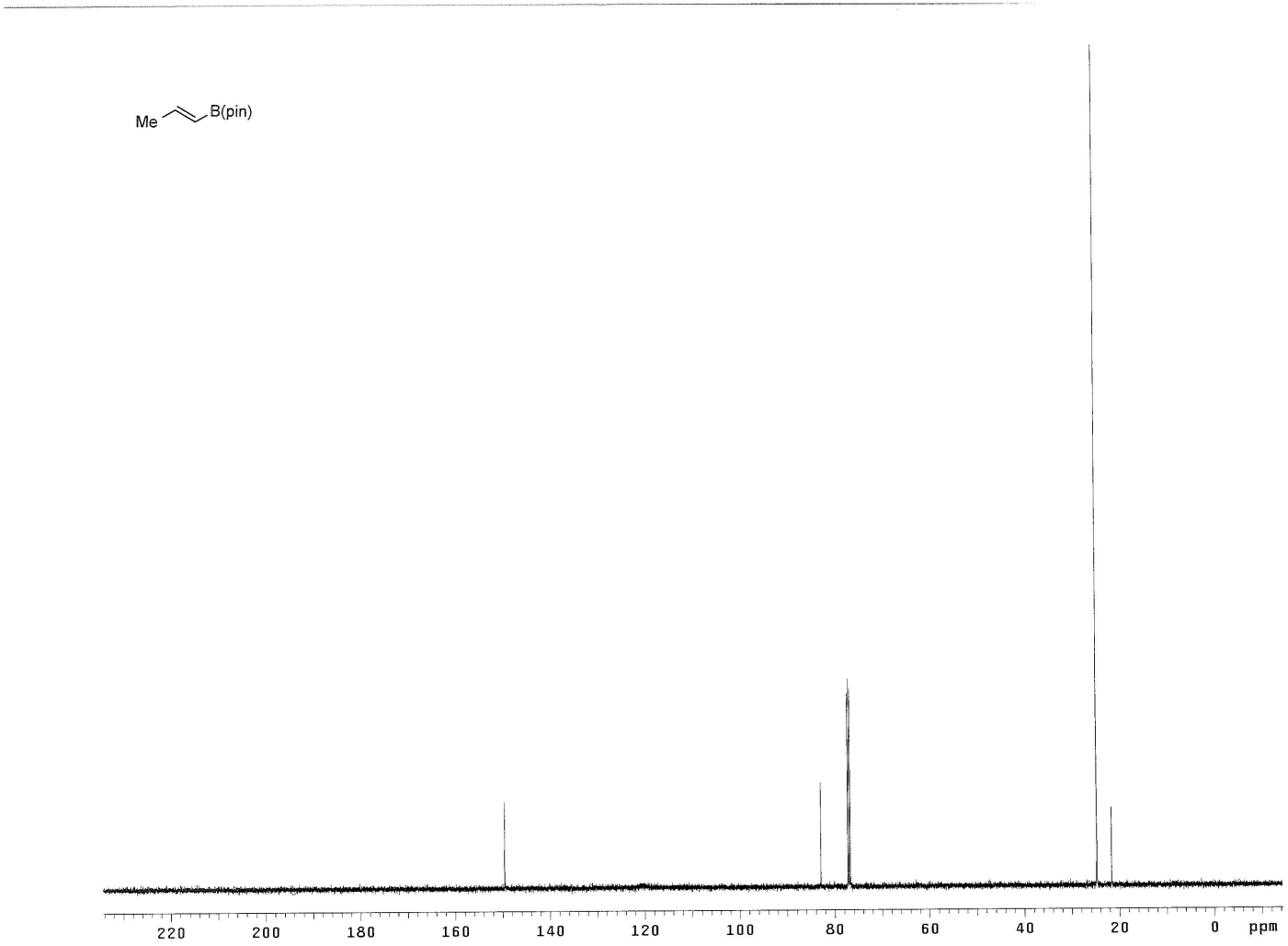
13.75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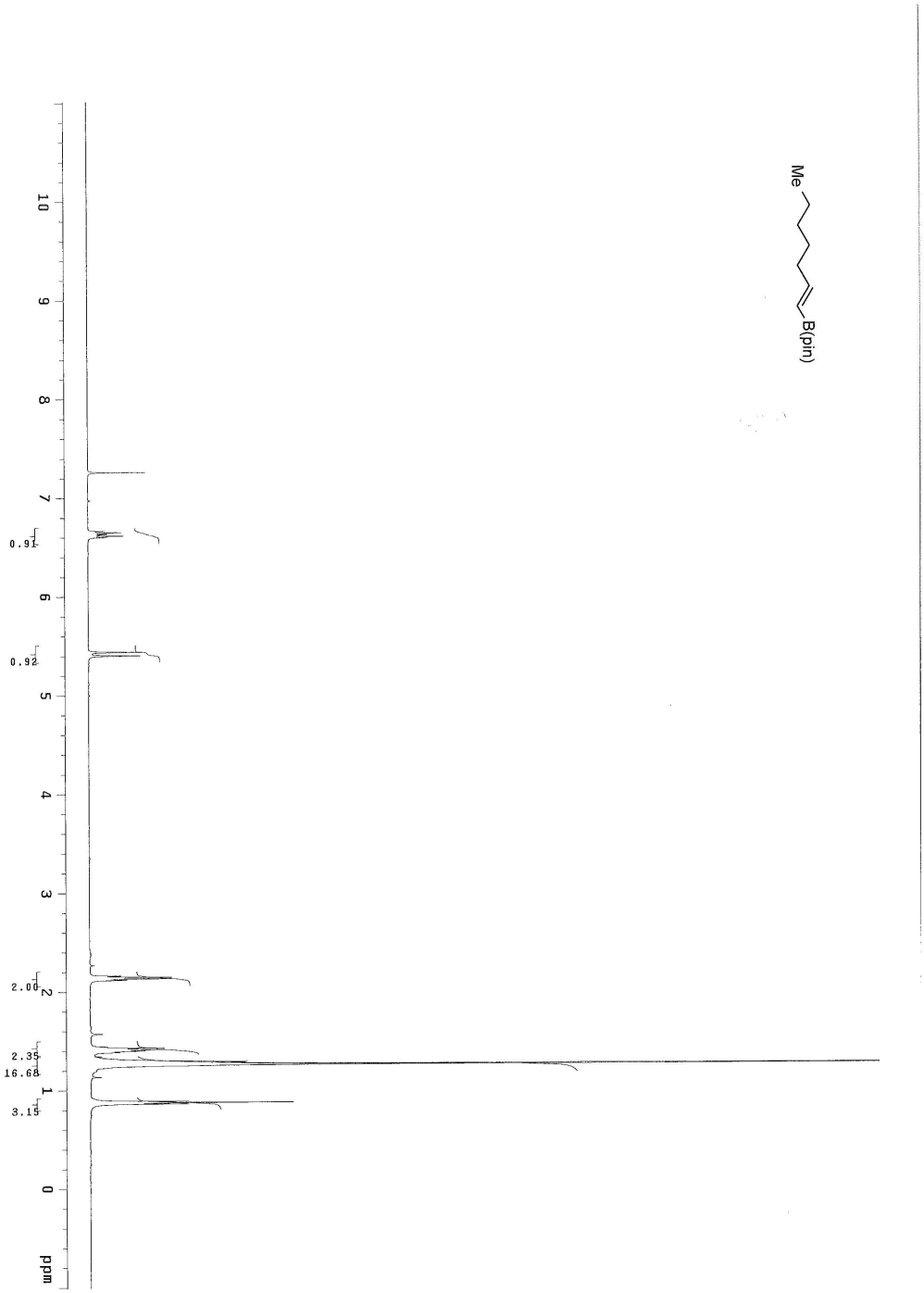
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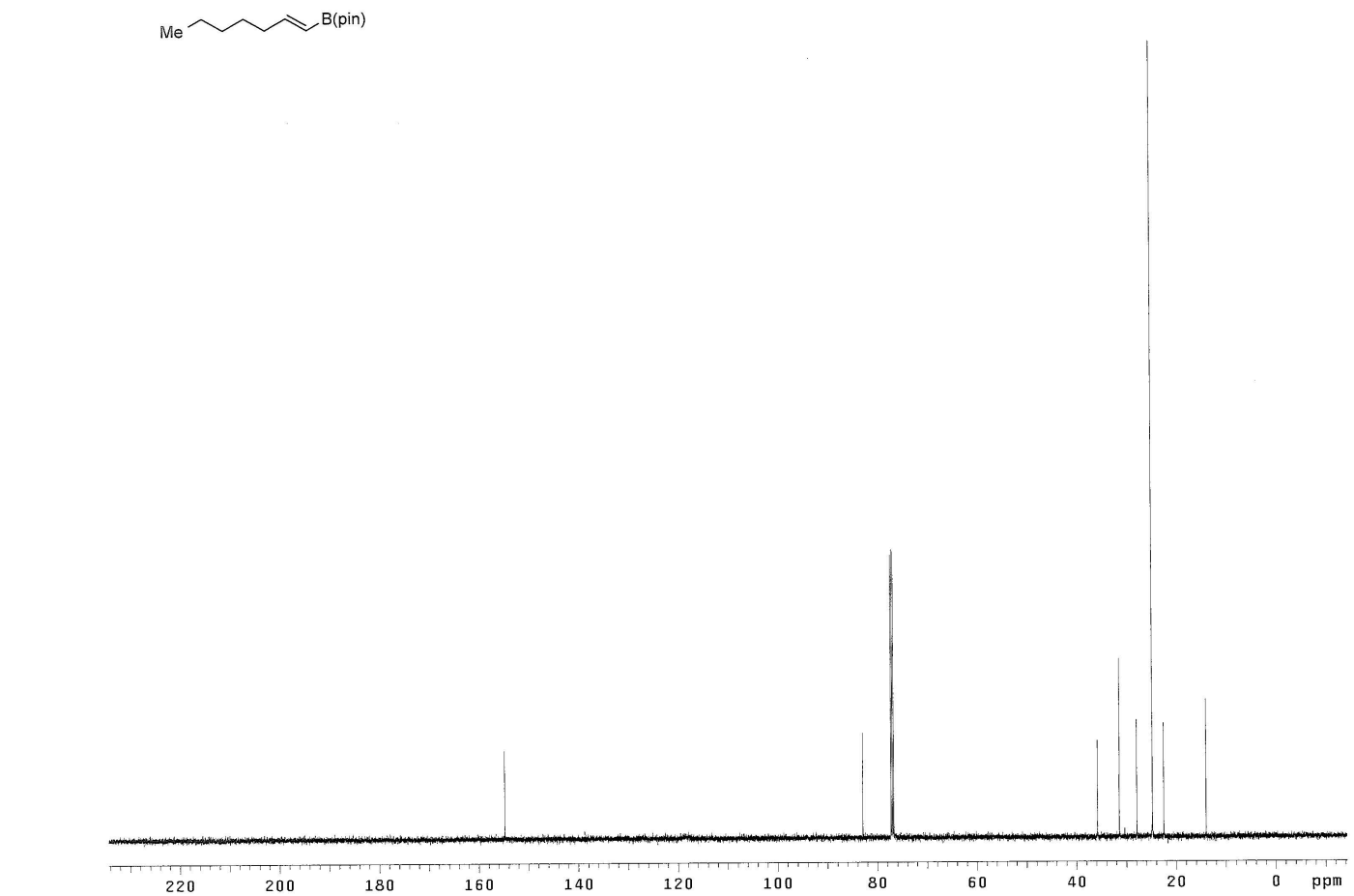
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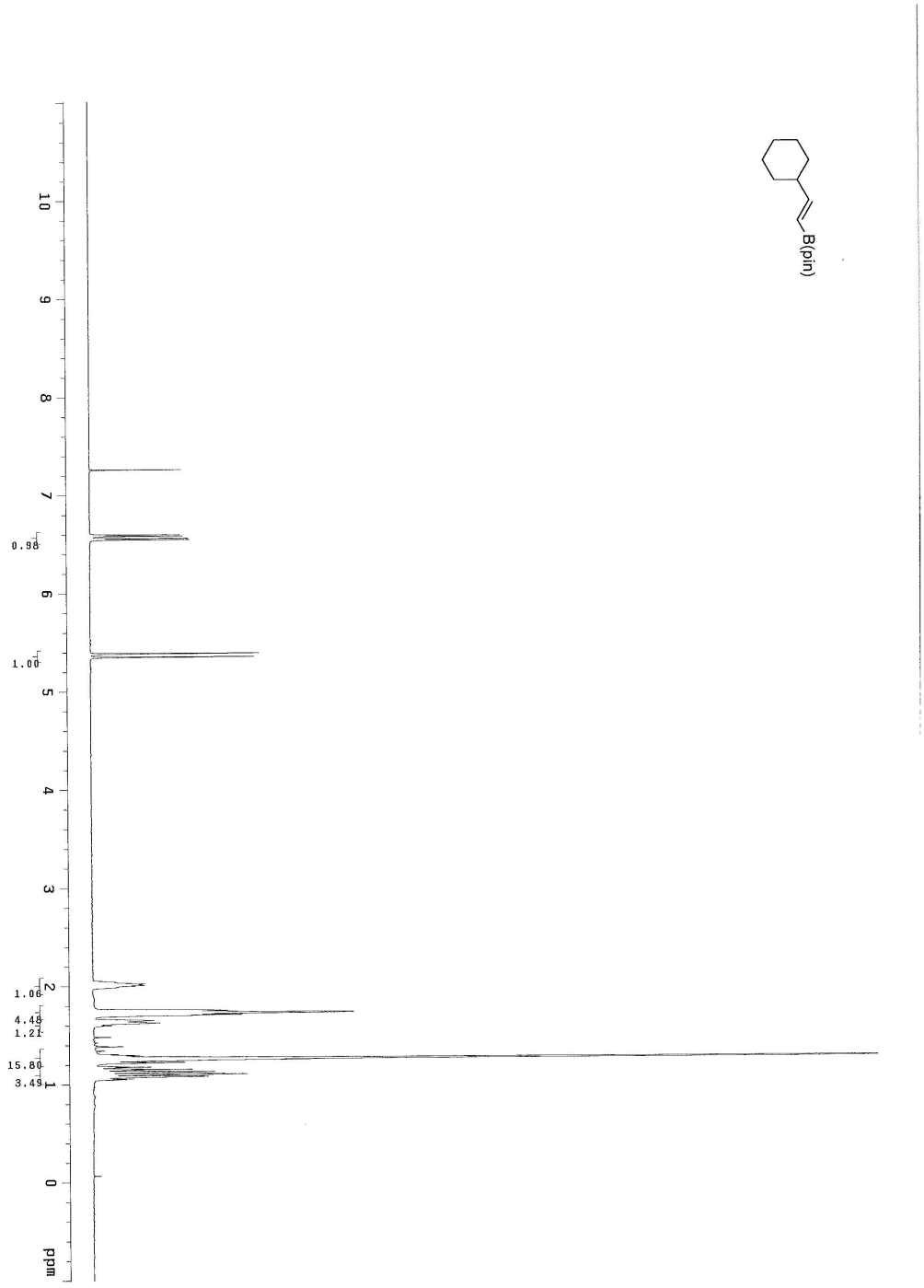
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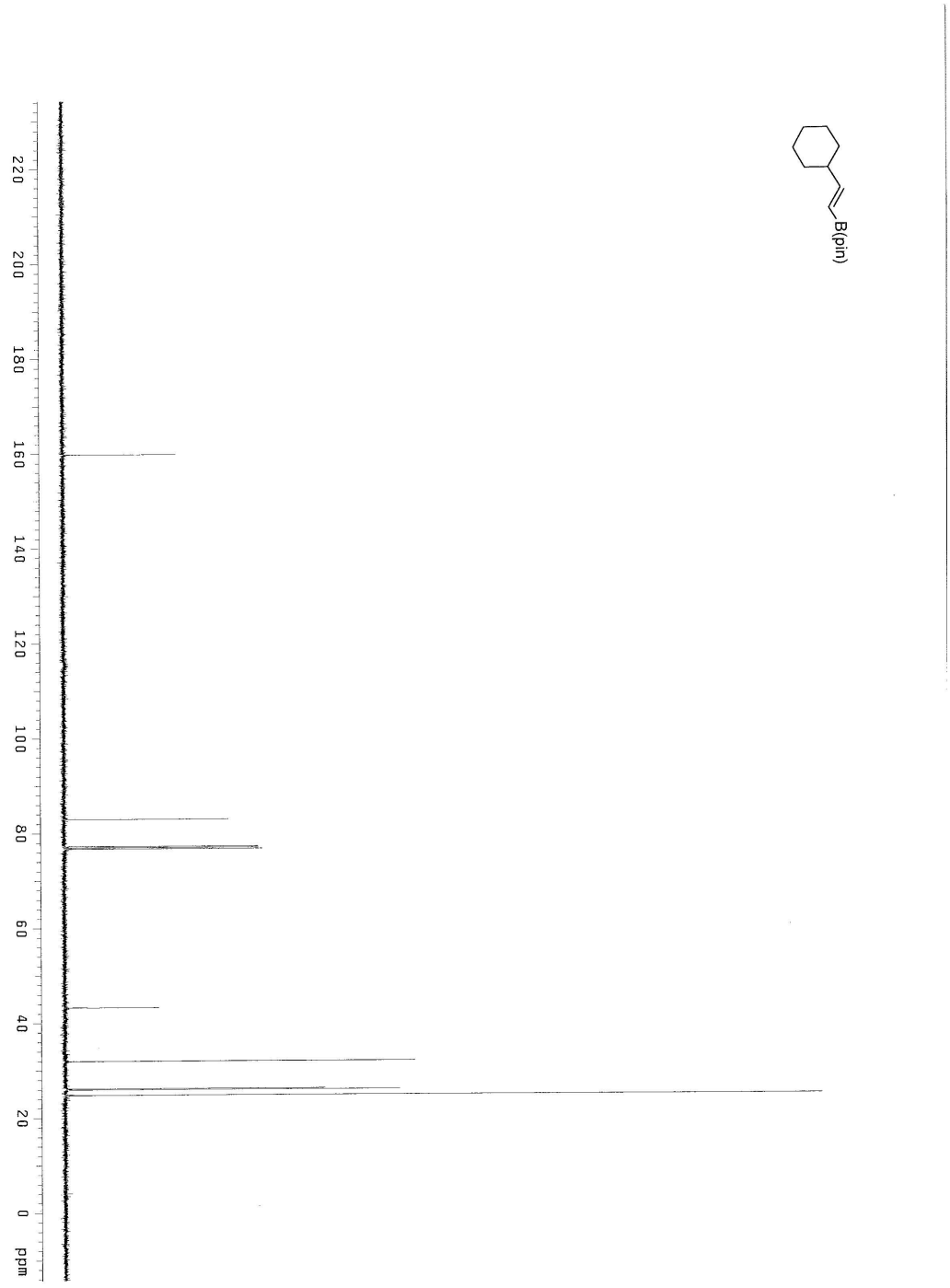
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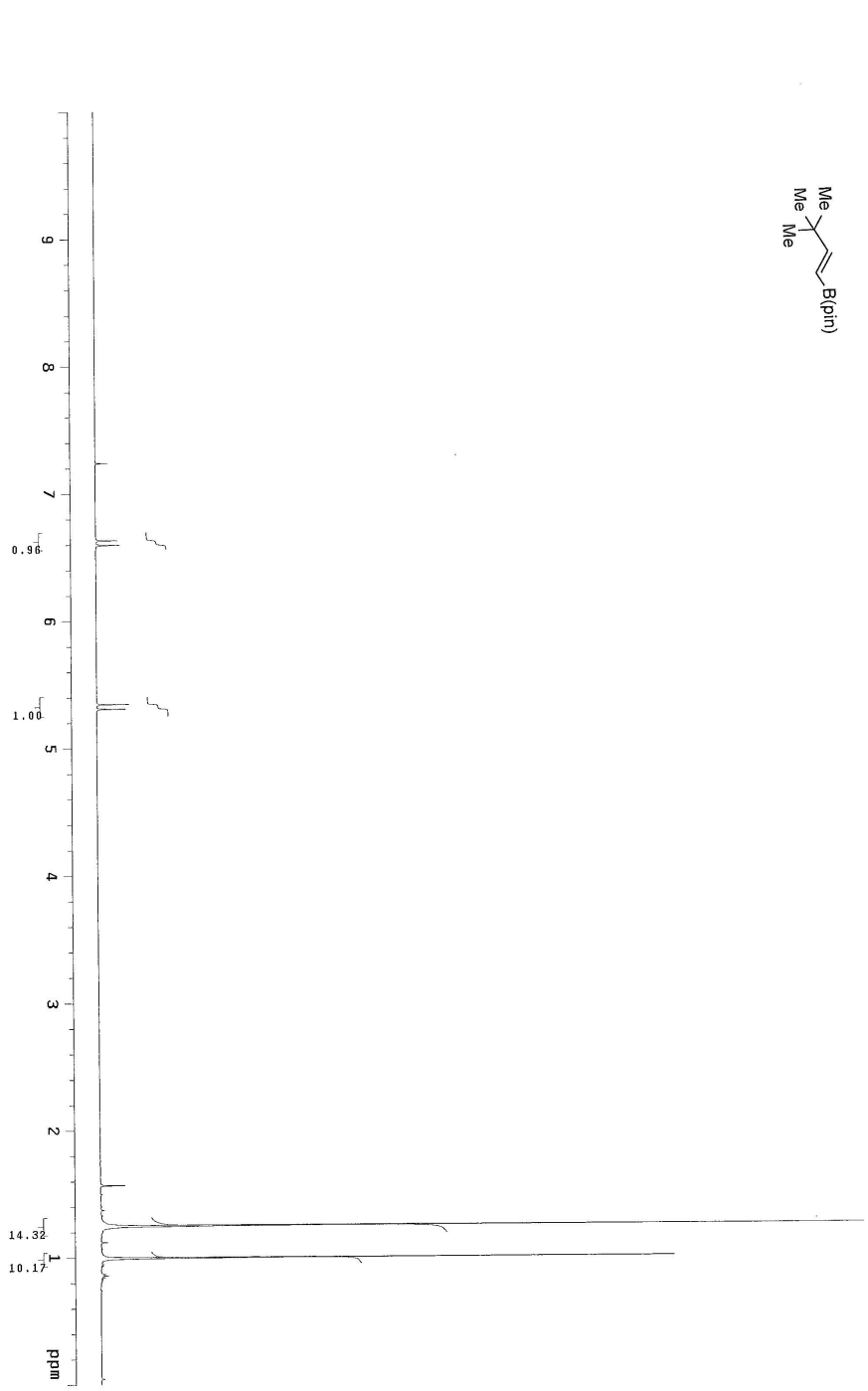
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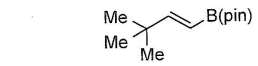
Me
Me
Me
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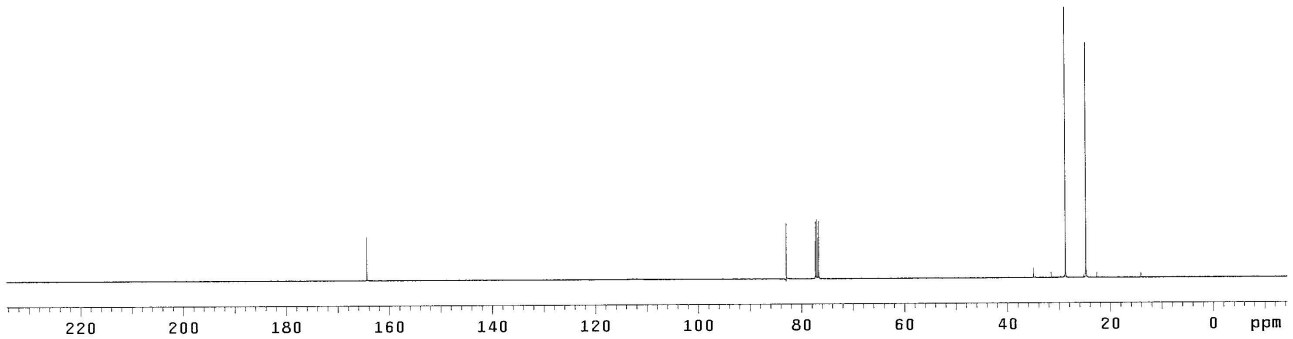
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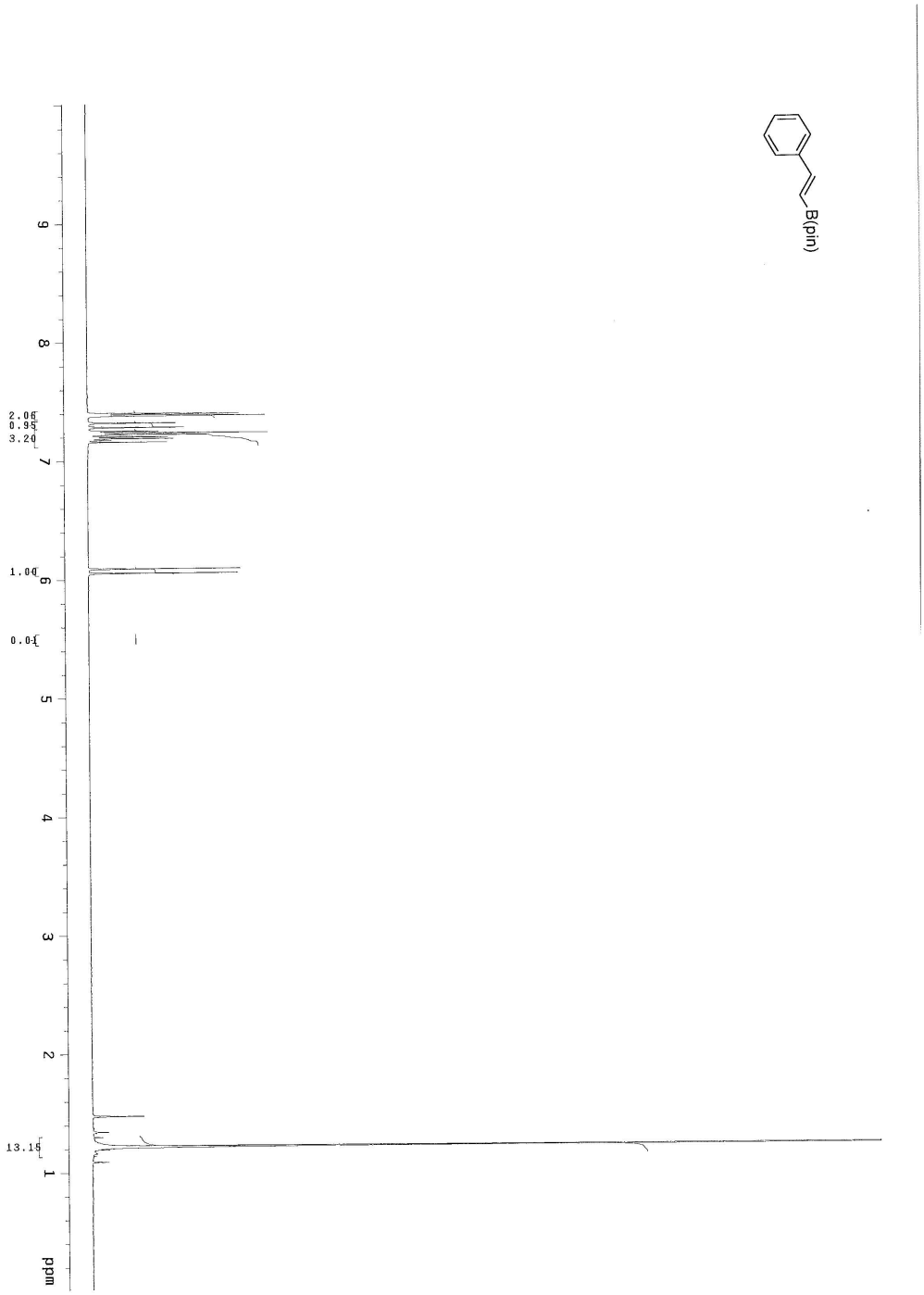
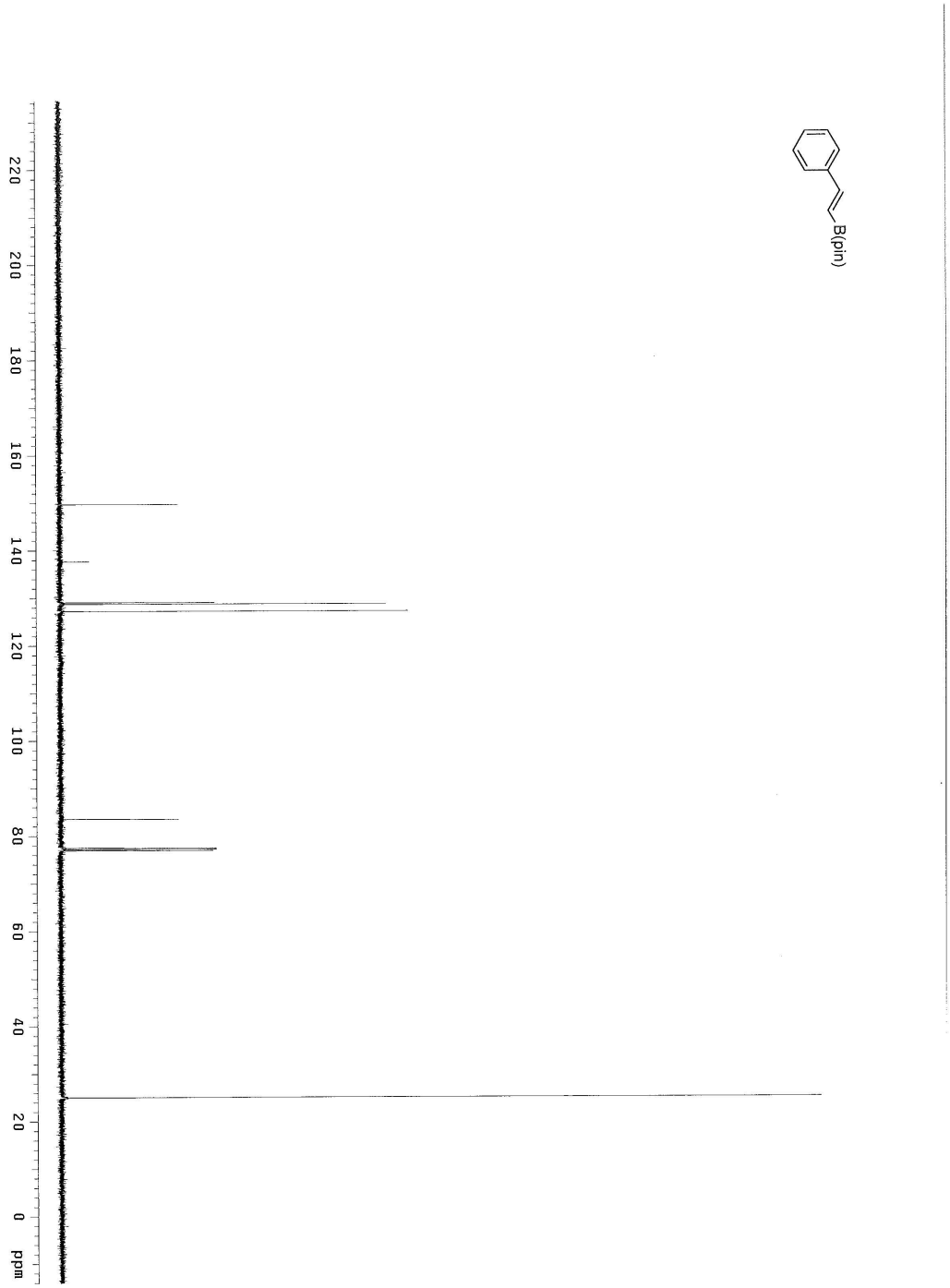
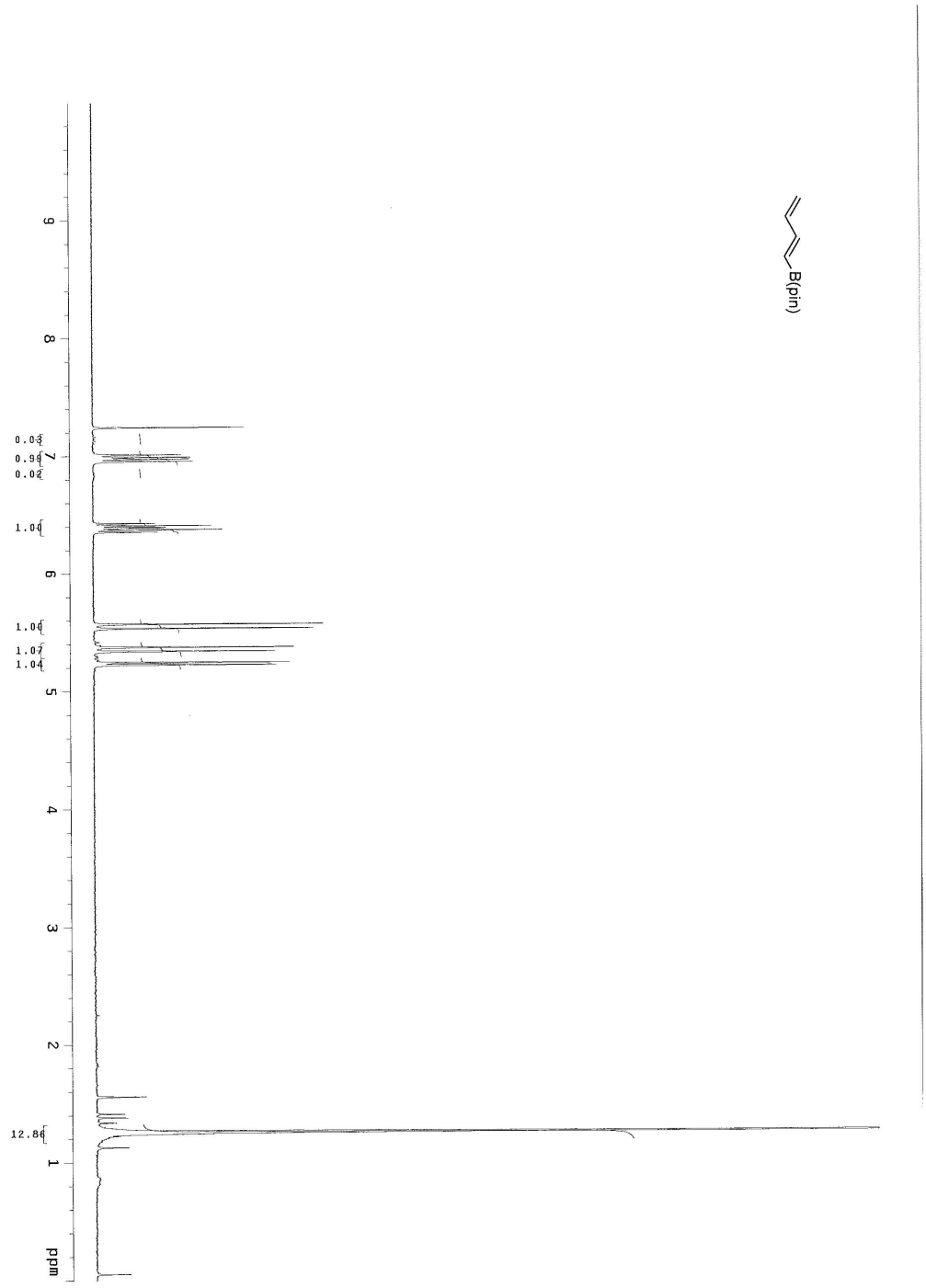
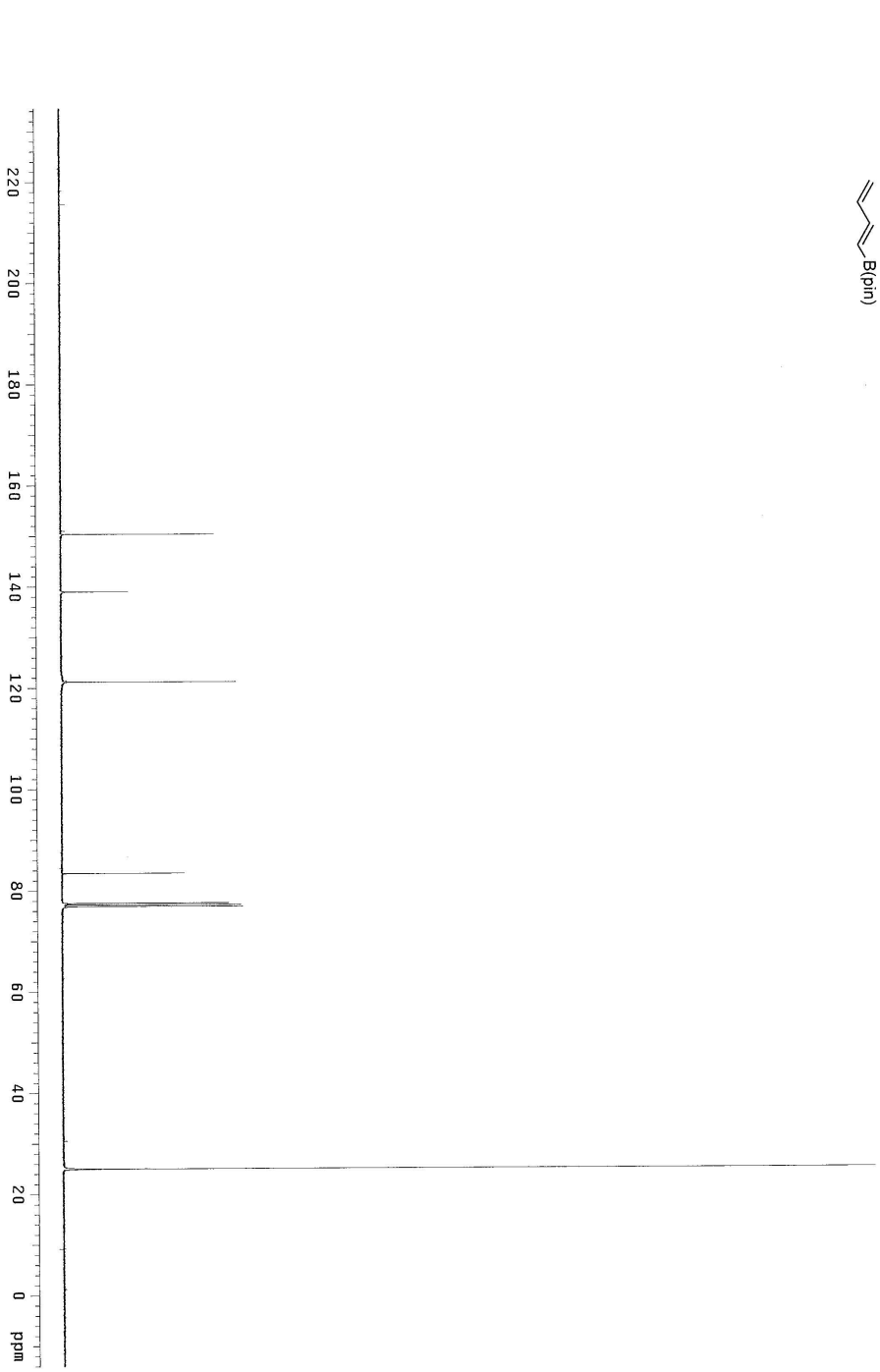
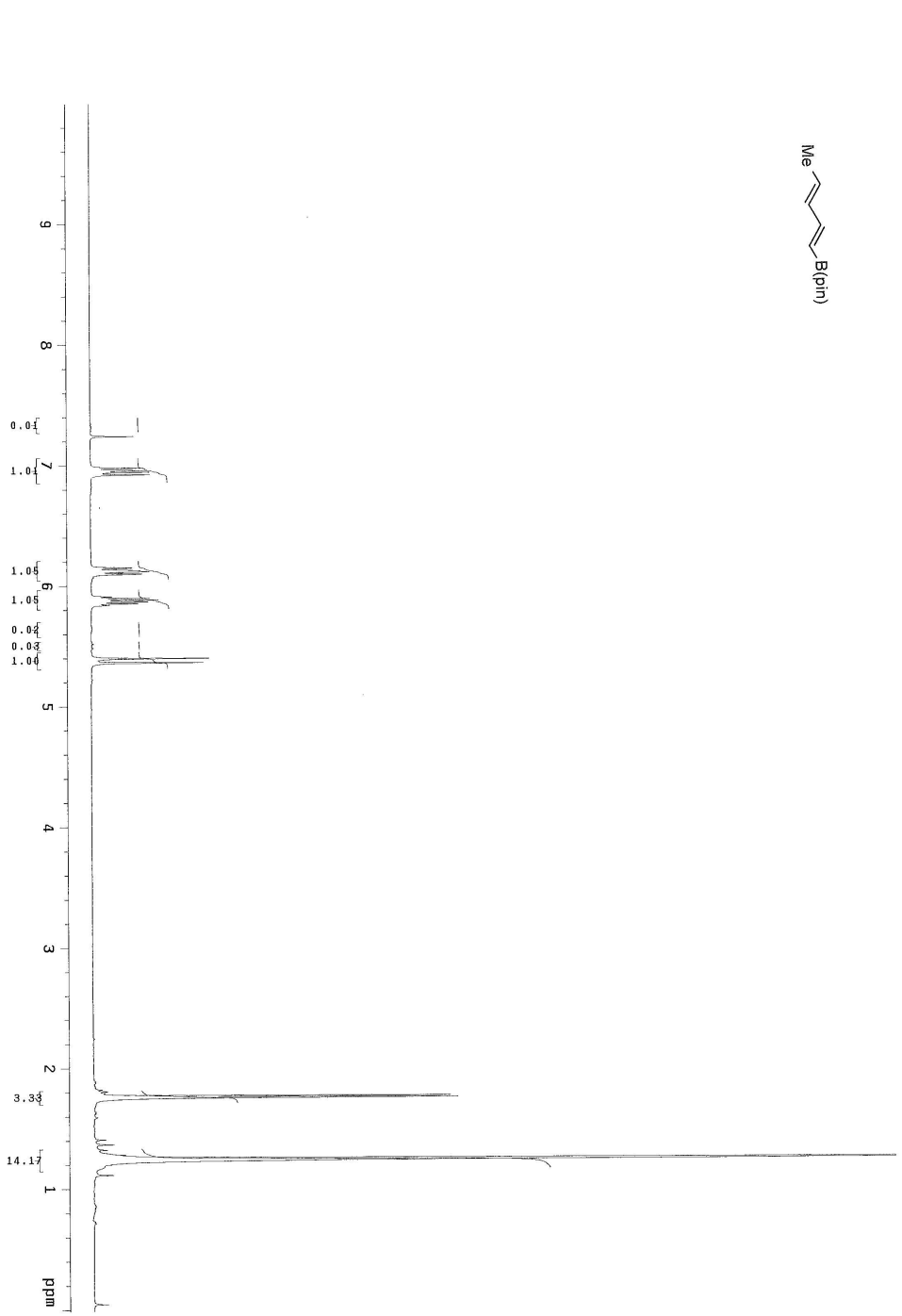
0
ppm

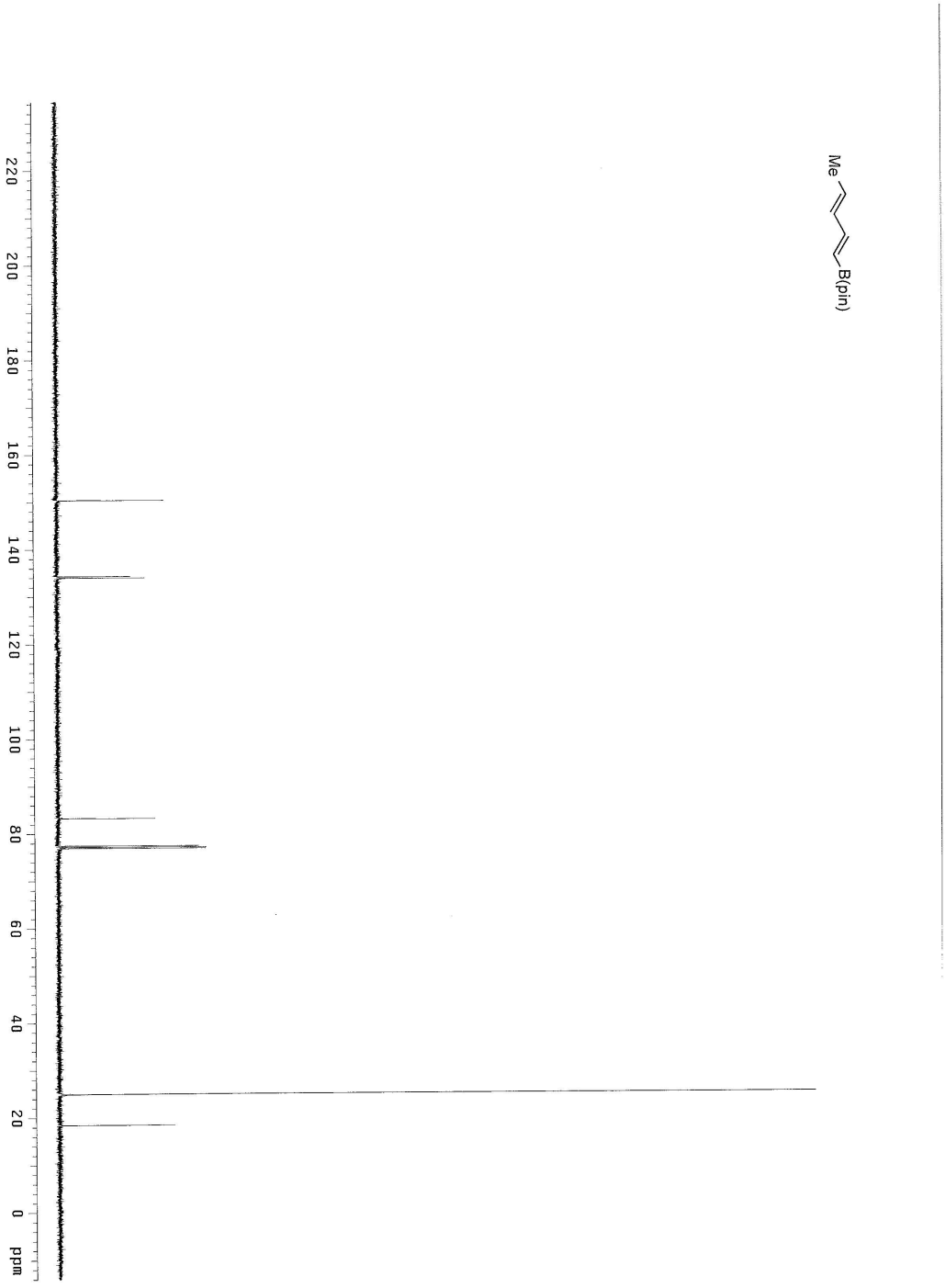

B(pin)
2.04
0.95
3.20
1.00
0.01
13.15
ppm

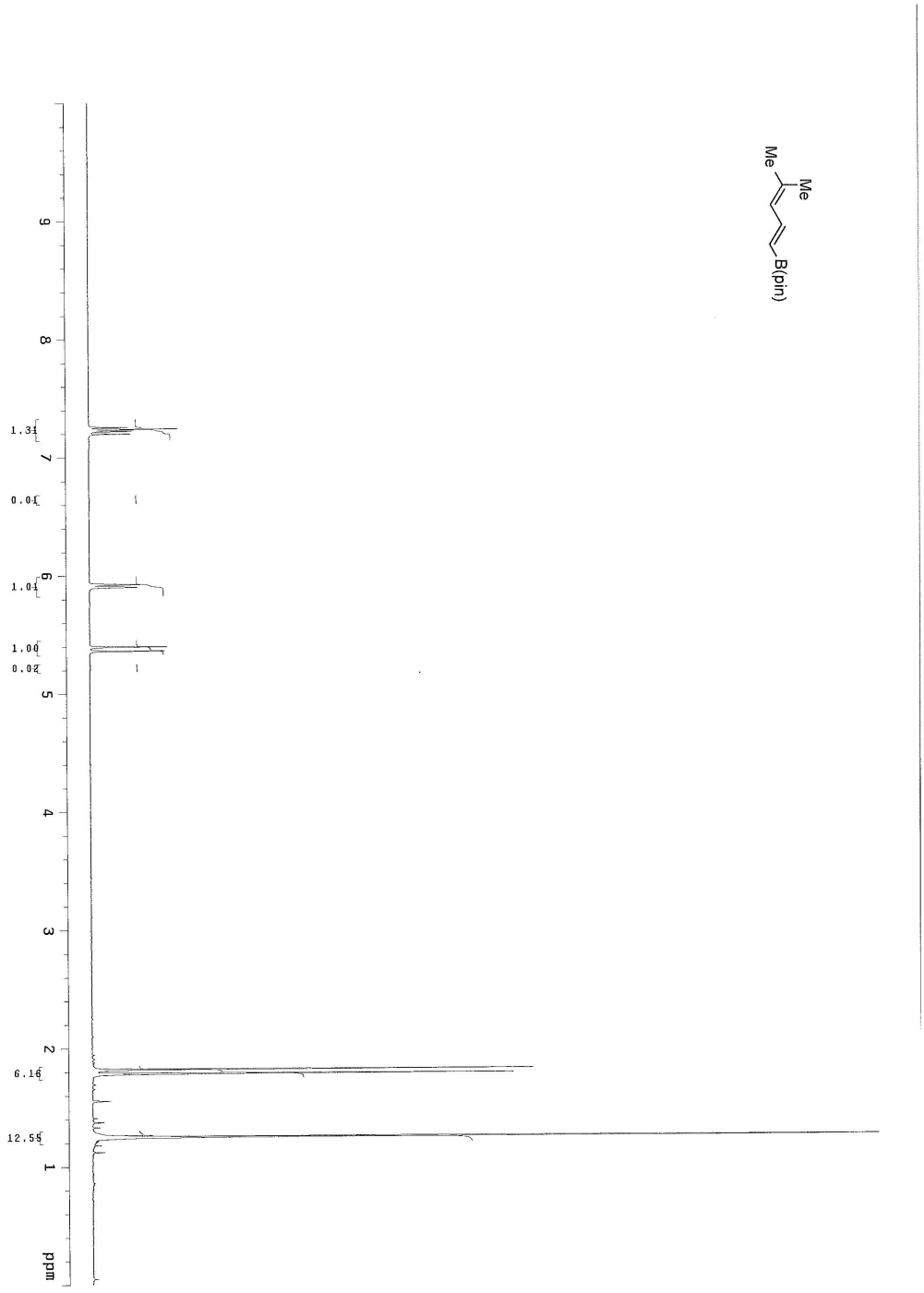

B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

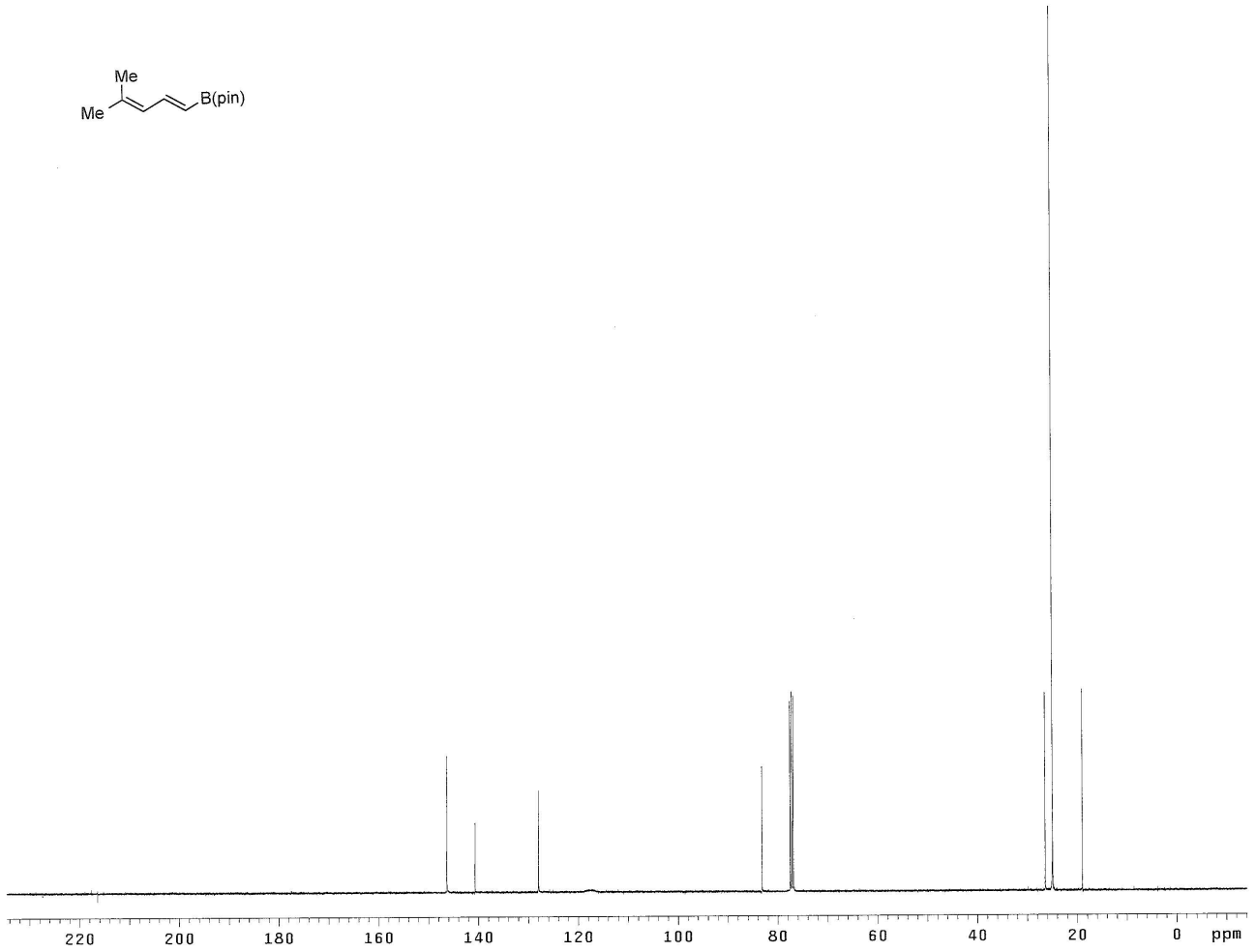

B(pin)
0.03
0.96
0.02
1.00
1.00
1.07
1.04
12.86
9
8
7
6
5
4
3
2
1
ppm

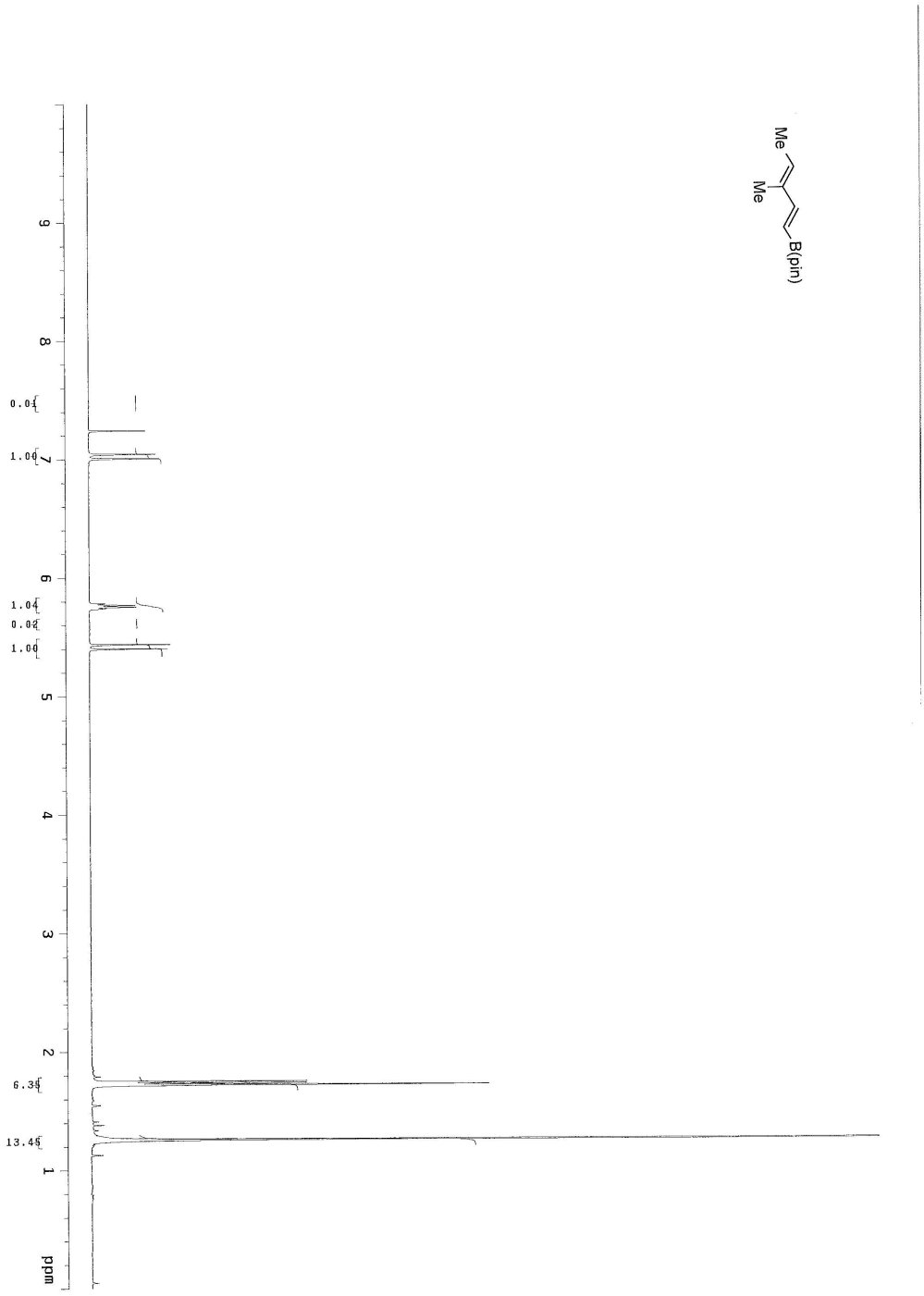

B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

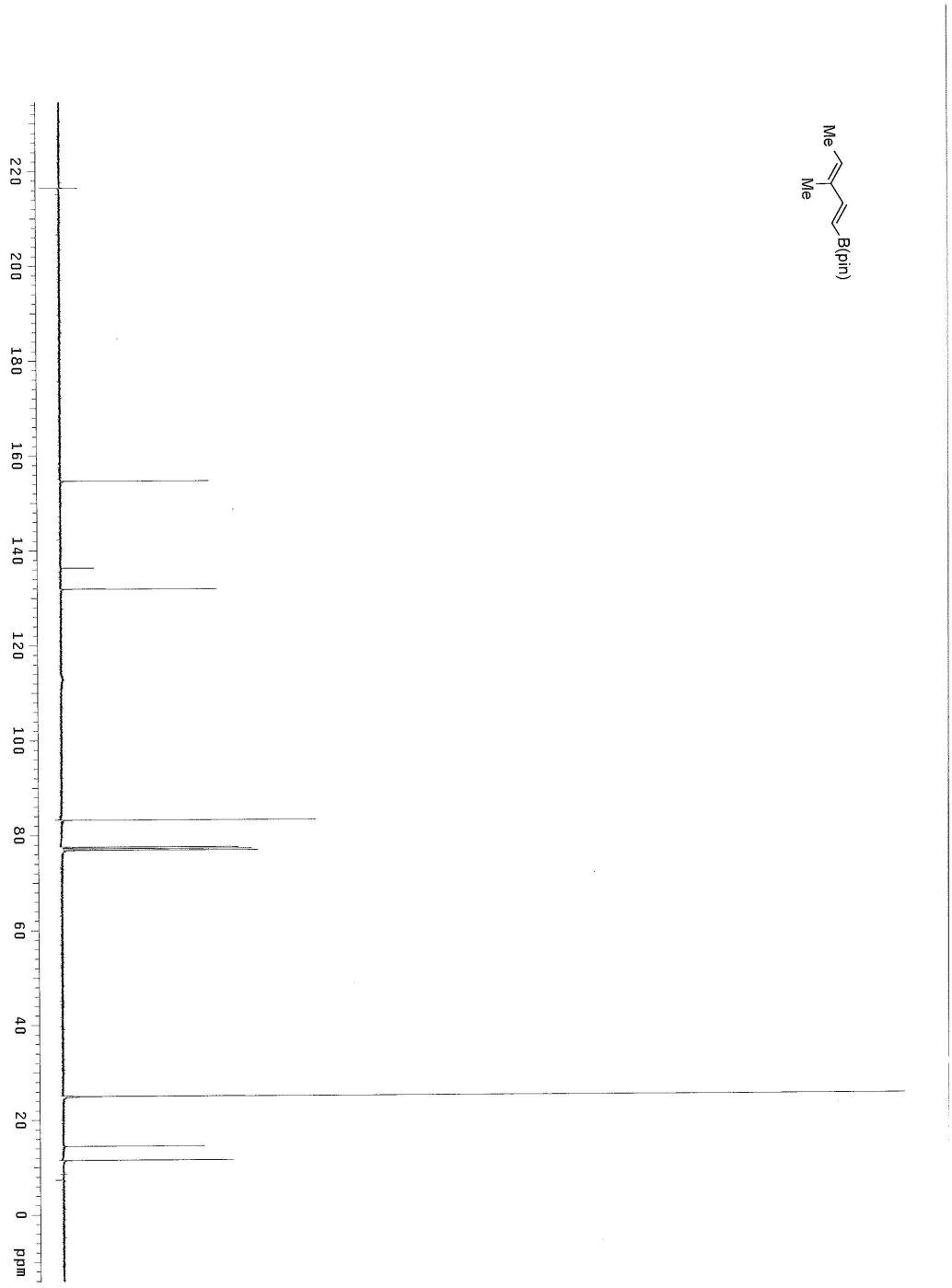

Me
B(pin)
0.01
1.01
1.05
1.05
0.02
0.03
1.00
3.33
14.17
9
8
7
6
5
4
3
2
1
ppm

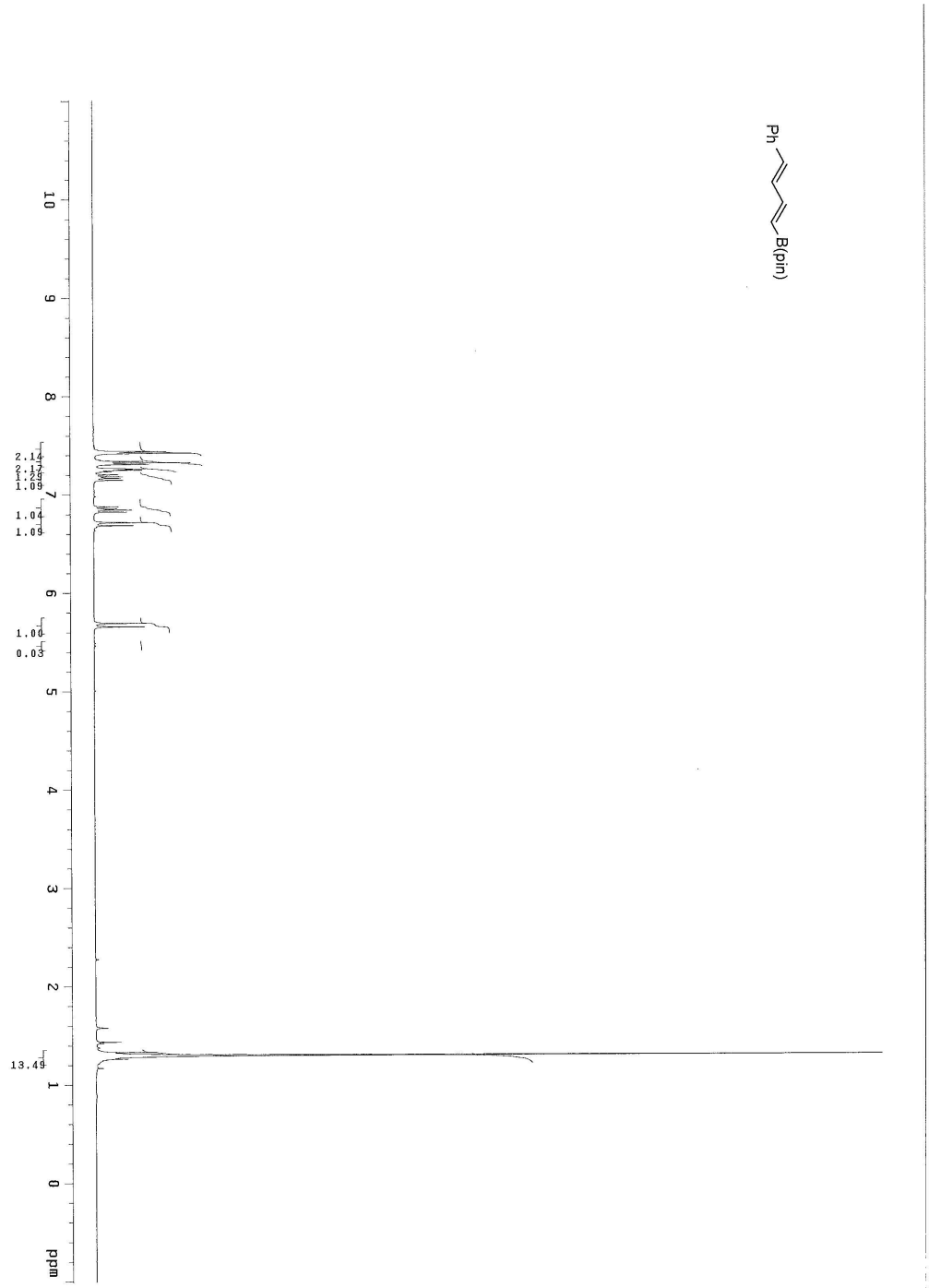

Me
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

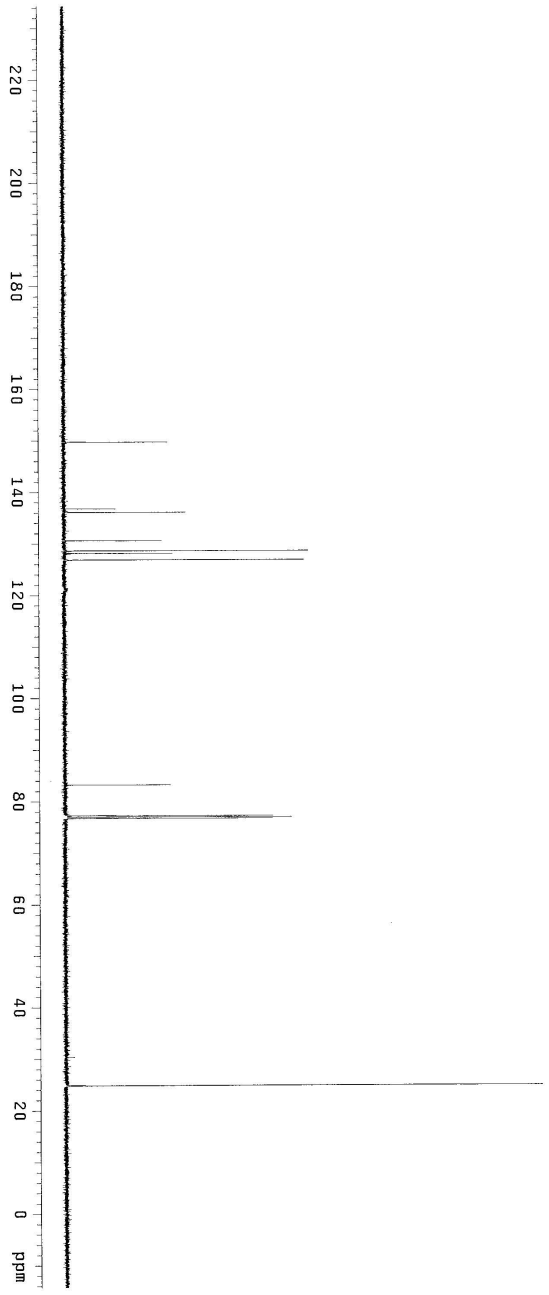

Me
Me
B(pin)
1.31
0.01
1.01
1.00
0.02
6.16
12.55
ppm


Me
Me
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

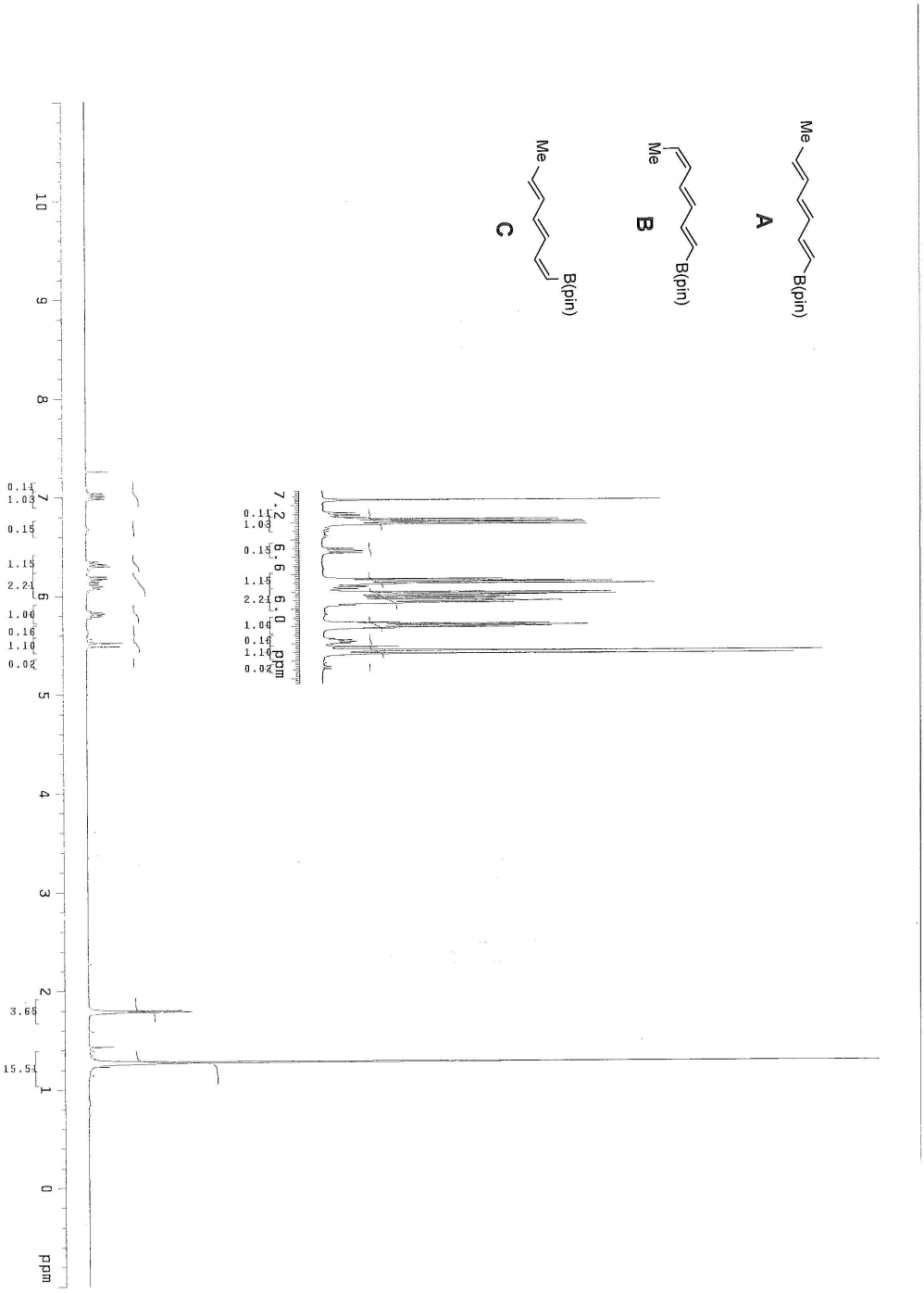

Me
Me
B(pin)
0.01
1.00
1.04
0.02
1.00
6.34
13.45
ppm

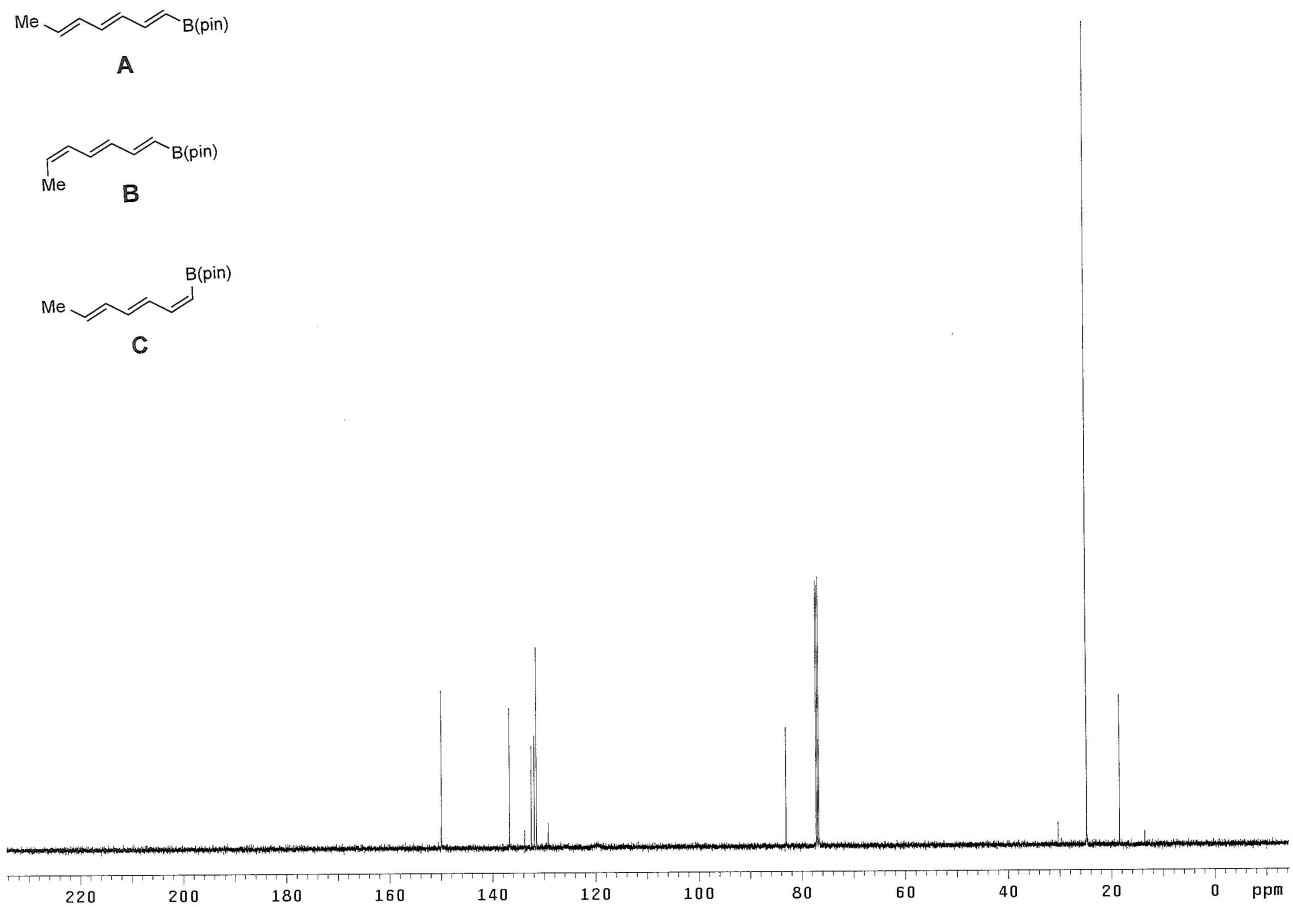

Me
Me
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

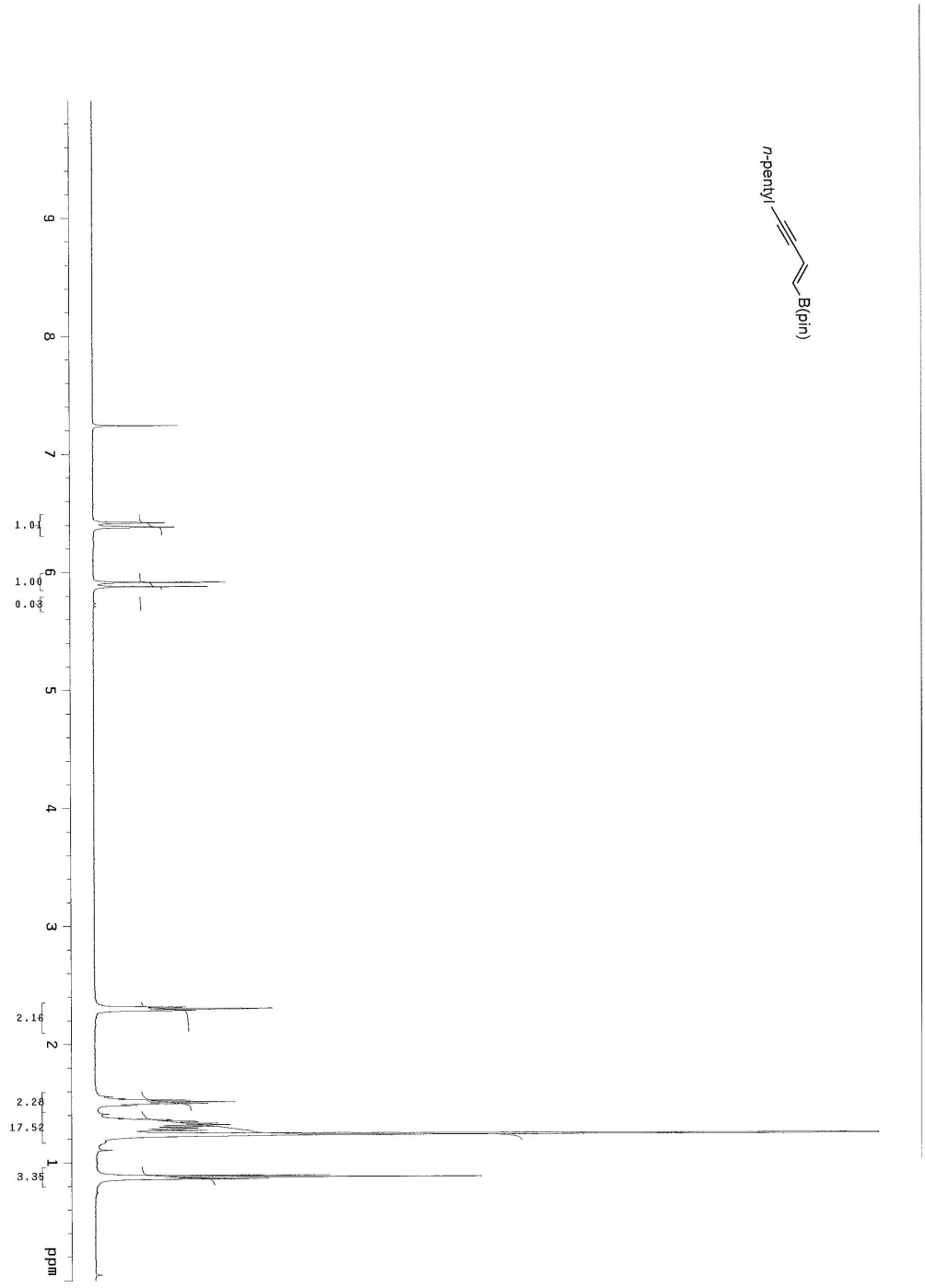

Ph
B(pin)
2.18
2.17
1.22
1.09
1.04
1.09
1.06
0.03
13.49
10
9
8
7
6
5
4
3
2
1
0
ppm

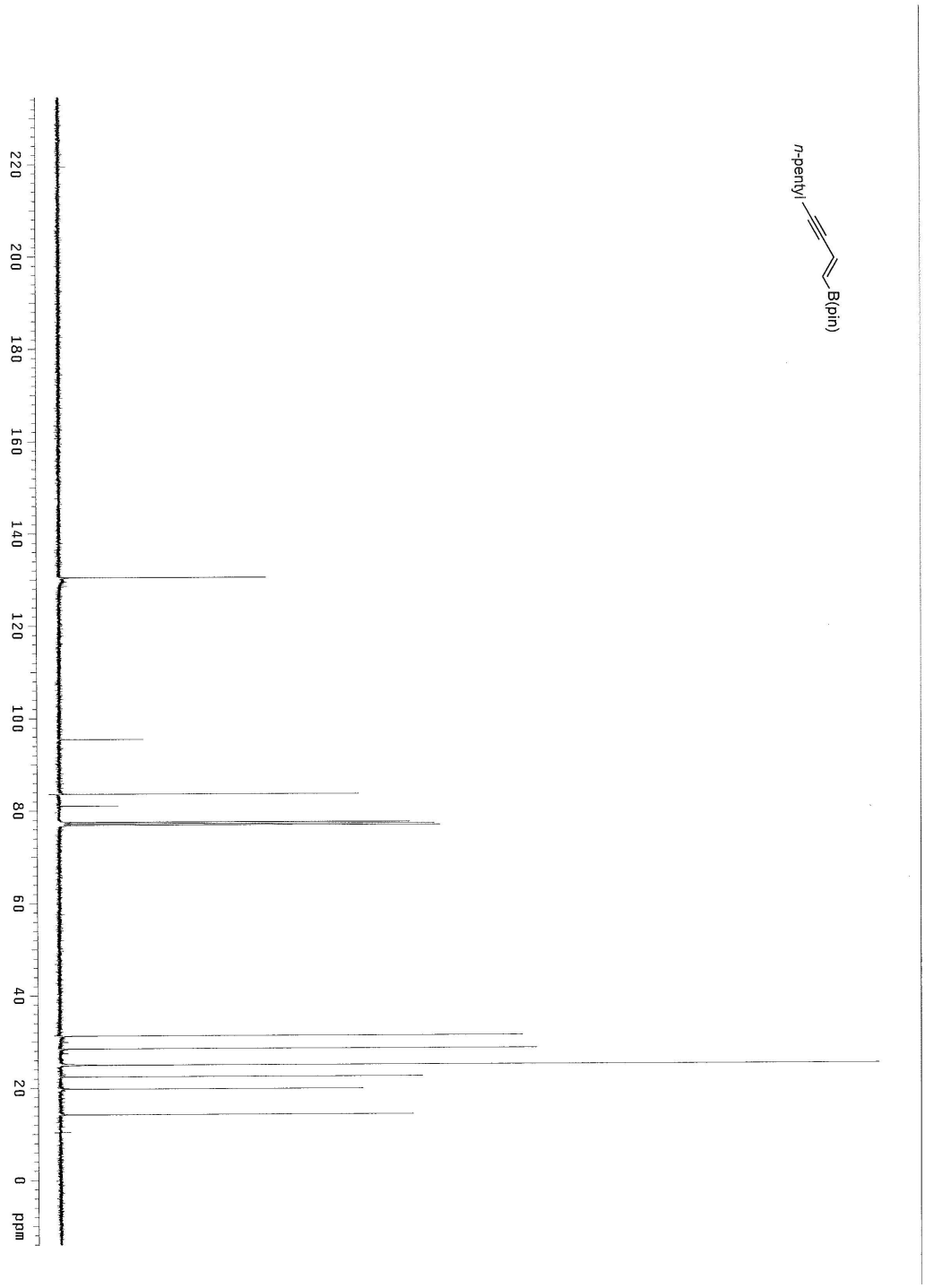

220
200
180
160
140
120
100
80
60
40
20
0
ppm

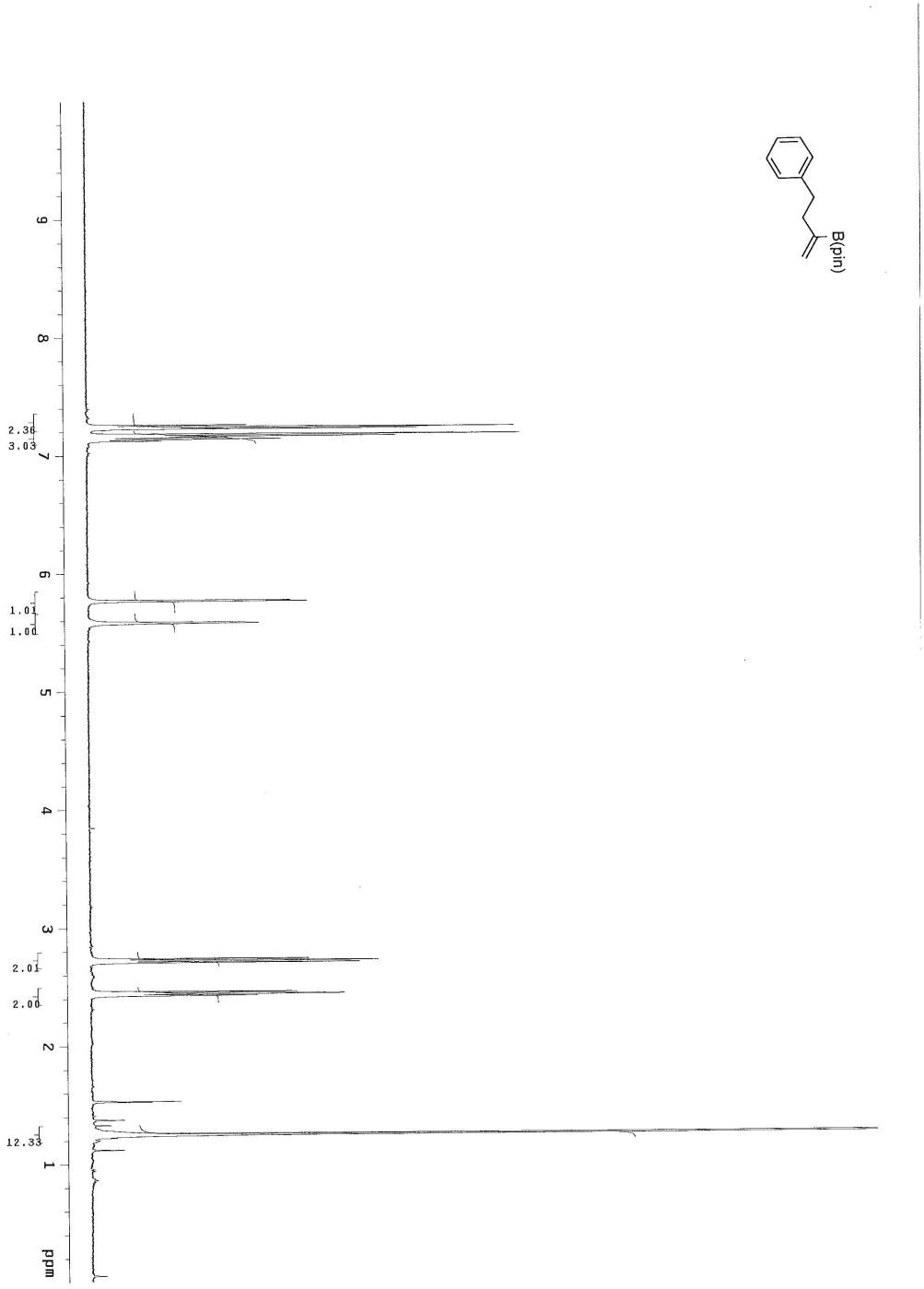

Ph
B(pin)

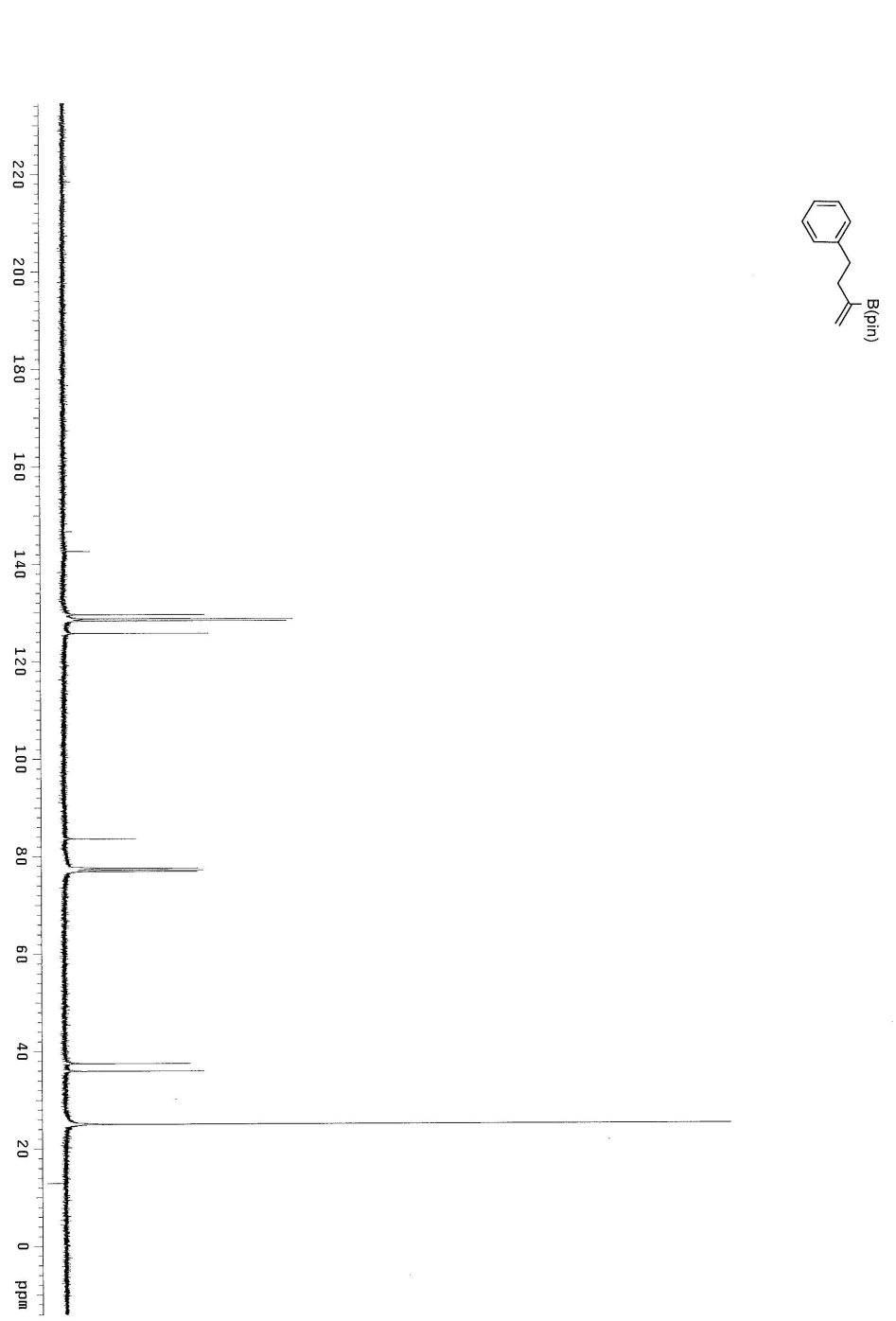

Me
B(pin)
A
Me
B(pin)
B
Me
B(pin)
C
0.11
1.03
0.15
1.15
2.21
1.00
0.16
1.10
0.02
3.65
15.51
ppm
7.2
6.6
6.0
ppm

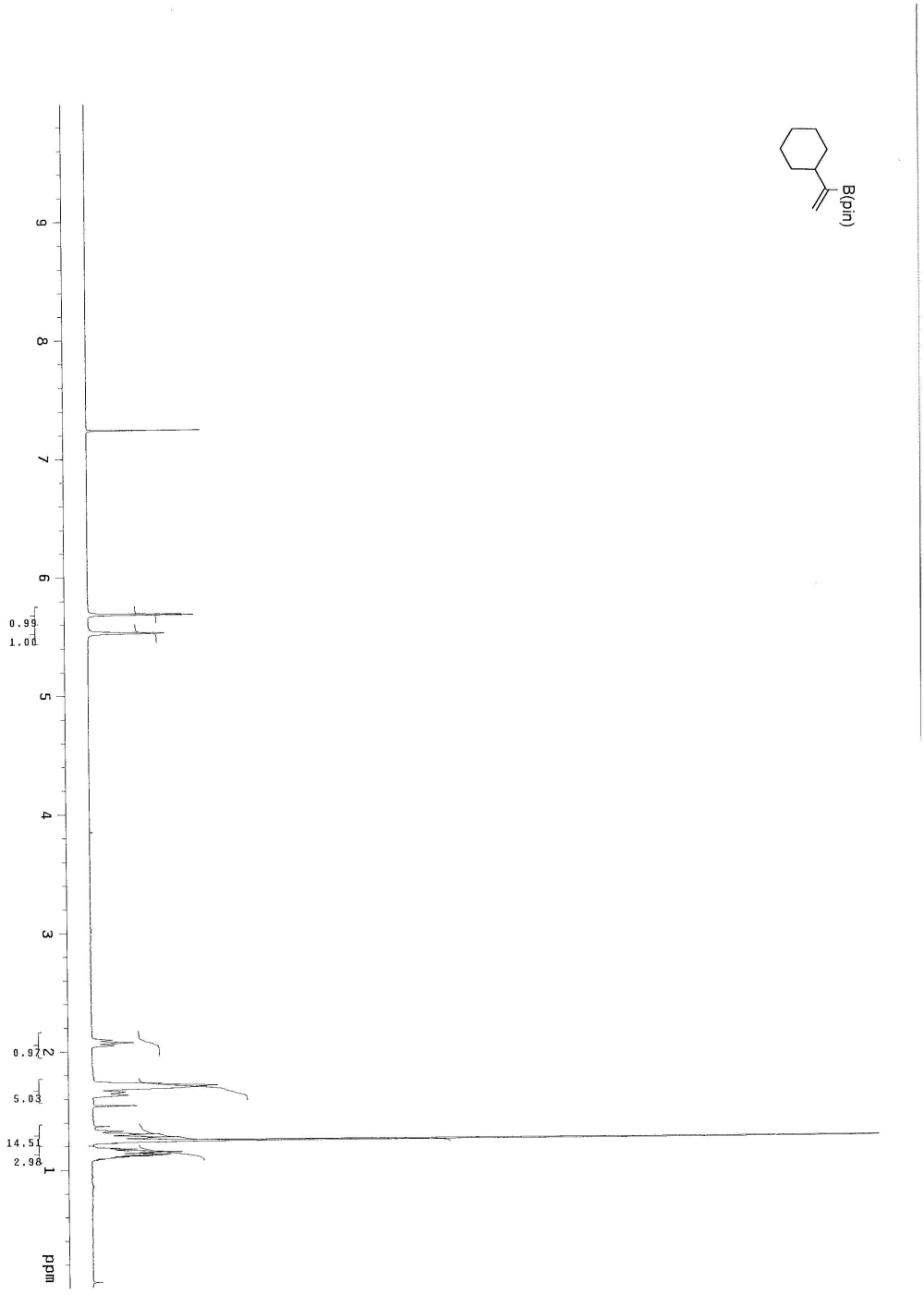

Me
B(pin)
A
B(pin)
Me
B
B(pin)
Me
C
220
200
180
160
140
120
100
80
60
40
20
0
ppm

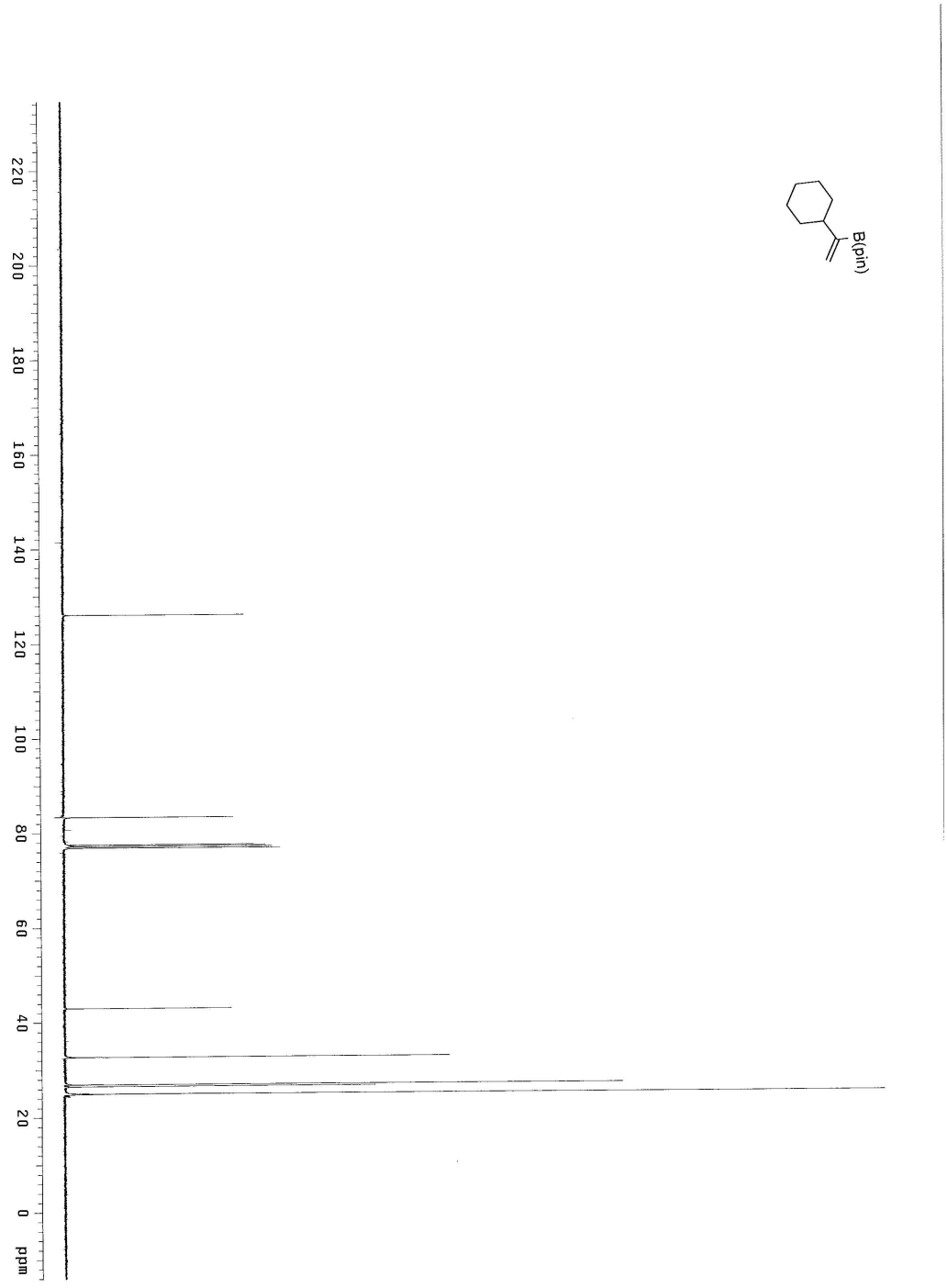

n-pentyl
B(pin)
9
8
7
6
5
4
3
2
1
ppm
1.01
1.00
0.03
2.16
2.28
17.52
3.35

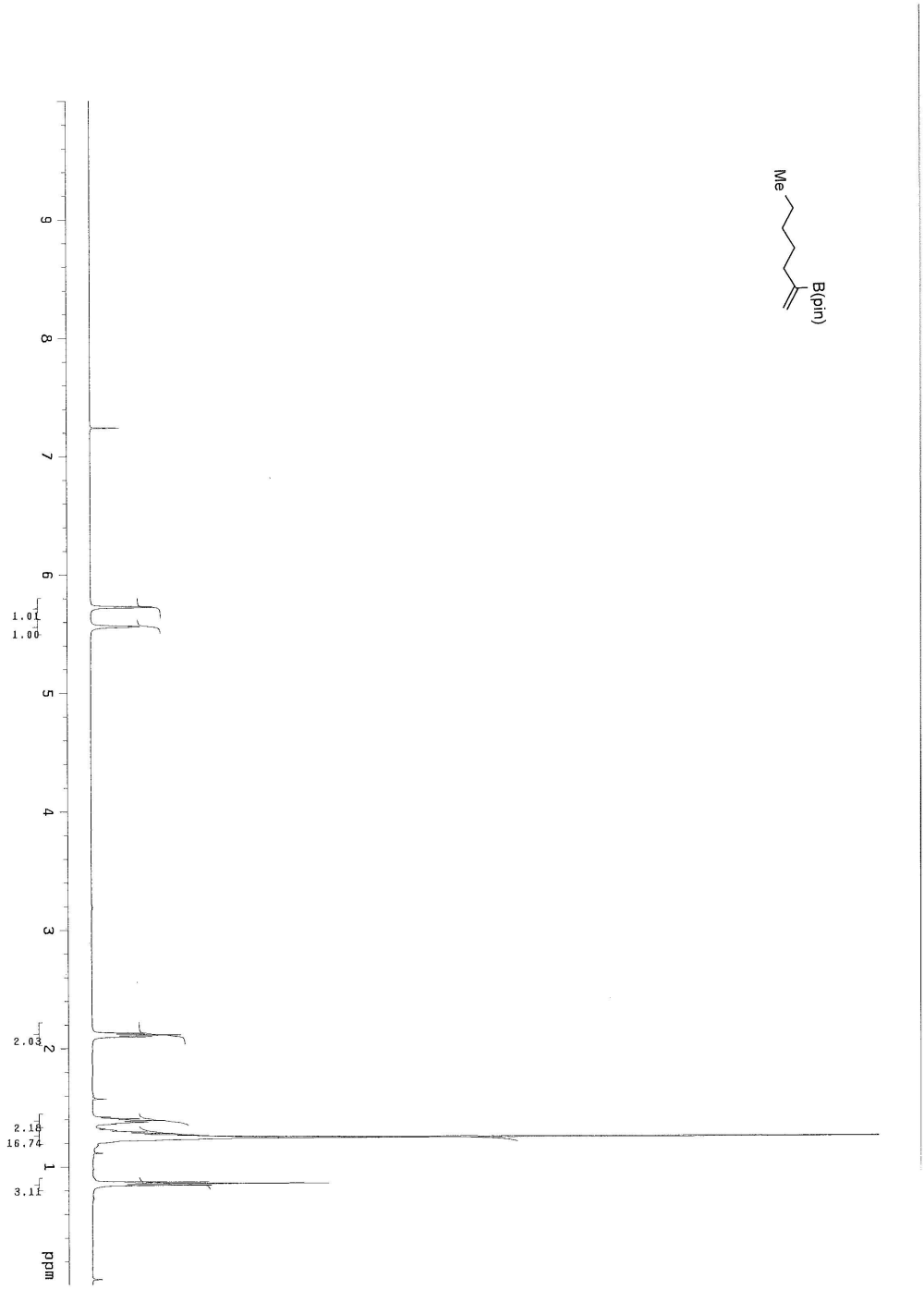

n-pentyl
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

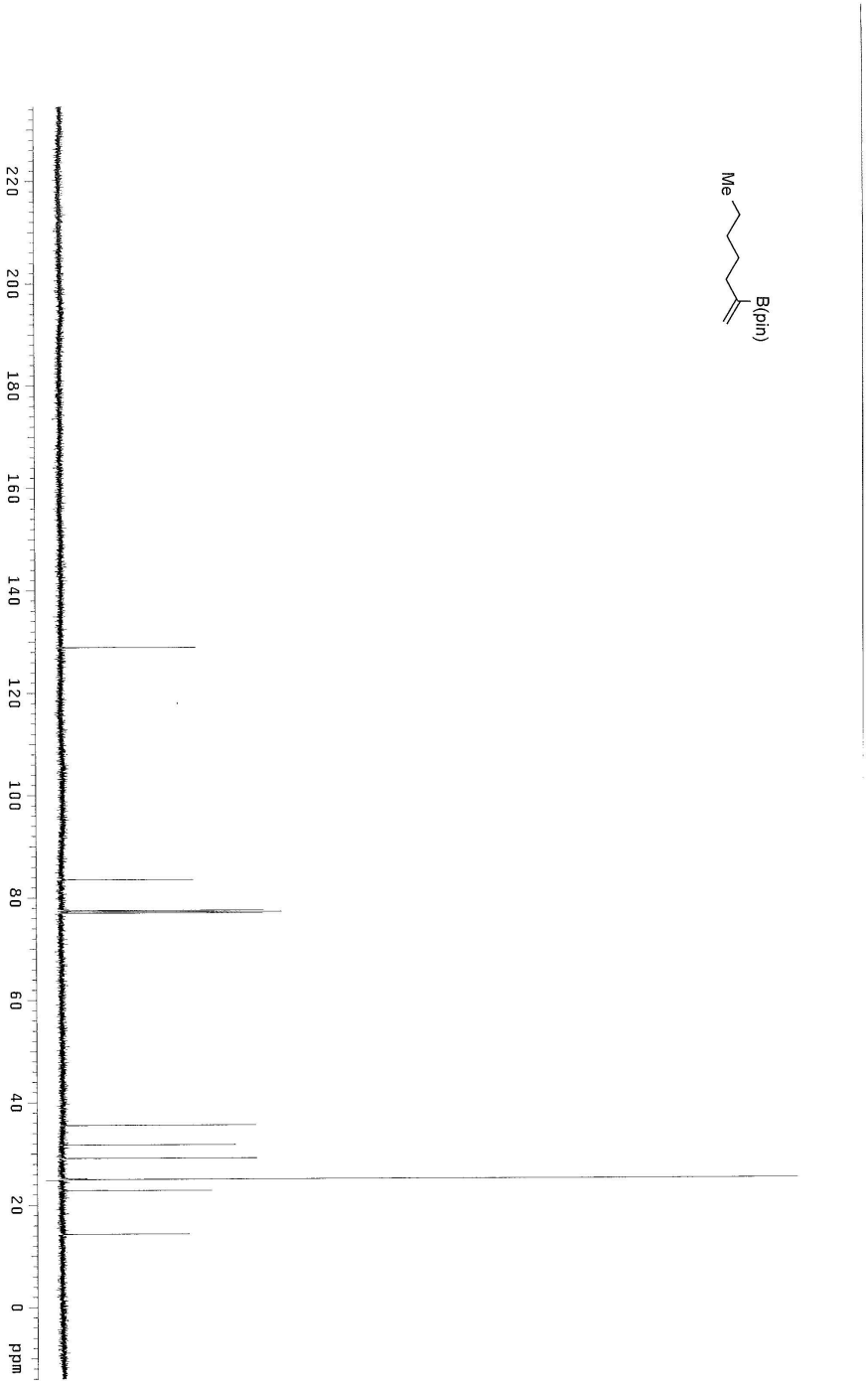

B(pin)
2.36
3.03
1.01
1.00
2.01
2.00
12.33
ppm

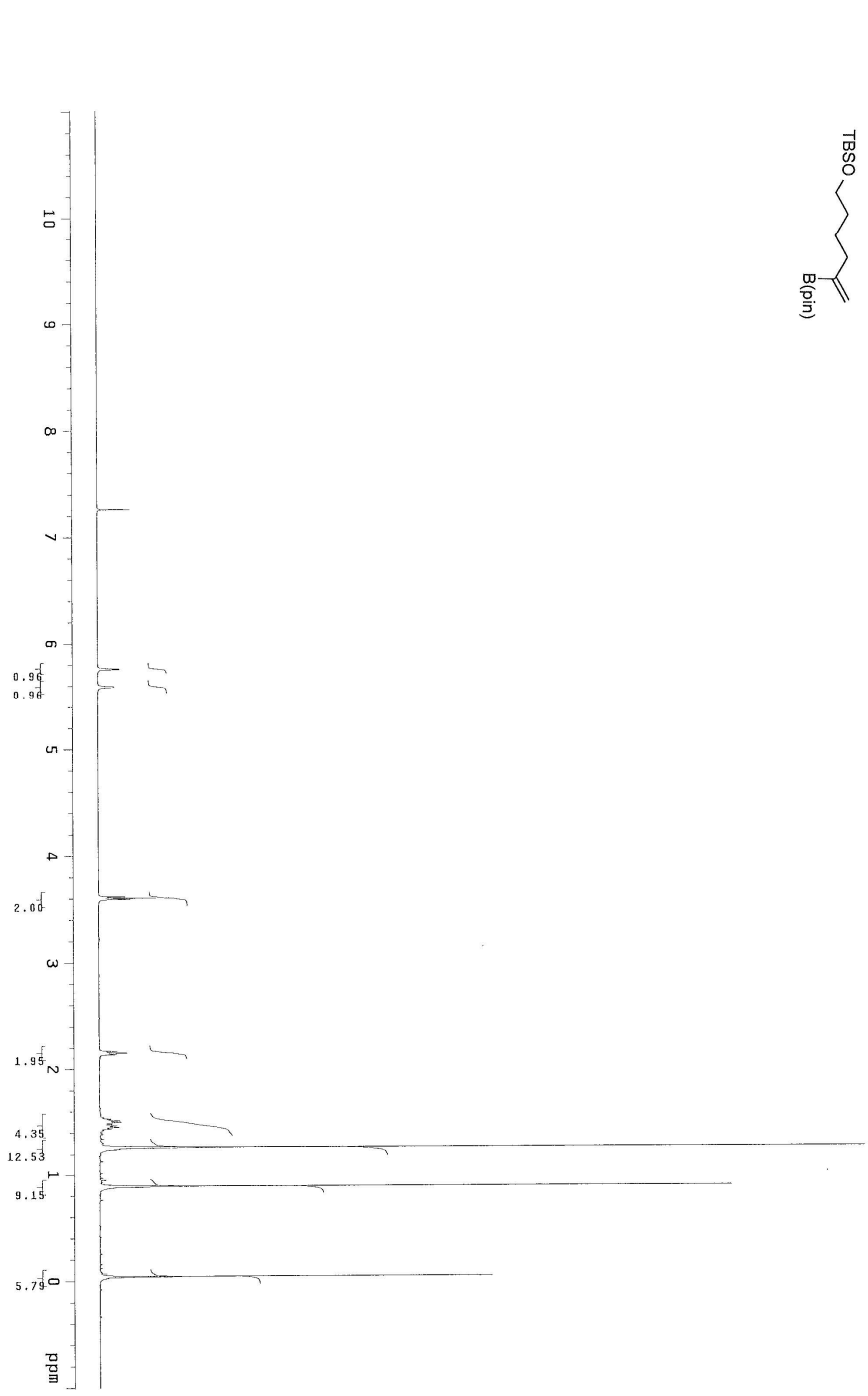

B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

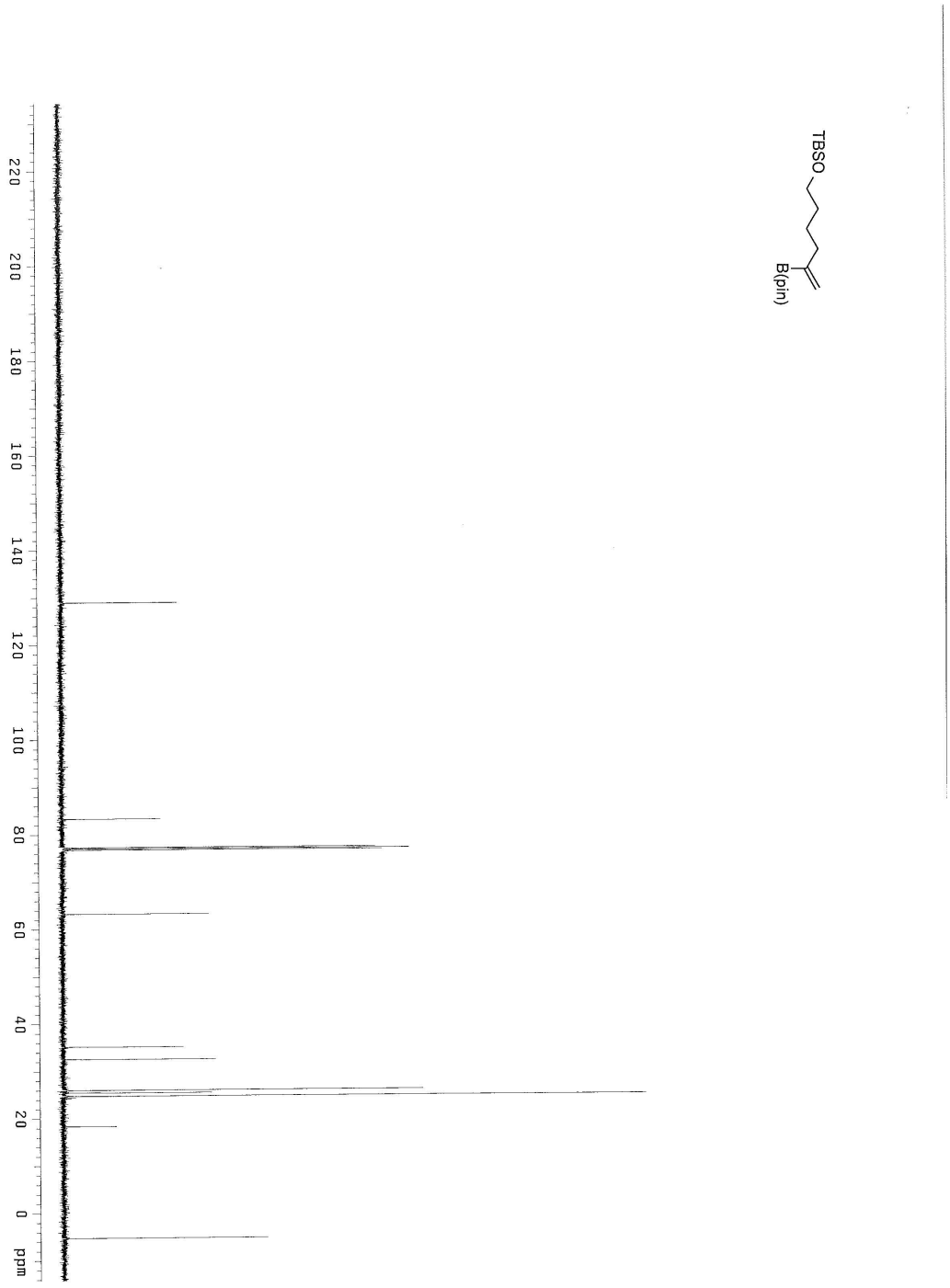

B(pin)
9
8
7
6
5
4
3
2
1
ppm
0.99
1.00
0.97
5.03
14.51
2.98

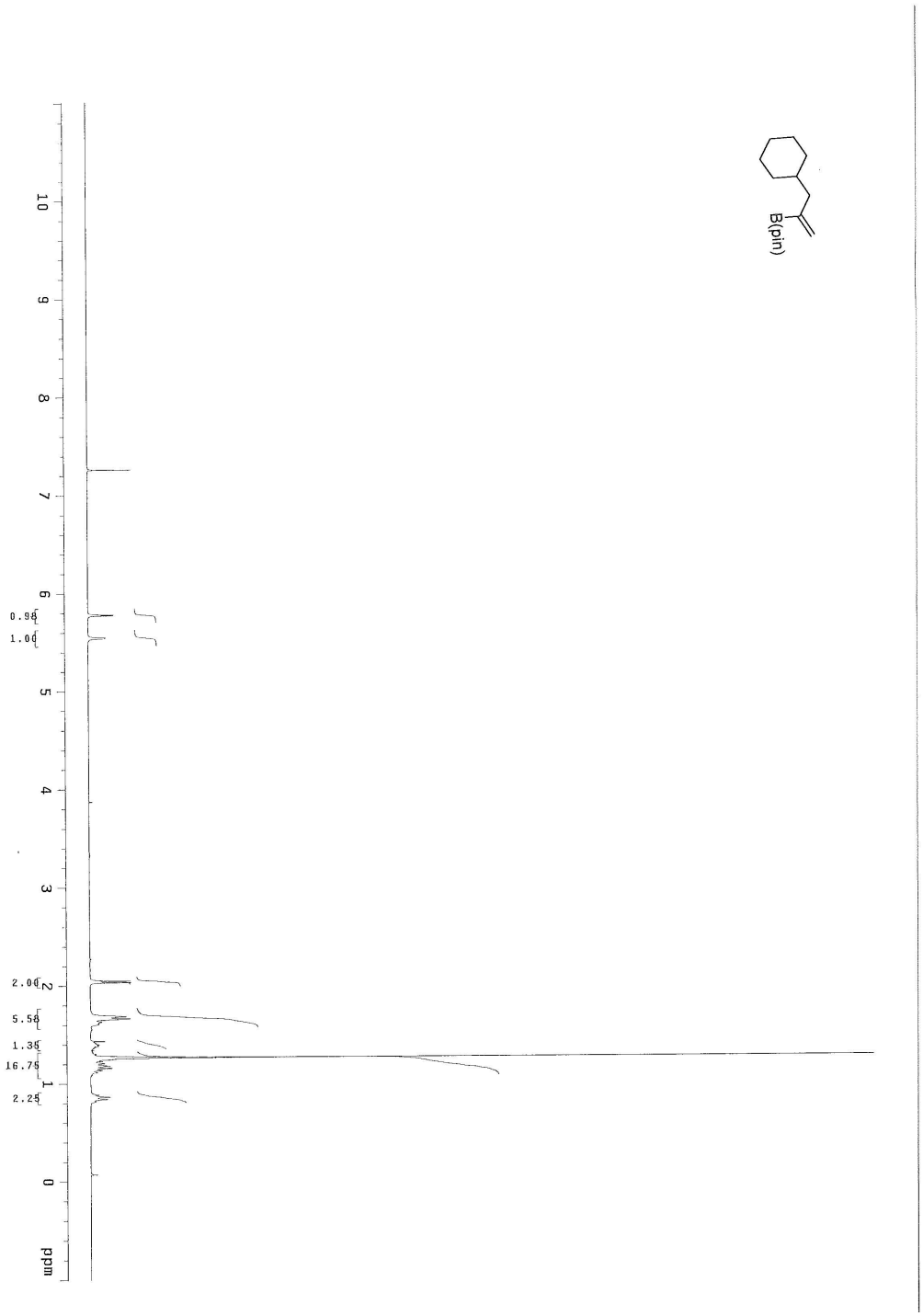

B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

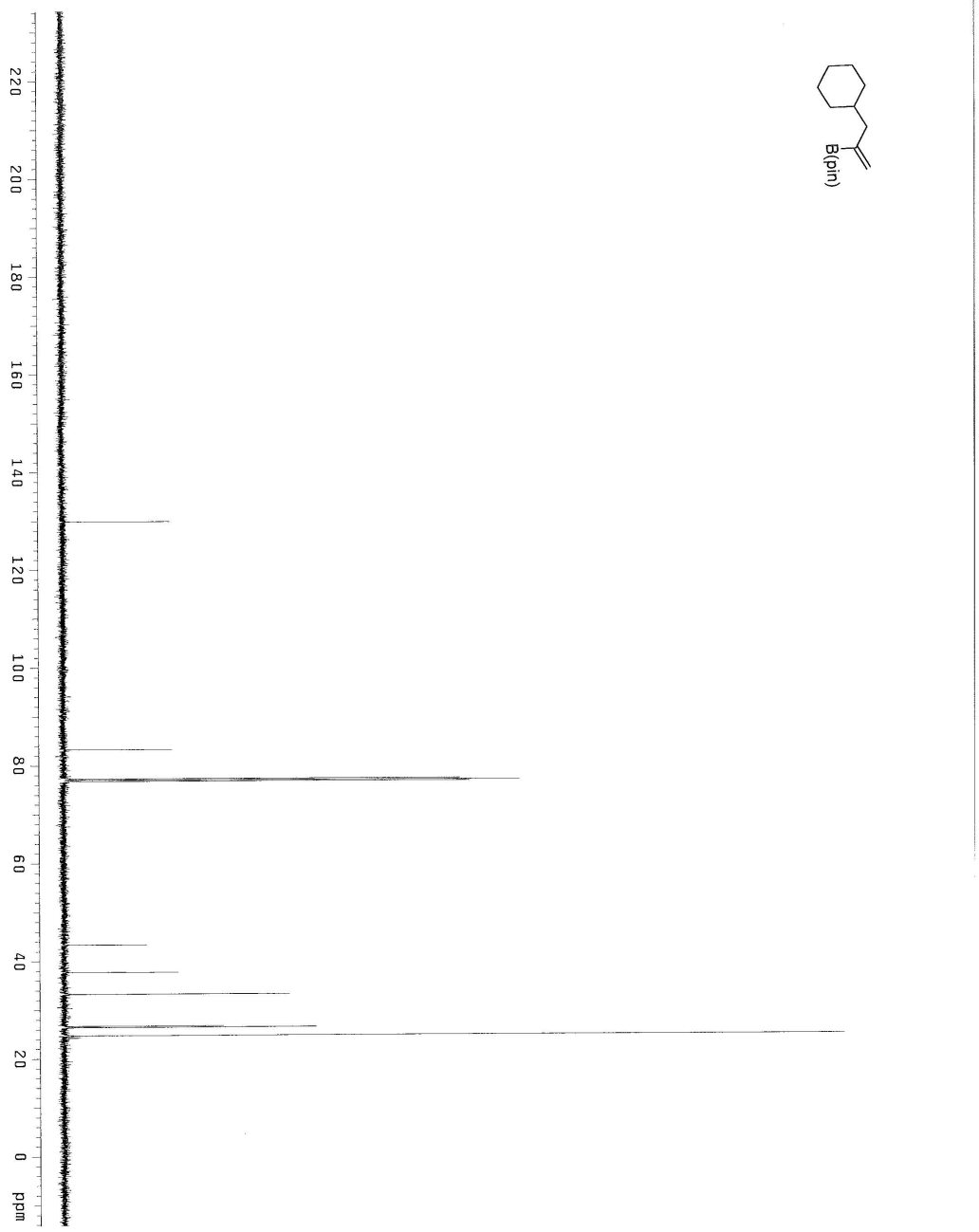

Me
B(pin)
1.01
1.00
2.03
2.18
16.74
3.11
ppm

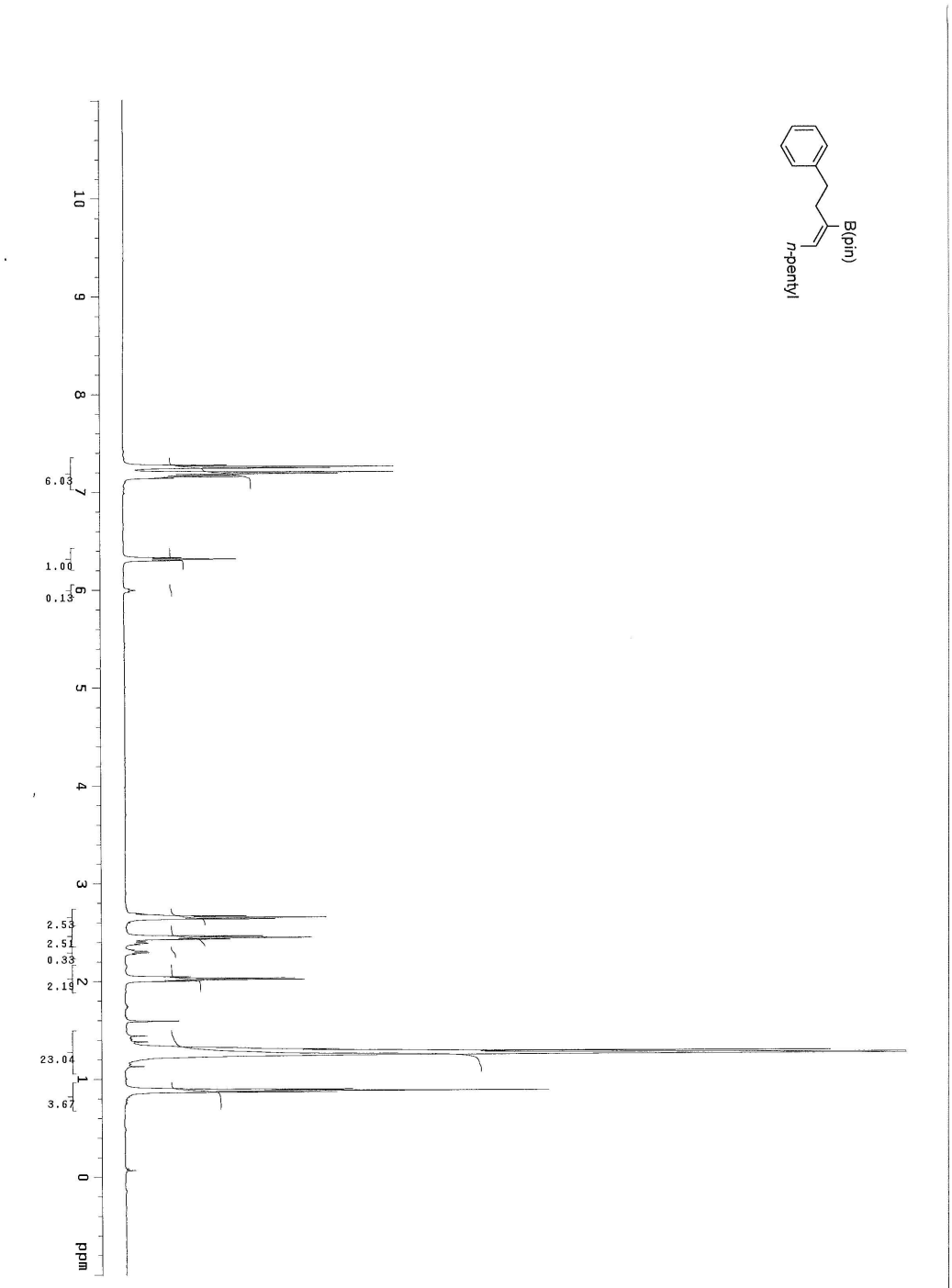

Me
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

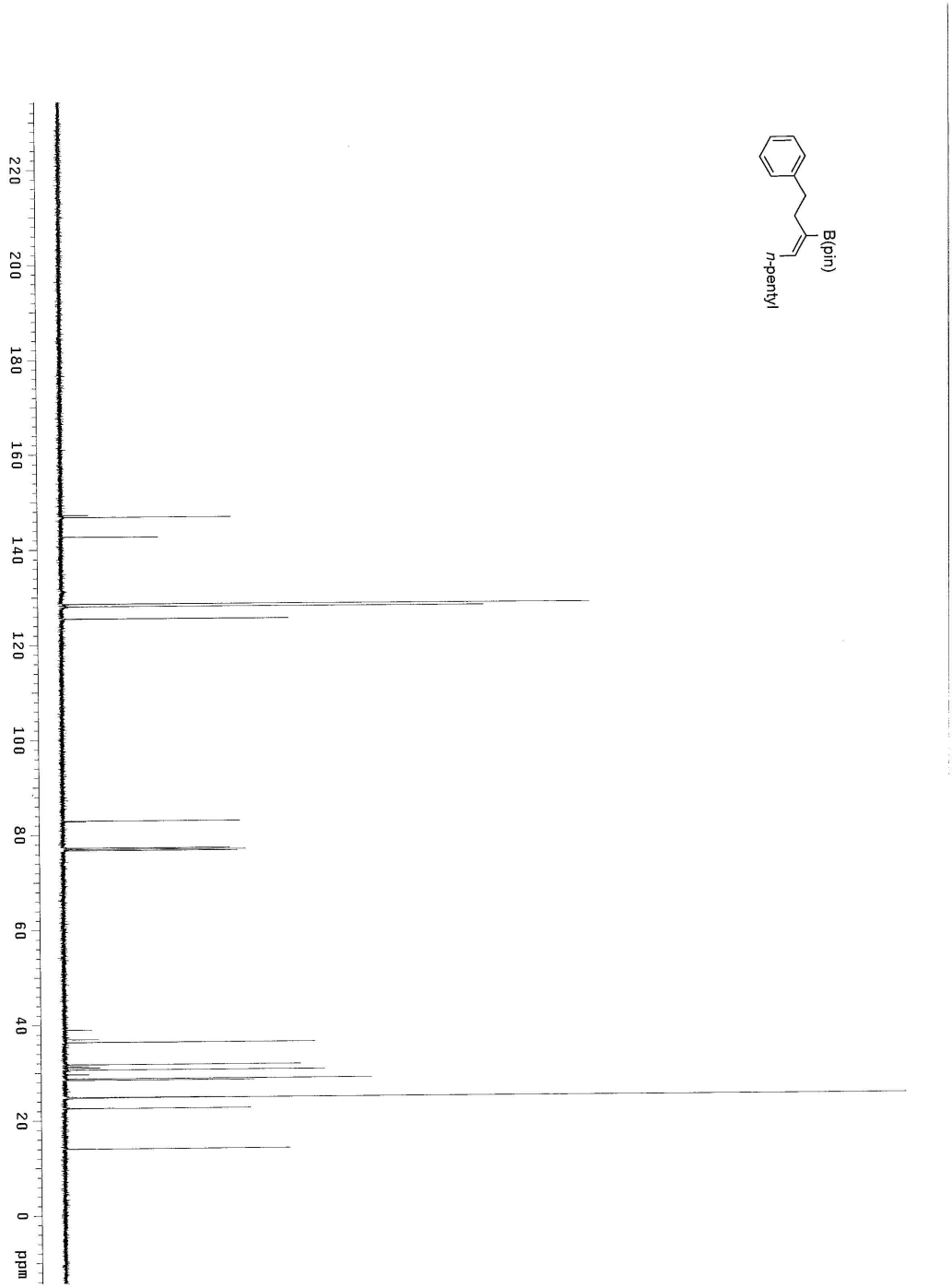

TBSO
B(pin)
10
9
8
7
6
5
4
3
2
1
0
ppm
0.96
0.96
2.00
1.95
4.35
12.53
9.15
5.79

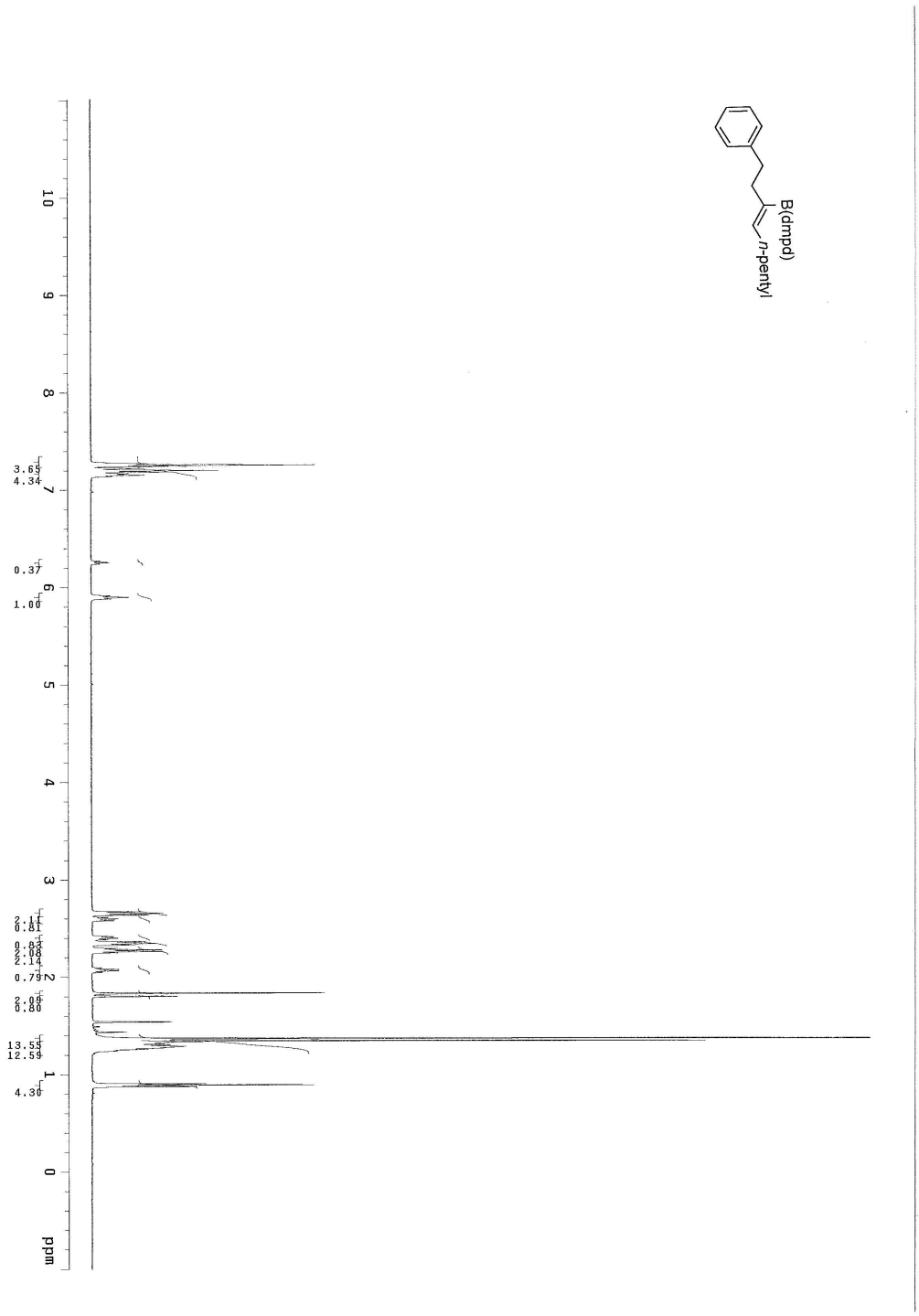

TBSO
B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

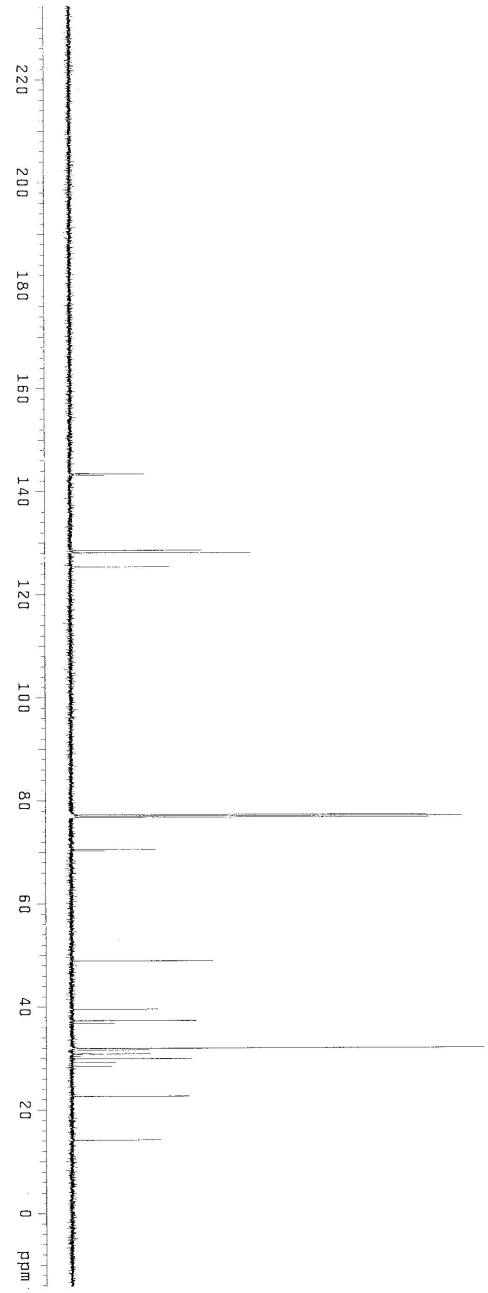

B(pin)
0.96
1.00
2.00
5.58
1.35
16.75
2.25
ppm

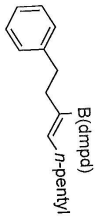

B(pin)
220
200
180
160
140
120
100
80
60
40
20
0
ppm

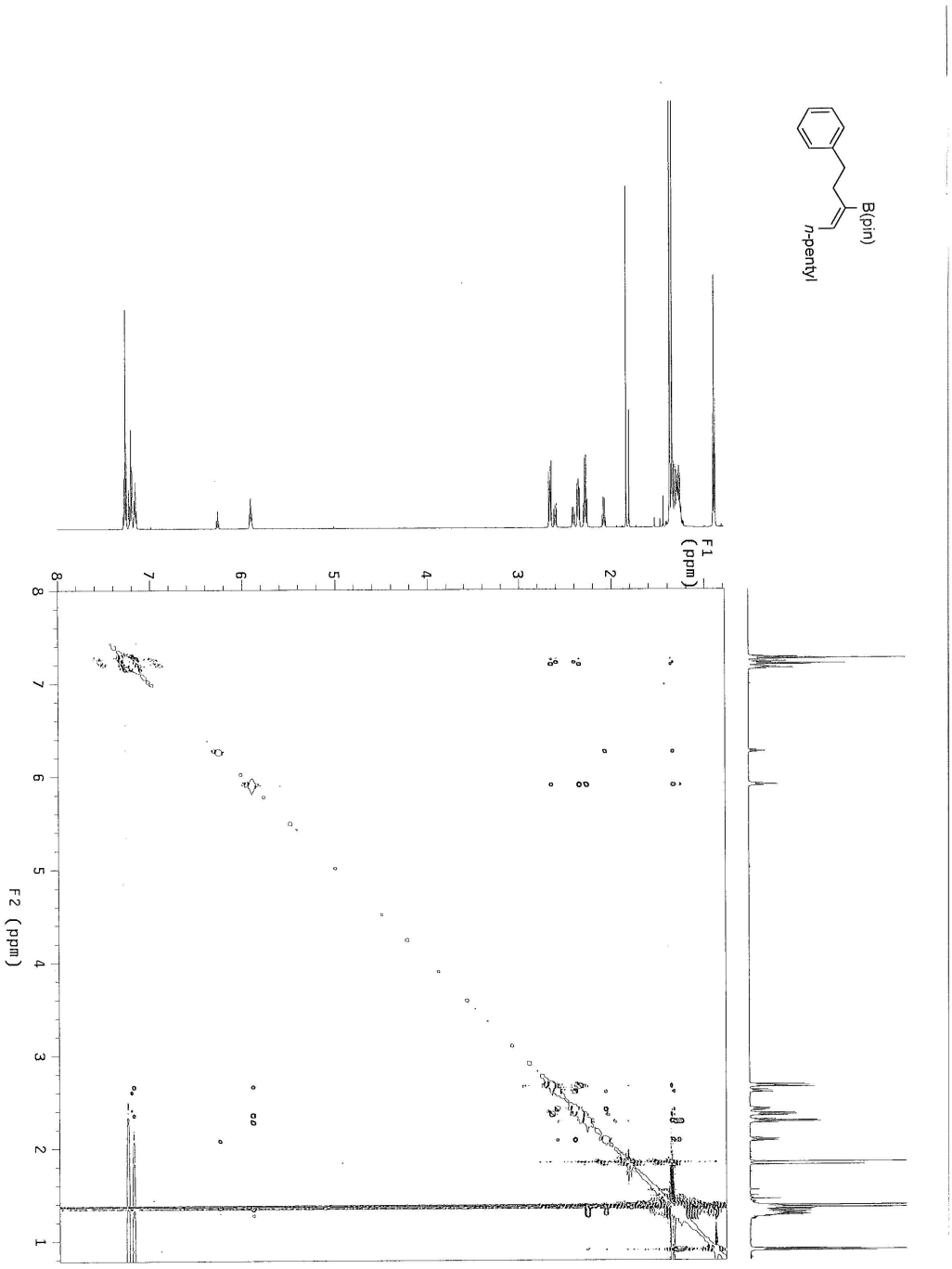

B(pin)
n-pentyl
6.03
1.00
0.13
2.53
2.51
0.33
2.19
23.04
3.67
ppm

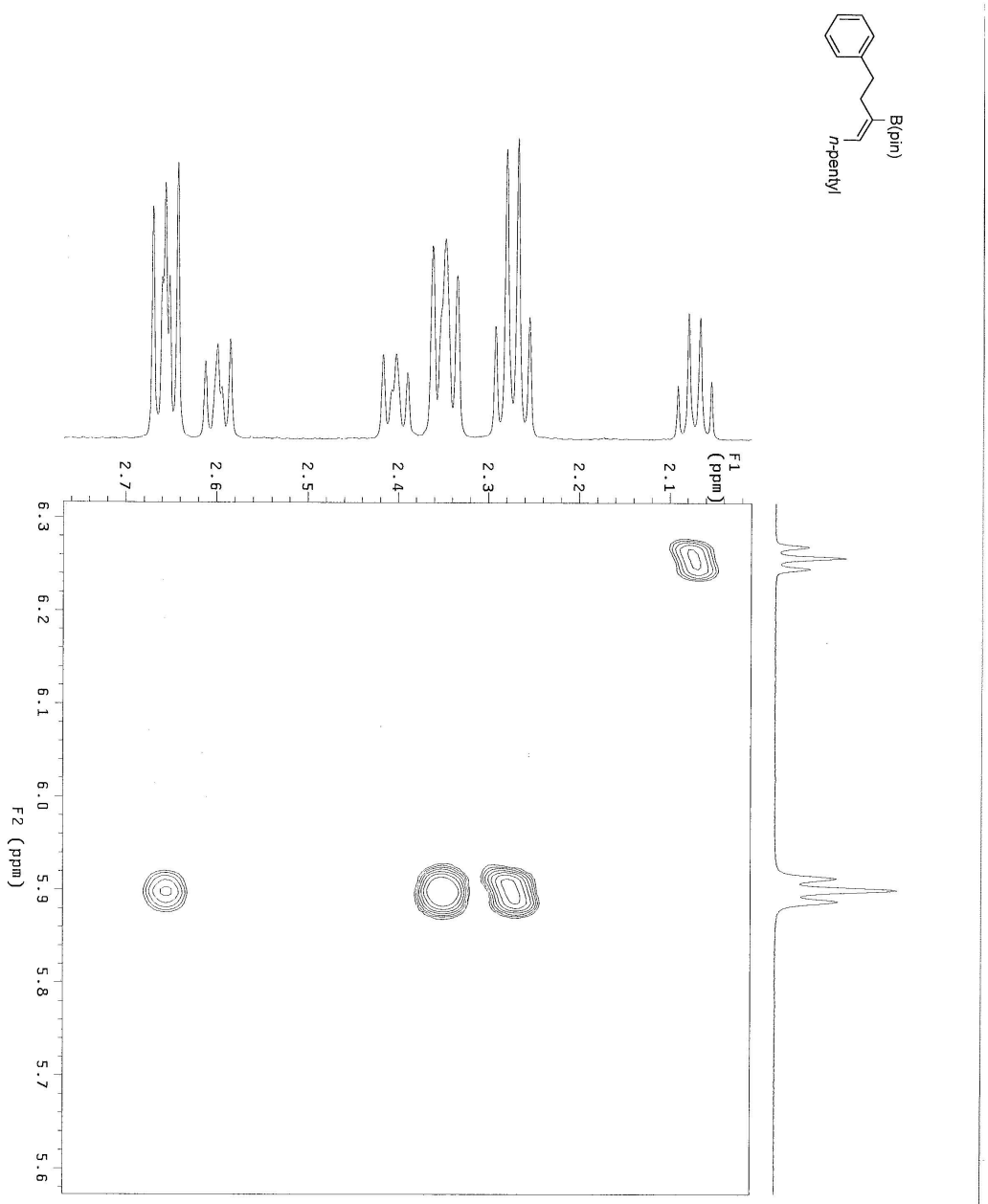

B(pin)
n-pentyl
220
200
180
160
140
120
100
80
60
40
20
0
ppm

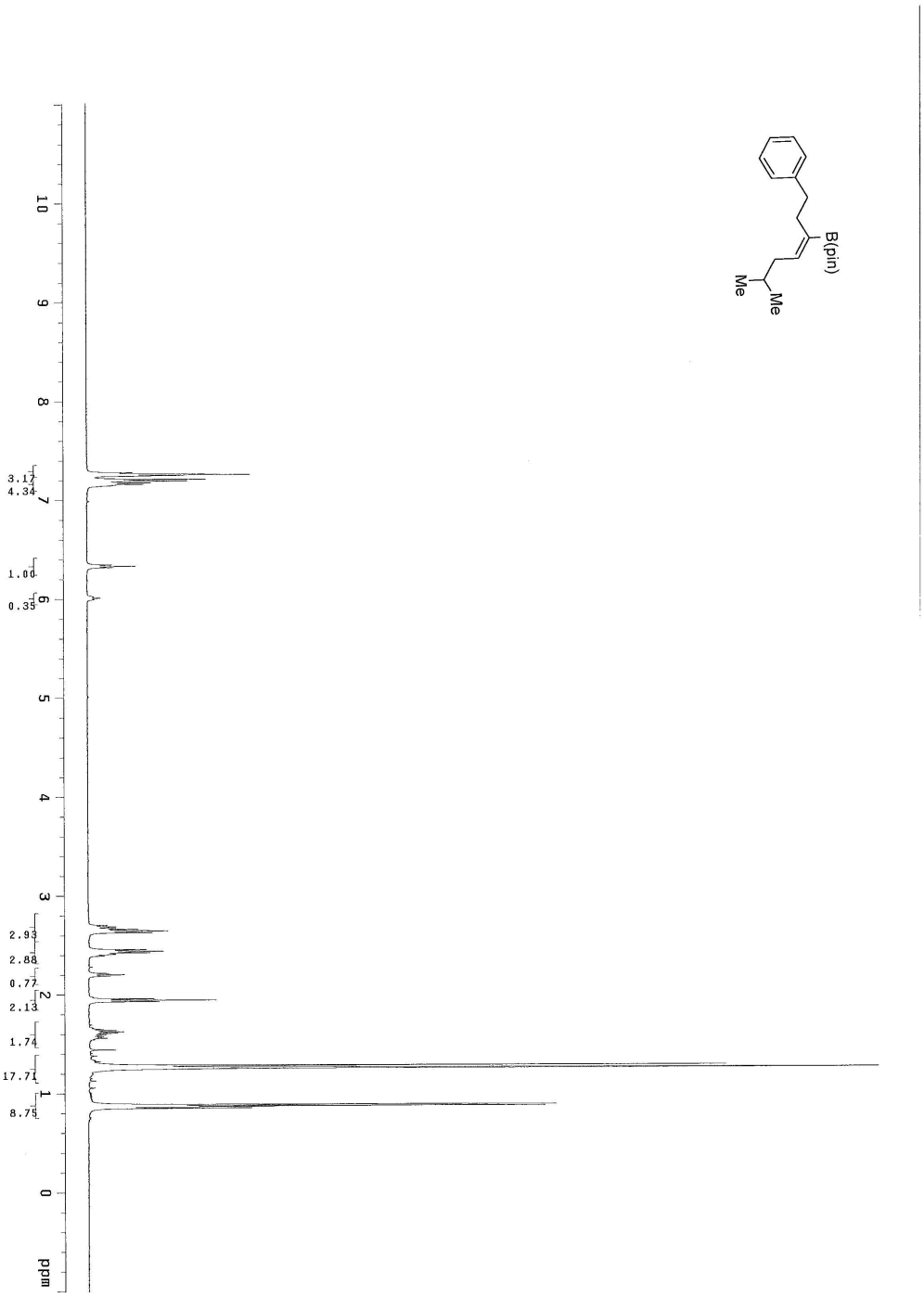

B(dmpd)
n-pentyl
3.65
4.34
0.37
1.00
2.11
0.81
0.83
2.05
2.14
0.79
2.05
0.80
13.55
12.59
4.30
ppm

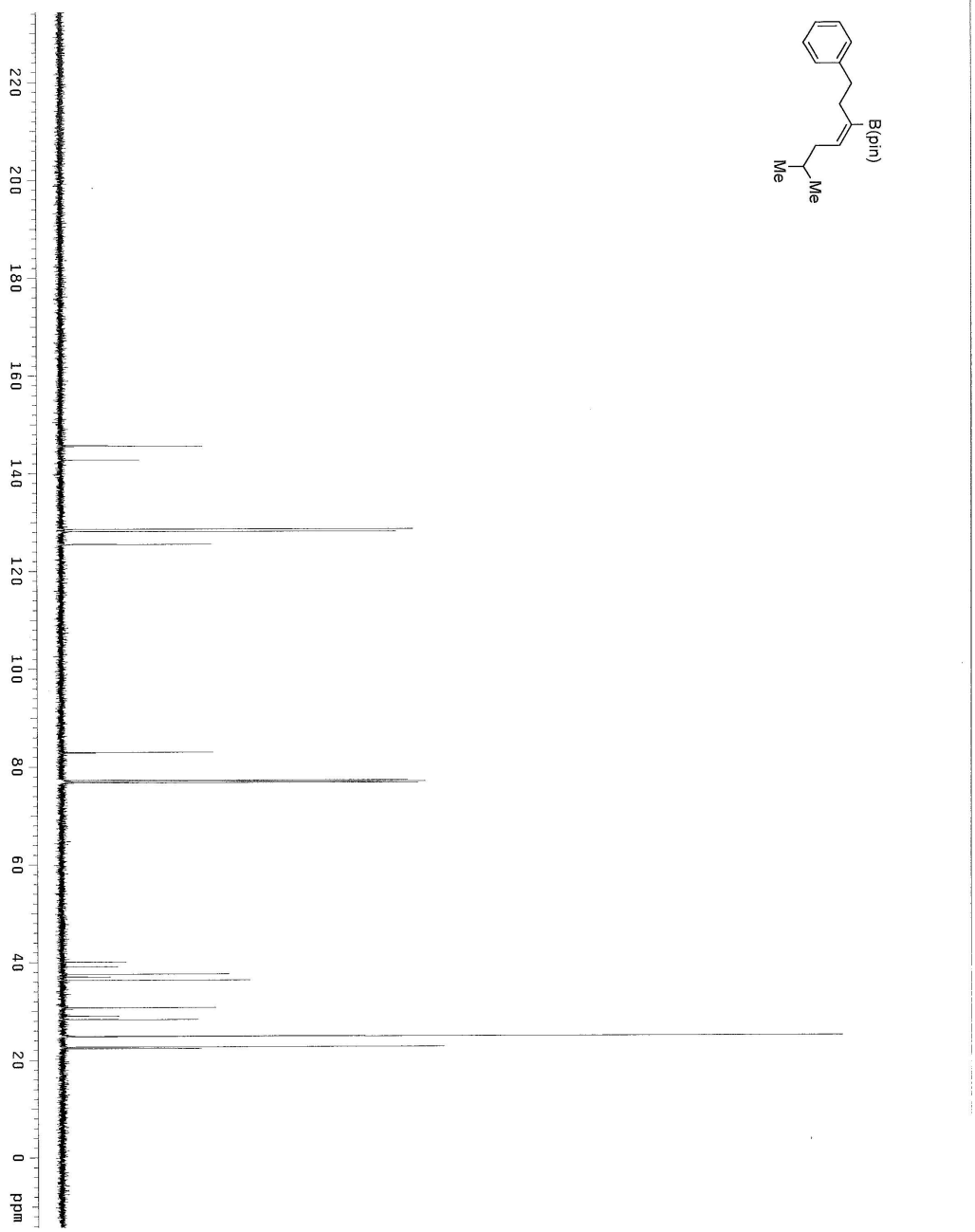

220
200
180
160
140
120
100
80
60
40
20
0
ppm

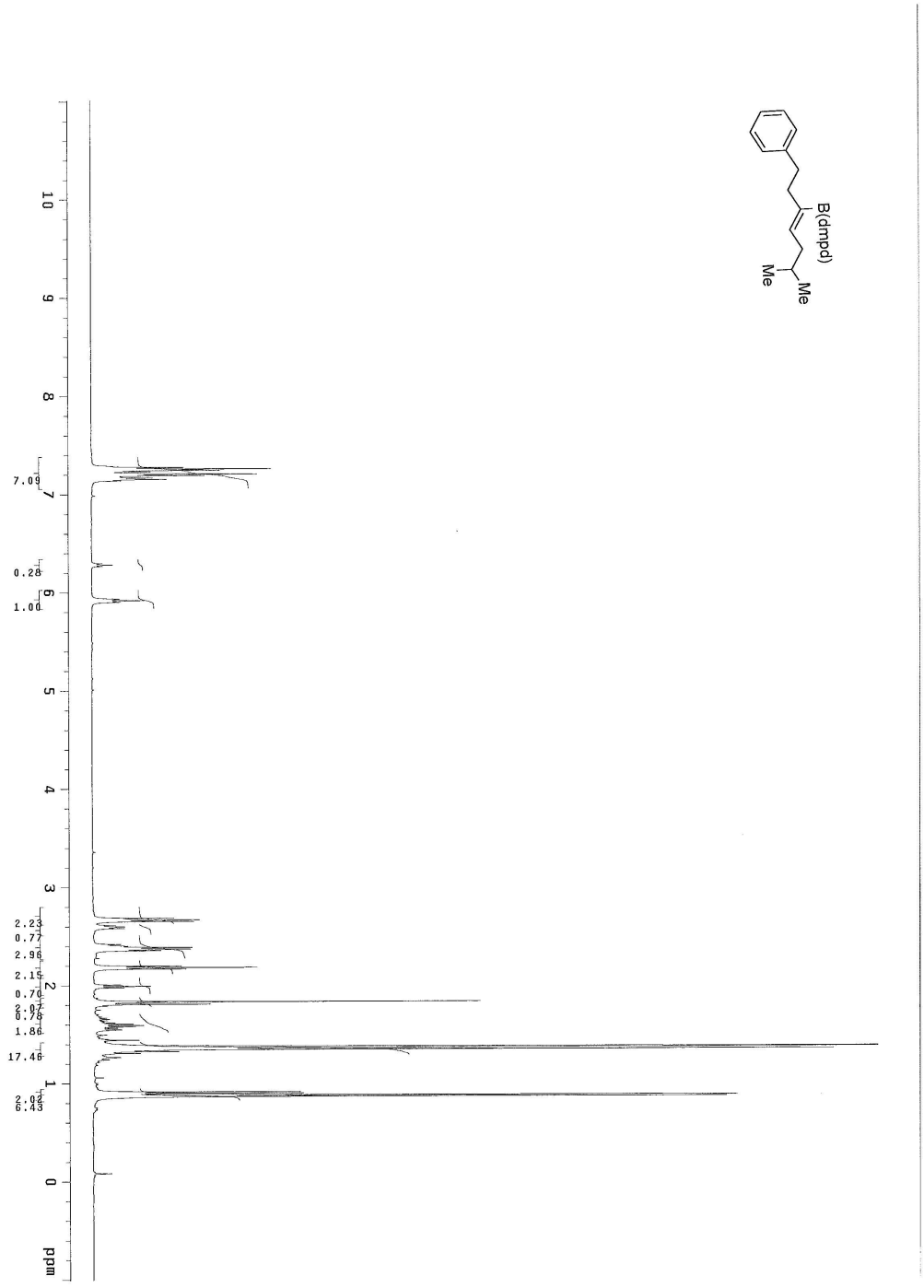

B(dmpd)
n-pentyl

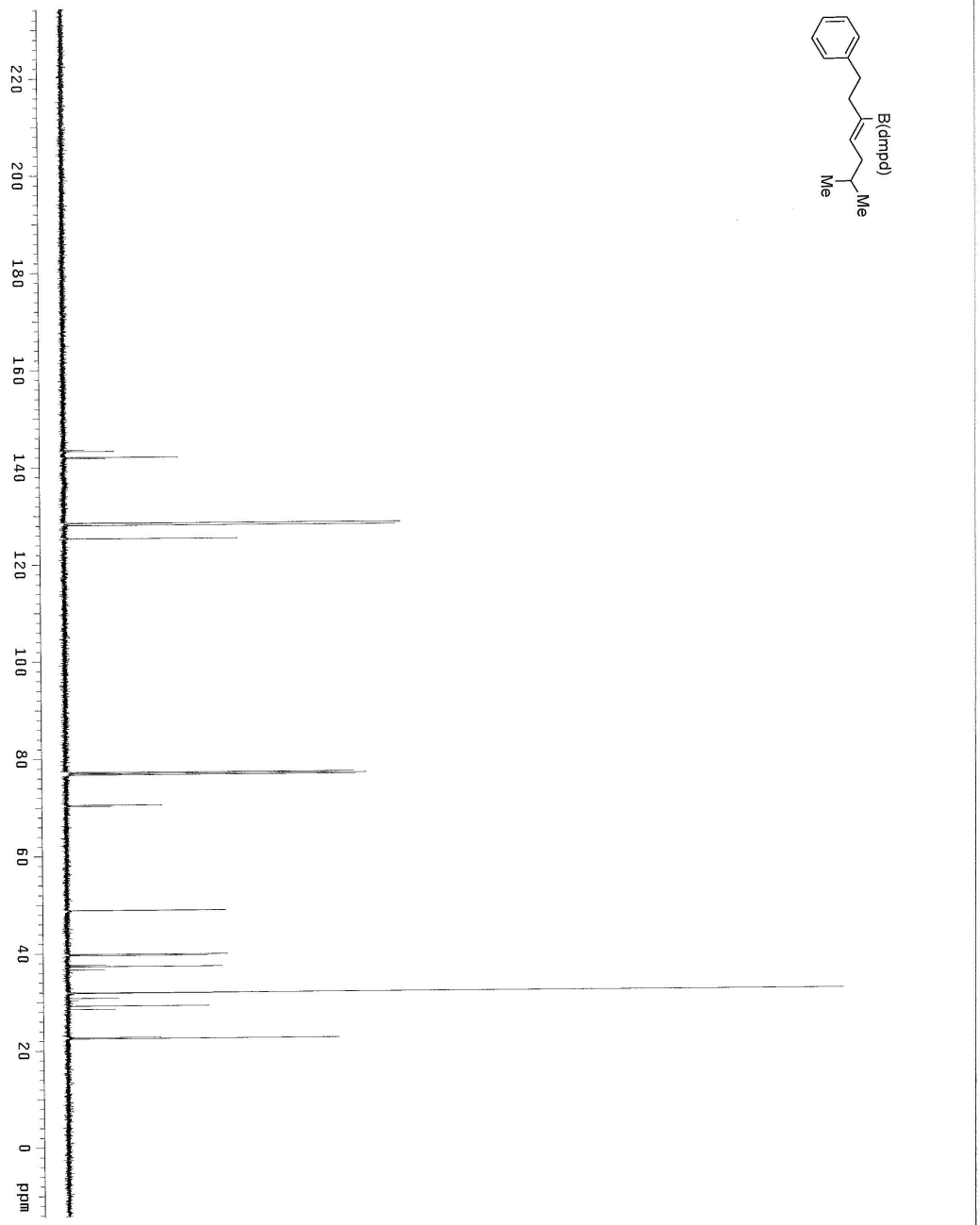

B(pin)
n-pentyl
F1 (ppm)
F2 (ppm)

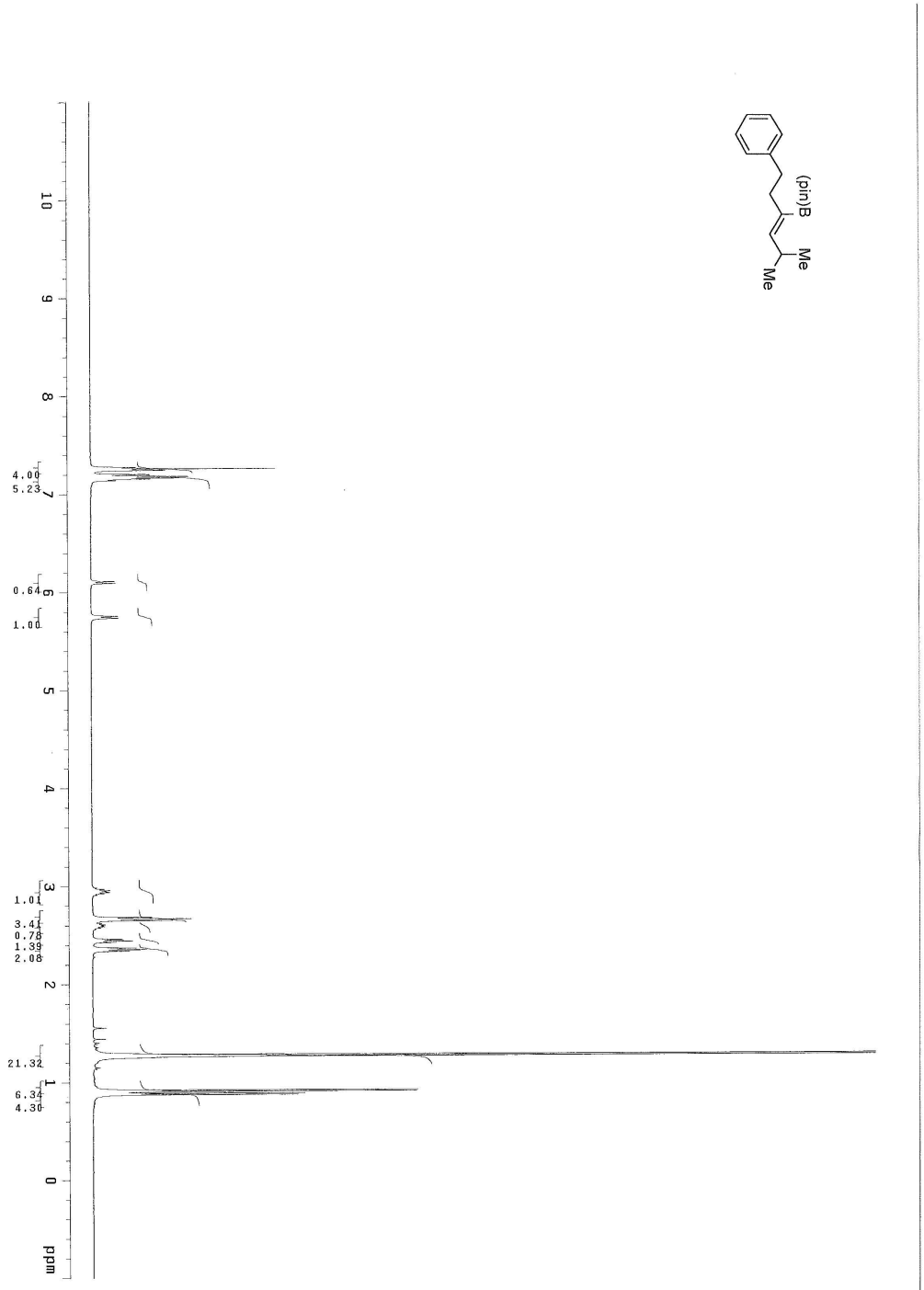

B(pin)
n-pentyl
F1 (ppm)
2.7
2.6
2.5
2.4
2.3
2.2
2.1
F2 (ppm)
6.3
6.2
6.1
6.0
5.9
5.8
5.7
5.6

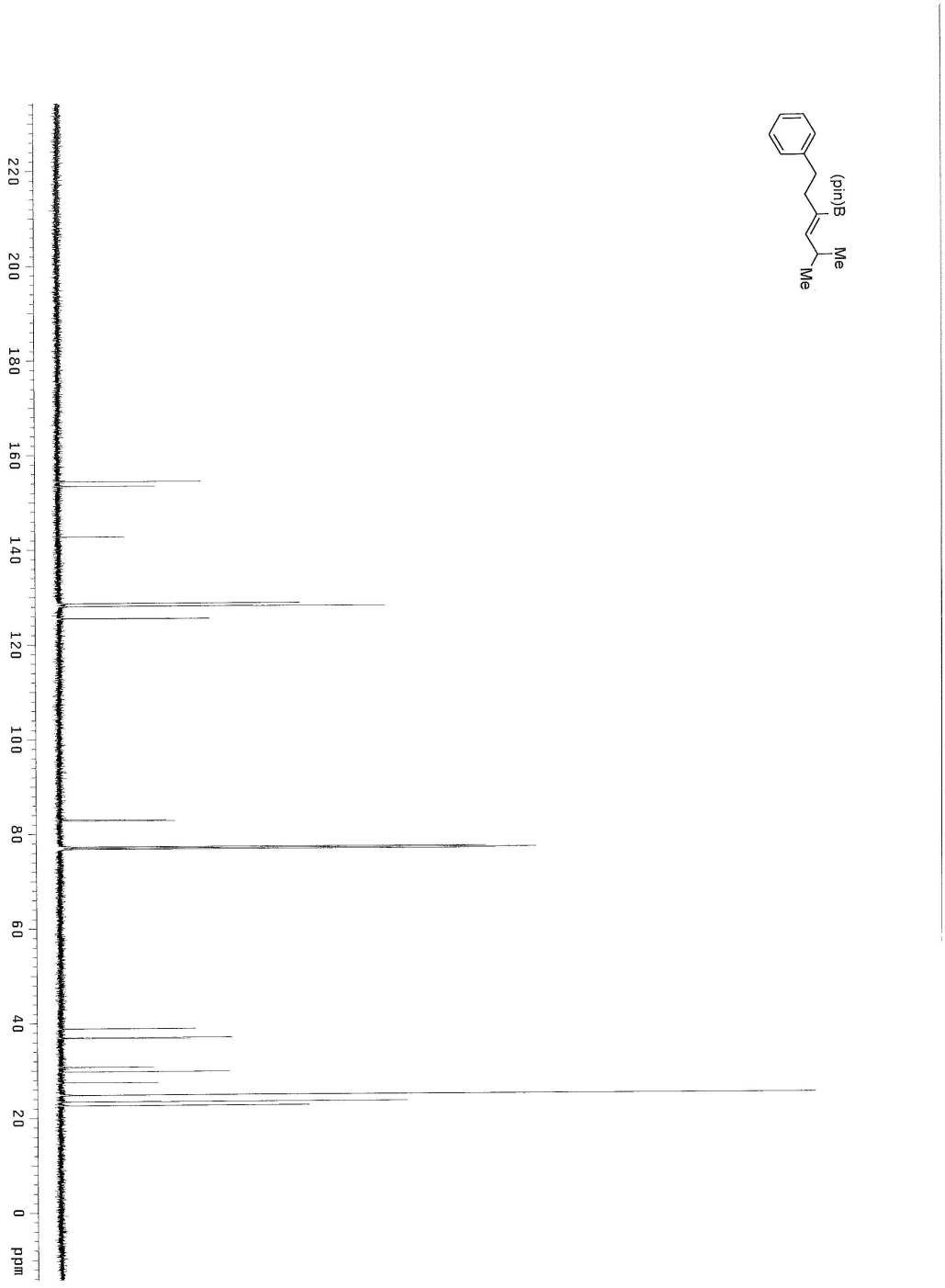

B(pin)
Me
Me
10
9
8
7
6
5
4
3
2
1
0
ppm
3.17
4.34
1.00
0.35
2.93
2.88
0.77
2.13
1.74
17.71
8.75

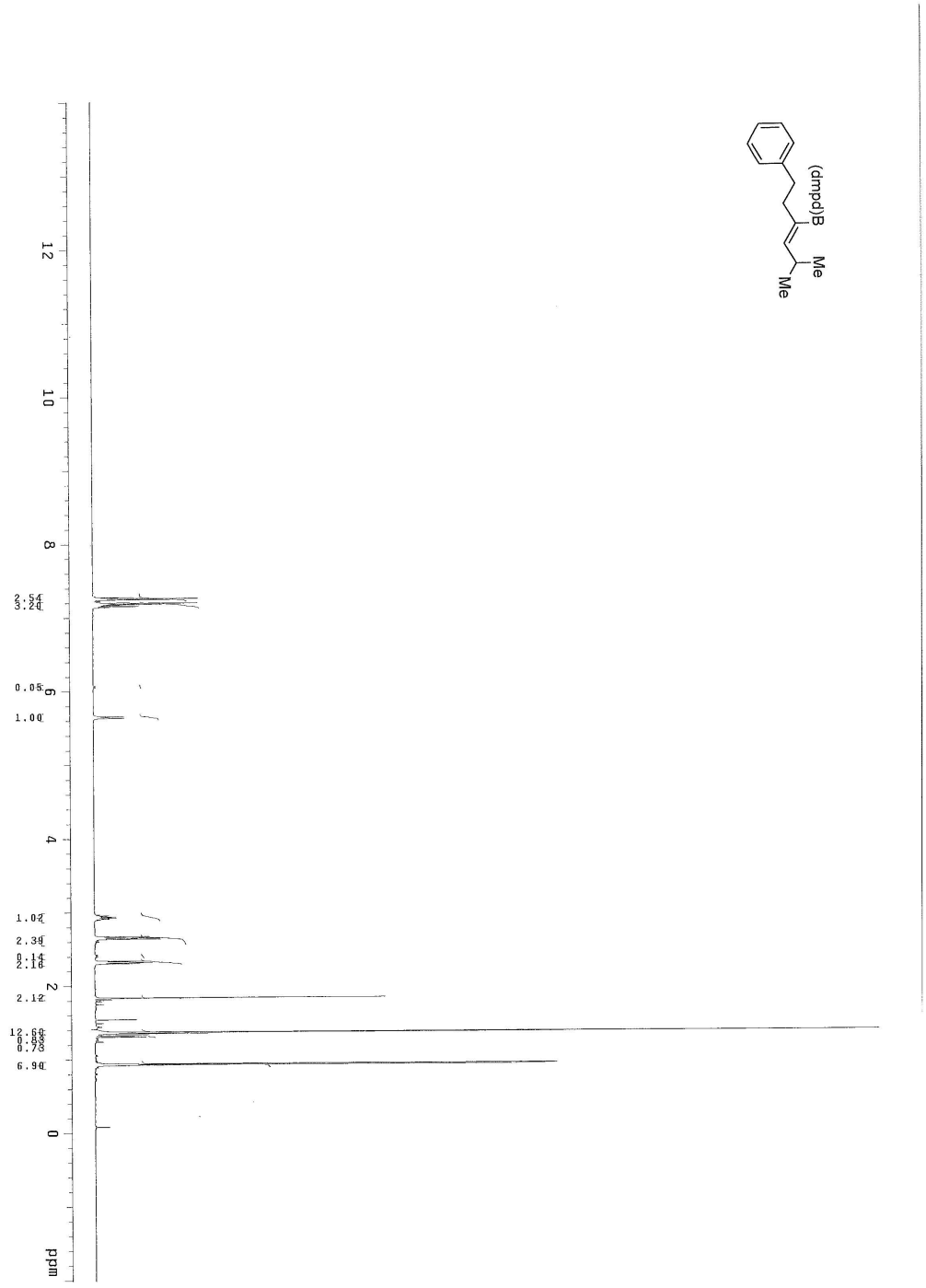

B(pin)
Me
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm

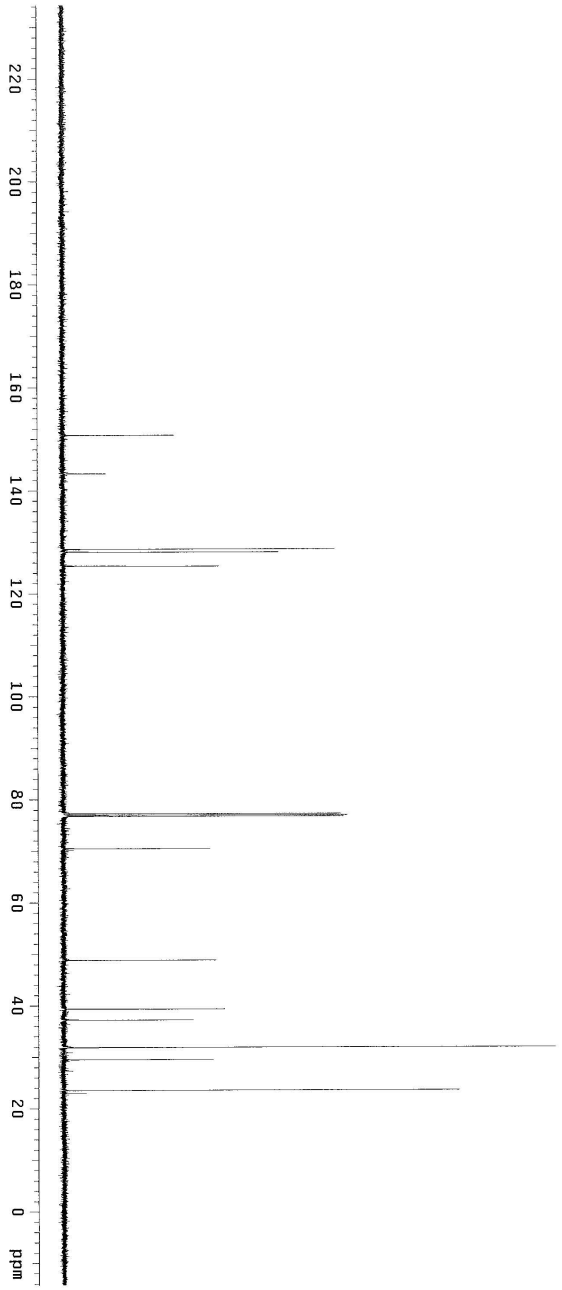

B(dmpd)
Me
Me
7.08
0.28
1.00
2.23
0.77
2.98
2.15
0.70
2.07
0.78
1.86
17.46
2.02
6.43
ppm

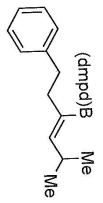

B(dmpd)
Me
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm

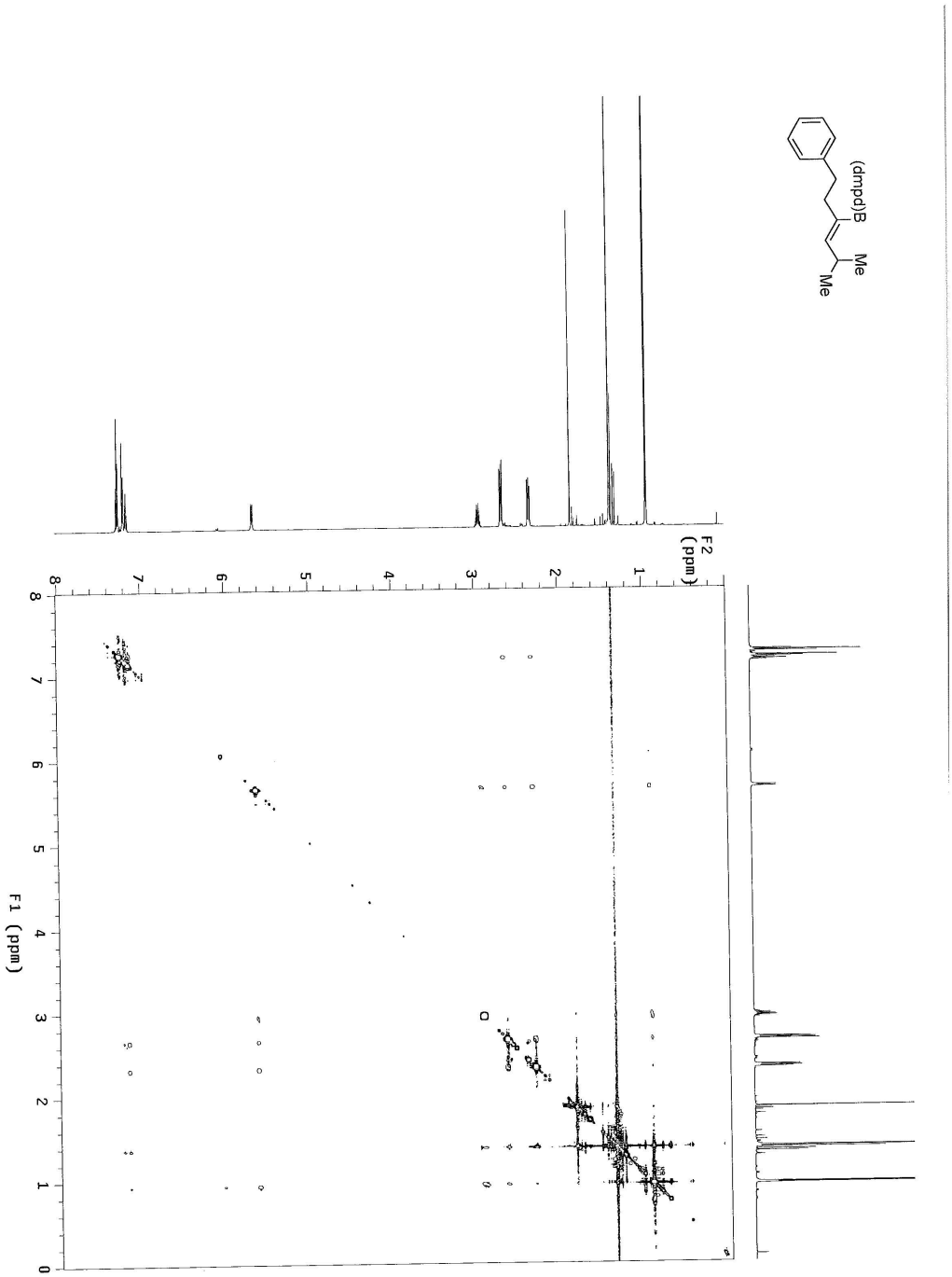

(pin)B
Me
Me
4.00
5.23
0.64
1.00
1.01
3.41
0.78
1.39
2.08
21.32
6.34
4.30
ppm

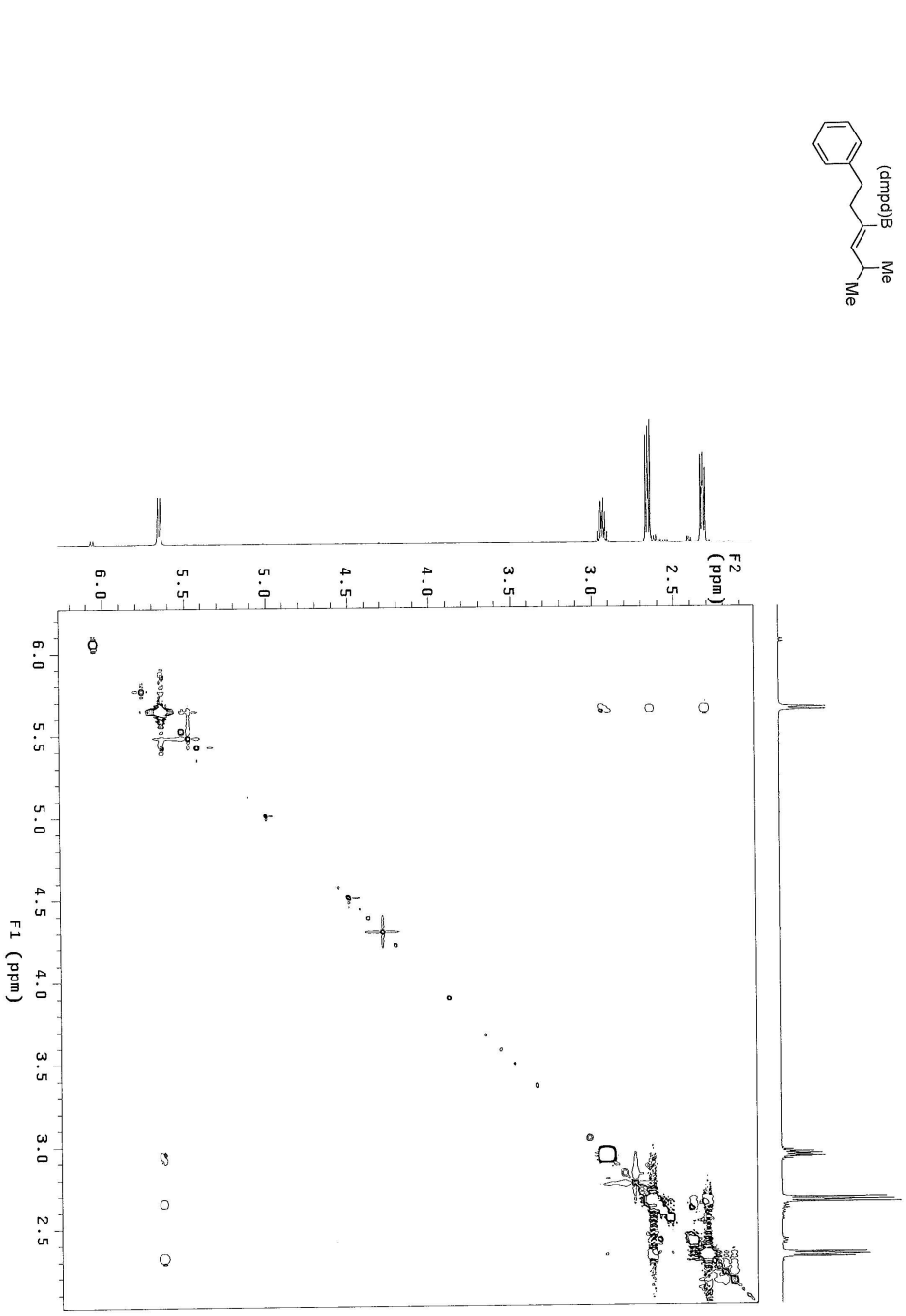

(pin)B
Me
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm

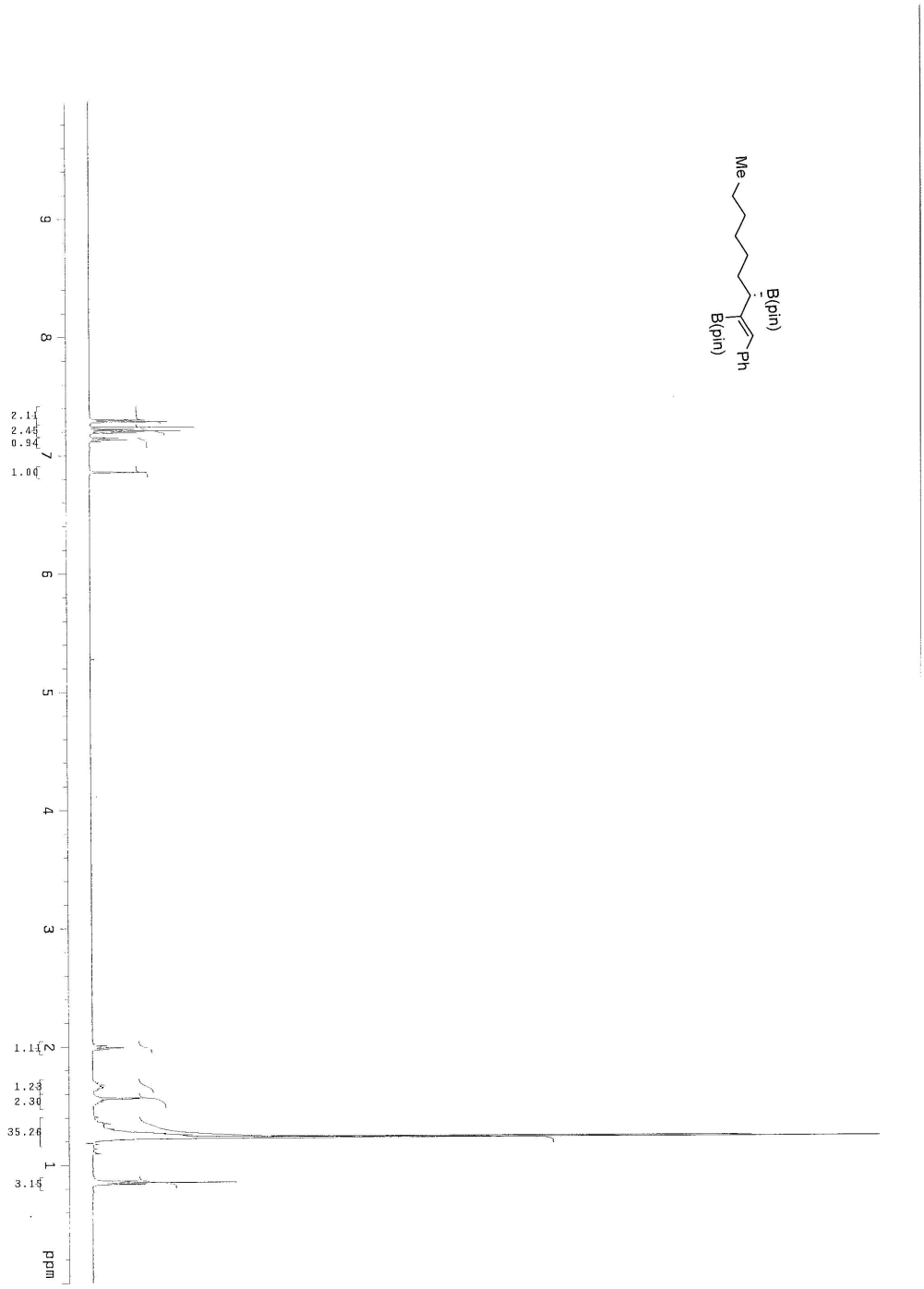

(dmpd)B
Me
Me
12
10
8
6
4
2
0
ppm
2.54
3.24
0.05
1.00
1.02
2.36
0.14
2.16
2.12
12.69
6.90

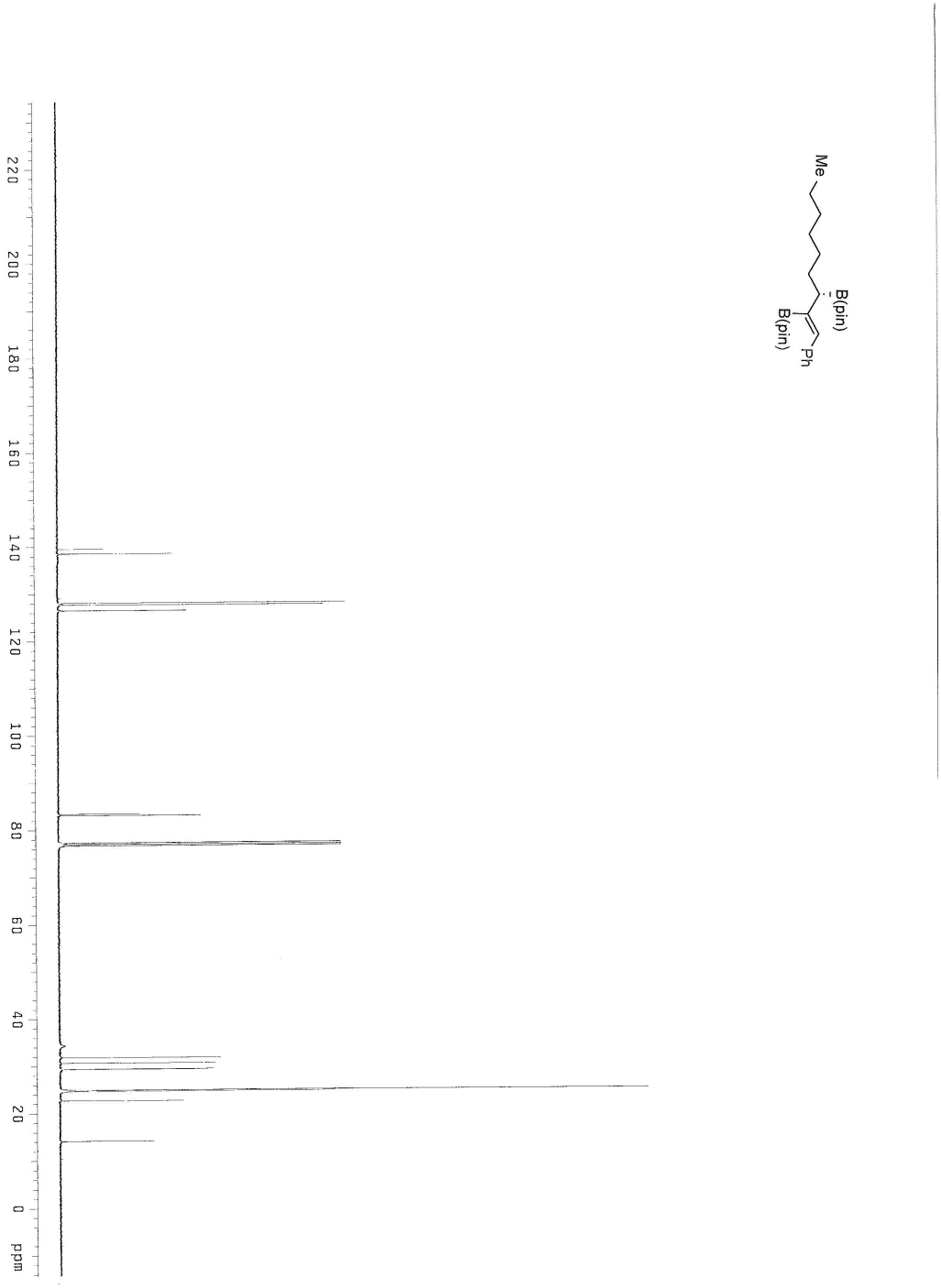

220
200
180
160
140
120
100
80
60
40
20
0
ppm

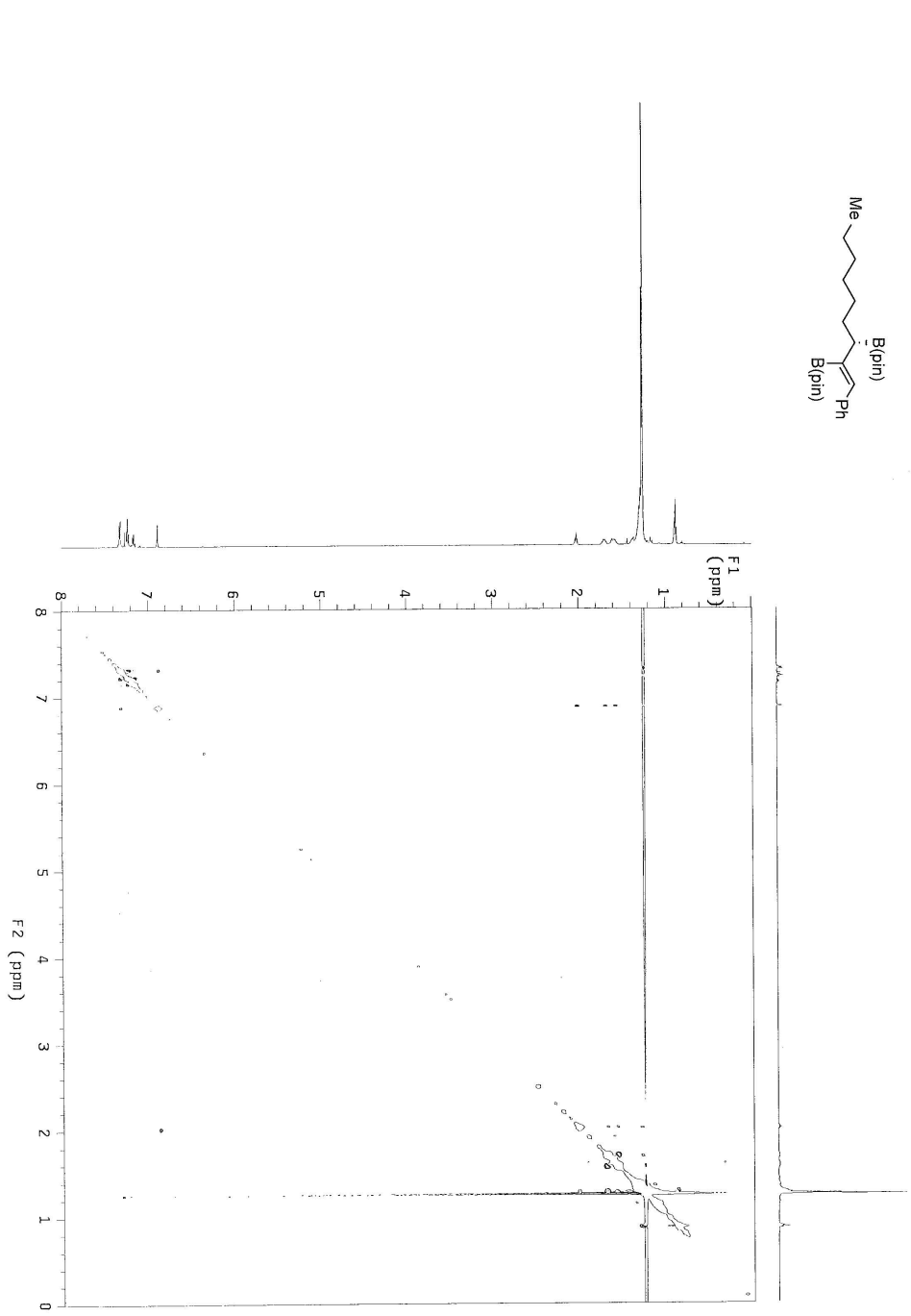

(dmpd)B
Me
Me

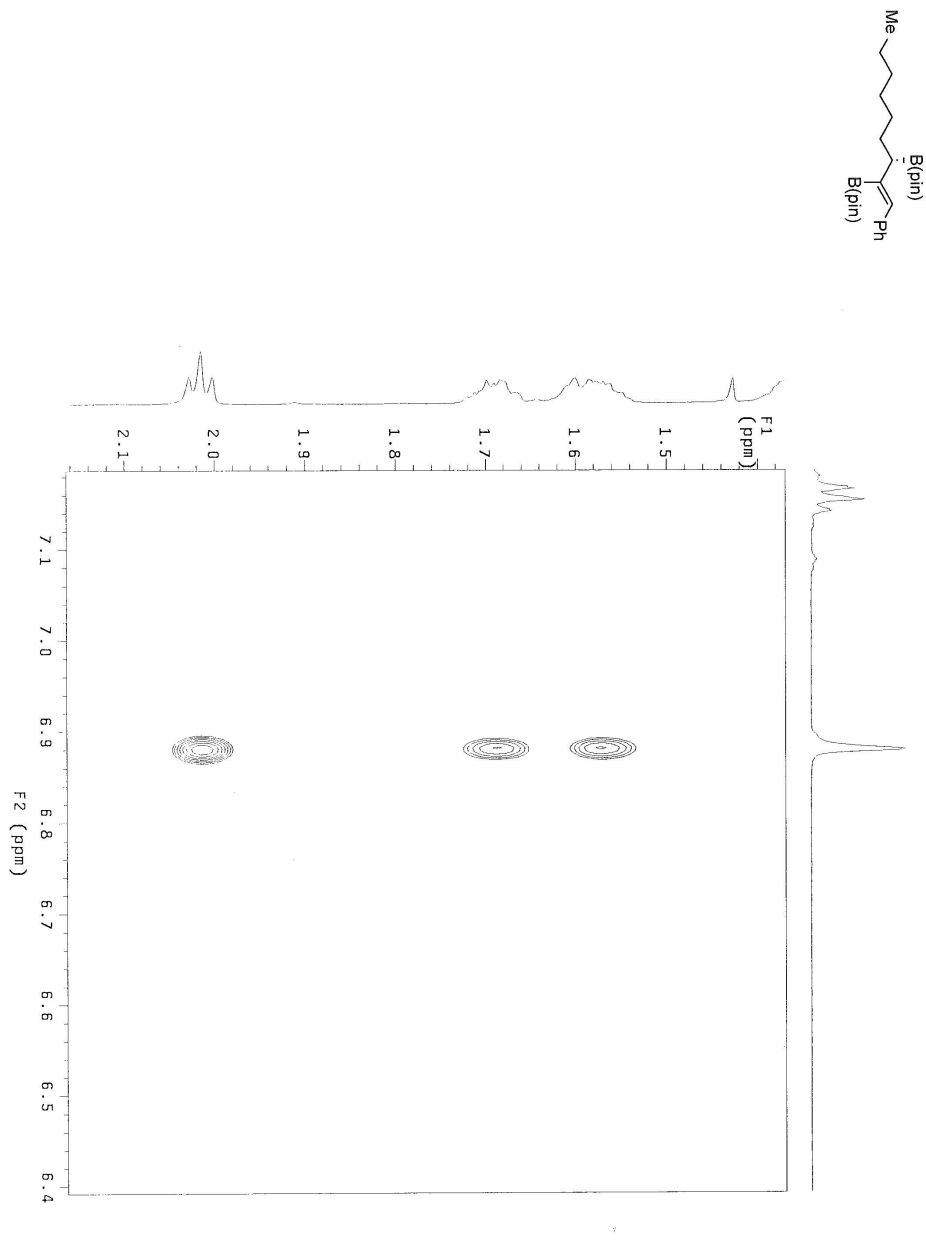

(dmpd)B
Me
Me
F2 (ppm)
F1 (ppm)

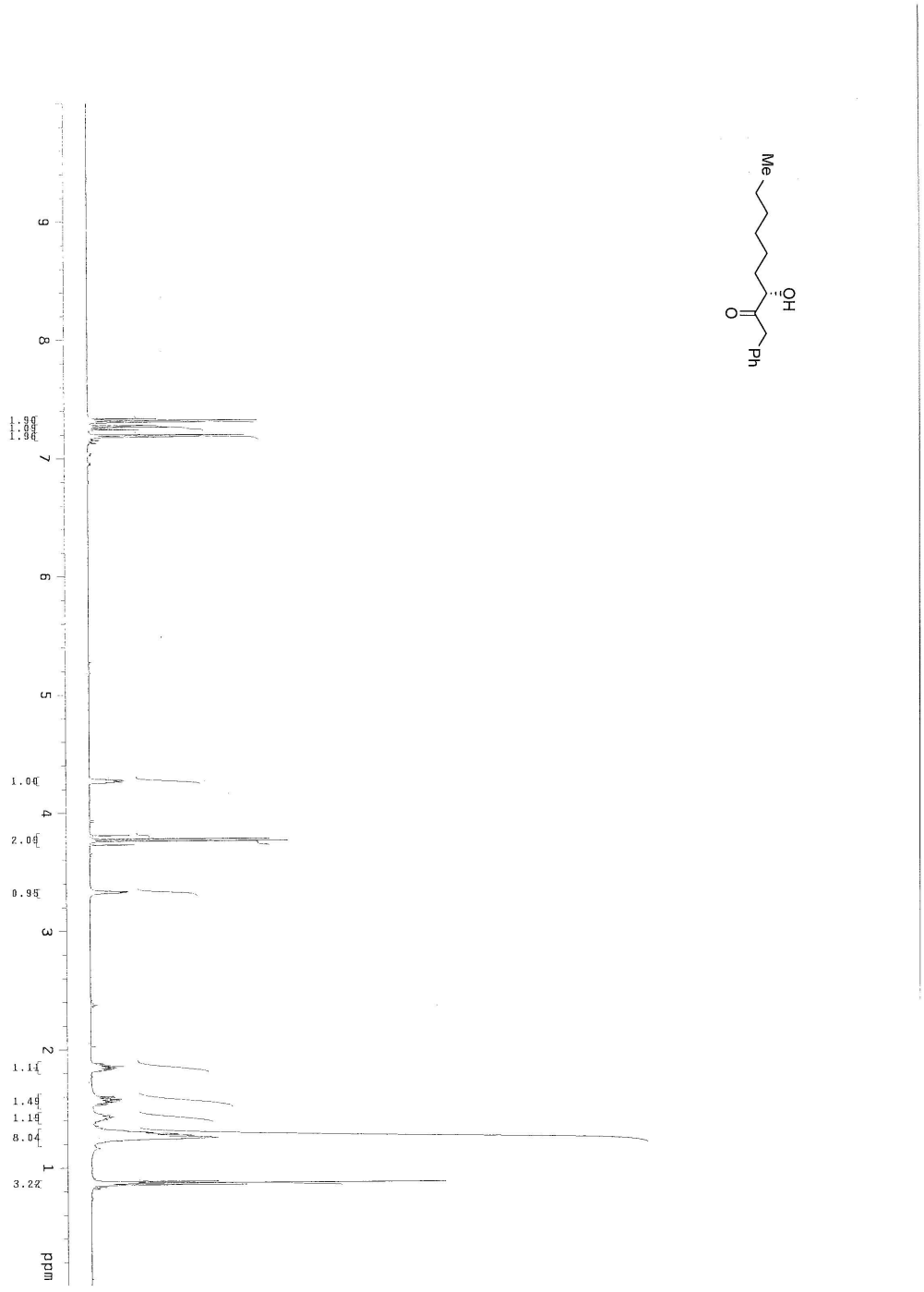

(dmpd)B
Me
Me
F2 (ppm)
F1 (ppm)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5

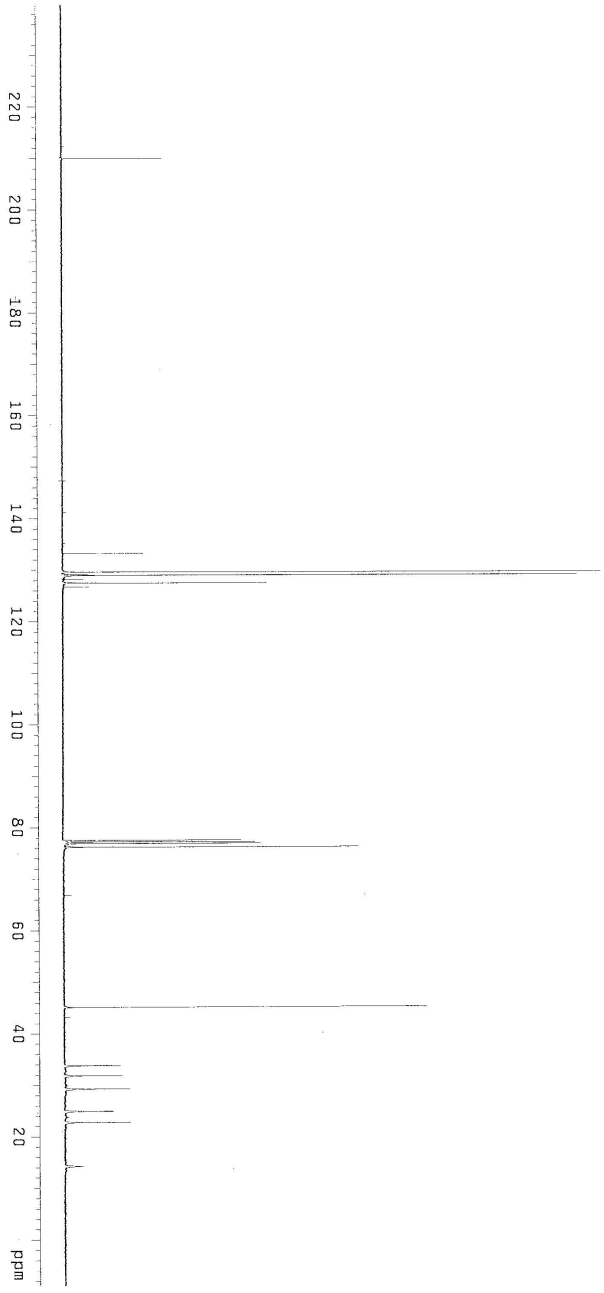

Me
B(pin)
B(pin)
Ph
2.11
2.45
0.94
1.00
1.14
1.23
2.30
35.26
3.15
ppm

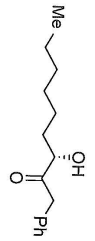

Me
B(pin)
B(pin)
Ph
220
200
180
160
140
120
100
80
60
40
20
0
ppm

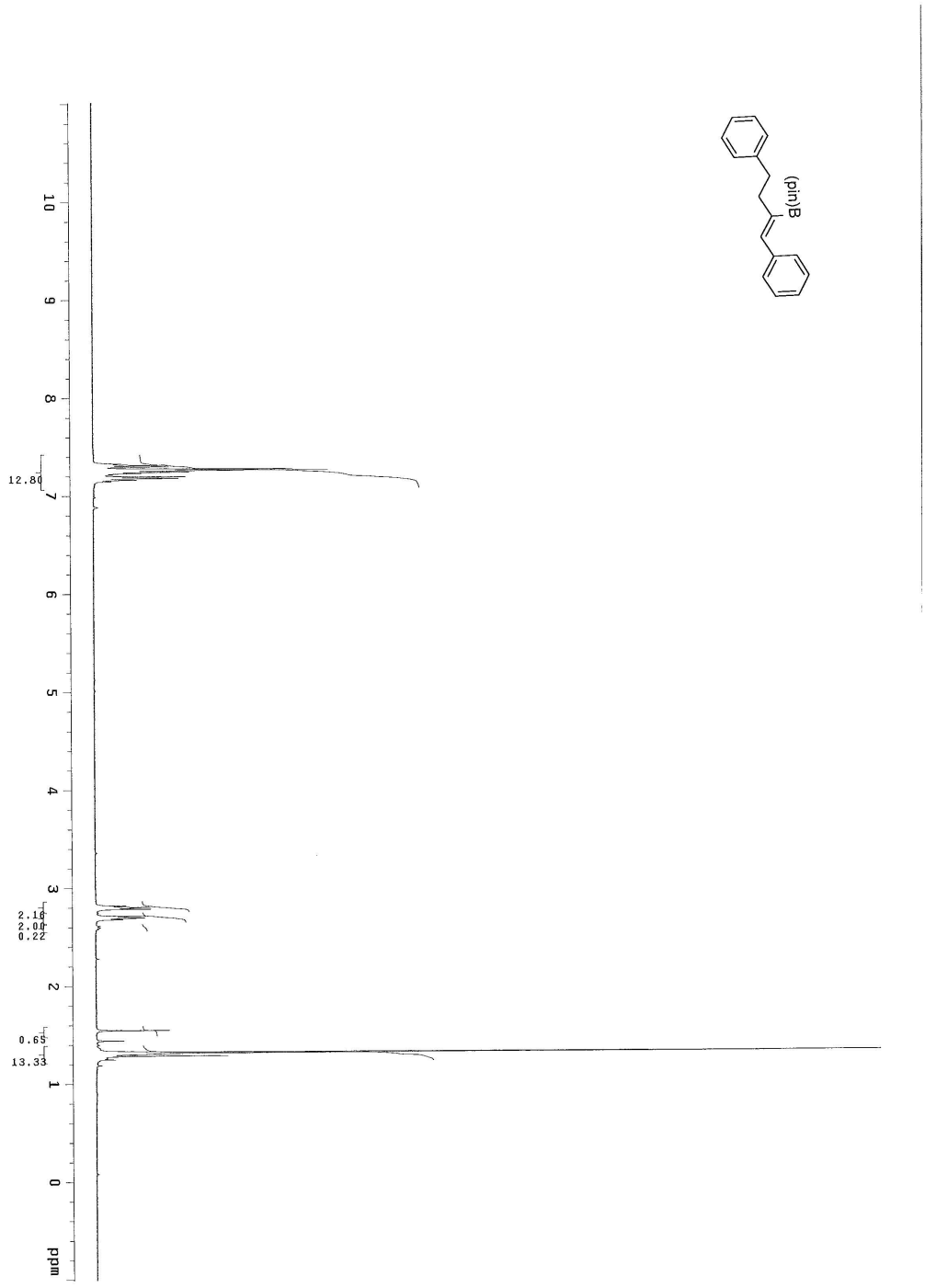

Me
B(pin)
B(pin)
Ph
F1 (ppm)
F2 (ppm)

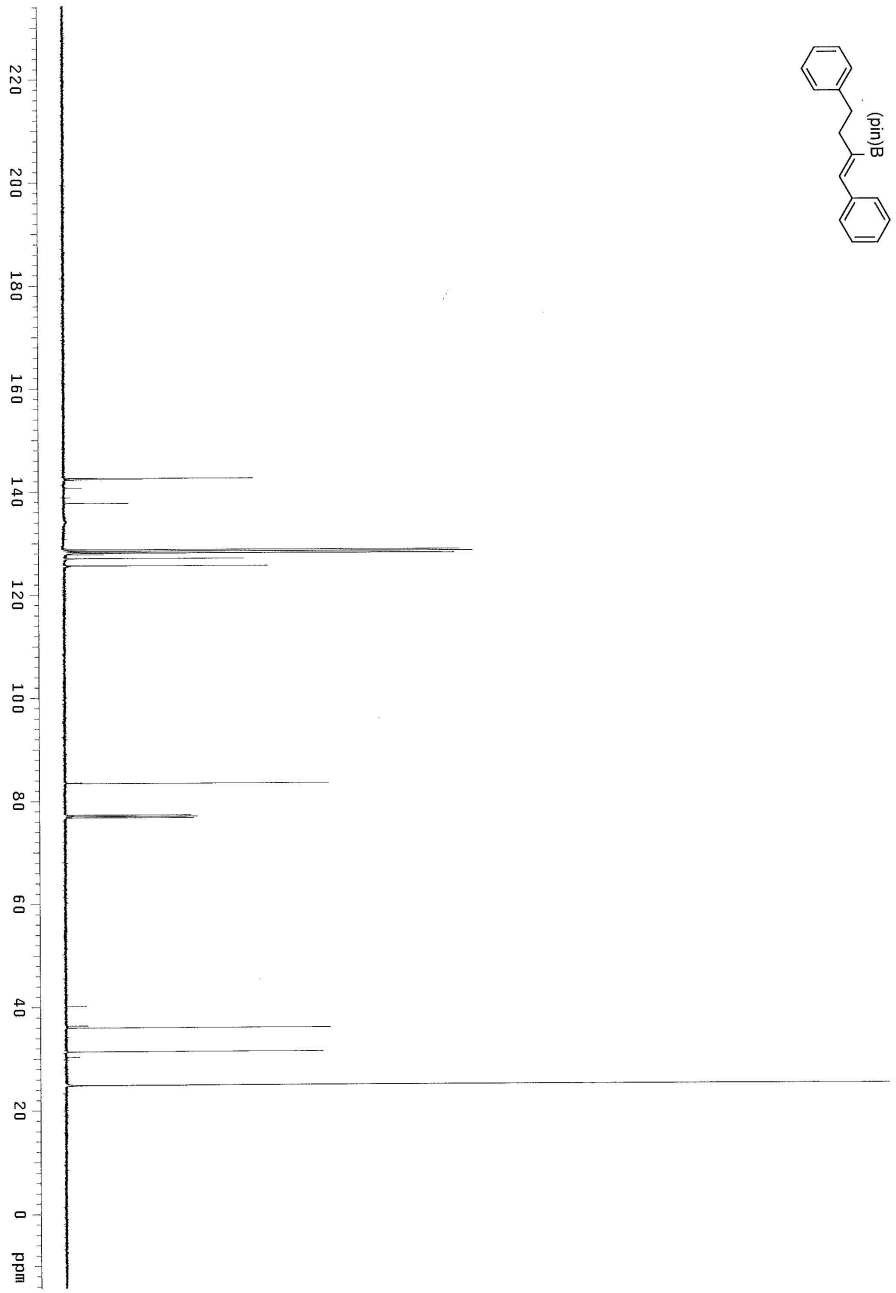

Me
B(pin)
B(pin)
Ph
F1 (ppm)
2.1
2.0
1.9
1.8
1.7
1.6
1.5
F2 (ppm)
7.1
7.0
6.9
6.8
6.7
6.6
6.5
6.4

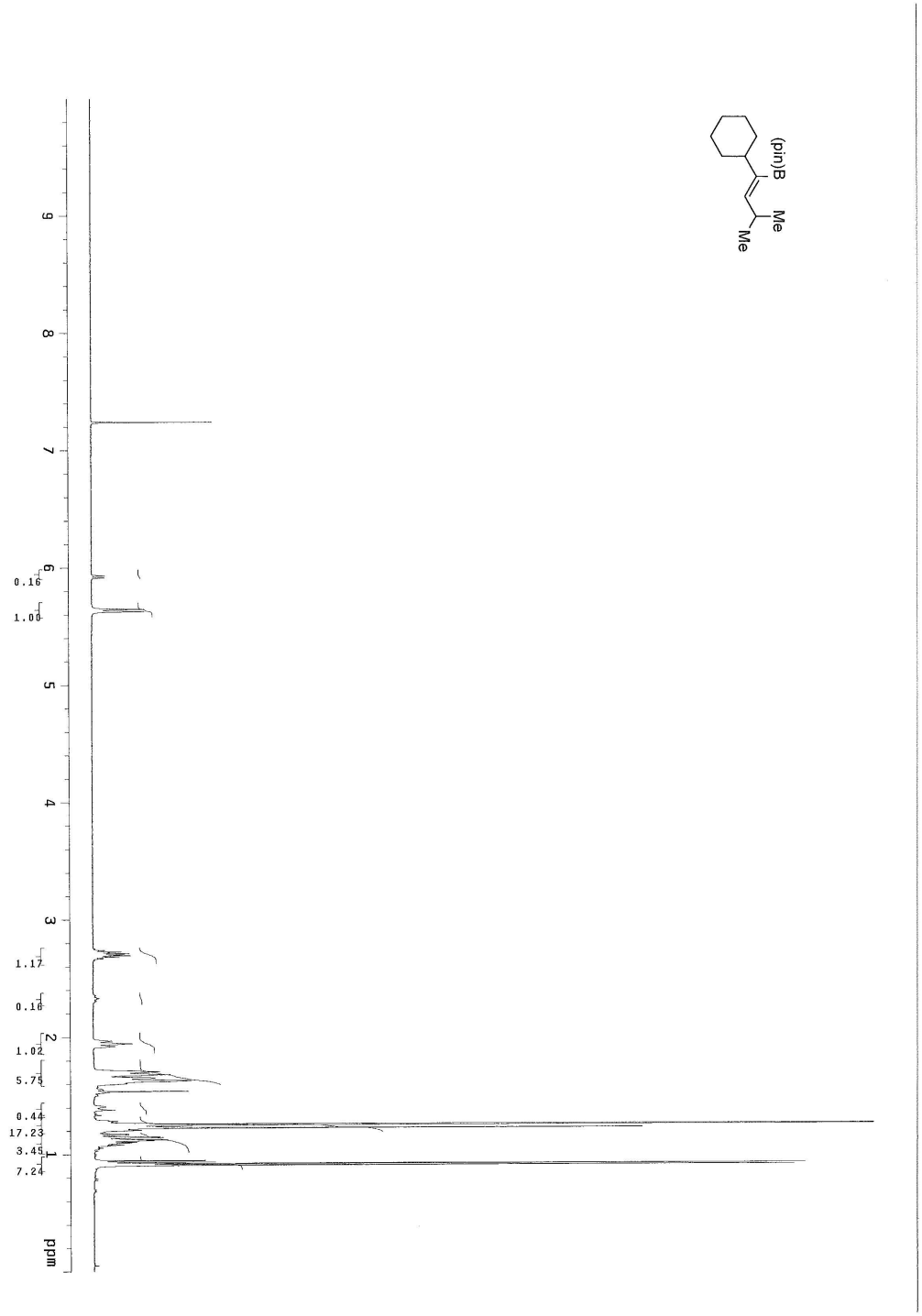

Me
OH
O
Ph
1.00
2.06
0.95
1.14
1.49
1.19
8.04
3.22
ppm

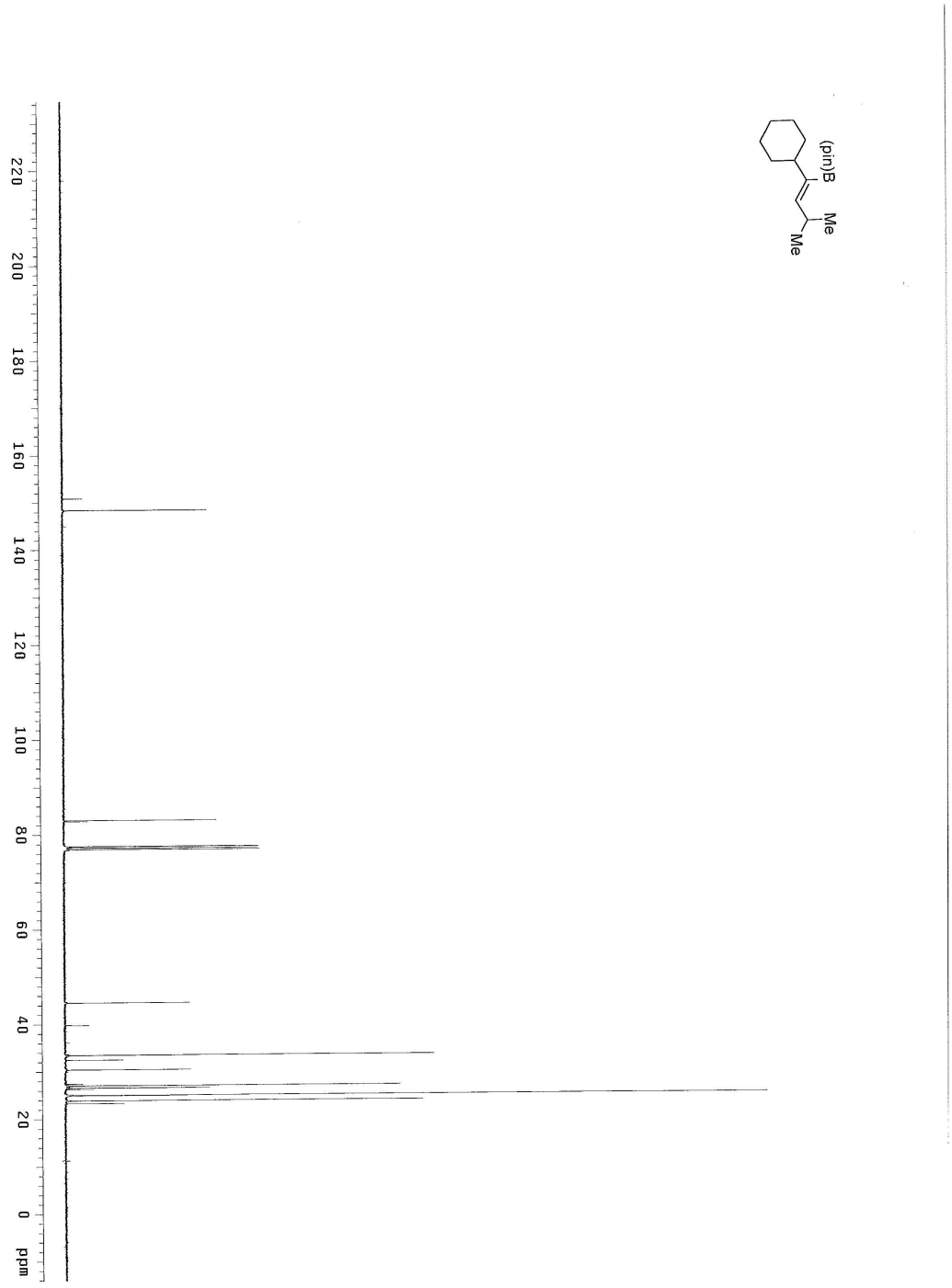

220
200
180
160
140
120
100
80
60
40
20
ppm

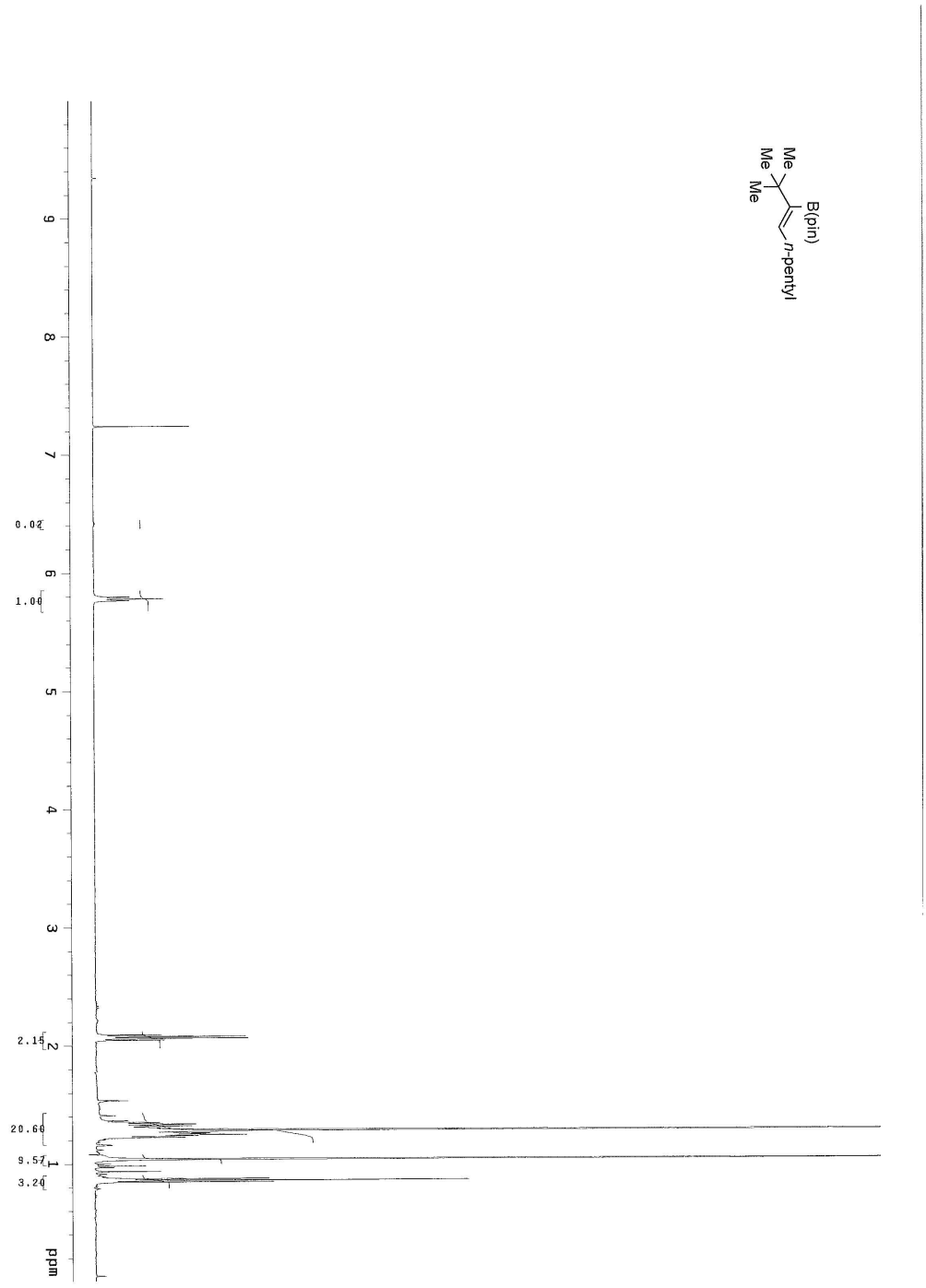

Me
OH
O
Ph

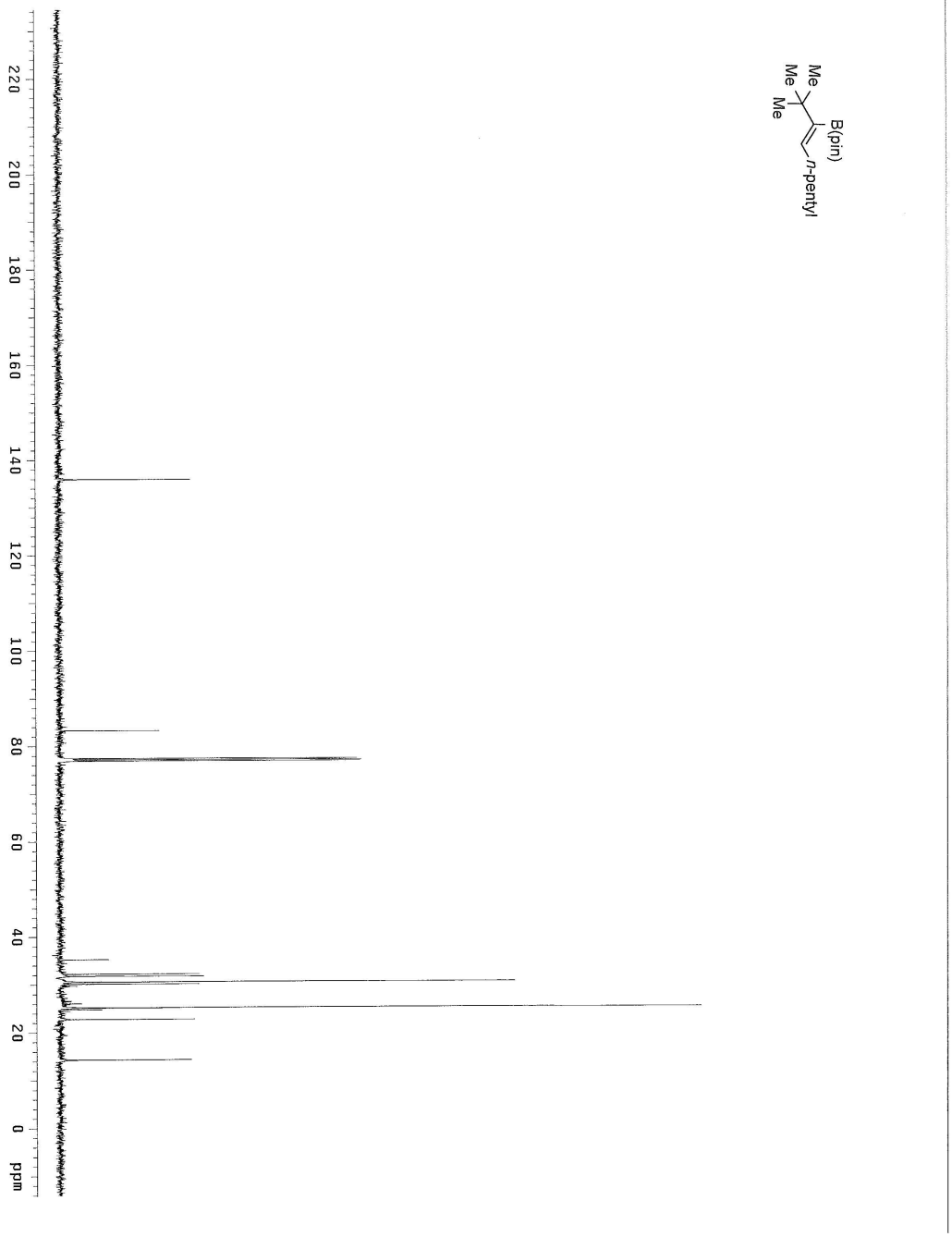

(pin)B
12.80
2.16
2.05
0.22
0.65
13.33
ppm

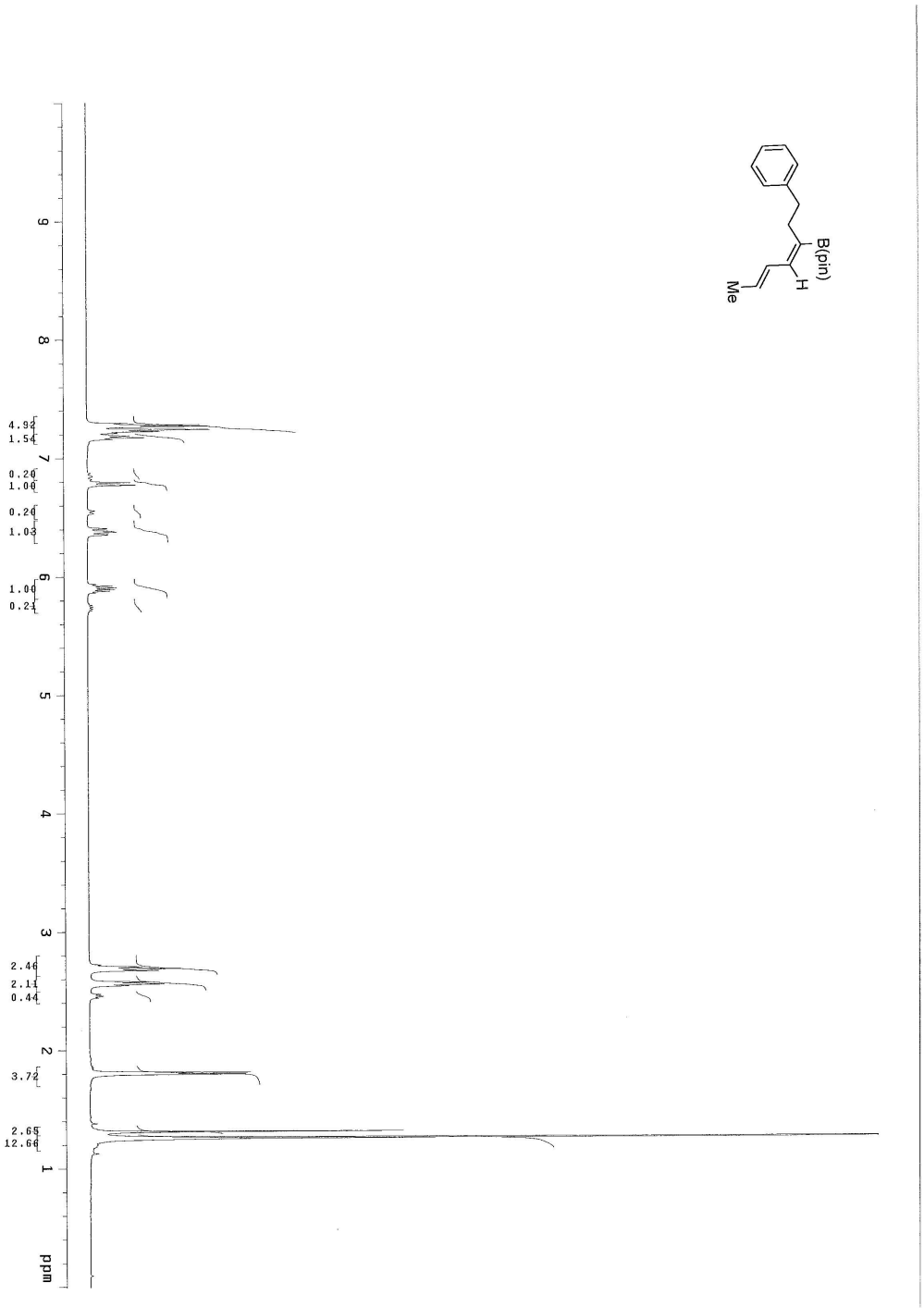

(pin)B
220
200
180
160
140
120
100
80
60
40
20
0
ppm

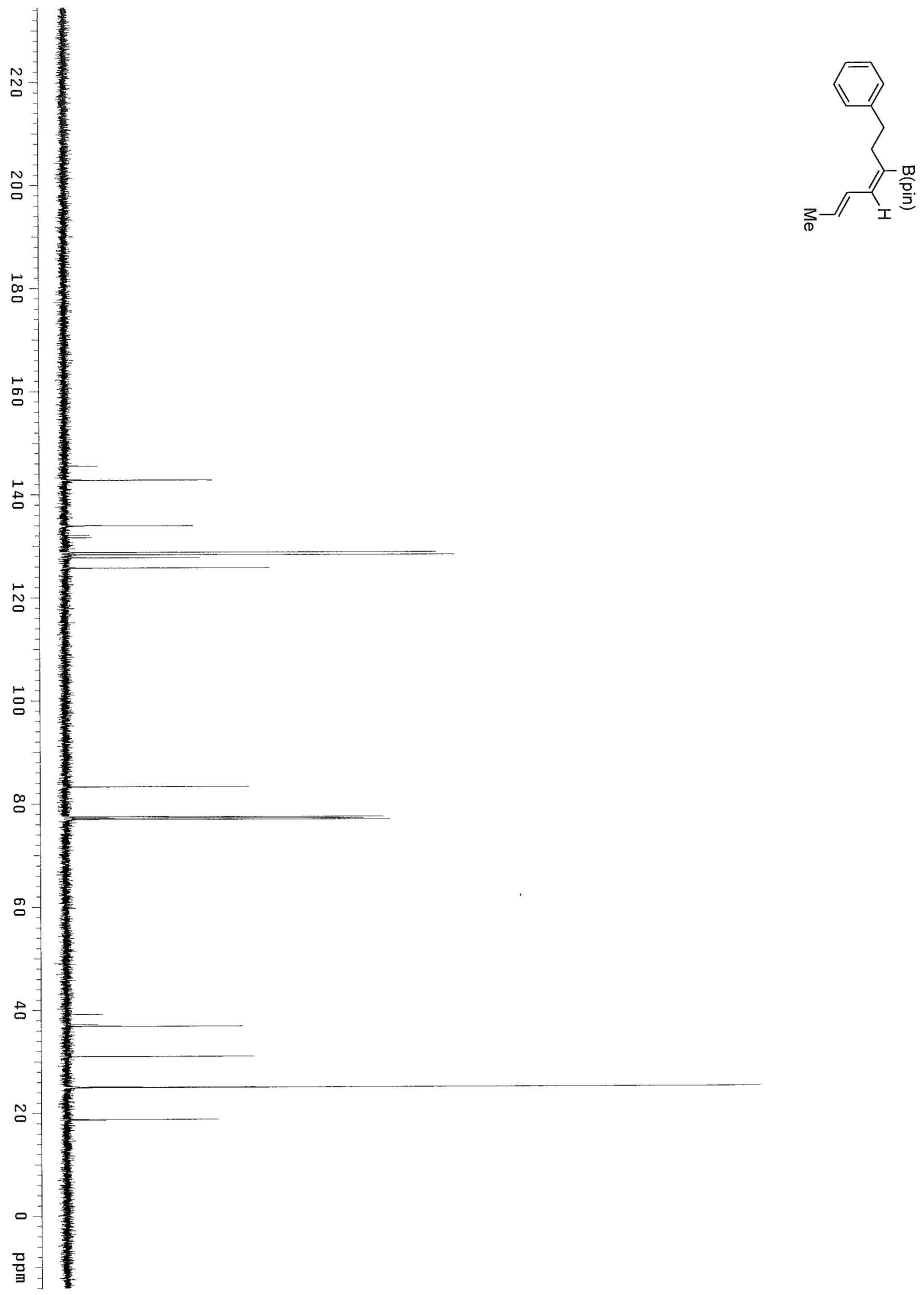

(pin)B
Me
Me
9
8
7
6
5
4
3
2
1
ppm
0.16
1.00
1.17
0.16
1.02
5.75
0.44
17.23
3.45
7.24

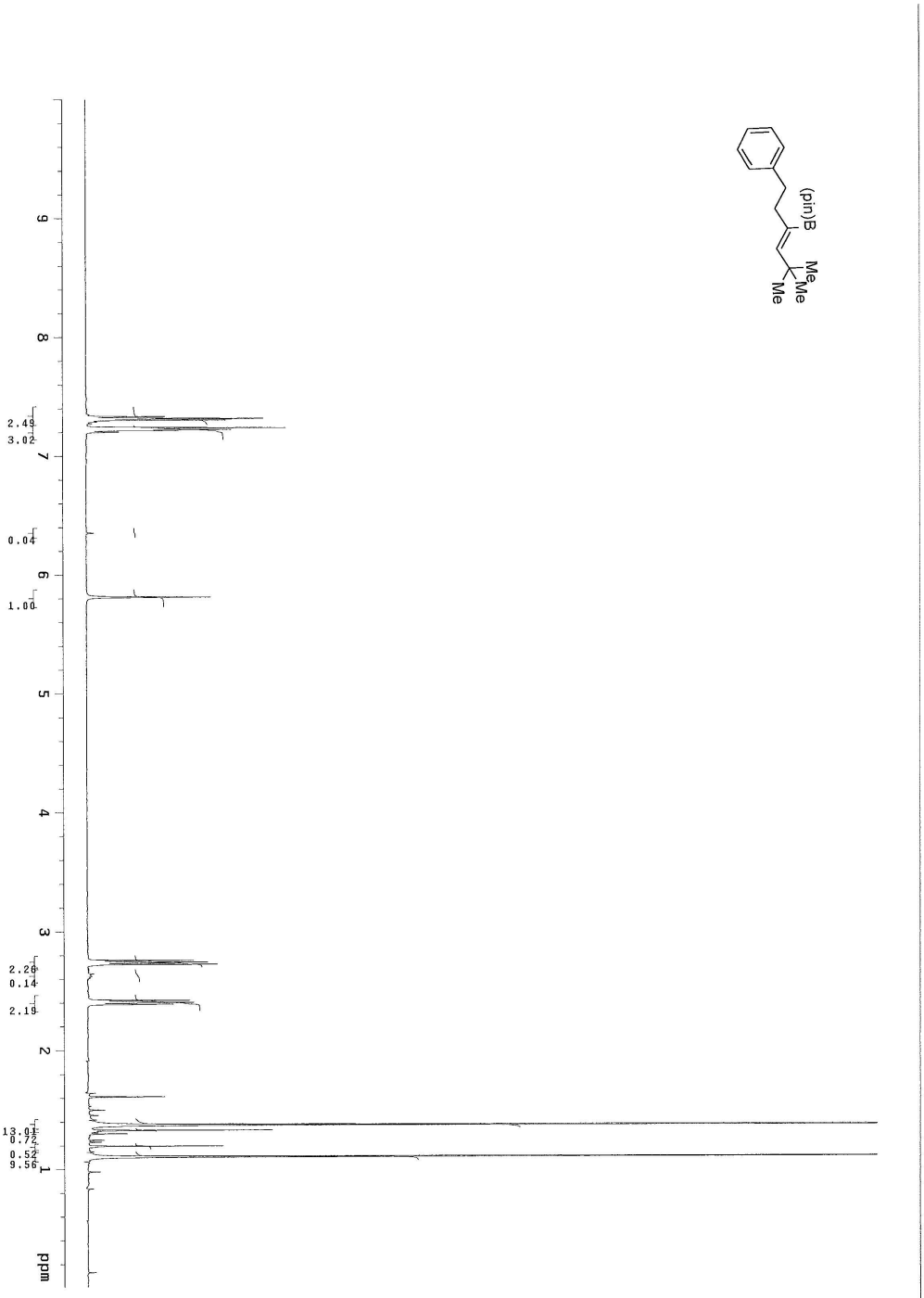

(pin)B
Me
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm

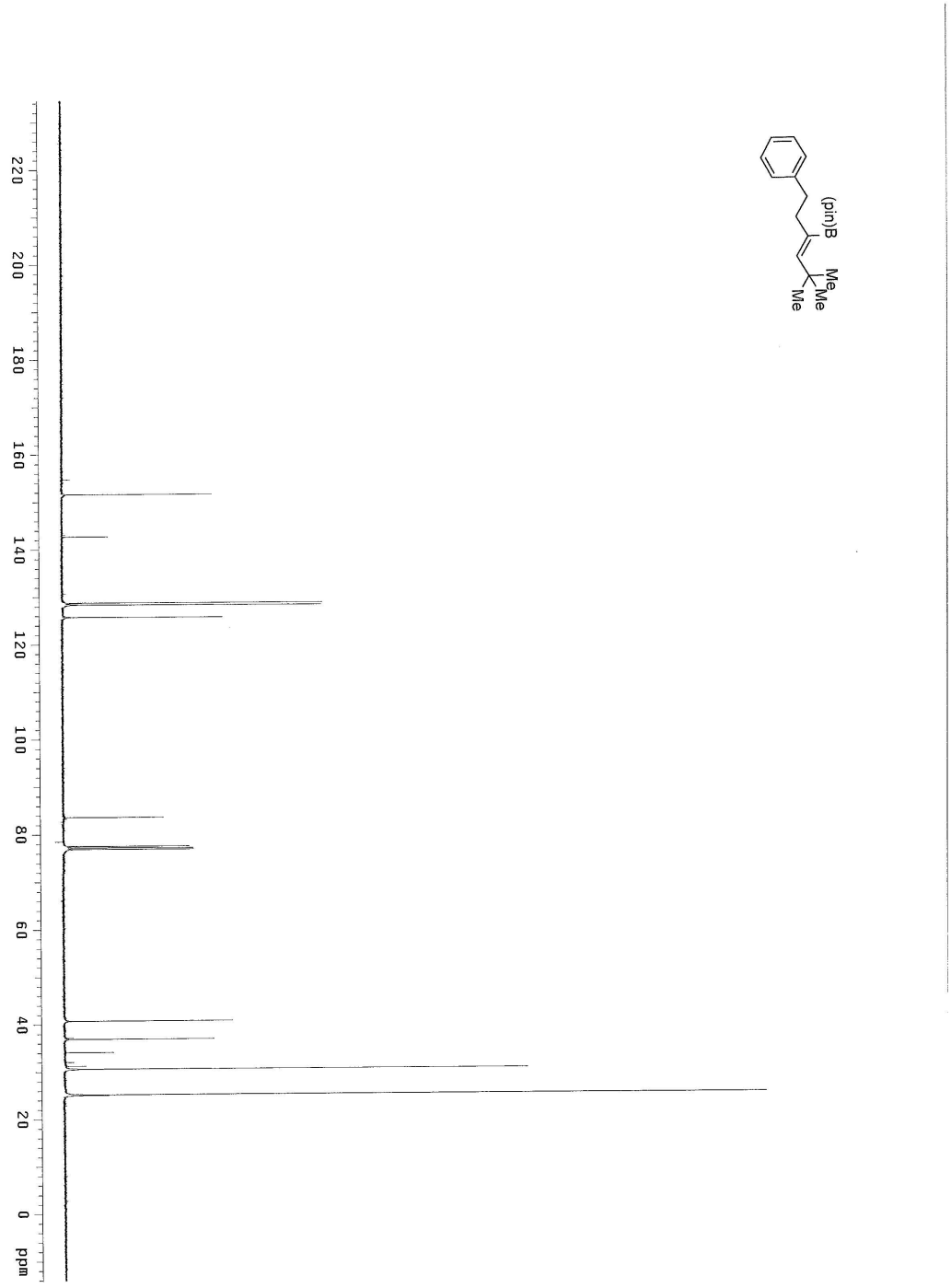

Me
Me
Me
B(pin)
n-pentyl
0.02
1.00
2.15
20.60
9.57
3.20
ppm

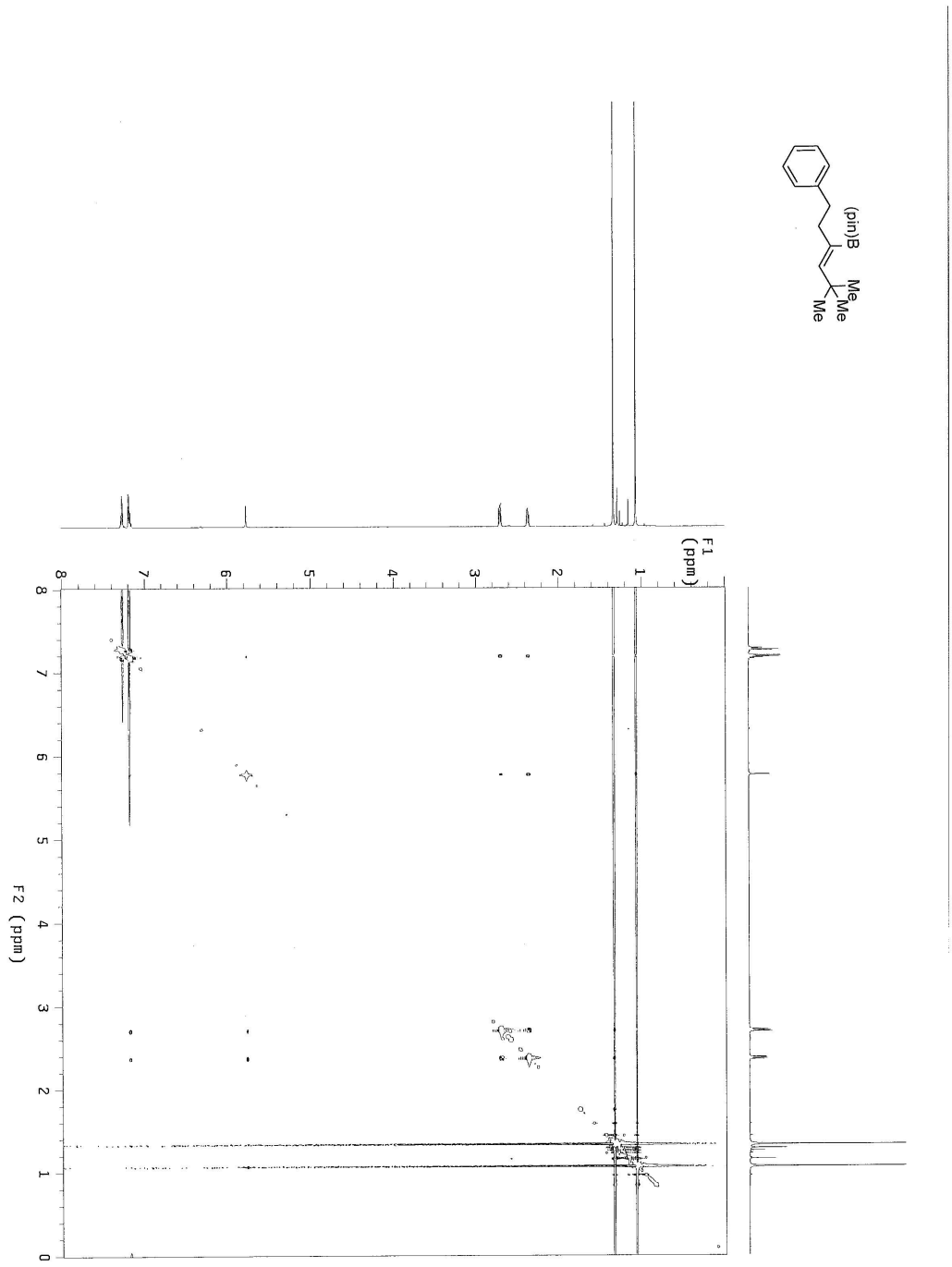

Me
Me
Me
B(pin)
n-pentyl
220
200
180
160
140
120
100
80
60
40
20
0
ppm

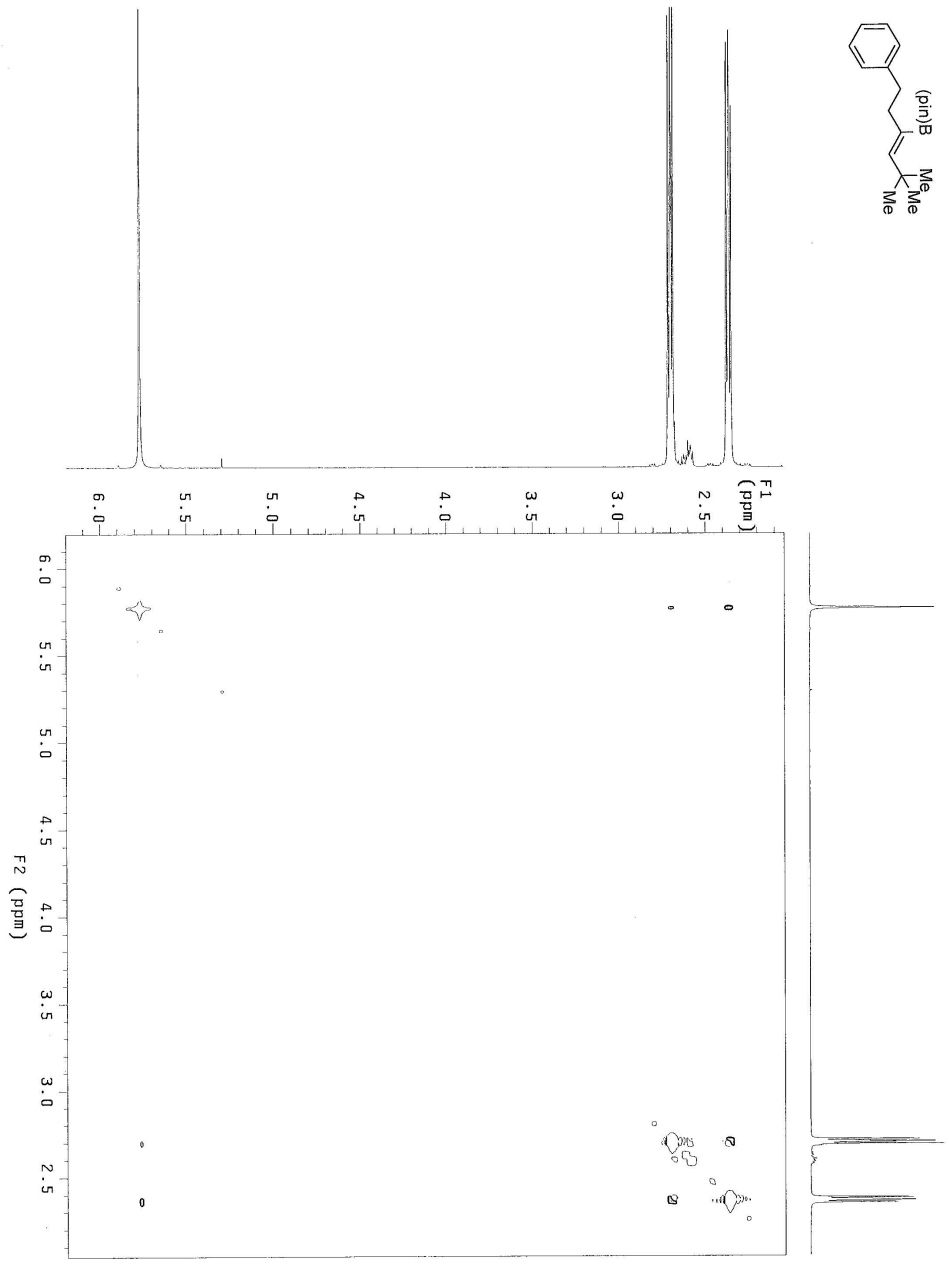

B(pin)
H
Me
4.92
1.54
0.20
1.06
0.20
1.03
1.00
0.21
2.46
2.11
0.44
3.72
2.65
12.66
ppm

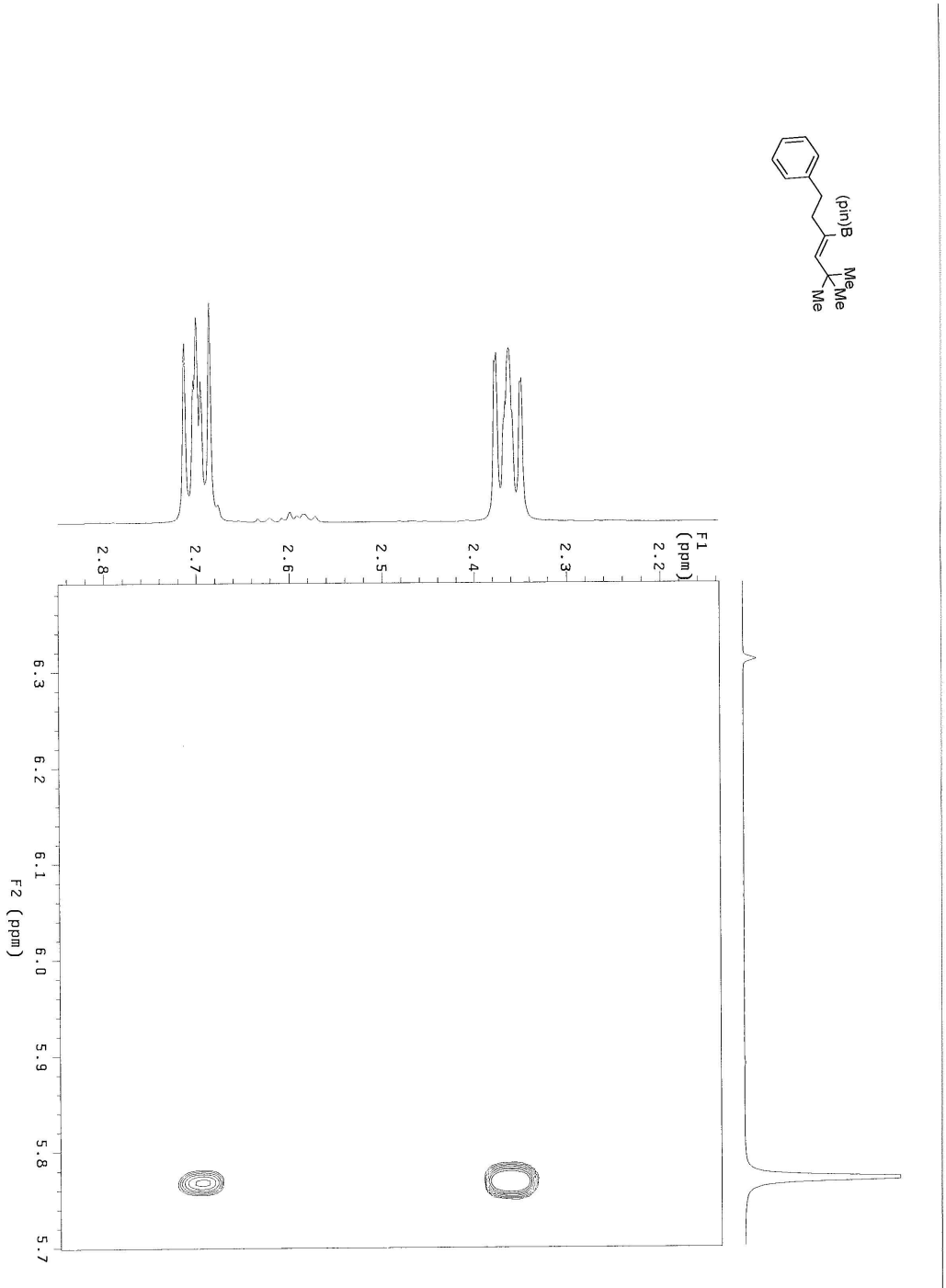

B(pin)
H
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm

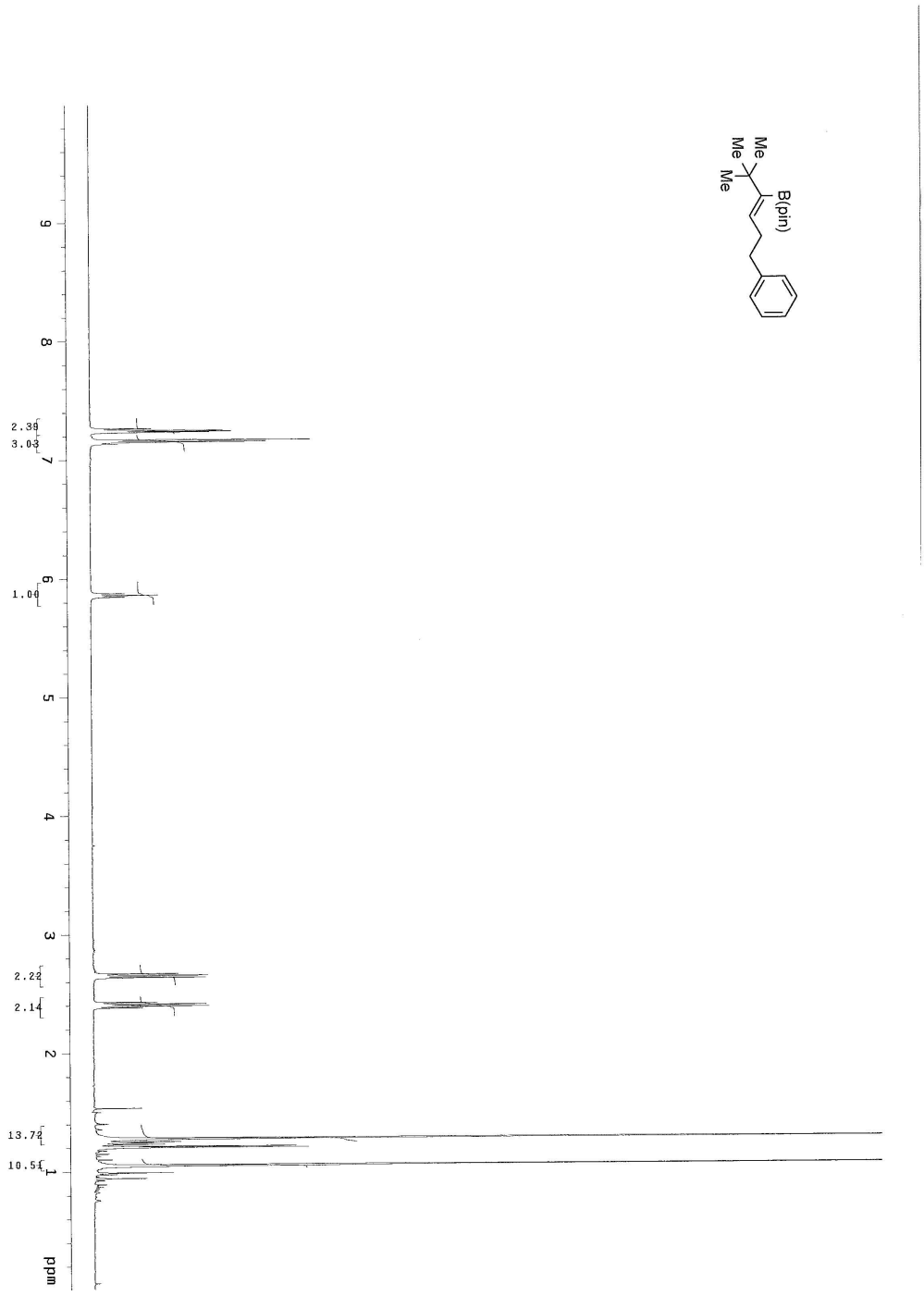

(pin)B
Me
Me
Me
2.49
3.02
0.04
1.00
2.20
0.14
2.19
13.91
0.72
0.52
9.56
ppm

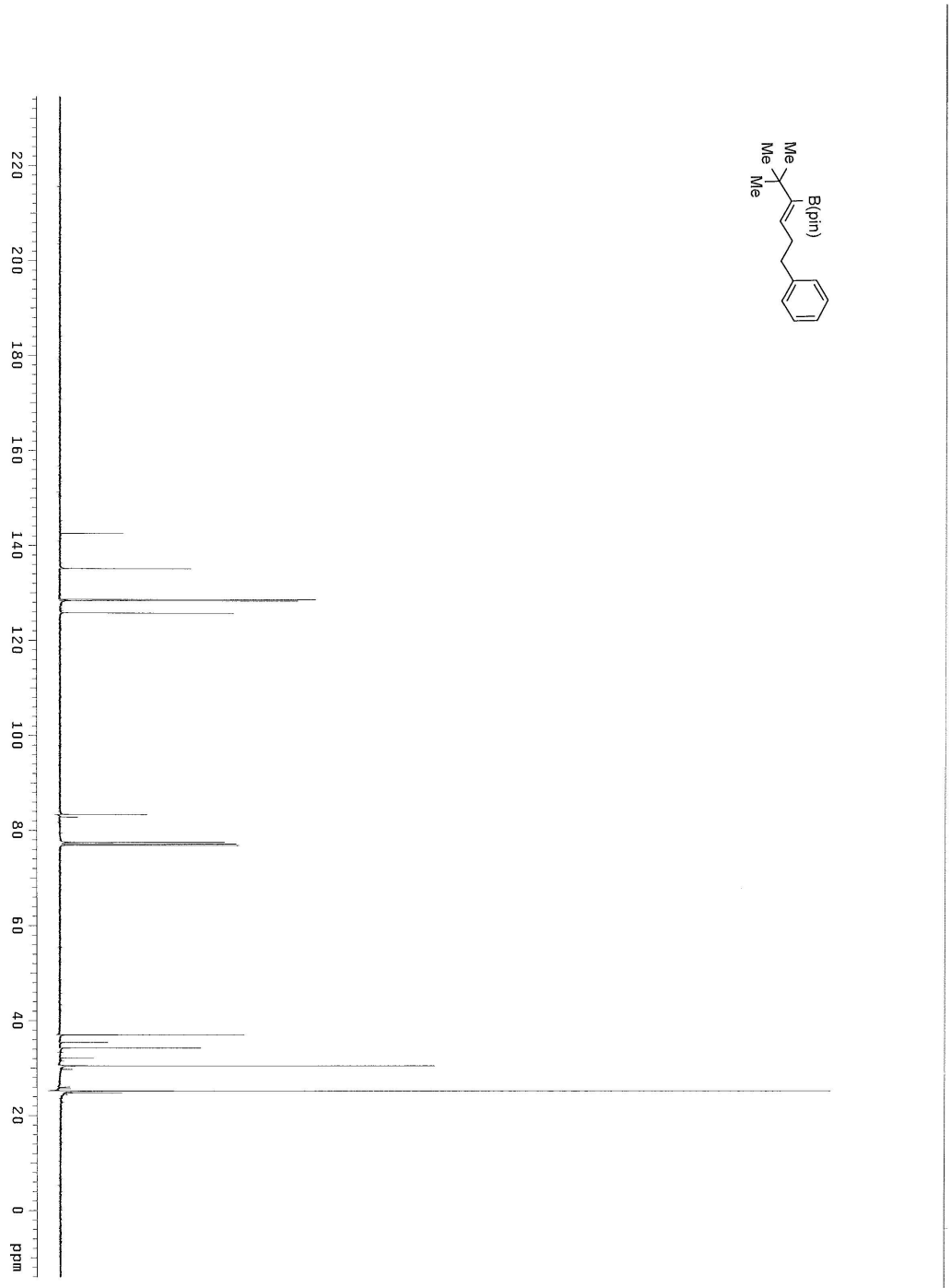

(pin)B
Me
Me
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm


(pin)B
Me
Me
Me
F1 (ppm)
F2 (ppm)


(pin)B
Me
Me
Me
F1 (ppm)
F2 (ppm)
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5


(pin)B
Me
Me
Me
F1 (ppm)
2.8
2.7
2.6
2.5
2.4
2.3
2.2
F2 (ppm)
6.3
6.2
6.1
6.0
5.9
5.8
5.7


Me
Me
Me
B(pin)
2.39
3.03
1.00
2.22
2.14
13.72
10.51
ppm


B(pin)
Me
Me
Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm